archaeologists' ability to understand ancient chronologies and build timelines. Frachetti and colleagues' work exemplifies the most recent surge in archaeological applications of spatial technologies, such as the use of drones[7] or the creation of 3D models using laser scanners and photographs[8].

A related approach, social network analysis (SNA), holds great potential for archaeological studies[9,10]. It builds on network-analysis techniques developed in mathematics, physics, biology, economics and sociology that focus not only on individual entities, but also on the interconnectedness and emergent properties that arise from relationships between nodes that form part of a larger system.

SNA could be used to extend Frachetti and colleagues' work using additional data about sites on the Silk Road network. Settlement-pattern analysis, a type of investigation that examines the distribution of hamlets, villages, towns and cities in a region, has been used in archaeology since the 1960s. However, many settlement-pattern analyses have treated archaeological sites merely as dots on maps, even though villages, towns and other locations often preserve a vast and diverse array of information about ancient human activities[11]. Using data about architecture, plant and animal remains, and artefacts from sites along the Silk Road for SNA might help to reveal the nature and strength of ties between sites, and perhaps identify sites or groups of sites where particular trade activities were concentrated.

Frachetti and colleagues' research is innovative in breaking new ground without breaking any actual ground. A logical next step might be to apply SNA to the Silk Road to help identify the economic, social and political dynamics of this important ancient network. ■

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NANOSCIENCE

Single-atom data storage

The ultimate limit of classical data storage is a single-atom magnetic bit. Researchers have now achieved the writing and reading of individual atoms whose magnetic information can be retained for several hours. SEE LETTER P.226

ROBERTA SESSOLI

In 1993, the observation[1] that a single molecule can behave like a magnet and store information opened a new field of research. It has since been shown that molecules can be targeted individually[2] and engineered to have magnetic stability at temperatures well above that of liquid helium[3]. However, an open question has been whether it is possible to go to even smaller scales — down to a single atom. Thanks to the continuous and ingenious development of scanning probe microscopy technology, and an improvement in our understanding of the mechanisms that govern magnetization dynamics on the nanoscale, Natterer *et al.*[4] now unambiguously achieve the ultimate limit of writing and reading information. On page 226, the authors show that single-atom data storage is possible using a holmium atom deposited on a thin magnesium oxide film.

Single atoms deposited on a surface represent a sort of extension of the periodic table, because they can have properties that are different from those seen when the atoms are part of a molecule or an extended lattice. For instance, when an atom of a lanthanide element such as holmium (Ho), which has many unpaired electrons, is positioned on an oxygen atom of a magnesium oxide (MgO) surface, it is subjected to an extremely asymmetric electrostatic potential-energy profile. Consequently, such an atom exhibits a large magnetic anisotropy — its response to a magnetic field depends strongly on the direction of the field.

A large magnetic anisotropy is the basis for magnetic bistability, whereby an atom has two stable magnetic states, defined by the orientation of its magnetic moment (spin). Reversing the atom's spin requires that a potential-energy barrier is overcome, which makes the process increasingly difficult as the temperature is decreased[5]. Ho atoms on MgO surfaces were

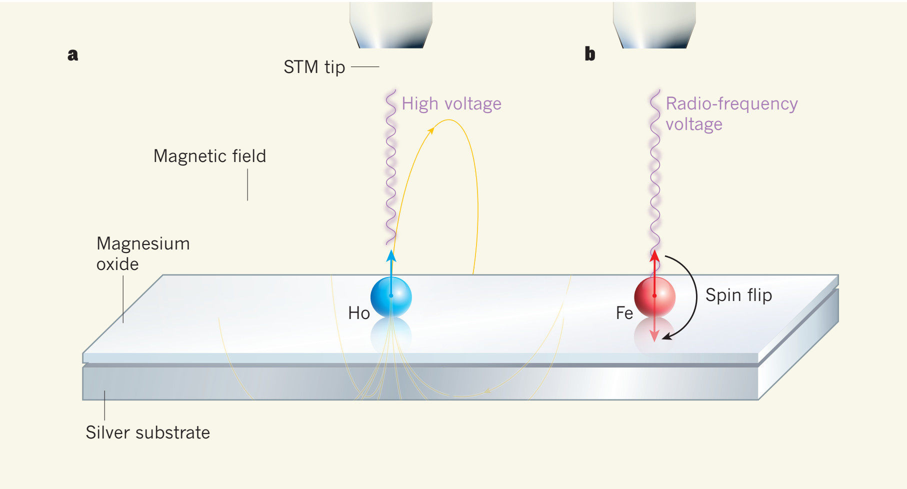

Figure 1 | Magnetic memory at the single-atom level. Natterer *et al.*[4] demonstrate the reading and writing of the magnetic state of a single holmium (Ho) atom, the ultimate limit of classical data storage. The authors' experiment consists of a Ho atom in the vicinity of an iron (Fe) atom on a thin magnesium oxide film that isolates the two atoms from a silver substrate. **a,** The authors first flip the Ho atom's magnetic moment (spin; blue arrow) by sending a high voltage through the tip of a spin-polarized scanning tunnelling microscope (STM). They then show that the spin is stable — the magnetic information is retained — for several hours. **b,** To confirm this, Natterer and colleagues use the Fe atom's spin (red arrow) as a sensor of the dipolar magnetic field generated by the Ho atom[9]. By applying a radio-frequency voltage from the microscope tip to the Fe atom, the authors detect an anomalous change in conductance when the frequency of this voltage coincides with the 'Larmor' frequency of the Fe atom's spin, which causes the spin to flip. The Larmor frequency depends on the local magnetic field at the site of the Fe atom, and therefore on the Ho atom's magnetic state.

recently found to exhibit magnetic bistability[6].

