11
Applications in bioinformatics, systems biology and artificial life

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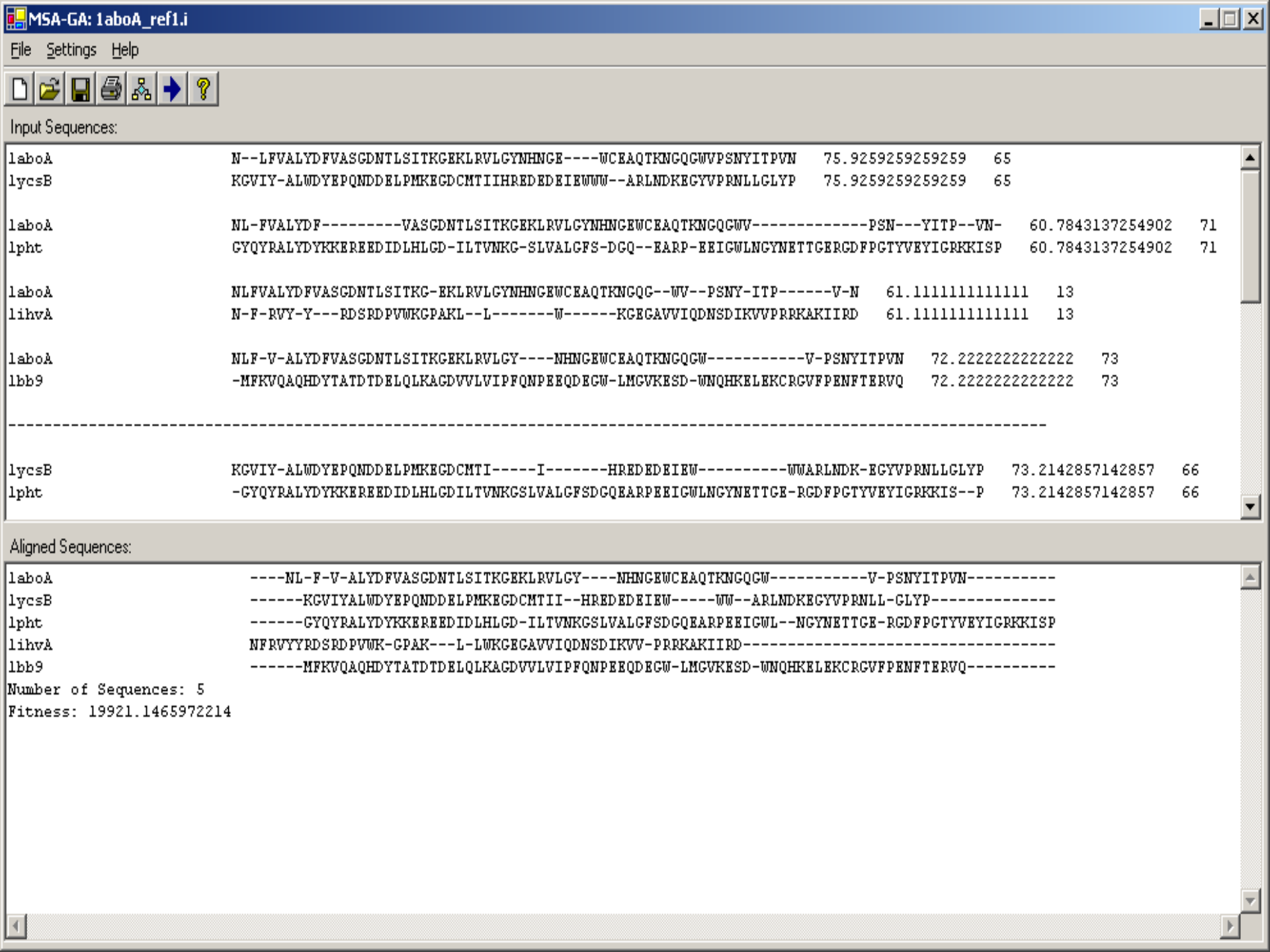
MSA-GA: 1aboA_ref1.i
File Settings Help
Input Sequences:
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lycsB KGVIY-ALWDYEPQNDDELPMKEGDCMTIIHREDEDEIEWWW--ARLNDKEGYVPRNLLGLYP 75.9259259259259 65
laboA NL-FVALYDF---------VASGDNTLSITKGEKLRVLGYNHNGEWCEAQTKNGQGWV----------PSN---YITP--VN- 60.7843137254902 71
lpht GYQYRALYDYKKEREEDIDLHLGD-ILTVNKG-SLVALGFS-DGQ--EARP-EEIGWLNGYNETTGERGDFPGTYVEYIGRKKISP 60.7843137254902 71
laboA NLFVALYDFVASGDNTLSITKG-EKLRVLGYNHNGEWCEAQTKNGQG--WV--PSNY-ITP------V-N 61.1111111111111 13
lihvA N-F-RVY-Y---RDSRDPVWKGPAKL--L-------W------KGEGAVVIQDNSDIKVVPRRKAKIIRD 61.1111111111111 13
laboA NLF-V-ALYDFVASGDNTLSITKGEKLRVLGY----NHNGEWCEAQTKNGQGW----------V-PSNYITPVN 72.2222222222222 73
lbb9 -MFKVQAQHDYTATDTDELQLKAGDVVLVIPFQNPEEQDEGW-LMGVKESD-WNQHKELEKCRGVFPENFTERVQ 72.2222222222222 73
lycsB KGVIY-ALWDYEPQNDDELPMKEGDCMTI-----I-------HREDEDEIEW----------WWARLNDK-EGYVPRNLLGLYP 73.2142857142857 66
lpht -GYQYRALYDYKKEREEDIDLHLGDILTVNKGSLVALGFSDGQEARPEEIGWLNGYNETTGE-RGDFPGTYVEYIGRKKIS--P 73.2142857142857 66
Aligned Sequences:
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lycsB ------KGVIYALWDYEPQNDDELPMKEGDCMTII--HREDEDEIEW-----WW--ARLNDKEGYVPRNLL-GLYP--------------
lpht ------GYQYRALYDYKKEREEDIDLHLGD-ILTVNKGSLVALGFSDGQEARPEEIGWL--NGYNETTGE-RGDFPGTYVEYIGRKKISP
lihvA NFRVYYRDSRDPVWK-GPAK---L-LWKGEGAVVIQDNSDIKVV-PRRKAKIIRD----------
lbb9 ------MFKVQAQHDYTATDTDELQLKAGDVVLVIPFQNPEEQDEGW-LMGVKESD-WNQHKELEKCRGVFPENFTERVQ----------
Number of Sequences: 5
Fitness: 19921.1465972214

