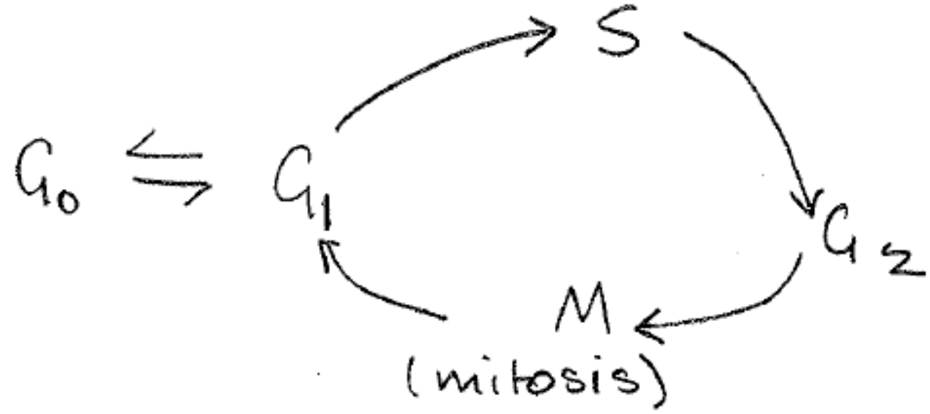
Populations Structured according to Age or Stage

For many population the age of individuals is less important than their size or maturity. For example, the effect of predation (and therefore death rates) in many species of fish are dependent not on the age of the fish but on their size. (More predators can eat little fish than can eat big fish.) The size of an individual fish depends not only on its age but on the environment where it lives, the food it eats and the genes it has inherited. Different fishes in the same population therefore may grow at different rates. A size structured model is most appropriate for this type of population.

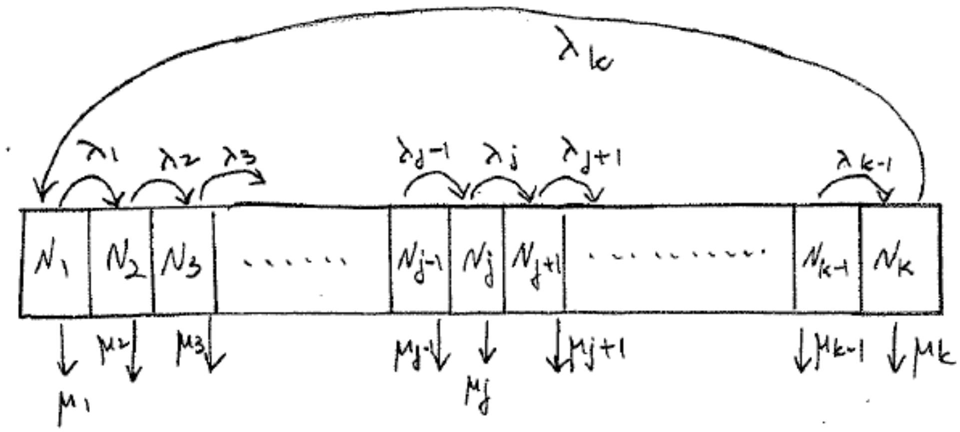
In these notes we first discuss a stage-structured model for a population of dividing cells. This model is continous in time but the population is divided into discrete stages. We then derive a continuous version of the cell model and relate this to size structured models and the Von Foerster equation (from last week).

Replicating cells go through a cycle of growth and change from one division to another. Immediately after mitosis (division) the cell enters the G_1 phase where the cell grows by synthesising protein and RNA. At this stage a cell may cease to replicate and enter the G_0 phase. A replicating cell, however will enter the S phase where it synthesises nuclear DNA. Before entering mitosis (the M phase) it undergoes another growth phase G_2. A schematic diagram of this cycle is shown below.



Models for such stage-structured cell populations have been used to help in designing chemotherapy regimes for treatment of cancer. Cancer cells replicate very rapidly and so a drug which kills the cells at certain points in the cell cycle can effectively reduce the size of the cancer. It also, however, affects other cells in the body which replicate rapidly, such as skin cells and the cells of the lining of the gut; hence the unpleasant side-effects of this type of therapy and the need to optimise drug delivery.

