WFLS2024 WORKSHOP

A Study on

Three Node Motifs Yielding Pattern Formation

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Contents:

- Motivation/ objectives
- Background/introduction
- Methodology
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- Results and Conclusions
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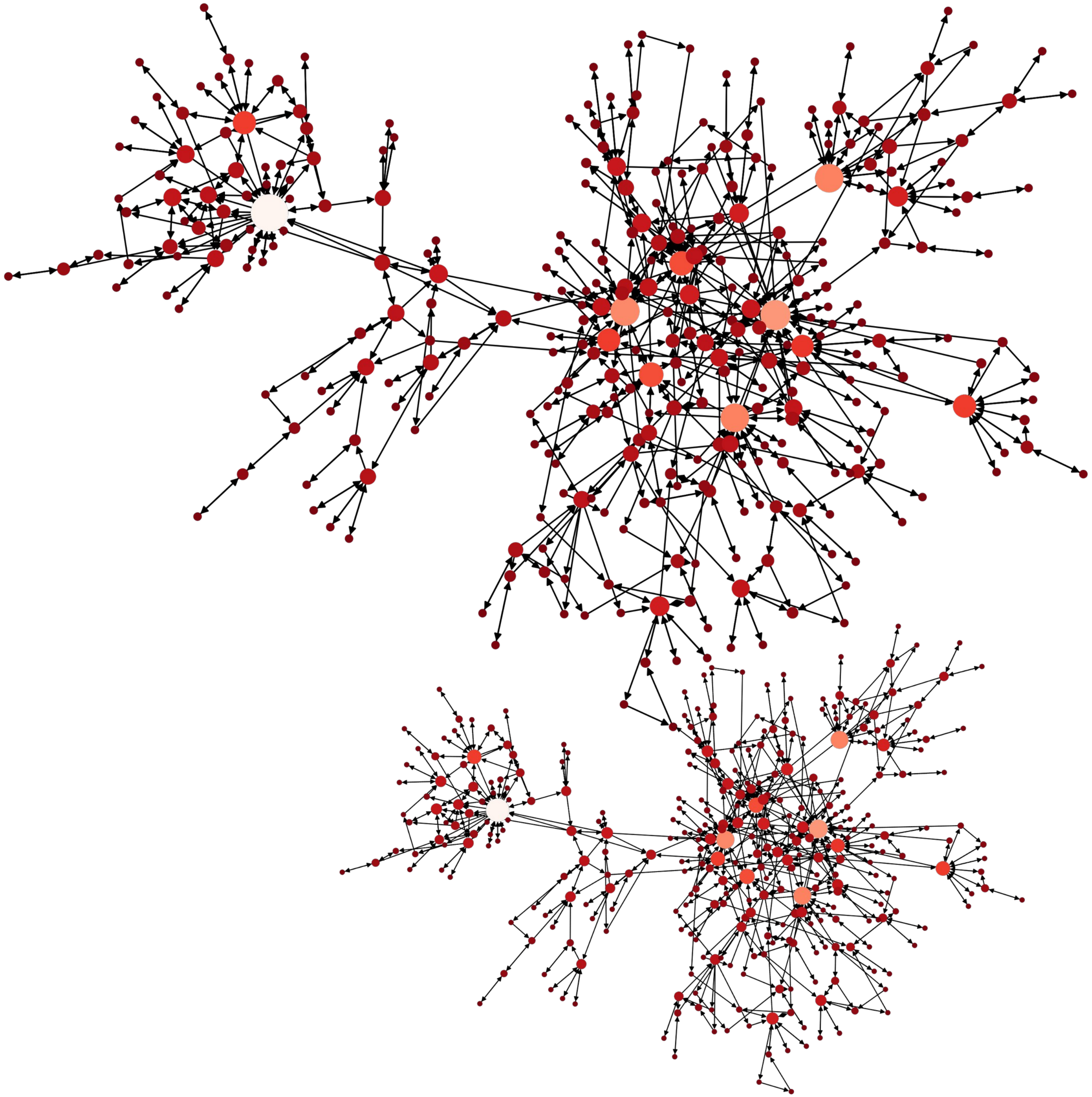
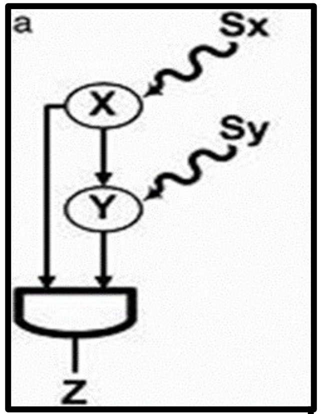


