

Supplemental File S2

Dynamic regulation of JAK-STAT signaling through the prolactin receptor predicted by computational modeling

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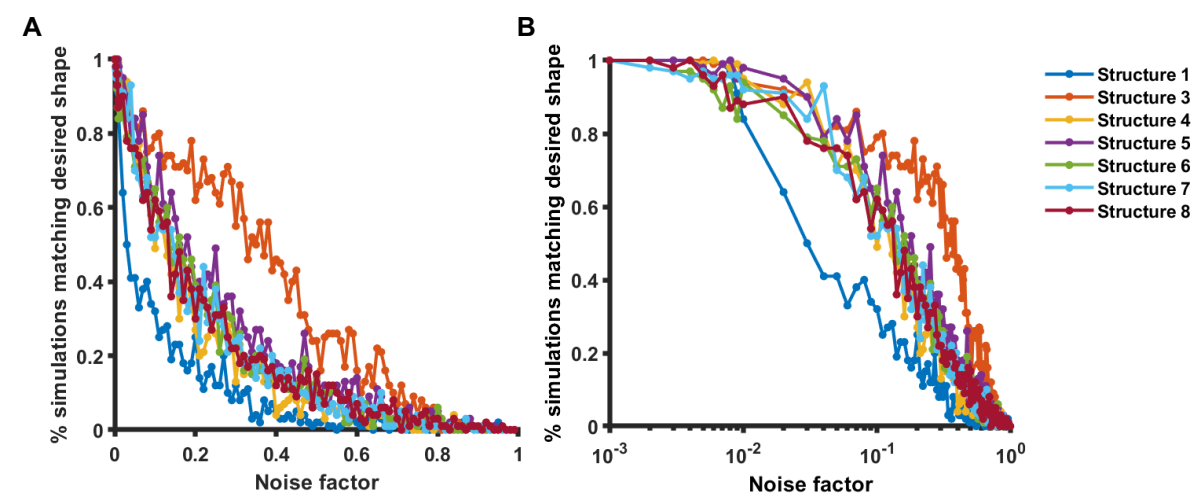
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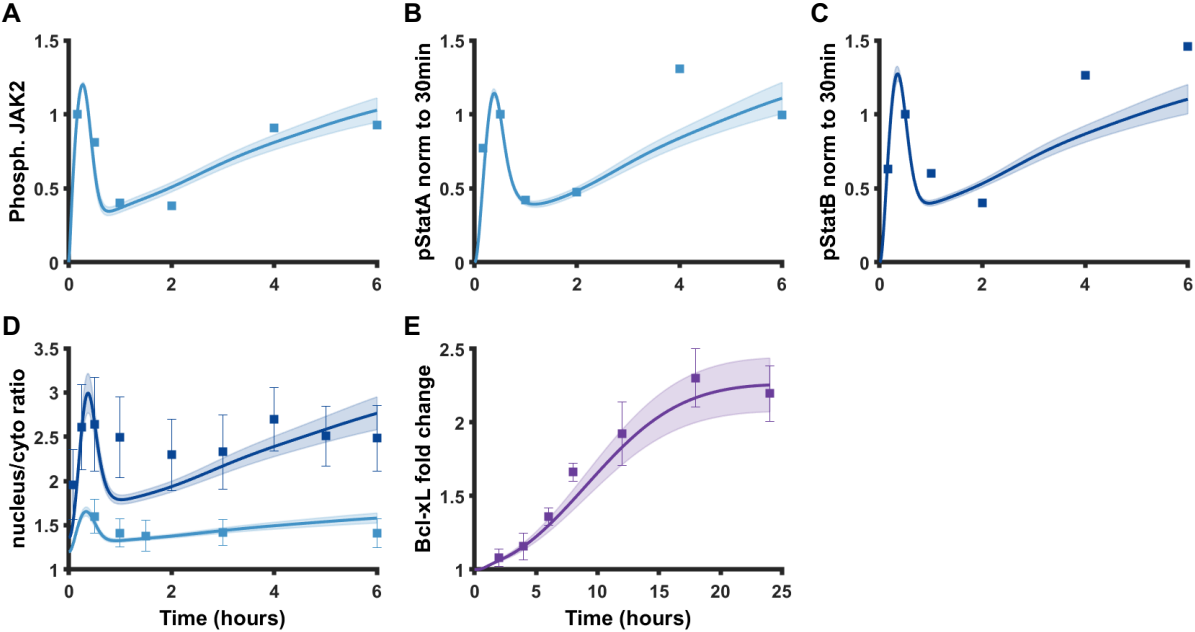
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Figure S2: Robustness of Monte Carlo Simulations. For each model structure which had some simulations matching the desired shape (Fig. 4), we added a specified noise factor (x) to each parameter value, representing $\pm x\%$ of the parameter value. We repeated 100 times at each value of the noise factor and quantified what percentage of simulations still matched the desired qualitative shape of STAT5 activation. **(A)** Results are for each model structure. **(B)** Results for each model structure with log-scale on the y-axis.



Figures S3: Model Calibration for Model Structure 5. Lines show mean value of model predictions with shading showing the standard. The letters in the top left correspond to which of the regulatory modules from Fig. 1 are included. Squares show experimental data points from Brelje *et al.* for panels A, B, C, and D or from Fujinaka *et al.* for panel E. Error bars are included for experimental data points that had error bars shown in the previously published work. All experimental data is for INS-1 cells treated with PRL at 200 ng/mL. *Dark blue*, STAT5A; *light blue*, STAT5B in panel D.

a b -



Figures S4: Model Calibration for Model Structure 7. Lines show mean value of model predictions with shading showing the standard. The letters in the top left correspond to which of the regulatory modules from Fig. 1 are included. Squares show experimental data points from Brelje *et al.* for panels A, B, C, and D or from Fujinaka *et al.* for panel E. Error bars are included for experimental data points that had error bars shown in the previously published work. All experimental data is for INS-1 cells treated with PRL at 200 ng/mL. *Dark blue*, STAT5A; *light blue*, STAT5B in panel D.

