Gene Interaction and Modularisation in a Model for Gene-Regulated Development

CoMo lab
Piet van Remortel
Bernard Manderick
Tom Lenaerts
VUB/ULB - Belgium

Overview

- Context
- Hypothesis
- Approach towards Hypothesis
- Biological Development
- A Model for Gene-Regulated Development
- Gene Interaction
- Genetic Modules
- Gene mutations/inversions
- Conclusions
- Future Work

Context

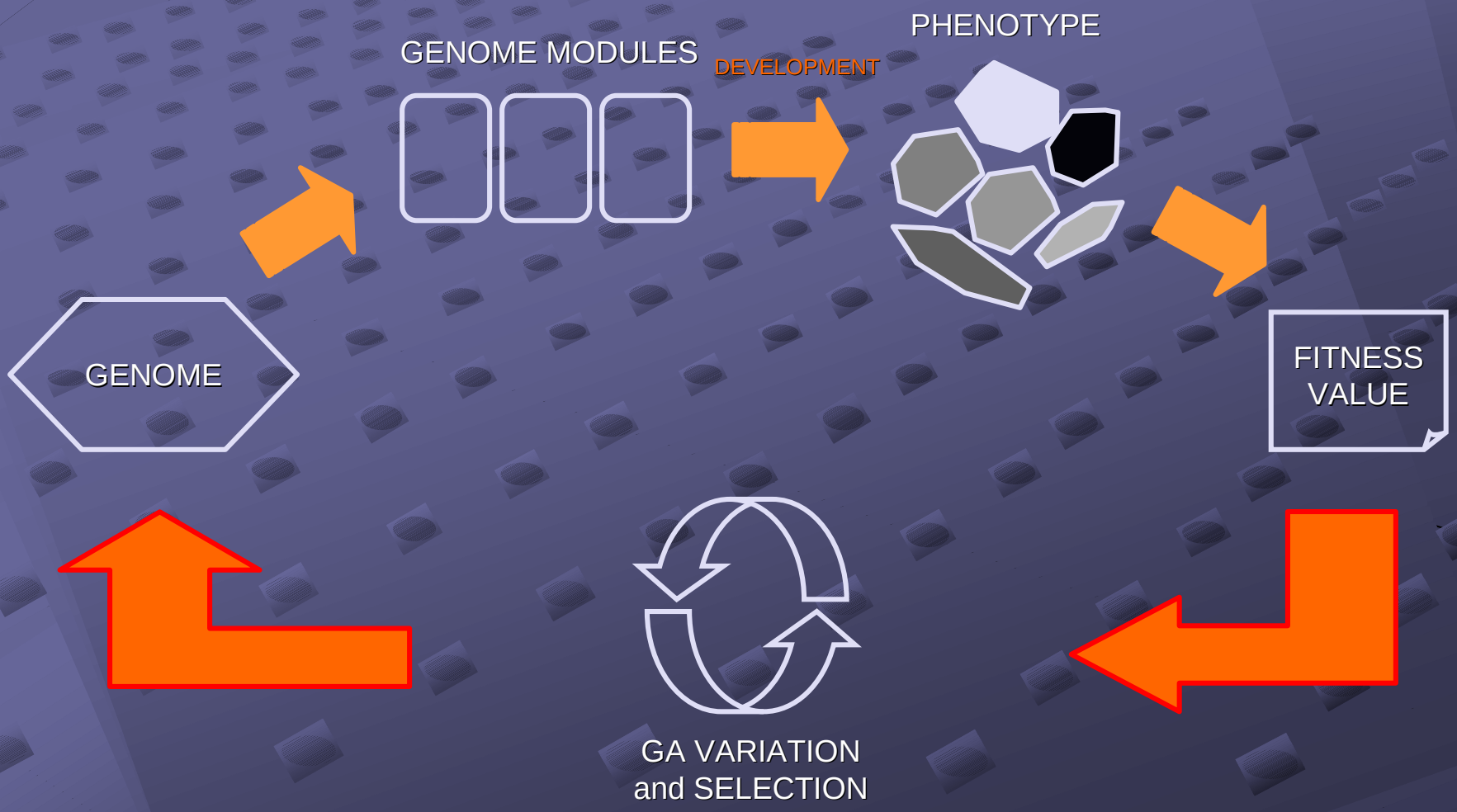
- GAs in EHW: scaling difficulties
- Possible (partial) solution: Development
- preferably *gene-regulated* development
- Our hypothesis:

  Naively Plugging (Gene-Regulated) Development into GAs does not work, because of evolutionary reasons.

