These transparencies were presented at the Computation in Cells workshop on Tuesday April 18, 2000 in Hertfordshire, UK and partially at the tutorial on Saturday April 15, 2000 at the Euro-GP-2000 conference in Edinburgh.

REVERSE ENGINEERING OF METABOLIC PATHWAYS

COMPUTATION IN CELLS
UNIVERSITY OF HERTFORDSHIRE
HATFIELD CAMPUS
TUESDAY — APRIL 18, 2000

John R. Koza
Stanford University, Stanford, California
koza@stanford.edu

William Mydlowec
Genetic Programming Inc., Los Altos, California
myd@cs.stanford.edu

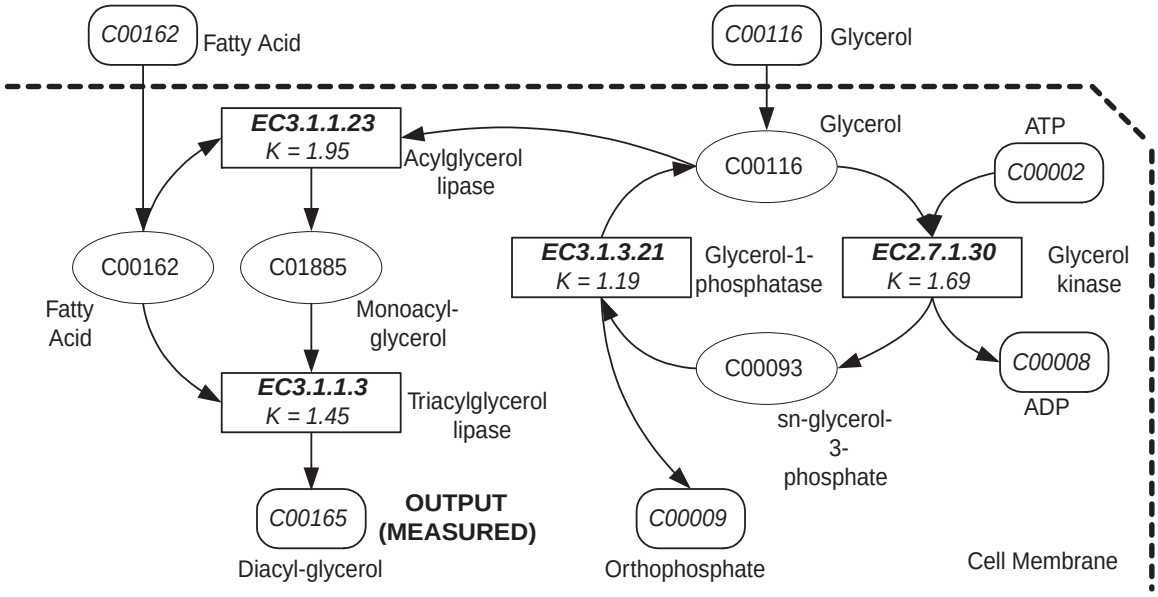
Guido Lanza
Genetic Programming Inc., Los Altos, California
guidissimo@hotmail.com

Jessen Yu
Genetic Programming Inc., Los Altos, California
jyu@cs.stanford.edu

Martin A. Keane
Econometrics Inc., Chicago, Illinois
makeane@ix.netcom.com

REVERSE ENGINEERING OF METABOLIC PATHWAYS

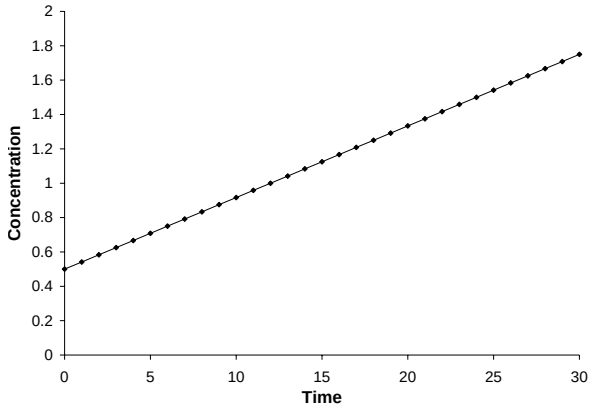
4-REACTION NETWORK IN PHOSPHOLIPID CYCLE



