Kinetics of Biopolymerization on Nucleic Acid Templates

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Synopsis

The kinetics of biopolymerization on nucleic acid templates is discussed. The model introduced allows for the simultaneous synthesis of several chains, of a given type, on a common template, e.g., the polyribosome situation. Each growth center [growing chain end plus enzyme(s)] moves one template site at a time, but blocks L adjacent sites. Solutions are found for the probability $n_j(t)$ that a template has a growing center that occupies the sites $j - L + 1, \ldots, j$ at time t. Two special sets of solutions are considered, the uniform-density solutions, for which $n_j(t) = n$, and the more general steady-state solutions, for which $dn_j(t)/dt = 0$. In the uniform-density case, there is an upper bound to the range of rates of polymerization that can occur. Corresponding to this maximum rate, there is one uniform solution. For a polymerization rate less than this maximum, there are two uniform solutions that give the same rate. In the steady-state case, only $L = 1$ is discussed. For a steady-state polymerization rate less than the maximum uniform-density rate, the steady-state solutions consist of either one or two regions of nearly uniform density, with the density value(s) assumed in the uniform region(s) being either or both of the uniform-density solutions corresponding to that polymerization rate. For a steady-state polymerization rate equal to or slightly larger than the maximum uniform-density rate, the steady-state solutions are nearly uniform to the single uniform-density solution for the maximum rate. The boundary conditions (rate of initiation and rate of release of completed chains from the template) govern the choice among the possible solutions, i.e., determine the region(s) of uniformity and the value(s) assumed in the uniform region(s).

INTRODUCTION

The syntheses of DNA and RNA on DNA templates, being catalyzed by exoenzymes, both have the property of progressing sequentially along their templates by the addition of monomers only. Similarly, protein synthesis is known to proceed sequentially from one end of a m-RNA template.[1] In the case where only one polymer chain is permitted to grow on a given template at a given time, but in which allowance is made for a possible back reaction (depolymerization), such a polymerization may be viewed as the diffusion of a single point "growing center" along a one-dimensional lattice. In a treatment of the kinetics of this case by Pipkin and Gibbs,[2] hereinafter referred to as Part I, an ensemble of systems was introduced, with each system consisting of a one-dimensional lattice of K sites and a single point (chain end) diffusing (polymerizing) on the lattice. $N_j(t)$ is the fraction of systems in which the diffusing point has reached lattice site j, i.e., in which the polymerization has proceeded to degree j with K the highest degree of polymerization (effective template length) allowed. When not too near equilibrium, the main effect of allowing for a back reaction is equivalent to the use, in a treatment ignoring the back reaction, of a somewhat lowered (effective) forward reaction rate. When the back-reaction rate is strictly negligible,[3,4] the solution for $N_j(t)$ reduces to a Poisson distribution, $N_j(t) = e^{-t}t^{j-1}/(j-1)!$ for all states except $j = K$.[3] For the more general results of allowance for the back reaction, the reader is referred to Part I, which, however, is not prerequisite to the following.

In order to incorporate some additional features known about certain biopolymerizations on nucleic acid templates, we now extend the model of Part I to a model analogous to the diffusion of several (or many) non-overlapping segments on each one-dimensional lattice. The price to be paid for this generalization is restriction of this discussion to two special types of solutions, uniform-density and steady-state solutions.

Electron micrographs and ultracentrifugation studies of appropriately radioactively labeled systems both indicate that more than one protein of a given type can be simultaneously synthesized on a m-RNA template (the polyribosome situation).[5] Experimental results also suggest that the same may be true for the synthesis of RNA on a DNA template.[6] In a discussion of such multiple synthesis on a given template one must consider the possibility of one growing chain end blocking the motion of another. In order to derive the effect of this blocking, it is necessary to know how many sites are occupied by a growing center. Although the growing chain probably occupies only one site at a time,[1] the enzyme catalyzing the polymerization is large compared to the distance between sites and can block more than one site. Ribosomes are particularly large. Thus, the polymerization should be viewed as the motion along a template of a growing center consisting of both the growing chain end and large enzyme (ribosome). The growing center moves one site at a time, but occupies L adjacent lattice sites (for ribosomes experimental evidence[7] indicates that $L = 27$). The process described is therefore analogous to the diffusion, in steps of single lattice site spacings, of segments occupying L adjacent lattice sites on a one-dimensional lattice. More than one segment is allowed on a lattice, as long as no segments overlap. Each system in the ensemble is thus comprised of a lattice plus the several segments diffusing on it.

GENERAL INFORMATION

The sites of each lattice are numbered 1, 2, . . ., K from beginning to end. If the number of adjacent sites covered by a segment is designated as L, the number of states available to each lattice site is $L + 1$ (i.e., L modes of occupation and one of emptiness). We designate a lattice site j as being in state 0 if it is empty, and in state s (where $s = 1, 2, \ldots, L$) if it is the sth site covered by the segment, i.e., if the sites occupied by the segment are $j - s + 1, \ldots, j - s + L$. For $s = 0, \ldots, L$, let $n_j^{(s)}(t)$ be the fraction of systems in the ensemble with site j in state s at time t.

Since the sum of these $L + 1$ probabilities for a given site must be unity, we have

$$\sum_{s=0}^{L} n_j^{(s)}(t) = 1 \tag{1}$$

From the definition of states, we have

$$n_j^{(s)}(t) = n_{j-s+L}^{(L)}(t) \tag{2}$$

for $s = 1, \ldots, L$. Combining eqs. (1) and (2) gives

$$n_j^{(0)}(t) = 1 - \sum_{s=1}^{L} n_j^{(s)}(t) = 1 - \sum_{s=1}^{L} n_{j-s+L}^{(L)}(t) = 1 - \sum_{s=1}^{L} n_{j+s-1}^{(L)}(t) \tag{3}$$

We can thus calculate $n_j^{(s)}(t)$ for all s in terms of the $n_i^{(L)}(t)$. Since the segment must move as a unit, we can examine its motion by considering only the motion of the end of the segment. We define $q_j(t)$ to be the flux of occupancy of type L from site j to site $j + 1$.

Now, conservation requires that

$$\frac{d}{dt} n_j^{(L)}(t) = q_{j-1}(t) - q_j(t) \tag{4}$$

In the most general case, the segment may move either forward or backward along the lattice. We may write

$$q_j(t) = q_j^{(f)}(t) - q_j^{(b)}(t) \tag{5}$$

where $q_j^{(f)}(t)$ is the forward flux from site j to $j + 1$ and $q_j^{(b)}(t)$ is the backward flux from site $j + 1$ to j.

In order to have forward flux of state L from site j to $j + 1$, we must have site j in state L and site $j + 1$ in state 0. Therefore

$$q_j^{(f)}(t) = k_f n_j^{(L)}(t) f_{j+1}(t)$$

where k_f is the forward rate constant and $f_{j+1}(t)$ is the conditional probability that site $j + 1$ is in state 0 at time t, given that site j is in state L at time t.

Without making any further assumptions, we do not have enough information to calculate $f_{j+1}(t)$. However, we can calculate $F_{j+1}(t)$, where $F_{j+1}(t)$ is the conditional probability that site $j + 1$ is in state 0 at time t, given that site j is in either state L or state 0 at time t. Since

$$n_j^{(0)}(t) + n_j^{(L)}(t) = n_{j+1}^{(0)}(t) + n_{j+1}^{(1)}(t)$$

from eqs. (1) and (2), $F_{j+1}(t)$ is also the probability that site $j + 1$ is in state 0 at time t, given that site $j + 1$ is in state 0 or 1. $F_{j+1}(t)$ can then be easily calculated,

$$F_{j+1}(t) = n_{j+1}^{(0)}/(n_{j+1}^{(0)} + n_{j+1}^{(1)})$$

or, from eqs. (2) and (3), we have

$$F_{j+1}(t) = \frac{1 - \sum_{s=1}^{L} n_{j+s}^{(L)}(t)}{1 - \sum_{s=1}^{L} n_{j+s}^{(L)}(t) + n_{j+L}^{(L)}(t)} \tag{6}$$

We assume

$$f_{j+1}(t) = F_{j+1}(t)$$

This is equivalent to the assumption that the conditional probability that site $j + 1$ is in state 0, given that site j is in state L, equals the conditional probability that $j + 1$ is in state 0, given that j is in state 0. We now have

$$q_j^{(f)}(t) = k_f \frac{n_j^{(L)}(t)[1 - \sum_{s=1}^{L} n_{j+s}^{(L)}(t)]}{1 - \sum_{s=1}^{L} n_{j+s}^{(L)}(t) + n_{j+L}^{(L)}(t)} \tag{7}$$

In order to have backward flux from site $j + 1$ to site j, we must have site $j + 1$ in state L and site $j - L + 1$ in state 0. The assumption used in calculating $q_j^{(f)}(t)$ gives also

$$\begin{aligned} q_j^{(b)}(t) &= k_b \frac{n_{j+1}^{(L)}(t) n_{j-L+1}^{(0)}(t)}{n_{j-L+1}^{(0)}(t) + n_{j-L+1}^{(L)}(t)} \\ &= k_b \frac{n_{j+1}^{(L)}(t)[1 - \sum_{s=1}^{L} n_{j-L+s}^{(L)}(t)]}{1 - \sum_{s=1}^{L} n_{j-L+s}^{(L)}(t) + n_{j-L+1}^{(L)}(t)} \end{aligned} \tag{8}$$

where k_b is the backward rate constant, $k_b < k_f$.

