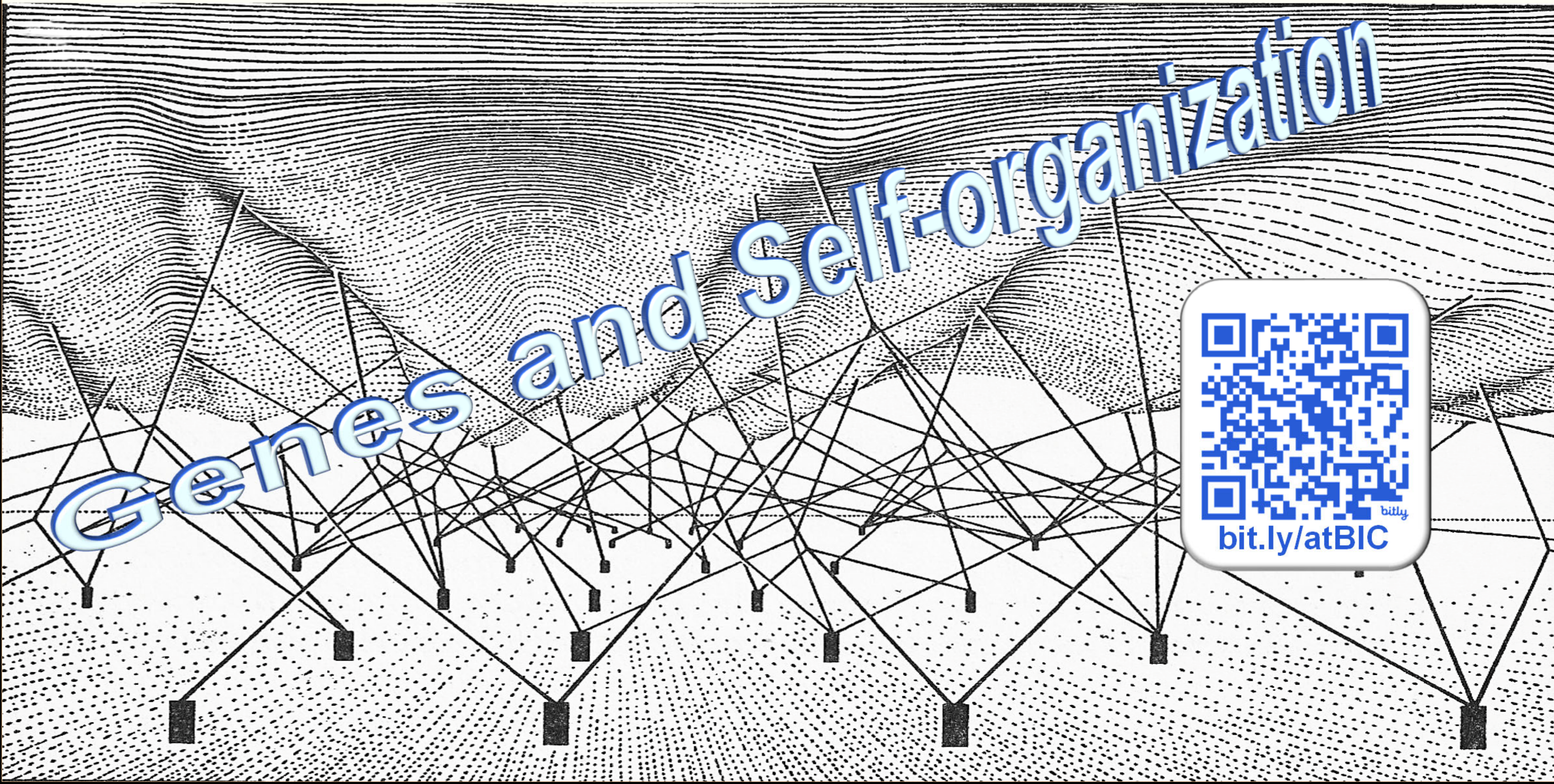
lecture 10

Genes and Self-organization



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key events coming up

- Labs: 35% (ISE-483)
  - Complete 5 (best 4 graded) assignments based on algorithms presented in class
    - Lab 3: March 11th
      - Cellular Automata and Boolean Networks (Assignment 3)
        - Delivered by SSIE583 Group 3
        - Due: March 18th
- SSIE – 583 -Presentation and Discussion: 25%
  - Present and lead the discussion of an article related to the class materials
    - Enginet students post/send video or join by Zoom
  - Dates TBA
    - Conrad, M. [1990]. "The geometry of evolution.“ *Biosystems* **24**: 61-81.
      - Mario Franco
    - Stanley, Kenneth O., Jeff Clune, Joel Lehman, and Risto Miikkulainen. “Designing Neural Networks through Neuroevolution.” *Nature Machine Intelligence* **1**, no. 1 (January 2019): 24–35.
      - Jessica Lasebikan
    - Lindgren, K. [1991]."Evolutionary Phenomena in Simple Dynamics." In: *Artificial Life II*. Langton et al (Eds). Addison-wesley, pp. 295-312.
      - Akshay Gangadhar
    - Salahshour, Mohammad. “Interaction between Games Give Rise to the Evolution of Moral Norms of Cooperation.” *PLOS Computational Biology* **18**, no. 9 (September 29, 2022): e1010429
      - Srikanth Iyer
    - Discussion by all

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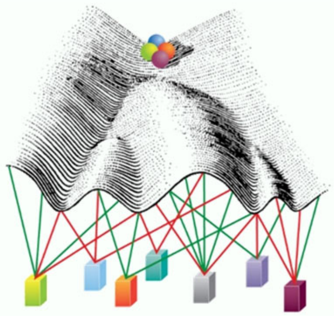
until now

- Class Book
  - Floreano, D. and C. Mattiussi [2008]. *Bio-Inspired Artificial Intelligence: Theories, Methods, and Technologies*. MIT Press. Preface, **Chapter 2.**
    - Nunes de Castro, Leandro [2006]. *Fundamentals of Natural Computing: Basic Concepts, Algorithms, and Applications*. Chapman & Hall. **Chapter 1,** pp. 1-23. Chapter 7, sections **7.1-7.4**, **Appendix B.3.1**, **Chapter 2**, Chapter 8, sections **8.1, 8.2, 8.3.10**
- Lecture notes
  - Chapter 1: What is Life?
  - Chapter 2: The logical Mechanisms of Life
  - Chapter 3: Formalizing and Modeling the World
  - Chapter 4: Self-Organization and Emergent Complex Behavior
    - posted online @ http://informatics.indiana.edu/rocha/i-bic
- Papers and other materials
  - Dynamical Systems
    - Kauffman, S.A. [1969]. "Metabolic stability and epigenesis in randomly constructed genetic nets". Journal of Theoretical Biology 22(3):437-467.
  - Optional
    - Prusinkiewicz and Lindenmeyer [1996] *The algorithmic beauty of plants*.
      - Chapter 1
    - Flake's [1998], *The Computational Beauty of Life*. MIT Press.
      - Chapters 10, 11, 14 – Dynamics, Attractors and chaos



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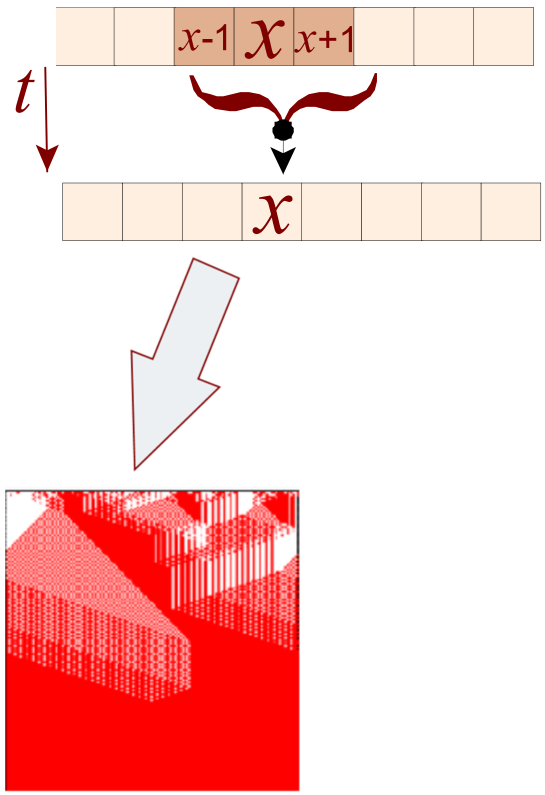
- Projects
  - Due by May 6th in Brightspace, "Final Project Paper" assignment
    - ALIFE 2023
      - Not to submit to actual conference due date (April 3rd , 2024)
      - https://2024.alife.org/
      - 8 pages, author guidelines:
      - https://2024.alife.org/call_paper.html
      - MS Word and Latex/Overleaf templates
    - Preliminary ideas **by March 15**
      - Submit to "Project Idea" assignment in Brightspace.
  - Individual or group
    - With very definite tasks assigned per member of group

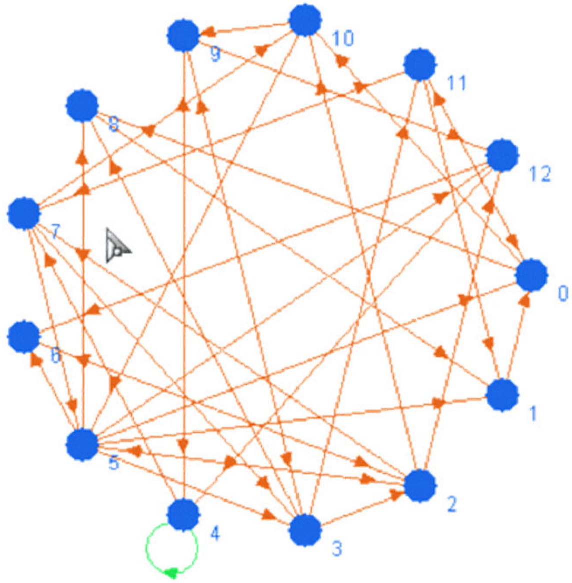
ALIFE 2024

Tackle a real problem using bio-inspired algorithms, such as those used in the labs.

examples

Cellular Automata





NK Boolean Network (N=13, K=3)

the drosophila segment polarity network

Based on the ODE model of von Dassow et al. (2000), consists of 4-cell parasegments, each cell with 15 interacting genes and proteins.

