Researchers reveal jamming in cellular motor protein traffic

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To keep a cell alive, molecular motor proteins constantly transport building blocks and waste across the cell, along its biopolymer network. Because of the high density of these proteins, jamming effects are believed to affect this transport, just like traffic jams affect street traffic. However, not much is known about such crowding effects in cellular traffic. Researchers in the groups of Erwin Peterman and Peter Schall at the LaserLaB (VU) and the Institute of Physics (UvA) have now found a way to directly visualize and measure these jamming effects in cellular traffic. Their results, which have been published in *Physical Review X* this week, yield new insight into motor interactions in the crowded molecular motor transport. This project is receiving funding from NWO's Complexity programme.

Living cells require a constant transport of nutrition and waste. This is achieved by molecular motor proteins that transport organelles and other building blocks along the network of biopolymers of the cytoskeleton, which spans the volume of the cell. The walking mechanism of the individual motors has been studied extensively: Kinesin-1, for example, an important representative of the Kinesin family of proteins, moves by the subsequent, hand-over-hand stepping of two motor domains in well-defined steps of 8 nanometers. What has so far remained unclear is how the motors walk and interact collectively. Due to their dense population, crowding effects could crucially affect the transport across the cell, but so far these effects could not be accessed in the densely populated regime.

Speed measurements

Researchers at the UvA and VU have now made significant progress on this issue by combining a new correlation imaging technique with physical modelling. Like in previous studies, they used fluorescently labelled motors under well-defined conditions on microtubules - components of the cell's cytoskeleton - assembled on a glass slide. By correlating the moving image points of the fluorescent motor proteins in space and time, the researchers could for the first time measure their velocity and run length along the filament at high densities.

These measurements revealed a remarkable slow-down of the motors as density increased, demonstrating the formation of traffic jams. These traffic jams were directly confirmed in the observed traces of the motors. Furthermore, the researchers showed that these traffic jams were well described by simple transport models, in which the motor proteins are modelled by hard particles that pile up as they get into each other's way. Surprisingly however, the different motor species showed very different lengths over which they interact: from their physical size as assumed in the simple model, up to a distance 30 times larger than this size.

While clarifying the mechanism behind this long-range interaction remains an intriguing open problem for future research, the current results already illustrate the very different characteristics of the motors. Learning more about these motor protein-specific properties could help to cope with, or even suppress jamming effects in the cellular traffic. For example, it is well known that, in diseases like Alzheimer's disease, neuronal transport is severely hampered, resulting in local accumulations of motor proteins and their cargos, which could play a role in neurodegeneration.

More information: Daniël M. Miedema et al. Correlation Imaging

Reveals Specific Crowding Dynamics of Kinesin Motor Proteins, *Physical Review X* (2017). DOI: 10.1103/PhysRevX.7.041037