drug dosing to a patient's specific needs.

Measuring drug levels continuously requires a technology that is reversible, so that the sensor's response rises and falls in concert with fluctuating drug concentrations. Moreover, the technology must be continuous, of course, and so should not rely on wash steps or other batch processes. Finally, it must be sufficiently selective to be used on whole blood. Unfortunately, although conventional analytical methods, including chromatography, spectroscopy and immunochemistry, often have one or more of these attributes, no general approach has achieved all these goals simultaneously. There are ways to measure a few specific molecules in the body in real time (for instance, blood glucose levels in patients with diabetes), but these are single-analyte sensors that are not easily generalizable to the detection of other molecules.

Ferguson *et al.* describe a sensor that cleverly links the above three technologies; they call it microfluidic electrochemical detector for *in vivo* continuous monitoring (MEDIC).

The sensing technology underlying this platform is a reagent-free electrochemical device[2,3] that uses the binding-induced folding of aptamers[4] (artificially selected nucleic acids that bind specific molecular targets) to signal the presence of a given analyte. This reagent-free, wash-free, sensing architecture has previously been shown[5] by some of the same authors to support continuous measurements in flowing, undiluted blood serum. The approach fails, however, when the sensor is challenged with whole blood, owing to the nonspecific adsorption of molecules onto the electrode surface, which progressively deactivates the associated aptamers — thereby leading to baseline drift in the output signal.

To eliminate this drift, Ferguson and colleagues took a two-pronged approach. The first was to place the sensors in a microfluidic device that insulates them with a micrometres-thick stream of buffer. Blood continuously collected from the subject (by a cannula) is drawn into the device, where it forms a laminar flow over this buffer (Fig. 1). Because the drug molecules are small, they quickly diffuse through the buffer layer to reach the sensor surface. The much larger blood cells and other large interfering agents diffuse too slowly to reach the buffer stream, so sensor fouling is essentially eliminated.

The authors' second advance was to interrogate their electrochemical aptamer probes using a method, known as square-wave voltammetry, operating at two discrete frequencies. Specifically, they identified matched frequency pairs at which the output signal drifts in concert while responding very differently to the presence of the target. Taking the difference between these two signals effectively eliminates drift. Combining the two approaches, the authors' device achieves multihour, continuous measurements on whole, undiluted blood with baseline stabilities in the submicromolar range of drug concentration.

The team demonstrated the ability of the MEDIC platform to monitor the chemotherapeutic drug doxorubicin and the antibiotic kanamycin in the blood of anaesthetized rats over the course of several hours. The pharmacokinetics derived correspond to long-established values[6] obtained by laboriously drawing blood samples and then, much later, measuring each by using chromatography. In the present paper, by contrast, the measurements were made in real time, which not only is convenient but also improves their precision.

There are some disadvantages to this platform, however. MEDIC requires continuous blood draws (of just a few hundred microlitres per hour) and a pump to maintain the flow of buffer through the device. It is therefore unsuitable for continuous, real-time monitoring of metabolites or drugs in the blood of a mobile patient going about their daily life. Nevertheless, by enabling convenient, high-precision measurements of pharmacokinetics in the clinic, the technology could fuel further advances in personalized medicine by supporting truly individualized dosing regimens. Indeed, the ability to monitor blood drug concentrations in real time could pave the way to proactive, high-precision dosing in which drug delivery is modulated on the go in response to hour-to-hour changes in a patient's metabolism or health status. Such feedback-controlled drug delivery could, in turn, open the door to therapies in which drugs with previously unduly complex dosing regimens or unacceptably narrow therapeutic indices are administered safely and effectively. ■

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QUANTUM PHYSICS

An atomic SQUID

Superconducting quantum circuits are the core technology behind the most sensitive magnetometers. An analogous device has now been implemented using a gas of ultracold atoms, with possible applications for rotation sensing.

