There is therefore a desire to redefine the SI second in terms of an optical-clock frequency and to move away from the current definition based on caesium. But before such a redefinition is possible, scientists must build confidence in the reproducibility of optical clocks through a series of clock comparisons. The target accuracy for these comparisons is at the level of parts in 10^{18} to clearly demonstrate the superiority of optical clocks over caesium clocks[5].

Clock comparisons are carried out by measuring ratios of the optical-clock frequencies using instruments called femtosecond-frequency combs. Until now, the best comparisons between optical clocks based on different atoms[6–11] have been at the level of parts in 10^{17}. The BACON Collaboration presents measurements of optical-frequency ratios reaching uncertainties at the level of parts in 10^{18}, bringing the redefinition of the SI second a step closer.

Such frequency-ratio measurements are no mean feat, and are equivalent to determining the distance from Earth to the Moon to within a few nanometres. Therefore, exceptional care is required to control any sources of frequency offset. The authors compared the aluminium-ion and ytterbium clocks at NIST and the strontium clock at JILA over several months to check reproducibility and reduce statistical uncertainties. They found that the day-to-day variation in the ratios was slightly larger than expected after accounting for all known effects. This observation suggests the existence of unknown effects, which are intrinsically hard to quantify. Nevertheless, the authors developed a statistical model to account for these uncertainties and to enable a rigorous assessment of the total measurement uncertainty.

The BACON Collaboration used redundant elements throughout the network of optical clocks to check for any sources of bias. In particular, the authors linked the clocks at NIST and JILA in two ways (Fig. 1). They used a 3.6-kilometre optical-fibre link — a tried-and-tested method for connecting signals between optical clocks at the required level of uncertainty. And, in what they believe to be a world first, they compared the clocks using a 1.5-km 'free-space' link by sending laser pulses through the air between NIST and JILA along a straight line joining the two institutes. They found that the two types of connection provided a similar level of uncertainty, apart from when data could not be obtained from the free-space link during a snowstorm.

The authors' demonstration that high-accuracy clocks can be connected by free-space links, without needing an optical-fibre infrastructure, is exciting because it opens up possibilities for applications outside the laboratory, such as land surveying[12]. According to Einstein's theory of relativity, Earth's gravity causes the frequency of an atomic clock to depend on its altitude. Consequently, the height difference between two remote clocks can be determined by measuring their difference in frequency. At the level of measurement uncertainty achieved in the latest work, clock comparisons could resolve centimetre-sized height differences. Therefore, clocks could provide new tools for long-term environmental monitoring of, for example, ice sheets or ocean levels.

The BACON Collaboration demonstrated another intriguing application of clock comparisons. The authors used the clock-frequency ratios to search for signs of possible interactions between atoms and dark matter — an elusive substance predicted to account for most of the matter in the Universe. According to current understanding, atoms do not interact with dark matter through electromagnetic forces. However, if these interactions were to exist, they would cause tiny changes in atomic-clock frequencies. The authors detected no such changes in their experiment, but a null result is still useful. Combined with previous data, the finding revealed that the maximum strength of any electromagnetic interactions between atoms and a particular type of dark matter was nearly ten times lower than previously determined.

Networks of optical clocks can also be used to explore many other aspects of physics, because their precision allows measurements of the world around us to be obtained at unprecedented resolution. Examples of such investigations include testing Einstein's theory of relativity at ever more stringent levels[13], and searching for possible changes in the values of physical constants[8]. Regardless of the application — whether in redefining the SI second, surveying or fundamental physics — the better the clock comparisons, the greater the impact. And with the current accuracy limits being set by technical issues, rather than fundamental limits, the prospects for even better measurements in the future are extremely promising.

