Chapter 5

Master equations II.

5.1 More on master equations

5.1.1 Birth and death processes

An important class of master equations respond to the *birth and death* scheme. Let us assume that "particles" of a system can be in the state X or Y. For instance, we could think of a person who is either sane or ill. The rates of going from X to Y is ω_1 while the rate from Y to X is ω_2 . Recall that both rates ω_1 and ω_2 are independent of each other. The process is indicated schematically as:

$$X \underset{\omega_2}{\overset{\omega_1}{\longleftrightarrow}} Y \tag{5.1}$$

Let n_1 be the number of particles in the state X while n_2 is the number of particles in the state 2. The total number of particles is $N = n_1 + n_2$, constant. We ask for the probability P(n;t) of having n particles in state X (and, consequently, N - n in state Y) at time t. The equation satisfied by P(n;t), the master equation, can be obtained by considering all transitions that can occur during the time interval $(t, t + \Delta t)$ and that lead that at time $t + \Delta t$ there are n particles in X. They are:

(1) There were n + 1 particles at X at time t and one of them jumped to Y during the time interval $(t, t + \Delta t)$. Since each one of the n + 1 particles can make the transition independently of the others with a probability $P(n; t + \Delta t | n + 1; t) = \omega_1 \Delta t + O(\Delta t)^2$, the total probability that any particle jumps is $(n + 1)\omega_1\Delta t$. We exclude the possibility that two (or more particles) made the transition $X \to Y$ since this is of order $(\Delta t)^2$ or larger.

(2) There were n - 1 particles at X at time t and one of the N - n + 1 particles at Y made a jump to X. This occurs with probability $P(n; t + \Delta t | n - 1; t) = (N - n + 1)\Omega_2\Delta t + O(\Delta t)^2$, again neglecting higher order terms.

(3) There were n particles at X at time t and no particle made a jump from X to Y o from Y to X. The probability that this happened is $1 - P(n; t + \Delta t|n; t)$, being $P(n; t + \Delta t|n; t) = n\omega_1\Delta t - (N-n)\omega_2\Delta t + O(\Delta t)^2$, the probability of the complementary event (a particle jumped from X to Y or a particle jumped from Y to X) happened.

No other possiblities can occur, according to the rules of the process. Putting all bits together we get:

$$P(n; t + \Delta t) = \sum_{k=-1,0,1} P(n+k; t) P(n; t + \Delta t | n; t)$$

$$= P(n; t) [1 - n\omega_1 \Delta t - (N - n)\omega_2 \Delta t] + P(n+1; t) (N - n + 1)\Omega_2 \Delta t + P(n-1; t)(n+1)\omega_1 \Delta t + O(\Delta t)^2$$
(5.2)
(5.2)
(5.2)

Arranging conveniently and taking the limit $\Delta t \to 0$ we arrive at the desired master equation:

$$\frac{\partial P(n;t)}{\partial t} = \omega_1(n+1)P(n+1;t) + \omega_2(N-n+1)P(n-1;t) - [\omega_1 n + \omega_2(N-n)]P(n;t)$$
(5.4)

or generalizing the definition of the step operator to $E^k[f(n)] = f(n+k)$:

$$\frac{\partial P(n;t)}{\partial t} = (E-1)[\omega_1 n P(n;t)] + (E^{-1}-1)[\omega_2 (N-n)P(n;t)]$$
(5.5)

Next, we need to solve this master equation. We use the generating function G(s, t), defined by (4.77). It is a matter of simple algebra to obtain:

$$\frac{\partial G(s,t)}{\partial t} = (1-s) \left[(\omega_1 + \omega_2 s) \frac{\partial G(s,t)}{\partial s} - \omega_2 N G(s,t) \right].$$
(5.6)

The solution to this differential equation with the initial condition $G(s, t = 0) = G_0(s)$, can be found by the method of the characteristics:

$$G(s,t) = \left[\frac{\omega_1 + \omega_2 s + \omega_2 e^{-(\omega_1 + \omega_2)t}(1-s)}{\omega_1 + \omega_2}\right]^N G_0\left(\frac{\omega_1 + \omega_2 s - \omega_1 e^{-(\omega_1 + \omega_2)t}(1-s)}{\omega_1 + \omega_2 s + \omega_2 e^{-(\omega_1 + \omega_2)t}(1-s)}\right)$$
(5.7)

with $\omega \equiv \omega_1 + \omega_2$. If initially there are no "life" particles, it is $P(n, t = 0) = \delta_{n,0}$ and $G_0(s) = 1$ which leads to

$$G(s,t) = \left[\frac{\omega_1 + \omega_2 s + \omega_2 e^{-\omega t} (1-s)}{\omega}\right]^N$$
(5.8)

a binomial distribution:

$$P(n,t) = \binom{N}{n} p(t)^n (1-p(t))^{N-n}, \text{ with } p(t) = \frac{\omega_2}{\omega} \left(1 - e^{-\omega t}\right).$$
(5.9)

If, on the other hand, at t=0 all N particles are alive, then $p(n,t=0)=\delta_{n,N}$, $G_0(s)=s^N$ and:

$$G(s,t) = \left[\frac{\omega_1 + \omega_2 s - \omega_1 e^{-\omega t} (1-s)}{k}\right]^N$$
(5.10)

again, a binomial distribution, but with $p(t) = \frac{\omega_2 + \omega_1 e^{-\omega t}}{\omega}$. Other initial distributions do not yield in general a binomial form for p(n, t). Note, however, that for $t \to \infty$ it is

$$G_{st}(s) = \lim_{t \to \infty} G(s, t) = \left[\frac{\omega_1 + \omega_2 s}{\omega}\right]^N$$
(5.11)

which is the generating function of a binomial distribution with $p_{st} = \frac{\omega_2}{\omega}$.

