

## **1 E. coli Glucose Simulations with $\alpha = 0.1$ , $\beta = 0$**

### E. coli model (aerobic growth on glucose), balanced kinetic data

(a) Metabolites

(b) Enzymes

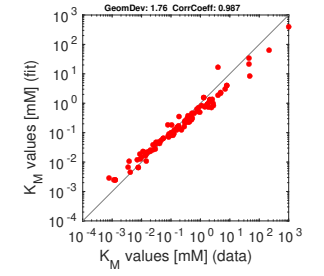
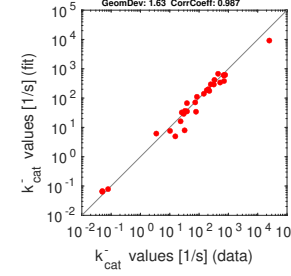
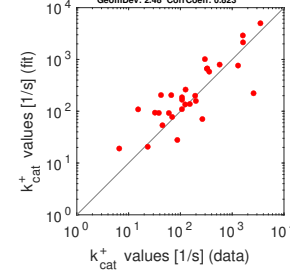
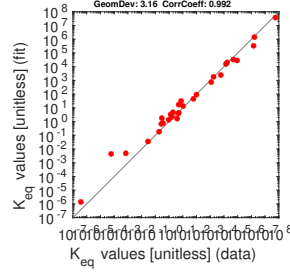
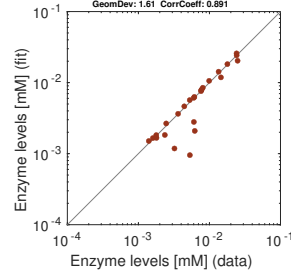
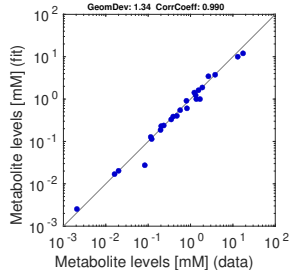
(c)  $K_{eq}$  values

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

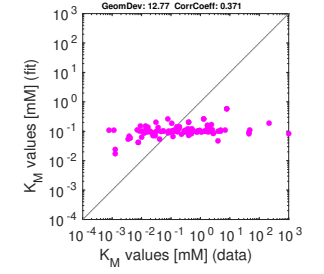
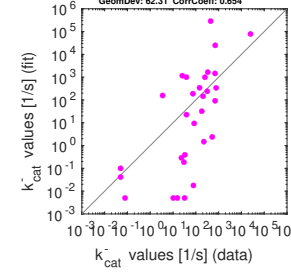
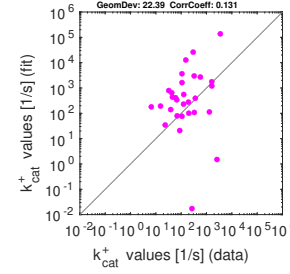
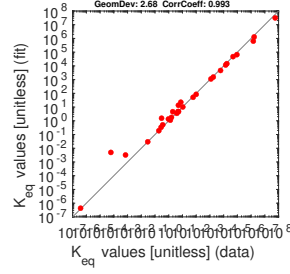
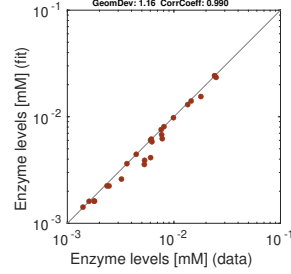
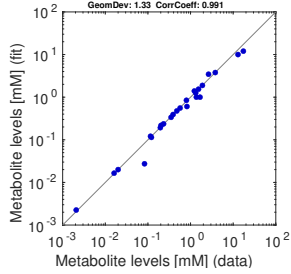
(e)  $k_{cat}^-$  values

(f)  $K_M$  values

With kinetic data



With  $K_{eq}$  data only



Without kinetic data

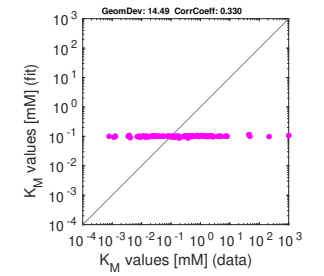
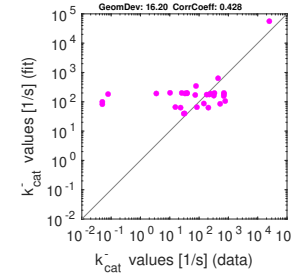
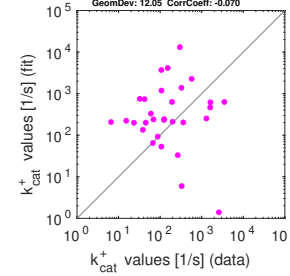
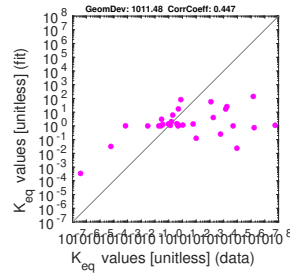
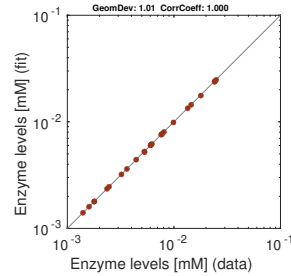
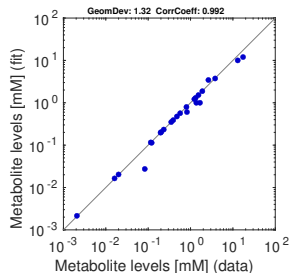


Figure 3: Results for *E. coli* central metabolism with experimental data (aerobic growth on glucose). The kinetic data stem from previous parameter balancing based on *in-vitro* data. Top: estimation using kinetic data. Centre: estimation using equilibrium constants as the only kinetic data. Bottom: estimation without usage of kinetic data. The same metabolite, enzyme, and kinetic data were used in [?].