Since all equations can be written in terms of $n_j^{(L)}(t)$ only, we now drop the superscript L and let $n_j^{(L)}(t) = n_j(t)$. In this notation, we can write

$$q_j(t) = k_f \frac{n_j(t)[1 - \sum_{s=1}^{L} n_{j+s}(t)]}{1 - \sum_{s=1}^{L} n_{j+s}(t) + n_{j+L}(t)} - k_b \frac{n_{j+1}(t)[1 - \sum_{s=1}^{L} n_{j-L+s}(t)]}{1 - \sum_{s=1}^{L} n_{j-L+s}(t) + n_{j-L+1}(t)} \tag{9}$$

The flux equation, eq. (9), holds true for values of j such that $2L - 1 \leq j \leq K - L$. At the ends it must be modified to incorporate the special boundary conditions.

We now examine two special sets of solutions of eq. (9), the uniform-density solutions for which $n_j(t) = n(t)$ and the steady-state solutions for which $dn_j(t)/dt = 0$.

UNIFORM-DENSITY SOLUTIONS

If $n_j(t) = n(t)$ for all j, we see from eq. (9) that $q_j(t) = q(t)$ for all j. Substitution of this into eq. (4) gives $n(t) = n$, and hence $q(t) = q$ from eq. (9). The flux equation, eq. (9), then becomes

$$q = (k_f - k_b)n(1 - Ln)/[1 - (L - 1)n] \tag{10}$$

The net effect of allowing the back reaction has been to give an effective forward rate constant of $(k_f - k_b)$.

It is convenient to define new variables, $Q = Lq/(k_f - k_b)$ and $N = Ln$. With this notation, eq. (10) becomes

$$Q = N(1 - N)/[1 - N + N/L] \tag{11}$$

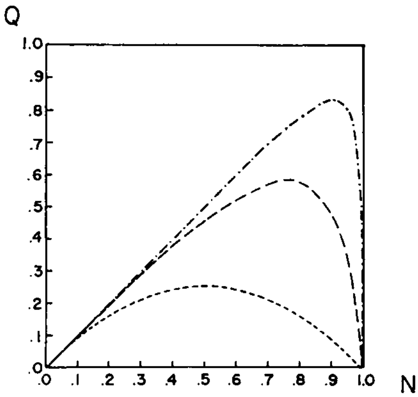


Fig. 1. The flux as a function of the occupation density. $Q = N(1 - N)/\{1 - [1 - (1/L)]N\}$, with $Q = L/(k_f - k_b) \times$ flux of segment end, $N = L \times$ occupation density of segment end.

The maximum value of Q occurs when $N_{\max} = \sqrt{L}/(1 + \sqrt{L})$ and has the value $Q_{\max} = N_{\max}{}^2$. The maximum flux, $q_{\max}$, is correspondingly $(k_f - k_b)Ln_{\max}{}^2$, where $n_{\max} = 1/\sqrt{L}(1 + \sqrt{L})$. Given a Q such that $Q < Q_{\max}$, there are two solutions with "flux" Q, a low-density solution $N < N_{\max}$ and a high-density solution, $(1 - N)/(1 - N + N/L)$. In terms of q and n, the latter solutions are $n(<n_{\max})$ and $(1 - Ln)/L[1 - (L - 1)n]$.

When $(1 - N)/N \gg 1/L$, the Q–N curve is closely approximated by the tangent to the curve at $N = 0$, i.e., $Q = N$. When $(1 - N)/N \ll 1/L$, the curve is closely approximated by the tangent at $N = 1$, i.e., $Q = L(1 - N)$. The Q–N curves for $L = 1$, 10, and 100 are shown in Figure 1.

STEADY-STATE SOLUTIONS

If $dn_j(t)/dt = 0$ for all j, then eq. (4) gives $q_j(t) = q(t)$, and eq. (9) gives $q(t) = q$. The flux equation, eq. (9), in this case is

$$q = k_f \frac{n_j(1 - \sum_{s=1}^{L} n_{j+s})}{1 - \sum_{s=1}^{L} n_{j+s} + n_{j+L}} - k_b \frac{n_{j+1}\,(1 - \sum_{s=1}^{L} n_{j-L+s})}{1 - \sum_{s=1}^{L} n_{j-L+s} + n_{j-L+1}} \tag{12}$$

General Behavior of Solutions for $L = 1$

In the special case $L = 1$, the flux equation, eq. (12), takes a particularly simple form:

$$q = k_f n_j(1 - n_{j+1}) - k_b n_{j+1}(1 - n_j)$$
$$j = 1, \ldots, K - 1 \qquad (13)$$

When $n_j \equiv n$, we have the uniform solutions described in the preceding section. The maximum flux,

$$q_{\max} = {}^1/_4(k_f - k_b) \qquad (14)$$

occurs when $n_j \equiv n = {}^1/_2$. Given that $0 \leq q < q_{\max}$, there are two solutions, $n_j \equiv n$ and $n_j \equiv 1 - n$, that give the same flux,

$$q = (k_f - k_b)n(1 - n) \qquad (15)$$

We now consider the general steady-state case. Equation (15) is preserved as the definition of n for this case. When $q = q_{\max}$, we have $n = {}^1/_2$. We will find below that, in this case, all steady-state solutions will approach the uniform solution $n_j = n = {}^1/_2$. When $0 \leq q < q_{\max}$, all steady-state

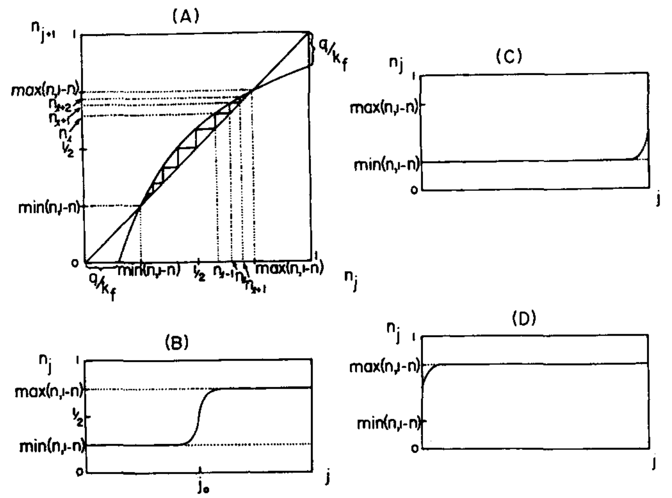


Fig. 2. Three of the five main classes of solutions of the flux equation with $(k_f - k_b)n \times (1 - n) = q < q_{\max} = {}^1/_4(k_f - k_b)$: ($A$) the graphical solution for $n_1 + n_K \simeq 1$, the analytical solution, $n_j = n + \{(1 - 2n)/1 + [f(n)]^{j-j_0}\}$, $0 \leq n \leq 1$; (B) the solution for $1 \ll j_0 \ll K$, which corresponds to the case in Fig. 2A; (C) the solution for $j_0 \simeq K$; (D) the solution for $j_0 \simeq 1$. The results are summarized in Table I. The other main cases are shown in Fig. 3.

solutions will either approach one of the two uniform solutions, n and $1 - n$, or approach a composite of both. When $q > q_{\max}$, i.e., when the steady-state flux is larger than the maximum flux allowed for the uniform-density case, the solution of the quadratic equation (15) for n is a complex number with $Re(n) = {}^1/_2$. In this case the solutions will approach the uniform solution $n = {}^1/_2$, provided the lattice is of proper length.

This nearly uniform behavior of the solutions can be seen easily by both analytical and graphical (Fig. 2A) methods. We first consider analytical solutions. Further detail is given in Appendix A.

