On the state space of the stochastic model

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Lecture on formal reaction kinetics
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- Structure of the state space for $M = 1$

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1. Reaction kinetic models (concepts to be used)

1. Reaction and mechanism

Definition. An ordered quadruple $<\mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}>$ is said to be a **reaction**, if $\mathcal{M}$ and $\mathcal{R}$ are finite, disjoint sets of M and R elements respectively ($M, R \in \mathbb{Z}^+$), $\boldsymbol{\alpha}, \boldsymbol{\beta} : \mathcal{M} \times \mathcal{R} \longrightarrow \mathbb{N}$ are functions sor matrices with some restrictions, see below.

The elements of $\mathcal{M}$, denoted by $X(m)$, are the (chemical) species, the elements of $\mathcal{R}$ are the reaction steps, and $\alpha(m,\ r)$ and $\beta(m,\ r)$ are the (reactant and product) stoichiometric coefficients expressing the number of $X(m)$ needed to and produced in the rth reaction step. The usual representation of the reaction $<\mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}>$ is:

$$\sum_{m=1}^{M} \alpha(m,\ r)\, X(m) \longrightarrow \sum_{m=1}^{M} \beta(m,\ r)\, X(m) \qquad (r = 1,\ 2,\ \ldots,\ R)$$

Now the restrictions are:
1. all the species take part in at least one reaction step;
2. all the reaction steps change the quantity of at least one species;
3. all the reaction steps are determined by their reactant and complex products.

Definition. The vector $\boldsymbol{\alpha}(.,\ r)$ is the rth **reactant complex vector**, $\boldsymbol{\beta}(.,\ r)$ is the **product complex vector**, the set

$$\{\boldsymbol{\alpha}(.,\ r) : r \in \mathcal{R}\} \cup \{\boldsymbol{\beta}(.,\ r) : r \in \mathcal{R}\}$$

is the set of **complex vectors**, the number of its elements is denoted by N, its elements are sometimes denoted by $\boldsymbol{y}(1),\ \boldsymbol{y}(2),\ \ldots,\ \boldsymbol{y}(N)$. The elements of $\mathcal{R}$ can be identified with pairs $(i,\ j)$ for which a reaction step $\boldsymbol{y}(i) \longrightarrow \boldsymbol{y}(j)$ occurs. The linear space $\mathcal{S}$ generated by the reaction vectors $\boldsymbol{\gamma}(.,\ r) := \boldsymbol{\beta}(.,\ r) - \boldsymbol{\alpha}(.,\ r)$ is the stoichiometric space.

The directed graph with the complexes as vertices and reaction steps as edges is the **Feinberg-Horn-Jackson graph** of the reaction.

Definition. If the reaction $<\mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}>$ together with the step

$$\sum_{m=1}^{M} \alpha(m,\ r)\, X(m) \longrightarrow \sum_{m=1}^{M} \beta(m,\ r)\, X(m) \qquad (r = 1,\ 2,\ \ldots,\ R)$$

also the step $\sum_{m=1}^{M} \beta(m,\ r)\, X(m) \longrightarrow \sum_{m=1}^{M} \alpha(m,\ r)\, X(m) \qquad (r = 1,\ 2,\ \ldots,\ R)$

occurs, then the reaction step is said to be **reversible**. If all the rection steps are reversible then the reaction is reversible.

Definition. An ordered quintuple $<\mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}, \boldsymbol{k}>$ is said to be a **mechanism**, if $<\mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}>$ is a reaction and $\boldsymbol{k} : \mathcal{R} \longrightarrow \mathbb{R}^{+}$ is a vector (or a function), the components (or values) of which are called **reaction rate coefficients**.

2. The deterministic model of reaction kinetics

Let us define te common continuous time continuous state (mass action type) deterministic model of the mechanism $<\mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}, \boldsymbol{k}>$.

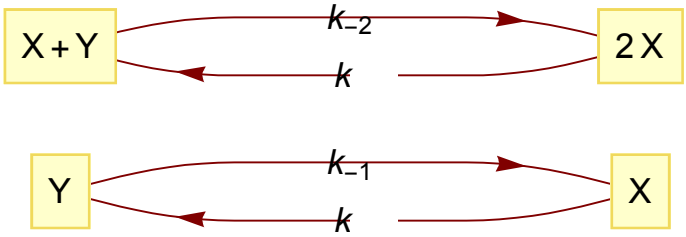
Definition. The deterministic model of the mechanism $<\mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}, \boldsymbol{k}>$ is the (autonomous) polynomial differential equation:

$$c_m'(t) = f_m(c(t)) := \sum_{r=1}^{R} (\beta(m,\ r) - \alpha(m,\ r))\, k_r \prod_{p=1}^{M} c_p(t)^{\alpha(p,r)}$$

$$c_m(0) = c_{m0} \in \mathbb{R}_0^{+} \qquad (m = 1,\ 2,\ \ldots,\ M)$$

The quantity $\mathbf{c}(t)$ is interpreted as the vector of concentrations of the species at time t. The model describes its time evolution.

Example: Wegscheider reaction



Species: X, Y

Reactions: $\mathcal{R} = \left\{ X \xrightarrow{k_1} Y,\ \ Y \xrightarrow{k_{-1}} X,\ \ 2X \xrightarrow{k_2} X + Y,\ \ X + Y \xrightarrow{k_{-2}} 2X \right\}$

Complexes ($N = 4$): X, Y, $2X$, $X + Y$

Complex vectors: $\mathbf{y}_1 = \begin{pmatrix} 1 \\ 0 \end{pmatrix},\ \mathbf{y}_2 = \begin{pmatrix} 0 \\ 1 \end{pmatrix},\ \mathbf{y}_3 = \begin{pmatrix} 2 \\ 0 \end{pmatrix},\ \mathbf{y}_4 = \begin{pmatrix} 1 \\ 1 \end{pmatrix}$

Reactions vectors: $\mathbf{v}_1 = \mathbf{y}_2 - \mathbf{y}_1,\ \mathbf{v}_2 = \mathbf{y}_1 - \mathbf{y}_2,\ \mathbf{v}_3 = \mathbf{y}_4 - \mathbf{y}_3,\ \mathbf{v}_4 = \mathbf{y}_3 - \mathbf{y}_4$

$$\alpha = \begin{pmatrix} 1 & 0 & 2 & 1 \\ 0 & 1 & 0 & 1 \end{pmatrix} \qquad \beta = \begin{pmatrix} 0 & 1 & 1 & 2 \\ 1 & 0 & 1 & 0 \end{pmatrix} \qquad \gamma = \beta - \alpha = \begin{pmatrix} -1 & 1 & -1 & 1 \\ 1 & -1 & 1 & -1 \end{pmatrix}$$

$$x'(t) = -k_1\, x(t) + k_{-1}\, y(t) - k_2\, x(t)^2 + k_{-2}\, x(t)\, y(t)$$

$$y'(t) = k_1\, x(t) - k_{-1}\, y(t) + k_2\, x(t)^2 - k_{-2}\, x(t)\, y(t)$$

3. The stochastic model of reaction kinetics

Let us define the most usual, continuous time discrete state stochastic model of the mechanism

$<\mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}, \boldsymbol{w}>$.

Definition. The stochastic model of the mechanism $<\mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}, \boldsymbol{w}>$ is a continuous time Markovian jump process with the state space $\mathbb{N}^M$ and with the transition rates (or infinitesimal transition probabilities) as follows:

$$q_{\mathbf{i},\mathbf{j}} := \sum_{r:\, \gamma(\cdot,r)=\mathbf{j}-\mathbf{i}} w_r(\mathbf{i}) \qquad (\mathbf{i}, \mathbf{j} \in \mathbb{N}^M)$$

where $w_r(\mathbf{i}) > 0 \iff \mathbf{i} \geq \boldsymbol{\alpha}(\cdot, r) \qquad (r \in \mathcal{R}, \mathbf{i} \in \mathbb{N}^M)$.

The most often used (combinatorial or Kurtz type) form for **w** is

$$w_r(\mathbf{i}) = \kappa_r(\mathbf{i})_{\boldsymbol{\alpha}(\cdot,r)} \qquad (r \in \mathcal{R},\ \kappa_r \in \mathbb{R}^+,\ \mathbf{i} \in \mathbb{N}^M)$$

where $(\mathbf{i})_{\boldsymbol{\alpha}(\cdot,r)} := \prod_{m=1}^{M} i_m(i_m-1)\ldots(i_m-\alpha(m,r)+1)$

is the **falling factorial power** of the vector **i** raised to the vectorial exponent $\boldsymbol{\alpha}(\cdot, r)$.

Remarks.
1) Here the quantities **i, j** are interpreted as the vector of possible numbers of molecules of the species. The model describes the time evolution of the transition and absolute probabilities of the vector $\boldsymbol{\xi}(t)$ representing the vector of the number of the individual species.

2) Let us denote the volume of the vessel in which the reactions take place by V, then the simple relation between the deterministic and stochastic reaction rate coefficients is as follows:

$$k_r\, V^{\sum_m \alpha(m,r)-1} = \kappa_r$$

Example: Wegscheider reaction

$$\mathcal{R} = \left\{ X \xrightarrow{k_1} Y,\ \ Y \xrightarrow{k_{-1}} X,\ \ 2X \xrightarrow{k_2} X+Y,\ \ X+Y \xrightarrow{k_{-2}} 2X \right\}$$

Let $\mathbf{i} = (n, p)$ and supposing that the initial state was $\mathbf{D} = (D_1, D_2)^T$, the state space is $\Phi = \{(n, p) \in \mathbb{N}\times\mathbb{N};\ n + p = D_1 + D_2\}$.

