in ref. 13). The other proteins in the cohesin complex lack any known enzymatic activity, but are required for the complex to form and to bind to DNA. One of these subunits, Scc1 (also called Mcd1), dissociates when the sister chromosomes separate[10,11], but only if Esp1 is active. These results suggest that the cohesin complex holds the sisters together, and that its removal from the chromosomes triggers sister separation[9]. The complex can establish this linkage only during DNA replication, possibly owing to activities that travel with the replication fork[12,14].

These studies set the stage for the work of Uhlmann and colleagues[1], who used a mixture of biochemistry and genetics to show that sister separation requires cleavage of Scc1. The biochemical analysis relied on extractology — the study of complex reactions in crude, but concentrated, cell extracts that can be manipulated by the addition or subtraction of individual proteins. When Uhlmann *et al.* added chromatin to such an extract, the Scc1 was cleaved into three fragments and it dissociated from the chromatin. The authors found that this reaction requires Esp1 and is inhibited by Pds1, reflecting the requirements for sister separation *in vivo*.

Is cleavage a cause or a consequence of sister separation? To answer this critical question, Uhlmann *et al.* mapped the cleavage sites, then made mutations that blocked them and reintroduced the mutant gene into cells. The results were dramatic. Although the mutant Scc1 protein established sister-chromosome linkage during DNA replication, it did not leave the chromosomes during mitosis, and the cells died because the linkage between the sisters was not dissolved. So, two different sorts of proteolysis are needed to initiate sister separation. The first is activation of the anaphase-promoting complex, which leads to the wholesale destruction of Pds1. This, in turn, frees Esp1 to introduce two surgical snips in Scc1, thereby destroying the cohesin complex (Fig. 1b).

Other studies indicate that changes in the cohesin subunits are responsible for the difference between chromosome segregation in mitosis and meiosis. In mitosis, the sisters separate their arms and centromeres (the specialized region that attaches them to the spindle) at the same time. But in meiosis, the arms separate in the first division whereas the centromeres separate in the second. In fission yeast, delayed separation of the centromeres can be induced by replacing components of the mitotic cohesion complex with variants that are made only during meiosis. This result indicates that a change in a single chromosomal protein may be enough to cause the altered pattern of chromosome segregation that is responsible for sexual reproduction (Y. Watanabe and P. Nurse, personal communication).

So, have we finally identified the physical glue that holds the sisters together? And is Esp1 the protease that destroys it? The answer to both questions is a resounding 'maybe'. We cannot exclude the possibility that the cohesin complex regulates the stability of some other, more fundamental linkage. Support for this possibility comes from studies of frog egg extracts, in which the cohesin complex helps to set up sister linkage, but leaves the chromosomes as they enter mitosis — well before the sisters separate[15]. Moreover, sequence gazing suggests that Esp1 is unlikely to cleave Scc1, because it lacks homology to any known protease. The answers probably lie beyond the realms of genetics and extractology, but the questions should stimulate biochemists to roll up their sleeves and dissect the reactions that promote cell reproduction by abolishing chromosomal sisterhood. □

Andrew Murray is in the Department of Physiology, University of California, 513 Parnassus Avenue, San Francisco, California 94143-0444, USA.
e-mail: amurray@socrates.ucsf.edu

1. Uhlmann, F., Lottspeich, F. & Nasmyth, K. *Nature* **400,** 37–42 (1999).
2. Holloway, S. L., Glotzer, M., King, R. W. & Murray, A. W. *Cell* **73,** 1393–1402 (1993).
3. Uzawa, S. & Yanagida, M. *J. Cell Sci.* **101,** 267–275 (1992).
4. Guacci, V., Hogan, E. & Koshland, D. *J. Cell Biol.* **125,** 517–530 (1994).
5. Straight, A. F., Belmont, A. S., Robinett, C. C. & Murray, A. W. *Curr. Biol.* **6,** 1599–1608 (1996).
6. Yamamoto, Y. A., Guacci, V. & Koshland, D. *J. Cell Biol.* **133,** 99–110 (1996).
7. Funabiki, H. *et al. Nature* **381,** 438–441 (1996).
8. Kumada, K. *et al. Curr. Biol.* **8,** 633–641 (1998).
9. Ciosk, R. *et al. Cell* **93,** 1067–1076 (1998).
10. Guacci, V., Koshland, D. & Strunnikov, A. *Cell* **91,** 47–57 (1997).
11. Michaelis, C., Ciosk, R. & Nasmyth, K. *Cell* **91,** 35–45 (1997).
12. Toth, A. *et al. Genes Dev.* **13,** 320–333 (1999).
13. Hirano, T. *Genes Dev.* **13,** 11–19 (1999).
14. Uhlmann, F. & Nasmyth, K. *Curr. Biol.* **8,** 1095–1101 (1998).
15. Losada, A., Hirano, M. & Hirano, T. *Genes Dev.* **12,** 1986–1997 (1998).

