Mass action networks with the isolation property

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(joint work with Carsten Conradi and Thomas Kahle)

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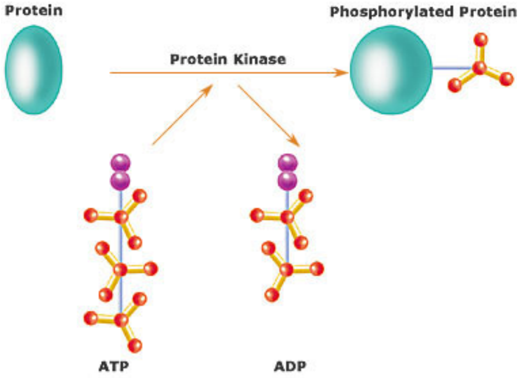
Phosphorylation



(Wikipedia)

Sequential Distributed Phosphorylations

$$A + E_1 \rightleftharpoons AE_1 \longrightarrow A_p + E_1$$

$$A_p + E_2 \rightleftharpoons A_pE_2 \longrightarrow A + E_2$$

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- Assume that A, E_1, ... are in some isolated, homogeneous reactor $\mathfrak{R}$.

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The rate of a chemical reaction is directly proportional to the product of concentrations of the reactants.

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Law of mass action

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Denote: $[A] = x_1$, $[E_1] = x_2$, $[AE_1] = x_3$, $[A_p] = x_4$, $[E_2] = x_5$, $[A_pE_2] = x_6$.

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$$x_1 x_2 \underset{k_2}{\overset{k_1}{\rightleftarrows}} x_3 \xrightarrow{k_3} x_2 x_4$$

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- Trajectory:

$$\dot{x}_1 = -k_1 x_1 x_2 + k_2 x_3 + k_6 x_6$$

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- Steady States ($\dot{x}_i = 0$):

$$0 = -k_1x_1x_2 + k_2x_3 + k_6x_6$$
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- Trajectory:

$$\dot{x} = \underbrace{\begin{pmatrix} -1 & 1 & 0 & 0 & 0 & 1 \\ -1 & 1 & 1 & 0 & 0 & 0 \\ 1 & -1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 1 & -1 & 1 & 0 \\ 0 & 0 & 0 & -1 & 1 & 1 \\ 0 & 0 & 0 & 1 & -1 & -1 \end{pmatrix}}_{S} \underbrace{\begin{pmatrix} k_1x_1x_2 \\ k_2x_3 \\ k_3x_3 \\ k_4x_4x_5 \\ k_5x_6 \\ k_6x_6 \end{pmatrix}}_{\phi(k,x)}$$

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Macaulay2 Experiment 1

```
i1 : needsPackage("Binomials");
i2 : K=QQ[k_1..k_6]; R=K[x_1..x_6];
i3 : I=ideal(-k_1*x_1*x_2+k_2*x_3+k_6*x_6,
       -k_1*x_1*x_2+k_2*x_3+k_3*x_3,
        k_1*x_1*x_2-k_2*x_3-k_3*x_3,
        k_3*x_3-k_4*x_4*x_5+k_5*x_6,
       -k_4*x_4*x_5+k_5*x_6+k_6*x_6,
        k_4*x_4*x_5-k_5*x_6-k_6*x_6);
i4 : associatedPrimes I
o4 : {ideal(k_3*x_3-k_6*x_6,
      k_4*x_4*x_5+(-k_5-k_6)*x_6,
      k_1*x_1*x_2-k_2*x_3-k_6*x_6)}
i5 : isBinomial I
o5 = false
i6 : gens gb I
o6 = | x_3k_3-x_6k_6 x_4x_5k_4-x_6k_5-x_6k_6
       x_1x_2k_1-x_3k_2-x_6k_6 |
```

