Genome-scale metabolic networks

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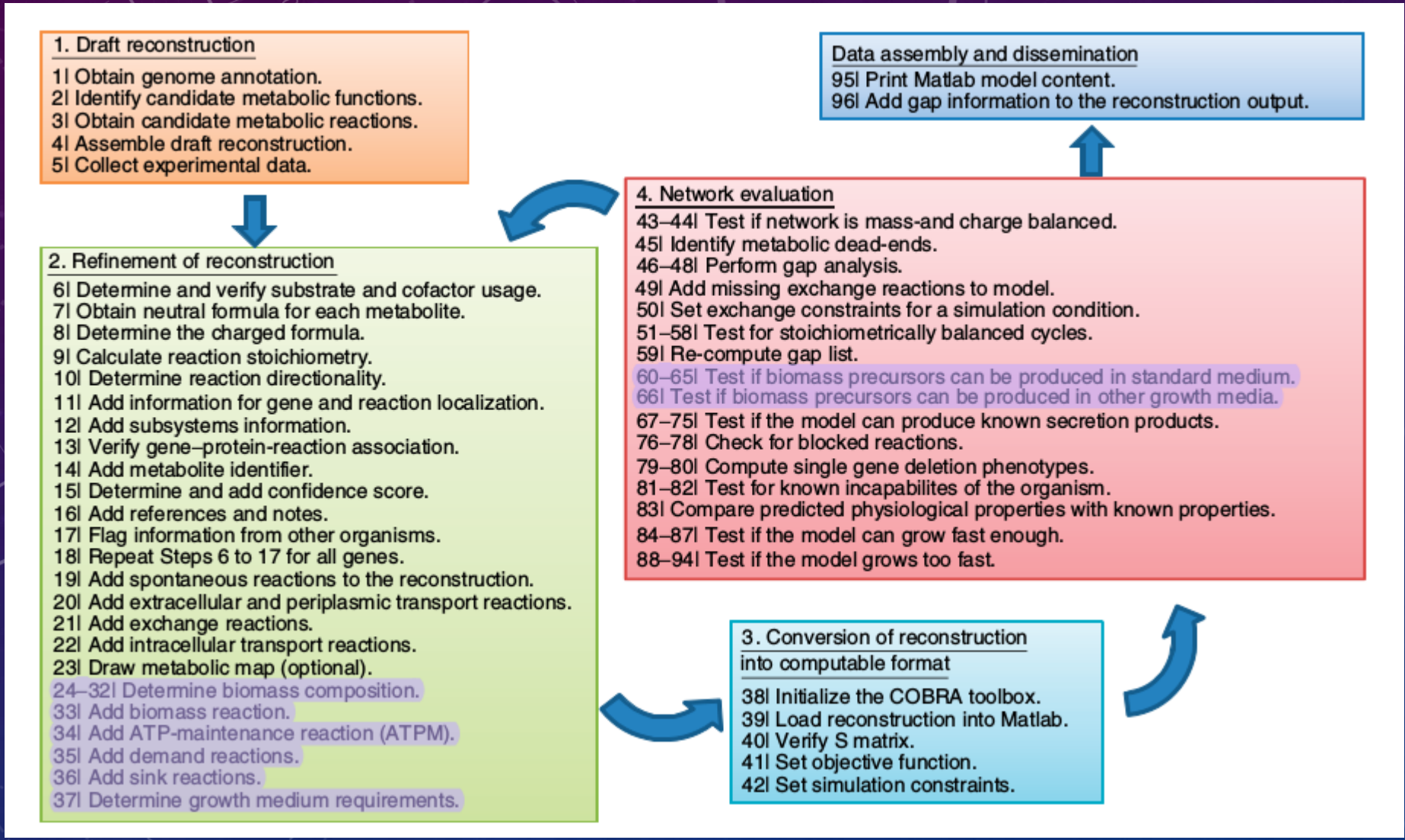


Thiele, Ines, and Bernhard Ø. Palsson. "A protocol for generating a high-quality genome-scale metabolic reconstruction." Nature protocols 5.1 (2010): 93-121.

