Supplementary Material: Exploring the effect of different dosing regimens of probenecid on influenza A infections with a quantitative systems pharmacology (QSP) model

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Overview

This supplement file describes how to use the data and code to reproduce all findings. It also contains additional results.

Code and file information

All code and data needed to reproduce the results are provided as supplement.

The data in a format that is ready for modeling is located in the `data` folder.

Scripts to fit the model to the data and run the simulations for different doses are located in the ‘code

Table 1: Another fit table.

Parameter	Value	Label
b	2.008741e-08	Virus infection rate
k	1.711872e-05	Adaptive response clearance rate
p	9.806772e+03	Virus production rate
kF	1.000000e-10	Innate response supression strength
cV	2.273026e+02	Virus removal rate
gF	8.304122e-03	Maximum innate response induction
hV	1.425410e-02	Half maximum of innate response induction
Fmax	9.942463e+01	Maximum innate response
hF	1.360302e-01	Innate response decay rate
gS	1.136927e+01	Symptom induction rate
cS	2.508052e-01	Symptom decay rate
Emax_F	8.069369e-01	Maximum innate response supression
C50_F	1.000000e-07	Half maximum of innate response effect
C50_V	8.653276e-05	Half maximum of virus suppression effect

Additional results

Table of parameter estimates

Estimates for parameter values that are fit to the model are provided in table Table 1 .

Values for fixed parameters are described in the methods section of the main text.

Additional tables of best fit estimates for all fixed parameter samples can be generated with the supplied code.

Residual plots

Figure Figure 1 shows the residual plots for the best fit model.

Additional figures of residual plots for all parameter samples can be generated with the supplied code.

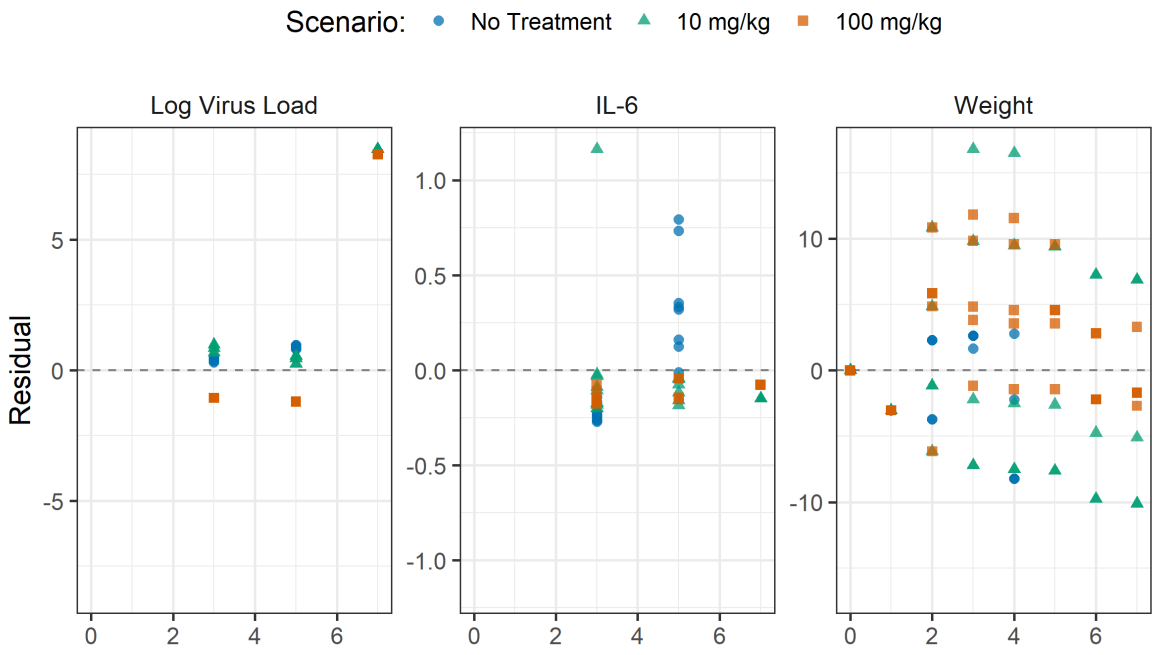

Figure 1: Residual plot for best fitting model.

