

S2 Table: Comparisons of the time needed to use various functions in PSAMM, COBRA, and RAVEN. The function is listed in the first column along with information on the parameters used in the simulation. The specific commands, running times for seven independent experiments, along with the 25th and 75th percentile times and the median time taken to run the commands are listed in the remaining columns.

	Experiment Number	PSAMM (Cplex 12.6) (including time to load model)	PSAMM (Cplex 12.6) (only solving)	COBRA (TOMLAB Cplex, Cplex 12.6)	RAVEN (MOSEK 7.1.0.36)
Load SBML model iJO1366, load from SBML file to memory representation. For PSAMM, converting to YAML format.		psamm-import sbml --source iJO1366.xml		model = readCbModel('iJO1366.xml')	model = importModel('iJO1366.xml', true, true)
	1	5.92	5.92	17.14	4.45
	2	5.76	5.76	17.22	3.93
	3	5.83	5.83	17.24	3.93
	4	5.95	5.95	17.37	3.95
	5	5.85	5.85	17.25	3.93
	6	5.92	5.92	17.06	3.77
	7	5.90	5.90	17.25	3.90
25% percentile	5.84	5.84	17.18	3.92	
Median	5.90	5.90	17.24	3.93	
75% percentile	5.92	5.92	17.25	3.93	
Standard FBA iJO1366, no thermodynamic constraints. Solver can use up to 20 threads.		psamm-model fba		sol = optimizeCbModel(model)	sol = solveLP(model)
	1	3.88	0.03	0.08	0.32
	2	3.10	0.03	0.07	0.29
	3	3.16	0.03	0.13	0.29
	4	3.13	0.03	0.11	0.29
	5	3.08	0.03	0.07	0.30
	6	3.13	0.03	0.09	0.29
	7	3.07	0.03	0.07	0.30
25% percentile	3.09	0.03	0.07	0.29	
Median	3.13	0.03	0.08	0.29	
75% percentile	3.14	0.03	0.10	0.30	
FBA with thermodynamic constraints iJO1366, with thermodynamic constraints. Solver can use up to 20 threads.		psamm-model fba --loop-removal=tfba		sol = optimizeCbModel(model, 'max', 0, false)	
	1	10.88	7.07	195.1	N/A
	2	10.13	7.20	195.4	N/A
	3	9.96	7.09	193.7	N/A
	4	9.80	6.99	194.7	N/A
	5	9.80	7.01	196.2	N/A
	6	9.78	6.92	191.8	N/A
	7	9.80	6.91	193.4	N/A
25% percentile	9.80	6.96	193.55	N/A	
Median	9.80	7.01	194.7	N/A	
75% percentile	10.05	7.08	195.25	N/A	
Robustness iJO1366, EX_o2(e), no thermodynamic constraints, 1000 steps. The number of parallel pool workers was set to one. Solver can use up to 20 threads.		psamm-model robustness --steps 1000 R_EX_o2_LPAREN_e_RPAREN_		[controlFlux, objFlux] = robustnessAnalysis(model, 'EX_o2(e)', 1000)	
	1	4.89	1.38	94.8	N/A
	2	4.05	1.38	100.7	N/A
	3	4.07	1.38	96.8	N/A
	4	4.04	1.38	100.8	N/A
	5	4.07	1.38	100.5	N/A
	6	4.19	1.38	101.2	N/A
	7	4.05	1.38	102.8	N/A
25% percentile	4.05	1.38	98.65	N/A	
Median	4.07	1.38	100.7	N/A	
75% percentile	4.13	1.38	101.00	N/A	
FVA iJO1366, no thermodynamic constraints. The number of parallel pool workers was set to one. Solver can use up to 20 threads.		psamm-model fva		[minFlux, maxFlux] = fluxVariability(model)	
	1	9.12	7.03	75.3	N/A
	2	8.85	7.06	75.3	N/A
	3	8.86	7.03	75.2	N/A
	4	8.26	7.01	75.1	N/A
	5	8.31	7.05	75.1	N/A
	6	8.27	7.02	75.4	N/A
	7	8.30	7.03	75.6	N/A
25% percentile	8.29	7.03	75.15	N/A	
Median	8.31	7.03	75.3	N/A	
75% percentile	8.86	7.04	75.35	N/A	
Random minimal network (randomsparse) iJO1366, gene-based, no thermodynamic constraints, 30% threshold. 100 random solutions.		psamm-model randomsparse --type genes 30%			
	1	1662	N/A	N/A	N/A
	2	1623	N/A	N/A	N/A
	3	1817	N/A	N/A	N/A
	4	1670	N/A	N/A	N/A
	5	1653	N/A	N/A	N/A
	6	1664	N/A	N/A	N/A
	7	1674	N/A	N/A	N/A
25% percentile	1657.5	N/A	N/A	N/A	
Median	1664.0	N/A	N/A	N/A	
75% percentile	1672.0	N/A	N/A	N/A	
Random minimal network (randomsparse) iJO1366, reaction-based, no thermodynamic constraints, 30% threshold. 100 random solutions.		psamm-model randomsparse --type reactions 30%			
	1	3502	N/A	N/A	N/A
	2	3512	N/A	N/A	N/A
	3	3524	N/A	N/A	N/A
	4	3538	N/A	N/A	N/A
	5	3698	N/A	N/A	N/A
	6	3486	N/A	N/A	N/A
	7	3534	N/A	N/A	N/A
25% percentile	3507.0	N/A	N/A	N/A	
Median	3524.0	N/A	N/A	N/A	
75% percentile	3536.0	N/A	N/A	N/A	

