arXiv:q-bio/0512046v1 [q-bio.MN] 28 Dec 2005

Uniqueness of steady states for a certain chemical reaction

Liming Wang and Eduardo Sontag
Department of Mathematics, Rutgers University

In [1], Samoilov, Plyasunov, and Arkin provide an example of a chemical reaction whose full stochastic (Master Equation) model exhibits bistable behavior, but for which the deterministic (mean field) version has a unique steady state.

The reaction that they provide consists of an enzymatic futile mechanism driven by a second reaction which induces "deterministic noise" on the concentration of the forward enzyme (through a somewhat artificial activation and deactivation of this enzyme). The model is as follows:

$$N + N \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} N + E$$

$$N \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} E$$

$$S + E \underset{k_{-3}}{\overset{k_3}{\rightleftarrows}} C_1 \overset{k_4}{\longrightarrow} P + E$$

$$P + F \underset{k_{-5}}{\overset{k_5}{\rightleftarrows}} C_2 \overset{k_6}{\longrightarrow} S + F\,.$$

Actually, [1] does not prove mathematically that this reaction's deterministic model has a single-steady state property, but shows numerically that, for a particular value of the kinetic constants k_i, a unique steady state (subject to stoichiometric constraints) exists. In this short note, we provide a proof of uniqueness valid for all possible parameter values.

We use lower case letters n, e, s, c_1, p, c_2, f to denote the concentrations of the corresponding chemicals, as functions of t. The differential equations are, then, as follows:

$$\begin{aligned}
n' &= -k_1 n^2 + k_{-1} ne - k_2 n + k_{-2} e \\
e' &= -k_3 se + k_{-3} c_1 + k_4 c_1 + k_1 n^2 - k_{-1} ne + k_2 n - k_{-2} e \\
s' &= -k_3 se + k_{-3} c_1 + k_6 c_2 \\
c_1' &= k_3 se - k_{-3} c_1 - k_4 c_1 \\
p' &= k_4 c_1 - k_5 pf + k_{-5} c_2 \\
c_2' &= k_5 pf - k_{-5} c_2 - k_6 c_2 \\
f' &= -k_5 pf + k_{-5} c_2 + k_6 c_2\,.
\end{aligned}$$

Observe that we have the following conservation laws:

$$e + n + c_1 \equiv \alpha\,, \quad f + c_2 \equiv \beta\,, \quad s + c_1 + c_2 + p \equiv \gamma\,.$$

Lemma 1. For each positive α, β, γ, there is a unique (positive) steady state, subject to the conservation laws.

Proof. Existence follows from the Brower fixed point theorem, since the reduced system evolves on a compact convex set (intersection of the positive orthant and the affine subspace given by the stoichiometry class).

We now fix one stoichiometry class and prove uniqueness. Let $\bar{n}, \bar{e}, \bar{s}, \bar{c}_1, \bar{p}, \bar{c}_2, \bar{f}$ be any steady state.

From $dn/dt = 0$, we obtain that:

$$\bar{e} = \frac{k_1 \bar{n}^2 + k_2 \bar{n}}{k_{-1}\bar{n} + k_{-2}}\,.$$

From $dc_1/dt = 0$, we have:

$$\bar{s} = \frac{(k_{-3} + k_4)\bar{c}_1}{k_3 \bar{e}}\,.$$

Solving $dc_2/dt = 0$ for p and then substituting $f = \beta - c_2$ gives:

$$\bar{p} = \frac{(k_{-5} + k_6)\bar{c}_2}{k_5(\beta - \bar{c}_2)}\,.$$

Finally, solving $d(p - f)/dt = 0$ with respect to c_2 gives:

$$\bar{c}_2 = \frac{k_4}{k_6}\bar{c}_1\,.$$

The derivative of $\bar{e}$ with respect to $\bar{n}$ is:

$$\frac{k_1 k_{-1}\bar{n}^2 + 2k_1 k_{-2}\bar{n} + k_2 k_{-2}}{(k_{-2} + k_{-1}\bar{n})^2} > 0,$$

and therefore $\bar{e}$ is strictly increasing on $\bar{n}$.

Since $\bar{c}_1 = \alpha - (\bar{e} + \bar{n})$, it follows that $\bar{c}_1$ is strictly decreasing on $\bar{n}$. Therefore $\bar{c}_2$, $\bar{s}$, and $\bar{p}$ are also strictly decreasing on $\bar{n}$.

Let $f(\bar{n}) = \bar{s} + \bar{c}_1 + \bar{c}_2 + \bar{p}$. Then, f is also decreasing function.

Thus, $\bar{n} = f^{-1}(\gamma)$ is uniquely defined, and, since all coordinates are functions of $\bar{n}$, it follows that the steady state is unique, too.

References

[1] M. Samoilov, S. Plyasunov, A.P. Arkin, "Stochastic amplification and signaling in enzymatic futile cycles through noise-induced bistability with oscillations," *Proc Natl Acad Sci USA* **102**(2005): 2310-2315