The evolution of the average number of particles and their variance can be found from Eq.(??) and Eq.(??), with the result:

$$\langle n(t) \rangle = N \frac{\omega_2}{\omega} \left(1 - e^{-\omega t} \right) + \langle n(0) \rangle e^{-\omega t},$$
(5.12)

and:

....

$$\sigma^{2}[n(t)] = \sigma^{2}[n(0)]e^{-2\omega t} + (1 - e^{-\omega t})\left[\langle n(0)\rangle \frac{\omega_{1} - \omega_{2}}{\omega}e^{-\omega t} + \frac{\omega_{2}}{\omega^{2}}N\left(\omega_{2}e^{-\omega t} + \omega_{1}\right)\right].$$
(5.13)

5.1.2 Birth and death from a reservoir

This is similar to the previous case, but now the particles are born out of a "reservoir". A reservoir is an unlimited source of particles. The reservoir is so large that the rate ω_A at which X particles are born out of the reservoir is suposed to be constant, independent on how many particles have been born already. Each X particle can "die" into the reservoir A at a rate ω_1 .

$$\bar{A} \underset{\omega_1}{\overset{\omega_A}{\longleftarrow}} X \tag{5.14}$$

(following Gillespie, the bar on top of the A means that its population is assumed to remain unchanged). If the (very large) number of particles of the reservoir is n_A we can think that the rate ω_A is proportional to the density $\frac{n_A}{\Omega}$, being Ω a measure of the volume of the reservoir, rather that to the number n_A . We write then, $\omega_A = \omega_2 n_A / \Omega$. The problem is then formally equivalent to the previously considered birth and death with a number of particles $N \to \infty$ and a vanishing rate ω_2 such that $\omega_A = \omega_2 N$ is finite. Its solution can be obtained using that limit, but we will start from scratch.

We want to find the master equation for the probability P(n;t) that there are n particles left in X at time t. We have now three elementary contributions to P(n;t+dt) according to what happened in the time interval (t,t+dt): (i) X had n particles at time t and none was lost to the bath and none was obtained from the bath; (ii) X had n+1 particles in time t and one particle was lost to the bath; (iii) X had n-1 particles and one was transferred from the bath. Combining the probabilities of these four events we get the evolution equation:

$$P(n; t + dt) = P(n; t)[1 - n\omega_1 dt][1 - \omega_A dt]$$
 case (i)
+ $P(n + 1; t)\omega_1(n + 1)dt$ case (ii)
+ $P(n - 1; t)\omega_A dt + o(dt)^2$ case (iii) (5.15)

or, taking the limit $dt \rightarrow 0$:

$$\frac{dP(n;t)}{dt} = -(\omega_1 n + \omega_A)P(n;t) + \omega_1(n+1)P(n+1;t) + \omega_A P(n-1;t).$$
 (5.16)

Again, this can be written using the step operator E as:

$$\frac{dP(n;t)}{dt} = (E-1)[\omega_1 n P(n;t)] + (E^{-1}-1)[\omega_A P(n;t)].$$
(5.17)

This equation is solved again by introducing the generating function G(s,t). The resulting partial differential equation is:

$$\frac{\partial G}{\partial t} = \omega_A(s-1)G - \omega_1(s-1)\frac{\partial G}{\partial s}.$$
(5.18)

The method of Lagrange gives us the general solution satisfying the initial condition $G(s, t = 0) = G_0(s)$:

$$G(s,t) = e^{\frac{\omega_A}{\omega_1}(s-1)(1-e^{-\omega_1 t})} G_0(1+(s-1)e^{-\omega_1 t})$$
(5.19)

If initially, there are no X particles, then $P(n, t = 0) = \delta_n$, $G_0(s) = 1$ and the corresponding solution is:

$$G(s,t) = e^{\lambda(t)(s-1)}, \qquad \lambda(t) \equiv \frac{\omega_A}{\omega_1} (1 - e^{-\omega_1 t}), \qquad (5.20)$$

which corresponds to a Poisson distribution $P(n,t) = e^{-\lambda(t)} \frac{\lambda(t)^n}{n!}$. This has first moment and variance:

Whatever the initial condition, in the stationary limit $t \to \infty$ we have from Eq.(5.19):

$$G_{st}(s) = G(s, t \to \infty) = e^{\frac{\omega_A}{\omega_1}(s-1)}$$
(5.22)

A Poisson distribution of parameter $\lambda = \frac{\omega_A}{\omega_1}$.

5.1.3 Reproduction and death

Particles reproduce at a rate ω and die at a rate γ . The schematic reactions are:

$$\begin{array}{cccc} X & \stackrel{\omega}{\longrightarrow} & 2X \\ X & \stackrel{\gamma}{\longrightarrow} & \emptyset \end{array} \tag{5.23}$$

The reproduction rate is $C_{-1}(n) = \omega n$ and the annihilation rate is $C_1(n) = \gamma n$. We write down directly the equation for the generating function $G(s,t) = \sum_{n=0}^{\infty} P(n,t)s^n$:

$$\frac{\partial G}{\partial t} = (s^{-1} - 1)\gamma s \frac{\partial G}{\partial s} + (s - 1)\omega s \frac{\partial G}{\partial s} = (1 - s)(\gamma - \omega s) \frac{\partial G}{\partial s}$$
(5.24)

If $\gamma \neq \omega$ the solution of this partial differential equation with the initial condition $G(s, t = 0) = G_0(s)$ is:

$$G(s,t) = G_0 \left(\frac{\gamma - \omega s + \gamma(s-1)e^{-\Gamma t}}{\gamma - \omega s + \omega(s-1)e^{-\Gamma t}} \right),$$
(5.25)

with $\Gamma=\gamma-\omega.$ The mean value and the variance can be obtained from the derivatives of G:

$$\langle n(t) \rangle = \langle n(0) \rangle e^{-\Gamma t}$$
 (5.26)

and

$$\sigma[n(t)]^2 = \sigma[n(0)]^2 e^{-2\Gamma t} + \langle n(0) \rangle \frac{\gamma + \omega}{\gamma - \omega} e^{-\Gamma t} (1 - e^{-\Gamma t}).$$
(5.27)

