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A THEORETICAL STUDY OF COOPERATIVE DUAL LINEAR AGGREGATION AND THE VERNIER EFFECT

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An introductory theoretical study is presented of cooperative dual linear aggregation, originating from a surface. That is, two kinds of molecules aggregate in side-by-side strands; lateral interactions cause the aggregation in the two strands to be cooperative. The vernier effect is a special case that is given particular attention: if the two kinds of molecules have different lengths, there will be certain combinations of numbers of molecules that will give the two strands the same length (a 'vernier structure'). Such a structure has extra thermodynamic and kinetic stability, literally because there are no loose ends. The increased lifetime of a vernier structure is, however, not very impressive unless some additional feature is incorporated into the model to enhance further such a structure. Aligned multi-stranded tubular aggregates are also discussed.

1. Introduction

A well-known problem in biophysics is the fact that some linear biopolymers seem to know when to stop growing. One suggestion, in the case of side-by-side dual linear aggregation of two components of different lengths, is that a vernier effect [1] may operate to terminate the growth. That is, growth will cease, because of extra stability, when the two adjacent aggregates happen to achieve exactly the same length.

Dual linear aggregation is in any case a problem of some general intrinsic interest. This paper considers some aspects of this problem, including the vernier effect. To anticipate: it is found that a simple vernier effect is probably inadequate for the purpose mentioned; some special source of extra stability needs to be involved at the 'vernier length.'

2. Simple dual aggregation

In this model, two species of monomers, 1 and 2, at concentrations c_1 and c_2, form a side-by-side linear aggregate at a nucleating site on a surface, as shown in fig. 1. The molecules (or subunits) usually have different lengths, $l_2 = 1$ (2 is assigned unit length and is always longer, if the lengths are unequal) and $l_1 \leqslant 1$. We always take l_1 to be a ratio of integers, i_2/i_1 ($l_1 = 2/3$ in fig. 1). The ratio $l_2/l_1 = i_1/i_2$ is denoted l and is used to designate the different cases (fig. 1 is the case $l = 3/2$). The number of molecules in strand 1 is N_1 and the number in strand 2 is N_2. The two strands have the same length if $N_1 l_1 = N_2 l_2$, i.e., if $N_1 : N_2 = i_1 : i_2$, $2i_1 : 2i_2$, etc. It is assumed that the two strands are continuous: there are no subunit vacancies. The strands might wrap around each other in helical fashion, but this is not shown.

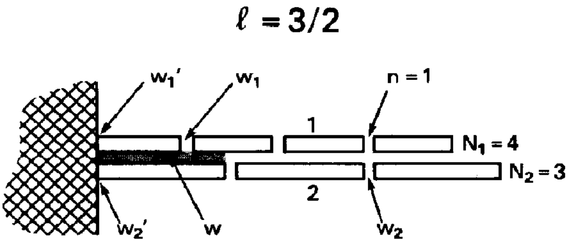

Fig. 1. Illustration of a simple dual polymer with $l = 3/2$. The interaction free energy w (see shaded area) refers to the interaction of one molecule of type 2 with the neighboring one and one-half type 1 molecules. The first vernier package is completed at $n = 1$.

The interaction free energy (fig. 1) between nearest neighbors in strand j is w_j; the interaction free energy with the surface is $w_j'(j = 1, 2)$. The lateral interaction free energy between the two strands is assumed to be simply proportional to the amount of overlap. This is measured in units of length of component 2, with a free energy w per unit, and is expressed as Nw. Thus, in fig. 1, $N = 8/3$. With this definition, N is the lesser of N_2 and N_1/l. It is convenient to define $y \equiv e^{-w/kT}$ and $y_0 \equiv y^{1/l}$. Of course w_j, w_j' and w are all negative, and $y \geqslant y_0 \geqslant 1$. In the special case $w = 0$ and $y = y_0 = 1$, the two strands aggregate independently of each other. A large value of y tends to favor vernier structures (3 : 2, 6 : 4, etc., in fig. 1) because in these structures there are no missing lateral interactions. A value $y = 1000$ corresponds to $w = -4.1$ kcal mol^{-1} at 25°C.

To avoid extra and unimportant (for present purposes) algebra, we shall take $w_j' = w_j (j = 1, 2)$, as if the nucleating site on the surface already contains a molecule of each type (or the equivalent) on which to build.

2.1. Partition function for an open system

We begin by considering the dual polymer when it is in equilibrium with monomers at concentrations c_1 and c_2 such that the polymer has a finite, though possibly large, mean size.

To introduce notation and method, let us review first the one-component special case $c_2 = 0$. The canonical partition function for strand 1 with a given size N_1 is

$$Q_{N_1} = \left(q_1 e^{-w_1/kT}\right)^{N_1}, \tag{1}$$

where q_1 is the partition function of a single subunit in the polymer (ignoring possible minor end effects). When N_1 is very large, the chemical potential of the bulk polymer (strand 1) is

$$\mu_1^\infty = -kT\, \partial \ln Q_{N_1}/\partial N_1 = -kT \ln\left(q_1 e^{-w_1/kT}\right). \tag{2}$$

The chemical potential of monomers at c_1 is

$$\mu_1 = \mu_1^0 + kT \ln c_1. \tag{3}$$

These two chemical potentials are equal, by definition, at the 'critical concentration,' $c_1 = c_1^e$. Hence,

$$c_1^e = \left(q_1 e^{-w_1/kT} e^{\mu_1^0/kT}\right)^{-1}. \tag{4}$$

Strand 1, in the presence of monomers at $c_1 < c_1^e$, is an open system with a finite mean size. The appropriate generalized partition function [2] for the open system is

$$\begin{aligned} \Upsilon &= \sum_{N_1=0}^{\infty} Q_{N_1} \lambda_1^{N_1} = \sum_{N_1=0}^{\infty} \left(q_1 e^{-w_1/kT} \lambda_1\right)^{N_1} \\ &= \sum_{N_1} x_1^{N_1} = \sum_{N_1} \left(c_1/c_1^e\right)^{N_1} \\ &= 1/(1 - x_1) = 1/\left[1 - \left(c_1/c_1^e\right)\right], \end{aligned} \tag{5}$$

where $\lambda_1 \equiv e^{\mu_1/kT}$ refers to the pool of monomers at c_1 (eq. 3) and

$$x_1 \equiv q_1 e^{-w_1/kT} \lambda_1 = \lambda_1/\lambda_1^\infty = c_1/c_1^e. \tag{6}$$

That is, x_1 is proportional to c_1. In eq. 6, $\lambda_1^\infty \equiv e^{\mu_1^\infty/kT}$ (eq. 2). The probability of a polymer of size N_1 is [2,3]

$$P_{N_1} = Q_{N_1} \lambda^{N_1}/\Upsilon = x_1^{N_1}(1 - x_1). \tag{7}$$

The mean size is $\bar{N}_1 = x_1/(1 - x_1)$. Note that $\bar{N}_1 \to \infty$ (bulk polymer) as $x_1 \to 1$ or $c_1 \to c_1^e$, as expected. Also, Υ diverges as $x_1 \to 1$.

The dual polymer of definite size N_1, N_2 has the canonical partition function

$$Q_{N_1 N_2} = \left(q_1 e^{-w_1/kT}\right)^{N_1} \left(q_2 e^{-w_2/kT}\right)^{N_2} y^N, \tag{8}$$

where (see above) $N = N_2$ if $N_1 > N_2 l$ (strand 1 is longer) or $N = N_1/l$ if $N_2 l > N_1$ (strand 2 is longer). In the former case $y^N = y^{N_2}$; in the latter case, $y^N = y_0^{N_1}$. The factor y^N arises from the free energy of interaction Nw between the two strands. The partition function for the open dual polymer, in contact with monomers at c_1, c_2, is

$$\Upsilon = \sum_{N_1, N_2 = 0}^{\infty} Q_{N_1 N_2} \lambda_1^{N_1} \lambda_2^{N_2} = \sum_{N_1, N_2} x_1^{N_1} x_2^{N_2} y^N, \tag{9}$$

where λ_2 and x_2 are defined in the same fashion as λ_1 and x_1 in eqs. 3, 5 and 6. The probability of a dual polymer of size N_1, N_2 is [2,3]

$$P_{N_1 N_2} = x_1^{N_1} x_2^{N_2} y^N / \Upsilon. \tag{10}$$

We shall see below that $P_{N_1 N_2}$ has local peaks in cases of interest at the vernier structures $N_1 : N_2 = i_1 : i_2, 2i_1 : 2i_2, \ldots$.

