THE BIOLOGICAL CHEMISTRY OF THE ELEMENTS

The Biological Chemistry of the Elements

The Inorganic Chemistry of Life

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Preface

The majority of present-day living organisms require rather strict environmental conditions: temperature from 0 to about 40°C, pressure of the order of 1 atm., salinity up to about 4 per cent, pH in the range 4 to 9, redox potential in the region of stability of water (-0.4 to $+0.8$ V at pH$=7$ versus the standard H^+/H_2 electrode), water activity between 0.7 and 1.0 mole fraction. In a few cases these limits can be greatly exceeded and it is known that, in the earth's past, conditions existed which were quite different from the present ones but did not hinder the development of life, although they did impose constraints upon the *forms* of life that could exist. Indeed, this is an essential feature of life itself: the continuous adaptation of living organisms to changing environmental conditions through the development of defence devices and mechanisms against those changes, while sometimes turning new (adverse) factors into favourable ones. The result was, and still is, the survival and predominant proliferation of the fittest, and the history of evolution, which started as development under constraints of fixed conditions, became the history of the continuous adaptation of living organisms to changing conditions. In fact, and as we shall see, organisms themselves have caused much of the chemical environmental change.

Although ideas concerning the evolution of species and forms are well accepted, they are less recognized when transferred to the small molecule chemistry scale, even though it has become customary to call 'chemical evolution' the series of events which is thought to have taken place between the beginnings of prebiotic synthesis of large organic molecules and the appearance of the first vesicles ('protocells') to which one might assign some 'vital' properties. Throughout the (unfinished) biological evolution there has been, in addition, a continual selection toward the best chemical components for the necessary functions and a continuous improvement in the conditions of their utilization, leading to the formation of separate compartments in cells, to the functional separation of cells, to the specialization of different multicellular organisms and to their diversification and development. As the species became more complex, so did their chemistry, as evidenced by the increased complexity of the materials used and the manipulation of dynamic factors. The development of materials is again well recognized in the evolution of biological polymers but it can only be thoroughly appreciated, we believe, in terms of the structures and patterns of the flow of elements and chemicals, of ionic and electronic charge, and of energy directed in biological space. The strict environmental conditions that are required today by living organisms also point to the necessity of strict internal control and regulation of these processes, and this again means time and space organization of the biological substances, both large and small, and of their reactions. Much of this control is included in the now well-known classical treatment of the organic chemistry of life but, diverging from the classical tradition, we shall regard it in this book as the interplay of not just the great number of small and very large organic molecules but also of a group of about 25 chemical elements, free as ions, combined as complexes, or as precipitates, organized in biological space and time. Most of these elements are classified as 'inorganic'. We shall go on to insist that a proper appreciation of living systems and their evolution cannot be obtained without reference to these elements.

Central to this group of elements is a series of metals, each one of them used in many ways within a given biological system. The position of each metal element in space and the variation of this position in time, as well as the exact chemical partners with which it interacts, have been selected and perfected by the demands of evolution seemingly in such a way that the element's function has become virtually optimal and its role separate and distinct. Hence, several such elements are essential for life. In order to fully appreciate the subtleties of the function that Nature makes of these *ca.* 15 metal elements, it is necessary to understand how they are selected, in terms of uptake, and how they are combined, transported, stored, and tuned to their specific functions. Evolution refined function by acting on the interaction of the metals with their partners (usually proteins) or by abandoning some in favour of others more appropriate to conditions. Much of this chemistry involves ionic interactions.

Of course, in the description of the way in which the chemical elements are involved in life we cannot concentrate on metal ions alone. Some non-metals actually function in ways not too different from those of the metals, but as anions not cations, e.g. Cl^-. Others, the major elements of life, C, N, O, and S, to which we refer to rather a small degree since their biological chemistry is well described elsewhere, behave very differently, much as their chemistry is also very different, being loosely called covalent rather than ionic. Between the extremes lies the chemistry of phosphorus, as phosphate in biology, and hydrogen, which have both ionic and covalent chemistry. Our point will be that all the elements we find in biology are used in some optimal manner developed from their chemical possibilities. Biological chemistry is concerned, therefore, with this intricate, interwoven, 'designed', and sometimes symbiotic use of organic (non-metal) molecules and inorganic (metal) chemical elements in cells and tissues and cannot be restricted or related to so-called organic chemistry rather than to so-called inorganic chemistry. This book is then about biological chemistry seen from a particular inorganic perspective where a certain inorganic *bias* is inevitable to compensate for the traditional approach which leans heavily on organic chemistry. Accordingly, we have named it *The biological chemistry of the elements*.

Before entering the main body of the text, the reader is warned that every biological device is unlikely to be the best of all possible devices. Not only has biology general chemical limitations, but it is also evolving in changing conditions, many of which are created by life itself. A consequence of this slow progression is that now and then a less than perfect feature will survive, which has evolved from a committed route earlier in evolution and then found a new semi-effective use. It also follows that, should environmental conditions, the air, the sea, or the land, change very rapidly, complex life forms are at risk. There is a very general warning here, as man's activities saturate the ability of the environment to buffer the chemical changes he makes.

The book is organized in the following manner. In Chapter 1 we analyse the occurrence of the chemical elements in biology showing that of the 92 elements in the periodic table some 25–30 are especially important in biology. Much of the reason behind this selection lies in the limitations imposed by the abundance of the elements (even in the universe) and their availability on earth. Availability is further constrained by the concentration in waters and in the air and depends on local conditions. In the absence of organic chemicals most elements are bound in simple oxygen- or sulphur-containing compounds, as hydrates or precipitates. On entering biology the elements undergo special combinations with organic molecules. In the next five chapters we shall be considering this chemical speciation in a great variety of compounds in biology. We shall describe in the first instance in Chapter 2 how the biological uptake of the elements from natural sources can be controlled by selective (energized) chemistry of the elements and leads on to selective chemical combinations, e.g. of metals, M, with organic ligands, L. In Chapter 3 we extend the discussion to physical transfer and separation of M, L, or ML across membranes into compartments. Only at this stage will it be possible to start to explore function. Function is dependent upon the ability of elements to undergo chemical change (within compounds). The kinetics of activity will therefore be analysed in Chapter 4. Chapter 5 will illustrate how energy is put into compounds within biology. This is an obvious necessity both in synthesis and in transfer. We shall then turn in Chapter 6 to one major concern of this book—the functionally necessary requirement for life of a variety of elements. Chapter 7 will be a rather lengthy but necessary interjection concerning the biopolymers of life. The second part of the book, Chapters 8 to 19, will consider the essential functions of individual inorganic elements in life's processes in detail and especially in relation to the principles we outline in the first part, before we attempt to pull all the (inorganic) chemistry of life together, in the last part of the book.

We begin the difficult final analysis with an enquiry into the nature of minerals in biology (Chapter 20), since this allows us to look at a peculiar biological problem, the relationship between chemical activity and morphology. Shape is so clearly an essential feature of living things. Having established some simple principles, we move in Chapter 21 to a consideration of the simultaneous homeostasis of shape and chemistry. It is here that the interactive feedback relationships between the functions of elements become so intriguing. It almost goes without saying at this stage that the balance of elements in life is related to the elements available and it follows that changing the availability must affect life. We look at problems of man's interference with the natural supply of elements in Chapter 22.

Each chapter has only a limited number of references and most of them are to reviews. We realize that this approach may offend some but we found it impossible to be sure that we could give proper priority amongst the vast number of primary sources we have used.

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