Supplement for "Quantifying the effect of remdesivir in rhesus macaques infected with SARS-CoV-2"

Hana M. Dobrovolny

In this supplement we present graphs showing the parameter distributions determined from bootstrapping. We also include a sensitivity analysis for the fixed parameter c.

1 Empirical model

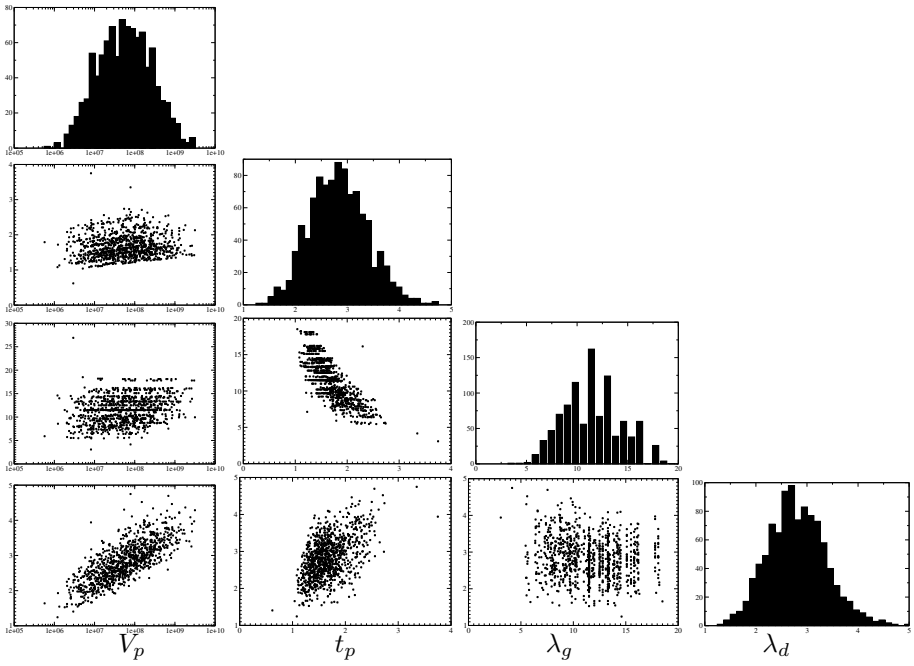

Figure 1: Parameter correlation plots and parameter distributions for empirical model fits to the data from animal 1.

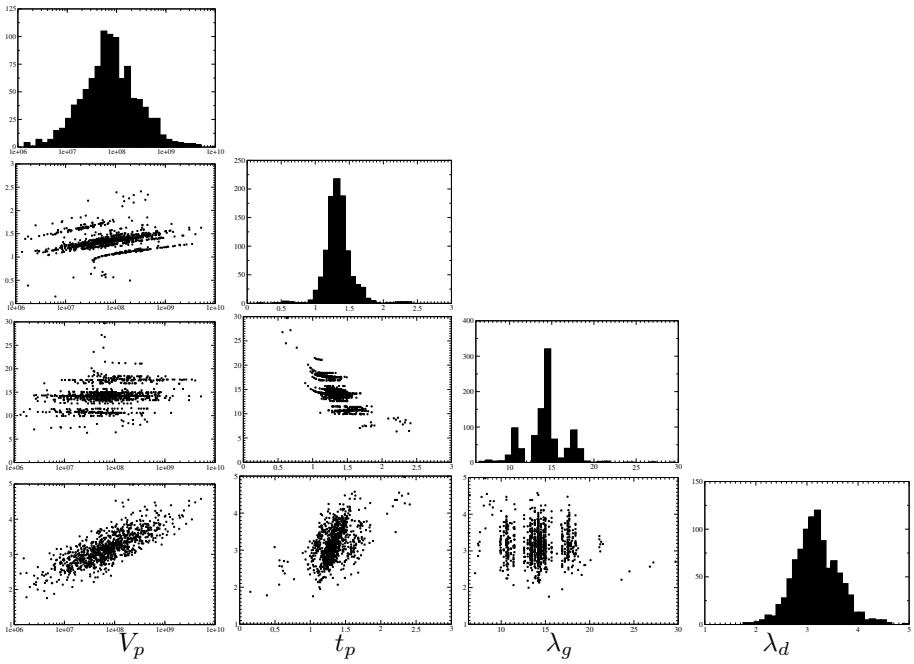

Figure 2: Parameter correlation plots and parameter distributions for empirical model fits to the data from animal 2.

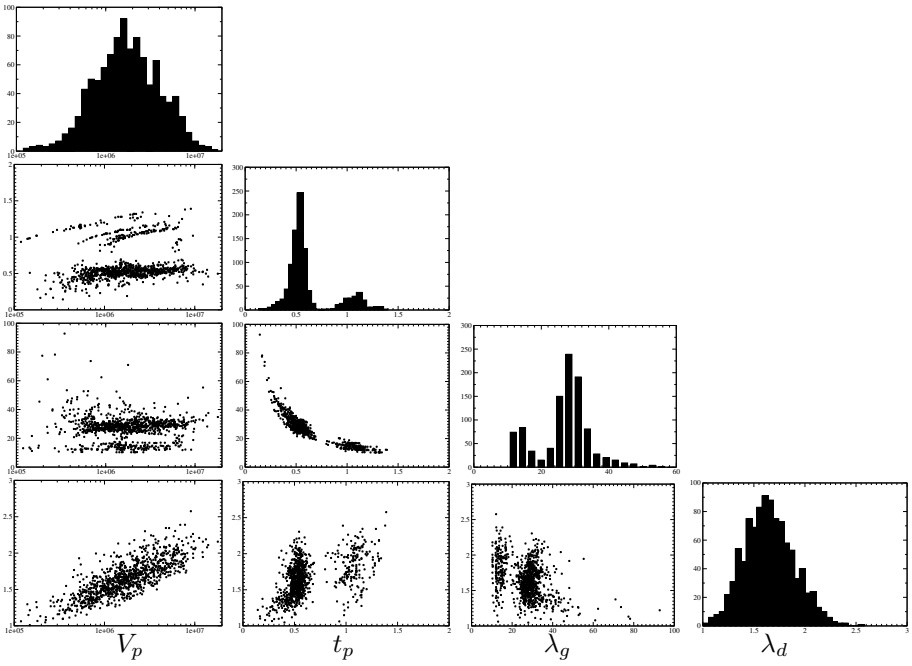

Figure 3: Parameter correlation plots and parameter distributions for empirical model fits to the data from animal 3.