The simplest way to find a closed expression for Υ is the following. The terms in eq. 9 are collected into three groups, according to whether the two strands are equal in length (vernier structures), strand 2 is longer, or strand 1 is longer. The three groups produce the following respective contributions to Υ:

$$\Upsilon = \frac{1}{1 - \Pi} + \frac{R_1(x_1 y_0)}{(1 - x_2)(1 - \Pi)} + \frac{R_2(x_2 y)}{(1 - x_1)(1 - \Pi)}, \tag{11}$$

where $\Pi = x_1^{i_1} x_2^{i_2} y^{i_2}$ (this is the partition function term of the smallest vernier package in eq. 9). $R_1(x_1 y_0)$ is an always positive polynomial in $x_1 y_0$ of degree $i_1 - 1$ with coefficients that are powers of x_2, and $R_2(x_2 y)$ is an always positive polynomial in $x_2 y$ of degree $i_2 - 1$ with coefficients that are powers of x_1. An example will be given below. However, the general form of eq. 11 suffices to show that Υ diverges (the polymer becomes very large) if $x_1 \to 1$, or $x_2 \to 1$, or $\Pi \to 1$. The case of primary interest in the present context is $x_1 \ll 1$, $x_2 \ll 1$, $y \gg 1$ and $\Pi \to 1$. That is, when y is large (strong attractive interaction between the two strands), bulk dual polymer is formed ($\Pi \to 1$) even though both x_1 and $x_2 \ll 1$. In other words, the aggregation is cooperative. It is easy to confirm, using eq. 8, that the equilibrium condition

$$\mu^{\infty}(i_1, i_2 \text{ package}) = i_1 \mu_1 + i_2 \mu_2, \tag{12}$$

between bulk dual polymer and monomers, is equivalent to $\Pi = 1$. More generally (i.e., $\Pi \geqslant 1$), if $X \equiv i_1 \mu_1 + i_2 \mu_2 - \mu^{\infty}$ is the thermodynamic force driving monomers to aggregate, then $\Pi = e^{X/kT}$. At equilibrium, $X = 0$.

Cooperative aggregation, arising from lateral interactions, can also occur in one-component polymers. For example, a bundle of laterally touching actin filaments would aggregate at a lower critical concentration than would a single actin filament (see section 6).

Let us now use the case $l = 4/3$ to illustrate eq. 11. In this example $\Pi = x_1^4 x_2^3 y^3$. The first term in eq. 11 arises from all vernier terms in eq. 9: $1 + \Pi + \Pi^2 + \ldots$. The second term (strand 2 is longer) in eq. 11 represents a vernier structure of any size plus 0, 1, 2, or 3 additional molecules of type 1, together with 1, 1, 2, or 3 molecules of type 2, respectively (so that strand 2 is longer), plus any number of additional molecules of type 2. The first of the above three components in the second term contributes the factor $1/(1 - \Pi)$, the second leads to $R_1(x_1 y_0)$, and the third gives $1/(1 - x_2)$. The explicit expression for R_1 is

$$R_1 = x_2 + x_2(x_1 y_0) + x_2^2 (x_1 y_0)^2 + x_2^3 (x_1 y_0)^3. \tag{13}$$

The maximum number of type 1 molecules in R_1 is $i_1 - 1 = 3$ (in order not to make another i_1, i_2 package).

The third term (strand 1 is longer) in eq. 11 is similar. There can be any number of vernier packages plus 0, 1, or 2 (i.e., $i_2 - 1$) type 2 molecules, together with 1, 2, or 3 type 1 molecules, respectively (so that strand 1 is longer), plus any number of additional type 1 molecules. The three contributions to the third term are then $1/(1 - \Pi)$, $R_2(x_2 y)$, and $1/(1 - x_1)$, respectively, where

$$R_2 = x_1 + x_1^2 (x_2 y) + x_1^3 (x_2 y)^2. \tag{14}$$

R_1 and R_2 are found in any example with arbitrary i_1, i_2, by comparing lengths as above.

The simplest special case (the two molecules have the same length) is $l = 1/1$, $\Pi = x_1 x_2 y$, $R_1 = x_2$ and $R_2 = x_1$. If the two components are the same, $x_1 = x_2 = x$ and $\Pi = x^2 y$, this case becomes essentially the two-stranded aligned model already treated in ref. 4 (and in section 6).

The separate terms in Υ are proportional to state probabilities (eq. 10). Hence, the three terms in eq. 11 are proportional to the probability of equal strands (vernier), strand 2 is longer, or strand 1 is longer, respectively. The separate terms in R_1 and R_2 have a similar probability interpretation. Because $1 - \Pi$ appears in all three terms in eq. 11, the probability that the polymer has n complete vernier packages (irrespective of additional molecules) is $\Pi^n(1 - \Pi)$, as in eq. 7. The mean value of n, $\bar{n}$, is $\Pi/(1 - \Pi)$.

If the common factor $1/(1 - \Pi)$ is removed from the three terms in eq. 11, the remaining partition function is the same (for this model) as the 'roughness' partition function Υ_0, introduced in section 6.

In any given case, the values of $x_1^{N_1} x_2^{N_2} y^N$ in eq. 10 are easily calculated and presented in an N_1, N_2 table, as illustrated in table 1. The probability of any vernier structure $N_1 = ni_1$, $N_2 = ni_2$ relative to its four immediate neighbors in the table is easily seen to be

$$P_{N_1 N_2}/P_{N_1+1,N_2} = 1/x_1, \quad P_{N_1 N_2}/P_{N_1-1,N_2} = x_1 y_0,$$
$$P_{N_1 N_2}/P_{N_1,N_2+1} = 1/x_2, \quad P_{N_1 N_2}/P_{N_1,N_2-1} = x_2 y. \tag{15}$$

In cases of interest for the vernier problem all of these quantities are greater than unity 1. That is, any vernier structure is represented by a local peak in the probability table. The peak is symmetrical in both directions ($1/x_1 = x_1 y_0$ and $1/x_2 = x_2 y$) for the particular values $x_1 = y_0^{-1/2}$ and $x_2 = y^{-1/2}$. For this choice of x_1 and x_2, $\Pi = 1$. The example in table 1 is of this type: $l = 3/2$, $y = 1000$, $y_0 = 100$, $x_1 = 0.1$ and $x_2 = 0.03162$. Because $\Pi = 1$, table 1 continues indefinitely with a repeating pattern (Υ diverges but the relative probabilities are significant). The vernier values ($\Pi^n = 1$) are underlined. If x_1 and x_2 are chosen so that $\Pi < 1$, the table converges (the vernier values are $\Pi^n < 1$). The highest peaks in table 1 are at the vernier values but there are smaller peaks at: $N_2 = 1$, $N_1 = 1$ or 2; $N_2 = 3$, $N_1 = 4$ or 5; etc. This occurs for any choice of l: the state probability is relatively high if the two strands have almost equal lengths, though not exactly equal lengths. Because of this feature, simple vernier structures do not have the dominant uniqueness required to produce the kind of vernier effect mentioned in section 1 [1]; there is significant competition from near-vernier structures.

Table 1

Values of $x_1^{N_1} x_2^{N_2} y^N = \Upsilon P_{N_1 N_2}$ for a case [a] with $l = 3/2$

N_1	N_2				
	0	1	2	3	4
0	$\underline{1.0000}$	0.0316	0.0010		
1	0.1000	0.3162	0.0100	0.0003	
2	0.0100	0.3162	0.1000	0.0032	0.0001
3	0.0010	0.0316	$\underline{1.0000}$	0.0316	0.0010
4	0.0001	0.0032	0.1000	0.3162	0.0100
5		0.0003	0.0100	0.3162	0.1000
6			0.0010	0.0316	$\underline{1.0000}$

[a] $y = 1000$, $x_1 = y_0^{-1/2}$, $x_2 = y^{-1/2}$, $\Pi = 1$.

2.2. Rate constants and kinetics

We take the on and off first-order rate constants for a single strand (as in eqs. 1–7) to be $\alpha_1 c_1$ and β_1, respectively, for component 1 and $\alpha_2 c_2$ and β_2 for component 2. Using $\alpha_1 c_1$ and β_1 in the kinetic diagram for $N_1 = 0, 1, 2, \ldots$, at equilibrium (detailed balance), it is easy to see that $P_N \sim (\alpha_1 c_1/\beta_1)^{N_1}$. Comparison with eq. 7 shows that $x_1 = \alpha_1 c_1/\beta_1$ and $x_2 = \alpha_2 c_2/\beta_2$.

In the dual polymer, the attractive interactions between the strands must influence the on and off rate constants. We shall assume throughout the paper that the full effect of these interactions appears in the off rate constants (e.g., the on rate constants are diffusion controlled).

