

# **1 E. coli metabolism point model Simulations with alpha = 0, beta = 0**

**E. coli metabolism model with artificial data (noise-free kinetic data, noise-free state data) - alpha = 0, beta = 0**

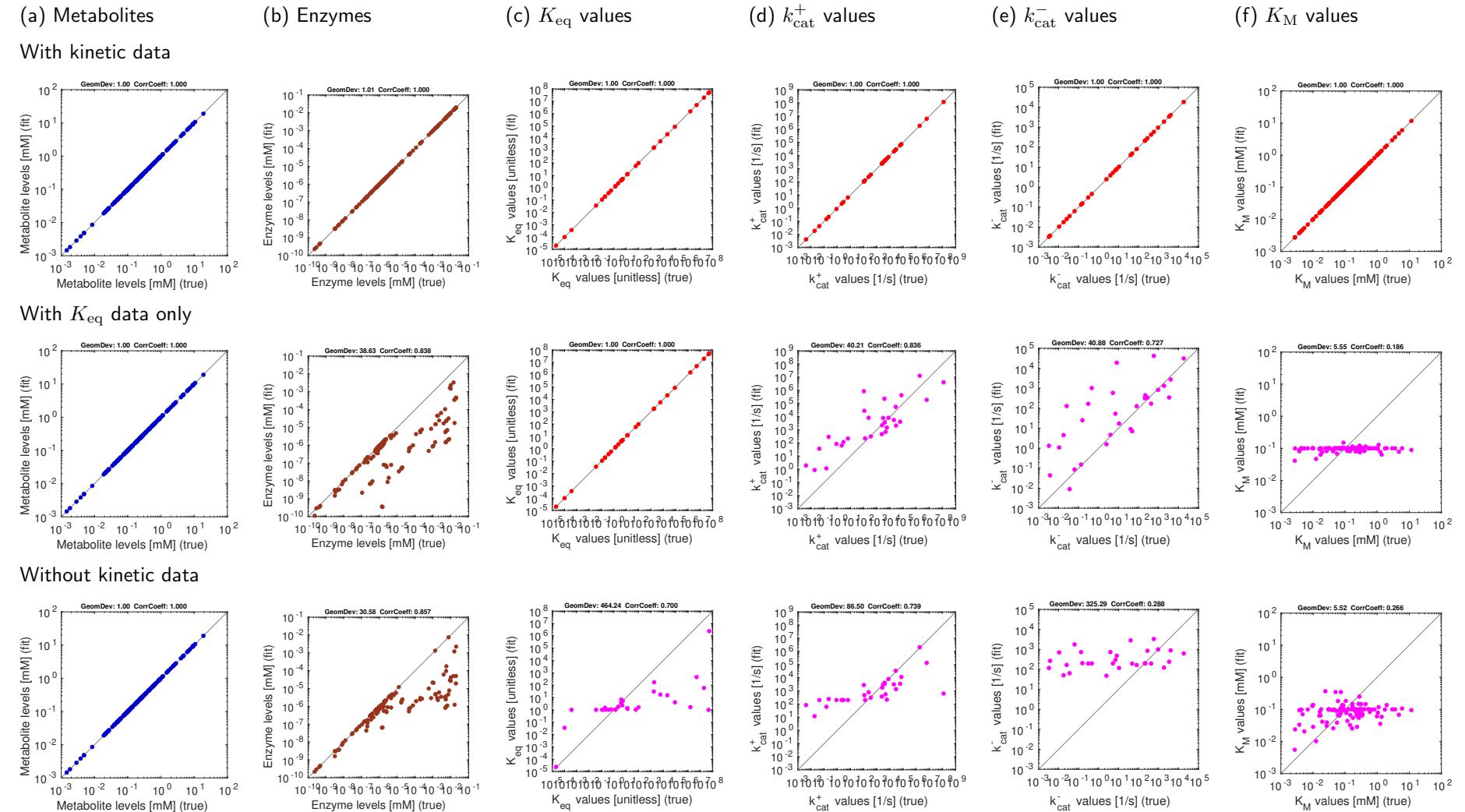
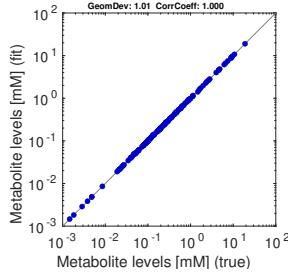


Figure 3: Model balancing results for E. coli metabolism model with artificial data. The model structure is shown in Figure ???. Each subfigure shows “true” values (x-axis) versus reconstructed values (y-axis). Similarities are quantified by geometric standard deviations (“GeomDev”) and Pearson correlation coefficients (“CorrCoeff”). (a) Metabolite levels. (b) Enzyme levels. (c)-(f) Different types of kinetic constants. Rows show different estimation scenarios (see Figure ) Upper row: simple scenario S1 (noise-free artificial data, data for kinetic constants). Centre row: scenario S1K (noise-free artificial data, kinetic data given only for equilibrium constants). Lower row: scenario S2 (noise-free artificial data, no data for kinetic constants). Depending on the scenario, kinetic constants are either fitted (red dots) or predicted (magenta dots).

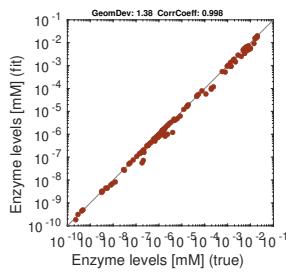
**E. coli metabolism model with artificial data (noisy kinetic data, noise-free state data) - alpha = 0, beta = 0**

(a) Metabolites

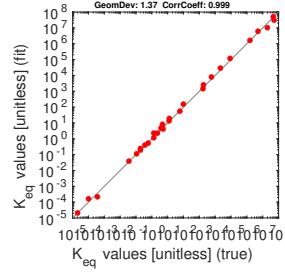
With kinetic data



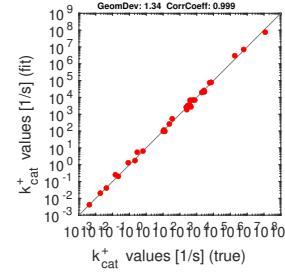
(b) Enzymes



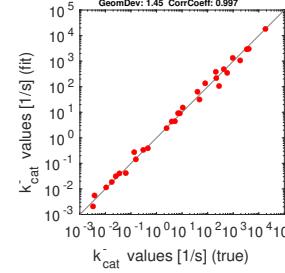
(c)  $K_{eq}$  values



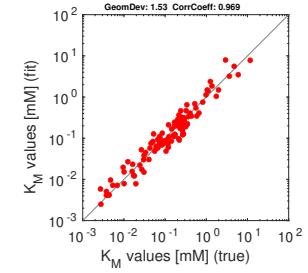
(d)  $k_{cat}^+$  values



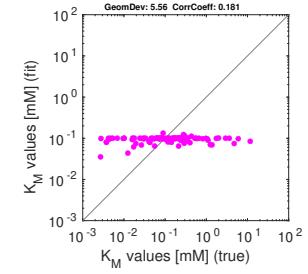
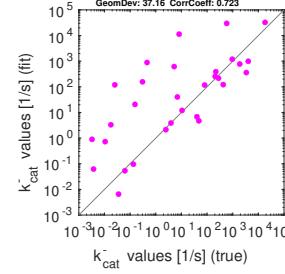
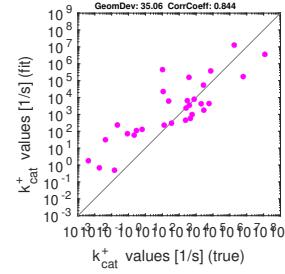
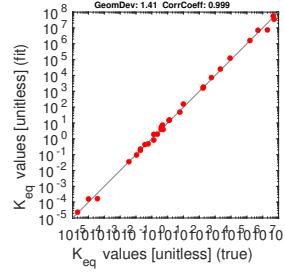
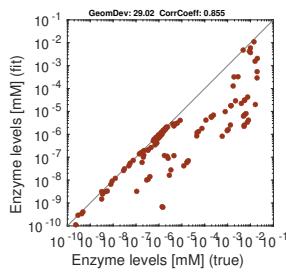
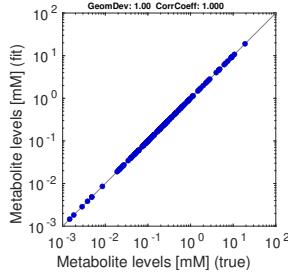
(e)  $k_{cat}^-$  values



