CHEME 5999: Modeling *in vitro* glycosylation on-chip

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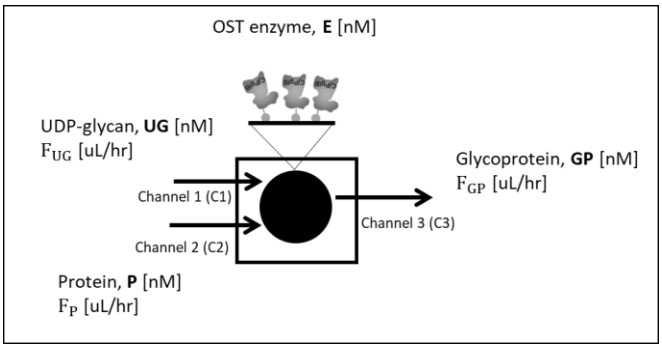
MODEL SIMULATION OF SYSTEM FOR ON-CHIP PROTEIN GLYCOSYLATION.



SUMMARY OF PARAMETERS GENERATED FROM SIMULATIONS

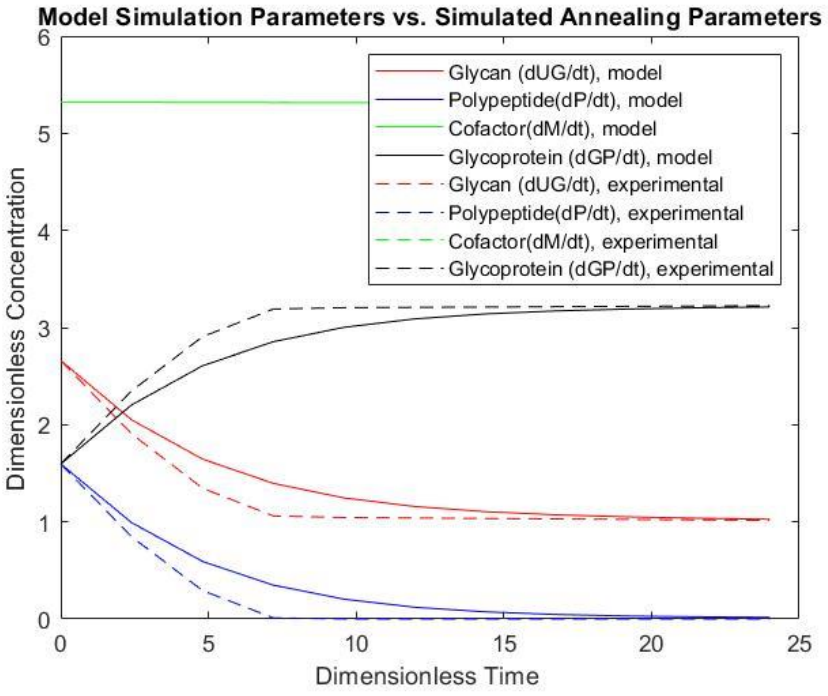
Parameters	Model simulation	Real parameters[1]	Simulated Annealing	Experimental Design
K_{M1}	1.02	4.58	1.4621	9.6746
K_{M2}	2* K_{M1}	0.06	1.7047	0.073039
k_{cat}	3600*1.5	5912.2	$2.1988*10^5$	$2.2741*10^5$
n	4	8.8	3.0326	3.926

[1] Gerber, S., et. al. (2013). *Journal of biological chemistry*, *288*(13), 8849-8861.

1. Model simulation vs. experimental data

Protocol: Ran *P1_experimental_model.m* to generate the graph.

