

Logbook

Our group worked on modelling the administration of NeuroTone and its interactions with the gut. We used two approaches: structural and dynamic.

Description of modelling

Notebook

Week 1: 22/06

This week was spent on reading papers on dynamic and structural modelling. Research into programs that may help or allow modelling to take place.

Week 2: 29/06

Over this week we were working to reproduce the results of some of the papers we read the week before.

Attempting to code a system of ODE's in MATLAB.

Week 3: 06/07

Software setup for COBRAPy, a python-based tool for structural modelling, and experimenting with parameters changes in the dynamic model. Learning the required skills to operate a biological model inside the python environment of COBRAPy.

Week 4: 13/07

COBRAPy guide. Fixing issues relating to the ability to load xml files as cobra models.

Installing and understanding COBRAPy before learning more Python and loading the 2019 model of *C.sporogeneses* to later be worked on as part of our modelling project.

Week 5: 20/07

COBRAPy guide and *C. sporogenes* model with errors exercise.

The *C. sporogenes* model provided by Nottingham's 2019 iGEM team has no metabolite formulas, so to allow for mass balancing to happen. The metabolite formulas for all 157 metabolites must be added, which is what we started work on for this week.

Got back to the last year's model since we are working with the same organism.

Week 6: 27/07

Looking over saw-tooth functions for modelling the level of glucose in the body.

All metabolite formulas have now been added to the model to enable mass balancing which will enable the model to better determine the feasibility of reactions.

Work in checking reactions that are not mass balanced for errors, and then if possible, correcting those errors.

Training in Elementary Mode Analysis took place this week for use in the future to help identify which pathway was most beneficial for our goal of DBHB production.

Week 7: 03/08

Drew the pathway we are using in Adobe Illustrator. Looking for functions to describe changes of glucose in the body. Worked on influx and outflux terms for the dynamic model of zeroth and first order.

Mass Balance work

Week 8: 10/08

More experimentation with influx and outflux, the step function describing the inflow of glucose was written.

Mass Balance work

Week 9: 17/08

Worked on incorporating the step function into the big dynamic model, which came with a lot of unexpected issues.

Finished mass balancing all possible reactions with the information available

Major progress this week with the two possible DBHB producing pathways being added to two separate copies of the base *C.sporogenes* model to allow for comparison between the two. These pathways were then loaded in Cell Net Analyzer (<https://www2.mpi-magdeburg.mpg.de/projects/cna/cna.html>) to use the elementary mode analysis function it offers.

Week 10: 24/08

Finally managed to have the step function work with the model and found appropriate parameters for it as well. Additionally, adjusted the Biomass outflow parameter so that it tends to 0, which means that the bacterium won't stay in the gut. Started learning LaTeX.

The biomass equation in the structural model was adjusted to better represent a real model of *C.sporogenes* and improve the accuracy of the report we were writing.

Week 11: 31/08

This week was spent on writing up initial findings to the modelling report in LaTeX.

Elementary mode analysis and some flux calculations in COBRApy have yielded the information we need to decide which pathway to choose as our focus for the remainder of the project. This allows for the kinetic model to be finalised, enabling an administration strategy to be developed.

A problem with the kinetic model arose, where the mutant switch was not working.

Week 12: 7/09

This week was spent on writing up findings to the modelling report and applying changes from feedback, as well as extra sections of analysis.

A problem with the switch in the kinetic model was fixed which allowed to investigate the strategy of administration.

Week 13: 14/09

The modelling report has now been finalised and proof read.