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1. Boulder Atomic Clock Optical Network (BACON) Collaboration. *Nature* **591**, 564–569 (2021).
2. Brewer, S. M. *et al. Phys. Rev. Lett.* **123**, 033201 (2019).
3. Bothwell, T. *et al. Metrologia* **56**, 065004 (2019).
4. McGrew, W. F. *et al. Nature* **564**, 87–90 (2018).
5. Riehle, F., Gill, P., Arias, F. & Robertsson, L. *Metrologia* **55**, 188–200 (2018).
6. Rosenband, T. *et al. Science* **319**, 1808–1812 (2008).
7. Nemitz, N. *et al. Nature Photon.* **10**, 258–261 (2016).
8. Lange, R. *et al. Phys. Rev. Lett.* **126**, 011102 (2021).
9. Origlia, S. *et al. Phys. Rev. A* **98**, 053443 (2018).
10. Dörscher, S. *et al. Metrologia* **58**, 015005 (2021).
11. Takano, T., Mizushima, R. & Katori, H. *Appl. Phys. Express* **10**, 072801 (2017).
12. Mehlstäubler, T. E., Grosche, G., Lisdat, C., Schmidt, P. O. & Denker, H. *Rep. Prog. Phys.* **81**, 064401 (2018).
13. Delva, P. *et al. Phys. Rev. Lett.* **118**, 221102 (2017).

Cell biology

Mitochondria are mixed during cell division

Till Klecker & Benedikt Westermann

Organelles called mitochondria have essential roles in the cell and must be inherited successfully as it divides. It turns out that three types of interaction with filaments of actin protein mix and partition mitochondria during cell division. **See p.659**

In 1855, the German physician Rudolf Virchow coined the phrase *Omnis cellula e cellula* — all cells come from cells. In other words, cells arise from the growth and division of existing cells. The genetic information stored in chromosomes is passed on to the next generation during cell division in a highly ordered process called mitosis. Biologists have spent many decades deciphering the molecular choreography of this fascinating process, but much less attention has been given to the inheritance of organelles called mitochondria. These are essential for energy metabolism and, because they cannot be generated *de novo*, they must be inherited, too. On page 659, Moore *et al.*[1] describe this process in an unprecedented level of detail.

Two major constituents of the cytoskeleton (a network of proteins that determines cellular architecture) are responsible for cellular dynamics. These are microtubules, structures that serve as tracks for long-distance transport of organelles; and actin filaments, which mediate transport over short distances and enable shape changes at the cell's outer boundary in a region called the cortex. The cytoskeleton is drastically remodelled during cell division. Microtubules build a structure called the

