Macromol. Symp. **2005**, *227,* 39-52

Coupling of the Polymer Threading a Membrane Transition to the Membrane Adsorption Transition

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Summary: A polymer molecule threading through a pore in a plane membrane is allowed to adsorb on either or both sides of the membrane. Further, it is confined to the vicinity of the membrane by two plane barriers lying on either side of the membrane. A lattice model of this problem is exactly solvable by matrix techniques. The equilibrium translocation behavior is described as a function of the polymer MW, the membrane adsorption energies, the solution properties, the barrier separations, applied force, and the temperature. The transition is first-order, meaning that small changes in any of these 9 quantities can in the limit of infinite MW, completely translocate the polymer. The work of Park and Sung who used Smoluchowski-like equations to calculate translocation transit times can be generalized by use of the sea-snake model which is relevant to isolated polymer chains in solution. The physics behind the sea-snake model is that if one monomer is pulled into the membrane, the distance the center of mass of the untranslocated portion of the chain moves is $MW^{-1/2}$ of the distance between monomer units. This reduces the effective friction coefficient by $MW^{1/2}$. It is found for the sea-snake model that the MW dependence of transit times varies as $MW^{3/2}$ or MW depending on whether we use a free draining or a non-free draining picture for the polymer.

Keywords: membrane translocation; polymer transition; polymer translocation; transit times

1. Introduction.

In this paper we will treat in depth the problem of a single polymer molecule threading a membrane at the same time as it can adsorb onto the surface, or surfaces, of the membrane. Earlier the polymer threading a membrane (PTM) problem was solved for a membrane surface that was a barrier but otherwise was neutral energetically [1]. Park and Sung have given an excellent treatment of the problem within the Gaussian approximation for the polymer[2]. The matrix method to be employed in our paper has, as we shall see, added capabilities. We now give three broad motivations for addressing this most important problem.

There are at least 5 separate phase transitions which occur in the isolated polymer molecule [3]. They are: the polymer threading a membrane (PTM) transition[1,4] which is first-order; the helix to random coil (HRC) transition which is diffuse for single stranded molecules[5,6] (polypeptides), second-order for double stranded molecules [7] (DNA), and first-order for triple stranded

DOI: 10.1002/masy.200550904

molecules[8] (collagen); the collapse (C) transition which can be second[9,10] or first-order[11], depending on solvent; the surface adsorption (SA) transition which is second-order[12,13]; a model of the equilibrium polymerization (P) transition which is first-order [3]. Except for the collapse transition these model systems have been solved exactly when simple models of the polymer are used. This solvability is due to the linear connectivity of the monomer units [3]. Things get both complicated and interesting when the transitions are coupled to one another. Complicated because of the coupling; interesting because of their exact solvability[4]. It is because of this comprehendible complexity that we limit ourselves to equilibrium statistical mechanics in this report. Dynamics will be discussed only to evaluate average translocation times as a function of molecular weight in Sec.2.4.

A previous paper[4] lists 15 different kinds of coupled pair transitions for a polymer threading a membrane. They are PTM-PTM, HRC-HRC, C-C, SA-SA, P-P, PTM-HRC, PTM-C, PTM-SA, PTM-P, HRC-C, HRC-SA, HRC-P, C-SA, C-P. SA-P. As an example the entry HRC-SA supposes that the solutions on sides A and B of the membrane can support a HRC transition on side A and a SA transitions on side B. Of these 15 entries the partition function for PTM-PTM, SA-SA, P-P, PTM-SA, PTM-P, SA-P was written down exactly with proper cognizance of the surface [4], while with the other 9 couplings the presence of the surface was not treated exactly. Of the 6 exactly treated cases 5 treat the surface as a barrier (no energetics) but with SA-SA not only is the surface a barrier (in the sense that monomer units on one side cannot penetrate the barrier except through the pore) but also the monomers can be attracted to the surface. It is this case that we treat in detail here.