- b c

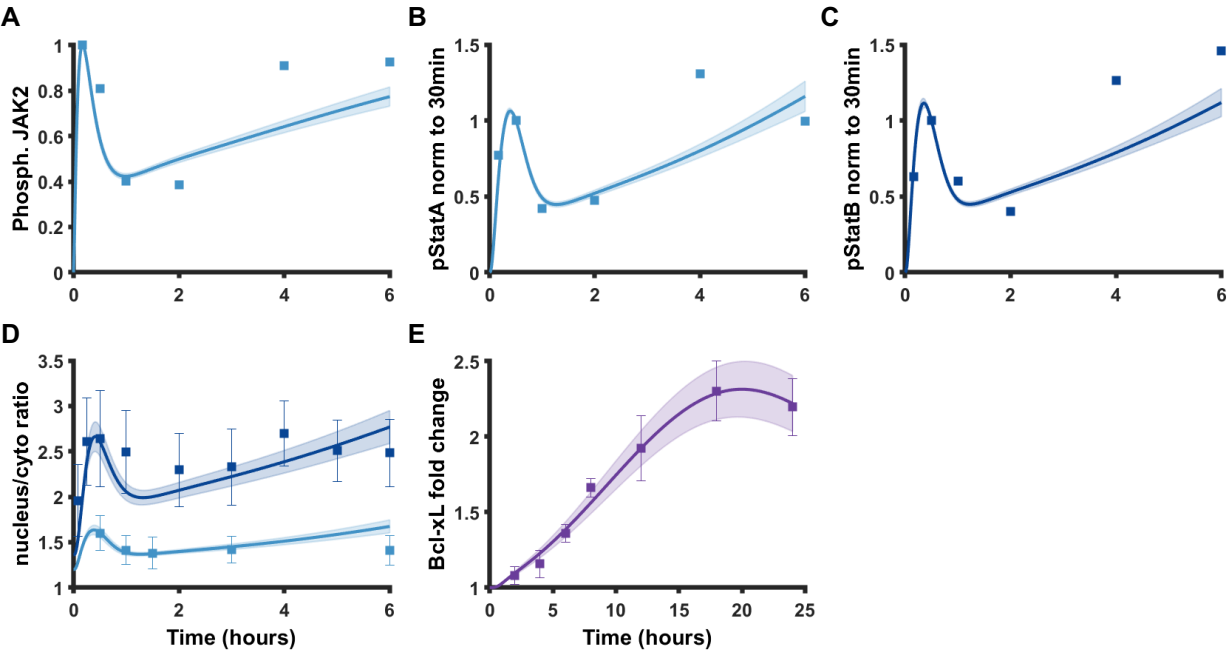
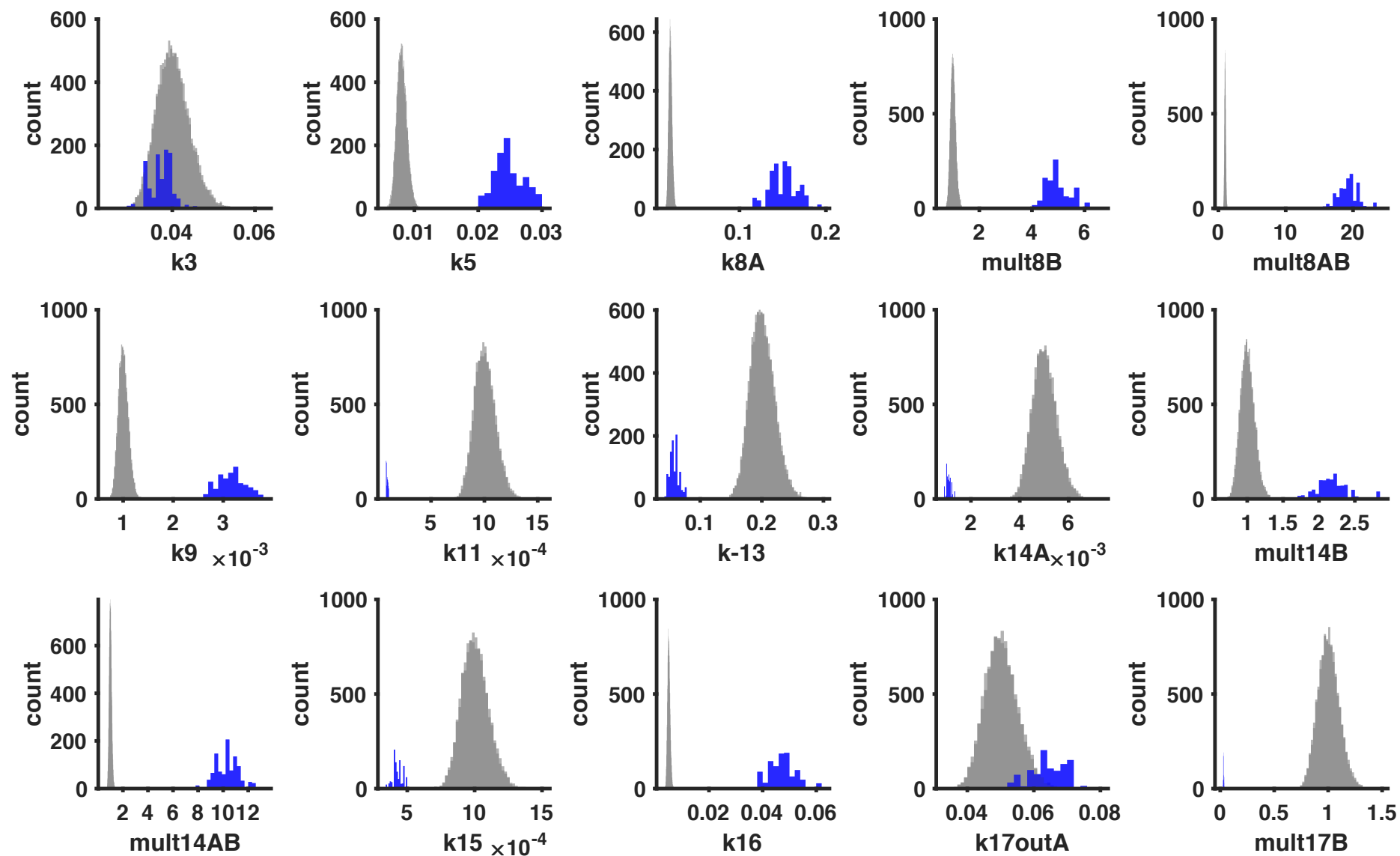
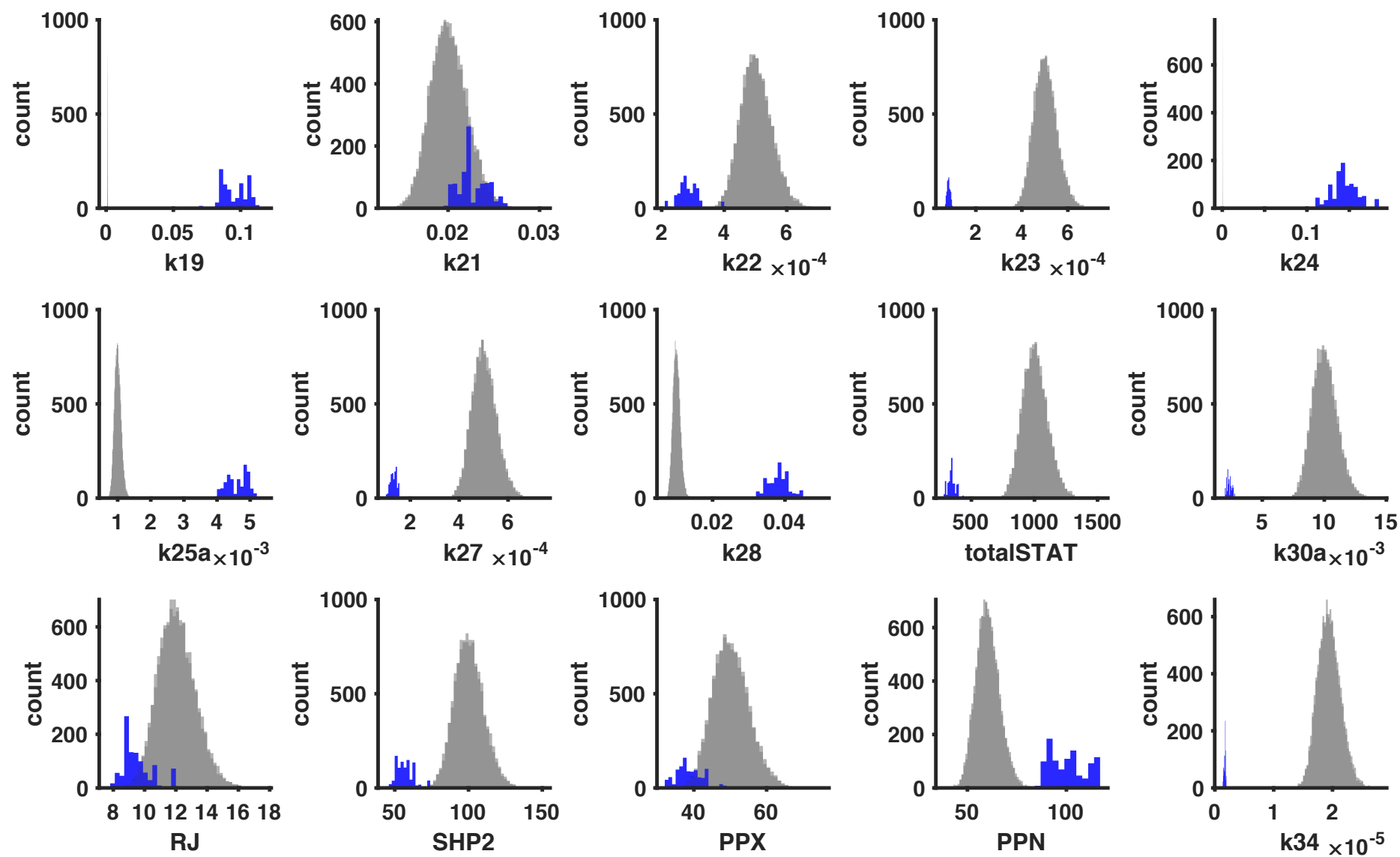


