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NANOMOTORS INTERNATIONAL CONFERENCE

Foster collaboration and highlight the positive impact of these technologies on society, promoting scientific advances and innovative applications.

2-5th JUNE · MUSEO DE LA CIENCIA CosmoCaixa · BARCELONA

PROGRAMME

MONDAY, JUNE 3

09:00	**Registration**
10:00	**Samuel Sánchez,** *Institute for Bioengineering of Catalonia, Spain*
10:20	Keynote talk: **Bradley Nelson**, *Swiss Federal Institute of Technology (ETH) Zurich, Switzerland*
10:50	Invited talk: Light Induced Active Phase Transition and New Material **Jinyao Tang,** *University of Hong Kong, Hong Kong*
11:10	Invited talk: Self-organization of micromotors in complex chemical media **Raymond Kapral**, *University of Toronto, Canada*
11:30	*Coffee break* + poster session
12:30	Keynote talk: Light-, chemically-, magnetically-driven active microparticles and microdroplets **Metin Sitti**, *Max Planck Inst. Inte. Systems Stuttgart, Germany*
13:00	Invited talk: Collagenase-based motors **Brigitte Stadler**, *Interdisciplinary Nanoscience Center (iNANO), Aarhus University, Aarhus Denmark*
13:20	Invited talk: Active Vesicles: From Understanding the Evolution of Biological Taxis to Directed Drug Delivery **Giuseppe Battaglia**, *Institute for Bioengineering of Catalonia, Spain*

13:40	*Lunch break*		
14:40	Keynote talk: Enzyme Motors and Pumps: From Transport to Collective Behavior **Ayusman Sen,** *Pennsylvania State University, USA*		
15:10	Invited talk: Synthetic Cells On The Move: Bottom-Up Engineering With Dna/Rna Nanotechnology **Kerstin Goepfrich**, *Max Planck Institute for Medical Research, Germany*		
15:30	Invited talk: Materials for Magnetic Small-Scale Robots **Salvador Pané**, *Swiss Federal Institute of Technology (ETH) Zurich*		
15:50	Invited talk: An insider's view of Nature journals **Raghavendra Palankar**, *Nature Nanotech*		
16:05	Group picture		
16:05	*Coffee break* + meet the editor		
16:30	*Parallel session 1* *Room: AGORA* ***Nanomotors for biomedicine 1*** *Chair:* *Juan Fraire,* *Institute for Bioengineering of Catalonia (IBEC), Spain*	*Parallel session 2* *Room: PI* ***Physics of active matter*** *Chair:* *Mykola Tasinkevych,* *Universidade de Lisboa, Portugal*	*Parallel session 3* *Room: DELTA* ***New materials for NM*** *Chair:* *Abdon Pena-Francesch,* *University of Michigan* *and* *Hamed Shahsavan,* *University of Waterloo*

	Combining nanocarrier design and self-propulsion for delivery of nucleic acids **Juan Fraire,** *Institute for Bioengineering of Catalonia (IBEC), Spain*	How to steer catalytic nanoswimmers? **Mykola Tasinkevych,** *Universidade de Lisboa, Portugal*	Bioinspired materials for stealth microrobots **Abdon Pena-Francesch,** *University of Michigan, USA*
16:45	Programmable Multifunctional Microrobots **Sambeeta Das,** *University of Delaware, USA*	Self-propulsion at the nanoscale: Exploiting Molecular Energy Relaxation Mechanisms **Carles Calero,** *University of Barcelona, Spain*	Tuning organic nanogels “à la carte” for a new generation of smart nanomotors **David Esporrín Ubieto,** *Institute for Bioengineering of Catalonia (IBEC), Spain*
17:00	Immune cell-based micromotors for active therapy **Zhiguang Wu,** *Harbin Institute of Technology, China*	Interactions in Active Colloids **Karnika Singh,** *Indian Institute of Technology Kanpur, India*	Micrometer-sized magnetic robots with piconewton-scale springs as on-board sensors and actuators **Haifeng Xu,** *Chinese Academy of Sciences, China*
17:15	Swarms of enzyme-powered nanomotors	Non-equilibrium thermodynamics of	Liquid Crystalline Materials and their

	enhance the diffusion of macromolecules in viscous media, **Noelia Ruiz González,** *Institute for Bioengineering of Catalonia (IBEC), Spain*	catalytic Janus particles self-organization, **Andrés Arango-Restrepo,** *University of Barcelona (UB), Spain*	Application in Small-scale Soft Robotics **Hamed Shahsavan,** *University of Waterloo*
17:30	Engineering Gated Nanoparticles as Chemical Communication Systems, **Antoni Llopis Llorente,** *Instituto Interuniversitario de Investigación de Reconocimiento Molecular y Desarrollo Tecnológico (IDM), Spain*	Impact of an inhomogeneous concentration field on the transport and self-assembly of active particles, **Juan David Torrenegra-Rico,** *University of Barcelona (UB), Spain*	Amyloid Peptide Nanotube based Nanomotors (Amylobots) for Complex Navigational Behaviour, **Dibyendu Das,** *Indian Institute of Science Education and Research (IISER), India*
17:45	–	Symmetrical catalytic colloids display Janus like motion **Stephen Ebbens,** *University of Sheffield, UK*	Communication Between Liposomal Nanomotors Based on Enzyme-Cascades **Yu-Ching Tseng,** *The Pennsylvania State University, USA*
18:00		Invited Short Talk:	

	_	Phoresis Kernel Theory for Passive and Active Spheres, **Amir Nourhani,** *University of Akron*	_
18:15	End		
18:30	Planetarium at the museum		
20:00	*Conference dinner at the Venue (inside the museum)*		

KEYNOTE LECTURES
INVITED LECTURES

Remote Magnetic Navigation at Clinical Scales for Micro and Nano Robots

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Abstract

More than seventy years ago remote magnetic navigation (RMN) was proposed for guiding magnetically tipped catheters [1]. The approach has been in clinical use for assisting surgeons during endocardial ablation procedures for more than two decades [2]. We have recently developed a portable RMN system, more specifically an electromagnetic navigation system (eMNS), called the Navion that has been used for steering magnetically tipped catheters, guidewires, and endoscopes [3], as well as micro and nano robots [4]. Our hope is that a clinically relevant system capable of guiding magnetic micro and nano robots will help propel the field of micro and nano robotics towards clinical adoption [5].

Figures

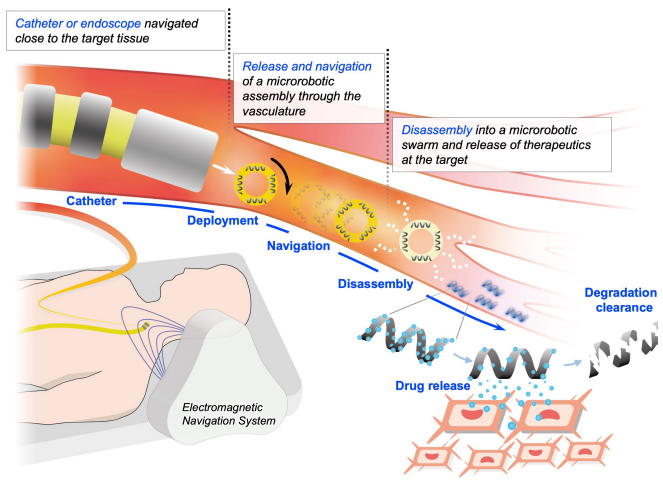

Figure 1. RMN (remote magnetic navigation) for delivering micro and nanorobots in a clinical scenario (credit Minsoo Kim, ETH Zurich).

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Light Induced Active Phase Transition and New Material

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Matters are assembled via interactions/forces between elementary building blocks. Controlling such interactions can, in principle, control the phases of matters and enable novel stimuli-responsive material. Traditionally, such control requires forming new bonds or changing the compositions, where different assemblies are formed statically.

Recently, synthetic active matter has aroused increasing interest due to its promising potential in biomedical applications and its ability to serve as the perfect model for non-equilibrium physics. It is known that non-equilibrium forces can be generated between active building blocks in active matter, which suggests additional knob for interaction and phase control, that is intrinsically dynamic and responsive. We propose that applying active matter as a fundamental building unit for new material may lead to a new class of functional materials that runs under non-equilibrium conditions and demonstrate unusual properties that are otherwise prohibited in any equilibrium system.

Among all dissipative interactions, light-driven chemistry is the most versatile due to excellent spatiotemporal controllability that can be tuned externally with rich light-matter physics. In this talk, I would like to discuss the recent discovery of the mechanical effect in photoinduced electron transfer processes. Starting with the photoactive colloid TiO2 particles (Figure 1), where the surface photoredox reaction as sensitized with dyes can produce apparent attractive potential, we will discuss the colloid phase transition under photochemical conditions. In this system, the light controls the reactivity of the active system, which changes the phase boundary.

Then, we present new results showing the universality of the apparent potential in photoactive systems even without traditionally used TiO2, where inert cargo particles from the molecular scale to the micrometer scale show similar attraction in photoactive system. Our experiment shows that the Photoinduced Electron Transfer (PET) process plays an essential role in generating the effective attraction potential of submerged particles even down to the molecular scale (Figure 2). A highly localized phase transition can be observed with focused light, leading to active transport similar to active nanomotors and new kinds of molecular machines that cause directed deposition of solute molecules to the focused laser point. This new phenomenon may be applied to formulate novel printing ink compatible with commercial laser 3D writer, allowing nanostructures to be printed with high resolution down to 100nm.

References

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Figures

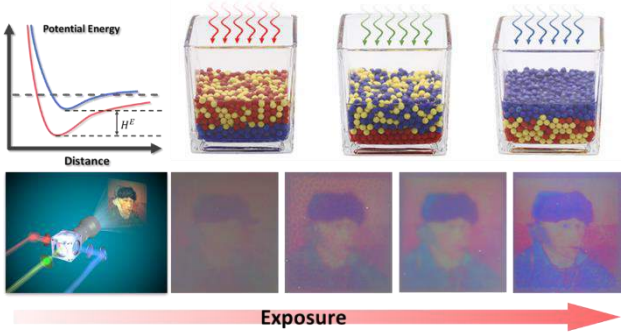

Figure 1. Photoactive particle interactions is tunned with incident light, which leads to spectral sensitive phase segregation and the overall photochromic behavior

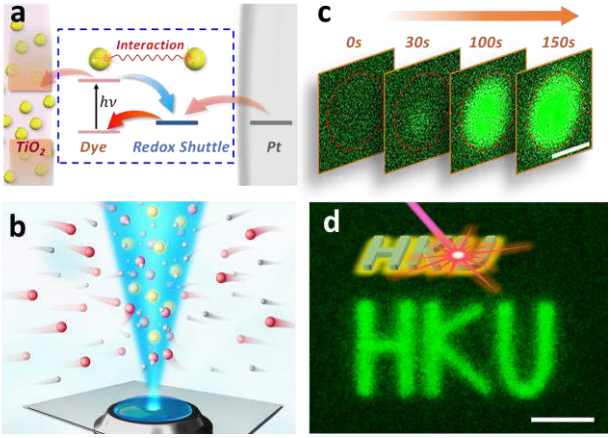

Figure 2. Photoinduced electron transfer process cycles electron between dye and redox shuttle molecules, which may lead to mechanical effect that cause active cargo delivery and active phase transition as observed in photoredox solution

Self-organization of micromotors in complex chemical media

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The collective behavior of active particles has been the subject of a considerable body of research that has elucidated the mechanisms that operate to produce a variety of nonequilibrium self-assembled structures. For the most part, the environments in which the micromotors move were simple fluids comprising fuel, product and solvent, with reactions confined to the catalytic surfaces of the active particles. Here we consider situations where the fluid environment is itself an active medium with broken detailed balance that drives the system out of equilibrium and may form chemical patterns. In this circumstance, when the chemical reactions that power active motion couple to reactions in the environment, new active system states are formed that involve both the active particles and their chemical environment. The phenomena observed under these conditions will be illustrated by mesoscale simulations of ensembles diffusiophoretic colloidal motors that allow one to probe aspects of various mechanisms leading to clustering that depend on the coupling of motor motion to reactions in the environment.[1] Moving to longer length and time scales, it will be shown how macroscopic densities of micromotors can respond to the gradients due to chemical patterns, and how the motors can, in turn, alter chemical patterns.[2]

References

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Figures

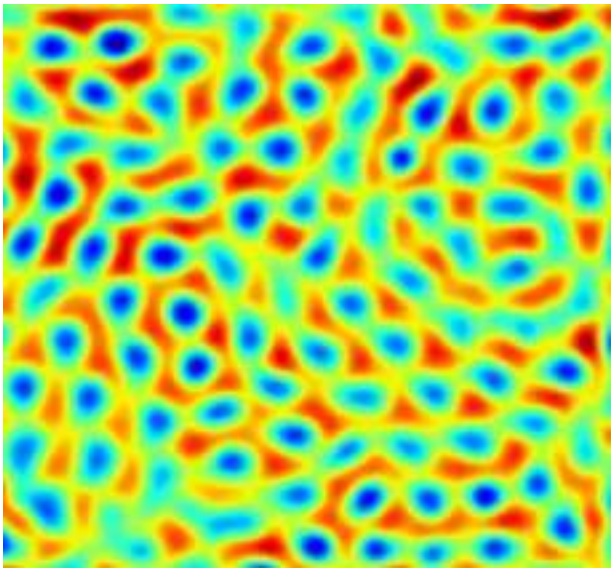

Figure 1. Micromotor density in an autocatalytic reactive medium

Light-, chemically-, magnetically-driven active microparticles and microdroplets

Prof. Dr. Metin Sitti

Active micronscale particles or droplets have the potential to improve the healthcare radically, since they have the unique capability of accessing, operating and possibly staying inside hard and currently not possible to reach target tight spaces inside the human body non-invasively. In this direction, light, chemical gradients and external magnetic fields are used to propel and steer microparticles or microdroplets. First, carbon nitride-based light-driven microswimmers with intrinsic photocharging ability and biocompatible propulsion in biological and ionic media are reported. Also, two types of COF microparticles are proposed as visible- and UV-light-powered microswimmers for targeted drug and other cargo delivery inside the human eye. They can also have responsive on-demand drug delivery function towards medical use. Next, magnetic nanoparticle cluster-embedded microdroplets are driven by surfactant gradients and magnetic fields. When continuously perturbed, achiral droplets exhibit emergent chiral motion with rotating fluidic flows. Such solid-fluid interactions remove barriers of specific emulsion chemistries and complements their inherent abilities thereby also enabling control over emergent collective behaviors of active droplets. Finally, using rotating external magnetic fields, magnetic Janus microparticles-based microrollers are used to move against the blood flow on the vessel walls. They can adhere to the specific cancer cells using their antibody coating and release drugs triggered by light.

Collagenase-based motors

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The extracellular matrix (ECM) is a network of molecules with collagen as a main component that provides structural and biochemical support to surrounding cells in tissues and organs. However, the ECM also possess a substantial hurdle for the tissue penetration of nanoformulations.
We developed collagenase-based motors that exhibited locomotion in collagen fiber environments[1] and in gelatin-based hydrogels[2]. In this context, polymer brush coated particles offered the most suitable scaffold for collagenase immobilization, resulting in the most efficiency motors in gelatin-based hydrogels.
These collagenase-based motors could penetrate cell spheroids and delivery heat when they were equipped with magnetic nanoparticles and exposed to an alternating magnetic field.[3]
Recently, we illustrated that these collagenase-based motors could be used as artificial organelles in artificial cells. When these artificial cells were co-cultured with hepatic cells, they could transfer their artificial subunits to the mammalian cells in the proximity.
Taken together, collagenase-based motors are a fast moving and versatile active nanomaterial with potential for biomedical applications.

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Active Vesicles: From Understanding the Evolution of Biological Taxis to Directed Drug Delivery

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With water as the quintessence of life's medium, we encounter a duality in molecular behavior: those akin to water, dispersing freely, and the hydrophobic, water-repelling molecules, which segregate and repulse. The convergence of these contrasting traits within a single entity, the amphiphile, harnesses both forces to orchestrate intricate molecular architectures. Among these, the membrane—a bilayer structure of aligned amphiphiles—is a paramount evolutionary achievement. Amphiphilic membranes possess the remarkable ability to self-assemble into well-defined compartments, enclosing distinct aqueous environments. These compartments serve as chemical potential reservoirs, fuelling many biochemical processes.

The vesicle is the basic unit of cellular compartments. It is derived from the Latin word "vesicula," which means "little bladder" or "fluid-filled blister." These structures are very similar to modern cells and have been suggested as a model for protocells because of their ability to self-assemble and replicate. Vesicles are found in all living organisms and are an essential component of cellular architecture. In unicellular organisms, the cell membrane separates the internal and external environments, while in eukaryotic cells, vesicles facilitate communication and signaling between different entities. Nature's profound mastery of compartmentalization and coordination is demonstrated from the humble vesicle to the intricate web of cellular communication.

Undoubtedly, vesicles have captured significant attention in unraveling life's origins. Their ability to maintain distinct aqueous compositions makes them ideal candidates for engineering reactors and diverse compartments. Whether these are done using natural membrane-forming phospholipids or synthetic surrogates, including polymers, vesicles are versatile carriers for myriad therapeutic and diagnostic interventions, showcasing their potential in biomedical applications. In the intricate tapestry of life's evolution, vesicles emerge as passive entities and dynamic vessels, harboring the promise of innovation and discovery.

Here, I propose to expand on such a concept of compartmentalization and explore how combining critical elements gives rise to more complex behavior such as locomotion. We aim to decipher the evolutionary journey from a mere Brownian energy reservoir to a dynamic entity capable of intricate behaviors, such as taxis—directed motion toward a specific source. This juncture is the focal point for research groups, including mine, as we endeavor to propel drug delivery beyond conventional paradigms toward more sophisticated, directed approaches. Concurrently, our endeavors contribute to unraveling a fundamental enigma of evolution: how the amalgamation of disparate elements can engender complex behaviors like taxis. The promise of advancing therapeutic interventions and unraveling the mysteries of life's evolutionary tapestry lies in this convergence of disciplines.

We demonstrated that chemotaxis can be achieved by creating a nanoscopic vesicle loaded with enzymes, whose membrane ave an asymmetric distribution of permeable domains[1].

When placed in a chemical gradient that acts as substrate for the enzyme, the asymmetric flow distribution across the vesicle membrane creates a biased slip velocity around the vesicles and a consequent propulsion. This, in turn, allows the vesicles to move chemotactically toward a higher substrate concentration, allowing long-range targeted delivery. Here, we will expand this concept using uniquely biological molecules to demonstrate that a minimal organization of biomolecules can create the conditions for complex behavior such as chemotaxis. The schematics of the system are shown in Figure 1, where we propose a simple vesicle formed by naturally occurring phospholipids that encapsulate[4] enzymes. This will be then placed in contact with pore-forming α-Hemolysin. This protein unimers assemble to form a heptameric pore with a pore diameter of 1.5 nm[3]. The pore is selective for the passage of any molecules with a mass lower than 1kDa and several cations, including K+, Na+, and Ca2+. We present and discuss the minimal number of elements required for cell-like vesicles to be chemotactic. Our study demonstrates that lipid vesicles can move in response to chemical gradients when a transmembrane protein and an encapsulated enzyme, including glucose oxidases or urea, are incorporated into the vesicle structure. This model serves as a proof of concept to show that even the simplest structured cell can undergo chemotactic navigation.

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Figures

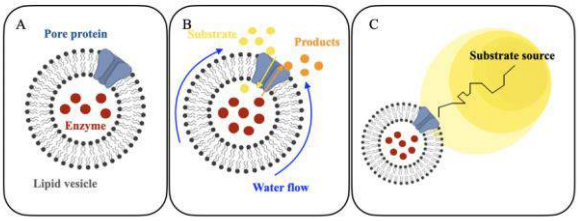

Figure 1. Schematic representation of a minimal chemotactic cell.

Enzyme Motors and Pumps: From Transport to Collective Behavior

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One of the more interesting recent discoveries has been the ability of enzymes to catalytically harness the chemical energy in their environment for mechanical work. Recent work from our group has shown that enzymes participating in catalytic cascades show surprising emergent behavior, ranging from directional chemotactic motility to dynamic assembly in response to chemical gradients. The resultant organization and collective behavior of interacting active enzymes show remarkable similarities to the biological world. When enzymes are anchored to surfaces, the catalytic reactions can propel the fluid. We will show that precise sculpting of fluid flow including flow enhancement and flow reversal becomes possible in coupled pump systems depending on the geometric placement of the pumps.

SYNTHETIC CELLS ON THE MOVE: BOTTOM-UP ENGINEERING WITH DNA/RNA NANOTECHNOLOGY

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Today's living cells emerge from the complex interplay of thousands of molecular constituents. Our vision is to create a simpler model of a cell that consists of a giant unilamellar lipid vesicle (GUV) and operates based on our own custom-engineered molecular machinery made from DNA and RNA nanotechnology. Recently, we demonstrated DNA-based mimics of cytoskeletons, capable of cargo transport, contractile ring formation and signal transduction [1-4]. We established the enzyme-driven rolling motion of GUVs based on a burnt-bridge mechanism and find that the motion of the GUVs differs significantly from the motion of a corresponding solid-state particle (**Figure 1**). Next, we aim for a prototype of a synthetic cell capable of evolution, by genetically encoding our molecular hardware inside of GUVs (**Figure 2**). This will be possible with a new technique, the co-transcriptional folding of RNA origami, which I will introduce in this talk. This may open up new opportunities for collaboration with the nanomotors community.

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Figures

Figure 1. Enzyme-driven rolling motion of GUVs. The rolling motion of GUVs differs from a corresponding solid-state particle.

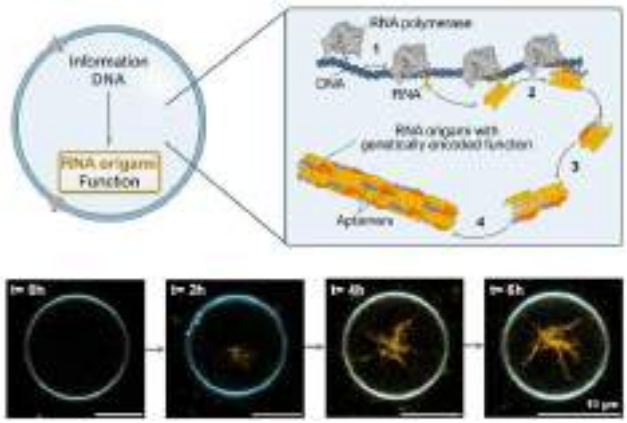

Figure 2. Co-transcriptional folding of RNA origami-based mimics of cytoskeletal filaments inside of GUVs.

Materials for Magnetic Small-Scale Robots

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Robots are revolutionizing surgical procedures by providing precise and controlled assistance in the operating room [1]. Among the medical robotic family, untethered micro- and nanorobots are gaining popularity. These miniaturized devices can move through fluids using external magnetic fields such as gradients, rotating, oscillating magnetic fields or combinations of these [2]. This distinctive feature renders them particularly intriguing for biomedical applications, for example, as vehicles for delivering therapeutic agents, including drugs and cells, to precise tissues within confined spaces of the human body [3]. Moreover, they can be employed as diagnostic tools or biochemical sensing instruments, further expanding their utility in advancing medical technologies.

The appealing feature of magnetic fields lies not only in their versatility for manipulating micro- and nanodevices but also in their minimal interaction with the human body. Magnetic fields offer biocompatibility across a broad spectrum of conditions in terms of frequency and magnetic field strengths. Fine-tuning both the magnetic input and the structure's geometry allows for a variety of locomotion mechanisms [4]. Additionally, incorporating soft, flexible components enriches the motion complexity of these magnetic engines. Beyond motion capabilities, magnetic fields can be used also to awake other functionalities to specific magnetic materials such as deformation in magnetoelastic compounds or heat in magnetic nanoparticles [5]. While numerous studies have been realized with magnetic micro- and nanorobots, including preliminary in vivo tests, significant challenges persist in their translation to clinical applications. These challenges extend beyond the selection of suitable magnetic materials and encompass aspects like drug loading capacity, biocompatibility, biodegradability, multifunctionality, swarm control, and the development of magnetic navigation setups compatible with healthcare facilities and clinical imaging [2].

In this talk, we will explore a range of material-based concepts and innovative fabrication techniques designed to surmount translational obstacles and bolster the capabilities of small-scale magnetic robotics. Our discussion will also delve into the aspect of multifunctionality, particularly with the integration of magnetoelectric composite multiferroics in micro- and nanorobotic platforms. Magnetoelectric composite materials, consisting of both magnetostrictive and piezoelectric parts in intimate coupling, exhibit electrical polarization in response to magnetic inputs. As such these materials, can be used in micro- and nanorobots to deliver electric fields wirelessly using external magnetic fields [6]. In this talk, we will particularly emphasize their application in electrostimulating cells and tissues, with a specific focus on potential implementations in the central nervous system. Specifically, we will show how these materials can be used to potentiate the proliferation of neuronal cells, stimulate their differentation into neuronal networks [7].

To conclude our talk, we will also show a more biocompatible alternative for wirelessly delivering electric fields with microrobots as well as a strategy for the deployment of magnetic micro- and nanorobots in the body.

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An insider's view of *Nature* journals

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We are excited to participate in the Nanomotors International Conference: 20th Anniversary, June 2-5, 2024, in Barcelona. We are looking forward to meeting and connecting with the community.

CHAIRS/INVITED SPEAKERS PARALLEL SESSION

Combining nanocarrier design and self-propulsion for delivery of nucleic acids

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Targeting the genetic bases of many diseases is rapidly being implemented, as demonstrated by the recent approval of various nucleic-acid-based therapeutics by the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA).[1] The promise of nanocarriers is to deliver nucleic acids (i.e., pDNA, mRNA or siRNA) selectively to the target tissues and cells with increased efficacy while reducing side effects. However, there are still remaining challenges, linked to the different physiological barriers that need to be overcome.[2] Self-propelled nanoparticles or nanomotors (NMs), have been proposed as the next generation of nanocarriers in nanomedicine. Among them, enzyme-powered NMs are at the forefront, since they can utilize physiologically relevant fuels to power motion under in vivo conditions.[3] Recent studies have demonstrated that urease presents high catalytic rates that confer to urease-functionalized motors higher self-propelling capabilities compared to other enzymes.[4] Moreover, their collective behavior (commonly referred as swarming behavior) was characterized in vitro[5] and in vivo[6] indicating that self-propulsion promotes collective displacement, convection and mixing.

In this talk, I will present our recently developed urease-powered platform based on biocompatible and biodegradable poly(lactic-co-glycolic acid) (PLGA) NPs. These NPs are used as scaffolds for layer-by-layer (LBL) self-assembly of nucleic acids-loaded PLGA NMs,[7] turning them into a versatile platform that can be tuned in terms of nucleic acids, polymers (directly linked to the complexation and intracellular release of the nucleic acids), and even enzymes (urease, urease/collagenase, etc.). In that sense, I will discuss the rational design of the nanocarrier, the functionalization process to synthesize the final NM formulation, and the evaluation of the collective behavior in drug delivery applications.

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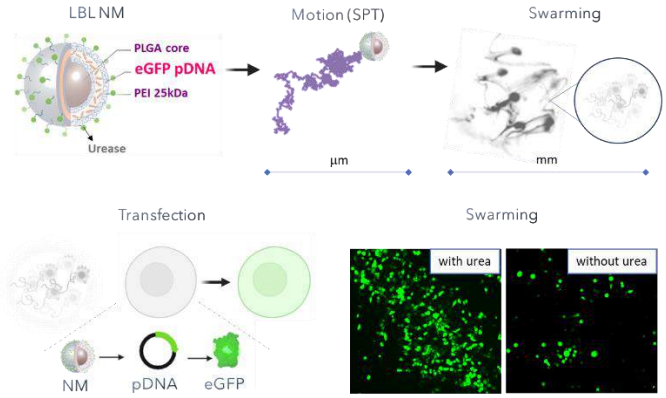

Figure 1. pDNA-loaded layer-by-layer NMs for cell transfection. Swarming significantly improved transfection efficiency in MB49 cells compared to the absence of urea, as evidenced by the expression of eGFP.

How to steer catalytic nanoswimmers?

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Self-propelled nanoparticles moving through liquids offer the possibility of creating advanced applications where such nanoswimmers can operate as artificial molecular-sized motors. Achieving control over the motion of nanoswimmers is a crucial aspect for their reliable functioning. While the directionality of micron-sized swimmers can be controlled with great precision, steering nano-sized active particles poses a real challenge. One of the reasons is the existence of large fluctuations of active velocity at the nanoscale. Here, we describe a mechanism that, in the presence of a ratchet potential, transforms these fluctuations into a net current of active nanoparticles [1]. We demonstrate the effect using a generic model of self-propulsion powered by chemical reactions. The net motion along the easy direction of the ratchet potential arises from the coupling of chemical and mechanical processes and is triggered by a constant, transverse to the ratchet, force. The magnitude of the rectified current sensitively depends on the amplitude and the periodicity of the ratchet potential and the strength of the transverse force. Our results highlight the importance of thermodynamically consistent modeling of chemical reactions in active matter at the nanoscale and suggest new ways of controlling dynamics in such systems.

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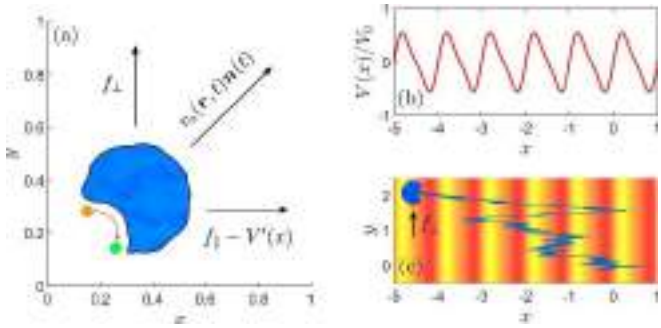

Figure 1. (a) An active nanoparticle, in (b) a ratchet potential $V(x)$, (c) exhibits net motion along the ratchet direction x when subject of a force $f\perp$ acting along perpendicular direction y .

Acknowledgements

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Bioinspired materials for stealth microrobots

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Micro/nanorobots offer transformative solutions for non-invasive medical therapy and diagnostics due to their small size and untethered operation inside the human body. However, they must face several biological barriers as a natural protection mechanism against foreign threats, including immune recognition and clearance. In this talk, we will introduce stealth strategies in robotic biomaterials development to avoid microrobot recognition from immune cells. We have developed zwitterionic photoresists for 3D printing of microrobots and functionalization of medical devices with tunable properties and antibiofouling stealth behavior. Stealth microrobots avoid non-specific adsorption of proteins and detection by macrophage cells of the innate immune system after exhaustive inspection. These versatile materials eliminate a major roadblock in the development of biocompatible microrobots, and will serve as a new toolbox of non-immunogenic materials for biomedical microrobot and other device technologies.

Liquid Crystalline Materials and their Application in Small-scale Soft Robotics

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Soft robotics is a multidisciplinary field that links different fields of research, such as chemistry, materials science, mechanical engineering, instrumentation and control, and artificial intelligence. During the last two decades, the development of novel materials and fabrication techniques have been two of the major challenges for further progress in this field. The synthesis and application of structural materials that a) have integrated sensing and actuating capabilities, b) can be programmed, and c) can be scaled down (or up) by various fabrication techniques are highly desirable for the fabrication of soft robots with a reduced number, size, and weight of components. In this seminar, I will talk about the importance of liquid crystalline materials in the design and fabrication of soft robotic components. I will present our recent progress in the development of artificial muscles and robotic constructs from LC materials that can be remotely stimulated by a variety of cues, such as heat, light, and electrical fields at different scales and media. I will also present opportunities to create novel solutions or augment the existing capabilities of microscale robotic systems with an emphasis on their future biomedical applications.

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Phoresis Kernel Theory for Passive and Active Spheres

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From a design perspective, we are interested in understanding how the distribution of activity over the surface of a self-phoretic active particle contributes to its dynamics, or how the composition of the surface of a passive particle determines its phoretic motion under an external field. The common practice involves obtaining the distribution of the driving field around the particle, calculating the slip velocity, and using a reciprocal theorem to obtain the translational and rotational velocities of the phoretic particle. We propose a phoresis kernel theory that bypasses the calculations of slip velocity and directly connects the velocities to the distribution of the field and its flux using integral kernels. These kernels quantify the local contribution of the field to the global dynamics of the phoretic particle, depend on the surface composition and phoretic mobility distribution, and are independent of the field's distribution around the particle.

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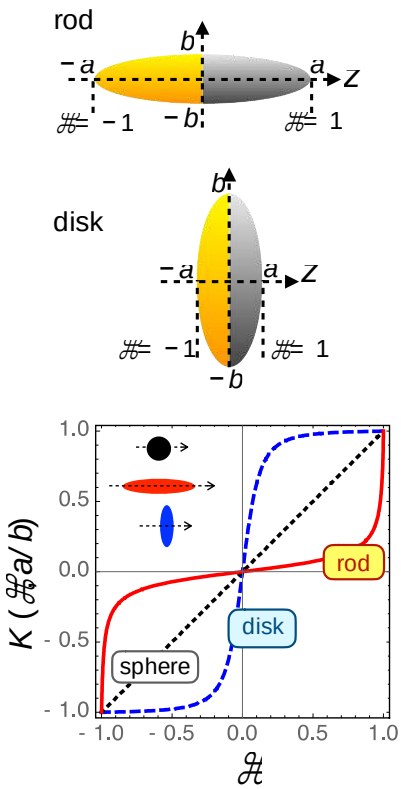

Figure 1. Translational phoresis kernel for spheroids

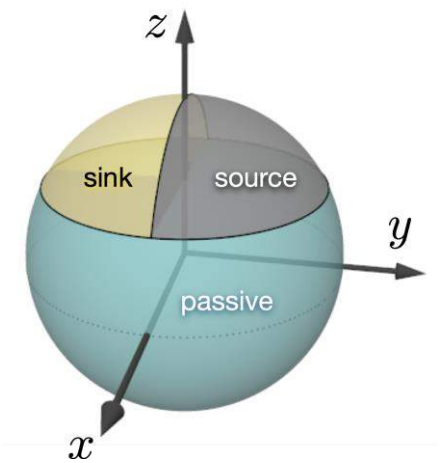

Figure 2. Translational and rotational dynamics of a self-phoretic sphere

PARALLEL SESSION

Programmable Multifunctional Microrobots

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The field of micro-robotics has emerged as an intriguing new area of research that has the potential for significant applications in biomedicine, both in vitro and in vivo, taking advantage of the untethered actuation and small size of the microrobots. Examples of applications of microrobots include targeted cargo delivery, microsurgery, and cellular manipulation. Of particular interest are multi-modal actuated microrobots which potentially offer greater adaptability, robustness, and capability to perform a variety of tasks. Additionally, modular microrobots provide exciting possible applications due to their ability to reconfigure into various shapes, create structures that may be difficult to fabricate as one whole unit, and be assembled on-site. Here, we present a microrobot that is actuated by both magnetic and acoustic fields and forms modular microstructures of various shapes. We demonstrate the use of these microrobots for cellular manipulation by creating patterns of cells on a surface.

Figures

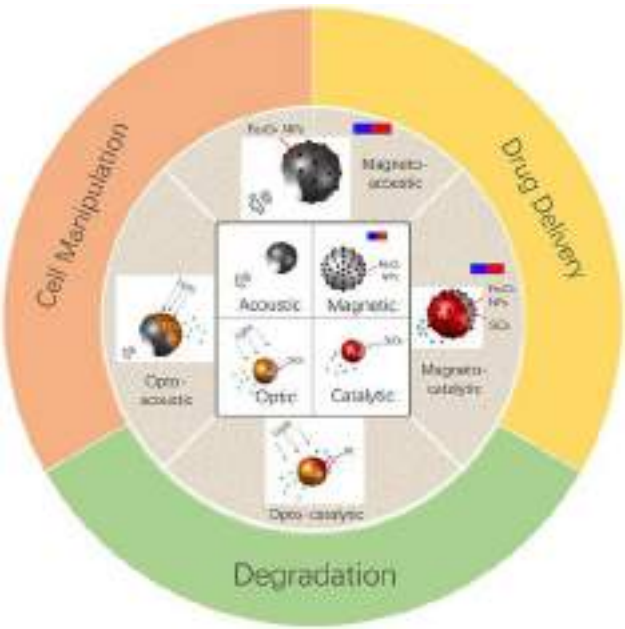

Figure 1. Representative examples of multifunctional microrobots for different applications

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Immune cell-based micromotors for active therapy

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Abstract

The biomedical micro/nanomotors have become an exciting field of research, thanks to their controllable locomotion in hard to-reach areas of the body for noninvasive drug delivery and treatment. However, current synthetic micro/nanomotors are susceptible to immune attack and clearance upon entering the body. Here, we report the recent progress of immune cell-based micromotors for active delivery tumors in vivo. On the other hand, various immune cells such as macrophages, with their ability to load drugs and target both tumor and inflammatory tissues, have gained attention in precision medicine.
Numerous macrophages-based delivery systems have been recently developed based on the capacity of monocytes to act as macrophages-based hitchhiking micromotors. Such immune cell-based have also shown chemotactic motility along the gradient inflammatory factors to penetrate various biological barriers. The strategy will significantly enhance the drug efficiency in tumors and thus offer promising potential in precise medicine.

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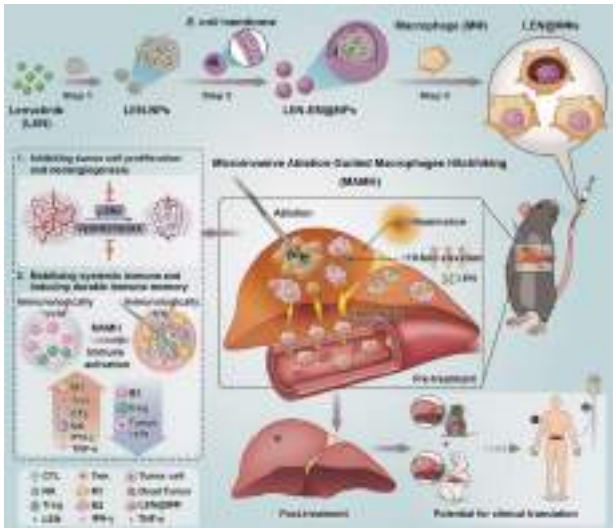

Figure 1. Chemotactic macrophage hitchhike as example of immune cell-based micromotors for active therapy

Swarms of enzyme-powered nanomotors enhance the diffusion of macromolecules in viscous media

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In recent decades, nanotechnology has made significant progress in drug delivery systems. The goal is to improve therapy effectiveness by precisely releasing drugs to specific tissues. However, there are still challenges to overcome. One major challenge is the presence of biological barriers,[1] such as viscoelastic fluids like synovial fluid in joints, which mainly contain hyaluronic acid. The complex network of these fluids hinders the transportation of nanosystems, causing conventional particles to get trapped and limiting their ability to reach the target area.[2,3] Therefore, there is a need for innovative technologies that can enhance the delivery of therapeutic agents.

To overcome the obstacles presented by complex media, one promising approach is the development of "active" nanoparticles or nanomotors (NMs).[4–6] However, the exploration of enzyme-powered nanomotors capable of navigating and influencing viscous fluids is still in its early stages. These enzyme-powered nanomotors offer great potential, as their coordinated movement can be driven by enzymatic reactions, effectively utilizing the biofuels present in the human body. Furthermore, some of these enzymatic nanomotors can modify the characteristics of the extracellular matrix by reducing its viscosity, thus facilitating improved diffusion of therapeutic agents.

In this study, we introduce a nanotechnological strategy using two swarms of nanomotors, namely hyaluronidase NMs (HyaNMs, Troop 1) and urease NMs (UrNMs, Troop 2), which synergistically enhance the diffusion of macromolecules within the synovial fluid. Troop 1 demonstrates the capability to break down the intricate network of synovial fluid, both in vitro and ex vivo, thereby reducing its viscosity. This enables Troop 2 to navigate more effortlessly through the viscous media. Moreover, the collective movement of Troop 2 significantly enhances the diffusion of Dextran macromolecules. These findings offer promising prospects for utilizing enzyme-powered NMs in the treatment of joint injuries, augmenting therapeutic effectiveness, and facilitating faster and more efficient delivery of therapeutic agents compared to conventional approaches.

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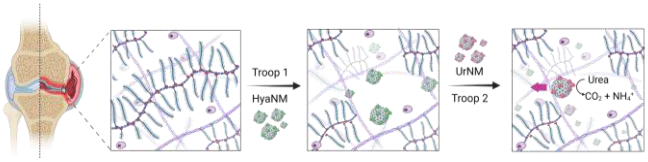

Figure 1. Conceptual idea of the novel approach using hyaluronidase NMs (HyaNMs) to interact with and reduce the viscosity of synovial fluid and urease NMs (UrNMs) for a more efficient transport of therapeutic agents in joints.

Engineering Gated Nanoparticles as Chemical Communication Systems

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Chemical communication based on the exchange of molecules as messengers allows different entities to share information, cooperate and orchestrate collective behaviors. In recent years, the development of strategies of chemical communication between micro/ nanosystems is becoming a key emergent topic in micro/nanotechnology, biomimicry and related areas.[1] Here we show recent progress by our group in the development of engineered gated nanoparticles for chemical communication. These gated nanoparticles are loaded with chemical messengers and functionalized with gatekeepers that control payload release in response to stimuli. Studies in this direction can be divided in two main categories: (i) communication between abiotic nanosystems[1-3] and (ii) communication between living and abiotic systems [5,6]. The engineering of chemical communication between micro/nanosystems represents a paradigm shift and may open a myriad of new concepts, applications and new technological possibilities in the near future in a number of research fields such as nanomedicine and synthetic biology.

Figure 1. Interactive communication with yeast cells. Sucrose is hydrolyzed into glucose by invertase located in periplasmic space of yeasts and diffuses to nanodevice ($S2_{gox}$) where is transformed into the corresponding acid by glucose oxidase on the Au face. The local drop in pH leads to the pH-sensitive nanovalve uncapping from the nanocarrier and the release of phleomycin (feedback messenger) that induces GFP expression (output) in yeasts.

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SELF-PROPULSION AT THE NANOSCALE: Exploiting Molecular Energy Relaxation Mechanisms

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Controlling the transport of micro and nano particles in liquids is a fundamental problem with the potential to revolutionize different emerging technologies [1]. The use of self-generated thermal gradients has been theoretically proposed and demonstrated in experiment to be a promising strategy to induce transport of microparticles in liquids [2]. Here we show that the anisotropic dissipation of excess molecular energy into the surrounding solvent can lead to the propulsion of nanoparticles [3]. We use all-atomic models of excited nanoparticles and of the solvent to investigate with molecular dynamics simulations the emergent particle propulsion as the excess energy is dissipated into the solvent. We report results in liquid water from: (i) nanoparticles functionalized with excited fluorophores [3]; (ii) high energy vibrationally excited molecules [4]. In both cases we find a marked energy flux anisotropy during relaxation which results in a temperature gradient across the nanoparticle and in a net propulsion that leads to significant enhanced diffusion when periodic excitations are applied (see Fig.1). In contrast to most models of self-phoresis, we find that propulsion occurs via short ($\lesssim$ 0.5ps) impulses (see inset in Fig.1), a possibility recently considered by Frenkel and co-workers [5]. From our all-atomic description we identify the source of propulsion as a transient force imbalance with the surrounding solvent when hydrogen bonds are broken as a result of the prescribed molecular excitations. Finally, strategies to direct the motion of functionalized nanoparticles in a given direction using confined environments are also discussed.

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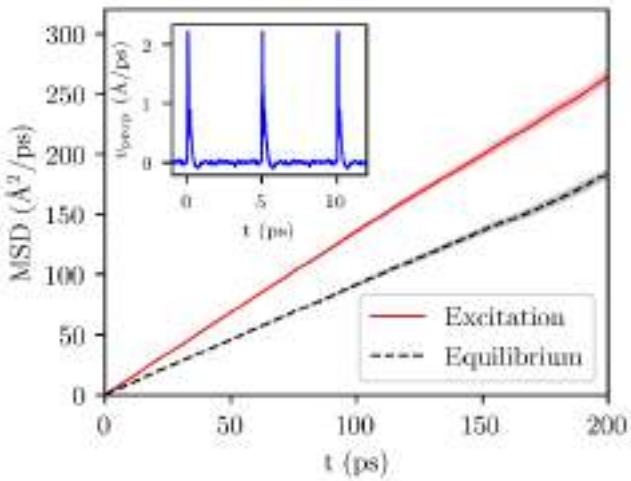

Figure 1. Mean square displacement of nanoparticle in equilibrium (dashed black line) and under repeated excitations (solid red line). Inset: velocity of propulsion of particle resulting from repeated excitations.

INTERACTIONS IN ACTIVE COLLOIDS

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Driven by the necessity to achieve a thorough comprehension of the bottom-up fabrication process of functional materials, our study investigates the pair-wise interactions or collisions between chemically active SiO_2-Pt Janus Colloids. The collisions are categorized based on the Janus colloids' orientations before and after they make physical contact.
In addition to the hydrodynamic interactions, the Janus colloids are also known to affect each other's chemical field, resulting in chemophoretic interactions, which depend on the degree of surface anisotropy in reactivity of Janus colloid, and the solute-surface interaction at play. Our study reveals that these interactions lead to a noticeable decrease in particle speed and changes in orientation that correlate with the contact duration and yield different collision types. Distinct configurations of contact during collisions, whose mechanisms and likelihood are found to be dependent primarily on the chemical interactions. Such estimates of collision and their characterization in dilute suspensions shall have key impact in determining the arrangement and time scales of dynamical structures and assemblies of denser suspensions, and potentially the functional materials of the future. Building on this study, we explored the interaction of particles in the well-known 'Coffee Ring Effect' (CRE). CRE, a widely observed phenomenon during the evaporation of colloidal droplets, has garnered attention in scientific and industrial domains such as inkjet printing, microfabrication, and biomedical diagnostics. Leveraging the unique characteristics of active Janus particles with anisotropic surface properties and self-propulsion via self-diffusiophoresis, our research delves into the intricate dynamics of CRE. The experiments reveal the delicate interplay between particle activity, interfacial interactions, and capillary attraction forces, offering insights into the effects on ring formation and particle distribution. By incorporating active Janus particles into the study of CRE, this research not only enhances our understanding of the phenomenon but also opens up promising avenues for advancing fundamental knowledge in colloidal science and expanding the applications of particle manipulation techniques.

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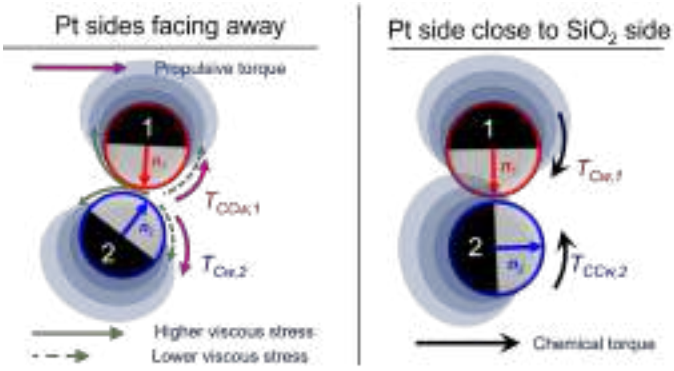
DOI: 10.1021/acs.langmuir.3c03415

Figures

Figure 1.



Non-equilibrium thermodynamics of catalytic Janus particles self-organization

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The study of the individual and collective behaviour of self-propelled particles, which convert the chemical energy of the surrounding fluid into mechanical energy, is fundamental to understanding the non-equilibrium nature of active matter of which many soft matter and biological systems are composed [1-2]. Being out of equilibrium raises questions such as how fluctuations behave and what are the mechanisms leading to the formation of self-assembling structures and instabilities at large length scales, to name but a few [3-4].

We investigate the energetic cost of Janus particle structure formation and analyse the dynamics of particle assembly to initially inhomogeneous fuel concentrations, revealing several emergent structures. The energy dissipation during structure formation is derived from the entropy production rate, exhibiting a non-monotonic behaviour that depends on the fraction of particles assembled within each self-assembly regime. Furthermore, we establish a thermodynamic criterion for structure formation by analysing the free energy of the particles, focusing on the behaviour of the non-equilibrium chemical potential with respect to the fraction of assembled particles [5].

In a complementary study, we delve into the motion of a catalytic Janus particle, exploring the interplay between self-thermophoresis and self-diffusiophoresis. We illuminate their individual behaviours and the possible coupling resulting from diffusion at the particle-medium interface, a previously neglected factor. Employing an out-of-equilibrium thermodynamic model, we determine crucial parameters such as effective diffusivities, phoretic coefficients and transport properties. By juxtaposing theoretical predictions with experimental data, we discern the conditions for coupled or independent phoretic dynamics. In particular, this work emphasises a detailed examination of particle surface interactions to elucidate the direction and magnitude of phoretic forces as well as their amplification due to collective phenomena, offering valuable information to advance drug delivery and nanomotors in materials science and medicine, promising customised transport properties at the nanoscale [6].