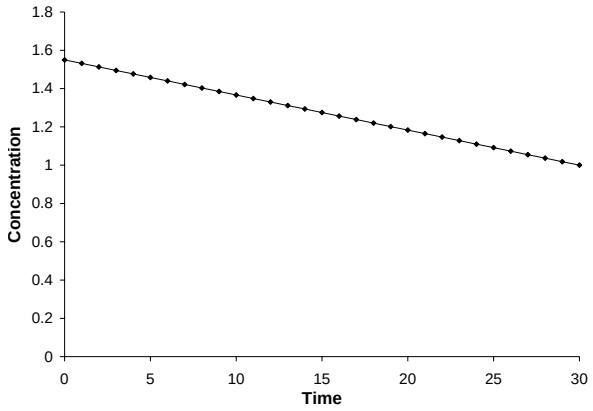
9 FITNESS CASES

Fitness Case	EC2.7.1.30	EC3.1.3.21	EC3.1.1.23	EC3.1.1.3
1	Slope-Up	Saw	Step-Down	Step-Up
2	Slope-Down	Step-Up	Saw	Step-Down
3	Step-Down	Slope-Up	Slope-Down	Step-Up
4	Step-Up	Slope-Down	Step-Up	Step-Down
5	Saw	Step-Down	Slope-Up	Step-Up
6	Saw	Step-Down	**Knock-Out**	Slope-Up
7	Saw	**Knock-Out**	Slope-Up	Step-Down
8	**Knock-Out**	Step-Down	Slope-Up	Saw
9	Step-Down	Slope-Up	Saw	**Knock-Out**