Let Nw be the lateral interaction free energy, as already defined, in an arbitrary state N_1, N_2. If $N_2 l \geqslant N_1$, then $N = N_1/l$; otherwise $N = N_2$. If a type 1 molecule is lost from the N_1, N_2 polymer, the value of N becomes, say, $N^{(1)}$. If now $N_2 l \geqslant N_1 - 1$, then $N^{(1)} = (N_1 - 1)/l$; otherwise $N^{(1)} = N_2$. If a type 2 molecule is lost, the value of N becomes $N^{(2)}$. If $(N_2 - 1)l \geqslant N_1$, then $N^{(2)} = N_1/l$; otherwise $N^{(2)} = N_2 - 1$. The two off rate constants are then

$$\beta_1' = \beta_1 y^{N^{(1)}-N} \text{ and } \beta_2' = \beta_2 y^{N^{(2)}-N}. \quad (16)$$

The above algorithm takes care of all possible cases except $\beta_1 = 0$ if $N_1 = 0$ and $\beta_2 = 0$ if $N_2 = 0$. The most common special cases are $\beta_1' = \beta_1$ if strand 1 is initially longer by at least one type 1 molecule, $\beta_2' = \beta_2$ if strand 2 is initially longer by at least one type 2 molecule, $\beta_1' = \beta_1/y_0$ if strand 2 is initially equal in length or longer, and $\beta_2' = \beta_2/y$ if strand 1 is initially equal in length or longer. These latter two rate constants are much reduced ($y \gg 1$) because the departing subunit must pull away from the adjacent attracting strand. There are also various 'fractional' cases (depending on l) in which only part of a molecular interaction is lost in the off transition.

In principle, one could now proceed to fill in all the rate constants in a two-dimensional kinetic diagram with states N_1, N_2 (as in table 1). If the kinetic system were allowed to come to equilibrium ($\Pi < 1$), the equilibrium distribution among states would be the same as in eq. 10 (using $x_1 = \alpha_1 c_1/\beta_1$ and $x_2 = \alpha_2 c_2/\beta_2$). However, to study transients and cases in which the polymer grows ($\Pi > 1$), it is necessary to use Monte Carlo calculations.

There are four principle steady regimes: (i) $\Pi < 1$ and equilibrium; (ii) $\Pi > 1$ with strand 1 always longer and growing faster than strand 2; (iii) $\Pi > 1$ with strand 2 always longer and growing faster than strand 1; and (iv) $\Pi > 1$ with the two strands growing together, i.e., maintaining equal lengths except for fluctuations. Regime (i) has been discussed already.

In regime (ii), the net mean subunit fluxes in the two strands are

$$J_1 = \alpha_1 c_1 - \beta_1 \text{ and } J_2 = \alpha_2 c_2 - (\beta_2/y). \quad (17)$$

The condition for strand 1 to be growing is $\alpha_1 c_1 > \beta_1$ or $x_1 > 1$. For strand 1 to be growing faster (so that strand 2 does not catch up), the condition is $J_1 > lJ_2$. This is equivalent to $z_1 > 1$, where

$$z_1 \equiv [\alpha_1 c_1 + (l\beta_2/y)]/(l\alpha_2 c_2 + \beta_1). \quad (18)$$

The term in $1/y$ is usually very small because $y \gg 1$.

In regime (iii),

$$J_1 = \alpha_1 c_1 - (\beta_1/y_0) \text{ and } J_2 = \alpha_2 c_2 - \beta_2. \quad (19)$$

The condition for strand 2 to be growing is $\alpha_2 c_2 > \beta_2$ or $x_2 > 1$. For strand 2 to be growing faster, $lJ_2 > J_1$. This is equivalent to $z_2 > 1$, where

$$z_2 \equiv [l\alpha_2 c_2 + (\beta_1/y_0)]/(\alpha_1 c_1 + l\beta_2). \quad (20)$$

For the strands to grow together, regime (iv), we need $\Pi > 1$ and also $z_1 < 1$ and $z_2 < 1$. The latter two conditions insure that whenever one strand becomes longer through a fluctuation, the other strand will, on average, grow faster and catch up. The actual rate of dual growth is not easy to express analytically except in the simple case $l = 1/1$ (see section 3). If successive pairs of N_1, N_2 values are followed (i.e., one transition at a time) in the course of a Monte Carlo simulation in a typical case of this kind (e.g., $l = 8/3$, $y \gg 1$), starting at $N_1 = 0$, $N_2 = 0$, the dual polymer is seen to increase in size stochastically but with significant pauses in the neighborhood of each vernier structure, ni_1, $ni_2 (n = 1, 2, \ldots)$, where there is extra stability. Thus, the mean rate of growth of the dual polymer is determined essentially by the mean first passage times from one vernier structure n to the next ($n + 1$ or $n - 1$).

A number of examples of the above four regimes have been followed by Monte Carlo simulation, especially for the case $l = 8/3$ and with $y = 10^3$–10^5. Both in regime (i) transients with $\Pi \leqslant 1$ and in regime (iv) with $\Pi > 1$, vernier structures ($n = 1, 2, \ldots$) do indeed exhibit the extra stability expected, but the additional lifetime spent by the kinetic system at and near the vernier structures ($n = 1$ is the most important structure for the vernier effect mentioned in section 1) does not appear to be sufficient for a particular such structure (e.g., $n = 1$) to have a good chance to be incorporated into some superstructure that would freeze the vernier structure permanently. Some additional source of stability of vernier structures seems to be needed. One possibility would be to have as a third component present in solution a ligand that binds very tightly to the end of both strands if both strands have exactly the same length. The bound ligand could then serve as a cap that prevents subunits of either type (1 or 2) from leaving or adding to the polymer. Because, in the growth process starting from $N_1 = 0$, $N_2 = 0$, the vernier structure $n = 1$ is encountered first, the cap would tend to stabilize this particular structure.

Three other mechanisms for stabilizing vernier structures, without using a third component, are discussed in section 4.

3. Simple dual aggregation with $l = 1/1$ and $l = 2/1$

The principal topic here is the intrinsically important case $l = 1/1$ (the two components have the same length). The case $l = 2/1$ will be mentioned briefly at the end of the section.

It has been pointed out already that in eq. 11, in the case $l = 1/1$, we have $R_1 = x_2$, $R_2 = x_1$, and $\Pi = x_1 x_2 y$. The aggregation is cooperative. Dual bulk polymer will form if $\Pi = x_1 x_2 y \geqslant 1$, even though $x_1 < 1$ and $x_2 < 1$.

In this case ($l = 1/1$) it is relatively simple to construct the two-dimensional kinetic diagram for the states N_1, N_2. From this one can write the master equations in $\mathrm{d}P_{N_1N_2}/\mathrm{d}t$ (for $N_1 > N_2$, $N_2 > N_1$ and $N_1 = N_2$) and then find the intuitively obvious subunit flux equations,

$$J_1 = \mathrm{d}\bar{N}_1/\mathrm{d}t = \alpha_1 c_1 - \beta_1 P_{N_2 < N_1} - (\beta_1/y) P_{N_2 \geqslant N_1}$$
$$J_2 = \mathrm{d}\bar{N}_2/\mathrm{d}t = \alpha_2 c_2 - \beta_2 P_{N_1 < N_2} - (\beta_2/y) P_{N_1 \geqslant N_2}, \tag{21}$$

where $P_{N_2 < N_1}$ is the sum of $P_{N_1 N_2}$ over all N_1 and over all $N_2 < N_1$, etc. These equations apply even in transients.

For steady dual growth of type (iv), discussed in section 2, it is of interest to find the P factors in eq. 21 in order to deduce explicit expressions for J_1 and J_2. This is easy to do using a one-dimensional kinetic diagram for the quantity $m \equiv N_2 - N_1$. This is shown in fig. 2. Although the polymer is growing, fig. 2 has a stationary solution for the probabilities p_m. That is, the tip of the growing polymer has a steady-state distribution of states m [4]. The probabilities p_m are found from the 'detailed balance' between neighboring pairs of states in the linear diagram [5]:

$$p_m = \frac{(1-z_1)(1-z_2)z_2^m}{1-z_1 z_2}, \qquad p_{-m} = \frac{(1-z_1)(1-z_2)z_1^m}{1-z_1 z_2} \qquad (m \geqslant 0) \tag{22}$$

where z_1 and z_2 are given by eqs. 18 and 20 with $l = 1$ and $y_0 = y$. We then find, for use in eq. 21,

$$P_{N_2 < N_1} = \frac{z_1(1-z_2)}{1-z_1 z_2}, \quad P_{N_1 < N_2} = \frac{z_2(1-z_1)}{1-z_1 z_2}$$
$$P_{N_2 \geqslant N_1} = \frac{1-z_1}{1-z_1 z_2}, \quad P_{N_1 \geqslant N_2} = \frac{1-z_2}{1-z_1 z_2}. \tag{23}$$

Eqs. 22 and 23 are valid provided that $z_1 < 1$ and $z_2 < 1$. Eqs. 21 become, then,

$$J_1 = \alpha_1 c_1 - \frac{\beta_1 z_1 (1-z_2)}{1-z_1 z_2} - \frac{\beta_1 (1-z_1)}{y(1-z_1 z_2)}$$
$$J_2 = \alpha_2 c_2 - \frac{\beta_2 z_2 (1-z_1)}{1-z_1 z_2} - \frac{\beta_2 (1-z_2)}{y(1-z_1 z_2)}. \tag{24}$$

The two strands in eqs. 24 ($\Pi > 1$, $z_1 < 1$, $z_2 < 1$) are in fact growing together. Hence, we should expect $J_1 = J_2$. Substitution of eqs. 18 and 20 (with $l = 1$ and $y_0 = y$) confirms this, after considerable algebra. In fact both fluxes simplify to the symmetrical expression

$$J_1 = J_2 = \frac{(\beta_1 + \beta_2)(\alpha_1 c_1 \alpha_2 c_2 y - \beta_1 \beta_2)}{y(\alpha_1 c_1 \beta_1 + \alpha_2 c_2 \beta_2) + \beta_1 \beta_2 (1+y)}. \tag{25}$$

Note that the numerator is proportional to $\Pi - 1$, i.e., to $e^{X/kT} - 1$, where X is the thermodynamic force driving aggregation of component 1, 2 pairs (see the discussion of eq. 12).

