



## 50 Years Ago

'Masters and Pupils' — The three books under review are approximately equal in price, but this is not true of their value. Two of them are hardy annuals; the third — the *Transactions of the International Ophthalmic Optical Congress, 1961* — appears ten years after the previous issue. Those who argue that opticians neglect research will find their fears both confirmed and confounded — confirmed when they read some of the uncritical work ... on contact lenses, and confounded by the high-quality work emanating from British and especially American sources. The trouble with a volume such as this is two-fold: every paper presented at the congress is reproduced, and, what is worse, reproduced in full. Verbosity is a smoke-screen for self-consciousness, and by George! what a difference a whiff of editorial air would have made to this tome. This is not to convey the notion that it does not contain any paper of merit. Le Grand, reproducing data by Bonnet on the cornea, is at his usual instructive best, Ball on dark-adaptation provocative ... By and large, all three volumes are well produced, adequately illustrated, and set in pleasing type. But they would be lighter, not to say cheaper, if editors kept pointing a pencil at the contributors, and — conscious of the rudeness of the gesture — kept asking them "Is this word really necessary?".

From *Nature* 25 May 1963

## 100 Years Ago

The Palaeolithic skull from Piltdown, Fletching, Sussex, just described in the *Quart. Journ. Geol. Soc.* By Dr. A. Smith Woodward as the type of a new genus and species (*Eoanthropus dawsoni*), has been placed on exhibition in a special case in the central hall of the Natural History Museum.

From *Nature* 22 May 1913

structure, one of the three transmembrane helices from a DgkA molecule is switched with that of another molecule.

The different structures might reflect the different conditions used in the two analyses, or the challenges involved in obtaining the NMR structure. However, given the extreme thermal stability of the membrane-embedded DgkA homotrimer (it can survive at temperatures as high as 100 °C)<sup>4</sup>, it is difficult to imagine a seamless switch between 'swapped' and 'unswapped' homotrimers. In the light of the high-resolution crystal structure described by Li and co-workers, the NMR results might need to be revisited.

The kinases are one of the largest and most extensively studied protein families, but DgkA shows that there are still surprises to be found. Its remarkable structure and composite active site add an intriguing twist to the kinome — the set of known kinases in an organism. The enzyme's ingenious design results in an active site that is much simpler than those of other kinases. Indeed, DgkA provides a new perspective for understanding the architecture and associated catalytic mechanisms of membrane

enzymes. As well as structural determination of ATP-bound and substrate-bound DgkA complexes, future work should include detailed investigation of the enzyme's catalytic mechanism and regulation, and resolution of the discrepancy between the NMR and crystal structures. ■

**Jimin Zheng** is in the College of Chemistry, Beijing Normal University, Beijing 100875, China. **Zongchao Jia** is in the Department of Biomedical and Molecular Science, Queen's University, Kingston, Ontario K7L 3N6, Canada.  
e-mail: jia@queensu.ca

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### PHYSICAL CHEMISTRY

# Handedness detected by microwaves

**Traditional methods for detecting and identifying the handedness of molecules — their chirality — have been based on the same theoretical concept. A technique has been reported that departs from this paradigm. SEE LETTER P.475**