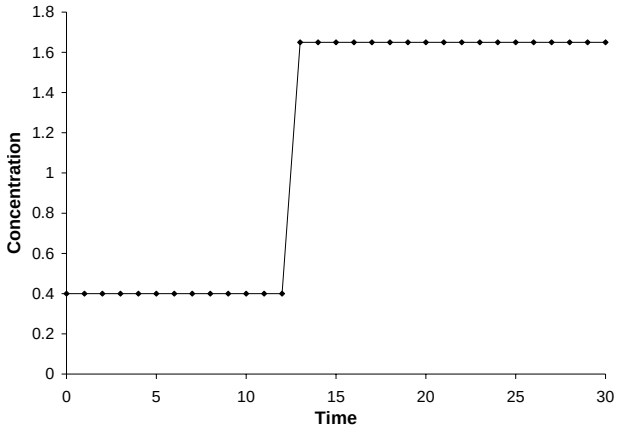
SLOPE-UP



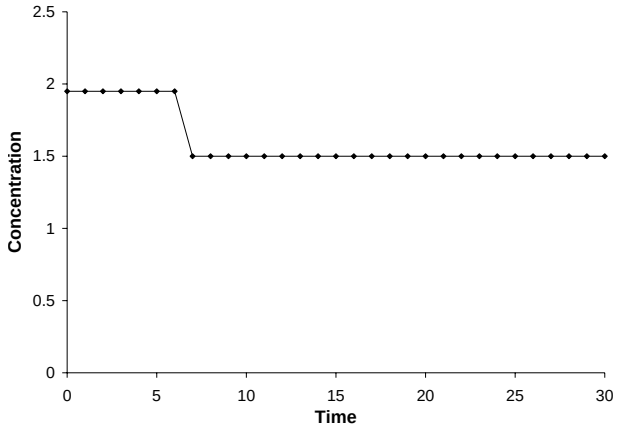
SLOPE-DOWN



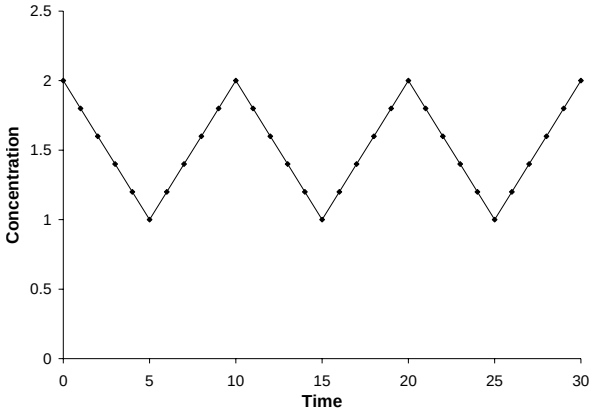
STEP-UP



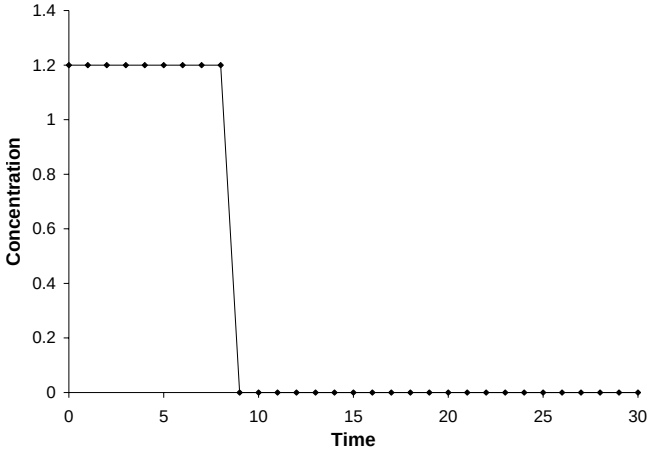
STEP-DOWN



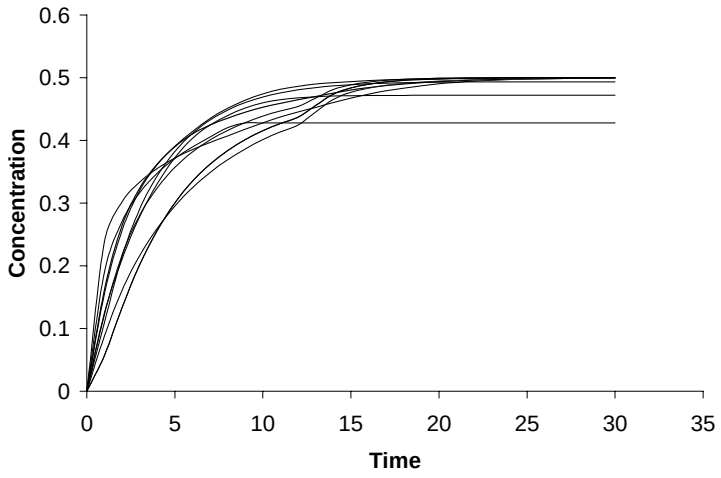
SAWTOOTH



KNOCK-OUT



CONCENTRATIONS OF PROBED PRODUCT C00165 - DIACYL-GLYCEROL FOR 9 FITNESS CASES



FIRST 15 SECONDS OF C00165

Time	Concentration of C00165
0	0
1	0.1221372
2	0.2168507
3	0.280057
4	0.324397
5	0.3568887
6	0.3815322
7	0.4007406
8	0.4160345
9	0.4284242
10	0.4386028
11	0.44706
12	0.4541539
13	0.4676479
14	0.4810823

FITNESS

- We vary the concentration of specified substance(s), such as substrates (inputs) or catalysts (enzymes), over time
- **In the example, the concentration of 4 enzymes is varied**
- **In the example, 9 different scenarios (fitness cases)**
- **In the example, each scenario is simulated for 30 seconds**