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Figures

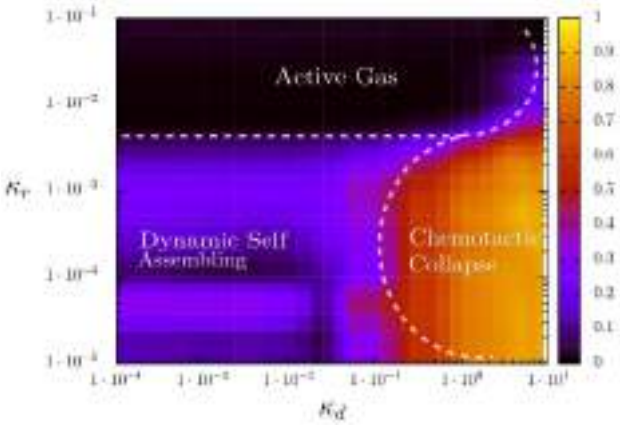

Figure 1 Fraction of assembled particles as a function of the chemophoretic coefficient κ_r and the difusiophoretic coefficient κ_d. We can identify the presence of three regimes: active gas (AG), dynamic self-assembly (DSA) and chemotactic-collapse (CC).

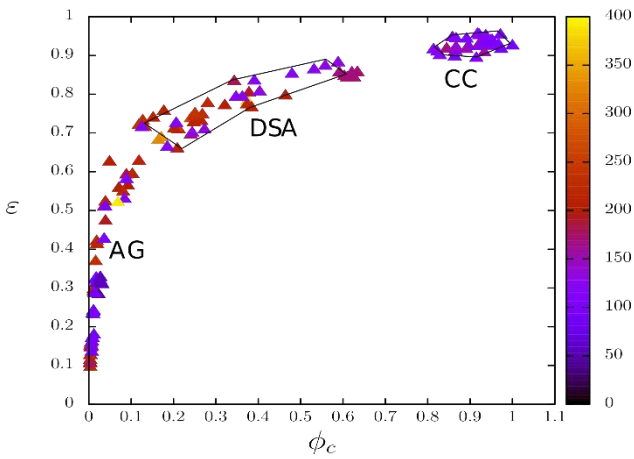

Figure 2 Sphericity ε as an function of the fraction of assembled particles ϕ_c. The triangles represent the values of the total entropy produced irreversibly Σ expressed by the colour bar.

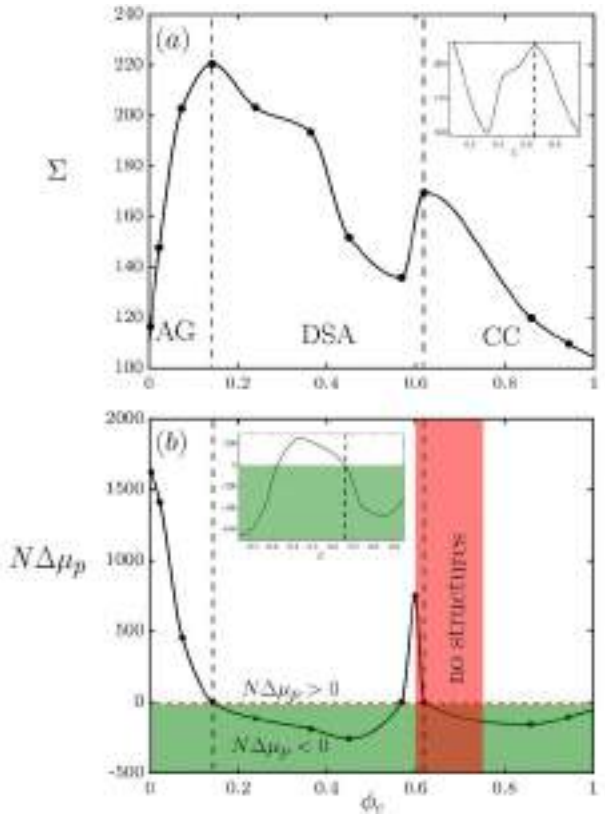

Figure 3 Thermodynamic criterion for the formation of structures (a) Total entropy production as a function of ϕ_c exhibiting two maxima at the transition points between aggregation regimes (dashed lines). The inset represents the entropy production as a function of ε. (b) Chemical potential difference between assembled and disassembled configurations $\Delta\mu_p$ as a function of ϕ_c and ε (inset). The figure shows the regions where ordered structures form (green stripes), where ordered structures do not form (white region), and where structure formation is unlikely (pink stripe).

Impact of an inhomogeneous concentration field on the transport and self-assembly of active particles.

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Active particles (AP) are known for consuming chemical energy from the medium and converting it into mechanical energy, facilitating their interaction with the environment to perform transport, chemotaxis, self-assemble process [1,2] . Numerous applications involving AP, such as drug delivery in situ medicine and environmental processes, necessitate consideration of fuel consumption to circumvent the need for external forces to propel particles through complex environments [1,3]. Moreover, the self-assembling process of AP could be contingent upon the amount of fuel the system consumes to attain a preferred state [1,4-6]. These observations underscore the necessity, particularly in defining models using the far-field approach, to account for the dependency of AP on the environment and fuel consumption [2,4-6]. This prompts inquiries into how chemical reactions on AP influence their transport through crowded environments and the impact of consumption on the mechanisms underlying the formation of self-assembling structures and potential instabilities.

Our investigations encompass two scenarios involving consumption: (I) the traversal of AP through diverse channels under oscillatory fuel conditions, assisted by environmental noise, to achieve optimal Signal-to-Noise ratio [7]. We discovered that intermittent substrate injection induces periodic forces Fig. 1 on particles, synchronized with noise, enhancing spectral amplification and optimizing transport, applicable in drug delivery and porous media penetration Fig .2 [7]. (II) Utilizing a self-consistent model of catalytic Janus particles, accounting for hydrodynamic interactions and non-uniform fuel concentration, we identified distinct aggregation regimes, elucidating free energy barriers and determining conditions conducive to particle clustering Fig . 3. We posit that the self-organization of active matter remodels the environment, engendering a feedback loop wherein evolving structures modulate environmental conditions to enhance stability.

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Figures

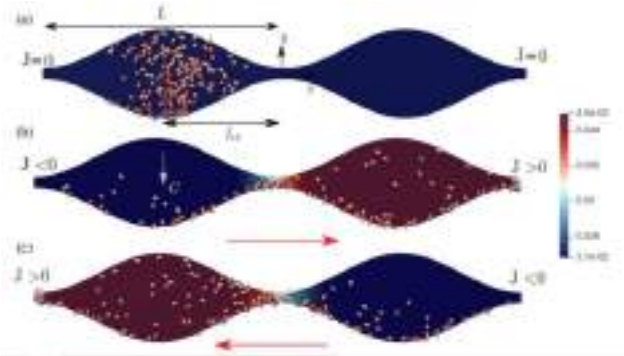

Figure 1 Scheme of the system. APs are driven by a constant force (white arrow) G in the orthogonal direction and by the substrate concentration gradient (color map) ρ(x, y, t) in the longitudinal direction whose flux is J.

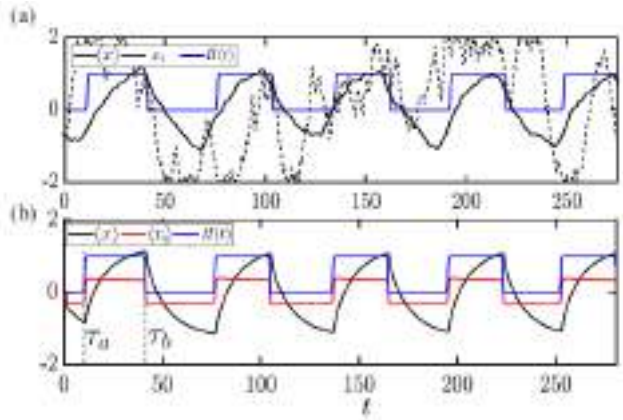

Figure 2 Active particle dynamics. APs mean position $\_x(t)\_$ (black solid line) and periodic signal $H(t)$ (blue solid line) (a) position of a single AP $x_i(t)$ (black dashed line), obtained from Langevin dynamics. (b) Substrate mean position $<x_s(t)>$ (red line). The oscillation period is $T = \tau_b - \tau_a$ while the frequency IS $\omega = \pi/T$. The values of the parameters used in the simulations are $J_{in} = 3.25D$, $G = 1.0$, $\omega = 0.114$, $k_d = 5$, and $k_{ch} = 10$.

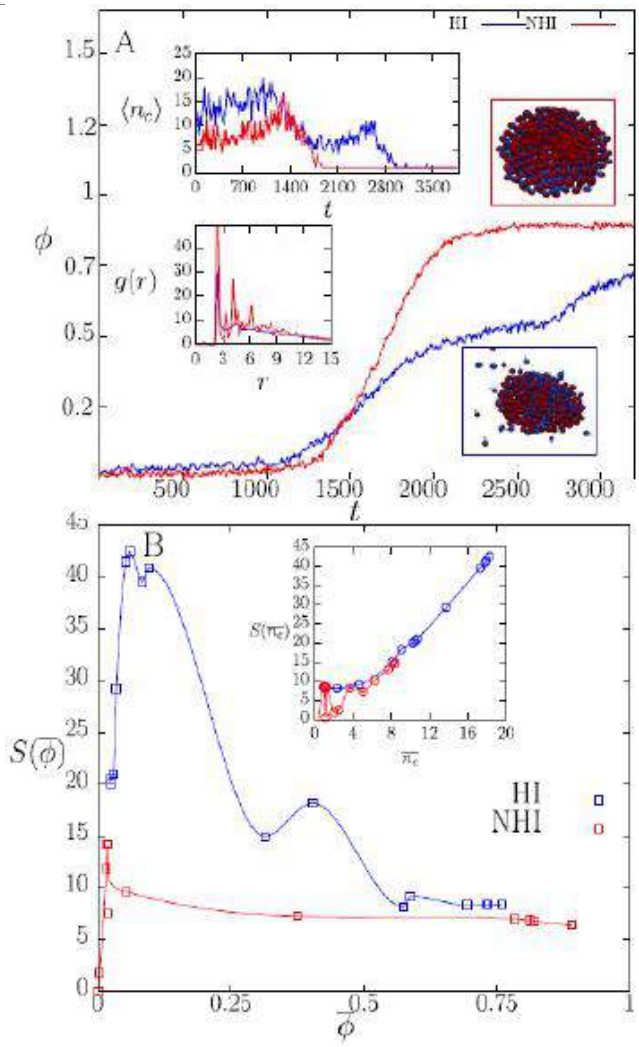

Figure 3 (A) number of clustered particles ϕ with Hydrodynamic interaction HI (blue lines) and with out Hydrodynamic interaction NHI (red solid lines). Insets are the number of clusters (nc) and the radial distribution function. (B) Entropy S as a function of the average number of aggregated particles $\overline{\phi}$, for HI and NHI. The inset depicts the entropy as a function of the averaged number of clusters formed nc.

Symmetrical catalytic colloids display Janus like motion

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Catalytic Janus colloids represent one of the most experimentally explored examples of self-motile active colloid systems, and are well known to exhibit Active Brownian Particle like trajectories [1]. The striking catalytic activity difference between the active and inactive hemispheres of such Janus colloids has been long held to be an essential requirement to produce motion [2]. Additionally, the various proposed mechanisms to explain motion in catalytic Janus colloids rely on significant asymmetrical activity. In this context, this study comparatively investigates the motile behavior of symmetrical catalytic colloids produced by a solution based metal salt reduction process.

Despite the significant differences in the distribution of catalytic activity, this study finds that the motion produced by symmetrical colloids is equivalent to that previously reported for Janus colloids. Experiments also show that introducing a Janus structure to the symmetrical colloids via masking does not significantly modify their motion, Figure 1. These findings could indicate that very subtle variations in surface reactivity can be sufficient to produce Janus-like active Brownian particle-type motion, or that a symmetry-breaking phenomena is present [3-4].

The study will consequently motivate fresh theoretical attention and also demonstrates a straightforward route to access large quantities of motile active colloids, which are expected to show subtly different phenomenology compared to those with Janus structures.

Figures

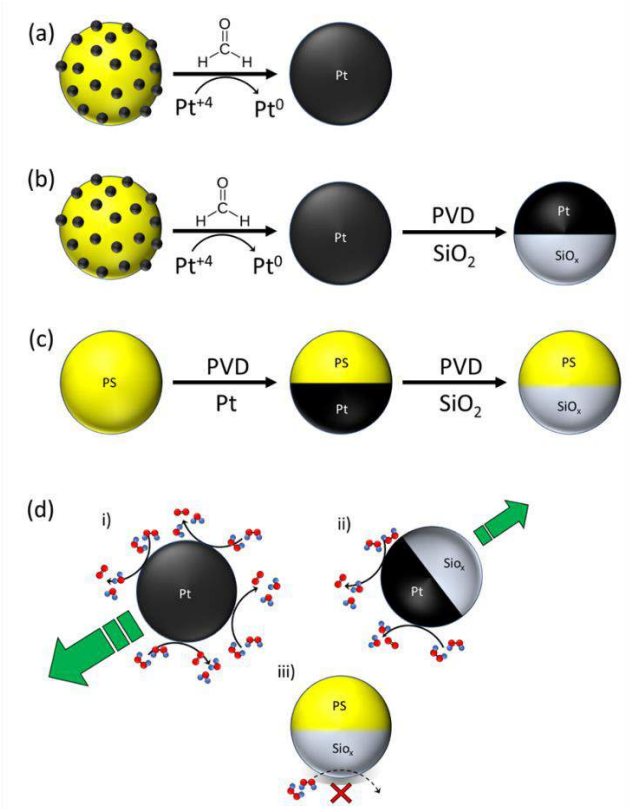

Figure 1. Schematics for the catalytic colloids investigated. (a) Converting Pt seeded colloids to continuous symmetrically Pt coated colloids via Pt salt reduction (b) Method to convert symmetrically coated Pt coated colloids to masked Janus structure colloids via plasma vapour deposition (PVD) of SiO_2. (c) Method to investigate the effectiveness of the SiO_2 mask, by applying a PVD SiO_2 mask to a PVD deposited Pt Janus coating. (d) Structure of the three colloids investigated here i) Symmetrical Pt coated colloid ii) Janus masked symmetrical Pt coated colloid iii) SiO_2 masked Pt Janus colloid.

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Tuning organic nanogels "à la carte" for a new generation of smart nanomotors

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In recent years, extensive efforts have been made to effectively transport drugs to precise targets within the human body. However, one significant challenge encountered is the entrapment of the drug within highly viscous media found in the entry routes of our bodies. For instance, one prominent difficulty arises when delivering therapeutic agents into the joints, specifically in the presence of synovial fluid (SF) – a protective layer composed of highly viscous hyaluronic acid. In order to tackle this issue, scientists have devised a solution by encapsulating the drug within nanoparticles (NPs).[1] Their primary focus has been on surface modifications of these NPs, aiming to reduce their interactions with biological matrices and effectively transform them into carriers for drug delivery.

In recent times, novel classes of self-propelled NPs, known as nanomotors, have emerged.[2] They possess the remarkable ability to propel themselves, enabling them to navigate through viscous media more swiftly compared to previous generations of materials. For instance, Janus silica nanorods-based motors have been developed, which utilize urease and hyaluronidase enzymes to disrupt HA and enable the nanorods to self-propel within the extracellular matrix. This propulsion mechanism relies on the catalytic activity of urease, requiring high concentrations of urea.[3] More recently, a tandem of silica nanomotors (non-Janus) has been employed. Initially, they were combined with hyaluronidase to reduce the viscosity of SF in a controllable manner. Subsequently, they were utilized with urease to propel particles through the medium via enzymatic activity.[4] Although this engineered system proved effective, it necessitated significant amounts of urea and approximately a 30% reduction in SF to ensure the motion of mesoporous-based nanomotors.

In this study, we introduce an innovative approach utilizing biocompatible organic gel-based nanomotors. The organic chassis is composed of a unique combination of p-N-Isopropylacrylamide co-polymerized with p-Itaconic acid, crosslinked with varying degrees of N,N-methylenebis(acrylamide) and bis(acryloyl)cystamine. To enable self-propulsion, the chassis has undergone enzymatic modification, leveraging its catalytic activity. This novel gel-based nanomotor not only exhibits the capability to navigate intricate matrices (e.g.: SF) autonomously (with a low amount of fuel) but also possesses controlled cargo encapsulation and release functionalities. Finally, we loaded small molecules into the materials and controlled their release upon pH and temperature. Also, we have conducted cytotoxicity tests on fibroblast cells to assess the materials, revealing significant biocompatibility. **Figure 1** illustrates the schematic representation of the four distinct nanogels developed in this study, accompanied by their respective chemical structures, SEM images showcasing the materials, and an assessment of cellular biocompatibility in fibroblasts. All our findings underscore the potential of nanogels as a promising organic option for developing the next generation of enzymatic nanomotors. They exhibit remarkable capabilities in navigating through viscous environments to deliver therapeutic payloads precisely to their intended targets.

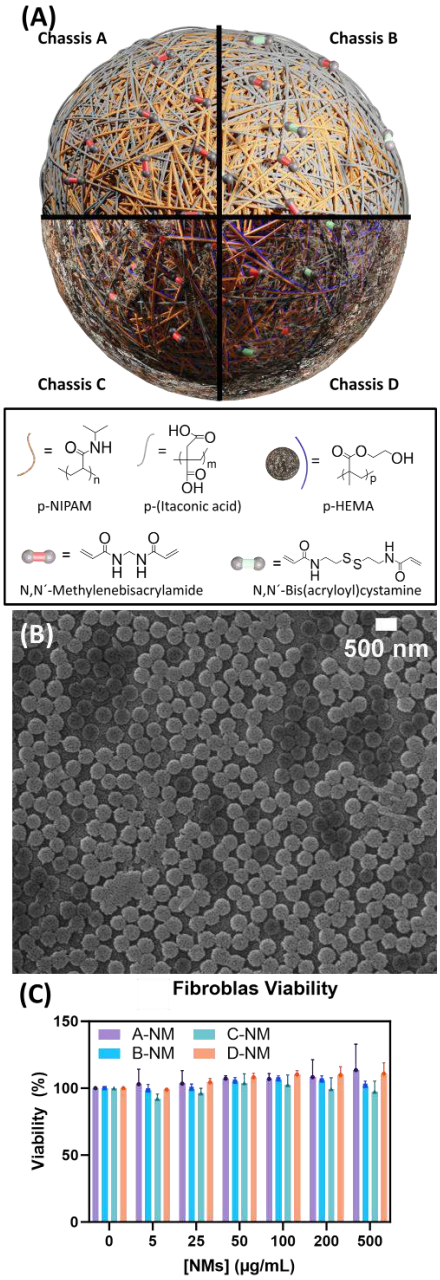

Figure 1. Nanogel-based Nanomotors: (**A**) Schematic depiction of the four distinct materials synthesized in this study along with their respective polymer structures. (**B**) SEM image showcasing the nanogels. (**C**) Assessment of cellular viability in fibroblasts.

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Micrometer-sized magnetic robots with piconewton-scale springs as on-board sensors and actuators

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Controllable magnetic microrobots hold great promise for manipulating cellular-level targets within small cavities in vivo, offering new possibilities for precision medicine. Due to the susceptibility of biological tissues and cells to damage by rigid structures, medical tasks require more compliant elastic micro/nanorobots. This presentation introduces a 4D nanofabrication strategy to produce highly compliant magnetic soft microrobots, with on-board soft sensors and actuators sensitive to sub-piconewton-scale forces, targeting the force sensing and manipulation of both dynamic and static cells[1]. Such 4D nanofabrication strategy with elasticity programmability enables to fabricate diverse shape-morphing micromachines including the microforcemeter for measuring the propulsion forces of various micromotors, the microgripper for microobject manipulation, and biomimetic microrobots with soft-actuation mechanisms. Specifically, the microforcemeter is capable of indicating the real-time propulsion force of various biohybrid, chemical and physical micromotors intuitively, with a precision of down to 500 fN. The microgripper performs complex manipulation of microobjects with the control of only the magnetic field. Starting from passive transportation manipulation, advancing to active transportation manipulation with specific recognition, and further to limitless free manipulation, such microrobots achieve the free manipulation of a series of complex actions such as force sensing, capturing, transportation, releasing, and rotating for various shapes and types of cells. Biomimetic micropenguin and microturtle perform soft actuation controlled only by the magnetic field without any other stimuli. Furthermore, by integrating microrobots with minimally invasive surgical robots, explorations of task execution by microrobots within organs across scales are conducted. This report will discuss the latest progress of such robots and how they will revolutionize therapeutic approaches in the biomedical field [2], [3].

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Figures

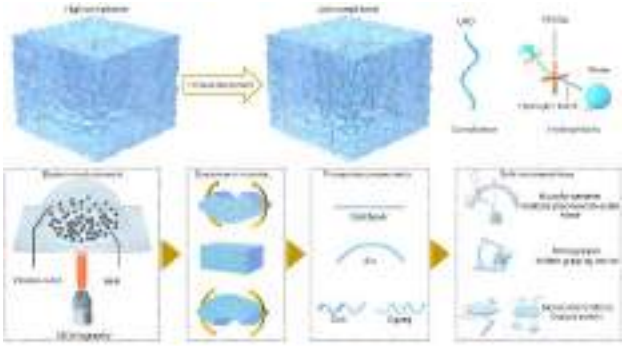

Figure 1. Soft micromachines based on piconewton-scale springs with programmable elasticity distributions.

Amyloid Peptide Nanotube based Nanomotors (Amylobots) for Complex Navigational Behaviour

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Shaped through millions of years of evolution, living cells exhibit intricate spatial localization of enzymes, orchestrating complex cascade reactions for coordinated multimodal functions. Integrating biological precursors into nanomotor chassis, powered by biocatalytic transformations, holds immense potential for future applications, particularly in emergent biomedical techniques. Utilizing the catalytic and templating abilities of cross-β amyloid nanotubes (amylobots) through a divergent cascade reaction, fluorescent microswimmers were designed. The amylobots showed remarkable binding capabilities to host dedicated enzymes for catalyzing orthogonal substrates to display chemotactic migration towards a substrate gradient. The design principle elucidated the utilization of distinct transport behaviours for chemotactic amylobots to overcome diffusion limitation in a biphasic environment and enhanced catalysis in organic solvents. Looking beyond, mimicking the emergent collective behaviour as observed in Nature, we aim to exploit time delayed and feedback triggered chemotactic migration of enzyme-bound amylobots thus displaying advanced interactive behavior in a complex chemical milieu.

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Figures

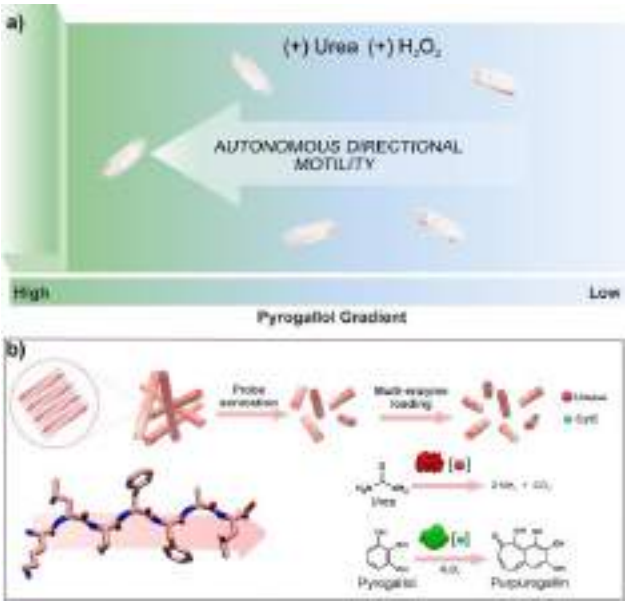

Figure 1. Scheme showing chemotactic motility of amylobots (amyloid peptide-based nanotubes). a. Representative cartoon of cytochrome C bound urease powered amylobots showing motile behaviour towards pyrogallol gradient (reservoir). **b.** Schematic illustration of amylobot design achieved by probe sonication of long nanotubes that lead to short nanotubes which were exposed with enzymes for binding.

Communication Between Liposomal Nanomotors Based on Enzyme-Cascades

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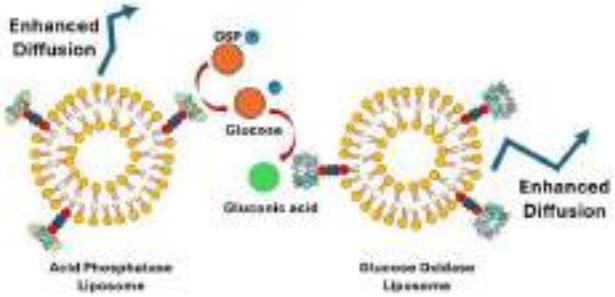

Figure 1. Schematic representation showing the communication of enzyme-attached liposomal nanomotors induced by enzyme cascade.

Abstract
In the world of biological systems, the detection and reaction to chemical signals are crucial for survival.[1] Traditional research efforts have aimed to mimic this communication involving chemical cues in synthetic cells, focusing on the chemical responses induced by such signals.[2, 3] However, by using enzyme-functionalized liposomes, we demonstrate how a chemical input can provoke a mechanical response (enhanced motility) through the communication between distinct populations of synthetic cells. In the presence of the substrate for the first population, a sequential catalytic reaction initiates across multiple populations, leading to enhanced diffusion of all involved synthetic cells. This approach allows for the control of the diffusion of up to three different enzyme-functionalized liposome populations using a single substrate via an enzyme cascade reaction. Furthermore, we apply substrate competition as a strategy to finely control the activation of enhanced motility. Our research not only presents the impact of chemical signal transduction on the motility of synthetic cells but also provides a robust and efficient approach for coordinating the motion of diverse protocell populations in reaction to mutual chemical cues.

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Figures

PROGRAMME

TUESDAY, JUNE 4

09:00	**Registration**
09:30	Keynote talk: Microelectronic morphogenesis: From microrobots to microelectronic life **Oliver Schmidt,** *University of Chemnitz, Germany*
10:00	Invited talk: Rotary FoF1-ATPase-propelled Supramolecular Colloidal Motor **Qiang He**, *Harbin Institute of Technology, Harbin, China*
10:20	Invited talk: Tailoring Functionality And Control In Living Robots Across Scales **Maria Guix,** *University of Barcelona, Barcelona, Spain*
10:40	Invited talk: Hydrodynamic description of swarming enzymatic nanomotors **Igor Aronson**, *Pen State University, USA*
11:00	*Coffee break* + poster session
12:00	Keynote talk: Microrobots Go In-Vivo: Our Journey from Test Tubes to Live Animals **Joseph Wang**, *University California San Diego, USA*
12:30	Invited talk: Driving micro/nanomotors and pumps by ion-exchange **Maria Jose Esplandiu,** *Catalan Institute of Nanoscience and Nanotechnology (ICN2), Spain*

12:50	Invited talk: Nano and microrobots for biofilm eradication and microplastics remediation **Martin Pumera,** *University of Chemistry and Technology Prague*
13:10	Keynote talk: **Peer Fischer,** *Heidelberg University and Max Planck Institute for Medical Research, Germany*
13:40	Lunch break
14:40	Keynote talk: Magnetic miniature robots for endoluminal intervention: from individual and modular designs to microswarm **Li Zhang**, *Chinese University of Hong Kong (CUHK), Hong Kong*
15:10	Invited talk: Engineering Photoactive Micromotors for Targeted Functions **Katherine Villa Gómez**, *Institute of Chemical Research of Catalonia, Spain*
15:30	Invited talk: Self-propelled magnetic nanomotors **Ambarish Ghosh**, *Indian Institute of Science, Bangalore, India*
15:50	Coffee break

16:20	*Parallel session 4* *Room: PI* ***Nanomotors for biomedicine 2*** *Chair:* *Yingfeng Haifeng,* *School of Pharmaceutical Sciences, Southern Medical University, China*	*Parallel session 5* *Room: TAU* ***Light-based Control 1*** *Chair:* *Stefano Palagi,* *The BioRobotics Institute, Pisa*	*Parallel session 6* *Room: DELTA* *Biomimetic systems* *Chair:* ***Loai Abdelmohsen,*** *Institute of Complex Molecular Systems (ICMS)* *and* *Claudia Contini, Imperial College London*
	Active therapy based on the byproducts of micro/nanomotors **Yingfeng Haifeng,** School of Pharmaceutical Sciences, Southern Medical University, China	Towards cell-inspired microrobots powered by catalytic micromotors **Stefano Palagi,** *The BioRobotics Institute, Pisa*	Exploiting Dynamicity to Induce Motility: Motion of Membranized Coacervate Motors, **Loai Abdelmohsen,** *Institute of Complex Molecular Systems (ICMS)*
16:35	Modularized microrobot for targeted cell delivery in bile duct **Lin Su,** *The Chinese University of Hong Kong, China*	Motion manipulation of photocatalytic nanomotors induced by an external magnetic field **Yufen Chen,** *Institute of Chemical Research of Catalonia (ICIQ), Spain*	How spontaneous curvature induces the morphogenesis of dendrimersome vesicles? **Nina Kostina**, *Institute for Bioengineering of Catalonia, Spain*

16:50	Glucose-Powered Gated Nanomotors for Enhancing Anticancer Efficacy via Deep Drug Penetration into Tumors **Alba García Fernández,** *Instituto Interuniversitario de Reconocimiento Molecular y Desarrollo Tecnológico (IDM), Spain*	Ultrafast Light-activated Polymeric Nanomotors **Jianhong Wang,** *Institute for Complex Molecular Systems, The Netherlands*	The minimal chemotactic cell **Barbara Borges Fernandes,** *Institute for Bioengineering of Catalonia, Spain*
17:05	Nitric Oxide-Propelled Nanomotors Induce Pyroptosis for Cancer Therapy **Mingchen Sun,** *Institute for Molecules and Materials, The Netherlands*	Micropumps and Micromotors from Smart Ionogels of Light-triggered Release **Dezhou Cao,** *Harbin Institute of Technology (Shenzhen), China*	Collective Self-Caging Of Active Filaments In Virtual Confinement **Leila Abbaspour,** *Max Planck Institute for Dynamics and Self-Organization (MPI-DS), Germany*
17:20	Urease-Powered Nanobots For Radionuclide Bladder Cancer Therapy **Meritxell Serra-Casablancas,** *Institute for Bioengineering of Catalonia (IBEC), Spain*	Transition Metal Dichalcogenides Meet Light-Driven Nanomotors **Víctor de la Asunción Nadal,** *University of Alcalá, Spain*	Mechanisms of self-propulsion of catalytic Janus particles for cell-inspired microrobots **Gaia Petrucci,** *The BioRobotics Institute, Sant'Anna School of Advanced Studies, Italy*

17:35	*Programmable Multifunctional Microrobots* ***Sambeeta Das,*** *University of Delaware, USA*	Photoactive Ru-based polymeric colloidal system for non-equilibrium assembly and micromotors **Majid Basharat,** *Institute of Chemical Research of Catalonia (ICIQ), Spain*	Bottom-Up Approaches to Designing Dynamic Behaviours in Artificial Cells **Claudia Contini,** *Imperial College London*
17:50	End		
20:00	Social Event: Cocktail at *Hotel Barceló Raval Rooftop*		

KEYNOTE LECTURES
INVITED LECTURES

Microelectronic morphogenesis: From microrobots to microelectronic life

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Microelectronic morphogenesis (MIMO) is the creation of form and structure under microelectronic control [1], and relies on our previous work on self-folding [2] and self-locomoting [3,4] thin film electronic modules, now carrying tiny silicon chiplets between the folds, for a massive increase in information processing capabilities. MIMO addresses key challenges in the field of micro- and microrobotics [4]. For instance, by controlling the robots' materials elasticity with nanoscale precision, cell-sized picoforce springs with remarkably large and tunable compliancy can be fabricated – allowing articulated motion in microrobots as well as micromanipulations and force sensing well beyond state of the art [5]. The storage and delivery of energy for truly autonomous operation of microrobotic systems represents another key challenge in the field [6] and will be addressed by producing tiny deep-submillimeter on-board integrated batteries and biosupercapacitors [7,8]. Finally, the talk will reveal how microelectronic life could evolve from interacting modular microrobots that undergo self-learning and evolutionary development [1].

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Rotary FoF1-ATPase-propelled Supramolecular Colloidal Motor

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Cells orchestrate the motion and force of hundreds of protein motors to perform various mechanical tasks over multiple length scales. However, engineering active biomimetic materials from protein motors that consume energy to propel continuous motion of micrometer-sized assembling systems remains challenging. In this talk, I will introduce our recent progress on rotary biomolecular motor (FoF1-ATPase)-powered supramolecular colloidal motors that is hierarchically assembled from a purified natural membrane containing FoF1-ATP synthase molecular motors, and different supramolecular assembled nanoarchitectures. These supramolecular motors with asymmetric distribution of rotary FoF1-ATPases can autonomously move under light illumination or proton gradients, and is collectively powered by hundreds of rotary FoF1-ATP synthase biomolecular motors. The self-propelled motion of these supramolecular motors accompanies the ATP biosynthesis inside or outside, which depend on the direction of proton gradients across the membrane of supramolecular motors. Also, their directional motion could be realized by modulating the light gradients or proton gradients. Such an active supramolecular architecture endowed with motility and biosynthesis offers a promising platform for intelligent colloidal motors resembling the propulsive units in swimming bacteria.

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Figures

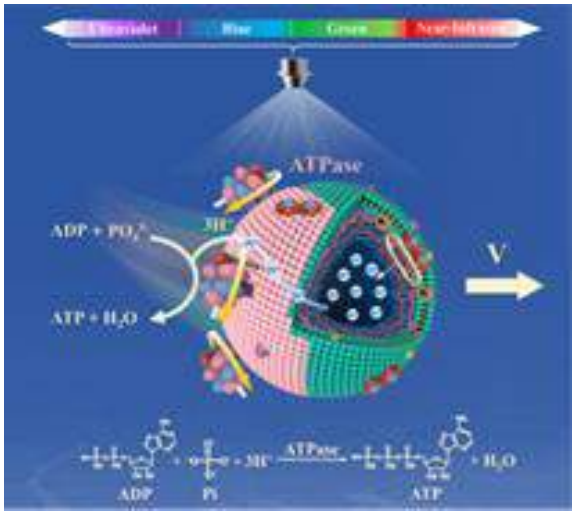

Figure 1. A hierarchically supramolecular colloidal motor is collectively powered by hundreds of nano-sized rotary biomolecular motors.

Tailoring Functionality And Control In Living Robots Across Scales

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Soft robotic systems often present bio-mimicking designs that resemble actuation mechanisms of certain biological organisms, as for example in swimmers resembling fish or flagellated organisms. However, some unique properties from living organisms that are specially challenging to obtain in their artificial counterparts, such as self-healing, adaptability, or bio-sensing capabilities.[1] Several bio-hybrid robotics platforms across different scales had been developed,[2] but the ones based on living muscles has attracted increasing attention.[3]

Regarding fabrication methods, 3D printing technologies have been particularly appealing for the fabrication of advanced living robots based on skeletal muscle cells, exploring new designs that are not bio-mimetic but especially efficient when it comes to mechanical self-stimulation (Figure 1A).[4] Additionally, the integration of nanomaterials in the cell-laden scaffold resulted in an enhanced force output.[5] Indeed, the overall robot design and materials implemented are key to achieve the desired functionality in the resulting bio-hybrid robotic platform. Alternative 3D printing techniques to generate living robots either at bigger or smaller scales to the cm-size range (mesoscale) will be presented.

Another important challenge in the development of such living robots is the integration of control systems, which could be either aimed toward guidance purposes of to gather real time information over the robot performance (i.e., exerted force). While very interesting control systems using light stimulation (Figure 1B)[6] and force-sensors integration[7] in genetically modified skeletal muscle constructs have been demonstrated, in the present talk it will be covered the implementation of strain sensors for real-time force detection in non-modified skeletal muscle actuators.

Overall, the key feature when designing these new generation of robots using living components as an active material will be discussed, as well as the main challenges and applications, both in the biomedical and the environmental field.

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Figures

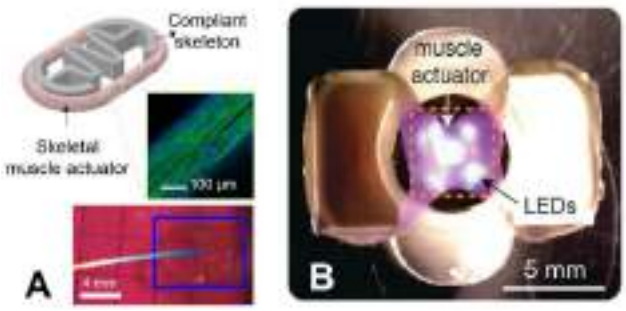

Figure 1. Skeletal muscle-based living robots, presenting a (A) 3D printed compliant skeleton for mechanical self-stimulation (adapted from Ref. [4]), and (B) on-board optoelectronics for independent stimulation of optogenetic skeletal muscles (adapted from Ref. [6]).

Hydrodynamic description of swarming enzymatic nanomotors

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Enzymatic nanomotors often exhibit collective swarming behavior reminiscent of bioconvection in aerobic microorganismal suspensions. While swarming has multiple advantages compared to individual nanomotor functionalities, the underlying physical mechanisms are not well understood. Our experimental studies have shown that swarming behavior is generated by the solutal buoyancy due to enzymatic activity [1]. In my talk, I'll present a coarse-grained hydrodynamic description of self-organization in suspensions of enzymatic nanomotors. We used two-fluid hydrodynamics to describe the co-evolution of solvent, particulate (nanomotors), and evolution of the fuel concentration. The analysis is extended to enzymatic swarms under vertical confinement. The approach successfully reproduced experimental observations, see Fig. 1, and made testable predictions for the evolution of enzymatic swarms.

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Figures

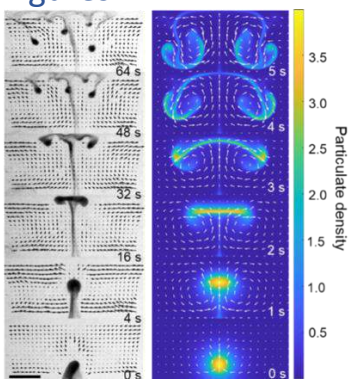

Figure 1. Left: A time-lapse sequence of images that show the collective movement of enzymatic nanomotors. Scale bar: 1 mm. Right: A time-lapse sequence of snapshots of computational results. The color bar indicates the nanomotor concentration and white arrows display the fluid velocity, From Ref. [1].

Microrobots Go In-Vivo: Our Journey from Test Tubes to Live Animals

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The field of microscale robots has grown rapidly over the past two decades, demonstrating new capabilities and offering exciting new opportunities. Such impressive capabilities, including greatly enhanced power and cargo-towing forces, multi-functionality, easy surface functionalization, and versatility, offer considerable promise for a variety of biomedical applications, and should have major impact on disease diagnosis, treatment, and prevention [1,2]. This talk will discuss our two-decade long journey towards designing powerful chemical-powered microrobots and moving them from test tube testing to the first in-vivo demonstration in live animals [3]. Our recent in-vivo applications using different types of biocompatible and biodegradable microrobots will be illustrated, including enhanced drug delivery towards enhanced treatment of stomach or lung infections, active vaccine delivery, and microrobot pills for oral delivery.

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Driving micro/nanomotors and pumps by ion-exchange

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Ion exchange is one of the most interesting processes occurring at the interface between aqueous solutions and polymers endowed with sulfonic groups, such as the well-known Nafion[1]. When exchanged ions possess varying diffusion coefficients, this process generates local electric fields that can be utilized to propel fluid motion[1,2]. In this study, we demonstrate the design and fabrication of self-propelling micro/nanoswimmers and pumps based on Nafion, powered by ion exchange and fueled by salts. These Nafion micromachines are created through different lithographic techniques (colloidal, stencil, photo or electron beam lithographies) shaping Nafion into asymmetric structures[3,4]. The resulting micro/nanoswimmers exhibit fascinating collective motion in water driven by the interplay of their self-generated chemical/electric fields and their capability to pump surrounding matter towards them. The pumping activity of the micro/nanoswimmers induces the formation of growing mobile clusters, whose velocity increases with size. Such dynamic structures are able to trap nearby micro/nano-objects while purifying the liquid, which acts both as the transport media and as fuel[3,4]. This phenomenon holds promise for potential applications in water remediation currently under development.

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Nano and microrobots for biofilm eradication and microplastics remediation

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Microrobots are emerging as revolutionary tools in combating environmental pollution and biofilm-related health issues, focusing on removing nanoplastics from water bodies and eradicating biofilms that hinder medical treatments and device functionality. These tiny engineered devices are designed to navigate challenges in healthcare and environmental preservation by directly targeting and disrupting the structure of biofilms to enhance treatment efficacy and adsorbing micro and nanoplastics to reduce aquatic pollution, respectively.[1,2,3]

Highlighting the innovative designs and mechanisms of nano and microrobots, this discourse delves into their recent advancements and potential in addressing stubborn problems in biomedical and environmental fields. It explores the capabilities of these robots in delivering targeted therapies, improving antibiotic effectiveness, and collecting harmful plastic particles, offering insights into their future development and the challenges that lie ahead in fully harnessing their potential for sustainable solutions.

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From diffusion to propulsion of nano-motors and a 'one shot' fablab of micromotors

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Diffusion is generally not an efficient mechanism for transport over larger distances. For this reason, many microorganisms, including pathogens, have developed swimming strategies. Nanomotors based on magnetic propulsion can be used to mimic these strategies and they are of interest for potential applications in nanomedicine [1,2]. Here, the choice of materials and suitable scalable fabrication approaches must be considered. Inspired from our group's recent invention of the acoustic hologram and its application in biofabrication [3,4], I will discuss our recent efforts towards a 'one-shot fablab for complex micromotors. It promises speed-ups that are many orders of magnitude faster than existing methods.

Apart from the fabrication and the powering of motors by physical fields, much simpler chemical nanomotors are also an important model system for nanomotors. They give rise to fascinating emergent phenomena as well as enhanced diffusion. It is therefore interesting to ask, if the mechanisms that power catalytically-active inanimate particles can translate to even smaller scales, such as proteins. The extension of these concepts to the nano- and molecular scale is, however, far from obvious. I will critically discuss the role of diffusion measurements in claims that enzymes and molecules can actively swim when they are catalytically active [5-11], and show how diffusion measurements may be used to realize a form of biosensing.

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Magnetic miniature robots for endoluminal intervention: from individual and modular designs to microswarm

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Robotics at small scales has attracted considerable research attention both in its fundamental aspects and potential biomedical applications. As the characteristic dimensions of the robots or machines scaling down to the milli-/microscale or even smaller, they are ideally suited to navigating in tiny and tortuous lumens inside the human body which are hard-to-reach by regular medical devices. Although the materials, structural design, and functionalization of miniature robots have been studied extensively, several key challenges have not yet been adequately investigated for in vivo applications, such as adaptive locomotion in dynamic physiological environments, in vivo localization with clinical imaging modalities, the efficiency of therapeutic intervention, biosafety, and their autonomy for the intervention tasks.

In this talk, I will first present our recent research progress on development of magnetic miniature robots, from individual [1] and modular designs [2] to microswarm [3-11], for endoluminal delivery and targeted therapy. Then the key challenges and perspective of using magnetic miniature robots for clinically relevant applications with a focus on endoluminal procedures will be discussed [12-13].

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Acknowledgements

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Engineering Photoactive Micromotors for Targeted Functions

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Optical actuation has emerged as a promising avenue for motion control in self-propelled micromotors, offering precise manipulation through wavelength, polarization, light intensity, and direction. [1]

In this presentation, I will introduce various strategies we have investigated to enhance the performance of photoactive micro/nanomotors with anisotropic morphologies.[2] For instance, by fine-tuning their surface properties with recognition sites, these micromotors can bind specifically to target molecules, leading to increased performance and faster motion efficiencies, all without the need for toxic chemical fuels.[3] Moreover, the integration of light and magnetic fields allows us to adjust charge transfer dynamics, ultimately leading to more effective light-driven nanomotors.

I will also highlight how these micromotors interact uniquely with their environment, when exposed to light irradiation.[4] Additionally, I will discuss achieving a precise steering of these nanomotors along predefined trajectories through controlled light patterning, showcasing the potential for programmable control in complex environments.

These different approaches, based on multifunctional photoresponsive micromotors, hold promising applications across diverse fields, such as micromanipulation, self-assembly, photocatalysis and selective oxidations.

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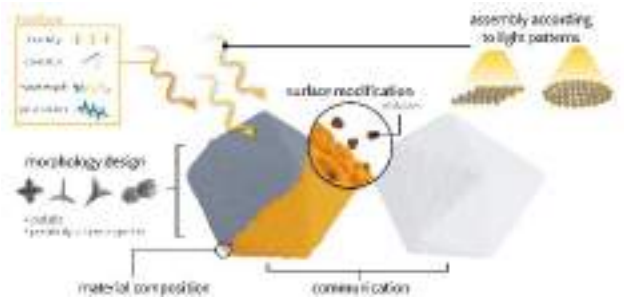

Figure 1. Schematic illustration of the different properties of light-driven micro/nanomotors and the diverse strategies used to tune their surface functionalities and interactions.

Self Propelled magnetic nanomotors

Ambarish Ghosh
AIndian Instituddress,

Unlike chemically powered nanomotors, magnetically driven colloids are typically not self-propelled. Recently, we used [1] the thermal rachet principle to render magnetic nanomotors autonomous. We will demonstrate biomedical applications [2] where these self-propelled colloids, even in the non-interacting limit, show clear superiority compared to driven colloids. At higher densities, the swimmers interact through hydrodynamic forces, where we observe interesting collective phenomena like chemical motors.

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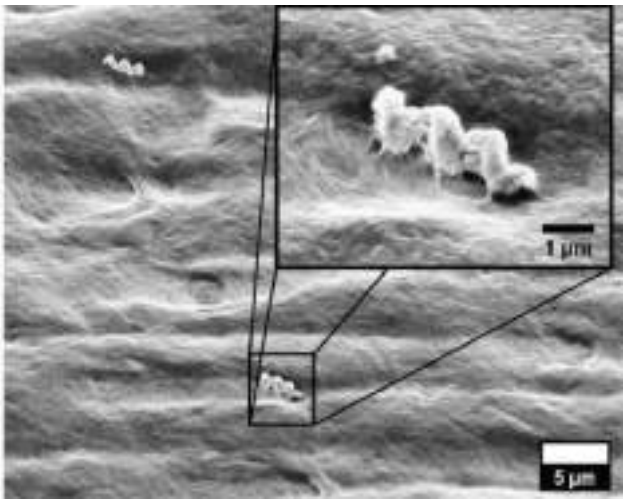

Figure 1. Magnetic nanomotors inside dentinal tubules

CHAIRS/INVITED SPEAKERS PARALLEL SESSION

Active therapy based on the byproducts of micro/nanomotors

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Self-propelled micro/nanomotors, as one of the hot research spots in nanotechnology, are capable of converting chemical or external energies (for example ultrasound, electric field, light, magnetic field etc) from surrounding environment into mechanical movement. Due to miniaturized size of micro/nanomotors, the produced motion can be used for complex functions with small scale or even microscale, ranging from environmental remediation, analysis and sensing, cargo transportation, drug delivery, tissue collection and even precise micro/nanosurgery. In the past decade, micro/nanomotors show huge potential in various fields. And how to further extend the biomedical applications of micro/nanomotors has become the key issue for the researchers. Recently, the speaker has been focusing on the development of mobile carriers based on micro/nanomotors, using the produced products from the motors to realize the active therapy of diseases. By successful utilization of the waste products, this is a new strategy for the biomedical application of micro/nanomotors.

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Figures

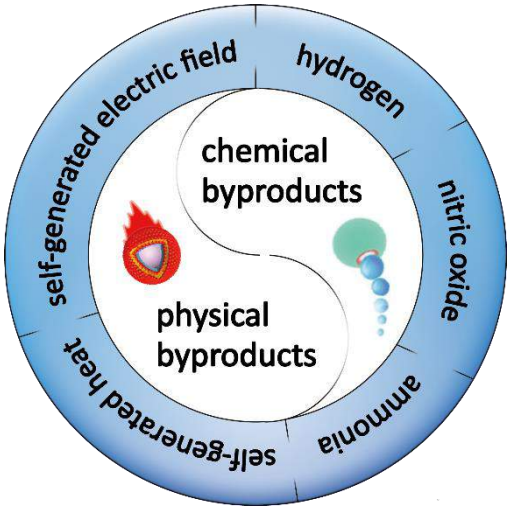

Figure 1. Schematic illustration of the byproducts of micro/nanomotors

Towards cell-inspired microrobots powered by catalytic micromotors

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One of the main challenges of microrobotics consists in making microrobots successfully move in body fluids and tissues. Biological micro-swimmers, such as bacteria, spermatozoa, and ciliates have served as a source of inspiration for microrobots that could swim [1]. Developing microrobots able to move through dense soft body tissues, however, requires different solutions compared to developing swimming microrobots and, thus, different sources of inspiration. Among these, we can identify cells that naturally move in such environments, such as some white blood cells. Instead of having appendages and propellers, they locomote by largely and continuously changing their body shape – known as amoeboid locomotion [2]. Nonetheless, this poses new challenges, as such cell-inspired microrobots – which we refer to as *celloids* – would need to change their body shape largely and continuously, being ultra-deformable and capable of self-sustained body-shape changes.

