Attractor stucture of Boolean networks of small canalizing depth

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DE PARIS

Plan of the talk

Main question: difference in dynamics between
"a random Boolean network" and "random canalizing Boolean network"

Plan

- Intro and problem statement
- Simulation results
- Theoretic results
- Remarks on the computation

Boolean networks and their structure

Definition

$\mathbf{F}_2$ is a field with two elements 0 (false / off) and 1 (true / on) and arithmetic operations:

$$x + y := x \text{ XOR } y, \quad xy := x \text{ AND } y.$$

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An n-dimensional Boolean network defined by n polynomials $f_1, \ldots, f_n \in \mathbb{F}_2[x_1, \ldots, x_n]$ is a discrete-time dynamical system such that

- states are points in $\mathbb{F}_2^n$
- and, the the state at time t is $\mathbf{a}_t = (a_{t,1}, \ldots, a_{t,n}) \in \mathbb{F}_2^n$, then

$$\mathbf{a}_{t+1} = (f_1(\mathbf{a}_t), \ldots, f_n(\mathbf{a}_t)).$$

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Example

Let $f_1(x_1, x_2) = x_1(x_2 + 1)$ and $f_2(x_1, x_2) = (x_1 + 1)x_2$:

$$(0, 1) \to (1, 0) \to (0, 1) \to \ldots$$

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Why: regulatory networks.

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Pros: we can define any dynamics!

Cons: we can define any dynamics...

Dynamics: attractors and basins

n-dimensional Boolean network $\implies$ directed graph on 2^n vertices

Network:

$$f_1 = x_1(x_2 + 1),$$
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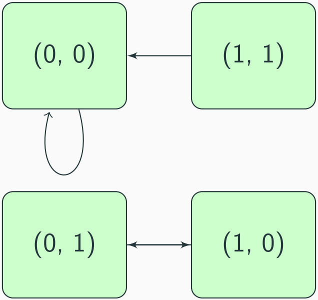

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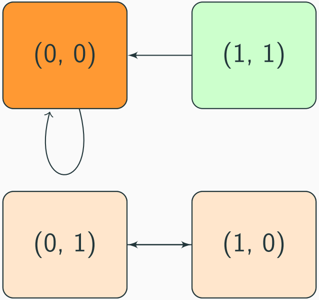

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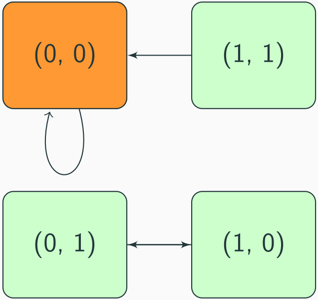

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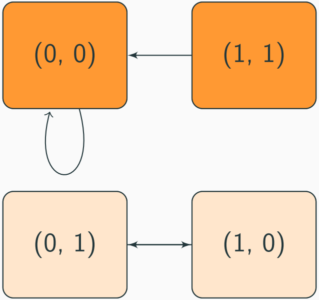

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  Each basin corresponds to an attractor and each attractor has its basin.

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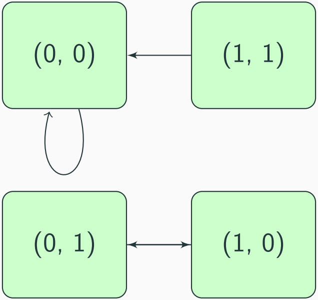

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Intuition
Attractors $\leftrightarrow$ Cell types
Length $\leftrightarrow$ number of experssion patterns

Canalization

One variable to rule them all

A nonconstant function $f(x_1, \dots x_n)$ is canalizing with respect to a variable x_i if there exists a canalizing value $a \in \{0, 1\}$ such that

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Why?

- Often appear in the published models.
- Make sense.

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Canalizing depth (Layne, Dimitrova, Macaulay, 2012)

We define canalizing depth recursively

1. noncanalizing function $\implies$ depth 0
2. if f is canalizing w.r.t. x_1 with value a, then

$$\text{depth}(f) = \text{depth}(f|_{x_1=1-a}) + 1.$$

Main question

Question: How does the canalization (and its depth) affect the attractor structure?

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Related results include: no chaos (Karlsson, Hörnquist), stability (Kauffman, Peterson, Samuelsson, Troein and Layne, Dimitrova, Macauley)

Experimental results

Setup

For each $n = 4, \ldots, 20$ and each $k = 0, \ldots, n$ we generate random Boolean networks

- of dimension n;
- with all the functions having canalizing depth k.

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Computed values

For each Boolean network we compute

N: the number of attractors

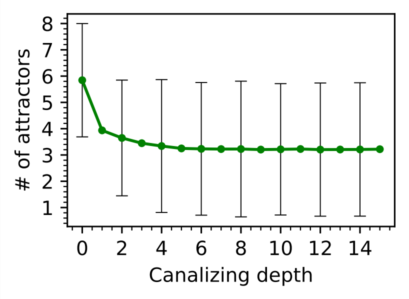
S: the total number of states in the attractors

AS: the average attractor size $= \frac{S}{N}$

Experimental results

For $n = 15$ based in 50k samples for each k.

