SINGLE-MOLECULE MAGNETS

# Iron lines up

For more than a decade, single-molecule magnets have relied on multinuclear transition metal clusters and lanthanide compounds. Now, a mononuclear, two-coordinate iron(I) complex has shown that single transition metals can compete with the lanthanides when certain design principles from magnetochemistry are borne in mind.

Eckhard Bill

The bottom-up synthesis of magnetic materials is a key aim of research in molecular magnetism. The goal is not to compete with bulk magnets, such as those decorating the fridge door at home or operating valves in your car, whose magnetism depends on the collective contributions of neighbouring magnetic atoms arranged with long-range order. Instead, molecules that are intrinsically magnetic — single-molecule magnets (SMMs) — are attractive because of their small size, versatile chemical composition and adaptable fabrication methods. They hold promise for spin-dependent electronics or magnetic information storage, with fields that put forth devices such as reading heads for hard disks or non-volatile computer memory components.

In particular, SMMs that contain just one spin centre should be ideal for future miniaturized spin-based computational devices that can store and process information by making use of the fascinating fundamental phenomena of quantum mechanics[1]. Jeffrey R. Long and his collaborators from spectroscopy and theoretical chemistry have now described[2] in *Nature Chemistry* a 'simple' mononuclear, two-coordinate iron(I) compound with impressive SMM properties. Their findings outline a few remarkable design principles for future advances.

The SMM nature of a compound manifests itself, among other features, through magnetic hysteresis: magnetization induced by an external field relaxes only slowly after the field is removed. Below a certain 'blocking temperature', the magnetization may even be stable for a period of time, from minutes to years, before the compound relaxes. This slow magnetic relaxation arises from coupling of the electronic spins with the orbital moments of the atoms. Among other effects, this spin–orbit coupling causes zero-field splitting (ZFS) of the atomic electronic ground states, which generates directionality for the molecular magnetic moments (magnetic anisotropy) and creates an energy barrier towards reversal of the magnetization. To be a good SMM, a compound must combine a high-spin ground state and a ZFS that is large and negative and provides a well-defined axis for easy magnetization.

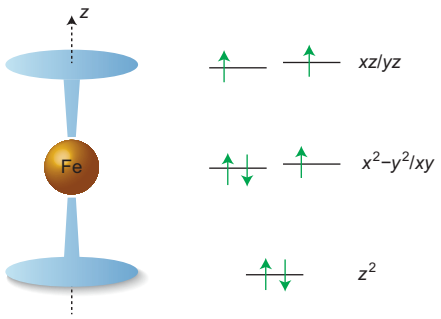


**Figure 1 |** A single-molecule magnet has been devised based on an iron(I) centre with linear symmetry. Schematic representation of the complex, emphasizing its axial symmetry (left). The corresponding ligand field at the metal affords a particular orbital scheme for the seven 3*d* electrons (right) that is the origin of a strong magnetic moment along the *z* direction.

An established strategy for building oligonuclear SMMs relies on clusters of transition metal ions with suitable local spins and large ZFS. To optimize the global cluster spin, ferro- or ferrimagnetic spin coupling is required between the metal centres, and these centres need to be organized in a geometry that favours build-up of large magnetic anisotropy. The latter in particular is not trivial, but successful schemes have been derived from the principles of classical magnetochemistry[3].

Recently, however, mononuclear complexes of terbium and dysprosium have surpassed all transition metal complexes by showing SMM behaviour with extremely large spin relaxation barriers[4] corresponding to thermal energies of more than 900 K — 10 times as high as those of transition metal clusters. This is because a single lanthanide spin centre can display large enough axial magnetic anisotropy to lead to high spin relaxation barriers. Since then, *f* elements have been considered 'silver bullets' for SMM developments.

In their present work, Long and co-workers have tuned the ligand field splitting of a 'simple' iron complex to achieve similar properties — a magnetic moment that has a suitable magnitude and strong anisotropy. The complex shows a spin relaxation barrier of 328 K, and is the first complex with a cheap and abundant transition element that may be able to compete as an SMM with lanthanide compounds. This is particularly noteworthy because the spin–orbit coupling (and thus anisotropy) of first-row transition metal ions is intrinsically lower than that of the lanthanides, and their larger ligand field effects in most coordination environments usually quench the orbital moment necessary for persistent magnetism to arise. Also, molecular vibrations in transition metal coordination complexes often perturb the degeneracy of *d* orbitals (for example through the Jahn–Teller effect); this weakens the ZFS and further limits the magnetic anisotropy.

The selection of the successful iron(I) SMM was guided by the consideration that a low coordination number of the *d*-metal ion, and a low oxidation state, should exhibit a high-spin *d*-electron configuration with unpaired electrons in close-lying *d* orbitals. This could provide unquenched orbital angular momentum, so that strong spin–orbit coupling is expected, which maximizes the magnitude and the anisotropy of the magnetic moment. In the new compound, this mechanism holds in particular for the $d_{x^2-y^2}$ and $d_{xy}$ orbitals (Fig. 1). The fact that the complex is linear inevitably provides a unique axis for easy magnetization and the preferential alignment of the magnetic moment.

