Until now, autophagy was the only process known to degrade whole organelles. However, in autophagy, degradation occurs by the delivery of organelles to lysosomes, which use enzymes called hydrolases to digest the organelle's various components, such as protein, DNA and lipids. The authors postulate that a phospholipase-dependent pathway could be more efficient than autophagy in circumstances such as lens development. This is because lens development requires the elimination of many types of organelle, including lysosomes, as opposed to the selective elimination of specific organelles, as occurs in autophagy. Indeed, this is the first report to describe the fate of lysosomes during lens development.

Lens differentiation is a spatio-temporally controlled process, in which organelles in the centre of the lens are degraded first, with degradation then continuing outwards to the lens periphery. Among the many transcription-factor proteins involved in this process, Hsf4 has a prominent role, and mutations in the gene encoding Hsf4 are associated with congenital cataracts[8]. Morishita and co-workers show that the development of small pores in the membranes of mitochondria and lysosomes in zebrafish occurs in an Hsf4-dependent manner, and that this acts as a signal for HRASLS-family phospholipases to relocate to these organelles. The authors report that pore formation in the lysosomal membrane triggers the partial release of its contents, including some DNA-degrading enzymes, into the cytosol. This occurs before phospholipase translocation to the lysosome results in the release of the entire contents of the organelle. Importantly, the authors demonstrate that lysosomal damage by pore-forming agents is sufficient to trigger phospholipase translocation to lysosomes.

This result underscores the key role of lysosomal-membrane permeabilization in physiological and developmental contexts, such as during cell division[9] or in the shrinkage of the mammary gland after lactation[10]. The authors further show that Hsf4-mediated permeabilization of the mitochondrial membrane is also required for HRASLS translocation to mitochondria in zebrafish, and that mitochondrial degradation is suppressed in Hsf4-deficient zebrafish.

Together, these observations suggest that the Hsf4-dependent partial permeabilization of organelle membranes is the signal required to trigger HRASLS translocation to target organelles in the lens. However, the permeabilization process seems to be cell-type dependent, because overexpression of Hsf4 and HRASLS3 in human HeLa cervical cancer cells does not induce HRASLS3 translocation to organelles (with the exception of organelles called peroxisomes) in those cells. Therefore, the precise mechanism by which Hsf4 specifically promotes the formation of pores in organelle membranes of lens cells remains to be determined. Hsf4 regulates lysosomal activity and lysosomal pH in lens cells[11]. It is therefore tempting to speculate that organelle degradation in the lens is mediated by an Hsf4-dependent connection between lysosomal pH and lysosomal pore formation, because pH alterations affect the membrane stability of lysosomes[12].

Further studies will be needed to explain the authors' observation that overexpression of HRASLS3 in HeLa cells results in the degradation of only one type of organelle — the peroxisome. Such selectivity might be mediated by protein–protein interactions, providing an extra control step, or perhaps it is due to differences between organelles, such as the composition or stability of their membranes. Yet another puzzle is why HRASLS proteins degrade the intracellular membranes of organelles in lens cells, but do not target the membrane lipids of the cell's outer boundary — the plasma membrane.

Given the high levels of expression of HRASLS3 in adipose tissue (which aids fat storage)[13], it will be interesting to learn whether HRASLS3 participates in organelle degradation during differentiation of the adipocyte cells in this tissue. Future studies could investigate whether these phospholipases can be engineered to degrade other membrane-bound structures of interest, such as those of harmful intracellular bacteria. It will also be worth investigating whether related forms of HRASLS proteins, of which there are five in humans and three in mice, also participate in organelle dismantling.

Morishita and colleagues' findings provide a wonderful example of how developmental processes are harnessed to solve complex problems. In this case, cell transparency for vision arises as a result of regulated organelle removal. Whether this process is involved in other developmental events, and whether abnormalities in it contribute to disease, remains to be determined.