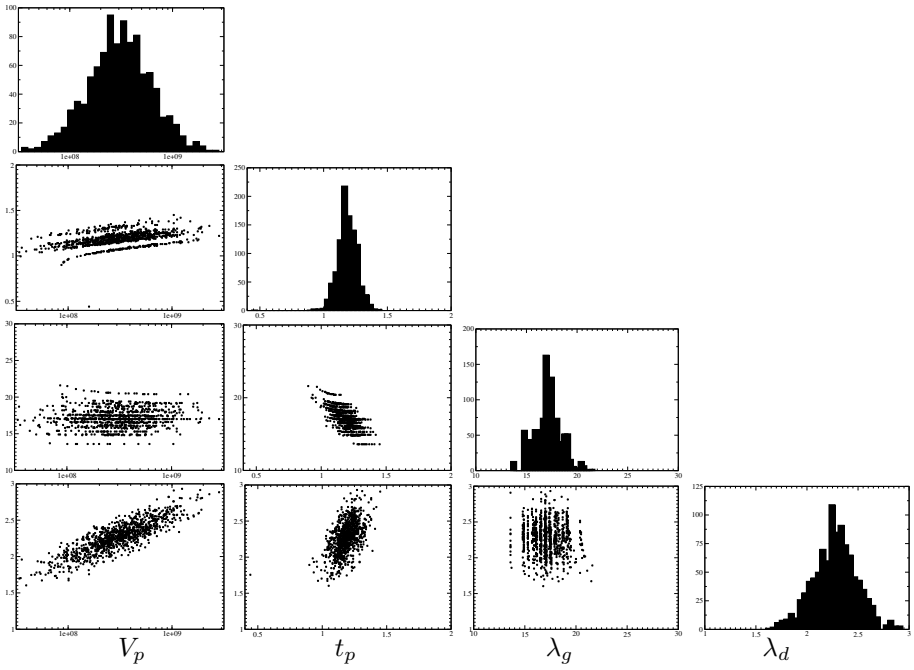

Figure 4: Parameter correlation plots and parameter distributions for empirical model fits to the data from animal 4.

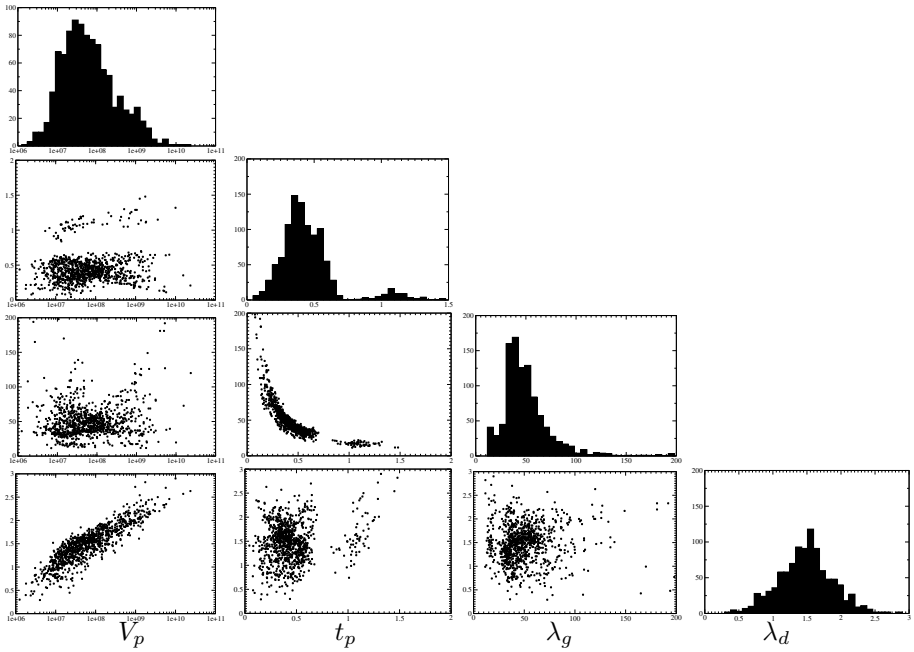

Figure 5: Parameter correlation plots and parameter distributions for empirical model fits to the data from animal 5.

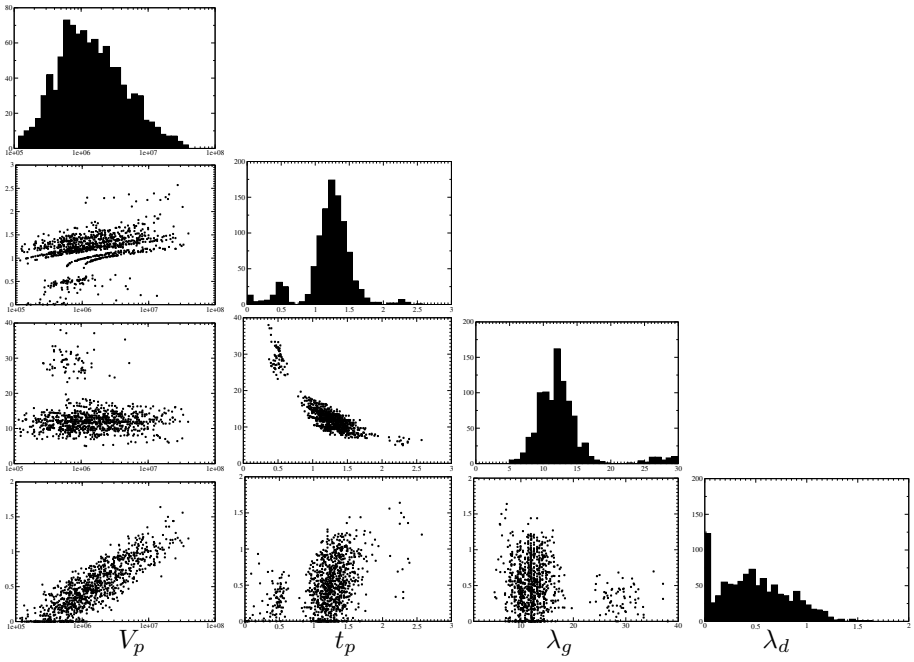

Figure 6: Parameter correlation plots and parameter distributions for empirical model fits to the data from animal 6.