# **E. coli central metabolism model (aerobic growth on glucose), in-vitro kinetic data**

(a) Metabolites

(b) Enzymes

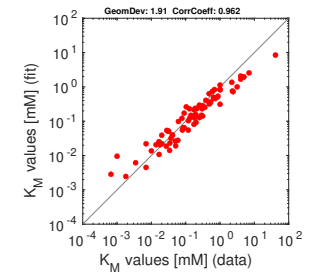
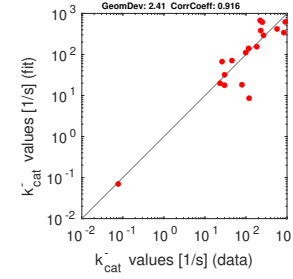
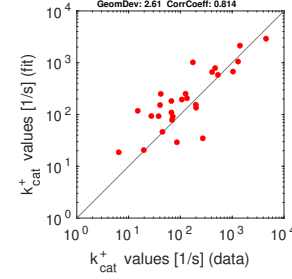
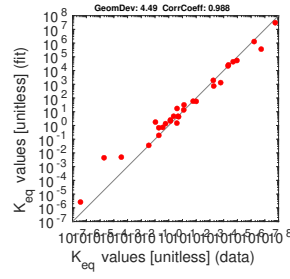
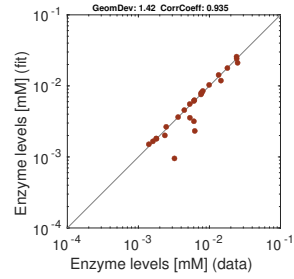
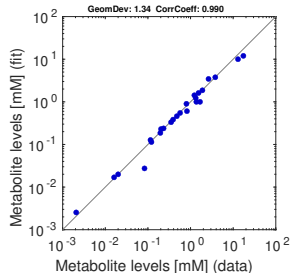
(c)  $K_{eq}$  values

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

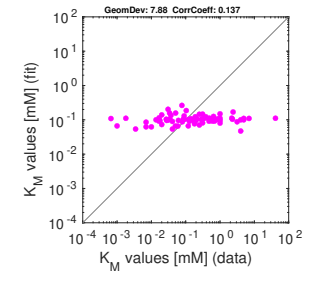
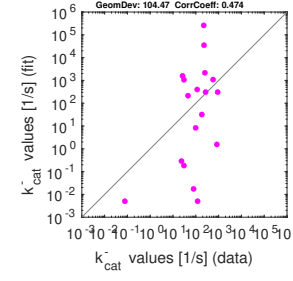
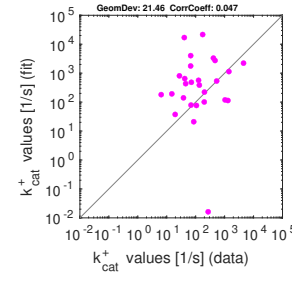
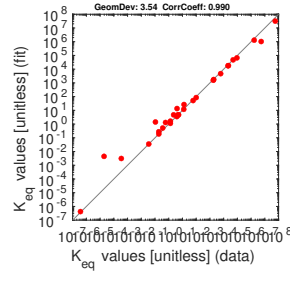
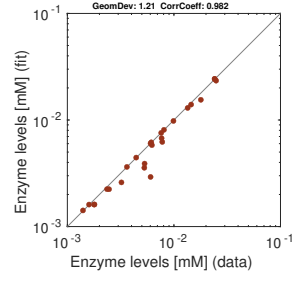
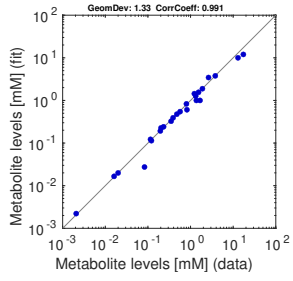
(e)  $k_{cat}^-$  values

(f)  $K_M$  values

With kinetic data



With  $K_{eq}$  data only



Without kinetic data

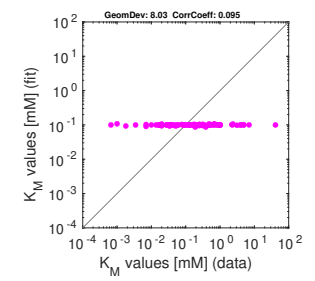
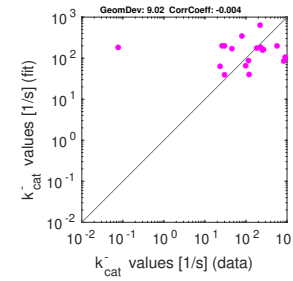
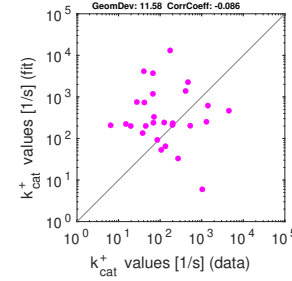
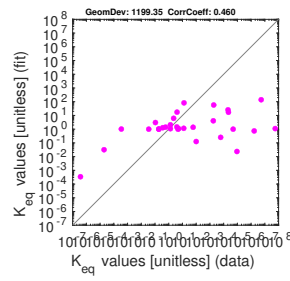
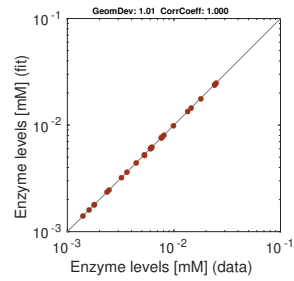
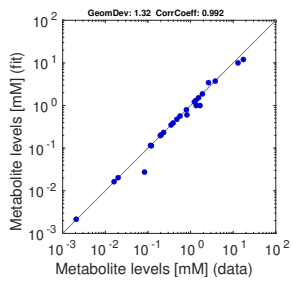


Figure 4: Results for *E. coli* central metabolism with experimental data (aerobic growth on glucose). Same as Figure 11, but based on original kinetic *in-vitro* data instead of balanced kinetic data.