Results:



2. Model simulation with learned parameters

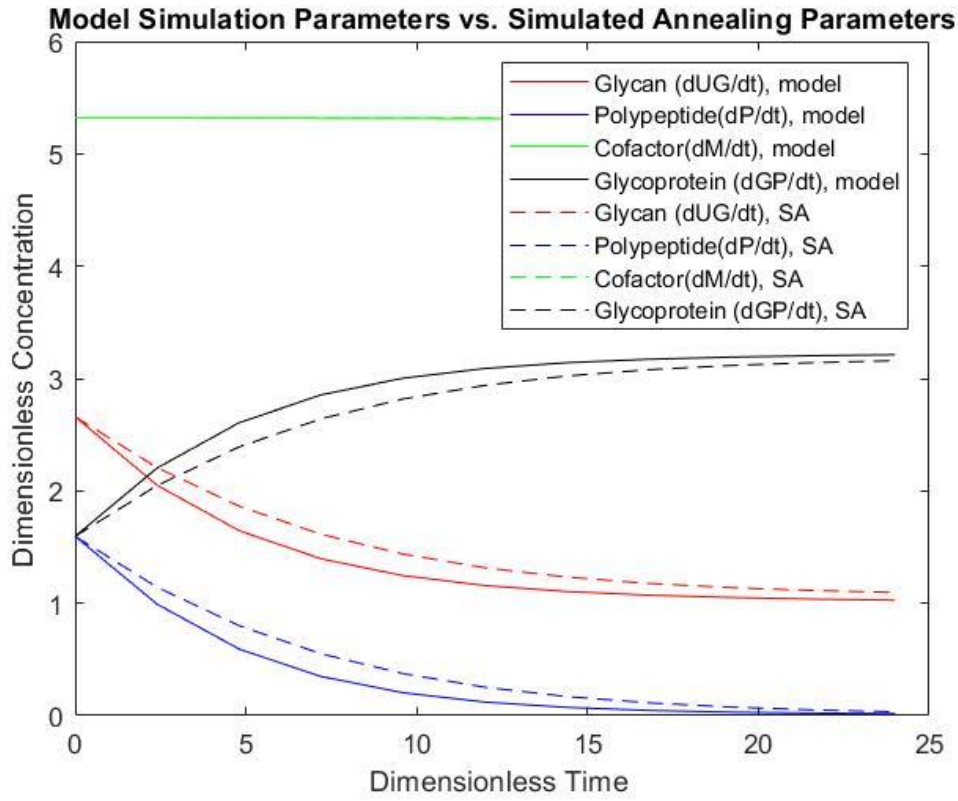
Protocol:

- Ran *P2a_Simulated_annealing_to_generate_parameters.m* to generate parameters in the Command Window, as shown below.

	kcat	Km1	Km2	n
Actual values	5400	1.02	2.04	4
simulated annealing values	2.1988e+05	1.4621	1.7047	3.0326

- Copied these parameters into *P2b_Model_using_simulated_annealing_parameters.m* for the following values: n_SA, kcat_SA, Km1_SA, and Km2_SA. Ran the code to generate the graph.

Results:

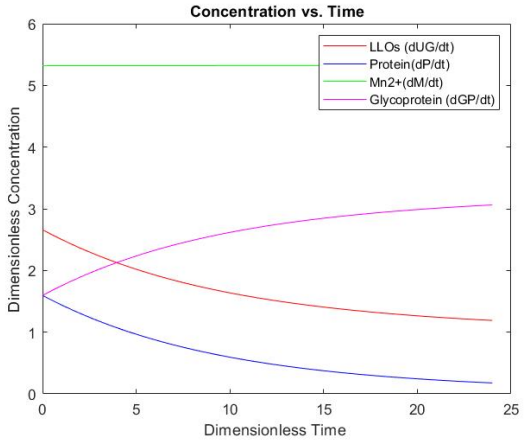


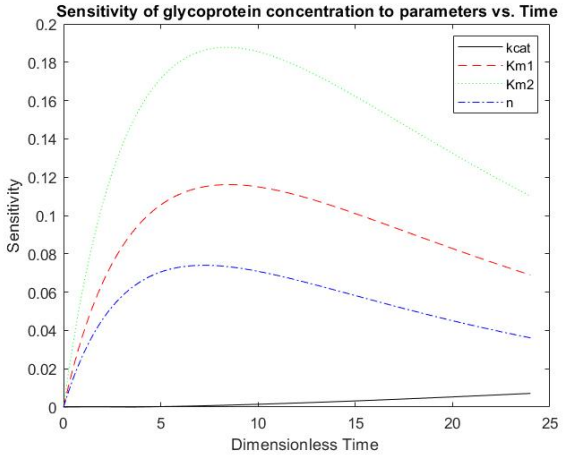
3. Experimental design approach

Protocol:

- Ran *P3_Sensitivity_analysis_of_parameters.m* to graph sensitivity of glycoprotein concentration to parameters over time.
- Decreased enzyme concentration from initial conditions in experiment 1. Graphed new results by running *P3_Sensitivity_EXP1.m*.
- Increased enzyme concentration from initial conditions in experiment 2. Graphed new results by running *P3_Sensitivity_EXP1.m*.
- Ran *P3a_Sensitivity_analysis_of_parameters.m* to generate graph of glycoprotein concentration sensitivity to parameter changes using initial conditions.

