Dynamic aspects of deterministic chemical systems

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MASS-ACTION SYSTEMS

\[ \begin{align*}
  X + Y & \xrightarrow{\kappa_{12}} 2Y \\
  & \xrightarrow{\kappa_{23}} X \\
  & \xrightarrow{\kappa_{31}} X
\end{align*} \]

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

\[
\begin{bmatrix}
  \dot{x} \\
  \dot{y}
\end{bmatrix} = \kappa_{12}xy \begin{bmatrix}
  -1 \\
  +1
\end{bmatrix} + \kappa_{23}y^2 \begin{bmatrix}
  +1 \\
  -2
\end{bmatrix} + \kappa_{31}x \begin{bmatrix}
  0 \\
  +1
\end{bmatrix}
\]
Mass-action systems

\[ \begin{align*}
X + Y & \xrightarrow{\kappa_{12}} Z \\
& \xrightarrow{\kappa_{31}} \quad \xrightarrow{\kappa_{23}} 2X \\
\end{align*} \]

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

\[ \begin{bmatrix} \dot{x} \\ \dot{y} \\ \dot{z} \end{bmatrix} = \kappa_{12}xy \begin{bmatrix} -1 \\ -1 \\ +1 \end{bmatrix} + \kappa_{23}z \begin{bmatrix} +2 \\ 0 \\ -1 \end{bmatrix} + \kappa_{31}x^2 \begin{bmatrix} -1 \\ +1 \\ 0 \end{bmatrix} \]

Since \( \dot{x} + \dot{y} + 2\dot{z} = 0 \),

\[ x(\tau) + y(\tau) + 2z(\tau) \equiv x(0) + y(0) + 2z(0) \]
**COMPLEXES ↔ VECTORS**

\[
\begin{align*}
X + Y & \rightarrow Z \\
2X & \\
y_1 & \rightarrow y_2 \\
y_3 & \\
y_1 &= \begin{bmatrix} 1 \\ 1 \\ 0 \end{bmatrix} \\
y_2 &= \begin{bmatrix} 0 \\ 0 \\ 1 \end{bmatrix} \\
y_3 &= \begin{bmatrix} 2 \\ 0 \\ 0 \end{bmatrix}
\end{align*}
\]
**MASS-ACTION ODE**

- for a single reaction:
  \[
  a_1 X_1 + a_2 X_2 + \cdots + a_n X_n \xrightarrow{\kappa} b_1 X_1 + b_2 X_2 + \cdots + b_n X_n
  \]

\[
\begin{bmatrix}
\dot{x}_1 \\
\dot{x}_2 \\
\vdots \\
\dot{x}_n
\end{bmatrix} = \kappa x_1^{a_1} x_2^{a_2} \cdots x_n^{a_n}
\begin{pmatrix}
b_1 \\
b_2 \\
\vdots \\
b_n
\end{pmatrix} -
\begin{pmatrix}
a_1 \\
a_2 \\
\vdots \\
a_n
\end{pmatrix}
\]

- for a collection \( \mathcal{R} \) of reactions:

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

with state space \( \mathbb{R}^n_+ \) or \( \mathbb{R}^n_{\geq 0} \)
**Mass-action ODE**

- for a single reaction:

\[
a_1 X_1 + a_2 X_2 + \cdots + a_n X_n \xrightarrow{\kappa} b_1 X_1 + b_2 X_2 + \cdots + b_n X_n
\]

\[
\begin{bmatrix}
\dot{x}_1 \\
\dot{x}_2 \\
\vdots \\
\dot{x}_n
\end{bmatrix} = \kappa \prod_{i=1}^n x_i^{a_i} \begin{pmatrix}
b_1 \\
b_2 \\
\vdots \\
b_n
\end{pmatrix} - \begin{pmatrix}
a_1 \\
a_2 \\
\vdots \\
a_n
\end{pmatrix}
\]

- for a collection \( R \) of reactions:

