Modeling Bacterial Aging

part of "Räumliche Organisation molekularbiologischer Prozesse"

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Assumption

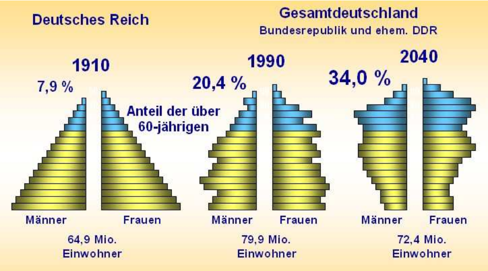
Morphological and functional symmetric and asymmetric cell division exists.

Question

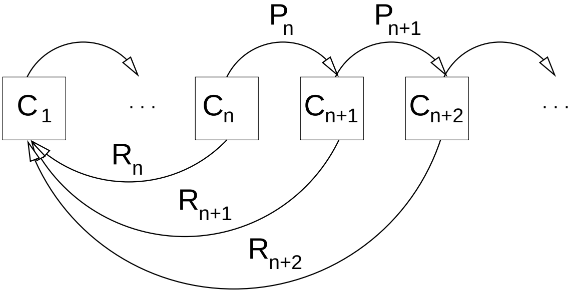
Is aging a conditional strategic choice or an inevitable outcome for bacteria?

Components Relevant for Aging

- a cell is made up of aged/aging components (i.e. pole-associated proteins)
- each component ages stepwise (passes from one age class to the next)
- newly synthetisized components start in the first age class
- the components of a cell can be represented by a age distribution similar to a population pyramid



- let's assume *m* discrete age classes
- C_n is the number of components in age class *n*
- R_n is the reproductive efficiency of the components in age class *n*
- P_n is the probability that a component of age class *n* survives to age class $n+1$



Age Distribution Changes

Given the age distribution of components at time t what is the age distribution at time $t+1$?

$$\begin{pmatrix} C_1 \\ C_2 \\ C_3 \\ \vdots \\ C_m \end{pmatrix}_{t+1} = \mathbf{LM} \times \begin{pmatrix} C_1 \\ C_2 \\ C_3 \\ \vdots \\ C_m \end{pmatrix}_{t}$$

Find a Matrix **LM** such that the above equation is fulfilled.

How to get the Matrix

Matrix Multiplication Rule

$$\begin{pmatrix} a & b \\ c & d \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix} = \begin{pmatrix} ax + by \\ cx + dy \end{pmatrix}$$

Generation of new components:

$$C_1^{t+1} = C_1^t R_1 + C_2^t R_2 + \cdots + C_m^t R_m$$

Components carried from age class n to $n + 1$:

$$C_{n+1}^{t+1} = C_n^t P_n \text{for } n \in 2, 3, \ldots, m - 1$$

The Leslie Matrix (**LM**)

$$\begin{pmatrix} R_1 & R_2 & \cdots & R_{m-1} & R_m \\ P_1 & 0 & \ddots & 0 & 0 \\ 0 & P_2 & \ddots & 0 & 0 \\ \vdots & \vdots & \ddots & 0 & 0 \\ 0 & 0 & \cdots & P_{m-1} & 0 \end{pmatrix}$$

Properties of the Leslie Matrix:

- the **eigenvector** corresponding to the dominant eigenvalue of the **LM** provides the stable age distribution
- the dominant **eigenvalue** of the **LM**, λ, gives the growth rate at the stable age distribution
- Once the stable age distribution has been reached, a population undergoes **exponential growth** at rate λ

Setting Parameters

Reproductive efficiency

$$R_n = R_1 - an^b$$

- the reproductive efficiency is highest in the first age class, $R_1 = 1$
- reproductive efficiency decreases with the age class n
- linear decline: $b = 1$, parameter a
- non-linear decline: $b > 1$ convex, $b < 1$ concave

Survival probability

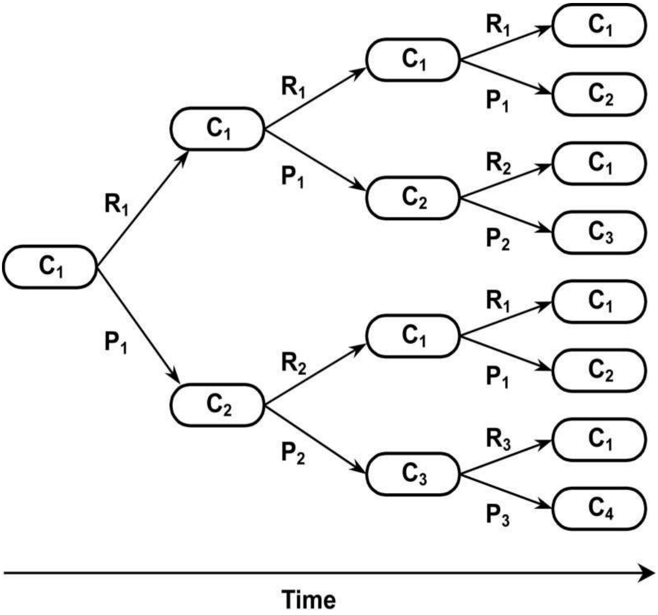
$$P_n = \begin{cases} 1 & \text{for } n \in 1, 2, \ldots, m-1 \\ 0 & \text{for } n = m \end{cases}$$

- all components of age class $m - 1$ are carried on to the next class
- all components in the last age class m do not survive

Asymmetric Division Model

- a cell with components C_n devides such that
  - all components of one cell are new, belong to C_1
  - all components of the other cell are old, belong to C_{n+1}
- $\Rightarrow$ **cell age class** is identical to the component age class
- $\Rightarrow$ the Leslie Matrix describes the age class distribution in the population of cells