Transition rates: $q_{(n,p),(n-1,p+1)} = k_1\, n + k_2\, n(n-1)$

$q_{(n,p),(n+1,p-1)} = k_{-1}\, p + k_{-2}\, n\, p$

Master equation: $P_{\mathbf{i}}'(t) = \sum_{\mathbf{j}} q_{\mathbf{j},\mathbf{i}}\, P_{\mathbf{j}}(t) - P_{\mathbf{i}}(t) \sum_{\mathbf{j}} q_{\mathbf{i},\mathbf{j}}$

$$\begin{aligned} P_{n,p}'(t) = {} & (k_1(n+1) + k_2(n+1)\, n)\, P_{n+1,p-1}(t) \\ & + (k_{-1}(p+1) + k_{-2}(n-1)\,(p+1))\, P_{n-1,p+1}(t) \\ & - (k_1\, n + k_{-1}\, p + k_2\, n(n-1) + k_{-2}\, n\, p)\, P_{n,p}(t) \end{aligned}$$

2. Structure of the transition graph, examples

1. Definitions

Here we are interested in the best possible description of the directed graph corresponding to the embedded Markov of the stochastic model of complex chemical reactions.

Definition. Let $\boldsymbol{\alpha}$, $\boldsymbol{\beta}$, $\mathbf{D} \in \mathbb{N}^M$ and let $K(\boldsymbol{\alpha}) := \{\mathbf{s} \in \mathbb{N}^M : \mathbf{s} \geq \boldsymbol{\alpha}\}$. If $\mathbf{D} \in K(\boldsymbol{\alpha})$, that is, $D_i \geq \alpha_i$ for all $i = 1, \ldots, M$, then the reaction step $\boldsymbol{\alpha} \longrightarrow \boldsymbol{\beta}$ proceeds starting from state **D** and we say that **D** is an acceptable (initial) state for this reaction step.

We say that **D** is an acceptable (initial) state for the mechanism $< \mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}, \boldsymbol{w} >$ if it is an acceptable (initial) state for at least one reaction step, that is, $\mathbf{D} \in \cup\{K(\boldsymbol{\alpha}(\cdot, r)) : r \in \mathcal{R}\}$.

Definition. If $\mathbf{D} \in \mathbb{N}^M \setminus \cup\{K(\boldsymbol{\alpha}(\cdot, r)) : r \in \mathcal{R}\}$ then the mechanism $< \mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}, \boldsymbol{w} >$ does not have any reaction step proceeding from **D**, that is, **D** is an isolated absorbing state.

Definition. Let $\Gamma(\mathbf{D})$ denote the transition graph of the machanism $< \mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}, \boldsymbol{w} >$ obtained starting from the initial state **D** and let

$$\Gamma := \bigcup\{\Gamma(\mathbf{D}) : \mathbf{D} \in \mathbb{N}^M\}$$

2. Examples for Γ: $R = 1$, $M = 1, 2$

a) $2X \longrightarrow 5X$

For the initial state $D = 4$,

$$\Gamma(4) = \{4 \longrightarrow 7 \longrightarrow 10 \longrightarrow 13 \longrightarrow \ldots\}$$

and Γ consists of 5 components:

$$\Gamma = \{0\} \cup \{1\} \cup \{2 \longrightarrow 5 \longrightarrow 8 \longrightarrow 11 \longrightarrow \ldots\} \cup \{3 \longrightarrow 6 \longrightarrow 9 \longrightarrow 12 \longrightarrow \ldots\} \cup \{4 \longrightarrow 7 \longrightarrow 10 \longrightarrow 13 \longrightarrow \ldots\}$$

b) $5X \longrightarrow 2X$

For the initial state $D = 16$,

$$\Gamma(16) = \{16 \longrightarrow 13 \longrightarrow 10 \longrightarrow 7 \longrightarrow 4\}$$

and Γ consists of 5 components:

$$\Gamma = \{0\} \cup \{1\} \cup \{2 \longleftarrow 5 \longleftarrow 8 \longleftarrow 11 \longleftarrow \ldots\} \cup \{3 \longleftarrow 6 \longleftarrow 9 \longleftarrow 12 \longleftarrow \ldots\} \cup \{4 \longleftarrow 7 \longleftarrow 10 \longleftarrow 13 \longleftarrow \ldots\}$$

c) $2Y \longrightarrow X$

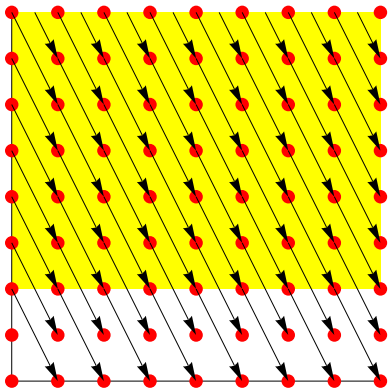
For the initial state $D = (0, 7)$,

$$\Gamma((0, 7)) = \{(0, 7) \longrightarrow (1, 5) \longrightarrow (2, 3) \longrightarrow (3, 1)\}$$

and Γ consists of the following components:

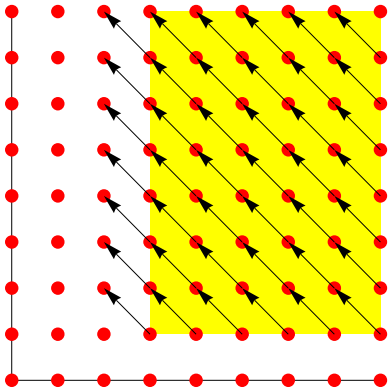
$$\Gamma = \{(0, 0)\} \cup \{(0, 1)\} \cup \left(\bigcup\{(0, s) \longrightarrow (1, s-2) \longrightarrow \ldots \longrightarrow (i, s-2i) : s - 2i \geq 0, i \in \mathbb{N}\}\right)$$

The points in the shaded region correspond to the points in $K((0, 2))$.



d) $3X + Y \longrightarrow 2X + 2Y$

The points in the shaded region correspond to the points in $K((3, 1))$.



3. Examples for $\Gamma(D)$, $R \geq 2$, $M = 2$

Algorithm for finding Γ(IS) if IS, $\alpha(1)$, ..., $\alpha(R)$, $v(1)$, ..., $v(R)$ are given

Programs: the FHJ graph and Γ(IS) in 2D

e) $R = 5$, $M = 2$

```
ClearAll[RC, RV, L, IS];
RC = {{1, 7}, {3, 3}, {5, 5}, {6, 1}, {8, 9}};
RV = {{1, 1}, {1, 0}, {-1, -1}, {2, 1}, {0, -1}};
IS = {{3, 8}}; L = {15, 12};
Reactions[RC, RV]
{FHJ[RC, RV, L, 400], Gamma2D[RC, RV, IS, 30, L, 400]}
```

