J D Bernal and the genesis of structural biology

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Abstract. I was invited to participate in this Symposium a month or so before the event. At that time however, I knew little about J D Bernal. I vaguely remembered a brief conversation on the topic over a decade ago with Professor Vittorio Luzzati as we ambled around the gardens at the Palace of Varsailles. Vittorio likely knew Bernal through his friend Rosalind Franklin who worked with Bernal at Birbeck College. But beyond that I knew nothing about the man or his science. And so it was most fortunate that Andrew Brown's book *J D Bernal: The Sage of Science* [1] appeared in 2005 and I was able to call on it. Indeed, much of the material included in this chapter is based on that source and on Dorothy Hodgkin's biographic memoir of J D Bernal [2], her postgraduate supervisor.

Given that this chapter is to be published in a Physics journal I thought it appropriate to provide some background to the theme of my presentation, structural biology. Accordingly, I will begin with an introduction to proteins, one of structural biology's central characters, and to which Bernal devoted much energy and attention. How the molecular structure of a protein determines its activity and function will then be described. Bernal's major contribution in this area was to X-ray crystallography, the primary method by which a protein's structure is determined. The method, and aspects of its development, will be described. I will also make reference to some of Bernal's additional contributions in related fields. Finally, Vincent Casey, the symposium organizer, asked that I comment on how structural biology might impact on society. I will attempt to address that at the close of my presentation.

1. Proteins: Form and Function

Bernal's major contribution to structural biology was in the area of proteins. Proteins are linear polymers of twenty different amino acids. They range in size from as few as a hundred to many thousands of amino acids arranged as beads on a string. The functional roles ascribed to proteins are many and varied. Transport is one such function. Thus, for example, haemoglobin is a blood protein that binds and moves oxygen around the body. Channeling of ions is another. Thus, in nervous tissue, ion channels play a role in impulse transmission. Many proteins have enzymatic activity, and digestion is a process that requires the action of myriad enzymes to break down for later assimilation and use the assorted proteins, fats and other constituents of the food we eat. There are protein-based machines that ensure life's blueprint molecule, deoxyribonucleic acid (DNA), can be passed from one generation to the next with extraordinary, but incomplete, fidelity. Defence is made possible by an array of antibody proteins produced in response to attack. Proteinaceous receptors communicate information between the inside and outside environments of the cell. Locomotion is made possible, in part by the muscle proteins. And then there are the 'billion dollar' fibrous proteins, the principle components of hair and nails. In sum, proteins have many activities or functions that are integral to life. Bernal's view

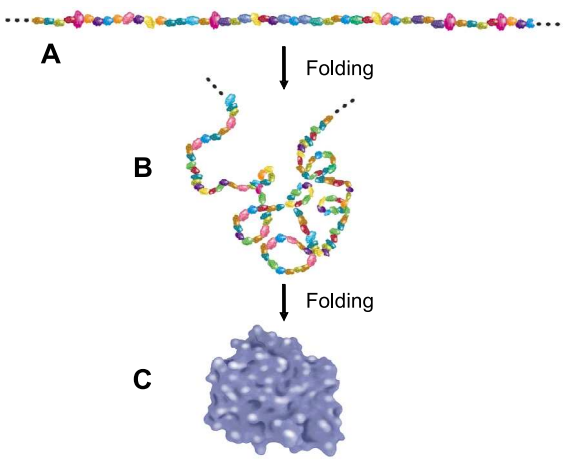

Figure 1. To become active and express functionality the long stretch of amino acids that make up a protein (A) must fold back on itself (B) and assume a well-defined three-dimensional form or structure (C). The individual amino acids, of which there are twenty, are represented as coloured beads on a string in (A) and (B). A surface contour representation of the folded protein is shown in (C).

from the outset was that to fully understand the workings of Nature's robots, as proteins have been referred to [3], we needed to know their molecular structure.

It is important to appreciate that a taut, stretched out string of amino acids in a protein has little or no activity and thus function. Why? Because it has the wrong form or structure. To have activity that same stretch of amino acid residues must fold back on itself and adopt a three-dimensional form or shape, as illustrated in figure 1. It is that properly folded object, with a well-defined form or structure, that now has activity and that can execute functions such as transporting oxygen or digesting fat. This serves to highlight the relationship between structure and function that occupies much of the attention of the structural biologist.