Particle physics

And you're glue

Frank Wilczek

It's a widely believed half-truth that protons and neutrons are made out of quarks. Actually, physicists are increasingly discovering that it's considerably less than half the truth. The modern theory of the strong force, which binds quarks inside protons and neutrons, and these particles in turn to make atomic nuclei, is quantum chromodynamics (QCD). The other ingredients of QCD, the colour gluons, were once conceived as mere paste that somehow links together more substantial stuff (their name reflects this). No longer. On closer inspection, the quarks appear as the showier, but gluons as the weightier and more dynamic, constituents of matter. Definitive images[1] from a microscope capable of looking inside protons, the HERA accelerator in Hamburg, Germany, reveal as well that there is more to gluons than meets the eye.

To understand these evolving views, you must consider how one goes about looking inside a proton, to 'see' what it is made of. An ordinary microscope, using ordinary light, is woefully inadequate, because the wavelength of light is about one billion times larger than the size of the proton. Even fancy electron or scanning tunnelling microscopes can barely resolve single atoms, and fall far short of seeing the nucleus inside. The right tool for the job is a high-energy accelerator. They produce virtual photons of very short wavelength (and lifetime), that can be used to take snapshots of the proton's interior (Box 1, overleaf).

There's a catch, however, to this seemingly straightforward procedure. You get to see only what the virtual photon allows you to see. And because the photons couple only to electrically charged particles, constituents of

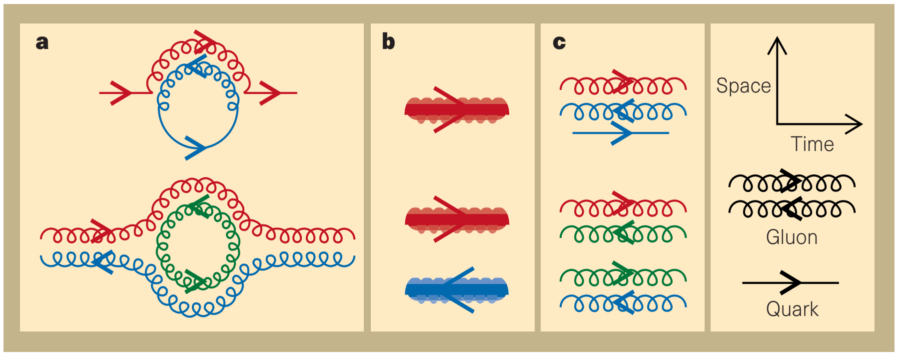

Figure 1 **What once appeared as fuzzy quarks or gluons are clearly imaged in a faster exposure, which reveals additional gluons.** a, **The flow of colour charge around a quark (top) or gluon (bottom) in time. Quarks carry a single unit of colour charge: red, blue or green. Gluons carry both positive and negative units of colour charge.** b, **Average views of the same quark and gluon with coarse time resolution** c, **In each case, a sharper-resolution view of the central time interval reveals the existence of an additional gluon.**

NATURE

100 YEARS AGO

A few interesting facts with regard to the kea, or sheep-eating parrot, of New Zealand are related in the July number of *Leisure Hour* by Dr. F. Truby King. The intense curiosity of these birds is stated to be sufficient to account for the habit of eating sheep acquired by them. Dr. King thinks it is probably a mistake to suppose that the kea designedly makes at once for the kidney fat of the sheep upon which it has pounced. It eats into various parts of the body, though perhaps more often into the region of the kidney, as it is there that the kea gets the firmest stand on the back of the running sheep. This view is strengthened by the fact that the bird prefers double-fleeced sheep – that is, such as have remained a whole season unshorn, on which it obtains a firmer grip.

From *Nature* 29 June 1899.

