

a year later, the authors documented three additional *csd* alleles. Gloag *et al.* propose that these three alleles were so rare that they had escaped detection in 2008. The authors showed that the rare alleles were not the result of new mutations because the alleles' DNA sequence was substantially different from those of the alleles found in 2008. It is also unlikely that these new *A. cerana* *csd* alleles were introduced by a secondary invasion, because the authors did not observe new alleles at the other DNA regions they examined. Rather, the presence of these three rare alleles in 2009 is best explained by balancing selection, in which bees that carried the rare *csd* alleles in 2008 contributed more offspring to the next generation.

Over the next six years, from 2009 to 2015, Gloag and colleagues found that the frequency of each of the seven *csd* alleles in the invasive population started to converge on an allele frequency of one-seventh, the theoretical frequency expected if balancing selection is assumed. By 2015, the authors estimated that one out of ten fertilized eggs developed into a diploid male, representing a 40% reduction in female mortality caused by diploid male production compared with the data from 2008 — this is a massive improvement in the fitness of the invasive population. Balancing selection at the *csd* gene has been indirectly inferred from studies of DNA-sequence change⁹ in native honeybee populations, and Gloag and colleagues' work provides a direct observation of this form of selection in real time.

Diploid males are typically found in invasive populations of ants¹⁰, bees¹¹ and wasps¹². The balancing selection at the *csd* gene documented by Gloag *et al.* might be a common process that enhances the success of social-insect invasions by correcting imbalances in the frequency of *csd* alleles that occur during founding events.

Although balancing selection clearly increased the fitness of invasive Asian honeybees in Australia, it is not clear whether this evolutionary force was essential for the successful establishment of the invasion. The invasive population of *A. cerana* still increased in size despite the skewed allele frequencies at the *csd* gene during the early stages of the invasion. Social-insect invaders might have other attributes that predispose them to be successful biological invaders. The intrinsic growth rates of some social insects might be so high that even a 25% increase in female mortality — the amount estimated by Gloag and colleagues to occur in the initial stages of *A. cerana*'s invasion — did not prevent population expansion.

Queen honeybees typically mate with 10–20 males, which spreads the consequences of diploid male production evenly across the invasive population; instead of some colonies producing a lot of diploid males, with others producing none, most colonies in the population would be expected to produce a

moderate level of diploid males¹³. Moreover, honeybee colonies recoup some of the costs of producing diploid males when they are cannibalized by workers. Perhaps the reduced genetic diversity found in invasive *A. cerana* reduces aggression between colonies as it does in invasive Argentine ants¹⁴. Nevertheless, Gloag and colleagues' study provides a clear example of how rapid evolutionary changes can affect the fitness of invasive populations. ■

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NANOSCIENCE

Flexible graphene strengthens friction

Previous observations showed that friction on graphene increases gradually when a probe starts to slide across the material's surface. Simulations now reveal that this effect is related to bending of the graphene sheet. [SEE LETTER P.541](#)

ASTRID S. DE WIJN

As anyone who has slipped on wet autumn leaves might realize, friction in layered materials can behave in peculiar ways. Such friction can be studied on small scales by looking at graphene, a material that consists of single sheets of carbon atoms. Experiments^{1,2} performed a few years ago using atomic force microscopy (AFM) revealed that friction is larger when the number of stacked graphene sheets is smaller. Moreover, when a probe begins to move across the surface of stacked graphene sheets, friction initially increases and then levels off². A wide range of suggestions has been proposed to explain these observations, but on page 541, Li *et al.*³ solve the mystery using computer simulations. They report that graphene's strange behaviour is related to distortions that strengthen friction on thin stacks of sheets.

Friction is so common in our daily lives that we barely think about it. Humans have been forced to deal with it since prehistoric times: the wheel is essentially a device for reducing friction when moving heavy loads, and rubbing sticks together to make fire makes use of the fact that friction generates heat. We have therefore developed a massive amount of phenomenological knowledge of friction under

specific circumstances, and especially of how to reduce it. But our fundamental understanding of how and why friction works is still sorely lacking.

Layered materials are a prime example of this knowledge gap. Some of them, such as graphite — stacked layers of graphene — and molybdenum disulfide are commonly used in powdered form as solid lubricants or as additives in liquid lubricants, and sometimes as low-friction coatings. We use these materials all the time, but are only now starting to understand their workings.

Graphene has received much attention in the past few years (see ref. 4, for example), largely because of its remarkable electronic properties — research into this material was rewarded with the Nobel Prize in Physics in 2010. But it is graphene's mechanical properties that are interesting when considering its friction. Most importantly for Li and colleagues' results, single sheets of layered materials bend easily. Although it might seem obvious that such bending must have a role in the friction of thin stacks of graphene, many explanations for the role of bending were possible.

To understand Li and co-workers' results, we need to know what surfaces in contact look like. Real surfaces are rough on microscopic scales, even if they look flat to the naked eye.