There are other pair interactions which do not involve threading a membrane. They are HRC_C, HRC_SA, HRC_P, C_SA, C_P, SA_P. Of these HRC_P, C_P and SA_P, are easily solved using the grand ensemble. HRC_SA [14] and C_SA [15] are difficult problems which have been solved by Carri and Muthukumar for homopolymers while HRC_C for copolymers is recognized as the globular protein collapse problem which has not yet been solved.

For our second motivation we observe that there are more than a few fundamental biological processes that involve translocation of polymers through membranes. Solving any of the above problems gives us insight into these important biological problems.

RNA and proteins translocate through the nuclear pore membrane as a normal process of cell metabolism [16]. Also viruses can infect by translocating their DNA (RNA) genes into the cell nucleus [16]. Finally, biotechnology procedures exist that depend on DNA managing to breach the nuclear cell membrane [17].

In a previous paper it was shown how the manufacture of proteins at the rough endoplasmic reticulum involve necessarily simultaneous polymerization and translocation of the growing protein^4. Undoubtedly translocation is occurring at the membrane(s) of mitochondria as well. Since these 3 processes are essential to the function of eukaryotic cells we can state that multi-cellular life itself would not exist without the various PTM processes.

Viruses also need to breach the cell membrane in order to enter the cell. In T-type viruses the process looks very much like the translocation through a pore process as does the reverse process of filling the newly created but empty virus capsules [1] with viral DNA.

There are many signaling molecules some of which are polymers embedded in the cell membrane. Translocation or partial translocation may be involved in the signaling process or at least in the initial incorporation of the signaling polymer into the membrane [16], since some singling molecules are known to span the membrane.

Our third motivation comes from the observation that cell division which is a necessary requirement of all evolved life involves the duplication during cell division of each of the many diverse cell structures using the starting structures of the parent cell as templates. Might phase transitions be involved? The 5 classes of phase transitions occurring within the isolated polymer molecule, when coupled to the 5 classes of phase transitions of ordinary non-polymeric matter, provide a vast number of different kinds of structures that could be (could have been) adapted to the needs of evolving life [3]. Might the necessity for the many diverse structures in biology, which only polymer systems can provide, be the reason why all life is polymeric? If, as we believe, polymer phase transition phenomena lie at the base of the various biological structures, it follows that understanding polymer phase transitions is a prerequisite to a predictive theory of evolution.

2. Theory

We herein describe the detailed system we shall be modeling (see Fig. 1). The membrane divides a volume into two regions, region A on the readers left and region B on the reader's right. We number the levels (parallel to the membrane) starting with the membrane as 1 and numbering away from the membrane. Thus A1, A2 are the first and second layer away from the membrane. B1 and B2 are the same for region B. By arbitrary designation, the layer on the left surface of the membrane is A1 and on the right surface it is B1. Thus if we have absorption on the surface of the membrane it will either be on A1 or B1 or perhaps both. We may also have absorption on some layer other than A1 or B1 (see below).

There are n segments on the left side which is denoted by A and N-n segments on side B. The polymer is constrained to have segments at the pore entrance and pore exit. Otherwise it is free.

Denote the partition function (PF) for n segments residing on side A of the membrane by $q_A(n)$ and the PF for the N-n segments (monomer units) residing on side B of the membrane by $q_B(N-n)$. The product of the two q's represents a polymer of N segments that has n segments on side A and N-n on side B. We are assuming the membrane thickness to be of unit thickness, but finite thickness is easily accommodated. We do not allow multiple threading.

