

kinetic gas theory and ends with body temperature. The human auditory system considers some basic concepts of sound, ending with defects in hearing. The treatment of electricity extends from Coulomb's law to neuronal action potentials. The nature of light and a geometric optics approach to vision is followed by a basic treatment of radioactive decay and its use in diagnostics and therapy. The book concludes with a chapter on pharmacodynamics based on compartment models. Here the mathematical aspect of differential equations is a bit more fleshed out. A notes section provides some cross-references for further reading in a chapter-wise manner.

If you have not read anything about the topic before, this book might whet your appetite. On the other hand, the reader may find many of the new and exciting results missing, such as the mechanics of barefoot versus shoe running (toe-first versus heel-first)¹ and non-Newtonian flows of blood². Other books by the same name exist, and one of them by Irving P. Herman³ deals with the subject in greater depth.

The book by McCall will serve well as an introductory source book on physics concepts and how they apply in normal and diseased functioning of the human body. The detailed chapter on pharmacodynamics will probably be an attractive and useful aspect of the book for referring to the various modes of modelling drug delivery and kinetics in the body. The target audience could well be interested high school and college students of pharmacy and biology as well as a interested layperson who wants to know 'how things work'⁴ in the machine that is the human body.

1. Lieberman, D. E. *et al.*, *Nature*, 2010, **463**, 531–535.
2. Fedosov, D. A. *et al.*, *Proc. Natl. Acad. Sci. USA*, 2011, **108**, 11772–11777.
3. Herman, I. P., *Physics of the Human Body*, Springer Verlag, 2007.
4. Selagat, R.-J., *How Things Work [Wie funktioniert das?]*, George Allen & Unwin Ltd, London, 1968.

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This volume effectively summarizes the excitement in the area of biophysics and structural biology in the past year. The choice of topics in this review is succinctly summarized in the first chapter by Peter Moore. In his essay entitled 'How should we think about the ribosome?', Moore makes a passionate case to re-examine dynamics in biological systems. Influenced, no doubt, by his sustained efforts to characterize the ribosome, he is forthright in making the case for visualizing the ribosome in action – a relevant observation for other large molecular machines as well. Most practitioners in this area of biophysics depict these mechanistic features as movies. He sounds a note of caution about this oversimplification based on static crystal structures, suggesting that this approach could lull researchers into believing these elegant visuals as factual data. He then goes on to predict that the post-structural era of the ribosome field could see more excitement and insight from kinetic measurements, thermodynamic analysis and computing than high-resolution crystal structures.

Cooperativity and allostery are two terms that link several topics in this review. From the chemo-mechanical coupling in the DEAD box helicases to the actin-binding protein, the focus, inevitably, is to understand the detached (weak) and attached (strong) binding events in these systems. This aspect is of critical importance in the case of the cyto-skeletal motors where strongly bound states are force-generating, whereas weakly bound (load-bearing) states represent intermediates that do work. Another noteworthy theme in this context is molecular machines that utilize ATP for their activity. In these systems, the ATP-hydrolysis competent and ADP-bound states are likely to be similar both functionally and structurally, but differ in their chemical states.

A significant number of articles in this volume focus on new methodologies for studies on biomolecules. These include zero-mode waveguides for single-molecule analysis by Zhu and Craighead, and

a review of single-molecule enzymatics by Puchner and Gaub. These topics could well be viewed as an indicator of an evolution in structural biology with a pronounced emphasis on the characterization of biomolecules in their entire dynamic splendour. Another chapter enticingly entitled 'Biomolecular simulation: a computational microscope for molecular biology' by Dror and colleagues is particularly revealing. The authors make a compelling case for the role of molecular dynamics (MD) simulations in structural analysis. In particular, researchers new to this area would find one figure on spatiotemporal resolution very informative (reproduced here as Figure 1). Figure 1 describes different techniques demonstrating the overlap in terms of information content. Indeed, the complementarity of techniques seen in Figure 1 is the gist of studies on biomolecular structure and function at the start of this decade.

Despite changes in techniques, and modern trends to emphasize the biological relevance of structural studies and other *in vitro* analysis, some topics and research themes still retain their charm. This is exemplified by the article 'Radical use of Rossmann and TIM barrel architectures for controlling coenzyme B12 chemistry' by Dowling, Croft and Drennan. This review succinctly describes another distinct step forward in protein engineering with the goal of embedding a new function into the versatile TIM barrel fold. Another fascination that appears to have sustained biophysicists over the ages is symmetry. The article on 'Allostery and Monod–Wyman–Changeux model after 50 years' by Jean-Pierre Changeux emphasizes this by the connection he draws between symmetry and regulation. Symmetry is also the theme that governs the chapter on 'Racemic protein crystallography' by Yeates and Kent. In this review, the thesis that racemic mixtures of proteins crystallize more readily has been discussed at length. The authors also comment on the choice of crystallographic symmetry that such systems could adopt vis-à-vis conventional protein crystals. This article would appeal to latter-day macromolecular crystallographers as it describes the theory regarding space-group preferences for small-molecule crystals in comparison to those preferred by macromolecules. After reading this article, one cannot help but wonder about

