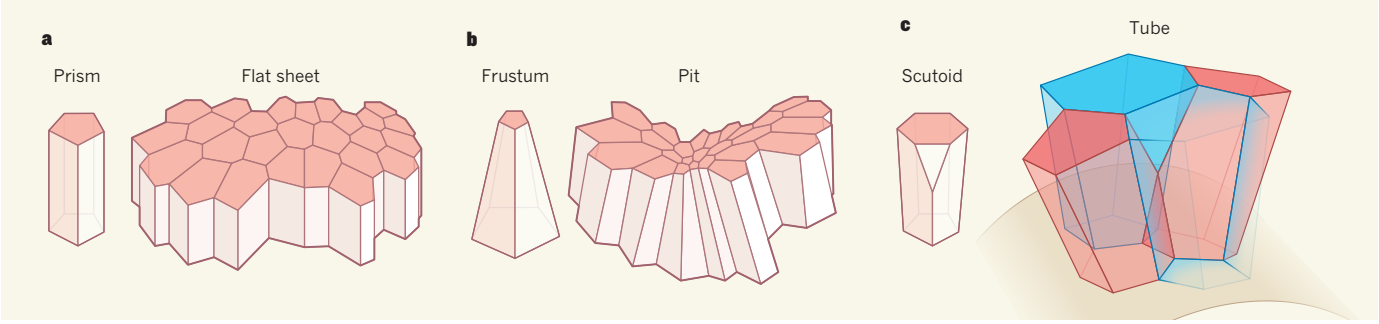

Figure 1 | 3D cell shapes in epithelial sheets. **a**, Sheets of cells called epithelia are most simply composed of prism shapes when flat. **b**, Frusta — prismatoids in which one end is constricted — bend epithelia into pits. **c**, Gómez-Gálvez *et al.*[1] provide evidence that cells can adopt a shape that the authors dub scutoid when epithelia form tubes. Scutoid cells have a triangular face towards one end and have different contacts with neighbouring cells at the inner and outer surfaces of the tube. For example, here the pink cells make contact only towards the inner surface of the tube. (Adapted from Fig. 1 of ref. 1.)

of tubes, they found topological differences between the inner and outer surfaces that required the cells to be scutoid. The authors then confirmed this finding using a mechanical model of the outer surface, in which the lengths of cell–cell interfaces were minimized, encouraging isotropic shapes.

Gómez-Gálvez and colleagues went on to search for scutoids *in vivo*. They found scutoid-shaped cells in snapshots of various embryonic epithelia, although, interestingly, not at the frequency predicted by their modelling. For example, the larval salivary glands of fruit flies have fewer scutoids than are predicted by the curvature of the gland tube. Furthermore, the authors found scutoids in the spherically curved surface layers of zebrafish embryos where none would be predicted.

There are several possible reasons for these discrepancies. First, scutoid predictions will be altered if they take into account other forces, either generated within the epithelium (for example, caused by anisotropic contractility) or acting on it. Second, in the current model, the authors used 2D modelling of the inner and outer surfaces of cells to infer 3D cell shapes — predictions might differ if modelling was extended to cell shapes that are explicitly 3D. However, a better understanding of the mechanics of the shared interfaces on the sides of cells will be needed before cell shapes more complex than prisms and frusta can be modelled accurately in three dimensions[6].

Third, the assumption that apical and basal cell shapes will tend towards isotropy is based on the assumption that the cells' cortex — a contractile, mesh-like network of proteins that gives cells their structure — acts as a ring at the cell–cell junctions at the ends of cells. But the cortex also spans the rest of the exposed apical and basal surfaces, and the contraction of this medial web seems not to tend to isotropic shapes in the same way[3]. Finally, scutoid formation might be highly dynamic in some epithelia, or might involve more-convoluted 3D shapes than those considered here, rendering measurement of scutoid frequency difficult.