We are therefore addressing the development of celloids, focusing on their ability to deform and squeeze through narrow openings. We are thus realizing microrobots with ultra-deformable bodies consisting of lipid Giant Unilamellar Vesicles (GUVs). The vesicle-based microrobots thus have a liquid body (tens of microns in size) enclosed by a nanometric thin membrane consisting of a phospholipid bilayer. The GUVs are produced by a method known as droplet transfer [3], which allows the vesicles to be loaded with molecules or particles of interest. At first, we loaded the vesicles with a ferrofluid (a stable suspension of superparamagnetic nanoparticles) and actuated the vesicle-based microrobots with magnetic fields and gradients. We are thus studying the role of the microrobots deformability (depending on the membrane composition and on the osmolarity of the liquid body with respect to the external environment) in transversing narrow and/or obstacles-filled environments, as well as devising specialized actuation strategies that exploit this inherent compliance. Our preliminary results show that these ultra-deformable magnetic microrobots can indeed move effectively through gaps smaller than their size. At the same time, we have been producing catalytic micromotors consisting of Janus particles made of inert (silica or polystyrene) microparticles half-coated with a metal catalyst for hydrogen peroxide. The micromotors are made by drop-casting a monolayer of inert particles on a substrate (silicon or glass) and then sputtering the metal (Pt or Pd) on top of it. In addition to characterizing the particles and their activity, we are looking more closely at their self-propulsion mechanism and at their interactions. We have also loaded such micromotors inside GUVs and confirmed that they remain active and able to move even inside very thin membrane protrusions. Enclosing the micromotors in the vesicles has the added advantage that the vesicle membrane shields them from ions and other solutes present in biological fluids and that can hinder the movement of the micromotors (depending on the specific self-propulsion mechanism). Indeed, we aim at making our celloids change shape spontaneously by exploiting the collective action of loaded catalytic micromotors. For this reason, we are at the same time running Active Brownian Particles (2D) simulations of micromotors in curved confinements. By experiments and simulations, we are addressing the following questions: how do the self-propulsion mechanism and inter-particle interactions affect the collective behaviors of the micromotors? how does the particles-membrane interaction affect the collective behaviors? can membrane curvature and deformation steer swarms of micromotors? can a swarm of micromotors deform the vesicle membrane? can a swarm of micromotors power the locomotion of the vesicle (inside confining environments)?

Future developments include the investigation of mechanical responses of the membrane to external environmental conditions that could be exploited to steer the inner micromotors swarm and the whole celloid along chemical gradients. Moreover, we will address the biocompatibility and biodegradability of the micromotors, including their constituent materials and the fuel. In the long term, we aim at cell-like, ultra-deformable, and micromotors-powered microrobots that can navigate dense soft biological tissues autonomously, release a treatment to a target they identify, and then degrade safely in the tissue.

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Figures

Figure 1. Vesicle with protrusion, enclosing catalytic self-propelled Janus particles (1 µm): one particle moves along the protrusion and back.

Exploiting Dynamicity to Induce Motility: Motion of Membranized Coacervate Motors

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Understanding how different building blocks can be assembled into synthetic systems displaying cell-like architectures and functions is a major scientific challenge. Scientists have considered this multidisciplinary challenge as a way to provide insight into the fundamental processes of living systems, concurrently developing diverse potential applications of cell-mimicking constructs. Noteworthy, compartmentalization, or separation of materials from the external environment by a physical boundary (membrane) is a key hallmark for the origin of life – lipid cellular membranes are essential for hosting vital biochemical processes and maintaining the integrity of living cells. Following a bottom-up approach, several synthetic strategies for the creation of artificial compartments at different length scales have been developed, such us the assembly of polymeric vesicles (polymersomes), lipid vesicles (liposomes), virus capsids, colloidosomes, and coacervates.
Remarkably, these compartments have been used for the reconstitution of certain cellular functions such as protein expression, metabolite synthesis, enzymatic cycles, transmembrane transport, and motion. Autonomous motion has been an important source of inspiration for scientists who, over the years, have created a variety of synthetic motor systems, imitating biological motility.
Notwithstanding, there is a fundamental difference in the way movement is regulated in synthetic and natural systems. Cellular autonomous motion (e.g., vesicular transport and motility), displays adaptive features as a result of random dynamic processes, which are governed by enzyme-mediated energy input and consumption, and molecular interactions. Mimicking dynamic behaviors in synthetic systems has recently drawn much attention from the scientific community. In this presentation I will show how we couple motility of coacervate compartments to a dynamic process, which is maintained by stochastic events and how we compartmentalize such coacervates in giant liposomes and investigate their motion in confinement.

Bottom-Up Approaches to Designing Dynamic Behaviours in Artificial Cells

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My research group focuses on the development of artificial constructs that simulate the structure and functionality of biological cells, using a combination of synthetic and hybrid molecular frameworks engineered for precise manipulation. By emulating the fundamental characteristics and behaviours of living cells, these cell-like systems offer insights into biological systems, paving the way for a variety of functional applications. A notable challenge in the field of bottom-up synthetic biology is the creation of these synthetic entities capable of dynamic behaviours, such as fusion, material uptake, and autonomous, directional movement in response to environmental stimuli, reflecting the intricate processes of biological communication and organization. The endeavour to construct life-like systems that are both manipulable and interpretable advances our comprehension of life's origins and drive scientific discovery. The fabrication of custom-designed, dynamic cell-like systems holds potential for application in biotechnological engineeringg, facilitating the creation of biomimetic tissues and materials with controlled spatiotemporal self-organization.

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PARALLEL SESSION

Modularized microrobot for targeted cell delivery in bile duct

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Abstract

The recent rise of magnetically actuated microrobots with miniature size and remote controllability promises major benefits in minimally invasive cell-based therapy via targeted delivery of specific cells to hard-to-reach regions inside living bodies [1-2]. However, current magnetic microrobots relying on the surface deposition or matrix encapsulation of magnetic agents generally suffer from an inevitable compromise between their magnetic responsiveness and biomedical functions, which would impair the simultaneous integration of effective actuation and cell-carrying capabilities.

Herein, we report a modularized microrobot that consists of specialized modules, i.e., a magnetic actuation (MA) module and a cell scaffold (CS) module, to achieve multifunctionalities in a division and cooperation manner. Through developing specific hydrogel printing materials, the MA module with strong magnetism and pH-responsive deformability, and the CS module with favorable cell loading and release capabilities were designed and fabricated by high-precision 3D printing technique. Subsequently, robust assembly of specialized modules into a modularized microrobot system was performed by designing a shaft-hole structure and elaborately customizing their relative dimensions, which enabled effective magnetic navigation of microrobot in tortuous, viscous and flowing environments, while not deteriorating the cellular functionalities. On-demand disassembly of modules at targeted lesion was then realized to facilitate in situ CS module delivery and post-operational retrieval of the MA module. Furthermore, the feasibility of our proposed system was validated in an ex vivo porcine bile duct and an in vivo rabbit bile duct under the real-time guidance of X-ray fluoroscopy or ultrasound imaging system. Therefore, this work presents a modular design–based strategy that enables uncompromised fabrication of multifunctional microrobots and stimulates their development for future cell-based therapy of bile duct diseases.

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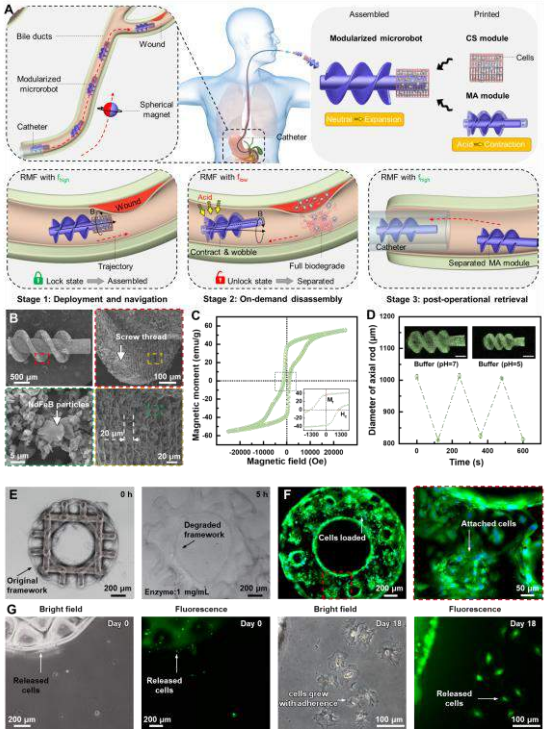

Figure 1. Modularized microrobot system. (A) Schematic of the modularized microrobot system for targeted cell delivery in Bile Duct. The system was prepared by assembling a CS module and an MA module, whose assembled state was locked and unlocked by the pH-responsive volume expansion and contraction of MA module, respectively. During the cell delivery process, the modularized microrobot was deployed by catheter to the vicinity of the lesion site and then navigated to the targeted region under the actuation of a rotating magnetic field (stage 1). Once arriving at the lesion site with acidic environment, on demand disassembly was performed by the combined application of a rotating magnetic field, contributing to the detachment of CS module for therapeutic purposes (stage 2). At stage 3, the individual MA module was retrieved by catheter under the actuation of a rotating magnetic field to minimize the potential biosafety risk. (B) Scanning Electron Microscopy images of the printed MA module. (C) Magnetic hysteresis loop of pH-responsive magnetic hydrogel for MA module doped with 33 wt% NdFeB particles. (D) The diameter variation of the MA module axial rod with the change of pH value between 7.0 and 5.0. Scale bar, 800 μm. Error bars represented the SD (n = 3). (E) SEM image of the printed CS module. (F) Fluorescence images of Mesenchymal Stem Cells (MSCs) loaded on CS module. (G) Fluorescence and optical images of the MSCs releasement from CS module after enzymatic treatment.

Acknowledgements This work is supported by the Hong Kong Research Grants Council (RGC) with project Nos. RFS2122-4S03, STG1/E-401/23-N, 14205823, 14301122, and 14300621. We also thank supports from the CUHK internal grants and the Multi-scale Medical Robotics Centre (MRC), InnoHK, at the Hong Kong Science Park.

Glucose-Powered Gated Nanomotors for Enhancing Anticancer Efficacy via Deep Drug Penetration into Tumors

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Efficient drug delivery to hard-to-reach areas such as tumors is of particular interest to improve antitumoral therapy. Due to their capacity to improve tumor reach, tumor infiltration, and tumor cell internalization, self-propelled and bio-inspired nano- and micromotors are a promising field in the biomedical sector, particularly in anticancer therapy. [1,2] Despite the advances, there are still some limitations to these new materials. The main issue is that external and toxic fuels are to generate their movement. The most used method to increase the diffusion or velocity of nanoparticles is hydrogen peroxide (H_2O_2), which is used at high concentrations.[3,4]

Herein, we describe a new versatile nanomotor capable of both self-propulsion and drug delivery for "smart" cancer therapy. It consists of a Janus-type nanoparticle with two opposing faces, a platinum (Pt) nanoparticle and a mesoporous silica nanoparticle (MSN). The MSN face acts as a container for the doxorubicin (DOXO) drug. The surface of the MSN is decorated through amide bonds with the enzyme glucose oxidase (GOx). The GOx enzyme acts as a "molecular gate" controlling the specific intracellular delivery of DOXO and as a trigger to initiate the propulsion reaction, converting the abundant glucose present in the tumor microenvironment into gluconic acid and H_2O_2. The Pt face is responsible for autonomous motion by catalytically decomposing the H_2O_2 produced by the GOx into water and oxygen (gas) (Figure 1).

The advantages of the Janus Pt-MSN (DOXO)-GOx lie in the bioavailability and non-toxicity of glucose in tumors and its geometry, enhancing their diffusive motion. The efficacy was examined in a HeLa tumor cell culture, tumor spheroids, and an in vivo mouse xenograft model. A strong anticancer effect is found and attributed to the synergistic combination glucose-induced propulsion, controlled drug delivery, elimination of glucose (by GOx) and ROS production (H_2O_2 generation by GOx). In addition, to better assess the therapeutic effectiveness of the nanomotors within a real clinical scenario, breast cancer patient-derived organoids (PDOs) were used. This serves as an ideal model due to its fibrotic nature and an immunosuppressive tumor microenvironment that hinder effective therapy.[5] The results demonstrated a high capacity for tumor infiltration and controlled DOXO release, which promoted a considerable cell viability decrease of PDOs.

Altogether, this study represents a major step in engineering nanomotors powered by endogenous fuels capable of working in vivo, and it demonstrates the potential of active particles in precise anticancer therapy toward clinical applications.

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Figures

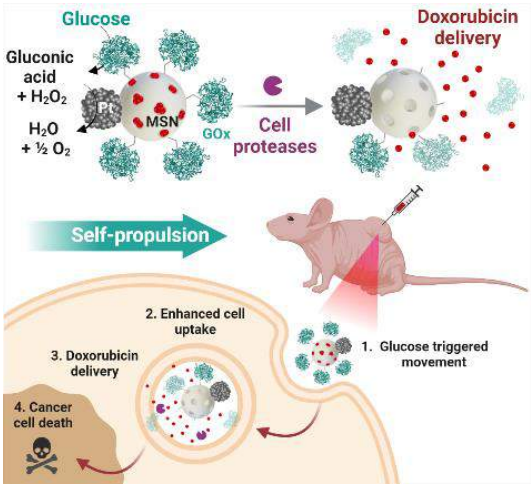

Figure 1. Illustration of the performance of the nanomotor. Step 1: Glucose induces self-propulsion via the catalytic activity of GOx and PtNds. Step 2: Nanomotors are internalized in cancer cells with subsequent doxorubicin release in response to lysosomal proteases, resulting in cancer cell elimination.

Nitric Oxide-Propelled Nanomotors Induce Pyroptosis for Cancer Therapy

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Immunologically cold tumors pose a persistent challenge in cancer therapy by evading immune surveillance and clearance, resulting in the failure of many immunotherapeutic interventions. Compared to the classical programmed cell death pathways, pyroptosis, characterized by the release of inflammatory factors, offers a promising opportunity to transform cold tumors into hot ones. Here, we present a pioneering study focusing on nitric oxide (NO)-propelled nanomotors with chemotactic motility towards the tumor microenvironment (TME). L-arginine converts to gaseous molecule NO under the oxidative TME to propel the nanomotors' movement while simultaneously causing mitochondrial damage. Remarkably, the release of mitochondrial cytochrome was followed by the activation of caspase-3, which ultimately leads to pyroptotic cell death of cancer cells. Employing a 3D tumor spheroid model, we validate the antitumor capacity of the nanomotors. Our study not only elucidates the mechanism underlying the pyroptosis induction by our nanomotor system but also highlights its promising application in cancer therapy, offering novel insights into nanomotor-driven approaches for revolutionizing cancer treatment paradigms.

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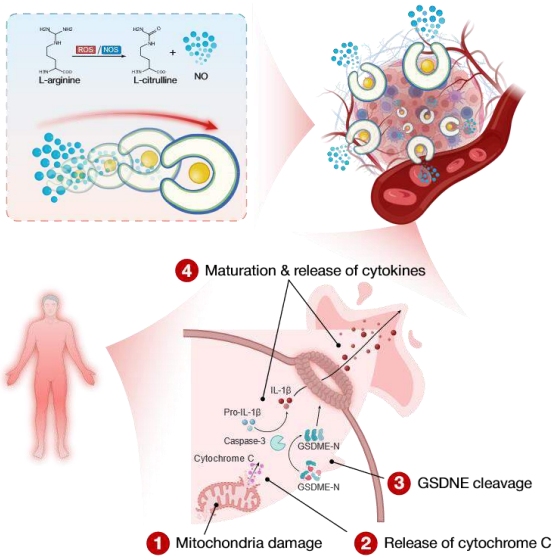

Figure 1. Nitric Oxide-Propelled Nanomotors Induce Pyroptosis for Cancer Therapy

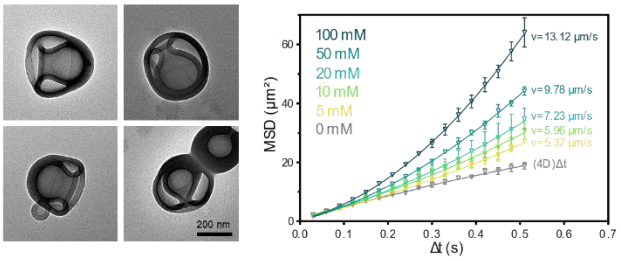

Figure 2. Morphology of the nanomotors by TEM (left) and the mean square displacement (MSD) under different concentrations of medium (right).

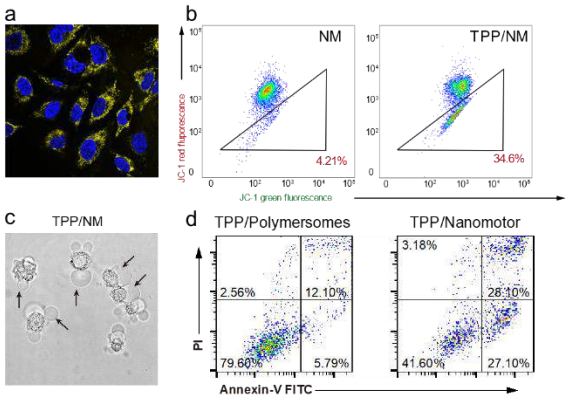

Figure 3. (a) The release of cytochrome C presented by yellow fluorescence. (b) Destruction in mitochondria membrane potential. (c) Pyroptotic cell death of Hela cells. (d) Pyroptosis of Hela cells characterized by flow cytometry.

Urease-Powered Nanobots For Radionuclide Bladder Cancer Therapy

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Enzyme-powered nanoparticles, known as nanobots, have emerged as a promising approach for performing tasks at the nanoscale, ranging from targeted drug delivery to precision medicine. Among these, urease-powered nanobots have shown improved diffusion and 3D navigation within biological environments [1] and drug delivery efficacy [2,3], compared to non-motile nanoparticles. The propulsion mechanism of these urease-powered nanobots, driven by urea (a readily available substance in the body), makes them particularly well-suited for potential applications in treating bladder cancer. Current treatments for this disease involve intravesical drug administration, which has shown good survival rates but limited therapeutic efficacy. Several factors, such as the sedimentation of therapeutic agents and the continuous addition of fresh urine, hinder the even diffusion of drugs throughout the entire bladder volume. Moreover, poor retention in the bladder and low penetration in the target site may leave certain subregions untreated, potentially leading to recurrence. To address these unresolved medical challenges, nanobots have emerged as a viable solution. In this context, our study demonstrates an enhanced accumulation of radiolabeled urease-powered nanobots within bladder tumors using an orthotopic murine model. Furthermore, we provide evidence that intravesically administered radio-iodinated nanobots exhibit a radionuclide therapeutic effect, resulting in significant tumor size reductions of approximately 90% when compared with non-treated mice [4]. These promising results firmly position nanobots as highly efficient nanosystems for bladder cancer therapy.

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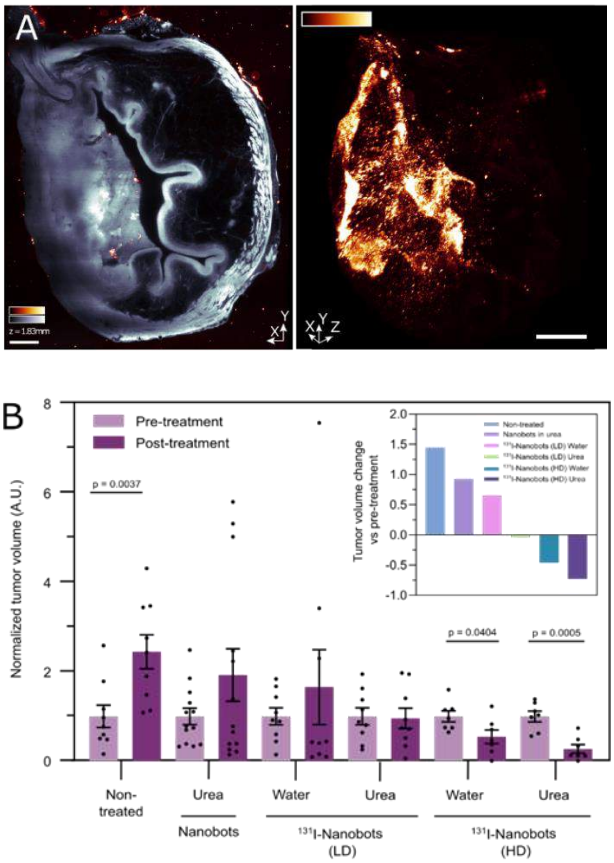

Figure 1. Nanobots penetrate and reduce bladder tumors size. A) Left: Plane in the center of the bladder showing autofluorescence (grey) and scattered light-sheet (sLS) signal. Right: Maximum intensity projection of sLS signal inside the bladder. B) Normalized tumor volume obtained by MRI pre- and post-treatment. LD denotes low dose and HD high dose of ^{131}I.

Motion manipulation of photocatalytic nanomotors induced by an external magnetic field

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Light-driven micro/nanomotors have raised considerate interests because of their superior controllable and programmable properties. Those based on photocatalytic materials can transfer both the optical and chemical energy from the photocatalytic reaction to induce the motion [1,2]. Nevertheless, simultaneous directional control for small-sized materials remains challenging, as Brownian motion randomizes the orientation [3]. To this end, combining optical forces with external fields, such as electrical, magnetic, and acoustic sources, has demonstrated to be a promising strategy for the motion manipulation of micro/nanomotors. In this work, we investigate the intricate interplay between optical and magnetic forces in actuating a rod-like TiO_2/NiFe photocatalytic nanomotors. The results indicate that under UV light illumination, the nanomotor can self-propel in a random direction; whereas under UV light + a magnetic field, the nanorod aligned with the direction of the external magnetic field, leading to a more directional trajectory. More interestingly, we also observed the promoted motion speed of nanomotors in the presence of a magnetic field. We propose that the applied magnetic field facilitates the electron transfer process on the TiO_2/NiFe nanomotors upon light irradiation and further accelerates their propulsion speed. Various techniques, such as photoluminescence, fluorescence lifetime and photoelectrochemical measurements, were used to demonstrate this improved charge separation efficiency. Additionally, by testing the photocatalytic performance of TiO_2/NiFe nanomotors for the conversion of benzene to phenol, we further validated the obtained magnetic field-induced enhancement of photoactivity.

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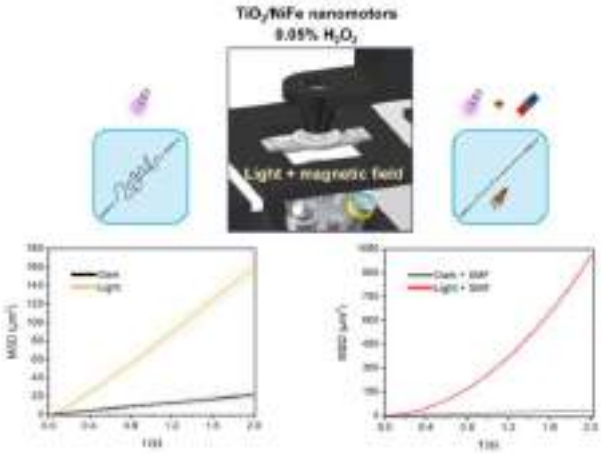

Figure 1. Enhanced motion efficiency of light-driven TiO_2/NiFe nanomotors in the presence of a magnetic field.

Ultrafast Light-activated Polymeric Nanomotors

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Synthetic micro/nanomotors have been extensively exploited over the past decade to achieve active transportation. This interest is a result of their broad range of potential applications, from environmental remediation to nanomedicine. Nevertheless, it still remains a challenge to build a fast-moving biodegradable polymeric nanomotor. Here we present a light-propelled nanomotor by introducing gold nanoparticles (Au NP) onto biodegradable bowl-shaped polymersomes (stomatocytes) via electrostatic and hydrogen bond interactions. These biodegradable nanomotors showed controllable motion and remarkable velocities of up to 125 µm s-1. This unique behavior was explained via a thorough three-dimensional characterization of the nanomotor, particularly the size and the spatial distribution of Au NP, with cryogenic transmission electron microscopy (cryo-TEM) and cryo-electron tomography (cryo-ET). Our in-depth quantitative 3D analysis revealed that the motile features of these nanomotors were caused by the nonuniform distribution of Au NPs on the outer surface of the stomatocyte along the z-axial direction. Their excellent motile features were exploited for active cargo delivery into living cells. This study provides a new approach to develop robust, biodegradable soft nanomotors with application potential in biomedicine.

Figures

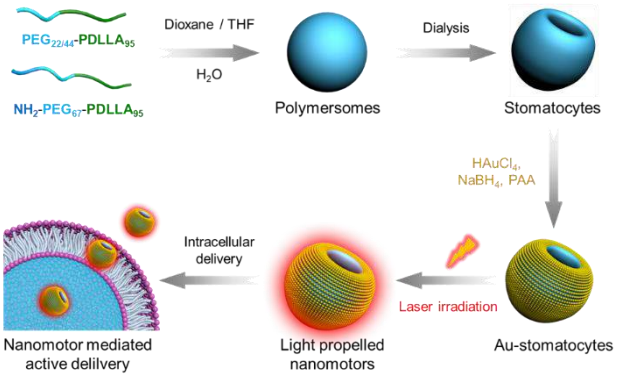

Figure 1. Schematic illustration of the preparation of light-propelled biodegradable stomatocyte nanomotors for efficient intracellular transport.

Micropumps and Micromotors from Smart Ionogels of Light-triggered Release

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Chemical micropumps drive fluid motion by creating localised chemical gradients through chemical reactions or chemical diffusion on the surface of colloids and the consequential self-generated electric field, which produces electrophoresis and electroosmosis[1]. When the symmetry of these gradients at the colloids surface is broken, the micropump transform into a self-propelled micro-motor. Chemical micropumps and motors that release substances on their own, rather than relying on chemical reactions, show clear advantages, especially in micro-environments requiring delicate manipulation, because they are not limited to specific types of chemical reactions and a wide range of chemicals with different diffusion rates and significant density differences, and they avoid violent bubble disturbances caused by chemical reactions in the system. However, several technical challenges remain, in particular the fact that colloidal micropumps and motors often lack non-invasive remote control mechanisms. Materials such as ion exchange resin microspheres, ZnO, MgO, CaCO3 and MOF microspheres, PVA and PNIPAM temperature-sensitive hydrogels lack effective control over their release in water. Although the positive action of light as an external energy source allows remote start or stop and avoids direct contact with the system, thus offering the possibility of flexible adjustment of pumping behaviour and range, these techniques usually require special activation mechanisms or the use of potentially hazardous substances. Therefore, the development of micropumps and motors with controlled release of substances by light in aqueous environments, with adjustable operating range and without the need for additional fuel, is of great importance for the advancement of the field, helping to broaden the application scenarios and increase their usefulness in a variety of micro-operations and precision control tasks. In this study, a new ionic liquid polymer with azobenzene structure, called "colloidal ionogel" microspheres, was successfully designed and synthesised with UV/visible light response and reversible release of ionic liquids, thus triggering diffusio-phoresis and diffusio-osmosis for effective fluid pumping. The light response is extremely sensitive, with response times of milliseconds, continuous pumping for more than 20 minutes for a single micropump, and a controlled range by adjusting the light intensity. When the symmetry of the ion gradient around the ionogels is broken, they exhibit self-propulsion, releasing ionic liquid without external fuel. This research provides a practical approach for the development of light-controlled drug release micropumps and motors, which can be extended in the future to release different functional drugs, which is crucial for the further design and production of stimulus-responsive, communicative colloidal materials to cope with environmental changes.

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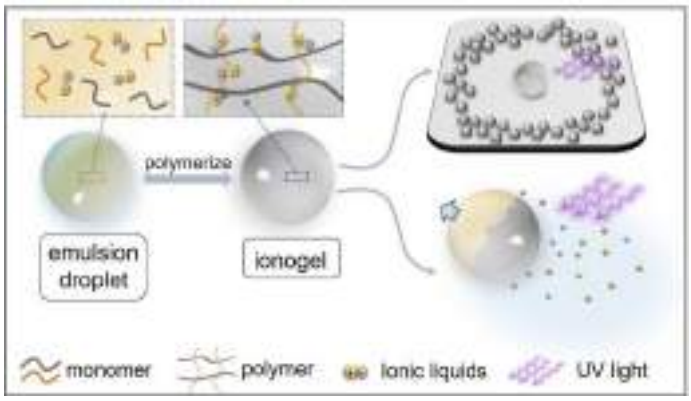

Figure 1. Construction of Intelligent light-actuated ionogel micropump and micromotor.

Transition Metal Dichalcogenides Meet Light-Driven Nanomotors

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Transition metal dichalcogenides (TMD) are 2D layered semiconductors with a MX_2 structure, where M is a transition metal and X is a chalcogen atom. Materials from the TMD group possess unique properties compared to those of other 2D materials, such as graphene, that can be exploited both for propulsion and advanced applications.

Notably, when nanostructured TMD-based microflakes are irradiated at a suitable wavelength, a fast collective motion is noted with record speeds up to 6000 µm s^{-1}. This process was studied both through experimental evidence and simulations, attributing this fast motion to a thermal phenomenon commonly described as photophoresis.[1]

Not only were impressive light-induced speeds recorded, but also due to the intrinsic properties of TMD, relevant applications were explored.

Due to the photocatalytic activity of TMD, reactive oxygen species (ROS) were employed to remove bacterial biofilms with an efficiency up to 87%.[2] Gold nanoparticles were also synthesized *in-situ* on the micromotors' surface (AuNPs@MoS_2) to generate smart surface-enhanced Raman spectroscopy (SERS) substrates. The smart light-driven SERS substrates can harvest and accumulate target analytes, increasing the SERS signal up to 18 times.[3] Finally, MoS_2@Fe_3O_4 composites were synthesized through a hydrothermal method to obtain hybrid magnetic/light-driven micromotors. Subsequently, MoS_2@Fe_3O_4-based motors were used for the degradation and removal of microplastics in contaminated water samples. [4]

Overall, TMDs exhibit exceptional potential as functional materials for advanced applications in light-driven micromotors, owing to their unique combination of photophoretic, photocatalytic, and photothermal properties. In light of this, the versatility of TMD-based micromotors allows for customization through various synthesis methods or modification with organic molecules and inorganic nanoparticles, tailoring the micromotors to meet the specific requirements of each application.

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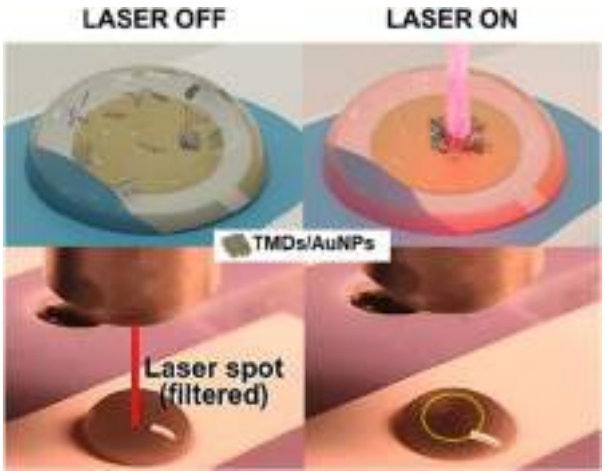

Figure 1. Light-induced harvesting and accumulation of analytes for SERS-readout using AuNPs@MoS_2 micromotors. Schematic representation (top) and images of an experimental setup (bottom).

Photoactive Ru-based polymeric colloidal system for non-equilibrium assembly and micromotors

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Abstract
Autonomous colloidal micromotors, also known as microrobots or micromachines, are specially designed devices at the nano/micro scale capable of converting various forms of energy into mechanical motion.[1] An ideal micromachine integrates actuation, power source, sensing, and other complex functions into a single body.[1,2] Recent efforts have been focused on developing these micromotors with the vision that they could revolutionize biomedical treatments for life-threatening diseases and environmental remediation.[3] In general, In general, micro/nanomotors can harness a variety of energy sources, such as chemical reactions, electric fields, magnetic fields, acoustic waves, and optical forces.[4] Compared to other energy sources, light presents greater sustainability and precise ON/OFF switching for motion control in micromotors. It offers enhanced versatility by allowing easy modulation of intensity, direction, wavelength, and polarization.[5] Moreover, these photoactive micromotors may also open new opportunities for the realization of photochemical reactions upon excitation with visible light turning light energy into chemical energy while moving in organic solvents. Considering the current challenges and future promises of such minuscule devices *i.e.,* drilling, stirring, dragging, and delivering cargos, the single electron transfer photocatalyst holds the potential to unlock unimaginable capabilities beyond their already intriguing intrinsic features. For instance, Ru-based complex, such as $Ru(bpy)_3^{2+}$, with an excited state reduction potential of E ½ III/*II= -0.81 V vs SCE and oxidation potential of E ½ *II/I= + 0.77 V vs SCE, fluorescence emission activity at 615 nm and long lifetime (1100 ns),[6] offer interesting properties for designing novel organic-based micromotors.

In this work, we present polymeric micromotors based on a **$Ru(bpy)_3^{2+}$ complex** fabricated in one pot synthesis. The as-developed colloids are fluorescent and demonstrate the visible light controlled dynamic assemblies in hydroquninone (H2Q) and benzoquninone (Q) aqueous medium. A variety of Janus **$Ru(bpy)_3^{2+}$** micromotors were fabricated by coating them with noble metals, such as Pt and Au, and semiconductors (TiO_2). Depending on the redox band potentials of each system, different motion speeds were observed as well as motion dynamics. Therefore, this work contributes to expand the applicability of photoactive colloidal systems in organic synthesis by providing a fundamental understanding of their design.

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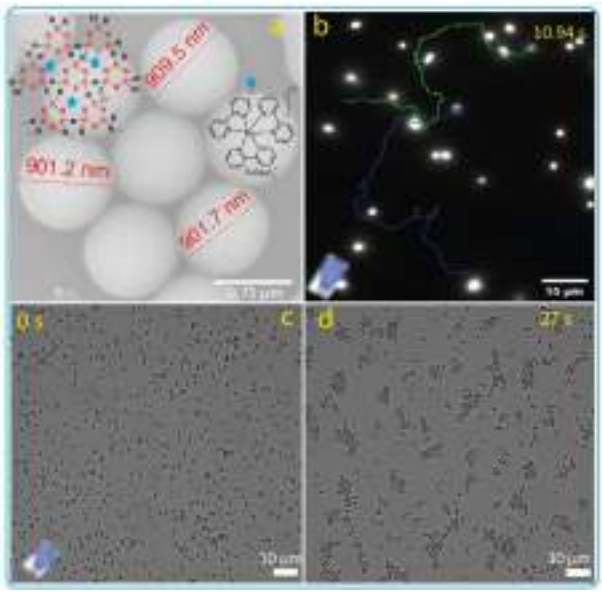

Figure 1. $Ru(bpy)_3^{2+}$ integrated cyclomatrix polyphsopahzene colloidal system. ESEM image of the as synthesized colloids (a). Tracking trajectories of the micromotors under light irradiation (b) and non-equilibrium assemblies (c, d) in hydroquinone and benzoquinone in blue light.

How spontaneous curvature induces the morphogenesis of dendrimersome vesicles?

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The vital functions of cell membranes require their ability to quickly change shape to perform complex tasks such as motion, division, endocytosis, and apoptosis. Membrane curvature in cells is modulated by a very complex processes such as changes in lipid composition, the oligomerization of curvature-scaffolding proteins and the reversible insertion of protein regions that act like wedges in the membrane. But, could much simpler mechanisms support membrane shape transformation? In this talk, I will discuss how the change of the amphiphile topology (shape) in the bilayer can drive morphogenesis of cell membrane models. [1] To tackle this, we have designed and synthesized new type of amphiphiles —Janus dendrimers— that self-assemble into uni- or multilamellar vesicles. [1,2,3,4, 5] Although these molecules do not exist in nature, the vesicles formed closely mimic the thickness, flexibility, lateral 2D organization of cell membranes. [1,2,3,4, 5] These properties are precisely encoded in the chemical structure, architecture, and topology of the macromolecular building blocks of the membrane. For these studies, we synthesized Janus dendrimers containing a photo-labile bond that upon UV-irradiation cleave losing part of the hydrophilic Dendron. This leads to a change from cylindrical to the wedge-shape of the amphiphile. The high lateral mobility of these dendrimers allows for the concentration of the wedge-shaped amphiphile and the generation of local spontaneous curvature. The concentration of the wedges and their rate of segregation allowed controlling the budding and generation of structures such as tubules, star-fish, and high genus vesicles. Our findings shed light on the fundamental principles governing membrane shape dynamics, offering insights into potential applications in biotechnology and medicine.

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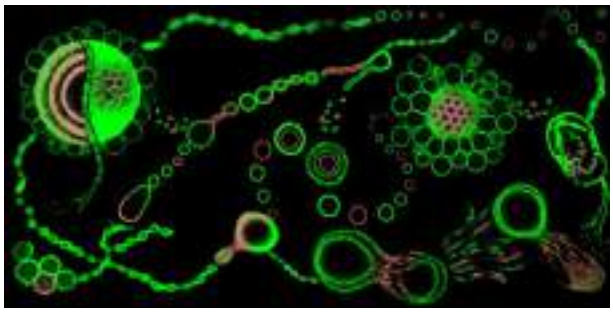

Figure 1. Using cell-mimetic dendrimersomes we demonstrated how changes in the molecular topology of amphiphilic Janus dendrimers forming the bilayer lead to the evolution of shape without the need for any active cellular machinery.

The minimal chemotactic cell

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The capacity of cells to perceive and react to chemical signals in their surroundings is vital for their survival and adaptability, making chemotaxis a decisive phenomenon in evolution. Our investigation explored the essential elements required for observing chemotaxis within a protocell model. This model comprised a liposome with an encapsulated enzyme and a transmembrane protein, specifically α-hemolysin. By employing this setup, we simplified the fundamental constituents of a cell to their bare minimum: the compartmentalization of a chemical reaction within a lipidic bilayer membrane. The α-hemolysin assembles into a heptametric pore within the liposome membrane, facilitating the transport of substrate and products into and out of the liposome. Consequently, when a liposome containing an encapsulated enzyme is situated in an environment with the corresponding substrate, an asymmetrical distribution of products emerges along its surface, promoting active motion.

Our focus extended to examining the motion of liposomes encapsulating glucose oxidase and urease, exposed to glucose and urea concentration gradients, respectively. The drift velocities were obtained by tracking single liposomes in a microfluidic device (μ-slide chemotaxis Ibidi) using a Confocal microscope. Parallel experiments, tracking polystyrene beads with diverse surface chemistries, allowed us to assess fluid flows induced by the concentration gradient in the microfluidic device. Observations revealed that high-concentration gradients induced advective flows, while low-concentration gradients led to flows induced by diffusion osmosis. The direction of diffusioosmotic flows depends on the interaction potential between the solute and the channel walls; glucose exhibited a positive interaction potential, while urea displayed a negative potential. The concentration gradient was limited to the range with no advective flows to track liposomes accurately.

The liposome drift results from diffusioosmophoresis and chemotaxis. The chemotactic component is absent for liposomes with no pores, as there is no asymmetry in the system. Liposomes lacking pores, encapsulating glucose oxidase, and urease showed a drift towards low substrate concentration, explained by diffusioosmophoresis. Introducing pores resulted in a diminished velocity drift towards lower concentrations, implying in positive chemotaxis component. Notably, liposomes encapsulating urease with an α-hemolysin-to-lipids ratio of 0.5 (by mass) exhibited a reversal of drift toward higher urea concentrations.

Our minimal chemotactic cell model showcased the achievement of chemotaxis by simply incorporating an enzyme and a transmembrane protein into liposomes. Furthermore, the chemotactic component showed an increase, corresponding to the increased concentration of α-hemolysin.

Collective Self-Caging Of Active Filaments In Virtual Confinement

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Filamentous cyanobacteria, ancient and prolific phototrophic prokaryotes, significantly contribute to atmospheric carbon fixation via photosynthesis. Their gliding motility, coupled with photophobic responses to light intensity gradients, drives accumulation in favorable light conditions. Our study unveils an intriguing aspect of photosensitivity: the formation of intricate super-filamentous aggregates with collective mechanical capabilities at boundaries of illuminated regions. We investigate the influence of light pattern, especially boundary curvature, on this aggregation process using an agent-based model for active, flexible filaments. While the ecological benefits remain uncertain, this behavior may empower colonies to regulate light exposure and achieve macroscopic movements [1].

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Figures

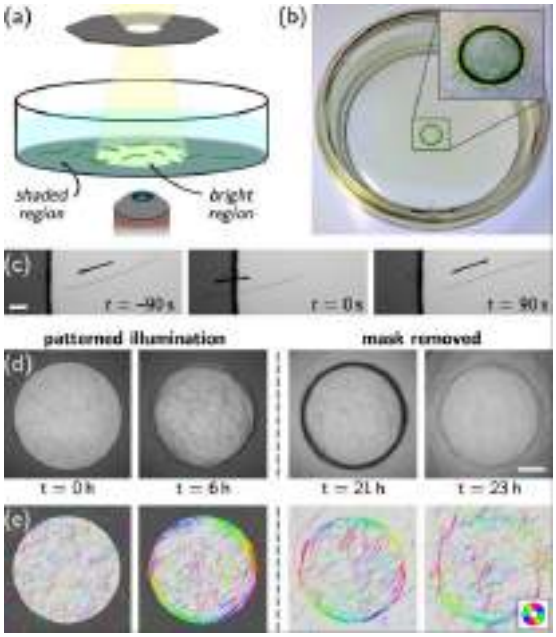

Figure 1. **Aggregation of filamentous cyanobacteria at light boundaries.** (a) Schematic of the experimental setup. Filaments glide at the bottom of a Petri dish, submersed in culture medium and illuminated from above with a pattern generated by the mask. (b) Macroscopic view of a ring structure of *O. lutea* that formed at the edge of a circular light patch (dashed yellow line), far from any physical boundary. The diameter of the Petri dish is 35 mm. (c) Scotophobic response of *O. lutea* when gliding into the dark, scale bar is 100 μm. (d) Formation (t = 0 h to 21 h) and dissolution (t = 21 h to 23 h) of the ring after removing the mask at t = 21 h, scale bar is 1 mm. (e) Numerical simulations of active filaments replicate the experimental observations from (d). The color wheel indicates the nematic orientation of individual filaments

Mechanisms of self-propulsion of catalytic Janus particles for cell-inspired microrobots

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Janus particles are structures, in most cases spherical, with two sides, each endowed with a different nature in such a way that their behavior in the presence of certain physico-chemical conditions is anisotropic space-wise. In the case of catalytic Janus particles, different parts of the particle participate differently to a chemical reaction, and relying on this asymmetry it is possible to generate motion [1]. Based on a widespread design, our Janus particles have an inert side and a metallic, catalytic side. The latter can decompose hydrogen peroxide (H_2O_2) to water and oxygen, and this localized decomposition reaction generates the motion of the particle. We are loading populations of these self-propelled particles into lipidic vesicles, where their individual and collective behaviors can change due to confinement and to the particle-particle and particle-membrane interactions [2]. Our aim is to leverage on these interactions and collective behaviors to realize cell-inspired microrobot that exploits swarms of self-propelled Janus particles as motors for the deformation and locomotion of the whole structure (Figure 1).

In the field of self-propelled catalytic Janus particles, platinum (Pt) is the most used metal as the catalytically active side. On the other hand, very few works have investigated palladium (Pd) as the metal catalyst for self-propelled particles, despite it is known to have similar physio-chemical and thus catalytic properties. Aiming at building a library of active particles with potentially different self-propulsions and interactions to be used in the development of our cell-inspired microrobots, we have realized both Pt- and Pd-based catalytic Janus particles and started to study and compare their activity.

We proceeded by producing monolayers of inert particles (silica or polystyrene) on glass, and then sputtering them with Pt or Pd in a magnetron-sputtering machine. After the lift-off in water, the motion of the particles was investigated through direct observation of the sample under an optical microscope in the presence of H_2O_2, followed by tracking and mean square displacement (MSD) calculation [3]. By comparing the behaviors of analogously produced Pt and Pd Janus particles, we found a substantial difference in terms of activity: while Pt particles self-propel as expected, Pd particles do not self-propel at all. Whereas we could expect a quantitative difference in the self-propulsion speed, such a stark qualitative difference was unexpected, especially considering that the decomposition of H_2O_2 is clearly taking place on Pd Janus particles too.

We have therefore resolved to elucidate the principles by which Janus particles with a Pt catalyst do propel, and to investigate and compare the corresponding behavior of Pd and Pd-based Janus particles (Figure 2).

Lyu *et al*. [4] observed that, due to the fabrication method, the metallic cap of Pt Janus particles has a different thickness at the equator and at the pole of the sphere and hypothesized that this induces a peculiar electrochemical behavior that generates electric fields and electrophoretic fluxes around the particle that sum up with the diffusiophoretic fluxes, substantially enhancing the self-propulsion speed of the particles. We thus aimed at reproducing their results with Pt, while also addressing the following questions regarding Pd: how does the oxygen evolution on Pd compare to that on Pt? Can Pd generate electrophoretic fluxes in presence of a thickness gradient, and how do they compare with those generated by Pt?

To address these questions, we compared Pt and Pd behavior in specific experimental conditions. The oxygen evolution rate of two continuous layers made of the two metals was compared collecting the volume of gas developed on them at specific time intervals. Pd showed the need of a higher H_2O_2 concentration to start producing oxygen constantly, as for concentrations lower than 20% v/v the oxygen bubbles were stuck on the metallic surface poisoning its catalytic activity. Although the oxygen generation could proceed differently on the particles surface, as no oxygen bubbles are formed, compared to the flat samples, where oxygen bubbles remain stuck on the surface preventing the reaction to keep going, the difference in oxygen evolution between the two metals suggests that the Pd-based particles should be slower than the Pt ones, at least in terms of self-diffusiophoresis.

For what concerns the electrochemical activity, three samples were realized for each metal on ITO electrodes: two metallic layers of the same thickness (40 nm) and a third thinner one (15 nm). They were coupled in an electrolytic solution and the current flowing between them was measured to corroborate the hypothesis of Lyu *et al*. [4]. As expected, the current flowing between analogous electrodes was very low, as being almost identical they are not able to delocalize the two semi-reactions of decomposition that generates the protons-electrons gradient. Instead, an opposite response was observed for the two metals when coupling thin and thick electrodes, suggesting that the electric field is pointing in the opposite direction in the case of Pd compared to Pt. On the Janus particles, this could result in electrophoretic fluxes that counteract, instead of enhancing, the diffusiophoretic ones.

Although further investigation is needed to assess these hypotheses, our observations could help to explain the reasons leading to a non-detectable motion of Pd Janus particles and further support the self-electrophoretic behavior of Pt Janus particles.

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This work has been supported by the European Research Council under Grant Agreement No. 948590, project "CELLOIDS".

Figures

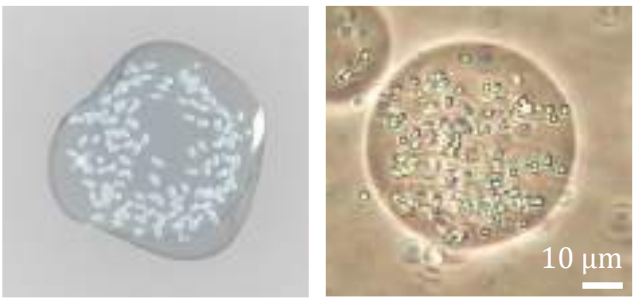

Figure 1. Sketch of the cell-inspired microrobot (left) and a phase-contrast microscopy image of an actual lipidic membrane encapsulating Janus microparticles (right).

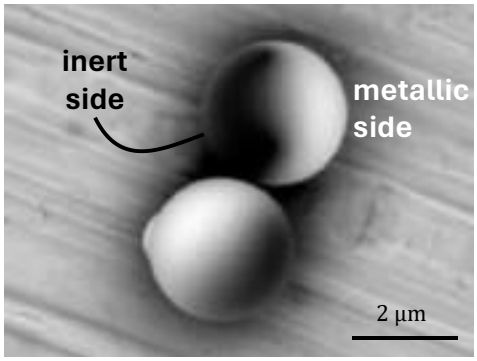

Figure 2. SEM image of the Janus microparticles.

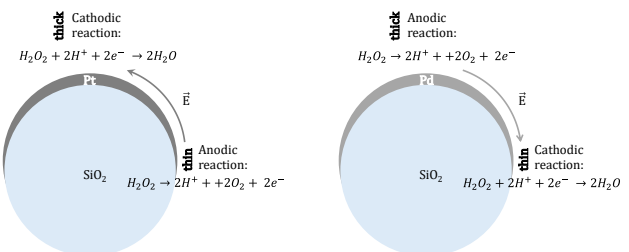

Figure 3. Envisaged mechanism for the hydrogen peroxide decomposition reaction at the particle surface. Left: mechanism for Pt, as reported in [4]; right: our hypothesis of analogous mechanism for Pd.