When $q \neq q_{max}$, the solution of eq. (13) can be seen by substitution to be

$$n_j = n + \frac{1 - 2n}{1 + C'[f(n)]^j}, \qquad j = 1, \ldots, K \tag{16}$$

with

$$f(n) = \frac{n + b(1 - n)}{1 - n + bn}$$

$$b = k_b/k_f \tag{17}$$

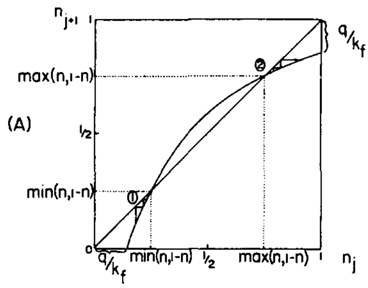
and with C' a constant (independent of j). This expression is derived in Appendix A. It includes several different cases which we discuss in turn.

When $0 \leq q < q_{max}$, solving eq. (15) for n gives n real, $0 \leq n \leq 1$, but $n \neq {}^1/_2$. In the limiting case, $C' = \pm\infty$, we have the uniform solution $n_j \equiv n$; in the case $C' = 0$, we have the uniform solution $n_j \equiv 1 - n$. Except for a limited range of values of j, all solutions are nearly uniform. To see this, let $C' = \pm[f(n)]^{-j_0}$ in eq. (16). Then eq. (16) gives n_j near to $\max(n, 1 - n)$ when $j - j_0 \gg 0$ and n_j near to $\min(n, 1 - n)$ when $j - j_0 \ll 0$.

If $C' > 0$, j_0 may assume any real value. The graphs of the possible solutions for $C' > 0$ are shown in Figures 2B–2D, and the results are summarized in Table I.

TABLE I
General Behavior of the Solution $n_j = n + \{(1 - 2n)/1 + [f(n)]^{j-j_0}\}$, with $0 \leq n \leq 1$, $(k_f - k_b)n(1 - n) = q < q_{max} = {}^1/_4(k_f - k_b)$

Value of j_0	Relationship of $(n_1 + n_K)$ and 1	Relationship of n_1, n_K, and ${}^1/_2$	Value(s) assumed by n_j in uniform region(s)
$j_0 \ll 1$	$n_1 + n_K > 1$	${}^1/_2 \leq n_1 \simeq n_K$	$n_j \simeq \max(n, 1 - n)$ for all j
$j_0 \simeq 1$	$n_1 + n_K > 1$	${}^1/_2 < n_K$	$n_j \simeq \max(n, 1 - n)$ for large j
$1 \ll j_0 \ll K$	$n_1 + n_K \simeq 1$	$n_1 \leq {}^1/_2 \leq n_K$	$n_j \simeq \max(n, 1 - n)$ for large j; $n_j \simeq \min(n, 1 - n)$ for small j
$j_0 \simeq K$	$n_1 + n_K < 1$	$n_1 \leq {}^1/_2$	$n_j \simeq \min(n, 1 - n)$ for small j
$j_0 \gg K$	$n_1 + n_K < 1$	$n_1 \simeq n_K \leq {}^1/_2$	$n_j \simeq \min(n, 1 - n)$ for small j



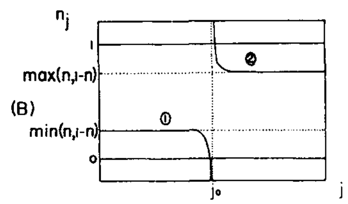


Fig. 3. Two of the five main classes of solutions of the flux equation with $q < q_{\max}$: (A) the two graphical solutions; (B) the analytical solution, $n_j = n + \{(1 - 2n)/1 - [f(n)]^{j-j_0}\}$, $0 \leq n \leq 1$. Curve *1* is the solution for $j_0 > K + 1 + \epsilon$; curve *2* for $j_0 < -\epsilon$, with $\epsilon = \{\ln [n/(1 - n)]/\ln [f(n)]\} - 1$. The results are summarized in Table II. The solutions for $q = q_{\max}$ can be obtained as a special limiting case of these solutions.

If $C' < 0$, j_0 must lie outside the lattice. In Appendix A we will show that for this case we must have $j_0 < -\epsilon$ or $j_0 > K + 1 + \epsilon$, where

$$\epsilon = \{\ln [n/(1 - n)]/\ln f(n)\} - 1$$

The graphs of the solutions for $C' < 0$ are shown in Figure 3B, and the results are summarized in Table II.

TABLE II
General Behavior of the Solution $n_j = n + \{(1 - 2n)/1 - [f(n)]^{j-j_0}\}$, with $0 \leq n \leq 1$, $q < q_{\max}$

Value of j_0[a]	Relationship of $(n_1 + n_K)$ and 1	Relationship of n_1, n_K, and $1/2$	Value assumed by n_j in uniform region
$j_0 \ll -\epsilon$	$n_1 + n_K > 1$	$1/2 \leq n_K \simeq n_1$	$n_j \simeq \max(n, 1 - n)$ for all j
$j_0 \lesssim -\epsilon$	$n_1 + n_K > 1$	$1/2 \leq n_K$	$n_j \simeq \max(n, 1 - n)$ for large j
$-\epsilon \leq j_0 \leq K + 1 + \epsilon$		Not allowed	
$j_0 \gtrsim K + 1 + \epsilon$	$n_1 + n_K < 1$	$n_1 \leq 1/2$	$n_j \simeq \min(n, 1 - n)$ for small j
$j_0 \gg K + 1 + \epsilon$	$n_1 + n_K < 1$	$n_K \simeq n_1 \leq 1/2$	$n_j \simeq \min(n, 1 - n)$ for all j

[a] $\epsilon = \{\ln [n/(1 - n)]/\ln [f(n)]\} - 1$. The solutions for $q = q_{\max}$ can be obtained as a special limiting case by letting $n = 1/2$ and $\epsilon = [(1 + b)/(1 - b)] - 1$.

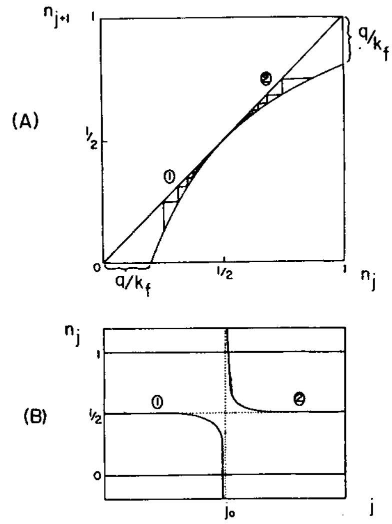


Fig. 4. The two main classes of solutions of the flux equation with $q = {}^1/_4(k_f - k_b) = q_{\max}$: (*A*) the two graphical solutions; (*B*) the analytical solution, $n_j = {}^1/_2[(k_f + k_b)/(k_f - k_b)]\{1/[2(j - j_0)]\}$; curve *1* is the solution for $j_0 > K + 1$; curve *2*, for $j_0 < 0$.

The case $q = q_{\max}$ can be obtained directly from eq. (13) or as a special limiting case of $q < q_{\max}$. The solution of eq. (13) in this case can be seen by substitution to be

$$n_j = \frac{1}{2} + \frac{k_f + k_b}{k_f - k_b} \frac{1}{(2j + C)} \qquad j = 1, \ldots, K \tag{18}$$

This expression is also derived in Appendix A. In the limiting case $C = \pm\infty$, we have the uniform solution $n_j = {}^1/_2$. All solutions are nearly uniform except for a limiting range of values of j. To see this, let $C = -2_{j_0}$ in eq. (18); n_j is close to ${}^1/_2$ except when j is near j_0. As in the case $q < q_{\max}$, $C' < 0$, j_0 must lie outside the lattice. In Appendix A we will show that we must have for this case $j_0 < 1 - [(1 + b)/(1 - b)]$ or $j_0 > K + [(1 + b)/(1 - b)]$. The graphs of the solutions for this case are shown in Figure 3*B*, and a summary of the results can be obtained from Table II as the special limiting case with $n = {}^1/_2$ and $\epsilon = [(1 + b)/(1 - b)] - 1$.