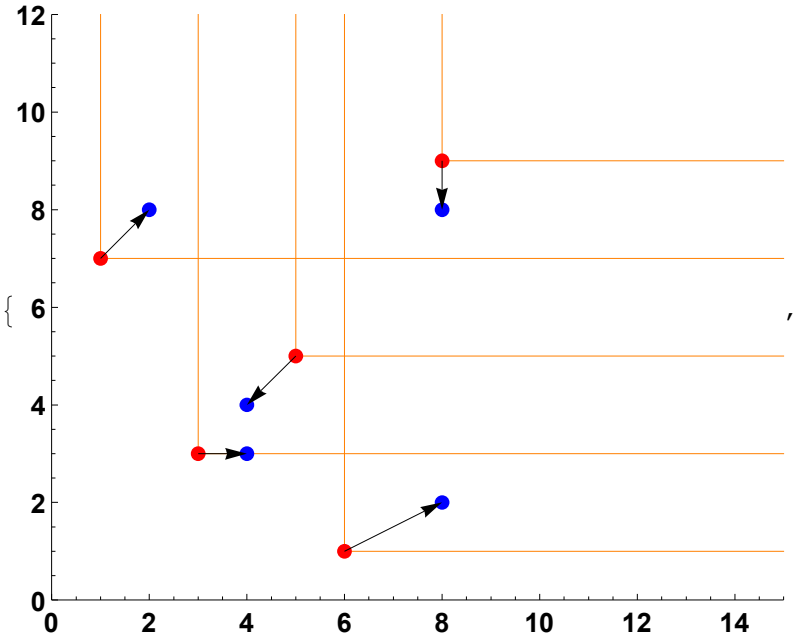
$X + 7\,Y \to 2\,X + 8\,Y$

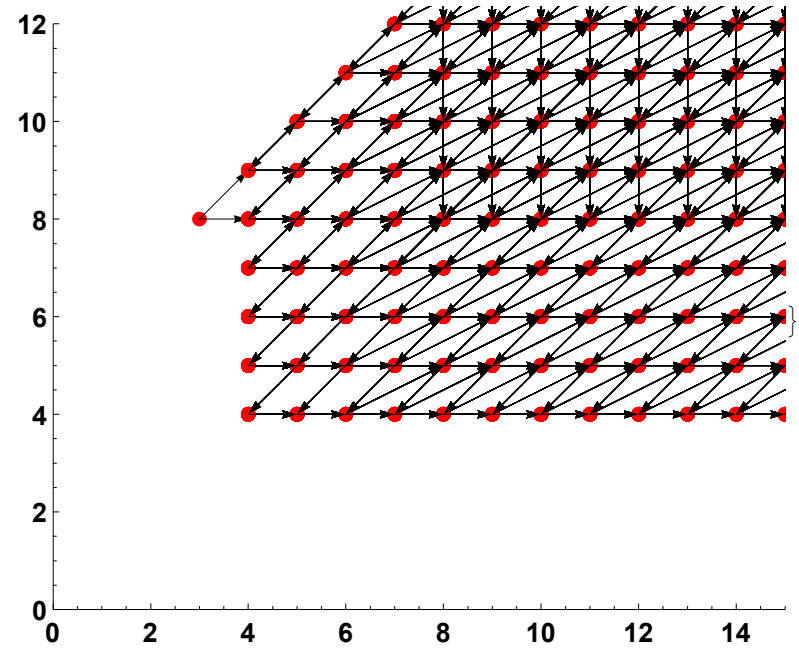
$3\,X + 3\,Y \to 4\,X + 3\,Y$

$5\,X + 5\,Y \to 4\,X + 4\,Y$

$6\,X + Y \to 8\,X + 2\,Y$

$8\,X + 9\,Y \to 8\,X + 8\,Y$



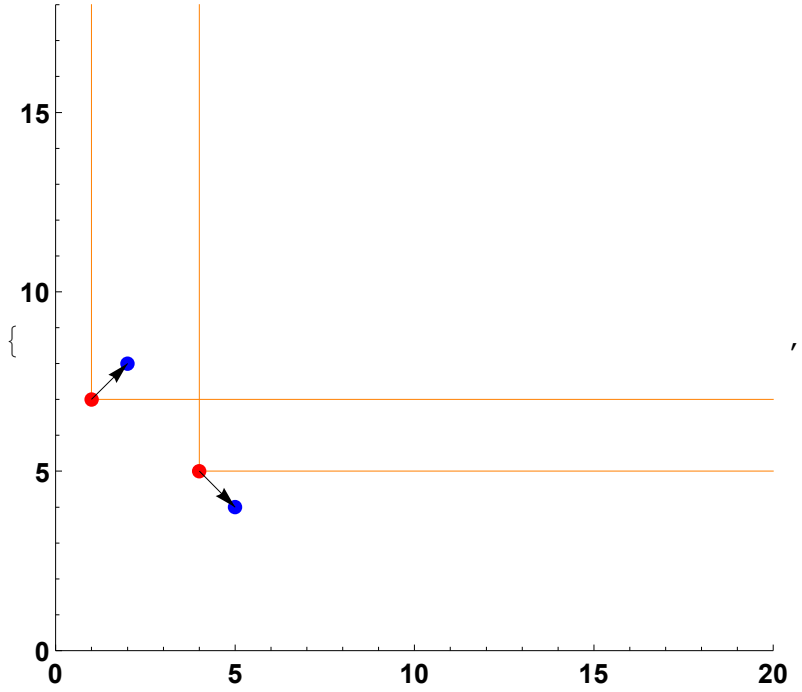


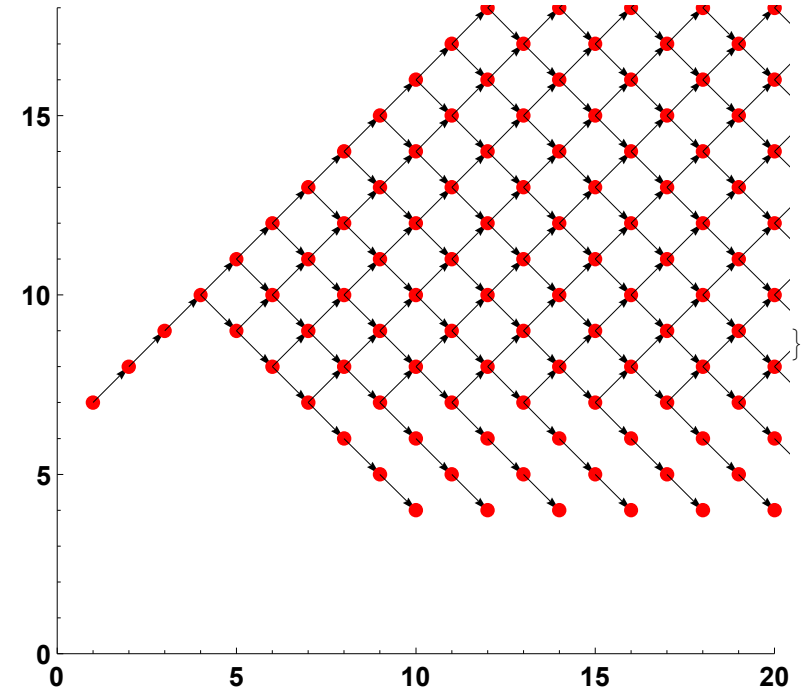
f) $R = 2,\ M = 2$

```
ClearAll[RC, RV, L, IS];
RC = {{1, 7}, {4, 5}}; RV = {{1, 1}, {1, -1}};
IS = {{1, 7}}; L = {20, 18};
Reactions[RC, RV]
{FHJ[RC, RV, L, 400], Gamma2D[RC, RV, IS, 30, L, 400]}
```

X + 7 Y → 2 X + 8 Y

4 X + 5 Y → 5 X + 4 Y



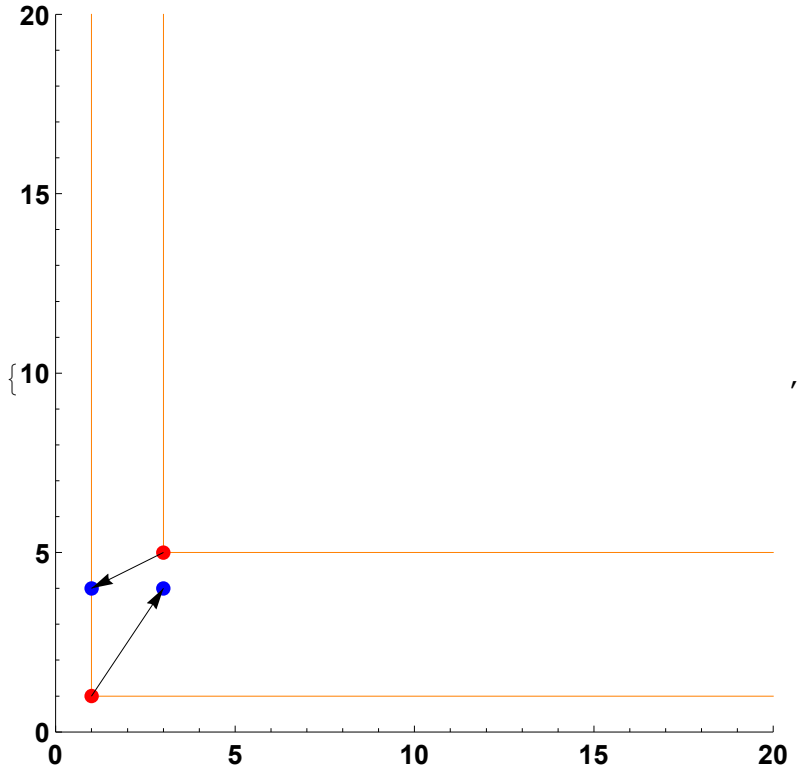


g) $R = 2,\ M = 2$

```
ClearAll[RC, RV, L, IS];
RC = {{1, 1}, {3, 5}}; RV = {{2, 3}, {-2, -1}};
IS = {{10, 3}}; L = {20, 20};
Reactions[RC, RV]
{FHJ[RC, RV, L, 400], Gamma2D[RC, RV, IS, 30, L, 400]}
```

$X + Y \to 3\,X + 4\,Y$

$3\,X + 5\,Y \to X + 4\,Y$



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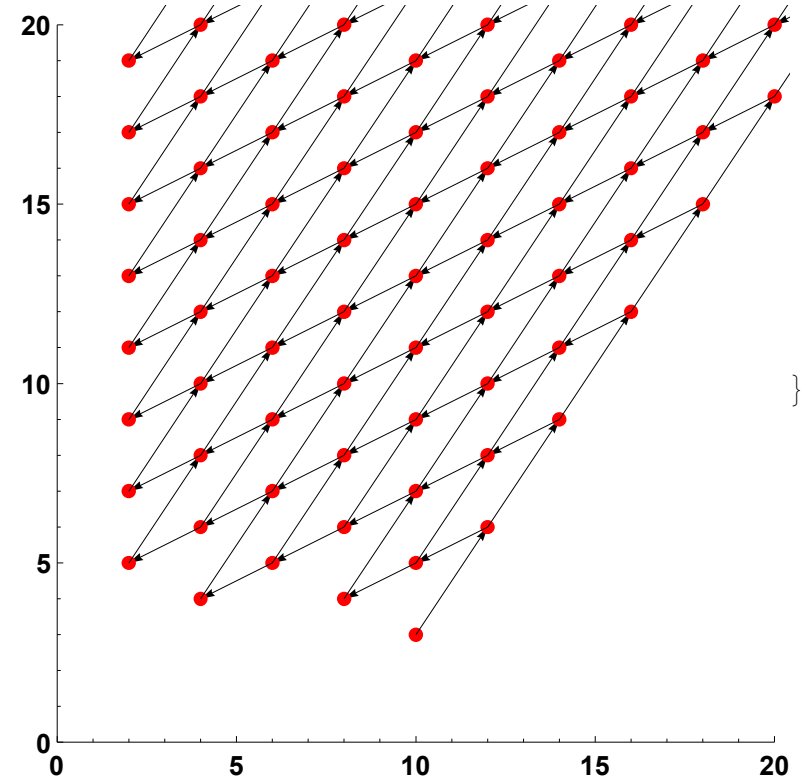


