DETERMINISTIC REACTION NETWORKS PART III - DYNAMICS

Balázs Boros

Symmetry and Perturbation Theory (SPT)
Chemical Reaction Networks (CRN)
Pula, Italy, June 10–14, 2024

Main characteristics of the model

This talk

- continuous-time
- deterministic
- state space is $\mathbb{R}^n_{\geq 0}$
- homogeneous in space
- future depends on the present only
- autonomous

Later this week, also

- stochastic
- state space is discrete or infinite dimensional
- inhomogeneous in space (PDE)
- future also depends on the past (delay)

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Mass-action systems

$$Z \underset{\kappa_2}{\overset{\kappa_1}{\rightleftarrows}} X \xrightarrow{\kappa_3} Y$$

$$2X + Y \xrightarrow{\kappa_4} 3X$$

species: X, Y, Z

complexes: X, Y, Z, $2X + Y$, $3X$

reactions: $Z \to X$, $X \to Z$, $X \to Y$, $2X + Y \to 3X$

$$\begin{bmatrix} \dot{x} \\ \dot{y} \\ \dot{z} \end{bmatrix} = \begin{bmatrix} 1 & -1 & -1 & 1 \\ 0 & 0 & 1 & -1 \\ -1 & 1 & 0 & 0 \end{bmatrix} \begin{bmatrix} \kappa_1 z \\ \kappa_2 x \\ \kappa_3 x \\ \kappa_4 x^2 y \end{bmatrix}$$

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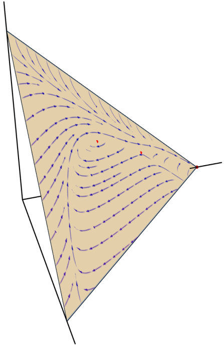
$$\dot{x} + \dot{y} + \dot{z} = 0 \Longrightarrow x(t) + y(t) + z(t) \equiv c$$



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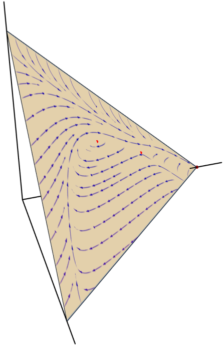


$$\dot{x} + \dot{y} + \dot{z} = 0 \Longrightarrow x(t) + y(t) + z(t) \equiv c$$

$$\dot{x} = N(\kappa \circ x^A) \text{ in } \mathbb{R}^n_+$$

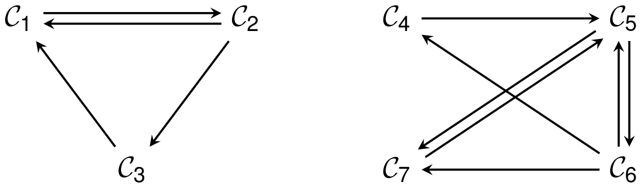
$$\mathcal{P} = (x_0 + \operatorname{im} N) \cap \mathbb{R}^n_+$$

Questions

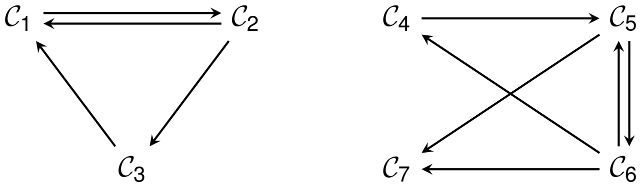
- existence/uniqueness/number of equilibria
- periodic orbits, limit cycles, centers, homoclinic orbits
- local/global asymptotic stability (of equilibria or periodic orbits)
- bifurcations (of equilibria or periodic orbits)
- multistability
- boundedness of solutions
- persistence
- permanence

Weak reversibility (WR)

each reaction is part of a cycle $\Longrightarrow$ WR



reaction $\mathcal{C}_6 \to \mathcal{C}_7$ is not part of any cycle $\Longrightarrow$ not WR



Deficiency

$$\delta = m - \ell - \operatorname{rank} N \geq 0$$

$$\dot{x} = N(\kappa \circ x^A)$$

$m = \#$ vertices

$\ell = \#$ connected components

$$N = \begin{bmatrix} -1 & 1 & 1 & 0 & 0 & 0 & 0 & 1 & 1 & 0 \\ 1 & -1 & -1 & 0 & -1 & 3 & -3 & -3 & 0 & 2 \\ 1 & -1 & -1 & 0 & 0 & 0 & 0 & -1 & 1 & 0 \\ 0 & 0 & 2 & -2 & 1 & -1 & 1 & 0 & -1 & 0 \\ 0 & 0 & 0 & 0 & -1 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 1 & 1 & -1 & -2 & -1 & -2 \end{bmatrix}$$

$$\delta = 7 - 2 - 5 = 0$$

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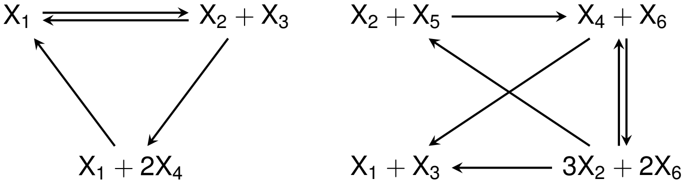


$$N = \begin{bmatrix} -1 & 1 & 1 & 0 & 0 & 0 & 0 & 1 & 1 & 0 \\ 1 & -1 & -1 & 0 & -1 & 3 & -3 & -3 & 0 & 2 \\ 1 & -1 & -1 & 0 & 0 & 0 & 0 & -1 & 1 & 0 \\ 0 & 0 & 2 & -2 & 1 & -1 & 1 & 0 & -1 & 0 \\ 0 & 0 & 0 & 0 & -1 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 1 & 1 & -1 & -2 & -1 & -2 \end{bmatrix}$$

$$\delta = 7 - 2 - 5 = 0$$

Deficiency-Zero Theorem

$$E_+ = \{x \in \mathbb{R}^n_+ \colon N(\kappa \circ x^A) = 0\} \qquad \mathcal{P} = (x_0 + \operatorname{im} N) \cap \mathbb{R}^n_+$$

Theorem (Horn–Jackson–Feinberg 1972)

WR, $\delta = 0 \Longrightarrow$

- $E_+ \neq \emptyset$
- $E_+ = \{x \in \mathbb{R}^n_+ \mid \log x - \log x^* \perp \operatorname{im} N\}$ *for each* $x^* \in E_+$
- $|E_+ \cap \mathcal{P}| = 1$ *for each* $\mathcal{P}$ *(denote the unique element by* $\overline{x}$*)*
- $\overline{x}$ *is locally asymptotically stable relative to* $\mathcal{P}$
- *all solutions are bounded*
- *there is no periodic solution*

Conjecture (Horn 1974)

even global asymptotic stability holds in the above theorem

The Horn–Jackson function as a global Lyapunov function

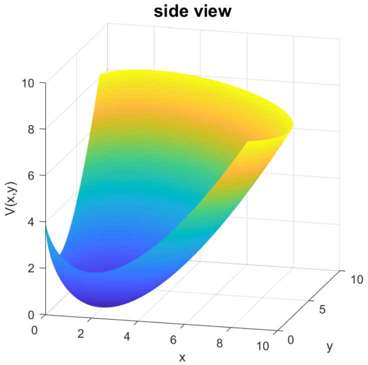
fix $x^* \in E_+$ and let $V(x_1, \ldots, x_n) = \sum_{i=1}^{n} \left[x_i \left(\log \frac{x_i}{x_i^*} - 1 \right) + x_i^* \right]$

Theorem (Horn–Jackson 1972)

WR, $\delta = 0 \Longrightarrow \frac{\mathrm{d}}{\mathrm{d}\tau} V(x(\tau)) < 0$ *whenever* $x(\tau) \notin E_+$

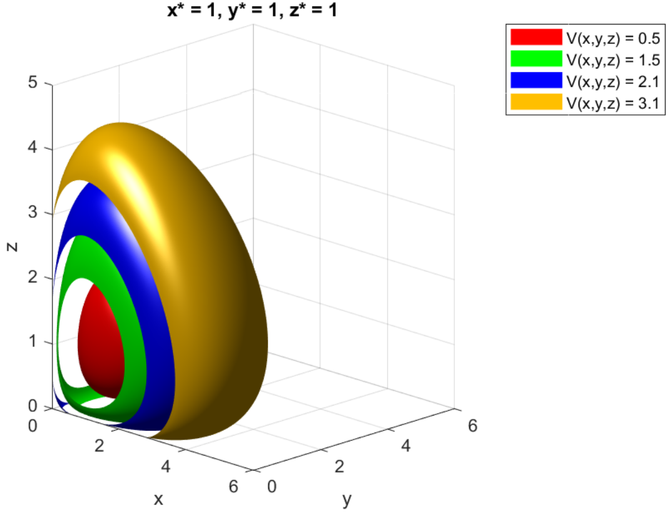
The Horn–Jackson function for $n = 2$

$$V(x,y) = \left[x\left(\log\frac{x}{x^*} - 1\right) + x^*\right] + \left[y\left(\log\frac{y}{y^*} - 1\right) + y^*\right]$$

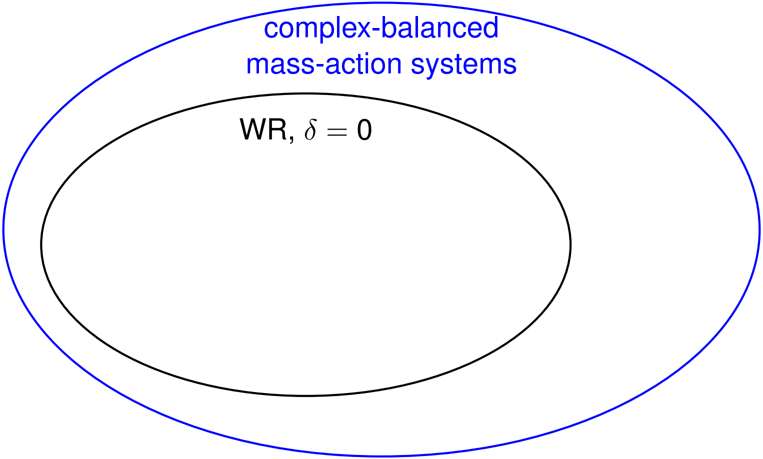


The Horn–Jackson level sets for $n = 3$

$$V(x,y,z) = \left[x\left(\log\frac{x}{x^*}-1\right)+x^*\right]+\left[y\left(\log\frac{y}{y^*}-1\right)+y^*\right]+\left[z\left(\log\frac{z}{z^*}-1\right)+z^*\right]$$



WR, $\delta = 0 \Longrightarrow$ COMPLEX-BALANCED SYSTEMS



Dfc-Zero-Thm extends to complex-balanced mass-action systems

Results on the Global Attractor Conjecture (GAC)

Conjecture (Craciun–Dickenstein–Shiu–Sturmfels 2009)

complex-balanced equilibria are globally asymptotically stable

- detailed balance, $\operatorname{rank} N = 2$, conservative
  Craciun–Dickenstein–Shiu–Sturmfels 2009
- all boundary equilibria are facet-interior or vertices of $\overline{\mathcal{P}}$
  Anderson–Shiu 2010
- $\operatorname{rank} N = 2$
  Anderson–Shiu 2010
- single connected component
  Anderson 2011, Gopalkrishnan–Miller–Shiu 2014, BB–Hofbauer 2019
- $\operatorname{rank} N = 3$
  Pantea 2012
- $n = 3$
  Craciun–Nazarov–Pantea 2013
- full generality
  Craciun 202?