If $\gamma > \omega$, the mean value and the fluctuations decay to 0 indicating that all particles eventually disappear. If $\gamma < \omega$, both increase exponentially. The case $\gamma = \omega$ can be treated as a limiting case, and it yields:

$$\langle n(t) \rangle = \langle n(0) \rangle \tag{5.28}$$

and

$$\sigma[n(t)]^2 = \sigma[n(0)]^2 + \langle n(0)\rangle(\gamma + \omega)t.$$
(5.29)

It is interesting to solve the case $\gamma = \omega$ directly. The differential equation for G(s,t) has the solution:

$$G(s,t) = G_0 \left(\frac{1 + (\gamma t - 1)(1 - s)}{1 + \gamma t(1 - s)} \right)$$
(5.30)

from where $\langle n(t) \rangle$ and $\sigma[n(t)]^2$ follow readily as before. If we take $G_0(s) = s^N$, corresponding to a situation in which there are exactly N particles at time t = 0, it is possible to expand this function in power series of s to find the time evolution of the probabilities:

$$P_N(0,t) = \frac{b(t)^N}{[1+b(t)]^N},$$
(5.31)

$$P_N(n,t) = \frac{b(t)^{n-N}}{[1+b(t)]^{N+n}} \sum_{\ell=0}^{N-1} \binom{N}{\ell} \binom{n-1}{N-\ell-1} b(t)^{2\ell}, \quad n \ge 1, \quad (5.32)$$

being $b(t) = \gamma t$. This shows an interesting behavior: as $\lim_{t\to\infty} P_N(0,t) = 1$ it means that eventually all particles disappear, but as the variance increases linearly $\sigma[n(t)]^2 = 2N\gamma t$, it means that there is a large tail in the distribution of $P_N(n,t)$. From

$$P_N(0,t) - P_N(1,t) = \frac{b(t)^{N-1}}{[1+b(t)]^{N+1}} (b(t)^2 + b(t) - N)$$
(5.33)

we derive that the collapse time t_c at which the probability at n = 0 begins to overcome the one at n = 1 is the solution of $b(t_c)^2 + b(t_c) = N$ or $t_c \sim \gamma^{-1} N^{1/2}$ for large N.

The probabilities can be written in the alternative form:

$$P_N(n,t) = \begin{cases} \frac{b(t)^{n-N}}{[1+b(t)]^{n+N}} \binom{n-1}{N-1} {}_2F_1(-N,1-N;n-N+1;b(t)^2), & \text{if } n \ge N, \\ \\ \frac{b(t)^{N-n}}{[1+b(t)]^{n+N}} \binom{N}{n} {}_2F_1(-n,1-n;N-n+1;b(t)^2), & \text{if } n \le N. \end{cases}$$
(5.34)

It is very easy to add immigration to this process, i.e. to consider:

The creation rate is now $C_{-1}(n) = \omega n + a$ and the generating function satisfies the equation:

$$\frac{\partial G}{\partial t} = (s^{-1} - 1)\gamma s \frac{\partial G}{\partial s} + (s - 1)(\omega s \frac{\partial G}{\partial s} + aG) = (1 - s)\left[(\gamma - \omega s)\frac{\partial G}{\partial s} - aG\right]$$
(5.36)

The solution is:

$$G(s,t) = \left[\frac{\gamma - s\omega + \omega(s-1)\mathrm{e}^{-\Gamma t}}{\gamma - \omega}\right]^{-a/\omega} G_0 \left[\frac{\gamma - s\omega + \gamma(s-1)\mathrm{e}^{-\Gamma t}}{\gamma - s\omega + \omega(s-1)\mathrm{e}^{-\Gamma t}}\right]$$
(5.37)

The mean value:

$$\langle n(t) \rangle = \langle n(0) \rangle e^{-\Gamma t} + \frac{a}{\Gamma} (1 - e^{-\Gamma t}).$$
 (5.38)

If $\Gamma > 0$ there is a limit distribution:

$$G_{st}(s) = \left[\frac{\gamma - s\omega}{\gamma - \omega}\right]^{-a/\omega} = \left(1 - \frac{\omega}{\gamma}\right)^{a/\omega} \left(1 - \frac{\omega}{\gamma}s\right)^{-a/\omega}$$
(5.39)

from where:

$$P_{st}(n) = \left(1 - \frac{\omega}{\gamma}\right)^{a/\omega} \frac{\Gamma\left(\frac{a}{\omega} + n\right)}{\Gamma\left(\frac{a}{\omega}\right)n!} \left(\frac{\omega}{\gamma}\right)^n$$
(5.40)

a negative-binomial distribution. The variance is $\sigma_{st}[n]^2 = \frac{a\gamma}{(\gamma - \omega)^2}$. For $\gamma = \omega$ this distribution is not normalizable. In fact, in this case, the population grows without limit as $\langle n(t) \rangle = \langle n(0) \rangle + at$.

5.1.4 The autocatalitic reaction

The process represents the birth of a particle from a reservoir mediated by the presence of another particle. Schematically:

$$\bar{A} + X \underset{\omega_1}{\overset{\omega_2}{\longrightarrow}} 2X \tag{5.41}$$

The rate at which one particle reproduces when in contact with the reservoir is ω_2 . However, the destruction of one particle requires that it finds another particle. If there are n particles, the rate at which one particle then dies is $\omega_2(n-1)$ since it can meet any of the other n-1 particles. Consequently, the rate at which n particles become n+1 is $\omega_1 n$ since any particle can interact with the reservoir. The rate at which n particles become n-1 is $\omega_1 n(n-1)$. We can now reason as we did in the previous examples to find the master equation for the probability of having n particles at time t:

$$\frac{dP(n;t)}{dt} = (E-1)[\omega_1 n P(n;t)] + (E^{-1}-1)[\omega_2 n(n-1)P(n;t)].$$
(5.42)

