The United Nations Environment Programme has been considering how evidence for cultural learning in animals should inform conservation policies. This is of particular note for animal populations that migrate through, or are located in, areas that cross national borders. A panel of scientists has recently assembled key evidence and recommendations related to this in a report for policymakers[6]. The findings of Jesmer *et al.* underscore the importance of such considerations if wild-animal populations develop skills that enhance their survival over a time span of centuries. In the case of migratory skills, the blocking of traditional migratory routes by human-made barriers such as roads could lead to the loss of animals' hard-won cultural knowledge.

Conservation efforts need to take into account the significance of such knowledge, the scope of which we are perhaps only starting to recognize[1,10], and our understanding of which is extended by long-term perspectives such as those reported by Jesmer and colleagues. Cumulative culture of this kind might be more widespread in nature than was previously assumed, and not unique to humans. Accordingly, understanding the gulf between these and our own species' cumulative cultures might require us to consider more-specific aspects of cultural transmission, including modes of learning such as intentional teaching, or cultural contents, such as adopting qualitatively improved materials for tools. As the latter example suggests, human culture could progress by incorporating qualitatively distinct innovations. It remains a controversial question whether this ability is also found in animals — can they go beyond just achieving gradual refinements in a skill, such as green-wave surfing, to add a transformative new approach to solve a particular problem? ■

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QUANTUM PHYSICS

Unexpected noise from hot electrons

Experiments reveal a previously unreported type of electronic noise that is caused by temperature gradients. The finding has practical implications, and could help in detecting unwanted hotspots in electrical circuits. **SEE LETTER P.240**

ELKE SCHEER & WOLFGANG BELZIG

A fundamental feature of any electrical measurement is noise — random and uncorrelated fluctuations of signals. Although noise is typically regarded as undesirable, it can be used to probe quantum effects and thermodynamic quantities. On page 240, Shein Lumbroso *et al.*[1] report the discovery of a type of electronic noise that is distinct from all others previously observed. Understanding such noise could be essential for designing efficient nanoscale electronics.

A century ago, the German physicist Walter Schottky published a seminal paper that described different causes and manifestations of noise in electrical measurements[2]. Schottky showed that an electric current produced by an applied voltage is noisy, even at absolute zero temperature, when all random heat-induced motion has stopped. This noise is a direct consequence of the fact that electric charge is quantized — it comes in discrete units. Because the noise results from the granularity of the charge flow, it is called shot noise.

It was already known at the time of Schottky's work that, in systems that are in thermal equilibrium, noise with distinctly different properties from shot noise comes into play at non-zero temperatures — this is known as thermal (Johnson–Nyquist) noise. Today, shot noise is a key tool for characterizing nanoscale electrical conductors, because it contains information about quantum-transport properties that cannot be revealed from mere electric-current measurements[3,4].

Shein Lumbroso *et al.* studied junctions composed of single atoms or molecules suspended between a pair of gold electrodes. The authors fabricated the electrodes by breaking a thin gold wire into two parts and bringing the parts gently back into contact. They evaporated hydrogen molecules on to this device, which is known as a mechanically controllable

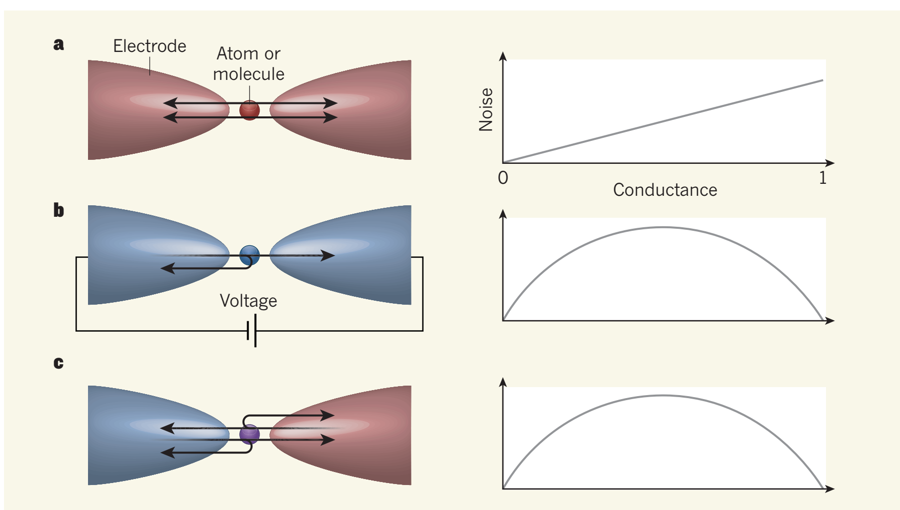

Figure 1 | Three types of electronic noise. Shein Lumbroso *et al.*[1] report experiments in which single atoms or molecules are suspended between the tips of two electrodes. **a**, At a non-zero temperature (red), electrons flow between the two electrodes (arrows). The electrical signal associated with this motion contains a type of noise called thermal noise, which varies linearly with electrical conductance (shown here in units of the quantum of conductance). **b**, If a voltage is applied to the device, electrons flow from one electrode to the other, and can be backscattered from the atom or molecule. The resulting signal contains 'shot' noise that is present even when the device is at absolute zero temperature (blue). Shot noise has a characteristic (non-monotonic) dependence on conductance. **c**, If a temperature gradient is applied to the device (indicated by rising temperatures from blue to purple to red), electrons flow from both of the electrodes and can be backscattered. The authors show that the resulting electrical signal contains a previously unreported type of noise, which they term delta-T noise. This noise has the same dependence on conductance as shot noise.

break junction, so that individual hydrogen atoms or molecules were captured between the tips of the electrodes, thereby establishing an electrical contact.

