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Authors

Barber, Diane L
Treat, Xavier

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Editorial overview: Cell dynamics: Integrating cell dynamics across scales

Diane L. Barber and Xavier Trepap



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Cell Dynamics

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Diane L. Barber

Department of Cell and Tissue Biology,
University of California San Francisco, San
Francisco, CA 94143, USA
e-mail: diane.barber@ucsf.edu

Diane Barber received her PhD from the University of California Los Angeles investigating signaling in endocrine cells. She is currently Endowed Professor and Chair of the Department of Cell and Tissue Biology at the University of California, San Francisco. Her research program addresses questions on the regulation of epithelial plasticity in stem and cancer cells, with a focus on cell behaviors regulated by intracellular pH and actin filament dynamics.

Xavier Trepap

Institute for Bioengineering of Catalonia,
Barcelona 08028, Spain
Faculty of Medicine, University of Barcelona,
Barcelona, Spain
Institució Catalana de Recerca i Estudis
Avançats (ICREA), Barcelona, Spain
Center for Networked Biomedical Research
on Bioengineering, Biomaterials and Nano-
medicine (CIBER-BBN), Barcelona, Spain
e-mail: xtrepap@ibebarcelona.eu

Xavier Trepap received his PhD from the Medical School at the University of Barcelona. In 2011, he became ICREA Research Professor at the Institute for Bioengineering of Catalonia (IBEC). His research aims to understand how cells and tissues grow, move, invade, and regenerate in a variety of processes in health and disease. To achieve this, he has developed technologies to measure the mechanical properties of cells and tissues.

Dynamics has its origins in the Greek word *dynamis*, meaning force or power. Dynamics is used as a descriptor ranging from personality traits to physics for bodies in motion. In cell biology, dynamics generally indicates changing as opposed to static. To highlight the importance of dynamics in cell biology, COCB initiated in 2016 special interest issues devoted to Cell Dynamics. Past issues on this topic focused on cell division, integrating cell behaviors and tissue architecture, cell decision-making, and unifying concepts in development, tissue remodeling, and cancer. Our current issue integrates cell dynamics across scales, from subcellular to supracellular to multicellular. As with overlapping and intersecting processes and paradigms in cell biology, the articles in this issue defy a best-fit organization, and we grappled with organizing our overview by thematic topics or scales. We settled on the latter because integrating dynamic processes across scales is a challenge cell biologists are increasingly addressing. We start with fundamental principles and building blocks within subcellular scales, segue to how these affect tissue organization, and conclude with tools and imaging modalities for controlling and quantitatively capturing cell dynamics in motion. Regardless of the organization of our overview, each article stands alone for an outstanding discussion of current work, insightful integration of multiple points of view, and importantly what we hope for the reader, thought-provoking ideas on how to advance new discovery.

Subcellular

A series of reviews in our issue describe subcellular processes with a focus on cytoskeleton and filament dynamics. **Webb and Kollman** present emerging evidence on the self-assembly of metabolic enzymes into filament-like polymers. The review includes an expanding list of metabolic enzymes that form filaments, how filament assembly is regulated by enzyme substrates and products, the distinction between enzyme filaments and stress granules, and differences in the structural features of some enzyme polymers, revealed mostly by cryo-EM. The review raises two intriguing questions. First, what is the functional significance of these filaments, which remains poorly understood? Second, with clear evidence

of metabolic filaments in cells, should we reconsider the components of what we classically define as the cytoskeleton?

With a focus on the more classically defined cytoskeleton, several reviews highlight the role of cytoskeleton dynamics as major driving forces for morphological changes. These forces are mediated through cytoskeleton anchoring by plasma transmembrane proteins, intracellular vesicle and organelle transport, and contractility from motor proteins. [Diz-Munoz and Sitarska](#) discuss the interplay between membrane tension and the cytoskeleton machinery. They highlight the role of the cell surface as a mechanobiological unit of the plasma membrane with membrane-interacting proteins and the underlying cytoskeleton. The article discusses current views on global compared with local propagation of membrane tension in regulating cell behaviors and concludes with a synopsis of available as well as needed toolkits to further understand the functional significance of dynamic membrane tension. Cell migration, a behavior regulated by membrane tension, is often described in the context of cytoskeleton dynamics with roles for actin filaments and microtubules. [Etienne-Manneville and van Bodegraven](#), however, call attention to understudied contributions from intermediate filaments in cell migration. They highlight recent work showing how the interaction between intermediate filaments and the actomyosin cytoskeleton regulates force generation and transmission at cell adhesions. They also discuss how the unique mechanical properties of intermediate filament networks protect the nucleus during cell migration through narrow pores.

Finally, two reviews within the topic of subcellular organization focus on biophysical properties. Physical methods, physical–chemical principles, and mathematical models are increasingly being applied to fundamental tenets governing dynamic cell organization and function. [Charras et al](#) focus on the biophysics of the actin cortex, a structure that governs shape and mechanics across biological scales, from subcellular protrusions to supracellular folding. They review the latest advances in our understanding of actin network organization, assembly, as well as connectivity and regulation of filament length, using mitosis as an example where all these features are tuned and integrated to drive shape changes. The biophysics of the actin cortex also determines phagocytosis, a process reviewed by [Thériot and colleagues](#). They discuss how phagocytic engulfment depends both on the mechanical properties of the cell surface and on the size and rigidity of the target particle.

