Figure 2 | Ice nucleation in wave clouds. Wave clouds — shown here — form when air is lifted up over a mountain, and water vapour in the upper reaches of the air current condenses to form water droplets. As the air current descends, the condensed water evaporates. Such an air current can bounce up and down, and with condensation at the crests of such undulations a wave-like cloud pattern can emerge. Durant and Shaw[2] argue that 'contact nucleation inside-out' may explain the extent of ice formation occurring in the downwind region of such currents.

becomes the thermodynamically preferred state. But the transformation first requires a germ of the crystal, a crystallite, to form. Such crystallites are created spontaneously as a result of the incessant jiggling around of molecules in the liquid, caused by thermal fluctuations. However, most of the crystallites dissolve back into the liquid. To grow, crystallites must overcome the barrier posed by surface tension — the unfavourable interactions between molecules in the crystalline arrangement and those in the surrounding liquid. A large enough crystallite that can overcome the barrier is termed the critical nucleus; the process by which it forms is called nucleation. Once formed, the critical nucleus will grow irreversibly and ice will form.

Water can be supercooled because crystal nucleation and growth may take a long time. But the processes become faster as the temperature falls, and they can be accelerated further by solid particles that act as a substrate for crystal nucleation. This is known as heterogeneous nucleation. It is of particular importance in the atmosphere, where water exists as small droplets that are suspended alongside particles that may act as heterogeneous ice nuclei. These nuclei may either be immersed in the bulk of the water droplet, or come into contact with the droplet surface.

Shaw and co-workers have examined the phenomenon of contact nucleation in lab experiments. As discussed in the first paper[1], they set out to compare the efficiency of an ice nucleus in causing crystallization when it is immersed in the droplet and when it is in contact with the droplet's surface. They used an experimental set-up in which the same drop of water, with the same ice nucleus immersed or in contact, is repeatedly cooled and heated hundreds of times. During each cooling run, they recorded the temperature at which the droplet froze. The result is an estimate of the most likely temperature at which droplets freeze, which in turn is a measure of the efficiency of the particular nucleation mechanism.

They find that the freezing temperature when the ice nucleus is in contact with the droplet is about 5 °C higher than when it is immersed in the droplet, showing that contact nucleation is a more effective mechanism than immersion nucleation. This conclusion is consistent with previous data. But the new results show that the efficacy of contact nucleation is not caused by transient effects related to an ice nucleus coming into contact with a water droplet, such as mechanical disturbance due to collision, or to the dissolution of part of the ice nucleus. Instead, it has simply to do with the fact that the nucleus is in contact with the droplet surface. This is a useful distinction, which may also be related to a proposal[3] that homogeneous nucleation (nucleation without an ice nucleus) is most effectively initiated at the droplet surface.

In the second paper[2], Durant and Shaw describe a variation of the experiment in which the ice nucleus is initially immersed in the droplet, but in conditions under which the droplet slowly evaporates as it is cooled and heated. The nucleus then eventually comes into contact with the surface of the droplet, but this time from inside the droplet (Fig. 1). In this situation, too, the authors observe a rise in the freezing temperature.

This 'contact nucleation inside-out' is evidently an efficient nucleation mechanism. But is it of special significance? Yes, claim the authors. They suggest that it may account for the high rates of ice nucleation in wave clouds (Fig. 2), when the cloud droplets are evaporating at temperatures that are too high for the rates to be explained by homogeneous nucleation. Re-examination of existing observational data may provide support for this idea.

Shaw and colleagues' results[1,2] will need to be validated, but they are appealing in their clarity and possible relevance to ice nucleation in the atmosphere. Extension of the experiments, perhaps with a clever choice of ice nuclei and varying droplet sizes, may also provide further evidence about homogeneous surface nucleation[4]. Another route forwards is through computer simulations, which have provided insight into heterogeneous nucleation[5] and homogeneous crystal nucleation in water[6]. Such simulations could be extended to provide a fresh angle on homogeneous and heterogeneous nucleation at surfaces. ■

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CELL BIOLOGY

Relays at the membrane

Roel Nusse

The Wnt signalling pathway is a major route by which the cell conveys information from its exterior to the nucleus. A gap in the sequence of signalling proteins has now been filled.

