Kinetic modelling

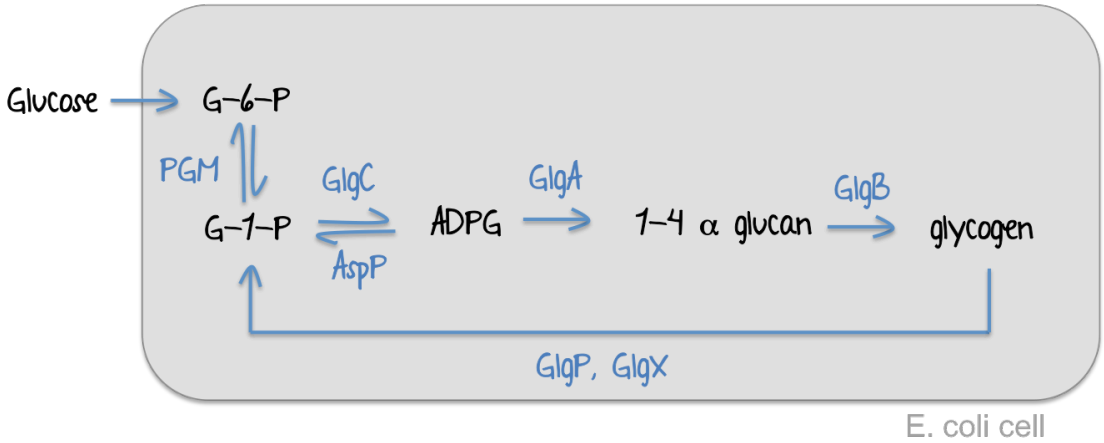
Assumptions: We generated a deterministic model taking into consideration the following assumptions:

- All enzyme concentrations are constant and similar. We fixed the enzyme concentrations to 1x10-5 mmol/mL
- Glucose is available in excess.
- Reactions follow simple reversible or irreversible Michaelis-Menten kinetics.
- There is no additional flux of substrates after the beginning of the simulation.
- The intracellular metabolite concentrations (ATP, AMP, ADP and PPi) are constant. They are all set to 1x10-5 mmol/mL.
- Only competitive inhibition by the product occurs. For simplicity, other external inhibitors are not considered in the model.

Enzyme kinetic rates

Enzyme	Km (mmol/mL)	Reference
Pgm(G1P)	2.9x10-4	(1)
Pgm(G6P)	5.6x10-6	(1)
GlgC(ADPG)	4x10-5	(2)
GlgC(ATP)	3.2x10-4	(2)
GlgA	3.5x10-5	(3)
GlgB(Glucan1-4)	1.42x10-5	(4)
GlgX (Glycogen)	1x10-6	-not found-
GlgP (Glycogen)	1x10-6	-not found-

Glycogen Pathway (5)

