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SPECTROSCOPY

NMR down to Earth

Janez Stepišnik

High-precision nuclear magnetic resonance spectroscopy generally requires the use of powerful magnets. But using Earth's magnetic field allows us to gain some of the same information on the cheap.

Are expensive superconducting magnets necessary to perform high-resolution nuclear magnetic resonance (NMR) spectroscopy? Not absolutely, say Stephan Appelt and his colleagues in the February issue of *Nature Physics*¹. They use a far less pricey source of magnetism — Earth's own magnetic field — to distinguish the chemical structures of various molecules containing hydrogen, lithium and fluorine. The level of accuracy they achieve is an order of magnitude better than that possible with the most advanced superconducting magnets.

When an external magnetic field is applied to an atomic nucleus, it induces a polarization in the direction of the intrinsic rotation, or 'spin', of that nucleus' constituent protons and neutrons. These spins align either parallel or antiparallel to the field, causing the quantum-mechanically allowed energy levels of the nucleus to split. At a frequency corresponding exactly to the difference between these energy levels, the nucleus can absorb electromagnetic radiation: the phenomenon known as nuclear magnetic resonance or NMR, first observed by Felix Bloch and Edward Mills Purcell in 1946 (for which achievement they won the Nobel Prize in Physics in 1952).

Soon after the initial discovery, it became clear that the effective magnetic field on a nucleus — and consequently the observed NMR frequency — is subtly changed by the effects of both orbiting electrons (the 'chemical shift')² and the spins of neighbouring nuclei ('J-coupling')³. This was the beginning of the triumphant success of NMR as a spectroscopic tool for exploring the composition and chemical environment of molecules in the liquid state. In the decades since, the need for higher sensitivity and lower spectral dispersion has demanded higher, more homogeneous magnetic fields, fuelling the development of powerful superconducting magnets.

Nowadays, the highest-resolution NMR techniques, using magnets producing field strengths of between 1 and 10 tesla, reproduce the hydrogen spectrum with a broadening of spectral lines caused by the instrumentation of less than a tenth of a hertz.

Compared with the fields that can be attained with superconducting magnets, Earth's magnetic field is weak: it varies from about 25 microtesla (μT) at the Equator to 75 μT at the poles, with geomagnetic field lines inclined, in Europe and North America, at an angle of about 60° to the (horizontal) surface. The field is not constant: currents in the ionosphere and disturbances from Earth's interior produce slow daily variations in the field with amplitudes of some 25 nanotesla (nT), and superimposed on these are further oscillations with periods of a few seconds and amplitudes of about 1 nT. Far enough from electric installations and other sources of artificial magnetic perturbation, however, proper shielding can reduce these shorter variations to about 0.1 nT s⁻¹, and local spatial gradients to below 1 nT m⁻¹. These variations are comparable to those found in the fields of artificial magnets.

The first observation of a nuclear magnetic effect in Earth's magnetic field — the free precession of proton spin⁴, akin to the precession of a spinning top in Earth's gravitational field — came not long after the discovery of NMR. The weakness of the geomagnetic field is such that it causes only a slight natural polarization in proton and neutron spins. Before an NMR measurement in the Earth field can be made, therefore, these spins generally have to be polarized by a high magnetic field, or polarization has to be transferred from more-readily polarizable electrons using a method known as dynamic nuclear polarization. Such techniques have been used for measurements of the precise 'Larmor' precession frequency for protons, of



50 YEARS AGO

...you reveal more than I think you were aware of when writing "a nation using...a minority language cannot escape bilingualism if it desires to attain high standards of scholarship". If the sentence is understood as referring to the use of minor languages for publishing, it is indisputable; but all too frequently it turns the other way — scholars within the major language groups neglecting the literature outside their own language... To illustrate this point I have made a small survey of world scientific literature... That our Soviet colleagues know more about 'Western' literature than the reverse is nothing new, but it is deplorable... That the English and even more the American literature should emerge as the narrowest is scarcely unexpected... It is a waste, and it is also inconsiderate, to publish primary scientific material in a minor language.

From *Nature* 18 February 1956.

100 YEARS AGO

Dr. H. Charlton Bastian re-expounds his well known biological heresies with a vigour and industry worthy of a better cause. The first heresy is that "archebiosis" is a present occurrence, that living organisms may here and now arise from non-living materials... we are recommended to take an infusion of turnip or fresh beef, to filter this through two layers of the finest Swedish paper, to let a drop fall on a cleaned microscope slip, to put a cover-glass on, to remove excess of fluid with blotting paper, to allow one or more air bubbles to remain in the film, to seal up with melted paraffin wax...to incubate at blood-heat for two to three hours, and to await events. The expected happens — multitudes of living particles appear... While we must stand aloof from Dr. Bastian's heresies, we cannot but admire his dogged support of what seems to us a lost cause. It is something to stand *unus contra mundum* with no loss of courage or good humour.