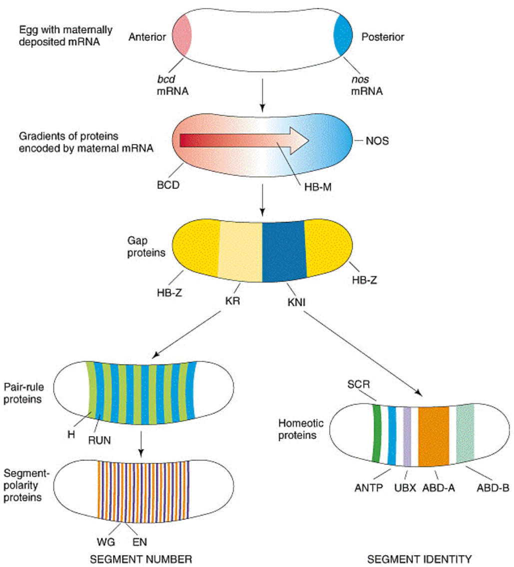
2^{60} network configurations

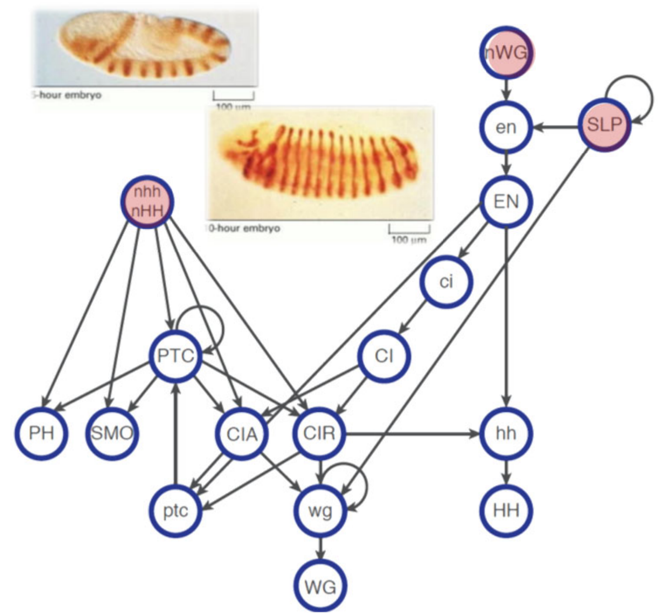
Reproduces wild-type and mutant gene expression patterns in development of fruit fly

2 intercellular inputs: **nhh** (*hedgehog*), **nWG** (*wingless*)

1 intracellular input: **SLP** (*sloppy paired*)

Node	*State – TransitionFunction*
SLP_i^{t+1}	$\leftarrow 0 \text{ if } i=1 \vee i=2; 1 \text{ if } i=3 \vee i=4;$
wg_i^{t+1}	$\leftarrow (CIA_i^t \wedge SLP_i^t \wedge \neg CIR_i^t) \vee (wg_i^t \wedge (CIA_i^t \vee SLP_i^t) \wedge \neg CIR_i^t)$
WG_i^{t+1}	$\leftarrow wg_i^t$
en_i^{t+1}	$\leftarrow (WG_{i-1}^t \vee WG_{i+1}^t) \wedge \neg SLP_i^t$
EN_i^{t+1}	$\leftarrow en_i^t$
hh_i^{t+1}	$\leftarrow EN_i^t \wedge \neg CIR_i^t$
HH_i^{t+1}	$\leftarrow hh_i^t$
ptc_i^{t+1}	$\leftarrow CIA_i^t \wedge \neg EN_i^t \wedge \neg CIR_i^t$
PTC_i^{t+1}	$\leftarrow ptc_i^t \vee (PTC_i^t \wedge \neg HH_{i-1}^t \wedge \neg HH_{i-1}^t)$
PH_i^t	$\leftarrow PTC_i^t \wedge (HH_{i-1}^t \vee HH_{i+1}^t)$
SMO_i^t	$\leftarrow \neg PTC_i^t \vee (HH_{i-1}^t \vee HH_{i+1}^t)$
ci_i^{t+1}	$\leftarrow \neg EN_i^t$
CI_i^{t+1}	$\leftarrow ci_i^t$
CIA_i^{t+1}	$\leftarrow CI_i^t \wedge (\neg PTC_i^t \vee hh_{i-1}^t \vee hh_{i+1}^t \vee HH_{i-1}^t \vee HH_{i+1}^t)$
CIR_i^{t+1}	$\leftarrow CI_i^t \wedge PTC_i^t \wedge \neg hh_{i-1}^t \wedge \neg hh_{i+1}^t \wedge \neg HH_{i-1}^t \wedge \neg HH_{i+1}^t$





Albert & Othmer [2003]. *J. Theor. Bio.* **223**: 1-18.

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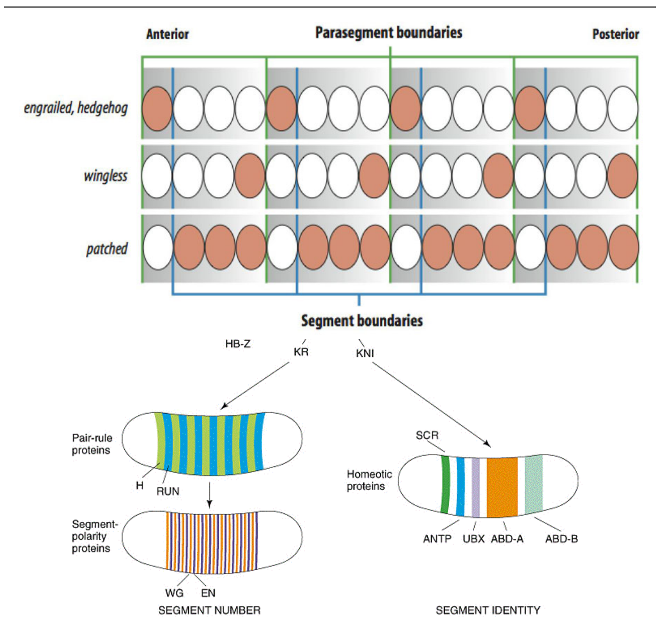
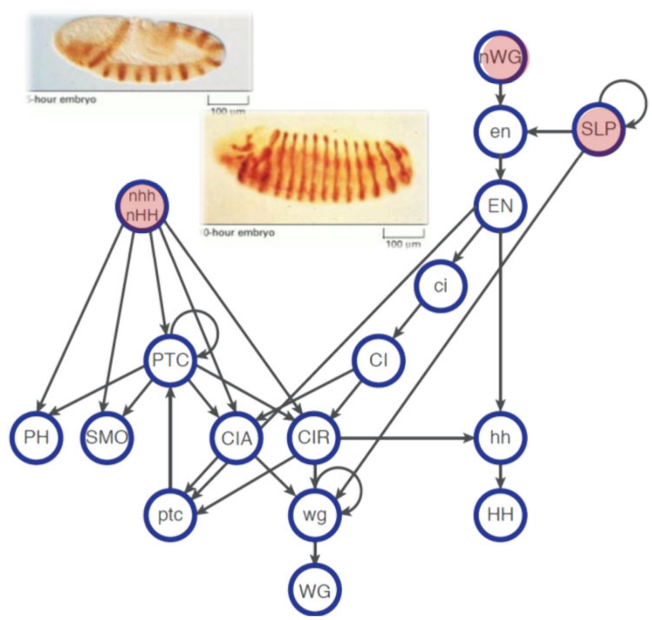
CIR_i^{t+1}	$\leftarrow CI_i^t \wedge PTC_i^t \wedge \neg hh_{i-1}^t \wedge \neg hh_{i+1}^t \wedge \neg HH_{i-1}^t \wedge \neg HH_{i+1}^t$





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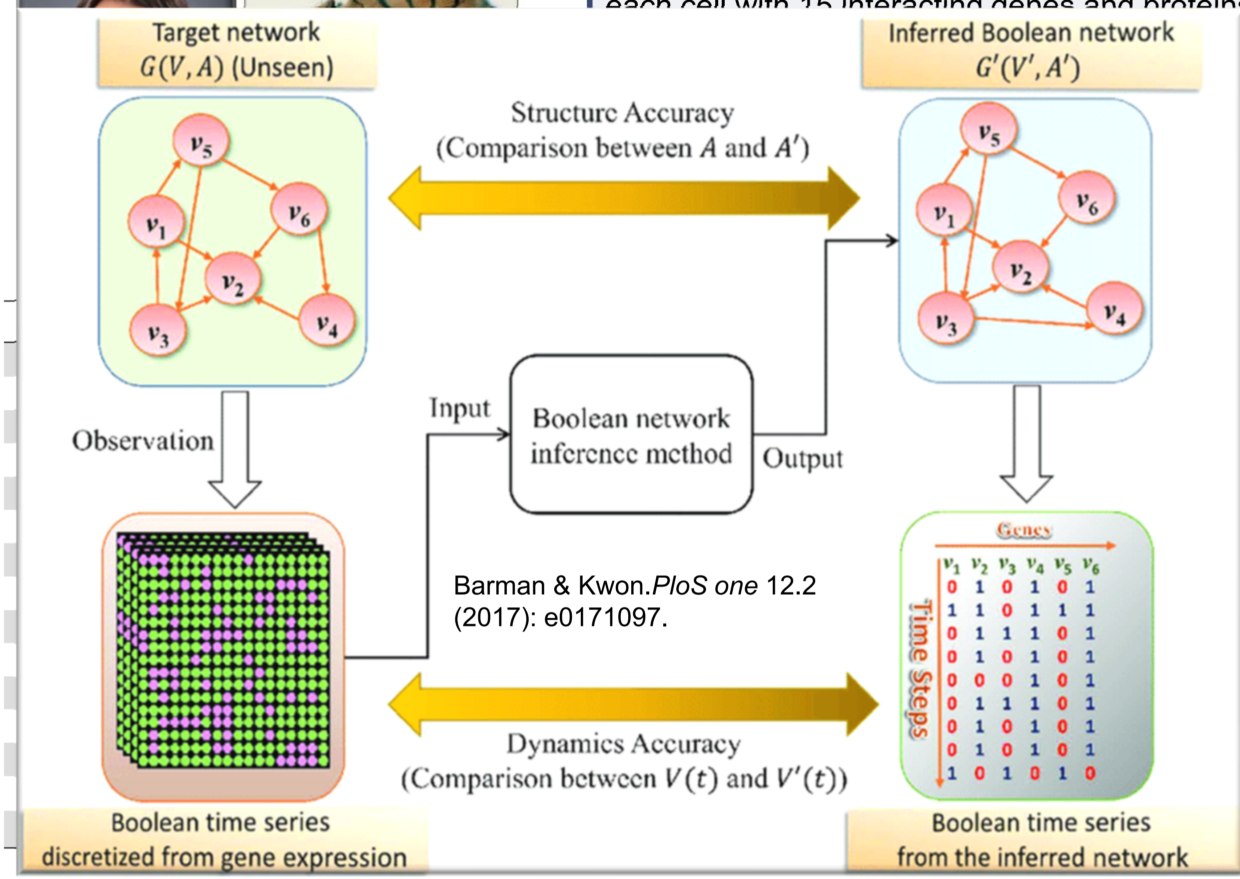
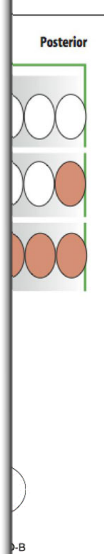
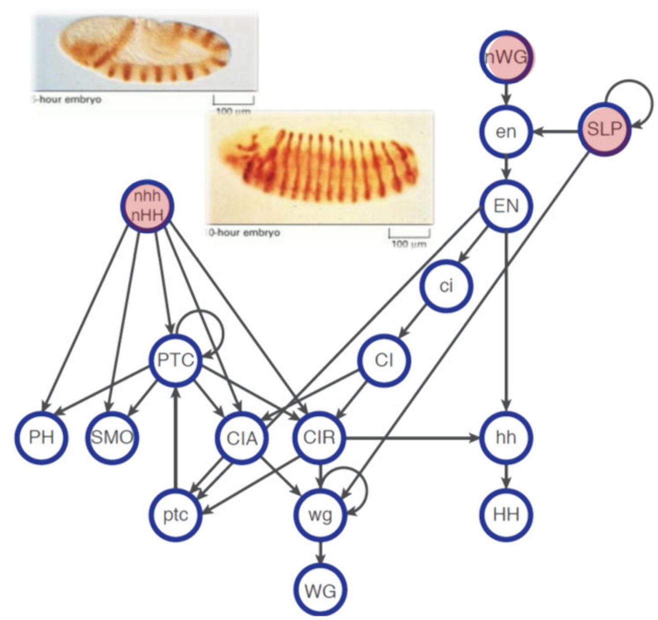


