hardly compatible with Bailey and colleagues' proposal.

No matter. Such quibbles do not diminish the central message of the authors' report, which is that, like all other theories about Precambrian animals, the classification of these fossils is far from resolved, even at the kingdom level. More data and critical analysis of the Doushantuo biota are required, such as that already provided by X-ray microtomography[2,7]. Only then can we assess whether any of its fossils address such overarching questions as the timing and embryological basis of animal origins. ■

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PARTICLE PHYSICS

Hard-core revelations

Frank Wilczek

Our description of how the atomic nucleus holds together has up to now been entirely empirical. Arduous calculations starting from the theory of the strong nuclear force provide a new way into matter's hard core.

Our quest to understand the force that holds atomic nuclei together has turned out to be a glorious adventure. Along the way we have found quarks, the coloured gluons that mediate the strong nuclear force, and a wonderful theory — quantum chromodynamics, or QCD. This theory has guided experimental research at the high-energy frontier, inspired dreams of 'unified field theories' that would embrace all nature's forces, and allowed theoretical physics to penetrate into the cosmology of the early Universe. In all this, the original problem of understanding nuclear forces has rather fallen by the wayside. That changes with what may come to be seen as a landmark paper by Ishii, Aoki and Hatsuda that has recently appeared on the arXiv preprint server[1].

Ironically, from the perspective of QCD, the foundations of nuclear physics appear distinctly unsound. Famously, nuclear physics is best understood by modelling atomic nuclei as assemblages of protons and neutrons moving at much less than the speed of light. Yet QCD tells us that protons and neutrons are themselves built from quarks and gluons that move at very nearly the speed of light. These more basic particles carry colour charges, leading to the additional requirement that they be confined within 'bags' whose contents are overall colour-neutral. So far, so good: we understand, at least roughly, how an unbalanced colour charge produces a growing cloud of virtual particles (the process known as vacuum polarization), which has to be neutralized. The neutral cluster holds together as a unit, like marbles in a bag.

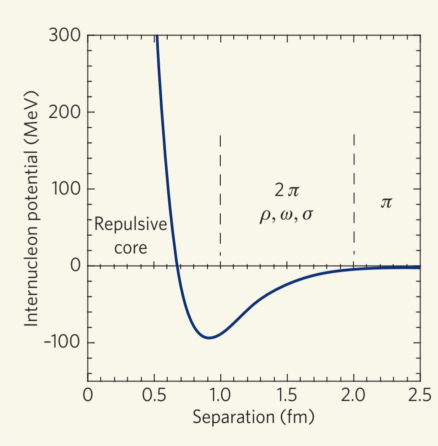

Figure 1 | The nucleon–nucleon potential. At distances of a few fermi, the force between two nucleons is weakly attractive, indicated by a negative potential. According to Hideki Yukawa's model[2], this force is mediated by the exchange of particles known as mesons. The π-meson, or pion, the lightest of the mesons, accounts for the attractive force at the largest distances where it is felt, whereas heavier mesons (ρ, ω, σ) take over closer in. The picture changes abruptly, however, below a separation of just under 1 fermi. Here the force becomes strongly repulsive, preventing nucleons merging. Ishii *et al.*[1] provide the first theoretical calculations from quantum chromodynamics, the theory of the strong force, that reproduce the empirical form of this potential.

But why don't the separate proton and neutron bags in a complex nucleus merge into one common bag? On the face of it, the one-bag arrangement has a lot going for it. It would allow quarks and gluons free access to a larger region of space, and so save on the energetic cost of localizing their quantum-mechanical wavefunctions. But in such a merger, protons and neutrons would lose their individual identities, and our traditional, quite successful model of atomic nuclei would crumble. What prevents that calamity?

We gain insight into this question by approaching it from the bottom up. Assuming that nucleons (protons and neutrons) are the appropriate starting point, what properties lead them to bind into atomic nuclei but to shun more intimate mergers? At an empirical level, the answer has been known for decades. The strong (that is, non-electromagnetic) internucleon force becomes significant at distances below a few fermi (1 fermi is 10^{-13} centimetres). It remains attractive down to about one fermi, but, at shorter distances, very strong repulsion abruptly sets in (Fig. 1). In atomic nuclei, nucleons arrange themselves close enough to take advantage of the attraction, but they stay away from the notorious hard core. In particular, they do not merge.

