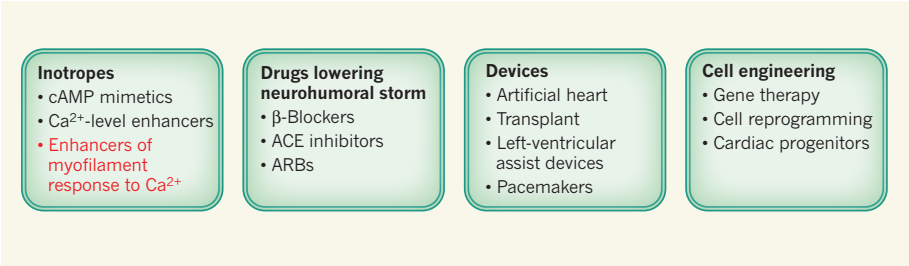

Figure 2 | Treating heart failure. There is an extensive array of therapeutic strategies for heart failure. Omecamtiv mecarbil, the subject of Malik and colleagues' investigation[2], is an inotropic drug (red). ARBs, angiotensin II-receptor blockers.

therapeutics being developed and used against it[1] (Fig. 2). Although cardiac transplantation is the only real cure for heart failure, artificial hearts and left-ventricular assist devices are beneficial, at least as bridges to transplantation and perhaps even as 'destination therapy'. Implantable devices such as pacemakers and resynchronization devices are also useful for treating heart failure, but devices and surgical interventions can be costly.

There is also great promise in emerging genetically based therapeutics that aim to replace or reprogram cardiac myocytes in order to boost heart function. For example, selective gene therapy targeted to cardiac myocytes might be able to break the neurohumoral storm and enhance myocyte contraction with fewer whole-body side effects than other therapies. Reprogramming of stem cells (either embryonic or inducible pluripotent), together with recruitment of cardiac progenitor cells to become functionally integrated muscle cells that can replace heart muscle lost to infarction, are promising areas under intensive study. The old notion that one cannot grow new heart cells in adulthood is probably incorrect. ■

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1. Tang, W. H. & Francis, G. S. *J. Am. Coll. Cardiol.* **55,** 688–696 (2010).
2. Malik, F. I. *et al. Science* **331,** 1439–1443 (2011).
3. Bers, D. M. *Nature* **415,** 198–205 (2002).
4. Kawase, Y., Ladage, D. & Hajjar, R. J. *J. Am. Coll. Cardiol.* **57,** 1169–1180 (2011).
5. Kushnir, A. & Marks, A. R. *Adv. Pharmacol.* **59,** 1–30 (2010).
6. Kass, D. A. & Solaro, R. J. *Circulation* **113,** 305–315 (2006).

METROLOGY

Filtering noise with a quantum probe

In the science of measurement, increasing the sensitivity to the quantity being measured while minimizing the susceptibility to noise is a challenge. A technique demonstrated with a single electron spin may help to tackle it. SEE LETTER P.61

JOHN J. BOLLINGER

Applications in both fundamental and applied science require ever greater sensitivity and higher spatial resolution for measurements of physical quantities such as magnetic and electric fields. The most sensitive and smallest measurement probes are inherently quantum mechanical. Examples include superconducting quantum-interference devices (SQUIDs)[1] and devices based on a few electron spins — or even a single spin[2]. However, greater susceptibility to noise usually accompanies extreme sensitivity, and so one of the challenges for metrologists is to separate a weak signal from large background noise.

On page 61 of this issue, Kotler and colleagues[3] describe a general technique in which a quantum probe is used to separate noise from the signal being measured, and they demonstrate it experimentally using a probe consisting of the spin of a valence electron of an individual atomic particle (a single strontium ion). The technique requires a controlled modulation of the quantity to be measured and a corresponding controlled manipulation of the quantum probe. It is reminiscent of noise-filtering techniques developed decades ago for classical signals and probes, but is described here for a general quantum probe for the first time.

