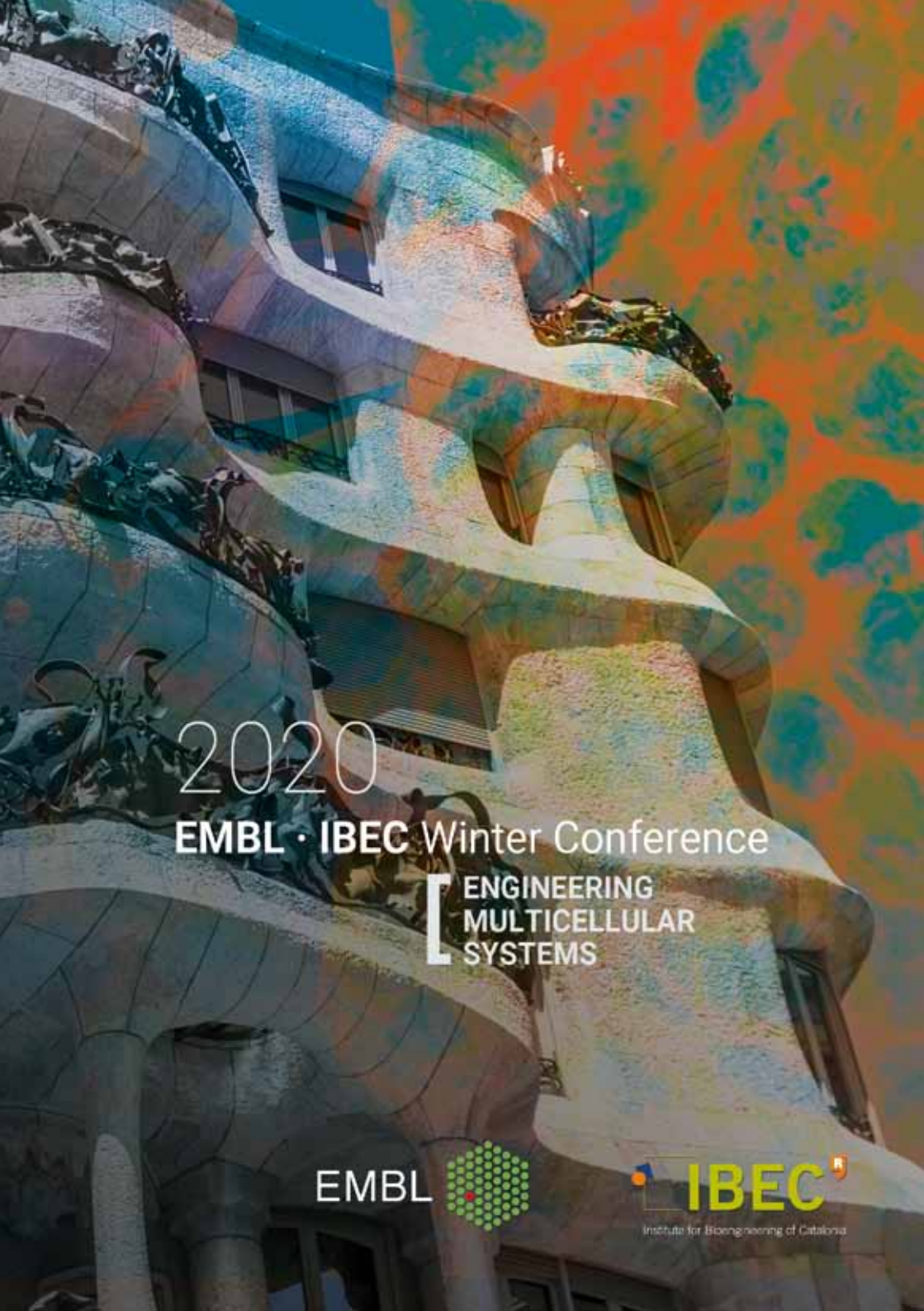
2020
EMBL · IBEC Winter Conference
ENGINEERING
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Welcome to EMBL · IBEC Winter Conference on ENGINEERING MULTICELLULAR SYSTEMS

Recent breakthroughs in stem cell biology, organ-on-chip assays, 3D Bioprinting, and cell mechanobiology have revolutionized our ability to design and assemble multicellular living systems, from organoids to embryos.

This conference will focus on how engineering multicellular living systems is boosting our understanding of tissue and organ function, with applications in disease modelling, drug screening, and tissue engineering.

Organizing Committee:

James Sharpe, EMBL · Chair
Xavier Trepat, IBEC · Chair
Miki Ebisuya, EMBL
Nuria Montserrat, IBEC
Josep Samitier, IBEC
Vikas Trivedi, EMBL

EMBL

IBEC
Institute for Bioengineering of Catalonia

EMBL Barcelona

Scientists at EMBL Barcelona explore how tissues and organs function and develop, in health and disease.

We combine a number of themes and approaches to achieve this:

- The development and use of 3D *in vitro* models, (organoids, vascular systems, and others) where the dynamic structure and function of multicellular systems is more accessible to measurement and manipulation than *in vivo*.
- Quantitative approaches and computational modelling, to create more a rigorous understanding and predictions of the dynamics of multicellular systems.
- 3D and 4D mesoscopic imaging tailored towards tissues, organs and organoids. We develop and improve these state-of-the-art technologies, as well as using them for our research.
- An engineering and synthetic philosophy, in which building and creating new biological models is a key part of understanding and controlling them.

Using these approaches, EMBL Barcelona studies a variety of multicellular questions:

- Organogenesis – how a complex mammalian organ (the limb bud) develops, grows and organises itself during development.
- Scaling – how dynamic patterning processes change their relative speeds and sizes, across different tissues and species.
- Self-organisation – how collectives of cells spontaneously break-symmetry and cooperate to organise themselves into functional tissues.
- Vasculogenesis – how blood vessels organise themselves into networks, and how this can be harnessed for improved tissue engineering and disease modelling.
- Vascular diseases – how genetic or infectious diseases interact with vascular system to cause pathologies, such as malaria.

Institute for Bioengineering of Catalonia (IBEC)

The Institute for Bioengineering of Catalonia (IBEC) is a leading-edge multidisciplinary research centre based in Barcelona that conducts research at the frontiers of basic and life sciences linked with engineering to generate new knowledge and applications to enhance health and quality of life.

IBEC creates wealth by putting together biophysics, cell engineering, nanomedicine, biomaterials, tissue engineering and the applications of information technology to health.

IBEC is a non-profit-making foundation set up in 2005 by the Departments of Health and Innovation, Universities and Enterprise of the Government of Catalonia, the University of Barcelona and the Technical University of Catalonia.

At IBEC, frontier research is combined with specific transfer targets to produce new applied technologies to be used in life and health sciences. We have the versatility to generate cutting-edge research and, at the same time, work with clinicians and industry to develop new diagnostic or treatment systems. The model envisaged by IBEC is inspired by a creative, innovative new ecosystem based on interaction between research experts in different enabling technologies (nano-bio-info-cogno) to generate new knowledge and engineering solutions in health technology.

The knowledge that exists in IBEC is placed at the service of science and society to progress in three major research programmes:

- **Bioengineering for future medicine**, with the aim of developing technology that goes beyond the existing paradigm of medical care in hospital to incorporate new areas such as personalize medicine, tailoring diagnostic and therapies to the individual, optopharmacology, diagnosis and therapies based on mechanobiology and nanomedicine.
- **Bioengineering for active ageing**, with the aim of developing care and technology and improve the quality of life of an increasingly older population. Assisted living technologies such as mobile health solutions, including home-based devices and services for remote monitoring, consultation and diagnosis are developed..
- **Bioengineering for regenerative therapies**, with the aim of developing regenerative technologies to allow the creation of implants able to bring about the regeneration of damaged tissues or organs and to develop cell therapies.

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ENGINEERING MULTICELLULAR SYSTEMS

Programme 10th February

08:15 – 09:00	Registration
09:00 – 09:30	Opening remarks
Session 1	Chair: Miki Ebisuya
09:30 – 10:00	Forward Engineering of multi-cellular biomachines. *Rashid Bashir, University of Illinois, USA*
10:00 – 10:30	Modelling malaria pathogenesis in 3D *in vitro* microvascular systems. *Maria Bernabeu Aznar, European Molecular Biology Laboratory, Spain*
10:30 – 10:45	Microengineered PEGDA Villus-like Hydrogels with Spatio-Chemical gradients for intestinal epithelium derived from intestinal organoids. *Aina Abad Lázaro, Institute for Bioengineering of Catalonia, Spain*
10:45 – 11:15	Using Human Organoids to Model Kidney Disease and Therapy. *Benjamin Freedman, University of Washington, Seattle, USA*
11:15 – 11:45	Coffee break
11:45 – 12:15	Engineering Tissue Patterning from the Bottom Up. *Pulin Li, Whitehead Institute, Cambridge, MA, USA*

12:15 – 12:30	Morphogenesis is stressful – Elastic properties of folding cell sheets. *Stephanie Hoehn, University of Cambridge, UK*
12:30 – 13:00	Mechanics of the intestinal crypt. *Xavier Trepat, Institute for Bioengineering of Catalonia (IBEC), Spain*
13:00 – 13:20	Group photo
13:20 – 14:50	Lunch and Poster session
Session 2	Chair: Nuria Montserrat
14:50 – 15:20	Gastruloids: A Self-engineered system for the study of early mammalian development. *Alfonso Martínez Arias, University of Cambridge, UK*
15:20 – 15:35	Three-dimensional culture of pancreas progenitors differentiated from mouse embryonic stem cells. *Shlomit Edri, Technion Israel Institute of Technology, Israel*
15:35 – 16:00	Coffee break
16:00 – 16:30	How is Ethics Relevant for the Engineering of Multicellular Systems? *Insoo Hyun, PhD Professor, Department of Bioethics, Harvard Medical School*
16:30 – 16:45	Collective Cell Movement and Cell State Transitions in Gastruloids Specify the Formation of Endoderm. *Ali Hashmi, Institut de Biologie du Développement de Marseille (IBDM), France*
16:45 – 17:15	Self-organization of stem cells into embryos: A window on early mammalian development. *Magdalena Zernicka-Goetz, Department of Physiology, Cambridge University*

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Programme 11th February

Session 3	Chair: Josep Samitier
09:00 – 9:30	Models of neurological disease. *Roger D. Kamm, Massachusetts Institute of Technology, USA*
9:30 – 10:00	Engineering approaches for human pluripotent stem cells derived kidney organoids: emulating tissue features through bioengineering design *Núria Montserrat, Institute for Bioengineering of Catalonia, Spain*
10:00 – 10:15	Mechanics and active cell behaviours contribute to self-organization of mesenchymal cells in the limb". *Xavier Diego, EMBL Barcelona, Spain*
10:15 – 10:45	From haploid stem cells to blood vessel engineering. *Josef Penninger, University of British Columbia, Canada*
10:45 – 11:15	Coffee Break
Session 4	**Chair: James Sharpe**
11:15 – 11:45	Vascular Integration towards improved disease modelling. *Kristina Haase, European Molecular Biology Laboratory, Spain*
11:45 – 12:00	A 3D Morphogenetic Model of Organogenesis in a Human Genetic Context. *Aimal Khankhel, University of California, Santa Barbara, USA*
12:00 – 12:30	Engineering Organoid Development. *Matthias Lütolf, École Polytechnique Fédérale de Lausanne, Switzerland*

