

STEADY-STATE HEAD-TO-TAIL POLYMERIZATION OF ACTIN OR MICROTUBULES

II. TWO-STATE AND THREE-STATE KINETIC CYCLES

TERRELL L. HILL, *Laboratory of Molecular Biology, National Institute of Arthritis, Metabolism and Digestive Diseases, National Institutes of Health, Bethesda, Maryland 20205 U.S.A.*

ABSTRACT In a previous paper, bioenergetic aspects of head-to-tail polymerization for a two-state actin ATPase cycle were discussed. In section 2, here, the steady-state polymer length distribution for this case is derived. The distribution has the same mathematical form as at equilibrium, but the parameters are different. In section 3, both bioenergetic topics and the polymer length distribution are considered for the more general and realistic case of a three-state actin ATPase cycle. Again, the mathematical form of the steady-state distribution is the same as at equilibrium, but the parameters are more complicated. In section 4, the question is examined of how much the mean and variance of a polymer length distribution, obtained from a finite experimental sample of polymer (aggregate) molecules, would be expected to deviate from the true mean and variance (from an infinite sample). Also considered briefly in section 4 is the effect of hard polymer-polymer interactions on the equilibrium polymer length distribution, at finite polymer concentrations.

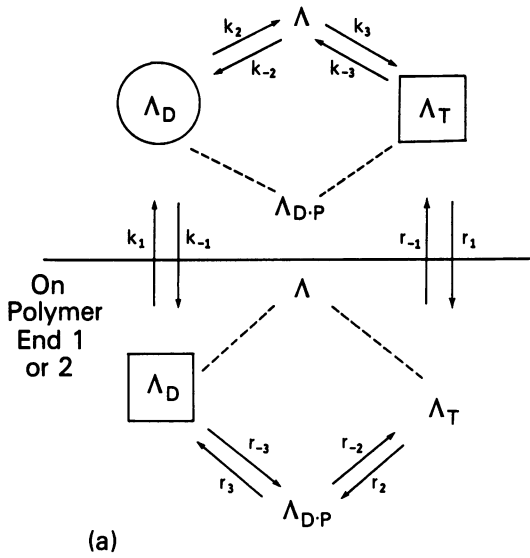
1. INTRODUCTION

This subject was introduced in a previous paper (1), which the reader should consult. The discussion is extended in four ways in the present paper: (a) the general steady-state polymer length distribution is derived for a two-state (Fig. 1) ATPase or GTPase cycle (section 2); (b) the significant aspects of the three-state cycle problem are analyzed in section 3 (the third state is monomer in solution with ADP or GDP bound—see Fig. 1); (c) fluctuations in the polymer length distribution itself, owing to observation of a finite experimental sample of polymers, are examined (section 4); and (d) first-order effects of polymer-polymer interactions, at equilibrium, on the polymer length distribution are deduced (section 4).

For proper perspective, we point out here the relationship of the present problem to recent work on general enzyme-enzyme interaction systems (2–6). In a small or large complex or aggregate of identical enzyme molecules, nearest-neighbor interactions between these molecules may alter the rate constants of the kinetic cycle catalyzed by the enzyme. Thus, these rate constants for a given molecule in the aggregate may depend on the number of nearest-neighbor molecules and also, in general, on the instantaneous states (in their cycles) of these nearest neighbors. For the most part, we have studied kinetic properties of aggregates of fixed size, but aggregates of variable size have also been considered (4).

In the present problem, monomers (G-actin molecules, or dimers of tubulin) are in a dynamic steady-state (we do not consider transients here) with a linear aggregate (several strands) of monomers. Thus, the aggregate size fluctuates. We also refer to an aggregate as a

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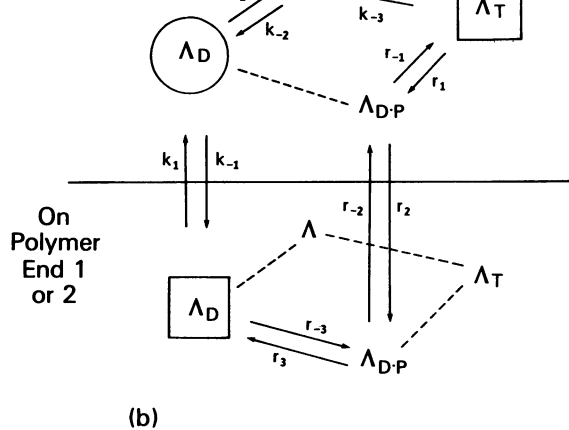


FIGURE 1 (a) Kinetic model for head-to-tail polymerization and NTP hydrolysis. Λ = monomer; T = NTP; D = NDP; P = P_i . Dashed lines represent very slow transitions. The dominant direction of the large (six-state) cycle is clockwise. The boxed species are used in the reduced two-state cycle; the circled species is included in the three-state cycle. See text. (b) Modification in which $\Lambda_{D,P}$ is the species that binds to the polymer (Brenner-Korn). See text.

polymer. A monomer, whether free in solution or as part of a polymer, is an enzyme; it is an ATPase (actin) or GTPase (tubulin). We use NTPase, below, to refer to either case. In general, owing to different nearest-neighbor numbers, one would expect different NTPase activity by monomers that are (a) free, (b) in the interior of a polymer, or (c) on either end of a polymer. As is well-known, this is indeed observed in this system, as follows. Interior monomers show essentially no NTPase activity, and are frozen in the cycle state Λ_D (Λ refers

to a monomer, D to NDP). End monomers and free monomers can both pass readily through parts of the NTPase cycle, but only slowly through the complete cycle; however, the two parts complement each other, thus allowing complete enzyme activity in combination with aggregation \rightleftharpoons disaggregation (on \rightleftharpoons off) transitions at either end of the polymer. Two specific possibilities (1, 7) are shown in Fig. 1 (ignore the rate constants in the figure for the present). The scheme outlined above is a special case of the general enzyme-enzyme interaction problem (2–6) summarized in the preceding paragraph.

One further point should be made. The combination invoked above of complementary partial enzymatic cycles together with on \rightleftharpoons off transitions of the enzyme is not novel. Essentially the same feature is used in muscle contraction models (8): part of the complete myosin-ATPase cycle is traversed when myosin-ATP is free and part when it is bound to an actin monomer of a thin filament.

2. POLYMER LENGTH DISTRIBUTION FOR MONOMERS WITH TWO-STATE CYCLES

As in reference 1, we base our main discussion on Fig. 1 *a*. The scheme in Fig. 1 *b* will be mentioned at the end of this section. We suppose (1, 9, 10) in this section that the only states in Fig. 1 *a* with significant population are the two in boxes: Λ_T in solution and Λ_D on either polymer end. Thus the kinetic diagram (now including the two ends separately) simplifies to Fig. 2. If the rate constants in Fig. 1 *a* are assumed to refer to end 1, then the rate constants of the two-state cycle are related to those of the six-state cycle by (1, 11)

$$\alpha_1 c = r_1 r_2 r_3 / (r_{-1} r_{-2} + r_{-1} r_3 + r_2 r_3) \quad (1)$$

$$\alpha_{-1} = r_{-1} r_{-2} r_{-3} / (r_{-1} r_{-2} + r_{-1} r_3 + r_2 r_3) \quad (2)$$

$$\alpha_2 = k_1 k_2 k_3 / (k_{-1} k_{-2} + k_{-1} k_3 + k_2 k_3) \quad (3)$$

$$\alpha_{-2} = k_{-1} k_{-2} k_{-3} / (k_{-1} k_{-2} + k_{-1} k_3 + k_2 k_3), \quad (4)$$

where c is the monomer concentration. There are, of course, completely analogous equations