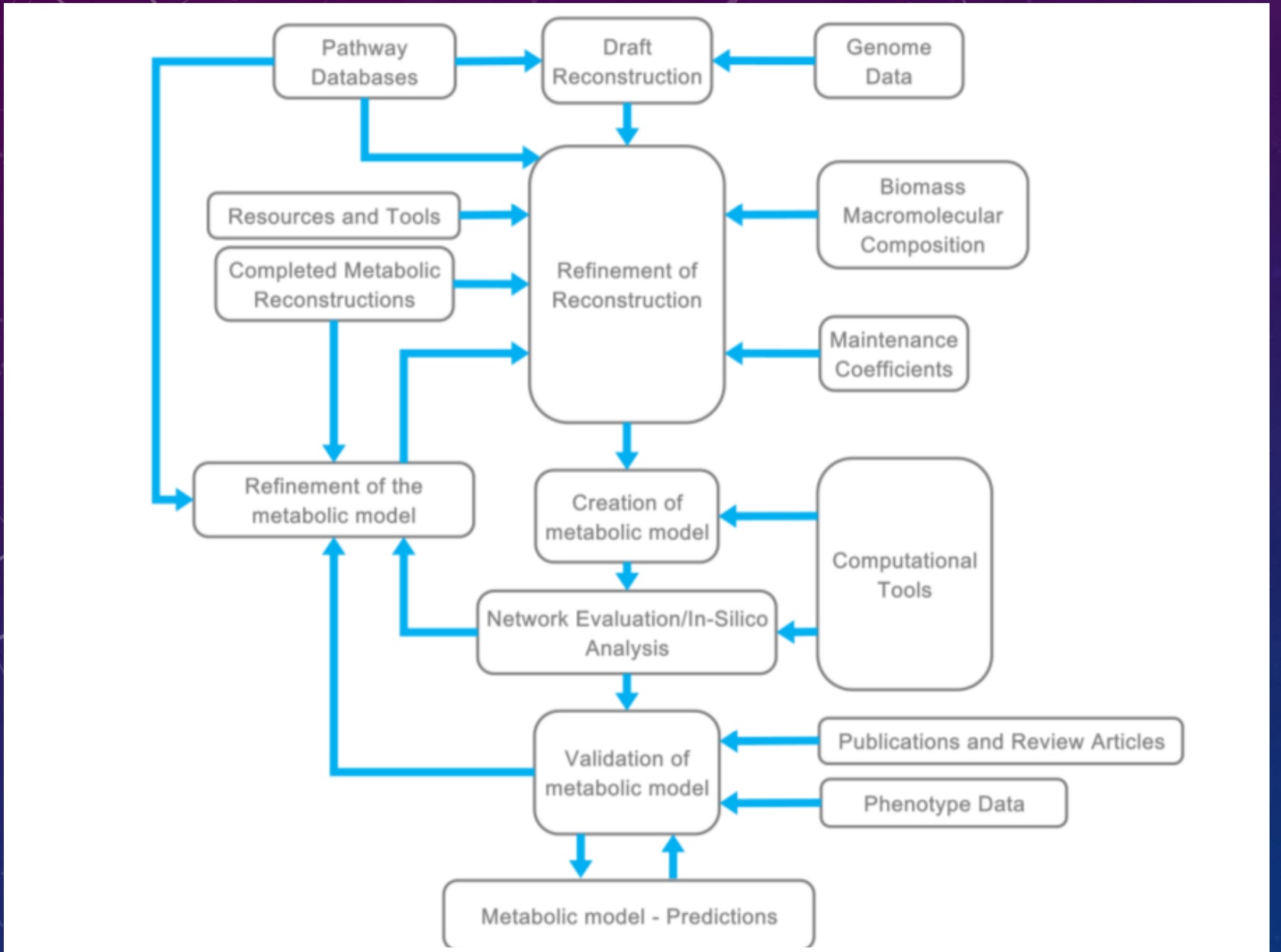