12:30 – 12:45	Induction of Synthetic Tissue Folding. *Guillermo Martínez Ara, EMBL Barcelona, Spain*
12:45 – 13:00	Onset and Patterning Rules of Mesendoderm and Definitive Endoderm in Embryoid Bodies. *Iftach Nachman, Tel Aviv University, Israel*
13:00 – 14:30	Lunch and Poster session
Session 5	Chair: Vikas Trivedi
14:30 – 14:50	Talk sponsored by Zeiss
14:50 – 15:20	Recreating Kidney Organogenesis *in vitro* with Human Pluripotent Stem Cells. *Ryuji Morizane, Harvard Stem Cell Institute, Cambridge, MA, USA*
15:20 – 15:35	Tension heterogeneity instructs morphogenesis and fate specification during heart development. *Rashmi Priya, Max Planck Institute for Heart and Lung Research, Germany*
15:35 – 16:00	Coffee break
16:00 – 16:30	Mechanoregulation of thrombus formation in the bloodstream. *Hongxia Fu, University of Washington, Seattle, USA*
16:30 – 16:45	A novel mathematical law to understand 3D self-organization in epithelial tubes. *Pedro Gómez-Gálvez, Instituto de Biomedicina de Sevilla (IBiS), Spain.*
16:45 – 17:15	Programming self-organizing tissues. *Wendell Lim, University of California, San Francisco, USA*
17:15 – 17:45	Synthetic Embryology: A new window on mammalian development. *Eric D Siggia, The Rockefeller University, New York, USA*

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Programme 12th February

Session 6	Chair: Xavier Trepat
09:00 – 9:30	3D Bioprinting for *in vitro* Tissue Engineering. *Wei Sun, Tsinghua University, China*
9:30 – 9:45	Contribution of stromal cells to the formation and stabalisation of blood vessels. *Negar Shahreza, University College London (UCL), UK*
9:45 – 10:15	Modeling epithelial cells-fibroblasts interactions in gut homeostasis and pre-invasive cancers. *Danijela Vignjevic, Institut Curie, Paris, France*
10:15 – 11:30	Coffee Break and poster session
11:30 – 12:00	Building and Breaking Tissues to Understand Development and Disease. *Zev Gartner, University of California, San Francisco, USA*
12:00 – 12:15	Shear-induced crystallization drives precise patterning of hair cells in the mammalian inner ear. *David Sprinzak, Tel Aviv University, Israel*
12:15 – 12:45	Feedback, Dynamics and the Control of Size and Scale. *Arthur Lander, University of California, Irvine, USA*
12:45 – 13:00	Awards ceremony
13:00 – 13:15	Closing remarks and farewell

Keynote Lectures

Forward Engineering of multi-cellular biomachines

Rashid Bashir, University of Illinois, USA

The integration of living cells with 3D printed soft scaffolds can enable the realization of cellular machines for a range of applications in engineering and medicine. In this talk, I will present our group's efforts towards developing such centimeter scale biological robots that actuated by skeletal muscles cells and our efforts to integrate neural control in these biological machines. These machines are controlled via electrical or optogenetic signals and demonstrated improved healing after a damage when exercised via optical stimulation. We also explore their lifetime and degradation in performance due to breakdown of the matrix that contains the cells. We will also present an approach to form functional *in vitro* neural tissue mimic (NTM) of different shapes using stem cells, a fibrin matrix, and 3D printed molds.

We used murine-derived embryonic stem cells for optimizing cell-seeding protocols, characterization of the resulting internal structure of the construct, and remodeling of the extracellular matrix, as well as validation of electrophysiological activity. We also characterized the effects of optogenetic stimulation during neural differentiation, by showing morphological changes in network formation. These cellular systems present many opportunities in the next decade and beyond with potential applications in drug delivery, power generation, and other biomimetic systems. As these cellular machines increase in capabilities, exhibit emergent behavior, and potentially reveal the ability for self-assembly and self-repair, important questions can also arise about the ethical implications of this work.

Rashid Bashir, University of Illinois, USA

Rashid Bashir is Dean of Engineering, the Grainger Distinguished Chair in Engineering and Professor of Bioengineering at the University of Illinois at Urbana-Champaign. Previously, he was the Executive Associate Dean at the Carle-Illinois College of Medicine (2017 – present), the Abel Bliss Professor of Engineering, Head of Department of Bioengineering (2013 – 2017), and Director of the Micro and Nanotechnology Laboratory (a campus-wide clean room research facility) (2007 – 2013). Prior to joining UIUC, he was at Purdue University (1998 – 2007) with faculty appointments in Electrical and Computer Engineering, and Bioengineering. From 1992 to 1998 he worked at National Semiconductor Corporation in Santa Clara, CA as Sr. Engineering Manager.

He graduated with a PhD in Electrical Engineering from Purdue University in 1992. He has authored or co-authored over 250 journal papers, over 200 conference papers and conference abstracts, and over 120 invited talks, and has been granted 49 patents. He received the NSF Faculty Early Career Award, the 2012 IEEE EMBS Technical Achievement Award, and the Pritzker Distinguished Lectureship Award from BMES in 2018. He is a fellow of IEEE, AIMBE, AAAS, BMES, IAMBE, RSC, APS, and NAI. He has been involved in 3 startups that have licensed his technologies. He was part of the core founding team and co-chair of the curriculum committee for the Carle Illinois College of Medicine, the world's first engineering based College of Medicine at the University of Illinois at Urbana-Champaign.

His research group is interested in developing new technologies for precision and personalized medicine, and 3D bio-fabrication of cellular systems. Using bionanotechnology, BioMEMS, and lab on chip, he is working at the interface of biology and engineering from the molecular to the tissue scale, and aiming to make an impact on grand challenges in health and medicine including cancer, sepsis, and others.

In addition to leading his own research group, he was the PI on an NSF IGERT on Cellular and Molecular Mechanics and Bionanotechnology and PI on an NIH Training Grant on Cancer Nanotechnology. He is also co-PI on a recently funded National Research Traineeship (NRT) from NSF. He is also Associate Director and UIUC site lead on an NSF Science and Technology Center on Emergent Behavior of Integrated Cellular Systems (with MIT, Georgia Tech, and other partners).

Modelling malaria pathogenesis in 3D *in vitro* microvascular systems

Maria Bernabeu, European Molecular Biology Laboratory, Spain

Caitlin Howard[2], Celina Gunnarsson[2], Christopher K. Arakawa[2], Maria Vishnyakova[3], Cole A. DeForest[2], Joseph D. Smith[3], Ying Zheng[2]

[2] Department of Bioengineering, University of Washington, Seattle, WA, USA
[3] Seattle Children´s Research Institute, Seattle, WA, USA

Severe malaria carries mortality rates of 15 – 20%, despite treatment with effective and fast-acting antimalarials. *Plasmodium falciparum* sequestration in the brain microvasculature is the main hallmark of severe malaria. However, the mechanisms of parasite sequestration are only partially understood due to the lack of a rodent malaria model that mimics *P. falciparum* sequestration. We have recently engineered two new *in vitro* 3D microvascular models to better understand *P. falciparum*-host interactions. The first model includes a 3D brain microvessel model that displays vessels of 100 µm of diameter arranged in a 13Ξ13 grid. This generates a wide range of wall shear stress within the same device. By using this system, we have shown that *P. falciparum* clonal lines, expressing different cytoadhesion ligands, respond differently to endothelium activation. In our second model, we have developed a robust method to build 3D endothelialized capillary-size vessels (5 – 10 µm).

Perfusion of wild-type parasites or those lacking either cytoadhesion ligands or membrane-stiffening knobs showed different spatiotemporal patterns of sequestration. These results reveal that while molecular interactions are the most important requisite to achieve microvascular obstruction, infected red blood cell reduced deformability plays a secondary role. Altogether, our systems represent a new platform to study the biomechanical and biological determinants of blood disorders that affect the microvasculature.

Maria Bernabeu, European Molecular Biology Laboratory, Spain

Maria Bernabeu received her PhD in 2013 from University of Barcelona where she studied the biology of the malaria parasite. She later moved to Seattle Children's Research Institute to study severe malaria pathogenesis. While in Seattle, she also worked at the Department of Bioengineering at the University of Washington, where she developed engineered models of brain microvessels. She recently has joint EMBL Barcelona as a Group Leader and her group focuses on the study of cerebral malaria pathogenesis.

Her lab uses a combination of bioengineering, computational and experimental tools to better understand cerebral malaria pathogenesis. By developing an in vitro 3D human blood-brain barrier model, they aim to understand how parasite and host factors interact to cause endothelial and perivascular damage. With this system, they will model the pathogenic mechanisms and signalling pathways that lead to BBB breakdown in patients with cerebral malaria.

Using Human Organoids to Model Kidney Disease and Therapy

Benjamin Freedman, University of Washington, Seattle, USA

A series of discoveries has recently revealed the potential of human pluripotent stem cells to differentiate into the renal lineage, culminating in the generation of kidney organoids with nephron-like segments *in vitro*. These beautiful structures contain diverse cell lineages and are capable of modeling complex disorders, such as polycystic kidney disease, glomerulosclerosis, and cystinosis. When transplanted *in vivo*, kidney organois exhibit potential for maturation. Could these lead to the 'holy grail' of immunocompatible regeneration? As kidney organoids approach their five year birthday, Dr. Freedman will look back at the beginnings of the field, reflect upon recent progress, and engage in a conversation about its future.

Benjamin Freedman, University of Washington, Seattle, USA

Dr. Benjamin Freedman is an Assistant Professor of Medicine at the University of Washington School of Medicine, Division of Nephrology. He is also a member of the Kidney Research Institute and the Institute for Stem Cell and Regenerative Medicine. Dr. Freedman received his Ph.D. in Cell and Developmental Biology in 2009 from the University of California at Berkeley.

He performed postdoctoral studies in the Renal Division of Brigham and Women's Hospital, at Harvard Medical School. Dr. Freedman is currently performing biomedical research using human pluripotent stem cells to model kidney disease pathophysiology and develop new therapies.

Engineering Tissue Patterning from the Bottom Up

Pulin Li, Whitehead Institute, Cambridge, MA, USA

How genes, operating in individual cells, generate coordinated multicellular behavior is a fundamental question in biology. Applying a bottom-up approach, we quantitatively analyzed how tissue patterning dynamics and precision arise from the underlying genetic interactions. Morphogens, forming concentration gradients in space, set the blueprint for tissue patterning. By reconstituting morphogen gradients *in vitro*, re-wiring genetic interactions, and using quantitative time-lapse imaging and mathematical modeling, we revealed how architectural features of morphogen pathways could improve patterning robustness.

Our ongoing work expands the morphogen platform to address the question of evolvability: how does the "same" morphogen pattern tissues of drastically different lengthscales? The ability to isolate patterning from concurrent developmental processes and to quantitatively analyze the patterning behavior under different biophysical parameters offers a new way to uncover developmental design principles and engineer multicellular patterning.

Pulin Li, Whitehead Institute, Cambridge, MA, USA

Pulin Li is a member of the Whitehead Institute for Biomedical Research, and an assistant professor of Biology at Massachusetts Institute of Technology. Her lab is interested in quantitatively understanding how genetic circuits create multicellular behavior in both natural and synthetically engineered systems. She obtained her B.S. at Peking University in China, and Ph.D. in Chemical Biology at Harvard University.

Her Ph.D. work used chemical genetic tools to control and understand the behavior of hematopoietic stem cells, under the mentorship of Dr. Leonard Zon. She then joined Dr. Michael Elowitz's group at California Institute of Technology to study developmental tissue patterning using synthetic and systems biology approaches.

Monday 10th February · 12:30

Mechanics of the intestinal crypt

Xavier Trepat, Institute for Bioengineering of Catalonia (IBEC), Spain

The intestinal epithelium is a highly dynamic tissue that self-renews every 3 – 5 days. Epithelial self-renewal is achieved through the action of stem cells that reside at the bottom of highly curved invaginations called crypts, where they coexist with secretory Paneth cells in a loose checker-board spatial pattern. To maintain homeostasis, stem cells constantly divide, giving rise to new cells that leave the niche, proliferate in the crypt neck, differentiate, and migrate to the tip of dome-like protrusions called villi, where they are extruded into the intestinal lumen. Each of these processes involves mechanical forces that have not yet been accessed experimentally.

