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A MORPHOGEN GRADIENT MODEL FOR PATTERN REGULATION. II. TIME DESCRIPTION OF GLOBAL MORPHOGEN FORMATION AND FIELD COMPARTMENTALIZATION

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In a model for pattern regulation, use was made of local and global morphogens S and Σ. Σ is produced from the S-degradation and it is decomposed by first order kinetics while it diffuses along the field. We solve exactly the partial differential equation for the distribution of Σ in one spatial dimension when its source S is monotonic (for simplicity, linear or generally a power function). Assuming that S and Σ react reversibly with an allosteric protein P according to a sequential scheme, we derive the evolution in time of the field separation into compartments. At equilibrium the relative extent of each compartment is constant (for variable field size) and so pattern regulation is achieved.

1. Introduction

In a preceding paper [1], we presented a model which, incorporated in reaction–diffusion theory, produces pattern regulation in an one-dimensional morphogenetic field. We started with a stable monotonic gradient of morphogen S which is generated by a Gierer-Meinhardt mechanism [2]. For a suitable range of parameter values, S is well approximated by the homogeneous function

$$S(x, L) = \alpha(L) f(x/L). \tag{1}$$

Here x is the position in the field varying from 0 to the total length L. $f(x/L)$ is a smooth sigmoid function of the relative distance x/L and $\alpha(L)$ is a scaling multiplicative factor depending on L. S is continuously produced and destroyed and from the first order S-decomposition we consider a by-product that we call Σ. Morphogen Σ degradates also by a first order reaction while diffusion tends to equalize its distribution along the field. Taking all three effects into account, we write the total rate equation for Σ in the form:

$$\partial\Sigma/\partial t = D\,\partial^2\Sigma/\partial x^2 + k_1 S - k_2\Sigma, \tag{2}$$

D is the diffusion constant of Σ while k_1 and k_2 are the rate constants for the decomposition of S and Σ respectively.

In section 2 the length L is considered fixed and, in order to avoid unessential complications, we approximate the source term by a simple linear x-dependence

$$k_1 S = cx, \tag{3}$$

where the constant c is

$$c = k_1\alpha(L)/L. \tag{4}$$

We solve then exactly eq. (2) with the linear source term (3) and some reasonable initial and boundary condi-

tions. In section 3 the time course is calculated towards a compartmental separation of the field. At equilibrium this separation is size-independent. Finally, in an Appendix the solution of eq. (2) is given when the source is a power function with exponent any natural number.

2. Solution of eq. (2) for a linear source term

Consider the partial differential equation

$$\partial\Sigma(x,t)/\partial t = D\,\partial^2\Sigma(x,t)/\partial x^2 + cx - k_2\Sigma(x,t), \tag{5}$$

where $0 \leqslant x \leqslant L$. We assume that the initial condition for Σ is:

$$\Sigma(x,0) = 0. \tag{6}$$

Furthermore, we impose the condition that there is no flow of substance Σ at both ends.

$$\frac{\partial\Sigma(x,t)}{\partial x} = 0 \quad \text{for } x = 0 \text{ and } x = L. \tag{7}$$

There are several ways [3] to handle eq. (5). We follow here the Laplace transformation method [3,4] which can be easily applied to cases with more complicated source term. We introduce the Laplace transform of $\Sigma(x,t)$

$$v(x,p) = \int_0^\infty \mathrm{e}^{-pt}\Sigma(x,t)\,\mathrm{d}t. \tag{8}$$

Eq. (5) is then transcribed into the ordinary differential equation for $v(x,p)$.

$$\mathrm{d}^2v/\mathrm{d}x^2 - (p + k_2)v/D + cx/Dp = 0. \tag{9}$$

Imposing the boundary conditions (7) we solve (9) in a straightforward way:

$$v(x,p) = c\sqrt{D}\left\{\left[\exp\left(\frac{(x-L)\sqrt{p+k_2}}{\sqrt{D}}\right) + \exp\left(-\frac{(x-L)\sqrt{p+k_2}}{\sqrt{D}}\right)\right] - \left[\exp\left(\frac{x\sqrt{p+k_2}}{\sqrt{D}}\right) + \exp\left(-\frac{x\sqrt{p+k_2}}{\sqrt{D}}\right)\right]\right\}$$
$$\times\left\{p(p+k_2)^{3/2}\left[\exp\left(\frac{L\sqrt{p+k_2}}{\sqrt{D}}\right) - \exp\left(-\frac{L\sqrt{p+k_2}}{\sqrt{D}}\right)\right]\right\}^{-1} + \frac{cx}{p(p+k_2)}. \tag{10}$$

