The inheritance of local bifurcations in mass action networks

Murad Banaji

UNIVERSITY OF OXFORD
Mathematical Institute

Formal Reaction Kinetics seminar, March 26, 2024

Credits

Joint work with **Balázs Boros** and **Josef Hofbauer**, mainly in the preprint

> *(B.–Boros–Hofbauer)* The inheritance of local bifurcations in mass action networks, `https://arxiv.org/abs/2312.12897`, *2023*

Inheritance of bifurcations

We are interested in results of the form:

A subnetwork $\mathcal{R}' \preceq \mathcal{R}$ admits a certain bifurcation $\mathcal{B}$ on some stoichiometric class as rate constants are varied.

$$\Downarrow$$

The full network $\mathcal{R}$ admits the bifurcation $\mathcal{B}$ on some stoichiometric class as rate constants are varied.

Mass action by example

$$0 \xrightarrow{\kappa_1} X$$
$$X \xrightarrow{\kappa_2} Y$$
$$Y + Z \xrightarrow{\kappa_3} 2Z$$
$$X + Z \xrightarrow{\kappa_4} 0$$

$$\begin{pmatrix} \dot{x} \\ \dot{y} \\ \dot{z} \end{pmatrix} = \begin{pmatrix} 1 & -1 & 0 & -1 \\ 0 & 1 & -1 & 0 \\ 0 & 0 & 1 & -1 \end{pmatrix} \begin{pmatrix} \kappa_1 \\ \kappa_2 x \\ \kappa_3 yz \\ \kappa_4 xz \end{pmatrix}.$$

$$\Gamma = \underbrace{\begin{pmatrix} 1 & -1 & 0 & -1 \\ 0 & 1 & -1 & 0 \\ 0 & 0 & 1 & -1 \end{pmatrix}}_{\text{stoichiometric matrix}}, \quad E = \underbrace{\begin{pmatrix} 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 1 \end{pmatrix}}_{\text{exponent matrix}}.$$

$$\mathrm{rank}\,\Gamma = 3, \quad \kappa = (\kappa_1, \kappa_2, \kappa_3, \kappa_4)^{\mathrm{t}}, \quad \boldsymbol{x}^{E^{\mathrm{t}}} = (1, x, yz, xz)^{\mathrm{t}}.$$

Mass action networks

Chemical reaction networks (CRNs) with mass action kinetics give rise to systems of ODEs which can be written succinctly as

$$\dot{x} = \Gamma(\kappa \circ x^{E^{\mathrm{t}}})\,.$$

If the CRN has n chemical species and m reactions, then

- $x \in \mathbb{R}^n_+$ is the vector of **species concentrations**,
- $\Gamma \in \mathbb{Z}^{n \times m}$ is the **stoichiometric matrix**,
- $\kappa \in \mathbb{R}^m_+$ is the vector of **rate constants**, and
- $E \in \mathbb{Z}^{n \times m}_{\geq 0}$ is the **reactant matrix** (or **left stoichiometric matrix** or **exponent matrix**).
- "$\circ$" is the entrywise product.

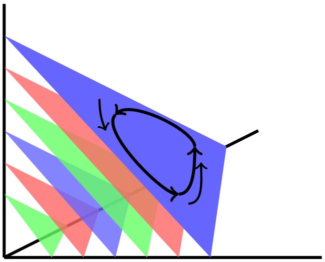
Stoichiometric classes (invariant polyhedra)

The ODE

$$\dot{x} = \Gamma\, v(x)$$

defines a vector field everywhere parallel to $\mathrm{im}\,\Gamma$, the **stoichiometric subspace**.

The intersections of cosets of $\mathrm{im}\,\Gamma$ with $\mathbb{R}^n_+$ are locally invariant polyhedra termed **positive stoichiometric classes**. These may be bounded or unbounded. The dimension of any positive stoichiometric class ($= \mathrm{rank}\,\Gamma$) is termed the **rank** of the CRN.



Inheritance results...

...infer **dynamical behaviours** in networks from "**subnetworks**".

- Give us natural partial orderings on mass action networks: $\mathcal{R} \preceq \mathcal{R}'$ if $\mathcal{R}'$ inherits behaviours from $\mathcal{R}$.
- Justify the intensive study of small networks as "motifs" in larger, real-world, networks.
- Help understand "emergent" behaviours.

[My own interest in this started from reading: Badal Joshi and Anne Shiu, **Atoms of multistationarity in chemical reaction networks**. *J. Math. Chem.*, 51(1):153–178, 2013.]

