groups will certainly be rushing to test this. But translation from proof-of-principle to any therapy has many challenges. First, human cells would have to be given a built-in drug-selectable pluripotent marker by some efficient means. Second, potentially cancer-causing factors such as c-Myc must be avoided. Third, factors would need to be introduced by a method other than retroviral transfection; retroviruses can cause activation of cancer-causing genes and are therefore risky. Transient gene expression by direct introduction of membrane-permeable transcription factors into cells might be one way to achieve this, and screens for small molecules that can replace the gene products would also be useful. Despite these challenges, direct reprogramming of adult cells is clearly the way of the future, and promises to open up new frontiers in human biology and future therapy.

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QUANTUM MECHANICS

Interference in the matter

Markus Kindermann

Like any particle, electrons are also waves that can interfere with each other. Remarkably, this interference can even happen between electrons from different sources that have never physically interacted.

That electrons are waves can be conclusively demonstrated by sending them through two parallel slits, and observing the interference patterns between them that result as they diffract. Such double-slit experiments led a recent ranking of the most beautiful experiments in the history of physics[1]. They were first performed with electrons in free space[2], but similar experiments performed later showed that the wave character also extends to electrons in small metallic conductors at very low temperatures[3]. Neder *et al.*[4], whose results appear on page 333 of this issue, have moved on to a next level: they have demonstrated compellingly that electron waves can interfere even if they originate from independent sources.

The statement that classical electromagnetic waves always add up ('superpose') no matter where they come from is quite intuitive, and typically taken for granted. The waves emitted by different light sources are thus able to interfere. This interference can even be observed for sources that are incoherent, or out of phase, through a phenomenon known as the Hanbury Brown–Twiss effect[5].

The same assertion made of electron waves is less obvious. The natural inclination is to describe each electron by its own matter wave that is independent of the waves associated with other electrons. And electrons with different origins are, one might think, evidently different.

This last assumption in fact turns out to be flawed. All electrons are intrinsically identical, and there is nothing besides their state at any particular moment that distinguishes two electrons (or any two elementary particles of the same kind) from each other. This is one of the fundamental postulates of quantum mechanics, and it follows that all electrons in the Universe are described by the same matter wave that invisibly connects them.

This strange fact has profound consequences. One of these is the phenomenon of 'anti-bunching': electrons tend to avoid getting too close to each other in space. Anti-bunching has been demonstrated with electrons in free space[6] and in electrical conductors[7,8]. But Neder and colleagues' painstaking demonstration of the interference of electron waves from independent sources[4] beautifully shows the fundamental mechanism underlying the anti-bunching phenomenon.

Quantum interference experiments in electrical conductors are typically performed[3] by splitting an electron beam from one source into two parts that propagate along different paths and merge again at a 'drain' (Fig. 1a). The phase difference between the two waves at the drain depends, through the so-called Aharonov–Bohm effect, on the magnetic flux between the two paths, which in turn is determined by the magnetic field in the area the two paths enclose. By tuning the magnetic flux, one can thus adjust the relative phases of the waves, and dictate whether the electron wave interferes constructively (if the peaks of the waves from each path arrive at the drain at around the same time) or destructively (if a peak and a trough arrive simultaneously). The electrical current at the drain accordingly oscillates as a function of the magnetic flux.

Neder *et al.*[4] have performed a similar experiment, but with two electron sources and drains (Fig. 1b). Their cleverly engineered interferometer, following a proposal by Samuelsson *et al.*[9], splits the source electron beams such that every emitted electron can reach both drain contacts, but the two parts of any one source wave cannot interfere with each other. Ordinary 'one-particle' interference is thus ruled out: at the drain contact, interference can take place only between waves originating from different sources.

As these sources are independent, the two waves should be emitted with random and uncorrelated phases. All effects of wave interference on the mean current in each of the

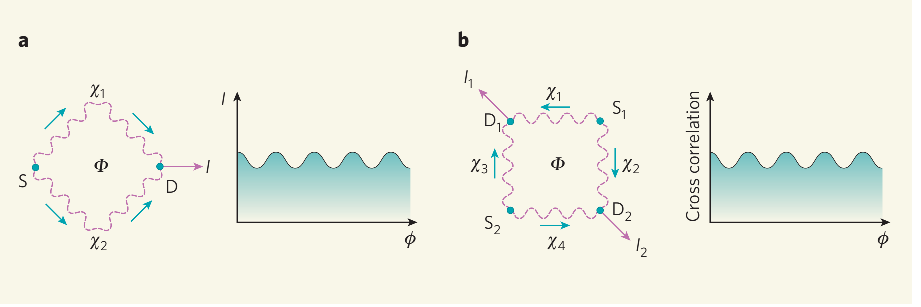

Figure 1 | One- and two-particle interferometers. a, In a single-electron interferometer, electrons enter from source S and choose between two paths to the drain contact D. The electron wave acquires different phases, χ_1 and χ_2, as it propagates along the two paths. In the presence of a magnetic flux, Φ, between the electron paths, the phase difference $\chi_1 - \chi_2$ depends on Φ. The electrical current, I, into D oscillates as a function of Φ. **b,** In the two-electron interferometer demonstrated by Neder *et al.*[4], electrons enter from two sources, S_1 and S_2. Every electron is able to reach two drain contacts D_1 and D_2, through which mean currents $\langle I_1 \rangle$ and $\langle I_2 \rangle$ flow. A magnetic flux, Φ, between the electron paths again influences the phases χ_1, χ_2, χ_3 and χ_4 acquired by the propagating electron waves. Interference takes place only between waves originating from different source contacts; this causes oscillations with Φ of the cross-correlations between the currents in the two drains, defined as $\langle I_1 I_2 \rangle - \langle I_1 \rangle\langle I_2 \rangle$. (For each electron to be able to reach both drains, the quantum mechanics of electron scattering requires two additional, but unmonitored drain contacts; for simplicity these are not shown.)

