Zuse Institute Berlin (ZIB)
Freie Universität Berlin
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11. Homework
Numerics for Bioinformaticians
WS 2016/17

Deadline: January 18, 10:00 (**before** the lecture)

The homework should be worked out in groups of two or three students. Each solution sheet must contain the names and student numbers ('Matrikulationnummer') of all group members and the exercise group (Wednesday/Friday). Solutions to exercise 1, 2 & 3.d must be handed in in paper form, either hand written or printed out if generated electronically. Please staple all sheets. Programming tasks must be submitted to max.kleist2@fu-berlin.de or BioInfNumerik@hotmail.com by email. Before sending it, please 'zip' it.

Exercise 1 (Explicit Integration, 2 points)
Compute the explicit/analytical solution of

$$\frac{\mathrm{d}}{\mathrm{d}t}x_1(t) = -x_1(t)\cdot\delta_1 - x_1(t)\cdot k_{12} + \lambda \tag{1}$$

$$\frac{\mathrm{d}}{\mathrm{d}t}x_2(t) = x_1(t)\cdot k_{12} - x_2(t)\cdot\delta_2 \tag{2}$$

with $x_1(t_0) = C_1$ and $x_2(t_0) = C_2$ and $t_0 = 0$.
Hint 0: First solve eq. (1), then plug it into eq. (2).

Exercise 2 (Implementation: Least-squares ↔ maximum likelihood, 6 Points)
Consider the structural model $\mathcal{M}$:

$$x(t_i) = D\left(\frac{k_a}{k_a - k_e}\right)\left(e^{-k_e\cdot t_i} - e^{-k_a\cdot t_i}\right)$$

with the dose $D = 200$ [mg], assuming an additive error

$$y_i = x_{i|k_e,k_a} + \eta_i$$

where $\eta_i \sim \mathcal{N}(0, \sigma_i^2)$.
With $\sigma^2 = \{4, 4, 16, 4, 1, 4\}$. The measurements are $y = \{48.52, 70.61, 82.57, 72.87, 35.09, 7.37\}$ for $t = \{1, 2, 5, 7, 12, 24\}$ [h] post dosing.
1) Make a contour (or surface-) plot of the negative log-likelihood of the data $-\ell_y$ for parameters $k_a \in (0.1, 0.4)$ and $k_e \in (0.15, 0.35)$. Use a 30 ×30 grid.
2) Make a contour (or surface-) plot of the sum of (ordinary) least-squares
3) Weigh the least-squares with their respective σ^2 and make a contour (or surface-) plot of the sum of weighted least-squares.
Hint: This should look like the graphic below

Exercise 3 (ODE Packages, Points 2)
Consider the Slögl model.

$$R_1 : 2x_1 \xrightarrow{k_1} 3x_1, \qquad R_2 : 3x_1 \xrightarrow{k_2} 2x_1 + \emptyset, \tag{3}$$

$$R_3 : \emptyset \xrightarrow{k_3} x_1, \qquad R_4 : x_1 \xrightarrow{k_4} \emptyset. \tag{4}$$

with parameter values are 1.5, 0.00015, 20.0 and 3.5 for $k_1, \ldots, k_4$ respectively. The initial value for x_1 is $x_1(0) = 400$.

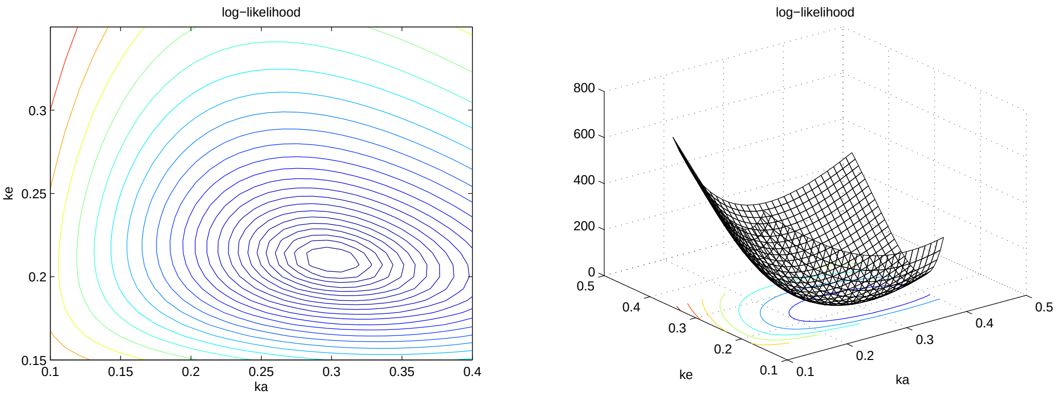

Figure 1: Exemplary contour and surface plots for the exercise.

- Deduce the ODE for the change in population of x_1.
- Use an existing ODE solver package (in your preferred programming language). Choose an explicit and implicit method.
- For both methods compute the solutions to $t_{final} = 5$.
- Print $x_1(5)$ for both methods.