On three equivalent methods for parameter estimation problem based on spatio-temporal FRAP data

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Seminář numerické analýzy a zimní škola

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Outline

1. 1D diffusion-reaction equation
2. Single parameter estimation problem
3. Implementation
4. Regularization
5. Numerical results

Outline

1D problem formulation

One-dimensional form of diffusion-reaction equation:

$$\frac{\partial y}{\partial \tau} - p\,\frac{\partial^2 y}{\partial x^2} = 0. \qquad (1)$$

The initial condition is

$$y(x, \tau_0) = f(x), \quad x \in [0, 1]. \qquad (2)$$

The time varying boundary conditions are either of the Dirichlet type

$$y(0, \tau) = g_0(\tau), \quad y(1, \tau) = g_1(\tau), \quad \tau \geq \tau_0, \qquad (3)$$

or of the Neumann type

$$-p\,\frac{\partial y}{\partial x}(0, \tau) = h_0(\tau), \quad p\,\frac{\partial y}{\partial x}(1, \tau) = h_1(\tau), \quad \tau \geq \tau_0. \qquad (4)$$

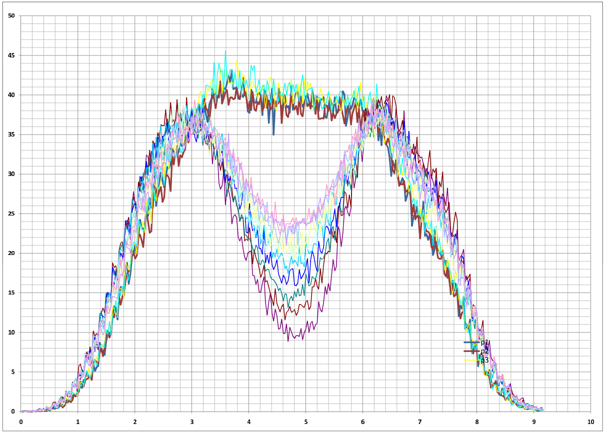
Based on FRAP experiments, we have a 2D dataset in form of a table with $(N+1)$ rows corresponding to the number of spatial points where the values are measured, and $(m+M+1)$ columns with m pre-bleach and $M+1$ post-bleach experimental values forming 1D profiles

$$y_{exp}(x_i, \tau_j), \quad i = 0 \dots N, \quad j = -m \dots M.$$

In fact the process is determined by

- m columns of pre-bleach data containing the information about the steady state and optical distortion
- $M+1$ columns of post-bleach data containing the information about the transport of unbleached particles (due to the diffusion) through the boundary

FRAP data: spatio-temporal image



Fluorescence intensity (in arbitrary units) vs. Distance [μm].
Experimental data from FRAP experiment with red algae *Porphyridium cruentum* describing the phycobilisomes mobility on thylakoid membrane.

Outline

We construct an objective function Y representing the disparity between the experimental and simulated time-varying concentration profiles, and then within a suitable method we look for such a value p minimizing Y.

The usual form of an objective function is the sum of squared differences between the experimentally measured and numerically simulated time-varying concentration profiles:

$$Y(p) = \sum_{j=0}^{M} \sum_{i=0}^{N} \left[y_{exp}(x_i, \tau_j) - y_{sim}(x_i, \tau_j, p) \right]^2 , \qquad (5)$$

where $y_{sim}(x_i, \tau_j, p)$ are the simulated values resulting from the solution of problem (1)–(4).

We have

$$x_0 = 0, \quad x_N = 1,$$

τ_0 corresponds to the first post-bleach measurement, and

- $y_{exp}(x_i, \tau_0)$, $i = 0 \dots N$, represents the IC,
- $y_{exp}(0, \tau_j)$, $j = 0 \dots M$, represents the left Dirichlet BC,
- $y_{exp}(1, \tau_j)$, $j = 0 \dots M$, represents the right Dirichlet BC,
- the Neumann BC for each j^{th} time instant is determined using the Fick's first law.

Simulated data $y_{sim}(x_i, \tau_j, p)$ (the solution of (1)–(4)) were found numerically using the Crank-Nicholson scheme for uniformly distributed nodes with the space steplength Δh and the variable time steplength $\Delta\tau$:

$$-\frac{\beta}{2}y_{i-1,j} + (1+\beta)y_{i,j} - \frac{\beta}{2}y_{i+1,j} = \frac{\beta}{2}y_{i-1,j-1} + (1-\beta)y_{i,j-1} + \frac{\beta}{2}y_{i+1,j-1}.$$

Here $\beta = \frac{\Delta\tau}{\Delta h^2}\, p$ and $y_{i,j} \equiv y_{sim}(x_i, \tau_j, p)$ are the computed values in nodes that enter the function Y.