Here we use intestinal organoids as a model system to provide maps of the forces that cells generate as they divide, differentiate, fold and migrate. Our data suggests that the crypt is a mechanical unit that folds through apical constriction. Apical tension reaches the first transient amplifying cells, which transmit the forces to the substrate, thus mechanically compartmentalizing the niche. We show, further, that stem cell division perturbs local tractions abruptly, but does not affect the overall force pattern at the crypt. Instead, cells leave the crypt through collective migration under tension, rather than being expelled by pressure as previously thought.

Xavier Trepat, Institute for Bioengineering of Catalonia (IBEC), Spain

Xavier Trepat received a BSc in Physics in 2000 and a BSc in Engineering in 2001. In 2004 he obtained his PhD from the Medical School at the University of Barcelona. He then joined the Program in Molecular and Integrative Physiological Sciences at Harvard University as a postdoctoral researcher. In 2008 he became a "Ramón y Cajal" researcher at the University of Barcelona and in January 2011 an ICREA Research Professor at the Institute for Bioengineering of Catalonia (IBEC).

He is Group Leader of the Integrative Cell and Tissue Dynamics research line at IBEC. In 2015 he won the Banc de Sabadell Award for Biomedical Research. In 2018 he was elected EMBO Member. He has been awarded with 3 grants from the European Research Council.

Gastruloids: a Self-engineered system for the study of early mammalian development

Alfonso Martinez Arias, University of Cambridge, UK

When small, specified numbers of Pluripotent Stem Cells (PSCs) are placed in defined culture conditions they aggregate and initiate a sequence of pattern forming events that mimic processes that take place in the embryo: they undergo symmetry breaking, gastrulation like movements, axial specification and germ layer organization. Over time, they assemble a spatially organize a genetic blueprint of the organism. In the case of mouse, gastruloids can be cultured for up to seven days to reach a stage comparable to E9.0 in the mouse embryo. We have recently extrapolated the system to human PSCs.

Gastruloids exhibit differences with mammalian embryos, most notably despite the spatial organization of gene expression they exhibit limited morphogenesis. This discrepancy suggests the existence of convergent but different modules involved in mammalian development. I shall be discussing specific examples and the implications that these observations have for the theoretical and practical understanding of developmental events in mammals.

References:

1. *Turner, D. et al. (2017) Anteroposterior polarity and elongation in the absence of extraembryonic tissues and spatialy organized signaling in Gastruloids, mammalian embryonic organoids. Development 144, 3894-3906*
2. *Van den Brink, S. et al. (2014) Symmetry breaking, germ layer specification and axial organisation in aggregates of mouse ES cells. Development 141, 4231-4242.*
3. *Beccari et al. (2018) Multiaxial self organization properties of mouse embryonic stem cells gastruloids. Nature 562, 272-276.*

Alfonso Martinez Arias, University of Cambridge, UK

Alfonso Martinez-Arias studied Biology at the Universidad Complutense in Madrid (Spain). After graduating in 1977, he obtained a Fullbright scholarship to study in the US and in 1978 he went to the Department of Biophysics of the University of Chicago, Chicago (USA). In 1983 he moved on to do a postdoc with Peter Lawrence at the MRC Lab of Molecular Biology in Cambridge, UK.

In 1987 he was awarded a Wellcome Senior Fellowship which he held until 2002 when he became a member of the University of Cambridge and since 2003, he is Professor of Developmental Mechanics. During this time, first in the department of Zoology and since 2000 in the Department of Genetics he has pursued his interests in the logic of animal development.

How is Ethics Relevant for the Engineering of Multicellular Systems?

Insoo Hyun, Harvard Medical School, Boston, MA, USA

Research into engineered multicellular systems is progressing at a rapid pace. Some observers may assume that ethical considerations for this new field amount only to regulatory issues concerning safety and/or informed consent concerns related to cell donors or patient recipients of investigational multicellular products. While these issues are important, they do not exhaust all the ways in which ethical considerations can affect the speed and direction of much of this research.

This talk will explain how a focus on bioengineering ethics can help facilitate rapid yet socially responsible progress in the engineering of multicellular systems for innovative research and clinical translation. A collaborative version of bioengineering ethics will be offered that brings researchers and ethicists together to help define an ethical approach that can be responsive to both the science and the ethical uncertainties that it may generate. Recent scientific examples will help illustrate the ways in which ethics remains relevant for the future development of multicellular systems engineering.

Insoo Hyun, Harvard Medical School, Boston, MA, USA

Insoo Hyun is Professor of Bioethics and Philosophy at Case Western Reserve University School of Medicine and Faculty Member in the Center for Bioethics at Harvard Medical School. As a Fulbright Scholar and Hastings Center Fellow, Dr. Hyun's interests include ethical and policy issues in stem cell research and new biotechnologies.

Currently, Dr. Hyun is the Principal Investigator of a BRAIN Initiative-funded project exploring the ethical issues surrounding human brain organoid research, in collaboration with leading scientists at Harvard and Stanford. He is the Co-Principal Investigator, along with colleagues at the Hastings Center, of an NIH grant identifying ways to improve the oversight of stem cell-based human-animal chimera research. And he is the Principal Investigator of a Greenwall Foundation project seeking to formulate a new bioengineering ethics framework for research involving the use of multi-cellular engineered living systems derived from human cells. This Greenwall project is in collaboration with scientists at Harvard, MIT, and the University of Michigan.

Dr. Hyun has been involved for many years with the ISSCR (International Society for Stem Cell Research), for which he has helped draft all of the ISSCR's international research guidelines and has served as their Chair of the Ethics and Public Policy Committee. He now serves as a member of the Neuroethics Subgroup of the BRAIN 2.0 Working Group of Advisory Committee to the Director, NIH.

Dr. Hyun received his BA and MA in Philosophy with Honors in Ethics in Society from Stanford University and his PhD in Philosophy from Brown University. He has been interviewed frequently on National Public Radio and has served on national commissions for the Institute of Medicine and the National Academy of Sciences in Washington D.C. Dr. Hyun is a regular contributor to Nature, Science, Cell Stem Cell, The Hastings Center Report, among many other journals. His book Bioethics and the Future of Stem Cell Research was published by Cambridge University Press in 2013.

Self-organization of stem cells into embryos: A window on early mammalian development

Magdalena Zernicka-Goetz, Department of Physiology, Cambridge University

Embryonic development is orchestrated by robust and complex regulatory mechanisms acting at different scales of organization. *In vivo* studies are particularly challenging for mammals after implantation, owing to the small size and inaccessibility of the embryo. The generation of stem cell models of the embryo represents a powerful system with which to dissect this complexity. Control of geometry, modulation of the physical environment, and priming with chemical signals reveal the intrinsic capacity of embryonic stem cells to make patterns. Adding the stem cells for the extraembryonic lineages generates three-dimensional models that are more autonomous from the environment and recapitulate many features of the pre- and postimplantation mouse embryo, including gastrulation.

Magdalena Zernicka-Goetz, Department of Physiology, Cambridge University

Magdalena carried out her Ph.D. at the University of Warsaw, Poland, under supervision of Andrzej Tarkowski. She came to Cambridge in 1995 to join Martin Evans group with the long-term aim of studying the mechanisms of regulative nature of development and spatial patterning in the mouse embryo. In 1997 she was awarded a Senior Research Fellowship from the Lister Institute to start her independent group at the Wellcome Trust/Cancer Research UK Gurdon Institute in Cambridge.

In 2001 she became a Wellcome Senior Research Fellow. In 2010, she became a Professor of Mammalian Development and Stem Cell Biology. In 1993 she received a Promising Young Scientist Prize from Foundation for Polish Science, in 2001, Young Investigator Award from EMBO, in 2007 she was elected to EMBO membership and in 2013 she became Fellow of British Academy of Medical Science.

Models of neurological disease

Roger D Kamm, Massachusetts Institute of Technology, USA

Many of the most debilitating and life-threatening diseases are associated with the central nervous system. Some, such as neurodegenerative diseases, predominately afflict our aging population. Yet others such as brain cancers and ALS are prevalent at all ages. In this presentation, models will be presented that attempt to recapitulate certain aspects of the central or peripheral nervous system, both to probe the disease process, and as a platform to screen for new therapeutics.

Four examples will be presented. First, a model for the healthy blood-brain barrier and neurovascular unit have been developed in order to capture the essential aspects associated with these diseases. Second, the blood-brain barrier model is used to study metastasis of cancers to the brain, as well as primary glioblastoma. In the third part of the talk, a model for the healthy and diseased neuromuscular junction will be presented as a step toward developing therapeutic strategies for treating ALS. Finally, a model for cerebral amyloid angiopathy, often associated with Alzheimer's disease, will be discussed as a disease model and for its drug screening potential.

Roger D Kamm, Massachusetts Institute of Technology, USA

Kamm is currently the Cecil and Ida Green Distinguished Professor of Biological and Mechanical Engineering at MIT, where he has served on the faculty since 1978. Kamm has long been instrumental in developing research activities at the interface of biology and mechanics, formerly in cell and molecular mechanics, and now in engineered living systems. Current interests are in developing models of healthy and diseased organ function using microfluidic technologies, with a focus on vascularization.

Kamm has fostered biomechanics as Chair of the US National Committee on Biomechanics (2006-2009) and of the World Council on Biomechanics (2006-2010). Kamm currently directs the NSF Science and Technology Center on Emergent Behaviors of Integrated Cellular Systems. He is the 2010 recipient of the ASME Lissner Medal (American Society of Mechanical Engineering) and the 2015 recipient of the Huiskes Medal (European Society of Biomechanics), both for lifetime achievements, and is the inaugural recipient of the ASME Nerem Medal for mentoring and education. He was elected to the National Academy of Medicine in 2010. Kamm is co-founder of two companies, Cardiovascular Technologies and AIM Biotech, a manufacturer of microfluidic systems for 3D culture.

Engineering approaches for human pluripotent stem cells derived kidney organoids: emulating tissue features through bioengineering design

Nuria Montserrat, Institute for Bioengineering of Catalonia (IBEC), Spain

The generation of human pluripotent stem cells (hPSCs) derived organoids is one of the biggest scientific advances in regenerative medicine. Recently, we have demonstrated that by lengthening the time that hPSCs are exposed to a three-dimensional microenvironment in the presence of defined renal inductive signals, we are able to generate kidney organoids that transcriptomically match second-trimester human fetal kidneys. Furthermore, we have recently developed a transplantation method that utilizes the chick chorioallantoic membrane (CAM). In our hands, this approach created a soft *in vivo* microenvironment that promotes the growth and differentiation of implanted kidney organoids, as well as providing a vascular component.

Through bioengineering, we have mimicked the stiffness of the chick CAM by fabricating compliant hydrogels. This approach resulted in the acceleration of kidney organoid formation proving that mechanical cues are determinant for the generation of hPSC-renal progenitor cells and kidney organoids. Overall, we will discuss how these preliminary findings are advancing our research towards the application of different bioengineering strategies (i.e., including 3D bioprinting and tissue engineering) for kidney organoid generation and human disease modeling.

Nuria Montserrat, Institute for Bioengineering of Catalonia (IBEC), Spain

Núria Montserrat is ICREA research professor since January 2019 and group leader of the "Pluripotency for organ regeneration" group at IBEC. She received BSc in Biology in 2006 at University of Barcelona and PostDoc at Fundaçao per a Ciência e Tecnologia (Portugal).