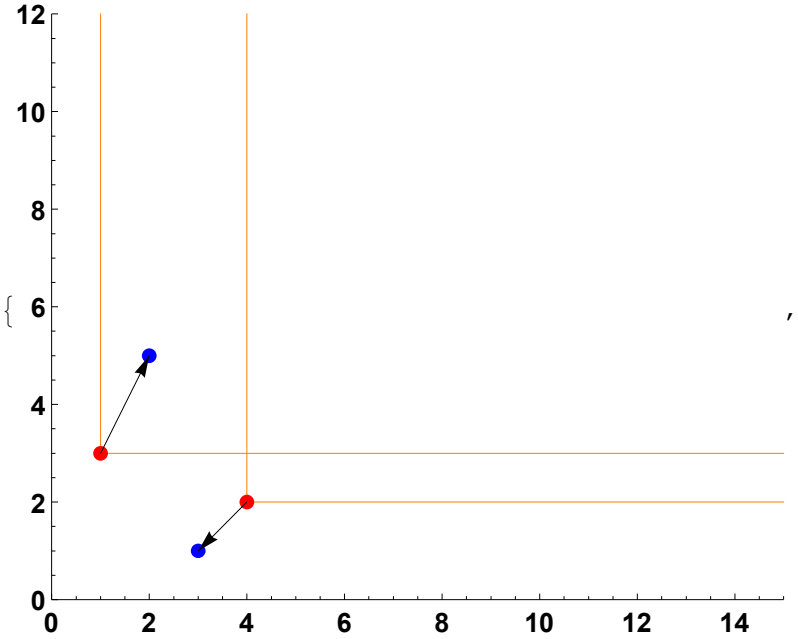
h) $R = 2,\ M = 2$, $\Gamma(D)$ and Γ

```
ClearAll[RC, RV, L, IS];
RC = {{1, 3}, {4, 2}}; RV = {{1, 2}, {-1, -1}};
IS = {{10, 3}}; L = {15, 12};
Reactions[RC, RV]
{FHJ[RC, RV, L, 400], Gamma2D[RC, RV, IS, 60, L, 400]}
```

X + 3 Y → 2 X + 5 Y

4 X + 2 Y → 3 X + Y

{



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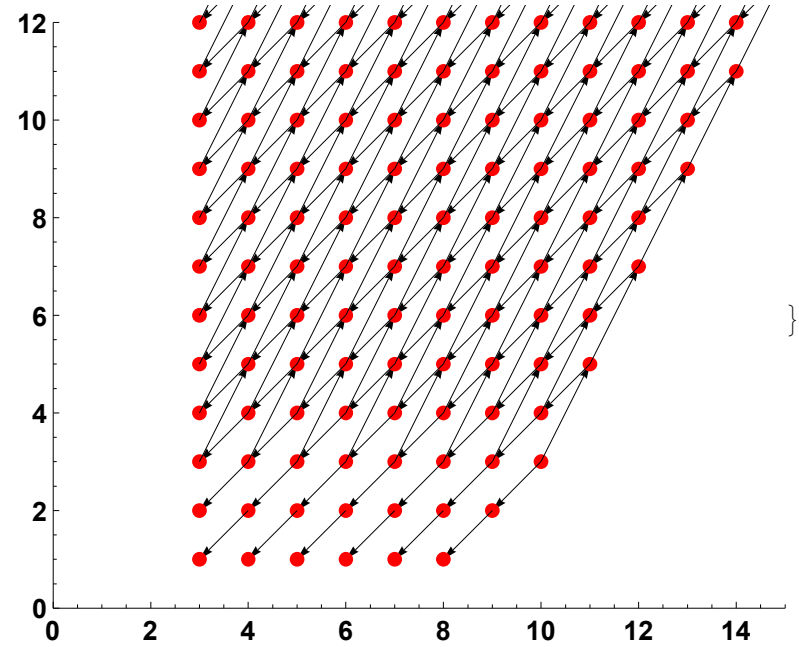

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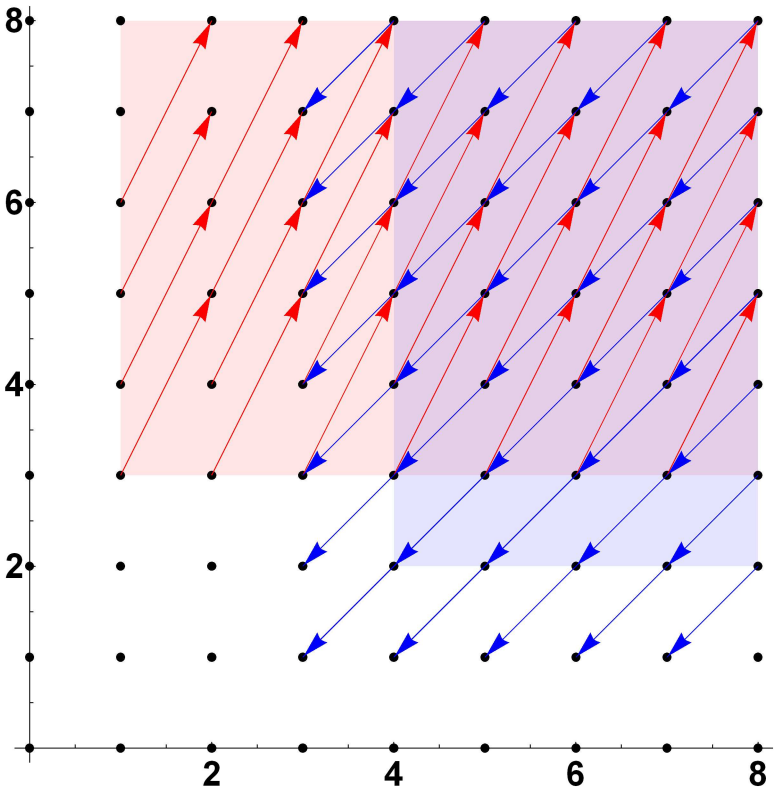


3. S-property

Definition

We say that the transition graph ($\Gamma(\boldsymbol{D})$ or Γ) has the s-property if for all states $\mathbf{i}, \mathbf{j} \in \mathbb{N}^M$, if it contains the edge $\mathbf{i} \longrightarrow \mathbf{j}$ then it also contains the edge $\mathbf{j} \longrightarrow \mathbf{i}$.

Remark

If $\Gamma(\boldsymbol{D})$ or Γ has the s-property then obvously it is irreducible.

Theorem

If the mechanism $< \mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}, \boldsymbol{w} >$ is reversible then $\Gamma(\mathbf{D})$ has the s-property for all acceptable initial states **D.**

Proof

Remark

It is obvious that for reversible reactions, Γ has the s-property as well.

Remark

The simple converse of the statement is not true, consider the reaction
$0 \rightleftarrows 2X$, $2X \to 4X$. Then, for all $k \in \mathbb{N}$,

if $D = 2k$, then $\Gamma(D) = \{0 \rightleftarrows 2 \rightleftarrows 4 \rightleftarrows 6 \rightleftarrows \ldots\}$;
if $D = 2k+1$, then $\Gamma(D) = \{1 \rightleftarrows 3 \rightleftarrows 5 \rightleftarrows 7 \rightleftarrows \ldots\}$.

Let us observe that in this irreversible reaction there corresponds at least two reaction steps to the same reaction vector.

Theorem

If the mechanism $<\mathcal{M}, \mathcal{R}, \boldsymbol{\alpha}, \boldsymbol{\beta}, \boldsymbol{w}>$ is not reversible and for every reaction vector there corresponds at most one reaction step, then there exists an initial state $\mathbf{D} \in \mathbb{N}^M$ such that $\Gamma(\mathbf{D})$ does not have the s-property.

Proof

Remark

The statement is also true for Γ as well since
if $\boldsymbol{\alpha}+\boldsymbol{\gamma} \in K(\boldsymbol{\alpha}+\boldsymbol{\gamma}+\boldsymbol{\delta}) \implies \boldsymbol{\alpha}+\boldsymbol{\delta} \longrightarrow \boldsymbol{\alpha}+\boldsymbol{\gamma}+\boldsymbol{\delta} \notin \Gamma$,
if $\boldsymbol{\alpha}+\boldsymbol{\gamma} \notin K(\boldsymbol{\alpha}+\boldsymbol{\gamma}+\boldsymbol{\delta}) \implies \boldsymbol{\alpha}+\boldsymbol{\gamma} \longrightarrow \boldsymbol{\alpha} \notin \Gamma$.

4. Structure of $\Gamma(\mathbf{D})$ for $R = 1$

Theorem

Consider the reaction $\boldsymbol{\alpha} \longrightarrow \boldsymbol{\alpha}+\boldsymbol{\gamma}$ where $\boldsymbol{\alpha} \in \mathbb{N}^M$, $\boldsymbol{\gamma} \in \mathbb{Z}^M \backslash \{\mathbf{0}\}$, $\boldsymbol{\alpha}+\boldsymbol{\gamma} \geq \mathbf{0}$ and let $\boldsymbol{D} \in K(\boldsymbol{\alpha})$ be an initial state.

(1) If $\boldsymbol{\alpha}+\boldsymbol{\gamma} \in K(\boldsymbol{\alpha})$ then $\Gamma(\boldsymbol{D}) = \{\boldsymbol{D}+s\,\boldsymbol{\gamma} \longrightarrow \boldsymbol{D}+(s+1)\,\boldsymbol{\gamma} : s \in \mathbb{N}\}$.

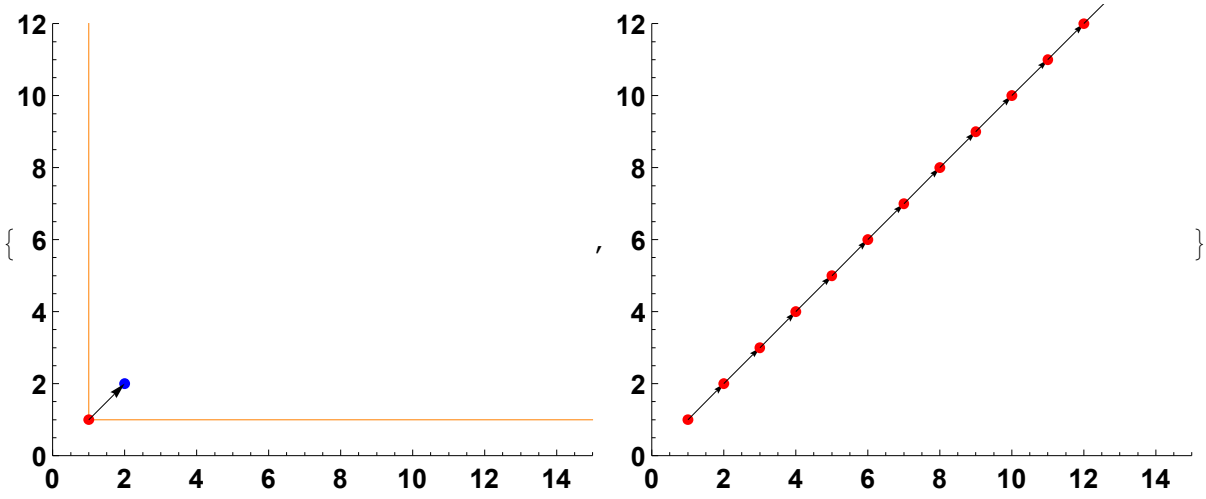
(2) If $\boldsymbol{\alpha}+\boldsymbol{\gamma} \notin K(\boldsymbol{\alpha})$ then $\Gamma(\boldsymbol{D}) = \{\boldsymbol{D}+s\,\boldsymbol{\gamma} \longrightarrow \boldsymbol{D}+(s+1)\,\boldsymbol{\gamma} : s \in \mathbb{N},\ 0 \leq s \leq k\}$

where $k \in \mathbb{N}$ such that $\boldsymbol{D}+k\,\boldsymbol{\gamma} \in K(\boldsymbol{\alpha})$ and $\boldsymbol{D}+(k+1)\,\boldsymbol{\gamma} \notin K(\boldsymbol{\alpha})$.