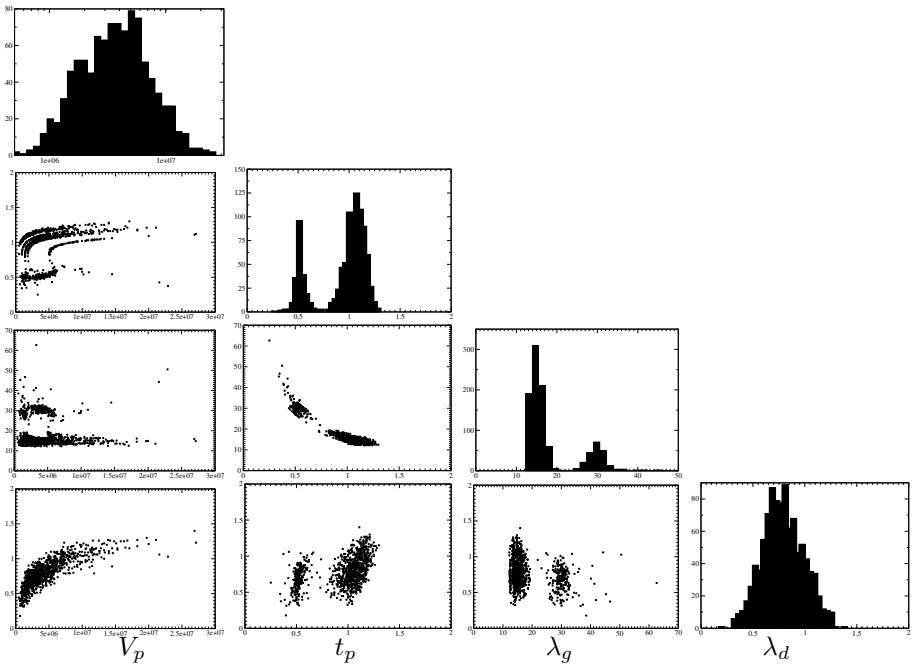

Figure 7: Parameter correlation plots and parameter distributions for empirical model fits to the data from animal 7.

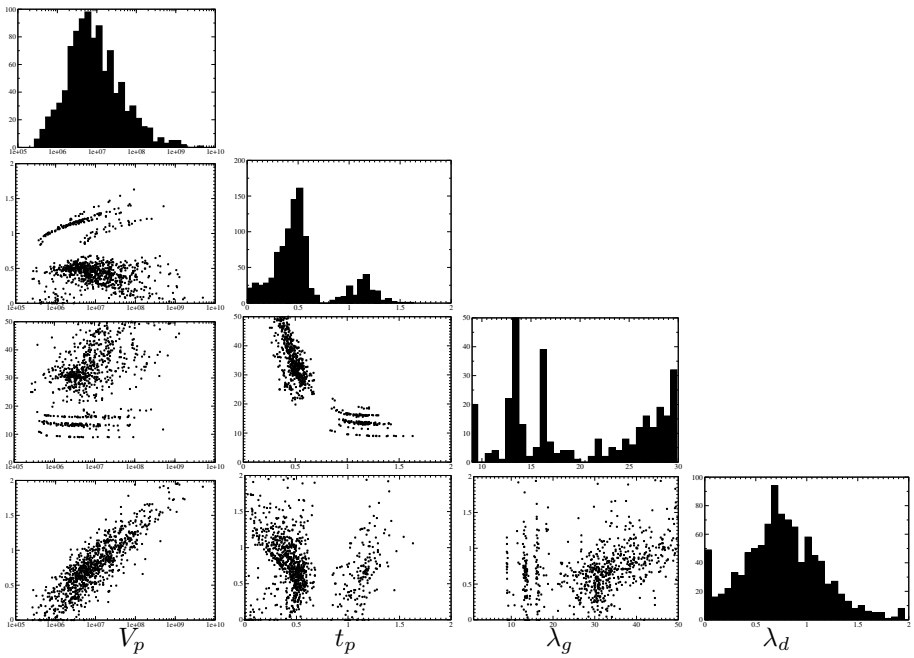

Figure 8: Parameter correlation plots and parameter distributions for empirical model fits to the data from animal 8.