Deficiency-One Theorem

Theorem (Feinberg 1979)

WR, $\ell = 1$, $\delta = 1 \Longrightarrow$

- $E_+ \neq \emptyset$
- $E_+ = \{x \in \mathbb{R}^n_+ \mid \log x - \log x^* \perp \operatorname{im} N\}$ *for each* $x^* \in E_+$
- $|E_+ \cap \mathcal{P}| = 1$ *for each* $\mathcal{P}$

Theorem (Feinberg 1979)

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$\times$ $\overline{x}$ is locally asymptotically stable relative to $\mathcal{P}$

? all solutions are bounded

$\times$ there is no periodic solution

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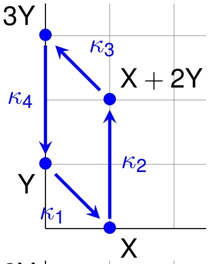
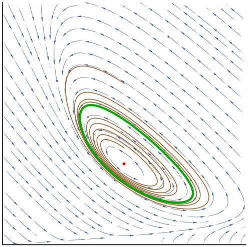
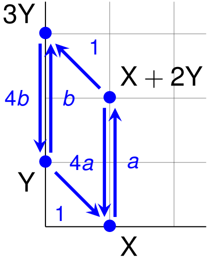
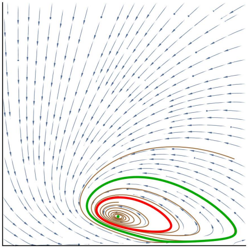
Limit cycles in deficiency-one networks (BB–Hofbauer 2021, 2022)





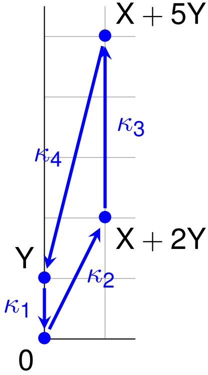
$\kappa_1 = 240$
$\kappa_2 = 8$
$\kappa_3 = 40$
$\kappa_4 = 3$





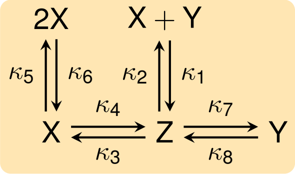
$a = 0.005$
$b = 0.18$

Limit cycles in deficiency-one networks (BB–Hofbauer 2021)



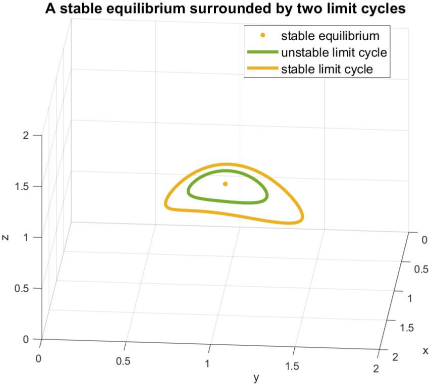
unstable equilibrium
stable limit cycle
unstable limit cycle
stable limit cycle

Limit cycles in deficiency-one networks (Feinberg–Berner 1979)

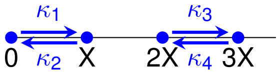


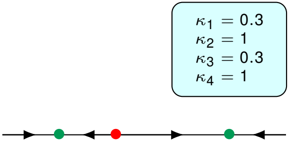
$$\dot{x} = -\kappa_1 xy + \kappa_2 z + \kappa_3 z - \kappa_4 x + \kappa_5 x - \kappa_6 x^2$$
$$\dot{y} = -\kappa_1 xy + \kappa_2 z + \kappa_7 z - \kappa_8 y$$
$$\dot{z} = \kappa_1 xy - \kappa_2 z - \kappa_3 z + \kappa_4 x - \kappa_7 z + \kappa_8 y$$

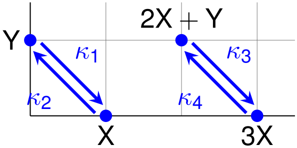
$\kappa_1 = 1$
$\kappa_2 = 0.2$
$\kappa_3 = 0.2$
$\kappa_4 = 0.2$
$\kappa_5 = 0.987$
$\kappa_6 = 0.187$
$\kappa_7 = 0.0052$
$\kappa_8 = 0.8052$

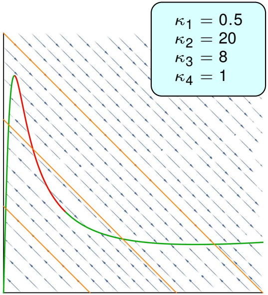


Multiple equilibria in deficiency-one networks (reversible Schlögl model 1971)

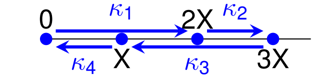


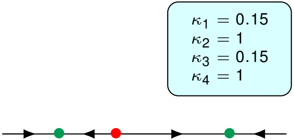


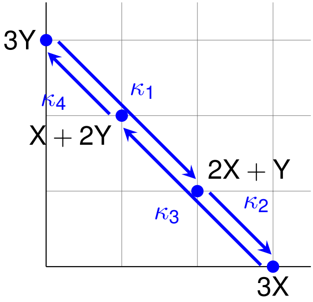


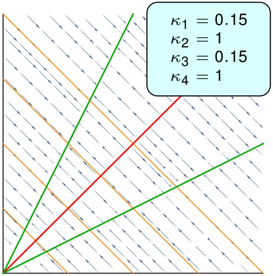


Multiple equilibria in deficiency-two networks (Horn–Jackson 1972)

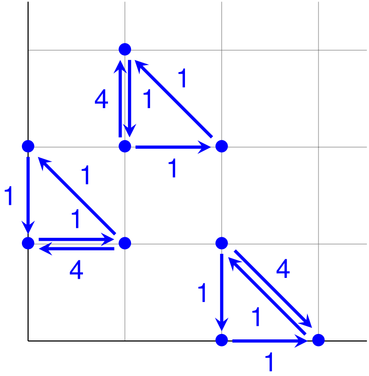


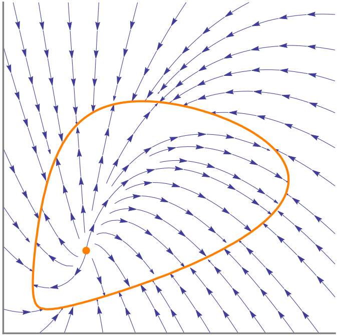






A continuum of equilibria in WR networks (BB–Craciun–Yu 2020)





$$\dot{x} = (x^2 + xy^2 + y - 4xy)[1 - x]$$
$$\dot{y} = (x^2 + xy^2 + y - 4xy)[x - y]$$

Boundedness

boundedness: for positive initial conditions,

$$\limsup_{\tau \to \infty} |x(\tau)| < \infty$$

Conjecture (Anderson 2011)

WR $\Longrightarrow$ boundedness

Theorem (Anderson 2011)

WR, $\ell = 1$ $\Longrightarrow$ boundedness

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Conjecture (Anderson 2011)

WR $\Longrightarrow$ *boundedness*

Theorem (Anderson 2011)

WR, $\ell = 1 \Longrightarrow$ *boundedness*

Persistence

- persistence: for positive initial conditions,

$$\liminf_{\tau \to \infty} x_s(\tau) > 0 \text{ for all } s = 1, \ldots, n$$

- if all the trajectories are bounded then persistence is equivalent to

$$\omega(\overline{x}) \cap \partial \mathbb{R}^n_{\geq 0} = \emptyset \text{ for each positive initial condition } \overline{x} \in \mathbb{R}^n_+$$

- persistence is the missing part of the Global Attractor Conjecture

Conjecture (Craciun–Nazarov–Pantea 2013)

WR $\Longrightarrow$ persistence

PERSISTENCE

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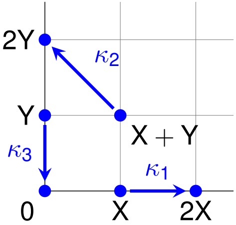
CONJECTURE (CRACIUN–NAZAROV–PANTEA 2013)

WR $\Longrightarrow$ *persistence*

Lotka reactions (solutions are bounded and persistent)



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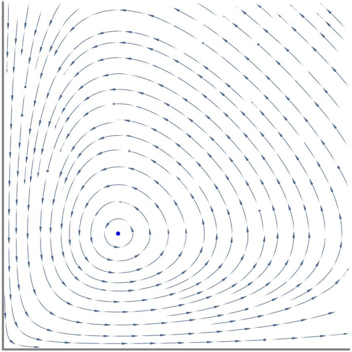
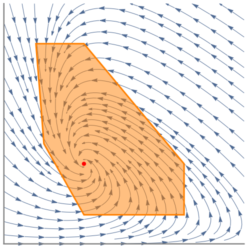


Permanence (more than boundedness + persistence)



permanence on $\mathcal{P}$:

$\exists K \subseteq \mathcal{P}$ compact s.t. every solution starting in $\mathcal{P}$ ends up in K

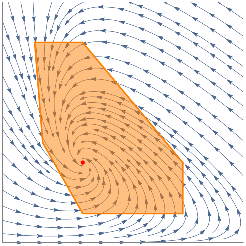
Conjecture (Craciun–Nazarov–Pantea 2013)

weak reversibility $\Longrightarrow$ permanence

Theorem (Simon 1995)

$n = 2$, reversibility $\Longrightarrow$ permanence

PERMANENCE (MORE THAN BOUNDEDNESS + PERSISTENCE)



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weak reversibility $\Longrightarrow$ permanence

THEOREM (SIMON 1995)

$n = 2$, reversibility $\Longrightarrow$ permanence

Existence of equilibria

Remark

permanence on $\mathcal{P} \implies E_+ \cap \mathcal{P} \neq \emptyset$

Theorem (BB 2019)

$WR \implies E_+ \cap \mathcal{P} \neq \emptyset$ *for all* $\mathcal{P}$

Existence of equilibria

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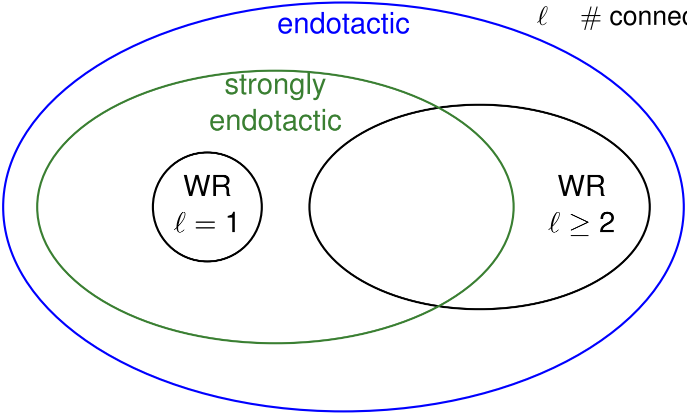
Extension of weak reversibility: endotacticity

Def. of *endotactic* networks is by Craciun–Nazarov–Pantea (2013)

Def. of *strongly endotactic* networks is by Gopalkrishnan–Miller–Shiu (2014)

WR weak reversibility

ℓ # connected components



The Extended Permanence Conjecture

- endotactic network:
  - 1D: either empty or has at least two source complexes and from the extreme ones reactions point inwards
  - nD: all 1D projections are endotactic
- time-dependent rate “constants”:

  $\exists \varepsilon \in (0,1)$ s.t. $\varepsilon \leq \kappa_{ij}(\tau) \leq \frac{1}{\varepsilon}$ for all $\tau \geq 0$ and for all $(i,j) \in \mathcal{R}$

Conjecture (Craciun–Nazarov–Pantea 2013)

endotactic $\Longrightarrow$ permanence (even for time-dependent κ)

The Extended Permanence Conjecture

- endotactic network:
  - 1D: either empty or has at least two source complexes and from the extreme ones reactions point inwards
  - nD: all 1D projections are endotactic

- time-dependent rate "constants":

  $\exists \varepsilon \in (0,1)$ s.t. $\varepsilon \leq \kappa_{ij}(\tau) \leq \frac{1}{\varepsilon}$ for all $\tau \geq 0$ and for all $(i,j) \in \mathcal{R}$

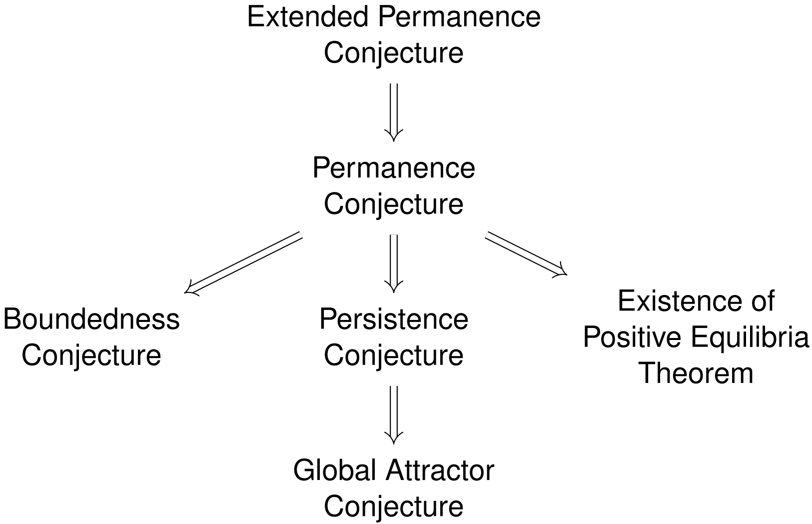
Conjecture (Craciun–Nazarov–Pantea 2013)

endotactic $\Longrightarrow$ permanence (even for time-dependent κ)

Results on persistence/permanence

- $n = 2$, reversible $\Longrightarrow$ permanence
  Simon 1995
- rank $N = 2$, WR $\Longrightarrow$ bounded trajectories are persistent
  Pantea 2012
- $n = 2$, endotactic $\Longrightarrow$ permanence (even for time-dependent κ)
  Craciun–Nazarov–Pantea 2013
- if the origin is repelling and all trajectories are bounded for all endotactic mass-action systems then the persistence conjecture holds
  Gopalkrishnan–Miller–Shiu 2013
- strongly endotactic $\Longrightarrow$ permanence (even for time-dependent κ)
  Gopalkrishnan–Miller–Shiu 2014, Anderson–Cappelletti–Kim–Nguyen 2020
- WR, $\ell = 1 \Longrightarrow$ permanence (even for time-dependent κ)
  Gopalkrishnan–Miller–Shiu 2014, BB–Hofbauer 2019,
  Anderson–Cappelletti–Kim–Nguyen 2020
- $n = 2$, tropically endotactic $\Longrightarrow$ permanence (even for time-dependent κ)
  Brunner–Craciun 2018

THE BIG CONJECTURES

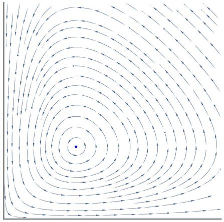


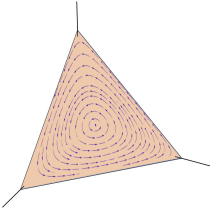
Models that show oscillation

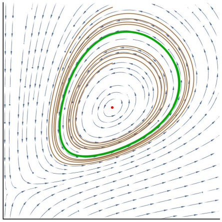
- Sel'kov's glycolytic oscillator
- Belousov–Zhabotinsky reaction
- mitogen-activated protein kinase (MAPK) cascade
- dual-site phosphorylation and dephosphorylation network (futile cycle)
- sequential and distributive double phosphorylation cycle
- phosphorylation and dephosphorylation of extracellular signal-regulated kinase (ERK)
- activation of lymphocyte-specific protein tyrosine kinase (Lck)
- ...

