Department of Mathematical Sciences, Sharif University of Technology

همایش ملی ریاضیات زیستی

Applications of Convex Optimization in Metabolic Network Analysis

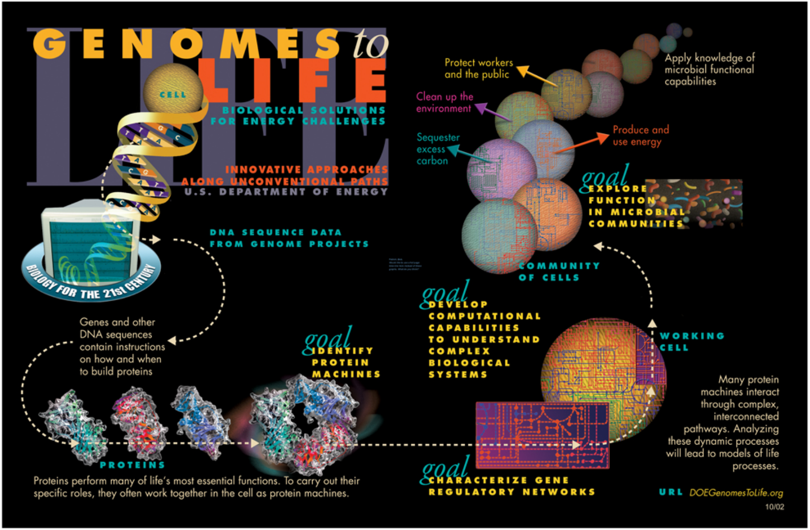
Mojtaba Tefagh

October 22, 2020

Outline

- Motivation
- Introduction
  - Systems Biology
  - COBRA
- Consistency Checking
- QFCA
  - Background
  - Flux Coupling Equations
  - Fictitious Metabolites
  - Implementation
  - Applications
- Metabolic Network Reductions
- Conclusions
- Further Topics

Motivation



GENOMES to LIFE
CELL
BIOLOGICAL SOLUTIONS FOR ENERGY CHALLENGES
INNOVATIVE APPROACHES ALONG UNCONVENTIONAL PATHS
U.S. DEPARTMENT OF ENERGY
BIOLOGY FOR THE 21st CENTURY
DNA SEQUENCE DATA FROM GENOME PROJECTS
Genes and other DNA sequences contain instructions on how and when to build proteins
goal IDENTIFY PROTEIN MACHINES
PROTEINS
Proteins perform many of life's most essential functions. To carry out their specific roles, they often work together in the cell as protein machines.
goal CHARACTERIZE GENE REGULATORY NETWORKS
goal DEVELOP COMPUTATIONAL CAPABILITIES TO UNDERSTAND COMPLEX BIOLOGICAL SYSTEMS
WORKING CELL
Many protein machines interact through complex, interconnected pathways. Analyzing these dynamic processes will lead to models of life processes.
COMMUNITY OF CELLS
goal EXPLORE FUNCTION IN MICROBIAL COMMUNITIES
Protect workers and the public
Clean up the environment
Sequester excess carbon
Produce and use energy
Apply knowledge of microbial functional capabilities
URL DOEGenomesToLife.org
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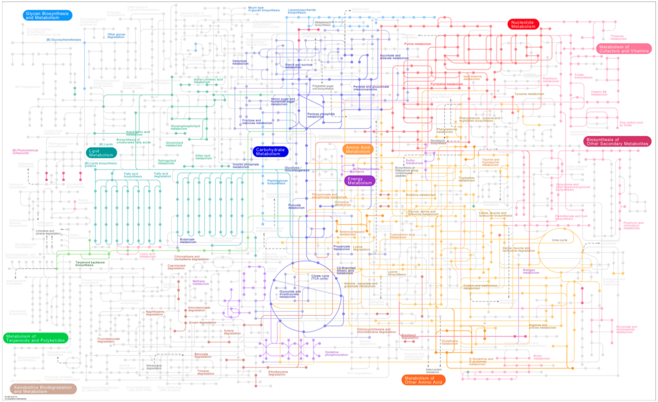
Introduction
Systems Biology

"However, many things have a plurality of parts and are not merely a complete aggregate but instead some kind of a whole beyond its parts."

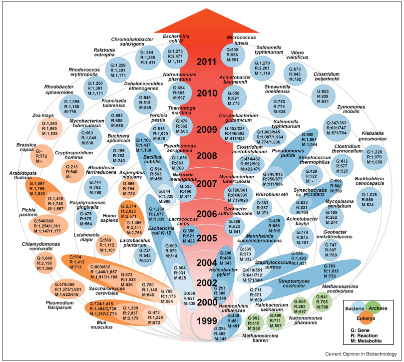
Aristotle, *Metaphysics* **8.6**



A metabolic network from KEGG pathway database

Introduction

COnstraint-Based Reconstruction and Analysis



Source: [Kim et al., 2012]

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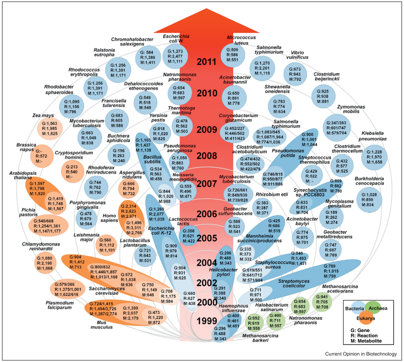

