



LUNDS  
UNIVERSITET

# Computer Aided Drug Design

2 days intensive hands-on course, 2 ECTS Credits

## OVERVIEW

A number of computational methods are used in order to increase the speed and lower the cost in drug discovery projects. Which methods are available and which ones do you apply in a particular project? This depends on a number of factors, for instance whether you know a ligand structure and/or its target receptor structure. We will discuss both the principles behind the optimization of ligand protein interactions and various computational methods applied in ligand based, de novo and structure based drug discovery projects. The participant will also be introduced to physicochemical property predictions and property filtering of compound databases.

## AIM

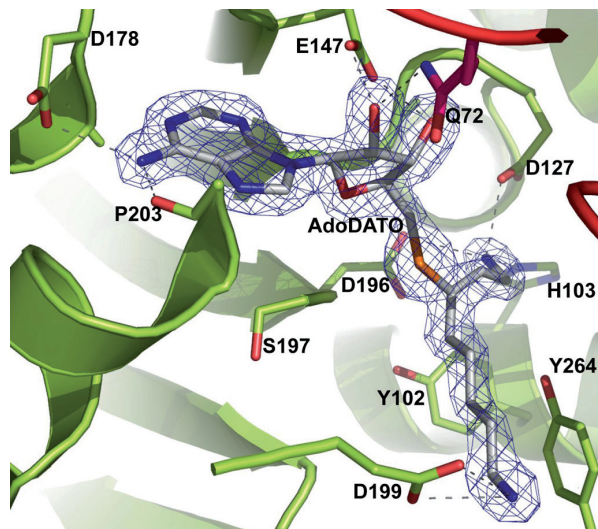
The course aims at providing the participants with basic understanding of computational modelling in the area of drug discovery. After finishing the course the participants will have:

- Basic understanding of ligand-protein interactions.
- Be familiar with a range of ligand and structure based computational methods.
- Performed computational modelling tasks using state of the art software.

The course will also serve as a meeting point and will provide networking opportunities with people from Sweden and Denmark.

## COURSE OUTLINE

- Introduction to basic principles of protein-ligand interactions and a number of concepts in modern drug discovery.
- Ligand based design approaches including traditional QSAR, Pharmacophore modelling and shape based methods.
- Property calculations and property filtering.
- Structure based methods, binding site analysis, docking, scoring functions and virtual screening.
- Success stories, possibilities and difficulties



*Binding of the potent inhibitor AdoDATO to the active site of the malaria protein spermidine synthase.*

*Computer tutorials during the course will include:*

- Application of ligand based and structure based methods as well as property prediction and database filtering. Hands-on training is made on state of the art software.

## COURSE PROGRAM

### Day 1

*Morning:* The principles behind ligand - protein interactions and an introduction to molecular mechanics. Explanation of concepts like lipophilicity, hydrogen bonding, electrostatic and steric interactions.

Introduction to ligand based methodologies. The traditional QSAR methodologies and its wide applicability. The pharmacophore concept, pharmacophore modeling and virtual screening. Molecular shape based methodologies.

*Afternoon:* Prediction of physicochemical properties like solubility, logP, logD, pKa, rigidity, polarity size and shape. Drug like properties, lipinsky rule of five and membrane permeability. Property filtering of compound databases. Hands-on exercises on ligand based modeling and demonstrations.

19.00 Course dinner



## Day 2

*Morning:* Introduction to structure guided drug discovery. Discussion on protein-ligand crystal structures and binding site analysis. Principles of docking, scoring functions and large compound library screenings.

*Afternoon:* More on structure guided drug discovery including possibilities, difficulties and success stories. Hands-on exercises on binding site analysis and dockings, and demonstrations.



Professor Salam Al-Karadaghi

### LECTURERS

Professor Salam Al-Karadaghi is the head of the Department of Molecular Biophysics, Lund University, and is responsible for organizing the course. He is also one of lecturers. Professor Al-Karadaghi has published more than 60 scientific papers in the field of protein structure and function and has contributed to 41 entries in the Protein Data Bank, PDB. Outside the university Al-Karadaghi has been involved in structure-guided design projects with several companies such as Active Biotech, Biovitrum, Leo Pharma, ALK-Abelló.

*Dr. Bo Svenssons* a founder and CSO of SARomics AB offering R&D support to pharmaceutical and biotechnology industries within the areas of structural biology and *in silico* drug discovery. Previously Bo was responsible for the computational chemistry activities at Active Biotech in Lund.

### MOLECULAR BIOPHYSICS AT LUND UNIVERSITY

Molecular Biophysics is one of the strong and expansive research fields at Lund University. The Department's focus is within the areas of three-dimensional structure, function and dynamics of key enzymes and macromolecular assemblies. It uses world-class experimental facilities and its research has been classified as "excellent to outstanding" in the recent international evaluation of research at Lund University, RQ -08.

Learn more about the fascinating world of structural bioinformatics and how it can facilitate your research on <http://www.protein-structures.com/> a site that is managed by professor Al-Karadaghi.

### WHO SHOULD ATTEND?

Scientists from the pharmaceutical and biotech industries, and from academia. Particularly, persons responsible for R & D, project leaders, medicinal chemists or those who want to get introduced into modern drug discovery by means of computational modeling will benefit from the course.