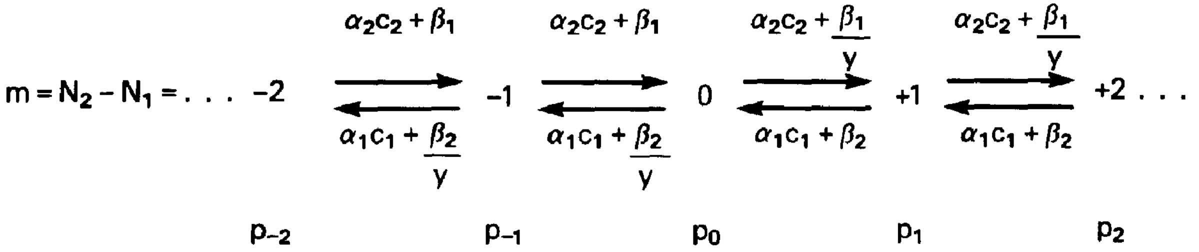

Fig. 2. State diagram, with rate constants, for $m = N_2 - N_1$ in the case of an $l = 1/1$ dual polymer, both of whose strands are growing steadily and together.

3.1. Dual aggregation in the case $l = 2/1$

This is the next simplest case, in which type 1 subunits are exactly half as long as type 2 subunits. Even for this case there seem to be only a few simple analytical results.

In the equilibrium regime, $\Pi = x_1^2 x_2 y < 1$, R_1 in eq. 11 is $x_2 + x_2(x_1 y_0)$ and R_2 is x_1, with $y_0 = y^{1/2}$. Eqs. 17–20, with $l = 2$, apply in regimes (ii) and (iii). In regime (iv), the two strands grow together, with $\Pi > 1$, $z_1 < 1$ and $z_2 < 1$. The one-dimensional kinetic diagram in $M \equiv 2N_2 - N_1$ is shown in fig. 3. The rate constants on the right and left of the figure persist at higher values of $|M|$; rate constants change only in the center of the diagram ($M = -1, 0, +1$). Fig. 3 is the analogue of fig. 2 for $l = 1/1$. The two strands have the same length at $M = 0$. There is a steady-state distribution of probability (p_M) among the states of fig. 3 even though the polymer is growing steadily. This distribution could be found numerically, by iteration, in any particular case, but a simple analytical solution probably does not exist.

The asymptotic form of p_M at large M is $p_M \sim s_2^M$, where $s_2 < 1$ for convergence. To find s_2 we equate the steady flow into an arbitrary state M with the steady flow out of this state:

$$\alpha_2 c_2 s_2^{M-2} + (\beta_1/y_0) s_2^{M-1} + \alpha_1 c_1 s_2^{M+1} + \beta_2 s_2^{M+2}$$
$$= \left[\beta_2 + \alpha_1 c_1 + (\beta_1/y_0) + \alpha_2 c_2\right] s_2^M. \qquad (26)$$

Division by s_2^{M-2} gives a quartic in s_2. One root of this is $s_2 = 1$. Factoring $s_2 - 1$ out, a cubic in s_2 remains:

$$\beta_2 s_2^3 + (\beta_2 + \alpha_1 c_1) s_2^2$$
$$- \left[\alpha_2 c_2 + (\beta_1/y_0)\right] s_2 - \alpha_2 c_2 = 0. \qquad (27)$$

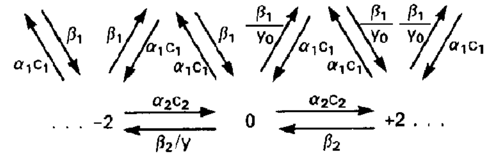

Fig. 3. State diagram, as in fig. 2, but for $M = 2N_2 - N_1$ in the case $l = 2/1$.

This determines s_2 as a function of rate constants and y_0. One root of the cubic is positive. This root approaches unity, $s_2 \to 1$, when $z_2 \to 1$, i.e., when (eq. 20)

$$2\alpha_2 c_2 + (\beta_1/y_0) \to \alpha_1 c_1 + 2\beta_2.$$

In the special case $\alpha_1 c_1 = 0$ and $\beta_1 = 0$, $s_2 = (\alpha_2 c_2/\beta_2)^{1/2}$. In the special case $\alpha_2 c_2 = 0$ and $\beta_2 = 0$, $s_2 = \beta_1/\alpha_1 c_1 y_0$.

There is a different asymptotic solution at large negative M: $p_M \sim s_1^{-M}$. The same kind of procedure leads to the cubic equation in s_1,

$$\alpha_2 c_2 s_1^3 + (\alpha_2 c_2 + \beta_1) s_1^2$$
$$- \left[\alpha_1 c_1 + (\beta_2/y)\right] s_1 - (\beta_2/y) = 0. \qquad (28)$$

The positive root $s_1 \to 1$ when $z_1 \to 1$ (eq. 18). In the special case $\alpha_1 c_1 = 0$ and $\beta_1 = 0$, $s_1 = (\beta_2/\alpha_2 c_2 y)^{1/2}$. In the special case $\alpha_2 c_2 = 0$ and $\beta_2 = 0$, $s_1 = \alpha_1 c_1/\beta_1$.

One can verify numerically that these asymptotic solutions at large $|M|$ do not persist to the center of the diagram (fig. 3).

The formal equations for the subunit fluxes, the analogues of eqs. 21, are (from fig. 3)

$$\begin{aligned} J_1 &= \alpha_1 c_1 - \beta_1 P_{M<0} - (\beta_1/y_0) P_{M\geqslant 0} \\ J_2 &= \alpha_2 c_2 - \beta_2 P_{M\geqslant 2} - (\beta_2/y_0) P_{M=1} \\ &\quad - (\beta_2/y) P_{M\leqslant 0}. \end{aligned} \qquad (29)$$

In steady growth, $J_1 = 2J_2$. However, the P terms in eqs. 29 are not available without a solution for all the p_M.

4. Dual aggregation with vernier enhancement

At the end of section 2 it was mentioned that, in simple dual aggregation, vernier structures are indeed favored as expected, but not in a very dominating way. A ligand that binds strongly to the tip of both strands of vernier structures only, essentially capping such a structure, could enhance the vernier effect considerably. In this section we discuss three other models for vernier enhancement that do not involve a third component (the ligand, above). The first of these models is actually unsatisfactory but is included for comparison. The other two models are rather similar. Kinetics and numerical results are discussed only for the third model.

4.1. Partition functions for an open system

The first model is shown schematically in fig. 4A, for the case $l = 3/2$. Both components have terminal appendages that interact with each other, with free energy $W < 0$, at each of the n vernier points in the dual polymer. This special interaction supplements the lateral interaction between strands, Nw, already introduced in section 2. We define $Y = e^{-W/kT}$. Because each vernier package in the polymer (whether there are additional subunits or not) is further stabilized by a factor $Y > 1$, eq. 11 for Υ is modified by replacing Π everywhere by ΠY. The polymer becomes very large when $\Pi Y \to 1$: the cooperativity between the two strands is stronger because of Y; the monomer concentrations needed for 'condensation' of bulk polymer are smaller. The equilibrium probability $P_{N_1 N_2}$ of a state N_1, N_2, when $\Pi Y < 1$, is $x_1^{N_1} x_2^{N_2} y^N Y^n / \Upsilon$.

