



Michael G. Rossmann, crystallographer

"It is still a very young science but especially active and very robust"

If change is the engine of adaptation, Michael Rossmann is a very adapted being. He was born in Frankfurt (Germany) 80 years ago, studied mathematics and physics in Glasgow (Scotland), founder of the bases of structural molecular biology in Cambridge (England) and has been directing a professorship of Biological Sciences at the Purdue University of West Lafayette, in Indiana (United States) for 30 years. When 50 years of the first X-rayed analysis of the three-dimensional structure of the proteins are being celebrated, having this researcher as a pioneer, Rossmann has come to Barcelona for a conference at the Biomedical Research Institute (IRB Barcelona), regarding the most elemental structures of life.

Jordi Montaner | 16 February 2010

Crystallography sounds like fragile science...

It is still a very young science but especially active and very robust. The crystallographic methods analyze the diffraction patterns that come from a matter when irradiating it with X-rays. These diffraction patterns allow us to understand how the atoms are structured in networks based in the three-dimensional repetition of its components. Also, the assisted X-ray crystallography currently allows us to obtain very valuable structural information about proteins and other organic macromolecules.

You were going to be a mathematician, what happened?

When I graduated from school in Glasgow, I did well in mathematics and physics, so I decided to train in those fields. However, I refused to do the military service (obligatory in those days) and I found many difficulties to get into the then leading universities like the one of Manchester or King's College of London. I had to content myself with continuing to study physics and mathematics at the Polytechnic University of Glasgow. There I met a crystallographer, Kathleen Lonsdale, with highly chemical training, who needed to resolve different mathematical equations (there were no computers then), and so I offered to decipher them. Then I started relating with another crystallographer, J. Monteath Robertson, from the University of Glasgow.

And hence the affection for crystallography.

The most exciting change came after a congress on crystallography in Montreal, where I met William Lipscomb and Max Perutz. Perutz invited me to join the team of crystallography at the University of Cambridge, a team integrated by several Nobel Prize winners, like Sir Francis Crick, co-finder of the helical structure of DNA. It was a tremendous optimal environment for doing research; I felt very motivated and I immediately set to work on identifying the three-dimensional structure of proteins. Thus, without sticking to the mathematics and physics, I was gradually approaching life sciences.

What is the Rossmann fold?

After finding the crystal structure of proteins, as from the Cambridge team and from other German and American universities, we began to study enzymes. I concentrated on the Lactate dehydrogenase, a molecule of capital importance in the metabolic functions. I found that, in attention to its molecular configuration, there wasn't only one, but several Lactate dehydrogenase; and also, I observed that all of them had a common nucleotide pattern. It happens that this pattern is repeated in almost all studied organic structures and can therefore be defined as the most primitive structural pattern and the most repeated in the evolution of living beings. This structure that repeats itself ended up by carrying my name. This proposition was at first very controversial but the years have finally shown that I was right.

Structure and function are interdependent in nature. Which is the egg and which is the chicken?

This is one of the most passionate debates in basic biology. My point of view is that all parts of some macromolecules are reconfigured in different ways, sensible to a series of environmental influences. So that we have a first function that is purely productive. From there, the natural selection undermines the products that aren't suited to the medium and premium ones that adapt well, so that there are different structures that are successful towards new functions which in turn, do not stop reproducing themselves and experiment.

The Jewels of your current crown are the viruses. To them you still dispense most part of your limited effort as researcher emeritus. Do such microbes deserve such dedication? What is its evolutionary origin?

Viruses are very interesting structures (not living beings). My interest, as you may have guessed, started from a determination of its structure in three-dimensions. This structure is intimately related to the function of parasitizing a host cell and interacting by neutralizing antibodies and spreading an infection.

And its origin?

There is no precise theory about its genesis, but my view, is that they never could have occurred if a protecting prior living cellular structure didn't exist. For example, it could be about shipwrecked macrostructures of a destroyed cell deciding to roam on other cells bypassing their defences and posing a new role... Time will tell.

In your conference you have also shown important things about viruses.

