

# 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 **analysis-code** folder. Code to generate figures and tables is located in the **plotting-code** folder.

NEEDS TO BE COMPLETED

Table 1: Another fit table.

Parameter	Value	Label
b	5.886119e-11	Virus infection rate
k	3.805840e-05	Adaptive response clearance rate
p	5.524383e+07	Virus production rate
kF	1.604213e-06	Innate response supression strength
cV	3.438261e+03	Virus removal rate
gF	6.171653e-03	Maximum innate response induction
hV	2.604149e-03	Adaptive response half-maximum induction
Fmax	1.149677e+02	Maximum innate response
hF	4.582016e-03	Adaptive response half-maximum induction
gS	1.416485e+01	Symptom induction rate
cS	3.409314e-01	Symptom decay rate
E <sub>max_F</sub>	9.993902e-01	Maximum drug effect on innate response
C <sub>50_F</sub>	1.000000e-07	Half maximum of innate response effect
C <sub>50_V</sub>	2.023443e-07	Half maximum of virus suppression effect
sigma_add_LogVirusLoad	1.773340e-01	Sigma of LogVirusLoad
sigma_add_IL6	3.162685e-01	Simga of IL6
sigma_add_WeightLossPerc	6.357825e+00	Sigma of WeightLossPerc

## Additional results

The following sections provide additional results from the model fitting and simulations.

### 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.

## Predicted versus observed plot

Figure 1 shows the (unweighted) predicted versus observed results for each fitted variable.

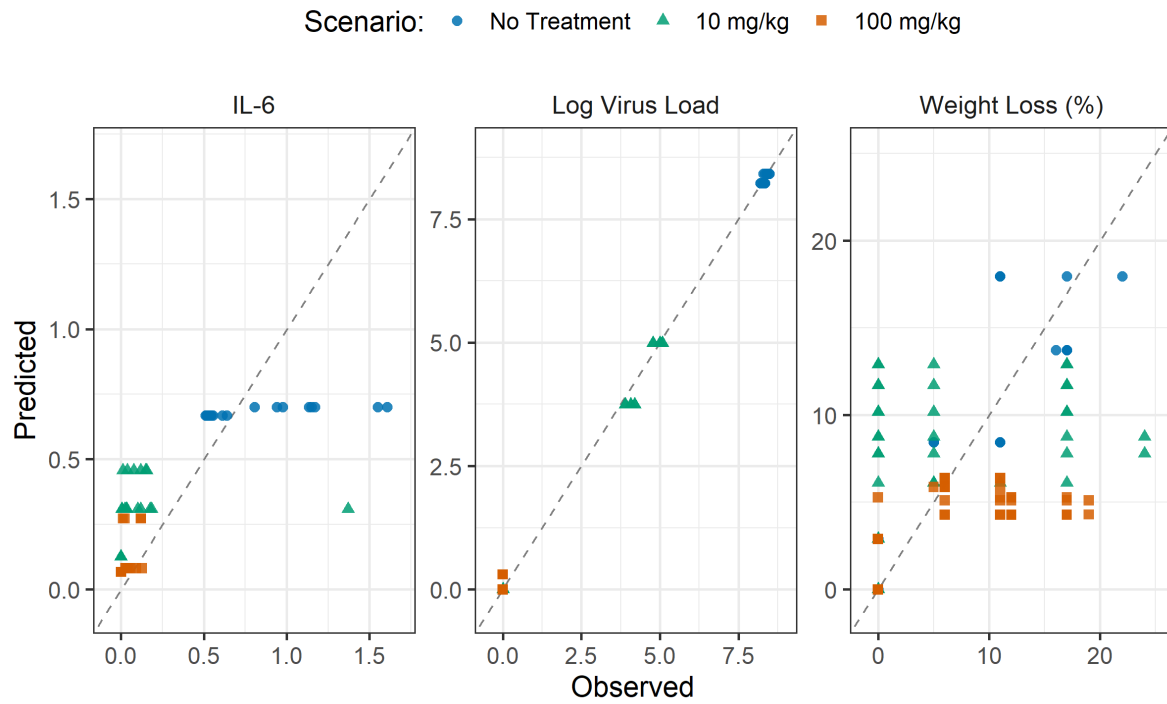


Figure 1: Predicted versus observed variables for best fitting model.