This empirical 'answer' serves only to frame more questions. Does the fundamental theory produce a force like that? If so, why? As originally proposed by Hideki Yukawa[2], the longest-range part of the strong internucleon force can be attributed to exchange of the lightest strongly interacting particles, known as π-mesons or pions. At shorter distances, exchanges of heavier mesons become important. As we approach hard-core distances, however, this meson-exchange picture becomes both unwieldy and dubious as the number of relevant mesons grows and their internal structure becomes resolved. Thus the existence of the hard core, which is absolutely crucial to the structure of matter as we know it, appears as a brute fact, opaque to theoretical analysis.

In principle, the equations of QCD contain all the physics of strong internucleon forces. But in practice, it is extremely difficult to solve the equations and calculate those forces. Ishii and colleagues' breakthrough calculation[1] required sophisticated algorithms, running on the biggest and fastest massively parallel computers currently available.

Why are the calculations so difficult? The main reason is simply that nucleons are complicated objects. It is often said that protons (and neutrons) are made from three quarks. That statement contains a kernel of truth, but it is a gross oversimplification. The kernel of truth is that a proton has the same conserved quantum numbers — charge and spin — as three quarks: two up (*u*) quarks and one down (*d*) quark, *uud*. Because these conserved quantities match, you can produce a proton by introducing three quarks and letting them settle down into a stable state of low energy.

In the process of settling down, however, the bare quarks dress themselves with a host of additional gluons and quark–antiquark pairs. Thus the wavefunction for a proton contains components with different numbers of gluons and quark–antiquark pairs, in addition to the basic three 'valence' quarks. To do that wavefunction justice, many different components must be sampled, and within each component the spatial distribution of its constituent quarks, antiquarks and gluons must be computed. The quantum-mechanical proton can contain all those configurations simultaneously. Existing

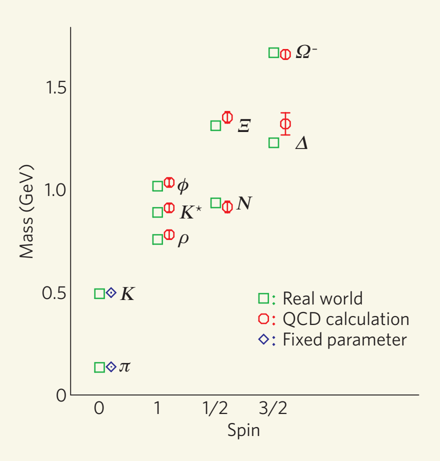

Figure 2 | Massive success. The fundamental equations of quantum chromodynamics contain three fixed parameters: the sum of the u and d quark masses, giving the pion mass; the mass of the s quark, which together with the $u + d$ mass sets the kaon mass (K); and an overall coupling strength fixed using the masses of mesons that contain heavier quarks (not shown). Given these, the masses of many observed particles have been computed with the precision indicated by the error bars. Notably here, N stands for nucleon (proton and neutron). Thus we have a first-principles account of the origin of the most of the mass of ordinary matter.

computers, based on classical physics, cannot. (For those familiar with the jargon: classical computers do not support superposition and entanglement.) The configurations must be laboriously constructed one by one, stored, and correlated. It is a job for teraflop machines running at full steam for months.

In recent years, first-principles calculations of the masses of strongly interacting particles — collectively known as hadrons and including the nucleons — have reached precisions of 5% or less, that precision being limited by computer power. This fundamental account of the origin of most of the mass of ordinary matter surely ranks as one of the greatest scientific achievements (Fig. 2). But yesterday's sensation is tomorrow's calibration, and the frontier of numerical QCD is set to expand into more difficult terrain. To study the nuclear force one must, of course, create two nucleons from scratch, and then study how the total energy depends on the distance between them.

That is exactly what Ishii *et al.*[1] have done. Their numerical results convincingly demonstrate that hard-core repulsion is a consequence of QCD: the strong internucleon force exhibits weak long-range attraction and strong short-range repulsion. Limitations of computer power did require the authors to use u and d quark masses slightly larger than the real-world values, so the magnitude and range of the hard core that they calculate should be taken as indicative, but not definitive.