That form, or structure, dictates function is not limited to the realm of proteins. Indeed, it is possible that the original idea of form and function arose with the Roman and the Greek architects of yore as they set about designing spaces in which to communicate effectively. The amphitheatres of old are fine examples of structures that beautifully satisfy this functional need. Similarly, the chair has been 'structured' with a seat, four legs, two arm rests and a back (figure 2A) to accommodate stably and comfortably an adult in a sitting posture. In like manner, we see a distinctly different expression of form matching function, this time in biology, as is illustrated by the giraffe (figure 2B) with its long neck and legs enabling it to forage at treetop level. It would appear therefore that the form-function relationship is ubiquitous.

As noted, to have functional activity a protein must assume its correctly folded, three-dimensional form or structure (figure 1C). However, a protein in isolation does not express that activity unless it is interacted with in some way. By analogy, let us reconsider the chair used to illustrate the structure-function relationship above (figure 2A). Whilst the chair in isolation might have aesthetic beauty, it is not functional until a person interacts with or sits in it. Similarly, to express the activity of a protein requires that the properly folded molecule interacts with something. That something might be a photon of light in the case of a photosynthetic protein, oxygen or a sugar molecule, or perhaps another protein. Thus, the folded protein must create a suitably crafted pocket or surface with which to engage in a productive interaction. By analogy with the seat of the chair, hemoglobin has an oxygen-binding pocket. The pocket

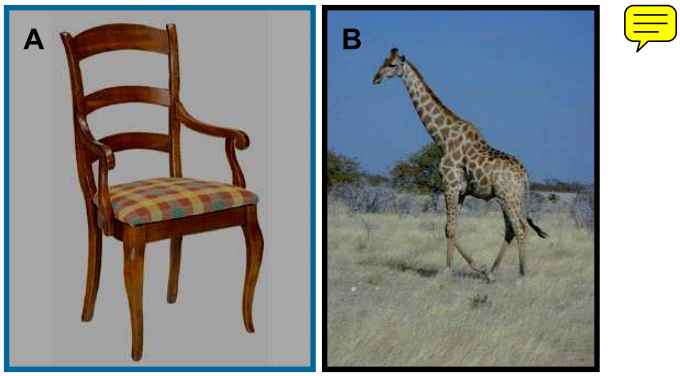

Figure 2. That function follows form or structure is illustrated here with reference to a chair (A) and a giraffe (B).

has the correct size, shape, accessibility and chemistry that enable specific interaction. It is the proper folding of the string of amino acids into a well-defined three-dimensional shape, with the proper humps and hollows, or structure, that creates the interaction site. Thus, the activity of the protein can be expressed when the interaction site and the ligand (oxygen, sugar, protein, etc.) are properly matched. Here again we see illustrated the relationship that exists between structure and function.

2. Structural Biology: A Primer

J D Bernal was one of the founding fathers of structural biology. The objective of the structural biologist is to determine the three-dimensional arrangement of atoms in biological macromolecules (proteins, nucleic acids, carbohydrates) and their assemblies. This arrangement is usually referred to as the 'structure' of the target molecule. While structure itself is interesting what the structural biologist really wants is to understand how these macromolecules and their assemblies function in, and indeed outside, the cell. It is as a result of establishing their three-dimensional structure that we come to know how they work at a molecular level. In addition to establishing structure, preferably at atomic resolution, the structural biologist is also interested in exploiting that knowledge for the purpose of advancing his/her own field of science. For some this will involve deciphering how cells communicate with one another or how light energy is harnessed as chemical energy in photosynthesis. For others, it concerns the design of a protein-digesting enzyme for use in laundry detergent or the crafting of the next blockbuster drug.

2.1. Bernal: Structure–Function

Bernal would have been acutely aware of the structure-function concept particularly since his postgraduate research concerned the atomic structure of graphite. Graphite and diamond are two forms of solid carbon, and two solids could not have more disparate physical properties. Graphite, familiar to us all as pencil lead, is soft, while diamond is extremely hard. At the time that Bernal was engaged in his doctorate studies the structure of diamond was known. In fact, its structure had been determined by W H Bragg, Bernal's mentor. Recall that W H Bragg and his son, W L Bragg, shared the 1915 Nobel Prize in Physics for their contributions to crystallography. Diamond consists of an extended network of carbon atoms each of which is bonded to four others in a tetrahedral arrangement (figure 3A). This three-dimensionally cross-linked and interconnected structure gives rise to a very hard material. The question posed by Bernal was, What about graphite? Accordingly, he set out to determine its structure

