How a molecular traffic jam impacts cell division

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Interdisciplinary research between biology and physics aims to understand the cell and how it organizes internally. The mechanisms inside the cell are very complicated. LMU biophysicist Professor Erwin Frey, who is also a member of the Cluster of Excellence "Nanosystems Initiative Munich" (NIM) is working with his group on one particular issue involved in the cell's life. The professor for statistical and biological physics and his team, Louis Reese and Anna Melbinger, investigate the interplay of so-called molecular motors with the skeleton of the cell, the cytoskeleton.

The cytoskeleton consists of many fiber-like structures called microtubules. Molecular motors move along these filaments and transport large macromolecules. Furthermore, these motors are necessary for cell signaling and microtubule regulation at the tip of these filaments.

Frey and his coworkers investigate molecular motors which are of particular interest for the regulation of the length of microtubules during cell division. Without these motors, cells are not able to divide properly. How does the lack of one single molecule, the molecular motor, have such tremendous impact on cellular behavior? The biophysicists confronted this question and studied the detailed functioning of the molecule and its potential regulatory mechanisms during cell division. They focused on the interplay of microtubules and motors that shorten (depolymerize) the filaments. Frey and his colleagues used a theoretical model which correctly accounts for the "traffic jam" phenomenon.

Using this model, the biophysicists were able to show that a traffic jam of motor molecules on the microtubule alters the shortening behavior of the filament significantly. The number of motors present in the surrounding solution (i.e. the cytosol) is of paramount importance. At a specific critical concentration of motors, traffic jams form at the tip of the microtubule. As soon as a motor has finished its severing activity, it diffuses with the microtubule-brick into solution. However, due to the traffic jam of motor proteins, a fresh supply is already present. Hence, the rate of microtubule shortening is directly connected to the speed at which the single molecular motor depolymerizes the microtubule.

The situation changes dramatically if there are significantly less motor proteins in solution. In this case, the supply of motor proteins becomes the limiting factor. The disassembly speed is now governed by the quantity of motors arriving at the microtubule tip. Consequently the disassembly mechanism differs significantly from the one for higher motor concentrations. In particular, the depolymerization speed becomes length dependent. "From existing experiments, we knew that these collective effects are important for the system. What we didn't expect is that the properties of single motors completely vanish behind the motor group's performance", tells Louis Reese first author of the study.

With their calculations, the physicists from Munich contribute to a better understanding of existing experiments on microtubule disassembly. For example, a phenomenon discussed among scientists is that the speed at which microtubules are depolymerized by motors depends on the microtubule length: the longer the microtubule, the more motor proteins can bind to it. Their theoretical model explains these basic functional properties of this system and in this vein it puts the existing experimental results into a larger context.

"With this work we as theorists pass the ball back to experiments", reckons Erwin Frey. "It is essential for the comprehension of biological

systems to identify and understand minimal functional units like the microtubule motor interaction. On this track the cell plays a central role with its multifarious building blocks and functions. To understand these effects in the living cell is a declared aim of biology and biophysics".

More information: Crowding of molecular motors determines microtubule depolymerization Louis Reese, Anna Melbinger, and Erwin Frey, *Biophysical Journal* (cover article), Volume 101, Issue 9, 2190-2200, 2. November 2011
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