j Strain model

The model is set up supposing intracellular concentrations of [µmol/gDW] and the extracellular concentrations [g/l]. To convert intracellular to extracellular concentrations a biomass concentrations of OD=1 [g/l] was considered. Molecular Weight for all extracellular species is set to 10[g/mol]. A conversion factor of cf=1e+06 is used to convert µmol to mol. Since the goal is to run the system at steady state the concentration of Sex is set [S_ex] = 4 g/l fixed. In the same way P_ex is set as fixed concentration because at steady state, being just produced, it only accumulates. They are set as parameters in the python files and as fixed concentrations in the Copasi file. Therefore, the first two ODEs here reported are the one to be used in case the model is run batch and not continuous. n= num strains. All equations are reported using j as index to indicate the considered strain.

ODEs

$$\frac{d[S_{ex}]}{dt} = \frac{\left(\sum_{j=1}^{n} -r_{1,j} * OD_{\ j}\right) * MW_S}{cf}$$

$$\frac{d[P_{ex}]}{dt} = \frac{\left(\sum_{j=1}^{n} r_{6,j} * OD_{\ j}\right) * MW_P}{cf}$$

$$\frac{d[S_j]}{dt} = r_{1,j} - r_{2,j}$$

$$\frac{d[A_j]}{dt} = r_{2,j} - r_{3,j} - r_{TAj}$$

$$\frac{d[B_j]}{dt} = r_{3,j} - r_{4,j} - r_{TBj}$$

$$\frac{d[Z_j]}{dt} = r_{2,j} + r_{4,j} - r_{3,j} - r_{5,j} - r_{TZj}$$

$$\frac{d[C_j]}{dt} = r_{4,j} - r_{5,j} - r_{TCj}$$

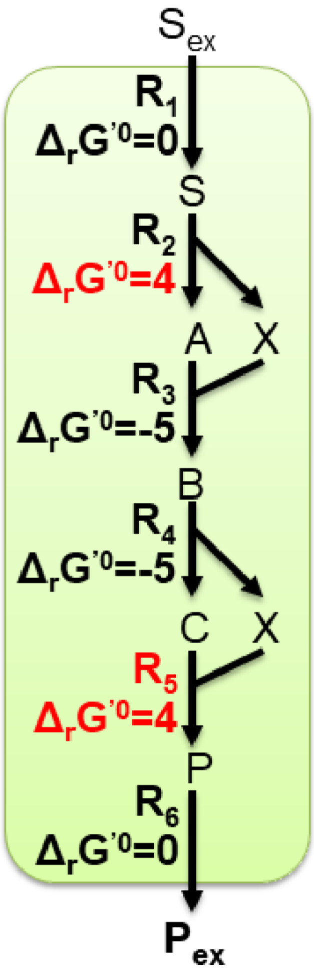
$$\frac{d[P_j]}{dt} = r_{5,j} - r_{6,j}$$

$$\frac{d[A_{ex}]}{dt} = \frac{\left(\sum_{j=1}^{n} r_{TAj} * OD_{\ j}\right) * MW_A}{cf}$$

$$\frac{d[B_{ex}]}{dt} = \frac{\left(\sum_{j=1}^{n} r_{TBj} * OD_{\ j}\right) * MW_B}{cf}$$

$$\frac{d[C_{ex}]}{dt} = \frac{\left(\sum_{j=1}^{n} r_{TCj} * OD_{\ j}\right) * MW_{CA}}{cf}$$

$$\frac{d[Z_{ex}]}{dt} = \frac{\left(\sum_{j=1}^{n} r_{TZj} * OD_{\ j}\right) * MW_Z}{cf}$$



INITIAL CONDITIONS

For all metabolites = 1e-05 umol/gDW – g/l.

REACTION KINETICS

The kinetics used are simple reversible Michaelis-Menten. For reactions from r2 to r5 the Vmax of the reaction is split in [enzyme]*kcat. For the other reactions just Vmax was used, (though also transporters can be overexpressed) because in this stage transport is not presenting any bottle neck.

