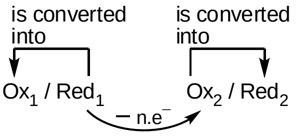
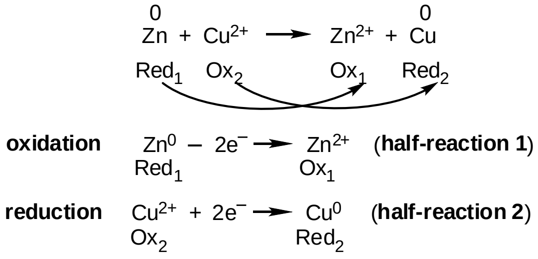
№ 14. CRITERIA FOR PREDICTING THE DIRECTION OF REDOX REACTIONS – THE NERNST EQUATION. RATE OF REDOX REACTIONS. REDOX CATALYSIS. BIOLOGICAL OXIDATION.

I. Electrode potential. Criteria for predicting the direction of a redox reaction. Nernst equation.



Two redox couples in contact are necessary in order to have a redox reaction. One substance from the first pair is oxidized; other substance from the second pair is reduced. The overall reaction can be expressed by two half-reactions of general form: $a\,\mathrm{Ox} + n.e^- \rightleftharpoons b\,\mathrm{Red}$

Every half-reaction of such type generates characteristic electrical potential (voltage). The potential is determined using electrochemical cells. An electrochemical cell is a device in which an electric current (a flow of electrons through a circuit) is either produced by a spontaneous chemical reaction or used to bring about a nonspontaneous reaction. We discussed earlier the spontaneous reaction when zinc rod is immersed in aqueous copper (II) sulfate solution. The redox reaction and its constituent half-reactions are:

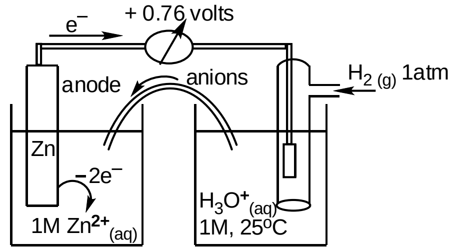


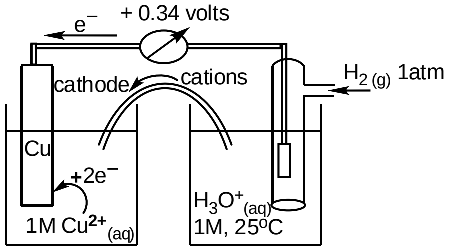
The potentials of these half-reactions can be measured (actually measured is potential difference, not individual potential) in electrochemical cells in comparison to the potential of standard hydrogen electrode. Its potential is set by convention to 0.00 volts. Standard hydrogen electrode is realized by immersing inert platinum plate into strong acid (e.g. HCl) with $[H^+] = 1$ mol/L (pH = 0) that is in equilibrium with H_2 gas with pressure p = 1 atm and the system is kept at standard temperature of 25°C, T = 298 K.

The half-reaction:

$Zn^0 - 2e^- \rightarrow Zn^{2+}$

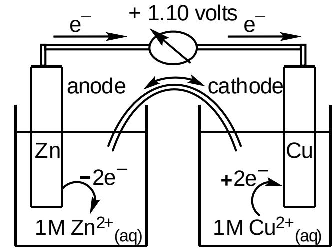
has standard electrode potential $E^o = +0.76$ V. The reversed reaction, reduction, has $E^o = -0.76$ V.





The **anode** is defined as the electrode at which electrons leave the cell and **oxidation occurs**. Electrons produced from oxidation flow out of compartment through a wire. Positive charge increases in the compartment due to the production of Zn^{2+} from Zn^0. To maintain neutrality, anions move in through the salt bridge (could be KCl with spectator ions).

The half-reaction: $Cu^{2+} + 2e^- \rightarrow Cu^0$ has standard electrode potential $E^o = +0.34$ V and the reversed reaction, oxidation – $E^o = -0.34$ V. **Cathode** as the electrode at which electrons enter the cell and **reduction occurs**. Electrons entering the copper compartment are consumed in the reduction of Cu^{2+} to Cu^0. Positive charge in solution decreases and cations migrate through the salt bridge to maintain the charge.



