

# **Combinatorial topological framework for nonlinear dynamics**

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# Lectures

Combinatorial topological framework - Theory

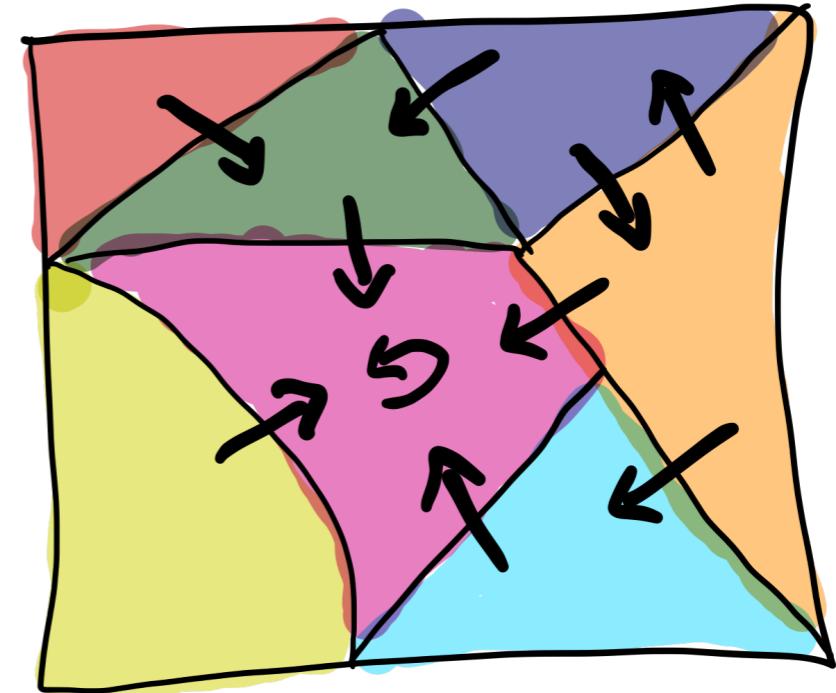
Combinatorial topological framework - ODEs

Combinatorial topological framework - Maps

Combinatorial topological framework - Data

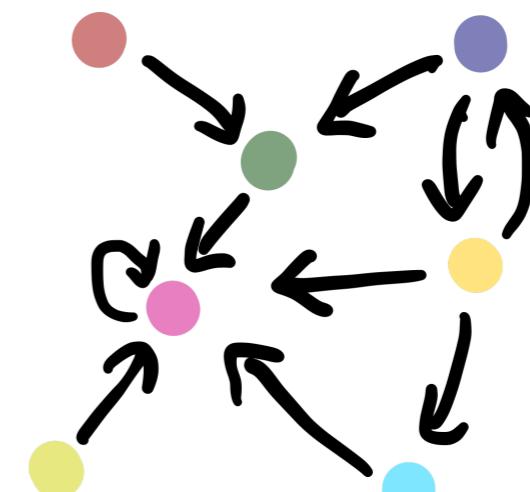
# Main Steps

Discretization of the domain and combinatorial representation of dynamics



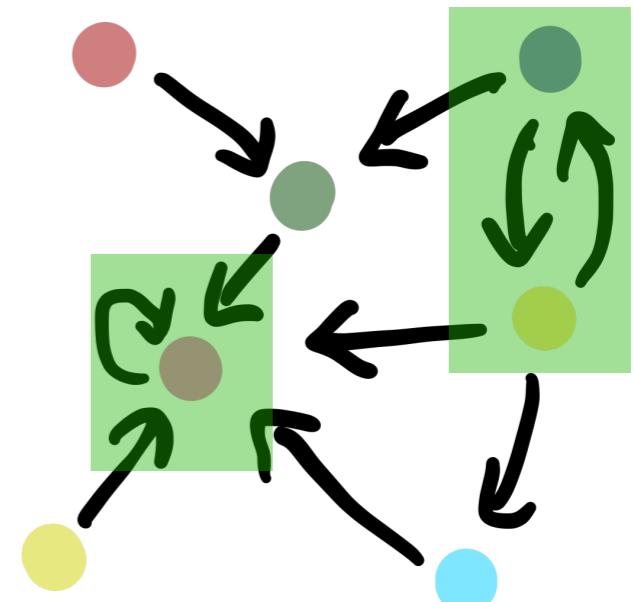
**Transversality model:** No arrow if flow is transverse in opposite direction

Combinatorial multivalued map  
(directed graph)  $\mathcal{F}: \mathcal{X} \rightrightarrows \mathcal{X}$   
(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 characterize the family of dynamical systems compatible with it

# Main Steps

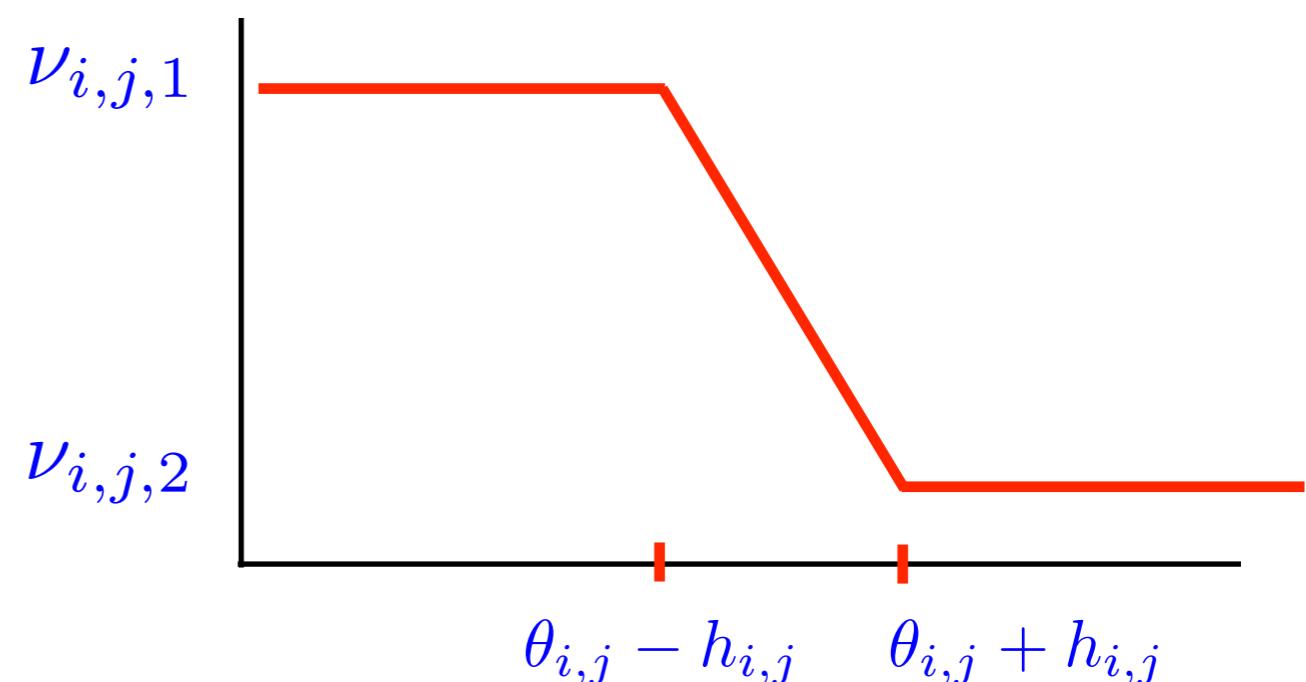
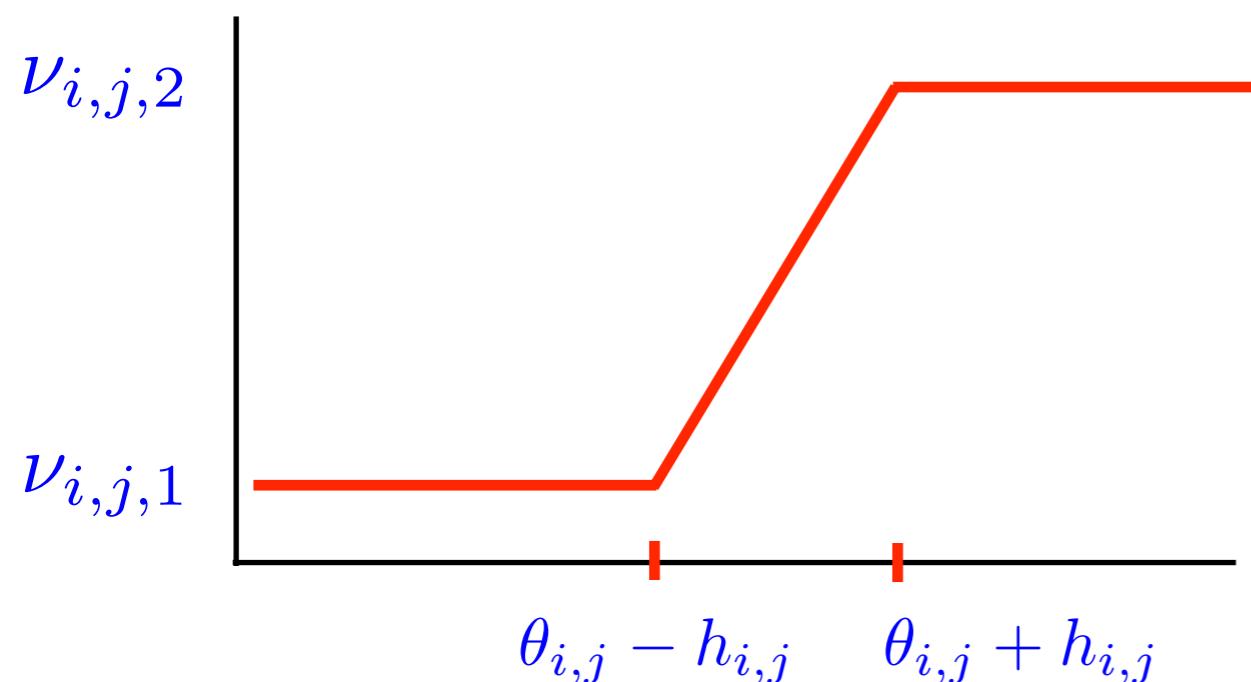
$$\dot{x}_1 = -\gamma_1 x_1 + r_{1,1}(x_1)r_{1,2}(x_2)$$

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

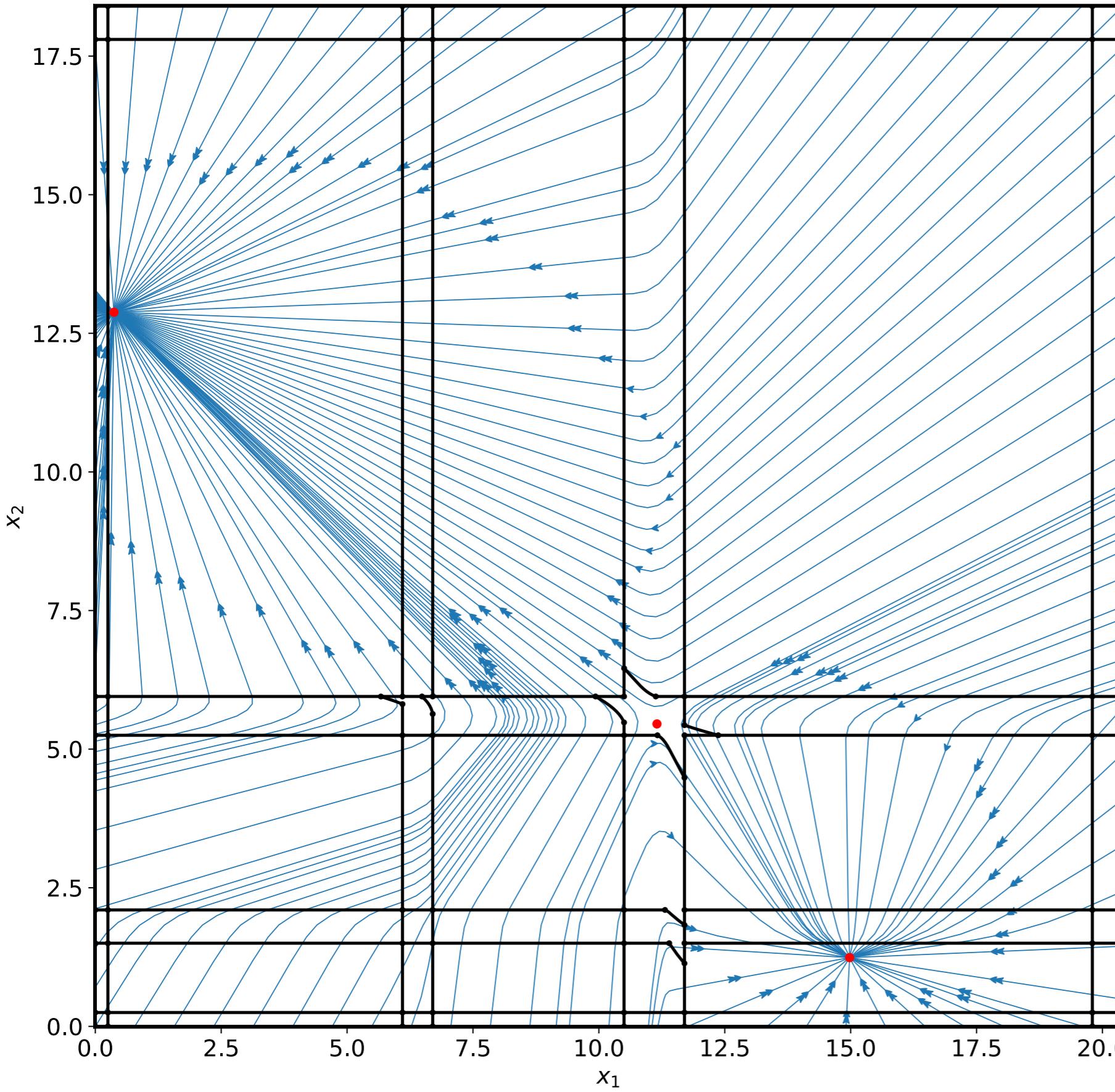
Ramp system

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

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



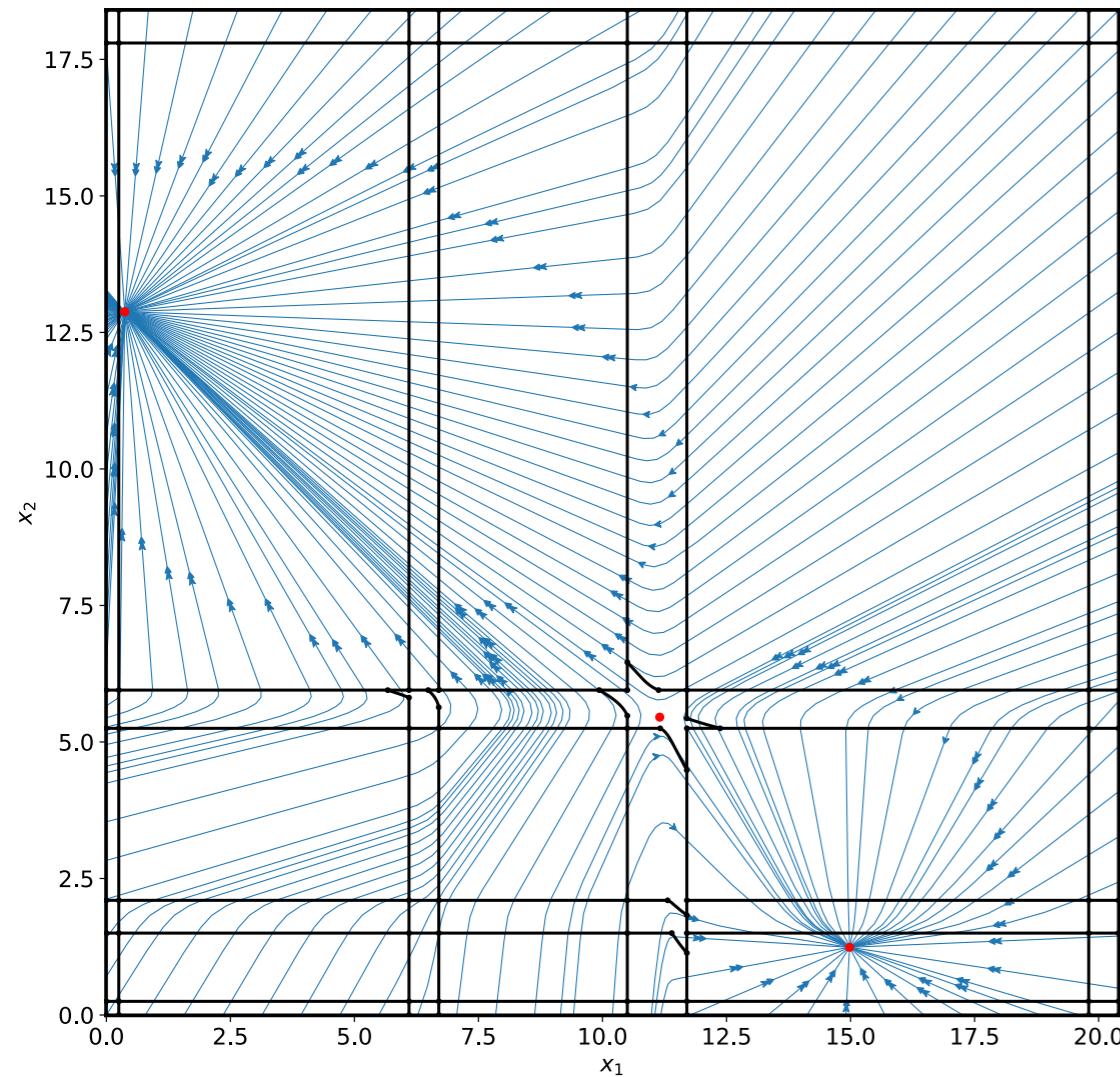
# Main Steps



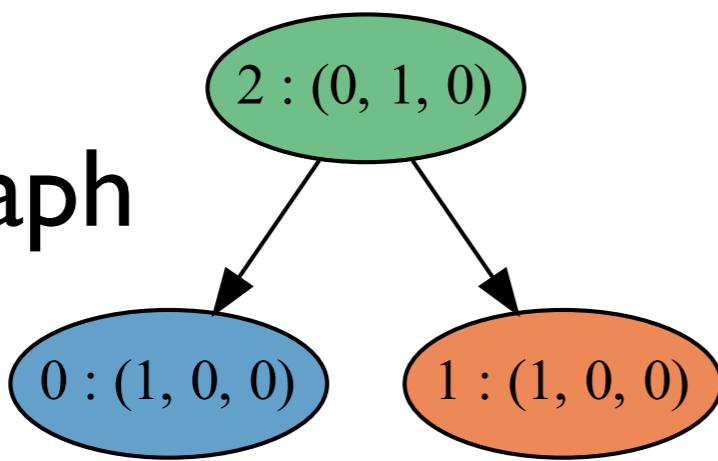
Phase space

Can define  $\mathcal{F}$

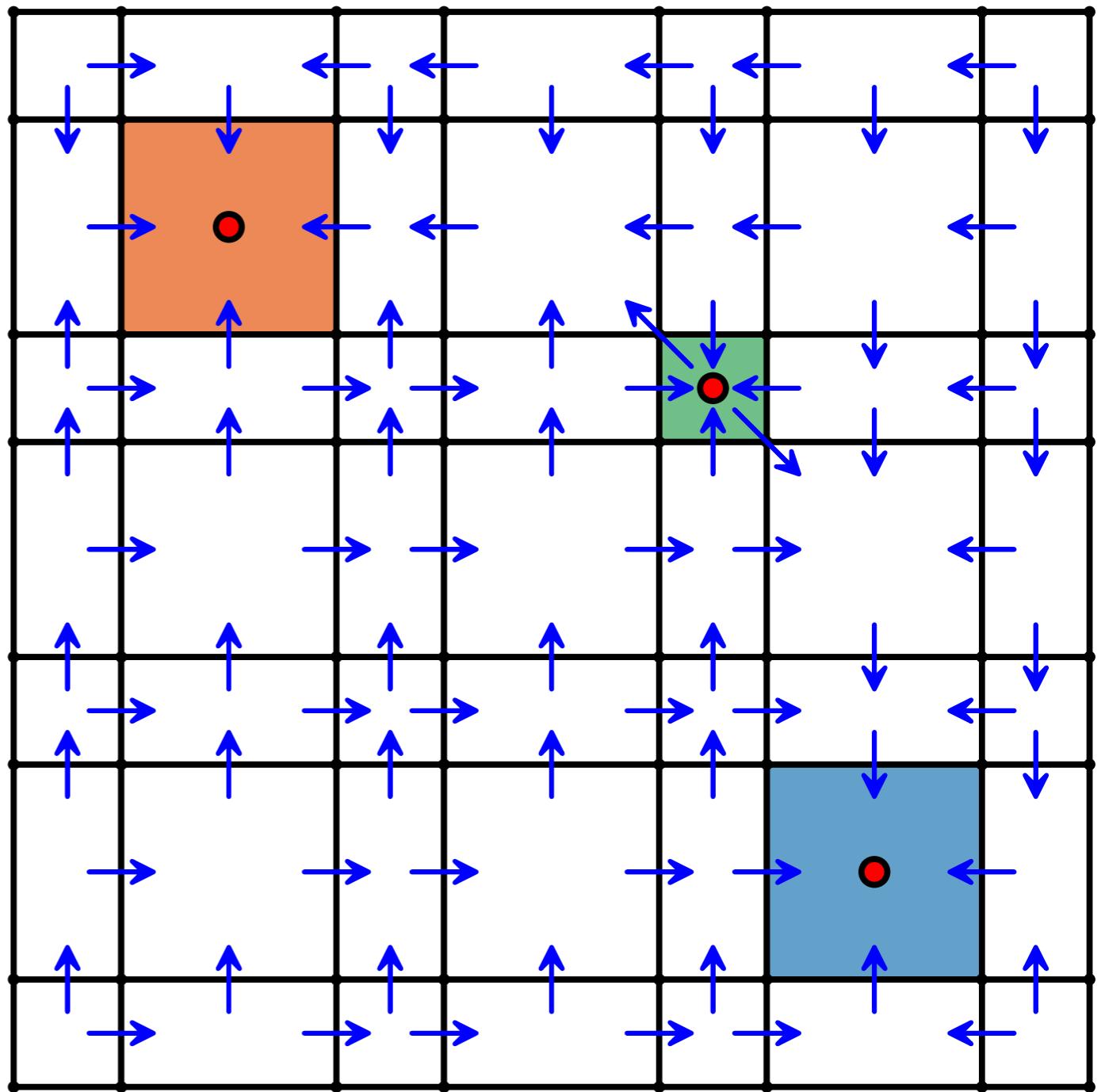
# Main Steps



Morse graph

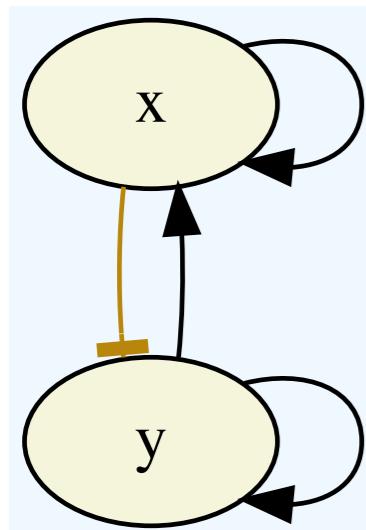


Abstract representation of  $\mathcal{F}$



# 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

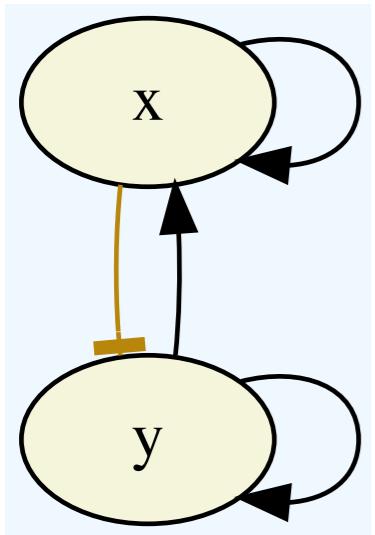
The nodes indicate the variables and the edges indicate coupling (interactions)