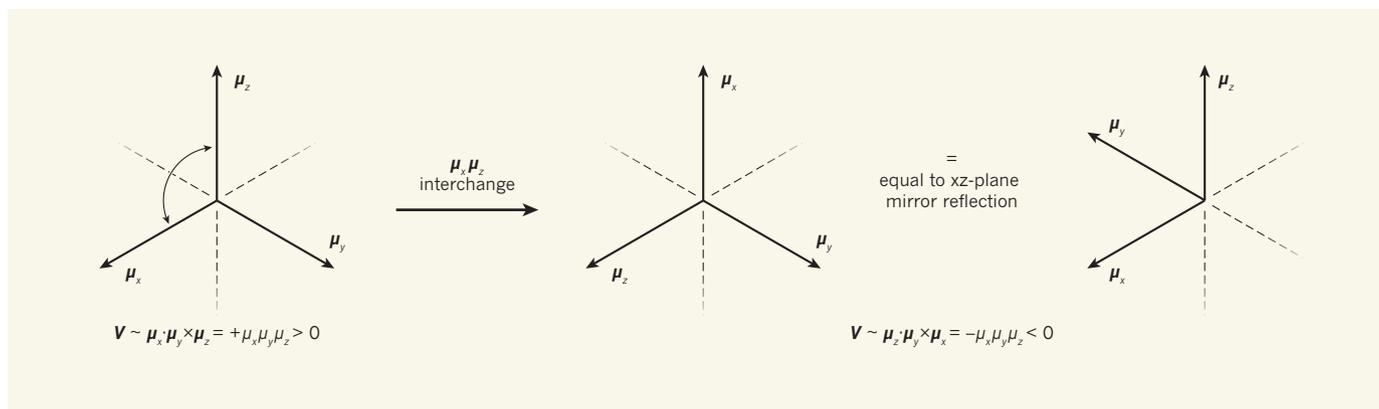
LAURENCE A. NAFIE

The property of handedness known as chirality is one of the most subtle and yet profound aspects of our world. Of particular relevance to chemistry and biology is the fact that molecular structures can be chiral: as with our left and right hands, chiral molecules have otherwise equivalent mirror-image isomers of the opposite chirality<sup>1</sup>. Such isomers are called enantiomers, and the ability to distinguish between them is called enantiomeric detection. On page 475 of this issue, Patterson *et al.*<sup>2</sup> describe a method that adds to the chemist's toolbox of techniques for detecting and identifying chirality in molecules<sup>3</sup>. They report that, when microwave radiation associated with transitions between rotational states is emitted by molecules of opposite chirality, the radiation is exactly out of phase, thus providing a clear signal of molecular chirality.

The building blocks of life are 'homochiral': naturally occurring amino acids, proteins,

sugars and nucleic acids exist as only one chiral form. If these building blocks had mixed chirality, molecular chaos would ensue and life would not be possible. Nature's lead is being followed by scientists, who have learned that single-enantiomer drugs are more efficient at binding to biological targets, and have fewer side effects, than the equivalent racemic drugs (which contain an equal mixture of opposite enantiomers). In fact, our bodies recognize drugs of the opposite chirality as different molecules, even though, apart from their chirality, they have the same structure. This is because the mirror symmetry of enantiomers is broken by the homochiral biochemistry of the human body, in the same way that only a right hand fits comfortably into a right-handed glove.

The mirror symmetry of enantiomers can also be broken by circularly polarized electromagnetic radiation. Circular polarization occurs when the electromagnetic field of radiation rotates either clockwise or anticlockwise, once per wavelength, as the beam propagates.



**Figure 1 | A new mechanism for chiroptical spectroscopy.** In Patterson and colleagues' method<sup>2</sup> for identifying molecular chirality, the measured quantity depends on the handedness of three mutually orthogonal electric-dipole rotational transition moments,  $\mu_x$ ,  $\mu_y$ , and  $\mu_z$ , which are associated with the three rotational degrees of freedom of a molecule. When microwave radiation interacts with these moments, energy transfer changes the rotational state of the molecule, generating a spectroscopic signal. The moments are vectors, and

can be represented by a scalar triple product of  $\mu_x \cdot \mu_y \times \mu_z$ . This product can be regarded as a dipole volume,  $V$ , that is equal to the product of the magnitudes of the three vectors. The sign of  $V$  depends on the order of the vectors. If any two vectors are interchanged (a process equivalent to a mirror reflection), the sign changes. Because  $V$  changes sign under spatial inversion (mirror reflection) and is even under time-reversal symmetry, it is a measure of true chirality<sup>8</sup>.

Two classical forms of 'chiroptical' spectroscopy have been developed on the basis of this symmetry breaking. The older form is optical rotation<sup>4</sup>, which measures the difference in refractive index for left-circularly polarized (LCP) and right-circularly polarized (RCP) radiation as it passes through chiral materials. The other is circular dichroism (CD), which measures the difference in the absorption of LCP and RCP radiation. Both techniques typically use ultraviolet or visible light and involve electronic transitions in molecules. Vibrational circular dichroism (VCD, which uses infrared radiation) and Raman optical activity (ROA, which mainly uses visible radiation) have also been added to the list of chiroptical spectroscopy techniques<sup>5–7</sup> and are based on the vibrational transitions of molecules.

Using these four techniques, two fundamental measures of chirality can be determined: enantiomeric excess, which is the excess of one enantiomer over the other in a sample; and absolute configuration, the specific handedness of an enantiomer. Every chiral drug substance approved for sale by the US Food and Drug Administration must have a known absolute configuration and a specified level of enantiomeric excess usually greater than 99% (see [go.nature.com/ujg17l](http://go.nature.com/ujg17l)).

Patterson and colleagues' use of microwave radiation to detect chirality is surprising, because microwave CD would be expected to be too small for detection by modern spectrometers. All previously measured forms of chiroptical intensity are inversely proportional to the wavelength of the probing radiation. Electronic CD in the ultraviolet–visible region is typically about 100 times larger than VCD in the longer-wavelength infrared region. Microwave CD should be at least 100 times smaller than VCD. This size argument derives from the mechanism underpinning

traditional chiroptical spectroscopy: optical activity arises from the interference between the electric-dipole transition moment and the weak magnetic-dipole transition moment (or, in some cases, the weak electric-quadrupole transition moment as well) that is detected when a chiral molecule is irradiated with alternating LCP and RCP light. The optical activity can be positive or negative depending on whether the electric- and magnetic-dipole transition moments point into the same or opposite halves of a sphere centred on the molecule.