Prisms, frusta and scutoids found in single-cell layered epithelia are discrete classes of shape, but belong in a continuum of cell shape and 3D arrangement. This continuum has recently been quantified as an additive combination of cell wedging and interleaving[2,7]. Wedging describes how cell shapes become wider or narrower with depth, whereas interleaving describes changes in how interdigitated a group of cells is with depth, equivalent to a rate of change of cell arrangement from bases to apices. Both wedging and interleaving can be quantified in units of radius of curvature, so are ideal for characterizing curved epithelia. A formal relationship between the degree of interleaving and the frequency of scutoids seems possible, which would make these continuous and discrete measures usefully interchangeable.

With Gómez-Gálvez and colleagues' characterization of the scutoid, we are beginning to recognize the kinds of 3D shapes and arrangements to look for in epithelia, and to develop the tools for quantifying them. Where else in nature should we expect scutoids? I would not bet against scutoids being found in plants, given the diversity of plant architectures. But because plant development is driven by cell growth and division without rearrangement, any mechanism of scutoid formation is likely to be rather different from that seen in animals. Nest comb construction by bees or wasps might also result in scutoids, particularly on curved surfaces, as in the nests of some paper wasps[8]. We shall have to wait and see. ■

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ENVIRONMENTAL SCIENCE

The future of tidal wetlands is in our hands

Computational simulations suggest that future losses of tidal wetlands attributable to sea-level rise could be greatly offset by the landward advance of these ecosystems into newly sea-inundated areas. SEE LETTER P.231

JONATHAN D. WOODRUFF

Coastal communities around the globe depend on tidal marshes and mangroves for the diverse ecological, economic and flood-mitigating services they provide. These relatively flat wetland systems (Fig. 1) commonly reside just above mean sea level, making them one of the ecosystems most at risk of being drowned by rising sea levels. But tidal wetlands will not disappear without a fight. On page 231, Schuerch *et al.*[1] present global-scale modelling that suggests that tidal wetlands are less vulnerable to sea-level rise than was thought. However, the scale of future wetland loss or gain depends greatly on the degree to which coastal communities accept or prevent the landward advances of these living coastal systems into newly inundated areas.

Tidal wetlands are dynamic, living systems

JOHANN SCHUMACHER/GETTY

Figure 1 | Tidal marshes at Jamaica Bay, New York. Schuerch and colleagues' modelling study[1] suggests that coastal management programmes could make a big difference to the future extent of tidal wetlands.

that have the ability to accelerate their growth as the sea level rises, using biophysical feedbacks — complex interactions between plant growth, water flow and sediment trapping. Furthermore, the flooding of low-lying areas by rising seas provides new locations that can accommodate tidal wetlands or allow them to grow. Are these adaptive mechanisms enough to save global wetlands from drowning in the future? Schuerch and colleagues' modelling study was framed to answer exactly this question.

The authors consider not only the adaptation potential of tidal wetlands to future sea-level rise in the vertical direction (upward growth) and horizontally (landward advance), but also the human response to their landward migration. Their modelling work was no small task, requiring the integration of large global data sets of shoreline topography, wetland distributions, concentrations of suspended sediments in wetland waters, tidal ranges (the vertical difference between high and low tides), and projected changes in sea level and coastal populations.

Schuerch *et al.* also incorporated a key feedback into their model to address the fact that the rate at which a wetland grows vertically to keep pace with sea-level rise is dictated not only by the plant matter it can produce, but also by how efficiently it traps sediment. So, in areas that have a sufficient sediment supply and tidal range, the model accounts for the acceleration of wetland growth that is due to the increased amount of sediment carried into and deposited on the wetland over a tidal cycle as sea levels rise.

As noted earlier, tidal wetlands can colonize new low-lying areas as they become flooded by sea-level rise, but little is known about the mechanisms that govern this inland migration. As a first cut, Schuerch and colleagues postulated that all newly inundated areas behind current wetlands and below a certain human population density will be converted to tidal wetlands — the second criterion is relevant because the size and extent of artificial barriers that impede inland wetland migration, such as roads, flood protection and other coastal infrastructure, are assumed to scale with population.