$i \rightarrow n$  Activating

$i \rightarrow n$  Repressing

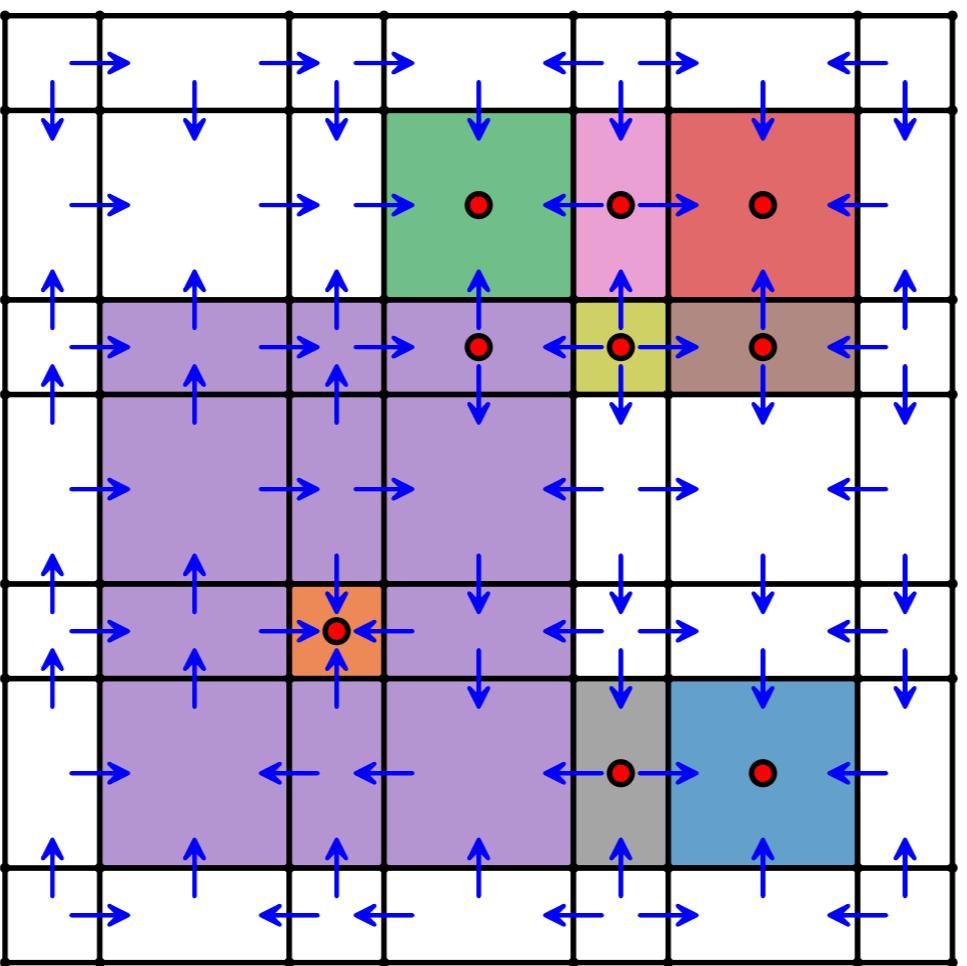
Start with a discretization and try to characterize the family of dynamical systems compatible with it

## Example

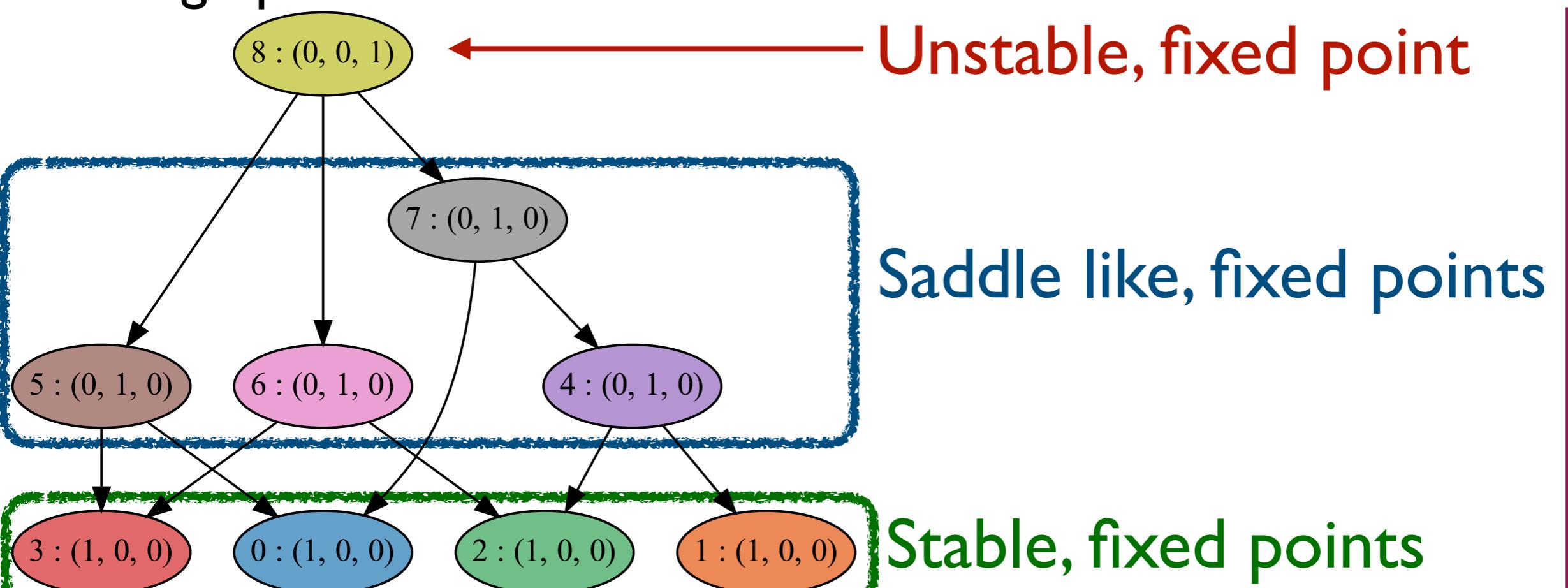


Network

Morse graph

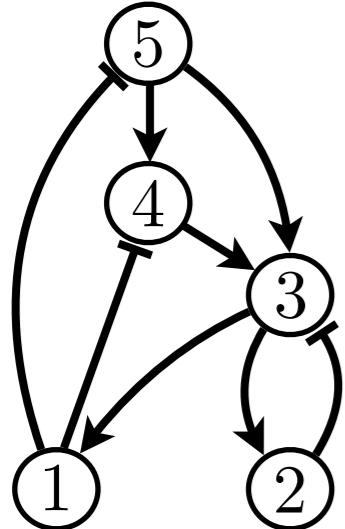


Combinatorial representation of dynamics for one parameter region



Theorems

# Dynamics of Networks

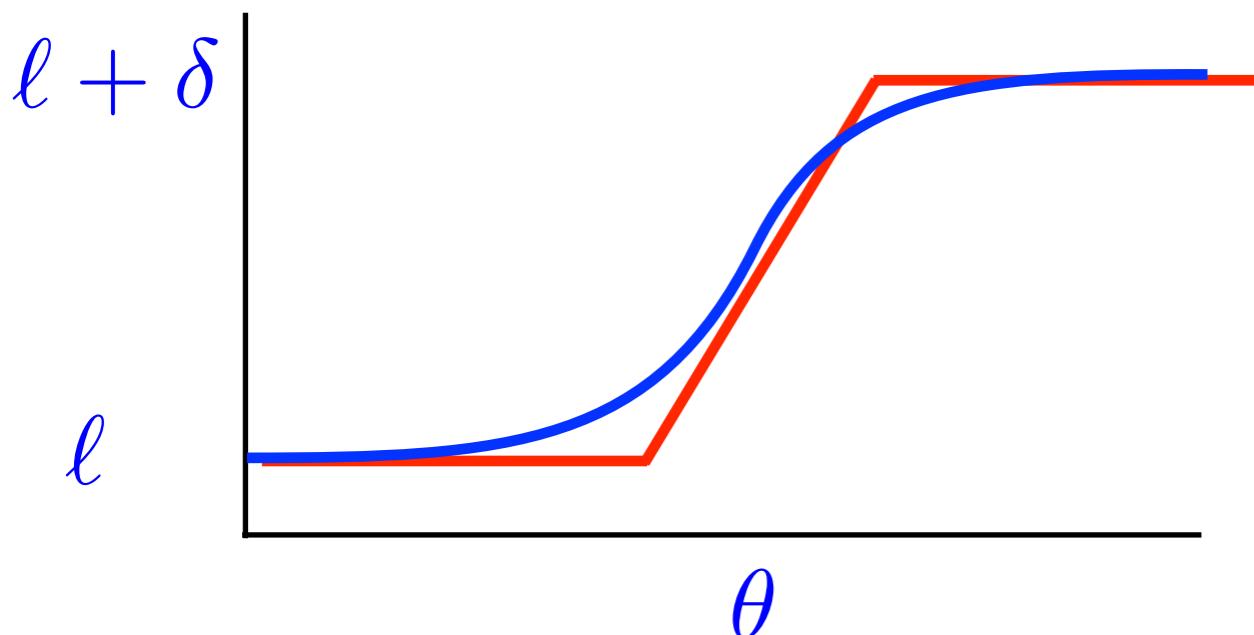


ODE model with unknown nonlinearities  
and parameters

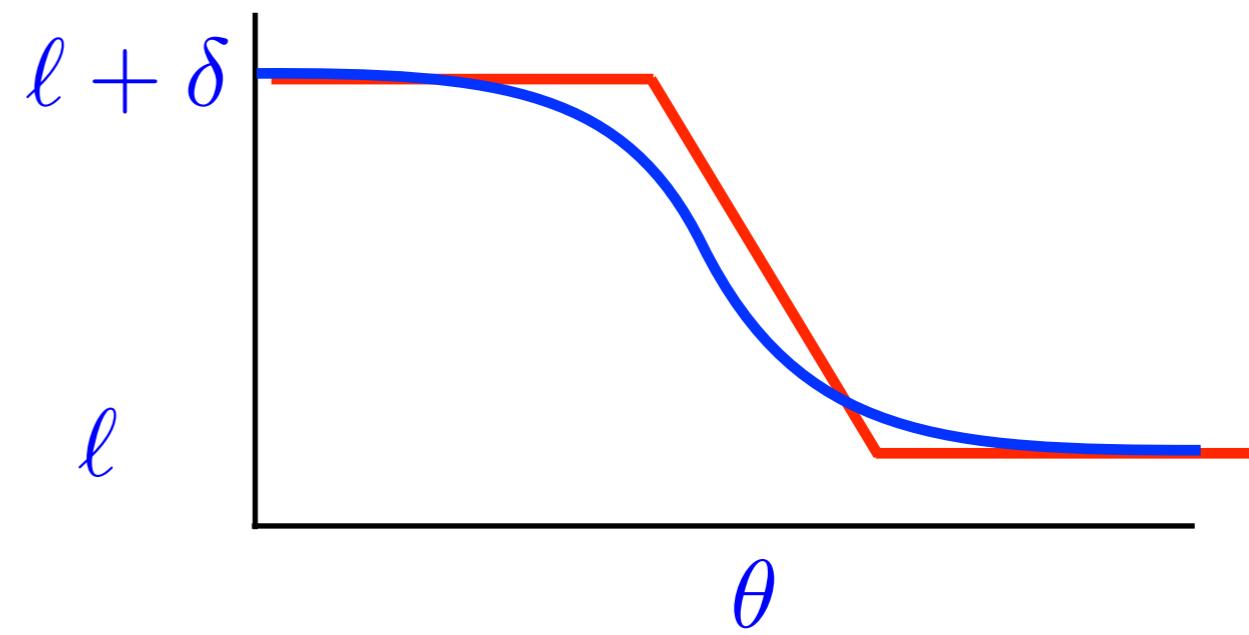
$i \rightarrow n$  Positive edge (activating, excitatory)

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

$i \rightarrow n$  Activating sigmoidal



$i \rightarrow n$  Repressing



Products or sums  
of sigmoidal

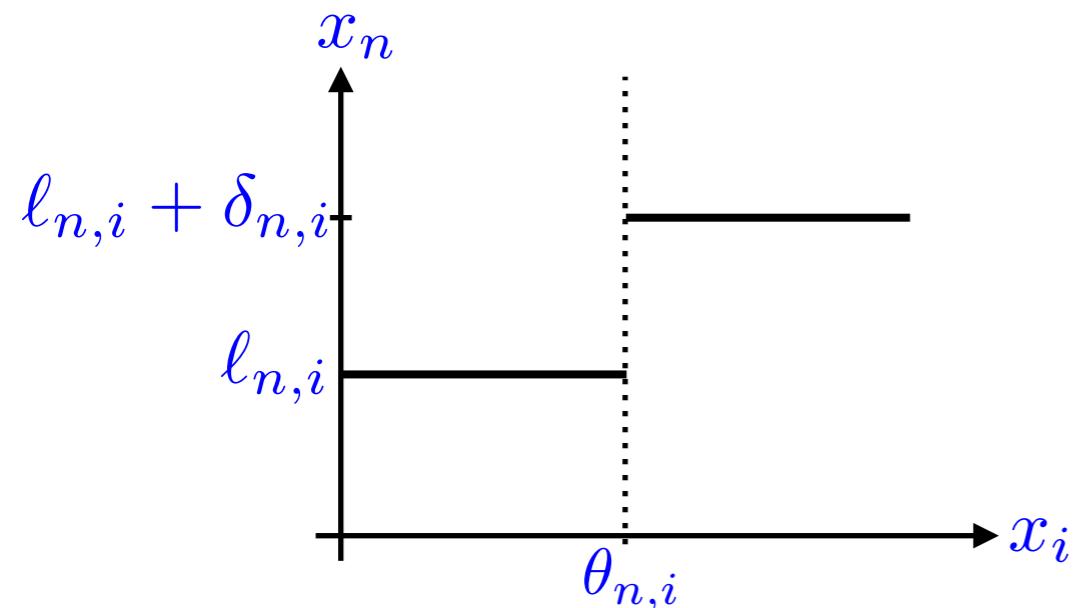
$$\dot{x}_n = -\gamma_n x_n + E_n(x)$$

# Dynamic Signatures Generated by Regulatory Networks (DSGRN)

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

$$i \rightarrow n$$

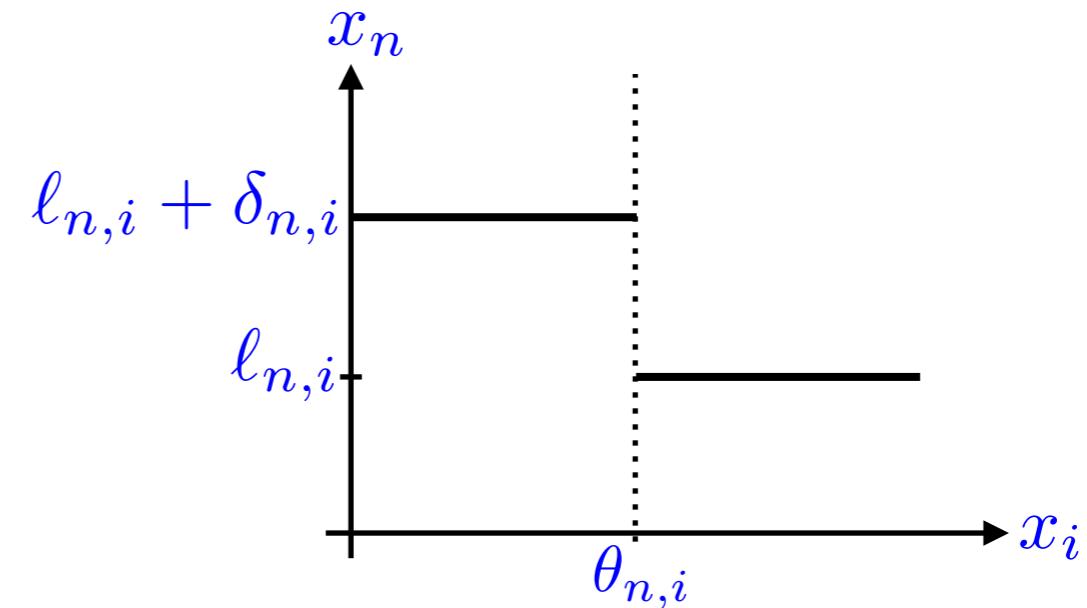
An increase in  $x_i$  increases the rate of production of  $x_n$



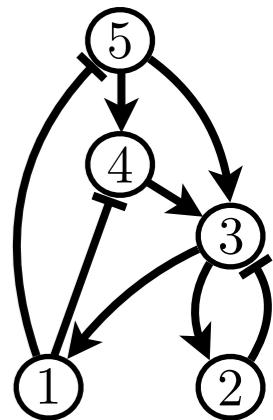
$$\sigma_{n,i}^+(x_i) = \begin{cases} l_{n,i}, & \text{if } x_i < \theta_{n,i} \\ l_{n,i} + \delta_{n,i}, & \text{if } x_i > \theta_{n,i} \end{cases}$$

$$i \rightarrow n$$

An increase in  $x_i$  decreases the rate of production of  $x_n$



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



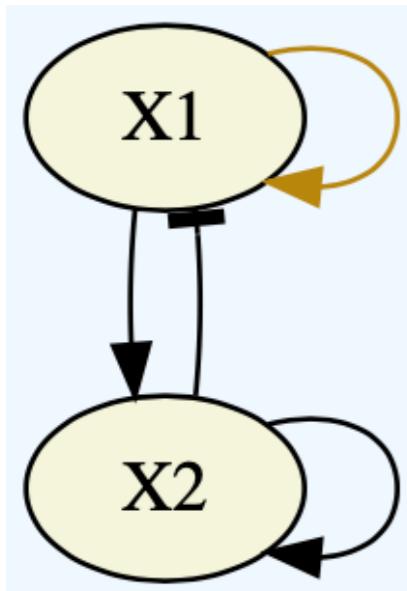
# DSGRN

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  $\sigma_{n,i}^\pm(x_i)$

**Example:**



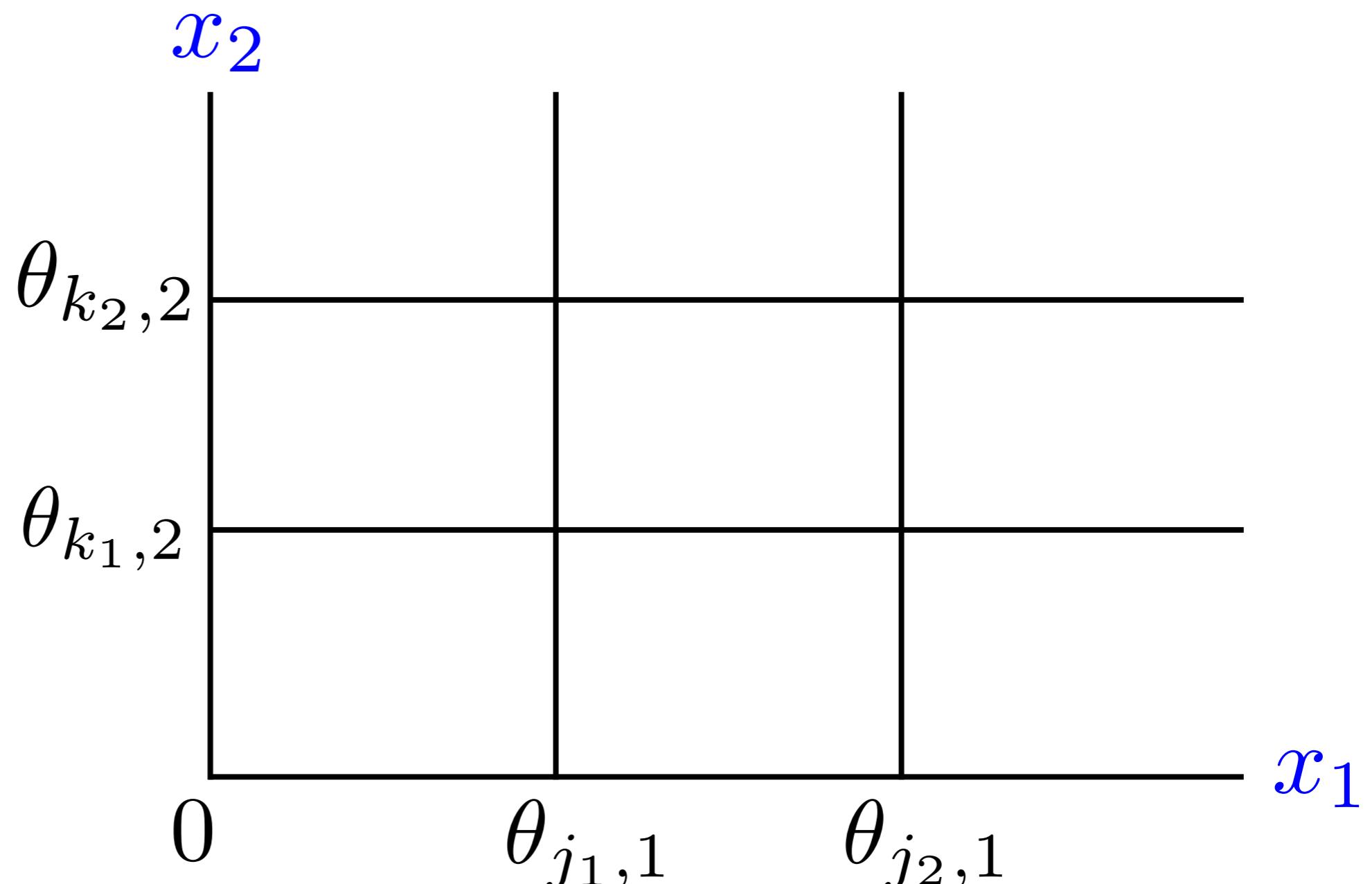
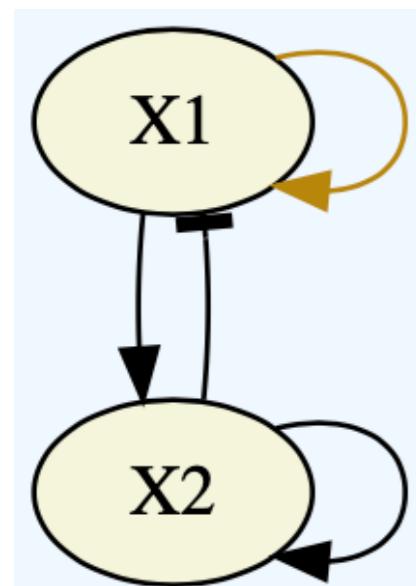
$$\begin{cases} -\gamma_1 x_1 + \sigma^+(x_1)\sigma^-(x_2) \\ -\gamma_2 x_2 + \sigma^+(x_1) + \sigma^+(x_2) \end{cases}$$