To model the reaction reversibility the ΔG°r was used in the following formula for computing the Keq. (R=8.315e-3 kJ/mol/K, T=298K)

$$k_{eq} = e^{\left(\frac{-\Delta G^{\circ} r}{RT}\right)}$$

For intracellular reaction the Haldane form for the numerator was preferred.

$$r_{1,j} = \frac{V_{max,r1,j} \cdot \left(\frac{[\mathrm{S_{ex}}]}{k_{r1,j,Sex}} - \frac{[\mathrm{S_j}]}{k_{r1,j,EQ}}\right)}{1 + \frac{[\mathrm{S_{ex}}]}{k_{r1,j,Sex}} + \frac{[\mathrm{S_j}]}{k_{r1,j,Sj}}}$$

$$r_{2,j} = \frac{E_{2,j} \cdot k_{cat,R2,j} \cdot \frac{[\mathrm{S_j}]}{k_{r2,j,Sj}} \left(1 - \frac{\frac{[\mathrm{Zj}] \cdot [\mathrm{Aj}]}{[\mathrm{Sj}]}}{k_{r2,j,EQ}}\right)}{1 + \frac{[\mathrm{S_j}]}{k_{r2,j,Sj}} + \frac{[\mathrm{Z_j}]}{k_{r2,j,Zj}} + \frac{[\mathrm{A_j}]}{k_{r2,j,Aj}}}$$

$$r_{3,j} = \frac{E_{3,j} \cdot k_{cat,R3,j} \cdot \frac{[\mathrm{A_j}]}{k_{r3,j,Aj}} \cdot \frac{[\mathrm{Z_j}]}{k_{r3,j,Zj}} \left(1 - \frac{\frac{[\mathrm{Bj}]}{[\mathrm{Zj}] \cdot [\mathrm{Aj}]}}{k_{r3,j,EQ}}\right)}{1 + \frac{[\mathrm{B_j}]}{k_{r3,j,Bj}} + \frac{[\mathrm{Z_j}]}{k_{r3,j,Zj}} + \frac{[\mathrm{A_j}]}{k_{r3,j,Aj}}}$$

$$r_{4,j} = \frac{E_{4,j} \cdot k_{cat,R4,j} \cdot \frac{[B_j]}{k_{r4,j,Bj}} \cdot \left(1 - \frac{\frac{[\mathrm{Cj}] \cdot [\mathrm{Zj}]}{[\mathrm{Bj}]}}{k_{r4,j,EQ}}\right)}{1 + \frac{[\mathrm{B_j}]}{k_{r4,j,Bj}} + \frac{[\mathrm{Z_j}]}{k_{r4,j,Zj}} + \frac{[\mathrm{C_j}]}{k_{r4,j,Cj}}}$$

$$r_{5,j} = \frac{E_{5,j} \cdot k_{cat,R5,j} \cdot \frac{[\mathrm{Cj}]}{k_{r5,j,Cj}} \cdot \frac{[\mathrm{Zj}]}{k_{r5,j,Zj}} \cdot \left(1 - \frac{\frac{[\mathrm{Pj}]}{[\mathrm{Cj}] \cdot [\mathrm{Zj}]}}{k_{r5,j,EQ}}\right)}{1 + \frac{[\mathrm{C_j}]}{k_{r5,j,Cj}} + \frac{[\mathrm{Z_j}]}{k_{r5,j,Zj}} + \frac{[\mathrm{P_j}]}{k_{r5,j,Pj}}}$$

$$r_{6,j} = \frac{V_{max,r6,j} \cdot \left(\frac{[\mathrm{P_j}]}{k_{r6,j,Pj}} - \frac{[\mathrm{P_{ex}}]}{k_{r6,j,EQ}}\right)}{1 + \frac{[\mathrm{P_{ex}}]}{k_{r6,j,Pex}} + \frac{[\mathrm{P_j}]}{k_{r6,j,Pj}}}$$

$$r_{TA1} = \frac{V_{max,TAj} \cdot \left(\frac{[\mathrm{A_j}]}{k_{TAj,Aj}} - \frac{[\mathrm{A_{ex}}]}{k_{TAj,EQ}}\right)}{1 + \frac{[\mathrm{A_j}]}{k_{TAj,Aj}} + \frac{[\mathrm{A_{ex}}]}{k_{TAj,Aex}}}$$

$$r_{TB1} = \frac{V_{max,TBj} \cdot \left(\frac{[\mathrm{B_j}]}{k_{TBj,Bj}} - \frac{[\mathrm{B_{ex}}]}{k_{TBj,EQ}}\right)}{1 + \frac{[\mathrm{B_j}]}{k_{TBj,Bj}} + \frac{[\mathrm{B_{ex}}]}{k_{TBj,Bex}}}$$

$$r_{TC1} = \frac{V_{max,TCj} \cdot \left(\frac{[\mathrm{C_j}]}{k_{TCj,Cj}} - \frac{[\mathrm{C_{ex}}]}{k_{TCj,EQ}}\right)}{1 + \frac{[\mathrm{C_j}]}{k_{TCj,Cj}} + \frac{[\mathrm{C_{ex}}]}{k_{TCj,Cex}}}$$

$$r_{TZ1} = \frac{V_{max,TZj} \cdot \left(\frac{[\mathrm{Z_j}]}{k_{TZj,Zj}} - \frac{[\mathrm{Z_{ex}}]}{k_{TZj,EQ}}\right)}{1 + \frac{[\mathrm{Z_j}]}{k_{TZj,Zj}} + \frac{[\mathrm{Z_{ex}}]}{k_{TZj,Zex}}}$$