Classical oscillators

Lotka 1920	Ivanova 197?	Frank-Kamenetsky and Salnikov 1943
$\mathsf{X} \longrightarrow \mathsf{2X}$	$\mathsf{Z} + \mathsf{X} \longrightarrow \mathsf{2X}$	$\mathsf{X} \longrightarrow \mathsf{2X} \longrightarrow \mathsf{3X}$
$\mathsf{X} + \mathsf{Y} \longrightarrow \mathsf{2Y}$	$\mathsf{X} + \mathsf{Y} \longrightarrow \mathsf{2Y}$	$\mathsf{X} + \mathsf{Y} \longrightarrow \mathsf{2Y}$
$\mathsf{Y} \longrightarrow \mathsf{0}$	$\mathsf{Y} + \mathsf{Z} \longrightarrow \mathsf{2Z}$	$\mathsf{Y} \rightleftarrows \mathsf{0}$





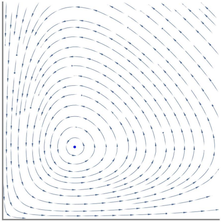


Classical oscillators

Lotka 1920

$$\begin{aligned} X &\longrightarrow 2X \\ X + Y &\longrightarrow 2Y \\ Y &\longrightarrow 0 \end{aligned}$$

bimolecular

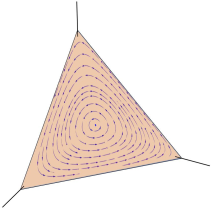


center

Ivanova 197?

$$\begin{aligned} Z + X &\longrightarrow 2X \\ X + Y &\longrightarrow 2Y \\ Y + Z &\longrightarrow 2Z \end{aligned}$$

bimolecular

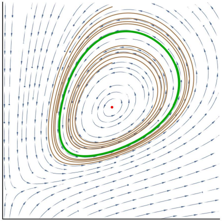


center

Frank-Kamenetsky and Salnikov 1943

$$\begin{aligned} X &\longrightarrow 2X \longrightarrow 3X \\ X + Y &\longrightarrow 2Y \\ Y &\rightleftarrows 0 \end{aligned}$$

bimolecular-sourced



limit cycle

Minimum rank of bimolecular oscillators

$$\dot{x} = N(\kappa \circ x^A)$$

Definition

The *rank* of a reaction network is $\operatorname{rank} N$.

Theorem (Póta 1985, BB–Hofbauer 2022)

bimolecular, isolated periodic orbit exists $\Longrightarrow$ *rank* ≥ 3

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Theorem (Póta 1985, BB–Hofbauer 2022)

bimolecular, isolated periodic orbit exists $\Longrightarrow$ *rank* ≥ 3

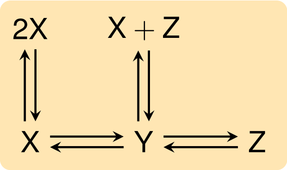
For the smallest oscillators, study

- rank-three, bimolecular or
- rank-two, bimolecular-sourced

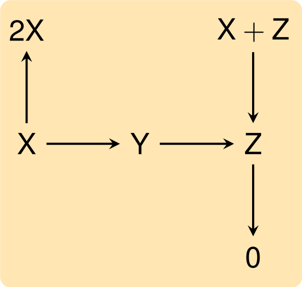
networks.

Rank-three, bimolecular oscillators (supercritical Andronov–Hopf bifurcation ⇒ stable limit cycle)

Feinberg–Berner 1979



Wilhelm–Heinrich 1995

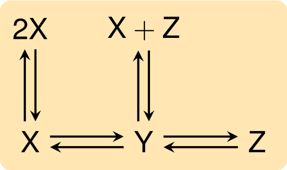


Wilhelm 2009

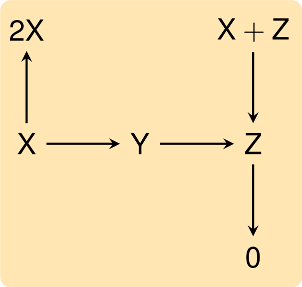
$$\mathsf{X} \longrightarrow \mathsf{2X}$$
$$\mathsf{X}+\mathsf{Z} \longrightarrow \mathsf{Y}+\mathsf{Z}$$
$$\mathsf{2Y} \longrightarrow \mathsf{Z}$$
$$\mathsf{2Z} \longrightarrow \mathsf{0}$$

Rank-three, bimolecular oscillators (supercritical Andronov–Hopf bifurcation $\Rightarrow$ stable limit cycle)

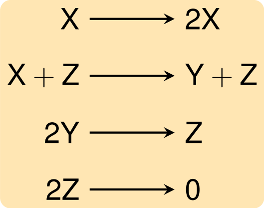
Feinberg–Berner 1979



Wilhelm–Heinrich 1995



Wilhelm 2009



only 4 reactions!

Rank-three, bimolecular oscillators (supercritical Andronov–Hopf bifurcation $\Rightarrow$ stable limit cycle)

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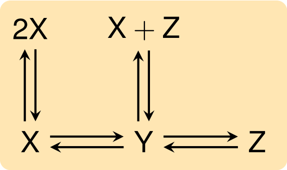
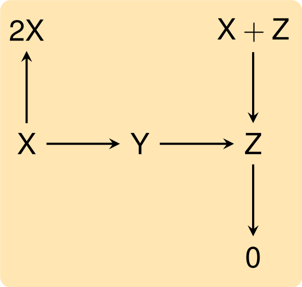
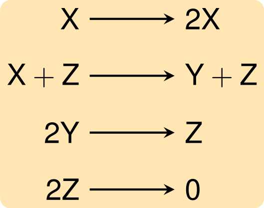


Wilhelm–Heinrich 1995



Wilhelm 2009



only 4 reactions!

Goal

Find all three-species, four-reaction, bimolecular networks that admit an Andronov–Hopf bifurcation. (Wilhelm's network is one such.)

Subtlety #1: loss of equilibrium

$$\begin{aligned} X &\longrightarrow 2X \\ X+Z &\longrightarrow 2Y \\ X+Y &\longrightarrow Z \\ Z &\longrightarrow 0 \end{aligned}$$

supercritical Andronov–Hopf

$$\begin{aligned} \dot{x} &= \kappa_1 x - \kappa_2 xz - \kappa_3 xy \\ \dot{y} &= 2\kappa_2 xz - \kappa_3 xy \\ \dot{z} &= -\kappa_2 xz + \kappa_3 xy - \kappa_4 z \end{aligned}$$

$$\begin{aligned} X &\longrightarrow 2X \\ X+Z &\longrightarrow Y \\ X+Y &\longrightarrow Z \\ Z &\longrightarrow 0 \end{aligned}$$

no positive equilibrium

$$\begin{aligned} \dot{x} &= \kappa_1 x - \kappa_2 xz - \kappa_3 xy \\ \dot{y} &= \kappa_2 xz - \kappa_3 xy \\ \dot{z} &= -\kappa_2 xz + \kappa_3 xy - \kappa_4 z \end{aligned}$$

Subtlety #2: loss of bifurcation

$$\begin{aligned} X &\longrightarrow 2X \\ 2X &\longrightarrow 2Y \\ Y &\longrightarrow 2Z \\ X + Z &\longrightarrow 0 \end{aligned}$$

$$\begin{aligned} \dot{x} &= \kappa_1 x - 2\kappa_2 x^2 - \kappa_4 xz \\ \dot{y} &= 2\kappa_2 x^2 - \kappa_3 y \\ \dot{z} &= 2\kappa_3 y - \kappa_4 xz \end{aligned}$$

supercritical
Andronov–Hopf
(even Bautin)

$$\begin{aligned} X &\longrightarrow 2X \\ 2X &\longrightarrow 2Y \\ Y &\longrightarrow Z \\ X + Z &\longrightarrow 0 \end{aligned}$$

$$\begin{aligned} \dot{x} &= \kappa_1 x - 2\kappa_2 x^2 - \kappa_4 xz \\ \dot{y} &= 2\kappa_2 x^2 - \kappa_3 y \\ \dot{z} &= \kappa_3 y - \kappa_4 xz \end{aligned}$$

positive equilibrium
asymptotically stable
(no bifurcation at all)

Andronov–Hopf bifurcation in 2D

[Kuznetsov, Section 3.5]

Theorem

$$\dot{x} = f(x, \alpha), \qquad x \in \mathbb{R}^2, \qquad \alpha \in \mathbb{R}$$

Suppose

- $f(0, \alpha) = 0$ *for sufficiently small* $|\alpha|$,
- $\mu(\alpha) \pm \omega(\alpha)i$ *are the eigenvalues with* $\mu(0) = 0$ *and* $\omega(0) > 0$.

Assume further

- *(transversality)* $\mu'(0) \neq 0$,
- *(nondegeneracy)* $\ell_1(0) \neq 0$ *(ℓ_1 is the first focal value).*

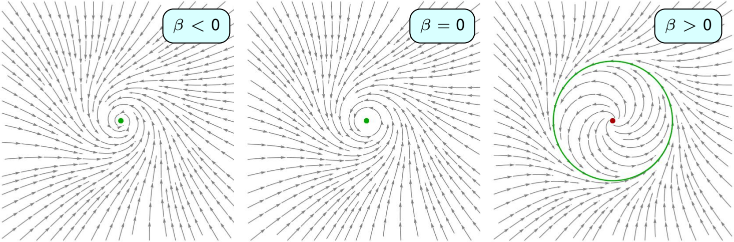
Then the system is locally topologically equivalent near the origin to

$$\begin{aligned} \dot{r} &= r(\beta + \sigma r^2), \\ \dot{\varphi} &= 1, \end{aligned} \qquad \textit{where } \sigma = \operatorname{sgn}(\ell_1(0)).$$

Analysis of the normal form

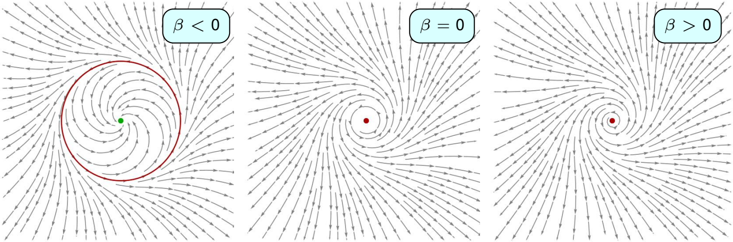
supercritical
$\ell_1(0) < 0$

$\dot{r} = r(\beta - r^2)$
$\dot{\varphi} = 1$

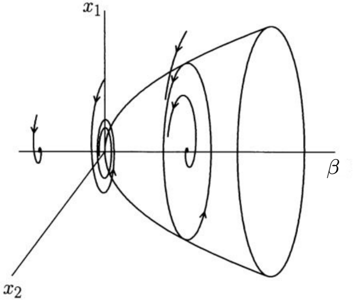


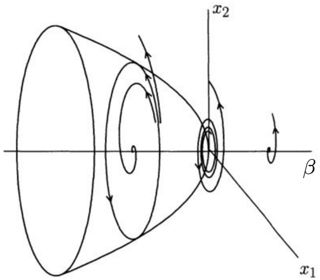
subcritical
$\ell_1(0) > 0$

$\dot{r} = r(\beta + r^2)$
$\dot{\varphi} = 1$



Super- and subcritical Hopf bifurcations [Kuznetsov, Section 3.4]





$\ell_1(0) < 0$: supercritical

stable limit cycle for $\beta > 0$
(a circle of radius $\sqrt{\beta}$)

$\ell_1(0) > 0$: subcritical

unstable limit cycle for $\beta < 0$
(a circle of radius $\sqrt{-\beta}$)

Names for $\ell_1(0)$ in the literature

- focal value
- Lyapunov value
- Lyapunov coefficient
- Lyapunov constant
- Lyapunov quantity
- Poincaré–Lyapunov coefficient
- Poincaré constant
- Bautin constant
- Strudelgröße
- Fokusgröße

$\ell_1(0)$ in 2D (when the Jacobian is in canonical form)

$$\dot{x} = -\omega y + \sum_{i+j\geq 2} \frac{f_{ij}}{i!j!} x^i y^j$$

$$\dot{y} = \omega x + \sum_{i+j\geq 2} \frac{g_{ij}}{i!j!} x^i y^j$$

$$A = \begin{bmatrix} 0 & -\omega \\ \omega & 0 \end{bmatrix}$$

$$\ell_1(0) = f_{30} + f_{12} + g_{03} + g_{21} + \frac{1}{\omega}\left[f_{11}(f_{20} + f_{02}) - g_{11}(g_{20} + g_{02}) + f_{02}g_{02} - f_{20}g_{20}\right]$$

Andronov–Hopf bifurcation in nd [Kuznetsov, Section 5.2]

$$\dot{x} = f(x, \alpha), \quad x \in \mathbb{R}^n, \quad \alpha \in \mathbb{R}$$

Suppose

- $f(0, \alpha) = 0$ for sufficiently small $|\alpha|$,
- $\mu(\alpha) \pm \omega(\alpha) i$ are the eigenvalues with $\mu(0) = 0$ and $\omega(0) > 0$,
- the other $n - 2$ eigenvalues have nonzero real part.

Then perform similar analysis on a 2d center manifold.

However, the computation of $\ell_1(0)$ gets more complicated.

