division.

Cells lacking CIP2A or TOPBP1, or that are deficient in the interaction between CIP2A and TOPBP1, are unable to cluster shattered chromosomes, leading to the dispersion of chromosomal fragments into the nuclei and cytoplasm of daughter cells. The presence of these fragments triggers a defence response (involving signalling pathways of innate immunity) after DNA is sensed in the cytoplasm.

Furthermore, both teams showed that this CIP2A–TOPBP1 complex not only accumulates on chromosome fragments but also acts specifically during mitosis, consistent with its having a tethering function at this stage of the cell cycle. Both studies also demonstrate that the loss of CIP2A-dependent chromosome tethering reduces the viability of micronucleus-bearing cells, possibly owing to the loss of genes essential for the cell's viability. Indeed, Lin *et al.* found that CIP2A-dependent clustering prevents loss of genetic material after chromosome pulverization, and Trivedi *et al.* carried out whole-genome sequencing and report that transient depletion of CIP2A results in a higher number of types of genetic alteration (deletions and inversions).

The typical chromothripsis seen in most cancer genomes is characterized by variations in the number of copies of DNA sequences (copy number)[1] arising from the loss of DNA fragments. However, the existence of a mitotic chromosome-end-tethering system suggests that this copy-number oscillation might not be a necessary outcome of chromosome shattering. Indeed, Lin *et al.* reanalysed cancer-genome sequencing data and found that they could detect a type of chromothripsis that they called balanced chromothripsis. This displays chromosomal rearrangement but without an oscillation in copy number that is typical of chromothriptic chromosomes.

Although the results of both studies are remarkably consistent, they differ in some details. Perhaps the most notable divergence pertains to the conclusion about the role in chromosome-fragment clustering of a protein named MDC1. Trivedi *et al.* conclude that MDC1 has a key role upstream of CIP2A–TOPBP1 in promoting shattered chromosome tethering, whereas Lin *et al.* observed only a minor contribution from MDC1. CIP2A–TOPBP1 has two modes of recruitment to mitotic DNA damage[8,9]: an MDC1-dependent mode that responds to chromosome breaks, and an MDC1-independent mode associated with defective DNA replication. Therefore, understanding how CIP2A–TOPBP1 associates with shattered chromosomes might help to reveal the origins of chromosome shattering, or to identify the elusive factor that recruits CIP2A–TOPBP1 to mitotic chromosomal DNA that has not replicated normally.

The results from Trivedi *et al.* and Lin *et al.* suggest that chromothripsis might be profoundly altered in the absence of CIP2A–TOPBP1-dependent clustering of shattered chromosomes, but this remains to be confirmed. Nevertheless, the identification that CIP2A–TOPBP1 acts as a mitotic chromosome tether is sure to unleash a flurry of further investigations. First and foremost on the to-do list is defining the biochemical basis of chromosome tethering by CIP2A–TOPBP1, which remains, for now, a complete mystery. The poor viability of micronucleus-bearing cells on CIP2A depletion, and the activation of innate-immune signalling caused by chromosome-fragment dispersion, suggest that it might be worth testing whether inhibition of CIP2A–TOPBP1 offers an attractive strategy for the treatment of some cancers, or a way of limiting chromothripsis-driven tumour evolution.

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1. Leibowitz, M. L., Zhang, C. Z. & Pellman, D. *Annu. Rev. Genet.* **49**, 183–211 (2015).
2. Lin, Y.-F. *et al. Nature* **618**, 1041–1048 (2023).
3. Trivedi, P. *et al. Nature* **618**, 1049–1056 (2023).
4. Carlson, J. G. *Proc. Natl Acad. Sci. USA* **24**, 500–507 (1938).
5. Warecki, B. & Sullivan, W. *Chromosome Res.* **28**, 229–246 (2020).
6. Orthwein, A. *et al. Science* **344**, 189–193 (2014).
7. Zirkle, R. E. & Bloom, W. *Science* **117**, 487–493 (1953).
8. Adam, S. *et al. Nature Cancer* **2**, 1357–1371 (2021).
9. De Marco Zompit, M. *et al. Nature Commun.* **13**, 4143 (2022).