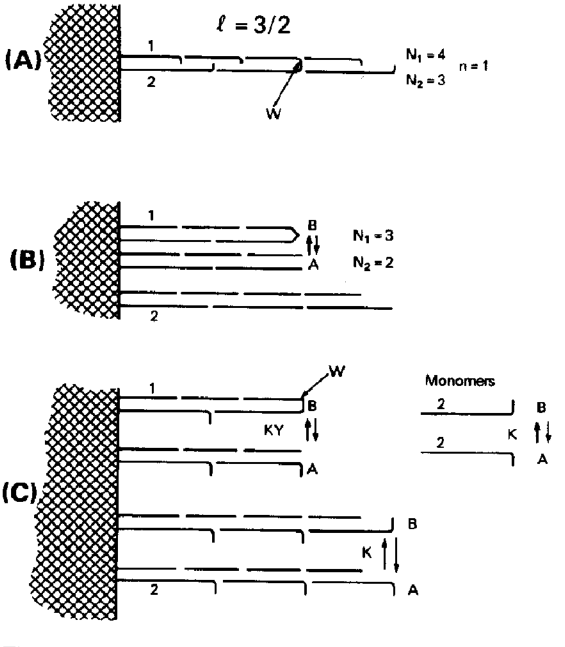

Fig. 4. (A) Model (the case $l = 3/2$ is shown) in which each vernier package has extra stability because of the interaction (W) between the aligned tips of the two components. (B) In this model the tips of the two components are flexible and can form (state B) a reversible bond, but only at the very end of the polymer (in a vernier structure). (C) A similar model in which component 2 (only) undergoes a conformational change (A ⇄ B) such that state B interacts strongly with the end of strand 1 in a vernier structure.

Although vernier packages i_1, i_2 receive extra stability in this model, this extra stability persists when additional subunits are added (e.g., the structure in fig. 4A is stabilized by a factor Y). That is, an exact vernier structure is enhanced by a factor Y relative to slightly smaller structures but not relative to slightly longer structures.

In the second model (fig. 4B) the distal tips of both components are assumed to have some flexibility, allowing a reversible bond to be formed (state B) between the two terminal subunits of a vernier structure. The bond is broken in state A. The equilibrium constant for A ⇄ B is $K \gg 1$. Because of the distortion at the subunit tips in the state B, further subunits cannot add to this state. The polymer can grow beyond a vernier structure only from state A. This model stabilizes only the final vernier package of a vernier structure. The A ⇆ B equilibrium is possible only in vernier structures. In effect, in this model, there is a reversible internal cap.

The contribution to Υ of the vernier structure $N_1 = ni_1$, $N_2 = ni_2$ (with $n \geqslant 1$) is $\Pi^{n-1} \cdot \Pi(1 + K)$ or $\Pi^n(1 + K)$. The factor $1 + K$ arises from the A ⇄ B equilibrium [5]. Hence eq. 11 becomes

$$\Upsilon = 1 + \frac{(1+K)\Pi}{1-\Pi} + \frac{R_1(x_1 y_0)}{(1-x_2)(1-\Pi)} + \frac{R_2(x_2 y)}{(1-x_1)(1-\Pi)}. \tag{30}$$

The individual state probabilities are as in eq. 10 except that each vernier structure ($n \geqslant 1$) has an extra factor $1 + K$. Thus, if K is large, the vernier structures can be very dominant in a probability table such as table 1.

The third model is similar. Type 1 molecules have no special properties but the distal end of a type 2 molecule can undergo a conformational change (A ⇄ B in fig. 4C), the main feature of which is that state B, in a vernier structure, interacts strongly (free energy $W < 0$) with the tip of strand 1. This stabilizes the vernier structure and forms a reversible internal cap (as in the second model).

Monomers of component 2 are in an A $\rightleftarrows$ B equilibrium. The concentrations are $c_{2\mathrm{A}}$ and $c_{2\mathrm{B}} = Kc_{2\mathrm{A}}$, where K is an equilibrium constant of order unity. The total concentration is $c_2 = c_{2\mathrm{A}} + c_{2\mathrm{B}}$.

Strand 2, by itself (i.e., $c_1 = 0$), has the following properties. A new monomer (A or B) can add only to a terminal subunit of the polymer that is in state A. Also, only the terminal subunit can undergo the A $\rightleftarrows$ B transitions (again with equilibrium constant K). Hence all internal subunits in strand 2 are in state A. Corresponding to eq. 5 (cf. also eq. 30), the open partition function for strand 2 alone is then

$$\Upsilon = 1 + \sum_{N_2=1}^{\infty} x_2^{N_2-1} \cdot x_2(1+K)$$

$$= 1 + \frac{(1+K)x_2}{1-x_2} = \frac{1+Kx_2}{1-x_2}, \tag{31}$$

where x_2 relates to $c_{2\mathrm{A}}$ (i.e., $x_2 = c_{2\mathrm{A}}/c_{2\mathrm{A}}^{\mathrm{e}}$) because the bulk polymer, when $x_2 \to 1$, is virtually all A.

When both strands are present, the A $\rightleftarrows$ B transition at the tip of strand 2 is possible only if strand 2 is at least as long as strand 1 (so that there is room for the structural change). If the strands have the same length (vernier structure), the A $\rightleftarrows$ B equilibrium constant is KY, where $Y = e^{-W/kT} \gg 1$. A vernier structure in state B cannot add a subunit of any type (1, 2A, 2B). A monomer of type 1 cannot add to the polymer if strand 2 is in state B and strand 2 is not longer than strand 1 by at least l_1 (otherwise there would be interference with the strand 2 tip). Similarly, a type 2 monomer in state B cannot add to the polymer unless the addition will make strand 2 at least as long as strand 1.

With this model, eq. 11 is modified to

$$\Upsilon = 1 + \frac{(1+KY)\Pi}{1-\Pi} + \frac{(1+K)R_1(x_1 y_0)}{(1-x_2)(1-\Pi)} + \frac{R_2(x_2 y)}{(1-x_1)(1-\Pi)}. \tag{32}$$

Table 2

Values of $\Upsilon P_{N_1 N_2}$ for a vernier enhanced case [a] with $l = 8/3$

N_1	N_2					
	0	1	2	3	4	5
0	1.000	0.304	0.046	0.007	0.001	
1	0.152	0.616	0.094	0.014	0.002	
2	0.023	1.249	0.190	0.029	0.004	0.001
3	0.004	0.534	0.385	0.058	0.009	0.001
4	0.001	0.081	0.780	0.119	0.018	0.003
5		0.012	1.580	0.240	0.037	0.006
6		0.002	0.285	0.487	0.074	0.011
7			0.043	0.987	0.145	0.023
8			0.007	101.000	0.304	0.046
9			0.001	0.152	0.616	0.094
10				0.023	1.249	0.190

[a] $y = 1000$, $Y = 100$, $K = 1$, $x_1 = x_2 = 0.15199$, $\Pi = 1$.

The values of K and Y have no effect on the condensation point $\Pi = 1$. Corresponding to eq. 32, the state probabilities in eq. 10 are multiplied by $1 + KY$ for vernier structures ($n \geqslant 1$) and by $1 + K$ whenever strand 2 is longer than strand 1. Because K is of order unity and $Y \gg 1$, vernier structures have unusually high probabilities.

We consider, as a numerical example, a case with $l = 8/3$ (as in ref. 1). We take as reasonable parameters $y = 1000$ (hence $y_0 = 13.34$), $Y = 100$, $K = 1$, and $x_1 = x_2 = 0.15199$. These values of x_1 and x_2 were chosen to give $\Pi = x_1^8 x_2^3 y^3 = 1$. Values of $\Upsilon P_{N_1 N_2}$ are given in table 2 for small values of N_1 and N_2. However, because $\Pi = 1$, the family of numbers between N_1, $N_2 = 0,0$ and 8,3 repeats itself between 8,3 and 16,6, between 16,6 and 24,9, etc. The vernier value of $\Upsilon P_{N_1 N_2}$ is always 101.0 ($n \geqslant 1$). Without this model's vernier enhancement (put $K = 0$), all values in table 2 above the dashed lines (strand 2 is longer) would be divided by 2 and 101.0 would become 1.0. It is apparent that vernier enhancement can produce the desired qualitative effect.

4.2. Rate constants and kinetics

The rate constants α_1 and β_1 are the same as in section 2. For component 2, we assume that α_2 and β_2 apply to both A and B conformations (but in general c_{2A} and c_{2B} are different: $c_{2B} = Kc_{2A}$). We then have $x_2 = \alpha_2 c_{2A}/\beta_2$. The new interaction parameter Y affects both β_1' and β_2' in eq. 16 (we assume Y has no effect on α_1 and α_2). Because Y applies to vernier structures only,

$$\beta_1' = \beta_1/y_0 Y \text{ and } \beta_2' = \beta_2/yY. \tag{33}$$

That is, the off rate constants are further reduced by the necessity to break the W 'bond'. For other than vernier structures, β_1' and β_2' are unchanged (eq. 16).