In order to derive $\Sigma(x,t)$ from its Laplace transform, we make use of the Inversion theorem:

$$\Sigma(x,t) = \frac{1}{2\pi\mathrm{i}}\int_{\gamma-\mathrm{i}\infty}^{\gamma+\mathrm{i}\infty} \mathrm{e}^{pt}v(x,p)\,\mathrm{d}p, \tag{11}$$

where γ is any constant positive number. All singularities of $v(x,p)$ in the complex p-plane lie to the left of the straight line $(\gamma - \mathrm{i}\infty, \gamma + \mathrm{i}\infty)$. (See fig. 1). $v(x,p)$ is a single-valued function, as can be easily seen by expanding the exponential expressions in the nominator and denominator of (10). The singularities then of the integrand of (11) are simple poles at $p = 0$, $p = -k_2$ and at these values of p, where $\sinh\{L\sqrt{(p+k_2)/D}\} = 0$.

For a parabolic arc ABCDE (see fig. 1) whose focus is fixed at the point O, we can show that

$$\int_{(\mathrm{ABCDE})} \mathrm{e}^{pt}v(x,p)\,\mathrm{d}p \to 0 \qquad \text{when } |\mathrm{OC}| \to \infty. \tag{12}$$

According to the Residue theorem

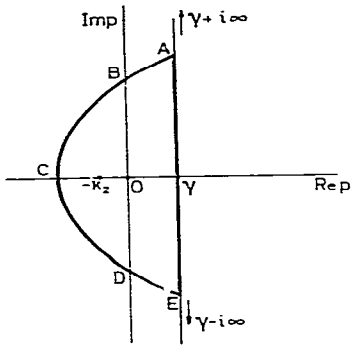

Fig. 1. The path C_N = (ABCDEA) for the integral of eq. (13) in the complex p-plane.

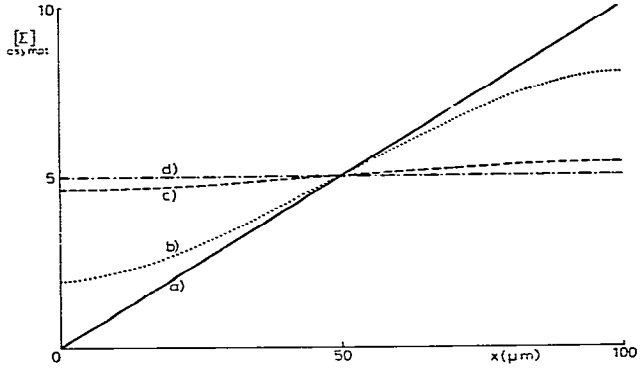

Fig. 2. The equilibrium concentration of Σ (in arbitrary units) as a function of position x. In an embryological scale the parameter values are: $c = 0.1$ (conc.)/(μm)(hour), $k_2 = 1$/(hour), $L = 100$ (μm). In a) $D = 0$ (μm)^2/(hour). Note: 1 (μm)^2/(hour) $\approx 2.78 \times 10^{-12}$ (cm)^2/(s). In b) $D = 400$ (μm)^2/(hour). In c) $D = 10^4$ (μm)^2/(hour). In d) $D = 10^6$ (μm)^2/(hour).

$$\int_{C_N} e^{pt} v(x, p)\, dp = 2\pi i[\text{sum of residues within } C_N] \tag{13}$$

and with the help of eqs. (11) and (12) we finally obtain for $\Sigma(x, t)$:

$$\Sigma(x, t) = \frac{c\sqrt{D}}{k_2\sqrt{k_2}}\left[\frac{\cosh\{(x - L)\sqrt{k_2/D}\} - \cosh\{x\sqrt{k_2/D}\}}{\sinh\{L\sqrt{k_2/D}\}}\right] + \frac{cx}{k_2}$$

$$- e^{-k_2 t}\left[\frac{cL}{2k_2} - \sum_{n=0}^{\infty} \frac{4cD\cos\{(\pi x/L)(2n+1)\}\exp\{-(\pi^2 D/L^2)(2n+1)^2 t\}}{L\{(\pi^2 D/L^2)(2n+1)^2\}\{(\pi^2 D/L^2)(2n+1)^2 + k_2\}}\right]. \tag{14}$$

