Life Cycle of Chlamy Cells

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Chlamydomonas reinhardtii with the short name chlamy is a unicellular photosynthetic alga, see **Fig. 1a**, which is studied within the ongoing project GoFORSYS on systems biology. Large populations of cells are cultivated in a fermenter at the MPI of Molecular Plant Physiology, varying several environmental conditions such as light spectrum, light intensity, temperature, and nutrient concentrations. Samples of about one million cells are extracted from the fermenter to perform measurements that should shed light onto several aspects of the intracellular activity. As a result of these measurements, the metabolite concentrations are obtained as averages over a very large number of cells.

In general, the cells that contribute to these average properties differ in their age, size, and molecular composition. It is, thus, not obvious how these average quantities are related to the properties of single cells. In order to address this question, our project considers theoretical models for cell populations. As shown schematically in **Fig. 1b**, each cell undergoes a cell cycle that starts with the growth phase (G 1), passes a commitment point for cell division, and then enters the other phases necessary for this division.
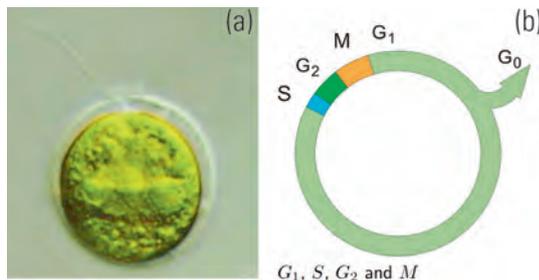

Fig. 1: (a) Image of one single cell of Chlamydomonas reinhardtii.
(b) Schematic representation of the cell cycle of a single cell. The phase denoted by G1 is the growth phase; the other three phases prepare the cell for division. The phase G0 is a dormant or rest phase.

It turns out, that chlamy cells remain in the growth phase for a random amount of time and thus attain a relatively broad distribution of cell sizes. This implies that each mother cell can produce a number of daughter cells roughly proportional to its size and, thus, can undergo multiple divisions.

One global property of each cell is its volume which should determine the overall rate of energy consumption. Our first objective was therefore to develop a model for the cell size distribution under time-independent conditions that may be implemented in the fermenter. The model can be used to calculate stationary distributions, two examples are shown in **Fig. 2** corresponding to binary and multiple divisions.
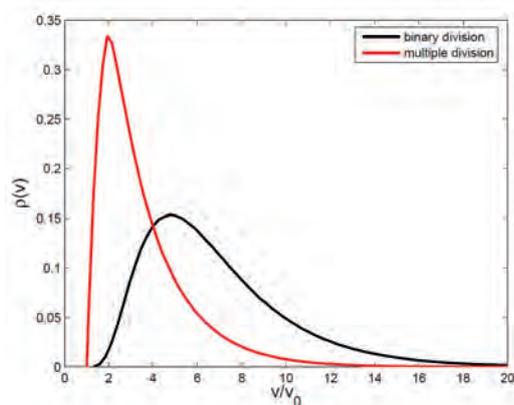

Fig. 2: Probability density for the cell volume under constant light conditions in units of the minimum volume v_0 of a viable cell. The two plots, computed with our model, compare two possible distributions assuming either binary divisions with two daughter cells or multiple divisions with more than two daughter cells as observed for chlamy cells.

Another set of experiments is performed by Martin Steup at the University of Potsdam, in which cells are synchronized by fixed periods of light and darkness. The cells are grown in a special medium that does not allow cell growth in the darkness. Synchronisation relies on the fact that, under certain general conditions, all cells would divide after the start of the dark period and the daughter cells would start to grow only when light is turned on again. By diluting the cells to a fixed density at every start of the light period and by renewing the cultivation medium, it is possible to observe the population over a long period of time under the same set of conditions.

This set-up has the advantage that both the average growth rate of the cells during the light period, the number of cells in the cultivation and, to a certain extent, the number of cell divisions can all be observed simultaneously. Moreover, during these synchronisation experiments, in which both the light and the dark periods typically last twelve hours, one can easily measure the cell size distribution of the cells. Our current aim is to adapt our model to predict the cell size distribution at the beginning of the light period.

