About sensitivity analysis (MCA)

I have based my thoughts on http://www.math.uwaterloo.ca/ bingalls/MMSB/Notes.pdf.

In MCA (Metabolic control analysis) the sensitivity of reaction is observed through two coefficients: *concentration control coefficient*,

$$C_{e_j}^{S_i} = \frac{e_j}{S_i}\frac{dS_i}{de_j},$$

where S_i is the steady state concentration of species i, and e_j is the concentration of enzyme j. *Flux control coefficients* are defined by

$$C_{e_j}^{J_k} = \frac{e_j}{J_k}\frac{dJ_k}{de_j},$$

where J_k is the flux through reaction k (i.e. the steady-state reaction rate k).

In this case we need to take the enzyme concentrations into account as can be seen from above formulas. We can build onto our existing very simple model and add enzyme concentrations to every reaction rate and assume the enzyme reaction occurs instantaneously compared to our time scale. (Then we'll have $k_i e_i[\textit{some other concentrations}]$.)

Now to obtain the steady state concentrations of our species in the reaction we need to set the differential equations to zero. I used notation that puts a as a first concentration, b as the second and so on, until the second last is g and then p for propane. The obtained concentrations are as follows. Notice that e_i for multiple i are not the same than $e(t)$.

$$b(t) = \frac{k_1 e_1 a^2}{k_2[NADPH]} \tag{1}$$

$$c(t) = \frac{k_2 e_2 b(t)[NADPH]}{k_3 e_3} \tag{2}$$

$$d(t) = \frac{k_3 e_3 c(t)}{k_4 e_4[NADH]} \tag{3}$$

$$e(t) = \frac{k_4 e_4 d(t)[NADH]}{k_5 e_5 [H2O]} \tag{4}$$

$$f(t) = \frac{k_5 e_5 e(t)[H2O]}{k_6 e_6 [ATP][H2O][NADPH]} \tag{5}$$

$$g(t) = \frac{k_6 e_6 f(t)[ATP][H2O][NADPH]}{k_7 e_7 [H]^2[O2][NADPH]^2} \tag{6}$$

Also, if we add a rate to propane to go away with parameter k_8, we get further from the last differential equation:

$$p(t) = \frac{k_7 e_7 g(t)[H]^2[O2][NADPH]^2}{k_8}.$$

Thus, all the steady state concentrations depend on the concentration of the first species, a, which we assume constant.

"Chains consisting of irreversible reactions display a simple behaviour: the first reaction has a fixed rate and so dictates the pathway flux. In this case, all of the reactions except the first have flux control coefficients of zero, while the first reaction—which exerts total control over the pathway flux—has a coefficient of one."

So the flux of the first reaction is one, others are zero. I don't see anything interesting arising from this. More interesting case would be if some of our reactions were reversible or if we had some branches. The latter is unlikely, but the first is actually quite probable. The question is where?

Another approach we tried was stoichiometric analysis. There we form matrix N so, that i, j-th component corresponds to the number of molecules of species i involved in reaction j. Now if we arrange the reaction rates as a column vector $\mathbf{v}$, then for the steady state holds $N\mathbf{v} = 0$. (This comes from the formula

$$\frac{d}{dt}s(t) = N\mathbf{v}.$$

However, the problem in this approach is that our matrix N is bad, and the only solution is $\mathbf{v} = \mathbf{0}$.

The conclusion is that the sensitivity analysis based on our knowledge and these simplified reactions is not useful. We need either measured data, or some more information of our reactions.