cell divisions of the embryo[7], and that Tet2 has a key role in blood-cell maintenance and is frequently mutated in human leukaemia[8]. But the biological function of Tet1 has been less clear, because no major developmental defects have been found in Tet1-deficient mice[9].

Yamaguchi *et al.* studied the physiological function of Tet1 by generating genetically modified mice that do not produce a functional full-length Tet1 protein. They show that the absence of Tet1 leads to decreased fertility and fewer pups in the litters than in normal mice. This finding is consistent with the high expression of Tet1 seen in the precursor cells of eggs and sperm, and was also observed recently in another model of Tet1-deficient mice[9].

Focusing on females, the authors report that Tet1 deficiency leads to a decrease in the size of the ovaries, an increased incidence of cell death in the ovaries and a reduced number of fully developed oocytes. They also show that the oocytes display meiotic defects, such as a failure to align and segregate chromosome pairs efficiently, together with defective genetic recombination (the 'shuffling' of DNA sequences that occurs during meiotic cell division). This failure to complete meiosis probably explains why a high proportion of developing oocytes in the Tet1-deficient mice are eliminated by apoptotic cell death.

To further study how Tet1 promotes meiosis, the authors examined gene-expression profiles of oocyte-precursor cells from wild-type and Tet1-deficient female mice. Strikingly, they observed that the mutant cells express reduced levels of several meiotic genes, such as those encoding components of the synaptonemal complex, which promotes chromosome alignment and recombination.

The obvious next question was, what is the role of Tet1 in activating these meiotic genes? Germ-cell precursors are known to undergo a genome-wide erasure of DNA methylation during their specification for becoming germ cells[3]. This affects all types of sequences, including the promoter regions of many meiotic genes that are repressed by DNA methylation in somatic (non-germ) cells and that need to be demethylated in germ cells[10,11]. (Promoter regions are the DNA sequences at which transcription of a gene is initiated.) Given the potential role of Tet proteins in DNA demethylation, it was tempting to speculate that Tet1 is involved in the demethylation of meiotic genes. To address this, the authors measured DNA methylation in the promoters of three meiotic genes and observed various degrees of residual DNA methylation in Tet1-deficient female germ cells, which could explain the genes' reduced expression.

The authors then investigated whether Tet1 is required for the broader erasure of DNA methylation in germ-cell precursors. They generated genome-scale maps of DNA methylation and, surprisingly, observed that the absence of Tet1 only marginally impairs genome-wide demethylation. This suggests that Tet1 is required only for demethylation of specific sequences, such as meiotic genes. Unfortunately, the authors' methylation data were at low coverage (meaning that each genomic position was measured only a small number of times), and this prevented detailed analysis of which sequences require Tet1 for demethylation in germ cells. Other aspects that need to be investigated include whether the role of Tet1 in meiotic-gene activation depends solely on its effect on 5-methylcytosine, and whether Tet1 has similar functions in males.

Since the discovery of Tet proteins, their role in epigenetic reprogramming in germ cells has been a matter of speculation. Yamaguchi and colleagues' study provides the first genetic clues about the specifics of this activity, by showing that Tet1 is not essential for general demethylation in germ cells but is required only at certain sequences. The finding raises many questions. Do other Tet proteins compensate for the absence of Tet1? What sequences are demethylated by Tet1, and how is the protein recruited to these DNA sites? What other mechanisms promote DNA demethylation in germ cells, and how do these processes interact? Could Tet1 be involved in human infertility? We are only beginning to understand the physiological and molecular roles of Tet proteins, and this work adds a new chapter to an exciting story. ■

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LOW-TEMPERATURE PHYSICS

Cool molecules

A sample of the hydroxyl radical has been cooled to a temperature of a few millikelvin. The result opens the door to observing phenomena such as Bose–Einstein condensation of molecules in their ground state. SEE LETTER P.396

PAUL S. JULIENNE

Since the advent of laser cooling and evaporative cooling more than two decades ago, ultracold trapped atoms at temperatures close to a millionth of a kelvin have been used in a wide range of research involving precision measurement and exotic quantum phenomena. Molecules, on the other hand, have resisted cooling down to even 1 millikelvin. On page 396 of this issue, Stuhl *et al.*[1] describe a breakthrough in molecular cooling. They demonstrate strong evaporative cooling that lowers the temperature from 50 mK to just a few millikelvin and increases the density of a decelerated and trapped sample of the chemically interesting hydroxyl radical (OH).

Why are cold atoms or molecules so interesting? First, cold means slow — the velocity of an ultracold atom or molecule is so low that its location in space becomes spread out and wave-like, in accordance with the Heisenberg uncertainty principle. The de Broglie wavelength, which is a measure of this quantum delocalization, can be many hundreds of nanometres or larger. Furthermore, an atom or molecule can be either a boson or a fermion, depending on its spin quantum number. The OH molecule is a composite boson, for example, having an integer spin quantum number. When the phase-space density (the number of atoms or molecules per cubic de Broglie wavelength) becomes large enough, approaching unity, the 'quantum degenerate regime' is reached. In this regime, bosons can exhibit exotic quantum phenomena, such as Bose–Einstein condensation, in which all the particles occupy a single wave-like quantum state. Other quantum phenomena are possible with cold fermions, including particle pairing similar to that seen in superconductivity.

Although cold molecules are in many ways similar to cold atoms, their more complex structure offers a richer range of phenomena. For example, for OH, which has an electric dipole moment, there are strong long-range forces between two molecules. These forces make it easy to control or engineer a wider range of condensed-matter quantum effects with molecules than with atoms[2,3]. Another difference is that molecules can take part in chemical reactions. Fast chemical reactions of molecular fermions can be turned off if they are cold enough, because the Pauli exclusion principle ensures that identical fermions cannot get close enough together to react. Flipping one nuclear spin to stop the molecules being identical can turn the reaction back on again[4]. The exquisite control of chemical reactants and molecular collision complexes should open up new vistas for chemistry involving ultracold molecules[5].

