Q1) 1 = least comfortable

3 = very comfortable

Mass-action systems:

From linear to non-linear inequalities

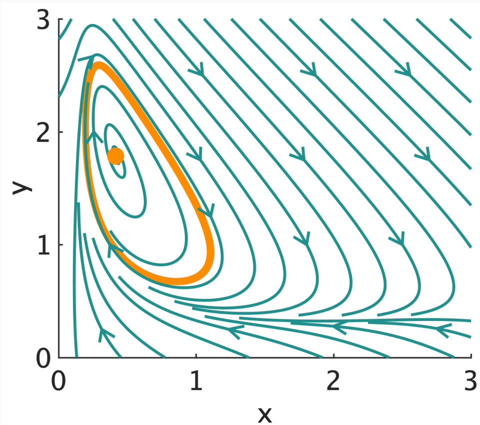
Poll: http://etc.ch/2oYS

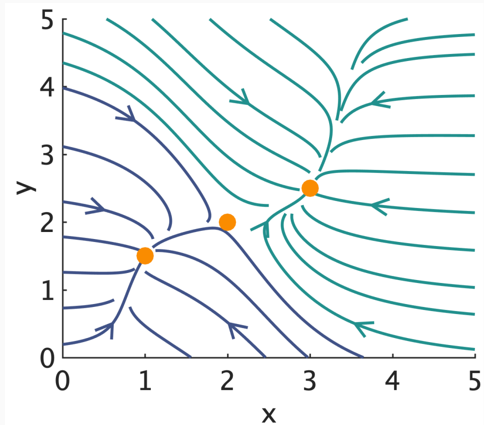
Polly Y. Yu

(Joint work with Gheorghe Craciun, Jiaxin Jin)
Department of Mathematics
University of Wisconsin-Madison

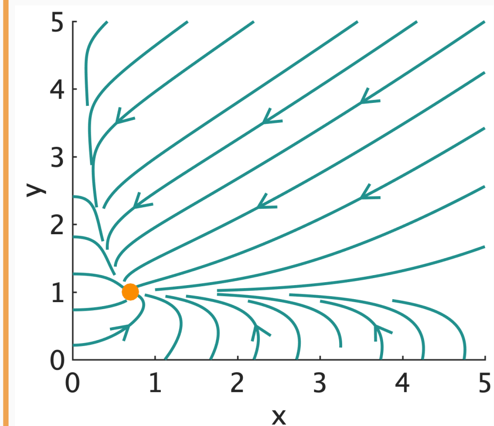
Model Theory of Differential Equations,
Algebraic Geometry, and their Applications to Modeling
June 2, 2020

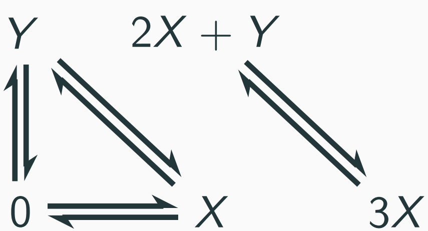
Possible dynamics of mass-action systems

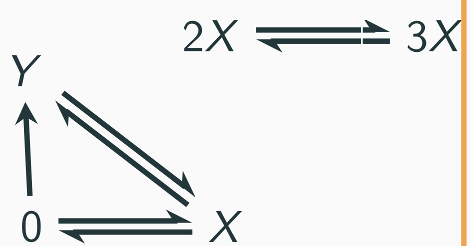


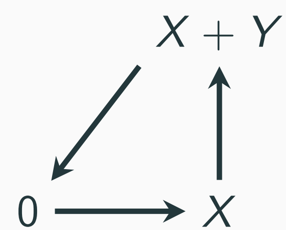


Our Focus



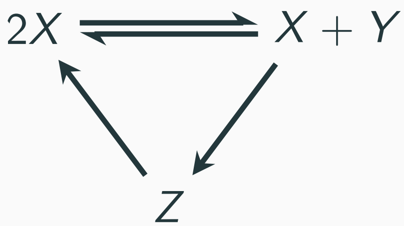






Reaction networks to polynomials

- **Reaction network** $G = (V, E)$



- **Mass-action system** $(G, \boldsymbol{\kappa})$ and associated ODE on $\mathbb{R}^n_{>0}$

$$\frac{d\boldsymbol{x}}{dt} = \sum_{(i,j)\in E} \kappa_{ij} \boldsymbol{x}^{\boldsymbol{y}_i} (\boldsymbol{y}_j - \boldsymbol{y}_i)$$

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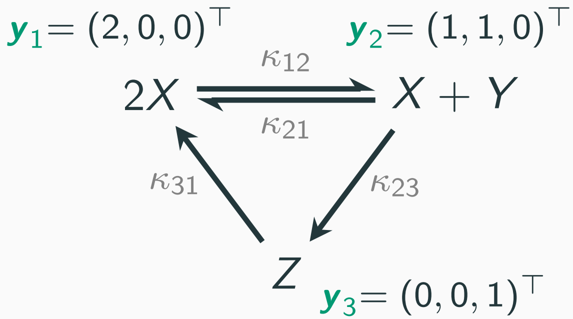

κ_{ij} = rate constants

$y_i \in \mathbb{Z}^n_{\geq 0}$, determine monomials

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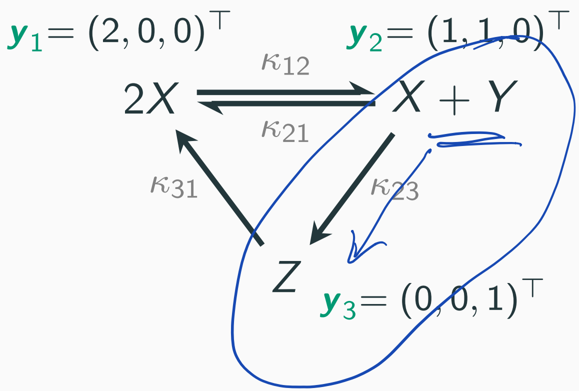