(f)  $K_M$  values



With  $K_{eq}$  data only



Without kinetic data

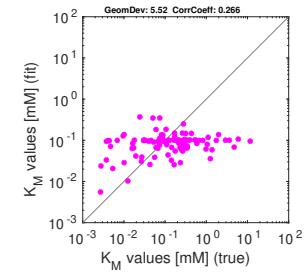
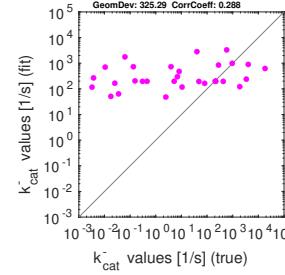
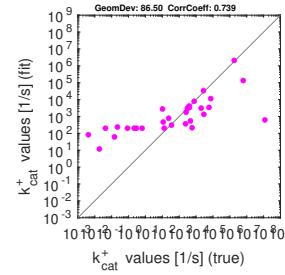
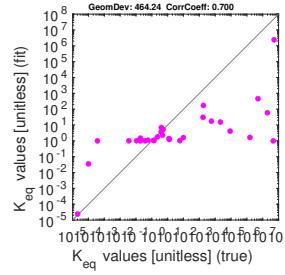
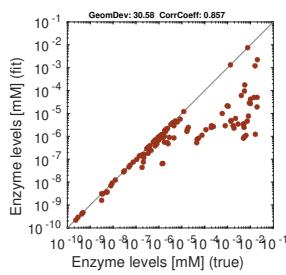
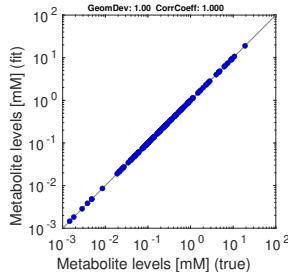


Figure 4: Same as Figure 13, with noisy kinetic data

**E. coli metabolism model with artificial data (noise-free kinetic data, noisy state data) - alpha = 0, beta = 0**

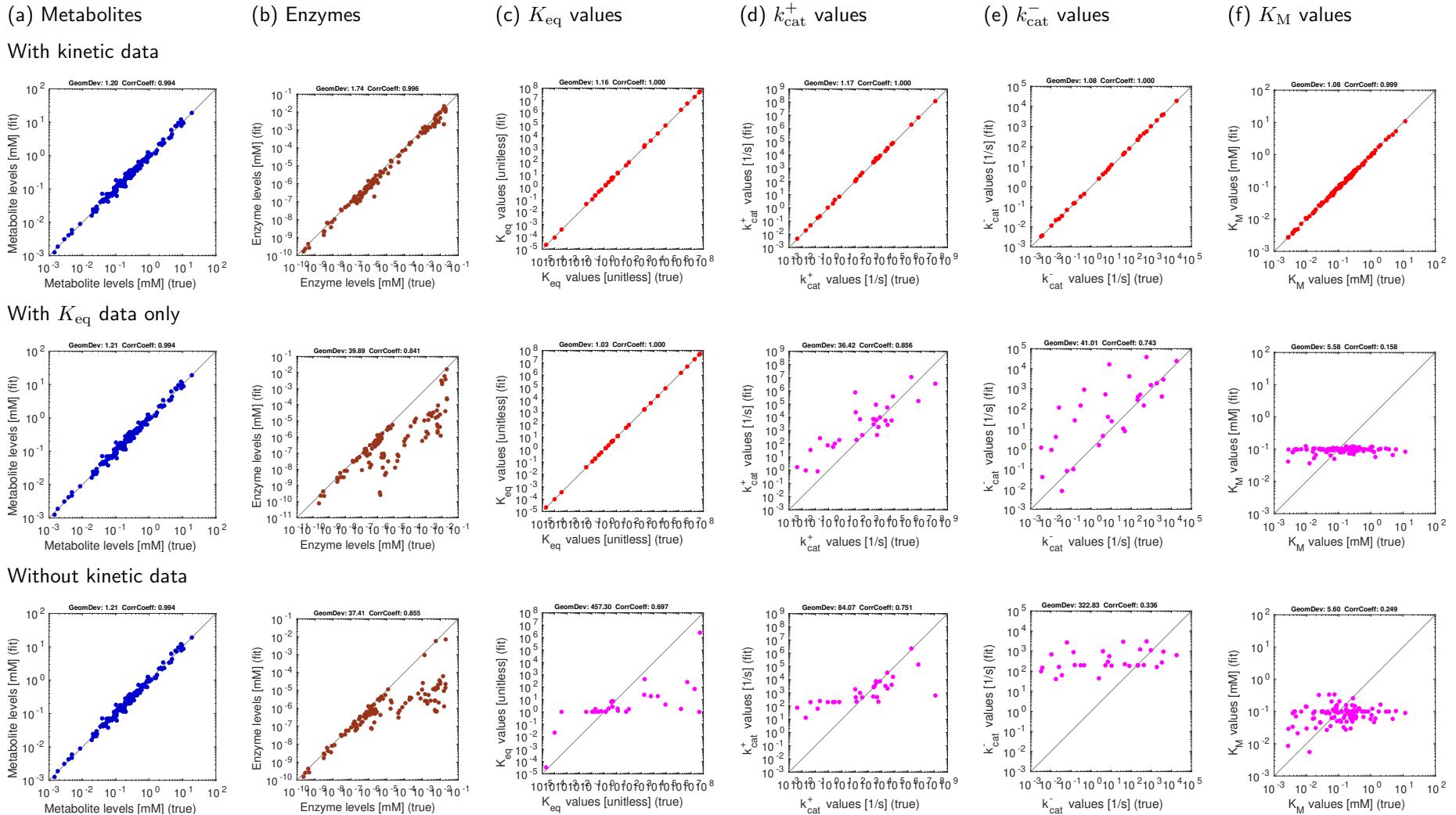


Figure 5: Results for E. coli metabolism with noisy artificial data. Top row: estimation scenario S3 (noisy artificial data, data used for kinetic constants). Centre row: estimation scenario S3K (noisy artificial data, data for equilibrium constants only). Bottom row: estimation scenario S4 (noisy artificial data, no data for kinetic constants).

