

in two ways. First, because epigenetic modifications regulate gene expression, epigenetic features probably differ between genomic regions within and outside genes, and also between genes that show drastically different expression levels or regulation (for example, those that are continuously expressed and those that are expressed only in certain tissues or in response to certain environmental factors). The relationship between the expression or regulation of a genomic region and the functional importance of the region might thus create a correlation between the epigenetic feature of a region and the probability that a mutation in the region would be deleterious. Consequently, selection might lead to the evolution of machinery that lowers mutagenesis in regions that exhibit an epigenetic feature that correlates with high probability of a mutation being deleterious (Fig. 1a).

Second, the association between a genomic or epigenetic feature and mutation rate might not be a result of selection for lower mutagenesis. Instead, it might be intrinsic to the feature (owing to its chemical nature) or a by-product of some other biological processes¹¹ (Fig. 1b). Intriguingly, although selection for lower mutagenesis should be orders of magnitude weaker in the non-selfing forest tree *Populus trichocarpa* than in the selfing *A. thaliana*^{9,10}, Monroe and colleagues present evidence suggesting similar mutation-rate profiles between the two species. This finding supports this second approach to explaining the origin of suppressed mutagenesis in important genomic regions.

It is worth emphasizing that, in both scenarios, the enrichment of certain genomic or epigenetic features at important regions occurs not because these regions have a high probability of deleterious mutations, but because of some correlates of that probability, such as gene expression or regulation. Hence, some variations in mutation rate across the genome might merely reflect these correlates. For example, Monroe *et al.* find that the outermost coding parts of a gene mutate more than other coding parts do. Moreover, genes that lack untranslated regions in their messenger RNAs have higher coding mutation rates than do other genes. And genes with few non-coding segments (introns) have higher coding mutation rates than do genes with more introns. Whether these mutational patterns are beneficial to the plant is unclear.

Even when mutagenesis-reducing machinery recognizes a particular genomic or epigenetic feature, selection for lower mutagenesis cannot drive the acquisition of the feature at an important genomic region. This is because the feature's beneficial effect on mutation rate in that one region is too small to overcome the effect of genetic drift^{6,8}.

Monroe *et al.* propose that, because *A. thaliana*'s mutation-rate profile reduces

the overall chance that a new mutation is deleterious, the profile increases the chance that a mutation is beneficial. This statement, however, need not be true, because lowering mutagenesis in crucial genomic regions could reduce the proportion of mutations that are deleterious as well as the proportion of those that are beneficial – provided that these types are concentrated, and neutral mutations under-represented, in important regions.

Mutation and selection are generally considered to be distinct evolutionary forces. But if mutation rate is shaped by selection to different extents in genomic regions of different importance, as Monroe *et al.* suggest, this distinction would be blurred, and many evolutionary phenomena would require reinterpretation. Most notably, differences between genomic regions in DNA-sequence variation within a species (known as polymorphism) and between species have been commonly explained by a variation in selection – but they might also be caused by a variation in mutation rate. Indeed, the authors observe a striking similarity between mutation-rate variation and polymorphism variation among genomic regions in *A. thaliana*, suggesting that the

latter is largely attributable to the former.

Although I am not ready to throw out the fundamental tenet of Luria and Delbrück, the intriguing mutation-rate pattern of *A. thaliana* makes me wonder whether the same pattern exists in many other species – and, if so, what the underlying mechanism is, and how it originated in evolution.

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Particle physics

Single magnetic charges in the largest of fields

Sonia Kabana

Collisions between lead ions have produced the largest measured magnetic field in the Universe, enabling a search for elusive exotic particles that carry an isolated magnetic charge. **See p.63**

Break a magnet into smaller pieces, and each part will have its own north and south pole. But in the subatomic realm, an exotic particle called a magnetic monopole can possess an isolated magnetic charge – existing as only a north pole or a south pole. On page 63, Acharya *et al.*¹ report the results of a search for these extraordinary particles using a very strong magnetic field.

The implications of the existence of magnetic monopoles are far reaching. For example, theories that attempt to unify the various forces in the Universe predict the existence of these particles, and such predictions motivated development of the most popular cosmological model, which holds that the early Universe underwent a period of inflation during which the volume of space expanded exponentially. Many investigations have looked for evidence of magnetic

monopoles – by searching in the cosmos, and by attempting to produce and detect them in high-energy particle collisions.

The Scottish mathematician James Clerk Maxwell offered the first hint of a possible unification of forces, by incorporating the electric and magnetic forces into a set of beautiful equations. These equations allow the existence of isolated electric charges in the Universe, but prohibit isolated magnetic charges. The discovery of an isolated magnetic charge would therefore motivate an update that provides symmetry to Maxwell's equations.

The idea of isolated magnetic charges was first mentioned formally in 1894 by French physicist Pierre Curie², and the English physicist Paul Dirac was the first to come up with a theory for a point-like particle (meaning a particle lacking a substructure) that could possess an isolated magnetic charge³. Remarkably, he

also showed that this hypothesis provided an explanation for the observation that electric charge is quantized (it takes only certain discrete values).

However, magnetic monopoles need not be point-like. In fact, magnetic monopoles are not point-like in many of the theories that have been proposed to go beyond the standard model of particle physics, the accepted model for describing the subatomic Universe. They are predicted to have a wide range of masses, and those with masses low enough to be produced in particle accelerators are predicted to have a substructure.

Most searches for magnetic monopoles in accelerators so far have looked for them in the products of collisions between elementary particles (such as electrons or quarks). But the strong coupling of magnetic monopoles to other particles and to each other (as predicted by Dirac's theory) makes it difficult to calculate the expected monopole yield. Therefore, searches using elementary-particle collisions are interpreted in terms of point-like magnetic monopoles, even though the monopoles that could possibly be produced by these experiments probably have substructure.