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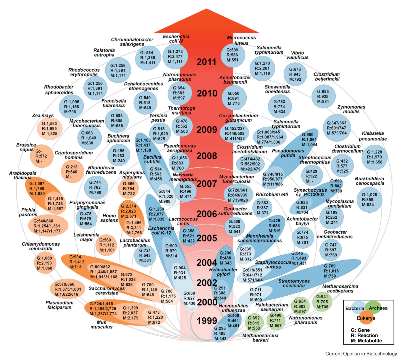

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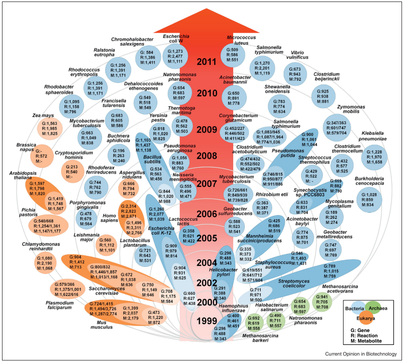

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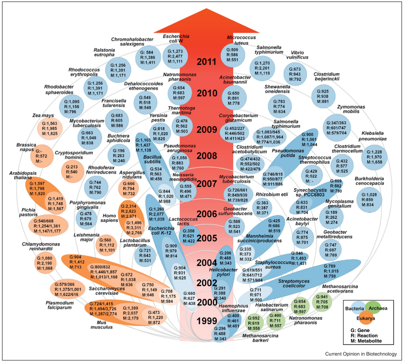

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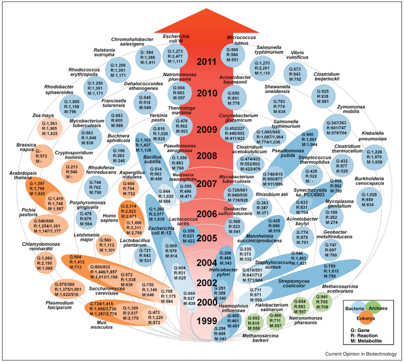

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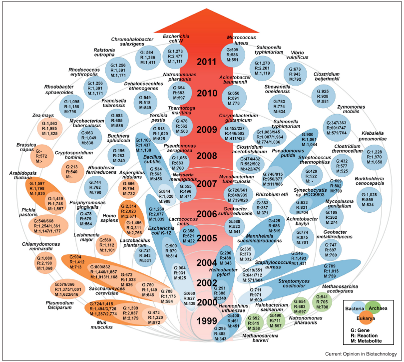

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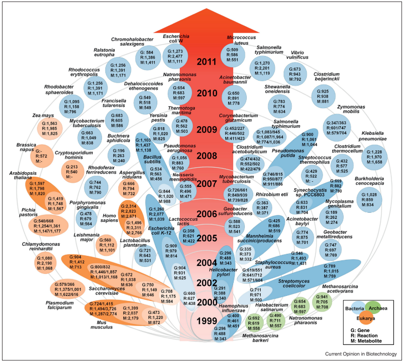

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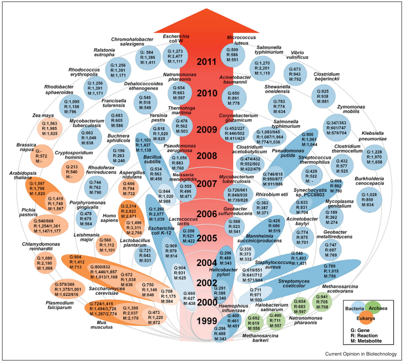

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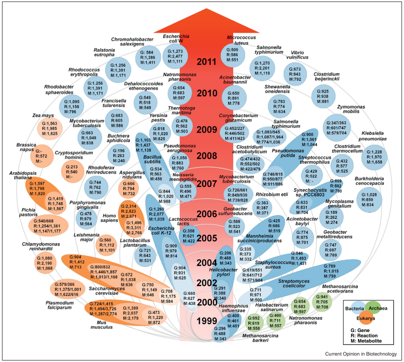

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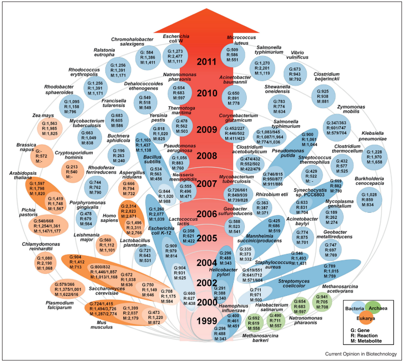
- We call $R_i \in \mathcal{R}$ a blocked reaction if $v_i = 0, \quad \forall v \in \mathcal{C}$.



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- *The forward direction:*

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$$\begin{aligned} \text{minimize} \quad & v_i \\ \text{subject to} \quad & v \in \mathcal{C} \\ & v_i \geq -1 \end{aligned}$$

- Identifying irreversible blocked reactions by,

$$\begin{array}{ll} \text{maximize} & \mathbf{1}^T \min(v_{\mathcal{I}}, \mathbf{1}) \\ \text{subject to} & v \in \mathcal{C}. \end{array}$$

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Consistency Checking

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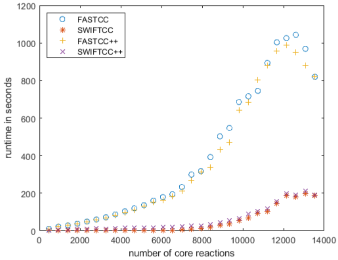
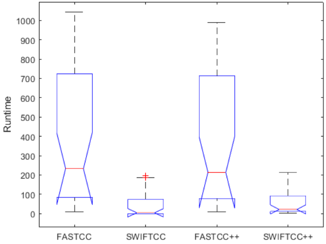
- Requires one QR decomposition.

Consistency Checking
Benchmark





SWIFTCC is more than 8× faster than FASTCC on average over 29 iterations of varying sizes for the Recon3D model.