Figure S5: Parameter Value Distributions from Best-Fit Likelihood Estimation for Structure 5. Histograms showing the posterior distribution of each parameter value from the last 1,000 iterations of Bayesian estimation, shown for the independent fit with the second lowest error for structure 5 (see Methods section).





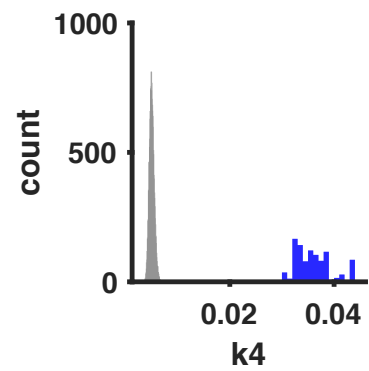
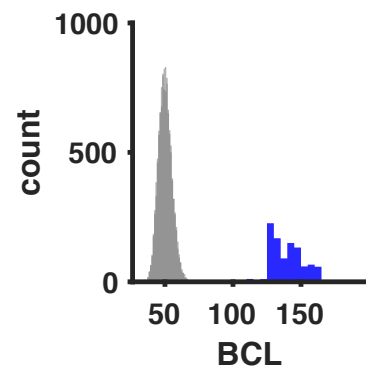
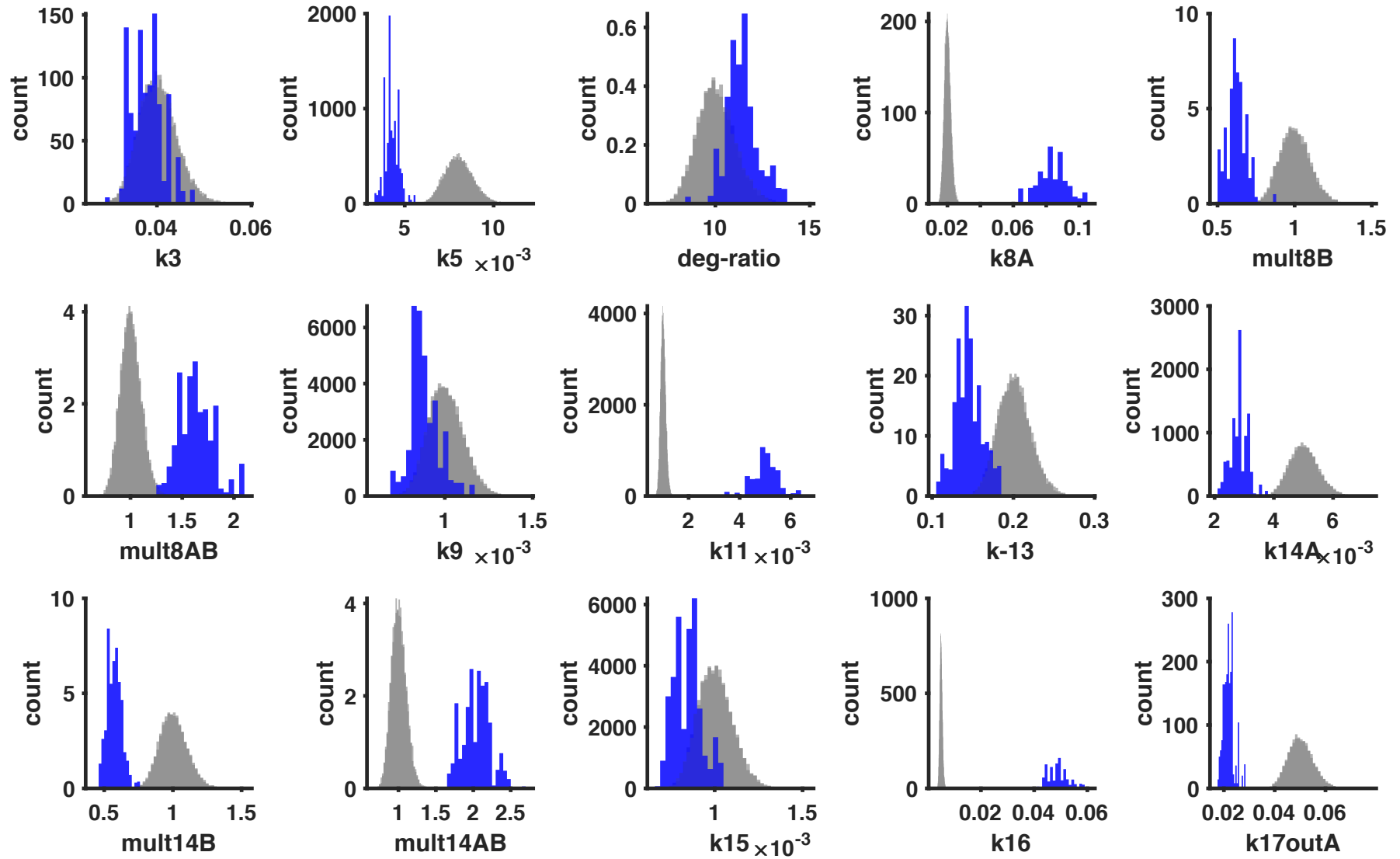


Figure S6: Parameter Value Distributions from Best-Fit Likelihood Estimation for Structure 7. Histograms showing the posterior distribution of each parameter value from the last 1,000 iterations of Bayesian estimation, shown for the independent fit with the lowest error for structure 7.



