PERMANENCE OF WEAKLY REVERSIBLE
MASS-ACTION SYSTEMS WITH A SINGLE LINKAGE CLASS

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Permanence of Weakly Reversible Mass-Action Systems with a Single Linkage Class

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Abstract. We give a new proof of the fact that each weakly reversible mass-action system with a single linkage class is permanent.

Key words. mass-action system, entropy, permanence

AMS subject classifications. 34C11, 34D23, 80A30, 92E20

https://arxiv.org/abs/1903.03071
\[ \dot{x}(\tau) = -\kappa_{12} x(\tau) y(\tau) + 2\kappa_{23} z(\tau) - \kappa_{31} x(\tau)^2 \]

\[ \dot{y}(\tau) = -\kappa_{12} x(\tau) y(\tau) + \kappa_{31} x(\tau)^2 \]

\[ \dot{z}(\tau) = + \kappa_{12} x(\tau) y(\tau) - \kappa_{23} z(\tau) \]
Mass-action system with bounded kinetics

\[
\begin{align*}
\dot{x}(\tau) &= -\kappa_{12}(\tau)x(\tau)y(\tau) + 2\kappa_{23}(\tau)z(\tau) - \kappa_{31}(\tau)x(\tau)^2 \\
\dot{y}(\tau) &= -\kappa_{12}(\tau)x(\tau)y(\tau) + \kappa_{31}(\tau)x(\tau)^2 \\
\dot{z}(\tau) &= +\kappa_{12}(\tau)x(\tau)y(\tau) - \kappa_{23}(\tau)z(\tau)
\end{align*}
\]

with \( \varepsilon \leq \kappa_{ij}(\tau) \leq 1/\varepsilon \)
**Permanence Conjecture**

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

endotactic $\implies$ permanence

Partial results:

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Author(s)</th>
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<td>$n = 2$, reversible</td>
<td>Simon</td>
<td>1995</td>
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<tr>
<td>$n = 2$, endotactic</td>
<td>Craciun, Nazarov, Pantea</td>
<td>2013</td>
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<td>$n = 2$, tropically endotactic</td>
<td>Brunner, Craciun</td>
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<td>strongly endotactic</td>
<td>Gopalkrishnan, Miller, Shiu</td>
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<td></td>
<td>Anderson, Cappelletti, Kim, Nguyen</td>
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<td>WR, $\ell = 1$</td>
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WR AND (STRONG) ENDOTACTICITY

\[ \ell = 1 \quad \text{WR} \]

\[ \ell \geq 2 \quad \text{WR} \]

endotactic

strongly endotactic
**TIME DERIVATIVE ALONG A TRAJECTORY**

Let

\[
\dot{x}(\tau) = \sum_{(i,j) \in \mathcal{R}} \kappa_{ij}(\tau) x(\tau)^{y_i} (y_j - y_i),
\]

\[
V(x) = \sum_{s=1}^{n} x_s (\log x_s - 1) + 1,
\]

\[
z_i = \frac{x^{y_i}}{\sum_{k \in \mathcal{C}} x^{y_k}} \text{ for } i \in \mathcal{C}.
\]

Then

\[
\frac{d}{d\tau} V(x(\tau)) = \left( \sum_{k \in \mathcal{C}} x(\tau)^{y_k} \right) \sum_{(i,j) \in \mathcal{R}} \kappa_{ij}(\tau) z_i(\tau) (\log z_j(\tau) - \log z_i(\tau)).
\]
A lemma from the proof of the existence of positive equilibria for WR mass-action systems

\[ \Delta^\circ = \{ z \in \mathbb{R}^m_+ \mid z_1 + \cdots + z_m = 1 \} \]

**Lemma**

Assume
- \( WR, \)
- \( \ell = 1, \)
- \( \varepsilon \leq \kappa_{ij}(\tau) \leq \frac{1}{\varepsilon}. \)

Then

\[
\sum_{(i,j) \in R} \kappa_{ij}(\tau) z_i (\log z_j - \log z_i) < 0
\]

whenever \( z \in \Delta^\circ \) and \( \min z \) is small enough.
The simplex $\Delta^\circ$ for 3 complexes

- **Dark red**: $z_1 + z_2 + z_3 = 1$ and $\min(z_1, z_2, z_3) \leq \delta$

- **Light red**: $z_1 + z_2 + z_3 = 1$ and $\min(z_1, z_2, z_3) > \delta$
A CRUCIAL OBSERVATION: EXAMPLE 1

\[ X_1 + 2X_2 \rightarrow 3X_1 \]

\[ 2X_1 + 3X_2 \rightarrow X_2 \]

basis of \( S \):

\[ X_1 + 2X_2 \rightarrow 3X_1 \]

\[ 2X_1 + 3X_2 \rightarrow X_2 \]
A CRUCIAL OBSERVATION: example 1

\[ X_1 + 2X_2 \rightarrow 3X_1 \]

