Moving story

Robert Simmons

Muscles and Molecules: Uncovering the Principles of Biological Motion. By Gerald Pollack. *Ebner: 1990. Pp.300. $55.*

GERALD Pollack, author of *Muscles and Molecules*, believes in the conspiracy theory of muscle contraction. He quotes with evident approval another renegade, the late Graham Hoyle: "in other disciplines, proponents of different theories may fight bitterly, but they do attend the same meetings and coexist in unresolved strife until new facts reset the battle lines. In the small subdiscipline that is muscle, not only are the dissenters from current orthodoxy forbidden to appear, but also their work disappears from the record by never being quoted. Muscle scientists have a unique record for simply losing the facts."

Hoyle's own pet theory of contraction involved the generation of force by "super-thin filaments" which others found less often and less interesting than he did. Ironically, this theory does not even get a mention in Pollack's book. Indeed, Pollack is even more assiduous than the supposed conspirators at editing the record, and there is hardly a page that is representative of what most people in the field thinks.

Pollack believes that striated muscle shortens in a stepwise way, and he has often demonstrated this to his own satisfaction, but most agree that the observed effect is artefactual. Pollack now espouses the view of Bill Harrington that the driving force for muscle contraction arises from a transition from helix to random coil (melting) in the rod part of the myosin molecule. But this ignores the fact that myosin subfragment 1, which lacks the rod portion, supports motility.

Pollack's idea is that the thick filaments shorten in a stepwise way as the myosin rods melt sequentially along the filament, continuity being provided by connecting filaments which anchor the ends of the thick filaments to the Z-line. Melting is supposedly triggered by phosphorylation, in turn mediated by another component of the thick filament, C-protein — a candidate myosin light-chain kinase. But the evidence for a link between phosphorylation and control of contraction is flimsy, at least in vertebrate skeletal muscle.

Shortening of thick filaments is central to Pollack's theory. In the original formulation of the sliding-filament theory in 1954, there were the observations by A. F. Huxley and Rolf Niedergerke and by H. E. Huxley and Jean Hanson that the A-bands (made up of the thick filaments) remain of constant length during most active and passive length changes, and that the I-bands (made up of the thin filaments) shorten as the thin filaments slide between the thick filaments. Pollack is fond of tabulating the number of papers supporting particular views, irrespective of their merit or relevance. He lists 28 papers published since 1954 showing more than 15 per cent shortening of the A-band and only 12 showing less than 15 per cent. But of 18 papers in the former category I managed to check, nine relate to *Limulus* muscle, generally agreed to be unusual. Of the remaining nine papers, there is not a single one that does not have a simple explanation for the observed A-band shortening, usually proffered by the original authors, and taken as a whole they are a thoroughly convincing body of evidence that the length of the A-band does not change under most physiological conditions.

The most flagrant example of misquoting by Pollack lies in the reproduction of micrographs by Alex and Françoise Fabiato, which indeed show A-band shortening, but without explaining fully that the (skinned) muscle fibre was allowed to shorten freely during maximum activation to reach the irreversible 'delta state', whereupon the A-band remained shortened after the fibre was released and then re-extended. The authors suggested that this might be an explanation of other reports of A-band shortening, citing one of Pollack's other references as an example.

Another of Pollack's contentions has been that the proportionality between isometric force and filament overlap, another of the major planks of the sliding-filament theory, is incorrect. In Pollack's hands, force does not fall much until overlap in nearly completely reduced. But when steps are taken to avoid potential artefacts arising from non-uniformities of sarcomere length along a fibre, a linear relationship is observed, and even he has had to concede recently that this is so. But he now states that this is true only for strictly isometric conditions and a small amount of shortening produces the alternative result.

In Pollack's theory, actin does not have a primary role and any interaction with myosin is incidental. Based mainly on his own electron micrographs he postulates that the myosin crossbridges form a lattice of A-bridges with neighbouring myosin molecules linked together rather than with actin, even, it seems, in rigor. Inexplicably, there is no reference to reconstructions of the insect fibrillar muscle lattice or decorated thin filaments, which clearly demonstrate the interaction between myosin and actin. According to Pollack, actin is permitted to slide by a ratchet-like interaction inside the cage formed by the A-bridges (or it may itself melt and shorten). The activation of the myosin ATPase by actin, one of the main pillars of conventional crossbridge theory, is dismissed airily, with the remark that other factors can activate the myosin ATPase. But none surely under physiological conditions and by the same basic kinetic pathway?

Again on the basis of his own electron micrographs, Pollack proposes that there are I-bridges between thin filaments and connecting filaments. He finds fault with the conventional structure of the thin filament, with tropomyosin and troponin acting as integral control proteins, and instead places tropomyosin in the connecting filament, with troponin forming the I-bridges to the thin filament. The tropomyosin molecules melt during contraction too, apparently. Some 40 years of painstaking research on thin-filaments structure and function which supports the conventional view barely receives a mention.

Much of Pollack's theory of contraction will sink without trace if it can be demonstrated in motility assays that the force between individual nonphosphorylated myosin molecules and actin is similar to the force per myosin in muscle itself. Nor is Pollack's book likely to stimulate much research, as the real areas of controversy lie elsewhere. *Muscles and Molecules* represents a missed opportunity as the field would benefit from a full-length critical text and Pollack's views could have been incorporated into such a text in their proper context. The book is instead solely a vehicle for his own flights of fancy, and these prove to be insubstantial outside his own area of expertise and quirky within it. □

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