Monotonicity and Almost-Monotonicity in Biological Systems

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A dynamical system is a type of continuous mathematical model which is frequently used to describe the behavior of physical systems over time. Dynamical systems are powerful modeling tools, and they have been successfully used for many applications, but they are conspicuously hard to study, especially when there is a high number of variables involved. One increasingly important application of dynamical systems modeling is the description of molecular biological processes at the cell level. It allows the modeler to incorporate a large amount of information about the process, such as what proteins influence which genes and at what rates these influences take place. A drawback for the modeler is precisely the fact that often there is a very large number of variables (proteins, genes, etc) involved. On the other hand, and for all the apparent complexity of the models, the behavior of the solutions over time is often relatively simple: the convergence of all solutions towards one or two points, or a stable oscillatory behavior, seem the rule rather than the exception. Moreover, the direct influence of one variable on another is often consistent: if a protein influences the production of a given gene, say, it often does so in order to consistently inhibit it or to consistently promote it.

A concept that allows to exploit these characteristics is that of a monotone dynamical system. In its simplest form, a monotone system is one in which all the influences among the variables are promoting, and no inhibitory influences are observed. But many systems with inhibitory reactions can also be monotone, as long as the indirect effect from any given variable to another is consistent along any path in the network. A necessary condition for a system to be monotone is for it to have consistent direct influences, which is commonly satisfied for molecular biological systems as described above. Also, monotone systems have a very stable behavior over time. By considering monotone systems with inputs and outputs and introducing a negative feedback, we were able to describe the behavior of systems that are not monotone ('almost-monotone') in terms of that of monotone systems, and to give sufficient conditions for such a system to converge globally towards

an equilibrium. This approach can potentially be used for a formal study of complex, non-monotone, large scale dynamical systems using techniques from monotone systems theory. We give a simple example of a testosterone dynamics model with delay, and show even in the presence of arbitrary delays all the solutions of the system converge.