Objectives:

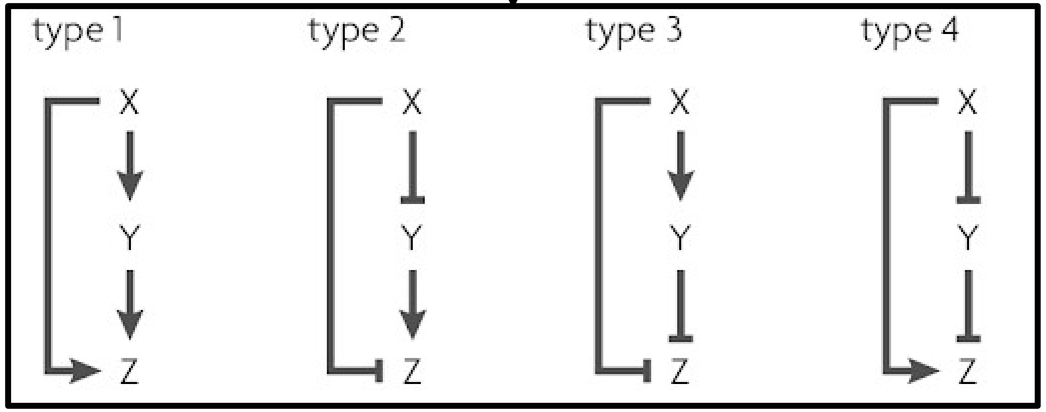
- FFLs confer to one of the most ***robust systems.***
- Associating them to pattern formation (symmetry breaking) would lead to ***spatiotemporally stable patterns***(crucial to development).
- Examining a ***hypothesis***: In a three-node motif (FFL with some alteration), enabling the output(Z) to diffuse spatially, may lead to pattern formation
- ***Expected observation***: some systematic heterogeneity to be observed at some scaling w.r.t. time and space(2D).

Feed-Forward Loops:

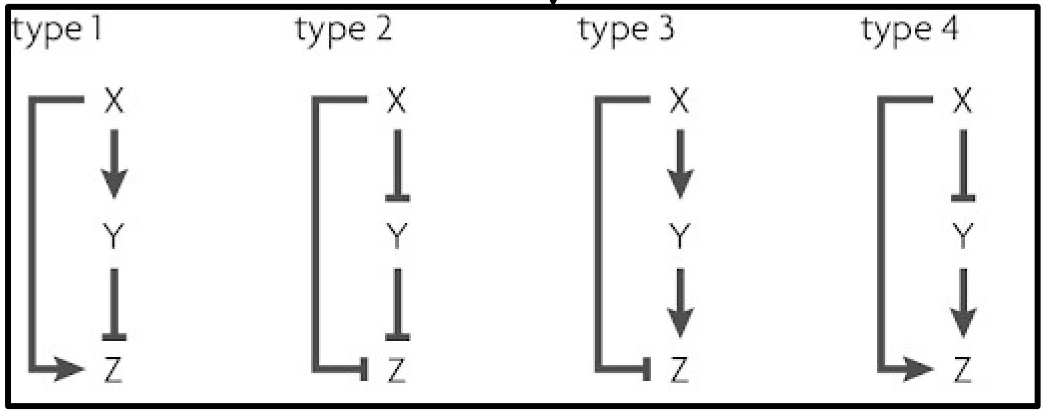


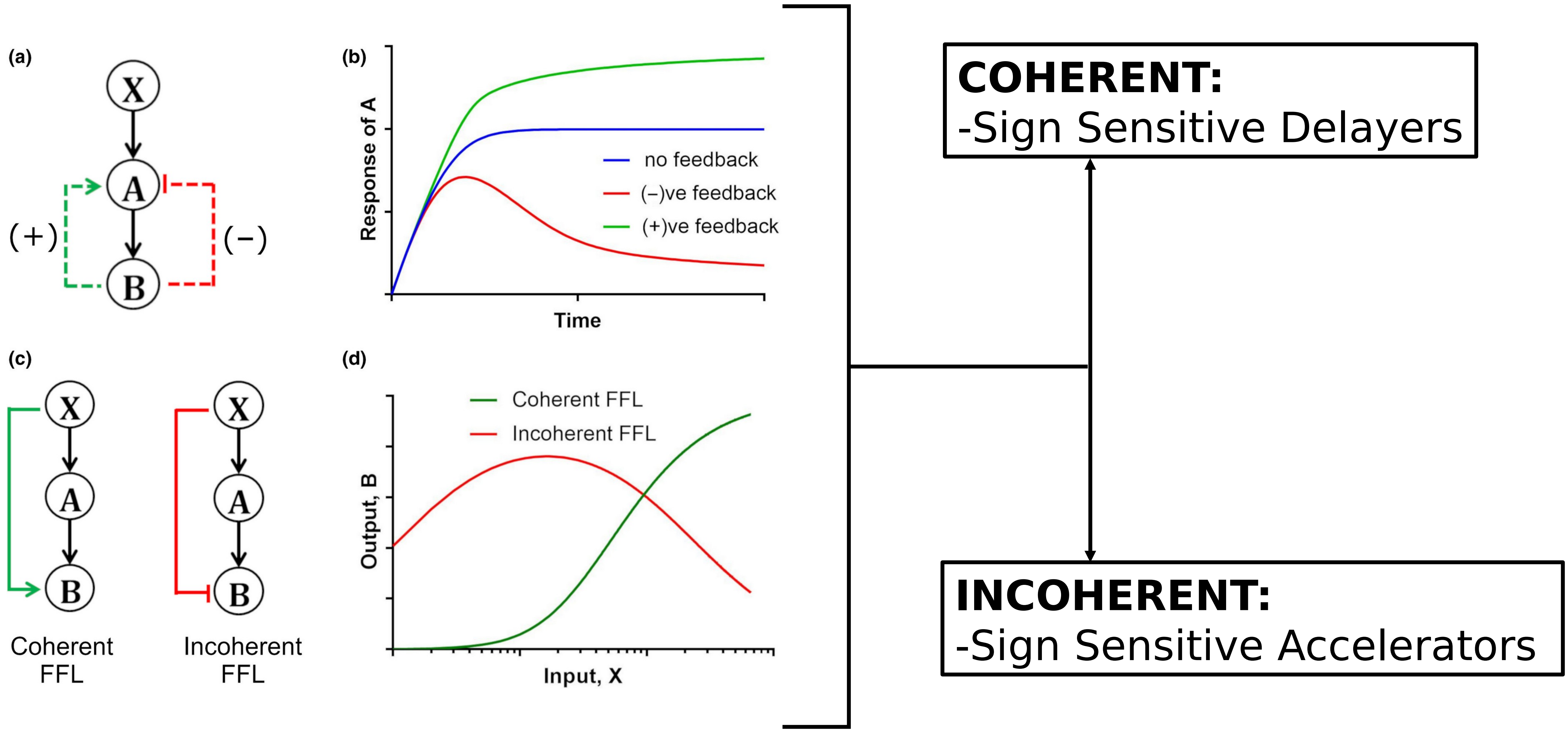
- -Three gene pattern
- -Two input transcription factors
- -Regulatory mechanism
- -Enhanced control systems
- -Unidirectional Flow
- -Optimization

Coherent (C)



Incoherent (I)




(a)
X
A
B
(+)
(−)
(b)
Response of A
Time
no feedback
(–)ve feedback
(+)ve feedback
(c)
X
A
B
Coherent FFL
Incoherent FFL
(d)
Coherent FFL
Incoherent FFL
Output, B
Input, X
COHERENT:
-Sign Sensitive Delayers
INCOHERENT:
-Sign Sensitive Accelerators

Methodology:

1.Considering all possible 3-node networks.
(Including the scope of NAR and PAR).

2.Hill's function to model the differential equations(rate equations) for the Factors at the three nodes.