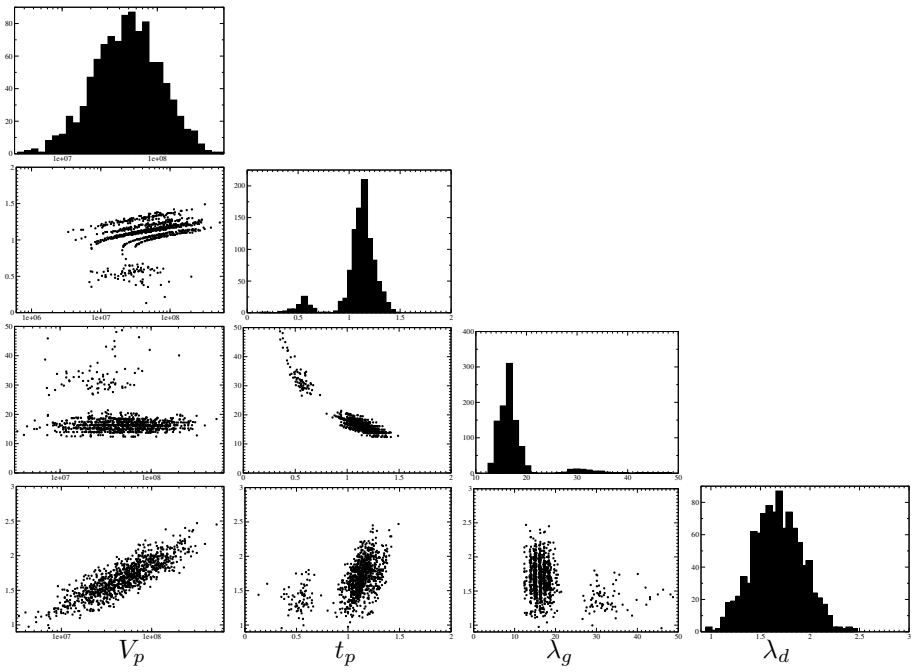

Figure 9: Parameter correlation plots and parameter distributions for empirical model fits to the data from animal 9.

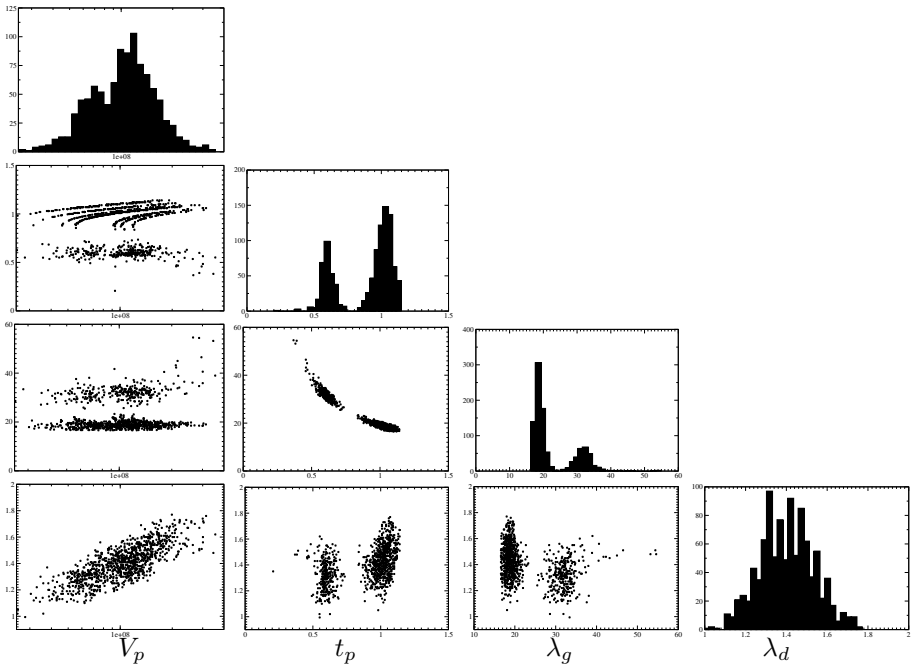

Figure 10: Parameter correlation plots and parameter distributions for empirical model fits to the data from animal 10.

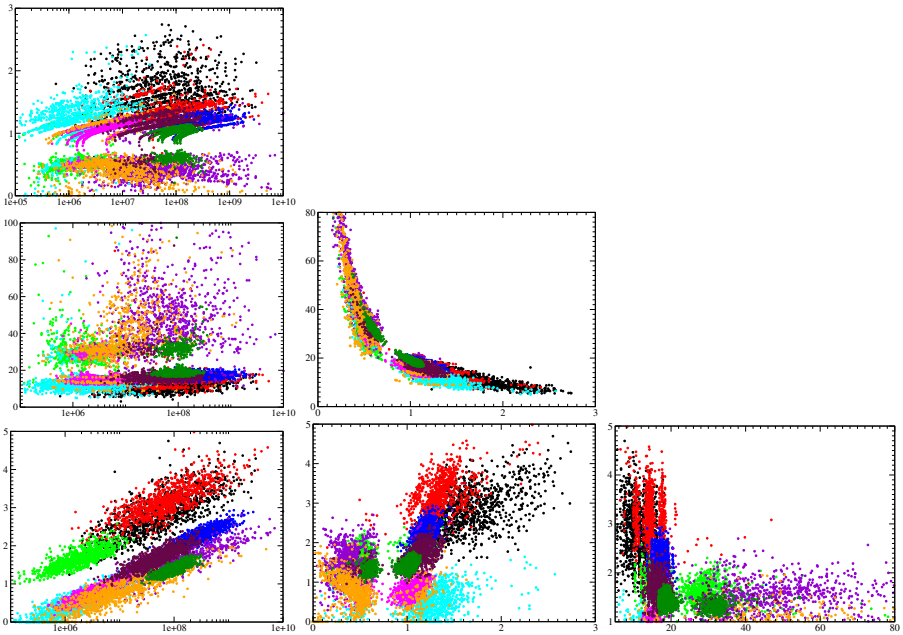

Figure 11: Parameter correlation plots for the empirical model for all animals. The parameter values for each animal are indicated by different colors.

