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 applica-

tion 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 progress¹ — 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 'trophoblast', 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 trophoblast, 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 trophoblast, and lowest in cells destined to contribute to the mural trophoblast. 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