When strand 2 is longer, the rate constant for A → B is k_1 and for B → A is k_2. Hence $K = k_1/k_2$. When the strands have the same length, we take

$$k_1' = k_1 Y^{1/2} \text{ and } k_2' = k_2/Y^{1/2}. \tag{34}$$

This divides the free energy effect (W) equally in the two directions. We need not be concerned with A ⇄ B monomer kinetics; we assume a large equilibrium reservoir of monomers with fixed c_{2A}, c_{2B} and c_1.

Table 3

Mean first passage times for the table 2 case

(1) Parameter change	(2) Π	(3) Mean no. transitions	(4) Mean time	(5) Escape high	(6) Time ratio
0,0 → 8,3	1	574	439	0.574	4.3
Out of 8,3		496	1901		
$c_1 \times 0.8$	0.168	1001	798	0.408	2.5
		520	1997		
$c_1 \times 1.2$	4.30	293	216	0.760	8.3
		465	1796		
$c_1 \times 2.0$	256	113	78	0.977	11.4
		225	891		
$c_{2A} \times 0.5$	0.125	993	989	0.268	2.3
		557	2270		
$c_{2A} \times 2.0$	8	317	181	0.852	6.0
		327	1089		
$K = 2$	1	553	332	0.581	7.4
		636	2450		
$k_2 = 0.5$	1	384	395	0.545	5.3
		303	2091		
$Y = 200$	1	489	374	0.577	11.1
		718	4144		
$y = 2000$	8	314	239	0.735	9.0
		549	2153		
$K = 0$	1	265	454	0.578	0.28
		71	126		
$K = 0,\ y = 10^4$	1	370	1175	0.600	0.28
c_1 [a], c_{2A} [a]		102	325		
$K = 0$	1	446	750	0.570	0.21
c_1 [b], c_{2A} [b]		92	161		

[a] $c_1 = c_{2A} = 0.081113$.

[b] $c_1 = y_0^{-1/2} = 0.2738$, $c_{2A} = y^{-1/2} = 0.0316$.

The discussion of the four steady regimes in section 2 still applies here except that in eqs. 17–20 c_2 is replaced by c_{2A}. In eq. 19, $\alpha_2 c_2$ must be divided by $1 + K$ because strand 2 can receive a new monomer only when the tip of the strand is in state A; this alters $\alpha_2 c_2$ to $\alpha_2 c_{2A}$.

Some kinetic properties of the first vernier structure in a number of cases related to table 2 ($l = 8/3$) are given in table 3. The first case in table 3 is a reference case with the same thermodynamic parameters (y, Y, K, x_1, x_2) as in table 2 and in addition the kinetic parameter choices $\alpha_1 = \alpha_2 = 1$ and $\beta_1 = \beta_2 = k_2 = 1$ (in arbitrary units of time and concentration). With these choices of α_i and β_i (which are not varied), $x_1 = c_1$ and $x_2 = c_{2A}$. Thus, in the reference case, $c_1 = c_{2A} = 0.15199$. The value of k_1 is not independent: $k_1 = k_2 K$. Thus, $k_1 = 1$ in the reference case. Except for the last two cases in table 3, where several parameters are changed, other cases in the table have only one parameter change from the reference set. These changes are indicated in column (1).

For each of the 13 cases in table 3, Monte Carlo simulations were carried out to determine the number of transitions of any kind and the time required (i) for a polymer originally in state $N_1 = 0$, $N_2 = 0$ (i.e., empty aggregation sites) to reach the first vernier structure $N_1 = 8$, $N_2 = 3$ and (ii) for a polymer originally in state $N_1 = 8$, $N_2 = 3$ to escape from the neighborhood of this vernier structure (which has a free energy minimum). Each of the 26 simulations was repeated between 100 and 200 times, and averages taken.

To be more precise, in process (i) the vernier structure was considered to have been reached when the conditions $N_1 \geqslant 8$ and $N_2 \geqslant 3$ were first simultaneously satisfied. In process (ii), escape from the neighborhood of the vernier structure was deemed to have occurred when either of the conditions $N_1 + N_2 = 5$ or $N_1 + N_2 = 17$ was satisfied (note that the first vernier structure, the starting point, has $N_1 + N_2 = 11$ and the second has $N_1 + N_2 = 22$).

Column (2) in table 3 gives the value of Π for each case (recall that $\Pi > 1$ would lead to indefinite polymer growth). Columns (3) and (4) give, in the first line of each case, the mean number of transitions and the mean time required to reach state 8,3 from 0,0 (i.e., to produce the vernier structure by aggregation, starting from nothing). The second line of each case gives the mean number of transitions and the mean time during which the first vernier structure survives in its own neighborhood (in the N_1, N_2 plane) before either the polymer dissolves (approaches $N_1 = 0$, $N_2 = 0$) or approaches the second vernier structure ($N_1 = 16$, $N_2 = 6$). The longer the dual polymer survives in the neighborhood of state 8,3, the more chance the vernier structure can be incorporated into some superstructure that will confer an indefinite lifetime on the vernier structure. Most of the time spent 'in the neighborhood of' state 8,3 is actually spent at 8,3 itself: in the reference case, over a long period of time, the fraction of time spent at each of the states N_1, N_2 would be proportional to the numbers in table 2 (at and around state 8,3). In fact this feature was used in several cases to check the Monte Carlo computer program.

Column (5) records the fraction of escapes from state 8,3 that occurred on the high side ($N_1 + N_2 = 17$ was reached first). This fraction tends to be high for $\Pi > 1$ and low for $\Pi < 1$, as expected. Column (6) gives the ratio of the mean survival time at state 8,3 to the mean formation time of this state, in each case.

The parameter changes (from the reference set) in table 3 are not meant to be exhaustive but rather are designed to show the influence of each parameter. The most favorable case listed (large survival time, large ratio in the last column) is $Y = 200$. This is not surprising because Y is the principal vernier enhancing parameter.

The last three cases in the table ($K = 0$) refer to simple dual polymers without vernier enhancement (as in section 2). State B does not exist. In the next to last case, we have $K = 0$, $y = 10^4$, and $c_1 = c_{2A}$ adjusted to give $\Pi = 1$ again. This is a simple dual polymer but with stronger lateral interactions. In the last case, we return to the reference value $y = 1000$ but choose c_1 and c_{2A} as prescribed following eq. 15. These three cases without vernier enhancement ($K = 0$) are seen to be the least satisfactory in the table. Vernier enhancement again seems necessary in order to obtain desired properties.

5. A further example of dual aggregation

In this section we obtain the equilibrium open partition function Υ for another kind of dual aggregation. This model is not concerned with the vernier effect; it is suggested by virus self-assembly.

The model is presented in fig. 5. Fig. 5A shows a transverse section through the dual polymer and fig. 5B is a very schematic longitudinal picture. Molecules of the two components, 1 and 2, have the same length but in each such unit of length in the polymer there may be two molecules of component 1 that wrap around one molecule of component 2 (fig. 5A). This is a lateral version of the longitudinal $l = 2/1$ case in section 2. The lateral interaction free energies of types 1-1 and 1-2 are denoted w and u, respectively, as shown in the figure. The longitudinal interaction free energies are denoted w_1 and w_2 (fig. 5B). There are three strands in the polymer, with numbers of molecules N_{11}, N_{12} and N_2 (fig. 5B). The strands have no vacancies. The polymer is nucleated by sites on a surface.

For definite values of N_{11}, N_{12} and N_2, the canonical partition function is (cf. eq. 8)

$$Q_{N_{11}N_{12}N_2} = \left(q_1 e^{-w_1/kT}\right)^{N_{11}+N_{12}} \times \left(q_2 e^{-w_2/kT}\right)^{N_2} y^{2N} z^{M}, \tag{35}$$

where $y \equiv e^{-w/kT}$, $z \equiv e^{-u/kT}$, N is the lesser of N_{11} and N_{12}, and M is the number of 1-2 interactions ($M = 5$ in fig. 5B). The partition function for an open system (in contact with monomers at c_1 and c_2) is then

$$\Upsilon = \sum Q_{N_{11}N_{12}N_2} \lambda_1^{N_{11}+N_{12}} \lambda_2^{N_2} = \sum x_1^{N_{11}+N_{12}} x_2^{N_2} y^{2N} z^{M}, \tag{36}$$