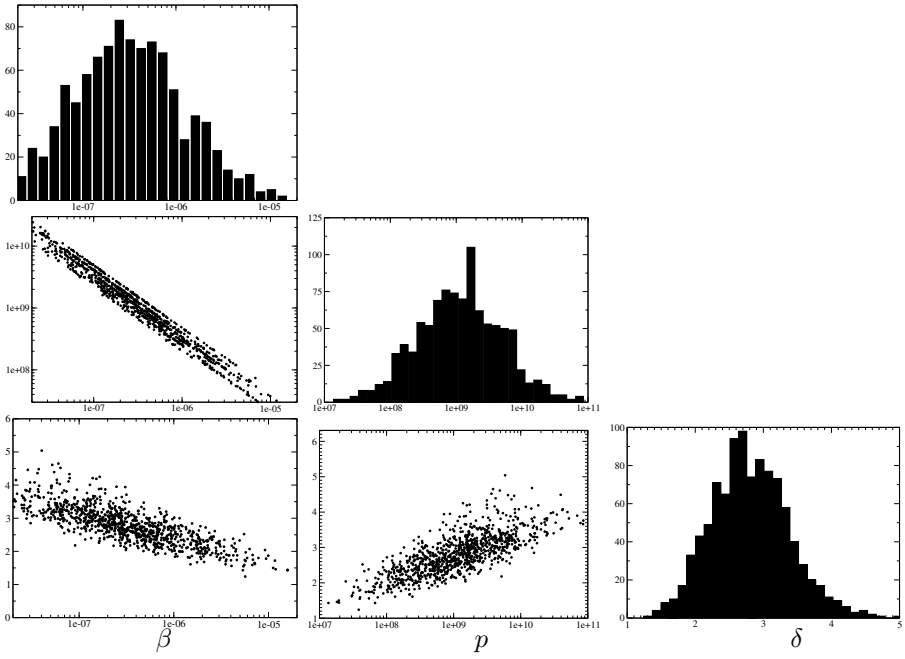

Figure 12: Parameter correlation plots and parameter distributions for viral kinetics model fits to the data from animal 1.

2 Viral kinetics model

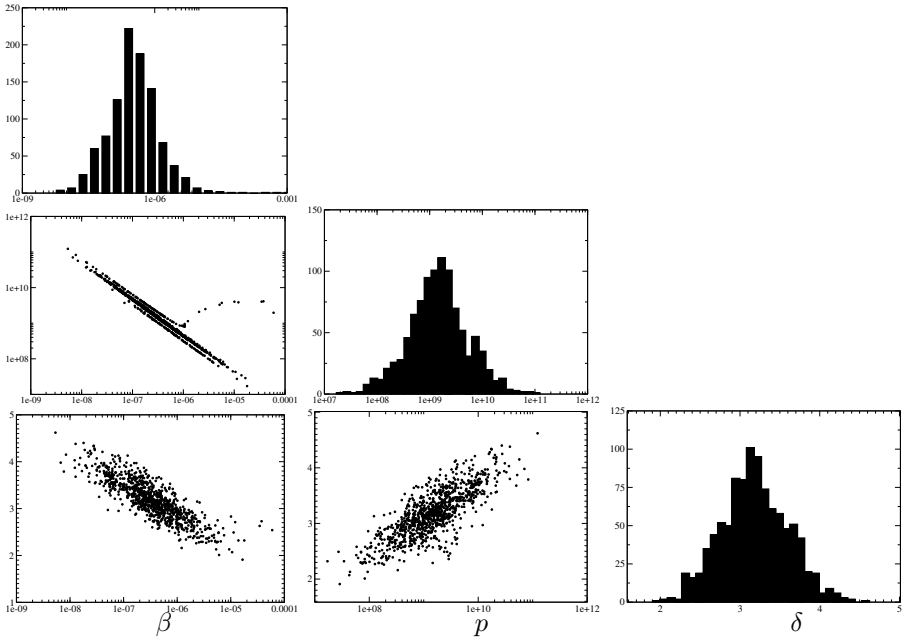

Figure 13: Parameter correlation plots and parameter distributions for viral kinetics model fits to the data from animal 2.

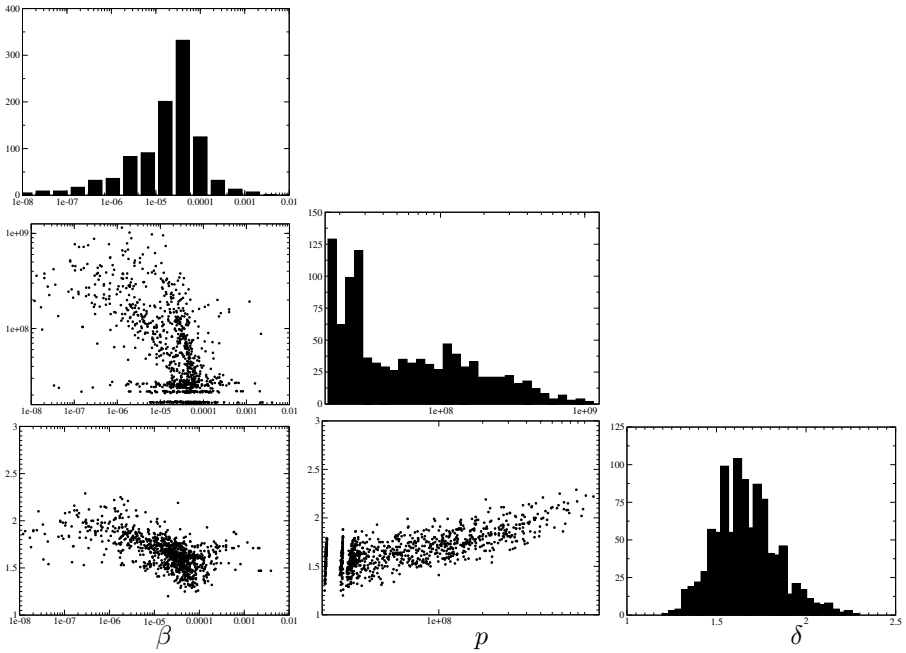

Figure 14: Parameter correlation plots and parameter distributions for viral kinetics model fits to the data from animal 3.