Intuitions supporting the hypothesis

1. Development largely based on *gene interaction*, while GAs dislike epistasis
2. Gene modules will arise, which require non-standard genetic operators
3. Gene module interdependence, typical for development, is likely to cause mismatch with an accretive GA.
4. GAs are accretive (<> compositional) when faced with poor variation and linkage.
5. Modular property must persist throughout genotype-fitness loop

Development in GAs: The Genome-Fitness loop



Research Approach

- Build a model for mutli-cellular, gene regulated development
- Investigate modularisation in a broad context
- Investigate impact of genetic operators on modules
- Investigate module interdependence

Biological Development (1/2)

- Converts genotype to multicellular phenotype
- Gene regulation: genes affect each others activation (proteins etc.)
- Cells:
  - Identical DNA (thus differential gene expression)
  - Communicate
  - Divide
  - Differentiate
  - (Move / die)

Biological Development (2/2)

What causes cells to change (simplified):

1. Cellular lineage: (= line of descent, cell divisions)

   "who are my parents ?"

   - Symmetric divisions and nuclear determinants
   - A-symmetric divisions

2. Cellular induction (= communication) :

   "who are my neighbours ?"

   - Cell context within phenotype
   - Important for regeneration etc.

A Development model: genes

- a gene: rule based

  <Antecedent> ?£ <consequent>

Reference/compare values:

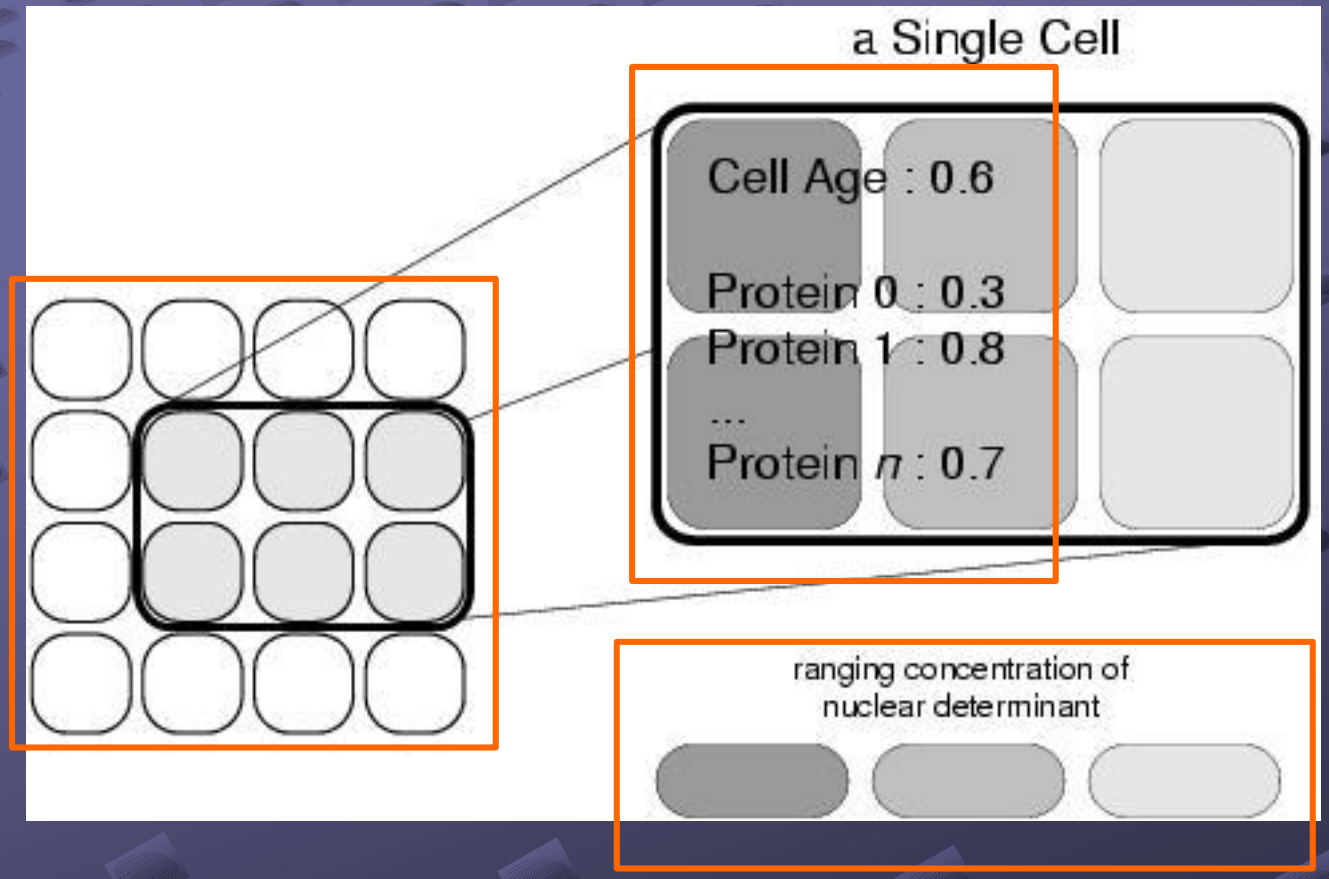
Cell age, protein conc, Nuclear determinant conc, global substances, ...