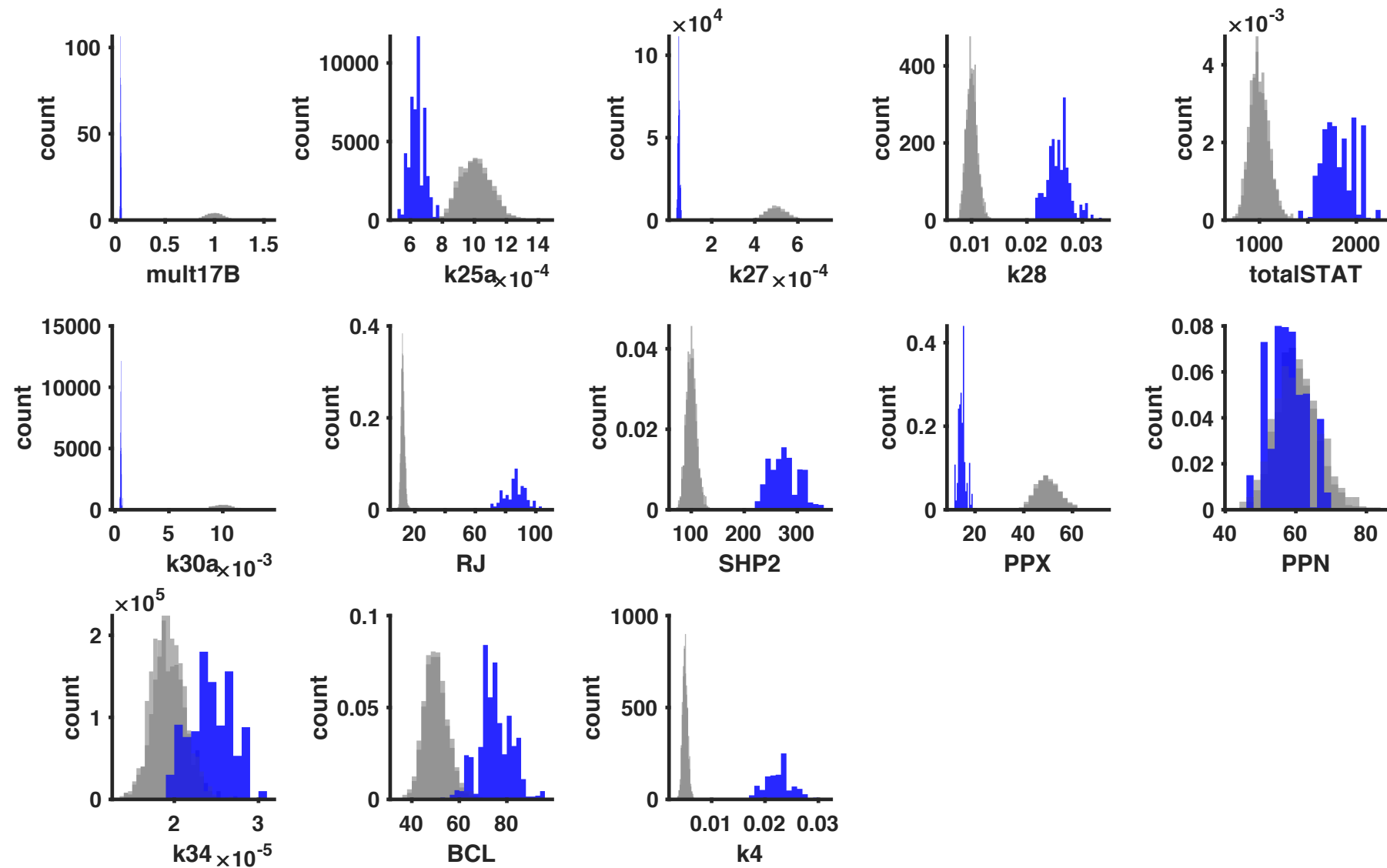
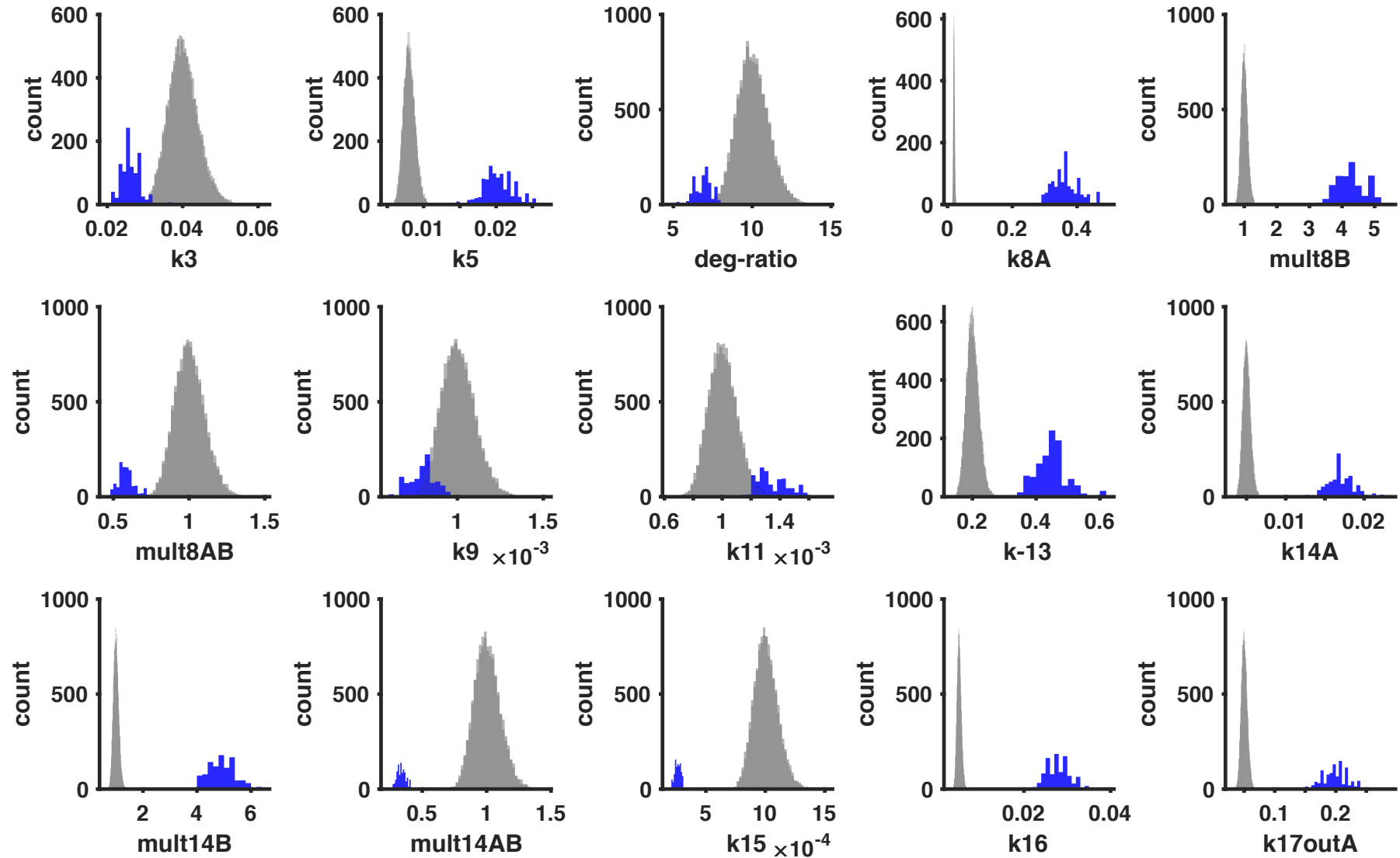
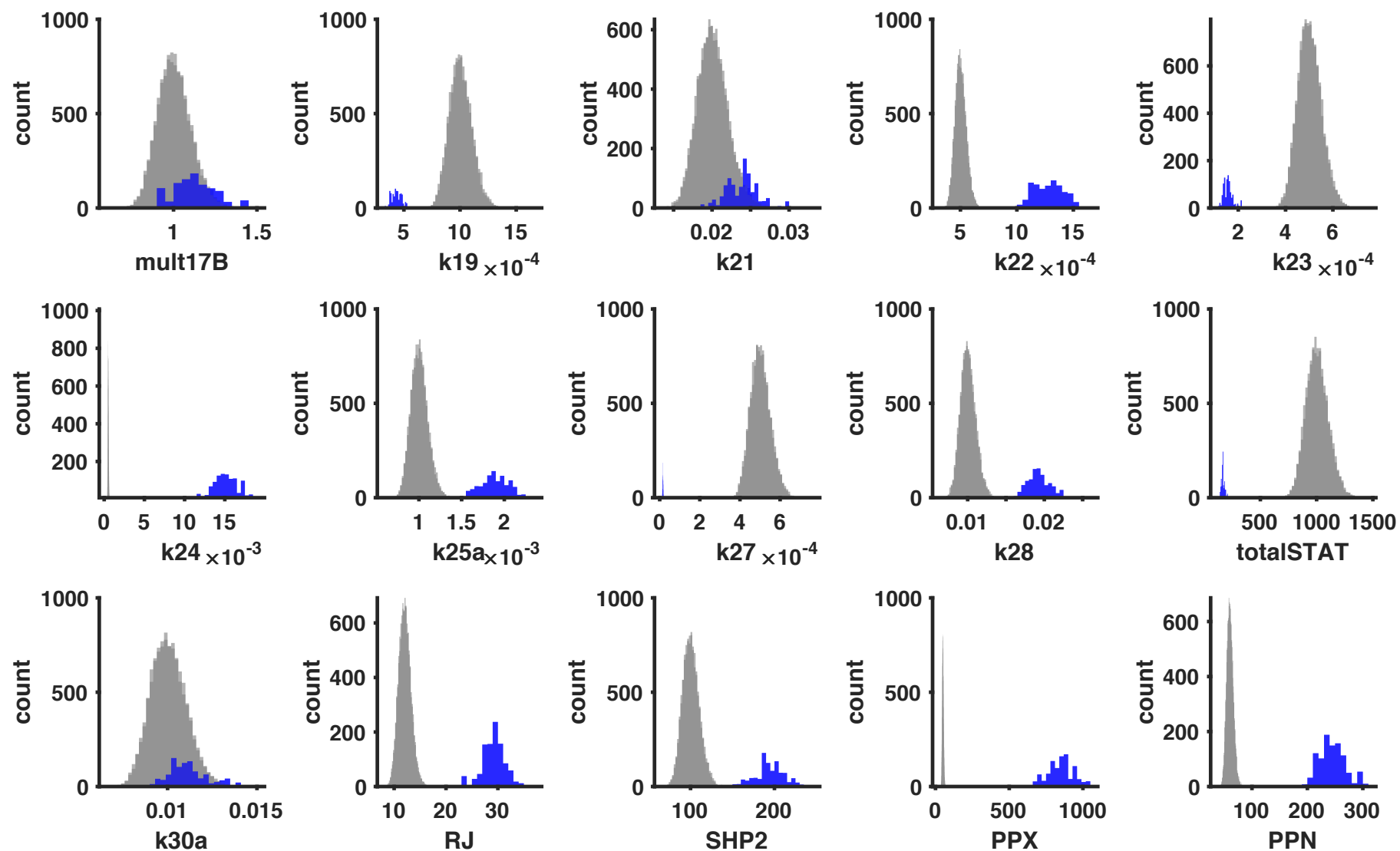


