Combinatorial topological framework for nonlinear dynamics

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Lectures

Combinatorial topological framework - Theory

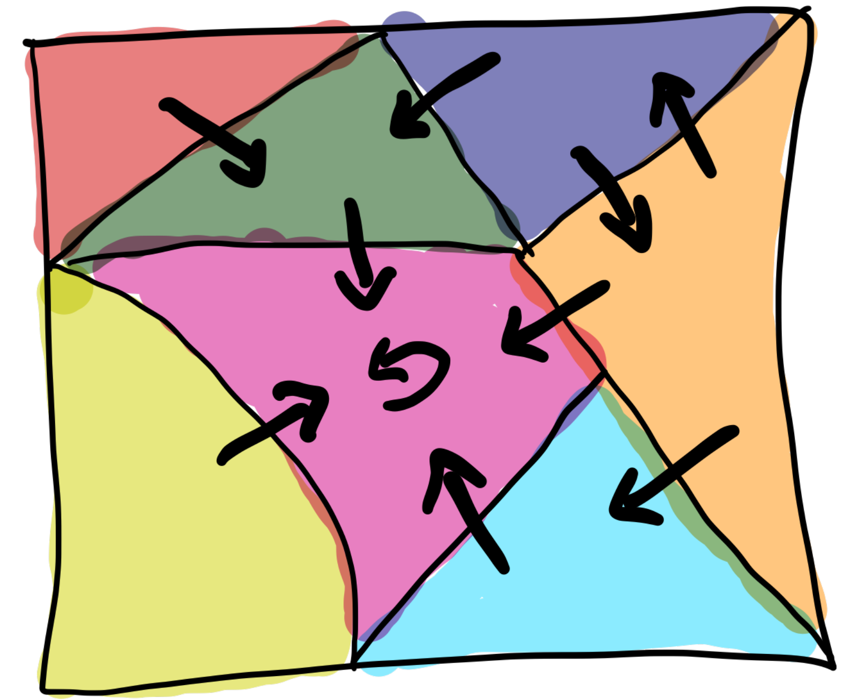
Combinatorial topological framework - ODEs

Combinatorial topological framework - Maps

Combinatorial topological framework - Data

Main Steps

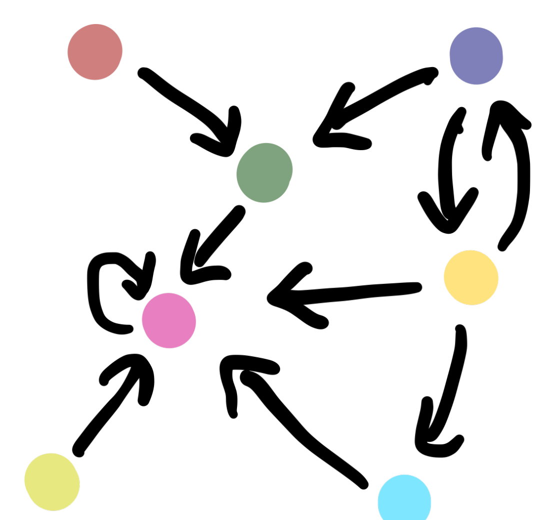
Discretization of the domain and combinatorial representation of dynamics



Transversality model: No arrow if flow is transverse in opposite direction

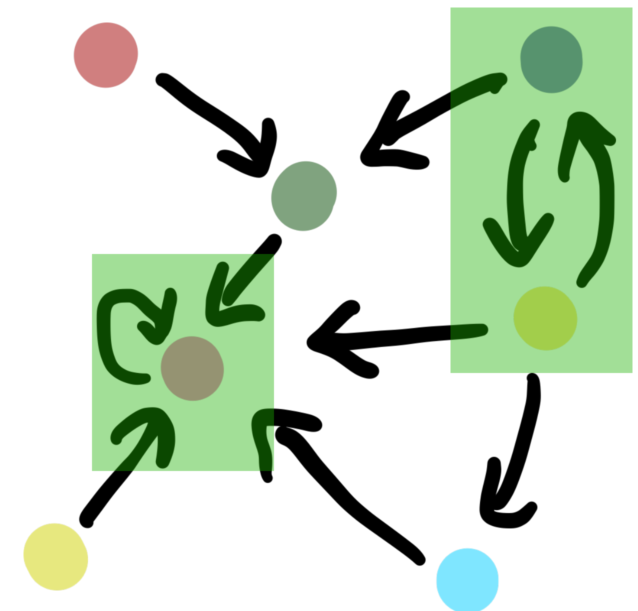
Combinatorial multivalued map (directed graph) $\mathcal{F}\colon \mathcal{X} \rightrightarrows \mathcal{X}$

(State Transition Graph)



Main Steps

Use graphs algorithms to find recurrent and gradient like dynamics



Compute algebraic topology (Conley index, connection matrix) to get rigorous information about dynamics

Our approach: Start with a discretization and try to characterized the family of dynamical systems compatible with it

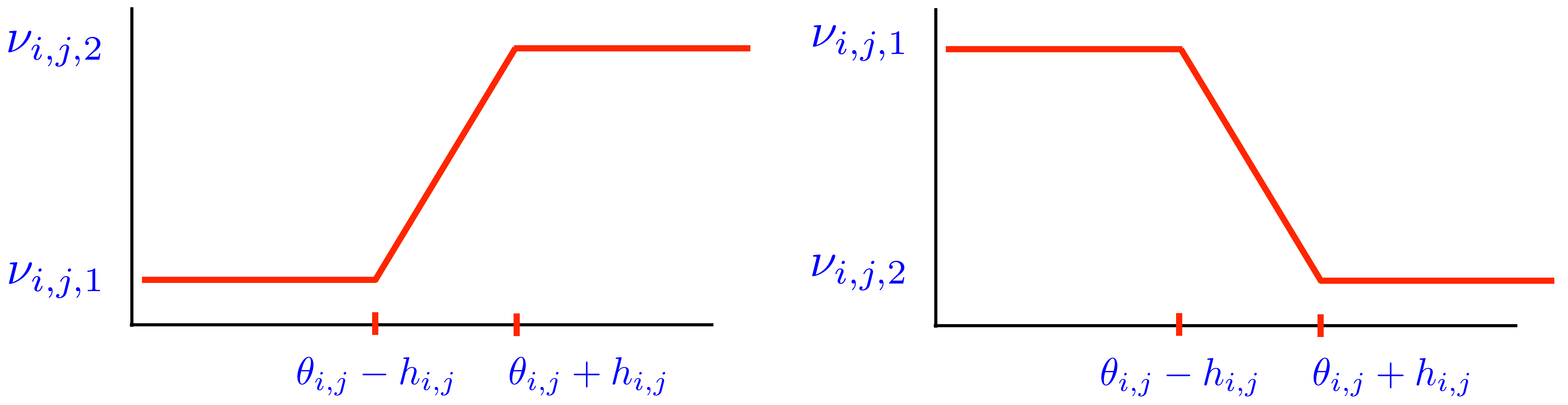
Main Steps

$$\dot{x}_1 = -\gamma_1 x_1 + r_{1,1}(x_1) r_{1,2}(x_2)$$
$$\dot{x}_2 = -\gamma_2 x_2 + r_{2,1}(x_1) r_{2,2}(x_2)$$

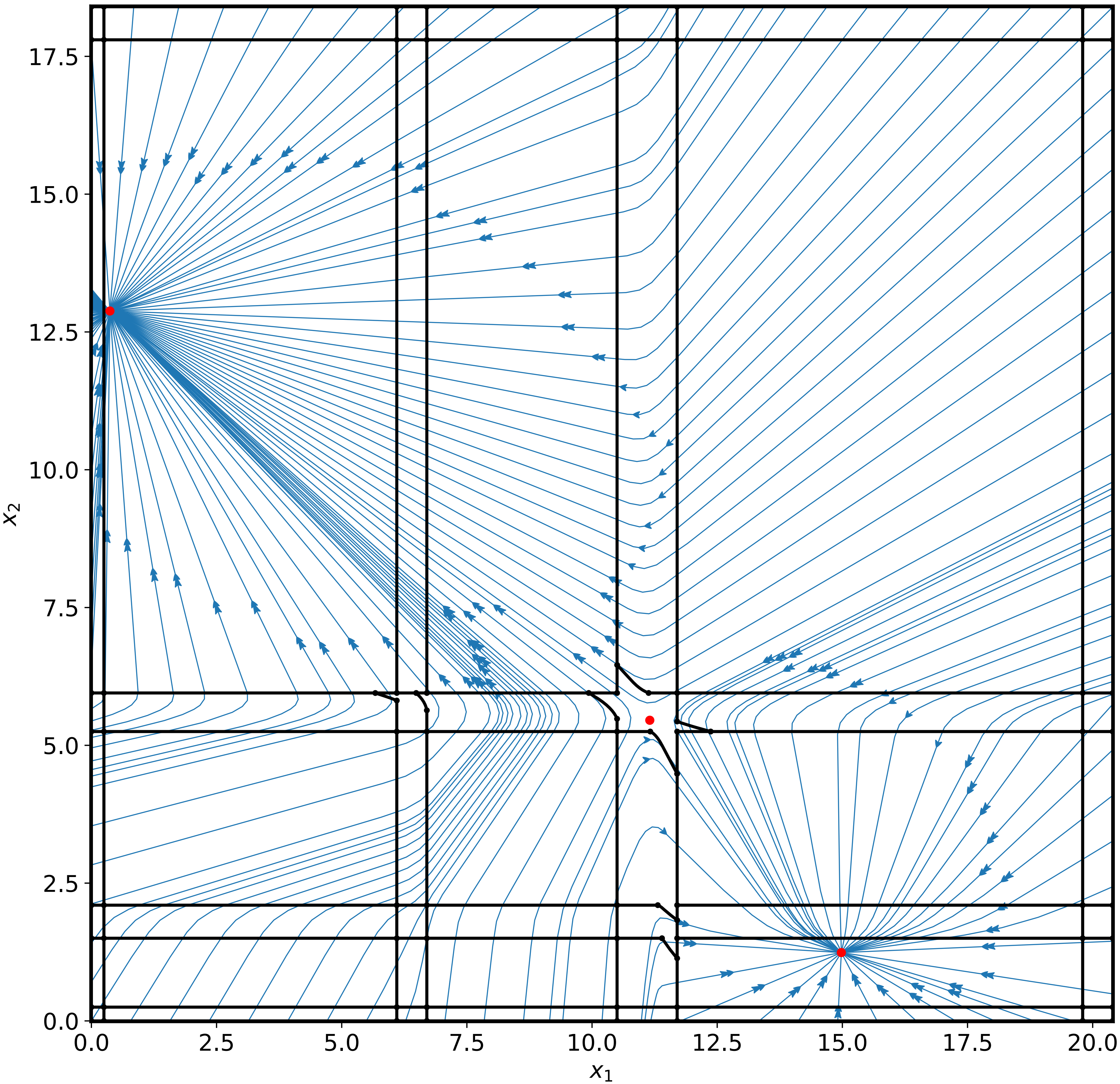
Ramp system

$$r_{i,j}(x) = \begin{cases} \nu_{i,j,1}, & \text{if } x < \theta_{i,j} - h_{i,j} \\ L_{i,j}(x), & \text{if } \theta_{i,j} - h_{i,j} \leq x \leq \theta_{i,j} + h_{i,j} \\ \nu_{i,j,2}, & \text{if } x > \theta_{i,j} + h_{i,j} \end{cases}$$

$$L_{i,j}(x) = \frac{\nu_{i,j,2} - \nu_{i,j,1}}{2h_{i,j}}(x - \theta_{i,j}) + \frac{\nu_{i,j,1} + \nu_{i,j,2}}{2}$$



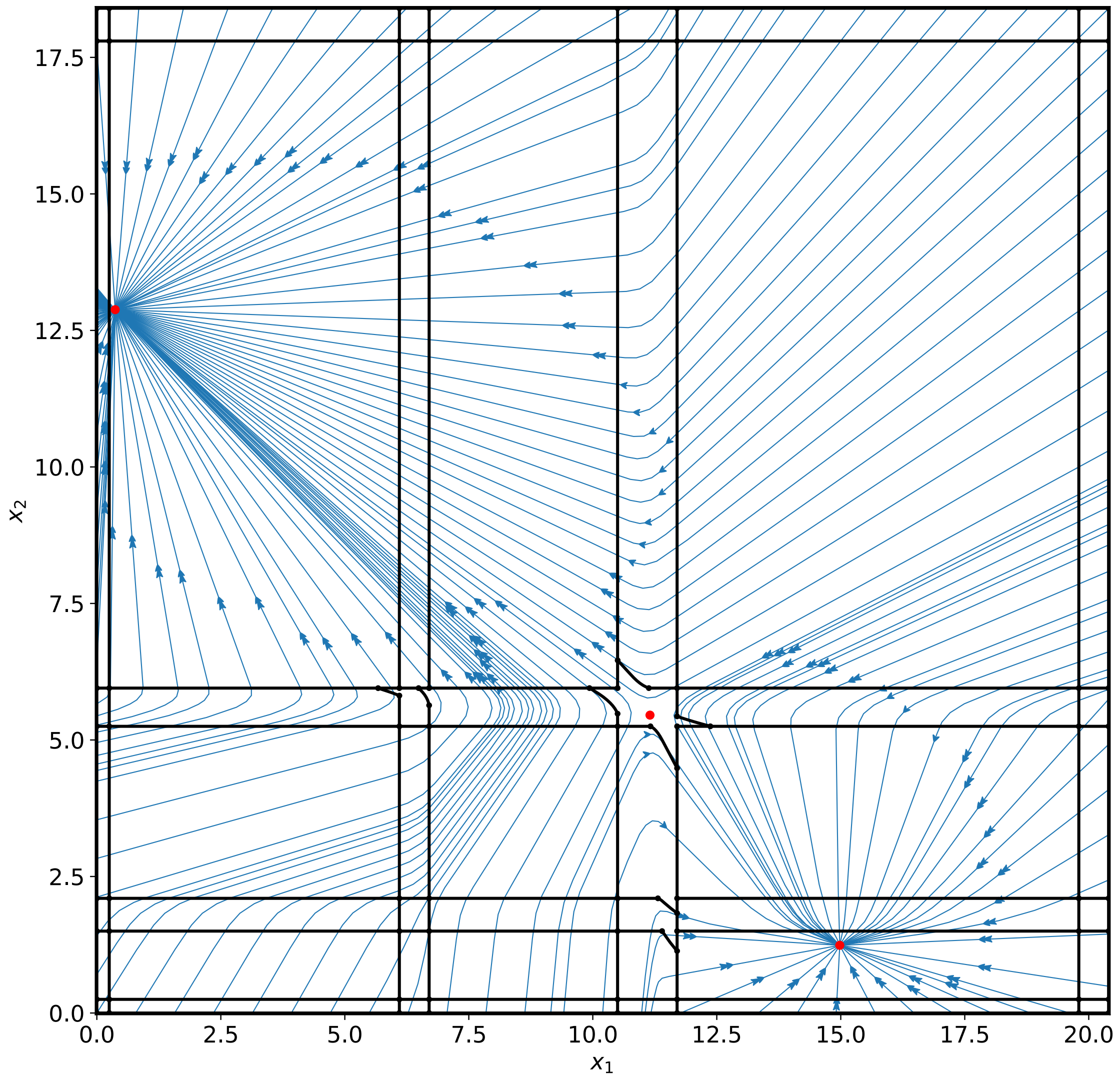
Main Steps



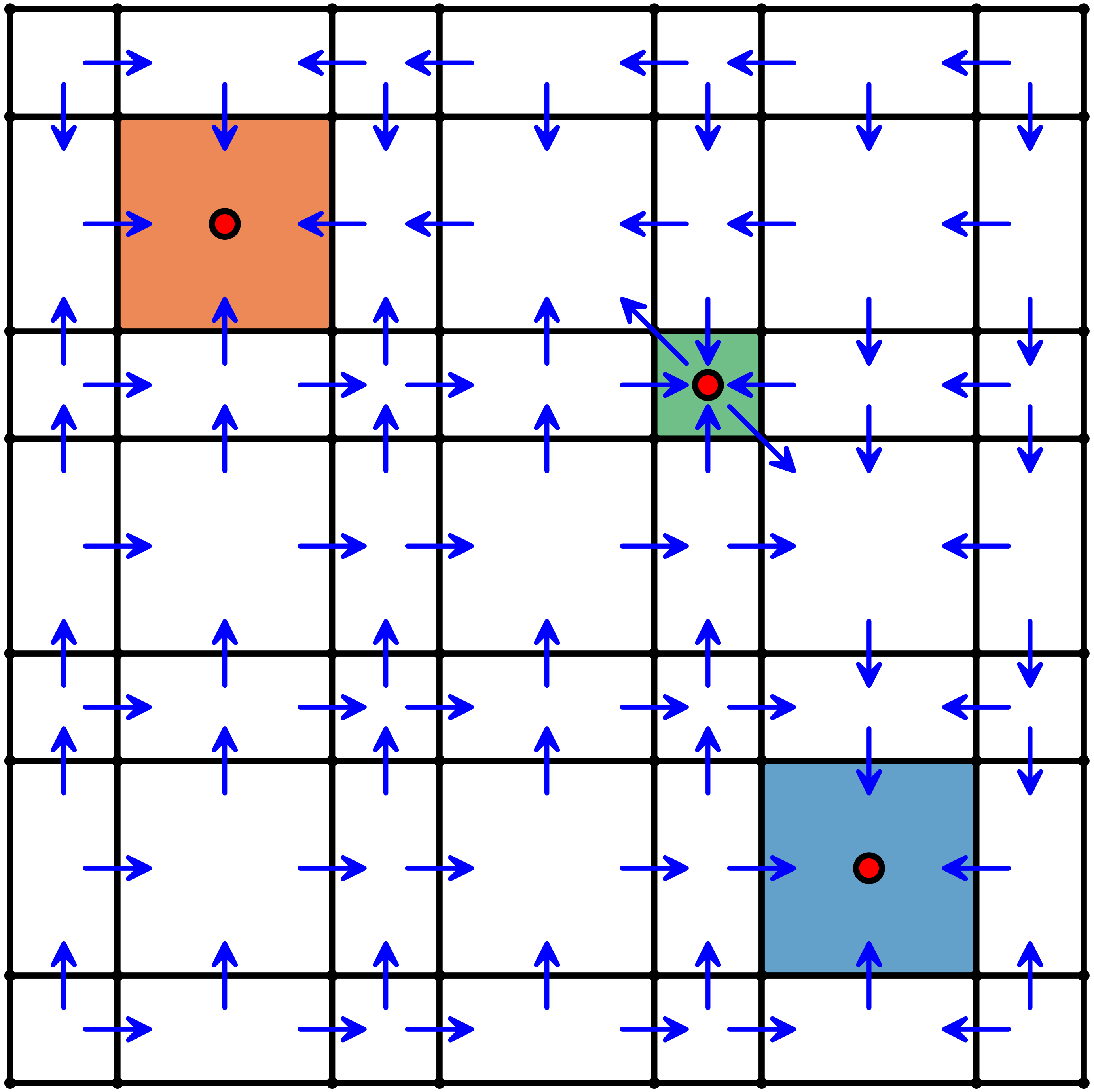
Phase space

Can define $\mathcal{F}$

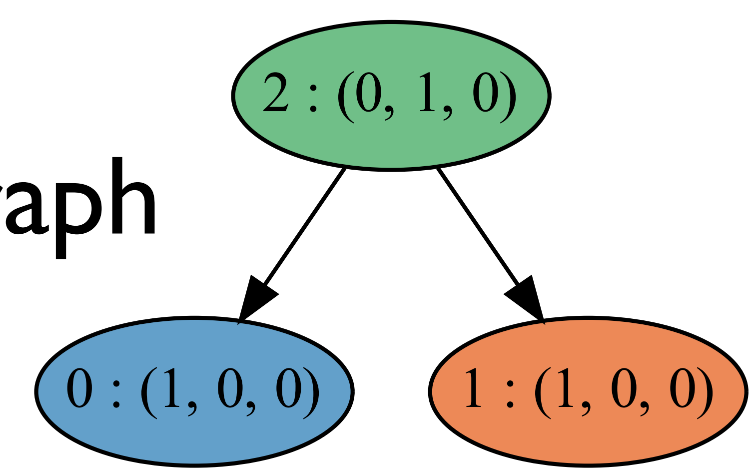
Main Steps



Abstract representation of $\mathcal{F}$

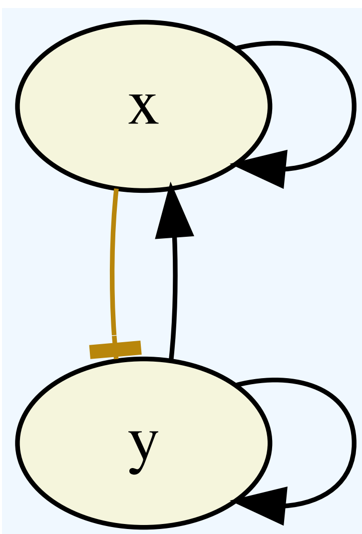


Morse graph



Main Steps

Our goal is to introduce an algorithmic approach to identifying the global dynamics of multi-parameter systems of ODEs



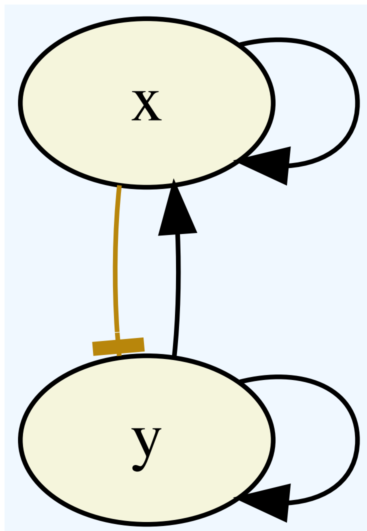
We represent a multi-parameter systems of ODEs by a network

The nodes indicate the variables and the edges indicate coupling (interactions)