! Can be ref of neighbouring cell's property: INDUCTION

Perform actions:

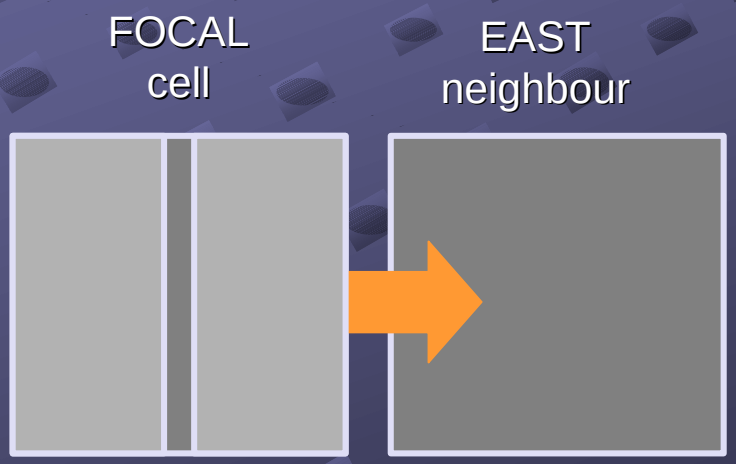
1. Increase/decrease protein concentration
2. Cell division (symetric/aymmetric : LINEAGE)
3. differentiation

Example of a Cel



Example of a gene

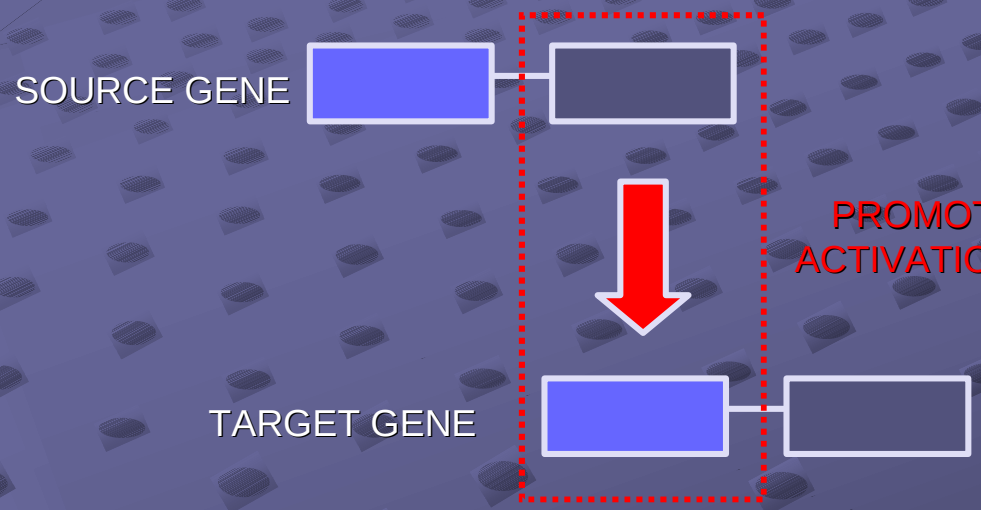
GENE: [cond: [0.4 OP< <prot E:0>] --> divide:[orient:N-S,size:0.5,…]]



Gene Interaction

- How does a development genome behave relative to genetic operators ?
- Key is: interaction
- *Independent* of fitness, interaction means: *a source gene influences the activation/inhibition of a target gene*
- How do genes interact in our model ?