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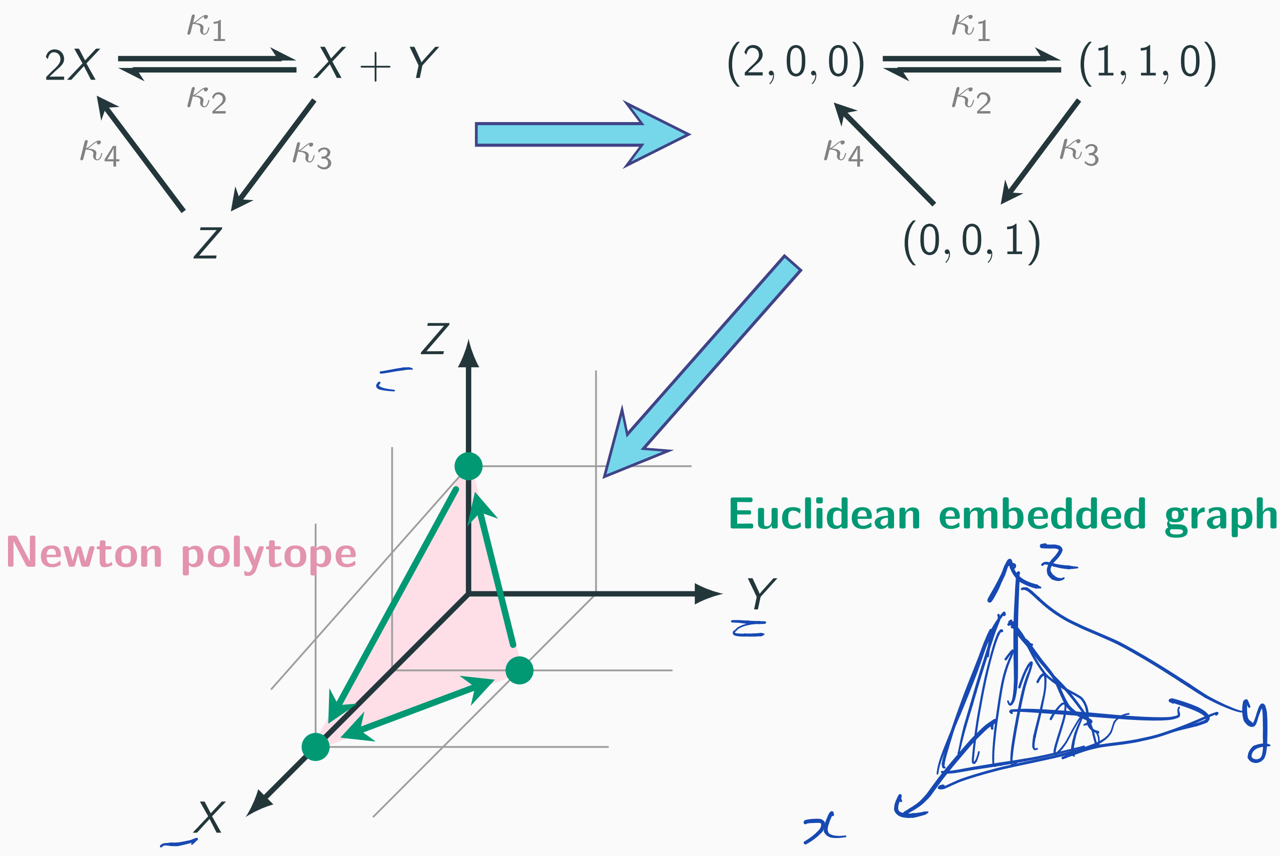
$$\kappa_{23}\, xy \begin{pmatrix} -1 \\ -1 \\ 1 \end{pmatrix}$$

Reaction networks: a geometric view

- Reaction graph $G = (V, E)$:

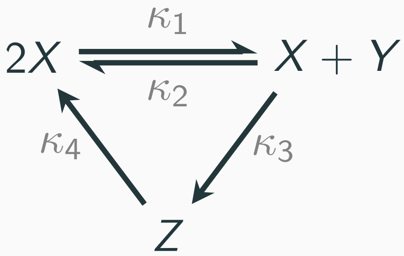


Complex-balanced systems

Complex-balanced steady states

- Steady state $\boldsymbol{x}^* > \boldsymbol{0}$ is **complex-balanced** if at each vertex $\boldsymbol{v}$

$$(\text{flux into } \boldsymbol{v}) = (\text{flux out of } \boldsymbol{v})$$



- E.g. $\kappa_2 xy + \kappa_4 z = \kappa_1 x^2$

$$\kappa_3 xy = \kappa_4 z$$

$$\kappa_1 x^2 = \kappa_2 xy + \kappa_3 xy$$

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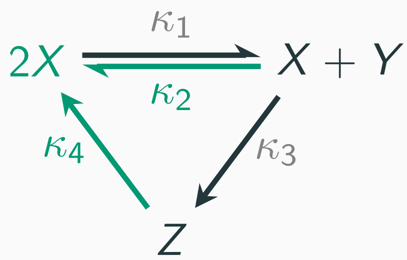

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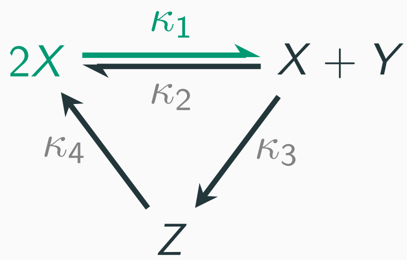

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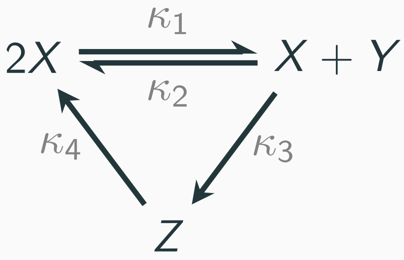
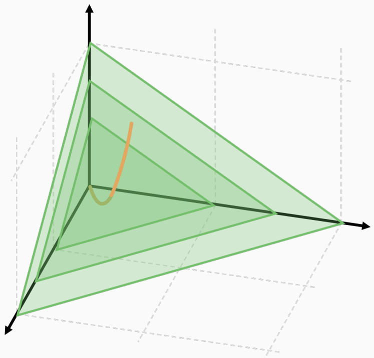
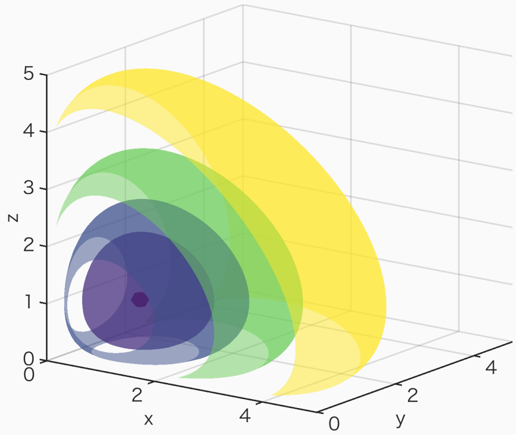


Complex-balancing is amazing

- If there is one CB steady state, then every positive steady state is CB
- monomial parametrization[a]
- Lyapunov function around CB $\boldsymbol{x}^*$
- Global Attractor Conjecture