Time-series for delayed treatment regimens

Figure 2 shows time-series for all model variables for 1, 10 and 100mg/kg doses with treatment starting 2 days post infection. Figure 3 shows the same for treatment starting 3 days post infection.

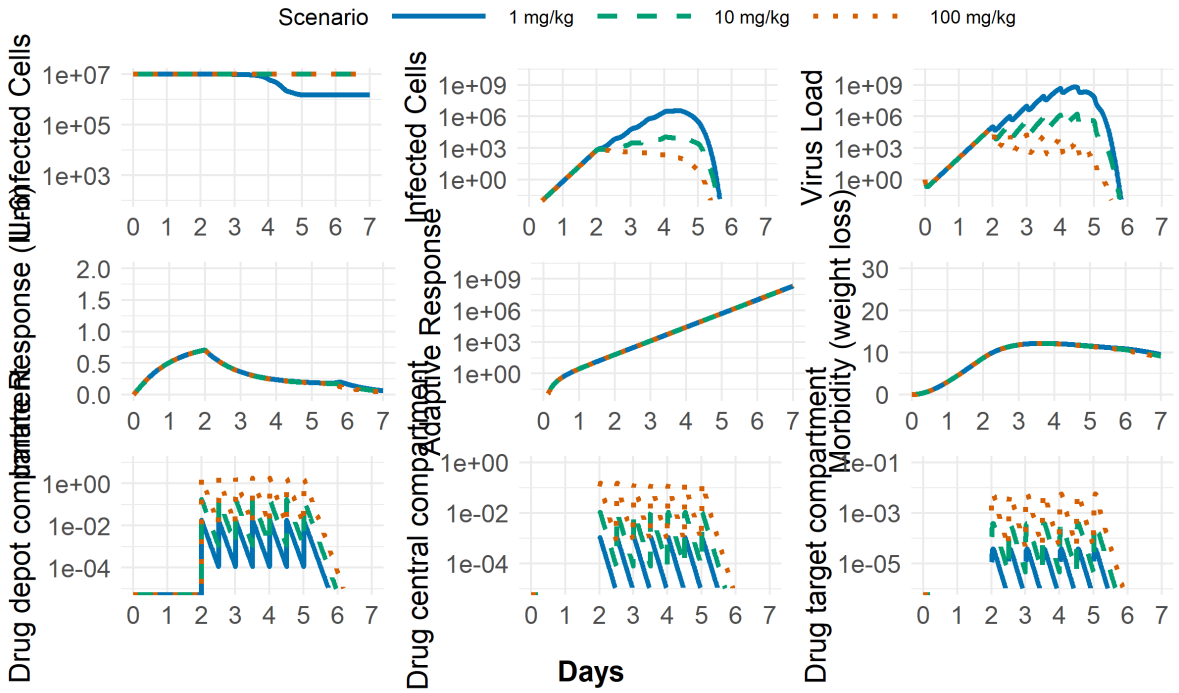

Figure 2: Time series of model simulations for 1, 10 and 100mg/kg dosing with treatment starting 2 days post infection.

Time-series for reduced treatment regimens

Figure 4 shows time-series for all model variables for 1, 10 and 100mg/kg doses with daily (instead of twice daily) treatment starting on day 1 post infection. Figure 5 shows the same for a single treatment on day 1 post infection.

