

BOOK REVIEWS

Annual Review of Cell and Developmental Biology, 2016. Randy Schekman, Larry Goldstein and Ruth Lehmann (eds). Annual Reviews, 4139 El Camino Way, Palo Alto, CA, 94303-0139, USA. Vol. 32. ix + 778 pages. Price: US\$ 109.

The present volume of *Annual Review of Cell and Developmental Biology* has 28 reviews. The introduction by Randy Schekman is worth mentioning as it deals with the important aspect of reproducibility of published results. Schekman argues that though scientific research is self-correcting and may work in the long run, the short-term problem with public acceptance of science will be a problem. He strongly argues for change in the culture that allows a distortion of the scientific method and suggests that the whole process of scientific publication should be such that the penalty for misrepresentation should be very high. This is highly relevant in areas related to clinical medicine as novel discoveries are linked to drug discoveries. Perhaps mere retraction of a paper is not enough!

The perspective in this volume is a personal account of research on pattern formation in *Drosophila* by Eric Wieschaus and Christiane Nüsslein-Volhard. It is technical-like a review and not only personal reminiscences. The article provides an insiders insight how using *Drosophila* they could unravel mechanisms related to pattern formation. They make an interesting statement 'we did not choose *Drosophila* as a model organism; in contrast, our screen pushed it to become one'.

The reviews cover several aspects of cell and developmental biology and are not specific to species or organisms. In fact, there are reviews related to development of plants as in the previous issues.

Palovaara *et al.* review aspects related to cellular basis of embryo development in 3 D and the genetic control of key developmental transition that shape the embryo in plants, particularly *Arabidopsis*. The authors opine that areas such as cell geometry and division, hormonal control and transcriptional networks, epigenetic control of embryo development and evolution of embryo patterning are potential areas of future research to address important unanswered questions. Bernardskaya and Christiaen discuss how tissue-specific transcriptional programs eventually determine complex morphogenetic events. The figures highlight

multiscale combination of modular sub-cellular processes and the process of mesenchymal to epithelial transition as well as tissue-specific gene regulatory networks.

Perera and Zoncu discuss recent discoveries that indicate a central role of the lysosome in nutrient-dependent signal transduction. The introduction details historical aspects starting with their discovery by Christian de Duve in 1955, and biochemical function to its current status as a key signalling node. Structural and functional organization of lysosomes, their emerging role in signalling metabolism and lysosomal activity in disease are described. Another review by Raben and Puertollano is related to the role of lysosomes as a key player in cellular processes linking lysosomes to cellular adaptation and stress. The authors focus on the role of specific transcription factors in the regulation of lysosomal function and biogenesis and the role of lysosomal pathway in cellular response to stress conditions as well as their potential as therapeutic targets.

The role of mechanical forces in various aspects of cell biology is increasingly being appreciated by cell biologists. Przybyla *et al.* deal with mechanical control of epithelial to mesenchymal transition in development and cancer. Mechanical regulation of cell surface proteins, intracellular mechanotransducers and transcriptional control of mechanically induced processes are discussed with illustrations that help in better appreciation of the processes. Te Boekhorst *et al.* review plasticity of cell migration *in vivo* and *in silico*. They discuss modes of cell migration, determinant controllers, migration modes, reciprocity of cell-tissue interaction and migration plasticity programs of cell migrations and multi-scale mathematical models of cell migration and plasticity. The authors are of the view that strategies in mathematical modelling in conjunction with wet-lab analysis are necessary to address the complex process of cell migration. Ramasamy *et al.* discuss key pathways and factors controlling endothelial cell behaviour in bones, the role of vessels in osteogenesis and the nature of vascular stem cell niches in bone marrow.

