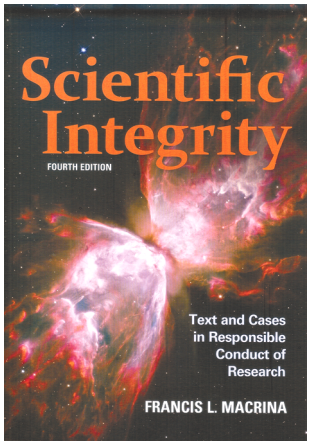

Scientific Integrity: Text and Cases in Responsible Conduct of Research. Francis L. Macrina. ASM Press, 1752 N St., N. W., Washington, DC 20036-2904, USA. 2014. 4th edn. 440 pp. Price: £ 42.00. ISBN: 978-1-5558-1661-2.

A recent message on a discussion group of editors began thus: 'In November last year, BioMed Central uncovered evidence of repeated and inappropriate attempts to manipulate the peer review process of several journals'. Last year, *Science* uncovered a racket that offered to add, on payment, the payer's name to the list of authors of a paper ready for publication, but not yet published. Then there are predatory journals that offer to publish virtually any paper that you may care to submit to them – and publish it fast – provided you pay upfront. These and similar instances of subverting the conduct of research is what the research establishment must guard itself against, because, as the foreword to the book under review reminds us, 'The advancement of science requires trust – trust in the literature, in our collaborators, in the data we are handed, and most of all in ourselves'.

I recall a survey conducted some years ago, in which scientists were found to be among the most trusted professionals in India. I hope the results today will be no different – and books such as *Scientific Integrity* can contribute a great deal to ensure that scientists continue to be worthy of the trust they enjoy.

The book 'aims to plant the seeds of awareness of existing, changing, and emerging standards in scientific conduct'. The wealth of material it offers by way of discussion questions, resources, case studies, exercises, and so on provides ample opportunities to learn and practice RCR, or responsible conduct of research, which is the focus of the book.

The book comprises 11 chapters and seven appendixes (which cover exercises, sample protocols and even instructions for maintaining laboratory notebooks). One chapter each is devoted to the following topics: methods of responsible conduct of research, ethics, mentoring, authorship and peer review, human subjects in experiments, animal subjects in experiments, conflict of interest, collaboration, data and intellectual property, and record keeping. The final chapter titled 'Science, technology, and society', seeks to 'stimulate thinking on scientific research and the ways it connects with and impacts on society' and 'encourage scientists to think deeply about the social responsibilities of their research and its implications'.

To assess the strengths of the book, I examined in detail the chapter on authorship and peer review, since I am more familiar with that topic than I am with any of the other ten. I was about to conclude that the book adds little to what is broadly known by most practising scientists until I came to the case studies – and was immediately rewarded. I then turned to case studies appended to other chapters as well, and was not disappointed. The book claims in as many words that its 'ultimate aim ... is to provide the opportunity to think' and succeeds in living up to that aim because the case studies are indeed thought provoking.

This book will prove a useful tool to all those who hold responsible positions in research for inculcating in all those they are responsible for the spirit of ethical conduct of research. To simply set this book as a required text is to do injustice to its spirit. In fact, the foreword goes to some length in describing how and when the contents of the book should be taught – at least 30 h spread over 5 years. This may sound impractical; yet, it is necessary if responsible conduct for research is to become part of our research culture and not another of those 'check in the box' items beloved of bureaucracies.

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Annual Review of Biophysics, 2014. Ken A. Dill and Xiaowei Zhuang (eds). Annual Reviews, 4139 El Camino Way, P.O. Box 10139, Palo Alto, CA 94303-0139, USA. Vol. 43. xi + 459 pp. Price: US$ 96.

This volume provides a glimpse of the new directions in biophysics in the recent past. The collection of articles reflects the convergence of diverse research interests with an underlying trend that is unmistakable – the focus increasingly is on understanding biological processes at the level of the organism. Nonetheless, this volume presents a delightful mix of the new methodologies with a few articles that represent traditional methods. The choice of reviews is perhaps best paraphrased in the words of the editors 'What is biophysics?' They then proceed to answer, 'Biophysics is the arena where the experimental tools and conceptual models of physical science are applied to problems of biology and biomedicine'.

The introductory article is by Ignacio Tinoco Jr – a familiar name to students in undergraduate and graduate schools as the co-author of their textbook in physical chemistry. This article is both informative and entertaining as it describes the research laboratory and environment at Berkeley that enabled groundbreaking research in RNA structure. Indeed the joy of the author as he describes this journey is evident even in his acknowledgement: 'The research and incidentally the fun has been supported by…'. This article is informative in another context. The enthusiasm to understand RNA structure was such that considerations of techniques and technology did not present unsurmountable roadblocks. Indeed, the techniques that were employed to understand RNA structure in his laboratory involved classical spectrophotometric methods, nuclear magnetic resonance (NMR) and single molecule visualization.