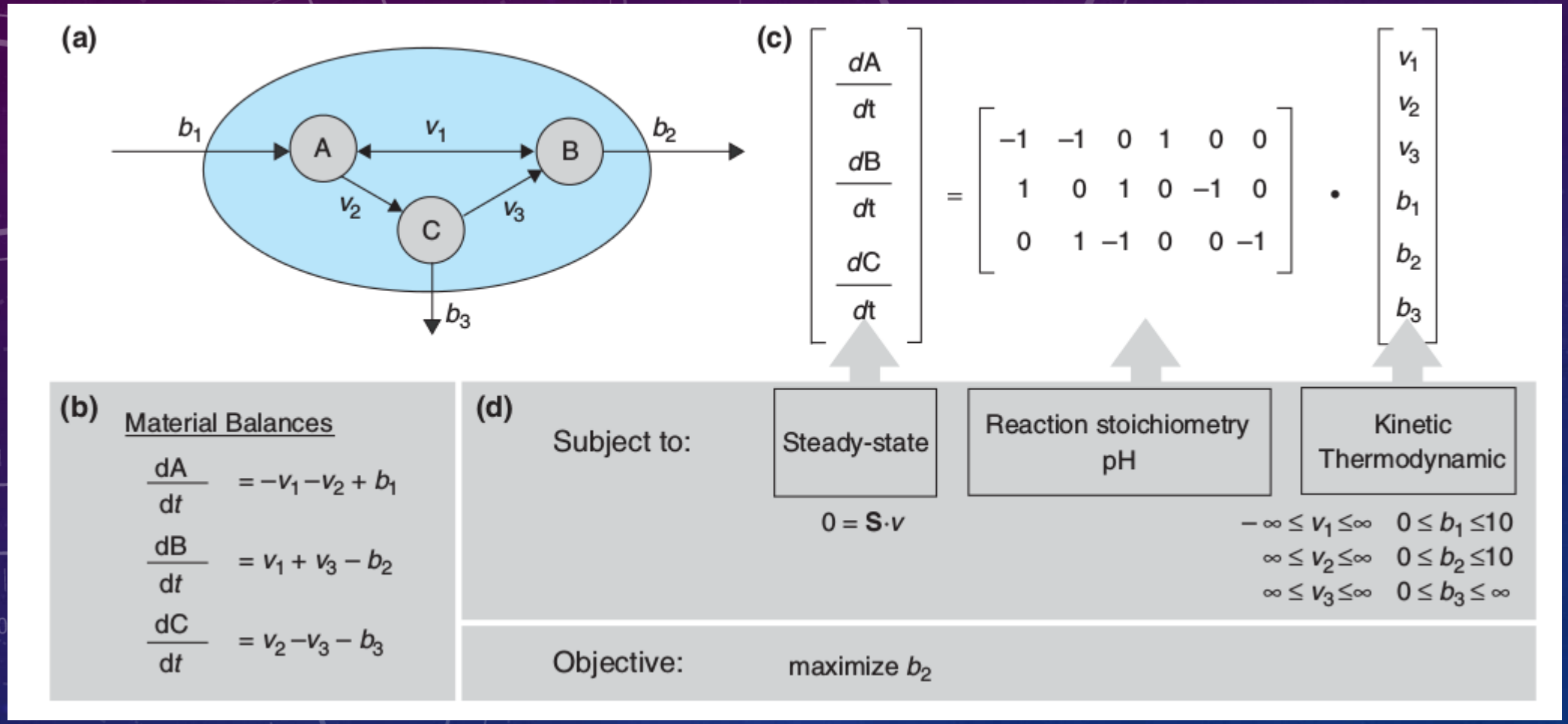


