Theory of acitve transport in filopodia and stereocilia

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Abstract:

The biological processes in elongated organelles of living cells, such as filopodia, stereocilia, microvilli or flagella, are often regulated by molecular motor transport. The molecular motors may be an important delivery mechanism of the building material to the end of such organelle, when the organelle is too long for diffusion to be fast enough. We determined the stationary spatial distributions of motors in such organelles, corresponding to a basic scenario when motors only walk along the substrate, bind, unbind, and diffuse. Surprisingly, these stationary distributions are universal for the given set of model parameters regardless of the organelle length, which follows from the form of the kinetic equations and the boundary conditions. We developed a mean-field model, with a good quality approximate analytical solution, which quantitatively reproduces elaborate stochastic simulation results as well as provides a physical interpretation of experimentally observed distributions of Myosin IIIa in stereocilia and filopodia. The mean-field model showed that the jamming of the walking motors is conspicuous, and therefore damps the active motor flux. This damping can negate any role of motors if it requires for them to be walking far from the organelle base.

The organelle length is often set up by fluxes of building material, mostly, G-actin. Since the motor distributions are decoupled from the lengths, it is straightforward to build a theory of active transport of G-actin monomers by this motors and solve it as a separate problem with motors distributions as external field. Corresponding G-actin distributions in the organelle define its length. We found that the concentration profile of G actin along the filopodium is rather nontrivial, containing a narrow minimum near the base followed by a broad maximum. For efficient enough actin transport, this nonmonotonous shape is expected to occur under a broad set of conditions. The maximum in G-actin concentration appears before the motor jam and effectively increases the concentration gradient for diffusion of G-actin towards the tip. The increase in the gradient is enough to speed up the diffusion to allow for severalfold longer filopodia. Thus the main role of transport is in locally bumping up the concentration to speed up the diffusion rather than to actually carry the monomers all the way to the tip.