We allow the time dependence of fluorescent particles diffusivity, hence for the minimization problem

$$Y(p) = \sum_{j=1}^{M} Y_j(p) = \sum_{j=1}^{M} \sum_{i=0}^{N} \left[y_{exp}(x_i, \tau_j) - y_{sim}(x_i, \tau_j, p)\right]^2 \to \min_{p>0} \quad (6)$$

we further consider two cases:

1. Taking both sums for i and j in (6) together. In this case, the scalar p is a result of minimization problem for Y:

$$p^* = \arg\min_{p>0} Y(p)$$

2. Considering each j^{th} time instant separately. In this case, the M solutions $p_1 \dots p_M$ correspond to each minimization problem for fixed j in sum (6) and we can observe a 'dynamics' of diffusion coefficient p_j evolution:

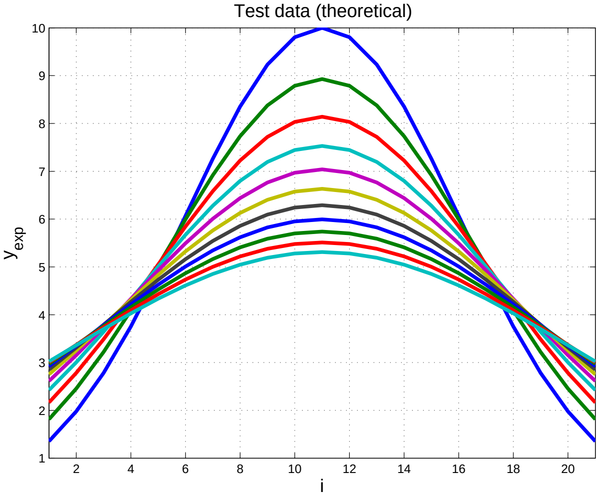
$$p_j^* = \arg\min_{p>0} Y_j(p), \quad j = 1 \dots M$$

