Coordination by remote control

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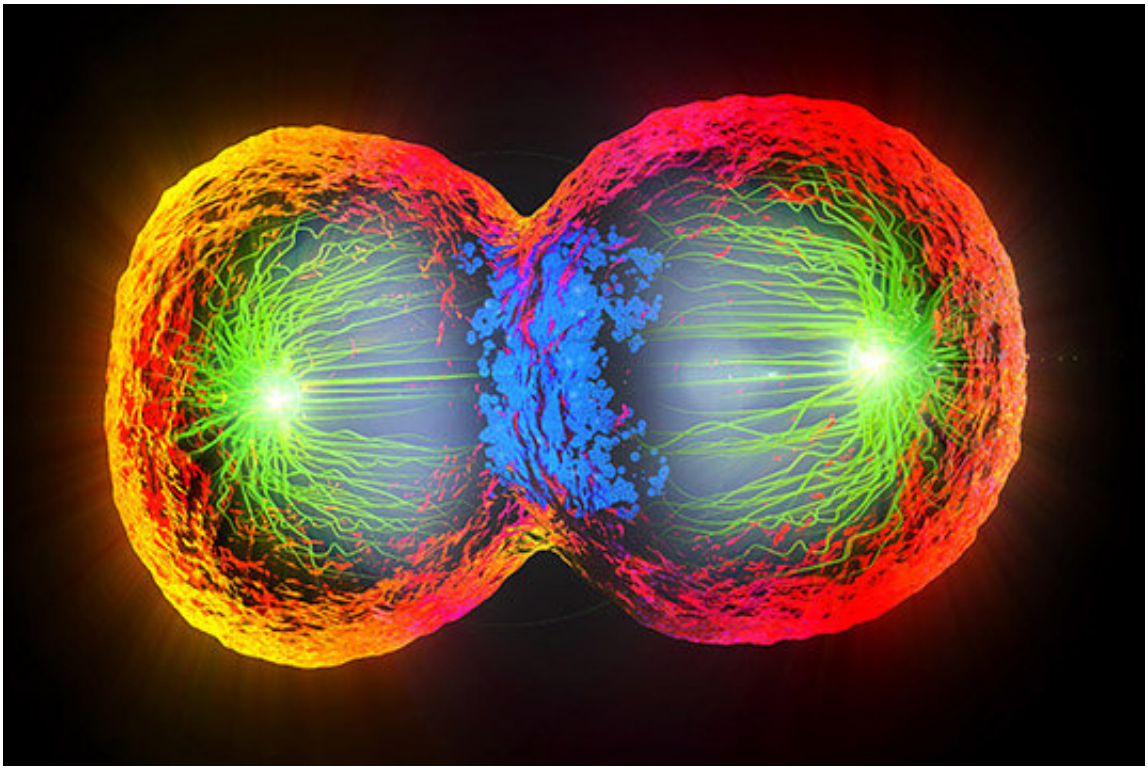

Many biological processes depend on the dynamic re-organization of the intracellular network of protein filaments and molecular motors. Probably the best known network of this type is the mitotic spindle. Credit: Ludwig Maximilian University of Munich

Protein filament systems within cells are subject to constant reorganization, which is in part mediated by the actions of motor proteins. LMU researchers have now shown that motor-driven movements can propagate through such networks.

Many biological processes depend on the dynamic re-organization of the cytoskeleton, which is comprised of several sets of proteins that are capable of actively altering cell shape and driving cell locomotion. These systems are essentially made up of intracellular networks of protein filaments and their associated molecular motors. The latter exert forces that alter filament configurations, which can result in changes in cell morphology. Probably the best known network of this type is the mitotic spindle. Following DNA replication, the spindle fibers attach to the duplicated chromosomes and actively pull them apart, thus distributing a complete set to each of the daughter cells during cell division. How the interactions between motor proteins and filaments give rise to such collective dynamics is a question that has not yet been satisfactorily answered. LMU physicist Erwin Frey and his team have now presented a new theoretical model which shows that movements within such a filament network can propagate over longer distances, and have used it to identify the mechanisms responsible for this phenomenon. Their findings are reported in an article in the *Biophysical Journal*.

The authors based their investigations on a simplified model, which includes filaments called microtubules and their molecular motors. Microtubules are cylindrical filaments made up of several protofilaments, each of which is composed of subunits. Protofilaments (and therefore microtubules) are polarized, i.e. they possess defined plus and minus ends. In the model, the filaments themselves can be oriented to the left or right. The motor proteins can bind simultaneously to subunits on two adjacent protofilaments and 'walk along them' in a stepwise fashion from one subunit to the next—always in the direction of the plus end. Furthermore, earlier experimental studies with isolated proteins had shown that these motors can also bind to neighboring microtubules that are oriented in an 'antiparallel' manner, such that their plus ends point in opposite directions. In this configuration, motor protein activity causes the two filaments to slide past one another, while parallel arrangements of microtubules remain static. "One would

intuitively expect that, in regions that contain lots of filaments disposed in antiparallel configurations, the average speed of filament motion should be higher than that in domains which encompass lesser numbers of antiparallel configurations," says Moritz Striebel, joint first author of the new study together with Isabella Graf. "However, previous experiments with mitotic spindles and in-vitro investigations of motor-filament networks have conclusively shown that this is not the case."

Thanks to the new model, Striebel and colleagues have identified a mechanism that can explain these observations. "We found that the mechanical forces exerted by the motor proteins propagate through the whole network. Since virtually all of the filaments are linked together by motors, those that are not coupled in an antiparallel fashion can still be caught up in the movements of the others," Striebel explains. The range over which these forces can propagate through a network is determined by the ratio of the viscous drag exerted by the cytosol (which acts as a braking force) to the forces generated by the motor proteins. "We were able to estimate the magnitudes of these two parameters for the mitotic spindle, and this showed that the characteristic length over which these motions can propagate is on the order of several filament lengths, which is in the same ballpark as the size of the spindle itself. In cellular terms, that's a large distance," says Frey. "More generally, our work yields new insights into the theory of active filament networks, which are indispensable for a better understanding of how the cytoskeleton functions."

More information: Moritz Striebel et al. A Mechanistic View of Collective Filament Motion in Active Nematic Networks, *Biophysical Journal* (2019). DOI: 10.1016/j.bpj.2019.11.3387

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