



UCD CASL

Complex & Adaptive Systems Laboratory

Dr. Miguel Nicolau

*Artificial Regulatory Network Models
Definition and Application*

COMP30290 Natural Computing

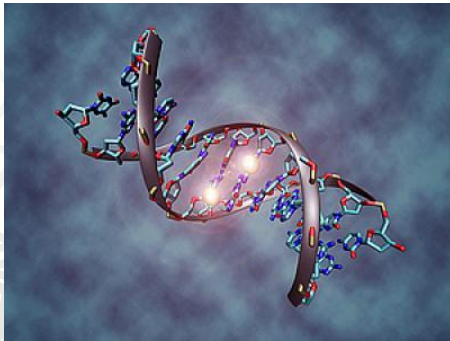
COMP41190 Natural Computing and Applications



Outline

- 1 **Gene Regulatory Networks**
- 2 **Artificial Model**
 - Representation
 - Example Dynamics
- 3 **I/O Extensions to Model**
- 4 **Pole-Balancing Experiments**
- 5 **Index Trading Experiments**
- 6 **Observations**

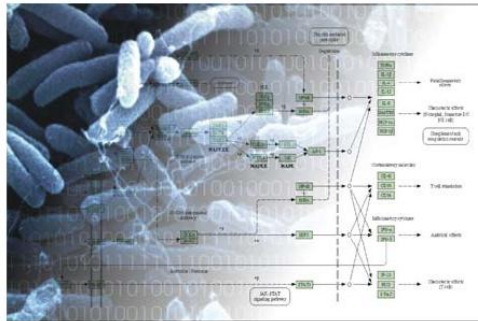
Genetic Regulatory Networks



Gene Expression

- ▶ Cells express proteins when needed;
- ▶ Regulatory processes enhance/inhibit expression of genes;
- ▶ Responsible for differentiation and morphogenesis.

Genetic Regulatory Networks



Transcription Regulation

- ▶ Genes are transcribed at different rates;
- ▶ Transcription Factors (TFs) influence expression of genes;
- ▶ Genes can produce TFs, thus forming **Regulatory Networks**.

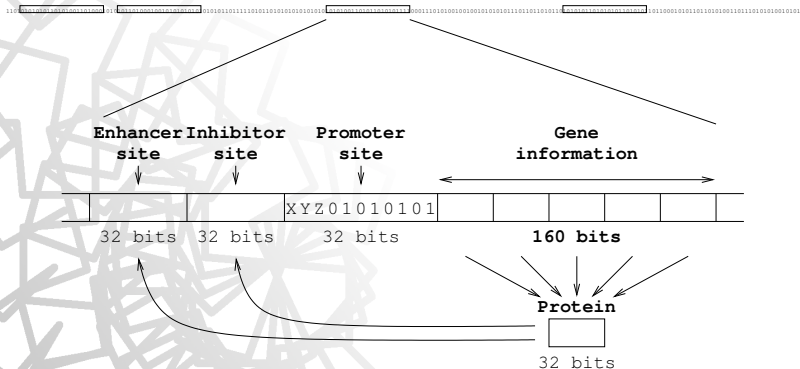


ARN: Computer Model

Wolfgang Banzhaf: Artificial Regulatory Networks and Genetic Programming. GPTP, 2003.

- ▶ Composition:
 - ▶ **Genome** (binary string);
 - ▶ Mobile **Proteins** (TFs).
- ▶ **Promoter Sites** identify genes;
- ▶ Genes composed of:
 - ▶ **Enhancer** and **Inhibitor** sites;
 - ▶ Gene information.

ARN: Computer Model



ARN: Computer Model

Dynamics

- ▶ Regulatory model is a closed world (no I/O);
- ▶ Production of proteins dictates their concentration: $\sum_i c_i = 1.0$
- ▶ Transcription factors bind to enhancer and inhibitor sites:
 - ▶ All TFs bind to all sites;
 - ▶ Strength of connection = # complementary bits (XOR):
 - ▶ Each gene has an **enhancing** and **inhibiting** signal:

$$e_i, h_i = \frac{1}{N} \sum_{j=1}^N c_j \exp(\beta(u_{i,j} - u_{max}))$$

$u_{i,j}$ = match between site and protein j

u_{max} = maximum match

β = scaling factor



ARN: Computer Model

Dynamics

- ▶ Concentration of each protein changes per iteration:
 - ▶ Regulated by differential equation:

$$\frac{dc_i}{dt} = \delta(e_i - h_i)c_i - \Phi$$

δ = scaling factor (time unit)

Φ = protein scaling factor ($\sum_i c_i = 1.0$)

- ▶ Concentrations change over time, depending on TFs matching sites;
- ▶ Rich dynamic regulatory network.