Fig. 1 Genome-scale metabolic network reconstruct process

杨毅. 大豆慢生根瘤菌基因组规模代谢网络构建与分析[D]. 华中农业大学, 2014.

MODEL DEVELOPMENT

The Stoichiometric Matrix



Constraints on Reaction Rates

Links to Genomic Information——GPR relationship

STOICHIOMETRIC NETWORK ANALYSIS

Structural Analysis: Characterizing the Nullspace

$$v = a\,1 \cdot K\,1 + a\,2 \cdot K\,2 + \ldots + a\,n \cdot K\,n = K \cdot a$$

$$\begin{bmatrix} v_1 \\ v_2 \\ \ldots \\ v_n \end{bmatrix} = \begin{bmatrix} k_{11} & k_{21} & \ldots & k_{n1} \\ k_{12} & k_{22} & \ldots & k_{n2} \\ \ldots & \ldots & \ldots & \ldots \\ k_{1n} & k_{2n} & \ldots & k_{nn} \end{bmatrix} \cdot \begin{bmatrix} a_1 \\ a_2 \\ \ldots \\ a_n \end{bmatrix}$$

RESULTS OF NULLSPACE ANALYSIS

1. If the kernel matrix contains a zero-row, the corresponding reaction cannot carry a (non-zero) flux. We can remove this reaction for all analysis employing the steady-state assumption.
2. If two matrix rows differ only by a constant factor, the two reactions are coupled, that is, the flux through one reaction is always a multiple of the flux through the other reaction; consequently either both reactions are active or both are passive. Such reactions are presumably co-regulated
3. Given reversibility constraints, inconsistent reaction coupling can be detected. For example, two coupled forward-only reactions with a negative coupling factor cannot carry a non-zero flux without violating an irreversibility constraint, since one reaction would have to operate in backward mode.