Gene Interaction: example



Interaction Weight

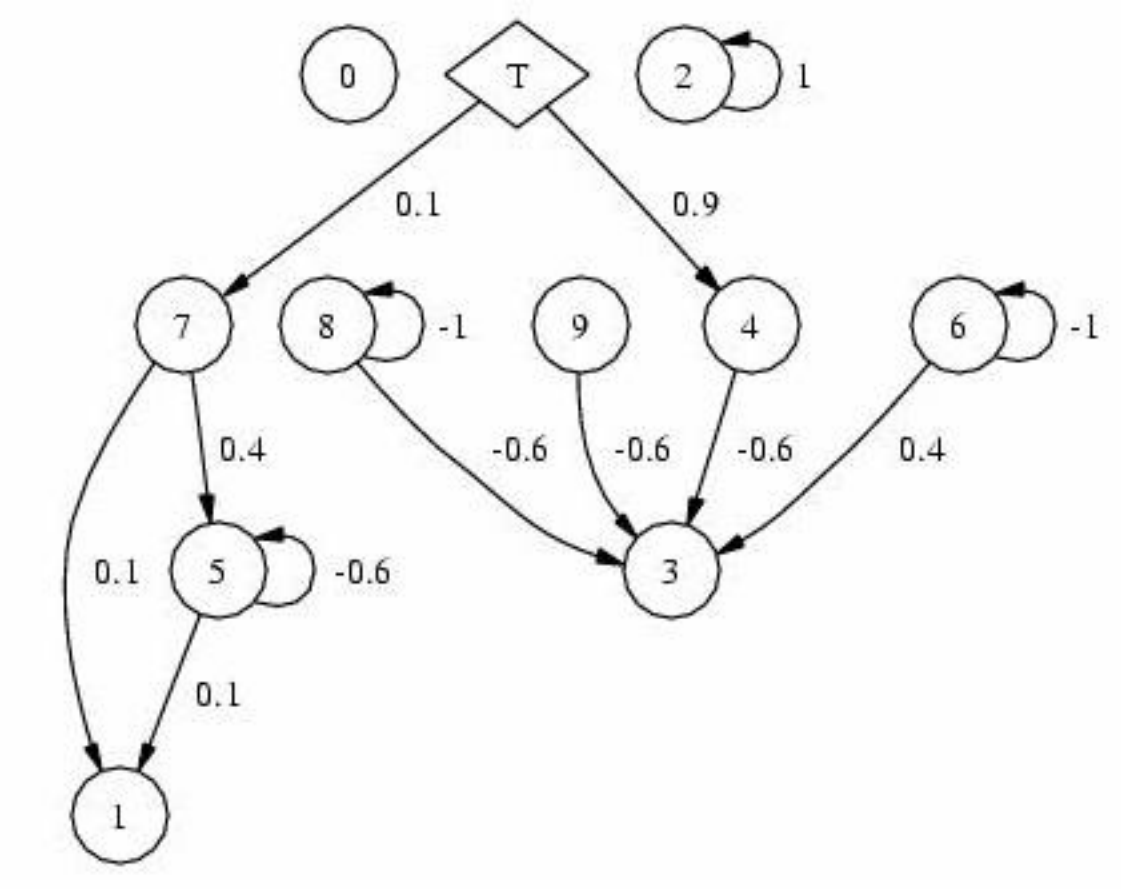
(~probability of propagation)

(see paper for details)

Examples:

- Source gene increases protein concentration, while target gene requires high protein concentratinos
- Source gene divides and makes young cells, while target gene activates in young cells

From Interactions to an Interaction Graph/Matrix



Contains interaction weights between all gene pairs in the genome.

