1 Branch point simulations with alpha = 0, beta = 0

Branch point model with artificial data (noise-free kinetic data, noise-free state data) - alpha = 0, beta = 0

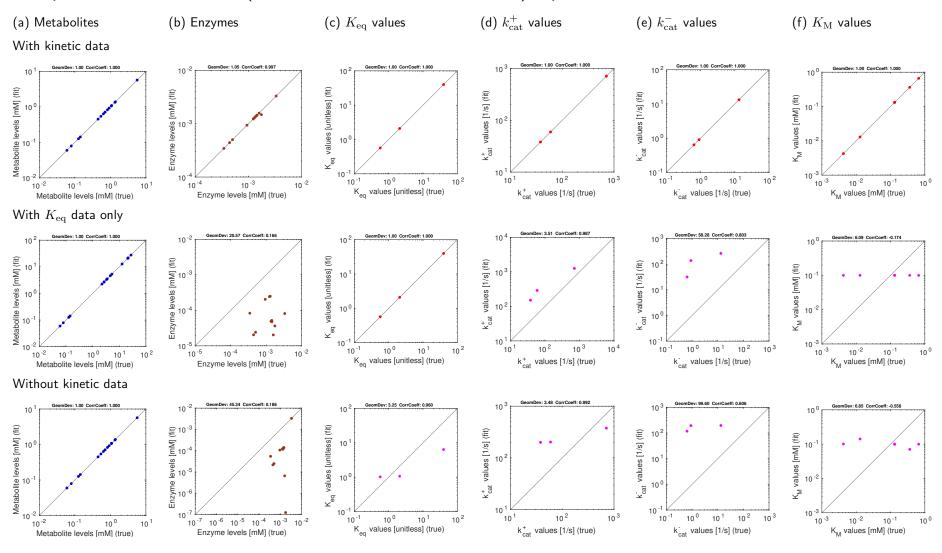


Figure 3: Model balancing results for Branch point model with artificial data. The model structure is shown in Figure ??. Each subfigure shows "true" values (x-axis) versus reconstructed values (y-axis). Similarities are quntified by geometric standard deviations ("GeomDev") and Pearson correlation coefficients ("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 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).

Branch point model with artificial data (noisy kinetic data, noise-free state data) - alpha = 0, beta = 0

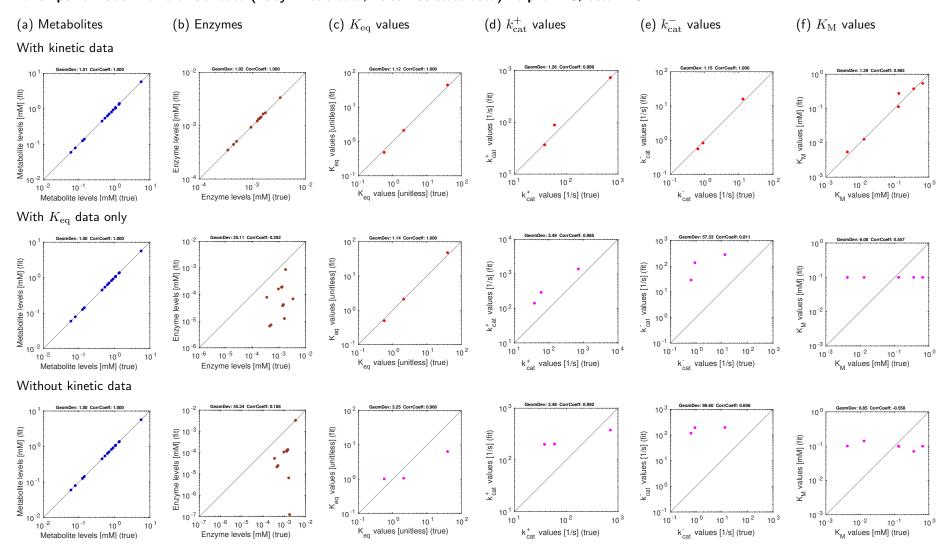


Figure 4: Same as Figure 8, with noisy kinetic data

Branch point model with artificial data (noise-free kinetic data, noisy state data) - alpha = 0, beta = 0