The authors tested what happens when the population threshold above which no wetland is created was set at either 5 or 20 people per square kilometre. These are considered to be the lower and upper bounds, respectively, of the population densities for which wetlands will migrate landward without any action being taken by humans to support or prevent the migration — that is, in 'business as usual' (BAU) scenarios. The authors also tested higher thresholds of 150 and 300 people per square kilometre, which they respectively describe as moderate and extreme nature-based adaptation scenarios, because they would require the replacement of current flood protection and infrastructure with alternatives that would allow wetlands to migrate into more-populated regions.

The authors' results suggest that global tidal wetland loss will be 0–30% by 2100 for the BAU scenarios in which wetlands migrate only into sparsely populated regions. These losses are well below those estimated in past studies[2–4], and highlight the need to consider adaptive feedbacks in future sustainability studies of tidal wetlands. Just as importantly, the nature-based adaptation scenarios suggest that wetland gains as high as 60% could be made when measures are taken that allow wetlands to migrate into more-populated areas.

Some of the findings are not too surprising. The study assumes an overly simple mechanism for inland wetland conversion, for which it is perhaps to be expected that the biggest increase in wetland extent will occur for the greatest sea-level rises under the most extreme nature-based adaptation scenarios. Other parts of the study are particularly interesting, however. For example, when the authors carried out simulations in which the concentration of sediments suspended in tidal wetland waters drops by 50% from present-day values, the extent of wetlands decreases by only 6%. Reductions in sediment supply caused by

damming and other human activities have been a primary concern as contributors to wetland loss[5], but Schuerch and co-workers' results indicate that the degree to which wetlands are allowed to migrate into newly flooded lowland areas could have a much greater impact on wetland sustainability.

One notable caveat to the current findings is that the analysis assumes new wetlands are initiated at a fairly high tidal level. Such super-elevated wetlands will eventually drown if they lack a sufficient sediment supply to sustain them. However, the timescale for this drowning in the simulations was relatively long, and did not occur by 2100, the end of the modelled period.

Schuerch and colleagues' results highlight major gaps in our knowledge of wetland sustainability. Most of the modelled wetland gains were for mangrove systems, which currently represent about 70% of tidal wetlands[1]. However, our understanding of adaptive feedbacks in mangroves is poor compared with our understanding of tidal marshes. Data describing the inland migration of wetlands are also extremely limited, and environmental factors such as pre-existing soil and vegetative conditions could restrict migration to much lower extents than those projected by Schuerch and colleagues. However, the authors' study is a crucial step towards realistic assessments of future wetland changes, and highlights the key roles of both sea-level rise and nature-based adaptation strategies in providing new spaces where lowlands can sustainably accommodate the growth of tidal wetlands. ■

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IMMUNOLOGY

Elusive inflammation insight uncovered

PINK1 and parkin proteins help to degrade damaged mitochondrial organelles, and abnormalities in these proteins are linked to Parkinson's disease. Mouse studies reveal that the proteins act to prevent inflammation. SEE LETTER P.258

ALEXANDRA STOLZ & IVAN DIKIC

Neurodegenerative conditions such as Parkinson's and Alzheimer's diseases constitute a major human-health burden. Although the symptoms, or the cells affected, can differ in such disorders, some neurodegenerative diseases have certain characteristics in common. These include a state of inflammation[1] and impaired elimination of defective mitochondrial organelles[2]. However, it remains to be determined whether such common alterations are interconnected, and whether they are a cause or a consequence of disease. On page 258, Sliter *et al.*[3] report their investigation of mice that have alterations in genes linked to Parkinson's disease. The authors identify a direct connection between the cellular process that eliminates damaged mitochondria — called mitophagy — and inflammation.

