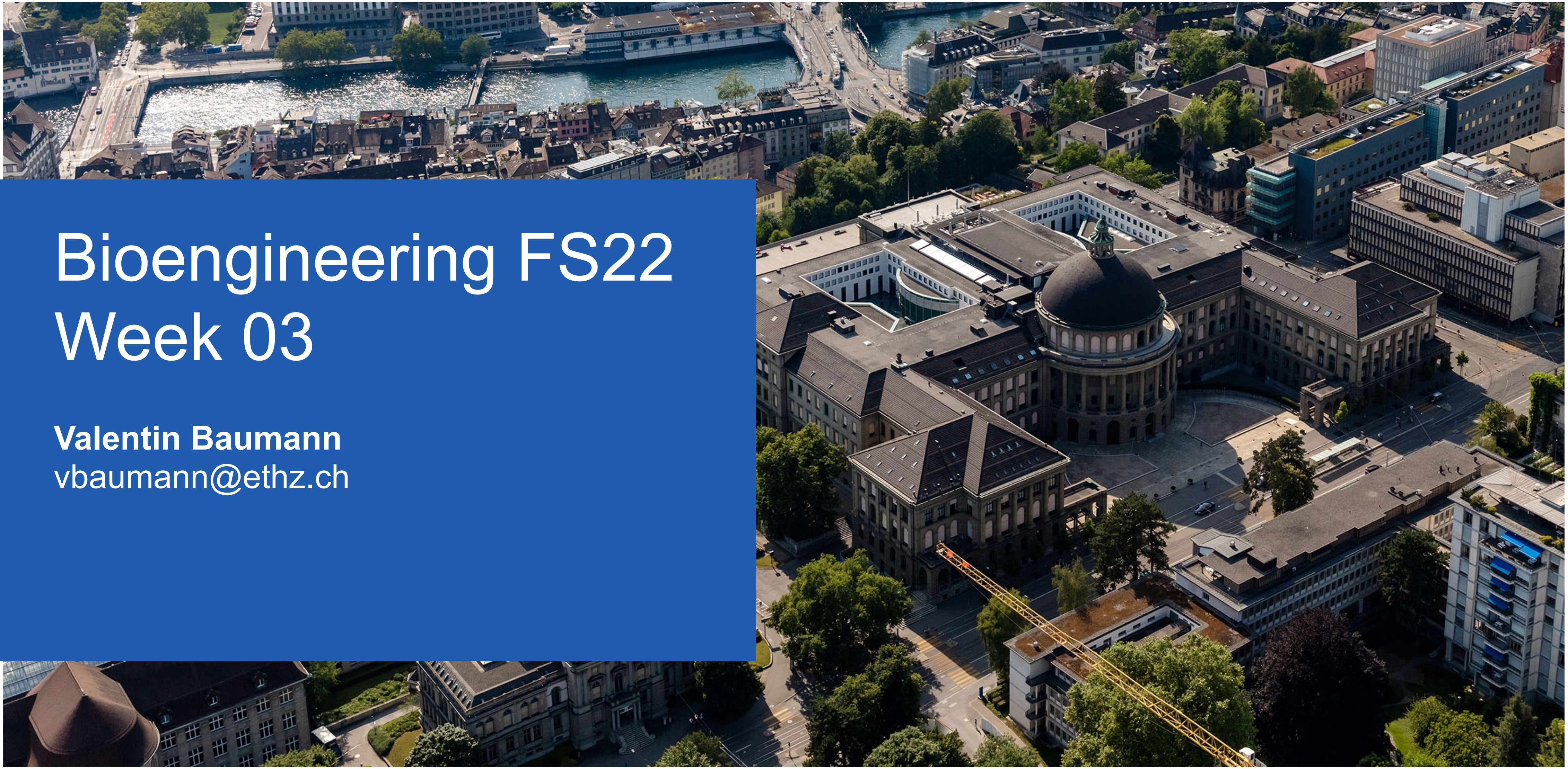

Bioengineering FS22
Week 03

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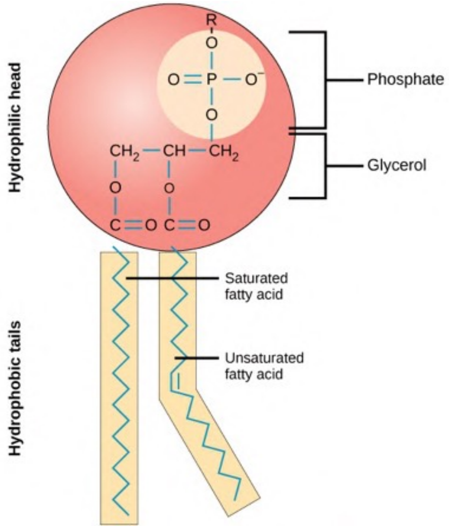
Agenda

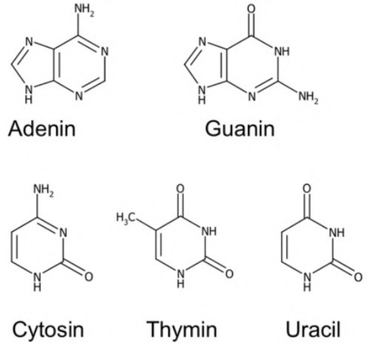
1. **Cell metabolism I**
    1. Cell nutrition
    2. Thermodynamics
    3. Principles of cell metabolism
    4. Metabolism example and ATP
    5. Enzymes
2. **Exercise 2**

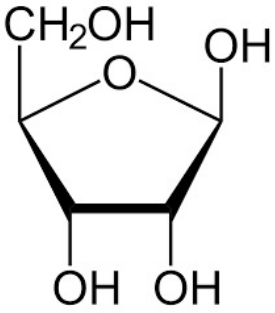
Cell nutrition – What is needed for survival?

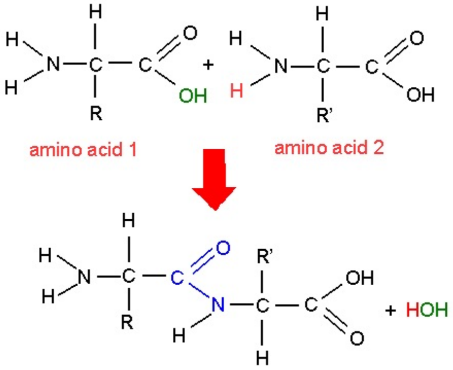
- Water (H_2O) is the most abundant component of cells. Macromolecules, phospholipids and ions make up the rest of the cell.
- In order for the cell to work properly, there are a few elements that need to be absorbed. The most important are: C, H, O, N, S, P, Mg, Fe.
  - **Proteins**: C, H, N, O, S
  - **DNA, RNA**: C, H, O, N, P
  - **Polysaccharids**: C, H, O
  - **Phospholipids**: C, H, O, P
  - **Catalysators and ligands**: Fe, Mg
- Where are these elements sourced?
  - Carbon: CO_2 and organic materials
  - Oxygen: Air, water, CO_2 and sugars
  - Sulfur: Sulfates and sulfidic acids
  - Nitrogen: Proteins, air and ammonium

  In conclusion: we consume the materials that our body needs to survive by eating, drinking and breathing!



