Introduction to Mass-Action Kinetics and Chemical Reaction Network Modeling

$\mathbb{Z}$ev Woodstock

May 2016
Nonlinear Dynamics (Math 441) Final Presentation

Outline

- Model Description
  - Applied to one reaction
  - Applied to a reaction network
- Computational Example (Euler's Method)
- Discussion on steady states of reaction networks
- Survey of methods to show multistationarity in CRN's

Definitions & Assumptions

$$2H_2 + O_2 \xrightarrow{r} 2H_2O$$

Definitions: *Species,*

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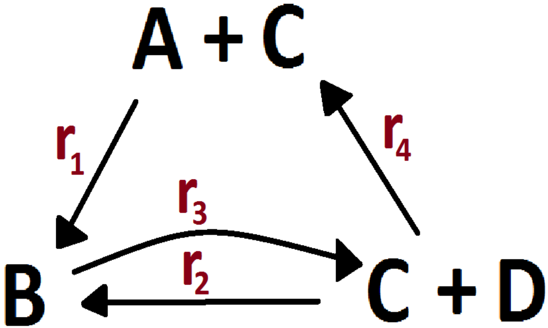
I.V. ODEs: $H_2(0), O_2(0), H_2O(0)$
Where $H_2(t)$, $O_2(t)$, and $H_2O(t)$ are functions of time.

Example: Reaction Network Model



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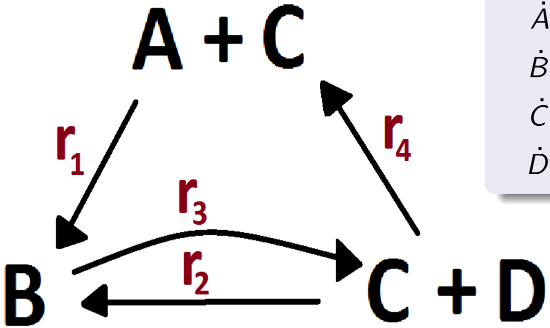

System of ODEs

$$\dot{A} = r_4 CD - r_1 AC$$
$$\dot{B} = r_1 AC + r_2 CD - r_3 B$$
$$\dot{C} = r_3 B - r_1 AC - r_2 CD$$
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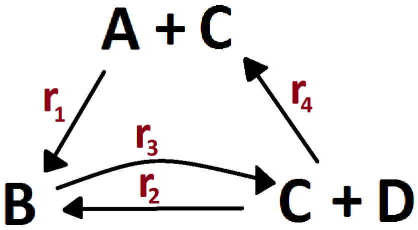
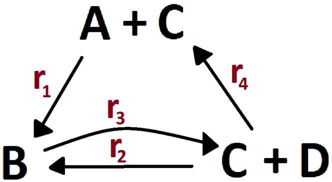


Linearization

We can re-express the ODEs in a linear system of a **Stoichiometric Matrix**, Γ, and a **Reaction vector**, ρ.

$$\begin{aligned} \dot{A} &= r_4 CD - r_1 AC \\ \dot{B} &= r_1 AC + r_2 CD - r_3 B \\ \dot{C} &= r_3 B - r_1 AC - r_2 CD \\ \dot{D} &= r_3 B - r_4 CD - r_2 CD \end{aligned} = \begin{pmatrix} -1 & 0 & 0 & 1 \\ 1 & 1 & -1 & 0 \\ -1 & -1 & 1 & 0 \\ 0 & -1 & 1 & -1 \end{pmatrix} \cdot \begin{pmatrix} r_1 AC \\ r_2 CD \\ r_3 B \\ r_4 CD \end{pmatrix}$$



Linearization

This is called the **Mass-Action Kinetics System**

$$\dot{\bar{x}} = \begin{pmatrix} -1 & 0 & 0 & 1 \\ 1 & 1 & -1 & 0 \\ -1 & -1 & 1 & 0 \\ 0 & -1 & 1 & -1 \end{pmatrix} \cdot \begin{pmatrix} r_1 AC \\ r_2 CD \\ r_3 B \\ r_4 CD \end{pmatrix} = \Gamma \cdot \rho(\bar{r}, \bar{x})$$

$\bar{x}$ is the vector of species **concentrations**, $\bar{r}$ is the vector of **reaction rates**

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- **Q:** Which networks are multistationary?