ARN: Dynamics of Model

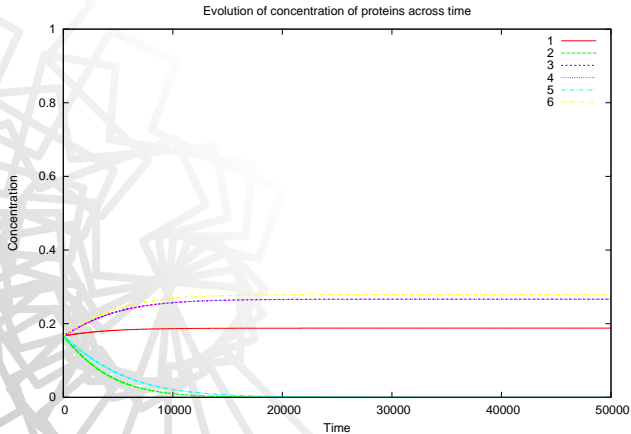
Dynamics

- ▶ Expression level of genes change over time:

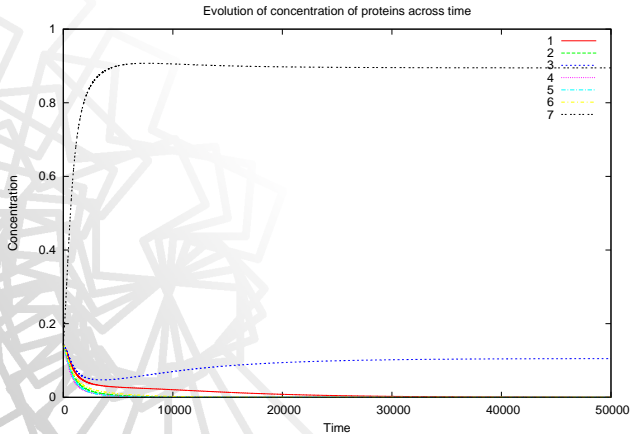
$$c_{t+1} = \text{signal} \times c_t$$

- ▶ Plot expression level of all genes across time;
- ▶ Different dynamics can be observed.

