Condensed-matter physics

Electron crystals come under the microscope

Carmen Rubio-Verdú

In 2D materials, electrons at low densities can freeze into well-defined positions and form exotic structures called Wigner crystals. A non-invasive technique has been developed to image these crystals directly. See p.650

In 1934, the physicist Eugene Wigner predicted that electrons could form crystals[1]. Evidence of such Wigner crystals has been seen in liquid helium-4 (refs 2,3), in 2D electron gases under strong magnetic fields[4,5] and in 2D semiconductors[6–8]. However, these crystals have been difficult to observe directly because they are fragile and can be altered by any small perturbation. On page 650, Li *et al.*[9] report the direct imaging of Wigner crystals in a 2D material.

Consider an electron moving through a metallic wire. It passes from one end of the wire to the other without being strongly affected by other electrons, and, thanks to this fact, we have electricity at home. Wigner crystals are states of matter in which electrons, instead of acting as freely flowing, independent units, interact with each other to form an ordered lattice. These crystals are collective phases — similar to those associated with magnetism or superconductivity — and their properties have fascinated physicists for decades.

A system of electrons in a material has two sources of energy: its kinetic energy is associated with the motion of each particle, and its potential energy is related to the repulsion between the particles. When the system has many electrons (which are therefore close to each other), the kinetic energy is dominant, because the motion of one particle causes nearby particles to move owing to repulsion. In this case, the system is said to be in a liquid phase. By contrast, when the system contains only a few electrons (which are thus, on average, far away from each other), the particles move more slowly and tend to localize. This process reduces the potential energy of the system and builds a Wigner crystal.

Li and colleagues used a combination of scanning tunnelling microscopy and spectroscopy to show that a particular 2D material can host Wigner crystals. This material comprises a monolayer of tungsten disulfide stacked above a monolayer of tungsten diselenide, forming a single object known as a heterostructure. These monolayers are transition-metal dichalcogenides — semiconductors less than one nanometre thick. The two monolayers are very similar, but the lattice spacing is slightly smaller in the tungsten disulfide monolayer than in the tungsten diselenide one.

This mismatch between the two atomic lattices produces an interference effect called a moiré pattern. Similar patterns can emerge in a wrinkled mesh shirt, or in a photograph of a television screen. The moiré pattern formed by mismatched lattices increases the effective mass of electrons, which in turn reduces their average kinetic energy. Wigner crystal phases therefore form more easily in moiré systems than in 'normal' materials.

In scanning tunnelling microscopy, an extremely sharp metallic tip is scanned across a sample. The main idea is that, by measuring the electric current that results from the 'tunnelling' of electrons between the tip and the sample under an applied voltage, one can extract the density of states — a quantity related to the material's electronic properties. However, measuring this tunnelling current requires a metallic contact on the sample, which has proved challenging for transition-metal dichalcogenides at low temperatures.

To avoid this issue, Li and colleagues placed their heterostructure under a layer of graphene (a single sheet of carbon atoms), and measured the tunnelling current on the graphene rather than on the heterostructure (Fig. 1a). A layer of an electrical insulator (hexagonal boron nitride) was also included to isolate the graphene from the tungsten disulfide. This set-up protected the heterostructure from external perturbations produced by the microscope tip. The local current between the tip and the graphene depends on the electron distribution in the 2D material, allowing Wigner crystals to be directly imaged.

Next, Li *et al.* used a process called electrostatic doping to add or remove electrons in the heterostructure. They found that the electrons arranged themselves differently in the moiré pattern depending on how many particles were injected or withdrawn. In particular, when one electron was introduced for every three unit cells (repeating units) of the moiré pattern, the density of states corresponded to a triangular electron lattice (Fig. 1b). By

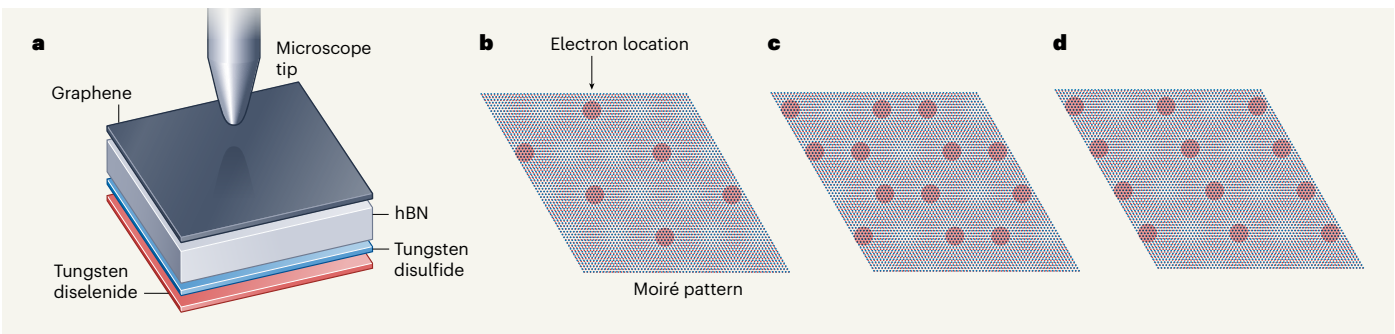

Figure 1 | Electron crystals in a 2D material. a, Li *et al.*[9] considered a 2D material comprising stacked monolayers of tungsten disulfide and tungsten diselenide. They placed a sheet of carbon atoms, known as graphene, above this 2D material, and scanned the surface of the graphene using the tip of a scanning tunnelling microscope. A layer of hexagonal boron nitride (hBN), an electrical insulator, separates the graphene from the tungsten disulfide. This technique allowed the authors to carefully probe the distribution of electrons in the 2D material. **b**, The stacked atomic lattices of tungsten disulfide and tungsten diselenide produced an interference effect called a moiré pattern. When one electron was added to the 2D material for every three unit cells (repeating units) of the pattern, the electrons formed a triangular lattice. **c**, When two electrons were introduced for every three moiré unit cells, the electrons arranged themselves into a hexagonal lattice. **d**, Finally, when one electron was added for every two unit cells, the electrons formed unidirectional stripes.

contrast, when two electrons were added for every three moiré unit cells, the density of states described a hexagonal lattice (Fig. 1c). Both of these arrangements maximize the distance between the electrons and minimize the potential energy of the system.

