Introduction.

The Principles of Biological Oxidation.

Whatever a cell does, it has to pay for it and the currency of living systems in which the cell has to pay, is energy. If there is no free energy, there is no life. The sole ultimate source of this energy is the radiation of the sun. This, however, cannot be utilized as such to maintain life, or else life would fail at night. Therefore the radiating energy is packed into small parcels by the chloroplasts of the chlorophyl-containing plants. If the cell needs energy, it does not use radiation but unpacks these parcels of energy, called "foodstuff molecules". The two fundamental reactions of life are: 1. The making of these packages and 2. their unpacking.

Energy
$$+ nCO_2 + nH_2O = nO_2 + C_nH_{2n}O_n$$
 . . . 1.
 $C_nH_{2n}O_n + nO_2 = nH_2O + nCO_2 + Energy$. . . 2.

Reaction 2 is the oposite of reaction 1. The first of the two reactions is performed only by chlorophyl-containing plant cells, while reaction 2 is performed by all cells, by the plant, or by the animal, which eats the plant (herbivores) or by the animal, which eats the animal, which ate the plant (carnivores).

This book is concerned with the mechanism of the second reaction.

The analogy of the coal heated steam engine suggests that the essence of this reaction is the coupling (oxidation) of the C with O_2 . C is the backbone of the whole molecule, and its reaction with oxygen is a rich source of energy, while the $H_{2n}O_n$ moiety (=nH₂O) of the foodstuff molecule represents no energy.

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The discovery that this is not so, is one of the greatest events in modern biochemistry and is linked with the name of H. Wieland.

According to *Wieland*, whose view is supported by the great bulk of modern literature, the oxidation of the foodstuff molecule consists of the splitting off of H atoms. The whole foodstuff molecule is in essence but a little parcel of Hydrogen, its C atoms are pegs, on which the H atoms are hung. To use *Wieland's* nomenclature, the foodstuff molecule is but an "H Donator". So in this book I will call the foodstuff simply "Donator".

The oxidation of the H, given off by the donator, drives the living engine. This reaction is the sole ultimate source of energy in higher organisms, which know but one fuel: Hydrogen. Hydrogen is the fuel of life.

The oxidation of H_2 to H_2O yields 68,000 cal., and is thus one of the reactions, richest in energy, known to the chemist. It is not the object of biological oxidation to liberate this energy. The object is, to liberate it in such a way that it can be transferred to cellular functions which need energy. Energy turned into heat is lost the living machine.

It seems that the quantity of energy, liberated in the oxidation of one single H atom is too big to be dealt with. The cell wants change. The H is thus not coupled at once with Oxygen, which coupling would yield the total energy, but it is linked in succession to a series of substances. At every new step energy is liberated. So the H is oxidised piecemeal and the liberation of energy distributed over a long series of reactions.

This piecemeal combustion of the H atom is one of the fundamental principles of biological oxidation and it was the object of my work to contribute to its knowledge.

Oxygen was thought of previously as the omnipotent master of oxidation which disintegrates the foodstuff molecule by its oxidising power. By *Wieland's* theory its function became reduced to the more modest rôle of an "H acceptor". The inspired oxygen does not come in touch with the foodstuff molecule at all. It does not even meet the H split off from the donator. Oxygen acts only in one single reaction, at one end of a long chain. It disappears from the scene at its first step and leaves behind no more than an electronic change on Fe atoms. Accordingly the O_2 moiety of the expired CO_2 is not derived from the inspired O_2 at all but it represents partly the oxygen contained in the foodstuff molecule, and is partly derived from the water molecules taken up by the donator to fill the place of the lost H atoms.

Naturally such generalisations hold only for the big bulk of respiration. Here and there a H may find its way to oxygen or an oxygen to some organic molecule. All the same there can be little doubt, that our outlook on oxidation has undergone profound changes. Biological oxidation was thought of before as an interaction of Foodstuff and Oxygen. To-day this process is pictured as a long chain of reactions in which Hydrogen is combusted. The central problem of biological oxidation is the mechanism of this piecemeal oxidation of the single H atoms. At one end of this chain of reactions stands the foodstuff molecule, having no other function than to give off its H atoms. At the other end stands O_2 giving up its electrons. It has been my chief object to contribute to the knowledge of the middle part of the reaction.



