Programme: Computational toxicology, November 19-23, 2018
Room 221, building 75, Retzius väg 13 a-b (Monday, Tuesday), Hall Rockefeller, Nobels väg 11 (Wednesday afternoon) and Room Gunnar Höglund, building BZ, Berzelius väg 3 (Wednesday morning, Thursday, Friday), Karolinska Institutet, Solna
Course leaders: Charlotte Nilsson and Annika Hanberg

Monday Nov 19	**Tuesday Nov 20**	**Wednesday Nov 21**	**Thursday Nov 22**	**Friday Nov 23**
9.00-9.30 Welcome and introduction to the course (CN/AH)	9.00-9.45 Non-linear machine learning (UN)	9.00-9.45 In silico methods in risk assessment of chemicals (SB)	9.00-9.45 Use of computational methods for exposure and kinetics modelling (DM)	9.00-9.45 Presentation and discussion of group work
9.30-10.30 Introduction of participants	9.45-10.15 Coffee break	9.45-10.15 Coffee break	9.45-10.15 Coffee break	9.45-10.15 Coffee break
10.30-11.00 Coffee break	10.15-11.00 Ensemble models. Applicability domain (UN)	10.15-11.00 Read-across, QSAR (SB)	10.15-11.00 Use of computational methods for exposure and kinetics modelling (DM)	10.15-12.30 Presentation and discussion of group work
11.00-11.30 Using In silico methods in risk assessment (BG) 11.30-12.00 Introduction to in silico methods in safety assessment in drug discovery and development (DM)	11.15-12.00 Exercise using Knime	11.15-12.00 Molecular modelling (DM)	11.15-12.00 Group work (exercise)	12.30-13.00 Course ending
12.00-13.00 Lunch	12.00-13.00 Lunch	12.00-13.00 Lunch	12.00-13.00 Lunch	Take home exam handed in at 17.00
13.00-13.45 Machine learning in drug discovery/toxicology (UN)	13.00-13.45 Exercise using Knime	13.00-14.00 Presentations on applications (invited lecturers: PA, DM, UN, SB, SK, PM)	13.00-13.45 Group work (exercise)	
13.45-14.15 Coffee break	13.45-14.15 Coffee break	14.00-14.30 Coffee break	13.45-14.15 Coffee break	
14.15-14.45 Introduction to group work (exercise) (UN)	14.15-15.00 Group work (exercise)	14.30-16.00 Presentations on applications (invited lecturers: PA, DM, UN, SB, SK, PM)	14.15-17.00 Group work (exercise) Hand in of results, prepare presentations Friday	
14.45-15.25 Introduction to Knime (DM)	15.00-15.15 Break			
15.25 – 15.40 Break	15.15-17.00 Group work (exercise)			
15.40-17.00 Exercise using Knime				

Teachers:
CN – Charlotte Nilsson, Swetox, KI
AH – Annika Hanberg, IMM, KI
DM – Daniel Mucs, Swetox, KI
UN – Ulf Norinder, Swetox, KI
SB – Scott Boyer, Swetox, KI

Invited lecturer:
BG – Björn Glinghammar, Swetox, KI
PA – Patrik Andersson, Umeå Univ
SK – Signe Klinting, Uppsala Univ
PM – Pär Matsson, Uppsala Univ

Course information

Purpose of the course:
The purpose of the course is to build knowledge and understanding on how computational methods and tools can be used for modelling and/or prediction in toxicology and risk assessment of chemical substances.

Learning outcomes:
After the course, the students should:
- be able to describe what computational methods and tools are available and their proper areas of use,
- have some basic practical skills in using selected software,
- be able to describe how computational methods are applied within some relevant regulations, and
- be able to reflect on the strengths and limitations of using computational toxicology in research and regulatory risk assessment.

Content of the course:
Computational, or in silico, toxicology, is a discipline that is focused on developing and using computer-based models to better understand and predict adverse effects caused by substances such as e.g. pharmaceuticals, chemicals and environmental contaminants. During the course, students will learn about concepts such as read-across, quantitative structure-activity relationships, quantitative structure-property relationships, machine learning, and molecular modeling. How to use computational methods for exposure and kinetics modelling will also be covered, as will regulatory guidelines relevant for this discipline. The utility of computational toxicology in various settings (such as in the REACH regulation, and in drug discovery and development) will be discussed. The students will get familiar with selected (mostly freely available) software that are used in computational toxicology.

Content of individual teaching and learning activities

Machine learning in drug discovery/toxicology (UN)
- Introduction to machine learning in drug discovery/toxicology
- Overview of methods and applications

Non-linear machine learning (UN)
- Concepts and principles of non-linear machine learning
- Different methods available (KNN, SVM, RF, PLS, NN)
- Pros and cons of different methods
- Method limitations

Ensemble models. Applicability domain (UN)
- Concepts and principles of ensemble methods
- Why ensemble methods?
- Concepts and principles of applicability domain estimation
- Pros and cons of different methods
- Method limitations

In silico methods in risk assessment of chemicals (SB)
- Concepts and principles of risk assessments
- Different methods available
- Applicability and pros and cons of different methods
- What is uncertainty in risk assessment and why is it important
- Methods to describe and quantify uncertainty

Read-across, QSAR
- Concepts and principles of read-across
- Different methods available
- Methods to describe and quantify uncertainty

Use of computational methods for exposure and kinetics modelling (DM)

- Concepts and principles of exposure and kinetics modelling
- Basic PK/TK and more complex PBPK/PBTK modelling
- Combination with other methods (for parametrization or information augmentation)

Molecular modelling (DM)

- Concepts and principles of molecular modelling approaches
- Different methods available (Docking, Pharmacophores, Dynamics, QM, Homology modelling)
- Combination with other methods

Exercise using Knime

- Practice on how to use different methods and nodes in KNIME
- How to build a KNIME workflow
- How to test and evaluate model performance in KNIME

Group work

- In the group work the participants will analyse an AMES dataset
- Predict the outcome of an unknown test set
- Estimate the expected performance the test set prediction
- Oral presentation of group work

Take home exam

- Short answer questions on factual knowledge of important principles
- Essay question/reflection on in silico methods and their utility in toxicology and risk assessment