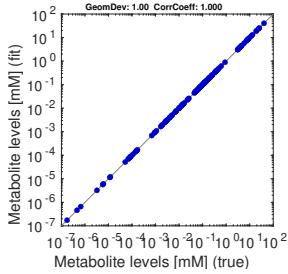


1 E. coli model Simulations with alpha = 0

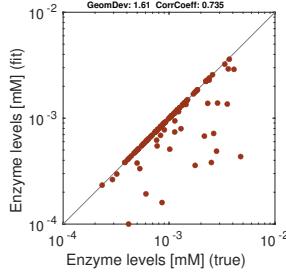
E. coli metabolism model with artificial data (noise-free kinetic data, noise-free state data)

(a) Metabolites

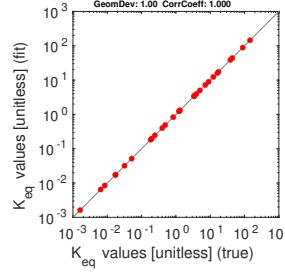
With kinetic data



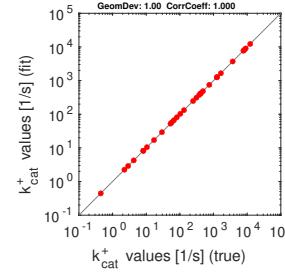
(b) Enzymes



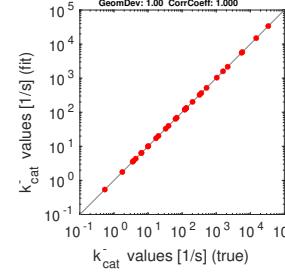
(c) K_{eq} values



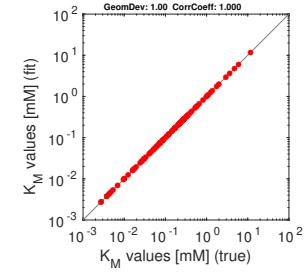
(d) k_{cat}^+ values



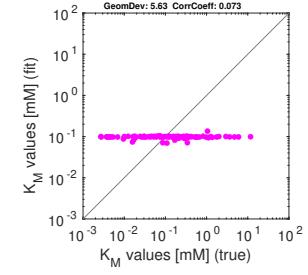
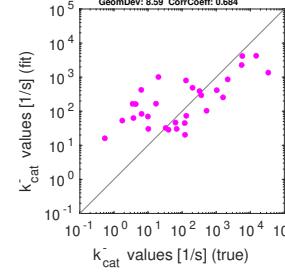
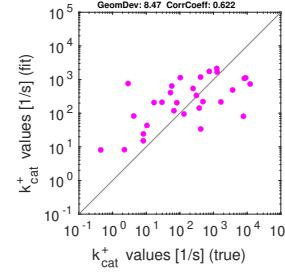
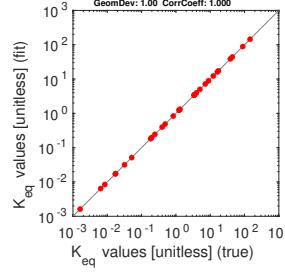
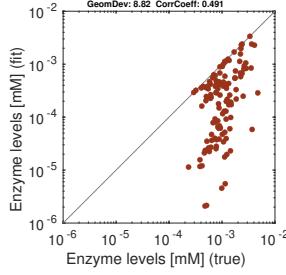
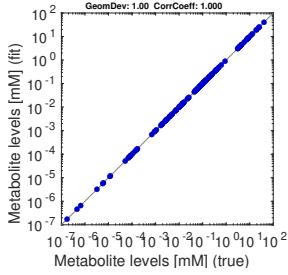
(e) k_{cat}^- values



(f) K_M values



With K_{eq} data only



Without kinetic data

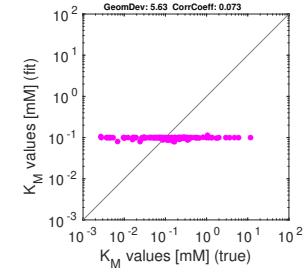
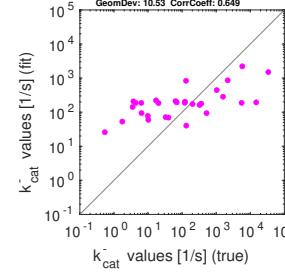
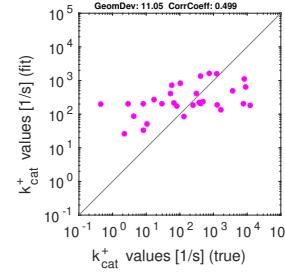
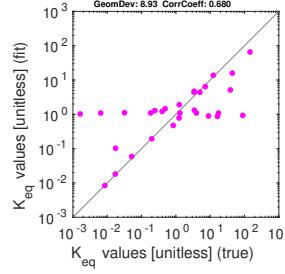
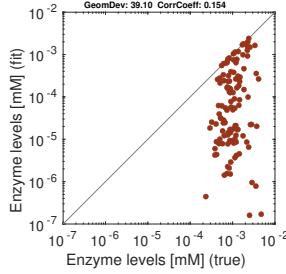
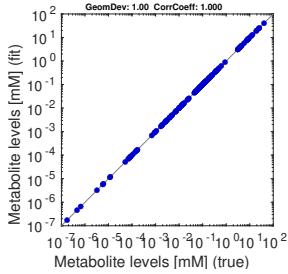
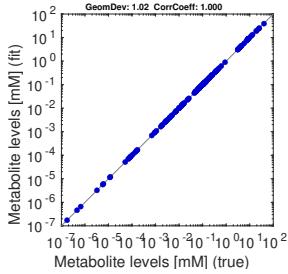


Figure 3: Model balancing results for E. coli metabolism model with artificial data. The model structure is shown in Figure ???. Each subfigure shows “true” values (x-axis) versus reconstructed values (y-axis). Similarities are quantified by geometric standard deviations (“GeomDev”) and Pearson correlation 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)

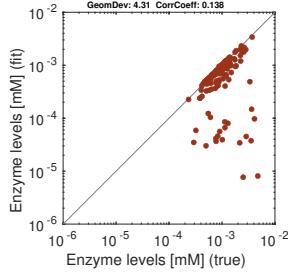
(a) Metabolites

With kinetic data



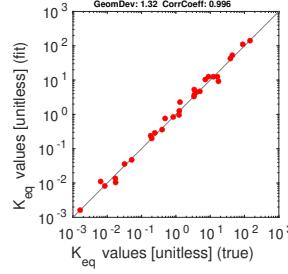
(b) Enzymes

With kinetic data



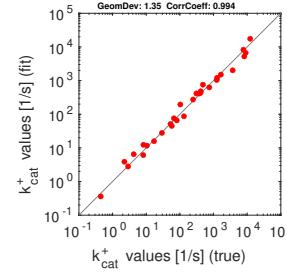
(c) K_{eq} values

With kinetic data



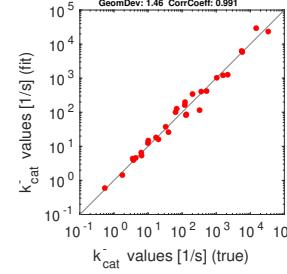
(d) k_{cat}^+ values

With kinetic data



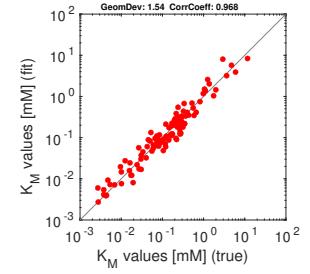
(e) k_{cat}^- values

With kinetic data

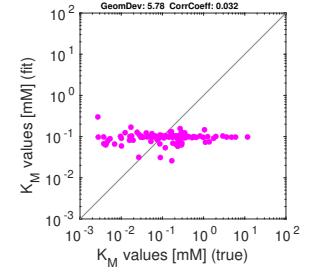
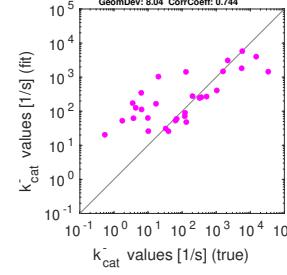
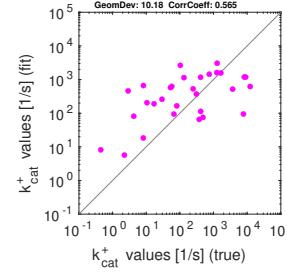
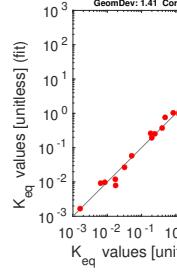
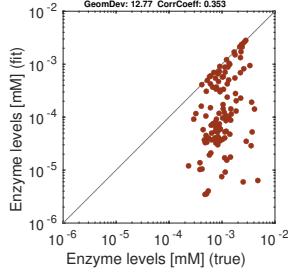
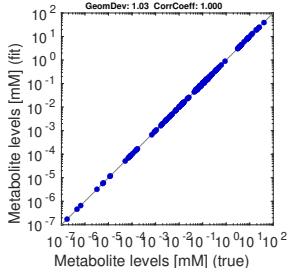


(f) K_M values

With kinetic data



With K_{eq} data only



Without kinetic data

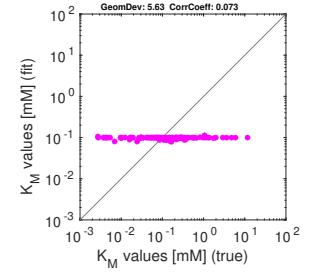
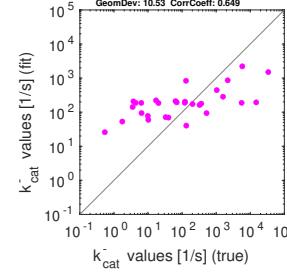
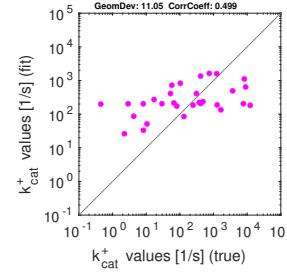
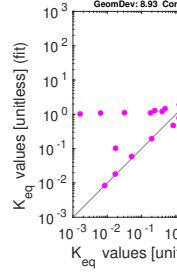
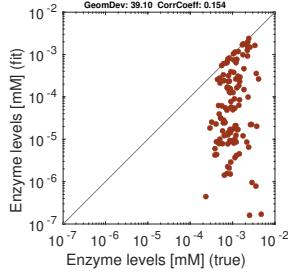
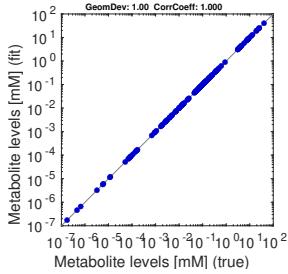
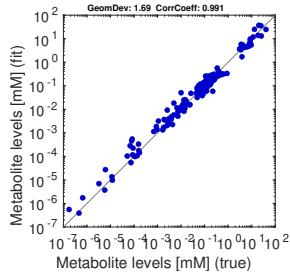


Figure 4: Same as Figure 28, with noisy kinetic data

E. coli metabolism model with artificial data (noise-free kinetic data, noisy state data)

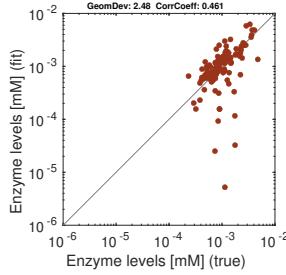
(a) Metabolites

With kinetic data



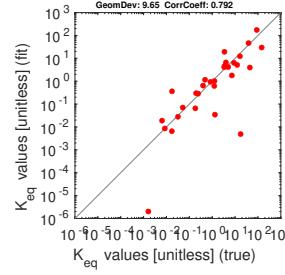
(b) Enzymes

With kinetic data



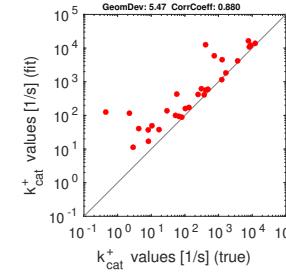
(c) K_{eq} values

With kinetic data



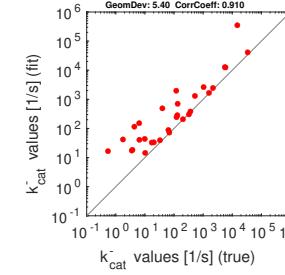
(d) k_{cat}^+ values

With kinetic data



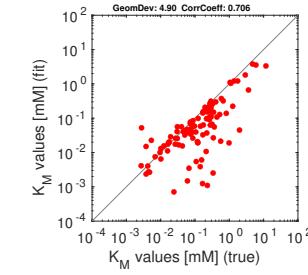
(e) k_{cat}^- values

With kinetic data

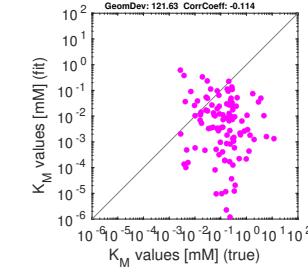
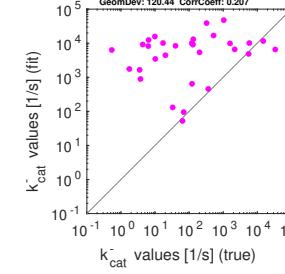
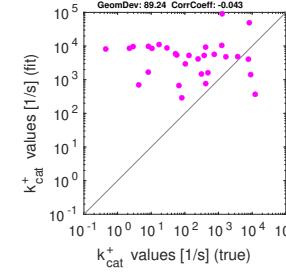
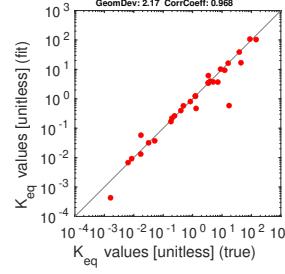
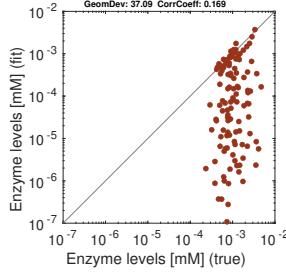
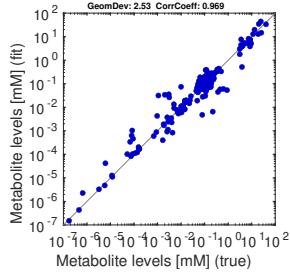


