turning to materials that draw inspiration from complex animals, such as octopuses, which are capable of sensing, decision-making and remarkable adaptability using a decentralized nervous system. To get there, transformative work is needed, and innovations such as the authors' metafluid are a step in the right direction.

Most achievements in mechanical metamaterials have been fuelled by progress in solid mechanics, paired with key advances in computing and digital fabrication (for example, 3D printing[9]). Fluids[10] and fluid mechanics[11] have yet to be considered substantial contributors to research in this field. The authors' metafluid provides an opportunity to transfer the now-mature ideas of solid metamaterials to the world of fluids. Many researchers will surely take inspiration from this study, and will work to better understand — and ultimately make use of — the characteristics of metafluids. This path is challenging, but future investigations will be able to draw on a long and rich history of research in fluid dynamics.

It's crucial to understand that metafluids do not flow in the same way as normal liquids. For example, when water flows through a small tube, its rate of flow is determined by the difference in pressure between two points, not by the magnitude of this pressure. For Djellouli and colleagues' metafluid, the magnitude also matters: a pressure difference across a system with spherical capsules will induce a behaviour that differs from that elicited by the same pressure difference across a fully collapsed suspension. In turn, this state will affect the viscosity and, thus, the flow.

This result is not surprising to anyone trained in fluid mechanics. However, the authors' ingenuity and profound understanding and control of the capsules' mechanics casts such flows in a new light — as versatile and tunable. Their metafluid is as multifunctional as a Swiss army knife. It could easily be integrated into robotics to form logic gates, but might also be applied in optics, thermodynamics and acoustics — metafluids can do it all.

P.-T. Brun is in the Department of Chemical and Biological Engineering, Princeton University, Princeton, New Jersey 08544, USA.
e-mail: pbrun@princeton.edu

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Cell biology

The race to find factors for organelle fission heats up

Shilpa Gopan & Thomas J. Pucadyil

Organelles called lysosomes fuse with cargo-carrying vesicles and degrade the cargo molecules. How lysosomes maintain their size despite constant vesicle fusion was unclear, but now factors that aid organelle fission have been found. **See p.630**

Lysosomes are acidic organelles that are involved in the degradation of molecules and proteins. They also represent a signalling hub for the maintenance and quality control of cellular functions[1–4]. Many of these functions are attributed to the delivery of specific molecular cargo to the lysosome by fusion of cargo-containing vesicles with the organelle. Although a lot is known about fusion[5], the pathways and mechanisms that enable the release of membrane-bound material through fission from the lysosome, which balances the size of the organelle, have remained elusive[6] until now. On page 630, Li *et al*.[7] reveal components that mediate lysosomal fission.

Li and colleagues examined the worm *Caenorhabditis elegans* and found that mutations in the gene *hpo-27* caused lysosomes to become extensively tubular. Such shape changes coincided with a decrease in acidity and degradative capacity of the organelle. This indicates that the shape of a lysosome is

From the archive

Early progress in predicting how proteins fold up, and Isaac Newton's use of the word 'axiom'.

50 years ago

In the right conditions, many proteins spontaneously and reversibly fold into their biologically active conformation ... Such observations have appropriately been interpreted as evidence that the linear sequence of amino acid residues ... carries all the necessary information for directing the folding process, and it is just a short step to speculation that artificial synthesis or genetic engineering of novel sequences will lead to conformations with novel catalytic and control functions. But which sequences will lead to the desired conformation, and achieve it in reasonable time? ... What does seem clear is that the final stages of folding will be the most difficult to ... predict ... [S]uccess will owe as much to the size and speed of future generations of computers as it does to the programs and data fed to them. But it is remarkable that one can now discuss the difficulty of predicting the final stages of folding, not the folding as a whole.

From *Nature* 19 April 1974

150 years ago

In reference to the controversy ... about Sir I. Newton's calling his laws of motion "axioms," it is to be observed that there is a certain ambiguity in the word ... Whatever may be considered the ground of Euclid's "axioms" so called, Euclid himself did not apply that name to them; but the first nine he called "common notions," and the last three ... he placed among the postulates ... and heads them with "let it be granted." Now it is clear, from Newton's own words, that in calling his Leges motûs "axioms," he does not imply that they are *necessary* judgments, but that ... they are postulates, like Euclid's last three "axioms." In our modern use of the words "axiom," "axiomatic," there is always implied the *ground* why a proposition is demanded as granted, viz., because its necessity is self evident; but this wider use is not required by etymology, or (I think) in interpreting all ancient writings.

