Molecular Mechanisms in Muscular Contraction

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Muscle cells provide a unique probe into the motile properties of all living systems. A full understanding of the molecular mechanisms within muscle cells is therefore important to many areas of biological research. It is now nearly 40 years since the postulation of the sliding filament model of muscle contraction yet only recently has sufficient evidence been produced to support a convincing model. This book marks a turning point in muscle research. It reviews the evidence that myosin cross-bridges do indeed swing on actin filaments during contraction, and starts to tackle the problems this raises: what are the geometrics of the attached states of cross-bridges on actin? How many states are there? What is the sequence of molecular events during muscle activation? And is the primary source of muscular force cross-bridge swinging or Helix-coil transition?

Contents: Organisation and Structure of Actomyosin Systems; J.M. Squire *et al* • The Nature of the Actin Molecule; C.E. Schutt & U. Lindberg • The Structure of F-Actin Calculated From X-Ray Fibre Diagrams and the 0.6nm Crystal Structure; K.C. Holmes *et al* • Discussion Muscle Mechanics and Biochemical Kinetics; B. Brenner • Crossbridge Patterns in Defined Static States in Insect Asynchronous Flight Muscle; M.C. Reedy *et al* • Nuclear Magnetic Resonance Studies of Calcium Modulated Proteins and Actin-Myosin Interaction; B.A. Levine *et al* • Crossbridge Movements Monitored by Extrinsic Probes; T.P. Burghardt & K. Aitai • Functional Aspects of the Myosin Rod in Contraction; W.F. Harrington *et al* • Equatorial X-Ray Diffraction Studies of Single-Skinned Muscle Fibres; L.C. Yu & R.J. Podolsky • Static and Time Resolved X-Ray Diffraction Studies of Contracting Fish Muscle; J.M. Squire & J. Harford • Index

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On the move

Peter Sheterline

Molecular Genetic Approaches to Protein Structure and Function. Edited by James A. Spudich. Liss: 1989. Pp.175. \$58, £40.

IF YOU are a subscriber to, or an avid reader of, the journal *Cell Motility and the Cytoskeleton*, you may pass on to the next item; this collection of review essays was published in a special issue of that journal last year. If you are still here then it may be dawning on you that although the title suggests a general review of molecular-genetic techniques in cell and developmental biology, the contents are concerned almost exclusively with examples from the study of proteins of the cytoskeleton and muscle. You will find mention of neither the elegant developmental work on *Drosophila* and *Caenorhabditis*, nor the exciting work on analysis of cell-cycle regulation in yeast.

Both these examples — there are certainly others — signal the power of molecular-genetic approaches for slicing manageable paths through the previously impenetrable undergrowth of complex cellular interactions. In these areas of cell biology recently opened up by molecular genetics, protein biochemistry has hardly had time to catch its breath. By contrast, knowledge of the cytoskeleton has been driven by studies on protein structure and function, mostly because the main proteins of the cytoskeleton constitute a significant proportion of total cell protein and are therefore relatively easy to isolate.

To those reared on strategies of grind, find, characterize and immunize, things molecular seem to be moving very fast and usually in redshift. How do molecular-genetic approaches clarify central questions pertaining to the structure and function of the cytoskeleton, questions which have matured over the past 20 years or more? Despite the panache of technique and the elegance of strategy, it is clear that the application of molecular-genetic approaches is still at an exploratory stage. The most commonly sought objectives fall into three main categories: first to express enough wild-type or engineered protein for structure and function studies; second, characterization of the phenotypic effects of expression or deletion of a protein in a suitable host cell; and third, identification and characterization of genes influencing cytoskeletal functions by conventional genetic approaches. Each of these areas is covered by one or more articles in this collection.

The expression of cytoskeletal proteins in prokaryotes, the most established vector, has turned out to be almost entirely unpredictable; gelsolin, a fragile

protein, can be isolated intact, but expression of actin, a jewel in the cytoskeletal crown, has not yet been achieved. The difficulties are not entirely unexpected and seem partly due to the lack of appropriate post-translational modification and, perhaps more darkly, to inappropriate protein-folding conditions.

Significant space is also given here to discussion of the possibilities of so-called pseudo-genetics, which involves the introduction of antisense messenger RNA into host cells to reduce their expression of selected proteins. With easy access to sequence databases and modest prices for synthetic oligonucleotides, this must be perfect entry-level 'genetics' for ex-protein biochemists.

Overall, I think that the professed objective of the editor to satisfy nascent geneticists has been successful. This success rests in part on the discussion in several papers of experimental avenues which were not directly useful or produced a quite unexpected result, but also because authors were consistent in clarifying their objectives and strategies.

Studies using cultured cells suggest that the cytoskeleton is a restless federation of structures which, by the exchange of component molecules, progressively adapts to suit prevailing conditions. The underlying mechanisms of change appear to exhibit the catastrophic behaviour of the new mathematics, and may therefore resist the linear reductionist descriptions applicable to simpler systems. There is no doubt that molecular genetics will contribute greatly to identification and structure-function relationships of component proteins, but we may have to wait for the mathematicians for any answer to the question of how the cytoskeleton works. □

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■ Also recently published, *The Cytoskeleton and Cell Motility* by T. M. Preston, C. A. King and J. S. Hyams is a short volume covering the topic for undergraduate and postgraduate students. Price is £30 hbk, £13.95 pbk, publisher is Blackie.

■ Published today is the third edition of David Aidley's textbook *The Physiology of Excitable Cells*, extensively revised and incorporating new information on the properties of single ionic channels and the molecular biology of membrane proteins. Publisher is Cambridge University Press, price £45, \$90.

■ *Turning the World Inside Out* by Robert Ehrlich contains 175 simple physics demonstrations. The book is a "treasure chest" of ideas to illustrate aspects of physical science in playful ways. Publisher is Princeton University Press, price \$50 hbk, \$14.95 pbk.

■ *Dead Heat*, by Michael Oppenheimer and Robert H. Boyle, is the latest book to describe "the race against the greenhouse effect", providing "a prescription for what America must do — before it is too late". Publisher is Basic Books, price \$19.95.