**E. coli metabolism model with artificial data (noisy kinetic data, noisy state data) - alpha = 0, beta = 0**

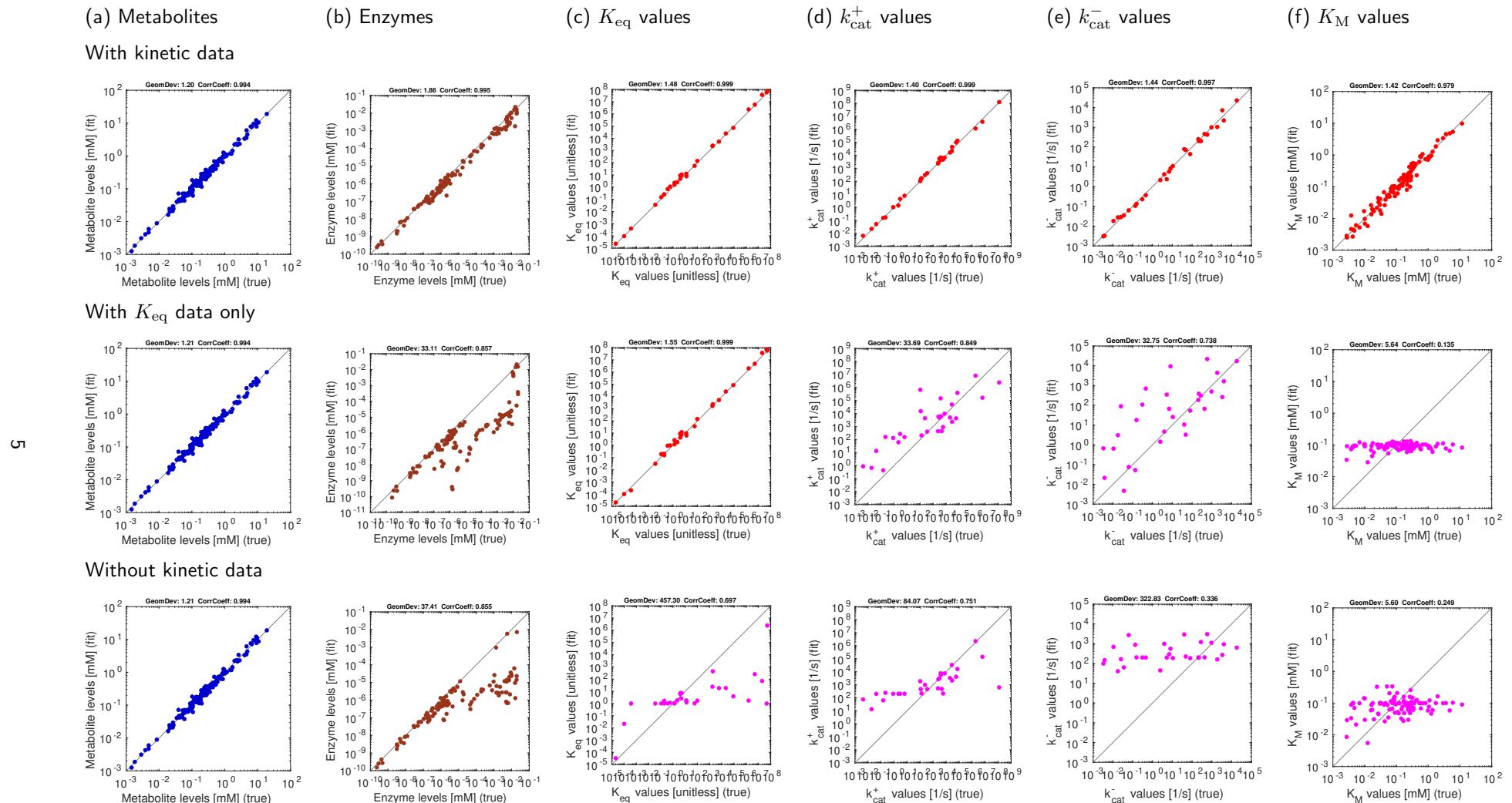


Figure 6: Same as Figure 15, with noisy kinetic data

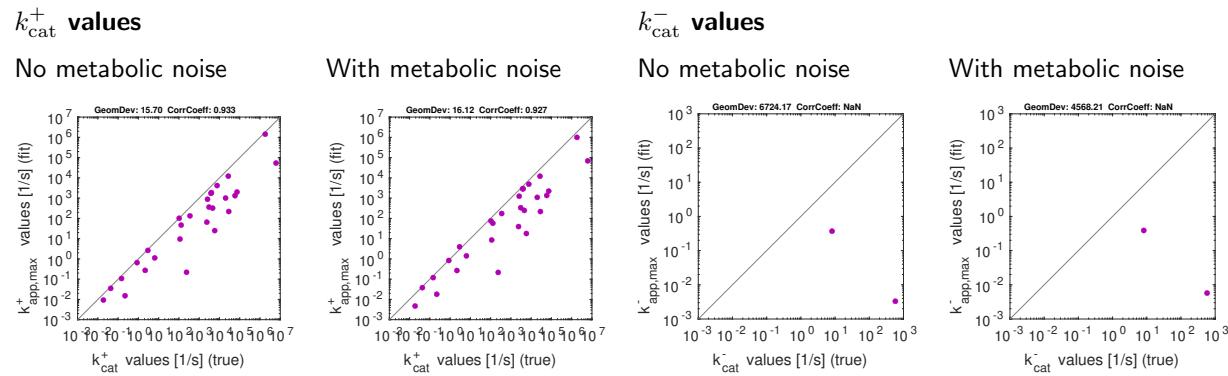


Figure 7: Catalytic constants in E. coli metabolism (artificial data), estimated by kinetic profiling [?]. Note that  $k_{\text{cat}}$  values can only be estimated in the direction of fluxes (e.g.  $k_{\text{cat}}^+$  for reactions with forward flux).

## **2 E. coli metabolism point model Simulations with alpha = 0.5, beta = 0**

**E. coli metabolism model with artificial data (noise-free kinetic data, noise-free state data) - alpha = 0.5, beta = 0**

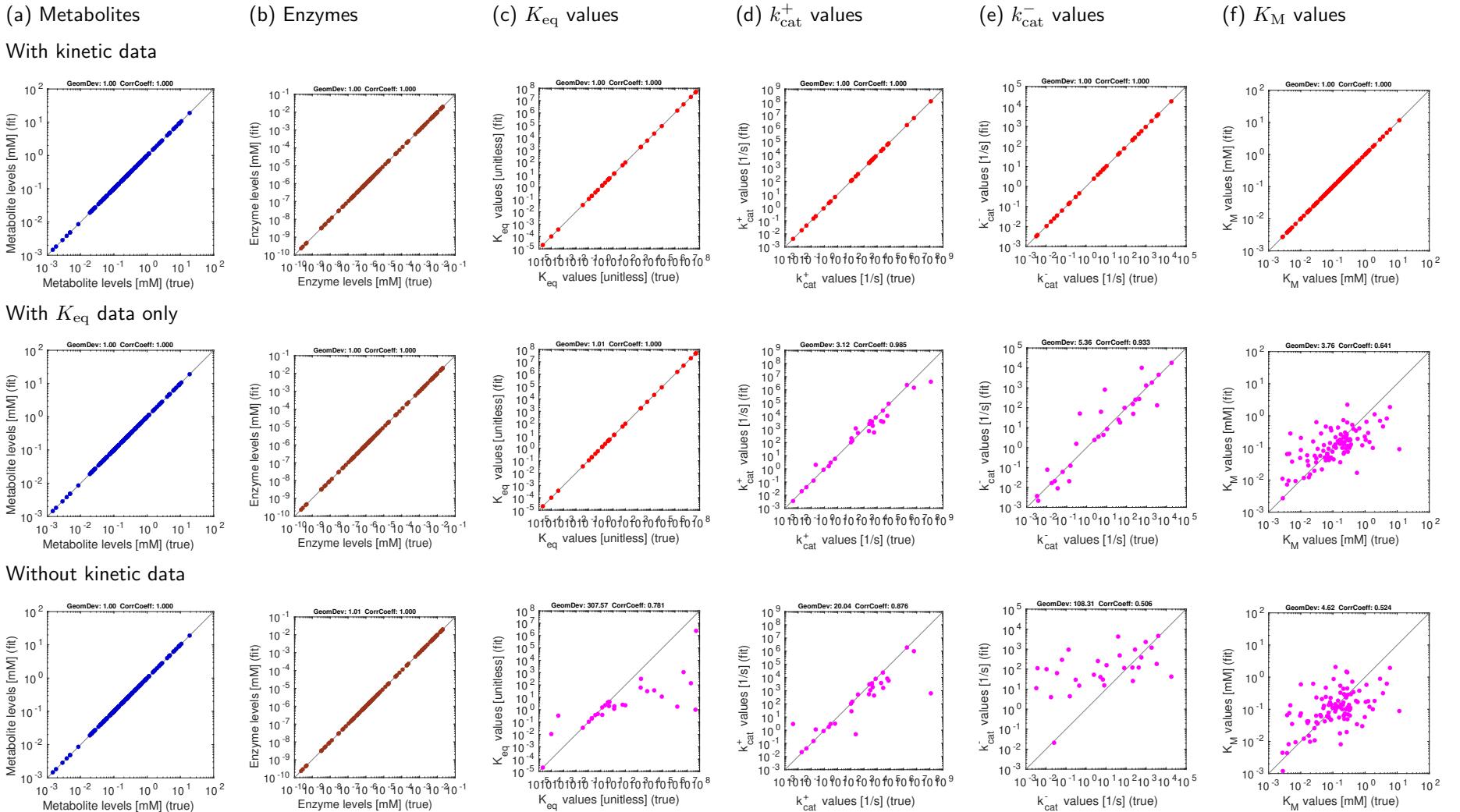
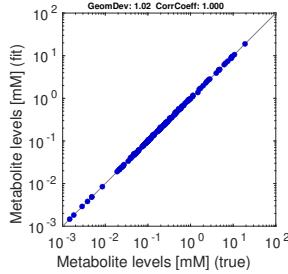