Figure S7: Parameter Value Distributions from Best-Fit Likelihood Estimation for Structure 8. Histograms showing the posterior distribution of each parameter value from the last 1,000 iterations of Bayesian estimation, shown for the independent fit with the lowest error for structure 8.





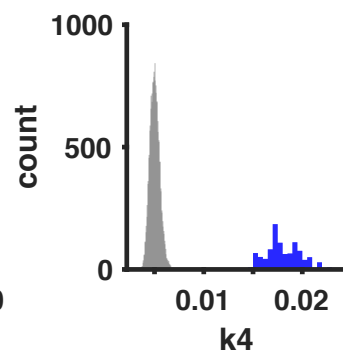
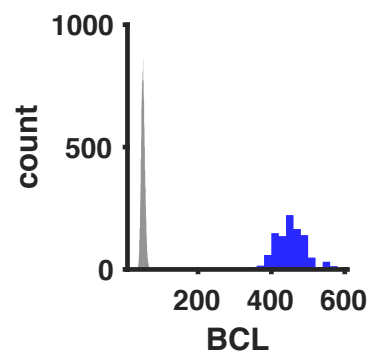
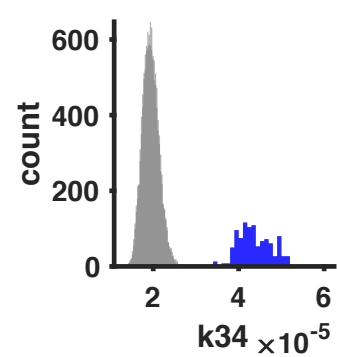
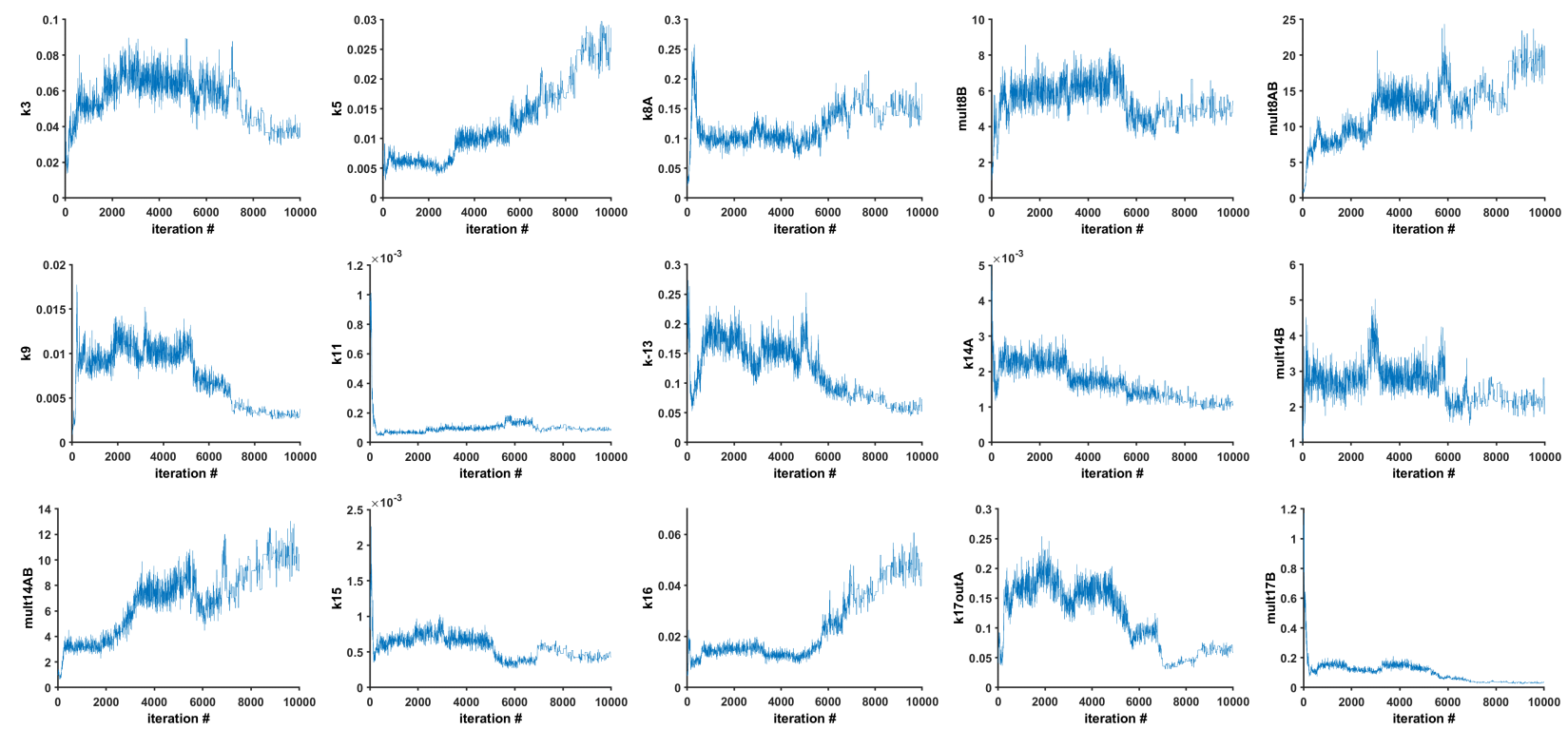


Figure S8: Parameter Trace Plots for Structure 5. Trace plots showing the value of each parameter over the course of 10,000 iterations of Bayesian estimation, shown for the independent fit with the lowest error for structure 5.