Formula balance check		psamm-model formulacheck		model = findSExRxnInd(model) model.SIntRxnBool(find(strcmp(model.rxn, ns, 'Ec_biomass_iJO1366_WT_53p95M')) = 0 [massImbalance, imBalancedMass, imBalancedCharge, imBalancedRxnBool, Elements, missingFormulaeBool, balancedMetBool] = checkMassChargeBalance(model, 2)	balance = getElementalBalance(model)	
iJO1366. COBRA combines formula check and charge check in one function. The time for COBRA is the time to run that function.	1		2.59	N/A	13.9	2.8
	2		2.32	N/A	13.8	2.7
	3		2.33	N/A	13.8	2.7
	4		2.40	N/A	13.7	2.7
	5		2.35	N/A	13.8	2.7
	6		2.44	N/A	14.0	2.7
	7		2.42	N/A	13.8	2.7
	25% percentile		2.34	N/A	13.80	2.70
Median		2.40	N/A	13.80	2.70	
75% percentile		2.43	N/A	13.85	2.70	
Charge balance check		psamm-model chargecheck			See above	
iJO1366.	1		1.67	N/A		N/A
	2		1.55	N/A		N/A
	3		1.62	N/A		N/A
	4		1.63	N/A		N/A
	5		1.63	N/A		N/A
	6		1.61	N/A		N/A
	7		1.67	N/A		N/A
	25% percentile		1.61	N/A		N/A
Median		1.63	N/A		N/A	
75% percentile		1.65	N/A		N/A	
Stoichiometric balance check		psamm-model masscheck		model = findSExRxnInd(model) model.SIntRxnBool(find(strcmp(model.rxn, ns, 'Ec_biomass_iJO1366_WT_53p95M')) = 0 [inform, m] = checkStoichiometricConsistency(model)		
iJO1366. Only compound imbalance check.	1		3.13	1.09	0.1	N/A
	2		3.10	1.05	0.1	N/A
	3		3.07	1.03	0.1	N/A
	4		3.15	1.16	0.1	N/A
	5		2.95	0.91	0.1	N/A
	6		2.86	0.83	0.1	N/A
	7		3.17	1.07	0.1	N/A
	25% percentile		3.01	0.97	0.09	N/A
Median		3.10	1.05	0.1	N/A	
75% percentile		3.14	1.08	0.09	N/A	
Flux consistency check (zero-flux reactions)		psamm-model fluxcheck		BlockedReaction = findBlockedReaction(model)		
iJO1366. Using FVA (without biomass constraint). The number of parallel pool workers was set to one. Solver can use up to 20 threads.	1		12.62	N/A	79.6	N/A
	2		12.02	N/A	79.5	N/A
	3		11.98	N/A	79.0	N/A
	4		11.88	N/A	78.5	N/A
	5		11.91	N/A	78.5	N/A
	6		11.90	N/A	78.5	N/A
	7		11.95	N/A	78.4	N/A
	25% percentile		11.91	N/A	78.50	N/A
Median		11.95	N/A	78.5	N/A	
75% percentile		12.00	N/A	79.25	N/A	
Flux consistency check (thermodynamic constraints)		psamm-model fluxcheck --tfba				
iJO1366.	1		7619	N/A	N/A	N/A
	2		7648	N/A	N/A	N/A
	3		7623	N/A	N/A	N/A
	4		7608	N/A	N/A	N/A
	5		7596	N/A	N/A	N/A
	6		7637	N/A	N/A	N/A
	7		7606	N/A	N/A	N/A
	25% percentile		7607.0	N/A	N/A	N/A
Median		7619	N/A	N/A	N/A	
75% percentile		7630.0	N/A	N/A	N/A	
Flux consistency check (fastcc)		psamm-model fluxcheck --fastcore		[A, v] = fastcc(model, 1e-5, 1)		
iJO1366.	1		14.52	N/A	22.0	N/A
	2		14.52	N/A	21.7	N/A
	3		14.62	N/A	21.8	N/A
	4		14.57	N/A	22.5	N/A
	5		14.50	N/A	21.6	N/A
	6		14.52	N/A	21.5	N/A
	7		14.68	N/A	21.6	N/A
	25% percentile		14.52	N/A	21.60	N/A
Median		14.52	N/A	21.7	N/A	
75% percentile		14.60	N/A	21.90	N/A	