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Two-Cell Stochastic Model of the Schlögl Reaction with Small Diffusional Coupling

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We study a stochastic theory of the two-cell model of the Schlögl reaction beyond the bistability threshold. We restrict ourselves to the case of a small diffusional coupling, where inhomogeneous steady states occur, and where a nucleationlike behavior is expected. Our analysis agrees with the deterministic analysis in the thermodynamic limit, and permits to calculate the long time evolution of the probability distribution function. We compare our results with a recent Monte Carlo simulation of this problem.

KEY WORDS: Bistable chemical reaction; multivariate master equation.

1. INTRODUCTION

The theoretical study of nonlinear reaction-diffusion systems has received much attention in recent years. These systems can exhibit a cooperative behavior which leads to a number of interesting situations such as bistability, limit cycle, spatial organization, and turbulence. Their deterministic description involves a set of coupled nonlinear equations, which can be successfully handled by using the bifurcation or catastrophe theories.[1,2] An interesting development consists in employing the stochastic Master Equation,[1,3] which permits the analysis of internal fluctuations far from equilibrium. This equation, which describes reaction and diffusion as random processes, is intuitively quite appealing. On the other hand, its solution is not simple. A number of theoretical investigations have been developed the last few years. Numerical calculations based on Monte Carlo methods[4] or on M.D. simulations[5] have proved to be valuable in this case, as in other domains of statistical mechanics. On a purely analytical level, one may

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quote works using the cumulant expansions,[6,7] the Fokker–Planck and Langevin Equation,[8] or the WKB expansions.[9–11] In the one variable case, the first two methods are satisfactory when the system presents only one stable stationary state, or in other words when the probability distribution is singly peaked. They fail in the case of bistability, when a second peak of the distribution appears. The WKB expansion applies even in the case of bistability, and permits to obtain an analytical expression of the stationary distribution.[10,11] Unfortunately, in the multivariate case, the Hamilton–Jacobi equation obtained in first order of this expansion cannot be solved exactly; a local expansion around each macroscopic steady states is then necessary.[12] The method bears similarities with the cumulant expansion, and does not apply beyond the bistability threshold since a nonlocal solution is necessary to connect the two steady states.

In this paper, we consider the most simple diffusion-reaction model involving bistability, namely, the two-cell model of the Schlögl reaction. This model has been studied numerically quite recently.[13]

In spite of its apparent simplicity, it exhibits all the difficulties inherent in the multivariate master equation. In particular, the stationary probability distribution cannot be calculated exactly. We shall limit ourselves to the case where the system is far beyond the bistability threshold and consider only the long-time behavior of the probability distribution. The short-time behavior can be handled conveniently by the various expansion methods mentioned earlier.[6,12] They predict a simple relaxation around each stable macroscopic stationary state and a formation of quasistationary peaks. The long-time behavior involves the equilibration of the different peaks of the quasistationary distribution, and has to be treated by a different method. The key asumption is that, at long times, the probabilities are locally in equilibrium around each stable steady state. This asumption has first been used by Kramers in the case of the Fokker–Planck equation with a double-well potential.[17] His precursory work has been widely discussed and improved ever since (see, for example, Refs. 18–23). In particular, extensions have been made to include nonpotential systems,[24,25] or non-Markovian dynamics.[26,27]

In Section 2, we briefly mention the deterministic model of the Schlögl reaction in a homogeneous cell, and the model consisting of two cells coupled by diffusion, following the work of W. Ebeling and H. Malchow.[14]

In Section 3, we study the stochastic theory of the two-cell model, starting from the master equation formalism. We restrict ourselves to the case of small diffusional coupling, and apply a calculation scheme suggested by our previous work on the homogeneous model of the Schlögl reaction.[15]

2. DETERMINISTIC ANALYSIS

2.1. Homogeneous System

Let us consider the Schlögl reaction[16]:

$$B \underset{k_3}{\overset{k_4}{\rightleftharpoons}} X, \qquad A + 2X \underset{k_2}{\overset{k_1}{\rightleftharpoons}} 3X \tag{1}$$

We suppose that this reaction takes place in a homogeneous box, and that the concentration of A and B are maintained constant. If $n(t)$ is the number of molecules X at time t, the kinetic equation of reaction (1) reads

$$\frac{dn}{dt} = w(n) - \bar{w}(n) \tag{2}$$

where $w(n)$ and $\bar{w}(n)$ stand for the rates of creation and destruction of the species X:

$$\begin{aligned} w(n) &= n_A \frac{k_2}{V^2} n^2 + k_3 n_B \\ \bar{w}(n) &= n\left(\frac{k_1}{V^2} n^2 + k_4\right) \end{aligned} \tag{3}$$

V is the volume of the cell; n_A, n_B represents the number of the molecules A, B, respectively. Putting

$$n = \bar{n}\frac{n_A k_2}{k_1}, \qquad t = \tau \frac{k_1 V^2}{(n_A k_2)^2}, \qquad \lambda = \frac{k_4 k_1 V^2}{(n_A k_2)^2}, \qquad \mu = \frac{k_3 k_1^2 n_B V^2}{(n_A k_2)^3} \tag{4}$$

eq. (2) yields

$$\frac{d\bar{n}}{d\tau} = -\bar{n}^3 + \bar{n}^2 - \lambda\bar{n} + \mu \tag{5}$$

For

$$\Delta = 4(\lambda - \tfrac{1}{3})^3 + 27(\mu - \lambda/3 + \tfrac{2}{27})^2 > 0$$

(2) admits one stationary solution α. For $\Delta < 0$, there are three stationary solutions $\alpha < \beta < \gamma$. A straightforward stability analysis shown that α and γ are stable while β is unstable.

2.2. The Two-Cell Model

We now consider the system consisting of two identical cells coupled by diffusion. In each of them takes place the Schlögl reaction described by (1), with the same pumping conditions for A and B.

The coupled differential equations for the numbers n_1 and n_2 of molecules of X in each cell are

$$\begin{aligned} \dot{n}_1 &= w(n_1) - \bar{w}(n_1) + D(n_2 - n_1) \\ \dot{n}_2 &= w(n_2) - \bar{w}(n_2) + D(n_1 - n_2) \end{aligned} \tag{6}$$

D is a diffusion coefficient, which can be related to Fick's diffusion coefficient d via the formula

$$D = \frac{d}{l^2} \tag{7}$$

where l stands for the length of each cell. The stationary solutions of (6) can be found graphically.[14] If the chemical equation $w(n) - \bar{w}(n) = 0$ admits itself one single solution α, the system (6) can be easily seen to admit only one homogeneous solution $(n_1, n_2) = (\alpha, \alpha)$. If the chemical equation has three possible solutions α, β, γ, we shall refer the reader to the detailed work of Ebeling and Malchow.[14] The system (6) then turns out to admit up to nine solutions. Two critical values D_{c_1} and D_{c_2} of D come out from this analysis. For $D < D_{c_1}$, both homogeneous and inhomogeneous solutions occur; the homogeneous solutions (α, α) and (γ, γ) are stable nodes, whereas (β, β) is an unstable point. The inhomogeneous solutions include two stable nodes and four saddles. For $D_{c_1} < D < D_{c_2}$, the two inhomogeneous stable nodes and two of the inhomogeneous saddle points disappear. For $D > D_{c_2}$, only the homogeneous solutions remain. (α, α) and (γ, γ) are still stable nodes while (β, β) becomes a saddle point.