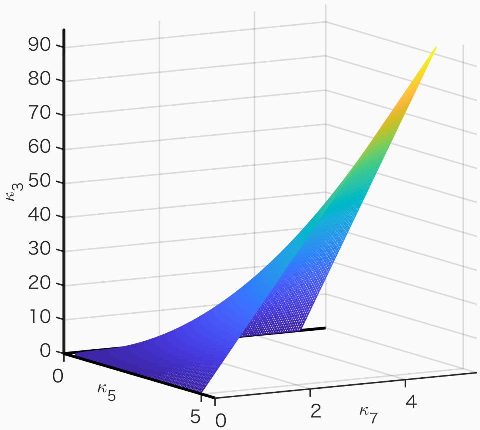
[a] Additional slide

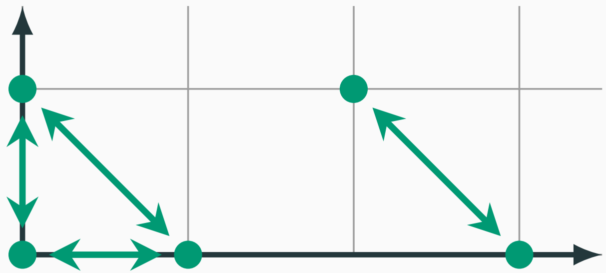
Algebraic conditions on κ

- CB $\iff$ κ_i satisfy some polynomial equations

- Number of equations $\approx$ **deficiency** δ

$$\delta = |V| - \ell - \dim S$$





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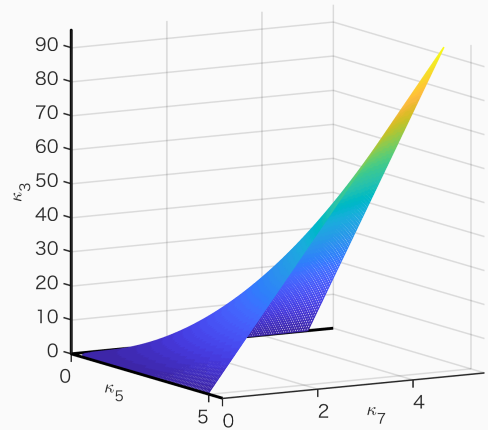

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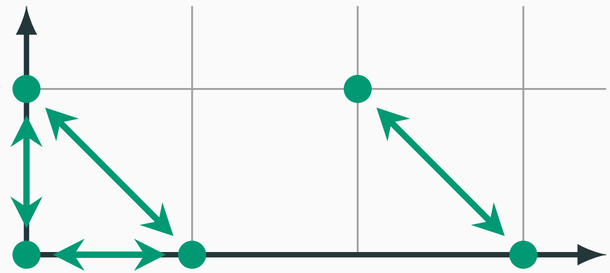
Poll!! What is $\delta = ??$



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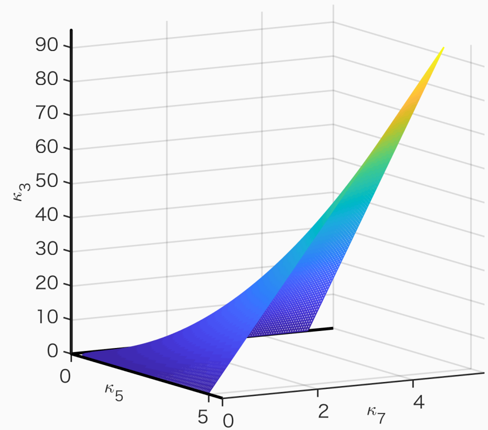

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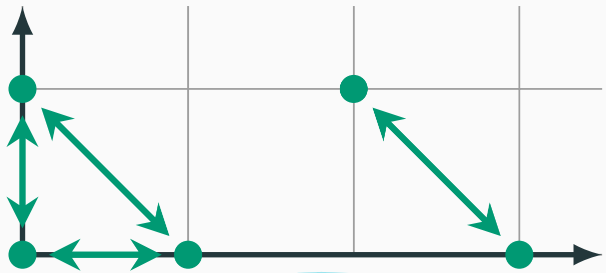
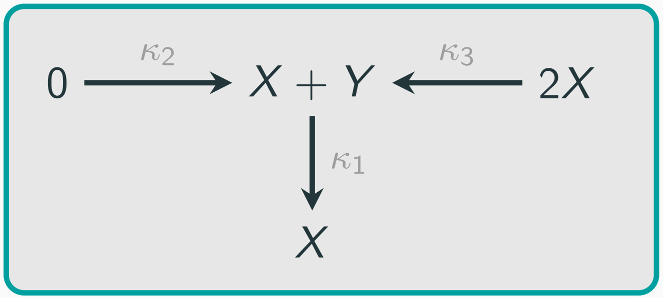


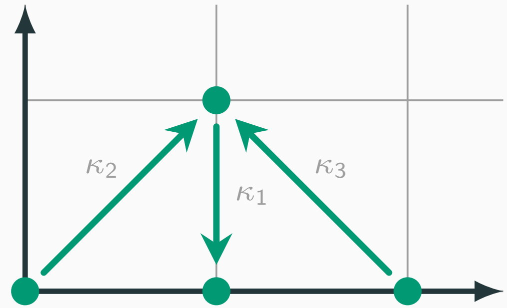
$\delta = 5 - 2 - 2 = 1$

Dynamical Equivalence

Dynamical Equivalence

$$\delta = 4 - 1 - 2 = 1$$





$$\frac{dx}{dt} = \cdots + \kappa_1 xy \begin{pmatrix} 0 \\ -1 \end{pmatrix}$$

Dynamical Equivalence

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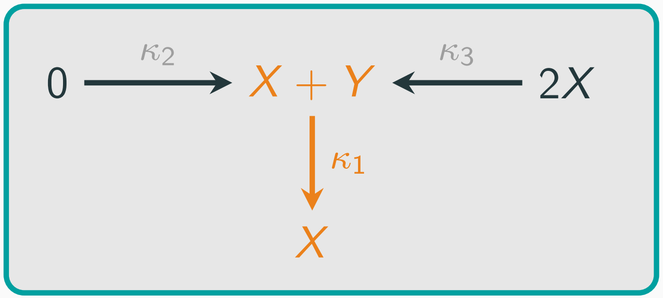

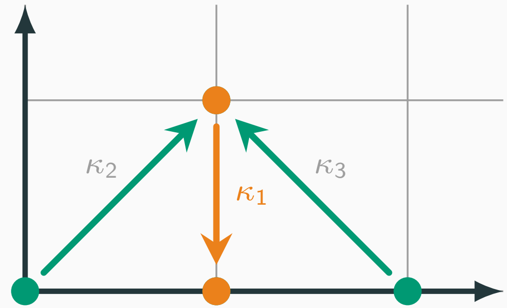

$$\frac{d\boldsymbol{x}}{dt} = \cdots + \kappa_1 xy \begin{pmatrix} 0 \\ -1 \end{pmatrix}$$

