Genetic Programming for structure characterization in dynamic metabolic modeling: a benchmark study

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Problem

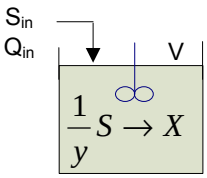
For optimally modeling metabolic networks not only data-based parameter estimation but also model structure characterization is needed, a task often neglected due to a field rather underdeveloped.

Objective

One promising tool for performing this structure characterisation is Genetic Programming (GP). Therefore, in this study a first assessment on the applicability of GP in metabolic modeling is performed by using GP to identify the kinetics of a fed-batch bioreactor system.

Fed-batch bioreactor system

System



S: reactor substrate conc.
X: reactor biomass conc.
y: yield
S_{in}: feed substrate conc.
Q_{in}: feed flow rate
V: volume reactor
K_d: decay rate
μ_{max}: kinetic parameter
K_S: kinetic parameter

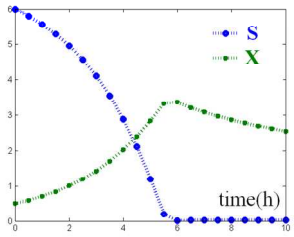
Model

$$\frac{dV}{dt} = Q_{in}$$

$$\frac{dS}{dt} = -\frac{1}{y}\cdot\frac{\mu_{max}\cdot S}{K_S + S}\cdot X + \frac{Q_{in}}{V}\cdot S_{in} - \frac{Q_{in}}{V}\cdot S$$

$$\frac{dX}{dt} = \frac{\mu_{max}\cdot S}{K_S + S}\cdot X - K_d\cdot X - \frac{Q_{in}}{V\cdot X}$$

Time course data



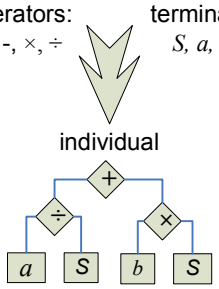
Can genetic programming identify the appropriate kinetics from the time course data?

Genetic Programming Strategy

Create initial population of kinetic models

operators: +, -, ×, ÷

terminals: *S, a, b*



Evolve model population during several generations

- assess fitness of each model from population, according to model fit
- select individuals of population in fitness proportional way
- generate new population from selected individuals

old pop. —recombination / mutation→ new pop.

- calibrate best individual of population with the simulated annealing algorithm and assess performance

Find best suited kinetic model

Results

After 8 generations of 100 individuals, the genetic programming algorithm succeeds in identifying the appropriate kinetics of the bioreactor system.

Conclusions

This result indicates an interesting perspective for genetic programming as a structure characterization tool in metabolic modeling.

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