GRNs an Overview

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Why bother about GRN Models?

- Huge amounts of Data are available.
  - Genome Projects.
  - temporal Gene Expression Patterns.
- Generic Model of a Genotype-Phenotype-Map.
  - Phenotype differs from the Genotype.
  - Abstract Proofs of Concept.
- Developmental Model.
  - Test fundamental Hypothesis.
  - Gene reuse, dense Encoding, Modularity ...

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Modeling Approaches for GRNs

Boolean Approach

Describes the state of genes in simple ON or OFF patterns.

Continuous Approach

Describes time course of gene product concentrations in terms of ODEs.

Hybrid Approach

Blends elements from the Boolean and the Continuous approaches.

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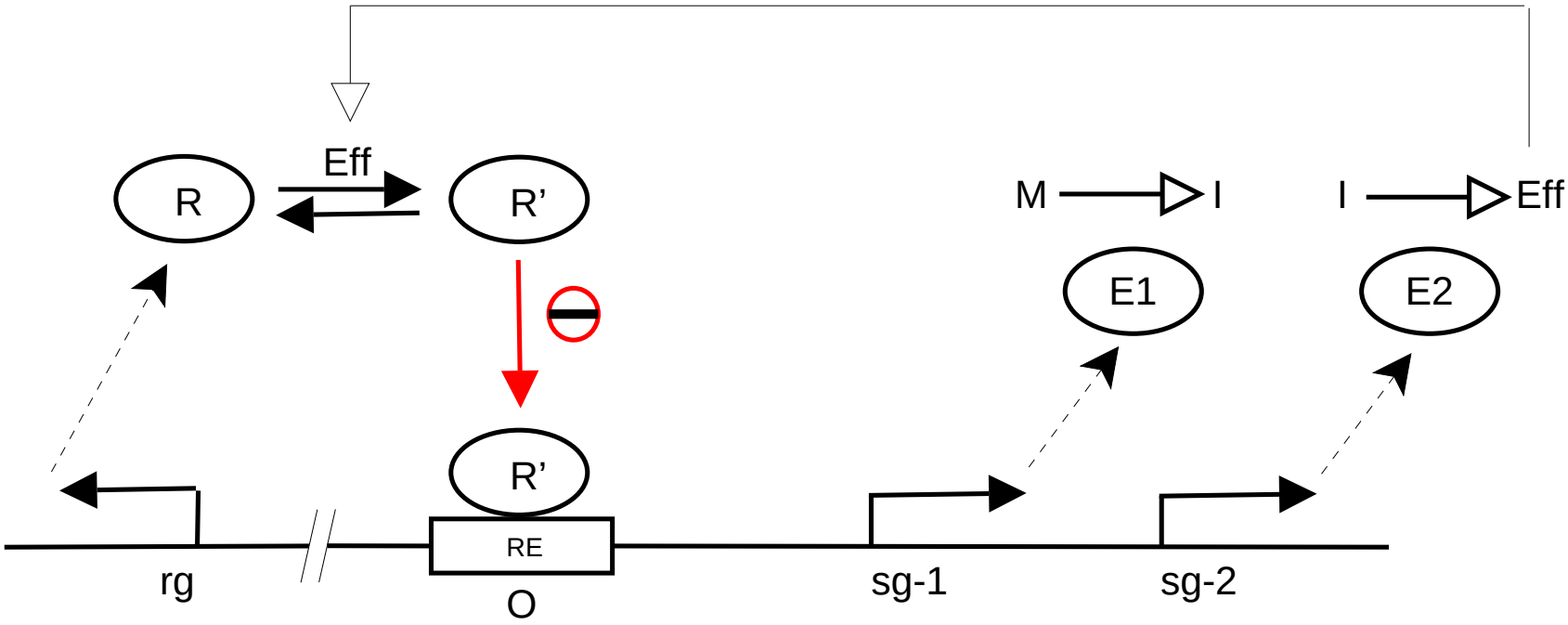
The Operon Model