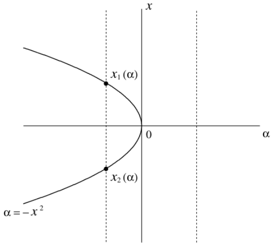
Bifurcations

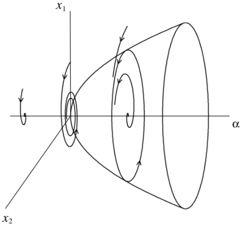
- Qualitative changes in behaviour as some parameters are varied (for us: rate constants).
- They "organise" the interesting behaviours in parameterised families of dynamical systems. (E.g., easier to look for Hopf bifurcations than directly search for periodic orbits.)
- Local bifurcations of equilibria: these are determined by local conditions in the neighbourhood of an equilibrium.
  - Generic codimension one: *fold*, *Andronov–Hopf*.
  - Generic codimension two: *cusp*, *Bautin*, *Bogdanov–Takens*, *fold–Hopf*, *Hopf–Hopf*.
  - Bifurcations of higher codimension...

Generic codimension-1 local bifurcations of equilibria

Pictures from Kuznetsov:

The birth/destruction of equilibria in a fold bifurcation;

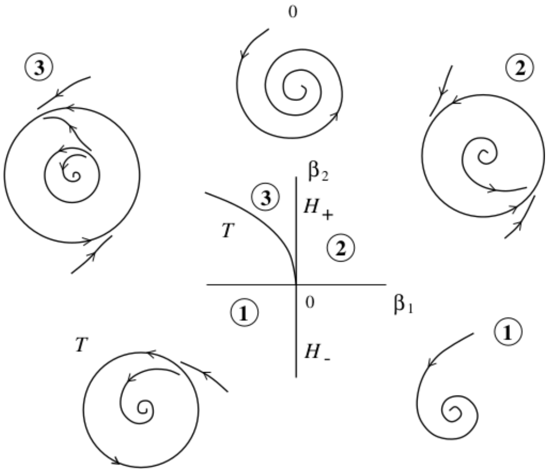




The birth of a limit cycle in a supercritical Andronov–Hopf bifurcation.

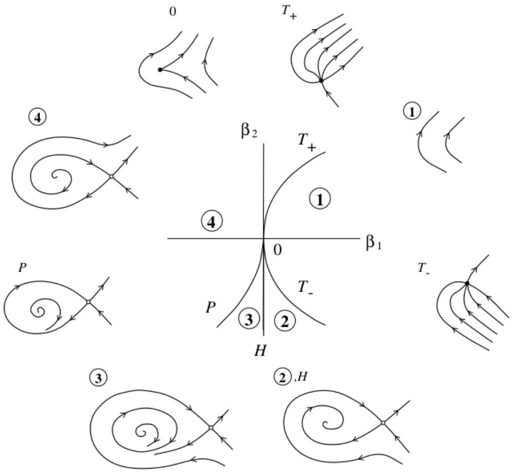
A Bautin bifurcation (co-dimension 2)

Again, from Kuznetsov:



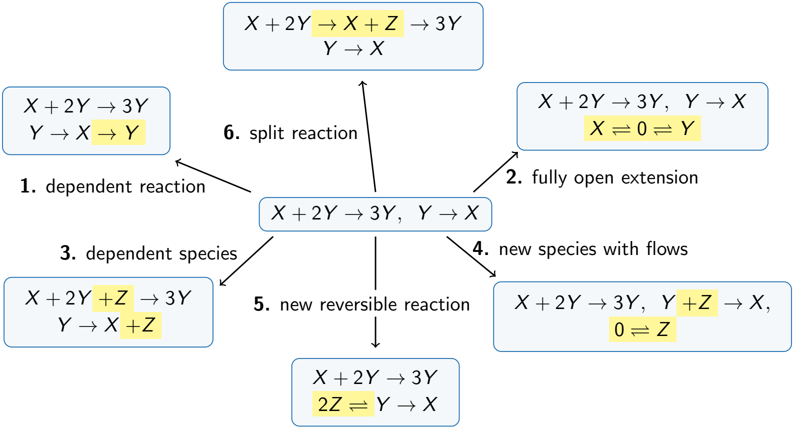
A Bogdanov–Takens bifurcation (co-dimension 2)

Again, from Kuznetsov:



The main result

Local bifurcations of equilibria are preserved by the following enlargements. (The list is *not* exhaustive.)



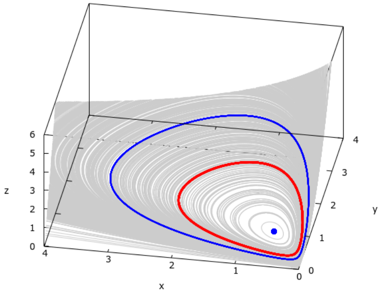
Remarks and caveats

- The result covers essentially any local bifurcation of equilibria of any codimension, provided...
  - The bifurcation is characterised by finitely many conditions on finitely many Taylor coefficients.
  - The bifurcation is unfolded transversely by the rate constants.
- We do not require the bifurcation to satisfy all its usual nondegeneracy conditions, but, if it does, then the same holds for the inherited bifurcation. (Note: checking transversality is often easier than checking nondegeneracy.)