# DSGRN

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

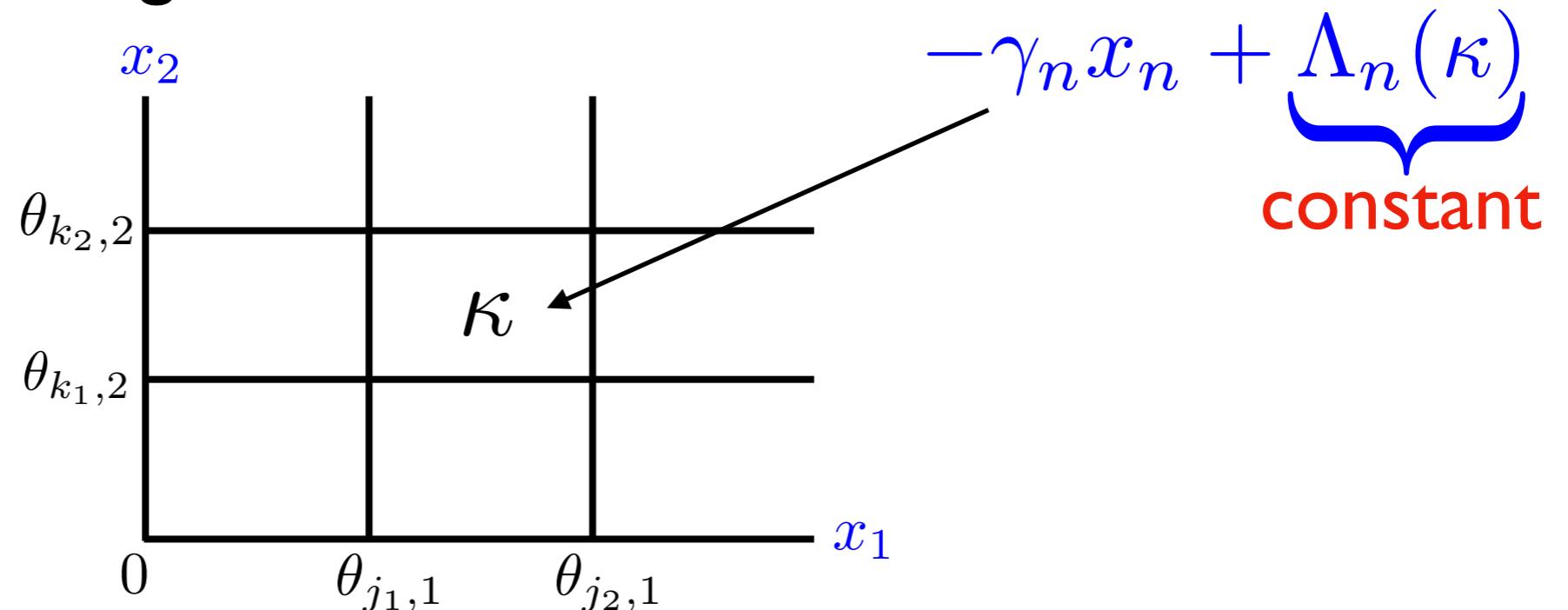
Hence we have a natural decomposition of phase space into rectangular regions

**out-edge threshold** 

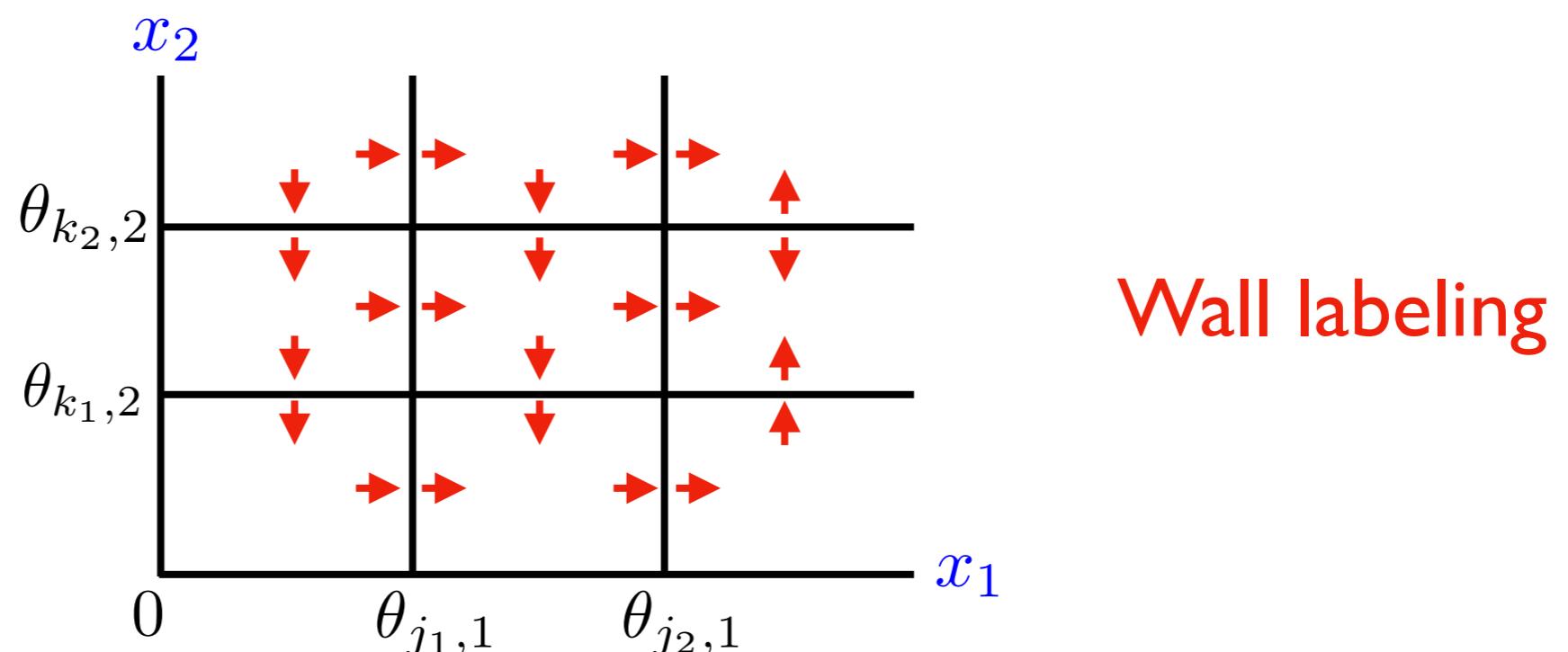


# DSGRN

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



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



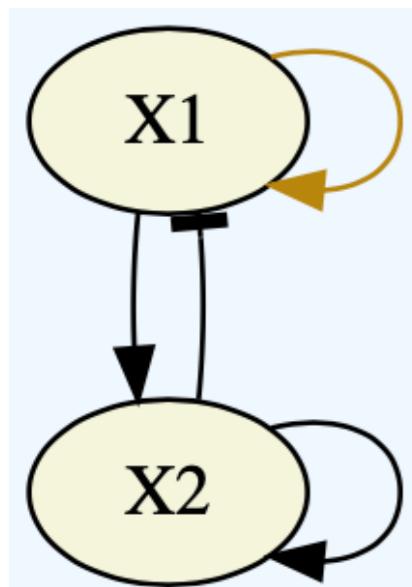
# Parameter graph

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

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

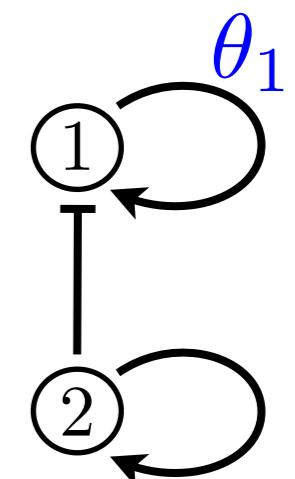
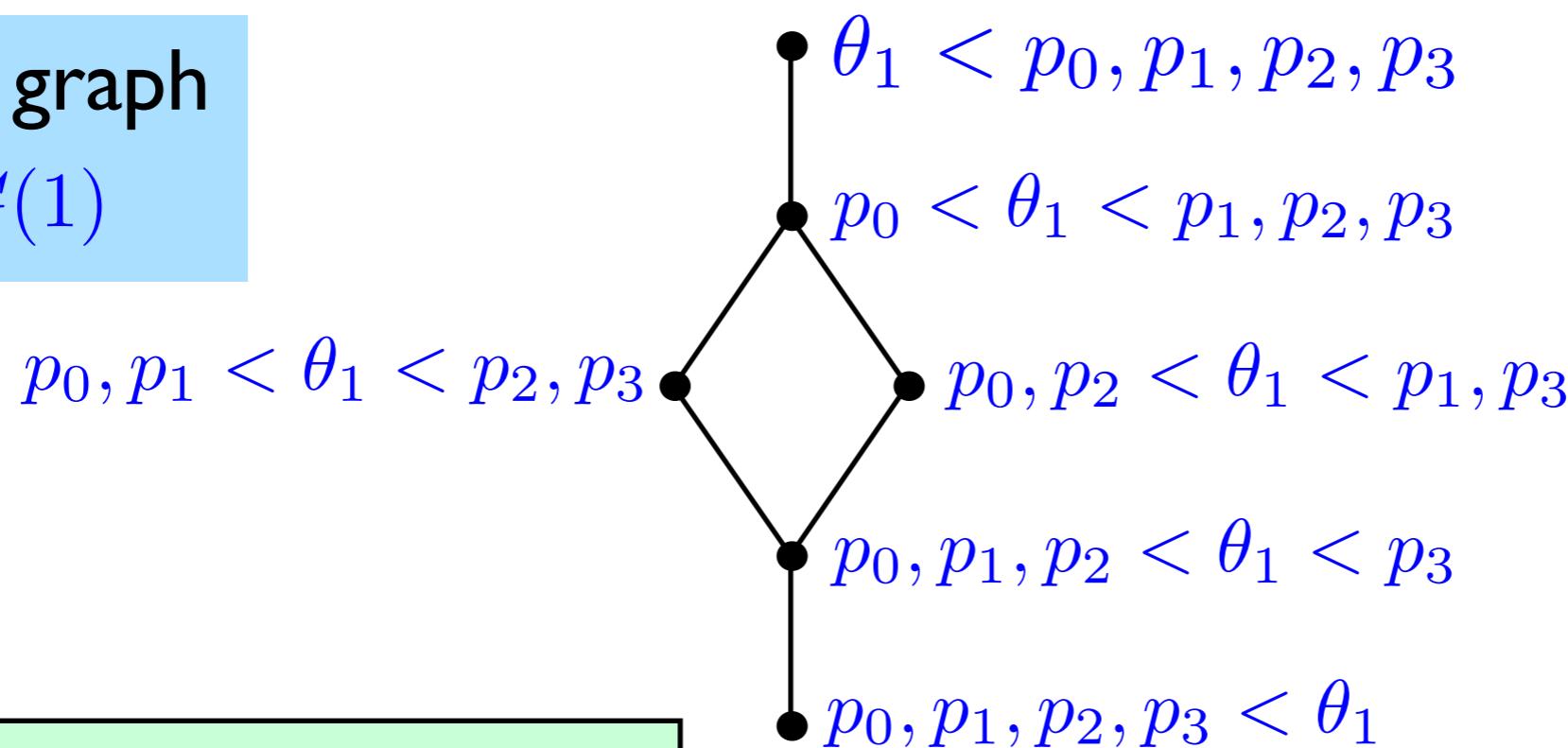
Total orders  $p_0 < p_1 < p_2 < p_3$  and  $p_0 < p_2 < p_1 < p_3$

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Factor graph

$PG(1)$

Poset



# Parameter graph

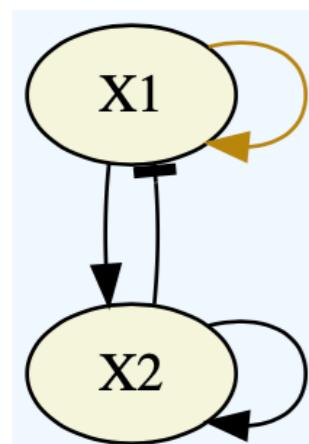
Parameter graph  $PG = \prod_{n=1}^N PG(n)$

Semi-algebraic sets (inequalities determining all sign combinations)

Each node determines all possible signs of

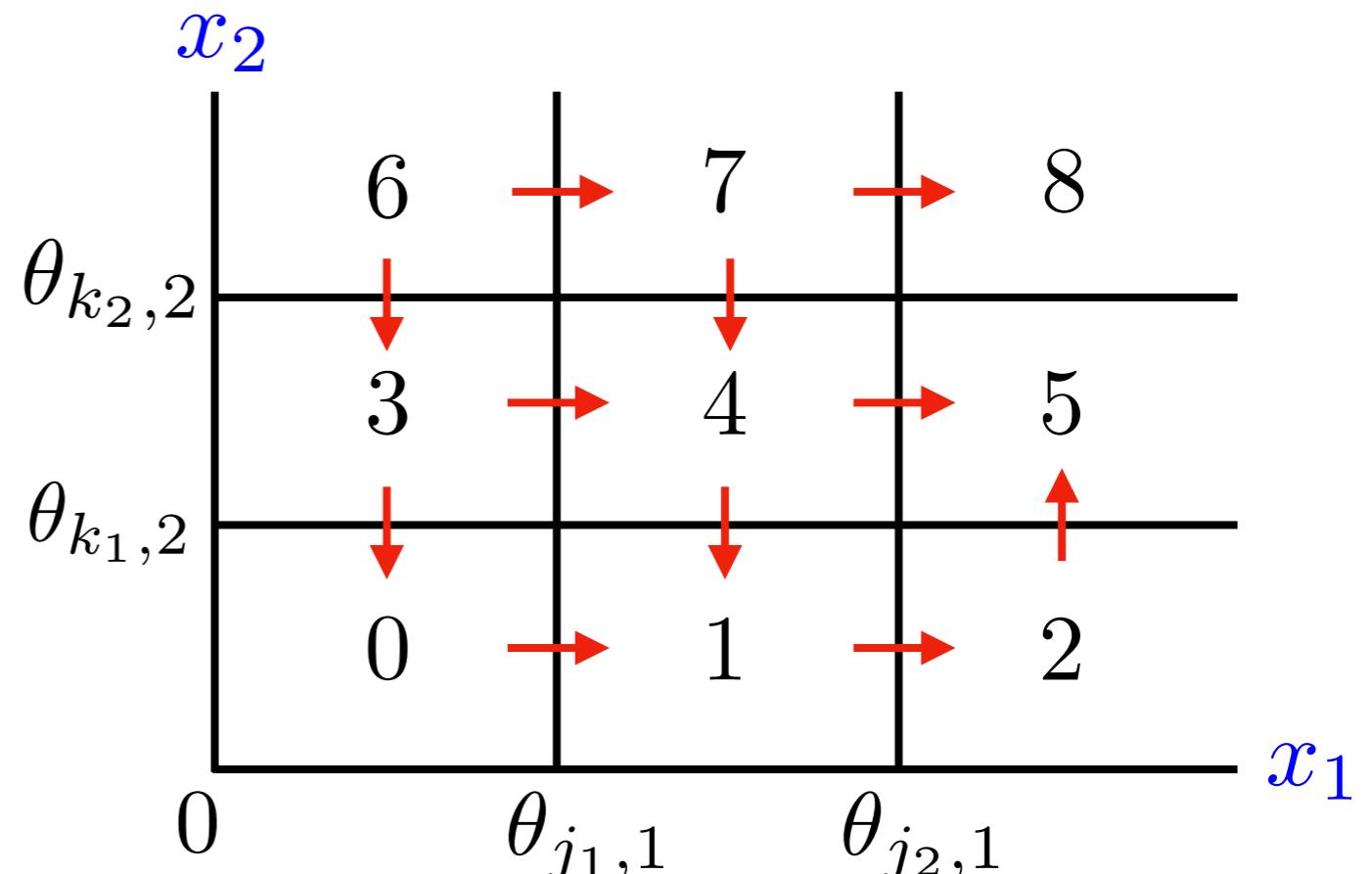
$$-\gamma_n \theta_{*,n} + \Lambda_n(x)$$

Edge means flip a single inequality



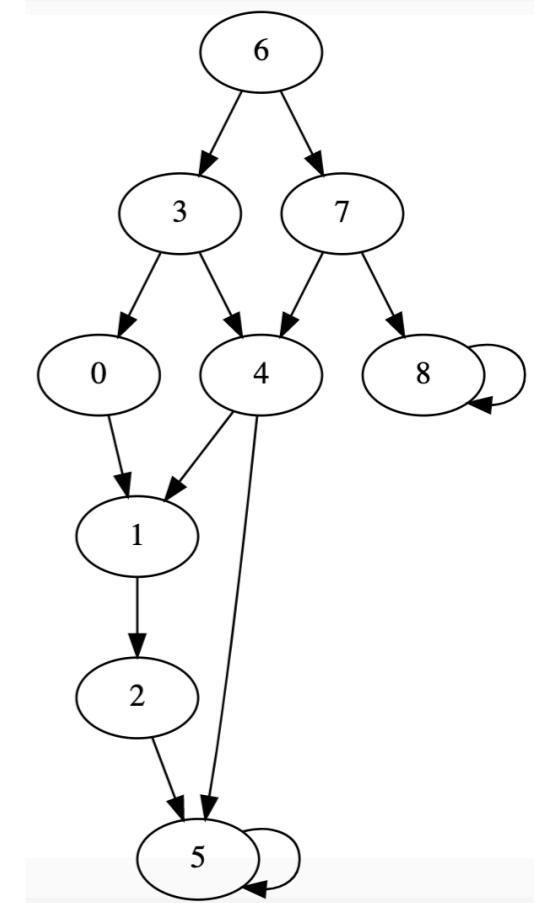
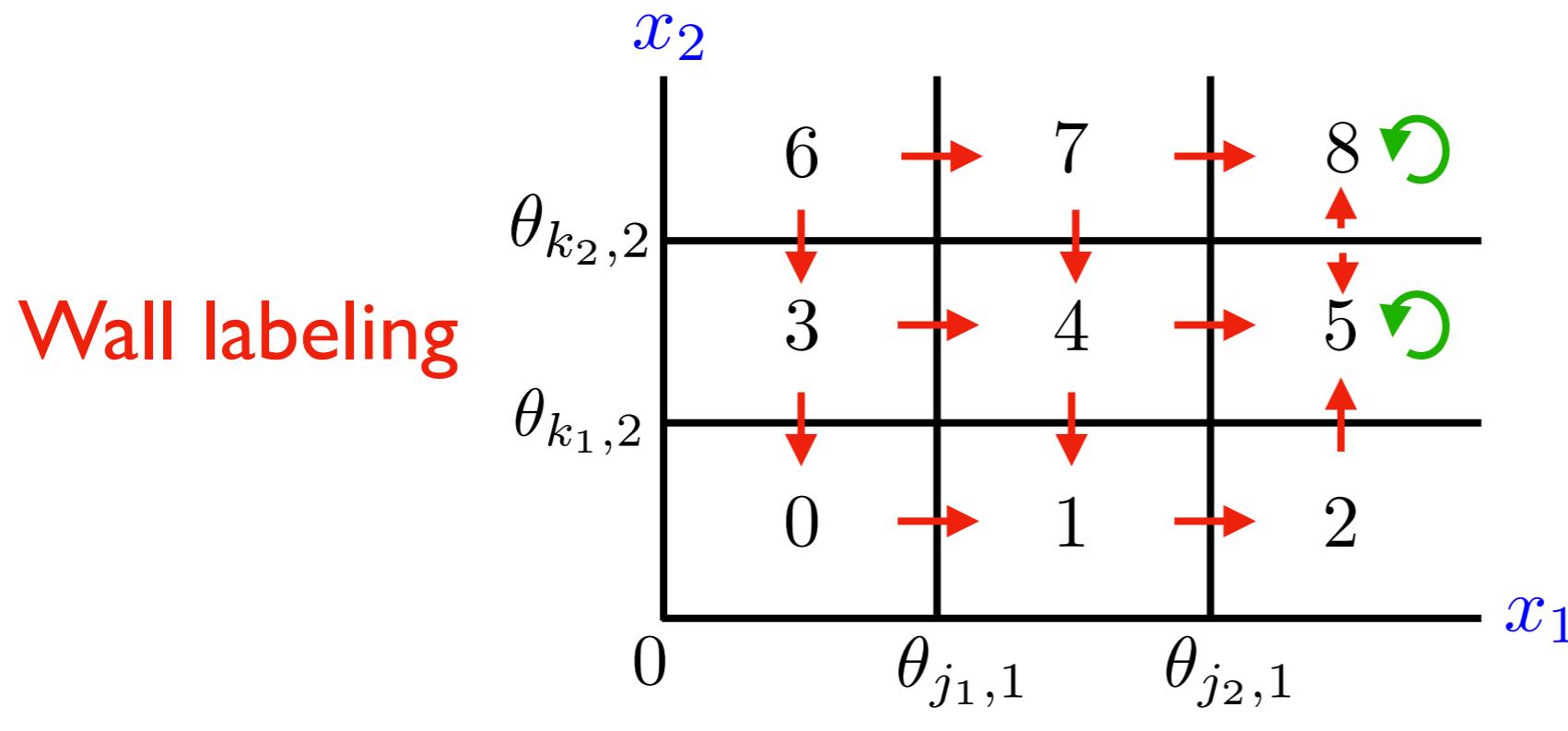
Parameter graph  
size: 1600