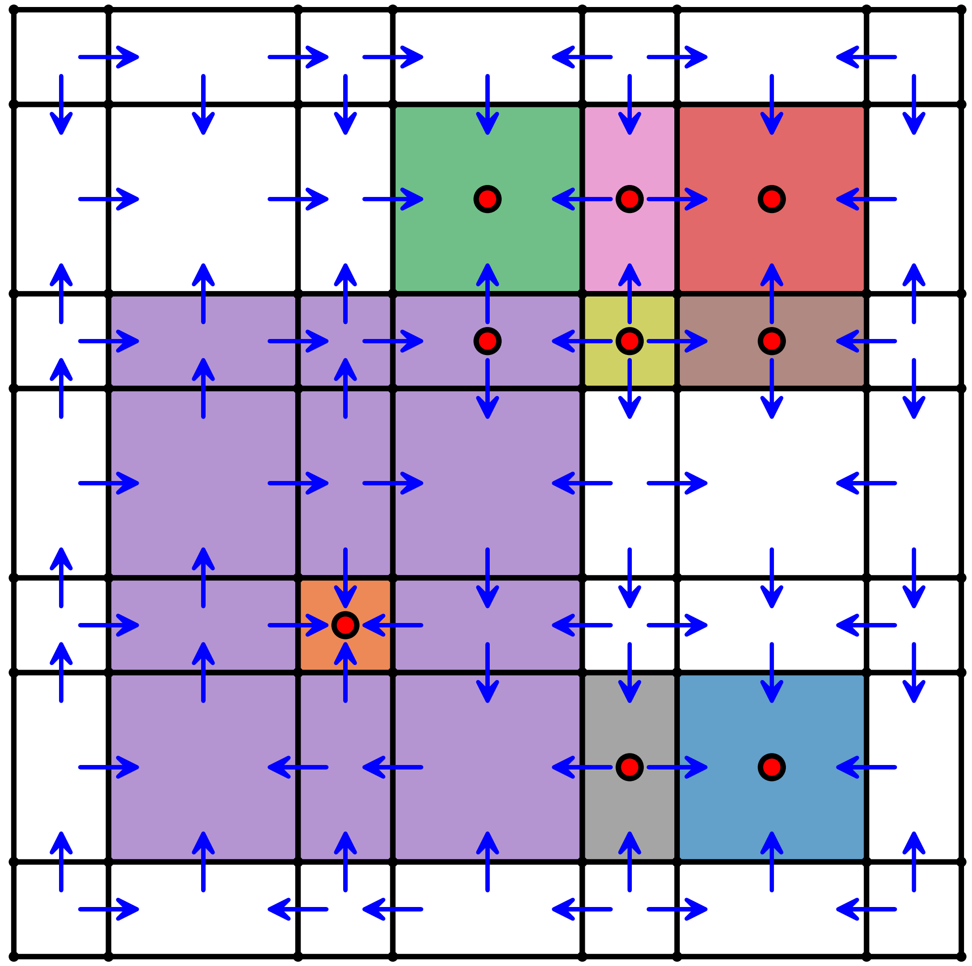
$i \longrightarrow n$ Activating $\qquad$ $i \dashv n$ Repressing

Start with a discretization and try to characterized the family of dynamical systems compatible with it

Example

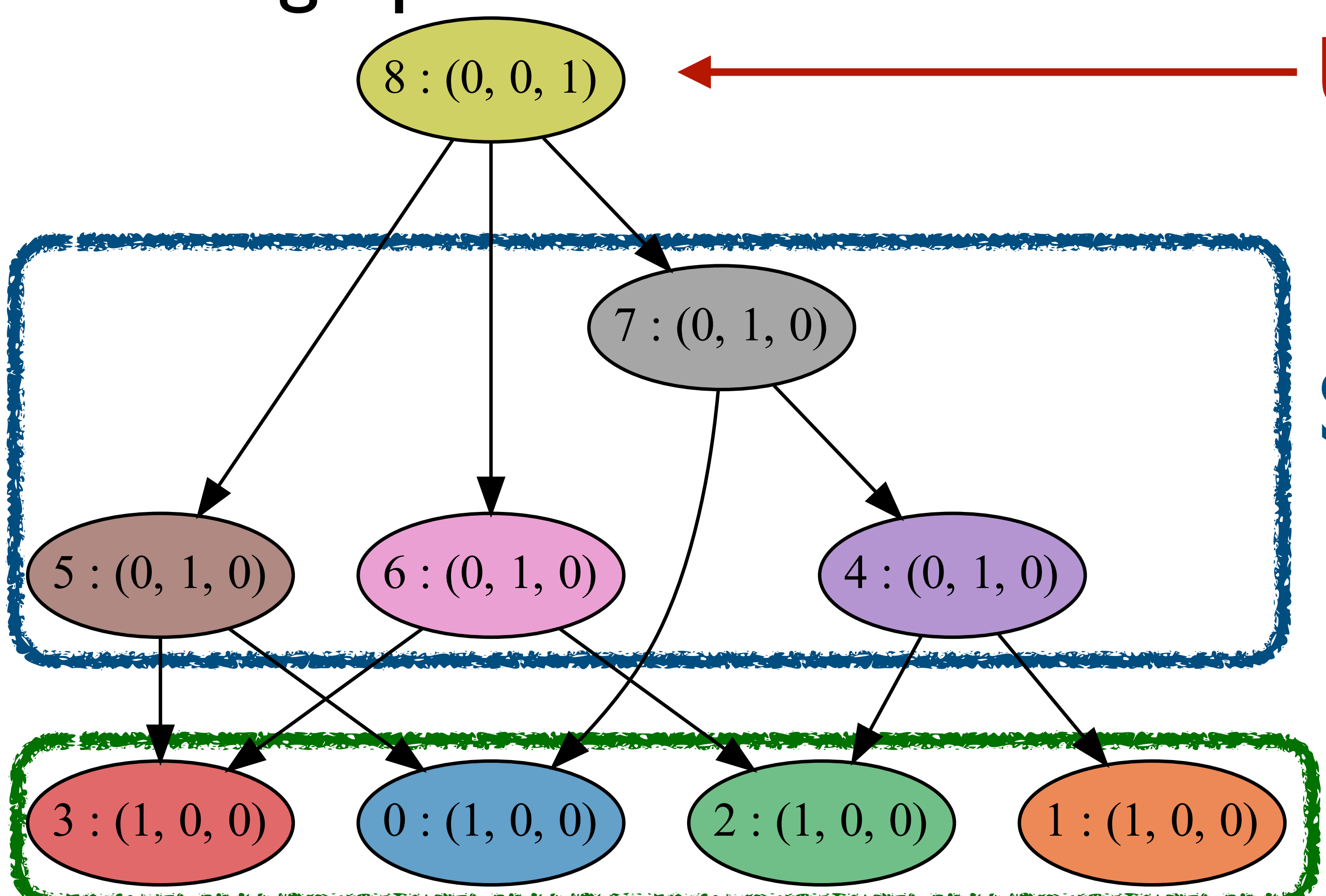


Network



Combinatorial representation of dynamics for one parameter region

Morse graph



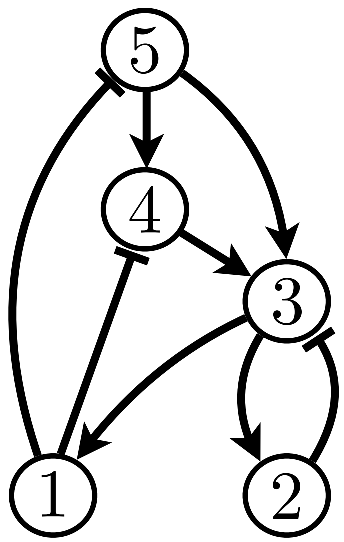
Unstable, fixed point

Saddle like, fixed points

Stable, fixed points

Theorems

Dynamics of Networks

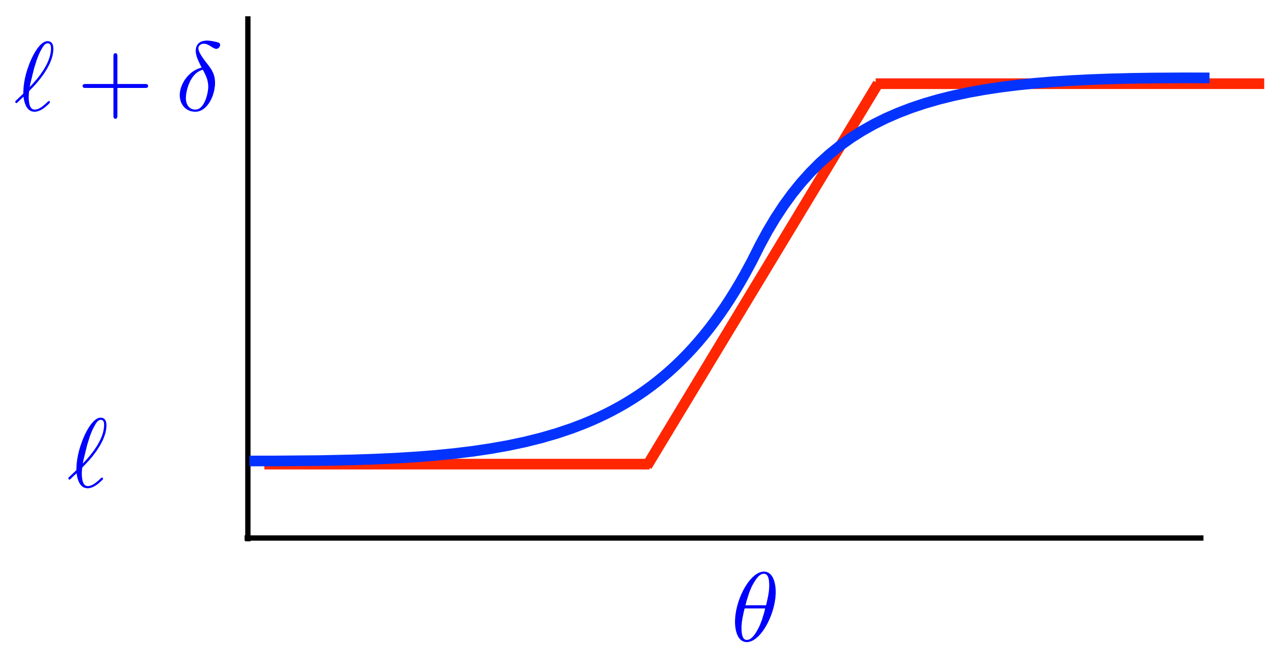


ODE model with unknown nonlinearities and parameters

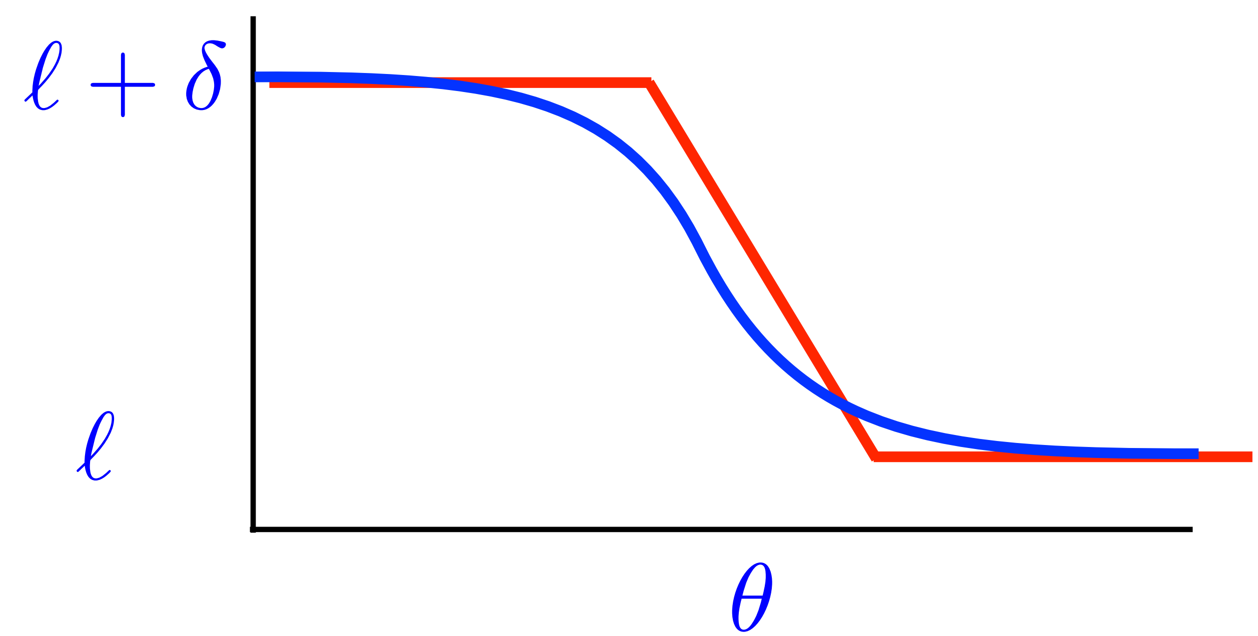
$i \longrightarrow n$ Positive edge (activating, excitatory)

$i \dashv n$ Negative edge (repressing, inhibitory)

$i \longrightarrow n$ **Activating sigmoidal**



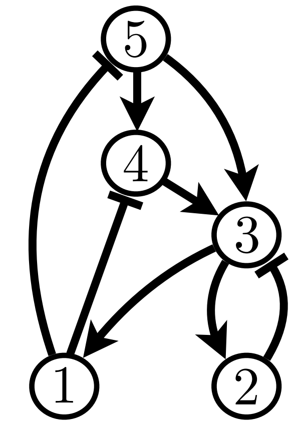
$i \dashv n$ **Repressing**



Products or sums of sigmoidal

$$\dot{x}_n = -\gamma_n x_n + E_n(x)$$

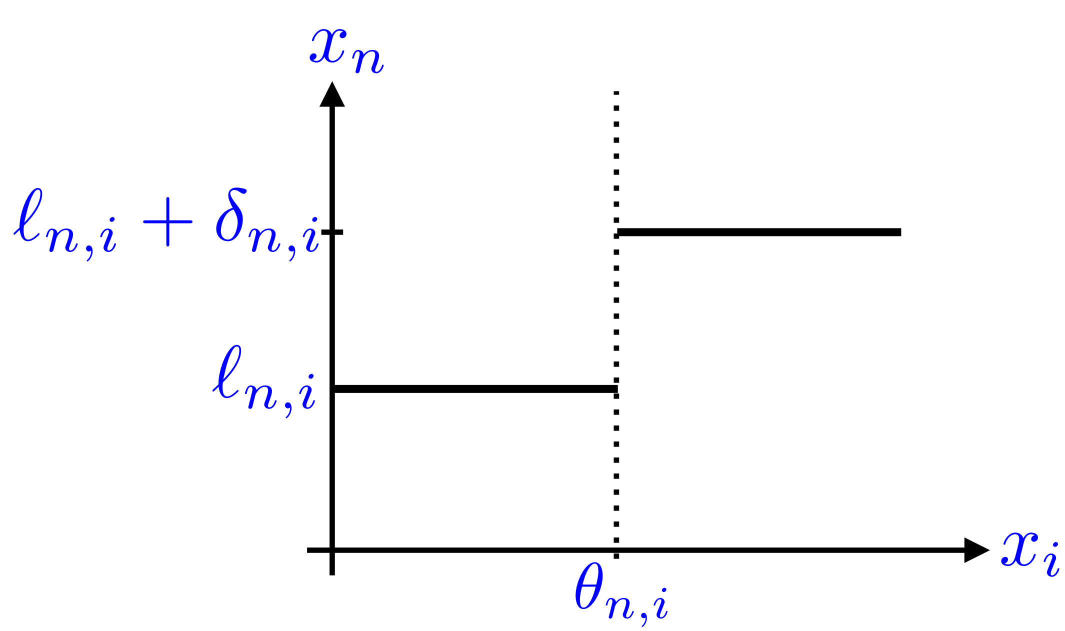
Dynamic Signatures Generated by Regulatory Networks (DSGRN)



Denote by x_n a quantity associated with node n and assume:

$i \longrightarrow n$

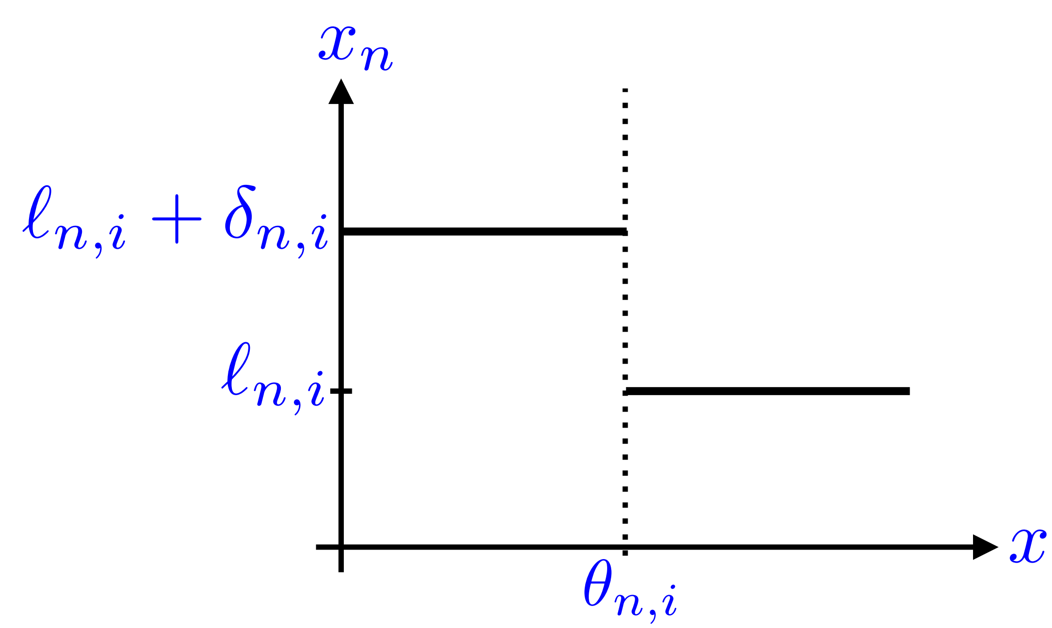
An increase in x_i increases the rate of production of x_n



$$\sigma^+_{n,i}(x_i) = \begin{cases} \ell_{n,i}, & \text{if } x_i < \theta_{n,i} \\ \ell_{n,i} + \delta_{n,i}, & \text{if } x_i > \theta_{n,i} \end{cases}$$

$i \dashv n$

An increase in x_i decreases the rate of production of x_n



$$\sigma^-_{n,i}(x_i) = \begin{cases} \ell_{n,i} + \delta_{n,i}, & \text{if } x_i < \theta_{n,i} \\ \ell_{n,i}, & \text{if } x_i > \theta_{n,i} \end{cases}$$

Cummins, et. al., SIADS, 2016

DSGRN

The rate of change of x_n is given by

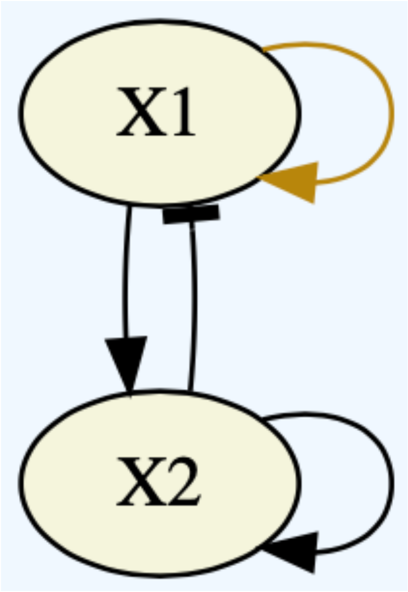
$$\cancel{\dot{x}_n} = -\gamma_n x_n + \Lambda_n(x)$$

decay

production

Product of sums of switching functions $\sigma^{\pm}_{n,i}(x_i)$

Example:



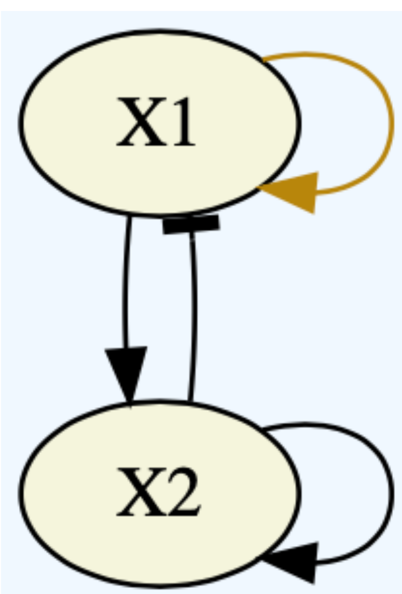
$$\begin{cases} -\gamma_1 x_1 + \sigma^+(x_1)\sigma^-(x_2) \\ -\gamma_2 x_2 + \sigma^+(x_1) + \sigma^+(x_2) \end{cases}$$