When $q > q_{\max}$, n is complex with $Re(n) = {}^1/_2$. However, if C' is complex, but $||C'|| = 1$, the solution, eq. (16), is real. The solution is nearly uniform to ${}^1/_2$ for a lattice of proper length. We will show in Appendix A that the maximum value of K that will permit this type of solution ($q > q_{\max}$) depends on the proximity of q to $q_{\max}$. In the limit as $q \to q_{\max}$, K and $q - q_{\max}$ are related by

$$\left(\frac{q - q_{\max}}{k_f - k_b}\right)^{1/2} < \frac{\pi}{2} \frac{k_f + k_b}{k_f - k_b} \frac{1}{K} \tag{19}$$

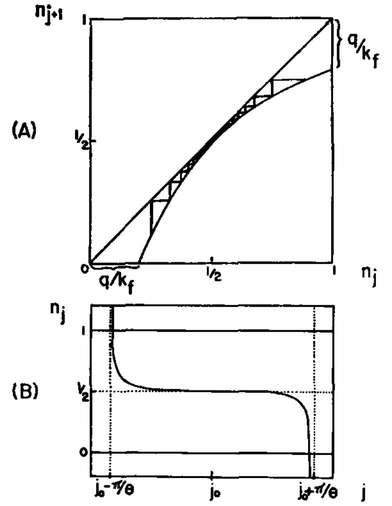


Fig. 5. Solution of the flux equation with $q = (k_f - k_b)(^1/_4 + \eta^2) > q_{max}, \eta > 0$; (A) the graphical solution; (B) one period of the periodic analytical solution, $n_j = n + \{(1 - 2n)/1 + [f(n)]^{j-j_0}\}, n = {^1/_2} + i\eta$.

The behavior of the solutions can also be seen by representing the flux equation graphically, as in Figures 2A, 3A, 4A, and 5A. Graphing eq. (13) with n_j as the abscissa and n_{j+1} as the ordinate gives a hyperbola symmetric along the axis $n_j + n_{j+1} = 1$. As a reference, we also graph the straight line $n_j = n_{j+1}$. For $0 \leq q < q_{max}$, the reference line intersects the hyperbola at two points, $n_j = n$ and $n_j = 1 - n$. When $q = q_{max}$, the line is tangent to the hyperbola at one point, $n_j = n_{j+1} = {^1/_2}$. If $q > q_{max}$, there is no intersection. The values of n_j can be read off the abscissa of each figure by following the stair-step diagram.

The detailed solution for $L = 1$ is given in Appendix A.

General Boundary Conditions for $L = 1$

In the preceding section and in Appendix A, all possible steady-state solution curves have been exhibited. In any particular case the boundary conditions dictate the choice among these curves (or sections thereof) which represents the appropriate solution. For boundary conditions we need equations describing the initiation and release steps. We assume that these two steps can be described by the same general mathematical form as the flux within the interior of the lattice. For the initiation, there should be a forward flux on to site 1 of the lattice proportional to the probability that site 1 is empty and a backward flux off the lattice proportional to the probability that site 1 is occupied. The rate constants for these do not need to be the same as the forward and backward rate constants in the interior, k_f and k_b. For release from the lattice, there is a forward flux off site K of the lattice proportional to the probability that site K is occupied and a flux back on to the lattice proportional to the probability that site K is empty.

The rate constants for these may be different from both the interior rate constants and the initiation rate constants. Because we are dealing here with the steady-state case, the net flux onto lattice site 1 and off lattice site K will be the same as the flux in the interior. The boundary conditions can be written as

$$q_0 = q = k_f\alpha(1 - n_1) - k_b\alpha' n_1 \tag{20a}$$

$$q_K = q = k_f\beta n_K - k_b\beta'(1 - n_K) \tag{20b}$$

where q is given by eq. (15). For initiation, the effective forward and backward rate constants are $k_f\alpha$ and $k_b\alpha'$, respectively; for release, $k_f\beta$ and $k_b\beta'$.

Given a particular set of values for α, α', β, and β', we can use eqs. (20) to calculate n_1 and n_K. After we know n_1 and n_K, we make the proper choice of solution curve by referring to the previous results.

Example, $L = 1$

As an illustration we consider the special case in which $\alpha' = \beta' = 0$. This corresponds to irreversibility of both initiation and release steps. In this case, the boundary conditions are

$$(1 - b)n(1 - n) = \alpha(1 - n_1) = \beta n_K \tag{21}$$

A detailed discussion is given in Appendix B of solutions valid in the limit of large K. The appropriate solution curve is determined by the relationship of α, β, and $^1/_2(1 - b)$.

If $\alpha < \beta$ and $\alpha < {}^1/_2(1 - b)$, the solution is the low-density solution (Fig. 2*C*) and is nearly uniform to $\alpha/(1 - b)$ except at the large j end.

If $\beta < \alpha$ and $\beta < {}^1/_2(1 - b)$, the solution is the high-density solution (Fig. 2*D*) and is nearly uniform to $1 = [\beta(/1 - b)]$ except at the small j end.

When α and β are nearly equal and also less than $^1/_2(1 - b)$, the solution is nearly uniform to $\alpha/(1 - b)$ for small j and nearly uniform to $1 - [\alpha/(1 - b)]$ for large j, with a transition from the low density solution to the high density solution in the interior (Fig. 2*B*).

If $\alpha > {}^1/_2(1 - b)$ and $\beta > {}^1/_2(1 - b)$, the solution is nearly uniform to $^1/_2$ except for very small j and for very large j (Fig. 5*B*).

In each case, the flux is given by

$$q = (k_f - k_b)m(1 - m) \tag{22}$$

with

$$m = \min\left(\frac{\alpha}{1 - b}, \frac{\beta}{1 - b}, \frac{1}{2}\right) \tag{23}$$

Solutions for $L > 1$

For $L > 1$, the flux equation, eq. (12), cannot be solved readily by analytical methods. It is, however, being treated by numerical methods with a computer. Steady-state solutions for $L > 1$, analogous to the various solutions for $L = 1$, can be obtained. The nearly uniform high-density region observed at large j for some solutions in the case of $L = 1$ is replaced in the case $L > 1$ by a region of oscillation around the appropriate uniform-density root. This oscillation is a consequence of our assumption that, irrespective of the large size of the growing center, the enzyme (ribosome) and newly synthesized polymer leave the template in one step when the growing chain end reaches template site K.

Meaningful application of the considerations of this paper to experimental data must await completion of the numerical calculations for $L > 1$ (particularly $L = 27$) and probably also furtherance of experimental investigations.

APPENDIX A

Detailed Solution for $L = 1$

In the case $L = 1$, the flux equation is

$$q = k_f n_j(1 - n_{j+1}) - k_b n_{j+1}(1 - n_j) \qquad j = 1, \ldots, K - 1 \tag{A-1}$$

where

$$q = (k_f - k_b)n(1 - n) \tag{A-2}$$

Substituting eq. (A-2) into eq. (A-1) gives

$$(k_f - k_b)n(1 - n) = k_f n_j(1 - n_{j+1}) - k_b n_{j+1}(1 - n_j) \qquad j = 1, \ldots, K - 1 \tag{A-3}$$

The substitution

$$n_j = [(u_{j+1})/(u_j)] + b/(b - 1) \tag{A-4}$$

with

$$b = k_b/k_f \tag{A-5}$$

gives a linear difference equation in the u_j,

$$(b - 1)u_{j+2} + (b + 1)u_{j+1} + \left[\frac{b}{b - 1} + (b - 1)n(1 - n)\right]u_j = 0 \tag{A-6}$$

Letting $u_j = A\gamma^j$ in eq. (A-6) and then dividing by γ^j gives a quadratic equation in γ which has the roots

$$\gamma_1 = \frac{1}{2}\left(\frac{1 + b}{1 - b}\right) + \frac{1}{2}(2n - 1) \tag{A-7a}$$

$$\gamma_2 = \frac{1}{2}\left(\frac{1 + b}{1 - b}\right) - \frac{1}{2}(2n - 1) \tag{A-7b}$$

If $q = q_{max}$, we have $n = {}^1/_2$, and eqs. (A-7) represent a double root,

$$\gamma = \frac{1}{2}\left(\frac{1+b}{1-b}\right) \tag{A-8}$$

In this case a general solution to eq. (A-6) is

$$u_j = A\gamma^j(1 + Dj) \tag{A-9}$$

Substitution of eqs. (A-9) and (A-8) into eq. (A-4) gives

$$n_j = \frac{1}{2} + \left(\frac{1+b}{1-b}\right)\frac{1}{2j+C} = \frac{1}{2} + \left(\frac{k_f+k_b}{k_f-k_b}\right)\frac{1}{2j+C}$$

$$j = 1, \ldots, K \tag{A-10}$$

When $q \neq q_{max}$, we have $n \neq {}^1/_2$, and the roots, eq. (A-7), are distinct. In this case a general solution to eq. (A-6) is of course

$$u_j = A\gamma_1^j + B\gamma_2^j \tag{A-11}$$

Substitution of eqs. (A-11) and (A-7) into eq. (A-4) gives

$$n_j = n + \frac{1-2n}{1 + C'[f(n)]^j},$$

$$j = 1, \ldots, K \tag{A-12}$$

We can obtain eq. (A-10) as a special case of eq. (A-12) by the following special limiting process. Let

$$C' = -1 + [(1-b)/(1+b)]C(1-2n) \tag{A-13}$$

The substitution of eq. (A-13) into eq. (A-12) gives

$$n_j = n + \frac{1-2n}{1 - [f(n)]^j + [(1-b)/(1+b)]C(1-2n)[f(n)]^j} \tag{A-14}$$

