New technique to accurately detect the 'handedness' of molecules in a mixture

June 24 2015

Scientists have demonstrated for the first time the ability to rapidly, reliably and simultaneously identify the 'handedness' of different molecules in a mixture.

The research, led by chemists at The University of Nottingham and the VU University Amsterdam, and published in the academic journal *Nature Communications*, could offer a new technique to easily distinguish whether a molecule is present in a left- or right-handed form.

The breakthrough could be important in developing effective molecules for use in a wide range of industries—everything from the development of safer new drugs and disease diagnosis to less toxic pesticides.

Many molecules exist in forms which are essentially identical, apart from being exact mirror images of one another. It is common for these so-called chiral molecules to exist in just one form in biological systems, although scientists still don't fully understand why. For example, although both forms of amino acid molecules—the building blocks of life itself—can be made in the laboratory, in nature they only occur in the left-handed form.

The chirality of these biomolecules also strongly affects the way in which they interact with other molecules, for instance with chiral drugs. Presently, more than 50 percent of all drugs produced are active in only one of their two handed forms.

Dr. Ivan Powis, professor of chemical physics in the University's School of Chemistry, who led the research, said: "It's similar with things like sugars and for much bigger macromolecules such as DNA. People will be familiar with the double helix but may not realise that, apart from some very rare cases, it always spirals in the same direction.

"The chemistry of life is selective to chirality. It's like having one glove from a pair which will only fit on the corresponding hand. Similarly, it is hard to shake with your right hand someone else's left hand—it's the same with molecules interacting. If you have a left-handed molecule it will have a preference for whether it interacts with a left- or right-handed molecule."

Handedness is significant because it can affect the properties and function of otherwise identical molecules, the impact of which can be large enough to be detectable by the human body.

A classic example is the hundreds of molecule pairs in which the left- and right-handed forms smell completely different. The molecule limonene—used as a citrus fragrance and de-greaser in a wide variety of household cleaning products—is well-known for its ability to smell of either oranges or lemons depending on the handedness of the particular form of the molecule.

In pharmaceuticals, handedness can be crucial because one form of a molecule can be associated with an effective result while the other can lead to associated (severe) side effects, for instance the well-known malformation of the limbs of infants of pregnant women taking the Thalidomide drug to relieve morning sickness that occurred around 1960.

An existing method of differentiating between the left and right forms, called circular dichroism, involves exposing the molecules to circularly polarised light and detecting the difference between how the molecules absorb the light. But the distinguishing effects are weak—tiny fractions of a per cent—so the technique struggles to approach the sensitivity of the human nose.

The latest research demonstrates a rapid new technique that can be used to identify the handedness of chiral molecules with more tangible effects and a greater degree of accuracy.

Mass-Selected PhotoElectron Circular Dichroism (MS-PECD) uses circularly polarised light produced by a laser to ionise the molecules—using a couple of photons to knock an electron out of the chiral molecule to leave a positively charged ion behind.

By tracking the direction that the electrons take when they travel out of the molecule—either forwards or backwards along the laser beam—it is possible to distinguish between left and right handed molecules with an accuracy of up to several tens of per cent rather than a fraction of a percent.

This is combined with a mass spectrometry experiment in which a small electrical potential is applied to the negatively-charged electron and positively-charged ion which draws them out in opposite directions. The scientists look for simultaneous detection of the ion and electron—those reaching the detectors simultaneously are very likely to have come from the same molecule. The mass of the ion can be measured and matched with its partner electron. By combining these methods, it is possible to identify both the handedness of individual molecules and the proportion of left- and right-handed molecules in a mixture.

The scientists can use gas-based samples rather than high concentrations in solution and the technique is much more detailed—by looking at energies involved scientists can see many other things about the molecule, not only whether it is left or right-handed but the shape which the molecule has taken and whether it interacts with other molecules.

The technique could have a wide range of applications. In addition to the development of effective new drugs and diagnosis methods for diseases including cancer, it could potentially lead to new 'green' pesticides using pheromones tailored specifically to attract pollinators or to repel destructive insects.

Chiral molecules are also emitted by some plants and trees when under stress and detectors to identify concentrations in air samples could be used to monitor our changing ecology.

While in the food industry, the technique could allow companies to refine the flavours of the food and drinks that we consume.

The research, Enantiomer Specific Analysis of Multi-Component Mixtures by Correlated Electron Imaging-Ion Mass Spectrometry, was funded by the Division of Chemical Sciences of the Netherlands Organisation for Scientific Research, with further European support from LASERLAB-EUROPE and the Marie Curie Initial Training Network ICONIC.

Provided by University of Nottingham