(f) K_M values

With kinetic data



With K_{eq} data only



Without kinetic data

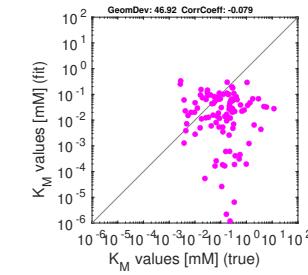
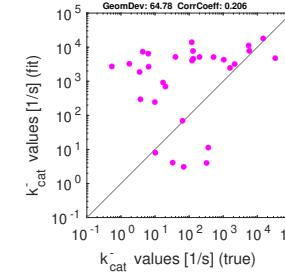
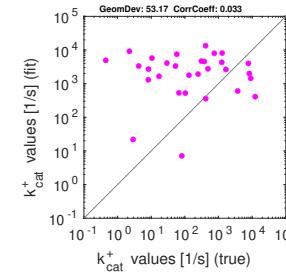
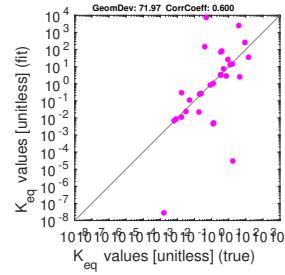
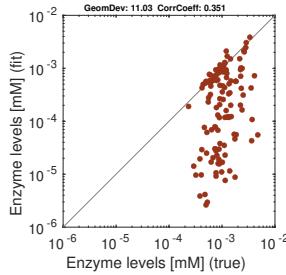
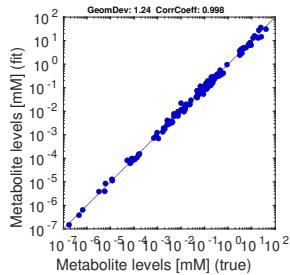
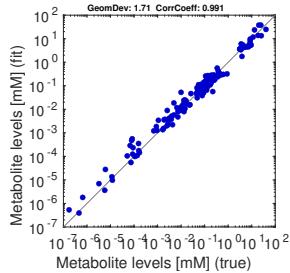


Figure 5: Results for E. coli metabolism with noisy artificial data. Top row: estimation scenario S3 (noisy artificial data, data used for kinetic constants). Centre row: estimation scenario S3K (noisy artificial data, data for equilibrium constants only). Bottom row: estimation scenario S4 (noisy artificial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

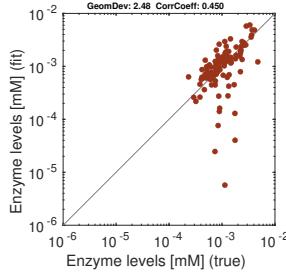
E. coli metabolism model with artificial data (noisy kinetic data, noisy state data)

(a) Metabolites

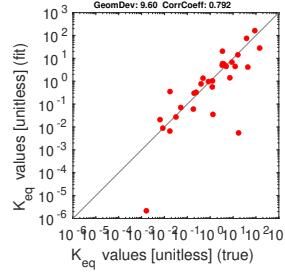
With kinetic data



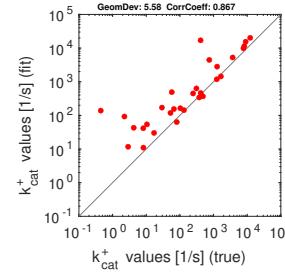
(b) Enzymes



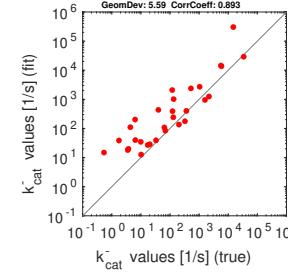
(c) K_{eq} values



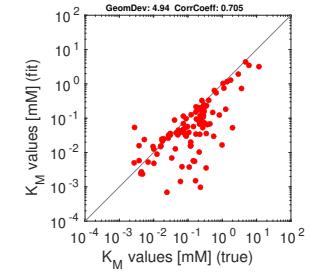
(d) k_{cat}^+ values



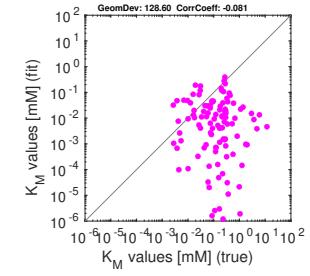
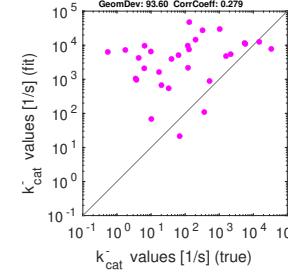
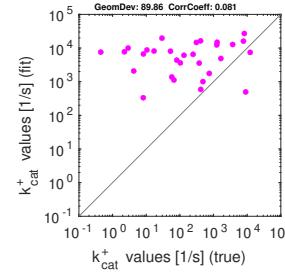
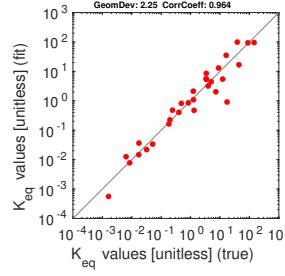
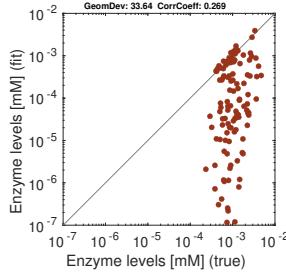
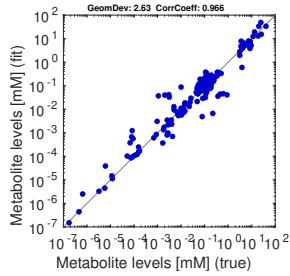
(e) k_{cat}^- values



(f) K_M values



With K_{eq} data only



Without kinetic data

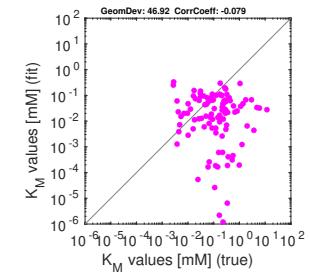
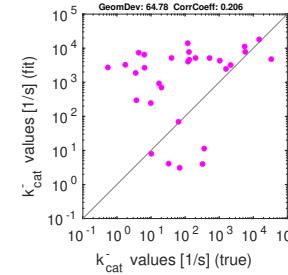
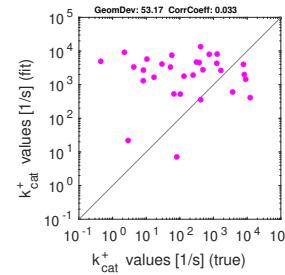
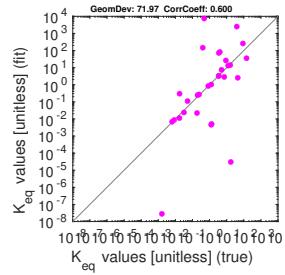
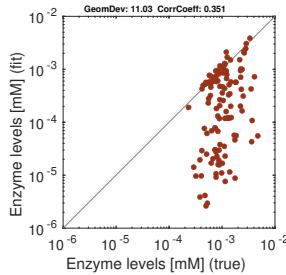
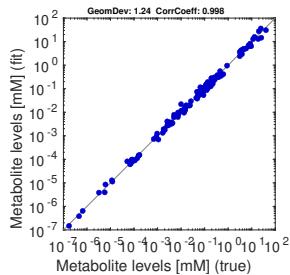


Figure 6: Same as Figure 30, with noisy kinetic data

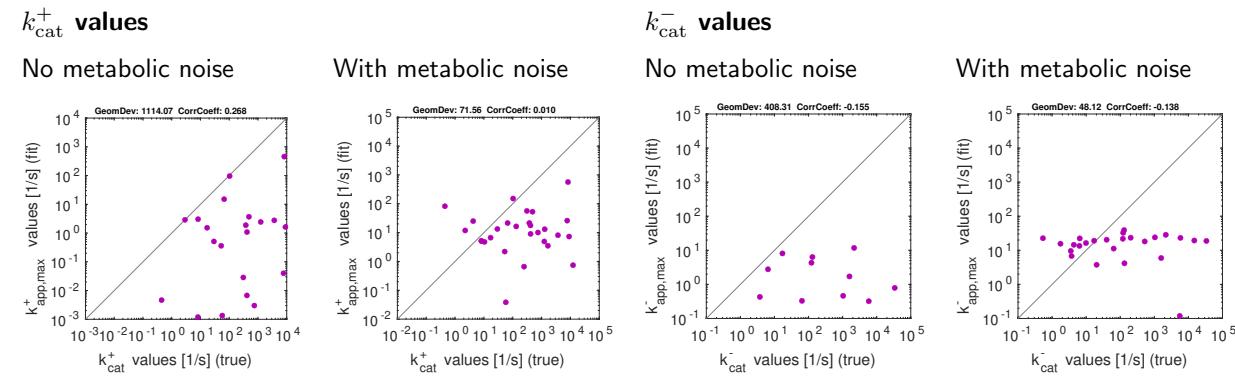


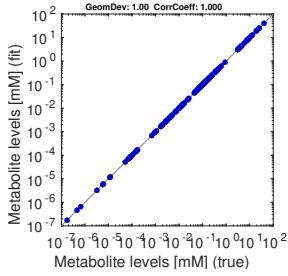
Figure 7: Catalytic constants in E. coli metabolism (artificial data), estimated by kinetic profiling [?]. Note that k_{cat} values can only be estimated in the direction of fluxes (e.g. k_{cat}^+ for reactions with forward flux).

2 E. coli model Simulations with alpha = 0.001

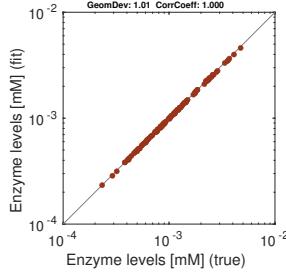
E. coli metabolism model with artificial data (noise-free kinetic data, noise-free state data)

(a) Metabolites

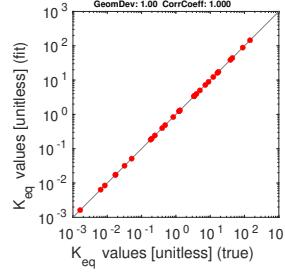
With kinetic data



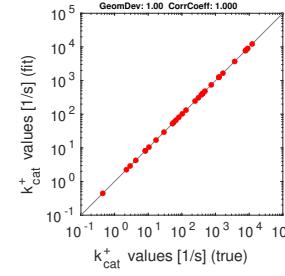
(b) Enzymes



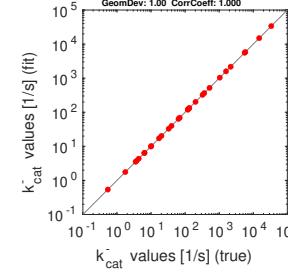
(c) K_{eq} values



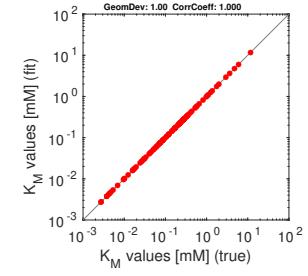
(d) k_{cat}^+ values



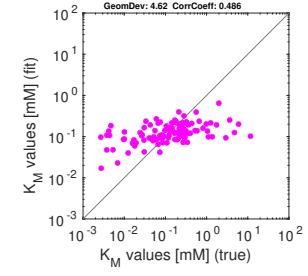
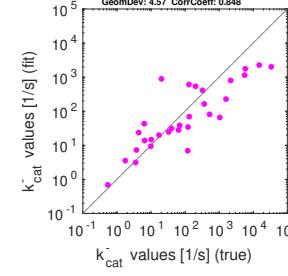
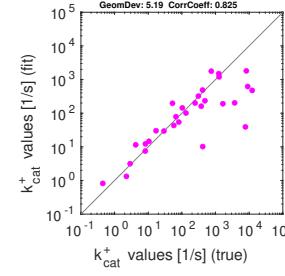
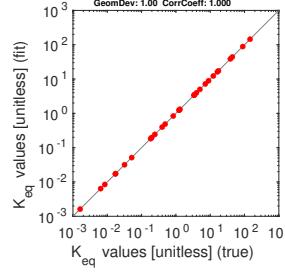
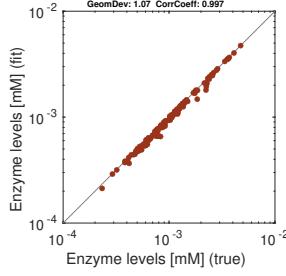
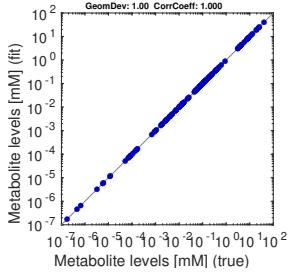
(e) k_{cat}^- values



(f) K_M values



With K_{eq} data only



Without kinetic data

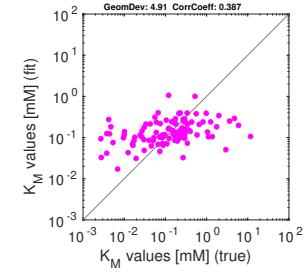
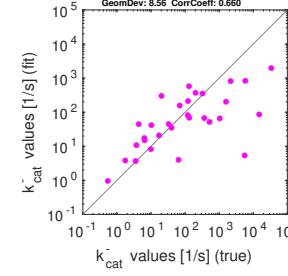
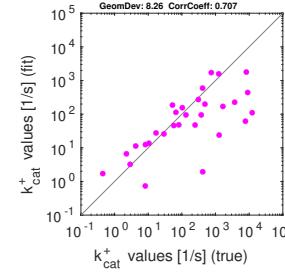
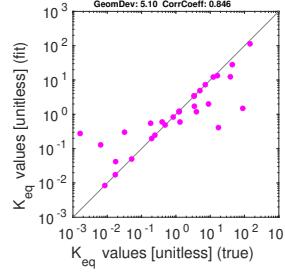
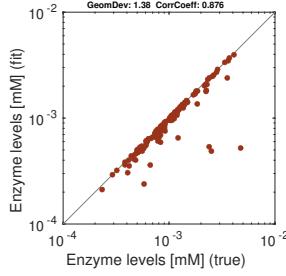
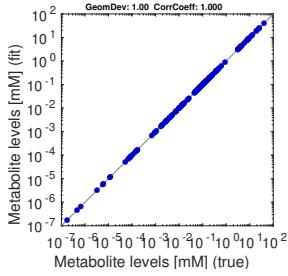


Figure 8: Model balancing results for E. coli metabolism model with artificial data. The model structure is shown in Figure ???. Each subfigure shows “true” values (x-axis) versus reconstructed values (y-axis). Similarities are quantified by geometric standard deviations (“GeomDev”) and Pearson correlation 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)

