Synergy between the parameter estimation and a design variable optimization for FRAP experiments

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We deal with the inverse problem of model parameters estimation using the spatio-temporal images acquired by the so-called FRAP method.

Consider a diffusion process with one single parameter: a diffusion coefficient D. The governing equation for the spatio-temporal signal $u(x,t)$ is the Fick diffusion equation

$$\frac{\partial u(x,t)}{\partial t} = D\Delta u(x,t), \quad x \in \Omega, \quad t \in [0,T]. \tag{1}$$

- Initial condition:
$$u(x,0) = u_0(x), \quad x \in \Omega.$$
- Boundary conditions:
$$u(x,t) = 0 \quad \text{or} \quad \frac{\partial}{\partial n} u(x,t) = 0 \quad \text{on} \quad \partial\Omega \times [0,T].$$

In FRAP experiments, IC (the first post-bleach profile) is often modeled as a Gaussian, which leads in the 1D case to IC of the form

$$u_0(x) = u_{0,0} e^{-\frac{2x^2}{r_0^2}},$$

- $u_{0,0} \geq 0$ is the maximum depth at time t_0 for $x = 0$,
- $r_0 > 0$ is the half-width of the bleach at normalized height (depth) e^{-2}, i.e. $\frac{u_0(r_0)}{u_{0,0}} = e^{-2}$.

The explicit solution for u in the one-dimensional free space case is

$$u(x,t) = u_{0,0} \frac{r_0}{\sqrt{r_0^2 + 8Dt}} e^{-\frac{2x^2}{r_0^2 + 8Dt}}.$$

We now discuss the parameter identification problem, where we try to infer about the parameter D by using direct measurements of u in some space-time domain. That is, we assume that the following discrete data are observed

$$u(x_i, t_i) \in \mathcal{R}, \quad i = 1, \ldots, N_{\mathrm{data}}.$$

Parameter identification problem

We define the forward map (also called the parameter-to-data map)

$$F : \mathcal{R} \to \mathcal{R}^{N_{\rm data}}, \quad F(D) = (u(x_i, t_i))_{i=1}^{N_{\rm data}}$$

Our regression model is now

$$F(D) = \mathrm{data} \tag{2}$$

where the data are modeled as contaminated with additive white noise

$$\mathrm{data} = F(D_T) + e = (u(x_i, t_i))_{i=1}^{N_{\rm data}} + (e_i)_{i=1}^{N_{\rm data}} .$$

Here $D_T \in \mathcal{R}$ denotes the true coefficient and $e \in \mathcal{R}^{N_{\rm data}}$ is a data error vector which we assume to be normally distributed with variance σ^2:

$$e_i = \mathcal{N}(0, \sigma^2), \quad i = 1, \ldots, N_{\rm data}.$$

The aim of the parameter identification problem is to find D such that (2) is satisfied in some appropriate sense:

$$\|F(D_c) - \mathrm{data}\|^2 = \min_D \|F(D) - \mathrm{data}\|^2. \tag{3}$$

This problem is usually ill-posed thus regularization has to be employed.

For the sensitivity analysis we require the Fréchet-derivative $F'[D] \in \mathcal{R}^{N_{\mathrm{data}}}$ of the forward map F, that is

$$F'[D] = \frac{\partial}{\partial D} F(D) = \left(\frac{\partial}{\partial D} u(x_1, t_1), \quad \ldots, \quad \frac{\partial}{\partial D} u(x_{N_{\mathrm{data}}}, t_{N_{\mathrm{data}}}) \right)^T \tag{4}$$

A corresponding quantity is the Fisher information matrix

$$M = F'[D]^T F'[D]$$

which collapses into the scalar quantity

$$M = \sum_{i=1}^{N_{\mathrm{data}}} \left(\frac{\partial}{\partial D} u(x_i, t_i) \right)^2$$

for the one single parameter case.

Now we can estimate confidence intervals. Suppose we have computed D_c as a least-squares solution to (3). Let us define the residual as

$$\mathrm{res}^2(D_c) = \|F(D_c) - \mathrm{data}\|^2 = \sum_{i=1}^{N_{\mathrm{data}}} \left[u_{D_c}(x_i, t_i) - \mathrm{data}_i\right]^2,$$

where u_{D_c} is a solution to (1) for the computed parameter value D_c.

Then it is possible to quantify an error between D_c and D_T. In fact, we have an approximate $1 - \alpha$ confidence interval

$$(D_c - D_T)^2 \sum_{i=1}^{N_{\mathrm{data}}} \left[\frac{\partial}{\partial D} u(x_i, t_i)\right]^2 \leq \frac{\mathrm{res}^2(D_c)}{N_{\mathrm{data}} - 1} f_{1, N_{\mathrm{data}}-1}(\alpha), \tag{5}$$

where $f_{1, N_{\mathrm{data}}-1}(\alpha)$ corresponds to the upper α quantile of the Fisher distribution with 1 and $N_{\mathrm{data}} - 1$ degrees of freedom.

Optimizing an experimental design variable

We can ask further questions concerning the optimal experimental design based on the sensitivity analysis by looking at further design variables.

We can try to look for such a bleach radius r_0 which leads to maximal sensitivity since this corresponds to minimal confidence intervals.

More precisely, we consider the case of a dense set of observations on a space-time cylinder $Q = [-\frac{L}{2}, \frac{L}{2}] \times [0, T]$ in 1D case and we try to infer about the optimal bleach radius r_{opt} yielding maximal sensitivity.

We approximate the sensitivity by integrals and forget the grid factor $\frac{1}{\Delta x \Delta t}$ which is assumed to be fixed. We introduce

$$S(r_0) = \int_0^T \int_{-\frac{L}{2}}^{\frac{L}{2}} \left| \frac{\partial}{\partial D} u(x,t) \right|^2 \mathrm{d}x\mathrm{d}t,$$

and we try to find out the maximal value of function

$$S(r_{opt}) = \max_{r_0 > 0} S(r_0).$$

For the special case of full spatial observation on the real line $\mathcal{R}$, i.e., $L = \infty$, we can actually find a formula for the optimal bleach radius:

$$S(r_0) = \frac{|u_{0,0}|^2}{D_c^3} r_0^3 K(\infty, \frac{TD_c}{r_0^2}),$$

where

$$K(\infty, t) = \frac{\sqrt{\pi}(1 + 12t + 24t^2)}{16(1 + 8t)^{\frac{3}{2}}} - \frac{\sqrt{\pi}}{16}$$

It turns out that in this setting the function $S(r_0)$ has a unique maximum

$$r_{opt} \approx 1.728\sqrt{TD_c}. \qquad (6)$$

Thus, this is the optimal bleach radius (with maximal sensitivity and hence minimal confidence interval).

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