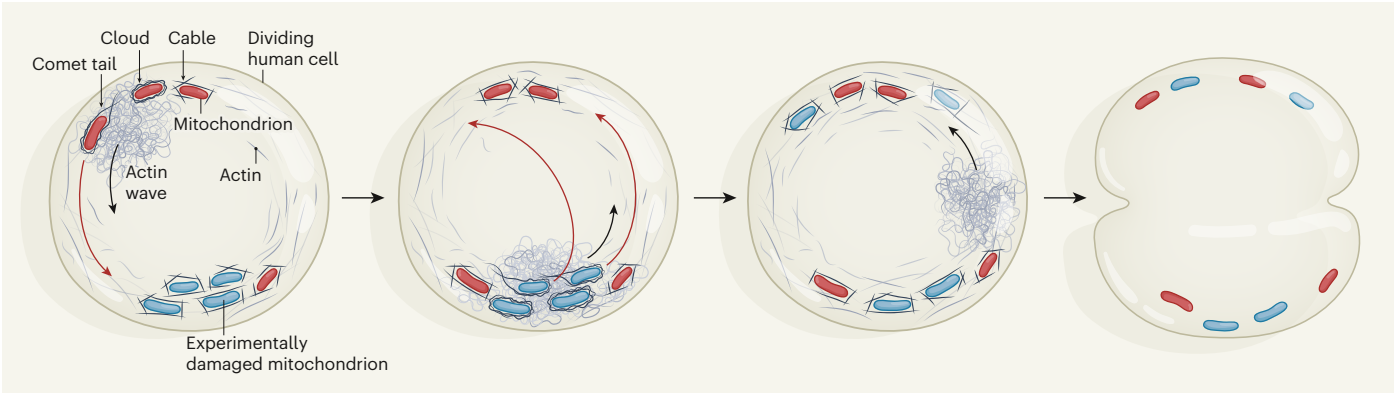

Figure 1 | How mitochondrial organelles are distributed during cell division. Moore *et al.*[1] report three types of interaction with filaments of the protein actin that aid the distribution of mitochondria when human cells divide. Using state-of-the-art microscopy, the authors observed that mitochondria can be tethered to cable structures. It has been reported[4] previously that some actin filaments in dividing cells form waves that revolve around the cell (black arrow) in a manner reminiscent of a radar display. In these waves, the authors observed two types of interaction between actin and mitochondria. Mitochondria were frequently encased in what looked like a cloud of actin filaments, restricting the organelles' mobility. Some mitochondria in the waves instead had comet-tail-like structures made of actin filaments, and these organelles moved rapidly (red arrow) in random directions. The authors tracked the fate of labelled mitochondria that were damaged using an experimental technique. The actin-mediated activities helped to mix and divide the mitochondria between the two daughter cells during cell division, resulting in an even distribution of the damaged organelles.

mitotic spindle that is needed to partition the chromosomes as the cell divides, and, later, actin filaments assemble a contractile ring that promotes cell separation.

Organelles are also extensively remodelled during mitosis. Mitochondria often form extended connected networks in human cells, and these mitochondria fragment into numerous small entities that lose their connection to microtubules during cell division[2,3]. It has long been thought that the partitioning of mitochondria as cells divide is a largely passive process, but this view is currently changing.

About ten years ago, researchers reported a discovery of the actin cytoskeleton in human cells behaving unusually[4]. A cluster of actin filaments was found to appear early during mitosis and then to revolve in cycles through the cytoplasm at a constant angular speed — time-lapse movies of cells with fluorescent filaments revealed circling waves (Fig. 1) that looked like a radar display[4]. Although extremely visually striking, the function of this odd phenomenon had remained a mystery. Moore *et al.* now shed light on this enigma. Using cutting-edge light-microscopy technology, the authors report evidence that these actin waves have a role in mitochondrial partitioning during mitosis of human cells. Like chromosomal partitioning, mitochondrial inheritance depends on dynamic processes orchestrated by the cytoskeleton — yet it turns out that these partitioning events occur in a completely different way.

The authors describe three modes of interaction between mitochondria and actin during mitosis (Fig. 1). Previous work[5] suggested that the myosin motor protein Myo19 dynamically tethers mitochondria to an actin network and maintains the distribution of mitochondria throughout the cytoplasm. First, Moore and colleagues observed this process in greater detail than had been reported previously, and found that it is independent of the presence of actin waves. Second, within a wave, mitochondria are encased by what looks like clouds of actin filaments that seem to immobilize the organelles. And third, sometimes these clouds 'opened', to be followed by an astonishing burst of mitochondrial movement. The organelles were propelled by the rapid growth (polymerization) of actin filaments. This generated what looks like a comet tail made of actin. These mitochondrial movements were rapid, randomly oriented, and covered substantial distances in the cell.

Moore and colleagues' observation of actin comet tails is particularly exciting. Two decades ago, it was suggested that actin polymerization drives mitochondrial motility in yeast cells[6]. However, this model is controversial because the transport of mitochondria into the bud that forms when yeast divides is mediated by a myosin motor protein 'walking' along actin cables[7], and mitochondrial comet tails of actin have not been documented in yeast. Nevertheless, movement that relies on actin dynamics is quite common in animal cells. Such processes contribute to the internalization of vesicles, and actin is hijacked by certain invading microorganisms to enable them to move in the cytoplasm of a host cell.

The authors present stunning images of twin actin tails emanating from the front of mitochondria and extending behind the organelle, similar to the contrails left in the sky by twin-engine aircraft. The comet tails that Moore and colleagues observed were often slightly twisted, and closely resemble the comet tails of actin generated by certain bacteria of the genus *Rickettsia* that infect cells and cause disease[8].