Both Zn/Cu half-reactions can be connected in one electrochemical cell, as shown. They create a potential of +1.10 volts at standard conditions. *But how to predict which substance will be oxidized, and which – reduced?*

Each half-reaction generates definite electrical potential depending on the conditions. **The electrode potential of a redox couple at any particular conditions is determined by Nernst equation**. The direction of a redox reaction depends on these potentials.

The general form of Nernst equation for a half-reaction $a\,\mathrm{Ox} + n.e^- \rightleftharpoons b\,\mathrm{Red}$ is:

$$E = E^o + \frac{RT}{nF}\ln\left(\frac{[Ox]^a}{[Red]^b}\right)$$

where **E** – the redox potential at used concentrations in volts (V) ;

E° – the standard redox potential in volts (for the standard state condition with 1mol/l solutions of ions, 1 atm of pressure for gases (1.10^5 Pa), 25°C temperature and pH=0) ;

n – number of moles of electrons stated in the half-reaction (redox capacity) ;
R – ideal gas constant (8.314 J/K.mol) ; **F** – Faraday constant (96 500 C/mol); (C = *Coulombs*) ;
T – temperature in Kelvin's (T = 273 + 25°C = 298 K) ; ***a, b*** – stoichiometric coefficients.

For calculations at standard conditions, the Nernst equation is simplified to: by substituting with numerical values R, F, T = 298 K, and changing *ln* into *lg.*

$$E = E^o + \frac{0.059}{n} lg\left(\frac{[Ox]^a}{[Red]^b}\right)$$

Organic redox reactions and, in particular biochemical oxidation / reduction reactions, are often accompanied by proton transfer. Therefore, the concentration $[H_3O^+]$ is included in Nernst equation as:

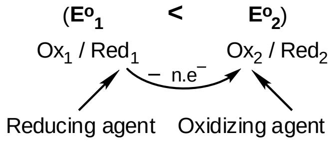
$$E = E^o + 0.059\,[H_3O^+] + \frac{0.059}{n} lg\left(\frac{[Ox]^a}{[Red]^b}\right) \qquad E = E^o - 0.059\,pH + \frac{0.059}{n} lg\left(\frac{[Ox]^a}{[Red]^b}\right)$$

The Nernst equation relates the redox couple potential E to the molar concentrations of Red and Ox species. The potential $E = E^o$ when the concentrations of oxidized and reduced forms are equal. In that case *ln* [Ox] / [Red] = 0 and $E = E^o$. The standard redox potentials have been determined for many couples and they are available in handbooks. By convention, the standard redox potentials are given for half-reaction written as reduction, therefore **E^o represent *reduction potentials***, e.g. Zn^{2+} (1M) I $Zn_{(s)}$ \ is – 0.76 V. **The standard reduction potential is a measure of how easily a substance can gain an electron.** High (positive) potential corresponds to very easy gain of e^- – *i.e.* strong oxidizers (F_2, MnO_4^-). Low (negative) potential means hard to get an e^- – *i.e.* strong reducing agents (Li, Na).

Some of the standard reduction potentials are:

Half-reaction	E^o (volts)	Half-reaction	E^o (volts)
$F_{2\,(g)} + 2e^- \longrightarrow 2F^-_{(g)}$	+ 2.87	$2H^+ + 2e^- \longrightarrow H_{2\,(g)}$	0.00
$MnO_4^- + 8H^+ + 5e^- \longrightarrow Mn^{2+} + 4H_2O$	+ 1.51	$Fe^{2+} + 2e^- \longrightarrow Fe_{(s)}$	– 0.45
$Cl_{2\,(g)} + 2e^- \longrightarrow 2Cl^-$	+ 1.36	$Zn^{2+} + 2e^- \longrightarrow Zn_{(s)}$	– 0.76
$Br_{2\,(l)} + 2e^- \longrightarrow 2Br^-$	+ 1.09	$Al^{3+} + 3e^- \longrightarrow Al_{(s)}$	– 1.66
$Ag^+ + e^- \longrightarrow Ag_{(s)}$	+ 0.80	$Ca^{2+} + 2e^- \longrightarrow Ca_{(s)}$	– 2.87
$Fe^{3+} + e^- \longrightarrow Fe^{2+}$	+ 0.77	$K^+ + e^- \longrightarrow K_{(s)}$	– 2.93
$Cu^{2+} + 2e^- \longrightarrow Cu_{(s)}$	+ 0.34	$Li^+ + e^- \longrightarrow Li_{(s)}$	– 3.04

