Surprisingly, it emerged later that fruitflies have circadian clocks not only in the brain, but also in every cell[4]. Moreover, studies in mice showed that many mammalian organs harbour circadian clocks[5]. The question was: do clocks outside the suprachiasmatic nucleus have physiological roles?

Two sets of findings suggested that mammalian clocks outside the brain participate in metabolic regulation. First, expression of enzymes, transporters and receptors that regulate metabolism fluctuate robustly throughout the day[6]. Second — and unexpectedly — circadian clocks outside the suprachiasmatic nucleus are adjusted on the basis of feeding time rather than the light–dark schedule[7,8]. For example, the cellular energy sensor AMPK controls the stability of cryptochromes and may contribute to nutrient entrainment of the clock in the liver[9].

General disruption of clock genes profoundly affects both locomotor activity and feeding behaviour, and so may indirectly alter metabolism. This problem can be overcome by organ-specific inactivation of genes such as *Bmal1*, which leaves general behavioural patterns intact. 'Conditional' ablation of *Bmal1* in this way demonstrated a role for retinal circadian clocks in visual perception[10] and for liver circadian clocks in glucose regulation[11]. Notably, liver-specific ablation of *Bmal1* caused lowered blood glucose levels only during the times of day when mice naturally fast. This observation supports a role for mammalian circadian clocks outside the brain in predicting recurrent daily changes in metabolic demand — in this case[11] leading to increased glucose production by the liver during times of expected fasting.

Despite these advances, many questions remain about the function of various circadian clocks. For instance, although disruption of *Bmal1* — either in all cells or specifically in the liver — alters metabolism, the effects are mild and, depending on the nature of disruption, metabolic outcomes differ. Do clocks in other organs counteract some of the effects of the liver clock?

Marcheva *et al.*[1] show that the mouse pancreas also harbours a functional circadian clock, with individual pancreatic islets having robust clock function even when outside their normal tissue environment. The islet clock seems to consist of the same components as other mammalian circadian clocks, and drives rhythmic expression of genes involved in insulin sensing, glucose sensing, and islet growth and development. These clocks are therefore crucial for the specific metabolic needs and functions of islet cells (Fig. 1).

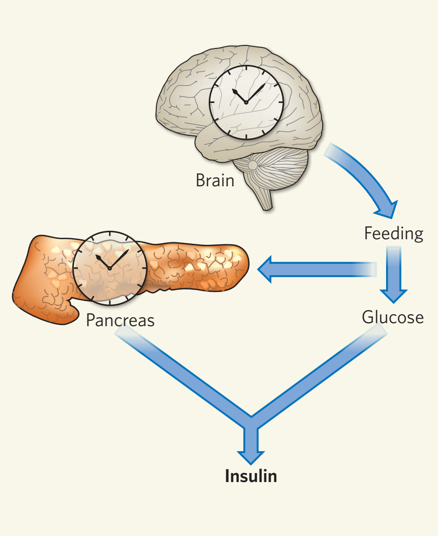

Figure 1 | Going by the local clock. In response to the daily light–dark cycle, the clock in the suprachiasmatic nucleus of the brain regulates metabolism by affecting rhythmic behaviour such as feeding. Marcheva *et al.*[1] show that the pancreas also has a local clock, which directly affects insulin secretion in response to high blood glucose levels.

The authors[1] find that, compared with normal mice, mice in which circadian-clock function is generally disrupted produce less insulin, both under resting conditions and after a shot of glucose. Moreover, these animals' pancreatic islets are smaller and less adept at insulin production than are those of normal mice. These results indicate that the islet clock directly regulates insulin production. But is reduced insulin secretion due to a loss of the islet clock specifically, or to indirect mechanisms associated with the loss of other circadian clocks? To answer this question, Marcheva *et al.* specifically disrupted the circadian clock in the pancreas by ablating *Bmal1* there. They note that the resulting mice have profoundly elevated levels of blood glucose under resting conditions, as well as impaired insulin secretion in response to a dose of glucose.