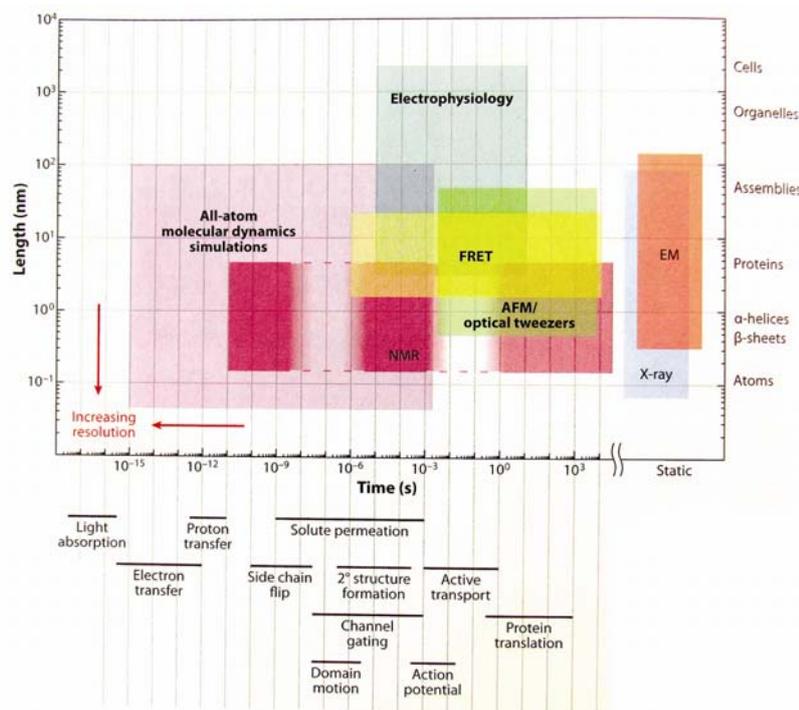


Figure 1. The spatio-temporal resolution of various biophysical techniques (reproduced from p. 432, Dror *et al.*).

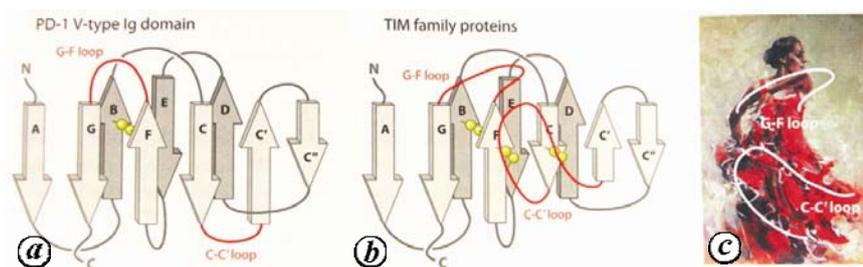


Figure 2. **a**, Topology diagram of a standard immunoglobulin domain and the disulphide bond shown in yellow. **b**, Representation of the T cell immunoglobulin mucin (TIM) protein that demonstrates how the disulphide dictates the tertiary structure. **c**, Painting that demonstrates conformational rearrangement wherein the lower fringes of the skirt become an upper-body accessory (reproduced from p. 73, Fass, D.).

what G. N. Ramachandran’s take on this experimental approach might have been.

This review also has authoritative essays on the assembly of larger macro-

molecular complexes. These include a chapter by Veessler and Johnson on virus maturation and another on the functional architecture of the nuclear pore complex

by Grossman, Medalia and Zwerger. Biophysicists nostalgic of the time when molecular tinkering using cysteine residues was a research theme of choice could well rejoice reading about the complexities that a disulphide bond brings about in a protein. Deborah Fass, in her article on disulphide bonding in protein biophysics, reviews diverse roles for disulphide bonding with a focus on proteins found in the extracellular environment. One sentence from this article could be of particular interest from a bioinformatics perspective – ‘Once the appearance of the disulfide permits the exploration of a new region of conformational space, other amino acid positions in the protein may subsequently evolve to support the new disulfide bonded geometry’. A figure from this chapter (reproduced below as Figure 2) is fascinating both for the sheer elegance of natural disulphide engineering and the apt metaphor of a flamenco dancer.

Put together, the volume provides an excellent description of biophysics in the early part of this decade. This review also seems to suggest that some research methodologies are likely to make the leap from being an exotic technique to an essential tool in biophysical research. The single-molecule techniques described in this review and the articles that detail the advances in our understanding of the dynamic properties of individual biomolecules and macromolecular assemblies are particularly noteworthy. It appears likely that these strategies would stretch the boundaries of biophysics and biomolecular structural analysis in the near future.

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