3. STOCHASTIC ANALYSIS OF THE TWO-CELL MODEL

3.1. Master Equation

Fluctuations of the number of molecules X in the system can be taken into account via the master equation formalism[1]; n_1 and n_2 are considered as random variables, and the evolution of $p(n_1 n_2)$ is given by

$$\begin{aligned} \frac{dp(n_1, n_2)}{dt} = {} & W_{n_1 - 1}\, p(n_1 - 1, n_2) - (W_{n_1} + \bar{W}_{n_1})\, p(n_1, n_2) \\ & + \bar{W}_{n_1 + 1}\, p(n_1 + 1, n_2) + W_{n_2 - 1}\, p(n_1, n_2 - 1) \\ & - (W_{n_2} + \bar{W}_{n_2})\, p(n_1, n_2) + \bar{W}_{n_2 + 1}\, p(n_1, n_2 + 1) \\ & - D(n_1 + n_2)\, p(n_1, n_2) + D(n_1 + 1)\, p(n_1 + 1, n_2 - 1) \\ & + D(n_2 + 1)\, p(n_1 - 1, n_2 + 1) \end{aligned} \tag{8}$$

The chemical reaction within each cell is there considered as a birth and death process; W_{n_i} and $\bar{W}_{n_i}$ are the birth and death rates from a state with n_i molecules of X in cell i. These transition rates are, in the notation of Section 2.1,[1]

$$W_{n_i} = n_A k_2 n_i(n_i - 1)/V^2 + k_3 n_B$$
$$\bar{W}_{n_i} = k_1 n_i(n_i - 1)(n_i - 2)/V^2 + k_4 n_i \tag{9}$$

The diffusion is described as a random exchange between cell 1 and 2, with passage probability per unit time from cell i to cell j equal to Dn_i. It should be noticed that no detailed balance exists in Eq. (8), and the stationary solution cannot be found exactly.

3.2. Quasistationarity Hypothesis

In the following we shall limit ourselves to the case where the chemical reaction is bistable, and the diffusion coefficient is small, namely, $D < D_{c_1}$. In this situation deterministic inhomogeneous steady states occur, and a nucleationlike behavior is expected, as has been shown by Monte Carlo simulation,[13] whereas for large diffusion coefficients the two-cell system behaves more or less like a single cell. In the case of small D, the stationary distribution has presumably the shape shown by Fig. 1. It presents two peaks concentrated on the homogeneous steady states (α, α) and (γ, γ), and two peaks which are symmetrical with respect to the main diagonal and concentrated on the inhomogeneous steady states (α', γ') and (γ', α'). For $D = 0$, one has $\alpha' = \alpha$ and $\gamma' = \gamma$. When D increases, α' and γ' are slightly shifted toward γ and α, respectively, as represented in Fig. 1.

In the plane (n_1, n_2), we can distinguish four regions where the probability distribution differs significantly from zero. They will be denoted by $(\alpha\alpha)$, $(\alpha\gamma)$, $(\gamma\alpha)$, $(\gamma\gamma)$, corresponding, respectively, to $(n_1 \in (\alpha), n_2 \in (\alpha))$, $(n_1 \in (\alpha), n_2 \in (\gamma))$, $(n_1 \in (\gamma), n_2 \in (\alpha))$, $(n_1 \in (\gamma), n_2 \in (\gamma))$, with $(\alpha) = \{i : i < m\}$ and $(\gamma) = \{i : i > M\}$, m and M being arbitrary states chosen sufficiently far from each side of β.

Starting from any initial distribution, the temporal evolution of $p(n_1, n_2)$ can be understood qualitatively as follows. On a short time scale, the four regions can be considered as disconnected from each other, and the distribution relaxes independently in each of them, giving four quasistationary peaks centered on the macroscopic steady states. The weight or total probability of these peaks corresponds to the respective weight of the initial distribution in each region. The long time evolution will be a slow

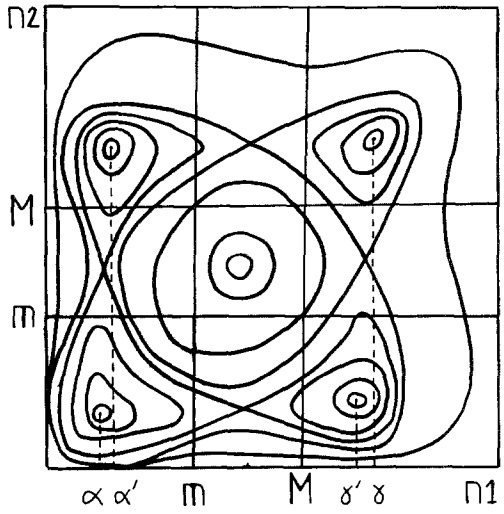

Fig. 1. Qualitative shape of the stationary distribution for small D.

exchange between the peaks without change of their shape until the stationary distribution is reached. This description is based on our main hypothesis, which amounts to assume that in each cell the exchanges between the regions (α) and (γ) are much slower than the relaxation inside these regions, in spite of the diffusion, if the diffusion coefficient D is small enough. This reasonable asumption is of course difficult to justify analytically, since the exact long time evolution is not known. However, we shall see that the consequences of this approximation agree fairly well with the results of numerical simulations, which confirms the validity of our methods.