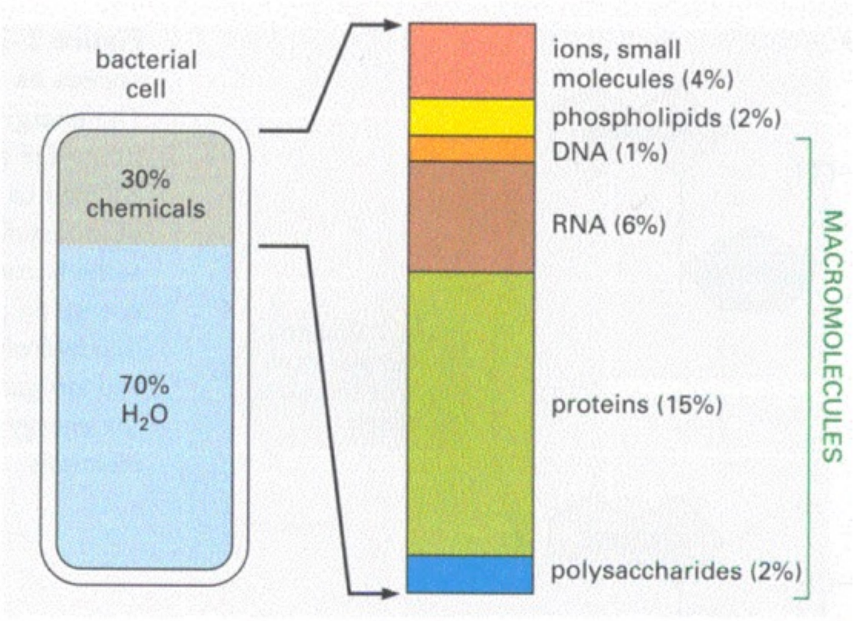






Cell nutrition and metabolism

- The materials that we take up are used to create the materials that we need to survive – macromolecules, phospholipids, ions and small molecules.
  In order for the synthesis of the macro- and micromolecules to take place, energy needs to be generated. This is another way of utilising the elemets that were taken up.
- **Cell metabolism**:
  - Conversion of food into energy (ATP)
  - Conversion of food into building blocks for proteins, lipds, nucleic acids and carbohydrates
  - Elimination of nitrogenous waste



Thermodynamics

- The same rules that you learned in theoretical physics courses also apply on a cellular level:
  - **First law of thermodynamics**

    Energy can be converted, but it cannot be created or destroyed
  - **Second law of thermodynamics**
    The universe gets more messy with every voluntary (spontaneous) process – thus the entropy of the universe constantly increases. Locally order can be created but the universe as a whole only gets «untidier». This untidyness can be experienced as heat – which is the messy form of energy and also the lowest quality.

- Gibbs free energy (ΔG)

  Free energy is the amount of energy that the system can transform into work. $\Delta G = \Delta H - T\Delta S$. T is constant under biological conditions and thus the free energy is a measure for the instability of a system.

  $\Delta G > 0$: Free enthaply (= energy) is needed in order for the reaction to take place – **endergonic reaction**.

  $\Delta G = 0$: Equilibrium and max. stability. There is no reaction

  $\Delta G < 0$: Free enthalpy is released during the reaction, thus the reaction happens spontaneously – **exergonic reaction**

Thermodynamics of (bio-)chemical reactions

- Reactions are driven by two forces: the reduction of bonding energy (since chemical systems strive to have the minimal energy possible) and increase in disorder (entropy).
- All reactions «strive» to reach equilibrium - ΔG = 0, since this is the state of maximal stability and thus minimal energy.
  During a chemical reaction, equilibrium is reached when there is no change in the concentration of the reactants and products:

$$aA + bB \leftrightharpoons pP$$

$$K_{\{eq\}} = \frac{[P]^p}{[A]^a * [B]^b}$$

- Keq is the equilibrium constant and it depicts the ratio of concentrations, at which the equilibrium of the reaction is reached.
- The reaction rate is determined by the change of concentrations over time. When the equilibrium is reached, the reaction rate is equal to zero.
- The Michaelis-Menten equation is the rate equation for a single substrate enzyme-catalysed reaction
- $V = \frac{V_{max} * [S]}{K_M + [S]}$ and $K_M = \frac{k_{-} + k_2}{k_1}$