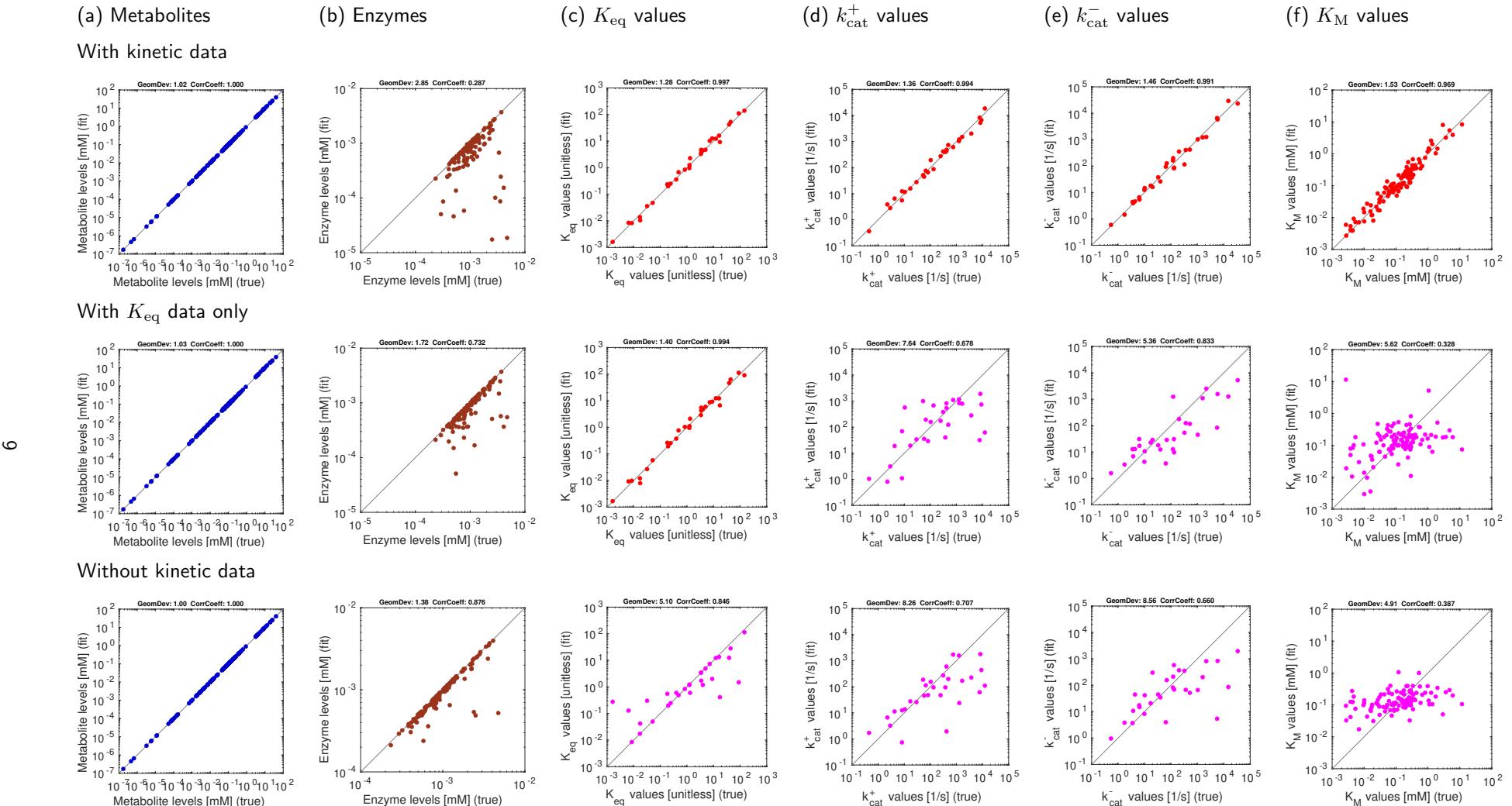


Figure 9: Same as Figure 28, with noisy kinetic data

E. coli metabolism model with artificial data (noise-free kinetic data, noisy state data)

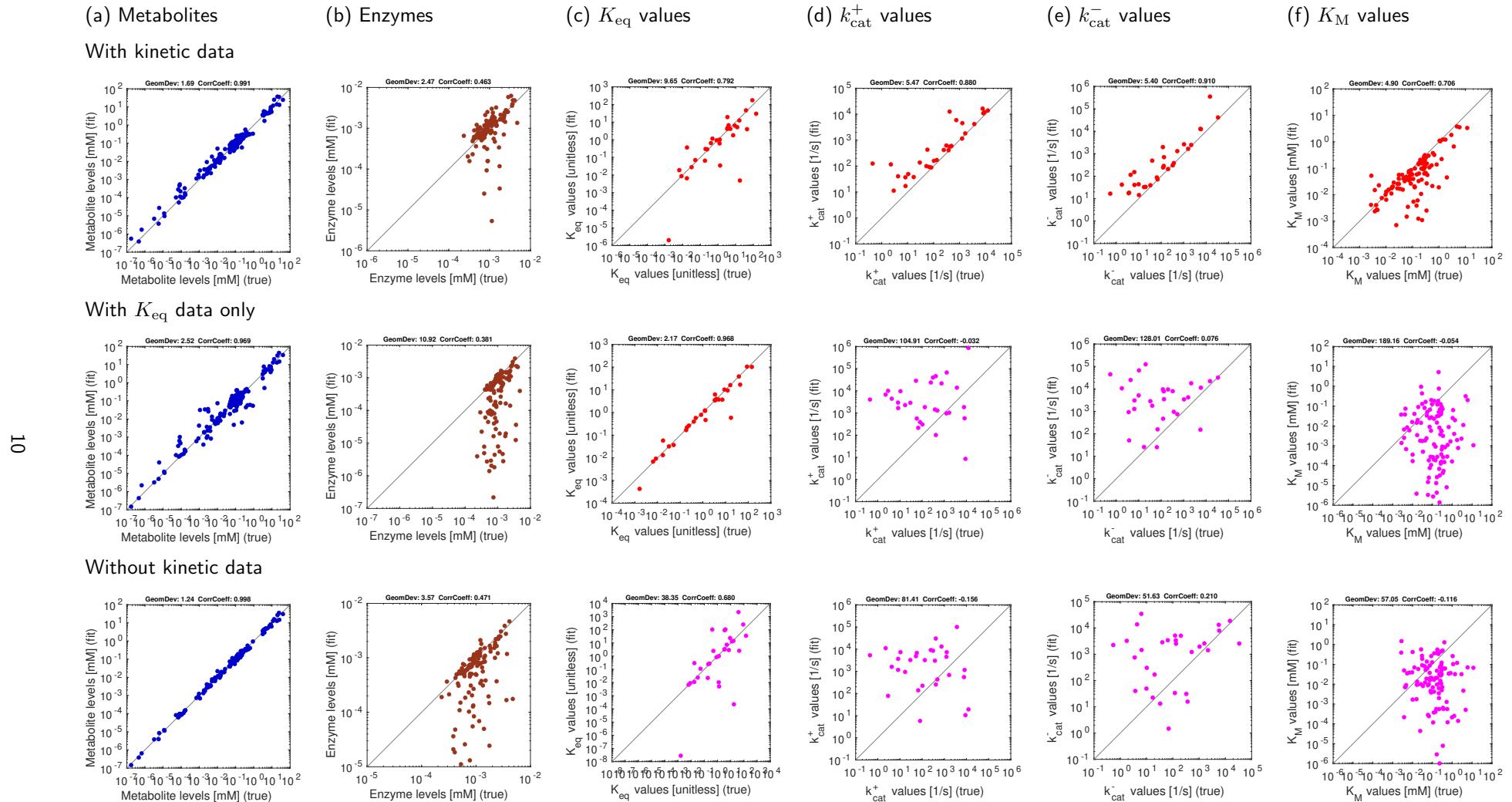
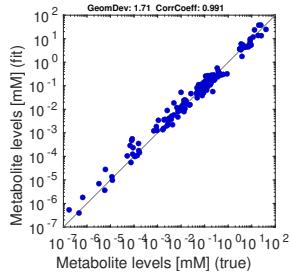


Figure 10: Results for E. coli metabolism with noisy artificial data. Top row: estimation scenario S3 (noisy artificial data, data used for kinetic constants). Centre row: estimation scenario S3K (noisy artificial data, data for equilibrium constants only). Bottom row: estimation scenario S4 (noisy artificial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

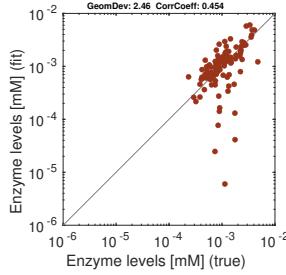
E. coli metabolism model with artificial data (noisy kinetic data, noisy state data)

(a) Metabolites

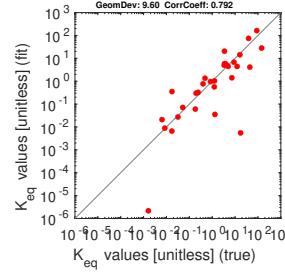
With kinetic data



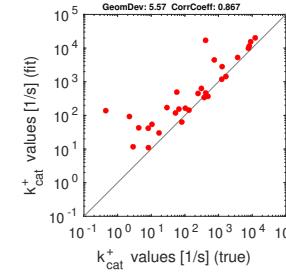
(b) Enzymes



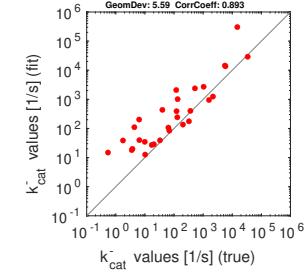
(c) K_{eq} values



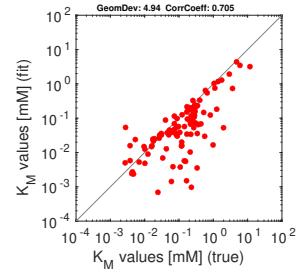
(d) k_{cat}^+ values



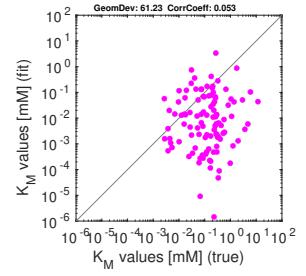
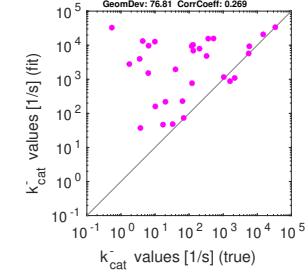
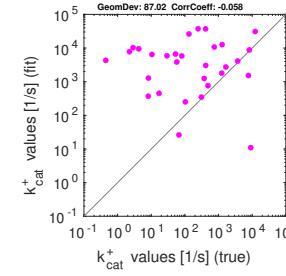
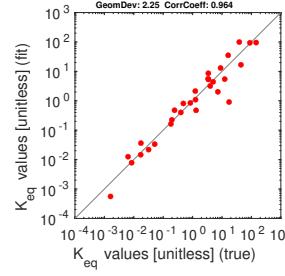
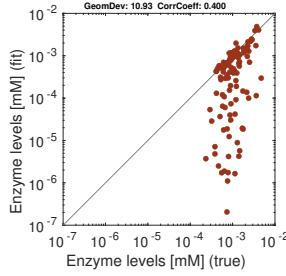
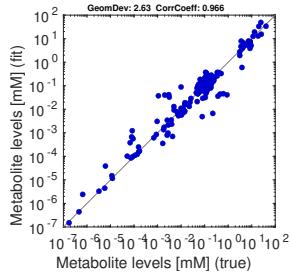
(e) k_{cat}^- values



(f) K_M values



With K_{eq} data only



Without kinetic data

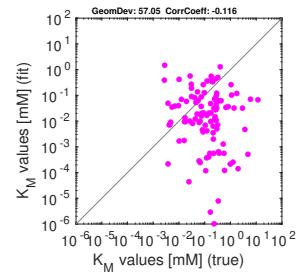
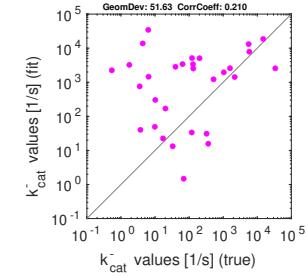
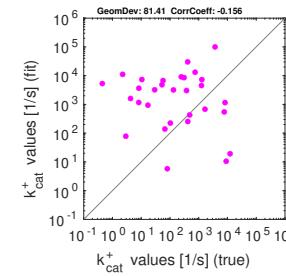
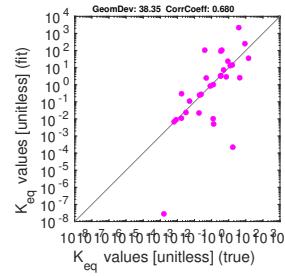
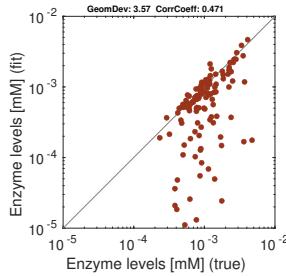
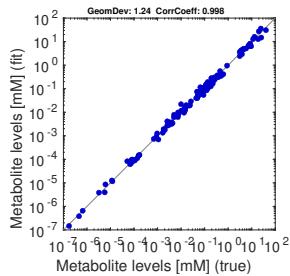


Figure 11: Same as Figure 30, with noisy kinetic data

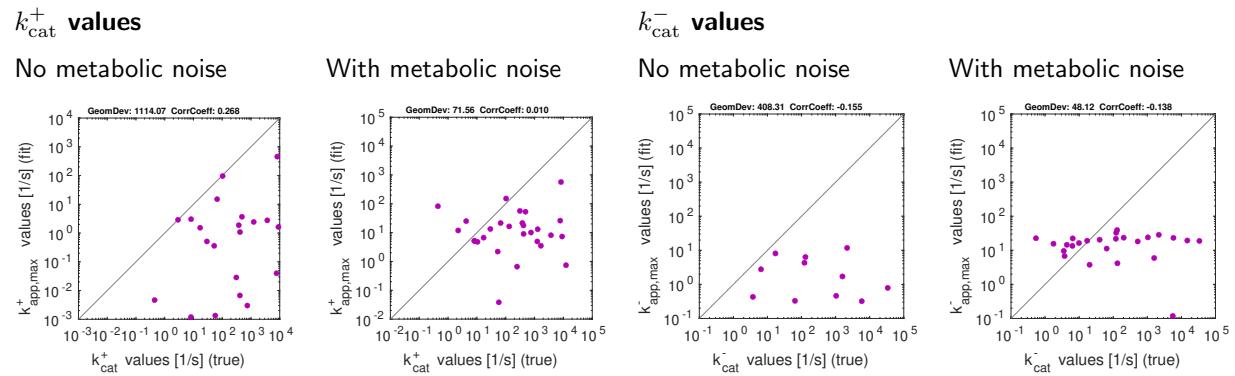


Figure 12: Catalytic constants in *E. coli* metabolism (artificial data), estimated by kinetic profiling [?]. Note that k_{cat} values can only be estimated in the direction of fluxes (e.g. k_{cat}^+ for reactions with forward flux).