Barman & Kwon. *PloS one* 12.2 (2017): e0171097.





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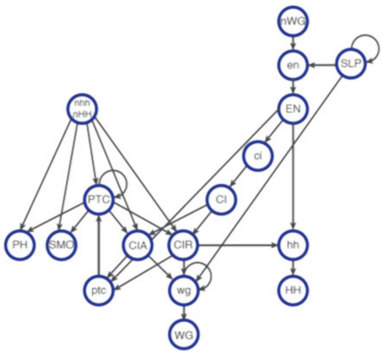
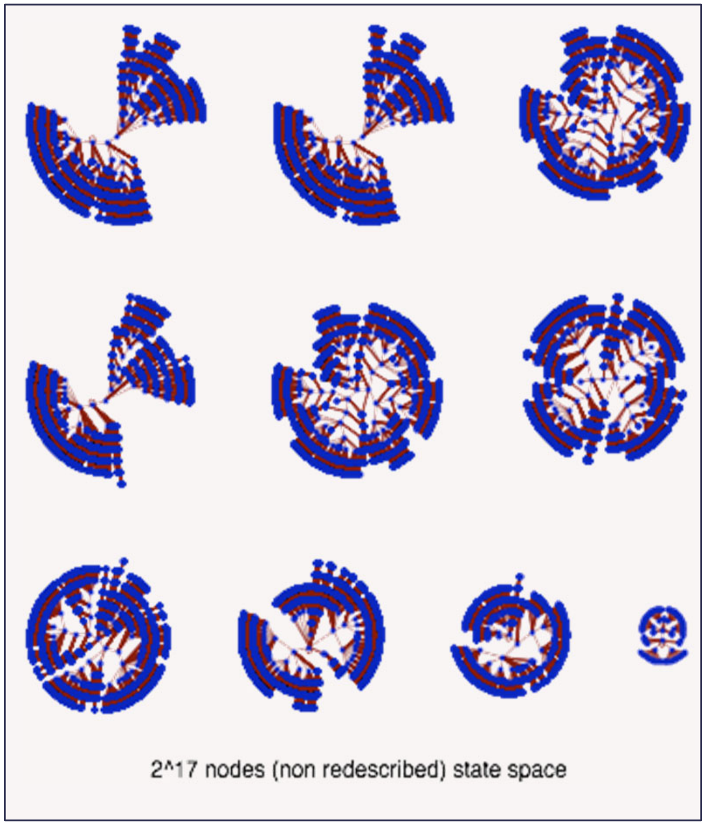
cell-types in a spatial arrangement





- Observing the state-transition graph
  - converges to one of 10 possible stable configurations
    - Steady-state attractors
- observed experimentally
  - wildtype
    - plus 3 variants
  - broad stripe
  - no-segmentation
  - Ectopic
    - plus 3 variants

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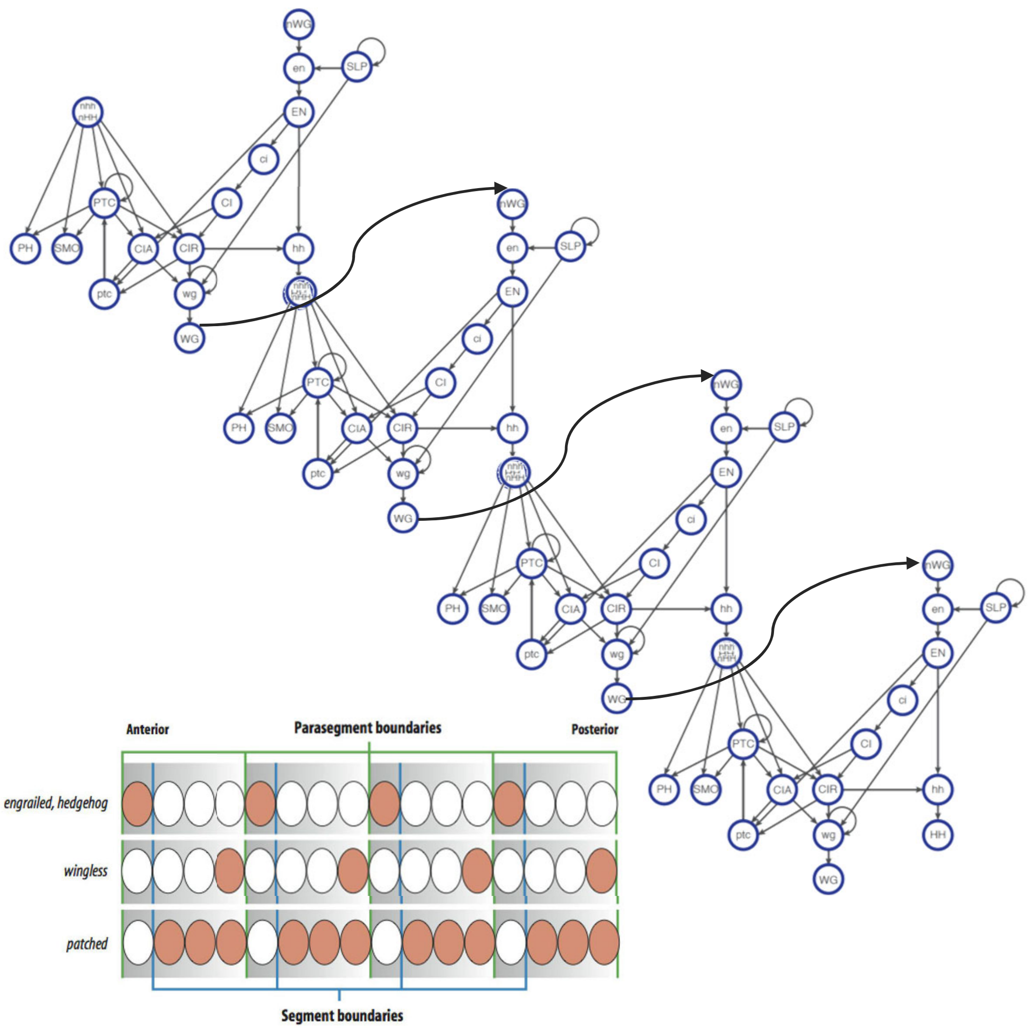