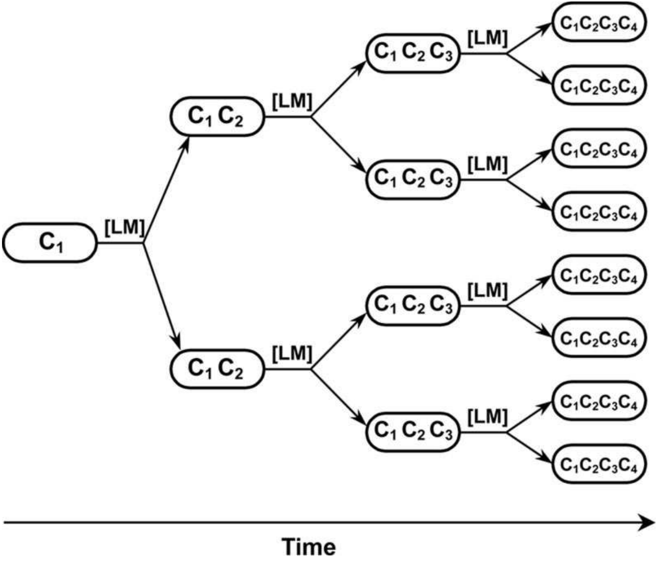
Asymmetric Division Model



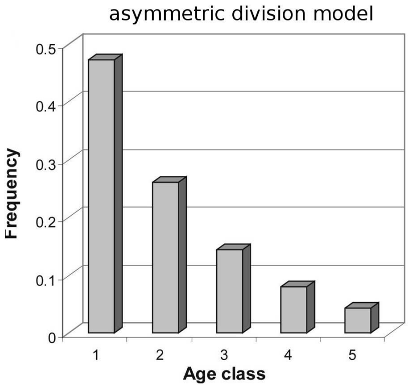
Symmetric Division Model

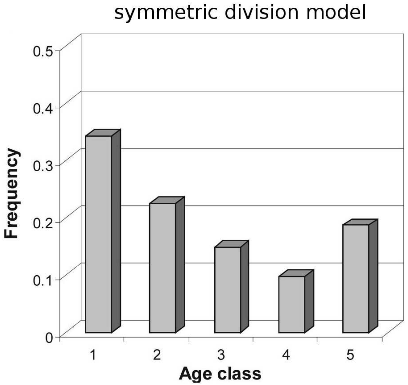
- at cell division, the components of each age class are distributed exactly equally (not stochastically)
- every cell has identical age class distribution of the components
- cells are assumed to be immortal as each cell has a majority of young components

Symmetric Division Model



Stabe Age Class Distribution





In the symmetric division model, the oldest age class has a higher frequency because of the accumulation of components.

Repair

- components of the highest age class, C_m, might be repaired with **repair efficiency** r
- rC_m are substracted from C_m (they are removed)
- rC_m are added to C_1 (they are as if they were newly synthesized)

At $r = 1$ the age class distribution for the symmetric division model is identical to that of the asymmetric divison model.

Growth Rate and Growth Yield

Growth rate

$$\frac{\ln(N(t_2)) - \ln(N(t_1))}{t_2 - t_1}$$

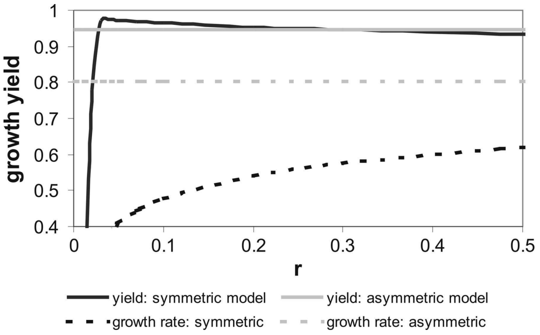
- $N(t_1)$ number of cells in the population at time t_1
- $N(t_2)$ number of cells in the population at time t_2

Growth yield

$$\frac{B(t_1, .., t_2) - D(t_1, .., t_2)}{B(t_1, .., t_2) + rC_m}$$

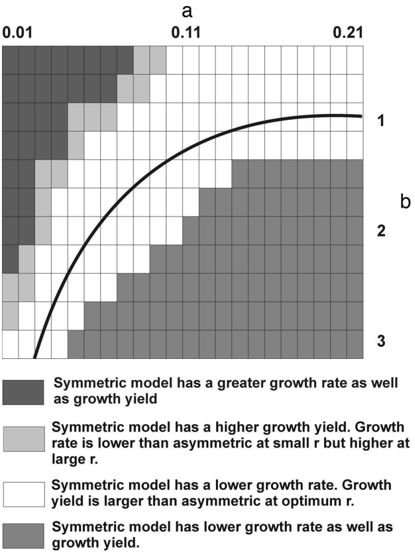
- $B(t_1, .., t_2)$ number of cells born in the time from t_1 to t_2
- $D(t_1, .., t_2)$ number of cells died in the time from t_1 to t_2

Growth Rate and Growth Yield



- The growth rate of the symmetric model is always less than the asymmetric one.
- The growth yield of the symmetric model at optimum repair efficiency is higher than the asymmetric model.

When is symmetric cell division beneficial over asymmetric cell division?



Literature

Milind Watve, Sweta Parab, Prajakta Jogdand and Sarita Keni (2006). *Aging may be a conditional strategic choice and not an inevitable outcome for bacteria.* PNAS 103(40):14831-14835