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colleagues' contrast-modulation method could be extended to many crystallized membrane proteins, facilitating this process. ■

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QUANTUM PHYSICS

Atomic envoy enables molecular control

A technique for manipulating molecules uses an intermediary atom to query a nearby molecule's energy state and produces 'quantum superpositions' of these states, a prerequisite for extremely high-precision spectroscopy. [SEE LETTER P.203](#)

WES CAMPBELL

Laser cooling and related techniques are routinely used to produce pure quantum states of atoms in the gas phase that enable the atoms to be measured and controlled with unprecedented precision. Put two atoms together in a molecule, however, and things become more than twice as difficult — the complexity of even simple molecules severely diminishes the effectiveness of tools based on repeated light scattering. But if an atomic ion is confined in the same electromagnetic trap as a molecular ion, as demonstrated last year by Wolf *et al.*¹, the atom can be cleverly used as an envoy to facilitate indirect communication with the molecule. On page 203, Chou *et al.*² extend this idea by cornering a molecule into a single quantum state using an atomic emissary, and then preparing and measuring quantum

superpositions (in which the molecule is simultaneously in more than one energy state), while retaining the molecule for subsequent measurements. This type of control over quantum superpositions is the gold standard for manipulating isolated quantum systems, and is a necessary ingredient of extremely high-precision spectroscopy.

Spectroscopy allows precision measurement of the energy states of atoms and molecules. It typically involves shining light on a sample and looking for a response that depends on the frequency of that incident light. To ensure that the energies being measured correspond to the species of interest (rather than its interaction with a solvent or substrate, which tends to shift these energies), the preferred method for recording high-resolution spectra uses gas-phase molecules isolated in a vacuum. However, because such molecules are free

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to rotate and vibrate, absorption of energy (whether from the probe light or, for instance, thermal radiation from the container) tends to chase molecules out of the energy state being probed, in a process called bleaching.

Bleaching creates a headache for the spectroscopist, who must then choose between sacrificing precision by working with a large, hot sample to guarantee that a few molecules can be found in each energy state, or working with a small, cold sample of molecules that can provide high precision, but only a few photons of signal. This conundrum is essentially unique to molecules, because their states pack the energy 'landscape' much more densely than even the most complicated atoms. New cooling methods^{3,4} might soon obviate this dilemma, but the strength of the atomic-envoy technique (known as quantum-logic spectroscopy⁵) is that it can produce plenty of signal while keeping the molecule inside the trap — the atom acts as a spokesperson to the outside world, but its conversations with the molecule occur strictly in whispers.

Chou and colleagues demonstrate their spectroscopy technique using a calcium atomic ion (Ca^+) and a calcium hydride molecular ion (CaH^+). Following the approach of Wolf *et al.*¹, the authors confine the two ions in an electromagnetic trap in an ultrahigh vacuum (Fig. 1a). The ions are coupled by their mutual electromagnetic repulsion, and therefore have shared motion. The authors cool the atomic ion using a laser, which causes this motion to

Figure 1 | Molecule manipulation. Chou *et al.*² report a technique for preparing and non-destructively detecting the internal quantum state of a molecular ion using an atomic ion, extending recent work by Wolf *et al.*¹. **a**, The authors confine a calcium ion (Ca^+) and a calcium hydride ion (CaH^+) in an electromagnetic trap (not shown). The two ions repel each other because both are positively charged, which causes the ions to have a shared motion (dotted line). The CaH^+ ion is initially in an unknown internal quantum state, illustrated here by a rotation in a random direction (white arrows). **b**, Chou and colleagues cool the Ca^+ ion using a laser, which causes the

ions' shared motion to cease. **c**, The authors then apply laser light to the CaH^+ ion. The frequency of the light is chosen so that the ion rotates in a particular direction if it started in a desired quantum state. This change in rotation transfers energy to the ions, which restores their shared motion. **d**, Finally, Chou *et al.* apply laser light to the Ca^+ ion. If the ions are moving, and therefore if the CaH^+ ion is in the desired quantum state, the light scatters off the Ca^+ ion. The authors can then apply further light to the CaH^+ ion to produce correlated states known as quantum superpositions, which are required for extremely high-precision spectroscopy.

stop (Fig. 1b). They then apply ‘modulated’ laser light to the molecular ion, changing its internal quantum state (Fig. 1c). This change is accompanied by a restoration of the ions’ shared motion. Subsequently applied laser light scatters off the atomic ion only if the ions are moving and therefore only if the molecular ion is in the desired quantum state (Fig. 1d).

By applying more laser light to the molecular ion, the authors produce quantum superpositions of molecular states. They are able to control the relative phase between the states — a key requirement for high-precision spectroscopy that the authors verify by repeating the state-preparation technique outlined above. The probability that the molecular ion is found in one of the two states used in the superposition oscillates as a function of time, which illustrates the close connection between the authors’ spectroscopy technique and the pendulum of a clock. Crucially, repeated trials of this protocol are possible because the detection method leaves the molecule not only in the trap, but also in the energy state revealed by the detection scheme itself.