Comparison

	msa-clustal	pre-clustal	msa-pre
better	12	17	8
worse	16	4	20
same	0	7	0
total	28	28	28

averages

MSA-GA	**0.59042857**
MSA-GA w/p	**0.65292857**
Clustal	**0.63978571**

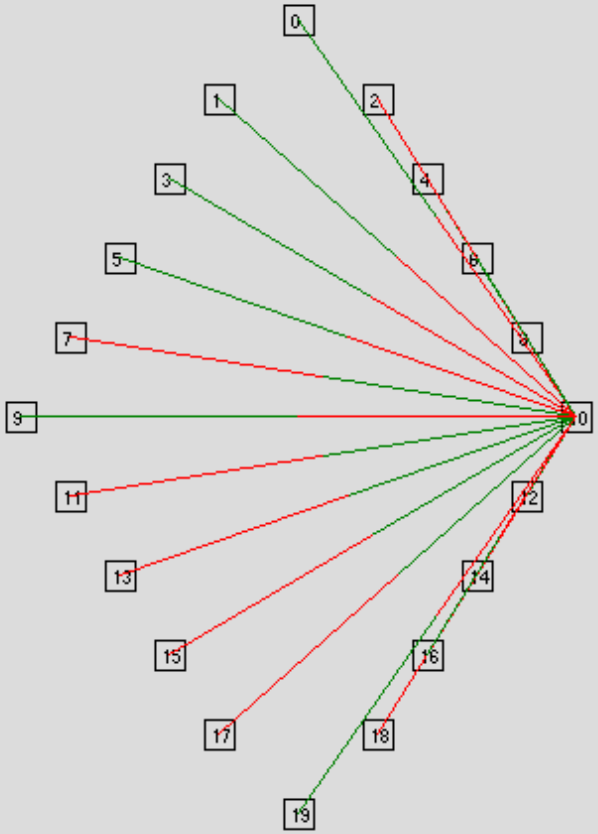
Optimization of Microarray Design

File Settings Run Zoom Help

Generation: 28719

Organism: 5 Fitness: -36.1

Cy3	0	10	10	10	5	6	10	10	19	4	10	10	12	16	3	10	10	9	1
Cy5	10	18	13	15	10	10	8	17	10	10	14	7	10	10	10	2	11	10	10



Parameters

Optimization Parameters

Population size:	100
Number of generations:	100000
Crossover rate:	0.9
Mutation rate:	0.05

Criterion Weights

☐	Minimize number of arrays:	0.0
☑	Minimize number of steps:	1
☐	Weight of contrasts:	0.0
☑	Balance Dyes:	1
☐	Variance (A-optimality):	0.0

Microarray Parameters

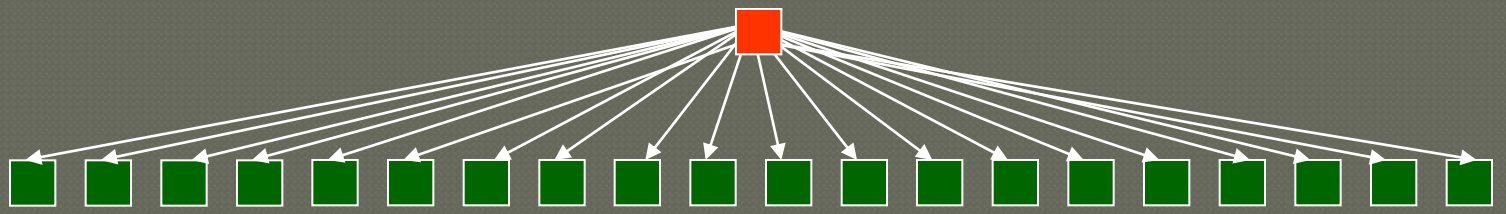
Maximum number of arrays:	4
Number of samples:	4

