100 YEARS AGO

Science is cosmopolitan. Electricity abolishes time and envelops both hemispheres with a new idea as soon as it has emerged from the brain of the Thinker. Mechanics, by its space-annihilating power, has reduced the surface of the planet to such an extent that the human race now possesses the advantage of dwelling, as it were, on a tiny satellite. Both these agencies, then, combine to facilitate a rapid exchange of new ideas and commodities, as well as of those who are interested in them in whatever capacity. These considerations indicate some of the most momentous changes which have occurred in the world's history since the last century dawned … The enormous and unprecedented progress in science during the last century has brought about a perfectly new state of things, in which the "struggle for existence" which Darwin studied in relation to organic forms is now seen, for the first time, to apply to organised communities, not when at war with each other, but when engaged in peaceful commercial strife. It is a struggle in which the fittest to survive is no longer indicated by his valour and muscle and powers of endurance, but by those qualities in which the most successful differs most from the rest.

From *Nature* 3 January 1901.

50 YEARS AGO

During the past hundred years or so a variety of techniques has been devised for transmitting messages electrically from one point to another. It is only of recent years, however … that means have been provided for assessing quantitatively the commodity which is transmitted, namely, the 'information' content of messages, and of determining the extent to which existing techniques fall short of what may be attainable. This recent work proves to have a significance beyond the sphere of electrical communications. A new branch of science is emerging which reveals and clarifies connexions between previously largely unrelated fields of research concerned with different aspects of the processes by which living organisms — in particular man — collect, classify, convert and transmit information. A confluence of different fields of investigation is, of course, no new phenomenon in the history of science, but the wide recognition of a new connecting link can seldom have been so rapid as in the present case.

From *Nature* 6 January 1951.

ner in which gas is removed from a protoplanetary disk could have as much influence on the ultimate configuration of the planetary system as does the lifetime of the disk. A planet gravitationally tugs surrounding disk material, and this interaction can alter planetary orbits substantially. Although the possibility of significant planetary migration was predicted more than two decades ago[6], this type of interaction was largely ignored, because theory suggested that a planet would move faster as it approached a star. Planets capable of migrating a significant distance were therefore expected to spiral inwards to a hot death.

The discovery of the first Jupiter-mass planet orbiting at only one-twentieth of the Earth–Sun distance from its star[7] (with an orbital period of 4.2 days) led to the suggestion that planetary migration could be stopped very close to the star. This could happen either because the planet enters a gas-free orbit, cleared by magnetic processes close to the star, or because the planet experiences counterbalancing forces resulting from tidal motion on the star that is induced by the planet[8]. But these models do not account for the many giant planets subsequently discovered with intermediate orbital periods ranging from a few weeks to a few years[9]. Such planets are still too close to their star to have grown *in situ*[10], yet too far away for the proposed stopping mechanisms to operate. Might these giant planets have been migrating inwards only to be stranded as the star cleared away disk material from the inside outwards? The Space Infrared Telescope Facility[11], to be launched by NASA in 2002, will be able to observe disks containing hydrogen at much higher resolution, so hundreds of nurseries will soon be available to test this and other ideas of giant-planet formation. ■

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Neurobiology

Background inhibition to the fore

Ivan Soltesz and Zoltan Nusser

Investigations of a neurotransmitter receptor required for 'background' neuronal inhibition in mice show the importance of such inhibition in keeping neuronal excitability under control.

Why would you put microphones outside a concert hall to record the music inside? All they would pick up is muffled noise, although the sound would vary according to the music's highs and lows. On the other hand, with sufficiently sensitive microphones you could monitor several concert halls simultaneously, and thus keep an ear on the musical life of the whole town. The festival halls of the nervous system are the tiny junctions, called synapses, between nerve cells. And the molecular microphones — neurotransmitter receptors — are indeed found outside synapses, as well as inside them, on the surface of nerve cells[1,2] (Fig. 1). In fact, there might be more receptors outside synapses than inside[3]. But despite their abundance, the function of these 'extrasynaptic' molecular microphones has been elusive. Writing on page 89 of this issue, Brickley and colleagues[4] make a significant contribution to deciphering their importance.

