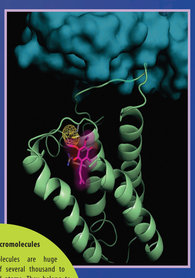
Using crystals to understand living organisms

To gain a better understanding of the way a living organism functions and the role played by different proteins, scientists have looked for ways of elucidating their structure. X-ray imagery (or radiocrystallography) has proved to be an extremely efficient technique in this respect. It does have one limitation, however: the proteins must be in crystal form.



Biological macromolecules

Biological macromolecules are huge molecules composed of several thousand to several hundred thousand atoms. They belong to one of two families:
- The **nucleic acids** which contain (**DNA**) or convey (**RNA**) the genetic coding of our organism.
- The **proteins** are the products of the translation of the genetic information; they catalyze chemical reactions (enzymes), transport other molecules (such as haemoglobin that carries oxygen), or may play a structural role (such as keratin which waterproofs the skin).

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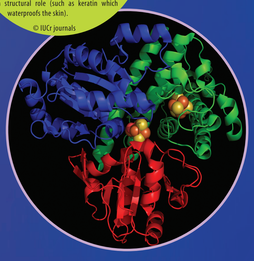

« Growing » protein crystals

Proteins, which are very large biological molecules (macromolecules) essential to life, are made of amino acids. Each protein has a specific function, directly linked to its three-dimensional structure, i.e. the manner in which the amino acids are laid out, one against the other, in space.
Proteins, however, do not form crystals naturally and these **crystals therefore have to be produced** artificially.

… in order to study them

There exists a very strong relationship between the atomic arrangement (the structure) of a biological macromolecule and its function: the precise knowledge acquired about its forms allows hypotheses to be made on its role and the way it carries out its function. This is fundamental research performed to acquire a precise **understanding of the biological processes** involved, and applied research performed to **synthesise new medicines**.

Bio-crystallography experiments consist of:
- the production of large quantities of ultra-pure macromolecules;
- the «growth» of the crystals - a long and empirical process, despite being highly automated;
- irradiation of these crystals with intense synchrotron X-rays (such as those produced by the ESRF in Grenoble or SOLEIL near Paris), for biological crystals are very small (~ 0.1mm) and give a weak signal.
- analysis of the diffraction patterns obtained, in order to determine the structure of the molecules under study.

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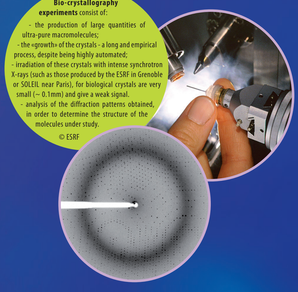

Biological crystals prepared for a diffraction experiment.

Like a crystal composed of inorganic molecules, a biological crystal is a perfect three-dimensional stack of macromolecules. - In these crystals, however, the large macromolecules are surrounded by channels allowing ions and water molecules to circulate. This means that these crystals cannot be handled in the open air, as they are liable to dry out and lose their properties.

Biological crystals are therefore frozen, before being studied under synchrotron light, a very intense form of X-ray.

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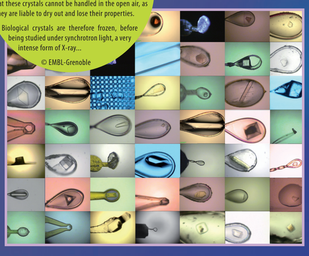

Malaria is transmitted by mosquito bites. It causes about three million deaths per year and its treatment is becoming less and less effective. Scientists are studying the structure of the relay proteins that transmit the parasite to the red blood cells as part of the search for new drugs.

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