3.3. Reduced Evolution Equation

The asumptions described earlier lead to a simple equation for the probability $p(x, y)$ to find cell 1 in region (x) and cell 2 in region (y):

$$p(x, y) = \sum_{n_1 \in (x)} \sum_{n_2 \in (y)} p(n_1, n_2) \tag{10}$$

As a matter of fact it will be shown that $p(x, y)$ satisfies an evolution equation which may be written in the form

$$\frac{dp(\alpha,\alpha)}{dt} = -2\mu^{\alpha}_{m-1}q^{\alpha}_{m-1}p(\alpha,\alpha) + \bar{\mu}^{\alpha}_{m}(p(m,\alpha)+p(\alpha,m)) + \varepsilon_{\alpha\alpha}$$

$$\frac{dp(\alpha,\gamma)}{dt} = -(\bar{\mu}^{\alpha}_{M+1}q^{\alpha}_{M+1} + \mu^{\gamma}_{m-1}q^{\gamma}_{m-1})p(\alpha,\gamma) + \mu^{\alpha}_{M}p(\alpha,M)$$
$$+ \bar{\mu}^{\gamma}_{m}p(m,\gamma) + \varepsilon_{\alpha\gamma} \tag{11}$$

$$\frac{dp(\gamma,\alpha)}{dt} = -(\bar{\mu}^{\alpha}_{M+1}q^{\alpha}_{M+1} + \mu^{\gamma}_{m-1}q^{\gamma}_{m-1})p(\gamma,\alpha) + \mu^{\alpha}_{M}p(M,\alpha)$$
$$+ \bar{\mu}^{\gamma}_{m}p(\gamma,m) + \varepsilon_{\gamma\alpha}$$

$$\frac{dp(\gamma,\gamma)}{dt} = -2\bar{\mu}^{\gamma}_{M+1}q^{\gamma}_{M+1}p(\gamma,\gamma) + \mu^{\gamma}_{M}(p(M,\gamma)+p(\gamma,M)) + \varepsilon_{\gamma\gamma}$$

where the coefficients μ, $\bar{\mu}$, and q are approximately constant and will be computed explicitly (see Appendix A), whereas the ε are very small and may be neglected. Equations (11) also involve the intermediate probabilities

$$p(\alpha,m) = \sum_{i\in(\alpha)} p(i,m) \tag{12}$$

and similar probabilities which can be eliminited by a projection procedure.

In order to define the quantities μ, q, ε and to derive equations (11), it is necessary to introduce the following conditional probabilities: (a) the conditional probability $p_{xy}(n_1,n_2)$ that cells 1 and 2 be, respectively, in states n_1 and n_2, knowing that they are in regions (x) and (y):

$$p_{xy}(n_1,n_2) = p(n_1,n_2)\Big/\sum_{i\in(x)}\sum_{j\in(y)} p(i,j)$$
$$= p(n_1,n_2)/p(x,y), \qquad \text{if } n_1\in(x),\ n_2\in(y) \tag{13}$$

(b) the conditional probability $p_x(n_1/n_2)$ that the cell 1 be in state n_1, knowing that this cell is in region (x) and that cell 2 is in state n_2:

$$p_x(n_1/n_2) = p(n_1,n_2)\Big/\sum_{i\in(x)} p(i,n_2), \qquad \text{if } n_1\in(x) \tag{14}$$

Similar conditional probabilities are defined by interchanging the cells 1 and 2. It should be noticed that, since these cells are entirely symmetrical from a physical point of view, one may write

$$p_{xy}(n_1,n_2) = p_{yx}(n_2,n_1)$$
$$\sum_{n_1\in(x)} n_1 p_x(n_1/j) = \sum_{n_2\in(x)} n_2 p_x(n_2/j) = \langle n/j\rangle_x \tag{15}$$

Equation (15) defines the conditional average number $\langle n/j \rangle_x$ of particles in one cell, knowing that this cell is in region (x) and that the other cell is in state j.

The time dependence of these quantities has not been indicated explicitly in order to simplify the notations. Our main hypothesis can now be stated precisely by assuming that for a small diffusion coefficient D the probability $p_x(n_1/n_2)$ remains approximately constant at long times, since this property holds true[15] if the homogeneous cell 1 is independent of the cell 2 (which corresponds to the limit of vanishing D).

As a result the conditional average number $\langle n/j \rangle_x$ defined by (15) is also stationary at long times, as well as the conditional probability $p_{xy}(n_1, n_2)$. Thus we recover the initial assumption that at long time the probabilities should evolve without change of shape in each region (xy).

Equation (11) is now obtained by summing the master equation (8) and by writing

$$\begin{aligned} \mu_j^x &= W_j + D\langle n/j \rangle_x \\ \bar{\mu}_j^x &= \bar{W}_j + Dj \end{aligned} \tag{16}$$

and

$$q_j^x = \sum_{n_1 \in (x)} p_{xy}(n_1, j) = \sum_{n_2 \in (x)} p_{yx}(j, n_2) \tag{17}$$

It is seen that the coefficients μ, $\bar{\mu}$, and q are stationary at long times, according to the previous assumptions. The ε terms of Eq. (11) are given by

$$\begin{aligned} \varepsilon_{\alpha\alpha}(t) &= -Dm(p(m-1, m) + p(m, m-1)) \\ \varepsilon_{\alpha\gamma}(t) &= D(M+1)\, p(M+1, m-1) + Dm\, p(m, M) \\ \varepsilon_{\gamma\alpha}(t) &= D(M+1)\, p(m-1, M+1) + Dm\, p(M, m) \\ \varepsilon_{\gamma\gamma}(t) &= -D(M+1)(p(M+1, M) + p(M, M+1)) \end{aligned} \tag{18}$$

They are probability fluxes from or to a highly improbable region where the two cells are in the neighbourhood of β. They can be considered negligible with respect to any other quantity in (11).

3.4. Adiabatic Elimination of the Intermediary Probabilities

In order to obtain a self-consistant equation for $p(x, y)$ from (11), the intermediary probabilities $p(x, m)$, $p(x, M)$ and the symmetrical quantities,

defined by (12), have to be computed from the master equation (8). One finds for any j in the intermediate region $(\beta) = \{j : m \leqslant j \leqslant M\}$

$$\frac{dp(x,j)}{dt} = \mu_{j-1}^x p(x, j-1) - (\mu_j^x + \bar{\mu}_j^x)\, p(x,j) + \bar{\mu}_{j+1}^x p(x, j+1) + \varepsilon_j^x(t) \tag{19}$$

with

$$\begin{aligned}
\varepsilon_j^{\alpha}(t) = &- W_{m-1} p(m-1, j) + \bar{W}_m p(m, j) + Dm\, p(m, j-1) \\
&- D(j+1)\, p(m-1, j+1) \\
\varepsilon_j^{\gamma}(t) = &- \bar{W}_{M+1} p(M+1, j) + W_M p(M, j) - D(M+1)\, p(M+1, j-1) \\
&+ D(j+1)\, p(M, j+1)
\end{aligned}$$

Here again, $\varepsilon_j^x(t)$ can be neglected, as it expresses probability fluxes from or to the highly improbable region $(\beta\beta)$. μ_j^x and $\bar{\mu}_j^x$ are defined by (16).