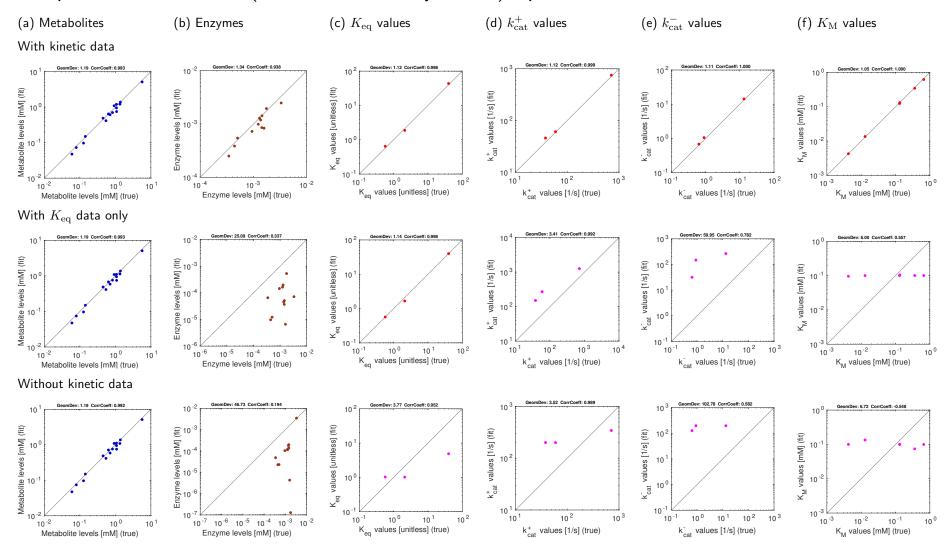


Figure 5: Results for Branch point with noisy artificial data. Top row: estimation scenario S3 (noisy artificial data, data used for kinetic constants). Centre row: estimation scenario S3K (noisy artificial data, data for equilibrium constants only). Bottom row: estimation scenario S4 (noisy artificial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

Branch point model with artificial data (noisy kinetic data, noisy state data) - alpha = 0, beta = 0(c) $K_{ m eq}$ values (d) $k_{\rm cat}^+$ values (e) $k_{\rm cat}^-$ values (a) Metabolites (b) Enzymes (f) $K_{ m M}$ values With kinetic data GeomDev: 1.22 CorrCoeff: 1.000 GeomDev: 1.19 CorrCoeff: 0.999 102 GeomDev: 1.28 CorrCoeff: 0.996 10 10² Metabolite levels [mM] (fit) values [unitless] (fit) Enzyme levels [mM] (fit) values [1/s] (fit) values [1/s] (fit) values [mM] (fit) 10¹ 10 10² 10 ⁰ 10⁰ 10 ⁻² + cat , cat 10² 10³ 10 ¹ 10² 10¹ 10² 10⁻⁴ 10 ⁻³ 10 ⁻² 10⁰ K_{eq} values [unitless] (true) k + values [1/s] (true) k_{cat} values [1/s] (true) K_M values [mM] (true) Metabolite levels [mM] (true) Enzyme levels [mM] (true) With K_{eq} data only GeomDev: 62.62 CorrCoeff: 0.726 GeomDev: 24.05 CorrCoeff: 0.433 GeomDev: 1.52 CorrCoeff: 0.991 10³ GeomDev: 6.04 CorrCoeff: 0.557 10 10-2 10 levels [mM] (fit) (fit) 10 -4 values [unitless] (fit) values [1/s] (fit) values [1/s] (fit) 10² values [mM] (fit) 10 10² 10 ¹ 10 ⁰ Metabolite Io 10⁰ , cat ⊼ 8 10² 10³ 10 ¹ 10² 10⁻¹ 10³ 10 ⁰ 10 ¹ 10² 10 ⁻³ 10⁰ 10⁻⁶ 10⁻⁵ 10⁻⁴ 10⁻³ 10 ⁰ 10 ¹ K_{eq} values [unitless] (true) k_{cat} values [1/s] (true) k at values [1/s] (true) K_M values [mM] (true) Metabolite levels [mM] (true) Enzyme levels [mM] (true) Without kinetic data GeomDev: 46.73 CorrCoeff: 0.194 GeomDev: 3.77 CorrCoeff: 0.952 GeomDev: 6.72 CorrCoeff: -0.548 103 10 10 -2 10 2 Metabolite levels [mM] (fit) (iti) [mM] (iti) 10⁻³ values [unitless] (fit) values [1/s] (fit) values [mM] (fit) values [1/s] (fit) 10² 10 ¹ 10² 10¹ 10 ⁰ (at 10°) κ cat