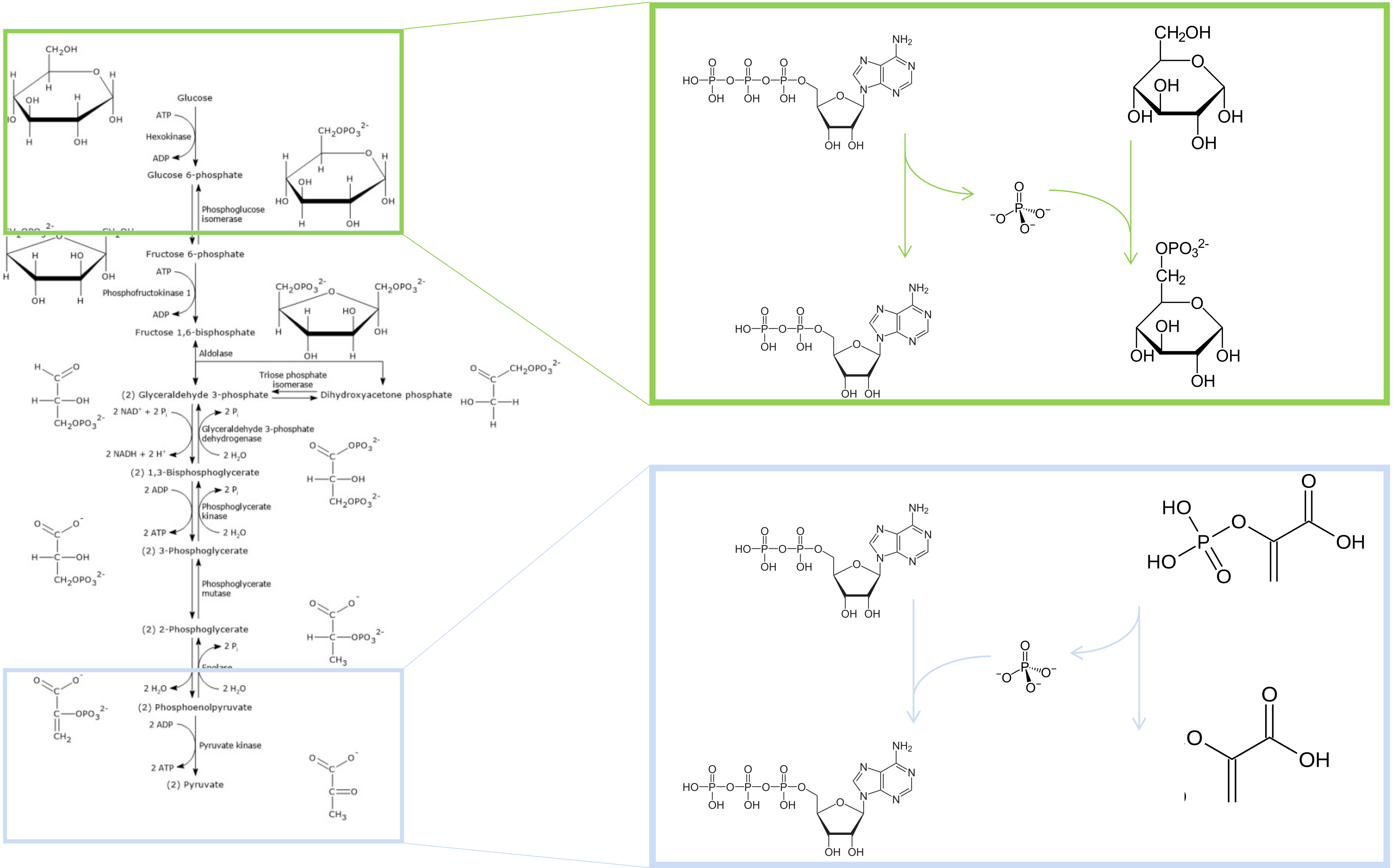
$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \overset{k_2}{\rightarrow} P + E$$