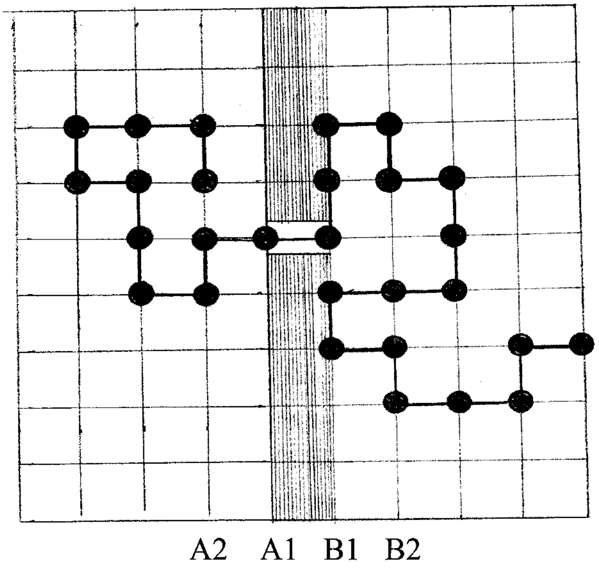

Fig. 1 shows the model of the chain crossing the membrane with some additional adsorption on B1. The energy of absorption of the polymer on layer A1 is given by ε_{A1} and on side B1 by ε_{B1}. For absorption on other surfaces like surface Aj the energy is given by ε_{Aj} . The energy of polymer interacting with the solution on side A is given by w_A. Notice for this model when the polymer has both absorption at A1 and solution energy in the A side of the membrane the total energy on the polymer segment at level A1 is $\varepsilon_{A1}+w_A$ while the energy at all other levels in A is w_A. Similarly for side B.

The total PF, not counting escape into the reservoir on either side is denoted by Q(N)

$$Q(N)=\sum q_A(n)q_B(N-n) \qquad (1)$$

$$0 \leq n \leq N$$

where q_A is the PF for that portion of polymer residing in side A. q_B samples all conformations of the polymer portion consistent with its one end being at the pore entrance. The summation of Eq. 1 is almost trivial. What is difficult is determining the form of q_A and of q_B. The polymer portions could be undergoing adsorption, polymerization, collapse or even undergoing a helix-random coil transition, or any combination of these, all in the presence of the surface. In this paper we restrict ourselves to considering only surface adsorption, but first we mention the previously solved non-adsorption case.

2.1 The PTM Transition: No Surface Adsorption

For the pure PTM transition

$$q_A(n) = z_A{}^n \exp(-nw_A/kT)/n^\theta, \quad q_B(n) = z_B{}^n \exp(-nw_B/kT)/n^\theta \qquad (2)$$

Here z_j allows for the configurational freedom of a monomer, which can depend on the nature of the solvent as well as the polymer structure, while w_j denotes the interaction with the solvent. The quantity θ depends on the nature of the constraint[1]; chain attached to surface only at one end, $\theta=1/2$; chain attached to surface at both ends but one end free to roam on the surface, $\theta=3/2$; Chain attached to surface at both ends but neither end free to roam $\theta=5/2$. The form of Eq. 2 encompasses other geometries as well. If the surface has the shape of a cone or of a wedge and the chain threads through the apex then the only effect is to alter the value of θ to a value determined by the wedge[18] or cone [19] angle. Additionally, one can approximately accommodate [20,21] the effects of excluded volume by adjusting the value of θ. In all cases the transition is first-order (in the limit of infinite molecular weight) and the temperature of the transition is independent of θ. The effect of different θ is only to give transitions variable width for finite N, the larger θ the more narrow the width. The location of the transition does not depend on θ and is determined only by z_A, z_B, w_A, w_B. Figure 2 shows the transition behavior for $\theta = 0$. Since it is first-order in the limit of infinite molecular weight and since larger θ give sharper transitions for each molecular weight [1] these $\theta>0$ transitions are first-order also.

Before leaving the pure PTM case we should point out that the reason for the occurrence of the transition lies in the fact that the monomers are covalently connected in a line which allows the monomers to be distinguishable from each other by virtue of the fact that they occur at different positions along the chain. If the monomers were not connected they would be indistinguishable from each other and there would be no transition. See Ref. 1 for a discussion of this important point. The occurrence of each of the 5 phase transitions of the isolated polymer is due to their linear covalent connectivity [1,3]. In a previous paper [4] we explored the effects of coupling the PTM transition to the 4 other transitions. In this paper we will treat in depth the coupling of the PTM transition with the surface adsorption transition.