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

with state space \( \mathbb{R}_+^n \) or \( \mathbb{R}_{\geq 0}^n \)
Questions

- existence/uniqueness/number of equilibria
- periodic solutions, limit cycles
- local/global asymptotic stability
- local/global centers
- multistability
- boundedness of solutions
- persistence
- permanence
STOICHIOMETRIC SUBSPACE

\[
\begin{bmatrix}
\dot{x} \\
\dot{y} \\
\dot{z}
\end{bmatrix} = \kappa_{12} xy \begin{bmatrix} -1 \\ -1 \\ +1 \end{bmatrix} + \kappa_{23} z \begin{bmatrix} +2 \\ 0 \\ -1 \end{bmatrix} + \kappa_{31} x^2 \begin{bmatrix} -1 \\ +1 \\ 0 \end{bmatrix}
\]

\[
S = \text{span} \left\{ \begin{bmatrix} -1 \\ -1 \\ +1 \end{bmatrix}, \begin{bmatrix} +2 \\ 0 \\ -1 \end{bmatrix}, \begin{bmatrix} -1 \\ +1 \\ 0 \end{bmatrix} \right\} \leq \mathbb{R}^3
\]
\textbf{STOICHIOMETRIC SUBSPACE}

\[
\begin{bmatrix}
\dot{x} \\
\dot{y} \\
\dot{z}
\end{bmatrix} = \kappa_{12} xy \begin{bmatrix} -1 \\ -1 \\ +1 \end{bmatrix} + \kappa_{23} z \begin{bmatrix} +2 \\ 0 \\ -1 \end{bmatrix} + \kappa_{31} x^2 \begin{bmatrix} -1 \\ +1 \\ 0 \end{bmatrix}
\]

\[S = \text{span} \left\{ \begin{bmatrix} -1 \\ -1 \\ +1 \end{bmatrix}, \begin{bmatrix} +2 \\ 0 \\ -1 \end{bmatrix}, \begin{bmatrix} -1 \\ +1 \\ 0 \end{bmatrix} \right\} \leq \mathbb{R}^3\]

Rest of this talk:
for simplicity, assume \( S = \mathbb{R}^n \)
**Complex-balanced equilibria**

Rate constant:

\[ \begin{align*}
    & X \\
    & \quad \overset{1}{\longrightarrow} \quad \overset{3}{\longrightarrow} \\
    3Y & \quad \underset{1}{\overleftarrow{\longrightarrow}} \quad \underset{29}{\longrightarrow} \\
    & Y + Z \\
    & \quad \overset{5}{\longrightarrow} \quad \overset{6}{\longrightarrow} \\
    & X + Z \quad \underset{1}{\overleftarrow{\longrightarrow}} \quad \underset{5}{\longrightarrow} \\
    & 2X + Y
\end{align*} \]

Flow at:

\[ \begin{bmatrix} x^* \\ y^* \\ z^* \end{bmatrix} \in \mathbb{R}_+^3 \]
**Complex-balanced equilibria**

Flow at

\[ \begin{bmatrix} x^* \\ y^* \\ z^* \end{bmatrix} \in \mathbb{R}^3_+ \]

Flow with

\[ \begin{bmatrix} x^* \\ y^* \\ z^* \end{bmatrix} = \begin{bmatrix} 2 \\ 1 \\ 5 \end{bmatrix} \]
LYAPUNOV FUNCTION FOR COMPLEX-BALANCED SYSTEMS

\[ V(x_1, \ldots, x_n) = \left[ x_1 \left( \log \frac{x_1}{x_1^*} - 1 \right) + x_1^* \right] + \cdots + \left[ x_n \left( \log \frac{x_n}{x_n^*} - 1 \right) + x_n^* \right] \]

THEOREM (HORN, JACKSON, 1972)

Assume

- \( S = \mathbb{R}^n \),
- there exists a complex-balanced equilibrium \( x^* \).