A CRN is **multistationary** if there exist reaction rates $\bar{r}$ and distinct non-trivial steady states $\bar{x}_1$ and $\bar{x}_2$ such that

$$\Gamma \cdot \rho(\bar{r}, \bar{x}_1) = \Gamma \cdot \rho(\bar{r}, \bar{x}_2) = \bar{0}$$

Example: Reaction Network Modeling

Euler's Method Simulations for $r_i = 1$

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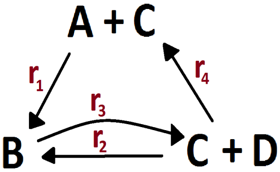
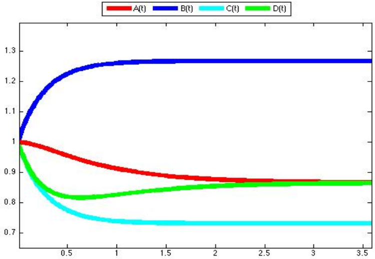
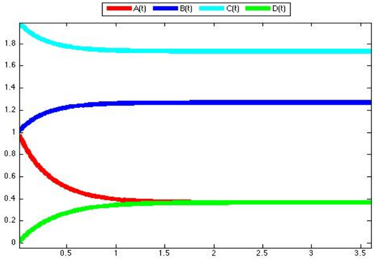


Initial Conditions: $[1, 1, 1, 1]$. $[1, 1, 2, 0]$





Determinant Optimization Method (Craciun & Feinberg)

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MULTIPLE EQUILIBRIA IN COMPLEX CHEMICAL REACTION NETWORKS: I. THE INJECTIVITY PROPERTY*

GHEORGHE CRACIUN† AND MARTIN FEINBERG‡

Abstract. The capacity for multiple equilibria in an isothermal homogeneous continuous flow stirred tank reactor is determined by the reaction network. Examples show that there is a very delicate relationship between reaction network structure and the possibility of multiple equilibria. We suggest a new method for discriminating between networks that have the capacity for multiple equilibria and those that do not. Our method can be implemented using standard computer algebra software and gives answers for many reaction networks for which previous methods give no information.

Key words. equilibrium points, chemical reaction networks, chemical reactors, mass-action kinetics

AMS subject classifications. 80A30, 37C25, 65H10

Linear Solution to nonlinear problem

Uses properties of the Stoichiometric matrix to prove multistationarity.

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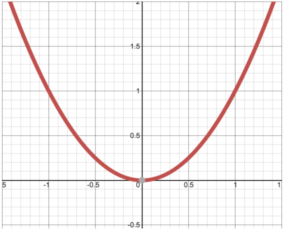
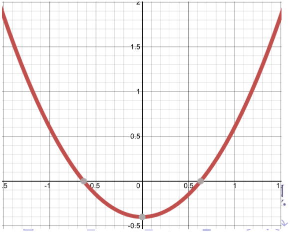
- *Proof Idea*
- Construct rates that satisfy $\det(J) > 0$, then use the IVT to force $\det(J) = 0$.
- They create one degenerate steady state, and perturb it to create two steady states (Bifurcation)





Embedded Subnetworks (Joshi & Shiu)

- If N is an embedded subnetwork of G, under certain hypotheses* then if N admits m positive non-degenerate steady states (for some fixed choice of reaction rates), then G also admits m positive, non-degenerate steady states (for some fixed choice of reaction rates).

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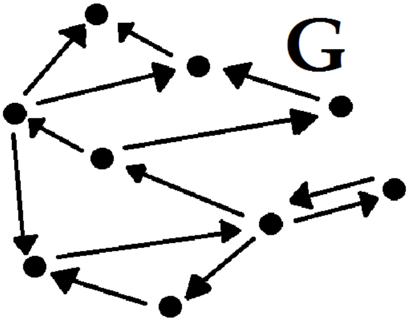

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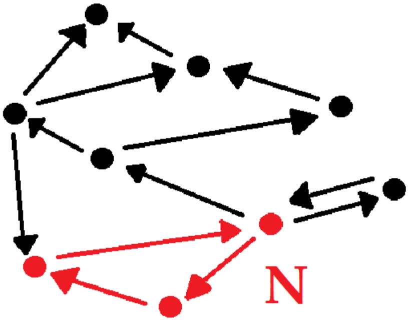