Problem (6) was solved using the methods from the **UFO system**

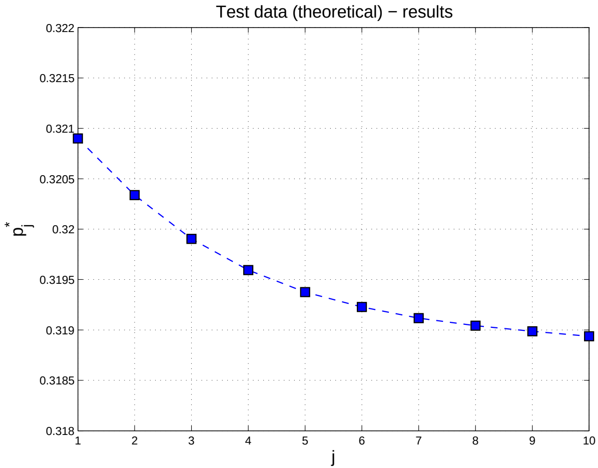
http://www.cs.cas.cz/luksan/ufo.html

Outline

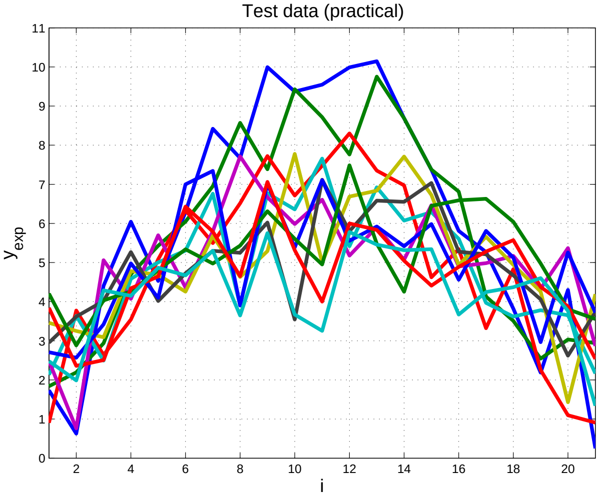
Test data (theoretical): noise = NO



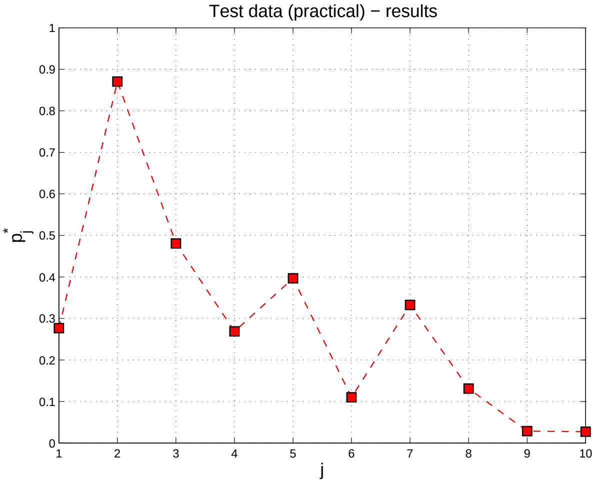
Numerical results: noise = NO



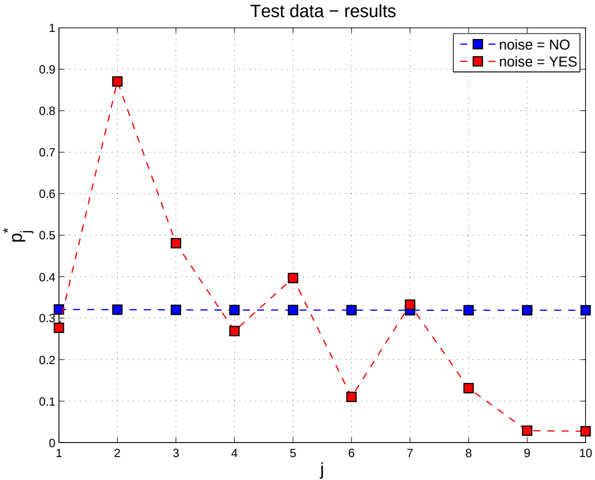
Test data (practical): noise = YES



Numerical results: noise = YES



Numerical results: with and without noise



Outline

Ill-posed problem: Necessity of regularization

Our problem is ill-posed in the sense that the solution, i.e. the diffusion coefficients $p_1 \ldots p_M$ do not depend continuously on the initial experimental data. This led us to the necessity of using some stabilizing procedure, formulation of regularized cost functions:

$$Y_j(p_j, p_{reg}, \alpha) = \sum_{i=0}^{N} \left[y_{exp}(x_i, \tau_j) - y_{sim}(x_i, \tau_j, p_j) \right]^2 + \alpha \left(p_j - p_{reg} \right)^2 \quad (7)$$

for $j = 1 \ldots M$, where $\alpha \geq 0$ is a regularization parameter, and p_{reg} is an expected value that is dynamically re-calculated with growing j ($p_{reg} := \o p_j^*(\alpha)$). Thus it is performed some kind of smoothing between consecutive values of p_j.

Tikhonov regularization

Values p_j^* and $p_j^*(\alpha)$ are approximate solutions of minimization problems

$$p_j^* = \arg \min_{p_j > 0, p_{reg}} Y_j(p_j, p_{reg}, 0), \quad p_j^*(\alpha) = \arg \min_{p_j > 0, p_{reg}} Y_j(p_j, p_{reg}, \alpha)$$

Now:

- It holds
$$\lim_{\alpha \to 0} p_j^*(\alpha) = p_j^*$$
- What we have for $\alpha \to \infty$:
  - :-) the variance of solutions $p_j^*(\alpha)$ is diminishing, i.e. $p_j^*(\alpha) \equiv p_{reg} \ \forall j$
  - :-(function values $\sum_j Y_j(p_j^*(\alpha), \alpha)$ become larger (although there is a *supremum*).

We look for such a value α^* for which both the $p_j^*(\alpha^*)$ variance (or $\mathcal{L}^2$-norm) and the residuum $Y(p)$, cf. (5) are 'small enough'.

A plot of a norm of regularized solution versus the corresponding residual norm is called the L-curve. We plot

- the value of objective function Y (without the regularization term)

$$Y(p_1^*(\alpha) \dots p_M^*(\alpha)) = \sum_{j=1}^{M} \sum_{i=1}^{N} \left[y_{exp}(x_i, \tau_j) - y_{sim}(x_i, \tau_j, p_j^*(\alpha)) \right]^2$$