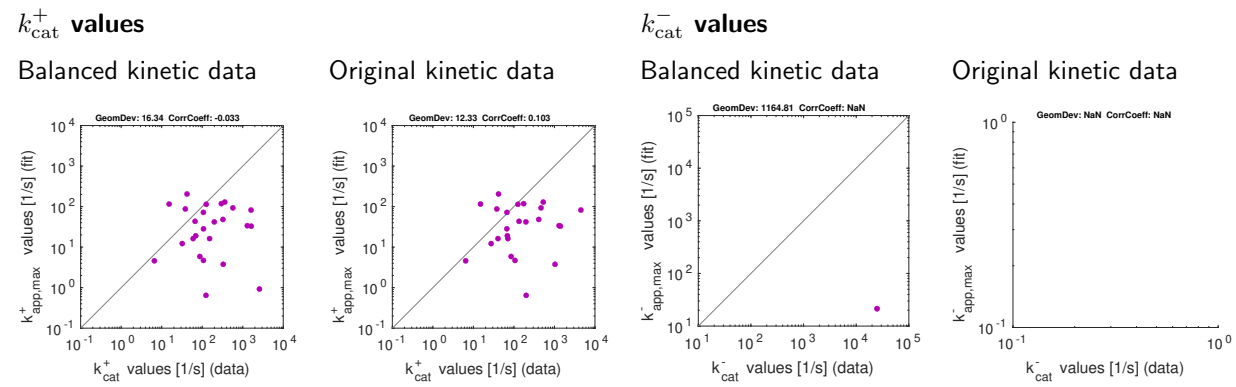
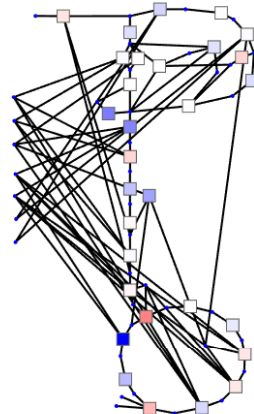
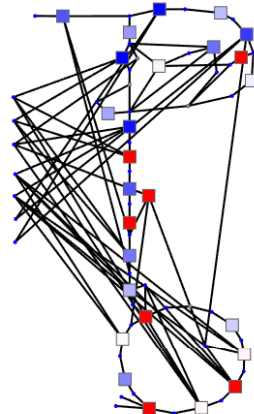
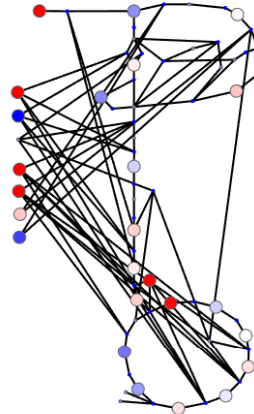
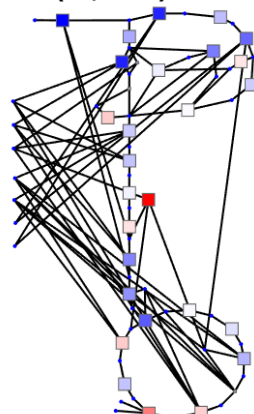


Figure 5: Catalytic constants in *E. coli* central metabolism model (aerobic growth on glucose), estimated by kinetic profiling [?].

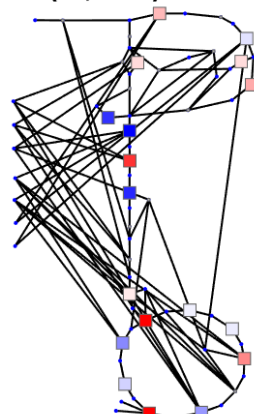
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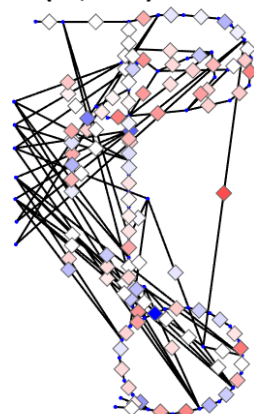
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Kcatr (fit/data) f.c.<13.95



KM (fit/data) f.c.<9.53



Reaction orientation w.r.t flux signs

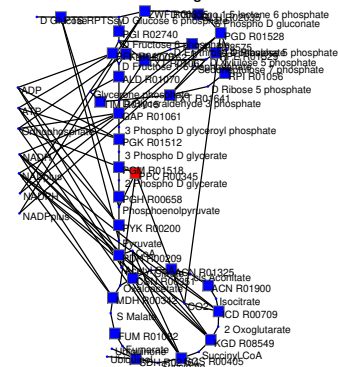


Figure 6: Diagnostic plots for fit with original kinetic data. Left: Relative fitting errors. Blue: fitted value too high. Red: fitted value too low. Maximal fold changes (whether up or down) are given by numbers. Right: Reaction orientatation (defining “forward” and “reverse”). Blue: in flux direction; Red: against flux direction.

## 2 E. coli Glucose Simulations with $\alpha = 0.5$ , $\beta = 0$

## E. coli model (aerobic growth on glucose), balanced kinetic data

(a) Metabolites

(b) Enzymes

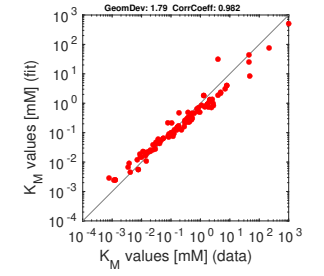
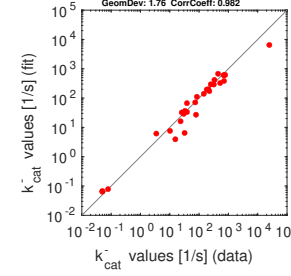
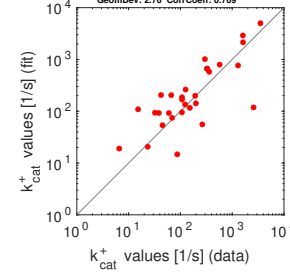
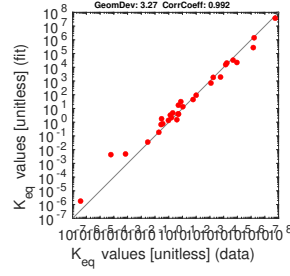
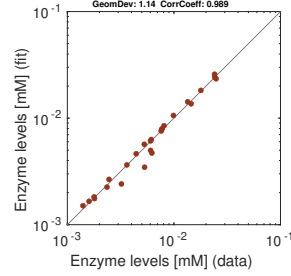
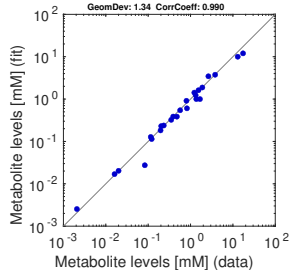
(c)  $K_{eq}$  values

