OVERVIEW TALK ON THE DYNAMIC ASPECTS OF DETERMINISTIC MASS-ACTION SYSTEMS

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Advances in Chemical Reaction Network Theory workshop at the Erwin Schrödinger International Institute for Mathematics and Physics (ESI) Vienna, Austria, October 15-19, 2018
Dynamical properties

- bounded solutions
- finite time blow-up
- persistence
- permanence
- local/global asymptotic stability
- local/global centers
- limit cycles
- multistability
- ...

...
**Mass-action ODE**

- ODE

\[
\dot{x}(\tau) = YA_\kappa x(\tau)^Y = \Gamma v_\kappa(x(\tau)) \quad \text{with state space } \mathbb{R}^n_+ \text{ or } \mathbb{R}^n_{\geq 0}
\]

- positive and boundary equilibria

\[
E_+ = \{ x \in \mathbb{R}^n_+ \mid YA_\kappa x^Y = 0 \}
\]

\[
E_0 = \{ x \in \partial \mathbb{R}^n_{\geq 0} \mid YA_\kappa x^Y = 0 \}
\]

- positive stoichiometric class

\[
\mathcal{P} = (p + \text{ran } \Gamma) \cap \mathbb{R}^n_+ \quad \text{for some } p \in \mathbb{R}^n_+
\]

- stoichiometric class

\[
\overline{\mathcal{P}} = (p + \text{ran } \Gamma) \cap \mathbb{R}^n_{\geq 0} \quad \text{for some } p \in \mathbb{R}^n_{\geq 0}
\]
**Deficiency-Zero Theorem**

**Theorem (Feinberg, Horn, Jackson, 1972)**

\[ WR, \delta = 0 \implies \]

- all solutions are bounded
- there is no periodic solution
- \( E_+ \neq \emptyset \)
- \( E_+ = \{ x \in \mathbb{R}_+^n \mid \log x - \log x^* \in (\text{ran} \, \Gamma)^\perp \} \) for each \( x^* \in E_+ \)
- \( |E_+ \cap \mathcal{P}| = 1 \) for each \( \mathcal{P} \) (denote the unique element by \( \bar{x} \))
- \( \bar{x} \) is locally asymptotically stable relative to \( \mathcal{P} \)

all of the assumptions (i.e., WR and \( \delta = 0 \)) are on the network, thus, the conclusions hold for all \( \kappa \)

**Conjecture (Horn, 1974)**

even **global** asymptotic stability holds in the above theorem
Deficiency-One Theorem

**Theorem (Feinberg, 1979)**

$W_{R}, \ell = 1, \delta = 1 \implies$

- $E_{+} \neq \emptyset$

- $E_{+} = \{ x \in \mathbb{R}^{n}_{+} \mid \log x - \log x^{*} \in (\text{ran } \Gamma)^{\perp} \}$ for each $x^{*} \in E_{+}$

- $|E_{+} \cap \mathcal{P}| = 1$ for each $\mathcal{P}$

- the result is independent of $\kappa$

- no general result on the dynamics

- examples are known with unstable $\bar{x}$ and a stable limit cycle (Andronov-Hopf bifurcation)
**Complex balanced (CB) equilibria**

\[ E^\text{CB}_+ = \{ x \in \mathbb{R}^n_+ \mid A_\kappa x^Y = 0 \} \]

**Theorem (Horn, Jackson, 1972)**

- \( E^\text{CB}_+ \neq \emptyset \implies \)
  - WR
  - \( E_+ = E^\text{CB}_+ \)
  - *all the conclusions of the Deficiency-Zero Theorem hold true*

- whether a WR system with \( \delta > 0 \) is CB or not depends on \( \kappa \)
- Global Attractor Conjecture (GAC) for complex balanced systems (Craciun, Dickenstein, Shiu, Sturmfels, 2009)
- convergence to the set \( (E_0 \cap \overline{\mathcal{P}}) \cup \{ \overline{x} \} \) (Siegel, MacLean 2000; Sontag, 2001)
detailed balance (DB), \( \text{rank } \Gamma = 2 \), conservative
Craciun, Dickenstein, Shiu, Sturmfels, 2009

all boundary equilibria are facet-interior or vertices of \( \overline{P} \)
Anderson, Shiu, 2010

\( \text{rank } \Gamma = 2 \)
Anderson, Shiu, 2010

\( \ell = 1 \)
Anderson, 2011; Gopalkrishnan, Miller, Shiu, 2014

strongly endotactic
Gopalkrishnan, Miller, Shiu, 2014

\( \text{rank } \Gamma = 3 \)
Pantea, 2012

\( n = 3 \)
Craciun, Nazarov, Pantea, 2013

full generality
Craciun, 20???
Persistency:

For all $x(0) \in \mathbb{R}_+^n$ we have $\lim \inf_{t \to \infty} x_s(t) > 0$ for all $1 \leq s \leq n$.

If all the trajectories are bounded then persistence is equivalent to $\omega(x(0)) \cap \partial \mathbb{R}_+^n = \emptyset$ for all $x(0) \in \mathbb{R}_+^n$.

