Faculty of Engineering
The University of Tokushima

Numerical Computation for Population Pharmacokinetics

Professor Toshiki Takeuchi

$$S = 2\omega_c^2 \sum_{j=1}^{m} \log c(t_j, \mathbf{x}) + \sum_{j=1}^{m} \frac{(c_j - c(t_j, \mathbf{x}))^2}{\{c(t_j, \mathbf{x})\}^2} + \omega_c^2 \sum_{i=1}^{n} \frac{(x_i - \mu_i)^2}{\omega_i^2 \mu_i^2}$$

(a) Objective function in nonlinear optimization problem

$C(t) = c(t, V_d, V_{max}, K_m)$: Concentration

$$\begin{cases} \dfrac{dX_a(t)}{dt} = -k_a X_a(t) \\ \dfrac{dC(t)}{dt} = \dfrac{F\, k_a\, X_a}{V_d} - \dfrac{V_{max}\, C}{V_d(K_m + C)} \end{cases} \qquad t_i \leqq t < t_{i+1} \qquad (i = 1, 2, \cdots)$$

$$X_a(t_i) = \begin{cases} D_1 \\ D_i + \lim\limits_{t \to t_i - 0} X_a(t) \end{cases} \qquad C(t_i) = \begin{cases} 0 & i = 1 \\ \lim\limits_{t \to t_i - 0} C(t) & i \geqq 2 \end{cases}$$

(b) Differential equations(phenytoin)

Fig. 1 Bayesian estimation for pharmacokinetics

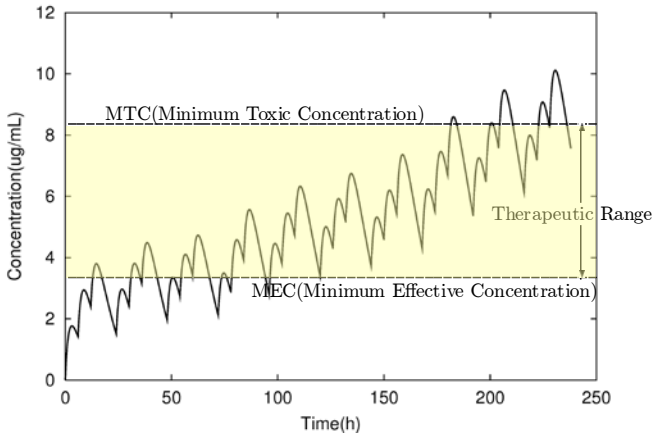

Fig. 2 Profile of the concentration and the therapeutic range

Content:

Pharmacokinetics plays an important role in efficacy and safety pharmacotherapy. The estimation of individual pharmacokinetic parameters from a few concentration data is desirable in quick therapy. Bayesian estimation using the population pharmacokinetic parameters is useful for the estimation of individual pharmacokinetic parameters. Here, population pharmacokinetic parameters mean statistic including average, variance and correlation coefficient. The numerical calculation of nonlinear optimization is essential to Bayesian estimation or computation for population pharmacokinetic parameters. In addition, the theoretical value of concentration data may be given with a nonlinear differential equation. The stable computation in nonlinear optimization for pharmacokinetics is difficult because of the strong nonlinearity. I am developing a stable and high-precision numerical method for nonlinear optimization problem in population pharmacokinetics and Bayesian estimation.

Keywords: Bayesian estimation, Nonlinear optimization

E-mail: takeuchi@pm.tokushima-u.ac.jp
Tel. +81-88-656-7544
Fax: +81-88-656-7544