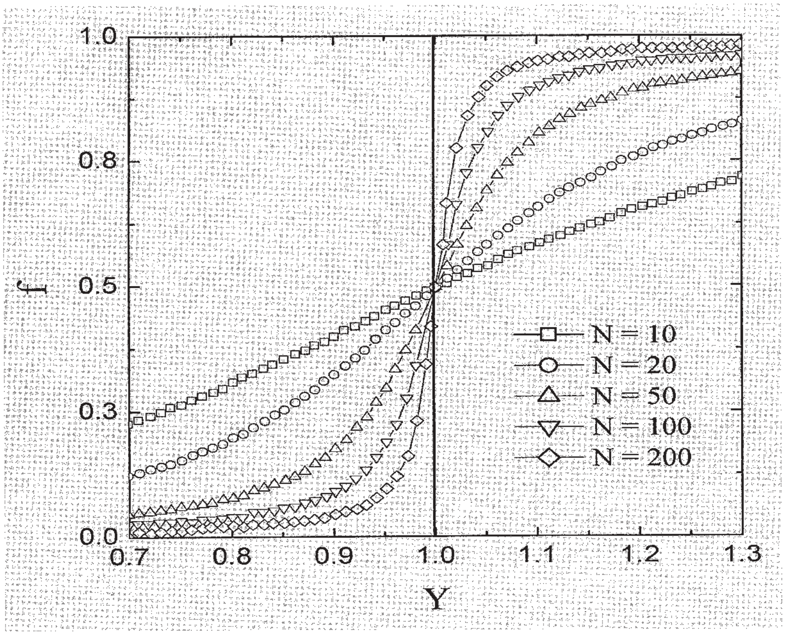

Fig. 2. Polymer threading a membrane transition when there is no surface adsorption . Y is the ratio of monomer partition functions, f is the fraction of monomers on side B, and N is the polymer length. For infinite molecular weight f(Y) is a step function. The energy is given by $U=Nf\varepsilon_B + N(1-f)\varepsilon_A$.

2.2 The PTM Transition: Surface Adsorption

We shall now use the powerful matrix method to evaluate q_A and q_B.

A polymer molecule whose one end is attached to a flat surface displays a transition when we allow attractive monomer-surface interaction [12,13]. The energy of monomers on the surface competes with the entropy favoring monomers off the surface. For this case the transition is second order in the Ehrenfest sense. This means that the extensive quantities entropy and energy are continuous across the transition but their derivatives are discontinuous. Several treatments of the isolated polymer attached to a surface at one end have been developed in the literature [22]. Perhaps the most powerful treatment is the matrix approach [23]. With this approach one can have an arbitrary interaction of the monomer for the surface. Also, copolymers are easily treated. In the original treatment [23] a minimal model was used in which the monomer-surface interaction energy was zero if the monomer was not touching the surface and ε_1 if it was. The polymer is confined to lie within (among) M layers and M is chosen large so that it is not a confinement restriction on the polymer. Using the notation of the Di Marzio-Rubin paper [23] we have

$$q_A(n)=\mathbf{U}^T z_A{}^n[\mathbf{W}_A(\theta_{A1,},\theta_{AM,})]^n\mathbf{P}(0)\exp(-nw_A/kT) \qquad (3)$$

where **P** is a column vector which sets the initial location of the starting segment. For our problem $\mathbf{P}^T=(1,0,0...0)$ which serves to fix one end at the surface. $\mathbf{U}^T$ is a unit row vector (1,1,1…1,1) which allows the free end to end up at any position. If we wished to force the free end to terminate at position j then each entry would be zero except for the jth which would be 1. $\mathbf{W}_A$ is an MxM matrix whose form is given, for M =5, by

$$\mathbf{W}= \begin{matrix} (1-a)\exp(\theta_1) & (a/2)\exp(\theta_1) & 0 & 0 & 0 \\ (a/2) & (1-a) & (a/2) & 0 & 0 \\ 0 & (a/2) & (1-a) & (a/2) & 0 \\ 0 & 0 & (a/2) & (1-a) & (a/2) \\ 0 & 0 & 0 & (a/2)\exp(\theta_5) & (1-a)\exp(\theta_5) \end{matrix} \qquad (4)$$

