Inferring Gene Networks from Microarray Data using a Hybrid GA

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Introduction

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- We combine the GA with a back-propagation local search

Microarray Data

- Goal: to decipher the connections of the genetic network
- Pathway: DNA → mRNA → protein
- Mircoarray technology provides a snapshot of mRNA levels
- mRNA levels are an indirect measurement of gene activity
- Multiple mRNA snapshots over time reveal the gene interactions
- Massive data sets: 6,000 genes for the yeast cell
- Too large to infer anything meaningful by hand

Genetic Algorithm: Approach

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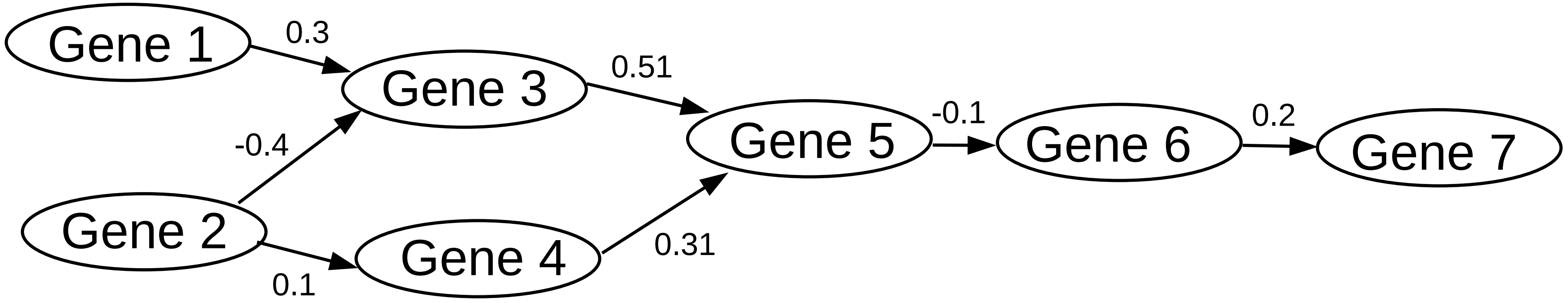
- Compare single population GA with an island model
- Compare with Friedman’s results on Rosetta data set

Example Gene Network



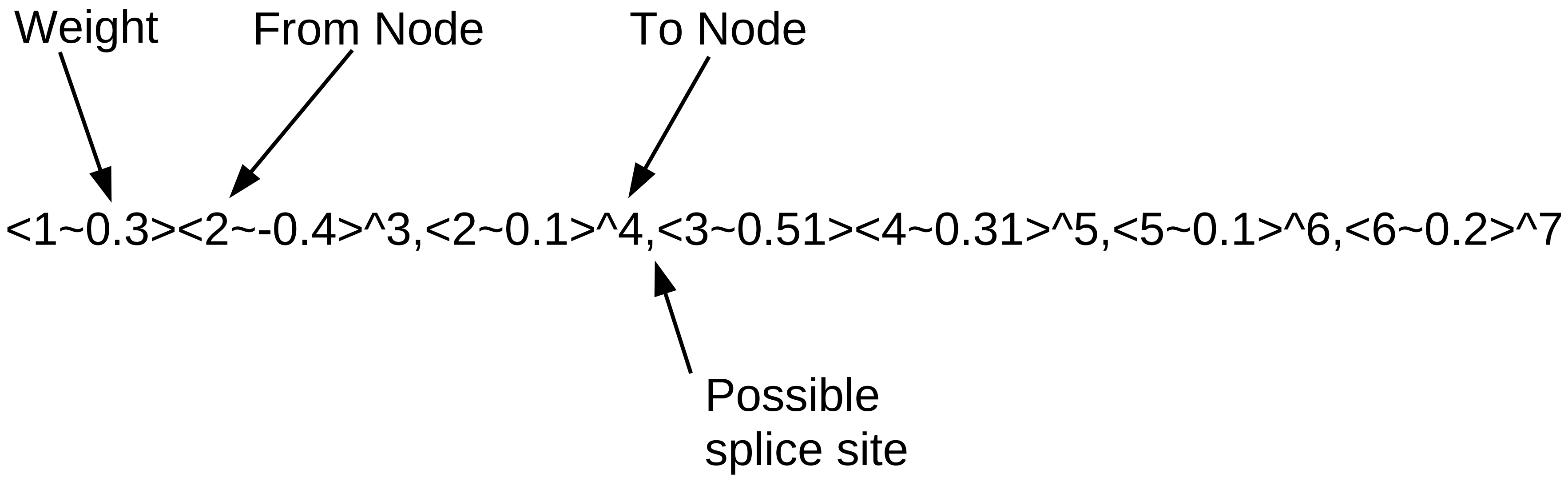
Representing Gene Networks

- Matrix representation:

$$\begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0.3 & -0.4 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0.1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0.51 & 0.31 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0.1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0.2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