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

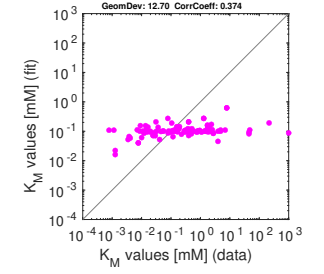
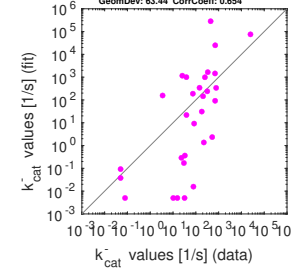
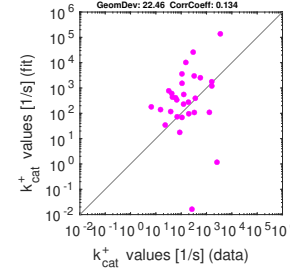
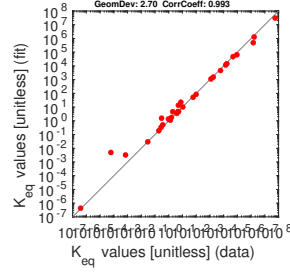
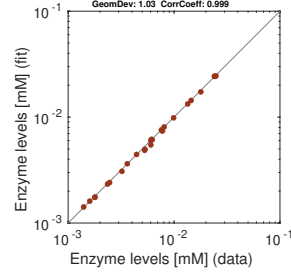
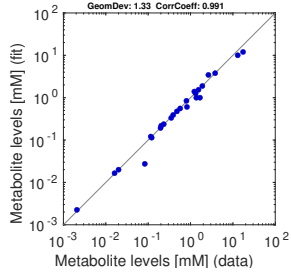
(e)  $k_{cat}^-$  values

(f)  $K_M$  values

With kinetic data



With  $K_{eq}$  data only



Without kinetic data

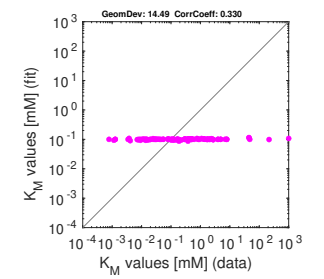
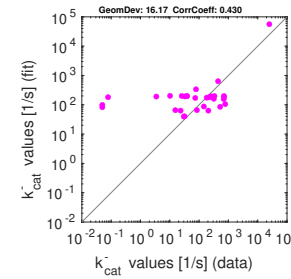
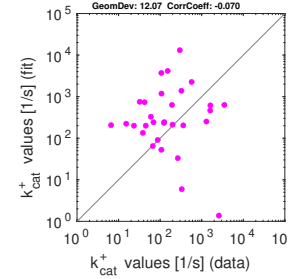
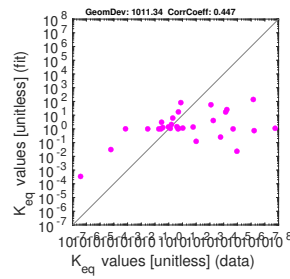
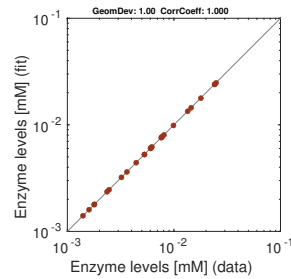
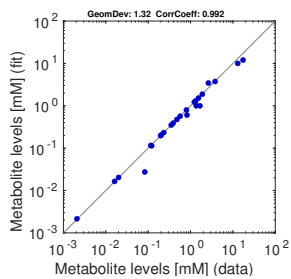


Figure 7: Results for *E. coli* central metabolism with experimental data (aerobic growth on glucose). The kinetic data stem from previous parameter balancing based on *in-vitro* data. Top: estimation using kinetic data. Centre: estimation using equilibrium constants as the only kinetic data. Bottom: estimation without usage of kinetic data. The same metabolite, enzyme, and kinetic data were used in [?].

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(a) Metabolites

(b) Enzymes

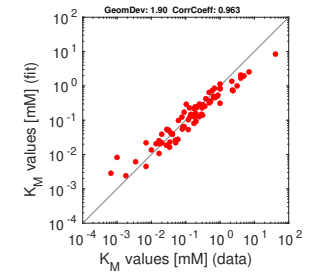
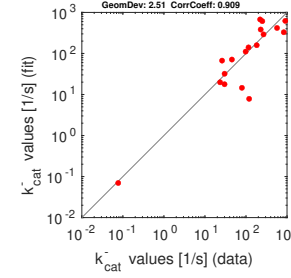
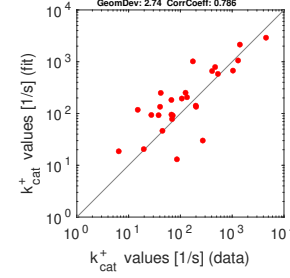
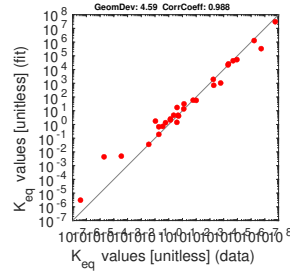
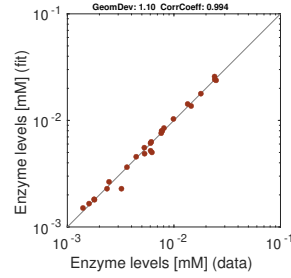
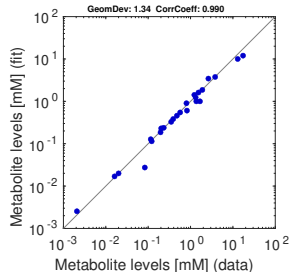
(c)  $K_{eq}$  values