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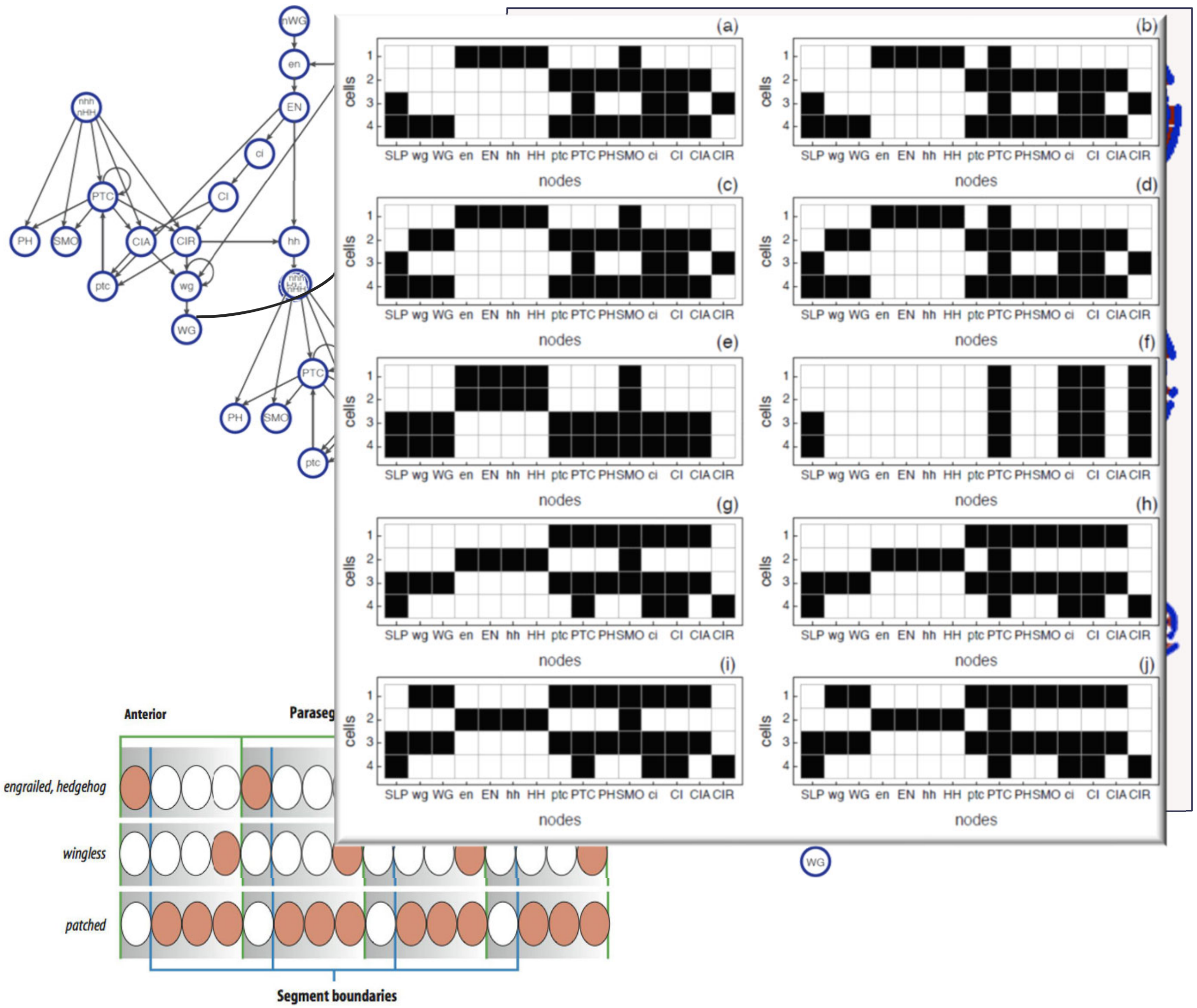

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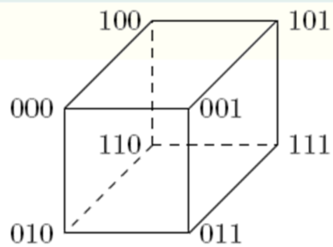
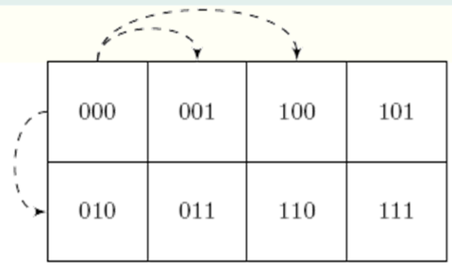
higher-dimensional hyper-cube representations

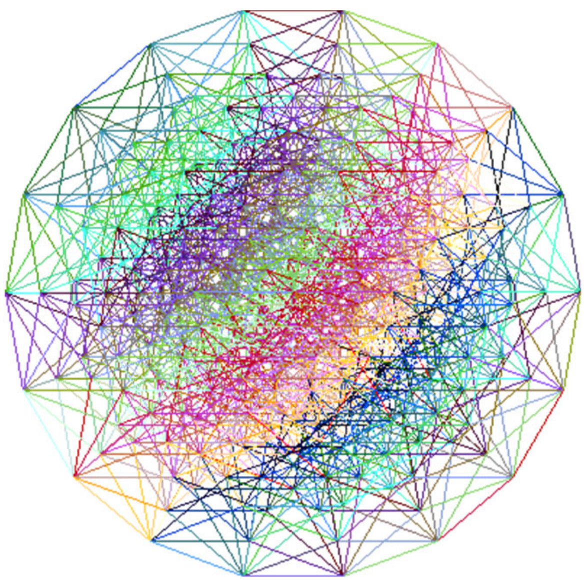


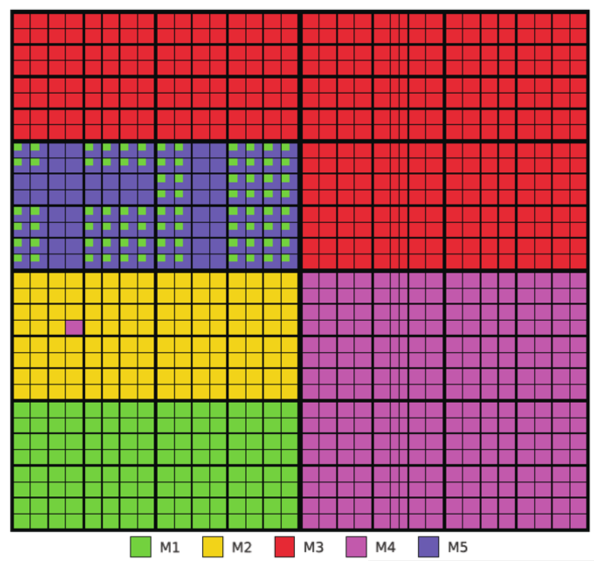


Planar representation

16 state drosophila segment polarity network (from Willadsen and Wiles , 2007

9-dimension representation





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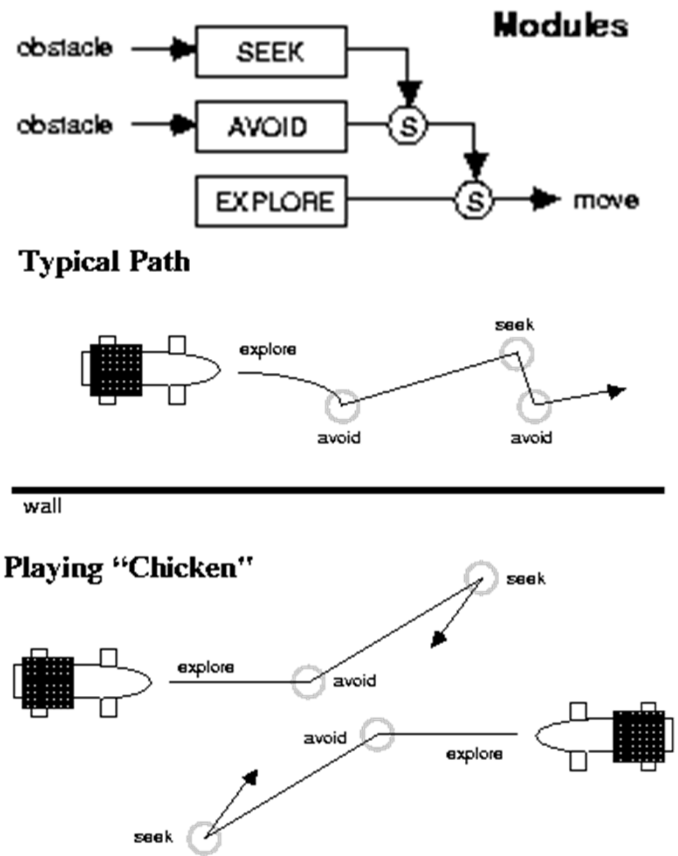
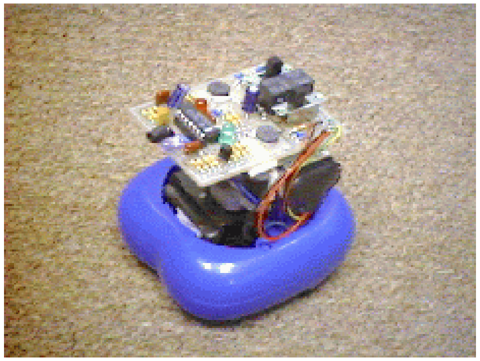
Robot example





Jonathan Connell 's Muramator

- Emergent Behavior from system/environment coupling
  - Classifies Walls and Other Robots
  - Self-organization
  - Embodied cognition

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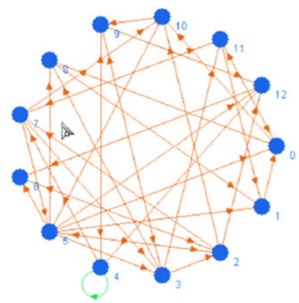
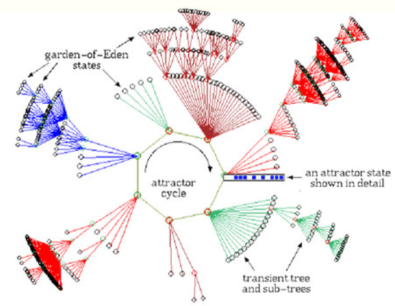
self-organization





- Discrete dynamical systems
  - Extremely large number o coupled elements
  - Systems of binary variables (0,1), coupled to one another in a network
    - The activity of each element depends on previous state of other elements
  - Simplifies continuous systems while maintaining essential behavior
- Statistical properties of sets of networks
  - Understanding of macroscopic, emergent properties
    - Similar to temperature
- Typically irreversible

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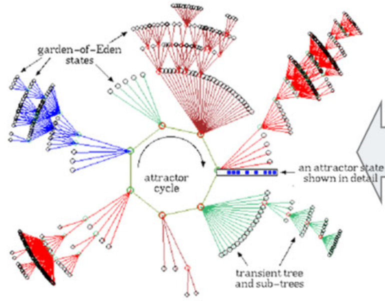
biological interpretations of attractor behavior

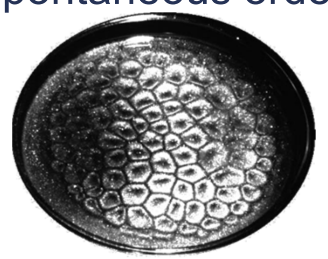
self-organization

- Genetic regulatory networks
  - Genes are on or off
  - Development, morphogenesis
  - Attractors interpreted as different cell types
- Classification in Immune networks
- Representation in artificial neural networks
- Stable patterns of species abundances in ecosystems

attractors



spontaneous order



To be improved by natural selection

Order is the raw material for evolution: how much of life is Natural Selection and how much is self-organization? (*credit assignment problem*)