From *Nature* 15 February 1906.

50 & 100 YEARS AGO

the relaxation time that spins require to return to their normal states following polarization, and of the strength of J-coupling between nuclei⁵. The method has also been applied to the magnetic resonance imaging of pieces of fruit and of phantoms standing in for human tissue⁶, and for the detection of groundwater reservoirs⁷.

The disadvantage of low-field NMR for chemical analysis is that the chemical shift of spectral lines is smaller than the broadness

that is due to the magnetic field. This renders effectively unobservable the direct information about a nucleus' chemical environment gained from the chemical shifts caused by the surrounding electrons' screening of the applied magnetic field. On the other hand, the J-coupling between nuclear spins caused by chemical bonds is almost independent of the magnetic field, so its effect is proportionately greater where the field is low. In J-coupling, the quantum states of shared electrons impose

information about the chemical environment through the indirect dipolar coupling between nuclei that are relatively close to one another. The effect of the resultant J-splitting on the NMR frequency is at an observable level of between a few tenths and a few tens of hertz.

In their experiments, Appelt *et al.*¹ measure the J-coupled spectra of various compounds containing hydrogen, lithium and fluorine. They first pre-polarized the nuclei of each sample in the field of a permanent magnet to a



CARTOGRAPHY

A popular perspective

Maps shape our perception of geographical realities, albeit often imperfectly. A world map, for instance, relies on some form of projection that transfers — with inevitable distortion — the unbounded surface of the globe to the bounded page. Mark Newman has taken this idea of distortion a stage further, producing a world map that gives each territory a size proportional to its population.

The idea of such density-equalized 'cartograms' is not new, and can be applied to a host of variables, besides population, whose distribution is geographically uneven. The innovation in Newman's map (pictured) is the use of the diffusion equation, familiar from the physics of heat transfer and molecular

mixing, to produce a map that smooths out population density, but keeps geographical distortion to a minimum.

The map follows on from work in which Newman and Michael T. Gastner applied the diffusion technique to (among other things) maps depicting the results of the 2000 US presidential election (*Proc. Natl Acad. Sci. USA* **101**, 7499–7504; 2004). For the world cartogram, a grid of 4,096 by 2,048 squares was overlaid on a rectangular world map based on a cylindrical equal-distance (plate carrée) projection. A starting population-density function was computed by dividing the population of each country equally between the squares covering its territory.

Population was then allowed to diffuse away from areas of higher

density to those of lower density, with national boundaries moving such that the net population flow through them was zero at all times. The displacement of the boundaries was recalculated throughout the diffusion process by integrating the diffusion-velocity field, until the population density was equalized over the land surfaces. Constituent parts of non-contiguous territories (such as nations divided between several islands) were treated as separate entities, and the oceans and unpopulated Antarctica were treated as a sea of uniform population density equal to the average density of the populated land areas. This ensured an end result that maintained the semblance of familiar geographical relationships.

Apart from the domination of Asian nations — China and India alone account for about a third of the world population of some 6.6 billion — the map throws up many other

interesting facets. The Americas are diminished; Russia and Canada, the two largest geographical territories, are reduced to Arctic buffer zones. Australia all but disappears, especially when compared with its near neighbour Indonesia.

The value of Gastner and Newman's technique lies in its intuitiveness and the relative simplicity of the algorithm, which requires a computation time of minutes. The diffusion method may also be extended readily to three dimensions, to create, for example, a three-dimensional 'homunculus' in which each part of the body is scaled according to the size of the brain region devoted to it. The potential of such techniques for producing startling representations that challenge our preconceptions seems — unlike world maps — unbounded.

Richard Webb

value about 10,000 times that attainable in the geomagnetic field, and transferred the sample within one second into the detection coil of an Earth-field NMR spectrometer. They investigated benzene, lithium chloride dissolved in water, tetramethylsilane, silicone oil, octamethylcyclotetrasiloxane and nonafluorohexane, demonstrating in each case that their spectrometer could image these compounds' molecular structure. The instrumental broadening of their spectrometer is only a few millihertz over a sample volume of 1 cm³ — less than the broadening of high-resolution NMR with advanced superconducting magnets. The spectral resolution is, however, limited by the shorter spin relaxation time to a few tenths of a hertz.

The authors predict that the combination of low-field NMR with advanced methods of spin hyperpolarization will allow time-resolved NMR spectroscopy of rare nuclei such as ⁶Li, ¹³C and ²⁹Si, and the separation of the corresponding J-couplings with high precision. Many applications of this mobile low-field NMR technique are also likely in medicine and materials science: the tracking of hyperpolarized ⁶Li⁺ and ⁷Li⁺ migrating through ion channels or membranes, for example, or the characterization of mineral oil in well-logging and the online detection of chemical reactions.