An example: Bautin bifurcation

$$\begin{gathered} X \longrightarrow 2X \\ X + Z \longrightarrow 2Y \\ Y \longrightarrow Z, \quad 2Z \longrightarrow 0 \end{gathered}$$

$$\begin{gathered} X \longrightarrow W, \quad V + W \longrightarrow 2X \\ X + Z \longrightarrow 2Y \\ Y \longrightarrow Z, \quad 2Z \longrightarrow 2V \end{gathered}$$



We can compute with symbolic algebra that the left CRN admits a Bautin bifurcation, hence coexistence of a stable periodic orbit and a stable limit cycle. It follows by **inheritance** that the same holds for the right CRN (which is homogeneous and has no one-step autocatalysis).

(B.–Boros), Nonlinearity 36(2) (2023) 1398–1433.

An example: the homogenised Brusselator

fold

$$X \longrightarrow Y$$
$$2X + Y \longrightarrow 3X$$

$\prec$

$$0 \rightleftarrows X \longrightarrow Y$$
$$2X + Y \longrightarrow 3X$$

Hopf

$\prec$

$$Z \rightleftarrows X \longrightarrow Y$$
$$2X + Y \longrightarrow 3X$$

fold, Hopf

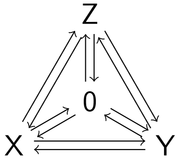
Bogdanov-Takens

(⇒ homoclinic)

Bautin

(⇒ fold of limit cycles)

$\preceq$



$$2X + Y \longrightarrow 3X$$

fold, Hopf

Bogdanov-Takens

(⇒ homoclinic)

Bautin

(⇒ fold of limit cycles)

Proof of the main result

- Calls on a number of previous results on the various enlargements.
- The main theoretical tools: regular and singular perturbation theory.
- Some challenges associated with
  - lifting parameterised families,
  - working in generality (rather than focussing on particular bifurcations).

Some ideas behind the proof, by example

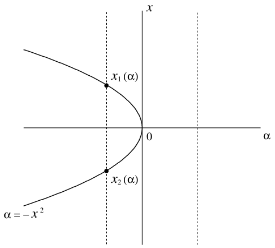
Consider the mass action CRN

$$X_1 + 2X_2 \xrightarrow{1} 3X_2, \quad X_2 \xrightarrow{\kappa} X_1 \ . \qquad (\mathcal{R}_0)$$

and the corresponding system of ODEs

$$\begin{pmatrix} \dot{x}_1 \\ \dot{x}_2 \end{pmatrix} = \begin{pmatrix} -1 & 1 \\ 1 & -1 \end{pmatrix} \begin{pmatrix} x_1 x_2^2 \\ \kappa x_2 \end{pmatrix} .$$

This CRN admits the simplest bifurcation: a **fold** bifurcation. On any given stoichiometric class, as κ decreases through some critical value, a pair of equilibria are born.



Some ideas behind the proof, by example

Choose a positive stoichiometric class, say,

$$\mathcal{S}_0 = \{(x_1, x_2) \in \mathbb{R}^2_+ : x_1 + x_2 = 2\}\,.$$

Define a local coordinate θ on $\mathcal{S}_0$ via

$$\begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = \begin{pmatrix} 1 \\ 1 \end{pmatrix} + \begin{pmatrix} -1 \\ 1 \end{pmatrix} \theta\,.$$

Then θ evolves according to

$$\dot{\theta} = (1+\theta)(1-\kappa-\theta^2) =: f(\theta,\kappa)\,.$$

$\mathcal{R}_0$ has a nondegenerate fold bifurcation at $(\theta,\kappa) = (0,1)$. We can check: $f(\theta,\kappa) = 0$, $f_\theta(\theta,\kappa) = 0$, and the nondegeneracy and transversality conditions $f_{\theta\theta}(\theta,\kappa) < 0$ and $f_\kappa(\theta,\kappa) < 0$.