Marcheva and co-workers' observations should put to rest any doubts as to whether CLOCK and BMAL1 have crucial roles in the regulation of metabolism, independently of their roles in controlling behaviour. They also provide further evidence for the idea that mammalian circadian clocks outside the brain enable animals to synchronize physiological processes with recurring, and therefore predictable, changes in metabolic demand.

One enduring difficulty in the study of circadian clocks' role in metabolism is whether disruption of CLOCK and BMAL1 leads to metabolic defects by affecting circadian rhythms or through activities unrelated to their clock function. Answering this question will require a technical breakthrough — for example, a small-molecule clock inhibitor — enabling selective disruption of clock function without ablating CLOCK or BMAL1 proteins entirely. Regardless of these semantic details, by linking CLOCK and BMAL1 activity to insulin production, Marcheva and co-workers' data hint at a potential alternative strategy for the treatment of diabetes, through enhancing the activity of these proteins. ■

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CONDENSED-MATTER PHYSICS

Bringing the noise

Chetan Nayak

Noise is usually viewed as the bane of measurements. But a neat experiment has confirmed a long-standing prediction for an exotic electronic state of matter through the increase of noise in charge transmission.

On page 585 of this issue, Bid *et al.*[1] report the observation of neutral particles propagating upstream along the edge of certain fractional quantum Hall systems — exotic electronic phases of matter that belong to the larger family of topologically ordered systems. The result confirms a never-before-verified theoretical prediction and has possible implications for quantum computation.

In a topologically ordered system[2], or topological phase of matter, the long-distance, low-frequency properties of the system are immune to local perturbations. A subset of these exotic systems, termed non-Abelian topological phases, are those in which a collection of the system's particle-like excitations, called quasiparticles, has many states with the same energy. (If there is a unique state, the topological order is said to be Abelian.) Braiding these quasiparticles — that is, winding their trajectories around one another to form a braid — causes these states to be rotated into each other in a way that depends only on the topological class of the braid and the particular form of topological order that is manifested in the phase. Thus, quantum information that is stored in these states is automatically protected from local perturbations. This property is the basis for proposed architectures for topological quantum computing[3,4]. But it also makes it very difficult to experimentally determine when a system is in a topological phase of matter and, if it is, which type of topological phase.

Fortunately, many topologically ordered systems have low-energy excited states that are confined to their boundaries[5]. These edge excitations can, in some topological phases, be particle-like in nature and are thus often called quasiparticles. They carry energy and may carry electrical charge. The topological properties of the bulk are imprinted on the dynamics of the edge excitations — an example of a 'holographic' correspondence. Thus, experiments that probe electrical charge transport along the edge can also shed some light on the braiding properties of quasiparticles in the bulk. However, the correspondence between bulk and edge is not one-to-one. The structure of the edge excitations depends not only on bulk properties but also on precisely how the edge of the system is engineered. As a general rule, the more sharply defined the edge of the system, the simpler the relationship to the bulk[6]. But even in the case of wider edges, experiments probing the edge can help identify a bulk topological phase.

Many topological phases have been found in the fractional quantum Hall regime, in which electrons are trapped at a planar interface or 'quantum well' in a semiconductor device and subjected to low temperatures and a strong magnetic field. They have been identified primarily by their Hall conductance, $\sigma = \nu e^2/h$, where e and h are the electrical charge of an electron and Planck's constant, respectively, and ν is a fraction (hence, the name fractional quantum Hall effect). The Hall conductance, a topological property of the bulk and also a dynamical property of the edge, is the ratio between the electric current and the voltage drop at right angles to the current; in a quantum Hall state in a large device there is no current parallel to the voltage drop, so the longitudinal conductance vanishes. When it has a constriction, or quantum point contact, the quantum Hall device is small at its narrowest point, and the electric current perpendicular to the voltage drop is suppressed from the quantized value that it assumes in a large device, whereas the current parallel to the voltage drop becomes non-zero. The dependence of the longitudinal electric current on the temperature and applied voltage is an important probe of the edge excitations of a quantum Hall state[5].