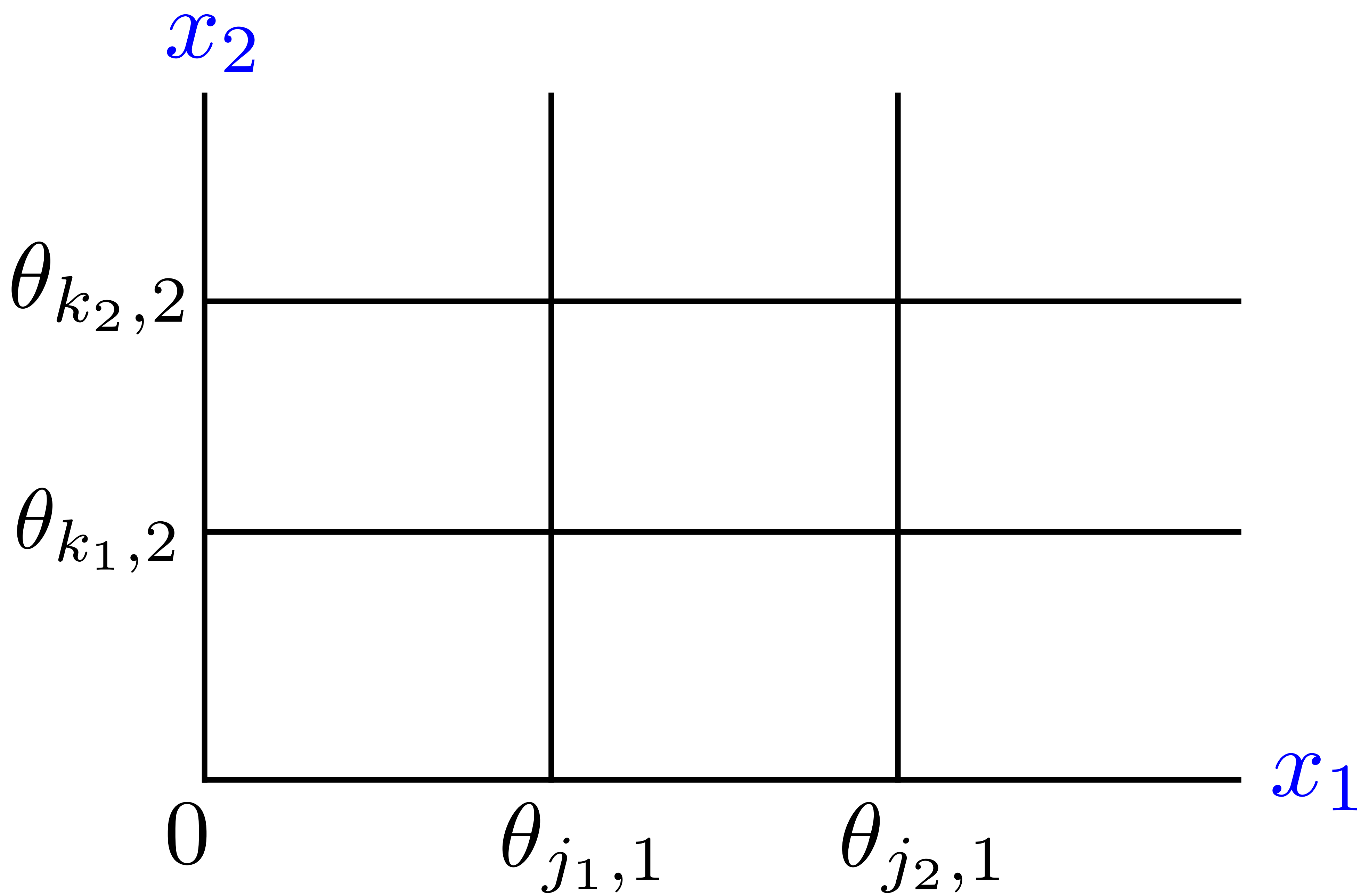
DSGRN

The function $\Lambda_n(x)$ is constant off the hyperplanes $x_i = \theta_{n,i}$

out-edge threshold

Hence we have a natural decomposition of phase space into rectangular regions

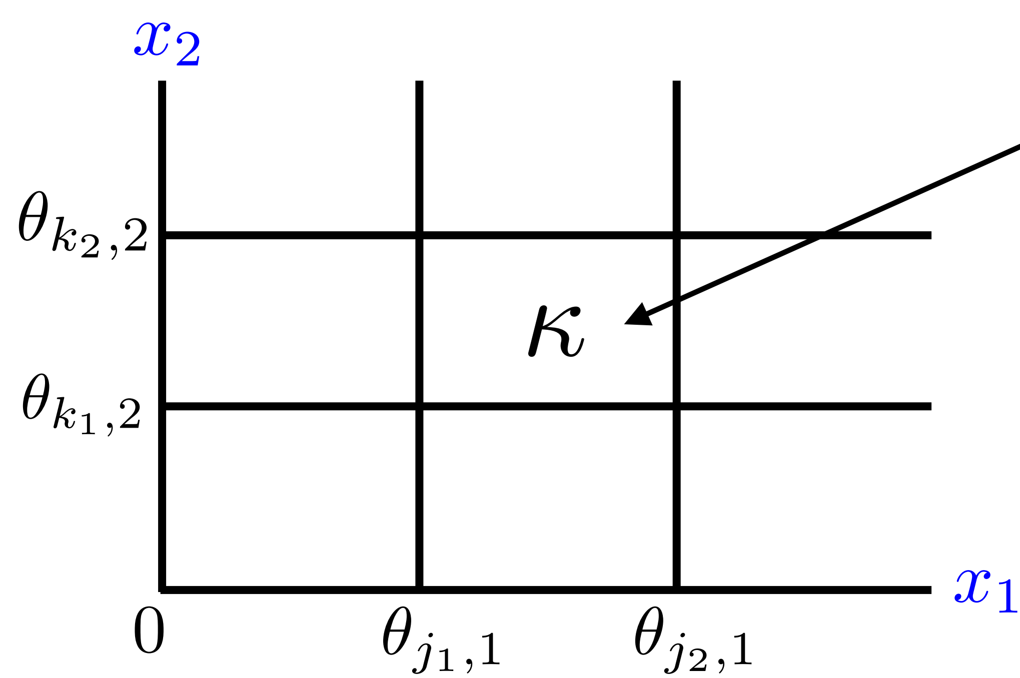




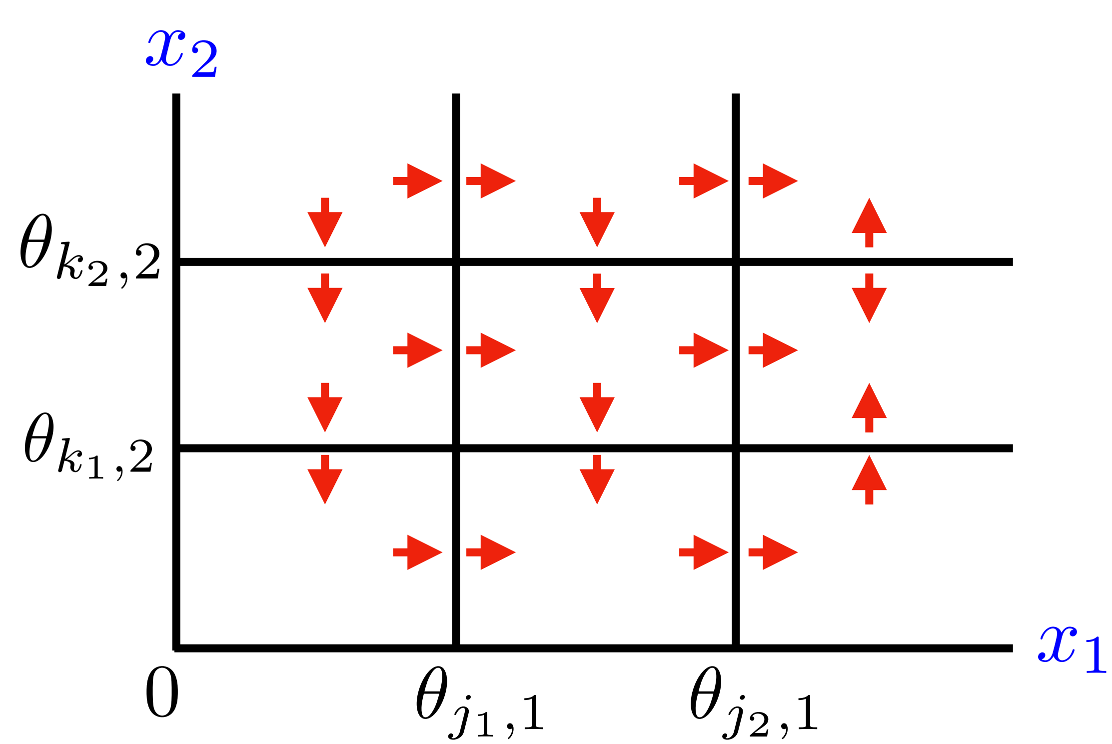
DSGRN

We want to determine whether x_n is increasing or decreasing within one of these regions

$$-\gamma_n x_n + \underbrace{\Lambda_n(\kappa)}_{\text{constant}}$$



We want to determine the signs of $-\gamma_n \theta_{*,n} + \Lambda_n(x)$



Wall labeling

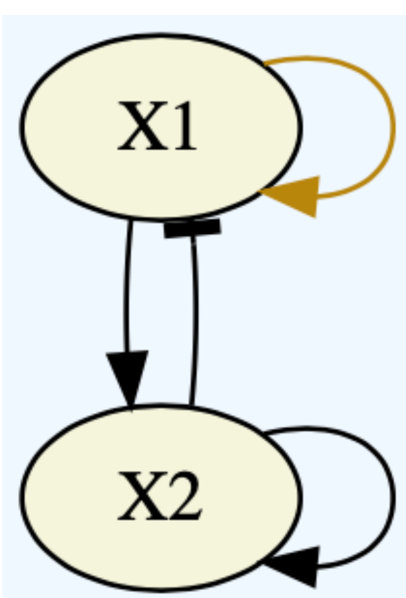
Parameter graph

We want wall labelings over the whole parameter space

To determine the signs of

$$-\gamma_n \theta_{*,n} + \Lambda_n(x)$$

Note that $\Lambda_1(x) = \sigma^+(x_1)\sigma^-(x_2)$ can take on the values



$$p_0 = \ell_{1,1}\ell_{1,2}$$
$$p_1 = (\ell_{1,1} + \delta_{1,1})\ell_{1,2}$$
$$p_2 = \ell_{1,1}(\ell_{1,2} + \delta_{1,2})$$
$$p_3 = (\ell_{1,1} + \delta_{1,1})(\ell_{1,2} + \delta_{1,2})$$

Parameter graph

Hence if we determine all admissible total orders of

$$\{p_0, p_1, p_2, p_3\}$$

We can determine all possible signs of

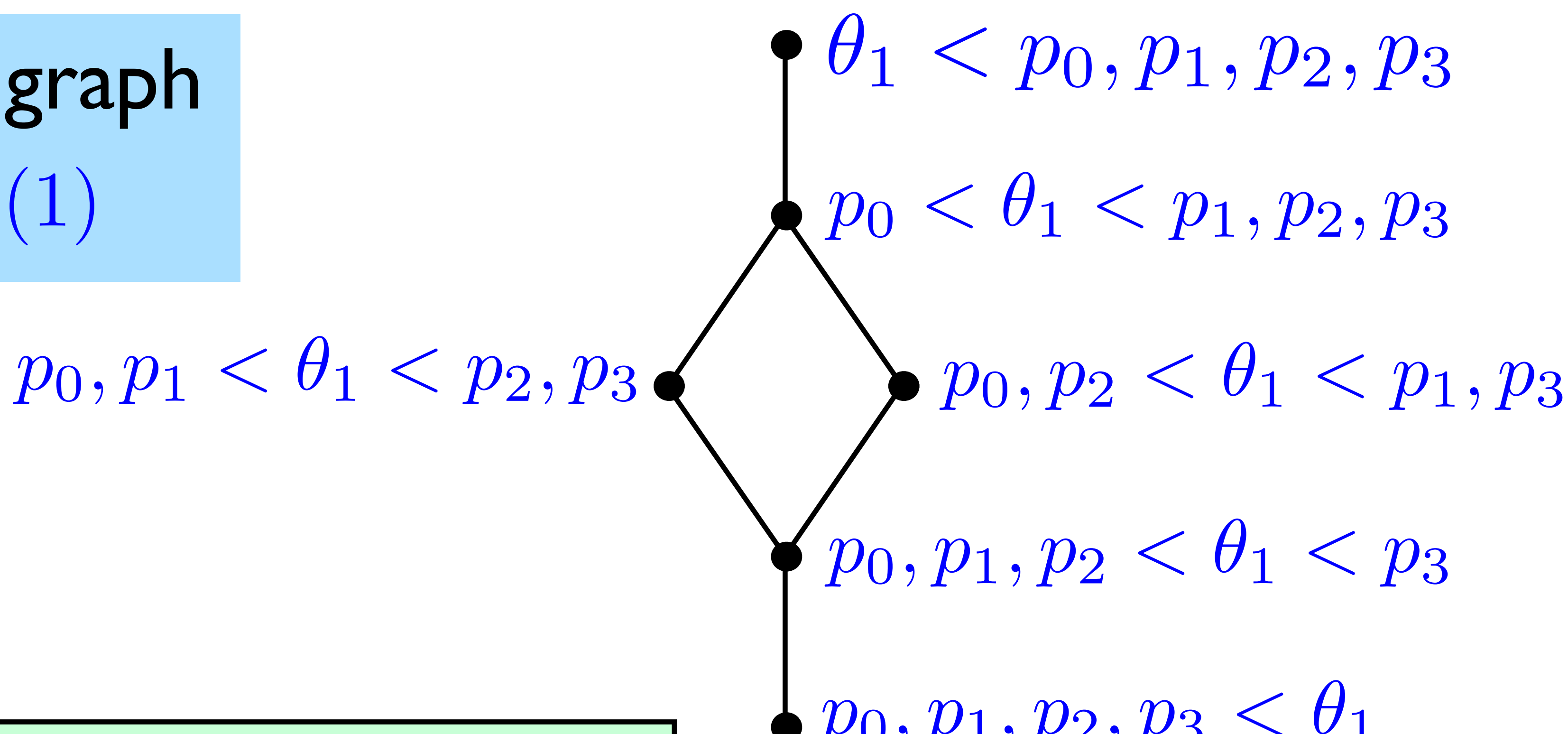
$$-\gamma_1\theta_{*,1} + \Lambda_1(x)$$

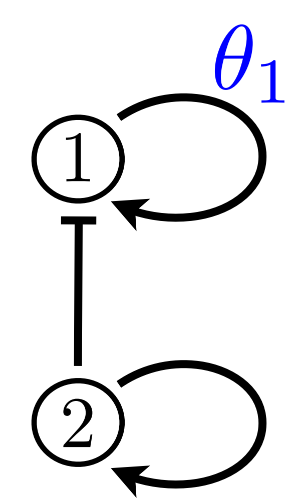
Total orders $p_0 < p_1 < p_2 < p_3$ and $p_0 < p_2 < p_1 < p_3$

Factor graph

$PG(1)$

Poset





Kepley, et. al., SIAM J. Appl. Algebra Geometry, 2021

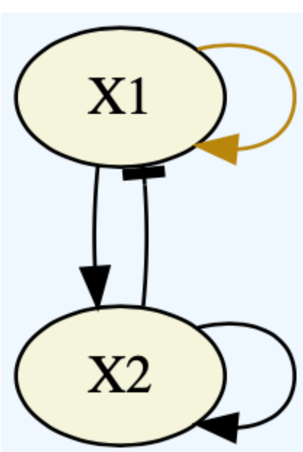
Parameter graph

Parameter graph $PG = \prod_{n=1}^{N} PG(n)$ Semi-algebraic sets (inequalities determining all sign combinations)

Each node determines all possible signs of

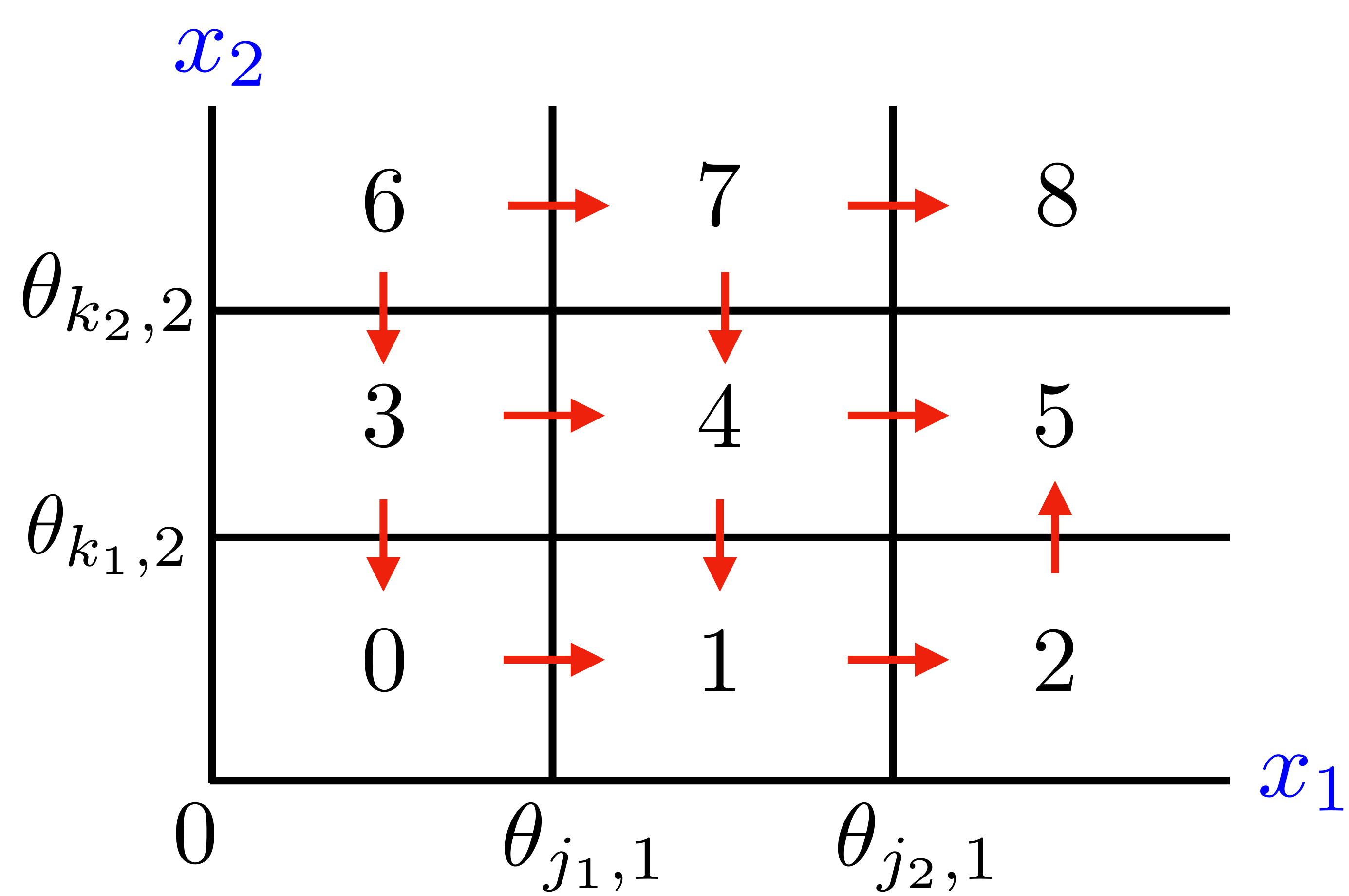
$$-\gamma_n \theta_{*,n} + \Lambda_n(x)$$

Edge means flip a single inequality



Parameter graph size: 1600

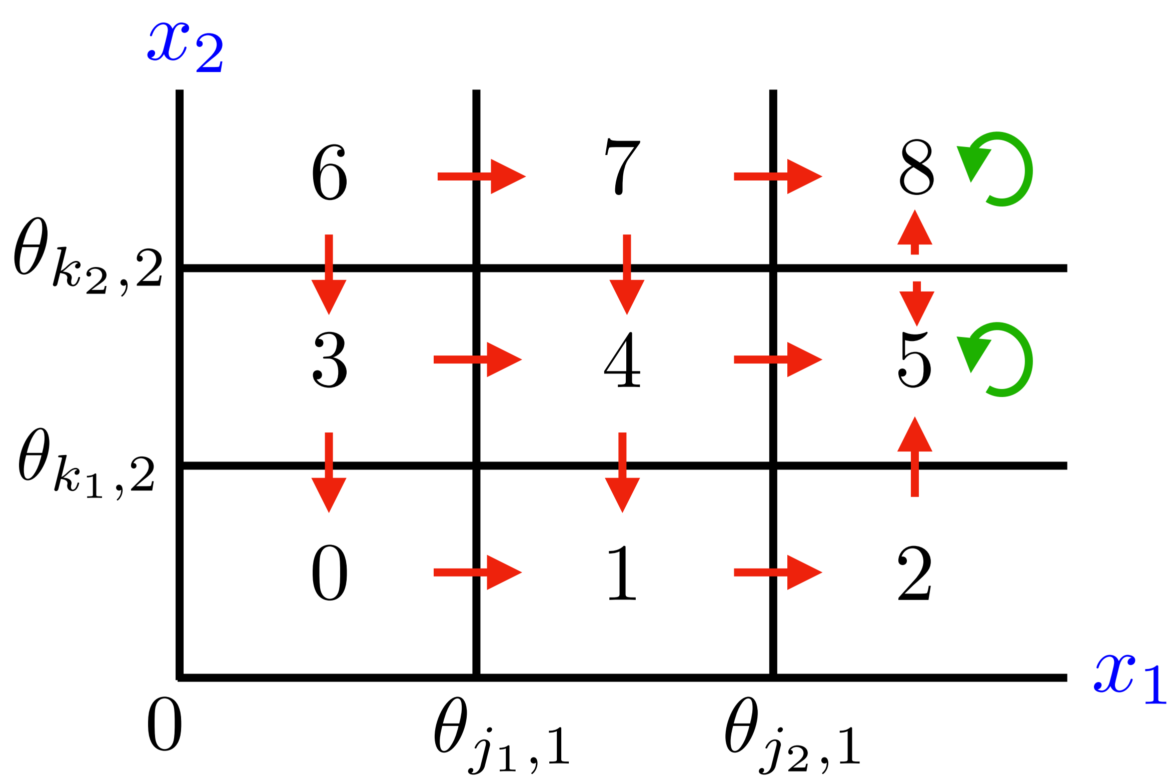
Parameter space dim: 14

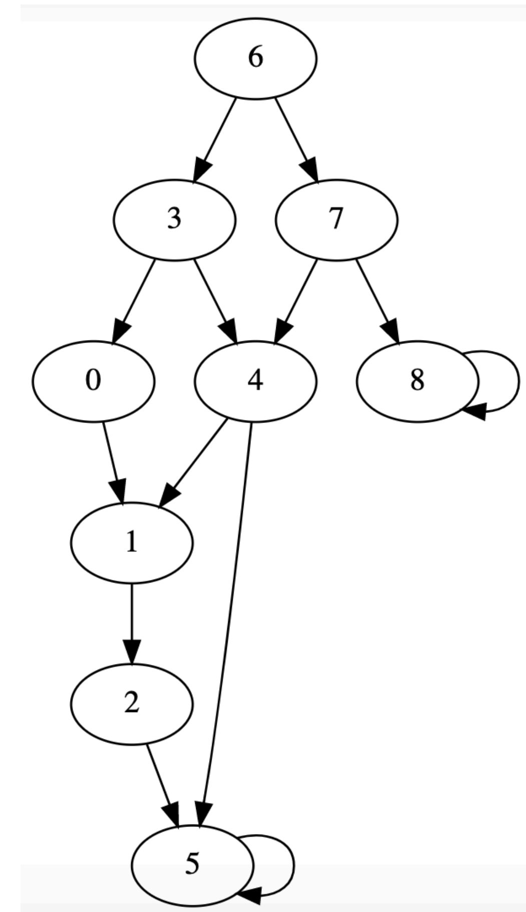


Multi-valued map

We could define the multi-valued map $\mathcal{F}$ using the top dimensional cells (DSGRN)