In keeping with the trend over the past few years, single-molecule techniques have dominated the discourse on biophysical analysis. In an article in this issue, Michael Woodslide describes the complexities of protein folding in exquisite detail. The fact that this is still an evolving field is evident from the discussions on multiple pathways for folding, reaction coordinate quality and effects of landscape multi-dimensionality. Indeed, it appears that further technical advances

in single-molecule techniques could perhaps force a rethink on model-dependent approximations that are currently employed to derive critical properties of the protein folding landscape. Another article on optical traps by Thomas T. Perkins dwells on the spatial resolution in visualizing single molecules (Figure 1). The technical advancements that are described in this article include specific corrections to minimize effects of Brownian motion – a serious limitation to spatio-temporal resolution. Other aspects, including eliminating mechanical drifts using an optically based reference system, suggest that detection and stabilization to 1 Å in three dimensions is indeed feasible. The advantage of visualizing biomolecules at this resolution in an optical trapping experiment is best exemplified from the insights that were revealed on the motion of the RNA polymerase enzyme. The high-stability optical trap measurements reveal aspects of the dynamics of an individual RNA polymerase relative to the DNA during a sequence-dependent pause. Sequence-specific regulatory pauses often govern co-transcriptional folding of the RNA – a conjecture that could only be resolved by the high spatio-temporal resolution achieved in these optical trapping experiments. Perkins provides an apt metaphor for this feature with this quote from Mozart – 'The music is not in the notes, but in the silence between.'

Two methodology papers exemplify the new territories that are likely to be widely employed in the near future – microfluidics, to examine microbial ecology, and live cell NMR. The information obtained from examining bacteria at single-cell level cannot be emphasized sufficiently enough given that it governs almost all aspects of pathogenesis and phenotypic variations that influence host–pathogen interactions and biofilm formation. Rusconi *et al.* describe specific experiments that exemplify the power of this methodology to understand chemotaxis at the molecular level, including the role of chemical gradients in governing microbial navigation strategies. The influence of this technology to understand microbe surface interaction, for example, is best exemplified in an analysis of *Pseudomonas aeruginosa* biofilm when examined over microscale topography (Figure 2).

Live cell NMR on the other hand, has fascinated researchers in biophysics over generations. Freedberg and Selenko

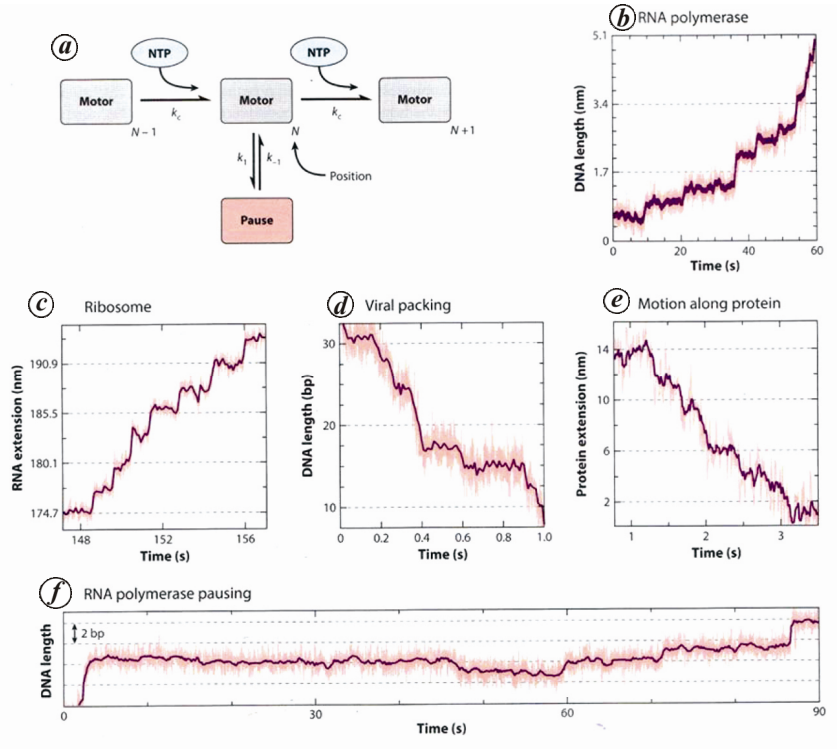

Figure 1. Measuring the motion of individual molecular motors (from the article in this volume by Thomas T. Perkins). ***a***, Kinetic diagram of a molecular motor to illustrate an off-pathway pause. ***b***, RNA polymerase motion along DNA showing 1-codon steps. ***c***, Ribosomal motion along RNA showing 1-codon steps. ***d***, A DNA packaging motor pulling in the DNA in 2.5 bp steps. ***e***, Movement of the ClpX protease moving along a protein substrate at 4–8 amino acids/step. ***f***, RNA polymerase motion showing forward steps interspersed with a long pause associated with 1 bp of backward motion.

