Development of a Bayesian-Based Framework for Identification of Most Probable Biochemical Reaction Network

Andrea L. Knorr and Ranjan Srivastava

When postulating the topology of a biochemical reaction network, multiple network architectures may be feasible. Identification of the correct network is not a trivial task. Using the technique of model discrimination (Stewart, Shon et al. 1998) it is possible to determine which network is most probable. Model discrimination is a Bayesian-based method in which the most likely network is determined from a pool of networks where experimental data for the system of interest is given. A framework is developed for carrying out model discrimination for an arbitrary number of biochemical reaction networks in order to identify the most probable one. Stochastic or deterministic reaction networks may be compared.

The framework is used to evaluate different postulated reaction networks of HIV-1 viral dynamics, as well as different postulated reaction networks of diabetes physiology. Each of the HIV-1 reaction networks accounts for some combination of infected cells, uninfected cells, free virus, and/or immune response. Interestingly, due to the high variance in the viral levels, any model incorporating free virus as a variable is heavily penalized. For the diabetes models, each of the reaction networks evaluated posits the existence of a hypothetical compartment to account for the efficiency of insulin usage. After identifying the most probable reaction network, it is possible to determine which prediction of insulin efficiency is most likely. Note that the insulin efficiency is virtually impossible to measure under normal circumstances.

Given these results, it can be seen that the developed framework may be used to identify likely biochemical reaction networks, as well as elucidate other qualities of networks based on which network is identified and which is ruled out.

References

Stewart, W. E., Y. Shon, et al. (1998). "Discrimination and Goodness of Fit of Multiresponse Mechanistic Models." AIChE Journal 44(6): 1404-1412.