Plenary Lectures

A1

Inorganic Elements in Biological Space and Time

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Inorganic chemists studying biological systems have been fascinated by the structure and properties of isolated (dead) compounds. This is but an extracted part of the interaction of inorganic elements with biological materials. *In vivo* we need to uncover the different compartments into which the elements are distributed and the timing of the distribution and its re-distribution. To this end we must define the time dependence of the chemical potential of elements in different parts of space. The chemical potential of an element itself can be broken down into concentration terms, field dependencies, and chemical bondings including oxidation state changes. The compartments for an element can be due to limitations upon physical diffusion, membrane control or to kinetically stable chemical traps. For simplicity I shall divide the elements first into two extreme groups: those that are restricted by physical diffusion only *e.g.* Na^+, K^+, Cl^-, and to a lesser degree Mg^{2+}, Ca^{2+}, and those that are confined by chemical traps *e.g.* Mo, Cu, Zn. We then observe that there are other elements of an intermediate category which are controlled by both types of traps and are mobile to a limited degree. While movement through membrane limitation is controlled by pumps and the synthesis of proteins controls the chemical traps some elements such as P, Fe, Mn both move between chemical traps and cross physical, membrane, barriers in very specific ways. The movement from the chemical traps often requires (catalysed) chemical reaction. We shall look at the movements of K, Ca, P, Fe, Cu and Mo asking about their residence time at any site.

Integrated over a very long period of time we can describe an average, though highly energised, distribution of any element. Over shorter periods there are found to be variations within this energised state. In other words elements have patterns of concentration and patterns of flow which are not constant in living systems—even of the simplest cells. The patterns of flow cause changes in local chemical potentials and hence in patterns of spatial activity especially since element movements trigger gross biological changes. The simplest examples of time dependences are the flows of electrons and ions, electronic and electrolytic currents, which can be connected to both chemical and mechanical devices *e.g.* the cytochrome chain activation and the nerve impulse. In more complicated situations the flow of an element is connected to differentiation and growth. Incidental changes in a biological system such as the storage of information or cell division (reproduction) are interwoven with changes in the patterns in space of elements. Iron movements are particularly interesting. I shall begin to explore some of these possibilities which will surely lead inorganic chemists closer to the nature of living systems. Very many elements are not inorganic and much of organic chemistry is inorganic.

A2

Mechanistic Aspects of Coenzyme B_{12}-dependent Rearrangements: Organometallics as Free Radical Precursors

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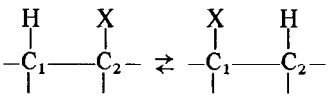
Coenzyme B_{12} (5′-deoxyadenosylcobalamin, abbreviated $[Co^{III}–R^-]$) serves as a cofactor for several enzymic reactions, a common feature of which involves the 1,2-interchange of a H atom and another group (X = OH, NH_2, $CH(NH_2)COOH$, *etc.*) on adjacent carbon atoms, *i.e.*,



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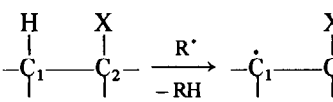
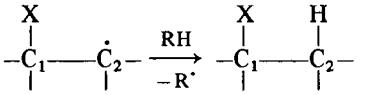
A widely accepted mechanistic interpretation of these reactions, supported by a variety of evidence from studies on the enzymic processes as well as on model systems, is,

$$[Co^{III}–R^-] \overset{\text{enzyme}}{\rightleftharpoons} [Co^{II}] + R^{\cdot} \qquad (2)$$





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