$\theta_{A1}=\varepsilon_{A1,}/kT$ is the energy of attraction of a monomer for the surface (layer A1) and $\theta_{AM,}$ that for layer M. a is the fraction of steps perpendicular to the layer, while 1-a is the fraction parallel. The coordination number of the lattice is z_A. For a simple cubic lattice a is 1/3 and z_A is 6 but other lattices can be accommodated as well[23]. It is immediately clear that the matrix method is applicable to systems that are confined in the direction normal to the surface. The confining wall at location M may be a barrier only or it can be energetically described. If we are not interested in confinement we simply make M large. It has been our experience that by choosing $\theta_{AM}=0$ and letting M be $2n^{1/2}$ gives results no different than if M were infinite [23-25].

Modern desktop computers easily handle the mathematics and using the matrix method has the added advantage that confined polymers can be treated.

A similar expression to that of Eq. 3 exists for $q_B(N-n)$. The energies of attraction of monomer for surface can be different on either side of the membrane, because the solutions are different and/or because the surfaces are different.

We now show that this coupled system displays a first-order phase transition. For large n, N-n, we expect the values of q_A and q_B to be given by

$$q_A(n) = \lambda^n, \quad q_B(N-n) = \mu^{(N-n)} \qquad (5)$$

where λ is the largest eigenvalue of $\mathbf{W}_A$, and μ that of $\mathbf{W}_B$. This gives

$$Q(N) = 3\lambda^{n}\mu^{(N-n)} = (\lambda^{N+1} - \mu^{N+1})/(\lambda - \mu) \tag{6}$$

The power series form for a partition function is known to give a perfectly sharp (first-order) phase transition at $\lambda(T)=\mu(T)$. To see this write

$$<n> = \lambda\partial\ln(3\lambda^{n}\mu^{(N-n)})/\partial\lambda = (N+1)\lambda^{(N+1)}/(\lambda^{(N+1)}-\mu^{(N+1)}) - \lambda/(\lambda-\mu) \tag{7}$$

which when plotted as a function of $Y=\lambda/\mu$ reproduces Fig. 2.

It is a straightforward matter to evaluate $q_A(n)$ and $q_B(N-n)$ for finite n, N and to evaluate the one-dimensional sum for Q(N) in Eq. 1. Using the thermodynamic relations

$$F = U-TS, \quad S = -\partial F/\partial T \tag{8}$$

and

$$F = -kT\ln Q(N) \tag{9}$$

we can plot U/kN and determine how surface adsorption determines the sharpness of the transition. A more useful quantity might be

$$<n> = \sum n q_A(n) q_B(N-n)/\sum q_A(n) q_B(N-n) \tag{10}$$

We wish to describe how widely applicable the matrix method can be by considering a generalization of the form for **W.**

$$\mathbf{W}= \begin{array}{ccccc} (1-a)\exp(\theta_{A1}) & (a/2)\exp(\theta_{A1}) & 0 & 0 & 0 \\ (a/2)\exp(\theta_{A2}) & (1-a)\exp(\theta_{A2}) & (a/2)\exp(\theta_{A2}) & 0 & 0 \\ 0 & (a/2)\exp(\theta_{A3}) & (1-a)\exp(\theta_{A3}) & (a/2)\exp(\theta_{A3}) & 0 \\ 0 & 0 & (a/2)\exp(\theta_{A4}) & (1-a)\exp(\theta_{A4}) & (a/2)\exp(\theta_{A4}) \\ 0 & 0 & 0 & (a/2)\exp(\theta_{A5}) & (1-a)\exp(\theta_{A5}) \end{array} \tag{11}$$