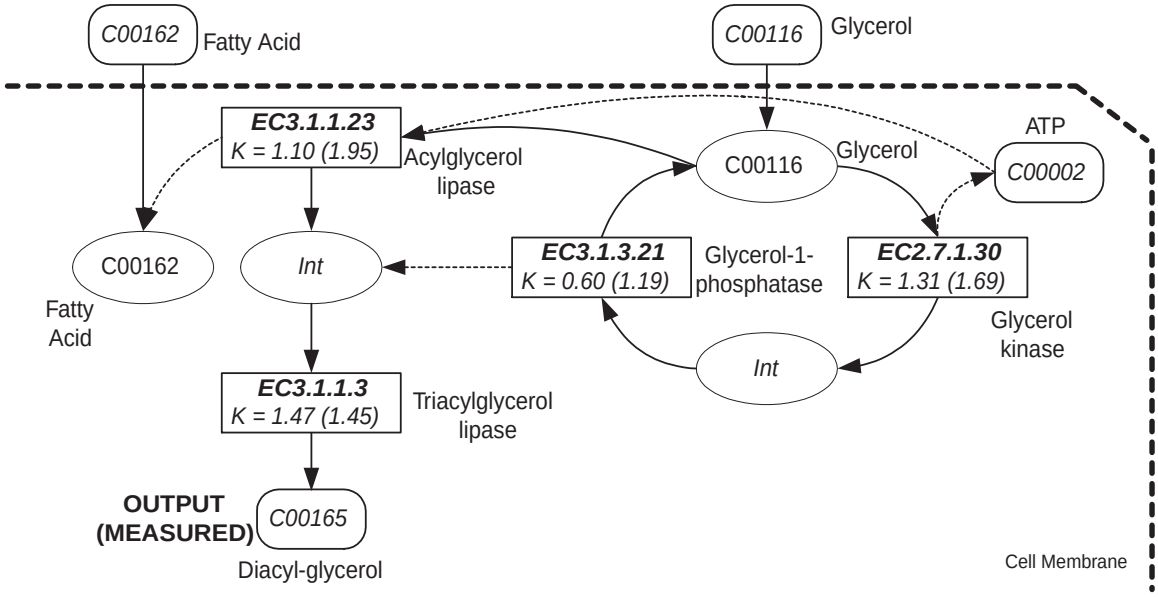
- We probe (as output) the concentration of specified product substance(s) produced by the network of reactions.
- **In the example, C00165 - Diacyl-glycerol is probed**

- Each actual network of reactions is exposed to the 9 30-second input scenarios (the fitness cases) and the actual concentration of the probed product substance(s) are recorded.

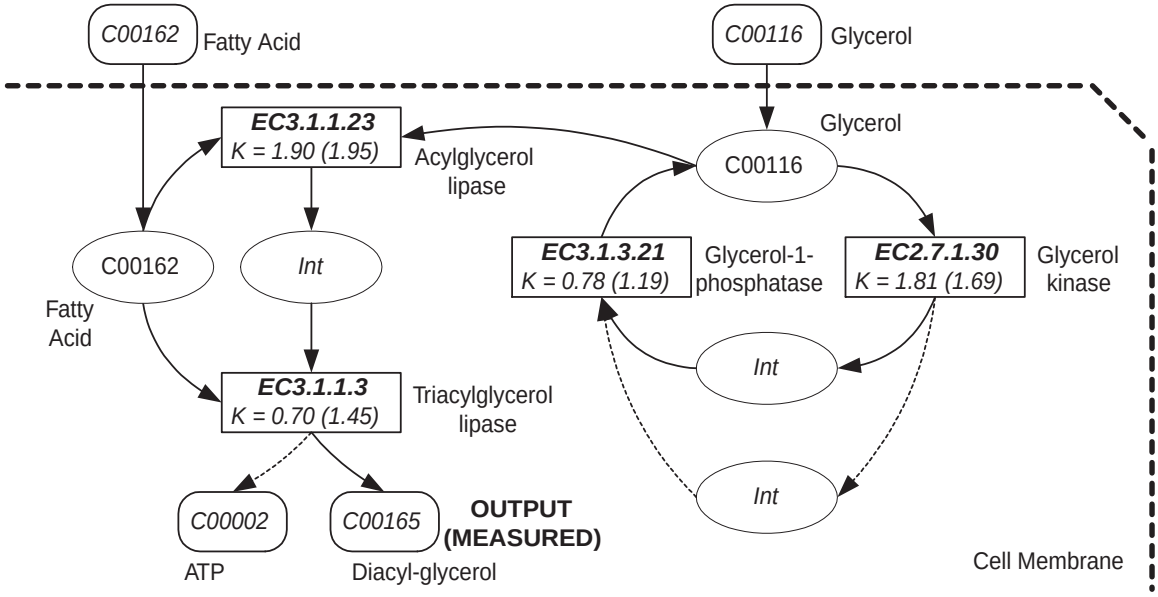
- Each individual network of reactions at each generation of the population is, at each generation, exposed to the same 9 30-second input scenarios (the fitness cases) and the concentration of the probed product substance(s) are recorded (for comparison).