Persistency is the missing part of the GAC

**Conjecture (Craciun, Nazarov, Pantea, 2013)**

$WR \implies persistence$
PERMANENCE

- permanence on a positive stoichiometric class $\mathcal{P}$:
  there exists $0 < \varepsilon < 1$ such that for all $x(0) \in \mathcal{P}$ we have
  $$
  \varepsilon < \liminf_{t \to \infty} x_s(t) \leq \limsup_{t \to \infty} x_s(t) < 1/\varepsilon
  $$
  for all $1 \leq s \leq n$

- in other words, there exists a compact set $K \subseteq \mathcal{P}$ such that every
  forward trajectory with $x(0) \in \mathcal{P}$ ends up in $K$

CONJECTURE (Craciun, Nazarov, Pantea, 2013)

$WR \implies$ permanence

THEOREM (Simon, 1995)

$n = 2$, reversible $\implies$ permanence
boundedness: \( \limsup_{t \to \infty} |x(t)| < \infty \) for all \( x(0) \in \mathbb{R}^n_{\geq 0} \)

**Conjecture (Anderson, 2011)**

\( WR \implies \text{boundedness} \)

**Theorem (Anderson, 2011)**

\( WR, \ell = 1 \implies \text{boundedness} \)
THE EXTENDED PERMANENCE CONJECTURE

- geometrically embedded reaction graph
  - 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 $\kappa$:
    - there exists $0 < \varepsilon < 1$ such that $\varepsilon \leq \kappa_{ij}(\tau) \leq 1/\varepsilon$
    - for all $\tau \geq 0$ and for all $(i, j) \in \mathcal{R}$

CONJECTURE (CRACIUN, NAZAROV, PANTEA, 2013)

endotactic $\iff$ permanence (even for time-dependent $\kappa$)
WR and (strong) endotacticity

\[ \ell = 1 \]

\[ \ell \geq 2 \]
RESULTS ON PERSISTENCE/PERMANENCE

- $n = 2$, reversible $\implies$ permanence
  Simon, 1995

- $\text{rank } \Gamma = 2$, $\text{WR} \implies$ bounded trajectories are persistent
  Pantea, 2012

- $\text{rank } \Gamma = 2$, lower-endotactic stoichiometric subnetworks, bounded trajectories $\implies$ persistence (even for time-dependent $\kappa$)
  Pantea, 2012

- $n = 2$, endotactic $\implies$ permanence (even for time-dependent $\kappa$)
  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 $\implies$ permanence (even for time-dependent $\kappa$)
  Gopalkrishnan, Miller, Shiu, 2014

- $\text{WR, } \ell = 1 \implies$ permanence (even for time-dependent $\kappa$)
  Gopalkrishnan, Miller, Shiu, 2014

- $n = 2$, tropically endotactic $\implies$ permanence (even for time-dependent $\kappa$)
  Brunner, Craciun, 2018
TROPICALLY ENDO TACTIC SYSTEMS IN 2D
**Example: the Lotka reactions with generalized mass-action kinetics**

\[
\begin{align*}
X & \quad (\alpha X) \quad \xrightarrow[]{} \quad 2X \\
X + Y & \quad (X + \beta Y) \quad \xrightarrow[]{} \quad 2Y \\
Y & \quad \xrightarrow[]{} \quad 0
\end{align*}
\]

\[
\begin{align*}
\alpha X & \quad \xrightarrow[]{} \quad (\alpha + 1)X \\
X + \beta Y & \quad \xrightarrow[]{} \quad (\beta + 1)Y \\
Y & \quad \xrightarrow[]{} \quad 0
\end{align*}
\]

\[
\begin{align*}
\dot{x} &= x^\alpha - xy^\beta \\
\dot{y} &= xy^\beta - y
\end{align*}
\]

**Question**

*For which \((\alpha, \beta) \in \mathbb{R}^2* is it permanent?*
**Example: the Lotka reactions with generalized mass-action kinetics**

\[
\begin{align*}
\dot{x} &= x^\alpha - xy^\beta \\
\dot{y} &= xy^\beta - y
\end{align*}
\]

<table>
<thead>
<tr>
<th>WR</th>
<th>$\alpha = 0, \beta = 0$</th>
</tr>
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<tbody>
<tr>
<td>endotactic</td>
<td>$\alpha \leq 0$, $\alpha - 1 \leq \beta \leq 0$</td>
</tr>
<tr>
<td>strongly endotactic</td>
<td>$\alpha \leq 0$, $\alpha - 1 \leq \beta \leq 0$</td>
</tr>
<tr>
<td>tropically endotactic</td>
<td>$\alpha &lt; 1$, $\beta \leq 1$, $\alpha \beta &gt; \alpha - 1$</td>
</tr>
<tr>
<td>permanent (BB, Hofbauer, 2018)</td>
<td>$\alpha \leq 1$, $\beta \leq 1$, $(\alpha, \beta) \neq (1, 1)$, $\alpha \beta &gt; \alpha - 1$</td>
</tr>
</tbody>
</table>
Example: the Lotka reactions with generalized mass-action kinetics

\[ \dot{x} = x^\alpha - xy^\beta \]
\[ \dot{y} = xy^\beta - y \]

WR
endotactic
strongly endotactic
tropically endotactic
permanent
**Example: planar S-systems (Savageau, 1969)**

\[
\begin{align*}
\dot{x}_1 &= \alpha_1 x_1^{g_{11}} x_2^{g_{12}} - \beta_1 x_1^{h_{11}} x_2^{h_{12}} \\
\dot{x}_2 &= \alpha_2 x_1^{g_{21}} x_2^{g_{22}} - \beta_2 x_1^{h_{21}} x_2^{h_{22}}
\end{align*}
\]

\[
\begin{align*}
\dot{u} &= e^{a_1 u + b_1 v} - e^{a_2 u + b_2 v} \\
\dot{v} &= e^{a_3 u + b_3 v} - e^{a_4 u + b_4 v}
\end{align*}
\]

- BB, Hofbauer, Müller, Regensburger, 2018
  - characterize local/global asymptotic stability for all rate constants
  - solve the local/global center problem
  - construct two limit cycles
- BB, Hofbauer, 2018
  - almost characterize permanence
  - construct three limit cycles