Inspecting (14) we draw the following conclusions:

1) For big values of t, the term involving $\exp(-k_2 t)$ will be very small. Asymptotically, for $t \to \infty$, the expression for Σ will become:

$$\Sigma(x)_{\text{asympt}} = \frac{c\sqrt{D}}{k_2\sqrt{k_2}} \frac{\cosh\{(x - L)\sqrt{k_2/D}\} - \cosh\{x\sqrt{k_2/D}\}}{\sinh\{L\sqrt{k_2/D}\}} + \frac{cx}{k_2}. \tag{15}$$

Once reached at equilibrium, the asymptotic value $\Sigma(x)_{\text{asympt}}$ is stable against any disturbance local or (and) temporal. This stability is due to the sign of term $k_2\Sigma$ in eq. (2).

2) Eq. (15) for $\Sigma(x)_{\text{asympt}}$ depends on the values of parameters k_2, c, L and D. In fig. 2 are plotted several cases where D varies while the other parameters are kept constant. In a) $D = 0$ and $\Sigma(x)_{\text{asympt}}$ is a straight line. This extreme case could be obtained directly from (5), when equilibrium is established ($\partial\Sigma/\partial t = 0$). Then

$$\Sigma(D = 0) = (c/k_2)x.$$

As D becomes bigger, the slope of the line drops rapidly. In c) $D = 10^4$ (μm)^2/hour (= 2.78×10^{-8}(cm)^2/s), and the corresponding Σ_c is almost a straight line parallel to the x-axis. In d) $D = 10^6$ (μm)^2/hour (= 2.78×10^{-6} (cm)^2/s) and Σ_d coincides with the expression when $D = \infty$. This extreme case can be directly estimated from (5)

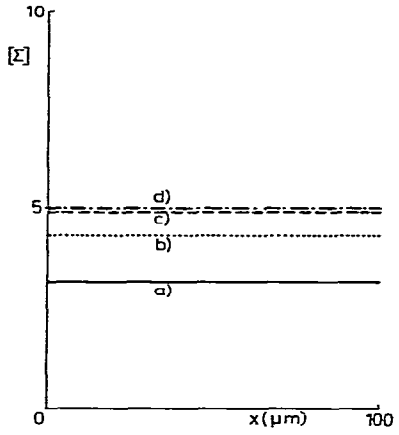

Fig. 3. Σ as a function of position for different values of time. $c = 0.1$ (conc.)/(μm)(hour), $k_2 = 1$/(hour), $D = 10^6$ (μm)^2/(hour), $L = 100$ (μm). For a) $t = 1$ hour, b) $t = 2$ hours, c) $t = 3$ hours, and d) $t \to \infty$.

since Σ diffuses instantly and is equally distributed along the whole length L. Hence

$$\Sigma(D=\infty) = \left(\int_0^L cx\,dx\right)\Big/ k_2 L = cL/2k_2.$$

3) It turns out that, for reasonable values of D, we obtain convenient expressions for $\Sigma(x)_{\text{asympt}}$ if we expand (15) in terms of the dimensionless parameter

$$\omega = L\sqrt{k_2/D}, \tag{16}$$

$$\Sigma(x)_{\text{asympt}} = \frac{cL}{k_2}\,\frac{[(x/L-1)^2 - x^2/L^2]\,\omega^2/2! + [(x/L-1)^4 - x^4/L^4]\,\omega^4/4! + \ldots}{\omega^2 + \omega^4/3! + \ldots} + \frac{cx}{k_2}. \tag{17}$$

Crick [5] calculated that for a morphogen of molecular weight about 500, the diffusion constant should be of the order $D \simeq 10^{-6}$ cm^2 s^{-1} ($\simeq 3.6 \times 10^5$ (μm)^2/hour). If Σ decomposes with a rate constant $k_2 = 1$/hour and the morphogenetic field is usually of the order $L = 200$ μm, as pointed out by Wolpert [6], then an estimate of ω is

$$\omega \approx 0.3$$

The above value indicates that it is quite reasonable to expect $\omega \lesssim 1$. We can therefore neglect in the expansion (17) all but the lowest power of ω. So we get:

$$\Sigma(x)_{\text{asympt}} \simeq cL/2k_2. \tag{18}$$

In this approximation (18) coincides with Σ_{asympt} for instant diffusion. In fig. 3 Σ is plotted from eq. (14) for different values of time. The asymptotic value is reached at a time characteristic of the time scaling in embryonic development.

