



Sampling the flux space of microbial metabolic networks

the example of SARS-CoV-2 on the human alveolar macrophage metabolic network

Haris Zafeiropoulos

Genome-scale metabolic reconstruction

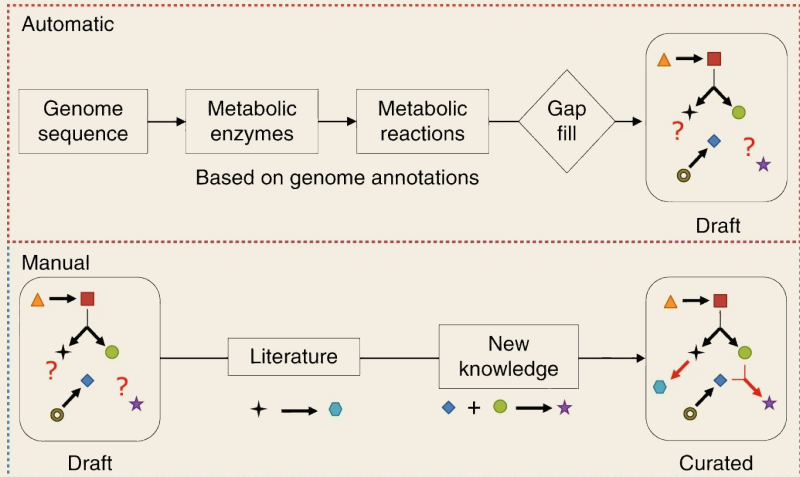










Figure from: Heirendt, Laurent, et al. Nature protocols 14.3 (2019): 639-702.

From a stoichiometric matrix to a constraint-based model

		Reactions				
		R ₁	R ₂	R ₃	R ₄	R ₅
Metabolites		-1	0	0	0	0
		1	-1	0	0	0
		0	1	-1	0	0
		0	1	0	0	-1
		0	0	1	0	0
		0	0	0	-1	0
		0	0	0	1	-1
		0	0	0	0	1

S-matrix

$$\times \begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

Flux vector

Flux Balance Analysis

Maximize minimize an
objective function:

$$\psi = c_1 v_1 + c_2 v_2 + \dots + c_5 v_5$$

such that:

$$S * v = 0$$

and for each reaction i :

$$lb_i \leq v_i \leq ub_i$$

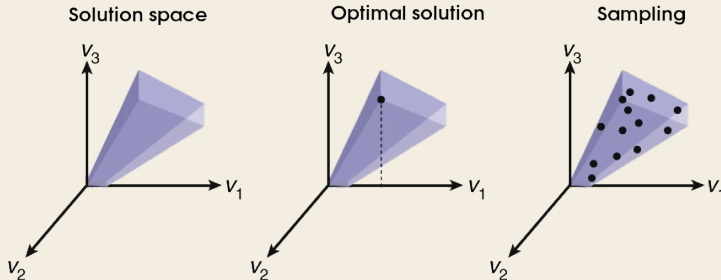
where lb : lower bound,

ub : upper bound and

S : the stoichiometric matrix

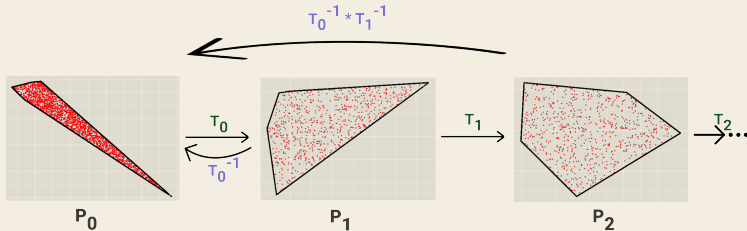
Flux sampling

an alternative approach



- enables the analysis of GSMMs without the need of an objective function
- determines the feasible solution spaces for fluxes in a network based on a set of conditions as well as the probability of obtaining a solution

Our Markov Chain Monte Carlo (MCMC) algorithm for flux sampling



Steps of an MMCS phase

- **sampling step:** using a variant of the **Billiard walk**
- **rounding step:** calculate a linear transformation T_i that puts the sample into isotropic position and then apply it on P_i to obtain the polytope of the next phase
- check several statistic tests

Chalkis, Fisikopoulos, Tsigaridas and Zafeiropoulos "Geometric Algorithms for Sampling the Flux Space of Metabolic Networks", SoCG 2021, DOI: 10.4230/LIPIcs.SocG.2021.21

Find possible anti-COVID19 targets

a flux sampling application

Bioinformatics, 36(26), 2020, i813–i821

doi: 10.1093/bioinformatics/btaa813

ECCB2020

OXFORD

Systems

FBA reveals guanylate kinase as a potential target for antiviral therapies against SARS-CoV-2

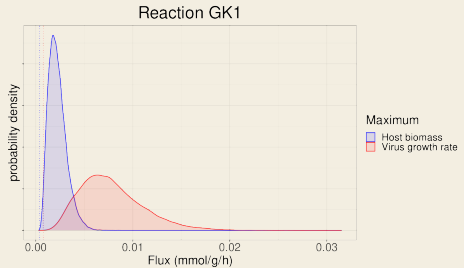
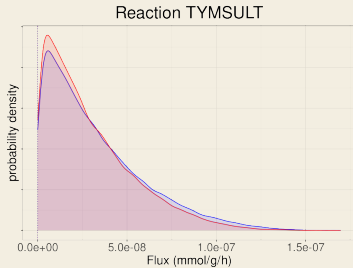
Alina Renz^{1,2,*}, Lina Widerspick¹ and Andreas Dräger^{1,2,3,*}

¹Computational Systems Biology of Infections and Antimicrobial-Resistant Pathogens, Institute for Bioinformatics and Medical Informatics (IBMI) and ²Department of Computer Science, University of Tübingen, Tübingen 72076, Germany and ³German Center for Infection Research (DZIF), partner site Tübingen, Germany

- Renz et al. '20 built the biomass function of Sars-Cov-2 to build a host - virus network
- Using FBA they computed an optimal steady state using
 - (i) human biomass maintenance,
 - (ii) virus growth rate
- They found reaction GK1 as a possible anti-viral target.

Find possible anti-COVID19 targets

a flux sampling application

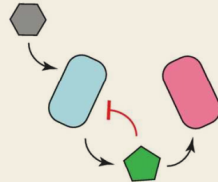


- Check if the flux distribution of a reaction changes.
- Find possible anti-viral targets and study further..

Further applications *of metabolic flux sampling*



Scott, William T., et al. "Metabolic flux sampling predicts strain-dependent differences related to aroma production among commercial wine yeasts." *Microbial cell factories* 20.1 (2021): 1-15.



Thank you for your attention

GitHub repository : <https://github.com/GeomScale/dingo/>
MMCS algorithm publication: 10.4230/LIPIcs.SoCG.2021.21

email : haris-zaf@hcmr.gr

Twitter : [haris_zaf](https://twitter.com/haris_zaf)

web-site : <https://hariszaf.github.io/>

