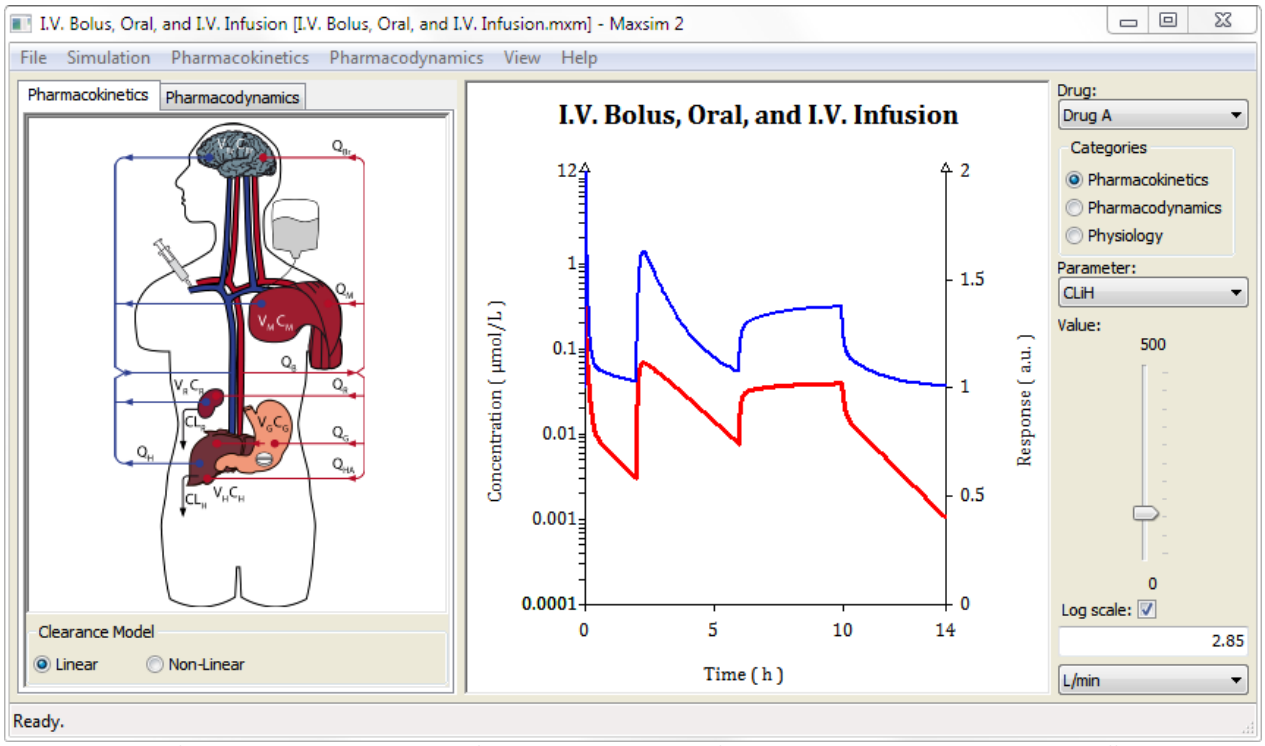
AUGUST 30, 2015

Maxsim2 – Interactive Pharmacokinetic and Pharmacodynamic Simulation

Maxsim2 is an easy to use, intuitive, and interactive application for pharmacokinetic and pharmacodynamic simulation. A gallery of common PK and PD models is provided by which one interacts using sliders, check boxes, and number fields, which in real time is mirrored in changes of concentration-time or response-time simulation profiles. This interactivity and direct visual feedback of what-if scenarios give a very good understanding of both the qualitative and quantitative impact of different parameters such as volumes of distribution, clearance, partition coefficients, potency, and dosage.



A screenshot of the Maxsim2 graphical user interface showing a simulation of plasma drug concentration (red) and drug effect (blue) in a human physiologically based pharmacokinetic model after three consecutive dose administrations: intravenous bolus, oral, and intravenous infusion, respectively. The slider, in this example, controls hepatic clearance, i.e., how fast the liver is able to remove the drug from the blood. Changes in this parameter are reflected in real time in the corresponding changes of the curves in the time-concentration/effect diagram.