N = # attractors



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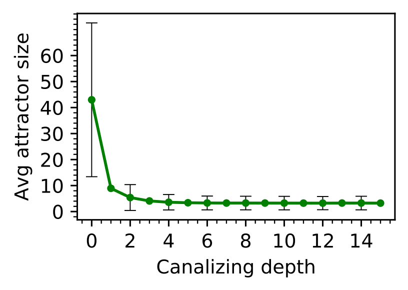

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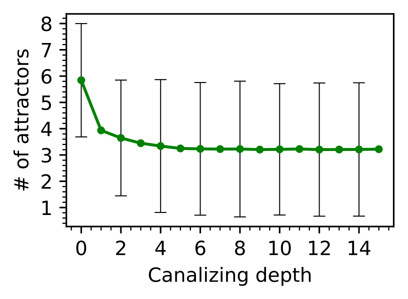

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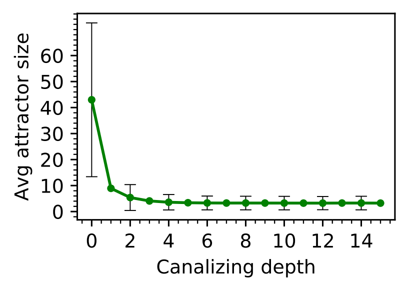

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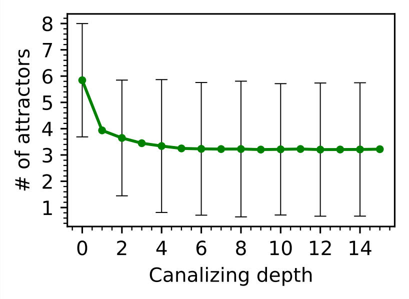

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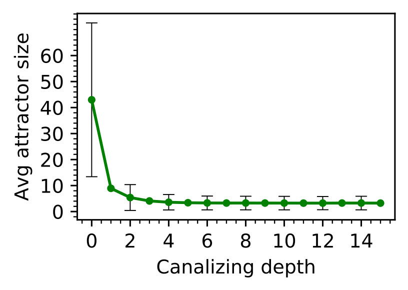

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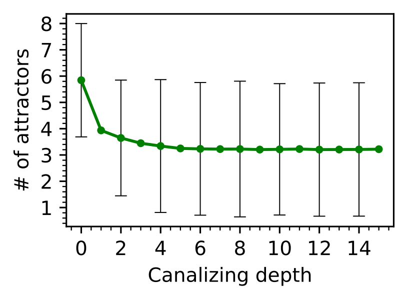

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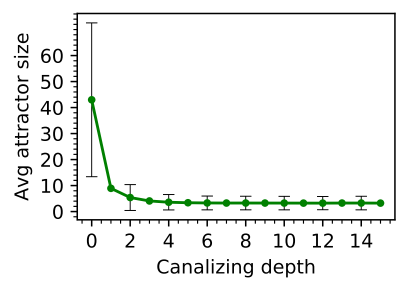


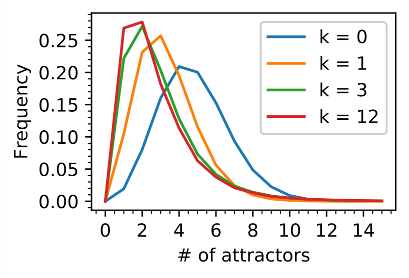
Analysis

- Depth increases $\implies$ number and sizes decrease
- Sizes decrease more substantially
- Most of the change happens between $k = 0$ and $k = 3$.

Experimental results

For $n = 12$ based in 300k samples for each k.

N = # attractors



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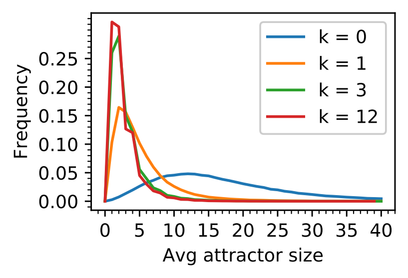

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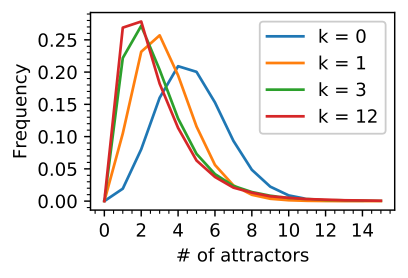

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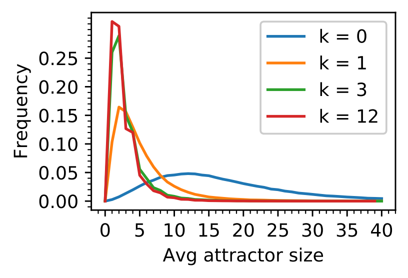

Analysis

- Confirms earlier conclusions
- Avg. size differs dramatically for $k = 0$ and $k = 1$

Theoretical results

Quantity of interest

$A_{\ell,n}$:= expected # of attractors of length ℓ in a random network of dimension n and depth one.

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Theorem

We give a formula for A_ℓ, in particular

- $A_\ell > \frac{1}{\ell}$ for $\ell > 0$;
- $A_1 = 1,\ A_2 = 0.66\ldots,\ A_3 = 0.3386\ldots,\ A_4 = 0.2856\ldots$

Summary

- canalization $\implies$ fewer attractors and they are much smaller
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- canalization $\implies$ fewer attractors and they are much smaller
  Biologically relevant!
- no big difference between small (but > 0) and large canalizing depths
  Applicable to a wide range of models

Remarks on the computation

Sampling:

- Relies on the structure theorem by He and Macaulay
- Complexity $\mathcal{O}(n2^n)$ almost optimal
  more precisely $\mathcal{O}(k^3 + (n-k)2^{n-k} + k2^n)$

Finding attractors: DFS

Open problems

Taking into account:

- sparsity
- uneven canalization profiles
  (i.e. only some of the functions are canalizing)
- collective canalization

Support

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