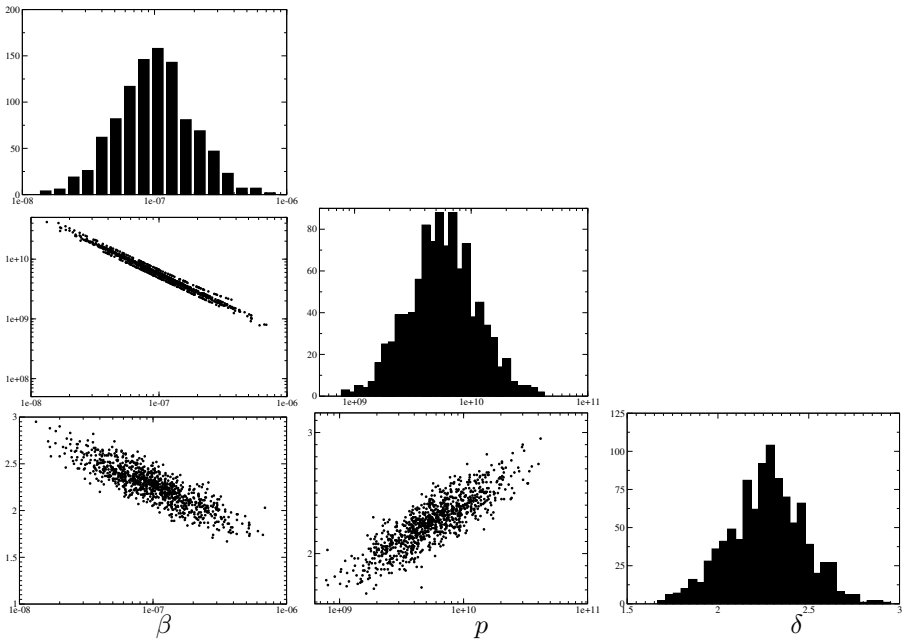

Figure 15: Parameter correlation plots and parameter distributions for viral kinetics model fits to the data from animal 4.

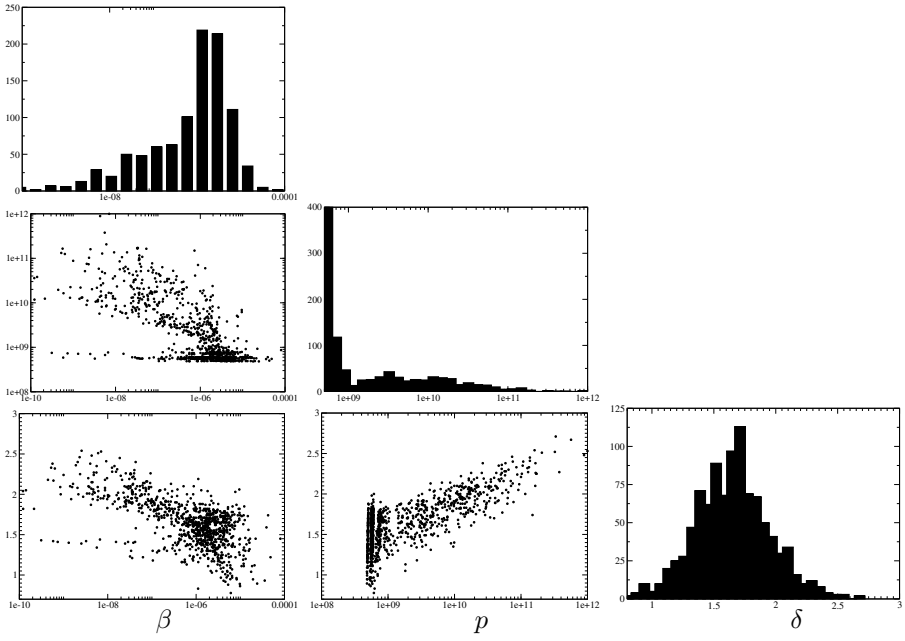

Figure 16: Parameter correlation plots and parameter distributions for viral kinetics model fits to the data from animal 5.

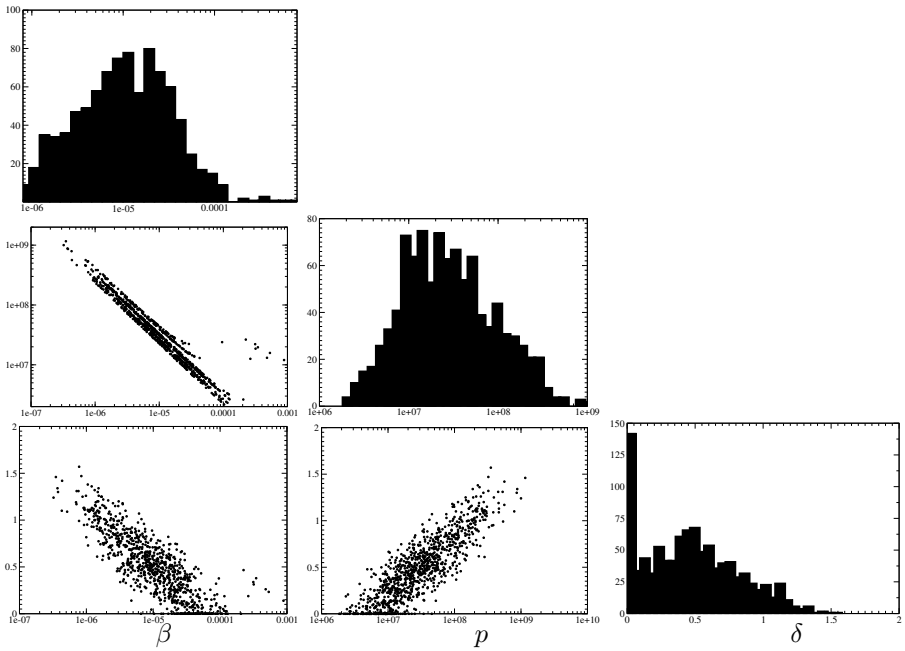

Figure 17: Parameter correlation plots and parameter distributions for viral kinetics model fits to the data from animal 6.

