

Book review for the Cell Press publication, Chemistry & Biology.

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Crystals and Life: A Personal Journey.
By Cele Abad-Zapatero

In many ways crystals and life are the very antitheses of each other. Regular and highly ordered structures, such as protein crystals or amyloid, are usually highly dangerous to living organisms and are certainly selected against over evolutionary time. Although living cells are as overcrowded as crystals, their order is much more complex and dynamic, with constant movement between cell compartments and between partners in multiprotein assemblies. Living organisms are “dissipative structures”, maintained far from thermodynamic equilibrium by a constant flux of matter and energy from outside. In contrast crystals and amyloid are “conservative structures”, stable after generation without further input of energy.

There are of course exceptions; protein crystals do occasionally occur in living organisms. In endocrine pancreas insulin is stored in crystalline granules in the β -cells of the islets of Langerhans. Indeed the tiny storage granules seem to be crystals of zinc-insulin hexamers, very similar to the crystals of insulin used to treat diabetes. In that context, crystals provide a mechanism for storing insulin until required after a meal, when the granules are delivered into the circulation. There the crystals dissolve, the hexamers disaggregate, and the insulin binds its receptors as a monomer, leading to a lowering of blood sugar. The insulin crystals are simply a safe place to keep the insulin! In a similar way some plant proteins are stored in microcrystals. But these examples are relatively rare.

So why then “crystals and life” I wondered, as I picked up this monograph with attractive graphics of a cubic crystal on its cover, decorated with inorganic, life and artistic themes. Was it a treatise on symmetry in crystals, viruses, protein assemblies, DNA and silk? Undoubtedly there would be a little Escher, certainly pictures of two-dimensional plane groups or even three-dimensional space groups of fishes transforming into birds. All crystallographers love these. And for a Spanish author there must be Alhambra, with all those Moorish majolica mosaics on the floors and walls, showing how to fill two-dimensional space with interlocking objects and no gaps, an inspiration to Escher as well of course. Well yes, there is some of this, attractively illustrated and described.

But Cele Abad-Zapatero has attempted something quite different. His objective is to communicate the beauty and power of crystallography, which has given us detailed molecular structures of many cell components, and which is now beginning to describe huge cell assemblies and molecular motors. He wishes to convey the excitement of discovery, and he focuses on his personal involvement in crystallography. Many of us teach this subject each year, with varying degrees of success. Some of us have even tried to write texts on the subject. Abad-Zapatero’s mentor, Michael Rossman, together with Edward Arnold, has recently produced the International Tables for Crystallography, Volume F, which seeks to achieve this objective. Louise Johnson and I tried hard to communicate the power of the technique in a long monograph in 1976. But I am sympathetic to what Rossman says in the

foreword about such efforts: our attempts are “mostly stripped of humanity” whereas *Crystals and Life* “radiates pleasure and fascination of the Universe”.

Cele Abad-Zapatero dips in and out of personal experiences, describing his first discovery of gypsum crystals, and discussing the analysis of macromolecular crystal structures, pausing to explain Bragg’s law, molecular replacement and much else. He places all in a gallery of music and pictures. Some of these themes I have tried myself, but many were new. I like his explanation of Fourier synthesis. His crystal becomes an orchestra on a rotating stage, and each instrument produces a wave from which the symphony is synthesised. The reader is invited to listen to the orchestra as the stage rotates, and then to imagine that the orchestra leaves the stage. The reader can then recall the music as the stage rotated and from the intensity of sound at each position of the stage derive where every instrumentalist was sitting. Not a bad explanation of reconstruction of an electron density map from the amplitudes. And the phases? Well that needs a little more work. I liked the idea of introducing Perutz with a tuba onto the stage without disturbing the other musicians. He is the “heavy atom” of his isomorphous replacement and we know where he sits. So we can work out where the rest are relative to the tuba. Actually we need a second instrumentalist – a Kendrew? – to define precisely where everyone is; it is multiple isomorphous replacement of course, and quite a long symphony as a result.

I enjoyed this book, because it constantly asks questions with which I have wrestled over the years. So it is great fun for someone working in the field. But would it work for those outside wishing to look in? I think so. Cele Abad-Zapatero really does attempt to teach it all, and not just the easy parts. We have synchrotrons – the ring – and Das Rheingold, and other ring themes with Frodo and modelling into electron density. There is even discussion of multiple anomalous dispersion. He pays homage to many practitioners of our subject – J D Bernal, Dorothy Hodgkin, Max Perutz, Michael Rossman, Wayne Hendrickson, Alwyn Jones and Hartmut Michel, all on my list of inspirational people.

I especially like the author’s historical background digressions. Most are informative and accurate, although the monograph covers a wide field. My own impression was that Astbury’s measurements on keratins and other fibres were more important to Pauling and Corey than the author gives credit, even though Astbury got the model wrong. Also it is fair to mention that Ramachandran and Kartha worked out the structure of collagen independently of Rich and Crick, and of course it isn’t a coiled-coil of three α -helices as Abad-Zapatero tells us, but a much more extended helix that will take a lot more strain than keratinous materials like hair.

Towards the end of the monograph Abad-Zapatero digresses a little to discuss some of the other molecular biological and genomic advances that have further empowered crystallography. He also has a chapter on more ephemeral and dissipative structures, describing the influence of listening to Pricogine’s lectures on non-equilibrium thermodynamics in the University of Texas at Austin. He begins to think about the evolution of life and the work of Manfred Eigen. At such a point in my lectures I also use analogy with art. In Muslim art the human form is not allowed, but Christian art was not so confined. So when Masaccio painted *The Trinity* he started with symmetry – conservative structures like mirror planes and triangles – but then subtly distorted it to give it life, albeit a dying Christ on the cross. Michaelangelo also broke symmetry

in his depiction of the beginning of life, The Creation of Man in the Sistine Chapel in Rome. Here the mirror plane possible between God's right hand and Adam's left is significantly twisted causing the spark of life to flow in one direction from God to Adam. But then Christians never discovered non-translational symmetry – Penrose tiling and all that – but the Muslims, not in Alhambra but further east, certainly did.

Crystals may be too conservative structures to be life forms, but the power of crystals as orienters and amplifiers in the labs of X-ray diffraction experts has certainly told us much about the molecular basis of life. The knowledge of those molecular structures is also contributing now to the design of new medicines, as Abad-Zapatero can tell us with authority as he works in Abbott labs. This is a fun book, worth reading. I recommend it to the cognoscenti as well as the aspiring beginner.