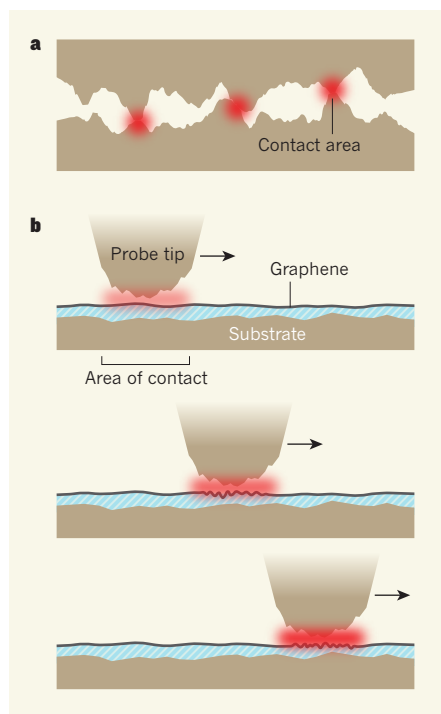


Figure 1 | Friction on graphene sheets. **a**, Surfaces that look smooth on a macroscopic scale are rough on the microscopic scale. Contact between surfaces thus occurs only between microscopic projections from the surfaces, and friction between the surfaces depends on the strength of the interactions between the contacting projections. **b**, Li *et al.*³ performed simulations to investigate what happens when a nanometre-scale probe is dragged along the surface of graphene on a silicon substrate. During the initial stages of sliding, the strength of the probe's interaction with the graphene increases gradually, thus increasing the friction between the probe and the graphene. The substrate-graphene interaction (blue) also plays a part in the observed effects, although its exact role is unclear.

Two surfaces in contact therefore never fit perfectly against each other, but meet only where microscopic projections come into contact (Fig. 1a). The actual area in contact is thus typically many orders of magnitude smaller than the apparent contact area.

These microscopic projections play a central part in friction. More specifically, the strength of the interaction between the microscopic contacts, which Li *et al.* refer to as the quality of the contact, is a key factor in the dissipation of the kinetic energy of sliding. The interaction strength can be affected by many factors, such as a material's properties, its chemistry and a mismatch of the crystal lattices in the contacting surfaces⁵, but also, in the case of graphene, by bending⁶.

The previously reported AFM experiments^{1,2} measured what happens at a single contact on stacks of graphene. Li *et al.* simulated those experiments numerically and investigated the strength of the interaction at a single contact. In the simulations, they put

one or several layers of graphene on top of a substrate (silicon) and rubbed the surface of the material with a tiny probe. They observed that bending distortions of the graphene sheets under the probe gradually increase as the probe moves; this increases the contact strength, and thereby also the friction (Fig. 1b). The effect is bigger if there are fewer layers, because thin stacks of graphene are more flexible than thicker stacks. The authors also find that the substrate underneath the graphene contributes to the increased contact strength.

It is worth noting that the authors checked carefully to make sure that the effect observed in their simulations was not related to the sliding speed. This was crucial, because current limitations to computational power make it impossible to simulate sliding at the low speeds used in AFM experiments.

Despite the fresh insight provided by Li *et al.*, many questions remain. What exactly causes the bending distortions to grow? And what is the role of the substrate under the graphene? When the authors altered the parameters of their model to increase the binding of the substrate to graphene, the contact strength no longer changed as the probe moved. The same was true when there was no substrate at all.

Moreover, both the substrate and the probe used by the authors were amorphous materials that lacked any structural order. It would

be interesting to see what happens if the simulations are repeated using an ordered substrate and/or probe. Graphene is often studied on ordered substrates in other contexts, and such a study might also provide insight into the mechanisms at play if the structures of the substrate and tip affect strengthening in some way.

Friction is a messy problem to study, because its effects are often found in highly complex systems that involve a variety of materials and chemistry. It is usually not clear which of these are essential for a specific friction effect, and which have little or no role. This makes meaningful study of such phenomena difficult. Li and colleagues' finding of increases in contact strength in a relatively simple system opens up the possibility of studying the strengthening process in a much more controlled way. ■

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CELL BIOLOGY

A mitochondrial brake on vascular repair

Injured blood vessels are repaired by vascular smooth-muscle cells. It emerges that the protein Fat1 regulates the proliferation of these cells by inhibiting the function of mitochondria. SEE LETTER P.575

CHARLES E. DE BOCK & RICK F. THORNE

After injury to the cells that line blood-vessel walls, vascular smooth-muscle cells (VSMCs) move to the injured region and proliferate to cover the damaged site. However, cellular overproliferation at the repair site might cause vessel-wall thickening that reduces blood flow through the vessel. In addition to naturally occurring damage, blood-vessel injury can be a consequence of surgical interventions such as transplants or procedures to open narrowed blood vessels. An understanding of the signals that regulate VSMC proliferation might enable the development of clinical approaches to limit this process and prevent blood-vessel narrowing. Cao *et al.*¹ demonstrate on page 575 that the Fat1 receptor protein, a negative regulator of VSMC

proliferation, has a direct and unexpected role in regulating energy production in mitochondria, the organelles that act as cellular powerhouses.

Fat1 is a member of the vertebrate Fat cadherins, a small family of proteins whose primary function is unclear². Previous work³ revealed that Fat1 enhances the migration and limits the proliferation of VSMCs, providing clues that Fat1 could have a role in vascular-cell remodelling.

The Fat1 receptor is normally present at the cell surface, and its structure consists of an extracellular domain, a transmembrane segment and an intracellular domain². Cao *et al.* used mass spectrometry to identify proteins that interact with the intracellular domain of mouse Fat1. They discovered that 22 Fat1 interactors are proteins of