FCA [Burgard et al., 2004]

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Directional Coupling: $R_i \longrightarrow R_j$ if

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Partial Coupling: $R_i \longleftrightarrow R_j$ if

$$v_i \neq 0 \Leftrightarrow v_j \neq 0, \quad \forall v \in \mathcal{C}.$$

Full Coupling: $R_i \Longleftrightarrow R_j$ if there exists a constant $c \neq 0$ such that

$$v_i = cv_j, \quad \forall v \in \mathcal{C}.$$

Problem

Given the stoichiometric matrix S and the subset of irreversible reactions $\mathcal{I}$, identify all the blocked reactions and the pairs of reactions which are directional, partially, or fully coupled.

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FFCA [David et al., 2011]

By $n(n_i + 2n_r) + 2n_p$ LP's:

$$\begin{array}{ll} \text{maximize} & v_i \\ \text{subject to} & v \in \mathcal{C} \\ & v_j = 0 \\ & v_i \leq 1. \end{array} \qquad \begin{array}{ll} \text{minimize} & v_i \\ \text{subject to} & v \in \mathcal{C} \\ & v_j = 0 \\ & v_i \geq -1. \end{array}$$

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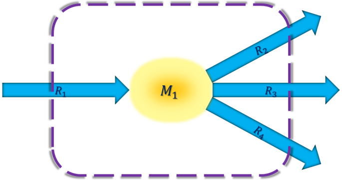
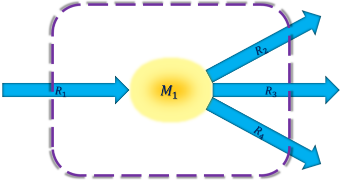


For $t = 2, 3, 4$, $R_t \longrightarrow R_1$ can be inferred from the DCE corresponding to M_1.

- For $R_{i_1}, R_{i_2}, \ldots, R_{i_l} \in \mathcal{I}$, there exists $c_{i_1}, c_{i_2}, \ldots, c_{i_l} > 0$, such that

$$v_j = c_{i_1} v_{i_1} + c_{i_2} v_{i_2} + \cdots + c_{i_l} v_{i_l}.$$



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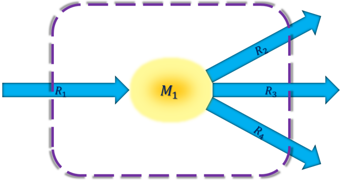
- There exists $c'_{i_{l+1}} \neq 0$,

$$v_j = c'_{i_1} v_{i_1} + c'_{i_2} v_{i_2} + \cdots + c'_{i_{l+1}} v_{i_{l+1}}.$$



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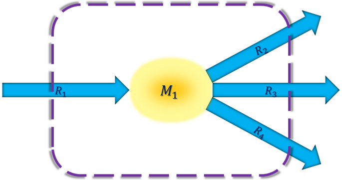


For $t = 2, 3, 4$, $R_t \longrightarrow R_1$ can be inferred from the DCE corresponding to M_1.

- $$(1+\frac{1}{c})v_j = (c_{i_1}+\frac{c'_{i_1}}{c})v_{i_1}+(c_{i_2}+\frac{c'_{i_2}}{c})v_{i_2}+\cdots+(c_{i_l}+\frac{c'_{i_l}}{c})v_{i_l}+\frac{c'_{i_{l+1}}}{c}v_{i_{l+1}}$$

Theorem ([Tefagh and Boyd, 2018])

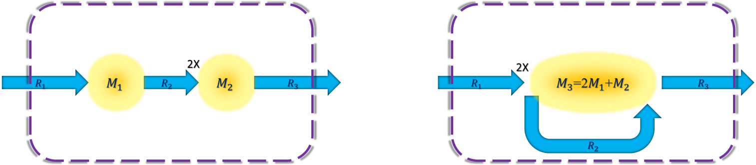
Suppose that $\mathcal{N} = (\mathcal{M}, \mathcal{R}, S, \mathcal{I})$ has no irreversible blocked reactions. Let R_j be an arbitrary unblocked reaction, and $\mathcal{D}_j \subseteq \mathcal{I}$ denote the set of all the irreversible reactions which are directionally coupled to R_j excluding itself. Then, $\mathcal{D}_j \neq \emptyset$ if and only if there exists $c_d > 0$ for each $R_d \in \mathcal{D}_j$, such that the following directional coupling equation (DCE)

$$v_j = \sum_{d:R_d \in \mathcal{D}_j} c_d v_d,$$

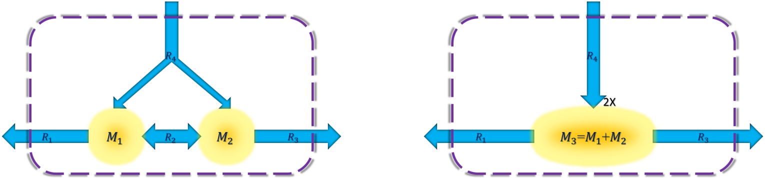
holds for all $v \in \mathcal{C}$. Moreover, for any unblocked $R_i \notin \mathcal{I}$, we have $R_i \longrightarrow R_j$ if and only if there exists an extended directional coupling equation (EDCE)

$$v_j = \sum_{d:R_d \in \mathcal{D}_j} c'_d v_d + c'_i v_i \qquad c'_i \neq 0,$$

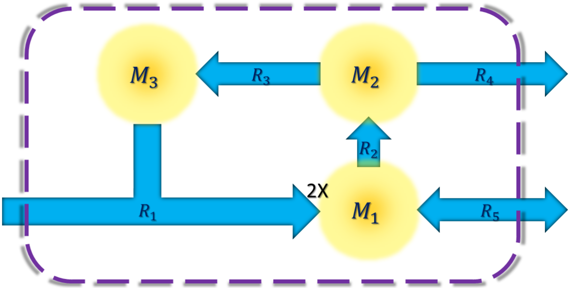
which holds for all $v \in \mathcal{C}$.