At each layer we have introduced an energy ε_{Aj} which assigns an energy ε_{Aj} ($\theta_{Aj} = \varepsilon_{Aj}/kT$) each time a monomer visits level j. This energy can represent a long range interaction with the surface or/and it can represent monomer solution interaction. We will in our computations use

$$\varepsilon_{Aj} = \varepsilon_A + w_A, \quad j=1; \qquad \varepsilon_{A1} = w_A, \; j \neq 1. \tag{12}$$

This means that there is a monomer-solution interaction w_A that does not depend on monomer distance from the surface, and a monomer–surface interaction ε_A that exists only when the monomer is in contact with the surface. But, we stress that much more complicated energies are treatable. Even the simple choice of Eq. 12 involves the 4 parameters w_A, w_B, ε_A, and ε_B, and if we allowed energy interaction with the confining walls we would have two more energies to complicate the picture. So the problem can be very complicated.

An important generalization is to copolymers where each monomer has its own energies. The formula for the partition function would then read

$$q_A(n) = \mathbf{U}^T z_A{}^n[\prod_k \mathbf{W}_k(\ldots\theta_{Aj,k}\ldots.)]\mathbf{P}(0) \tag{13}$$

Where there is a separate matrix for each monomer with energies appropriate to that monomer, and the product is an ordered product. The sequence order of the product must be observed because the matrices do not commute. This can be a big effect. To understand why this might be, imagine the monomer-surface interaction to be extremely strong for only one of the monomers. Then, depending on its location, we would have a tail or a loop (plus tail). These objects have widely different entropies.

2.3 Pulling on the end with a force f

There are two approaches; the canonical ensemble approach and an analogue of the isobaric ensemble. The justification of these ensembles can be found in the book [26] by Terrell Hill. Schrodinger's book [27] gives a more rigorous treatment of the Canonical ensemble case. We will give both treatments.

The canonical partition function is

$$Q(x) = \sum \exp(-\beta\varepsilon_j(x)) \tag{14}$$

while the constant force partition function is

$$\Delta(f) = \int\sum \exp(-\beta\varepsilon_j(x))\exp(-\beta xf)dx = \int Q(x)\exp(-\beta xf)dx \tag{15}$$

Since Q(x) and Δ(f) are Laplace transform (LT) pairs they have equivalent information. Eq. 14 gives

$$F(T,N,x) = -kT\ln Q(x) \tag{16}$$

The relationship

$$\partial\langle\varepsilon_j(x)\rangle/\partial x=\langle\partial\varepsilon_j(x)/\partial x\rangle=\sum(\partial\varepsilon_j(x)/\partial x)\exp(-\beta\varepsilon_j(x))/\sum\exp(-\beta\varepsilon_j(x) = -kT\partial\ln Q/\partial x \qquad (17)$$

allows us to identify $\partial F(T,N,x)/\partial x$ with the thermodynamic force $\partial\langle\varepsilon_j(x)\rangle/\partial x$. Our matrix method easily handles the case where one end of the polymer is at the origin (on the surface and the other end is at x. In actual practice we shall use the canonical ensemble approach.

The fundamental relation Π obtained from Eq. 15 is

$$\Pi(T,N,f) = -kT\ln\Delta(f) \qquad (18)$$

Similarly a relation analogous to Eq. 17 gives

$$\langle x\rangle = \int\sum x\exp(-\beta\varepsilon_j(x)-\beta xf)dx/\int\sum\exp(-\beta\varepsilon_j(x)-\beta xf)dx = -kT\partial\ln\Delta/\partial f \qquad (19)$$

This allows us to identify $M\Pi/Mf$ with the expectation value of x ($\langle x\rangle$).

Notice that for large N the integrand of Eq. 15 is a sharply peaked function of x. We can find this maximum by setting the derivative of the integrand equal to zero which gives

$$F = -\langle\partial\varepsilon_j(x)/\partial x\rangle \qquad (20)$$

This shows that the LT variable f is to be identified with the force. Thus, in the limit of large N (the thermodynamic limit) one can obtain a Laplace transform by simply doing a Legendre transform since we know that Π(f) is the Legendre transform of F(x). Similarly, the inverse Laplace transform can be obtained from the (inverse) Legendre transform of Π(f).