Brickley *et al.* have studied inhibitory neuronal signalling mediated by the neurotransmitter γ-amino-butyric acid (GABA). Inhibition takes place as a consequence of GABA binding to its receptors — the so-called $GABA_A$ receptors (Fig. 1). The result is a decrease in the probability that a neuron reaches its threshold for firing an action potential, the signal of a nerve cell. In an earlier study[5], the same group described two distinct types of inhibition in a group of neurons — the cerebellar granule cells — that are involved in coordinating movements. 'Phasic' inhibition of these cells is mediated by discrete pulses of high concentrations of GABA released at synapses, where GABA acts on synaptic $GABA_A$ receptors. In contrast, 'tonic' (continuous) inhibition is due to the persistent activation of extrasynaptic $GABA_A$ receptors by the low concentrations of GABA in the extrasynaptic space — rather like the continuous, muffled music from many concert halls picked up by the microphones.

The $GABA_A$ receptors underlying these two forms of inhibition differ in terms of their molecular composition and proper-

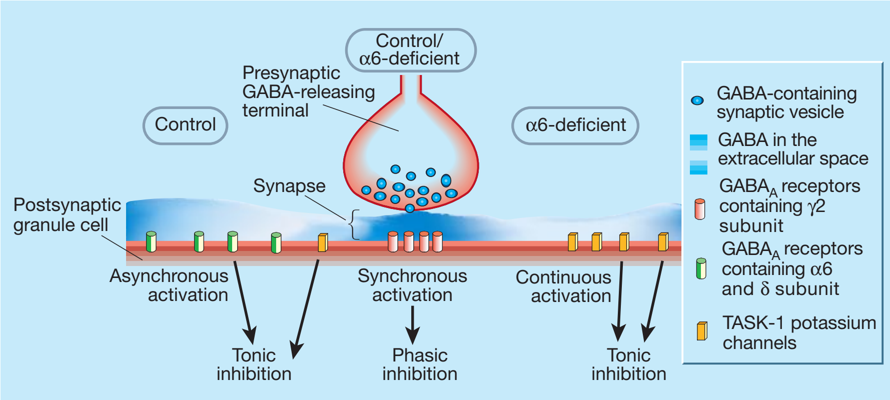


Figure 1 **Background and synaptic inhibition of neuronal firing. The excitability of cerebellar granule neurons is regulated by inhibition, which is generated by the opening of certain ion channels. This increases the membrane's electrical 'leakiness' (conductance), making the cells less responsive to excitatory inputs. Inhibition can result from the binding of the neurotransmitter GABA to its receptors, and/or from the opening of potassium channels. Centre, in control mice and those that lack the α6 subunit of the GABA$_A$ receptor, the release of GABA from synapses opens intrasynaptic, γ2-subunit-containing GABA$_A$ receptors, generating a quickly rising, quickly decaying (phasic) inhibitory conductance. Left, in control mice, GABA diffusing away from several synapses activates extrasynaptic GABA$_A$ receptors in an asynchronous manner, generating noisy, tonic inhibition. This is akin to music from several concert halls being picked up by a microphone outside the halls. Right, in α6-deficient mice the extrasynaptic GABA$_A$ receptors containing the α6 and δ subunits are missing. But, as shown by Brickley *et al.*[4], tonic inhibition is restored because the granule cells increase their expression of TASK-1 potassium channels.**

ties[6]. Receptors containing α6 and δ subunits are only present outside synapses, whereas receptors comprising the γ2 subunit are concentrated inside synapses[7]. As a result, the extrasynaptic receptors have higher sensitivity (affinity) for GABA, and are not desensitized by the prolonged presence of this neurotransmitter. This makes them ideal for mediating tonic inhibition. So, to determine the importance of tonic inhibition in controlling neuronal excitability, Brickley *et al.*[4] used mice that had been engineered to lack the α6 subunit[8].

The authors could not detect any GABA$_A$-receptor-mediated tonic inhibition in brain slices from the genetically altered mice, an observation that fits well with the known role of the α6-containing extrasynaptic receptors in generating tonic inhibition. In control animals, drugs that block the GABA$_A$ receptors have a significant effect on the amount of excitation required to bring a granule cell to its firing threshold. These drugs had no such effect in the α6-deficient animals[4]. As it is only the tonic form of GABA$_A$-receptor-mediated inhibition that is missing in these mice, this lack of an effect shows that this type of inhibition controls the excitability of granule neurons.

But if extrasynaptic GABA$_A$ receptors were truly important, one might expect that deleting them would result in severe alterations in excitability within the neuronal circuits of the cerebellum. This brain region is important in coordinating movements, so specific defects in the behaviour of α6-deficient mice would be predicted. But these mice do not show any measurable behavioural problems[8]. Had the story ended here, sceptics might have mused that tonic inhibition is not named background inhibition for nothing. Fortunately, Brickley *et al.* avoided this hasty conclusion, and go on to provide a surprising solution to the puzzle.