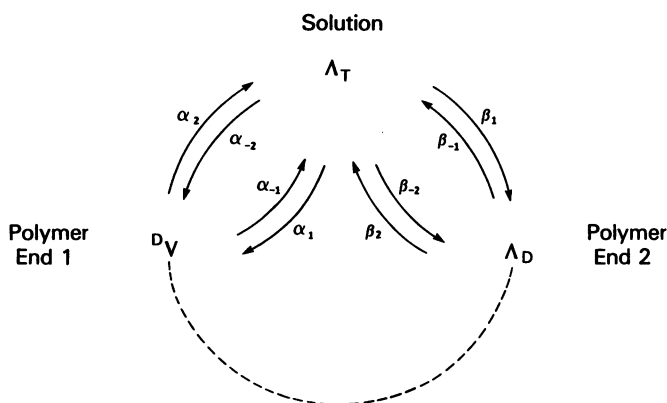


FIGURE 2 Simplified kinetic diagram with only the two boxed states retained from Fig. 1. The two polymer ends are shown separately in this figure, with related two-state kinetic cycles. Dominant direction in cycles is clockwise. Dashed line represents the polymer.

for the β 's (polymer end 2) in Fig. 2; in general, there are different sets of r 's and k 's at the two ends (except that $k_{\pm 2}$ and $k_{\pm 3}$ are shared). Detailed discussion of the kinetic order of the rate constants in Eqs. 1–4 is deferred until section 3.

We have nothing to add here to the discussion in reference 1 of the steady-state kinetics and bioenergetics of this two-state system. What we do provide, though, is a more general treatment of the steady-state polymer length distribution (only a very special case was considered in reference 1). It may well be that the true steady-state distribution is very difficult to achieve experimentally. However, this distribution has intrinsic theoretical interest (it is not the conventional exponential distribution). Also, the kinetics of aggregation depend on the same considerations.

To begin with, we consider the equilibrium system, in Fig. 1 *a*, in which only the transitions k_1, k_{-1} can occur (all other transitions inhibited), at one end or the other. Then we have, from the appropriate partition function for an ensemble of these systems (1, 12),

$$P_N^e = [\ln(c_{\infty}/c)]^{n+1} N^n (c/c_{\infty})^n / \Gamma(n+1), \quad (5)$$

where P_N^e is the normalized equilibrium probability of observing a polymer containing N monomers, when the monomer concentration is c , n is a statistical-mechanical constant of order 5 (1), Γ is the Gamma function [$\Gamma(n+1) = n!$, if n is zero or a positive integer], and c_{∞} is the "critical" concentration (i.e., c_{∞} is the solubility of infinite polymer). The normalization in Eq. 5 is valid when c is close to c_{∞} , so that large polymers dominate (say, $\bar{N} > 50$ or 100); this is the case we consider throughout. The value of n mentioned above would apply to completely free polymer molecules in solution; n originates from translation, rotation, and vibration in the finite polymer (1). If some degrees of freedom are lost, for example, if the polymers are attached to a surface at one end (13), then n would be smaller. The usual exponential distribution has $n = 0$, which is not justified.

Detailed balance at equilibrium requires that

$$P_{N-1}^e k_{-1} c = P_N^e k_1(N), \quad k_{-1} c_{\infty} = k_1(\infty), \quad (6)$$

where k_{-1} is a second-order rate constant that is independent of c . In fact, we shall assume that k_{-1} is diffusion-controlled and also independent of N . Thus the N -dependence of the binding equilibrium constant k_{-1}/k_1 for a finite polymer is contained entirely in $k_1(N)$. From Eqs. 5 and 6 we deduce that

$$k_1(N) = k_1(\infty) [(N-1)/N]^n. \quad (7)$$

In a more general treatment, $[(N-1)/N]^n$ would be divided up arbitrarily between both k_1 and k_{-1} , but the only natural and simple special case is the one we consider here (k_{-1} is constant). In the future, other cases may prove worthy of study. In particular, in investigating the kinetics of the early stages of aggregation, k_{-1} may be N -dependent for small N , even if diffusion-controlled, because the polymer is not large compared with the monomer. But this is not important at steady state, where only rather large values of N are significant.

Similarly (1), we also find

$$r_{-1}(N) = r_{-1}(\infty) [(N-1)/N]^n. \quad (8)$$

These N -dependences obviously apply at either end of the polymer. They also apply whether

or not the ensemble of polymer molecules is at equilibrium, even though equilibrium was used to deduce the result. The other k 's and r 's do not, or are assumed not to, depend on N (1).

On noting the positions of k_1 and r_{-1} in Eqs. 1–4, we conclude that the N -dependences of the α 's and β 's in Fig. 2 take the following forms:

$$\alpha_1(N) = \alpha_1(\infty) \left/ \left[g_\alpha + (1 - g_\alpha) \left(\frac{N-1}{N} \right)^n \right] \right. \quad (9)$$

$$\alpha_{-1}(N) = \alpha_{-1}(\infty) \left(\frac{N-1}{N} \right)^n \left/ \left[g_\alpha + (1 - g_\alpha) \left(\frac{N-1}{N} \right)^n \right] \right. \quad (10)$$

$$\alpha_2(N) = \alpha_2(\infty) \left(\frac{N-1}{N} \right)^n, \quad \alpha_{-2} = \alpha_{-2}(\infty), \quad (11)$$

where g_α is a constant (see below). The expressions for the β 's are the same: replace all α 's by β 's (including $g_\alpha \rightarrow g_\beta$). The explicit expression for g_α is

$$g_\alpha = r_2 r_3 / [r_2 r_3 + (r_{-2} + r_3) r_{-1}(\infty)], \quad (12)$$

and similarly for g_β (using the r 's related to polymer end 2). Clearly, g_α and g_β are fractions. Under usual steady-state conditions, far from equilibrium, g_α and g_β are presumably close to unity (r_{-1} and r_{-2} small). The only steady-state polymer length distribution considered in reference 1 was for the important special case $\alpha_{-1} = \alpha_{-2} = \beta_{-1} = \beta_{-2} = 0$, $g_\alpha = g_\beta = 1$.

Although k_{-1} and r_1 might reasonably be expected to be diffusion-controlled, this is not true of α_{-2} and α_1 , which are composite rate constants.

To simplify notation, from this point we shall understand α_1 , etc., to refer to $\alpha_1(\infty)$, etc. Also, we use c and c_∞ for the steady-state monomer concentrations (c_∞ is the steady-state critical concentration; $c \leq c_\infty$). In reference 1 we used \bar{c}_1 and $\bar{c}_1(\infty)$ for these quantities.

The master equation for P_N at steady state is, from Fig. 2,

$$\begin{aligned} \frac{dP_N}{dt} = 0 = & P_{N+1}[\alpha_2(N+1) + \beta_2(N+1) + \alpha_{-1}(N+1) + \beta_{-1}(N+1)] \\ & - P_N[\alpha_1(N) + \beta_1(N) + \alpha_{-2} + \beta_{-2}]c \\ & + P_{N-1}[\alpha_1(N-1) + \beta_1(N-1) + \alpha_{-2} + \beta_{-2}]c \\ & - P_N[\alpha_2(N) + \beta_2(N) + \alpha_{-1}(N) + \beta_{-1}(N)]. \quad (13) \end{aligned}$$

A solution, P_N , for only the first two lines on the right,

$$0 = P_{N+1}[N+1] - P_N[N]c, \quad (14)$$

is also a solution for only the third and fourth lines; hence, a solution of Eq. 14 is also a solution for the complete Eq. 13. Thus, we need consider only Eq. 14, which can be solved seriatim: P_3 is expressed in terms of P_2 , P_4 is expressed in terms of P_3 and then in terms of P_2 , etc. Thus, by repeated application of Eq. 14, P_N can be found, for arbitrary N , with P_2 absorbed into the normalization constant. Although the system is not at equilibrium, we can exploit a kind of "detailed balance" here, Eq. 14 (compare Eq. 6). This is possible because aggregates of different sizes are characterized by only a single variable, N (14). We could not

use this convenient mathematical feature if monomers belonging to the aggregate could exist in several kinetic states that had to be taken into account (section 1).