The standard hydrogen electrode (with Pt electrode at 1 mol/L H^+, 1 atm H_2, and T = 298 K) for the reaction $2H^+ + 2e^- \longrightarrow H_2$ has arbitrary assigned $E^o = 0.00$ V. **Meaning of standard reduction potential E°:** (1) **A large positive E° means the element or compound is easy to reduce.** Example: $F_2 + 2e^- \longrightarrow 2F^-$ has E°=+2.87 volts and it is easy to add electrons to F_2 (this reduction is with positive E°, negative ΔG°, favorable transformation). **A large positive E° means the oxidized species of the couple is very oxidizing.** Elemental fluorine is strong oxidizing agent. (2) **A large negative E° means the element or compound is hard to reduce.** Example: $Li^+ + e^- \longrightarrow Li$ has E°= –3.04 volts and it is hard to add electrons to Li^+ (negative E°, positive ΔG°, not favorable transformation). If we ask: "Is Li^+ a good oxidizing agent?", the answer is plain "NO" – just the opposite, lithium metal is very good reducing agent. A large negative E° means the reduced species of the couple is very reducing. The more positive the redox potential is, the greater is the tendency of an oxidized form to be reduced. **More positive redox potential have couples of stronger oxidizing agents, where the tendency is to convert into a reduced form.** In the reversed reaction, the reduced form is very weak reducing agent – it is hard to oxidize it (like F^-). **More negative redox potential have pairs with greater tendency of the reduced form to be oxidized.** With more negative redox potential, the oxidized form is weaker oxidizing agent



and the reduced form is strong reducing agent (like Li). In general terms: When **$E°_2 > E°_1$ the oxidized Ox_2 form will oxidize the reduced Red_1 form**.

$$\overset{2.1e^-}{\overleftarrow{F_2 + 2\,Li}} \longrightarrow 2\,F^- + 2\,Li^+ \quad \text{spontaneous}$$

F_2 I $2F^-$	Li^+ I Li
E^o=+2.9 V	E^o=–3.0 V
tendency to reduced F^-	tendency to oxidized Li^+

When fluorine (gas) and lithium are in contact, the spontaneous reaction is oxidation of lithium metal with simultaneous reduction of fluorine molecules, whereas the reversed reaction is not spontaneous. How to determine the direction of a redox reaction (when two redox couples are in contact, as in an electrochemical cell)? How to find in which direction the reaction is spontaneous? The thermodynamic criterion for **a spontaneous reaction is the decrease of Gibbs free energy: $\Delta G° < 0$.** In a cell, where a spontaneous redox reaction drives the cell to produce an electric potential, Gibbs free energy change ΔG° must be negative, in accordance with the following equation: **$\Delta G^o = -\,n\,F\,\Delta E°_{cell}$**

(where **n** is number of moles of electrons per mole of products and **F** is the Faraday constant). If **$\Delta E°_{cell} > 0$**, **then the process is spontaneous** (as in galvanic cells and batteries). If **$\Delta E°_{cell} < 0$**, **then the process is nonspontaneous** (as in an electrolytic cell).

A redox reaction may occur spontaneously either in an electrochemical cell of after mixing the reactants. In such cases the standard redox potentials and the Nernst equation are used to predict the spontaneity of an oxidation-reduction reaction. The potential of an electrochemical cell is determined as:

$\Delta E°_{cell} = E°_{cathode} - E°_{anode}$ In order to have **$\Delta G° < 0$, $\Delta E°_{cell}$ must be positive**. For the familiar example:
The reduction of Cu^{2+} to Cu^o is at the cathode, the oxidation Zn^{2+} to Zn^o is characteristic for anode. The electrode potential of the latter must be with opposite sign to that listed as standard reduction potential of +0.76 V. Therefore, **$\Delta E°_{cell}$** is positive, and the reaction from left to right is spontaneous. The reversed reaction does not happen spontaneously.