Then

\[ \frac{d}{d\tau} V(x(\tau)) < 0 \text{ whenever } x(\tau) \neq x^*. \]
THE HORN-JACKSON FUNCTION FOR $n = 2$

$$V(x, y) = \left[ x \left( \log \frac{x}{x^*} - 1 \right) + x^* \right] + \left[ y \left( \log \frac{y}{y^*} - 1 \right) + y^* \right]$$
Horn-Jackson level sets for $n = 3$

\[ V(x, y, z) = \left[ x \left( \log \frac{x}{x^*} - 1 \right) + x^* \right] + \left[ y \left( \log \frac{y}{y^*} - 1 \right) + y^* \right] + \left[ z \left( \log \frac{z}{z^*} - 1 \right) + z^* \right] \]
Corollary (Horn, Jackson, 1972)

Assume

- $S = \mathbb{R}^n$,
- there exists a complex-balanced equilibrium $x^*$.

Then

- $x^*$ is the only positive equilibrium,
- $x^*$ is locally asymptotically stable,
- all solutions are bounded,
- no solution converges to the origin,
- there is no periodic solution.

Conjecture (Horn, 1974)

$x^*$ is globally asymptotically stable
Corollary (Horn, Jackson, 1972)

Assume
- \( S = \mathbb{R}^n \),
- there exists a complex-balanced equilibrium \( x^* \).

Then
- \( x^* \) is the only positive equilibrium,
- \( x^* \) is locally asymptotically stable,
- all solutions are bounded,
- no solution converges to the origin,
- there is no periodic solution.

Conjecture (Horn, 1974)

\( x^* \) is globally asymptotically stable
**Global Attractor Conjecture (allow $S \subseteq \mathbb{R}^n$)**

**Conjecture (Craciun, Dickenstein, Shiu, Sturmfels, 2009)**

*complex-balanced equilibria are globally asymptotically stable*

- detailed balance, $\dim S = 2$, conservative
  
  Craciun, Dickenstein, Shiu, Sturmfels, 2009

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

- $\dim S = 2$
  
  Anderson, Shiu, 2010

- single connected component
  
  Anderson, 2011; Gopalkrishnan, Miller, Shiu, 2014; BB, Hofbauer, 2019

- $\dim S = 3$
  
  Pantea, 2012

- $n = 3$
  
  Craciun, Nazarov, Pantea, 2013

- full generality
  
  Craciun, 202?
**Extend the class of complex-balanced systems**

**Definition (Weak Reversibility)**

A directed graph is said to be *weakly reversible* if a partition $V = V_1 \cup V_2$ of its vertex set as follows is not possible:

![Diagram of weakly reversible partition]

**Lemma**

Every complex-balanced system is weakly reversible.

**Proof**

The inflow is the same as the outflow not just at each vertex, but for each subset of vertices. However, the above type of partition would result in a subset $V_1$ with zero inflow and positive outflow.
**Definition (Weak Reversibility)**

A directed graph is said to be *weakly reversible* if a partition 
\( V = V_1 \cup V_2 \) of its vertex set as follows is **not** possible:

\[
\begin{array}{c}
V_1 \\
\rightarrow \\
\rightarrow \\
\rightarrow \\
\rightarrow \\
V_2
\end{array}
\]

**Lemma**

*Every complex-balanced system is weakly reversible.*

**Proof**

The inflow is the same as the outflow not just at each vertex, but for each subset of vertices. However, the above type of partition would result in a subset \( V_1 \) with zero inflow and positive outflow.
Characterizations of Weak Reversibility

Example of a weakly reversible graph:

Equivalent formulations of weak reversibility:

- Every directed edge is part of a directed cycle.
- Every weak component is strongly connected.
- Existence of a directed path from $i \in V$ to $j \in V$ implies the existence of a directed path from $j$ to $i$. 
Dynamics of weakly reversible systems?

- Uniqueness of a positive equilibrium does not hold true in general.
- Even a unique positive equilibrium can be unstable.
- There could be limit cycles.
Uniqueness of a positive equilibrium does not hold true in general.

Even a unique positive equilibrium can be unstable.

There could be limit cycles.

