These results[5] provide new insight into how organs develop a blood supply — a question with significance for tissue regeneration and tumour growth. For tumours to grow or tissues to regrow (for example, during the healing of burned skin), they need oxygen, which at first reaches cells by simple diffusion from existing blood vessels. But when the gap between the rapidly multiplying cells and the blood vessels exceeds the limit of diffusion, distant cells become deprived of oxygen (hypoxic). These cells increase their expression of VEGF and other angiogenic molecules by activating hypoxia-inducible transcription factors, so attracting new blood vessels, which restore oxygenation[1,4,7]. When such hypoxic upregulation of VEGF is impaired, angiogenesis in tumours is reduced[8] and, surprisingly, motor neurons degenerate[6].

LeCouter *et al.* show that the expression of EG-VEGF is also upregulated by hypoxia, providing a molecular explanation as to how growing endocrine glands acquire not only more numerous but also more specialized blood vessels. Moreover, because arteries are produced from different precursors to veins, and smooth-muscle cells are generated from distinct precursors in different organs[4,9], their results also raise the possibility that tissue-specific angiogenic molecules control these processes, too.

Do tissue-specific blood-vessel regulators contribute to the excessive angiogenesis that occurs in cancers and inflammatory disorders? We don't yet know, but we should perhaps hope that they do. LeCouter *et al.*[5] show that the forced overexpression of extrinsic EG-VEGF in rat ovaries leads to the production of cysts, with excessive numbers of blood vessels nearby. If the abnormal expression of intrinsic EG-VEGF likewise contributes to angiogenesis in ovarian disorders, then it might be possible to develop drugs that selectively block this process. Inhibition of VEGF does block deregulated ovarian angiogenesis[10] but, because VEGF is non-selective, such drugs might increase the risk of motor-neuron degeneration[6] and heart failure because of poor blood supply[1]. Blocking EG-VEGF would be expected to have fewer side effects.

On the flip side of the treatment coin, LeCouter *et al.*'s results might also have implications for inducing the growth of new blood vessels in blood-deprived (ischaemic) tissues. A good blood supply is crucial; for example, a lack of blood supply to the heart can cause heart failure[1]. VEGF and other general angiogenic molecules have been tested for their ability to stimulate angiogenesis in ischaemic heart tissue, and have proved successful in animals.

But the downside of the long-term use of such general molecules is that they might also stimulate angiogenesis elsewhere — in hidden tumours, for example[11]. Moreover, although these molecules work in animals, initial results from clinical trials reveal only modest long-term benefit, so it remains unknown whether VEGF alone can induce the necessary formation of stable blood vessels. Additional angiogenic molecules might be needed, such as placental growth factor, which amplifies the activity of VEGF in ischaemic but not normal heart tissue[12]. However, this combination has not yet been shown to stimulate angiogenesis. Given that coronary vessels are derived from different precursors to vessels in other tissues, heart-specific angiogenic molecules might be necessary, and safer than more general molecules.

Research into angiogenesis has arrived at the critical stage of translating the findings from studies of mice to humans. LeCouter *et al.*'s study[5] has raised the hope that we might be able to achieve this goal more rapidly, and more safely, than we thought. ■

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Quantum engineering

Protecting the quantum world

Juan Pablo Paz

When quantum systems interact with the environment, classical properties emerge — a process known as decoherence. Although decoherence is unavoidable, it may still be possible to manipulate the outcome.

The world around us looks classical even though the fundamental laws of physics are based on quantum mechanics. At the atomic level, electrons and protons are blurred entities that cannot be described as point-like particles following trajectories. But macroscopic objects have well defined properties: they are either here or there, and not everywhere. So how does the classical world arise from the quantum?

The consensus today is that classical behaviour is an emergent property of quantum systems, induced by their interaction with the environment. This interaction, a fact of life for complex macroscopic objects, is responsible for the process of decoherence[1,2], which is the biggest obstacle to building a viable quantum computer. An attractive idea to control decoherence is to manipulate the environment — so-called environment engineering. As Carvalho *et al.*[3] describe in *Physical Review Letters*, a cold trapped ion could be manipulated in this way by applying a number of judiciously chosen laser fields to create an environment in which the stable state of the ion can be chosen (almost) at will.

Decoherence makes most of the states of a quantum system unstable, so that only a small subset of all possible states, the 'pointer

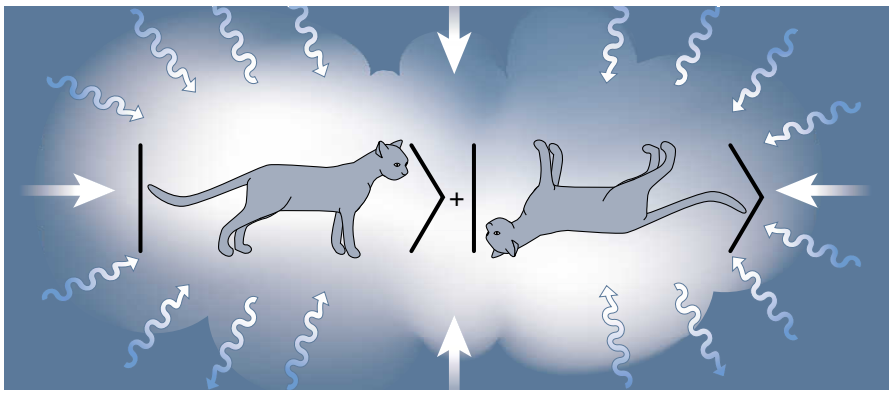

Figure 1 **Environment engineering. Quantum states are unstable against the process of decoherence, which is induced by their interaction with the environment. But by using the ideas of environment engineering, physicists can protect some quantum states and prevent their natural degradation. A proposal by Carvalho *et al.*[3] suggests that it is possible to do precisely this with the motional state of a cold, trapped ion. This system, when illuminated with an appropriately chosen set of laser fields, can exist in a state that is a small version of the famous dead-and-alive Schrödinger cat state.**

states', survive the interaction with the environment. So pointer states, dynamically selected by the environment, are the only ones in which macroscopic systems are allowed to exist. In the real world, pointer states are selected by nature. But in recent years, physicists have found valuable ways to modify the properties of the decoherence process in some systems. They do this by creating an artificial environment that is tailored to control the properties of pointer states.