A proof of this principle has already been obtained[5–8], when SMM behaviour was observed for linear iron(II) compounds with spin $S = 2$. These compounds exhibit impressive relaxation barriers of up to 260 K or so, but their magnetization was short-lived — even at low temperatures — unless a polarizing magnetic field was

applied. This was not entirely surprising, because this type of integer-spin system ($S$ = 2, 4…) provides magnetic decay pathways 'around' the spin relaxation barrier. In contrast, half-integer spins (with $S$ = 3/2, 5/2…) are not at risk from that, owing to the different polarization of their magnetic levels. The Long group therefore chemically reduced one of the known iron(II) precursor complexes[5–7] to obtain an iron(I) compound with spin state $S$ = 3/2. The resulting complex not only shows, as anticipated, a record high relaxation barrier (for iron) of 328 K, significant magnetic hysteresis below 29 K and magnetic 'blocking' below 4.5 K, but also has improved permanence in zero field. Unfortunately, the stability at weak fields close to zero was not as good as expected, but this deviation touches on fundamental questions about the role of spin tunnelling and weakest interactions for magnetic decay and deserves further study.

Detailed spectroscopic and quantum-chemical characterization of the linear iron(I) compound revealed an electronic structure that many inorganic chemists familiar with ligand-field models would probably not have guessed correctly. The theoreticians in the research team showed — with spectroscopy-oriented multireference methods[9] and ligand-field analyses based on computation of all electronic multiplets for the $3d^7$ configuration — that strong $4s$–$3d_{z^2}$ mixing readily stabilizes the $d_{z^2}$ orbital in the linear symmetry, as sketched in Fig. 1 (right). The result is well supported by comprehensive spectroscopic characterization, and the calculated orbital degeneracies nicely explain the unquenched orbital moment. Interpreted through the ligand field model (derived *ab initio*), the calculations provide a solid understanding of the compound and a wealth of chemical information, which will stir things up in the field. ❐

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POLYMER CHEMISTRY

# Proteins in a pill

Protein drugs are important therapies for many different diseases, but very few can be administered orally. Now, a cationic dendronized polymer has been shown to stabilize a therapeutic protein for delivery to the gut.

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Proteins are widely used as drugs — over 130 are approved by the US Food and Drug Administration (FDA). These therapeutics make up for deficiencies, supplement or boost existing pathways, and block deleterious agents[1]. Proteins are found in vaccines and other treatments for diseases that range from diabetes, osteoporosis and cancer. Most of these drugs must be given by injection, and this has associated difficulties including pain, discomfort and inconvenience for patients. Oral administration in the form of a pill would be a much better alternative, yet there are many challenges associated with this method of delivery.

The gastrointestinal tract has evolved to cleave proteins into small fragments and to denature them, a beneficial feature that enables us to digest our food and obtain essential nutrients. Unfortunately for delivery of therapeutic proteins, this degradation also results in loss of biological activity. Another problem facing oral delivery is the rapidity with which materials are moved through the gastrointestinal system by gastric emptying and peristalsis. Despite these problems, there are a few proteins that need oral administration because their action is required within the gastrointestinal tract[2], for example enzymes for treating maladies such as pancreatic insufficiency and lactose intolerance. Some are relatively stable in the gut, but most are not. Various strategies have been investigated to retain activity of these proteins; however, it has proved difficult to preserve biological activity, especially within specific places in the gastrointestinal tract. Now writing in *Nature Chemistry*, Jean-Christophe Leroux and co-workers report[3] that by covalently attaching a polymer to a proline-specific endopeptidase (PEP), the enzyme was stabilized and retained in the upper gastrointestinal tract (Fig. 1).

Proline-specific endopeptidases are a promising treatment for coeliac disease — commonly known as gluten intolerance. Coeliac disease comes about when a person launches an immune response against large gluten fragments in the small intestine[4]. These fragments typically contain high proportions of the amino acids proline and glutamine, which our natural enzymes do not recognize. Cleaving gluten into tiny peptides before passing them to the intestine has been proposed as one method of mitigating the pathology of gluten intolerance. Bacteria-derived PEPs target proline-rich regions of the gluten and have been explored as a way of reducing its immunotoxicity[5]. However, some of the candidate enzymes are easily inactivated in the stomach, and yet any therapeutic would require prolonged enzymatic activity there to ensure that the gluten is effectively broken down before it moves into the small intestine. Leroux and co-workers show that by attaching a positively charged polymer to a PEP, the enzyme was not only active in the stomach, it was retained there.

Conjugation of synthetic polymers to proteins is often used to protect injected proteins from enzymatic degradation and to increase the time it takes for the biomolecule to be excreted out of the body[6]. This results in increased circulation times and reduced dosage frequency. The polymer that is most widely utilized for this purpose is the linear polyether poly(ethylene glycol) (PEG), and many so-called PEGylated proteins and peptides have been approved as treatments by the FDA. Leroux and co-workers tried PEGylation of the PEP but found, however, that although this standard polymer