Natterer and colleagues now demonstrate that this phenomenon can arise in a single Ho atom. Even more impressively, they show that the atom's magnetic state can be written and read using a scanning tunnelling microscope. The authors first apply a high voltage (above about 150 millivolts) to the microscope tip to flip the atom's spin[7] — this is the writing process. Because the tip is magnetic, electrical conductance through the probed atom varies depending on the direction of the atom's spin with respect to the magnetization of the tip. The authors then read the atom's magnetic state by measuring this conductance[8]. They show that if low voltages (below about 75 mV) are used, the magnetic state can be stable for many hours.

It is often assumed that a system is unaffected by the process of taking measurements. However, this is not the case for experiments that use a scanning tunnelling microscope, in which what is actually probed is a larger system that comprises the tip, the targeted atom or molecule and a substrate. To prove unambiguously that the observed changes in conductance are caused by spin flips, Natterer and colleagues use a complex architecture in which the Ho atom is deposited alongside an iron (Fe) atom on a MgO bilayer that isolates the two atoms from a silver substrate (Fig. 1). The authors then use an ingenious scanning probe microscopy technique — described in a study published this year by the same research group[9] — to probe the dipolar magnetic field generated by the Ho atom.

By applying a radio-frequency voltage from the microscope tip to the Fe atom, Natterer *et al.* detect an anomalous change in conductance when the frequency of the applied voltage matches the 'Larmor' frequency of the Fe atom's spin, which causes the spin to flip. In this way, the authors perform a sort of 'single-spin' version of a spectroscopic technique called electron paramagnetic resonance, which is another remarkable achievement of their research group[10]. Because the Larmor frequency depends on the local magnetic field, the Fe atom 'senses' the magnetic state of the Ho atom, whose spin dynamics are no longer perturbed by the tunnelling current.

Natterer and collaborators find that the magnetic field generated by the Ho atom is stable for several hours, including at liquid-helium temperatures. Moreover, by placing two Ho atoms at slightly different distances from the Fe-atom sensor, the authors can detect the frequency shift associated with the four possible spin combinations, representing the four numbers that can be stored in a two-bit memory.

Although Natterer and colleagues' work is still far from having real-world applications, their advancement of scanning probe microscopy techniques has shown that the storage and retrieval of magnetic information in a single atom is feasible. Several issues need to be resolved. In terms of reading and writing data, the techniques involved are not the most user-friendly or affordable. Even if other sensing methods are developed, the peculiar magnetic properties of Ho atoms exploited by the authors can be realized only in extreme conditions, such as in an ultrahigh vacuum.

In this respect, the molecular approach, which is at the heart of this research field, could assist us by providing chemically stable objects that can be robustly tethered to a surface. However, in addition to efficient control of the magnetic anisotropy[3] and molecular vibrations[11], interactions between the molecule and its surroundings must be maintained to encode and read information. These are antithetical requirements whose fulfilment will not be straightforward. ■

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IMMUNOLOGY

The chronicles of T-cell exhaustion

T cells of the immune system often fail to target cancer cells because they enter a dysfunctional state known as exhaustion. Molecular analysis of T-cell exhaustion provides insights into the clinical use of these cells.

ROBERT A. AMEZQUITA & SUSAN M. KAECH

The T cells of the immune system that express the surface protein CD8 ($CD8^+$ T cells) combat viral infection and cancer through their ability to 'search and destroy' infected or abnormal cells. However, $CD8^+$ T cells often become dysfunctional, entering a state known as exhaustion, during certain chronic infections or when they enter a suppressive tumour microenvironment[1]. Although advances in immunotherapy have revealed that the immune system can be harnessed to fight cancer and other chronic diseases, much remains to be learnt about how T cells become dysfunctional and how they might be revitalized. Writing in *Science*, Pauken *et al.*[2] and Sen *et al.*[3] describe key molecular changes that occur in exhausted T cells. Their findings will improve our understanding of how these cells develop and whether their state can be manipulated by certain immunotherapies.

When $CD8^+$ T cells enter an exhausted state, there is an increase in the cells' expression of several inhibitory receptor proteins, including PD-1, TIGIT, LAG3 and TIM3 (ref. 4). In addition, exhausted cells have a diminished capacity to produce immune signalling molecules called cytokines, such as IFN-γ and TNF-α (ref. 5). The inhibitory receptor proteins desensitize the cells so that they do not respond to the presence of the specific antigen molecule that they usually recognize.

Antibody-mediated blockade of these inhibitory receptor proteins, such as PD-1 or its ligand the PD-L1 protein, has emerged as a transformative mode of cancer immunotherapy, removing the 'brakes' on a T cell's immune response to boost antitumour immunity and provide durable tumour regression for a subset of people treated[6]. However, central questions remain about such immunotherapies. Are exhausted T cells in an irreversible developmental state, or can blockade of PD-1 and PD-L1 signalling induce long-term reprogramming to return them to being functional T cells known as effector T cells that can launch a productive immune response? One way in which such changes in developmental state might be monitored is by analysing epigenetic changes, the structural alterations that occur in the DNA–protein complex called chromatin.

Pauken *et al.* and Sen *et al.* dive into the genetic underpinnings of $CD8^+$ T-cell exhaustion, examining the cells' transcriptional and epigenetic states from the onset of exhaustion through to subsequent treatment with anti-PD-L1 blockade[5,6]. As $CD8^+$ T cells become exhausted, many changes occur to their