utilization of science underwent a sea-change in the twentieth century, particularly during and after the Second World War. Science now involves large organizations, huge funds and mega projects. Much of science is in the firm grip of governments and corporates. Commodification of science has also progressed apace. The author dwells on the negative consequences of the globalized techno-capitalism. However, the intellectual excitement of pursuing science shines through the entire narrative.

The final chapter briefly recapitulates the material presented in the previous chapters. The concluding thoughts of the author are summarized in a section called 'Afterword'. They do not easily lend themselves to critical scrutiny. They are, of course, naturally in consonance with the narrative in the body of the book.

The book provides a panoramic view of the theory and history of knowledge production from antiquity to the present day, with Science at the centre stage. The study of the book has enriched me. I recommend the book to working scientists and others who are engaged in intellectual pursuits.

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Annual Review of Biophysics, 2018. Ken A. Dill (ed.). Annual Reviews, 4139 El Camino Way, PO Box 10139, Palo Alto, California 94303-0139, USA. Vol. 47, vii + 677 pages. Price: US$ 112.

The *Annual Review of Biophysics 2018*, edited by Ken Dill of Stony Brook University, is part of a series published every year since 1972. Each volume in the series combines reviews of those developments in biophysics that have attracted attention in the recent past. The only requirement placed on the contributions, apart from the fact that they should be reasonably current, is that they must represent areas where physics and biology speak to each other. At 677 pages this year, the hard-back version of this book is weighty in every sense of the word.

This year's reviews, 30 of them, cover much ground. Some themes are common to more than one article. These include the structural basis for GPCR signalling, the structure and biophysical aspects of membrane proteins, regulation across multiple scales and mechanobiology. There is something here to satisfy biophysicists of every stripe.

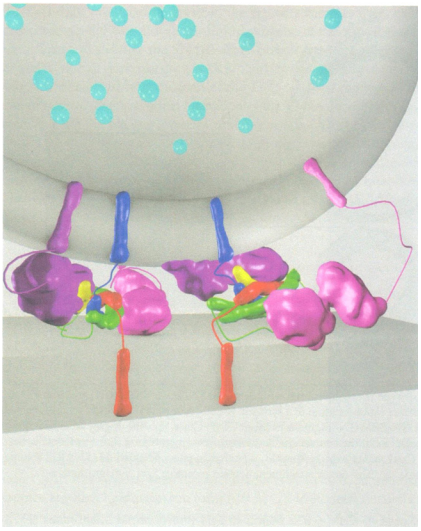
Some of these topics represent scientific directions that have remained largely the same over the past decade or more. What usually changes from year to year are advances marked by the introduction of novel tools, analysis methodologies and, occasionally, the flash of exceptional insight that upends a field. In this review, I will try to isolate those broader trends that appear to motivate a reasonable fraction of the biophysical community at this point in time, as manifest in the contributions to this volume.

Erlandson *et al.* describe recent advances in the understanding of how GPCR conformation switching underlies the activation of effector proteins. Such allostery appears to be pervasive. Stauch and Cherezov study the ultra-fast dynamics of GPCRs using X-ray free-electron lasers. Wand and Sharp study questions of the thermodynamic landscape governing protein–ligand interactions. Theory and simulations suggest that solution NMR relaxation measurements should yield a dynamical proxy for changes in conformational entropy upon ligand binding.

Newer microscopies, as usual, provide fresh insights into structure. Hashem and Frank review the structural biology of the eukaryotic translation initiation process, focusing on X-ray and cryo-EM methods. Wilkinson *et al.* summarize achievements in using cryo-EM to study the structures of spliceosomes captured in different assembly and catalytic states. Mandala *et al.* describe solid-state NMR measurements of membrane proteins, elucidating the role of the protonation state of polar residues in determining structure and function as well as the importance of structural plasticity in cases where membrane remodelling happens. Kiselar and Chance provide a review of assessment of proteins structure through the technology of hydroxyl radical footprinting (HRF) of proteins with mass spectrometry (MS). Smith and collaborators review the use of dynamical neutron scattering techniques to examine vibrations in proteins, the temperature dependence of protein motions, as well as new concepts that emerge from these studies.

The organization of cell membranes, of membrane-bound proteins and of membrane–membrane interactions are dealt with in multiple articles. Betune and Wielend describe the current state of knowledge of the organization of coat proteins, including the COPI and COPII coats, using cryo-EM. McLean *et al.* note that many complex multi-protein assemblies involved in cellular communication require an integral membrane protein and a membrane surface for assembly as well as for information transfer to soluble partners in a signalling cascade. Incorporating these protein components into nanodiscs provides a native bilayer environment with a precisely controlled composition of lipids, cholesterol and other components. Boonstra and collaborators describe biophysical studies of influenza haemagglutinin (HA) mediated membrane fusion. HA mediates binding of the virus particle to the host–cell membrane, also catalysing the fusion of the viral membrane with that of the host. These authors provide a thorough biophysical description of the membrane fusion process, describing our current understanding of how HA conformation changes and their membrane interactions might together lower barriers between fusion intermediates.