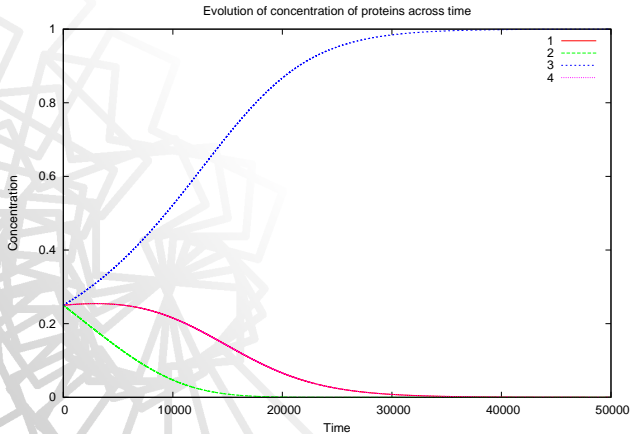
ARN: Dynamics of Model



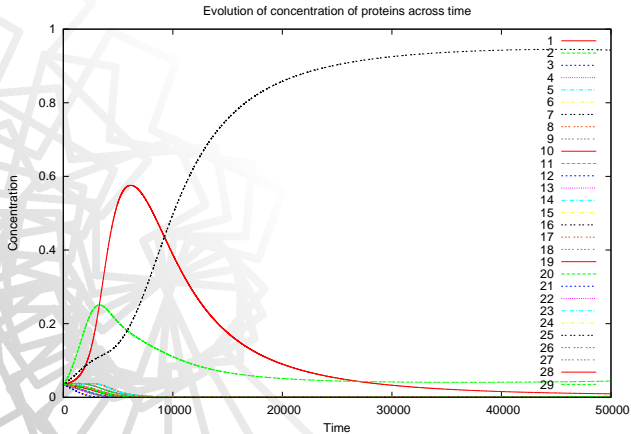
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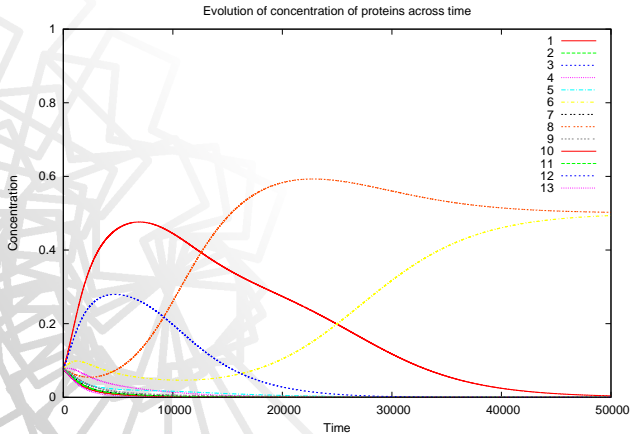
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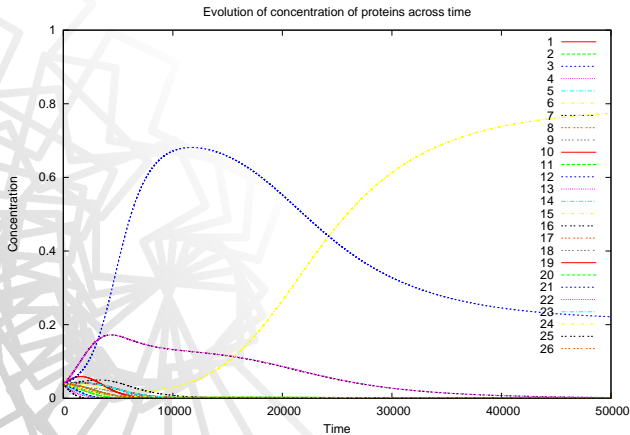
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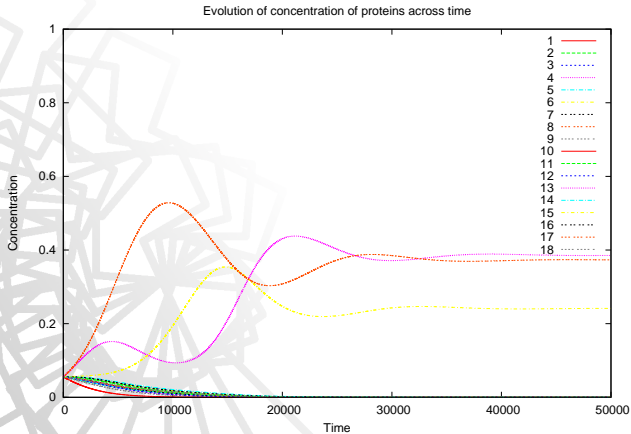
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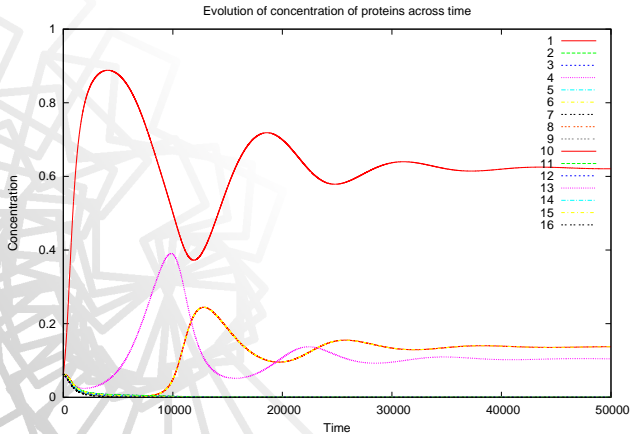
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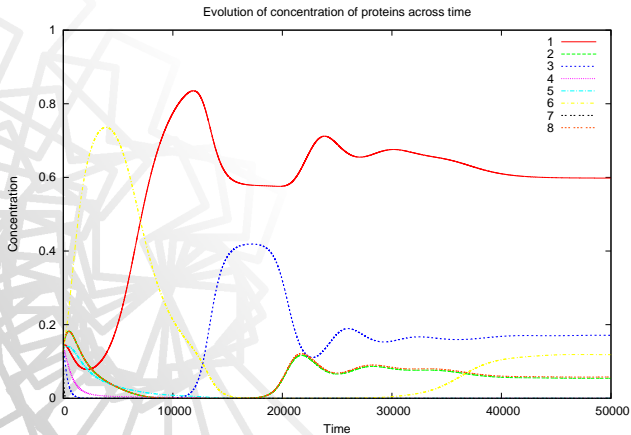
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ARN: I/O Extensions