Parameter space dim: 14



# Multi-valued map

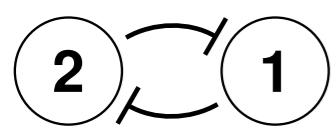
We could define the multi-valued map  $\mathcal{F}$  using the top dimensional cells (**DSGRN**)



This does not capture dynamics on lower dimensional cells

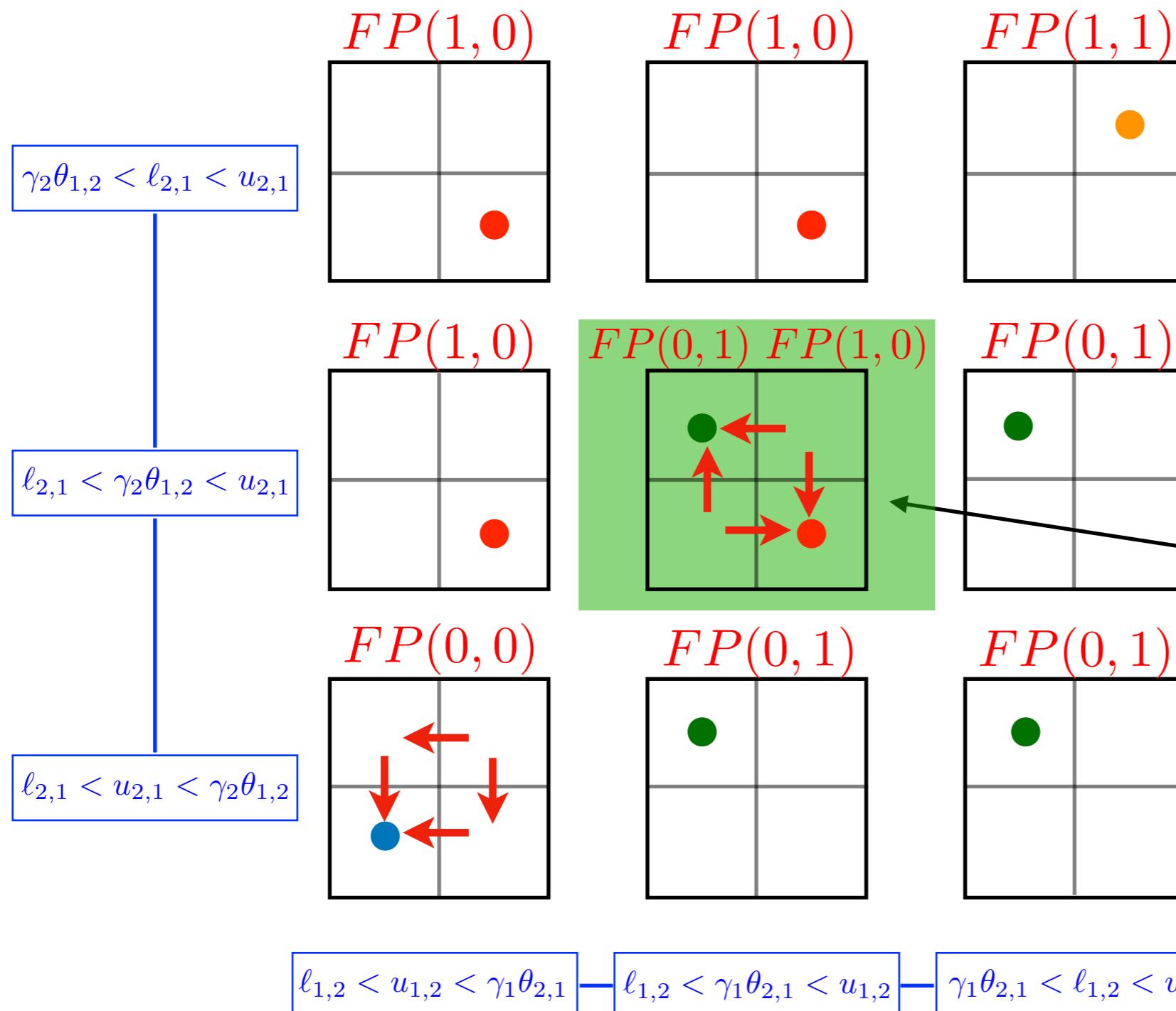
So we want to include the lower dimensional cells in the multi-valued map

# 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

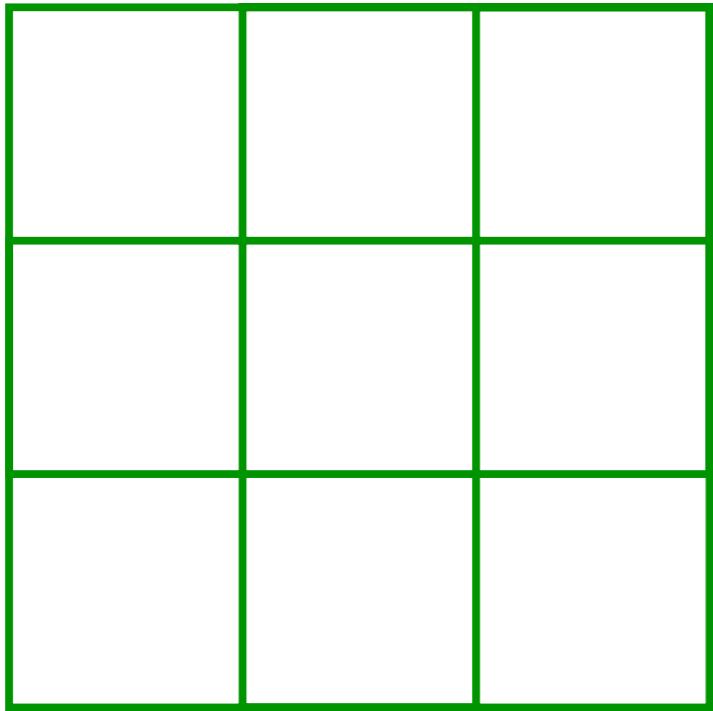


Parameter graph decomposes entire parameter space

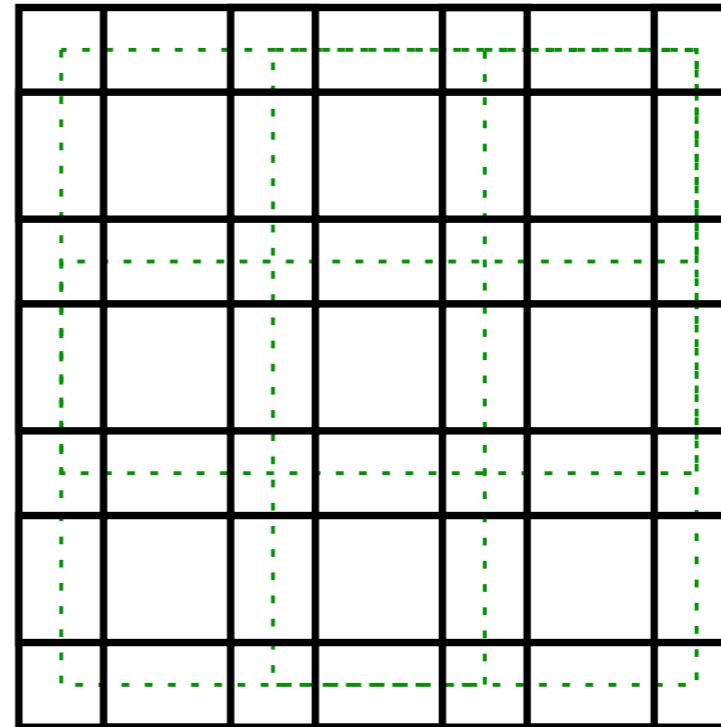
Essential parameter node

# Cubical blowup complex

Cubical complex

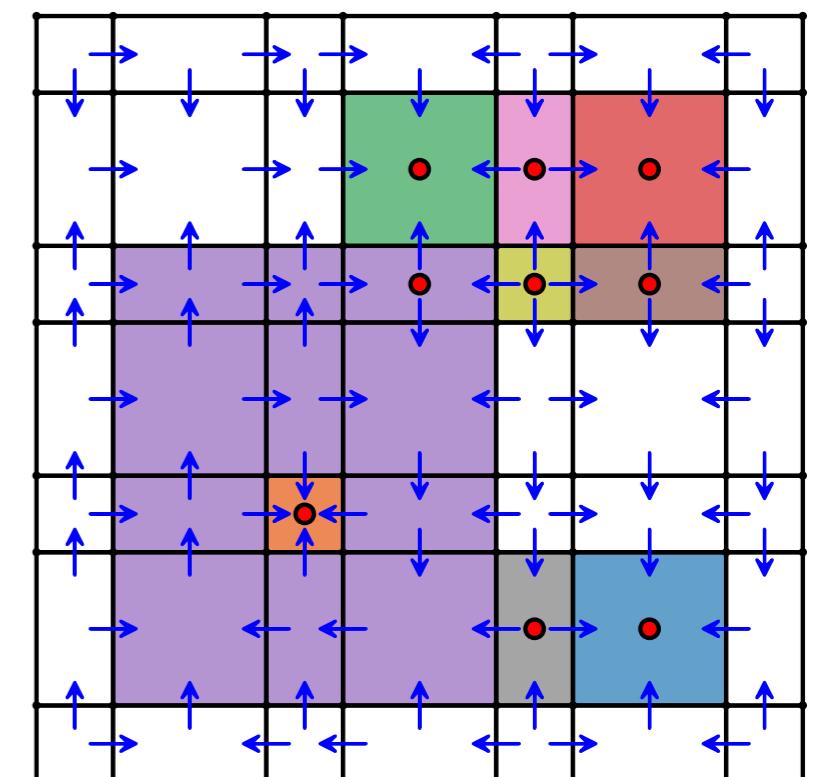


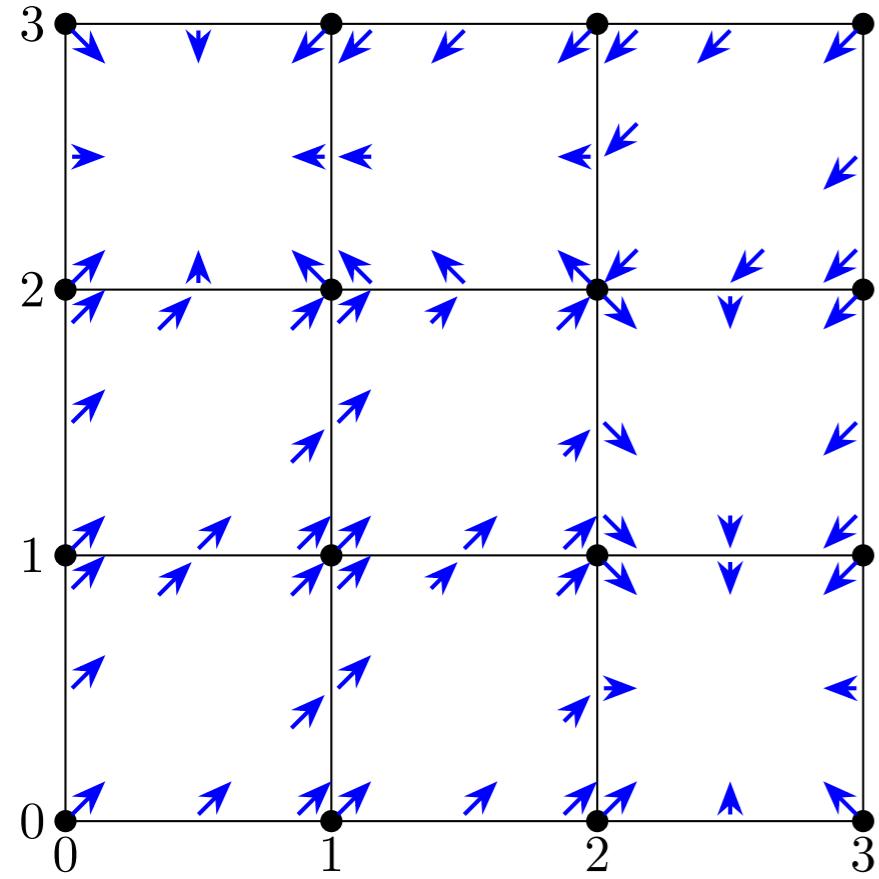
Cubical “blowup complex”



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**

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

Rook field is used to define combinatorial dynamics

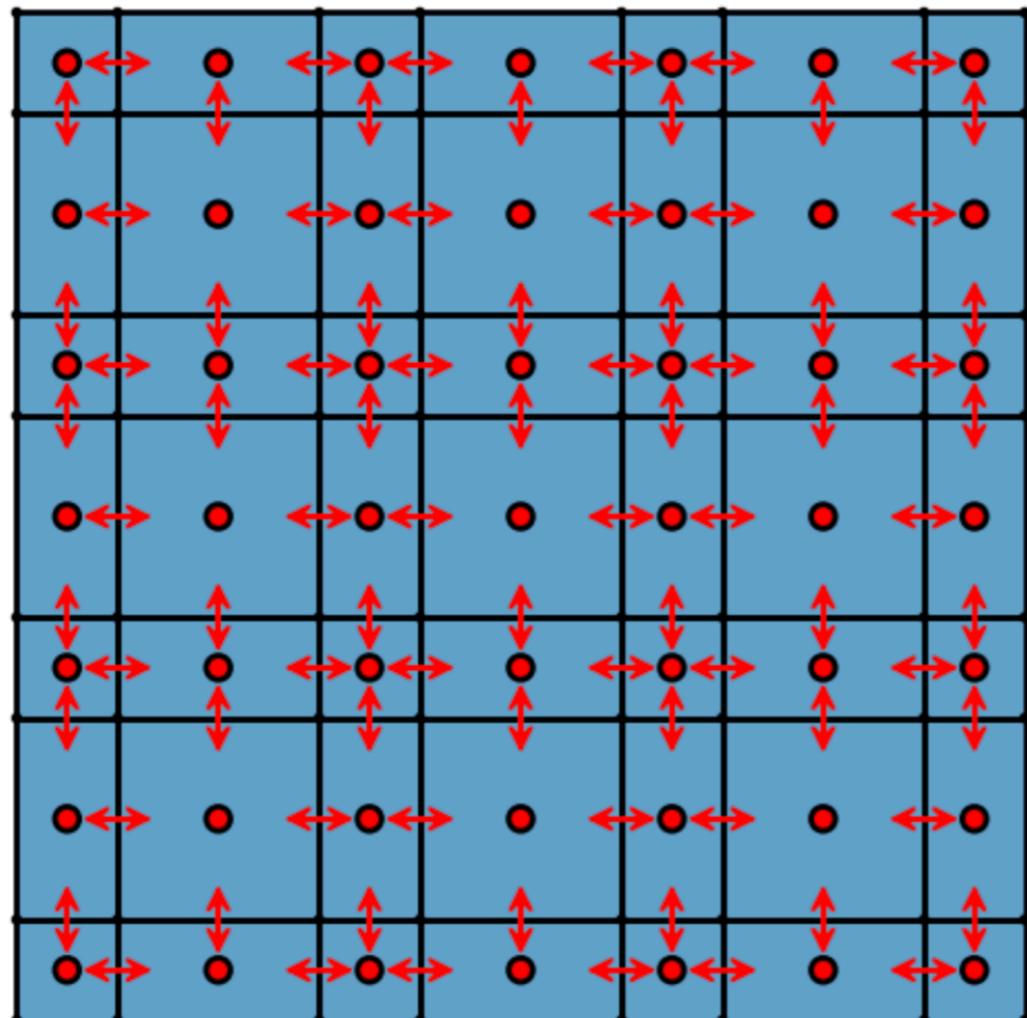
From a rook field we define multi-valued maps

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

# Multi-valued map

Define multi-valued map from rook field

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



Face relation

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

Morse graph

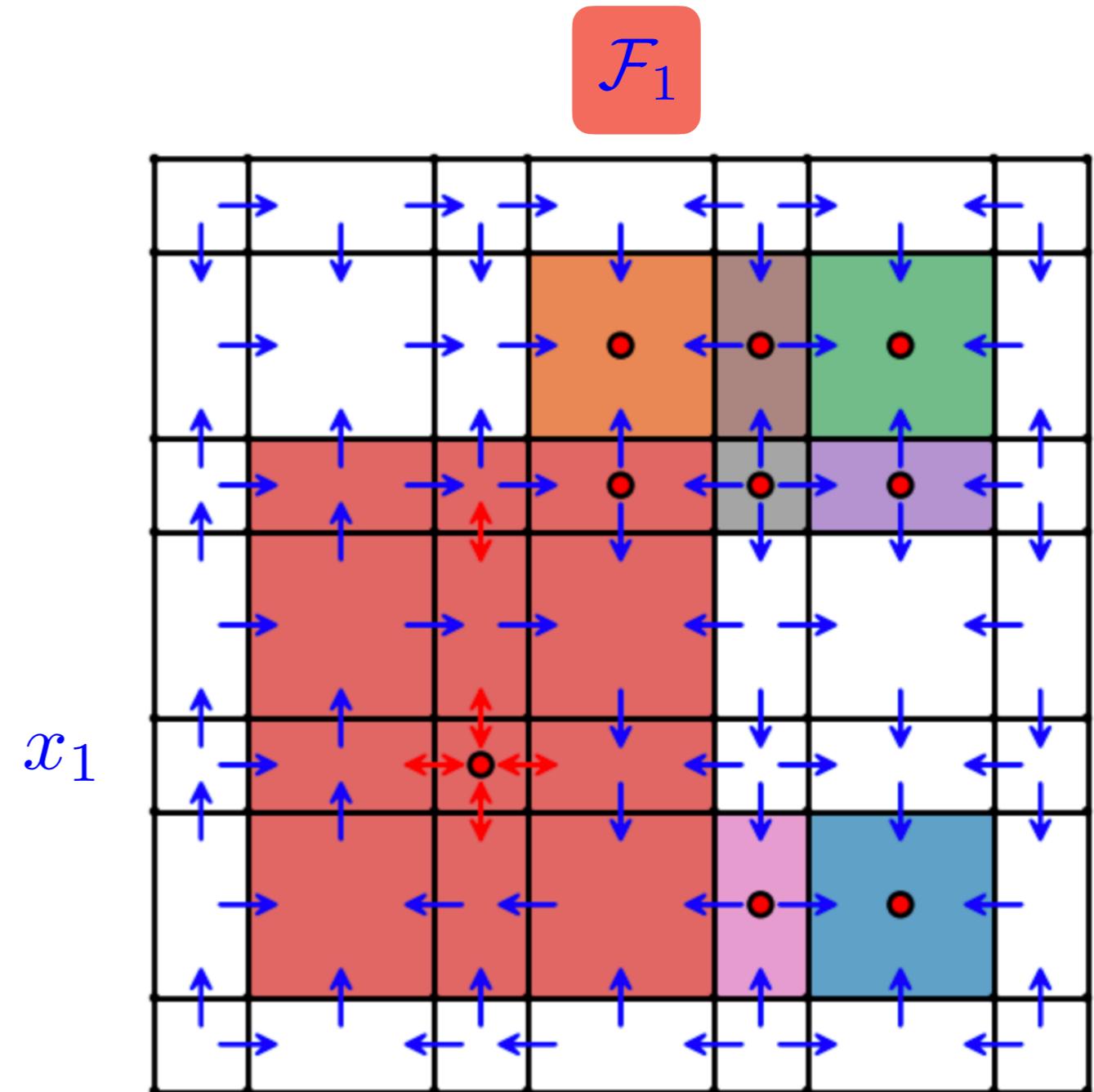
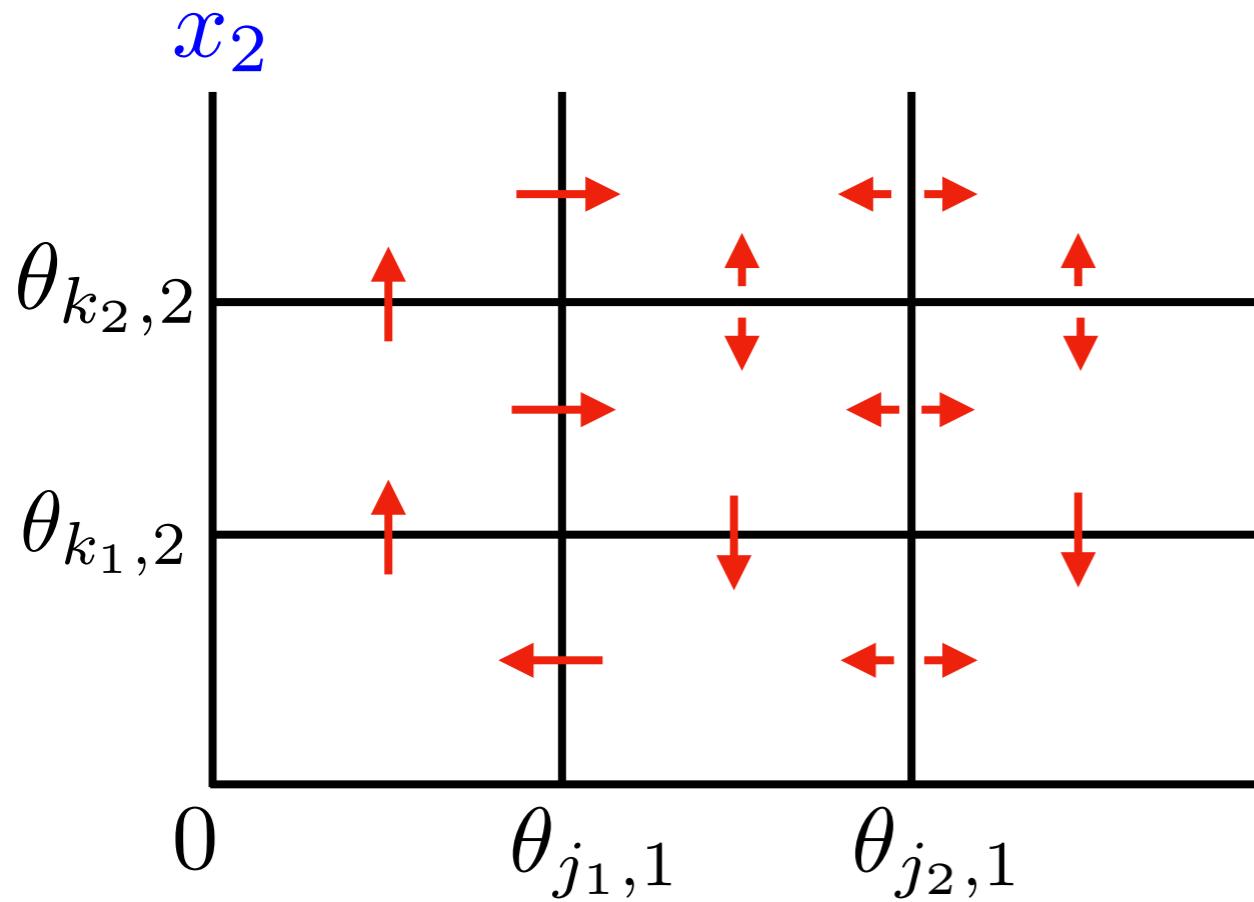
0 : (1, 0, 0)