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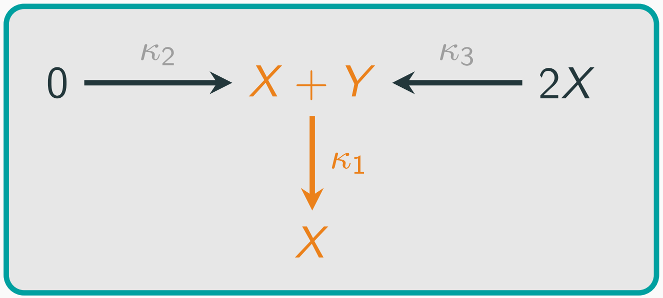
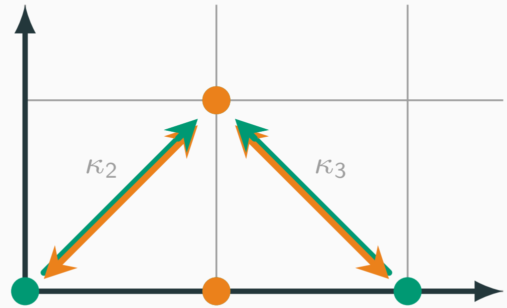




$$\frac{d\boldsymbol{x}}{dt} = \cdots + \kappa_1 xy \begin{pmatrix} 0 \\ -1 \end{pmatrix}$$

$$\delta = 3 - 1 - 2 = 0$$

$$= \cdots + \frac{\kappa_1}{2} xy \begin{pmatrix} -1 \\ -1 \end{pmatrix} + \frac{\kappa_1}{2} xy \begin{pmatrix} 1 \\ -1 \end{pmatrix}$$

Dynamical equivalence

- MAS $(G, \boldsymbol{\kappa})$ and $(G', \boldsymbol{\kappa}')$ are **dynamically equivalent (DE)** if they generate same ODE

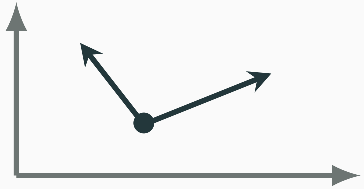
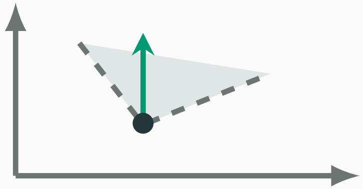
$$\sum_{(i,j)\in G} \kappa_{ij} \boldsymbol{x}^{\boldsymbol{y}_i}(\boldsymbol{y}_j - \boldsymbol{y}_i) = \sum_{(i,j)\in G'} \kappa'_{ij} \boldsymbol{x}^{\boldsymbol{y}_i}(\boldsymbol{y}_j - \boldsymbol{y}_i)$$

$\iff$ for each monomial $\boldsymbol{x}^{\boldsymbol{y}_i}$ $(\boldsymbol{y}_i \in V \cup V')$,

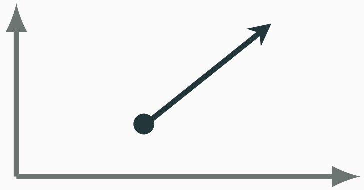
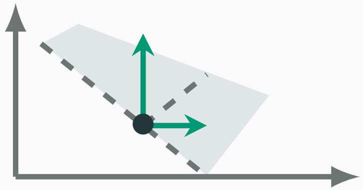
$$\sum_{(i,j)\in G} \kappa_{ij}(\boldsymbol{y}_j - \boldsymbol{y}_i) = \sum_{(i,j)\in G'} \kappa'_{ij}(\boldsymbol{y}_j - \boldsymbol{y}_i)$$

Some allowed operations

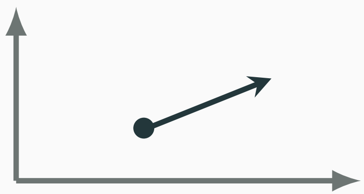
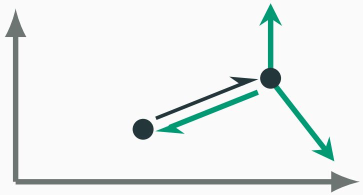
- Combining vectors:

- Breaking up a vector:

- Creating new complex:

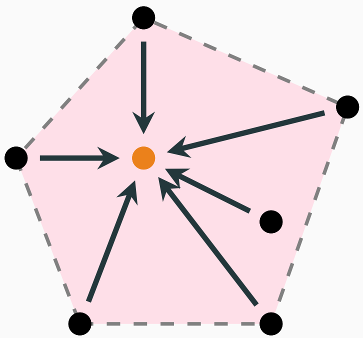



Dynamically equivalence to complex-balancing?

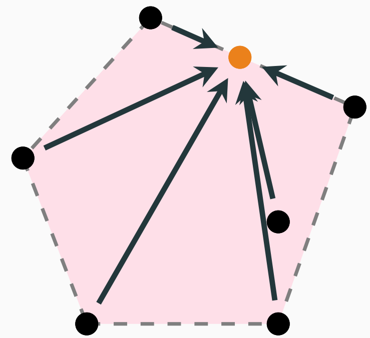
Single-target network

- Poll: One of these is not a single-target network:

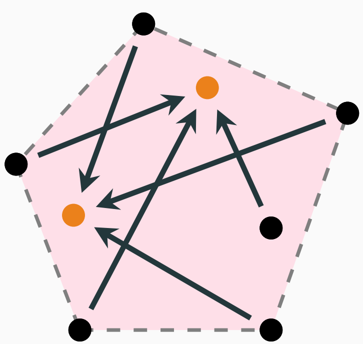
(a)



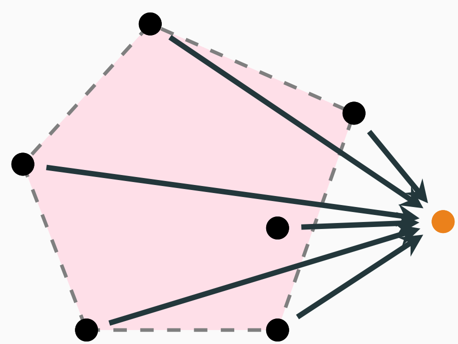
(b)



(c)



(d)



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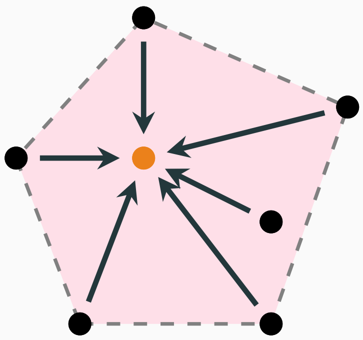

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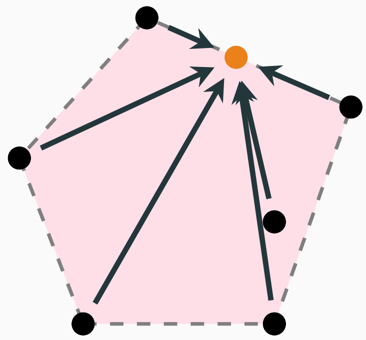

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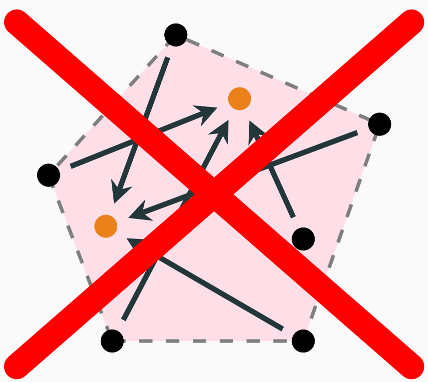