More than half a century ago, Robert Dicke invented the lock-in amplifier[4]. This powerful tool is now used extensively in all branches of experimental science to extract signal from a noisy background. As an example of lock-in detection, consider the measurement of a weak fluorescent signal in the presence of strong background light. If the clever experimentalist can devise a way to periodically modulate the weak fluorescent signal at a frequency f_m, for example by modulating the number of fluorescing molecules, then the overall detected signal will contain a contribution whose time dependence is given by a known sinusoidal reference signal of frequency f_m. The lock-in amplifier electronically multiplies the overall signal (for example, the voltage output of the sensor with which the fluorescence is detected) and the reference signal, and averages the result for a period of time. An output is therefore generated that is proportional to the signal components around some narrow band of frequencies centred at f_m. Noise tends to be spread across a broad range of frequencies, and the lock-in amplifier filters out noise at frequencies other than f_m. By choosing f_m judiciously, the signal-to-noise ratio of the measurement can be significantly improved.

The classical lock-in amplifier is based on the nonlinear process of multiplying the output of the sensor and the reference signal. However, quantum dynamics is described by a linear differential equation (the Schrödinger equation), and so it is not immediately clear how the concept of lock-in detection could be generalized to a quantum-mechanical probe. Kotler and colleagues[3] show that the application of operations that do not commute with the quantum-mechanical operators describing the detected signal and noise, along with a synchronous modulation of the signal to be measured, provides a form of quantum lock-in detection.

This abstract idea is actually familiar to anyone acquainted with the concept of spin echoes, a ubiquitous technique in nuclear magnetic resonance[5]. Consider a single electron or nuclear spin that is set precessing about an externally applied magnetic field. As a result of magnetic-field fluctuations, the spin accumulates some unknown precession. For slow noise fluctuations, this unknown precession can be reversed by means of a spin-echo pulse — a quick 180° rotation about an axis orthogonal to the magnetic field. Mathematically, rotations about orthogonal axes do not commute. Spin echo is a simple example of a more general class of technique called dynamical decoupling[6], which relies on stringing together many spin-echo pulses in succession.

Dynamical-decoupling sequences improve the coherence of quantum systems by acting

as high-pass filters, removing the effects of environmental fluctuations (noise) across a wide spectral bandwidth. However, such suppression of noise comes at a price in metrology experiments, because the intrinsic high-pass filtering prevents certain quantities from being measured. For example, because the spin echo 'erases' the accumulation of unwanted precession in a quantum system, one cannot measure the rate at which any precession accumulates.

To get around this, Kotler *et al.*[3] exploit a quirk of dynamical-decoupling sequences: high-frequency noise is not passed uniformly, allowing the authors to home in on the quantum effects of a desired signal in a narrow-frequency passband. The passband is controlled by the dynamical-decoupling sequence of the spin-echo pulses they apply. Changing the periodicity of the applied pulses tunes the central frequency of this band, and by synchronously modulating the signal of interest, the quantum lock-in amplifier preserves the signal while the dynamical decoupling filters the noise — the authors can have their cake and eat it too.

They experimentally demonstrate the quantum lock-in technique using a probe consisting of the valence-electron spin of a singly ionized strontium atom that is laser-cooled and stored in an electromagnetic trap. The spin-flip frequency of the unpaired valence electron is sensitive to an applied magnetic field, and the authors demonstrate a magnetic-field sensitivity of 15 picoteslas of magnetic-field strength in a 1-second measurement period — a record for a single-spin probe. In addition, they apply the technique to measure small shifts in the spin-flip frequency of the valence electron caused by a weak applied laser field. This demonstration is particularly intriguing because it provides a way to use dynamical decoupling to stabilize the frequency of a laser to that of an atomic transition. Lasers stabilized to narrow-linewidth atomic transitions currently provide the world's most stable atomic clocks[7,8]. ■

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1. Bending, S. J. *Adv. Phys.* **48,** 449–535 (1999).
2. Taylor, J. M. *et al. Nature Phys.* **4,** 810–816 (2008).
3. Kotler, S., Akerman, N., Glickman, Y., Keselman, A. & Ozeri, R. *Nature* **473,** 61–65 (2011).
4. Horowitz, P. & Hill, W. *The Art of Electronics* 1031 (Cambridge Univ. Press, 1989).
5. Haeberlen, U. *High Resolution NMR in Solids* (Adv. Magn. Res. Ser.) (Academic, 1976).
6. Biercuk, M. J. *et al. Nature* **458,** 996–1000 (2009).
7. Chou, C. W., Hume, D. B., Koelemeij, J. C. J., Wineland, D. J. & Rosenband, T. *Phys. Rev. Lett.* **104,** 070802 (2010).
8. Ludlow, A. D. *et al. Science* **319,** 1805–1808 (2008).