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

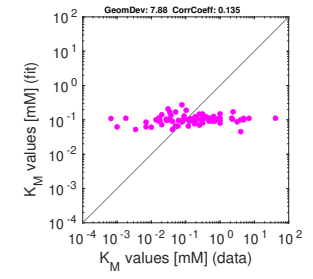
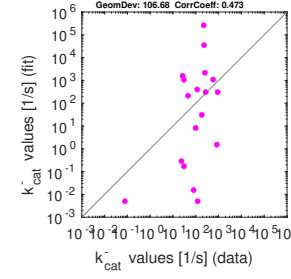
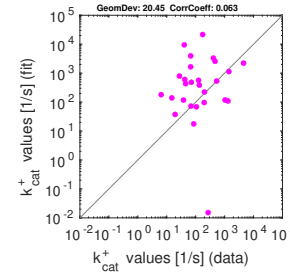
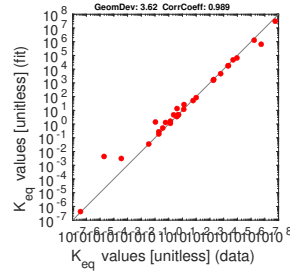
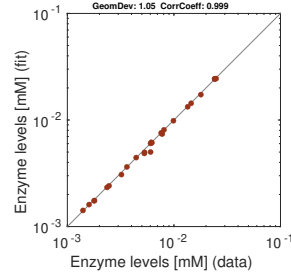
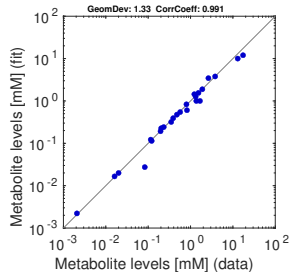
(e)  $k_{cat}^-$  values

(f)  $K_M$  values

With kinetic data



With  $K_{eq}$  data only



Without kinetic data

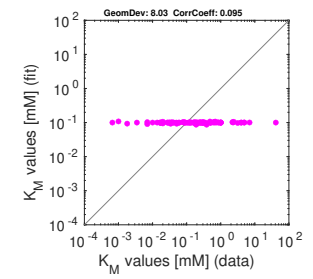
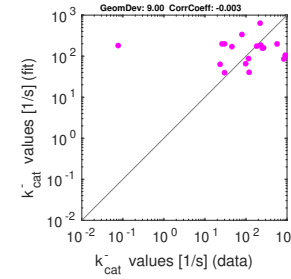
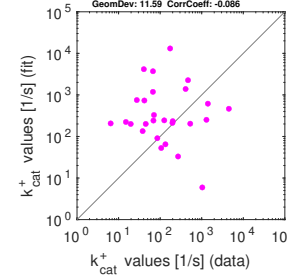
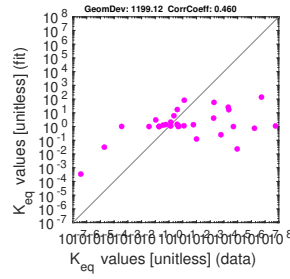
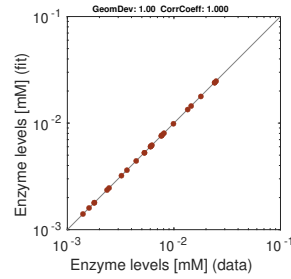
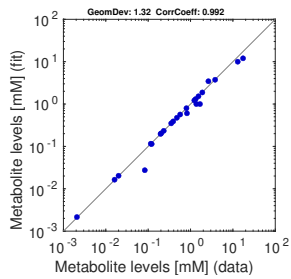


Figure 8: Results for *E. coli* central metabolism with experimental data (aerobic growth on glucose). Same as Figure 11, but based on original kinetic *in-vitro* data instead of balanced kinetic data.



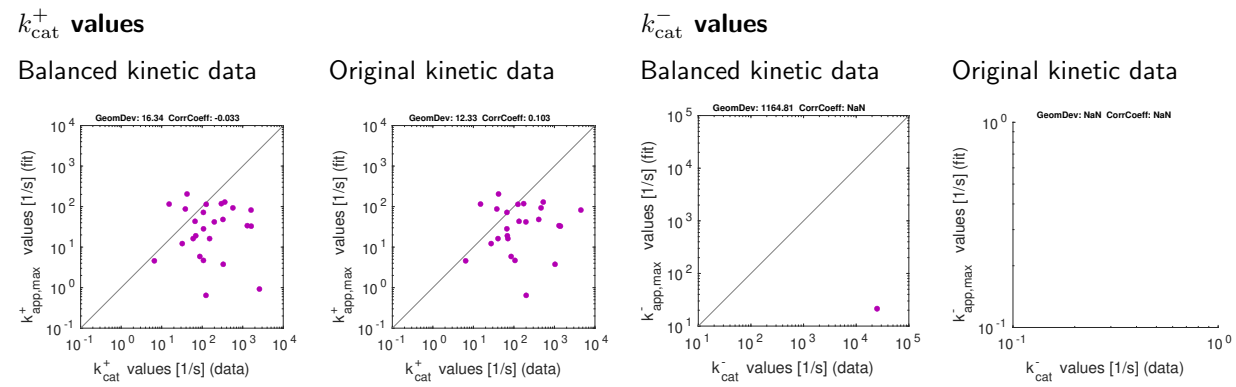
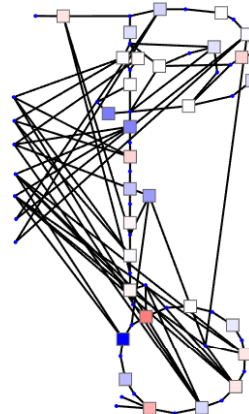
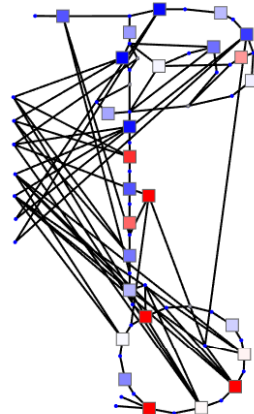
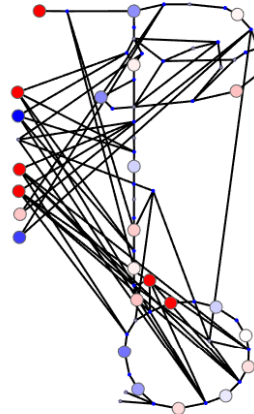
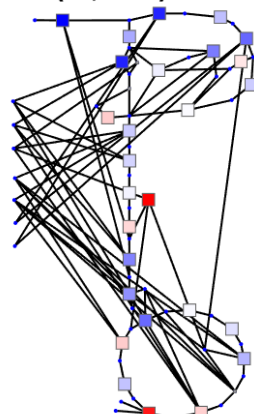


Figure 9: Catalytic constants in *E. coli* central metabolism model (aerobic growth on glucose), estimated by kinetic profiling [?].