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1. GBD 2019 Blindness and Vision Impairment Collaborators. *Lancet Glob. Health* **9**, e144–e160 (2021).
2. Morishita, H. *et al. Nature* **592**, 634–638 (2021).
3. Wistow, G. J. & Piatigorsky, J. *Annu. Rev. Biochem.* **57**, 479–504 (1988).
4. Cvekl, A. & Ashery-Padan, R. *Development* **141**, 4432–4447 (2014).
5. Wride, M. A. *Phil. Trans. R. Soc. Lond. B* **366**, 1219–1233 (2011).
6. Matsui, M., Yamamoto, A., Kuma, A., Ohsumi, Y. & Mizushima, N. *Biochem. Biophys. Res. Commun.* **339**, 485–489 (2006).
7. Morishita, H. *et al. J. Biol. Chem.* **288**, 11436–11447 (2013).
8. Bu, L. *et al. Nature Genet.* **31**, 276–278 (2002).
9. Hämälistö, S. *et al. Nature Commun.* **11**, 229 (2020).
10. Sargeant, T. J. *et al. Nature Cell Biol.* **16**, 1057–1068 (2014).
11. Cui, X. *et al. Biochim. Biophys. Acta Gen. Subj.* **1864**, 129496 (2020).
12. Wang, F., Gómez-Sintes, R. & Boya, P. *Traffic* **19**, 918–931 (2018).
13. Hummasti, S., Hong, C., Bensinger, S. J. & Tontonoz, P. *J. Lipid Res.* **49**, 2535–2544 (2008).

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Engineering

Large-scale origami locks into place under pressure

Sigrid Adriaenssens

Inflatable, metre-scale origami structures have been designed to transform from flat structures into expanded forms and then to lock into their new shape. This technology opens the way to the use of large origami structures for engineering. **See p.545**

It might seem surprising that origami, the ancient Japanese art of paper folding, is an integral part of engineering. However, origami structures can be folded up compactly and deployed at the nano- and macroscales seemingly without effort. They are therefore well suited for a wide range of applications, including robotics[1], arrays of solar panels[2] and engineered structures known as metamaterials[3]. On page 545 Melancon *et al.*[4] report triangular origami facets that snap into 3D shapes when filled with a pressurized fluid. The authors' work provides a new method for designing large origami enclosures that can be deployed and locked into shape through inflation.

In engineering, a deployable structure is one that can change shape in a way that greatly alters its size — large-scale examples include scissor lifts and bouncy castles. Conventional deployable structures are transformed into a larger shape through the extension of linkages

REF. 4

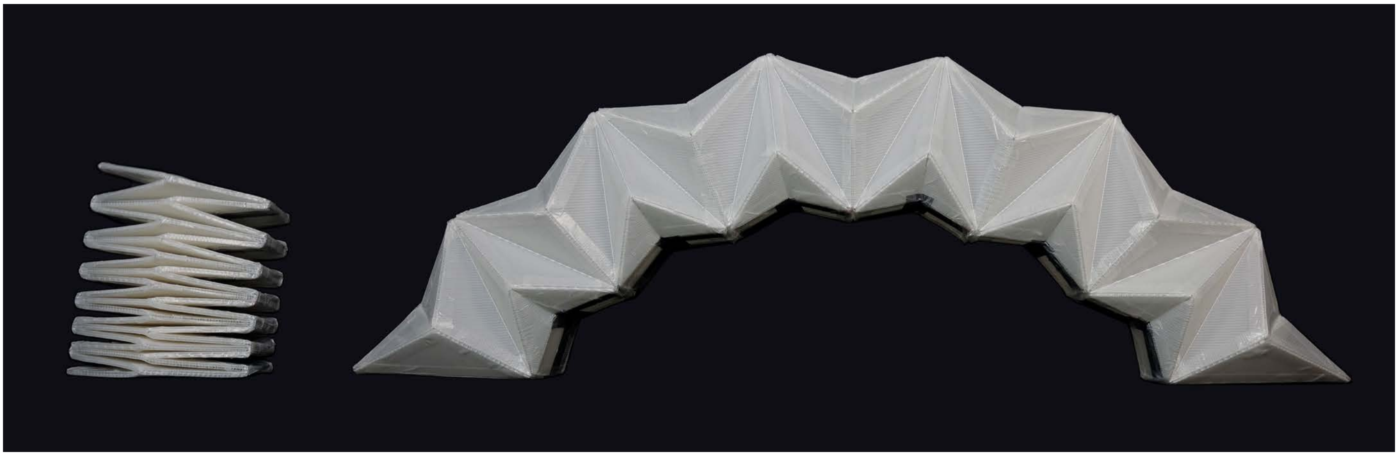

Figure 1 | An inflatable origami archway. Melancon *et al.*[4] report the design of inflatable, metre-scale origami structures, such as this archway, that transform from a compact shape into an expanded one when inflated. Moreover, the structure retains its expanded shape without the need for constant air pressurization.