The generating function satisfies the differential equation:

$$\frac{\partial G}{\partial t} = s(1-s)\frac{\partial}{\partial s} \left[\omega_2 \frac{\partial G}{\partial s} - \omega_1 G\right].$$
(5.43)

which should be solved with the initial condition $G(s, t = 0) = G_0(s)$, but I am unable to find this general solution. The stationary solution can be found by setting $\frac{\partial G}{\partial t} = 0$. This yields: $G_{st}(s) = c_1 e^{\lambda s} + c_2$ with $\lambda = \frac{\omega_1}{\omega_2}$ and c_1 , c_2 integration constants. To find them we use the general relation G(s = 1, t) = 1 and, in this case, we note that the probability that there are n = 0 particles is exactly equal to 0, as particles meet in pairs but only one gets annihilated. This means that $G_{st}(0) = P_{st}(0) = 0$. Implementing these two conditions we find:

$$G_{st}(s) = 1 + \frac{e^{\lambda(s-1)} - 1}{1 - e^{-\lambda}} = \frac{1}{e^{\lambda} - 1} \sum_{n=1}^{\infty} \frac{\lambda^n}{n!} s^n,$$
(5.44)

which implies that

$$P_{st}(n) = \frac{1}{\mathrm{e}^{\lambda} - 1} \frac{\lambda^n}{n!}, \qquad n \ge 1,$$
(5.45)

almost a Poisson distribution.

5.1.5 Gene transcription

A modification of the above death and birth process has been proposed as a very simple and crude model for gene transcription. The model assumes that a gene A (a portion of DNA) is copied into a messenger-RNA (mRNA) at a rate ω_T . The mRNA then degradates at a rate γ . The schematic reactions are:

$$\begin{array}{ccc} A & \stackrel{\omega_T}{\xrightarrow{\gamma}} & mRNA \\ mRNA & \stackrel{\omega_T}{\xrightarrow{\gamma}} & \emptyset \end{array}$$
(5.46)

The master equation describing this process of creation and degradation of mRNA is:

$$\frac{\partial P(n;t)}{\partial t} = \omega_T P(n-1;t) - \omega_T P(n;t) + \gamma(n+1)P(n+1;t) - \gamma n P(n;t)$$
(5.47)

This equation can be solved using the generating function technique to find that in the steady state the probability of finding n mRNA's is a Poisson distribution of parameter ω_T/γ . Hence, the average number of mRNA's molecules is $\langle n \rangle = \omega_T/\gamma$. Typically, a gen of about 1500 base pairs will take 60s for transcription. That gives us an idea of the order of magnitude of $\omega_T \approx 1/60s$. The degradation rate is of the order of 4 times smaller, $\gamma \approx 1/240s$. Hence the average number of mRNA's transcribed by a particular gene is of the order of $\langle n \rangle \approx 4$. This is correct experimentally, but the model has a problem: the variability is too high. This is because the fluctuations in the Poisson distributions, as measured by the root mean square $\sigma = \sqrt{\langle n \rangle} \approx 2$, which is a variability of the 50% in the number of mRNA molecules. This is too high.

We might want to include some other effects present in gene expression. We know that mRNA is translated into proteins inside the ribosomes. A codon is a sequence of three nucleotides (Adenin, Thymin, Cytosin or Guanin) and each codon is translated into one of the possible 20 aminoacids (this is the *genetic code*). This translation is mediated by 20 different tRNA's. Each tRNA couples to the right codon to generate the aminoacid. The sequence of aminoacids Hence we have the following process¹: genes create mRNA molecules at a rate ω_r . An mRNA molecule can either degradate at a rate γ of produce a protein at a rate ω_p . The protein finally degradates at a rate γ .

If we introduce the probability P(r, n; t) of having r mRNA's, n proteins at time t, we can write the master equation of the standard dogma as:

$$\frac{\partial P(r,n;t)}{\partial t} = \omega_r P(r-1,n;t) - \omega_r P(r,n;t) \qquad \text{transcription} \\
+ \omega_p r P(r,n-1;t) - \omega_p r P(r,n;t) \qquad \text{translation} \\
+ \gamma_r(r+1) P(r+1,n;t) - \gamma_r r P(r,n;t) \qquad \text{degradation of mRNA} \\
+ \gamma_p(n+1) P(r,n+1;t) - \gamma_p n P(r,n;t) \qquad \text{degradation of protein} \\
(5.48)$$

We can use now the generating function technique to compute the mean values and the

¹This whole process is known as the *standard dogma* of molecular biology.

fluctuations in the steady state. The result is

$$\langle r \rangle = \frac{\omega_r}{\gamma_r} \tag{5.49}$$

$$\sigma^2[r] = \tag{5.50}$$

$$\langle n \rangle = \frac{\omega_r \omega_p}{\gamma_r \gamma_p} \tag{5.51}$$

$$\frac{\sigma^2[n]}{\langle n \rangle} = 1 + \frac{\omega_p}{\gamma_r + \gamma_p}$$
(5.52)

The last equation shows that in this model the distribution of proteins is super-Poissonian, since the fluctuations are larger that in the Poisson distribution. This has been named as *noise amplification*. The situation is then even worse that it was in the previous model, as far as the magnitude of the variability is concerned. It is believed that the number of proteins is regulated by a feedback mechanism between different genes. A gene B can regulate the production of gene A by producing proteins that bind to the promotors of gene A.

A recent modification of this model [A. Oudenaidon, PNAS **98**, 8614 (2001)], includes the presence on inhibitory circuits in gene expression. Basically it amounts to replacing ω_r by $\omega_r(1 - \epsilon n)$ with ϵ a small number (a more realistic approach could be to include some non-linear saturation terms). One can now solve the master equation and after a lengthy calculation find that the average number of proteins decreases to $\langle n \rangle = \frac{\omega_r}{\gamma_r} \left(1 - \epsilon \frac{\omega_r}{\gamma_r}\right)$. The variance is then reduced to:

$$\frac{\sigma^2[n]}{\langle n \rangle} = 1 + \frac{\omega_p}{\gamma_r + \gamma_p} - \epsilon \frac{\omega_r \omega_p}{\gamma_r \gamma_p}$$
(5.53)

5.1.6 The prey-predator Lotka-Volterra model

Rate and master equations are commonly used in other fields, such as population dynamics and the kinetics of chemical reactions (including those occuring in living beings). However, some sort of approximation is usually needed to derive them.