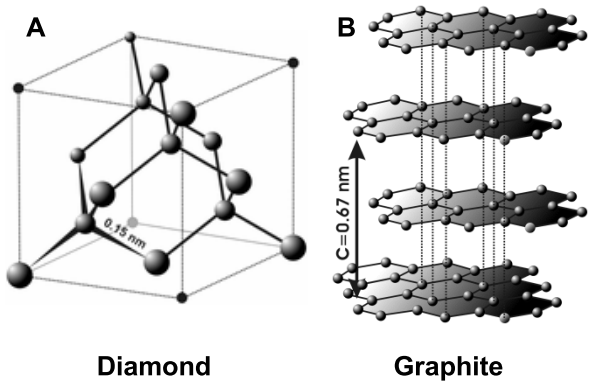

Figure 3. The three-dimensional structure of diamond (A) and graphite (B). Carbon atoms are represented as shaded spheres. Covalent bonds between carbon atoms are shown as solid lines.

crystallographically. One can only imagine Bernal's delight upon finding that in graphite the carbon atoms are arranged in planar sheets (figure 3B). Further, while the bonding within the sheets is strong that between the layers is feeble in the extreme enabling those sheets to slide over one another and accounting for graphite's familiar softness. This would have imprinted indelibly on the young Bernal the very direct relationship that exists between a material's molecular structure – how its constituent atoms are strung together in three-dimensional space – and its physical (and chemical) properties which in turn dictate its functionality. It is this concept, gleaned from an elemental form of carbon, that he felt applied equally well to the very much more complex macromolecules on which life depends. And, as with diamond and graphite, he recognized that the route to macromolecular structure was by the tried and true method of X-ray crystallography.

2.2. Protein Crystals Do Diffract!

Bernal solved the structure of graphite using X-ray crystallography. It is with this same methodology that he and his colleagues embarked on the quest to establish the structure of proteins and other macromolecules as a preliminary to understanding the molecular details of how they function. The method subsequently became known as macromolecular crystallography. Inherent to the method is the need for a crystal of the target molecule (figure 4). This is so because crystalline order is required for the probing X-rays to be scattered in a way that is coherent and that can be processed to provide the corresponding structure. Thus, while it is relatively straightforward to get crystals of diamond, graphite or table salt, it was considered a different matter altogether to procure crystals of a protein that are of diffraction quality. The emphasis here is on diffraction quality because at that time in the early 1930's it was known that certain proteins could be crystallized and the technique of crystallization was used as a purification tool. However, no one knew if a protein crystal would have the inherent order to diffract well enough to yield its molecular structure.

In order to pursue his dream of using crystallography to determine the structure of a protein, Bernal needed a suitable protein crystal. However, despite his many and varied talents, he was not a biochemist, nor did he have direct access to biological materials and the wherewithal to produce the highly purified protein required to grow crystals. Such was his good fortune that a friend, Glen Millikan, returning from a trip that included a visit to the Svedberg's lab in Uppsala, brought back with him a tube of pepsin crystals, exactly what Bernal was looking for.

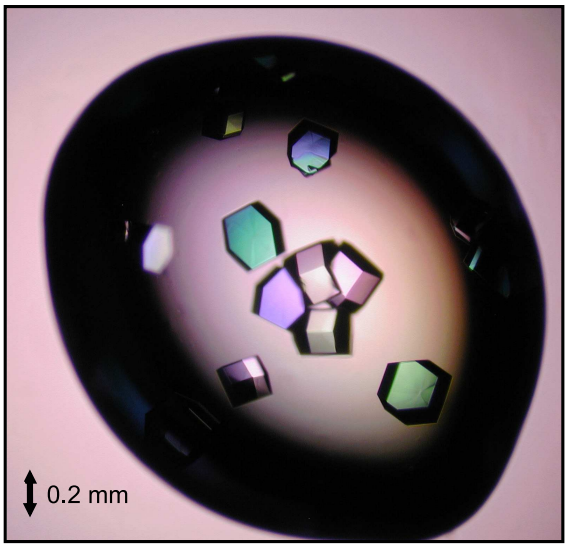

Figure 4. Crystals of the protein lysozyme, a carbohydrate cleaving enzyme found in egg white and in tears. The crystals are growing in a small volume of mother liquor and are viewed with a polarizing light microscope.

Pepsin is a digestive enzyme that breaks down, or hydrolyses, protein.