The authors show that the amount of excitation needed for granule cells to emit an action potential when the GABA$_A$ receptors are not blocked by drugs is similar in control and α6-deficient mice. They argue — on the basis of their electrophysiological and molecular data — that a compensation mechanism is at work in mice lacking the α6 subunit (Fig. 1). They suggest that this mechanism involves the increased expression of a continuously active type of potassium channel. Their results point to the so-called TASK-1 channels[9], which also inhibit cellular excitability in a continuous (tonic) manner.

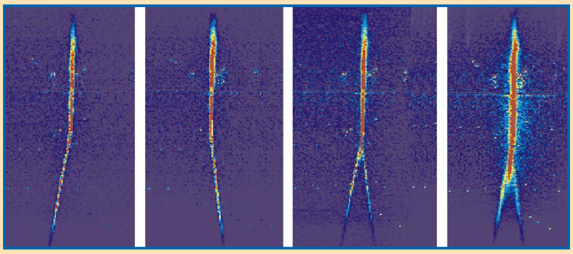
These data are the best evidence yet that the extrasynaptic GABA$_A$ receptors regulate neuronal excitability. Given that biology tends not to fix things that are not important, the fact that neurons found a way to compensate precisely for the loss of extrasynaptic GABA$_A$ receptors suggests just how significant the receptors are. Although Brickley *et al.* did their experiments in brain slices *in vitro*, compensation by the TASK-1 channels took place in the intact brain — a strong indication that tonic inhibition also existed *in vivo*. But the level of expression of many other GABA$_A$-receptor subunits (as well as that of the TASK-1 channels) is also altered in the α6-deficient mice[10].

Atom optics

A matter of choice

Similar to how light fibres transformed optics, physicists hope guided atom beams will revolutionize atom optics. Two groups have developed an atomic analogue of a beam splitter, which until now has only been used to separate atoms moving in free space. By guiding atoms along a surface, greater control has been achieved by D. Cassettari *et al.* (*Phys. Rev. Lett.* **85**, 5483–5487; 2000) and D. Müller *et al.* (http://xxx.lanl.gov/abs/physics/0003091).

Modern atom interferometers use beam splitters to split up matter waves and recombine them to produce sensitive interference patterns, used in precision measurements of gravity and the rotation of the Earth. But such free-space beam splitters can only separate beams by small angles thus limiting the scope of the experiments.



J. SCHMIEDMAYER

In their study, Cassettari *et al.* guided cold lithium atoms along a Y-shaped current-carrying wire patterned on the surface of a semiconductor chip. Fluorescence images taken of the wire show the beam splitter in action (see above). When current was passed through only one of the output wires, the atoms take the left or right fork (left two images). By varying the current in each arm, the splitting fraction of the atoms can be changed continuously (50:50 in right images). The angle between the two beams is 15°.

In similar work, Müller *et al.* split a beam of cold rubidium atoms along two current-carrying wires on a glass substrate. Neither of these studies split a coherent matter wave — in which all the atoms are in step with one another. This has been shown for atoms in free space, but needs to be done with guided atoms if they are to be used in precision atom interferometers. One solution might be to use a coherent atom source, such as a Bose–Einstein condensate. **Sarah Tomlin**

Developing 'inducible-knockout' mice, in which the expression of the α6 or δ subunits can be stopped quickly, might avoid the problems of compensatory alterations and may clarify the roles of tonic inhibition in brain function.

The next major advance in this field might not come from studies of genetically altered mice. The development of drugs that specifically block receptors containing the δ subunit, for example, would provide tools for unravelling the precise function of background inhibition, not just in the cerebellum but also in other brain areas where such receptors are expressed extrasynaptically. The task of understanding the function and importance of extrasynaptic $GABA_A$ receptors is an exciting one, and it is clear that neuroscientists have already lost their inhibition about listening to background noise. ■

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Quantum engineering

Squeezing entanglement

Nick Bigelow

Quantum entanglement between two particles is a spooky connection that means measuring one has an instant effect on the other. Connecting many atoms in this way would be the first step towards a quantum computer.

If a street magician with two identical coins told you he could predict which way up your coin would land — heads or tails — simply by tossing his coin first, you probably wouldn't believe him. But what if he told you that, because of the laws of physics, your toss had to turn out the same as his toss? Not convinced, you try it and find that, yes, it is true. And it remains true, time after time, toss after toss. By some mechanism, there is a surprising correlation between the behaviour of the two coins. What's going on? Well, it could be that these two coins have somehow been prepared in a remarkable quantum state known as an entangled state. On page 63 of this issue Sørensen *et al.*[1] provide physicists with an exciting new recipe for creating such entangled states from an unusual sample of atoms known as a Bose–Einstein condensate.