3. Time evolution of field compartmentalization

In [1] we introduced a sequential scheme of chemical reactions where an allosteric protein P interacts reversibly with S and Σ while in every step an active site of P is occupied. Furthermore, the equilibrium active state distributions are written down for the general case of a protein with any number of active sites.

We are going to calculate now the time course towards equilibrium for the simple case of a protein P with 2 active sites reacting with the morphogens according to:

$$P_0 + S \underset{k_4}{\overset{k_3}{\rightleftarrows}} P_1 + \Sigma, \qquad P_1 + S \underset{k_6}{\overset{k_5}{\rightleftarrows}} P_2 + \Sigma. \tag{19}$$

P_0, P_1 and P_2 are the states of P with none, one and two active sites occupied respectively. The sites are reversibly occupied, with equilibrium constants given by:

$$K_1^{eq} = k_3/k_4, \qquad K_2^{eq} = k_5/k_6.$$

The protein P is produced in all cells at equal quantities and it is a quite large molecule. Therefore, it is considered indiffusible.

At each position x we can write down the kinetic equations for P_0, P_1 and P_2

$$dP_0/dt = -k_3 S P_0 + k_4 \Sigma P_1, \quad dP_1/dt = k_3 S P_0 - (k_4 \Sigma + k_5 S) P_1 + k_6 S P_2, \quad dP_2/dt = k_5 S P_1 - k_6 \Sigma P_2. \tag{20}$$

The quantity of protein found in the three states P_0, P_1 and P_2 is constant and the same for all x and all times

$$P_{tot} = P_0 + P_1 + P_2. \tag{21}$$

At $t = 0$: $P_0 = P_{tot}, P_1 = P_2 = 0$.

Since $S(x)$ and $\Sigma(L)$ are stable, we can solve the system (20) for two independent functions, e.g. P_0, P_1 while P_2 is fixed from (21). In a straightforward calculation we find:

$$\begin{aligned} P_0 &= A\, e^{\lambda_1 t} + B\, e^{\lambda_2 t} + P_{tot} \frac{k_4 k_6 \Sigma^2}{k_3 k_5 S^2 + k_3 k_6 S\Sigma + k_4 k_6 \Sigma^2} \\ P_1 &= \frac{1}{k_4 \Sigma} [A\lambda_1 e^{\lambda_1 t} + B\lambda_2 e^{\lambda_2 t}] + \frac{k_3 S}{k_4 \Sigma} \left[A\, e^{\lambda_1 t} + B\, e^{\lambda_2 t} + P_{tot} \frac{k_4 k_6 \Sigma^2}{k_3 k_5 S^2 + k_3 k_6 S\Sigma + k_4 k_6 \Sigma^2} \right]. \end{aligned} \tag{22}$$

Here λ_1 and λ_2 are the roots of the second-order equation in λ:

$$\lambda^2 + (k_3 S + k_4 \Sigma + k_5 S + k_6 \Sigma)\lambda + (k_3 k_5 S^2 + k_3 k_6 S\Sigma + k_4 k_6 \Sigma^2) = 0$$

and

$$A = P_{tot} \frac{(k_4 k_6)\Sigma^2 \lambda_2 - (k_3 k_5 S^2 + k_3 k_6 S\Sigma + k_4 k_6 \Sigma^2)(\lambda_2 + k_3 S)}{(\lambda_1 - \lambda_2)(k_3 k_5 S^2 + k_3 k_6 S\Sigma + k_4 k_6 \Sigma^2)},$$

$$B = P_{tot} \frac{-(k_4 k_6)\Sigma^2 \lambda_1 + (k_3 k_5 S^2 + k_3 k_6 S\Sigma + k_4 k_6 \Sigma^2)(\lambda_1 + k_3 S)}{(\lambda_1 - \lambda_2)(k_3 k_5 S^2 + k_3 k_6 S\Sigma + k_4 k_6 \Sigma^2)}$$