When n is near ${}^1/_2$, we can expand $[f(n)]^j$ in powers of $(1-b)(1-2n)/$

$$(1-n+bn)\ [f(n)]^j = [1 - \frac{(1-b)(1-2n)}{1-n+bn}\ ]^j$$

$$= 1 - \frac{(1-b)(1-2n)}{1-n+bn}j + 0[(1-2n)^2] \tag{A-15}$$

Substituting eq. (A-15) into eq. (A-14) and taking the limit as $n \rightarrow {}^1/_2$ gives

$$\lim_{n\to 1/2} n_j = \lim_{n\to 1/2} \left\{ n + \frac{1-2n}{j\dfrac{(1-b)(1-2n)}{(1-n+bn)} + \left(\dfrac{1-b}{1+b}\right)C(1-2n) + 0[(1-2n)^2]} \right\}$$

$$= \lim_{n\to 1/2} \left\{ n + \frac{1-2n}{j\left(\dfrac{1-b}{1-n+bn}\right) + \left(\dfrac{1-b}{1+b}\right)C + 0[(1-2n)]} \right\}$$

$$= \frac{1}{2} + \left(\frac{1-b}{1+b}\right)\frac{1}{2j+C}$$

We now consider the behavior of the solutions in more detail. The solution eq. (A-12) satisfies the flux equation, eq. (A-3), for any n and C', including the cases in which n and C' are complex. However, because n_j must be real, $0 \leq n_j \leq 1$, for $j = 1, \ldots, K$, we shall find that there are certain restrictions on the values that n and C' can assume.

We first consider $C' \geq 0$, $C' = [f(n)]^{-j_0}$. In the limiting case $j_0 = +\infty$, we have the uniform solution $n_j \equiv \max(n, 1-n)$; and for $j_0 = -\infty$, we have $n_j \equiv \min(n, 1-n)$. By requiring that j_0 be finite and hence $C' \neq 0$, $C' \neq \infty$, we obtain the solutions that are not completely uniform. We have

$$n_j = n + (1-2n)/\{1 + [f(n)]^{j-j_0}\} \tag{A-16}$$

Since we are considering only finite j_0, we have $\min(n, 1-n) < n_j < \max(n, 1-n)$ for all j_0, and therefore $0 < n_j < 1$ for all j. For $C' > 0$, there are no restrictions on the finite values that j_0 can assume. Because $(1-2n)$ and $[1-f(n)]$ always have the same sign, we have

$$n_{j+1} - n_j = \frac{f(n)^{j-j_0}(1-2n)[1-f(n)]}{\{1+[f(n)]^{j-j_0}\}\{1+[f(n)]^{j-j_0+1}\}} > 0$$

We therefore must always have $n_1 < n_K$. Since

$$(n_{j+1} - n_j) - (n_j - n_{j-1}) = \frac{[f(n)]^{j-j_0}(1-2n)[1-f(n)]^2[f(n)^{j-j_0}-1]}{\{1+[f(n)]^{j-j_0}\}\{1+[f(n)]^{j-j_0+1}\}\{1+[f(n)]^{j-j_0-1}\}}$$

we have

$$(n_{j+1} - n_j) - (n_j - n_{j-1}) \begin{cases} > 0 & j - j_0 < 0 \\ < 0 & j - j_0 > 0 \end{cases}$$

The solution curve therefore has a first difference that is positive everywhere and a second difference that is positive for $j < j_0$ and negative for $j > j_0$.

The solution curve is shown in Figure 2. Depending on the value of j_0, we may have as our solution any of various different parts of the curve in this Figure 2 (B, C, or D).

The various possible results for $C' > 0$ are summarized in Table I.

We now consider $C' \leq 0$, $C' = -[f(n)]^{-j_0}$. If $j_0 = +\infty$, we have the uniform solution $n_j \equiv \max(n, 1 - n)$; and if $j_0 = -\infty$, we have $n_j \equiv \min(n, 1 - n)$. To obtain the solutions that are not completely uniform, we require that j_0 be finite and hence $C' \neq 0$, $C' \neq -\infty$. The solution is of the form

$$n_j = \frac{1 - 2n}{1 - [f(n)]^{j - j_0}} \tag{A-17}$$

For $j < j_0$, we have $n_j < \min(n, 1 - n)$; and for $j > j_0$, we have $n_j > \max(n, 1 - n)$. We now show that in this case where $C' < 0$ the requirement that $0 \leq n_j \leq 1$ for $j = 1, \ldots, K$ can be satisfied only if j_0 lies outside the lattice.

We first eliminate the case $q = 0$, $C' < 0$ as this means both $\min(n, 1 - n) = 0$ and $\max(n, 1 - n) = 1$, which imply that $n_j < 0$ for $j < j_0$ and $n_j > 1$ for $j > j_0$.

Substitution of the requirement $n_j < 1$ for $j = 1, \ldots, K$ into eq. (A-17) yields

$$1 > n + \frac{1 - 2n}{1 - [f(n)]^{j - j_0}} \qquad j = 1, \ldots, K \tag{A-18}$$

The solution of this inequality gives

$$K < j_0 \tag{A-19a}$$

or

$$j_0 < -\epsilon \tag{A-19b}$$

with ϵ defined by

$$\frac{n}{1 - n} = [f(n)]^{1+\epsilon} \tag{A-20a}$$

or

$$\epsilon = \{\ln [n/(1 - n)]/\ln f(n)\} - 1 \tag{A-20b}$$

For $b = 0$, we have $\epsilon = 0$; for $b \neq 0$, $\epsilon > 0$.

Since we also require $n_j > 0$, we have in addition

$$0 < n + \frac{1 - 2n}{1 - [f(n)]^{j - j_0}} \qquad j = 1, \ldots, K \tag{A-21}$$

There are two possible solutions to this inequality,

$$K + 1 + \epsilon < j_0 \tag{A-22a}$$

or

$$j_0 < 1. \tag{A-22b}$$

The combination of requirements eq. (A-19) and eq. (A-22) amounts to

$$K + 1 + \epsilon < j_0 \tag{A-23a}$$

$$j_0 < -\epsilon \tag{A-23b}$$

For both $2 \leq j \leq K < j_0 - (1 + \epsilon)$ and $j_0 + (1 + \epsilon) < 2 \leq j$, we can show that $n_j - n_{j-1} < 0$. We therefore have $n_1 > n_K$ for all allowed cases with $C' < 0$. In the first case, in which eq. (A-23a) holds, we see that the minimum value of j_0 allowed is related to K as well as n. There is no such restriction by chain length K, in the second case, in which eq. (A-23b) holds. Although both cases have solution curves with a first difference that is negative everywhere, the first case has a negative second difference and the second case a positive second difference,

$$(n_{j+1} - n_j) - (n_j - n_{j-1}) \begin{cases} <0 & 2 \leq j \leq K - 1 < j_0 - (1 + \epsilon) \\ >0 & j_0 + (1 + \epsilon) < 2 \leq j \end{cases}$$

The solution curve is illustrated in Figure 3. Depending on the value of j_0, we have part or all of the curve *1* or part or all of the curve *2*, but never a portion of both curves.

The various possible results are summarized in Table II.

In the preceding discussion we have considered $0 \leq q < q_{\max}$. We now consider the case in which $q = q_{\max}$. Here the solution is of the form

$$n_j = \frac{1}{2} + \frac{1 + b}{1 - b}\frac{1}{2j + C} \tag{A-24}$$

In the limiting case $C = \pm\infty$, we have the uniform solution $n_j = {}^1/_2$. For any C, all solutions are nearly uniform to ${}^1/_2$ except for a limited range of values of j. The solution is illustrated in Figure 4.

These results for $q = q_{\max}$ can also be obtained as a special limiting case of the results for $q < q_{\max}$. Since we made the substitution $C' = -1 + [(1 - b)/(1 + b)]C(1 - 2n)$, in the limit $n \rightarrow {}^1/_2$ we have $C' < 0$. We can find ϵ quite easily by taking the limit $n \rightarrow {}^1/_2$ in eq. (A-20b), obtaining $\epsilon = [(1 + b)/(1 - b)] - 1$.