\[ 2X_1 + 3X_2 \rightarrow X_2 \]

basis of \( S \):

\[ X_1 + 2X_2 \rightarrow 3X_1 \]

\[ 2X_1 + 3X_2 \rightarrow X_2 \]
**A crucial observation: example 1**

\[
\begin{align*}
X_1 + 2X_2 & \rightarrow 3X_1 \\
2X_1 + 3X_2 & \rightarrow X_2
\end{align*}
\]

basis of $S$:

\[
\begin{align*}
X_1 + 2X_2 & \rightarrow 3X_1 \\
2X_1 + 3X_2 & \rightarrow X_2
\end{align*}
\]

\[
\mathcal{P}
\]

\[
\begin{pmatrix} x_1 \ x_2 \end{pmatrix}
\]

\[
\mathbb{R}^{\dim S}_+
\]

\[
\begin{pmatrix} x_1^3 \ x_2^2 \ x_3 \\ x_1 x_2^2 \ x_1^3 \end{pmatrix}
\]

$\psi$ is a homeomorphism!
A crucial observation: example 2

\[ X_1 + X_2 \rightarrow 2X_1 \]
\[ 2X_3 \leftarrow X_2 + X_3 \]

basis of \( S \):

\[ X_1 + X_2 \rightarrow 2X_1 \]
\[ 2X_3 \]
\[ X_2 + X_3 \]
A CRUCIAL OBSERVATION: example 2

\[ X_1 + X_2 \rightarrow 2X_1 \]

basis of \( S \):

\[ 2X_3 \]

\[ X_2 + X_3 \]

\[ \mathbb{R}^\text{dim } S \]

\[ \left( \frac{x_1^2}{x_1 x_2}, \frac{x_2 x_3}{x_1^2} \right) \]
A CRUCIAL OBSERVATION: EXAMPLE 2

\[ X_1 + X_2 \rightarrow 2X_1 \]

basis of \( S \):

\[ 2X_3 \]

\[ X_2 + X_3 \]

\[ x_1, x_2, x_3 \]

(\( P \))

\[ \Psi \]

\[ \mathbb{R}^{\dim S} \]

\[ \left( \frac{x_1^2}{x_1 x_2}, \frac{x_2 x_3}{x_1^2} \right) \]

\( \Psi \) is a homeomorphism!
A CRUCIAL OBSERVATION: GENERAL STATEMENT

**Lemma**

Let $\mathcal{R}' \subseteq \mathcal{R}$ be such that $\{y_j - y_i \mid (i, j) \in \mathcal{R}'\}$ is a basis of $S$. Then

$$\Psi : P \rightarrow \mathbb{R}_{+}^{\dim S}$$

$x \mapsto \left( \frac{xy_j}{xy_i} \right)_{(i, j) \in \mathcal{R}'}$ is a homeomorphism.

**Proof**

$\Psi : P \rightarrow \mathbb{R}_{+}^{\dim S}$ is bijective

$\uparrow$

$P \cap \{x \in \mathbb{R}_{+}^{n} \mid \log x - \log x^* \in S^\perp\}$ is a singleton for each $x^* \in \mathbb{R}_{+}^{n}$
A CRUCIAL OBSERVATION: general statement

Lemma

Let $\mathcal{R}' \subseteq \mathcal{R}$ be such that $\{y_j - y_i \mid (i, j) \in \mathcal{R}'\}$ is a basis of $S$. Then

$$\Psi : \mathcal{P} \rightarrow \mathbb{R}_{\dim S}^+$$

$$x \mapsto \left( \frac{xy_j}{xy_i} \right)_{(i,j) \in \mathcal{R}'}$$

is a homeomorphism.

Proof

$\Psi : \mathcal{P} \rightarrow \mathbb{R}_{\dim S}^+$ is bijective

$$\uparrow$$

$\mathcal{P} \cap \{x \in \mathbb{R}_+^n \mid \log x - \log x^* \in S^\perp\}$ is a singleton for each $x^* \in \mathbb{R}_+^n$
Theorem

Assume WR, $\ell = 1$, $\varepsilon \leq \kappa_{ij}(\tau) \leq \frac{1}{\varepsilon}$.

Fix a positive stoichiometric class $\mathcal{P}$ and assume it is unbounded. Then

- $\frac{d}{d\tau} V(x(\tau)) < 0$ whenever $x(\tau) \in \mathcal{P}$ and $\max x(\tau)$ is big enough,
- all solutions are bounded.
No solution can approach the origin

\[ V(x) = \sum_{s=1}^{n} x_s (\log x_s - 1) + 1 \]

\{ V = c \} with \( n - 1 < c < n \)

**Theorem**

Assume \( WR, \ell = 1, \varepsilon \leq \kappa_{ij}(\tau) \leq \frac{1}{\varepsilon} \).

Fix a positive stoichiometric class \( \mathcal{P} \) and assume \( 0 \in \overline{\mathcal{P}} \).