$$Zn + Cu^{2+} \rightleftarrows Zn^{2+} + Cu$$

$$Cu^{2+} + 2e^- \longrightarrow Cu^0 \quad (E^o = +0.34V)$$

$$Zn^{2+} + 2e^- \longrightarrow Zn^0 \quad (E^o = -0.76V)$$

$$E^o_{cell} = \Delta E^o = 0.34 - (-\,0.76) = +1.10\ V$$

$\longrightarrow$ spontaneous
$\longleftarrow$ nonspontaneous

II. Relationship between free energy change, the redox potential and the equilibrium constant

$$Ox_1 + Red_2 \rightleftarrows Red_1 + Ox_2$$

oxidation at anode: $Red_2 \longrightarrow Ox_2$
reduction at cathode: $Ox_1 \longrightarrow Red_1$

For any redox reaction, let's set standard conditions: (t^o=25°C, P=1 atm, and $C_{ox1}=C_{red2}=C_{red1}=C_{ox2}$= 1 mol/L). Then, the reaction will occur **spontaneously from left to right if $\Delta E° > 0$, $\Delta G^o < 0$ and $K_C >> 1$**.

The change of Gibbs free energy must be negative: **$\Delta G^o = -\,n\,F\,\Delta E^o$**

We have already learned that Gibbs free energy change is related to the equilibrium constant by:

$$\Delta G^o = -\,R\,T\,\ln K_C$$

Therefore **$-\,n\,F\,\Delta E^o = -\,R\,T\,\ln K_C$** and **$n\,F\,\Delta E^o = R\,T\,\ln K_C$**. It follows

$$\ln K_c = \frac{n\,F}{R\,T}\,\Delta E^o$$

or in simplified form (at 298 K, using the values of constants R and F, and common logarithm to base 10) :

$$\lg K_c = \frac{n}{0.059}\,\Delta E^o$$

The last equation indicates that the redox reactions **is almost complete to the right when ΔE^o has large, positive value!** The equilibrium constant (**K_C**) and the standard free energy change (**ΔG^o**) can be calculated from tabulated data on standard redox potentials of two half-reactions using the derived last equations and the relation **$\Delta G^o = -\,n\,F\,\Delta E^o$** . Under nonstandard conditions (when temperature is not 25°C, and all concentrations and pressures are not equal to unity), the Nernst equation relates **ΔG** to the redox potential **E**.

One remarkable feature of redox reactions, in contrast to most other chemical reactions, is that they occur over such a wide range of equilibrium constant values. For a two-electron reaction, a voltage difference of 6 V corresponds to an equilibrium constant $\mathbf{K_C}=10^{200}$! This means that only rarely will two half-reactions have potentials so similar that the equilibrium constant for the overall reaction will be of moderate size. **Most redox reactions either go to completion (effectively) or do not go at all.**

III. Rate of redox reactions Redox catalysis

Many chemical reactions proceed spontaneously when the reactants are mixed together. Mixing a strong acid with a strong base in aqueous solutions results in a very rapid neutralization reaction between very mobile ions.

$$HCl_{(aq)} + NaOH_{(aq)} \rightarrow NaCl_{(aq)} + H_2O \quad (\Delta G^o < 0)$$

$$2\,H_2 + O_2 \rightarrow 2\,H_2O \quad (\Delta G^o < 0)$$

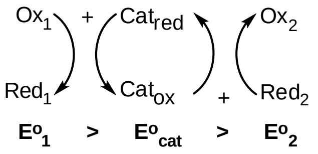
In contrast, many redox reactions, such as that between H_2 and O_2 to produce water, do not occur at all at room temperature. However, when the temperature is high enough, the reaction between H_2 and O_2 takes place with enormously high rate (explosion). Both of these reactions are ***energetically favourable in thermodynamic terms***, because they both occur with a large decrease of Gibbs free energy (**$-\Delta G$**). There are practical limitations on predictions of the direction of spontaneity for a chemical reaction, the most important arising from **the problem of reaction rates**. An analogy can be made with the simple physical system of a block on a sloping plane. Because of the favorable energy change, the block tends spontaneously to slide down, rather than up, the slope, and, at mechanical equilibrium, it will be at the bottom of the slope, since that is the position of lowest gravitational energy. How rapidly the block slides down is a more complex question, since it depends on the amount and kind of friction present. The direction of spontaneity for a chemical reaction is analogous to the downhill direction for a sliding block, and chemical equilibrium is analogous to the position at the bottom of the slope; the rate at which equilibrium is approached depends on the efficiency of the available reaction processes. **Between zinc metal and aqueous copper (II) ions, the reaction proceeds without observable delay, but various other spontaneous redox processes proceed at imperceptibly slow rates under ordinary conditions.** There is no simple way to predict which redox reaction will go fast and which – slow; some redox reactions proceed with higher rate due to lower kinetic barrier, lower activation energy than others. As stated before, besides the **thermodynamical condition** for a spontaneous reaction, we must also **consider the kinetic factors** governing the reaction. The reaction between H_2 and O_2, as many other redox reactions, does not occur rapidly at room temperatures because of a **kinetic barrier (high activation energy E_a)**.

