A trivial connection between parameter estimation and “TDDR”

Larry Lok

January 31, 2006

Suppose that we view our concentrations as a vector function of time, $C(t) = (c_1(t), \ldots, c_m(t))$, and that we have rate constants $R = (r_1, \ldots, r_k)$. Our usual “mass-action” equation looks like this:

$$\frac{dC}{dt} = F(C(t), R).$$

If we want to add time-dependent stimuli, $S(t) = (s_1(t), \ldots, s_l(t))$, then the equation becomes “non-autonomous,”

$$\frac{dC}{dt} = F(C(t), S(t), R). \tag{1}$$

Assume that we have a way, given an trajectory sample, $C(t_1) = C_1, C(t_2) = C_2, \ldots, C(t_j) = C_j$, obtained from observations in the laboratory, to estimate the rate parameters R. (Kouichi has recently sent around papers describing high-powered ways of doing this.) That is, suppose that we have a solution to the “plain” parameter estimation problem.

If we have a collection of test stimulus function, such as those that Ty used in his simulations,

$$\mathbf{S}(t) = (S^{(1)}(t), S^{(2)}(t), \ldots, S^{(n)}(t)),$$

and we denote the corresponding solutions to Eq. 1 by

$$\mathbf{C}(t) = (C^{(1)}(t), C^{(2)}(t), \ldots, C^{(n)}(t)),$$

then we have

$$\frac{d\mathbf{C}}{dt} = \mathbf{F}(\mathbf{C}(t), \mathbf{S}(t), R),$$

where

$$\mathbf{F}(\mathbf{C}, \mathbf{S}, R) = \left(F(C^{(1)}, S^{(1)}, R),\ F(C^{(2)}, S^{(2)}, R),\ \ldots,\ F(C^{(n)}, S^{(n)}, R)\right).$$

This system of equations is of exactly the same form as our original Eq. 1. While it's very much larger, parameter estimation should apply to it as it would to Eq. 1.

Doing parameter estimation on this expanded system of equations (after collecting sample response trajectories of the response to each of the time-dependent stimuli) amounts to using our time-dependent responses to time-dependent doses to infer parameter values.

Kouichi points out some issues that pertain to all parameter estimation from sample trajectories, and therefore to this “tddr estimation” in particular:

1. We will never have sample trajectories of all the species, only a few. The initial conditions for these species become, in effect, more parameters for estimation, making it all more difficult, especially when the rate parameters and/or unobserved species are numerous.

2. This is nothing new, of course, being so completly trivial. But nobody was saying it around the Institute, and it seemed to need saying, so here we are.

3. Parameter estimation algorithms may impose restrictions on the right-hand side of Eq. 1, and hence on the stimulus functions $S(t)$.