News & views

Precision upheld for exotic atoms confined by liquid

Yukari Matsuo

High-precision measurements of exotic atoms containing antimatter are shown to be equally precise when the atoms are immersed in superfluid helium. Such immersion could be used for other atoms in studies of dark matter. **See p. 411**

The structure and composition of matter can be revealed by examining how it interacts with light. Atoms absorb or emit a unique range of light frequencies appearing as lines on a spectrum, which can be measured with a technique known as laser spectroscopy. For isolated atoms, these lines are extremely narrow, offering a remarkable precision of up to 19 significant figures[1]. Confining atoms in fluid can make measurements more efficient by increasing the density of atoms, but it can also broaden and shift the spectral lines. On page 411, Sótér et al.[2] report a very narrow spectral line for an exotic form of helium engulfed in liquid helium, which might make such confinement useful for studies of the fundamental physics governing the subatomic Universe.

Spectroscopy is key to current efforts to check whether the physics of all particles is the same as that of their antiparticles, by making precise frequency measurements of protons and antiprotons[3,4]. One way of approaching this task uses exotic atoms, such as pionic helium — a helium atom in which one of its two electrons is replaced by a subatomic particle known as a pion. Laser spectroscopy has been performed on pionic helium immersed in liquid helium[5], but such measurements are difficult because only a small number of

> **"When an impurity atom is implanted in superfluid helium, a defect called a bubble-like state emerges."**

antimatter particles can be detected (around three per billion exotic atoms), and they have a lifetime of only nanoseconds.

By contrast, antiprotonic helium, in which one of the electrons of a helium atom is replaced by an antiproton, has a relatively long lifetime of several microseconds. Antiprotonic helium has been studied extensively

in helium gas using laser spectroscopy[6]. But the confining effect of the gas increases the pressure exerted on the antiprotonic helium atoms, which broadens and shifts the spectral lines relative to those for isolated atoms. To overcome this effect, spectra are typically measured at different helium pressures, and frequencies are then estimated by extrapolating to zero pressure.

A complementary approach is to swap the helium gas for liquid helium, which has a much higher density. Sótér and colleagues found that this method could be used to measure very narrow lines in the spectrum of antiprotonic helium, just below the temperature at which normal fluid helium transitions to superfluid helium (an ideal superfluid has zero viscosity).

Superfluid helium usually causes problems for precision spectroscopy. When an impurity atom is implanted in superfluid helium, a defect called a bubble-like state emerges. This state induces an interaction between the impurity atom and the surrounding helium atoms, which in turn shifts and broadens the spectral lines, reducing spectroscopic precision (Fig. 1a). This is especially noticeable when the impurities are atoms of alkali metals or alkaline-earth metals, which have been studied for more than two decades[7].

The changes to the spectral lines occur typically when an s electron — the outermost electrons of alkali and alkaline-earth metals — is excited, because the surrounding helium atoms affect the transition frequency at which this occurs. However, the transition frequency at which an inner-shell electron is excited does not change much, because the s electrons in the outer shell shield it from the surrounding helium, resulting in the observation of a narrow line. This occurs in atoms such as europium, gold and dysprosium, which can have narrow excitation spectra[8].

The antiprotonic helium that Sótér and colleagues studied has a key feature that allowed the authors to emulate the conditions seen in atoms with inner-shell excitations. Namely, the antiproton excited by the laser orbits the atomic core at a smaller radius than that of the atom's s electron (Fig. 1b), which means that this state is protected from the surrounding helium. However, this was not the case for all temperatures and pressures measured.