However, some more global properties (are conjectured to) hold true!
**PERSISTENCE**

- **persistence**: for positive initial conditions, 
  \[ \liminf_{\tau \to \infty} x_{s}(\tau) > 0 \text{ for all } 1 \leq s \leq n \]

- if all the trajectories are bounded then persistence is equivalent to 
  \[ \omega(\bar{x}) \cap \partial \mathbb{R}^n_{\geq 0} = \emptyset \text{ for each positive initial condition } \bar{x} \in \mathbb{R}^n_+ \]

- persistence is the missing part of the Global Attractor Conjecture

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

weak reversibility \(\iff\) persistence
PERSISTENCE

- **persistence:** for positive initial conditions,
  \[ \liminf_{\tau \to \infty} x_s(\tau) > 0 \text{ for all } 1 \leq s \leq n \]

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- persistence is the missing part of the Global Attractor Conjecture

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

*weak reversibility* \(\implies\) *persistence*
**Boundedness**

boundedness: for positive initial conditions,

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

**Conjecture (Anderson, 2011)**

weak reversibility \(\implies\) boundedness

**Theorem (Anderson, 2011)**

weak reversibility and single connected component \(\implies\) boundedness
boundedness: for positive initial conditions,

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

**Conjecture (Anderson, 2011)**

weak reversibility \(\Rightarrow\) boundedness

**Theorem (Anderson, 2011)**

weak reversibility and single connected component \(\Rightarrow\) boundedness
Lotka reactions
(solutions are persistent and bounded)

\[ \begin{align*}
    x & \xrightarrow{\kappa_1} 2x \\
    x + y & \xrightarrow{\kappa_2} 2y \\
    y & \xrightarrow{\kappa_3} 0
\end{align*} \]

\[ \begin{align*}
    \dot{x} &= \kappa_1 x - \kappa_2 xy \\
    \dot{y} &= \kappa_2 xy - \kappa_3 y
\end{align*} \]
PERMANENCE (more than persistence + boundedness)

permanence: there exists a compact set $K \subseteq \mathbb{R}_+^n$ such that every forward trajectory with positive initial condition ends up in $K$

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

weak reversibility $\implies$ permanence

**Theorem (Simon, 1995)**

$n = 2$, reversibility $\implies$ permanence
PERMANENCE (more than persistence + boundedness)

permanence: there exists a compact set \( K \subseteq \mathbb{R}_+^n \) such that every forward trajectory with positive initial condition ends up in \( K \)

CONJECTURE (CRAICIUN, NAZAROV, PANTEA, 2013)
\[
\text{weak reversibility} \implies \text{permanence}
\]

THEOREM (SIMON, 1995)
\[
n = 2, \text{ reversibility} \implies \text{permanence}
\]
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
time-dependent rate constants:

there exists an $0 < \varepsilon < 1$ such that $\varepsilon \leq \kappa_{ij}(\tau) \leq \frac{1}{\varepsilon}$

for all $\tau \geq 0$ and for all $(i, j) \in \mathcal{R}$
The Extended Permanence Conjecture

time-dependent rate constants:

there exists an $0 < \varepsilon < 1$ such that $\varepsilon \leq \kappa_{ij}(\tau) \leq \frac{1}{\varepsilon}$

for all $\tau \geq 0$ and for all $(i, j) \in \mathcal{R}$

Conjecture (Craciun, Nazarov, Pantea, 2013)

$\text{endotactic} \iff \text{permanence (even for time-dependent } \kappa)$
**PERSISTENCE/PERMANENCE RESULTS (ALLOW $S \subseteq \mathbb{R}^n$)**

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

- $\dim S = 2$, WR $\implies$ bounded trajectories are persistent
  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; Anderson, Cappelletti, Kim, Nguyen, 2018

- WR, $\ell = 1$ $\implies$ permanence (even for time-dependent $\kappa$)
  Gopalkrishnan, Miller, Shiu, 2014; Anderson, Cappelletti, Kim, Nguyen, 2018; BB, Hofbauer, 2019

- $n = 2$, tropically endotactic $\implies$ permanence (even for time-dependent $\kappa$)
  Brunner, Craciun, 2018
Sanity test for permanence ✓