We now consider $q > q_{\max}$. We define η, $\eta > 0$, by

$$q = (k_f - k_b)({}^1/_4 + \eta^2) = (k_f - k_b)n(1 - n) \tag{A-25a}$$

or, equivalently,

$$q/k_f = (1 - b)({}^1/_4 + \eta^2) = (1 - b)n(1 - n) \tag{A-25b}$$

The solution of eq. (A-25) is just eq. (A-12), with $n = {}^1/_2 \pm i\eta$. Although eq. (A-12) is satisfied for any complex C', we find below that $||C'||$ must equal 1 in order to satisfy the requirement that n_j be real. We choose n to be the root $n = {}^1/_2 + i\eta$. Since $n^* = {}^1/_2 - i\eta = 1 - n$, then $f({}^1/_2 + i\eta)^* = 1/f({}^1/_2 + i\eta)$, and therefore $||f({}^1/_2 + i\eta)|| = 1$. Thus f can be represented by

$$f({}^1/_2 + i\eta) = e^{i\theta} \tag{A-26}$$

In the most general case, let

$$C' = cf({}^1/_2 + i\eta)^{-j_0} = ce^{-ij_0\theta} \tag{A-27}$$

with $c = ||C|| > 0$. Substituting eqs. (A-26) and (A-27) into eq. (A-12) and separating into real and imaginary parts gives

$$n_j = \frac{{}^1/_2(1 + c^2) + c[\cos (j - j_0)\theta - 2\eta \sin (j - j_0)\theta]}{1 + c^2 + 2c \cos (j - j_0)\theta} + i\frac{\eta(c^2 - 1)}{1 + c^2 + 2c \cos (j - j_0)\theta} \tag{A-28}$$

Since n_j is real, and $c > 0$, it follows that $c = 1$. The solution thus becomes

$$n_j = {}^1/_2 - \eta \frac{\sin (j - j_0)\theta}{1 + \cos (j - j_0)\theta}. \tag{A-29}$$

The analytical solution, eq. (A-29), is periodic with period $2\pi/\theta$. The period bounded by $j_0 - \pi/\theta$ and $j_0 + \pi/\theta$ is shown in Figure 5*B*, and the results are summarized in Table III.

TABLE III
General Behavior of the Solution $n_j = n + \{(1 - 2n)/1 + [f(n)]^{j-j_0}\}$, with $n = {}^1/_2 + i\eta$, $\eta > 0$.

Value of j_0	Relationship of $(n_1, + n_K)$ and 1	Relationship of n_1, n_K, and ${}^1/_2$	Value assumed by n_j in uniform region
$j_0 \lesssim 1$	$n_1 + n_K < 1$	$n_K < n_1 \leq {}^1/_2$	$n_j \simeq {}^1/_2$ for small j
$1 < j_0 < K$	Indeterminate	$n_K < {}^1/_2 < n_1$	$n_j \simeq {}^1/_2$ for $1 \ll j \ll K$
$j_0 \gtrsim K$	$n_1 + n_K > 1$	${}^1/_2 \leq n_K < n_1$	$n_j \simeq {}^1/_2$ for large j

We now show that the physical solution is contained in only one such period. The substitution of the requirement $0 < n_j < 1$ into eq. (A-29) gives

$$\left|\frac{\eta \sin (j - j_0)\theta}{1 + \cos (j - j_0)\theta}\right| < \frac{1}{2} \tag{A-30}$$

which has the solution

$$\cos (j - j_0)\theta > (1 - 4\eta^2)/(1 + 4\eta^2) \tag{A-31}$$

The other solution of eq. (A-30), $\cos (j - j_0)\theta < -1$, must be discarded. Let ϕ be the angle such that

$$\cos \phi = (-1 + 4\eta^2)/(1 + 4\eta^2) \qquad 0 \leq \phi < \pi \tag{A-32}$$

The inequality eq. (A-31) then gives

$$-\phi < (j - j_0)\,\theta + 2m_j\,\pi < \phi, \qquad m_j \text{ an integer} \tag{A-33}$$

or, equivalently,

$$j\theta/2\pi - \phi/2\pi + m_j < j_0\theta/2\pi \tag{A-34a}$$

$$j_0\theta/2\pi < j\theta/2\pi + \phi/2\pi + m_j \tag{A-34b}$$

Letting $j = j' + 1$ in eq. (A-34a) and $j = j'$ in eq. (A-34b) gives

$$(j' + 1)\theta/2\pi - \phi/2\pi + m_{j'+1} < j'\theta/2\pi + \phi/2\pi + m_{j'} \tag{A-35}$$

Since $\theta > 0$ and $0 \leq \phi < \pi$, the inequality eq. (A-35) gives $m_{j'+1} < 1 + m_{j'}$. However, it is clear from graphing the entire solution eq. (A-29) that $m_{j'} \leq m_{j'+1}$. Therefore $m_{j'} = m_{j'+1} = m$, and all the j for $j = 1, \ldots, K$ must be contained within the same period. We choose this period to be the one corresponding to $m = 0$, which contains j_0. The inequalities in eq. (A-34) then become

$$j - \phi/\theta < j_0 < j + \phi/\theta \qquad j = 1, \ldots, K \tag{A-36}$$

which gives

$$K - \phi/\theta < j_0 < 1 + \phi/\theta \tag{A-37}$$

From (A-37), we can get an estimate of the value of η and hence the maximum flux that can be supported on a lattice of length K. From the stair-step diagram (Fig. 5*A*), it is clear that q must be very close to $q_{\max}$ when K is large, and therefore η very close to 0. Separating $f(^1/_2 + i\eta)$ into real and imaginary parts gives

$$\sin \theta = \mathrm{Im}[f(^1/_2 + i\eta)] = (1 - b)(1 + b)\eta/[^1/_4(1 + b)^2 + (1 - b)^2\eta^2]$$

In the limit as $\eta \to 0$, $\theta \to 0$, and therefore $\theta \to \sin \theta$. Then

$$\theta \simeq 4\eta(1 - b)/(1 + b) \tag{A-38}$$

As $\eta \to 0$, $\phi \to \pi$ and therefore $\phi \to \pi - \sqrt{2(1 + \cos \phi)}$, giving

$$\phi \simeq \pi - 4\eta^2. \tag{A-39}$$

Combining eqs. (A-38) and (A-39) gives, in the limit $\eta \to 0$,

$$\phi/\theta \simeq [(\pi/4\eta) - 1](1 + b)/(1 - b) \tag{A-40}$$

Substituting eq. (A-40) into eq. (A-37) and solving for η gives

$$\eta < \frac{\pi}{2} \; \frac{(1 + b)/(1 - b)}{K - 1 + 2(1 + b)/(1 - b)} \tag{A-41}$$

For K large, eq. (A-41) gives an approximate upper bound to η, hence determining the maximum flux, $q = (k_f - k_b)(^1/_4 + \eta^2)$, that can be supported by the lattice. For very large K, eq. (A-41) becomes

$$\left(\frac{q - q_{\max}}{k_f - k_b}\right)^{1/2} < \frac{\pi}{2}\left(\frac{1 + b}{1 - b}\right)\frac{1}{K}$$

From Figures 4*B* and 5*B* it appears that the solution curve for $q > q_{\max}$ is almost indistinguishable from the two curves for $q = q_{\max}$, pieced together in a certain way. For j near $j_0 + \pi/\theta$,

$$\sin\,(j - j_0)\theta/[1 + \cos\,(j - j_0)\theta] \rightarrow 2/[\pi - (j - j_0)\theta]$$

Substituting this result and eq. (A-38) into eq. (A-29) gives

$$n_j \simeq \frac{1}{2} + \frac{1 + b}{1 - b}\,\frac{1}{2[j - (j_0 + \pi/\theta)]} \qquad j > j_0 \tag{A-42}$$

Similarly, for j near $j_0 - \pi/\theta$,

$$n_j \simeq \frac{1}{2} + \frac{1 + b}{1 - b}\,\frac{1}{2[j - (j_0 + \pi/\theta)]} \qquad j < j_0 \tag{A-43}$$

The two solutions eqs. (A-42) and (A-43) are also valid for j near j_0, as the second term is very small when η is small. The solution eq. (A-42) corresponds to curve *1* in Figure 4*B* with $j_0 \rightarrow j_0 + \pi/\theta$, while the solution eq. (A-43) corresponds to curve *2* with $j_0 \rightarrow j_0 - \pi/\theta$.