Then, using the stationarity condition of $p_{xy}(n_1, j)$ at $j = m-1$ and $j = M+1$, Eq. (19) yields for j in the intermediate region (β):

$$\begin{aligned}
\frac{dp(x,j)}{dt} = &\sum_{k=m}^{M} L_{jk}^x p(x,k) + \mu_{m-1}^x q_{m-1}^x \delta_{jm}\, p(x, \alpha) \\
&+ \bar{\mu}_{M+1}^x q_{M+1}^x \delta_{jM}\, p(x, \gamma)
\end{aligned} \tag{20}$$

Here δ_{jk} is the Kronecker symbol; L_{jk}^x is an element of a triagonal matrix L^x:

$$\begin{aligned}
L_{jj}^x &= -(\mu_j^x + \bar{\mu}_j^x) \\
L_{j-1,j}^x &= \bar{\mu}_j^x \\
L_{j+1,j}^x &= \mu_j^x \\
L_{jk}^x &= 0 \qquad \text{otherwise}
\end{aligned} \tag{21}$$

Equation (20) can be solved formally as

$$\begin{aligned}
p(x, j; t) = &\sum_{k \in (\beta)} [e^{L^x t}]_{jk}\, p(x, k; 0) \\
&+ \mu_{m-1}^x q_{m-1}^x \int_0^t [e^{L^x \tau}]_{jm}\, p(x, \alpha; t-\tau)\, d\tau \\
&+ \bar{\mu}_{M+1}^x q_{M+1}^x \int_0^t [e^{L^x \tau}]_{jM}\, p(x, \gamma; t-\tau)\, d\tau \qquad \text{if } j \in (\beta)
\end{aligned} \tag{22}$$

The region (β) is an unstable region connecting the two stable regions (α) and (γ). The internal relaxation time in (β), which is of the order of magnitude of $|\lambda_1|^{-1}$($|\lambda_1|$ being the smallest eigenvalue of L^x in absolute value) is supposedly very small on the scale of the long time evolution of $p(n_1, n_2)$. Thus, for any time $t \gg |\lambda_1|^{-1}$, the first term on the right-hand side of (22) can be discarded, the integrals extended from zero to infinity, and $p(x, y; t-\tau)$ replaced by $p(x, y; t)$. Then from (11)

$$\frac{dp(\alpha,\alpha)}{dt} = -2\mu^{\alpha}_{m-1} q^{\alpha}_{m-1} k^{\alpha}_f \, p(\alpha,\alpha) + \bar{\mu}^{\alpha}_{M+1} q^{\alpha}_{M+1} k^{\alpha}_b (p(\alpha,\gamma) + p(\gamma,\alpha)) \tag{23a}$$

$$\frac{dp(\alpha,\gamma)}{dt} = \mu^{\alpha}_{m-1} q^{\alpha}_{m-1} \bar{k}^{\alpha}_f \, p(\alpha,\alpha) - (\mu^{\gamma}_{m-1} q^{\gamma}_{m-1} k^{\gamma}_f + \bar{\mu}^{\alpha}_{M+1} q^{\alpha}_{M+1} \bar{k}^{\alpha}_b) p(\alpha,\gamma) + \mu^{\gamma}_{M+1} q^{\gamma}_{M+1} k^{\gamma}_b \, p(\gamma,\gamma) \tag{23b}$$

$$\frac{dp(\gamma,\gamma)}{dt} = \mu^{\gamma}_{m-1} q^{\gamma}_{m-1} \bar{k}^{\gamma}_f (p(\alpha,\gamma) + p(\gamma,\alpha)) - 2\bar{\mu}^{\gamma}_{M+1} q^{\gamma}_{M+1} \bar{k}^{\gamma}_b \, p(\gamma,\gamma) \tag{23c}$$

and the equation obtained from (23b) by changing $p(\alpha,\gamma)$ in $p(\gamma,\alpha)$. The quantities $k^x_f, k^x_b, \bar{k}^x_f, \bar{k}^x_b$ are defined as

$$\begin{aligned} k^x_f &= 1 - \int_0^{\infty} \bar{\mu}^x_m [e^{L^x t}]_{mm} \, dt \\ k^x_b &= \int_0^{\infty} \bar{\mu}^x_m [e^{L^x t}]_{mM} \, dt \\ \bar{k}^x_f &= \int_0^{\infty} \mu^x_M [e^{L^x t}]_{Mm} \, dt \\ \bar{k}^x_b &= 1 - \int_0^{\infty} \mu^x_M [e^{L^x t}]_{MM} \, dt \end{aligned} \tag{24}$$

The matrices L^x given by (21) are particular nonstochastic tridiagonal matrices similar to the matrices of the single box problem that we have studied in an earlier paper.[15] We recall briefly in Appendix B how the $k^x, \bar{k}^x$ can be calculated exactly. Putting

$$g^x_i = \frac{\mu^x_{i-1} \mu^x_{i-2} \cdots \mu^x_0}{\bar{\mu}^x_i \bar{\mu}^x_{i-1} \cdots \bar{\mu}^x_1} \tag{25}$$

it comes out that

$$\begin{aligned} k^x_f = \bar{k}^x_f &= \frac{1}{\bar{\mu}^x_m g^x_m} \times \left[\sum_{k=m-1}^{M} \frac{1}{\mu^x_k g^x_k} \right]^{-1} \\ k^x_b = \bar{k}^x_b &= \frac{1}{\mu^x_M g^x_M} \times \left[\sum_{k=m}^{M+1} \frac{1}{\bar{\mu}^x_k g^x_k} \right]^{-1} \end{aligned} \tag{26}$$

Furthermore it is possible to express the q_j^x as a function of the g_i^x, as shown in Appendix A:

$$q_j^x = \frac{g_j^x}{\sum_{k\in(y)} g_k^x} \qquad \text{for } j\in(y),\ y=\alpha,\gamma \tag{27}$$

Thus the $p(x, y)$ satisfy the simple evolution Eq. (23), which may be written

$$\frac{d}{dt}\begin{bmatrix} p(\alpha,\alpha) \\ p(\alpha,\gamma) \\ p(\gamma,\alpha) \\ p(\gamma,\gamma) \end{bmatrix} = \begin{bmatrix} -2K_f^\alpha & K_b^\alpha & K_b^\alpha & 0 \\ K_f^\alpha & -K_b^\alpha - K_f^\gamma & 0 & K_b^\gamma \\ K_f^\alpha & 0 & -K_b^\alpha - K_f^\gamma & K_b^\gamma \\ 0 & K_f^\gamma & K_f^\gamma & -2K_b^\gamma \end{bmatrix} \begin{bmatrix} p(\alpha,\alpha) \\ p(\alpha,\gamma) \\ p(\gamma,\alpha) \\ p(\gamma,\gamma) \end{bmatrix} \tag{28}$$