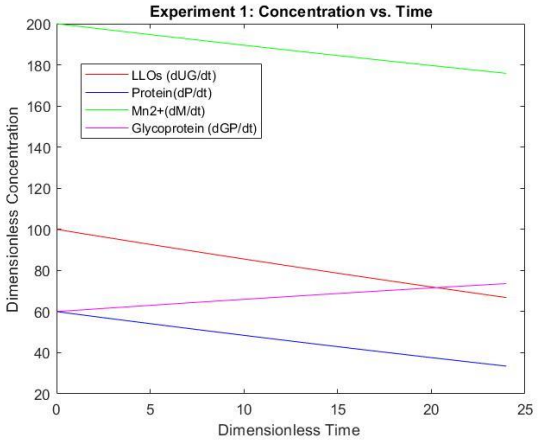
INITIAL CONDITIONS UNCHANGED FROM PREVIOUS SIMULATIONS.

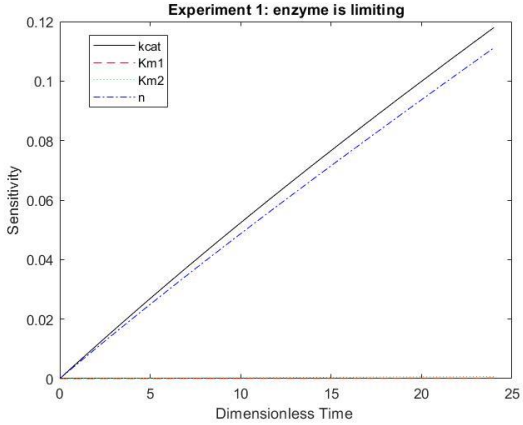




- Ran *P3b_Sensitivity_EXP1.m* to generate graph of glycoprotein concentration sensitivity to parameter changes with the enzyme as the limiting reagent.

EXPERIMENT 1: INITIAL CONDITIONS WITH ENZYME AS LIMITING REACTANT.



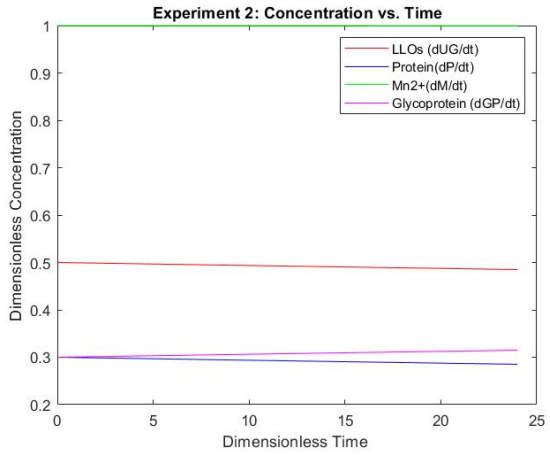


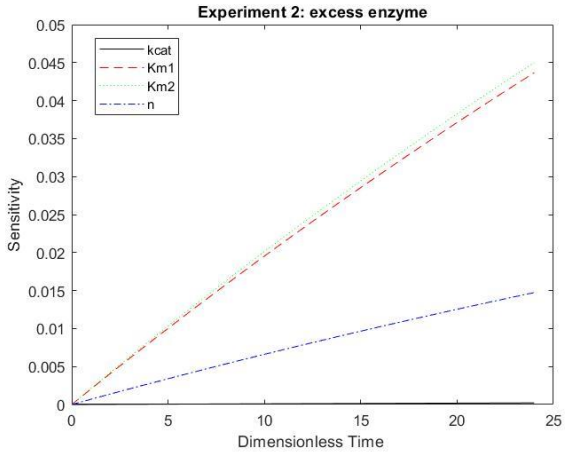
- Because sensitivity was highest at time=24, new initial conditions and concentrations at this timepoint were plugged into *P3c_EXP1_conditions_simulated_annealing.m* and simulated annealing was used to determine k_{cat} and n values.