An alternative approach is analogous to a phenomenon first described in 1951 by the US physicist Julian Schwinger⁴. Schwinger showed that electrically charged particles could be produced by the decay of a strong electric field. The fact that electric and magnetic fields are linked through the principle of electromagnetic duality suggests that pairs of magnetic monopoles and their antiparticle twins could be produced by the Schwinger mechanism in a sufficiently strong magnetic field. This production mechanism is easier to describe theoretically than is the mechanism involving elementary-particle collisions, and it is expected to yield more magnetic monopoles⁵.

Acharya *et al.* took this route to search for magnetic monopoles produced in the enormous magnetic field that is induced by collisions between lead ions accelerated by the Large Hadron Collider (LHC) at CERN, Europe's particle-physics laboratory near Geneva, Switzerland. This magnetic field can reach strengths of 10^{16} tesla (ref. 6), making it the largest magnetic field measured on Earth, and, indeed, in the Universe. For example, the maximum magnetic field produced in the experiment was more than 10,000 times stronger than the magnetic field found on the surfaces of neutron stars.

The team attempted to detect magnetic monopoles that could be produced by the huge magnetic field to which the MoEDAL (Monopole and Exotics Detector at the LHC) experiment was exposed (Fig. 1). This experiment uses detectors made from the aluminium isotope ^{27}Al , the nucleus of which can trap particles that carry a magnetic charge. Acharya

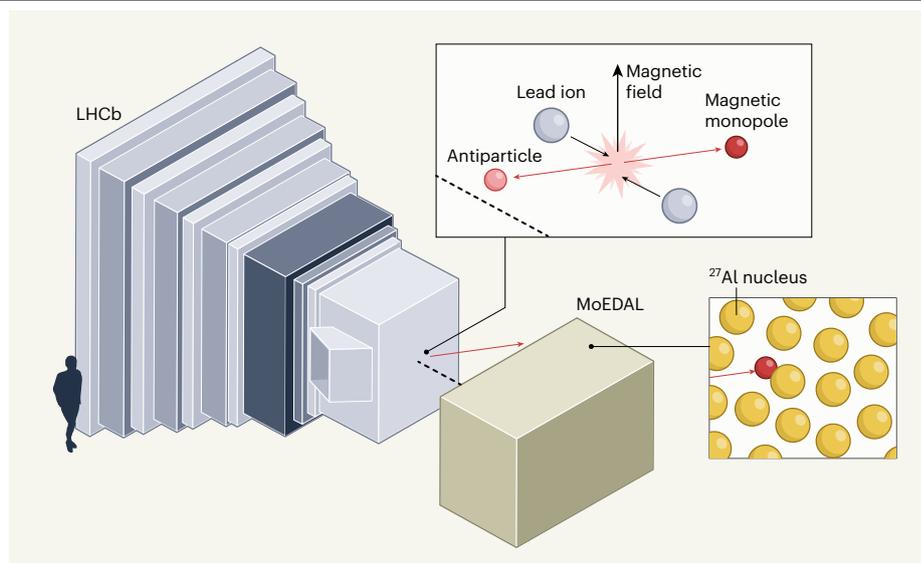


Figure 1 | An experiment to prove the existence of particles with isolated magnetic charges. Acharya *et al.*¹ searched for particles with single magnetic charges (magnetic monopoles) in a large magnetic field generated by collisions of lead ions accelerated in the Large Hadron Collider (LHC) at CERN, Europe's particle-physics laboratory near Geneva, Switzerland – in the interaction region of an experiment known as LHCb. The collisions are expected to produce a magnetic monopole and its antiparticle. The authors placed a detector known as MoEDAL (Monopole and Exotics Detector at the LHC) near the area in which the lead ions collide. (In reality, MoEDAL partially surrounds this area.) The detector contains the aluminium isotope ^{27}Al , which is expected to be able to trap particles carrying a magnetic charge. The experiment did not detect magnetic monopoles, but set limits on the expected yield of magnetic monopoles produced by strong magnetic fields. Dashed line represents the axis along which lead–lead collisions occur.

et al. positioned these detectors near the area in which the lead ion collisions take place in the LHCb experiment. They then scanned the detectors with a type of magnetometer that can directly sense magnetic charges.

This is one of the most unambiguous methods used so far to detect magnetic monopoles. Acharya *et al.* combined this detection approach with the most promising means of yielding a high production rate of mono-

“The maximum magnetic field produced was more than 10,000 times stronger than the magnetic field found on neutron stars.”

poles that can also have a substructure, in a process that can be described well by theory. The results are therefore much more reliable than those from previous methods at colliders.

The authors did not find a statistically significant signal of a magnetic charge trapped in their detector, and therefore ruled out the existence of Schwinger monopoles with masses up to $75 \text{ GeV } c^{-2}$ (GeV stands for gigaelectronvolt; c is the speed of light in a vacuum) for magnetic charges ranging from 1 to 3 Dirac units of magnetic charge.

The absence of such a signal effectively

sets limits on the expected yield of magnetic monopoles produced by strong magnetic fields. Such limits are the basis of the method by which the standard model is tested and improved: they are taken into account when planning new experimental searches and developing the theoretical concepts required to explain observations, as well as the lack of observations.

Acharya and colleagues' result is therefore a great success in the context of particle-physics research, because it opens up a new avenue for studies of magnetic monopoles. It also maps out the limits within which we can further hunt for magnetic monopoles. Future experimental searches – both in particle colliders and through non-collider experiments – will no doubt benefit from the limits set by the authors, to enable the detection of these intriguing, elusive particles.

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