Rademacher and colleagues' results demonstrate the potential of STD NMR for the rapid, unequivocal identification of small molecules that bind to proteins. The technique offers several benefits — for example, no structural information about the protein is required, and the mode of binding of the molecules is also revealed. It has already been shown that, of all the current NMR screening techniques^{9–11}, STD NMR is the most efficient at identifying false-positive hits from high-throughput biological assays. Rademacher *et al.*¹ have provided further compelling arguments for the routine use of this technique in drug development. ■

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QUANTUM PHYSICS

Debut of the quarter electron

Eduardo Fradkin

A particle-like object with a quarter of an electron's charge is the latest find in a hotbed of quantum-physical experimentation, the fractional quantum Hall fluid. Its significance is more than esoteric.

On page 829 of this issue, Dolev *et al.*¹ report the detection of vortices in a fluid of electrons confined to two dimensions within a semiconductor structure that carry just 1/4 of the electron's charge. These 'quasiparticles' are an exciting find: according to theoretical predictions, their collective behaviour should be described by an unusual type of particle statistics known as non-abelian statistics. Above all, that could make them useful in an exotic, but highly promising, brand of quantum computer — the topological quantum computer (see News Feature on page 803)².

It is an established fact that, if a large magnetic field is applied perpendicular to the plane confining a soup of mobile electrons in a gallium arsenide semiconductor structure, the confined electrons can be made to enter correlated states with very unusual properties. When an electric field is applied in the plane, and at certain values of the 'filling fraction' ν (defined as the ratio of the number of electrons in the fluid to the number of magnetic field quanta penetrating through the sample), the electrons will flow without encountering any resistance. In such states, the conductivity transverse to the electric field, the Hall conductivity, takes on the universal value ve^2/h , where e is the electron charge, h is Planck's constant and $\nu = 1/m$; m is an odd integer.

This 'fractional quantum Hall effect' was discovered³ in 1982, and explained theoretically⁴ a year later — achievements that were rewarded with a Nobel prize in 1998. In the theoretical treatment, a quantum Hall state at

filling fraction $1/m$ will involve quasiparticles of fractional electric charge e/m . Such quasiparticles were first detected in 1997 through measurements of the statistical fluctuations of electrical current ('shot noise') on a single point contact in a quantum Hall device^{5,6}.

As well as having a charge somewhere between 0 and 1, these quasiparticles obey an intermediate form of quantum statistics that lies somewhere between the two established forms, Fermi–Dirac statistics and Bose–Einstein statistics. Fermi–Dirac statistics applies to systems of spin-1/2 'fermions', which obey the Pauli exclusion principle; particles covered include electrons, protons, neutrons, quarks, neutrinos and atoms with an odd number of constituent particles. Bose–Einstein statistics governs the behaviour of collections of integer-spin 'bosons': atoms with an even number of constituents such as photons, gluons and the yet-to-be-found Higgs particle.

A crucial difference between fermions and bosons is that a wavefunction describing two bosons is symmetrical when the two particles are swapped around in space: it does not change sign, and the wavefunctions before and after the particle exchange are said to have a phase factor of 0. The wavefunction describing two fermions, on the other hand, is antisymmetrical, flipping sign when particles are exchanged (phase factor π). But the phase of the wavefunction representing two quasiparticles in a two-dimensional system such as a quantum Hall fluid can change by an arbitrary phase factor, not just 0 or π . The precise value of this phase

50 YEARS AGO

'Recent discoveries at Olduvai Gorge, Tanganyika' By Dr. L. S. B. Leakey — Work has, in the main, been concentrated upon two sites: BK II at the lowest level of Bed II Olduvai, where it rests uncomfortably upon the eroded top of Bed I, and at SHK II at a level about 10 ft. above the base of Bed II ... At each of these two sites, living floors of Chellean man have been found, with big accumulations of stone tools, waste flakes and the fossilized remains of the animals upon which Chellean man lived ... In addition [were found] ... two hominid teeth. It was hoped that this important discovery, made at the close of the 1955 season, was the precursor of further finds of hominid material, but the hope has not been fulfilled and, therefore, a preliminary description of these teeth is given here.

From *Nature* 19 April 1958.

100 YEARS AGO

'The condensation of helium' — In *NATURE* of March 12 I have found a note referring to my experiments on the expansion of helium, made in consequence of my determinations on the isothermals of helium, at -252°C . and -259°C ., which yielded nearly -5°K . for the critical temperature of helium. The prosecution of the experiments has shown that what I observed in expanding the gas was not the evaporation of solid helium, but solution phenomena of solid hydrogen in gaseous helium. I have communicated to the Amsterdam Academy a note on my experiments, which at the moment leave the condensation of helium a yet undecided question. Of course, I have written the details to Sir James Dewar, and I hoped to do so to you to-day, but by pressing duties I cannot do it before to-night, and you will probably go to press before that letter reaches you. So I beg to be allowed to send you this first short notice.