The resulting junctions constituted a single quantum-mechanical transport channel in which electrons could be transmitted from one electrode to the other with a probability that could be adjusted by varying the openness of the channel. This set-up provided an ideal test bed for exploring the properties of the so-far-overlooked noise contribution.

The authors observed a strong increase in electronic noise when they applied a temperature difference between the two electrodes, compared with when the electrodes were at the same temperature. The additional noise, which the authors call delta-T noise, scaled with the square of the temperature difference. It exhibited the same dependence on electrical conductance as shot noise (Fig. 1).

Shein Lumbroso and colleagues explained their finding using the quantum theory of charge transport, known as the Landauer theory[5], which has been developed in the past few decades. This theory incorporates both shot noise and thermal noise, and has been tested intensively down to the atomic and molecular scale[3]. It has been found to accurately describe many experimental observations obtained when working entirely in thermal equilibrium, or when applying small voltages. The authors took a closer look at the theory, and found that it includes a noise component that occurs when solely a temperature difference is applied across a junction: delta-T noise.

It is well established that an electric current can arise from a temperature difference in the absence of an applied voltage — a phenomenon called the Seebeck effect. However, delta-T noise is not the shot noise associated with this thermally induced current. The authors' results indicate that delta-T noise is larger than this shot noise, and has a different dependence on the temperature difference. Instead, the results suggest that delta-T noise arises from the discreteness of the charge carriers mediating the heat transport.

Because the Landauer theory is widely used, it is surprising that delta-T noise has not previously been observed. The importance of carefully considering all of the spatial temperature differences and resulting electric currents to understand the current flow in atomic and molecular contacts was pointed out in a 2013 paper[6], but implications for noise were not addressed.

Shein Lumbroso *et al.* found that the Landauer theory accurately describes all of the characteristic properties of delta-T noise. In this sense, their experiments are yet another beautiful demonstration of the theory. But the work also conveys a key message: careful design and rigorous analysis of experiments are required when studying any of the details of quantum transport.

The authors' discovery also has practical implications. In particular, quantum-transport experiments that are not entirely in thermal equilibrium could show strongly enhanced noise, which might be mistaken for noise arising from interactions between the charge carriers or from other subtle effects. Experimentalists who wonder about finding unexpectedly high noise in their electric-current measurements might wish to revisit their set-ups to search for unintentional temperature gradients. The most practical application of the authors' work is probably that the enhanced noise could be used to detect unwanted hotspots in electrical circuits.

For the future, researchers could explore the relationship between delta-T noise and shot noise that has a nonlinear dependence on applied voltage, which was observed earlier this year in high-voltage experiments on atomic junctions[7]. Such studies could also be expanded to more-complex quantum-transport experiments — for instance, those on artificial atoms called quantum dots. Because of the sensitivity of delta-T noise to the properties and interactions of charge carriers, the phenomenon might become a valuable tool in quantum-transport investigations. ■

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CANCER

Thousands of short cuts to genetic testing

Gene editing has now been used to introduce every possible single-nucleotide mutation into key protein-coding regions in the cancer-predisposition gene *BRCA1*, to identify the variants that are linked to cancer risk. **See Article p.217**

STEPHEN J. CHANOCK

For decades, cancer geneticists have been trying to understand which changes in the sequence of the *BRCA1* gene predispose affected individuals to developing breast or ovarian cancer. Extensive efforts have focused on interpreting the plethora of genetic variants in *BRCA1*, using clinical observations to determine whether this or that variant warrants patient counselling about options for medical intervention[1]. Generally, *BRCA1* variants are sorted into three categories[2,3]: benign variants, which cause no concern; deleterious variants, which can confer a high risk of cancer; and an unsettling intermediate known as variants of uncertain significance (VUS). Hardest to classify are variants that arise only rarely, of which there are thousands for *BRCA1*. Conventionally, genetic sleuthing has focused on families or populations within which certain mutations occurred at an unusually high frequency, exposing the effects of deleterious variants. But on page 217, Findlay *et al.*[4] report an innovative laboratory-based approach to assessing the effect of thousands of variants across protein-coding regions of *BRCA1*.

The BRCA1 protein is a key tumour suppressor, and is essential for a DNA-repair pathway called homology-directed repair. Mutations that prevent this function lead to the death of cultured human cells of a strain called HAP1 (ref. 5). Findlay and colleagues made clever use of this property of HAP1 cells to screen for deleterious *BRCA1* variants.

The authors used a gene-editing approach called CRISPR–Cas9 to accurately mutate each nucleotide in 13 crucial protein-coding regions (exons) of *BRCA1* into every other possible base, one nucleotide at a time — an exhaustive technique known as saturation genome editing (SGE). In each experiment, they edited 1 exon of *BRCA1* in 20 million HAP1 cells simultaneously. They left the cells to grow *in vitro* for 11 days, then sequenced the edited exon to gauge the frequency at which each variant was present in the cell population. From these data, they designated each variant as functional (if its frequency indicated that homology-directed repair was active in cells harbouring that variant), non-functional (if the frequency was lower than average, indicating that the variant led to cell death), or intermediate (Fig. 1).

Findlay *et al.* found that their results fit well with those obtained from a complementary assay designed to test whether homology-directed repair occurs normally in *BRCA1* mutant cells,