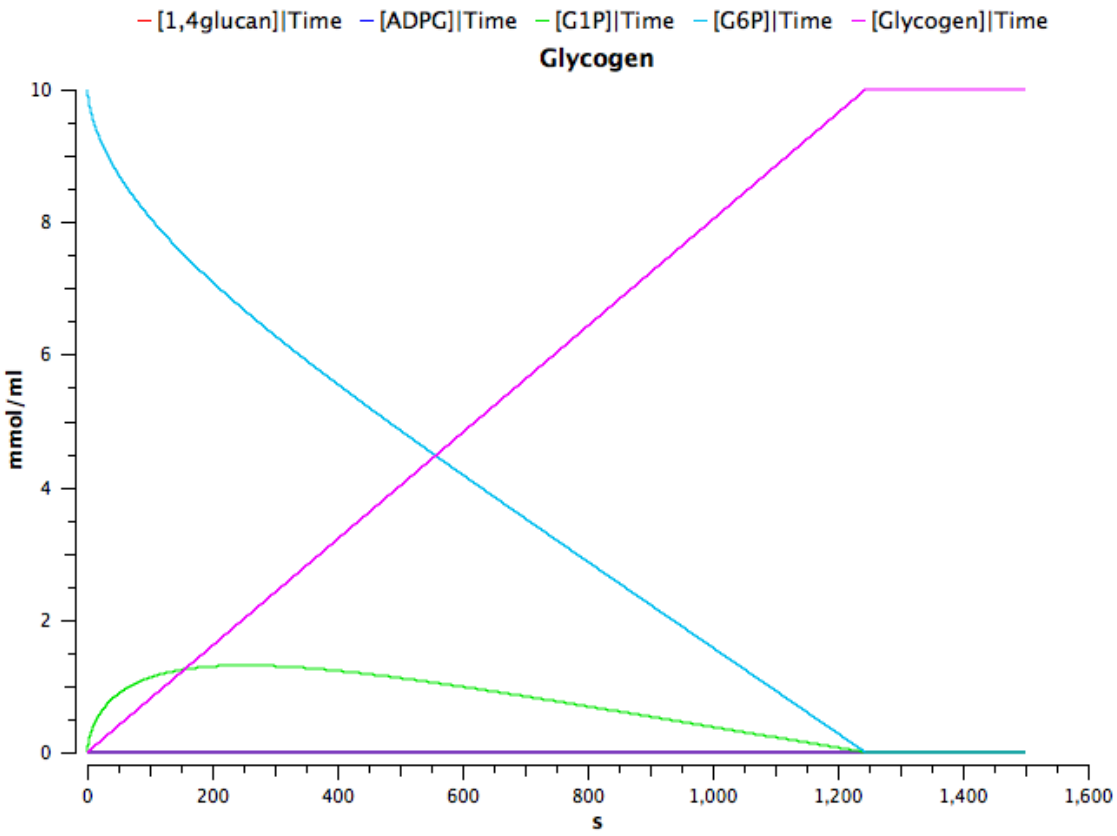


GlgB catalyzes 2 consecutive reactions. First, it cleaves an alpha 1,4 glycosidic linkage in a 1,4-alpha-D-glucan to form a non-reducing-end oligosaccharide chain that is transferred to a C-6 hydroxyl group of the same or another alpha-1,4-D-glucan.(Preiss, J. 2009. Glycogen Biosynthesis.) GlgX and GlgP were considered together as the action of both enzymes is required to get debranching of glycogen.

2 substrate irreversible reaction: Vmax*substrateA*substrateB/(KmB*substrateA* + *kmA*substrateB + substrateA*substrateB)

All the reactions of the pathway are highly efficient, as all the initial glucose-6-P converted to glucose-1-P and ADP-glucose is used in the production of glycogen. Part of the glucose-1-P is recovered due to the GlgX debranching activity.

We run our model for 2500 seconds and collect the data in intevals of 0.05 seconds starting with a concentration of 10 mmol/mL of Glucose-6-P (G6P). After the time course, the majority of the starting glucose has been used to produce glycogen and only a small part of the glucose stays unbranched.


[1,4glucan]|Time
[ADPG]|Time
[G1P]|Time
[G6P]|Time
[Glycogen]|Time
Glycogen
mmol/ml
10
8
6
4
2
0
0
200
400
600
800
1,000
1,200
1,400
1,600
s

Differential equations

$$\frac{\mathrm{d}([\mathrm{G6P}])}{\mathrm{d}t} = -\left(\frac{\frac{\mathrm{Vf}_{(\mathrm{Pgm})}\cdot[\mathrm{G6P}]}{\mathrm{Kms}_{(\mathrm{Pgm})}} - \frac{\mathrm{Vr}_{(\mathrm{Pgm})}\cdot[\mathrm{G1P}]}{\mathrm{Kmp}_{(\mathrm{Pgm})}}}{1+\frac{[\mathrm{G6P}]}{\mathrm{Kms}_{(\mathrm{Pgm})}}+\frac{[\mathrm{G1P}]}{\mathrm{Kmp}_{(\mathrm{Pgm})}}}\right)$$