It turns out that the roots λ_1 and λ_2 are always real and non-positive. Hence, the asymptotic values of P_0, P_1 and P_2 are:

$$\begin{aligned} P_{0,asympt} &= P_{tot} \frac{k_4 k_6 \Sigma^2}{k_3 k_5 S^2 + k_3 k_6 S\Sigma + k_4 k_6 \Sigma^2}, \quad P_{1,asympt} = P_{tot} \frac{k_3 k_6 S\Sigma}{k_3 k_5 S^2 + k_3 k_6 S\Sigma + k_4 k_6 \Sigma^2}, \\ P_{2,asympt} &= P_{tot} - P_{0,asympt} - P_{1,asympt}. \end{aligned} \tag{23}$$

The expressions for P_0, P_1 and P_2 from (22) are quite complicated in terms of x, L and t. The asymptotic values (23) in contrast, are not only time independent but the dependence on x and L is of particular simplicity.

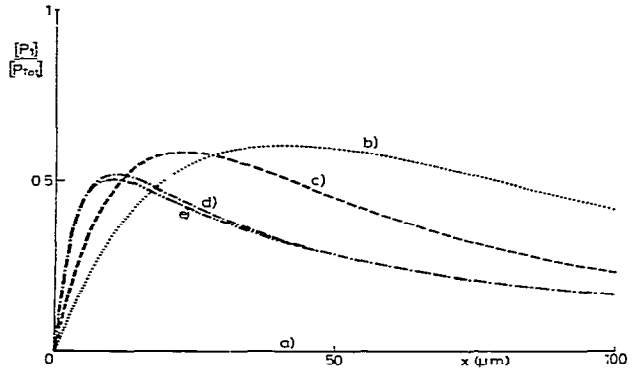

Fig. 4. P_1 plotted for different values of the time following eq. (22). S and Σ are given by (3) and (18) respectively. We take for the ratio $k_1/k_2 = 0.1$. The other constants measured in units (hour)$^{-1}$ (μm)$^{-1}$ are: $(\alpha k_3) = 0.1$, $(\alpha k_4) = 0.1$, $(\alpha k_5) = 0.025$, $(\alpha k_6) = 0.1$. The length L is 100 μm. a) $t = 0$ hour, b) $t = 0.5$ hour, c) $t = 1$ hour, d) $t = 4$ hours, and e) $t \to \infty$ following eq. (24).

If we substitute from (3) and (18) the expressions for S and Σ we find that at equilibrium the concentrations will be:

$$P_{0,\,\text{asympt}} = P_{\text{tot}}\left\{1 + \frac{2k_2K_1^{\text{eq}}}{k_1}\left(\frac{x}{L}\right) + \frac{4k_2^2K_1^{\text{eq}}K_2^{\text{eq}}}{k_1^2}\left(\frac{x}{L}\right)^2\right\}^{-1},$$

$$P_{1,\text{asympt}} = P_{\text{tot}}\left\{\frac{k_1}{2k_2K_1^{\text{eq}}}\left(\frac{L}{x}\right) + 1 + \frac{2k_2K_2^{\text{eq}}}{k_1}\left(\frac{x}{L}\right)\right\}^{-1} \tag{24}$$

$$P_{2,\text{asympt}} = P_{\text{tot}}\left\{\frac{k_1^2}{4k_2^2K_1^{\text{eq}}K_2^{\text{eq}}}\left(\frac{L}{x}\right)^2 + \frac{k_1}{2k_2K_2^{\text{eq}}}\left(\frac{L}{x}\right) + 1\right\}^{-1}.$$

It is clear from (24) that the equilibrium concentrations depend on the rate constants k_1, k_2 and the equilibrium constants K_1^{eq}, K_2^{eq}. They depend on x and L in such a manner that only the ratio x/L appears in (24). Therefore expressions (24) are explicitly scale invariant. From (36) we note that the equilibrium distributions are size-invariant as long as S is of the form (1) and Σ behaves as a global morphogen ([1], eq. (5)).