Before deriving P_N , as outlined above, we note that summation of Eq. 14 over N yields

$$c = (\bar{\alpha}_2 + \bar{\beta}_2 + \bar{\alpha}_{-1} + \bar{\beta}_{-1}) / (\bar{\alpha}_1 + \bar{\beta}_1 + \alpha_{-2} + \beta_{-2}), \quad (15)$$

where $\bar{\alpha}_2$ is the mean value of $\alpha_2(N)$,

$$\bar{\alpha}_2 = \sum_N P_N \alpha_2(N), \quad (16)$$

etc. At the critical concentration, the corresponding relation is

$$c_\infty = \sum_{\text{off}} / \sum_{\text{on}}, \quad (17)$$

where

$$\sum_{\text{off}} \equiv \alpha_2 + \beta_2 + \alpha_{-1} + \beta_{-1}, \quad \sum_{\text{on}} \equiv \alpha_1 + \beta_1 + \alpha_{-2} + \beta_{-2}.$$

That is, Eq. 15 refers to finite polymers and Eq. 17 to infinite polymers.

For use below we define, for $\alpha_2, \beta_2, \alpha_{-1}$, and β_{-1} ,

$$\langle \alpha_2 \rangle \equiv \alpha_2 / \sum_{\text{off}}, \quad (18)$$

etc., and for $\alpha_1, \beta_1, \alpha_{-2}$, and β_{-2} ,

$$\langle \alpha_1 \rangle \equiv \alpha_1 / \sum_{\text{on}}, \quad (19)$$

etc. The eight quantities $\langle \rangle$ are fractions; the first four add to unity, as do the second four.

At equilibrium, Eq. 17 simplifies to

$$c_\infty = \alpha_2 / \alpha_{-2} = \beta_2 / \beta_{-2} = \alpha_{-1} / \alpha_1 = \beta_{-1} / \beta_1. \quad (20)$$

There is detailed balance in each transition pair (but not at steady state).

To find P_N , we start with Eq. 14, substitute Eqs. 9–11 for the α 's and β 's, and use Eqs. 17–19. The result is

$$P_{N+1} = P_N \left(\frac{N+1}{N} \right)^n \cdot \frac{c}{c_\infty} \cdot \frac{X_N}{Y_{N+1}}, \quad (21)$$

where

$$X_N = \frac{\langle \alpha_1 \rangle}{[g_\alpha, N]} + \frac{\langle \beta_1 \rangle}{[g_\beta, N]} + \langle \alpha_{-2} \rangle + \langle \beta_{-2} \rangle \quad (22)$$

$$Y_{N+1} = \langle \alpha_2 \rangle + \langle \beta_2 \rangle + \frac{\langle \alpha_{-1} \rangle}{[g_\alpha, N+1]} + \frac{\langle \beta_{-1} \rangle}{[g_\beta, N+1]}, \quad (23)$$

and $[g_\alpha, N]$ represents the denominator in Eq. 9 or 10. As already mentioned, we are concerned only with cases in which c is close to c_∞ so that \bar{N} is fairly large. Thus, the significant values of N are also fairly large: $N \gg 1$. For large N ,

$$[g_\alpha, N] = [g_\alpha, N + 1] = 1 - (1 - g_\alpha)(n/N)$$

$$[g_\beta, N] = [g_\beta, N + 1] = 1 - (1 - g_\beta)(n/N).$$

Thus we find

$$X_N = 1 + [\langle \alpha_1 \rangle (1 - g_\alpha) + \langle \beta_1 \rangle (1 - g_\beta)](n/N) \quad (24)$$

$$Y_{N+1} = 1 + [\langle \alpha_{-1} \rangle (1 - g_\alpha) + \langle \beta_{-1} \rangle (1 - g_\beta)](n/N). \quad (25)$$

We now apply Eq. 21, successively, for $N = 2, 3, \dots, N$, to obtain an expression for P_N . The product of X 's (or Y 's) encountered in this procedure can be evaluated by taking the logarithm of the product, replacing summation by integration, and using $\ln(1 + \delta) = \delta$ in the integrand. The result, after normalization, is

$$P_N = [\ln(c_\infty/c)]^{nx+1} N^{nx}(c/c_\infty)^N / \Gamma(nx + 1), \quad (26)$$

where

$$x = 1 + (\langle \alpha_1 \rangle - \langle \alpha_{-1} \rangle)(1 - g_\alpha) + (\langle \beta_1 \rangle - \langle \beta_{-1} \rangle)(1 - g_\beta). \quad (27)$$

Eq. 26 is the main result of this section. This is the probability distribution in N (polymer length distribution) at steady state. The notable feature of Eq. 26 is that the distribution has exactly the same mathematical form as the equilibrium distribution, Eq. 5. However, nx replaces n and c_∞ replaces $c_{e\infty}$.

Using the relations (1)

$$\alpha_1/\alpha_{-1} = \beta_1/\beta_{-1}, \quad \alpha_2/\alpha_{-2} = \beta_2/\beta_{-2} \quad (28)$$

$$\alpha_1\alpha_2/\alpha_{-1}\alpha_{-2} = \beta_1\beta_2/\beta_{-1}\beta_{-2} = e^{X/RT}, \quad (29)$$

where X is the thermodynamic force (the free energy of hydrolysis of NTP), Eq. 27 can be rewritten as

$$x = 1 + \frac{(\alpha_2 + \beta_2)[(1 - g_\alpha)\alpha_1 + (1 - g_\beta)\beta_1](1 - e^{-X/RT})}{\Sigma_{\text{on}} \Sigma_{\text{off}}}. \quad (30)$$

At equilibrium ($X = 0$), $x = 1$ as expected (in agreement with Eq. 5). If $g_\alpha = g_\beta = 1$, we also find $x = 1$. In the important special case of essentially one-way cycles (X large, $\alpha_{-1} = \beta_{-1} = \alpha_{-2} = \beta_{-2} = 0$),

$$x = 2 - [(\alpha_1 g_\alpha + \beta_1 g_\beta)/(\alpha_1 + \beta_1)]. \quad (31)$$

If $g_\alpha = g_\beta = 0$, $x = 2$. If $g_\alpha = g_\beta$, $x = 2 - g$. The range in x , at steady state, is from 1 to 2, with x , presumably, usually near the lower limit. When $x > 1$ and hence $nx > n$, the distribution P_N is somewhat sharper than at equilibrium (see Fig. 4 of reference 1). If nx could be deduced from a steady-state P_N distribution, for example, from the variance and mean (1),

$$(\overline{N^2} - \overline{N}^2)/\overline{N}^2 = (\text{wt av.}/\text{No. av.}) - 1 = 1/(nx + 1), \quad (32)$$

it would not be quite safe to ascribe the value of nx to the statistical-mechanical quantity n (1) alone because it may be that $x > 1$.

Other properties of the steady-state P_N in Eq. 26 are (1)

$$\bar{N} = (nx + 1)/\ln(c_\infty/c) \quad (33)$$

$$N_m = nx/\ln(c_\infty/c) \quad (34)$$

$$\bar{N}^{-1} = N_m^{-1} = \ln(c_\infty/c)/nx, \quad (35)$$

where $N = N_m$ at the maximum in P_N .