$$\frac{\mathrm{d}([\mathrm{G1P}])}{\mathrm{d}t} = +\left(\frac{\frac{\mathrm{Vf}_{(\mathrm{Pgm})}\cdot[\mathrm{G6P}]}{\mathrm{Kms}_{(\mathrm{Pgm})}} - \frac{\mathrm{Vr}_{(\mathrm{Pgm})}\cdot[\mathrm{G1P}]}{\mathrm{Kmp}_{(\mathrm{Pgm})}}}{1+\frac{[\mathrm{G6P}]}{\mathrm{Kms}_{(\mathrm{Pgm})}}+\frac{[\mathrm{G1P}]}{\mathrm{Kmp}_{(\mathrm{Pgm})}}}\right) - \left(\frac{\mathrm{Vmax}_{(\mathrm{GlgC})}\cdot[\mathrm{G1P}]\cdot[\mathrm{ATP}]}{\mathrm{KmB}_{(\mathrm{GlgC})}\cdot\mathrm{KmA}_{(\mathrm{GlgC})}+\mathrm{KmB}_{(\mathrm{GlgC})}\cdot[\mathrm{G1P}]+\mathrm{KmA}_{(\mathrm{GlgC})}\cdot[\mathrm{ATP}]+[\mathrm{G1P}]\cdot[\mathrm{ATP}]}\right) + \left(\frac{V_{(\mathrm{GlgX-GlgP})}\,[\mathrm{Glycogen}]}{\mathrm{Km}_{(\mathrm{GlgX-GlgP})}+[\mathrm{Glycogen}]}\right) + \left(\frac{V_{(\mathrm{AspP})}\cdot[\mathrm{ADPG}]}{\mathrm{Km}_{(\mathrm{AspP})}+[\mathrm{ADPG}]}\right)$$

$$\frac{\mathrm{d}([\mathrm{ADPG}])}{\mathrm{d}t} = -\left(\frac{V_{(\mathrm{GlgA})}\cdot[\mathrm{ADPG}]}{\mathrm{Km}_{(\mathrm{GlgA})}+[\mathrm{ADPG}]}\right) + \left(\frac{\mathrm{Vmax}_{(\mathrm{GlgC})}\cdot[\mathrm{G1P}]\cdot[\mathrm{ATP}]}{\mathrm{KmB}_{(\mathrm{GlgC})}\cdot\mathrm{KmA}_{(\mathrm{GlgC})}+\mathrm{KmB}_{(\mathrm{GlgC})}\cdot[\mathrm{G1P}]+\mathrm{KmA}_{(\mathrm{GlgC})}\cdot[\mathrm{ATP}]+[\mathrm{G1P}]\cdot[\mathrm{ATP}]}\right) - \left(\frac{V_{(\mathrm{AspP})}\cdot[\mathrm{ADPG}]}{\mathrm{Km}_{(\mathrm{AspP})}+[\mathrm{ADPG}]}\right)$$

$$\frac{\mathrm{d}([1,4\mathrm{glucan}])}{\mathrm{d}t} = +\left(\frac{V_{(\mathrm{GlgA})}\cdot[\mathrm{ADPG}]}{\mathrm{Km}_{(\mathrm{GlgA})}+[\mathrm{ADPG}]}\right) - \left(\frac{V_{(\mathrm{GlgB})}\cdot[1,4\mathrm{glucan}]}{\mathrm{Km}_{(\mathrm{GlgB})}+[1,4\mathrm{glucan}]}\right)$$

$$\frac{\mathrm{d}([\mathrm{Glycogen}])}{\mathrm{d}t} = +\left(\frac{V_{(\mathrm{GlgB})}\cdot[1,4\mathrm{glucan}]}{\mathrm{Km}_{(\mathrm{GlgB})}+[1,4\mathrm{glucan}]}\right) - \left(\frac{V_{(\mathrm{GlgX-GlgP})}\cdot[\mathrm{Glycogen}]}{\mathrm{Km}_{(\mathrm{GlgX-GlgP})}+[\mathrm{Glycogen}]}\right)$$

References

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5. Wilson WA, Roach PJ, Montero M, Baroja-Fernández E, Muñoz FJ, Eydallin G, Viale AM, Pozueta-Romero J: Regulation of glycogen metabolism in yeast and bacteria. FEMS Microbiol Rev 2010, 34:952–85.