Chou and colleagues’ technique is particularly powerful because it does not require laser light that has a frequency anywhere near the resonance frequency associated with a molecular electronic transition. This means that other molecules should be amenable to the same method, with few changes. Scattering of light near the envoy atom’s electronic resonance allows the state of the molecule to be determined, whereas the laser light that is applied directly to the molecule is hundreds of terahertz (1 THz is 10^{12} Hz) from the closest electronic resonance. A further advantage of working with such far-off-resonant light is that the authors’ technique should be applicable to the hydrogen molecular ion H_2^+ , which does not have a (strongly bound) excited electronic state for near-resonant spectroscopy techniques. This is exciting because, although H_2^+ is conceptually the simplest molecule possible — and is described by high-precision theoretical calculations — it has been difficult to test these calculations using conventional tools.

Although the type of quantum-logic spectroscopy reported by Chou *et al.* shows promise for its applicability to other molecules, its technological aspects are demanding. Because the far-off-resonant light interacts with the molecule only extremely weakly, the technique could require high laser power, potentially generating unintended laser-light scattering that must be avoided. Additionally, any high-precision measurement of this kind will, by definition, require relatively long interaction times. This imposes some constraints on the immediate applicability of the authors’ technique to molecules other than diatomic hydrides — more-complex species might be bleached by room-temperature thermal radiation faster than the requisite interaction time, and would therefore need a cryogenic

environment to reach high resolution.

Finally, a crucial ingredient of Chou and colleagues’ technique is a fully functioning, co-trapped envoy atom, which is effectively a simple quantum computer⁵ and challenging to construct. Nevertheless, growing numbers of research groups have access to these tools, as applications proliferate for well-controlled quantum systems. It might therefore not be long before this type of molecular spectroscopy can be used to probe fundamental physics and to realize other promising proposed applications for cold molecules^{6,7}. ■

MOLECULAR BIOLOGY

The long and short of a DNA–damage response

Ultraviolet light can damage DNA, triggering a general shutdown of gene transcription — yet some genes are activated by UV light. An investigation of this counter-intuitive behaviour reveals a surprising gene-regulation mechanism.

ANTONIO CONCONI & BRENDAN BELL

DNA damage can lead to mutations, cancer and even cell death, and activates several biological processes^{1,2}. These include: DNA repair that removes lesions from the double helix; checkpoints that arrest cell-cycle progression to prevent the transmission of damaged DNA to daughter cells; apoptosis, a form of cell death that eliminates cells with heavily damaged genomes; and a transcription response that changes the cellular RNA profile. Much is known about how cells orchestrate these processes, but the transcription response is arguably the least well understood of the four. Writing in *Cell*, Williamson *et al.*³ describe a mechanism for the transcription response to DNA damage caused by ultraviolet light. Their findings reveal a remarkable circuit that triggers the formation of non-coding RNA molecules from a gene. Moreover, these molecules oppose the action of the protein that is produced from the same gene in the absence of UV damage.

DNA-damaging agents induce the transcription of specific gene classes. Several genes can be induced by more than one DNA-damaging agent, whereas others are induced mainly by one agent. The resulting gene products are associated with many different cellular processes, including DNA repair, intercellular signalling and responses to oxidative stress.

Irradiation by UV light elicits a response from a large subset of damage-induced genes, through a series of intracellular processes

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that starts at or near the cell membrane⁴. But a general shutdown of transcription also occurs soon after UV irradiation. This is because UV exposure causes chemical modifications in DNA known as pyrimidine dimers (PDs). When present on the transcribed strand of a gene, PDs stall the enzyme RNA polymerase II (RNAPII), which elongates nascent RNA chains. A process called transcription-coupled nucleotide excision repair rapidly removes these defects, allowing fast resumption of transcription. Cells that fail to resume transcription are eliminated by the ultimate DNA damage-response pathway: apoptosis^{5,6}.

How can some genes be activated by UV light if transcription in general has been shut down by PDs? It is tempting to speculate that PDs on the transcribed strand of UV-activated genes are repaired particularly quickly, or that fewer PDs form in those genes. The number of PDs that form in a gene is usually proportional to gene size, because PDs form almost randomly in typical DNA sequences. It is therefore interesting that the genes activated by cytotoxic doses of UV light are compact, and contain a small number of short introns⁷ (non-coding sequences).

Williamson *et al.* now reveal a regulatory mechanism for UV-activated genes. They report that the transcription of several such genes by RNAPII proceeds slowly after UV exposure, and is restricted to regions of DNA that are close to promoters (promoter sequences are those that initiate gene transcription). Intriguingly, these changes in RNAPII behaviour correlate with the emergence of