Sótér and colleagues introduced antiprotons into cold helium gas and bulk liquid helium (in the normal and superfluid phases) to produce antiprotonic helium atoms. After exciting the sample with a laser, the authors observed the annihilation of antiprotons and measured their spectra. They then changed the conditions of the experiment, for example the density and temperature of the helium, and measured the effect of this on the pressure-induced
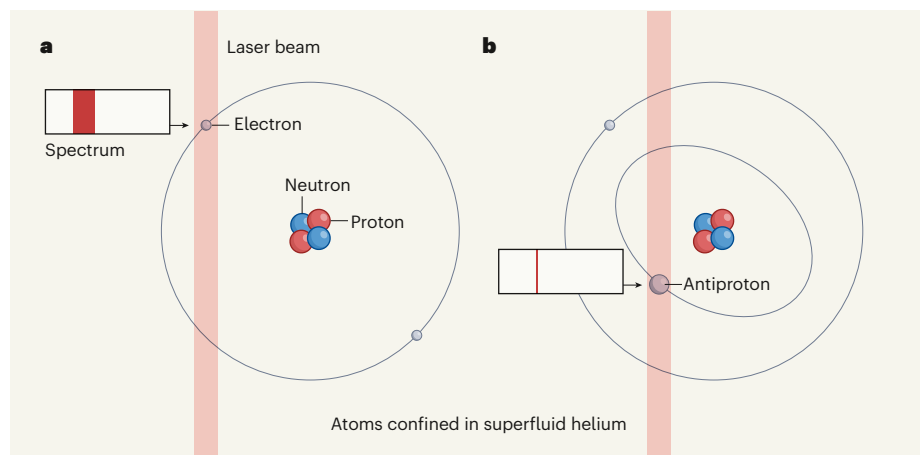
Figure 1 | Maintaining high precision in measurements on confined atoms. An electron in an atom is excited by a laser at a frequency that produces a narrow line on a light spectrum. **a**, Immersing the atom in superfluid helium broadens and shifts this line owing to interactions between the atom and the surrounding liquid. **b**, Sótér et al.[2] showed that the spectrum for a helium atom in which one of the two electrons is replaced by an antiproton does not have this line broadening. This is because the excited antiproton orbits the atomic core at a radius that is smaller than that of the outermost electron, which shields the antiproton from the atoms in the surrounding liquid.

broadening and shifting of the spectral lines.

A very narrow spectral line was observed at a temperature just below the phase-transition temperature to superfluid helium. This line was four times narrower than that observed for the inner-shell excitation of dysprosium[8]. It was even narrow enough to reveal a splitting of the atoms' energy levels, known as hyperfine splitting, which arises as a result of interactions between the electron and the antiproton. The measured resolution (one part per million of the transition frequency) is remarkable in liquid helium.

If this resolution can be matched for other exotic atoms, it might be possible to test theories proposing that dark matter decays or is annihilated in the Milky Way[9]. Current estimates[5] of the spectral linewidth of pionic helium suggest that it is up to 100 times that of the antiprotonic helium measured by Sótér and colleagues. However, if a transition with a similarly narrow linewidth also exists in pionic helium immersed in liquid helium, it might be a good candidate for such investigations. Finding the optimal combinations of energy levels and liquid-helium conditions will undoubtedly require guidance from theoretical calculations.

The fact that the linewidth measured by Sótér *et al.* narrowed suddenly at a temperature close to that at which normal fluid helium transitions to superfluid helium, and broadened again at a lower temperature, is intriguing from the viewpoint of chemical physics. Although not discussed in depth by the authors, the reason for this seems to be unrelated to the phase transition itself, but instead to be linked to the characteristics of bulk helium. More research is needed to reveal the relevance of this temperature, its relationship to the properties of helium, and the physics behind this connection.

Yukari Matsuo is in the Department of Advanced Sciences, Hosei University, Tokyo 184-8584, Japan.
e-mail: yukari.matsuo@hosei.ac.jp

1. Bothwell, T. *et al. Metrologia* **56**, 065004 (2019).
2. Sótér, A. *et al. Nature* **603**, 411–415 (2022).
3. Hori, M. *et al. Science* **354**, 610–614 (2016).
4. Ulmer, S. *et al. Nature* **524**, 196–199 (2015).
5. Hori, M., Aghai-Khozani, H., Sótér, A., Dax, A. & Barna, D. *Nature* **581**, 37–41 (2020).
6. Hori, M. *et al. Phys. Rev. Lett.* **87**, 093401 (2001).
7. Toennies, J. P. & Vilesov. A. F. *Annu. Rev. Phys. Chem.* **49**, 1–41 (1998).
8. Moroshkin, P., Borel, A. & Kono, K. *Phys. Rev. B* **97**, 094504 (2018).
9. Cuoco, A., Krämer, M. & Korsmeier, M. *Phys. Rev. Lett.* **118**, 191102 (2017).