## Residual plots

Figures Figure 2 and Figure 3 show the weighted residual plots for the best fit model, one separated for each variable, and one combined.

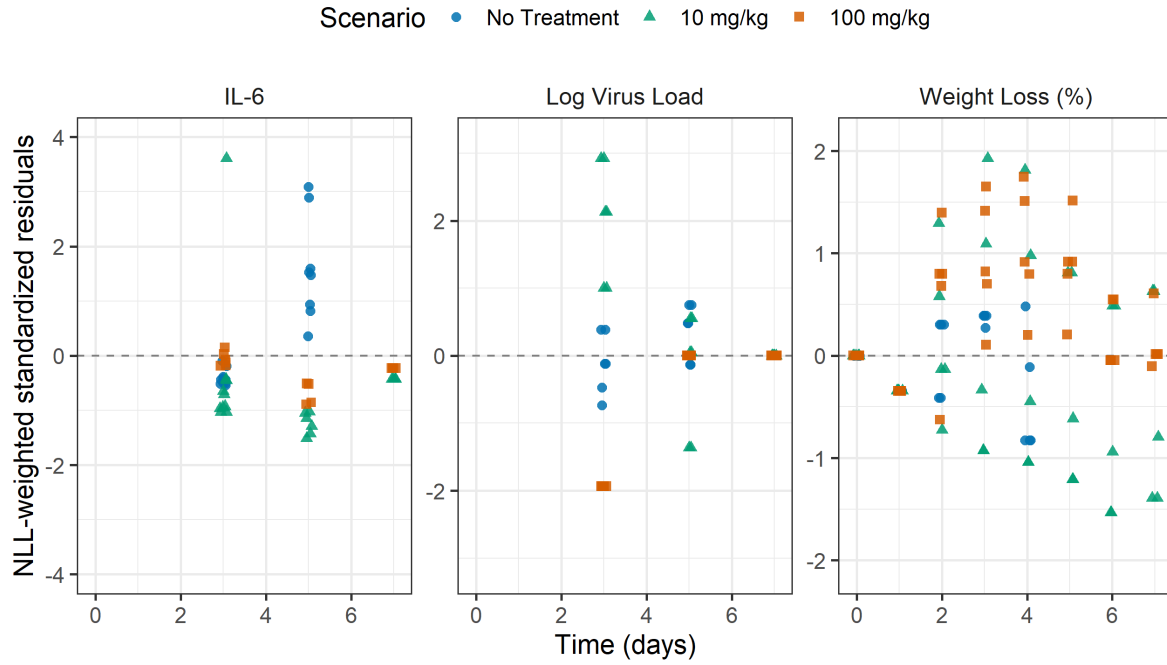


Figure 2: Per-variable weighted residual plot for best fitting model.

