Introduction

EVROPSKÁ UNIE
Evropské strukturální a investiční fondy
Operační program Výzkum, vývoj a vzdělávání

MINISTERSTVO ŠKOLSTVÍ, MLÁDEŽE A TĚLOVÝCHOVY

What is advanced biochemistry?

Biochemistry has been a part of chemistry curriculum at UCT Prague (previously ICT Prague) as Biochemistry I and Biochemistry II till 2011. That time there was only a 5-year “inženýr” program. Biochemistry I included structure and function of proteins, enzymes, nucleic acids and other components of life. This was followed by Biochemistry II, which was about metabolism.

Since 2011, studies were split into bachelor and master studies. This resulted into change of biochemistry to a basic and advanced biochemistry. The basic biochemistry is the part of curriculum of all students. Advanced biochemistry is the part of the curriculum of students of biochemistry, biotechnology, food sciences and related specializations.

Both courses cover similar topics, but the advanced biochemistry goes into details. **Basic knowledge of biochemistry is needed for advanced biochemistry**.

What is advanced biochemistry?

1. Introduction
2. Non-covalent Interactions in Biological Sciences
3. Oxygen
4. Essential Factors: Vitamins, Cofactors, Coenzymes and Prosthetic Groups
5. Regulation of Enzymatic Activity
6. Signal Transduction – Receptors
7. Biochemistry of Human Organs and Tissues I
8. Biochemistry of Human Organs and Tissues II
9. Metabolism of other Organisms
10. Gene Technologies I
11. Gene Technologies II
12. Clinical Biochemistry
13. History of Biochemistry
14. Testing your Knowledge

What is biochemistry about?

Biochemistry is chemistry of living systems. In last decades this term was evolving.

Molecular biology studies genetic information and its expression (replication, transcription and translation) at the molecular level.

Cell biology studies signaling in the cell and its structural elements (receptors, organels, cytoskeleton, cell cycle etc.).

Biochemistry is nowadays mostly understood as a chemistry of metabolism.

Biotechnology applies results of these disciplines in technology.

Omics approaches study biological systems in high throughput.

All these fields are overlapping.

What is biochemistry about?

The main role of molecular genetics, cell biology, biochemistry, omics and other fields is to find cures to diseases. How can biochemistry (metabolism research) contribute? It seemed for many years that biochemistry is dead. Basic metabolic pathways have been determined decades ago. Since that time it seemed that there is nothing to discover. Metabolic enzymes were believed as poor targets for drugs. If you inhibit a metabolic enzyme you inhibit or kill the cell, sick as well as healthy. However, in last decade or so biochemistry is back in Vogue due to these findings.

This can be illustrated on examples of isocitrate dehydrogenase research, “global” enzymes and rise of synthetic biology – topics that triggered a renaissance of biochemistry.

What is biochemistry about?

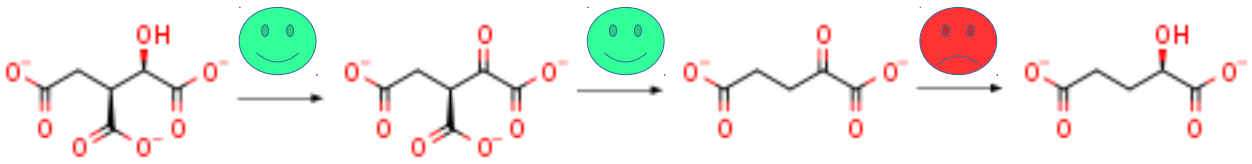
IDH story

Isocitrate dehydrogenase (IDH) catalyses oxidation of isocitrate by NAD^+ followed by decarboxylation, producing 2-oxoglutarate. It is an enzyme of citrate cycle, which implies that it is an “innocent” enzyme in cancer, poor target for drugs. Mutation of an enzyme from the main metabolic pathway was supposed to kill the cell, rather than give it some advantage.

However, it was found that IDH is frequently mutated in cancers. This implies that mutation provides some advantage for cancer cells.

In 2009 it was found that IDH mutant catalyses alternative reaction producing D-2-hydroxyglutarate.

What is biochemistry about?



IDH story
D-2-Hydroxyglutarate accumulate in cancer cells. This causes:

- changes in methylation of DNA

- changes in modification of histons

- hypoxia and D-2-hydroxyglutarate support each other

Cancer cells are more aggressive due to different gene expression and due to tolerance to lack of oxygen.

What is biochemistry about?

