Study sheds light on how cells transport materials along crowded intercellular 'highways'

December 13 2012

The interior of an animal cell is like a small city, with factories—called organelles—dedicated to manufacturing, energy production, waste processing, and other life functions. A network of intercellular "highways," called microtubules, enables bio-molecular complexes, products, and other cargo to move speedily about the cell to keep this vital machinery humming. A new paper published online in the journal *Proceedings of the National Academy of Sciences* sheds new light on how cells manage to keep traffic flowing smoothly along this busy transportation network that is vital to the survival of cells and whose failure can lead to a variety of diseases, including Alzheimer's and cancer.

The study, "Motor transport of self-assembled cargos in crowded environments", is co-authored by Jennifer Ross, assistant professor of physics at the University of Massachusetts Amherst, Erkan Tüzel, assistant professor of physics at Worcester Polytechnic Institute (WPI), and Leslie Conway and Derek Wood, graduate students of physics at UMass Amherst. It examines how proteins called motors (the trucks of the intercellular transport network) cooperate to minimize traffic jams and maximize the distance traveled by cargos.

In the study, the researchers used quantum dots (nanometer-sized semiconductors that reflect brightly in microscopy images) as cargo. In the laboratory, they attached these tiny cargos to individual motor

proteins and then allowed those proteins to attach to a microtubule. Motor proteins are able to "walk" along microtubules by attaching and detaching parts of their structure to the microtubule, much like the hand-over-hand motion of a person climbing a rope. The researchers observed how the quantum dots moved along the microtubule as they created more and more traffic by adding more and more motor proteins to the highways of this simplified transportation system.

They found that the dots moved more slowly as the traffic increased, but that they were able to travel farther before becoming detached from the microtubule. They also observed the pausing of the quantum dots, with the number of pauses increasing, but the length of the pauses decreasing, as the concentration of motor proteins is increased. The authors hypothesize that as the concentration of motor proteins increased, several of them became bound to each quantum dot. Much like trucks driving side-by-side down a multilane highway, the motor proteins likely became attached to different protofilaments along the microtubule (microtubules are made of 13 parallel protofilaments arranged into a hollow tube).

As an individual protein encountered an obstacle (another motor protein, for example), the motion of the dot would pause until the force exerted by the other proteins attached to the dot caused it to become detached from the blocked protein. The greater the number of proteins pulling the dot along the microtubule, the greater the force acting on it and the more quickly it would become detached from blocked proteins (and thus, the briefer the pauses in its forward motion).

In this way, motor proteins were able to cooperate to move cargo around roadblocks and to keep cargo attached to the microtubules despite heavy traffic, Tüzel says. "This is the first study to really look at the operation of the intracellular transportation system crowded conditions that are typical of living cells," he noted.

"It is important to understand how this system works and what can keep it from functioning properly because it is vital to the survival of all animal cells and motor proteins that make many fundamental biological processes, such as cell division, possible," he adds. "When the transport mechanism fails to work properly, it can lead to a variety of illnesses, including neurodegenerative diseases like Huntington's and Alzheimer's, and to cancer."

Provided by Worcester Polytechnic Institute