Representing Gene Networks

- String representation:



Weight

From Node

To Node

<1~0.3><2~-0.4>^3,<2~0.1>^4,<3~0.51><4~0.31>^5,<5~0.1>^6,<6~0.2>^7

Possible
splice site

Evaluating Network Fitness

- Estimate gene expression levels at time $t+1$ given levels at time t:

$$s_i(t+1) = \sum_{j=0}^{n} w_{ji} x_j(t)$$

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$$s_i(t+1) = \sum_{j=0}^{n} w_{ji} x_j(t)$$

- Pass estimate through a sigmoid function for biological realism:

$$x_i(t+1) = \frac{n_j}{1 + e^{-n_j(s_i(t+1))}}$$

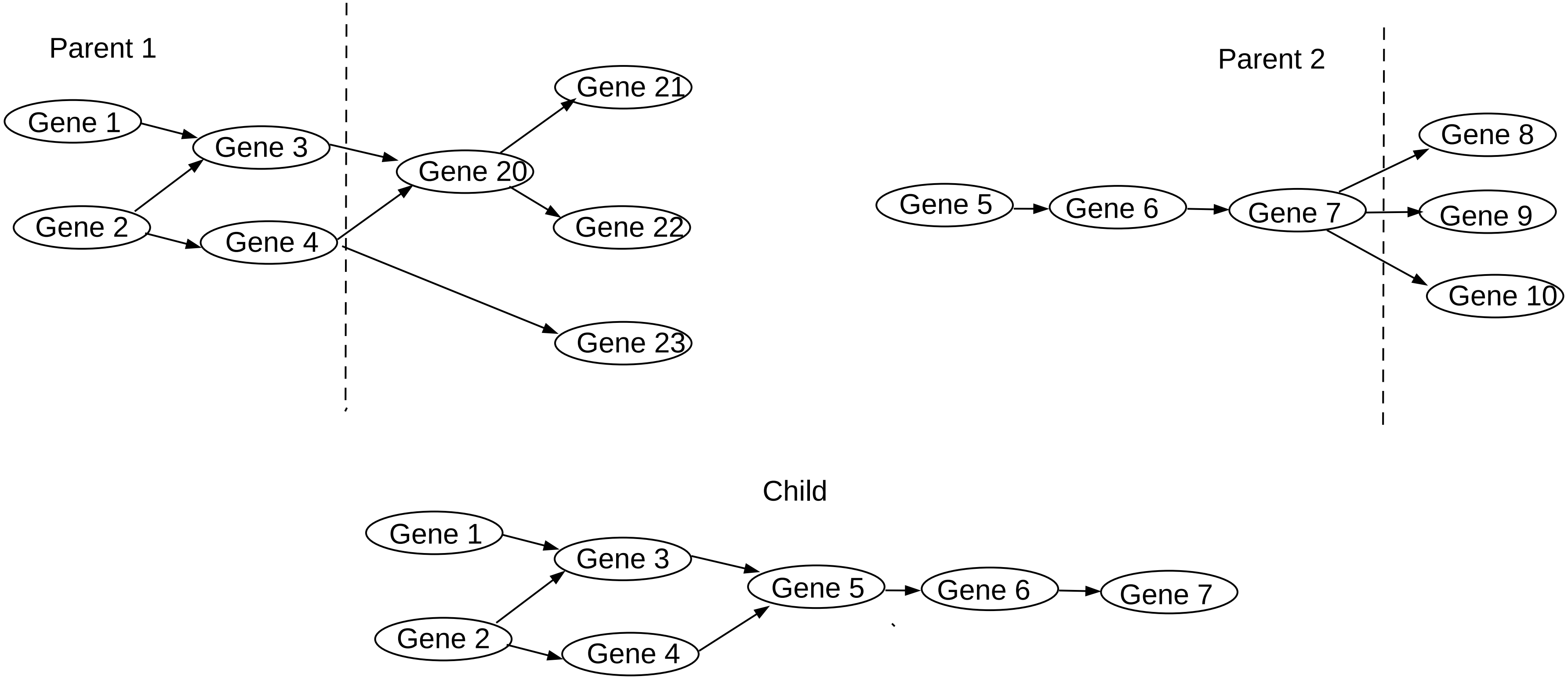
Evaluating Network Fitness

- Overall network fitness:

$$fitness = \sum_{i=0}^{n} \sum_{t=0}^{T} |y_i(t) - x_i(t)| + num\_nodes/b$$

- Imposed bias towards smaller networks

Single Point Network Crossover



Single Machine Results

Initial Pop	Net Size	GA Fitness	BP Error	Markov matches	Time
2000	50	186.60	2.032	6	30 min
2000	20	257.16	1.200	0	2 mins
5000	50	180.43	1.200	8	35 min
5000	20	221.40	0.8323	6	5 min