Extensive research in the area of transport of proteins from the endoplasmic reticulum to the Golgi complex has revealed how high selectivity and directional transport is achieved. Barlowe and Helenius address cargo capture and bulk

flow in the early secretory pathway in their review. They describe the trans-membrane cargo receptors, many of them identified recently. The authors highlight several questions that still need to be addressed. The role of intracellular membranes in segregation of specialized compartments has been the subject of intense research. The review by Gallo *et al.* specifically dwells on the structure and the function of membrane contact sites (MCSs), between two membrane bound organelles. The review details proteins that play a role in establishing connection between membranes and their topology, non-vesicular lipid transport including the biochemistry of lipid transfer proteins and possible areas that require detailed investigations such as thermodynamics of the reactions involving lipid transfer in MCSs. The role of phosphatidylinositol (PI) as a key player in the regulating membrane dynamics has been appreciated for several years. Schink *et al.* focus on PI effectors that directly control various membrane-related processes in cells such as exocytosis, endocytic processes, autophagy, cell division and migration and epithelial cell polarities. Castro-Castro *et al.* discuss the role of membrane-anchored metalloproteinases in particular, the membrane-anchored type 1 proteinase (MT1)-MMP in cancer cell invasion leading to metastasis. The conclusion highlights possible areas for further investigation such as control of (MT1)-MMP trafficking and other components that are involved in cancer invasion.

Quinlan reviews cytoplasmic streaming in the *Drosophila* oocyte. The author introduces advection, in which objects within the cytoplasm are moved with the flow of cytoplasm. In the introduction, general aspects of fluid flow with respect to morphology in several species are highlighted. Claveria and Torres review the mechanisms driving cell competition in metazoans and its physiological roles in tissue dynamics. The review also shows how *Drosophila* is a good system to study this phenomenon.

Liu describes the enzyme cytidine triphosphate synthase (CTPS) which is compartmentalized in cytoophidia, an intracellular compartment that is conserved across prokaryotes and eukaryotes. The nomenclature used to describe CTPS containing filamentous structures is introduced. This should be a handy reference to researchers working on filamentous structures in cells. Cytoophidia is specific to CTPS and another enzyme

inosine monophosphate dehydrogenase and not other metabolic enzymes. Liu makes a strong case for further research on cytoophidia by interdisciplinary approaches.

Neely and Flajnik review emergence and evolution of secondary lymphoid organs. Specifically, they discuss various aspects of spleen development along with evolution of adaptive immunity that is nicely illustrated. The authors start with mouse spleen and go to cover Agnathans (jawless vertebrates such as lamprey and hagfish), Chondrichthyes that include cartilaginous fishes, teleost fish, amphibians as well as reptiles and birds. The review highlights the importance of studying such immunological aspects in species across the evolutionary scale.

Daneva *et al.* review functions and regulation of programmed cell death (PCD) in plant development, an area that has attracted interest in recent years. They provide an overview of genes and miRNA that directly regulate different PCD processes, and describe various aspects of cell death during plant reproductive development, vegetative development as well as comparison with apoptosis in animal systems. The review should provide impetus for plant researchers looking for problems in newer areas.

Directed cell migration is crucial to development process in organisms. Paluch *et al.* discuss physical mechanisms proposed for cell body translocation during focal adhesion-independent migration. The illustrations show requirements for migration on 2D substrates versus 3D confinement, mesenchymal and amoeboid migration, conditions favouring non adhesive migration and different physical mechanisms of force generation and transmission during focal adhesion-independent migration. According to the authors, a multifaceted approach that includes biophysics and engineering of micro environment that would model in vivo situation would be essential in understanding the process. The physics aspect of forces in biology is increasingly being appreciated. García-Cardena and Slegtenhorst discuss biomechanical forces related to arterial venous, specifically lymphatic development and endothelial to haematopoietic transition.

Ogura and Busch discuss system biology approaches to study genotypes, networks and phenotypes in *Arabidopsis thaliana* that include flowering time, traits and root growth traits. They opine that studying system biology linked to natural variation would go a long way in

addressing the genotype to phenotype questions.

Pathogenic bacteria have exquisite mechanics to overcome cellular barriers and establish infection. The review by Jimenez *et al.* discusses newer investigations that reveal how pathogens gain control over the actin cytoskeleton and intracellular organelles. They discuss the individual effector proteins and toxins that target cell structure and function and relevance to drug discovery.

