Cell biology

Gel models for cell motility

from Harriet Harris

ACTIN filaments in many motile cells are randomly orientated in complex networks rather than in the parallel arrays of striated muscle, raising the question of how they participate in the organized movement of cells. The groundwork for attempting to answer that question was laid some years ago when it was demonstrated that soluble extracts of cells, prepared in the cold, formed gels on warming. Actin was a major component of the gels, some of which contracted in the presence of ATP, and myosin was identified in contracted material. However, crude gels may contain a bewildering assortment of components so it has been profitable to turn to reconstituted gels to test the effects of characterized proteins on actin behaviour. In particular, this allows the assessment of the combined effects of proteins which have such apparently opposing actions on actin as gelation and contraction. Two papers in the *Journal of Cell Biology* demonstrate the progress being made in the study of reconstituted gels from sea urchin eggs[1] and macrophages[2].

Macrophages contain a long flexible actin-binding protein (ABP) that cross-links actin filaments into gels[3]. If myosin is included with actin and ABP in the gels, they contract in an ATP-dependent manner; moreover, the effect of cross-linking the actin filaments with ABP is to lower substantially the amount of myosin required for contraction[4]. This is likely to resemble the physiological situation because, when phagocytic cells extend pseudopodia around a particle which is destined for ingestion, both myosin and ABP concentrate within the pseudopodia[5,6]. A further degree of sophistication is imparted by the addition of macrophage gelsolin, a protein which solates actin gels in the presence of calcium ions[7]. When calcium is present it abolishes the amplifying effect of ABP on actomyosin contraction. In a gradient of calcium concentration, the gelsolin-containing gels contract away from the highest calcium concentration[4]; thus the ionic gradient imposes directionality on the movement of a randomly orientated macromolecular array.

A quantitative analysis of the structure of gels formed by the assembly of actin in the presence of ABP shows marked differences from networks of actin filaments alone [2]; the filaments are shorter and form a perpendicularly branching network, whereas free filaments cross each other at random angles. If the structural and mechanical properties of these gels can be correlated in detail, the properties of networks in cells may be deduced.

The popularity of sea urchin eggs for studies of cytoskeletal behaviour is largely due to the substantial changes in actin organization that occur on fertilization: the cortical actin polymerizes[8,9] and microvilli, containing cores of actin[10] and fascin[11], form on the cell surface. Subsequently, cytoskeletal contraction occurs in the cleavage furrow during cell division. The questions posed by this system are, first, what are the precise changes in the structural organization of actin and, second, how are these changes regulated? To approach these problems Kane and colleagues have studied the gelation properties of sea urchin egg extracts. Upon warming, soluble extracts from unfertilized eggs form gels[12] which, if prepared under conditions such that the myosin remains active, contract in the presence of ATP[13].

Recently Kane has prepared synthetic mixtures of purified components which form stable gels at low ATP concentration and contract when the ATP concentration is increased[1]. The minimal requirements for such contractile gels are actin, cross-linking proteins and myosin. Superficially, therefore, both crude extracts and synthetic gels from sea urchin eggs appear analogous to their macrophage counterparts; the detailed organization of the actin filaments is, however, different. In the eggs, the cross-linking proteins are the 58,000-molecular-weight fascin and a 220,000-molecular-weight polypeptide. Fascin links the actin filaments into needle-like bundles, which are then linked into gels by the 220,000-molecular-weight component, which has no independent cross-linking effect on actin[14]. The gel thus consists of sets of actin bundles whereas the macrophage gel consists of separate filaments[2,3].

It is unclear whether this network of bundles is a useful model for the organization of actin in the egg cortex. The behaviour of actin–fascin bundles in a network might be rather different from their physiological role in the cores of microvilli. The synthetic gels are also deficient in some important biochemical properties of the crude system; for example, fascin is excluded from crude gels upon contraction, but retained in synthetic actomyosin contraction. Until these points have been clarified, Kane's synthetic gels cannot be assumed to be a good model for sea urchin egg cortical actin. Nevertheless, they should provide a useful assay for additional regulatory components as these are found and purified.

An intriguing property of randomly ordered macromolecular systems is that directed movements may be brought about by directed stimuli. Examples are the response of macrophage gels to calcium gradients and sea urchin gels to ATP, but the scope could be broadened to include gels containing gradients of selected protein components. In this respect, the behaviour of gels may be seen as a direct contrast to that of muscle, in which directed movement is brought about by the action of a uniform stimulus on an ordered system of filaments. □

1. Kane, R.E. *J. Cell Biol.* **97**, 1745 (1983).
2. Niederman, R., Amrein, P.C. & Hartwig, J. *J. Cell Biol.* **96**, 1400 (1983).
3. Stossel, T.P. & Hartwig, J.H. *J. Cell Biol.* **68**, 602 (1976).
4. Stendahl, O.I. & Stossel, T.P. *Biochem. biophys. Res. Commun.* **92**, 675 (1980).
5. Stendahl, O.I., Hartwig, J.H., Brotschi, E.A. & Stossel, T.P *J. Cell Biol.* **84**, 215 (1980).
6. Valerius, N.H., Stendahl, O., Hartwig, J.H. & Stossel, T.P. *Cell* **24**, 195 (1981)
7. Yin, H.L. & Stossel, T.P. *Nature* **281**,583 (1979).
8. Spudich, A. & Spudich, J.A. *J. Cell Biol.* **82**, 212 (1979).
9. Begg, D.A. & Rebhun, L.I. *J. Cell Biol.* **83**, 241 (1979).
10. Burgess, D.R. & Schroeder, T.E. *J. Cell Biol.* **74**, 1032 (1977).
11. Otto, J.J., Kane, R.E. & Bryan, J. *Cell Motil.* **1**, 31 (1980).
12. Kane, R.E. *J. Cell Biol.* **71**, 704 (1976).
13. Kane, R.E. *J. Cell Biol.* **86**, 803 (1980).
14. Bryan, J. & Kane, R.E. *J. molec. Biol.* **125**, 207 (1978).

Harriet Harris is at the ARC Institute of Animal Physiology, Babraham, Cambridge CB2 4AT.

Free-electron lasers

Past the visible light barrier

from C. R. Pidgeon

ALTHOUGH many experiments have successfully demonstrated the free-electron laser (FEL) as an amplifier of laser light, until a year ago the gain threshold for actual laser oscillation in a mirrored optical cavity had only twice been surpassed. A renewed burst of activity in the last twelve months has resulted in demonstrations of FEL oscillation in three new wavelength regions.

In a FEL amplifier, one observes or infers the amplification of an external laser beam as it interacts with an undulating electron beam passing through the periodic magnetostatic structure of a 'wiggler'. By contrast, a FEL oscillator produces a laser beam without the need for an external laser. The spontaneous radiation generated by undulating electron bunches in the wiggler is reflected back and forth between a pair of end-mirrors, generating enough stimulated emission in successive electron bunches to produce and sustain a laser beam.

The first such FEL laser oscillator was reported by Deacon *et al.* (*Phys. Rev. Lett.* **38**, 891; 1977), who used the electron beam from a superconducting linac at Stanford University to produce infrared laser beams with wavelengths around 3 μm. Shortly thereafter, a Columbia University–Naval Research Laboratory collaboration