3 E. coli model Simulations with alpha = 0.01

E. coli metabolism model with artificial data (noise-free kinetic data, noise-free state data)

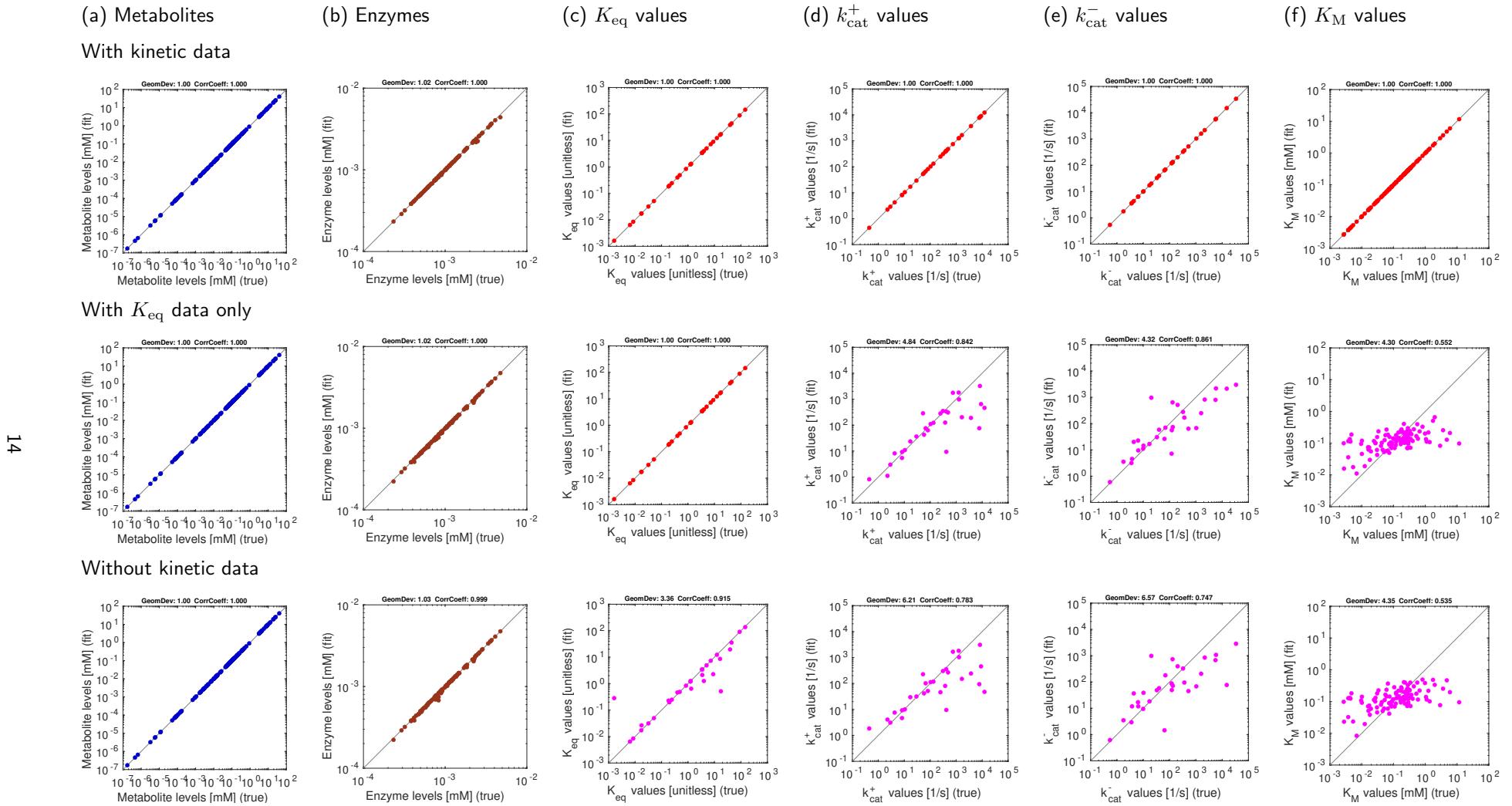


Figure 13: Model balancing results for E. coli metabolism model with artificial data. The model structure is shown in Figure ???. Each subfigure shows “true” values (x-axis) versus reconstructed values (y-axis). Similarities are quantified by geometric standard deviations (“GeomDev”) and Pearson correlation 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)

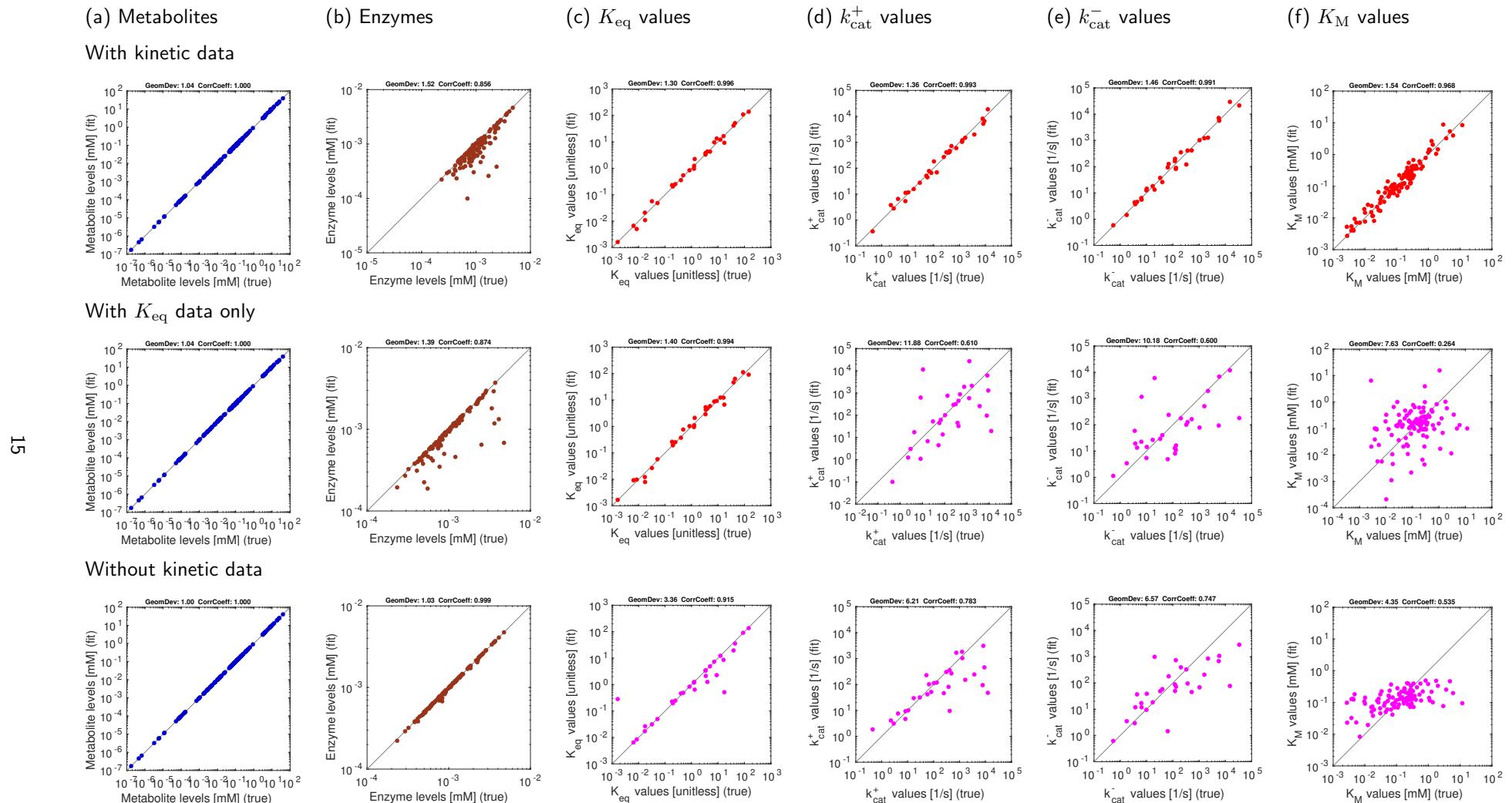
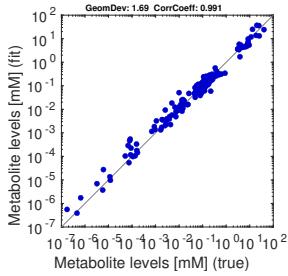


Figure 14: Same as Figure 28, with noisy kinetic data

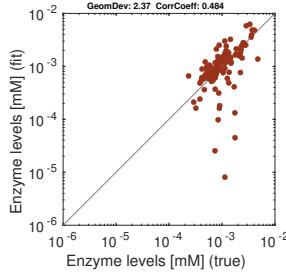
E. coli metabolism model with artificial data (noise-free kinetic data, noisy state data)

(a) Metabolites

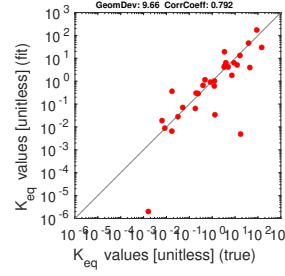
With kinetic data



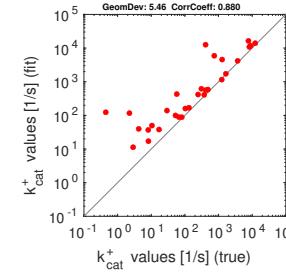
(b) Enzymes



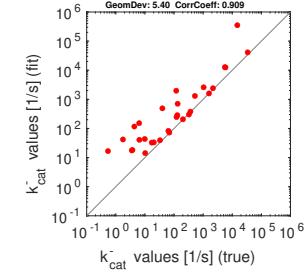
(c) K_{eq} values



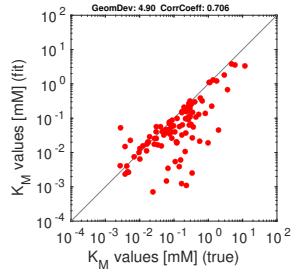
(d) k_{cat}^+ values



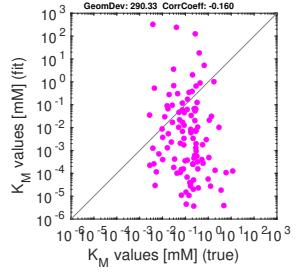
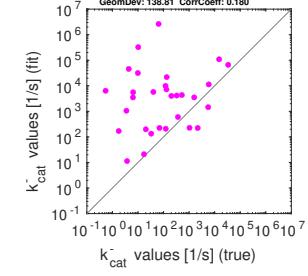
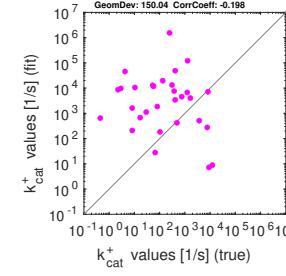
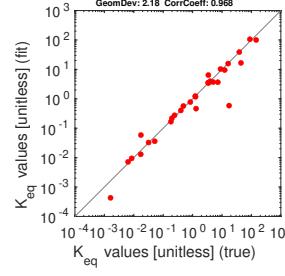
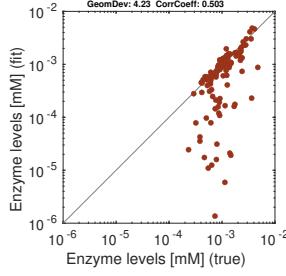
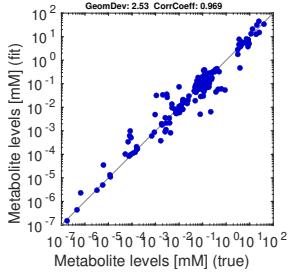
(e) k_{cat}^- values



(f) K_M values



With K_{eq} data only



Without kinetic data

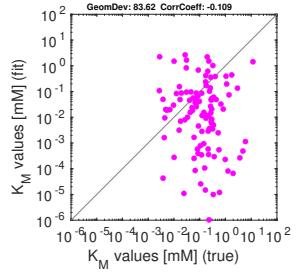
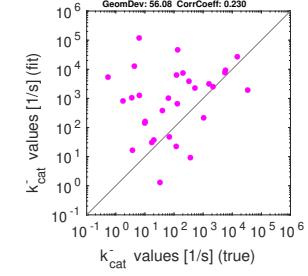
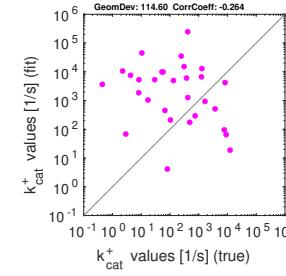
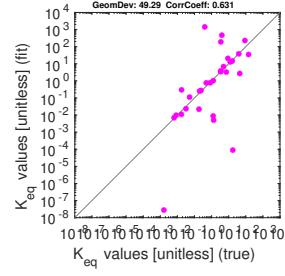
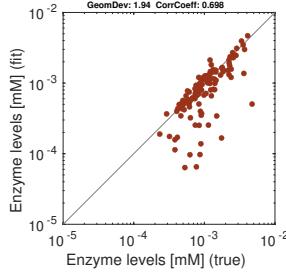
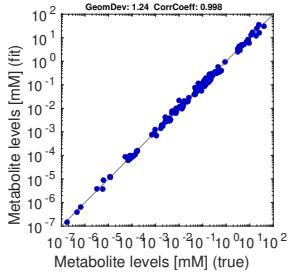


Figure 15: Results for E. coli metabolism with noisy artificial data. Top row: estimation scenario S3 (noisy artificial data, data used for kinetic constants). Centre row: estimation scenario S3K (noisy artificial data, data for equilibrium constants only). Bottom row: estimation scenario S4 (noisy artificial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