PROGRAMME

WEDNESDAY, JUNE 5

09:00	Registration	
09:30	*Parallel session 7* *Room: AGORA* ***Control 2*** *Chair:* *Anna Bakenecker, Fraunhofer Research Institution for Individualized and Cell-Based Medical Engineering*	*Parallel session 8* *Room: TAU* ***Biosensing and environmental applications*** *Chair:* *Alberto Escarpa, Universidad de Alcalá & Chemical Research Institute "Andres M. del Rio"*
	Magnetic-enzymatic nanomotors depicting a collective swarming behavior and directional navigation abilities, **Anna Bakenecker,** *Fraunhofer Research Institution for Individualized and Cell-Based Medical Engineering*	Micromotors for smart bioassays: towards disruptive diagnosis. **Alberto Escarpa,** *Universidad de Alcalá & Chemical Research Institute "Andres M. del Rio"*
09:45	Magnetically Induced Thermal Effects For A Programmed Disassembly Of Protein Cages On Nanocomposites With Magnetotactic Behavior **Verónica Salgueiriño,** *CINBIO, Universidade de Vigo, Spain*	Engineering light-driven micro-nanomotors for on-demand and local pH sensing applications **Dhruv Pratap Singh,** *Department of Physics, IIT Bhilai, India*

10:00	Chemical Micromotors Move Faster at Oil-Water Interfaces **Jiayu Liu,** *Harbin Institute of Technology (Shenzhen), China*	Fighting Bacteria With Micromotors **Beatriz Jurado,** *Universidad de Alcala, Spain*
10:15	Nanorod-colloid propellers: from bidirectional transport to energetic efficiency **Pietro Tierno,** *University of Barcelona, Spain*	COFBOTs: Covalent Organic Framework-Based Microrobots for Versatile Biomedical and Environmental Applications **Andrea Veciana,** *Institute of Robotics and Intelligent Systems ETH Zurich, Switzerland*
10:30	Ultrasound-powered micro- and nanorobots **Amirreza Aghakhani,** *University of Stuttgart, Germany*	CoffeeBots: Magnetic Coffee Ground-Based Micromotors for Water Treatment **Jeffrey Moran,** *George Mason University, USA*
10:45	Built-In Metal Organic Frameworks Into Tubular Micromotors With Multiple Propulsion Modes **Enrique Solano Rodríguez,** *Universidad de Alcala, Spain*	Towards Efficient Environmental Remediation: Light-Driven Hybrid Nano/Microrobots for Emerging Pollutant Degradation **Bahareh Khezri,**

		Institute of Chemical Research of Catalonia (ICIQ-CERCA), Spain
11:00	*Coffee Break*	
11:30	Keynote Speaker: Nanomotors as active matter: a reflection on the conceptual developments **Ramin Golestanian,** *Max Planck Institute for Dynamics and Self-Organization, Germany*	
12:00	Invited talk: Colloidal Metamachines **Jeremy Palacci,** *Institute of Science and Technology, Austria*	
12:20	Invited talk: Utilizing Sperm as Vectors for Gynaecological Cancer Treatment **Mariana Medina**, *CIC Nanogune, Spain*	
12:40	Invited talk: Microfluidic tools for the bioinspired synthesis of artificial functional materials **Josep Puigmartí**, *University of Barcelona, Barcelona, Spain*	
13:00	*Lunch Break*	

14:00	Keynote talk: Electric Robotization from nanoscale to decimeters: Innovation Through Science-Driven Design **Emma Fan**, *University of Texas, USA*
14:30	Invited talk: Phagocytic synthetic cells: non-living predators to fight bacteria **César Rodriguez**, *Institute for Bioengineering of Catalonia (IBEC), Spain*
14:50	Invited talk: Synthetic DNA-based swimmers: harnessing programmable molecular patterning to control motion dynamics **Tania Patiño**, *Eindhoven University of Technology, Eindhoven, The Netherlands*
15:10	Invited talk: Emerging morphologies and effective interactions in active colloids **Ignacio Pagonabarraga**, *University of Barcelona, Spain*
15:30	*Coffee Break*
16:00	Keynote talk: Engineering with biomolecular motors **Henry Hess**, *Columbia University, New York, USA*
16:30	Awards Ceremony
16:50	Concluding remarks

KEYNOTE LECTURES
INVITED LECTURES

Nanomotors as active matter: a reflection on the conceptual developments

Ramin Golestanian[1,2]
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My talk will be composed of two parts. In the first part, I will reflect on some of the developments in the past twenty years in the field of chemical nanomotors, highlighting the conceptual developments and some of my personal experiences. In the second part, I will discuss some of the more recent developments on non-reciprocal active matter across the scales.

Before working on nanomotors, I had two major fascinations. The first one, which formed my PhD work, was on a topic called dynamical Casimir effect, which was effectively concerned with how one can exchange energy and forces between conducting bodies that move or change shape and the quantum electromagnetic vacuum that constantly undergoes fluctuations [1]. I remember that at some point I developed a design for a flying carpet in quantum vacuum, and at a moment of tactlessness I told someone at NASA about the idea. When I received a call from them on my office phone at the (Kavli) Institute for Theoretical Physics at UCSB in the summer of 1999 where I was a postdoc, I was obliged to put in numbers in the equations to check if the idea was feasible, and was embarrassed by how small the effect was. My second fascination was about electrolytes and polyelectrolytes with strong correlation effects, such as like-charge attraction, which was at the time being studied intensely, but only under equilibrium conditions. The next natural step for me was to combine these two perspectives and study electrolytes in non-equilibrium conditions. This was a hard topic to make any reasonable progress in, especially if one was concerned with conceptual developments and aimed at making analytical calculations. While I was frustrated and stagnated with these developments, I spent some time in Paris during the years 2000-2002, where I learned about two things: hydrodynamics at low Reynolds number, which was fascinatingly similar to electrostatics at a formal level, and molecular motors, which at a conceptual level were operating in a similar fashion to the problems concerning how one can extract work from fluctuating vacuum. It was at this time that I felt I had all the ingredients that I needed to start working on models of artificial motors and swimmers at the nanoscale. Our first paper on this topic was the introduction of the simple three-sphere model of a micro- or nano-swimmer in 2004 [2], which was widely popularized in the media as a possible conceptual starting point of the “fantastic voyage” dream. Our next contribution was the development of a model that uses catalytic activity for a direct conversion of chemical energy into mechanical work, using self-diffusiophoresis which is a force-free transport mechanism [3], its subsequent experimental realization as well as theoretical and mechanistic characterization [4,5], and systematic extension of the model towards a comprehensive understanding of the collective behaviour of many such active particles.

More recently, I have been fascinated by the possibilities provided – both conceptual and practical – by non-reciprocal active matter. Broken action-reaction symmetry has been recently explored in active matter in the context of nonequilibrium phoretic interactions between catalytically active colloids and enzymes [6], and hydrodynamic interactions [7,8], among others. It has been shown to lead formation of self-propelled active molecules that break time-reversal symmetry [9], oscillating active complexes that break time-translation symmetry [10], chiral bound-states [11], and active phase separation with specified stoichiometry [12,13,14]. Non-reciprocal interactions have been found to lead to rich physical phenomena involving various forms of spontaneous symmetry-breaking in other related nonequilibrium contexts [15,16]. Recent applications of non-reciprocal active matter have revealed exotic behaviour such as the appearance of effervescent travelling patterns [17] and shape-shifting multifarious self-organization [18], spontaneous escape of kinetic barriers [19], dynamical pattern formation in quorum-sensing active matter [20], as well as implications of the physics of non-reciprocal interactions on the origin of life [21,22,23].

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Colloidal Metamachines

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We take inspiration from nature, whereby an "Organism, or natural Machine, [is] a machine in which each part is a machine" [Leibniz] to devise functional and autonomous machines at the microscale. Metamachines, as machines made of machines, translate this concept from the biological real towards engineering joining approaches of colloidal assembly and active matter.

We will present an experimental approach leveraging optical and active forces to design and template colloidal Metamachines, as machines built from active colloids. We will show how our approach allows to obtain a library of autonomous micromachines with programmable dynamics [1, 2]. In particular, we will investigate an active polymer, which static and dynamical properties are controlled by non-equilibrium interactions [3].

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Figures

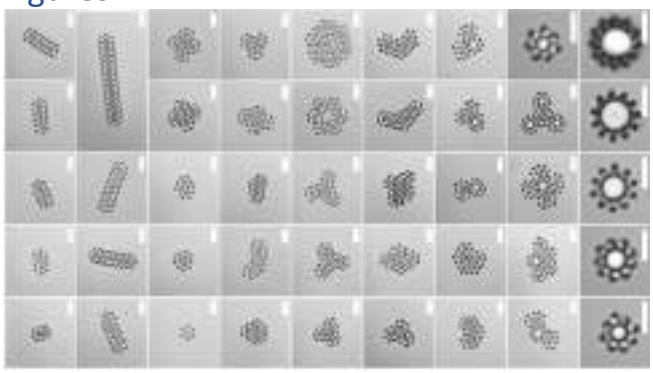

Figure 1. Examples of Colloidal Metamachines (all scale bars are 5µm)

Utilizing Sperm as Vectors for Gynaecological Cancer Treatment

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Sperm are motile gametes capable of traversing the gynecological tract from the uterine cavity to the ampulla site of the fallopian tube. Due to their high motility, and non-proliferative nature, sperm have shown promise as biocompatible carriers for therapeutic substances in the treatment of gynecological cancers. In this talk, I will highlight our contributions, focusing on the use of various sperm-microstructure configurations and different sperm species to locally deliver anticancer drugs and tumor microenvironment regulators. These approaches aim to target solid tumors, modify the tumor microenvironment, and enhance drug diffusion and efficacy. While most results are from in vitro models of cervical and ovarian cancers, advancements in controlling therapeutic drug delivery with sperm swarms and imaging techniques such as ultrasound and photoacoustics suggest promising potential for their future in vivo implementation.

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Figure

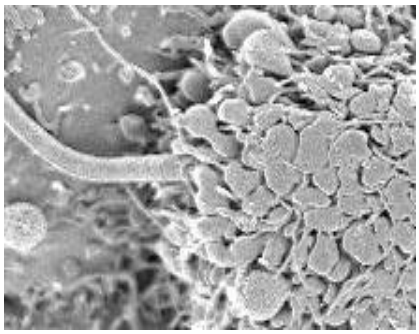

Figure 1. Sperm cells fuse with cancer cells, delivering Doxorubicin at the sub-cellular level. Apoptotic bodies are commonly observed on the surface of the cells.

Microfluidic tools for the bioinspired synthesis of artificial functional materials

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The incorporation of both covalent and non-covalent interactions has been pivotal in crafting artificial functional materials capable of mimicking the properties and functions observed in natural counterparts. Similar to nature, achieving precise control over the positioning of functional artificial building blocks holds the key to establishing rationalized structure-property correlations, a longstanding pursuit in the realms of chemistry, physics, and materials science. Despite its potential, understanding the pathways and mechanisms governing the formation of artificial functional materials remains a formidable challenge. To advance the engineering of artificial functional materials, it is crucial to understand the complexities of their nucleation and growth mechanisms, which can ultimately lead to the realization of nature-inspired functions. This presentation will highlight the innovative use of microfluidic devices to replicate reaction conditions found in nature. I will show that microfluidic approaches not only unravel the complexity of crystallization pathways but also enable the manipulation of pathway selection.

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Electric Robotization from nanoscale to decimeters: Innovation Through Science-Driven Design

D. Emma Fan[1,2,3], Huaizhi Li[1], Zexi Liang[1], and Xianfu Luo[1]
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In this talk, I will discuss our recent innovations in robotic devices and systems enabled by exploring the rich science of electric-materials-water interaction controlled across a wide range of length scales. At the nanoscale, I will discuss 3D electrokinetic tweezers, an ultra-precision tool invented in my lab, which can be used to manipulate nanowires with a precision of 20 nm in position and 0.5° in 3D orientation in solution under a standard microscope. With this technique, designed nanostructures are maneuvered as untethered probes for detecting metabolites from single bacterial cells. At the chip scale, I will describe a novel optoelectric mechanism that permits unparalleled capability in dynamically patterning micromotor swarms with accurate modal, spatial, and temporal control. At the decimeter scale, I will show a novel device scheme and the associated material design that can expand the 2D local electric effect into 3D long-range interaction for bottle-sized water disinfection, which practically brings heavily polluted water from Waller Creek at UT-Austin to a drinkable level.

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Figures

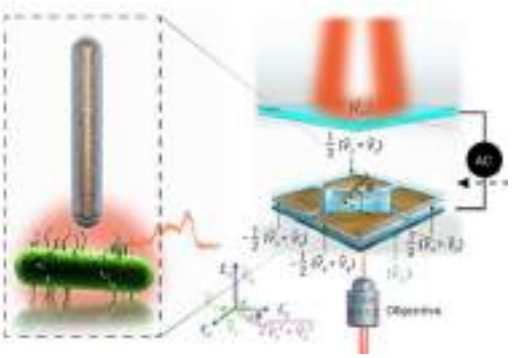

Figure 1. Nanoscale: 3D electrokinetic tweezers manipulate nanostructures as untethered tools for programmable single cell probing. The precision reaches 20 nm in position and 0.5° in 3D orientation in solution under a standard microscope (patent application No. 63/498,247, 2023).

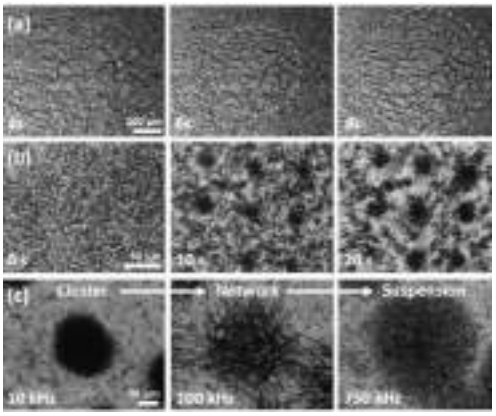

Figure 2. Chip-scale: novel optoelectric mechanism for dynamic patterning and mode-switching of micromotor swarms. (a-b) Semiconductor micromotor swarms instantly pattern according to light and (c) switch between multiple operation modes by actively tuning the ratio of electrostatic attraction and electrorotation in high-frequency asynchronous rotating electric fields.

Figure 3. Decimeter Scale: Portable, bottle-sized water disinfection via electrically capturing live bacteria with highly branched graphite foams—bringing heavily pathogen-polluted water from Waller Creek at UT-Austin to drinkable level (patent application #63/548,533, 2023).

Phagocytic synthetic cells: non-living predators to fight bacteria

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I will introduce Phagocytic Synthetic Cells (PSCs) that recognize, capture, engulf and kill antibiotic-resistant bacteria without generating selection pressure for resistance recapitulating the most salient steps of phagocytosis.[1] The PSCs are synthetic vesicles that can selectively bind to bacteria and exploit the binding energy to drive engulfment. From a thermodynamic point any vesicle can engulf a bacterium if the adhesive energy surpasses the bending energy of vesicle's membrane. However, the high curvature intermediates present during engulfment have prevented the use of the state-of-the-art vesicles for this task. We invented a new family of biomimetic vesicles, called i-combisomes that, despite having the same flexibility of superflexible liposomes, exhibited unsurpassed ability to quantitatively engulf nano- and micro-objects including bacteria which they killed upon engulfment.[2] This superpredatory behavior is rooted in the statistic nature of the molecular topology of their building blocks, ionically-linked comb polymers. When assembled in water, their collective behavior follows a mean-field description, smearing the heterogeneity by forcing molecules with non-zero spontaneous curvature into a flat membrane acquiring a strained conformation, with the concomitant local-mean curvature mismatch. When engulfment begins, these molecules migrate to the non-zero curvature regions and adopt their more favorable conformation, therefore reducing the kinetic barriers, a trait that membranes assembled from a single low molecular weight amphiphile cannot achieve. By the same token, few minutes after engulfment of an antibiotic-resistant bacterium, the close apposition of the phagosome and bacterial membranes resulted in their fusion and the death inside the i-combisome. The remarkable element of this concept is that the killing occurs inside the PSCs, separated from the environment and because it targets a highly conserved element of the pathogen, its membrane, the killing action cannot be avoided by evolution. Remarkable, the PSCs could be engineered to be safe for eukaryotic cells and human organoids.

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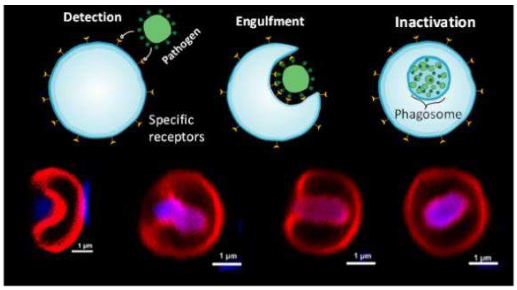

Figure 1. Phagocytic synthetic cells engulfing a living *E. coli* by simple physical interactions.

Synthetic DNA-based swimmers: harnessing programmable molecular patterning to control motion dynamics

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A plethora of different materials have been employed for the design of biocatalytic micro- and nanoswimmers, including polymers, lipids, silica, gold or platinum. However, achieving precise and predictable control over the assembly of structural and functional building blocks remains a challenge, limiting their translation into applications. Specially, for enzyme-powered nanoswimmers, the molecular distribution of enzymes is crucial to achieve effective motility [1]. Therefore, although enzyme-powered swimmers have strong potential for different applications, including bladder cancer therapy [2], there is a growing need to control their molecular design features.

Here, we employ synthetic DNA strands as building blocks to engineer highly integrated catalytic swimmers with enhanced motion capabilities and integrated functionalities. Thanks to the hierarchical self-assembly of single-stranded DNA oligonucleotides, we can design building blocks that consist of highly ordered DNA-based nanostructures that can be functionalized with enzymes with high programmability. By combining different DNA-based building blocks, we have achieved precise control over enzyme patterning on the surface of the nanostructures, leading to different motion dynamics. Moreover, we used the unique programmability of synthetic DNA to engineer "molecular brakes" to control the motility of the swimmers in an on/off fashion [4]. We strongly believe that the unique features of synthetic DNA can be harnessed to further control molecular patterning onto catalytic swimmers, which holds a tremendous potential for unlocking new emergent behaviours and functionalities in artificial micro-nanorobotic systems that resemble those observed in natural systems.

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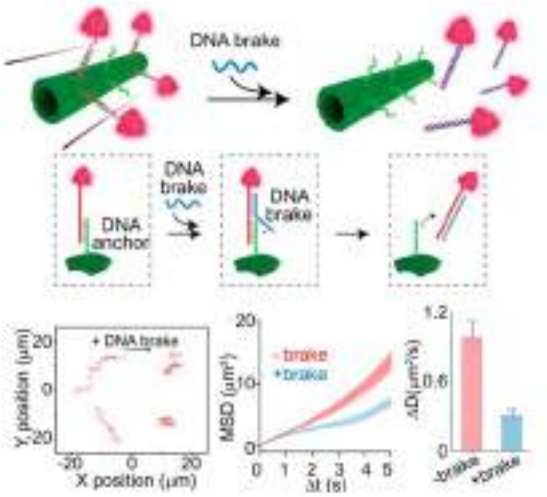

Figure 1. DNA-based nanoswimmers that can be controlled using molecular brakes.

Emerging morphologies and effective interactions in active colloids

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Abstract

Active colloids use a variety of mechanisms to self-propel. They usually involve an exchange of matter or energy with the medium in which they are suspended. Because of the intrinsic non-equilibrium nature of such coupling, the properties and regimes of the emergent structures due to their activity are richer and more varied than the ones associated to their underlying equilibrium properties[1].

In this presentation I will analyze the implications that the dynamic coupling of active colloids and reactants may have in how colloids self-propel[2] and how such dynamical couplings can be used to control and manipulate the individual and collective motion of colloids. I will also analyze the interplay between self-propelled colloids and heterogeneous environments. Specifically, I will analyze the co-assembly morphologies produced due to the interactions among active colloids and the geometrical constraints of a phase separating binary mixture[3], as well as the subtle role that activity plays in the emergence of effective interactions among passive inclusions[4].

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Engineering with biomolecular motors

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Motor proteins, including kinesin, together with their associated filaments, such as microtubules, can serve as biological components in engineered hybrid nanosystems. Our recent work focused on degradation mechanisms in these nanosystems, including microtubule breaking and shrinking. Mechanical failure of such biological nanostructures due to forces exerted by biomolecular motors has been studied by us in great detail and explained with the principles of mechanochemistry and mechanical fatigue. Molecular motors also introduce an interesting new element into self-assembly processes by accelerating transport, reducing unwanted connections, and enabling the formation of non-equilibrium structures. Our recent work created a molecular system that is capable of dynamically assembling and disassembling its building blocks while retaining its functionality, and demonstrates the possibility of self- healing and adaptation.

Recent publications

G. Saper, S. Tsitkov, P. Katira, H. Hess*: “Robotic end-to-end fusion of microtubules powered by kinesin”, Science Robotics, 6(60), abj7200 (2021)

Y. Zhang, H. Hess*: “Chemically-powered swimming and diffusion in the microscopic world”, Nature Reviews Chemistry, 5, 500-510 (2021)

G. Saper, H. Hess*: “Synthetic systems powered by biological molecular motors”, Chemical Reviews, 120(1), 288-309 (2020)

Y. Zhang, S. Tsitkov, H. Hess*: “Substrate competition as a path to complex spatio-temporal dynamics”, Nature Catalysis, 1, 276–281 (2018)

CHAIRS/INVITED SPEAKERS PARALLEL SESSION

Magnetic-enzymatic nanomotors depicting a collective swarming behavior and directional navigation abilities

Anna C. Bakenecker[1,2*], Xavier Arqué[1], Juan Fraire[1], Huimin Wei[2], Heiko Lemcke[2], Paul Soto Rodriguez[3,4], Sandra Prévéral[3], Damien Faivre[3], and Samuel Sánchez[1,5*]

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Many treatments are based on the systemic administration of high amounts of therapeutic drugs, which leads to side effects and limited accumulation at the target side. Therefore, methods to efficiently administer, penetrate and locally release the drugs such as smart nanoparticles (NPs) for precision medicine are highly needed. For this, NPs with self-propelling properties, which are called nanomotors, have been proposed as drug delivery systems able to overcome these limitations [1].

Nanomotors show self-propelling behavior due to the catalytic reaction of enzymes decorated on the NPs surface. The propulsion mechanism is based on the consumption of an enzyme-specific substrate serving as a fuel. On a single particle level, enhanced diffusion coefficients have been reported. For drug delivery approaches however, many particles are needed and therefore the collective swarming effect of nanomotors has been brought into focus [2]. It has been recently shown that actively propelled nanomotors can cross extracellular barriers [3], show enhanced penetration into tumor tissue [4] and enable the movement through complex media such as the synovial fluid [5].

On the other hand, several approaches have been demonstrated of using magnetic NPs for an enhanced administration of drugs by applying magnetic fields and steering the particles towards their targeted site. Also, for the actuation of magnetic NPs, the collective behavior has attracted interest [6].

To combine the properties of active self-propulsion and magnetic guidance, we present enzymatic functionalized magnetic NPs. These magnetic-enzymatic nanomotors show on one hand an active swarming behavior due to the catalytic reaction of the enzymes and on the other hand the magnetic properties allow for a directional steering of the nanomotors in magnetic gradient fields. The figure shows representative snapshots of the video taken from nanomotors which were pipetted into a petri dish either containing water or fuel. Furthermore, these nanomotors have the potential to be visualized by means of Magnetic Particle Imaging (MPI) as well as to be used for Hyperthermia treatments.

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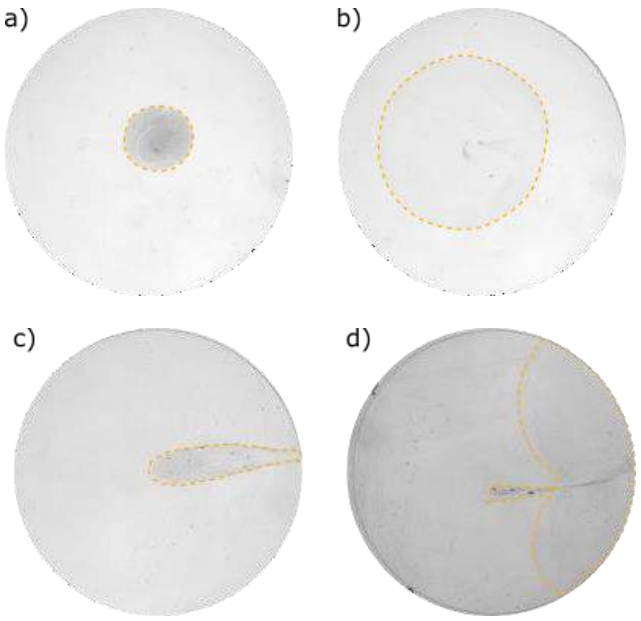

Figure 1. Representative snapshots of the dispersion behavior of magnetic-enzymatic nanomotors in a) water b) fuel c) water + magnetic force (pointing towards right side) d) fuel + magnetic force (pointing towards right side). The area occupied by nanomotors is encircled in yellow for better visibility.

Micromotors for smart bioassays: towards disruptive diagnosis.

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Micromotors represent one of the most exciting horizons in analytical chemistry. The utilization of self-propelled micromotors in (bio)chemical assays has led to a fundamentally new approach where their continuous movement around the sample and the mixing associated effect, all this as a collective behavior, greatly enhances the target-receptor interactions and hence the performance of the bioassay [1,2].

In our lab, we are focusing on the design and development of micromotors which are constituted by (nanostructured) layers (tubular-based shape) and particles (Janus-based shape) that confer them self-propulsion using (photo)-catalytic propulsion [3] and magnetic guidance with compatibility in biological media due its tremendous significance [4,5] They also smartly incorporate nanomaterials and molecular recognition-based functionalization to obtain sensitivity and exquisite selectivity [5-7] on board using electrochemical and fluorescence detection approaches [6-7], even integrated on smartphones [8] or as smart SERS substrates [9]. In our experience, we humbly found that micromotor technology is an attractive alternative to performing fast, and reliable bioassays and diagnostic testing, especially when an extremely low volume of samples is available or when the analysis must be performed in a micro-size environment.

In this communication selected micromotors-based bioassays with potential in relevant diagnostics, and some future directions will be discussed.

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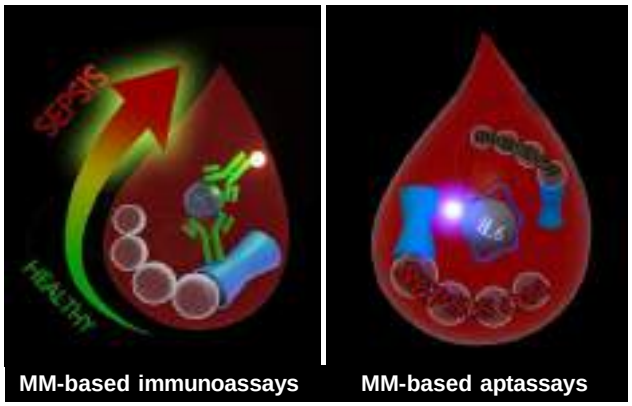

Figure 1. Fluorescence bioassays on board on micromotors.

Acknowledgment

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PARALLEL SESSION

Magnetically Induced Thermal Effects For A Programmed Disassembly Of Protein Cages On Nanocomposites With Magnetotactic Behavior

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Protein cages offer exciting potential for precisely delivering therapeutics and imaging agents through customizable disassembly strategies. In this study, we developed hybrid nanocomposites of polystyrene spheres (PS) comprising tobacco mosaic virus (TMV) and magnetic iron oxide nanoparticles (IONPs), engineered to function as swimmers capable of navigating in a magnetic field gradient. These nanocomposites are designed to disrupt viral protein cages through magnetically induced heat release, leveraging the magnetic manipulation. Additionally, we investigated the impact of magnetic hyperthermia on the programmed disassembly of viral protein capsids. Significantly, our findings indicate that the degree of protein cage disassembly depends on factors such as the specific absorption rate (SAR) of the magnetic nanoparticles - reflecting their heating efficiency - and the spatial relationship between the protein cage and the heating sources within the nanocomposite. Enhancing our understanding of and optimizing this interplay will facilitate precise spatiotemporal control for targeted drug and gene delivery using protein cages within magnetotactic or self-propelled nanomotors..

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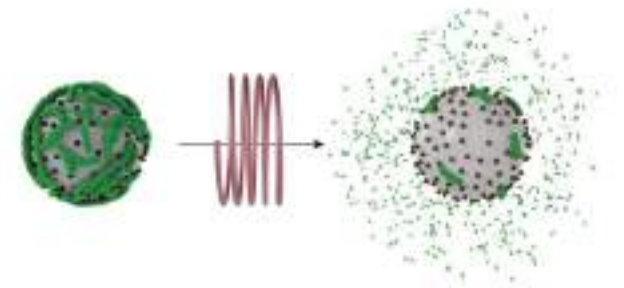

Figure 1. Scheme of the magnetotactic swimmers, made of PS spheres on which tobacco mosaic viruses and iron oxide nanoparticles were deposited (PS@IONPs/TMV), before and after exposed to an alternating magnetic field for a programmed disassembly of the protein cages.

BUILT-IN METAL ORGANIC FRAMEWORKS INTO TUBULAR MICROMOTORS WITH MULTIPLE PROPULSION MODES

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Tubular micromotors (MM) are fascinating materials in the current scientific scenario due to its dynamic motion that have demonstrated its capabilities in many fields such as analytical, environmental, or biomedical [1,2]. On the other hand, metal organic frameworks (MOFs) are crystalline materials with a periodic network of organic ligand linkers bonded with metal ion nodes to create one, two or three-dimensional structures. MOFs have been positioned as versatile materials thanks to their huge number of functionalizable sites and extensive surface area [3,4]. The combination of both micromotors and MOFs has been pursued and achieved in the past, but with certain limitations remains, mainly complicated synthesis approaches [5,6] and limited stability of MOFs in aqueous medium [7], preventing thus practical applications.

Herein we present a new, easy-to-obtain, and environmentally friendly route for the synthesis of tubular MOF-MM based on HKUST-1. As can be seen in Figure 1, tubular Cu/Pt, Cu/Ni and Cu/Ni/Pt MM prepared by template electrodeposition are used as nucleation spots for the synthesis of HKUST-1 MOFs by incubation with the specific ligand, benzene-1,3,5-tricarboxylic acid. Furthermore, we have explored different propulsion mechanisms to have a wide range of MM depending on the final application: magnetic, catalytic, and both magnetic and catalytic. These MOF-MM have proved their suitability in drug delivery and water decontamination, and they are placed as a tool with endless applications in the short-range future.

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Figures

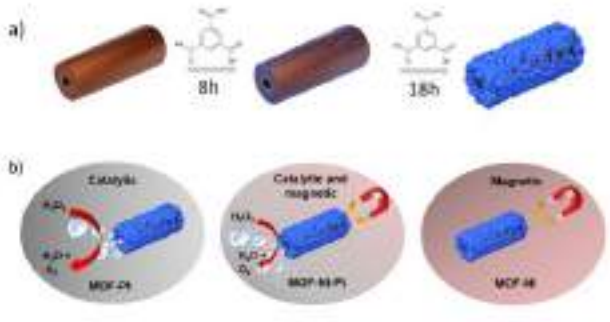

Figure 1. Schematic representation of the synthesis of MM (a) and the three different mechanisms of propulsion (b)

Nanorod-colloid propellers: from bidirectional transport to energetic efficiency

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Field-driven direct assembly of nanoscale matter has an impact in disparate fields of science. In microscale systems, such concept has been recently exploited to optimize propulsion in viscous fluids [1]. Despite the great potential offered by miniaturization, using self-assembly to achieve transport at the nanoscale remains an elusive task [2]. In this talk, I will introduce an hybrid propeller, composed by a ferromagnetic nanorod and a paramagnetic microsphere, Figure 1, can be steered in a fluid in a variety of modes, from pusher to puller, when the pair is dynamically actuated by a simple oscillating magnetic field. This unique design can be exploited to build more complex structures capable of carrying several colloidal cargos as microscopic trains that quickly disassemble at will under magnetic command. In addition, this prototype can be extended to smaller nanorods below the diffraction limit, but still dynamically reconfigurable by the applied magnetic field [3].
Using the nanorod-colloid propeller, I will show how to obtain experimentally the Lighthill's energetic efficiency of the swimmer by measuring the power consumed during propulsion and the energy required to translate the propeller at the same speed. Finally, I will discuss how the efficiency of our microswimmer could be increased upon suitable tuning of the different experimental parameters [4].

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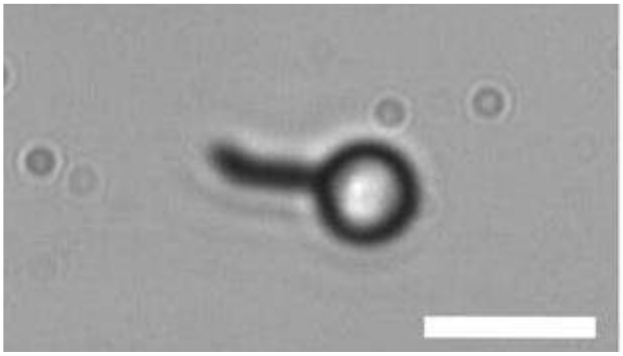

Figure 1. Optical microscope image of a paramagnetic sphere (1 micron diameter) and a ferromagnetic nanorod (200 nanometer thick, length 2 micron) assembled by a square wave magnetic field. Scale bar is 5 microns,

Ultrasound-powered micro- and nanorobots

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Abstract

Ultrasound technology offers a promising and biologically safe method for both the actuation and imaging of medical micro and nanorobots. This presentation introduces a novel category of acoustic microrobots designed for enhanced maneuverability and high-speed locomotion on various surfaces, including both flat and curved environments. These microrobots employ a unique propulsion mechanism that incorporates a trapped air bubble to leverage acoustic waves, achieving thrust forces significantly surpassing those of natural microorganisms like algae and bacteria by two to three orders of magnitude [1], [2]. Further discussion will highlight the microrobots' exceptional propulsion capabilities, enabling effective navigation through complex biological fluids—such as blood and mucus—that exhibit non-Newtonian characteristics [3]. The production process involves the use of advanced 3D microprinting technology, specifically two-photon polymerization (2PP), facilitating the creation of these microrobots with a typical size of approximately 25µm. The presentation will also showcase a recent innovation in our acoustic microrobot design featuring a negative acoustic contrast factor [4]. This characteristic permits the microrobots to be precisely localized and maintained at the focal point of focused ultrasound waves, even under rapid fluid flow conditions. Such dynamic control and stability in manipulation pave the way for targeted therapeutic applications and minimally invasive procedures within the restricted confines of the human body, offering significant potential for the future of medical interventions.

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Chemical Micromotors Move Faster at Oil-Water Interfaces

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Micromotors, which can convert external energy into autonomous motion, hold great promise as a core platform for next-generation autonomous multifunctional microrobotics[1] with broad application prospects.[2-3] In these applications, various types of confinement exist, such as solid-liquid, liquid-liquid, and liquid-gas interfaces, which can significantly alter the individual and collective dynamics of micromotors. These interfaces can be found in environmental remediation and biological samples.[4-5] Compared to other types of interfaces, micromotors moving at liquid-liquid interfaces are less explored and understood. This is also poorly understood for chemically active colloids that release chemicals into their environment. We report[6] that chemically driven micromotors move several times faster than those moving at a glass-water interface. Typical speed increases were 3-6 times, but speed increases of an order of magnitude were also frequently observed. The robustness of this speed increase observation is confirmed with several types of chemically powered micromotors and with different types of oils. We propose that the reported speed increase is primarily due to faster chemical reaction rates at an oil-water interface, an effect that is supported by some experimental evidence. Our discovery of the fast speeds of chemical micromotors at oil-water interfaces reveals interesting dynamics of micromotors in confined environments where reaction kinetics, distributions of physicochemical fields, and flows are intricately coupled. Such an increase in speed can inspire faster micromotor designs with better energy efficiency, which is particularly useful for environmental remediation, micromixing, or food processing applications involving oil-water emulsions. In addition, chemical micromotors could serve as a local probe of the reaction rate at an oil-water interface, providing real-time, visual, and quantifiable monitoring of interfacial reaction kinetics that are both important and elusive.

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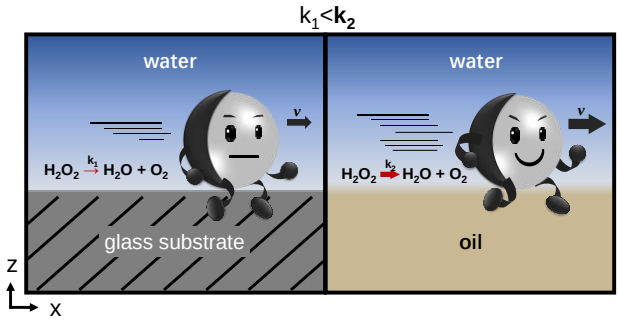

Figure 1. A schematic diagram illustrating the significant acceleration of chemically powered micromotors due to faster chemical reactions at an oil-water interface.

Engineering light-driven micro-nanomotors for on-demand and local pH sensing applications

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Abstract

Local pH measurements are very important in various areas e.g., in cell biology measurement of pH is critical for the detection of cancer cells as well as for elucidating the mechanisms of disease development and investigating drug effects [1]. Similarly, they also play an important role in chemical reactions or electrochemistry to ensure the reaction sites and reaction quality [2]. Here, we demonstrate the design of light-driven micro and nanomotors (MNMs) as an efficient and controlled mobile probe for on-demand and local pH sensing measurements. The MNMs are spherical Janus particles with multiple functional coatings that provide them interesting features, like, a dual optical response i.e., controlled swimming under UV light and pH-dependent fluorescence signal emission when excited with blue light, and moving path guidance using the weak external uniform magnetic field [3,4] (see Fig. 1a,b). All these features allow the micromotors to sense the pH of the medium on-demand and locally or of a target location by guiding them to swim to the target location. The pH-dependent change in the fluorescent signal intensity is used for the measurement of the local pH of the medium (see Fig. 1c). It is observed that the careful measurement of small pH changes requires a spectrometer that precisely measures the intensity change. However, the fluorescence signal of micromotors was good enough to provide a clear visual demarcation for large pH changes. Systematic experimental studies supported by controlled experiments are performed to optimize the system as well as to calibrate the micromotors for local pH sensing applications. A schematic in Fig. 2 briefly shows the approach adopted for demonstrating the on-demand and local pH sensing applications of the micromotors. The characteristics like easy-to-design structure, light activation, directional swimming, and ability to measure the pH on-demand and locally prove that micromotors have the potential to revolutionize pH monitoring in various domains including lab-on-a-chip devices, biomedical research, environmental monitoring, and quality control in industrial processes, etc.

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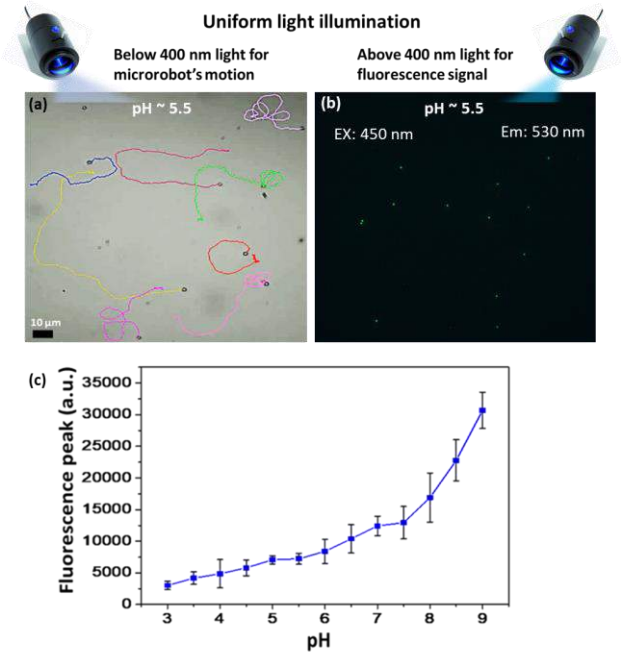

Figure 1. Illumination and observation. (a) Swimming: trajectories of micromotors under UV light in aqueous peroxide medium (b) Fluorescence: green dots are the fluorescence signal emitted by micromotors under the illumination of blue light. (c) fluorescence signal intensity depends on the pH value of the medium

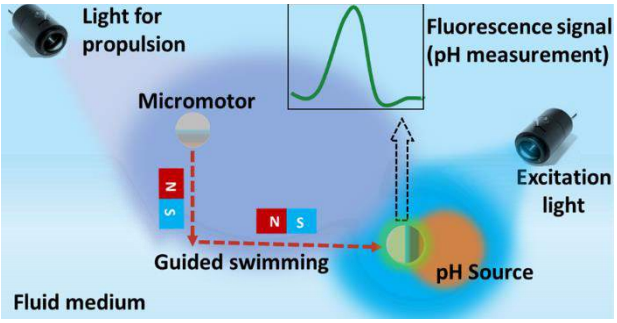

Figure 2. Schematic shows the application of light-driven and externally-guided micromotors for fluorescence signal-based local pH sensing in the fluid medium.

FIGHTING BACTERIA WITH MICROMOTORS

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Antimicrobial resistance (AMR) is considered a major threat worldwide, causing up to 6 million deaths every year [1]. Bacterial biofilms are one of the key issues to tackle in the battle against AMR. An undesired side effect is the burden to healthcare systems worldwide. As such, new methods for prompt bacteria detection and inactivation are needed. The unique features of micromotors, such as high towing force to reach hardly accessible areas and the enhanced fluid mixing generated during its autonomous movement, make them promising candidates for the sensing and eradication of bacteria [2].

In this communication, selected examples of fuel-free micromotors to fight and detect bacteria will be presented. In the first example, light-driven unmodified MoS_2 and WS_2 microflakes for highly efficient biofilm destruction will be described. The strategy combines the force of multiple moving swarms as collision platforms along with radical oxygen species generation (see **Figure 1**) [3, 4]. Another important core of this communication will be based on the use of 2D nanomaterials magnetic Janus micromotors. Thus, in a second example, we will present its modification with antimicrobial peptides for targeted bacterial biofilm inactivation [5]. Also, such Janus micromotors can be engineered with bacteriophages for highly selective bacteria detection in real clinical applications. As will be described, a simple microplate reader can be used for colorimetric detection in less than 2 hours, avoiding cumbersome bacteria culture approaches, for fast treatment. The new micromotor-based strategies described in this communication hold considerable promise to fight against AMR.

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Figures

Figure 1. A micromotor swarm inactivating bacteria. Green: live bacteria. Red: dead bacteria. The top part at the right of the figure illustrates the “swarm”.

COFBOTs: Covalent Organic Framework-Based Microrobots for Versatile Biomedical and Environmental Applications

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In the realm of small-scale robotics, the utilization of biotemplating techniques has facilitated the creation of micro- and nanorobots with diverse morphologies for a wide range of applications [1-4]. Expanding on this paradigm, we explore the integration of highly porous crystalline materials, specifically metal-organic frameworks (MOFs) and covalent organic frameworks (COFs), with magnetic biotemplates [5]. Due to their porous nature, large surface area, and chemical stability, these materials offer promising prospects for enhancing the functionality of magnetic microrobots. In this study, we present the pioneering development of covalent organic framework-based microrobots (COFBOTs) by integrating them with COF-300 nanoparticles and nanorods [6]. We introduce a water-based nanoreactor technology capable of producing processable sub-40 nm 3D COF nanoparticles under ambient conditions, thereby enhancing the processability of 3D COFs. Leveraging the inherent magnetic properties of iron oxide nanoparticles, these COFBOTs can be remotely controlled through the application of a rotating magnetic field, resulting in the displacement of the microrobots in water. The versatility of COFBOTs extends to both biomedical and environmental applications, illustrating their potential impact in diverse fields.

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Figures

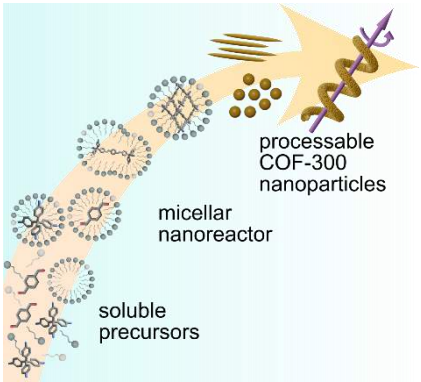

Figure 1. Water-based nanoreactor technology for the synthesis of processable sub-40 nm 3D COF nanoparticles that can be integrated into magnetic microrobots [6].

CoffeeBots: Magnetic Coffee Ground-Based Micromotors for Water Treatment

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Water pollutants such as oil spills, industrial dyes, and microplastics threaten public health and aquatic ecosystems. There are considerable challenges in removing water contaminants using traditional methods, especially in communities with limited resources. Several studies have been conducted recently focusing on developing novel water treatment materials, some of which are based on self-propelled or magnetically-propelled particles. Although these preliminary works constitute an important proof of principle, scalability and cost continue to pose practical challenges. Herein, we report the facile synthesis of spent coffee ground (SCG)-derived magnetic microrobots, which we dub "CoffeeBots", to remove oil, organic dyes, and microplastic pollution from contaminated seawater. To meet eco-friendly, high-yield and low-cost requirements, iron oxide nanoparticles (IONPs) were deposited on biodegradable SCGs using green chemistry. The CoffeeBots' magnetic properties facilitate magnetic navigation and recycling, microswarm assembly, and ease of retrieval after water remediation tasks. CoffeeBots' intrinsic surface hydrophobicity enables efficient on-the-fly capture and removal of oil droplets and microplastics from contaminated water with remote magnetic guidance. CoffeeBots were also functionalized with ascorbic acid (AA@CoffeeBots) to remove methylene blue (MB) dye contaminants from polluted seawater. SCGs and AA act as bioadsorbent and reducing agent, respectively, for MB dye removal whereas magnetic propulsion enhances mixing and accelerates MB decolorization. These CoffeeBots can be recycled numerous times for removing oil spills, organic dyes, and microplastics from the seawater. CoffeeBots hold considerable potential as sustainable, recyclable, and low-cost remediation agents for water treatment in the near future.

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Figures

Figure 1. Graphical depiction of potential applications of CoffeeBots to remove diverse pollutants from water [1].

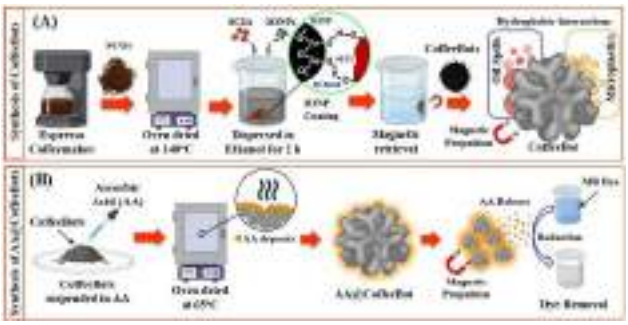

Figure 2. Scheme of synthesis and application of CoffeeBots for water treatment [1]

Towards Efficient Environmental Remediation: Light-Driven Hybrid Nano/Microrobots for Emerging Pollutant Degradation

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The quest for efficient and sustainable solutions for the degradation of emerging pollutants has led to significant interest in light-driven nano/microrobots. In this study, we explore the enhancement of the motility and photocatalytic activity light-driven nano/microrobots through the integration with hybrid materials such as MXenes, quantum dots, and polyoxometalates. By leveraging the unique properties of these hybrids, we aim to address the limitations associated with the speed and efficiency of existing photocatalytic nano/microrobots.

Our research methodology involved the microwave synthesis of hybrids, followed by a comprehensive evaluation of their photocatalytic performance under visible light irradiation. The incorporation of MXenes, known for their excellent electrical conductivity, quantum dots with superior light absorption capabilities, and polyoxometalates for their redox versatility, has resulted in a significant enhancement in the speed and degradation efficiency of the nano/microrobots. [1-2]

The performance of the final hybrid nano/microrobots was assessed through the degradation of a set of emerging pollutants under simulated environmental conditions. The results demonstrate a marked improvement in the speed and efficiency of pollutant degradation, highlighting the potential of these hybrid nano/microrobots in environmental remediation applications.

This study not only paves the way for the development of highly efficient light-driven nano/microrobots but also contributes to the broader field of nanotechnology and environmental science by providing a viable solution for the removal of emerging pollutants from water bodies.