(a) the original metabolic network (b) the transformed metabolic network



$R_2 \longrightarrow R_4$ can be inferred from the EDCEs corresponding to M_1 and M_2.



M_1 and $M_1 + M_3$ provide EDCEs, M_2 and $M_2 + M_3$ provide DCEs, and M_3 provides an FCE.

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We call $\lambda \in \mathbf{R}^n$ a fictitious metabolite if there exists $\nu \in \mathbf{R}^m$ such that $\lambda = S^T \nu$.

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Theorem

Suppose that in a given metabolic network specified by S and $\mathcal{I}$, there are no irreversible blocked reactions. Then for any $\lambda \in \mathbf{R}^n$, λ is a fictitious metabolite if and only if

$$\lambda^T v = 0, \quad \forall v \in \mathcal{C}.$$

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Lemma

Suppose that in a given metabolic network specified by S and $\mathcal{I}$, there are no irreversible blocked reactions. Then for any $\lambda \in \mathbf{R}^n$,

$$\lambda^T v = 0, \quad \forall v \in \mathcal{C} \Leftrightarrow \lambda^T u = 0, \quad \forall u \in \ker(S).$$

$$
\begin{aligned}
M = & 4 \times 13dpg[c] + 2 \times 2pg[c] + 2 \times 3pg[c] \\
& + 4.8756 \times 6pgc[c] + 3.8756 \times 6pgl[c] + 2 \times actp[c] \\
& - 2 \times adp[c] - 4 \times amp[c] + 2 \times dhap[c] \\
& - 1.8756 \times e4p[c] + 2 \times f6p[c] + 4 \times fdp[c] \\
& + 2 \times g3p[c] + 2 \times g6p[c] + 2 \times pep[c] \\
& + 2 \times pi[c] + 1 \times pi[e] - 5.7513 \times r5p[c] \\
& + 5.8756 \times ru5p - D[c] - 1.8756 \times s7p[c] \\
& + 5.8756 \times xu5p - D[c]
\end{aligned}
$$

$$
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M =\, & 4 \times 13dpg[c] + 2 \times 2pg[c] + 2 \times 3pg[c] \\
& + 4.8756 \times 6pgc[c] + 3.8756 \times 6pgl[c] + 2 \times actp[c] \\
& - 2 \times adp[c] - 4 \times amp[c] + 2 \times dhap[c] \\
& - 1.8756 \times e4p[c] + 2 \times f6p[c] + 4 \times fdp[c] \\
& + 2 \times g3p[c] + 2 \times g6p[c] + 2 \times pep[c] \\
& + 2 \times pi[c] + 1 \times pi[e] - 5.7513 \times r5p[c] \\
& + 5.8756 \times ru5p - D[c] - 1.8756 \times s7p[c] \\
& + 5.8756 \times xu5p - D[c]
\end{aligned}
$$

- 3-Phospho-D-glyceroyl-phosphate
- D-Glycerate-2-phosphate
- 3-Phospho-D-glycerate
- 6-Phospho-D-gluconate
- 6-phospho-D-glucono-1-5-lactone
- Acetyl-phosphate
- ADP
- AMP
- Dihydroxyacetone-phosphate
- D-Erythrose-4-phosphate
- D-Fructose-6-phosphate
- D-Fructose-1-6-bisphosphate
- Glyceraldehyde-3-phosphate
- D-Glucose-6-phosphate
- Phosphoenolpyruvate
- Phosphate (pi[c])
- Phosphate (pi[e])
- alpha-D-Ribose-5-phosphate
- D-Ribulose-5-phosphate
- Sedoheptulose-7-phosphate
- D-Xylulose-5-phosphate

Table: a bird's eye view of QFCA

	positive certificates	negative certificates	A
$\mathcal{B}_R$ EDCE FCE	$(S^{(A)})^T x = e_i^{(A)}$	$S^{(A)} u = 0$ ${e_i^{(A)}}^T u = 1$	$\emptyset$ $\mathcal{D}_j \cup \{R_j\}$ $\{R_j\}$
$\mathcal{B}_I$ DCE	maximize $\mathbf{1}^T \min(\lambda^{(A)}, \mathbf{1})$ subject to $S^T \nu = \lambda$ $\lambda_i = 0, \quad i \notin \mathcal{I}$ $\lambda_i \geq 0, \quad i \in \mathcal{I} \setminus A$	maximize $\mathbf{1}^T \min(v_{\mathcal{I}}, \mathbf{1})$ subject to $v \in \mathcal{C}$ $v_A = 0$	$\emptyset$ $\{R_j\}$

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- Certificates as potential differences

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- Certificates as potential differences
- Certificates as fictitious metabolites

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- Certificates as potential differences
- Certificates as fictitious metabolites
- Certificates as generalizations of fully coupling constants

$$v_1 = -\frac{\lambda_2}{\lambda_1} v_2 - \frac{\lambda_3}{\lambda_1} v_3 - \cdots - \frac{\lambda_l}{\lambda_1} v_l$$

QFCA

Input: $\mathcal{M}, \mathcal{R}, \mathcal{S}, \mathcal{I}$
Output: A, b

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Input: $\mathcal{M}, \mathcal{R}, \mathcal{S}, \mathcal{I}$
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identifying and removing the blocked reactions from the metabolic network