K_f^x and K_b^x express for each cell the forward passage rate from (α) to (γ), and the backward passage rate from (γ) to (α), knowing that the second cell is in region (x). According to (25)–(27), they have the following expressions:

$$\begin{aligned} K_f^x &= \left(\sum_{j\in(\alpha)} g_j^x \sum_{k=m-1}^{M} \frac{1}{\mu_k^x g_k^x} \right)^{-1} \\ K_b^x &= \left(\sum_{j\in(\gamma)} g_j^x \sum_{k=m}^{M+1} \frac{1}{\mu_k^x g_k^x} \right)^{-1} \end{aligned} \tag{29}$$

With an obvious reindexing of the $p(x, y)$:

$$p(\alpha,\alpha)=p_1, \qquad p(\alpha,\gamma)=p_2, \qquad p(\gamma,\alpha)=p_3, \qquad p(\gamma,\gamma)=p_4$$

Eq. (28) yields

$$p_i(t) = \sum_{k=1}^{4} \frac{\bar{x}_k^j \underline{x}_i^k}{\sum_{l=1}^{4} \bar{x}_k^l \underline{x}_l^k} e^{\lambda_k t} \qquad \text{for } p_i(0)=\delta_i^j \tag{30}$$

$\lambda_k, \bar{x}_k^i, \underline{x}_i^k$ are, respectively, the eigenvalues, and the left and right eigenvectors of the evolution matrix (21).

The eigenvalues prove to be

$$\begin{aligned} \lambda_1 &= 0 \\ \lambda_{2,3} &= -\left(K_f^\alpha + K_b^\gamma + \frac{K_f^\gamma + K_b^\alpha}{2}\right) \pm \left[\left(K_f^\alpha - K_b^\gamma - \frac{K_f^\gamma + K_b^\alpha}{2}\right)^2 + 2K_f^\alpha K_b^\gamma \right]^{1/2} \\ \lambda_4 &= -(K_b^\alpha + K_f^\alpha) \end{aligned} \tag{31}$$

and are associated with the (nonnormalized) right eigenvectors:

$$\underline{x}_1^i = \frac{2K_b^\alpha}{2K_f^\alpha + \lambda_i}, \qquad \underline{x}_2^i = \underline{x}_3^i = 1, \qquad \underline{x}_4^i = \frac{2K_f^\gamma}{2K_b^\gamma + \lambda_i}, \qquad i = 1, 2, 3$$
$$\underline{x}_1^4 = \underline{x}_4^4 = 0, \qquad \underline{x}_2^4 = -\underline{x}_3^4 = 1 \tag{32}$$

and with the left eigenvectors:

$$\bar{x}_i^1 = \frac{2K_f^\alpha}{2K_f^\alpha + \lambda_i}, \qquad \bar{x}_i^2 = \bar{x}_i^3 = 1, \qquad \bar{x}_i^4 = \frac{2K_b^\gamma}{2K_b^\gamma + \lambda_i}$$
$$\bar{x}_4^1 = \bar{x}_4^4 = 0, \qquad \bar{x}_4^2 = -\bar{x}_4^3 = 1 \tag{33}$$

It is seen that the first three eigenvectors are symmetrical and the fourth eigenvector is unsymmetrical. The symmetry between $p(\alpha, \gamma)$ and $p(\gamma, \alpha)$ in (28) is only broken by the initial conditions: starting from a symmetrical distribution, for instance, concentrated on one of the homogeneous steady states, the equality of $p(\alpha, \gamma)$ and $p(\gamma, \alpha)$ propagates in time. Thus in the spectral decomposition (31), $k = 4$ can be discarded; the evolution of $p_i(t)$ reduces to the decay of two exponentials, of characteristic times $|\lambda_2|^{-1}$ and $|\lambda_3|^{-1}$. For times $t \gg |\lambda_2|^{-1} > |\lambda_3|^{-1}$, a stationary distribution is reached, which is given by

$$p(\alpha, \alpha) = N^{-1}\left(\frac{K_b^\alpha}{K_f^\alpha}\right), \qquad p(\alpha, \gamma) = p(\gamma, \alpha) = N^{-1}, \qquad p(\gamma, \gamma) = N^{-1}\left(\frac{K_f^\gamma}{K_b^\gamma}\right) \tag{34}$$

where N is the normalization factor $(2 + (K_b^\alpha/K_f^\alpha) + (K_f^\gamma/K_b^\gamma))$.

4. NUMERICAL RESULTS

The computation of the passage rates K_f^x, K_b^x makes sense as long as the conditional averages $\langle n_i/n_j \rangle_x$ can be calculated with a sufficient accuracy. As mentionned previously, the analysis of this important point is reported in Appendix A. It is shown that in the thermodynamic limit, $\langle n_1/n_2 \rangle_x$ is the solution of the equation

$$w(n_1) + \bar{w}(n_1) + Dn_2 \frac{w(n_2) + Dn_1}{\bar{w}(n_2) + Dn_2} - Dn_1 \frac{\bar{w}(n_2) + Dn_2}{w(n_2) + Dn_1} = 0 \tag{35}$$

which belongs to the region (x); w and $\bar{w}$ are the deterministic birth and death rates defined by (3). $\langle n_2/n_1 \rangle_x$ verifies the symmetrical equation with respect to n_1, n_2. It can be easily seen that (35) and its symmetrical are

simultaneously satisfied for the steady states of deterministic Eq. (6). We have represented graphically their solutions in the plane (n_1, n_2), for the chemical rates used by Frankowicz and Gudowska-Nowak in their Monte Carlo simulation[13]:

$$W_n = AV(n(n-1)/V^2 + C/A)$$
$$\bar{W}_n = n((n-1)(n-2)/V^2 + B) \tag{36}$$
$$A = 1.55, \quad B = 0.595, \quad C = 0.0604965, \quad V = 100$$

and for different values of the diffusion coefficient D. In agreement with the deterministic analysis of Ebeling and Malchow,[14] three regions of D can be distinguished:

(i) For small D (Fig. 2a), (35) admits three solutions for any n_2 (more precisely, in our case, for $n_2 > 150$. We do not take care of the regions of the plane (n_1, n_2) far beyond the second peak since, in terms of probabilities, their contribution is very small). The two stable solutions correspond to the conditional averages in region (α) and (γ), or equivalently, in the thermodynamic limit, to the maximum of the conditional probabilities in region (α) and (γ). The unstable solution belongs to the region (β). Although its meaning in terms of conditional average is not obvious, this solution can likely be assimilated to the minimum of the conditional probabilities. We can see in Fig. 1a that this is both consistent with the deterministic analysis of Section 2.2 and with the approximative shape of the stationary distribution given by Fig. 1. The surface presents four peaks separated by saddle points. The region $(\beta\beta)$ surrounds an unstable state and has supposedly a negligeable probability weight.

