Introduction

The first half of the twentieth century saw the discovery of the chemical processes of life, including a sense of wonderment that yeast and humans used the same metabolic processes to burn sugar; the second half saw the unravelling of the processes whereby chromosomal deoxyribonucleic acid (DNA) is duplicated, the DNA sequence determines protein sequence and structure, and protein structure explains the magic of enzyme action. Together, these discoveries constitute the secret of life: the processes of life were revealed in their underlying physicochemical simplicity but cloaked in a bewildering complexity.

In the 1930s, John Desmond Bernal thought that the secret of life would be revealed by using X-ray crystallography to solve the structures of crystalline proteins. Max Perutz was Bernal's student in Cambridge, England. Twenty-five years later, Perutz and his co-worker John Kendrew realised Bernal's dream by determining the atomic structures of the oxygen-carrying proteins haemoglobin and myoglobin. In the end, the secret of life entailed more than protein structures, but structures are indeed an essential part of learning that secret. Proteins fulfil many functions: hair, skin, enzymes, pumps, or the multitude of nanomachines and motors that make muscles move and cells divide. Structure, together with the genetic approach founded by Salvador Luria and Max Delbrück, became the twin pillars of a new science, Molecular Biology.

Aaron Klug developed methods for structure determination of macromolecular assemblies at the atomic level – a prerequisite for understanding how life's clockwork actually operates. Aaron entered the field of structural molecular biology just as it was beginning. Thus our account perforce embraces many historical aspects of the development of Molecular Biology.

Aaron Klug was born in Zelva (other spellings include Zhelva or Želva), Lithuania, in 1926. His family emigrated to Durban, South Africa, when he was two. He attended the Durban High School and won a scholarship to Witwatersrand University in Johannesburg at 15. He attained his degree from Wits when he was 19 and moved to Cape Town University, where he took a master's degree. There, he worked with the crystallographer R. W. James, who had an important formative effect. During this time, Aaron's first scientific publication appeared in the scientific periodical *Nature*. Two more papers published in *Acta Crystallographica* earned him an 1851 British Empire Fellowship and a Trinity College (Cambridge) Rouse Ball scholarship. He married Liebe Bobrow, a dancer and musician, in 1948, and in 1949 the young couple repaired to Cambridge, England, where Aaron did a PhD with Douglas R. Hartree on the kinetics of the formation of steel. For an ensuing year in Cambridge he did theoretical studies for Jack Roughton on the kinetics of oxygen uptake by the blood pigment haemoglobin. This experience reawakened his interest in biological phenomena.

Armed with a Nuffield Fellowship, Aaron joined John Desmond Bernal's Biomolecular Research Laboratory at Birkbeck College, London. Here he met Rosalind Franklin: after working on the structure of DNA at King's College London, Franklin had moved to Bernal's laboratory to lead a small group working on virus structure by X-ray diffraction. Meeting Franklin at Birkbeck College was Aaron's epiphany. This encounter determined his scientific future: solving the structures of macromolecular assemblies such as viruses. After Franklin's untimely death, he took over direction of the virus group. Together with John Finch, his collaborator for 40 years, he showed that poliovirus and small spherical plant viruses have closely related structures. A fruitful collaboration with Donald Caspar established the geometric rules for assembling 'spherical' viruses. In 1960 the virus group was invited to join the newly founded Medical Research Council's Laboratory of Molecular Biology (LMB) in Cambridge.

At the LMB, while working out the structures of spherical viruses by electron microscopy, Aaron developed the first applicable method for computing three-dimensional images from a set of two-dimensional projections of a structure (tomography). He and his collaborators solved the structure of tobacco mosaic virus. His group worked out the first atomic structure of an RNA-containing macromolecule, tRNA – a molecule containing thousands of atoms. Aaron also carried out structural analysis of the large macromolecular complexes involved in packaging DNA in chromatin (nucleohistones) and mapped out the organisation of the nucleohistone core. He discovered zinc fingers, protein domains that bind to specific DNA sequences, and he pioneered their application in gene therapy.

In 1982, Aaron Klug was awarded the Nobel Prize for Chemistry. Between 1985 and 1995, he was Director of the Laboratory of Molecular Biology. As Director he was also instrumental in getting the British part of the Human Genome project started. From 1995 to 2000, he was President of the Royal Society of London. He was knighted in 1988 and awarded the Order of Merit in 1995.

Science is much held back because scientists concern themselves with that which is not worth knowing, and that which cannot be known[1]. Aaron was careful never to fall into either of these traps – he chose subjects that were at once topically important and likely to yield answers. Moreover, he never let himself be beholden to a technique. Aaron moved fluently between structure determination by X-ray diffraction or electron microscopy, and biochemistry. His endeavours were guided by an ability to choose topics that would yield to a sustained investigation. His consummate skill as a teacher and leader enabled him to draw forth exceptional performance from his co-workers and collaborators.

[1] *Die Wissenschaft wird dadurch sehr zurückgehalten, daß man sich abgibt mit dem, was nicht wissenwert, und mit dem, was nicht wißbar ist.* Goethe, J. W. in *Maximen und Reflexionen* (ed. H. Koopmann) p. 83 Deutsche Taschenbuch Verlag München (2006)