$\ell_1(0)$ in 3D (when the Jacobian is in canonical form)

$$\begin{aligned}
\dot{x} &= -\omega y + \sum_{i+j+k\geq 2} \frac{f_{ijk}}{i!j!k!} x^i y^j z^k \\
\dot{y} &= \omega x + \sum_{i+j+k\geq 2} \frac{g_{ijk}}{i!j!k!} x^i y^j z^k \\
\dot{z} &= \varrho z + \sum_{i+j+k\geq 2} \frac{h_{ijk}}{i!j!k!} x^i y^j z^k
\end{aligned}$$

$$A = \begin{bmatrix} 0 & -\omega & 0 \\ \omega & 0 & 0 \\ 0 & 0 & \varrho \end{bmatrix}$$

$$\begin{aligned}
\ell_1(0) = {} & f_{300} + f_{120} + g_{030} + g_{210} \\
& + \frac{1}{\omega} \left[f_{110}(f_{200} + f_{020}) - g_{110}(g_{200} + g_{020}) + f_{020}g_{020} - f_{200}g_{200} \right] \\
& - \frac{h_{200}}{\varrho(\varrho^2 + 4\omega^2)} \left[(3\varrho^2 + 8\omega^2) f_{101} - 2\varrho\omega f_{011} - 2\varrho\omega g_{101} + (\varrho^2 + 8\omega^2) g_{011} \right] \\
& - \frac{2h_{110}}{\varrho^2 + 4\omega^2} \left[2\omega f_{101} + \varrho f_{011} + \varrho g_{101} - 2\omega g_{011} \right] \\
& - \frac{h_{020}}{\varrho(\varrho^2 + 4\omega^2)} \left[(\varrho^2 + 8\omega^2) f_{101} + 2\varrho\omega f_{011} + 2\varrho\omega g_{101} + (3\varrho^2 + 8\omega^2) g_{011} \right]
\end{aligned}$$

$\ell_1(0)$ IN nD (A NEED NOT BE IN CANONICAL FORM)

Write

$$f(x,0) = Ax + \frac{1}{2}B(x,x) + \frac{1}{6}C(x,x,x) + O(\|x\|^4), \text{ where}$$

$$B_j(x,y) = \sum_{k,l=1}^{n} \left.\frac{\partial^2 f_j(\xi,0)}{\partial\xi_k \partial\xi_l}\right|_{\xi=0} x_k y_l, \quad C_j(x,y,z) = \sum_{k,l,m=1}^{n} \left.\frac{\partial^3 f_j(\xi,0)}{\partial\xi_k \partial\xi_l \partial\xi_m}\right|_{\xi=0} x_k y_l z_m$$

for $j = 1, \ldots, n$. Further, let $p, q \in \mathbb{C}^n$ be such that

$$Aq = \omega i q,$$
$$A^\top p = -\omega i p,$$
$$\langle p, q \rangle = 1.$$

$\ell_1(0) = \frac{1}{2\omega} \operatorname{Re}\langle p, v \rangle$, where

$$v = C(q,q,\overline{q}) + 2B\left(q, (-A)^{-1} B(q,\overline{q})\right) + B\left(\overline{q}, (2\omega i \operatorname{Id} - A)^{-1} B(q,q)\right)$$

details: http://www.scholarpedia.org/article/Andronov-Hopf_bifurcation
(by Kuznetsov)

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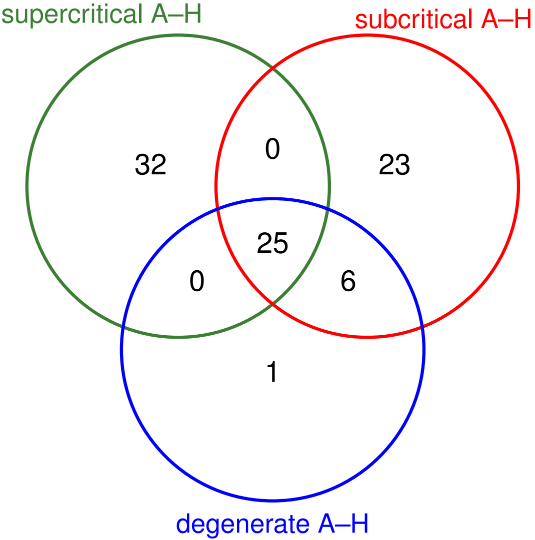
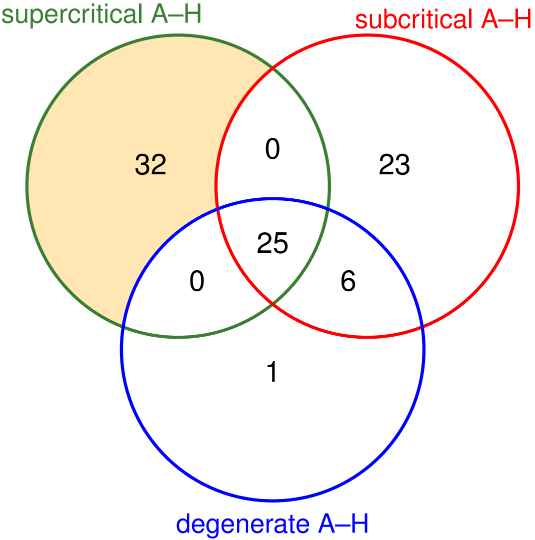
THEOREM (BANAJI–BB 2023):

ALL 3-SPECIES, 4-REACTION, BIMOLECULAR ADMITTING A–H



Theorem (Banaji–BB 2023):

all 3-species, 4-reaction, bimolecular admitting A–H



unstable equilibrium
stable limit cycle

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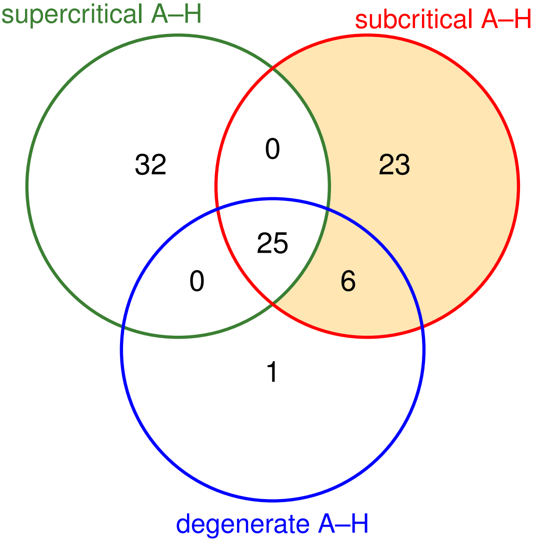

stable equilibrium
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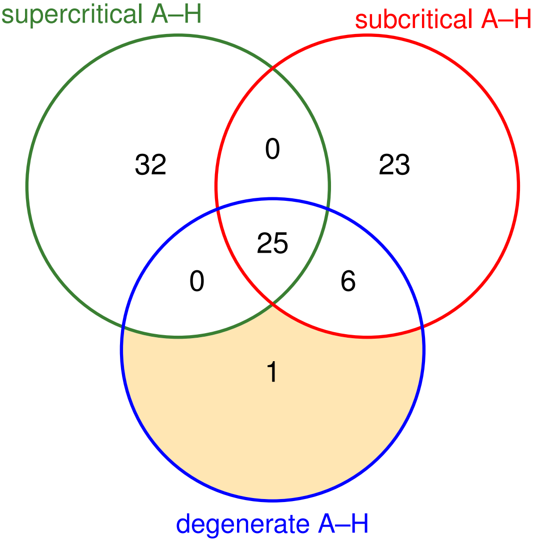
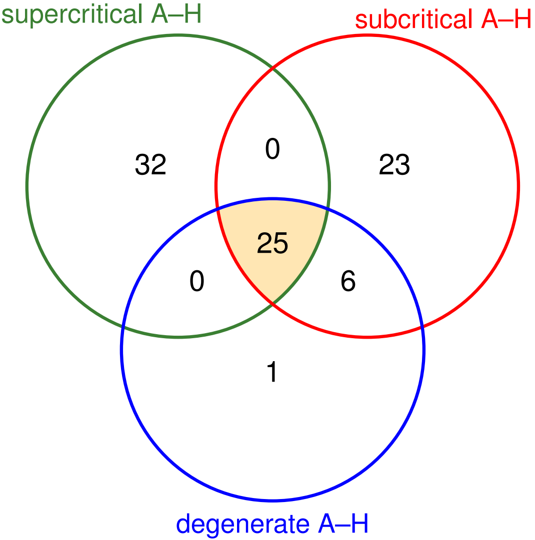


$$Z + X \longrightarrow 2X$$
$$X + Y \longrightarrow 2Y$$
$$Y + Z \longrightarrow 0 \longrightarrow 2Z$$

$$\pm\omega i \in \sigma(A) \Rightarrow L_1 = 0$$

Theorem (Banaji–BB 2023):

all 3-species, 4-reaction, bimolecular admitting A–H



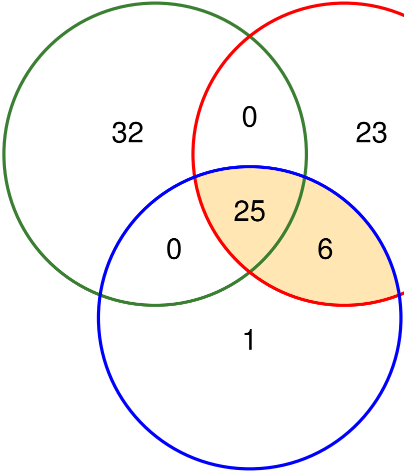
unstable equilibrium
stable limit cycle

or

stable equilibrium
unstable limit cycle

Theorem (Banaji–BB 2023):

all 3-species, 4-reaction, bimolecular admitting A–H



Can two limit cycles coexist?
(codimension-two bifurcation)

Bautin bifurcation in 2D
[Kuznetsov, Section 8.3]

Theorem

$$\dot{x} = f(x, \alpha), \qquad x \in \mathbb{R}^2, \qquad \alpha \in \mathbb{R}^2$$

Suppose

- $f(0, \alpha) = 0$ *for sufficiently small* $|\alpha|$,
- $\mu(\alpha) \pm \omega(\alpha) i$ *are the eigenvalues with* $\mu(0) = 0$ *and* $\omega(0) > 0$,
- $\ell_1(0) = 0$.

Assume further

- *(transversality)* $\alpha \mapsto (\mu(\alpha), \ell_1(\alpha))^\top$ *is regular at* $\alpha = 0$,
- *(nondegeneracy)* $\ell_2(0) \neq 0$ *(*ℓ_2 *is the second focal value).*

Then the system is locally topologically equivalent near the origin to

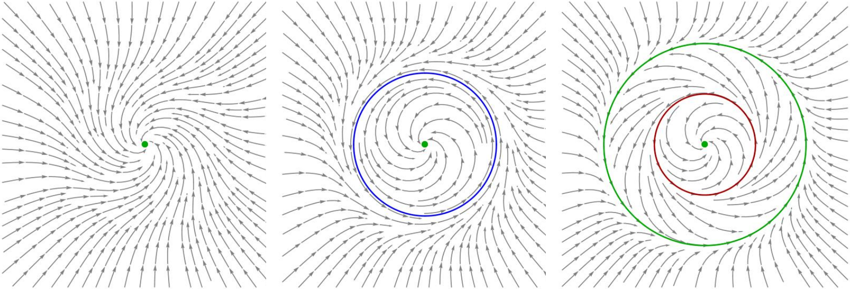
$$\dot{r} = r(\beta_1 + \beta_2 r^2 + \sigma r^4), \qquad \dot{\varphi} = 1,$$

where $\sigma = \operatorname{sgn}(\ell_2(0))$.