The enzymes PINK1 and parkin act in a pathway that attaches a protein called ubiquitin to cellular proteins; such ubiquitin-tagged components are targeted for cellular destruction. These enzymes assist with the process of mitophagy[4], in which non-functional mitochondrial fragments are rapidly sequestered into a membrane-bound vesicle that is degraded when it fuses with an organelle known as a lysosome.

Mutations that prevent the normal expression of PINK1 or parkin are linked to an early-onset form of Parkinson's disease[5], and there is evidence that failure to successfully eliminate damaged mitochondria results in a higher risk of developing the disease[5]. However, mice that are deficient in PINK1 or parkin do not develop symptoms of the type observed in people who have abnormalities in the expression of these proteins; such symptoms include movement problems arising from the loss of neuronal cells that produce the neurotransmitter molecule dopamine[5,6]. Nor do these animals have the high level of inflammation that is a hallmark of Parkinson's disease[5,6].

The finding that the loss of PINK1 or parkin has a minimal effect on animals was surprising, because it was long thought that the removal of damaged mitochondria serves a key role in protecting cells from oxidative damage[5]. Defective mitochondria represent a severe threat to cells because ruptured mitochondria might release reactive oxygen species (ROS) that cause substantial cellular damage[6,7]. For example, ROS might increase the burden of potentially toxic

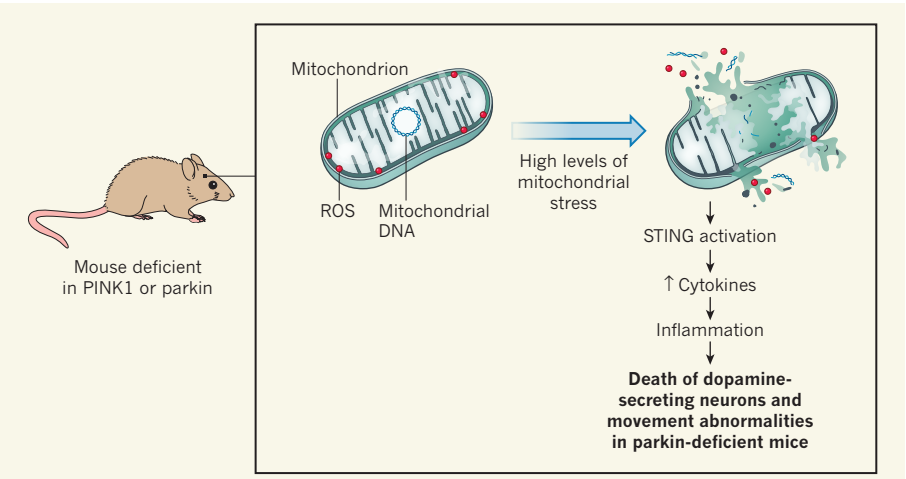

Figure 1 | How the absence of PINK1 or parkin proteins leads to inflammation. Abnormalities in the proteins PINK1 or parkin are linked to early-onset Parkinson's disease in humans[5]. Mice that lack either protein are defective in the process that removes damaged organelles called mitochondria[5,6] in a controlled manner; this process is necessary to prevent organelle rupture and the release of reactive oxygen species (ROS) and mitochondrial DNA into the cytoplasm. However, these animals do not have the types of symptom found in human Parkinson's disease[5,6]. Sliter *et al.*[3] induced high levels of mitochondrial stress in these mice (by use of excessive levels of exercise or by a high level of mitochondrial-DNA mutations) and found that activation of the STING protein — which can mediate inflammation when mitochondrial DNA enters the cytoplasm — increases the expression of inflammation-inducing cytokine molecules. This indicates that PINK1 and parkin protect against inflammation, and might shed light on the inflammation that is commonly observed in people with Parkinson's disease[5,6]. In old mice that lack parkin, STING-mediated inflammation correlates with movement abnormalities and the loss of neuronal cells that secrete the neurotransmitter dopamine[10].