Figure 6: Same as Figure 10, with noisy kinetic data

10¹

K_{eq} values [unitless] (true)

10⁻⁷ 10⁻⁶ 10⁻⁵ 10⁻⁴ 10⁻³ 10⁻²

Enzyme levels [mM] (true)

10 ⁰

10 ⁻¹

Metabolite levels [mM] (true)

10¹

10¹

10²

k + values [1/s] (true)

10³

10⁻¹

10²

10 ⁻³

10⁻²

K_M values [mM] (true)

10 ⁰

10 ¹

k-at values [1/s] (true)

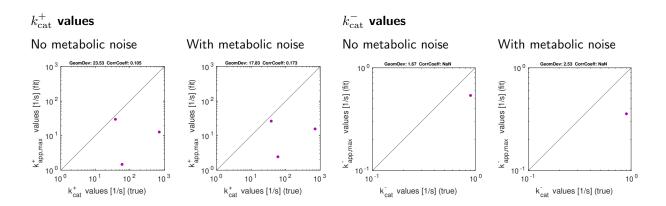


Figure 7: Catalytic constants in Branch point (artificial data), estimated by kinetic profiling. Note that $k_{\rm cat}$ values can only be estimated in the direction of fluxes (e.g. $k_{\rm cat}^+$ for reactions with forward fluxe).

2 Branch point simulations with alpha = 1, beta = 0

Branch point model with artificial data (noise-free kinetic data, noise-free state data) - alpha = 1, beta = 0

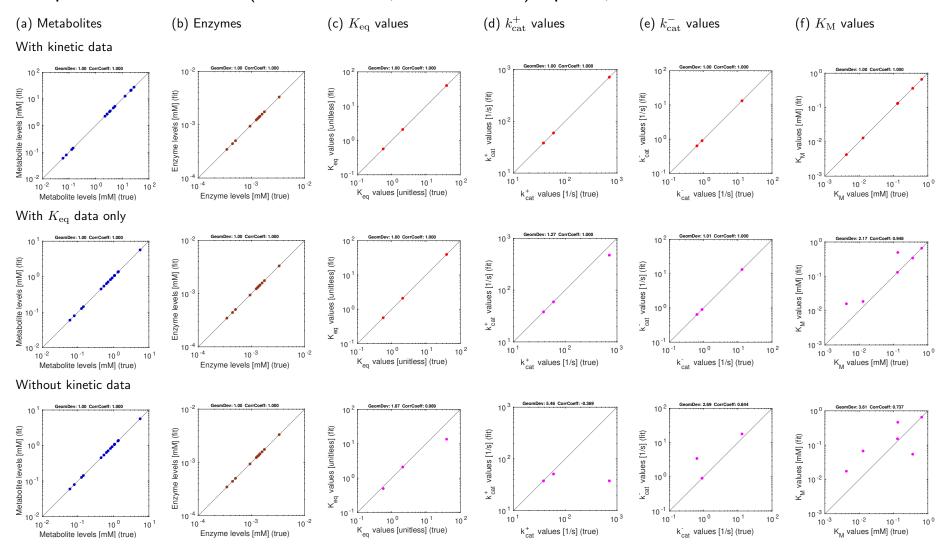


Figure 8: Model balancing results for Branch point model with artificial data. The model structure is shown in Figure ??. Each subfigure shows "true" values (x-axis) versus reconstructed values (y-axis). Similarities are quntified by geometric standard deviations ("GeomDev") and Pearson correlation coefficients ("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 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).

10⁻²

10 ⁻¹

Metabolite levels [mM] (true)

10 ⁰

10¹

10 -4

10⁻⁴

10 ⁻³

Enzyme levels [mM] (true)