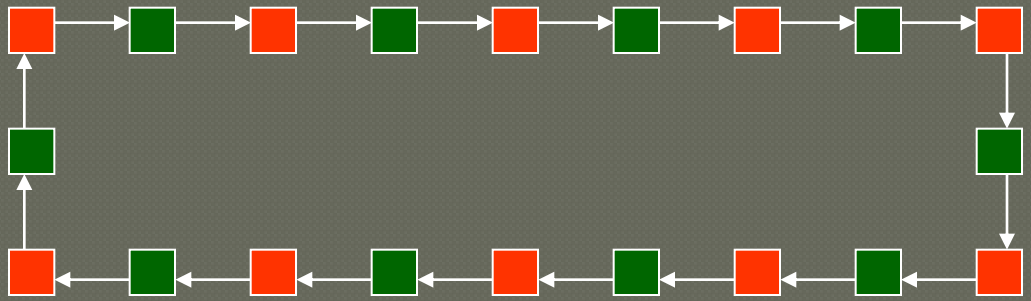
◉ Maximize Contrasts

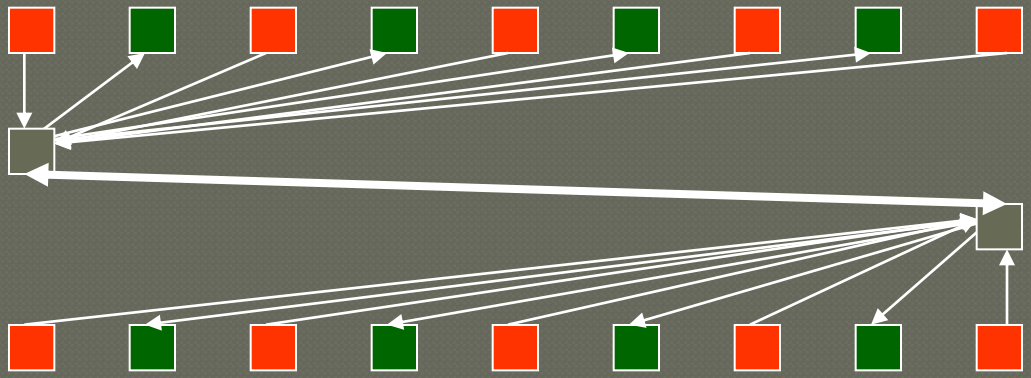
○ Minimize Contrasts

OK Cancel

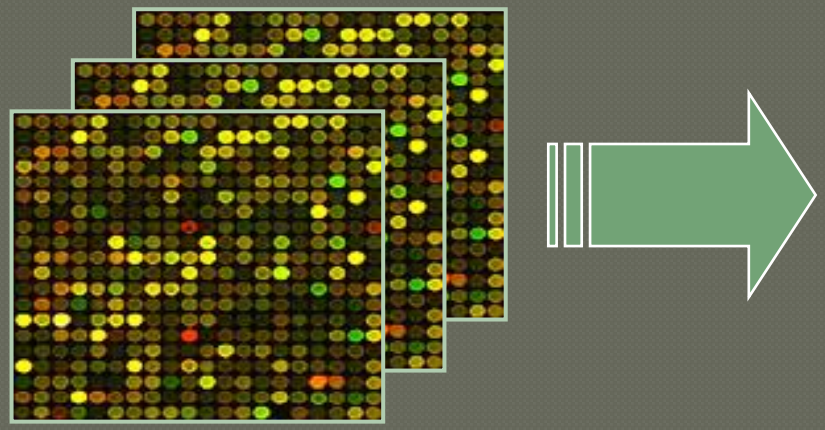
Generation: 28719



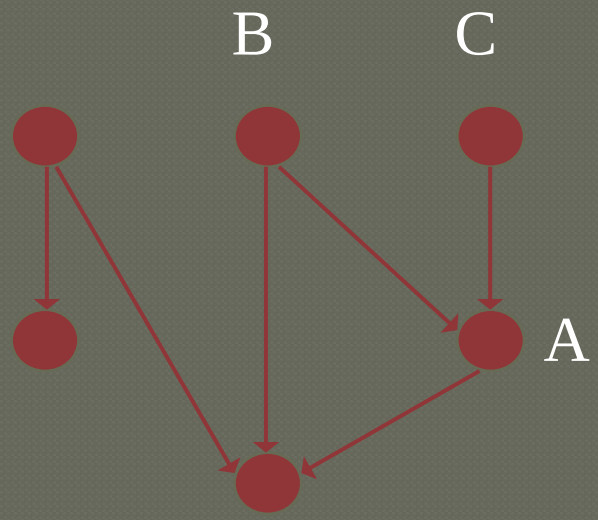




Biological Process Reconstruction



Microarray gene expression data



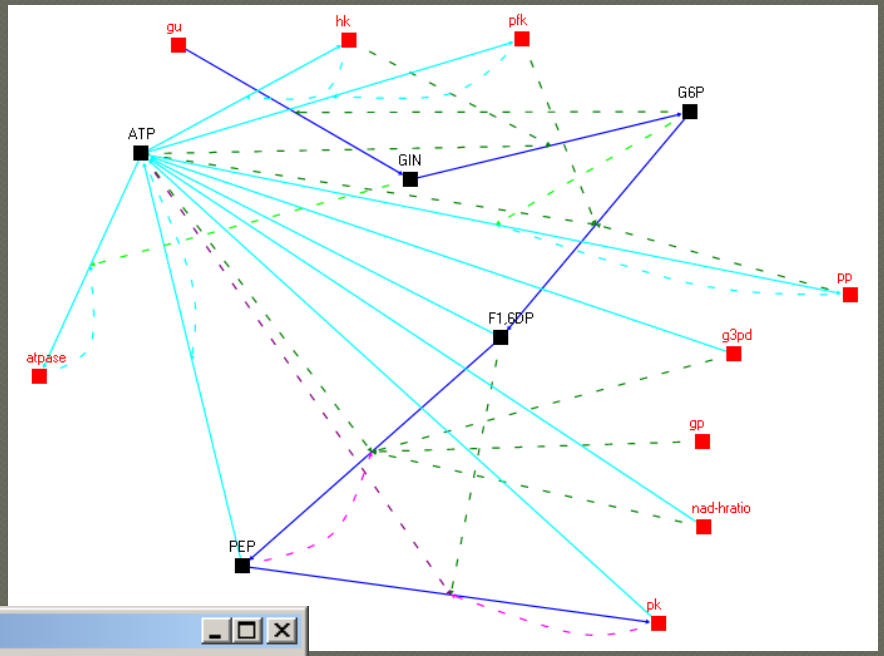
Genetic network

Objectives

- To find a mathematical model that:
  - predicts how a biological process changes over time
  - predicts measurable outputs of the process
  - Helps explain/understand how the process operates
- Parameterize the model with realistic biological parameters
  - Estimate how parameter changes affect the process

Parameterization of S-Systems Equations
Fermentation pathway in *Saccharomyces cerevisae*

$$\dot{X}_i = \alpha_i \prod_{j=1}^{n+m} X_j^{g_{ij}} - \beta_i \prod_{j=1}^{n+m} X_j^{h_{ij}}$$