There are no formal requirements on academic qualifications, however in order to be able to absorb as much as possible from the course content it is advisable that the participants have a background in chemistry/biochemistry/molecular biology or are involved in R & D work within these areas. Participants with other backgrounds can expect to get a broad overview of principles and computational modeling tools within drug discovery.

### SCHEDULE AND FEE

May 19-20, 2011

The course will take place at the Chemistry Centre, Lund University. Course fee is 11.000 SEK, VAT exclusive. The fee comprises diploma, course literature, coffee, lunch and course dinner.

Each day will include morning (9-12) and afternoon (13.15-17) sessions. Lunch will be at 12, coffee will be served at 10 and 15. Morning sessions will be mostly lectures, while afternoon sessions will be focused on computer tutorials.

*Registration deadline:* March 30, 2011. The registration is binding. At cancellation 5 weeks before the course start the participant will be billed 3000 SEK. At cancellation less than 3 weeks before the course start the participant will be billed full amount. Substitution of participants is allowed at any time and without charges, but it is advisable that such should take place at the start of the course.



*For information about the course and application* please contact Mirka Fahlander at Lund University Commissioned Education (Ph. +46-46-222 0777 or [mirka.fahlander@education.lu.se](mailto:mirka.fahlander@education.lu.se)).

*For information about the course and research* in molecular biophysics please contact professor Salam Al-Karadaghi at Department of Molecular Biophysics, Lund University (Ph. +46-46-222 4512 or [salam.al-karadaghi@mbfys.lu.se](mailto:salam.al-karadaghi@mbfys.lu.se)).



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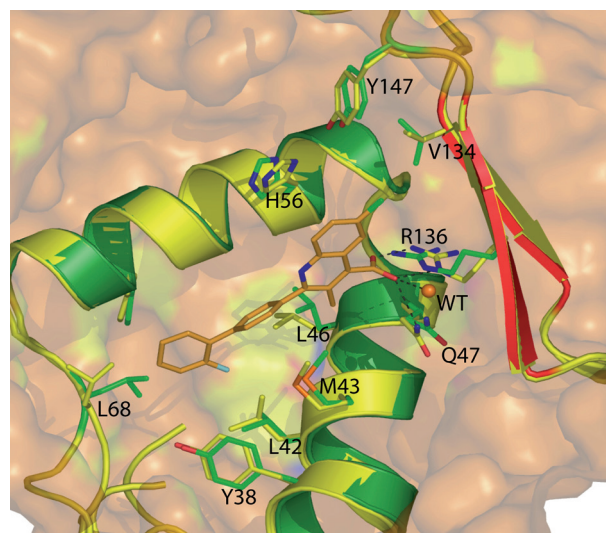
### COURSE ORGANISER

Professor Al-Karadaghi has been involved in several projects of biomedical interest. His academic projects include studies of the molecular mechanisms of inhibition of enzymes from tropical parasites, *Leishmania donovani* and *Plasmodium falciparum*, the causative agents of leishmaniasis and malaria. In addition, in collaboration with the Lund-based company Active Biotech, Professor Al-Karadaghi has been involved in a structure-guided design project aimed at developing new inhibitors against the human enzyme dihydroorotate dehydrogenase, a drug target in the treatment of rheumatoid arthritis, psoriasis, autoimmune diseases, and cancer. Through his activities in SARomics Biostructures AB, a company in which he is one of the co-founder, Professor Al-Karadaghi has been involved in structure-guided design projects with Biovitrum AB, Active Biotech AB, Leo Pharma A/S, ALK-Abelló A/S and some other companies.

Professor Al-Karadaghi has extensive teaching experience. He is responsible for and teaches at the course Principles in Molecular Protein Science at Lund University. The course is focused on structural bioinformatics, protein modelling and structural aspects of drug design.

### MOLECULAR BIOPHYSICS AND THE CENTRE FOR MOLECULAR PROTEIN SCIENCE AT LUND UNIVERSITY: OUTSTANDING RESEARCH AND WORLD-CLASS FACILITIES

The Department of Molecular Biophysics together with two other departments, Biochemistry and Biophysical Chemistry, has in 2005 established the Centre for Molecular Protein Science (CMPS). CMPS brings together protein scientists involved in fundamental research on proteins, with a strong focus on molecular structure, function and dynamics.



*Conformational changes in response to inhibitor binding in the enzyme dihydroorotate dehydrogenase.*

Modern structural biology relies on advanced instrumentation and CMPS is uniquely equipped in this regard. The conditions for X-ray crystallography, the main technique for protein structure determination, are ideal, with convenient access to MAX-lab, the Swedish National Laboratory for Synchrotron Radiation Research. MAX-lab is equipped with several beamlines dedicated to structural studies of proteins. A modern crystallisation laboratory equipped with nano-drop robotics for screening and optimisation of protein crystallisation conditions is also placed at MAX-lab. CMPS scientist also operate three nuclear magnetic resonance (NMR) laboratories with eight state-of-the-art NMR-instruments. These large-scale facilities put CMPS scientists at the very forefront of research in structural biology.