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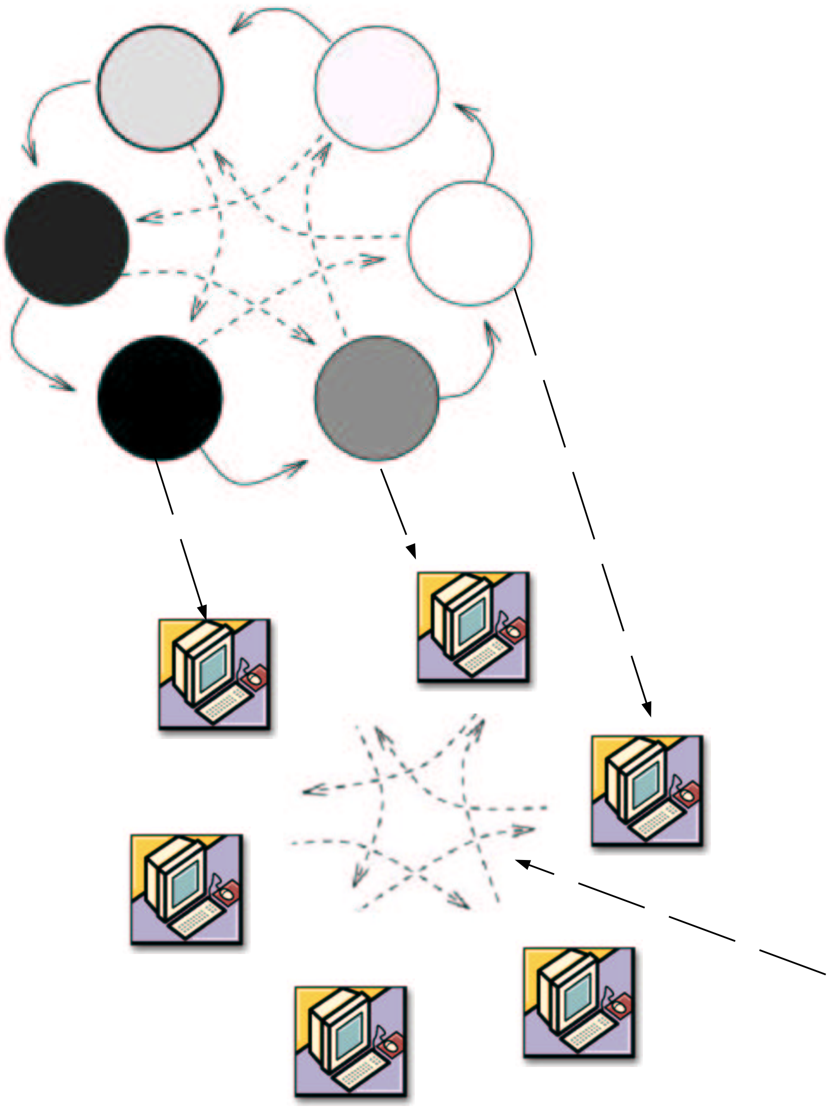
- But a different (sub-)network every time
- Impossible to validate results

Island Model GA



after each generation each island sends it best individual to all the other islands

Island Model Results

Nodes	Pop	Size	GA Fitness	BP Error	Markov matches	Time
4	2000	50	225.60	2.214	6	30 min
4	2000	20	257.16	1.334	2	7 mins
4	5000	50	223.43	2.200	4	42 min
4	5000	20	227.30	1.542	7	9 min
8	2000	50	122.60	2.635	9	30 min
8	2000	20	117.16	1.986	5	6 mins
8	5000	50	116.22	1.256	7	40 min
8	5000	20	132.30	0.623	5	11 min

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- Better fitness, but same problem as before
- Results with simulated data demonstrate validity of the technique

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- The GA can find highly fit networks that explain the test data
- Back-propagation can be used to fine tune the network weights
- The island model markedly improves the fitness level achieved
- Simulation may be able to provide benchmark data