The authors' method does not arise by this interference mechanism. Instead, the authors detect chirality by applying two orthogonally polarized, microwave-timescale electric fields (oriented in the  $x$  and  $z$  directions) to a sample. This causes the molecules in the sample to emit microwave radiation polarized along a third orthogonal direction ( $y$ ), the intensity of which is proportional to the product of each molecule's three orthogonal rotational electric-dipole moments ( $\mu_x$ ,  $\mu_y$ , and  $\mu_z$ ). This product is independent of the molecule's orientation, but is sensitive to the handedness of the directions of the three rotational dipole moments. It therefore changes sign if any two of the moments are interchanged or, equivalently, if the molecule is exchanged for its opposite enantiomer, and so is a new measure of true chirality<sup>8</sup> (Fig. 1).

Patterson and colleagues' approach has several advantages over existing chiroptical spectroscopy techniques. Because it does not depend on a weak magnetic-dipole transition moment, the chiral signal is nearly as large as that of the applied microwaves. Furthermore, the method requires extremely cold, gaseous molecules, which exhibit sharp, narrow lines in their microwave spectra. Molecules of interest can therefore be resolved in the presence of other interfering molecules. Moreover,

measurement times can be as fast as tens of seconds; measurements for traditional chiroptical spectroscopy techniques take minutes to hours.

Of course, a few drawbacks remain to be ironed out. Any molecule investigated must be sufficiently volatile to be sampled in the gas phase, potentially placing an upper limit on the size of molecules that can be analysed. And for large molecules that have high conformational freedom, it may be difficult to identify the conformation associated with the microwave line being analysed. Additionally, enantiomeric excess measured using the technique is accurate to only about 5%, and so further development is needed to reach a more desirable level of accuracy.

Finally, the determination of absolute configuration for a sample of unknown chirality has yet to be demonstrated. The scalar triple product of  $\mu_x \cdot \mu_y \times \mu_z$  will be positive or negative depending on the enantiomer in the sample. But how can one say which enantiomer produces a positive product and which a negative one? This information might be obtained by determining whether the chiral microwave emission of a particular enantiomer has the same phase as the driving field, or the opposite one. However, this information would still need to be connected to the absolute configuration of a chiral molecule, most probably by carrying out a quantum-mechanical calculation to determine the signs of the dipole-moment components. Most other chiroptical spectroscopy techniques require such a calculation to connect measured spectra to the molecule's absolute configuration.

If Patterson and co-workers' method can be widely applied to determine the enantiomeric excess and absolute configuration of previously unassigned chiral molecules, particularly those of pharmaceutical interest,

then their paper will be extremely important. But even if its applicability is at first limited (either for sampling reasons or by instrumentation), the unexpected demonstration of a conceptually new form of chiroptical spectroscopy makes this work a landmark in the 200-year-old history of optical activity in chemistry. ■

**Laurence A. Nafie** is in the Department of Chemistry, Syracuse University, Syracuse, New York 13244, USA.  
e-mail: lnafie@syr.edu

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## MATERIALS SCIENCE

# When two is better than one

**Aerogels have many potential applications but usually suffer from poor elasticity. The synergistic assembly of carbon nanotubes and graphene has now allowed multifunctional, ultra-lightweight and super-elastic aerogels to be made.**

WENCAI REN & HUI-MING CHENG

Solids are normally stronger but heavier than gases because their atoms are bound together more tightly. Writing in *Advanced Materials*, however, Sun *et al.*<sup>1</sup> describe how they have used two carbon-based nanomaterials — graphene and carbon nanotubes — to make a strong carbon aerogel that is lighter than air, is super-elastic and has a variety of useful properties.

Aerogels are highly porous solid foams that have an interconnected network of thin, solid walls. They have an extremely low density and a high specific surface area — the total surface area per unit mass. But they tend to suffer from poor strength and low elasticity: pressing them firmly can cause a catastrophic breakdown of the network. The first aerogel to be reported<sup>2</sup> was prepared from a silica gel by supercritical drying, in which the liquid component of the gel is dried off in a controlled manner. This

silica aerogel is transparent and has the lowest thermal conductivity of any known solid, making it suitable as a thermal insulating material.