Let us start with the Lotka-Volterra model. We consider an animal species X (the prey, think on rabbits) which reproduces by eating grass, A. The schematic reaction is as follows:

$$\bar{A} + X \to 2X \tag{5.54}$$

with some rate ω_0 . We'll use the notation $\omega_A = \omega_0 n_A$. At the same time, the species Y (the predator, think on foxes) reproduces by eating species X. Again schematically:

$$X + Y \to 2Y \tag{5.55}$$

with a rate ω_1 . Finally, the species Y can die of natural causes at a rate ω_2 :

$$Y \to \emptyset \tag{5.56}$$

Of course, this is a very simplified model of population dynamics, but let us analyze it in some detail.

We denote by $P(n_1, n_2; t)$ the probability that there are n_1 animals of species X and n_2 animals of species Y at time t. The master equation can be obtained by enumerating the elementary processes occuring in the time interval (t, t + dt) that might contribute to $P(n_1, n_2; t + dt)$ namely:

(i) The population was (n_1, n_2) at time t and no rabbit reproduced and no rabbit was eaten and no fox died.

- (ii) The population was $(n_1 1, n_2)$ at time t and a rabbit reproduced.
- (iii) The population was $(n_1, n_2 + 1)$ at time t and a fox died.
- (iv) The population was (n_1+1, n_2-1) at time t and a fox ate a rabbit and reproduced.

The contributions to the probability are, respectively:

$$P(n_1, n_2; t + dt) = P(n_1, n_2; t)[1 - \omega_A n_1 dt][1 - \omega_1 n_1 n_2 dt][1 - \omega_2 n_2 dt]$$
 case (i)
+ $P(n_1 - 1, n_2; t)\omega_A(n_1 - 1)dt$ case (ii)
+ $P(n_1, n_2 + 1; t)\omega_2(n_2 + 1)dt$ case (iii)
+ $P(n_1 + 1, n_2 - 1; t)\omega_1(n_1 + 1)(n_2 - 1)dt$ case (iv)
(5.57)

Taking the limit $dt \rightarrow 0$ we obtain the desired master equation:

$$\frac{\partial P(n_1, n_2; t)}{\partial t} = -(\omega_A n_1 + \omega_1 n_1 n_2 + \omega_2 n_2) P(n_1, n_2; t) + \omega_A(n_1 - 1) P(n_1 - 1, n_2; t) + \omega_2(n_2 + 1) P(n_1, n_2 + 1; t) + \omega_1(n_1 + 1)(n_2 - 1) P(n_1 + 1, n_2 - 1; t)$$
(5.58)

In deriving this equation we have made a very strong assumption: that all foxes eat all rabbits with the same rate. Hence the term $\omega_1 n_1 n_2$ which is directly proportional to the number of pairs of rabbits and foxes. However, this is unlikely to be true in a real situation. Some rabbits will be closer to some foxes and those pairs will have an enhanced probability of leading to the loss of a rabbit and the birth of a fox. This is a *homogeneity* assumption in the sense that the spatial distribution of the animals is completely neglected² in which. It might be close to true in a case in which there is a fast movement, migration, of animals from a place to another, but in general it has to be seen as an unjustified approximation. In any event, it is not reasonable to assume that a prey can be eaten with equal probability by **all** possible predators, so the corresponding term is proportional to $\omega_1 n_1 n_2$. It is more likely that this terms is proportional to the local density of predators, n_2/Ω , being Ω a measure of the volume of the system where prey and predator live. Hence, we correct this term by writing it as $\omega_1 n_1 n_2/\Omega$. Now ω_1 is the rate per unit volume and has units of volume/time. Similarly the corresponding rate for the eating of grass by the prey is proportional to the local concentration of grass,

²It can also be considered as a kind of mean field approach, since spatial inhomegeneities are not considered. However, we will using shortly the name *mean-field* to denote a situation in which correlations between the populations of prey and predators are neglected.

not to the total amount of grass, ans we write the corresponding term as $\omega_A n_A/\Omega$, or $\omega_A c_A$ being c_A the concentration of grass. We will use the notation $\bar{\omega}_1 = \omega_1/\Omega$ and and $\bar{\omega}_A = \omega_A/\Omega$. We will see that only with this rescaling is possible to recover the determistic equations in the limit of Ω large.

One might try to solve the master equation by introducing the generating function:

$$G(s_1, s_2, t) = \sum_{n_1 = -\infty}^{\infty} \sum_{n_2 = -\infty}^{\infty} s_1^{n_1} s_2^{n_2} P(n_1, n_2; t)$$
(5.59)

5.2 General results

The most general master equation appears to be of the form:

$$\frac{\partial P(n,t)}{\partial t} = \sum_{k} (E^{k} - 1) \left[C_{k}(n) P(n,t) \right], \qquad (5.60)$$

begin $C_k(n)$ some coefficients and E the linear step operator such that $E^k[f(n)] \equiv f(n+k)$ and k runs over the integer numbers. The k-th term of this sum corresponds to the process in which -k particles are created (hence destroyed if k > 0) at a rate C_k .