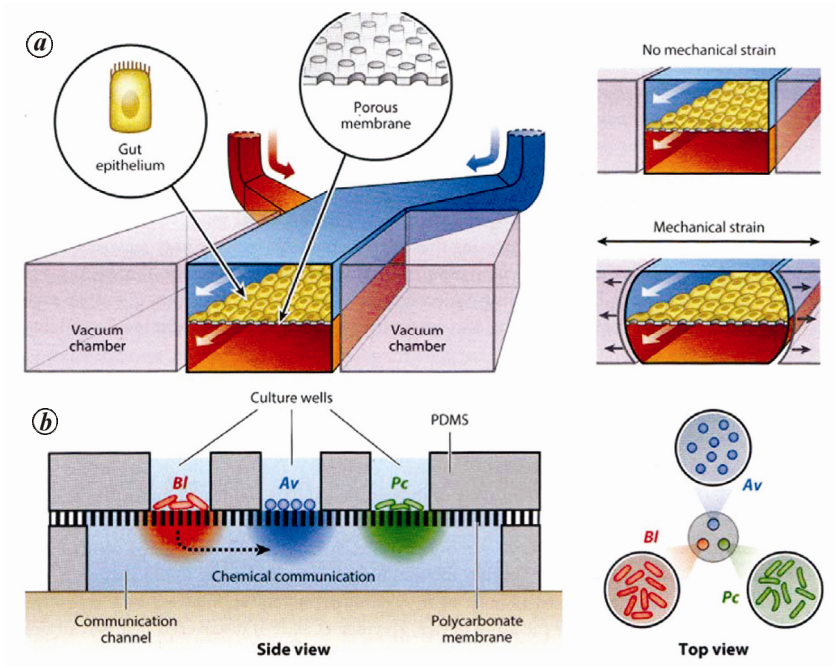

Figure 2. Multilayer microfluidic devices allow coculturing (from the article in this volume by Rusconi *et al.*). ***a***, Schematic of a gut-on-a-chip device showing the porous membrane lined by gut epithelial cells. ***b***, Schematic of a microfluidic device used to coculture three species of soil bacteria by imposing spatial structure on three culture wells and providing a chemical communication channel.

provide a glimpse of what is feasible with current-day technology. Indeed the article is dedicated to early studies in this area on haemoglobin in red blood cells (RbCs) – an enticing model system due to the high concentration of haemoglobin (ca. 5 mM) in the RBCs. The information provided by live cell NMR is clearly unique as it provides atomic resolution insights into the native cell states of proteins and macromolecular complexes. If anything, the challenges associated with this technique appear to be worthwhile given that artificial crowding agents like Ficoll and polyethylene glycol do no recapitulate the full range of biological contributions that proteins experience inside cells.

The trend over the past decade of biophysics and structural biology-oriented approaches to neurobiology is adequately represented in this volume. While previous volumes dwelt on structural studies (high-resolution structures of membrane proteins, ion channels, transporters that provide a mechanistic basis for neurodegenerative disorders) and patch-clamp analysis, the article by Han and Dong on itch mechanisms and circuits in this volume provide a glimpse of the complexities in this area. The molecules, cells and circuits that mediate the itch sensation as well as the pathophysiology of chronic itching conditions reveal a complex network of stimuli and molecular factors. While several groups of spinal neurons (such as $GPCR^+$ neurons) have been identified as mediators of itch sensations, the finding that psychogenic itch can be generated by solely visual stimuli suggests multiple overlapping pathways and circuits. Another article by Encalada and Goldstein describes our current understanding of motor cargo deficiencies and neurodegeneration. The authors describe studies which demonstrate that various cargoes travel at velocities that can be correlated with the kinesin number, a finding that has perplexed researchers in this area. This volume is notable for the discussion on the role of axonal transport in neurodegeneration. The studies on two pathways involving genetic mutations and protein aggregation suggest that further quantification of motor cargo transport parameters in axons is clearly needed for a molecular understanding of neurodegenerative disorders.

Three classical structural biology papers in this volume are likely to be of interest to macromolecular crystallographers and biochemists. These include one on Fanconi anemia DNA repair pathway by Walden and Deans, ubiquitin-like conjugation by Streich and Lima, and a review of metals in protein–protein interfaces by Song *et al.* The article on metals in proteins provides an intriguing dataset for bioinformaticians due to the sheer variety of permanent and transient interactions between proteins and protein subunits mediated by metal ions. Computational biology and bioinformatic analysis is also adequately represented in another article describing conserved RNA secondary structure in transcriptomes and genomes. The many functional non-coding RNAs identified in this analysis suggest that the current controversy of pervasive transcription and long non-coding RNAs is unlikely to die away soon.

Put together, this volume suggests that the boundaries of biophysics research are being redrawn by inputs from diverse science and engineering disciplines. Indeed, the research areas described in the articles here encompass micro- and cellular biology to neurobiology and large data genome studies to single-molecule bioassays – covering both the breadth and scale of modern day biology.

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