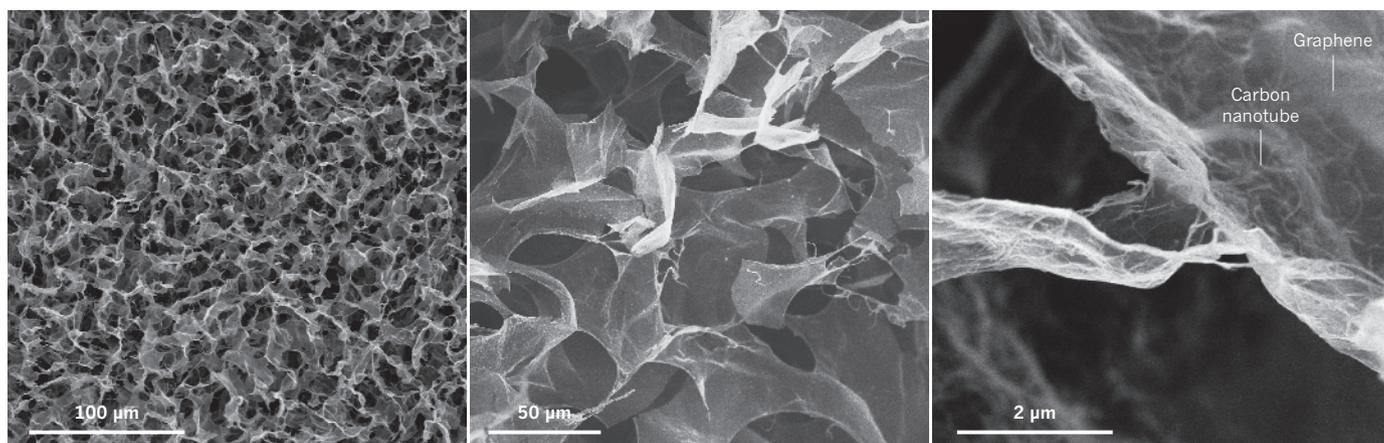
Several aerogels have since been made, including oxide and carbon aerogels. However, the synthesis of ultralight aerogels with high elasticity has remained a challenge. Aerogels with these qualities would find many uses, for example as media for energy absorption<sup>3,4</sup> or as reusable absorbents for liquids<sup>1</sup>, and as pressure-responsive sensors<sup>1</sup>.

The prospects for making ultralight, highly elastic aerogels have changed with the development of carbon nanomaterials, however, especially carbon nanotubes (CNTs) and graphene. Graphene is a single layer of carbon atoms arranged in a perfect honeycomb structure<sup>5</sup>. A CNT is a tubular material seamlessly rolled from a graphene sheet<sup>6</sup>. Both materials have a host of useful properties: low density, high strength and stiffness, high electrical and thermal conductivity, high specific surface

area, excellent flexibility, and good chemical stability<sup>5,6</sup>. They therefore hold great promise as building blocks for aerogels with multiple functionalities.

Both graphene and CNTs have been used separately to make aerogels that have low density and high elasticity<sup>3,4,7</sup>. For instance, a graphene aerogel with a density of 5.1 milligrams per cubic centimetre has been shown to sustain its structural integrity under a load of more than 50,000 times its own weight and can rapidly recover from 80% compression<sup>3</sup>. However, the low elastic bending stiffness of graphene sheets limits improvement in the elasticity of graphene aerogels when their density is decreased<sup>1,3</sup>. Also, in CNT aerogels, the bundling or permanent buckling of the CNTs usually results in inefficient load transfer between the CNTs, and significant irreversible deformation of the aerogels<sup>1,8</sup>.

Sun *et al.*<sup>1</sup> used giant graphene oxide (GO) sheets, tens of micrometres across, to build an ultralight structural framework, and used CNTs as 'ribs' to reinforce the framework, taking advantage of their good elasticity (Fig. 1). The authors fabricated their hybrid graphene–CNT aerogels by freeze-drying an aqueous solution of GO sheets and CNTs, and then chemically reducing the GO to graphene. This procedure resulted in a graphene–CNT aerogel that is lighter than air (it has a density of 1.0 mg cm<sup>-3</sup>, compared with 1.2 mg cm<sup>-3</sup> for air at ambient conditions) and that could recover its original macroscopic shape and microstructure after being repeatedly compressed by 50% in 1,000 cycles of compression



**Figure 1 | Synergistically assembled carbon aerogels.** Sun *et al.*<sup>1</sup> report the assembly of multifunctional, ultra-lightweight and super-elastic carbon aerogels from reduced graphene oxide sheets and carbon nanotubes. The

microscopic structure of the aerogels, which consists of an interconnected network of randomly oriented graphene walls and carbon nanotube 'ribs', is seen here at three different scales.