Equations: Anaerobic Fermentation

File Options

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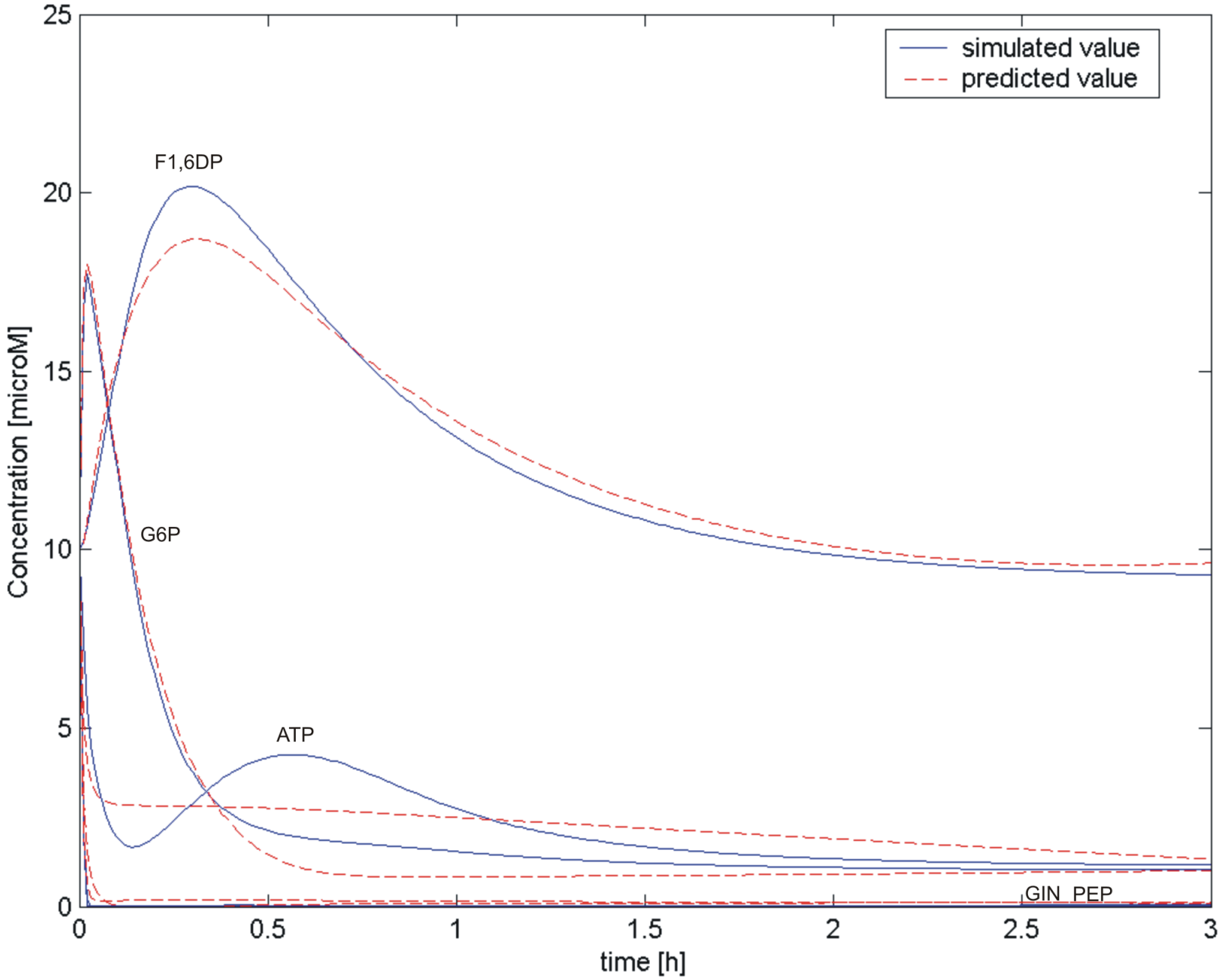
Equations:
GIN = 0.8122*gu^1*G6P^-0.2344 - 2.8632*GIN^0.7464*ATP^0.0243*hk^1

G6P = 2.8632*GIN^0.7464*ATP^0.0243*hk^1 - 0.5239*G6P^0.735*ATP^-0.394*pfk^0.999*pp^0.001

F1,6DP = 0.5232*G6P^0.7318*ATP^-0.3941*pfk^1*pp^0 -
0.0148*F1,6DP^0.584*ATP^0.119*g3pd^0.944*gp^0.056*nad-hratio^-0.575*PEP^0.03

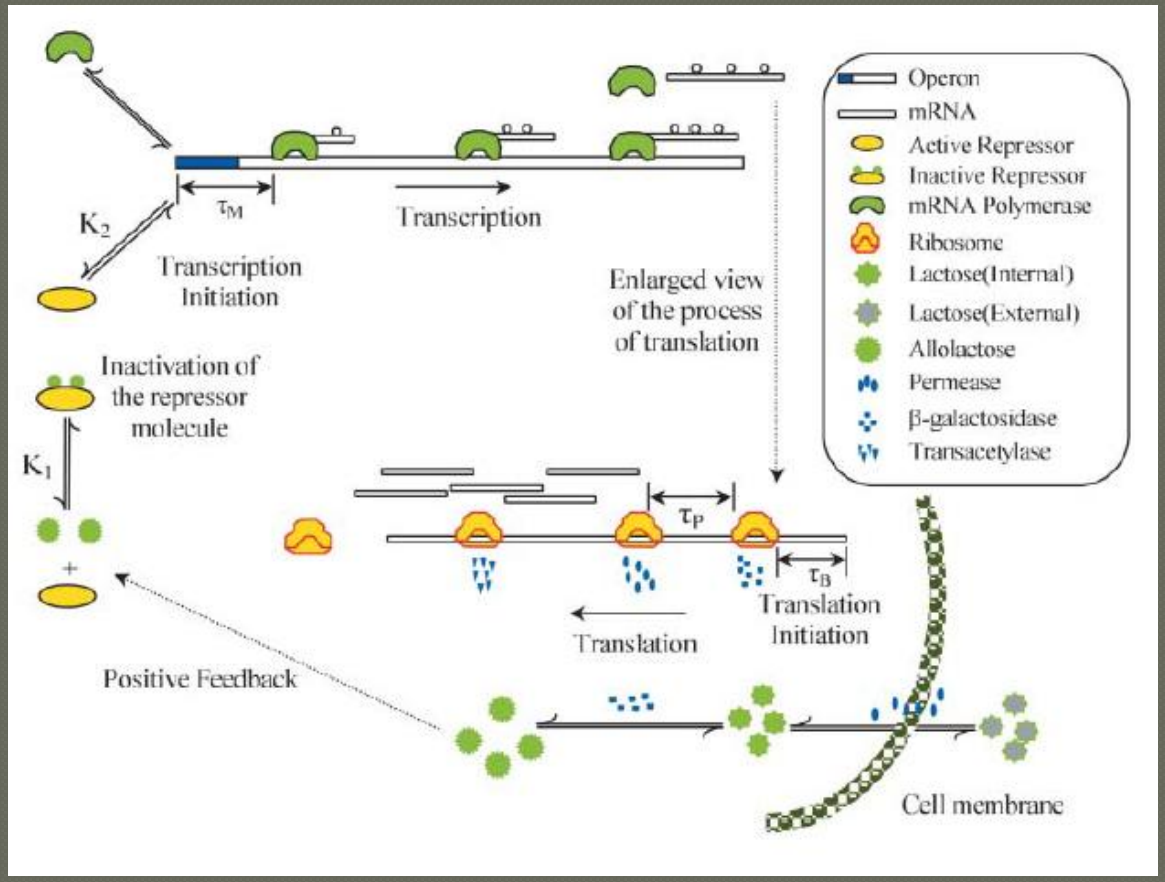
PEP = 0.022*F1,6DP^0.6159*ATP^0.1308*g3pd^1*gp^0*nad-hratio^-0.6088*PEP^0 -
0.0945*PEP^0.533*F1,6DP^0.05*ATP^-0.0822*pk^1