What might be the function of these actin dynamics in mitochondrial inheritance? Mitochondria contain their own genome, which encodes essential proteins required for energy generation through a pathway called the respiratory chain (also known as the electron-transport chain). If there is an accumulation of mitochondria with mutations in the DNA that encodes such components, a cell's energy production would be compromised. Moreover, if a cell inherits a high load of mitochondria with mutated DNA from its mother cell, each subsequent cell division would pass on these energy defects to the progeny cells. Abnormalities could therefore spread to a large part of the tissue and ultimately impair organ function. This possibility suggests why actin dynamics might actively contribute to the distribution of mitochondria being inherited.

Moore *et al.* used what are called optogenetic tools to generate cells with damaged mitochondria. The authors triggered the production of damaging reactive oxygen species in a subset of mitochondria and at the same time specifically labelled these mitochondria. They observed that the dispersion of damaged organelles depends on the presence of cycling actin waves. The authors fed their experimental data into computer models, and the results suggest that the actin waves trigger bursts of movement driven by comet tails that randomly distribute mitochondria during cell division. This activity promotes organelle dispersion, and ensures that the burden of damaged mitochondria is evenly split between the two daughter cells of the mitotic division (Fig. 1).

The authors' discoveries reveal several intriguing aspects worthy of further study. It will be interesting to determine the molecular pathways that regulate actin dynamics on the mitochondrial surface. A previous study[9] reported that revolving actin waves regulate the balance between the division and fusion of

mitochondria during the interphase stage of the cell cycle, which precedes mitosis. It will be important to discover whether mitochondrial movement, interconnectivity and dispersion are processes that mutually affect each other.

Certain types of cell divide asymmetrically and generate daughter cells with different fates. During the division of a stem cell, the older mitochondria in the dividing cell are preferentially partitioned to the daughter cell that is destined to differentiate, whereas the younger and 'fitter' mitochondria are apportioned to the daughter cell that maintains stem-cell properties[10]. One can predict, therefore, that mitochondria mixing is suppressed in these cells and that other, as yet unknown, mechanisms ensure the asymmetric inheritance of mitochondria. Clearly, mitochondrial research will yield many more surprises in the future.

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1. Moore, A. S. *et al. Nature* **591**, 659–664 (2021).
2. Taguchi, N., Ishihara, N., Jofuku, A., Oka, T. & Mihara, K. *J. Biol. Chem.* **282**, 11521–11529 (2007).
3. Chung, J. Y., Steen, J. A. & Schwarz, T. L. *Cell Rep.* **16**, 2142–2155 (2016).
4. Mitsushima, M. *et al. J. Cell Biol.* **191**, 453–462 (2010).
5. Rohn, J. L. *et al. Curr. Biol.* **24**, 2598–2605 (2014).
6. Boldogh, I. R. *et al. Proc. Natl Acad. Sci. USA* **98**, 3162–3167 (2001).
7. Förtsch, J., Hummel, E., Krist, M. & Westermann, B. *J. Cell Biol.* **194**, 473–488 (2011).
8. Van Kirk, L. S., Hayes, S. F. & Heinzen, R. A. *Infect. Immun.* **68**, 4706–4713 (2000).
9. Moore, A. S., Wong, Y. C., Simpson, C. L. & Holzbaur, E. L. *Nature Commun.* **7**, 12886, (2016).
10. Katajisto, P. *et al. Science* **348**, 340–343 (2015).

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Genomics

Sowing the seeds of multi-genome rice

Diane R. Wang

Having more than two sets of chromosomes can help plants to adapt and evolve, but generating new crops with this type of genome is challenging. A road map for doing just that has now been developed using wild rice.

We all sometimes wish we could do more than one thing at once – run errands, catch up on work deadlines and perhaps grab that long-overdue coffee with a friend. A genetic state known as polyploidy helps some plant genomes to do just this. Most plants, like humans, are diploid, with two sets of every chromosome. But polyploid plants have four, six or even eight sets of chromosomes. These additions allow different copies of a gene to take on different roles, and provide a buffer against potentially harmful mutations. Accordingly, polyploidy has served as a common mode of evolution in flowering plants[1]. Writing in *Cell*, Yu *et al.*[2] outline a viable approach to producing a domesticated form of polyploid rice using gene editing. Their advance could allow us to reap the benefits of polyploidy in one of the world's most important crop species.