In 2008 she moved to the Center of Regenerative Medicine in Barcelona (CMRB) as an associate-researcher, supported by a Juan de la Cierva fellowship. In 2014 she was awarded with the European Research Council Starting Grant aiming at studying kidney development. and disease using hiPSC-derived kidney organoids.

From haploid stem cells to blood vessel engineering

Josef Penninger, University of British Columbia, Canada

We have previously generated murine stem cells with a single set of chromosomes, termed haploid ES cells. Using such cells we have been able to rapidly mine essential biological pathway and to use revertible mutagenesis to identify novel mediators of angiogenesis. Recently we have expanded our work to engineer human blood vessel organoids that can be transplanted into mice to establish a fully human vascular tree. We have used this system to model the pathogenesis of diabetes vasculopathies.

Josef Penninger, University of British Columbia, Canada

Josef Penninger, MD was formerly a lead researcher at the Amgen Research Institute in Toronto. Since 2002 Josef Penninger was the founding and scientific director of the newly established Institute of Molecular Biotechnology (IMBA) of the Austrian Academy of Sciences in Vienna, Austria. In 2018 he accepted the appointment as Director of the Life Sciences Institute (LSI) at the University of British Columbia (UBC) in Canada.

Major achievements include pioneering insights into the molecular basis of osteoporosis and breast cancer, as well as the study of metastatic spread. Josef Penninger's major awards include the Descartes Prize, the Wittgenstein Prize of the Austrian Federal Government, the Ernst Jung Prize for medical excellence, an AAAS Award, the Innovator Award from Era of Hope/U.S. Department of Defense and a second ERC Advanced grant.

Vascular Integration towards improved disease modelling

Kristina Haase, European Molecular Biology Laboratory, Spain

The development of ever more complex *in vitro* models has increased drastically over the last two decades. Now, in 2020, we expect that 3D models should make the leap from the bench to the bedside. However, a lack of adoption thus far results from the inability of these models to accurately predict clinical outcomes. Despite advances in patient-specific iPSC and gene-editing technologies, the lack of functional vasculature is hypothesized as a likely key factor in the limited predictability of current *in vitro* models. Given its role in regulating oxygen tension, nutrient delivery and immune cell interactions, functional vasculature is required for the development and long-term maintenance of normal tissue physiology. To overcome this limitation, we develop disease-specific models integrating microvasculature on millimetre-scale chips.

This talk will provide an overview of several vascularized models (placental, ischemic, and tumor) where we exploit the self-assembly process of primary endothelial and combined stromal cells. Generating perfusable microvessels in a tissue-dependent context allows us to investigate specific cell-cell interactions and the effects of mechanical cues, such as luminal flow, on the regulation of microvessel morphology and permeability. In addition, drug dissemination studies can be performed and examined in the context of perfused microvessels. These physiologically relevant systems hold significant promise for development into more accurate preclinical models – a major focus of our new lab.

Kristina Haase, European Molecular Biology Laboratory, Spain

Kristina Haase is a mechanical engineer by training. She holds a Masters degree in Mechanical Engineering and a Ph.D. in Biophysics from University of Ottawa.

Her post-doctoral work was carried out in the bio-engineering lab of Prof. Roger Kamm at MIT in Massachusetts, USA.

Since October 2019 she has started a new lab at EMBL Barcelona, focusing on tissue engineering and disease-specific modeling.

Tuesday 11th February · 12:00

Engineering Organoid Development

Matthias Lütolf, École Polytechnique Fédérale de Lausanne (EPFL), Switzerland

Organoids form through poorly understood morphogenetic processes in which initially homogeneous ensembles of stem cells spontaneously self-organize in suspension or within permissive three-dimensional extracellular matrices. Yet, the absence of virtually any predefined patterning influences such as morphogen gradients or mechanical cues results in an extensive heterogeneity. Moreover, the current mismatch in shape, size and lifespan between native organs and their *in vitro* counterparts hinders their even wider applicability. In this talk I will discuss some of our ongoing efforts in developing next-generation organoids that are assembled by guiding cell-intrinsic self-patterning through engineered stem cell microenvironments.

Matthias Lütolf, École Polytechnique Fédérale de Lausanne (EPFL), Switzerland

Professor Matthias Lutolf is Director of the Laboratory of Stem Cell Bioengineering at Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland. His highly innovative and cross-disciplinary research program is focused on the development of bio- and tissue-engineering strategies for improving organoid culture and enabling its translation to real-life applications.

Recreating Kidney Organogenesis *in vitro* with Human Pluripotent Stem Cells

Ryuji Morizane, Harvard Stem Cell Institute, Cambridge, MA, USA

We have developed an efficient, chemically defined protocol for differentiating human pluripotent stem cells into multipotent nephron progenitor cells (NPCs) that can form kidney organoids. By recapitulating metanephric kidney development *in vitro* we generate SIX2+SALL1+WT1+PAX2+ NPCs with 80 – 90% efficiency within 8 – 9 days of differentiation. NPCs form kidney organoids containing epithelial nephron-like structures expressing markers of podocytes, proximal tubules, loops of Henle and distal nephrons in an organized, continuous arrangement that resembles the nephron *in vivo*. The organoids express genes reflecting many transporters seen in adult metanephric-derived kidney, enabling assessment of transporter-mediated drug nephrotoxicity. Stromal cells are also generated with the presence of PDGFRβ+ fibroblasts/pericytes, and CD31+ endothelial cells. This kidney differentiation system can be used to study mechanisms of human kidney development.

Repetitive injury to tubular cells causes interstitial fibroblast expansion with characteristics of myofibroblasts, indicating kidney organoids can be used to model kidney fibrosis *in vitro*. Polycystic kidney disease (PKD) patient-derived organoids exhibit cystic phenotypes. Hence the generated kidney organoids are effective tools to study genetic disorders of the kidney as well as mechanisms of kidney injury and fibrosis. Microphysiological platforms *in vitro* facilitate kidney organoid vascularization and maturation, which may lead to the development of functional bioengineered kidneys in the future.

Ryuji Morizane, Harvard Stem Cell Institute, Cambridge, MA, USA

Ryuji is currently a Principal Investigator at Brigham and Women's Hospital, Harvard Medical School. He has pioneered research in stem cell differentiation and kidney organoids. Ryuji directs research groups focused on kidney regenerative medicine, genome editing in stem cells, and kidney disease modelling. His research also extends to simulation of kidney microenvironment using organ-on-chip systems. At the Wyss, Ryuji is collaborating with Professor Jennifer Lewis aiming to create functional vascularized kidney tissues in vitro.

Ryuji's research has been recognized internationally, and he has received various awards including the Research Excellence Award at Discover Brigham in 2015 and 2016 and Career Development Award at Brigham and Women's Hospital in 2016. He is a recipient of funding from the Uehara Memorial Foundation, Japan Society for the Promotion of Science, ReproCELL, Harvard Stem Cell Institute, and the Diabetic Complications Consortium.

Mechanoregulation of thrombus formation in the bloodstream

Hongxia Fu, University of Washington, Seattle, WA, USA

A thrombus is like a double-edged sword in blood vessels: on the positive side, it can stop bleeding at sites of injury, but on the negative side, it can cause vascular occlusion in many cardiovascular diseases, such as thrombosis, stroke, and sepsis. Endothelial cells (ECs) on the interior surface of blood vessels play an important role in regulating thrombus formation. We are interested in how a blood protein called von Willebrand factor (VWF), which is synthesized by ECs, mediates platelet adhesion and aggregation on the blood vessel wall and controls the initiation and development of thrombi in bloodstream.

Combing stem cells, microfluidics, and single molecule biophysics tools, our studies have unveiled a novel mechanoregulatory mechanism for VWF to be locally activated by hydrodynamic force induced by blood flow during hemorrhage or in diseased vessels, but rapidly deactivated downstream in normal blood circulation.

Hongxia Fu, University of Washington, Seattle, WA, USA

Hongxia Fu obtained her Ph.D. at the National University of Singapore, where she studied DNA biomechanics using single-molecule force manipulation tools and theoretical models. She continued her postdoctoral research training in biophysics and mechanobiology at the National University of Singapore and Harvard Medical School, where her research focused on developing and applying tools combining single-molecule fluorescence imaging and force manipulation techniques, microfluidics, and cell biology to study protein functions under force.

Currently she is an Assistant Professor in the Division of Hematology, University of Washington (UW) School of Medicine, the Institute for Stem Cell and Regenerative Medicine, the Department of Bioengineering at UW, and Bloodworks Northwest Research Institute in Seattle, USA. Her current research focuses on understanding the mechanisms of mechanosensory proteins in blood clotting, studying related blood diseases, such as thrombosis and bleeding disorders, based on vascular, molecular, and single-molecule models of health and disease, and seeking new methodologies for therapeutics testing and treatment of blood and circulatory system disorders.

Programming self-organizing tissues

Wendell Lim, University of California, San Francisco, USA

Satoshi Toda, Jonathan Brunger, Adam Stevens, Wesley McKeithan, Pilar Lopez

Multicellular organisms have evolved cell-cell communication programs that specify the robust self-organization of diverse body-plans and tissues. It is remarkable that genetically encoded programs can so compactly store the information to construct macroscopic tissues and organisms. Although we have identified many common themes seen in diverse developmental programs, many fundamental questions remain unclear.

What are the minimal components required for multi-cellular self-organization, and how might metazoan multi-cellularity have arisen? Can we understand the language of self-organization sufficiently to be able to genetically program the formation of new types of tissues, or to drive developmental programs in response to novel inputs and niches (i.e. for regenerative medicine etc.)? We have been developing a set of orthogonalized molecular parts that facilitate the construct defined, user-designed cell-cell interaction networks. Using these components (including orthogonal juxtacrine signals, paracrine signals, and adhesion/assembly systems) we have begun exploring how to program the formation of simple synthetic tissues from the bottom-up, as well as to modulate and control natural developmental programs.

Wendell Lim, University of California, San Francisco, USA

Wendell A.Lim obtained his Ph.D. in Biochemistry&Biophysics in 1991 at the Massachusetts Institute of Technology and his Postdoc in 1996 at Yale University. He is currently Professor & Chair, Department of Cellular and Molecular Pharmacology at UCSF and Director of UCSF Center for Systems & Synthetic Biology.

His general scientific interests are in understanding how genetically encoded molecular programs can yield the remarkable behaviors observed in biological organisms, at multiple scales. His research career began as a biophysical chemist and structural biologist studying problems such as the evolutionary optimization of enzymes, how protein structure is encoded in sequence, and the determinants of protein-protein interaction specificity. Now,his research has gradually shifted towards utilizing this mechanistic understanding of molecules as a foundation to study how systems of interacting molecules assemble to yield cellular or organismal signaling behaviors – complex behaviors in both space and time. His lab is interested in both the fundamental principles governing these molecular programs, as well as the way such programs have evolved.

Synthetic Embryology: A new window on mammalian development

Eric D. Siggia, The Rockefeller University, New York, USA

The embryo evolved to make a fetus and thus multiple modes of regulation conspire to ensure a robust outcome. This makes the task of quantifying the pathways defining the mammalian embryo particularly difficult. Embryonic stem cells (ESC) give rise to all cells of the body proper. We have shown several years ago, how merely confining human ESC to two dimensional patterns, causes the cells to recapitulate the spatial patterning seen in the mouse embryo at the onset of gastrulation. We have dissected the cascade of secreted factors and the location of receptors driven by apical-basal polarity responsible for the patterns.

A prediction for how morphogens are targeted in the mouse was recently confirmed by another group. Our assay can be extended to three dimensions and the model epiblast shown to spontaneously break symmetry and form a primitive streak. A second layer of extraembryonic like cells adds additional realism and new interactions. Synthetic systems allow one to peal back the layers of regulation that make embryonic development so robust. They are easy to manipulate and suggest targeted experiments to pursue in-vivo.

