Redox (oxidation–reduction) reactions occur everywhere in biochemistry. The transfer of a hydride ion to or from carbon is a fundamental redox reaction, usually mediated by a flavin or pyridinium nucleotide (both organic co-factors). However, there are areas of redox biochemistry where metals (Fe, Cu, Mo, Mn, Co) have an essential role, most notably in electron transfer and the handling of certain small inorganic species [8].

With metal co-factors, we can distinguish groups solely involved in electron transfer from those involved in substrate redox reactions. The former are protected from solvent by their protein environment, and electrons are passed to or from the active metal via the protein in some way. The latter, on the other hand, are ‘open-sided’ groups, and allow co-ordination or close approach of substrate molecules as well as electron transfer if required.

In this chapter we shall look at some of the general properties that suit metals for these roles, and at some of the well characterized electron transfer chromophores (haem, ‘blue’ copper, and iron–sulphur clusters) as they occur in simple and complex proteins. Then follow sections on Mo and Co (coenzyme B_{12}) enzymes, and finally a survey of the components of the electron transfer chains of respiration and photosynthesis. In the next chapter we shall describe one particular group of proteins with open-sided metal co-factors – those which react with dioxygen species.

3.1 Metals as redox catalysts

Transition metals, with their labile d-electron systems, are well suited to catalyse redox reactions, for the following reasons. (1) A range of accessible oxidation states enables them to transfer electrons. (2) The redox potentials ($E_\text{red}$) for such transfer can be varied by alteration of ligand type or geometry. (3) Metals mediate atom transfer reactions. (4) Stable paramagnetic states are common, facilitating reaction with radical substrates. (5) The degree of paramagnetism (spin-state) can be varied. (6) Metals can bind neutral as well as anionic ligands. The last four points apply especially to open-sided sites.

Most organic redox co-factors, including the ubiquitous hydride carriers NAD(P)H, deal in the transfer of pairs of electrons ($H^- \equiv H^+ + 2e^-$), thus avoiding unstable or readily autoxidizable intermediates. However, all the metal chromophores referred to above have working capacities in vivo of only one electron, with no atom transfer. (It is
the alternation of these two types of redox carrier which permits the translocation of protons, p. 44.) Open-sided sites have greater capacities for change in oxidation state, as atom transfer or ion-binding nearby can offset local charge changes induced by electron transfer. Haem Fe, for instance, can vary from +2 to +5 in various reactions, and Mn and Mo are capable of similar changes in vitro at least.

The range of redox potentials at which metal co-factors are reported to operate is very wide, from −300 to ca. +800 mV (haem in cyt P450 and cyt a3), from +180 to +767 mV (blue Cu in plastocyanin and fungal laccase), and from −490 to +350 mV (iron–sulphur in ferredoxin and HiPIP). $E_\text{f}$ for a group may even be varied during the course of a reaction, with the effect of controlling electron flow. Organic groups rarely reach the oxidizing extremes of metals (perhaps in photosynthesis?), but flavodoxin substitutes functionally for ferredoxin in Fe-deficient Clostridium pasteurianum, with flavin $E_\text{f}$ values of −170 and −380 mV for two-step reduction.

Co in coenzyme B12 enzymes is probably the only metal catalysing C-atom transfer reactions. However, metals have an important role in O-atom ('oxene') transfer. This occurs in the splitting of peroxide, and probably in oxygenation and in the reduction of the oxyanions of N and S. The first step in the reactions of the peroxidases, for instance, is probably (see p. 58) of the form

$$\text{Fe}^{\text{III}} - \text{O-H} \rightarrow \text{Fe}^{\text{IV}} \text{O}^2^- (\text{cpd I}) + \text{OH}^-$$

Here transfer of oxene from peroxide to FeIII in haem raises the formal Fe oxidation state from +3 to +5, though the charge on oxide (−2) and porphyrin (−2) serve to keep the net charge at +1. (The formation of oxycations such as FeIVO2− is a feature of the chemistry of Fe, Mn and Mo, though not particularly of Cu. Nevertheless, Cu catalysis is responsible for splitting the O–O bond in laccase.) By means of such atom transfer, and by the assembly of groups of redox chromophores, metalloproteins can act as electron converters in redox transfer chains. Cytochrome oxidase converts the four oxidizing equivalents of O2 rapidly into single units carried by cyt c, and nitrogenase enables six electrons to react with N2 to yield ammonia. (In a similar way, flavin can act as a two-to-one converter by hydride and electron transfer.)

Paramagnetic states of metals are commonly used in initial activation of the stable diradical O2, although O2 reacts satisfactorily with haemocyanin, which is diamagnetic in its cuprous form. The spin state of a metal reflects the degree to which its electrons are paired with each other. From our point of view, one important aspect of electron pairing is that it affects the interaction of a metal with its ligands. Fe in haem, for instance, may adopt an octahedral co-ordination, lying in the haem plane, with two axial ligands. This induces a low-spin state, in which FeII is diamagnetic. In the high-spin state, ligand bonds are weakened and lengthened, and Fe shifts slightly