ATP = 0.0913*F1,6DP^0.333*PEP^0.266*g3pd^0.5*pk^0.5*nad-hratio^-0.304*ATP^0.024 -
3.2097*ATP^0.372*pp^0.0002*atpase^0.47*pfk^0.265*hk^0.265*GIN^0.198*G6P^0.196
```


simulated value
predicted value
F1,6DP
G6P
ATP
GIN_PEP
Concentration [microM]
time [h]
0
5
10
15
20
25
0
0.5
1
1.5
2
2.5
3

Lac Operon – A Well Characterized System

- Classic model of gene regulation
- Few elements
- Well studied and parameterized
- Biological measurements available
- Various mathematical models



A System of Delay Differential Equations for the lac operon in *E. coli* – I

- 4 time delay differential equations
- 8 parameters
- 6 functions:
  - Plus
  - Minus
  - Power
  - Division
  - Multiplication
  - Time delay

$$\frac{dM}{dt} = \frac{1 + k_1 y_4^{\rho}}{1 + y_4^{\rho}} - b_1 y_1$$

$$\frac{dP}{dt} = y_1 - b_2 y_2$$

$$\frac{dB}{dt} = r_3 y_1 - b_3 y_3$$

$$\frac{dL}{dt} = S y_2 - y_3 y_4$$

Mahaffy and Savev 1999

A System of Delay Differential Equations for the lac operon in *E. coli* – II

- 3 time delay differential equations
