Leaving the structured world of Oxford

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For me as a post-graduate student, the Oxford laboratory of Dorothy Hodgkin in the mid 1960s seemed like the center of the world. Dorothy had just been given the Nobel prize. Distinguished crystallographers from all over the world visited to talk about vitamin B12 and to ask of progress with insulin. Young researchers joined from USA, China, India, Chile, New Zealand, Australia, Canada and all over Europe, eager to participate in the excitement. The successful lysozyme team of David Phillips moved to Oxford in 1966 and those working on insulin relocated alongside in Old Physiology. It was a very stimulating environment for a young scientist!

In 1969, thirty five years after Dorothy had observed the first diffraction from rhombohedral insulin crystals, Guy and Eleanor Dodson, Ted Baker, M. Vijayan and I were lucky to be around when the insulin structure (Fig. 1) was finally solved, the first protein hormone to be successfully subjected to X-ray analysis[1,2]. The excitement intensified again, with interest from the international scientific community and the press. Nobel prize winners — Perutz, Kendrew, Sanger, Anfinsen and many others — came to see Dorothy and we were asked to write reviews and give lectures at prestigious meetings.

However, life after the successful insulin analysis was much more complex and sometimes much less satisfying. Of course, we enjoyed discussions with chemists, biologists, clinicians and colleagues in pharmaceutical companies, learning more about the molecular physiology of insulin and relating our structural results to other data. That was a lot of fun, and we did make progress[3] as well as many friendships. We were the center of much attention; even Margaret Thatcher, a student of Dorothy in earlier years, came to see us, although Dorothy thought it was probably better that I was not around that day, given my political views. But we had lost the clear objective of solving the structure, and the focus that it brought to our everyday work. It was also obvious that all of us had to leave eventually to develop our careers elsewhere.

After a period of relative abstention from my other passion of the time, politics, I found myself elected to the City Council in 1970 and eventually in charge of planning in Oxford. Although I played with the idea of going into politics nationally, it all seemed much more difficult than I had anticipated. The challenge of making decisions with insufficient data was more acute than in protein crystallography. The need to balance and decide between morally equivalent options in the face of scientific uncertainty left me with a permanent respect for politicians. It also encouraged me to leave Oxford and retreat to a quieter place where I could focus once more on scientific objectives alone.

But arriving in the School of Biological Sciences in Sussex University in early 1973 was really a shock. I was faced by an empty, new building. There was an urgent need to write my lectures. None of my small team, a post doc and three students, had done any protein crystallography, although I was lucky to recruit Ian Tickle who was already an outstanding crystallographer. We had to set up biochemistry, crystallography and computing on a small grant designed for the purchase of a rotating anode generator and precession cameras. Nobody came to visit; it certainly was not anywhere near the center of the world! Nevertheless, we continued the work on pancreatic hormones — including other insulins, from a range of different species, and glucagon — and in 1975, we determined the structure of glucagon using anomalous scattering[4,5], a technique learned through the earlier work on the insulin project.

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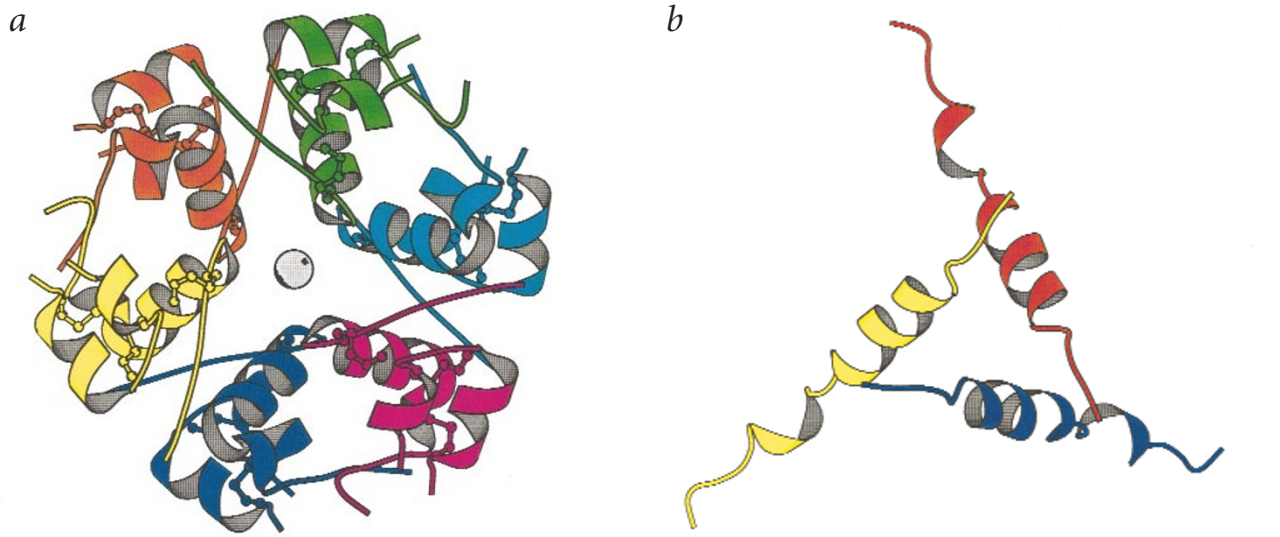

Fig. 1 Structures of ***a***, a zinc insulin hexamer and ***b***, a glucagon trimer.