Eric D. Siggia, The Rockefeller University, New York, USA

Dr Siggia was trained as a physicist and worked in the areas of statistical mechanics of phase transitions, quantum magnetism, fluid mechanics and nonlinear dynamics. He moved to Rockefeller University from Cornell in 1998, and converted to biology.

He collaborated on projects in the areas of protein trafficking, bioinformatics of gene regulation, evolution of antibiotic resistance, cell cycle in yeast. In the last decade he worked with Ali Brivanlou and others on dynamics of vertebrate signaling pathways and synthetic embryology using human embryonic stem cells.

3D Bioprinting for *in vitro* Tissue Engineering

Wei Sun, Tsinghua University, China

3D Bio-Printing uses living cells as building blocks to fabricate *in vitro* biological models. The printed 3D tissue models have been widely applied to the field of regenerative medicine, disease study, drug discovery and drug toxicity testing. This presentation will report our recent study on printing cells for construction of *in vitro* tissue models, disease models, tumor models and micro-organ chips with application to cancer and drug toxicity study. An overview of 3D Bioprinting on *in vitro* tissue engineering will be given. Enabling techniques for cell printing to construct 3D biological models will be introduced.

Examples of 3D printing *in vitro* tissue models for: 1) cervical tumor *in vitro* with tumor morphology, MMP and genes expressions, chemo-resistance, and epithelial-mesenchymal transitions study; 2) micro-liver-organ for drug metabolism study; and 3) printing hepatocytes for drug hepatotoxicity study; and 4) printing cell models for renal filtration and nephrotoxicity test. Comparison of biological data derived from 3D printed models with 2D planar petri-dishes models will be conducted. Discussions on challenges and opportunities of 3D Bio-Printing model as alternative tissue models for drug development and testing will also be presented.

Wei Sun, Tsinghua University, China

Dr. Wei Sun is Albert Soffa Chair Professor of Mechanical Engineering, Drexel University, and Professor and Director of Biomanufacturing Research Center, Tsinghua University, Beijing, China. Dr. Sun's research has been on Biofabrication, Cell Printing and Tissue Engineering. His research has been sponsored by the US National Science Foundation (NSF), Defense Advanced Research Projects Agency (DARPA), National Aeronautics and Space Administration (NASA), Chinese Ministry of Science and Technology (MOST) and Chinese Ministry of Education (MoE).

Dr. Sun has published 160+ journal papers, with 9500+ SCI citations, 45 issued patents, and conducted 360+ invited presentations in the field of his research. Dr. Sun is the Founding President for International Society of Biofabrication (2010-2014), and the Founding Editor-in-Chief for international journal Biofabrication (2009-present).

Dr. Sun received Award of Distinguished Visiting Fellow from the Royal Academy of Engineering in UK (2018), the Senior Investigator Award from International Society of Biofabrication (2017), MII / Fralin Visiting Scholar Award from Virginia Tech (2015), Outstanding Research Award, College of Engineering, Drexel University (2009), William Mong Fellow Award, the University of Hong Kong (2008) and Ralph R. Teetor Educational Award, International Society for Automotive Engineers (2003).

Modeling epithelial cells-fibroblasts interactions in gut homeostasis and pre-invasive cancers

Danijela Vignjevic, Institut Curie, Paris, France

Fibroblasts are one of the most abundant cell types in the stroma of many tissues. They produce the extracellular matrix (ECM) and factors that modify its biochemical and physical properties. They also secrete growth factors and cytokines that affect proliferation, migration, and survival of neighboring cells. As such, they play an essential role in gut organogenesis, homeostasis, and tumor invasion.

We have developed a microstructured device that allows the study of the interaction of fibroblasts with the epithelial cells. Based on a 3D collagen I scaffold, the device has the typical topography of the mouse gut, an array of villi surrounded by crypts. Rigidifying the scaffold by cross-linking collagen fibers with threose preserves its cytocompatibility and enables the incorporation of fibroblasts reproducing the gut stromal compartment. Mouse organoids deposited into crypts, open up and epithelize the scaffold, generating a polarized monolayer containing proliferative and differentiated cells. Applying physical strain to the epithelium maintains its long-term integrity. Using this device, we found that primary intestinal fibroblasts are required to stimulate the efficient epithelialization of the scaffold while maintaining the apicobasal polarity of the epithelial cells.

In cancer, fibroblasts surrounding a tumor are generally called cancer-associated fibroblasts (CAFs). At the early stage of tumor progression, before the onset of invasion, cancer cells and CAFs are segregated. CAFs accumulate at the tumor periphery, forming a continuous and cohesive layer that surrounds the tumor. How is this organization of early-stage tumors achieved it is not clear. Using hollow alginate capsules, we found that CAFs do not spontaneously envelop cancer cells. Instead, confinement, the buildup of compressive stress, and reorganization of the fibronectin network were necessary to induce fibroblasts spreading over the aggregates of tumor cells. We propose that the compressive stress generated by the tumor growth represents a mechanism by which CAFs enwrap the tumor.

Danijela Vignjevic, Institut Curie, Paris, France

Danijela Matic Vignjevic was trained as a molecular biologist at the University of Belgrade, Serbia, and University of Wisconsin-Madison, US. She did her Ph.D. in cell biology, working on the role of the actin cytoskeleton in cell migration in the lab of Gary Borisy at Northwestern University, Chicago, US. She then did a post-doc in the lab of Daniel Louvard at Institut Curie, working on mouse models for colon cancer metastasis as a HFSP fellow.

After being recruited as an INSERM researcher, she continued working on cell migration-related questions. She started her independent team in 2013 when she got interested in how epithelial cells interact with their microenvironment (focusing on ECM and fibroblasts) in homeostasis and during cancer invasion. Her research strategy combines molecular and cell biology techniques with live-cell imaging using different model systems such as 2D and 3D in vitro cell cultures, tissue slices cultured ex vivo, and different transgenic mouse models.

She is the recipient of ERC Starting grant (2013-2017) and Consolidator grant (2018-2023), and she received several awards such as "Grand Prix" in Cancer research, Foundation Simone et Cino del Luca, and Dandrimont-Benicourt, French Academy of Science.

Building and Breaking Tissues to Understand Development and Disease

Zev Gartner, University of California, San Francisco, USA

Cells are living materials – their physical properties are not static but change dynamically in response to the environment. This property of cells as materials gives them the capacity to self-organize into complex three dimensional structures. Self-organization is critical to tissue developmental and repair, and a better understanding of how tissues self-organize will generate new strategies to slow the breakdown of tissue structure that contributes to the initiation and progression of diseases like breast cancer. In this presentation I will discuss our efforts to understand the physical mechanisms used by primary human epithelial cells to self-organize into a bilayered mammary epithelium. I will then describe how this program of self-organization becomes dysregulated by the activation of breast cancer driver genes contributing to disease progression.

Zev Gartner, University of California, San Francisco, USA

Professor Zev Gartner obtained his Ph.D. in Chemical Biology in 2004 at Harvard University and his PostDoc in 2008 at University of California. He is Professor, Department of Pharmaceutical Chemistry, UCSF and Co-director, Center for Cellular Construction.

His lab is working to understand how cells assemble into multicellular tissues, how the structure of tissues controls the behaviour of individual cells, and how changes to tissue structure drive the progression of diseases like cancer. Toward these goals, they build, perturb, and model human tissues in vitro using techniques from the chemical, engineering, physical and biological sciences.

Feedback, Dynamics and the Control of Size and Scale

Arthur D. Lander, University of California, Irvine, USA

Animal development is a remarkable feat of engineering, capable of reaching precise endpoints in the face of massive internal and external unreliability. That precision is reflected in the sizes of macroscopic structures (tissues and organs), the spatial patterns of cell behavior within those structures, and the scaling relationships that couple pattern and size. On rare occasions reliable outcomes are the result of finely-tuned initial conditions, but far more often they depend on feedback processes involving morphogens and other intercellular signals.

Understanding how such feedback circuits are constructed is one of the oldest and most pressing goals of developmental biology. I will discuss recent experimental and modeling results on the role of feedback in pattern scaling in Drosophila, and its relationship to the control of size.

Arthur D. Lander, University of California, Irvine, USA

Arthur Lander obtained his Ph.D. in Neuroscience in1985 at University of California and his PostDoc in 1987 at Columbia University College of Physicians & Surgeons, New York, NY.

Arthur Lander is the Donald Bren Professor of Developmental and Cell Biology and holds joint appointments in the Departments of Biomedical Engineering, and Logic & Philosophy of Science. He serves on the editorial board of BMC Biology, and is a member of the American Society for Clinical Investigation, a fellow of the American Association for the Advancement of Science, and a member of the Science Board of the Sante Fe Institute. He holds visiting professor appointments at National Taiwan University and the University of Tsukuba (Japan).

Research in the Lander lab is focused on the Systems Biology of Development and Disease, and deals with topics in Developmental Biology, Cell Biology, Mathematical/ Computational Biology, Glycobiology, Neurobiology, Cancer Biology and Engineering.

Short talks

Microengineered PEGDA Villus-like Hydrogels with Spatio-Chemical Gradients for Intestinal Epithelium Derived from Intestinal Organoids

Gizem Altay[1], **Aina Abad-Lazaro**[1], Emilio J. Gualda[2], María García-Díaz[1], Núria Torras[1], Jordi Folch[1], Sébastien Tosi[3], Vanesa Férnandez[1], Eduard Batlle[4,5,6], Pablo Alvarez-Loza[3], Elena Martínez[1,7,8]

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[2] *SLN Research Facility, The Institute of Photonic Sciences (ICFO), The Barcelona Institute of Science and Technology (BIST), Castelldefels 08860, Barcelona, Spain*

[3] *Advanced Digital Microscopy Core Facility (ADMCF), Institute for Research in Biomedicine (IRB Barcelona), The Barcelona Institute of Science and Technology (BIST), Baldiri Reixac 10-12, Barcelona 08028, Spain*

[4] *Colorectal Cancer Laboratory, Institute for Research in Biomedicine (IRB Barcelona), The Barcelona Institute of Science and Technology (BIST), Baldiri Reixac 10-12, Barcelona 08028, Spain*

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[8] *Department of Electronics and Biomedical Engineering, University of Barcelona (UB), Martí i Franquès 1, Barcelona 08028, Spain*

The small intestinal epithelium is formed by finger-like protrusions called villi and invaginations called crypts. The intestinal epithelium cell turnover relies on intestinal stem cells (ISCs) located at the crypt base that divide giving rise to proliferative cells that migrate up along the villi while differentiating into mature epithelium. Differentiated cells die at the tips of the villi and exfoliate into the lumen. This homeostasis is tightly controlled by biomolecular gradients of EGF, Wnt and BMP signalling pathways formed along the crypt-villus axis [1]. The development of three-dimensional (3D) *in vitro* culture methods has made possible the use of primary ISCs to create organoids1. One of the main drawbacks of intestinal organoids is their 3D closed geometry which hinders the access to the organoid lumen limiting their use in many applications. Therefore, there is a need for engineering culture platforms that overcome this limitation and provide physiologically cellular microenvironment combining all key features of the intestinal epithelium: 3D architecture, distinct stem/proliferative and differentiated cell types, and gradients of ISCs niche biomolecules.

