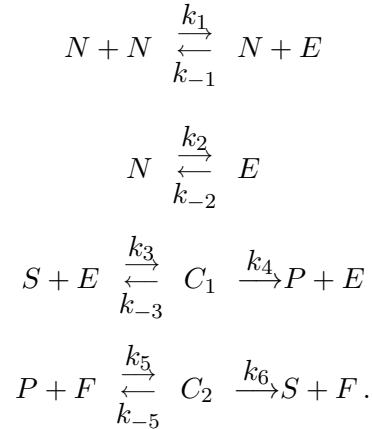


# Uniqueness of steady states for a certain chemical reaction

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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:



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:

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

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  $\alpha, \beta, \gamma$ , there is a unique (positive) steady state, subject to the conservation laws.

*Proof.* Existence follows from the Brouwer 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