

provides the bacterium with the ability to switch rapidly and reversibly between a vast number of possible combinations of physical attributes.

Other types of repetitive DNA allow further diversity, mediating genomic recombination both within and between different meningococcal strains. Recombination between strains makes use of the natural ability of the meningococcus to acquire DNA from its environment and is undoubtedly helped by the prevalence of DNA-uptake sequences — specific nucleotide sequences that enable the acquisition of DNA by other meningococci — in the genomes. All of these mechanisms provide the bacterium with the means to overcome the host's immune response to both infection and vaccination. Such concerns have been raised recently with regard particularly to the ability of meningococcal strains to exchange the genes responsible for biosynthesis of their capsules⁴.

Fortunately, as well as highlighting the extent of the problem, meningococcal genomics also provides possible solutions. Pizza *et al.*⁵ have screened the serotype B genome for genes encoding cell-surface antigens that are highly conserved in all meningococcal strains. Their aim is to make use of these antigens as vaccine components. This approach, although giving encouraging results in an animal model⁵, must now be proved in clinical studies. The comparison of different meningococcal genomes might also reveal genes that distinguish the relatively small number of hypervirulent strains from all other meningococci, and provide the basis for a strategy that specifically targets the properties encoded by such genes.

We do not yet know which strategy, or combination of strategies, will provide an

effective solution to the problem of meningococcal disease. But the public availability of the two genome sequences is bound to hasten the development of comprehensive vaccines that offer protection against all virulent meningococci. ■

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Particle physics

Backyard exotica

Frank Wilczek

All atoms follow the same body plan. They consist of a small, massive nucleus of positive charge surrounded by a cloud of negative electrons, bound together by the electromagnetic force. One might say that all atoms belong to a single phylum. Hadrons, elementary particles that are governed by the strong nuclear force, are known to populate three extremely well documented phyla. Baryons (such as protons and neutrons) are based on three quarks having different colour charges, one each of red, white and blue. Antibaryons are similarly constructed from triads of antiquarks, and mesons are based on bound quark–antiquark pairs, carrying equal and opposite colour charges. Each of these hadron phyla supports dozens of species. For many years now, physicists have been on the lookout for exotic new species, requiring more hadron phyla. We might now have the first hint from a theoretical analysis by Alford and Jaffe¹ of something suitably exotic.

What are these new particles? Among the range of possibilities dreamt up by theorists are various types of glueball, made from either two or three colour gluons (the particles that bind quarks together). Or there are centaurons (also called hybrids) made from a quark, an antiquark and a gluon. Finally, we have a hypothetical phylum that does not yet have an accepted name, based on two quarks and two antiquarks. It seems irresistible to call these quartets. Alford and Jaffe use ingenious computer experiments to argue that some long familiar, but hitherto enigmatic, particles are best interpreted as quartets¹.

Hundreds of different strongly interacting particles have been identified. Most are very short-lived (less than 10^{-20} seconds), and are observed only as enhancements in particle production rates, known as resonances. The observed properties of many of these particles match up with the predicted properties of different arrangements of quarks and antiquarks conforming to one of the baryon, antibaryon or meson body plans. Within each plan, one has the freedom to choose different properties for the quarks,

which can result in states with different total energies (or masses, according to $E = mc^2$). By this reasoning, the pattern of resonances can be seen as a 'spectrum', wholly analogous to the pattern of stationary states of an atom (as observed from its spectral lines).

The logical development of this line of thought is the quark model². The quark model was cultivated during the 1960s and early 1970s, finally reaching its most mature form in the so-called bag model³. According to the bag model, hadrons consist of relativistic, nearly free quarks (and/or antiquarks) confined to a finite region of space by a universal, constant vacuum pressure. The quark/bag model accounts, semi-quantitatively, for an enormous range of data. But it is not a satisfactory fundamental theory. For example, simply trying to compute what happens when bag-hadrons move results in mathematical ambiguities.

The fundamental theory of the strong force, quantum chromodynamics or QCD, emerged from the study of extremely high-energy collisions. QCD accepts quarks and antiquarks as fundamental ingredients, but also requires colour gluons. Indeed, the exchange of colour gluons is fully responsible for the strong interactions between quarks, much as the exchange of photons is responsible for electromagnetic interactions. Unlike the quark/bag model, QCD is a proper, precisely defined fundamental theory.

If correct, QCD should be able to predict the major properties and strong interactions of hadrons. Unfortunately, however, the equations of QCD are very difficult to solve. Computations that strain at the limits of modern, massively parallel computers succeed in producing, within a few per cent accuracy, the masses of a dozen or so of the lowest states of the hadron spectrum⁴. This is a remarkable achievement and confirms the correctness of a beautiful, parameter-free theory⁵. Yet to understand the rest of the hadron spectrum one will need, for the foreseeable future, to build upon older, but more manageable, concepts and models. Within this humbler approach, QCD does not dic-

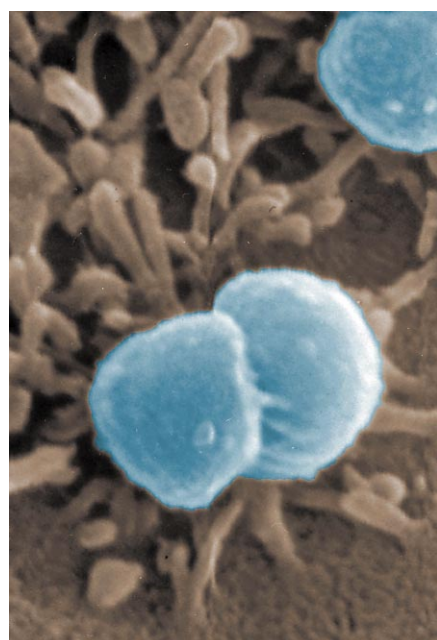


Figure 1 The meningococcus — a bacterium with unprecedented potential for diversity^{1,2}.