Ignacio Cirac, Peter Zoller and co-workers[4] originally devised the idea of environment engineering in 1996. Their work contained the basis for a general method that has been tested by impressive experiments[5] in which an ion is stored and laser-cooled in a special trap. Ion traps use a particular configuration of oscillating electromagnetic fields to confine the ions to a well-defined region of space, and have been used successfully in high-precision spectroscopy, as well as to demonstrate the feasibility of quantum information processing. The trapped ion can be made to interact with an environment whose properties are designed by the experimenter.

Carvalho *et al.*[3] propose a way of preparing pointer states that can persist even in the presence of the form of decoherence that is most effective in disturbing the motion of an ion in a trap: that generated by the interaction with random fields in the trap electrodes. Even with this disturbing interaction, the authors claim their method can be used to select a single pointer state for the centre of mass of a trapped ion, which becomes stable under the effect of the artificial environment. This quantum state can be chosen at will by manipulating the frequency and intensity of the applied laser fields. The method will only protect a single stable state, so rather than specifying several pointer states, which may be relatively stable, the procedure prepares and protects a single specified state in the presence of natural decoherence. The proposal seems to be within the reach of current technology but would require 'stiffer' traps than those used in current experiments.

The method's basic strategy is simple. Suppose that you want to prepare and protect a given quantum state, ψ. The first step of the procedure is to find an operator, D, such that ψ is the only state annihilated by D (that is, $D\psi = 0$). The authors then explain how to design the laser fields, which drive internal transitions of the ions into rapidly decaying states, in such a way that the artificial environment interacts with the ion precisely through the operator D. The key feature of the method is that the net effect of the laser fields is to drive the irreversible decay of the motional state of the ion towards ψ. If the desired state is a given superposition of energy eigenstates (with given coefficients), the method determines the necessary values of the amplitudes of the driving laser fields.

There is a practical limitation to the method. To protect a state in which the ion occupies two positions at once separated by a distance of about 80 nanometres, it is necessary to apply about 15 laser beams to the ion. This is because the number of laser beams is proportional to the number of terms in the expansion of ψ. Increasing the separation into the mesoscopic domain becomes increasingly hard. This kind of quantum state (in which the ion occupies two locations at once) illustrates the most counterintuitive features of quantum mechanics, and is a laboratory cousin of the famous Schrödinger's cat (whose fate is to be in a superposition of alive and dead states). Thus, while the method does not seem to be useful for preparing mesoscopic or macroscopic Schrödinger cat states, it could serve to prepare and protect states of small and tender quantum kittens. The authors also describe in detail how to prepare other interesting quantum states.

A remarkable feature of the debate on the transition between quantum and classical behaviour is that, for the first time in its rather long history, experiments are probing this boundary and playing an important role[6,7]. Environment engineering, as discussed by Carvalho *et al.*[3], is a useful proposal that will certainly be tested soon in more detail. Moreover, there are other fertile proposals on how to fight decoherence. Many of these ideas, which were born in the context of studies on quantum information processing[8] (such as quantum error correction), are also being examined experimentally. Most of these are 'controlled decoherence' experiments, which a few years ago appeared to be just thought experiments exploring the nature of the transition from quantum to classical physics. In the near future, a new generation of experiments, in which decoherence is caught in the act, will be able to probe the fuzzy border between the quantum and the classical worlds. ■

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Immunology

Antibody alterations

Alberto Martin and Matthew D. Scharff

In an immune response, antibody molecules are altered so they can bind to intruders more strongly. Some of the molecules that determine which alteration process predominates have now been tracked down.

One of the ways in which the immune system fights off intruders is to produce antibodies, which bind to and neutralize foreign molecules (antigens). The immune system — specifically B cells — must be able to generate enough different antibodies to recognize every possible antigen, so extraordinary antibody diversity is generated before exposure to foreign antigens. But these primary antibodies almost always have low affinity for their targets, and cannot neutralize pathogens or toxins. So, after exposure to an antigen, the variable (V) regions of the antibody genes, which encode the antigen-binding site, acquire many changes — some of which result in higher-affinity binding sites. In some species, this occurs by a process known as gene conversion; in others, by 'somatic hypermutation'[1–3]. On page 921 of this issue, Sale and colleagues[4] describe how they used a chicken B-cell line, which normally undergoes gene conversion, to search for factors involved in the diversification of the variable regions. Their results answer some questions, and raise new ones, about the relationship between gene conversion and somatic hypermutation.

In some species, such as chickens, rabbits, pigs and cows, the diversification of the V region occurs mainly by gene conversion. This process basically involves the acquisition of new DNA sequences, copied from parts of nearby pseudogenes (regions of DNA that are similar to genes but cannot encode a protein) on the same chromosome. In other species, such as sharks, frogs, mice and humans, the V regions of the antibody genes acquire large numbers of single base changes, by somatic hypermutation[1–3]. It is not clear why these two different processes evolved, and why their species distribution is so sporadic[1]. Moreover, the biochemical mechanisms underlying gene conversion and somatic hypermutation have been hard to identify. These questions formed the backdrop for Sale *et al.*'s work[4].

The authors used the chicken DT40 B-cell line, which is unusual among cultured animal cells because it can undergo high