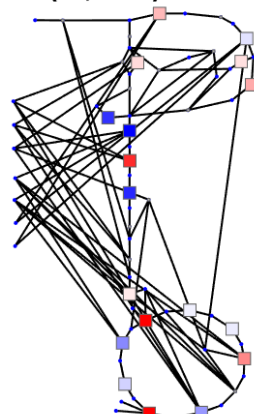
met (fit/data) smpl 1 f.c.<3.03 enz (fit/data) smpl 1 f.c.<1.41 Keq (fit/data) f.c.<226.29



Kcatf (fit/data) f.c.<8.99



Kcatr (fit/data) f.c.<15.22



KM (fit/data) f.c.<8.25

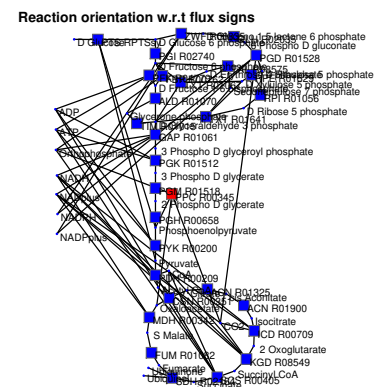
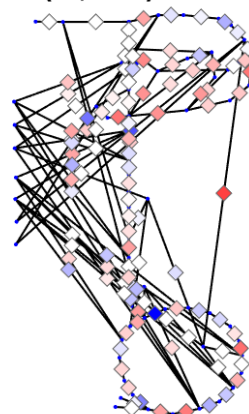


Figure 10: Diagnostic plots for fit with original kinetic data. Left: Relative fitting errors. Blue: fitted value too high. Red: fitted value too low. Maximal fold changes (whether up or down) are given by numbers. Right: Reaction orientation (defining “forward” and “reverse”). Blue: in flux direction; Red: against flux direction.

### **3 E. coli Glucose Simulations with $\alpha = 1$ , $\beta = 0$**

# **E. coli model (aerobic growth on glucose), balanced kinetic data**

(a) Metabolites

(b) Enzymes

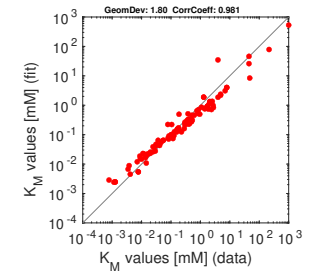
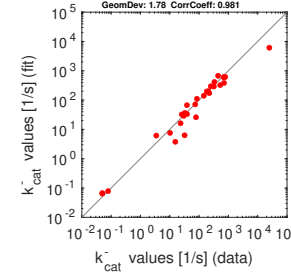
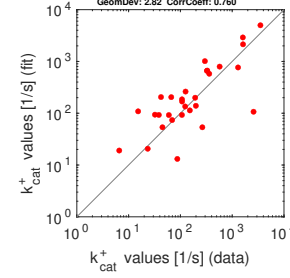
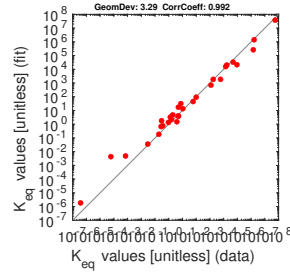
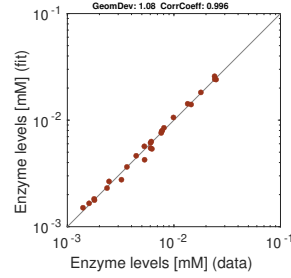
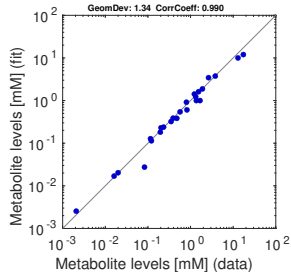
(c)  $K_{eq}$  values

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

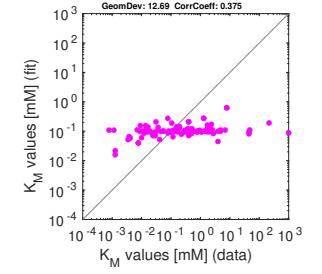
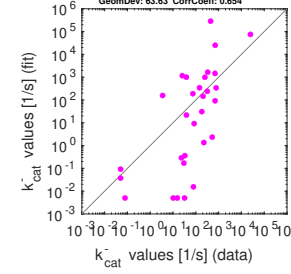
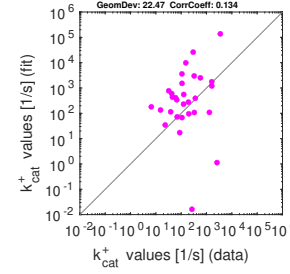
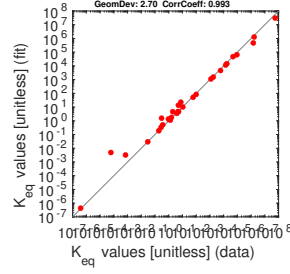
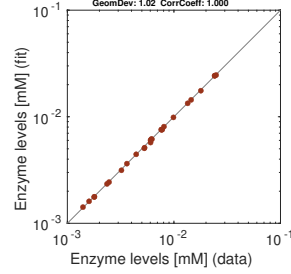
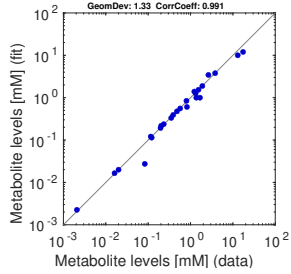
(e)  $k_{cat}^-$  values