The process of signal transduction allows a cell to receive messages from its environment and transfer this signal from the membrane through the cytoplasm and into the nucleus. Here the signal alters the expression of the various genes that contribute to the cell's response. Regardless of the signal's nature, the general logic of the transduction pathways that are triggered by protein ligands is roughly the same. The signalling protein binds to a receptor on the cell's surface, which consequently undergoes a conformational change. Commonly, the receptor is then tagged with a phosphate group by an associated protein kinase enzyme. The phosphorylation allows the receptor to recruit cytoplasmic signalling

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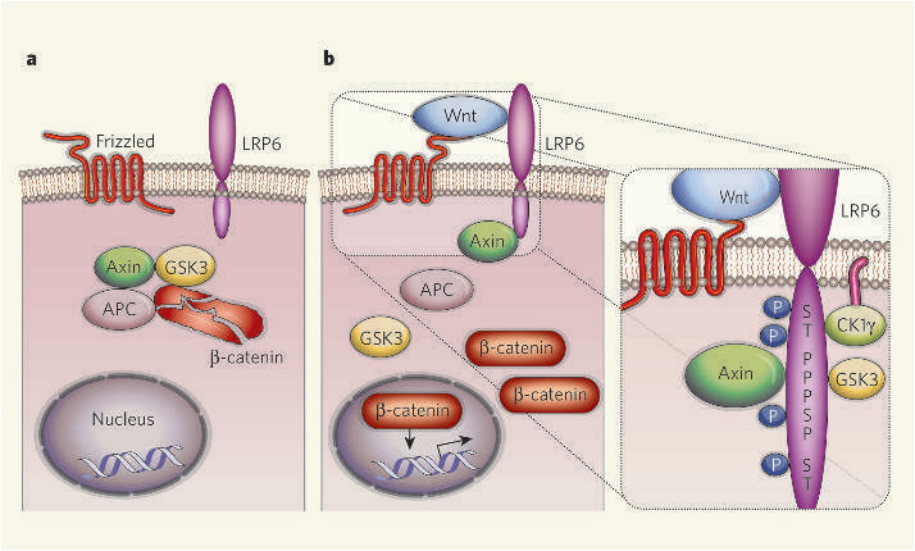

Figure 1 | Crucial kinases. **a**, In cells not activated by Wnt, a complex between β-catenin, Axin, APC and GSK3 causes phosphorylation of β-catenin and its consequent destruction. The Wnt receptors LRP6 and Frizzled are unoccupied. **b**, Without Axin, β-catenin is stabilized and it enters the nucleus to control gene expression. Inset, binding of Wnt to cells results in phosphorylation (P) of LRP6 residues in its cytoplasmic tail. Zeng *et al.*[1] and Davidson *et al.*[2] show that this is catalysed by the GSK3 and CK1γ protein kinases. CK1γ is attached to the membrane by a lipid anchor domain. Several other sites on LRP6 that become phosphorylated are not shown here. The phosphorylated LRP6 recruits Axin, removing it from the β-catenin destruction complex and stabilizing β-catenin.

components that initiate a cascade of events resulting in changes in gene expression. Two papers in this issue[1,2] show that signal transduction initiated by the protein Wnt — a major regulator of developmental processes — follows a similar strategy but with some interesting new twists.

Compared with other signalling cascades, the Wnt pathway[3] is exceptional in its complexity, with numerous components and intricacies that go beyond this short overview. One of the key players in the pathway is β-catenin, a protein that resides in the cytoplasm and, once activated, is responsible for relaying the signal into the nucleus. When cells are not exposed to Wnt, β-catenin is destined to be destroyed (Fig. 1a). This process is triggered by phosphorylation of β-catenin, catalysed by the protein kinase GSK3 and assisted by the β-catenin-binding partners Axin and APC. The Wnt signal activates two membrane receptors, the Frizzled and LRP6 molecules, which form a complex and trigger signalling to the cytoplasm that halts the breakdown of β-catenin[4]. But how are the events at the receptor level coupled to β-catenin, and how does β-catenin escape degradation?

The discovery, several years ago, that the Axin protein can bind to the cytoplasmic tail of the LRP6 receptor[5], provided a mechanism by which Axin is seized from β-catenin[6]. This changes the fate of β-catenin: instead of being destroyed, it accumulates and enters the nucleus, where it executes a programme of Wnt-induced gene expression (Fig. 1b). Crucially, the binding of Axin to the LRP6 tail is promoted by phosphorylation of LRP6 (ref. 7), suggesting that protein kinases must be recruited to the receptor after activation by Wnt[8].