IDH story
2009 – discovery of production of D-2-hydroxyglutarate by mutant IDH

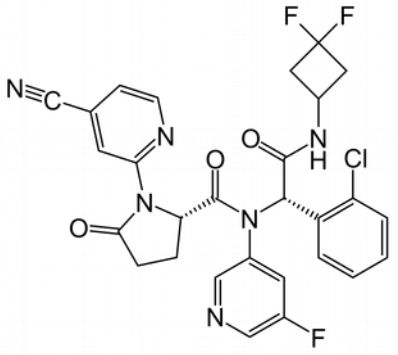
2011 – D-2-hydroxyglutarate alters DNA methylation

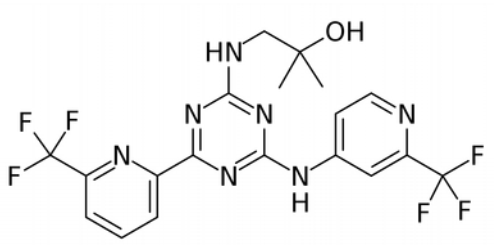
2011 – D-2-hydroxyglutarate alters histon modification

2015 – D-2-hydroxyglutarate levels is elevated by hypoxia

2018 – Ivosidenib – phase III clinical trial for acute myeloid leukemia
and cholangiocarcinoma

2018 – Enasidenib (IDHIFA) – approved for acute myeloid leukemia





What is biochemistry about?

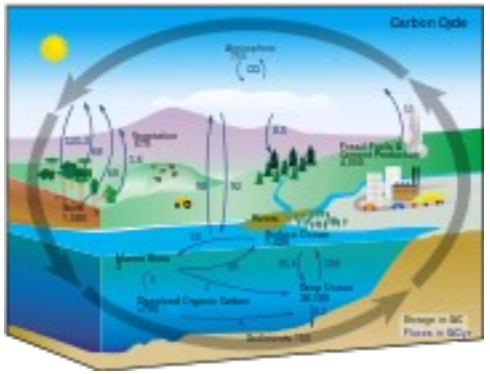
“Global enzymes” story

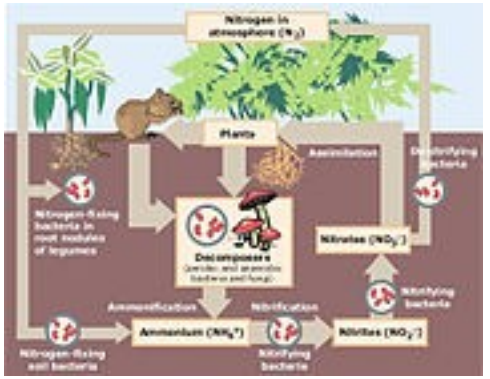
Replacement of fossil fuels by biofuels caused rise of food prices in last decade. Therefore researchers study tools for production of biofuels from cheap and waste materials, such as straw, saw dust, wooden chips and other materials.

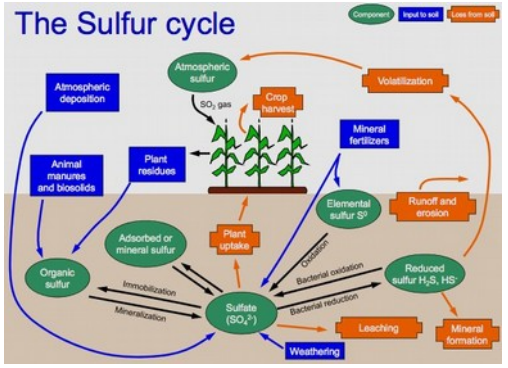
Cheep materials for biofuel production contain saccharides in the form of cellulose. There is a never-ending struggle in nature between plants and cellulolytic microorganisms. Plants have evolved highly durable cell walls containing cellulose, other polysaccharides, lignin and other protective compounds that make enzymatic hydrolysis of cellulose difficult.

On the other hand, cellulolytic microorganisms have developed sophisticated cellulases, carbohydrate-binding modules, other cellulose-degrading enzymes (e.g. oxygenases), cellulosome and other systems.

What is biochemistry about?







“Global enzymes” story

Cycles of elements in nature have become a hot topic due to climate change and other environmental topics. Nitrogen cycle involves nitrogen fixation forming ammonium, nitrification of soil ammonium to nitrites, their nitrifying to nitrates and decomposition (denitrifying) of nitrates to nitrogen. Ammonium, nitrites and nitrates can be assimilated by plants or microogranisms. Ammonium can be produced by microbial biomass degraders. Similar cycles driven by microorganisms exist for sulfur, phosphorus and other elements. These cycles take place in huge quantities in soil, in oceans and in other environments and can be sensitive to changes of conditions.

What is biochemistry about?

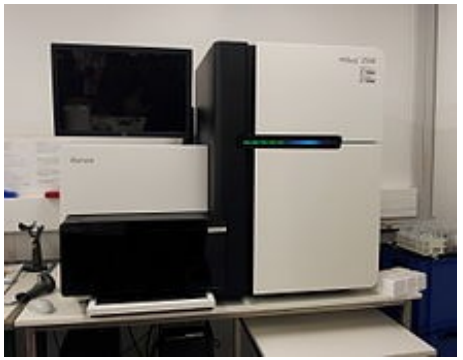
Synthetic biology

The concept of synthetic biology has been known for a long time, but recently it became real owing to solution of problems related to co-expression of multiple enzymes. It is possible to clone whole metabolic pathways from one organism to another. This requires knowledge of metabolism and knowledge of enzyme kinetics.

As a curiosity, we can mention a report (*Nature*, **521**, 281-283, 2015) that two groups of researchers independently cloned the first and the second half of morphine biosynthesis pathway from poppies into yeast *S. cerevisiae*. This has raised concerns that leaking of these yeast strains to public would enable home “brewing” of opiate drugs.