Wall labeling

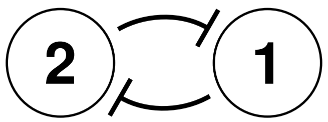




This does not capture dynamics on lower dimensional cells

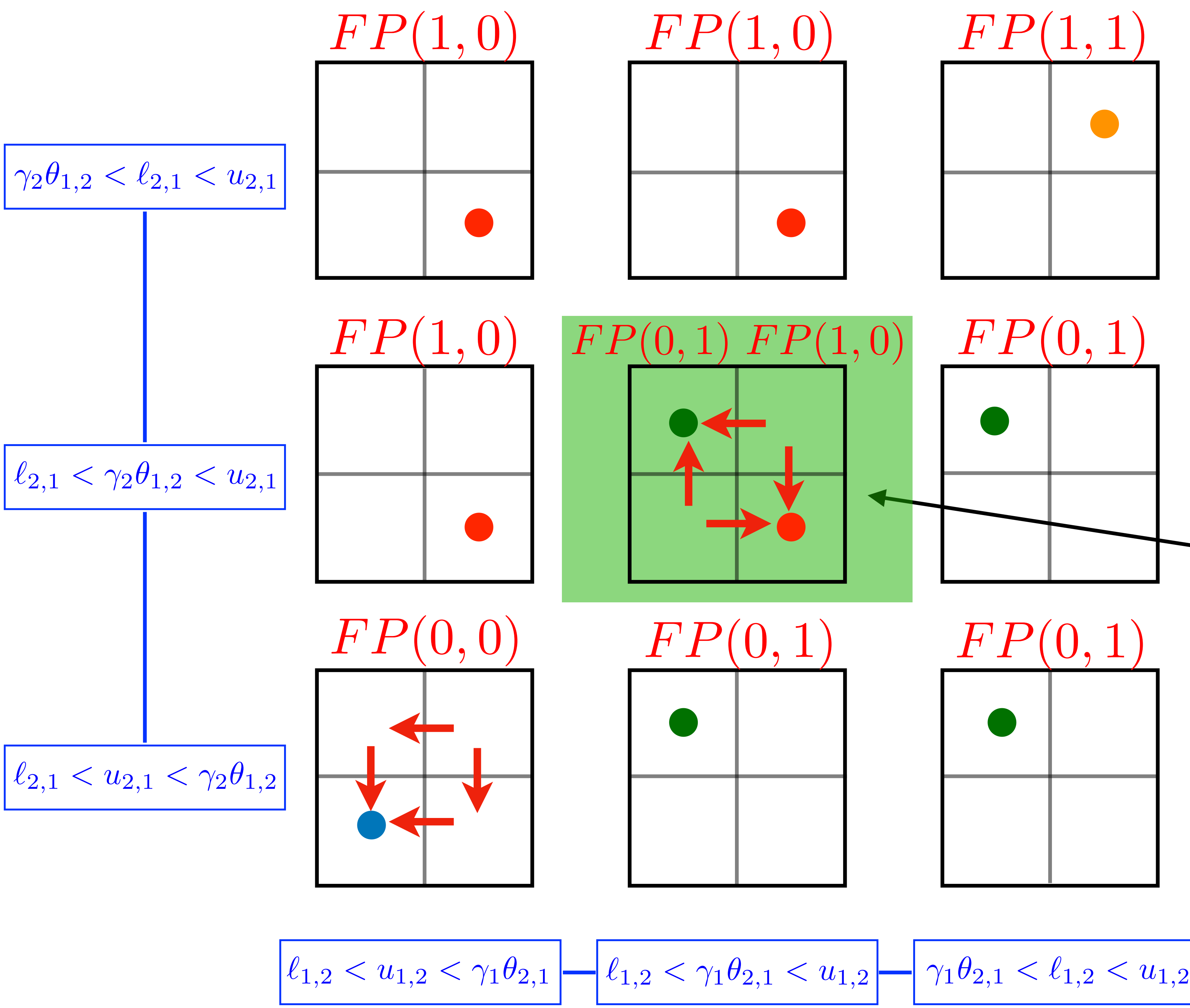
So we want to include the lower dimensional cells in the multi-valued map

Parameter Graph



$$\begin{cases} -\gamma_1 x_1 + \sigma^-(x_2, \ell_{1,2}, u_{1,2}, \theta_{1,2}) \\ -\gamma_2 x_2 + \sigma^-(x_1, \ell_{2,1}, u_{2,1}, \theta_{2,1}) \end{cases}$$

8-D parameter space

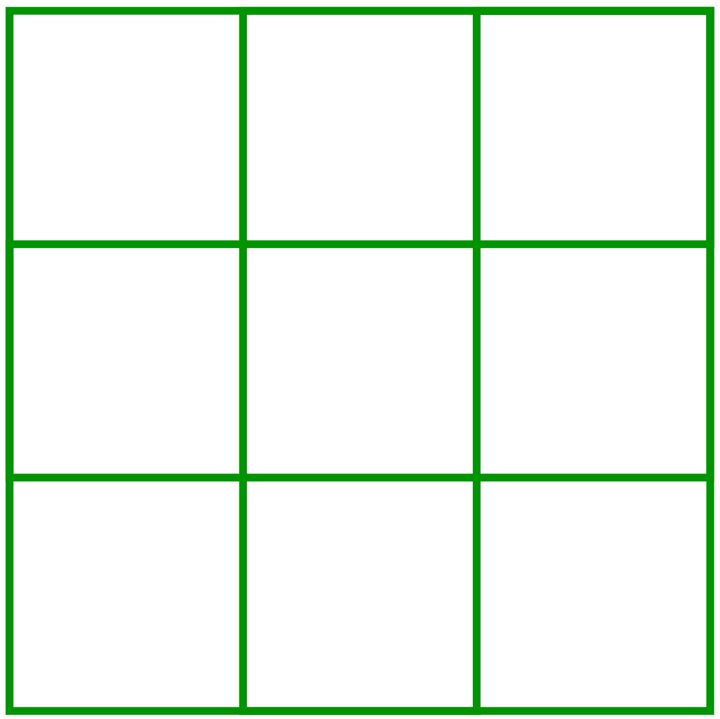


Parameter graph decomposes entire parameter space

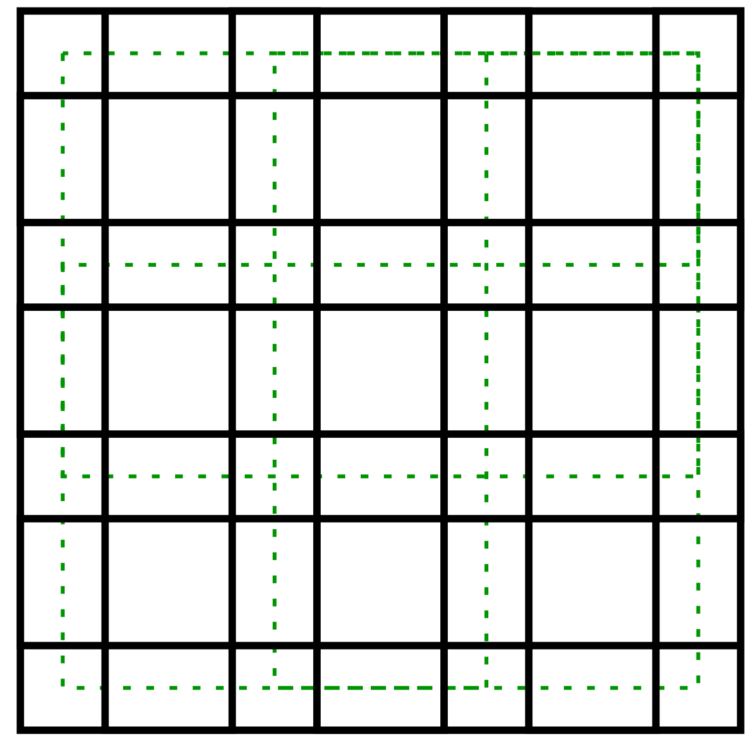
Essential parameter node

Cubical blowup complex

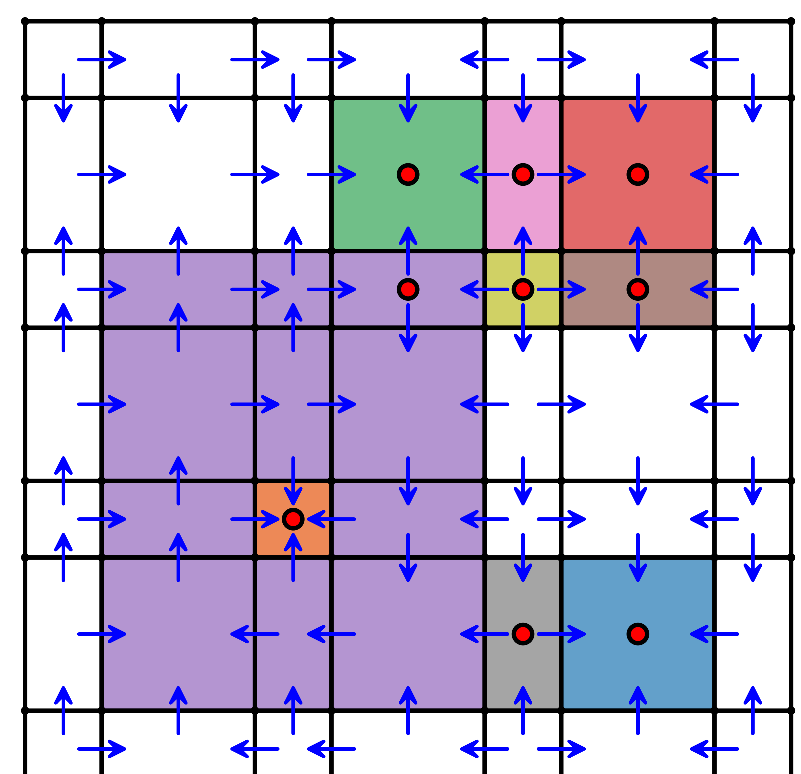
Cubical complex



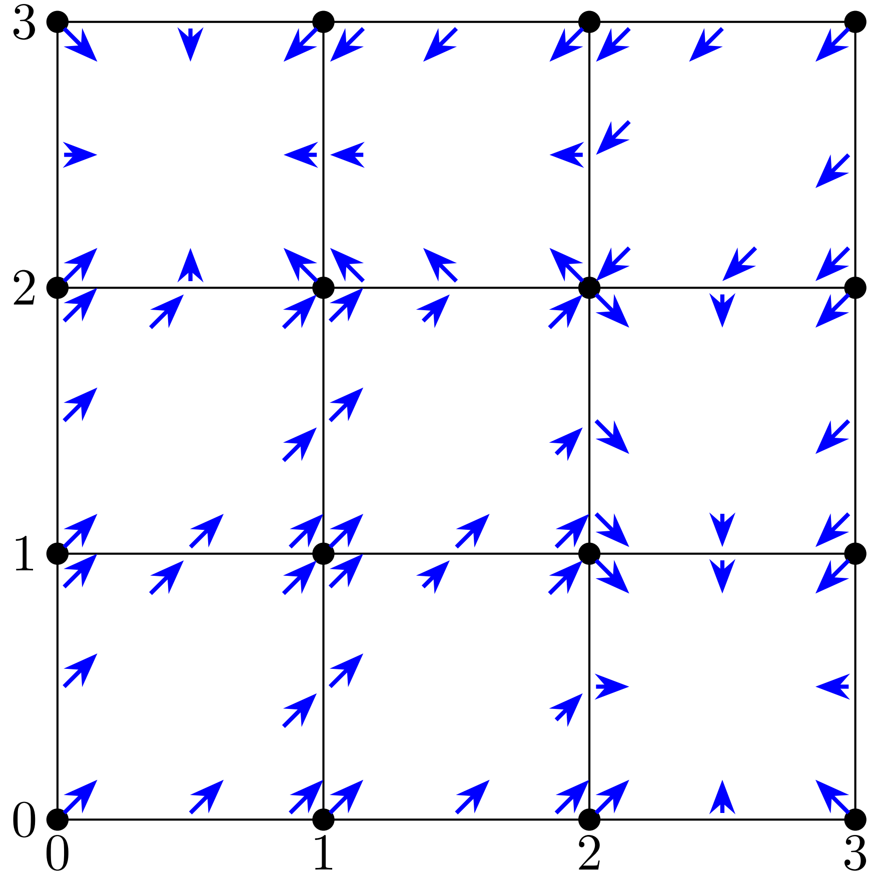
Cubical “blowup complex”



Bijection between cells of the original complex and the top cells of the cubical blowup complex



Can do the algebraic topology computations



Rook Field

A wall labeling defines a rook field

$$\Phi(\xi, \kappa) \in \{0, \pm 1\}^N \qquad \xi \preceq \kappa \in \mathcal{X}^{(N)}$$

Rook field is used to define combinatorial dynamics

From a rook field we define multi-valued maps

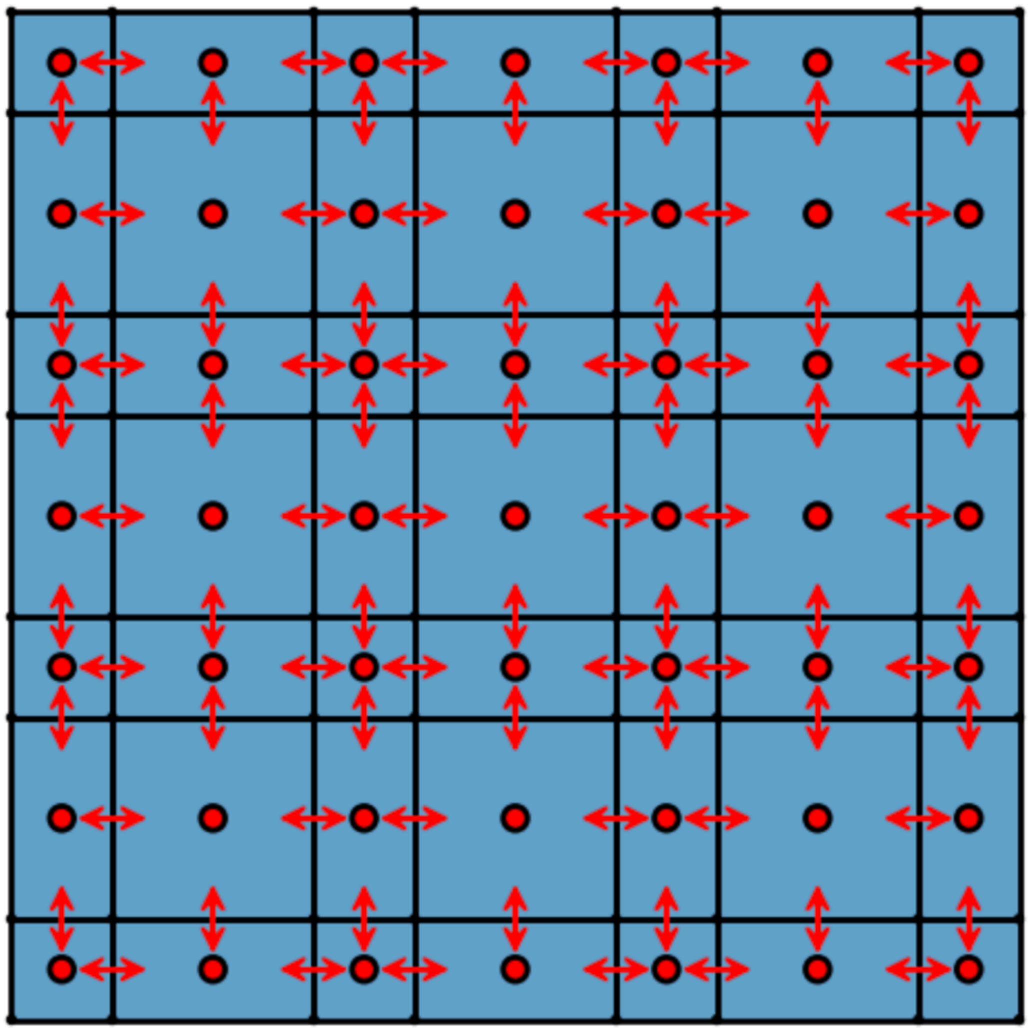
$$\mathcal{F}_i : \mathcal{X} \rightrightarrows \mathcal{X}, \quad i = 0, 1, 2, 3$$

Multi-valued map

Define multi-valued map from rook field

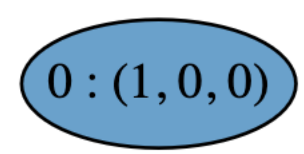
$$\mathcal{F}_0 : \quad \sigma \in \mathcal{F}_0(\xi) \text{ iff } \sigma \preceq \xi \text{ or } \xi \preceq \sigma$$

Face relation



Double arrows between every cell and its faces (trivial dynamics)

Morse graph

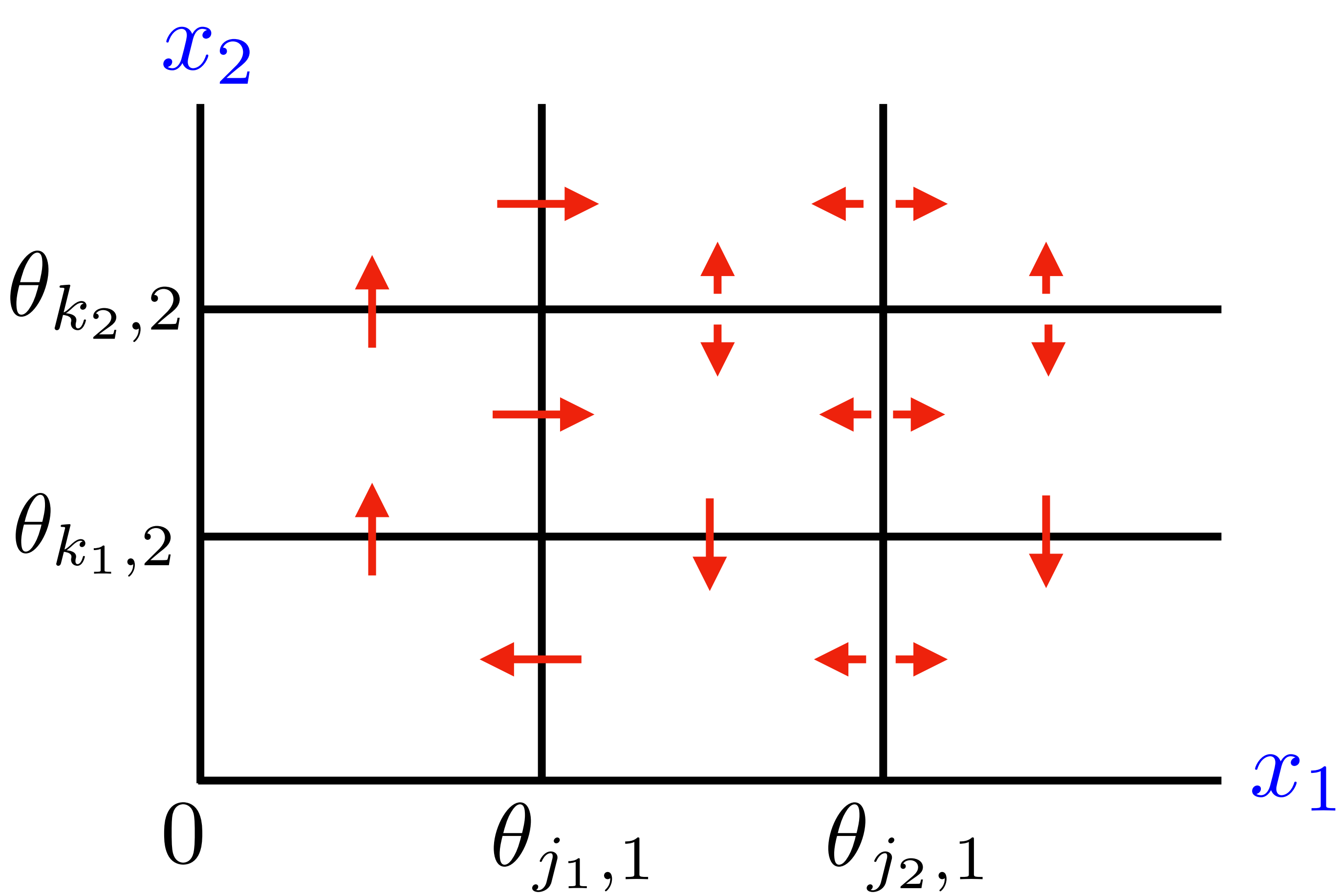


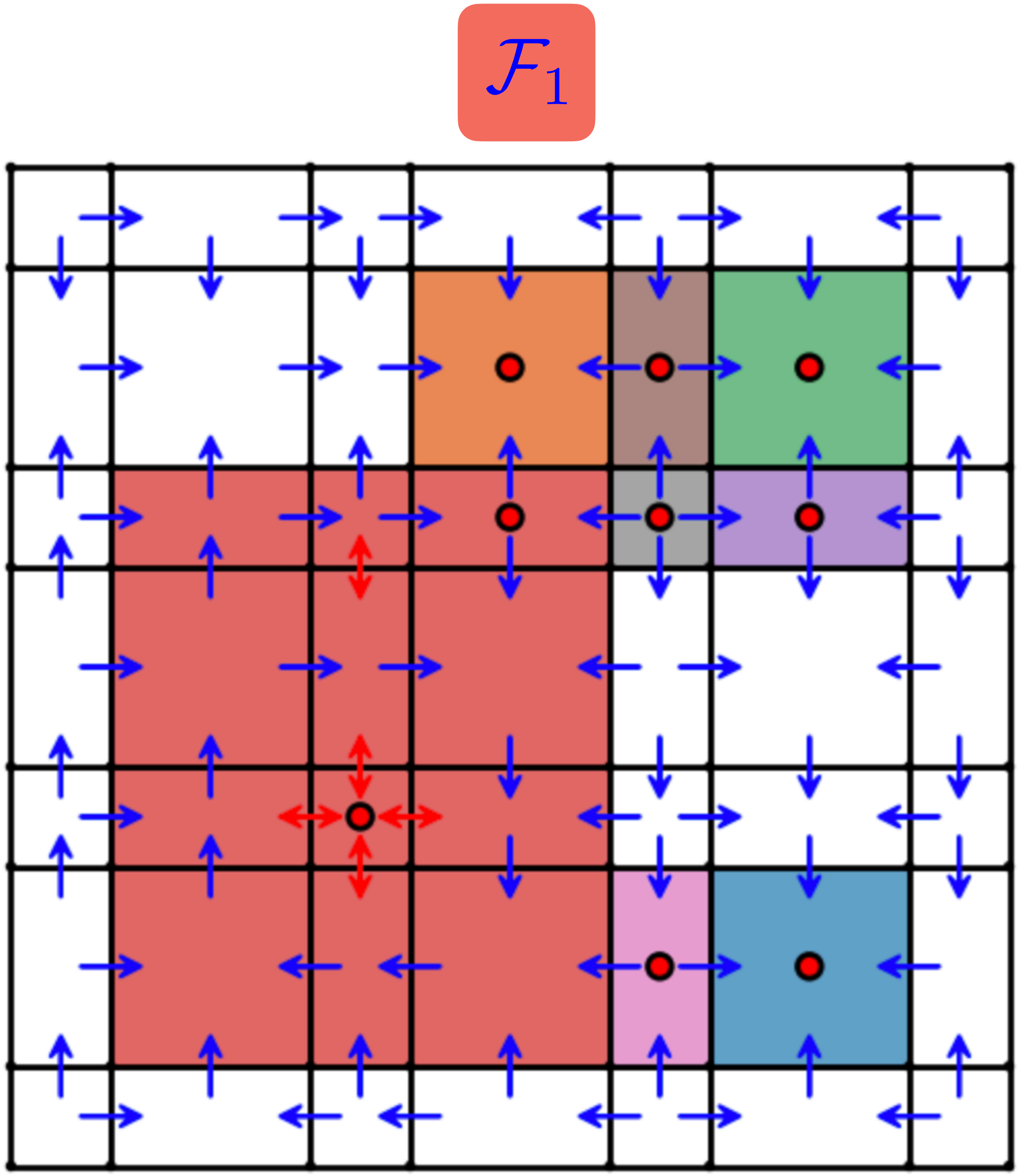
Other maps eliminate double arrows (refinements)