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Condensed-matter physics

Widespread waves spark superconductor search

Hui Chen & Hong-Jun Gao

Periodic waves of changing electron density are linked to the ability of some materials to conduct electricity without resistance. Four studies reveal that such waves could emerge in more materials than expected. **See p.921, p.928, p.934 & p.940**

Superconductors are materials that exhibit zero electrical resistance when cooled to temperatures of just a few kelvin. But harnessing this remarkable property for practical applications — in energy transmission and electronics, for example — requires materials that superconduct at higher temperatures. And to induce such behaviour, it must first be understood. A particular class of high-temperature superconductor has shown an intriguing phenomenon that involves a periodic modulation of electron density, known as a pair density wave[1]. Now, writing in *Nature*, four research groups[2–5] report that pair density waves are actually more prevalent than was previously thought, with evidence for these waves in three separate materials.

Electrons in superconductors form what are known as Cooper pairs, which were first thought to move together with zero momentum and condense into a state that allows them to traverse the material without electrical resistance[6]. However, around 60 years ago, two teams of physicists independently predicted that strong magnetic fields could be applied to give these pairs non-zero momentum and make them oscillate spatially as they moved through the material[7,8]. This prediction was confirmed experimentally[9], and subsequent work[10–12] suggested that such oscillations could occur even in the absence of a magnetic field in systems that are characterized by strong interactions between electrons. These oscillations are referred to as pair density waves — but observing them is not a trivial task.

A powerful tool in the search for pair density waves is known as scanning tunnelling microscopy (STM) — a technique that visualizes the quantum states in a material with atomic resolution. There are different ways of looking for pair density waves using STM. One approach involves searching for signatures of superconductivity at low temperatures, and simultaneously observing another phase known as a charge density wave, in which the concentration of electric charge varies periodically through a material. This is because pair density waves are expected to transition into a charge-density-wave phase, which can persist at high temperatures. Another approach is to detect a periodic variation in the 'superconducting gap', which is a gap in the allowed energies of electrons in a material that directly relates to the density of Cooper pairs.