In short order, Bernal set about determining if and how well the crystals diffracted. His first measurement was made with the crystal exposed to air whilst being irradiated with a collimated X-ray beam (figure 5A). He must surely have been crestfallen as the photographic film emerged from the developing solution only to reveal – no diffraction! However, as was his wont Bernal did not rely on a single technique and he kept an eye on the crystal's birefringence, which can correlate with internal order, using polarized light microscopy. He noted that the exposed crystal, which had started out birefringent when fresh and surrounded by mother liquor, had lost its birefringence by the end of the data collection period. This suggested that the crystal had likely dried out during the exposure and, in the process, had become disordered. Bernal reasoned that if the diffraction measurement were made instead with the crystal in a sealed environment whilst bathed in its mother liquor where it could not dry out, order and diffraction quality, if present, would be retained. He was right! And with an arrangement that included a thin-walled glass capillary in which the crystal and its mother liquor were housed (figure 5B) Bernal and his postgraduate student Dorothy Crowfoot (later Hodgkin who subsequently was awarded the Nobel Prize in Chemistry) went on to demonstrate that these crystals of a soluble protein diffracted X-rays.

That the crystals diffracted was a profound result and its significance was not lost on Bernal. The implications were that the original protein was not a disordered colloidal particle, as some had suspected, but that it had a definite size and shape, and that it did pack in an orderly way within the lattice of the crystal. Accordingly, it should be possible to use the crystallographic method, as with diamond, graphite, and small molecules, to determine its three-dimensional structure. This observation, along with Bill Astbury's diffraction studies on the fibrous proteins, set the stage for the development of the field of structural biology.

And the simple, sealed capillary approach (figure 5B) devised by Bernal in the mid-1930's became the method of choice for collecting diffraction data on macromolecules and their assemblies for at least the next half a century.

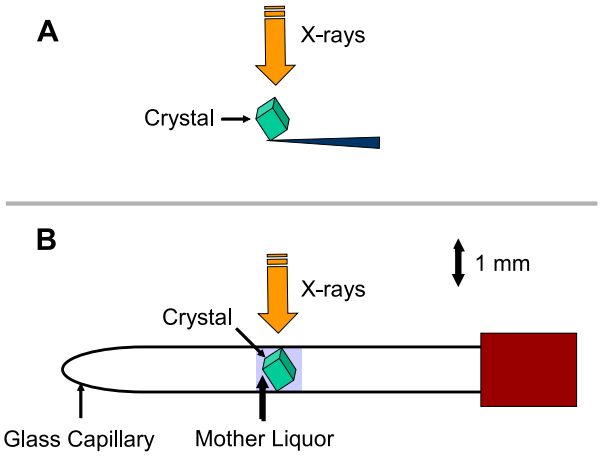

Figure 5. To solve a protein's structure using macromolecular crystallography requires that a crystal of the protein diffract X-rays to high resolution. Shown in (A) is a cartoon representation of how Bernal and Crowfoot are likely to have made the first such measurements with the crystal exposed to air in an X-ray beam. By sealing the crystal inside a thin-walled glass capillary whilst bathed in mother liquor as in (B) X-ray diffraction data could be recorded without the crystal drying out, becoming disordered and loosing the ability to diffract.

2.3. Macromolecular Crystallography

While an important result and an indicator of things to come, the diffraction pattern itself is just a part of a long and complex process that eventually leads to the atomic-resolution structure of a protein. The diffraction pattern consists of an array of reflections that appear as spots on a detector which, back then, was a piece of photographic film (figure 6). In the case of a typical protein, many thousands of such spots must be recorded, their location in the pattern identified and their intensity (degree of blackness in the case of photographic film) measured. One additional piece of information is needed; the phase of the diffracted X-rays which, it turns out, affects the intensity of each and every reflection. It took one of Bernal's students, Max Perutz, over a decade to solve this so-called 'phase problem'. By so doing he was able to solve the structure of haemoglobin, the oxygen-binding and transporting protein in blood, and the field of macromolecular crystallography was born. For this Herculean effort he shared in the Nobel Prize with John Kendrew, another physicist-turned structural biologist drawn to the field by Bernal.

> Acknowledging the enormity of Bernal's contributions to the emerging field of structural biology, in 1962 John Kendrew was to send him a note in which he referred to Bernal as having 'fathered' five Nobel Prize winners in that year alone. They included Dorothy Hodgkin, Aaron Klug, Max Perutz, Maurice Wilkins and the note writer himself.

