any unique alterations, including unknown components, are specifically engaged in the mitochondrial sorting of aggregating proteins.

From the perspective of cellular physiology and pathological processes, the most exciting questions are about the functionality of mitochondria that are busy disposing of aggregates, their role in maintaining cellular-protein homeostasis and how they affect the failure of this process in disease. Ruan and colleagues provide evidence that mitochondrial aggregate disposal is active not only during heat stress but also under a broader range of physiological conditions. In a final set of experiments, they observed a similar phenomenon in human cells. Together, these data indicate that the mechanism could be widespread and evolutionarily conserved. Defects in mitochondrial function and an inability to deal with aberrant proteins are common features of age-related and neurodegenerative diseases in humans. Perhaps defects in mitochondrial aggregate clearance are a part of the mechanisms that trigger and accompany cellular degeneration during disease.

The mitochondrial pathway of aggregate clearance is likely to form an important addition to our knowledge of the mechanisms involved in maintaining cellular-protein homeostasis. Interestingly, the efficiency of mitochondrial protein import affects the ability of cells to clear proteins in the cytosol[11]. Ruan and colleagues' work provides another fascinating example of the crosstalk between the mitochondrial import machinery and cytosolic-protein homeostasis. It is becoming increasingly clear that maintaining a productive dialogue between cellular compartments is a crucial task — one that we are just beginning to understand. ■

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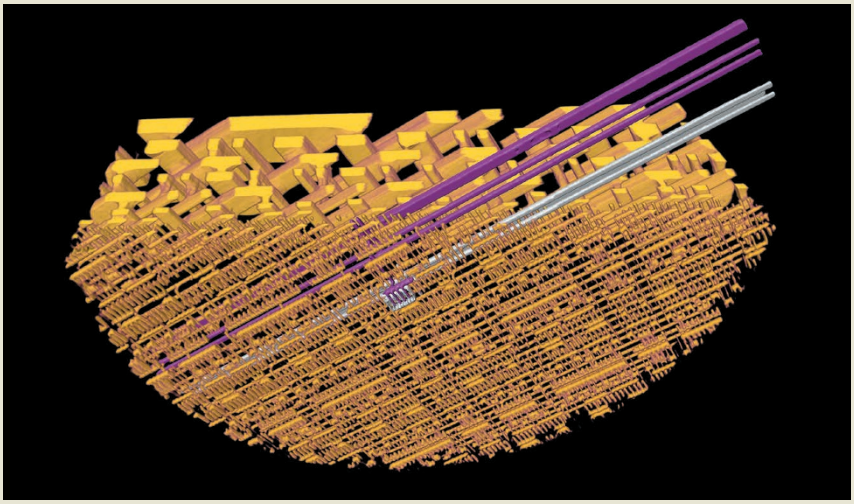
APPLIED PHYSICS

3D imaging for microchips

Semiconductor-based devices called integrated circuits (ICs) are used extensively in modern electronics. However, techniques for producing 3D images of these devices are often inefficient or destructive. In this issue, Holler *et al.* report a method for generating high-resolution images of ICs that overcomes these problems (M. Holler *et al. Nature* **543,** 402–406; 2017).

The authors adapt an imaging technique called X-ray ptychography. First, they scan the IC using a beam of non-destructive X-rays and observe the diffraction pattern produced at each point using high-speed detectors. They then feed these patterns into a computer program that builds a 3D image (pictured).

Holler *et al.* create maps of ICs that have spatial resolutions down to 14.6 nanometres, allowing smaller features to be distinguished than with usual X-ray techniques. Their work will improve IC inspection, with applications from health care to aviation. **Ryan Wilkinson**



MIRKO HOLLER

MOLECULAR BIOLOGY

A hidden competitive advantage of disorder

The cellular response to low oxygen levels is regulated by a process in which one protein is ousted from a binding site by another. It emerges that protein disorder allows the displacement to occur remarkably efficiently. **SEE LETTER P.447**

P. ANDREW CHONG & JULIE D. FORMAN-KAY

Imagine two different ligand molecules, either of which can individually bind to the same site on a protein. Now imagine those ligands competing with each other to bind to a population of the protein molecules: a mixture of two complexes will form, in which either one or the other ligand is bound to the protein. It is generally assumed that the proportions of the complexes in the mixture will be defined by the binding affinities of the ligands for the protein. But on page 447, Berlow *et al.*[1] report an unexpected result that challenges this assumption — a finding that could alter our understanding of the behaviour of protein-interaction networks.

The authors studied hypoxia-inducible factor 1α (HIF-1α), a protein whose production increases when cellular oxygen levels are low. HIF-1α binds the protein CBP, and together they initiate a response to the low oxygen level[2]. This response is tempered by a feedback mechanism[3] in which HIF-1α promotes production of the protein CITED2. CITED2 in turn displaces HIF-1α from the

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