Research Roundup

Motor tug-of-war is productive

A
tug-of-war between microtubule motors creates cooperation that makes cargo transport a snap, according to a mathematical model from Melanie Müller (Max Planck Institute of Colloids and Interfaces, Potsdam, Germany) and colleagues.

Microtubule-based transport runs in two directions: motors such as kinesin pull cargo toward filament plus ends, whereas dynein heads to minus ends. Both motor types can bind at once to a single cargo, suggesting that they should hinder each other’s progress.

Some researchers propose that the two motor sets are coordinated by a regulatory complex to ensure that only one team is bound to the track at a given time. But the new model indicates that motors can fight it out themselves and still bring cargo to its destination.

The motors were characterized mathematically using previously measured properties such as motor speed, strength, and binding and unbinding rates. The calculations revealed that fast, directional transport was possible due to what the authors call an unbinding cascade. Random fluctuations in the number of motors bound to the microtubule give one motor team an advantage. If the force generated by the winning team is enough to detach a losing motor, each remaining losing motor bears a greater force and thus becomes even more likely to fall off until only the winning team is attached.

Small variations in the properties of one motor, such as might be caused by mutations or cellular regulatory pathways, altered the probability that one team or the other would win. Plugging such alterations into the model reproduced actual changes in transport behavior seen in developing fly embryos.

Müller would like to see the model tested further. “I’m not an experimentalist,” she says, “So I hope someone else builds an in vitro assay—bind microtubules to a surface and add beads with both motors attached. If you lower ATP concentrations to decrease motor velocity, does it then do what our model predicts?” The biggest obstacle might be getting dynein, which Müller calls the “diva” of motors, to behave reproducibly in vitro.

Müller, M.J.I., et al. 2008. Proc. Natl. Acad. Sci. USA. doi:10.1073/pnas.0706825105.

Spine actin for memory

Tiny spines on dendrites harbor three separate pools of actin, say Naoki Honkura, Haruo Kasai (University of Tokyo, Japan), and colleagues. The trapping of one pool helps form memory.

Memory is thought to stem from long-term potentiation (LTP)—the lasting enhancement of communication between two neurons at a synapse. On the postsynaptic side, information is collected in tiny bulbous membrane protrusions called spines, whose enlargement helps create LTP. Enlargement requires actin polymerization, prompting the authors to examine spine actin organization in brain slices before and after synaptic stimulation.

Unstimulated spines contained a stable pool of actin filaments near the base of the spine and a more dynamic pool throughout. The behavior of the dynamic set resembled that of actin in axonal growth cones, where actin is assembled by Rac at the leading edge and disassembled further back.

A third actin pool appeared in spines that swelled after repeated stimulation with glutamate. Polymerization of this pool seemed to cause the spine expansion, as its appearance correlated with membrane ruffling at spine edges. Its polymerizing enzyme is not yet known, but the group found that it required calcium and especially high concentrations of actin monomers.

In some spines, the enlargement-associated pool was quickly pushed out en masse into the dendrite body through the bud neck, and the spine shrunk back to its former size. The pushing force probably stems from surrounding glia and other neurons.

Lasting growth required more of the stable actin filaments, which might originate from the enlargement pool. Only spines that held onto their enlargement pool for longer than six minutes were still enlarged an hour later. Confinement of the pool required CaM-dependent kinase II, which the authors hypothesize helps cross-link the new filaments, making them stiffer and more difficult to squeeze through the bud neck. Smaller spine necks also helped hold them in.

The findings explain why larger spines have proportionately more glutamate receptors, since the receptors dock to the ends of actin filaments. The resulting increased responsiveness to glutamate in turn helps LTP set in. Enlargement itself probably assists. “So many enzymes are needed for LTP,” says Kasai. “The spine becomes a sort of incubator, and the extra space allows subsequent events to happen.” JCB

Honkura, N., et al. 2008. Neuron. 57:719–729.