Other maps eliminate double arrows (refinements)

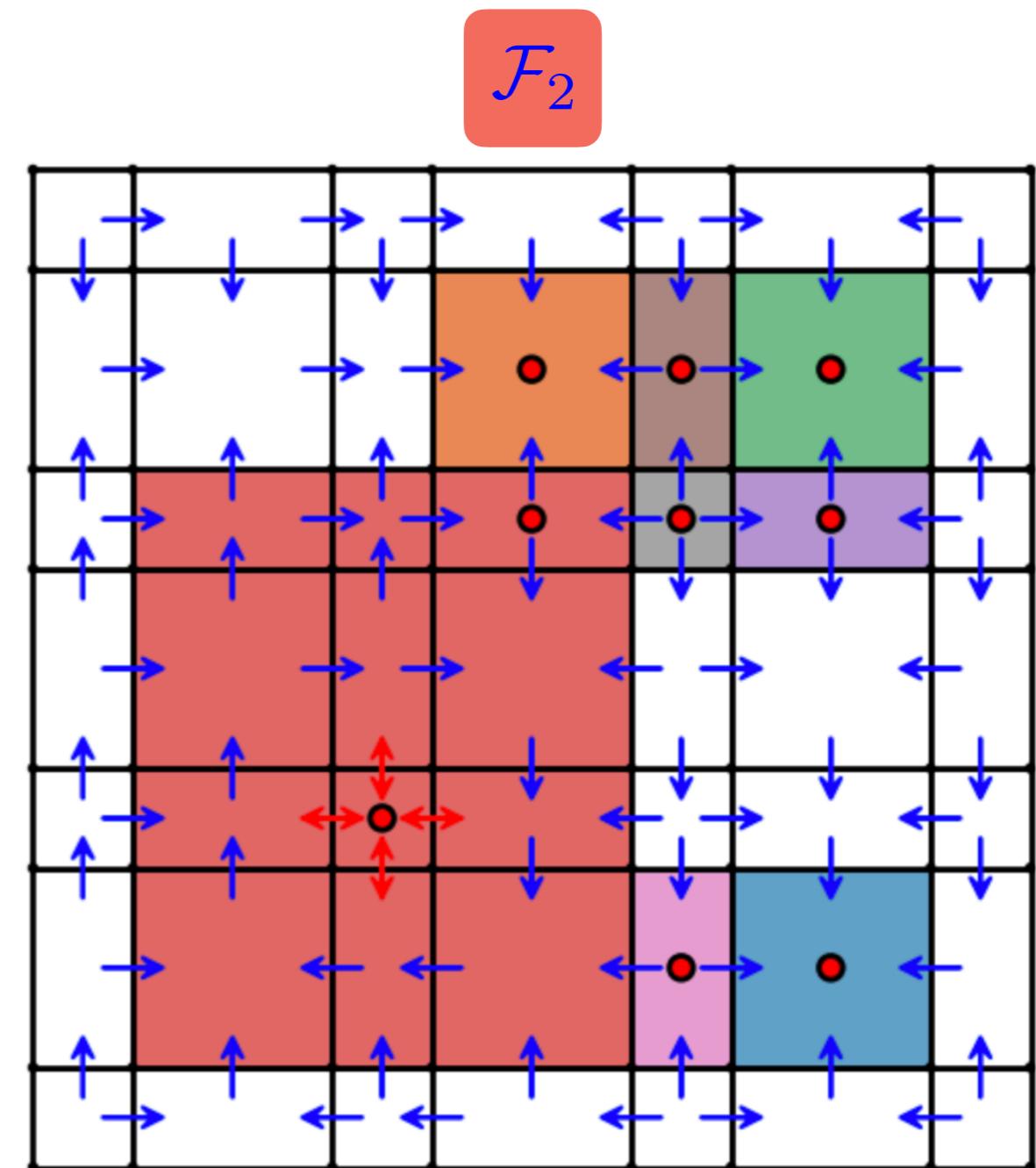
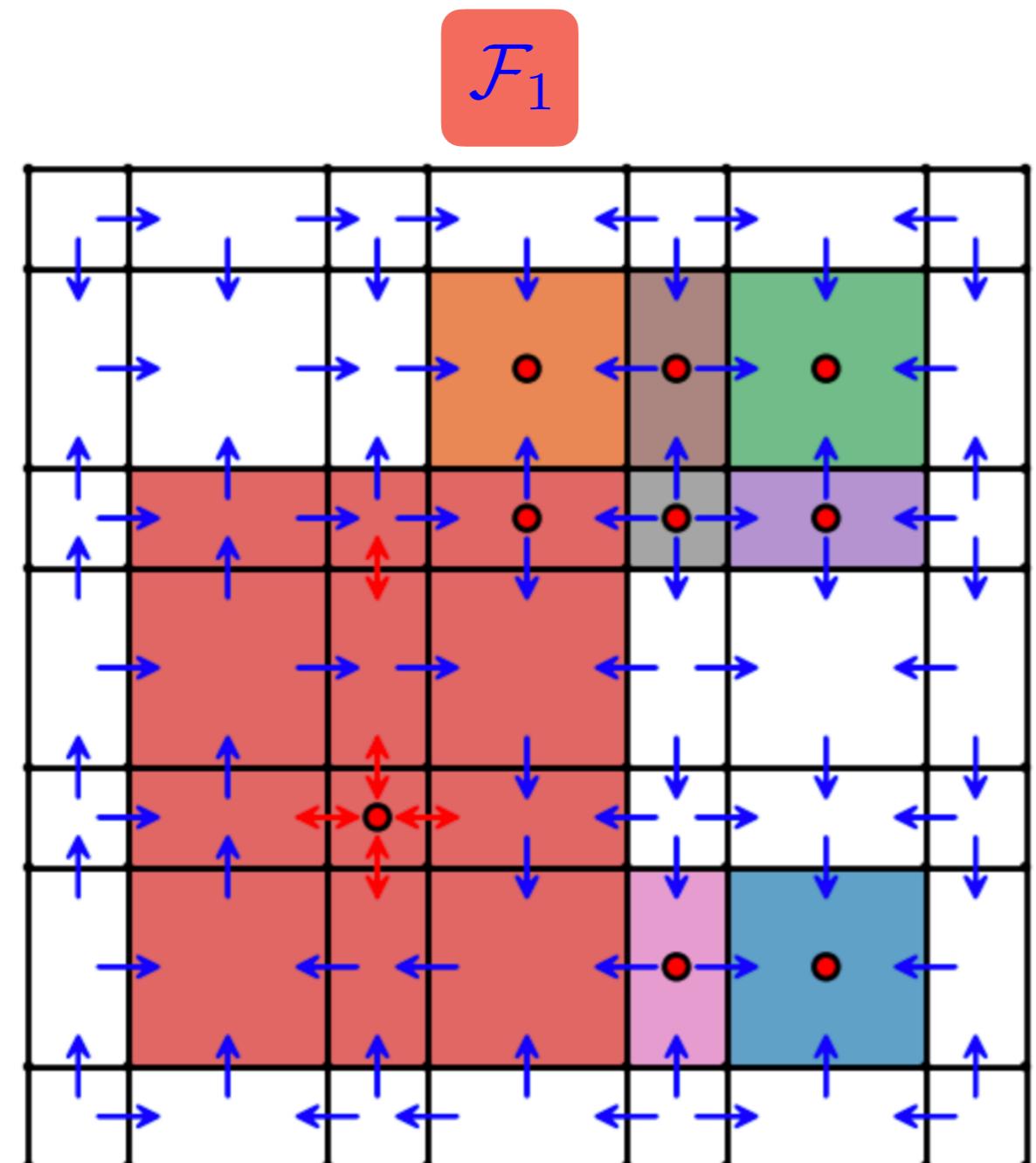
# Multi-valued map refinements