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identifying and removing the blocked reactions from the metabolic network
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identifying and removing the blocked reactions from the metabolic network
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identifying the fully coupled pairs of reactions and merging each pair

QFCA

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identifying and removing the blocked reactions from the metabolic network
aggregating all the isozymes and removing the newly blocked reactions
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computing the set of fully reversible reactions and reversibility type pruning

QFCA

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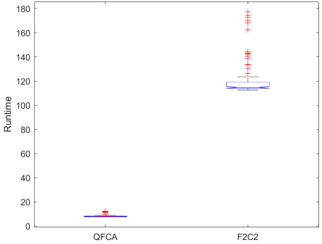
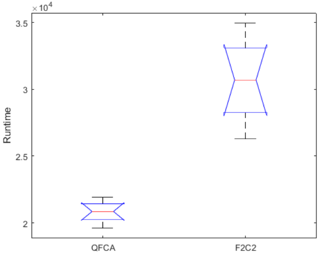
identifying and removing the blocked reactions from the metabolic network
aggregating all the isozymes and removing the newly blocked reactions
identifying the fully coupled pairs of reactions and merging each pair
computing the set of fully reversible reactions and reversibility type pruning
finding the directional and partial coupling relations by positive certificates



(a) YEASTNET v3.0 with 2292 reversible and 49 irreversible reactions



(b) Recon3D with 5238 reversible and 5362 irreversible reactions

QFCA average runtime is 7% and 68% of F2C2 average runtime, respectively.

- A quantitative approach to FCA

$$v_j \geq c v_i$$

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Equivalently the optimal value of the following LP is zero.

$$\begin{array}{ll} \text{minimize} & v_j - cv_i \\ \text{subject to} & v \in \mathcal{C} \end{array}$$

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Deriving the dual,

$$\begin{array}{ll} \text{maximize} & 0 \\ \text{subject to} & S^T \nu + e_j - c e_i = \lambda \\ & \lambda_i = 0, \quad i \notin \mathcal{I} \\ & \lambda_i \geq 0, \quad i \in \mathcal{I} \end{array}$$

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As a result,

$$(1 - \lambda_j^\star) v_j = (c + \lambda_i^\star) v_i + \sum_{d \neq i,j} \lambda_d^\star v_d,$$

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- Sensitivity analysis

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- Sensitivity analysis
- The metabolic gap-filling problem

Metabolic Network Reductions

A Toy example

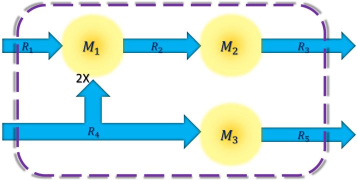
$$\mathcal{N} = (\mathcal{M}, \mathcal{R}, S, \mathcal{I})$$

$$\mathcal{M} = \{M_1, M_2, M_3\}$$

$$\mathcal{R} = \{R_1, R_2, R_3, R_4, R_5\}$$

$$\mathcal{I} = \mathcal{R}$$

$$S = \begin{bmatrix} +1 & -1 & 0 & +2 & 0 \\ 0 & +1 & -1 & 0 & 0 \\ 0 & 0 & 0 & +1 & -1 \end{bmatrix}$$



the original metabolic network

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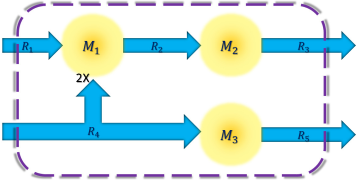
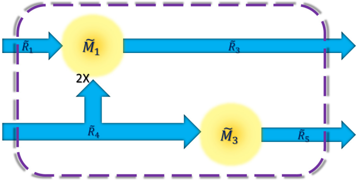


the original metabolic network

$$v = \begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix} = \begin{bmatrix} v_1 \\ v_3 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix} = \begin{bmatrix} +1 & 0 & 0 & 0 \\ 0 & +1 & 0 & 0 \\ 0 & +1 & 0 & 0 \\ 0 & 0 & +1 & 0 \\ 0 & 0 & 0 & +1 \end{bmatrix} \begin{bmatrix} v_1 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix}.$$

$$\tilde{S} = \begin{bmatrix} +1 & -1 & +2 & 0 \\ 0 & 0 & +1 & -1 \end{bmatrix}$$

$$\begin{aligned} \tilde{R}_1 &\xrightarrow{r_1} \{R_1\} \\ \tilde{R}_3 &\xrightarrow{r_1} \{R_2, R_3\} \\ \tilde{R}_4 &\xrightarrow{r_1} \{R_4\} \\ \tilde{R}_5 &\xrightarrow{r_1} \{R_5\} \end{aligned}$$



the reduced metabolic network

Metabolic Network Reductions

A Toy example

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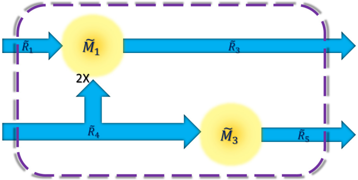

the reduced metabolic network

$$Sv = S \begin{bmatrix} +1 & 0 & 0 & 0 \\ 0 & +1 & 0 & 0 \\ 0 & +1 & 0 & 0 \\ 0 & 0 & +1 & 0 \\ 0 & 0 & 0 & +1 \end{bmatrix} \begin{bmatrix} v_1 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix} = \begin{bmatrix} +1 & -1 & +2 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & +1 & -1 \end{bmatrix} \begin{bmatrix} v_1 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix}$$