50 YEARS AGO

According to Darwin the long neck of the giraffe is the result of natural selection acting through the animal's tree-feeding habit. He wrote: "the individuals which were the highest browsers and were able during dearths to reach even an inch or two above the others will often have been preserved." There are serious objections to this argument. (1) During dearths … the recurrent wastage of young giraffes would threaten the species with extinction. (2) Under such extreme conditions of dearth the grass-eating African ungulates would also have been so short of food that it is difficult to see why more of them did not develop the leaf-eating habit and the excessively long neck. (3) Bull giraffes tend to be several inches taller than the cows, so that during each dearth males would be naturally selected at the expense of the females – another factor likely to lead to rapid extinction. An alternative theory free from these criticisms has occurred to me. … The giraffe is actively preyed upon by lions and leopards. It is reasonable, therefore, to explain the excessive length of its forelegs as the effect of natural selection acting continually through the hunter–hunted relationship. … That the neck has elongated to a degree only just sufficient to keep pace with the increasing length of the legs is suggested by the fact that the giraffe has to splay its forelimbs awkwardly to drink.

From *Nature* 2 July 1949.

Box 1: Designer photons

The basic principle of the powerful microscopes used to examine proton interiors is extremely simple. Electrons (or positrons) are accelerated to high energy, and made to collide with protons (or other atomic nuclei). The main interactions of electrons are through the well-understood processes of electrodynamics. In quantum electrodynamics (QED), its modern version, these interactions are pictured and calculated as the exchange of real or virtual photons.

Real photons are completely characterized by their energy. Their momentum is simply equal to their energy (divided by the speed of light). For virtual photons, which exist only for a limited time, the energy and momentum are independent variables. In either case, real or virtual, the wavelength is inversely proportional to the momentum.

When an electron at SLAC interacts with a proton it generally gets deflected, so that its energy and momentum change. The difference is carried off by a virtual photon. If the momentum of this virtual photon is large, it will have a short wavelength and provide excellent spatial resolution. If, in addition, it is a 'highly virtual' photon – that is, if there is a big mismatch between its energy (divided by the speed of light) and momentum, then it has a very short lifetime and provides excellent time resolution. By analysing how frequently virtual photons of different kinds get absorbed – that is, by noting how frequently you observe different electron deflections – you can effectively take snapshots, with adjustable spatial and time resolutions, of the charge distribution inside protons. **F. W.**

the proton that are electrically neutral do not show up in these snapshots. (Biologists face a similar problem, in that they are often interested in materials that are basically transparent. They use various tricks, such as staining or attaching fluorescent molecules, to work around this difficulty.) What you see in an accelerator is quarks[2]. Although these unusual particles are notoriously 'well confined', that is, impossible to isolate, they show up quite clearly in these short-time-exposure snapshots. You can even measure their peculiar fractional electric charges, their spin and the energy and momentum they carry.

When this is done, and the results analysed, physicists discover that they have a missing-mass problem on their hands,

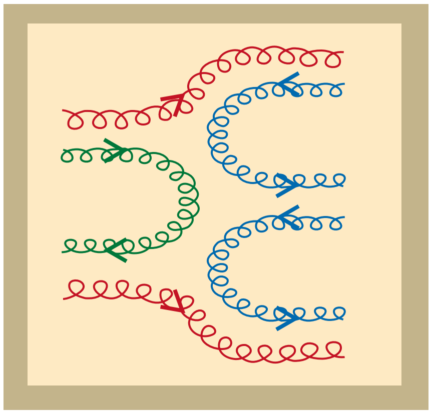

Figure 2 **Recombination of gluons. In Fig. 1, a single smudgy gluon was resolved into two sharp ones. If gluon seas were always dilute, then two separate smudgy gluons should be resolved into four sharp ones. But when gluons are more densely packed (as shown), two could be resolved into three, suggesting recombination has taken place.**

rather similar to the one faced by astronomers. The total energy in all the quarks does not add up to the energy in the proton. It is less than half. In the early days of this subject, Richard Feynman (who first carried out this kind of analysis) greatly annoyed his colleague Murray Gell Mann (a paladin of quarks) by calling the constituents of protons 'partons', and refusing to acknowledge that partons are quarks. As it turns out, each rival had part of the truth. Some of the partons are quarks, but many are gluons. The quarks carry all the electric charge, but most of the energy is in the colour gluons.