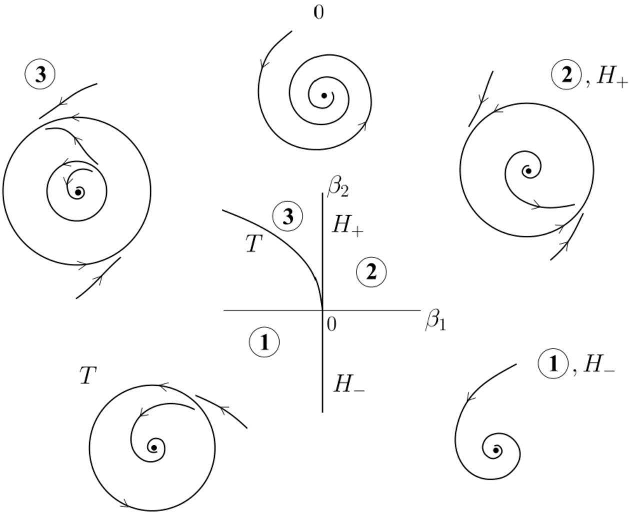
Analysis of the normal form for $\ell_2(0) < 0$, $\beta_1 < 0$

$$\frac{\ell_2(0) < 0}{\begin{aligned} \dot{r} &= r(\beta_1 + \beta_2 r^2 - r^4) \\ \dot{\varphi} &= 1 \end{aligned}}$$

$\beta_1 < 0$, $\beta_2 < 2\sqrt{-\beta_1}$	$\beta_1 < 0$, $\beta_2 = 2\sqrt{-\beta_1}$	$\beta_1 < 0$, $\beta_2 > 2\sqrt{-\beta_1}$



Bautin bifurcation diagram (case $\ell_2(0) < 0$) [Kuznetsov, Section 8.3]



$\ell_2(0)$ in 2D (quadratic case)

$$\dot{x} = -y + \frac{1}{2}(f_{20}x^2 + 2f_{11}xy + f_{02}y^2)$$
$$\dot{y} = \quad x + \frac{1}{2}(g_{20}x^2 + 2g_{11}xy + g_{02}y^2)$$

$$\begin{aligned}
\ell_2(0) = {} & 5f_{11}f_{02}^3 + 5g_{02}f_{02}^3 - 9f_{11}f_{20}f_{02}^2 - 14f_{20}g_{02}f_{02}^2 - 6f_{11}g_{11}f_{02}^2 - 11g_{02}g_{11}f_{02}^2 \\
& + 5f_{20}g_{20}f_{02}^2 + 5g_{11}g_{20}f_{02}^2 - 24f_{11}^3f_{02} - 43g_{02}^3f_{02} - 57f_{11}f_{20}^2f_{02} - 133f_{11}g_{02}^2f_{02} \\
& - 32f_{11}g_{11}^2f_{02} - 6g_{02}g_{11}^2f_{02} - 5f_{11}g_{20}^2f_{02} - 5g_{02}g_{20}^2f_{02} - 114f_{11}^2g_{02}f_{02} - 53f_{20}^2g_{02}f_{02} \\
& - 84f_{11}f_{20}g_{11}f_{02} - 54f_{20}g_{02}g_{11}f_{02} - 22f_{11}^2g_{20}f_{02} + 20f_{20}^2g_{20}f_{02} - 20g_{02}^2g_{20}f_{02} \\
& + 22g_{11}^2g_{20}f_{02} - 42f_{11}g_{02}g_{20}f_{02} + 42f_{20}g_{11}g_{20}f_{02} - 43f_{11}f_{20}^3 + 6f_{20}g_{02}^3 + 24g_{02}g_{11}^3 \\
& - 5f_{20}g_{20}^3 - 5g_{11}g_{20}^3 - 53f_{11}f_{20}g_{02}^2 - 32f_{11}f_{20}g_{11}^2 + 86f_{20}g_{02}g_{11}^2 + 11f_{11}f_{20}g_{20}^2 \\
& + 14f_{20}g_{02}g_{20}^2 + 6f_{11}g_{11}g_{20}^2 + 9g_{02}g_{11}g_{20}^2 - 24f_{11}^3f_{20} - 6f_{20}^3g_{02} - 86f_{11}^2f_{20}g_{02} \\
& + 43g_{02}^3g_{11} - 78f_{11}f_{20}^2g_{11} + 78f_{11}g_{02}^2g_{11} + 32f_{11}^2g_{02}g_{11} + 53f_{20}^2g_{02}g_{11} + 43f_{20}^3g_{20} \\
& + 24g_{11}^3g_{20} + 53f_{20}g_{02}^2g_{20} + 114f_{20}g_{11}^2g_{20} + 6f_{11}^2f_{20}g_{20} + 54f_{11}f_{20}g_{02}g_{20} \\
& + 32f_{11}^2g_{11}g_{20} + 133f_{20}^2g_{11}g_{20} + 57g_{02}^2g_{11}g_{20} + 84f_{11}g_{02}g_{11}g_{20}
\end{aligned}$$

$\ell_2(0)$ in nD (quadratic case)

$f(x,0) = Ax + \frac{1}{2}B(x,x) \Longrightarrow \ell_2(0) = \frac{1}{12\omega}\operatorname{Re} c_2$, where

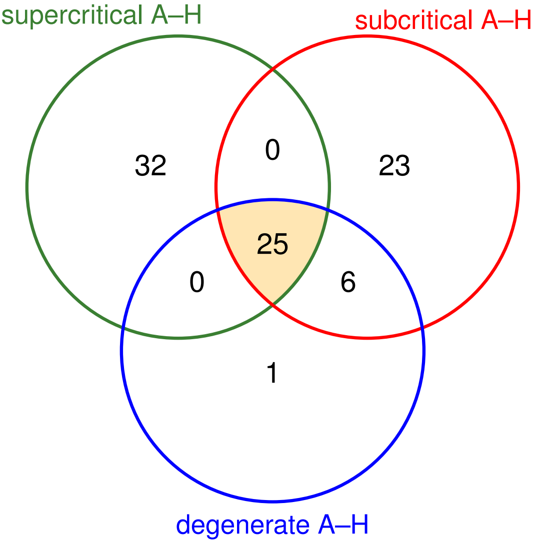
$$
\begin{aligned}
c_2 &= \langle p, 2B(\overline{q}, h_{31}) + 3B(q, h_{22}) + B(\overline{h_{20}}, h_{30}) + 3B(\overline{h_{21}}, h_{20}) + 6B(h_{11}, h_{21})\rangle \\
h_{20} &= (2\omega i \operatorname{Id} - A)^{-1} B(q,q) \\
h_{11} &= -A^{-1} B(q, \overline{q}) \\
c_1 &= \tfrac{1}{2}\langle p, 2B(q, h_{11}) + B(\overline{q}, h_{20})\rangle \\
h_{21} &: \begin{bmatrix} \omega i \operatorname{Id} - A & q \\ \overline{p}^\top & 0 \end{bmatrix} \begin{bmatrix} h_{21} \\ s \end{bmatrix} = \begin{bmatrix} 2B(q, h_{11}) + B(\overline{q}, h_{20}) - 2c_1 q \\ 0 \end{bmatrix} \\
h_{30} &= 3(3\omega i \operatorname{Id} - A)^{-1} B(q, h_{20}) \\
h_{31} &= (2\omega i \operatorname{Id} - A)^{-1}(3B(h_{20}, h_{11}) + B(\overline{q}, h_{30}) + 3B(q, h_{21}) - 6c_1 h_{20}) \\
h_{22} &= -A^{-1}(2B(h_{11}, h_{11}) + 2B(q, \overline{h_{21}}) + 2B(\overline{q}, h_{21}) + B(\overline{h_{20}}, h_{20}))
\end{aligned}
$$

(recall: $\pm\omega i \in \sigma(A)$, $Aq = \omega i q$, $A^\top p = -\omega i p$, $\langle p, q\rangle = 1$)

details: http://www.scholarpedia.org/article/Bautin_bifurcation

(by Guckenheimer and Kuznetsov)

THEOREM (BANAJI–BB 2023): SIGN OF $\ell_2(0)$



all 25: generic Bautin

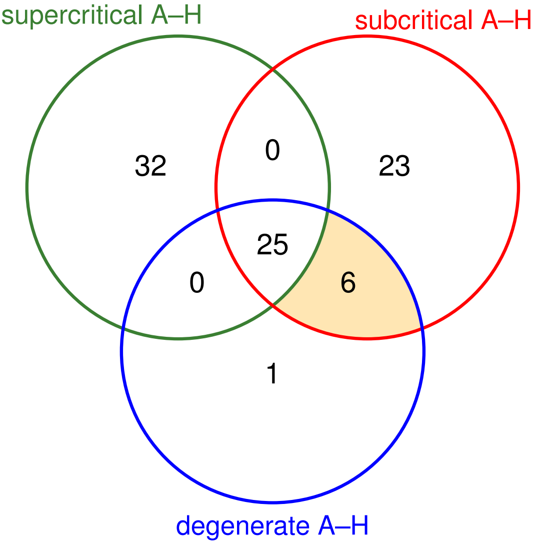
23 of 25: $L_2 < 0$

stable equilibrium
unstable limit cycle
stable limit cycle

2 of 25: $L_2 > 0$

unstable equilibrium
stable limit cycle
unstable limit cycle

Theorem (Banaji–BB 2023): sign of $\ell_2(0)$

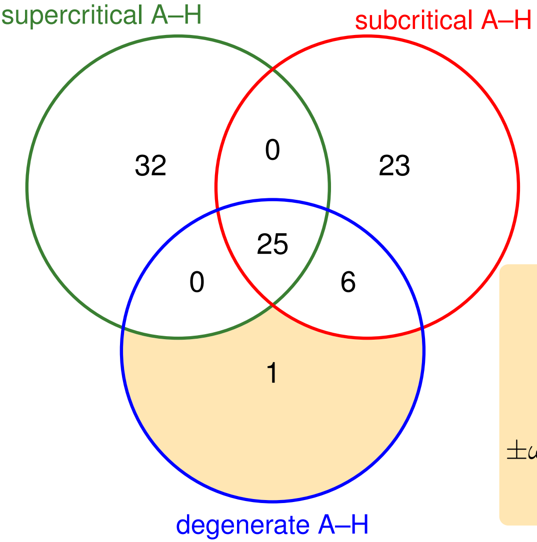


transversality of the Bautin *fails* for all six

for all six: $L_2 < 0$

stable equilibrium
unstable limit cycle
stable limit cycle

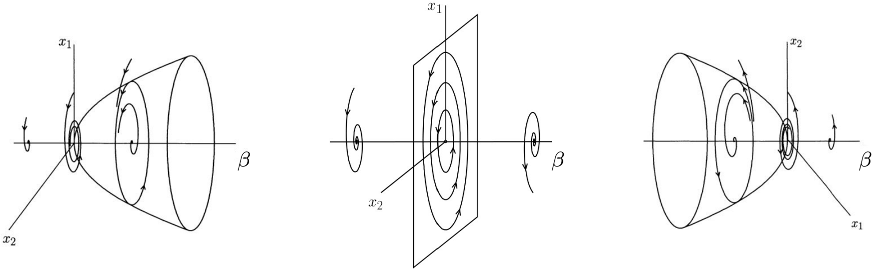
THEOREM (BANAJI–BB 2023): SIGN OF $\ell_2(0)$



$$\mathsf{Z} + \mathsf{X} \longrightarrow 2\mathsf{X}$$
$$\mathsf{X} + \mathsf{Y} \longrightarrow 2\mathsf{Y}$$
$$\mathsf{Y} + \mathsf{Z} \longrightarrow 0 \longrightarrow 2\mathsf{Z}$$

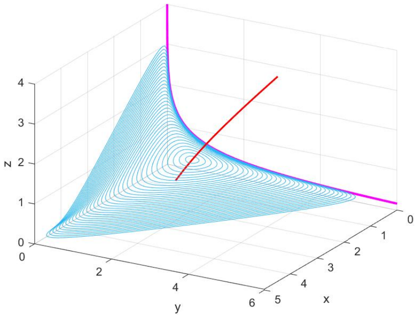
$$\pm\omega i \in \sigma(A) \Rightarrow L_1 = L_2 = 0$$
is it a center?

Vertical Andronov–Hopf bifurcation
[Kuznetsov, Section 3.4]



supercritical A–H	vertical A–H	subcritical A–H
$\ell_1(0) < 0$	$\ell_k(0) = 0$ for all $k \geq 1$	$\ell_1(0) > 0$
stable limit cycle when $\beta > 0$	continuum of periodic orbits at $\beta = 0$	unstable limit cycle when $\beta < 0$

The exceptional network shows a vertical Andronov–Hopf bifurcation



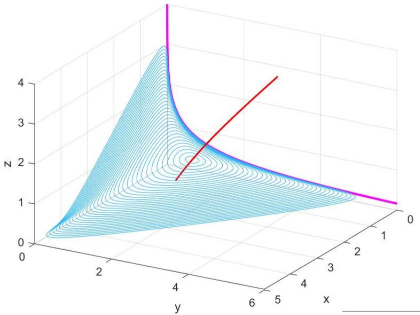
$$Z + X \xrightarrow{\kappa_1} 2X$$

$$X + Y \xrightarrow{\kappa_2} 2Y$$

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

$$\kappa_1 = \kappa_2 + \kappa_3$$

The exceptional network shows a vertical Andronov–Hopf bifurcation



$$Z + X \xrightarrow{\kappa_1} 2X$$

$$X + Y \xrightarrow{\kappa_2} 2Y$$

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

$$\kappa_1 = \kappa_2 + \kappa_3$$

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The smallest bimolecular mass-action system with a vertical Andronov–Hopf bifurcation

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[b] Department of Mathematics, University of Vienna, Austria

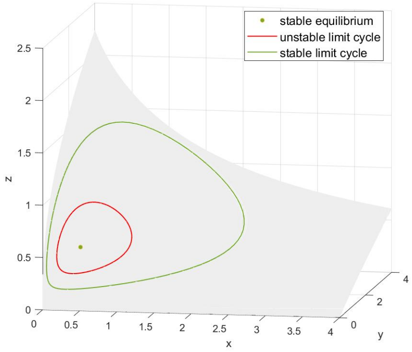
MULTISTABILITY: A STABLE EQUILIBRIUM AND A STABLE LIMIT CYCLE COEXIST

#23

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

$$\dot{x} = \kappa_1 x - \kappa_2 xz$$
$$\dot{y} = 2\kappa_2 xz - \kappa_3 y$$
$$\dot{z} = -\kappa_2 xz + \kappa_3 y - 2\kappa_4 z^2$$

$\kappa_1 = \frac{7235}{10000}$, $\kappa_2 = \frac{4}{3}$, $\kappa_3 = 1$, $\kappa_4 = \frac{1}{2}$