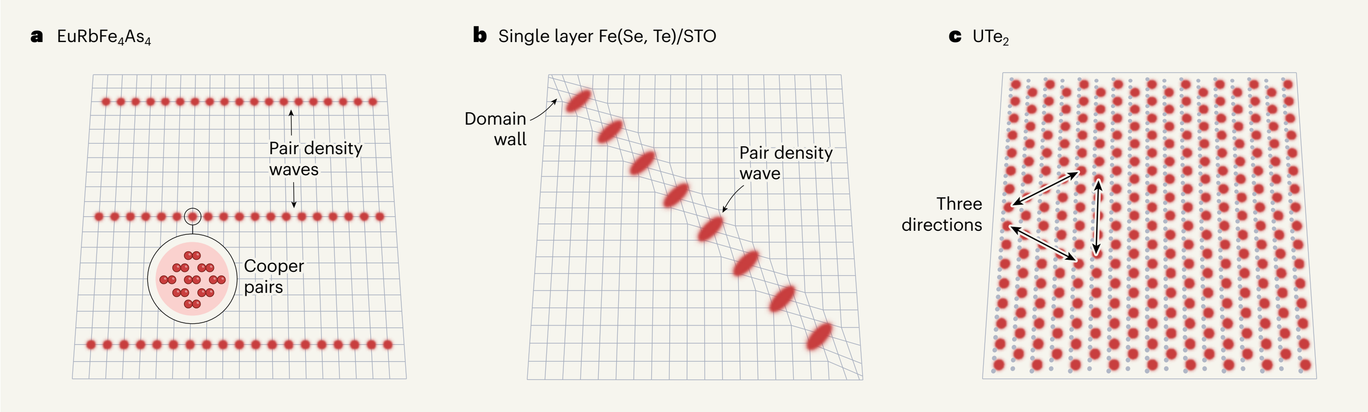

Figure 1 | Pair density waves in various superconductors. The electrons in superconductors (materials that display zero electrical resistance when cooled) form pairs called Cooper pairs. Strong interactions between electrons can make these pairs undergo oscillations, known as pair density waves, that are associated with the properties of certain high-temperature superconductors[1]. Four research groups have shown that these waves arise in various superconducting materials. **a**, Zhao *et al.*[2] observed a stripe-like pattern of pair density waves in a material containing europium (Eu), rubidium (Rb), iron (Fe) and arsenic (As). **b**, Liu *et al.*[3] found a pair density wave in a single layer of a film of iron and either selenium or tellurium (Fe(Se, Te)), grown on strontium titanate (STO). The pair density wave was localized at the boundaries between different types of crystal lattice. **c**, Aishwarya *et al.*[4] and Gu *et al.*[5] both studied the superconductor uranium ditelluride (UTe_2), which exhibits a complex pair density wave that propagates in three directions.

STM experiments have already detected pair density waves in cuprates, materials with layers that comprise of copper oxide[13]. They have also been used to observe the waves in kagome compounds (in which atoms lie on a crystal lattice formed by a pattern of overlapping triangles)[14] and in atomically thin chalcogenide materials (which contain elements such as selenium and tellurium)[15]. But it has been unclear whether pair density waves are prevalent in most superconducting materials or just these specific few. However, theory suggests that they should exist in others[1], so researchers continue to use STM to search for pair density waves in other superconductors.

One promising candidate for hosting pair density waves is a class of superconductor made from iron-containing compounds[16]. These materials are similar to cuprates, in that they exhibit various electronic states, including nematic (liquid crystalline) order and stripe-like patterns of a certain type of magnetic order. On the basis of this similarity, Zhao *et al.*[2] investigated the iron-based superconductor $EuRbFe_4As_4$, which contains europium (Eu), rubidium (Rb) and arsenic (As). This material becomes superconducting when cooled to temperatures of around 37 kelvin, and also exhibits magnetism. The authors detected pair-density-wave order in this material, manifesting as a stripe pattern that repeated after every eight unit cells (the smallest repeating units) of the crystal lattice formed by the Rb atoms (Fig. 1a).

Iron-based superconductors are layered materials, and some superconduct at higher temperatures when they exist as single layers than they do when they are multilayered – an increase that could be a result of interface effects. Liu *et al.*[3] investigated a pair density wave that arises in a single layer of a film containing iron and either selenium or tellurium, when it is grown on strontium titanate. Pair density waves were previously observed in large areas on the surface of cuprates[13]. By contrast, Liu and colleagues' pair density wave was localized at the boundaries between different types of crystal lattice (Fig. 1b). This film therefore provides a 2D platform for studying the interplay between states that arise through interactions between electrons, as well as unconventional Cooper pairing in high-temperature superconductors.

Aishwarya *et al.*[4] investigated uranium ditelluride. Researchers in the group had previously used STM to show a special type of superconductivity known as chiral superconductivity in this material[17]. Building on this discovery, the authors unveiled an unusual kind of charge-density-wave order, which propagates in three directions, is closely associated with superconductivity and is sensitive to magnetic fields. Because charge density waves are not expected to interact strongly with external magnetic fields, the researchers propose that the observed wave might be related to an underlying pair density wave in uranium ditelluride.

