

# Analysis of practical identifiability of a viral infection model

Van Kinh Nguyen<sup>1,2,3</sup>, Frank Klawonn<sup>4,5</sup>, Rafael Mikolajczyk<sup>6,7,8,9</sup>, Esteban A. Hernandez-Vargas<sup>1,\*</sup>

**1** Systems Medicine of Infectious Diseases, Department of Systems Immunology and Braunschweig Integrated Centre of Systems Biology, Helmholtz Centre for Infection Research, Braunschweig, Germany, **2** Epidemiology Department, Ho Chi Minh University of Medicine and Pharmacy, Ho Chi Minh, Vietnam. **3** PhD Programme “Epidemiology”, Braunschweig-Hannover, Germany **4** Biostatistics, Helmholtz Centre for Infection Research, Braunschweig, Germany, **5** Department of Computer Science, Ostfalia University, Wolfenbüttel, Germany, **6** Epidemiological and Statistical Methods, Helmholtz Centre for Infection Research, Braunschweig, Germany. **7** German Centre for Infection Research, site Hannover-Braunschweig, Germany **8** Hannover Medical School, Hannover, Germany **9** [Institute of] Medical Epidemiology, Biometry and Informatics, Martin-Luther University Halle-Wittenberg, Germany

\* [esteban.vargas@helmholtz-hzi.de](mailto:esteban.vargas@helmholtz-hzi.de)

## S1 Text

**Limited-memory BFGS (L-BFGS-B) algorithm settings.** Maximum likelihood estimation was done with the L-BFGS-B algorithm implemented in R [2]. The parameter boundaries are shown in Table 1 (main text). The relative tolerance was set at  $10^{-8}$ . The parameter estimation was conducted in log base ten for both the states and parameters.

**Differential Evolution (DE) algorithm settings.** The parameter estimation was conducted in log base ten for both the states and parameters. The parameter boundaries are shown in Table 1 (main text). Root mean squared error (RMSE) was used as the cost function. The DE algorithm was run with recommended configurations from [1]. In particular, set the number of parents  $NP$  to 10 times the number of parameters (40), select differential weighting factor  $F = 0.8$  and crossover constant  $CR = 0.9$ . A consecutive thirty iterations without an improvement in the root mean squared error (RMSE) ( $10^{-8}$ ) will stop the optimizer. Note that the maximum number of iterations needs to be set to an arbitrarily large number ( $10^4$ ) to prevent DE algorithm stops early in problematic data. The algorithm was run in parallel mode. The weighted bootstrapping was done the same as described in [3], i.e., assigning to the cost function a vector of random weights with length equal the sample size from the exponential distribution with mean one and variance one.

## References

1. Storn R, Price K. Differential Evolution – A Simple and Efficient Heuristic for global Optimization over Continuous Spaces. *Journal of Global Optimization*. 1997;11(4):341–359.
2. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria; 2014.
3. Ma S, Kosorok MR. Robust semiparametric M-estimation and the weighted bootstrap. *Journal of Multivariate Analysis*. 2005;96(1):190 – 217.