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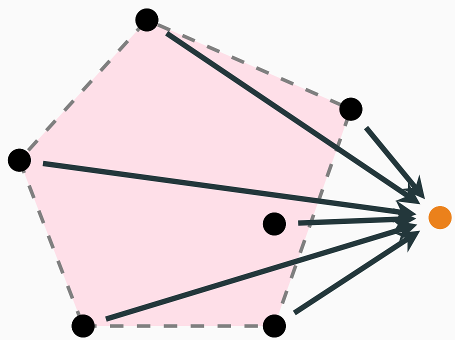
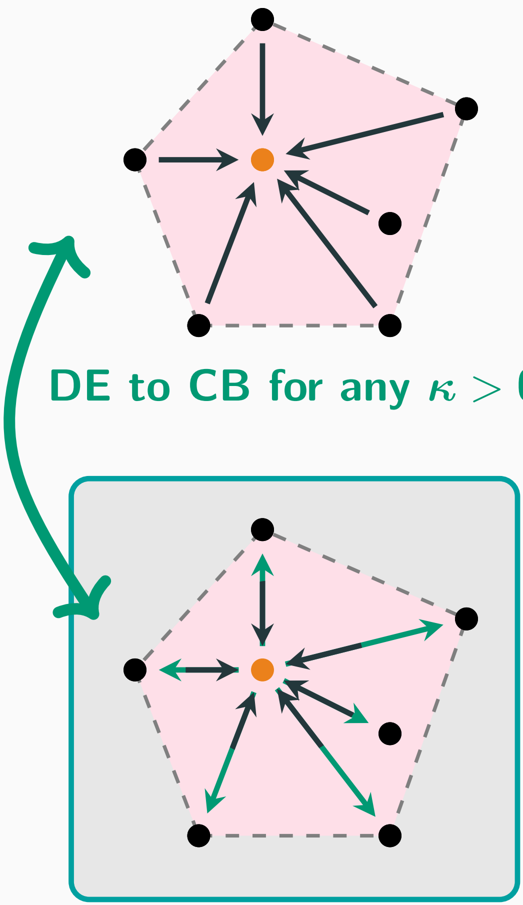
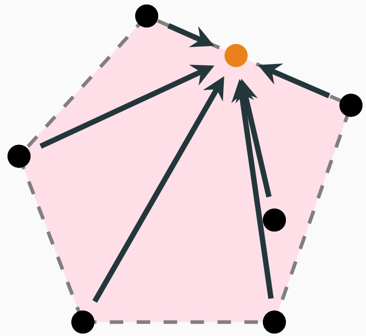
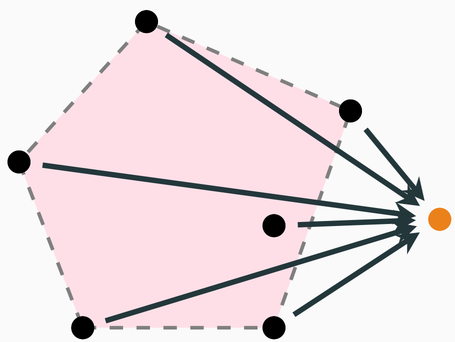


Theorem (2020):





No pos. steady state for any $\kappa > 0$



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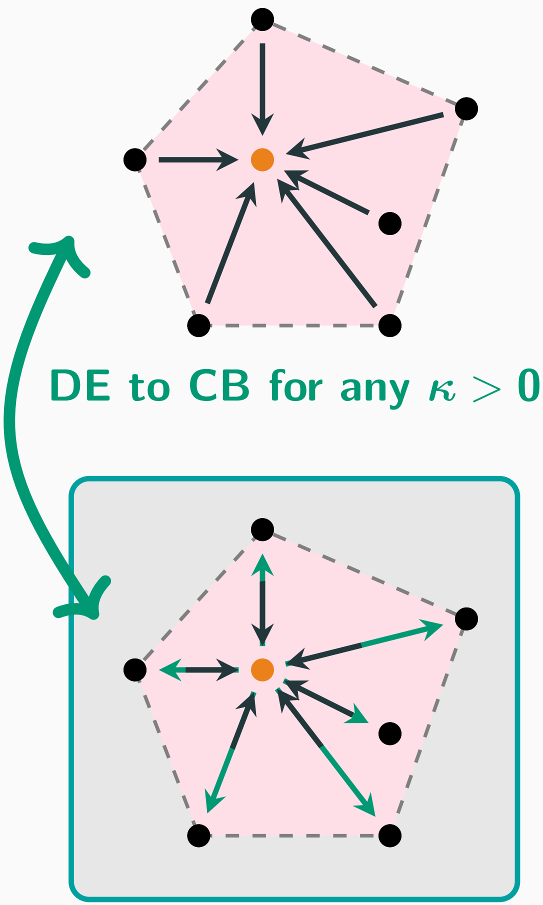
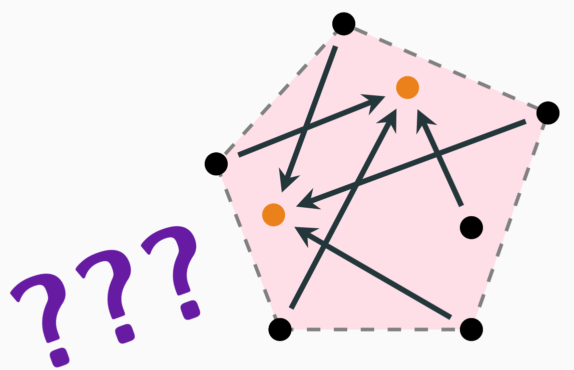
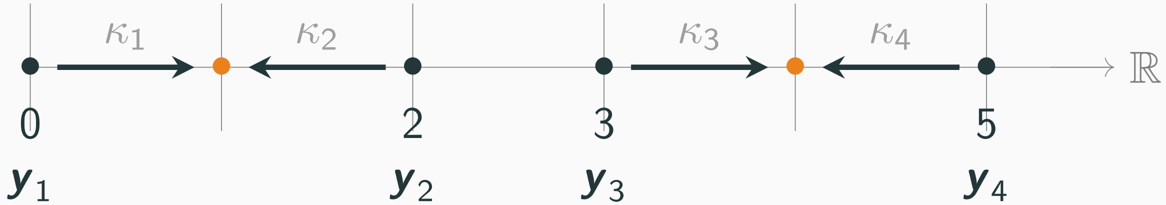


Thm: Only need nodes from monomials



Q: What about 2 targets inside Newton polytope?

