Analysis of practical identifiability of a viral infection model

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S4 Text

Implementation of simulation and extrapolation approach. Let t denote the true time point when an observed value actually happens; the corresponding time point in experimental scale is $t^* = t + v, v \sim N(0, \Sigma_v)$, where v is an unknown time shift. The following steps are done (adapted from [1]): (1) Define Σ_v such that t varies in a biological range according to the model; (2) Generate a sequence of λ_i in $\{0, ..., K\}$; (3) For each λ_i, add time shifts to the original data with the noise equal to $\lambda_i \Sigma_v$ and fit the model. The new time shift for each data point thus is equal to $(1 + \lambda_i)\Sigma_v$; (4) Repeat step 3 B times (B sufficiently large) and obtain the average parameter estimates for each λ_i; (5) Use statistical models to make extrapolation of parameter values at $\lambda = -1$.

In the IAV kinetics, the shift v could be assumed varying from a few minutes to a day which can be illustrated by a truncated normal distribution. The λ sequence length of ten and $K = 1$ are chosen such that the simulated data have realistic time scale and maximum time shift of one day, $B = 1000$ simulations is used. The results showed that applying simulation step in the model resulted in a non-linear pattern of parameter estimates over λ (Fig. T4). Thus it is not possible to make extrapolation properly to where theoretically no error at $\lambda = -1$.
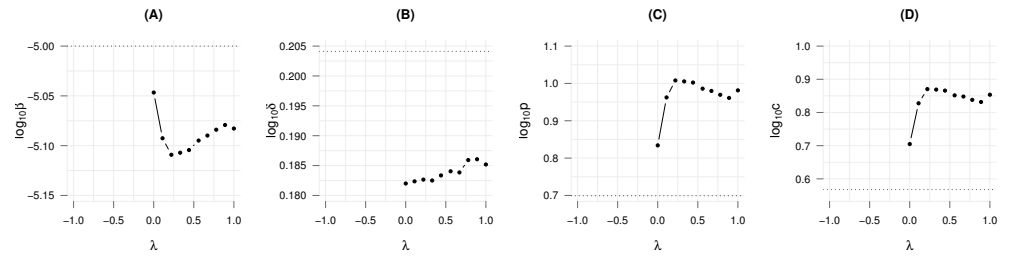
Figure T4. Simulation and extrapolation approach in the target-cell limited model. The horizontal dashed line corresponds to the reference values, each dot is the mean of 1000 simulations of time shifts.

References

1. Althubaiti A, Donev A. Non-Gaussian Berkson errors in bioassay. Statistical Methods in Medical Research. 2012;.