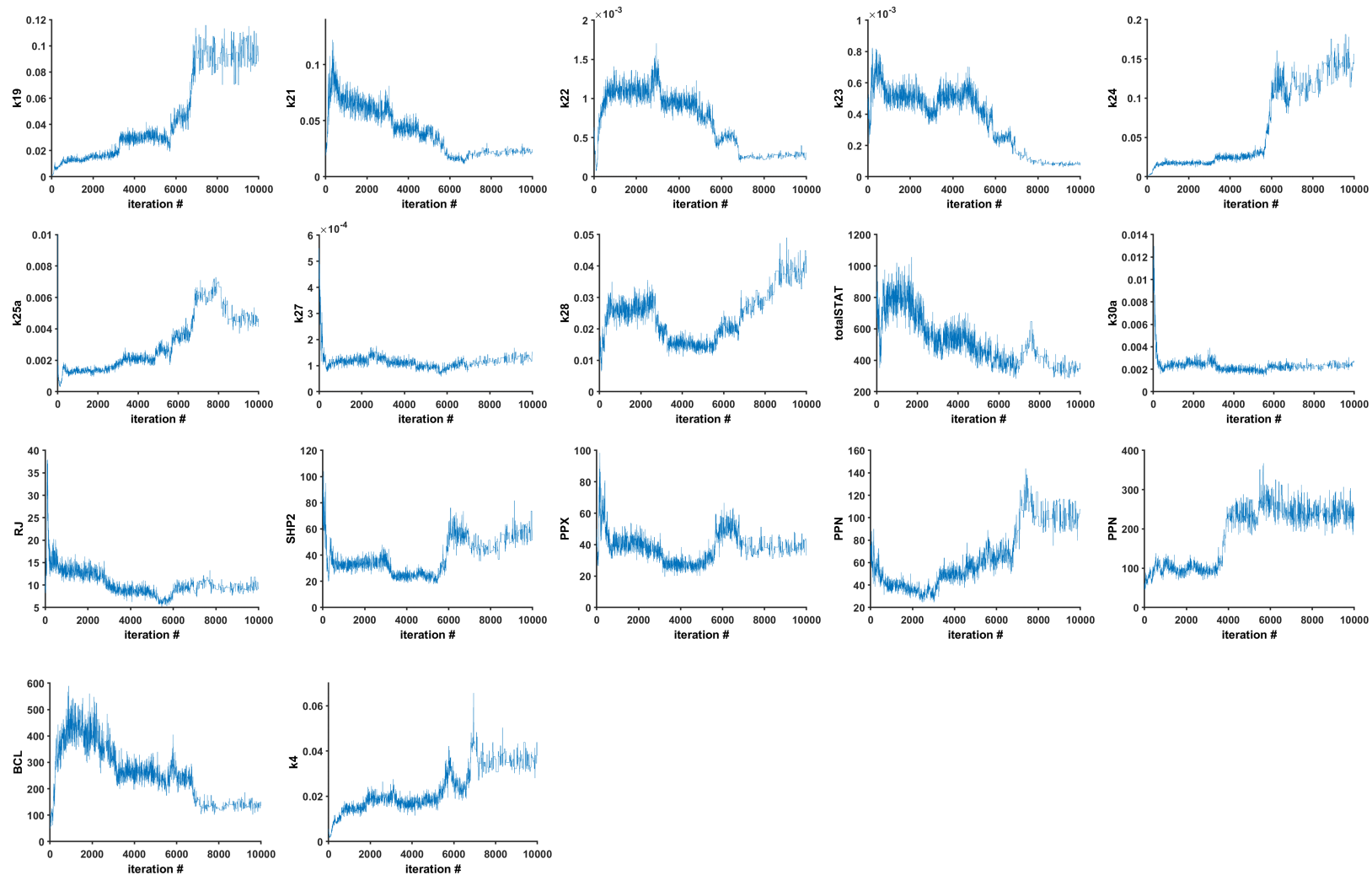
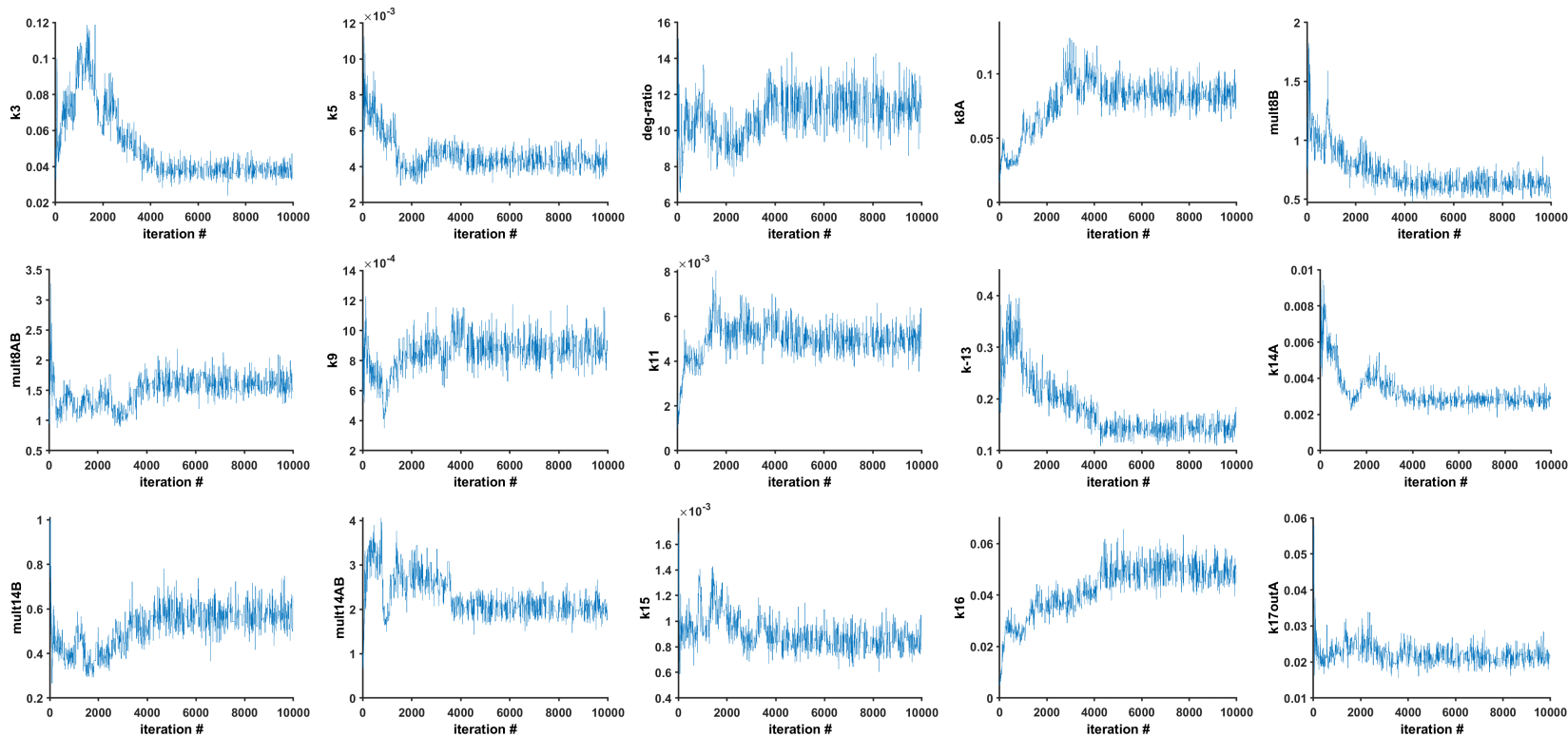