STOICHIOMETRIC NETWORK ANALYSIS

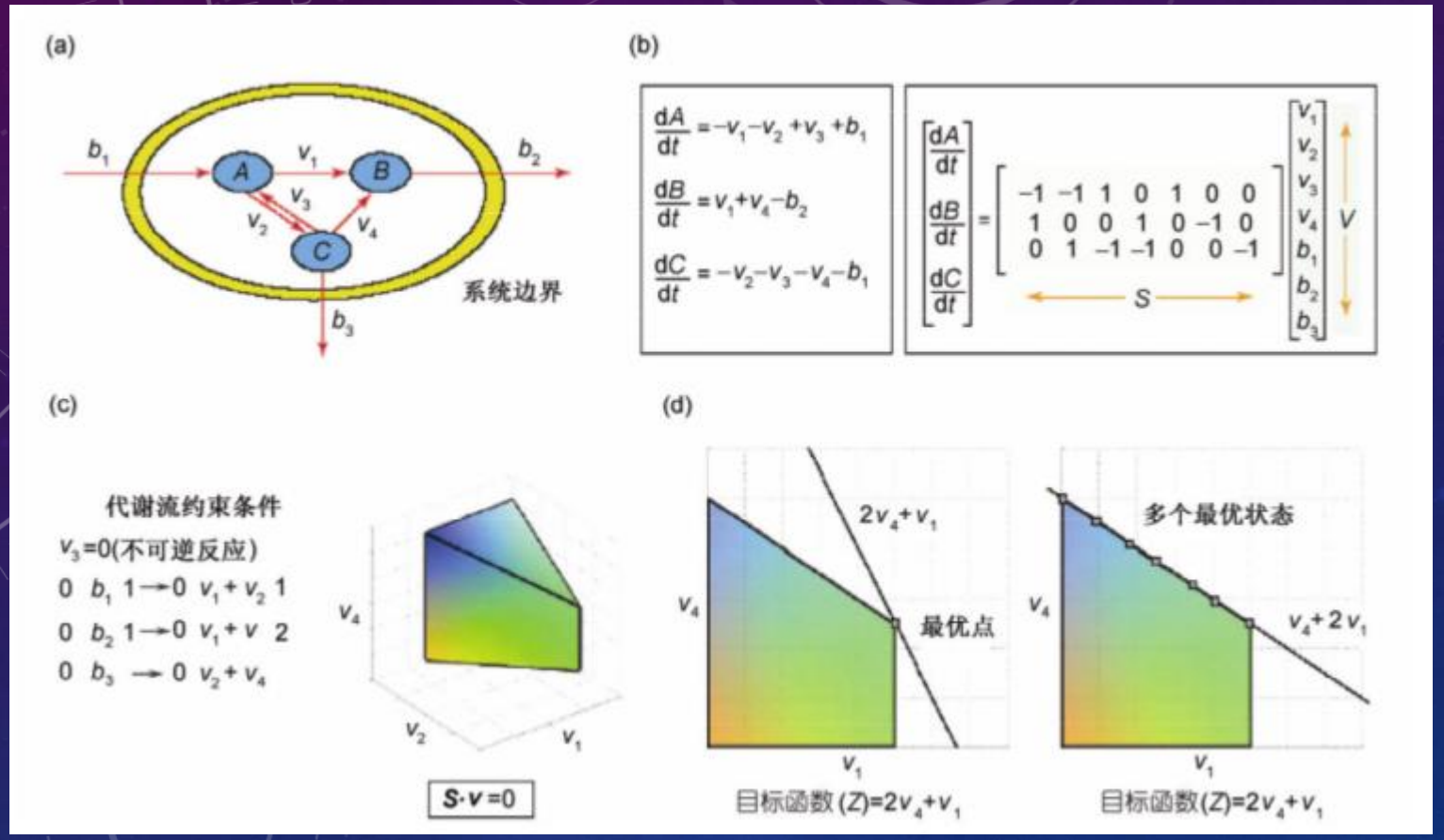
MODEL CONSISTENCY

1. Minimize and maximize the flux value for each reaction.

   (a) If min and max value are zero, the reaction is a zero flux reaction, that is, it cannot have a flux value other than zero. It can be removed if no model corrections are made, without affecting the outcome of subsequent simulations.
   (b) If min or max value is zero and the reaction is reversible, we have an unsatisfied reversibility. Either the reversibility constraint is too lax or another component is missing, disabling the operation in one direction. Tightening this constraint might lead to better simulation performance.
   (c) If the minimal and maximal values are non-zero and have equal sign, the reaction is essential. Deletion of the reaction, for example, by gene knockout, is predicted to be lethal.

2. For reactions not of type (1c), set the bounds to zero. If biomass cannot be produced, the reaction is essential. Again, reaction removal is associated with lethality.

