

Last Time: $\overline{X}^r \Rightarrow \overline{X}$ where a.s. $\overline{X}$ satisfies the equation:

$$\begin{aligned}\frac{d\overline{X}}{dt} &= \sum_{k=1}^K \tilde{\kappa}_k(\overline{X}(t))^{\nu_k} (\nu'_k - \nu_k) \\ \overline{X}(0) &= \overline{X}_0\end{aligned}$$

where $c^{\nu_k} = \prod_{i=1}^n c_i^{\nu_{ik}}$ for $c \in \mathbb{R}_{\geq 0}^n$. The differential equation above can be rewritten as

$$\begin{aligned}\frac{d\overline{X}}{dt} &= S r(\overline{X}(t)) =: f(\overline{X}(t))\end{aligned}\tag{1}$$

(2)

where the ik entry of the stoichiometric matrix S is $\nu'_{ik} - \nu_{ik}$ and the k^{th} element of the vector $r(\overline{X}(t))$ is $r_k(\overline{X}(t)) = \tilde{\kappa}_k(\overline{X}(t))^{\nu_k}$. Thus, $f(\cdot)$ is nonlinear.

Topics for this time and next time:

(1) Unique equilibria for $\frac{dc}{dt} = f(c), c \in \mathbb{R}_{\geq 0}^n$ (in the setting of a CF-STR=Continuous Flow Stirred Tank Reactor with inflows and outflows for all species).

(2) Equilibria for $\frac{dc}{dt} = f(c), c \in \mathbb{R}_{\geq 0}^n$, where there can be more than one stoichiometric compatibility class and there is a connection to stationary solutions for the original stochastic model.

References for Topic (1):

(i) Craciun & Feinberg: Multiple equilibria in complex chemical reaction networks I. *SIAM J. Appl. Math.*, 65(2005), 1526-1546 (Mass-action kinetics)

(ii) Craciun & Feinberg: Multiple equilibria in complex chemical reaction networks II. (Species-reaction graph)

(iii) Craciun, Helton and Williams: Homotopy methods for counting reaction network equilibria.

(iv) Also see the slides posted on the webpage.

Dynamical System Model:

$$\frac{dc}{dt} = f(c), c \in \mathbb{R}_{\geq 0}^n\tag{3}$$

where $f : \mathbb{R}_{\geq 0}^n \rightarrow \mathbb{R}^n$ is smooth.

Key Condition (DetSign): The determinant of the Jacobian $\frac{\partial f}{\partial c}(\cdot)$ of f is either strictly positive or negative on its domain.

When this condition holds, on the domain we have

$$|\text{degree of } f| = \# \text{ zeros of } f \quad (4)$$

We seek conditions for invariance of the degree as parameters in f are changed continuously.

Consequence of Homotopy Invariance of Degree:

Define $\kappa^\lambda := \lambda \tilde{\kappa} + (1 - \lambda) \tilde{\kappa}$, $\lambda \in [0, 1]$, hence,

$$f_\lambda(c) = f(c, \kappa^\lambda) : \overline{\Omega} \longrightarrow \mathbb{R}^n, c \in \Omega \quad (5)$$

where Ω is a bounded domain in $\mathbb{R}_{>0}^n$.

Conditions to check: (a) For each λ , f_λ has no zeros on $\partial\Omega$; (b) For all $c \in \Omega$, $\det(\frac{\partial f_\lambda}{\partial c}) \neq 0$ for $\lambda = 0, 1$.

If conditions (a) & (b) are satisfied, then

$$\# \text{ of zeros of } f_0 \text{ in } \Omega = \# \text{ of zeros of } f_1 \text{ in } \Omega.$$

Example of Arcak and Sontag (not mass action):

Here Ω is $[0, 1]^3$: $c \in [0, 1]^3$. We can check that there are no equilibria on the boundary and $\det(\frac{\partial f}{\partial c}(c, \tilde{\kappa})) \neq 0$ on $[0, 1]^3$ for all positive $\tilde{\kappa}$. It follows that there is a unique equilibrium for each value of $\tilde{\kappa}$.

CFSTR:

$$\frac{dc}{dt} = f(c) = c_{in} - c + g(c) \quad (6)$$

where $c_{in} \in \mathbb{R}_{>0}^n$, and g is smooth and such that for all $c \in \mathbb{R}_{>0}^n$, such that 1) if $c_j = 0$, then $g_j(c) \geq 0$, for $j \in \{1, 2, \dots, n\}$; 2) $\exists m \in \mathbb{R}_{>0}^n$ s.t. $m \cdot g(c) = 0$ for all $c \in \mathbb{R}_{\geq 0}^n$.

Theorem: For the above system: $\dot{c} = f(c) = c_{in} - c + g(c)$, there are no equilibria on the boundary of $\mathbb{R}_{\geq 0}^n$. And if $\det(\frac{\partial f}{\partial c}) \neq 0$ on $\mathbb{R}_{>0}^n$, there is precisely one equilibrium point in $\mathbb{R}_{>0}^n$.

Proof. Let $f_\lambda(c) := c_{in} - c + \lambda g(c)$, $\lambda \in [0, 1]$. One can readily check due to the presence of inflows and conditions on g that there are no zeros of f_λ on the boundary of $\mathbb{R}_{\geq 0}^n$ for any $\lambda \in [0, 1]$.

We have (DetSign) for $\lambda = 1$, and $\frac{\partial f_0}{\partial c} = -I$ for $\lambda = 0$.

Let $\Omega_{up} = \{c \in \mathbb{R}_{>0}^n : m \cdot c = L\}$ for L large. Then

$$\begin{aligned} \frac{d}{dt}(m \cdot c_\lambda) &= m \cdot \frac{dc_\lambda}{dt} = m \cdot c_{in} - m \cdot c_\lambda \\ &= m \cdot c_{in} - L \text{ on } \Omega_{up} \end{aligned} \quad (7)$$

$$< 0 \text{ for all } L \text{ sufficiently large} \quad (8)$$

Then there are no zeros for f_λ on Ω_{up} for $\lambda \in [0, 1]$.

Thus,

$$\# \text{ of zeros of } f_0 = \# \text{ of zeros of } f_1 = 1 \text{ (when } \Omega \text{ is big enough)} \quad (9)$$

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