- Example in 1D: (with $J_i = \kappa_i \boldsymbol{x}^{\boldsymbol{y}_i}$ and $Q_{ij} = \kappa'_{ij} \boldsymbol{x}^{\boldsymbol{y}_i}$)



- Steady state equation:

  $J_1 + J_3 = J_2 + J_4$

- DE condition:

  $J_1 = 2Q_{12} + 3Q_{13} + 5Q_{14}, \ldots$ + 3 more eqs

- CB condition:

  $Q_{12} + Q_{13} + Q_{14} = Q_{21} + Q_{31} + Q_{41}, \ldots$ + 3 more eqs

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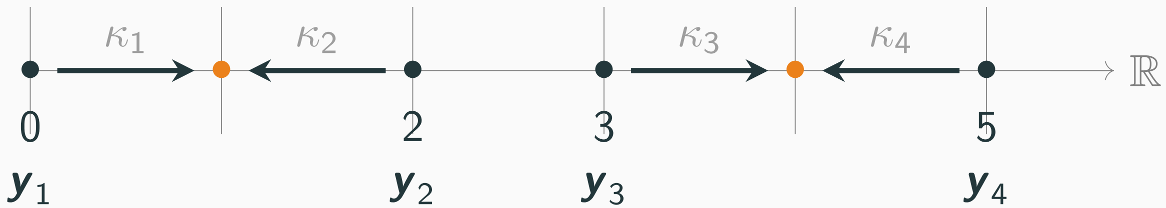

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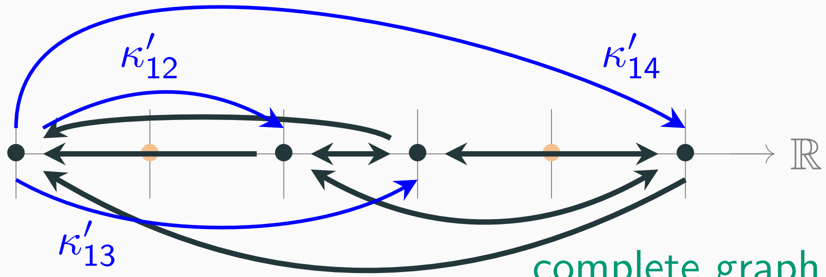

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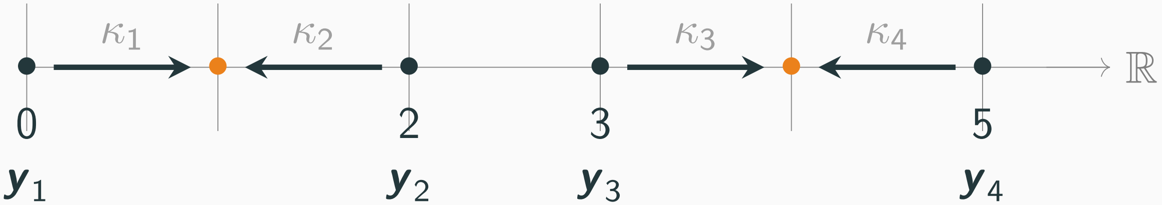

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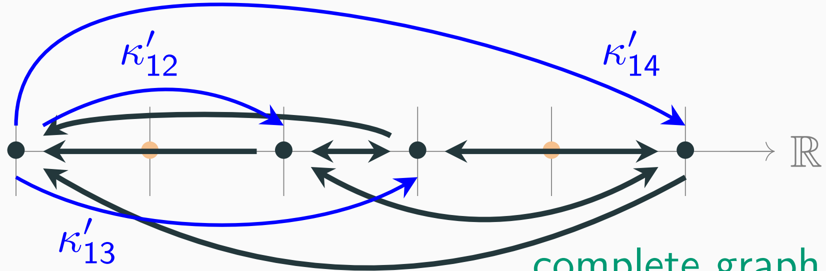

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Q: What about 2 targets inside Newton polytope?

- Linear in $J_i > 0$ and $Q_{ij} \geq 0$:

$$J_1 + J_3 = J_2 + J_4 \tag{ss}$$

$$J_1 = 2Q_{12} + 3Q_{13} + 5Q_{14} \tag{DE1}$$

$$-J_2 = -2Q_{21} + Q_{23} + 3Q_{24} \tag{DE2}$$

$$J_3 = -3Q_{31} - Q_{32} + 2Q_{34} \tag{DE3}$$

$$-J_4 = -5Q_{41} - 3Q_{42} - 2Q_{43} \tag{DE4}$$

$$Q_{12} + Q_{13} + Q_{14} = Q_{21} + Q_{31} + Q_{41} \tag{CB1}$$

$$Q_{21} + Q_{23} + Q_{24} = Q_{12} + Q_{32} + Q_{42} \tag{CB2}$$

$$Q_{31} + Q_{32} + Q_{34} = Q_{13} + Q_{23} + Q_{43} \tag{CB3}$$

$$Q_{41} + Q_{42} + Q_{43} = Q_{14} + Q_{24} + Q_{34} \tag{CB4}$$

Q: What about 2 targets inside Newton polytope?

- DE + CB (slide above)

  $\implies \quad J_1 \geq J_2$ and $J_4 \geq J_3$

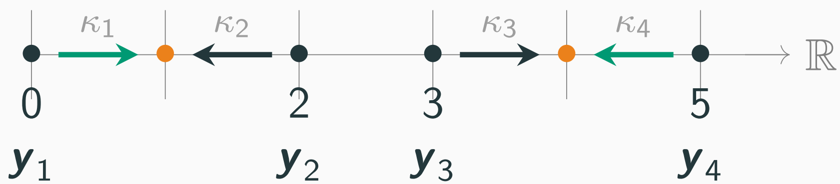
  $\implies \quad J_1 J_4 \geq J_2 J_3$, i.e.,

$$J_1 J_4 - J_2 J_3 = x^5 \left(\kappa_1 \kappa_4 - \kappa_2 \kappa_3\right) > 0$$

- can show:

$$\text{DE to CB} \quad \iff \quad \kappa_1 \kappa_4 - \kappa_2 \kappa_3 > 0$$

- brute force calculation



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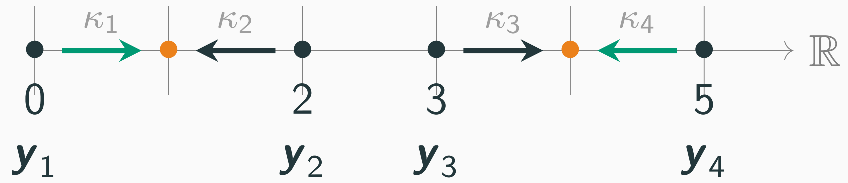
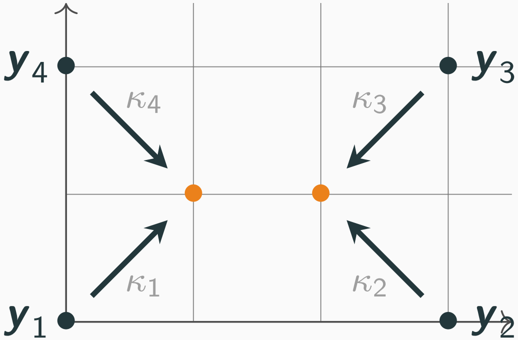


