Terms to know

This list presents important terms and nomenclature, which will be covered by the examination test. Students are supposed to have the basic knowledge of the following points. Consult the materials for individual lectures in the Moodle course.

Lecture 1

- computer-aided drug design (CADD), 'hit' and 'lead', high-throughput screening (HTS), high-throughput virtual screening (HTVS), *in silico*
- molecular mechanics (MM) *vs* quantum mechanics (QM)
- principals of energy calculations in molecular mechanics
- Structure-Based Drug Design (SBDD) *vs* Ligand-Based Drug Design (LBDD)
- X-ray crystallography, homology modelling
- pharmacophore models
- fragment-based drug discovery (FBDD)
- energy minimization, conformation, force field
- molecular dynamics (MD)

Lecture 2

- drug targets at the molecular level
- types of interactions (covalent bond, ionic interaction, ion-dipole, dipole-dipole, hydrophobic interaction, π-π interaction)
- solvation energy
- strength (energy) and relative importance of the above-mentioned interactions for ligand-receptor binding
- protein structure, peptide bond properties
- biogenic amino acids and their division according to side chain properties (polar, lipophilic, charged, uncharged, aliphatic, aromatic, acidic, basic)
- elements of the secondary structure (α-helix, β-folded sheet, turn/loop, coil)
- super-substructure, structural domains
- enzyme, holoenzyme, apo-enzyme, cofactor
- binding site, active site, catalytic site, allosteric site
- catalytic triad

Lecture 3

- databases important for drug design - their content and their usage – Cambridge Structural (Crystallographic) Database (CSD); ZINC; ChEMBL; DrugBank; Brookhaven Protein Databank (PDB)
- basic principles of methods for experimental determination of 3D structure (X-ray crystallography; NMR)
- parameters for quality assessment of 3D protein structures (resolution, R-value, R-free, Ramachandran plot)
- basic principles of homology modelling

Lecture 4

- molecular docking – definition
- search functions
- scoring functions
- terminology – ligand, receptor, pose, binding mode, scoring, ranking
- special docking applications – consensus docking, consensus scoring, ensemble docking, blind docking, protein-protein docking, covalent docking

Lecture 5

- definition of (3D) pharmacophore
- procedures that can be used for building a 3D pharmacophore
- pharmacophore features
- fingerprints, Tanimoto coefficient (index)
- use of pharmacophore models, fingerprints, similarity searching

Lecture 6

- molecular dynamics (MD)
- time scales of molecular dynamics simulation
- boundary conditions of the MD simulation system
- analysis of MD trajectory, RMSD, RMSF
- applications and usage of MD

Knowledge and skills gained in seminars

Seminar 1

- preparation of a small molecule – ligand
    1. Structure check – errors, bonds, chain breaks, alternates
    2. Protonation state and/or tautomer selection
    3. Check of stereochemical aspects, *R*/*S*, *cis*/*trans*
    4. Calculation of partial charges (according to the chosen force field)
    5. Energy minimization according to the force field

Seminar 2

- working with databases
- preparation of the receptor (protein) for docking

Seminar 3

- selection of receptor structure from the PDB database, assessment of its quality
- downloading the receptor and its preparation
- re-docking of the original ligand
- ligand-receptor interaction, interaction diagram
- HTVS, induced-fit docking

Seminar 5

- creation of a pharmacophore model based on the crystallographic structure of the ligand-receptor complex
- pharmacophore-based searching