Figure 8: Model balancing results for E. coli metabolism model with artificial data. The model structure is shown in Figure ???. Each subfigure shows “true” values (x-axis) versus reconstructed values (y-axis). Similarities are quantified by geometric standard deviations (“GeomDev”) and Pearson correlation coefficients (“CorrCoeff”). (a) Metabolite levels. (b) Enzyme levels. (c)-(f) Different types of kinetic constants. Rows show different estimation scenarios (see Figure ) Upper row: simple scenario S1 (noise-free artificial data, data for kinetic constants). Centre row: scenario S1K (noise-free artificial data, kinetic data given only for equilibrium constants). Lower row: scenario S2 (noise-free artificial data, no data for kinetic constants). Depending on the scenario, kinetic constants are either fitted (red dots) or predicted (magenta dots).

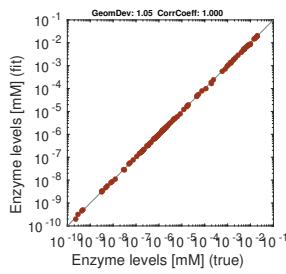
**E. coli metabolism model with artificial data (noisy kinetic data, noise-free state data) - alpha = 0.5, beta = 0**

(a) Metabolites

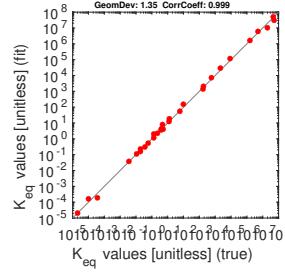
With kinetic data



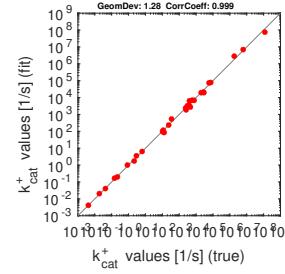
(b) Enzymes



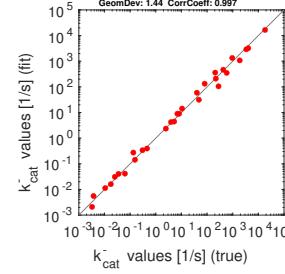
(c)  $K_{eq}$  values



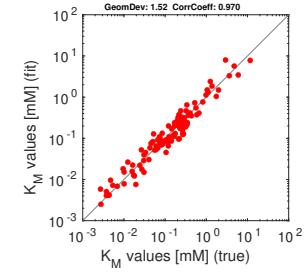
(d)  $k_{cat}^+$  values



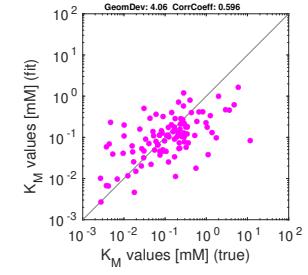
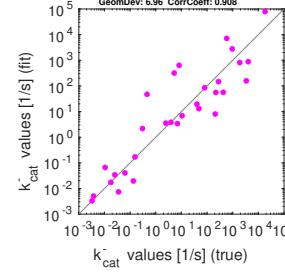
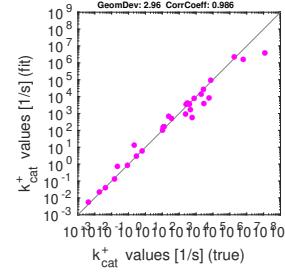
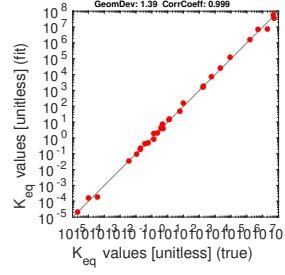
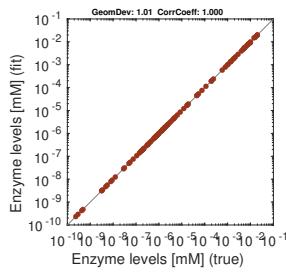
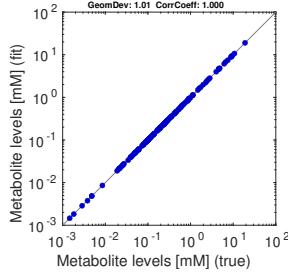
(e)  $k_{cat}^-$  values



(f)  $K_M$  values



With  $K_{eq}$  data only



Without kinetic data

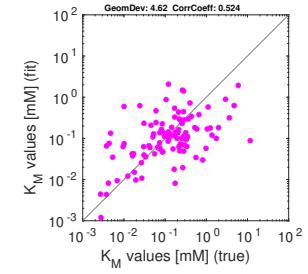
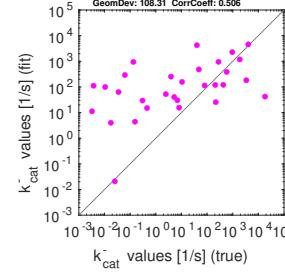
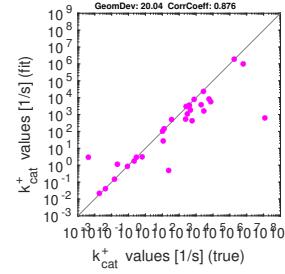
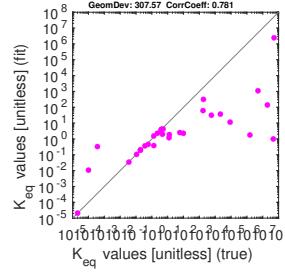
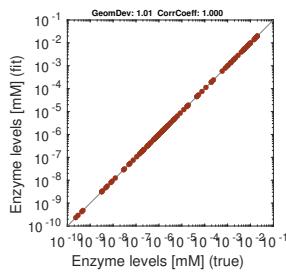
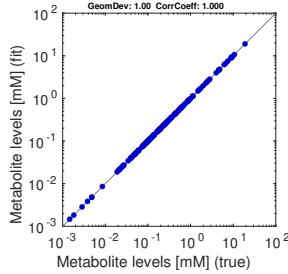