Motivated by Aishwarya and colleagues' discovery, Gu *et al.*[5] explored the possibility of finding this pair density wave. They used an advanced experimental STM technique involving a microscope equipped with a superconducting tip, which offers high precision that has previously proved effective in detecting pair density waves in cuprates[13]. Their study identified the presence of three pair density waves along the same directions as those of Aishwarya and co-workers' charge density wave (Fig. 1c). Gu *et al.* hypothesized that the observed pair density waves are analogous to those detected in superfluid helium, which behaves as though it has zero viscosity.

These investigations represent a crucial step forward in the study of pair density waves, but they also raise several questions. On a technical level, the observations relied heavily on atomically resolved imaging techniques at ultra-low temperatures. However, this method provides information only about the structure and charge distribution of a material, making it challenging to distinguish pair density waves from other types of density wave. Hence, techniques other than STM are crucial for further exploration of the pair density waves in superconductors.

The results of these investigations have already inspired the search for pair density waves in other platforms in which superconductivity arises through unconventional mechanisms. For instance, high-temperature superconductors containing nickel exhibit similar phenomena to cuprates, suggesting the existence of pair density waves in them. Organic superconductors are similarly worth investigating, because the Cooper pairs that they exhibit are formed through a mechanism that differs from that seen in other superconductors.

Finally, it's worth noting that the experimental study of pair density waves is still in its early stages. Signatures of such waves have been observed in various superconductors, but the ordered states that emerge from these waves, and the way that they interact with other states in superconductors, remain largely unexplored. Developing an effective theoretical description of pair density waves has also proved challenging, and further work is needed in this direction. The studies presented here provide ample motivation for this endeavour, and reveal the diverse systems in which these fascinating waves can emerge.

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From the archive

The use of symbols in chemistry, and excitement at an aquarium over an octopus baby boom.

100 years ago

Symbols are both an aid and an obstacle to thought ... There is always the danger ... faced by the student of chemical science, for without symbols systematic advance is impossible: the symbols are based on a theory and permit the representation of that theory in detail ... The first symbols ... for the metals known to the ancients, indicated ... their supposed association with the planets and the gods ruling them. Thus the solar disk stood for gold, the lunar crescent for silver ... and so on. Towards the end of the eighteenth century we see the beginnings of our present system of elementary symbols ... [A] system ... of formulation in use at the present time for the representation of elements and the composition of compounds ... is never likely to be superseded ... [W]hether the symbols we use are simple or complicated, we should always be clear as to their true significance, and be on our guard against their distracting our thoughts from the realities which they partly reveal and partly obscure.

From *Nature* 30 June 1923

150 years ago

The fine specimen of the Octopus brought to the Brighton Aquarium from the French Coast ... and suspected at the time ... to be a female, has just verified this anticipation by depositing numerous eggs ... within a few inches of the front glass of its tank; thus affording every facility ... to watch their progress towards maturity from day to day. The eggs were deposited on Thursday last ... since which time the parent has vigilantly guarded them, usually encircling and partly concealing the whole within a coil of one or more of her snake-like arms ... The mate of the interesting parent is a fine fellow brought from the Cornish Coast last February. On the arrival of his fair companion he immediately vacated his oyster grotto in her favour and for many subsequent days lavished upon her the most assiduous attention.

