An Analytic Approach to ARGESIM Comparison C15 'Renal Clearance Identification' using Maxima/LISP

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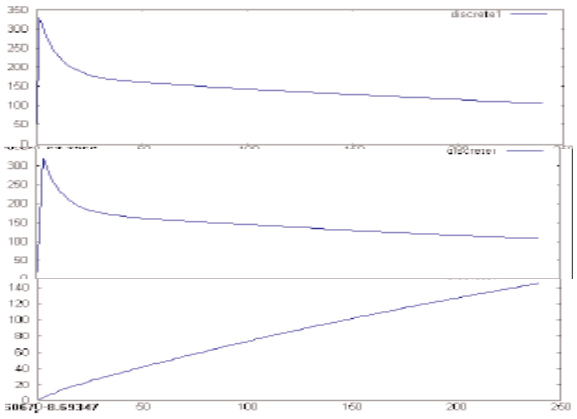
Simulator. *Maxima* is an open source symbolic mathematics package (MAXIMA.SOURCEFORGE.NET). Maxima is an open version of Macsyma, which originally was developed at MIT from 1967 on. Macsyma and Maxima are written in LISP, a functional programming language, and therefore allow executing LISP-like scripts. Plots can be performed with the help of *GNUPLOT*.

Model. The model is defined as system of differential equations in Maxima / Macsyma notation, in textual form (similar to Mathematica). Maxima can solve this system analytically using the Maxima command `desolve`. Because of the discontinuity of the input function *f(t)* (square pulse), the differential equation system has to be solved two times.

A - Task: Simulation with bolus input. The ODEs are solved analytically twice. First they are solved with initial conditions $x_1(0)=0$ and $x_2(0)=0$ and $f(t) = D/\tau$, which yields $c(t)$ for $0 \le t \le \tau$. Then the system is solved with initial conditions at $x_1(\tau)$ and $x_2(\tau)$ taken from the first solution, which yields $c(t)$ for $\tau \le t \le 240$. The two resulting functions are concatenated piecewise in the respective ranges, giving the solutions for three different bolus injections (Figure 1 - 3), and difference of concentrations (Figure 4).
The desired state values are: $\tau = 0.5$, $x_1(\tau+1) = 2342.55$; $\tau = 3$, $x_1(\tau+1) = 2208.83$; $\tau = 240$, $x_1(\tau) = 1060.40$.



Figures 1-3: Simulated concentrations for $\tau = 0.5$, $\tau = 3$ and $\tau = 240$ min.

k_{01}	k_{12}	k_{21}	V_1	max(c)	clear	res.
0.00416	0.0591	0.0499	7.298	342.5	30.4	261

Table 1: Identified parameters and algorithm results.

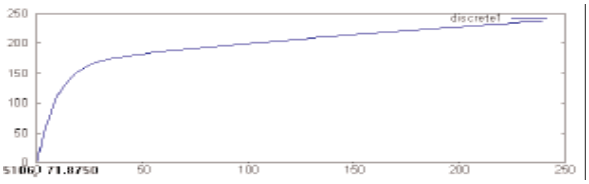


Figure 4: Difference concentration of injection - concentration in the compartment.

B - Task: Identification of model parameters. The parameters k_{01}, k_{12}, k_{21}, and V_1 are estimated using the Levenberg-Marquardt algorithm, a gradient descent method using least squares and adaptation. Maxima does not offer functions for numerical optimization, so this algorithm had to be implemented in LISP.

Programming an identification algorithm in LISP is a non-trivial task. Maxima as symbolic tool is able to calculate analytical solutions parameterised with k_{01}, k_{12}, k_{21}, and V_1 , giving a formula input to the identification algorithm (results in Table 2 and Figure 5).

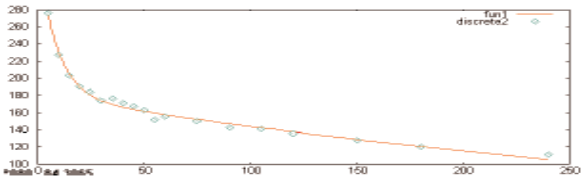


Figure 5: Comparison of simulation and measurements.

C - Task: Error estimation. A loop programmed in LISP performs the identification of the perturbed data. As LISP is interpretative and very slow, only 100 samples have been drawn (results in Table 2).

	k_{01}	k_{12}	k_{21}	V_1
mean	0.004112	0.05922	0.04956	7.331
std. dev.	0.0001620	0.001958	0.001799	0.1170

Table 2: Mean and standard deviation for parameters, 100 samples.

Classification: Analytical simulation approach
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