

SUPPLEMENTARY INFORMATION

Coupling Flux Balance Analysis with Reactive Transport Modeling through Machine Learning for Rapid and Stable Simulation of Microbial Metabolic Switching

Hyun-Seob Song^{1,2,*}, Firnaaz Ahamed^{1,†}, Joon-Yong Lee^{3,†}, Christopher S. Henry⁴, Janaka N. Edirisinghe⁴, William C. Nelson³, Xingyuan Chen³, J. David Moulton⁵, Timothy D. Scheibe^{3,*}

¹Department of Biological Systems Engineering, University of Nebraska-Lincoln, Lincoln, NE

²Department of Food Science and Technology, Nebraska Food for Health Center, University of Nebraska-Lincoln, Lincoln, NE

³Earth and Biological Sciences Directorate, Pacific Northwest National Laboratory, Richland, WA

⁴Division of Mathematics and Computer Science, Argonne National Laboratory, Argonne, IL

⁵Theoretical Division, Los Alamos National Laboratory, Los Alamos, NM

*Correspondence: hsong5@unl.edu (H-SS); tim.scheibe@pnnl.gov (TDS)

†Current address: Taylor's University, Subang Jaya, Malaysia (FA); PrognomiQ Inc., San Mateo, CA (J-YL)

Table S1. The number of nodes and layers in ANN models. The two numbers in the parenthesis respectively denote the numbers of nodes and layers chosen for predicting output variables. MISO = multi-input single-output, and MIMO = multi-input multi-output.

Input variables	Output variables in MISO models				Output variables in MIMO models
	Oxygen uptake rate	Biomass production rate	Pyruvate production rate	Acetate production rate	All
Upper limit to the uptake rates of lactate and oxygen	(6,2)	(6,2)	(8,2)	(10,3)	(10,5)
Upper limit to the uptake rates of pyruvate and oxygen	(6,2)	(4,2)	N/A	(6,2)	(8,4)
Upper limit to the uptake rates of acetate and oxygen	(4,2)	(6,2)	N/A	N/A	(6,2)

Table S2. Composition of minimum growth media used for FBA simulations. Carbon sources (i.e., lactate, pyruvate, and acetate) are not included in this table.

Compound ID	Name	Formula	Lower bound of exchange reaction [mmol/gDW/h]	Upper bound of exchange reaction [mmol/gDW/h]
cpd00149	Co ²⁺	Co	-1000	1000
cpd00099	Cl ⁻	Cl	-1000	1000
cpd00067	H ⁺	H	-1000	1000
cpd00063	Ca ²⁺	Ca	-1000	1000
cpd00058	Cu ²⁺	Cu	-1000	1000
cpd00048	Sulfate	O ₄ S	-1000	1000
cpd00034	Zn ²⁺	Zn	-1000	1000
cpd00030	Mn ²⁺	Mn	-1000	1000
cpd00013	NH ₃	H ₄ N	-1000	1000
cpd00009	Phosphate	HO ₄ P	-1000	1000
cpd00001	H ₂ O	H ₂ O	-1000	1000
cpd00007	O ₂	O ₂	Constrained by kinetics	1000
cpd00205	K ⁺	K	-1000	1000
cpd00254	Mg	Mg	-1000	1000
cpd00971	Na ⁺	Na	-1000	1000
cpd10515	Fe ⁺²	Fe	-1000	1000
cpd10516	Fe ⁺³	Fe	-1000	1000
cpd11574	Molybdate	MoO ₄	-1000	1000
cpd00244	Ni ²⁺	Ni	-1000	1000
cpd00159	L-Lactate	C ₃ H ₅ O ₃	$-r_{Lac}^{kin}$ in Table 1	1000
cpd00020	Pyruvate	C ₃ H ₃ O ₃	$-r_{Pr}^{kin}$ in Table 1	1000
cpd00029	Acetate	C ₂ H ₃ O ₂	$-r_{Ace}^{kin}$ in Table 1	1000