- 17 parameters
- 6 functions:
  - Plus
  - Minus
  - Power
  - Division
  - Multiplication
  - Time delay

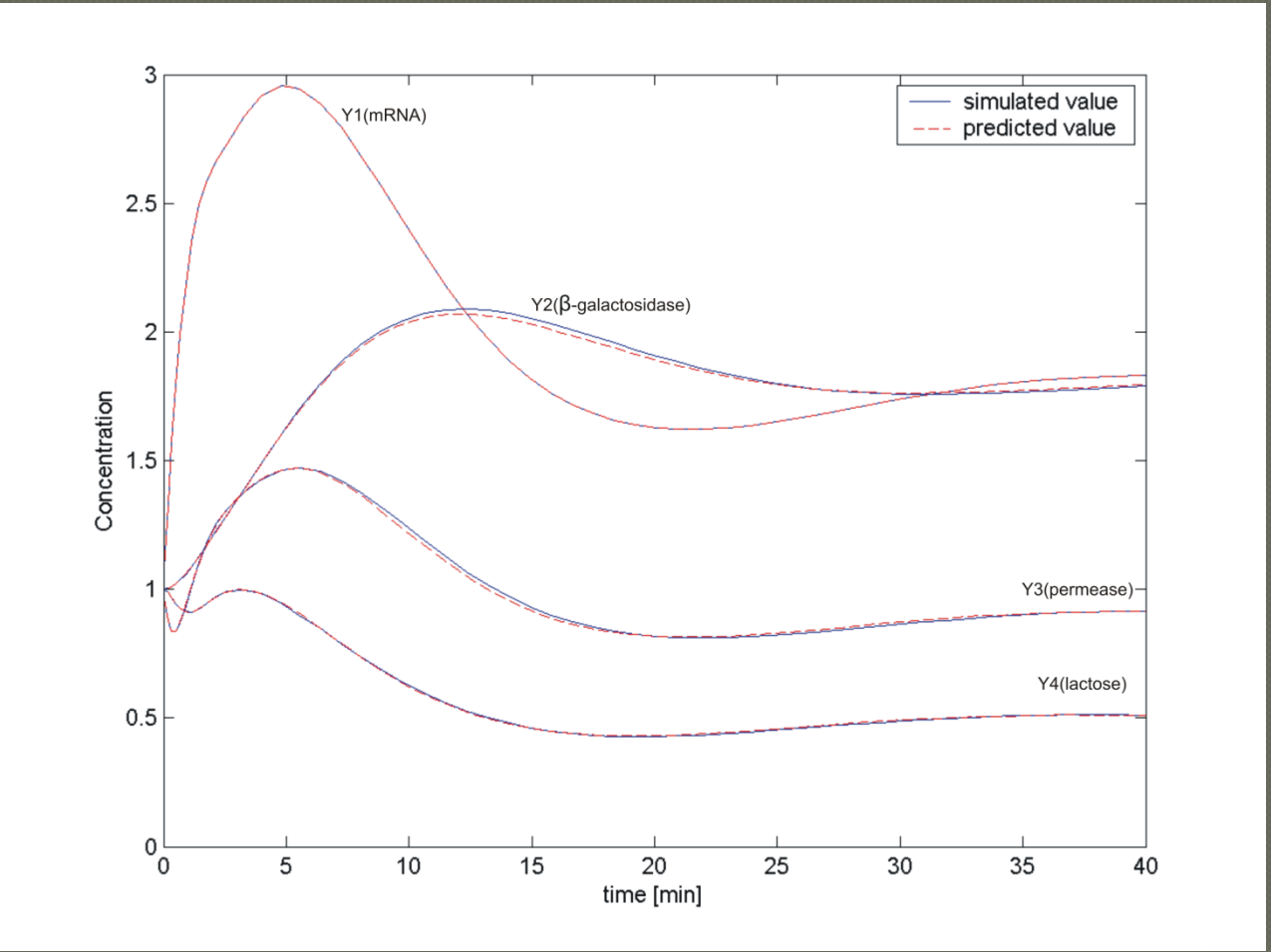
$$\frac{dM}{dt} = \alpha_M \frac{1 + k_1 (e^{-\mu \tau_M} A_{\tau_M})^n}{k + k_1 (e^{-\mu \tau_M} A_{\tau_M})^n} - \tilde{Y}_M M$$

$$\frac{dB}{dt} = \alpha_B e^{-\mu \tau_B} M_{\tau_B} - \tilde{Y}_B B$$

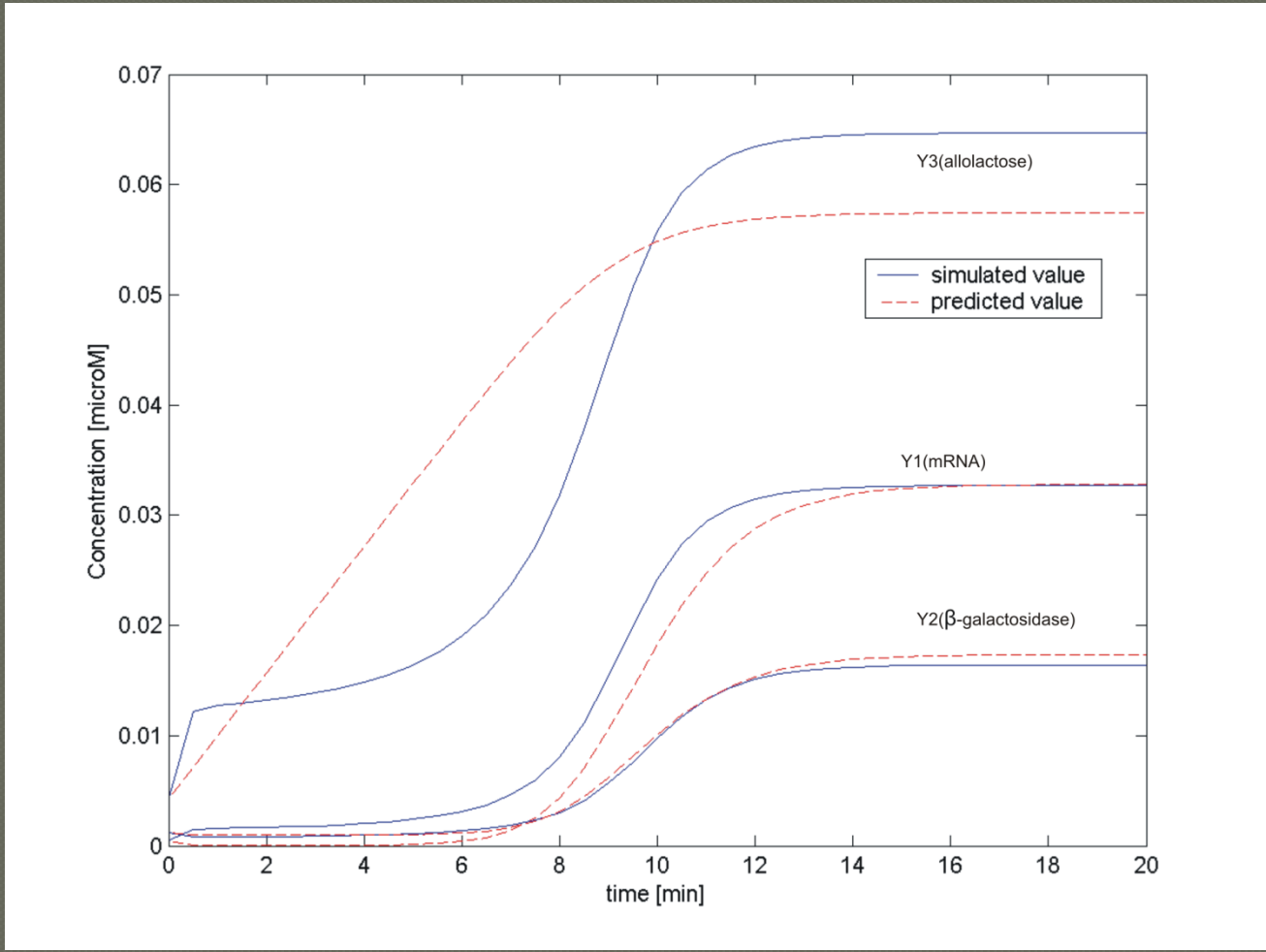
$$\frac{dA}{dt} = \alpha_A B \frac{L}{K_L + L} - \beta_A B \frac{A}{K_A + A} - \tilde{Y}_A A$$

Yildirim *et al.* 2004

Goodness of Fit Model I



Goodness of Fit Model II



Evolved solutions

$$y1 = \frac{4.9987\, y_4^{t-0.64} y_4^{t-0.64} + 1}{y_4^{t-0.64} y_4^{t-0.64} + 1} - y_1$$

$$y2 = y_1 - (y_2 + y_2)$$

$$y3 = y_1 / 10.1023 - y_3 / 10.1023$$

$$y4 = y_2 - y_3 y_4$$

$$\frac{dM}{dt} = \frac{1 + k_1 y_4^{\rho}}{1 + y_4^{\rho}} - b_1 y_1$$

$$\frac{dP}{dt} = y_1 - b_2 y_2$$

$$\frac{dB}{dt} = r_3 y_1 - b_3 y_3$$

$$\frac{dL}{dt} = S y_2 - y_3 y_4$$

$$y1 = 0.123003^{8.1379 - \left(\frac{y3}{y1 + y1 + 8.7614}\right)} - y1$$