The 86 networks that admit nondegenerate Andronov–Hopf

$L_1 < 0$	1	0 → X	X → Y	Y + Z → 2Z	X + Z → 0
	2	0 → X	X → 2Y	Y + Z → 2Z	X + Z → 0
	3	0 → X	X + Y → 2Y	Y → Z	X + Z → 0
	4	0 → X	X + Y → 2Y	Y → X + Z	X + Z → 0
	5	Z → X + Z	X + Y → 2Y	Y + Z → 0	0 → Z
$L_1 \gtrless 0$	6	0 → X	X + Y → 2Y	Y → 2Z	X + Z → 0
$L_1 > 0$	7	0 → X + Y	X + Z → Y + Z	Y + Z → 2Z	Z → 0
$L_1 \geq 0$	8	0 → X + Y	X + Z → Y	Y + Z → 2Z	Z → 0
	9	0 → X + Y	X + Z → 2Y	Y + Z → 2Z	Z → 0
	10	0 → X	X + Z → Y + Z	Y + Z → 2Z	Z → 0
	11	0 → X	X + Z → 2Y	Y + Z → 2Z	Z → 0
	12	0 → X + Z	X + Y → 2Y	Y → Z	Y + Z → X
	13	0 → X + Z	X + Y → 2Y	Y → 2Z	Y + Z → X

$L_1 < 0$	14	X → 2X	X + Z → Y + Z	Y → 2Z	2Z → 0
	15	X → 2X	X + Z → Y + Z	Y → Z	2Z → 0
	16	X → 2X	X + Z → Y + Z	Y → Z	2Z → Y
	17	X → 2X	X + Z → Y + Z	X + Y → Z	Z → 0
	18	X → 2X	X + Z → Y + Z	X + Y → 2Z	Z → 0
	19	X → 2X	X + Z → Y	X + Y → 2Z	Z → 0
	20	X → 2X	X + Z → 2Y	X + Y → 2Z	Z → 0
	21	X → 2X	X + Z → 2Y	X + Y → Z	Z → 0
$L_1 \gtrless 0$	22	X → 2X	X + Z → 2Y	Y → Z	2Z → Y
	23	X → 2X	X + Z → 2Y	Y → Z	2Z → 0
	24	X → 2X	X + Z → 2Y	Y → 2Z	2Z → 0
	25	X → 2X	X + Z → Y	Y → 2Z	2Z → 0
	26	X → 2X	2X → 2Y	Y → 2Z	X + Z → 0
	27	Z → 2X	X + Y → 2Y	Y → 0	2X → 2Z
$L_1 > 0$	28	Y → 2X	X + Z → Y + Z	2Y → Z	Z → 0
	29	Y → 2X	X + Z → Y + Z	2Y → Z	Z → X
	30	Y → 2X	X + Z → Y + Z	2Y → Z	Z → Y
	31	Y → 2X	X + Z → Y + Z	2Y → X + Z	Z → 0
	32	Y → 2X	X + Z → Y + Z	2Y → 2Z	Z → 0
	33	Y → 2X	X + Z → 2Y	2Y → 2Z	Z → 0
	34	Z → 2X	X + Y → 2Y	Y → Z	2Z → Y

$L_1 < 0$	35	0 → X	2X → Y	Y + Z → 2Z	X + Z → 0
	36	0 → X	2X → 2Y	Y + Z → 2Z	X + Z → 0
	37	0 → X	X + Y → 2Y	Y + Z → 2Z	X + Z → X
	38	0 → X + Y	X + Y → 2Y	Y + Z → 2Z	X + Z → X
	39	0 → X + Z	X + Y → 2Y	Y + Z → Z	X + Z → X

$L_1 < 0$	40	X → 2X	X + Z → Y + Z	2Y → Z	2Z → 0
	41	X → 2X	X + Z → Y + Z	2Y → Z	2Z → Y
	42	X → 2X	X + Z → Y + Z	2Y → Z	2Z → 2Y
	43	X → 2X	X + Z → Y + Z	2Y → Z	Y + Z → 0
	44	X → 2X	X + Z → Y + Z	2Y → Z	Y + Z → Y
	45	X → 2X	X + Z → Y + Z	2Y → Z	Y + Z → 2Y
	46	X → 2X	X + Z → Y + Z	2Y → 2Z	2Z → 0
	47	X → 2X	X + Z → Y + Z	2Y → 2Z	2Z → Y
	48	X → 2X	X + Z → Y + Z	2Y → 2Z	Y + Z → 0
	49	X → 2X	X + Z → Y + Z	2Y → 2Z	Y + Z → Y
	50	X → 2X	X + Z → Y + Z	Y + Z → 2Z	2Z → 0
	51	X → 2X	X + Z → Y + Z	Y + Z → 2Z	2Z → Y
	52	X → 2X	2X → Y	Y + Z → 2Z	X + Z → 0
	53	X → 2X	2X → 2Y	Y + Z → 2Z	X + Z → 0
$L_1 \gtrless 0$	54	X → 2X	X + Y → 2Y	2Y → Z	X + Z → Y
	55	X → 2X	X + Z → Y	X + Y → 2Z	2Z → 0
	56	X → 2X	X + Z → Y	X + Y → 2Z	Y + Z → Y
	57	X → 2X	X + Z → 2Y	2Y → 2Z	2Z → 0
	58	X → 2X	X + Z → 2Y	2Y → 2Z	2Z → Y
	59	X → 2X	X + Z → 2Y	2Y → 2Z	Y + Z → 0
	60	X → 2X	X + Z → 2Y	2Y → 2Z	Y + Z → Y
	61	X → 2X	X + Z → 2Y	X + Y → Z	2Z → 0
	62	X → 2X	X + Z → 2Y	X + Y → Z	2Z → Y
	63	X → 2X	X + Z → 2Y	X + Y → Z	Y + Z → Y
	64	X → 2X	X + Z → 2Y	X + Y → 2Z	2Z → 0
	65	X → 2X	X + Z → 2Y	X + Y → 2Z	Y + Z → Y
	66	X → 2X	X + Z → 2Y	X + Y → X + Z	Y + Z → 0
	67	X → 2X	X + Z → Y + Z	X + Y → Z	2Z → 0
	68	X → 2X	X + Z → Y + Z	X + Y → Z	2Z → Y
	69	X → 2X	X + Z → Y + Z	X + Y → Z	Y + Z → Y
	70	X → 2X	X + Z → Y + Z	X + Y → 2Z	2Z → 0
	71	X → 2X	X + Z → Y + Z	X + Y → 2Z	Y + Z → Y
$L_1 > 0$	72	X → 2X	X + Z → 2Y	2Y → 0	X + Y → X + Z
	73	X → 2X	X + Z → 2Y	Y + Z → Z	X + Y → X + Z
	74	X → 2X	X + Z → 2Y	Y + Z → Z	2Y → 2Z
	75	X → 2X	X + Z → 2Y	Y + Z → 2Z	2Z → 0
	76	X → 2X	X + Z → 2Y	Y + Z → 2Z	2Z → Y
	77	X → 2X	X + Z → Y + Z	2Y → X + Z	Y + Z → 0
	78	X → 2X	X + Y → 2Y	2Y → Z	X + Z → 0
	79	X → 2X	X + Y → 2Y	2Y → 2Z	X + Z → 0
	80	Y → 2X	2X → 2Y	Y + Z → 2Z	X + Z → 0
	81	Y → 2X	X + Z → 2Y	Y + Z → 2Z	2Z → 0
	82	Y → X + Y	2X → Y + Z	Y + Z → Z	X + Z → 0
	83	Y → X + Y	2X → Y + Z	Y + Z → 2Z	X + Z → 0
	84	Y → X + Y	2X → Y	Y + Z → 2Z	X + Z → 0
	85	Y → X + Y	2X → 2Y	Y + Z → 2Z	X + Z → 0
	86	Z → X + Z	2X → Y + Z	X + Y → 0	Y + Z → X + Y

Rank-two, bimolecular-sourced oscillators

Theorem (Póta 1985, BB–Hofbauer 2022)

bimolecular, isolated periodic orbit exists $\Longrightarrow$ rank ≥ 3

$$\begin{aligned} \mathsf{X} &\longrightarrow 2\mathsf{X} \longrightarrow 3\mathsf{X} \\ \mathsf{X}+\mathsf{Y} &\longrightarrow 2\mathsf{Y} \\ \mathsf{Y} &\rightleftarrows 0 \end{aligned}$$

Frank-Kamenetsky–Salnikov 1943

bimolecular-sourced

Andronov–Hopf

Rank-two, bimolecular-sourced oscillators

Theorem (Póta 1985, BB–Hofbauer 2022)

bimolecular, isolated periodic orbit exists $\Longrightarrow$ *rank* ≥ 3

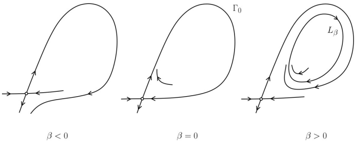
$$\begin{aligned} X &\longrightarrow 2X \longrightarrow 3X \\ X+Y &\longrightarrow 2Y \\ Y &\rightleftarrows 0 \end{aligned}$$

Frank-Kamenetsky–Salnikov 1943
bimolecular-sourced
Andronov–Hopf

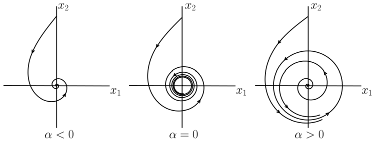
Papers on rank-two, bimolecular-sourced mass-action systems:

- Banaji–BB–Hofbauer
  Oscillations in three-reaction quadratic mass-action systems
  Studies in Applied Mathematics, 2024
- Banaji–BB–Hofbauer
  Bifurcations in planar, quadratic mass-action networks with few reactions and low molecularity
  In preparation, 2024

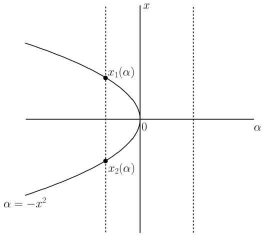
BOGDANOV–TAKENS BIFURCATION [KUZNETSOV, CHAPTERS 3, 6, 8]



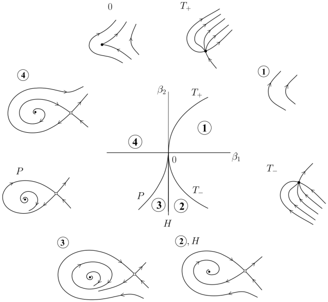
homoclinic



Andronov–Hopf



fold (a.k.a. saddle-node)

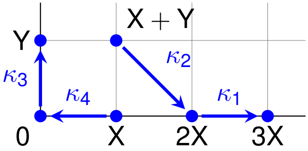


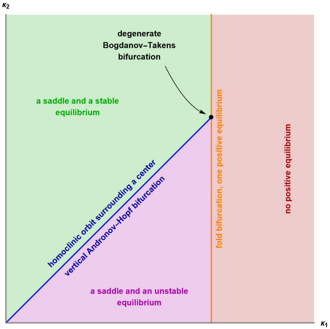
Bogdanov–Takens

The smallest planar, quadratic networks admitting Bogdanov–Takens bifurcation

supercritical B–T	1	$2X \to 3X$	$X + Y \to 2Y$	$Y \to 0$	$0 \to Y$
	2	$2X \to 3X$	$X + Y \to 3Y$	$Y \to 0$	$0 \to Y$
	3	$2X \to 3X$	$X + Y \to 2Y$	$Y \to 0$	$X \to Y$
	4	$2X \to 3X$	$X + Y \to 3Y$	$Y \to 0$	$X \to Y$
	5	$2X \to 3X$	$X + Y \to 2Y$	$Y \to 0$	$X \to 2Y$
	6	$2X \to 3X$	$X + Y \to 3Y$	$Y \to 0$	$X \to 2Y$
	7	$2X \to 3X$	$X + Y \to 2Y$	$Y \to 0$	$X \to 3Y$
	8	$2X \to 3X$	$X + Y \to 3Y$	$Y \to 0$	$X \to 3Y$
vertical B–T	9	$2X \to 3X$	$X + Y \to 2X$	$0 \to Y$	$X \to 0$
	10	$2X \to 3X$	$X + Y \to 3X$	$0 \to Y$	$X \to 0$
subcritical B–T	11	$2X \to 3X$	$X + Y \to 2X$	$0 \to X + 2Y$	$X \to 0$
	12	$2X \to 3X$	$X + Y \to 3X$	$0 \to X + 2Y$	$X \to 0$
	13	$2X \to 3X$	$X + Y \to 2X$	$0 \to X + Y$	$X \to 0$
	14	$2X \to 3X$	$X + Y \to 3X$	$0 \to X + Y$	$X \to 0$
	15	$2X \to 3X$	$X + Y \to 2X$	$0 \to 2X + Y$	$X \to 0$
	16	$2X \to 3X$	$X + Y \to 3X$	$0 \to 2X + Y$	$X \to 0$
	17	$2X \to 3X$	$X + Y \to X$	$Y \to X + 2Y$	$X \to Y$
	18	$2X \to 3X$	$X + Y \to X$	$Y \to X + 2Y$	$X \to 2Y$
	19	$2X \to 3X$	$X + Y \to X$	$Y \to X + 2Y$	$X \to 3Y$
	20	$2X \to 3X$	$X + Y \to 0$	$Y \to 2X$	$X \to 2Y$
	21	$2X \to 3X$	$X + Y \to 0$	$Y \to 3X$	$X \to 2Y$
	22	$2X \to 3X$	$X + Y \to 0$	$Y \to X$	$X \to 3Y$
	23	$2X \to 3X$	$X + Y \to 0$	$Y \to 2X$	$X \to 3Y$
	24	$2X \to 3X$	$X + Y \to 0$	$Y \to 3X$	$X \to 3Y$
	25	$2X \to 3X$	$X + Y \to 0$	$Y \to X$	$X \to X + Y$
	26	$2X \to 3X$	$X + Y \to 0$	$Y \to 2X$	$X \to X + Y$
	27	$2X \to 3X$	$X + Y \to 0$	$Y \to 3X$	$X \to X + Y$
	28	$2X \to 3X$	$X + Y \to Y$	$2Y \to 0$	$X \to 2X + Y$
	29	$2X \to 3X$	$X + Y \to Y$	$2Y \to X$	$X \to 2X + Y$
	30	$2X \to 3X$	$X + Y \to Y$	$2Y \to 2X$	$X \to 2X + Y$
	31	$2X \to 3X$	$X + Y \to Y$	$2Y \to 3X$	$X \to 2X + Y$
	32	$2X \to 3X$	$X + Y \to Y$	$2Y \to 2X + Y$	$X \to 2X + Y$
	33	$2X \to 3X$	$X + Y \to 2Y$	$2Y \to 0$	$0 \to X + 2Y$

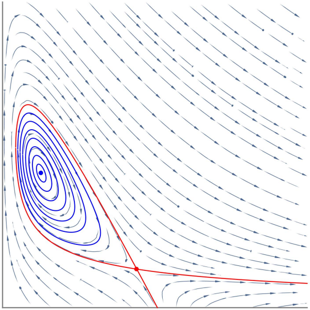
Vertical Bogdanov–Takens bifurcation





bifurcation diagram

(κ_3, κ_4 fixed)



phase portrait

($4\kappa_1\kappa_4 < \kappa_3^2$ and $\kappa_1 = \kappa_2$)

Inheritance results...

