saturation of DNA-binding components of the cytoplasm. These components have not been identified but Newport and Kirschner provide reasonable arguments that they are unlikely to be core histones.

An analogous abrupt switch in the cell cycle has been observed in other amphibian embryos (see refs 1 and 2 for references) and in *Drosophila* embryos, where McKnight and Miller⁵ have shown that it is correlated with the sudden onset of transcription. It will now be interesting to see whether Newport and Kirschner's findings are widely applicable. Already it is clear that they can have a substantial impact on embryology by integrating several lines of research and formulating clear questions on the relationship between chromosome replication and gene expression in early development. □

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Dynein structure

A delicate molecular bouquet

from Jeremy Hyams

THE beating of the billions of cilia lining your respiratory tract (and, in some cases, oviduct) is driven by the ATPase protein dynein. The dynein molecule forms paired projections, or arms, which extend like rabbit ears from each of the nine doublet microtubules that form the circumference of the ciliary axoneme (the cilium minus its surrounding membrane). By making a transient ATP-sensitive connection with the neighbouring doublet, the dynein arms cause the microtubules to slide over one another, a displacement that is converted into bending by other axonemal structures.

Elucidating the detailed structure of the dynein molecule has long been regarded as essential to understanding its function. The traditional electron microscope (EM) image based on axoneme cross-sections is of a hook¹ which tapers towards its point of attachment to the A-subfibre of the microtubule doublet (see the figure). This is undoubtedly a fairly crude view, however, as a typical EM section is around 80 nm thick and, with arms spaced at intervals of 24 nm, what you see is in fact a superimposition of as many as three different images. Better resolution is obtained from negative staining, although, for reasons that are not entirely clear, this visualizes only the outer of the two arms. These appear as a rod of three subunits² or as a club-shaped projection supported by a thinner spur³.

A radically different interpretation of the structure of the outer dynein arm and its cross-bridge cycle has recently been suggested from replicas of quick-frozen deep-etched axonemes from various ciliated or flagellated cells⁴. The technique gives a spectacular three-dimensional view of the dynein molecule and shows it to be composed of several distinct components. Essentially, these are a pyramid of three globular subunits associated with the A-subfibre and a slender stalk which spans the remaining distance to the B-subfibre of

the next doublet. The relationship between the different elements is reported to show a systematic variation depending on the condition of the axonemes before preparation. In rigor axonemes prepared by the rapid depletion of ATP by dilution and in which the arms are assumed to be physically locked in place⁵, the dynein molecules stand erect, like rows of soldiers. Re-addition of the nucleotide induces the relaxed state in which the arms detach and at the same time undergo a distinct baseward tilt. The basis of this configurational shift is a change in the association between the three globular subunits, and several possible scenarios whereby this could be translated into force-generation have been proposed⁴.

Diagram showing how the EM image of the outer dynein arm can vary with different methods of preparation. From the top: hook (thin section); three-subunit rod (isolated dynein negatively stained); club (*in situ* arm negatively stained); three-subunit mouse (deep freeze etch); three-head bouquet (STEM). Each doublet consists of a complete microtubule (the A-subfibre) and an incomplete one (the B-subfibre). (From ref. 6.)

Now, almost before the significance of these novel ideas have had a chance to be fully digested, their validity has been brought sharply into question. In the most recent issue of *The Journal of Cell Biology*, K. Johnson and J. Wall⁶ describe observations, using the scanning transmission electron microscope (STEM) at the Brookhaven National Laboratory, of isolated unstained dynein outer arms obtained from the ciliate *Tetrahymena*, at low electron dose. What they saw was yet another new image of the dynein molecule which they describe as a bouquet of three globular heads connected by separate stalks to a common base. From mass-distribution analysis of dynein molecules that had been rebound to microtubules, Johnson and Wall predict that the root-like base of the dynein molecule forms the permanent structural attachment to the A-subfibre and the globular heads contain the ATP-sensitive sites which interact with adjacent B-subfibres. Johnson and Wall point out that whilst the arrangement they describe is consistent with descriptions of the dynein arm based on other methods of preparation, the same cannot be said of the deep-etched images — although these would be obtained if the stalks of the bouquet collapsed during etching.

Outer dynein arms isolated from the flagella of the green alga *Chlamydomonas* have also been examined under the Brookhaven STEM⁷. Unlike *Tetrahymena* where the outer arm can be isolated as a single particle, the *Chlamydomonas* arm dissociates into two distinct ATPases⁸. The larger of these consists of two heads connected by two strands to a base whilst the smaller appears as a single globular unit. Interestingly, a similar Y-shaped or two-headed dynein arm structure was described some time ago by more conventional EM methods⁹.

Clearly, there is a lot more of the dynein story still to come but it is encouraging that the structure of the ciliary and flagellar arms is at last starting to reflect their biochemical complexity^{10,11}. The fact that several laboratories are currently raising monoclonal antibodies to different arm components should mean that the relationship between structure and function in the ciliary and flagellar axoneme should continue to become clearer. In the meantime, those with a nose for this sort of thing might conclude that Johnson and Wall's bouquet has the right smell about it. □

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