

comment

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In reply

Sir — While it is true that we have not published a detailed description of a model of F-actin based on our ribbon-to-helix conjecture, we have outlined our reasons for believing that an alternative to the Holmes' model is necessary and possible¹. Our recent determination of the crystal structure of an 'open-state' of actin has enabled us to find the shear and hinge-like regions of the actin monomer² by comparison with the previously determined 'tight-state' structure³. With this information, we are carrying out our programme⁴ to obtain a model of F-actin that can be compared with X-ray fiber diffraction and other structural data. Upon completion of this analysis, we will submit it for publication.

We never requested three-dimensional maps from the author of ref 9. of decorated F-actin because the helical symmetry in the published images⁵ gave us enough independent views (at the resolution of the data) to fit our preliminary F-actin model to the density. Figs 3 and 4 of our News & Views article⁶ show that the chemical cross-links to F-actin for calponin-homology domain and gelsolin can be explained by our model.

It is incorrect to assume that F-actin in the presence of ADP, ADP-P_i, or ATP analogues has the same structure as

F-actin in the overlap region with myosin in muscle fibers. Electron micrographic analysis has shown that the structure of F-actin is perturbed by the binding of myosin^{7,8}. The evidence cited by Egelman *et al.*⁹ does not contradict our proposal, nor does it invalidate our suggestion that the ends of growing filaments involve such conformational changes. Furthermore, the fact that the average length change in an actin monomer is only 0.08 Å in contracting muscle fibers¹⁰, does not preclude that a few are extended to a greater extent, as dictated by our model¹¹. In any event, X-ray measurements do not exclude length changes in the overlap region, where short stretches of actively shortening actin filaments are bound between successive crowns of myosin heads. The reason is that actin ribbon segments are commensurate with the 143 Å spacings of the myosin heads and, therefore, would contribute to changes in scattering at these layer lines, and not just to those commonly referred to as 'actin layer lines'¹¹.

We are not convinced that the position of the N terminus of actin in filaments has been localized using antibodies¹². Only when the contour threshold in the images was dropped to the point where the included volume was twice that of an actin filament did a small 'lollipop' of difference density appear at high radius. This density, comprising only 12% of that expected for an Fab fragment, was claimed, without further substantiation,

to be the combining site with the N terminus of actin. The antibody might well be located within the ordered density occupied by the fattened actin filament.

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