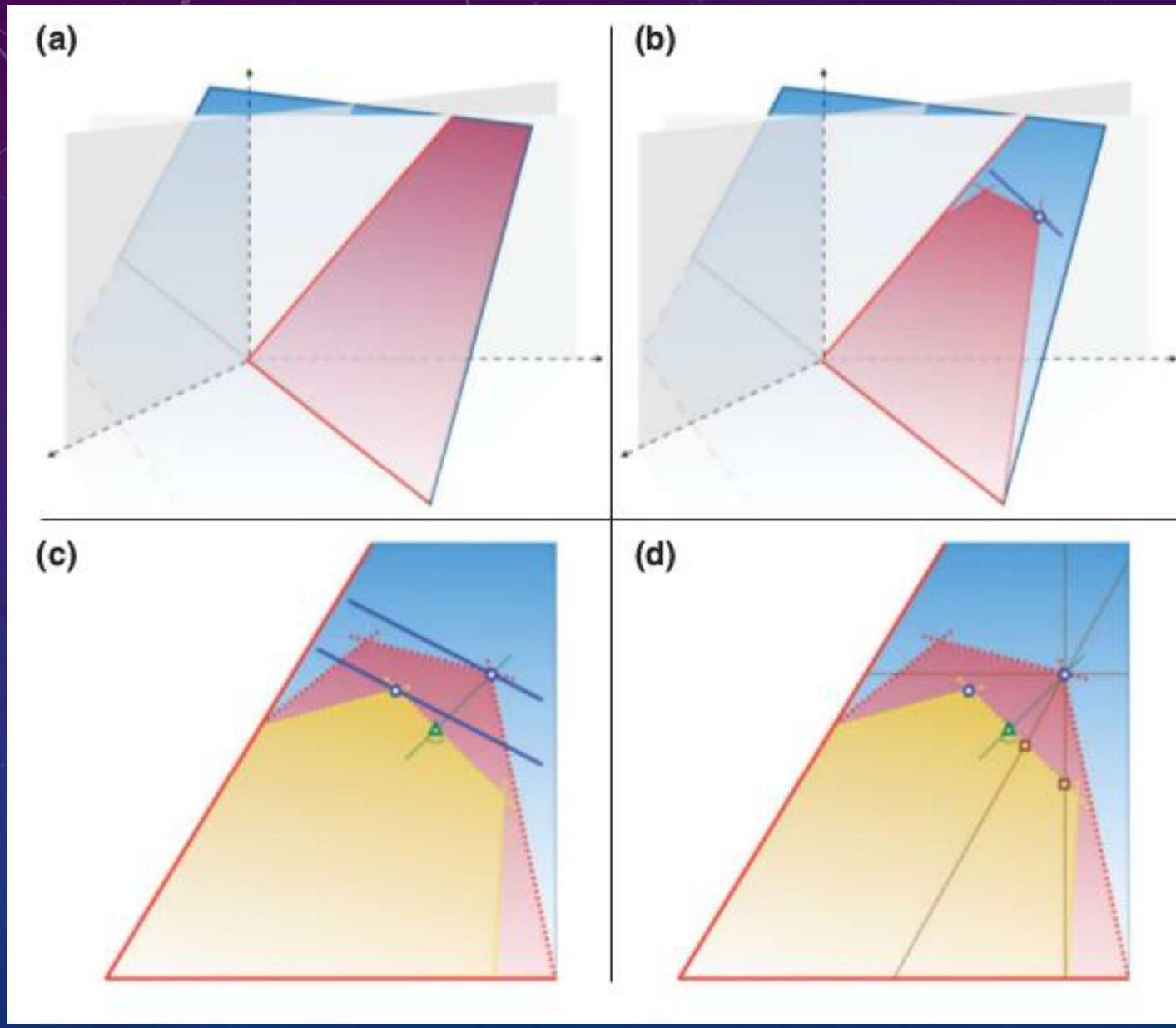
FBA——flux balance analysis



Deletion Strain Phenotypes

Minimization of metabolic adjustment (MoMA)

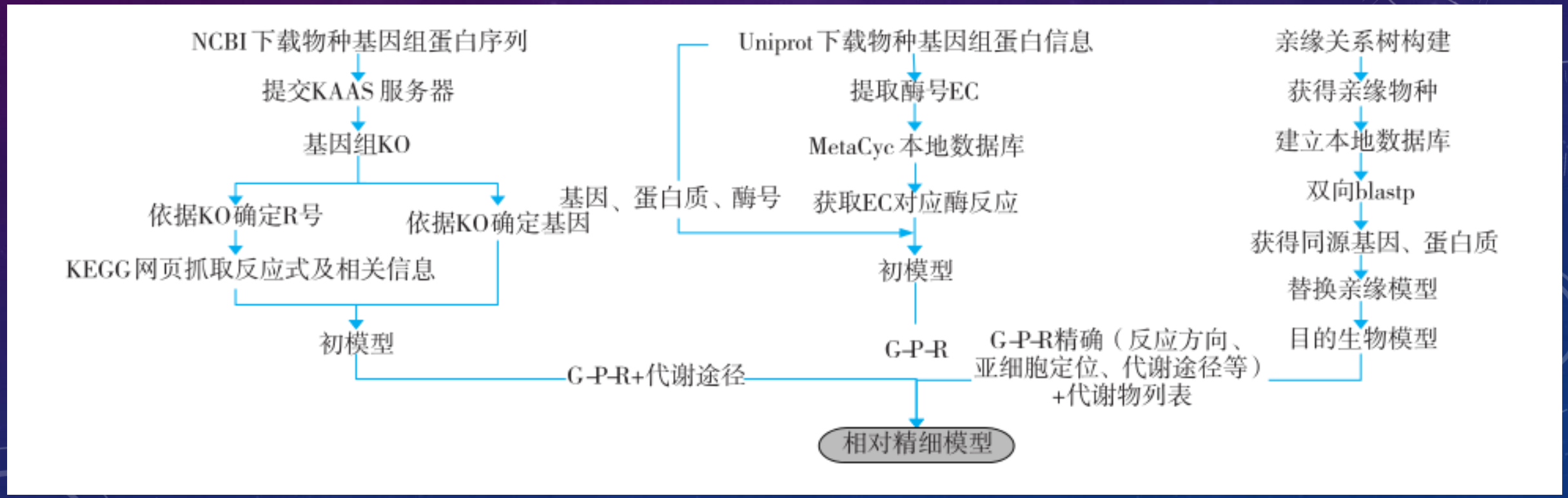
Regulatory on/off minimization (ROOM)



	CellNetAnalyzer FluxAnalyzer	BioSPICE MOMA	COBRA Tool-box	FluxExplorer	MetaFluxNet	Pathway Analyser	Fbatool
图形化界面	有	有	无	有	有	无	无
网络构建方法	Four Network Element files	SBML files	SBML files	Mannually	SBML files	SBML files	SBML files
适用操作系统	Windows (Matlab)	Windows Linux	Windows (Matlab)	Windows	Windows	Linux UNIX	Corona
网络分析算法	MFA SNA	FBA MOMA	FBA MOMA DFBA FVA	FBA MOMA EPA SVD	MFA	FBA MOMA	FBA
适用网络规模	中	大	大	小	大	大	大
操作难易程度	易	难	中	易	易	中	中
软件可用性	优	良	优	中	良	良	中