I have focused on the structure and function of the dengue virus and other human pathogens counterparts, like the yellow fever virus or the one of the West Nile. They are the so called 'emerging viruses', and their nature currently capitalizes the interest of biomedicine. We have learned that the structure reveals important aspects of these pathogens. They are viruses that are still presenting an immature structure in the cells interior, acquiring their maturity and infectious ability in the extracellular medium and through endocytosis, when they finally acquire their definitive fusogenic structure. These viruses have been studied through cryonography and electronic microscopy, and their proteic components have been three-dimensioned through X-rays. It seems that, in their transition from immature to mature, the

mentioned viruses require a rotational structural reconfiguration of up to 180 degrees. These configurationally changes can be detected through neutralizing antibodies.

OF, BY AND FOR VIRUSES

All the curiosity maintaining Michael Rossmann active is currently focused on viruses. In his department of Purdue, the team researches the de glycosylation of the alpha-virus to be able to characterize the proteic crystallography better, as well as the fusion of this alpha-virus with liposome.

Through the cryonographic reconstruction through the computer, Rossmann's team also researches the mature and immature particles of *flaivivirus*; specifically, conformational changes of the E-glycoprotein, antibodies and hydrophobic complex. More: bacteriophages macro virus, human and canine *parvovirus*, Coxsackie virus, polio and Mimi virus. These last ones remind Rossmann of the Farnese statue at the National Archaeological Museum of Naples, representing Atlas holding an enormous Earth globe on his back. Atlas represents the humanity, carrying the most complex virus known today, whose genome is tightly related with the one of the bacteria.

Profiles

Biomedicine and Molecular Biology



> **Michael G. Rossmann**

**Distinguished Professor of
Biological Sciences at the
University of Purdue**

Michael G Rossmann (Frankfurt [Germany], 1930) got his degree and licensed in mathematics and physics at the [Polytechnic University of Glasgow](#) (Scotland). He did well in the two sciences and he had the intention of working professionally in both. But several contacts with people linked to crystallography (amongst them [Kathleen Lonsdale](#), [William Lipscomb](#) and [Max Perutz](#)) gave place to a change of direction in his career, towards life sciences and organisms. This is how Rossmann slowly started a career full of findings, becoming one of the most valued scientists in his field, this young and peculiar discipline, from which he knew how to make the most of it.

As a student, Rossmann did a Postdoctoral stay at the [University of Minnesota](#) with William Lipscomb (1956-1958). In 1964 he started in the labour world as an associated researcher at the [MRC Laboratory of Molecular Biology](#), of the University of Cambridge, where he worked until 1964. He then became Professor of the Department of Biological Sciences at the [University of Purdue](#) (Indiana, United States), a place that has become his working site until now, and from where he has done his major contributions.

His merits started with the study and knowledge of the three-dimensional structure of proteins. The finding of course notoriously widened the research abilities, and so he went to do research on enzymes. His insistency would give way to the well-known Rossmann Fold (1973), a common structural pattern of nucleotides in all organic structures. His finding, despite the initial resistance, has been internationally recognized.

But Rossmann didn't stop and continued to be interested in deciphering further structures. After finding the mentioned structural pattern, the crystallographer has passed to study the three-dimensional structure of the viruses, a research he does whilst directing the [Laboratory of X-rays Crystallography](#) at the University of Purdue.

He has received many honours. A few should be highlighted: he is a member of the [American Academy of Arts and Sciences](#) (1978), of the [National Academy of Sciences](#) (1984), of the [Royal Society](#) of London (1996) and of the [American Association for the Advance of Science](#) (1999). He has also been named Honorary doctorate by the [University of Uppsala](#) (Sweden), the [Strasbourg](#) (France), the [Vrije Universiteit Brussel](#) (Belgium), the [University of Glasgow](#) (Scotland), the [University of York](#) (England) and the [Institute Armand-Frappier](#) at the University of Quebec (Canada). Last, one also has to point out the Medal of Honour of the University of Purdue, which he was awarded with in 1995.