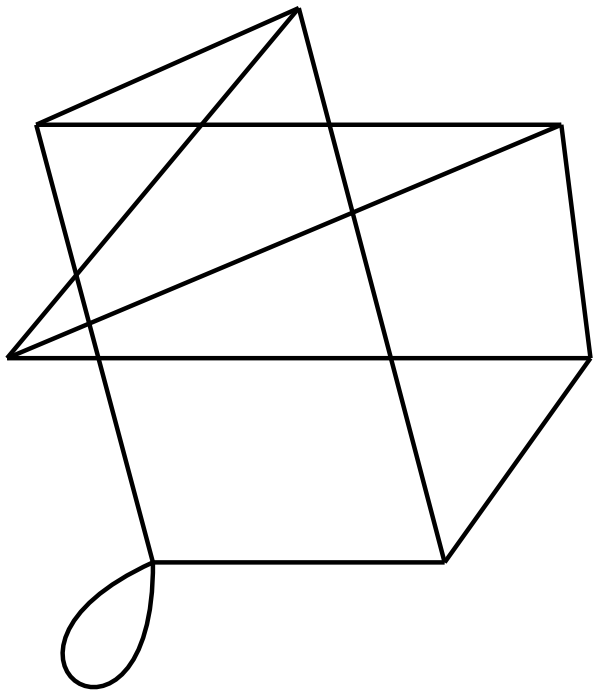


Jacob & Monod 1961

Random Boolean Networks – The Dinosaur

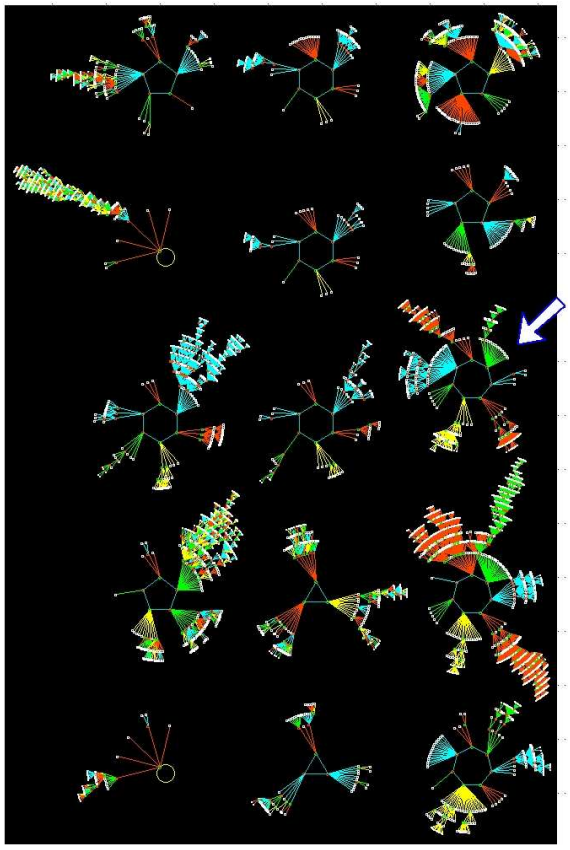
Behavior depends only on 2 parameters:

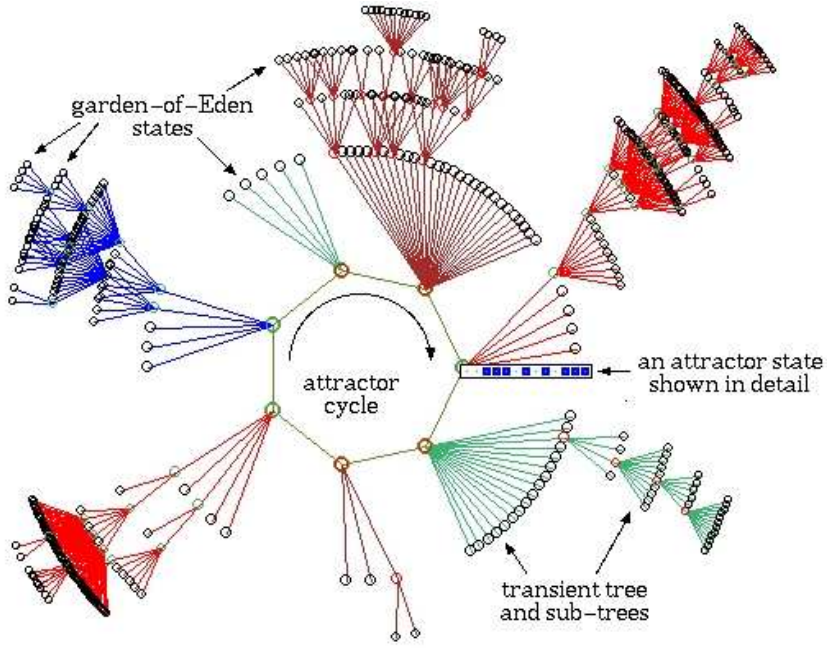
1. The number of genes
2. The degree of connectivity between genes.



A	B	C	
0	0	0	0
0	0	1	1
0	1	0	1
0	1	1	0
1	0	0	1
1	0	1	1
1	1	1	0
1	1	0	0

Random Boolean Networks – State Transition Graph





Andrew Wuensche (2002)

tbi

Random Boolean Networks – Pros and Cons

Pros:

- RBNs are computationally cheap.
- RBNs settle into a small number of cycle attractors.
- RBNs show a considerable degree of homeostasis.

Cons:

- RBNs are difficult to treat analytically.
- RBN nodes represent gene interactions, rather than genes themselves.
- RBN nodes are updated synchronously, which is clearly not observed in nature.

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The Continuous Approach

- based on the reaction-diffusion model.
- becomes manifest in ODEs.

$$\frac{\partial C}{\partial t} = F(C) + D\nabla^2 C$$

Temporal changes of the gene products are cause by ...

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. . . reactions between the gene products and . . .

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. . . diffusion of the gene products . . .

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. . . so the Eq describes reactivity and diffusion at a point in space.

The Continuous Approach – Pros and Cons

Pros:

- More accurate physical representation.
- There is a lot of theory and methodology.

Cons:

- Computationally rather demanding.
- Assumption of specific kinetic schemes.