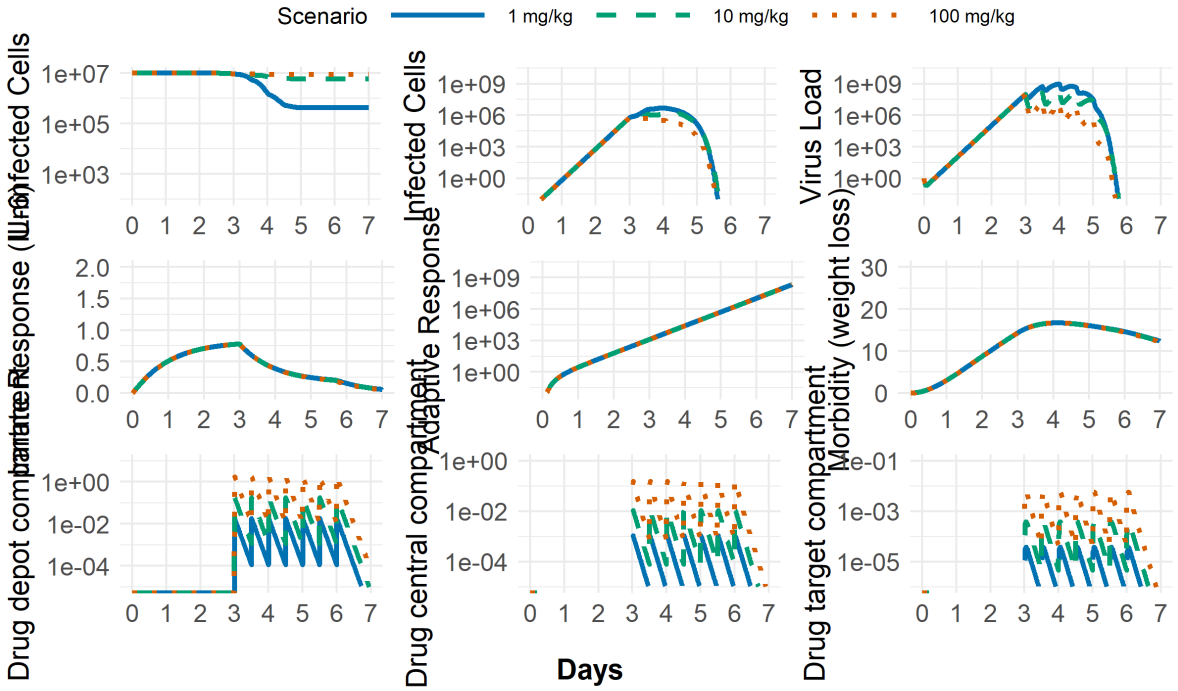

Figure 3: Time series of model simulations for 1, 10 and 100mg/kg dosing with treatment starting 3 days post infection.