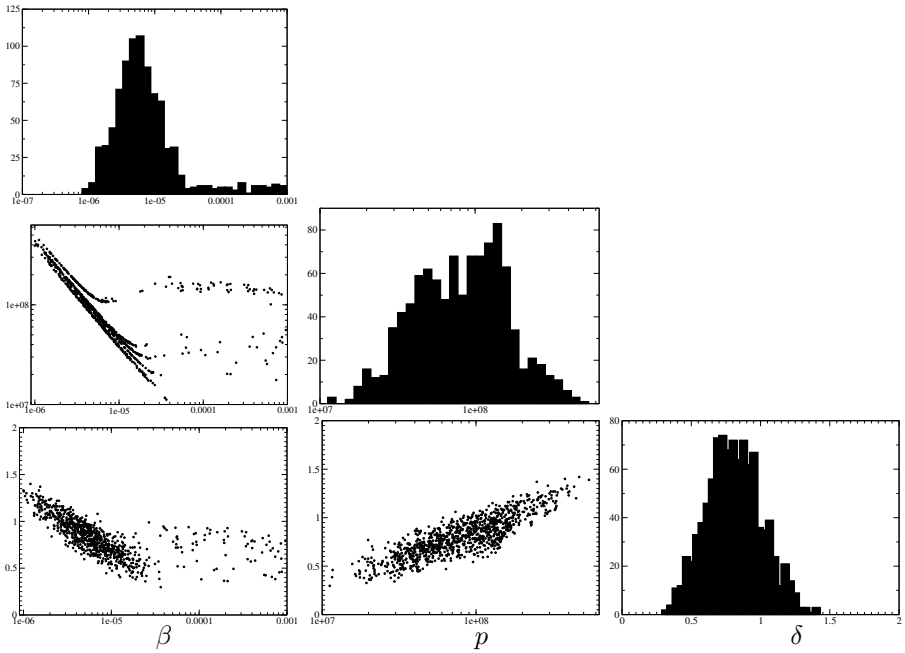

Figure 18: Parameter correlation plots and parameter distributions for viral kinetics model fits to the data from animal 7.

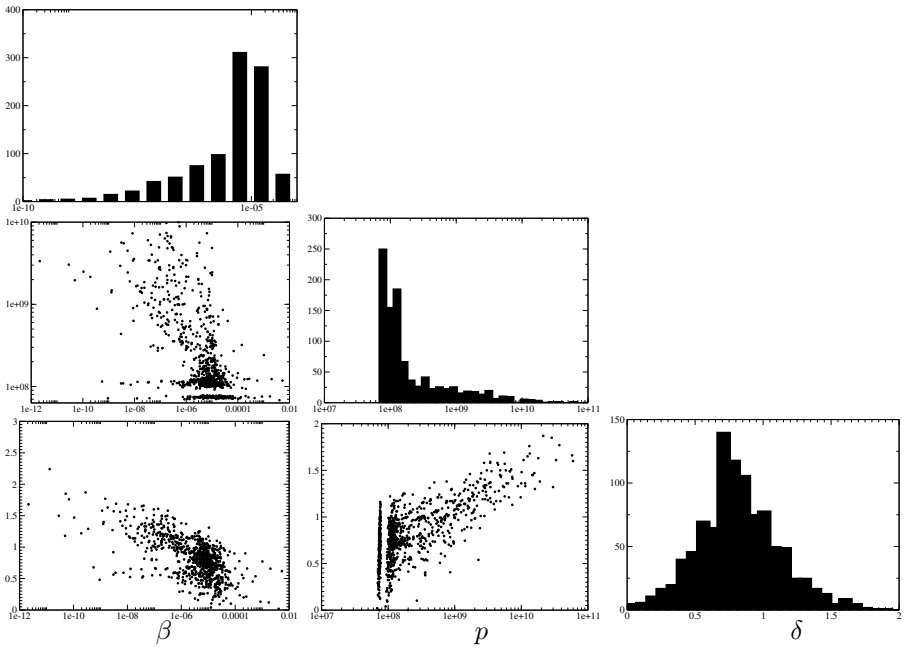

Figure 19: Parameter correlation plots and parameter distributions for viral kinetics model fits to the data from animal 8.

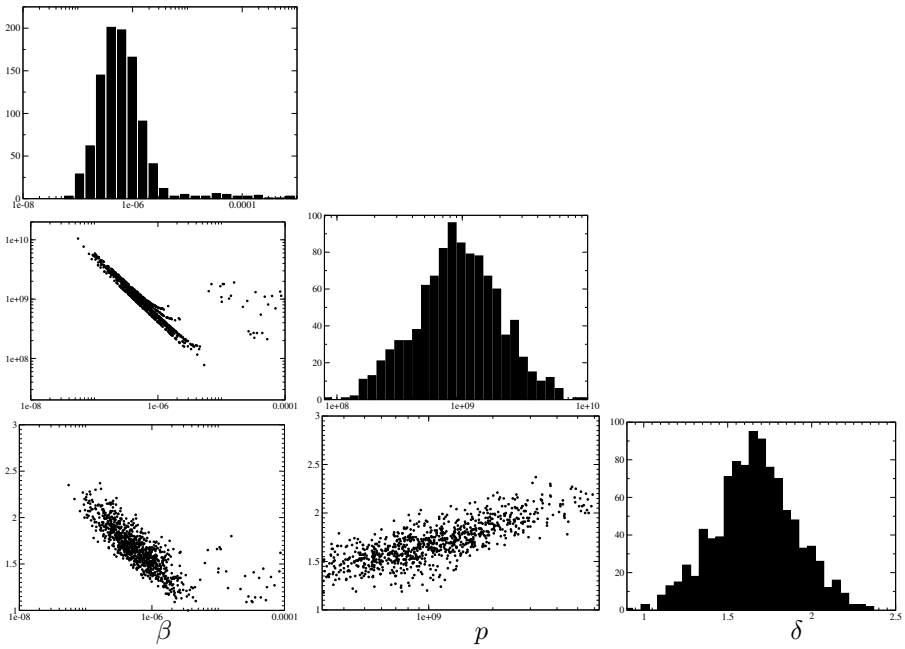

Figure 20: Parameter correlation plots and parameter distributions for viral kinetics model fits to the data from animal 9.