Examples

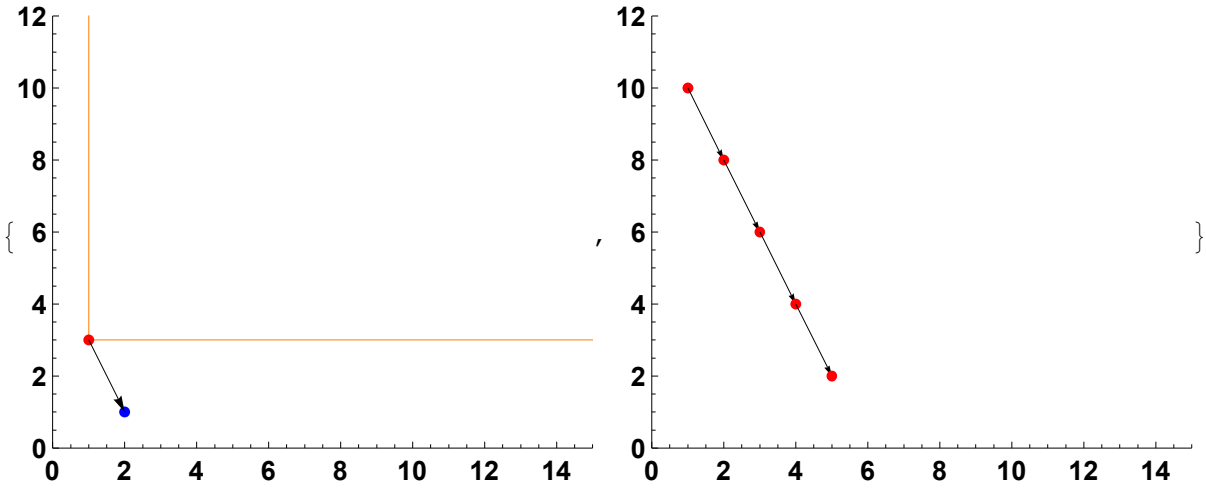
```
ClearAll[RC, RV, L, IS];
RC = {{1, 1}};
RV = {{1, 1}};
IS = {{1, 1}};
L = {15, 12};
Reactions[RC, RV]
{FHJ[RC, RV, L, 300], Gamma2D[RC, RV, IS, 30, L, 300]}
```

X + Y → 2 X + 2 Y



```
ClearAll[RC, RV, L, IS];
RC = {{1, 3}};
RV = {{1, -2}};
IS = {{1, 10}};
L = {15, 12};
Reactions[RC, RV]
{FHJ[RC, RV, L, 300], Gamma2D[RC, RV, IS, 30, L, 300]}
```

X + 3 Y → 2 X + Y



Proof

Remark

In case (1), $\Gamma(\boldsymbol{D})$ has no nonisolated absorbing states and all states are transient.

In case (2), $\boldsymbol{D}+(k+1)\,\boldsymbol{\gamma}$ is the only nonisolated absorbing state in $\Gamma(\boldsymbol{D})$ and all the other states are transient. From this it follows that the set of nonisolated absorbing states in Γ is $K(\boldsymbol{\alpha}+\boldsymbol{\gamma})\backslash K(\boldsymbol{\alpha})$.

Remark

Consider the reversible reaction $\boldsymbol{\alpha} \Longleftrightarrow \boldsymbol{\alpha}+\boldsymbol{\gamma}$ (where $\boldsymbol{\alpha} \in \mathbb{N}^M$, $\boldsymbol{\gamma} \in \mathbb{Z}^M \backslash \{\mathbf{0}\}$, $\boldsymbol{\alpha}+\boldsymbol{\gamma} \geq \mathbf{0}$).

If $\boldsymbol{D} \geq \boldsymbol{\alpha}$ then $\boldsymbol{D}+\boldsymbol{\gamma} \geq \boldsymbol{\alpha}+\boldsymbol{\gamma}$ and so $\boldsymbol{D} \longrightarrow \boldsymbol{D}+\boldsymbol{\gamma} \in \Gamma(\boldsymbol{D})$ and $\boldsymbol{D}+\boldsymbol{\gamma} \longrightarrow \boldsymbol{D} \in \Gamma(\boldsymbol{D})$.
Similarly, if $\boldsymbol{D} \geq \boldsymbol{\alpha}+\boldsymbol{\gamma}$ then $\boldsymbol{D}-\boldsymbol{\gamma} \geq \boldsymbol{\alpha}$ and so $\boldsymbol{D} \longrightarrow \boldsymbol{D}-\boldsymbol{\gamma} \in \Gamma(\boldsymbol{D})$ and $\boldsymbol{D}-\boldsymbol{\gamma} \longrightarrow \boldsymbol{D} \in \Gamma(\boldsymbol{D})$.

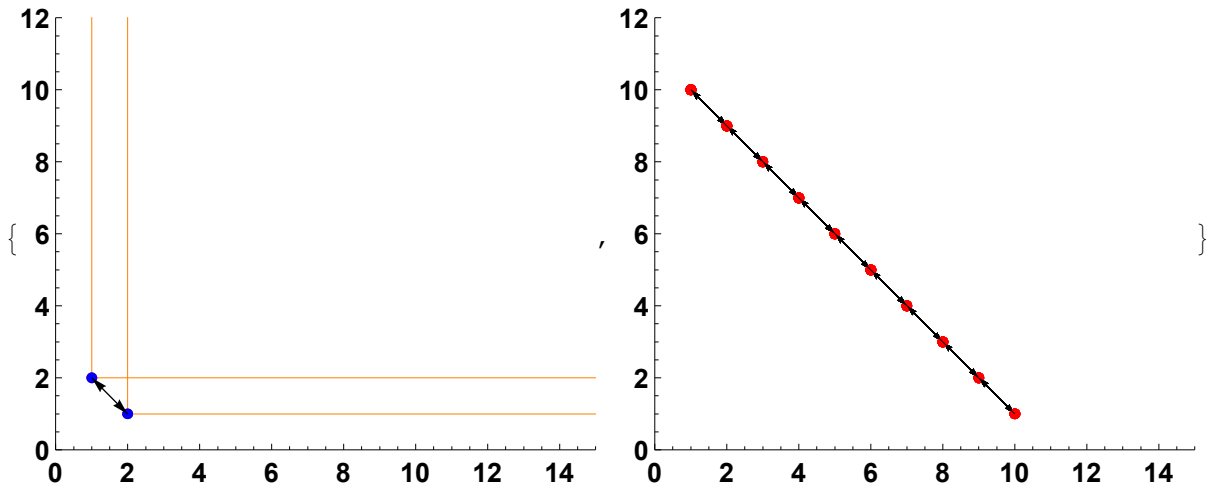
Therefore, $\Gamma(\boldsymbol{D})$ does not have any nonisolated absorbing states, it is irreducible and periodic with period 2 for all $\boldsymbol{D} \in K(\boldsymbol{\alpha}) \cup K(\boldsymbol{\alpha}+\boldsymbol{\gamma})$

Example

```
ClearAll[RC, RV, L, IS];
RC = {{1, 2}, {2, 1}};
RV = {{1, -1}, {-1, 1}};
IS = {{1, 10}};
L = {15, 12};
Reactions[RC, RV]
{FHJ[RC, RV, L, 300], Gamma2D[RC, RV, IS, 30, L, 300]}
```

X + 2 Y → 2 X + Y

2 X + Y → X + 2 Y



5. Structure of $\Gamma(D)$ for $M = 1$, $R = 2$

The following theorem deals with the conditions of periodicity in the simplest case when $M = 1$ and the reaction consists of an increasing and decreasing reaction step.

Theorem

Suppose that a mechanism consists of the reaction steps

$\alpha X \longrightarrow (\alpha+n)\,X,\ (\beta+k)\,X \longrightarrow \beta X$

starting from the initial state D where α, β, $D \in \mathbb{N}$ and k, $n \in \mathbb{Z}^+$. Let $n = p\,d$ and $k = q\,d$ where p, q, $d \in \mathbb{Z}^+$ and p and q are relative primes. Then the following statements hold.

(1) If $\alpha \leq \beta$ then $\Gamma(D)$ is periodic with period $p + q$ if and only if $D \geq \beta$.

(2) If $\beta < \alpha$ then $\Gamma(D)$ is periodic with period $p + q$ if and only if $\alpha \leq D$ and there exists a nonnegative integer D^* such that $D \equiv D^* \pmod{d}$ and $\alpha \leq D^* \leq \beta + d - 1$.

In both cases, the number of components of Γ is d.