Earth-field NMR cannot replace the diagnostic capabilities of the chemical shift measurements available with the high-field method. But particularly in combination with

superconducting quantum interference device (SQUID) detectors⁸, the technique could give limited, but potentially very useful, information about the coupling of many molecules. ■

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CHEMISTRY

Brevity for bonds

Jay S. Siegel

Fashion design? Game-playing? Designing the shortest bond between two carbon atoms can seem to have elements of such apparently ephemeral pursuits. But it can also stretch the chemist's creativity.

Carbon–carbon (C–C) bonds could be tailored shorter this coming season, according to Deborah Huntley and colleagues, who include the Nobel laureate Roald Hoffmann. Their predictions appear in an unlikely fashion magazine, the journal *Angewandte Chemie International Edition*¹. The authors highlight several ways to sport short bonds, but it will be no small task for manufacturers to bring these designs into reality.

Molecular fashion has long been the chemist's playground² — no wonder, given chemistry's unique position in the design and synthesis of new forms of matter. The pursuit of novel molecular structures has led chemists to uncover material properties that cannot be revealed by observational science alone. Such creativity blends the hard science of chemistry with the engineering and aesthetic components of architecture and sculpture — or even *haute couture*. A question that often stems from a molecular-design hypothesis is “Can we make that?”. Whether the answer is yes or no, addressing such questions in a scholarly manner can generate great chemical insight.

In their paper, Huntley and colleagues¹ ask how many ways a C–C bond can be squeezed, and what is the resultant degree of shortening. They cite precedent from Henning Hopf's 1976 essay “*Wie kurz kann eine Einfachbindung werden? Wie stark lässt sie sich stauchen?*” (“How short can a single bond be? How strongly can it be compressed?”)³. As such, their call for a renewed interest in short bonds can be seen as a revivalist trend, which could signal a return to training chemists in

their basic trade: the synthesis and characterization of new molecular entities.

The authors propose three basic approaches to squeezing C–C bonds: caging, crowding and clamping. They evaluate all three computationally, using a reasonable computational level for the rough screening of structures. Such simulations represent a departure by

Hoffmann from his normally more poetic approach to theory. But given the goal of designing the shortest bond, one is left to grind out the numbers, or grind out the synthesis and structure determination.

In the end, investigating the concept of relative molecular compressibility teaches us more about the behaviour of molecules than can the size of the deviation from the ‘normal’ bond length of 1.53 Å. Huntley *et al.* predict a world record of 1.32 Å, but there is a chemistry lesson to be learnt from any compound that bears a C–C single bond less than 1.4 Å long, for example.

The shape of the ‘potential-energy well’ for stretching a C–C bond — the curve showing the relationship between the system's potential energy and the distance between two carbon atoms — is asymmetric; distortions to longer

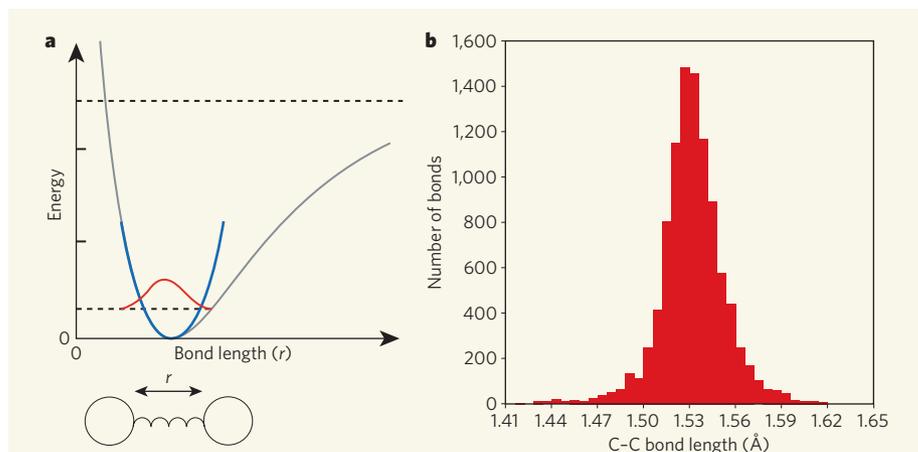


Figure 1 | Bonding energy potential and carbon–carbon bond-length distribution. **a**, The C–C bond can be considered energetically as two balls joined by a spring. Pulling them apart becomes increasingly harder (requires more energy) the longer the bond gets. Pushing them together will also become more difficult as they almost come into contact. But somewhere in the middle is a stable state. Although this approximation (the blue line) works fairly well, especially at the bottom of the energy well, a more realistic energy profile (grey line) is asymmetrical because the energy of stretching the bond is limited by the bond dissociation energy. The energy of interaction decreases as the atoms move apart; the red line shows a qualitative expectation of the distribution observed for **b**. **b**, Distribution of observed bond lengths, compiled from data from the Cambridge Structural Database⁵. Skew towards longer bonds becomes evident only past the 3σ level of deviation beyond the ‘normal’ bond length of 1.53 Å.