Remove double arrow if there is a clear flow direction

No self-arrow if there is a gradient direction

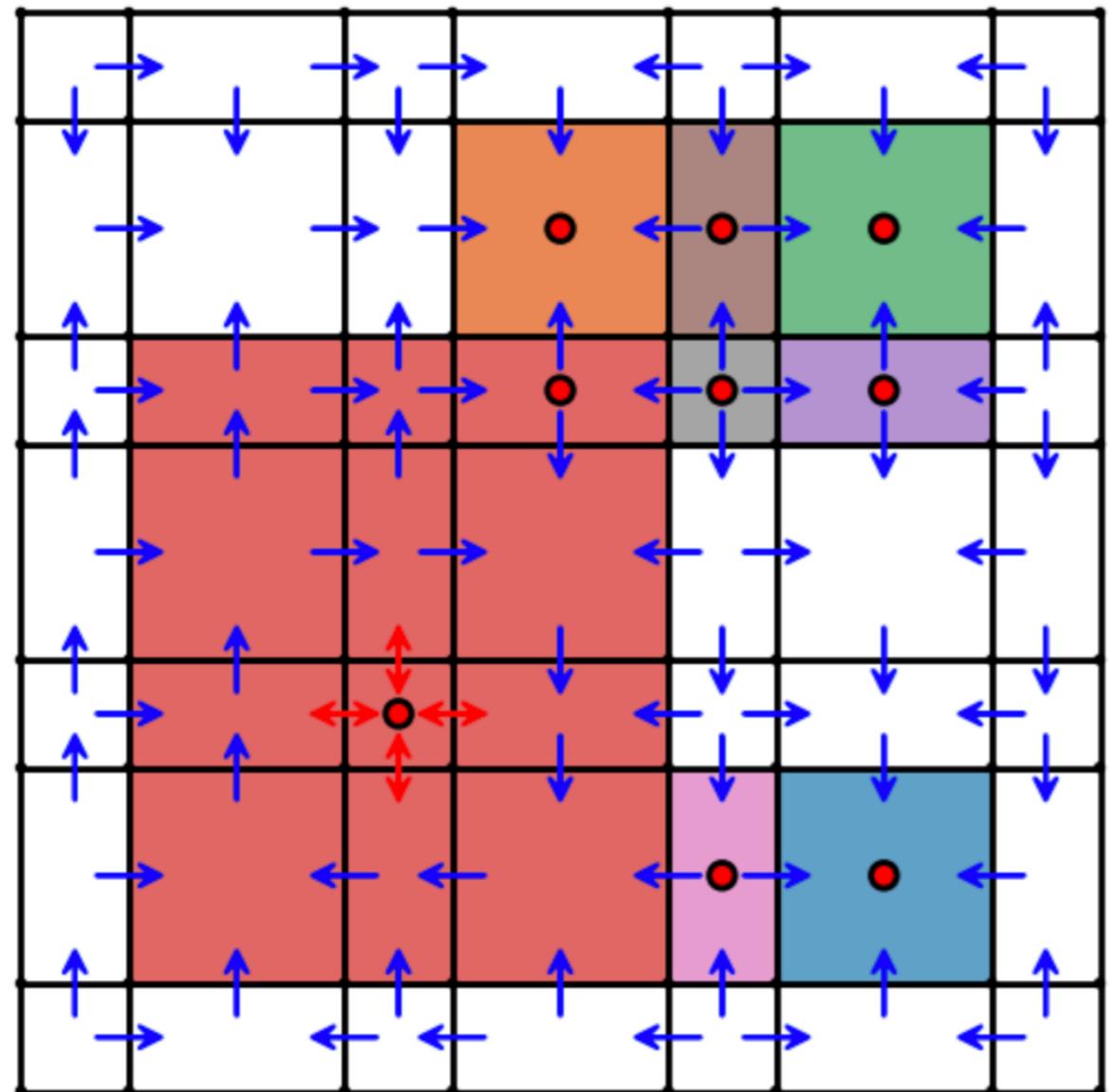


# Multi-valued map refinements

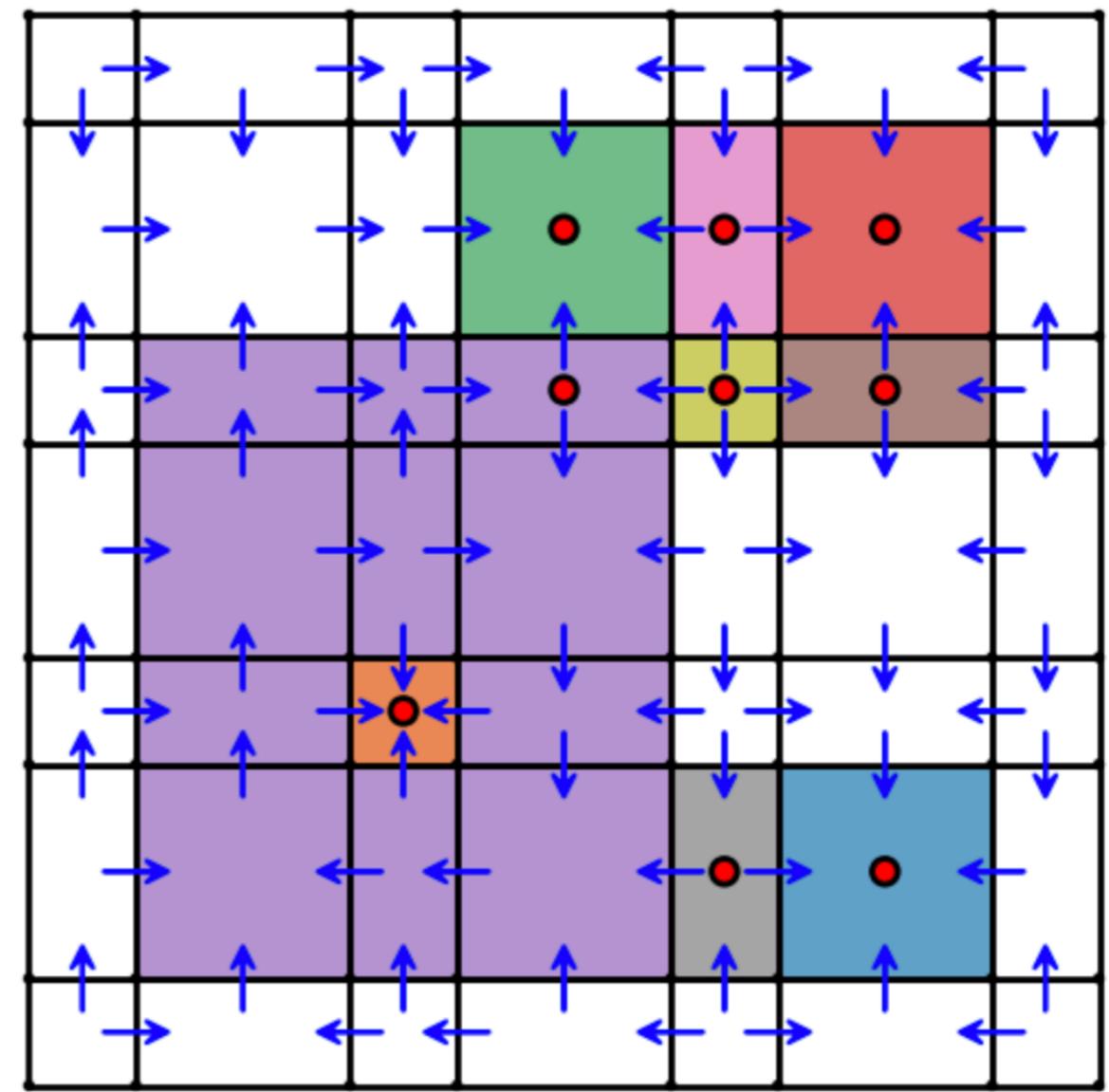


# Multi-valued map refinements

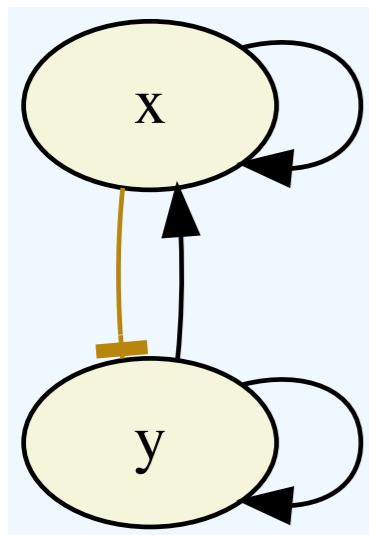
$\mathcal{F}_2$



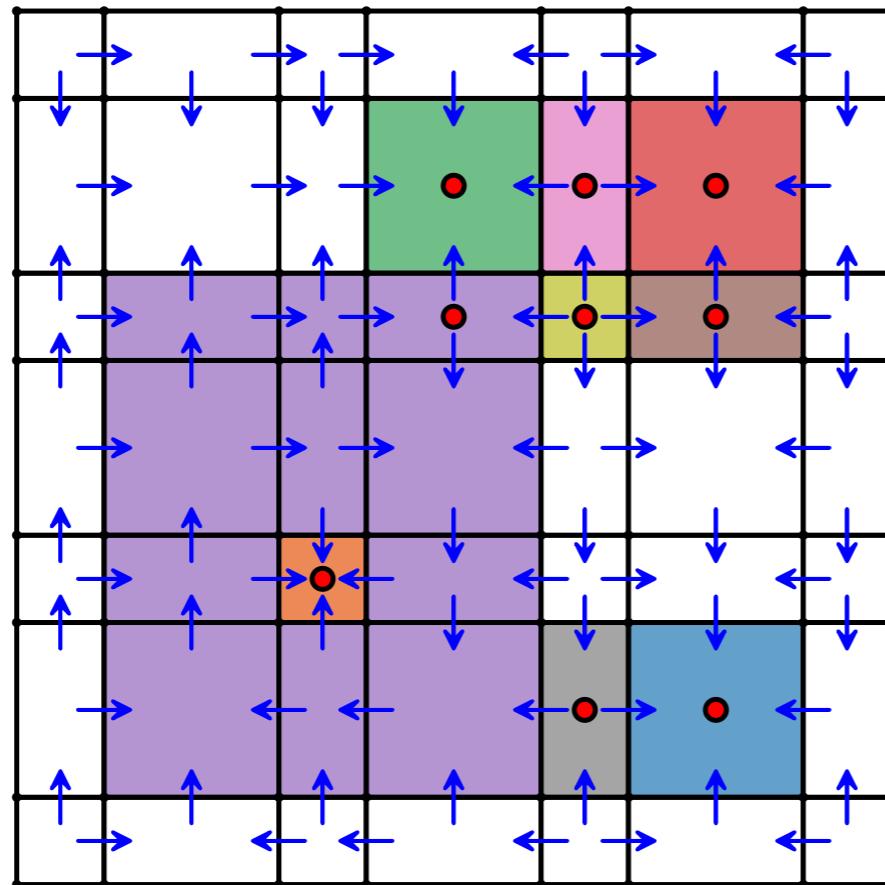
$\mathcal{F}_3$



# Combinatorial Dynamics



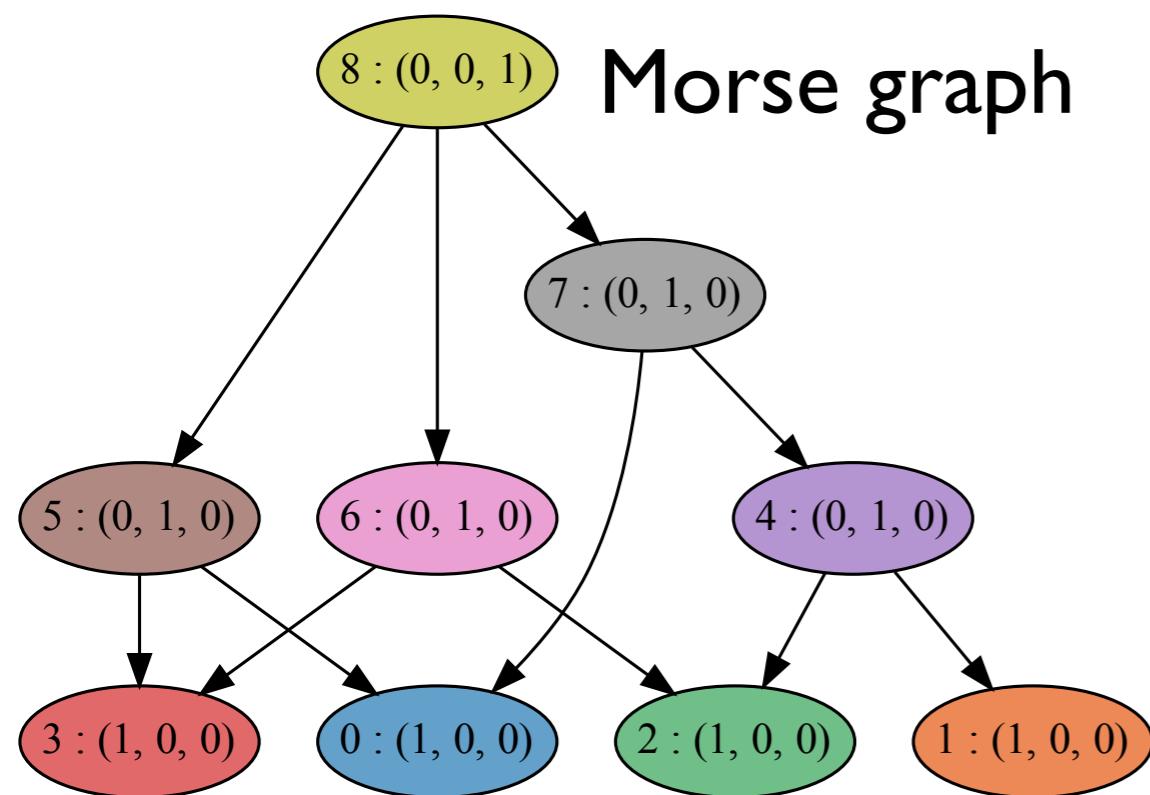
Network



Abstract cell complex

Algebraic topology  
computations

Dynamics valid for  
whole parameter region



Morse graph

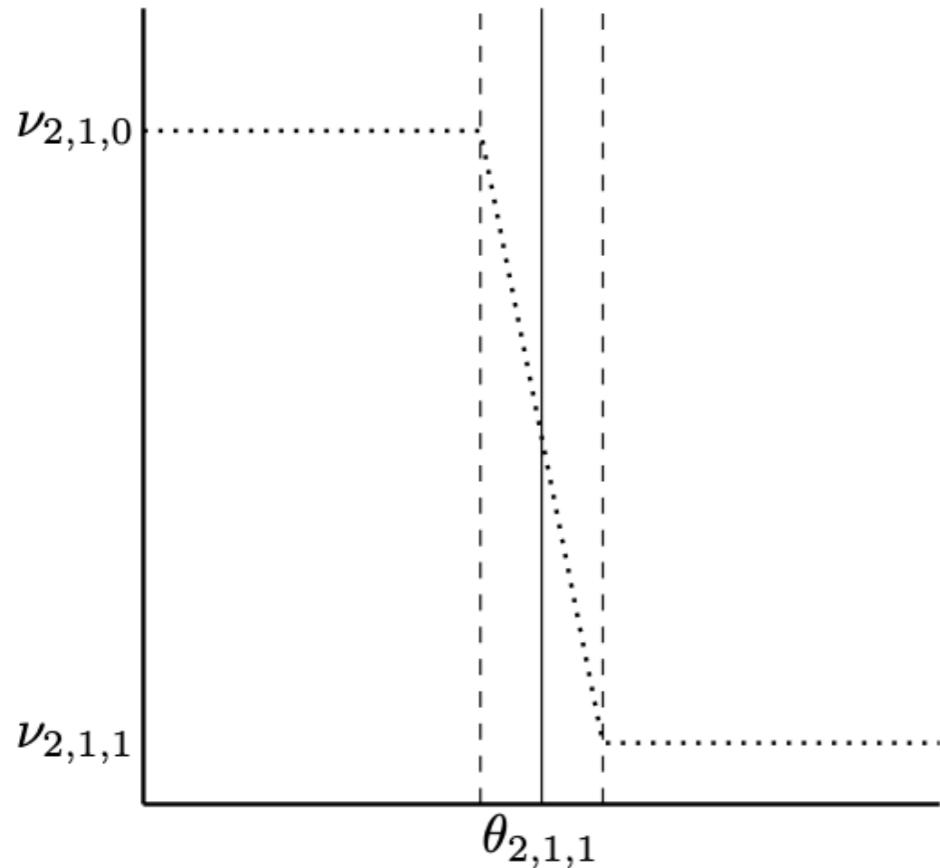
Dynamics is valid for which  
families of ODEs?

To get ODE dynamics we  
need transversality

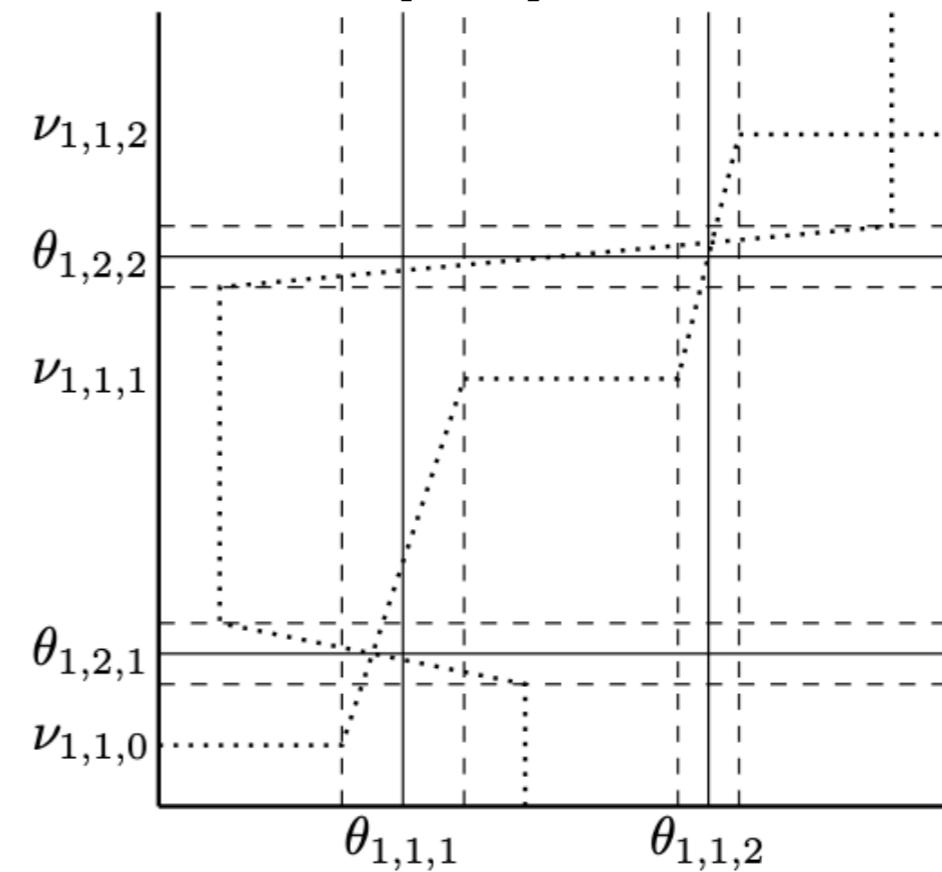
# Ramp systems

“Replace” step functions by ramp functions

Ramp function



Ramp system

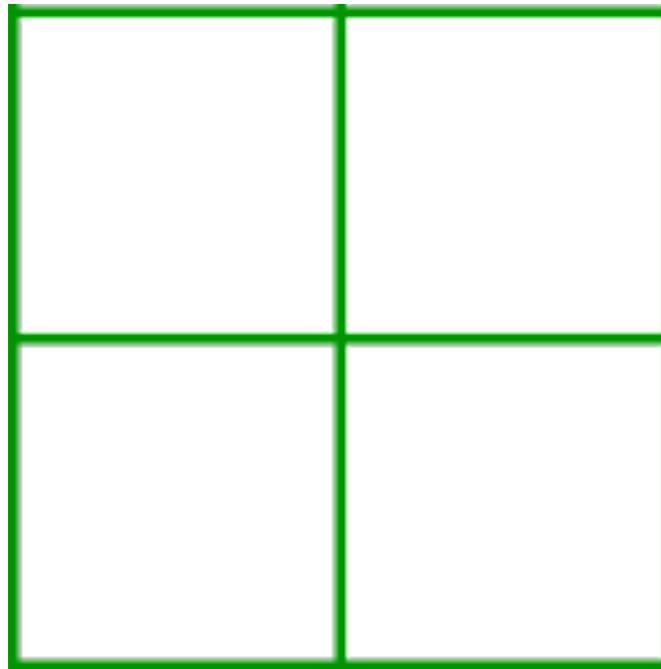


Sums and products of ramp functions

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

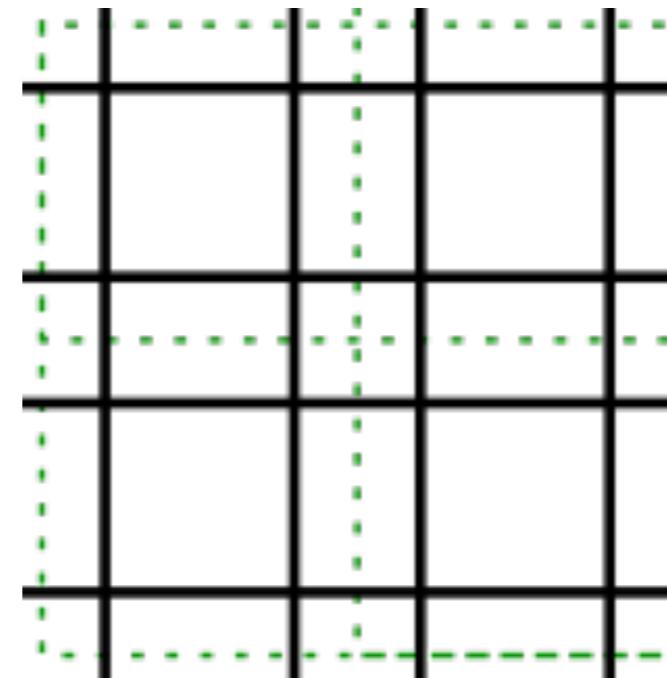
# Ramp systems

Cubical complex



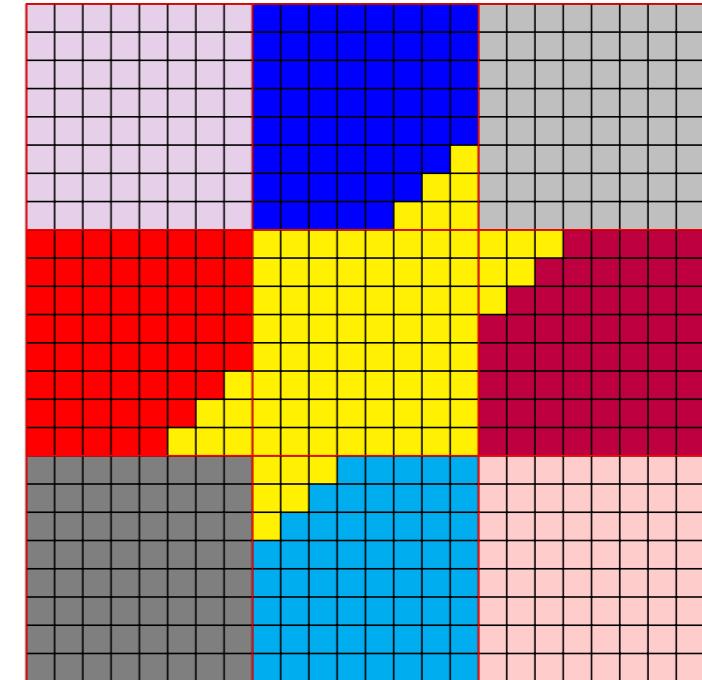
$\chi$

Blowup complex



$\chi_b$

Janus complex

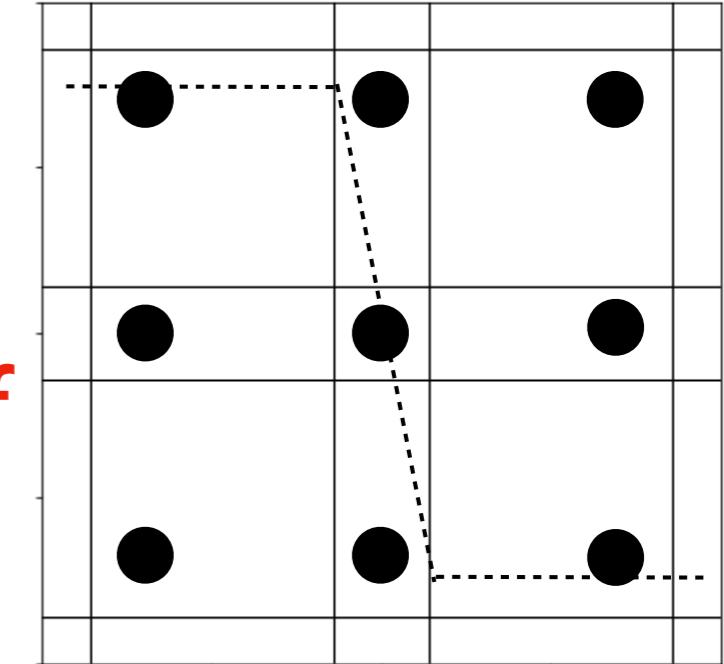


$\gamma$

Chain homotopy

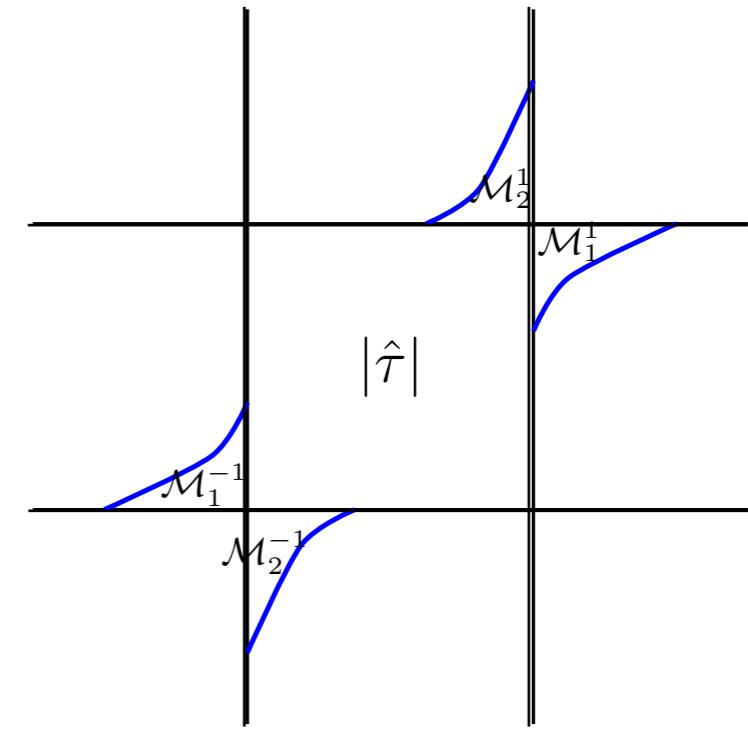
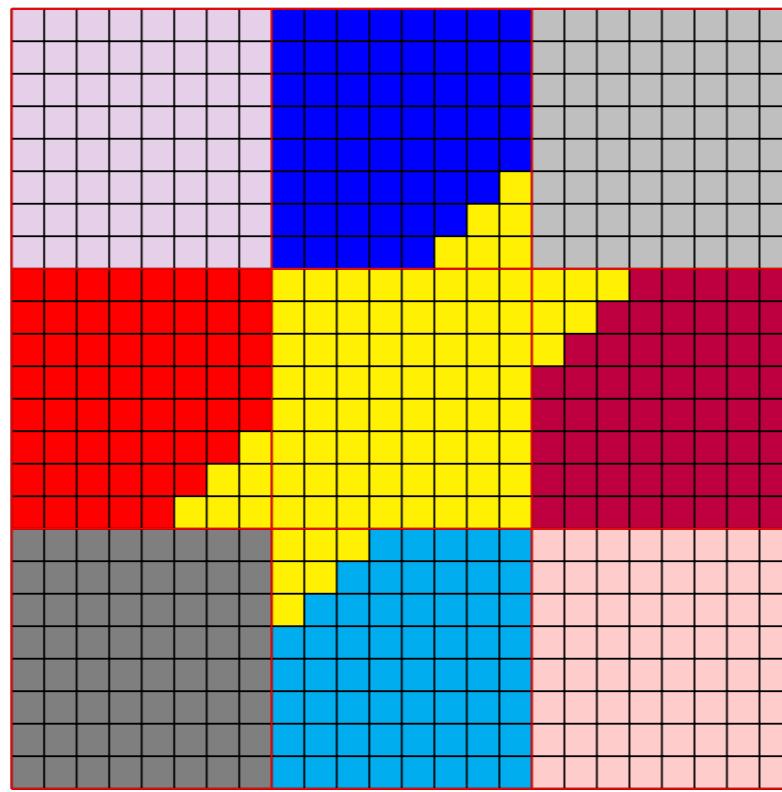
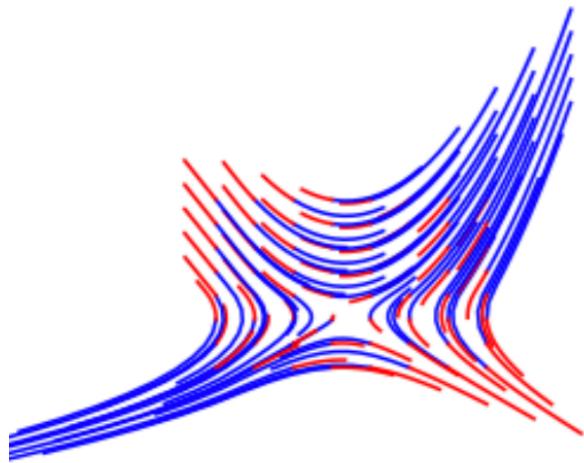
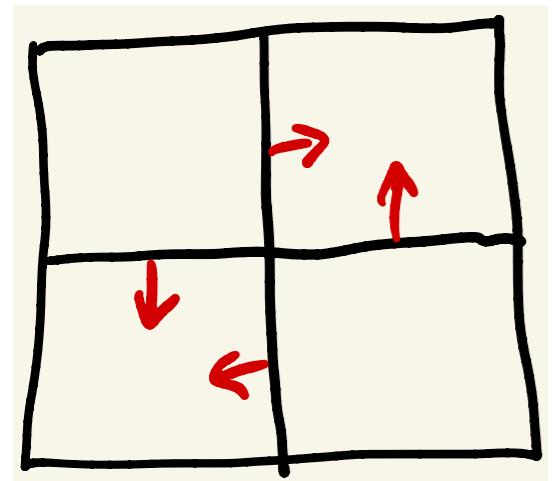
Transversality:  
geometric realization of  
the modified complex

Local modifications



$2h$

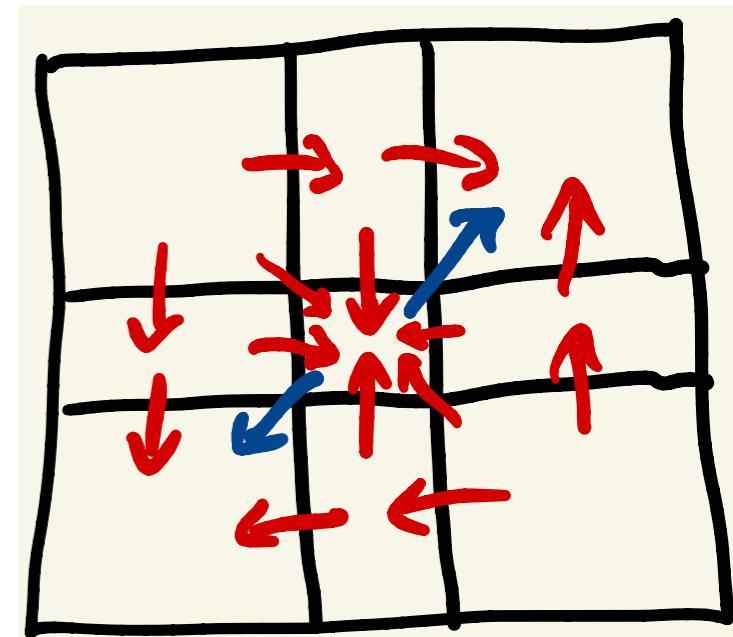
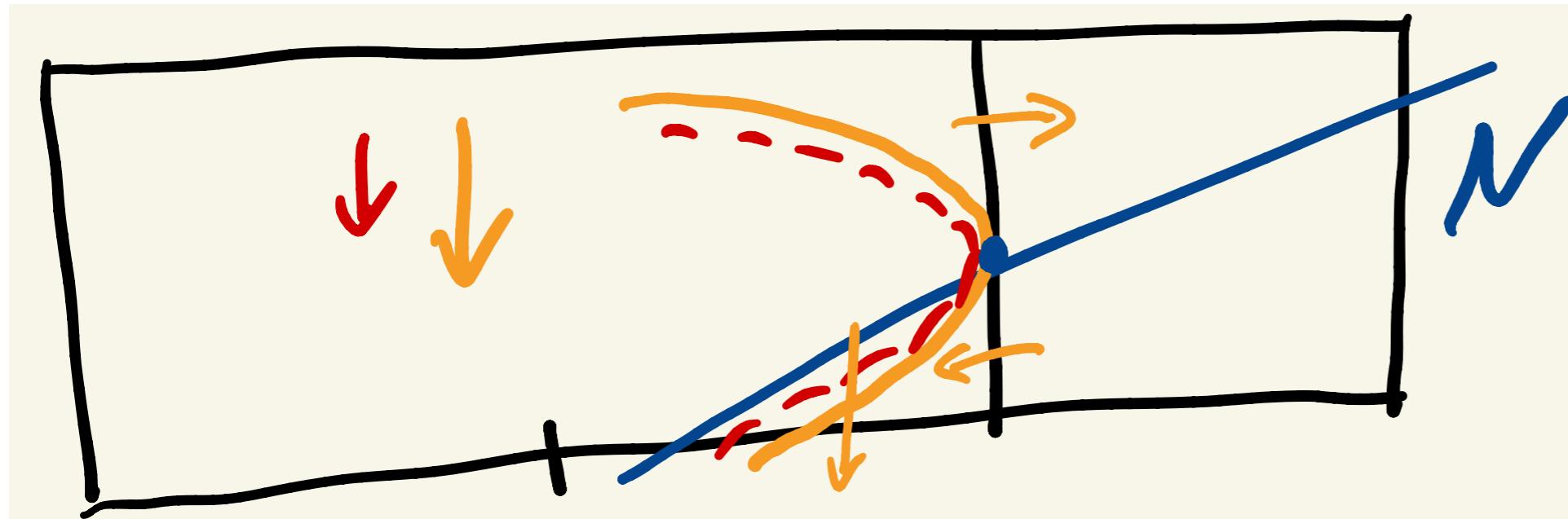
# Ramp systems