E. coli metabolism model with artificial data (noisy kinetic data, noisy state data)

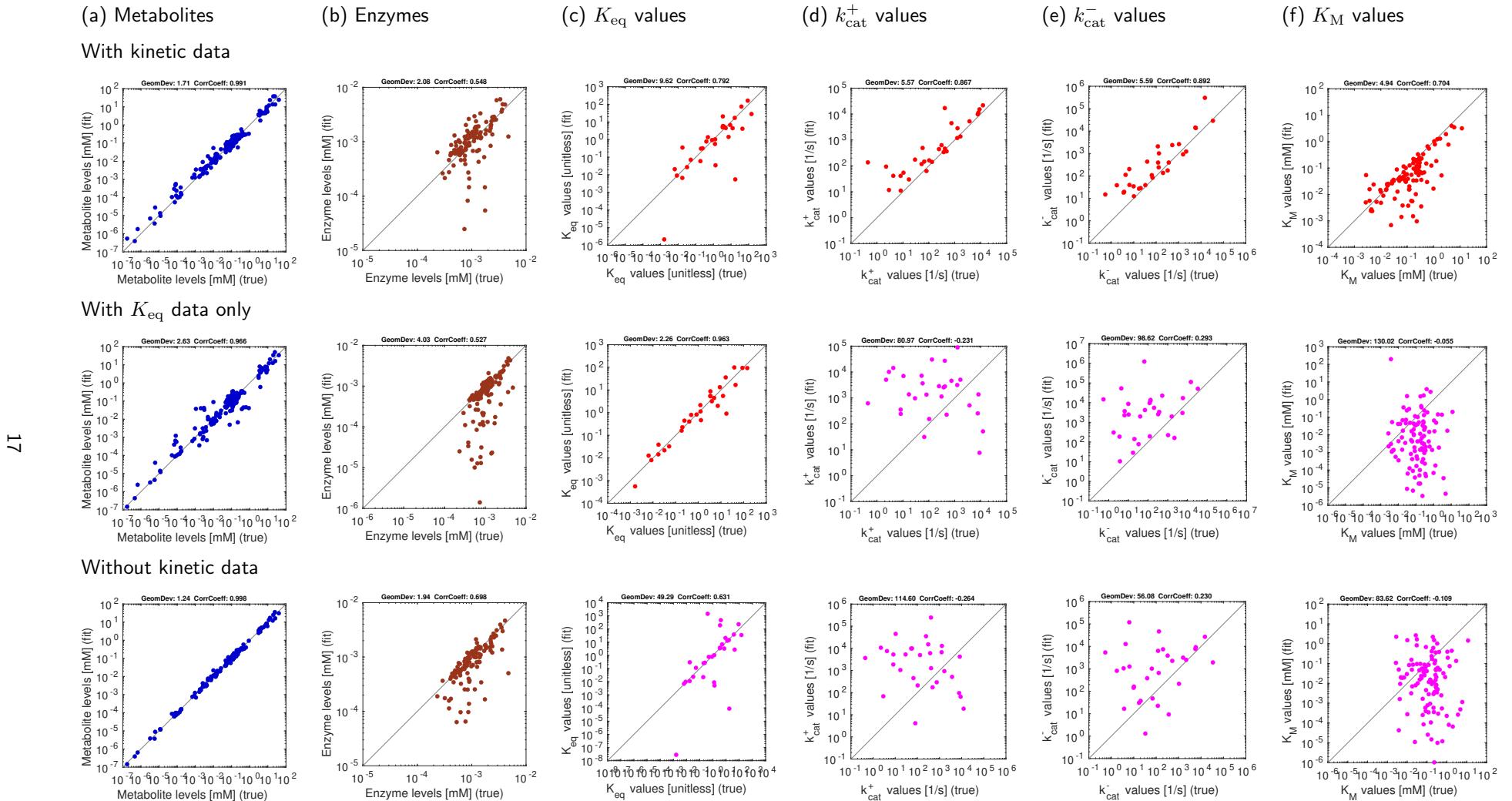


Figure 16: Same as Figure 30, with noisy kinetic data

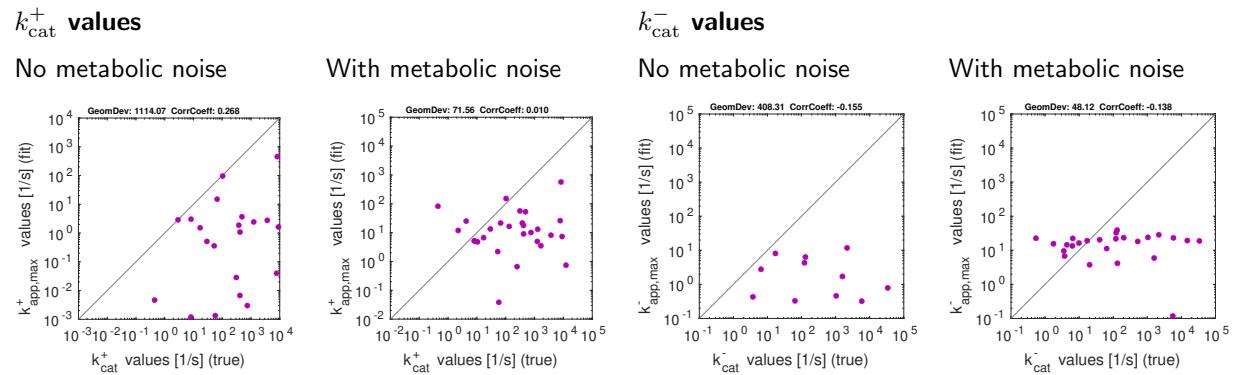


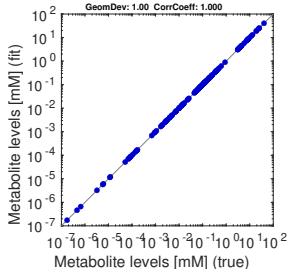
Figure 17: Catalytic constants in *E. coli* metabolism (artificial data), estimated by kinetic profiling [?]. Note that k_{cat} values can only be estimated in the direction of fluxes (e.g. k_{cat}^+ for reactions with forward flux).

4 E. coli model Simulations with alpha = 0.1

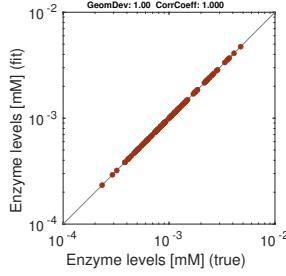
E. coli metabolism model with artificial data (noise-free kinetic data, noise-free state data)

(a) Metabolites

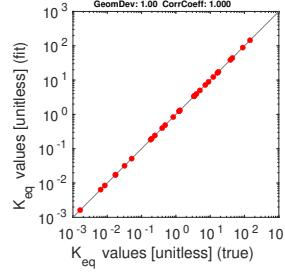
With kinetic data



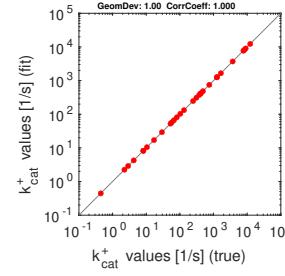
(b) Enzymes



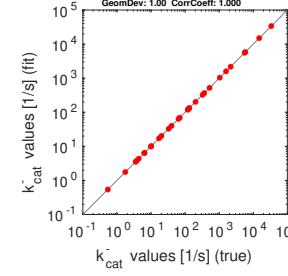
(c) K_{eq} values



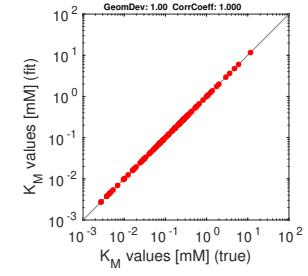
(d) k_{cat}^+ values



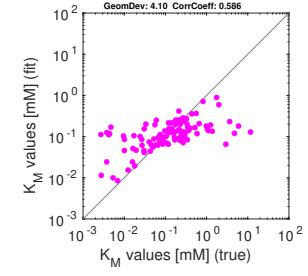
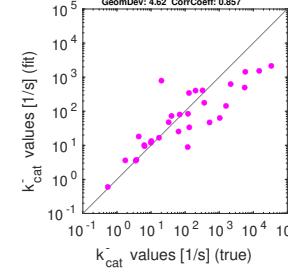
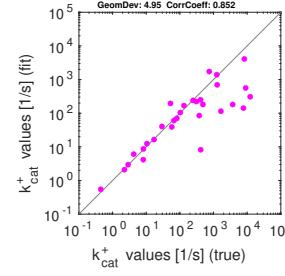
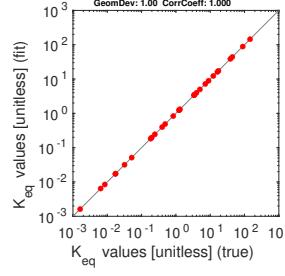
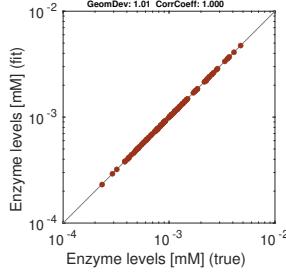
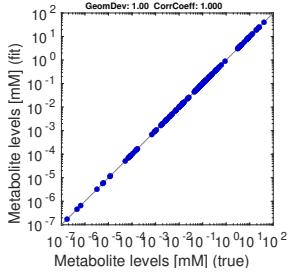
(e) k_{cat}^- values



(f) K_M values



With K_{eq} data only



Without kinetic data

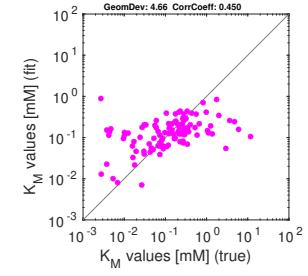
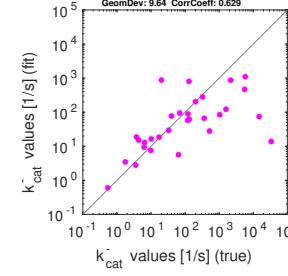
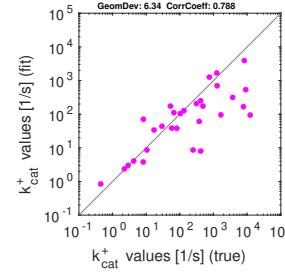
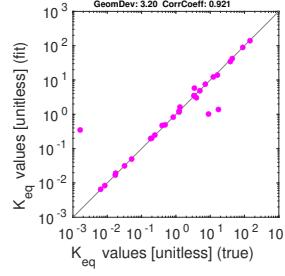
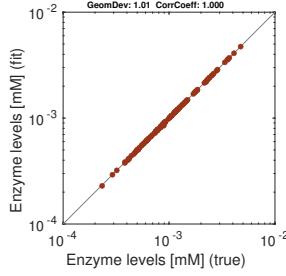
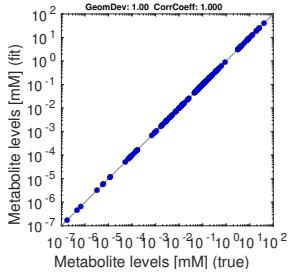


Figure 18: Model balancing results for E. coli metabolism model with artificial data. The model structure is shown in Figure ???. Each subfigure shows “true” values (x-axis) versus reconstructed values (y-axis). Similarities are quantified by geometric standard deviations (“GeomDev”) and Pearson correlation 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)

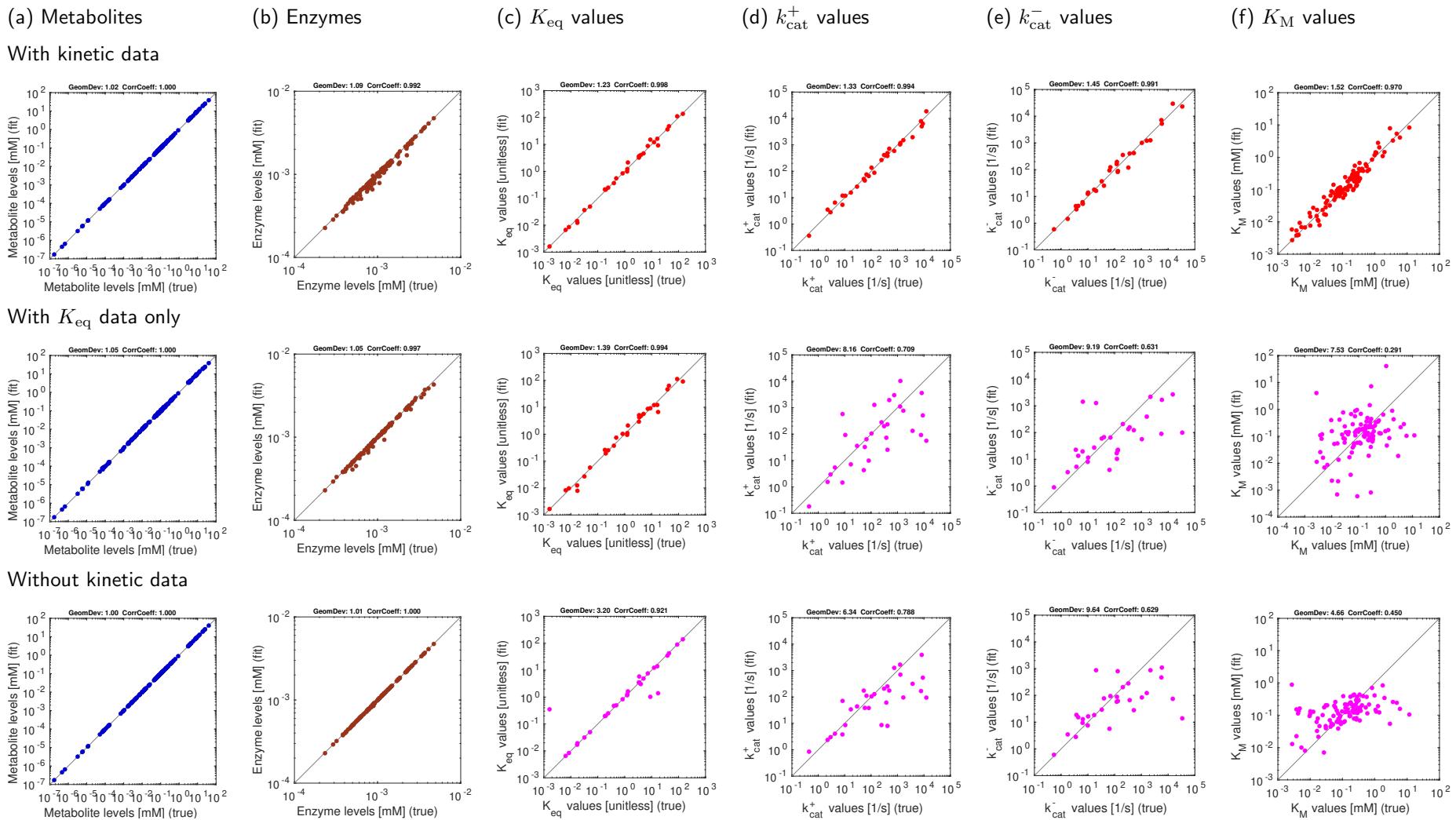


Figure 19: Same as Figure 28, with noisy kinetic data

E. coli metabolism model with artificial data (noise-free kinetic data, noisy state data)

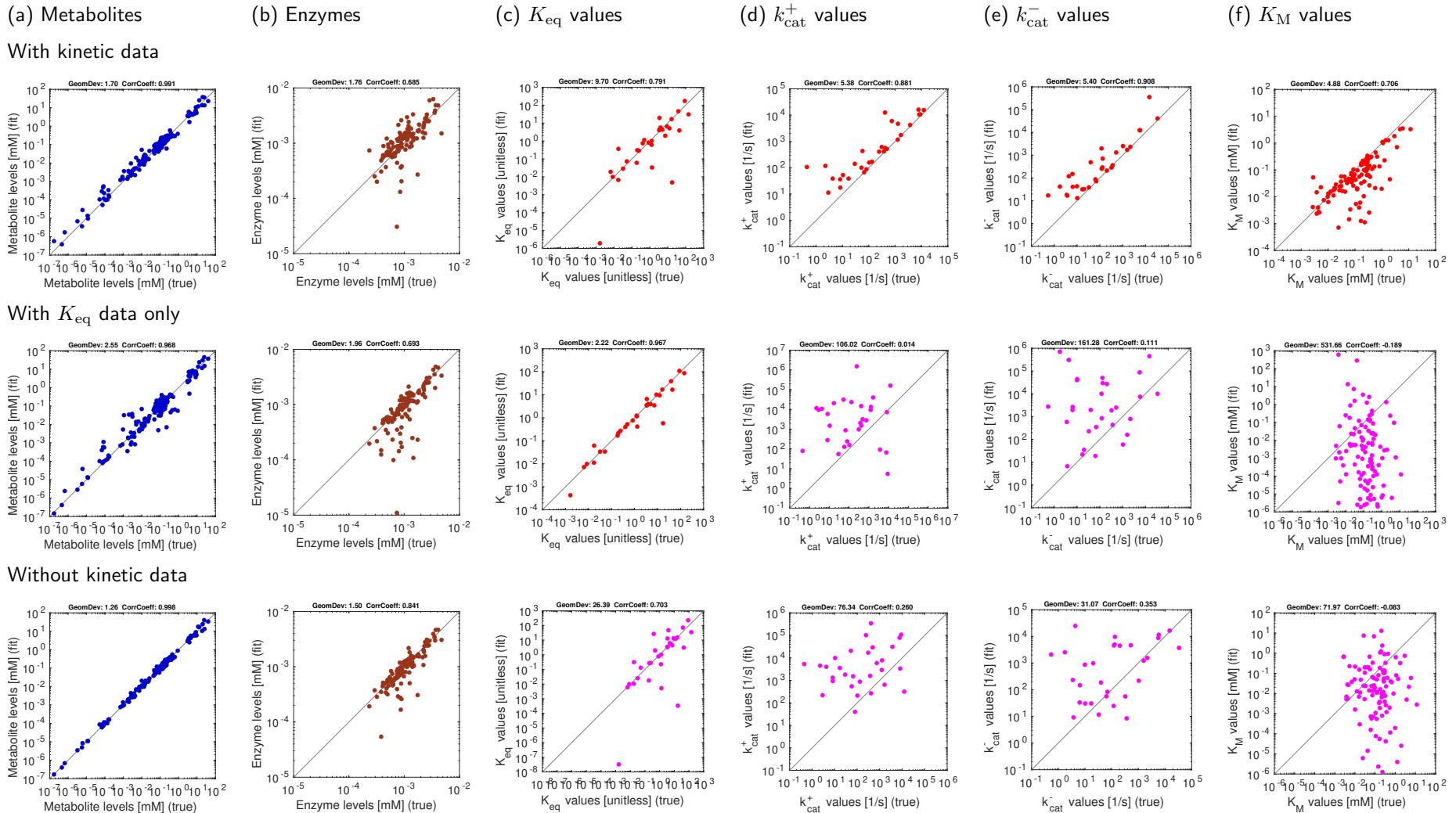


Figure 20: Results for E. coli metabolism with noisy artificial data. Top row: estimation scenario S3 (noisy artificial data, data used for kinetic constants). Centre row: estimation scenario S3K (noisy artificial data, data for equilibrium constants only). Bottom row: estimation scenario S4 (noisy artificial data, no data for kinetic constants).