Figure S9: Parameter Trace Plots for Structure 7. Trace plots showing the value of each parameter over the course of 10,000 iterations of Bayesian estimation, shown for the independent fit with the lowest error for structure 7.



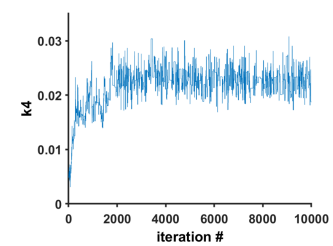
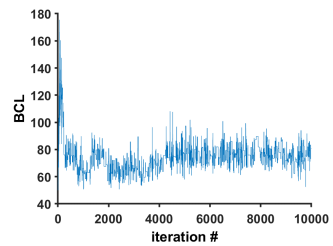
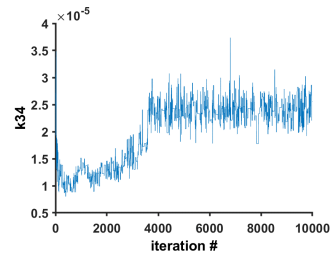
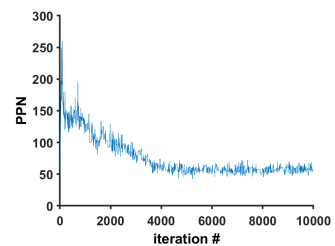
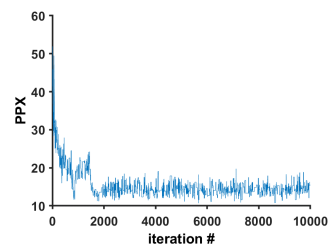
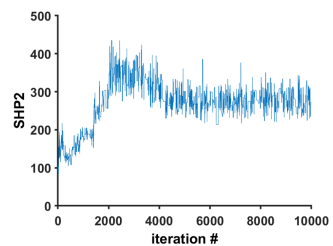
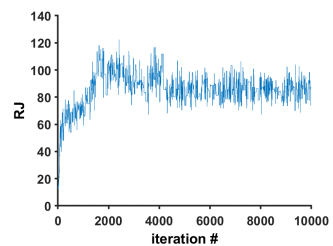
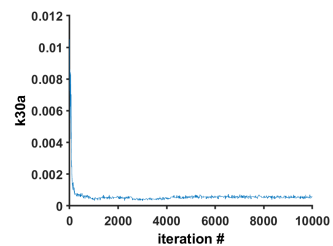
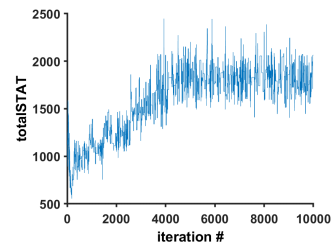
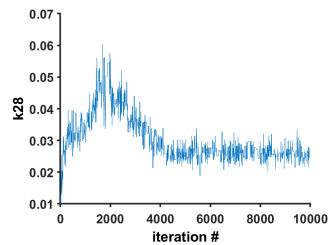
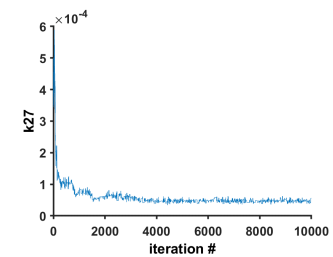
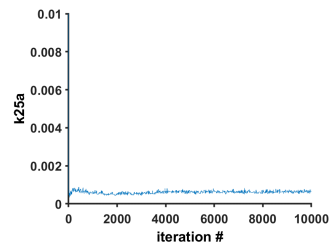
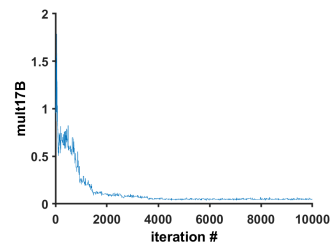
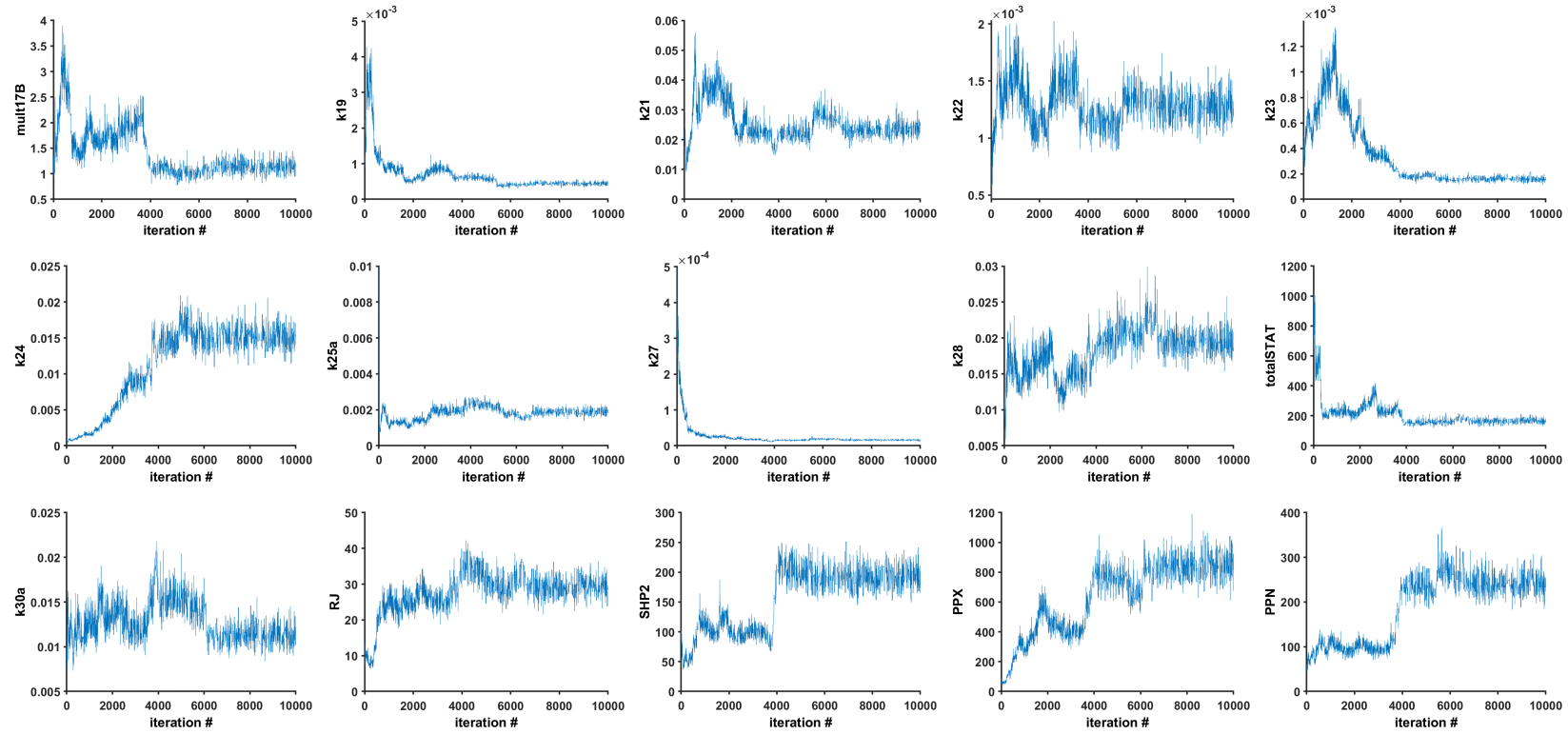