10 ⁻²

Branch point model with artificial data (noisy kinetic data, noise-free state data) - alpha = 1, beta = 0(c) $K_{ m eq}$ values (d) $k_{\rm cat}^+$ values (e) $k_{\rm cat}^-$ values (a) Metabolites (b) Enzymes (f) $K_{ m M}$ values With kinetic data GeomDev: 1.25 CorrCoeff: 0.990 GeomDev: 1.22 CorrCoeff: 0.999 10 102 GeomDev: 1.39 CorrCoeff: 0.985 10² 10² Metabolite levels [mM] (fit) values [unitless] (fit) Enzyme levels [mM] (fit) 0 6 values [1/s] (fit) values [1/s] (fit) values [mM] (fit) 10¹ 10 10² 10⁰ 10⁰ 10⁰ 10 ⁻² + cat , cat 10² 10³ 10 ¹ 10² 10¹ 10² 10⁰ 10⁻⁴ 10 ⁻³ 10 ⁻² 10 ⁻¹ 10⁰ 10 ¹ K_{eq} values [unitless] (true) k + values [1/s] (true) k_{cat} values [1/s] (true) K_M values [mM] (true) Enzyme levels [mM] (true) Metabolite levels [mM] (true) With K_{eq} data only GeomDev: 1.24 CorrCoeff: 0.999 10 10² GeomDev: 2.18 CorrCoeff: 0.943 10 10-2 10 Metabolite levels [mM] (fit) Enzyme levels [mM] (fit) values [unitless] (fit) values [1/s] (fit) values [1/s] (fit) values [mM] (fit) 10 ¹ 10 10² 10⁰ 10 ⁰ , cat 10 -10² 10³ 10 ⁰ 10⁻¹ 10 ¹ 10² 10 ⁰ 10 ¹ 10² 10 ⁻³ 10⁰ 10⁻⁴ 10 ⁻³ 10 ⁻² 10 ⁻¹ 10 ⁰ 10 ¹ K_{eq} values [unitless] (true) k + values [1/s] (true) k at values [1/s] (true) K_M values [mM] (true) Metabolite levels [mM] (true) Enzyme levels [mM] (true) Without kinetic data Dev: 1.00 CorrCoeff: 1.000 GeomDev: 1.87 CorrCoeff: 0.989 GeomDev: 2.69 CorrCoeff: 0.844 GeomDev: 3.61 CorrCoeff: 0.737 102 10 10 -2 10 2 Metabolite levels [mM] (fit) Enzyme levels [mM] (fit) values [unitless] (fit) values [1/s] (fit) values [1/s] (fit) values [mM] (fit) 10 ¹ 10 ¹ 10² 10⁰ 10 ⁰ , cat

Figure 9: Same as Figure 8, with noisy kinetic data

10¹

K_{eq} values [unitless] (true)

κ cat

10¹

10²

k + values [1/s] (true)

10³

10⁻¹

10 ⁰

k at values [1/s] (true)

10 ¹

10²

10 ⁻³

10⁻²

K_M values [mM] (true)

10 ⁰

Branch point model with artificial data (noise-free kinetic data, noisy state data) - alpha = 1, beta = 0

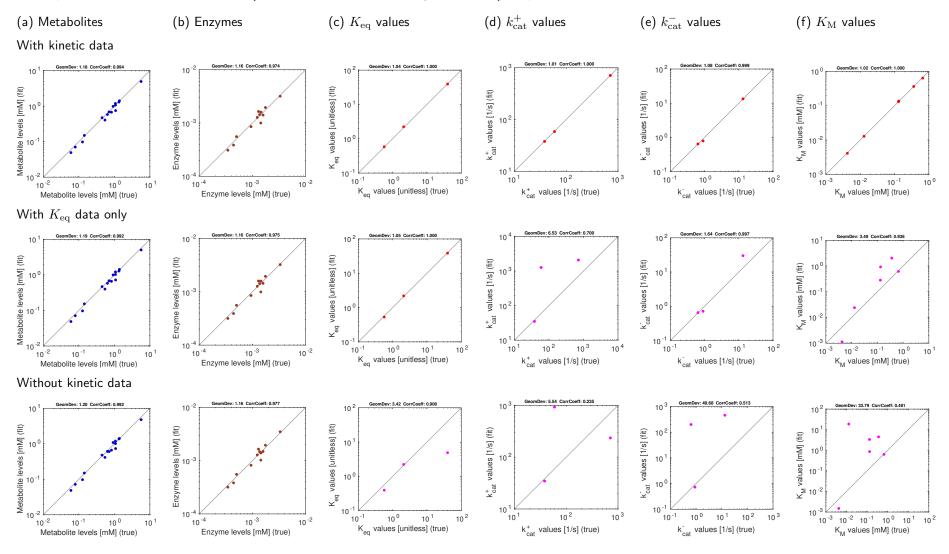


Figure 10: Results for Branch point with noisy artificial data. Top row: estimation scenario S3 (noisy artificial data, data used for kinetic constants). Centre row: estimation scenario S3K (noisy artificial data, data for equilibrium constants only). Bottom row: estimation scenario S4 (noisy artificial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