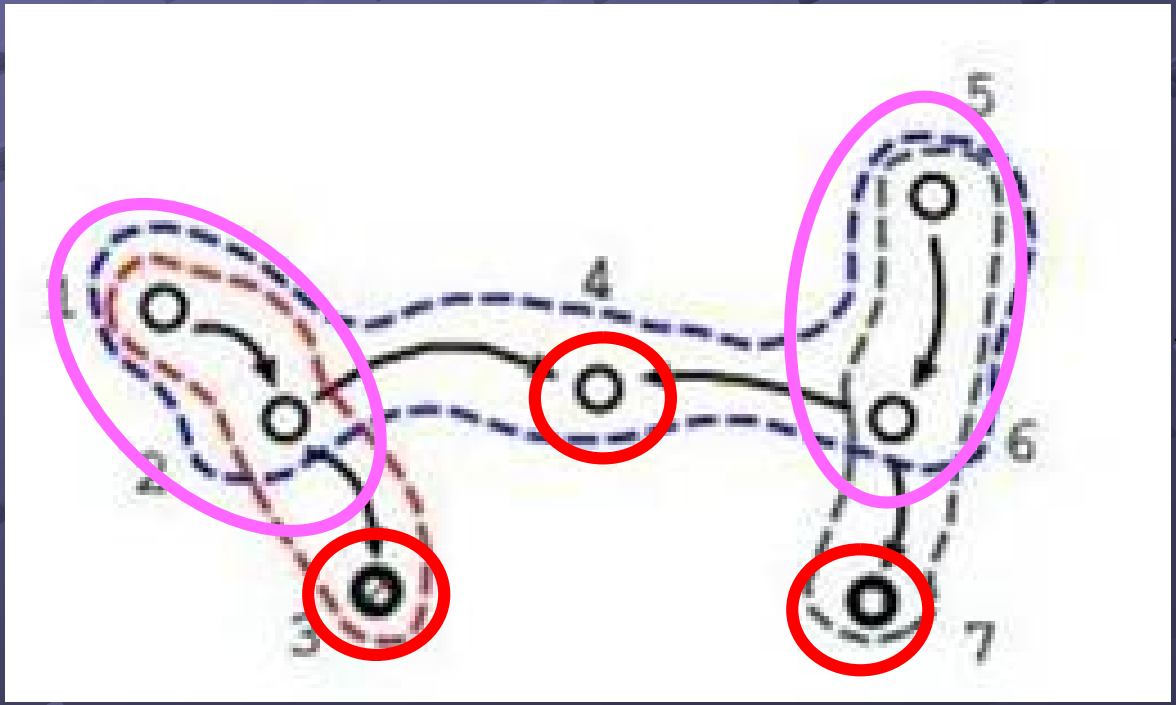
(~functional genomics in bio-informatics)

Modules of Gene interaction

- Modules identified by genes that have no outgoing interactions (genes 3, 4 and 7)
- Extend with all genes that influence these genes

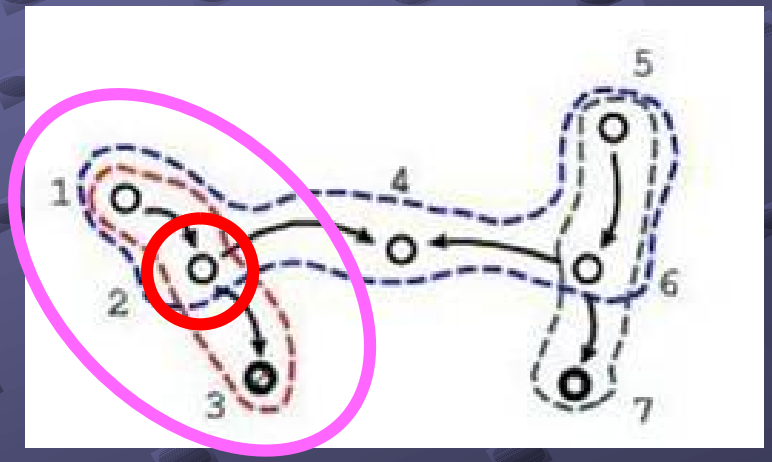
Result is 3 modules,

With partly overlapping genes



Properties of genes in modules

- 1 module
  - Size in number of genes
  - Max. Propagation depth in number of genes
- 1 gene
  - Number of in/out going interactions
  - Number of modules it is shared in (“module overlap”)
  - Its type (division, protein change, ...)