**Theorem (BB, 2019)**

weak reversibility $\implies$ existence of positive equilibria
A weakly reversible example with a continuum of positive equilibria (BB, Craciun, Yu, 2019)

\[
\begin{align*}
\dot{x} & = (1 + x^2 + x^2 y^2 + y^2 - 5xy)(1 - xy) \\
\dot{y} & = (1 + x^2 + x^2 y^2 + y^2 - 5xy)(x - y)
\end{align*}
\]
Relation of the Big Conjectures

Extended Permanence Conjecture

Permanence Conjecture

Boundedness Conjecture

Persistence Conjecture

Existence of Positive Equilibria Theorem

Global Attractor Conjecture
EXTENSION OF MASS-ACTION KINETICS

Classical mass-action kinetics:

\[
a_1X_1 + \cdots + a_nX_n \xrightarrow{\kappa} b_1X_1 + \cdots + b_nX_n
\]

\[
\begin{bmatrix}
\dot{x}_1 \\
\vdots \\
\dot{x}_n
\end{bmatrix} = \kappa \underbrace{x_1^{a_1} \cdots x_n^{a_n}}_{\chi^a} \left( \begin{bmatrix} b_1 \\ \vdots \\ b_n \end{bmatrix} - \begin{bmatrix} a_1 \\ \vdots \\ a_n \end{bmatrix} \right)
\]

Generalized mass-action kinetics (Müller, Regensburger, 2012):

\[
a_1X_1 + \cdots + a_nX_n \xrightarrow{\kappa} b_1X_1 + \cdots + b_nX_n
\]

\[
(\alpha_1X_1 + \cdots + \alpha_nX_n) \xrightarrow{\kappa} b_1X_1 + \cdots + b_nX_n
\]

\[
\begin{bmatrix}
\dot{x}_1 \\
\vdots \\
\dot{x}_n
\end{bmatrix} = \kappa \underbrace{x_1^{\alpha_1} \cdots x_n^{\alpha_n}}_{\chi^\alpha} \left( \begin{bmatrix} b_1 \\ \vdots \\ b_n \end{bmatrix} - \begin{bmatrix} a_1 \\ \vdots \\ a_n \end{bmatrix} \right)
\]
**Extension of Mass-action Kinetics**

Classical mass-action kinetics:

\[
\begin{align*}
a_1X_1 + \cdots + a_nX_n & \quad \xrightarrow{\kappa} \quad b_1X_1 + \cdots + b_nX_n \\
\begin{bmatrix}
\dot{x}_1 \\
\vdots \\
\dot{x}_n
\end{bmatrix} & = \kappa \underbrace{x_1^{a_1} \cdots x_n^{a_n}}_{\chi^a} \left( \begin{bmatrix} b_1 \\ \vdots \\ b_n \end{bmatrix} - \begin{bmatrix} a_1 \\ \vdots \\ a_n \end{bmatrix} \right)
\end{align*}
\]

Generalized mass-action kinetics (Müller, Regensburger, 2012):

\[
\begin{align*}
a_1X_1 + \cdots + a_nX_n & \quad (\alpha_1X_1 + \cdots + \alpha_nX_n) \quad \xrightarrow{\kappa} \quad b_1X_1 + \cdots + b_nX_n \\
\begin{bmatrix}
\dot{x}_1 \\
\vdots \\
\dot{x}_n
\end{bmatrix} & = \kappa \underbrace{x_1^{\alpha_1} \cdots x_n^{\alpha_n}}_{\chi^\alpha} \left( \begin{bmatrix} b_1 \\ \vdots \\ b_n \end{bmatrix} - \begin{bmatrix} a_1 \\ \vdots \\ a_n \end{bmatrix} \right)
\end{align*}
\]
Matrix Form of the Mass-Action ODE

Classical mass-action:

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

Lemma

\(x^* \in \mathbb{R}^n_+\) is a complex-balanced equilibrium if and only if \(A_\kappa(x^*)^Y = 0\)