3.An ODE model with:
input: 2 D lattice of initial concentrations
output: Pattern formation (expected)
parameters:
- Degradation rates (b_x , b_y , b_z)
- Scaling factor in Hills' function (k_x , k_y , k_z)
- Maximum rate of production (v_x , v_y , v_z)
- Hill's Coefficient (h_x , h_y , h_z)

4.
- Assigning sets of random initial conditions
- periodic boundary condition
- Tuning parameters

5.
- Visualizations
- Selection and eliminations

Mathematization of the Sample Networks:

Model system-1 (AND gate to Z)

1. $$\frac{dx}{dt} = v_x \left(\frac{k_z^{h_z}}{k_z^{h_z} + z^{h_z}} \right) - b_x \cdot x$$

2. $$\frac{dy}{dt} = v_y \left(\frac{x^{h_x}}{k_x^{h_x} + x^{h_x}} \right) - b_y \cdot y$$

3. $$\frac{dz}{dt} = v_z^2 \left(\frac{x^{h_x}}{k_x^{h_x} + x^{h_x}} \right) \left(\frac{y^{h_y}}{k_y^{h_y} + y^{h_y}} \right) - b_z \cdot z + D_z \cdot \nabla^2 z$$

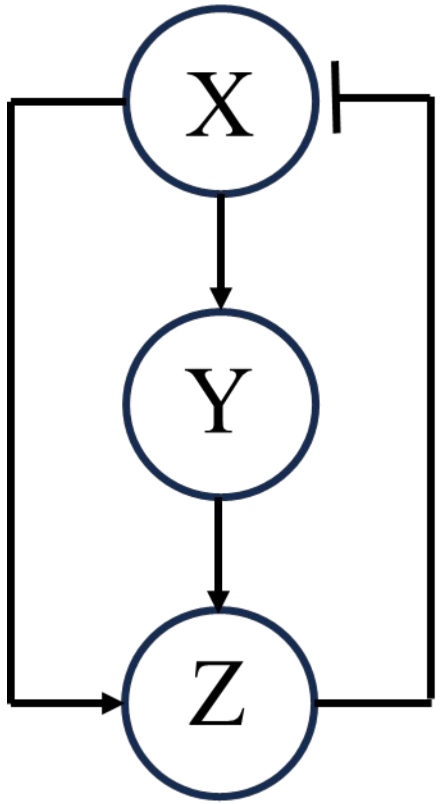


Fig.(a)

Model system-2 (AND gate to Z)

1. $$\frac{dx}{dt} = v_x \left(\frac{k_x^{h_x}}{k_x^{h_x} + x^{h_x}} + \frac{z^{h_z}}{k_z^{h_z} + z^{h_z}} \right) - b_x x$$

2. $$\frac{dy}{dt} = v_y \left(\frac{x^{h_x}}{k_x^{h_x} + x^{h_x}} \right) - b_y y$$

3. $$\frac{dz}{dt} = v_z^2 \left(\frac{x^{h_x}}{k_x^{h_x} + x^{h_x}} \right) \left(\frac{y^{h_y}}{k_y^{h_y} + y^{h_y}} \right) - b_z z + D_z \cdot \nabla^2 z$$

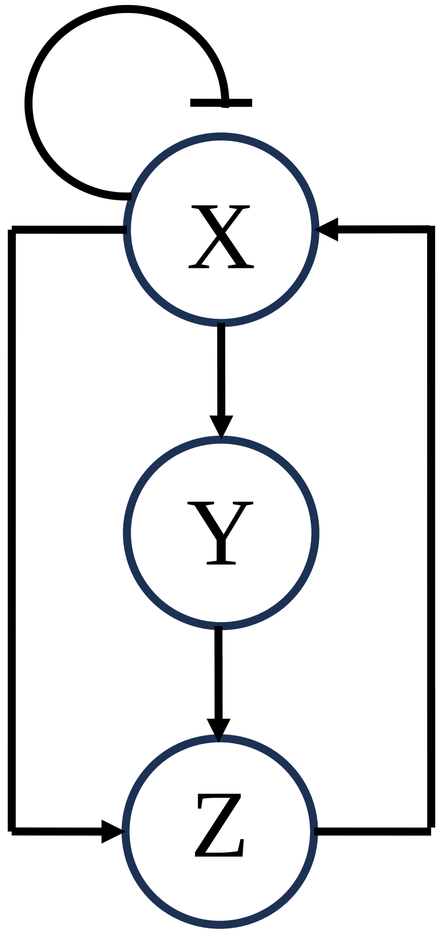


Fig.(b)

Model system-3 (OR gate to Z)

1. $\frac{dx}{dt} = -b_x x + \frac{v_x\left(\frac{z}{k_z}\right)^{h_z}}{1+\left(\frac{z}{k_z}\right)^{h_z}}$