It is possible to obtain the general form of the equation for the generating function $G(s,t) = \sum_{n} s^{n} P(n;t)$, starting from:

$$\frac{\partial G}{\partial t} = \sum_{k} (s^{-k} - 1) \sum_{n} s^{n} C_{k}(n) P(n, t).$$
(5.61)

If we now assume the Taylor expansion $C_k(n) = \sum_a C_k^a n^a$ and use that $s^{n+a} = (s\frac{\partial}{\partial s})^a s^n$, we arrive at:

$$\frac{\partial G}{\partial t} = \sum_{k} (s^{-k} - 1)C_k \left(s\frac{\partial}{\partial s}\right) G(s, t).$$
(5.62)

From (5.61) we get the (exact) equations for these first two moments, as:

$$\frac{d\langle n\rangle}{dt} = -\sum_{k} \langle kC_k(n)\rangle, \qquad \frac{d\langle n^2\rangle}{dt} = \sum_{k} \langle k(k-2n)C_k(n)\rangle.$$
(5.63)

5.3 The mean-field theory

The mean-field theory is interested in the evolution of the mean values, neglecting fluctuations. In some cases, it is possible to obtain exact equations for the evolution of the mean values, but in most cases the evolution equations will necessarily involve some sort of approximation. Let us begin by the radiactive substance. Let us call X(t) the average value of the number of radiactive atoms remaining:

$$X(t) = \sum_{n} nP(n;t)$$
(5.64)

We know that $X(t) = X(0)e^{-\omega t}$, but we want to obtain directly from the master equation a differential equation for X(t). Taking the derivative of the previous equation and substituting Eq.(??):

$$\frac{dX(t)}{dt} = \sum_{n} n \frac{\partial P(n;t)}{\partial t} = \sum_{n} n \left[-\omega n P(n;t) + \omega(n+1) P(n+1;t) \right]$$
(5.65)

we now make changes of variables $n + 1 \rightarrow n$ in the second term of the sum to obtain:

$$\frac{dX(t)}{dt} = -\omega \sum_{n} nP(n;t)$$
(5.66)

or

$$\frac{dX(t)}{dt} = -\omega X(t) \tag{5.67}$$

the desired mean-field equation, exact in this case.

If we do the same for the birth and death process, we obtain again an exact equation for the mean value:

$$\frac{dX(t)}{dt} = -\omega_1 X(t) + \omega_A \tag{5.68}$$

whose solution is

$$X(t) = X(0)e^{-\omega_{1}t} + \frac{\omega_{A}}{\omega_{1}} \left(1 - e^{-\omega_{1}t}\right)$$
(5.69)

in agreement with the previous treatment.

Example which is not linear.

We turn now to the pre-predator Lotka-Volterra model. We need to compute two averages $X(t) = \langle n_1(t) \rangle$ and $Y(t) = \langle n_2(t) \rangle$. After some careful calculation one obtains:

$$\frac{dX(t)}{dt} = \bar{\omega}_A X(t) - \bar{\omega}_1 \langle n_1(t) n_2(t) \rangle$$

$$\frac{dY(t)}{dt} = \bar{\omega}_1 \langle n_1(t) n_2(t) \rangle - \omega_2 Y(t)$$
(5.70)

And the equations are not closed. This is typical of non-linear problems. We could now compute the evolution of $\langle n_1(t)n_2(t)\rangle$ but then it would be coupled to higher and higher order moments, a complete mess! Mean-field approach assumes that the populations are independent and hence $\langle n_1(t)n_2(t)\rangle = \langle n_1(t)\rangle\langle n_2(t)\rangle = X(t)Y(t)$. This is simply not true, but ...

$$\frac{dX(t)}{dt} = \bar{\omega}_A X(t) - \bar{\omega}_1 X(t) Y(t)$$

$$\frac{dY(t)}{dt} = \bar{\omega}_1 X(t) Y(t) - \omega_2 Y(t)$$
(5.71)

Now we can derive the evolution equation for the density of species $x(t) = \frac{X(t)}{\Omega}$, $y(t) = \frac{Y(t)}{\Omega}$. With the above definitions we get: $\frac{dx(t)}{dt} = \omega_A c_A x(t) - \omega_1 x(t) y(t)$ (5.72)

$$\frac{dy(t)}{dt} = \omega_1 y(t) y(t) - \omega_2 y(t)$$
(5.72)

being $c_A = n_A/\Omega$ the concentration of food. Now all the parameters in the equations are intensive. These are the celebrated Lotka-Volterra equations.

5.3.1 The enzimatic reaction

We now look at a very simple enzymatic reaction, where one substrate molecule S binds to the enzyme E which then decays into one product P plus an uncombined enzyme, one might write

$$S + E \rightleftharpoons ES \rightleftharpoons P + E$$
. (5.73)

In 1913 the two scientists Maud L. Menten (1879-1960) and Leonor Michaelis (1875-1949) published a famous work on the function of invertase (or saccharase). Invertase is an enzyme, found for example in yeast, which catalyses the breakdown of sucrose. What Menten and Michaelis postulated and reasoned was the following: the reaction starts with the relatively fast combination of the complex

$$S + E \underset{\omega_{-1}}{\overset{\omega_1}{\longleftarrow}} ES \tag{5.74}$$

and is followed by a rather slow decay into the product and the enzyme

$$ES \underset{\omega_{-2}}{\overset{\omega_2}{\underset{\omega_{-2}}{\longrightarrow}}} P + E.$$
(5.75)

By assuming a high energy barrier for the combination of a product with an enzyme the backwards rate ω_{-2} can be neglected. In this way one can write down a set of differential equations for the dynamical variables s(t), e(t), c(t) and p(t), resembling substrate, enzyme, complex and product concentration respectively:

$$\dot{s}(t) = \omega_{-1}c(t) - \omega_{1}s(t)e(t)$$
 (5.76)

$$\dot{e}(t) = (\omega_{-1} + \omega_2)c(t) - \omega_1 s(t)e(t)$$
 (5.77)

$$\dot{c}(t) = -(\omega_{-1} + \omega_2)c(t) + \omega_1 s(t)e(t)$$
(5.78)

$$\dot{p}(t) = \omega_2 c(t) \tag{5.79}$$

After a short time of rapid complex building the rates of complex formation and breakdown will be in a steady state of flow, leading to a constant concentration c(t)

meaning $\dot{c}(t) = 0$. The sum of bound and unbound enzyme molecules is constant $c(t) + e(t) = e_0$ and one can eliminate e(t) in (5.79). The steady state concentration of complexes is

$$c(t) = \frac{e_0 s(t)}{s(t) + \frac{\omega_{-1} + \omega_2}{\omega_1}} \equiv \frac{e_0 s(t)}{s(t) + K_M}$$
(5.80)

and K_M is called the Michaelis-Menten constant. When this equation is substituted into the dynamics of the product one finds:

$$\dot{p}(t) = \frac{\omega_2 e_0 s(t)}{s(t) + K_M} \equiv V_{max} \frac{s(t)}{s(t) + K_M},$$
(5.81)

which is a form that can easily be compared with an experiment. For large substrate concentrations the production velocity saturates at V_{max} whereas low substrate concentrations lead to velocities of $V_{max}s/K_M$. The constants K_M and V_{max} have been determined for many enzymes.