- ...infer **dynamical behaviours** in networks from **subnetworks**.
- ...give us a **partial ordering** on 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.

Enlargements

$$\mathsf{X} \longrightarrow \mathsf{Y}$$
$$2\mathsf{X} + \mathsf{Y} \longrightarrow 3\mathsf{X}$$

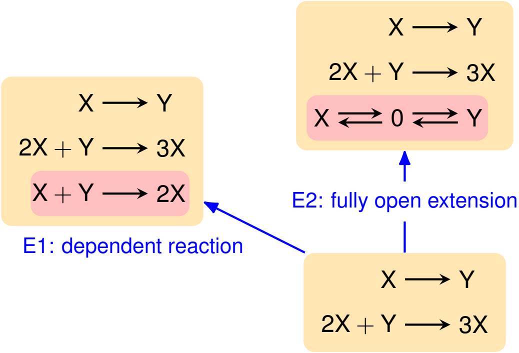
Enlargements

$$\begin{aligned} X &\longrightarrow Y \\ 2X + Y &\longrightarrow 3X \\ X + Y &\longrightarrow 2X \end{aligned}$$

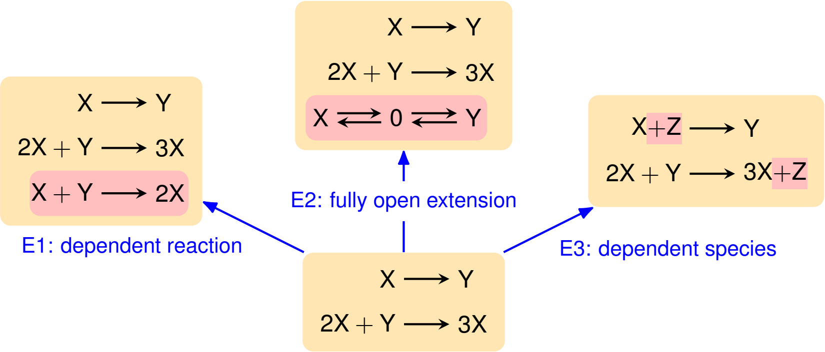
E1: dependent reaction

$$\begin{aligned} X &\longrightarrow Y \\ 2X + Y &\longrightarrow 3X \end{aligned}$$

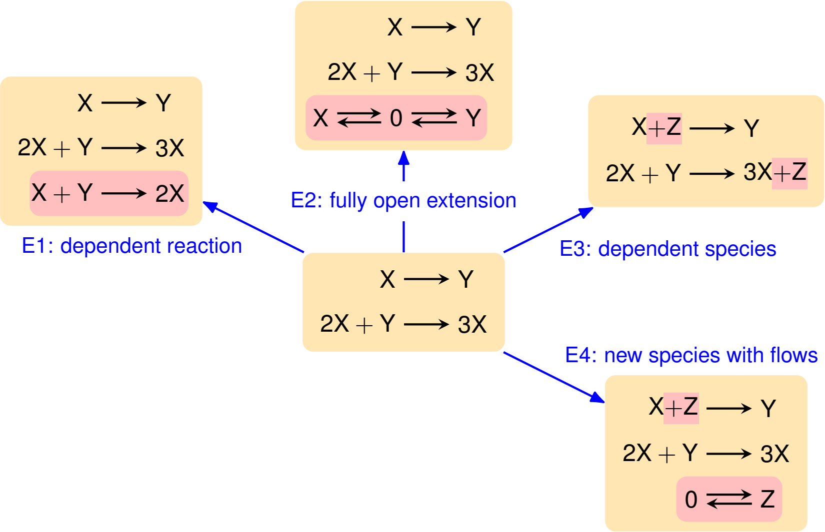
ENLARGEMENTS



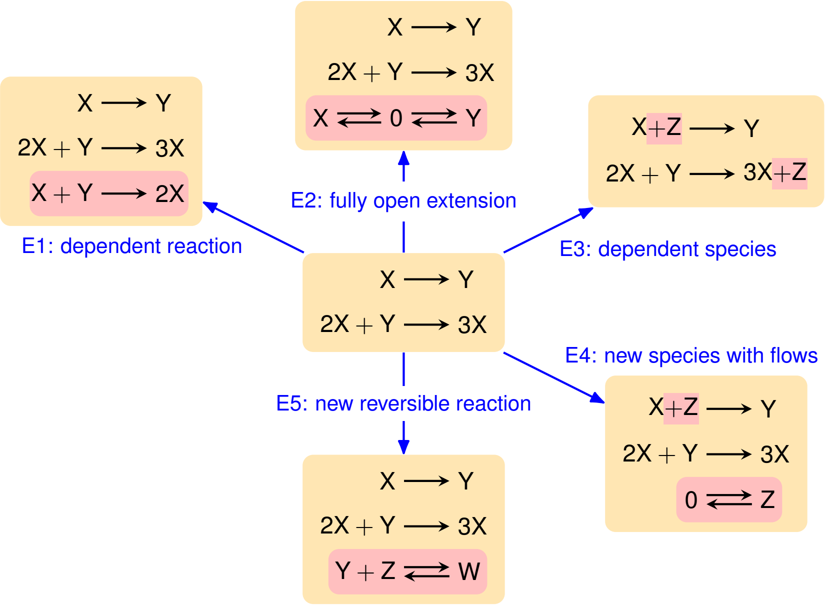
ENLARGEMENTS



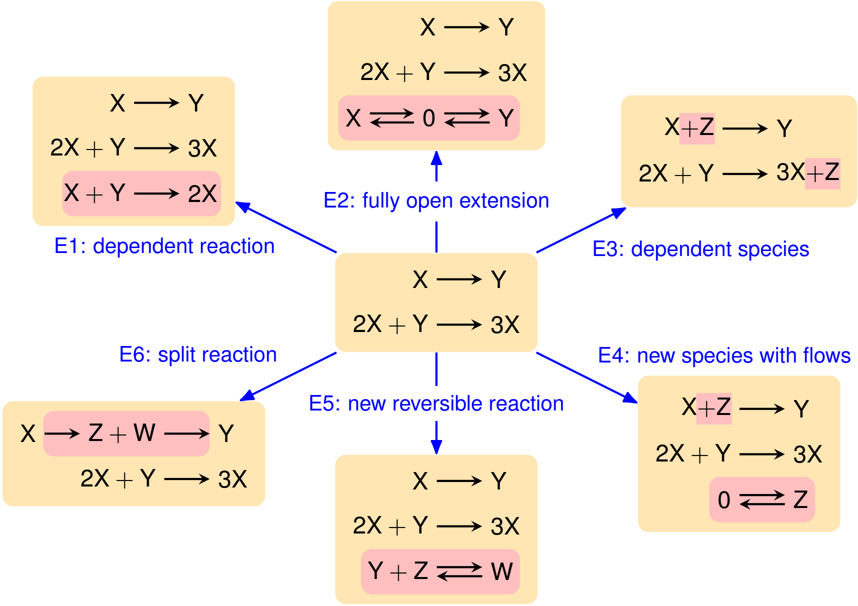
ENLARGEMENTS



ENLARGEMENTS



ENLARGEMENTS (NOT EXHAUSTIVE)



The Inheritance Theorem

- E1 A new linearly dependent reaction.
- E2 The fully open extension.
- E3 A new linearly dependent species.
- E4 A new species and its inflow-outflow.
- E5 New reversible reactions involving new species.
- E6 Splitting reactions.

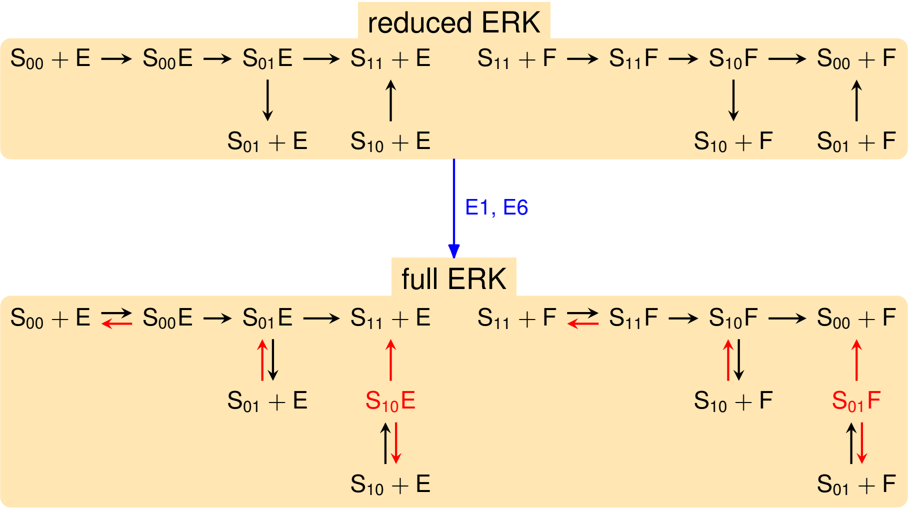
Theorem (Banaji et al.)

E1–E6 preserve equilibria, periodic orbits, and bifurcations

Proof

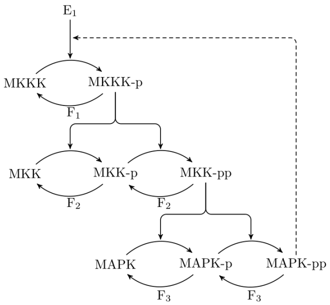
Apply regular (E1, E2, E3) or singular (E4, E5, E6) perturbation theory.
Very technical. □

Phosphorylation and dephosphorylation of extracellular signal-regulated kinase (ERK)



the full ERK inherits the oscillation that is present in the reduced ERK

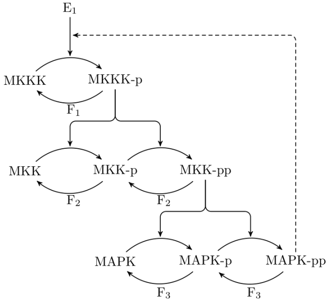
Mitogen-activated protein kinase (MAPK) cascade with negative feedback



$n = 24$, $m = 36$, $r = 17$ (stable oscillation)

$$\begin{aligned}
&E_1 + Z \rightleftharpoons E_1\text{–}Z \rightarrow E_1 + Z\text{-p},\\
&F_1 + Z\text{-p} \rightleftharpoons F_1\text{–}Z\text{-p} \rightarrow F_1 + Z\\
&Z\text{-p} + Y \rightleftharpoons Z\text{-p–}Y \rightarrow Z\text{-p} + Y\text{-p} \rightleftharpoons Z\text{-p–}Y\text{-p} \rightarrow Z\text{-p} + Y\text{-pp}\\
&F_2 + Y\text{-pp} \rightleftharpoons F_2\text{–}Y\text{-pp} \rightarrow F_2 + Y\text{-p} \rightleftharpoons F_2\text{–}Y\text{-p} \rightarrow F_2 + Y\\
&Y\text{-pp} + X \rightleftharpoons Y\text{-pp–}X \rightarrow Y\text{-pp} + X\text{-p} \rightleftharpoons Y\text{-pp–}X\text{-p} \rightarrow Y\text{-pp} + X\text{-pp}\\
&F_3 + X\text{-pp} \rightleftharpoons F_3\text{–}X\text{-pp} \rightarrow F_3 + X\text{-p} \rightleftharpoons F_3\text{–}X\text{-p} \rightarrow F_3 + X\\
&E_1 + X\text{-pp} \rightleftharpoons E_1\text{–}X\text{-pp}\\
&E_1\text{–}X\text{-pp} + Z \rightleftharpoons E_1\text{–}X\text{-pp–}Z\\
&E_1\text{–}X\text{-pp–}Z \rightleftharpoons E_1\text{–}Z + X\text{-pp}.
\end{aligned}$$

Mitogen-activated protein kinase (MAPK) cascade with negative feedback



$n = 24$, $m = 36$, $r = 17$ (stable oscillation)