Why are molecules much harder to cool than atoms? Laser cooling is generally ineffective because molecules have a more complex internal structure than atoms. Two atoms that are already cold can sometimes be coaxed together using magnetic fields and light to make a molecule in its quantum ground (lowest-energy) state[6,7], but only a few species can be created this way. Stark deceleration, which uses a pulsed sequence of electric fields to slow a beam of polar molecules, provides a general technique for a variety of species[6]. However, the temperature of such molecules is still relatively high, about 50 mK, and the density in a molecular trap is very low. What has been missing is a method to cool the molecules further, and to increase their density — especially their phase-space density.

Stuhl *et al.* take advantage of the OH molecule's unusual properties. It has both an electric dipole moment, which means that it can be decelerated in a standard Stark decelerator, and an unpaired electron, which gives it a magnetic moment, so that it can be confined in a magnetic trap. The OH molecule's ground state has the useful property of being split into two quantum levels of nearly the same energy but with different parity quantum numbers. Molecules in the higher energy state are trapped, but those in the lower energy state are expelled from the trap. Evaporative cooling involves a slow reduction of the trap depth, allowing the warmer trapped molecules to escape while the cooler molecules achieve thermal equilibrium through collisions with one another that do not change their state. For evaporative cooling to work, the rate of such thermalizing collisions must remain high compared with the rate of loss collisions that convert the molecules to the untrapped lower energy state.

Evaporative cooling is not possible for most molecules because the ratio of thermalizing to loss collision rates is not favourable. But for OH and similar molecules, the upper state can survive for many collisions, allowing evaporative cooling to proceed. The theoretical model described by Stuhl *et al.* explains how two molecules in the upper state experience repulsive van der Waals forces when they are far apart, as a consequence of the opposite parity of the two ground-state levels of OH that have nearly the same energy. These repulsive forces ensure that fast thermalizing collisions occur while keeping the molecules far enough apart to prevent loss collisions.

Stuhl *et al.* lowered their effective trap depth by introducing a microwave-frequency 'knife' that converts trapped molecules to untrapped ones on the outer edges of the trap. By changing the microwave frequency, they could cut closer and closer to the centre of the trap, where the coldest molecules accumulate. Their tenfold decrease in temperature, with small molecular loss, implies a dramatic thousand-fold increase in phase-space density. The temperature may be even lower than reported, because in this low-temperature regime the molecules are at the limit at which temperature can be measured with the current apparatus.

This is an extremely promising advance in molecular cooling. The theoretical model suggests that evaporation should be even more effective as the molecules get colder. There is every reason to expect that an improved experimental apparatus could lower the temperature and increase the phase-space density enough to make a Bose–Einstein condensate from OH molecules. If the same degree of cooling can be achieved in OD, using deuterium (D, or ^{2}H), a quantum degenerate gas of fermions could also be observed.

It seems that evaporative cooling will soon join the method of associating two ultracold atoms as a way of making an ultracold molecule. Laser cooling of at least some species may not be far behind[8,9]. An era of doing real quantum science with ultracold molecules is now upon us. ■

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EARTH SCIENCE

Go with the lows

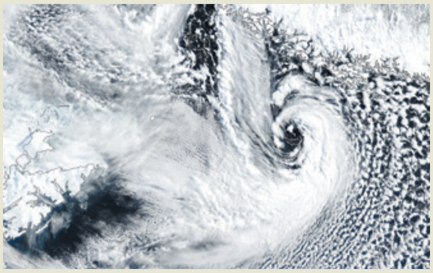
Before Father Christmas sets off from the North Pole, he will want to know if his flight will be disrupted by polar lows — storms (pictured) that afflict subpolar seas. Unfortunately for him, the effects of polar lows are not usually included in climate and seasonal forecasting models. Writing in *Nature Geoscience*, Condron and Renfrew report that they should be (A. Condron and I. A. Renfrew *Nature Geosci.* http://dx.doi.org/10.1038/ngeo1661; 2012).

Polar lows are typically too small (less than 250 kilometres in diameter) and fleeting (24–48 hours in duration) to be well resolved in global meteorological and climate models. Nevertheless, their intensity is often high enough to affect convection in the underlying ocean. Deep open-ocean convection is one of the mechanisms that renews the North Atlantic Deep Water, the main water mass that drives large-scale ocean circulation in the Atlantic Ocean.

Condron and Renfrew used state-of-the-art computational models to simulate circulation in the northeast Atlantic during 1978–98, in the presence or absence of polar lows. They found that models that incorporated the effects of the storms indicated more open-ocean convection, at greater depths, than those that omitted polar lows.

Furthermore, the strengths of two gyres — large systems of rotating ocean currents — in the region were more frequently high when the effects of polar lows were simulated. This in turn increased the renewal of deep water in the Greenland Sea, the transport of that water flowing south across the Greenland–Iceland–Scotland ocean ridge, and the northward movement of heat to Europe and North America.

The authors conclude that the effects of polar lows should be incorporated in ocean, climate and seasonal forecasting models. They also point out that the Intergovernmental Panel on Climate Change predicts that these storms will shift northwards in the future, and will occur less frequently than now. If so, this could greatly affect the deep waters of the North Atlantic, potentially reducing their southward flow. **Andrew Mitchinson**



NEODAAS DUNDEE SATELLITE RECEIVING STATION