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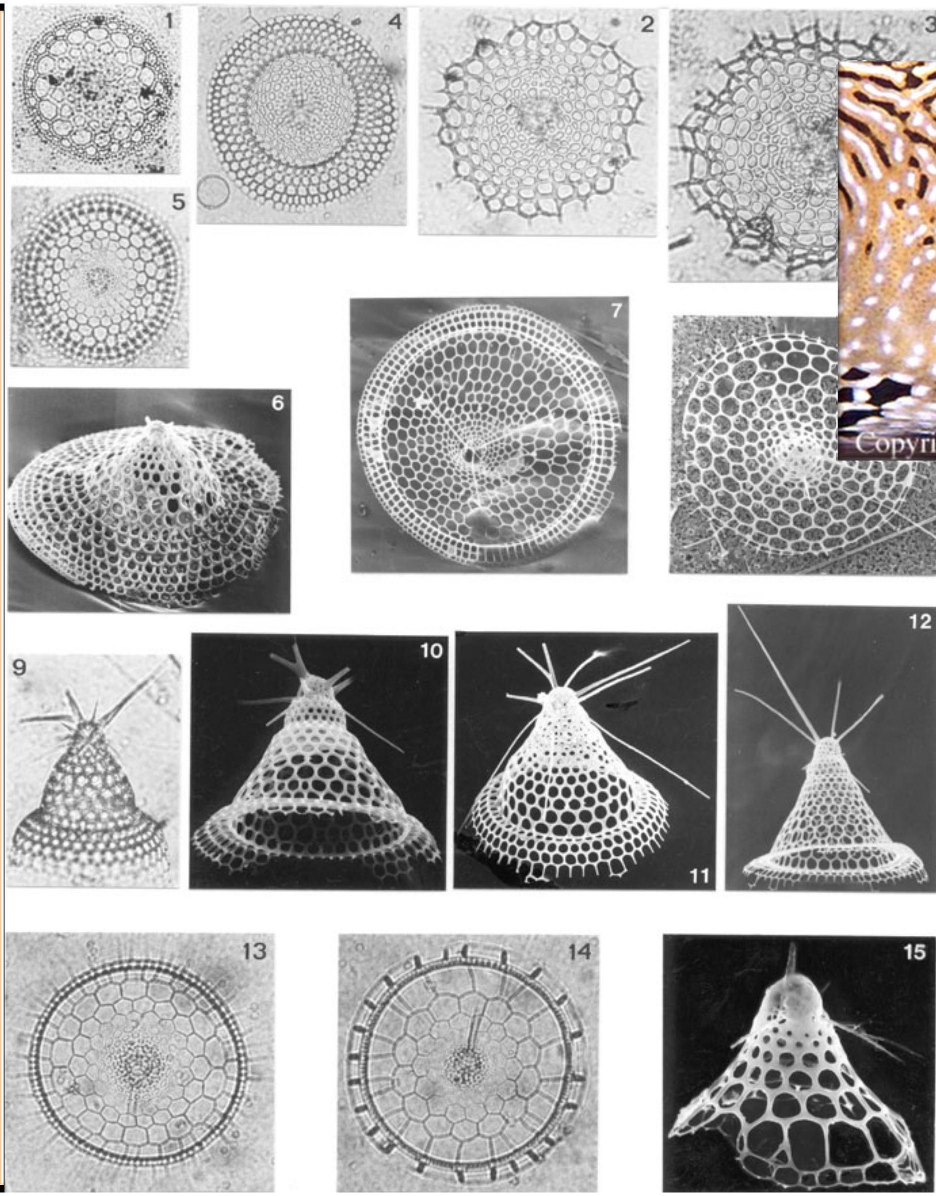


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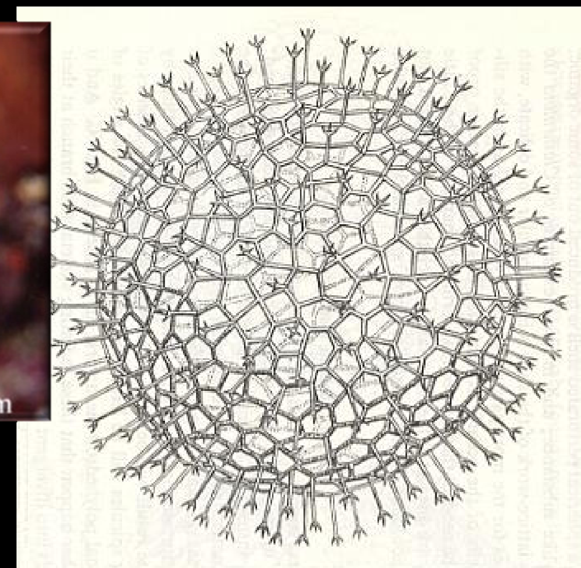
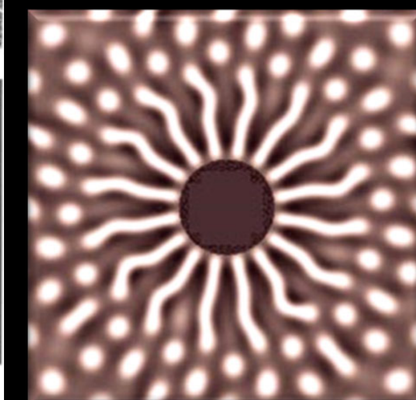
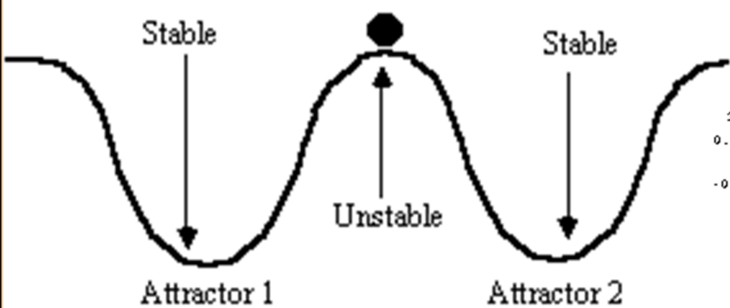
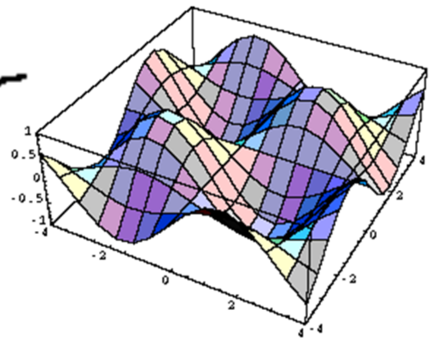


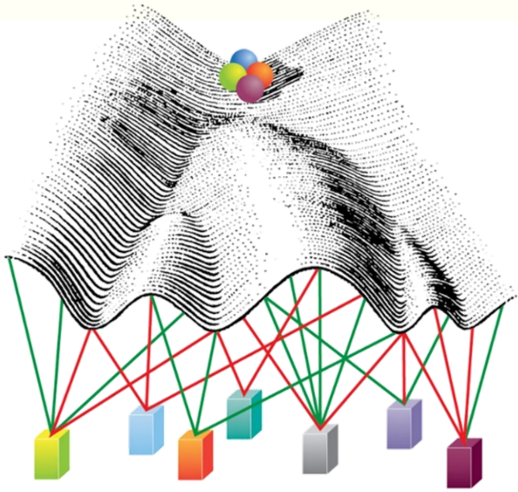


(energy) landscape metaphor

- Phase-space as landscape
  - State of the system as a drop of water released in hills and valleys