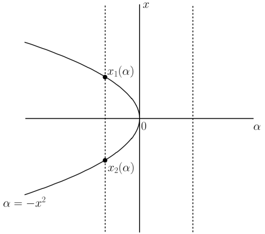
$E_1 + Z \rightleftharpoons E_1\text{–}Z \to E_1 + Z\text{-p},$
$F_1 + Z\text{-p} \rightleftharpoons F_1\text{–}Z\text{-p} \to F_1 + Z$
$Z\text{-p} + Y \rightleftharpoons Z\text{-p–}Y \to Z\text{-p} + Y\text{-p} \rightleftharpoons Z\text{-p–}Y\text{-p} \to Z\text{-p} + Y\text{-pp}$
$F_2 + Y\text{-pp} \rightleftharpoons F_2\text{–}Y\text{-pp} \to F_2 + Y\text{-p} \rightleftharpoons F_2\text{–}Y\text{-p} \to F_2 + Y$
$Y\text{-pp} + X \rightleftharpoons Y\text{-pp–}X \to Y\text{-pp} + X\text{-p} \rightleftharpoons Y\text{-pp–}X\text{-p} \to Y\text{-pp} + X\text{-pp}$
$F_3 + X\text{-pp} \rightleftharpoons F_3\text{–}X\text{-pp} \to F_3 + X\text{-p} \rightleftharpoons F_3\text{–}X\text{-p} \to F_3 + X$
$E_1 + X\text{-pp} \rightleftharpoons E_1\text{–}X\text{-pp}$
$E_1\text{–}X\text{-pp} + Z \rightleftharpoons E_1\text{–}X\text{-pp–}Z$
$E_1\text{–}X\text{-pp–}Z \rightleftharpoons E_1\text{–}Z + X\text{-pp}.$

E1, E3, E5, E6

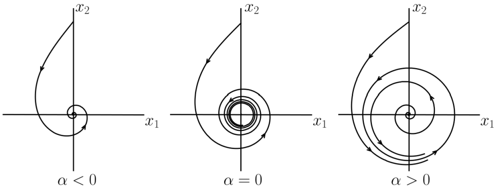
$n = 8$, $m = 14$, $r = 8$ (stable oscillation)

$E_1 \to E_1 + Z\text{-p},$
$Z\text{-p} \to 0$
$Z\text{-p} \to Z\text{-p} + Y\text{-p} \to Z\text{-p} + Y\text{-pp}$
$F_2 + Y\text{-pp} \to F_2 + Y\text{-p} \to 0 \to F_2$
$Y\text{-pp} + X \to Y\text{-pp} + X\text{-p} \to Y\text{-pp} + X\text{-pp}$
$X\text{-pp} \to 0 \to X\text{-p} \to X$
$E_1 + X\text{-pp} \rightleftharpoons 0$

Codimension-one bifurcations of equilibria [Kuznetsov, Chapter 3]

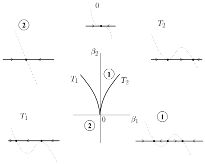


fold (a.k.a. saddle-node)

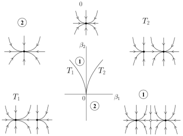


Andronov–Hopf

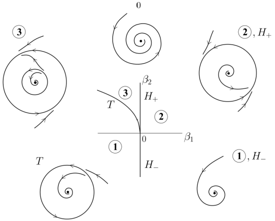
Codimension-two bifurcations of equilibria (in scalar or planar ODEs) [Kuznetsov, Chapter 8]



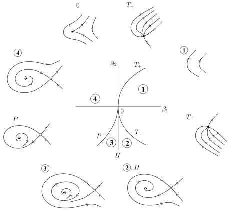
cusp (in 1d)



cusp (in 2d)



Bautin



Bogdanov–Takens

The homogenised Brusselator

Banaji–BB–Hofbauer 2022

$$\mathsf{X} \longrightarrow \mathsf{Y}$$
$$2\mathsf{X} + \mathsf{Y} \longrightarrow 3\mathsf{X}$$

fold

$$0 \rightleftarrows \mathsf{X} \longrightarrow \mathsf{Y}$$
$$2\mathsf{X} + \mathsf{Y} \longrightarrow 3\mathsf{X}$$

Andronov–Hopf

The homogenised Brusselator

Banaji–BB–Hofbauer 2022

$$\mathsf{X} \longrightarrow \mathsf{Y}$$
$$2\mathsf{X} + \mathsf{Y} \longrightarrow 3\mathsf{X}$$

fold

E5

$$\mathsf{Z} \rightleftarrows \mathsf{X} \longrightarrow \mathsf{Y}$$
$$2\mathsf{X} + \mathsf{Y} \longrightarrow 3\mathsf{X}$$

fold
Andronov–Hopf
Bogdanov–Takens
(⇒ homoclinic)
Bautin
(⇒ fold of limit cycles)

E3

$$0 \rightleftarrows \mathsf{X} \longrightarrow \mathsf{Y}$$
$$2\mathsf{X} + \mathsf{Y} \longrightarrow 3\mathsf{X}$$

Andronov–Hopf

The homogenised Brusselator

Banaji–BB–Hofbauer 2022

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

fold

E5

E3

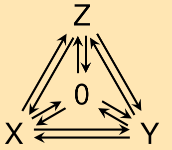
$$0 \rightleftarrows X \longrightarrow Y$$
$$2X + Y \longrightarrow 3X$$

Andronov–Hopf

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

fold
Andronov–Hopf
Bogdanov–Takens
(⇒ homoclinic)
Bautin
(⇒ fold of limit cycles)

E1, E2



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

fold
Andronov–Hopf
Bogdanov–Takens
(⇒ homoclinic)
Bautin
(⇒ fold of limit cycles)

Analysis of large networks: the long-term goal

- build a directory of **motifs/atoms**:

  classify small networks with certain behaviours

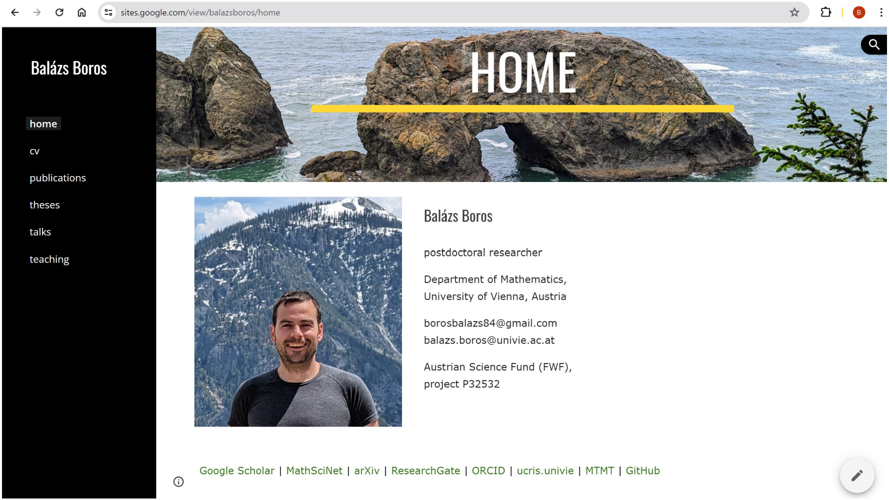
- establish **inheritance results**:

  infer behaviours in large network from subnetworks

- develop **algorithms**:

  find motifs/atoms of certain behaviours in a large network

My homepage


sites.google.com/view/balazsboros/home
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project P32532
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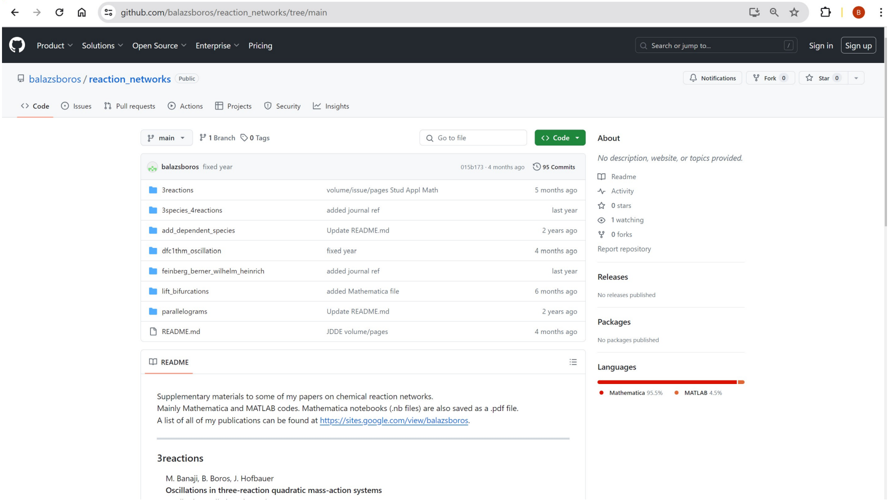
My GitHub


github.com/balazsboros/reaction_networks/tree/main
Product
Solutions
Open Source
Enterprise
Pricing
Search or jump to...
Sign in
Sign up
balazsboros / reaction_networks
Public
Notifications
Fork 0
Star 0
Code
Issues
Pull requests
Actions
Projects
Security
Insights
main
1 Branch
0 Tags
Go to file
Code
balazsboros fixed year
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95 Commits
3reactions
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parallelograms
Update README.md
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README.md
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README
Supplementary materials to some of my papers on chemical reaction networks.
Mainly Mathematica and MATLAB codes. Mathematica notebooks (.nb files) are also saved as a .pdf file.
A list of all of my publications can be found at https://sites.google.com/view/balazsboros.
3reactions
M. Banaji, B. Boros, J. Hofbauer
Oscillations in three-reaction quadratic mass-action systems
About
No description, website, or topics provided.
Readme
Activity
0 stars
1 watching
0 forks
Report repository
Releases
No releases published
Packages
No packages published
Languages
Mathematica 95.5%
MATLAB 4.5%

COMPUTING THE FOCAL VALUES IN MATHEMATICA

```
(* F[i,j] computes the polynomial F_i(h_j) *)
F[i_, j_] := Module[{coeffs, M, mtx},
   coeffs = CoefficientList[D[R_i h_j, {z, 1}], {z, w}];
   M = Dimensions[coeffs][[1]] - 1;
   mtx = (coeffs + Transpose[coeffs*]) Table[If[k + l == M && k ≠ l, 1/(k - l), 0], {k, 0, M}, {l, 0, M}];
   I z^Range[0,M] . mtx . w^Range[0,M]
  ];

(* H[k,j] computes H_k(h_j), note that one of k and j is even, the other one is odd in all of the interesting cases *)
H[k_, j_] := Module[{coeffs},
   coeffs = CoefficientList[h_j, {z, w}];
   Sum[Coefficient[R_k, z^a w^(k-a)] × coeffs[[((k - 2 a + 1) + j)/2 + 1, (j - (k - 2 a + 1))/2 + 1]], {a, (k + 1 - j)/2, (k + 1 + j)/2}]
  ];
```

```
(* compute the focal values L_1,L_2,...,L_m *)
FocalValues[m_, coefficient_, isquadratic_] := Module[{cd, R2cd, coeffsxy, cond, cd2FG, Ls, quadratic, FG2fg},

   (* coefficient is either "Taylor" (F_ij and G_ij) or "derivative" (f_ij and g_ij), where F_ij=f_ij/(i!j!) and G_ij=g_ij/(i!j!); default is Taylor *)

   cd = {}; R2cd = {};
   For[k = 2, k ≤ 2 m + 1, k++, For[i = 0, i ≤ k, i++, {cd = Join[cd, {c_k,i, d_k,i}], R2cd = Join[R2cd, {R_k,i → c_k,i + d_k,i I}]}]];
   coeffsxy = CoefficientList[ComplexExpand[Sum[Sum[R_k,i z^(k-i) (z*)^i, {i, 0, k}], {k, 2, 2 m + 1}] /. R2cd /. {z → x + y I}], {x, y}];
   cond = True;
   For[k = 2, k ≤ 2 m + 1, k++, {
      For[i = 0, i ≤ k, i++, {
         cond = cond && (F_i,k-i == ComplexExpand[Re[coeffsxy[[i + 1, k - i + 1]]]]) && (G_i,k-i == ComplexExpand[Im[coeffsxy[[i + 1, k - i + 1]]]])
        }];
    }];
   cd2FG = Solve[cond, cd][[1]];
   If[isquadratic, {
     quadratic = {};
     For[i = 0, i ≤ 2 m + 1, i++, For[j = 0, j ≤ 2 m + 1 - i, j++, If[i + j ≥ 3, quadratic = Join[quadratic, {F_i,j → 0, G_i,j → 0}]]]];
     cd2FG = cd2FG /. quadratic;
    }];

   For[k = 2, k ≤ 2 m + 1, k++, R_k = Sum[R_k,i z^(k-i) w^i, {i, 0, k}]];

   h_0 = 1;
   For[k = 1, k ≤ 2 m - 1, k++, h_k = Sum[F[k + 1 - l, l], {l, 0, k - 1}]];

   Ls = ConstantArray[Null, m];
   For[j = 1, j ≤ m, j++, {
     Ls[[j]] = Simplify[ComplexExpand[2 π Re[Sum[H[2 j + 1 - l, l], {l, 0, 2 j - 1}]] /. R2cd /. cd2FG]];
    }];
   If[coefficient == "derivatives", {
     FG2fg = {};
     For[i = 0, i ≤ 2 m + 1, i++, For[j = 0, j ≤ 2 m + 1 - i, j++, FG2fg = Join[FG2fg, {F_i,j → f_i,j/(i! j!), G_i,j → g_i,j/(i! j!)}]]];
     Ls = Simplify[Ls /. FG2fg];
    }];
   Ls
  ];

{L_1, L_2, L_3} = FocalValues[3, "derivatives", True];
```