Modelling output

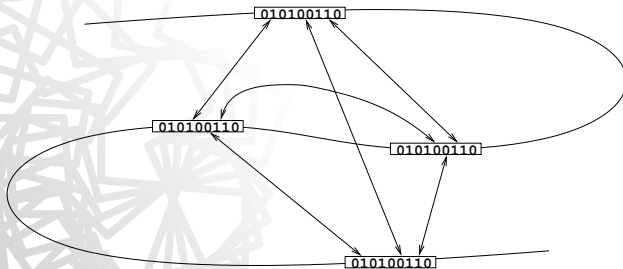
- ▶ Genes produce 2 types of genes:
 - ▶ *TF-genes*: produce TFs;
 - ▶ *P-genes*: produce **product proteins** (output signals).
- ▶ Different promoter site signatures identify different genes.

Modelling input

- ▶ Model input through extra regulatory (TF) proteins:
 - ▶ Not produced by any gene (external signals);
 - ▶ Co-regulate all genes with existing TFs.



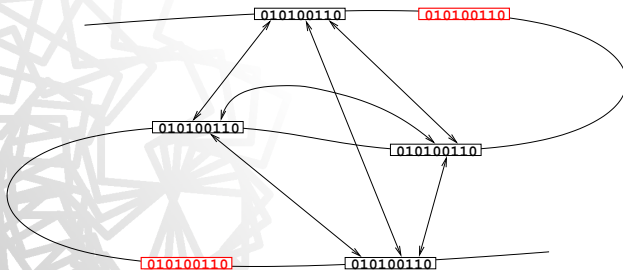
ARN: I/O Extensions



Standard regulation network.

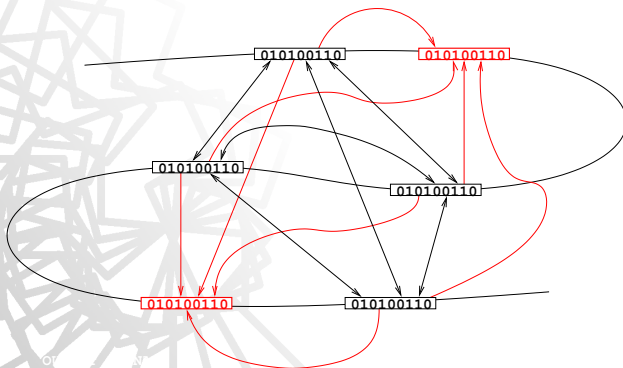


ARN: I/O Extensions



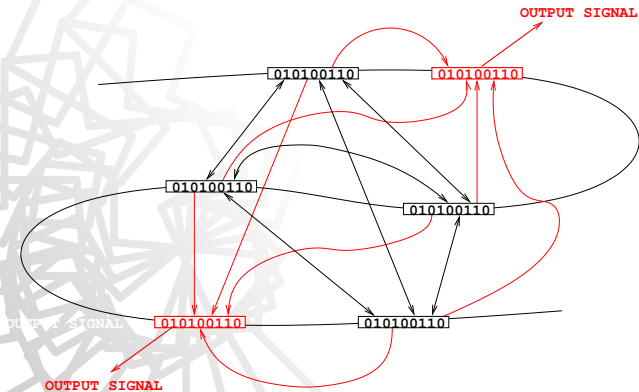
Detection of one or more P-genes.

ARN: I/O Extensions



P-genes are regulated by all TF-genes.

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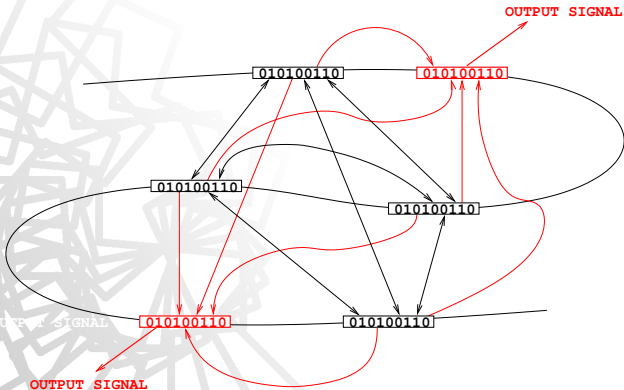


Expression signals are extracted.