So what's new? The latest and greatest accelerators allow us to take snapshots with ever shorter time exposures. We can thereby resolve in ever finer detail the dynamical processes going on inside protons. When this is done, a remarkable result emerges. In the shorter-exposure pictures, one finds that the balance of energy tilts more and more toward gluons. What previously appeared as a blurry quark is on sharper examination revealed as part quark, part gluon. Nor is the concept of gluons free from challenge. They, too, on sharper examination, are revealed to be composites of several lower-energy gluons (Fig. 1). The closer we look, the more a proton (or neutron) appears as a bundle of soft glue[1].

This remarkable phenomenon — the gluonization of the proton — was predicted theoretically[3]. Indeed, it reflects quite directly one of the most profound features of the fundamental theory of quarks and gluons. According to QCD, the very powerful, complicated forces that confine quarks, preventing them from drifting away over long periods of time, are due to the accumulated effect of a surrounding cloud of short-lived virtual gluons, each of which individually interacts weakly and simply. Now we've got pictures to prove it.

Predicted as a possibility, but not yet observed, is the inverse process, where gluons become so densely packed that they start recombining. This happens when two nearby fuzzy gluons are resolved, on closer inspection, into three (rather than the expected four — two from each) sharp gluons (Fig. 2). It can even turn out that false images are dissolved away: what appears at first as three fuzzy-looking gluons can turn out to be the image of two less fuzzy ones that partially overlap. A fascinating equilibrium of splitting and recombination should eventually result[4]. It is a considerable theoretical challenge to calculate this equilibrium in detail — how a proton eventually appears, as you peer in closer and closer.

In an accelerator, rapidly approaching nuclei appear to one another as pancakes, because of relativistic contraction, and thereby produce the densest gluon seas[5]. Their use, now an active frontier of experimental physics, will open the recombination regime to experimental investigation. The accumulation of glue inside the proton is not only of interest for its own sake. It will also be important for the interpretation of future experiments using ultra-high-energy protons as an exploratory tool, particularly searches for the Higgs particle and the particles predicted by supersymmetry at the CERN Large Hadron Collider. Because many of these particles are produced primarily by the fusion of gluons found within colliding protons, their production rate is controlled by the gluons' densities[6].

In any duel of insults, the old saying, "I'm rubber, and you're glue, so whatever you call me bounces back and sticks to you", is a feeble last resort. Well, you are, you know. □

Frank Wilczek is at the Institute for Advanced Study, School of Natural Sciences, Olden Lane, Princeton, New Jersey 08540, USA.
e-mail: wilczek@sns.ias.edu

1. Abramowicz, H. & Caldwell, A. *Rev. Mod. Phys.* (submitted); http://xxx.lanl.gov/abs/hep-ex/9903037
2. Roberts, R. *The Structure of the Proton* (Cambridge Univ. Press, 1990).
3. De Rujula, A. *et al. Phys. Rev.* **10,** 1649–1652 (1974).
4. Gribov, L., Levin, E. & Ryskin, M. *Phys. Reps* **100,** 1–146 (1983).
5. McLerran, L. http://xxx.lanl.gov/abs/hep-ph/9903536
6. Kilian, W. & Zerwas, P. http://xxx.lanl.gov/abs/hep-ph/9809486

Palaeobiology

A refugium for relicts

Zhexi Luo

The transition between the Late Jurassic and Early Cretaceous, 157–100 million years (Myr) ago, is a defining time in the history of terrestrial biodiversity. It witnessed the descent of birds from two-legged, meat-eating dinosaurs[1,2], and their early diversification[3–5]; the rapid evolution of non-bird dinosaurs; diversification of the major mammalian groups[6,7]; the origins of flowering plants (angiosperms)[8]; and diversification of the nectar-feeding flies — the finest early examples of plant–insect coevolution[9,10]. These emerging lineages came to dominate the world's terrestrial biotas, and some are still thriving today.

A window with a grand view of this evolutionary spectacle is the Yixian Formation in China's Liaoning Province, one of the richest and most important sources of fossils from the Mesozoic era (245–65 Myr ago; see map on page 59). On page 58 of this issue[11], Carl Swisher, Yuan-qing Wang and their colleagues show that the Yixian beds are 124 Myr old, placing them firmly within the Early Cretaceous. Such precisely dated rich fossil assemblages are rare in the Early Cretaceous[12], making the new work a welcome step towards a better temporal calibration of the Mesozoic terrestrial biotas.