Even at fixed temperature and applied voltage, the electric current through a point contact fluctuates in time because it is due to a series of discrete events at which electrical charge passes through the point contact. Remarkably, the fluctuations, or noise, in the current are another probe of the edge excitations of a quantum Hall state[7]. In some temperature and voltage regimes, the noise is proportional to the average current through the point contact, and the ratio between the two gives a measure of the electrical charge of the quasiparticles responsible for carrying current. The fractional charge of quasiparticles in the $\nu = 1/3$ state was measured[8,9] in this way.

There is broad agreement between experimental observations and the theoretically predicted properties of edge excitations, although a few puzzles and discrepancies remain. In my opinion, these are due to overly simplistic modelling of quantum point contacts and uncertainty about the sharpness of the edge, and they will disappear as we learn more about these devices. However, there is one crucial aspect of the theory of edge excitations that has not been experimentally confirmed. All fractional quantum Hall states must have at least one branch of edge excitations that propagate in the direction prescribed by the magnetic field — 'downstream'. But some states are also predicted to have one or more branches that propagate in the opposite direction — 'upstream'[10]. However, it has not, until now, been possible to directly observe the upstream excitations[11].

In their study, Bid and colleagues[1] have developed a novel method by which they could observe these upstream excitations through their effect on noise at a quantum point contact. The authors excite neutral quasiparticles downstream from the point contact by running current from an external source downstream from the point contact to an external drain even further downstream. Because none of the injected current makes it to the point contact, this cannot affect the total average current through it. However, the electric current creates neutral quasiparticles at the current source and along the edge. If the neutral quasiparticles are counter-propagating, they will then move upstream to the point contact, where they will increase the current noise. Bid *et al.* find such an effect at those fractional quantum Hall states at which theory predicts neutral quasiparticles with an upstream mode of propagation, namely $\nu = 2/3$, $3/5$ and $5/2$. They do not see such an effect at those values of ν at which theory predicts that all modes propagate downstream, such as $\nu = 2/5$.

The authors' observation of a counter-propagating neutral mode for the $\nu = 5/2$ state is particularly intriguing. Theoretical work[12–14] suggests that this state is non-Abelian in nature and, therefore, might provide a platform for topological quantum computation[15]. There is some indirect experimental evidence that the state is non-Abelian[16]. There is also one experiment[17] that may, at $\nu = 5/2$, have directly observed the effects of the peculiar statistics that non-Abelian quasiparticles obey, but more data are needed to unambiguously establish this result. There are two primary non-Abelian candidate theories: the Moore–Read (MR) Pfaffian state[12] and the anti-Pfaffian state[18,19]. Although they are very similar, they differ in several ways, including the nature of their edge quasiparticles. The anti-Pfaffian state will always have upstream neutral edge quasiparticles. The MR Pfaffian state can have upstream neutral edge quasiparticles in a wide edge but not in a sharply defined one[20]; it is not known whether the edge in Bid and colleagues' experiments is wide enough to be in the former situation. The most plausible Abelian candidate state does not have upstream modes. Thus, the observation of upstream modes at $\nu = 5/2$ is indirect evidence that this state is non-Abelian.

It would be premature to conclude at this stage that the $\nu = 5/2$ state is the anti-Pfaffian state. But if the sharpness of the edge can be more fully understood, and if the increase in noise can be made more quantitative, then an experiment of this type could even distinguish between these two non-Abelian candidates. Even without making this finer distinction, however, Bid and colleagues' technique has already confirmed a key aspect of the theory of edge excitations of fractional quantum Hall states. It has also produced further independent evidence that the $\nu = 5/2$ state is non-Abelian, which would make it a candidate platform for fault-tolerant quantum computation. ■

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