Figure 9: Same as Figure 13, with noisy kinetic data

**E. coli metabolism model with artificial data (noise-free kinetic data, noisy state data) - alpha = 0.5, beta = 0**

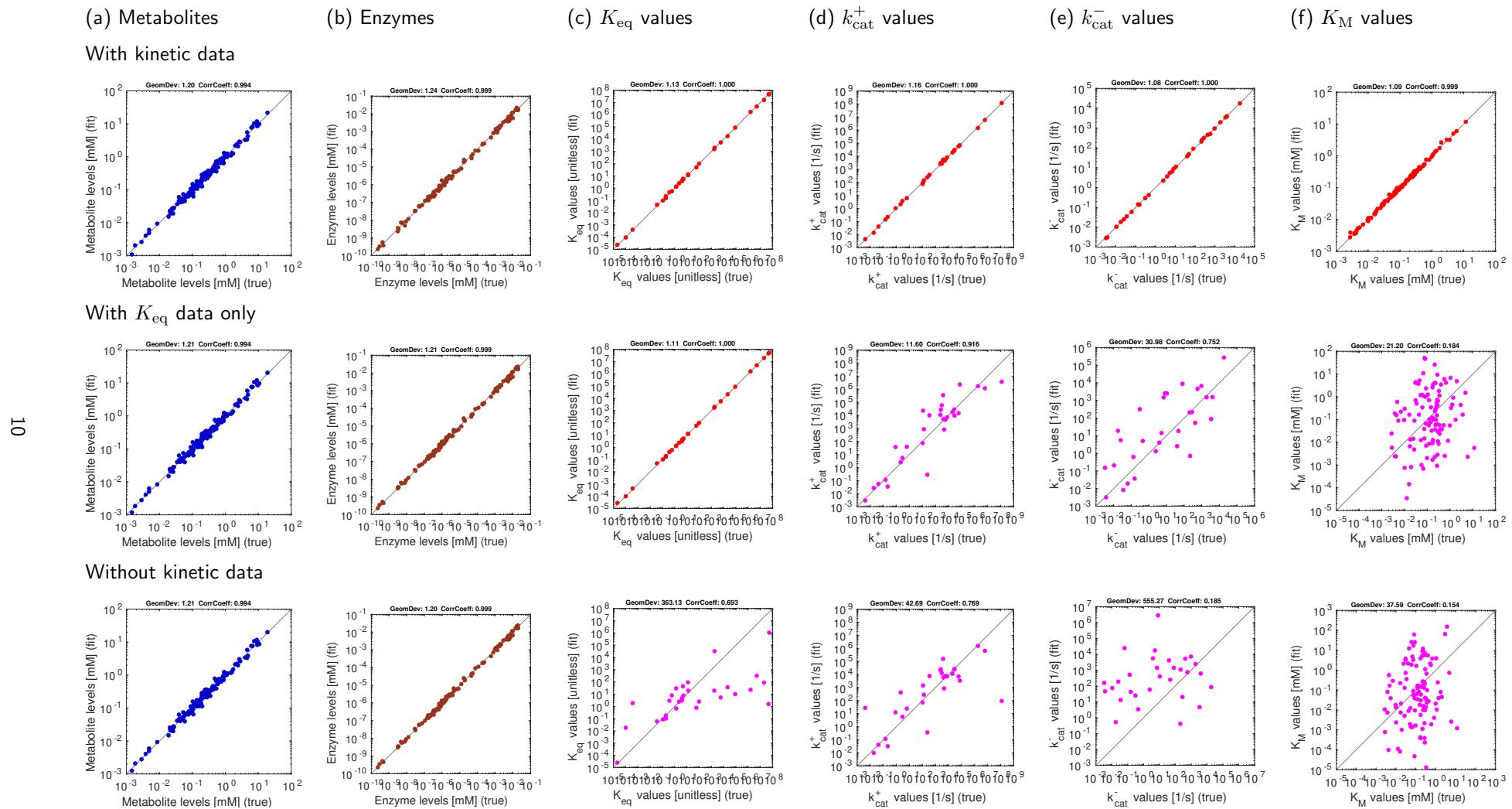
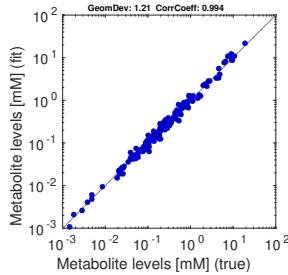


Figure 10: Results for E. coli metabolism with noisy artificial data. Top row: estimation scenario S3 (noisy artificial data, data used for kinetic constants). Centre row: estimation scenario S3K (noisy artificial data, data for equilibrium constants only). Bottom row: estimation scenario S4 (noisy artificial data, no data for kinetic constants).

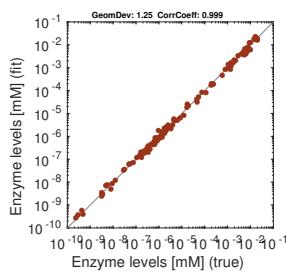
**E. coli metabolism model with artificial data (noisy kinetic data, noisy state data) - alpha = 0.5, beta = 0**

(a) Metabolites

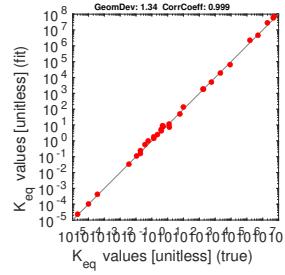
With kinetic data



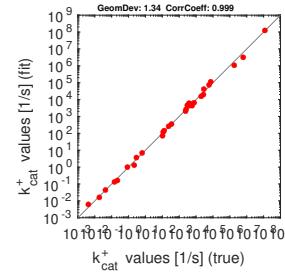
(b) Enzymes



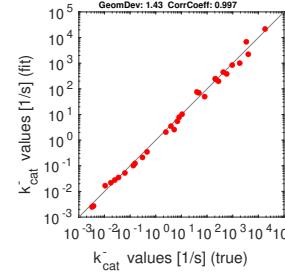
(c)  $K_{eq}$  values



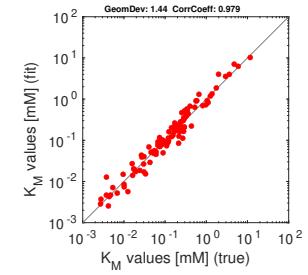
(d)  $k_{cat}^+$  values



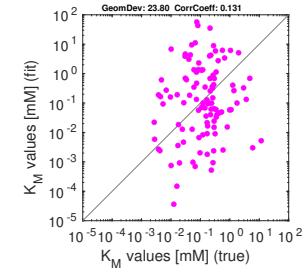
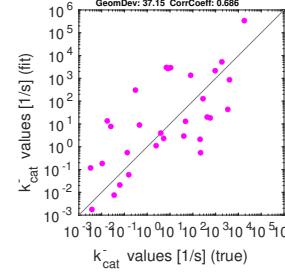
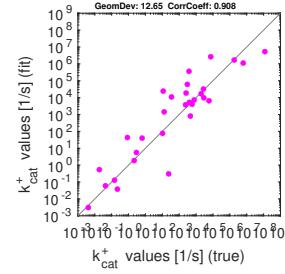
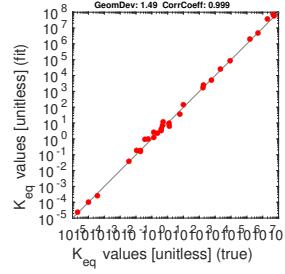
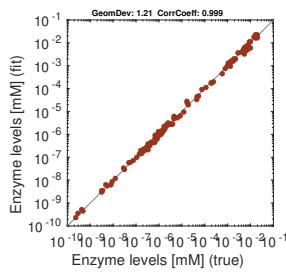
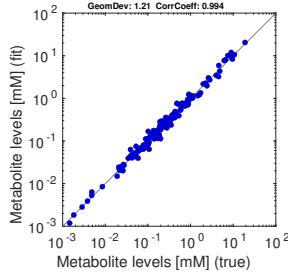
(e)  $k_{cat}^-$  values