From *Nature* 26 June 1873

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1. Agterberg, D. F. *et al. Annu. Rev. Condens. Matter Phys.* **11**, 231–270 (2020).
2. Zhao, H. *et al. Nature* **618**, 940–945 (2023).
3. Liu, Y. *et al. Nature* **618**, 934–939 (2023).
4. Aishwarya, A. *et al. Nature* **618**, 928–933 (2023).
5. Gu, Q. *et al. Nature* **618**, 921–927 (2023).
6. Bardeen, J., Cooper, L. N. & Schrieffer, J. R. *Phys. Rev.* **108**, 1175 (1957).
7. Fulde, P. & Ferrell, R. A. *Phys. Rev.* **135**, A550 (1964).
8. Larkin, A. I. & Ovchinnikov, Y. N. *Sov. Phys. JETP* **20**, 762–770 (1965).
9. Singleton, J. *et al. J. Phys. Condens. Matter* **12**, L641 (2000).
10. Himeda, A., Kato, T. & Ogata, M. *Phys. Rev. Lett.* **88**, 117001 (2002).
11. Agterberg, D. F. & Tsunetsugu, H. *Nature Phys.* **4**, 639–642 (2008).
12. Lee, P. A. *Phys. Rev.* **4**, 031017 (2014).
13. Du, Z. *et al. Nature* **580**, 65–70 (2020).
14. Chen, H. *et al. Nature* **599**, 222–228 (2021).
15. Liu, X., Chong, Y. X., Sharma, R. & Davis, J. C. S. *Science* **372**, 1447–1452 (2021).
16. Paglione, J. & Greene, R. L. *Nature Phys.* **6**, 645–658 (2010).
17. Jiao, L. *et al. Nature* **579**, 523–527 (2020).

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Cell death

The role of NINJ1 protein in programmed destruction

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The protein NINJ1 drives membrane rupture associated with certain types of cell death. Investigation of NINJ1 reveals mechanistic details of how it functions, raising the possibility of developing new therapeutics. **See p.1065 & p.1072**

Programmed cell death (PCD) is a central process for the removal of damaged or unwanted cells in the context of cancer and development. It also has a key role in the normal functioning of the immune system[1]. In the realm of immune-system defences, PCD can rob a bacterium or virus of its host-cell home and thereby halt the spread of infection[1]. The control of death is so important in life that at least three complex pathways for PCD – termed apoptosis, pyroptosis and necroptosis – have evolved[1]. Writing in *Nature*, Degen *et al.* (page 1065)[2] and Kayagaki *et al.* (page 1072)[3] shed light on how the protein NINJ1 functions in the final stages of certain types of PCD.

PCD and the mechanisms behind genetically encoded death have long fascinated biologists. The most-studied form of PCD, originally observed and reported by Karl Vogt in 1842 and now termed apoptosis, generally ends 'quietly' with the dying cell shrivelling up and fragmenting before being ingested by macrophage cells, which handle such garbage disposal. By contrast, both pyroptosis and necroptosis end with a bang – the plasma membrane that surrounds the cell and is crucial for cellular integrity ruptures and the cell contents leak out[4]. In certain circumstances, apoptotic cells can progress to a secondary phase (called secondary necrosis of apoptosis), in which the dying cells develop 'bubble-like' structures and the plasma membrane eventually ruptures[1].

If cells rupture in this fashion and their cytoplasmic contents spill out, proteins such as lactate dehydrogenase (LDH) and large pro-inflammatory molecules, termed damage-associated molecular patterns (DAMPs), which are normally contained in the cellular cytoplasm, escape from the cell (Fig. 1). The presence of DAMPs outside cells indicates to the immune system that all is not well, and a sustained and sometimes extremely intense inflammatory response develops to counter the threat[1,4]. Pyroptosis, necroptosis and plasma-membrane rupture in apoptosis can all be triggered in response to infection by viruses or bacteria, and all underlie tissue damage in many chronic conditions, including cancers and neurodegenerative diseases[1,4].

Central to pyroptosis is the pore-forming protein GSDMD (refs 5, 6). This normally exists in soluble form in the cytoplasm, but when activated during pyroptosis, it assembles to form pores in the plasma membrane. These pores are quite small (around 21 nanometres in diameter) – large enough to let pro-inflammatory molecules escape the dying cell but too small to permit the release of large DAMPs and LDH. For a long time, GSDMD pores were thought to promote a passive process of cell rupture through the non-selective flux of ions and the induction of osmotic stress. However, this view was overturned by a study[7] demonstrating that plasma-membrane rupture and the release of LDH and DAMPs in pyroptosis require NINJ1. As that study and the work by Kayagaki *et al.* show, NINJ1 is also needed for plasma-membrane rupture in