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Extension

How binding oxygen triggers changes in haemoglobin

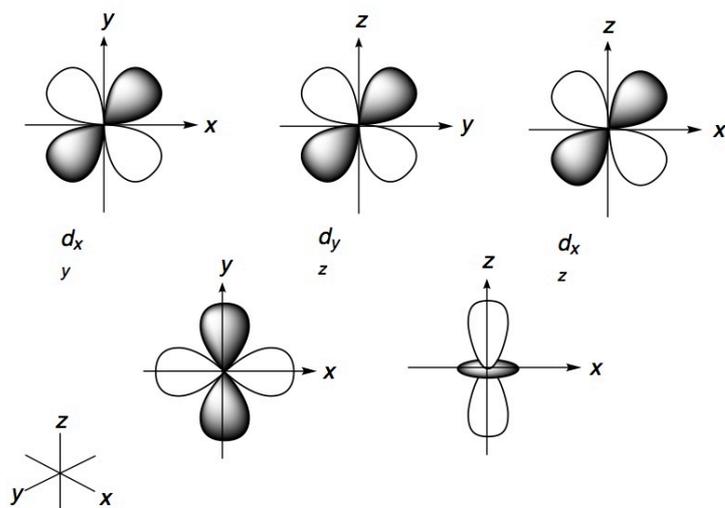
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The article 'Iron in the blood' (see CHEMISTRY REVIEW, Vol. 25, No. 4, pp. 16–22) discusses how haemoglobin, a protein packed into red blood cells, transports oxygen from the lungs to the rest of the body. Oxygen is transferred from the haemoglobin to a similar protein, myoglobin, which is found in muscle cells. Both haemoglobin and myoglobin contain iron, in the form of Fe^{2+} , and it is the iron that binds to oxygen molecules. Haemoglobin consists of four subunits, each formed by a polypeptide chain, with a haem group (a porphyrin) bearing an Fe(II) ion. In an area of low oxygen concentration, haemoglobin gives up its cargo of four oxygen molecules, due to a change in shape of the subunits, as explained here.

In the deoxy- forms of haemoglobin and myoglobin, the Fe^{2+} ion lies some 0.4 \AA ($1 \text{ \AA} = 0.1$ nanometres (nm), 10^{-10} m) out of the plane of the porphyrin ring, as iron is in the high-spin d^6 state and is too large to fit into the cavity in the middle of the porphyrin ring.

When oxygen binds to the iron atom, the Fe^{2+} ion changes to the low-spin d^6 state and is now slightly smaller (the radius decreases by around 0.15 \AA), so that it is able to move into the cavity, in the plane of the ring, dragging the histidine after it (see Figure 6 on p. 20 of the article).

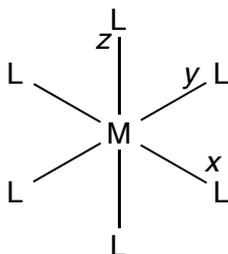
In the free metal ions, like Fe^{2+} , the five d orbitals all have the same energy, they are *degenerate*:



Shapes of d orbitals

That is not the case in complexes, where ligands are bound to the metal ion.