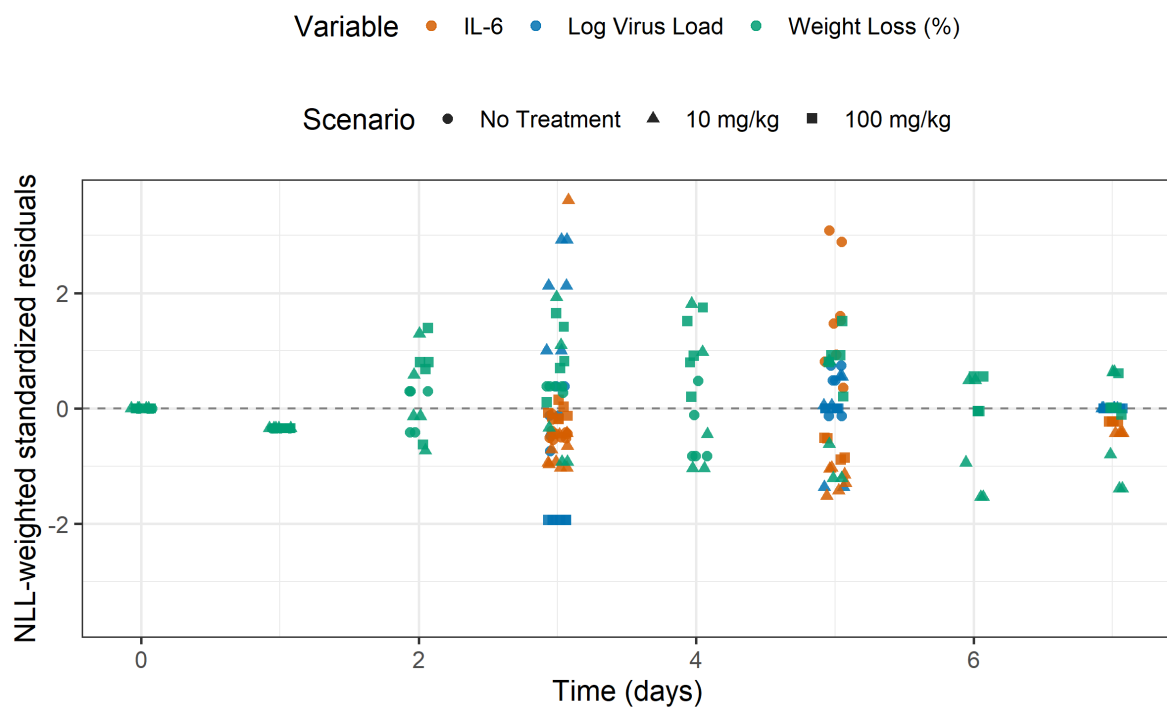


Figure 3: Combined weighted residual plot for best fitting model.

## Time-series for delayed treatment regimens

Figure 4 shows time-series for all model variables for 1, 10 and 100mg/kg doses with treatment starting 2 days post infection. Figure 5 shows the same for treatment starting 3 days post infection.

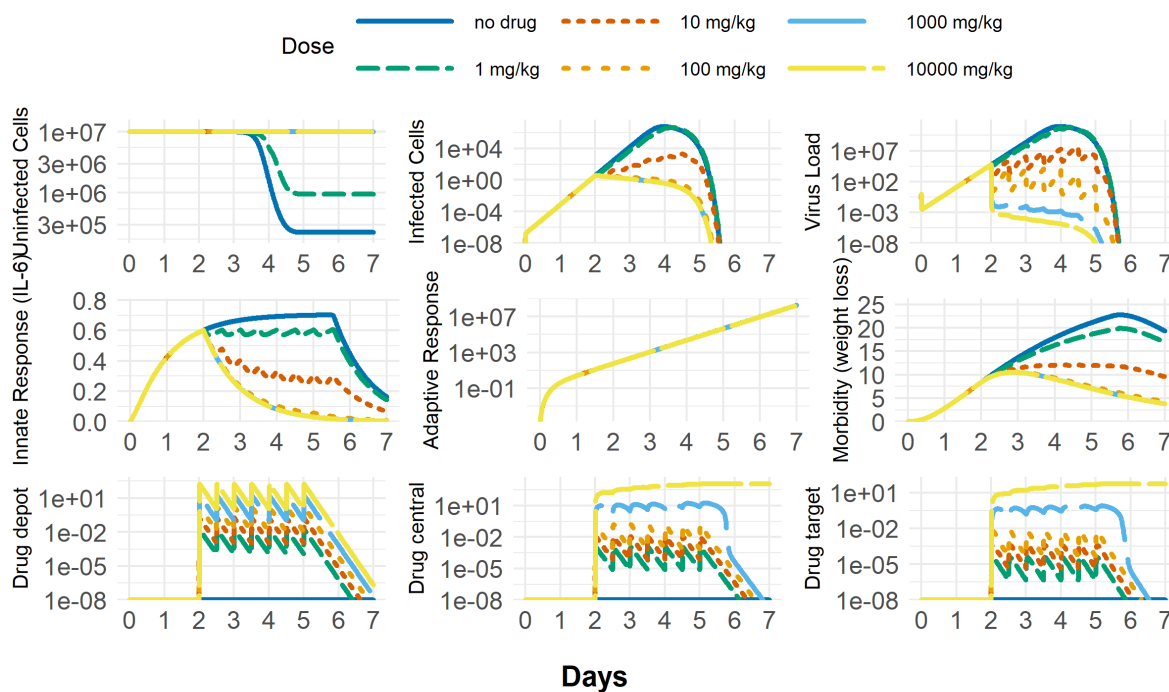


Figure 4: Time series of model simulations for several dosing levels with treatment starting 2 days post infection.

