M196

Diffusion as a ruler: Modeling kinesin diffusion as a length sensor for intraflagellar transport.

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An important question in cell biology is whether cells are able to measure size, either whole cell size or organelle size. Perhaps cells have an internal chemical representation of size that can be used to precisely regulate growth, or perhaps size is just an accident that emerges due to constraint of nutrients. The eukaryotic flagellum is an ideal model for studying size sensing and control because its linear geometry makes it essentially one-dimensional, greatly simplifying mathematical modeling. The assembly of flagella is regulated by intraflagellar transport (IFT), in which kinesin motors carry cargo adaptors for flagellar proteins along the flagellum and then deposit them at the tip, lengthening the flagellum. The rate at which IFT motors are recruited to begin transport into the flagellum is anticorrelated with the flagellar length, implying some kind of communication between the base and the tip and possibly indicating that cells contain some mechanism for measuring flagellar length. Although it is possible to imagine many complex scenarios in which additional signaling molecules sense length and carry feedback signals to the cell body to control IFT, might the already-known components of the IFT system be sufficient to allow length dependence of IFT? Here, we investigate a model in which the anterograde kinesin motors unbind after cargo delivery, diffuse back to the base, and are subsequently reused to power entry of new IFT trains into the flagellum. By modeling such a system at three different levels of abstraction we are able to show that the diffusion time of the motors can in principle be sufficient to serve as a proxy for length measurement. In all three implementations, we found that the diffusion model can not only achieve a stable steady-state length without the addition of any other signaling molecules or pathways, but also is able to produce the anticorrelation between length and IFT recruitment rate that has been observed in quantitative imaging studies.

M197

Mechanical force induces mitochondrial fission via the canonical fission machinery.

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Eukaryotic cells are densely packed with macromolecular complexes and intertwining membranous organelles that continually change shape and engage in active trafficking. It is intriguing that organelles avoid clashing and entangling with each other during such dynamic movements in such limited space. Here we describe a mechanism that explains how mitochondria orderly cohabit with other organelles in the crowded space of the cytoplasm. Mitochondria form extensive networks that are constantly remodeled by fission and fusion events. While the molecular machineries that execute mitochondrial fission and fusion processes are relatively well documented, little is known about what triggers these events and determines the fusion and fission sites. We show here that mechanical stimulation of mitochondria – via the encounter with motile intracellular pathogens, via external pressure applied by an atomic force microscope, or via cell migration across uneven microsurfaces – resulted in the recruitment of the canonical mitochondrial fission machinery and subsequent fission. The mitochondrial fission factor (MFF) acts as a membrane-bound force sensor preferentially accumulating at mitochondria of reduced diameter, then recruiting the fission machinery to sites of mechanical strain. Thus, mitochondria may avoid entanglement with itself and other cellular structures by responding to biomechanical cues. These results shed new light on mitochondrial dynamics, an important process that