Figure 1 The doubly quantized vortex observed by Blaauwgeers and colleagues. The cones indicate the direction of the Cooper-pair angular momentum. The angular momentum makes a full turn in direction on going round the circular and hyperbolic cores. The circulation is given by the rotation of the cones about their axes. This makes a full 4π , double turn, following round the perimeter.

because the direction of both the nuclear and the orbital spins, as well as the phase of the wavefunction, can make a 2π change around the axis, then many different vortex structures are possible and the energy restriction on all but singly quantized vortices is lifted.

In their experiment, Blaauwgeers and colleagues identify a doubly quantized vortex (that is, $n=2$) in superfluid ^3He from its NMR signature. This vortex is shown in Fig. 1. The cones point in the direction of the orbital angular momentum of the Cooper pairs. The circulation depends on the angle of rotation of the coloured bands around the cone axis. Following around the perimeter of Fig. 1, the cones make two full turns, corresponding to a 4π rotation.

In ^3He , several quantities are changing simultaneously, so there is no singularity along the axis (the air-filled core in the plug-hole version) and all quantities vary smoothly across the axis. The vortex is also rather large, of order 10 micrometres in diameter, or not far off the size of a small snowflake. Indeed, this is a new snowflake, a natural

structure having its own beautiful symmetry and the added bonus of stable symmetrical flow. Because superfluid ^3He can only exist below 2.6 mK above absolute zero, these new 'snowflakes' are even more fugitive than those of ice.

Vortices in this superfluid are not simply aesthetic structures in an arcane fluid. The symmetry of the wavefunction of superfluid ^3He mimics surprisingly closely the metric of the Universe. Vortices are the superfluid analogue of cosmic strings. In the Universe, cosmic strings, if they indeed exist, are the relics of cosmic turbulence frozen into space-time by rapid phase transitions in the Universe shortly after the big bang. In the experiment of Blaauwgeers *et al.* the vortices are under strict control and can be injected one by one into the liquid as the rotation rate is increased. Indeed, this is how the experiment is done. Until we find real cosmic strings to study, vortices in superfluid ^3He are the best substitute.

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*Science*². These papers represent a milestone in meningococcal research. As well as providing the basis for future studies of the biology and the disease-causing mechanisms of this important pathogen, they highlight the potential of bacterial genomics to provide mankind with new solutions to intractable infectious diseases. However, the data also show us that a headlong rush to evaluate new vaccine candidates should be tempered with caution. Both genomes are replete with an unprecedented number of genetic elements that contribute to both genome fluidity and physical variability, attesting to the adaptability of *N. meningitidis* and its potential to evade the human immune response.

Neisseria meningitidis is a major cause of bacterial meningitis and septicaemia, diseases that all too frequently result in death or disability. Serogroup A organisms are responsible for large epidemics in sub-Saharan Africa, whereas serogroup B and C organisms account for sporadic cases and numerous localized outbreaks worldwide³.

Despite the reputation it has earned as an aggressive pathogen, *N. meningitidis* is more frequently found as a harmless commensal — an organism that lives with, but does not harm, the host — in the human nose and pharynx. It has been estimated that, at any given time, between 5% and 10% of people carry the organism. Sporadic cases of disease occur at the much lower annual rates of 1 to 5 per 100,000. The bacterium lives only in humans, passing from one person to another in aerosols; there are no other animal or environmental niches that it can colonize. It is therefore highly adapted to living in humans and has evolved a variety of mechanisms to evade our defences, including the ability to produce polysaccharide capsules that provoke a poor immune response, and very variable cell-surface proteins that represent an ever-changing target for the immune system.

The genetic basis for the adaptability of *N. meningitidis* is evident from the analyses of the genome sequence data by Parkhill *et al.*¹ and Tettelin *et al.*². These data reveal an abundance of diverse repeat sequences in each meningococcal strain. These sequences are likely to have a key role in mediating variation within each genome and hence in promoting the adaptability of the organism. A large proportion of repeat sequences is associated with genes encoding cell-surface structures that are involved in the interaction of the organism with the host and thus represent possible targets for vaccine development. Tettelin *et al.*² estimate that the expression of as many as 65 genes in the serogroup B strain MC58 might be altered by the gain or loss of nucleotides within iterative sequence motifs as a result of inaccurate DNA replication. The effect of such sequence changes on the expression of these genes and, ultimately, on the synthesis of the proteins they encode,

Bacterial genomics

ABC of meningococcal diversity

Ian M. Feavers

Meningococcal disease is dreaded by parents and medical practitioners alike for its rapid onset and the difficulty of obtaining a timely and accurate diagnosis. Although the causative bacterium, *Neisseria meningitidis* (Fig. 1, overleaf), is responsive to antibiotic therapy, these features of the disease pose a particular problem for treatment. Prevention of the disease through effective immunization is thus a more attractive alternative than therapy. For example, during the past five months new

vaccines have been introduced into the UK vaccination programme that, for the first time, offer protection to young infants against disease caused by *N. meningitidis* serogroup C. The success of this programme emphasizes the need for the development of vaccines against all pathogenic strains of *N. meningitidis*.

The complete genome sequences of the serogroup A and B organisms are now reported by, respectively, Parkhill *et al.* on page 502 of this issue¹ and Tettelin *et al.* in

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 centaurs (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 quarklets. Alford and Jaffe use ingenious computer experiments to argue that some long familiar, but hitherto enigmatic, particles are best interpreted as quarklets¹.

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}.