E. coli metabolism model with artificial data (noisy kinetic data, noisy state data)

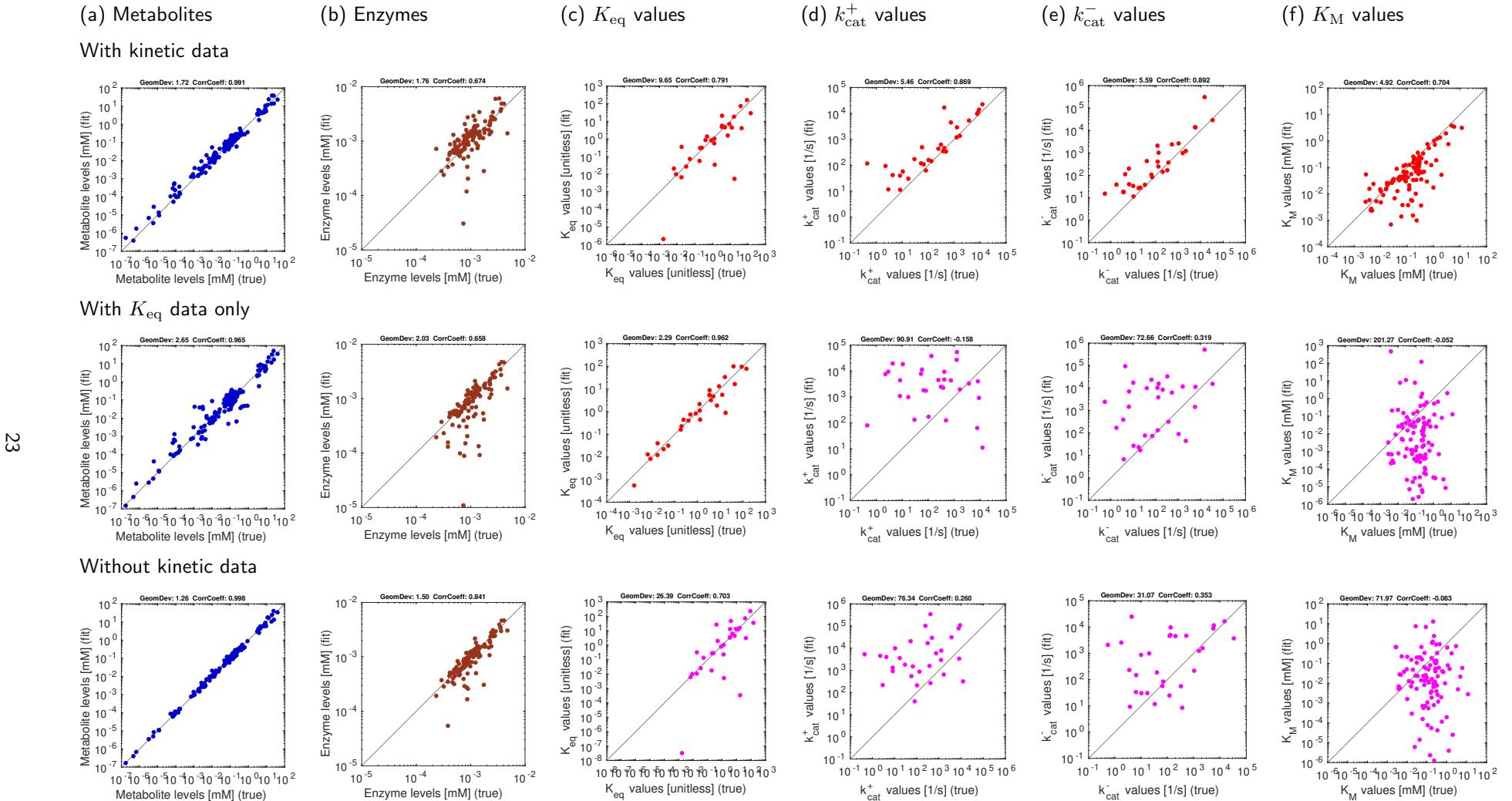


Figure 21: Same as Figure 30, with noisy kinetic data

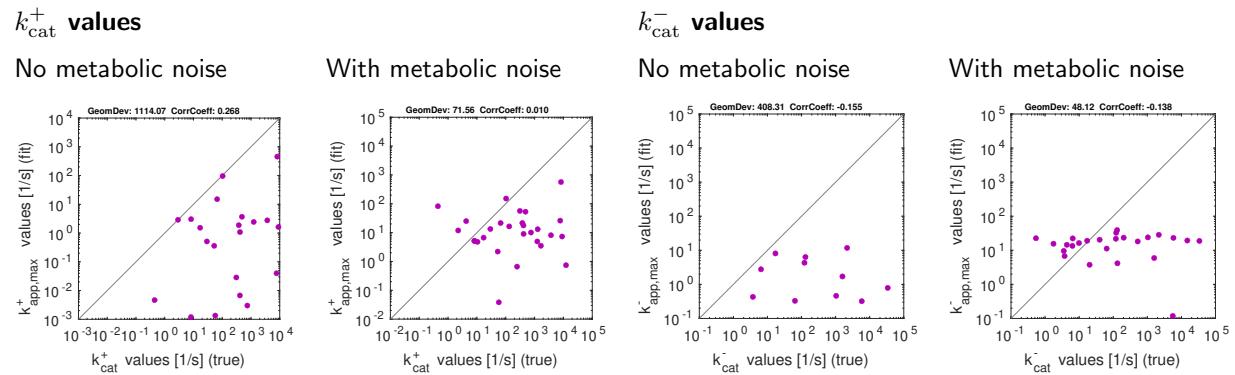


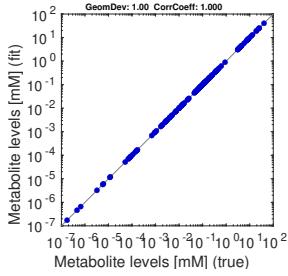
Figure 22: Catalytic constants in *E. coli* metabolism (artificial data), estimated by kinetic profiling [?]. Note that k_{cat} values can only be estimated in the direction of fluxes (e.g. k_{cat}^+ for reactions with forward flux).

5 E. coli model Simulations with alpha = 0.5

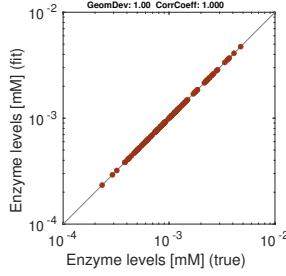
E. coli metabolism model with artificial data (noise-free kinetic data, noise-free state data)

(a) Metabolites

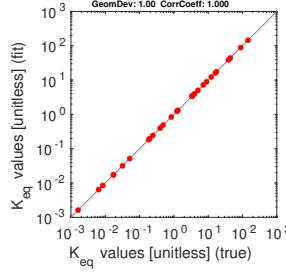
With kinetic data



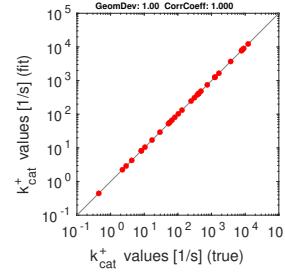
(b) Enzymes



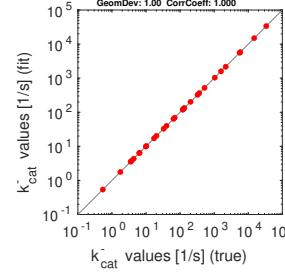
(c) K_{eq} values



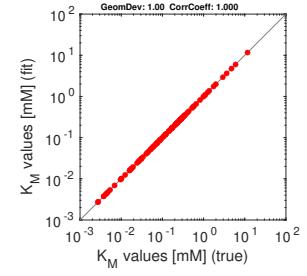
(d) k_{cat}^+ values



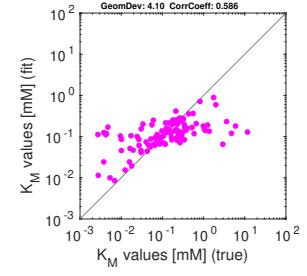
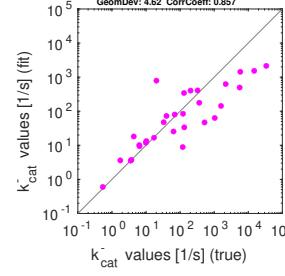
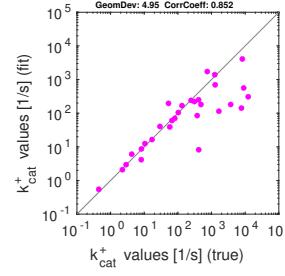
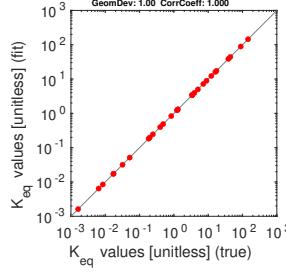
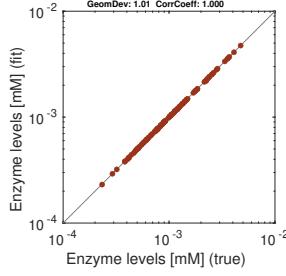
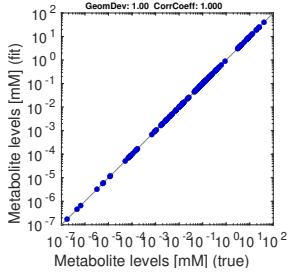
(e) k_{cat}^- values



(f) K_M values



With K_{eq} data only



Without kinetic data

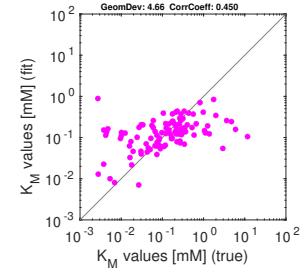
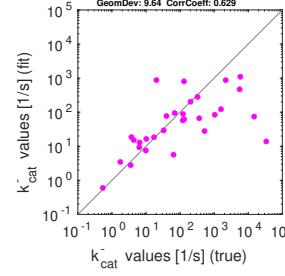
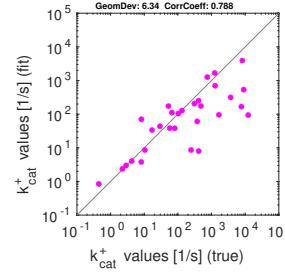
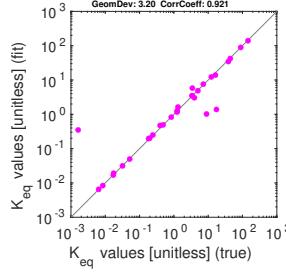
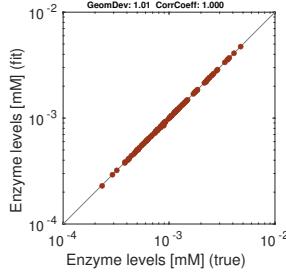
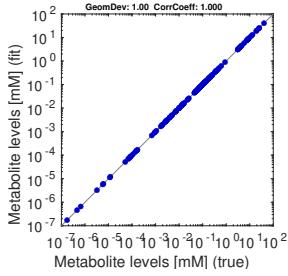


Figure 23: Model balancing results for E. coli metabolism model with artificial data. The model structure is shown in Figure ???. Each subfigure shows “true” values (x-axis) versus reconstructed values (y-axis). Similarities are quantified by geometric standard deviations (“GeomDev”) and Pearson correlation 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)