Although Li and colleagues' work is remarkable, it raises some questions that will surely drive further experiments and theoretical studies. For instance, the authors found that when one electron was introduced for every two moiré unit cells, the density of states corresponded to unidirectional stripes that do not follow the moiré triangular structure (Fig. 1d). Future work should provide a more complete picture of this particular Wigner-crystal state.

The importance of this study goes beyond the direct observation of Wigner crystals. The work opens a path for studying fragile states of matter that might be obscured by a probe — in this case, a microscope tip. The authors' technique allows quantum phases to be imaged that were previously unobservable.

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Cancer

Insights into the origins of pancreatic cancer

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The initial events that give rise to pancreatic cancer are not fully understood. Evidence from mice now implicates the enzyme Tert in setting the stage for the formation of this type of tumour. **See p.715**

The pancreas secretes enzymes that are required for the digestion of food in the intestine. Two main pancreatic cell types are involved in this — acinar cells, which secrete these enzymes, and ductal cells, which line channels to the intestine. The most common type of pancreatic cancer arises in a form that recapitulates such pancreatic ducts, both in its gland-like structure and in its pattern of protein expression. Yet, despite this similarity, substantial uncertainty remains regarding the cell type (cell of origin) that gives rise to pancreatic cancer.

Most genetically engineered mouse models of pancreatic cancer express cancer-promoting genes in cells of the acinar lineage, suggesting that, at least in mice, acinar cells can be the cell of origin[1]. However, whether all acinar cells are equally capable of generating pancreatic cancers, or whether certain prerequisites must also be met in a subpopulation of these cells for cancer to develop, has not been rigorously examined. On page 715, Neuhöfer *et al.*[2] provide key insights relevant to this long-standing question.

Working in mice, the authors focused on a particular subset of acinar cells — those expressing the enzyme telomerase reverse transcriptase (Tert). This enzyme enables dividing cells to maintain the lengths of structures at their chromosome ends called telomeres by facilitating the reaction that adds nucleotides to these chromosomal tips. The shortening of telomeres results in the activation of Tert to maintain telomere length and thereby avoid catastrophic genomic damage. Technical challenges have previously limited the options available to visualize the expression of Tert in cells, so Neuhöfer and colleagues used genetically engineered mice in which cells that express Tert are labelled by the expression of a fluorescent protein. This system allowed the authors to determine the prevalence of Tert expression in different populations of cells in the pancreas, and to assess the cellular lineages arising from Tert-expressing cells.

Neuhöfer and colleagues discovered that acinar and not ductal cells expressed Tert (Fig. 1). The authors also generated mice with acinar cells that were randomly labelled irrespective of their Tert-expression status. Only the Tert-expressing acinar cells formed 'expanded clones' — groups of cells arising from single parental cells. This was true both with increasing age and acutely, in response to injury in the form of chemically induced pancreatic inflammation.

To determine the role of these Tert-expressing acinar cells in initiating pancreatic cancer, the authors used a version of their mouse model in which a mutation in the gene *Kras* that is associated with the formation of pancreatic cancer[3] was restricted to the Tert-expressing acinar cells. Neuhöfer *et al.* found that the *Kras* mutation accelerates the growth of clones of acinar cells expressing Tert, compared with the growth of acinar cells that were randomly labelled irrespective of their Tert-expression status.

In addition, compared with mice that had mutant *Kras* in random cells, mice in which mutant *Kras* was restricted to Tert-expressing cells had a greater number of precancerous growths. Both the expanded clones (in which cells are normally shaped) and precancers (in which cells have shape changes indicative of progression towards cancer) in these mice had signs of activation of the MAPK pathway, one pathway known to act downstream of cancer-associated *Kras* mutations to promote cancer growth.

The authors tested whether their findings might have relevance for human cancer by examining samples of human pancreas removed during surgery to treat cancer or other types of pancreatic disease. This revealed clusters of acinar cells with signs of MAPK-pathway activation in around half of the samples analysed. Intriguingly, a subset of these MAPK-activated acinar cell clusters also contained mutations in the *KRAS* gene. The authors suggest that the Tert-expressing acinar cell clones in mice represent an 'abnormal field' for the accumulation of extra cancer-promoting changes, such as genetic alterations, or modifications (termed epigenetic changes) to the DNA–protein complex in the nucleus. Such an accumulation of alterations on this abnormal field eventually results in the development of precancers.

The study of the earliest steps in the formation of pancreatic tumours is exceedingly challenging in humans, because normal tissue is largely unavailable for research and it is not ethically justifiable to repeatedly sample the same non-cancerous pancreas over time. Mouse models are a useful tool to assess cellular and molecular events during the initiation of pancreatic tumours, and the integration of findings made in such animal models with those from the analysis of human samples is crucial to ensuring that the results are of clinical relevance.

A notable advance in the mouse system used by the authors is its capacity to activate a mutant form of *Kras* in specific small