We fabricated poly(ethylene) glycol diacrylate (PEGDA) based 3D villus-like scaffold by a simple photolithographic technique [2]. We generated ISCs niche biomolecules

gradients through the microstructured hydrogels, based on the free diffusion of the factors from a source to a sink chamber. We performed in silico models to simulate these spatio-chemical gradients. For the characterization, we designed and fabricated a fluidic chip allocating the hydrogel. We used fluorescently labelled proteins and Light-sheet fluorescence microscopy to visualize the gradients. We functionalized the scaffolds with collagen type I by EDC/NHS chemistry after co-polymerizing PEGDA with acrylic acid. We seeded cells derived from intestinal organoids on the scaffolds bearing the gradients of ISCs niche biomolecules.

Using in silico models and microscopic characterization, we demonstrated that the steady state gradient profiles could be obtained in our system by periodically replenishing the media in the source and the sink chambers. We could obtain full coverage of the scaffold surface, bearing the biomolecular gradients, by primary intestinal epithelial cells. As a proof of concept, we demonstrated that different ISCs niche biomolecular gradients profiles and composition affect the proportion and positioning of the different intestinal organoid-derived cell types along the vertical axis of our scaffold.

We believe our 3D *in vitro* intestinal model with physiologically relevant physico-chemical characteristics will allow for a thorough *in vitro* analysis of the intestinal epithelial cells' biology under physiological and pathological conditions.

1. *Sato T et al. Growing self-organizing mini-guts from a single intestinal stem cell: mechanism and applications. Science. 2013;340(6137):1190-1194.*
2. *Castaño AG, et al. Dynamic photopolymerization produces complex microstructures on hydrogels in a moldless approach to generate a 3D intestinal tissue model. Biofabrication. 2019;11.*

Morphogenesis is stressful – Elastic properties of folding cell sheets

Stephanie S.M.H. Höhn, Pierre A. Haas, Kyriacos C. Leptos and Raymond E. Goldstein

Department of Applied Mathematics and Theoretical Physics, University of Cambridge, UK

Living tissues are intelligent materials that can change their mechanical properties while they develop. In spite of extensive studies in multiple model organisms we are only just beginning to understand these dynamic properties and their role in tissue development. Although many tissues are known to exhibit visco-elastic properties, it is unclear which properties dominate three-dimensional shape changes of cellular monolayers, such as epithelia.

The embryonic inversion process in the micro-algal order Volvocales is uniquely suited for comparative studies on epithelial morphogenesis. Volvocalean embryos consist of cup-shaped or spherical cellular monolayers which invert their curvature in order to expose their flagella. Volvox globator exhibits one of the most striking processes of cell sheet folding (Fig. 1): Through inwards folding at the equator of the initially spherical cell sheet adopts a mushroom shape and eventually turns itself entirely inside-out through an anterior opening [1]. These global deformations are driven by several waves of active cell shape changes [2, 3]. A combination of advanced imaging and computational analyses is used to explore the role of tissue contractility in the occurring invagination and involution. The associated internal stresses as well as the elastic properties of the dynamic cell sheet are determined through laser ablation experiments.

[1] Höhn S and Hallmann A. BMC Biology 9, 89 (2011).

[2] Höhn S, Honerkamp-Smith AR, Haas PA, Khuc Trong P, and Goldstein RE. Physical Review Letters 114, 178101 (2015).

[3] Haas PA, Höhn S, Honerkamp-Smith AR, Kirkegaard JB, and Goldstein RE. PLOS Biology 16, e2005536 (2018).

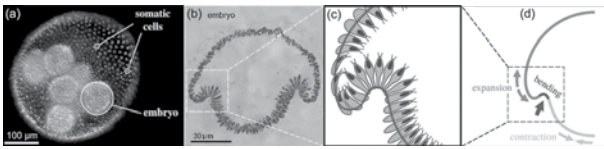

Fig. 1 (a) Volvox globator with embryos; (b) Cross-section of inverting embryo; (c) cell shapes, red line: cytoplasmic bridges (cell-connections); blue: nuclei; (d) tissue deformations in early inversion.

Three-dimensional culture of pancreas progenitors differentiated from mouse embryonic stem cells

Shlomit Edri[1], Ariel Szklanny[1], Ben Kaplan[1], Francesca Spagnoli[2] and Shulamit Levenberg[1]

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[2] *Centre for Stem Cells & Regenerative Medicine, King's College London, UK*

Over the last few years the establishment of three-dimensional (3D) cell culture methods allow embryonic stem cells (ESCs), induced pluripotent stem cells (iPSCs) or stem/progenitor cells to recapitulate many aspects of their differentiation programs and development *in vitro*. Specifically, ESCs can be coaxed into specific structures resembling *in vivo* tissues and organs, like eye caps, intestine, forebrain and liver, which termed organoids. The ability of cells to aggregate in this way has been referred as self-organization. With the great potential the organoids hold, they have limitations: they are small and lack mechanical support and vasculature.

In our study we focus on differentiation mouse ESCs to pancreas identity. We developed a robust and efficient differentiation protocol of adherent mouse ESCs to pancreas progenitors, which we aggregated to pancreatic organoids. To supply the mechanical support for the aggregates, we created 3D spatially defined highly porous polymeric scaffolds using a 3D printing technique. Seeding pancreas endothelial cells and mesenchymal support cells on this scaffold, allowed the formation of vessel-like networks inside the entire scaffold. Utilizing the self-organization of the organoids and the scaffold support, we integrate pancreas organoids and vessel-like networks in the polymeric scaffold, mimicking the complex structure of the developing pancreas, which in future will enable the functional maturation upon implantation.

Our study provides a new approach that combines the inherent self-organization of ESCs, engineered vessel networks and mechanical support to better resemble the developing pancreas, which has enormous potential in the fields of regenerative medicine and developmental biology.

Collective Cell Movement and Cell State Transitions in Gastruloids Specify the Formation of Endoderm

Ali Hashmi[1], Pierre Perrin[1], Sham Tlili[1], Alfonso Martinez Arias[2], Pierre-François Lenne[1]

[1] *Aix Marseille University, CNRS, IBDM, Turing Centre for Living Systems, Marseille, France*

[2] *Department of Genetics, University of Cambridge, UK*

In recent years, "gastruloids" have emerged as an alternative model system to dissect the complex intricacies of gastrulation and early morphogenesis. By utilizing a smaller number of embryonic stem cells (ESC) for gastruloids it is now possible to investigate the earliest symmetry breaking events and the formation of germ layers in a controlled fashion.

In this study we generated small aggregates from mouse ESC, primed to behave more epithelial-like in presence of FGF, to study the emergence of the endoderm. Despite the absence of an extraembryonic tissue, the aggregates that are given a Chiron pulse (a Wnt agonist) grow and elongate to attain a teardrop morphology with the emergence of a tip after 4 days. We found that the tip contains a group of cells that are endodermal-like as shown by the expression of various markers. We used imaging on fixed and live gastruloids to dissect the mechanisms leading to the formation of this region and focused on E-cadherin (E-cad) dynamics in relation with the transcription factors T/Brachury (T/Bra) and Sox17, which are markers of mesendoderm and endoderm, respectively.

The distribution of E-cad, which is initially homogeneous, exhibits temporal inhomogeneities, that exacerbate after the Chiron pulse. At the macroscopic scale, the elongation of the aggregates is preceded by a polarized expression of E-cad and T/Bra. A large population of cells that express both E-cad and T/Bra lose E-cad expression over time, all the while retaining a small fraction of pluripotent Ecad cells that do not express T/Bra to begin with. This cell-state switching and maintenance of local pluripotency lead to the formation of small islands of E-cad rich cells that are surrounded by cells that are expressing T/Bra. The islands move in a directional manner to the region of the aggregate which forms the tip. The E-cad islands eventually combine to form a single cluster wherein the cells commit towards an endoderm fate, marked by expression of Sox17 and FoxA2.

Our data suggest that the endoderm can emerge from epithelial-like cells, without cycles of epithelial-to-mesenchymal transition (EMT) and the reverse transition (MET).

Mechanics and active cell behaviours contribute to self-organization of mesenchymal cells in the limb

Xavier Diego[1*], A. Malandrino[1*], H. Cardona[1*], X. Trepat[2,3], J. Sharpe[1,3]

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[3] *Institute for Bioengineering of Catalonia, Spain*

** Equal contributions*

A reaction-diffusion mechanism is believed to govern the formation of digits during development. However, mechanics and active cell behaviors could also have a role in this process, an hypothesis that has been proposed before but has not been investigated systematically.

Thus, we decided to test the importance of mechanics for self-organization by culturing mesenchymal cells from mouse limbs on substrates of different rigidities. For the first time, we demonstrate that purely mechanical properties clearly influence the emergent patterns.

Combining live imaging and traction force microscopy we have quantified the evolution of cell forces, velocities and densities during the first three days of the patterning process.

Our observations suggest that the mechanism of self-organization in the limb mesenchyme requires feedback between a reaction-diffusion program and the mechanical and migratory state of cells, which is dynamically modulated over time. Computational modeling and transcriptomics allows us to characterize the physical and molecular nature of this feedback.

A 3D Morphogenetic Model of Organogenesis in a Human Genetic Context

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During embryogenesis, tissue layers undergo morphogenetic flows that rearrange and fold the embryo and its organs into specific shapes. While characteristic signaling pathways and morphogenetic features have been identified using animal models, extrapolating this information to human systems is challenging. Moreover, mammalian embryos exhibit species-specific differences in morphology, and many molecular markers have not been confirmed. Here we report a novel *in vitro* technique to produce large arrays of 3D pluripotent epithelial cultures composed of human pluripotent stem cells (hPSCs).

Using this technique, we are able to robustly control initial conditions such as shape, cell number, and cell density for the generation of organoids. We exploit this control and under subsequent differentiation obtain reproducible fate-patterning in our 3D organoids. Upon differentiation, we observe spontaneous symmetry breaking and morphological changes. Time-lapse imaging reveals tissue folding and stratification, driven by cellular rearrangements, which is a key motif of organogenesis. Our reproducible on-chip approach establishes a new model system to study organ development and enables opportunities to direct morphogenetic systems.

Induction of Synthetic Tissue Folding

Guillermo Martínez Ara[1], Nuria Taberner Carretero[2], Mami Takayama, Casandra Villava Robles[1], Miki Ebisuya[1]

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During the last years, several developmental processes such as patterning and cell differentiation have been reconstituted *in vitro* to improve our understanding of them. However, 3D tissue shape is still mainly achieved through tissue engineering methods, based on the use of structures that will direct cells to acquire different tissue morphologies. However, initial changes in tissue shape will condition the following developmental stages, and therefore are essential for the development of functional tissues and organs. For this reason, we aim to reconstitute 3D morphogenetic processes *in vitro*.

How can cell-level processes provoke changes in tissue shape during development? Many essential genes need to be expressed for changes in tissue shape to occur. Some of these genes have also been observed to be sufficient to cause changes in cell shape, proliferation or migration. To find out to what extent each of these proteins and cellular events can drive morphogenesis, we use a minimal setting in which we study how epithelial tissues acquire new shapes.

In our latest work, we induce apical constriction in a sheet of MDCK (Madin-Darby Canine Kidney) cells set on a soft substrate, to test which types of tissue deformation can be provoked by this process. This change in cell shape (from cuboidal to trapezoidal) is induced through the expression of one single protein: Shroom3, and it is sufficient to cause curvature of epithelial colonies and eventually folding. To further test how different patterns of apical constriction can create different 3D shapes, we have developed an optogenetic version of the protein.

In this setting in which unknown forces and interactions with other tissues are minimized, we plan to analyze which are the necessary conditions to achieve different tissue shapes. Our main focus is now to investigate how size and initial shape of cell colonies can affect these deformations.