2.4. Structure–Function: Examples

The efforts of macromolecular crystallography result in a three-dimensional structure of the type shown in figure 7. Here, we see that the location in space of all the non-hydrogen atoms (mostly carbon, oxygen, nitrogen and sulphur) has been defined. The protein used in this illustration is a phospholipase, an enzyme that plays a part in the inflammatory response. It does so by breaking a lipid (also known as a fat) molecule in two. One of the resulting fragments goes on to form what are called prostaglandins and thromboxanes that elicit the inflammatory response

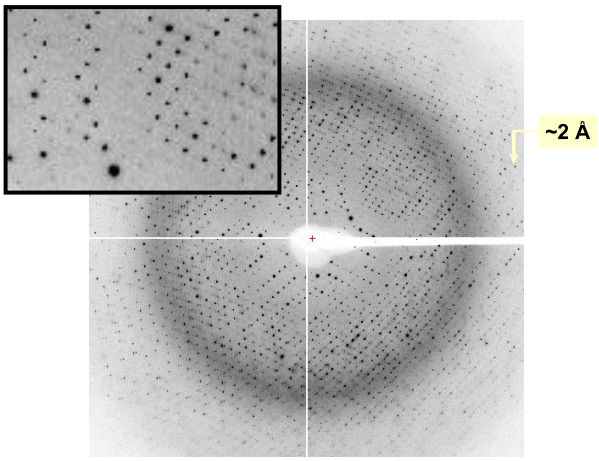

Figure 6. X-ray diffraction pattern recorded using a crystal of lysozyme. The pattern consists of hundreds of discrete Bragg reflections that appear as black spots on the detector. An expanded view of a section of the pattern at low angles is shown in the inset. The shadow created by a bead of lead used to block the direct incident X-ray beam that has passed through the crystal surrounds the red cross at the centre of the pattern. The reflections at the edge of the pattern correspond to diffraction from planes spaced 2Å apart.

familiar to us all in the form of a headache or a painful sprain. The molecular structure reveals an obvious gap in its otherwise rugby ball shape (figure 7A); it is in the gap that the active site of the enzyme resides and into which the lipid substrate fits as a prelude to the cleavage event. One might speculate that in order to prevent the inflammatory response, and the attendant pain, the active site could be blocked in such a way that the substrate cannot bind. And how right one would be, for shown in figure 7B is the structure of that same phospholipase enzyme as a complex with aspirin! The analgesic is exactly where it is expected to be, smack bang in the active site. This example serves to illustrate why the pharmaceutical industry has such an interest in protein structure. Structure-based rational drug design is one of its major thrusts.

The area of structural biology of particular interest to the author concerns membrane proteins. Here too we find examples of function being informed by structure. The potassium channel is a case in point and it serves as a model for certain of the proteins that are involved in nerve impulse transmission. The protein creates a pore or channel that enables potassium ions to cross from one side of the membrane to the other with exquisite selectivity and lightning speed (figure 8). Thus, it can discriminate between sodium and potassium, two remarkably similar ions, whilst shuttling at the rate of an ion every billionth of a second. The structure of the protein, solved at close to atomic resolution by the MacKinnon group at Rockefeller University, provides a detailed understanding of how the channel works at a molecular level. For his efforts, Rod MacKinnon was recently awarded a share in the Nobel Prize in Chemistry.

2.5. Structure Work Today

It took Max Perutz over a decade to work through the phase problem and to solve the structure of haemoglobin. By contrast, today it is possible to determine a protein's structure in minutes – under favourable circumstances. And those few minutes can include the time required to collect and to process the X-ray diffraction data upon which the structure is based. Several important advances have enabled this extraordinary acceleration in the rate at which macromolecular structures can be solved. These include advances in the power and speed of computing and