(f)  $K_M$  values



With  $K_{eq}$  data only



Without kinetic data

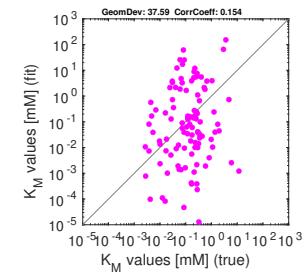
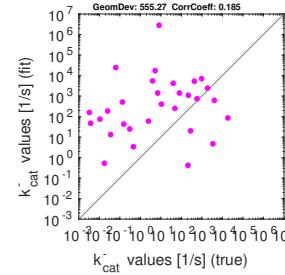
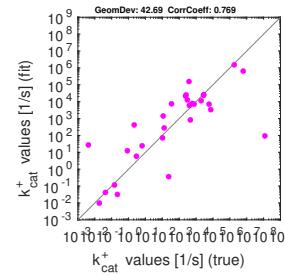
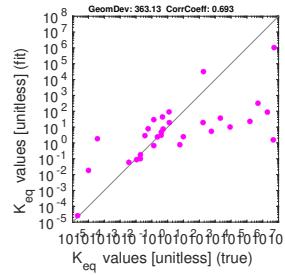
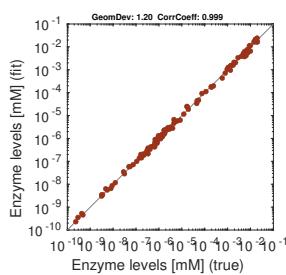
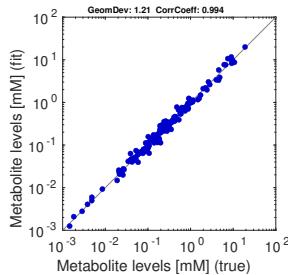


Figure 11: Same as Figure 15, with noisy kinetic data

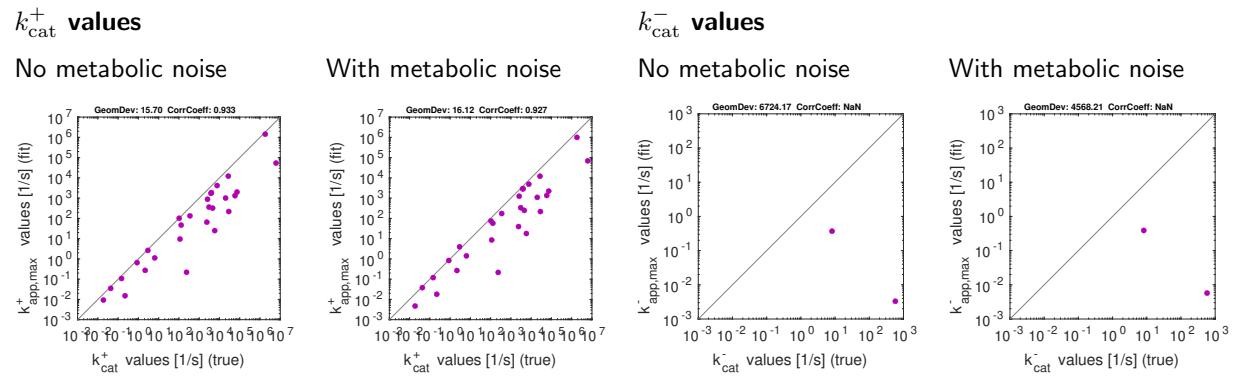


Figure 12: Catalytic constants in *E. coli* metabolism (artificial data), estimated by kinetic profiling [?]. Note that  $k_{\text{cat}}$  values can only be estimated in the direction of fluxes (e.g.  $k_{\text{cat}}^+$  for reactions with forward flux).

### **3 E. coli metabolism point model Simulations with alpha = 1, beta = 0**

**E. coli metabolism model with artificial data (noise-free kinetic data, noise-free state data) - alpha = 1, beta = 0**

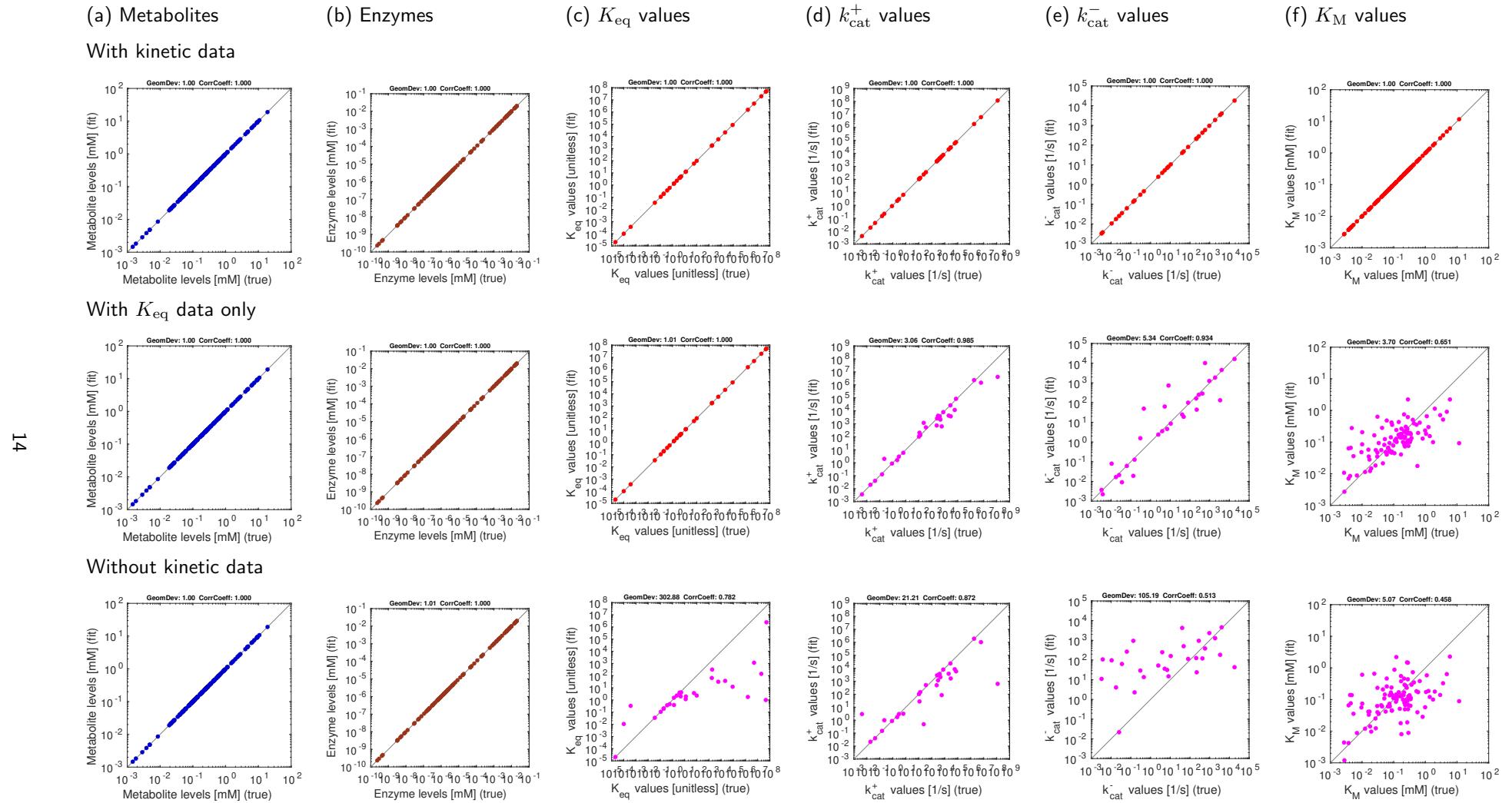
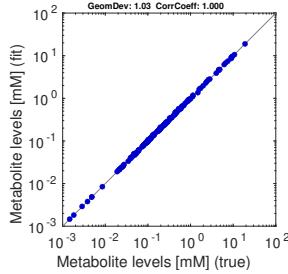


Figure 13: Model balancing results for E. coli metabolism model with artificial data. The model structure is shown in Figure ???. Each subfigure shows “true” values (x-axis) versus reconstructed values (y-axis). Similarities are quantified by geometric standard deviations (“GeomDev”) and Pearson correlation coefficients (“CorrCoeff”). (a) Metabolite levels. (b) Enzyme levels. (c)-(f) Different types of kinetic constants. Rows show different estimation scenarios (see Figure ) Upper row: simple scenario S1 (noise-free artificial data, data for kinetic constants). Centre row: scenario S1K (noise-free artificial data, kinetic data given only for equilibrium constants). Lower row: scenario S2 (noise-free artificial data, no data for kinetic constants). Depending on the scenario, kinetic constants are either fitted (red dots) or predicted (magenta dots).