An oracle for gene regulation

Andreas Wagner

A long-standing goal of biology is the ability to predict gene expression from DNA sequence. A type of artificial intelligence known as a neural network, combined with high-throughput experiments, now brings this goal a step closer. **See p.455**

Gene expression affects every aspect of life, from the survival of bacteria in specific environments to the anatomy and physiology of the human body. The ability to accurately predict how strongly a gene is expressed on the basis of the DNA sequences that regulate such expression would transform how researchers study biology. But the biochemical machinery that regulates gene expression is tremendously complex, and this goal has eluded biologists' best efforts for more than 50 years. On page 455, Vaishnav *et al.*[1] take advantage of two key technologies to produce a successful 'oracle' for gene expression in the yeast *Saccharomyces cerevisiae*.

The first technology used by the authors is a means of measuring the expression of a gene that encodes yellow fluorescent protein (YFP) in every cell of a large population of yeast cells[2]. In this population, different cells carry different regulatory DNA sequences, called promoters, that are located close to the *yfp* gene on a small piece of circular DNA — their proximity to *yfp* enables them to drive the gene's expression. Specifically, the authors used a collection of more than 30 million different promoters, each 80 base pairs long, and quantified the production of YFP by each cell containing one of these promoters.

Vaishnav *et al.* fed the resulting expression data into the second technology, an artificial intelligence (AI) called a convolutional neural network, and trained the network to predict gene expression from the data. They then validated the network's ability to predict gene expression on an impressive scale (Fig. 1).

For example, the authors synthesized thousands more promoter sequences not used for training, measured their ability to drive gene expression, and showed that the neural network very accurately predicts how well each will drive gene expression. In addition, the authors presented the network with random starting sequences, and showed that its ability to predict gene expression from sequence could be used to transform these starting sequences, through ten rounds of computer-simulated evolution, into promoter sequences predicted to drive extreme (very high or very low) YFP expression. The group then synthesized 500 of these sequences and measured their ability to drive YFP expression.
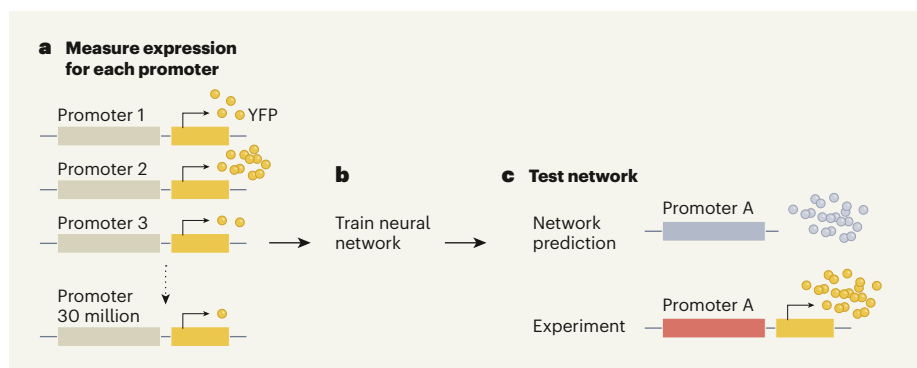
Figure 1 | Learning to predict gene expression. a, Vaishnav *et al.*[1] created a library of 30 million promoters — 80-base-pair-long DNA sequences that drive gene expression. They measured how well each could drive expression of the gene that encodes yellow fluorescent protein (YFP) in yeast cells. **b**, The group used these data to train a neural network to predict how well different promoter sequences drive gene expression. **c**, The authors then tested network's predictive ability. The group designed thousands more promoters (only one is shown here, for simplicity), and showed that the network could predict, extremely accurately, how well each promoter would drive gene expression.