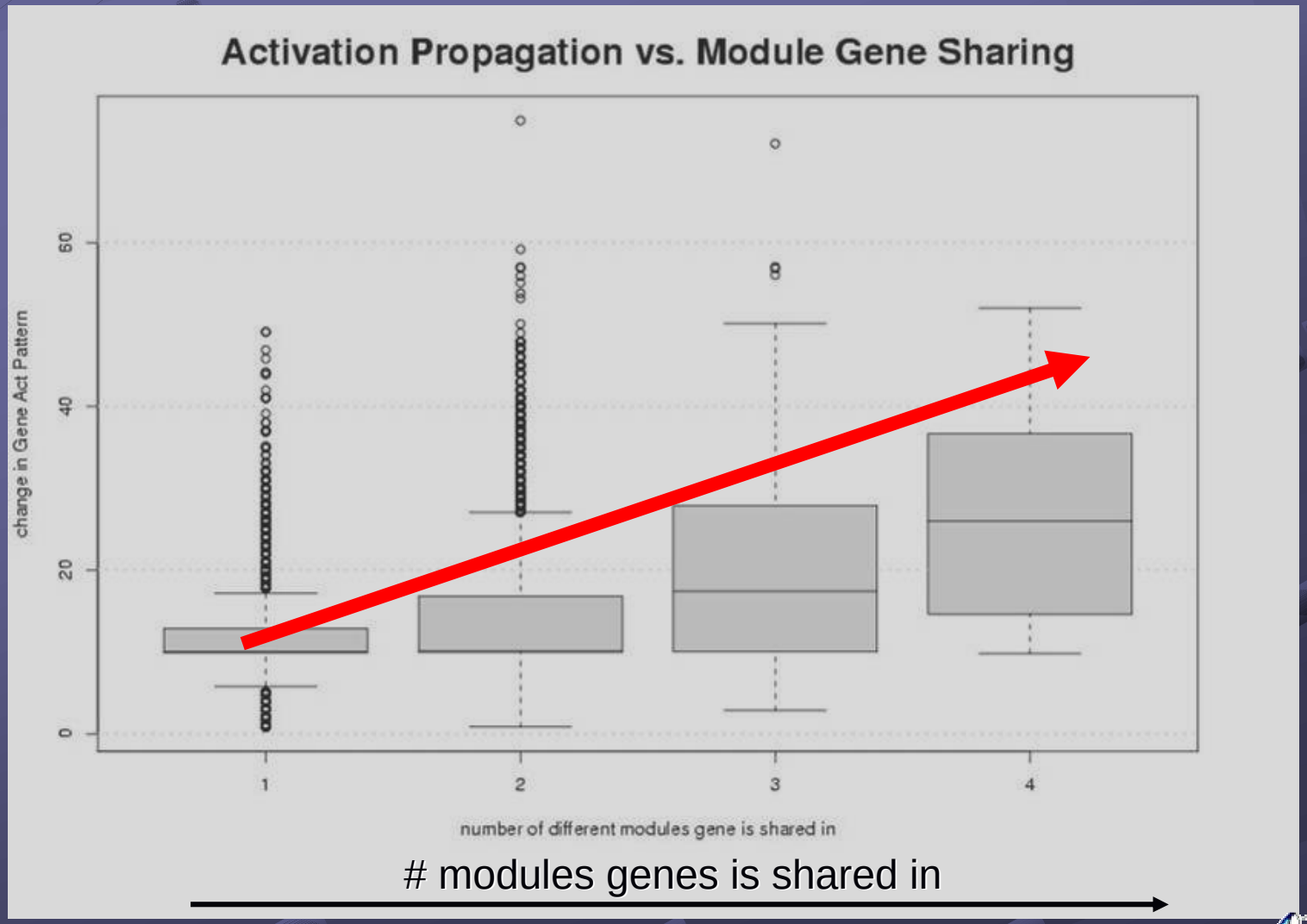


Mutations on Genes in Modules

- Mutation: accretive view on GAs
  "sequential accumulation of small variations"
- Mutations change modules in genome
- First investigate effect of gene in static modular context ?ñ gene inversions
- Genes remains, antecedent *result* is Boolean inverted
- Observe effect of inversion on rest of genome