APPENDIX B

Example for $L = 1$

For the special case $L = 1$ with $\alpha' = \beta' = 0$, the boundary conditions are

$$(1 - b)n(1 - n) = \alpha(1 - n_1) = \beta n_K \tag{B-1}$$

From the boundary conditions eq. (B-1) we can solve for n_1 and n_K,

$$n_1 = 1 - (1 - b)n(1 - n)/\alpha \tag{B-2a}$$

$$n_K = (1 - b)n(1 - n)/\beta \tag{B-2b}$$

Solving eq. (16) for C' gives

$$C' = \frac{1 - n - n_j}{n_j - n} f(n)^{-} \tag{B-3}$$

Substituting eqs. (B-2a) and (B-2b) into eq. (B-3) with $j = 1$ and $j = K$ gives

$$C'(n) = \frac{1 - n - n_1}{n_1 - n} f(n)^{-1}$$
$$= \left[\frac{(1-b)(1-n) - \alpha}{\alpha - n(1-b)}\right]\left[\frac{n}{1-n}\right] f(n)^{-1} \quad \text{(B-4a)}$$

$$C'(n) = \frac{1 - n - n_K}{n_K - n} f(n)^{-K}$$
$$= \left[\frac{\beta - (1-b)n}{(1-n)(1-b) - \beta}\right]\left[\frac{1-n}{n}\right] f(n)^{-K} \quad \text{(B-4b)}$$

By setting the two expressions for $C'(n)$ equal, we obtain an equation of high degree in n. Rather than solving it exactly, we consider approximate solutions valid in the limit of large K.

Given values of α and β, we need to be able to choose the appropriate solution curve. In the case in which $q < q_{\max}$, knowing whether $n_1 + n_K$ is less than, approximately equal to, or greater than 1 is sufficient to determine the region(s) where the solution is nearly uniform. However, knowing the value of $n_1 + n_K$ is not sufficient information to determine whether we have $q \leq q_{\max}$ or $q > q_{\max}$.

From eq. (B-1) it is clear that

$$\alpha \simeq \beta \Longleftrightarrow n_1 + n_K \simeq 1 \quad \text{(B-5a)}$$

$$\alpha < \beta \Longleftrightarrow n_1 + n_K < 1 \quad \text{(B-5b)}$$

We let η be defined as before and let $\gamma > 0$ be defined by

$$^1/_4(k_f - k_b)(1 - \gamma^2) = q < q_{\max} \quad \text{(B-6)}$$

From eq. (B-1) we can see that

$$\alpha > \frac{1}{2}(1-b) \Longleftrightarrow \begin{cases} n_1 > {}^1/_2 + 2\gamma^2 & q < q_{\max} \\ n_1 > {}^1/_2 & q = q_{\max} \\ n_1 > {}^1/_2 - 2\eta^2 & q > q_{\max} \end{cases} \quad \text{(B-7a)}$$

$$\beta > \frac{1}{2}(1-b) \Longleftrightarrow \begin{matrix} n_K < {}^1/_2 - 2\gamma & q < q_{\max} \\ n_K < {}^1/_2 & q = q_{\max} \\ n_K < {}^1/_2 + 2\eta^2 & q > q_{\max} \end{matrix} \quad \text{(B-7b)}$$

We first examine the case in which $\alpha < \beta < {}^1/_2(1 - b)$. In this case we can have only $q < q_{\max}$, since otherwise we have from eq. (B-7) that $n_1 < {}^1/_2$ and $n_K > {}^1/_2$, for which there are no solutions, with $q \geq q_{\max}$. From eq. (B-5), we have $n_1 + n_K < 1$. Referring to Tables I and II for $q < q_{\max}$, we see that the solution is nearly uniform for small j, $n_1 \simeq \min(n, 1 - n)$. Substitution of this into eq. (B-1) gives $n_1 \simeq \alpha/(1 - b)$. The uniform solution $n_j = n = \alpha/(1 - b)$ should be a good approximation except near

$j = K$. To obtain an improved approximation for large j, we substitute eq. (B-4b) into eq. (16), and then set $n = \alpha/(1 - b)$, obtaining

$$n_j = \frac{\alpha}{1-b} + \frac{1 - \dfrac{2\alpha}{1-b}}{1 + \left[\dfrac{\beta - \alpha}{(1-b) - \alpha - \beta}\right]\left[\dfrac{(1-b) - \alpha}{\alpha}\right]\left[f\left(\dfrac{\alpha}{1-b}\right)\right]^{j-K}}$$

$$= \frac{\alpha}{1-b} + \frac{\left[1 - \dfrac{2\alpha}{1-b}\right][(1-b) - \alpha - \beta]}{\beta - \alpha}$$

$$\times \frac{\left[\dfrac{\alpha}{(1-b) - \alpha}\right]\left[f\left(\dfrac{\alpha}{1-b}\right)\right]^{K-j}}{1 + \left[\dfrac{(1-b) - \alpha - \beta}{\beta - \alpha}\right]\left[\dfrac{\alpha}{(1-b) - \alpha}\right]\left[f\left(\dfrac{\alpha}{1-b}\right)\right]^{K-j}} \tag{B-8}$$

Since $\alpha < {}^1/_2(1 - b)$, we have $\alpha/[(1 - b) - \alpha] < 1$ and $f[\alpha/(1 - b)] < 1$; therefore $\{\alpha/[(1 - b) - \alpha]\}\{f[\alpha/(1 - b)]\}^K$ is very small when K is large. We thus have n_j approximately equal to $\alpha/(1 - b)$ except when j is close to K. The flux is approximately

$$q = (k_f - k_b)[\alpha/(1 - b)]\{1 - [\alpha/(1 - b)]\}$$

The solution is shown in Figure 2*C*.

Here the initiation step is so slow that it is the rate-controlling factor. As is expected in such a case, we have the low-density solution associated with the flux q.

We next consider the case in which $\beta < \alpha < {}^1/_2(1 - b)$. As in the previous case, we must have $q < q_{\max}$. However, here we have $n_1 + n_K > 1$. The uniform solution, $n_j = n = 1 - [\beta/(1 - b)]$, should be a good approximation except near $j = 1$. In order to obtain an improved approximation for small j, we substitute eq. (B-4a) into eq. (16) and then set $n = 1 - [\beta/(1 - b)]$, obtaining

$$n_j = 1 - \frac{\beta}{1-b}$$

$$- \frac{1 - 2\dfrac{\beta}{1-b}}{1 + \left[\dfrac{\alpha - \beta}{(1-b) - \alpha - \beta}\right]\left[\dfrac{(1-b) - \beta}{\beta}\right]\left[f\left(1 - \dfrac{\beta}{1-b}\right)\right]^{j-1}} \tag{B-9}$$

Since $\beta < {}^1/_2(1 - b)$, we have $[(1 - b) - \beta]/\beta > 1$ and $f\{1 - [\beta/(1 - b)]\} > 1$. We therefore have n_j approximately equal to $1 - [\beta/(1 - b)]$ except when j is small. The solution is shown in Figure 2*D*.

Here the release step is so slow as to be rate controlling. In this case we have the high density solution. The flux in this case is approximately

$$q = (k_f - k_b)[\beta/(1 - b)]\{1 - [\beta/(1 - b)]\}$$

In the two examples considered, we have assumed that α and β are not even nearly equal. If $\alpha - \beta$ is very small, the approximate solutions given above are not correct. We now consider separately the case $\alpha \simeq \beta$, $\alpha < {}^1/_2(1 - b)$. Since $\alpha \simeq \beta$, we have $n_1 + n_K \simeq 1$. Because $\alpha < {}^1/_2(1 - b)$ and $\beta < {}^1/_2(1 - b)$; we must have $q < q_{\max}$. In this case, we have two uniform regions, a low-density one for small j and a high-density one for large j. We let $n = \alpha/(1 - b)$ in eq. (16) and write

$$\text{eq. } C' = \pm\left[f\left(\frac{\alpha}{1 - b}\right)\right]^{-j_0}$$

The solution is

$$n_j = \frac{\alpha}{(1 - b)} + \frac{1 - [2\alpha/(1 - b)]}{1 \pm \{f[\alpha/(1 - b)]\}^{j - j_0}} \tag{B-10}$$

Except when j is near j_0, we have n_j near to $\alpha/(1 - b)$ when $j_0 < j$ and n_j near to $1 - [\alpha/(1 - b)]$ when $j_0 > j$. Since $\alpha \simeq \beta$, both boundary conditions are satisfied with negligible error. The $\pm$ sign takes the sign of $(\beta - \alpha)$. The value of j_0 is very sensitive to the precise value of $\beta - \alpha$. To obtain a good approximation to j_0, let $n_K = 1 - [\beta/(1 - b)]$ in eq. (A-9) with $j = K$, obtaining

$$f\left(\frac{\alpha}{1 - b}\right)^{K - j_0} = \frac{\alpha - \beta}{(1 - b) - \alpha - \beta} \tag{B-11}$$

Solving eq. (B-11) for j_0, we obtain

$$j_0 = K - \frac{\ln\left[\dfrac{1}{|\alpha - \beta|}\right] - \ln\left[\dfrac{1}{(1 - b) - \alpha - \beta}\right]}{\ln\left[\dfrac{1}{f\left(\dfrac{\alpha}{1 - b}\right)}\right]}$$

The solution is illustrated in Figure 2*B*.