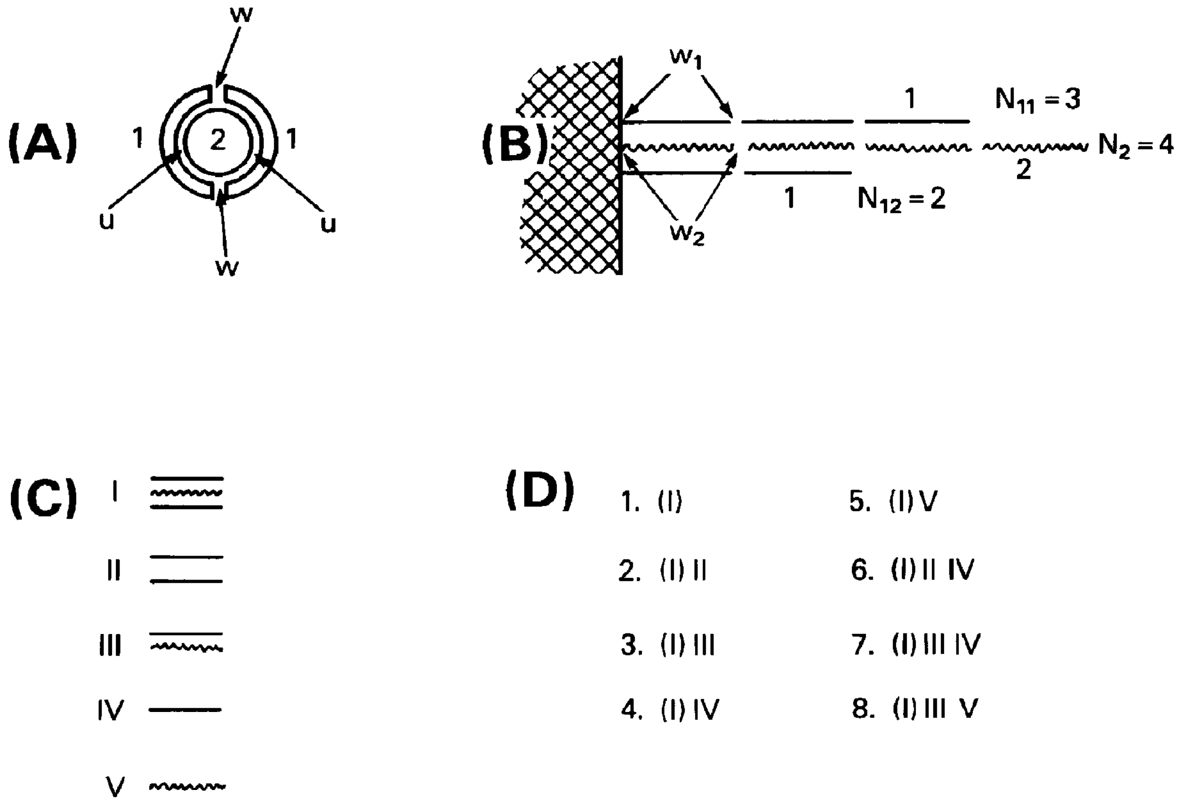

Fig. 5. (A) Transverse section in a simple dual aggregation model in which two components have the same length but each level may be comprised of two molecules of component 1 and one molecule of component 2. (B) Very schematic longitudinal diagram of the same model. (C) Possible types of combinations of molecules at any level of the polymer. (D) Possible sequences of combinations, each of which contributes a term to Υ.

where the sum is over N_{11}, N_{12} and N_2 (from 0 to ∞), and x_1 and x_2 are defined as in section 2. The probability of particular values of N_{11}, N_{12} and N_2, in the open system at equilibrium, is

$$P_{N_{11}N_{12}N_2} = x_1^{N_{11}+N_{12}} x_2^{N_2} y^{2N_2} z^{M}/\Upsilon. \tag{37}$$

The easiest way to deduce a closed expression for Υ in eq. 36 is to use a modification of the method introduced for eq. 11. At any level of the polymer, there are five possible types of combinations of molecules, labelled I–V in fig. 5C. For example, the successive levels in fig. 5B are I, I, III, V. In such a sequence, because vacancies are not allowed, a I can be followed by any one of I,...,V, a II can be followed by a II or a IV, a III can be followed by a III, IV, or V, and a IV or V only by a IV or V, respectively. These possibilities then allow the eight types of sequences shown in fig. 5D, where (I) indicates any number of successive I combinations, including zero, and II, III, ... indicate any number of successive II, III, ... combinations, not including zero. Each of these sequences contributes terms to Υ. That is, $\Upsilon = \Upsilon_1 + \ldots + \Upsilon_8$, where

$$\Upsilon_1 = \frac{1}{1-\Pi}, \quad \Upsilon_2 = \frac{1}{1-\Pi} \cdot \frac{x_1^2 y^2}{1 - x_1^2 y^2}$$

$$\Upsilon_3 = \frac{1}{1-\Pi} \cdot \frac{2x_1 x_2 z}{1 - x_1 x_2 z}, \quad \Upsilon_4 = \frac{1}{1-\Pi} \cdot \frac{2x_1}{1 - x_1}$$

$$\Upsilon_5 = \frac{1}{1-\Pi} \cdot \frac{x_2}{1 - x_2},$$

$$\Upsilon_6 = \frac{1}{1-\Pi} \cdot \frac{x_1^2 y^2}{1 - x_1^2 y^2} \cdot \frac{2x_1}{1-x_1} \qquad (38)$$

$$\Upsilon_7 = \frac{1}{1-\Pi} \cdot \frac{2x_1 x_2 z}{1 - x_1 x_2 z} \cdot \frac{x_1}{1-x_1}$$

$$\Upsilon_8 = \frac{1}{1-\Pi} \cdot \frac{2x_1 x_2 z}{1 - x_1 x_2 z} \cdot \frac{x_2}{1-x_2},$$

where $\Pi = x_1^2 x_2 y^2 z^2$ and factors of 2 have been included where a degeneracy requires it. The quantity Υ_i/Υ is the probability of observing a sequence of type i. A more compact form for Υ follows on combining 1,2,4,6 and 3,7 and 5,8:

$$\Upsilon = \frac{1 + x_1}{(1-\Pi)(1 - x_1^2 y^2)(1 - x_1)} + \frac{2x_1 x_2 z}{(1-\Pi)(1 - x_1 x_2 z)(1 - x_1)} + \frac{x_2(1 + x_1 x_2 z)}{(1-\Pi)(1 - x_1 x_2 z)(1 - x_2)}. \qquad (39)$$

Condensation of bulk dual polymer occurs when $\Pi = x_1^2 x_2 y^2 z^2 \to 1$. The equations

$$\bar{N}_2 = \partial \ln \Upsilon / \partial \ln x_2,$$
$$2\bar{N}_{11} = 2\bar{N}_{12} = x_1\, \partial \ln \Upsilon / \partial \ln x_1, \qquad (40)$$
$$\bar{N} = \partial \ln \Upsilon / \partial \ln y^2, \quad \bar{M} = \partial \ln \Upsilon / \partial \ln z$$

can be used to find the mean values indicated but we do not pursue this.

In the special case $x_1 = 0$, we have $\Upsilon = 1/(1 - x_2)$, as in eq. 5. If $x_2 = 0$,

$$\Upsilon = (1 + x_1)/(1 - x_1)(1 - x_1^2 y^2). \qquad (41)$$

This is the $l = 1/1$ case, with $x_1 = x_2 = x$, already mentioned following eq. 14, except that here there are two contacts, w, between the two strands. If there are no lateral interactions ($y = 1$, $z = 1$), eq. 39 simplifies to

$$\Upsilon = 1/(1 - x_1)^2(1 - x_2), \qquad (42)$$

as expected (the three strands are independent).

6. Aligned tubular models at equilibrium

In a previous paper [4] we examined the 'roughness' at an end of a long tubular aggregate of s strands where the subunits in the different strands might be either aligned or staggered relative to each other. This section is essentially an appendix that uses the method of the previous section to extend some of the results given in ref. 4 for aligned tubular models at equilibrium. There is only one type of subunit; the vernier effect is not involved.

We consider an aligned tubular aggregate of s strands, initiated by sites on a surface (as in the other sections of this paper). The aggregate is at equilibrium and has a finite size. In ref. 4, the only equilibrium state considered was at the critical concentration c_e of free subunits where bulk polymer is formed. Here we generalize to $c \leqslant c_e$.

Fig. 6A and B shows transverse sections for $s = 2$ and $s = 3$. Note that there are two lateral interactions, w, in fig. 6A. This is in contrast with the non-tubular two-stranded model in fig. 6C (the $l = 1/1$ case of section 2, with $x_1 = x_2$), which has only one lateral interaction w. We define, as usual in this paper, $y = e^{-w/kT}$ and $x = qe^{-w_1/kT}\lambda$, where λ is proportional to c (eqs. 3 and 6).