All crop species evolved from wild ancestors, as humans saved and propagated plants that had favourable attributes – loss of seed-dispersal mechanisms, for instance, and larger seeds and fruits[3] – over hundreds or thousands of years. The world's main rice crop, the Asian species *Oryza sativa*, was domesticated about 9,000 years ago from its wild progenitor, *Oryza rufipogon*, through processes thought to have occurred across multiple regions in Asia[4,5]. Both species are diploid, carrying two sets of 12 chromosomes.

For rice scientists, the idea of developing polyploid cultivated rice is tantalizing as a potential means for future crop improvement, especially in the face of climate variability[6]. The plant's extra gene copies might enable rapid adaptation in response to major changes in the environment without the loss of favourable features[7]. But generating a polyploid rice from a cultivated diploid plant is hugely technically challenging. With that in mind, Yu *et al.* took an entirely different approach. The authors started with a distant, wild polyploid cousin of *O. sativa* and *O. rufipogon*, and domesticated it using biotechnological approaches (Fig. 1).

The authors first spent time identifying an appropriate starting strain. The ideal candidate needed to be amenable to callus induction and regeneration – a process in which plant tissues are cultured to produce a mass of partially undifferentiated cells called a callus, from which new plants are generated. These properties are essential for gene-editing techniques. The selected individual also needed to have high biomass and tolerance to various abiotic and biotic stresses – heat and insect resistance, for example. After screening 28 polyploid wild rice lines, a strain of *Oryza alta* was selected, and named polyploid rice 1 (PPR1).

Oryza alta has four sets of chromosomes (it is tetraploid), and is found in Central and South America[8]. The species arose as a result of hybridization between two ancestors that had diploid genomes, designated C and D. The PPR1 strain selected by Yu *et al.* looks quite different from cultivated *O. sativa*. For instance, it is very tall – more than 2.7 metres, compared with 1 metre or less for typical *O. sativa*. It produces abundant biomass, and has broad leaves and sparse, small seeds adorned with awns (spiky protrusions thought to aid seed dissemination). As such,

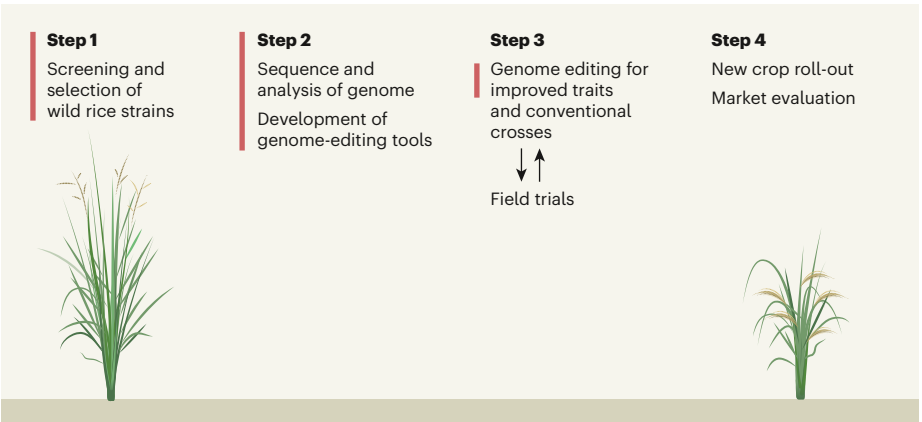

Figure 1 | A fast track to cultivated polyploid rice. Yu *et al.*[2] have developed a strategy for rapid domestication of wild polyploid rice (which has more than two sets of chromosomes, unlike the rice commonly grown as a food crop). The first step is to select a wild strain that has favourable characteristics for gene editing and crop production. This is followed by genomic analysis and method optimization. Iterative cycles of genome editing, conventional crossing and testing are then needed before the new crop is rolled out to farmers and evaluated. Red highlights indicate sections of the road map completed by the authors for the wild rice *Oryza alta*.