Multi-valued map refinements

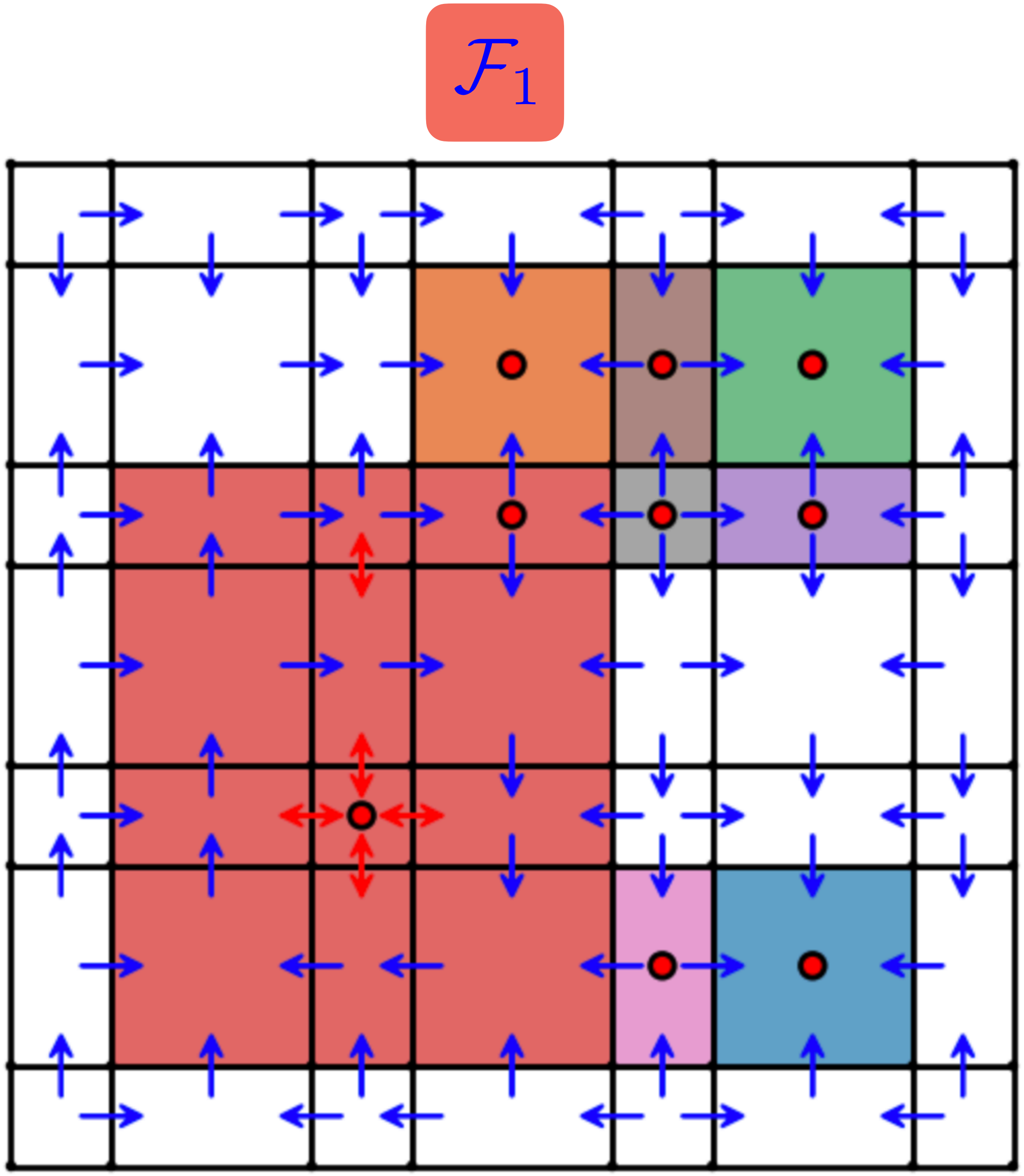
Remove double arrow if there is a clear flow direction

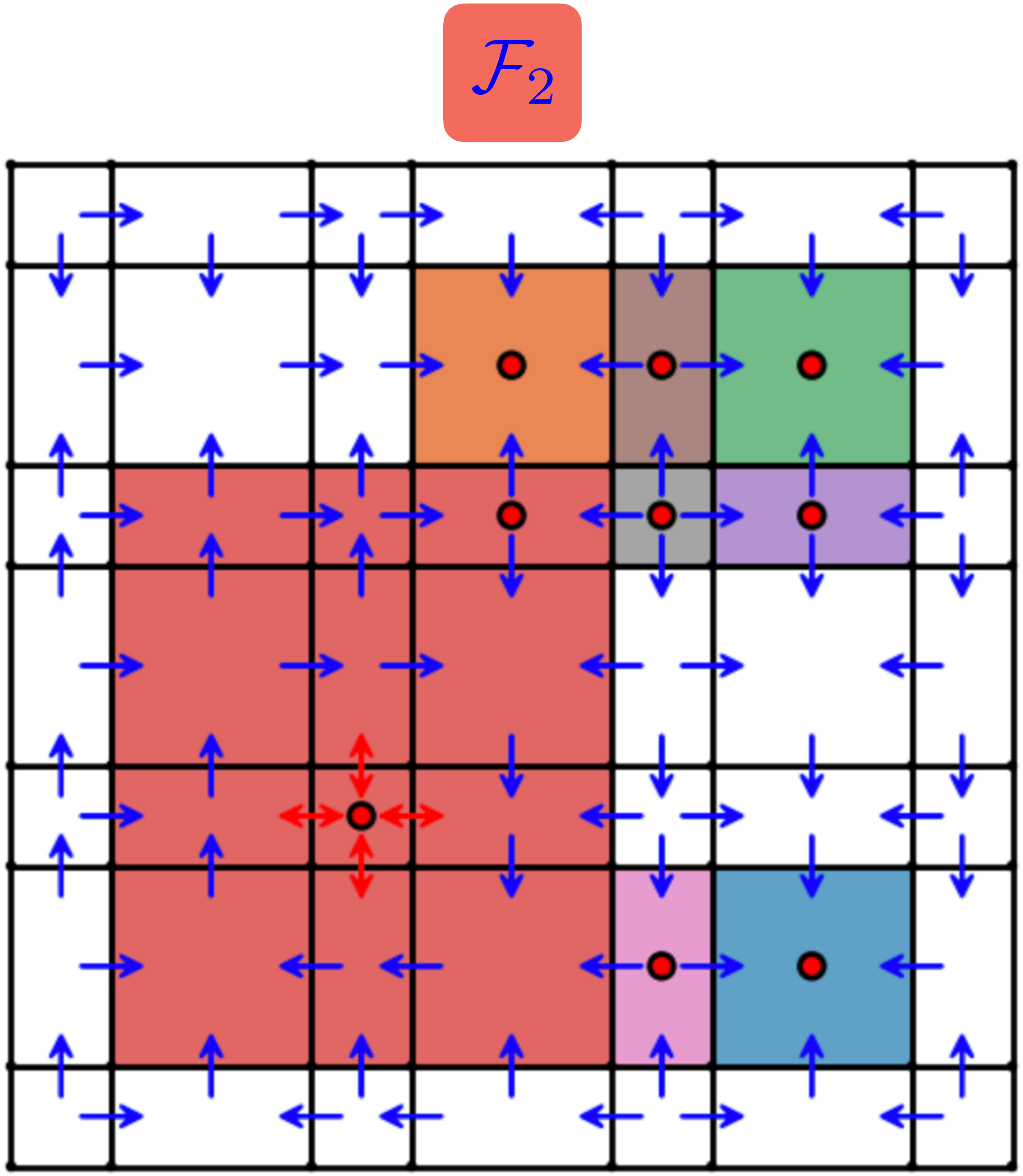
No self-arrow if there is a gradient direction