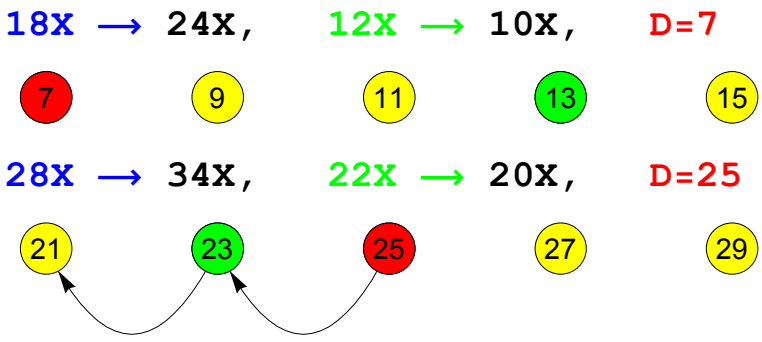
Proof

Program

Examples

a-b) $D < \alpha$

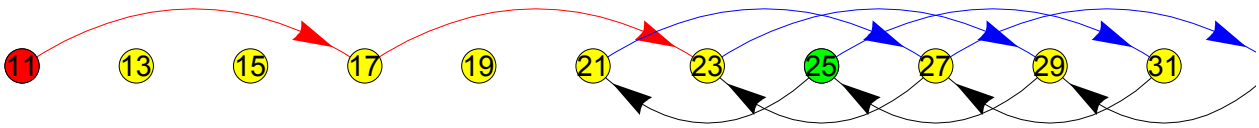
```
p[18, 10, 6, 2, 7, 400]
p[28, 20, 6, 2, 25, 400]
```



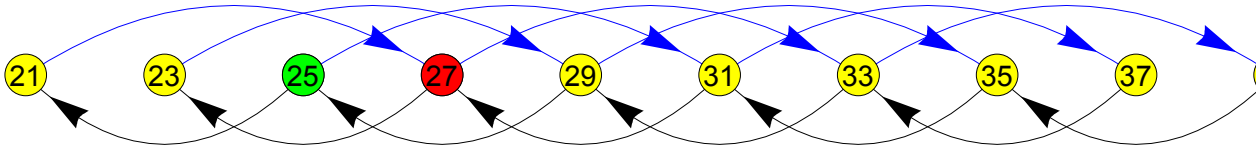
c) $\alpha \leq D$ and $\alpha \leq \beta$

```
p[8, 20, 6, 4, 11, 700]
p[8, 20, 6, 4, 27, 700]
```

8X ⟶ 14X, 24X ⟶ 20X, D=11



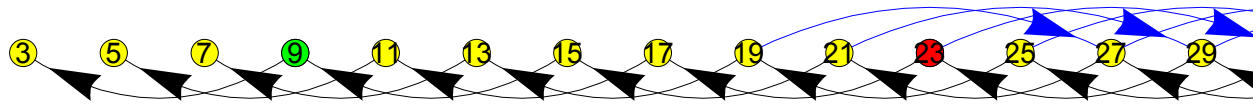
8X ⟶ 14X, 24X ⟶ 20X, D=27



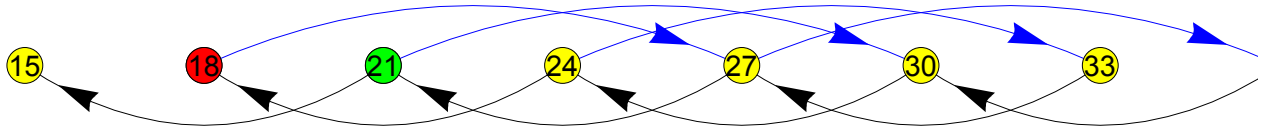
d) $\beta < \alpha \leq D$ and the graph cannot be periodic: $\alpha > \beta + d - 1$

```
p[18, 2, 8, 6, 23, 900]
p[18, 15, 9, 6, 18, 700]
p[18, 15, 9, 6, 19, 700]
p[18, 15, 9, 6, 20, 700]
p[18, 15, 9, 6, 21, 700]
```

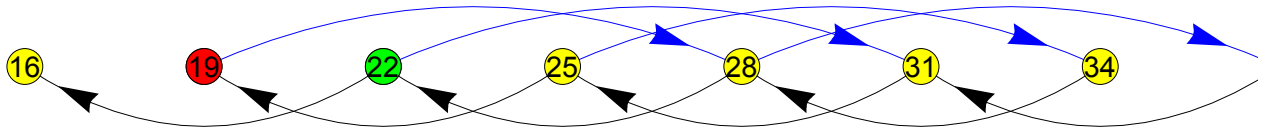
18X ⟶ 26X, 8X ⟶ 2X, D=23



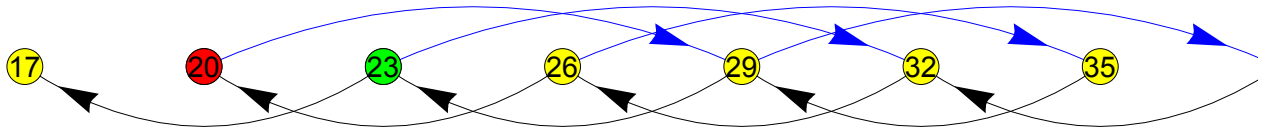
18X ⟶ 27X, 21X ⟶ 15X, D=18



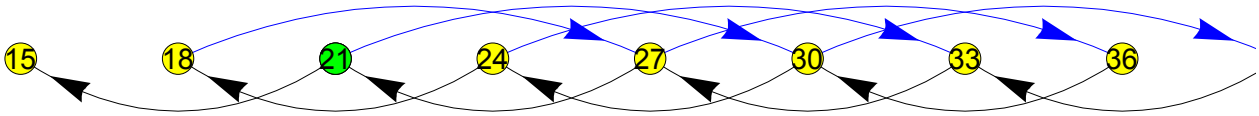
18X ⟶ 27X, 21X ⟶ 15X, D=19



18X ⟶ 27X, 21X ⟶ 15X, D=20



18X ⟶ 27X, 21X ⟶ 15X, D=21

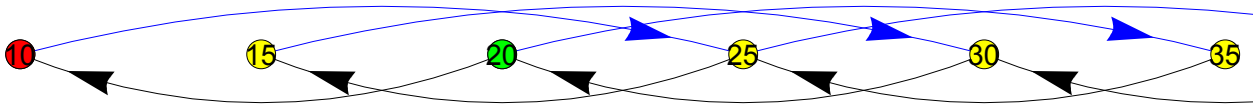


d) $\beta < \alpha \leq D$ and the graph can be periodic;

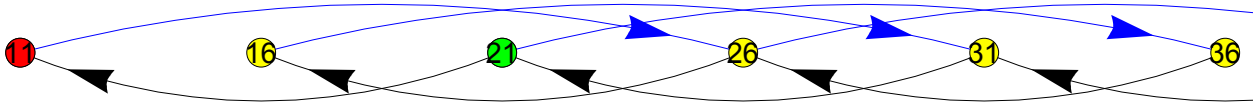
$\exists\, D^* : D \equiv D^* \pmod 5 : \quad 10 \leq D^* \leq 8 + 5 - 1 = 12$

```
p[10, 8, 15, 10, 10, 800]
p[10, 8, 15, 10, 11, 800]
p[10, 8, 15, 10, 12, 800]
p[10, 8, 15, 10, 13, 800]
p[10, 8, 15, 10, 14, 800]
p[10, 8, 15, 10, 15, 800]
```

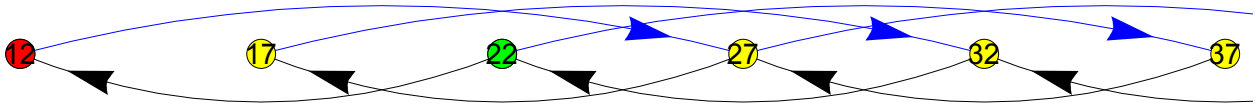
10X ⟶ 25X, 18X ⟶ 8X, D=10



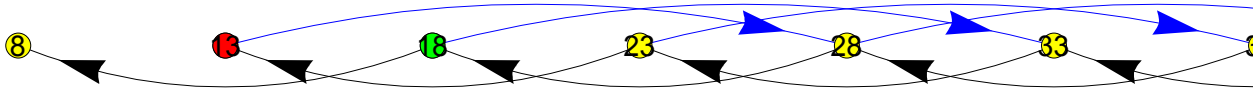
10X ⟶ 25X, 18X ⟶ 8X, D=11



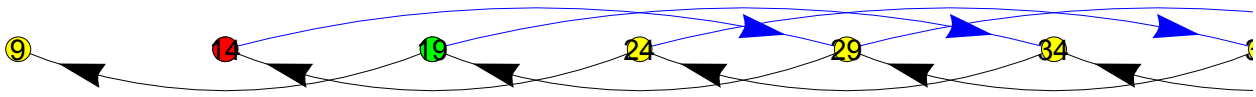
10X ⟶ 25X, 18X ⟶ 8X, D=12



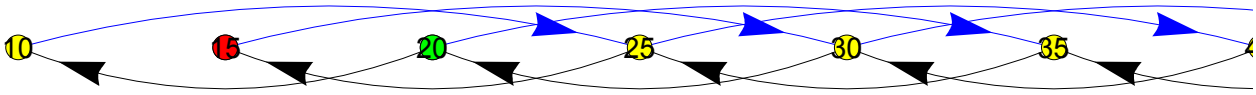
10X ⟶ 25X, 18X ⟶ 8X, D=13



10X ⟶ 25X, 18X ⟶ 8X, D=14



10X ⟶ 25X, 18X ⟶ 8X, D=15



6. The transition graph for reversible reactions, $M = 1$

Theorem

Suppose that a mechanism consists of the reaction steps

$\alpha_r X \Longleftrightarrow (\alpha_r + \gamma_r) X \qquad (r = 1, \ldots, R)$

where $\alpha_r \in \mathbb{N}$ and $\gamma_r \in \mathbb{Z}^+$. Let $\gamma_r = 2^{g(r)} h(r)$ where $h(r)$ is not divisible by 2 $(r = 1, \ldots, R)$ and let
$D_0 = \min\{\alpha_1, \ldots, \alpha_R\}$ and
$\Gamma_0 = \cup\{\Gamma(D) : D \geq D_0\}$. Then the full classification of Γ_0 is the following.