The immunological synapse is related to the intracellular contact between T cells and antigen presenting cells and has been the subject of intense research over 16 years. The review by Dustin and Choudhuri discusses how evolutionally conserved strategies for polarized cell communication contribute to immune defense by T cells via immunological synapse formulation. Areas that need to be investigated such as cell biology of adaptive lymphocytes from agnathans and interaction of gnathostome innate lymphocytes are highlighted. They expect that recent technological advances in microscopy will enable deeper insights into how the immunological synapse mount effective immune responses. Gascoigne *et al.* review T cell receptor (TCR) signal strength and T cell development. They discuss TCR signal strength in positive and negative selection, molecular mechanism of signal strength modulation during T cell development, signal longevity versus signal strength and how thymoproteasome and immune proteasome influence selection. They predict that control by micro RNAs and long noncoding RNAs will in the coming years contribute to better understanding of thymocyte development.

The review by Escobedo and Oliver is in the area of Lymphangiogenesis. The historical perspective on lymphatic components indicates awareness since 460 BC and highlights pioneering work in this area since then. The review discusses various aspects of arteries, veins, sources of lymphatic endothelial cells needed to form functional lymphatics as well as commitment and differentiation of lymphatic endothelial cells. The illustrations provide an excellent overview of the development process and of molecular players and signalling pathways involved. The review by Ito and Ito describes the importance of metabolism in stem cell biology. Important aspects of metabolism in stem cells including the role of mitochondria in stem cell division are discussed. The authors conclude that

study of stem cell fate control would be relevant to metabolic requirement for cancer stem cells and have possible therapeutic applications.

The review related to neurogenesis and gliogenesis by Frisén is directed towards providing an overview of cell generation in the adult central nervous system and also addressing emerging concepts and outstanding questions. The figures showing new cells in old brains, how to recognize a new cell, recruitment of resident astrocytes to the neurogenic lineage and the origin of scar tissue in the injured central nervous system gives an excellent overview. The author makes an important point that there are dramatic differences between rodents and humans in various aspects of neurogenesis and cautions that mouse models may not be directly relevant to humans, particularly when questions related to disease and therapeutics are addressed. Seiradake *et al.* discuss structure–function relationships of ephrins, semaphorins and cell adhesion molecules. Their discussion draws heavily on the crystal structures of the receptors and morphogens. The review emphasizes the importance of research efforts including determination of crystal structures, electron microscopy and cell biology in conjunction with genetics to study the complex phenomenon of axon guidance.

The importance of white adipose tissue (WAT) as an important regulator of metabolic processes is becoming increasingly evident. In their review, Shook *et al.* discuss the roles of WAT in the homeostasis and regeneration of epithelial, muscle and immune tissue and how they contribute to the pathology of several disorders. The diseases discussed are skin disorders, skin infection, fibrosis, cancer, obesity and diabetes. The importance of WAT in normal metabolism and dysfunctional WAT leading to disease conditions make it a target translational biology to the authors.

Tissue cleaning and staining has played an important role in the visualization of cellular architecture. The review by Tainaka *et al.* describes chemical principles for cleaning protocols and recent chemical staining methods. The tables summarize tissue cleaning and tissue staining protocols for a quick reference. The figures clearly indicate the chemistry behind the various steps which would help in appreciating what actually happens in the process. It is evident that understanding the chemical principles of tissue engineering and staining is essential

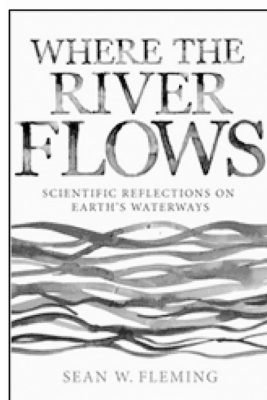
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for a better understanding of not only a static picture but possibly also of dynamics. The review will be useful for researchers working on method development for visualization in cell biology.

The reviews provide a wealth of information and problems that remain to be addressed in the coming years. Since several diseases are linked to the cellular malfunctioning, many reviews comment on translational aspects, that is increasingly stressed upon by various funding agencies world over.

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Where the River Flows: Scientific Reflections on Earth's Waterways. Sean W. Fleming. Princeton University Press, Oxford. 2017. 216 pp. Price: US\$ 26.95.