In order to derive the time evolution of the compartmental division of the field in analytic form we have imposed an artificial separation of the whole process in discrete steps. Firstly, we considered the establishment of global morphogen Σ (from the already existing gradient S) and at a second stage we calculated the approach towards equilibrium distributions P_0, P_1 and P_2. It would be more realistic if both processes were simultaneously taken into account. In that case, however, we could evaluate the distributions only numerically. In fig. 4, P_1 is plotted as a sample from eqs. (22) for different time intervals.

Consider now that L is a variable quantity. For any finite time, as in fig. 4 a, b, c and d, we note that the distributions are not size-independent since they depend on both x and L. In contrast, the asymptotic curve e depends on a single variable x/L, according to eq. (24), and is therefore manifestly scale invariant.

Although eq. (24) is independent of the scaling function $\alpha(L)$, this is not true for intermediate distributions as is seen from eqs. (22). Consequently, $\alpha(L)$ affects the time course towards equilibrium.

Our compartmentalization is based on an economical assumption for allosteric protein P: Each active state of P initiates a distinct pathway of molecular differentiation. To our knowledge such a specific enzymatic function has not been observed. This does not invalidate the model to the least, since we can introduce a set of enzymes each one with a characteristic active state. It is easy then to obtain a coincidence of these active state distributions with $P_0, P_1, \ldots$ of ([1], 9). Specific molecular differentiation is localized to that area of the field where the active state of the corresponding enzyme is dominant.

Appendix

Solution of eq. (2) when S is a power function

In section 2 we solved exactly eq. (5) when the source term is linear in x. In a straightforward generalization of the method used there, we can derive the solution of eq. (2) when the S-term is proportional to a power of x.

Consider the equation:

$$\partial\Sigma(x,t)/\partial t = D\,\partial^2\Sigma(x,t)/\partial x^2 + cx^\nu - k_2\Sigma(x,t), \tag{A.1}$$

where D, c, k_2 are constants and ν is a positive integer. We impose again the conditions (6) and (7). If we define $v(x,p)$ as the Laplace transform of $\Sigma(x,t)$, eq. (A.1) becomes:

$$d^2v/dx^2 - (p+k_2)v/D + cx^\nu/Dp = 0. \tag{A.2}$$

If ν = odd, the solution of (A.2) is

$$v_{\text{odd}}(x,p) = C_1\exp\left(\sqrt{\frac{p+k_2}{D}}\,x\right) + C_2\exp\left(-\sqrt{\frac{p+k_2}{D}}\,x\right) + \frac{c}{p(p+k_2)}\left[x^\nu + \frac{\nu(\nu-1)D}{(p+k_2)}x^{\nu-2} + \ldots + \frac{\nu(\nu-1)\ldots 1D^{(\nu-1)/2}}{(p+k_2)^{(\nu-1)/2}}x\right], \tag{A.3}$$

where the constants C_1 and C_2 are:

$$C_1 = c\sqrt{D}\left\{p(p+k_2)^{3/2}\left[\exp\left(\sqrt{\frac{p+k_2}{D}}\,L\right) - \exp\left(-\sqrt{\frac{p+k_2}{D}}\,L\right)\right]\right\}^{-1} \times \left\{\frac{\nu!}{(p+k_2)^{(\nu-1)/2}}\exp\left(-\sqrt{\frac{p+k_2}{D}}\,L\right)D^{(\nu-1)/2} - \left[\nu L^{\nu-1} + \frac{\nu(\nu-1)(\nu-2)DL^{\nu-3}}{(p+k_2)} + \ldots + \frac{\nu(\nu-1)\ldots 1D^{(\nu-1)/2}}{(p+k_2)^{(\nu-1)/2}}\right]\right\}$$

$$C_2 = c\sqrt{D}\left\{p(p+k_2)^{3/2}\left[\exp\left(\sqrt{\frac{p+k_2}{D}}\,L\right) - \exp\left(-\sqrt{\frac{p+k_2}{D}}\,L\right)\right]\right\}^{-1} \times \left\{\frac{\nu!}{(p+k_2)^{(\nu-1)/2}}\exp\left(\sqrt{\frac{p+k_2}{D}}\,L\right)D^{(\nu-1)/2} - \left[\nu L^{\nu-1} + \frac{\nu(\nu-1)(\nu-2)DL^{\nu-3}}{(p+k_2)} + \ldots + \frac{\nu(\nu-1)\ldots 1D^{(\nu-1)/2}}{(p+k_2)^{(\nu-1)/2}}\right]\right\}. \tag{A.4}$$