$$y2 = y1 - y1^{t-0.53614}$$

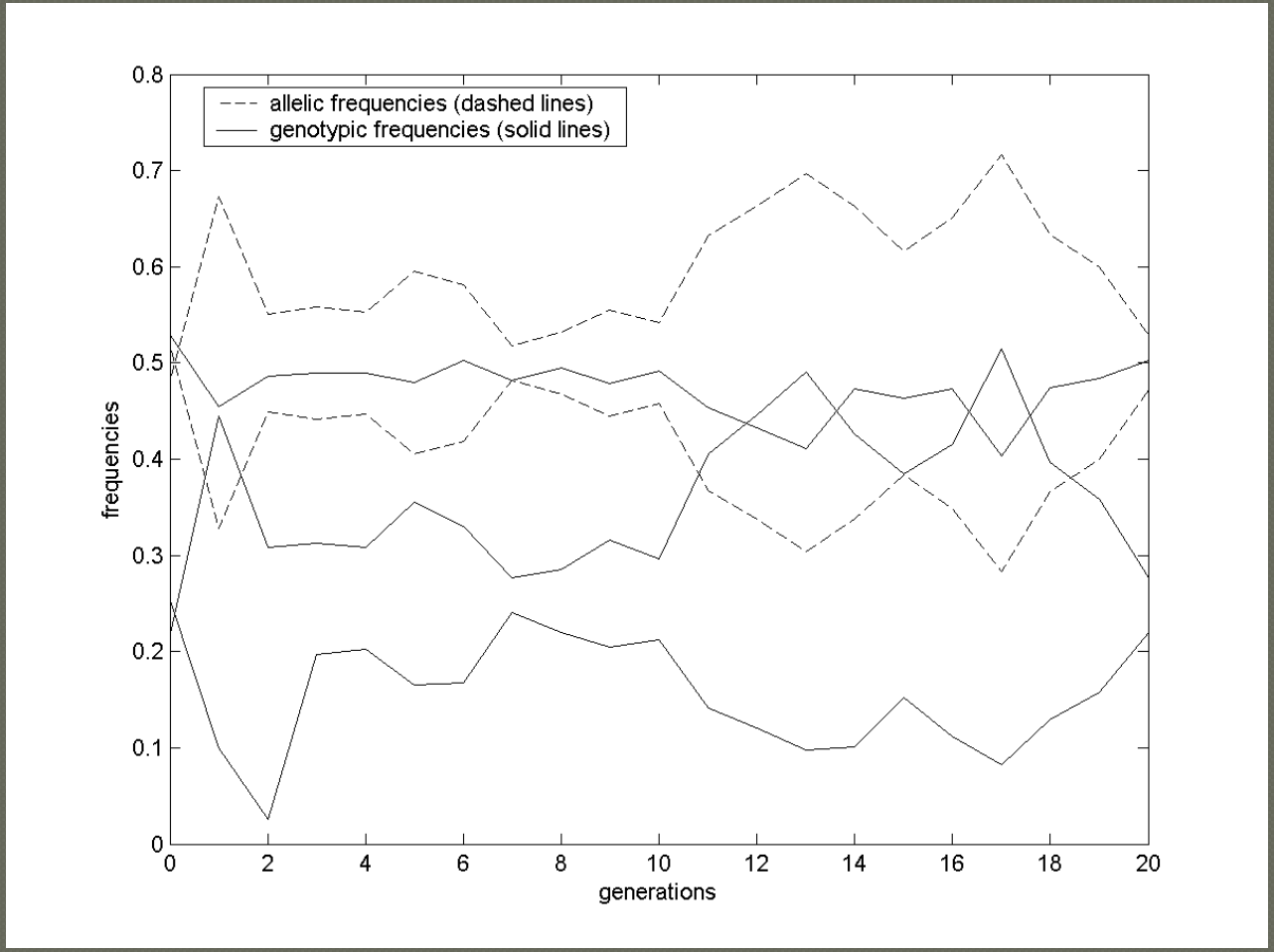
$$y3 = 0.12303 - (y2^{0.516968})$$

$$\frac{dM}{dt} = \alpha_M \frac{1 + k_1 (e^{-\mu \tau_M} A_{\tau_M})^n}{k + k_1 (e^{-\mu \tau_M} A_{\tau_M})^n} - \tilde{Y}_M M$$

$$\frac{dB}{dt} = \alpha_B e^{-\mu \tau_B} M_{\tau_B} - \tilde{Y}_B B$$

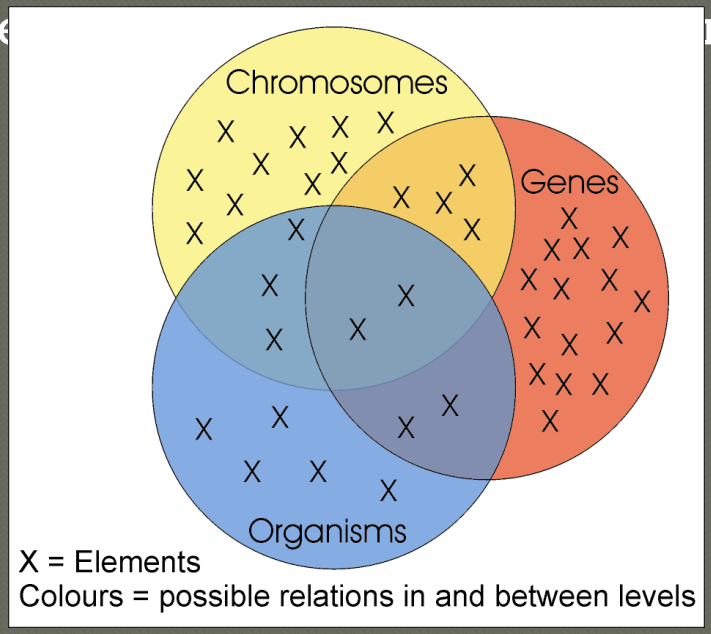
$$\frac{dA}{dt} = \alpha_A B \frac{L}{K_L + L} - \beta_A B \frac{A}{K_A + A} - \tilde{Y}_A A$$

Alife – stealing it back

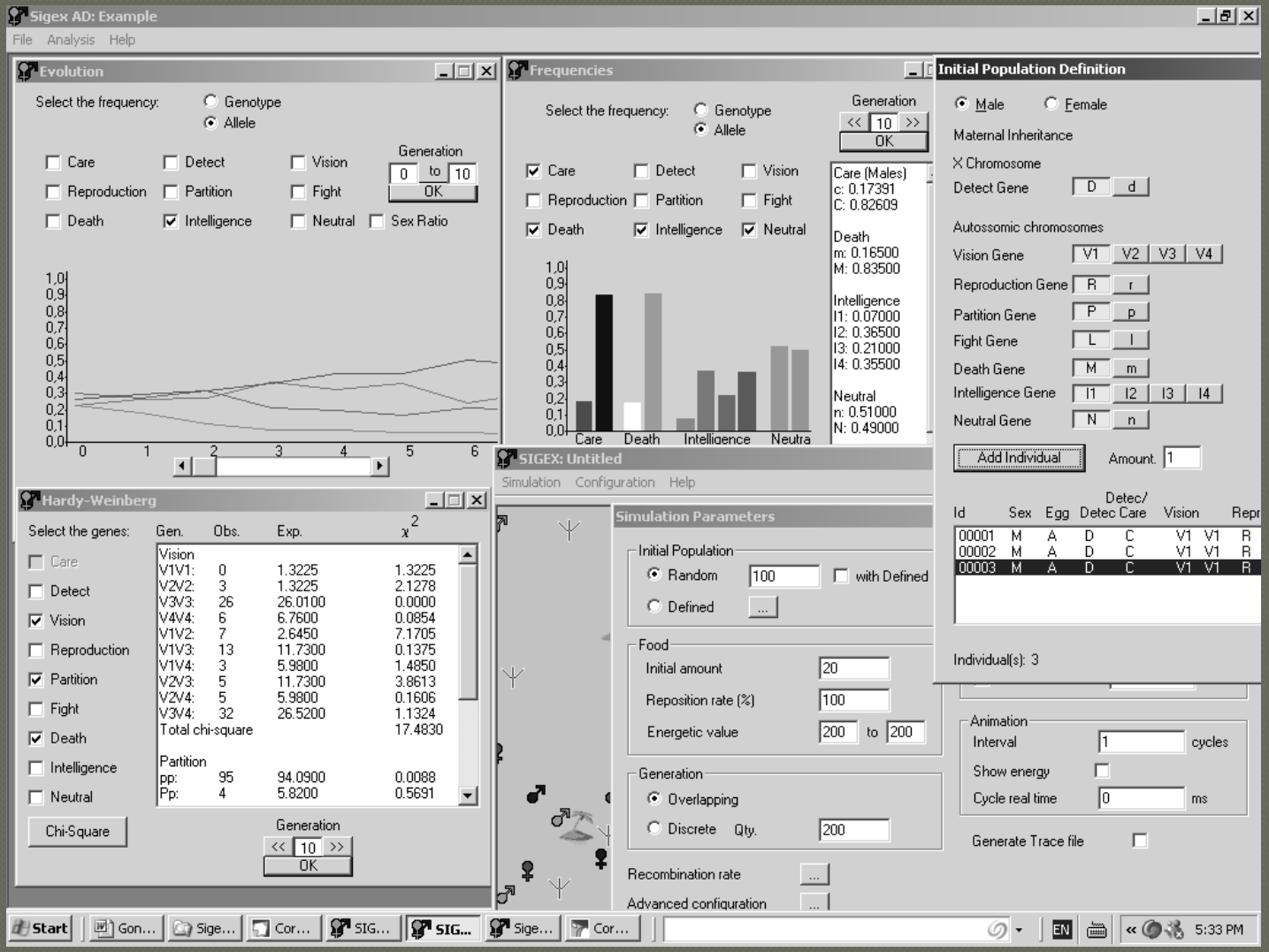


A conceptual model of Mendelian populations

- Empirical model / echo model – simplified abstraction of the main mechanistic properties of biological populations
  - Universe – environment and population
  - Organisms – chromosomes, genes and alleles
  - Phenotypic correlation of the ment and other organisms



Population genetics and evolution simulation



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Metaheuristics can solve sudoku puzzles

Rhyd Lewis