drains should therefore average to zero. But the product of these two currents, as measured by a quantity known as a cross-correlation, has interference contributions where these random phases appear in pairs with opposite signs. This interference should not average out: it should oscillate as a function of the magnetic flux between all electron paths from the sources to the drains. This is precisely what Neder *et al.* observe.

Although the above discussion conveys the essence of the correct quantum-mechanical description, it is considerably simplified. Formally, the measured current cross-correlations are described by quantum-mechanical amplitudes of two-electron processes. Cross-correlations receive contributions from two processes: when an electron from source 1 travels to drain 1, while an electron from source 2 flows into drain 2; and when an electron from source 1 goes to drain 2, while that from source 2 finishes up in drain 1.

Because the electrons are indistinguishable, one cannot say which of these two things has happened, and the quantum-mechanical probability amplitudes for the two processes interfere. Because, however, the two events involve electron waves propagating along different paths, they do so with a phase difference that oscillates with the magnetic flux. This is thus two-particle interference that occurs without the two particles ever having physically interacted.

Experiments such as that of Neder and colleagues are pushing into a new and exciting area of nanoelectronics: the coherent control of many-particle quantum states. This control is one of the fundamental requisites for quantum information processing with electrons. Indeed, it has been proposed that one of the core resources for a quantum computer — entanglement, where the states of two remote particles become correlated at the quantum-mechanical level — can be created and detected in the next generation of such experiments[9,10]. Moreover, cross-correlation measurements reveal central aspects of the physics of interacting many-electron systems[11], including characteristics of their quantum state[12]. More beautiful fundamental physics, and more exciting applications, should be expected from this fascinating field of endeavour. ■

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NEUROBIOLOGY

New order for thought disorders

Lorna W. Role and David A. Talmage

Can we really learn about complex human psychiatric disorders through genetic manipulations in mice? Yes, according to studies of how altering the gene encoding neuregulin 1 affects signalling in the mouse brain.

Schizophrenia is a spectrum of disorders. Its causes lie in a complex interplay of genetic, prenatal and developmental factors, as well as precipitating events in later life. Given the complexity of this uniquely human disorder, surely it is hubris to think that poking around at a rodent gene or two could shed light on the processes underlying it? Results from Li *et al.*[1] and Woo *et al.*[2], published in *Neuron*, suggest not. Building on a link first made in 2002 between schizophrenia and a protein called neuregulin 1 (Nrg1) and its signalling partners, the ErbB receptors[3,4], these authors highlight how targeted manipulation of Nrg1 in mice can help to illuminate the workings of neural circuits gone awry.

The devastating array of psychotic, emotional and cognitive symptoms that comprise schizophrenia is thought to be caused by an imbalance in the fine tuning, or 'synaptic plasticity', of connections between neurons in the brain. This plasticity reflects the ability, in healthy individuals, to adjust, adapt and alter the levels of excitability of the myriad synapses and circuits that link different brain regions in a manner precisely coupled to ever-changing demands.

Li *et al.*[1] and Woo *et al.*[2] use a range of techniques to manipulate the levels of Nrg1–ErbB signalling with high precision in space and time. They examine the effects of this regulation on different electrical, neurochemical and morphological measures of synaptic plasticity and reach two fundamental conclusions: first, that synaptic plasticity requires precisely the correct level of Nrg1–ErbB signalling; and second, that the absolute levels of Nrg1–ErbB

50 & 100 YEARS AGO

50 YEARS AGO

When the history of the twentieth century is written, the year 1957 will surely be noted, *inter alia*, as the one when women really began to press their claims for equal career opportunities with men... In one sphere, however, they have made little progress. This, of course, is the world of industry... [Some] manufacturers will only take women applicants when there are no suitable male applicants... Women should think carefully before deciding on particular careers in industry. In such careers as general management, personnel management, and industrial medicine, a break for marriage and child-bearing should be no handicap and should enable the middle-aged woman to return to industry even more fitted for her job. In rapidly evolving specialist fields, however, where knowledge of chemistry, physics and other natural sciences are involved, she may find it easy to secure a post before marriage but difficult to return to it afterwards.
From *Nature* 20 July 1957.

100 YEARS AGO

Notwithstanding the much improved statistics recently issued by the Lunacy Commissioners, thoroughly satisfactory materials are still wanting for solving the question whether the prevalence of insanity is or is not increasing. The importance of the problem... imparts special interest to a paper by Mr. Noel A. Humphreys on the alleged increase of insanity... This paper shows in a striking manner the value of scientific statistics in checking crude figures. The author expresses a decided opinion that there is no absolute proof of actual increase of occurring insanity in England and Wales, and that the continued increase in the number and proportion of the registered and certified insane is due to changes in the degree and nature of mental unsoundness for which asylum treatment is considered necessary, and to the marked decline in the rate of discharge (including deaths) from asylums.
From *Nature* 18 July 1907.