To do justice to existing data, and to validate the method, much more work will be required. Realistic quark masses must be used, and the discretization errors that result from calculating continuous functions with the discrete bits of a computer processor must be carefully assessed. The dependence of the force on spin, which the authors averaged over, and velocity, which is known empirically to be quite complicated, must also be calculated.

Once all that is achieved, an exciting application will be to calculate the forces that occur in more extreme conditions than can be studied in terrestrial laboratories, such as those involving unstable hyperons. These particles are analogues of protons and neutrons that contain a valence strange (s) quark instead of a u or d, and are very difficult to study experimentally. Hyperons are copiously produced during supernova explosions, and they occur inside neutron stars, where the enormous ambient pressure stabilizes them. Our ignorance of hyperon behaviour renders current models of supernovae and neutron stars wildly uncertain. Numerical QCD could sharpen our insight into these and many other issues in nuclear astrophysics.

It will also be fun, and important, to consider how forces get modified as we change the masses of the u, d and s quarks, apply pressure, or otherwise tinker with the underlying theory. Over what range of parameters does the hard core persist, and so allow complex nuclear chemistry? That will provide fresh ideas in our understanding of how 'fine-tuned' the fundamental parameters must be in order to produce a user-friendly Universe. Such investigations might also provide something that is still conspicuously missing, despite the recent dramatic progress[1] — a simple qualitative explanation for the existence of the hard core.

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DEVELOPMENTAL BIOLOGY

Marked from the start

Not all cells in the early mammalian embryo are created equal. Even at the four-cell stage, embryonic cells that follow a particular pattern of division already have their developmental fate assigned to them. No cell will contribute exclusively to a specific cell type in the later embryo. But the progeny of some cells make a greater contribution to the 'inner cell mass' — the stem cells destined to become the fetus — and its surrounding 'trophectoderm', which forms extraembryonic structures such as the placenta. The progeny of other cells will make a greater contribution to other extraembryonic structures.

Reporting on page 214 of this issue, Maria-Elena Torres-Padilla and colleagues find that the key to the cells' destiny lies, at least in part, outside their genes (M.-E. Torres-Padilla *et al. Nature* **445,** 214–218; 2007).

To fit into the nucleus, DNA is wound around histone proteins. Both the DNA and the histones can be studded with a variety of additional chemical groups — notably, methyl groups — that affect how tightly the structure is packed. These 'epigenetic marks' determine how accessible the genes in certain regions are, and they can interact directly with gene regulatory factors to activate or silence nearby genes.

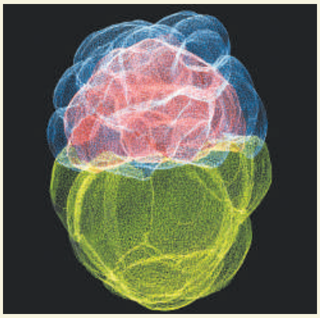
Specific patterns of these marks are associated with particular cell fates in later stages of development, and with allowing stem cells to maintain the ability to develop into many different cell types (pluripotency). So Torres-Padilla *et al.* speculated that epigenetic instructions might also help to determine the fate of early embryonic cells.

The authors concentrated on an epigenetic mark related to gene activation — methylation of an arginine amino acid in the histone H3 protein. They looked for differences between the cells destined for different fates in mouse embryos. An embryo is pictured here at the 32-cell stage, with the inner cell mass shown in red and the two types of trophectoderm, polar and mural, shown in blue and green respectively.

In the four-cell embryo, methylation of H3 was highest in cells that were due to become the inner cell mass and polar trophectoderm, and lowest in cells destined to contribute to the mural trophectoderm. To see whether this epigenetic mark really affected developmental fate, the authors manipulated the cells to overexpress the enzyme that carries out arginine methylation in two-cell embryos. This caused all the cells' progeny to become part of the inner cell mass — and increased the expression of certain proteins associated with pluripotency.

Epigenetic marks thus seem to be among the first developmental instructions that the embryonic cell receives.

Helen Dell



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