From *Nature* 16 April 1874

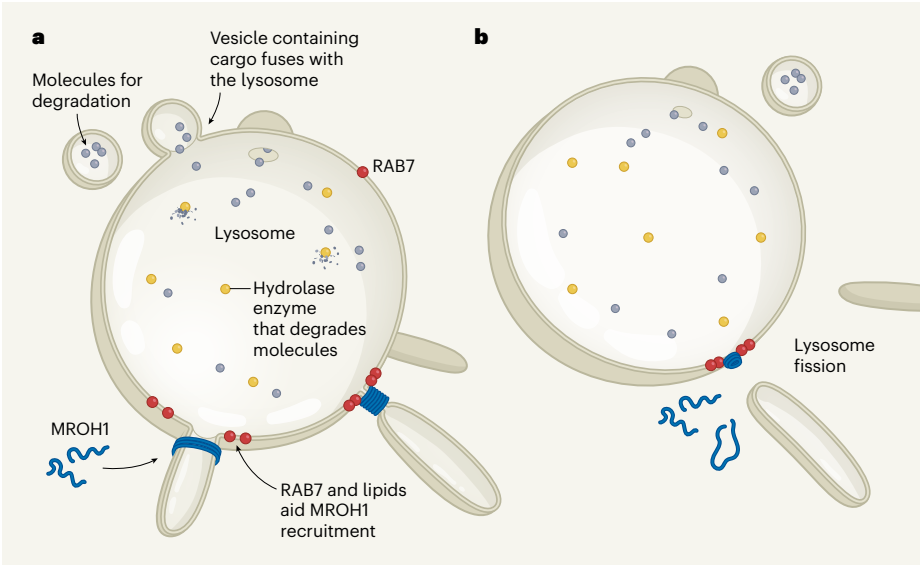

Figure 1 | Factors needed for the process of fission of lysosomal organelles. **a**, Lysosomes maintain their size through a balance of membrane fusion, which is associated with the merger of the lysosome and vesicles carrying cargo molecules that are destined for degradation inside this organelle, and a counterbalancing removal of membrane-bound material through the process of fission. Li *et al.*[7] report that the protein MROH1 is recruited to a site of organelle fission through interactions with the protein RAB7 and specific lipids (not shown) present on lysosomes. MROH1 assembles around tubules that emerge from the lysosome. **b**, MROH1 mediates the fission of these tubules by a mechanism that probably involves tubule constriction and severing.

intricately linked to its functions. The mammalian protein MROH1 is equivalent to the protein encoded by the worm gene *hpo-27*, and lysosomes look extensively tubular when MROH1 is removed from mammalian cells. Together, these results indicate that the pathway for maintaining lysosome shape and function is evolutionarily conserved.

MROH1 is known to bind to the protein RAB7, which is located on the lysosome, where it facilitates the movement (trafficking) of proteins out of the organelle[8–10]. But the exact functions of MROH1 have remained unclear. Li and colleagues show that RAB7 recruits MROH1 to the lysosome. MROH1 was also found to directly bind to phosphatidic acid, which is a type of molecule (an anionic lipid) that is present on lysosomes. MROH1 proteins assemble as discrete clusters on lysosomes, sometimes even coating the tubules that emerge from the organelle (Fig. 1). These tubules undergo fission over time. Therefore, the localization of MROH1 correlates with sites of fission.

Li and colleagues then examined an *in vitro* system to model lysosomes, consisting of artificial membrane 'nanotubes' that contained small amounts of phosphatidic acid and that mimicked the tubules emerging from the lysosome. Remarkably, the addition of purified MROH1 resulted in the proteins assembling as discrete clusters that constricted and severed the nanotube. This result is consistent with the model that MROH1 is sufficient for fission of lysosomes.

MROH1 contains a structural motif called a HEAT repeat that consists of two subunits (antiparallel α-helices) linked by a short turn of amino-acid residues. An extension of this repeat or the association of identical proteins containing the motif in a complex (termed oligomerization) can produce extended curved structures that are shaped like a coil of wire (solenoid). MROH1 is predicted to contain 37 HEAT repeats, and deletion of a HEAT repeat from either end of the protein affects its ability to oligomerize. These deletion mutants are unable to sever membrane nanotubes and fail to associate with lysosomes. The fission mechanism therefore probably involves a membrane-active oligomer or a scaffold of MROH1 that wraps around and constricts the underlying tubule.

"The pathway for maintaining lysosome shape and function is evolutionarily conserved."

Members of the dynamin superfamily of proteins are well-established fission proteins associated with vesicle formation. However, the authors report that deletion of the gene encoding dynamin in *C. elegans* did not alter lysosome shape. This indicates that dynamin is not involved in lysosome fission. Dynamins are enzymes that break down (hydrolyse) the cellular molecule GTP, and they associate with membranes and oligomerize into helical scaffolds. GTP hydrolysis by these enzymes drives a conformational change in the scaffold, causing it to constrict the underlying tubule, which results in fission[11]. However, MROH1 does not have any obvious enzymatic activity, and the precise mechanism by which it constricts the membrane tubules of lysosomes remains unclear.

Li and colleagues extended their findings to examine the physiological role of lysosome fission. *C. elegans* embryos that lacked the gene *hpo-27* had low survival rates and the few survivors showed notable growth defects and enhanced susceptibility to fungal infections. Furthermore, these worms displayed an early onset of protein aggregation, which is a hallmark of premature ageing. Surprisingly, the cellular basis for these adverse effects arises from the loss of lysosomal integrity. Lysosomes in these worms were prone to rupture, leading to the release of their contents into the cytoplasm. This caused substantial widespread damage to the function of other organelles such as mitochondria and the endoplasmic reticulum. In the long term, these effects caused a decrease in the lifespan of the worms. Lysosome fission therefore represents a key mechanism that maintains proper organelle function.

The discovery of MROH1 as a lysosome-fission factor is a notable observation and it raises some exciting questions. The finding that such a factor is both necessary and sufficient for lysosome fission provides an avenue for addressing some of these questions. This is because scientists now have a defined target that can be used to help establish links between lysosome functions and cellular and organismal physiology.

Shilpa Gopan and **Thomas J. Pucadyil** are at the Indian Institute of Science Education and Research, Pune 411008, Maharastra, India.
e-mail: pucadyil@iiserpune.ac.in

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