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POSTERS

Poster number	Name	Surname	Affiliation:	Title of the abstract:
1	Xavier	Arqué Roca	CNRS Gulliver Unit, ESPCI ParisTech, PSL Research University	Effect of Catalytic Microbots on Cytoskeletal Microtubules
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3	Michalis	Chatzittofi	Max Planck Institute for Dynamics and Self-Organization	Enzymes as stochastic oscillators: a basic mechanistic description and novel opportunities for design and control
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6	Carmen	Cuntín Abal	Universidad de Alcalá (UAH)	BiOCl-Biotemplate Magnetic Micromotors For Inhibition Of Bacterial Growth
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19	Zichang	Guo	Ma Xing Group, Harbin Institute of Technology（Shenzhen）, Shenzhen, Guangdong Province, China	Carbon nitride-composite gallium-based liquid metal micromotors that can control movement speed and enhance antibacterial treatment with ultraviolet light
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22	Hyungmok	Joh	The University of Texas at Austin	Massively Parallel Microbubble Nano-Assembly
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38	Xuan Dieu Linh	Nguyen	University of Rovira i Virgili	Visible light-driven BiVO4-based microswimmers for water remediation
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41	Xia	Peng	Central European Institute of Technology, Brno University of Technology	Biohybrid microrobots for sustainable removal of micro\/nanoplastics
42	Remi	Peters	Radboud University	Soft Self-assembled Nanomotors: Unveiling Cilia-Like Motion through Photoisomerization
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44	Anna	Pushkareva		
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46	Alberto	Rodríguez Castillo	Universidad de Alcalá	Affinity peptide modified magnetic micromotors for OFF-ON protein S detection: towards fast COVID-19 determination.
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48	Twan David	Smits	IBEC	On the chemotactic behaviour of natural trafficking vesicles
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54	Qinglong	Wang	The Chinese University of Hong Kong	Real-time tracking and navigation of a microswarm under laser speckle contrast imaging for targeted delivery in vivo
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59	Zili	Yang	Wuhan University of Technology	Ultrasmall Enzyme-Powered Janus Nanomotor Working in Blood Circulation System
60	Florian	Peter	Max Planck Institute for Medical Research	Reactive, cargo-carrying and degradable micro- and nanomotors

Effect of Catalytic Microbots on Cytoskeletal Microtubules

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Catalytically propelled micro- and nanobots hold great promise for biomedical applications as active drug delivery systems[1] capable of targeting locations as specific as the interior cells.[2] However, there is a lack of understanding regarding the effect of these tiny robots on the functionality and organization inside living cells. Actively moving therapeutic micro- and nanobots will certainly interact with ubiquitous elements such as cytoskeletal microtubules responsible for cell division, intracellular transport, and overall cell shape. Most importantly, intracellular treatments such as DNA/RNA modifications like RNA interference or certain enzyme replacement therapies require for the optimal function of the cell after treatment. Hence, it is of crucial relevance to study the interaction of navigating micro-/nanobots with the intracellular environment of collectively moving cytoskeletal microtubules.

Herein, we study the influence of i) inactive microparticles, ii) chemical-releasing microparticles and iii) self-propelling catalytic microbots on an *in vitro* model of actively moving microtubules. The experimental setup is based on the formation of microtubule-kinesin complexes at an oil-water interface confined within a circular PDMS compartment.[3,4] Hence, the different types of SU-8 particles are studied in this two-dimensional platform of active microtubules organized in a nematic distribution.[5]

Under this framework, multiple particle parameters are investigated such as shape, size, surface charge, chemical-releasing function, and self-propulsion, and the effect these parameters induce on the particle trajectory and the structural and dynamical properties of the microtubule nematic state. The sizes considered comprise between 25 and 150 µm, and the surface properties are modified through surface functionalization with positively and negatively charged groups.

Next, different intracellularly delivered compounds are encapsulated inside the SU-8 structure, such as anticancer drugs (doxorubicin) and RNA interference (siRNA) to test the effect of their release on the active microtubule mesh. We also consider the release of catalytic products in enzyme replacement therapy by attaching enzymes to the surface of the particles through glutaraldehyde linker. This chemical-release function added to the inactive microparticles offers the additional possibility of controlling the active motion of the surrounding microtubules through release of ATP by attaching the enzymatic combo of Pyruvate kinase and Lactic dehydrogenase (PK-LDH) on the microparticles. Hence, creating a local activation system that can be triggered on demand by adding the ATP-releasing sources to induce complex activity gradients and patterns.

Finally, certain chemical-releasing microparticles present self-propulsion powered by the catalysis of well-known catalysts such as urease, catalase or platinum, hence, resulting in catalytic microbot systems. These self-propelling microdevices combine both a propelling force and the release of chemicals to their surroundings, which effect is monitored to assess modifications in the normal functioning of the microtubule active nematic. Further, the release of ATP from the navigating microbots allow for a tunable and transportable activation source of the microtubules.

Concerning the analysis of the experimental conditions and their comparability, multiple technical approaches are applied: On the one hand, the analysis of microparticle motion is performed through microscopy videos analyzed with an open-access tracking software to extract the trajectory of microparticles and compare the propulsive (speed) and diffusive regimes (effective diffusion) of the mean squared displacement (MSD) between types of particles. On the other hand, the emergence of topological defects on the nematic state resulting from breaking or curvature of the microtubule bundles is explored through confocal microscopy videos analyzed by means of particle image velocimetry (PIV).

Thus, this research investigates the effects of different particle-based agents on the cytoskeletal active environment, examining their influence on structure, dynamics, and network behavior and assessing their effect on cytoskeletal functionality. This approach provides fundamental insights on the principles of self-organizing subcellular structures involved in cell division and organelle organization and transport, whilst contributing to upgrade active drug delivery systems for future intracellular biomedical applications.

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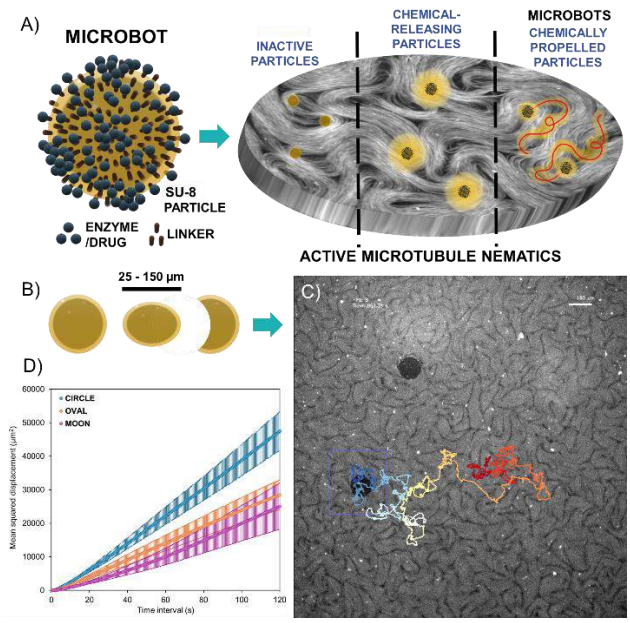

Figure 1. Effects of different particle-based agents on active cytoskeletal microtubules. A) Schematic of a microbot and the application of i) inactive microparticles, ii) chemical-releasing microparticles and iii) self-propelling catalytic microbots on actively moving microtubule nematics. B) Schematic of different particle shapes and sizes. C) Representative tracking trajectory of an inactive particle in the flowing microtubule nematic phase. D) Mean squared displacement (MSD) representing the area explored by particles of different shapes in the active microtubule nematics (mean ± standard error of the mean),

Enzyme-Powered Nanomotors for Enhanced siRNA Delivery in Bladder Cancer Therapy

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Bladder cancer (BC) poses a significant global health burden, with a substantial number of new cases and deaths annually. Non-muscle-invasive bladder cancer (NMBIC) represents the majority of BC cases and is notorious for its high recurrence rates. Conventional treatment options such as intravesical therapy, chemotherapy, surgery, or Bacille Calmette-Guérin (BCG) immunotherapy are limited by efficacy issues and adverse effects, leaving a critical need for the development of innovative therapies [1].

In recent years, gene therapy, particularly utilizing small interfering RNA (siRNA), has emerged as a promising strategy for targeted cancer therapy by silencing specific genes involved in tumorigenesis [2]. However, the clinical translation of siRNA-based therapeutics has been hindered by challenges related to efficient delivery, including susceptibility to degradation and limited cellular uptake. Addressing these difficulties requires the development of sophisticated delivery systems capable of protecting and transporting siRNA to target cells with high specificity and efficacy [3].

Nanoparticles (NPs) have gained significant attention as potential carriers for siRNA delivery due to their tunable properties, biocompatibility, and ability to encapsulate and protect nucleic acid. Among NPs, nanomotors (NMs) have emerged as a promising class of drug delivery vehicles, capable of autonomous motion, which could facilitate targeted drug delivery and enhance therapeutic efficacy. Enzyme-powered NMs, fueled by endogenous substances such as urea, hold promise for *in vivo* applications due to their biocompatibility and ability to harness physiological fuels for motion. Moreover, in recent studies it has been highlighted that there is a significant tumor accumulation of NMs in a bladder cancer mouse model [4].

This study focuses on the development and characterization of urease-powered NMs for the targeted delivery of siRNA to bladder cancer cells, concretely MB49 cell line. The synthesis of NMs involved the fabrication of biocompatible and biodegradable poly(lactic-co-glycolic acid) (PLGA) nanoparticles as a scaffold for siRNA loading. A layer-by-layer approach was employed to load selected siRNAs targeting genes involved in BC tumorigenesis and immunogenicity onto the PLGA NPs. Afterwards the incorporation of urease was performed to develop the NM.

The efficacy of urease-powered NMs was evaluated through *in vitro* studies, including motion analysis, siRNA delivery efficiency, cell viability assays, and knockdown efficiency analyses. The results demonstrated successful synthesis and characterization of urease-powered NMs with optimal physicochemical properties, efficient motion in the presence of urea, and robust siRNA delivery capabilities. Importantly, cell viability remained unaffected across tested concentrations of NMs and fuel.

In conclusion, urease-powered NMs represent a promising approach for the targeted delivery of siRNA in bladder cancer therapy. Leveraging endogenous fuel sources such as urea in the urinary tract, these NMs offer a biocompatible and efficient platform for siRNA delivery, addressing critical challenges associated with conventional therapeutic modalities. This study contributes to advancing the field of nanomedicine and underscores the potential of enzyme-powered NMs as a versatile and effective strategy for cancer therapy, with implications for the development of precision medicine approaches in the management of bladder cancer and other malignancies.

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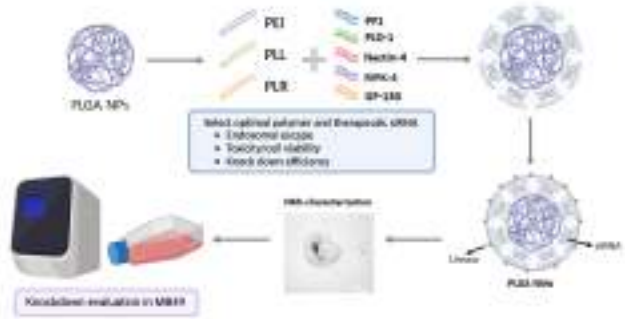

Figure 1. Workflow structure of the project.

Enzymes as stochastic oscillators: a basic mechanistic description and novel opportunities for design and control

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Enzymes are the catalysts of all chemical processes that take place in living organisms. These processes, during which chemical energy is converted to mechanical energy and heat, occur stochastically as a result of a noise-activated barrier-crossing event. Conformational changes of the enzymes during the catalytic cycle have been considered in the past to explain enhanced spatial diffusion [1] and the emergence of cooperativity in mechanically coupled enzymes [2-4]. Here, we show how conformational changes can be exploited to design an active enzyme that uses the free energy released by a thermodynamically favourable reaction to drive a thermodynamically unfavourable one.

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AlphaLISA based on magnetic photosensitive nanomotors

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Magnetic nanomotors have been widely applied in biomedical assays due to facile fabrication and excellent properties for separation and precise control [1][2].
AlphaLISA has the advantages of no background fluorescence interference and a wash-free homogeneous process. However, low incubation efficiency and interference due to strong non-specific binding are difficulties in the application of this technology. In this study, Fe_3O_4@mSiO_2 magnetic nanomotors loaded with the photosensitizer Ce6 were prepared as the magnetically controlled donor beads, and polystyrene nanospheres loaded with the europium chelate Eu(DBM)$_3$Phen and the thioxene derivative PCU [3] were prepared as the acceptor beads, respectively. The magnetically controlled donor beads are a core-shell structure with an average particle size of about 500 nm, which are readily dispersed in water and produce singlet oxygen ($^1O_2$) under 680 nm light, and can be separated by the magnet and precisely controlled by 3D Helmholtz coils. The acceptor beads are regular spheres of uniform size, with an average particle size of about 200 nm, which are readily dispersed in water and can emit 615 nm light with $^1O_2$. Incubation and separation can be performed by the precise control of complex swarm motion of the beads in magnetic field [4], which shortens the time cost and suppresses the interferences.

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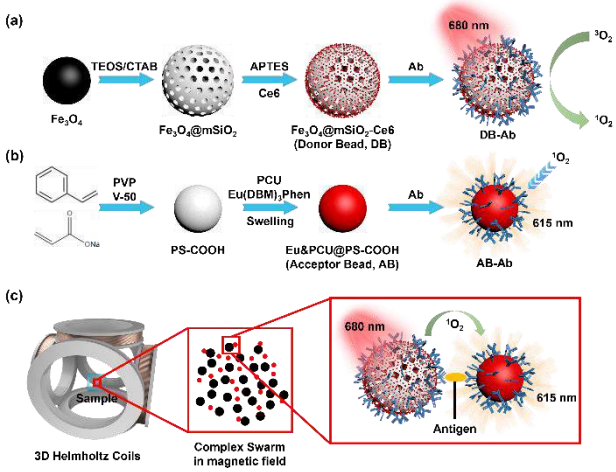

Figure 1. Schematic illustration of AlphaLISA based on magnetic photosensitive nanomotors

Convective Dynamics of Swarming Enzymatic Nanomotors

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Enzymatic nanomotors harvest kinetic energy through the catalysis of chemical fuels. When a group of self-propelled nanomotors is placed in a fuel-rich environment, they assemble into ordered groups and exhibit intriguing swarming behaviors akin to the self-organization observed in bacterial colonies, bioconvection of aerobic microorganismal suspensions, and the coordinated movements of fish, ants, and birds. This swarming behavior presents numerous advantages compared to individual nanomotors, including expanded coverage and prolonged propulsion duration.[1,2] However, the physical mechanisms underlying the swarming have yet to be fully elucidated. Our study investigates the formation of enzymatic swarms using experimental analysis and computational modeling. We show that the directional movement of enzymatic nanomotor swarms is due to their solutal buoyancy. We investigated various factors that impact the movement of nanomotor swarms, such as particle concentration, fuel concentration, fuel viscosity, and vertical confinement. We examine the effects of these factors on swarm self-organization to gain a deeper understanding. In addition, the urease catalysis reaction produces ammonia and carbon dioxide, accelerating the directional movement of active swarms in urea compared with passive ones in the same conditions. The numerical analysis agrees with the experimental findings. Our findings are crucial for the potential biomedical applications of enzymatic nanomotor swarms, ranging from enhanced diffusion in bio-fluids and targeted delivery to high- efficiency cancer therapy.

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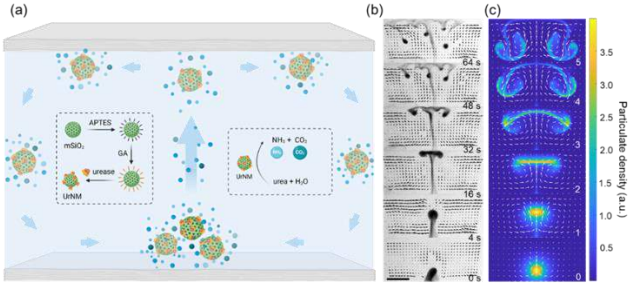

Fig. 1 Swarming behavior of enzymatic nanomotors viewed from the side. (a) Schematics illustrating the preparation of enzymatic nanomotors and the mechanism of solutal buoyancy resulting in swarming behavior. (b) A time-lapse sequence of images that show the directional and collective movement of enzymatic nanomotors in fuel. The fluid flow is analyzed by adding tracer particles and is shown in black arrows. Scale bar: 1 mm. (c) A time-lapse sequence of snapshots of computational results according to the assumed mechanism. The color bar indicates the nanomotor concentration and white arrows display the fluid velocity.

BiOCl-Biotemplate Magnetic Micromotors For Inhibition Of Bacterial Growth

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Multidrug-resistant infections are responsible for millions of deaths each year [1]. As an alternative to traditional antibiotics, which are responsible for this resistance, new treatments are being developed. Among them, micromotors are considered a viable option as a new alternative because of the possibility of avoiding resistance and their capability to be directed to the infection point autonomously [2].

This communication presents a new magnetic micromotor created from an *Escherichia coli* (*E. coli*) bio template decorated with bismuth oxychloride (BiOCl) crystals on its surface. BiOCl is a photocatalytic compound that is excited by near ultraviolet (UV) wavelength [3]. When these micromotors are irradiated, oxygen-reactive species (ROS) are produced. These ROS can interact with bacteria present in the solution, causing damage to the bacteria's outer membrane and, therefore, causing the death of the microorganism [3] (**Figure 1**). For the determination of these ROS, biocompatible electrochemical cells were designed by 3D printing. Apart from yielding reliable electrochemical measurements, the proposed cell allows the use of a small amount of sample and is easily adapted to the experimental conditions.

Different crystallization and photocatalytic responses were also studied. The results (not published) obtained for the growth inhibition of *E. coli* present these new micromotors as a viable alternative to traditional antibiotics for bacterium diseases, water, or surface decontamination.

Figures

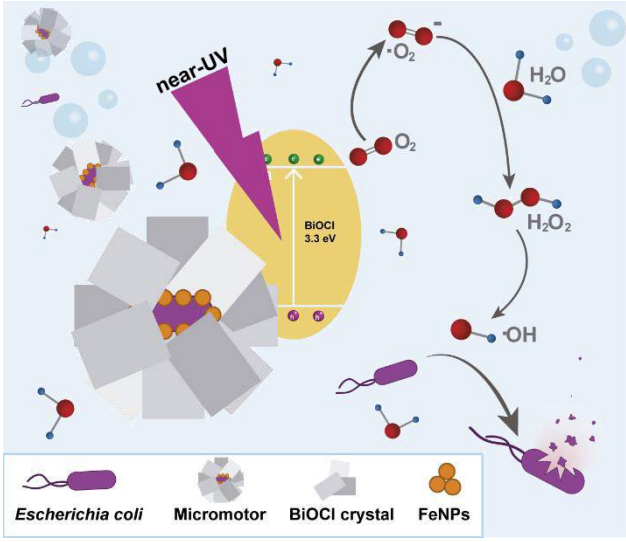

Figure 1. BiOCl micromotors are irradiated by near UV radiation, producing ROS, and causing bacteria damage.

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Chemotactic Directionality of Alkaline Phosphatase Mediated by a Trade-off between Carbohydrates & Metal Ions

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The importance of biomolecular behavior in spatiotemporal control over biological processes and stimuli-responsive nano or micro-machine systems is drawing interest from a wide range of disciplines especially, biomolecular behavior related to taxis in response to chemical gradient at nano- and microscale environment.[1] Since the previous ten years, one of the key areas of discussion in this context has been how to understand chemotactic ability and directionality of enzymes in the presence of their substrate gradient. There is mounting evidence that suggests that during the catalytic process, enzyme mobility increases, despite some inconsistent studies that do not agree with this notion.[2] However, the degree of chemotactic drift and directionality are two essential facts that are crucial for the micro- to macroscale prediction and design of biochemical spatiotemporal response patterns. The majority of the time, enzymes including urease, catalase, acetylcholine esterase, kinase, phosphatase, DNA polymerase, and many more are known to have the ability to chemotactically move in response to a gradient of their substrate in a microfluidic environment. Here, positive chemotaxis, or the general propensity of the enzyme to migrate up the substrate gradient, has been observed. Also, Sen et al. have demonstrated that, depending on the nature of the catalyzed products, liposomes can exhibit both positive and negative chemotaxis when an enzyme is bound to them.[3] Thus, new questions are posed: what will be the taxis behavior for only enzymes with respect to physiologically relevant ions or carbohydrates in a solely non-catalytic environment. Notably, there are few studies addressing how interactive or non-interactive ions or molecules affect an enzyme's chemotactic directionality when it is not catalysing. Herein, we report the extent and directionality of the chemotactic property of the membrane-bound glycoprotein alkaline phosphatase (ALP), a physiologically and clinically significant enzyme, in relation to a gradient of metal ions (Na+, Ca2+), including its metal ion co-factors (Mg2+ and Zn2+) and carbohydrates osmolytes (glucose, fructose and sucrose).

It was observed that ALP migrates slightly away from the gradient of carbohydrates, while the direction of migration for divalent metal ions is opposite and more pronounced. This differential phoresis is due to Hofmeister effect driven change in ALP surface zeta potential and osmotic pressure imbalance.[4] The ability to regulate an enzyme's chemotactic extent and direction in response to entirely non-catalytic conditions may prove useful in the fabrication of environment-responsive nanomachines.

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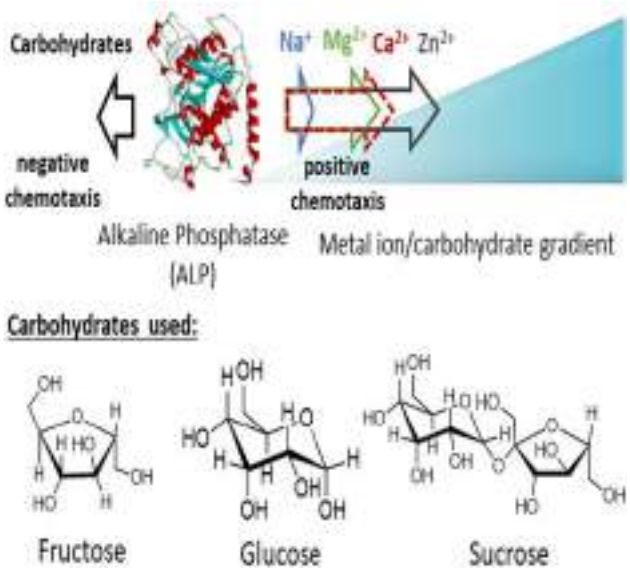

Figure 1. Schematic representation of the extent and directionality of chemotactic drift in response to the gradient of salts and carbohydrates.

SEGREGATION TRANSITION FOR INERTIAL SELF-SPINNING DISKS

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Self-spinners convert external energy into persistent rotational motion. Due to this unique feature, assemblies of self-spinning particles are recognised as a novel class of active materials, that evolve out of thermal equilibrium and undergo several types of collective behaviours and self-organisation. In the case of spinners, broken chiral symmetry gives rise to self-sustained global vorticity, as recently observed in experiments of starfish embryos [1]. During the early stages of their growth, a large amount of self-spinning embryos can assemble in a hexagonal bidimensional crystal, which persists for a long time. Interestingly, due to the inherent broken chiral symmetry, these clusters can sustain a global rigid body rotation.

Experimental evidence of collective chiral motion is also available for synthetic spinners. A layer of self-spinning macroscopic discs, powered by an upward air flow, shows collective vortical motion [2]. Most interestingly, the global vorticity of the system undergoes a chirality transition for increasing upflow, from the same sense as the one of the single discs to the opposite one.

Inspired by these experiments, we have designed a minimal model of self-spinning particles immersed in a 2D thermal bath, interacting through a conservative repulsive potential and tangential contact friction. This allows conversion from rotational to translational motion upon collisions between particles.

For high enough friction and self-spinning rates, we observe that the system spontaneously segregates into dense regions with non-zero vorticity w_P, leaving behind empty regions with sustained edge currents. Fig. 1 shows a typical example of such behaviour. We have studied the emergence of this phenomenon, as a function of the relevant parameters, deriving the phase diagram of the model. We found out that particles' inertia is fundamental to trigger segregation. Moreover, we have investigated the properties of the two coexisting phases the role of the edge currents in sustaining the segregation.

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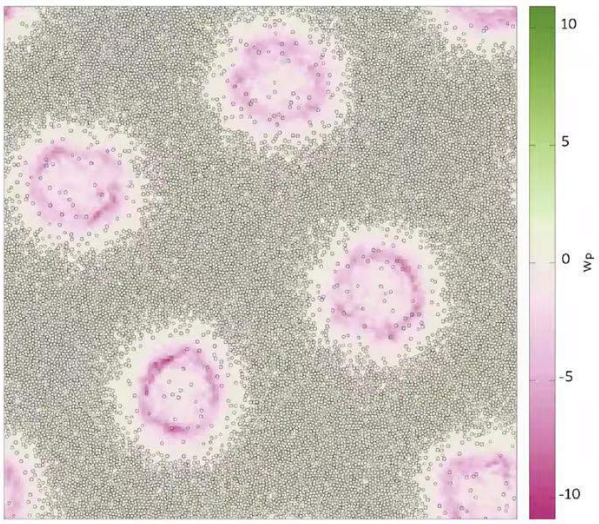

Figure 1. Clustering of self-spinning particles. Green regions have non-zero counterclockwise local vorticity w_P, while pink regions show clockwise edge currents.

Tubular MnO_2-based micromotors for ammonia generation

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Micromotors have emerged as promising tools for environmental remediation, thanks to their ability to autonomously navigate and perform specific tasks at the microscale. In this study, we present the development of bio-catalytic MnO_2 micromotors modified with laccase for enhanced oxidation of organic pollutants by providing an additional catalytic pathway for organic pollutant oxidation. These modified micromotors exhibit efficient ammonia generation through the catalytic decomposition of urea, suggesting their potential application for green energy generation. Compared to bare micromotors, the MnO_2 micromotors modified with laccase exhibit a 20% increase in rhodamine B degradation. Moreover, the generation of ammonia increased from 2 to 31 ppm in only 15 min, evidencing their high catalytic activity. To enable precise tracking of the micromotors and measurement of their speed, a deep-learning-based tracking system was developed.[1] Overall, this work expands the potential applicability of bio-catalytic tubular micromotors in the energy field.[2]

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Figures

Figure 1. Scheme of ammonia generation and pollutant removal by MnO_2-based tubular micromotors for the production of green energy.

Urease-powered nanomotors for chemotherapeutic bladder cancer therapy

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In recent years, enormous research efforts have been made to minimize the side effects of drugs and to increase their therapeutic efficiency in the treatment of cancer by making drugs more efficient and designing drug delivery systems based on nanoparticles. Bladder cancer, for example, is one of the most common cancer types worldwide for which current therapies prolong patient survival but still show high relapse rates and thus making it urgent to improve existing therapies. Using the catalytic reaction of enzymes that consume bioavailable fuels to propel micro- and nanoparticles (nanomotors) has revolutionized the field of nanomedicine. Combining nanoparticles containing therapeutic cargo [1,2] and targeting moieties [3] with the ability to move and navigate in complex biological environments [4,5] has the potential to overcome current challenges in drug delivery. Here, we present urease-powered nanomotors based on mesoporous silica nanoparticles (MSNP) loaded with clinically relevant chemotherapeutic drugs for the potential treatment of bladder cancer. The procedure of nanoparticle synthesis to obtain homogeneous particle size distributions and ensure proper pore opening for subsequent drug loading of the nanoparticles has been optimized. To achieve the highest possible drug loading efficiency of urease-nanomotors, different drug loading approaches have been tested. Furthermore, we tested whether the drugs influence the properties of the urease-powered nanomotors using SEM, DLS and enzymatic activity assay. Additionally, we were monitoring the *in vitro* swarming behaviour of drug-loaded and non-loaded nanomotors by optical microscopy in ionic and proteinaceous media in presence of different concentrations of urea (0 mM up to 300 mM). Additionally, we investigated the biocompatibility of nanomotors and tested the therapeutical efficiency of drug-loaded nanomotors *in vitro* using mouse bladder carcinoma cells. We employed metabolic activity tests and LIVE/DEAD assay for biocompatibility evaluation, and spectral flow cytometry to access the delivery efficiency of the nanomotors. We demonstrated the capability of urease-nanomotors to be loaded with different clinically relevant drugs without inducing changes in their collective motion. Furthermore, nanomotors showed 2.3x fold enhanced cell internalization in presence of 100 mM urea compared to passive nanoparticles (MSNP-BSA) after only 1 h of incubation. Additionally, urease-nanomotors showed high biocompatibility at different concentrations tested whereas drug-loaded nanomotors showed high therapeutical efficiency *in vitro* after only 4 h of incubation in presence of fuel. These results are pathing the way for using nanomotors based on mesoporous silica nanoparticles as delivery platform for chemotherapeutic drugs for the potential treatment of bladder cancer.

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Pollen-Based BioBots for Navigated Cancer Therapy

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Innovative approaches in cancer therapy are crucial for enhancing treatment efficacy and patient outcomes. Our study presents a novel method for the development and application of magnetic sunflower pollen-based biological robots (SFPµP-BioBots) for targeted cancer therapy. Utilizing electron beam evaporation, we asymmetrically deposited thin metal layers (Au, Co, Au) on one side of defatted sunflower pollen microparticles, ensuring magnetic actuation capabilities while preventing cobalt oxidation with gold layers. This preparation technique preserved the microparticles' structural integrity and non-allergenic properties, as confirmed by scanning electron microscopy (SEM) and energy-dispersive X-ray spectroscopy (EDS) analyses.

The magnetic SFPµP-BioBots exhibited precise directional control under a transversal rotating magnetic field, demonstrating linear, circular, and undulatory motions. This control is critical for their potential use in biological systems. In this study we have used the SFPµP-BioBots for manipulating and transporting ovarian cancer cells via electrostatic interactions. The BioBots' surface, positively charged, attracts the negatively charged cancer cells, facilitating targeted drug delivery.[1]

Furthermore, our study evaluated the doxorubicin (DOX) loading efficiency on these BioBots, revealing a strategic decrease in binding efficiency due to the metal layer coating. Despite this, the BioBots successfully delivered DOX to ovarian cancer cells, significantly enhancing the therapeutic efficacy of DOX under the influence of a transversal rotating magnetic field. The enhancement of DOX anti-cancer activity in A2780 human ovarian cancer cells mediated by SFPµP-BioBots under transversal rotating field was 17.4% ± 3.8, 16.0% ± 18.5, 20.0% ± 16.5, and 6.3% ± 7.6, for 0, 0.5, 1, 5 × 10^{-6} m of DOX, respectively.

This research not only underscores the feasibility of using magnetic SFPµP-BioBots for targeted drug delivery but also highlights the potential of these BioBots in advancing cancer therapy. By leveraging the natural, non-allergenic properties of sunflower pollen and incorporating magnetic actuation, we present a novel, efficient, and promising approach to combat ovarian cancer.[2]

This work was supported by funds from the Ministry of Health of the Czech Republic (NU21-08-00407).

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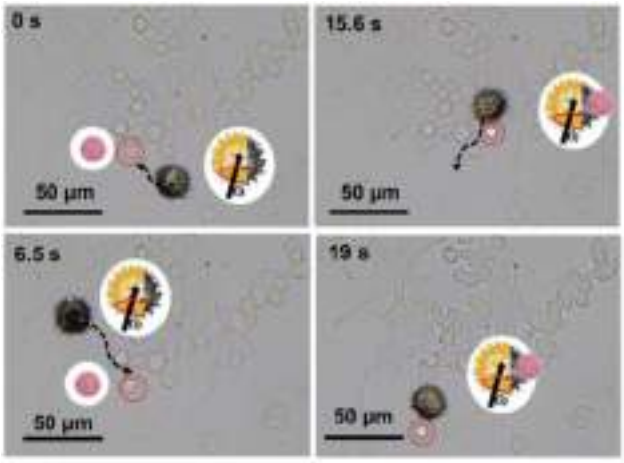

Figure 1. Manipulation of A2780 human ovarian cancer cell by magnetic SFPµP-BioBots. Time lapse images of magnetic SFPµP-BioBots attracting and transporting a free cancer cell as well as interaction with seeded cancer cells.

Multi-Stimulus-Responsive Programmable PNIPAM Hydrogels for Small-Scale Robotics

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Abstract:

In this work, we investigate a poly(*N*-isoproylacrylamide-*co*-acrylic acid) (PNIPAM-AA) hydrogel reinforced with aligned cellulose nanocrystals (CNC), superparamagnetic Fe_3O_4 nanoparticles (MNP), and Fe^{3+} as a physical ionic crosslinker. This copoylmer and these additives have been reviewed in literature individually [1,2,3], but it is the combination of these components that grant the studied hydrogel proficiency in six important categories in polymeric soft actuators: structural anisotropy for programmable deformation upon actuation, henceforth termed programmability; ability to be easily produced and to be made into complex structures, henceforth termed processability; hydrogel biocompatibility; mechanical strength; actuation reversibility; and multi-responsiveness. Many works have explored the use of Fe_3O_4 nanoparticles for magnetic actuation [4,5,6,7,8], but the selected preparation method (solvent casting, manual cutting and pasting) does not give the hydrogels sufficient processability. Some works have explored CNC and its optical and anisotropic properties [9,10,11,12,13] but have not investigated robotic capability and actuation. Other works have explored ionic complex formation methods to establish physical crosslinking networks [14,15,16,17,18] but have not added multi-stimulus-responsiveness to their hydrogels. With the proposed combination of PNIPAM-AA, which gives intrinsic and reversible thermo- and pH-responsiveness to the hydrogels, CNC, which bestows the precursor with shear-thinning properties for easy processability and structural anisotropy, MNP, which provides photo- and magneto-responsiveness, and Fe^{3+}, which works in conjunction with the acrylic acid to form ionic complexes to improve mechanical integrity, the formulated biocompatible hydrogel demonstrates great potential for use in biomedical applications.

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ENZYMATICALLY MEDIATED, DYNAMIC ASSEMBLIES IN SURFACE FUNCTIONAL STOMATOCYTES

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One recent focus in micro/nanomotors (MNMs) is the study of bacterial movement and collective behavior. These events range from population-based signaling networks to predation and motility, the plethora of communications falling within quorum sensing and predator/prey models.[1,2] In the emerging pursuit of recreating swarming and predatory behaviors, we present urease-loaded polymersome stomatocytes with basic quorum-like behaviors that, much like bacteria, are capable of signal production, reception, and response by transiently clustering with surface complementary artificial species.

The intended reversible behavior is transient and is based on the widely known complex-forming behavior of nitrilotriacetic acid (NTA) and histidine (His) moieties, in the presence of nickel ions and high pH. The attachment of such functional groups to the surfaces of stomatocytes would induce their grouping in the presence of nickel ions and, ultimately, allow the control of cluster and individual motors' motion regimes by pH. Upon the addition of urea, the urease stomatocytes are able to alter the environmental pH and the surface histidines on the complementary species and transiently cluster.

The clustering behaviors of stomatocyte nanomotor populations at different ratios and fuel concentrations were analyzed in ultrapure water and buffered systems by dynamic light scattering and microscopy. In both continuous phases, the stomatocytes display a maximum clustering interaction at pH between 6.3 and 7.3 and interparticle repulsive behaviors outside the range. Within the detectable region of the dynamic light scattering, individual stomatocytes can aggregate to agglomerates 20x their volumes.

Understanding population behavior in chemotactic colloids can facilitate the achievement and execution of remote navigation and cooperative tasks not feasible for individual MNMs.[3]

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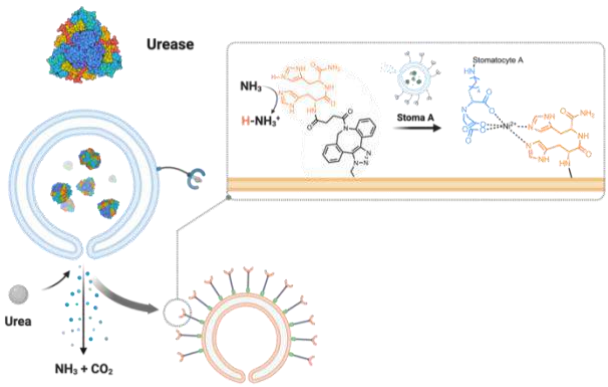

Figure 1. System design for stomatocyte communication for dynamic assemblies. Nitrilo triacetic acid functional, urease-loaded stomatocytes catalyze the production of the signal ammonia, which deprotonates the surface of the surface complementary histidine-functional stomatocytes. Upon deprotonation, the histidine is able to form a complex the Ni^{2+}-NTA surface moieties of the complementary motors and colloidal clustering occurs.

Microrobotic Superstructures for Transport and Delivery of Magnetic Micromachines

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In the field of biomedical small-scale robotics, the combination of metals and polymers offers opportunities for novel functionalities. Microrobots consisting of metals and organic materials leverage the unique properties of both material classes. Integration of metallic components with polymer structures by combining 3D-Lithography, mold casting and electroplating, yields elevated magnetic responsiveness, increased drug loading capacity, shape adaptability, and elasticity.[1,2] The approach facilitates diverse microrobotic locomotion modes and controlled swarm delivery, demonstrating its versatility across applications.[3] Furthermore, a microrobotic superstructure is introduced comprising interconnected magnetic units organized via a transient physical gelatin chassis. This superstructure, composed of electroplated magnetic helical micromachines interlocked by a gelatin nanocomposite containing iron oxide nanoparticles, exhibits responsive motion and controlled disassembly under various magnetic inputs.[4] Practical demonstrations include swarm navigation in large channels utilizing gradient magnetic fields, disassembly and micromachine release via high-frequency alternating magnetic fields, and corkscrew locomotion of single micromachines through small channels using rotating magnetic fields. This adaptable superstructure holds promise for intricate delivery procedures within the human body, offering a paradigm shift in confined environment navigation.

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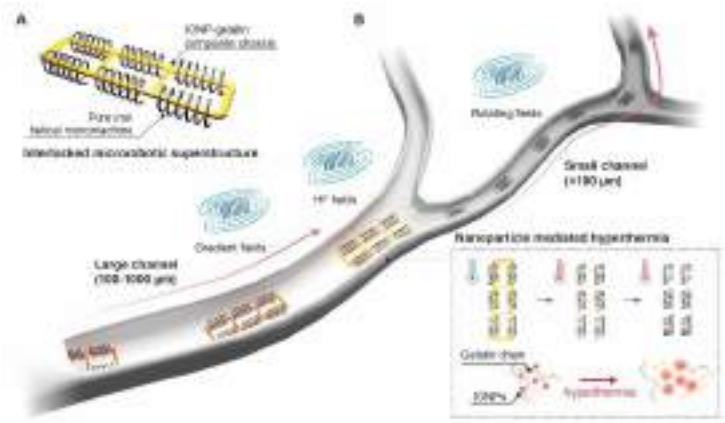

Figure 1. A swarm of helical micromachines, interlocked by a transient gelatin nanocomposite, is delivered to a vessel bifurcation by magnetic gradient fields. By applying a high frequency magnetic field at the bifurcation, the hyperthermia nanoparticles in the nanocomposite trigger the heat mediated dissolution of the chassis, releasing the micromachines. The micromachines can further advance in intricate vessels to a site of interest by application of a rotating magnetic fields.

Integrating *In Vitro* and *In Vivo* Studies for Comprehensive Evaluation of Nanoparticle-Based Drug Delivery Systems

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Nanoparticle-based drug delivery systems hold immense potential for transforming disease treatment by enhancing drug efficacy, improving targeting specificity, and minimizing off-target effects. However, their successful translation from laboratory to clinical settings demands a thorough understanding of safety, efficacy, and translational potential. This abstract highlights the pivotal role of integrating both in vitro and in vivo studies for a comprehensive evaluation of nanoparticle-based drug delivery systems (DDS). Furthermore, it introduces the concept of precision medicine to tailor innovations that address biological barriers and patient heterogeneity. In vivo and in vitro settings replicate distinct contexts encountered during DDS administration within the body. While the former involves navigating through the intricate network of tissues, organs, and barriers to distribution and clearance, the latter focuses on interactions at target tissues, including cellular membranes and intracellular compartments. In vitro experiments offer invaluable insights into initial screening, mechanistic understanding, and early-stage safety assessment of DDS. Through high-throughput screening assays, we rapidly evaluate biological activity, cellular uptake kinetics, and potential nanoparticle toxicity in a controlled laboratory setting. These in vitro studies enable identification of promising formulations, elucidation of mechanisms of action, and selection of safe and biocompatible candidates for further assessment. However, in vitro experiments alone cannot fully replicate the complex physiological and pathophysiological conditions present in living organisms. Therefore, complementing in vitro studies with in vivo experiments using animal models is essential to mimic human physiology and assess pharmacology effects, biodistribution, and pharmacokinetics of DDS. In vivo toxicology studies provide critical insights into systemic toxicity, organ-specific toxicity, and long-term effects of nanoparticle exposure, informing their safety profile and translational potential. Understanding the design of our system and applying in vitro and in vivo settings considering the context in which we are working is essential, as not all tests will fit all purposes. Unfortunately, there is still the probability that the system will not work under desired conditions. Several factors can influence the failure of a drug delivery systems. As a final consideration, there is one approach underexplored in DDS design, which could be key to generate successful biomedical applications: the heterogeneity present both in biological diseases and amongst the patients. DDS are typically engineered without prior knowledge of the disease and then applied. However, this conventional approach may explain why only a few nanomedicines are recommended as first-line treatments and demonstrate improvements in only a small subset of patients. What if we turned this conventional approach upside down and we started by applying precision medicine principles to the design process, using patient data to guide the engineering of DDS tailored to specific disease contexts and patient populations. This shift in approach could potentially revolutionize the field, leading to more effective and personalized treatments. Integrating in vitro and in vivo approaches is crucial for obtaining a comprehensive understanding of the biological, pharmacological, and toxicological properties of DDS. By combining the controlled and mechanistic insights gained from in vitro studies with the physiological relevance provided by in vivo experiments, we can bridge the gap between laboratory findings and clinical applications. Moreover, by incorporating new design approaches that utilize precision medicine principles, we can set the stage for the next generation of DDS that are better suited to address the complexities of individual patients and diseases, ultimately enhancing treatment outcomes and patient care.

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Magnetic Janus micromotors for biosensing tacrolimus in human oral fluids

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Self-propelled micromotors have revealed themselves as a disruptive technology for fast (bio)sensing in biological systems. The high towing force of micromotors, their directional control, and their ability to interact with target analytes make them particularly attractive for the direct detection of clinically relevant compounds in microvolume samples. Indeed, the autonomous movement of the micromotors generates an enhanced mixing of fluids at the microscale allowing access to areas not reachable by other static diffusion-based sensors; accelerating the kinetics of the reaction and allowing the detection of the analyte in a few minutes [1]. In this communication, a new micromotor-based competitive assay for the detection of Tacrolimus (FK506), an immunosuppressive drug widely used to prevent organ rejection after transplantation, is described (Figure 1). FK506 exhibits high inter- and intra-patient pharmacokinetic variability, which, together with its narrow therapeutic window, makes its monitoring extremely necessary to ensure graft survival [2]. The analysis of FK506 is usually performed using immunoassays or chromatographic techniques, which are cumbersome and require antibodies or expensive instrumentation [3]. The immunosuppressive capacity of the drug is due to the complex formed with immunophilin FKBP1A, which inhibits calcineurin, affecting the activation and proliferation of T-cells [4]. As such, FKBP1A, shows a good specificity and affinity for the drug, being thus a useful alternative to commonly applied antibodies for FK506 analysis.

The micromotor bioassay developed here relies on the recognition of FK506 by a recombinant FKBP1A fused to an emerald-green fluorescent protein (EmGFP) [5]. Polycaprolactone (PCL) magnetic Janus micromotors, synthesized by a simple oil-in-water emulsion approach [6] and modified with the target FK506, are used. Thus, the principle behind the assay relies on a competitive binding between the target immunosuppressant and the FK506 immobilized in the micromotor surface for the recognition site of the recombinant FKBP1A-EmGFP. The optimized fluororeceptor-based assay meets therapeutic requirements and shows potential for developing sensitive antibody-free FK506 detection systems.

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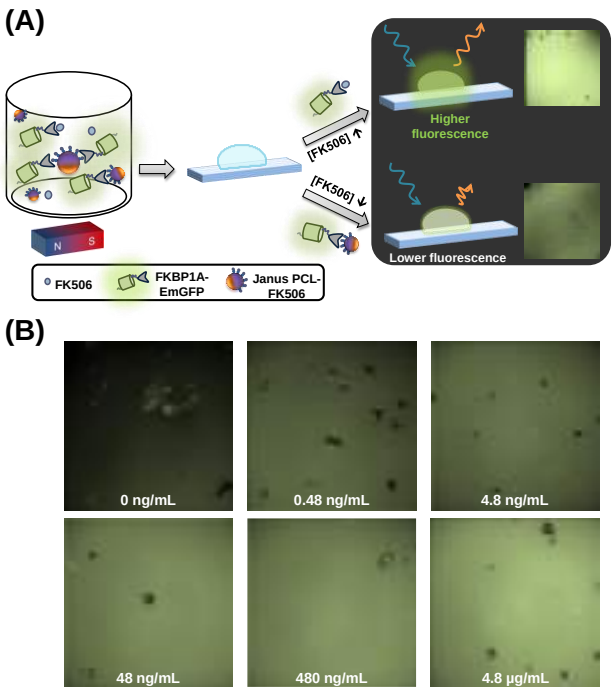

Figure 1. (A) Scheme of the assay protocol for detecting FK506 using PCL/Fe_2O_3 magnetic-propelled micromotors. As a result of competition, an increased fluorescence signal is localized in the solution due to a higher concentration of the analyte. In contrast, a lower concentration causes localization of the fluorescence on the surface of the micromotors and consequently decreases in the solution. **(B)** Micromotor-based fluorescence assay. Real-time fluorescent images related to the different FK506 concentrations assayed.

Chemically-fueled $NaYF_4$:Yb,Er@SiO_2@ZnO-Pt Janus particles for thermometry

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Chemically fueled micromotors are small devices that uses chemical reactions as a source of power by either producing bubbles or chemical gradients to propel the particles, and can be utilized for sensing and delivery, to cite a few [1,2]. On the other hand, measurement of temperature in small scales has become a challenge for miniaturized devices, such as microelectronics due to the inherent lack of spatial resolution of traditional thermometers [3]. One way to obtain thermal readouts is to use upconversion luminescence, where two or more photons are absorbed by the material generating emission from thermally coupled states, *i. e.* excited states in which their emission intensity is dependent on the temperature, allowing for temperature calculation [3]. Combining the active motion nature of chemically fueled micromotors with thermal sensing has potential to be applied in microelectronics and microfluidics, to cite a few. Therefore, we aimed to synthesize $NaYF_4$@SiO_2@ZnO core@shell@shell particles and partially coat them with Pt to form a Janus structure. By infrared laser excitation these particles emit in the green region of the electromagnetic spectrum, that ultimately can be used to calculate temperature. Additionally, the Pt coated size can catalytically decompose H_2O_2 as fuel, leading to propulsion, achieving a self-propelled thermometer.

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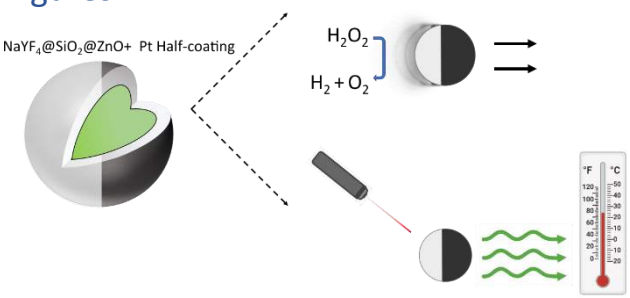

Figure 1. Schematic representation chemically fueled motor-luminescent thermometer micromotor.

An Isotropic Microdroplet Motor Triggered and Traced by Self-Supplied Fuel Induced Crystal Growth

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In the last decade, a significant number of self-propelled micro/nanomotors (MNMs) have been developed. For these MNMs, the most common constructing strategy is to build innate asymmetric active surfaces, like Janus structure [1], or cavity structure [2,3]. Another common constructing strategy is to induce the acquired asymmetric active surface on the isotropic MNMs with external stimuli [4]. The self-propelled MNMs fabricated through different constructing strategies exhibit featured motion behaviors and functionalities. Nevertheless, the existed constructing strategies that are tightly bonded with anisotropic active surfaces impose restrictions on the development of the self-propelled MNMs. Therefore, developing innovative constructing strategies that can bypass anisotropic active surfaces may contribute more intriguing motion behaviors and functionalities to self-propelled MNMs. Herein, we report a kind of microdroplets that can be propelled by the growth of nearby crystal seeds (**Figure 1**). They were prepared by dispersing a pretreated oil solution containing 2,2-azobisisobutyronitrile (AIBN) into surfactant solution through magnetic stirring. When the oil microdroplets approach free AIBN crystal seeds, they were observed to be self-propelled by continuously providing the AIBN solutes to crystal growth, leaving a visible crystal trajectory. The growth of AIBN crystal seeds creates an asymmetric concentration gradient field around the droplet surface and propels the droplet via nonelectrolyte-diffusiophoresis without any alteration of its surface features. The propulsion strategy that the droplet motion occurred simultaneously with crystal growth were further confirmed experimentally and numerically. In this unique propulsion strategy, the movement of the microdroplet is closely related to the crystal growth kinetics and can be manipulated by changing the AIBN concentration (c_{AIBN}) around the crystal and the crystal structure. What's more, a new crystal seed or a magnetic field can also exert an extra propulsive force or torque on the microdroplet. Given the traceable feature, this micromotor is expected to work for the fabrication of the crystal micropatterns via modulating its motion. By introducing an extra flow field to the micromotor system, we observed the reciprocating motion of a microdroplet, forming a half-arrow sequence pattern as shown in **Figure 2**, indicating a potential micropatterning strategy with great simplicity.