IV. Biological reduction-oxidation reactions. The vast majority of valuable to an organism redox reactions have high kinetic barriers preventing their spontaneous occurrence in the living cell. **Such high kinetic barrier is usually overcome *in vivo* by the action of enzyme catalyst**. A particularly significant illustration of the role of mechanisms in determining the rates of redox reactions concerns **respiration, the central energy-producing process of life**. Foodstuffs that are oxidized by molecular oxygen during respiration are quite unreactive with oxygen before ingestion. **Such high-energy foods as grains and sugar can resist the atmosphere indefinitely but are rapidly converted into carbon dioxide and water through combination with oxygen during respiratory metabolism**. The situation is exemplified by the behavior of glucose at ambient temperatures. *"You remember the exciting story of the grave of the Egyptian emperor. At its opening the breakfast of the emperor was found unburned though it had been exposed to the action of oxygen during several thousand years at a temperature that was not very different from 37° C. Had the king risen and consumed his breakfast, as he had anticipated doing, **the food would have been oxidized in no time**, that is to say the cells of the emperor would have made reactions take place that would not run spontaneously" (from Albert V. Szent-Györgyi, On Oxidation, Fermentation, Vitamins, Health and Disease).* **Living systems are able to use respiratory oxidation as an energy source only because the same reactions are slow outside the cell**. In return for providing an efficient mechanism for the oxidation of foods, the cell gains control over the disposition of the liberated chemical energy. Otherwise the result would be overheating from "uncontrolled burning". Examples such as the chemistry of respiration make clear the importance of determining the rates and mechanisms of redox reactions. Often questions are difficult to answer even in regard to relatively simple reactions. It has been pointed out that many redox processes can be categorized as oxygen-atom-, hydrogen-atom-, or electron-transfer processes. These categories describe the net changes that are involved but provide no insight into the mechanisms of the reactions.

Redox-catalyst is a reversible redox system that has intermediate value of standard redox potential in respect to the two redox couples participating in a reaction.

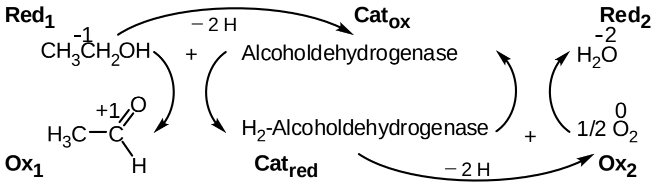
$$Ox_1 + Red_2 \rightleftharpoons Red_1 + Ox_2$$
$$E^o_1 \quad > \quad E^o_2$$
$$Ox_1 / Red_1 \quad Ox_2 / Red_2$$

Consider a redox reaction that is thermodynamically favorable to proceed from left to right but it is slow. This reaction can be accelerated by a redox catalyst (redox couple **Cat_{ox} I Cat_{red}** as shown in the next scheme) **if the catalyst has an intermediate value of standard redox potential and if the catalytic Red / Ox forms can react rapidly with Ox_1 and Red_2.**



Redox catalysts in biochemical reactions are enzymes called oxido-reductases.