The identity of these kinases is the subject of the papers by Zeng *et al.* (page 873 of this issue)[1] and Davidson *et al.* (page 867)[2]. To appreciate their function, some detail is necessary. Phosphorylation of LRP6 occurs on several clusters of serines and threonines, with a central proline-rich motif (PPPSP) as a hallmark (Fig. 1b; inset). As in many other cases of cluster phosphorylation, there is a priming phosphorylation event after which the remaining residues become modified as well. Proline-rich environments are conducive to phosphorylation by GSK3, so Zeng *et al.*[1] tested the PPPSP motif on LRP6 for activity. They found that the serine in the motif is indeed modified by GSK3, leading to activation of signalling. Strikingly, GSK3 is now known to phosphorylate a number of Wnt signalling components, including β-catenin, Axin and APC. GSK3 used to be thought of as a negative component in Wnt signalling: when it was deleted genetically, Wnt-response genes were activated because β-catenin was no longer phosphorylated or degraded. But we now know that it acts positively on LRP6, activating Wnt signalling — an effect missed in the genetic experiments because of its negative involvement further down the pathway.

Residues next to the PPPSP motif also get phosphorylated. What is the enzyme? Based on an expression screen, Davidson *et al.*[2] identify this kinase as a member of the CK1 family, CK1γ. Beyond biochemical experiments showing that CK1 can phosphorylate the LRP6 tail, Davidson *et al.* demonstrate that the gene encoding CK1γ is required for Wnt signalling to occur, and that overexpression of this gene is sufficient to activate the pathway.

As with GSK3, the diminutive name CK1 does not do justice to the numerous functions of the CK1 family in cell physiology. Within this family, CK1γ is an outlying relative, and, interestingly, it has a membrane anchor in the form of a fatty-acid attachment site. Eliminating the fatty-acid anchor domain from CK1γ results in loss of Wnt signalling, implying that this kinase needs to be associated with the membrane to act.

So now there are two LRP6 kinases, raising the question of how these enzymes become activated by the Wnt signal. Here the two papers differ in their conclusions. Zeng *et al.* suggest that the GSK3-dependent phosphorylation of the PPPSP motif is induced by Wnt. By contrast, Davidson *et al.* conclude that PPPSP is usually phosphorylated in cells, in the absence of Wnt; that is, it is constitutively phosphorylated. They propose that it is the subsequent modification of neighbouring residues, catalysed by CK1γ, that is dependent on the Wnt signal. This discrepancy needs to be resolved, but if phosphorylation of LRP6 by GSK3 is indeed signal dependent, it would be an exception to the general rule that GSK3 activity is constitutive in cells. GSK3 is involved in many signalling pathways, but it acts on all its multitude of targets without being triggered by a signal from outside. By contrast, CK1γ activity is clearly stimulated by Wnt signalling, as adding Wnt protein to cells leads to modification within a few minutes.

There are many questions remaining. For example, it is not known how CK1γ activity is regulated or whether the enzyme becomes physically associated with LRP6. Because of its unique function, this enzyme provides an attractive novel target for Wnt-specific inhibitors.

When we now compare Wnt signalling events at the receptor level to other signalling pathways, there are many parallels but one difference. In the Wnt signalling pathway, ligand binding triggers the formation of a receptor complex, and protein kinases modify the receptor tails, leading to recruitment of cytoplasmic factors. In other signalling pathways, however, receptor-induced protein phosphorylation amplifies the signal, and the receptor-associated kinase acts as a catalyst for the modification of many substrate molecules. In this regard, Wnt signalling is peculiar: Wnt-induced LRP6 phosphorylation acts by titrating away a negative regulator of signalling, Axin. This implies a stoichiometric rather than a catalytic mechanism of signal transduction. On the other hand, Axin is present in very low concentrations in cells, much lower than the other components in the β-catenin destruction complex[9]. So, is it possible that Axin actually plays a dynamic role, shuttling between the receptor and the destruction complex and acting as an amplifier of Wnt signalling rather than as a simple scaffold? ■

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QUANTUM INFORMATION

Remember that photon

Philippe Grangier

Storing single photons in atomic memories, and releasing them at a later time, is a required step on the way to quantum repeaters and long-distance quantum cryptography networks. This step has now been taken.

The basic unit of quantum information, the quantum bit or qubit, can be encoded in various physical quantities, such as the polarization states of photons, or the spin states of atomic nuclei. To make qubits practically useful, random coupling of them with the external world — an effect known as decoherence — must at all costs be avoided or corrected. This makes photons (the quanta of light) particularly suitable for qubit transmission, as they can travel over very long distances with very little decoherence. For qubit storage, encoders such as atoms come into their own: they can be kept in 'traps' for long periods, again avoiding deleterious decoherence effects from outside.