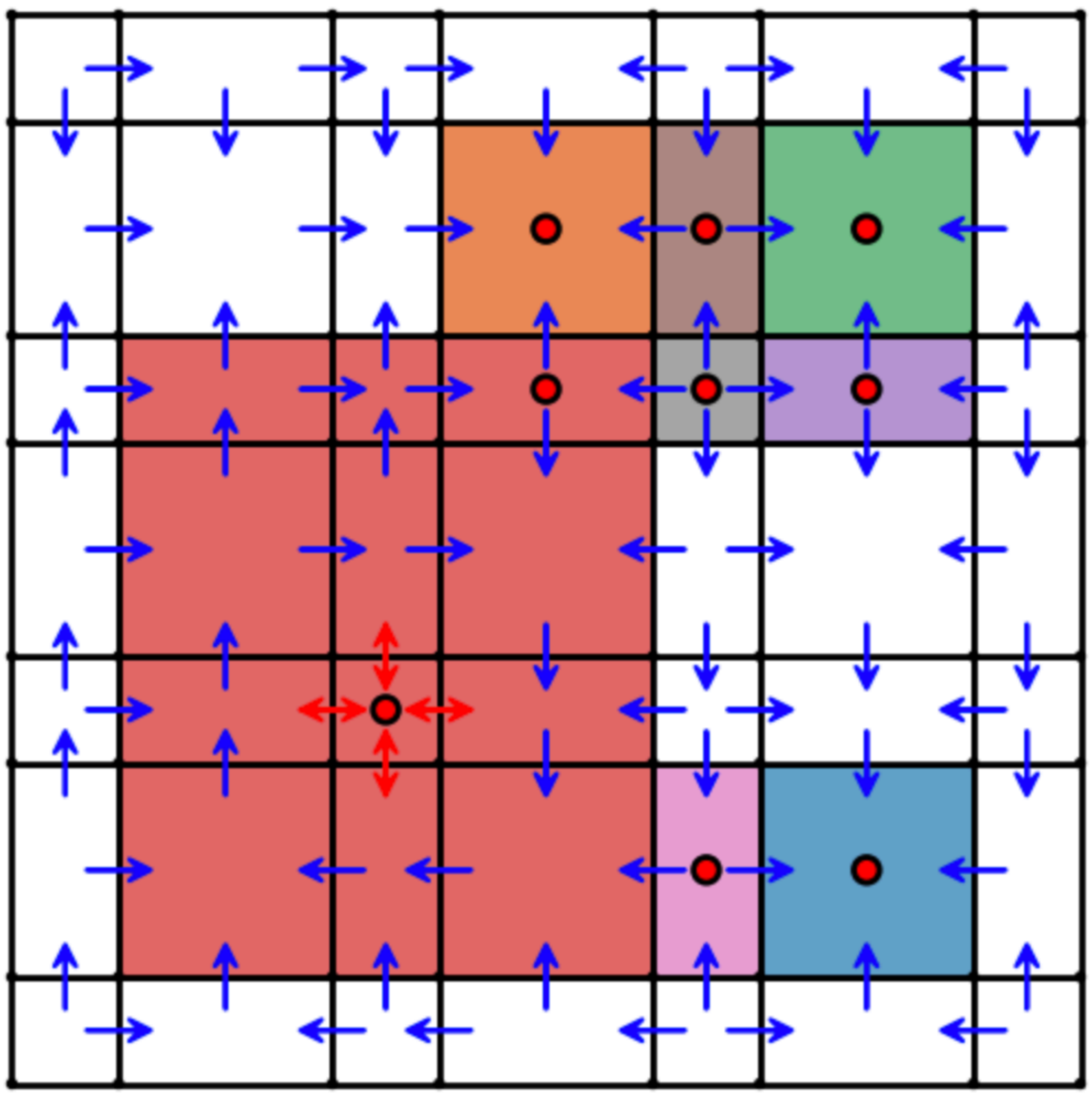
Multi-valued map refinements



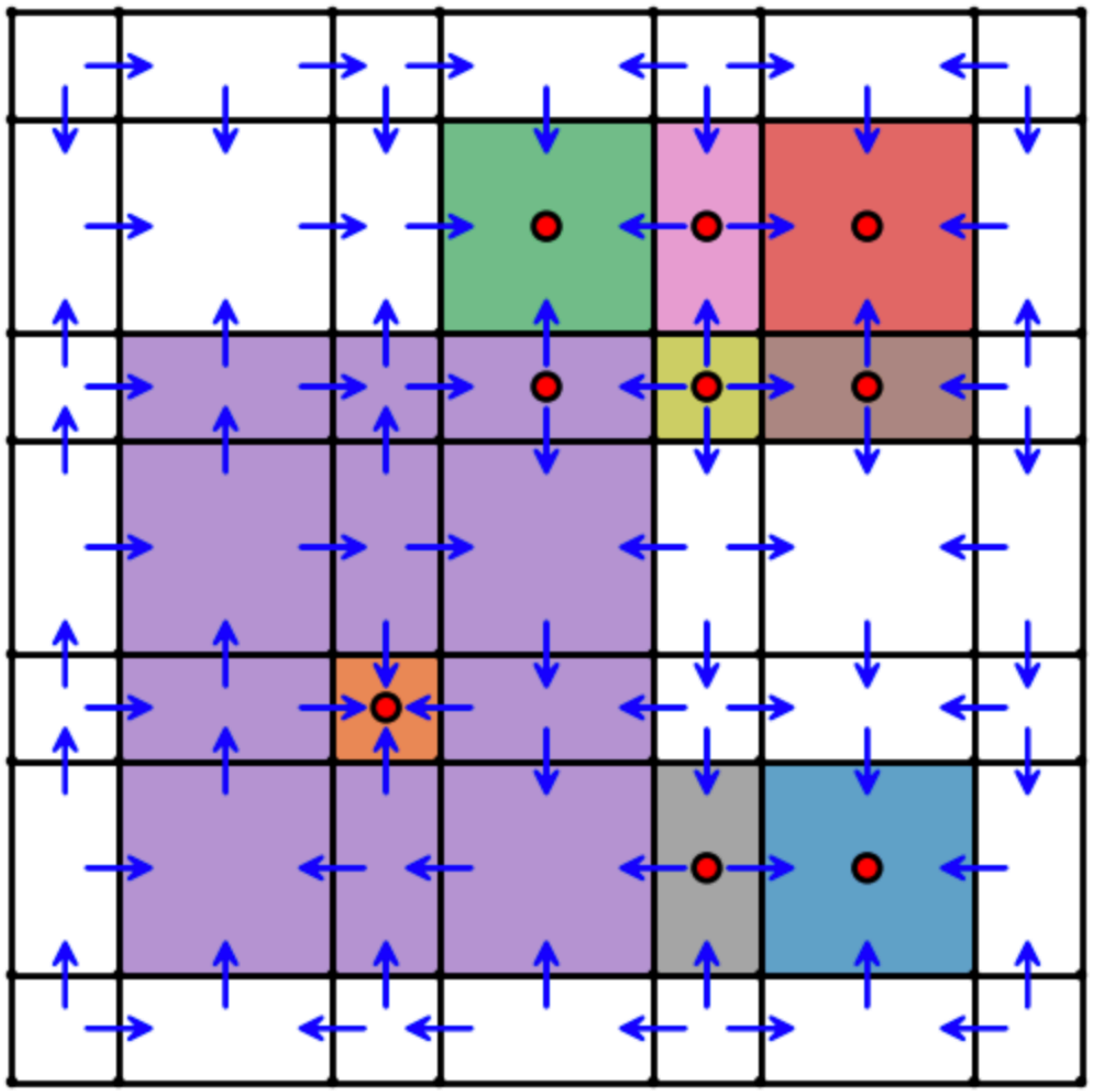


Multi-valued map refinements

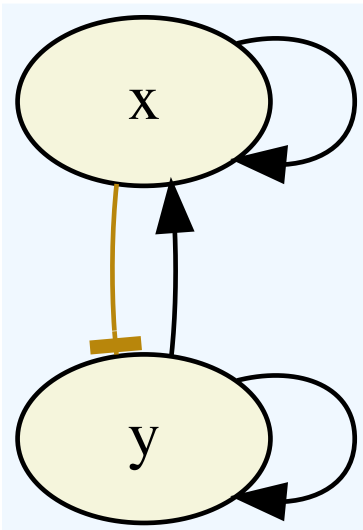
$\mathcal{F}_2$



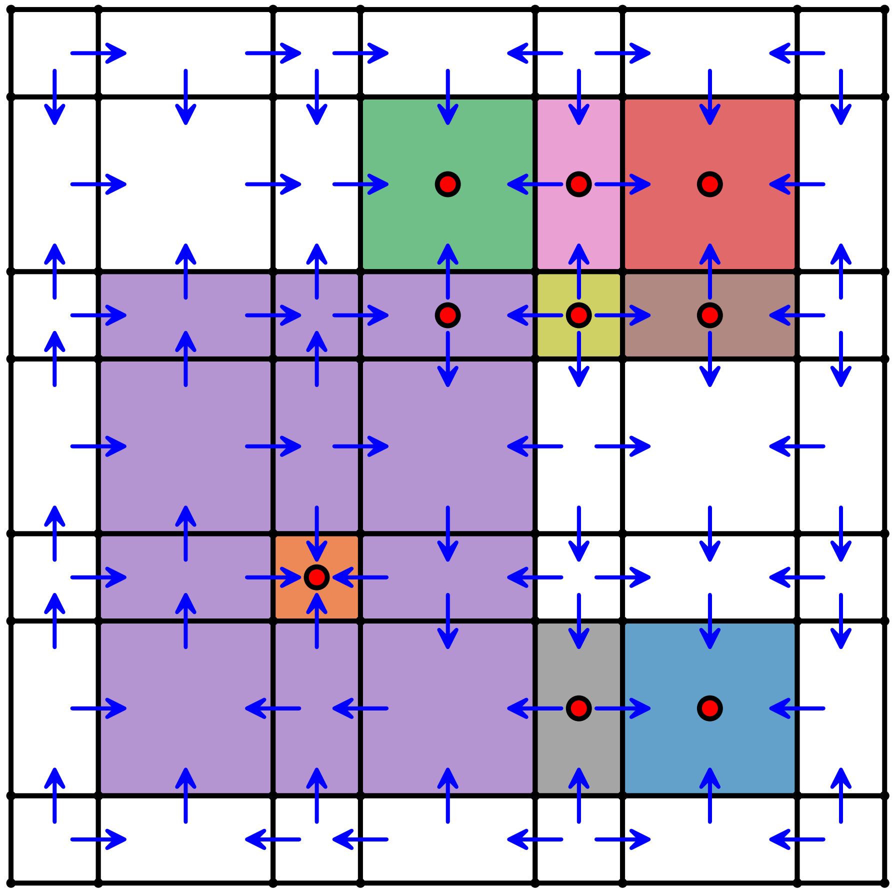
$\mathcal{F}_3$



Combinatorial Dynamics



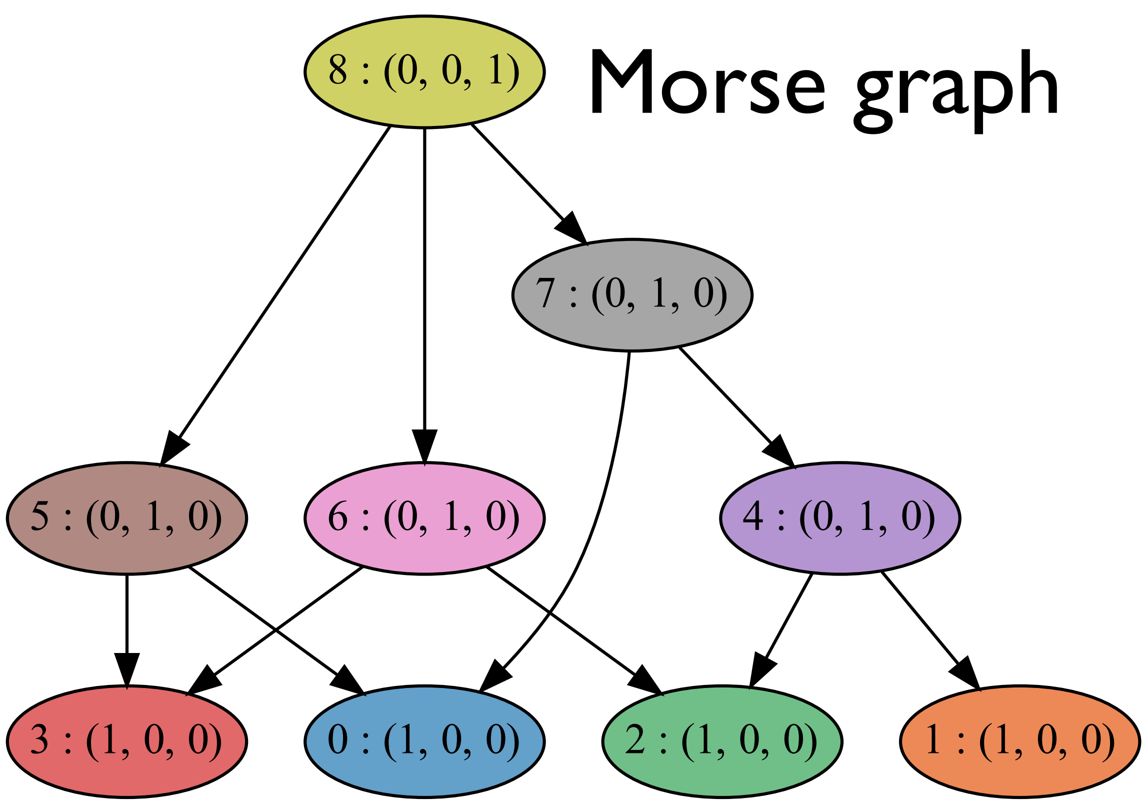
Network



Abstract cell complex

Algebraic topology computations

Dynamics valid for whole parameter region



Morse graph

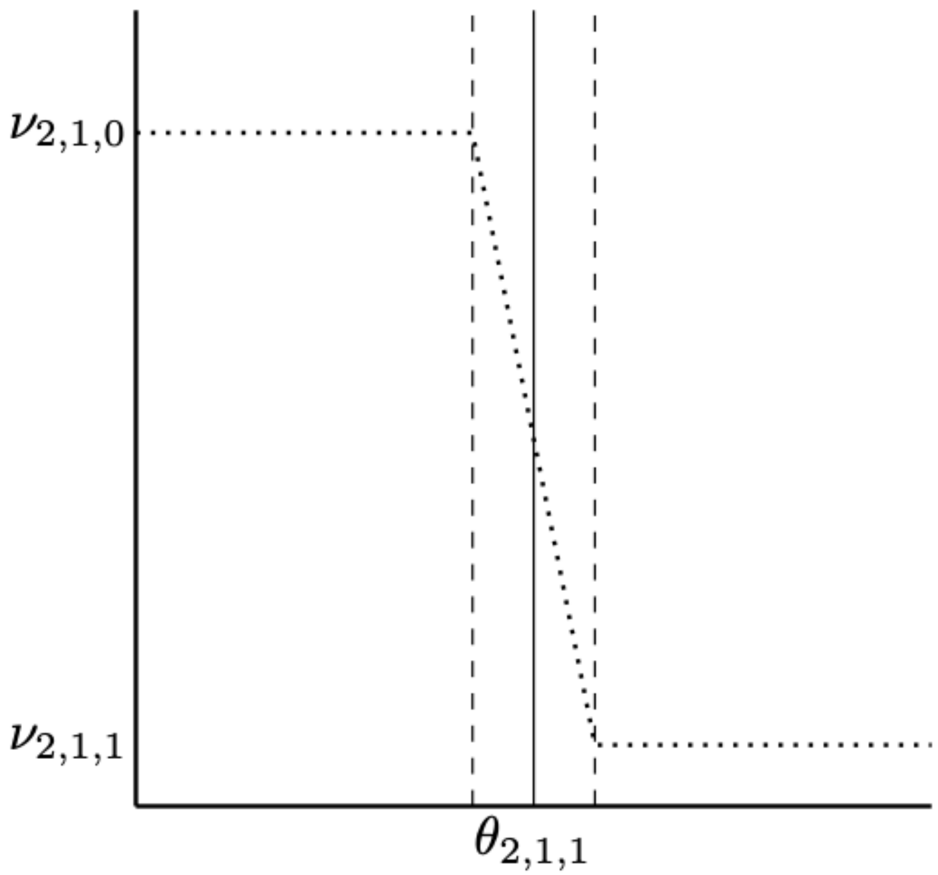
Dynamics is valid for which families of ODEs?

To get ODE dynamics we need transversality

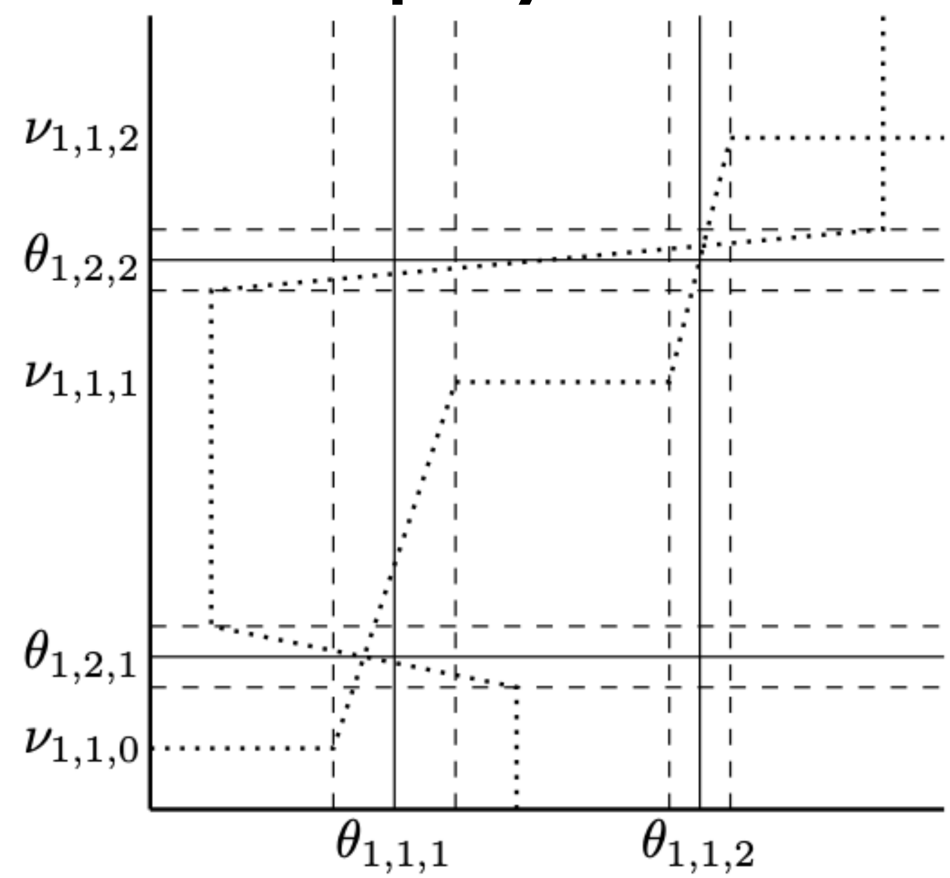
Ramp systems

"Replace" step functions by ramp functions

Ramp function



Ramp system

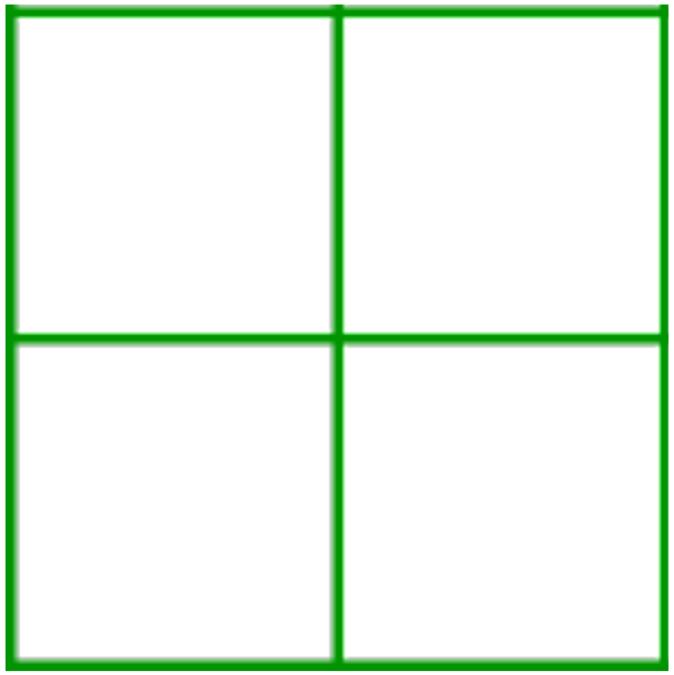


Sums and products of ramp functions

$$\dot{x}_n = \mathbf{E}_n(x) = -\gamma_n x_n + E_n(x;\nu,\theta,h) \quad n = 1,\dots,N$$

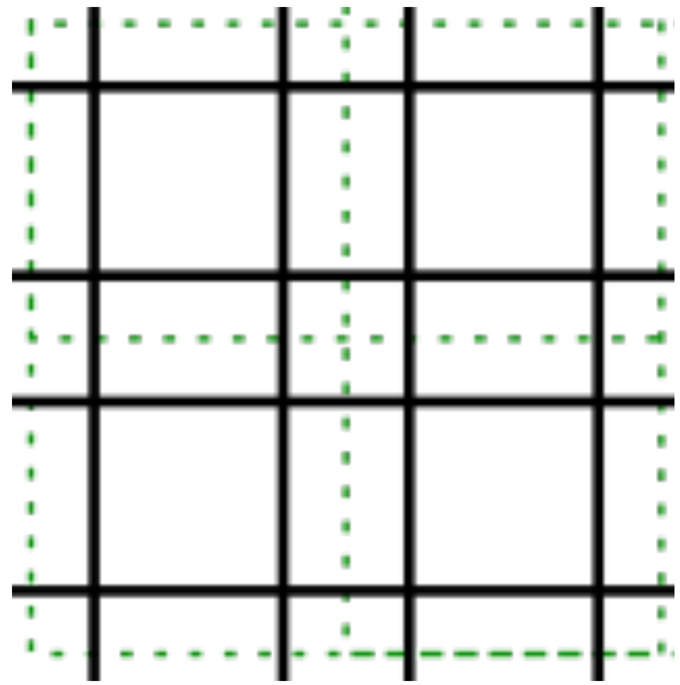
Ramp systems

Cubical complex



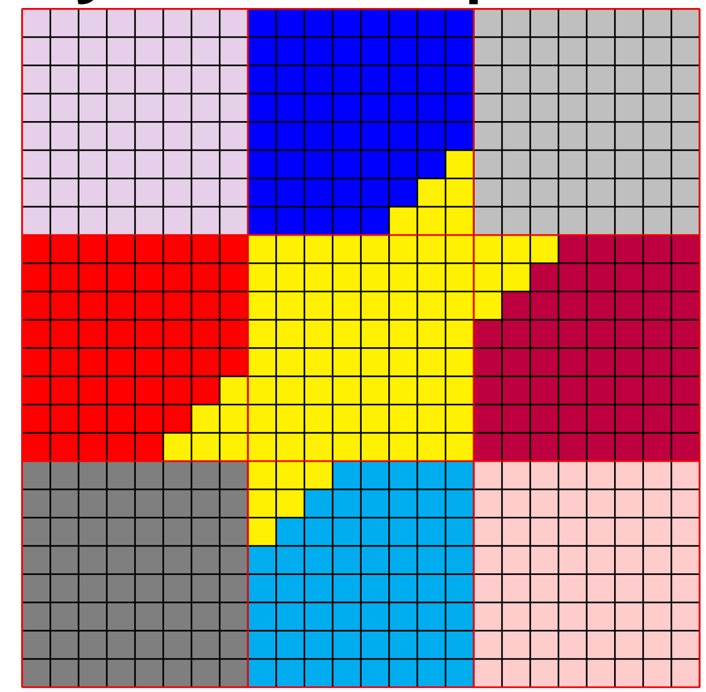
$\mathcal{X}$

Blowup complex

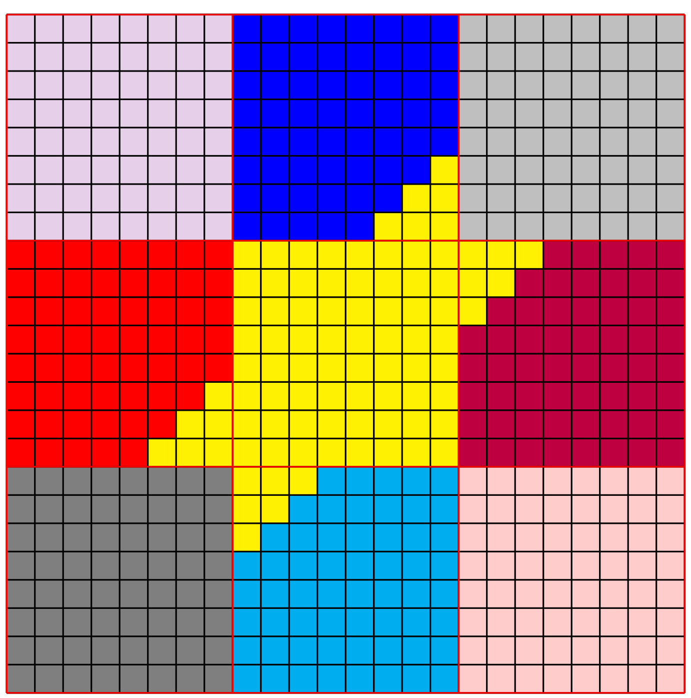


$\mathcal{X}_b$

Janus complex



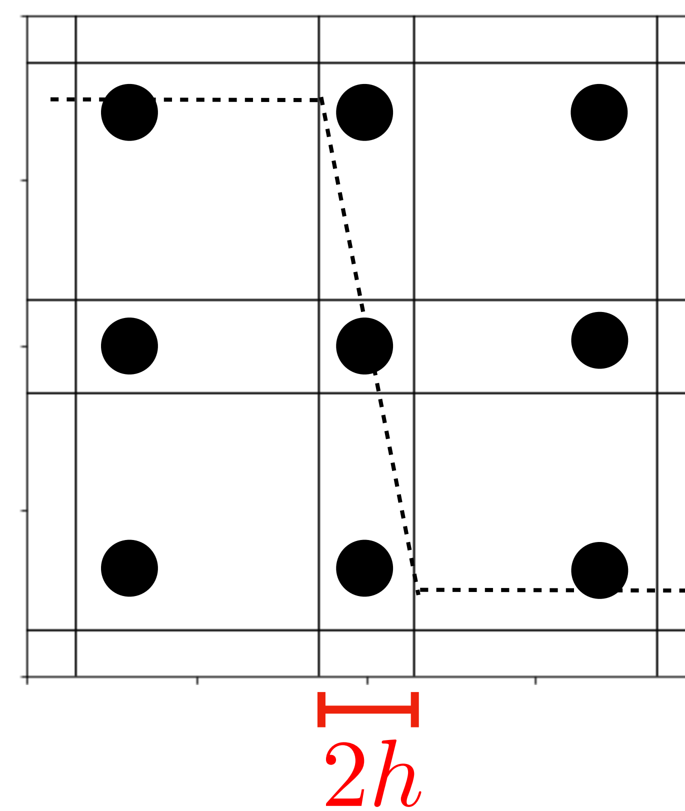
$\mathcal{Y}$



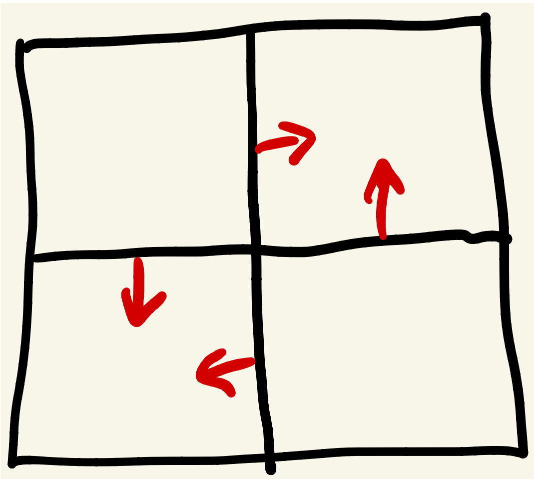
Local modifications

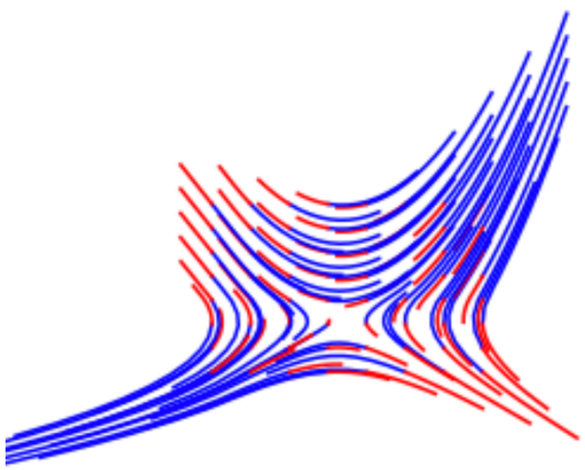
Chain homotopy

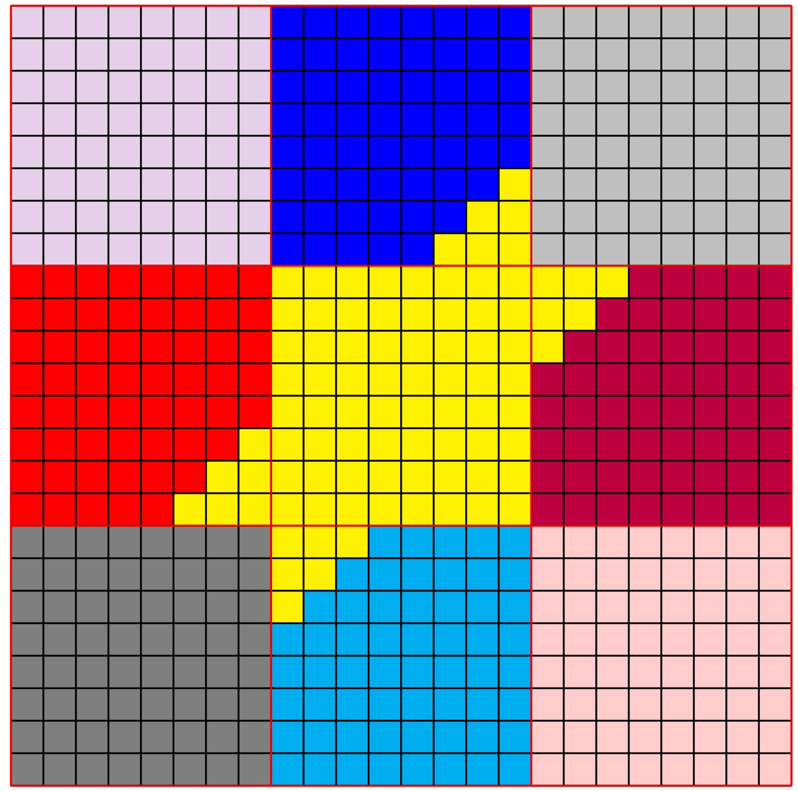
Transversality: geometric realization of the modified complex

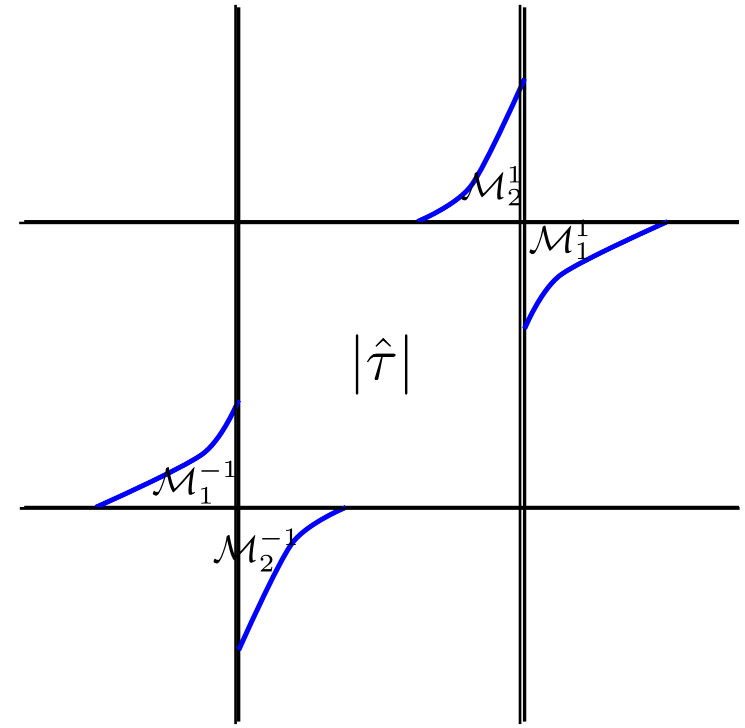


Ramp systems



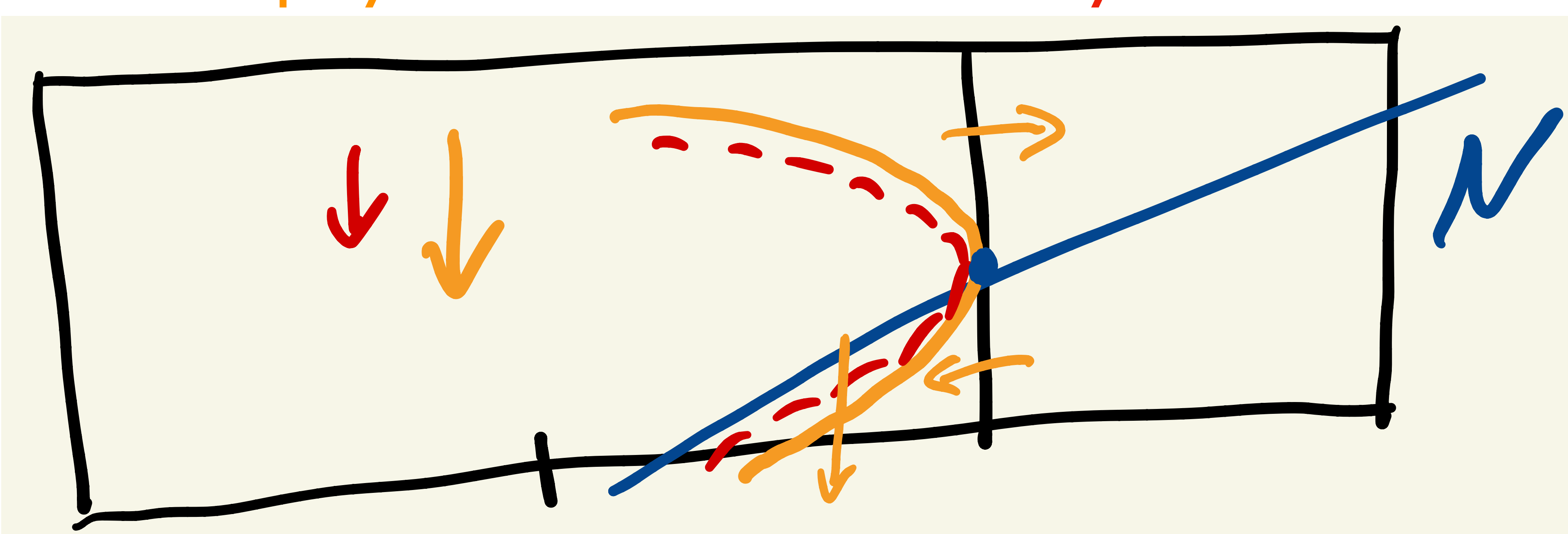


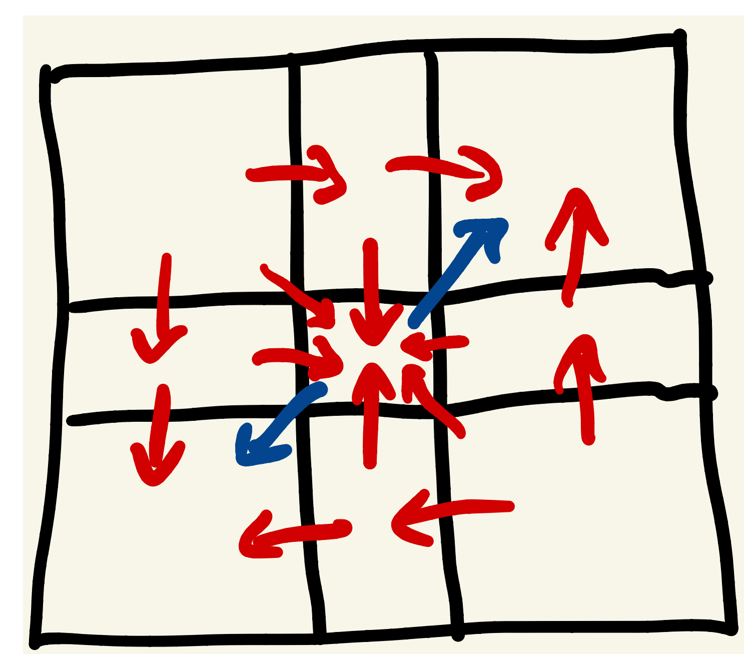




Geometric realization

Ramp system Perturbed system





Ramp systems

Dynamics identified by $\mathcal{F}_0$, $\mathcal{F}_1$, and $\mathcal{F}_2$ is valid for N-dim ODEs

