Stick and slide: Computer simulation advances understanding of molecular motors

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A new study reveals how molecular motors that power important subcellular movements can generate cyclical motion. The research, published by Cell Press in the December issue of the *Biophysical Journal*, opens a new door to understanding motor molecules by using a computer program that faithfully simulates movement of hair-like cellular projections.

Many cells and single-celled organisms have tiny appendages called cilia and flagella that can wave or oscillate to move fluid across the cell surface or propel the cell forward. Each flagellum (or cilium) has nine pairs of fused microtubules, called outer doublets, arranged in a cylinder. Thousands of motor protein molecules, called dyneins, are arranged along each doublet. Each dynein motor attaches and detaches to the neighboring doublet, causing a sliding motion between the doublets, which causes oscillatory bending of the flagellum.

"We do not understand how the action of these motors is coordinated to produce useful bending patterns. In particular, the fundamental mechanism that generates oscillation has not been established," says study author Dr. Charles J. Brokaw from the Division of Biology at the California Institute of Technology. "The theories that have been proposed are difficult to test because of the complex structure of flagella."

Earlier studies in the laboratory of Dr. Ritsu Kamiya at the University of Tokyo used partially disintegrated flagella from green algae and

provided the first clear mechanism of a dynein-driven oscillation. Specifically, dyneins generated sliding forces that caused a lone pair of doublets to split apart near their bottom ends, which were still firmly attached together. Further sliding enlarged the separation and caused it to extend to the full length of the doublet pair, until it was completely dissociated. The doublets then reassociated, starting at their basal ends, until the dyneins were able to reinitiate sliding and repeat the cycle.

To fully exploit this simplified model system, Dr. Brokaw developed a computer program that could compute the movement of a doublet pair resulting from realistic dynein forces. The simulation confirmed what was inferred from the earlier study, that dynein-driven sliding is turned off when the separation between the doublets becomes too large, and is turned on again when the doublets reassociate.

"Perhaps more importantly, the new simulation demonstrated that dyneins must produce an adhesive force that keeps the doublets close together to produce sliding forces," explains Dr. Brokaw. "This first step will lead to programs in which ideas about the detailed chemical kinetics and structural mechanics of individual dyneins can be tested as the source of the sliding and adhesive forces."

Source: Cell Press (news : web)