H. Kamerlingh Onnes

From *Nature* 16 April 1908.

50 & 100 YEARS AGO

depends on both the nature of the two quasiparticles and how their paths through space-time intertwine or 'braid' — a latitude that led to these quasiparticles being dubbed 'anyons' (see also 'Braiding anyons'² on page 804). Anyons in a fractional quantum Hall fluid with filling factor $1/m$ are predicted to have fractional statistical phase π/m .

And indeed, the fractional quantum Hall states observed so far do largely follow that prediction. But remember that m is supposed to be an odd number; thus, the discovery some 20 years ago⁷ of a no-resistance quantum Hall state with an even denominator, at a filling factor of $5/2$, was initially puzzling. This state was soon realized to have very special properties^{8,9}: the associated quasiparticles would also have fractional charge, but would obey non-abelian statistics.

The definition of non-abelian statistics is complex, but one facet is that the state of a system of many quasiparticles obeying non-abelian statistics cannot be completely determined by knowing the quasiparticles' spatial coordinates. Several linearly independent wavefunctions are possible: a system with four quasiparticles, for instance, can have two different states. In this situation, the final state of an exchange interaction is a linear combination of the two initial states, and the braiding process as particles interact and their trajectories intertwine is encoded in a two-by-two matrix. More generally, for a system with $2n$ quasiparticles, there are 2^{n-1} states. In general, because any pair of quasiparticles in the quantum fluid can become intertwined, these states do not commute with each other — in other words, the order in which the exchange interactions between quasiparticles occur will determine the system's final state. This order-dependence of the state is crucial to the proposed use of non-abelian quasiparticles as the basic 'qubits' of information in a topological quantum computer^{2,10,11}.

Dolev and colleagues' detection¹ of a quasiparticle of charge $e/4$ is a first step in that direction. The discovery was made in a shot-noise experiment similar to those in which the original quasiparticle states were found^{5,6}. But the new measurement was much harder to make than those pioneering experiments: the $5/2$ state is so delicate that to study it requires a sample quality such that the mean free path of electrons before they collide with impurities in the semiconductor structure is very long (about 0.5 millimetres). It also requires low temperatures so that thermal fluctuations do not obscure the state.

Naively, one would have expected that the quasiparticle in the $5/2$ state, with its denominator of 2, would have a charge of $e/2$ (the multiplier of 5 in the numerator is not relevant to these considerations). But through a series of non-trivial consistency checks, Dolev *et al.* show that the charge at filling fraction $5/2$ is consistent with $e/4$, but not with $e/2$ (at integer filling fraction, the measured charge is just e and at a filling fraction $1/3$ it is $e/3$). For that reason, this

quasiparticle is also called a 'half-vortex' state.

Measuring the charge to be $e/4$ is a necessary, but not sufficient proof of a non-abelian state: there is a conceivable (but very unlikely) possible 'strongly paired' abelian state with the same filling fraction and charge. But an independent (and as-yet unpublished)¹² direct-current transport measurement at a point contact has not only measured the same value of the fractional charge, but also a tunnelling probability consistent with the predictions for a non-abelian state.

Further tests of the statistics of these intriguing quasiparticles at single point contacts will be the next step. They will be the key to the development of well-controlled, multi-contact quantum interferometers that are needed to test the properties of these intriguing quasiparticles, and thus to construct the qubits of a topological computer. ■

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SYSTEMS BIOLOGY

Genome rewired

Matthew R. Bennett and Jeff Hasty

Within a genome, genes are connected to each other through a complex network of interactions. One way to assess how robust and evolvable such genomic networks are is to introduce new links between unrelated genes.

Change in the genetic code is the driving force of classical evolution. Typically, it is thought that mutations in single nucleotides within the DNA sequence ensure such change, but other random alterations such as deletion, duplication and recombination of gene sequences can also occur. The robustness of organisms to such changes, which are necessary for evolution, is of fundamental interest, and so previous studies have investigated the sturdiness of gene-regulatory networks by either deleting¹ or overexpressing² individual genes. On page 840 of this issue, Isalan *et al.*³ describe a different

approach. They used high-throughput assay techniques to systemically rewire the architecture of the genetic network of the bacterium *Escherichia coli*. Their findings provide insight into not only the robustness but also the evolvability of this network.

The DNA sequence of a given gene generally consists of two parts: a regulatory promoter and an open reading frame (ORF). The promoter interacts with gene transcription factors to either increase or decrease the level of the gene's expression. Once transcription is initiated, the gene's ORF is transcribed into

Figure 1 | Intra-network communication. A simplified example of Isalan and colleagues' experiment³, in which they rewired the network of genes for *E. coli* transcription factors to create new network connections, is shown. Here, the existing network consists of four genes. The promoter of gene 3 (P_3) can be fused to the ORF of gene 1 (ORF_1) to create a new gene. On insertion of this 'hybrid' gene into the normal cell, the new gene creates new regulatory links (shown in red) that could alter the functionality of the network.