Our intuition is that as a function of f, Δ(T,N,f) gives a first order transition even for finite N. Pulling a monomer off of a surface involves a loss of an energy ε and movement of a distance a. If ε/a is less than f we expect the monomer to leave the surface even for finite N.

Skvortsov, Gorbunov and L. I. Llushin have treated the problem of a force on a chain at a surface in the Gaussian limit [28,29]. Interestingly, they show that the Landau-Lifshits approach is not valid for this system. We can gain some insights from their work.

2.4 Translocation Transit Times

In this section we wish to comment on the time for a polymer of length L to transit the membrane. Park and Sung show[2] that if there is no force pulling the polymer then the transit time varies as L^3 while if there is a force (which in our case is imagined to arise because of the adsorption on the trans side) then the transit time varies as L^2. We wish to expand these results.

In a previous paper we showed that the transit time is model dependent [30]. If we used a reptation model in which the polymer is imagined to be pulled along (within) a confining tube then indeed $t \propto L^2$ while if there is no such tube $t \propto L^{3/2}$. To understand these results we use the relation

$$F= \eta v = -\eta dL/dt \tag{21}$$

where F is the force, η the viscosity and $v=-dL/dt$ is the velocity of a monomer segment as it passes perpendicularly through the membrane. Inertial and spring constant effects are being ignored which is to say that the process is occurring slowly. In the reptation model the friction coefficient is proportional to L ($\eta=\eta_0 L/a$) so that

$$\frac{dL}{dt} = -aF/\eta_0 L \tag{22}$$

which leads immediately to $t \propto L^2$. In the sea snake model [30] we take cognizance of the fact that the chain is a random walk and we ask how the center of mass moves when we pull the chain one unit , a , through the membrane. The answer is that it moves a distance $(2(N+1))^{1/2}$ a $-(2N)^{1/2}$ a = $ad(2N)^{1/2}/dt = 2^{1/2}$ a $N^{-1/2}$. Thus, when one monomer transits the membrane the other monomers move towards the membrane surface a distance proportional to the inverse of the square root of N. Their average velocity is not dL/dt but rather $2^{1/2}N^{-1/2}dL/dt$ which when we substitute into the left hand side of Eq. 22 gives

$$2^{1/2}N^{-1/2}dL/dt = - aF/ \eta_0 L \tag{23}$$

And this leads immediately to $t \propto L^{3/2}$.

Now the above treatment is a free-draining model because each monomer sees a friction coefficient η_0, so we must also consider the non free-draining model where the friction coefficient is a property of the whole molecule and according to Stokes law is proportional to the radius of the molecule, which varies a $N^{1/2}$. If we were moving the polymer in free space the effective friction would be proportional to $N^{1/2}$. But in moving the one monomer a distance a through the membrane the polymer moves only a distance$2^{1/2}$ a $N^{-1/2}$. These factors cancel resulting in a power dissipation that is independent of N.

$$\frac{dL}{dt} = -AF \tag{24}$$

And this leads to immediately to t $\propto$ L. Summarizing we have,

t $\propto$ L, non free-draining model; t $\propto$ $L^{3/2}$, free-draining model
t $\propto$ L^2 , tube model; t $\propto$ L^3 , no force on end of chain

These results hold only if the chain is not allowed to escape from the cis side because the probability of returning to the pore is less than 1 in 3-dimensions (for an infinite cis volume) so that the first passage times would all become infinite. So we must imagine a chemical blob to be attached to the chain on the trans side thereby preventing pop out to the cis side.

We did not take into account the 6/5ths law, which would modify the results in an obvious way. We did not take into account the hydrodynamic interaction of the chain with the wall. We did not account for the possibility that application of the force has its own time constant arising from the rearrangement times of adsorption and desorption of the monomers onto the trans side of the membrane and/or the time scales of the monomer-solvent interaction.