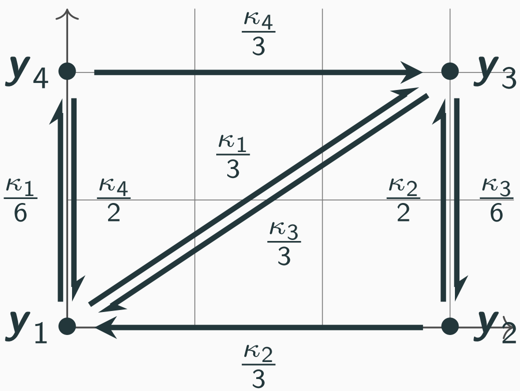
Another example (2D)



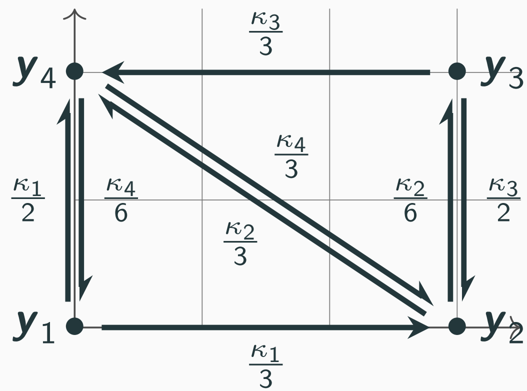
- DE to CB $\iff$

$$\frac{1}{25} \leq \frac{\kappa_2\kappa_4}{\kappa_1\kappa_3} \leq 25$$

- Possible with



or



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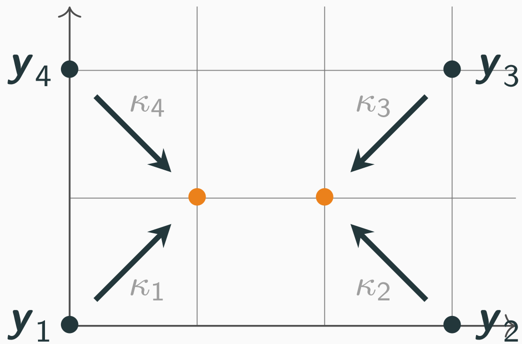


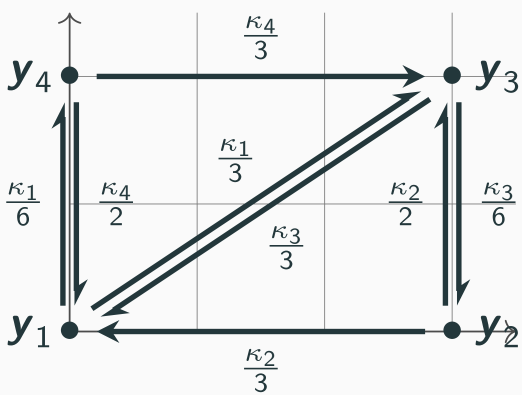
- DE to CB $\iff$

$$\frac{1}{25} \leq \frac{\kappa_2 \kappa_4}{\kappa_1 \kappa_3} \leq 25$$

Coincidence?

Or good question?

- Possible with



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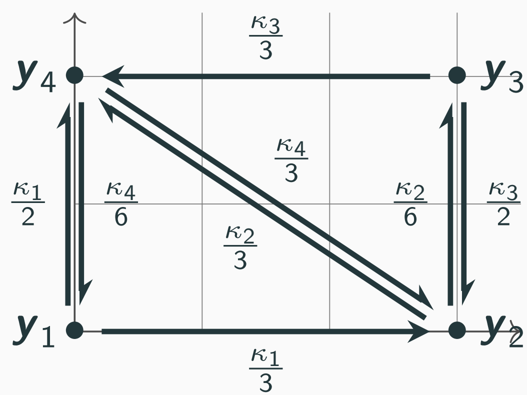


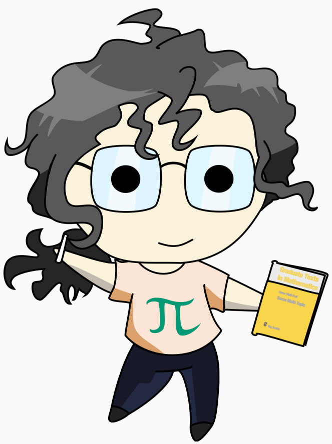
Summary

- Linear feasibility problem→

$$\text{Linear inequalities } J_i > 0,\ Q_{ij} \geq 0$$

- Eliminate $\boldsymbol{x}$ from $J_i = \kappa_i \boldsymbol{x}^{\boldsymbol{y}_i}$ for non-linear inequalities on κ_{ij}?

Real quantifier elimination??



Related talk: Fri Jun 5 at 9:40 (MT)

Miruna-Stefana Sorea:

Disguised toric dynamical systems

References

- G. Craciun, A. Dickenstein, A. Shiu, B. Sturmfels *Toric Dynamical Systems.* 2009.
- G. Craciun, J. Jin and P.Y. Yu, *An efficient characterization of complex-balanced, detailed-balanced, and weakly reversible systems.* 2020.
- G. Craciun, J. Jin and P.Y. Yu, *Single-target networks. On arXiv soon.*

$$\frac{d\vec{x}}{dt} = \sum k_i \vec{a}_i x^{y_i}$$

Thanks!

Additional slides

Monomial parametrization for complex-balancing

- Complex-balanced set

$$Z_{\boldsymbol{\kappa}} = \left\{ \boldsymbol{x} > \boldsymbol{0} \mid \underbrace{\log \boldsymbol{x} - \log \boldsymbol{x}^* \in S^\perp}_{} \right\}$$

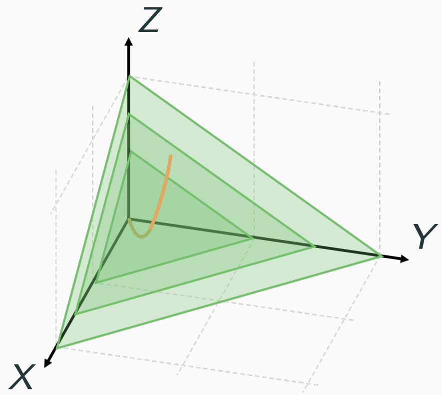
$$\log\left(\frac{\boldsymbol{x}}{\boldsymbol{x}^*}\right) \in S^\perp$$

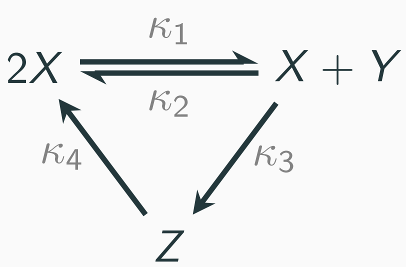
$$\iff \quad \frac{\boldsymbol{x}}{\boldsymbol{x}^*} \in \exp S^\perp$$

$$\iff \quad \boldsymbol{x} \in \boldsymbol{x}^* \circ \exp S^\perp$$

- E.g. $S^\perp = \operatorname{span}(1, 1, 2)$

$$E_{\boldsymbol{\kappa}} = \left\{ (a_1 t, a_2 t, a_3 t^2) \mid t > 0 \right\}$$