(as in scissor lifts) or by inflation (bouncy castles). Both types of structure are then secured into their new shape by an external agent: a lock and the sustained application of air pressure, respectively. However, neither can secure themselves.

To address this problem, Melancon *et al.* draw inspiration from origami. The authors first define geometric parameters enabling the deployment of origami structures that enclose a space using fluidic pressure. Their innovative approach is then to design enclosed origami shapes that have two or more stable equilibrium states (conformations in which the energy of the system is minimized). Because they are at equilibrium, these states stay in place without the use of an external agent — in the same way that a ball comes to rest when it rolls to the bottom of a valley.

However, to switch between the stable states as they are inflated, the authors' origami shapes must overcome an energy barrier. This is because the facets that make up the origami shape cannot bend or stretch, and so are geometrically incompatible with each other during the deployment process. To overcome this problem, Melancon *et al.* connect the rigid facets with stretchable hinges. These hinges deform to resolve the geometric incompatibility, and thus allow the system to shift from one local minimum-energy state to another.

Melancon and colleagues demonstrate that their approach can be used to deploy and lock into place an inflatable archway 60 centimetres tall and 150 cm wide (Fig. 1), and a prototype for a tent-like shelter that has an expanded shape 2.5 × 2.6 × 2.6 m in size. These are remarkable achievements, because the deployment and locking of origami structures at such large scales is challenging. The authors show that the secret to success is to integrate multistability with inflation and the use of flexible hinges to resolve geometric incompatibility of the facets. The findings therefore pave the way to an unexplored realm of deployable, stable origami structures at large scales.

Moreover, because these origami structures can embody two or more mutually exclusive stable states, it should be possible to design structures that can be switched between a variety of shapes — a desirable property for one-shape-fits-all emergency shelters, especially in situations in which the enclosures are to be deployed in an unknown context.

However, scaling issues might limit the potential of these origami systems for engineering applications at very large scales (10–100 m). The authors' understanding of the processes needed to fold flat sheets of materials to produce self-locking, inflatable structures derives from numerical simulations and physical prototypes constructed at the metre scale, deployed in the controlled environment of a laboratory. The material is assumed to be (practically) massless — and thus lacking internal stresses — and infinitely rigid. But these assumptions do not hold for very large objects. For example, a previously reported numerical analysis of an origami footbridge[5] that spans 56 m reveals that its substantial self-weight produces both compressive and tensile stress variations and deformations across its hinges and facets.

Large-span structures also need to be strong and stiff at all phases of deployment to satisfy building regulations. This means that they must be able to resist extreme loading, such as asymmetrical wind suction and pressures produced by hurricanes. This is particularly true for emergency shelters in disaster areas. The effects of combinations of extreme loading on the structural behaviour of Melancon and colleagues' origami systems remain to be determined.

Scaling issues can also arise because origami processes that work for sheets of paper, which have essentially zero thickness, might not work at larger scales for other, thicker materials. Materials used for architectural or structural applications not only need to be strong, but must also have a long lifespan and fulfil other functions, such as regulating heat transfer into an enclosure. The facets of such structures will therefore be much thicker than paper. This challenge could be addressed by using systems of facets that have variable thickness (variable within one facet, or having different facets of variable thicknesses). Because hinges are often the most costly and weakest elements in any engineering design, minimizing the number of creases would help to lower manufacturing costs and strengthen the origami structure.

The use of Melancon and co-workers' origami structures in engineering could save on storage space, transportation costs and setting-up times, and the self-locking inflation system would enable easy and robust deployment, a win–win situation for deployable structures. As noted earlier, several issues will need to be addressed before the structures can be used at large scales on Earth. But having the ability to transport large objects in compact forms is also highly desirable for space missions. Moreover, the reduction of gravitational force — and the absence of building regulations — in space would also facilitate the use of the new origami technology.

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1. Felton, S., Tolley, M., Demaine, E., Rus, D. & Wood, R. *Science* **345**, 644–646 (2014).
2. Zirbel, S. A. *et al. J. Mech. Des.* **135**, 111005 (2013).
3. Filipov, E. T., Tachi, T. & Paulino, G. H. *Proc. Natl Acad. Sci USA* **112**, 12321–12326 (2015).
4. Melancon, D., Gorissen, B., García-Mora, C. J., Hoberman, C. & Bertoldi, K. *Nature* **592**, 545–550 (2021).
5. Nagy, L., Rhode-Barbarigos, L., Adriaenssens, S. & Kilian, A. *Int. J. Space Struct.* **30** (2), 75–84 (2015).