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A missing link in the network, can we ever find it?

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Flavonoids are plant secondary metabolites and as such an integral part of the human diet. There is increasing evidence that these polyphenols may explain the beneficial effects of a diet rich in fruits and vegetables on the prevention of several chronic and age-related diseases. To control the amount that these micronutrients are present in our daily food, we need to understand the molecular pathways that lead to the accumulation of these compounds. In our earlier work on flavonoid pathway inference [1-3], we have found ourselves in what seems to be a typical situation in systems biology, where the molecular interactions are fairly well known, the kinetic parameters are completely unknown and where the network topology is almost known [4]. This means that we have only a few missing links in our network structure. There is an abundant literature that describe methods for finding such missing links accompanied with results, when these methods are a pplied to real data. Some of them are top-down and very abstract [5], others are more context-dependent relying on the existing knowledge on the features of the specific system dynamics [6]. Here we want to turn the problem setting upside down and ask how dramatic can the effect of a missing link be to the inference results. When the network is robust against structural changes in topology, the effect of such missing links on the network performance can be limited [7]. We focus here on dynamic networks and consider three different ordinary differential equation-(ODE) based models: a linear model, a non-linear Michaelis-Menten-type model and a complex non-linear model for gene regulatory networks as in the DREAM2012 challenge [8]. We investigated the discrepancy between the true and inferred network as a function of number of edges removed and their average connectivity.
To measure the degree of failure, we look at the percentage of lost/red undant edges as well as the errors in the inferred parameters. We believe that our findings can be instructive and useful for the biological network inference practitioners.

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