CURRENT CHALLENGES

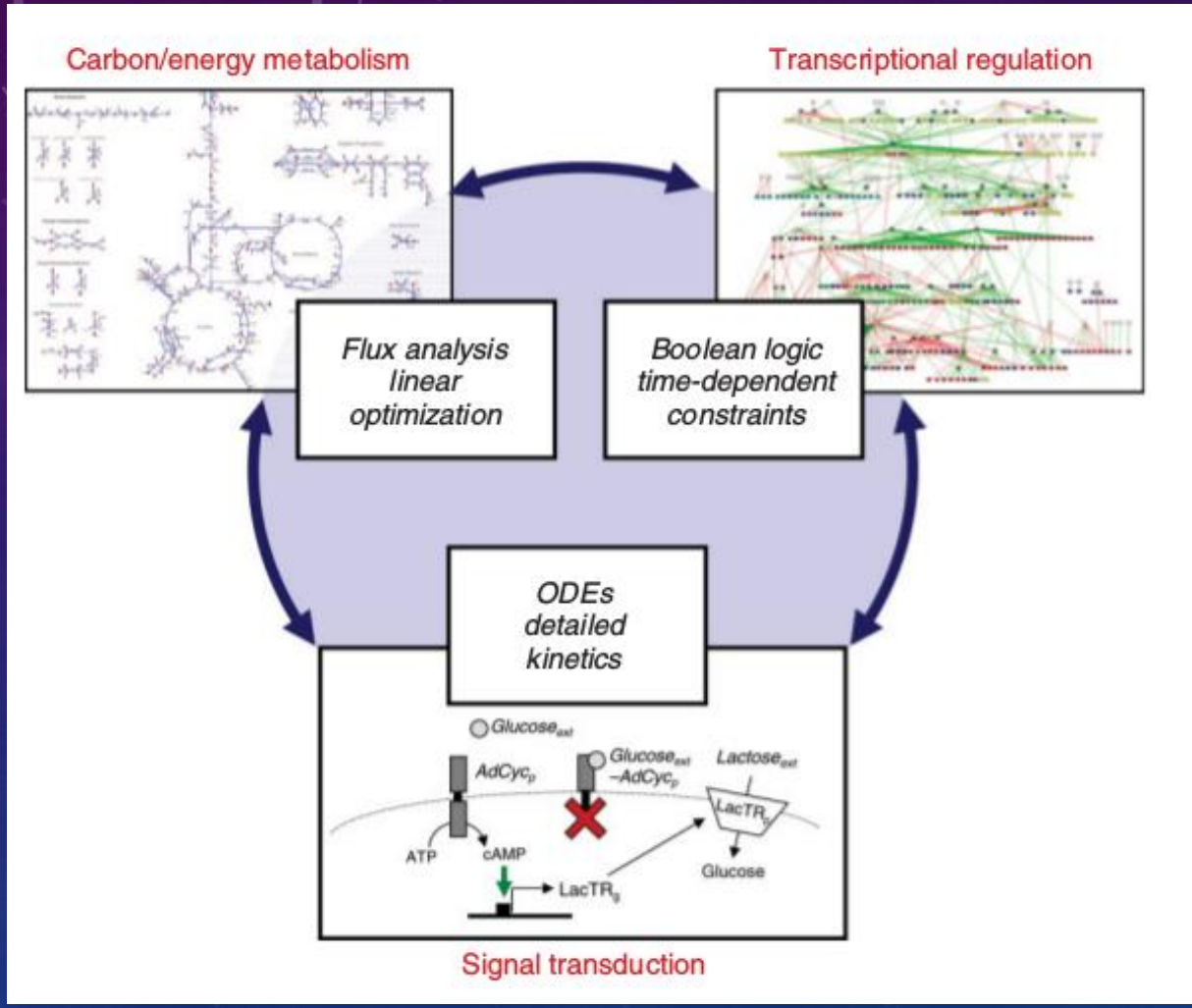
1、Automated Network Reconstruction



CURRENT CHALLENGES

2、Cellular Optimality and Design

3、Toward Large-Scale Network Integration and Dynamics



Thanks for your listening!