- The fitness of an individual reaction network is the sum of the absolute weighted differences (errors)
- **The weight is 1 if the error is within 5%**
- **The weight is 10 if the error is greater than 5%**

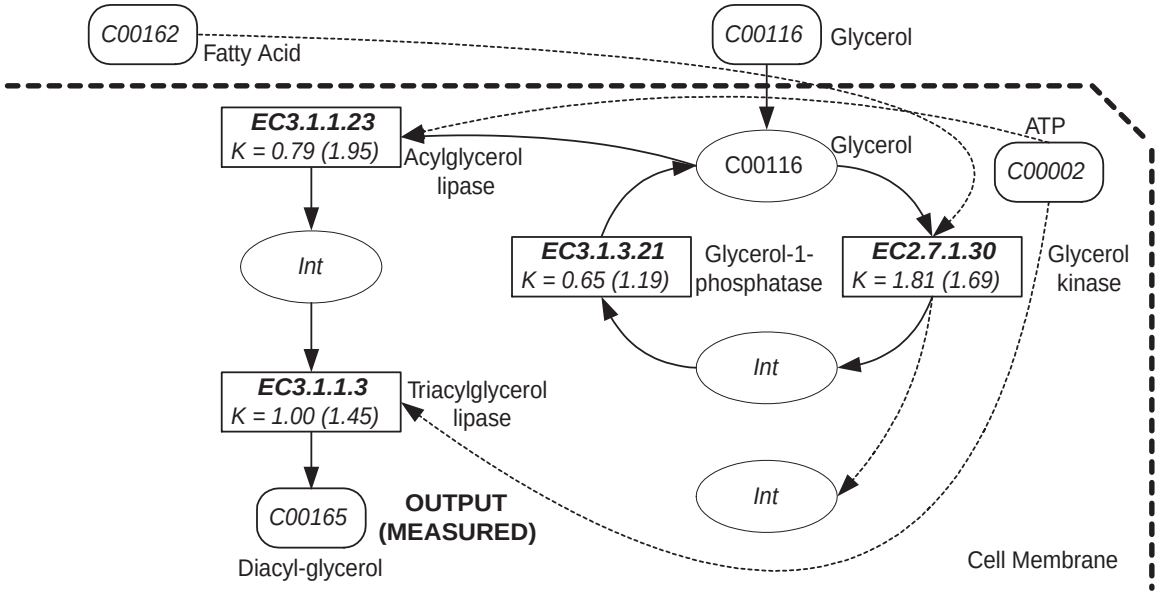