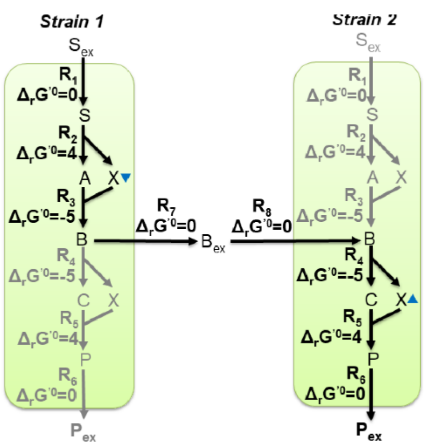
Parameter	Value	Unit of measurement
$V_{max,r1,j}$	6	[µmol/gCDW/s]
$k_{r1,j,Sex}$	0.18	[µmol/gCDW]
$k_{r1,j,EQ}$	1	[µmol/gCDW]
$k_{r1,j,Sj}$	2.5	[µmol/gCDW]
$E_{2,j}$	1	[µmol/gCDW]
$k_{cat,R2,j}$	5	[1/s]
$k_{r2,j,Sj}$	0.4	[µmol/gCDW]
$k_{r2,j,EQ}$	0.1952	[-]
$k_{r2,j,Zj}$	2.1	[µmol/gCDW]
$k_{r2,j,Aj}$	3.1	[µmol/gCDW]
$E_{3,j}$	1	[µmol/gCDW]
$k_{cat,R3,j}$	8	[1/s]
$k_{r3,j,EQ}$	7.7	[-]
$k_{r3,j,Aj}$	4.6	[µmol/gCDW]
$k_{r3,j,Zj}$	0.4	[µmol/gCDW]
$k_{r3,j,Bj}$	2.5	[µmol/gCDW]
$E_{4,j}$	1	[µmol/gCDW]
$k_{cat,R4,j}$	9	[1/s]
$k_{r4,j,EQ}$	7.7	[-]

$k_{r4,j,Bj}$	0.5	[µmol/gCDW]
$k_{r4,j,Zj}$	3.1	[µmol/gCDW]
$k_{r4,j,Cj}$	0.9	[µmol/gCDW]
$E_{5,j}$	1	[µmol/gCDW]
$k_{cat,R5,j}$	10	[1/s]
$k_{r5,j,EQ}$	0.1952	[-]
$k_{r5,j,Cj}$	1.5	[µmol/gCDW]
$k_{r5,j,Zj}$	2.6	[µmol/gCDW]
$k_{r5,j,Pj}$	6.8	[µmol/gCDW]
$V_{max,r6,j}$	24	[µmol/gCDW/s]
$k_{r6,j,Pj}$	0.01	[µmol/gCDW]
$k_{r6,j,EQ}$	1	[µmol/gCDW]
$k_{r6,j,Pex}$	14	[µmol/gCDW]
$V_{max,TAj}$	0 - 100	[µmol/gCDW/s]
$k_{TAj,EQ}$	1	[µmol/gCDW]
$k_{TAj,Aj}$	2	[µmol/gCDW]
$k_{TAj,Aex}$	2	[µmol/gCDW]
$V_{max,TBj}$	0 - 100	[µmol/gCDW/s]
$k_{TBj,EQ}$	1	[µmol/gCDW]
$k_{TBj,Bj}$	2	[µmol/gCDW]
$k_{TBj,Bex}$	2	[µmol/gCDW]
$V_{max,TCj}$	0 - 100	[µmol/gCDW/s]
$k_{TCj,Cj}$	2	[µmol/gCDW]
$k_{TCj,EQ}$	1	[µmol/gCDW]
$k_{TCj,Cex}$	2	[µmol/gCDW]
$V_{max,TZj}$	0 - 100	[µmol/gCDW/s]
$k_{TZj,Zj}$	2	[µmol/gCDW]
$k_{TZj,EQ}$	1	[µmol/gCDW]
$k_{TZj,Zex}$	2	[µmol/gCDW]

Simulate exchange

To simulate the exchange of B between strains as in figure just set

Parameter	Value	Unit of measurement
$V_{max,r1,2}$	0	[µmol/gCDW/s]
$E_{4,j}$	0	[µmol/gCDW]
$V_{max,TB1}$	100	[µmol/gCDW/s]



$V_{max,TB2}$	100	[µmol/gCDW/s]