In this case where the initiation and release rates are of comparable magnitude, but slow, there is a transition from the low-density solution at the low j end to the high-density solution at the large j end. The flux is approximately

$$q = (k_f - k_b)[\alpha/(1 - b)]\{1 - [\alpha/(1 - \mathrm{b})]\}$$

We now consider the case in which $\alpha > {}^1/_2(1 - b)$ and $\beta > {}^1/_2(1 - b)$. If $q \leq q_{\max}$, then $n_1 > {}^1/_2$ and $n_K < {}^1/_2$. Since there can be no solutions with $n_1 > {}^1/_2$ and $n_K < {}^1/_2$ for $q \leq q_{\max}$, we must have $q > q_{\max}$. Therefore $n_1 > {}^1/_2 - 2\eta^2$ and $n_K < {}^1/_2 + 2\eta^2$. Since we wish to consider the solution in the limit of large K, we need η very small. If $\alpha \gg {}^1/_2(1 - b)$ and $\beta \gg {}^1/_2(1 - b)$, then $n_1 \gg {}^1/_2$ and $n_K \ll {}^1/_2$.

In this case neither α nor β is the controlling factor; both initiation and release are sufficiently fast that they are not rate-controlling. We have a high initial density and a low terminal density, with the solution in the interior being nearly uniform to ${}^1/_2$.

The flux in this case is so close to $q_{\max}$ that we can obtain a good approximation to the solution by piecing together two separate solutions for the case in which $n = {}^1/_2$.

Solving eq. (18) for C gives

$$C = \frac{1 + b}{1 - b}\frac{1}{n_j - {}^1/_2} - 2j \tag{B-12}$$

Substituting the boundary conditions eqs. (B-2a) and (B-2b) with $n = {}^1/_2$ into eq. (B-12) with $j = 1$ and $j = K$ gives

$$\begin{aligned} C &= \frac{1 + b}{1 - b}\frac{1}{n_1 - {}^1/_2} - 2 \\ &= \frac{1 + b}{1 - b}\frac{2}{\{1 - [(1 - b)/2\alpha]\}} - 2 \end{aligned} \tag{B-13a}$$

$$C = \frac{1 + b}{1 - b}\frac{1}{n_K - {}^1/_2} - 2K = \frac{1 + b}{1 - b}\frac{2}{\{[(1 - b)/2\beta] - 1\}} - 2K \tag{B-13b}$$

Substituting these two expressions for C into eq. (18) gives

$$n_j = \frac{1}{2} + \frac{1}{2}\,\frac{\alpha - [(1 - b)/2]}{(j - 1)[(1 - b)/(1 + b)]\{\alpha - [(1 - b)/2]\} + \alpha} \tag{B-14a}$$

$$n_j = \frac{1}{2} - \frac{1}{2}\,\frac{\beta - [(1 - b)/2]}{(K - j)[(1 - b)/(1 + b)]\{\beta - [(1 - b)/2]\} + \beta} \tag{B-14b}$$

For the case $n = {}^1/_2$, eqs. (B-14a) and (B-14b) both give the same expression for n_j, as α and β are not independent. In the case in which $n = {}^1/_2 + i\eta$, eq. (B-14a) is a good approximation for n_j for small j, and eq. (B-14b) is a good approximation for n_j for large j. In this case, α and β are independent, and eqs. (B-14a) and (B-14b) are not the same solution. An approximation that is accurate for all j is obtained by combining eqs. (B-14a) and (B-14b) in the form

$$n_j = \frac{1}{2} + \frac{1}{2}\,\frac{\alpha - \dfrac{1 - b}{2}}{(j - 1)\left(\dfrac{1 - b}{1 + b}\right)\left(\alpha - \dfrac{1 - b}{2}\right) + \alpha} - \frac{1}{2}\,\frac{\beta - \dfrac{1 - b}{2}}{(K - j)\left(\dfrac{1 - b}{1 + b}\right)\left(\beta - \dfrac{1 - b}{2}\right) + \beta} \tag{B-15}$$

This approximation does not satisfy the recursion equation, eq. (19), exactly. The solution is shown in Figure 5*B*.

In each of the cases discussed so far, information about the relative magnitudes of α, β, and $^1/_2(1 - b)$ has been sufficient to determine the one correct solution curve. In the two cases that will now be discussed, $\alpha < {}^1/_2(1 - b) < \beta$ and $\beta < {}^1/_2(1 - b) < \alpha$, more than one consistent solution curve can be obtained. Further information is needed in order to determine which solution curve is the correct one.

We first consider the case in which $\alpha < {}^1/_2(1 - b) < \beta$. Then eq. (B-5b) gives $n_1 + n_K < 1$. If $q < q_{\max}$, the solution is nearly uniform for small j to the value $\alpha/(1 - b)$, and the solution eq. (B-8) is a good approximation for all j. If $\alpha + \beta < (1 - b)$, substituting $n = \alpha/(1 - b)$ into the expression eq. (B-4b) gives $C' > 0$. In this case the solution curve is that shown in Figure 2*C* as in the case $\alpha < \beta < {}^1/_2(1 - b)$. If $\alpha + \beta > (1 - b)$, then $C' < 0$ and hence the solution curve is curve *1* in Figure 3*B*. In each case, the flux is approximately

$$q = (k_f - k_b)[\alpha/(1 - b)]\{1 - [\alpha/(1 - b)]\}$$

If $q \geq q_{\max}$, the negatives of the equivalence relations in eq. (B-7a) give $n_1 < {}^1/_2$ and hence $n_K < n_1 < {}^1/_2$. Since we are dealing with large K, n_1 must be very close to $^1/_2$, and hence α very close to $^1/_2(1 - b)$. This solution can then be regarded as a special limiting case of $q < q_{\max}$, with $\alpha + \beta > 1 - b$ and $\alpha \rightarrow {}^1/_2(1 - b)$.

We next consider the case in which $\alpha > {}^1/_2(1 - b) > \beta$. Then eq. (B-5b) gives $n_1 + n_K > 1$. If $q < q_{\max}$, the solution is nearly uniform to the value $1 - [\beta/(1 - b)]$ for large j and the solution eq. (B-9) is a good approximation for all j. If $\alpha + \beta < (1 - b)$, the solution curve is that shown in Figure 2*D*. If $\alpha + \beta > (1 - b)$, the solution curve is curve *2* in Figure 3*B*. In each case the flux is approximately

$$q = (k_f - k_b)[\beta/(1 - b)]\{1 - [\beta/(1 - b)]\}$$

If $q \geq q_{\max}$, eq. (B-7b) gives $n_K > {}^1/_2$ and hence $n_1 > n_K > {}^1/_2$. Since we are dealing with large K, n_K must be very close to $^1/_2$ and hence β is very close to $^1/_2(1 - b)$. This solution can then be regarded as a special limiting case of $q < q_{\max}$, with $\alpha + \beta > 1 - b$ and $\beta \rightarrow {}^1/_2(1 - b)$.

In each of the solutions, the flux is given by

$$q = (k_f - k_b)m(1 - m) \qquad \text{(B-16a)}$$

with

$$m = \min\left(\frac{\alpha}{1 - b}, \frac{\beta}{1 - b}, \frac{1}{2}\right) \qquad \text{(B-16b)}$$

The effect of varying b, the ratio of the backward-rate constant to the forward-rate constant, can be seen quite easily from eq. (B-16). As the back reaction becomes more important (b becomes larger), the initiation or termination step must become slower (α or β smaller) in order to be the rate-controlling step. With an important back reaction, polymerization is the rate-controlling factor for a much broader range of values of α and β. If either α or β is small enough to be rate-controlling, a larger b gives a lower flux, even though the density in the uniform region is closer to $^1/_2$.

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