(ii) For intermediate D (Fig. 2b), there is a critical value n_c inferior to γ such that Eq. (35) admits three solutions for $n_2 < n_c$ and only one solution for $n_2 > n_c$. The line of maximum conditional probabilities for n_1 in the region (α) does not interest anymore the line of maximum conditional probabilities for n_2 in the region (γ). The two stable inhomogeneous steady states have disappeared, while two inhomogeneous saddle points still exist.

(iii) For larger D (Fig. 2c), the inhomogeneous saddle points have disappeared. A valley where the conditional probabilities for both n_1 and n_2 are minimum intersects perpendicularly the main diagonal at the point (β, β). This point is presumably a saddle point, while (α, α) and (γ, γ) are still stable points.

In their Monte Carlo simulation of the two-cell model, Frankowicz and Gudowska-Nowak have computed the mean first passage time from the state

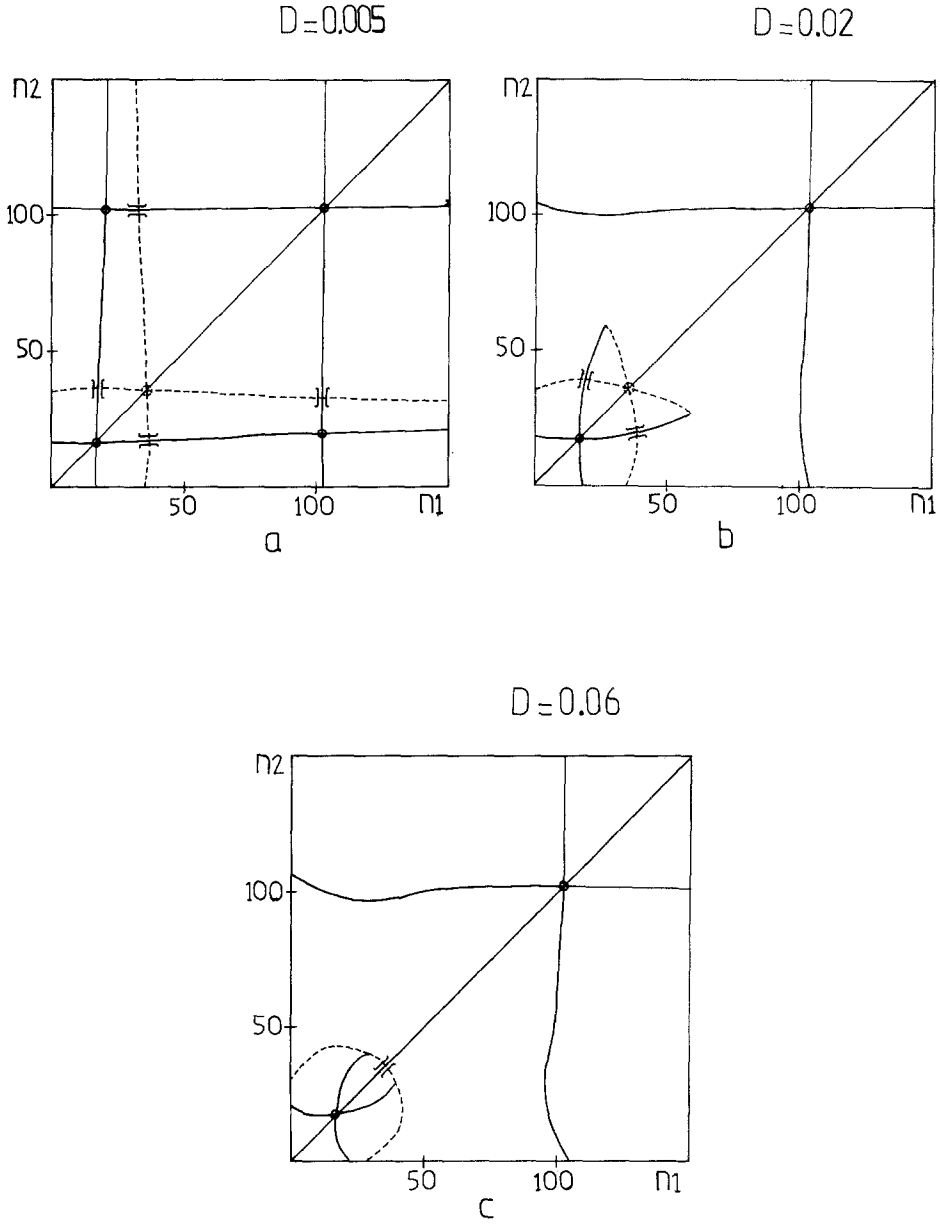

Fig. 2. Maximum (——) and minimum (------) of the conditional probabilities, in both directions, and for different values of D. The intersection of two solid lines gives a stable node (O). The intersection of one solid line and one dashed line gives a saddle point (≍). The intersection of two dashed lines give an unstable point (◌).

(α, α) to the state (γ, γ) for the set of constants (36). In our theory, this mean first passage time is qualitatively given by the quantity

$$T_{\alpha\gamma} = \frac{1}{2}\left(\frac{1}{K_f^{\alpha}} + \frac{1}{K_f^{\gamma}}\right) \tag{37}$$

which expresses the mean passage time from the region $(\alpha\alpha)$ to the region $(\gamma\gamma)$ through $(\alpha\gamma)$ and $(\gamma\alpha)$.

We have computed the stationary distribution (34) and the passage time $T_{\alpha\gamma}$ for the constants (36). Our results are given in Table Ia. They have to be considered with some caution, since $V = 100$ is a small volume, and the potential barriers between the steady states are very low; our basic hypothesis of quasistationarity around each steady state is thus not well verified. However, we recover the main points brought out by the Monte Carlo simulation. When D is increased from $D = 0$, where the two cells are independent, to the first critical value D_{c_1} of D, we find that (a) the relative stability of the inhomogeneous steady state is decreased, (b) the relative stability of the homogeneous steady state with higher concentration is increased, and (c) the passage time from (α, α) to (γ, γ) decreases and seems to reach a minimum beyond $D = 0.015$. This minimum was observed by Frankowicz and Gudowska-Nowak for $D = 0.02$.