The distribution function P_N , which can in principle be measured (15), is quite sensitive to how close c is to c_∞ . Thus, if we define ϵ by $c/c_\infty = 1 - \epsilon$, then $\ln(c_\infty/c)$ in Eqs. 33–35 is equal to ϵ . In Fig. 10 (b) of reference 15, for actin, $nx = 3.5$, $N = 2,180$, and $\epsilon = 0.0021$, if we assume, for purposes of illustration, that this is a true steady-state distribution.

In all of the above discussion, if, say, the polymer is attached to a surface at end 2 (13), then all of the β 's are to be set equal to zero.

Mean Values of the Rate Constants

The two-state cycle rate constants depend on N , as shown in Eqs. 9–11 (with analogous expressions for the β 's). We note first that

$$\alpha_1(N)\alpha_2(N)/\alpha_{-1}(N)\alpha_{-2} = \alpha_1\alpha_2/\alpha_{-1}\alpha_{-2} = e^{X/RT}, \quad (36)$$

using Eq. 29 (and similarly for the β 's). This is to be expected, because the thermodynamic force in the cycle depends on NTP, NDP, and P_i concentrations, not on the state of the polymer. The thermodynamic quotients in Eqs. 28 become

$$\begin{aligned} \alpha_1(N)/\alpha_{-1}(N) &= \beta_1(N)/\beta_{-1}(N) \\ &= (\alpha_1/\alpha_{-1})[(N-1)/N]^{-n} \end{aligned} \quad (37)$$

$$\begin{aligned} \alpha_2(N)/\alpha_{-2} &= \beta_2(N)/\beta_{-2} \\ &= (\alpha_2/\alpha_{-2})[(N-1)/N]^n. \end{aligned} \quad (38)$$

The mean rate constants $\bar{\alpha}_i$, etc., averaged over P_N , differ immeasurably from α_i , etc., but are of some theoretical interest. Thus (for large \bar{N} and N , as usual)

$$\begin{aligned} \alpha_1(N) &= \alpha_1[1 + (1 - g_\alpha)(n/N)] \\ \bar{\alpha}_1 &= \alpha_1[1 + (1 - g_\alpha)n\bar{N}^{-1}] \\ &= \alpha_1[1 + (1 - g_\alpha)(\epsilon/x)] \\ &= \alpha_1(c/c_\infty)^{-(1-g_\alpha)/x}. \end{aligned} \quad (39)$$

Also,

$$\bar{\alpha}_{-1} = \alpha_{-1}(c/c_\infty)^{g_\alpha/x}, \quad \bar{\alpha}_2 = \alpha_2(c/c_\infty)^{1/x}, \quad (40)$$

with analogous expressions for the β 's (replace α by β everywhere). As checks, we note that

$$\bar{\alpha}_1\bar{\alpha}_2/\bar{\alpha}_{-1}\bar{\alpha}_{-2} = \alpha_1\alpha_2/\alpha_{-1}\alpha_{-2} = e^{X/RT}, \quad (41)$$

and that, using $c/c_\infty = 1 - \epsilon$ again, we can verify Eq. 15.

The Mechanism of Brenner and Korn

Suppose the mechanism in Fig. 1 *b* (7) is the origin of the two-state cycle (boxed states in Fig. 1), instead of Fig. 1 *a*. This change in mechanism would not effect the role played (1) by the concentrations of NTP, NDP, and P_{*i*} (designated *c_T*, *c_D*, and *c_P*, respectively). This follows because these ligands enter the cycle in the transitions *k₃*, *k₋₂*, and *r₋₃*, respectively, whereas the mechanism change under consideration involves only *r_{±1}* and *r_{±2}*.

Turning to the polymer length distribution, and related questions, as discussed in this section, there is again essentially no effect on our results. The *N*-dependent rate constants in Fig. 1 *b* are *k₁*, as before, and *r₋₂* instead of *r₋₁* (Eq. 8). Examination of Eqs. 1 and 2 shows that we again obtain Eqs. 9 and 10, but the definition of *g_α* is different:

$$g_{\alpha} = (r_{-1} + r_2)r_3 / [(r_{-1} + r_2)r_3 + r_{-1}r_{-2}(\infty)]. \quad (42)$$

This is the only alteration required. As before, if *r₋₁* and *r₋₂* are small, *g_α* is near unity.

Thus, the physical properties discussed in this paper and in reference 1 are unlikely to be useful in distinguishing between the mechanisms in Fig. 1 *a* and *b*.

3. MONOMERS WITH THREE-STATE CYCLES

So far our analysis has referred to the two-state kinetic cycle used by Wegner (9) and by Bergen and Borisy (10). The work of Neidl and Engel (16) suggests that it would be worthwhile to extend the theory to include a third state in the reduced kinetic cycle, namely, the solution species Λ_D in Fig. 1 (encircled). This is the subject of the present section. After an initial digression on the definition of rate constants, we first consider several steady-state bioenergetic topics (corresponding to reference 1 for a two-state cycle) and then turn to the polymer length distribution (corresponding to section 2 for a two-state cycle.)

We start again with Fig. 1 *a*, which refers to either end of a polymer molecule, and reduce this six-state kinetic cycle to the three-state cycle shown in Fig. 3, where both ends are included explicitly. Λ in solution is assumed to be an unimportant transient intermediate; in Fig. 2, both Λ and Λ_D in solution are considered to be transient intermediates. The relationship between the rate constants in Fig. 1 *a* (assuming, to be specific, that they refer to polymer end 1) and those in Fig. 3 are (11):

$$\alpha_2 = k_1, \quad \alpha_{-2} = k_{-1} \quad (43)$$

$$\gamma = k_2k_3 / (k_{-2} + k_3) \quad (44)$$

$$\gamma_- = k_{-2}k_{-3} / (k_{-2} + k_3), \quad (45)$$

with α_1 and α_{-1} still given by Eqs. 1 and 2. The β 's, referring to polymer end 2, are expressed similarly. At this point we digress to provide more details concerning the rate constants in Eqs. 1-4 and 43-45.

Rate Constant Definitions

We first examine the meaning of the *k*'s in Fig. 1. Let us denote the concentrations of the monomer species Λ_D , Λ , and Λ_T , in the solution of volume *V*, by

$$c_{1D} = N_{1D}/V, \quad c_{10} = N_{10}/V, \quad c_{1T} = N_{1T}/V, \quad (46)$$

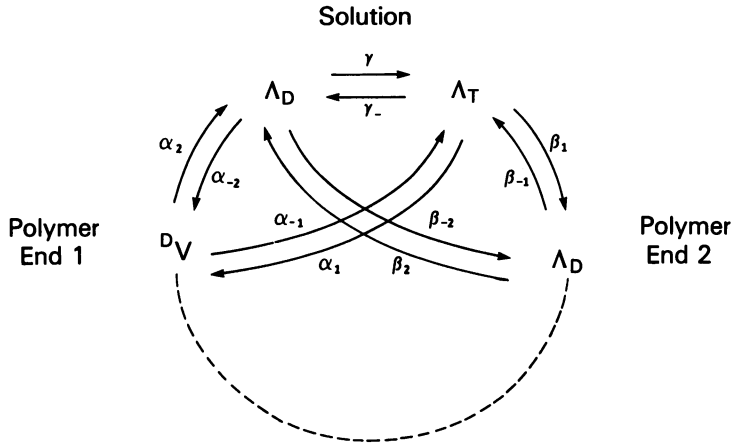


FIGURE 3 Extension of Fig. 2 to three-state cycles when the circled state in Fig. 1 is included, as well as the two boxed states.

respectively. Also, the concentration of polymer (aggregate) molecules is $c_a = N_a/V$. The rate equation for N_{1D} (considering polymer end 1 only) suffices to clarify the definition of the k 's:

$$dN_{1D}/dt = k_1 N_a - k_{-1} c_{1D} N_a + k'_{-2} N_{10} - k'_2 N_{1D}. \quad (47)$$