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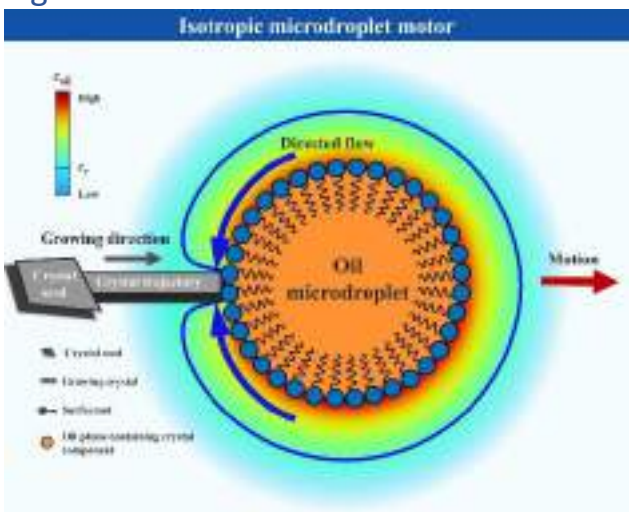

Figure 1. Schematic illustration of the isotropic microdroplet motor driven by the growth of a crystal seed.

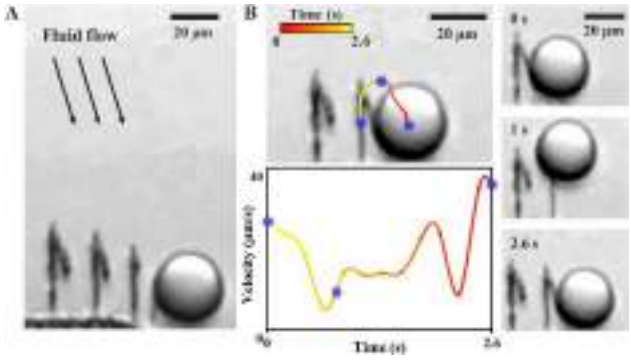

Figure 2. Patterned crystals leaving by the microdroplet motor. (A) Complete half-arrow sequence crystal micropattern leaving by the microdroplet motor under the influence of a fluid flow. (B) Formation process of single half-arrow crystal pattern, including the microscopic images (top left), the velocity profile (bottom left) and three typical moments (right).

Carbon nitride-composite gallium-based liquid metal micromotors that can control movement speed and enhance antibacterial treatment with ultraviolet light

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Liquid Metal Micro/Nano Motors (LM-MNM) are poised for a wide array of applications[1], yet their practical utilization is hindered by the presence of an inhibitive oxide layer on their surfaces.

In this work, we introduce a novel photoregulated liquid metal micro/nanorobot, denoted as GaGCN@Pt, which exhibits unique properties allowing for the ultraviolet light-controlled modulation of its movement speed and antibacterial capabilities[2]. These micro/nanorobots harness hydrogen peroxide as a fuel to achieve propulsion via electrophoresis. Under UV light exposure, the carbon nitride nanosheets anchored on the gallium particles facilitate the separation of electron-hole pairs, thereby enhancing the transfer of electrons within the gallium particles. This process not only augments the electrophoresis effect but also significantly increases the motor's velocity.

Furthermore, the generated singlet oxygen radicals ($^1O_2$) by GaGCN@Pt act as potent antibacterial agents, effectively eradicating Escherichia coli (E.coli) [3]. Notably, this antibacterial action is bolstered by the motors' enhanced mobility, markedly speeding up the healing process of wounds infected with bacteria in vivo.

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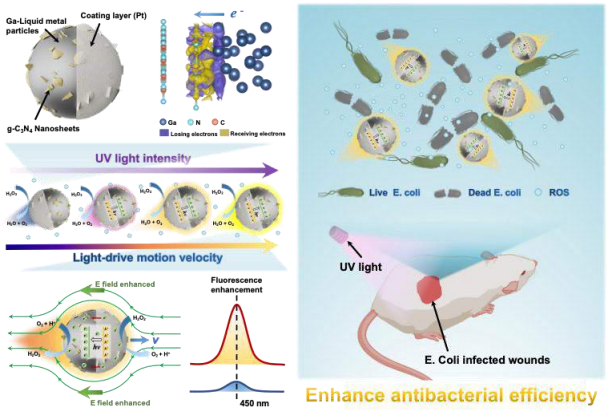

Figure 1. Light-regulated movement mechanism of liquid metal micromotors and their antibacterial applications.

Pixel-based reconfigurable organisms

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A comparative examination reveals that living organisms possess a broader spectrum of resilience, diver- sity, complexity, and capacity to sustain human existence compared to any previously developed technology. However, the current scope of our ability to engineer novel life forms is confined to the modification of exist- ing organisms or the creation of organoids within controlled laboratory settings. Recent endeavors have been made towards the design of reconfigurable organisms [1].

In this investigation, we delved into a theoretical scenario wherein a matrix of materials exhibits behavior akin to that of a beating myocardium cell, while the remaining elements maintain a passive resemblance to skin cells in a fluid domain. The central inquiry pertains to the repercussions of infinite permutations as these square units transition from a four-by-four to a thousand-by-a-thousand configuration.

Leveraging methodologies such as reinforcement learning [3]and graph neural networks [5], we propose potential refinements to the design process of microswimmers. Specifically, we envisage the assignment of distinct functionalities to individual pixels within a matrix, with certain pixels acting as active agents while others assume a passive role. Strategies for orchestrating their behavior and determining the activation status of each pixel, especially in the context of specifying particular destinations, were discussed.

Moreover, we contemplate the ramifications of attaining the capability to control pixel activation through optogenetics [2] or pacemakers [4]. This advancement would enable modulation of pixel states alongside the manipulation of cellular composition, facilitating precise coordination of movements. Such granular control would permit the choreography of intricate pixel dynamics, thereby augmenting maneuverability to levels surpassing conventional constraints.

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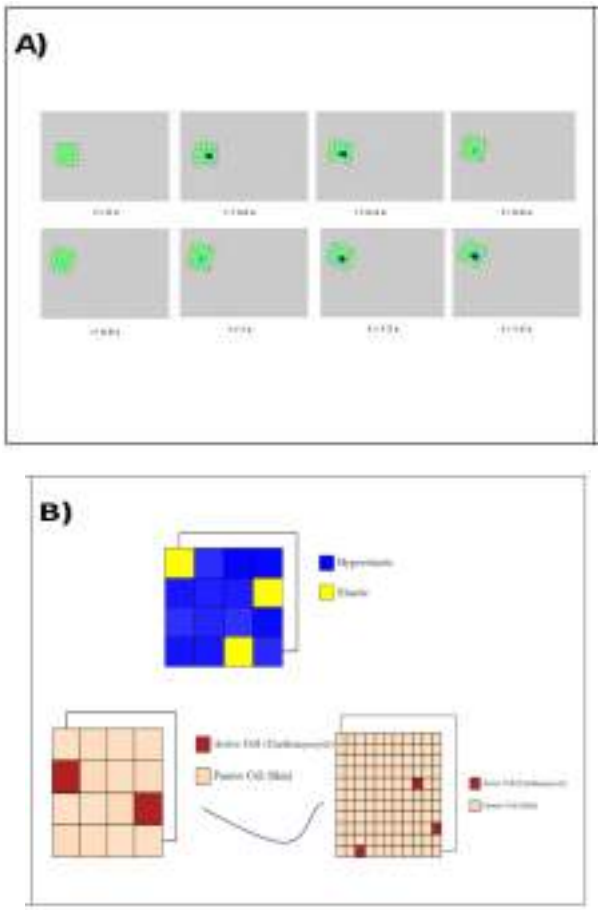

Figure 1: A: The time-dependent fluid-interaction simulation of a microswimmer in an aquarium. In this simulation, the [3,3] pixel is assigned as a myocardium cell, while the other pixels represent skin cells, characterized as passive- B.1: A representation illustrating the concept of selecting different material properties for microswimmer design: rigid, elastic, or Hyperelastic- B.2: We demonstrate the capability to transform the units of these squares from four-by-four to a thousand-by-a-thousand, allowing for the assignment of different configurations to achieve desired microswimmer behaviors for various destinations

Active Colloidal Metamachines

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Directional assembly of complex active architectures from colloidal motors consuming energy offers a promising strategy to operate the microscopic world, resembling life processes such as muscle contraction driven by the interaction between myosin and actin, and fueled by the hydrolysis of ATP.[1] However, precisely modulating the non-reciprocal interactions of different motors to create active colloidal metamachines with specific dynamic properties remains challenging.[2-4] Here, we report the shape-directed dynamic self-assembly of active colloidal metamachines by utilizing peanut-shaped TiO_2 colloidal motors and Janus spherical Pt/SiO_2 colloidal motors as basic agents. The anisotropic flow fluid dominated by peanut TiO_2 motors promotes Janus Pt/SiO_2 motors sequentially sensing, aligning and assembling, while the fluid flow from the passive SiO_2 face to the active Pt face affects their assembly sites. The coupling between motors' autogenetic fluid fields determines the configuration and self-propulsion of active colloidal metamachines, as depicted in components' shapes. These colloidal metamachines move along predetermined paths under structured light gradients. Such self-propelled colloidal metamachines with self-adaptive and interactive functions provide new strategy for fabricating active soft materials and intelligent robotic systems.[5]

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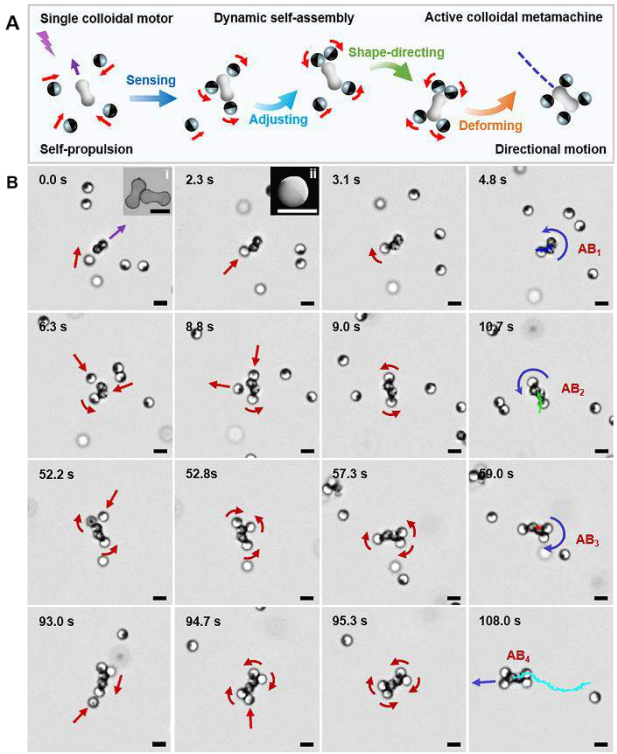

Figure 1. The shape-directed dynamic self-assembly process of two kinds of active colloidal motors, including sensing, adjusting, shape-directing and deforming. Schematic illustrations (A) and time-lapse images (B) show the dynamic self-assembly process of a peanut TiO_2 motor and multiple Janus Pt/SiO_2 motors. The insets of (B) are the transmission electron microscope image (TEM, i) of the peanut TiO_2 motors and the scanning electron microscopy image (SEM, ii) of the Janus Pt/SiO_2 motor, the former of which shows that the peanut TiO_2 motor is a peanut-shaped hollow shell and the latter shows that the Janus Pt/SiO_2 motor has two different sides. The purple, red, and blue arrows in figures show the motion direction of the peanut TiO_2 motor, Janus Pt/SiO_2 motor, and colloidal metamachines, respectively. Scale bar, 2 µm.
Active colloidal metamachines (ABn, n = 1~7) with self-propulsion, adaptive and interactive functions are manufactured by the shape-directed dynamic self-assembly of different types of active colloidal motors.

Massively Parallel Microbubble Nano-Assembly

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Microbubbles in aqueous suspensions have demonstrated vast applications ranging from pumping and mixing,[1-5] drug delivery,[6,7] and in the propulsion of micro/nanorobots.[8-11] However, it has been a formidable challenge to create large areas of individually addressable microbubble patterns. In this work, we report an opto-electrochemical method (**Figure 1**) for creating microbubbles on demand with controlled sizes ranging from a few microns to ~140 µm. The patterns can be formed in less than a second. The shapes include rings, squares, lattices as well as complex images (**Figure 2**). The required minimum light intensity (532 nm) of ~0.1 W/cm^2 is several orders of magnitudes lower than the state-of-the-art of optothermal/optoelectronic printing methods, which facilitates robust and large-scale bubble creation. We showcase the first rapid assembly and printing of nanocolloids into different patterns with light-addressed electrochemical microbubbles across millimeters with a spatial accuracy of ~2 µm. The technique is general and permits a wide spectrum of particles to be assembled from suspension, ranging from 40-nm silver nanocrystals, 200 nm polymer nanospheres, to 2-µm-E-coli bacterial cells. We also realize the first hybrid nanosensor-cell arrays, where plasmonic Ag nanosensors and bacterial cells are positioned in pairs to detect cells' metabolites (**Figure 3**). The reported advance opens new opportunities in particle assembly, nanomanipulation, nanomanufacturing, single-cell biotechnology, and optoelectronics.

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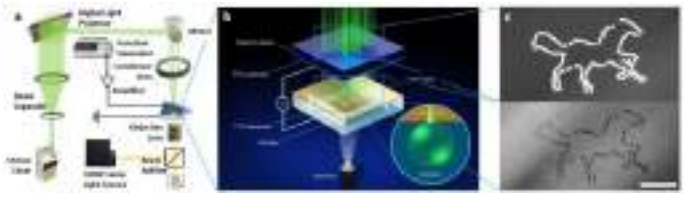

Figure 1. a) Schematic of the DLP device used for large-area bubble patterning. b) Close-up of the setup during bubble generation and subsequent particle patterning. c) Laser pattern of a horse (top) and corresponding bubble pattern (bottom). Scale bar: 100 µm.

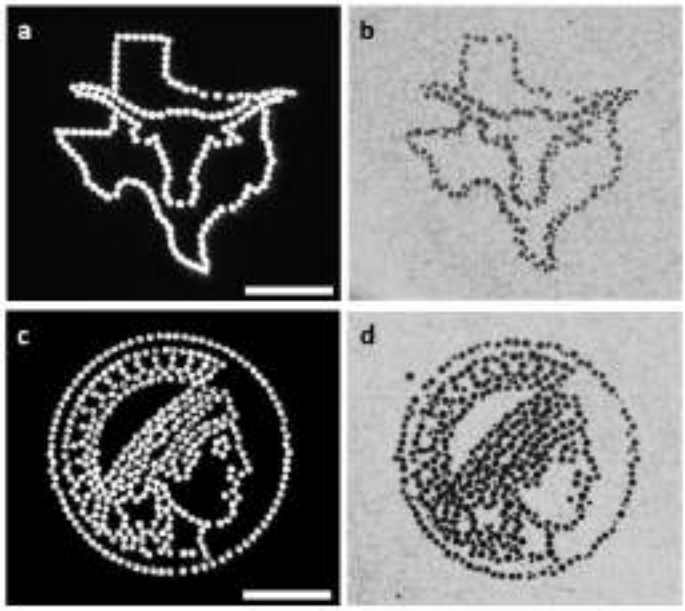

Figure 2. a) Laser profile and b) corresponding bubble pattern of a Bevo superimposed on the map of Texas (Bevo is UT-Austin's copyrighted logo). c) Laser profile and corresponding d) bubble pattern of the Max Planck Institute logo. Scale bars: 100 µm.

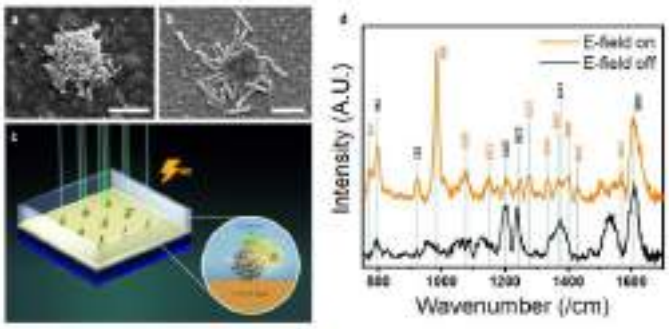

Figure 2. Assembly and SERS of Ag-nanoclusters with a precise co-localization of E-coli: SEM images of a) bubble-deposited assemblies of silver nanoparticle and b) E-coli cells. Scale bars: 1 µm, 3 µm, respectively. c) Schematic of E-coli attraction to bubble-assembled silver nanoparticle arrays via light-directed dielectrophoresis. d) Baseline-corrected SERS spectra with E-field on (in orange) and off (in black) of one Ag-nanocluster

from an assembly of 3 x 4 Ag-nanoclusters. Peaks labeled in orange font are from E-coli cells, those in black are from Ag nanoparticles alone.

Enhancing Nanorobot Propulsion with Single-Atom Catalysts

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Nanorobots receive great attention for their move-sense-and-act capabilities. Autonomous movement enables the micro/nanorobots to navigate within complex environments[1] and perform encoded tasks. Among the designs, chemically-powered micro/nanomotors can harness the catalytic power of enzymes that convert chemical fuels to motion. The motion is often induced by catalytic decomposition of the fuel, but the efficiency of fuel conversion of these nanomachines remains low. In the past decade, single atom engineering has demonstrated exceptional efficiency in catalysis, energy-related technologies, and medicine. Downsizing functional nanoparticles to single atoms[2] not only enhances catalytic activities and metal utilization efficiency but also facilitates the possibility of coupling cascade reactions in one confinement with structural simplicity[3]. In this study, we present a novel approach involving point defect engineering and the incorporation of single atoms and atomic level species onto the surface of dioxide-based nanomaterials. We investigate the impact of catalytic single atoms on the propulsion capabilities of nanorobots. Single atom decorated nanorobots demonstrated enhanced motion due to maximized catalytic effect of dispersed catalyst species. The developed nanorobots have demonstrated remarkable efficiency toward biomedical and environmental applications, offering promising advances in related technologies.

Figures

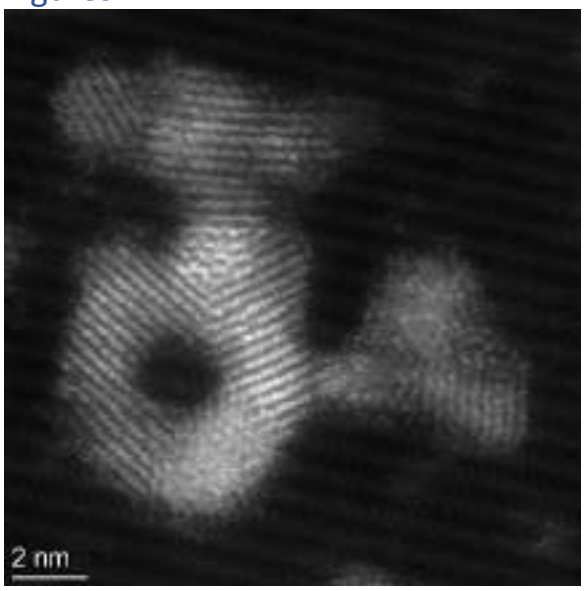

Figure 1. High-resolution STEM image identifying gold single atoms on cerium oxide support.

Acknowledgement

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Dynamics of Torque-Mediated Clustering in Self-Propelled Bimetallic Au-Rh Nanorods

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Self-assembly of elongated rod-shaped particles has attracted considerable attention across interdisciplinary research domains due to their potential applications in diverse fields[1-5]. In this study, we explore the intricate dynamics of nanorod assembly at miniature scales by investigating the clustering kinetics of self-propelled bimetallic gold and rhodium (Au-Rh) nanorods synthesized via template-assisted electrodeposition and driven by self-electrophoresis motion in hydrogen peroxide solution (H_2O_2)[6]. The synthesized Au-Rh nanorods, with dimensions 2-5 µm in length and 200-300 nm in diameter, exhibit self-propulsion at approximately 10 µm/s, with the rhodium end leading in dilute H_2O_2. An electroosmotic flow around the nanorods builds up, generating torque[7] in nearby tracer particles and other micromotors. Our experimental observations, complemented by Brownian dynamics and COMSOL simulation, reveal the remarkable phenomenon of tetratic clusters(see Figure 1) formed by self-propelled Au-Rh nanorods. At lower population densities(<0.1%), undisturbed wedge-shaped assemblies persist, facilitating the integration of individual nanorods into clusters through pairwise phoretic interactions[8]. Increasing the particle fraction, these clusters exhibit an alternating arrangement of parallel or perpendicular orientation, reminiscent of overlapping wedge shapes, and continue to evolve into larger, structurally consistent clusters dominated by a hydrodynamic torque (1.72×10-19 N·m) and an electrophoretic torque (5.43×10-20 N·m), both forming vortices in a way that facilitates a “wedge” shape dimer. Notably, clusters comprised of at least four bundles of nanorods aligned at 90-degree angles emerge as a common occurrence, particularly at higher fuel concentrations. Analyzing the dynamics of cluster growth reveals a two-phase process, with initial slow growth driven by pairwise interactions followed by rapid growth, eventually leading to stable non-motile clusters. Our findings suggest that cluster growth accelerates with increasing population density and activity, with stronger activity potentially leading to an earlier transition. As we commemorate the 20th anniversary of the first seminal work[9] in the field of self-propelled nanorod motors, our study contributes to advancing our understanding of torque-mediated clustering dynamics in bimetallic nanorod assemblies. These insights pave the way for designing and engineering functional nanomaterials with tailored properties and enhanced performance for diverse applications.

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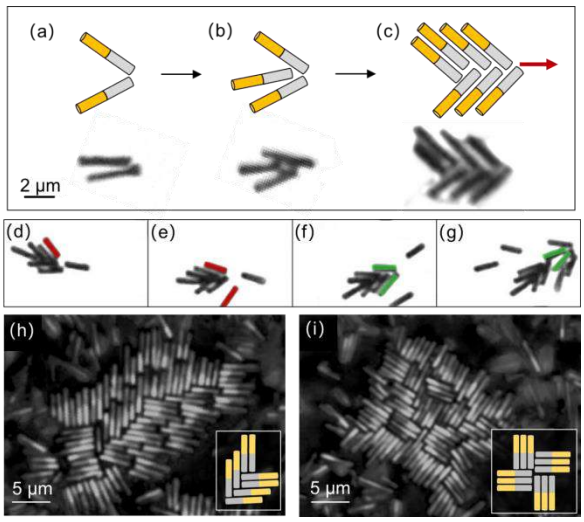

Figure 1. (a-c) Cartoon and microscopic images of cluster growth with Rh, represented by grey, and Au, represented by yellow color coding. (d-g) Dynamic clustering assisted by torque and hindered by drag is shown as the addition of (red) rods and (green) escape of nanorods. (h) Microscopic image of bidirectional tetratic cluster formed by nanorods at low fuel concentrations. (i). Microscopic image of quadrilateral tetratic cluster formed by nanorods at low fuel concentrations.

Dynamic Oscillation and Motion of Droplet Micromotors

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Abstract

Active droplets serve as suitable model systems for comprehending the intricate behaviors of living organisms.[1] The interplay of interfacial tensions on droplets manifests a spectrum of self-propelled motions that mimic those observed in living systems, providing a tuneable model for comprehending their complex non-equilibrium behavior. Oscillations and spontaneous shape deformations are fundamental features seen in nature but challenging to replicate in synthetic systems.[2] In this study, we demonstrate the occurrence of rapid oscillatory behavior in sessile oil-in-water emulsions. The characteristics of the droplet oscillation is contingent upon factors such as the nature and concentration of the surfactant, the chemical composition of the oil, and the wettability of the solid substrate.[3] Through side-view optical microscopy, we observe rapid changes in the contact angle per oscillation. We hypothesize that these changes stem from fluctuations in the interfacial tension of the oil droplets, driven by the surfactant's partitioning into the oil phase and the movement of self-emulsified oil out of the parent droplets, resulting in rhythmic variations in the droplet's contact line (as shown in Figure 1). The ability to regulate and comprehend droplet oscillation holds promise for modeling similar phenomena in non-equilibrium natural systems and reproducing biomimetic behavior in artificial systems, with potential applications spanning microfluidic lab-on-a-chip technologies and adaptive materials.

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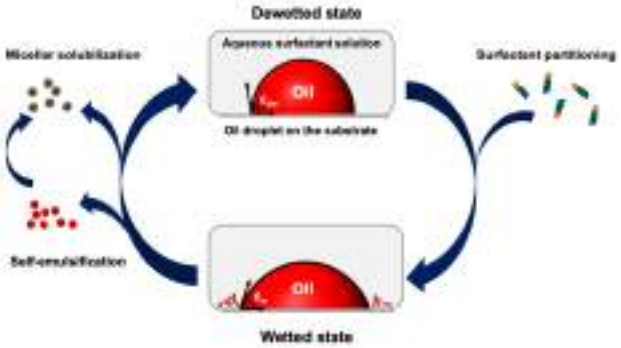

Figure 1. Schematic diagram of droplet wetting/dewetting as the mechanism for oscillation and motion.[1] The direction of motion depends on spontaneous symmetry breaking during the wetting step. The intersection of surfactant partitioning, spontaneous emulsification, and substrate wettability generates a unique type of motion, droplet oscillation, rarely reported in the literature for oil-in-water emulsion systems.

Active chiral microswimmer: emergent behavior of suspensions mediated by hydrodynamic interaction

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Abstract

The non-axisymmetric chiral squirmer [1], implemented within a Lattice Boltzmann code tailored for complex fluid dynamics [2], serves as a versatile tool to study the emergent behavior of microswimmer suspensions. Utilizing this model, we delve into the characterization of interactions between pairs of squirmers and explore their behavior in proximity to solid walls, as well as within the context of active chiral suspensions.

Our study encompasses a diverse spectrum of scenarios, ranging from individual interactions to more complex systems such as run-and-tumble dynamics, monolayers of rotors and rollers on walls, and beyond. By leveraging the capabilities of our computational framework, which solves the Stokes equations to accurately capture the hydrodynamics of active microswimmer suspensions, we gain insights into the intricate interplay of hydrodynamic forces, chirality, and confinement effects.

Through systematic simulations and analysis, we elucidate the mechanisms governing the interaction dynamics between non-axisymmetric chiral squirmers, unveiling emergent collective behaviors and patterns. Moreover, we investigate the influence of solid interfaces on the motion and orientation of squirmers, providing valuable insights into boundary effects in active suspensions.

Furthermore, our study extends to the realm of active chiral suspensions, where we explore the collective behavior and rheological properties of these systems. By characterizing the response of chiral squirmers to external stimuli and confinement, we contribute to a deeper understanding of the rich dynamics exhibited by active fluids.

In summary, our research advances the understanding of non-axisymmetric chiral squirmers in complex fluid environments, offering valuable insights into their interactions, behavior near solid interfaces, and implications for active chiral suspensions. These findings pave the way for future studies aimed at harnessing and controlling the dynamics of active microswimmers for various applications in fields such as microfluidics, biomedicine, and soft robotics.

Keywords: Non-axisymmetric chiral squirmers, Lattice Boltzmann simulations, complex fluids, active microswimmers, interaction dynamics, solid interfaces, active chiral suspensions.

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Figures

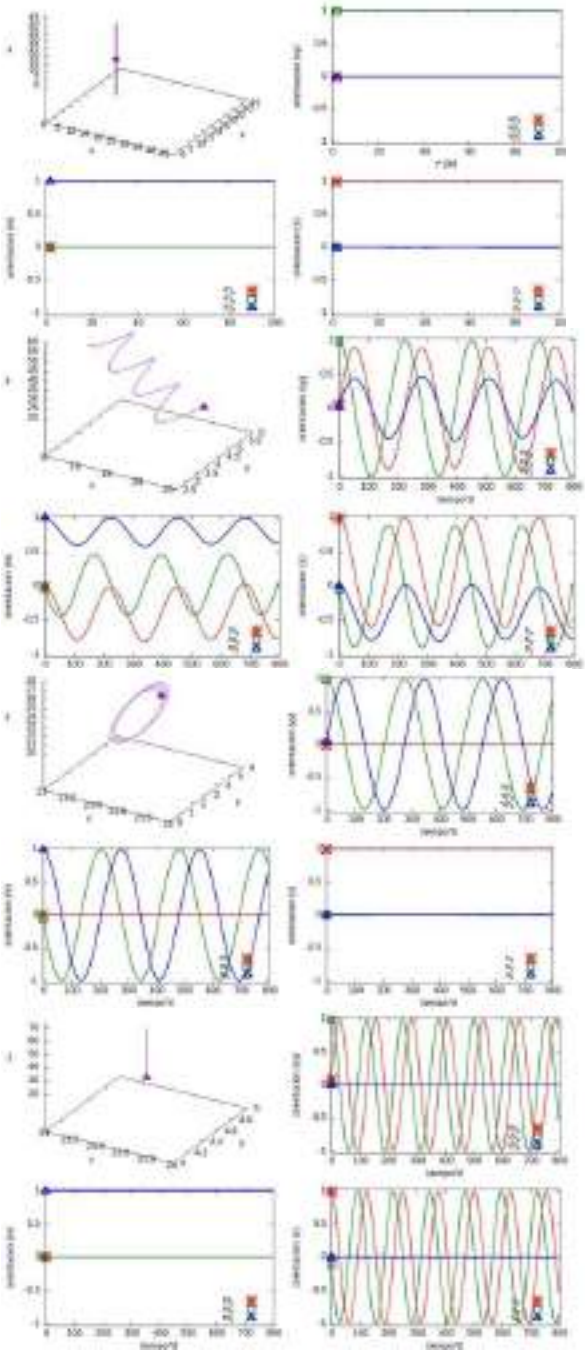

Figure 1. Types of swimming described by active microswimmers.

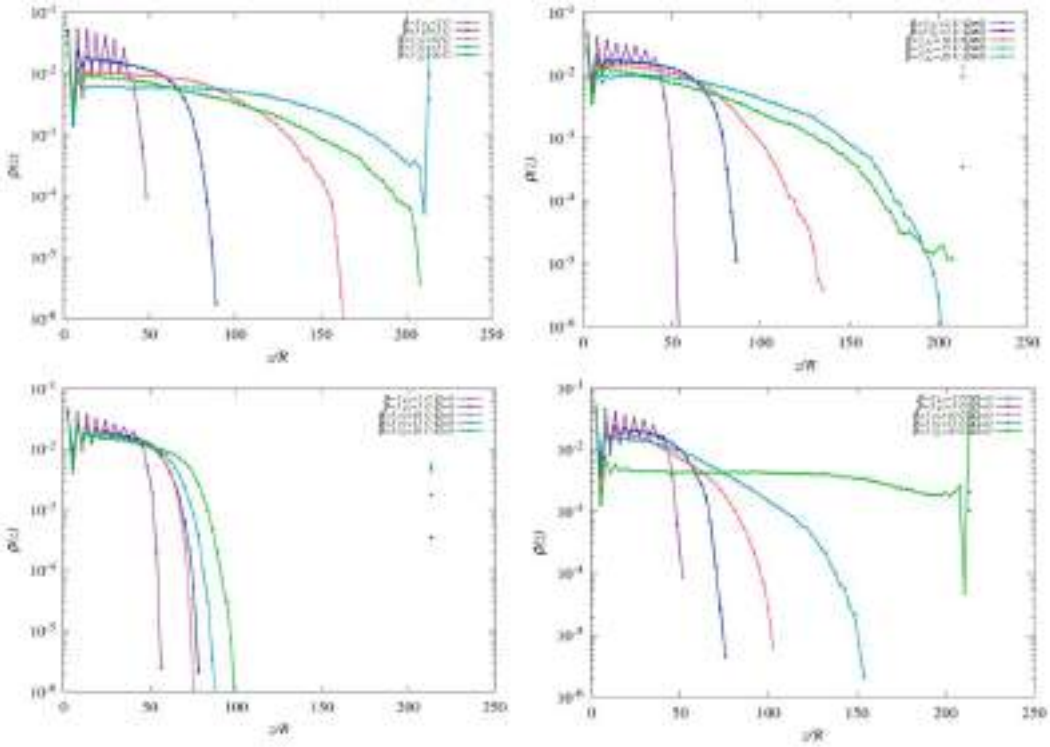

Figure 2. Density profiles of active run and tumble suspensions with different types of swimming.

Advancing Biomedical Frontiers: The Role of Nanobiosupercapacitors and Biocompatible Engines in Motile Microsystems for Enhanced Therapeutic and Targeted Drug Delivery

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The integration of microelectronics with biomedical applications has significantly advanced targeted drug delivery and diagnostic tools. The development of micro/nano motors, in particular, shows great potential in overcoming biological barriers and delivering therapeutic payloads with exceptional precision [1]. This abstract offers a detailed review of recent progress in motile microsystems [2], with a focus on the use of nanobiosupercapacitors (nBSCs) to overcome energy constraints and enhance performance for clinical applications.

Initial research by Mei and co-authors brought forward groundbreaking concepts for the use of self-propelled catalytic microengines [3]. Following studies have sought to improve the energy efficiency and control of locomotion to meet the complex requirements of biomedical applications [4]. A significant development we introduced is the integration of a square coil into a flexible polymer platform, which enables wireless energy transfer via inductive coupling. Additionally, the creation of bifunctional catalytic microengines facilitates localized heating and precise directional control, as demonstrated in Figure 1a. This electronic control of catalytic engines marks a pioneering advancement in the field of micro motors. The platform's ability to support onboard wireless energy also enables the integration of light-emitting diodes (LEDs) and a thermoresponsive micro-arm, crucial for performing grasp-and-release tasks in drug delivery systems.

Moreover, we present the development of nBSCs as a novel energy storage solution, occupying a minimal volume of 1/1000 mm³ (equivalent to 1 nanoliter) [5]. By employing biocompatible materials such as PEDOT:PSS and biological electrolytes derived from bull blood, along with a compact tubular geometry akin to biofluidic channels, this innovation proves the feasibility of incorporating an efficient energy storage system into real biological settings, thereby enhancing performance, as demonstrated in Figure 1b. This method not only tackles the energy limitations of traditional biomedical devices but also enables precise pH detection by monitoring capacitance changes. The integration of nBSCs in our systems ensures uninterrupted power, extending the operational range beyond that of wireless energy. Furthermore, we have developed an electrochemical twin-jet motile microsystem, proficient in water splitting (see Fig. 2). This system utilizes water as an actuation fuel, enabling traversal through diverse environment, including the human body, which comprises approximately 70 % water. The transition from conventional hydrogenperoxide (H_2O_2) chemical fuel to water renders this novel digitally controlled twin-jet microsystem fully biocompatible and environmentally sustainable.

The clinical implications of these advancements and the synergy between catalytic microengines and nBSCs have the potential to transform targeted drug delivery, enabling prolonged operation, supporting minimally invasive surgeries without the risk of toxicity, and enhancing diagnostic imaging capabilities by detecting variations in biological signals.

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Figures

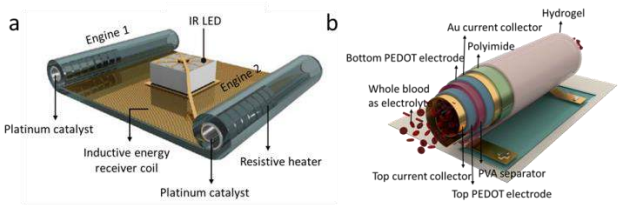

Figure 1. Schematic illustration of **(a)** the motile twin-jet-engine microsystem (MTJEMS) integrated with an IR-LED [4] and **(b)** the nano-biosupercapacitor (nBSC) with all active components [5]

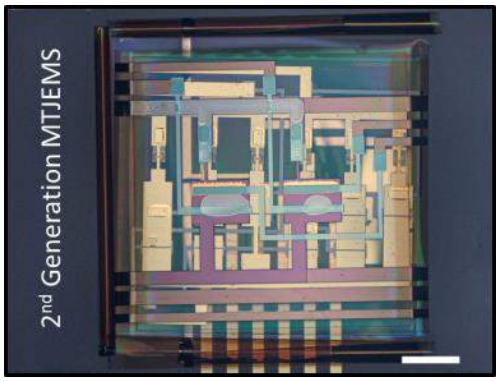

Figure 2. Microscope image of the second generation MTJEMS integrated with digital logic, wireless energy harvester, biocompatible energy storage system and an electrochemical twin-jet engines. Scale bar, 500 µm.

Magnetic controlled micro robot for targeted sampling of bronchial micro lesions

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Based on then ability to manipulate movements in complex biological environments, micro/nanorobots are anticipated to become a new tool capable of achieving controlled targeting for lung sampling, facilitating minimally invasive, high-precision sampling of small lesions in the lungs. However, research in this area is relatively limited. Currently, most studies primarily utilize external stimuli to achieve single manipulation and grasping actions. Aimed at the targeted sampling needs of small lesions in the early diagnosis of lung cancer, A cylindrical magnetic controlled sampling micro robot was constructed using two-photon laser printing technology, and a dual-mode motion strategy of clockwise rolling and counterclockwise sampling is achieved through magnetic field manipulation. Furthermore, under the guidance of medical imaging, controllable targeting and sampling of micro lesions in the lung tracheal environment are completed, ultimately achieving pathological detection of recovered sampled tissues.

Figures

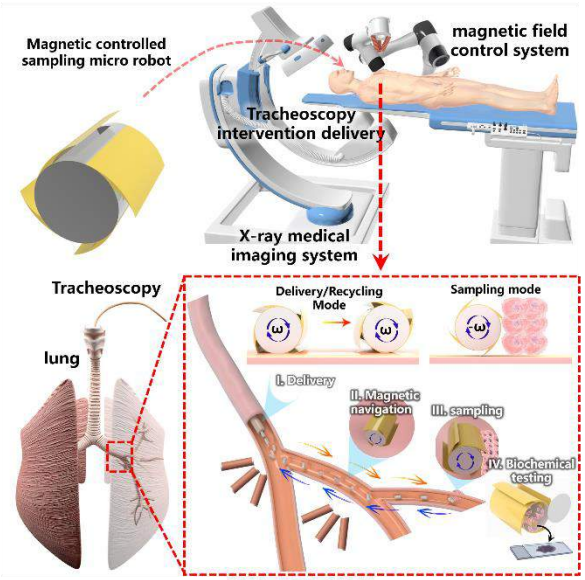

Figure 1. Schematic diagram of a lung sampling micro-robot

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Cuberdon-inspired microrocket for oral drug delivery

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Abstract

Oral administration of active pharmaceutical ingredients (APIs) is a preferred route of drug delivery. Compared to intravenous and intramuscular injections, oral drug delivery (ODD) is a more convenient, non-invasive, and well-obedience method for patients and does not require professional staff for administration. However, many APIs (e.g., protein/peptide drugs) typically have poor bioavailability and fail to induce a clinical response due to low mucosal permeability, low dissolved concentration in gastrointestinal liquids, epithelium layer barrier, and degradation in gastrointestinal environments before absorption [1]. Micromotors are miniaturized machines powered by external physical fields (*e.g.,* magnetic/ultrasound/light field), chemical fuels (*e.g.,* H_2O_2/H_2O/acid), and biological components (bacteria/microalgae). Taking advantage of their small size and unrestricted maneuverability, they could navigate through intricate and confined environments, leading to significant advances in fields such as biopsy, biosensing, precision drug delivery, and minimally invasive surgery. Among them, self-propelling micromotors are receiving much attention in ODD due to their drug-loading capacity, localized delivery, adherence to the mucosal matrix, and even penetrating the mucosa to attach or through the epithelial cells [2-4]. Here, we developed a Cuberdon-inspired microrocket (CIM) for oral drug delivery in the intestine. A two-step fabrication process was used to prepare the CIM in a PDMS mold, including casting the outer polymer layer (i.e., drug layer) and loading the inner fuel layer (*i.e.,* acetic acid and sodium bicarbonate). As shown in Figure 1a, the diameter of the CIM is 300 µm at the bottom, 25 µm at the top, and 800 µm high. The CIM showed a pink color as we currently use Rhodamine B as a model drug, which can be replaced by other drugs such as insulin, vaccines, antibiotics, etc. When CIM was placed in the PBS solution, the fuel part generated bubbles from the bottom and propelled the whole CIM structure (Figure 1b) with an average swimming speed of 1860 µm/s (about 2.3 times the body length). Figure 1c shows the time-lapse photos illustrating the swimming trajectory for 4 s, and the swimming direction could not be controlled at present. For further experiments, we will integrate magnetic particles into the CIM to navigate the movement along a defined path. After 60 s, the generation of bubbles stopped, indicating that the fuel part was exhausted, leading to the cessation of swimming behavior. In addition, the drug layer of the CIM was intact but with a deteriorating pink color as Rhodamine B was gradually released from the polymer (Figure 1d). In conclusion, we have developed a Cuberdon-inspired self-propelled microrocket that can be actuated in a biological environment in a biocompatible manner without producing any hazardous by-products and is a promising candidate for increasing the bioavailability of oral drugs by prolonging the retention time. In the following experiments, we will further characterize swimming performance, drug loading/release behavior, and delivery efficacy *in vitro* and *in vivo*.

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Figures

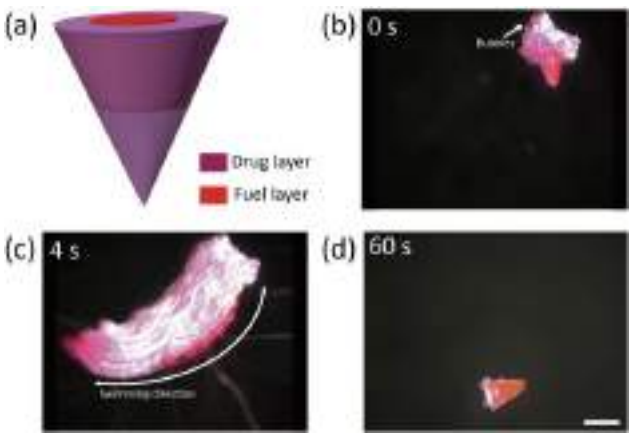

Figure 1. (a) The scheme of CIM. The pink part represents the drug layer, and the red part represents the fuel layer. (b) The morphology of CIM before swimming forward (0 s) and the bubbles generated by CIM. (c) The swimming trajectory of CIM within 4 s. (d) The morphology of CIM after stopping swimming showed a deteriorating pink color. Scale bar: 800 µm.

Glucose-Fueled Bienzyme Cascade Reaction-Powered Nanomotors for Efficient Treatment of Diabetic Wounds

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Micro/nanomotors, serving as an active delivery platform, show improved delivery efficiency compared to passive diffusion-based systems. However, they still pose challenges in applications of effectively treating diabetic wounds due to limitations in regulating complex and heterogeneous microenvironments on-demand. Here, we propose glucose-fueled nanomotors powered by bienzyme cascade reactions, operating at physiological concentrations, capable of targeted glucose reduction combined with comprehensive microenvironment regulation, and thus expediting diabetic wound healing. These nanomotors, composed of Janus dendritic mesoporous silica nanospheres modified with glucose oxidase and catalase, exhibit enhanced diffusion in ion- and protein-rich fluids containing few to tens of millimoles of glucose. They autonomously respond to endogenous glucose gradients and accumulate in hyperglycemic regions on-demand, such as interfaces between wound seepage and tissue, facilitating deep penetration. Consequently, efficient diabetic wound treatments can be achieved through targetedly consuming glucose combined with pH reduction, reactive oxygen species scavenging, and oxygen delivery by leveraging bienzyme cascade reactions. In vivo experiments demonstrate high treatment efficacy and biosafety, as evidenced by near-complete closure of wounds within 10 days without any observable organ damage or inflammatory lesions. This finding offers valuable insights into efficient management of diabetic wounds using nanomotors, which enable targeted and comprehensive regulation of wound microenvironment.

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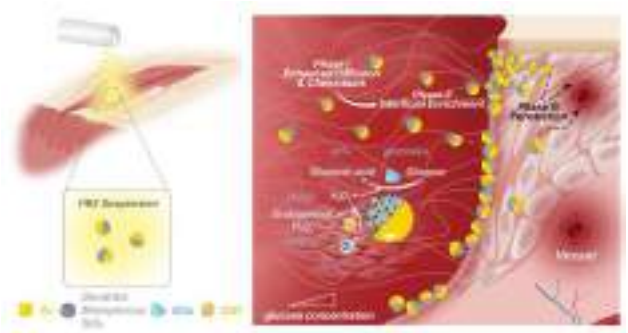

Figure 1. Schematic illustration of JNDMSNs nanomotors for efficient treating diabetic wounds through targetedly and comprehensively regulating the wound microenvironment. Fuelled by glucose within the wound microenvironment, the nanomotors perform effectively enhanced diffusion and autonomously respond to endogenous glucose gradients moving towards the regions with high glucose concentrations (Phase I). The enhanced mobility and unique chemotaxis contribute to their "on-demand" accumulation at the wound interfaces (Phase II), which facilitates the deep tissue penetration (Phase III). Moreover, the movement by taking advantages of GOx and CAT cascade reaction allows for the simultaneous reduction of glucose and pH levels, scavenging of reactive oxygen species and delivery of oxygen for targeted and comprehensive regulation of the diabetic wound microenvironment, thereby expediting the wound healing.

Light-responsive MXene Micromotors with controllable swarming motion

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Since the first development of $Ti_2C_3T_x$ MXene in 2011 [1], emphasis has been placed on the mechanical, physical, and optical properties of this class of two-dimensional inorganic compounds. Therefore, it has seen extraordinary exponential development in a wide range of applications such as cancer treatment, antibacterial agents, sensors, solar energy conversion, and supercapacitors, among others [2]. In this communication, we describe the combination of MXenes with micromotors towards controlled motion and enhanced propulsion, combining the remarkable properties of such material with enhanced fluid mixing.

Herein, ferrite@$Ti_3C_2T_x$ micromotors are synthesized by liquid phase exfoliation of Ti_2C_3Tx using an ultrasonic probe in the presence of ferrite. The use of the photothermal properties of ferrite@$Ti_3C_2T_x$ MXene as light-driven micromotor engines has been explored. In this way, the light-induced swarming effect, and the behavior of Ti_2C_3 MXene as a micromotor under UV and VIS light irradiation due to the photophoretic effect have been explored [3]. Different wavelengths of incident radiation were used: UV = 385 nm, blue = 475 nm, green = 550 nm, and red = 621 nm (see **Figure 1**). The dissipation of this energy induces a thermal effect due to the efficient thermal conversion of MXenes [4] that heats the surrounding media. The dissipation of the heat generates a hydrodynamic flow, and consequently, a self-thermophoretic motion as a swarm, which can be additionally controlled by a magnetic field.

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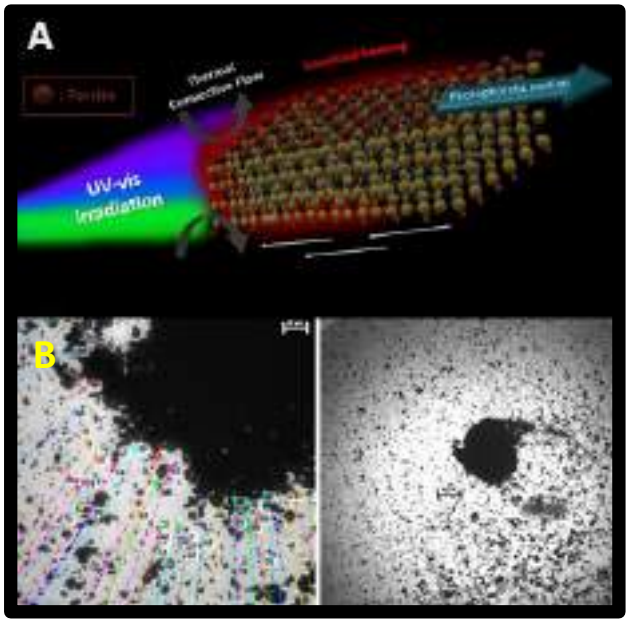

Figure 1. Photophoretic Ti_2C_3 nanocomposite-based micromotors with swarming motion. (A) Schematic of the proposed propulsion mechanism. (B) Tracking lines and swarm of Ti_2C_3 micromotors under 550 nm irradiation.

Mannosylated Supramolecular Nanomotors for Active Cancer Cell Targeting

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Active cancer cell targeting remains a promising strategy for utilizing biological nanomotors in the field of nanomedicine, particularly for precise cancer therapy. In this study, we introduce a novel nanomotor design, the mannosylated compartmentalized cross-linked enzymatic nanomotor (c-CLEnM), which exhibits specific and efficient targeting of Hep G2 cells through autonomous motion. To achieve this, biodegradable bowl-shaped stomatocytes were employed to encapsulate glucose oxidase and catalase within their nanocavity. A subsequent crosslinking reaction was performed to guarantee stable encapsulation, facilitating the autonomous motion of stomatocytes in the presence of glucose. Furthermore, the stomatocytes were modified with mannose glycopolymer, enabling binding with receptor overexpressed on Hep G2 cells. These mannosylated c-CLEnM operates with autonomous motion fueled by glucose, exhibiting speed acceleration and high targeting efficiency in the context of autonomous cell targeting within a short timeframe. Notably, this nanomotor demonstrates effective active targeting to the cancer cell with strong affinity, underscoring its potential for precise and enhanced cancer therapy.