Onset and Patterning Rules of Mesendoderm and Definitive Endoderm in Embryoid Bodies

Naor Sagy[1], Maayan Pour[1], Shaked Slovin[1], Abhishek S. Kumar[2], Gaya Savyon[1], Maya Allalouf[1], Jonathan Boxman[1], Alexander Meissner[2], **Iftach Nachman**[1]

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In vitro models of early mammalian development, such as embryoid bodies (EBs) and gastruloids, provide accessible systems for the study of basic rules shaping cell fate and patterning during embryogenesis. Using high-throughput live 3D imaging, we study two early differentiation decisions in mESC-derived EBs and tetraploid-complementation embryos: the formation of primitive streak and mesendoderm progenitors (using Bra-GFP), and the downstream emergence of definitive endoderm (DE), using Sox17-RFP.

We find that mechanical, biochemical and neighboring cell cues predict or affect the positioning of a primitive streak-like locus, determining the AP axis. Bra onset is biased by EB contact points with surfaces, can be maneuvered to a specific locus, two loci, or to an isotropic peripheral pattern. The EB can integrate separate mechanical and biochemical signal sources, resulting in a single locus. Interestingly, Foxa2 onset provides a predictive earlier symmetry-breaking event, explained by a local Wnt gradient.

In contrast, DE cells arise from within the mesendoderm population in a temporally-synchronized, yet spatially stochastic “salt-and-pepper” pattern. This is followed by a self-sorting phase of the Sox17+ cells, leading to aggregation or lumenogenesis as the in-vitro counterpart to intercalation in the embryo. Self-sorting correlates with up-regulation of E-cadherin, and is not essential for DE differentiation or proliferation. We find that a small subpopulation of Bra-high cells are committed to their Sox17+ fate independent of external Wnt signal.

The remarkably different strategies demonstrated in these two fate decisions may be explained in the context of embryo dynamics.

Sagy et. al., Development 146 (20), dev181917, 2019
Pour et. al., bioRxiv, 728642, 2019

Tension heterogeneity instructs morphogenesis and fate specification during heart development

Rashmi Priya, Srinivas Allanki, Alessandra Gentile, Shivani Mansingh, Hans-Martin Maischein and Didier Stainier

Department of Developmental Genetics, Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany.

Embryogenesis entails generation of diverse cell fates and emergence of complex morphogenetic patterns. A key question remains as to how morphogenesis and mechanics contribute to cell fate decisions in a complex and growing organ. During cardiac development, the myocardial wall transforms from a monolayer to an intricate topological structure consisting of two distinct types of cardiomyocytes (CMs): outer compact and inner trabecular layer CMs. This process of cardiac trabeculation is crucial for cardiac function as aberrations lead to congenital cardiomyopathies and embryonic lethality. Yet, the mechanisms underlying the emergence and specification of trabecular CMs remain unknown. Using the zebrafish heart in combination with high-resolution quantitative microscopy, *in vivo* measurements of tension/subcellular dynamics, genetic mosaic tools and embryological interventions, we now report that contractility couples morphogenesis and cell fate to ensure robust self-organization of CMs into compact versus trabecular layer.

Proliferation induced crowding triggers symmetry breaking by generating local differences in cellular contractility. These effects lead to stochastic delamination of CMs from the outer compact layer to seed the inner trabecular layer. By manipulating contractility at the single cell-level, we show that reducing contractility abrogates delamination while inducing contractility augments delamination, and strikingly, inducing contractility is sufficient to drive delamination even in the absence of critical trabeculation signals like Nrg/Erbb2 or blood- flow. Further, using controlled perturbations to decouple mechanical cues from biochemical signaling, we find that mechanical cues drive CM fate specification. Inducing tension heterogeneity (and thereby CM delamination) by manipulation of cell density or contractility is sufficient to generate differential Notch activity as well as apicobasal polarity. Overall, our study reveals how form and function emerge as a collective product of individual cell behaviors, and argues for system-level approach integrating mechanics with regulatory circuits for a cogent understanding of multicellular organization *in vivo*.

A novel mathematical law to understand 3D self-organization in epithelial tubes

Pedro Gómez-Gálvez[1,2,*], Pablo Vicente-Munuera[1,2,*], Samira Anbari[3,*], Antonio Tagua[1,2,*], Carmen Gordillo-Vázquez[1,2], Ana M. Palacios[1,2], Antonio Velasco[1], Carlos Capitán-Agudo[1], Clara Grima[5], Valentina Annese[1,2], Rafael Robles[5], Alberto Márquez[5], Javier Buceta[3,4], Luis M. Escudero[1,2]

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The analysis of epithelial organization as tiles on planar surfaces has been essential to the understanding of animal development. However, realistic insight into organogenesis requires a three-dimensional perspective able to deal also with tissue bending. In that regard, apico-basal cell intercalations (scutoids) have been shown as a key factor to optimize energy expenditure in folding epithelia. Yet, the consequences of this new morphogenetic paradigm remain uncharacterized. Until now, two mathematical principles have been widely used to investigate morphogenesis quantitatively: Euler´s formula and Lewis' law.

The importance of these laws resides in two fundamental aspects. First, their applicability to different tissues from different organisms and, therefore, their character as driving developmental principles. Second, their biological implications since they connect geometrical traits with key functionality features such as patterning, fate establishment, cell division, and tissue growth. Importantly, the certainty of these principles in 3D has been taken for granted. However, our recent discovery of scutoids questions their truthfulness. We have found a relationship between the 3D topology of epithelia and the inherent geometrical and physical constraints of tissues. We will show how the scutoids presence implies a breakdown of Euler's principle in 3D and will present what we have called the "Flintstones' law": the thickness and curvature of epithelial tubes are logarithmically related to the cellular connectivity of the tissue via energetic cues. The existence of this novel, and universal, law is supported by data and technical advances from four different disciplines: computed-aided image analysis of 3D bended tissues; computational models imitating the 3D cellular packing; mathematical analyses of cellular organization and a stochastic biophysical model able to predict the "Flintstones' law" based on the energetic cost needed to increase the number of 3D cells contacts.

In conclusion, our research shows how mathematical and physical principles, arranged in the form of simple rules, underlie the emergence of functionally complex developmental structures.

Contribution of stromal cells to the formation and stabalisation of blood vessels.

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Vasculogenesis, the creation of new blood vessels, occurs due to an inherent ability of endothelial cells (ECs) to self-assemble. These cells proliferate, migrate, elongate and self-assemble to from tubules. Thus, without doubt, ECs are the most important participants in the formation of blood vessels. However, many studies have shown that stromal cells, connective tissue cells of any organ, including fibroblasts (FBs) play key roles in the formation and stabilisation of these vessels, mostly chemically by producing and secreting growth factors. In this study, employing a 3-channel microfluidic device we aimed to address mechanical roles of FBs in vasculogenesis.

Mono-culturing, embedding only ECs within a hydrogel, and co-culturing, embedding ECs and FBs within a hydrogel, showed that presence of FBs is crucial for formation functional blood vessels, as mono-cultured ECs failed to form interconnected vascular networks while ECs mixed co-cultured with FBs formed highly inter-connected vascular networks which lasted for 21 days (Figure 1-1). Although treating mono-cultured ECs with conditioned medium, a medium consisted of growth factors secreted by FBs, improved vessel formation but the vessels formed were not functional proving that chemical interaction is essential but not sufficient to support the formation of functional vessels. Also, perturbing genes belonging to mechanotransduction passways by either applying chemical inhibitors or siRNAs knockdown showed that mechanical support of FBs plays an important role in vessel formation and stabilisation as perturbation of these genes resulted in the formation either non-functional or less functional blood vessels.

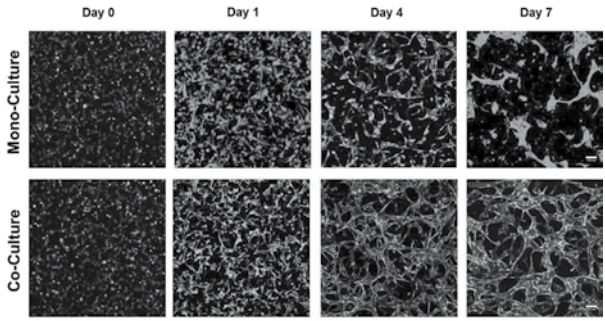

Figure 1-1: GFP-HUVECs formed **well-connected** networks when co-cultured with **NHLFs.**

Shear-induced crystallization drives precise patterning of hair cells in the mammalian inner ear

Roie Cohen[1,2], Liat Amir-Zilberstein[1,#], Micha Hersch[3,4], Shiran Woland[1], Shahar Taiber[1,5], Fumio Matsuzaki[6], Sven Bergmann[3,4,7], Karen B. Avraham[5], and **David Sprinzak**[1]

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Precise periodic organization of cells is required for the function of many organs and tissues. It is often unclear, however, how such precise patterns emerge during development. The mammalian hearing organ, the organ of Corti, consists of a remarkably organized pattern of four rows of hair cells interspersed by non-sensory supporting cells. This checkerboard-like pattern of HCs and SCs emerges from a disordered epithelium over several days, yet the transition to an ordered cellular pattern is not well understood. Using time-lapse imaging of mouse cochlear explants and mathematical modeling, we show that hair cells rearrange gradually over 2-3 days through a tissue-wide shear motion that coordinates intercalation and delamination events to achieve precision patterning.

A mathematical model, where tissue morphology is described in terms of the mechanical forces that act on cells and cellular junctions, suggests that global shear and local repulsion forces on hair cells are sufficient to drive the tissue into the final checkerboard-like pattern. Our findings suggest that mechanical forces drive the transition from disordered to ordered cellular patterns in a process strikingly analogous to the process of shear-induced crystallization in physics.

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Gerry Sexton Ph.D, 3D Microscopy Specialist, Zeiss

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Activation using Surface
nyography

Caroline J Jolley[1,4], Raimon Jané[2,3]

ology (BIST), Barcelona, Spain
CIBER-BBN), Barcelona, Spain
ona Tech, Barcelona, Spain
ndon, United Kingdom
United Kingdom
g's College London, King's Health Partners, London, United Kingdom

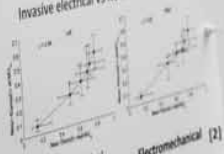
te assessment of inspiratory muscle activity is therefore
nctioning. The current **gold standard assessment** of human
or crural diaphragm electromyography ($oesEMG_d$). These

nical and electrical activation during contraction, respectively
over the lower intercostal spaces ($sMMG_{ics}$ and $sEMG_{ics}$
ctly compared to gold standard P_{di} and $oesEMG_d$ measures

RESULTS

Invasive mechanical VS Non-invasive mechanical [1]

Invasive electrical VS Non-invasive electrical [1]



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RMS

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Invasive electrical VS Non-invasive mechanical

Electromechanical coupling [2]

for the assessment of inspiratory muscle function in health and disease.