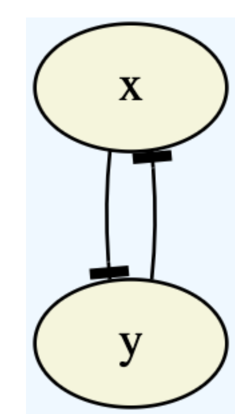
Dynamics identified by $\mathcal{F}_3$ is valid for 2 and 3-dim ODEs

Dynamics valid for every parameter value in DSGRN parameter region

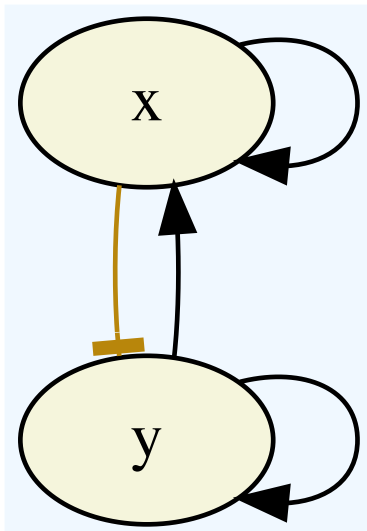
Valid for ramp systems with h less than explicit upper bound

For the toggle switch

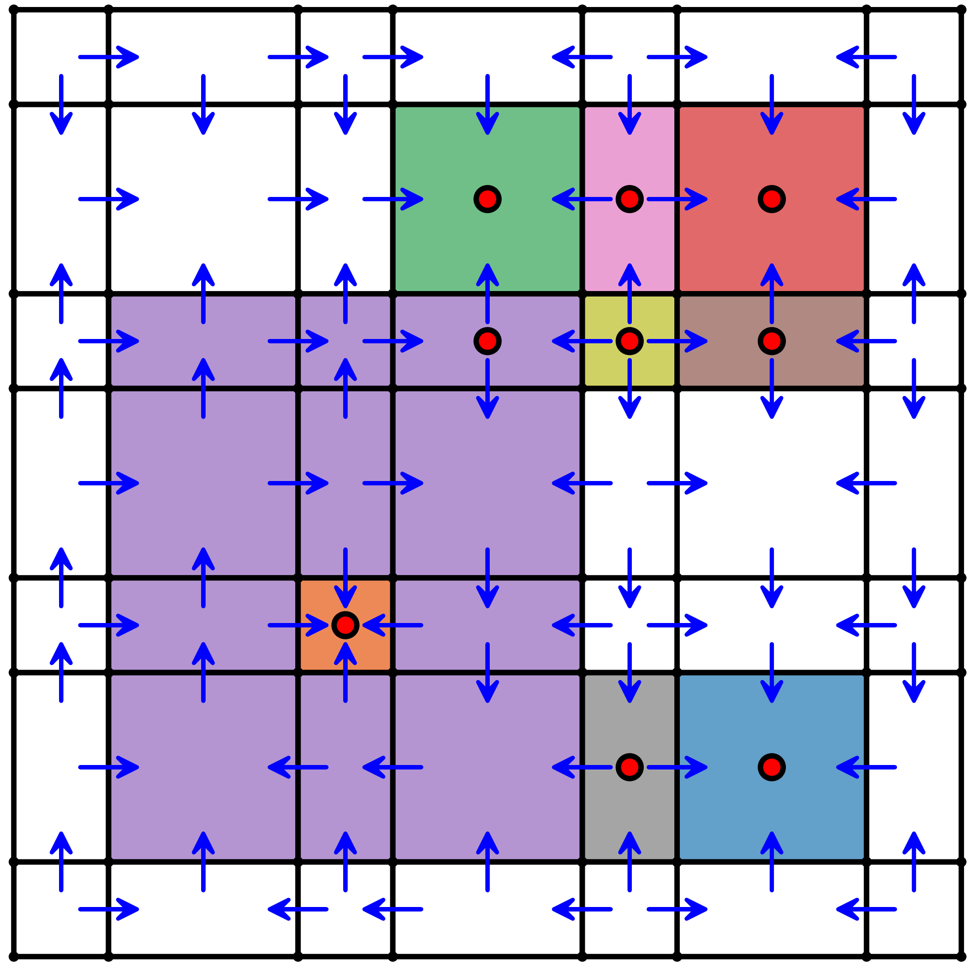
$$h < \min\{|\ell - \theta|, |\ell + \delta - \theta|\}/\gamma$$



Example



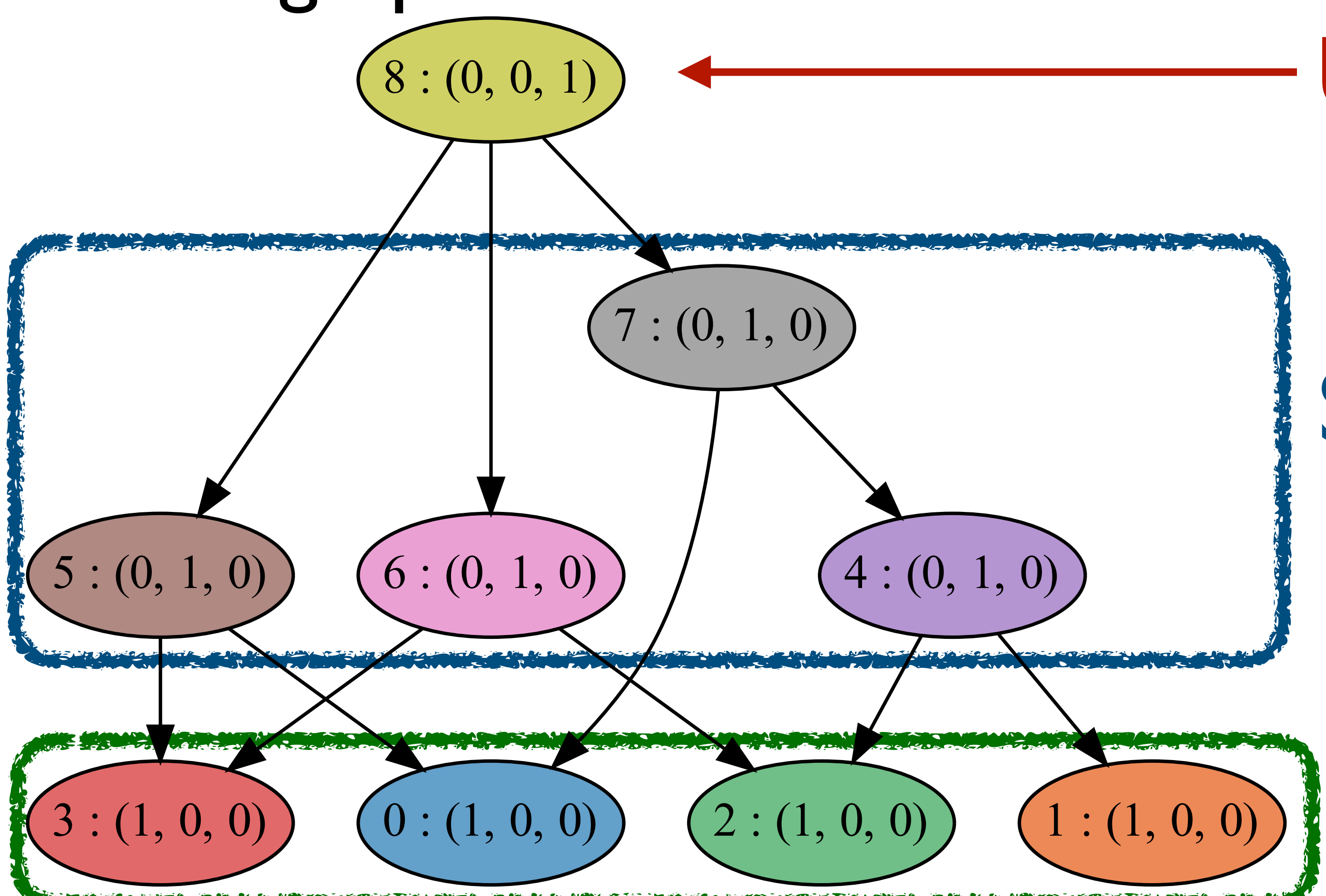
Network



Combinatorial representation of dynamics for one parameter region

$\mathcal{F}_3$

Morse graph



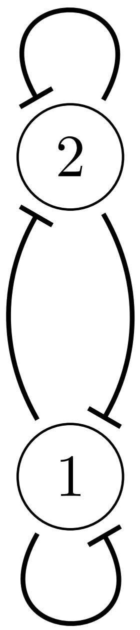
Unstable, fixed point

Saddle like, fixed points

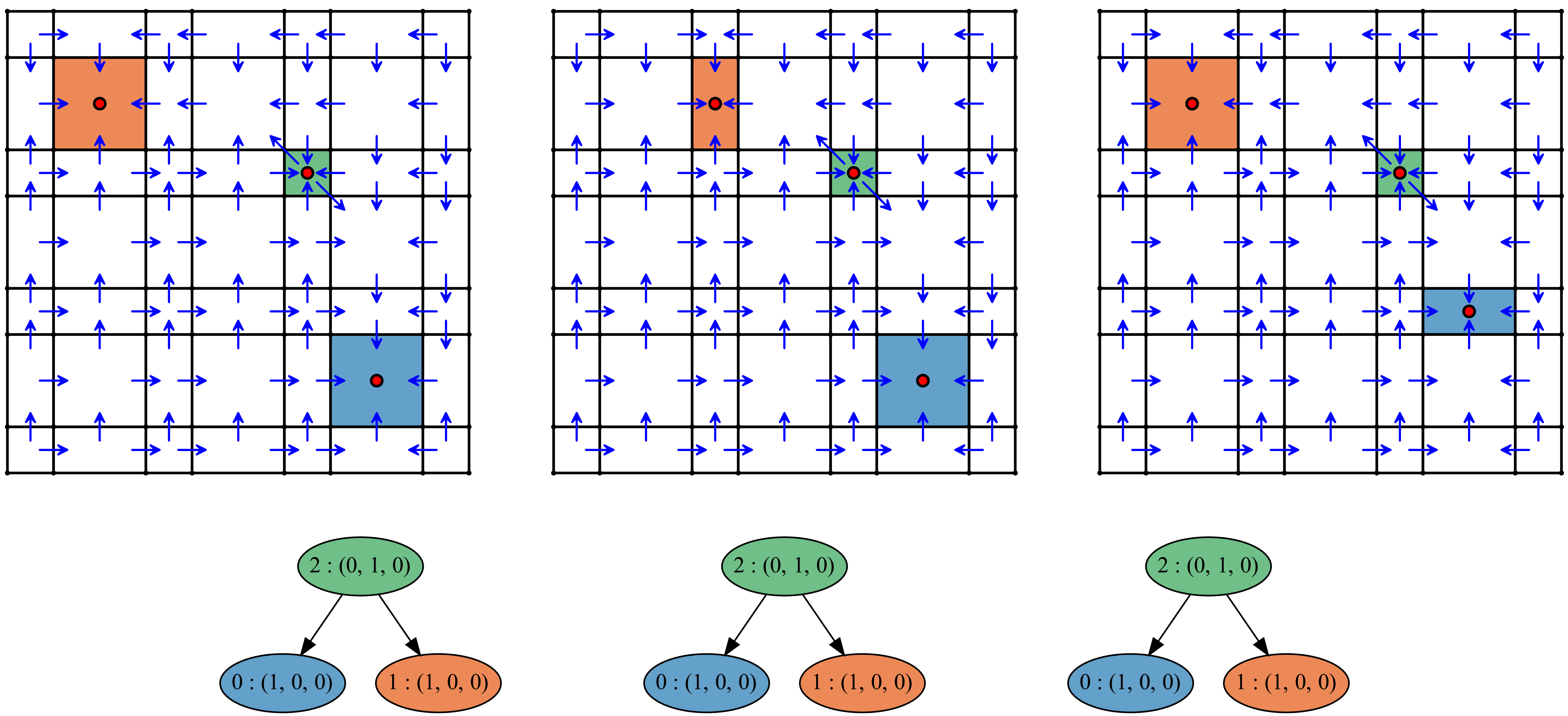
Stable, fixed points

Theorems

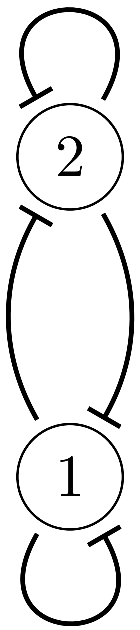
Example



Parameter node 974	$x_1 : p_0, p_1 < \gamma_1\theta_{1,1} < \gamma_1\theta_{2,1} < p_2, p_3$ $x_2 : p_0, p_2 < \gamma_2\theta_{2,2} < \gamma_2\theta_{2,1} < p_1, p_3$
Parameter node 975	$x_1 : p_0 < \gamma_1\theta_{1,1} < p_1 < \gamma_1\theta_{2,1} < p_2, p_3$ $x_2 : p_0, p_2 < \gamma_2\theta_{2,2} < \gamma_2\theta_{2,1} < p_1, p_3$
Parameter node 1054	$x_1 : p_0, p_1 < \gamma_1\theta_{1,1} < \gamma_1\theta_{2,1} < p_2, p_3$ $x_2 : p_0 < \gamma_2\theta_{2,2} < p_2 < \gamma_2\theta_{2,1} < p_1, p_3$

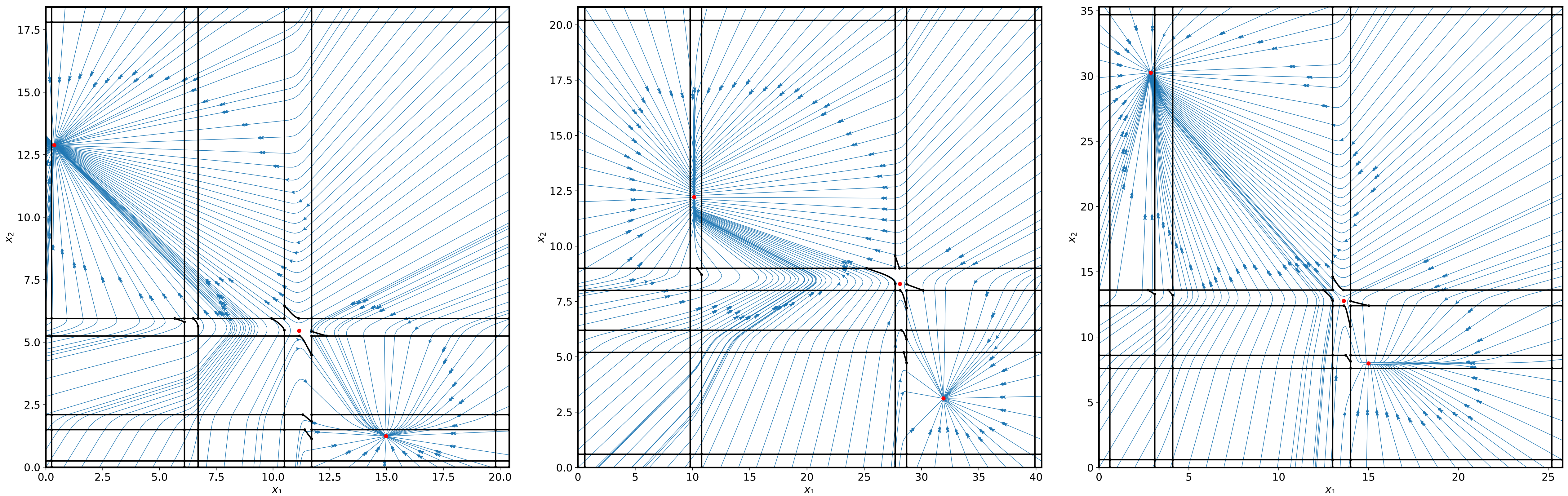


Example

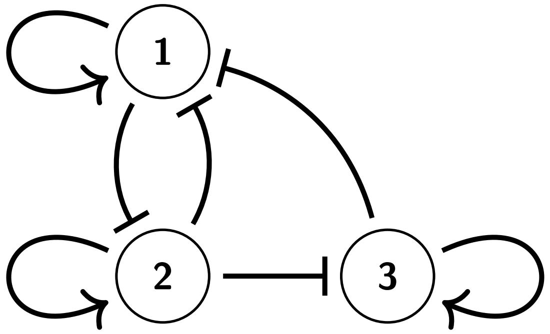


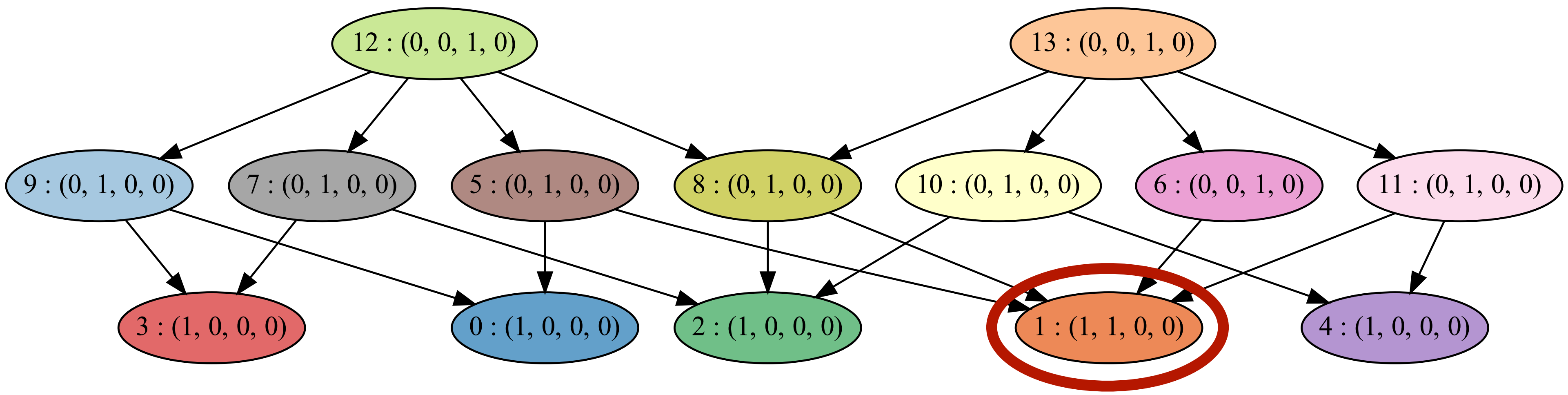
Parameter set 1	Parameter set 2	Parameter set 3
$\nu_{1,1,1} = 3.7,\ \nu_{1,1,2} = 1.4$	$\nu_{1,1,1} = 6.5,\ \nu_{1,1,2} = 4.2$	$\nu_{1,1,1} = 7.2,\ \nu_{1,1,2} = 5$
$\nu_{1,2,1} = 10.7,\ \nu_{1,2,2} = 0.1$	$\nu_{1,2,1} = 7.6,\ \nu_{1,2,2} = 1.7$	$\nu_{1,2,1} = 3,\ \nu_{1,2,2} = 0.4$
$\nu_{2,1,1} = 9.2,\ \nu_{2,1,2} = 0.2$	$\nu_{2,1,1} = 4.7,\ \nu_{2,1,2} = 0.6$	$\nu_{2,1,1} = 5.5,\ \nu_{2,1,2} = 1$
$\nu_{2,2,1} = 6.2,\ \nu_{2,2,2} = 1.4$	$\nu_{2,2,1} = 5.2,\ \nu_{2,2,2} = 2.6$	$\nu_{2,2,1} = 9,\ \nu_{2,2,2} = 5.5$
$\theta_{1,1} = 6.4,\ \theta_{1,2} = 5.6$	$\theta_{1,1} = 10.3,\ \theta_{1,2} = 8.5$	$\theta_{1,1} = 3.6,\ \theta_{1,2} = 13$
$\theta_{2,1} = 11.1,\ \theta_{2,2} = 1.8$	$\theta_{2,1} = 28.2,\ \theta_{2,2} = 5.7$	$\theta_{2,1} = 13.5,\ \theta_{2,2} = 8.1$
$h_{1,1} = 0.3,\ h_{1,2} = 0.35$	$h_{1,1} = 0.5,\ h_{1,2} = 0.5$	$h_{1,1} = 0.5,\ h_{1,2} = 0.6$
$h_{2,1} = 0.6,\ h_{2,2} = 0.3$	$h_{2,1} = 0.5,\ h_{2,2} = 0.5$	$h_{2,1} = 0.5,\ h_{2,2} = 0.5$
$\gamma_1 = 1,\ \gamma_2 = 1$	$\gamma_1 = 1,\ \gamma_2 = 1$	$\gamma_1 = 1,\ \gamma_2 = 1$