Toricity in complex-balancing

$-\underline{\mathbf{A}}_{\kappa}^{\top}$ = Laplacian matrix of G

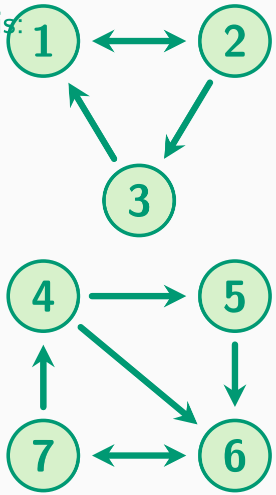
- CB $\iff \boldsymbol{x}^{\underline{\mathbf{Y}}} \in \ker \underline{\mathbf{A}}_{\kappa} \iff \boldsymbol{x}^{\underline{\mathbf{Y}}} \perp (\ker \underline{\mathbf{A}}_{\kappa})^{\perp}$

basis:

Matrix-Tree Theorem

$$(K_2, -K_1, 0, 0, 0, 0, 0)^{\top}$$
$$(0, K_3, -K_2, 0, 0, 0, 0)^{\top}$$

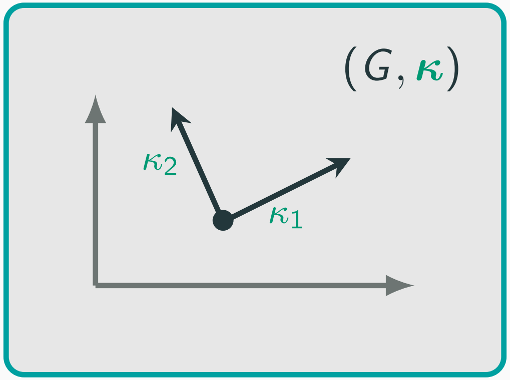
$$(0, 0, 0, K_5, -K_4, 0, 0)^{\top}$$
$$(0, 0, 0, 0, K_6, -K_5, 0)^{\top}$$
$$(0, 0, 0, 0, 0, K_7, -K_6)^{\top}$$



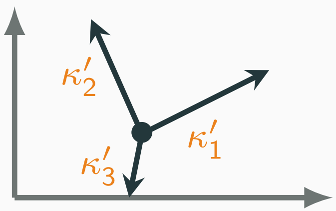
$$\iff \begin{cases} K_2 \boldsymbol{x}^{\boldsymbol{y}_1} - K_1 \boldsymbol{x}^{\boldsymbol{y}_2} = 0 \\ \vdots \\ K_7 \boldsymbol{x}^{\boldsymbol{y}_6} - K_6 \boldsymbol{x}^{\boldsymbol{y}_7} = 0 \end{cases}$$

Dynamical equivalence: Test your understanding

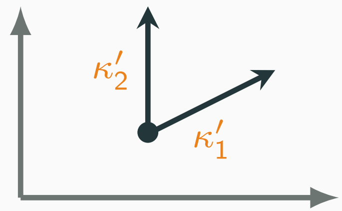
- For which $(G', \boldsymbol{\kappa}')$, $\forall \kappa_j > 0 \; \exists \kappa'_j \geq 0$: $(G, \boldsymbol{\kappa})$ and $(G', \boldsymbol{\kappa}')$ are DE?



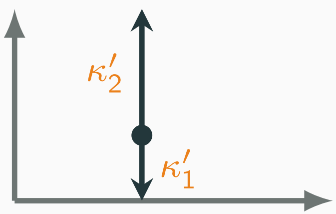
(a)



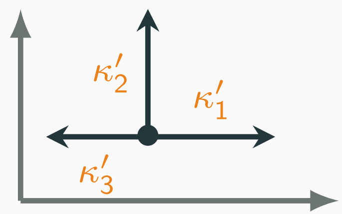
(b)



(c)

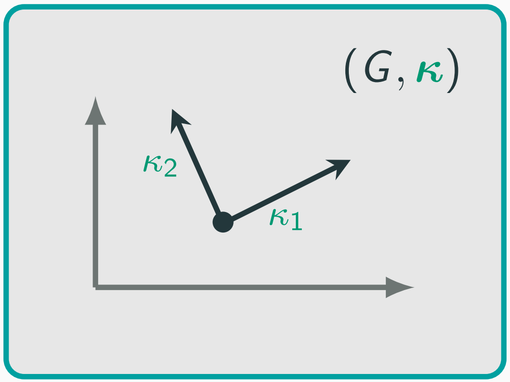


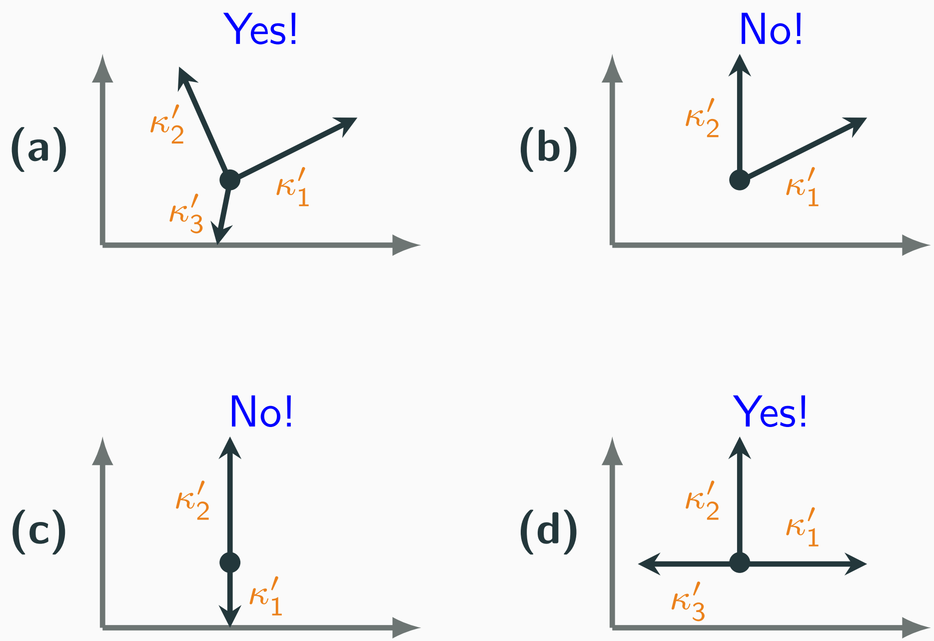
(d)



Dynamical equivalence: Test your understanding

- For which $(G', \boldsymbol{\kappa}')$, $\forall \kappa_j > 0 \; \exists \kappa'_j \geq 0$: $(G, \boldsymbol{\kappa})$ and $(G', \boldsymbol{\kappa}')$ are DE?





Basically can be embed cone generated by vector into those of G'