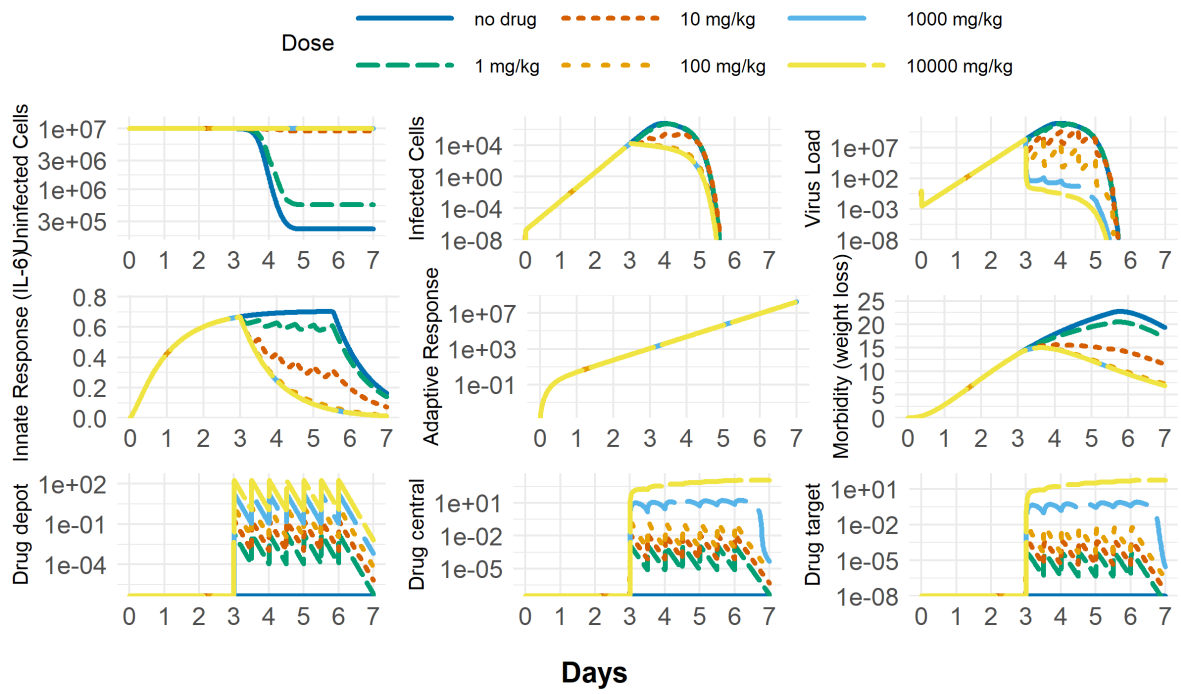


Figure 5: Time series of model simulations for several dosing levels with treatment starting 3 days post infection.



## Time-series for reduced treatment regimens

Figure 6 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 7 shows the same for a single treatment on day 1 post infection.