CHARLES A. SACKETT

When a magnetic field needs to be measured with the utmost precision, a superconducting quantum interference device (SQUID) is the instrument of choice[1]. Its exquisite sensitivity derives directly from a macroscopic manifestation of quantum mechanics, making it an archetype of quantum engineering. Reporting in *Physical Review Letters*, Ryu and colleagues[2] demonstrate an analogue of a SQUID using an ultracold gas of neutral atoms known as a Bose–Einstein condensate. Here, the analogue to the magnetic field is a physical rotation, so the atomic device could prove useful for rotation sensing and vehicle navigation. More broadly, it strengthens the correspondence between atomic and solid-state systems. Because atomic systems are better understood and more easily controlled than their solid-state counterparts, atoms might eventually serve as a design platform for complex solid-state quantum devices.

A conventional SQUID is a small ring of superconducting material cut in half by two non-superconducting barriers. Wire leads connected to each side of the device allow a current to pass through it (Fig. 1a). Within each of the superconducting regions, electrons act like a coherent quantum wave. Because the current passing through the SQUID can take either path around the ring, the two corresponding waves can interfere: they can add constructively with the peaks of the waves lined up, or cancel destructively with the peaks of one wave aligned to the troughs of the other. The total current through the ring depends sensitively on the type of interference. For charged particles such as electrons, the way that the waves align is set largely by the magnetic field threading the ring, which makes the SQUID a good magnetometer.

In the atomic analogue demonstrated by Ryu and colleagues, the superconducting electrons are replaced by a Bose–Einstein condensate consisting of a few thousand rubidium atoms at nanokelvin temperature, isolated in an ultra-high-vacuum chamber[3]. Like the electrons, the atoms in a Bose–Einstein condensate act as a wave, allowing similar physics to be probed. Here, the atoms are held in a ring-shaped trap that has two small potential-energy barriers through which the atoms can tunnel (Fig. 1b). The authors created the ring trap using a technique known as a painted potential. For

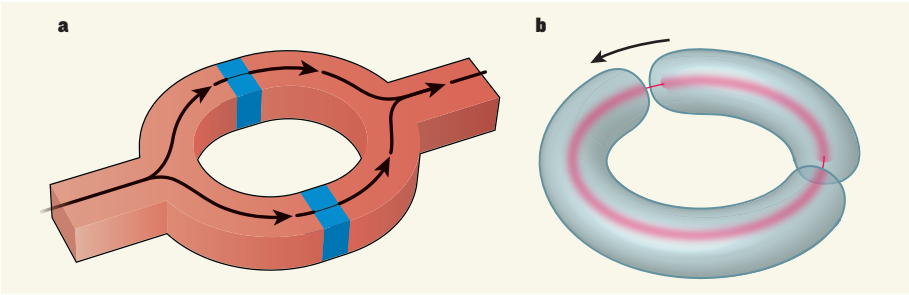

Figure 1 | Quantum interference devices. **a**, A conventional superconducting device consists of a ring of superconducting wire split by two non-superconducting barriers (blue). The current (thick black lines) through the loop must tunnel through the barriers (thinner lines). **b**, The atomic version demonstrated by Ryu *et al.*[2] is a Bose–Einstein condensate (red) held in a ring-shaped trap. The ring is broken by two potential-energy barriers. Instead of passing the atoms through the barriers, here one of the barriers is moved around the ring so as to pass through the atoms, as indicated by the arrow. The distribution of the atoms between the two regions reveals the dynamics of atom motion, which corresponds well to the electron currents in the superconductor.

this, a laser beam is rapidly scanned across the trapping region and selectively turned on so as to illuminate only a ring-shaped area. The atoms are attracted to the laser light and confined within the ring. The tunnelling areas are produced by reducing the light intensity at two spots on the ring.