	kcat	Km1	Km2	n
Actual values	5400	1.02	2.04	4
simulated annealing values	2.2741e+05	0.010147	0.039819	3.926

- Ran *P3d_Sensitivity_EXP2.m* to generate graph of glycoprotein concentration sensitivity to parameter changes with the enzyme in excess.

EXPERIMENT 2: INITIAL CONDITIONS WITH ENZYME IN EXCESS.



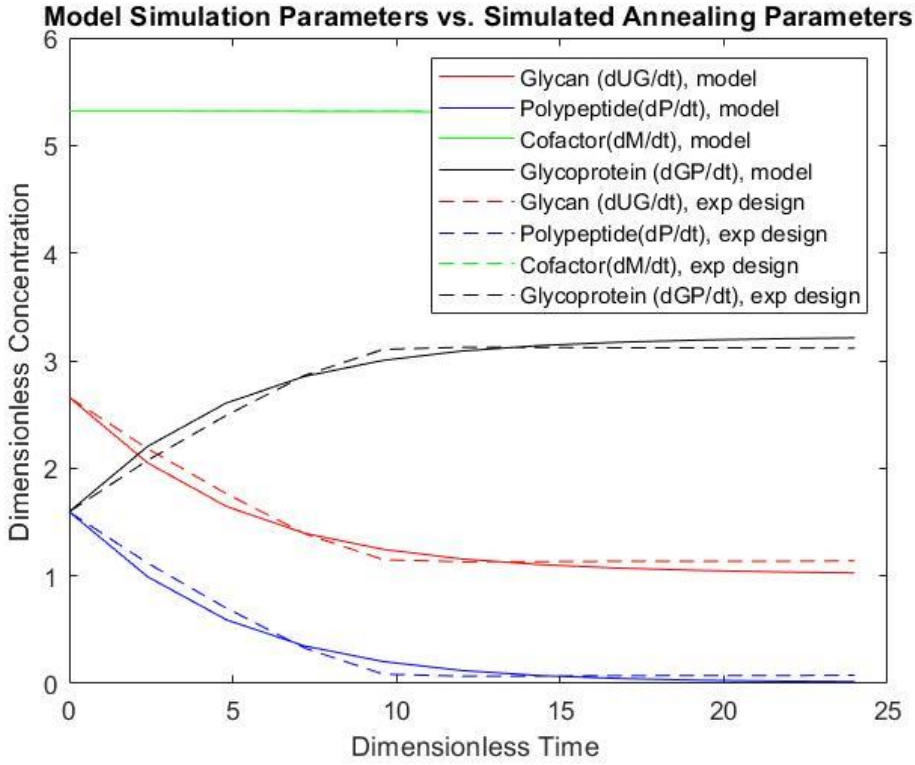


- Because sensitivity was highest at time=24, new initial conditions and concentrations at this timepoint were plugged into *P3e_EXP2_conditions_simulated_annealing.m*. The values determined previously for k_{cat} and n were fixed and simulated annealing was used to determine K_{M1} and K_{M2} values.

	Km1	Km2
Actual values	1.02	2.04
simulated annealing values	9.6746	-0.073039

- Plugged experimental design parameters determined in this section into *P3f_Model_using_experimental_design_parameters.m* to generate graph.

Results:


Model Simulation Parameters vs. Simulated Annealing Parameters
Glycan (dUG/dt), model
Polypeptide(dP/dt), model
Cofactor(dM/dt), model
Glycoprotein (dGP/dt), model
Glycan (dUG/dt), exp design
Polypeptide(dP/dt), exp design
Cofactor(dM/dt), exp design
Glycoprotein (dGP/dt), exp design
Dimensionless Concentration
Dimensionless Time
0
1
2
3
4
5
6
0
5
10
15
20
25

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