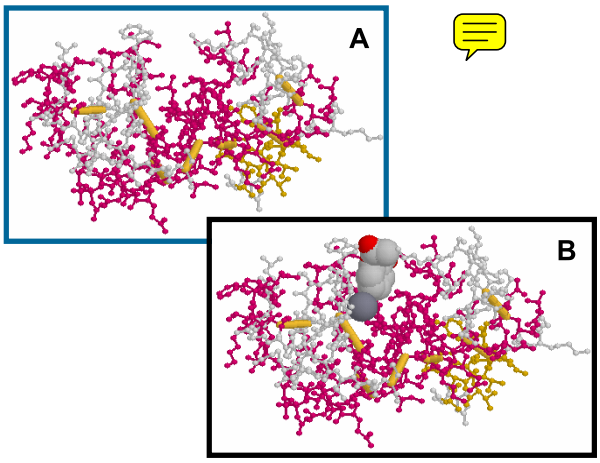

Figure 7. The three-dimensional structure of phosopholipase A2, an enzyme that plays a key role in the inflammatory response. The active site of the enzyme appears as a gap at the upper surface of the protein in (A). In (B), the blocked and inactive form of the enzyme is shown complexed with the analgesic small molecule, aspirin. The small shaded spheres represent non-hydrogen atoms (carbon, oxygen, nitrogen, sulfur) and the solid lines are covalent bonds. In (B), the aspirin molecule is shown in space-filling form. Taken from the Protein Data Bank (www.rcsb.org/pdb/) and formatted using Protein Explorer (www.proteinexplorer.org).

visualization. Thus, gone are the days of the punched computer card, and the stacks of contour-lined plastic sheets that were used to aid the interpretation of electron density data. The second significant advance has been in the area of X-ray generation. Today we avail of synchrotron sources offering wavelength tunability and unprecedented brightness where diffraction patterns, that took days and possibly weeks to collect in Bernal's time, can now be recorded in fractions of seconds. The rate-limiting step in the overall process of structure determination has now shifted 'upstream' in the direction of protein production and crystallization. The latter are benefiting enormously from advances in molecular biology by means of which the protein of interest and its variants can be produced and purified rapidly and in quantities large enough for crystallographic analysis. Crystallogenesis is being aided and abetted by automation, robotics and miniaturization, and by the availability of commercial screening kits.

2.6. The Spate and Its Cost

With these advances has come a veritable avalanche of structural information. This is captured convincingly in figure 9 where the number of structures deposited annually in the Protein Data Bank is shown as a function of time. It is worthwhile perusing these data mindful of the fact that in the early days it took many years to produce a single structure. Currently, the output rate exceeds a whopping 5,000 structures annually (figure 9). Importantly, this figure does not include proprietary structures produced by industry.

It is interesting also to reflect on the monetary cost of this endeavour. In the not too distant past, a single structure was estimated to require an investment of several hundred thousand US dollars. The funding agencies are actively supporting methods and technology developments that will enable the cost per structure to drop by at least an order of magnitude. It is fair to say that J D Bernal played a significant hand in getting this entire enterprise underway.

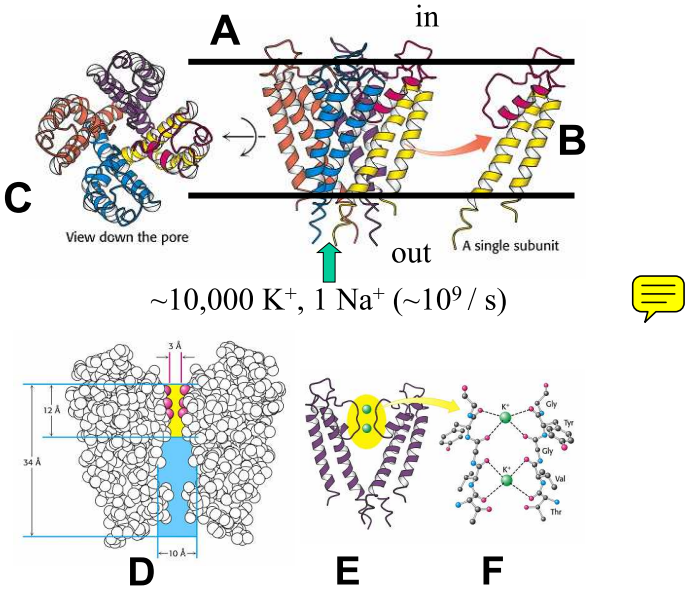

Figure 8. Crystal structure of a potassium channel membrane protein solved by the MacKinnon group. The black horizontal lines in (A) and (B) represent the inner and outer surface of the membrane in which the protein is embedded. The protein crosses the membrane as a homotetramer, a collection of four identical protein subunits that assemble to create a transmembranal pore. A side vew of the channel from within the membrane is shown in (A). For clarity, a single subunit on its own is shown in (B). A view down the pore is presented in (C). The protein is shown in space-filling model form in (D) and the details of how the protein interacts with potassium ions (K^+) in the channel are shown in (E) and (F). Taken from Berg et al [4].