5.4 The Ω expansion of the master equation

The exact solution of the master equation for the probabilities P(n;t) is very difficult in the vast majority of cases. If we are just interested in the evolution of the mean value $\langle n(t) \rangle$ we can use the mean-field approach. Unfortunately, this does not give us neither the standard deviation $\sigma[n(t)]$ of the process, neither the evolution of the probabilities P(n;t). By considering that n is a continuous variable we obtained a way of reducing the (infinite) set of differential equations (master equation) to a partial differential equation (Fokker-Planck) equation. However, the way we derived the Fokker-Planck equation was very unsatisfactory as it was based on an uncontrolled Taylor expansion cut off at second order without much justification. In this section we present a method developed by van Kampen which uses the large parameter Ω of the problem to derive a systematic series expansion in powers of Ω . As a general exposition is quite complicated, we develop the formalism for a specific example and let the reader to refer to the book by van Kampen for a more systematic exposition of the theory including problems with more than one variable.

We consider then, as an example, the autocatalytic reaction:

$$\begin{array}{ccc} A & \stackrel{k}{\longrightarrow} & X, \\ X + X & \stackrel{k'}{\longrightarrow} & B. \end{array}$$

$$(5.82)$$

The number of A is considered to be constant (reservoir) and equal to $n_A = \phi_A \Omega$, being Ω a measure of the (macroscopic) size of the reservoir. If n is the number of X's, the reaction rates are, in the notation of the previous chapters,

$$\Omega(n \to n+1) = kn_A = k\phi_A\Omega, \quad \Omega(n \to n-2) = \frac{k'}{\Omega}n(n-1).$$
(5.83)

The master equation is then

$$\frac{\partial P(n;t)}{\partial t} = k\phi_A \Omega(E^{-1} - 1)P(n;t) + \frac{k'}{\Omega}(E^2 - 1)[n(n-1)P(n;t)].$$
(5.84)

If we record the variable n as a function of time it will oscillate around a well defined average value, say $\phi(t)$. The basic idea of van Kampen's expansion is to split the evolution variable in a time-dependent determinist component plus fluctuations and to assume that the deterministic component is proportional to Ω while the fluctuating part is of order $\Omega^{1/2}$, namely:

$$n = \Omega \phi(t) + \Omega^{1/2} \xi. \tag{5.85}$$

Alternatively, we could understand this as a change of variables from the stochastic variable n to the new stochastic variable $\xi = \Omega^{-1/2}n - \Omega^{1/2}\phi(t)$. We introduce the pdf $\Pi(\xi;t)$ of the variable ξ . The relation between the two probability functions is

$$P(n;t) = \Pi(\xi;t) \left| \frac{\partial \xi}{\partial n} \right| = \Omega^{-1/2} \Pi(\xi;t).$$
(5.86)

We are going now to replace P(n;t) by $\Pi(\xi;t)$ in the master equation. For this we need to compute the time derivative as taking into account that the change of variables from n to ξ is time dependent (through the dependence on $\phi(t)$). Hence:

$$\frac{\partial P(n;t)}{\partial t} = \frac{\partial}{\partial t} \left[\Omega^{-1/2} \Pi(\xi;t) |_{\xi = \Omega^{-1/2} - \Omega^{1/2} \phi(t)} \right]$$
(5.87)

$$= \Omega^{-1/2} \left(\frac{\partial \Pi(\xi;t)}{\partial \xi} \frac{\partial \xi}{\partial t} + \frac{\partial \Pi(\xi;t)}{\partial t} \right)$$
(5.88)

$$= \Omega^{-1/2} \left(\frac{\partial \Pi(\xi;t)}{\partial \xi} (-\Omega^{-1/2} \dot{\phi}(t)) + \frac{\partial \Pi(\xi;t)}{\partial t} \right)$$
(5.89)

$$= -\dot{\phi}(t)\frac{\partial\Pi(\xi;t)}{\partial\xi} + \Omega^{-1/2}\frac{\partial\Pi(\xi;t)}{\partial t},$$
(5.90)

being $\dot{\phi}=\frac{d\phi(t)}{dt}.$ For the step operators we use

$$\frac{\partial}{\partial n} = \frac{\partial \xi}{\partial n} \frac{\partial}{\partial \xi} = \Omega^{-1/2} \frac{\partial}{\partial \xi},\tag{5.91}$$

which allows to write the step operator as $E = e^{\frac{\partial}{\partial n}} = e^{\Omega^{-1/2} \frac{\partial}{\partial \xi}}$ and expanding the exponential:

$$E^{-1} - 1 = -\Omega^{-1/2} \frac{\partial}{\partial \xi} + \frac{\Omega^{-1}}{2} \frac{\partial^2}{\partial \xi^2} + O(\Omega^{-3/2}),$$
 (5.92)

$$E^{2} - 1 = 2\Omega^{-1/2} \frac{\partial}{\partial \xi} + 2\Omega^{-1} \frac{\partial^{2}}{\partial \xi^{2}} + O(\Omega^{-3/2}).$$
 (5.93)