MATERIALS CHEMISTRY

Catalytic accordions

Single chains of a specially designed polymer fold up in water to form an encapsulated catalytic chamber. This supramolecular assembly strategy mimics the one used by enzymes in nature.

NICOLAS GIUSEPPONE & JEAN-FRANÇOIS LUTZ

The catalytic properties of an enzyme result from the three-dimensional folding of a single protein chain, which brings together a well-defined set of amino-acid residues to form the enzyme's active site. This pocket is a highly organized domain that binds tightly and selectively to the enzyme's substrate, which becomes trapped and polarized in a network of supramolecular interactions. In this way, active sites lower the energy of transition states for reactions, so that products form up to billions of times faster than in the uncatalysed reactions. A challenge for chemists has been to devise systems that mimic enzyme activity, and a breakthrough has now been reported by Terashima *et al.*[1] in the *Journal of the American Chemical Society*. They have synthesized a polymer, single chains of which fold in water to form an inner compartment that acts, through its supramolecular structure, as an 'active site' for a catalytic reaction.

Supramolecular chemistry is fundamental to catalysis, because the transition states of chemical reactions represent a special class of supramolecular complex in which some covalent bonds are being formed while others are being broken. What's more, numerous self-assembled supramolecular objects have been designed to act as catalysts[2], in particular by acting as templates that bring reagents together to react. Examples of these include cages or capsules made of discrete small molecules[3] or proteins[4], and multi-component matrices[5] such as micelles or vesicles, made of surfactants or polymers. But these self-assemblies are relatively poor catalysts in comparison with highly organized enzymes.

Other options for developing artificial enzymes have therefore been studied. For instance, it is possible to prepare fully synthetic enzymes from amino acids by using well-established chemistry to make polypeptide fragments, and then joining the fragments together to construct proteins in so-called ligation reactions[6]. However, such approaches are still rather challenging and time-consuming.

Simpler alternatives are obviously required. Given that enzymes are macromolecular, the idea of performing catalytic reactions in other discrete macromolecular entities, such as polymer molecules, seems logical. Macromolecular objects made from branched polymers have received much attention in this regard[7], because they contain isolated domains that could be used as catalytic active sites. But the three-dimensional structures of branched polymers are not obtained through straightforward supramolecular folding, as is the case for enzymes. They are instead the topological result of complex synthetic routes.

Terashima *et al.*[1] now suggest an original solution to this problem. Instead of synthesizing a polymer that has a complex, three-dimensional topology, they investigated whether a single linear polymer chain can be folded to make an enzyme-like object for catalysis. To do this, the authors carefully designed a polymer chain that was constructed from three different monomers (Fig. 1a): a hydrophilic monomer that contained a water-soluble group; another that bore a self-assembling motif; and a third monomer that contained a diphenylphosphine ligand, which forms a catalytic complex with ruthenium ions.

These monomers were not, however, randomly incorporated into a polymer backbone. Using an approach known as living radical polymerization[8], the authors controlled the locations of the different monomers in the polymer chains[9]. For instance, they specifically incorporated the ruthenium-binding monomers into the middle of the chains, whereas the other types of monomer were distributed along the whole length of the chains. What's more, because the polymerization reaction required a ruthenium catalyst, the diphenylphosphine groups in the chains formed complexes with ruthenium ions from that catalyst. The arrangement of monomers in the resulting chains caused the molecules to fold up in water (Fig. 1b), as a result of intramolecular hydrophobic and hydrogen-bonding interactions. In particular, the self-assembling units incorporated into the polymer formed compact helical structures, so that the linear macromolecules collapsed like supramolecular accordions.

Terashima *et al.* found that, as hoped, their macromolecules folded into unimolecular objects in which a catalytically active inner region (the domain containing ruthenium complexes) was stabilized by a hydrophilic shell. This compartmentalization was thus a good — albeit simplified — mimic of the