Our calculation of the passage times does not apply to the intermediate and high values of D, where $T_{\alpha\gamma}$ should increase. We give in Table Ib a second set of results for a larger volume, which fits better to the hypothesis

Table I. Stationary Distribution and Mean Passage Time from (αα) to (γγ) for Different Values of D

a. $A = 1.55$, $B = 0.595$, $C = 0.0604695$, $V = 100$

D	$p(\alpha, \alpha)$	$p(\alpha, \gamma)$	$p(\gamma, \gamma)$	$T_{\alpha\gamma}$
0.000	0.070	0.195	0.540	159
0.005	0.058	0.126	0.690	135
0.01	0.047	0.082	0.789	127
0.015	0.036	0.055	0.854	126

b. $A = 1.49$, $B = 0.595$, $C = 0.06048965$, $V = 400$

D	$p(\alpha, \alpha)$	$p(\alpha, \gamma)$	$p(\gamma, \gamma)$	$T_{\alpha\gamma}$
0.000	0.444	0.222	0.111	8986
0.005	0.424	0.084	0.407	6932
0.01	0.271	0.023	0.683	8753
0.015	0.170	0.007	0.817	11920

of quasistationarity. We have used slightly different constants, in order to make the weight of the regions $(\alpha\alpha)$ and $(\gamma\gamma)$ of comparable magnitude. The main features described above are conserved. The decrease of the stability of the inhomogeneous steady state is emphasized. The value of D corresponding to the minimum is shifted toward zero. It would be interesting to compare these results to other Monte Carlo simulations with a larger volume, but such simulation are not available up to now, since the computing time is expected to increase drastically with V.

5. DISCUSSION

In conclusion, it should be pointed out that our calculation depends on two basic assumptions: (a) the quasistationarity of the conditional probabilities inside each region (α), (γ) and (b) the hypothesis of low coupling between the cells, permitting to calculate the conditional averages.

The limits of these approximations are difficult to evaluate. Nevertheless, they have merit to lead to a very simple equation governing the evolution of the probability distribution, and to give directly the weight of the different peaks of the stationary distribution. This cannot be achieved by any other analytical theory at the moment. The comparison with the Monte Carlo calculation of Frankowicz and Gudoska-Nowak seems encouraging. On the other hand, the determination of the conditional averages of the Appendix A gives a better idea of the shape of the stationary distribution. The results agree with those of the deterministic analysis for any value of D in the thermodynamic limit. However, the treatment of the passage times for intermediate and large D remains outside the scope of the present theory.

APPENDIX A

On a short time scale, the conditional probabilities $p_x(n_1/n_2)$, $x = \alpha, \gamma$, relax towards a quasistationary distribution which is approximatively identical to the stationary probability distribution obtained when reflecting barriers are introduced at $n_1 = m$ and $n_1 = M$, which is now assumed. Owing to the definition (14), the evolution equation of $p_x(n_1/n_2)$ then reads

$$\frac{dp_x(n_1/n_2)}{dt} = \frac{1}{p(x, n_2)} \frac{dp(n_1, n_2)}{dt} - \frac{p_x(n_1/n_2)}{p(x, n_2)} \frac{dp(x, n_2)}{dt} \tag{A1}$$

$dp(x, n_2)/dt$ can be straightforwardly obtained by summing the master equation (8) over the region (x), and by taking into account the reflecting boundary conditions:

$$\frac{dp(x, n_2)}{dt} = W_{n_2-1}\, p(x, n_2 - 1) - (W_{n_2} + \bar{W}_{n_2})\, p(x, n_2) + \bar{W}_{n_2+1}\, p(x, n_2 + 1)$$
$$+ D(n_2 + 1)\, p(x, n_2 + 1) + D\langle n_1/n_{2-1}\rangle_x\, p(x, n_2 - 1)$$
$$- D(n_2 + \langle n_1/n_2\rangle_x)\, p(x, n_2) \tag{A2}$$

In particular, the stationary solution of (A2) verifies a detailed balance condition:

$$\frac{p(x, n_2 + 1)}{p(x, n_2)} = \frac{W_{n_2} + D\langle n_1/n_2\rangle_x}{\bar{W}_{n_2+1} + D(n_2 + 1)} = \frac{\mu^x_{n_2}}{\bar{\mu}^x_{n_2+1}} \tag{A3}$$

Owing to the definitions (13) and (17), we have

$$q^x_{n_2} = \sum_{n_1 \in (x)} p_{xy}(n_1, n_2) = \frac{p(x, n_2)}{p(x, y)}, \qquad n_2 \in (y) \tag{A4}$$

so that (A3) yields

$$\frac{q^x_{n_2+1}}{q^x_{n_2}} = \frac{\mu^x_{n_2}}{\bar{\mu}^x_{n_2+1}} \tag{A5}$$

from which formula (27) can be recovered.

Now the evolution of $p_x(n_1/n_2)$ can be found explicitly from (A1), (A2), and from the master equation (8). At this point, we introduce the following complementary hypothesis: when the diffusional coupling between cells 1 and 2 is low, $p_x(n_1/n_2)$ should be a slowly varying function of n_2, and depends mostly on n_1. This statement enables us to proceed to a useful approximation in the evolution equation of $p_x(n_1/n_2)$; we shall write

$$p_x(n_1/n_2 - 1) \simeq p_x(n_1/n_2) \simeq p_x(n_1/n_2 + 1) \tag{A6}$$

so that Eq. (A1) reduces to

$$\frac{dp_x(n_1/n_2)}{dt} = \left[W_{n_1-1} + D(n_2 + 1)\frac{p(x, n_2 + 1)}{p(x, n_2)}\right] p_x(n_1 - 1/n_2)$$
$$- \left[W_{n_1} + \bar{W}_{n_1} + Dn_1 + D(n_2 + 1)\frac{p(x, n_2 + 1)}{p(x, n_2)}\right.$$
$$\left. + D\langle n_1/n_2\rangle_x \left(\frac{p(x, n_2 - 1)}{p(x, n_2)} - 1\right)\right] p_x(n_1/n_2)$$
$$+ \left[\bar{W}_{n_1+1} + D(n_1 + 1)\frac{p(x, n_2 - 1)}{p(x, n_2)}\right] p_x(n_1 + 1/n_2) \tag{A7}$$

The approximation scheme that we have used above is classically used to solve multivariate master equations (see Ref. 2, Chap. 7.5). (A7) has to be

completed by the evolution of the conditional averages. Multiplying (A7) by n_1 and summing over (x), we get

$$\frac{d\langle n_1/n_2\rangle_x}{dt} = \langle W_{n_1} - \bar{W}_{n_1}/n_2\rangle_x + D(n_2+1)\frac{p(x,n_2+1)}{p(x,n_2)}$$
$$- D\langle n_1/n_2\rangle_x \frac{p(x,n_2-1)}{p(x,n_2)} + D\langle \delta n_1^2/n_2\rangle_x \left[\frac{p(x,n_2-1)}{p(x,n_2)} - 1\right] \quad \text{(A8)}$$

where $\langle \delta n_1^2/n_2\rangle_x$ is the conditional variance in region (x). The variances of any order make sense, since the conditional probabilities have been constructed to be singly peaked. With the definition (9) of W_{n_1} and $\bar{W}_{n_1}$, it is easy to show that

$$\langle W_{n_1} - \bar{W}_{n_1}\rangle_x = W_{\langle n_1/n_2\rangle_x} - \bar{W}_{\langle n_1/n_2\rangle_x} - \frac{k_1}{V^2}\langle \delta n_1^3/n_2\rangle_x$$
$$+ \frac{1}{V^2}\langle \delta n_1^2/n_2\rangle_x [n_A k_2 - k_1(3\langle n_1/n_2\rangle_x - 3)] \quad \text{(A9)}$$