Some ideas behind the proof, by example

Let's now enlarge $\mathcal{R}_0$ with a new intermediate complex:

$$\mathsf{X}_1 + 2\mathsf{X}_2 \xrightarrow{1} 3\mathsf{X}_2, \quad \mathsf{X}_2 \xrightarrow{\kappa} \mathsf{Y}_1 + \mathsf{Y}_2 \xrightarrow{\varepsilon^{-1}} \mathsf{X}_1\,. \qquad (\mathcal{R}_1)$$

We obtain the ODE

$$\begin{pmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{y}_1 \\ \dot{y}_2 \end{pmatrix} = \begin{pmatrix} -1 & 1 & -1 \\ 1 & -1 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x_1 x_2^2 \\ \kappa x_2 \\ \kappa x_2 - \varepsilon^{-1} y_1 y_2 \end{pmatrix}.$$

Compare with the original ODE system:

$$\begin{pmatrix} \dot{x}_1 \\ \dot{x}_2 \end{pmatrix} = \begin{pmatrix} -1 & 1 \\ 1 & -1 \end{pmatrix} \begin{pmatrix} x_1 x_2^2 \\ \kappa x_2 \end{pmatrix}.$$

Some ideas behind the proof, by example

We focus attention on the 2D, positive, stoichiometric class of $\mathcal{R}_1$:

$$\mathcal{S}' = \{(x_1, x_2, y_1, y_2) \in \mathbb{R}^4_+ \colon x_1 + x_2 + y_1 = 2,\; y_2 - y_1 = 1\}\,.$$

Define θ by $\left(\begin{array}{c} x_1 + y_1 \\ x_2 \end{array}\right) = \left(\begin{array}{c} 1-\theta \\ 1+\theta \end{array}\right)$, and define $w = \varepsilon^{-1} y_1$.

For any fixed $\varepsilon > 0$, (θ, w) is a local coordinate on $\mathcal{S}'$. We get, in these coordinates,

$$\begin{array}{rcl} \dot{\theta} & = & (1+\theta)(1-\kappa-\theta^2-\varepsilon w(1+\theta))\,, \\ \varepsilon \dot{w} & = & \kappa(1+\theta) - w - \varepsilon w^2\,, \quad \dot{\kappa} = 0\,. \end{array}$$

Compare with the original

$$\dot{\theta} \;=\; (1+\theta)(1-\kappa-\theta^2), \quad \dot{\kappa} = 0\,.$$

Some ideas behind the proof, by example

We now have a **singular perturbation problem**. For sufficiently small $\varepsilon > 0$, the system has an attracting, locally invariant, manifold $\mathcal{E}_\varepsilon$ close to

$$\mathcal{E}_0 = \{(\theta, w, \kappa) : \; w = \frac{1}{\kappa(1+\theta)}\},$$

on which (in local coordinates) the dynamics is a regular perturbation of the original dynamics.

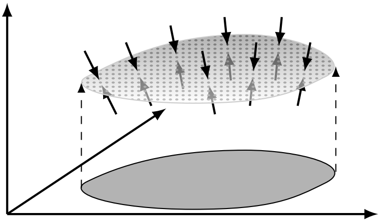
We can now conclude that for any sufficiently small $\varepsilon > 0$, $\mathcal{R}_1$ has a nondegenerate fold bifurcation on $\mathcal{S}'$ as the rate constant κ is varied.

More generally

Broadly the template set out in the previous example "works". For each enlargement, via appropriate choices of rate constants and appropriate transformations, we recast the problem as a **regular or singular perturbation** problem.

We end up with two sets of parameters: the original bifurcation parameters, say κ; and new perturbation parameters, say, ε.

In the singular perturbation case, the interesting dynamics now occurs on an attracting "slow" manifold.



Conclusions and remarks

The main result has a number of immediate corollaries, for example for

- *Fully open* networks;
- *Enzymatic* processes.

The results justify a program of identifying **minimal networks** admitting certain bifurcations.

The enlargements covered so far are not a complete list.

Extensions to global bifurcations are implicit in the proofs, but present some technical challenges.

References

*(B.–Boros–Hofbauer) *The inheritance of local bifurcations in mass action networks*, `https://arxiv.org/abs/2312.12897`, 2023.

(B.–Boros) *The smallest bimolecular mass action reaction networks admitting Andronov–Hopf bifurcation*, Nonlinearity 36(2) (2023) 1398–1433.

(B.) *Splitting reactions preserves nondegenerate behaviours in chemical reaction networks*, SIAM J Appl Math 83(2) (2023) 748–769.

(B.–Boros–Hofbauer) *Adding species to chemical reaction networks: preserving rank preserves nondegenerate behaviours*, Applied Math Comput 426 (2022) p127109.

(B.) *Building oscillatory chemical reaction networks by adding reversible reactions*, SIAM J Appl Math 80(4) (2020) 17511777.

(B.–Pantea) *The inheritance of nondegenerate multistationarity in chemical reaction networks*, SIAM J Appl Math 78(2) (2018) 11051130.

(B.) *Inheritance of oscillation in chemical reaction networks*, Applied Math Comput 325 (2018) 191209.

Thank you for listening!