XAVIER NASSIF

tate answers, but rather suggests ideas. For example, the overall colour-charge neutrality of three-quark baryons and quark–anti-quark mesons explains why they have special status as stable objects. So QCD sanctions the semi-empirical approach of the quark/bag model, much as quantum theory validates the chemists' models of valence and bonding.

But it is important, and perhaps more exciting, that beyond endorsing old working assumptions, QCD suggests new questions and possibilities. Notably, QCD predicts each of the alternative body plans described earlier. Such beasts ought to exist, and they probably do. Unfortunately, particles or resonances observed in the laboratory do not come tidily labelled 'glueball', 'centauron' or 'quarktet'. Although candidate glueballs and centaurons have been vigorously advocated, other more conventional interpretations have not yet been firmly excluded.

The new work¹ concerns a family of resonances known as 0^{++} mesons, with names such as $\sigma(660)$, $f_0(980)$ and $a_0(980)$. 0^{++} refers to the spin (0), parity (even or +) and charge conjugation parity (+). (I won't try to explain these technicalities here.) The numbers in parentheses are the approximate masses of the resonances in megaelectron volts. (In these units, the electron mass is 0.5 and the proton mass is 938.) Here, a_0 actually refers to a related trio of particles, a so-called isotriplet.

If we attempt to explain the f_0 and a_0 particles within the conventional meson body plan, then we must combine either an up or a down quark with either an up or a down antiquark, using special, rather complicated wavefunctions. But then one would expect to find another heavier meson of the same kind, made from the heavier strange quark and its antiquark, whereas the σ is found to be lighter. On the other hand, the quarktet picture provides a very pretty, though slightly intricate, explanation of the observed pattern, based on the fundamental forces between quarks^{6,7}.

Such arguments⁸ are already quite suggestive, but Alford and Jaffe have raised the discussion to a new level, by formulating and performing a crucial (numerical) experiment. In pure QCD, the 0^{++} particles decay rather rapidly into pairs of 'pseudoscalar' mesons (π , K , η), which complicates their study and interpretation. So Alford and Jaffe study a slightly modified version of QCD, in which the masses of the quarks are taken to be larger than their real-world values, where this can't happen. They also 'improve' on reality by removing the possibility of quark–anti-quark annihilation, thereby sharpening the distinction between mesons and quarktets. They find that pairs of pseudoscalar mesons feel attractive forces, which will cause them to form stable bound states

whose qualitative properties (spin, parity and mass) match those of the observed 0^{++} particles. As each pseudoscalar is a quark–anti-quark meson, the combination is a quarktet!

More accurate and extensive work is required to prove that the bound states really do form, and to verify that nothing untoward happens when we swap modified for real QCD. If everything checks out as expected, then in the search for exotic hadrons it seems that, after voyages into realms of extravagant energy and strangeness, we "arrive where we started, and know the place for the first time"⁹.

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Ancient DNA

Neanderthal population genetics

Matthias Höss

Authenticity is all in research on ancient DNA. Experience has taught us that even the most exciting claims of the retrieval of ancient DNA are not worth much if they cannot be independently reproduced. Hence the importance of a paper on page 490 of this issue, in which Ovchinnikov *et al.*¹ describe the extraction, amplification and sequencing of DNA from 29,000-year-old archaeological bone material of a Neanderthal recovered from the Mezmaiskaya Cave in the northern Caucasus (see map on

page 490). This is the second time that such a claim has been made, the first being in 1997 (ref. 2). The paper by Ovchinnikov *et al.* is probably the more important of the two, for it provides invaluable corroboration for the authenticity of Neanderthal DNA sequences. Moreover, sequences of the DNA from a second Neanderthal offer more detailed insight into the contentious evolutionary relationship between Neanderthals and modern humans.

Research into ancient DNA enjoys high

Box 1 Studying ancient DNA

Research on ancient DNA developed in the mid-1980s from molecular evolutionary research, with the aim of extending phylogenetics (studies of evolutionary relationships) and population genetics to extinct species and populations.

Mitochondrial DNA (mtDNA) is used mainly for research into ancient DNA. Such DNA has advantages for evolutionary research in general. In addition, the large number of copies of mitochondrial genes (up to 1,000 times more copies of mitochondrial DNA are available per cell, compared with single-copy nuclear genes) makes mtDNA a better option when hunting for surviving ancient DNA molecules.

The polymerase chain reaction (PCR) is the most important tool in this field. The

exponential DNA amplification provided by this technique is highly efficient and, in theory, a single DNA molecule can be amplified to provide enough material for sequencing. Without PCR, it would be impossible to study the sequences of ancient DNA molecules.

However, contamination of samples by modern DNA molecules is a severe problem, in part because of the efficiency of PCR. Because only tiny amounts of target (ancient) DNA molecules tend to be retrieved, even low levels of contamination with modern DNA will distort the result. Human remains are particularly difficult to work with, owing to the difficulty of identifying contaminating, generally human, sequences.

Water and oxygen, which

cause hydrolysis and oxidation of DNA, respectively, are the main causes of DNA decay over time. Any burial conditions that limit or exclude water and/or oxygen will improve the survival of DNA in archaeological samples. Low temperatures during the burial period also seem to increase the chance of DNA survival, by slowing its breakdown by hydrolysis and oxidation. The age limit for successful retrieval of DNA depends to a large extent on the burial conditions. So far, the upper limit seems to be around 100,000 years.

Finally, the resurrection of extinct species is, and will stay, impossible. The reason? Only small, insufficient amounts of ancient DNA can ever be recovered, even under ideal conditions.

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