Because the atoms are neutral, the condensate version is not especially sensitive to magnetic fields. However, if the whole apparatus rotates, then the atoms will experience the Coriolis force, which twists the path of any object moving on a rotating platform. For example, on the Earth, the Coriolis force causes the circulating air flow of hurricanes and cyclones. It affects the atomic waves much like a magnetic field affects electrons. By measuring how the atoms move through the ring, even a tiny Coriolis force can be detected, making the system useful for sensing rotation[4].

Ryu and colleagues' work builds on previous demonstrations (see, for example, ref. 4) of atomic systems similar to a SQUID, but for the first time uses the complete geometry of a ring with two barriers. The observed behaviour of the authors' atoms is in good accord with the phenomenological model used to describe superconducting devices. Indeed, for the atomic case, the expected behaviour can be derived nearly from first principles, so the system is on firm theoretical ground.

Rotation sensors are useful for vehicle navigation and other geophysical applications, and the atomic SQUID shows promise for advancing these technologies. A greater impact, however, may derive from the demonstration of how atomic systems can replicate solid-state devices. Although solid-state circuits have the practical benefit of not requiring lasers and vacuum chambers, developing a new device involves painstaking fabrication and characterization work. By contrast, the size and shape of an atom trap can be modified simply by reprogramming the behaviour of the laser beam. The atom system could thus serve as a design tool for complicated circuits, in which the geometry could be developed and optimized before being applied to superconductors. Although ordinary computer simulation can serve a similar purpose, a physical device can easily become too complex for simulation to be practical. Such complexity is common in quantum systems in which particle interactions are important and non-trivial, including high-temperature superconductors and, perhaps one day, quantum computers.

The idea that ultracold atoms could be used to simulate and explain solid-state systems has been a driving force in the atomic-physics community since the first observations of Bose–Einstein condensation[5]. Ryu and colleagues' demonstration that a useful device such as a SQUID can be implemented with atoms is a milestone in this effort. Nonetheless, substantial challenges remain. An immediate issue is the difficulty of using atomic systems to model macroscopic currents: the number of atoms in a condensate is relatively small, so there is no simple way to create a large current. The authors sidestep this problem by measuring a small current flowing through a barrier, rather than a large current passing through the ring as a whole (compare Fig. 1a and b). Although this set-up can be used for rotation measurements, it does not reflect the actual operation of a superconducting SQUID. A larger question is how well the correspondence between atoms and solid-state systems will hold up as the system's complexity grows. Until the systems become too complicated for computer simulation, the utility of the atomic experiments as a design platform for solid-state systems will probably be limited. Meeting the challenges involved will not be easy, but the steady progress in this field exemplified by Ryu and colleagues' achievement is encouraging. ■

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HIV

Ringside views

Two crystal structures reveal that the Vif and Vpx proteins of human and simian immunodeficiency viruses mediate evasion of host defences by reprogramming the cellular protein-degradation machinery. SEE LETTERS P.229 & P.234

MICHAEL H. MALIM

The human immune system uses myriad adaptive and innate mechanisms to fight HIV infection and AIDS. Prominent among these is a collection of widely expressed cellular proteins called restriction factors, which can potently suppress viral replication[1]. But human and simian immunodeficiency viruses, including HIV-1, encode several dedicated regulatory proteins that enable them to evade restriction factors, thus ensuring their survival and propagation. Two papers[2,3] in this issue show how the viral Vif and Vpx regulatory proteins bind to key host-cell partners and targets, culminating in the removal of restriction factors from infected cells.

The substrates for Vif are members of the APOBEC3 (A3) protein family, namely A3D, A3F, A3G and A3H; the substrate for Vpx is the SAMHD1 protein. These are all enzymes that interfere with reverse transcription, an essential phase of HIV replication in which the viral RNA genome is copied into DNA. The APOBEC3 proteins are cytidine deaminases that are captured by virus particles as they assemble. The proteins induce destructive hypermutation of nascent viral DNA and suppress its synthesis[1]. SAMHD1 is a deoxynucleoside triphosphate