Its global prevalence notwithstanding, the state of water in nature reflects our inadequate understanding of its intricate flow dynamics. Despite abundance, its access eludes millions of living beings and the consequent stress on the ecosystem of which it is an integral part is only growing. That currently more than one billion people lack access to clean water and in near future the global demand for water will be twice as much are numerical manifestations of a deep crisis. With nothing that can substitute this life nurturing fluid, the soul-stirring lyrics 'i'll give you answers to the questions you have yet to ask.' from the album 'Where the river flows' offer sound advice to ask right questions for getting past the prevailing hydrological muddle.

Sean Fleming may have listened to this album or the lyrics may have intuitively echoed to him in his quest for seeking interconnectedness between disparate disciplines to get answers to some unusual questions about and on rivers. Intriguing and exciting as these may sound, questions like 'why rivers are where they are' and 'how do rivers remember' propose exciting new ways of understanding varying levels of causality and complexity of the system and how these interact with one another. Plate tectonics may have carved a river's course, but its meandering flow is an aggregate of multiple factors, from the changing climate overhead to the dynamic geomorphology underneath. The sum total is that rivers have manifest identity in sky, land and us.

All rivers are alike in a broader sense, but have varied meandering curves, diverse aquatic fauna, and distinct morphological features. Unravelling this distinctiveness and the (unknown) variables that contribute to it are the challenges that confront hydrologists. Existing watershed models do not provide all the answers and the modelers themselves do not rate the results too high in getting a sophisticated description of river hydrology. Part of the problem, in the words of Belgian Nobel Laureate Ilya Prigogine, rests on our innate desire to reduce systems into sub-systems which only helps in learning more about less. Such an approach does not do much good to our understanding of river hydrology; as the challenge rests on addressing uncertainty in an array of environmental factors that contribute to stream flow and the aquifer beneath it. Rivers are at the centre of human civilization, and warrant compassionate understanding of their existence in time and space.

Where the River Flows offers a paradigm shift in understanding the rivers. It calls for a radical shift outside of the disciplinary box, as rivers are but a reflection of profound interrelationships between landscapes, ecosystems and societies. Fractal mathematics alongside chaos and information theory can be applied to generate a new set of data on the overall pattern created by the river system and the resultant decision-support system. As anthropogenic impacts like climate change accelerate democratically across the world, there is a need for as much finer details (will my farm get rain next week) as about big picture (will river topple its banks this coming season) of how the system works as a whole.

This would be critical in understanding the common but differentiated pattern rivers generate under varying geomorphological settings.

But a counter narrative has kept pace as science struggles to get a better sense of river hydrology. Sustained tempering of rivers on account of damming, diversion and contamination continues to throw formidable challenges in sustaining healthy stream flows for human welfare and the environment. Be it the Mississippi, Ganges or Yangtze, the story of river degradation threatens to off balance the dynamic equilibrium between ever-increasing human populations and their relentless aspiration to stay adequately watered. The United States may have leveled off its water use to 1970 rates in spite of both population and economic growth, the health of its rivers continues to remain alarming. While every drop of water pumped out from the Colorado river is used at least 17 times, which may sound like a good news, its net impact on the Gulf of California has grossly disrupted the hydrological cycle as river water has not reached the delta since 1960.

Fleming's scientific reflections on rivers emerge in the backdrop of such contrasting realities. Calling for an entirely new way of viewing the natural environment, he suggests processing of vast and complex information to reconceptualize the natural environment for recognizing problems differently, and in many cases identify altogether new problems. But can reams of hard data, quantitative modelling techniques, and classical statistical approaches get a better sense of a system that is not only dynamic but a living entity too? Not without reason had Heraclitus said that 'you can't step twice into the same river', highlighting that river is in a continuous flux. As the need for more accurate, precise and consistent forecast move center stage in our dealings with the rivers, the need for factoring the cultural perspectives of riverine societies must get the desired emphasis. All it needs is sharpening scientific skills to convert human observations into quantifiable information. After all, there is a reason for humans to have evolved along the rivers!

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