Metabolic Network Reductions

A Toy example

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$$\tilde{R}_1 \xrightarrow{r_2} \{R_1, R_2\}$$
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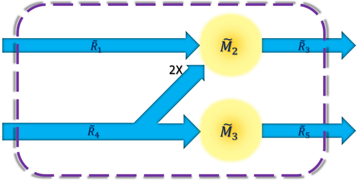

a DCE-induced reduction

Metabolic Network Reductions

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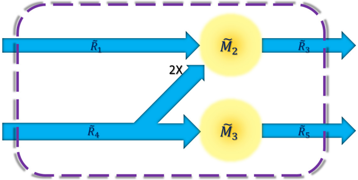

a DCE-induced reduction

$$v = \begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix} = \begin{bmatrix} v_1 \\ v_1 + 2v_4 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix} = \begin{bmatrix} +1 & 0 & 0 & 0 \\ +1 & 0 & +2 & 0 \\ 0 & +1 & 0 & 0 \\ 0 & 0 & +1 & 0 \\ 0 & 0 & 0 & +1 \end{bmatrix} \begin{bmatrix} v_1 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix}$$

- First, we eliminate all the blocked reactions.

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- Third, we remove the eligible reactions by the DCE-induced reductions.

Metabolic Network Reductions

QFCA Reductions

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- Third, we remove the eligible reactions by the DCE-induced reductions.

$$\mathcal{N} \xleftarrow{\phi_1, r_1} \tilde{\mathcal{N}}_1 \xleftarrow{\phi_2, r_2} \cdots \xleftarrow{\phi_{n-\tilde{n}}, r_{n-\tilde{n}}} \tilde{\mathcal{N}}_{n-\tilde{n}}$$

$$\tilde{S} = SPA$$

$$\phi^{n-\tilde{n}}(\tilde{v}) = PA\tilde{v}$$

$$A = \begin{pmatrix} \begin{matrix} 0 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & 0 \end{matrix} & \\ I_{\tilde{n}\times\tilde{n}} & \\ \begin{matrix} \lambda_{11} & & & 0 \\ \vdots & & & \\ \lambda_{a_1 1} & & & \\ & \lambda_{12} & & \\ & \vdots & & \\ & \lambda_{a_2 2} & & \\ & & \ddots & \\ & & & \lambda_{1f} \\ & & & \vdots \\ 0 & & & \lambda_{a_f f} \end{matrix} & 0 \\ C & \end{pmatrix}$$

We say that the metabolic network $\tilde{\mathcal{N}} = (\tilde{\mathcal{M}}, \tilde{\mathcal{R}}, \tilde{\mathcal{S}}, \tilde{\mathcal{I}})$ is a reduction of $\mathcal{N} = (\mathcal{M}, \mathcal{R}, \mathcal{S}, \mathcal{I})$ if

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$$r(\tilde{R}_i) \nsubseteq \bigcup_{k \neq i} r(\tilde{R}_k) \quad \forall \tilde{R}_i \in \tilde{\mathcal{R}},$$

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3. and the following diagram commutes

$$\begin{array}{ccc} \tilde{\mathcal{C}} & \xrightarrow{\text{supp}} & \mathcal{P}(\tilde{\mathcal{R}}) \\ {\scriptstyle\phi}\downarrow & & \downarrow{\scriptstyle\tilde{r}} \\ \mathcal{C} & \xrightarrow{\text{supp}} & \mathcal{P}(\mathcal{R}) \end{array}$$

where $\tilde{r} : \mathcal{P}(\tilde{\mathcal{R}}) \to \mathcal{P}(\mathcal{R})$ is defined by

$$\tilde{r}(\{\tilde{R}_i\}_{i \in I}) = \bigcup_{i \in I} r(\tilde{R}_i).$$

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$$\exists \tilde{R}_j \in r_2(\tilde{R}_i) \backslash \bigcup_{k \neq i} r_2(\tilde{R}_k) \Rightarrow \exists R_t \in r_1(\tilde{R}_j) \backslash \bigcup_{k \neq j} r_1(\tilde{R}_k) \Rightarrow R_t \in \tilde{r}_1 \circ r_2(\tilde{R}_i) \backslash \bigcup_{k \neq i} \tilde{r}_1 \circ r_2(\tilde{R}_k),$$

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and the following diagram commutes

$$\begin{tikzcd}
\tilde{\mathcal{C}}_2 \arrow[r, "\mathrm{supp}"] \arrow[d, "\phi_2"'] & \mathcal{P}(\tilde{\mathcal{R}}_2) \arrow[d, "\tilde{r}_2"] \\
\tilde{\mathcal{C}}_1 \arrow[r, "\mathrm{supp}"] \arrow[d, "\phi_1"'] & \mathcal{P}(\tilde{\mathcal{R}}_1) \arrow[d, "\tilde{r}_1"] \\
\mathcal{C} \arrow[r, "\mathrm{supp}"] & \mathcal{P}(\mathcal{R})
\end{tikzcd}$$

because for any $\tilde{v} \in \tilde{\mathcal{C}}_2$

$$\mathrm{supp}(\phi_1 \circ \phi_2(\tilde{v})) = \tilde{r}_1(\mathrm{supp}(\phi_2(\tilde{v}))) = \tilde{r}_1 \circ \tilde{r}_2(\mathrm{supp}(\tilde{v})).$$

Definition ([Schuster and Hilgetag, 1994])

We call a nonzero feasible flux distribution $0 \neq v \in \mathcal{C}$ an *elementary mode* (EM), if its support is minimal, or equivalently, if there does not exist any other nonzero feasible flux distribution $0 \neq u \in \mathcal{C}$ such that $\mathrm{supp}(u) \subset \mathrm{supp}(v)$.

