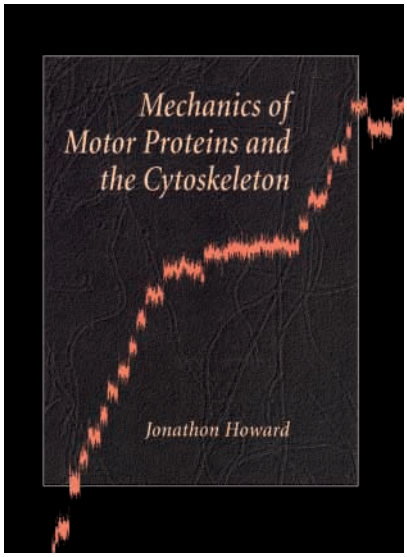
Size matters



Mechanics of Motor Proteins and the Cytoskeleton

by Jonathon Howard

Sinauer Associates (2001) 367 pages. ISBN 0-87893-334-4
£44.99/US$62.95

The recent developments in single molecule technology, especially in the field of single molecule mechanics and fluorescence measurements, have made it possible to study the basic mechanisms of cellular motility, such as intracellular vesicle trafficking, endo- and exocytosis, muscle contraction and cell locomotion, in unprecedented detail. Cellular motility is a form of nanotechnology devised by nature and has come into focus not only for biologists but also for engineers and physicists who are on the look out for novel solutions to technical questions in the man-made world.

Mechanics of Motor Proteins and the Cytoskeleton by Jonathon Howard is an excellent introduction into the molecular mechanisms that underlie the morphology and motility of cells. The book is aimed at an interdisciplinary readership, including students of biology, physics and engineering. Howard has divided his book into three parts. The first deals with the physical principles of protein mechanics. The second is about the structures of the cytoskeleton and the forces and motilities it can generate. Finally, he discusses the structures and functions of motor proteins and how these account for the macroscopic properties of complex motile systems like muscles. The author, Professor at the Department of Physiology and Biophysics at the University of Washington and Director at the Max Planck Institute for Molecular Cell Biology and Genetics in Dresden, is one of the leading experts in the field of protein mechanics for his experimental and theoretical contributions.

Size matters! This is the take home message of part one of the book. Throughout this section Howard contrasts the well known physics of motion of macroscopic systems – like a football, whose motions are determined by inertial and gravitational forces – to motions on the level of single proteins, where inertia and gravity are irrelevant and, instead, damping and elasticity dominate. While the mass of an object goes down with the third power of its length, its damping decreases only linearly. The motions of proteins and protein domains are therefore very different from a football. Howard illustrates this fact very clearly by examples such as a bacterium swimming through water at a speed of 25 μm/s. Although much bigger than a single protein, once the driving force has ceased, the bacterium will stop after just 5 picometres (much less than the diameter of a water molecule!) because of the viscous forces from the surrounding fluid. Howard uses the scaling argument also to explain why thermal forces are crucial for the mechanics of protein machines but not for macroscopic man-made machines. The chemical energy used by molecular machines is of the same order as thermal energy provided by their diffusive environment, and the transition states of the chemical reactions can therefore be reached by thermal fluctuations. Among many other important topics covered in part one of the book, Howard discusses chemical forces and how molecular motors convert chemical energy directly into mechanical work. Again he makes useful comparisons with man-made machines that must first generate intermediates such as heat or electrical energy.

In part two, Howard gives interesting insights into the mechanical properties of cytoskeletal filaments that determine the morphology and mechanical properties of cells. He discusses energetic aspects of the polymer biochemistry of actin filaments and microtubules, and explains how the growth and shrinkage of the filaments might be used in the cell to generate compressive and tensile forces. These forces are used in cells to produce mechanical work – for example, the polymerisation-driven motility of the intracellular bacterium *Listeria*, which propels itself through the cytoplasm by inducing polymerisation of an actin filament-containing 'comet tail'. Here, the reader finds an interesting treatment of the free energy of these multi-stranded cytoskeletal filaments and how the coupling of nucleotide hydrolysis to polymerisation provides energy for mechanical work (e.g. a microtubule of 100,000 subunits stores the mechanical energy equivalent to the free energy of 40,000 ATPs). Howard emphasises the dynamic aspects of cytoskeletal polymers and his emphasis on thermodynamics encourages the reader to consider the cytoskeleton in quantitative mechanical and energetic terms, rather than as a static structure.