Here, k_1 , k'_{-2} , and k'_2 are first-order constants, whereas k_{-1} is a conventional second-order binding constant. N_a is considered to be a constant. We rewrite the last two terms in Eq. 47 as

$$(k'_{-2}/c_a)(N_{10}/V)N_a - (k'_2/c_a)(N_{1D}/V)N_a.$$

Then Eq. 47 becomes, if we divide by N_a ,

$$d(N_{1D}/N_a)/dt = k_1 - k_{-1} c_{1D} + k_{-2} c_{10} - k_2 c_{1D}, \quad (48)$$

where we have defined

$$k_{-2} \equiv k'_{-2}/c_a, \quad k_2 \equiv k'_2/c_a. \quad (49)$$

Eq. 48 is a "working" equation, on a per polymer molecule basis (1). The left-hand side can also be written as $d(c_{1D}/c_a)/dt$. It is seen that "normalization" with c_a is necessary in the definition of $k_{\pm 2}$, because of the per polymer molecule basis being used. The same is of course true for $k_{\pm 3}$. These four constants ($k_{\pm 2}$, $k_{\pm 3}$) become larger relative to k_{-1} if c_a is small.

In summary, in Fig. 1, k_1 is a first-order constant, whereas k_{-1} , $k_{\pm 2}$, and $k_{\pm 3}$ are second-order constants (of two different types). Consequently, in Eqs. 3 and 4 (Fig. 2), α_2 is first order and α_{-2} is second order. Also, in Eqs. 43–45 (Fig. 3), α_2 is first order and α_{-2} , γ , and γ_- are second order. The values of γ and γ_- depend on c_a (Eq. 49). Of course, $\beta_{\pm 2}$ have the same properties as $\alpha_{\pm 2}$.

The definition of the r 's in Fig. 1 *a* is more straightforward, because pure solution reactions do not have to be normalized relative to polymer, as above. Again considering polymer end 1 only, the terminal monomer in the polymer can be in state Λ_T , $\Lambda_{D,p}$, or Λ_D . Correspondingly,

we subdivide N_a as follows:

$$N_a = M_T + M_{DP} + M_D. \quad (50)$$

The rate equation for M_T suffices for our purposes:

$$dM_T/dt = r_1^* c_{1T} M_D - r_{-1} M_T + r_{-2} M_{DP} - r_2 M_T. \quad (51)$$

It is obvious from this equation that, in Fig. 1 *a*, r_{-1} , $r_{\pm 2}$, and $r_{\pm 3}$ are first-order rate constants, whereas r_1^* is second order and $r_1 \equiv r_1^* c_{1T}$ is pseudo first order. Thus, all of the r 's in Eqs. 1 and 2 are first order; hence α_1 (or β_1) is second order and α_{-1} (or β_{-1}) is first order.

Finally, we consider the r 's in the Brenner-Korn mechanism (7) in Fig. 1 *b*. Because of the hybrid aspect of this case, we need to use features from both Eqs. 47 and 51. The nature of all the rate constants can be seen from the two rate equations

$$dN_{1DP}/dt = r_1' N_{1T} - r_{-1}' N_{1DP} + r_{-2} M_{DP} - r_2 c_{1DP} M_D \quad (52)$$

$$dM_{DP}/dt = r_2 c_{1DP} M_D - r_{-2} M_{DP} + r_{-3} M_D - r_3 M_{DP}, \quad (53)$$

where $M_D + M_{DP} = N_a$. All of these rate constants are first order except r_2 . We now define

$$r_{-1} \equiv r_{-1}'/c_a, \quad r_1^* \equiv r_1'/c_a, \quad r_1 \equiv r_1^* c_{1T}. \quad (54)$$

Then, on dividing by N_a , Eqs. 52 and 53 become

$$d(N_{1DP}/N_a)/dt = r_1 - r_{-1} c_{1DP} + r_{-2} (M_{DP}/N_a) - r_2 c_{1DP} \quad (55)$$

$$d(M_{DP}/N_a)/dt = r_2 c_{1DP} - r_{-2} (M_{DP}/N_a) + r_{-3} - r_3 (M_{DP}/N_a), \quad (56)$$

where we have simplified a little by using $M_D/N_a \approx 1$ (recall that $\Lambda_{D,P}$ on the polymer end is assumed here to be a transient intermediate). Thus, in Eqs. 1 and 2 for this case, r_{-1} and r_2 are second order but all the other r 's are first order. Also, α_1 (and β_1) are second order and α_{-1} (and β_{-1}) are first order.

Steady-State Kinetics

We turn now to the kinetic scheme in Fig. 3, with rate constants given by Eqs. 1, 2, and 43–45. We ignore the negligible effects of finite N here; these effects are important only for the polymer length distribution, and related topics (see below). The polymer is considered essentially infinite in length.

The rate constants in Fig. 3 are interrelated by (1)

$$\alpha_1/\alpha_{-1} = \beta_1/\beta_{-1}, \quad \alpha_2/\alpha_{-2} = \beta_2/\beta_{-2} \quad (57)$$

$$\alpha_1 \alpha_2 \gamma / \alpha_{-1} \alpha_{-2} \gamma_{-} = \beta_1 \beta_2 \gamma / \beta_{-1} \beta_{-2} \gamma_{-} = e^{X/RT}, \quad (58)$$

where the thermodynamic force X (free energy of hydrolysis of NTP) is determined by ligand concentrations, as follows:

$$X = \mu_T - \mu_D - \mu_P$$

$$\mu_i = \mu_i^0 + RT \ln c_i \quad (i = T, D, P). \quad (59)$$

The net mean rate of addition of monomers to ends 1 and 2, per polymer molecule, are, respectively.

$$dn_1/dt = \alpha_1 c_{1T} - \alpha_{-1} + \alpha_{-2} c_{1D} - \alpha_2 \quad (60)$$

$$dn_2/dt = \beta_1 c_{1T} - \beta_{-1} + \beta_{-2} c_{1D} - \beta_2. \quad (61)$$

The rate equations for the numbers of monomers in solution, N_{1D} and N_{1T} , per polymer molecule, are

$$d(N_{1D}/N_a)/dt = \alpha_2 + \beta_2 - (\alpha_{-2} + \beta_{-2})c_{1D} + \gamma_- c_{1T} - \gamma c_{1D} \quad (62)$$

$$d(N_{1T}/N_a)/dt = \alpha_{-1} + \beta_{-1} - (\alpha_1 + \beta_1)c_{1T} + \gamma c_{1D} - \gamma_- c_{1T}. \quad (63)$$

At steady state, the sum of the right-hand sides of Eqs. 60 and 61 is equal to zero, as are the separate right-hand sides of Eqs. 62 and 63. This provides three equations in the two unknowns c_{1D}^∞ and c_{1T}^∞ ; one equation is redundant. The superscript “ ∞ ” refers to infinite-length polymer at steady state (as, for example, in Eq. 17). Though total polymer growth is zero at steady state, one end may grow at the expense of the other (9, 10). We therefore define the “monomer flux,” at steady state, per polymer molecule, by

$$J_m = dn_1/dt = -dn_2/dt. \quad (64)$$

We find for the steady-state c_{1D}^∞ and c_{1T}^∞ ,

$$c_{1D}^\infty = [(\alpha_1 + \beta_1)(\alpha_2 + \beta_2) + \gamma_- \Sigma_{\text{off}}]/\Sigma \quad (65)$$

$$c_{1T}^\infty = [(\alpha_{-1} + \beta_{-1})(\alpha_{-2} + \beta_{-2}) + \gamma \Sigma_{\text{off}}]/\Sigma, \quad (66)$$

where Σ_{off} was introduced in Eq. 17 and

$$\Sigma = (\alpha_1 + \beta_1)(\alpha_{-2} + \beta_{-2}) + \gamma(\alpha_1 + \beta_1) + \gamma_-(\alpha_{-2} + \beta_{-2}). \quad (67)$$