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Activity Patterns on Networks

The biosphere contains many networks built up from rather different elements such as molecules, cells, or organisms. In spite of their diversity, these networks exhibit universal features and generic properties. The basic elements of each network can be represented by nodes or vertices. Furthermore, any binary relation between these elements can be described by connections or edges between these vertices.

By definition, the degree k of a given vertex is equal to the number of edges connected to it, i.e., to the number of direct neighbors. Large networks containing many vertices can then be characterized by their degree distribution, P(k), which represents the probability that a randomly chosen vertex has degree k. Many biological networks are found to be scale-free in the sense that their degree distribution behaves as

$$P(k) \sim 1/k^{\gamma} \text{ for } k > k_0$$

which defines the scaling exponent γ. Another structural property of networks is their assortativity and dissortativity. Networks are assortative or dissortative if vertices with large degree are primarily connected to other vertices with large or small degree, respectively. Biological networks tend to be dissortative.
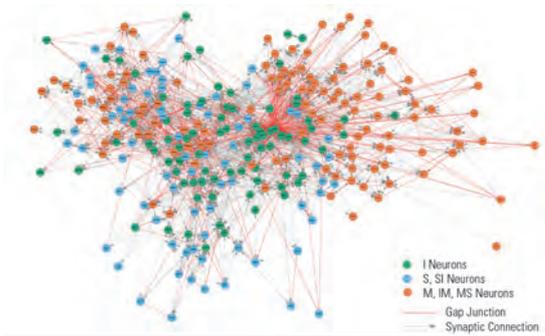

Fig. 3: Graphical representation of the neural network of C. Elegans. The vertices correspond to sensor (S), Inter (I), and motor (M) neurons; the edges represent chemical links via synapses and electrical connections via gap junctions. The input signal is received by the S neurons, processed by the I neurons, and eventually transmitted to the M neurons.

In general, the elementary units or vertices of biological networks are dynamic and exhibit various properties or internal degrees of freedom that evolve with time. A more detailed description of the network is then obtained in terms of dynamical variables that are defined for each vertex of the network. Two examples for such dynamical processes are provided by genetic networks that exhibit a changing pattern of active and inactive genes as well as by neural networks that can be characterized by firing and nonfiring neurons. A relatively simple example for a neural network is shown in **Fig. 3** corresponding to the 302 neurons of the worm C. Elegans.

In general, the dynamics of each vertex is determined by the local interactions of this vertex with its neighbours. One instructive example is provided by local majority rule dynamics which is defined as follows: If, at a certain time, most direct neighbors of a certain vertex are active or inactive, this vertex will become active or inactive at the next update of the pattern.

If one starts with a certain pattern of active and inactive vertices, the synchronous update of all vertices according to their local rules determines the time evolution of the activity pattern on the whole network, see **Fig. 4**. For long times, all activity patterns evolve towards one of the attractors (fixed points, limit cycles, etc) of the global dynamics.

Local majority rule dynamics has always two fixed points corresponding to two completely ordered patterns, the all-active pattern and the all-inactive one. In fact, for random scale-free networks without degree-degree correlations, these two fixed points are the only attractors of the dynamics as has been shown in previous studies. **[1]**
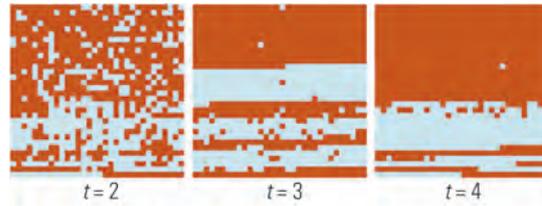

Fig. 4: Time evolution of activity pattern towards an attractor that switches back and forth between the two patterns for t = 3 and t = 4. In each panel, the vertices are arranged according to their degree starting with the smallest degree in the upper left corner and ending with the largest degree in the lower right corner.

This situation changes drastically for majority rule dynamics on scale-free networks with degree correlations. In the latter case, the activity patterns are governed by a large number of attractors. One example corresponding to a limit cycle of period two is displayed in **Fig. 4**. In fact, dissortative scale-free networks have the interesting property that the number of attractors exhibits a maximum as a function of network size. **[2]**

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