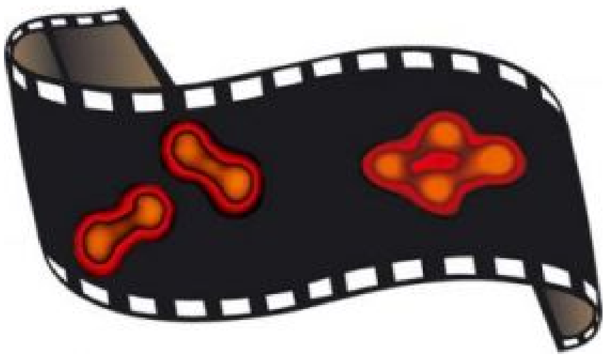
Everything starts with recognition

April 23 2007



An STM image of individual L and D Di-phenylalanine molecules adsorbed onto Cu (110). A human body has more than one thousand trillion trillion molecules with about one hundred thousand different shapes and functions. The researchers have followed the interaction between two molecules to show the basic mechanism underlying chiral recognition. Credit: Max Planck Institute for Solid State Research

A human body has more than 10 to the power of 27 molecules with about one hundred thousand different shapes and functions. Interactions between molecules determine our structure and keep us alive. Researchers at the Max Planck Institute for Solid State Research in Stuttgart in collaboration with scientists from the Fraunhofer Institute in Freiburg and the King's Collage London have followed the interaction of only two individual molecules to show the basic mechanism underlying recognition of dipeptides.

By means of scanning tunnelling microscopy movies and theoretical simulations they have shown how dynamic interactions induce the molecular fit needed for the transfer of structural information to higher levels of complexity. This dynamic picture illustrates how recognition works at the very first steps, tracking back the path in the evolution of complex matter. (*Angewandte Chemie International* April 20th 2007)

If one thinks that there are thousands of times more molecules forming our body than stars in the universe it is astonishing how all these molecules can work together in such an organised and efficient way. How can our muscles contract to make us walk? How can food be metabolised every day? How can we use specific drugs to relieve pain?

To work as a perfect machine, our body ultimately relies on the capability of each little part (molecule) to know a specific function and location out of countless possibilities. To do this, molecules carry information in different ways. An international team at the Max Planck Institute for Solid State Research in Stuttgart, in collaboration with scientists from the Fraunhofer Institute in Freiburg and the King's College London are seeking to find out how the information can be passed on at the very first steps: from the single molecule level to structures of increasing complexity and functionality.

The key to understanding all biological processes is recognition. Each molecule has a unique composition and shape that allows it to interact with other molecules. The interactions between molecules let us - as well as bacteria, animals, plants and other living systems - move, sense, reproduce and accomplish the processes that keep all living creatures alive.

A very common example of recognition can be experienced in daily life whenever one meets someone and shakes right hands. In principle, one can also shake left hands; the fact that we do it with the right has historically been a sign of peace, used to show that both people hold no weapon. But, have you ever attempt to shake the right hand of a person using your left hand? No matter how the two hands are oriented, you will never fit your left hand with the right hand of your friend.

Many molecules can recognise each other and transfer information exactly in the same way, they can either be "right handed" (D) or "left handed" (L). This property called "chirality" is a spectacular way to store information: a chiral molecule can recognise molecules that have the same chirality (same "handedness", L to L or D to D) and discriminate the ones of different chirality (L to D and D to L).

Probably one of the most exciting mysteries of Nature is why the building blocks of life, i.e. amino acids (the building blocks of proteins) are exclusively present in the chiral L form and sugars (which constitute DNA) are all in the D form. Once more, the reason for this preference is "historical", but this time goes back millions of years till the origins of the biological world. Scientists believe that current life forms could not exist without the uniform chirality ("homochirality") of these blocks, because biological processes need the efficiency in recognition achieved with homochiral substances. In other words, the separation of molecules by chirality was the crucial process during the Archean Era when life first emerged.

Researchers of the Max Planck Institute for Solid State Research have now used the "nanoscopic eye" of a scanning tunnelling microscope to make movies following how two adsorbed molecules (diphenylalanine, the core recognition motif of Alzheimer amyloid polypeptide) of the same chirality can form structures (pairs, chains) while molecules of different chirality discriminate and cannot form stable structures.

As it occurs when you shake the hand of your friend, the fact that the two homochiral hands are complementary by shape is not enough, you both have to dynamically adapt and adjust your hands to reach a better fit, a comfortable situation. By a combination with theoretical simulations done at Kings College London, the researchers have shown for the first time this dynamic mechanism of how two molecules "shake hands" and recognise each other by mutually induced conformational changes at the single molecule level.

We live in houses, wear clothes and read books made of chiral cellulose. Most of the molecules that mediate the processes of life like hormones, antibodies and receptors are chiral. Fifty of the top hundred best-selling drugs worldwide are chiral. With this contribution to the basic mechanism of chiral recognition, the researchers have not only tracked back to the very first steps in the evolution of living matter but have also shed light on our understanding and control of synthetic (man-made) materials of increasing complexity.

Related link: Molecular handshake (film) -- www.fkf.mpg.de/kern/videos/videoV1.mpg

Source: Max-Planck-Gesellschaft