If ν = even, the solution of (A.2) is

$$v_{\text{even}}(x,p) = -c\sqrt{D}\left\{p(p+k_2)^{3/2}\left[\exp\left(\sqrt{\frac{p+k_2}{D}}\,L\right) - \exp\left(-\sqrt{\frac{p+k_2}{D}}\,L\right)\right]\right\}^{-1} \times \left(\nu L^{\nu-1} + \frac{\nu(\nu-1)(\nu-2)DL^{\nu-3}}{(p+k_2)} + \ldots + \frac{\nu(\nu-1)\ldots 2D^{(\nu-2)/2}L}{(p+k_2)^{(\nu-2)/2}}\right)\left[\exp\left(\sqrt{\frac{p+k_2}{D}}\,x\right) + \exp\left(-\sqrt{\frac{p+k_2}{D}}\,x\right)\right] + \frac{c}{p(p+k_2)}x^\nu + \frac{\nu(\nu-1)Dc}{p(p+k_2)^2}x^{\nu-2} + \ldots + \frac{\nu(\nu-1)\ldots 1D^{\nu+2}c}{p(p+k_2)^{\nu+2}}. \tag{A.5}$$

In order to determine the asymptotic (equilibrium) concentration $\Sigma_{\text{asympt}}(x)$ it suffices to evaluate the residue of $v(x,p)$ at $p=0$. In terms of the dimensionless parameter ω of eq. (16) we obtain

$$\Sigma^{\text{odd}}_{\text{asympt}}(x) = \frac{cL}{k_2\omega(e^{\omega} - e^{-\omega})}\left\{\frac{v!L^{v-1}[e^{\omega(x-L)/L} + e^{-\omega(x-L)/L}]}{\omega^{v-1}} - \left[vL^{v-1} + \frac{v(v-1)(v-2)L^{v-1}}{\omega^2}\right.\right.$$

$$\left.\left. + \ldots + \frac{v(v-1)\ldots 1L^{v-1}}{\omega^{v-1}}\right](e^{\omega x/L} + e^{-\omega x/L})\right\} + \frac{c}{k_2}\left\{x^v + \frac{v(v-1)x^{v-2}L^2}{\omega^2} + \ldots + \frac{v(v-1)\ldots 1xL^{v-1}}{\omega^{v-1}}\right\} \tag{A.6}$$

for v = odd.

If v = even, the asymptotic function $\Sigma^{\text{even}}_{\text{asympt}}(x)$ is

$$\Sigma^{\text{even}}_{\text{asympt}}(x) = \frac{-cL}{k_2\omega(e^{\omega} - e^{-\omega})}\left\{vL^{v-1} + \ldots + \frac{v(v-1)\ldots 1L^{v-1}}{\omega^{v-2}}\right\}(e^{\omega x/L} + e^{-\omega x/L})$$

$$+ \frac{c}{k_2}\left\{x^v + \frac{v(v-1)x^{v-2}L^2}{\omega^2} + \ldots + \frac{v(v-1)\ldots 1L^v}{\omega^v}\right\}. \tag{A.7}$$

The exact asymptotic forms (A.6) and (A.7) can be expressed in terms of power series of ω. If the positive parameter ω is close to zero, approximate expressions for $\Sigma_{\text{asympt}}(x)$ can be found by neglecting all but the lowest order term in the ω expansion. We find finally the global expression for Σ when $\omega \to 0$ and for v being odd or even:

$$\Sigma_{\text{asympt}}(x) = cL^v/(v+1)k_2. \tag{A.8}$$

References

[1] S. Papageorgiou, Biophys. Chem. 11 (1980) 183.
[2] A. Gierer and H. Meinhardt, Kybernetik 12 (1972) 30.
[3] H.S. Carslaw and J.C. Jaeger, Conduction of heat in solids (Clarendon Press, Oxford, 1959, second edition).
[4] R.V. Churchill, Operational mathematics (McGraw Hill, N.Y. 1958, second edition).
[5] F.H.C. Crick, Nature 225 (1970) 420.
[6] L. Wolpert, Current topics in Developmental Biology 6 (1971) 183.