Pharmacokinetics

Maxsim2 provides standard compartment models as well as physiologically based pharmacokinetic (PBPK) models. Compartment models ranges from simple one compartment models with linear or nonlinear elimination to highly nonlinear target mediated drug disposition models whose qualitative behavior dramatically changes with dosage. This model type finds its application for example in studying biological compounds, where both target-receptor saturation and target-receptor complex elimination play important roles. In the PBPK models the pharmacokinetic processes are defined in terms of physiologically, anatomically, and biochemically interpretable parameters and mechanisms. These models are used in medical applications to describe the potency or efficacy of a substance and how it is transported and distributed via the blood to different organs in the body as a function of time. Each organ is represented by one or several compartments, which are interconnected by blood flows. These models are excellent tools for real-time presentation of the interplay between physiology, pharmacology, and pharmacokinetic processes.

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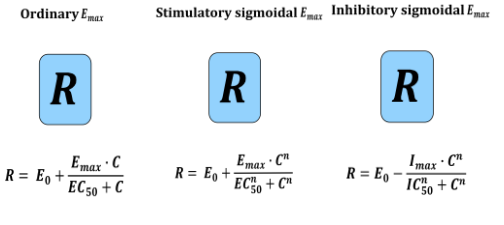
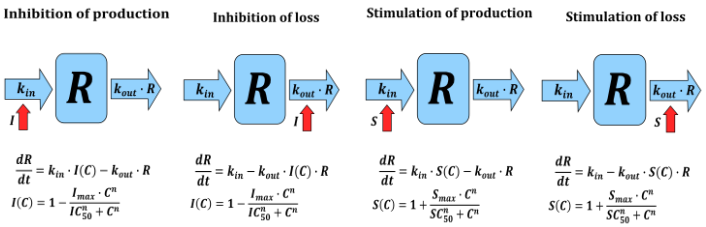
Pharmacodynamics

The pharmacodynamic models available in *Maxsim2* are both instantaneous concentration-response models and indirect concentration-response models also known as turnover models. The indirect models include both inhibition and stimulation of build-up and loss, respectively. The instantaneous models feature both excitatory and inhibitory sigmoidal *Emax* models.



Instantaneous response models.



Indirect response models.

Dosage

The user interface of *Maxsim2* makes it easy to specify different dosage schemes such as single dose, repeated dose, or varying amounts of dose but also specifying different dosage regimens such as oral, intravenous bolus, intravenous infusion, or combinations. Using state-of-the-art graphical user interface controls it is easy to set up simulation scenarios such as repeated oral dosage of a specific compound to study the dynamic effect of a missed dose as well as a "double dose" compensation – under what conditions does this lead to toxic effects? Or, what is the difference in temporal profiles of the plasma concentration of the drug given an oral dose, intravenous bolus dose, or intravenous infusion for a limited period of time.

List of Features

- Pharmacokinetic and pharmacological processes defined in terms of compartment models
  - One- and two-compartment models and target-mediated drug disposition models
  - Physiologically based pharmacokinetic models (human, rat, cat, dog, horse)
- Pharmacodynamics defined in terms of instantaneous response models and indirect response models
  - Ordinary *Emax*, stimulatory sigmoidal *Emax*, and inhibitory sigmoidal *Emax* response models
  - Inhibition/stimulation of build-up and inhibition/stimulation of loss of effect
- Flexible interface to specify dosage
  - Oral, intravenous bolus, intravenous infusion
  - Single or multiple doses of same or different kind
  - Specification of amount or rate and time of administration
- Highly interactive graphical user interface
  - Drop-down menus and radio buttons for quick selection of parameters
  - Slider and number field for interactive parametric changes of simulation results
  - User configurable concentration-time/response-time diagram
  - Linear or logarithmic plotting scales
  - User selection of curves for drug concentration *vs* time in different compartments

Maxsim2 is an excellent tool for dynamic interactive presentation of the interplay between physiology, pharmacology, and pharmacokinetic processes. Its ease of use yet wide scope makes it is an ideal application for both educational and professional users where thorough understanding and communication of pharmacodynamic and pharmacokinetic phenomena are important. *Maxsim2* has been developed in close collaboration with Dr Johan Gabrielsson, a world leading authority in the field of pharmacokinetic and pharmacodynamic data analysis.

Trial version: 30-days trial version, www.maxsim2.com.
System Requirements: Windows XP/Vista/7/8/10 and Mac OSX

About FCC

The purpose of FCC is to promote and undertake scientific research, development, and education in the field of applied mathematics, in close co-operation with universities and other scientific and industrial agencies, and promote the use of mathematical models, methods, and results in industrial activities.

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