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Minimal conserved pool identification (MCPI)

Replace FCA by *Metabolite concentration coupling analysis* (MCCA) and everything works!

Theorem (The reduction theorem)

Suppose that $\tilde{\mathcal{N}} = (\tilde{\mathcal{M}}, \tilde{\mathcal{R}}, \tilde{S}, \tilde{\mathcal{I}})$ *is a metabolic network reduction of* $\mathcal{N} = (\mathcal{M}, \mathcal{R}, S, \mathcal{I})$ *by the surjection* $\phi : \tilde{\mathcal{C}} \to \mathcal{C}$ *and the reduction map* $r : \tilde{\mathcal{R}} \to \mathcal{P}(\mathcal{R})$. *For each* $\tilde{R}_i, \tilde{R}_j \in \tilde{\mathcal{R}}$ *such that* $\tilde{R}_i \longrightarrow \tilde{R}_j$, *any reaction in* $r(\tilde{R}_i) \setminus \bigcup_{k \neq i} r(\tilde{R}_k)$ *is directionally coupled to any reaction in* $r(\tilde{R}_j)$. *Conversely, if there exists a reaction in* $r(\tilde{R}_i)$ *which is directionally coupled to some reaction in* $r(\tilde{R}_j) \setminus \bigcup_{k \neq j} r(\tilde{R}_k)$, *then* $\tilde{R}_i \longrightarrow \tilde{R}_j$.

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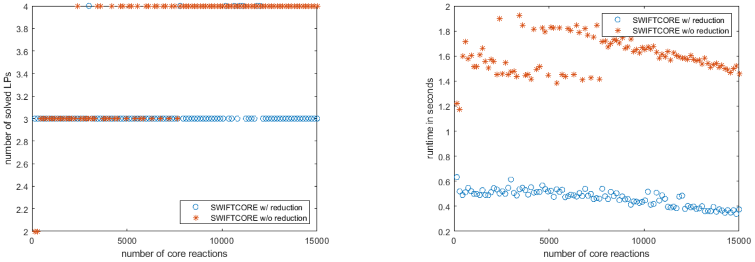
Remark

By setting $i = j$ in the reduction theorem, any reaction in $r(\tilde{R}_i) \setminus \bigcup_{k \neq i} r(\tilde{R}_k)$ is directionally coupled to any reaction in $r(\tilde{R}_i)$.



SWIFTCORE runs more than 3× faster on the reduced BiGG universal model

$$m = 13249, n = 24311, nnz(S) = 95774$$

$$\tilde{m} = 1278, \tilde{n} = 10255, nnz(\tilde{S}) = 56457$$

The DCE reduced reactions are...

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- essential reactions

Essential reactions are the symmetric counterpart of the blocked reactions.

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- exchange reactions
- of older evolutionary age
- evolutionary more conserved
- essential in a wide range of conditions

Essential reactions are the symmetric counterpart of the blocked reactions.

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- the reactions enriching the vital metabolic processes of the cell

Essential reactions are the symmetric counterpart of the blocked reactions.

Conclusions

- QFCA

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  - Flux coupling equations

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Further Topics

- Closure of a metabolic network

Further Topics

- Closure of a metabolic network
- SWIFTCC++

Further Topics

- Closure of a metabolic network
- SWIFTCC++
- SWIFTCORE

Further Topics

- Closure of a metabolic network
- SWIFTCC++
- SWIFTCORE
- SWIFTGAPFILL

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- SWIFTCC++
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- SPARSEQFCA

Further Topics

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- Inhibition analysis

Further Topics

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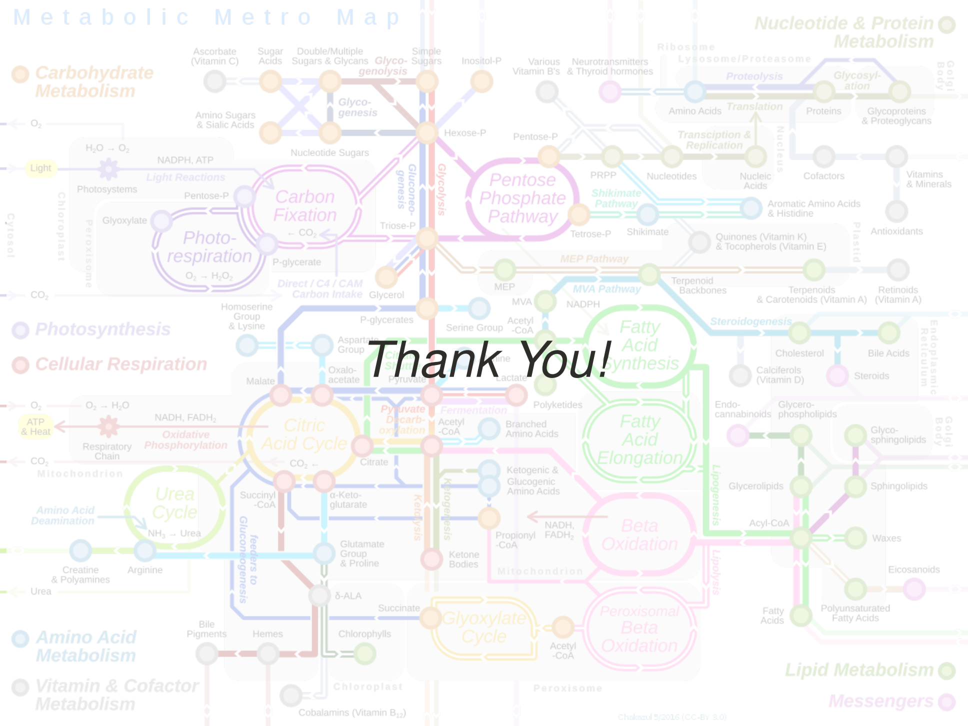
Thank You!