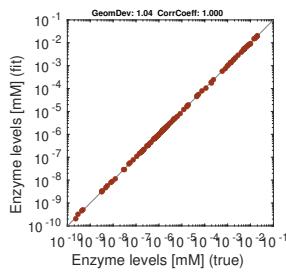
**E. coli metabolism model with artificial data (noisy kinetic data, noise-free state data) - alpha = 1, beta = 0**

(a) Metabolites

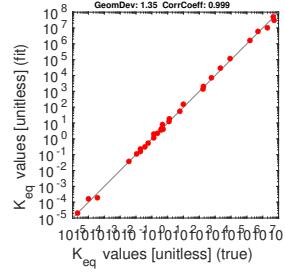
With kinetic data



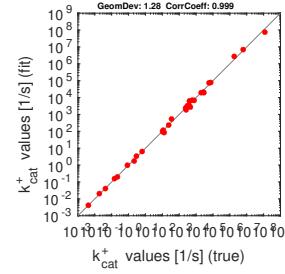
(b) Enzymes



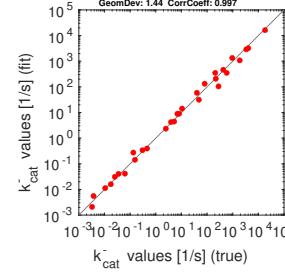
(c)  $K_{eq}$  values



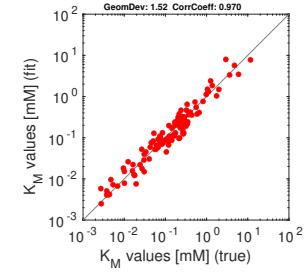
(d)  $k_{cat}^+$  values



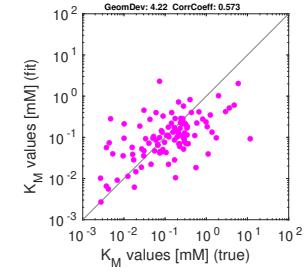
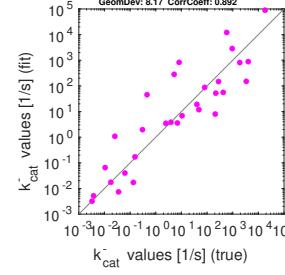
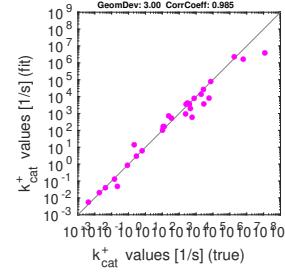
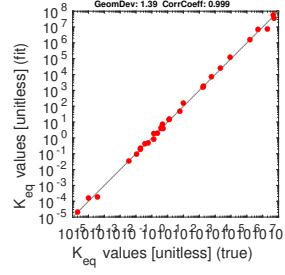
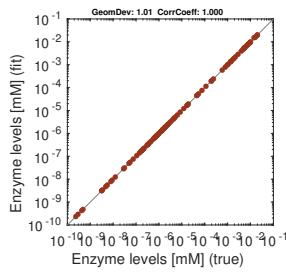
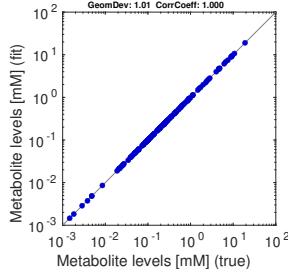
(e)  $k_{cat}^-$  values



(f)  $K_M$  values



With  $K_{eq}$  data only



Without kinetic data

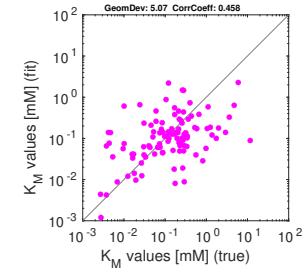
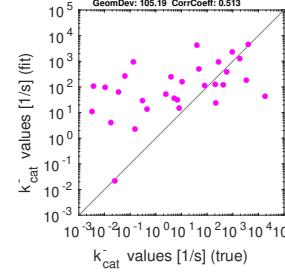
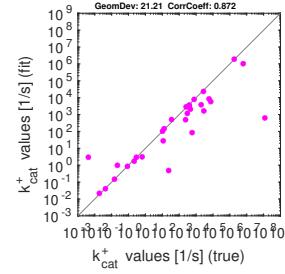
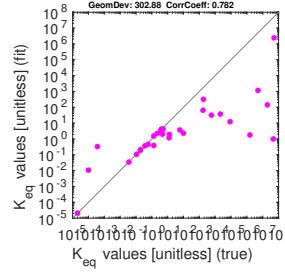
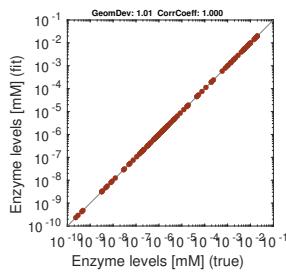
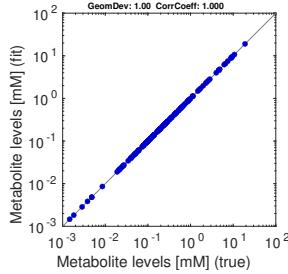