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

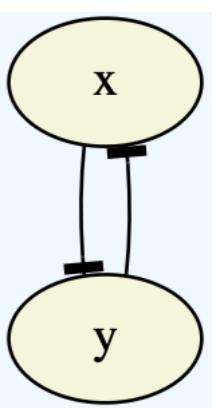
Dynamics identified by  $\mathcal{F}_3$  is valid for 2 and 3-dim ODEs

Dynamics valid for every parameter value in DSGRN parameter region

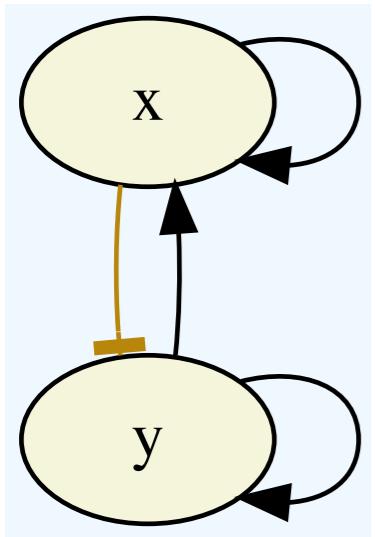
Valid for ramp systems with  $h$  less than explicit upper bound

For the toggle switch

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

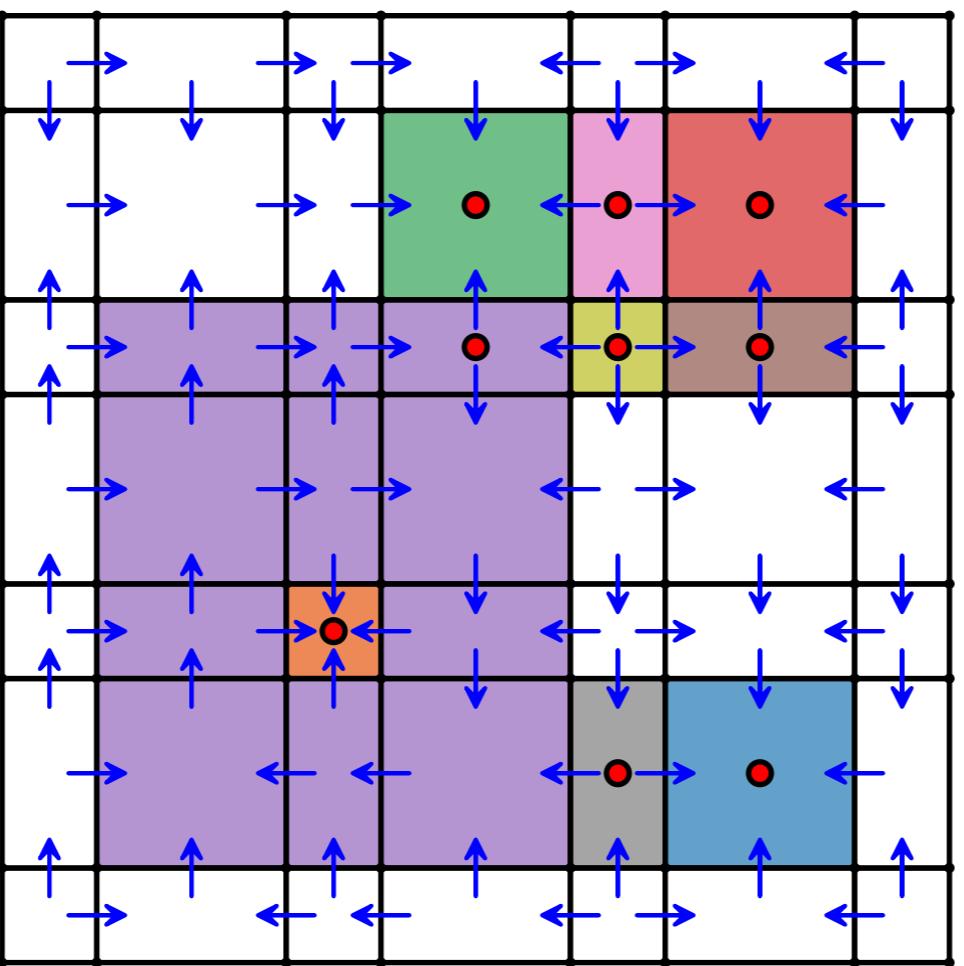


## Example



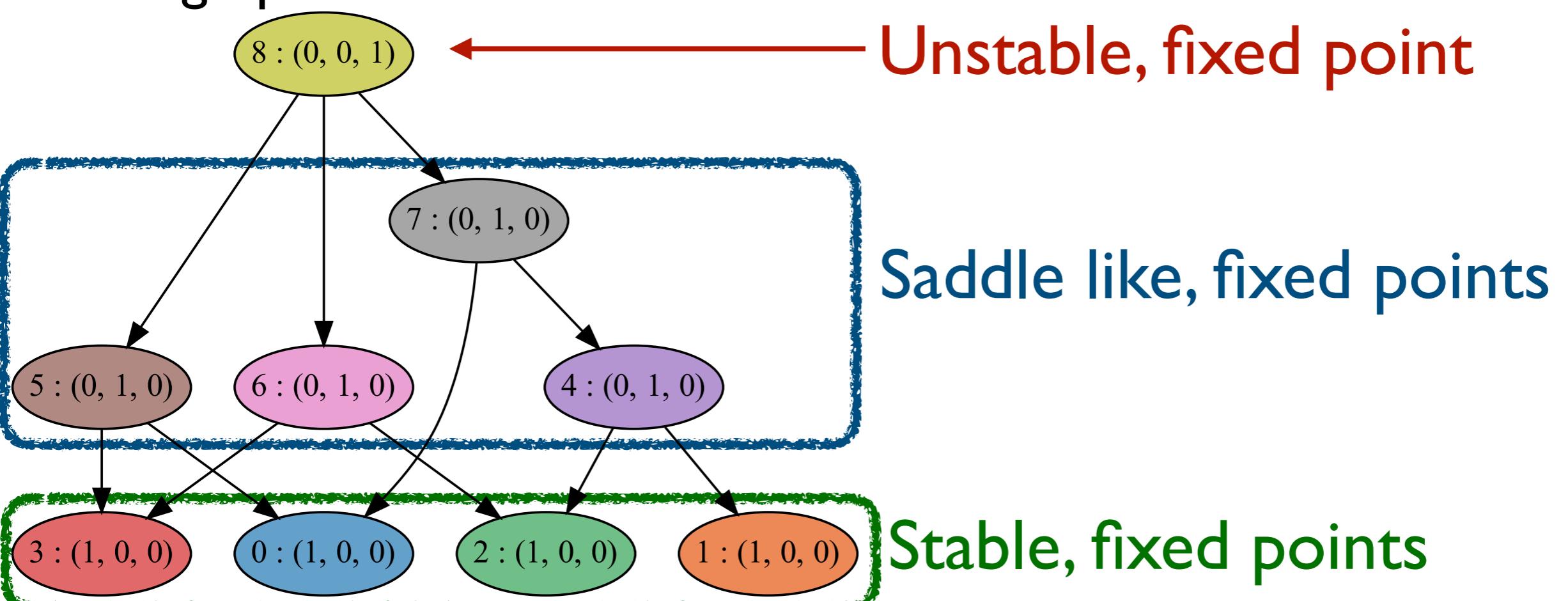
Network

Morse graph



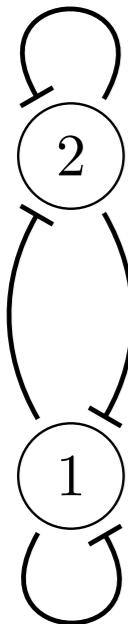
Combinatorial representation of dynamics for one parameter region

$\mathcal{F}_3$



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

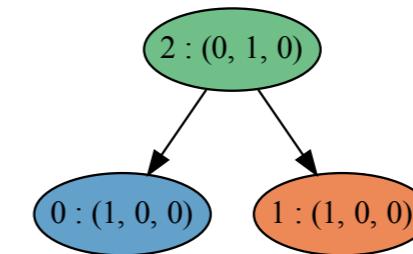
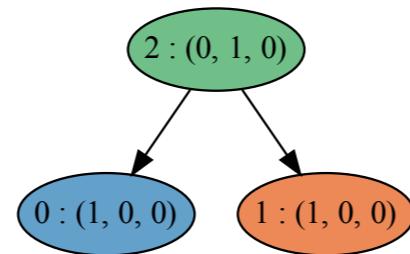
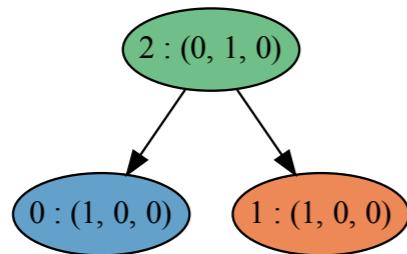
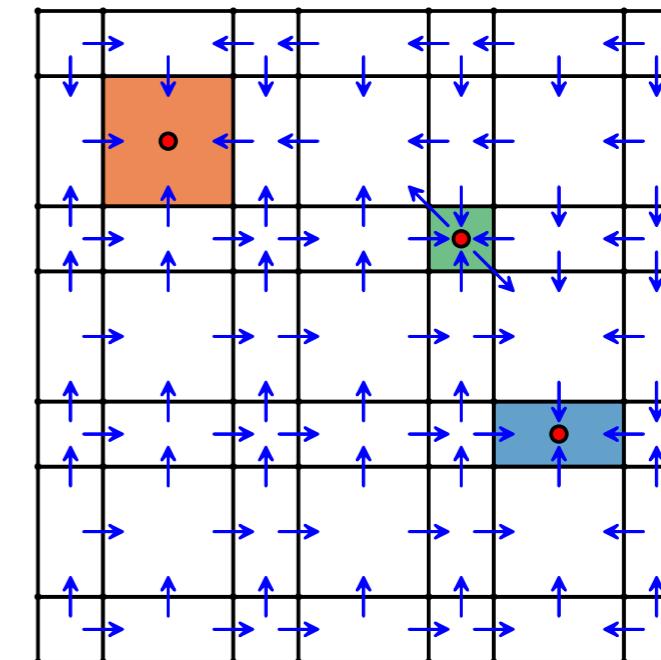
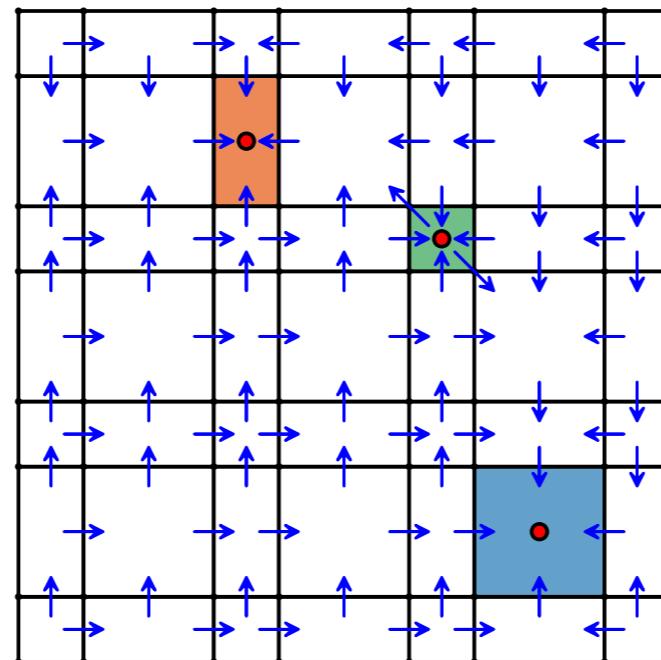
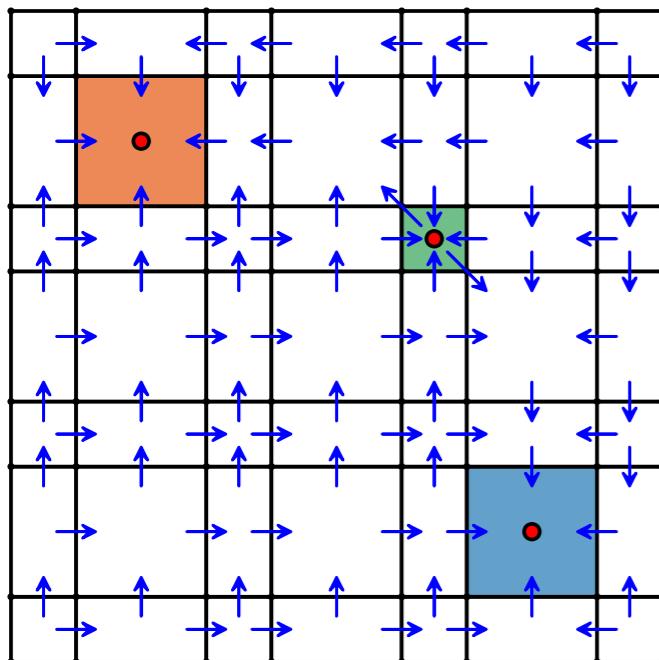
$$x_1 : p_0 < \gamma_1 \theta_{1,1} < p_1 < \gamma_1 \theta_{2,1} < p_2, p_3$$

$$x_2 : p_0, p_2 < \gamma_2 \theta_{2,2} < \gamma_2 \theta_{2,1} < p_1, p_3$$

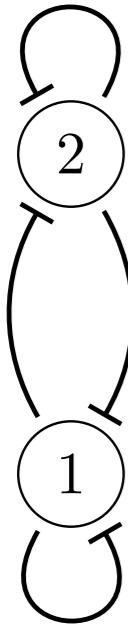
Parameter node 1054

$$x_1 : p_0, p_1 < \gamma_1 \theta_{1,1} < \gamma_1 \theta_{2,1} < p_2, p_3$$

$$x_2 : p_0 < \gamma_2 \theta_{2,2} < p_2 < \gamma_2 \theta_{2,1} < p_1, p_3$$

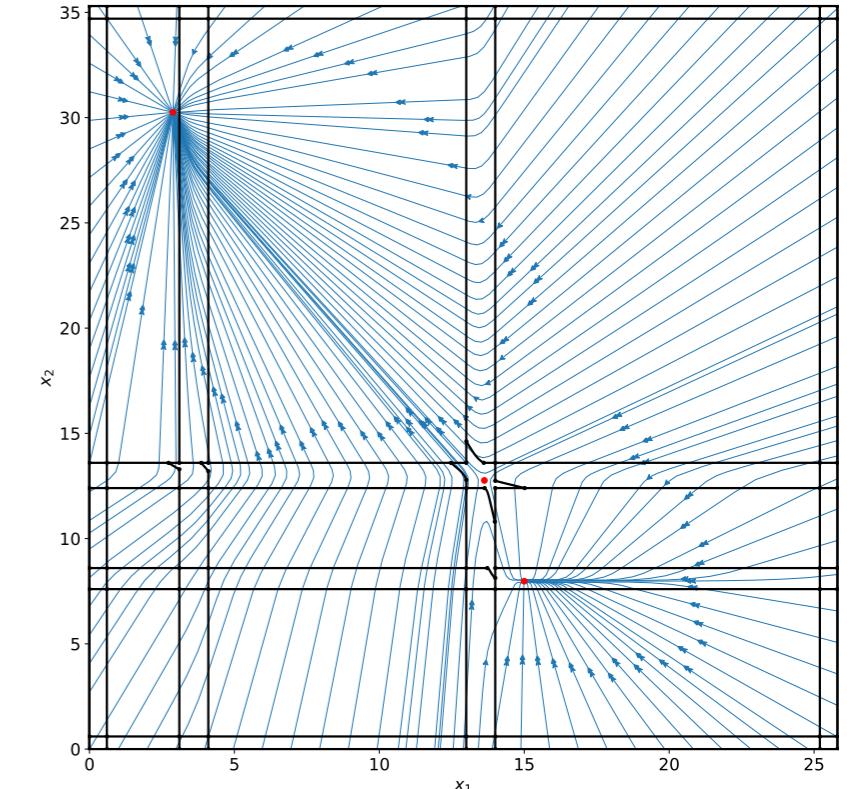
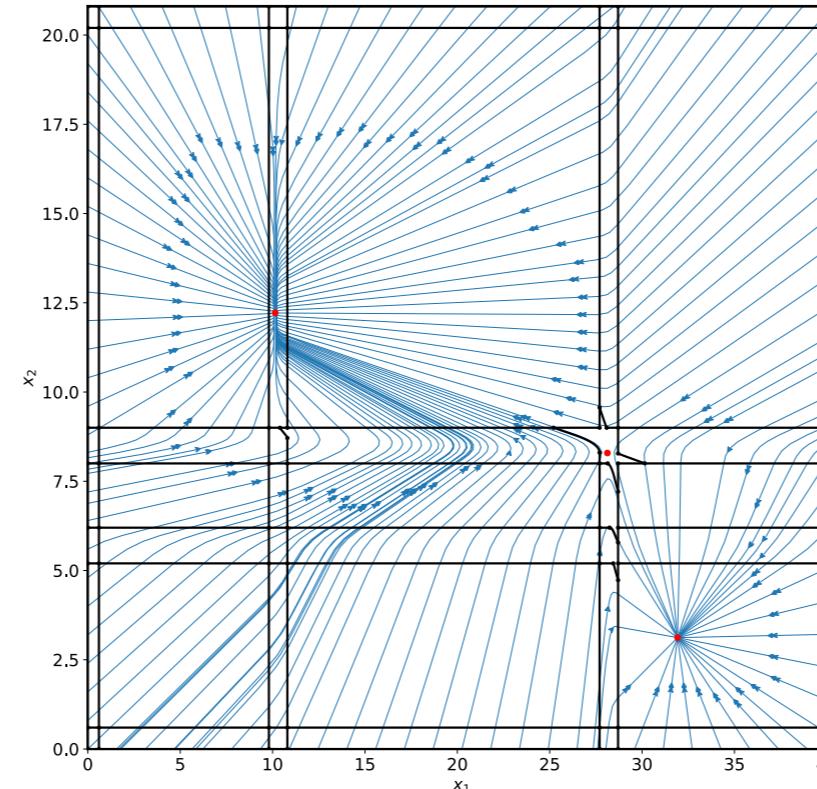
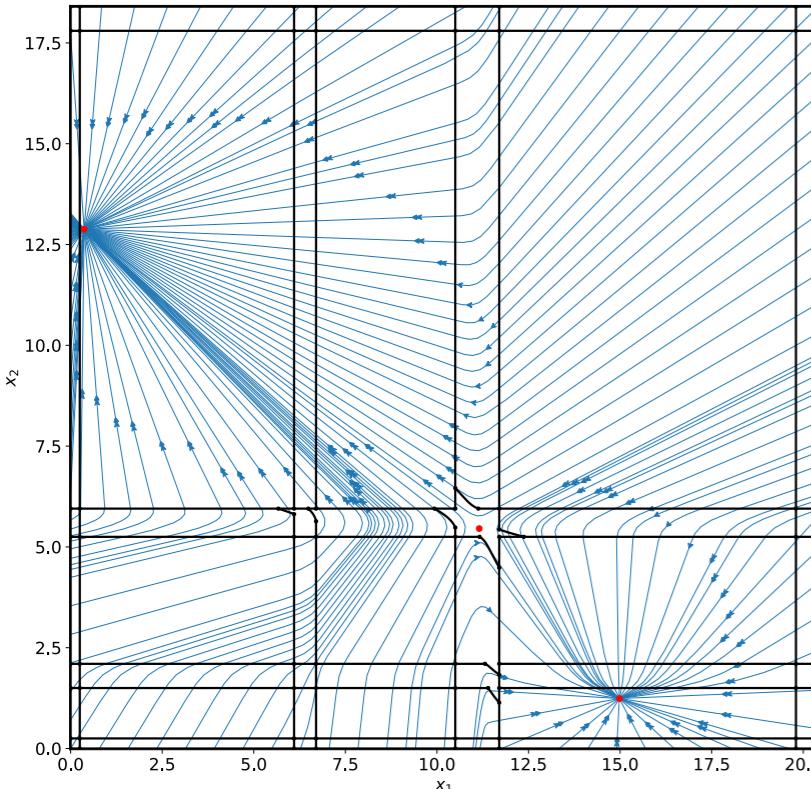


