My project has been looking at how to find elementary flux modes (EFMs) in large metabolic networks. The number of EFMs in a metabolic network increases exponentially with the size of the network. The classic way of generating these has been through the double description method. However, as the size of the network grows, this method must check an increasingly large number of combinations. In addition, there is no way to specify which EFMs should be extracted. When using this method, the only way to find EFMs that have certain properties is to extract all of them then throw away those that are not wanted.

For my project I have been looking at using linear programming to generate only the EFMs that satisfy certain constraints. Currently, these constraints can either be ‘this reaction must be included in a forward/reverse direction’ or ‘this reaction must not be included’. A single EFM that satisfies these constraints can be generated quickly using linear programming. This will take the form of a list of reactions to be included and their relative fluxes. An additional solution can be generated by taking any of the reactions included in the previous solution, adding an additional constraint to exclude this reaction (i.e. knock this reaction out), then running the linear programming solver again. By successively knocking out reactions, many EFMs that correspond to the original constraints can be found.

This technique struggles to enumerate all the EFMs that correspond to a particular network. However, enumerating all possible EFMs in a large network is very time consuming and difficult. The aim of this project is to try and extract EFMs in a more ‘intelligent’ manner. By using linear programming with constraints specified beforehand, only the EFMs of interest will be extracted, thereby avoiding the need to explore the entire solution space.

Currently I am working on trying to figure out the best way to choose reaction to knock out and how to determine when the search should be stopped.