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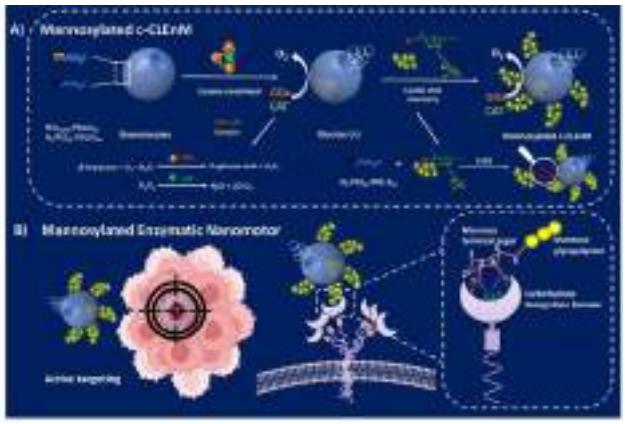

Figure 1. Schematic illustration of mannosylated compartmentalized cross-linked enzymatic nanomotor (c-CLEnM). A) Biodegradable copolymers self-assembled into stomatocytes, encapsulating catalase (CAT) and glucose oxidase (GOx), which were then crosslinked within the stomatocytes cavity. By modifying mannose glycopolymer on c-CLEnM, they achieved autonomous motion in glucose fuel. **B)** Mannosylated c-CLEnM exhibits active targeting to the cancer cell. The binding of c-CLEnM to carbohydrate recognition domain such as mannose-binding lectin (MBL) occurs through hexose sugars possessing hydroxyl groups in the equatorial position, thereby fitting into the binding pocket stabilized by calcium ions.

Construction of compartmentalized cross-linked enzymatic nanomotor (c-CLEnM)

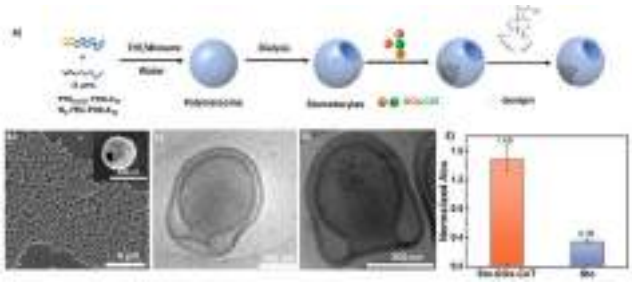

Figure 2. Preparation and characterization of crosslinked enzyme-driven nanomotor (c-CLEnM). A) Schematic illustration of supramolecular assembly of the c-CLEnM. B) SEM image of empty stomatocytes. C) Morphological characterization of empty stomatocytes using cryo-TEM. D) Cryo-TEM image revealing the structure of the c-CLEnM. E) UV-vis spectrum of empty stomatocytes and c-CLEnM.

Mannosylated nanotomor binding with Mannose binding lectin (MBL)

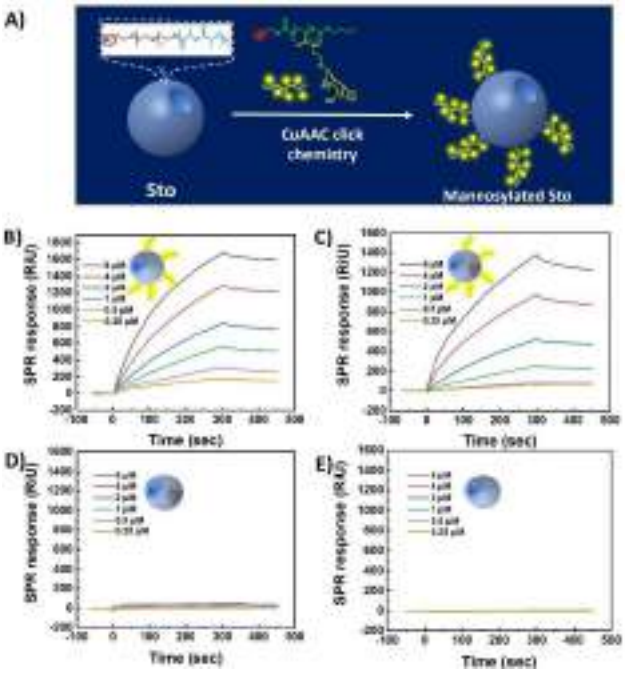

Figure 3. **Characterization of Mannosylated stomatocytes.** A) Schematic illustration of conjuagting mannose glycopolymer to the surface of stomatocytes. B) Surface plasmon resonance (SPR) analysis illustrating the binding of mannosylated stomatocytes with MBL C)SPR analysis demonstrating the binding of mannosylated c-CLEnM with MBL. D) SPR analysis showing the binding of c-CLEnM with MBL. E) SPR analysis showing the binding of empty stomatocytes with MBL.

Movement behaviors of c-CLEnM evaluated by calculating mean square displacement (MSD)

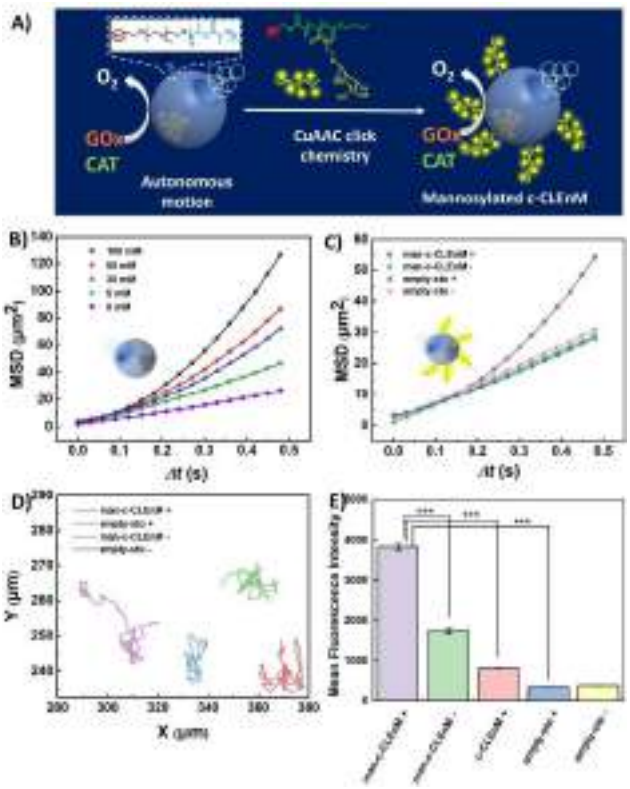

Figure 4. Motion behaviors of mannosylated compartmentalized cross-linked enzymatic nanomotor(c-CLEnM). A) Schematic illustrates the conjugation of mannose glycopolymer to c-CLEnM and the motion meachnism of motile behavior of c-CLEnM in the glucose fuel. Two enzymes, catalse (CAT) and glucose oxidase (GOx,) were encapsulated and crosslinked in the carvity of stomatocytes. Upon addition of fuel glucose, the mannosylated c-CLEnM exhibited autonomous motion. B) MSD of c-CLEnM as a function of a range of glucose concentrations. C) MSD of mannosylated c-CLEnM and empty stomatocytes were compared in the presence of glucose and in the absence of glucose. D) Representative tracking trajectories of mannosylated c-CLEnM and empty stomatocytes were observed in the presence of glucose and in the absence of glucose. E) Flow cytometry mean fluorescence intensities of Hep G2 cells treated with representative nanoparticles were measured (n=2).

Active cell targeting based on Specific Receptor-Dependent binding

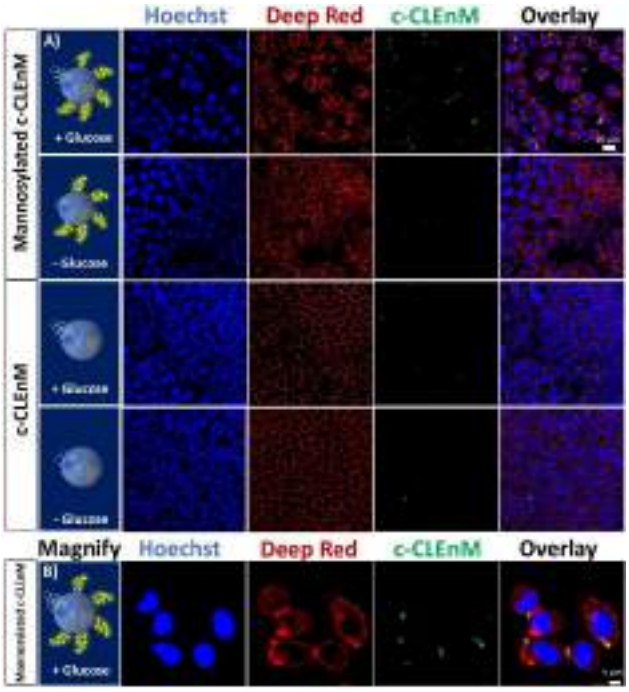

Figure 5. Evaluation of active cell targeting of mannosylated c-CLEnM using Hep G2 cells. A) CLSM images of Hep G2 cells incubated with mannosylated c-CLEnM and c-CLEnM for 2 h under conditions of presence or absence of glucose. The cells were stained with Hoechst 33342 and deep red, scale bar = 20 μm. B) Magnified CLSM images of Hep G2 cells incubated with mannosylated c-CLEnM for 2 h in the presence of glucose, scale bar = 5 μm. (+) : in the presence of glucose, (-) : in the absence of glucose.

Nanoengineered Motors for Targeted Pollutant Decomposition and SERS Monitoring

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Light-driven photocatalytic nanomotors possess the remarkable ability to propel themselves by harnessing external energy from the surrounding environment.[1] By integrating surface recognition sites, these photoactive motors can selectively capture and degrade persistent organic pollutants and pathogenic microorganisms.[2,3] The addition of plasmonic components to these multifunctional swimmers enables simultaneous monitoring of reaction mechanisms through Surface-Enhanced Raman Scattering (SERS).[4] This approach also tackles two significant challenges in SERS: selectively capturing target molecules to overcome matrix interferences using Molecularly Imprinted Polymers (MIP) and facilitating close contact between SERS probes and analytes within the detection area to enhance signals. This is achieved by leveraging the active motion of microswimmers, which exhibit positive phototaxis, guiding them toward the target location. In this study, star-shaped $BiVO_4$ micromotors are synthesized and subsequently coated with gold nanostars (Figure 1). The surface of the gold-coated nanostars is further modified by surface molecular imprinting with the selected target pollutant. Upon light irradiation, these micromotors effectively degrade organic pollutants such as methylene blue (MB) in a selective manner. Therefore, this study shows the potential of light-driven micromotors for the simultaneous monitoring and removal of water contaminants, contributing to their application in the environmental field and analytical chemistry.

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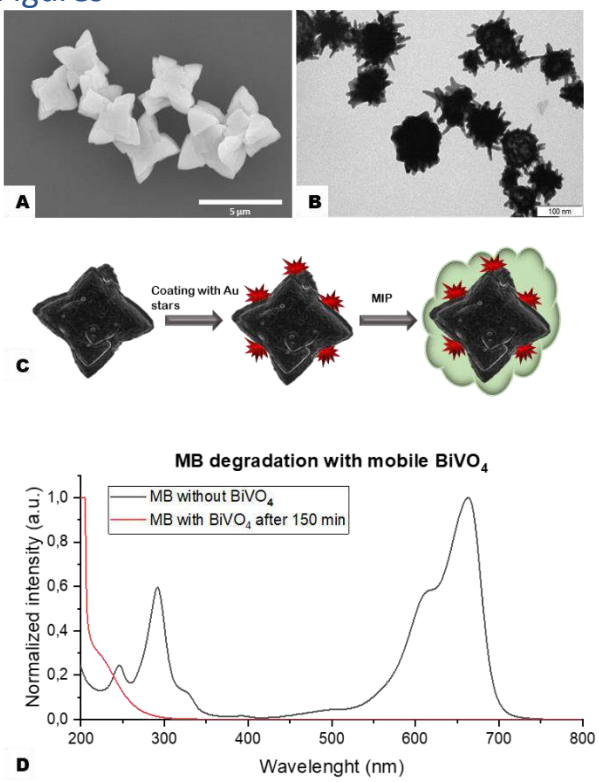

Figure 1. A) SEM image of the star-shaped $BiVO_4$ micromotors. B) TEM image of Au nanostars. C) Scheme of Au-coating and surface modification procedure. D) UV-VIS spectrum of the degradation of methylene blue by $BiVO_4$ micromotors in the presence of H_2O_2.

Microfluidic Design of Streamlined Alginate Hydrogel Motors with Run and Tumble Motion Patterns

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Autonomous nano/micromotors demonstrate remarkable advancements in biomedical applications. A noteworthy example is streamlined motors, which display enhanced movement efficiency with low fluid resistance. However, existing streamlined motors, primarily constructed from inorganic materials, present challenges due to their complex fabrication procedures and lack of a soft interface for interaction with biological systems. Herein, a novel design of biodegradable streamlined alginate hydrogel motors with a tear-drop shape by microfluidics is introduced. The platform enables the high-throughput fabrication of monodisperse motors with varied dimensions. By incorporating Pt-coated Fe_3O_4 nanoparticles, motors are equipped with dual capabilities of catalytic propulsion and accurate magnetic guidance. Through precisely tuning the localization regions of catalysts within the motors, the streamlined hydrogel motors not only exhibit enhanced propelling efficiency, but also accomplish distinct motion patterns of run and tumble. The design provides insights for developing advanced motors capable of executing intricate tasks across diverse application scenarios.

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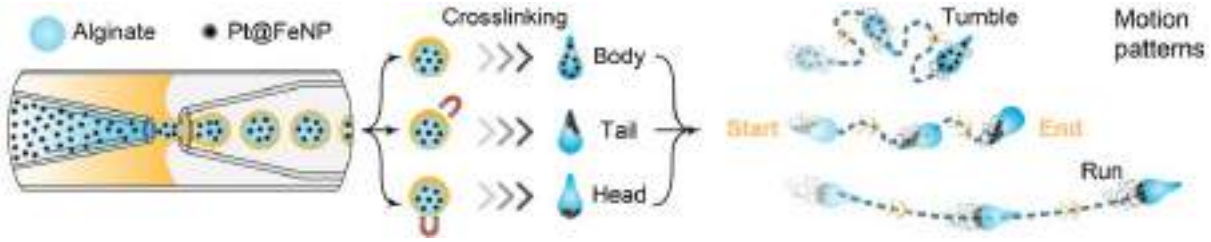

Figure 1. Streamlined alginate hydrogel micromotors with a teardrop shape by microfluidics are generated by microfluidics, enabling high-throughput fabrication of monodisperse micromotors with precisely varied dimensions. Tuning the localization regions of catalysts within the streamlined hydrogel micromotors enhances propelling efficiency and accomplishes distinct motion patterns of run and tumble.

Urease-powered Drug-loaded PLGA nanomotors as a new approach for Bladder Cancer Therapy

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Bladder cancer is the 7th most common cancer type worldwide, with more than 500.000 new cases and 200.000 deaths annually. Current bladder cancer treatments are limited by drug sedimentation and poor retention in the bladder, resulting in high recurrence rates and low long-term surveillance.

In recent years, nanomotors (NMs) have been developed as drug delivery systems for therapeutic agents. Nanomotors are self-propelled nanoparticles capable of moving by converting the chemical energy from the surrounding environment into mechanical propulsion. This motion allows nanomotors to avoid their sedimentation and significantly improve their internalization in bladder tumors *in vivo* compared to passive nanoparticles. However, the designs used so far present different limitations regarding clinical applications due to their inorganic chassis such as silica. Due to this, there is a need to develop new nanobots based on organic materials, which are more biocompatible, biodegradable and FDA-approved.

In this study, we developed a new design of nanomotors based on poly(lactic-co-glycolic acid) (PLGA) for the delivery of Mitomycin C (MMC), the standard of care for bladder cancer.

PLGA nanoparticles loaded with MMC were synthetized by the double emulsion method, obtaining a loading efficiency of 50% and a polydispersity index (PDI) of 0.1. After that, drug-loaded nanoparticles were functionalized with urease by first coating them with polyethylenimine (PEI) to gain a positive layer and then adding glutaraldehyde (GA) as linker for the enzyme attachment. The drug loading did not show a significant effect on the nanomotors' polydispersity and neither nanomotor enzymatic activity nor motion, when comparing drug loaded and non-loaded PLGA nanomotors.

Finally, drug loaded PLGA nanomotors treatment efficacy was assessed by evaluating the viability of bladder mice carcinoma cell line (MB49) compared to passive nanoparticles and free drug.

First of all, the benefits of the nanomotor's movement were demonstrated by the significant reduction on the number of viable MB49 cells in samples treated with drug-loaded nanomotors compared to drug-loaded passive nanoparticles. Additionally, drug-loaded nanomotors showed a faster therapeutical effect compared to the free drug, with an important decrease on the viability of MB49 cells after only 1 hour treatment with MM-C-loaded nanomotors.

From these results, we can conclude that PLGA urease-powered nanomotors are promising nano-systems for drug delivery that could be used as a new approach for bladder cancer treatment.

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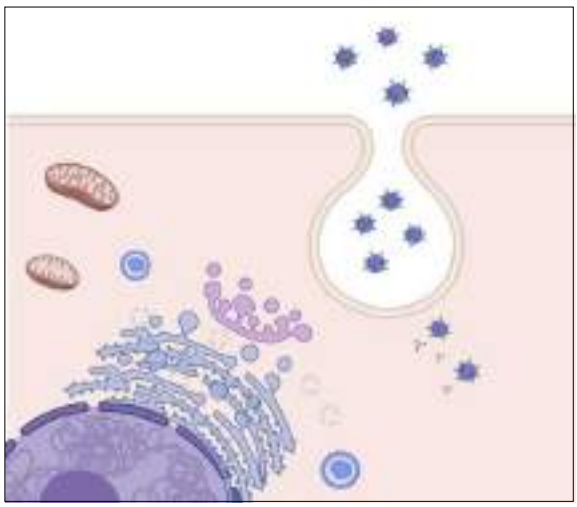

Figure 1. Scheme of the internalization and drug release of MMC-loaded PLGA nanomotors into bladder cancer cells.

Motion Dynamics and Performance of Photoactive Nanomotors inside Microreactors

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Two decades have elapsed since the first generation of self-propelled nanomotors, marking the onset of an expansive exploration within this field. This period has witnessed the synthesis of a diverse array of nanomotors, characterized by variations in materials, shapes, sizes, and propulsion mechanisms [1]. However, with this rich diversity comes a host of new challenges and fundamental inquiries, particularly concerning practical applications. Research in nanomotors is primarily directed towards drug delivery, pollutant degradation, sensing, and other areas requiring thorough investigations. These domains require comprehensive examinations into dynamics within confined spaces characterized by diverse obstacles and geometries such as spheres, channels, and pores [2-4]. Here, we investigate the capabilities of light-driven nanomotors to keep functioning within a silica-based spherical matrix. Moreover, we delve into the impact of confinement on the photocatalytic efficiency and motion behaviors of various types of nanomotors. Consequently, this study represents a novel "lab-in-a-drop" approach, coupled with the inherent advantages of self-propulsion. This, in turn, paves the way for exploring new frontiers in understanding nanomotor behaviors within confinement and unlocking their potential applications in biomedicine, sensing, and environmental contexts.

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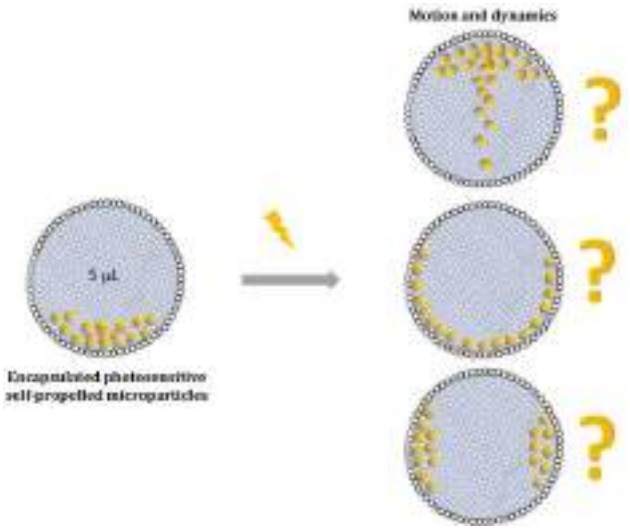

Figure 1. Scheme of nanomotor behaviour inside a spheric confinement made of silica nanoparticles.

From Vision to Control: Developing Advanced Imaging Systems for Microrobotics in Healthcare

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Microrobots present significant potential to revolutionize healthcare by enabling minimally invasive procedures, precise drug delivery, and assisted fertilization at the microscale [1]. However, navigating complex biological environments poses considerable challenges, especially in imaging and control [2]. Addressing these challenges necessitates the development of a universal computer vision solution compatible with existing hospital imaging modalities, as effective microrobot control is contingent upon accurate visual perception.

State-of-the-art imaging modalities are primarily limited to ultrasound [3] and photoacoustic imaging [4]. In light of these considerations, our current focus is on enhancing visual feedback for the closed-loop control system. We have developed a methodology to accurately extract data on microrobot position and orientation from each frame. Utilizing Optical Flow, we track microrobot motion as observed by US, while artificial videos simulating helical microrobot motion are employed for algorithm refinement and training deep learning models (Figure 1i, ii).

Furthermore, we have integrated a Rotation Frequency Extraction Module with the motion tracking and deep learning systems (Figure 2i, ii). This module utilizes a helical robot adorned with reflective materials to capture distinctive patterns in PA imaging, which correspond to the robot's rotational frequency. As the robot rotates, the reflective materials produce two distinct shining areas indicative of rotational frequency. These points are utilized to reconstruct the robot's geometry, even within visually challenging environments.

Beyond mere localization, our integrated approach empowers us to map the surrounding environment by reading changes in the robot's frequency of rotation. The robot's resonant frequency, influenced by excitation frequency, geometry, and hydrodynamic pressure, becomes a key indicator of environmental conditions. Our simulations demonstrate the system's capability to respond to different conditions, such as the decrease in angular velocity as the robot approaches a block (Figure 3, 4). By systematically analyzing motion, object, and frequency in US/PA frames, our approach promises to overcome current limitations in accurately extracting microrobot position and orientation, thus providing essential feedback to the control unit.

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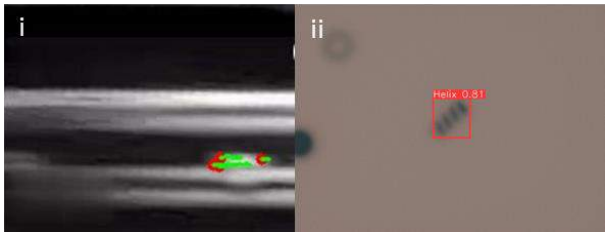

Figure 1. i) Robot localization by optical flow and ii) simulation of micro-helix motion to train the deep learning model

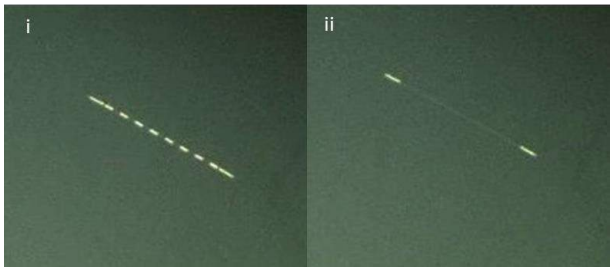

Figure 2. shining area variation over a cycle of rotation as an indicator of frequency of rotation i) maximum appearance ii) minimum appearance

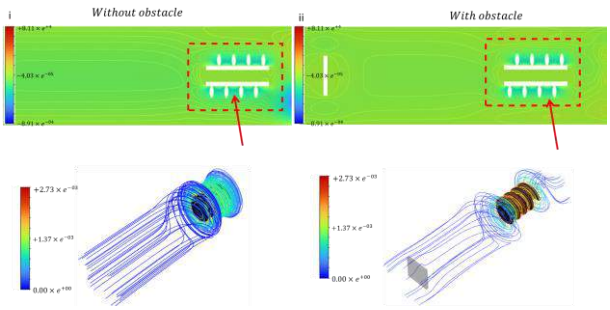

Figure 3. CFD simulation showing flow streamlines around helix, color maps indicate helix' z-velocity i) Open fluid without obstacle ii) in the presence of a block

Visible Light driven $BiVO_4$/MXene microrobots for Environmental degradation

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Advancements in light-driven microswimmers have marked a significant milestone in the utilization of solar energy for environmental applications, particularly in water remediation. In this work, bismuth vanadate ($BiVO_4$) microswimmers, varying in shape and size, have been successfully fabricated using a straightforward, quick, and surfactant-free microwave-assisted method. We demonstrated that the morphology of these $BiVO_4$ microswimmers could be fine-tuned by modifying the pH, the concentration and type of the base, and the temperature during synthesis. The photocatalytic capabilities of these microswimmers were evaluated by their effectiveness in degrading emergent pollutants under visible light. Remarkably, their photocatalytic performance was significantly enhanced when $BiVO_4$ was combined to form a heterojunction with MXene, attributed to MXene's role in improving visible light absorption, facilitating charge regeneration, and reducing the recombination rates of electron-hole pairs. This research lays the groundwork for developing cost-efficient and highly effective BiVO4-based microswimmers, offering a promising solution for large-scale water purification using solar energy.

Acoustically Actuated Microneedles for Oral Drug Delivery

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Acoustic manipulation of particles has been extensively investigated in a variety of fields. For example, within the areas of microfluidics and biomedicine for the trapping and guiding of particles and cells. Recently, due to its non-invasive nature, the use of ultrasound as a method of manipulating particle movement for human drug delivery has been investigated. [1] The streaming effects on microswimmers with an encapsulated air bubble shows a relatively fast motion which can be directed with the help of magnetic field and is one interesting field in this area. [2] Separately, a variety of microneedle (MN) structures for drug delivery in the gastrointestinal tract have been researched. For these, drug delivery is ordinarily accomplished by mechanical forces within the gastrointestinal tract, such as peristalsis or spring-release mechanisms within the device itself. [3-4] In this work, we combine the idea of a MN with the concept of microswimmers, to produce a MN capable of locomotion by ultrasonic stimulation. The purpose being non-invasive delivery of pharmaceuticals to the close vicinity of the epithelium in the small intestine. In a one-step process, we fabricate MNs with a base diameter of 300 µm, top diameter of 25 µm and a height of 800 µm. The inner cavity is a capsule shape with a length of 350 µm and width of 150 µm. For a visual representation, see Figure 1a. The composition of the MNs consists of a hydrophobic polymer to allow for easier encapsulation of the air bubbles. According to previous research, the air bubble should theoretically experience three distinct forces: a primary Bjerknes force, a streaming propulsive force and a secondary Bjerknes force, of which the streaming propulsive force will be largest in the absence of a rigid boundary. [2] To characterize the motion, a MN was stimulated using a piezoelectric disc (CTS Ferroperm) attached to the side of a cuvette (Figure 1b) and observed under a microscope at 5x magnification. The piezoelectric disc was connected to a signal generator (Agilent 33220A), generating a sine wave at 225 kHz and at 10 V_{p-p}, which is the maximum output voltage of the signal generator. The MN (Figure 1c) travelled 1670 µm and had an average velocity of 783 µm/s in the direction of the ultrasonic wave. This is equivalent to a speed of 0.98 body lengths/s assuming the body length as the height of the needle structure. Curiously, the MN oriented itself with the needle tip towards the cuvette wall before colliding with it (Figure 1d), which is likely due to secondary Bjerknes forces. This could be a valuable feature during further trials to achieve a drug release through the mucus layer present within the small intestine. The directionality of the motion is not fully determined, however. For future trials, MNs with incorporated magnetic particles will be investigated to see whether this can enhance the directionality of the motion. The material composition of the MN will be modified and quantitative measurements of drug release from the MNs will be done. With a well optimized system, the MNs could bypass the low pH environment in the stomach and then be ultrasonically actuated to localize in the mucus layer of the small intestine allowing for the release of pharmaceuticals close to the intestinal epithelium, increasing the drug uptake of macromolecules. Furthermore, the system could allow for localized treatment of GI-tract diseases such as intestinal cancer. Additional studies would also have to be conducted to determine the effect on epithelial tissue around injection.

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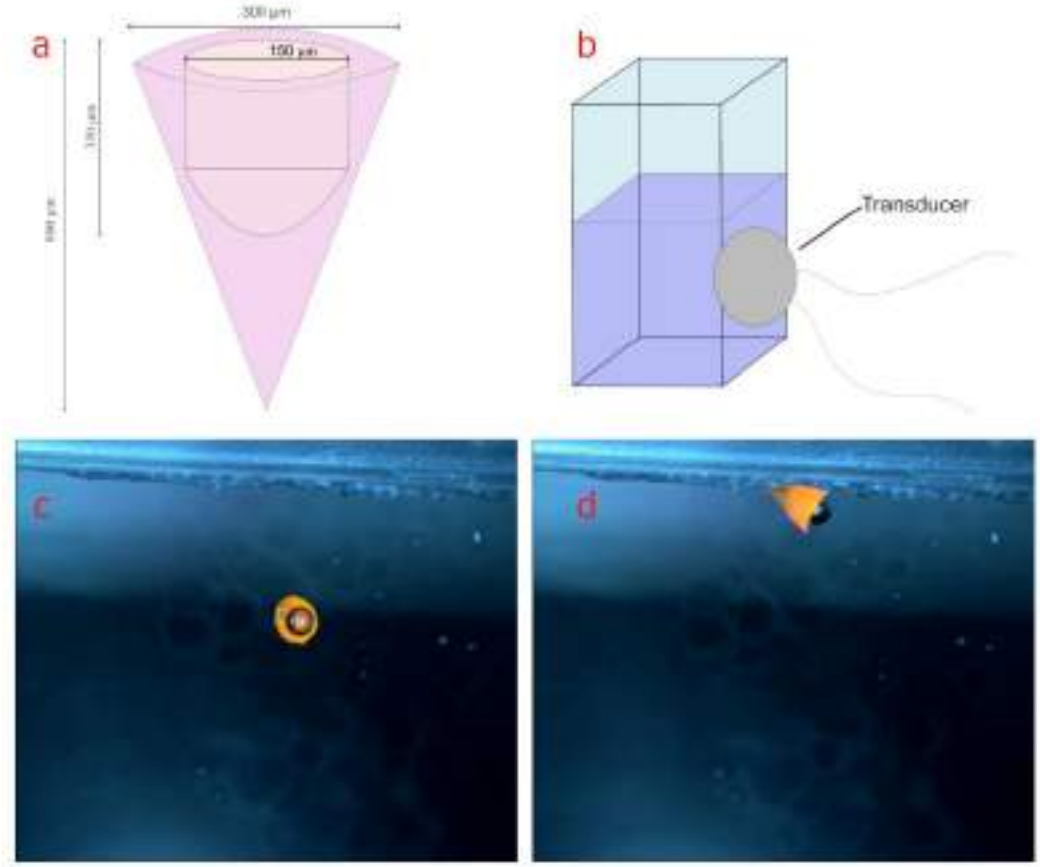

Figure 1. a) A schematic of the MN structure with the cylindrical air cavity in the middle. b) The setup used for ultrasonic stimulation. c) An image of a needle with the air cavity facing towards the microscope indicates the presence of an air bubble. d) The same needle after 2s of ultrasound stimulation at 225 kHz and 10 $V_{p\text{-}p}$.

RADIOPAQUE NANOROBOTS FOR LOCALIZED IMAGING OF THE GASTROINTESTINAL TRACT

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Magnetic nanorobots offer unprecedented access to hard-to-reach areas of the body for targeted diagnosis and therapy [1]. Though magnetic nanorobots require imaging-based guidance to reach target areas, it is challenging to detect the nanorobots under *in vivo* settings [2,3]. Here, we demonstrate the utilization of microcomputed tomography (microCT) for imaging magnetic nanorobots localized in the gastrointestinal (GI) tract of mice. The nanorobots consist of a contrast agent, barium sulfate ($BaSO_4$), decorated with magnetite (Fe_3O_4) nanoparticles. The presence of Fe_3O_4 nanoparticles allows magnetic actuation of the nanorobots in a microfluidic channel used to simulate confined areas of the body. The nanorobots' intrinsic radiopacity reveals the microfluidic channel's internal structure by X-ray contrast. Additionally, microCT scans of mice demonstrate the nanorobots' localization in the GI tract, indicating the effective magnetic response of the nanorobots even in the presence of natural peristaltic movements. The findings highlight the competence of imaging modalities based on X-ray to detect nanorobots that can be used as mobile robotic contrast agents for comprehensive examination of inner body parts.

Acknowledgements

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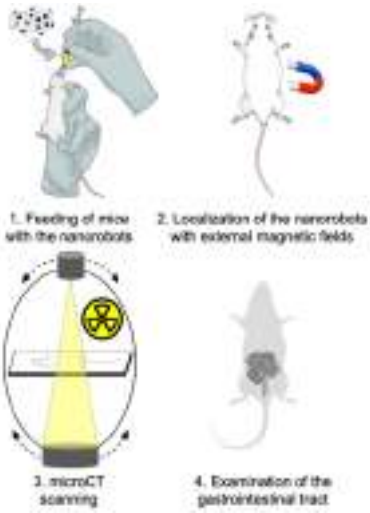

Figure 1. Localized imaging of the GI tract via $Fe_3O_4/BaSO_4$ nanorobots.

Biohybrid microrobots for sustainable removal of micro/nanoplastics

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The proliferation of micro/nanoplastics derived from the fragmentation of plastic waste released in the environment represents an increasingly alarming issue with adverse implications for aquatic ecosystems worldwide.[1, 2] Conventional approaches for mitigating such contamination are inadequate in removing plastic fragments with exceptionally tiny sizes.[3, 4] Therefore, it is highly urgent to develop efficient strategies to address the threats posed by micro/nanoplastics. Here, we demonstrate biohybrid microrobots that integrate the magnetic properties of Fe_3O_4 nanoparticles for the dynamic removal of micro/nanoplastics from various aquatic environments via high-precision magnetic actuation and reliable electrostatic interactions. After the surface decoration with Fe_3O_4 nanoparticles, algae cells can achieve precise locomotion and wireless manipulation by regulating an external magnetic field. Taking advantage of this active movement, magnetic algae robots (MARs) display considerable capture and removal efficiencies for micro/nanoplastics in water with extensive application scenarios. The reusability of MARs was also investigated, proving great recyclable performance. The growth and cell viability experiments elucidate that the presence of Fe_3O_4 nanoparticles may result in hormesis stimulation of algae growth. Such recyclable microrobots with eco-friendly and low-cost characteristics offer an attractive strategy for sustainably tackling micro/nanoplastics pollution.

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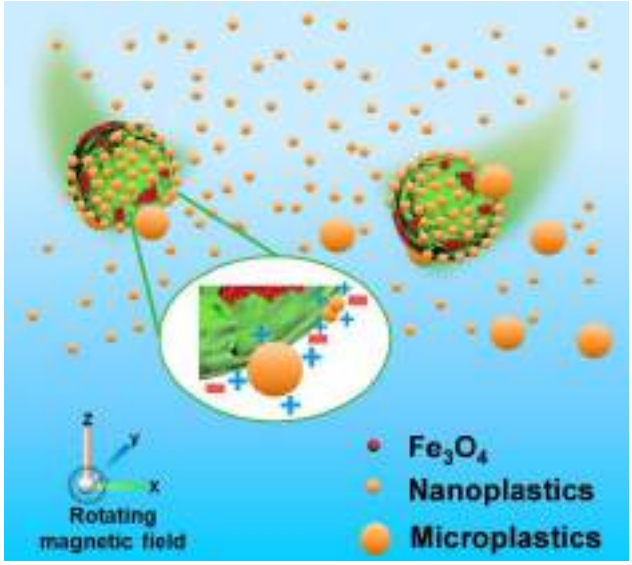

Figure 1. Utilizing magnetic actuation and electrostatic interactions, MARs facilitate the removal of micro/nanoplastics from water by drawing them to their surface.

Acknowledgements

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Soft Self-assembled Nanomotors: Unveiling Cilia-Like Motion through Photoisomerization

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Interest in leveraging nanoparticles for drug delivery systems is rapidly increasing. Polymeric nanoparticles, in particular, offer a soft interface between the particle and its biological environment, enhancing compatibility and functionality . Beyond their primary role in drug delivery, these versatile particles also open avenues for studying biological systems under precisely controlled conditions. This dual capability not only advances therapeutic strategies but also enriches our understanding of biological processes at the molecular level.

Our research group developed many strategies for the design of soft anisotropic nanomotors via a bottom-up self-assembly approach, utilizing chemical energy and a variety of catalysts for propulsion [1]. In this study, we explored the use of photoisomerization of azobenzene as an alternative propulsion mechanism for PEG-PS stomatocytes, deviating from the traditional catalyst-driven approach [2].

While we observed motion in the resultant nanomotor, understanding the underlying mechanism posed a challenge. Potential contributing factors, including the Marangoni effect and mechanical force from photoisomerization, were explored [3, 4]. Through meticulous control experiments aimed at isolating these influences, we determined that the motion of these particles closely resembles the ciliary motion observed in bacteria.

This finding not only advances our understanding of nanoscale motion but also paves the way for the development of more biomimetic nanomotors. Such systems hold promise for elucidating the fundamental requirements for nanoscale motion and could open avenues for creating life-like nanomotor designs.

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Figures

Figure 1. i: PEG-PS block copolymers undergo co-assembly with amine-functionalized PEG-PS through a solvent exchange process. ii: Addition of PEG to the polymeric vesicle induces its transformation into a stomatocyte structure. iii: The photoswitchable unit is conjugated to the vesicle membrane utilizing HOBT and, culminating in the formation of the final nanomotor.

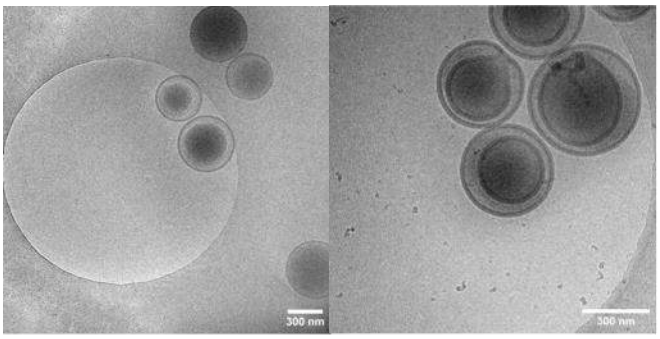

Figure 2. In the first panel the polymeric vesicle can be observed after self-assembly. In the second panel the stomatocyte shape can be seen after shapetransformation.

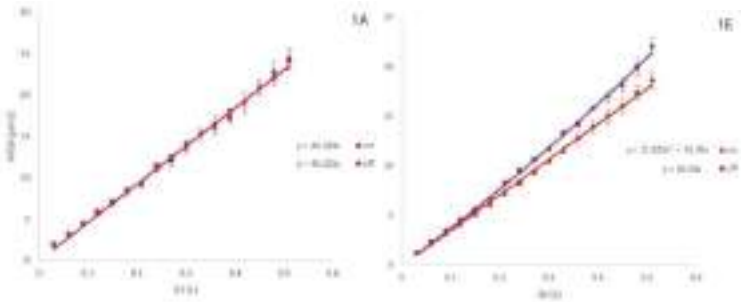

Figure 3. In Panel 1A, the stomatocyte is depicted both with (purple) and without (red) irradiation, in the absence of a photoswitchable molecule. Under these conditions, no enhanced motion is detected. Conversely, Panel 1E showcases the same particle, this time with azobenzene conjugated to its membrane. Following irradiation, a noticeable enhancement in motion is observed.

Exploring the Movement of Enzymatic-PLGA Nanobots in Human Skin Models

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Nanobots have brought wide attention as the next generation of vehicles for drug delivery.[1] Their active motion and especially collective behavior have shown an enormous advantage in terms of movement in complex medias,[2] overcoming biological barriers[3] and enhancing tumor penetration[4] not only *in vitro* but also in *in vivo* studies.[5] Nevertheless, there is a general concern about the side effects associated to the composition of the most extended nanobot designs, which may hinder their clinical applications. Therefore, there is still the need to develop a simple and biodegradable enzymatic nanobot based on organic materials, which would be more appealing for industry and clinicians.

Here, we present the design and characterization of a new kind of nanobot based on (poly(lactic-co-glycolic acid) (PLGA), an FDA-approved material already used in clinics.[7] By conforming a positive layer of polyethylenimine (PEI), glutaraldehyde chemistry was used for functionalizing their surface with urease, resulting in PLGA-PEI-Urease Nanobots. By incubating these nanobots in different biological environments we have studied for the first time the differences on the degradation profile of passive and active nanobots based on enzymatic propulsion. After one week, PLGA-PEI-Urease nanobots showed some degradation in an aqueous media, and interestingly, their degradation rate increases as the pH varies during the catalytic reaction of active nanobots. The basic pH of the products of the reaction enhances the degradation of PLGA nanoparticles and PLGA-PEI-Urease nanobots.

In order to explore the safety and potential of PLGA-based nanobots as drug delivery platform, their biocompatibility and penetration in skin models were tested. Skin is the largest organ in the body, representing a promising target site as it offers a minimally invasive administration route, but also a significant challenge due to skin natural defensive function, conforming a formidable chemical and physical barrier.[6] *In vitro* models of epidermis and dermis were developed using neonatal Human Epidermal Keratinocytes (HEKn) for mimicking a full epidermis, while neonatal Human Dermal Fibroblasts (HDFn) were cultured in a 3D fibrin matrix. The movement and distribution of PLGA-PEI-Urease nanobots with and without the presence of fuel on the dermal and epidermal model were explored to study how far and deep do nanobots go in skin and how do they interact with the skin cells and the different biological environments present in native skin. Firstly, biocompatibility of PLGA-PEI-Urease nanobots was assessed in a 2D culture of HDFn, with non-toxicity observed. Regarding our studies in dermal models, we have observed how active nanobots in presence of fuel (urea) are able to expand and penetrate significantly more in a 3D fibrin matrix. Now, the same experiments will be carried out in a 3D dermal model with HDFn.

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Figures

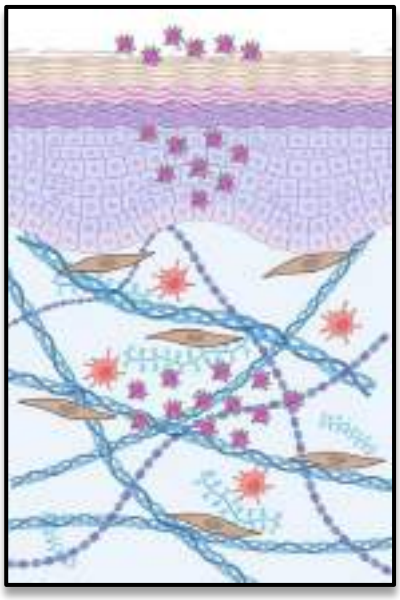

Figure 1. Graphical abstract of nanobots in skin

Computer Vision for Swarming Analysis

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Nanobots interact with the environment and with each other, developing a coordinated collective motion known as swarming behavior [1]. This behavior is especially relevant in biomedicine, as it can have applications in targeted drug delivery [2]. In this context, one of the most important characteristics of this phenomenon is the area covered by the swarm of nanobots, which can be recorded using microscopical imaging systems. Over the last few years, different approaches for analyzing swarming recordings have been developed, mostly based on algebraic methods [3]. However, computer vision has recently emerged as a promising tool for video analysis [4].

Thus, the aim of this work is to compare algebraic (AM) and computer vision (CV) based methods for analyzing the area covered by swarming nanobots.

For this, an AM-based software [3] for swarming analysis and a custom CV-based code developed in Python were considered. To validate and test the sensitivity of both methods to different parameters, a series of 36 simulated grayscale videos (of 25 seconds each) were created in Python. These videos simulated a swarming behavior with a growing circle on a gray background, varying in contrast (high, intermediate, low), growth speed (5, 35, 300 pixels/second), and noise level (0.00, 0.25, 0.50, 0.75). Poisson noise was used to mimic typical camera noise.

The CV-based method showed robustness under various conditions. With intermediate contrast, the covered area measurements were consistent across different noise levels and matched the theoretical values. In low contrast scenarios, the CV method could still track temporal changes despite some noise-induced variations, whereas the AM method lost accuracy and consistency. High noise levels significantly impacted the AM method, making its results unreliable, while the CV method maintained a reasonable degree of accuracy in tracking temporal evolution.

CV-based methods were shown to be more reliable than AM-based ones, thus showing the potential of using machine learning methods for this purpose (Fig. 1).

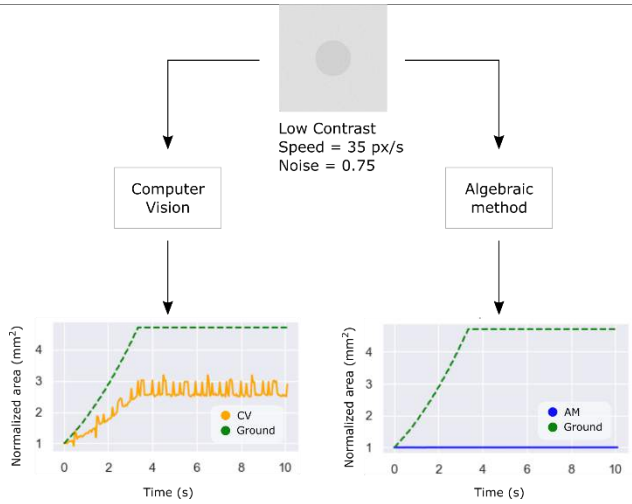

Figure 1. Normalized covered area (mm²) over time (s) obtained using CV and AM-based methods for the simulated video with the most unfavorable contrast and noise conditions. Ground truth corresponds to theoretical values.

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Molecular Shuttles and Macroscopic Actuators from Biomolecular Motors

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Biological motor proteins have evolved over millions of years to be highly scalable and efficient molecular-scale converters of chemical energy into mechanical work. Integrating motor proteins and cytoskeletal filaments into hybrid engineered systems enables the exploration of new devices and active matter systems, such as molecular shuttles and contractile materials [1]. Molecular shuttles are systems capable of transporting nanoscale cargo (Figure 1), such as molecules or vesicles, from one location to another. One of the most studied molecular shuttle systems consists of arrays of kinesin-1 motor proteins that propel cargo-carrying cytoskeletal filaments useful for biosensing or biocomputational tasks [2,3]. The lifetime of these molecular shuttles is limited by the degradation of the cytoskeletal filaments, which shrink and break as they are propelled by the motor proteins [4,5]. We will describe how the investigation of motor-induced degradation motivated the development of reversibly binding motor proteins that mimic the self-repair mechanisms of biological systems [6]. The capability to dynamically reorganize which results from reversible attachment can potentially be exploited to assembly contractile materials. Recent work demonstrated contractile gels which form after light activation and rely on the random attachment of engineered protein filaments to each other [7]. However, the tensile stresses generated by these muscle-like materials are still a thousand-fold lower than those generated by muscle tissue. We are working towards realizing a biohybrid actuator by spatially organizing biomolecular motors from the bottom-up to create large-scale functional arrays. By spatially organizing the motor proteins on synthetic scaffolds, we aim to more accurately mimic the sarcomere in its dense arrangement of proteins to maximize force production (Figure 2). We plan to achieve this through the dynamic self-assembly of swarming microtubules that attach to synthetic sheets functionalized with Ni-NTA complexes that allow for the reversable binding of kinesin and dynein motor proteins. Future applications of such structures include prosthetic and implantable actuators for biomedicine and force transducers for transport systems [8].

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Figures

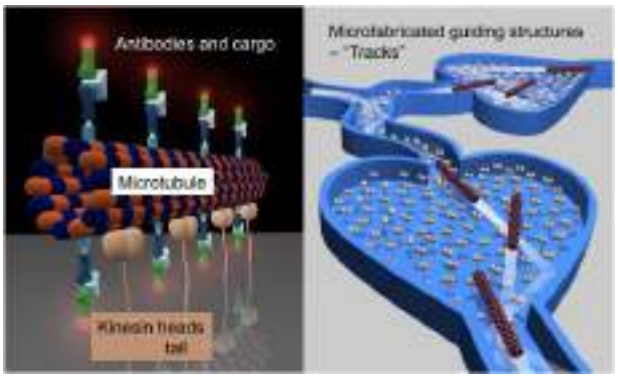

Figure 1. Molecular shuttles – Antibody-functionalized microtubules propelled by surface-adhered kinesin motors carry molecular cargo. Microfabricated, open channels can guide the movement of shuttles.