10 -4

10 ⁰

10 ⁻¹

Metabolite levels [mM] (true)

10¹

10⁻⁴

10 ⁻³

Enzyme levels [mM] (true)

10 ⁻²

Branch point model with artificial data (noisy kinetic data, noisy state data) - alpha = 1, beta = 0(c) $K_{ m eq}$ values (d) $k_{\rm cat}^+$ values (e) $k_{\rm cat}^-$ values (a) Metabolites (b) Enzymes (f) $K_{ m M}$ values With kinetic data GeomDev: 1.16 CorrCoeff: 1.000 GeomDev: 1.18 CorrCoeff: 0.993 GeomDev: 1.25 CorrCoeff: 1.000 102 GeomBey: 1.31 CorrCoeff: 0.996 10 10² Metabolite levels [mM] (fit) values [unitless] (fit) Enzyme levels [mM] (fit) 0 6 values [1/s] (fit) values [1/s] (fit) values [mM] (fit) 10¹ 10 10² 10 ⁰ 10⁰ 10 ⁻² + cat , cat 10² 10³ 10 ¹ 10² 10¹ 10² 10⁻⁴ 10 ⁻³ 10 ⁻² 10⁰ K_{eq} values [unitless] (true) k + values [1/s] (true) k_{cat} values [1/s] (true) K_M values [mM] (true) Metabolite levels [mM] (true) Enzyme levels [mM] (true) With K_{eq} data only GeomDev: 1.68 CorrCoeff: 0.949 10 10² GeomDev: 5.08 CorrCoeff: 0.858 10 10-2 10 levels [mM] (fit) values [1/s] (fit) 0 10 2 2 Enzyme levels [mM] (fit) values [unitless] (fit) values [1/s] (fit) 10⁰ values [mM] (fit) 10¹ 10 10⁰ 10 ⁰ Metabolite Io , cat ×8 10 " 10³ 10 ⁰ 10² 10⁴ 10⁻¹ 10 ¹ 10² 10 ¹ 10² 10⁻² 10⁻¹ 10⁰ 10⁻⁴ 10 ⁻³ 10 ⁻² 10 ⁻¹ 10 ⁰ 10 ¹ K_{eq} values [unitless] (true) k at values [1/s] (true) k_{cat} values [1/s] (true) K_M values [mM] (true) Metabolite levels [mM] (true) Enzyme levels [mM] (true) Without kinetic data nDev: 1.16 CorrCoeff: 0.977 GeomDev: 3.42 CorrCoeff: 0.908 GeomDev: 33.79 CorrCoeff: 0.481 10³ 10 10 -2 10 2 10² Metabolite levels [mM] (fit) values [unitless] (fit) Enzyme levels [mM] (fit) values [1/s] (fit) values [mM] (fit) values [1/s] (fit) 10² 10 ¹ 10⁰ 10² 10 ¹ 10 ⁰ (at 10°) κ cat

Figure 11: Same as Figure 10, with noisy kinetic data

10¹

K_{eq} values [unitless] (true)

10¹

10²

k + values [1/s] (true)

10³

10⁻¹

10²

10 -3 10 -2 10 -1 10 0 10 1

K_M values [mM] (true)

10 ¹

k-at values [1/s] (true)

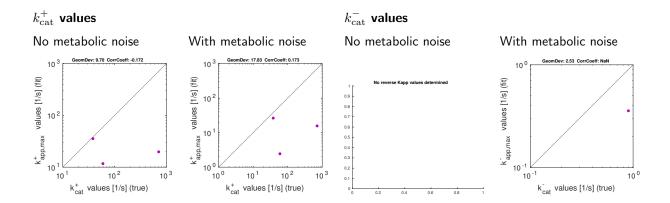


Figure 12: Catalytic constants in Branch point (artificial data), estimated by kinetic profiling. Note that $k_{\rm cat}$ values can only be estimated in the direction of fluxes (e.g. $k_{\rm cat}^+$ for reactions with forward fluxe).