Abstract

Microorganisms are commonly grown in continuous culture systems called chemostats, which typically have fixed volume and flow rate, so that population size and growth stage are set by limiting nutrition. In a less common type of continuous culture system called a turbidostat, feedback between culture density and flow rate is adjusted so that population is not nutrition-limited and can grow more freely. The goal of this research was to develop an individual-based computer model to simulate evolution as it occurs in a turbidostat as compared to a chemostat. We developed a Matlab computer model that uses a simple set of 3 genes with 5 positions each. Initially, we hypothesized that yeast population diversity would be greater in a turbidostat because more genetic combinations could be successful without nutrition limitation. Preliminary results analyzed with a genetic diversity algorithm were consistent with this hypothesis. However, additional runs of the program under different conditions suggested that the different population turnover rates in the systems were the primary predictor of population diversity and changes in fitness. Ongoing research focuses on modeling interactions between multiple genes, and working with different mutation rates.

Approach, cont.

Organism fitness was calculated as a simple Gene Fitness. Diversity was characterized using an adaptation of the Nucleotide Diversity Equation (Nei and Li, 1979). Graphs of population, diversity, fitness, and food (nutrition) over time were generated from simulation results (Figs. 2-4). Computer modeling was used to test hypotheses ‘In silico’ and to serve as a platform for efficient design of costly laboratory experiments.

The simulation was designed to:

Calculate “fitness” of each gene based on similarity of its sequence to an externally defined ideal “most fit” sequence. The model starts with a small, homogeneous population.

Calculate the overall fitness of the organism based on the weighted fitness of each gene as determined by how important the gene is, as determined externally.

Simulate removal of some of the culture as occurs in chemostats and turbidostats, by removing a percentage of the organisms on a schedule dictated by the user (chemostat) or as determined by organism growth rate (turbidostat).

Let each organism attempt to replicate once each “cycle”, with probability of success dependent on the organism’s fitness and culture nutrient concentration. Allow the user to plot simulation results over time.

Results

The Fitness Coefficient (CF) of each gene is calculated as:

\[ FC = 1 - (Fi*GD) \]

Where GD = how numerically distant the gene is from the user defined ideal (0 ≥ GD ≥ 1) and Fi = the fitness impact of that gene on the organism, defined by user (0 ≥ Fi ≤ 1). The FCs are multiplied to calculate the cumulative fitness.

Example of Chemostat Results

![Chemostat](image1)

![Turbidostat](image2)

![Figure 1. Comparison of Chemostat and Turbidostat](image3)

The Fitness Coefficient (CF) of each gene is calculated as:

\[ FC = 1 - (Fi*GD) \]

Where GD = how numerically distant the gene is from the user defined ideal (0 ≥ GD ≥ 1) and Fi = the fitness impact of that gene on the organism, defined by user (0 ≥ Fi ≤ 1). The FCs are multiplied to calculate the cumulative fitness.

Results, cont.

Example of Turbidostat Results

![Figure 3. Changes in Average Gene Fitness (left), Food and Population](image4)

![Figure 4. Example of changes in Sequence Diversity over time for simulations shown in Figures 2 and 3. Note slight differences in y axes.](image5)

Comparison of Sequence Diversity

![Chemostat](image6)

![Turbidostat](image7)

![Time (run time/10)](image8)

![Time (run time/10)](image9)

These example simulations show general behaviors expected for chemostats and turbidostats in terms of food use and population size.

Some interesting detailed behaviors were apparent:

1. In both the chemostat and the turbidostat, average gene fitness increased over time
2. In the turbidostat, gene fitness oscillated, which is expected given the small population size.
3. Average gene fitness at the end of the run (time = 1000) was greater in the turbidostat than in the chemostat.
4. Faster population turnover rate in the turbidostat appeared to play an important role in the faster increase in fitness.
5. Sequence diversity was slightly greater in the turbidostat than in the chemostat, consistent with my hypothesis that greater diversity should be tolerated with less selection pressure.

Results, cont.

Further analysis aimed at finding the reason for these differences in behavior in the chemostat and turbidostat. Eventually, it was discovered that when average turnover rate was controlled for by running the simulations for different times, average gene fitness and diversity in the two systems reached the same levels. This suggests that the primary factor contributing to the faster evolution and greater diversity in the turbidostat is the turbidostat’s much faster turnover rate.

Conclusions and Implications

The models produced data that were consistent with our expectations. Organisms in the turbidostat attained greater fitness and slightly greater population diversity during the simulation. Although these differences appear to be more the result of differences in turnover rate than differences in selective pressure. Although this is a relatively simplistic model, it allows for ‘In-silico experiments’ that could prove useful for designing laboratory experiments to minimize time and costs of analyses and/or for testing competing evolutionary hypotheses.

Directions for Future Research

• In the current model, the mutation rate is set very high. A lower mutation rate would be more realistic, and could significantly change the results.
• Different ways of calculating diversity might be necessary to better understand a population’s diversity with a lower mutation rate.
• In the model, genes act independently of one another but in real organisms, genes are often linked functionally. Often, there must be several deleterious mutations in interconnected genes before a positive change in fitness can occur. Such linkages need to be added for realism.
• As with any model, comparison with actual (lab) observations is needed.

Reference and Acknowledgments


Chemostat photo by P. DaSilva