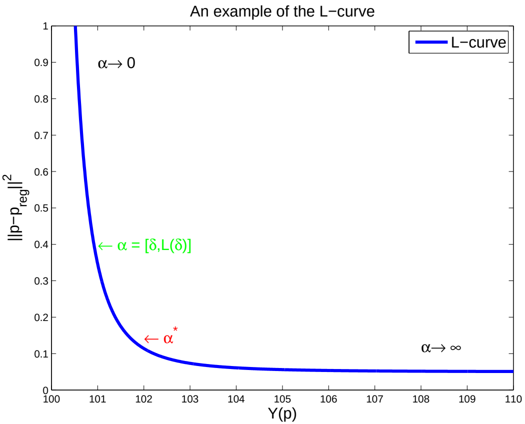
against

- the (relative) deviation σ of $p_j^*(\alpha)$ from their average value $\o p_j^*(\alpha)$

$$\sigma = \frac{1}{\o p_j^*(\alpha)} \sqrt{\frac{1}{M} \sum_{j=1}^{M} [p_j^*(\alpha) - \o p_j^*(\alpha)]^2}$$

The L-curve optimal parameter α^* then usually corresponds to the point with maximal curvature.

L-curve in theory by Hansen



P.C. Hansen: *Rank-Deficient and Discrete Ill-Posed Problems: Numerical Aspects of Linear Inversion.* SIAM, 1997.

Let δ^* be a measure of the noise in input data. If we denote

- $y_{exp}^{\delta^*}(x_i, \tau_j)$ as really measured data with the noise
- $y_{exp}(x_i, \tau_j)$ as data that would be measured without the noise

then

$$\sum_{j=1}^{M} \sum_{i=1}^{N} \left[y_{exp}^{\delta^*}(x_i, \tau_j) - y_{exp}(x_i, \tau_j) \right]^2 \leq c\delta^*$$

where $c > 0$.

There exists α^* such that

$$\alpha^* = [\delta^*, L(\delta^*)]$$

and this α^* is „noise" optimal.
Such a solution $p_1^*(\delta^*) \ldots p_M^*(\delta^*)$ is based on the discrepancy principle.

V.A. Morozov: *On the solution of functional equations by the method of regularization.* Soviet Math. Dokl., 7 (1966), pp. 414-417.

Equivalent problems to Tikhonov's method

Hansen claims: Tikhonov regularization is equivalent to the following two optimization problems with a nonlinear constraint (note that $Y(p) = \sum_{j=1}^{M} Y_j(p_j)$ with $p = (p_1, \ldots, p_M)^T \in \mathcal{R}^M$):

$$p^*(\delta) = \arg\min_p \|p - p_{\mathrm{reg}}\|^2, \quad \text{st.} \quad \sum_{j=1}^{M} Y_j(p_j) \le \delta, \quad p_j \ge 0 \qquad (8)$$

and

$$p^*(\delta) = \arg\min_p \sum_{j=1}^{M} Y_j(p_j), \quad \text{st.} \quad \|p - p_{\mathrm{reg}}\|^2 \le L(\delta), \quad p_j \ge 0 \qquad (9)$$

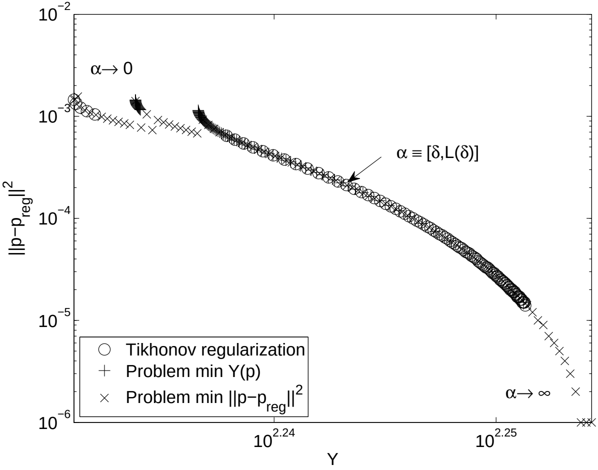
By theory, L-curve is continuous and decreasing which means that both constraints in (8) and (9) are attained on the boundary. Thus each value δ (specifying the noise) corresponds the value $L(\delta)$ so that

$$\sum_{j=1}^{M} Y_j(p_j) = \delta \quad \Leftrightarrow \quad \|p - p_{\mathrm{reg}}\|^2 = L(\delta)$$