We now replace these results in the master equation after replacing $P(n;t) = \Omega^{-1/2} \Pi(\xi;t)$, to obtain:

$$-\dot{\phi}(t)\frac{\partial\Pi(\xi;t)}{\partial\xi} + \Omega^{-1/2}\frac{\partial\Pi(\xi;t)}{\partialt} =$$

$$k\phi_a\Omega\left[-\Omega^{-1/2}\frac{\partial}{\partial\xi} + \frac{\Omega^{-1}}{2}\frac{\partial^2}{\partial\xi^2} + O(\Omega^{-3/2})\right]\left[\Omega^{-1/2}\Pi(\xi;t)\right]$$

$$+\frac{k'}{\Omega}\left[2\Omega^{-1/2}\frac{\partial}{\partial\xi} + 2\Omega^{-1}\frac{\partial^2}{\partial\xi^2} + O(\Omega^{-3/2})\right]\left((\Omega\phi + \Omega^{1/2}\xi)(\Omega\phi + \Omega^{1/2}\xi - 1)\Omega^{-1/2}\Pi(\xi;t)\right),$$
(5.94)

Expanding carefully and arranging in powers of Ω we get:

$$\Omega^{0} \Rightarrow -\dot{\phi}\frac{\partial\Pi}{\partial\xi} = -k\phi_{A}\frac{\partial\Pi}{\partial\xi} + 2k'\phi^{2}\frac{\partial\Pi}{\partial\xi}, \qquad (5.95)$$

$$\Omega^{-1/2} \quad \Rightarrow \quad \frac{\partial \Pi}{\partial t} = \frac{k\phi_a}{2} \frac{\partial^2 \Pi}{\partial \xi^2} + 2k' \left(\phi^2 \frac{\partial^2 \Pi}{\partial \xi^2} + 2\phi \frac{\partial(\xi\Pi)}{\partial \xi} \right)$$
(5.96)

Or,

$$\Omega^0 \Rightarrow \frac{\partial}{\partial \xi} \left[(-\dot{\phi} + k\phi_A - 2k'\phi^2)\Pi \right] = 0,$$
(5.97)

$$\Omega^{-1/2} \Rightarrow \frac{\partial \Pi}{\partial t} = 4k'\phi \frac{\partial(\xi\Pi)}{\partial\xi} + \left(\frac{k\phi_A}{2} + 2k'\phi^2\right) \frac{\partial^2\Pi}{\partial\xi^2}.$$
 (5.98)

From the first equation (order Ω^0) we get

$$(-\dot{\phi} + k\phi_A - 2k'\phi^2)\Pi(\xi;t) = \text{constant},$$
(5.99)

imposing boundary conditions $\Pi(\xi \to \pm \infty; t) = 0$, the constant is equal to zero and we find the equation for the deterministic part of the trajectory:

$$\frac{d\phi(t)}{dt} = k\phi_A - 2k'\phi^2,\tag{5.100}$$

whose solution is

$$\phi(t) = \frac{\phi(0) + \frac{k\phi_A}{2k'} \tanh(2k't)}{\frac{2k'}{k\phi_A}\phi(0) \tanh(2k't) + 1}.$$
(5.101)

Note that, independently on the initial condition, it is $\phi(t \to \infty) = \frac{k\phi_a}{2k'}$.

Equation (5.97) is closed in $\Pi(\xi;t)$. However, since there are further equations to lower orders $\Omega^{-1}, \Omega^{-3/2}, \ldots$ involving $\Pi(\xi;t)$ we still need to assume the expansion $\Pi(\xi;t) = \Pi_0(\xi;t) + \Omega^{-1/2}\Pi_1(\xi;t) + \ldots$ At the lowest order given by (5.97) we have:

$$\frac{\partial \Pi_0}{\partial t} = 4k'\phi \frac{\partial(\xi \Pi_0)}{\partial \xi} + \left(\frac{k\phi_A}{2} + 2k'\phi^2\right) \frac{\partial^2 \Pi_0}{\partial \xi^2}.$$
(5.102)

This complicated partial differential equation accepts a simple answer: if the initial condition $\Pi_0(\xi; 0)$ is a Gaussian function, then $\Pi_0(\xi; t)$ is a Gaussian function for all values of t. The proof is valid for a slightly more general equation of the form:

$$\frac{\partial \Pi_0}{\partial t} = a(t) \frac{\partial (\xi \Pi_0)}{\partial \xi} + b(t) \frac{\partial^2 \Pi_0}{\partial \xi^2},$$
(5.103)

for arbitrary functions a(t), b(t). The proof consists in assuming the Gaussian ansatz

$$\Pi_0(\xi;t) = \frac{1}{\sigma(t)\sqrt{2\pi}} e^{-\frac{(\xi-\mu(t))^2}{2\sigma(t)^2}}.$$
(5.104)

As $\mu(t)$ is the mean value of ξ it can be computed from

$$\mu(t) = \langle \xi(t) \rangle = \int d\xi \, \xi \Pi_0(\xi; t). \tag{5.105}$$

Taking the time derivative and replacing (5.104) we obtain:

$$\frac{d\mu}{dt} = \int d\xi \,\xi \frac{\partial \Pi_0(\xi;t)}{\partial t} = \int d\xi \,\xi \left[a(t) \frac{\partial (\xi \Pi_0)}{\partial \xi} + b(t) \frac{\partial^2 \Pi_0}{\partial \xi^2} \right].$$
(5.106)

Integration per parts (including the boundary conditions $\Pi_0(\xi \to \pm \infty; t) = 0$) gives

$$\frac{d\mu(t)}{dt} = -a(t)\mu(t),$$
(5.107)

of solution

$$\mu(t) = \mu(0)e^{-\int_0^t ds \,a(s)} \tag{5.108}$$

It is also possible to derive the equation for the second moment $\mu_2(t) = \langle \xi(t)^2 \rangle = \int d\xi \, \xi^2 \Pi_0(\xi; t)$ as

$$\frac{d\mu_2(t)}{dt} = -2a(t)\mu_2 + 2b(t)$$
(5.109)

and for the variance $\sigma^2 = \mu_2 - \mu_1^2$,

$$\frac{d\sigma(t)}{dt} = -a(t)\sigma(t) + \frac{b(t)}{\sigma(t)},$$
(5.110)

of solution:

$$\sigma(t) = e^{-\int_0^t ds \, a(s)} \sqrt{\sigma(0)^2 + 2 \int_0^t dt' \, b(t') e^{\int_0^{t'} ds \, a(s)}}$$
(5.111)