Advanced Systems Biology - Modelling the central carbon metabolism of three cancer cells using carbon 13 data

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Ten percent of all colon cancer cases have an activating KRAS mutation. Cases with this kind of mutation do not respond to the usual drug treatment. Interestingly, KRAS mutated colon cancer cells have an accumulation of lactate, which would be an option as treatment target. To understand the reason for the accumulation of lactate I am comparing a KRAS mutated colon cancer cell line with two other common colon cancer cell lines to investigate the following question:

Can the difference of the central carbon metabolism in the three different colon cancer cell lines be understood only by changes of enzyme concentrations?

To answer this question, my project is about building a kinetic model of the central carbon metabolism for the three colon cancer cell lines. The comparison of the three models and exchanging the enzyme concentrations in between models will give a clue about the extent of the effect of the enzyme concentrations alone. Obviously, the identifiability of the parameter in each model affects majorly the outcome of this project, therefore it has priority.

To achieve these goals I use flux data, metabolomics data, carbon 13 metabolomics data, and proteomics data. The flux and metabolomics data give constraints to my kinetics, whereas the carbon 13 metabolomics data, which shows the change of carbon 12 to carbon 13 metabolites and therefore the dynamics of metabolites over time, defines the kinetics.

Finally, either three separate models or one combined model will be analyzed to see the differences in their behavior, and how the differences in behavior arise. The model is then used to suggest the best targets to influence the accumulation of metabolites.