Metabolic Metro Map
Carbohydrate Metabolism
Photosynthesis
Cellular Respiration
Amino Acid Metabolism
Vitamin & Cofactor Metabolism
Nucleotide & Protein Metabolism
Lipid Metabolism
Messengers
Ascorbate (Vitamin C)
Sugar Acids
Double/Multiple Sugars & Glycans
Glycogenolysis
Simple Sugars
Inositol-P
Amino Sugars & Sialic Acids
Glycogenesis
Nucleotide Sugars
Hexose-P
Carbon Fixation
Photorespiration
Light Reactions
Photosystems
Light
Pentose-P
Glyoxylate
P-glycerate
Triose-P
Direct / C4 / CAM Carbon Intake
Glycerol
Gluconeogenesis
Glycolysis
Pentose Phosphate Pathway
Tetrose-P
Shikimate Pathway
Shikimate
PRPP
Nucleotides
Nucleic Acids
Various Vitamin B's
Neurotransmitters & Thyroid hormones
Ribosome
Lysosome/Proteasome
Proteolysis
Glycosylation
Amino Acids
Translation
Proteins
Glycoproteins & Proteoglycans
Transcription & Replication
Cofactors
Vitamins & Minerals
Aromatic Amino Acids & Histidine
Quinones (Vitamin K) & Tocopherols (Vitamin E)
Antioxidants
MEP Pathway
MEP
MVA Pathway
MVA
NADPH
Terpenoid Backbones
Terpenoids & Carotenoids (Vitamin A)
Retinoids (Vitamin A)
Homoserine Group & Lysine
P-glycerates
Serine Group
Acetyl -CoA
Fatty Acid Synthesis
Steroidogenesis
Cholesterol
Bile Acids
Calciferols (Vitamin D)
Steroids
Aspartate Group
Oxalo-acetate
Malate
Pyruvate
Lactate
Polyketides
Citric Acid Cycle
Pyruvate Decarboxylation
Fermentation
Branched Amino Acids
Fatty Acid Elongation
Endocannabinoids
Glycerophospholipids
Glycosphingolipids
Oxidative Phosphorylation
Respiratory Chain
ATP & Heat
Citrate
Succinyl -CoA
α-Keto-glutarate
Ketogenic & Glucogenic Amino Acids
Glycerolipids
Sphingolipids
Lipogenesis
Urea Cycle
Amino Acid Deamination
Ketolysis
Ketogenesis
Propionyl -CoA
Beta Oxidation
Acyl-CoA
Waxes
Creatine & Polyamines
Arginine
Glutamate Group & Proline
Ketone Bodies
Lipolysis
Eicosanoids
Urea
δ-ALA
Succinate
Glyoxylate Cycle
Peroxisomal Beta Oxidation
Fatty Acids
Polyunsaturated Fatty Acids
Bile Pigments
Hemes
Chlorophylls
Cobalamins (Vitamin B_{12})
Mitochondrion
Chloroplast
Peroxisome
Cytosol
Nucleus
Plastid
Endoplasmic Reticulum
Golgi Body
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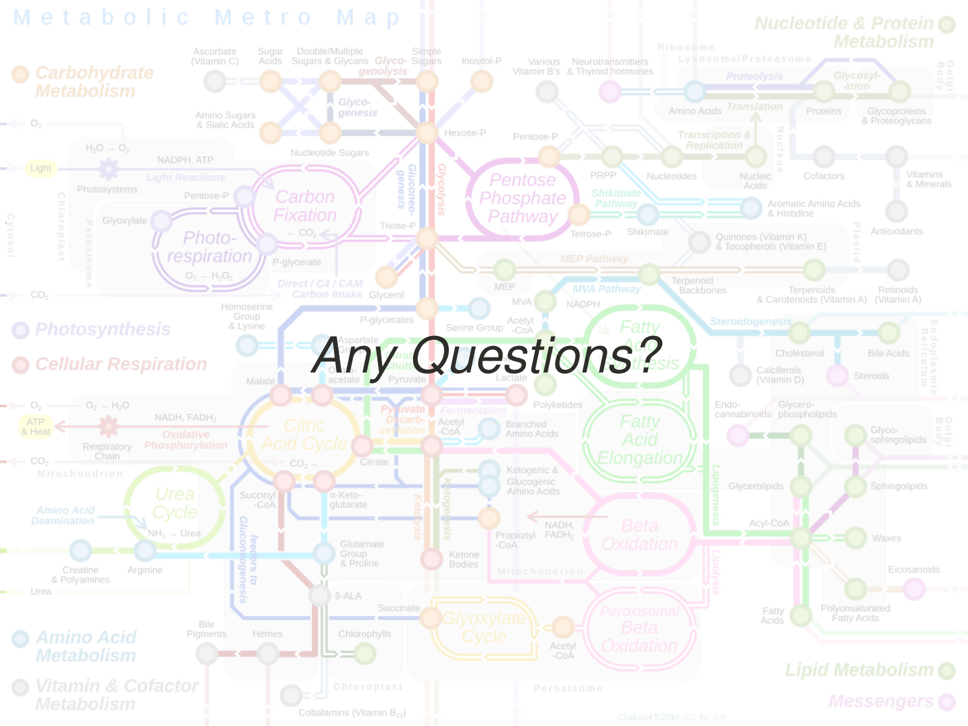
Any Questions?



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