For example, the enzyme alcoholdehydrogenase can catalyze oxidation of ethyl alcohol to acetaldehyde:



Characteristic features of biochemical oxidation / reduction reactions

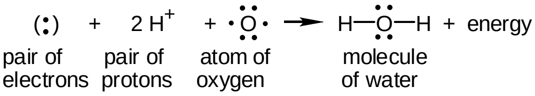
1. **Typically biological oxidation is a dehydrogenation reaction. The reduction reactions are hydrogenation reactions.** By no means is a H_2 molecule involved – one hydrogen atom is transferred with electron pair, as a hydride anion, the second hydrogen atom is transferred as proton.
2. Biological oxidation-reduction reactions are almost always due to **two-electron transfer (both e^- coming with H^-, hydride anion)**.
3. **The ultimate acceptor of electrons is frequently (but not always) oxygen.**
4. The overall chemical transformation is:

$$\overset{Red_1}{\overset{0}{2\,H}} + \frac{1}{2}\overset{Ox_2}{\overset{0}{O_2}} \rightleftharpoons \underbrace{\overset{Ox_1}{\overset{+1}{2\,H}} + \overset{Red_2}{\overset{-2}{O}}}_{H_2O}$$

and the standard reduction potentials at pH = 7 in human body are: $E^o_{1/2\,O_2\,I\,O^{-2}} = +0.82$ V $\quad E^o_{2\,H^+\,I\,H_2} = -0.41$ V

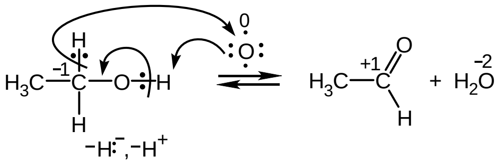
5. **The electron pair is usually not transferred directly to oxygen from a substrate that is oxidized.** The electron acceptor in many biological oxidations is one of several coenzymes. They are specialized molecules to carry forth and back electrons and protons. As a result of such reversible hydrogen transfers, the coenzymes exist in oxidized and reduced forms. The order of intermediates in **an electron acceptors chain** that is responsible for transport of H^-/H^+ from reduced coenzymes to oxygen is governed by the standard redox potentials of participants in that chain.
6. The oxido-reductases are redox catalysts that increase the rate of a biochemical oxidation reaction.

The **biochemical oxidation** is more often a dehydrogenation reaction. **That is, removal of two electrons as a hydride (H^-) and removal of one H^+**, which is expressed as:

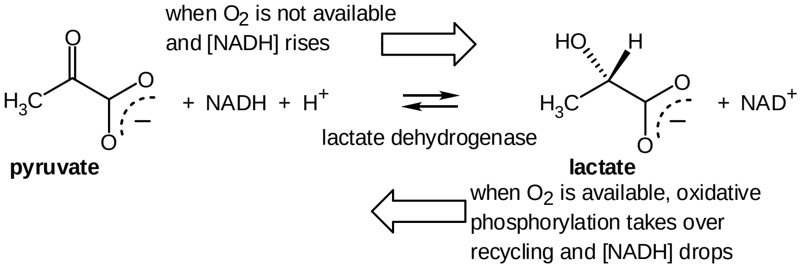


Reduction in living cells is addition of two electrons as a hydride anion and addition of one proton – overall hydrogenation.

In the body, the enzyme alcohol dehydrogenase (ADH) oxidizes CH_3OH (wood alcohol) to formaldehyde (HCHO) which has toxic effect and can cause blindness and death.



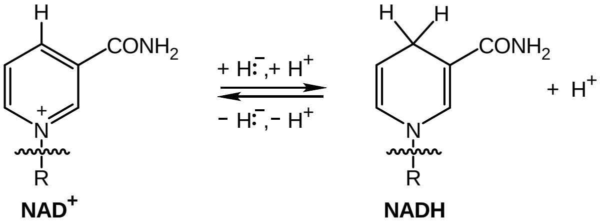
Typical example of **reversible biochemical redox reaction is the oxidation of lactate to pyruvate and reduction of pyruvate to lactate:**



The oxidized form of coenzyme NAD^+ takes one hydride anion (H^-) and one H^+ from the lactate substrate to convert it into pyruvate and the coenzyme is reduced to NADH. In the reversed reduction reaction NADH supplies one H^- and the substrate takes one H^+ to obtain lactate.

NAD^+ – nicotinamide adenine dinucleotide in oxidized form;

NADH – nicotinamide adenine dinucleotide in reduced form.



Quinones (oxidized form, as in Coenzyme Q_{10}) can redox cycle with their conjugate hydroquinones (reduced form, as in Ubiquinol).