Summary of the Four Scenarios for Enthalpy and Entropy Changes

	ΔH > 0 (endothermic)	ΔH < 0 (exothermic)
ΔS > 0 (increase in entropy)	ΔG < 0 at high temperature ΔG > 0 at low temperature Process is spontaneous at high temperature	ΔG < 0 at any temperature Process is spontaneous at any temperature
ΔS < 0 (decrease in entropy)	ΔG > 0 at any temperature Process is nonspontaneous at any temperature	ΔG < 0 at low temperature ΔG > 0 at high temperature Process is spontaneous at low temperature

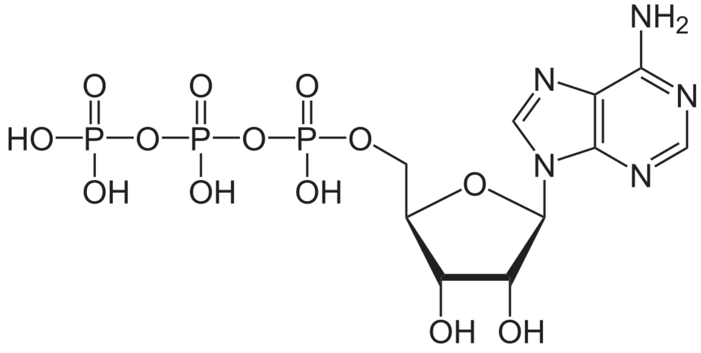
Principles of cell metabolism

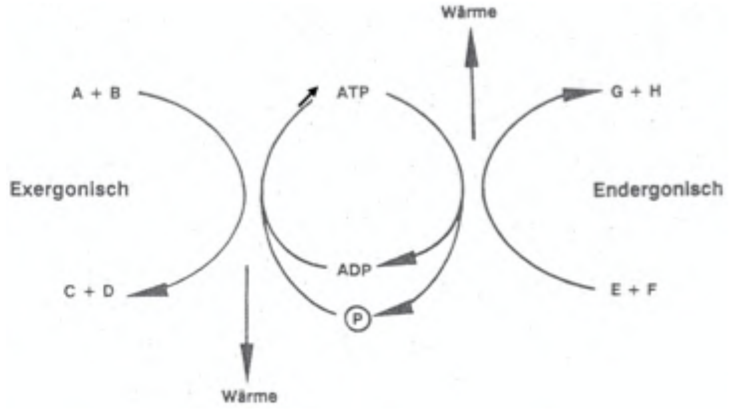
- Metabolism is the umbrella term for thousands of chemical interactions that either generate energy (**Catabolism**) or synthesise cell compounds (**Anabolism**)
  - **Catabolism**: degradation of energy rich molecules to obtain energy and synthesis components – generally **exergonic**
  - **Anabolism**: construction of cell components using energy – **generally endergonic**
- The previously discussed laws of thermodynamics apply on a cellular level and can be explained using metabolism as an example:
  - During **anabolism**, cells build structured matter – and thus locally reduce the entropy – by using energy. The energy is generated from light or chemical components using **catabolism**. During the synthesis of structured matter, cells usually release smaller molecules (H2O during protein synthesis) and heat which in turn increases the entropy.
    Conclusion: Energy enters the system as light and is metabolised with catabolic and anabolic processes. The energy then leaves the system as heat.
    However, it is important to note that the coupling of catabolism and anabolism does NOT happen in one quick reaction, but in many small reactions, that amount to large reactions in a cell.
    The energy that is produced in the beginning (catabolism) is stored in ATP to be used later in anabolic reactions


Glucose
ATP
Hexokinase
ADP
Glucose 6-phosphate
Phosphoglucose isomerase
Fructose 6-phosphate
ATP
Phosphofructokinase 1
ADP
Fructose 1,6-bisphosphate
Aldolase
Triose phosphate isomerase
(2) Glyceraldehyde 3-phosphate
Dihydroxyacetone phosphate
2 NAD+ + 2 Pi
2 Pi
Glyceraldehyde 3-phosphate dehydrogenase
2 NADH + 2 H+
2 H2O
(2) 1,3-Bisphosphoglycerate
2 ADP
2 Pi
Phosphoglycerate kinase
2 ATP
2 H2O
(2) 3-Phosphoglycerate
Phosphoglycerate mutase
(2) 2-Phosphoglycerate
2 Pi
2 H2O
2 H2O
(2) Phosphoenolpyruvate
2 ADP
Pyruvate kinase
2 ATP
(2) Pyruvate