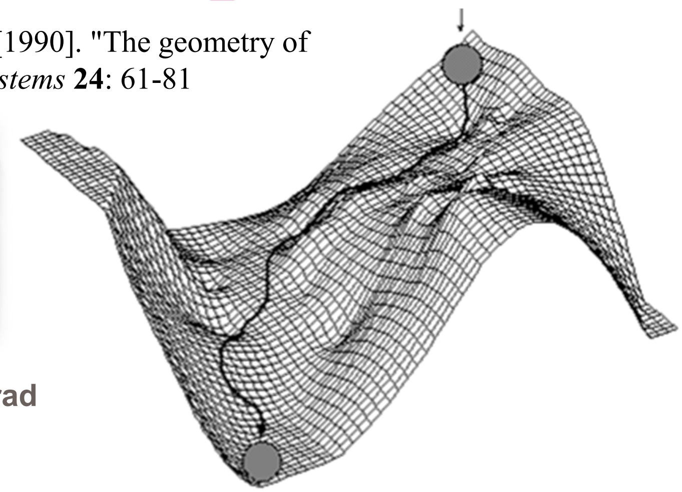


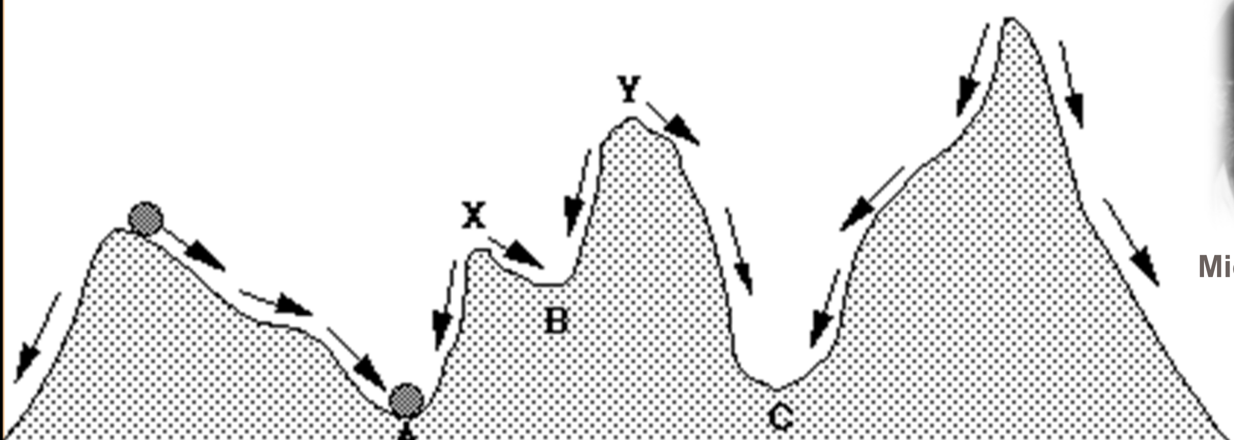


See: Conrad, M. [1990]. "The geometry of evolution." *Biosystems* **24**: 61-81

Waddington CH (1942). *Nature*.**150** (3811):563–565

Michael Conrad





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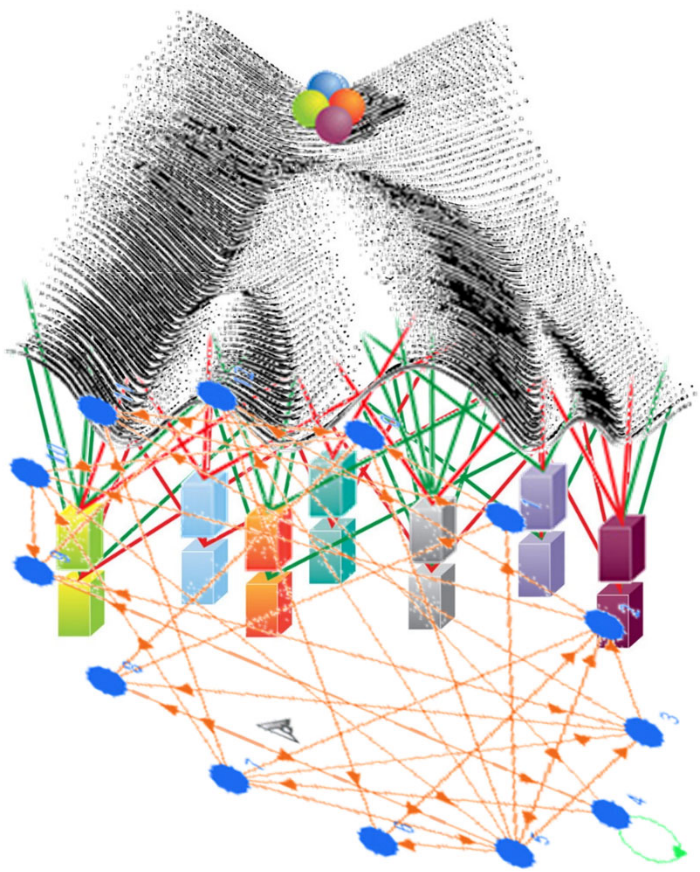
self-organization as a key mechanism for order and robustness

evolution does not need to encode all details and is constrained



Kauffman, S. A. (1984). *Phys. D Nonlinear Phen*.**10**,145–156.

Waddington CH (1942). *Nature*.**150** (3811):563–565

robustness of phenotypes is the result of a ***buffering*** of the developmental process.

dynamics of gene networks provides buffering (***self-organization***).

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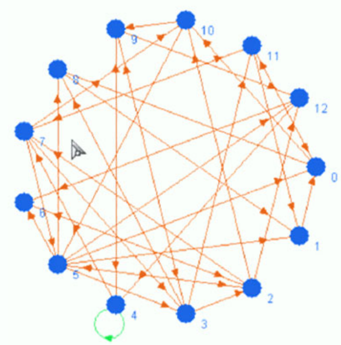
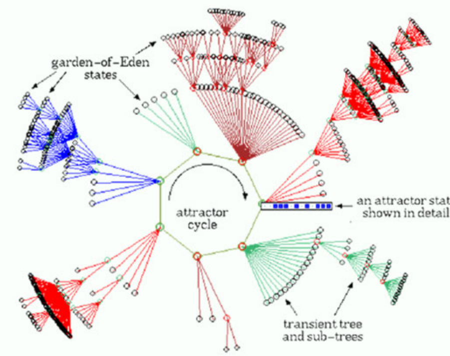
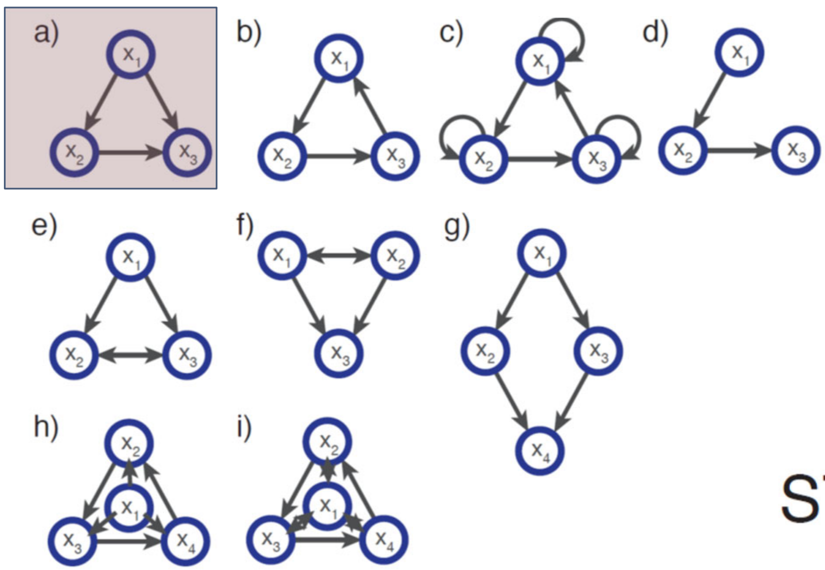
definitions

- basin of attraction
  - All states in trajectories leading to an attractor (state cycle)
- length of cycle
  - Number of states in cycle
    - 1 to 2^N
- perturbation (minimal)
  - Flipping of one node to the opposite state
- Damage
  - Change in behavior from a perturbation
- Structural perturbation
  - Permanent in connections or Boolean rules in the network





ensemble dynamics for same structure



different Boolean networks for same structure

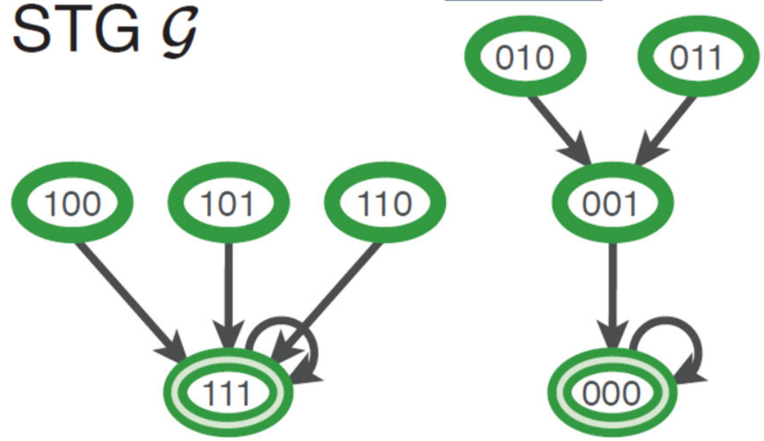
$$\prod_{i=1}^{N} 2^{2^{k_i}}$$

a) 64

Variable Logic

Variable	Logic
x_1	-
x_2	x_1
x_3	$x_1 \vee x_2$

STG $\mathcal{G}$



Gates & Rocha [2016]. *Sci. Rep.* **6**, 24456.

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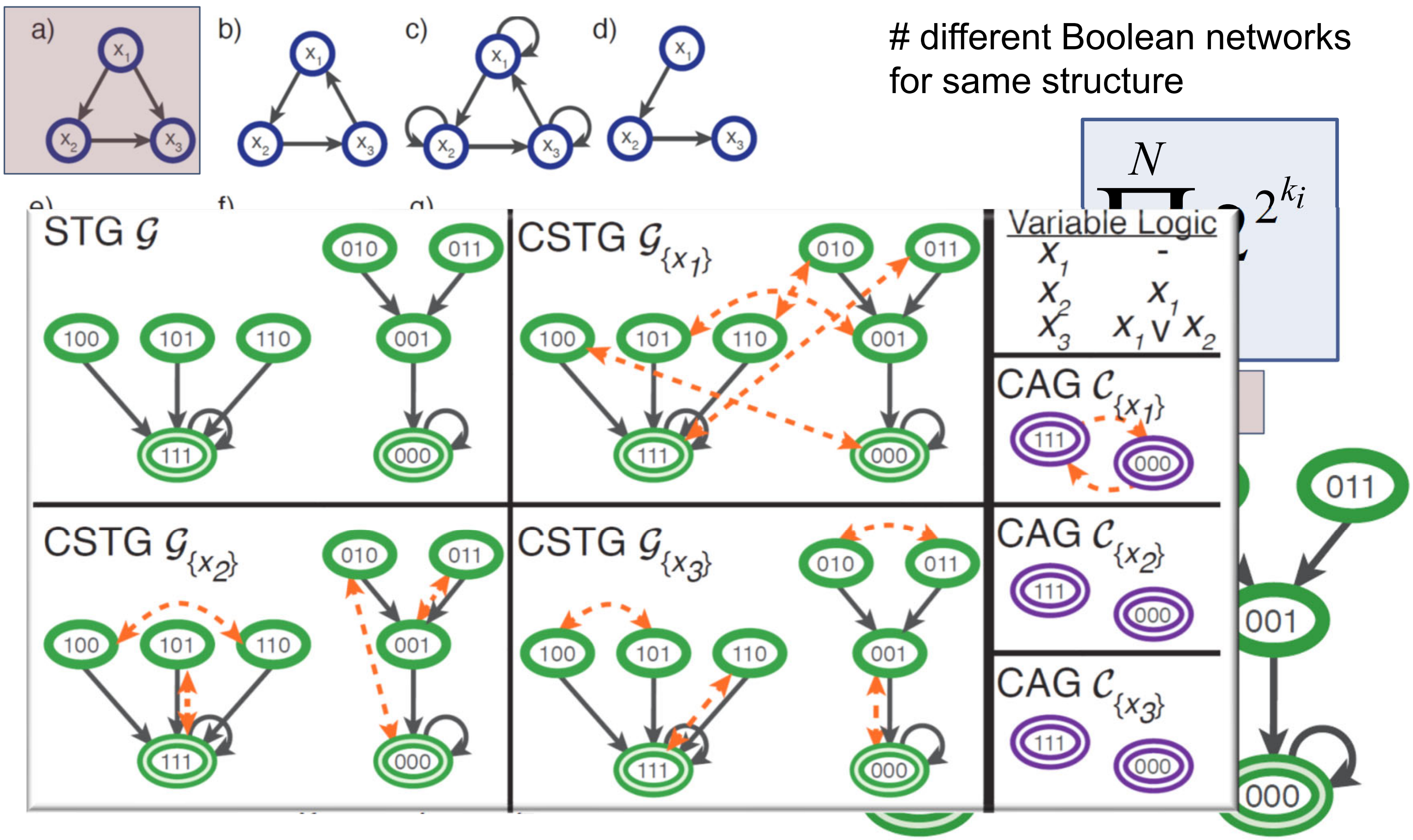
ensemble dynamics for same structure



different Boolean networks for same structure

$$\prod^{N} 2^{2^{k_i}}$$

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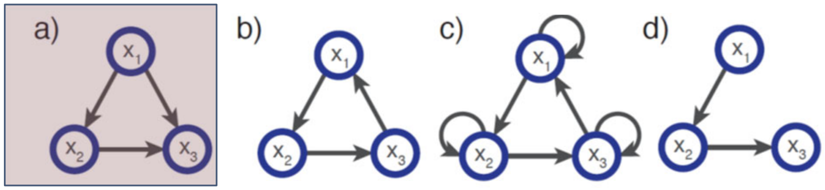