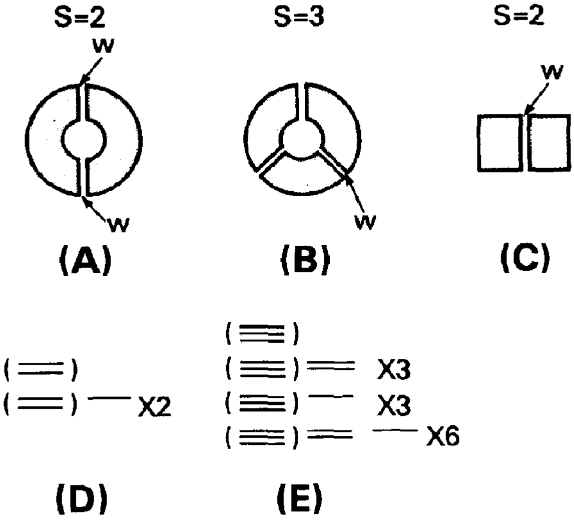

Fig. 6. (A) Cross-section of a tube with two strands. (B) Cross-section of a tube with three strands. (C) Cross-section of a non-tubular two-stranded aggregate. (D) Types of configurations in the $s = 2$ (tube) case. (E) Types of configurations in the $s = 3$ case.

We first adapt the method used in fig. 5D to the $s=2$ case (fig. 6A). The open partition function Υ for this aggregate has two contributions, shown diagrammatically in fig. 6D:

$$\Upsilon=\frac{1}{1-\Pi}+\frac{2x}{(1-\Pi)(1-x)}, \qquad (43)$$

where $\Pi=x^2y^2$. The first term represents any number of complete packages x^2y^2, from 0 to ∞, attached to the surface. The second term includes this contribution plus at least one additional subunit (1 to ∞) on one of the two strands. All possible configurations of the aggregate are included in the two terms in Υ. Bulk condensation of the aggregate occurs when $\Pi \to 1$, i.e., when $x \to 1/y$ (recall that x is proportional to the subunit concentration c). Eq. 43 is valid for $\Pi<1$ or $x<1/y$. Note that eq. 43 is the same as eq. 41, as expected.

Let us digress at this point to compare critical concentrations (proportional to x when $\Pi=1$). For a single strand (with no lateral interactions), $\Upsilon=1/(1-x)$ (eq. 5) and condensation occurs as $x \to 1$. For a two-stranded aggregate with only one lateral interaction (fig. 6C), $\Pi=x^2y$ in eq. 43 and $x \to 1/y^{1/2}$ determines the critical concentration. That is, the critical concentration is reduced ($y>1$) by the lateral interactions, as expected, because these interactions increase the stability of the condensed phase (i.e., they lower its chemical potential). With two lateral interactions at each level (fig. 6A), $x \to 1/y$ (see above), which gives a still lower critical concentration (for the same value of w). In fact, for an aligned tubular aggregate of s strands ($s>1$), $\Pi=x^sy^s \to 1$, and $x \to 1/y$ for any s. This simple result occurs because there is one lateral interaction per subunit in a complete tubular package of any size, $s>1$.

We return now to the main argument. One can factor $1/(1-\Pi)$ out of both terms in eq. 43, leaving

$$\Upsilon_0=1+\frac{2x}{1-x}=\frac{1+x}{1-x}, \qquad (44)$$

which is valid for $x \leqslant 1/y$ (see below). The physical significance of the partition function Υ_0 is that it represents the sum over all aggregation states of the polymer beyond the last complete package (x^2y^2). This is, then, a surface roughness partition function [4]. Incidentally, the fact that $1/(1-\Pi)$ can be factored out of Υ for all of these models (i.e., for any s) corresponds to the fact that the distribution of rough states is the same for any number n of underlying complete packages x^sy^s. In the simple $s=2$ case, roughness can arise only from extra subunits on one strand or the other. The reason y does not appear in eq. 44 is that no lateral interactions can occur with one strand only.

The polymer becomes infinitely long when $x=1/y=e^{w/kT}$, but Υ_0, which we have denoted by Q in this limit [4], remains well-behaved (i.e., the singularity has been removed from Υ). The result (using $x=e^{w/kT}$) is the same as eq. 21 of ref. 4. However, eq. 44 is more general; it applies whenever $x \leqslant 1/y$.

From eq. 44, the mean number of subunits beyond the last complete package is

$$\bar{m}=\partial \ln \Upsilon_0/\partial \ln x=2x/(1-x^2). \qquad (45)$$

We turn now to $s=3$ (fig. 6B), an aligned aggregate of three strands. All possible configurations of such an aggregate are represented by the four diagrams in fig. 6E. For example, the last diagram refers to configurations with any number (0 to ∞) of complete packages x^3y^3 as a base, supplemented by at least one level (i.e., 1 to ∞) with subunits in two strands (three choices), and this supplemented by at least one further subunit on one of these two strands (two choices). The four diagrams in fig. 6E correspond to four terms in Υ:

$$\Upsilon=\frac{1}{1-\Pi}+\frac{3x^2y}{(1-\Pi)(1-x^2y)}+\frac{3x}{(1-\Pi)(1-x)}+\frac{6x^3y}{(1-\Pi)(1-x^2y)(1-x)}, \qquad (46)$$

where $\Pi=x^3y^3$. This equation is valid for $x<1/y$. The separate terms are proportional to the probability of observing configurations of the different types. The roughness partition function Υ_0 follows on factoring out $1/(1-\Pi)$. After simplification,

cation, we find

$$\Upsilon_0 = (1 + 2x + 2x^2y + x^3y)/(1 - x^2y)(1 - x). \tag{47}$$

This agrees with eq. 24 of ref. 4 in the limit $x = 1/y = e^{w/kT}$ but eq. 47 is more general: it is valid for $x \leqslant 1/y$.

For any $s \geqslant 3$, Υ_0 will be a function of x and y, as in eq. 47. The derivative $\partial \ln \Upsilon_0/\partial \ln x$ then gives the mean number of subunits in the aggregate beyond the last complete package x^sy^s. Also, $\partial \ln \Upsilon_0/\partial \ln y$ gives the mean number of lateral interactions, w, in this part of the aggregate. If we subtract the latter from the former, we obtain

$$\bar{m} = \partial \ln \Upsilon_0/\partial \ln x - \partial \ln \Upsilon_0/\partial \ln y, \tag{48}$$

where $\bar{m}$ is one-half the mean number of 'missing' interactions in the aggregate. This terminology, introduced in ref. 4, refers to the fact that in bulk (i.e., very long) polymer there is one lateral interaction per subunit (as in a complete package, x^sy^s), but in the rough part of the aggregate, beyond the last complete package, there are more subunits than lateral interactions. That is, some lateral interactions are missing, compared to bulk polymer; one-half the mean number of these is given by eq. 48. A special case is eq. 45 for $s = 2$, where $\partial \ln \Upsilon_0/\partial \ln y = 0$. The rougher the end of the aggregate, i.e., the more exposed surface, the larger the value of $\bar{m}$. Thus $\bar{m}$ is a useful index of surface roughness [4].

The two derivatives, in the $s = 3$ case, are

$$\frac{\partial \ln \Upsilon_0}{\partial \ln x} = \frac{3x(1 - x^2y)(1 + x^2y) + 6x^2y(1 - x)(1 + x)}{(1 - x^2y)(1 - x)(1 + 2x + 2x^2y + x^3y)} \tag{49}$$

$$\frac{\partial \ln \Upsilon_0}{\partial \ln y} = \frac{3x^2y(1 + x)}{(1 - x^2y)(1 + 2x + 2x^2y + x^3y)}. \tag{50}$$

Then

$$\bar{m} = \frac{3x(1 - x^2y)(1 + x^2y) + 3x^2y(1 - x)(1 + x)}{(1 - x^2y)(1 - x)(1 + 2x + 2x^2y + x^3y)}. \tag{51}$$

This agrees with eq. 27 of ref. 4 when $x = 1/y$.

The algebra becomes rather lengthy for the $s = 4$ case, so we abbreviate the discussion. There are now 12 diagrams of the type shown in fig. 6E, and there are 12 corresponding terms in Υ. If we factor $1/(1 - \Pi)$ out of each term, where $\Pi = x^4y^4$, the 12-term expression for Υ_0 can then be simplified somewhat to give

$$\Upsilon_0 = \frac{\begin{gathered}[(1 - x^4y)(1 + 3x + 3x^2y + 3x^3y^2 + x^4y^2) + \\ x^2(1 - x)(1 + xy + x^2y^2 + x^3y^3) + 3x^4y(y -\end{gathered}}{(1 - x^3y^2)(1 - x^2y)(1 - x^2)(1 - x)} \tag{52}$$

This equation is valid for $x \leqslant 1/y$. This reduces properly to eq. 32 of ref. 4 if $x = 1/y$ and to $(1 - x^4)/(1 - x)^4$ if $y = 1$. That is, $\Upsilon = 1/(1 - x)^4$ in the latter case (four independent strands).

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