A cornucopia of beautiful fossils has been unearthed, in unprecedented quantities, from the Yixian Formation. The discovery of such exceptionally complete fossils has filled the gaps in our knowledge about lineages that were previously represented only by sparse, fragmentary fossils. Although the Yixian beds have yielded fossil fish, plants and arthropods since the 1920s, most of these species are restricted to eastern and central Asia. Likewise, the abundant dinosaurs, such as the horned psittacosaurs and enigmatic therizinosaurs found in the Yixian Formation, were also endemic to Asia during the earliest Cretaceous[13]. Without fossils from outside Asia, it has been difficult to correlate the Yixian biota with the worldwide geological timescale.

Ideally, to date fossil beds we need 'index' fossils that are abundant, broadly distributed and have rapid evolution. Age correlation of terrestrial biotas — as in the case of the Yixian — can be more difficult, because the preservation of terrestrial fossils is rarer, less complete and more uneven geographically than in marine environments. So, for decades, divergent opinions have waxed and waned about the age of the Yixian biota, which was suggested to be either Late Jurassic or Early Cretaceous — or anywhere in between.

The controversy has implications for both temporal and geographical patterns in the evolution of Mesozoic plants and animals, as many fossils from the Yixian beds occupy critical positions on their respective family trees. For instance, *Sinosauropteryx*[1] is the most primitive coelurosaurian dinosaur with downy feathers. *Protarchaeopteryx* and *Caudipteryx*[2] are basal in the maniraptoran dinosaur lineage that also includes *Archaeopteryx* and other birds, suggesting that true feathers evolved before the origin of avian flight. Other examples include the symmetrodont mammal *Zhangheotherium*[6], which is basal to the diverse spalacotheriid tree[14], and *Jeholodens*, a close relative of the triconodontids[7] that were found around the world in the Late Jurassic and Early Cretaceous. Then there are *Confuciusornis* and *Changchengornis*, the primitive beaked birds capable of powered flight, which are relatives of the enantiornithine birds that dominated the global avian faunas in the Cretaceous[3,15].

Similar examples abound in plants and invertebrates. The primitive angiosperm *Archaefructus*, for instance, has a typical angiosperm carpel (the female reproductive structure) but no flower petals[8]. It tells us much about the early anatomical evolution

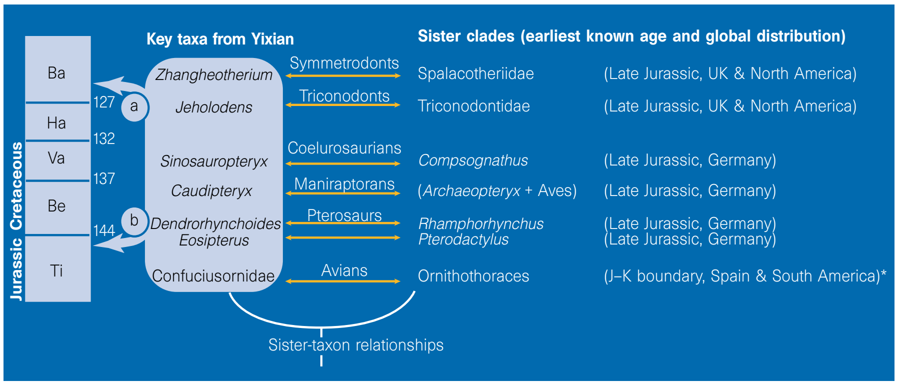

Figure 1 **Correlation of taxa from the Yixian Formation with their close relatives from the Lower Jurassic or earliest Cretaceous in other continents. Several endemic taxa, such as *Psittacosaurus*, therizinosaurs and *Liaoningornis*, are not considered here, because they were restricted to northern China and Central Asia before the end of the Early Cretaceous, and cannot be correlated with the taxa on other continents.** a, **Correlation of the Yixian Formation, according to the results of Swisher *et al.*[11].** b, **Correlation of vertebrates from Yixian with their respective sister taxa from the Late Jurassic on other continents. Epochs are: Ba, Barremian; Ha, Hauterivian; Va, Valanginian; Be, Berriassion; Ti, Tithonian.**