MENTS
nish Ministry of Economy and Competitiveness through the project DPI2015-68862p
als and Nanomedicine (CIBER-BBN) [Instituto de Salud Carlos III/FEDER]. M. Lozano-

Posters Session

EMBL · IBEC Winter Conference

ENGINEERING MULTICELLULAR SYSTEMS

Poster Session 10th February

N	Name	Affiliation	Title
1	Vanesa Fernández Majada	Institute for Bioengineering of Catalonia (IBEC)	Myofibroblast-derived mechanical cues direct Epithelial Migration
2	Elena Garreta	Institute for Bioengineering of Catalonia (IBEC)	Efficient Generation of Human Pluripotent Stem Cell-derived Kidney Constructs by 3D Bioprinting of cell-laden Kidney Specific Bioinks
3	Tom Golde	Institute for Bioengineering of Catalonia (IBEC)	The role of intermediate filaments in stress resistance in 3D epithelial structures
4	Carmen M. Gordillo Vázquez	Universidad de Sevilla	Natural variation in 3D tissue organization
5	Judith Guasch	Institute of Materials Science of Barcelona (ICMAB-CSIC)	Steps towards Mimicking the Lymph Nodes to Enhance T Cell Expansion
6	Maria Guillot-Ferriols	Biomaterials and Nanomedicine (CIBER-BBN)	Elastin-like recombinamers as poly(vinylidene fluoride) membrane coatings, a new approach for mesenchymal stem cell culture and differentiation
7	Ju Yeon Han	EMBL Barcelona	To what extent is digit patterning a Turing system?
8	Mathieu Hautefeuille	Universidad Nacional Autónoma de México	Fabrication of biphasic microstructures for viscoelastic cell culture substrates
9	Mathieu Hautefeuille	Universidad Nacional Autónoma de México	Impact of the ECM stiffness and geometry in the collective dynamics of epithelial and mesenchymal lung cells

10	Joseph Hill	SUPA School of Physics	Embryonic Forces: Illuminated by Microlasers
11	Kazuya Horibe	Osaka University	A surface geometry of living things induces a topological change of a chemical traveling wave during morphogenesis
12	Akanksha Jain	ETH-Zurich	Studying developmental dynamics and pattern emergence in human cerebral organoids
13	Jenny Kechagia	Institute for Bioengineering of Catalonia (IBEC)	The Integrin β4-keratin link impairs mechanosensing by protecting the nucleus form mechanical loading.
14	Akshada Khadpekar	Indian Institute of Technology	Asamataxis: Mechanical inhomogeneity driven cell migration leading to long-range self-patterning of cells
15	Gülistan Kocer	INM-Leibniz Institute for New Materials	Anisotropic materials with dual functionality for cardiac tissue engineering
16	Hui-Shun Kuan	Friedrich-Alexander Uni Erlangen-Nürnberg	Material properties of pilus mediated cellular aggregates
17	Adrián López Canosa	Institute for Bioengineering of Catalonia (IBEC)	Design of a Microphysiological System to Model Ischemic Cardiac Tissue
18	Erik Mailand	Ecole polytechnique fédérale de Lausanne (EPFL)	The Role of Surface Stresses in Fibrous Tissue Morphogenesis
19	Andrea Malandrino	EMBL Barcelona	*In Vitro* Modeling of Micro-Emboli and Their Effect on Microvascular circulation And Endothelium Mechanics
20	Andrés Marco Gimenez	Institute for Bioengineering of Catalonia (IBEC)	Engineering human Pluripotent Stem Cells (hPSCs) lines with CRISPR/Cas9 for inducible Knock Out in Kidney Organoids
21	Ariadna Marín Llauradó	Institute for Bioengineering of Catalonia (IBEC)	Linking epithelial geometry to tension and pressure
22	Elena Martínez Fraiz	Institute for Bioengineering of Catalonia (IBEC)	Self-organized intestinal epithelial monolayers in crypt and villus-like domains show effective barrier function

23	Marina Matsumiya	EMBL Barcelona	Recapitulating the somitogenesis *in vitro* to identify novel causative genes for congenital bone diseases
24	Antoni Matyjaszkiewicz	EMBL Barcelona	LIMBNET: online image-based computational modelling of limb development
25	Torsten Müeller	Bruker Nano GmbH	Quantitative characterization of adhesion and cytomechnics of living cells on biomaterials and tissues
26	Jose Munoz	Universitat Politècnica de Catalunya (UPC)	Stability and oscillatory evolution of Drosophila Central Nervous System depends on tissue rigidity and adhesive contributions
27	Anastasiia Mykuliak	Tampere University	*In Vitro* Vascular Networks for Bone Tissue Engineering
28	Erik Noetzel-Reiss	Institute of Complex Systems Biomechanics (ICS-7)	Physical and chemical basement membrane disruption modes synergistically promote the invasiveness of MCF10A breast acini.
29	David Oriola	EMBL Barcelona	Inferring the network topology driving mesoderm differentiation from single cell time-course data
30	Adam Ouzeri	Universitat Politècnica de Catalunya (UPC)	Upscaling active gel models of the actin cortex to epithelial mechanics
31	Raghavendra Palankar	University Medicine Greifswald	Platelet and Thrombus Biomechanics: The Need for Vasculature-on-Chip
32	Patricia Prado	Institute for Bioengineering of Catalonia (IBEC)	Differentiation of Human Pluripotent Stem Cells into Ureteric Bud-like Cells and Assessment of their Renal Potential by the Use of ex vivo Kidney Reconstruction Assays
33	Bernad Raquel	Institute for Research in Biomedicine (IRB Barcelona)	CDK8/19 inhibition stabilizes human naive pluripotency
34	Laura Rijns	Eindhoven University of Technology	Biofunctionalized Hydrogels based on Benzene-1,3,5-tricarboxamides (BTAs) for Kidney Regeneration

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ENGINEERING MULTICELLULAR SYSTEMS

Poster Session 11th February

N	Name	Affiliation	Title
35	Alicia Roig Merino	German Cancer Research Center (DKFZ)	SMARt engineering: Generation of isogenic Stem Cells and transgenic models utilising a non-integrative and autonomously replicating DNA vector system
36	William Roman	Instituto de Medicina Molecular	Generation of an *in vitro* neuromuscular junction at the cellular resolution
37	Aurelien Roux	University of Geneva	Topological defects organize morphogenetic stresses
38	Gerard Rubí	Institute for Bioengineering of Catalonia (IBEC)	Development of an *in vitro* three-dimensional colorectal tumor model for drug screening
39	Christian Schröter	University of Copenhagen	Generation and maintenance of robust cell fate proportions by FGF/ERK signaling
40	Lucia Selfa	Institute for Bioengineering of Catalonia (IBEC)	Studying Wilms' Tumor 1 (WT1) function in human kidney development and disease using human pluripotent stem cells-derived organoids and genome editing
41	Yvenn Sermeus	KU Leuven	Individual cell based modeling of limb bud outgrowth to predict shape and mechanical properties
42	Tiziano Serra	AO Research Institute Davos	A sound-induced technology for spatial orchestration of functional large-scale microvascular networks
43	Shayan Shamipour	IST Austria	Bulk Actin Dynamics Drive Phase Segregation in Zebrafish Oocytes

44	Apeksha Shapeti	KU Leuven	Quantifying invasion and 3D traction forces during multicellular angiogenic sprouting upon CCM-2 loss shows a ROCK-dependent increase in contractility and invasiveness
45	Aleksandra Slabikova	Ryazan State Medical University	Examination of proliferative activity and cell viability during neurogenic differentiation from iPSCs in 3D culture of cerebral organoids
46	Aki Stubb	University of Turku	Superresolution architecture of cornerstone focal adhesions in human pluripotent stem cells.
47	Alejandro Torres-Sánchez	The Francis Crick Institute	Interacting Cellular Meshes: A new theoretical and computational framework to investigate tissue reorganisation during morphogenesis
48	Manuela Urban	German Cancer Research Center (DKFZ)	Non-viral episomal S/MAR DNA vectors for the persistent genetic engineering of hiPSCs and their progenies
49	Johnick Van Sprang	Eindhoven University of Technology	Supramolecular Hydrogels For Kidney Organoid Development
50	Jef Vangheel	KU Leuven	Exploring the Cell Jamming Phase Diagram Using a 3D Deformable Cell Model
51	Chiara Venturini	Universitat Politècnica de Catalunya (UPC)	A generalized clutch model to explain cell adhesion mechanics
52	Tacker Vivek	Global Health Institute	Lung-on-a-chip microphysiological systems for studies of host-pathogen interactions in Tuberculosis
53	Sara Watson	University College London	Development of an *in vitro* microfluidic model of thymocyte extravasation
54	Justina Yeung	The Francis Crick Institute	Spatial Regulation of Proneural Gene Expression in the Hindbrain
55	Ayushi Agrawal	University College London	Integrated *in vitro* model of tumour vasculogenesis and cancer cell intravasation
56	Enrico Almici	Institute for Bioengineering of Catalonia (IBEC)	Engineered cell-derived matrices as 3D tumor stroma models

57	Krisztina Arato	EMBL Barcelona	A Study on Actomyosin Influencing the Formation of Spatial Asymmetries in Early Embryonic Organoids
58	Melis Asal	Izmir Biomedicine and Genome Center	Lacrimal Gland on Chip Derived from Induced Pluripotent Stem Cells
59	Jordina Balaguer	Institute for Bioengineering of Catalonia (IBEC)	Magnetic bead-based immunosensing platform for in-situ detection of secreted cytokines in response to oligonucleotide treatment
60	Natalia Basalova	Lomonosov Moscow State University	Decellularized multicellular fibroblast sheets for mimicking the profibrotic microenvironment *in vitro*
61	Sara Bonavia	Université Paris Diderot	An *in vitro* system for the mouse Epiblast to investigate the establishment og the anterposterior polarity
62	Carlo Brighi	Italian Institute of Technology	Modeling Fragile X syndrome with iPSC-derived neurons in 2D and 3D tissue culture conditions.
63	Isabel Calvo	Institute for Research in Biomedicine (IRB Barcelona)	Visualization of Mediator complexes in naive and primed embryonic pluripotent cells
64	Ignasi Casanellas	Institute for Bioengineering of Catalonia (IBEC)	Cell-matrix nanoscale adherence continually modulates intercellular communication in morphogenesis
65	Sandra Clara-Trujillo	Biomedical Research Networking Center on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN)	From 2D to 3D cell culture with biomimetic microgels
66	Laura Clua	Institute for Bioengineering of Catalonia (IBEC)	Micro-Spheroids For β-like Cell Encapsulation
67	Mar Cóndor	KU Leuven	Cellular force generation during sprouting angiogenesis
68	James Cotterell	EMBL Barcelona	A Local, Self-Organizing Reaction-Diffusion Model Can Explain Somite Patterning in Embryos.

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ENGINEERING MULTICELLULAR SYSTEMS

Poster Session 12th February

N	Name	Affiliation	Title
69	Ross Cowie	University of St Andrews	Quantifying biomechanical stresses in 3D cellular environments via micro-droplet laser spectroscopy
70	Eleni Dalaka	University of St Andrews	Measurement of invadopodia forces in 2D and 3D environments
71	Giovanni Dalmasso	EMBL-Barcelona	The role of SOX9 in vasculature re-modelling: an *in vitro* study
72	Malik Dawi	Universitat Politècnica de Catalunya (UPC)	Vertex Modeling and Three-dimensional Tissue Reorganization
73	Simone de Jong	Eindhoven University of Technology	The Introduction of Fc-Fusion Bioactive Proteins in Supramolecular Biomaterials
74	Rocky Diegmiller	Princeton University	Cell and Nuclear Growth Dynamics in Developing Drosophila Germline Cysts
75	Camille Douillet	Poietis	Morphogenesis control of dermal tissues produced by Laser-Assisted Bioprinting (LAB)
76	Arthur Douillet	LaTIM & Poietis	An Agent-Based Modeling Framework To Predict Bioprinted Tissue Morphogenesis
77	Aleksey Emelin Ryazan	State Medical University	Efficiency evaluation of iPSCs neurogenic and myogenic differentiation in organoids composition

78	Ismail Es	University College London	Formation of tumor spheroid models using 3D-printed micromolds
79	Elena Garreta	Institute for Bioengineering of Catalonia (IBEC)	Substrate Stiffness Impacts the Differentiation of Kidney Organoids Derived from Human Pluripotent Stem Cells
80	Gemma Gabriel	IMB-CNM	Organ-on-chip monitoring
81	Maria Gallo	Institute for Bioengineering of Catalonia (IBEC)	Developing kidney-specific bioinks for human pluripotent stem cells 3D Bioprinting into kidney organoids
82	Jad Saleh	Institut Jacques Monod Université Paris Diderot/CRNS	Mechanical impact on stem cell niche morphogenesis

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