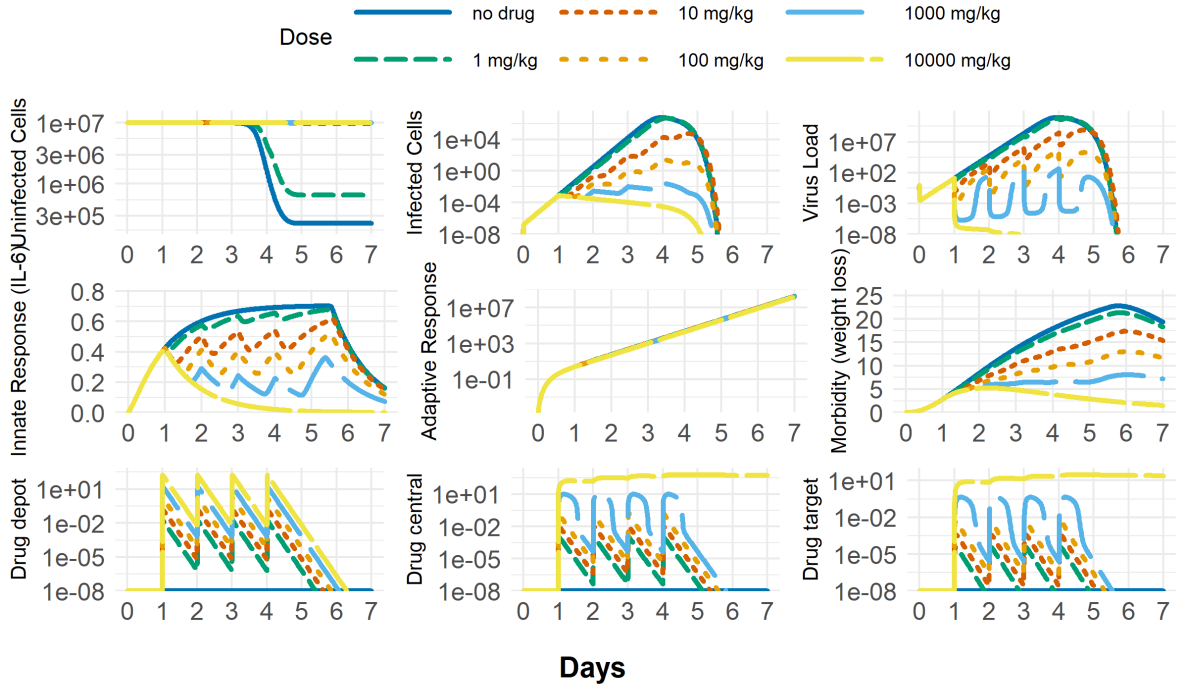


Figure 6: Time series of model simulations for several dosing levels with daily treatment starting on day 1 post infection.

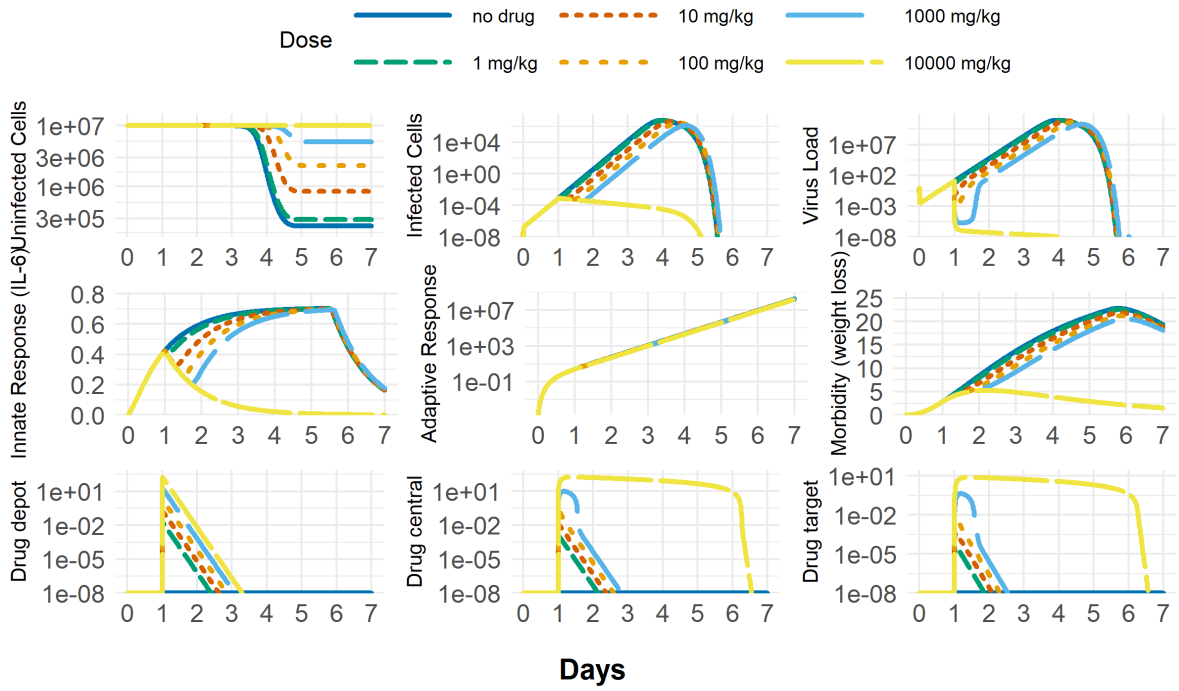


Figure 7: Time series of model simulations for several dosing levels with a single treatment at day 1 post infection.

## References