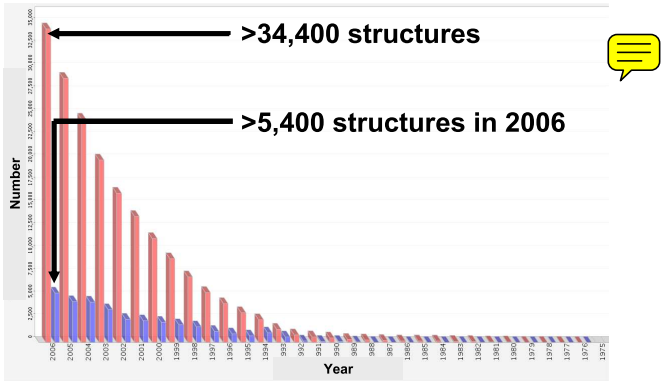

Figure 9. Growth in the number of macromolecular structures solved by X-ray crystallography that have been deposited in the Protein Data Bank (www.rcsb.org/pdb/). Yearly output is shown in blue; cummulative figures are shown in pink. Sourced from the Protein Data Bank on 12 December 2006.

3. Related Contributions

In addition to his very direct contributions to the area of structural biology and macromolecular crystallography, Bernal made other important and relevant contributions. From an early age, he was very well versed in physics and mathematics. This, combined with a precocious nature, likely accounts for his ability and perseverance in working out the 32 crystal shapes that are possible in two-dimensions and in deriving the complete space group set, of which there are 230, whilst an undergraduate student at Cambridge. We are told too that he likely devised then what has since been referred to as the Ewald sphere, an ingenious and convenient geometrical construction for visualizing the relationship between planes in a crystal and the X-ray reflections they generate that are seen on a detector [2]. He introduced the rotation X-ray camera to his group at The Royal Institution, London. For this purpose, he cleverly improvised a wind-up alarm clock and extended the spindle axis by gluing to it a carpenter's nail (figure 10). A crystal was mounted at the sharp end of the nail which rotated steadily in the X-ray beam. In this period he made important contributions by determining the structure of several amino acids, sterols and sex hormones. Along with Fankuchen he made some of the first diffraction measurement on viruses. This was later to be followed up on by one of Bernal's postdoctoral fellows, Aaron Klug, who later went on to win the Nobel Prize in Chemistry in 1982.

Bernal had a very active and engaged mind, and advanced many hypotheses over the years. As often as not, the hypotheses were put forward and then left for others to test and to develop more fully, presumably as he hastened on to his next new idea. Among these is the so-called zipper hypothesis of how genetic material (DNA) is packaged as paired strands stabilized by, what later became known as, the hydrophobic effect. This was long before Watson and Crick reported their landmark discovery of the double helical nature of DNA in 1953. He had a great and a long-lived interest in the origins of life and his many proposals placed much emphasis on clays. He was also convinced early on of the primacy of RNA which has since been demonstrated convincingly. He proposed a way to solve the crytallographic 'phase problem' in structure determination by a process that involved 'swelling' under controlled hydration conditions. While the problem was eventually solved by Perutz using the isomorphous replacement method, the swelling idea has subsequently been used in the area of biomembranes and lipids to determine the electron density distribution in liquid crystalline arrays. Bernal also reasoned for the existence of subunits as an element of structural hierarchy within proteins and expounded on the possibility that gene replication was fundamentally a 2-dimensional issue. Later Crick acknowledged that this was one of the alternative mechanisms he had failed to consider.

Bernal was instrumental in establishing the first crystallographic journal, Acta Crystallographica, the International Union of Crystallography and the Cambridge Crystallographic Data Centre. His realization that scientists are not necessarily gifted librarians, but that they need immediate and easy access to the latest publications to advance their work, led him to propose a 'centralized reprint system'. This idea was developed by Eugene Garfield, and with time and much iteration led to the widely used and very powerful information retrieval tool known as the Science Citation Index (SCI). Bernal was the first to recognize how such a tool could be used to track scientific trends. The ability to monitor citations in a quantitative way has lead to the well-known Impact Factor which is used, particularly by administrators with a penchant for numbers, as a measure of the 'quality' of a journal or publication, and by extension, the 'quality' of its authors.