Inversions on Genes in Modules

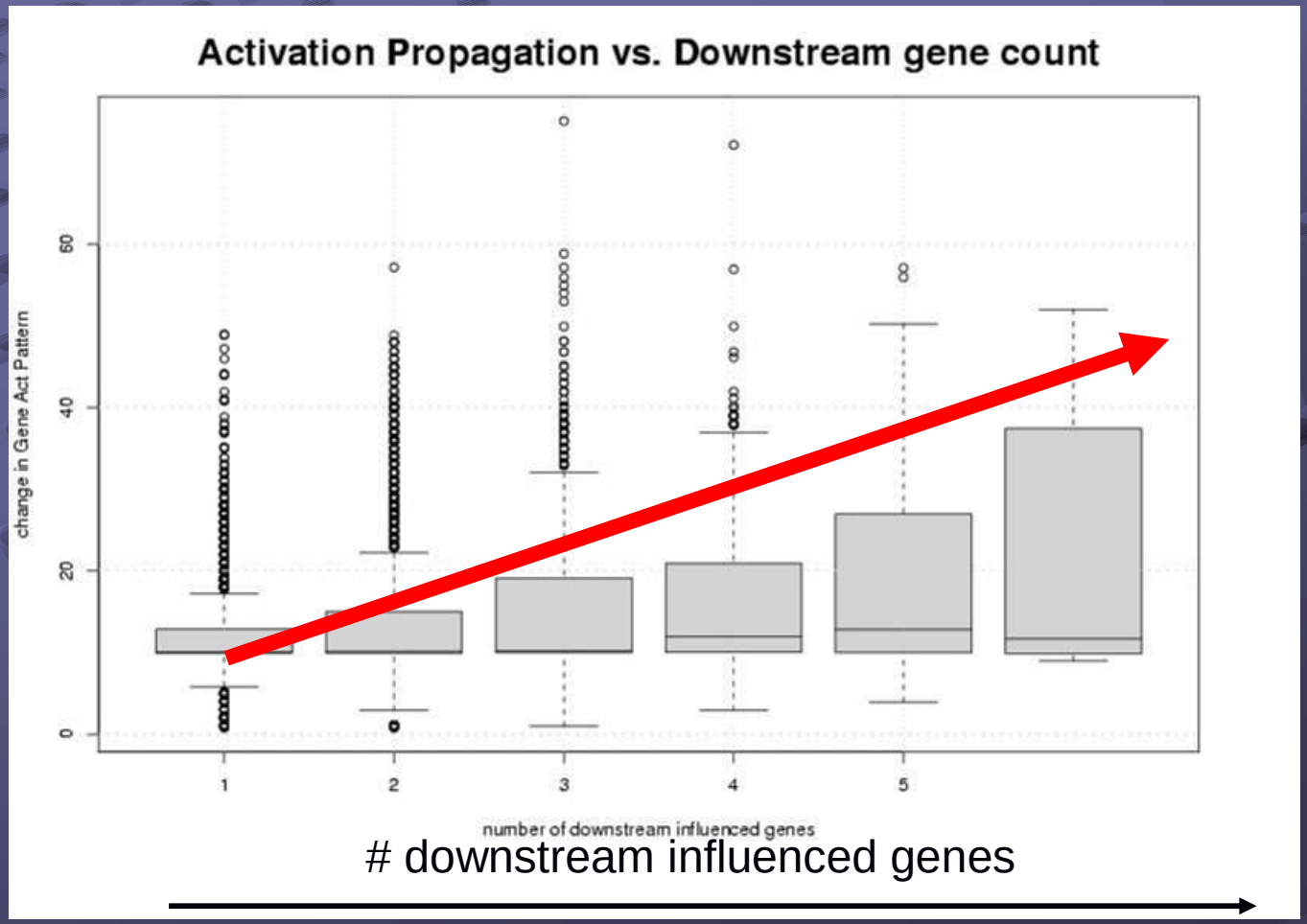
Change in activation sequence



modules genes is shared in

Inversions cont'd

Change in activation sequence



downstream influenced genes

Some conclusions

- GAs + Development : beware ...
- (another) development model
  - Aimed at investigating evolvability issues
- Gene regulation: genes cluster in modules
- Identify using activation propagation
- Modules with # properties
- Observability of effect of properties
  - supports the approach
  - Usable in the line of e.g. reasoning about mutation

Future work...

- Crossover on modules:
  - How do modules depend on each other ?
- What about the linkage issue ?
  - Multiple-context usability of genes in development increases chance of bad linkage
- Modularity in the loop: from genome to fitness
  - Un-modular fitness functions absorb beneficial effects of previous modular effects

Questions ...

- Piet van Remortel
- CoMo – lab, VUB, Belgium
- pvremort@vub.ac.be

Thanks !