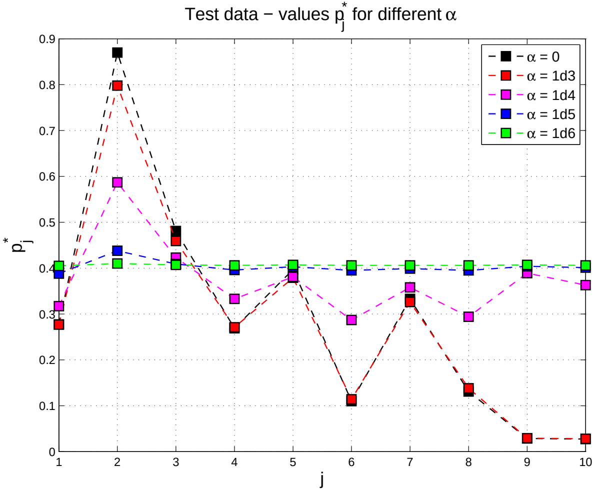
Outline

Results of 3 EQUIVALENT(?!) methods on L-curve plot

Figure 3: Test data with noise: L-curves

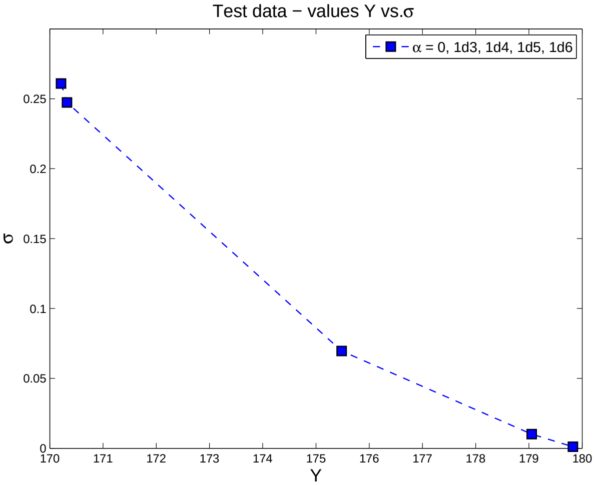


Test data with noise: Solution p_j^* for different α

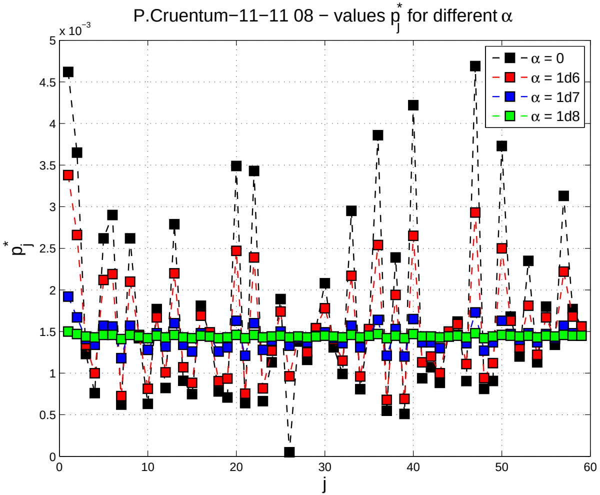


Values Y against σ

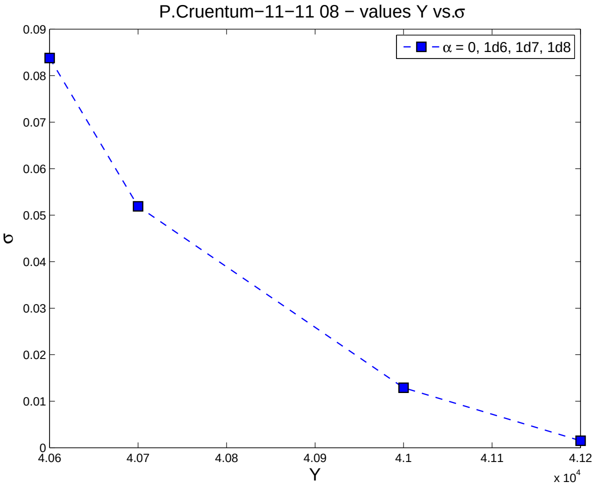
Test data with noise: Values Y against σ



P.Cruentum-11-11 08: Solution p_j^* for different α



P.Cruentum-11-11 08: Values Y against σ



- Our method improves on other (closed form) models by accounting for experimentally measured post-bleaching fluorescence profiles and time-dependent boundary conditions.
- Due to the ill-posedness and noisy data a suitable **regularization technique** and a **robust optimization procedure** have to be implemented.
- The *discrepancy principle* based methods are appealing because the experimental FRAP protocol allows an adequate assessment of the measurement noise.
- Based on simulation results, cf. Fig. 3, we argue that all three methods are for the practical purposes equivalent, thus we can choose the most suitable one...

- 2D extension of our method (the membrane is 2D) based on FD, CN.
- Uncertainty assessment or error analysis, i.e. to assess *how the measurement noise influences the result* (in terms of mean and SD).
- The analysis of sensitivity (Fischer information matrix), should lead us to the **optimal experimental design** (time interval between measurements, size of the bleach spot, etc.).

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