Computational methods and strategies in structure-based drug design

Structure-based computational methods are currently routinely used in the drug design process, when potential drug targets are known or can be identified. Simulations allow for a better understanding of interactions between small molecules and their targets, and thus allow for efficient design and optimization of drugs, e.g., protein inhibitors.

In this course we will present the principles of simulation methods applicable to drug design and the practical aspects of structure-based drug design strategies. We will focus on such techniques as small molecule docking, molecular dynamics and binding free energy estimation methods.

Recommended reading:

- computational drug design: Sliwoski et al. "Computational Methods in Drug Discovery", Pharmacol. Rev. 66:334–395, 2014.

- reference handbook about modelling and simulation methods: Andrew R. Leach "Molecular Modelling. Principles and Applications (2nd edition)", Pearson Education, 2001.

Day 1 - December 4, 2017

morning (10am-1pm)

- Introduction to drug design

- Physical representations of molecules in computational studies: force fields and interaction field maps

- Identification, mapping and comparison of potential drug binding sites

afternoon (2.30pm-5.30pm)

- Demonstration session: binding site mapping and molecular docking

- Predicting drug binding positions with molecular docking: searching and scoring

Day 2 - December 5, 2017

morning (10am-1pm)

- How to prepare structural data for docking, and discussion of the factors that can influence the results

- Introduction to molecular dynamics simulations

- Applications of molecular dynamics simulations in drug design: prediction of protein-drug binding affinities

afternoon (2.30pm-5.30pm)

- Going beyond affinity prediction: the importance of kinetics in drug design

- Overcoming the imitations of standard automated docking procedures: receptor flexibility, more accurate hydration treatment etc.

- Lead design strategies with examples