



Fig. 2 Schematic drawing of a myosin molecule showing the two heavy chains (tail) and four light chains (head). The ATPase is contained in the heads.

images of filaments in the electron microscope readily allows a head count of the number of myosin molecules, 12–14 in each filament, and indicates a longitudinal spacing between the heads of around 43 nm. Using the further observation that the smooth muscle myosin rod also forms minifilaments under the same conditions, Trybus and Lowey demonstrate, in mixing experiments, a rapid subunit exchange between filaments occurring within minutes. By the same mechanism, smooth muscle myosin minifilaments readily incorporate skeletal muscle myosin molecules. Using different conditions, Kendrick-Jones and co-workers⁶ independently demonstrate critical concentrations of monomer for assembly into filaments for smooth muscle, thymus and brush border myosins. The dynamic nature of myosin monomer–polymer transitions is thus brought into the limelight. Surprisingly, these transitions have also been seen in skeletal muscle myosin¹⁵.

But what about the folded state described above? Cross and colleagues⁷ show that folding is concomitant with ATP hydrolysis and causes the trapping of the hydrolysis products in the myosin head. They demonstrate that the folding reaction blocks not only the ATPase but also the self-assembly of myosin molecules so that the folded molecules represent an inert storage form of myosin. This result readily explains the apparent increase in critical concentration for polymerization induced by MgATP⁶ — the critical concentration for polymer-competent myosin remains unchanged against an increased background of redundant folded monomers. It is not known how these myosins fold or what amount of folded myosin occurs in systems such as smooth muscle *in vivo*. But some interesting transition forms to the folded state are providing clues about filament construction (Fig. 1). Trybus and Lowey^{3,4} and Onishi and Wakabayashi¹² have identified a stable 15S folded dimer that apparently unfolds to form an anti-parallel bipolar unit with a tail overlap of 40–50 nm. Such a building unit, as suggested earlier¹⁰, would explain the characteristic absence of a central bare zone and the ‘mixed’ or ‘side-polar’ appearance of long filaments assembled from smooth and non-muscle myosins^{8,16,17}.

How does myosin head phosphorylation fit into the picture? It is generally

agreed that phosphorylated myosin filaments, apart from being enzymatically competent to interact with actin, are more stable. But the new results differ concerning whether all or only a proportion of phosphorylated molecules can confer resistance to solubilization by MgATP. Trybus and Lowey find⁴ that dephosphorylated smooth muscle myosin is readily dissociated from smooth muscle minifilament copolymers containing phosphorylated and dephosphorylated myosin, whereas Citi *et al.* observe⁵ stabilization in comparable non-muscle myosin copolymers containing as little as 30 per cent phosphorylated myosin. In the latter case, however, Citi *et al.* used longer filaments rather than minifilaments, which could be significant.

As is clear from the images of Trybus and Lowey³, the myosin heads in the minifilaments are all far removed from the overlapping tails and cannot directly affect tail–tail interactions. It is conspicuous, however, that the growth of smooth muscle minifilaments into larger filaments occurs first laterally, reminiscent of the side-to-side, slightly oblique stacking of *Acanthamoeba* myosin minifilaments¹⁸. This staggered annealing of minifilaments leads to the population of more crossbridge levels and to the appearance of the characteristic 14-nm myosin helical repeat^{8,16,18} that can, with subsequent growth, extend to the centre of the filament⁸. Once this occurs, in filaments longer than about 300 nm, head–tail interactions, modifiable by head phosphorylation, could take place. The filaments could then be stabilized by submaximal levels of myosin phosphorylation. A consequence of such a building mode is that filament growth need not be restricted to the addition of bipolar dimers but could just as well proceed by the annealing of more minifilaments or larger assemblies⁸ (Fig. 1a). □

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Daedalus

Encapsulated breath

A FIRE on an aircraft kills more by smoke-inhalation than by flame. One defence is to provide the passengers with smoke-hoods that give a few minutes’ protection. Daedalus now proposes a more fundamental approach. He points out that the absorption area of the stomach and intestines is about 20 per cent of that of the lungs. Because the lungs extract oxygen from air containing only 20 per cent of that gas, we should be able to ‘breathe’ quite effectively through the stomach and intestines if they were provided with pure oxygen.

To do its new job properly, the stomach would also have to dispose of respired carbon dioxide. In this connection Daedalus recalls that sodium peroxide reacts with carbon dioxide to release oxygen: not in perfect replacement-ratio, but enough to make it useful in air-purifiers for submarines. So DREADCO’s chemists are exploring alkali-metal peroxide chemistry in search of a suitable composition for a ‘stomach-breathing pill’. The best bet seems to be a balanced mixture of sodium superoxide and lithium oxide: it contains about 38 per cent of available oxygen, and releases it in exchange for the equivalent quantity of carbon dioxide.

These ferocious oxides cannot just be swallowed. They react energetically with water to form highly caustic alkalis. The DREADCO team is encapsulating its formulations into thousands of tiny silicone-rubber-coated granules, to make a sort of micro-sago or ‘oxygenated caviar’. The silicone rubber safely retains the solid reagents and excludes water, but is permeable to oxygen and carbon dioxide. A gut charged with oxygenated caviar should smoothly take over the function of the lungs. A mere hundred grams of this powerful but insipid nostrum should enable the swallower to hold his breath effortlessly for at least an hour.

Thus the smoke-hood can be replaced by something only slightly less palatable than standard airline food. Gorged on the new emergency rations, passengers will be able to stroll to safety through the thickest smoke. Firemen will need no breathing apparatus. Even a victim already overcome by smoke might be revived by force-feeding with oxygenated caviar.

The new ability to stop breathing will also be welcomed by skin-divers, high-altitude mountaineers and beleaguered non-smokers. But stomach respiration will pose yet another chemical problem for sports authorities. Oxygenated both through lungs and stomach, athletes will break ever more records while denying that they are making use of unnatural stimulants.

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