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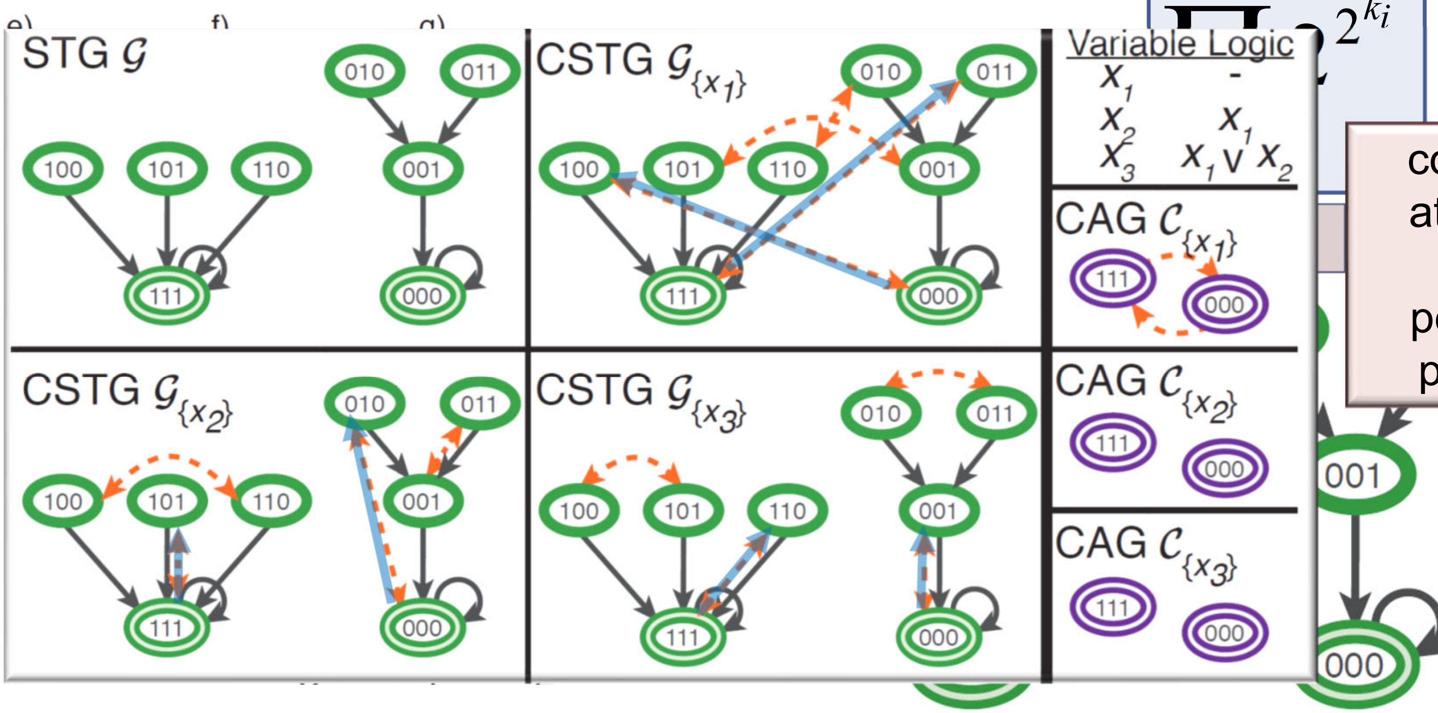

configuration vs attractor control and perturbation vs. pinning control

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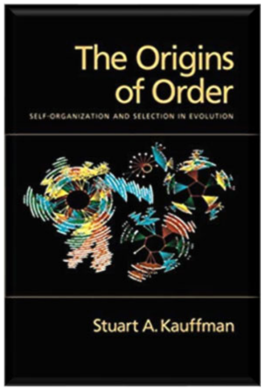
Of NK-Boolean Networks

- Random networks
  - Started with random initial conditions
    - Self-organization is not a result of special initial conditions
- Statistical analysis
  - $K \leq 2$
    - Steady state, ordered, crystallization
  - ($5 \leq K$ to) K=N
    - Disordered, chaotic
    - Mean length of cycles: $0.5 \times 2^{N/2}$
    - Mean number of cycles: N/e
    - High reachability, sensitive to perturbation
      - Number of other state cycles system can reach after perturbation
  - K=2
    - Mean length: $n^{1/2}$
    - Mean number of cycles: $n^{1/2}$
    - Low reachability
    - Percolation of frozen clusters (isolated subsets)
    - Not very sensitive to perturbation

Kauffman, S. A. (1984). *Phys. D Nonlinear Phen.* **10**,145–156.



Kauffman, SA. *J. theoretical biology* **22**.3 (1969): 437-467.

criticality

- $2 \leq K \leq 5$
  - Good for evolvability?
  - Some changes with large repercussions
  - Best capability to perform information exchange
    - Information can be propagated more easily
- Problems with analysis
  - Network topology is random
    - Not scale-free, as later explored by Aldana
  - Real genetic networks tend to have lower values of K (in ordered regime)
  - Genes as simply Boolean may be oversimplification
    - Though a few states can approximate very well continuous data

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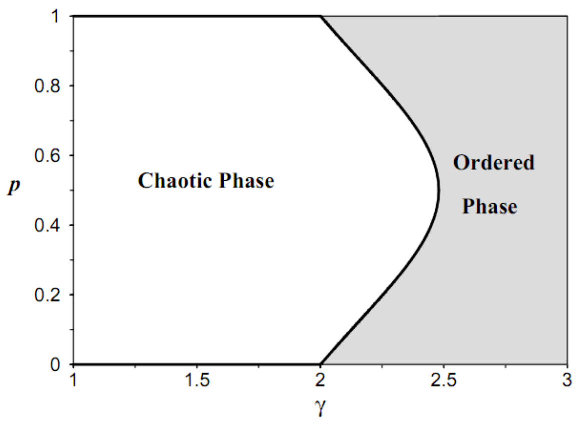
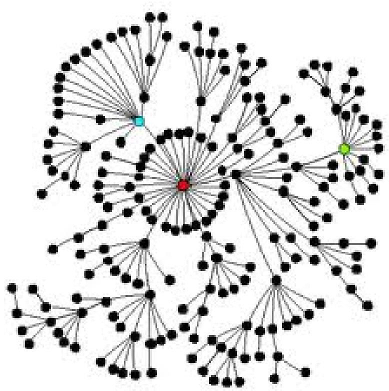
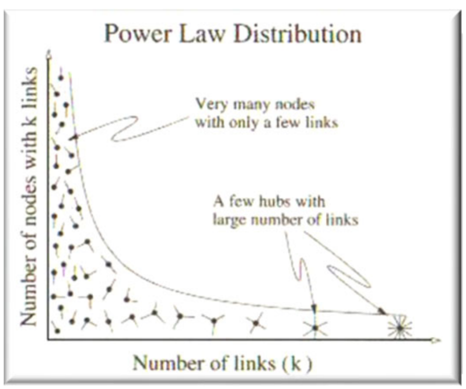
dynamical behavior of ensembles of networks



scale-free topology

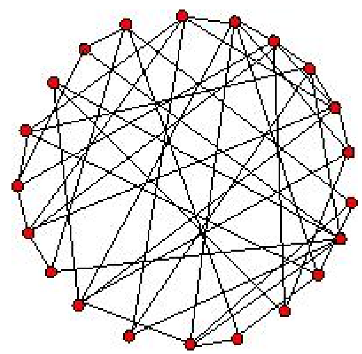
$$P(k) = c.k^{-\gamma}$$

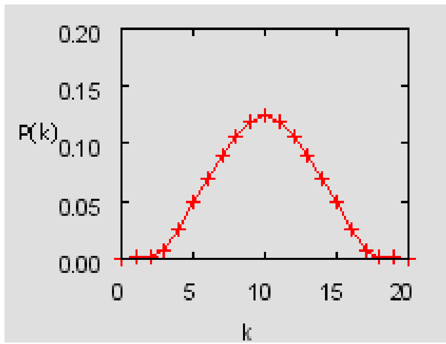


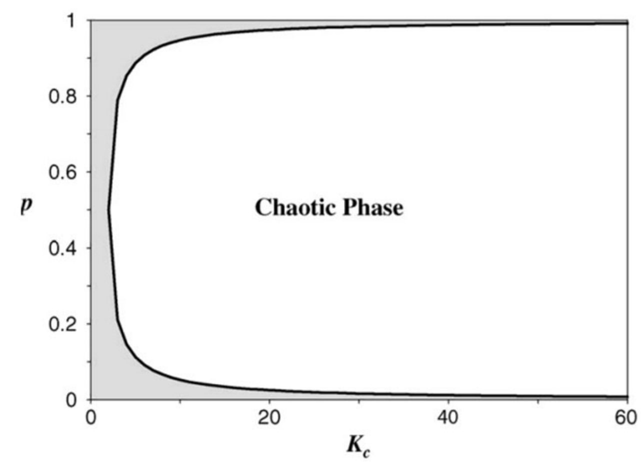


Aldana, M. [2003]. *Physica D*. **185**: 45–66

Random topology







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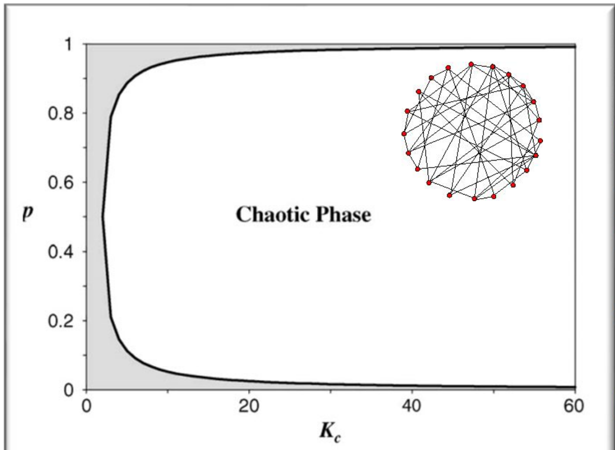
self-organization easily chaotic

evolution requires life in critical regime which is small, how come life is not chaotic?