(1) If $R = 1$ and $\gamma_1 = 1$ then Γ_0 is irreducible and of period 2.
(2) If $R > 1$, $(\gamma_1, \ldots, \gamma_R)=1$ and $g(1) = \ldots = g(R)$ then Γ_0 is irreducible and of period 2.
(3) If $R > 1$, $(\gamma_1, \ldots, \gamma_R)=1$ and not all $g(r)$s are equal then Γ_0 is irreducible and aperiodic.
(4) If $R = 1$ and $\gamma_1 = d > 1$ then Γ_0 consists of d irreducible subgraphs all of which are of period 2.
(5) If $R > 1$, $(\gamma_1, \ldots, \gamma_R) = d > 1$ and $g(1) = \ldots = g(R)$ then Γ_0 consists of d irreducible subgraphs all of which are of period 2.
(6) If $R > 1$, $(\gamma_1, \ldots, \gamma_R) = d > 1$ and not all $g(r)$s are equal then Γ_0 consists of d irreducible, aperiodic subgraphs.

Proof

Structure of the state space for $M \geq 1$

Paulevé, Loïc, Gheorghe Craciun, and Heinz Koeppl. “Dynamical properties of discrete reaction networks.”
Journal of mathematical biology 69.1 (2014): 55-72.

1. Definitions

Notation: $x \longrightarrow y$ if and only if y can be reached by the occurence of a single reation step from x
$x \longrightarrow^* y$ if and only if there exists a sequence of reaction occurences from x leading exactly to y

Irreducibility:
Γ is *irreducible* if any point in $\mathbb{Z}_{\geq 0}$ can be reached from any other point in $\mathbb{Z}_{\geq 0}$, that is, if and only if

$\forall\, x,\ y \in \mathbb{Z}_{\geq 0},\ x \longrightarrow^* y$ and $y \longrightarrow^* x$.

Recurrence:
Γ is *recurrent* if and only if for all $x,\ y \in \mathbb{Z}_{\geq 0},\ x \longrightarrow^* y \Longrightarrow y \longrightarrow^* x$.

Remark: Irreducibility $\Longrightarrow$ Recurrence.

We also investigate less resctrictive dynamical properties, when assuming the species are present at a large copy number (LCN):

LCN irreducibility:
Γ is *LCN irreducible* if and only if $\exists\ M_0 \in \mathbb{Z}^d_{\geq 0}$ such that $\forall\, x,\ y \in \mathbb{Z}_{\geq 0}$ with $x \geq M_0$ and $y \geq M_0$, $x \longrightarrow^* y$ and $y \longrightarrow^* x$.

LCN recurrence:
Γ is *LCN recurrent* if and only if $\exists\ M_0 \in \mathbb{Z}^d_{\geq 0}$ such that $\forall\, x,\ y \in \mathbb{Z}_{\geq 0}$ with $x \geq M_0$ and $y \geq M_0$,
$x \longrightarrow^* y \Longrightarrow y \longrightarrow^* x$.

Remark: LCN Irreducibility $\Longrightarrow$ LCN Recurrence.

Remark: A reaction network that has any conservation laws cannot be irreducible or LCN irreducible.

2. Two examples

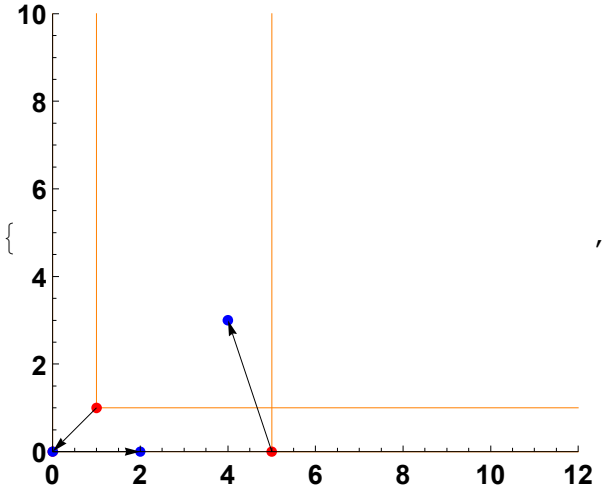
Example a)

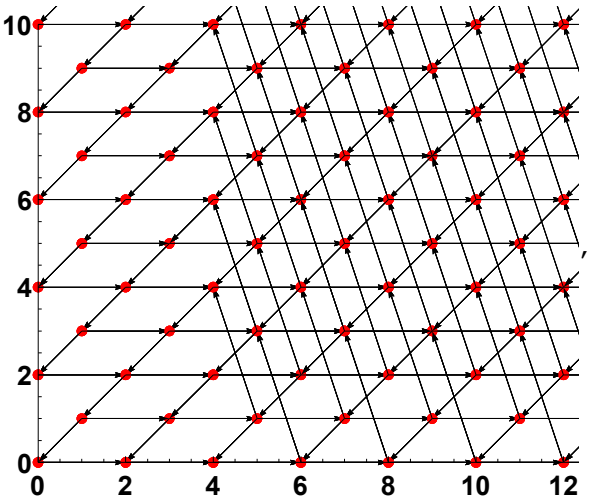
```
ClearAll[RC, RV, L, IS];
RC = {{0, 0}, {1, 1}, {5, 0}}; RV = {{2, 0}, {-1, -1}, {-1, 3}};
L = {12, 10}; Reactions[RC, RV]
{FHJ[RC, RV, L, 300], Gamma2D[RC, RV, {{0, 0}}, 30, L, 300],
 Gamma2D[RC, RV, {{1, 0}}, 30, L, 300]}
```

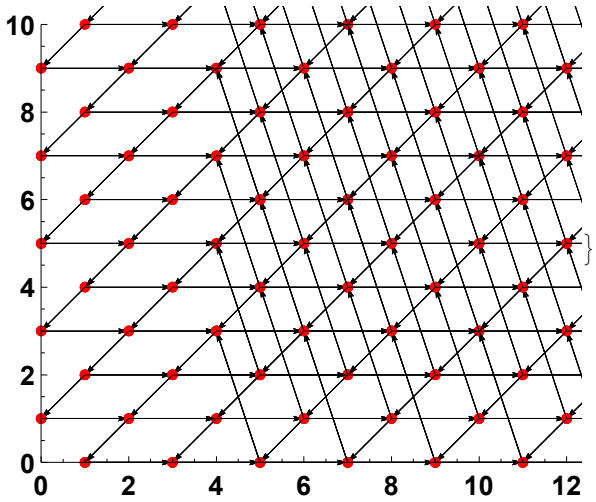
$0 \to 2\,X$

$X + Y \to 0$

$5\,X \to 4\,X + 3\,Y$







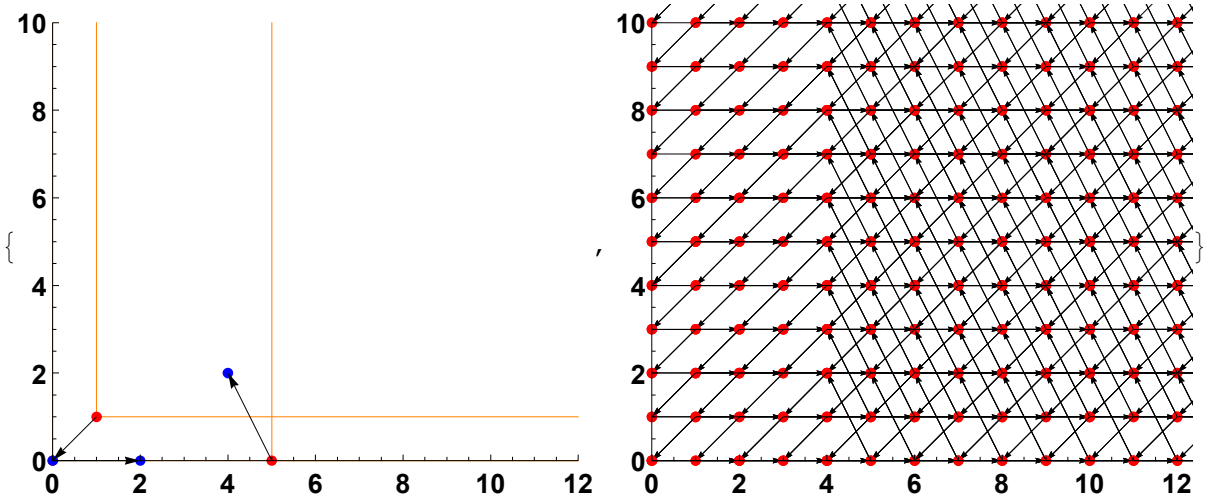
Example b)

```
ClearAll[RC, RV, L, IS];
RC = {{0, 0}, {1, 1}, {5, 0}}; RV = {{2, 0}, {-1, -1}, {-1, 2}};
L = {12, 10}; Reactions[RC, RV]
{FHJ[RC, RV, L, 300], Gamma2D[RC, RV, {{0, 0}}, 30, L, 300]}
```

$0 \to 2\,X$

$X + Y \to 0$

$5\,X \to 4\,X + 2\,Y$



3. Deciding irreducibility

3.1. LCN irreducibility

Theorem

Γ is LCN irreducible $\Longleftrightarrow$ $\text{span}_{\mathbb{R}_{>0}}\,\gamma = \mathbb{R}^M$ and $\text{span}_{\mathbb{Z}}\,\gamma = \mathbb{Z}^M$.