Axel Brunger and colleagues summarize the current knowledge of synaptic proteins central to synaptic vesicle fusion in presynaptic active zones, including



Model of primed prefusion SNARE/Cpx1/Syt1 complexes. Article by Brunger *et al.* on p. 469.

SNAREs, synaptotagmin, complexin, Munc18 and Munc13. They highlight recent insights into how these proteins might cooperate for neurotransmitter release. Crispin *et al.* review biophysical methods for the study of the complex structure of the glycan shield of HIV, a barrier that vaccines encounter. Finally, Alonso and Goni study ceramides, sphingolipids containing a sphingosine or a related base, to which a fatty acid is linked through an amide bond. Although found in small amounts in cell membranes, this class of sphingolipids has unique properties. These authors comment on the relative paucity of physical studies of these as opposed to biochemical ones, stressing the gap between pathophysiological observations and physicochemical data.

The field of mechanobiology is one in which ideas from physics are most intimately linked to the description of biological phenomena. Harris *et al.* examine issues of mechanotransduction in the actin cytoskeleton. The actin cytoskeleton responds to a mechanical load by shaping its composition, organization and function. The review describes our current understanding of how mechanical signals at the cytoskeletal level are converted into biochemical ones. Expanding on important work initiated in the Needleman lab, Oroiola, Needleman and Brugues study physical forces in the development of the mitotic spindle, bringing in concepts of rheology (the study of flow) and of active matter (the spindle as an active liquid crystal). Finally, Hu *et al.* review 3-D studies of cell migration, discussing the pros and cons of several well-characterized 3D cell culture systems for performing migration studies and pointing out that little is known about what determines and regulates cell polarization in 3-D migration.

Holehouse and Pappu use a polymer physics framework to describe how the interplay among side-chains, backbone units and solvent determine the driving forces favouring collapsed or expanded states of proteins in aqueous solvents. Ho *et al.* review the classic problem of the determinants of cell size, discussing mathematical formulations of this problem. Kaneko and Furasawa present a theoretical formulation for the plasticity, robustness, and evolvability of biological responses and their fluctuations. They suggest that a macroscopic potential for phenotypic evolution can be provided by the growth rate (or fitness), represented as a function of environmental and evolutionary changes. Shis *et al.* provide an overview of bacterial gene expression, showing how recording gene expression dynamics in single cells and in populations, coupled with mathematical modelling, can enable help in the understanding of how these responses are shaped by the underlying regulatory networks.

Tutucci *et al.* review how single-mRNA detection can be used to study gene expression in both fixed and live cells. Current state-of-the-art measurements can track mRNA with single molecule resolution, across transcription to decay, in single cells. They can be used to study how single molecule interactions generate phenotype. Engel *et al.* describe structural studies that show that the mechanisms of transcription initiation and its regulation differ between Pol I and Pol II. Pavlov and Ehrenberg review how induced fit affects the accuracy of initial codon selection on the ribosome, from the point of view of both structure and detailed biochemical studies. Globyte *et al.* describe studies of target search and recognition, focusing on single-molecule advances in understanding these in the Argonaute and CRISPR systems. Finally, Waite *et al.* review variability in chemotactic response in *E. coli*, in particular how cell-to-cell differences in protein abundance map onto differences in individual chemotactic abilities, with the larger aim of describing how phenotypic variability affects the performance of the population.

Synthetic biology aims to establish engineering rules for the forward synthesis of cellular function. Bashor and Collins describe the use of synthetic gene circuit engineering research to refine our understanding of regulation. Fox and collaborators carefully discuss the delicate issue of enthalpy/entropy (H/S) compensation in biomolecular recognition, illustrating the many ways in which this compensation might happen. They stress the little understood role of water and molecular motions, suggesting that these play a crucial role in compensation. In a fascinating review, Gradinaru and collaborators describe the use of hydrogen tissue chemistry to study component localization, accompanied by the idea of thinking of metazoans as metareactants, or positionally defined three-dimensional graphs of constituent chemicals, made available for ongoing functionalization, transformation and readout.

The real value of up-to-date and comprehensive annual reviews, written by experts in the field, is that they let us assess the status of a sub-field at a snapshot in time. They also let us track major shifts in what the community as a whole works on, such as when a novel technique becomes a central component of the studies that these reviews report. (The explosion of cryo-EM-based structure analysis over the past 5–10 years is one such example; the need to distil exponentially growing amounts of biological data into usable information using machine-learning-based computational methods may well dominate a future set of such reviews.)

I enjoyed this volume from a number of points of view. Among them was the feeling of examining my own field from a distant and more objective vantage point, where broad trends but not individual contributions, were easily visible. Reading it was fun, even those articles not directly in my field, also because the articles were well written, well illustrated and appropriately comprehensive. I look forward to using it as a reference and can recommend it in no uncertain terms to interested readers of *Current Science*.

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