Received: 7 July 2005 / Revised: 15 March 2006 /
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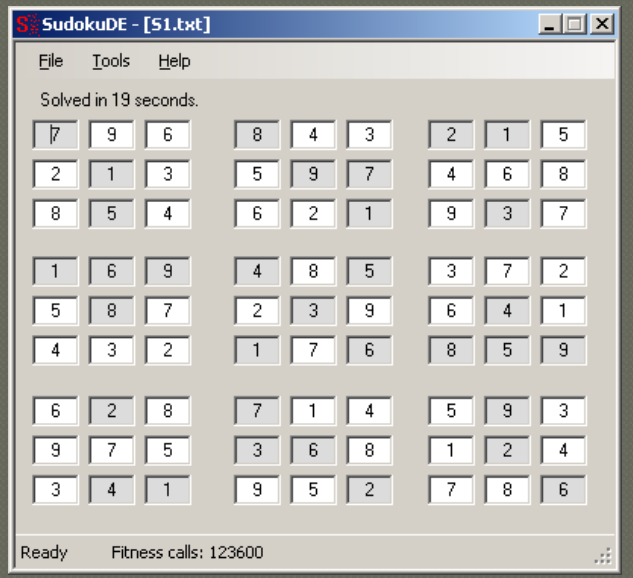
Abstract In this paper we present, to our knowledge, the first application of a metaheuristic technique to the very popular and NP-complete puzzle known as 'sudoku'. We see that this stochastic search-based algorithm, which uses simulated annealing, is able to complete logic-solvable puzzle-instances that feature daily in many of the UK's national newspapers. We also introduce a new method for producing sudoku problem instances (that are not necessarily logic-solvable) and use this together with the proposed SA algorithm to try and discover for what types of instances this algorithm is best suited. Consequently we notice the presence of an 'easy-hard-easy' style phase-transition similar to other problems encountered in operational research.

Keywords Metaheuristics · Sudoku · Puzzles · Phase-transition



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