The concept of entanglement is one of the most fundamental features of quantum mechanics, yet it is one of the most puzzling, non-intuitive and 'non-classical' aspects of the theory. The consequences of entanglement are so disturbing that Albert Einstein called them "spooky action-at-a-distance". But is entanglement real? Can we actually create entangled states? More importantly, can we observe the effects of entanglement? The answer to all of these questions is yes, at least on the rather remote and microscopic scale of a single pair of photons. More recently, entanglement has also been demonstrated using an ensemble of four carefully prepared atoms[2,3]. So far, though, entanglement has not been observed in any macroscopic (human-sized) system.

The physics of entangled states is also at the heart of a new generation of futuristic technologies, including recent plans for quantum computers and strategies for quantum teleportation. Making entanglement a tangible, exploitable phenomenon, however, requires the creation of entangled states of many particles — entanglement on a macroscopic scale. Moreover, it is important to achieve this with massive particles that can easily be stored and transported, rather than with photons, which have no mass. One of the exciting aspects of the work of Sørensen *et al.*[1] is that, by following their guidelines, researchers may soon be able to do just that — entangle the many particles within a Bose–Einstein condensate (BEC). A BEC is a large sample of particles (as many as 10 million ultracold atoms) that share exactly the same quantum state.

For the purposes of entanglement, theorists[1,4–6] are especially interested in a type of BEC in which the atoms have multiple internal states. This was first achieved experimentally for a 'double condensate' composed of two clouds of rubidium atoms,[7] each cloud having a different internal spin, which can be thought of as a tiny bar magnet. More recently, researchers have been able to transfer a BEC of sodium atoms from a magnetic trap into an optical trap formed from a focused laser beam[8]. Unlike a magnetic trap, this new laser-trapping technique is not sensitive to the spin state of the atoms, so physicists can vary the complex magnetic properties of these 'spinor' condensates[9,10].

In the quest to create entangled states for large collections of atoms, the 'squeezed' state is of particular interest. To appreciate the relationship between squeezing and entanglement, it is important to have a sense for quantum 'noise'. At the heart of quantum theory is the idea that nature is inherently probabilistic. In classical physics you can predict the outcome of a coin toss if you know the exact starting conditions. But in quantum theory you can speak only of the probability of a certain outcome, no matter how much detail of the problem is known. Inherent in this picture is the idea that the measurable properties of a given state are accompanied by unavoidable fluctuations.

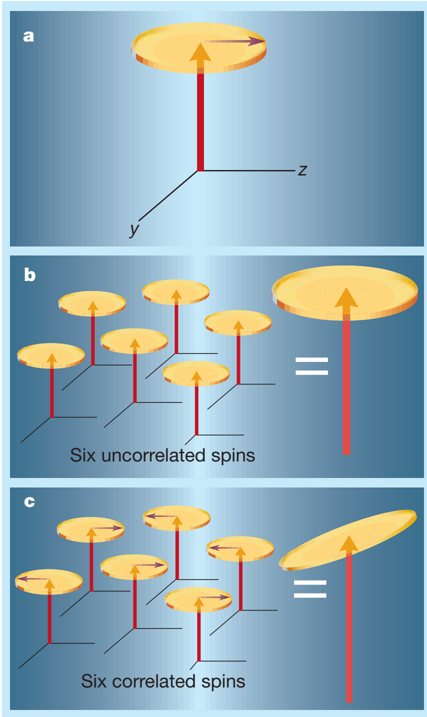

Figure 1 **Putting the squeeze on spin. Simple particles, such as electrons, have a quantum mechanical 'spin', which can be either up or down.** a, **This quantum spin is aligned mostly in the 'up' direction, but there is a quantum mechanical uncertainty in the component of the spin in the transverse direction, which is represented by a small circular disk.** b, **In a dilute gas of** ***N*** **atoms with uncorrelated spins, the collective uncertainty is a disk of diameter** $\sqrt{N}$ **times each individual uncertainty disk.** c, **In a gas of atoms with correlated spins, such as the Bose–Einstein condensate modelled by Sørensen** ***et al.***[1]**, the uncertainty disk becomes an ellipse, which is narrower along the** ***y*****-axis than the** ***z*****-axis. This means that measuring the left–right component of the spin is 'noisier' than the in–out component — it has been squeezed.**