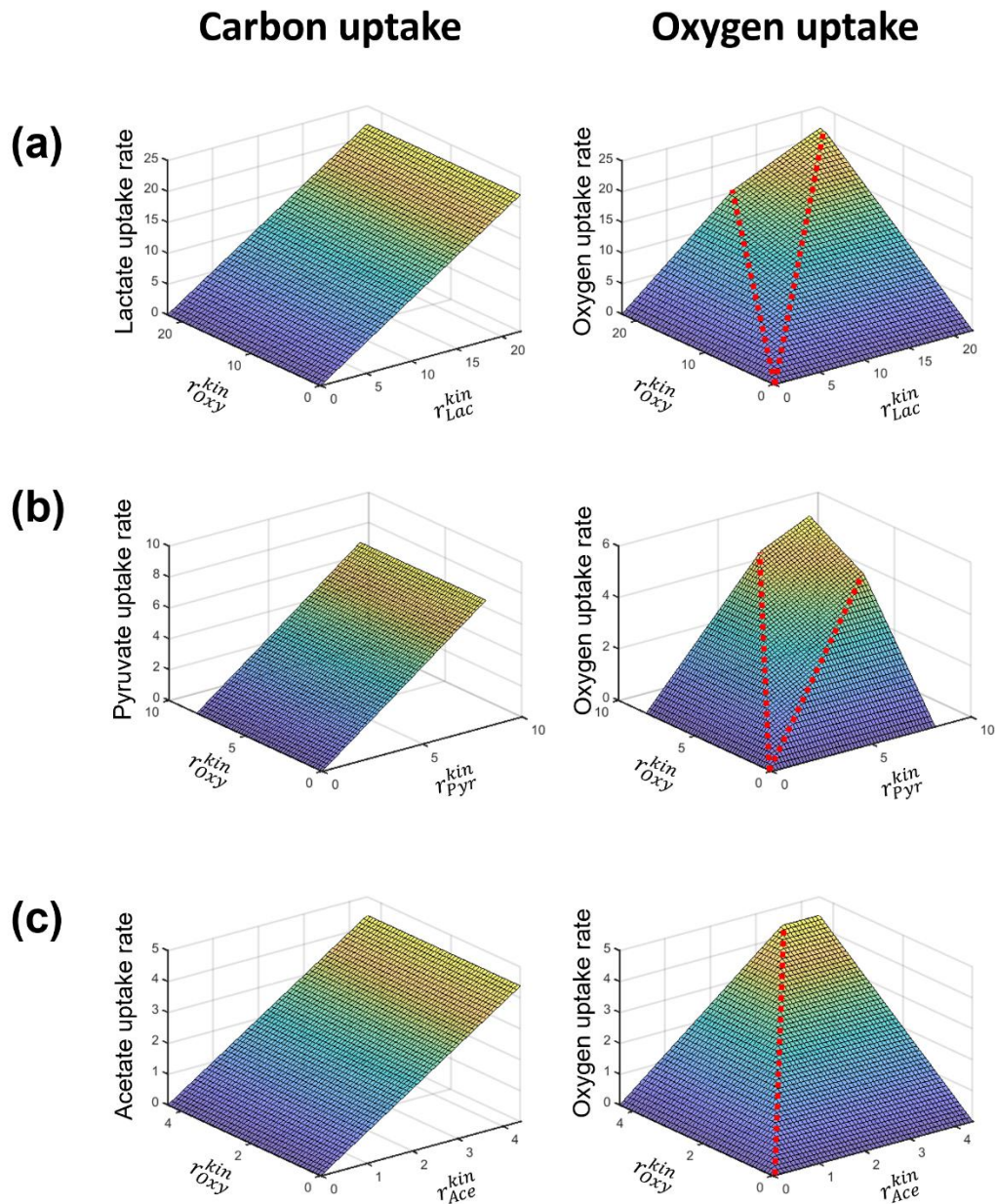


Figure S1. Carbon source-specific FBA-determined carbon uptake rates and oxygen uptake rates in the growth of *S. oneidensis* MR-1. Carbon source: (a) lactate, (b) pyruvate, and (c) acetate.

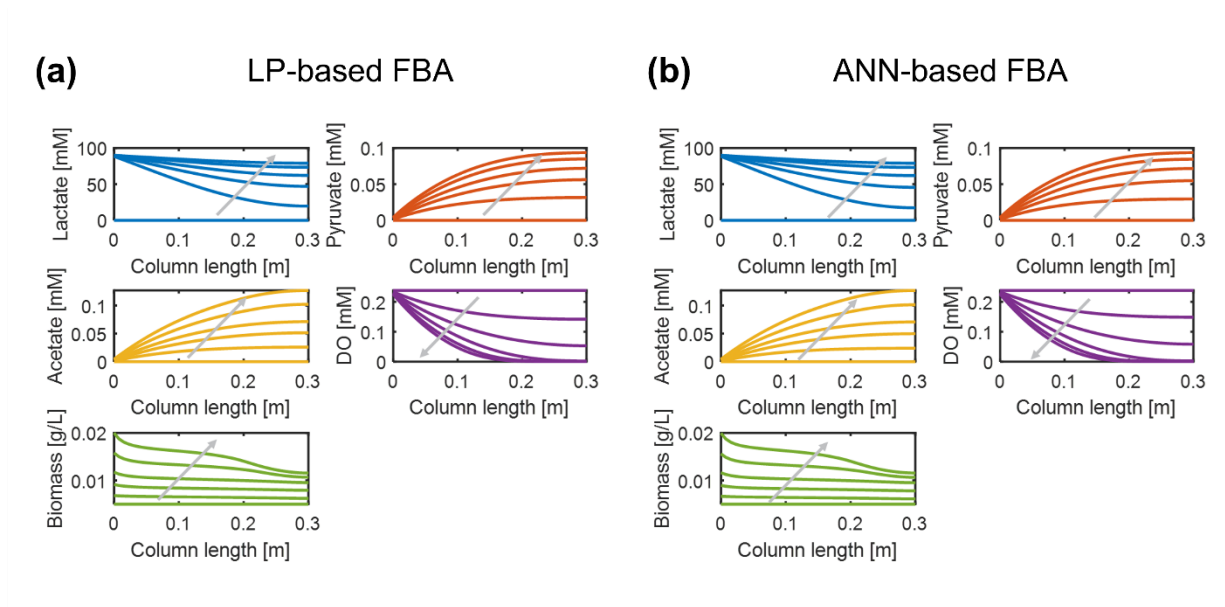


Figure S2. FBA-based dynamic simulations of aerobic growth of *S. oneidensis* MR-1 in a 1-D column reactor: (a) LP-based FBA and (b) ANN-based FBA. DO denotes dissolved oxygen. Grey arrows indicate time progression.