In the final part, he scrutinizes the stars of the show, the motor proteins. He compares two well-studied examples, skeletal muscle myosin II and conventional kinesin, in great detail and thereby illustrates how molecular motors have been adapted for different cellular functions. The problem of coupling the biochemical and mechanical cycles of the motors and their adaptation to a wide diversity of functions are discussed in the context of the duty cycle ratio. The duty cycle ratio has been defined as the fraction of time a motor spends attached to its filament during its biochemical cycle. Using this concept, Howard gives an elegant explanation why some motors can work on their own as cellular porters (e.g. conventional kinesin), although at the cost of low speed, while others work in a team assembled into a polymer structure containing thousands of molecules, to produce higher forces and faster movement (e.g. muscle myosin II). In order to understand the workings of the motors, various information about

their structures, biochemistry and mechanics have to be combined. The short but clear summary of these aspects and the extensive literature list will be very helpful to the newcomer in the field. Howard also provides a short introduction into the basics of single molecule mechanical studies, which allow direct measurement of the working distance and force generated by an individual molecule. The author concludes his book with current models for both muscle contraction and kinesin movement. At this point it would have been beneficial for readers unfamiliar with the field if the original models by Huxley (Huxley, 1957) and Huxley and Simmons (Huxley and Simmons, 1971) had been presented more clearly. These models have become slightly lost in the author's own interpretations and views.

We highly recommend the book to those interested in the cytoskeleton, motor proteins, molecular machines, protein mechanics, protein structures and nanotechnology in general. One of its many strengths is that it uses units expressed per molecule rather than mole, making it easy to relate the energetics – for example, the energy of ATP hydrolysis – to molecular mechanical parameters such as force and displacement. It is also very well illustrated with figures, tables and numerical examples. By highlighting some of the controversial issues, such as the question whether or not the acto-myosin ATPase is tightly coupled to force generation, Howard encourages experts in the field to go away and do better experiments to answer the many remaining unsolved questions about the *Mechanics of Motor Proteins and the Cytoskeleton*.

References

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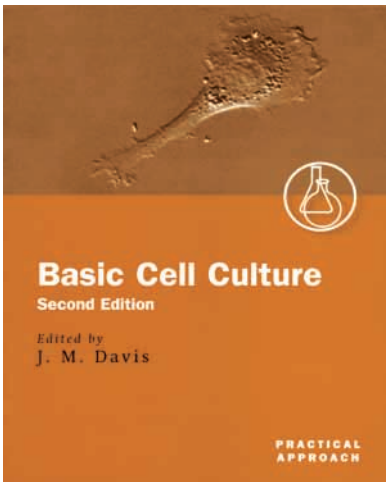
A guidebook for the cell culture facility



Basic Cell Culture, 2nd edn

edited by J. M. Davis

Oxford University Press (2002) 381 pages. ISBN 0-19-963853-5
£30

If you are planning to set up any functional cell culture facility, small- or large-scale, *Basic Cell Culture* could be very useful. The book has high practical and scientific value. It contains details about how to design the laboratory, and describes not only cell culture techniques but also other basic skills, such as how to load and run an autoclave. The text is compact and it is easy to find specific information. It contains useful tables and, most importantly of all, ready-to-use protocols for routine cell culture procedures. The book describes which cell culture medium and additional factors (e.g. growth factors) should be used for various animal cell lines. Different microscopy techniques are presented together with instructions for how to use microscopes, how to align illumination sources and how to analyse cell biology data statistically.

There are further descriptions of basic cell culture techniques, such as cell freezing and thawing, and the establishment and maintenance of various common cell lines. The book explains how to make primary cell cultures from different types of tissue and at various developmental stages, and how to establish immortal cell lines. In addition, it presents several protocols for modern DNA and chromosome analyses, together with brief descriptions of gene transfer techniques and cloning. Theoretical short overviews of, for example, the cell cycle, are followed by more detailed descriptions of methods to analyse these processes. This information can also be found elsewhere – for example, in original papers and, sometimes, in protocols from life science companies – but it is definitely convenient to have it all in one place. For work involving plants and invertebrate primary cell cultures, however, the information is lacking and other books should be consulted for practical advice on media and dissociation of tissues.

Websites for additional specific aspects of cell biology (such as protocols, image analysis, genome projects and bioinformatics), homepages of some of the larger life science companies, and educational resource websites are listed at the end of the book. These, together with the book itself, provide a valuable tool for teachers of cell biology.

With its low budget cover, *Basic Cell Culture* will probably not stand out on the bookshelf; however, this may have reduced the cost of the book to a reasonable level. Over all, the book provides a guide for any university or pharmaceutical company laboratory, with or without good laboratory practise (GLP) standards, that aims to obtain consistent cell biological data.

I suggest this book could serve as a handy reference guide and recommend it for managers of cell culture facilities and any person practising cell culture work. Although a lot of helpful practical information can be provided by life science and chemical companies, this book takes on a wider and more conclusive attitude to the cell culture process. Personally, I have placed it in the lab I am working in, and my colleagues and I have found it to be very handy when working at the bench or planning future studies.

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