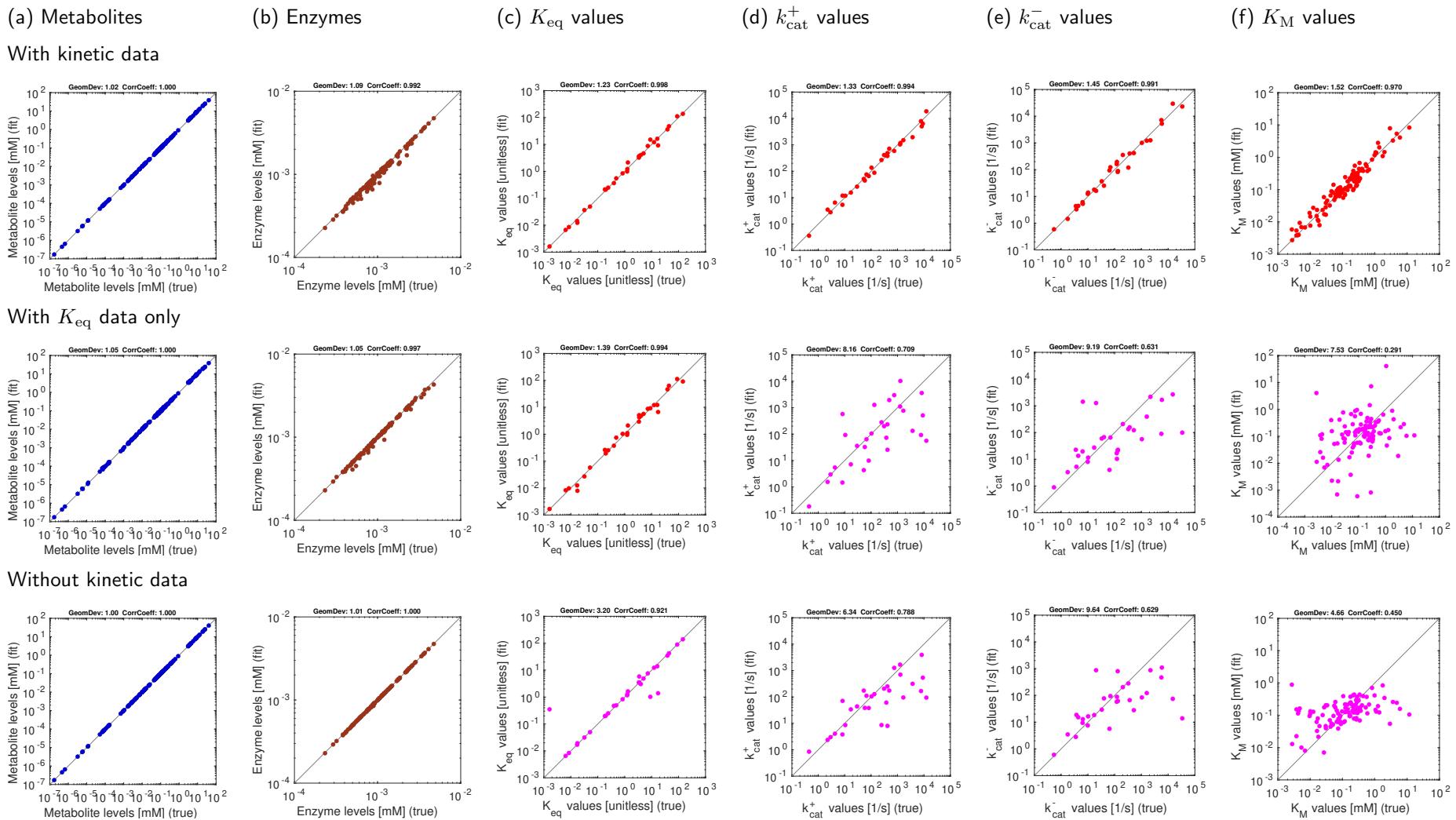


Figure 24: Same as Figure 28, with noisy kinetic data

E. coli metabolism model with artificial data (noise-free kinetic data, noisy state data)

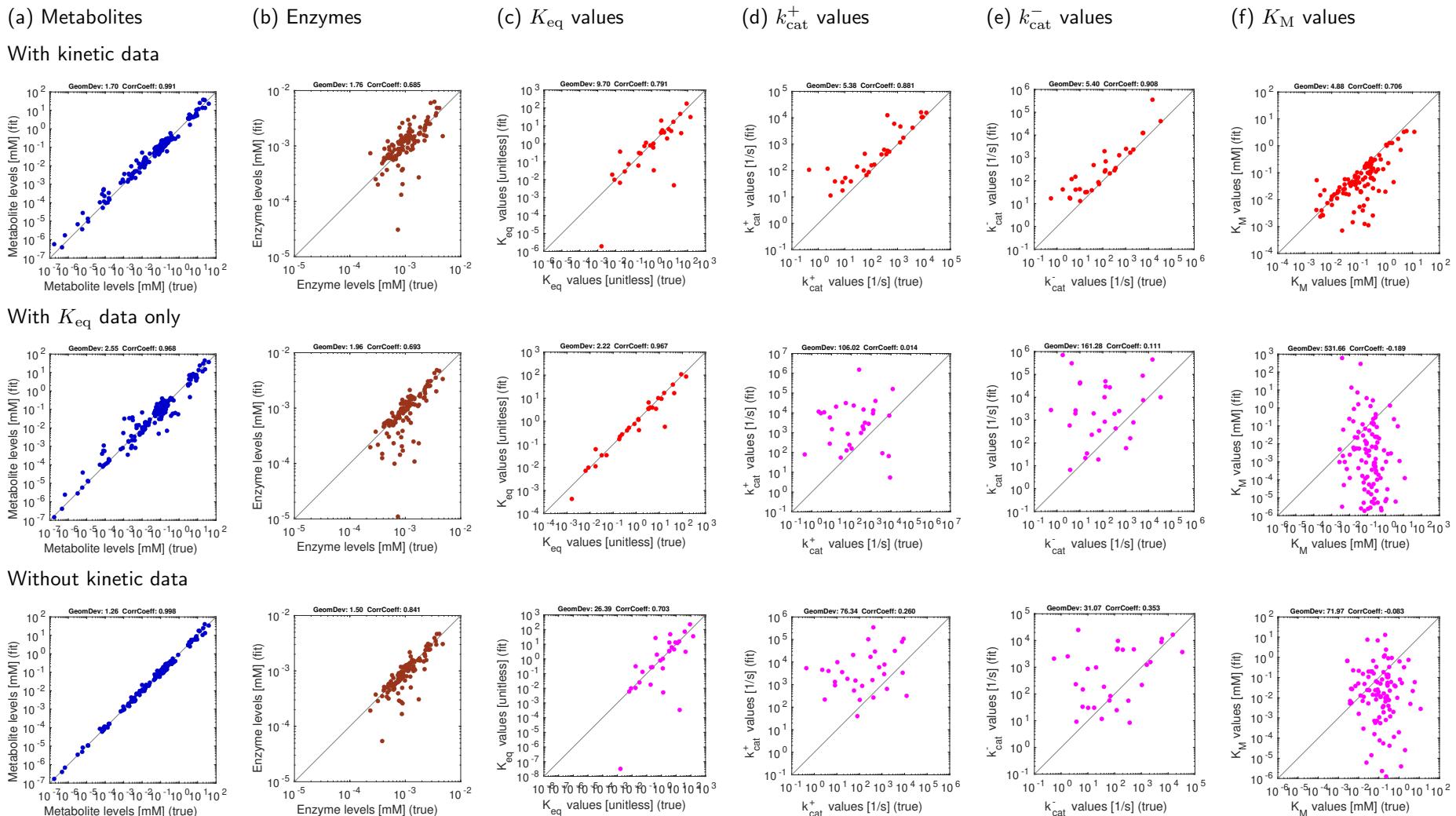


Figure 25: Results for E. coli metabolism with noisy artificial data. Top row: estimation scenario S3 (noisy artificial data, data used for kinetic constants). Centre row: estimation scenario S3K (noisy artificial data, data for equilibrium constants only). Bottom row: estimation scenario S4 (noisy artificial data, no data for kinetic constants).

E. coli metabolism model with artificial data (noisy kinetic data, noisy state data)

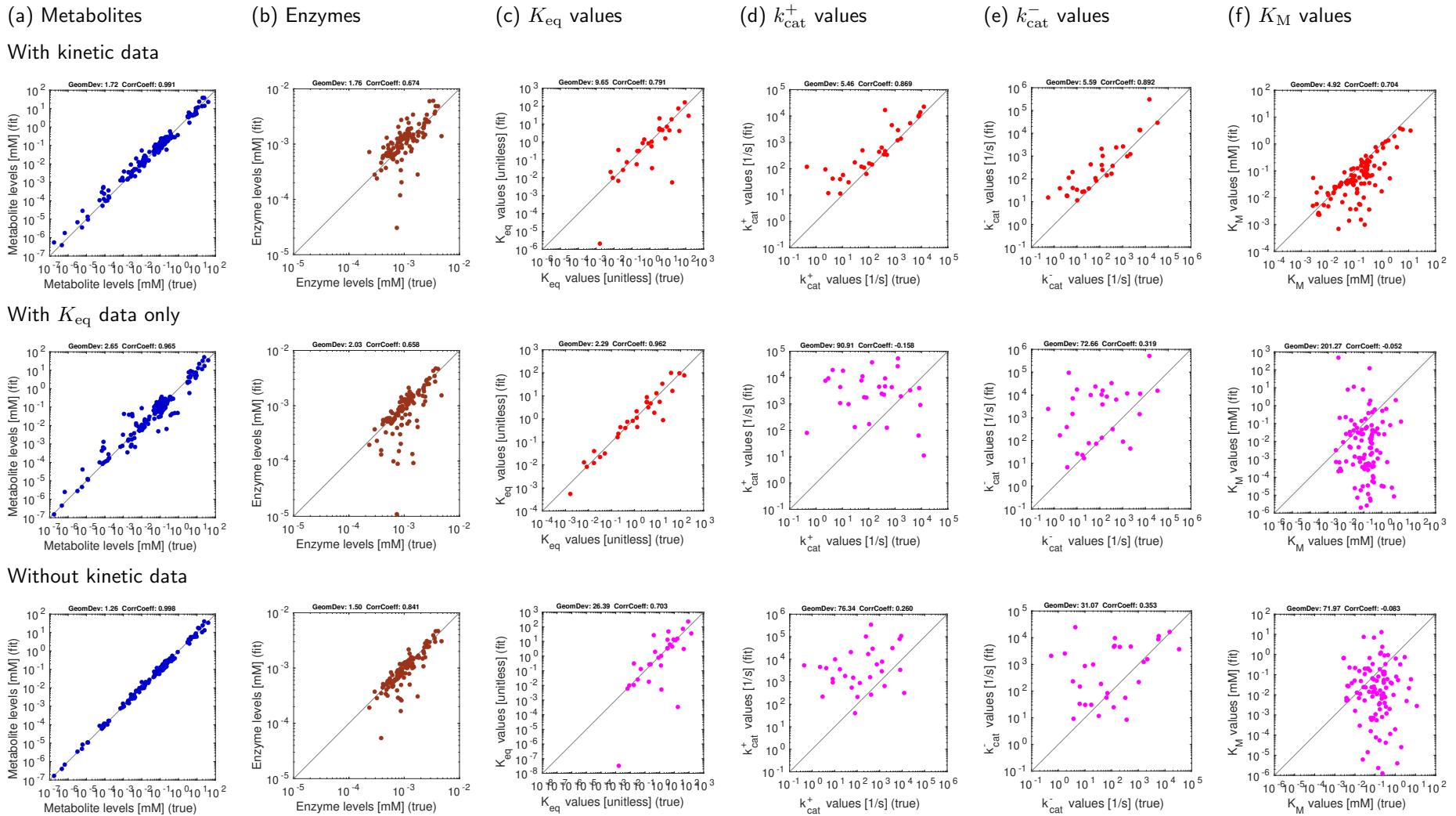


Figure 26: Same as Figure 30, with noisy kinetic data

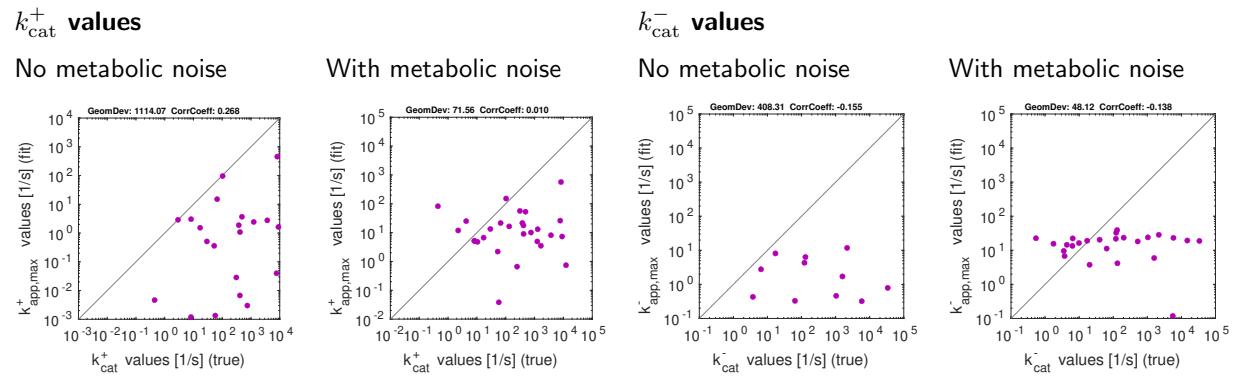


Figure 27: Catalytic constants in *E. coli* metabolism (artificial data), estimated by kinetic profiling [?]. Note that k_{cat} values can only be estimated in the direction of fluxes (e.g. k_{cat}^+ for reactions with forward flux).

6 E. coli model Simulations with alpha = 1

E. coli metabolism model with artificial data (noise-free kinetic data, noise-free state data)

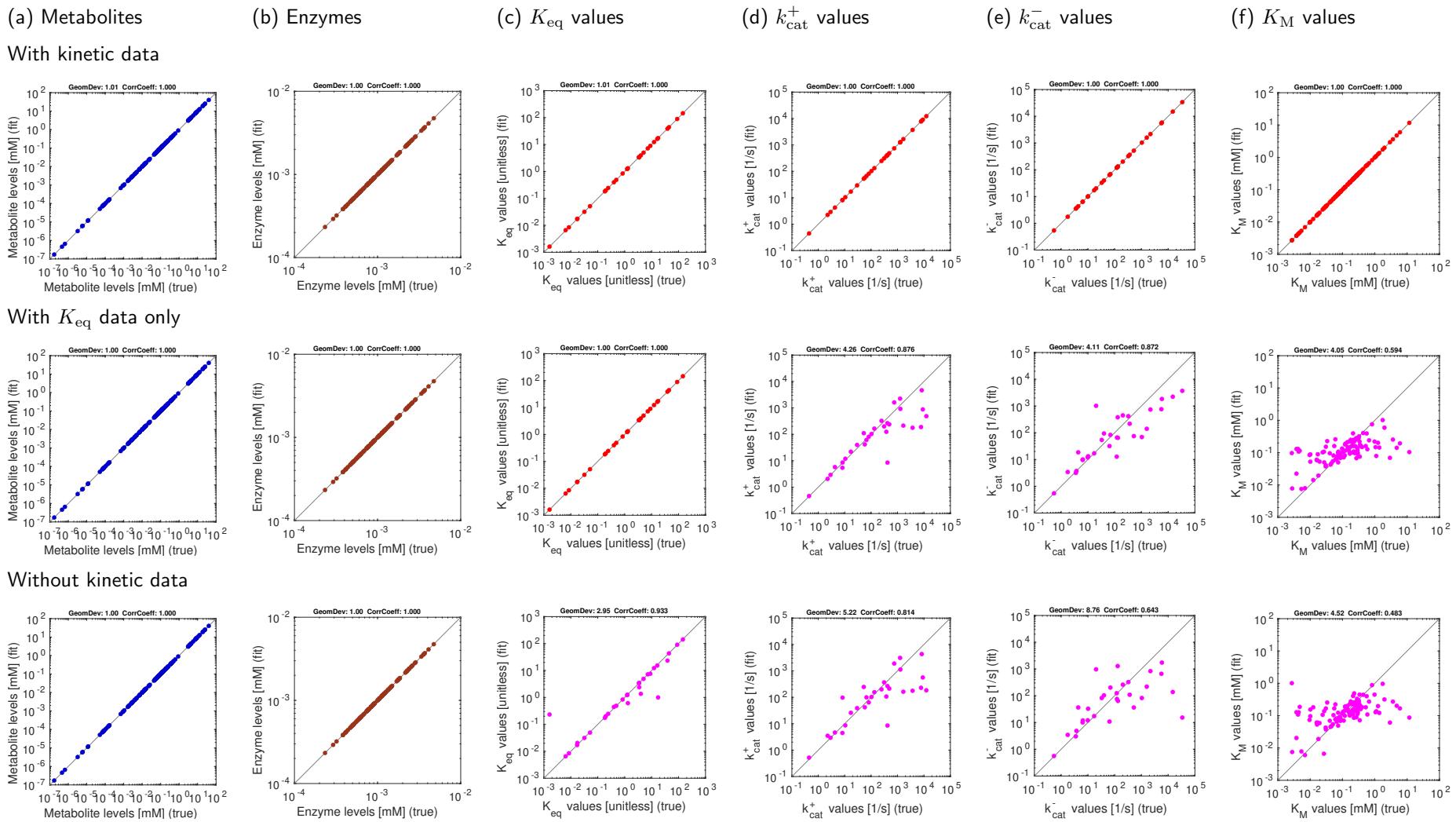


Figure 28: Model balancing results for E. coli metabolism model with artificial data. The model structure is shown in Figure ???. Each subfigure shows “true” values (x-axis) versus reconstructed values (y-axis). Similarities are quantified by geometric standard deviations (“GeomDev”) and Pearson correlation 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)