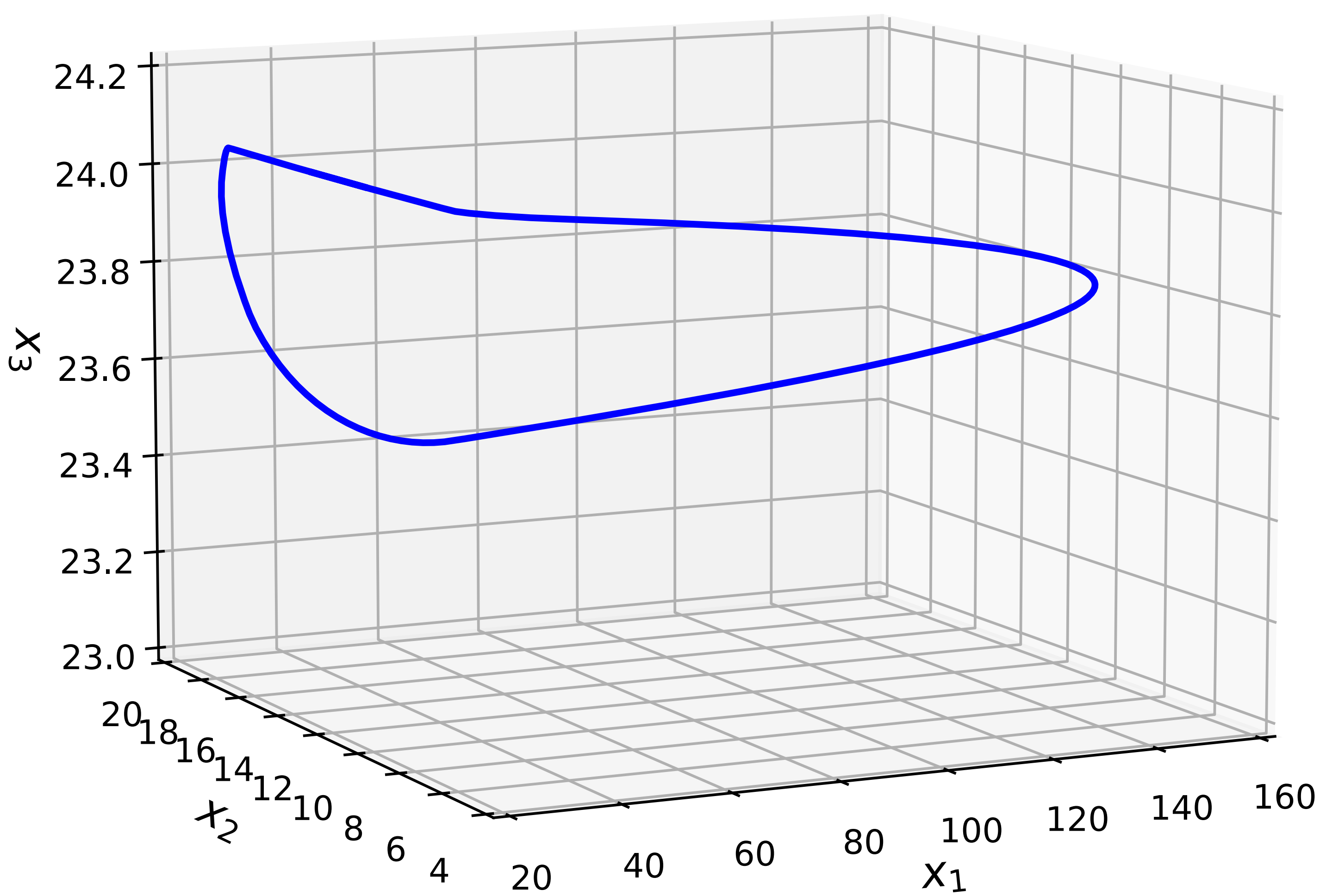
Ramp system



Example







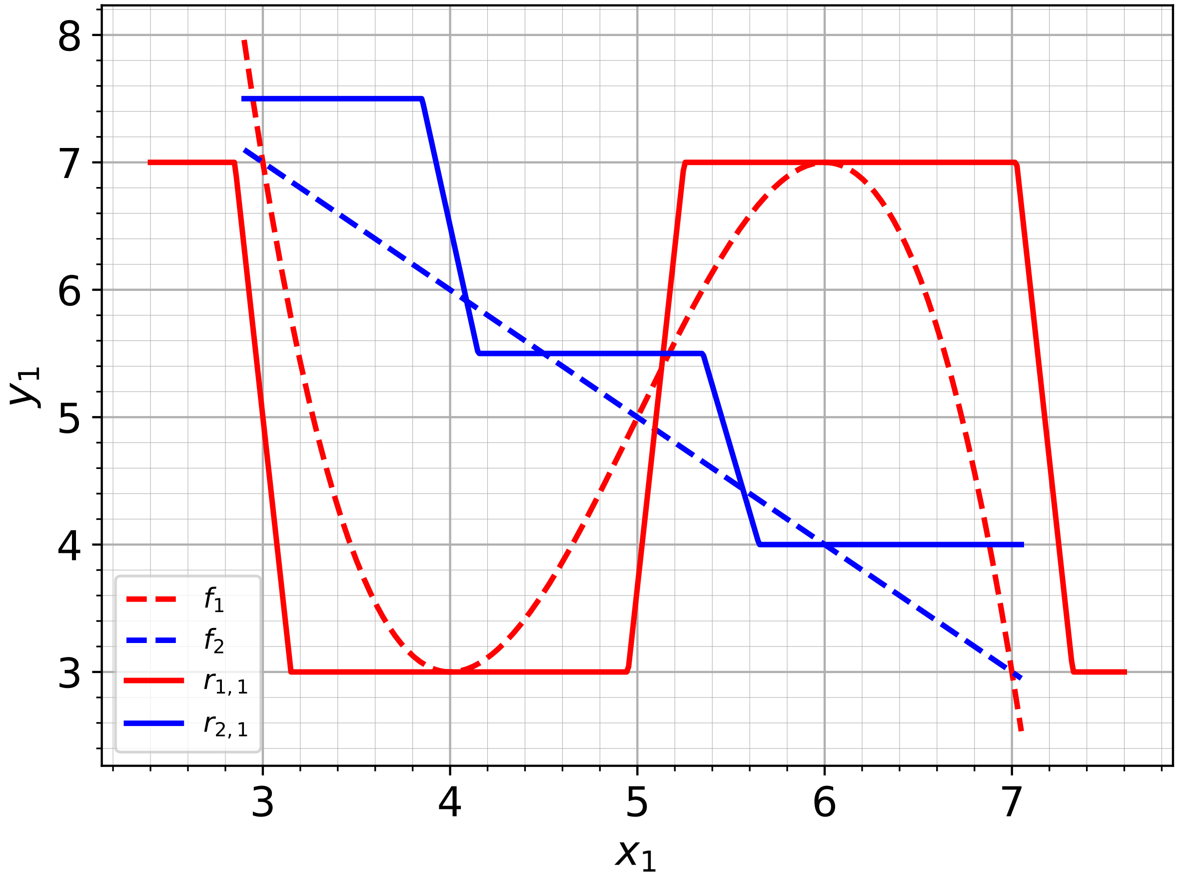
Indicates existence of a periodic orbit

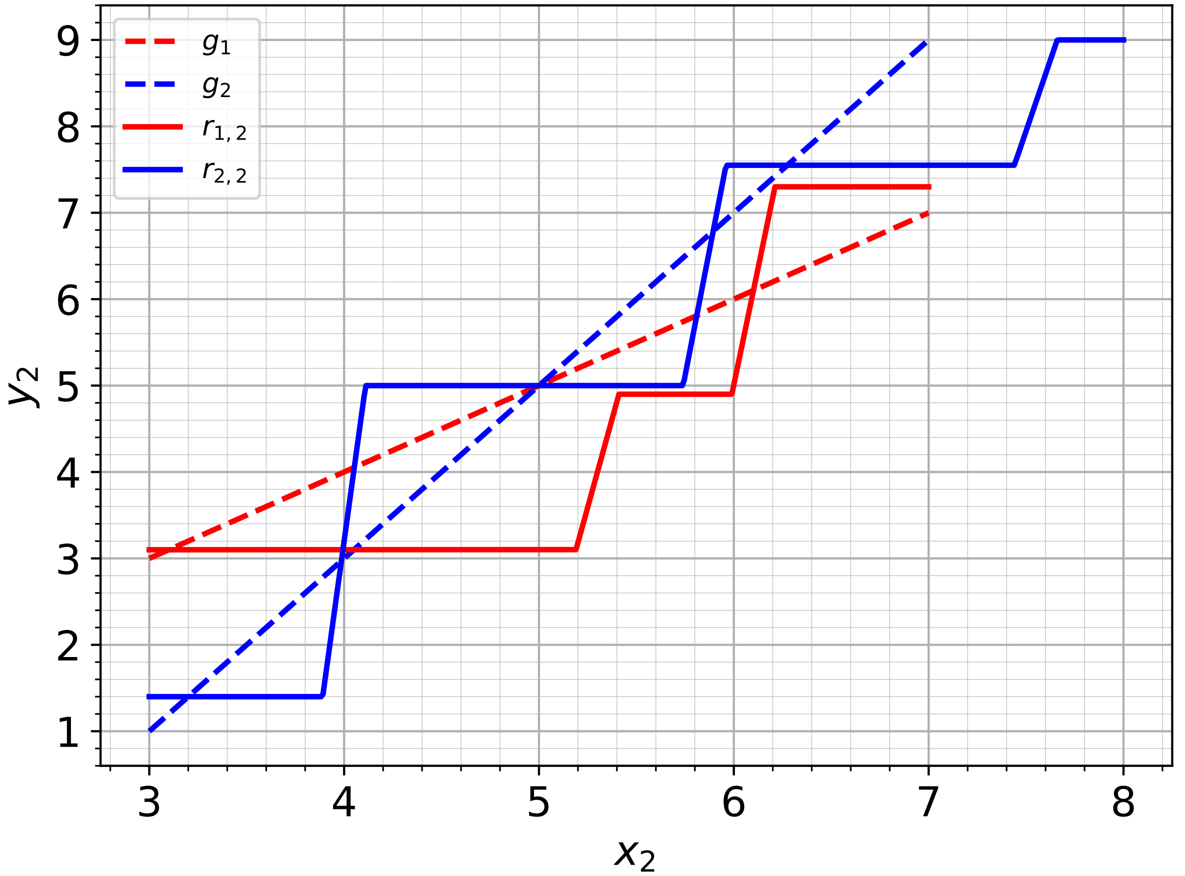
Example

$$\dot{x_1} = -\gamma_1 x_1 + r_{1,1}(x_1) + r_{1,2}(x_2)$$
$$\dot{x_2} = -\gamma_2 x_2 + r_{2,1}(x_1) + r_{2,2}(x_2)$$

Ramp system

$\nu_{1,1} = (7,3,7,3)$	$\theta_{1,1} = (3,5.1,7.17)$	$h_{1,1} = (0.15,0.15,0.15)$
$\nu_{1,2} = (3.1,4.9,7.3)$	$\theta_{1,2} = (5.3,6.1)$	$h_{1,2} = (0.11,0.11)$
$\nu_{2,1} = (7.5,5.5,4)$	$\theta_{2,1} = (4,5.5)$	$h_{2,1} = (0.15,0.15)$
$\nu_{2,2} = (1.4,5,7.55,9)$	$\theta_{2,2} = (4,5.85,7.55)$	$h_{2,2} = (0.11,0.11,0.11)$
$\gamma_1 = \gamma_2 = 2$		

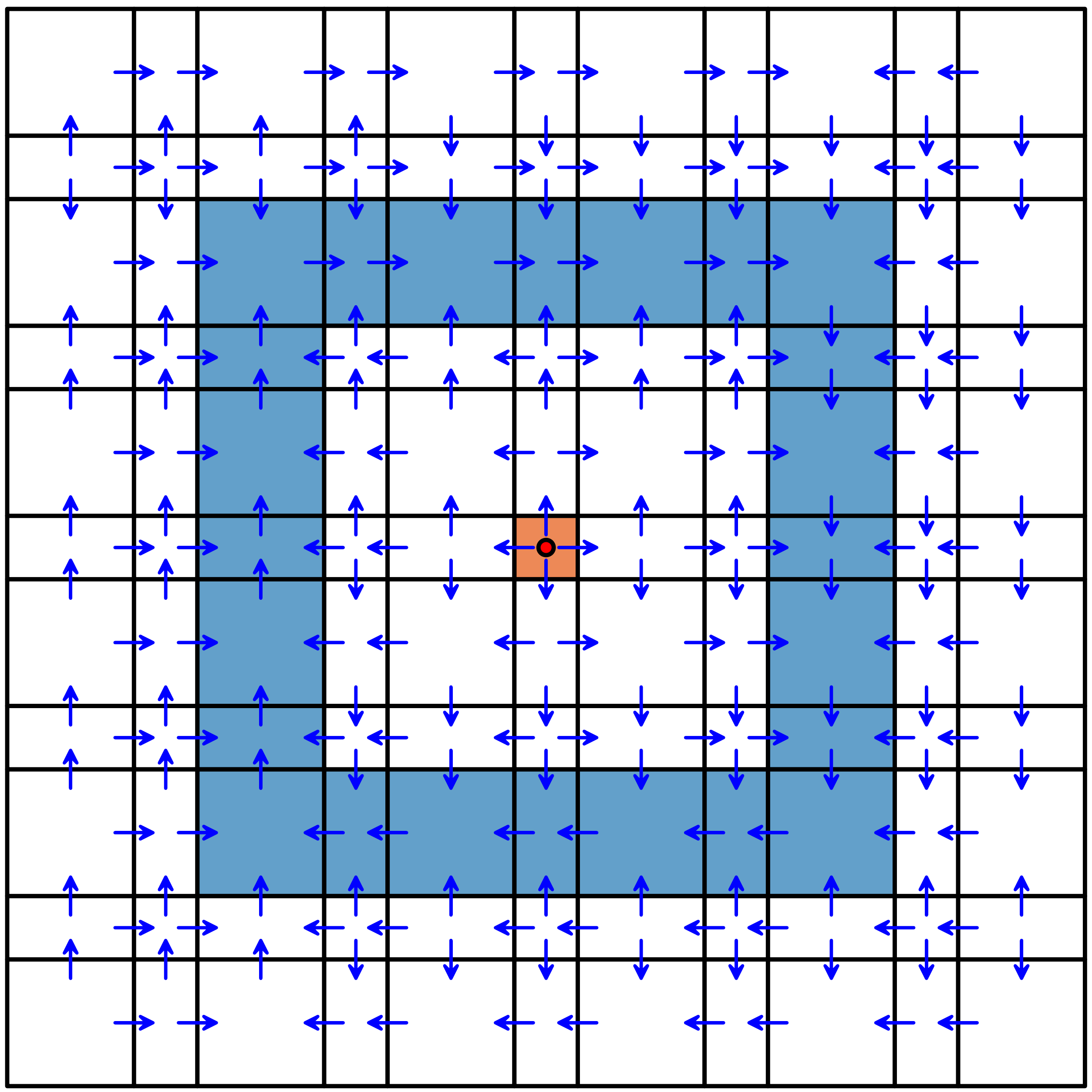


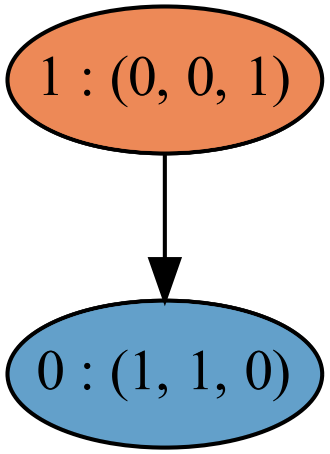


Example

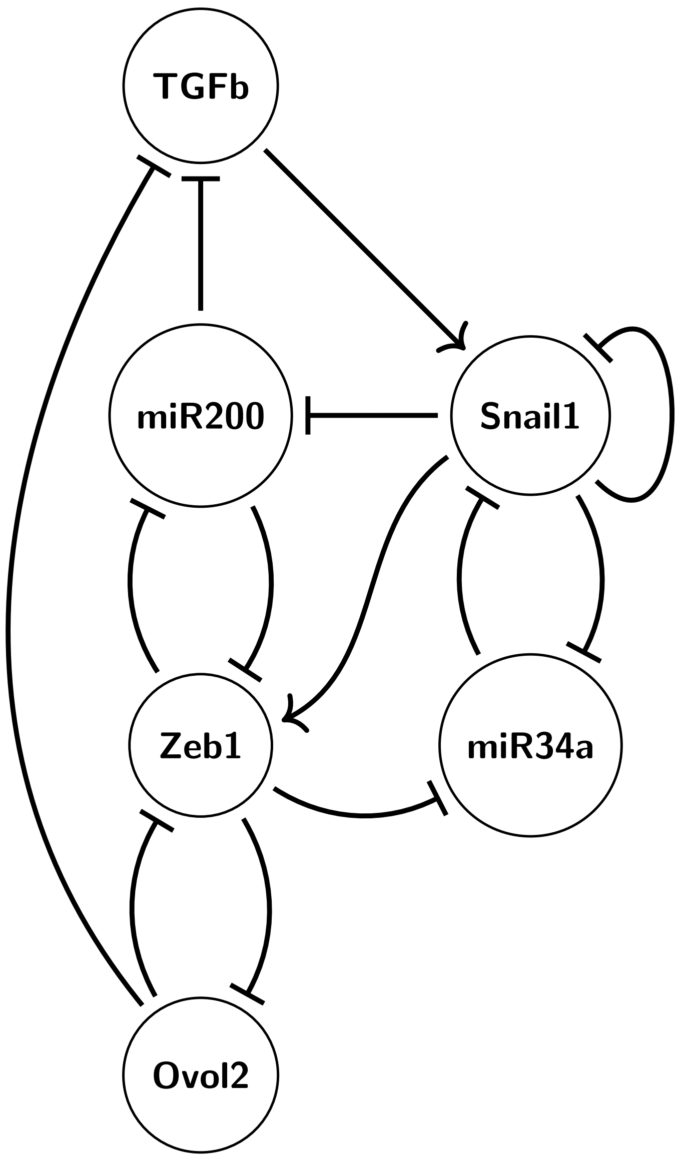
$$\dot{x_1} = -\gamma_1 x_1 + r_{1,1}(x_1) + r_{1,2}(x_2)$$
$$\dot{x_2} = -\gamma_2 x_2 + r_{2,1}(x_1) + r_{2,2}(x_2)$$

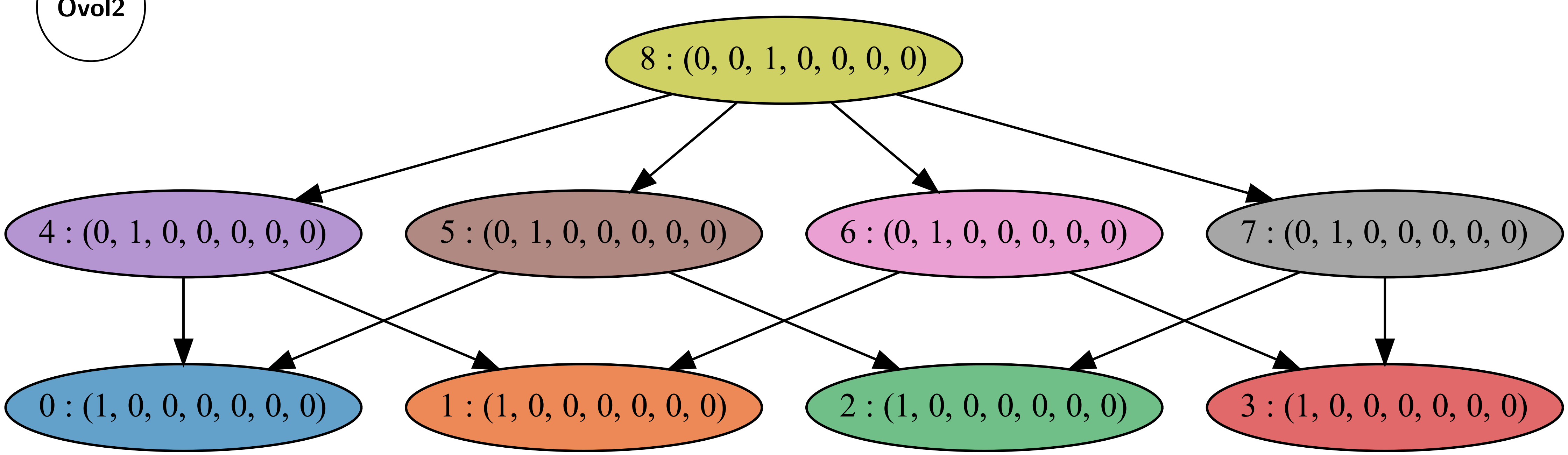
Ramp system





6D Example


TGFb
miR200
Snail1
Zeb1
miR34a
Ovol2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4 : (0, 1, 0, 0, 0, 0, 0)
5 : (0, 1, 0, 0, 0, 0, 0)
6 : (0, 1, 0, 0, 0, 0, 0)
7 : (0, 1, 0, 0, 0, 0, 0)
0 : (1, 0, 0, 0, 0, 0, 0)
1 : (1, 0, 0, 0, 0, 0, 0)
2 : (1, 0, 0, 0, 0, 0, 0)
3 : (1, 0, 0, 0, 0, 0, 0)

More Examples

Jupyter Notebooks:

https://github.com/marciogameiro/CTD_Tutorial_CRM

Thank you for your attention!

Rutgers:

- K. Mischaikow
- B. Rivas
- E. Vieira
- D. Gameiro

Toledo:

- W. Kalies

Montana State:

- T. Gedeon
- B. Cummins
- W. Duncan

Kyoto:

- H. Kokubu
- H. Oka

DSGRN software

https://github.com/marciogameiro/DSGRN

https://github.com/marciogameiro/PyCHomP2