Supplementary Information

Title: A U–system approach for predicting metabolic behaviors and responses based on an alleged metabolic reaction network

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Simple Michaelis-Menten system

A simple model of a linear pathway with inhibition is sketched in Figure S1.

![Figure S1. Linear pathway with inhibition](image)

Figure S1. Linear pathway with inhibition (эффект). \(X_1\) and \(X_2\) represent metabolites whereas \(Y_1\) and \(Y_2\) represent enzyme activities for the \(X_1\) influx and \(X_2\) efflux, respectively.

Flux expressions and parameters for this pathway were constructed in the typical Michaelis-Menten format where the enzymatic reaction velocity is usually determined by an in vitro experiment [6]. The usual Michaelis-Menten model with inhibition is presented in equations (S1) and (S2),

\[
\frac{dX_1}{dt} = Y_1 - \frac{V_{\text{max}} X_1}{X_1 + K_m (1 + X_2 / K_i)} \tag{S1}
\]

\[
\frac{dX_2}{dt} = \frac{V_{\text{max}} X_1}{X_1 + K_m (1 + X_2 / K_i)} - Y_2 X_2 \tag{S2}
\]

where \(V_{\text{max}}=100.0, K_m=10.0, K_i=5.0, Y_1=5.0, Y_2=2.0\), and the steady state is \(X_1^* = 0.789, X_2^* = 2.50\).

The corresponding GMA model with U–system simplifications is presented in equations (S3) and (S4),

\[
\frac{dX_1}{dt} = Y_1 - X_1 X_2^{0.5} \tag{S3}
\]
\[
\frac{dX_2}{dt} = X_1 X_2^{-0.5} - X_2
\]  

(S4)

where \(Y_1 = 5.0, X_1^* = 11.180, \) and \(X_2^* = 5.0\)

The dynamics of the time-varying metabolite concentrations was calculated for the Michaelis-Menten equations and the U–system approach of the GMA model. Specifically, the initial value of either \(X_1\) or \(X_2\) at \(t=0\) was increased to twice the steady-state concentrations and the following trajectories were computed. Figure S2 shows the comparison of calculations from both models. It is clear that the results from both models are numerically quite different but qualitatively comparable. For both scenarios, when \(X_1\) was perturbed, \(X_2\) increased until it reached its maximum and decreased back to its steady-state, whereas \(X_1\) continuously decreased. The results indicate that the qualitative shapes of the trajectories of metabolite concentrations strongly depend on the network structure, but less so on specific parameter values, as it was observed elsewhere [7]. Nonetheless, the metabolite concentrations at each time point and the time-scale of metabolite concentrations are quite different.
Figure S2. Comparisons of time courses of $X_1$ and $X_2$ obtained by the Michaelis-Menten model and those by the simplified U–system approach of the corresponding GMA model.

The x-axis represents time, while the y-axis represents the concentrations of $X_i$. The red lines pertain to the actual system in left and bottom axes whereas the blue dotted lines are for U–system in right and top axes.

a The $X_1$ U–system concentration compared with real concentration when the values of $X_1$ was increased two-fold at $t=0$.

b The $X_2$ U–system concentration compared with real concentration when the values of $X_1$ was increased two-fold at $t=0$.

c The $X_1$ U–system concentration compared with real concentration when the values of $X_2$ was increased two-fold at $t=0$.

d The $X_2$ U–system concentration compared with real concentration when the values of $X_2$ was increased two-fold at $t=0$. 
Branched pathway

These supplements contain additional figures for the branched pathway model while the details for *Arabidopsis* model are provided in Usystem_SupplementaryModel.pdf with the U-system simulations comparing with experimental data from metabolome and amino acids analysis in Usystem_SupplementaryFigures.pdf, as mentioned in the body of the text.

Figure S3. Normalized concentrations of $X_i$ with variations of parameters $\alpha_i$ which value from 0.5 (red), 1, 5, 10, 15, 20, 25, 50, 75 to 100 (blue)
Figure S4. Normalized concentrations of $X_i$ with variations of parameters $\beta_i$ which value from 0.5 (red), 1, 5, 10, 15, 20, 25, 50, 75 to 100 (blue)
Figure S5. Normalized concentrations of $X_i$ with variations of parameters $g_{ij}$ which range from 0.1 (or –0.1; red) to 1.0 (or –1.0; blue)
Figure S6. Normalized concentrations of $X_i$ with variations of parameters $h_{ij}$ which range from 0.1 (red) to 1.0 (blue)