Let us consider a model for a population of replicating cells where each cell goes through k stages before dividing. Let N_j be the number of cells in the jth stage. Cells enter this stage at a rate of $\lambda_{j-1}N_{j-1}$ and progress onto the next stage at a rate of $\lambda_j N_j$. Cells in stage j also die at a rate of $\mu_j N_j$. Once a cell has matured to the kth stage it divides into β new cells which all enter stage 1. This is shown diagrammatically below.



Of course for mitosis, $\beta = 2$ but there are other types of cellular organisms such as slime moulds, where either a cell or a fruiting body splits open at maturity to produce a larger number of spore which grow into cells. To model such populations we would set $\beta > 2$. If we write this model as a set of ordinary differential equation, the equation for the change in the number of cells in the jth stage is

$$\frac{dN_j}{dt} = \lambda_{j-1}N_{j-1} - \lambda_j N_j - \mu_j N_j. \tag{1}$$

This applies to the stages 2 to k. For the first stage, the differential equation is

$$\frac{dN_1}{dt} = \beta\lambda_k N_k - \lambda_1 N_1 - \mu_1 N_1. \tag{2}$$

These equations can be solved explicitly for the special case where all the λ_j's are equal, the death rates are all zero and $\beta = 2$. Then the equations become

$$\frac{dN_j}{dt} = \lambda(N_{j-1} - N_j) \tag{3}$$

$$\frac{dN_1}{dt} = \lambda(2N_k - N_1). \tag{4}$$

A solution is then

$$N_j(t) = \left(\frac{\lambda_j}{(j-1)!}\right)^{j-1} e^{\lambda t}. \tag{5}$$

In this model the process of maturity is represented as a series of transitions from one stage to another. We can also think about maturation as being a continuous process. Let α be the maturation variable with $0 < \alpha < 1$. That is, newly divided cells have $\alpha = 0$ and mature cells divide when $\alpha = 1$. We can use the discrete model to define this continuous model. Let

$$N_j(t) = n(\alpha_j, t)\Delta\alpha \tag{6}$$

where $\alpha_j = j\Delta\alpha$. Here $n(\alpha, t)$ is the cell age distribution. It is similar to the age distributions $n(a, t)$ discussed in Set 2 but now $d\alpha/dt$ is not necessarily unity, nor need it be the same for every cell.

We will derive a partial differential equation for $n(\alpha, t)$. We start by Taylor expanding $n(\alpha_{j-1}, t) = n(\alpha_j - \Delta\alpha, t)$:

$$n(\alpha_{j-1}, t) = n(\alpha_j, t) - \frac{\partial n}{\partial \alpha}(\alpha_j, t)\Delta\alpha + \frac{\partial^2 n}{\partial \alpha^2}(\alpha_j, t)\frac{(\Delta\alpha)^2}{2} - \frac{\partial^3 n}{\partial \alpha^3}(\alpha_j, t)\frac{(\Delta\alpha)^3}{6} + \dots \tag{7}$$

If we assume that λ is the same for all j and substitute into equation (1), neglecting terms of order $(\Delta\alpha)^3$ and higher we have,

$$\frac{1}{\lambda}\frac{\partial n}{\partial t}(\alpha_j, t) = -\frac{\mu}{\lambda}n(\alpha_j, t) - \frac{\partial n}{\partial \alpha}(\alpha_j, t)\Delta\alpha + \frac{\partial^2 n}{\partial \alpha^2}(\alpha_j, t)\frac{(\Delta\alpha)^2}{2}. \tag{8}$$

If we assume that there are k equal subdivisions of the “maturity scale” then we can put $\Delta\alpha = 1/k$ to get

$$\frac{\partial n}{\partial t} + \frac{\lambda}{k}\frac{\partial n}{\partial \alpha} = \frac{1}{2}\frac{\lambda}{k^2}\frac{\partial^2 n}{\partial \alpha^2} - \mu n \tag{9}$$

By setting $\nu = \lambda/k$ and $D = \nu/(2k)$, this equation can be rewritten as

$$\frac{\partial n}{\partial t} + \nu\frac{\partial n}{\partial \alpha} = D\frac{\partial^2 n}{\partial \alpha^2} - \mu n. \tag{10}$$

(Note that ν and D are related to one another). This equation describes the population dynamics where maturity does not increase at the same rate for all individuals. It is similar to equation for convective transport in fluids. If $D = 0$ we return to the Von Foerster equation discussed in Set 2. The diagram below illustrates how different terms in the equation model different effects by considering what happens to a particular cohort of newly divided cells.