(f)  $K_M$  values

With kinetic data



With  $K_{eq}$  data only



Without kinetic data

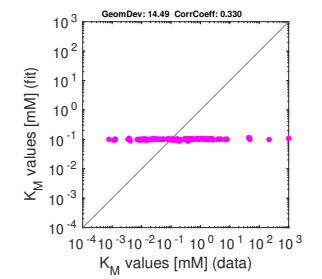
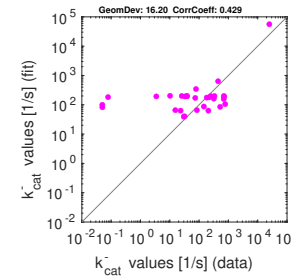
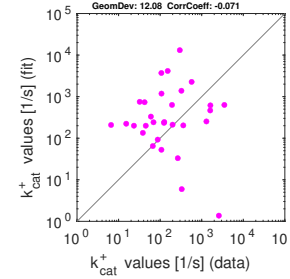
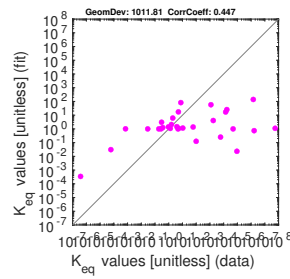
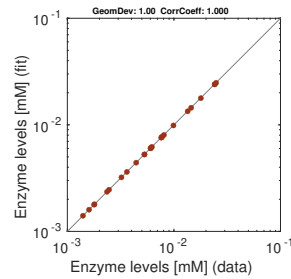
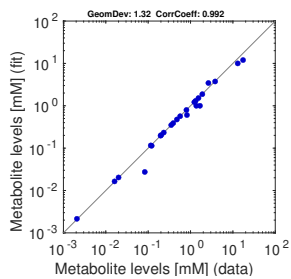


Figure 11: Results for *E. coli* central metabolism with experimental data (aerobic growth on glucose). The kinetic data stem from previous parameter balancing based on *in-vitro* data. Top: estimation using kinetic data. Centre: estimation using equilibrium constants as the only kinetic data. Bottom: estimation without usage of kinetic data. The same metabolite, enzyme, and kinetic data were used in [?].

# **E. coli central metabolism model (aerobic growth on glucose), in-vitro kinetic data**

(a) Metabolites

(b) Enzymes

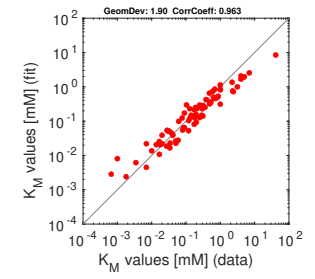
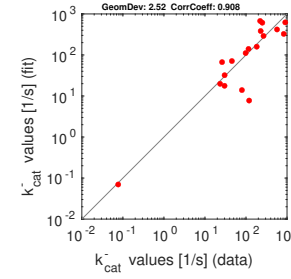
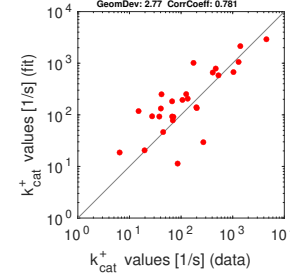
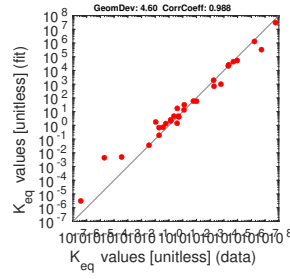
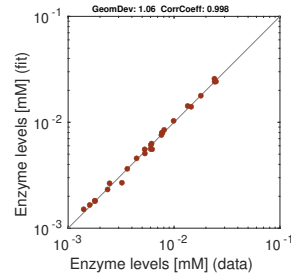
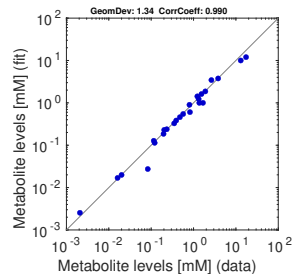
(c)  $K_{eq}$  values

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

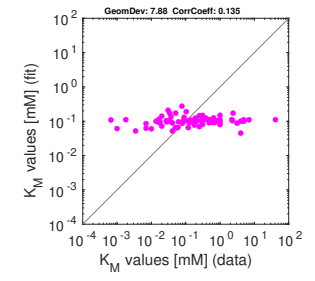
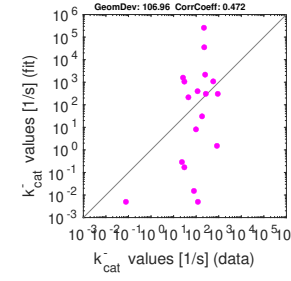
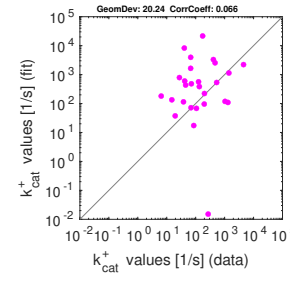
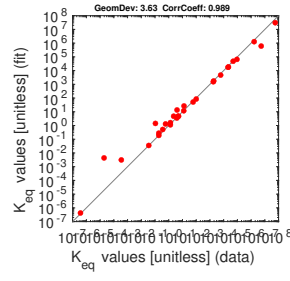
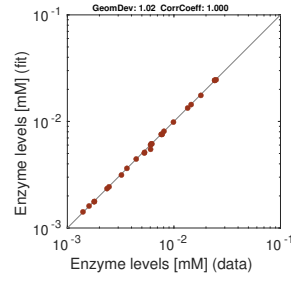
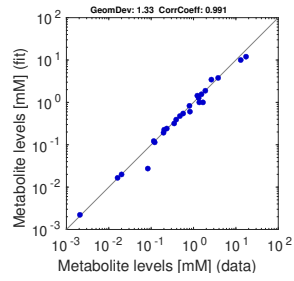
(e)  $k_{cat}^-$  values