Although the linear and 3/2 laws were derived for small forces and slow processes we can show on physical grounds that they must hold aside from entanglement problems for large tugs. To see this follow the chain from the pore to the first place that the tangent to the chain turns towards the surface. The contour length of this loop is proportional to the Kratky-Porod persistence length. Pulling on this loop will result on the motion of the loop but not on the rest of the chain since there is no way to transfer tension to the remainder of the chain until this loop is straightened. Thus instantaneously the resistance is independent of N. If we pass a plane parallel to the membrane surface but a distance from the plane proportional to √N it will cut the polymer at √N places (actually proportional to √N). Pulling on one of the segments of length √N we can hardly imagine that the other (√N-1) segments will be affected. The average number of monomer units between cuts is √N. These are the basic reasons for the √N dependence quoted above applying also to large tugs.

For polymer chains of length of 100 to 1000 monomers the t $\propto$ L and t $\propto$ $L^{3/2}$ laws result in transit times that are orders of magnitude smaller than the t $\propto$ L^2 law. This may be important to biology. That short transit times are important to biological systems is proved by the existence of helper molecules.

3. Conclusions

We here list the coupled pair systems that have been solved exactly. Carri and Muthukumar have solved the problem of a single stranded molecule undergoing a helix to random coil transition (HRC) near a surface[14]. Di Marzio and Mandell have solved the problem of a polymer threading a membrane[1] (PTM-PTM transition). Di Marzio and Kasianowicz have solved the problem of a polymerizing polymer threading a membrane [4] (PTM-P transition). In addition these latter authors have written down the partition functions for a polymer that is threading a membrane simultaneously with it undergoing a HRC, SA, C or P transition on one side or both sides of the membrane. Given that the solutions on either side are sufficiently diverse there are 15 possible translocation pair couplings. They are PTM-PTM, HRC-HRC, C-C, SA-SA, P-P, PTM-HRC, PTM-C, PTM-SA, PTM-P, HRC-C, HRC-SA, HRC-P, C-SA, C-P, SA-P. To illustrate the marvelously comprehensible complexity of these exactly solvable systems the HRC-HRC system was examined and it was shown that there are 8 classes of behavior resulting in back and forth translocations of from zero to three times [4].

However all the results of the preceding paragraph were for very simple models of the polymer molecule. We might call them vanilla models. The PTM-SA and SA-SA treatments we have given in this paper add flavor. We have allowed the polymer to adsorb onto the membrane surfaces thus initiating an investigation into the interplay of surface forces with translocation phenomena. Our method is easily generalized to treat the case when 1) we have an arbitrary copolymer (see Eq. 13), 2) the interaction energy with the surface has arbitrary distance from the surface dependence (see Eq. 11), 3) the polymer is volume confined on one or both sides of the membrane (this is determined by the matrix size M), 4) there is a force tugging on the end of the polymer (see Sec. 2.3). These are exactly solvable problems using the matrix approach. Also, one can generalize the matrix method to include some aspects of pore structure such as the length of the pore, vestibule volume and wall energy. Also some aspects of polymer structure such as chain stiffness have been treated [23]. Also, as Ambjornsson and Metzler show, certain aspects of chaperone assisted translocation can be solved by using appropriate chemical potentials which they calculate [31] for the A and B sides (represented by our w_A and w_B).

If the insight of nobelist Gerald Edelman is correct to the effect that the most important determinants of biological structure are the surface active CAM, SAM and CJMs molecules [32] then perhaps the surface problem we have solved is of some value in those areas as well as for translocation.

Finally, in Sec. 2.4 we have calculated the translocation transit time τ arising from monomer-solution bead friction coefficients. In addition to $\tau \propto L^2$, (tube model) we have derived $\tau \propto L$, (non free-draining model) and $\tau \propto L^{3/2}$, (free-draining model) by a variation of the reptation model which we call the sea-snake model [30].

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