As a first approximation we can neglect all the variances in Eq. (A8). Owing to the detailed balance condition (A3), the stationary value of $\langle n_1/n_2\rangle_x$ then verifies a closed equation:

$$0 = W_{\langle n_1/n_1\rangle_x} - \bar{W}_{\langle n_1/n_2\rangle_x} + D(n_2+1)\frac{W_{n_2} + D\langle n_1/n_2\rangle_x}{\bar{W}_{n_2+1} + D(n_2+1)}$$
$$- D\langle n_1/n_2\rangle_x \frac{\bar{W}_{n_2} + Dn_2}{W_{n_2-1} + D\langle n_1/n_2\rangle_x} \quad \text{(A10)}$$

which can be solved numerically in a straightforward way and thus allow us to calculate the coefficients μ and $\bar{\mu}$ of Eq. (16). The approximation procedure can be refined by writing the equation verified by $\langle \delta n_1^2/n_2\rangle_x$, and vanishing only the variances of order superior or equal to 3. Without entering the detailed calculation, it is possible to obtain the two coupled equations:

$$0 = W_{\langle n_1/n_2\rangle_x} - \bar{W}_{\langle n_1/n_2\rangle_x} + D(n_2+1)\frac{p(x,n_2+1)}{p(x,n_2)} - D\langle n_1/n_2\rangle_x \frac{p(x,n_2-1)}{p(x,n_2)}$$
$$+ \langle \delta n_1^2/n_2\rangle_x \left\{ D\left(\frac{p(x,n_2-1)}{p(x,n_2)} - 1\right) + \frac{1}{V^2}[n_A k_2 - k_1(3\langle n_1/n_2\rangle_x - 3)]\right\} \quad \text{(A11)}$$

$$0 = W_{\langle n_1/n_2\rangle_x} + \bar{W}_{\langle n_1/n_2\rangle_x} + D(n_2+1)\frac{p(x,n_2+1)}{p(x,n_2)} + D\langle n_1/n_2\rangle_x \frac{p(x,n_2-1)}{p(x,n_2)}$$
$$- \langle \delta n_1^2/n_2\rangle_x \left\{ 2D\frac{p(x,n_2-1)}{p(x,n_2)} + \frac{1}{V^2}[n_A k_2(1 - 4\langle n_1/n_2\rangle_x)\right.$$
$$\left. + k_1(6\langle n_1/n_2\rangle_x^2 - 15\langle n_1/n_2\rangle_x - 15\langle n_1/n_2\rangle_x + 7)] + 2k_4\right\}$$

$\langle \delta n_1^2/n_2 \rangle_x$ can be expressed as function of $\langle n_1/n_2 \rangle_x$ in the second equation and then be substituted in the first one, so that a closed equation for $\langle n_1/n_2 \rangle_x$ is obtained. Notice that in the thermodynamic limit, if V represents the volume of each cell, all the terms of order V^i, $i \leqslant 0$, can be discarded in (A10), and this equation reduces to

$$0 = w(\langle n_1/n_2 \rangle_x) - \bar{w}(\langle n_1/n_2 \rangle_x) + Dn_2 \frac{w(n_2) + D\langle n_1/n_2 \rangle_x}{\bar{w}(n_2) + Dn_2}$$
$$- D\langle n_1/n_2 \rangle_x \frac{\bar{w}(n_2) + Dn_2}{w(n_2) + D\langle n_1/n_2 \rangle_x} \tag{A12}$$

where w and $\bar{w}$ are the deterministic rates defined by (3). This last formula permits us to recover the results of the deterministic analysis, as mentioned in Section 4. This is an encouraging consequense of the approximation scheme that we have used, and which consists in considering $p_x(n_1/n_2)$ and $\langle n_1/n_2 \rangle_x$ as slowly varying functions of n_2.

APPENDIX B

Let L^x be the matrix (21). We want to calculate the quantities k_f^x and $\bar{k}_f^x$ defined by

$$k_f^x = 1 - \bar{\mu}_m^x \int_0^\infty [e^{L^x t}]_{mm}\, dt$$
$$\bar{k}_f^x = \mu_M^x \int_0^0 [e^{L^x t}]_{Mm}\, dt \tag{B1}$$

The integrals can be expressed in terms of the minors D_{ij} and of the determinant D and L_x:

$$\int_0^\infty [e^{L^x t}]_{mm}\, dt = -L_{mm}^{x\,-1} = -\frac{D_{mm}}{D}$$
$$\int_0^\infty [e^{L^x t}]_{Mm} = -L_{Mm}^{x\,-1} = -\frac{D_{Mm}}{D} \tag{B2}$$

Let Δ_k' be the determinant of the submatrix obtained by suppressing the first k lines and columns of L^x. It follows that

$$D = \Delta_0', \qquad D_{mm} = \Delta_1' \tag{B3}$$

It is easy to show that the Δ'_k verify a recurrence relation:

$$\Delta'_{M-m+2} = 0, \qquad \Delta'_{M-m+1} = 1$$

$$\Delta'_k = -(\mu_{k+m} + \bar{\mu}_{k+m})\Delta'_{k+1} - \mu_{k+m}\bar{\mu}_{k+m+1}\Delta'_{k+2}$$
$$\text{for } 0 \leqslant k \leqslant M-m \tag{B4}$$

so that the Δ'_k can be proved to have the following expressions:

$$\Delta'_k = (-1)^{M-m+1-k}\mu_M \mu_{M-1} \cdots \mu_{m+k}\left(1 + \frac{\bar{\mu}_{m+k}}{\mu_{m+k}} + \cdots + \frac{\bar{\mu}_{m+k}\cdots\bar{\mu}_M}{\mu_{m+k}\cdots\mu_M}\right) \tag{B5}$$

On the other hand, D_{mM} is obtained directly from the matrix L^x:

$$D_{mM} = W_{M-1}W_{M-2}\cdots W_m \tag{B6}$$

With the preceding formulas, it is easy to recover the expression (26) for k_f^x and $\bar{k}_f^x$. k_b^x and $\bar{k}_b^x$ can be calculated in a similar manner.

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