2. $\frac{dy}{dt} = -b_y y + \frac{v_y}{1+\left(\frac{x}{k_x}\right)^{h_x}}$

3. $\frac{dz}{dt} = -b_z z + \frac{v_z\left(\left(\frac{x}{k_x}\right)^{h_x}+\left(\frac{y}{k_y}\right)^{h_y}\right)}{\left(\frac{x}{k_x}\right)^{h_x}+\left(\frac{y}{k_y}\right)^{h_y}+1} + D_z \cdot \nabla^2 z$

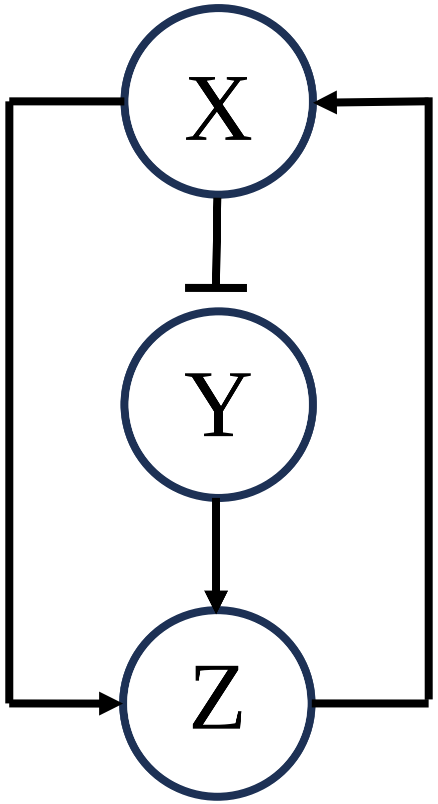
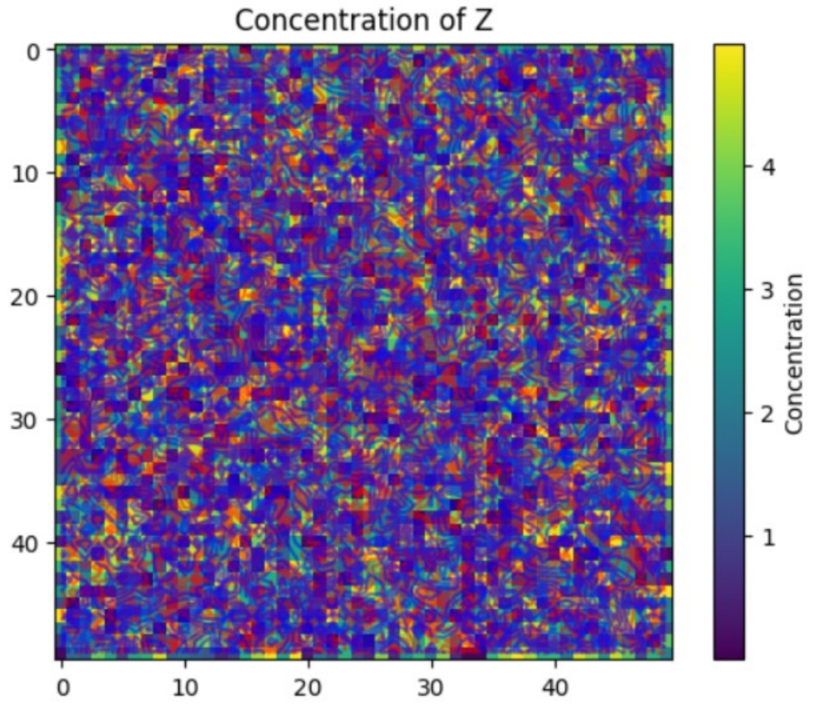
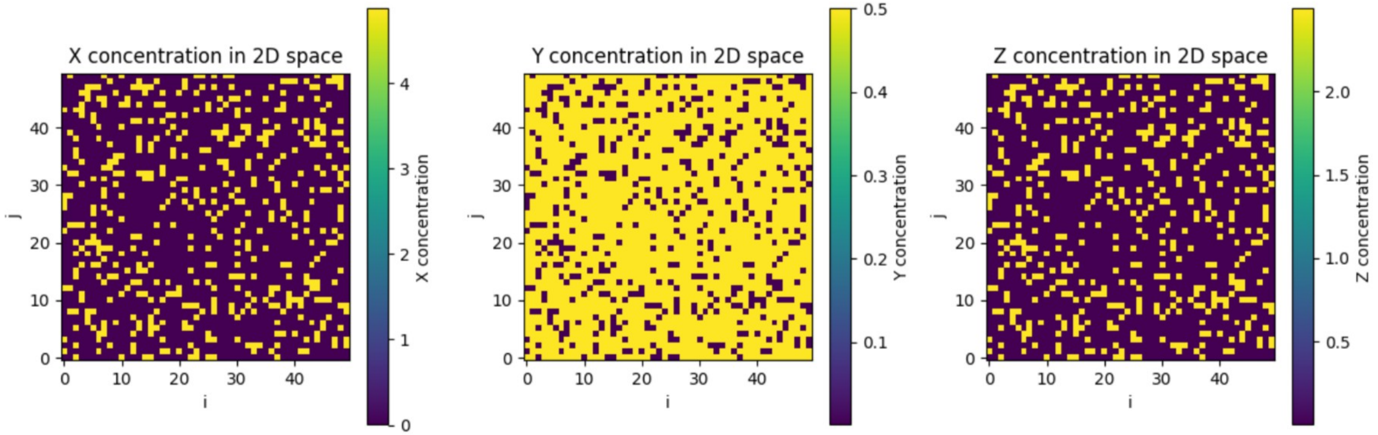