# Example

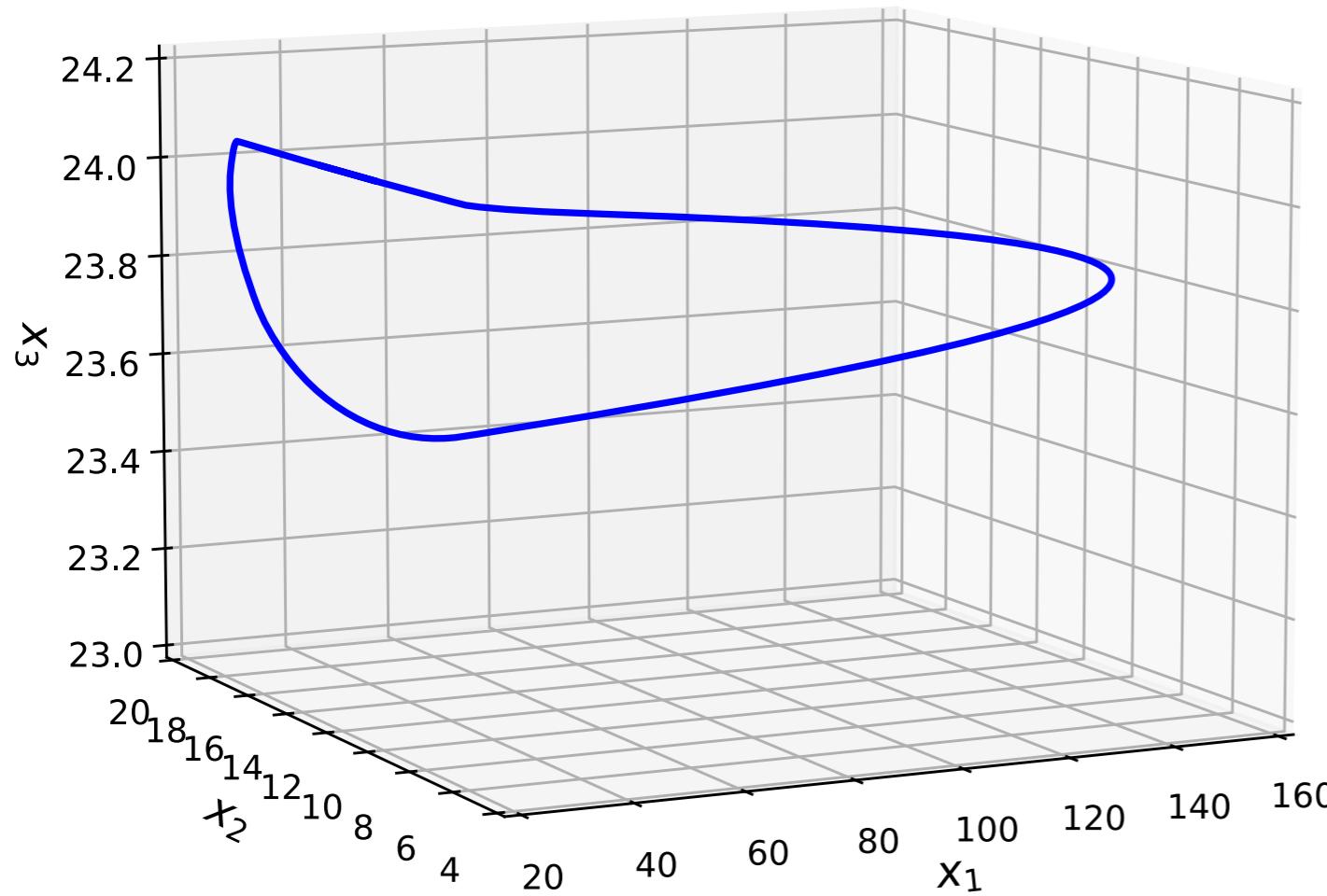
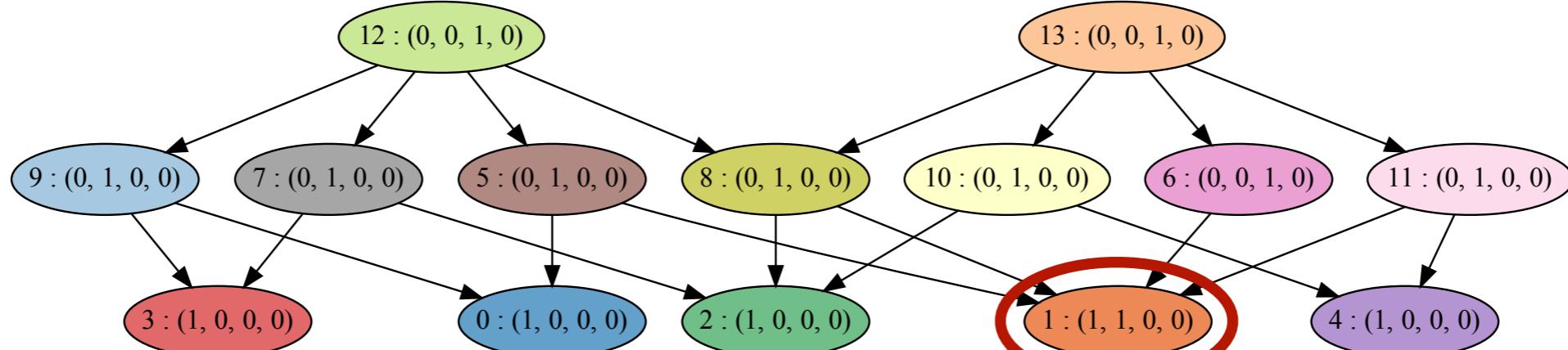
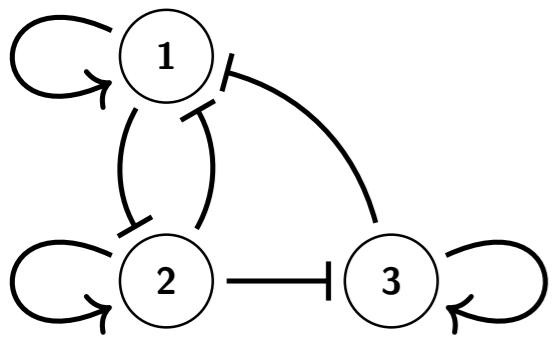


Parameter set 1	Parameter set 2	Parameter set 3
$\nu_{1,1,1} = 3.7, \nu_{1,1,2} = 1.4$	$\nu_{1,1,1} = 6.5, \nu_{1,1,2} = 4.2$	$\nu_{1,1,1} = 7.2, \nu_{1,1,2} = 5$
$\nu_{1,2,1} = 10.7, \nu_{1,2,2} = 0.1$	$\nu_{1,2,1} = 7.6, \nu_{1,2,2} = 1.7$	$\nu_{1,2,1} = 3, \nu_{1,2,2} = 0.4$
$\nu_{2,1,1} = 9.2, \nu_{2,1,2}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

## 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

$$\nu_{1,1} = (7, 3, 7, 3)$$

$$\theta_{1,1} = (3, 5.1, 7.17)$$

$$h_{1,1} = (0.15, 0.15, 0.15)$$

$$\nu_{1,2} = (3.1, 4.9, 7.3)$$

$$\theta_{1,2} = (5.3, 6.1)$$

$$h_{1,2} = (0.11, 0.11)$$

$$\nu_{2,1} = (7.5, 5.5, 4)$$

$$\theta_{2,1} = (4, 5.5)$$

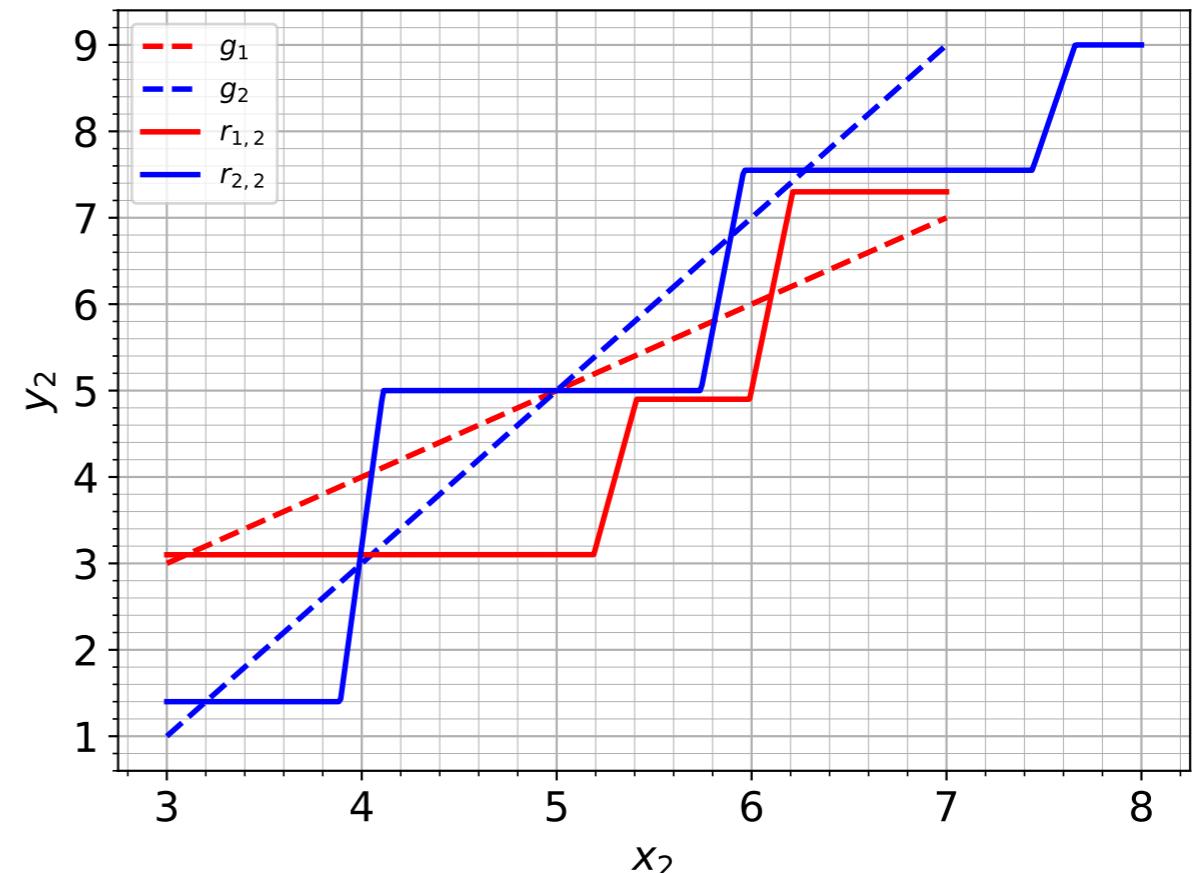
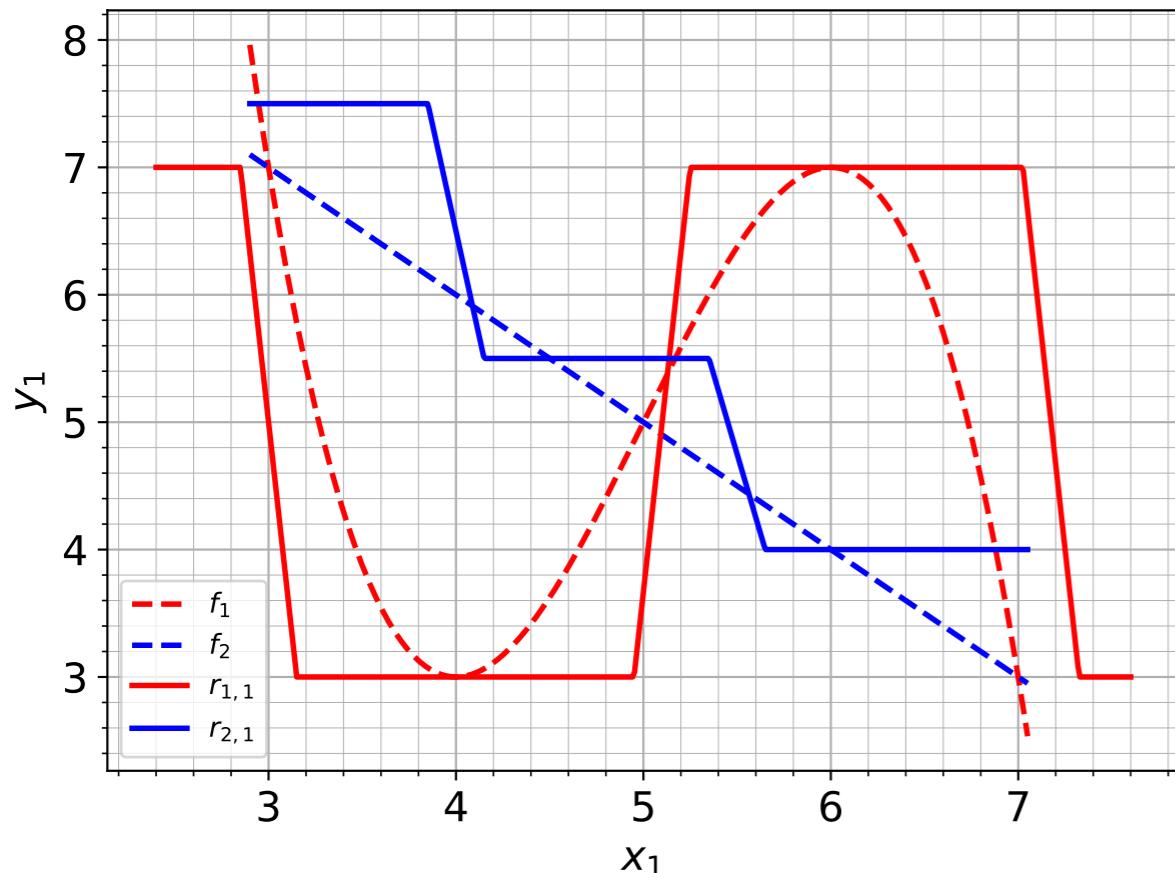
$$h_{2,1} = (0.15, 0.15)$$

$$\nu_{2,2} = (1.4, 5, 7.55, 9)$$

$$\theta_{2,2} = (4, 5.85, 7.55)$$

$$h_{2,2} = (0.11, 0.11, 0.11)$$

$$\gamma_1 = \gamma_2 = 2$$

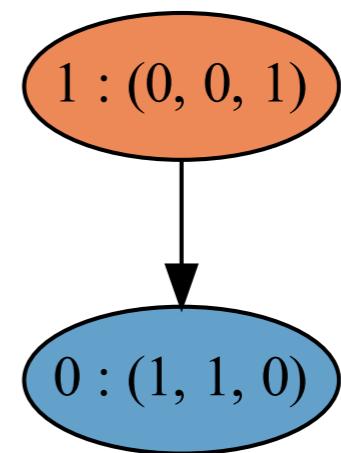
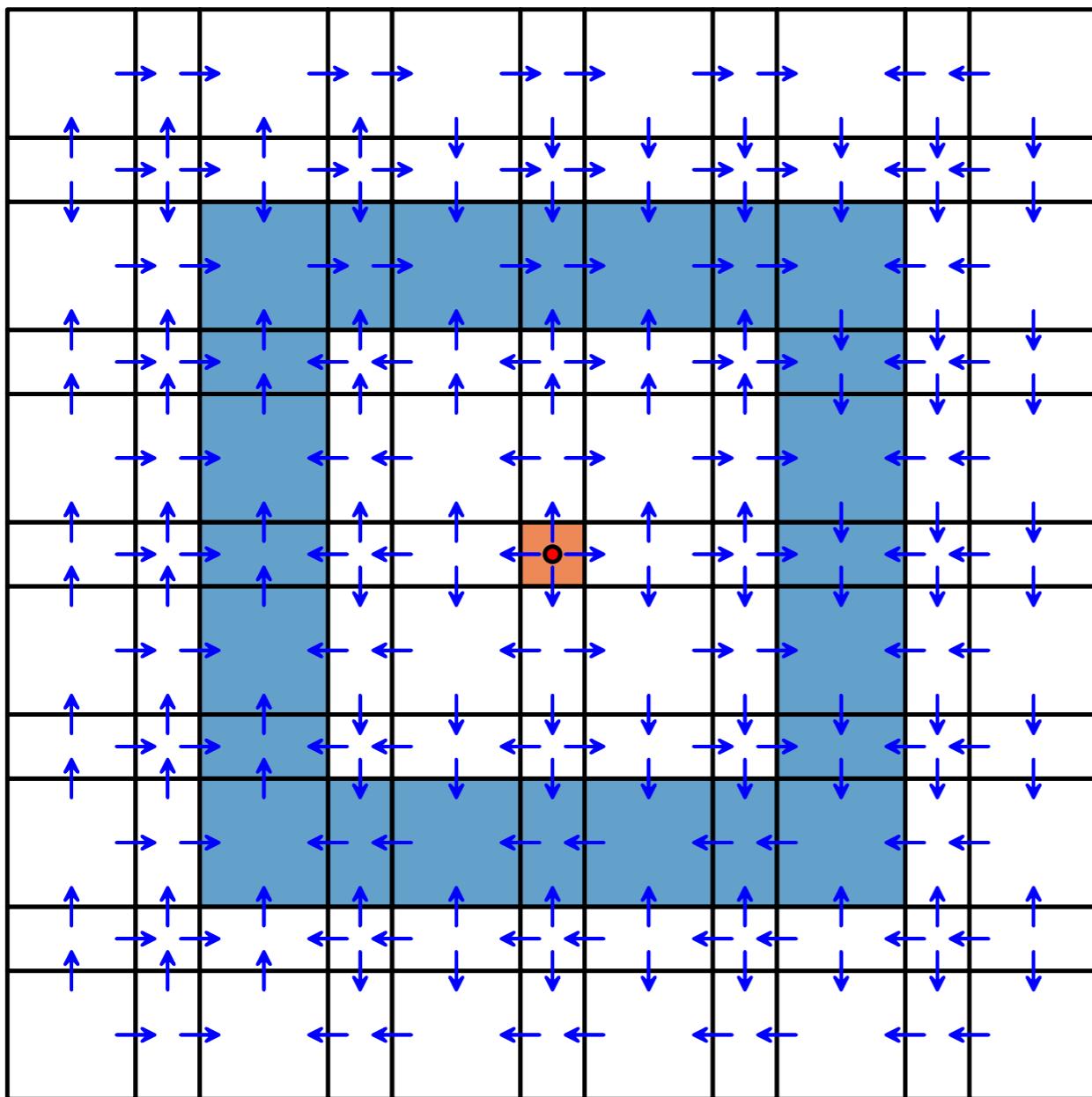


# Example

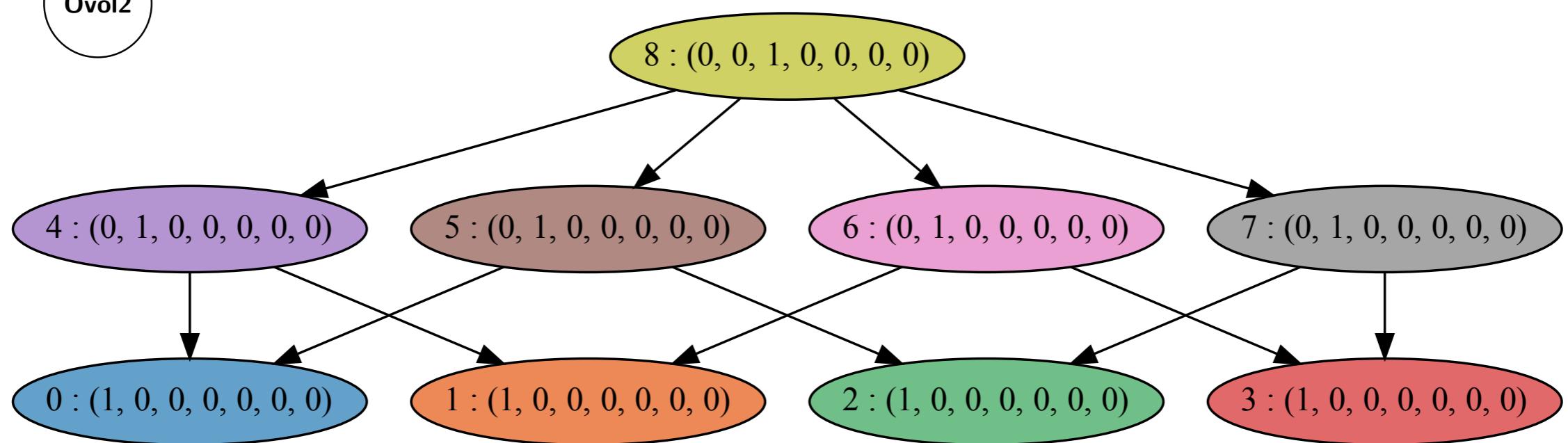
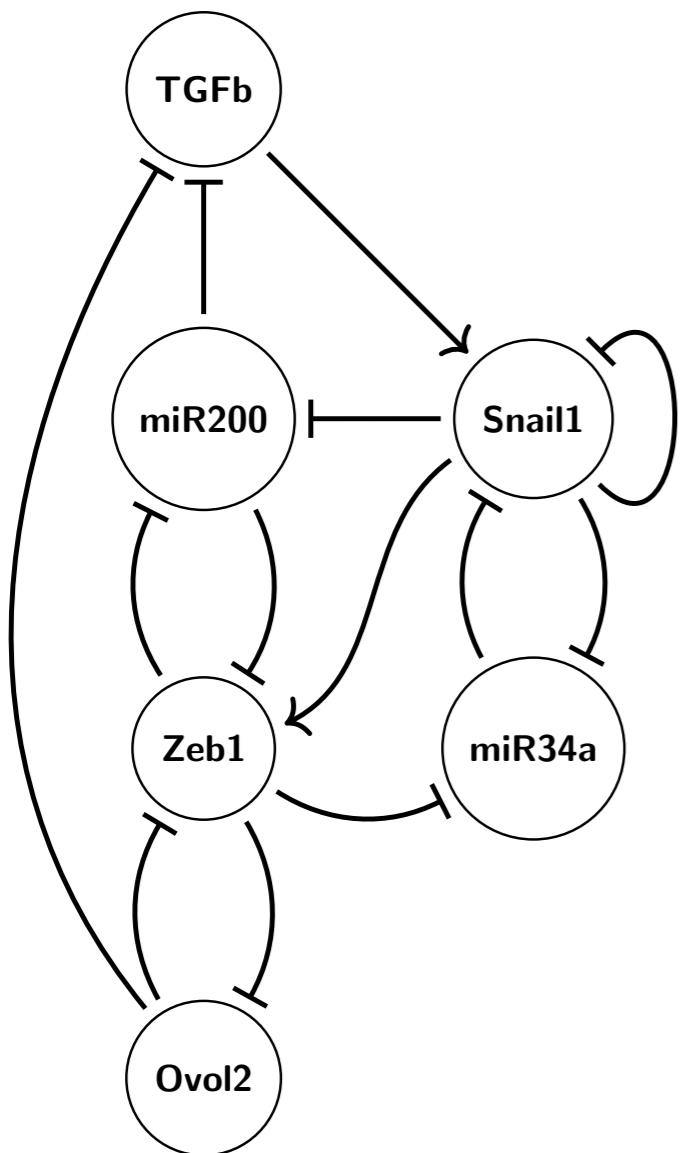
$$\dot{x}_1 = -\gamma_1 x_1 + r_{1,1}(x_1) + r_{1,2}(x_2)$$

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

Ramp system



# 6D Example



# More Examples

Jupyter Notebooks:

[https://github.com/marciogameiro/CDTutorial\\_CRM](https://github.com/marciogameiro/CDTutorial_CRM)

# Thank you for your attention!

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- 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>



National Institute of  
General Medical Sciences