Figure 14: Same as Figure 13, with noisy kinetic data

**E. coli metabolism model with artificial data (noise-free kinetic data, noisy state data) - alpha = 1, beta = 0**

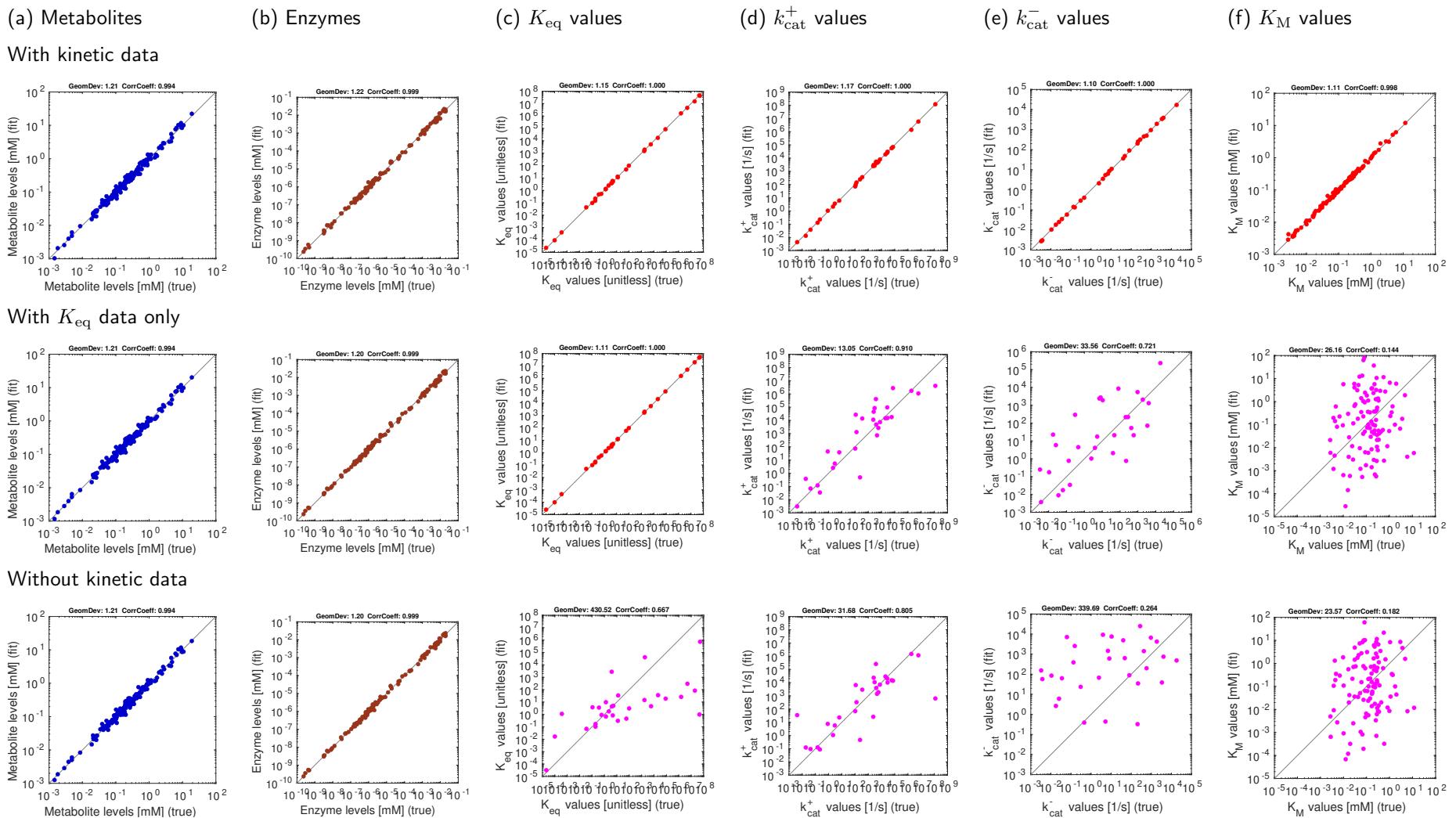


Figure 15: Results for E. coli metabolism with noisy artificial data. Top row: estimation scenario S3 (noisy artificial data, data used for kinetic constants). Centre row: estimation scenario S3K (noisy artificial data, data for equilibrium constants only). Bottom row: estimation scenario S4 (noisy artificial data, no data for kinetic constants).

**E. coli metabolism model with artificial data (noisy kinetic data, noisy state data) - alpha = 1, beta = 0**

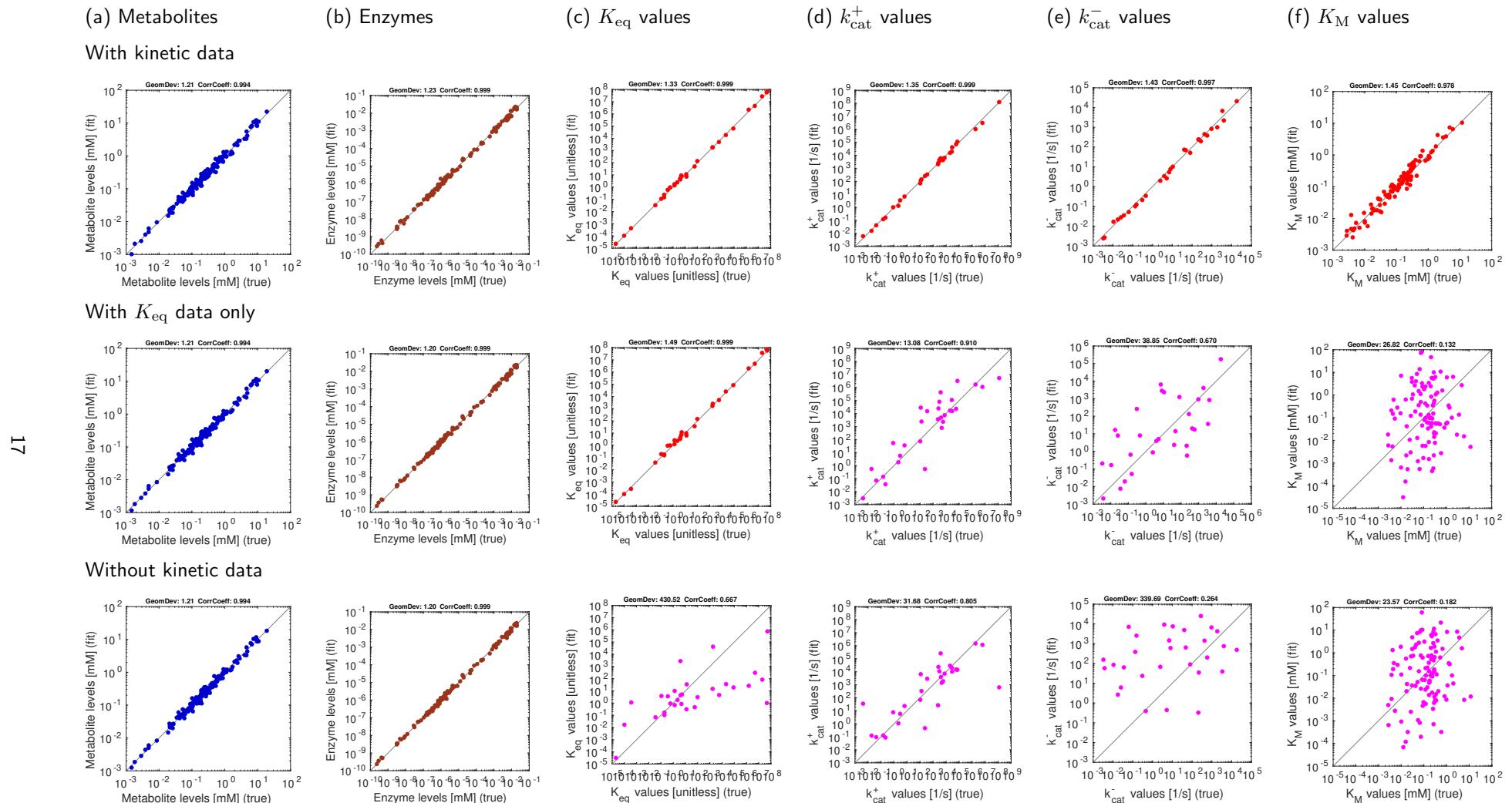


Figure 16: Same as Figure 15, with noisy kinetic data

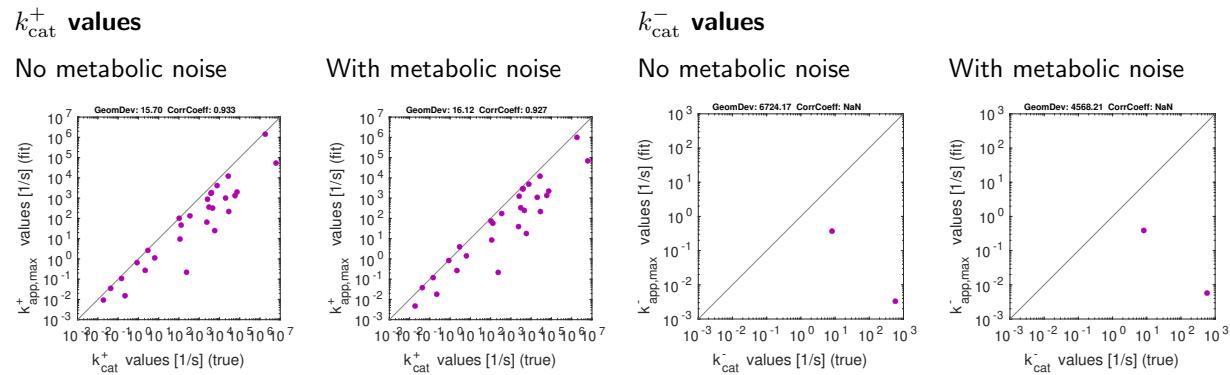


Figure 17: Catalytic constants in *E. coli* metabolism (artificial data), estimated by kinetic profiling [?]. Note that  $k_{\text{cat}}$  values can only be estimated in the direction of fluxes (e.g.  $k_{\text{cat}}^+$  for reactions with forward flux).