Figure S10: Parameter Trace Plots for Structure 8. Trace plots showing the value of each parameter over the course of 10,000 iterations of Bayesian estimation, shown for the independent fit with the second lowest error for structure 8 (see Methods section).



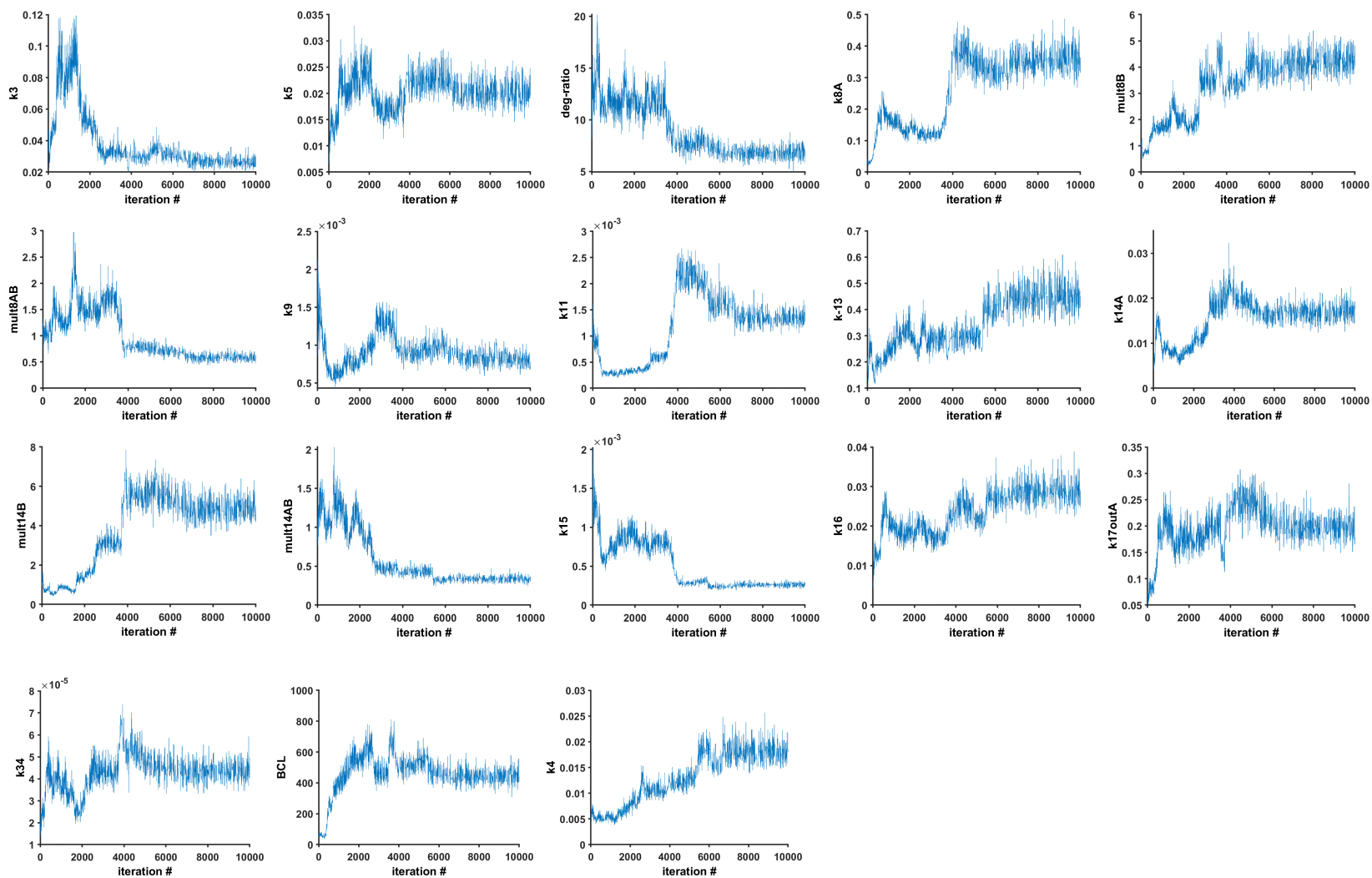


Figure S11: Error Values for 50 Independent Fits for Each Model Structure. Histogram showing the distribution of error values for 50 independent fits (left). The error value plotted against the number of fits, ranked by lowest error (right). **(A)** Model structure 5, **(B)** Module structure 7, **(C)** Model structure 8.

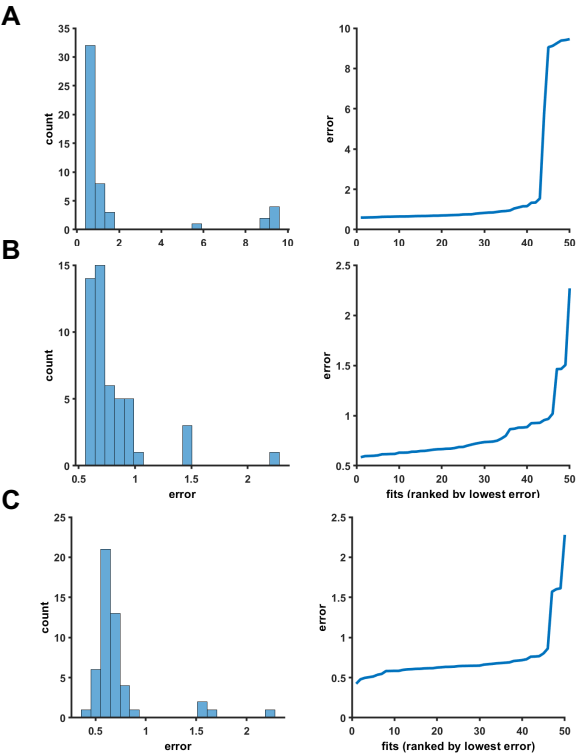


Figure S12: Effect of Varying Single Parameters on Model Predictions. Each of the parameters (**Panel A**, k_2 ; **Panel B**, k_{12}) or initial values (**Panel C**, PPX ; **Panel D**, RJ) were varied one order of magnitude smaller and larger than the fitted value in order to evaluate how perturbations to single parameter values affect model predictions. Lines indicate the mean model prediction from the 1,000 posterior parameter sets. STAT5A predictions are shown separately from STAT5B for ease of viewing. *Dark blue*, STAT5A; *light blue*, STAT5B; *purple*, Bcl-xL. Note the different y-axis limits for Panel D.