ARN: I/O Extensions

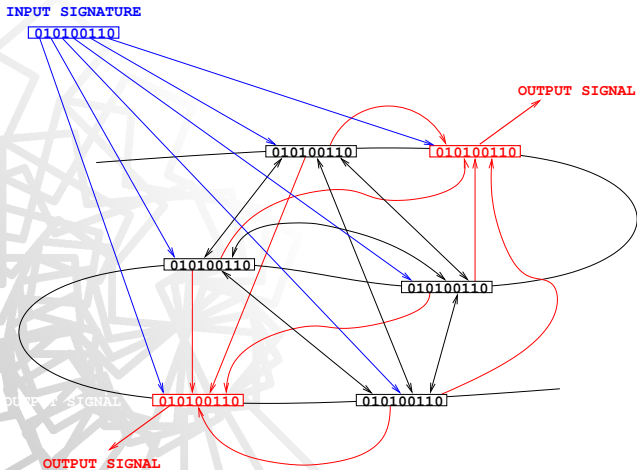
INPUT SIGNATURE

010100110



One or more extra proteins (EPs) are added to network.

ARN: I/O Extensions

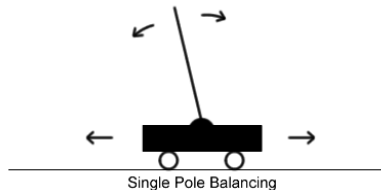


They regulate all types of genes.

Pole-Balancing Experiments

Single-Pole Balancing (Inverted Pendulum)

- ▶ Famous dynamic control benchmark;
- ▶ Cart with rigid pole attached to it;
- ▶ Control cart along 1-dimensional track:
 - ▶ Apply constant force to either side of cart each 0.2s;
 - ▶ Keep pole within acceptable angle;
 - ▶ Keep cart within track boundaries.



Pole-Balancing Experiments

Pole-Balancing

- ▶ 4 inputs, 1 output:
 - ▶ $x \in [-2.4, 2.4]$ m = position of the cart relative to the centre;
 - ▶ $\theta \in [-12, 12]^\circ$ = angle of the pole with the vertical;
 - ▶ $\dot{x} \in [-1, 1]$ m/s = cart velocity;
 - ▶ $\dot{\theta} \in [-1.5, 1.5]^\circ/s$ = rate of change of the angle.
 - ▶ $F(t) = \pm 10 N$ = bang-bang force applied to cart.

Experimental Setup

- ▶ (250+250)-ES (1% mutation rate, adapted);
- ▶ $0.2s = 2000$ time steps in model;
- ▶ Measure concentration of chosen P-gene:
 - ▶ $> .5$ = push cart right, $< .5$ = push cart left.

Pole-Balancing Experiments

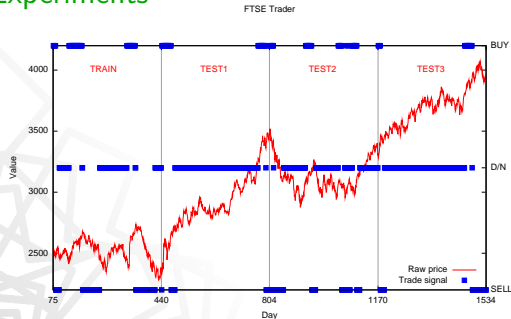
Results

	Best	Worst	Mean
random genomes	422	3	202.18
DM genomes	416	23	235.68

Analysis

- ▶ Results close to optimum (457 or less);
- ▶ Not far from best in literature (446).

Index Trading Experiments



GRN Trader

- ▶ **Index Trading;**
- ▶ Inputs: MA(n), SO(n), MC(n);
- ▶ Output is buy/sell/nothing;
- ▶ FTSE, DAX, Nikkei;
- ▶ Investment \$1000/\$10000, fixed term;
- ▶ Results equally good/better than B&H;
- ▶ Proof of concept.



Observations

Regulatory Networks as computational models

- ▶ Use of GRNs as new representation for GP;
- ▶ Investigation of more complex biological models for evolutionary computation.
 - ▶ Clear computational potential with current model;
 - ▶ Adaptation of such complex models often not obvious.

Future Work

- ▶ Calibration of parameters not easy;
 - ▶ Signature and concentration of extra proteins;
 - ▶ Calibration of biological and physical model.
- ▶ Dynamic control problems seem adequate.

Next Classes

- ▶ Discussion group (Thursday) 15h - 16h:
 - ▶ Toribash paper (blood and guts).