BEST-OF-GENERATION 0



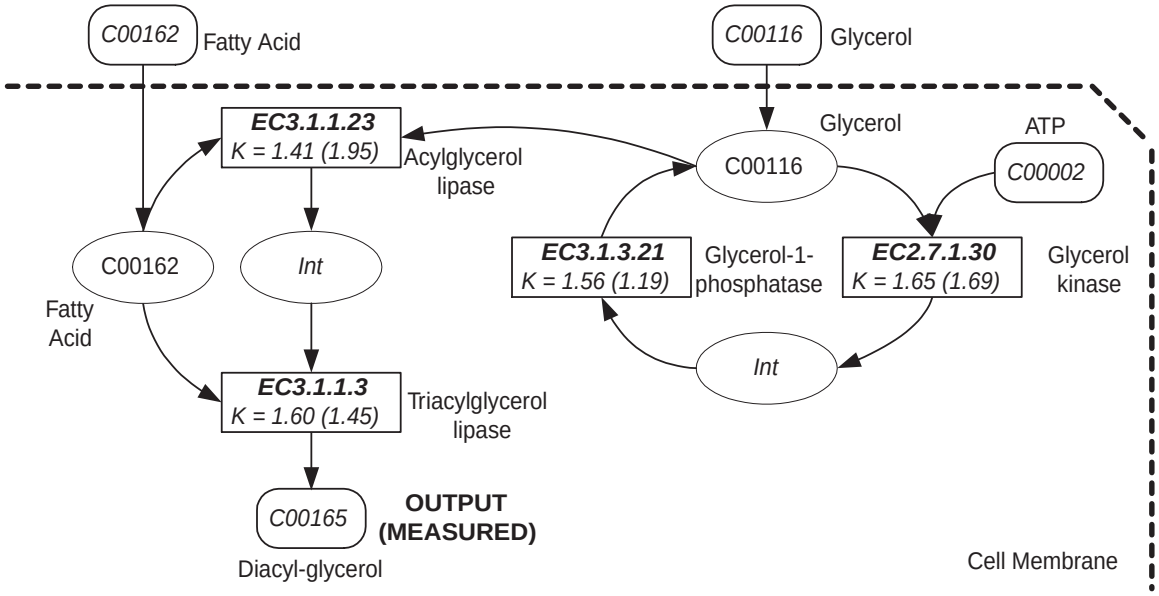
BEST-OF-GENERATION 9



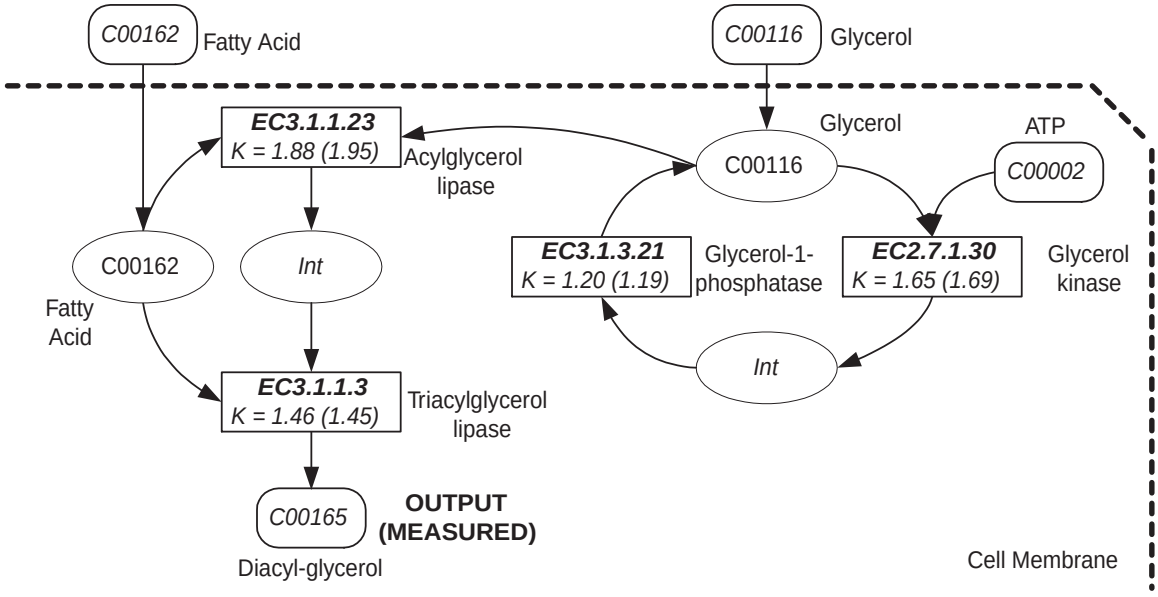
BEST-OF-GENERATION 17



BEST-OF-GENERATION 19



BEST-OF-GENERATION 66



DESIRED