In experiments detailed in two papers in this issue, Chanelière *et al.* (page 833)[1] and Eisaman *et al.* (page 837)[2] contrive to combine the two crucial aspects of transport and storage: they generate a single photon on demand, catch it and store it in a remote atomic memory, and release it some time later. The advance is potentially highly significant for the field of quantum cryptography, also known as quantum key distribution (QKD). This emerging technology promises absolutely secure transmission of the key codes that are essential to decipher any encrypted message (Box 1).

Previous advances in quantum key distribution have owed much to the fact that photons that are used to encode the keys are very good qubit carriers: apart from maintaining a robust quantum state throughout transmission, they can be detected efficiently and with low levels of noise. But light signals cannot — whether viewed classically or quantum-mechanically — propagate over infinite distances in optical fibres. They are in fact dampened exponentially with distance: by a factor of two over 15 kilometres, and by a factor of a hundred over 100 kilometres. In classical optical telecommunications, this problem is solved by using simple, readily available devices known as repeaters, which can amplify and reshape the transmitted signal. But a good classical repeater is no use in the quantum regime: it is much too noisy, and creates so many errors that any quantum key being transmitted would not survive. To put the problem in more quantum-mechanical terms, a classical repeater breaks down quantum entanglement. This delicate phenomenon is associated with very strong, non-classical correlations between the states of two widely separated qubits, and is a crucial element of all quantum communication schemes: in effect, it allows any useful qubit to be 'teleported' directly to its destination, avoiding transmission losses[3].

So quantum communication must reinvent the repeater concept, using quantum hardware that preserves coherence. This is feasible in principle[4]: a quantum repeater would be nothing more than a small quantum processor. The exact number of qubits that would have to be stored and processed in such a repeater to ensure high-fidelity quantum communication over thousands of kilometres is an open issue. But it is likely to be in the range of tens or hundreds — much lower than the number required for a fully fledged quantum computer. The proposal in 2001 of the so-called DLCZ quantum information protocol[5], in which an ensemble of many atoms stores just one qubit, was a significant step towards a functioning quantum repeater. This protocol uses a process known as spontaneous Raman scattering, in which an incident photon is scattered inelastically (that is, with a change in its frequency) between two atomic ground states.

Chanelière *et al.*[1] and Eisaman *et al.*[2] exploit the DLCZ protocol to set up a controllable single-photon source for further experimentation. After initially preparing all the atoms of an ensemble in one ground state, a weak laser pulse (which nevertheless contains many photons) is used to induce a Raman transition of just one atom within the ensemble. As a consequence, a single spontaneous Raman photon is scattered, and its detection heralds the creation of a collective, delocalized, single-atom excitation of the ensemble. This excitation can be stored for as long as all the atomic levels in the sample maintain a constant phase relationship (a period known as the coherence time of the ensemble). This excitation can be converted back into a single-photon light field of controllable direction, intensity and frequency using another pump pulse (for a review of recent experimental work in this area, see ref. 6).

Once a single photon has been generated, the second stage is to catch it, and then release it again, in a second, remote atomic ensemble. The trick here is to use a second atomic ensemble that is opaque to the photon — absorbing rather than transmitting it — and that can only be made transparent by using an extra laser beam. This transparency arises through a neat and extensively studied interference phenomenon, electromagnetically induced transparency (EIT). If the EIT laser

Box 1 | Key codes: classical versus quantum cryptography

The purpose of quantum key distribution is to share a secret key among legitimate users that allows them and only them to decode messages. Some sort of key that allows a message to be deciphered is essential to all forms of encryption. Common, classical schemes used in electronic commerce can set up a key by relying on computationally difficult problems, such as the splitting of a very large number into two prime-number factors, that are in fact — given unlimited patience and computational power — breakable.

The only totally secure classical encryption system is the 'one-time pad', which uses a key that is as long as the message itself and that may be used only once. This solution leads to what is known as the key distribution problem: as the key must be transmitted between sender and recipient, it is itself susceptible to interception by an eavesdropper. In the classical world, someone can listen in on such a signal passively without changing the bits that make it up at all, so neither sender nor recipient need ever know that their communication has been intercepted.

Not so in the world of quantum communication. Qubits do not possess definite values such as the 0 or 1 of classical bits; rather, they represent a so-called coherent superposition of physical states such as the polarizations of a photon. A fundamental feature of quantum mechanics is that the mere act of observing such a superposition will cause it to 'collapse' into a definite state. This means any attempt by an eavesdropper to intercept a key made of qubits can be easily spotted by sender and recipient. Given this knowledge, and as long as the errors created by the eavesdropper (or any other perturbation) are not too large, it should be possible to build up an errorless and perfectly secure key. **P.G.**