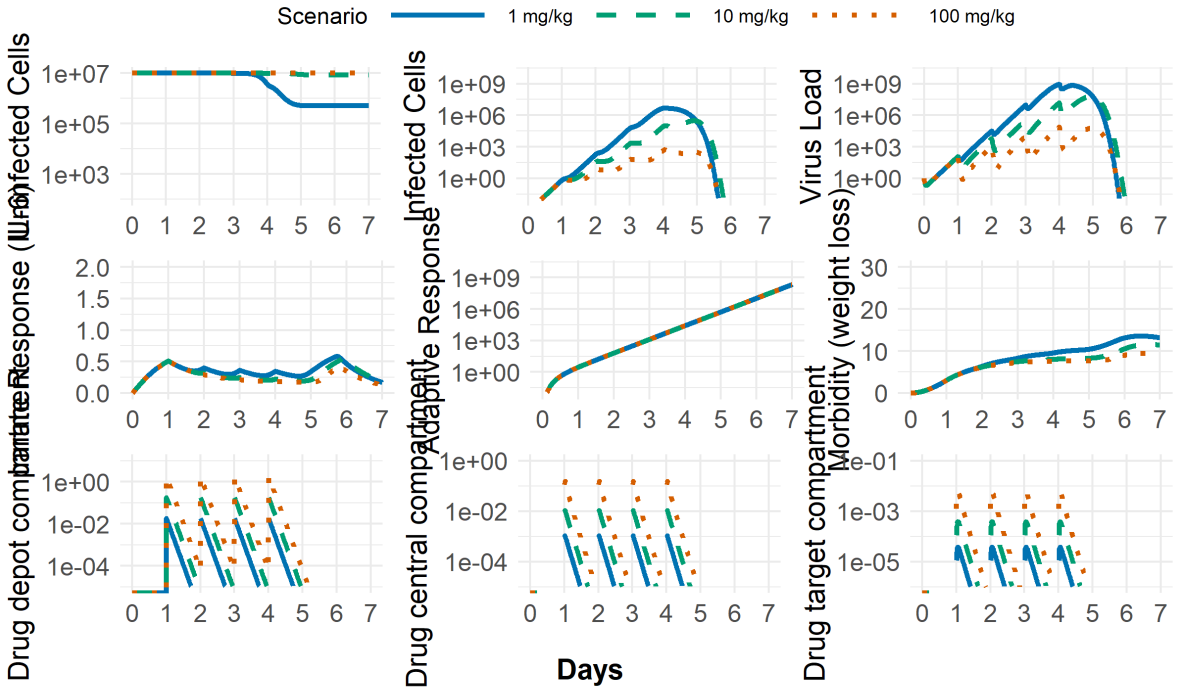

Figure 4: Time series of model simulations for 1, 10 and 100mg/kg dosing with daily treatment starting on day 1 post infection.

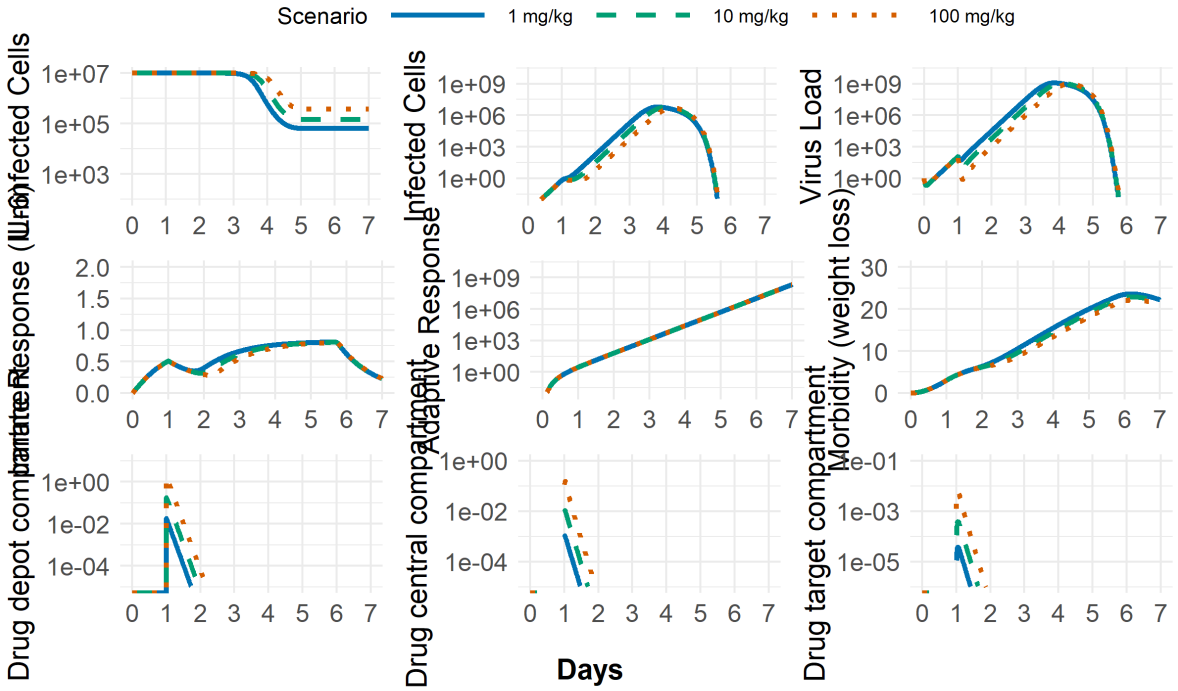

Figure 5: Time series of model simulations for 1, 10 and 100mg/kg dosing with a single treatment at day 1 post infection.

References