

# Sampling the flux space of microbial metabolic networks









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

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# From a stoichiometric matrix to a constraint-based model

		Reactions				
		R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>
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  $i$ :

$$lb_i \leq v_i \leq ub_i$$

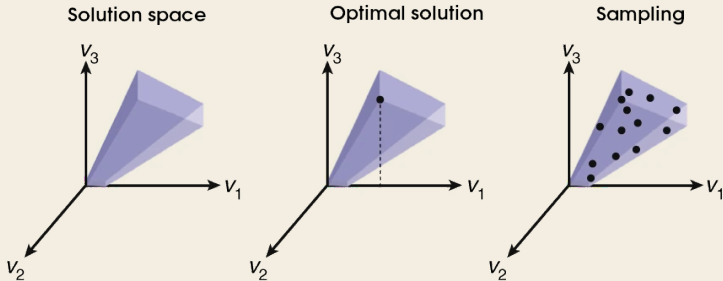
where  $lb$ : lower bound,

$ub$ : upper bound and

$S$ : the stoichiometric matrix

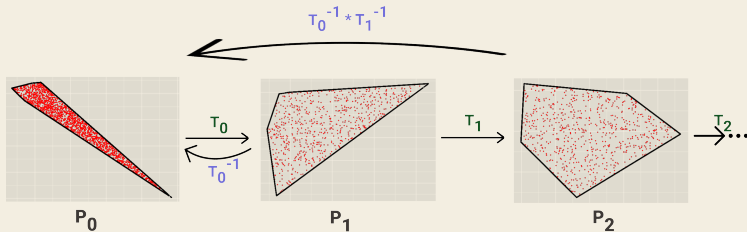
# Flux sampling

*an alternative approach*



- enables the analysis of GEMs 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 targets against SARS-CoV-2

*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<sup>1,2,\*</sup>, Lina Widerspick<sup>1</sup> and Andreas Dräger<sup>1,2,3,\*</sup>**

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

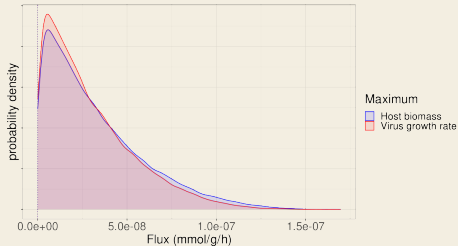
- Renz et al. '20 built the biomass function of Sars-Cov-2 to build a host - virus network
- Using FBA they computed an optimal steady state using
  - (i) human biomass maintenance,
  - (ii) virus growth rate
- They found reaction GK1 as a possible anti-viral target.

# Find possible targets against SARS-CoV-2

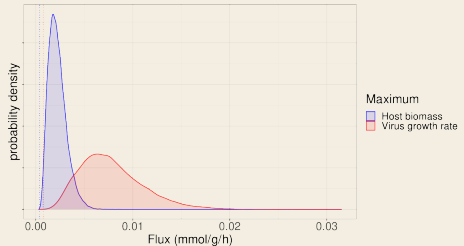
## *a flux sampling application*



Reaction TYMSULT



Reaction GK1

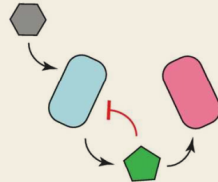


- Check if the flux distribution of a reaction changes
- Find possible anti-viral targets and study further

## 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.



What about microbial interactions ?

# dingo: a Python library

*for flux sampling*



<https://github.com/GeomScale/dingo>

how to GCollab notebook





Thank you for your attention

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GitHub repository : <https://github.com/GeomScale/dingo/>

MMCS algorithm publication: [10.4230/LIPIcs.SoCG.2021.21](#)



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