Macaulay2 Experiment 2

```
i1 : needsPackage("Binomials");
i2 : K=frac(QQ[k_1..k_6]); R=K[x_1..x_6];
i3 : I=ideal(-k_1*x_1*x_2+k_2*x_3+k_6*x_6,
       -k_1*x_1*x_2+k_2*x_3+k_3*x_3,
        k_1*x_1*x_2-k_2*x_3-k_3*x_3,
        k_3*x_3-k_4*x_4*x_5+k_5*x_6,
       -k_4*x_4*x_5+k_5*x_6+k_6*x_6,
        k_4*x_4*x_5-k_5*x_6-k_6*x_6);
i4 : associatedPrimes I
stdio:4:1:(3): error: expected base field to be QQ or ZZ/p
i5 : isBinomial I
o5 = true
i6 : gens gb I
o6 = | x_3-k_6/k_3x_6 x_4x_5+(-k_5-k_6)/k_4x_6
       x_1x_2+(-k_2k_6-k_3k_6)/k_1k_3x_6 |
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- Let $V := \{x \in \mathbb{R}^6 : f(x) = 0, \ \forall f \in I\}$,
  $V_{\geq 0} := V \cap \mathbb{R}^6_{\geq 0}$ and $V_{>0} := V \cap \mathbb{R}^6_{>0}$.

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- As I is binomial, the Zariski closure of $V_{>0}$ is toric.
- Therefore $V_{>0}$ has a monomial parametrization:

$$\begin{array}{ccc} \mathbb{R}^3_{>0} & \to & \mathbb{R}^6_{>0} \\ (t_1, t_2, t_3) & \mapsto & \left(\frac{k_6(k_2+k_3)}{k_1 k_3} \frac{t_3}{t_1}, t_1, \frac{k_6}{k_3} t_3, \frac{k_5+k_6}{k_4} \frac{t_3}{t_2}, t_2, t_3 \right). \end{array}$$

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    - Primary decomposition is computationally expensive.
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  - Look at simpler cases (e.g., systems with the isolation property)

The kernel of the stoichiometric matrix

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- Let E be a matrix whose columns are the extreme rays of $\ker(S) \cap \mathbb{R}^r_{\geq 0}$. Let n_i denote the i^{th} row of E.
- If E has p columns, let $\Lambda(E) := \{\lambda \in \mathbb{R}^p_{\geq 0} : E\lambda > 0\}$.

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- Let $\mathfrak{R}$ denote the union of all preclusters.
- A **cluster** is an element of the maximal partition of $\mathfrak{R}$ induced by the preclusters.

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Definition

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Theorem [2017; Conradi, I., Kahle]

If a mass action network $\mathcal{N}$ has the isolation property, then the set of positive steady states $V_{>0}$ of $\mathcal{N}$ has a monomial parametrization.

Idea of the proof (definitions)

- Let $\mathcal{Y}$ denote the matrix whose i^{th} column is the exponent vector of the source of the i^{th} arrow.

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- Let U^{doub} denote a matrix with r rows which has a column $e_i - e_j$ for each superdoubling set $\{i, j\}$.

Idea of the proof (definitions)

- Let $\mathcal{Y}$ denote the matrix whose i^{th} column is the exponent vector of the source of the i^{th} arrow.
- If $\{i, j\}$ is a superdoubling set, then $e_i - e_j \in \ker(\mathcal{Y})$, where $\{e_1, \ldots, e_r\}$ is the cannonical basis of $\mathbb{R}^r$.
- Let U^{doub} denote a matrix with r rows which has a column $e_i - e_j$ for each superdoubling set $\{i, j\}$.
- Let $\tilde{U}$ denote a matrix such that the columns of $(U^{\text{doub}}|\tilde{U})$ span $\ker(\mathcal{Y})$.

Idea of the proof

Lemma I [2010; Conradi, Flockerzi]

If i and j belong to the same cluster J, then
$\log\left(\frac{n_i\nu}{n_i\lambda}\right) = \log\left(\frac{n_j\nu}{n_j\lambda}\right) := \psi_J(\nu,\lambda)$ for all $\nu, \lambda \in \Lambda(E)$.

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Definition

If $\mathcal{N}$ has γ clusters, $J_1, \ldots, J_\gamma$, let:

$$\begin{array}{rccc} \psi : & \Lambda^2(E) & \rightarrow & \mathbb{R}^\gamma \\ & (\nu, \lambda) & \mapsto & (\psi_{J_1}(\nu,\lambda), \ldots, \psi_{J_\gamma}(\nu,\lambda)). \end{array}$$

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Lemma II [2010; Conradi, Flockerzi]

If $\mathcal{N}$ has the isolation property then imψ is a linear space.

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Let $\Pi \in \{0,1\}^{r\times\gamma}$ be such that the support of its i^{th} column is J_i

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Lemma III [2010; Conradi, Flockerzi]

There are two positive steady states $x^* \neq x^{**}$ with and common k^* if and only if $\exists \kappa \in \text{im}\psi$ with $\mathcal{Y}^T(\log(x^{**}) - \log(x^*)) = \Pi\kappa$ and $\tilde{U}^T \Pi \kappa = 0$.

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Lemma IV [2017; Conradi, I., Kahle]

For every steady state x^* of $\mathcal{N}$ and for every $\kappa \in \text{im}\psi$ and $\mu \in \mathbb{R}^n - \{0\}$ with $\tilde{U}^T \Pi\kappa = 0$ and $\mathcal{Y}^T \mu = \Pi\kappa$, there is another steady state $x^{**} = e^{\mu} \circ x^*$.

Thank you for your attention!

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