Energy storage in ATP (Adenosine Triphosphate)

- ATP: Adenosine Triphosphate (Base, Sugar, Phosphate) – high energy
  ADP: Adenosine Diphosphate – low energy
- In endergonic reactions, **ATP** is hydrolysed into **ADP + P** by the addition of H_2O. The hydrolysis of ATP frees energy, which can be used for the reaction. During the endergonic reaction, the extra phosphate group, that was split off, is added to the second reactant – the reactant is **phosphorylised**.
- In exergonic reactions, **ADP + P** is condensed into **ATP** by removing H2O. This reaction requires energy, which is generated by dephosphorylation of another molecule.





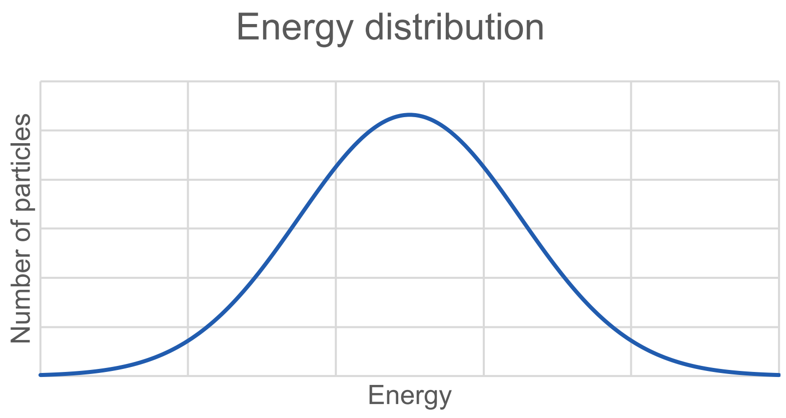
Enzymes and chemical reactions

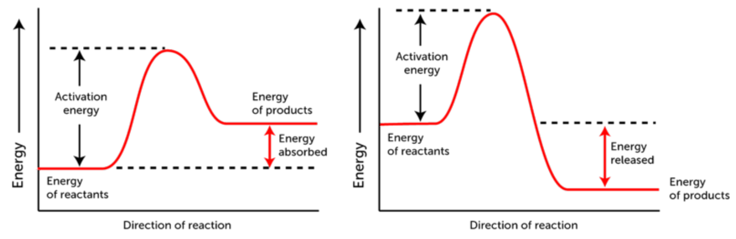
- Activation energy is the minimal amount of energy that is needed in order for a chemical reaction to take place. In a system, there are always some particles that have the required energy. When lowering the activation energy, then a larger part of the particles have the required energy and more will react. This increases the reaction rate – NOT the velocity of the reaction!
- Enzymes are substances that act as catalysts in living organisms. They can either be proteins or proteins and a co-factor (metal ions or complex organic molecules)
- It is important to note that enzymes are not used in the reaction. This is why they do not count towards the formula that we estabilished earlier.

$$aA + bB + Enzyme \leftrightharpoons cC + dD + Enzyme$$

$$K_{\{eq\}} = \frac{[C]^c * [D]^d * [Enzyme]}{[A]^a * [B]^b * [Enzyme]}$$

- An exothermic reaction, by definition, releases energy. Looking at the two graphs on the right, which reaction do you think is exothermic? How can you justify calling a reaction exothermic when you need to add energy in order for the reaction to take place?





Chemical reactions with enzymes

- Enzymes not only catalyse a reaction by changing the fold of the protein they bind to, changing the fold of the protein can also affect its function.
- Enzymes bind to proteins following the lock-key principle: An enzyme fits the substance it is supposed to bind perfectly. Once bound, they change the fold of the proteins and either activate (or deactivate) it.