Supracellular

Reviews within the supracellular category focus on the dynamics of morphogenesis or cell migration. Decades of outstanding work contributed to our current

understanding of transcriptional and epigenetic control of morphogenetic behaviors, but less clear is the fundamental mechanics of cell biology. The first two articles in this section discuss emerging concepts interfacing cell morphology dynamics and developmental processes with a focus on mechanics and roles for mechanical signaling. [Bush and colleagues](#) present the different elements involved in the integration of cell mechanics and biochemistry, including dedicated mechanosensors, cell adhesions, and transcriptional regulators. They discuss how these elements work together to drive multiscale processes in development, including rhombomere formation in the hindbrain, tract valve development in the heart, and morphogenesis of the pharyngeal arch. Multiscale integration is also the central theme of the review by [Özgüç and Maitre](#), who discuss how actomyosin contractility governs morphogenesis of the preimplantation mouse blastocyst at different time scales. They present how the shape of the embryo is defined by a combination of rapid contractile processes that operate in the time scale of seconds, such as periodic waves of contraction, and slow ones that evolve over the course of hours to days, such as the changes in cortical surface tension that drive compaction.

As an integrated process necessary for morphogenesis, collective cell migration is discussed in two reviews. [Das and colleagues](#) focus on mechanisms that give rise to large protrusive cells at the edge of motile groups. They discuss how recent advances in the physics of active jammed materials can explain the emergence of length scales that predict the location, separation, and strength of these ‘leader cells’. While [Das and colleagues](#) focus on mechanically accessible systems *in vitro*, [Bronner and colleagues](#) discuss how cells migrate to reach their targets *in vivo*. They review how the epithelial to mesenchymal transition displays a spectrum of intermediate states that define different migration modes. They discuss how these modes enable single and collective cell migration during development of the neural crest.

Two reviews discuss experimental approaches for investigating morphogenesis. [Martinez-Arias and colleagues](#) present two-dimensional micropatterns and three-dimensional stem cell culture systems as a way to recreate the architecture and interactions of particular cell populations during development. They highlight the strengths and suitability of different approaches in modeling early mammalian development and describe the value of free-floating gastruloids for understanding the intrinsic capacity for self-organization of embryonic stem cells and body plan specification. [Gartner and colleagues](#) present the latest approaches to engineer mammary gland organoids. They discuss the advantages and limitations of these approaches to model mammary gland morphogenesis and disease, placing particular emphasis on the need to incorporate stromal cell types.

Integrating morphogenesis, mechanical forces, and complex cellular components, [Abuwarda and Pathak](#) review the mechanobiology of neural development. They discuss how mechanics influences this process at multiple steps, including neural tube closure, neural crest cell migration, and neural progenitor proliferation and differentiation. They discuss how traction forces and tissue rigidity guide neuronal migration and axon guidance. Finally, they highlight the potential of organoids to study neural development, illustrating that these model systems unveiled how cytoskeletal forces drive cortical folding.

Multiscale (tools)

In addition, included are a series of articles on experimental approaches and imaging modalities to inform readers of recent advances in controlling and quantitatively capturing cell dynamics. Two reviews discuss using optogenetics or light-activated systems to experimentally control protein localization and function in time and space. [De Renzis and colleagues](#) discuss using optogenetics to decode complex developmental processes and address system-level questions of multicellular morphogenesis. They describe new optogenetic tools to quantitatively perturb protein function *in vivo*. These new approaches *in situ* allow linking cell and tissue behaviors to understand developmental robustness, emergent self-organized systems, and multiscale causality. [Wittmann and colleagues](#) highlight the design principles, as well as advantages and limitations, of currently used optogenetic switches for understanding cytoskeleton-regulated cell behaviors. They discuss how these new tools allow us to move from observing molecules to controlling them in real time to understand dynamic cell biology. For cytoskeleton systems, in particular, that assemble, disassemble, and reorganize within minutes, optogenetics allows experimental approaches over rapid time scales compared with genetically ablating or mutating proteins.

[McDole and Lemon](#) present an outstanding overview of current imaging modalities for revealing cell biology dynamics. The review includes a useful table of modalities and their strengths and limitations. In addition, the authors address the challenge of extensive post-acquisition analysis and postprocessing requirements and emphasize that it is the experimentalist's responsibility to understand how they are processing or quantifying images.

Conclusions and outlook

As new tools in cell biology and microscopy enable an increasingly quantitative description of the building blocks of the cell, integration of dynamic processes across scales is now becoming our most challenging task. In this issue, we provided an overview of different processes in cell biology that operate at different length scales, from subcellular filament assembly to supracellular tissue movements. Reviews in this issue emphasize that a biological function can only be understood when mechanisms are studied and integrated across scales. We include articles that address integration through bottom-up approaches, whereby a process is understood by engineering its building blocks. Other articles focus on top-down approaches, whereby a process is deconstructed to understand the role of its components. Regardless of the approach, a central theme of the issue is the need to integrate tools and concepts in biology and physics to address cell dynamics. In this regard, this issue highlights that the concept of dynamics in cell biology is evolving back to its ancient Greek meaning; the only way to fully understand movement in a biological system is to know the underlying forces.

Conflict of interest statement

Nothing declared.