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The cutting edge

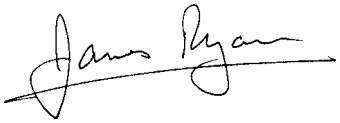
T. H. White's book *The Sword in the Stone* tells the story of the childhood of England's King Arthur. Growing up in obscurity in the Forest Sauvage outside London, Arthur is one day sent to retrieve his older brother's sword for a jousting tournament. Not being able to find his brother's sword, he searches for another, coming across one stuck fast through an anvil on a stone. There is an inscription reading "*Whoso Pulleth Out the Sword of the Stone and Anvil, is Rightwise King Born of All England.*" Where many before him have failed, Arthur succeeds in pulling the sword free and becomes king. Of course, the magical sword is not just a weapon to vanquish Arthur's enemies. What Arthur symbolically gained with the sword was an entitlement to use his knowledge for the betterment of those over whom he would rule. So in a way, what he pulled from the anvil and stone was information—vital information, accompanied by the right to use it.

In this month's issue of *MDD*, we show how information today can be pulled from other stones, or rather crystals. Of course, chemists have been gathering crystallographic information for almost as long as there has been chemistry. In 1670, Robert Boyle, perhaps more famous for his law of gases, showed how the structure of a crystal allowed it to cleave in a particular manner. In 1914, Max von Laue won the Nobel Prize for his work in showing that X-rays can be diffracted by crystals. A year later, another Nobel award went to W. H. and W. L. Bragg, father and son, for their work showing that X-rays could be used to reveal chemical structure.

Dorothy Crowfoot Hodgkin's seminal work in the X-ray analysis of biological molecules beginning in the 1930s opened up new avenues of research, encouraging scientists to tackle the complex crystal structures of proteins. Note must also be made of the work of Rosalind Franklin. Her X-ray diffraction data showed evidence of both the sugar–phosphate backbone and the basic helical structure of the DNA molecule, and it is now widely recognized that James Watson and Francis Crick formulated their double-helix model on the basis of Franklin's work. X-ray crystallography has been an indispensable tool in understanding genomics.

This tool that had much to do with commencing the genomic age is now becoming a key part of the strategy of deciphering proteomics. In David Bradley's feature on the automation of protein structure determination, "Cutting-edge crystallography" (p 26), we show that the storehouse of knowledge and skill that has been amassed for crystallography is now being applied to unearthing the atomic configuration not only of isolated proteins, but also of those in combination with specific and nonspecific ligands to understand and predict precisely how small-molecule drug candidates bind to their potential targets. Furthermore, the concepts of automation are being stirred into the mix to transform the five steps of protein crystallography—expression, purification, crystallization, diffractometry, and data analysis—from a time-intensive, very specialized task to a high-throughput, user-friendly technique for pharmaceutical scientists.

There are those who think that instrumentation for proteomics is composed only of highly refined mass spectrometers and powerful computer databases. But crystallography has always been an important part of the chemical world, and its importance to the protein world is likely to become ever greater. To continue our rise in the understanding of genomes and their protein progeny, we'll have to continue to wield all the tools at our command.



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