Fig.(c)

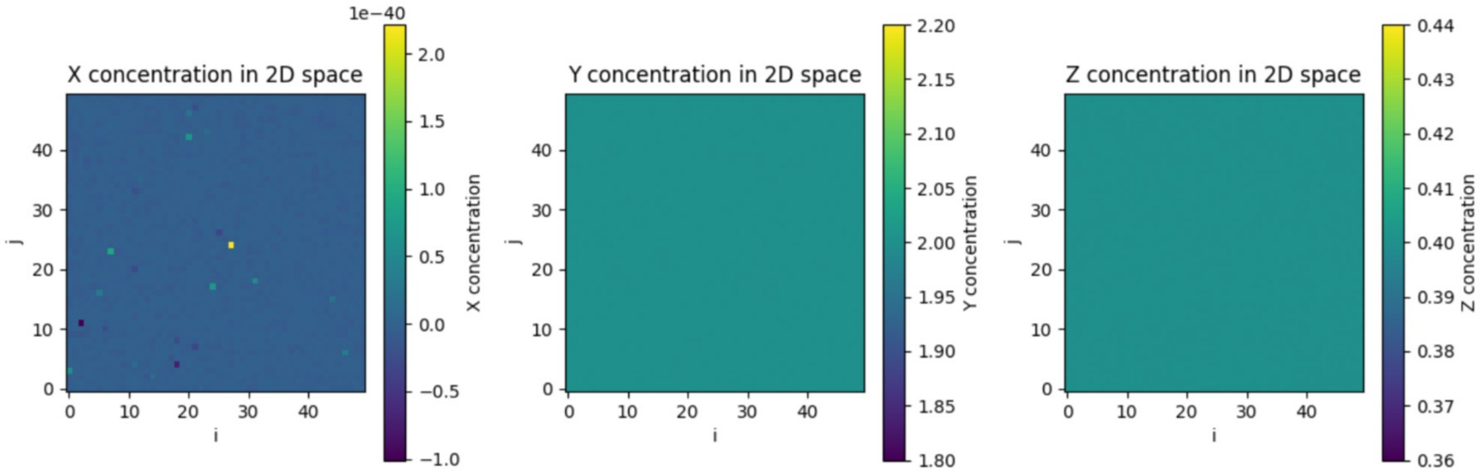


In the absence of diffusion when initial conditions are different for each cell. (x in red, y in blue, z based on the gradient)



Result for the network in **Fig.(c)**

(At 10000 time steps)



Result for the networks in **Fig.(a)** and **Fig(b)**

Future Aspects:

- Scan parameter space for stable pattern formation.
- Scan parameter space more thoroughly for other networks.
- Primarily ask the question “what network topologies are amenable to single morphogen patterning?”.

References:

Multistability, oscillations and bifurcations in feedback loops

Article *in* Mathematical Biosciences & Engineering · January 2010
DOI: 10.3934/mbe.2010.7.83 · Source: PubMed

2 authors:

Maria C.A. Leite
Yunjiao Wang

High-throughput mathematical analysis identifies Turing networks for patterning with equally diffusing signals

Luciano Marcon[1], Xavier Diego[2,3], James Sharpe[2,3,4], Patrick Müller[1*]

Cell Systems

Article

Periodic spatial patterning with a single morphogen

Graphical abstract

Authors

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