Generalized mass-action:

\[
\dot{x} = \sum_{(i,j) \in \mathcal{R}} \kappa_{ij} x^\tilde{y}_i (y_j - y_i) \iff \dot{x} = YA_\kappa x^{\tilde{Y}}
\]

Lemma

\(x^* \in \mathbb{R}^n_+\) is a complex-balanced equilibrium if and only if \(A_\kappa(x^*)^{\tilde{Y}} = 0\)
Matrix form of the mass-action ODE

Classical mass-action:

\[
\dot{x} = \sum_{(i,j) \in \mathcal{R}} \kappa_{ij} x^y_i (y_j - y_i) \quad \iff \quad \dot{x} = Y A_{\kappa} x^Y
\]

Lemma

\(x^* \in \mathbb{R}^n_+\) is a complex-balanced equilibrium if and only if \(A_{\kappa}(x^*)^Y = 0\)

Generalized mass-action:

\[
\dot{x} = \sum_{(i,j) \in \mathcal{R}} \kappa_{ij} x^{\tilde{y}}_i (y_j - y_i) \quad \iff \quad \dot{x} = Y A_{\kappa} x^{\tilde{Y}}
\]

Lemma

\(x^* \in \mathbb{R}^n_+\) is a complex-balanced equilibrium if and only if \(A_{\kappa}(x^*)^{\tilde{Y}} = 0\)
Stability of linear ODEs

Theorem (Lyapunov)

Let $A \in \mathbb{R}^{n \times n}$ and consider the linear ODE

$$\dot{x} (\tau) = Ax (\tau).$$

Then the following are equivalent.

1. $0 \in \mathbb{R}^n$ is asymptotically stable
2. each eigenvalue of $A$ has negative real part
3. there exists a $P = P^\top > 0$ for which the quadratic function $V(x) = x^\top Px$ is a strict Lyapunov function:

$$\frac{d}{d\tau} V(x(\tau)) < 0 \text{ whenever } x(\tau) \neq 0 \in \mathbb{R}^n$$

4. there exists a $P = P^\top > 0$ such that $PA + A^\top P < 0$
**Theorem (Hartman-Grobman)**

An equilibrium $x^* \in \mathbb{R}^n$ of the ODE $\dot{x}(\tau) = f(x(\tau))$ is asymptotically stable if each eigenvalue of the Jacobian matrix $J(x^*) \in \mathbb{R}^{n \times n}$ has negative real part.

In this case, $x^*$ is said to be *linearly stable*. 
\[
\dot{x} = YA_x x^Y \\
J(x) = YA_x \text{diag}(x^Y) Y^\top \text{diag}(1/x)
\]

**Theorem (Johnston, 2011)**

Assume \( S = \mathbb{R}^n \) and let \( x^* \) be a complex-balanced equilibrium. Then \( x^* \) is linearly stable (i.e., \( \sigma(J(x^*)) \subseteq \mathbb{C}_- \)).

In fact, \( x^* \) is even *diagonally stable*:
there exists a positive diagonal matrix \( D \) such that

\[
DJ(x^*) + J(x^*)^\top D < 0.
\]
**Linear stability of complex-balanced equilibria:**

**Generalized mass-action**

\[
\dot{x} = YA_\kappa x \tilde{Y}
\]

\[
J(x) = YA_\kappa \text{diag}(x \tilde{Y}) \tilde{Y}^\top \text{diag}(1/x)
\]

**Theorem (BB, Müller, Regensburger, 2020)**

Assume \( S = \mathbb{R}^n \) and that the reaction graph is a cycle. Then the following are equivalent.

- Complex-balanced equilibria are linearly stable (for all complex-balancing \( \kappa \)).
- The matrix \( YA_\kappa \equiv 1 \tilde{Y}^\top \) is D-stable.

**Definition (D-stability)**

A matrix \( A \in \mathbb{R}^{n \times n} \) is said to be D-stable if \( \sigma(AD) \subseteq \mathbb{C}_- \) for all positive diagonal matrix \( D \).