(f)  $K_M$  values

With kinetic data



With  $K_{eq}$  data only



Without kinetic data

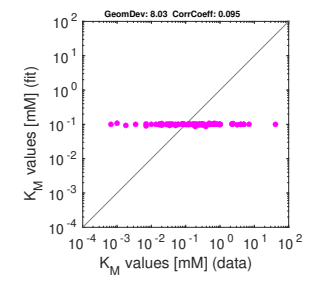
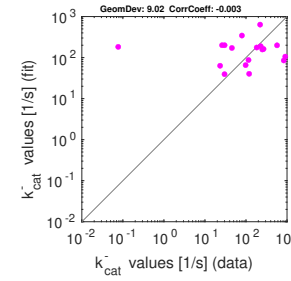
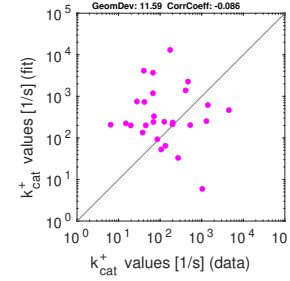
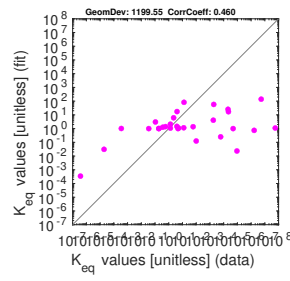
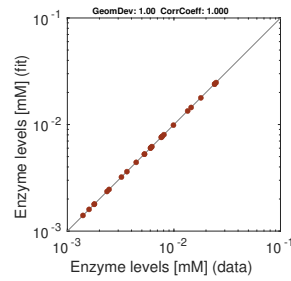
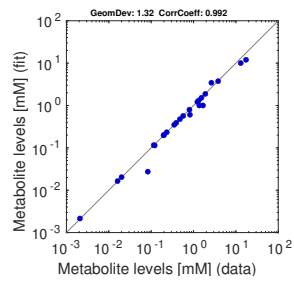


Figure 12: Results for *E. coli* central metabolism with experimental data (aerobic growth on glucose). Same as Figure 11, but based on original kinetic *in-vitro* data instead of balanced kinetic data.

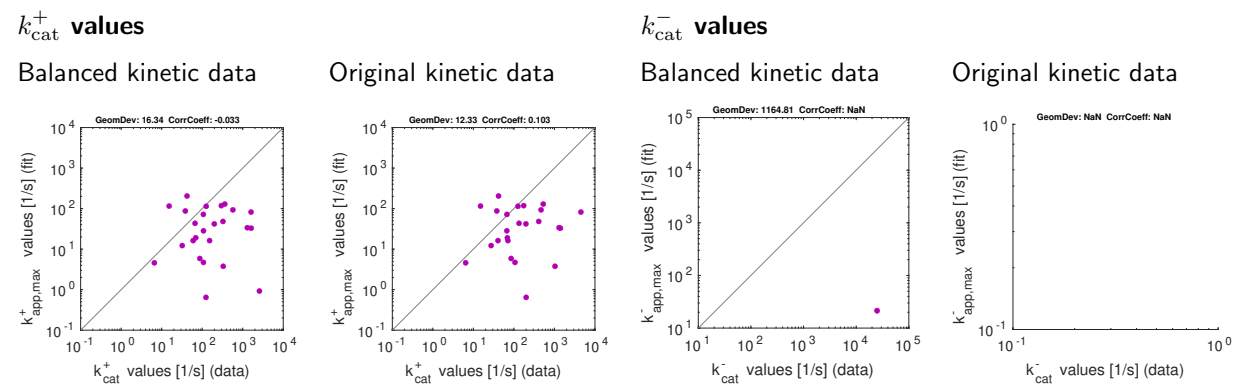
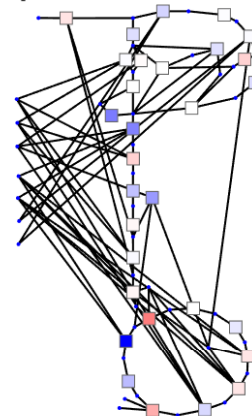
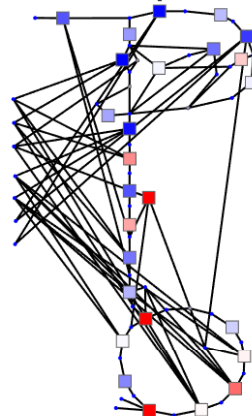
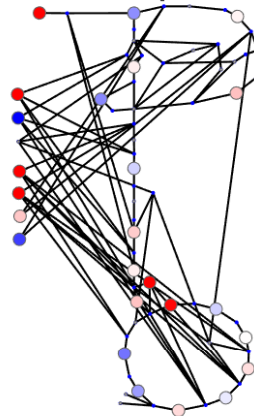
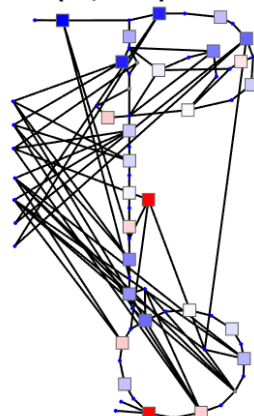


Figure 13: Catalytic constants in *E. coli* central metabolism model (aerobic growth on glucose), estimated by kinetic profiling [?].

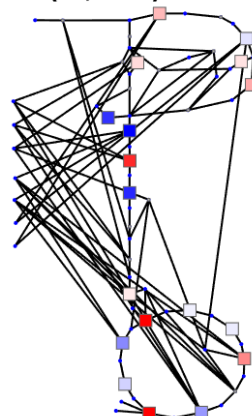
met (fit/data) smpl 1 f.c.<3.03 enz (fit/data) smpl 1 f.c.<1.20 Keq (fit/data) f.c.<225.93



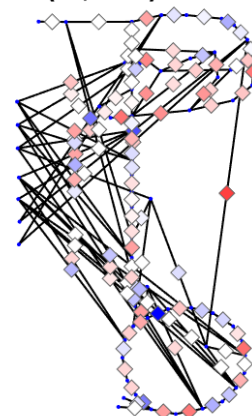
Kcatf (fit/data) f.c.<9.16



Kcatr (fit/data) f.c.<15.41



KM (fit/data) f.c.<8.08



Reaction orientation w.r.t flux signs

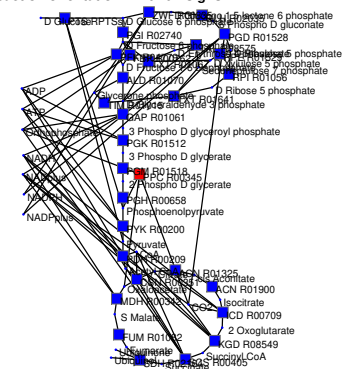


Figure 14: Diagnostic plots for fit with original kinetic data. Left: Relative fitting errors. Blue: fitted value too high. Red: fitted value too low. Maximal fold changes (whether up or down) are given by numbers. Right: Reaction orientation (defining “forward” and “reverse”). Blue: in flux direction; Red: against flux direction.