At equilibrium ($X = 0$),

$$c_{1D}^\infty = \alpha_2/\alpha_{-2} = \beta_2/\beta_{-2}, \quad c_{1T}^\infty = \alpha_{-1}/\alpha_1 = \beta_{-1}/\beta_1, \quad c_{1T}^\infty/c_{1D}^\infty = \gamma/\gamma_-. \quad (68)$$

When Eqs. 65 and 66 are substituted into Eq. 60 to obtain the monomer flux J_m , the result can be written in the form (1)

$$J_m = \gamma(\alpha_1\beta_2 - \alpha_2\beta_1)(1 - e^{-X/RT})/\Sigma. \quad (69)$$

The steady-state NTP flux J_T , per polymer molecule, can be found most simply from $\gamma c_{1D} - \gamma_- c_{1T}$. Using Eqs. 65 and 66, we find that

$$J_T = \gamma(\alpha_1 + \beta_1)(\alpha_2 + \beta_2)(1 - e^{-X/RT})/\Sigma. \quad (70)$$

The kinetic “efficiency” (1), $\eta \equiv J_m/J_T$, is simply

$$\eta = (\alpha_1\beta_2 - \alpha_2\beta_1)/(\alpha_1 + \beta_1)(\alpha_2 + \beta_2), \quad (71)$$

as for a two-state cycle (1).

We define (9, 10) a parameter s by J_m/Σ_{off} . Thus

$$s = \gamma(\alpha_1\beta_2 - \alpha_2\beta_1)(1 - e^{-X/RT})/\Sigma\Sigma_{\text{off}}. \quad (72)$$

All of the above results resemble closely the corresponding two-state cycle properties derived in reference 1, so we omit much discussion.

The most important special case is no doubt the one-way cycle (X large; γ_- , α_{-1} , β_{-1} , α_{-2} , β_{-2} negligible):

$$c_{1D}^{\infty} = (\alpha_2 + \beta_2)/\gamma, \quad c_{1T}^{\infty} = (\alpha_2 + \beta_2)/(\alpha_1 + \beta_1) \quad (73)$$

$$c_{1T}^{\infty}/c_{1D}^{\infty} = \gamma/(\alpha_1 + \beta_1) \quad (74)$$

$$J_m = (\alpha_1\beta_2 - \alpha_2\beta_1)/(\alpha_1 + \beta_1) \quad (75)$$

$$J_T = \alpha_2 + \beta_2 \quad (76)$$

$$\eta = s = (\alpha_1\beta_2 - \alpha_2\beta_1)/(\alpha_1 + \beta_1)(\alpha_2 + \beta_2). \quad (77)$$

These results are the same as for a one-way two-state cycle (1), except that c_{1D}^{∞} may not be negligible and appears here explicitly. If we use the values (16) $c_{1D}^{\infty}/c_{1T}^{\infty} = 0.0057$ at equilibrium and 0.1 at steady-state, we deduce, from Eqs. 68 and 74, that

$$\gamma = 175\gamma_- = 10(\alpha_1 + \beta_1). \quad (78)$$

The ratio $c_{1T}^{\infty}/c_{1D}^{\infty}$ in Eq. 74 might just possibly be used to distinguish between the mechanisms in Figs. 1 *a* and *b*. If Fig. 1 *a* is correct, $c_{1T}^{\infty}/c_{1D}^{\infty} \sim 1/c_a$, because $\gamma \sim 1/c_a$ (Eqs. 44 and 49). If Fig. 1 *b* is correct, $c_{1T}^{\infty}/c_{1D}^{\infty}$ should be independent of polymer concentration, because $\alpha_1 + \beta_1 \sim 1/c_a$ also (Eqs. 1 and 54). Incidentally, in a third mechanism in which, in Fig. 1 *b*, $\Lambda_{D,P}$ is an important solution species in place of Λ_T , we would again have $c_{1DP}^{\infty}/c_{1D}^{\infty} \sim 1/c_a$ (as in Fig. 1 *a*).

Free Energy Levels and Dissipation

Following the discussion in reference 1, as one goes around the three-state cycle in Fig. 3 in the dominant (clockwise) direction, in the order $\Lambda_T(s)$, Λ_D (end 1 or 2), $\Lambda_D(s)$, $\Lambda_T(s)$ ($s = \text{solution}$), the respective basic free energy levels (11) are

$$\mu_{AT}^0, \mu_{AD} + \mu_P, \mu_{AD}^0 + \mu_P, \mu_{AT}^0 - X, \quad (79)$$

and the respective gross free energy levels (11) are

$$\begin{aligned} \mu_{AT}^0 + RT \ln c_{1T}^{\infty}, \mu_{AD} + \mu_P, \mu_{AD}^0 + RT \ln c_{1D}^{\infty} + \mu_P, \\ \mu_{AT}^0 + RT \ln c_{1T}^{\infty} - X, \end{aligned} \quad (80)$$

where μ_P and X are defined in Eq. 59, μ_{AT}^0 and μ_{AD}^0 refer to monomer in solution, and μ_{AD} refers to monomer in the infinite polymer. Successive basic free energy level differences are related to rate constant ratios (1, 11):

$$\begin{aligned} RT \ln (\alpha_1/\alpha_{-1}) &= RT \ln (\beta_1/\beta_{-1}) = \mu_{AT}^0 - (\mu_{AD} + \mu_P) \\ RT \ln (\alpha_2/\alpha_{-2}) &= RT \ln (\beta_2/\beta_{-2}) = \mu_{AD} - \mu_{AD}^0 \\ RT \ln (\gamma/\gamma_-) &= (\mu_{AD}^0 + \mu_P) - (\mu_{AT}^0 - X). \end{aligned} \quad (81)$$

On adding these equations, we recover Eq. 58.

We omit the details but, just as in reference 1, it is easy to show that the total rate of free

energy dissipation, namely, the sum over the five transition pairs ij in Fig. 3 of the product $J_{ij}\Delta\mu_{ij}$, where J_{ij} is the net transition flux and $\Delta\mu_{ij}$ is the corresponding gross free energy level difference from Eq. 80, is equal to $J_T X$. This verifies (1) that there is no transduction of any of the ATP free energy into another form of free energy in this model.

Again, if the polymer molecules are attached to a surface at, say, end 2, then all the β 's above (and below) would be set equal to zero.

Concentration Dependences of Rate Constants

We see from Fig. 1 *a* or *b* that (1)

$$k_{-2} \sim c_D, \quad k_3 \sim c_T, \quad r_{-3} \sim c_P. \quad (82)$$

Consequently, in either case, from Eqs. 1, 2, and 43–45, the only ligand concentration-dependent rate constants in Fig. 3 are $\alpha_{-1} \sim c_P$, $\beta_{-1} \sim c_P$, and γ, γ_- , which have dependences of the form

$$\gamma \sim c_T/(Ac_D + Bc_T), \quad \gamma_- \sim c_D/(Ac_D + Bc_T). \quad (83)$$

Note that these relations are consistent with Eqs. 58 and 59: $e^{X/RT} \sim c_T/c_P c_D$. Some of these results could become significant experimentally if wide variations in c_T, c_P , and/or c_D are used.