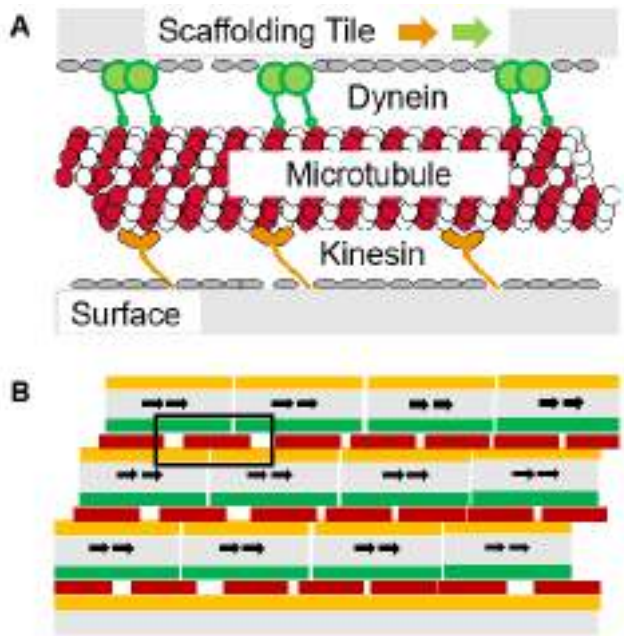

Figure 2. a) Schematic of the proposed design of the contractile unit for the macroscopic actuator. Arrays of microtubules and kinesin/dynein motors will enable the coordinated actuation of synthetic sheets. b) The scaling up of force will be achieved through the stacking of two-dimensional arrays of contractile units.

Affinity peptide modified magnetic micromotors for OFF-ON protein S detection: towards fast COVID-19 determination.

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The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) caused the COVID-19 pandemic that started in December 2019, leading to thousands of deaths and lockdowns around the world. One of the main tools to reduce the spreading of the virus has been testing using molecular and serological methods like RT-PCR (which requires long analysis times and specialized personnel) and commercial antigen tests (which present low sensitivity) [1]. Herein, we present an "on-the-fly" fluorescence approach for SARS-CoV-2 determination based on magnetically propelled MoS_2/Ni micromotors modified with a rhodamine B-labelled peptide that showed a nanomolar affinity for the Spike protein S1 (RBD) via electrostatic and Van der Waals forces (see **Figure 1**). In this approach the micromotors move through the sample, inducing an enhanced fluid mixing, and thus increasing the number of peptide-Spike protein biorecognition events and allowing for efficient operation in just 1 µL of samples [2]. As a result, the peptide desorbs from the micromotors and target-dependent increase of the fluorescence intensity in the solution was measured using fluorescence microscopy. Our method was performed during an assay time of 1 minute and displayed a linear range from 50 pg ml^{-1} to 50 ng ml^{-1}, with a limit of detection of 3 pg ml^{-1}. The method also provides good results with real nasopharingeal samples (checked out by RT-PCR), allowing for detection without sample treatment.

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Figures

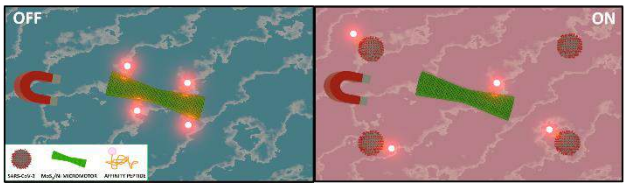

Figure 1. OFF-ON Spike protein detection scheme.

Enhancing nanomotor stability: the role of enzymatic protection

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In the last few decades, advancements in nanotechnology have paved the way for harnessing the power of enzymes through their integration with micro- nanoparticles, endowing them self-propulsion features[1–3]. Among these enzymes, **catalase (CAT)** has gained significant prominence due to its intrinsic properties, i.e., high turnover number and dismutation of hydrogen peroxide in water and oxygen bubbles which drive to enhanced motion properties by means of jet-like mechanism or buoyancy effect[4]. Recently they have been successfully applied in biomedical applications[5]. However, the presence of biomacromolecules with high potential to produce immune response hindering its application in clinic. In this regard, **single enzyme nanogles (SENs)** is an emerging technology which provides polymeric mantle around the enzyme protecting them from the media. It has been reported that this technology could increase the enzyme stability against temperature and organic solvents in addition to potential functionalities for further applications [6–8].

Here, we show the synthesis of catalase nanogels **(CAT@NGs)** functionalized with amine groups **(Figure 1)** and its immobilization covalently onto **mesoporous silica nanoparticles (MSNPs)** to fabricate for first time CAT@NGs-based nanomotors **(Figure 2)**. The preliminary results showcased not only the **preservation of catalytic properties** in the CAT@NGs but also upon immobilization we demonstrated its ability to exhibit enhanced self-propulsion at the **single particle level** and **collective behavior (swarm)**. Finally, we have demonstrated that the motion remains unaffected by temperature, attributed to the polymeric protection surrounding the enzyme.

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Figures

Figure 1. Schematic representation of CAT@NGs. Radical polymerization was performed with the monomers N-(3-aminopropyl)methacrylamide (APM), acrylamide (AAm), and N,N´-Methylenebis(acrylamide) (MBAAm) as a crosslinker to form catalase-based nanogels.

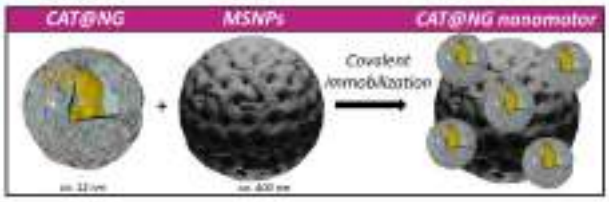

Figure 2. Schematic representation of CAT@NGs-based nanomotors manufacturing. The amines groups provided by CAT@NGs promote the covalent attachment onto MSNPs.

On the chemotactic behaviour of natural trafficking vesicles

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Chemotaxis refers to the behavioral phenomena of directed motion either positive or negative in response to a chemical stimulus. This phenomenon is present throughout all of nature from a singular ant following a trail of sugar to the vastly complex collective dynamics of wound healing. Within the human body, chemical gradients are widely used to direct active transport. The most common of these is regulated by so called 'trafficking vesicles'. These are membrane bound compartments with size varying from tens to thousands of nanometers. The most studied systems are exosomes which are vesicles released by most cells for exchanging macromolecular cargo and controlling signaling[1]. Exosomes were found to be the most prominent extracellular vesicles deployed by murine stem cells[1]. It was shown that these exosomes exhibit specific L-asparaginase activity allowing them to alter the metabolic microenvironment by consuming Asparagine and releasing Aspartate. L-asparaginase activity arises from the asparaginase-like protein 1 (Asrgl1), which is a metabolic enzyme that the exosomes carry from their donor neural stem cells[2].
The goal of our research is to investigate if the exosomes could use their independent L-Asparaginase activity to induce movement along L-Asparagine gradients and thus display chemotactic behavior. Such a finding could have broader implications indicating the possibility that chemophoresis of metabolite gradients within the body contribute to the observed directed motion of exosomes displayed in their role as trafficking vesicles.

We thus set out to prove the existence of super or 'active' diffusion of exosomes under an L-Asparagine gradient. To create this environment, we made use of a commercially available single channel microfluidic device capable of upholding linear chemical gradients for up to one hour. We then tracked the movement of the exosomes in a confocal microscope and analyzed the data using TrackPy in python. All measurements were performed at 37°C to mimic mammalian physiological conditions, and this temperature was closely monitored to avoid unwanted thermal drift. To enable tracking of exosomes in the confocal microscope we made use of neural stem cells derived from mice genetically engineered to express red fluorescent protein at CD63 biomarkers. Exosomes were then collected from the cell supernatant through differential centrifugation.

In this experimental setup, the measured dynamics of these exosomes can be divided into three main components. We name these components fluid flow, Brownian motion, and phoresis.
The overarching fluid flow within the microchannel arises from the specific interaction between the channel wall and the chemical gradient and will exhibit distinct fluid flow regimes as a function of the concentration of said gradient. For nonelectrolyte concentration gradients, the system will show advective flow under relatively high concentration gradients, and diffusioosmotic flow or no flow at increasingly low concentrations[3]. Thus, to account for this inherent fluid flow created by the chemical gradient of L-Asparagine, we performed control experiments where we tracked polystyrene beads under different concentrations. The goal here was not only to better understand the overarching dynamics of our experimental setup but also to find an optimum between the fluid flow velocity and the chemical concentration needed to observe active motion. When performing these control experiments with beads, we made sure to make use of differently functionalized beads to also account for passive drift or diffusioosmophoresis.
Brownian motion within the system could be theoretically predicted from the particle size and corroborated with experimental findings. By understanding all components, we can finally assess if the exosomes' drift has a chemotactic component according to the concentration gradient of L-asparagine.

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Design and construction of hybrid coacervate-based artificial cells: Nanomotor-driven coacervates

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Cells are highly complex and advanced microreactors, which are regarded as the basic building blocks of all life. Over the last decades, scientists have been motivated to combine diverse non-living materials in creative bottom-up ways to construct living cell equivalents called artificial cells. A further step towards assembling multifunctional artificial cells would involve the capacity of locomotion. Artificial cells that can implement directed motion have drawn much attention, and progress in designing these powerful motor systems has led to advances in biomedical applications, such as directed drug delivery, cell sensing, and therapy.

In my work, our aim is to develop a novel hierarchical coacervate based micromotor composed of coacervates and nanomotors. Our final goal is to use nanomotors to drive micro-sized coacervate droplets. First, multiple nanomotors will be incorporated in a single coacervate droplet where they must work in unison to achieve a net displacement. Secondly, the kinetic energy of the nanomotors must be transferred to the larger compartment to enable motion of the entire system. The localization of the nanomotors on the coacervate droplet will be further investigated and the relationship between the motion of the nanomotors and the motion of the whole coacervate droplet will be further discussed.

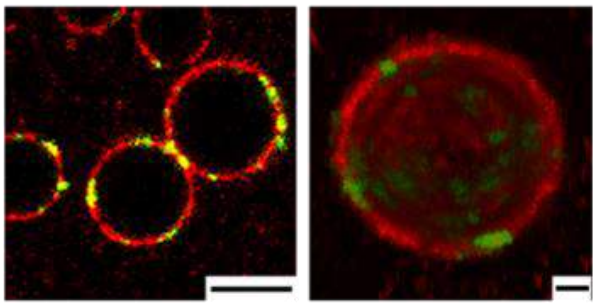

Figure 1. Terpolymer and nanomotors dual stabilized coacervate droplets

Sonodynamic Bacterial Inactivation Enhanced by an Actuator-Integrated Mechanism

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Sonodynamic bacterial inactivation, a reactive oxygen species (ROS)-empowered approach featuring high penetration depth and low health risk, has been explored for antibiotics-free antibacterial treatment. However, the low yield and inadequate diffusion of ROS negatively affect the antibacterial efficacy of sonodynamic treatment, thus hindering its further developments. Here we propose an actuator-integrated mechanism for enhancing the sonodynamic efficacy of loaded sonosensitizers through motion-induced hydrodynamic effects, demonstrated by a porphyrin-decorated gold nanomotor, which can produce ROS for bacterial inactivation while performing multimodal motion via actuation using low-frequency ultrasound (**Figure 1**). Corroborated by numerical simulation, our experimental results show that the motor's stirring motion substantially increases the yield and diffusion of ROS through fluid flow and frequent interaction between the motor and bacterial targets, resulting in doubled antibacterial efficiency in comparison to a still motor (**Figure 2**). Furthermore, the flow-induced shear forces combining frequent interaction constitutes a source of mechanical damage and can form a synergy with the antibacterial attributes of ROS, enabling an efficient biofilm eradication that is inaccessible by freely suspended porphyrin (**Figure 3**).

- This study introduces TPPS-decorated Au NRs as ultrasound-powered sonodynamic nanomotors (TPPS@Au) to enhance ROS-based bacterial inactivation. These nanomotors are fabricated through electrodeposition and surface modification, utilizing PDEA-mediated electrostatic adsorption.
- Under low-frequency ultrasound, TPPS@Au nanomotors exhibit various motions, release ROS, and interact with bacteria effectively, resulting in enhanced antibacterial efficacy for both planktonic bacteria and biofilms.
- This study offers a promising strategy to improve sonodynamic antibacterial treatments by leveraging nanomotor motion-induced effects and ROS production, addressing challenges in traditional sonodynamic therapy. Future work will focus on precise motion control, understanding motion-related effects, nanomotor swarming behavior, and potential applications.

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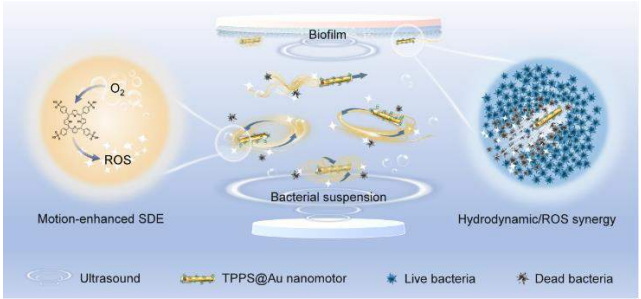

Figure 1. Schematic illustration of an ultrasound-propelled sonodynamic nanomotor for enhanced bacterial inactivation.

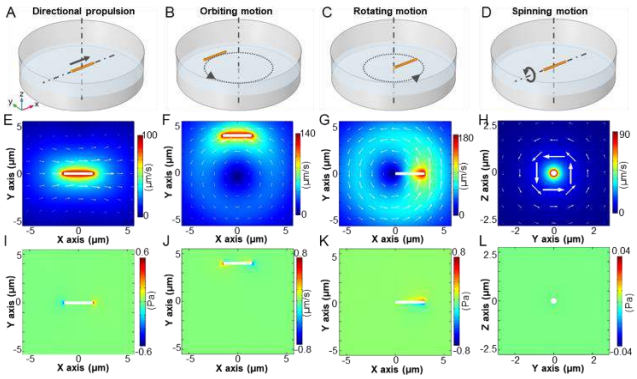

Figure 2. Numerical simulation of fluid flows and relevant velocity gradients induced by the locomotive, rotating, spinning and orbiting motion of TPPS@Au. COMSOL Multiphysics software 5.6 is used for the simulation.

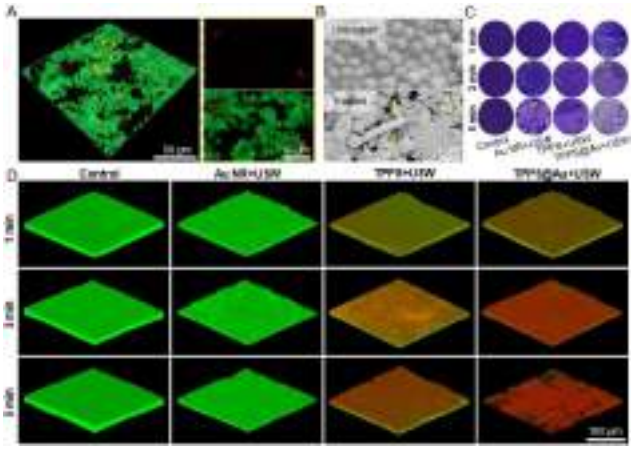

Figure 3. Structural characterization and quantitative analysis of the TPPS@Au-dominant eradication of MRSA biofilms.

Collapse Dynamics of Flexible Active Polymer

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The active matter systems feature the perpetual conversion of chemical energy or other forms of energy into mechanical motion that drives the system out-of-equilibrium. In this work, we are interested in studying one particular branch of such active systems, that is the active polymer which exhibits various interesting dynamics like self-propulsion, swelling, shrinkage, loop formation, spontaneous oscillation, spiral formations, enhanced diffusion etc. The linear and circular structures in many synthetic or natural systems simultaneously experience local and long-range forces. In this work, we use numerical simulations to investigate the concurrent effect of a local polar and attractive long-range activity on the active polymer. The source of activity on the polymer is the self-generating, nonequilibrium solvent gradient caused by the chemical reaction at different sites on the polymer. The chemical gradient then leads to the generation of both local and long-range force along the filament. Here we present the effect of activity on the configurational dynamics of a flexible chain emphasizing globulelike transformation for linear topology. However for rings, while the long-range attraction leads to a systematic collapse, the polar activity tends to swell the shorter rings and crumple the larger ones. We show that the steady-state conformation of such an active ring strongly depends on the kind of activity. The dominance of local tangential activity for very short rings, while the long-range activity at intermediate length scales is observed. However, in contrast to our intuition, we observe the dominance of local polar activity again for very large rings. We quantify these observations by comparing the scaling laws and local structures with the passive polymers. Further, the relaxation dynamics of the polymer were characterized by the Rg, and a nonmonotonic behavior was observed for polar activity for rings.

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MXene based Micromotors for Biomedical applications.

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Abstract.

MXenes are a class of two-dimensional transition metal carbides, nitrides, and carbonitrides that exhibit a range of remarkable properties which has enabled diverse applications across various branches of electrochemistry. Their unique layered structure, combined with excellent electrical conductivity, mechanical strength, and surface chemistry, makes them highly versatile materials. MXenes have been extensively investigated for use in lithium-ion batteries, supercapacitors, and fuel cells, where their large surface area enables efficient charge storage and transfer [1]. MXenes' ability to selectively adsorb molecules and ions has also led to their utilization in sensing and water purification. Moreover, their biocompatibility makes them promising candidates for biomedical applications.

Building on the recent success of MXene-based micro/nanorobots for selective nanoplastics removal in wastewater treatment [2], this study explored the potential of functionalizing MXene-based micromotors for biological toxins neutralization. We exploit the unique surface properties and exceptional adsorption capabilities of MXenes to design micromotors that can effectively target and neutralize biological toxins. This research has significant implications for both nanomedicine and environmental protection, offering a promising new approach for toxin removal.

Figures

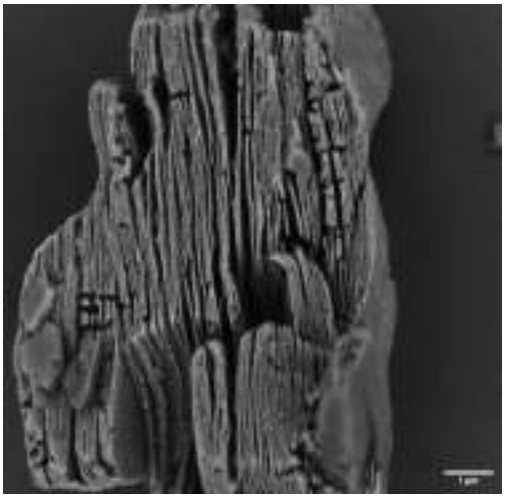

Figure 1. SEM image of Ti3C2TX MXene micro motor

Acknowledgment

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Programmable Negative Chemotaxis of Polymeric Vesicles

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Chemotaxis enables organisms and cells to move either toward or away from specific cues. Artificial protocells capable of integrating both positive and negative chemotaxis into one system are still very rare outside the biological realm and often require elaborately designed catalytic reactions with complex adaptation processes. Furthermore, the chemotactic mechanism of artificial systems is not yet fully investigated and understood especially at the molecular level. Here, we introduce binding interaction as a new propulsion mechanism for chemotactic polymeric vesicles, requiring no external modification of the system. The vesicles can be selectively programmed for negative chemotaxis by detecting specific signaling molecules. We systematically examined the possible mechanisms of the chemotaxis by a flow-chart toolbox approach and highlight the mechanism of the binding-induced breaking effect on water structure. The programmable negative chemotaxis driven by binding interaction represents a conceptually novel way to guide the design of artificial chemotactic protocells and opens a new route in fields such as the active delivery or artificial communication under out-of-equilibrium conditions.

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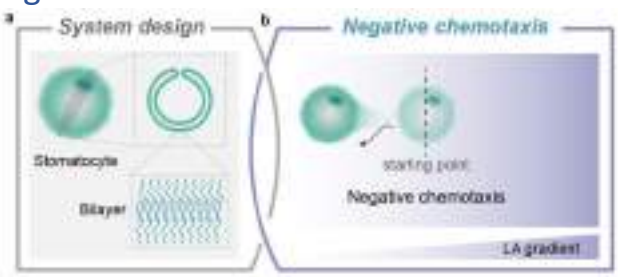

Figure 1. Programmable negative chemotaxis of polymeric vesicles. a, Design of a biodegradable bowl-shaped stomatocyte made from poly(ethylene glycol)-*b*-poly(D,L-lactide) (PEG-*b*-PLA). b, Schematic representation of negative chemotaxis of a PEG-*b*-PLA stomatocyte. LA, lactic acid.

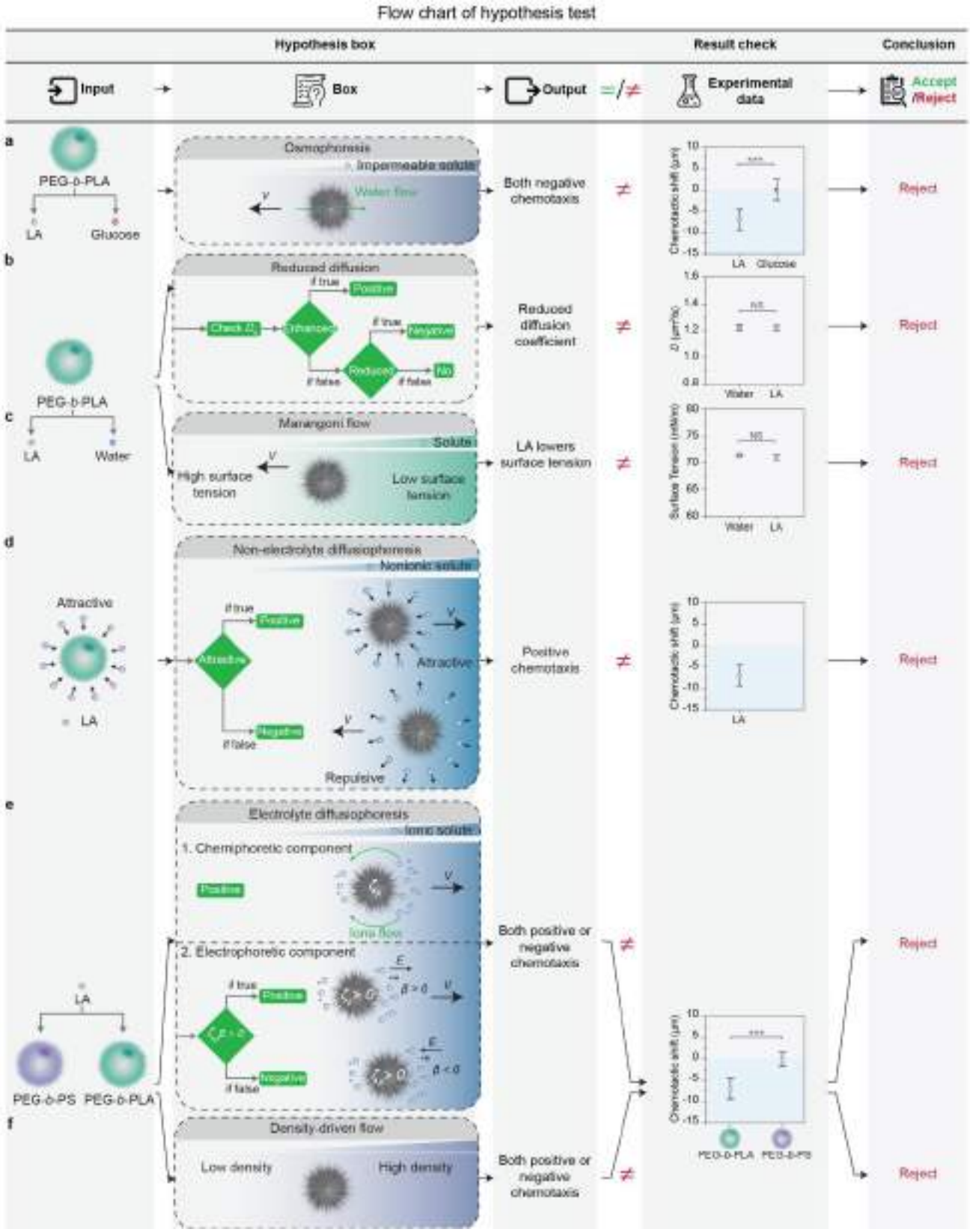

Figure 2. Ruling out alternative mechanisms by using a flow chart of hypothesis tests. The *Hypothesis box* contains the elements of *Input* (experimental design), *Box* (description of alternative mechanisms), and *Output* (the outcome by passing the path *Input* through *Box*). The *Output* column is then compared with the column *Experimental data*, and via the column *Accept/Reject* used to verify/rule out the corresponding hypothesis. The following mechanisms are tested: osmophoresis (a), reduced diffusion (b), Marangoni flow (c), non-electrolyte diffusiophoresis (d), electrolyte diffusiophoresis (e), and convection (f). The mean and standard deviations are plotted in *Experimental data* (n = 4). Statistical analysis: ANOVA test and Tukey's HSD post hoc test, ***$P < 0.001$, NS: not significant ($P > 0.05$).

Real-time tracking and navigation of a microswarm under laser speckle contrast imaging for targeted delivery in vivo

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Micro/nanorobotic swarms consisting of numerous tiny building blocks show great potential in biomedical applications due to their collective delivery ability, enhanced imaging contrast, and environment-adaptive capability.[1-4] However, in vivo real-time imaging and tracking of micro/nanorobotic swarms remain a challenge, considering the limited imaging size and spatial-temporal resolution of current imaging modalities.[5-6] Here, we propose a strategy that enables real-time tracking and navigation of a microswarm in stagnant and flowing blood environments by using laser speckle contrast imaging (LSCI), featuring full-field imaging, high temporal-spatial resolution, and non-invasiveness. The change of dynamic convection induced by the microswarm can be quantitively investigated by analyzing the perfusion unit (PU) distribution, offering an alternative approach to investigate the swarm behavior and its interaction with various blood environments. Both the microswarm and surrounding environment are monitored and imaged by LSCI in real time, and the images are further analyzed for simultaneous swarm tracking and navigation in the complex vascular system. Moreover, our strategy realized real-time tracking and delivery of a microswarm in vivo, showing promising potential for LSCI-guided active delivery of microswarm in the vascular system.

Here, we report a LSCI-based tracking method to navigate a microswarm in endovascular environments with real-time monitoring (Figure. 1A). Fe_3O_4@SiO_2 nanoparticles with a diameter of 300-400 nm (fig. S1) were used as the tiny building blocks. A sphere magnet was applied to generate a rotating magnetic field, which can control the microswarm formation and navigation process.[7-9] In stagnant blood environments, the microswarm showed a relatively strong imaging contrast in both the pseudo color pattern and the gray pattern (Figure. 1B). The hydrodynamic convection generated by the rotating motion of the microswarm effectively agitated surrounding RBCs. The movement of RBCs was detected by LSCI and transformed into imaging signals. Two types of imaging modes, including pseudo color pattern and gray pattern, were captured. Compared with the gray pattern in stagnant blood, the pseudo color pattern exhibited a better imaging profile and provided more details in the contrast change. In flowing blood, the microswarm showed a smaller imaging profile (Figure. 1B). The microswarm mainly exhibited an imaging profile of itself in the dynamic environment, which was distinguished by the difference in imaging contrast between the microswarm and bloodstream. The gray pattern was more suitable for the flowing conditions due to the differentiation between the microswarm and surrounding RBCs signals. Moreover, the hydrodynamic convection can be evaluated by the motion of RBCs, and quantitative analysis was achieved by monitoring the PU change. Such an exclusive feature allowed us to optimize the parameters to improve hydrodynamic convention and benefit the delivery process. Our work presents a non-invasive and high-resolution approach for the tracking and navigation of a microswarm in an endovascular system with a large imaging field that allows real-time feedback.

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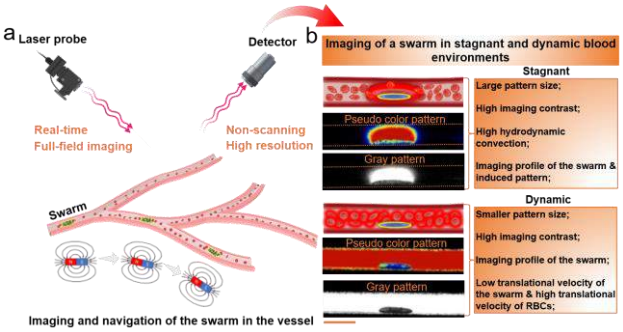

Figure 1. Schematic illustration of LSCI-based real-time tracking of a microswarm. (A) Schematic illustration of the imaging and navigation of a magnetic microswarm in a blood vessel. (B) Photographs depict the real imaging of a magnetic swarm in the vessel with both stagnant and flowing blood. The scale bar is 5 mm.

Acknowledgements

This work is supported by the Hong Kong Research Grants Council (RGC) with project Nos. RFS2122-4S03, STG1/E-401/23-N, 14205823, 14301122, and 14300621. We also thank supports from the CUHK internal grants and the Multi-scale Medical Robotics Centre (MRC), InnoHK, at the Hong Kong Science Park.

Light-Driven Micro/Nanomotor for Biomimetic Optical Communication

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In nature, organisms respond to environmental stimuli through their light-responsive properties. Further the process of optical communication is accomplished by physiological activities via signaling pathways. Light-driven micro/nanomotors have drawn considerable attention due to their unique dynamic behaviors at the microscale. Meanwhile, emerging research on collective behaviors and molecular communication brings promising advancements for biomimetic applications. However, it remains challenging to integrate these key concepts to build biomimetic micro/nanomotor systems with collective intelligence. This study explores the self-propulsion and collective behaviors of light-driven micro/nanomotors, mimicking the response of organisms to light stimuli, followed by the signal transmission via molecular communication [1]. Herein, we prepared Cu_2O micro/nanomotors with negative phototactic properties as information carriers. Also, we established a microscope-based experimental platform for microscale communication, relying on optical microscopy equipment, which offers high controllability and precision. By real-time observation and recording of communication processes at the microscale, we achieved macroscopic demonstration and analysis of biomimetic molecular communication. By controlling the motion of Cu_2O particles with light signals, we regulate their go-stop and directional movement in the transmission channel, which in turn induces changes in the density distribution. Further, signal detection is achieved by detecting the distribution of particles in microscopic view, employing three threshold-based low-complexity detectors for information recovery from received signals. Experimental results demonstrate successful control and modulation of self-propelled micro/nanomotor, enabling low bit error rate information transmission through molecular communication mechanisms. Our research provides new solutions for the construction and practical applications of biomimetic micro/nanomotor systems. Moreover, it offers significant insights for the design and development of micro/nanoscale intelligent systems in an intradisciplinary background.

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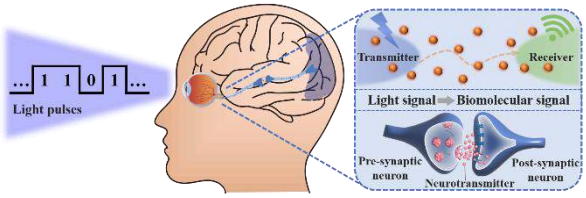

Figure 1. Schematic diagram of bionic molecular communication in the optical nervous system and clustered micro/nanomotors.

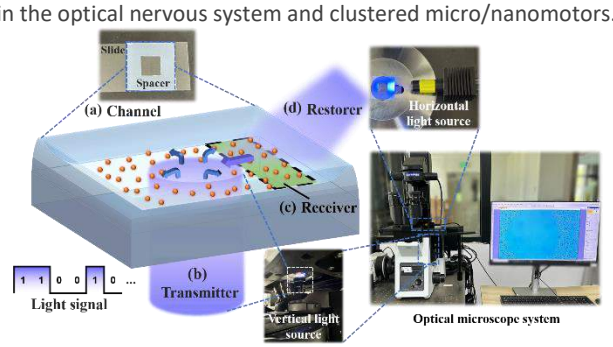

Figure 2. Schematic diagram of experimental setup for light-driven Cu_2O micro/nanomotor based molecular communication.

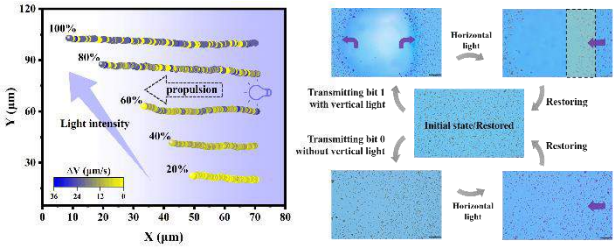

Figure 3. (a) Motors' trajectories under different light intensities. (b) Processes of motor movement under horizontal and vertical light in the microscopic view.

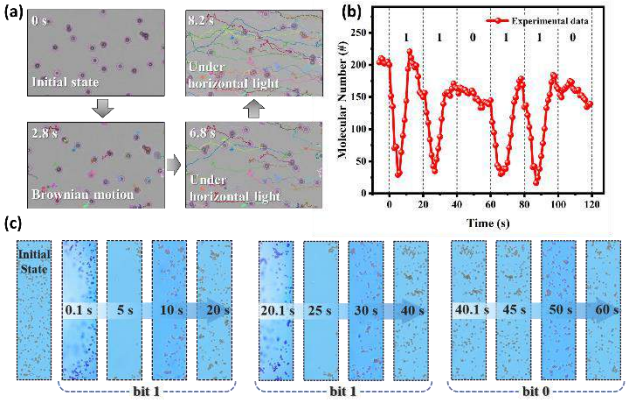

Figure 4. (a) Trajectory of Cu_2O micro/nanomotors. (b) Numbers of motors estimated by pixel-based detector. (c) Distribution of motors over time for 60 s transmission of [110] bit sequences.

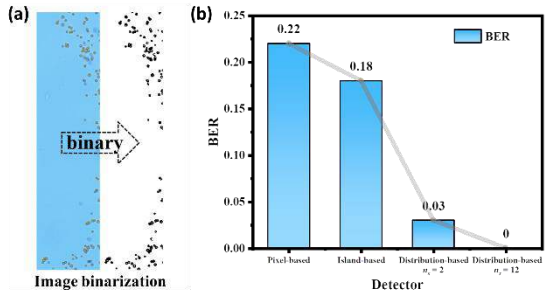

Figure 5. (a) Captured images and the corresponding binary images. (b) Bit error rate (BER) comparison of the proposed three detection schemes for 100 bits of experimental data.

Development and control of magnetic microrobot-assisted recanalization system for nasolacrimal duct obstruction

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Nasolacrimal duct obstruction (NLDO) is the most common obstructive cause of tearing. If left untreated, NLDO may be complicated by infections (dacryocystitis, cellulitis, and postoperative endophthalmitis). External dacryocystorhinostomy (DCR) is the primary treatment for NLDO. However, this method is an invasive surgery that may lead to complications and leave scars on the patient. On the other hand, endoscopy dacryocystorhinostomy is a new treatment in this field, the visual feedback provided by micro endoscopes improves operation safety. However, this method requires expensive equipment and professional doctors to operate. In contrast, the lacrimal duct probing and tube intubation method does not change the anatomical structure of the lacrimal duct, and restores the physiological passage of the lacrimal duct, ensuring smooth drainage of tears. By combining with advanced drug delivery technology, it can achieve good performance. However, this method usually needs to be carried out manually by doctors, which lacks accurate control of force. Therefore, it is sometimes difficult to determine the location of blocked part accurately [1]. If the operation is improper, there will be potential risks, such as damage to the nasolacrimal duct (NLD), bleeding, and the false passage creation.

Miniature robots have emerged as a promising approach for minimally invasive medicine. Many strategies have been proposed to manipulate the motion of these tiny robots, and the magnetic field is one of the most promising tools for biomedical applications [2]. To date, the helical magnetic microrobots show good potential for biomedical applications. They need no on-board actuators and processors, instead, the external magnetic actuation system can actuate and navigate them by controlling the magnetic field parameters. These features make helical magnetic miniature robots a good candidate for NLDO treatment. However, the retrieval of these tiny agents is still challenging. On the other hand, the catheter-based microrobots are widely developed for various medical treatment [3]. Whereas, in the existing application scenarios, real-time control of robots relies on visual feedback. However, the NLD is embedded in the skull, so the ultrasound device is not suitable for this situation. Fluoroscopy exposes patients and doctors to radiation for a long time, which can cause health problems. In this way, the navigation and control of the microrobot in the NLD becomes difficult. Because of lacking visual feedback, the actual state of the robot in operation is hard to determine.

In this study, a magnetic microrobot system that integrates the force feedback method for NLDO is proposed to address the aforementioned challenges. A schematic diagram is shown in **Figure 1**. The system consists of a magnetic micro-driller, a magnetic navigation system and a motion control system. An automatic insert procedure is developed to show the low-risky and minimally invasive feature of microrobot-assisted solution for nasolacrimal duct recanalization. The proposed procedure has several stages. First, the microrobot can be inserted into the NLD from the lacrimal canaliculus. Then, it is navigated and manipulated in the duct by a magnetic actuation system, and drills through the blockage during the process. In addition, if the driller gets stuck in the phantom, the contact force in the guidewire will increase. In this way, the control system could get the states of the microrobot. Finally, the microrobot can be safely taken out of the NLD after completing the task. Experimental results show that the microrobot can drill through the obstruction and achieve recanalization directly and effectively in the phantom.

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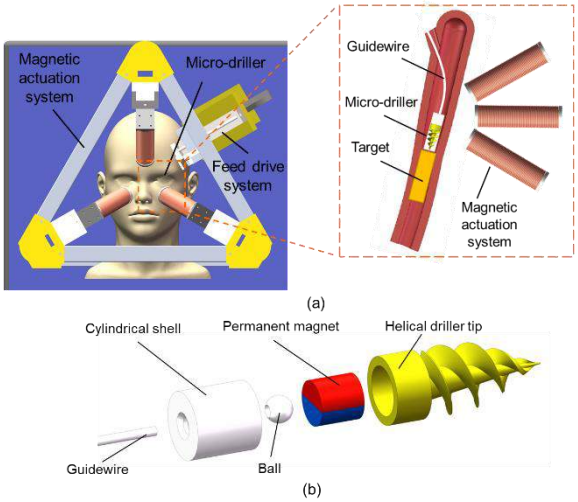

Figure 1. Schematic diagram of the magnetic microrobot-assisted recanalization system. (a) The microrobot is inserted into the NLD and controlled by the magnetic actuation system. (b) Structure design of the magnetic micro-driller robot.

Acknowledgements This work is supported by the Hong Kong Research Grants Council (RGC) with project Nos. RFS2122-4S03, STG1/E-401/23-N, 14205823, 14301122, and 14300621. We also thank supports from the CUHK internal grants and the Multi-scale Medical Robotics Centre (MRC), InnoHK, at the Hong Kong Science Park.

Controlling Pattern Transformation Rates of Magnetic Colloidal Microswarms in Complex Fluids

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In nature, living organisms form swarms through collective behaviors to accomplish life activities that would be unachievable by individuals alone. Natural swarms exhibit deformable overall patterns, demonstrating exceptional adaptability to surrounding environments. For instance, the structure of bird flock changes during migration, the shape of fish schools is influenced by predator attacks, and honey bee swarms actively alter their form under dynamic loads to enhance stability. These fascinating natural swarm phenomena have inspired the development of various artificial micro/nanorobot swarms (microswarms) with transformable patterns, reflecting the immense application potential of adaptive microswarms in various fields, especially in biomedicine.[1]

Natural swarms are often required to complete pattern transformations as quickly as possible in response to rapid and unpredictable environmental changes. For example, *Bacillaria paradoxa* (a widely distributed diatom) swarms can transform between fully extended and contracted states under light stimulation within tens of seconds. To date, the shape deformation of artificial microswarms has been extensively developed, and multi-mode, reversible, and large-scale pattern transformations have been realized through various strategies.[2] Compared with natural counterparts, pattern transformation rates of artificial microswarms are relatively low and difficult to control, hindering their further applications. Improving pattern transformation rates can enhance the operational efficiency, stability, and environmental adaptability of microswarms, facilitating applications in complex environments. However, research on pattern transformation of microswarms primarily focuses on achieving various types and large-scale transformation, and the on-demand control of transformation rates still needs further exploration.

This study proposes a strategy for controlling the pattern transformation rates of two different types of deformable microswarms, *i.e.*, ribbon-like and vortex-like microswarms.[3] We first develop a theoretical model to quantify the magnetic and hydrodynamic interactions between nanoparticle chains. Theoretical analysis and experimental results reveal the relationship between microswarm pattern transformation rates and magnetic field parameters, including field ratio, input field strength, and frequency. Based on these theoretical and experimental findings, we propose a strategy to control the transformation rate by adjusting the field parameters, as illustrated in Figure 1. Using this strategy, we increase the pattern transformation rates of ribbon-like and vortex-like microswarms to 820% and 568% of the original, respectively. We further prove that this strategy is applicable to various environments, including viscous Newtonian fluids (viscosity: 1–4 mPa·s), non-Newtonian biological fluids (diluted blood, plasma, whole blood), and flowing fluids. This study indicates that the pattern transformation rate of magnetic colloidal microswarms can be regulated by adjusting external inputs, and such a concept is expected to be extended to various swarming systems. Our work also deepens the fundamental understanding of small-scale swarming behavior and provides new insights for enhancing the environmental adaptability and controllability of microswarms.

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Figures

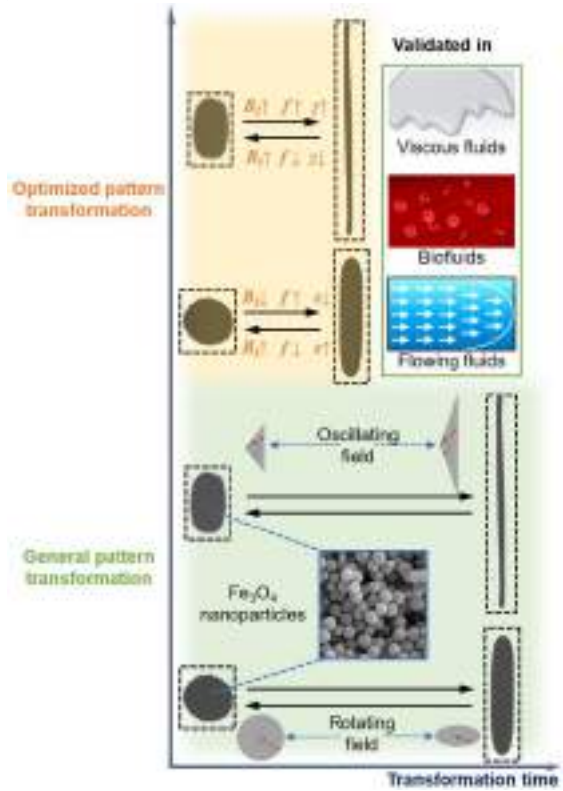

Figure 1. Schematic illustration of microswarm pattern transformation rates control strategy. B_I is the input field strength. f is the frequency. γ and ε indicates the field ratio of oscillating and rotating magnetic fields, respectively.

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The Design of Heterogeneous Catalysts

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In heterogeneous catalysis, chemical reactions usually take place on the heterogeneous interface between the catalytic material and the reactive species. The physical and chemical properties of catalytic materials are crucial for catalytic reaction[1]. Investigating structure-activity relationship by designing the structure of catalysts plays a crucial part in heterogeneous catalysis. However, modulating the structure of catalysts precisely to achieve effective catalysis remains challenging. Here, we report on the improvement of catalytic performance for sulfur conversion reaction by introducing strain engineering and defect engineering in MoS_2 nanosheets to modulate the electronic and geometric structure accurately (Figure 1). The tensile strain regulates the adsorption of polysulfides by raising the D-band center of Mo. Meanwhile, the strain elongates the lattice spacing of MoS_2, which weakens the S-S and Li-S bonds in polysulfides to accelerate the sulfur conversion reaction[2]. In order to deal with the stability issue of oxygen vacancies in surface of catalysts, the charge distribution and the formation energies of oxygen vacancies in the surface of BiOCl nanosheets were modulatd by doping S element, which achieved a balance between catalytic activity and stability (Figure 2) [3]. These designs of catalytic systems provide new strategies for the preparation of efficient and stable heterogeneous catalysts.

Figures

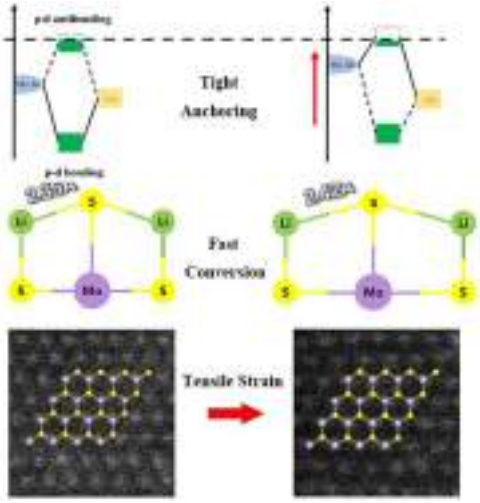

Figure 1. Schematic of MoS_2 with strain and defect modulating the electronic and geometric structure.

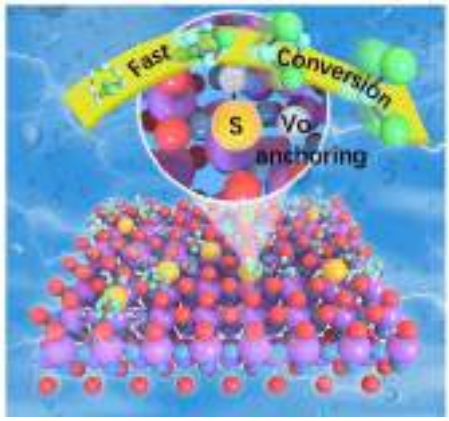

Figure 2. Schematic of doped S affecting the catalytic activity and stability of oxygen vacancies

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Ultrasmall Enzyme-Powered Janus Nanomotor Working in Blood Circulation System

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Injectable chemically powered nanomotors may revolutionize biomedical technologies, but to date, it is a challenge for them to move autonomously in the blood circulation system and they are too large in size to break through the biological barriers therein[1–4]. Herein, we report a general scalable colloidal chemistry synthesis approach for the fabrication of ultrasmall urease-powered Janus nanomotors (UPJNMs) that have a size (100−30 nm) meeting the requirement to break through the biological barriers in the blood circulation system and can efficiently move in body fluids with only endogenous urea as fuel. In our protocol, the two hemispheroid surfaces of eccentric Au−polystyrene nanoparticles are stepwise grafted with poly(ethylene glycol) brushes and ureases via selective etching and chemical coupling, respectively, forming the UPJNMs. The UPJNMs have lasting powerful mobility with ionic tolerance and positive chemotaxis, while they are able to be dispersed steadily and self-propelled in real body fluids, as well as demonstrate good biosafety and a long circulation time in the blood circulation system of mice. Thus, the as-prepared UPJNMs are promising as an active theranostics nanosystem for future biomedical applications.

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Figures

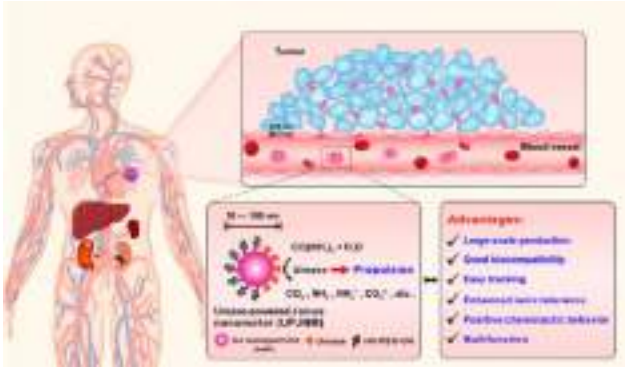

Figure 1. Schematic illustration of the biological barriers faced by nanocarriers when they work in blood circulation system. The inset shows the design strategy and advantages of the urease-powered Janus nanomotors (UPJNMs).

Reactive, cargo-carrying and degradable micro- and nanomotors

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Micro- and nanomotors are promising candidates for targeted drug or gene delivery. In order to be used in in-vivo environments a number of requirements are imposed on the material properties. Naturally they need to be biocompatible, while offering functionalization capabilities for cargo loading. Additionally, they must be addressable by external stimuli to facilitate active, guided transport to the target site with subsequent release of their payload. Finally, to avoid long-term biosafety concerns microswimmers need to be degradable under physiological conditions – an aspect that has been difficult to achieve in previous designs.[1]

Taking inspiration from macroscopic orthopedic implants that are made from magnesium (Mg) and zinc (Zn) and that are fully biocompatible and degradable, we show that we can grow complex microstructures, including micropropellers, with these characteristics. By varying the relative content of magnesium, we demonstrate that we can tune the corrosion time of the microstructures from hours to over a month. Incorporation of biocompatible hard-magnetic iron-platinum in the L10 phase permits the controlled motion of the nanopropellers via small external magnetic fields with a minimum amount of magnetic material.[2] The surface of the MgZn structures can be functionalized with different potential cargoes, like liposomes, enzymes or molecules, and due to their structural degradation in aqueous media, allow for a time-dependent release of their cargo.

When moving to sub-micrometer length scales live imaging of nanomotors becomes increasingly difficult. We are thus investigating alternative tracking methods for nanomotors beyond conventional size limitations using well-characterized chemically-active Janus-particles.

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