Then

- \( \exists \) a neighborhood \( U \) of the origin s.t.
  \[ \frac{d}{d\tau} V(x(\tau)) < 0 \text{ whenever } x(\tau) \in U \cap \mathcal{P}, \]
- no solution can approach the origin.
The truncated Horn-Jackson function

\[ V_{\{1,2\}}(x_1, x_2, x_3) = (x_1(\log x_1 - 1) + 1) + (x_2(\log x_2 - 1) + 1) \]

\[ \text{sgn} \overline{x} = (0, 0, +) \]

\{ \overline{V_{\{1,2\}}} = c \} \text{ with } 1 < c < 2
**Generic boundary point**

- For $\bar{x} \in \partial \mathbb{R}^n_{\geq 0}$ let $W = \{ s \mid \bar{x}_s = 0 \}$.

- Truncated Horn-Jackson function: for $W \subseteq \{1, \ldots, n\}$ let

$$V_W(x) = \sum_{s \in W} x_s (\log x_s - 1) + 1.$$ 

**Theorem**

Assume WR, $\ell = 1$, $\varepsilon \leq \kappa_{ij}(\tau) \leq \frac{1}{\varepsilon}$.

Fix a positive stoichiometric class $\mathcal{P}$ and an $\bar{x} \in \overline{\mathcal{P}} \cap \partial \mathbb{R}^n_{\geq 0}$.

Then $\exists$ a neighborhood $U$ of $\bar{x}$ s.t.

$$\frac{d}{d\tau} V_W(x(\tau)) < 0 \text{ whenever } x(\tau) \in U \cap \mathcal{P}.$$ 

**Proof**

As for the origin, but for the *projected* mass-action system.
**Projected mass-action system**

**Original**

\[
\begin{align*}
3X_3 & \xrightarrow{\kappa_{12}(\tau)} X_3 \\
X_1 + 2X_2 & \xrightarrow{\kappa_{56}(\tau)} 2X_1 \\
2X_1 & \xleftarrow{\kappa_{45}(\tau)} 2X_1 + X_2
\end{align*}
\]

**Projected to** \( W = \{1, 2\} \)

\[
\begin{align*}
0 & \xrightarrow{\kappa_{12}(\tau)X_3^3(\tau)} 0 \\
X_1 + 2X_2 & \xrightarrow{\kappa_{61}(\tau)} X_1 + 2X_2 \\
2X_1 & \xleftarrow{\kappa_{45}(\tau)} 2X_1 + X_2
\end{align*}
\]
A bit of hand waiving

permanence

= persistence + boundedness + a little more
**Theorem**

Assume WR, $\ell = 1$, $\varepsilon \leq \kappa_{ij}(\tau) \leq \frac{1}{\varepsilon}$.

Fix a positive stoichiometric class $\mathcal{P}$ and assume it is unbounded. Then there exists a $c > n$ such that

- $\{V \leq c\} \cap \mathcal{P}$ is bounded and forward invariant,
- solutions starting in $\{V > c\} \cap \mathcal{P}$ reach $\{V = c\} \cap \mathcal{P}$ in finite time.
Little more 2: The origin is uniformly repelling

\[ V(x) = \sum_{s=1}^{n} x_s (\log x_s - 1) + 1 \]

\{ V = c \} \text{ with } n - 1 < c < n

**Theorem**

Assume WR, \( l = 1, \varepsilon \leq \kappa_{ij}(\tau) \leq \frac{1}{\varepsilon} \).

Fix a positive stoichiometric class \( P \) and assume \( 0 \in \overline{P} \).

Then there exists a \( c \in (n - 1, n) \) such that

- \( P \setminus (\{ V > c \} \cap (0, 1)^n \cap P) \) is forward invariant,
- solutions starting in \( \{ V > c \} \cap (0, 1)^n \cap P \) reach \( \{ V = c \} \cap (0, 1)^n \cap P \) in finite time.
CONSTRUCTION OF THE COMPACT AND FORWARD INVARIANT GLOBAL ATTRACTOR IN CASE $\mathcal{P} = \mathbb{R}_+^n$

- cut away infinity
- cut away the origin
- cut away the $n$ axes
- cut away the $\binom{n}{2}$ 2-dimensional faces
- cut away the $\binom{n}{3}$ 3-dimensional faces
- ... 
- cut away the $n$ facets
Construction of the compact and forward invariant global attractor for any fixed $\mathcal{P}$

- cut away infinity (if $\mathcal{P}$ is unbounded)
- cut away the vertices of $\mathcal{P}$
- cut away the edges of $\mathcal{P}$
- cut away the 2-dimensional faces of $\mathcal{P}$
- cut away the 3-dimensional faces of $\mathcal{P}$
- $\ldots$
- cut away the $(\dim S - 1)$-dimensional faces of $\mathcal{P}$
Example: the Horn-Jackson function is not a Lyapunov function at the origin.
Example: The Horn-Jackson function is not a Lyapunov function at infinity.