Polymer Length Distribution

Eqs. 7–12 apply, unchanged, to the present problem (three-state cycle). Of course, γ and γ_- are independent of N because they refer to monomers in solution. In Eq. 14, $[N + 1]$ is the same here as in Eq. 13, but $[N]c$ becomes

$$[\alpha_1(N) + \beta_1(N)]c_{1T} + (\alpha_{-2} + \beta_{-2})c_{1D}. \quad (84)$$

These respective concentrations are near to but less than c_{1T}^∞ and c_{1D}^∞ (for a finite but fairly large \bar{N}). The fact that two concentrations appear in Eq. 84, instead of one, introduces some complications.

Summation of Eq. 14 over N gives

$$(\bar{\alpha}_1 + \bar{\beta}_1)c_{1T} + (\alpha_{-2} + \beta_{-2})c_{1D} = \bar{\alpha}_2 + \bar{\beta}_2 + \bar{\alpha}_{-1} + \bar{\beta}_{-1}. \quad (85)$$

For the infinite polymer (Eqs. 60 and 61),

$$(\alpha_1 + \beta_1)c_{1T}^\infty + (\alpha_{-2} + \beta_{-2})c_{1D}^\infty = \alpha_2 + \beta_2 + \alpha_{-1} + \beta_{-1}. \quad (86)$$

Also, Eqs. 65 and 66 apply to the finite polymer, as well as to the infinite polymer, if we use mean rate constants on the right-hand sides and c_{1D} and c_{1T} on the left. This follows because the analogues of Eqs. 60–63 can be written for the finite polymer case.

The procedure to find P_N is essentially the same as that already used in section 2, so we pass directly to the final result, corresponding to Eq. 26:

$$P_N = [\ln(1/w)]^{nx+1} N^{nx} w^N / \Gamma(nx + 1), \quad (87)$$

for \bar{N} large, as usual, where

$$w = [(\alpha_1 + \beta_1)c_{1T} + (\alpha_{-2} + \beta_{-2})c_{1D}] / [(\alpha_1 + \beta_1)c_{1T}^\infty + (\alpha_{-2} + \beta_{-2})c_{1D}^\infty] \quad (88)$$

$$x = 1 + \frac{[\alpha_1(1 - g_\alpha) + \beta_1(1 - g_\beta)]c_{1T}}{(\alpha_1 + \beta_1)c_{1T} + (\alpha_{-2} + \beta_{-2})c_{1D}} - \frac{\alpha_{-1}(1 - g_\alpha) + \beta_{-1}(1 - g_\beta)}{(\alpha_1 + \beta_1)c_{1T}^\infty + (\alpha_{-2} + \beta_{-2})c_{1D}^\infty}. \quad (89)$$

This distribution, P_N , given by Eq. 87, has the same shape (N -dependence) as in Eq. 26 (two state, steady state) or Eq. 5 (equilibrium). This shape is shown in Fig. 4 of reference 1. However, the parameters of the distribution are different here. In place of c/c_∞ in Eq. 26 we now have w (which involves c_{1T} , c_{1D} , c_{1T}^∞ , and c_{1D}^∞). Also, the parameter x in Eq. 89 has a new and more elaborate definition than in Eq. 27.

The complication referred to above is that c_{1T} and c_{1D} can be calculated from the mean rate constants and Eqs. 65 and 66, as already mentioned, but the mean rate constants themselves (see below) are found from P_N which depends on c_{1T} and c_{1D} through w and x . Thus, a numerical iteration procedure would be needed to calculate c_{1T} and c_{1D} , given the sum $c_{1T} + c_{1D}$ (which is experimentally adjustable) and the "infinite" rate constants.

In Eqs. 32–35, we of course have to use x from Eq. 89 and replace c_∞/c by $1/w$.

At equilibrium ($X = 0$),

$$\begin{aligned} w &= c_{1T}/c_{1T}^\infty = c_{1D}/c_{1D}^\infty \\ c_{1T}/c_{1D} &= c_{1T}^\infty/c_{1D}^\infty = \gamma/\gamma_- \\ x &= 1. \end{aligned} \quad (90)$$

Note also that $x = 1$ if $g_\alpha = g_\beta = 1$.

In the important one-way cycle special case, $w = c_{1T}/c_{1T}^\infty$ and x is given by Eq. 31, just as for a two-state one-way cycle. Also,

$$\begin{aligned} c_{1D} &= (\bar{\alpha}_2 + \bar{\beta}_2)/\gamma, \quad c_{1T} = (\bar{\alpha}_2 + \bar{\beta}_2)/(\bar{\alpha}_1 + \bar{\beta}_1) \\ c_{1T}/c_{1D} &= \gamma/(\bar{\alpha}_1 + \bar{\beta}_1). \end{aligned} \quad (91)$$

The mean rate constants are determined by Eqs. 39 and 40, with the understanding that x is defined by Eq. 89 and c/c_∞ is to be replaced by w in Eq. 88. In the one-way cycle case,

$$\bar{\alpha}_1 = \alpha_1(c_{1T}/c_{1T}^\infty)^{-(1-g_\alpha)/x}, \quad \bar{\beta}_1 = \beta_1(c_{1T}/c_{1T}^\infty)^{-(1-g_\beta)/x} \quad (92)$$

$$\bar{\alpha}_2 = \alpha_2(c_{1T}/c_{1T}^\infty)^{1/x}, \quad \bar{\beta}_2 = \beta_2(c_{1T}/c_{1T}^\infty)^{1/x}, \quad (93)$$

with x here given by Eq. 31. From Eqs. 91 and 93,

$$c_{1D}/c_{1D}^\infty = (c_{1T}/c_{1T}^\infty)^{1/x}. \quad (94)$$

Thus, in this case, it is easy to calculate c_{1D} and c_{1T} , given, say, $c_{1D} + c_{1T}$ and the properties of the infinite polymer. Because $1 \leq x \leq 2$ (Eq. 31),

$$c_{1D}/c_{1D}^\infty \geq c_{1T}/c_{1T}^\infty. \quad (95)$$

4. FLUCTUATIONS IN THE LENGTH DISTRIBUTION

In this section we consider a quite different question, which is more general than the present problem. But we shall apply the general results to our particular problem. Suppose P_N is the normalized probability of observing N for for a given polymer or system. For an infinitely

large ensemble of systems, P_N would be the fraction of systems in the ensemble with N . The mean of the distribution P_N is \bar{N} and the variance is $\overline{N^2} - \bar{N}^2$. Eqs. 26, 32, and 33 provide examples. Now in a particular experiment (15), suppose only a finite sample M of these polymers or systems is observed; say $M = 200$ or 300 rather than $M = \infty$. In this sample, let the number of systems with k be M_k (we use k as the index for the finite sample M , and N as the same index for the "true" or $M = \infty$ distribution). Let \mathbf{M} represent the complete set of numbers M_k ($\sum_k M_k = M$). For the set \mathbf{M} , the mean and variance are denoted \bar{k} and v . A practical question is: how much are \bar{k} and v likely to differ from \bar{N} and $\overline{N^2} - \bar{N}^2$, respectively? It seems unlikely that these questions are new. We merely sketch the necessary derivations.

For a sample of size M , the normalized probability of observing the particular set \mathbf{M} is

$$p(\mathbf{M}) = M! \prod_k P_k^{M_k} / \prod_k M_k! \quad (96)$$

If M_k , M_k^2 , etc., are averaged over all sets \mathbf{M} , we find the well-known results

$$\overline{M_k} = \sum_{\mathbf{M}} M_k p(\mathbf{M}) = M P_k \quad (97)$$

$$\overline{M_k^2} = M P_k + M(M-1) P_k^2 \quad (98)$$

$$\overline{M_k M_l} = M(M-1) P_k P_l \quad (k \neq l) \quad (99)$$

etc.