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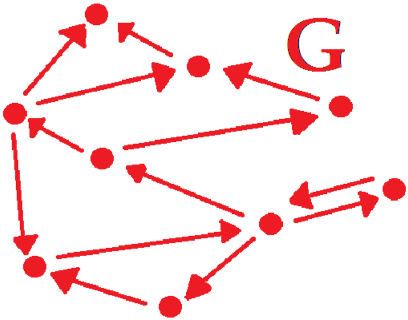

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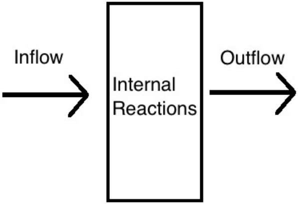
- ... As long as we know a lot about these smaller *embedded networks*.
- This motivates creating a **catalog** of multistationary networks with **positive non-degenerate** steady states.

* The hypothesis we will consider is when "N is a CFSTR embedded in the fully open network G"



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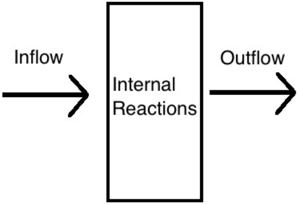

Our Network

$$\widetilde{K}_{m,n} = \begin{cases} X_1 + X_2 \to 0 \\ \quad\vdots \\ X_{n-1} + X_n \to 0 \\ X_1 \to mX_n \\ X_i \leftrightarrow 0 \quad \forall\ i \in \{1, 2, ..., n\} \end{cases}$$

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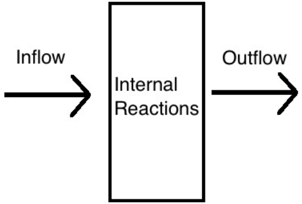

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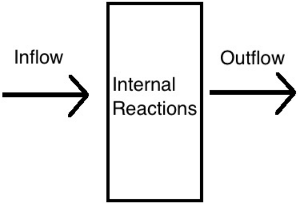

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$\widetilde{K}_{m,n}$ is known to be multistationary for odd n. However, **non-degeneracy** is required for this family to be added to the catalog.

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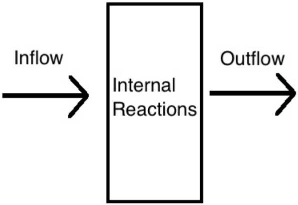

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Definition (Non-degeneracy)

Intuitively, this means it is a "friendly" steady state.
Mathematically, a steady state $\bar{x}$ is **non-degenerate** if $Im(\Gamma) = Im(\text{Jacobian of } \bar{x})$

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- We proved the Stoichiometric matrix Γ is always full rank, thus we need to show $\det(\text{Jacobian}(\bar{x})) \neq 0$ for both steady states.
- **The Problem:** We need to characterize the steady states and reaction rates for $\widetilde{K}_{m,n}$.
- Most methods of proving multistationarity are not even constructive... But in some cases (with some work) the Determinant Optimization Method of Craciun and Feinberg can produce closed forms.

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1. We altered the Determinant Optimization Method to produce **closed-form** concentrations and reaction rate steady states for $\widetilde{K}_{m,n}$.
2. We numerically verified the conjecture for small values of n and m
3. then we considered the case for $n = 3$ and any m.
4. (n $=$ 3) We found the determinant as a function of m, and bounded it with a polynomial in m, proving non-degeneracy for infinitely many values of m.

It was messy

$$\delta_k = \delta_1 \lambda \cdot \frac{(\sqrt{4\lambda\epsilon+\epsilon^2} - (2\lambda+\epsilon))^k - (-\sqrt{4\lambda\epsilon+\epsilon^2} - (2\lambda+\epsilon))^k}{2^k \lambda^k \sqrt{4\lambda\epsilon+\epsilon^2}}$$

$$\eta_{2n}^0 = \frac{(m+1)(m\lambda^n + \lambda(m+1)\daleth_{n-2})}{(\lambda(m+2)+\epsilon)\daleth_{n-2} - \lambda^2 \daleth_{n-3}} - \lambda(m+1)$$

... But when the smoke cleared, we proved this method for the case $n = 3$:

Theorem[Félix, Shiu & Woodstock]

The chemical reaction system $\widetilde{K}_{m,3}$ has multiple positive non-degenerate steady states for any $m \geq 2$.

Conclusion

Today, we discussed:

- The Law of Mass-Action applied to Chemical Reaction Networks
- Steady states of these reaction networks (and difficulties in determining their behavior)
- Several methods on how to show a CRN is multistationary

Thank you!