The hydrophobic effect, which is at the heart of spontaneous self-assembly and macromolecular folding, stability and interactions, has its origins in what I sometimes refer to as the 'narcissistic properties' of water; the fact that water has an enormous affinity for itself [5]. For the longest time I was of the opinion that the original concept was Walter Kauzmann's to be championed subsequently by Charles Tanford [6]. However, upon reading Andrew Brown's book I came to learn that Bernal, following up on a conversation with Ralph Fowler while on

Figure 10. Improvised rotation X-ray camera made using a wind-up alarm clock. Gluing to it a nail has extended the spindle. A crystal was mounted at the sharp end of the nail which rotated steadily in the X-ray beam. Bicycle clips were used to hold the photographic film against the inner surface of a metal cylinder. The X-ray beam entered the camera through a porthole half way up the cylindrical chamber.

a 12 hour delay at Moscow airport in 1932, would have been amongst the first to describe this profound and ubiquitous effect. The flight was held up by heavy fog and during the protracted wait the pair got into deep conversation and thought on the properties of water that enable it to exist as microscopic droplets of which fog is composed. Subsequent work led to the proposed 'pseudo-crystalline' nature of liquid water and to hydrogen bonding where hydrogen can, under the right circumstances, be considered to have a 'valence of two'. In 1940, Bernal described in detail the affinity that water has for itself and how this attraction drives the separation of oil and water and the pairing of chromosomes as in the zipper hypothesis, referred to above. Bernal's interest in water and liquid structure continued throughout his scientific career. His last PhD student, John Finney, continues to work on the structure of water and ice as Quain Professor of Physics at University College London, and is a contributor to this Meeting and to its Proceedings.

4. Concluding Remarks

Bernal teemed with ideas and his interests were catholic. And he was generous to a fault with those ideas, as noted. He was erudite, articulate and insightful. The range of his knowledge was matched only by its depth. He was after all a very good mathematician and physicist, and an expert crystallographer. Coupled with an unbridled enthusiasm, optimistic outlook and vision meant that he attracted the very highest calibre students, staff and associates. As we know, several of these went on to win major awards including the Nobel Prize. Bernal was a persuasive, interesting and an engaging conversationalist and communicator. He obviously had the 'gift of the gab'. And he was courteous and an inspiration to all. Combined with his boundless energy and his penchant for travel meant that he had an extensive and worldwide network of colleagues and friends. This served him and his team well in their scientific pursuits as is evidenced, for example, when the pepsin crystals landed on his desk, brought to him by a friend on a return trip from Scandinavia.

As noted, the structural biologist seeks to understand how molecular structure impacts on functional activity with a particular emphasis on macromolecules and the assemblies they form. In so doing, the fund of scientific knowledge grows as does our understanding of how the natural world works. Whilst intellectually satisfying, the process of doing this science also contributes significantly to the gainful employment of a skilled workforce. All of this must surely be to the good of society.

The information gained from establishing the link between macromolecular structure and function has many practical applications and utilities, which again are to the betterment of society. Consider for a moment the rational design of drugs for disease prevention and treatment. Insulin is a recent case in point. As a result of knowing the structure of insulin and the form in which the protein crystallizes, an inhalable form of the drug is now available. Perhaps this will signal the end to the burdensome daily injection schedule of the diabetic with an obvious positive impact on the quality of life and performance of the patient. Likewise, structural biology is making major contributions to animal and plant health which, in turn, impact on agriculture and aquaculture. The food, feed and the personal care products industries are also beneficiaries of advances in structural biology. Biosensors, designed based on a knowledge of how signalling macromolecules work, have enormous potential in the medical and security fields. Solar cells, built to mimic Nature's ability to harness light energy and to convert it to a useful form of chemical energy, are inspired by our understanding of how the assorted photosynthetic protein complexes in microorganisms and plants are structured and how they work at a molecular level. Nanotechnology and nanofabrication take some of its lead from Nature which has crafted molecular motors that turn chemical and electrical gradients into useful forms of energy for synthesis and locomotion. There can be little doubt therefore that structural biology contributes in a very direct, positive and multifaceted way to society.

It is fitting that we got to celebrate the life and times of J D Bernal here at this IOPI meeting in Limerick, just a 'stone's throw' from where Bernal spent his formative years. It is unfortunate however that the man's genius and enormous contributions to science and society were not recognized in any official capacity here in Ireland during his lifetime. Still, better late than never, and it is likely that this event has set the stage for many more. Accordingly, it is important that we avoid repeating such mistakes by making every effort to recognize and to celebrate home-grown talent and genius, regardless of where it is located, and to do so whilst such inspired individuals are still in the flesh!

References

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