What is biochemistry about?

New tools and techniques



Add on - Genetically Engineer Any Brewing or Baking Yeast to Fluoresce

$80.00

Not Rated

Bacterial CRISPR and Fluorescent Yeast Combo kit

$209.00

Not Rated

Bacterial CRISPR Kit Replacement Perishables

$30.00

Not Rated

Custom CRISPR

$150.00

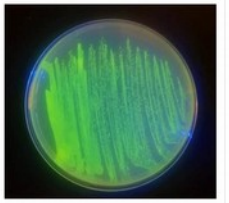
Not Rated

DIY Bacterial CRISPR Refill/Classroom Kit

$75.00

DIY Bacterial Gene Engineering CRISPR Kit

$159.00



Genetic Design Starter Kit - Glowing Jellyfish Bacteria

$29.00

Not Rated

Genetic Engineering Home Lab Kit

$1,699.00

Genetically Engineer Any Brewing or Baking Yeast to Fluoresce

$159.00

Not Rated

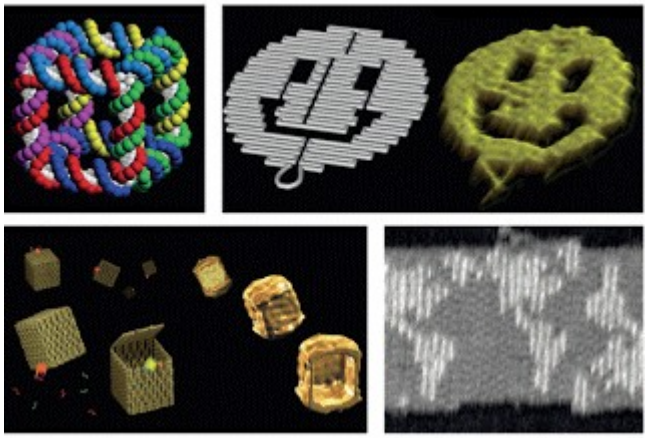
Starter Kit for iGEM Competitors

$100.00

What is biochemistry about?

New tools and techniques

Nanotechnology



http://philipball.blogspot.com/2014/06/programmable-matter-kicks-off.html

What is biochemistry about?

New tools and techniques

Gene silencing and editing

RNA interference (RNAi) – specific degradation of mRNA

Zinc finger nucleases, TALENs, CRISPR/Cas9 –
specific disruption of a gene or its specific modification

Cost-effective sequencing

High throughput sequencing methods

Electron and optical microscopy at high resolution

What is biochemistry about?

Holy Grails of biochemistry

Full understanding of human genome – detailed understanding of all genes, their functions, relationships between genes, population differences etc.

Detailed models of cells and organisms – doing “experiments” on mathematical models

Medicine based on genomics, individual medicine, systems medicine

More drug targets – discovery of new drugs is slow, partially due to lack of new drug targets, old targets have been explored

Protein folding – atomistic simulations of protein folding on a routine basis

Keeping track with bacterial, viral and cancer resistance

Enzymatic production of cost-effective energy sources

Required knowledge

Biochemistry

Building blocks of biomacromolecules:
Amino acid structure, properties (polar/nonpolar/acidic/basic...), peptide bond,
Nucleic acid bases, nucleosides, nucleotides
Basic monosaccharides

Structure of biomacromolecules
Protein structure (primary, secondary, tertiary and quaternary structure)
DNA structure (chemical structure, formation of double helix, orientation of strands)
Basic polysaccharides (e.g. glycogen, starch, cellulose)

Structure of other biomolecules
Phospholipids, membranes
Triacylglycerols

Required knowledge

Biochemistry

Bioenergetics (equilibrium, steady state, homeostasis)

Bioenergetics of synthesis/hydrolysis of biomacromolecules

Metabolism, catabolism, anabolism

ATP (structure, production by membrane and substrate phosphorylation, ATP consumption in biosyntheses, motion, active transport etc.)

Required knowledge

Biochemistry

Digestion of proteins, nucleic acids, polysaccharides and lipids

Electron transport chain

Krebs cycle (TCA, citric acid cycle)

Glycolysis, gluconeogenesis, pentose phosphate pathway

Lipid metabolism (degradation and synthesis pathway)

Amino acid metabolism (transamination, glutamate dehydrogenase, ammonium metabolism)

Localization of these processes in an eukaryotic cell

Required knowledge

Molecular genetics

Gene, genome

Replication, DNA polymerase

Transcription, RNA polymerase

Translation, ribosome, tRNA

Biology

Organization of a cell, organels, compartmentalization

Human organs (digestive tract, blood and immune system, liver,
adipose, kidney, muscles, connective tissues, brain, senses)

Final exam

Test

Written test with 10 questions (10 % each), typically short or few sentence answers, thinking is more important than memorizing

50 % required in order to pass to the oral exam

Oral exam

Discussion on the test results, clarification of your answers, extending questions, questions testing your in-deep knowledge