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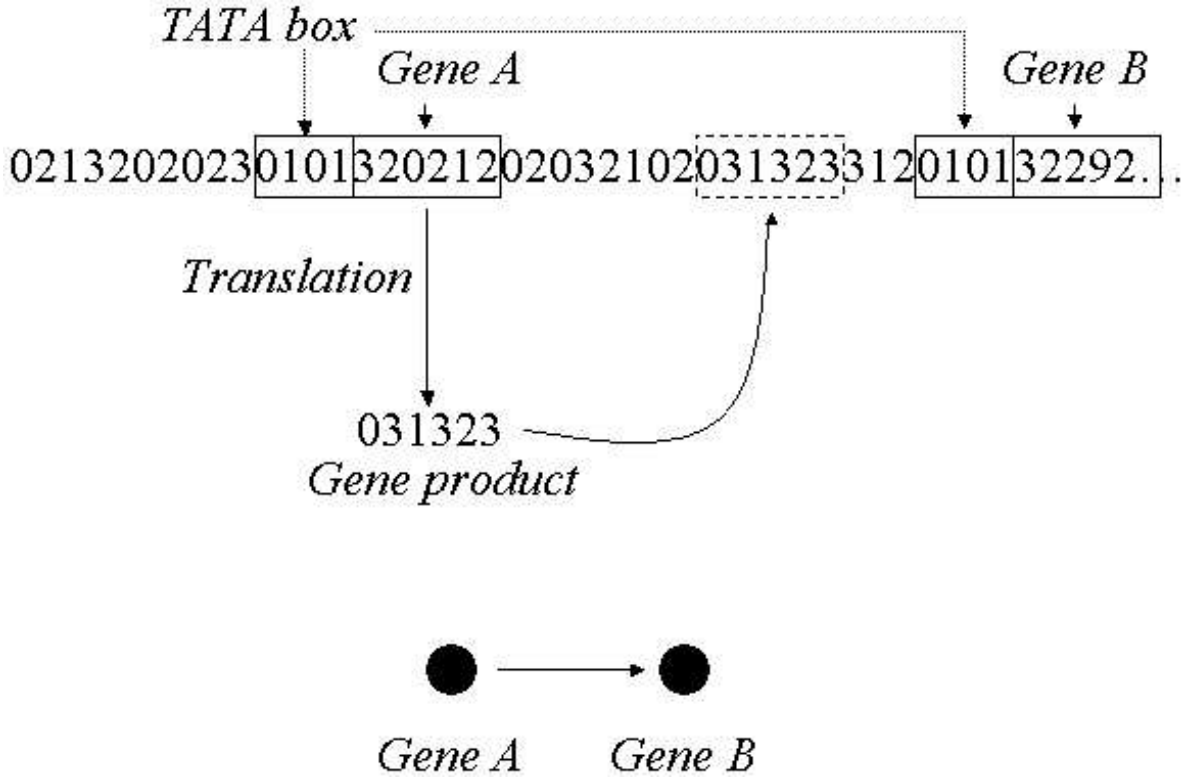
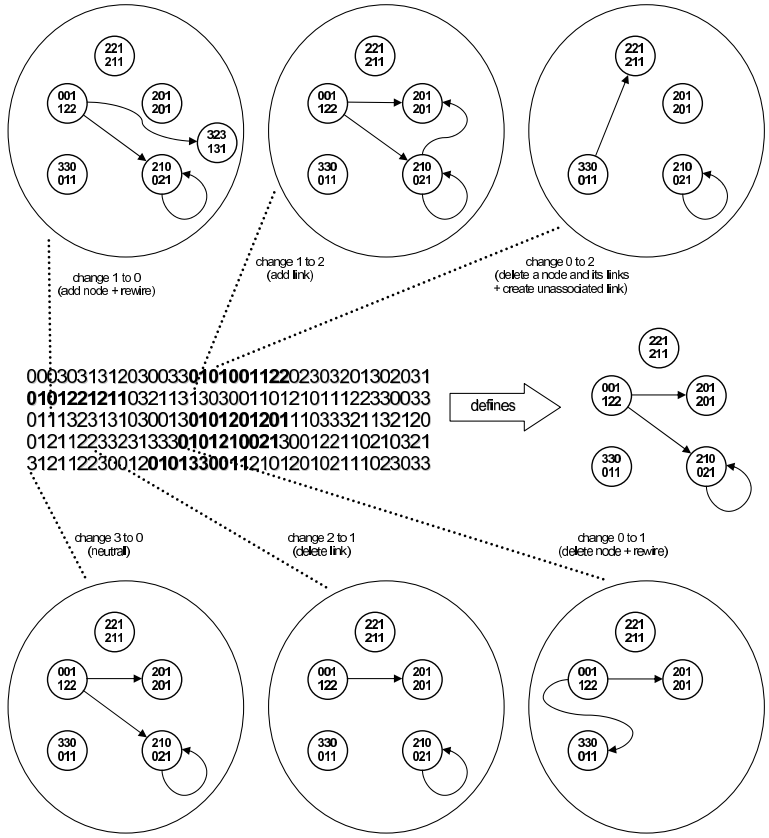
The Mother of the Models



Torsten Reil (ECAL 1999)

Effect of Point Mutations a GRN



James Watson et. al. (IPCAT 2003),