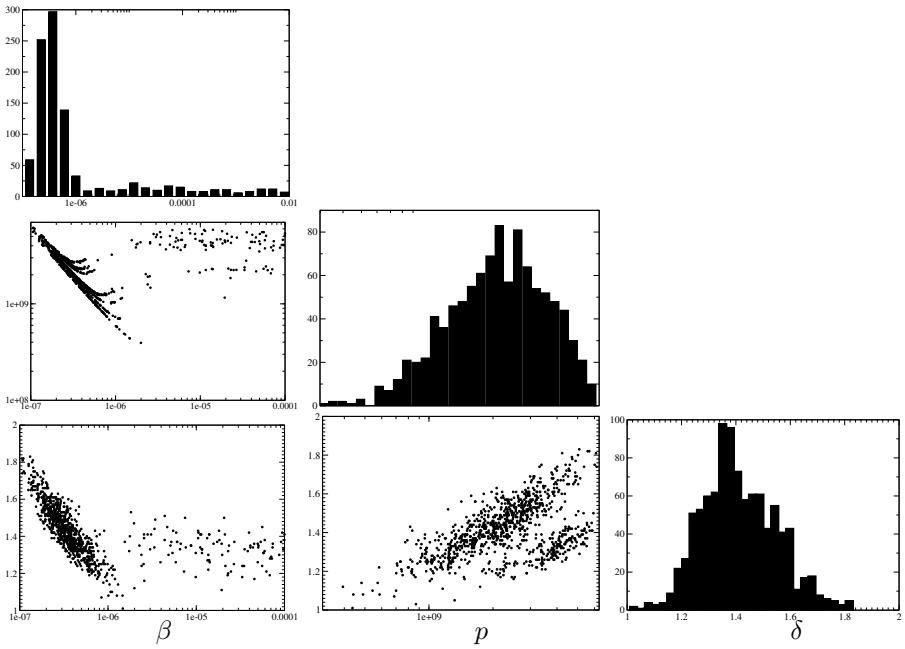

Figure 21: Parameter correlation plots and parameter distributions for viral kinetics model fits to the data from animal 10.

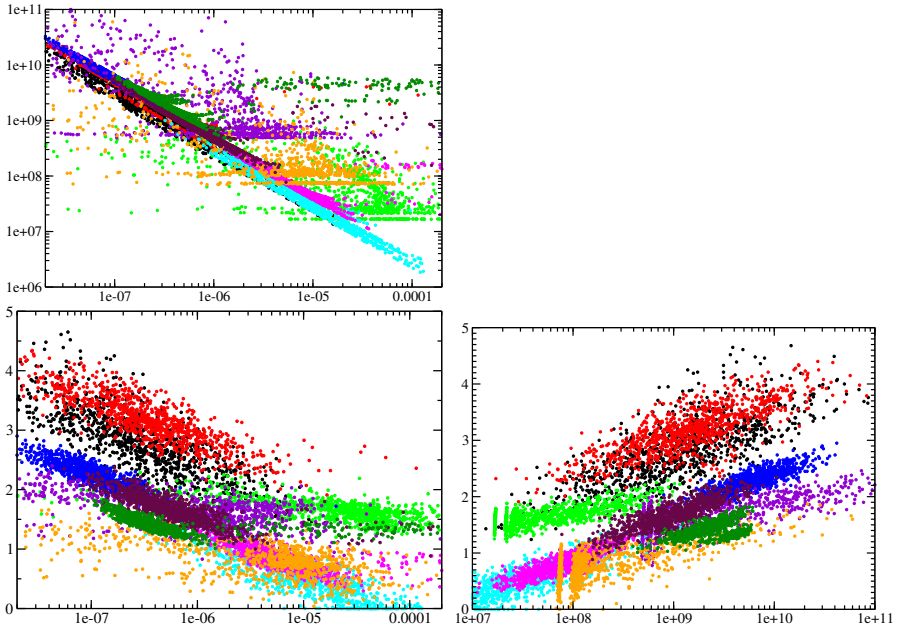

Figure 22: Parameter correlation plots for viral kinetics model fits for all animals. The parameter values for each animal are indicated by different colors.

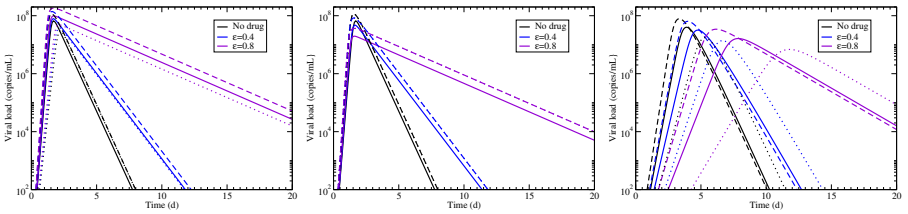

Figure 23: Effect of different values of viral clearance on predicted drug effect curves. Solid lines give the predictions shown in the main text with $c = 10$ /d; dashed lines give predictions for $c = 5$ /d; and dotted lines give predictions for $c = 20$ /d. Left figure is a drug that changes the cell death rate; center figure is a drug that changes infection rate, cell death rate, and production rate; and right figure is a drug that changes k.

Due to the limited amount of data, we fixed the parameter c to 10 /d as in [1]. We assess how this affects the predicted effects of the different drug models presented in the manuscript by running model simulations using $c = 5$ /d and $c = 20$ /d. Results are shown in Fig. 23 that show a drug on δ only (left), a drug on δ, β, and p (center), and a drug on k (right). Solid lines are the original parameters ($c = 10$ /d), dashed lines are the smaller value of viral clearance ($c = 5$ /d), and dotted lines are the larger value of viral clearance ($c = 20$ /d). In all cases, the viral decay rate is the same for the different values of c. We do, however, observe a shift in the timing and height of the peak viral titer, although the general trend as amount of drug is increased remains the same.

References

[1] A. Gonçalves, J. Bertrand, R. Ke, E. Comets, X. de Lamballerie, D. Malvy, A. Pizzorno, O. Terrier, M. R. Calatrava, F. Mentré, P. Smith, A. S. Perelson, J. Guedj, Timing of antiviral treatment initiation is critical to reduce SARS-CoV-2 viral load, medRXivdoi:10.1101/2020.04.04.20047886.