For the proof

- **Lemma 3.1:** Γ is irreducible $\Longleftrightarrow$ $\forall\, i \in \{1, \ldots, M\}$, $\mathbf{0} \longrightarrow^* e_i$ and $e_i \longrightarrow^* \mathbf{0}$.
- **Lemma 3.2:** Γ is LCN irreducible $\Longleftrightarrow$ $\text{span}_{\mathbb{Z}_{\geq 0}}\,\gamma = \mathbb{Z}^M$.
- **Lemma 3.3:** $\text{span}_{\mathbb{R}_{>0}}\,\gamma = \mathbb{R}^M \Longleftrightarrow \text{span}_{\mathbb{Q}_{>0}}\,\gamma = \mathbb{Q}^M$.

Remark: - verification of $\text{span}_{\mathbb{Z}_{\geq 0}}\,\gamma = \mathbb{Z}^M$: integer programming techniques
- verification of $\text{span}_{\mathbb{R}_{>0}}\,\gamma = \mathbb{R}^M$ and $\text{span}_{\mathbb{Z}}\,\gamma = \mathbb{Z}^M$: linear programming and computing the Hermite normal form of γ^T

Application for Examples a) and b)

$\text{span}_{\mathbb{R}_{>0}}\,\gamma = \mathbb{R}^M$ holds for examples a) and b) but only example b) verifies $\text{span}_{\mathbb{Z}}\,\gamma = \mathbb{Z}^M$
$\Longrightarrow$ a) is not LCN irreducible, b) is LCN irreducible

Application for $M = 1$

Consider the system $\alpha_i \longrightarrow \alpha_i + v_i$, $\alpha_i \in \mathbb{Z}_{\geq 0}$, $v_i \in \mathbb{Z}\backslash\{0\}$, $i = 1, \ldots, R$.

If $R = 1$: $\text{span}_{\mathbb{R}_{>0}}\,\gamma = \mathbb{R}$ does not hold.
If $R \geq 2$: $\text{span}_{\mathbb{R}_{>0}}\,\gamma = \mathbb{R}$ holds if and only if among $v_1, v_2, \ldots, v_R$ there are two integers of opposite sign
$\text{span}_{\mathbb{Z}}\,\gamma = \mathbb{Z}$ holds if and only if among $v_1, v_2, \ldots, v_R$ there are two integers that are relative primes

LCN recurrence $\Longleftrightarrow$ among $v_1, v_2, \ldots, v_R$ there are two integers that are relative primes and of opposite sign

3.2. Full irreducibility

Definition: Γ is **self-starting** if and only if there exists a strictly positive point $x \in \mathbb{Z}^d_{>0}$ such that $\mathbf{0} \longrightarrow^* x$.
Definition: Γ is **self-stopping** if and only if there exists a strictly positive point $x \in \mathbb{Z}^d_{>0}$ such that $x \longrightarrow^* \mathbf{0}$.

Theorem

Γ is irreducible if and only if it is LCN irreducible, self-starting and self-stopping.

For the proof

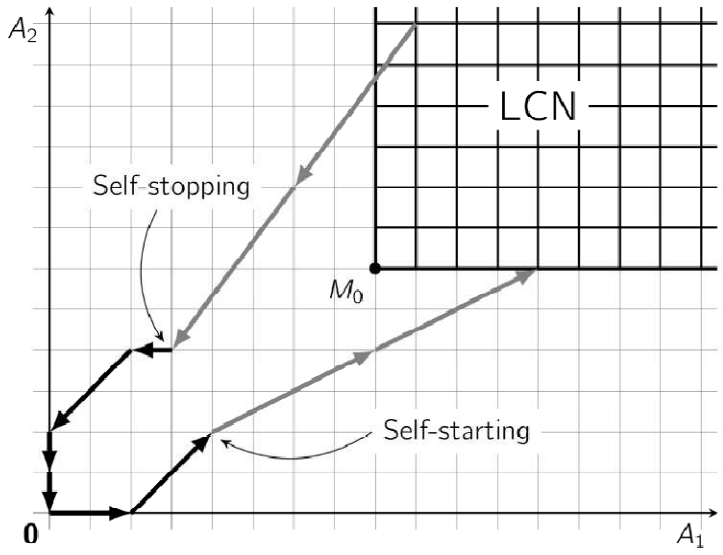
- Lemma 1: Γ is self-starting $\Longleftrightarrow$ there exists a sequence of M reactions (not necessarily unique) such that for each dimension at least one reaction has a positive drift along that reaction and such that the origin of the kth reaction belongs to the positive real span of the $k-1$ preceding drift vectors (the first reaction having necessarily **0** as origin). The existence of such an ordering of reactions can be verified by a backtrack algorithm.

- Lemma 2: Given $x, y \in \mathbb{Z}^d_{\geq 0}$, $x \longrightarrow^* y \Longrightarrow \forall\, \delta \in \mathbb{Z}^d_{\geq 0},\ x + \delta \longrightarrow^* y + \delta$
- Lemma 3: $\mathbf{0} \longrightarrow^* x \Longrightarrow \forall\, \alpha \in \mathbb{Z}_{>0},\ \mathbf{0} \longrightarrow^* \alpha\, x$.

($\Longrightarrow$) obvious.

($\Longleftarrow$) Γ is self-starting $\Longrightarrow \exists\, x \in \mathbb{Z}^d_{>0}$ such that $\mathbf{0} \longrightarrow^* x \overset{\text{Lemma 3}}{\Longrightarrow} \exists\, y \geq M_0$ such that $\mathbf{0} \longrightarrow^* y$.
Γ is self-stopping $\Longrightarrow \exists\, z \geq M_0$ such that $z \longrightarrow^* \mathbf{0}$.

Γ is LCN recurrent $\Longrightarrow$ any pair of points above M_0 is reversebly reachable $\overset{\text{Lemma 2}}{\Longrightarrow}$ there exists a reversible path from **0** to all $e_i,\ i \in \{1, \ldots, M\}$.



Application for Examples a) and b)

a) and b): self-starting and self-stopping

self-starting: a) two reacton vectors: (2,0), (-1,3): there is a positive coordinate in each direction
self-stopping: a) one reaction vector: (-1,-1): there is a negative coordinate in each direction

a) is not LCN irreducible, b) is LCN irreducible

$\Longrightarrow$ a) is not irreducible, b) is irreducible

Application for $M = 1$

Consider the system $\alpha_i \longrightarrow \alpha_i + v_i,\ \alpha_i \in \mathbb{Z}_{\geq 0},\ v_i \in \mathbb{Z}\backslash\{0\},\ i = 1, \ldots, R$.

It is irreducible $\Longleftrightarrow$ among the reaction steps $0 \longrightarrow v_1$ and $v_2 \longrightarrow 0$ occur where v_1 and v_2 are positive integers and relative primes.

4. Deciding recurrence

4.1 LCN recurrence

Theorem

Γ is LCN recurrent $\Longleftrightarrow \mathbf{0} \in \text{span}_{\mathbb{R}_{>0}}\, \gamma$

Application for Examples a) and b)

b) is irreducible $\Longrightarrow$ recurrent

a) is not irreducible but LCN recurrent

Application for $M = 1$

Consider the system $\alpha_i \longrightarrow \alpha_i + v_i,\ \alpha_i \in \mathbb{Z}_{\geq 0},\ v_i \in \mathbb{Z}\backslash\{0\},\ i = 1, \ldots, R$.

It is LCN recurrent $\Longleftrightarrow$ among $v_1, v_2, \ldots, v_R$ there are two integers of opposite sign.

4.2 Full recurrence

Theorems

1. If Γ is LCN recurrent and $\exists\ z \in \mathbb{Z}_{>0}^M$ such that $\mathbf{0} \longrightarrow^* z \longrightarrow^* \mathbf{0}$ then Γ is recurrent.

2. Consider the system $\alpha_i \longrightarrow \alpha_i + v_i,\ \alpha_i \in \mathbb{Z}_{\geq 0}^M,\ v_i \in \mathbb{Z}^M\backslash\{\mathbf{0}\},\ i = 1, \ldots, R$. Then Γ is recurrent $\Longleftrightarrow$ $\alpha_i + v_i \longrightarrow^* \alpha_i$ for all $i = 1, \ldots, R$.

3. Any weakly reversible reaction network is recurrent.

Remark: There is no efficient general method to verify the conditions is statements 1. and 2.

Proof of 1.: Let $\alpha \in \mathbb{Z}_{>0} :\ \alpha z \geq M_0$. If $x \longrightarrow^* y \implies x + \alpha z \longrightarrow^* y + \alpha z \overset{\text{LCN rec.}}{\Longrightarrow} y + \alpha z \longrightarrow^* x + \alpha z \implies y \longrightarrow^* x$.

Application for Examples a) and b)

b) is irreducible $\Longrightarrow$ recurrent

a) reaction vectors: $v_1 = \begin{pmatrix} 2 \\ 0 \end{pmatrix},\ v_2 = \begin{pmatrix} -1 \\ -1 \end{pmatrix},\ v_2 = \begin{pmatrix} -1 \\ 3 \end{pmatrix}$

$4\,v_1 + 2\,v_3 = \begin{pmatrix} 6 \\ 6 \end{pmatrix},\ 6\,v_2 = \begin{pmatrix} -6 \\ -6 \end{pmatrix} \Longrightarrow \mathbf{0} \longrightarrow^{*} (6, 6) \longrightarrow \mathbf{0} \Longrightarrow$ recurrent (but not irreducible)

Application for $M = 1$

Consider the system $\alpha_i \longrightarrow \alpha_i + v_i,\ \alpha_i \in \mathbb{Z}_{\geq 0},\ v_i \in \mathbb{Z}\backslash\{0\},\ i = 1, \ldots, R$.

It is recurrent $\Longleftrightarrow$ among the reaction steps $0 \longrightarrow v_1$ and $v_2 \longrightarrow 0$ occur where v_1 and v_2 are positive integers.