To answer the first question above, we average $(\bar{k} - \bar{N})^2$ over all sets \mathbf{M} :

$$\sum_{\mathbf{M}} p(\mathbf{M}) \left(\sum_k k \frac{M_k}{M} - \bar{N} \right)^2 = \sum_{k,l} kl \frac{\overline{M_k M_l}}{M^2} - \bar{N}^2.$$

The sum is over all k and l . We can use the expression in Eq. 99 in this sum, but there is an extra contribution $M P_k$ from Eq. 98 when $k = l$. Thus we find

$$\overline{(\bar{k} - \bar{N})^2} = (\overline{N^2} - \bar{N}^2) / M. \quad (100)$$

This is the simple final result for the mean value \bar{k} . In our polymer example, Eq. 32,

$$\overline{(\bar{k} - \bar{N})^2} / \bar{N}^2 = 1 / (nx + 1) M. \quad (101)$$

Thus, if $M = 200$ and $nx = 5$, the root-mean-square deviation of \bar{k} from \bar{N} is $0.029\bar{N}$.

Turning now to the variance, we first calculate the mean of $v(\mathbf{M})$, averaged over all sets \mathbf{M} :

$$\begin{aligned} \bar{v} &= \sum_{\mathbf{M}} p(\mathbf{M}) \left[\sum_k \frac{M_k}{M} k^2 - \left(\sum_k \frac{M_k}{M} k \right)^2 \right] \\ &= \overline{N^2} - \sum_{k,l} kl \frac{\overline{M_k M_l}}{M^2} \end{aligned} \quad (102)$$

$$= [(M-1)/M] (\overline{N^2} - \bar{N}^2). \quad (103)$$

Our primary interest is not in \bar{v} itself but in the variance in the variance, $\overline{v^2} - \bar{v}^2$. For this, we need $\overline{v^2}$:

$$\overline{v^2} = \sum_{k,l} k^2 l^2 \frac{\overline{M_k M_l}}{M^2} - 2 \sum_{k,l,m} k^2 l m \frac{\overline{M_k M_l M_m}}{M^3} + \sum_{k,l,m,n} k l m n \frac{\overline{M_k M_l M_m M_n}}{M^4}. \quad (104)$$

These sums are handled essentially as above (though they are more complicated), taking due care whenever two or more indices are equal. We find for the three sums:

$$\sum_{kl} = \frac{(M-1)}{M} (\overline{N^2})^2 + \frac{1}{M} \overline{N^4} \quad (105)$$

$$\sum_{klm} = \frac{(M-1)(M-2)}{M^2} \overline{N^2} \overline{N^2} + \frac{2(M-1)}{M^2} \overline{N^3} \overline{N} + \frac{(M-1)}{M^2} (\overline{N^2})^2 + \frac{1}{M^2} \overline{N^4} \quad (106)$$

$$\begin{aligned} \sum_{klmn} = & \frac{(M-1)(M-2)(M-3)}{M^3} (\overline{N})^4 + \frac{6(M-1)(M-2)}{M^3} \overline{N^2} \overline{N^2} \\ & + \frac{4(M-1)}{M^3} \overline{N^3} \overline{N} + \frac{3(M-1)}{M^3} (\overline{N^2})^2 + \frac{1}{M^3} \overline{N^4}. \quad (107) \end{aligned}$$

The final result can be put in the relatively compact form (for $M \geq 3$)

$$\overline{v^2} - \bar{v}^2 = M^{-1} (1 - M^{-1})^2 (\overline{N - \bar{N}})^4 - M^{-1} (1 - M^{-1}) (1 - 3M^{-1}) [(\overline{N - \bar{N}})^2]^2 \quad (108)$$

$$\approx M^{-1} \{(\overline{N - \bar{N}})^4 - [(\overline{N - \bar{N}^2})]^2\}. \quad (109)$$

Using the distribution in Eq. 32,

$$\frac{\overline{v^2} - \bar{v}^2}{\bar{v}^2} = \frac{2M^{-1}[nx + 4] - M^{-1}(nx + 7) + 3M^{-2}}{(1 - M^{-1})^2(nx + 1)} \quad (110)$$

$$\approx 2M^{-1}(nx + 4)/(nx + 1). \quad (111)$$

For example, if $M = 200$ and $nx = 5$, the root-mean-square deviation from \bar{v} is $0.015 \bar{v} = 0.015 (\overline{N^2} - \bar{N}^2)$.

A final deviation we consider, from the true P_N , is the average over all sets \mathbf{M} of $\sum_k (M_k - MP_k)^2$. This is the sum of the squares of the differences, over the entire distribution (all k), between each M_k and the corresponding "true" value MP_k . This average is easily found to be

$$\sum_{\mathbf{M}} p(\mathbf{M}) \sum_k (M_k - MP_k)^2 = M \left(1 - \sum_k P_k^2 \right). \quad (112)$$

To normalize, both sides of the equation should be divided by M^2 , because the absolute magnitude of the deviation $M_k - MP_k$ should be compared with MP_k , the sum of which over k is M .

With the distribution in Eq. 32, we find

$$\sum_k P_k^2 = \Gamma(2nx + 1) \ln(c_\infty/c) / \Gamma(nx + 1)^2 2^{2nx+1}. \quad (113)$$

Because $\ln(c_\infty/c)$ is a small quantity, this sum is negligible in Eq. 112. For example, if $nx = 5$, $\sum_k P_k^2 = 0.123 \ln(c_\infty/c)$. Thus the right-hand side of Eq. 112 becomes M .

Effect of Polymer-Polymer Interactions on $P(N)$

This is essentially an appendix. In this paper and in the previous one (1) we have assumed that the polymer concentration is so low that these aggregates are independent of each other. Here we examine the first-order effect of hard polymer-polymer interactions on the aggregation by taking into account the second virial coefficient. We treat the equilibrium problem only; the general steady-state problem is much more difficult (4).

We denote the equilibrium polymer distribution (Eq. 5) at very low polymer concentration ($c_a \rightarrow 0$) by P_N^0 , with mean \bar{N}^0 and variance $\bar{N}^{20} - (\bar{N}^0)^2$ (Eqs. 32 and 33, with $x = 1$). The polymers are considered to be long hard right cylinders with fixed diameter d and variable length l (proportional to N). Onsager (17) showed that the second virial coefficient between two such cylinders, of lengths l_1 and l_2 , is $B(l_1, l_2) = (\pi d/4)l_1 l_2$, if $l_1, l_2 \gg d$. We shall write this as $B_{NN'} = \kappa NN'$, for two aggregates with N and N' monomers.

The distribution P_N , to the linear term in c_a , is then given by (18, 19)

$$P_N = P_N^0 \left[1 + 2c_a \left(B - \sum_{N'} B_{NN'} P_{N'}^0 \right) + \dots \right] \quad (114)$$

$$B = \sum_{N, N'} B_{NN'} P_N^0 P_{N'}^0. \quad (115)$$

In our case, Eq. 5, we find easily

$$B = \kappa (\bar{N}^0)^2 = \kappa (n+1)^2 / \ln^2(c_\infty/c) \quad (116)$$

$$P_N = P_N^0 \{ 1 + 2Bc_a [1 - (N/\bar{N}^0)] + \dots \} \quad (117)$$

$$\bar{N} = \bar{N}^0 \left(1 - \frac{2Bc_a}{n+1} + \dots \right) \quad (118)$$

$$\bar{N}^2 - \bar{N}^2 = [\bar{N}^{20} - (\bar{N}^0)^2] \left(1 - \frac{4Bc_a}{n+1} + \dots \right). \quad (119)$$

Both the mean and the variance of P_N are smaller than for P_N^0 , owing to the hard interactions between aggregates. But the effective n that would be calculated from Eq. 32 (with $x = 1$) is not changed.

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