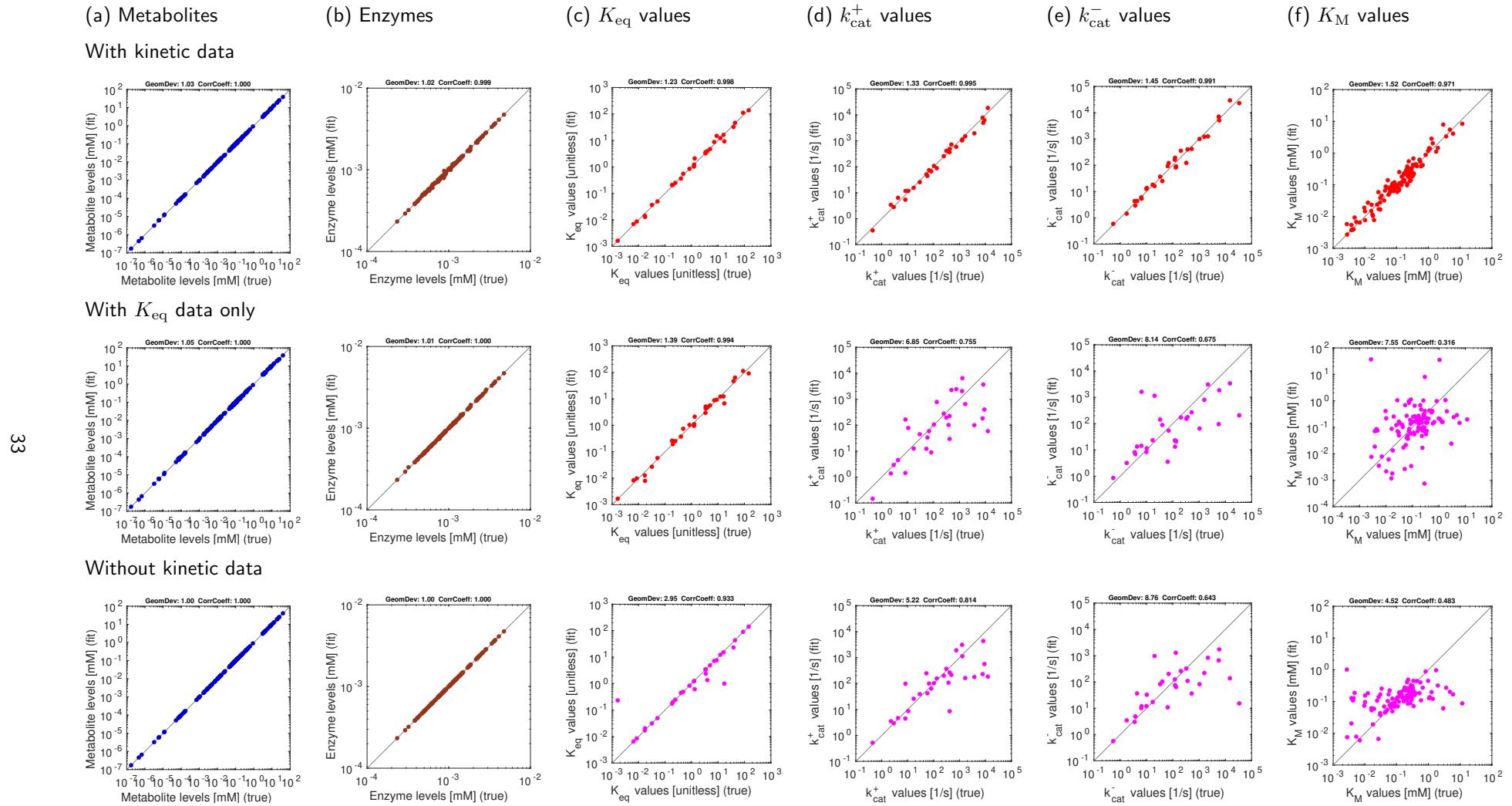


Figure 29: Same as Figure 28, with noisy kinetic data

E. coli metabolism model with artificial data (noise-free kinetic data, noisy state data)

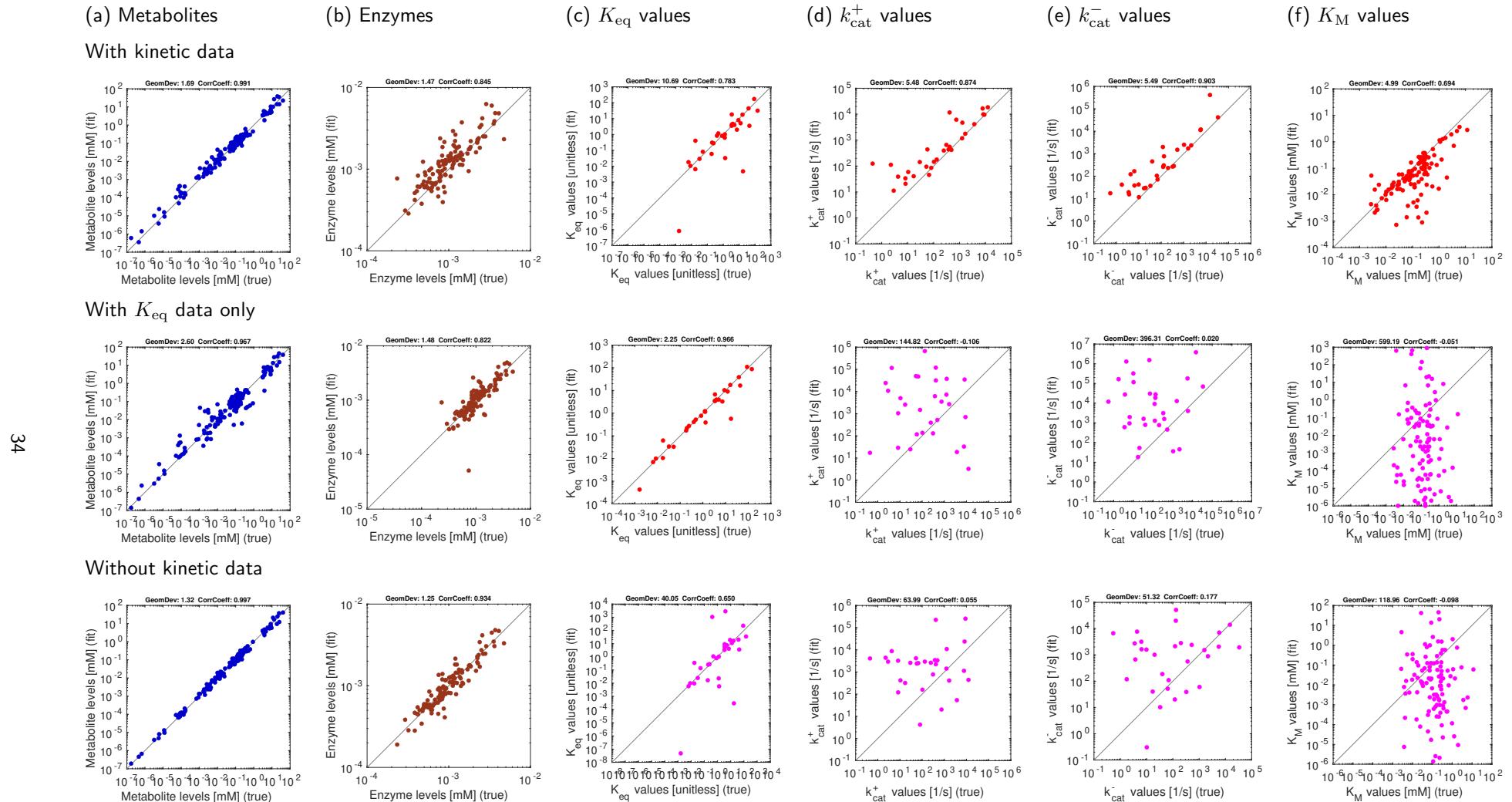
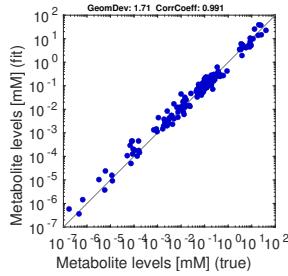


Figure 30: Results for E. coli metabolism with noisy artificial data. Top row: estimation scenario S3 (noisy artificial data, data used for kinetic constants). Centre row: estimation scenario S3K (noisy artificial data, data for equilibrium constants only). Bottom row: estimation scenario S4 (noisy artificial data, no data for kinetic constants).

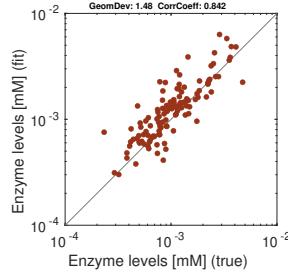
E. coli metabolism model with artificial data (noisy kinetic data, noisy state data)

(a) Metabolites

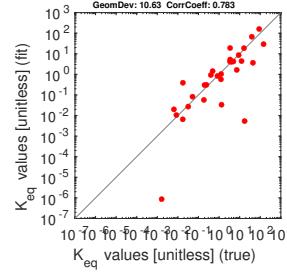
With kinetic data



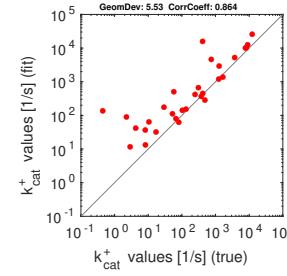
(b) Enzymes



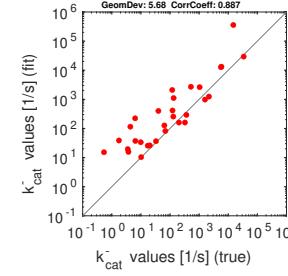
(c) K_{eq} values



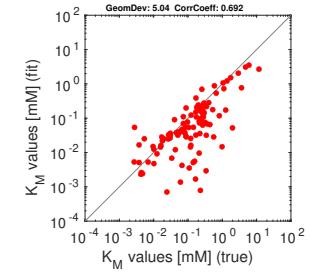
(d) k_{cat}^+ values



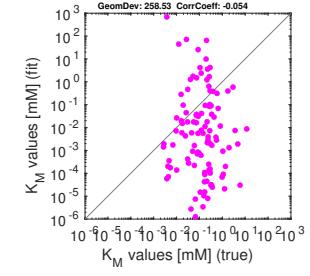
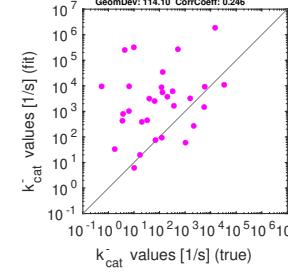
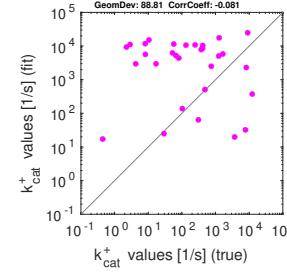
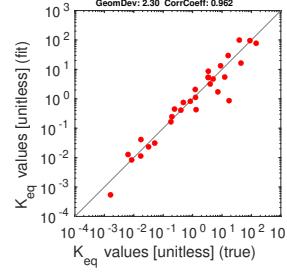
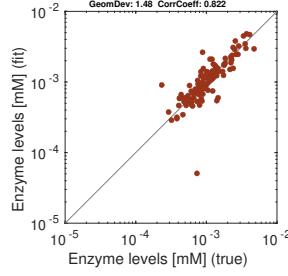
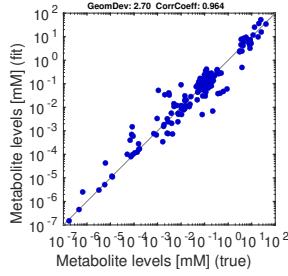
(e) k_{cat}^- values



(f) K_M values



With K_{eq} data only



Without kinetic data

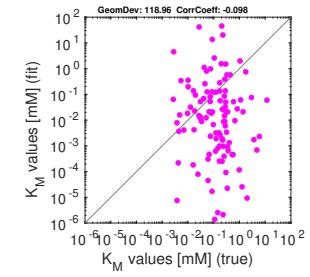
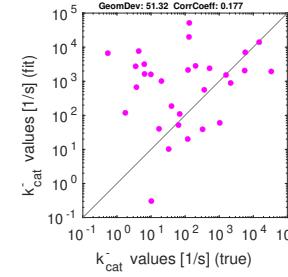
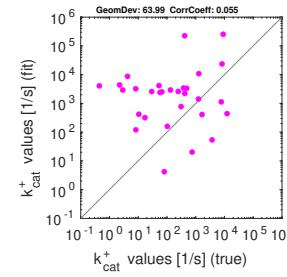
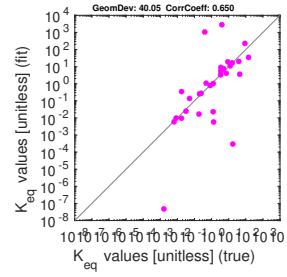
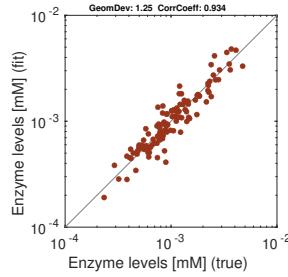
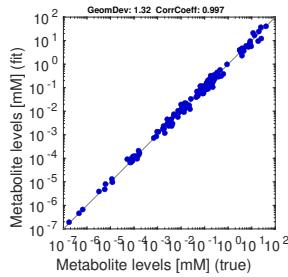


Figure 31: Same as Figure 30, with noisy kinetic data

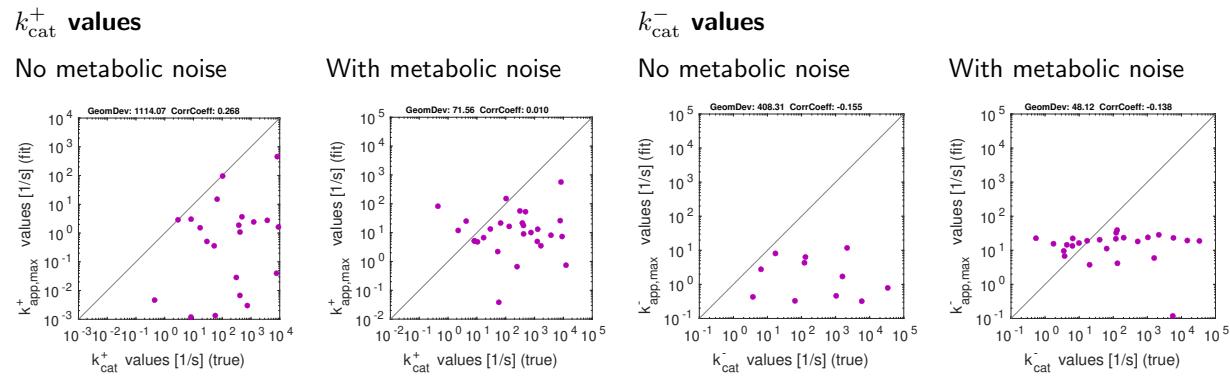


Figure 32: Catalytic constants in *E. coli* metabolism (artificial data), estimated by kinetic profiling [?]. Note that k_{cat} values can only be estimated in the direction of fluxes (e.g. k_{cat}^+ for reactions with forward flux).