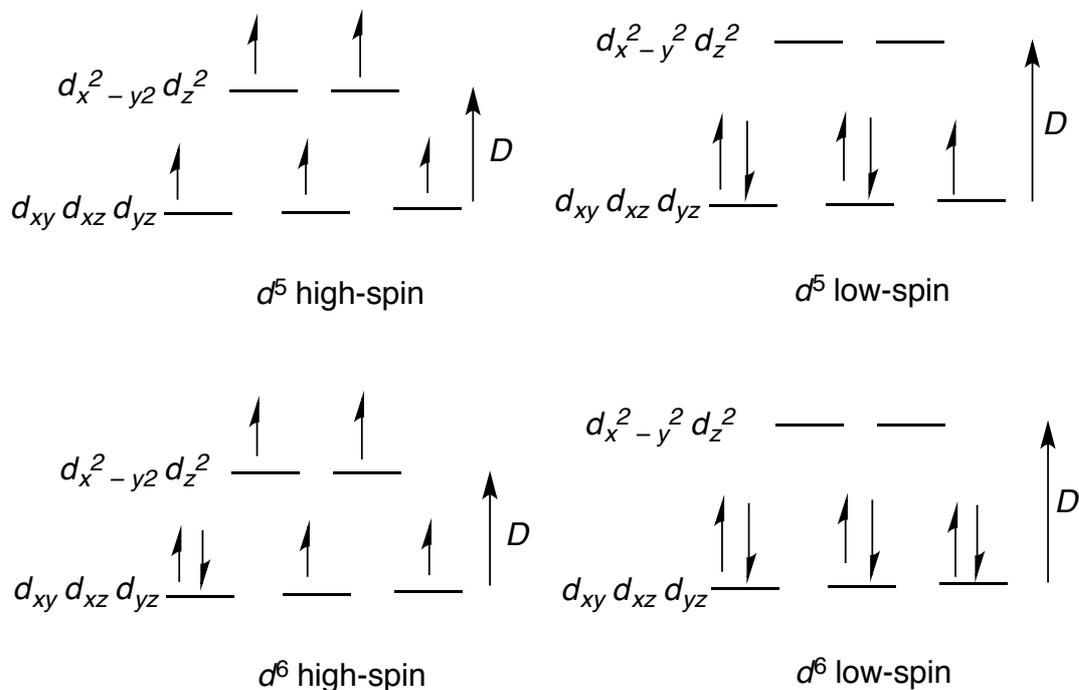
In an octahedral complex, the ligands are considered to lie along the x, y and z axes. Ligands have a lone pair of electrons that they donate to the metal ion (into empty metal orbitals):



Because the $3d_{xy}$, $3d_{xz}$ and $3d_{yz}$ orbitals point *between* the axes, they are further from the ligand electrons than are the $3d_{x^2-y^2}$ and $3d_z^2$ orbitals, which point *along* the axes. There are two consequences of this that concern us here.

The repulsive force between the ligand electrons and the electrons in d orbitals causes their energy to be raised, but it will be raised more for electrons in the orbitals which point directly at the ligands, the $3d_{x^2-y^2}$ and $3d_z^2$ orbitals. The difference in energy between these two sets of orbitals, $3d_{xy}$, $3d_{xz}$ and $3d_{yz}$, and $3d_{x^2-y^2}$ and $3d_z^2$, is known as the crystal field splitting, Δ . The size of the splitting depends upon several factors, including the identity of the ligands (halides produce small Δ values, cyanide produces large Δ values).

In the case of both iron(III), with its $3d^5$ arrangement of the $3d$ electrons, and iron(II), with its $3d^6$ arrangement, two electron arrangements are possible. If the difference in energy, Δ , is small, it is energetically more favourable for electrons to occupy as many of the $3d$ orbitals as possible, the 'high-spin' arrangement, which results in the maximum number of unpaired electrons. If Δ is big, greater than the 'pairing energy', the repulsion caused when putting two electrons in the same orbital, then the 'low-spin' arrangement, which maximises pairing of the d electrons, is the more stable state:



Distribution of electrons between orbitals in different spin arrangements

In deoxy-myoglobin and haemoglobin, the value of Δ is such that the Fe^{2+} ion has the $3d^6$ high-spin arrangement. When O_2 is attached to the iron, this causes an increase in Δ sufficient to change to the $3d^6$ low-spin arrangement.

In the high-spin arrangement, electrons occupy the two orbitals that point directly at the ligands, $3d_{x^2-y^2}$ and $3d_z^2$, whereas in the low-spin arrangement this is no longer the case. The extra repulsion in the high-spin case means that high-spin Fe^{2+} ions have a slightly greater radius than the low-spin Fe^{2+} ions, which is why the low-spin Fe^{2+} ions are able to fit into the cavity in the middle of the porphyrin ring in oxymyoglobin and oxyhaemoglobin.

Useful site

d orbitals: <http://www.chemguide.co.uk/inorganic/complexions/colour2.html>

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