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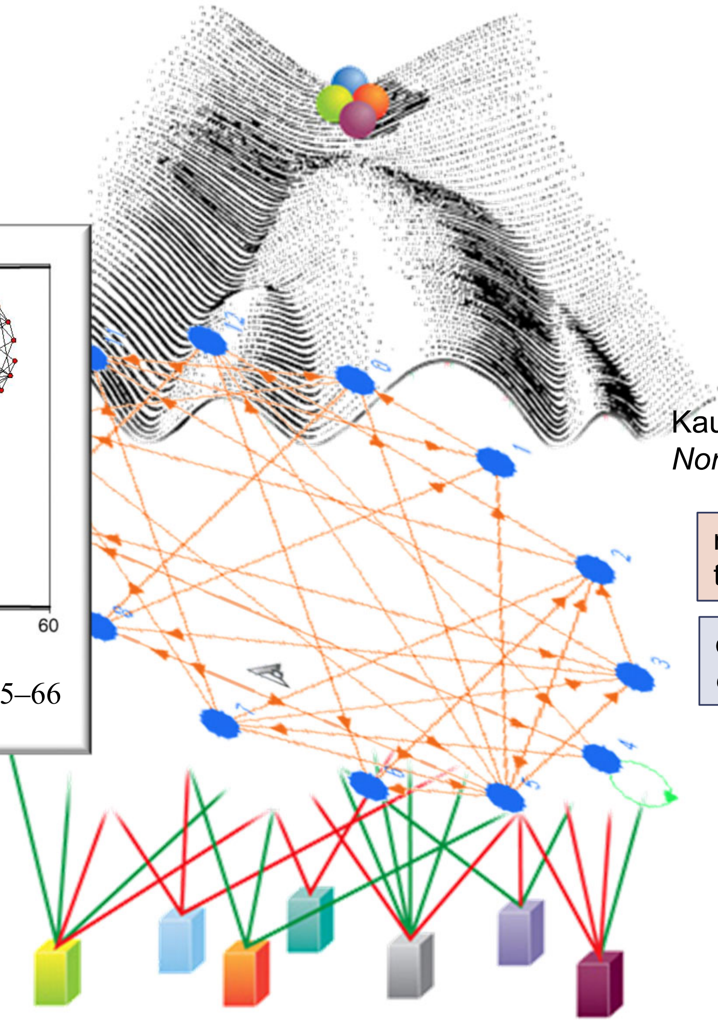

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robustness of phenotypes is the result of a ***buffering*** of the developmental process.

dynamics of gene networks provides buffering (***self-organization***). But still easily chaotic.

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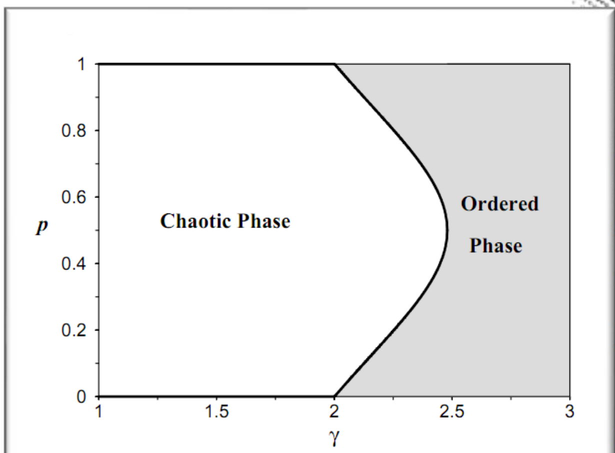

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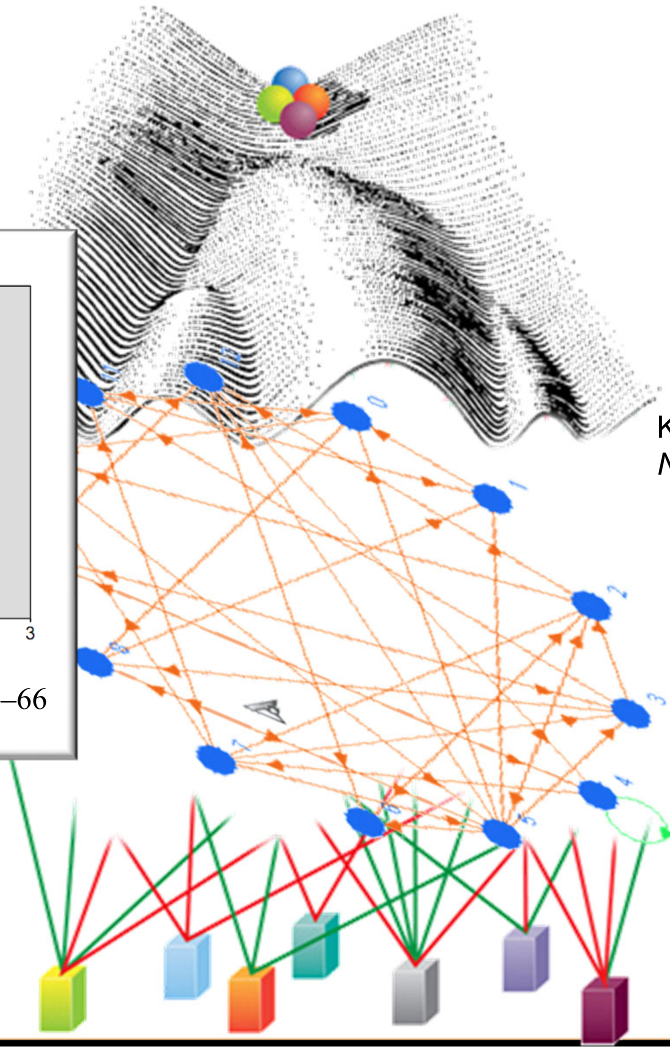

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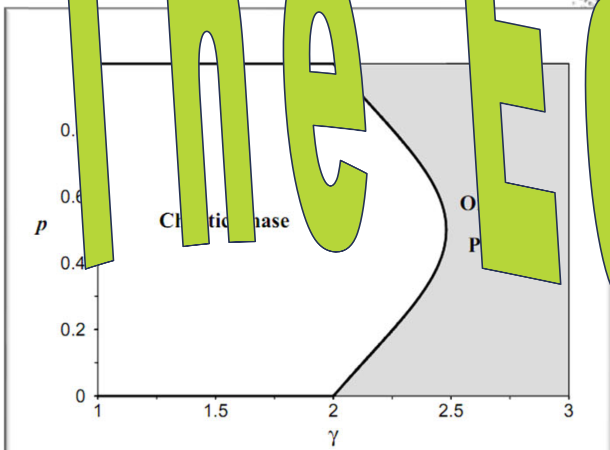
The Edge of Chaos?



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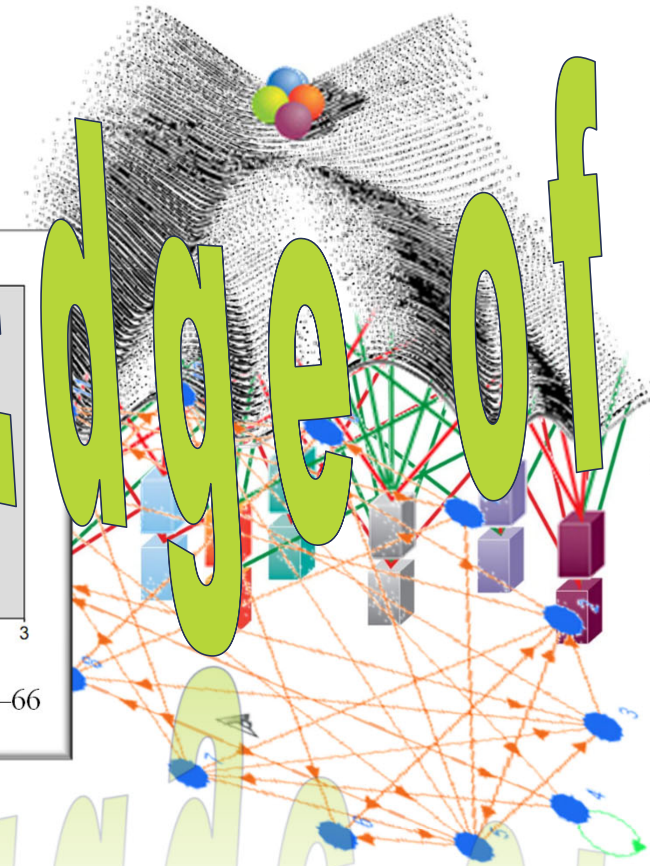

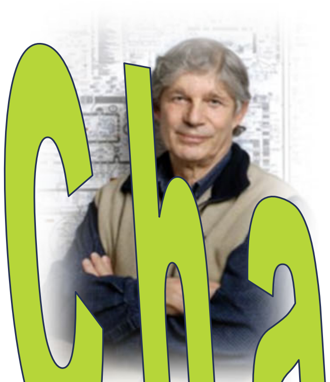

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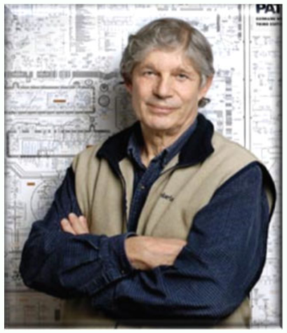
The Criticality Hypothesis

readings

- Class Book
  - Floreano, D. and C. Mattiussi [2008]. *Bio-Inspired Artificial Intelligence: Theories, Methods, and Technologies*. MIT Press.
    - **Chapter 2**.
- Lecture notes
  - Chapter 1: What is Life?
  - Chapter 2: The logical Mechanisms of Life
  - Chapter 3: Formalizing and Modeling the World
  - Chapter 4: Self-Organization and Emergent Complex Behavior
    - posted online @ http://informatics.indiana.edu/rocha/i-bic



- Papers and other materials
  - Optional
    - Nunes de Castro, Leandro [2006]. *Fundamentals of Natural Computing: Basic Concepts, Algorithms, and Applications*. Chapman & Hall.
      - Chapter 2, all sections
      - Chapter 7, sections 7.3 – Cellular Automata
      - Chapter 8, sections 8.1, 8.2, 8.3.10
    - Flake's [1998], *The Computational Beauty of Life*. MIT Press.
      - Chapters 10, 11, 14 – Dynamics, Attractors and chaos

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