pH-Controlled Gating in Polymer Brushes

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A crucial function in the survival of biological cells is the ability to regulate the boundary between the local environment and the interior of the cell. A mechanism that has evolved for this purpose is the inclusion of channels in the cell membrane, which permit the selective transport of molecules in and out of the system.[1] The channels are lined with chains that are highly sensitive to variations in the surrounding environment, such as changes in pH or salt concentration. In response to such fluctuations, the chains can change their conformations and thereby cause the pores to open or close. An intriguing challenge lies in designing synthetic polymer systems that can mimic this gating behavior. Of particular interest is fabricating "smart" polymer channels that sense and respond to changes in the environment. Applications for such systems would be manifold, including controlled release, selective filtration, electronic devices, or sensors.

In this paper, we use a two-dimensional self-consistent mean-field (SCF) theory to design a polymer channel that can be made to open and close by varying the pH of the solvent. Polymer systems exhibiting this behavior have been fabricated;[2-4] however, there have been few fundamental or systematic studies of their properties.[5] Our studies provide a theoretical framework for understanding the mechanism by which polymers can act as pH-dependent "valves". The distinct advantage of performing the calculations in two dimensions is that we can determine how both the vertical and lateral properties of the grafted layer are affected by surrounding solvent conditions. By systematically varying the relevant parameters, we can determine the optimal design criteria for synthesizing smart polymer pores.

We consider a system of chains that are uniformly anchored or grafted to a solid surface, forming a polymer brush. The middle of the grafting surface, however, contains a bare patch: no chains are tethered to this central region. In this way, the chains bordering the bare domain define and form the walls of a well or channel (see Figure 1). (By assuming this geometry, the results of our calculations are applicable to the interesting case where the chains are grafted onto a porous substrate that contains real holes and the channels are "bottomless". This would in fact be the situation in controlled release devices or capsules.[2,4]) The chains in the brush are polyacids: they contain groups (carboxylic groups, for example) whose charge is a function of the local pH.[6] The acid groups become negatively charged through the dissociation of a proton, or

$$HA \rightleftharpoons A^- + H^+ \tag{1}$$

The degree of dissociation, α, depends on the pH of the solution, the local electrostatic field, ψ, and the pK_a according to the following equation:[7]

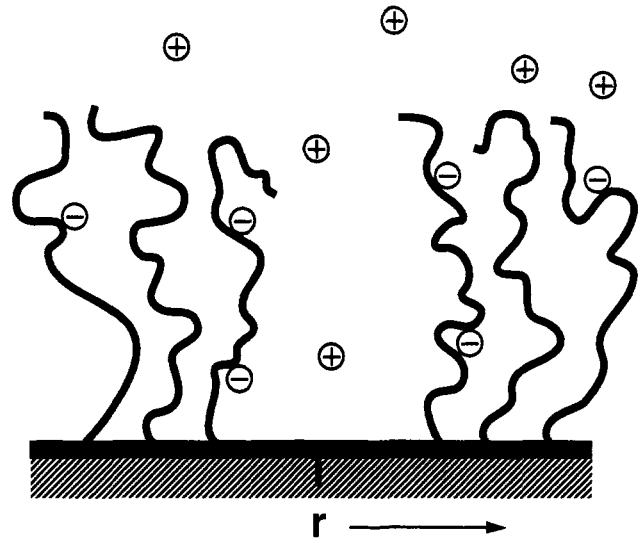

Figure 1. Schematic drawing of the grafted polyacid chains. The length of the chains is held fixed at 35 lattice sites. No chains are grafted at $|r| < 8$, whereas a grafting density of 10% is chosen for $|r| \geq 8$. The negative charges on the chains arise from the dissociated acid groups. (The charges are assumed to be randomly distributed along the lengths of the chains.) The positive counterions, on the other hand, arise from the finite salt concentration that is added to screen the charges in the brushes.

$$\log(\alpha/(1-\alpha)) = \mathrm{pH} - \mathrm{p}K_a + \psi \tag{2}$$

At low pH, the degree of dissociation is relatively weak and the chains are essentially neutral. At high pH, however, the acid groups are driven to dissociate and the grafted chains behave as a charged brush.

To determine the properties of our system of grafted polyacids (see Figure 1), we adopt the SCF lattice model developed by Scheutjens and Fleer (SF)[7,8] to calculate the density distribution, $\phi(\mathbf{r})$, for each of the four components present in the system: grafted polymers, solvent, ions, and counterions. In this model, the free energy of the system is a sum of the following entropic and energetic interactions:

$$F = k \ln \Omega - \sum_{\mathbf{r}} [\rho(\mathbf{r})\,\psi(\mathbf{r})/2 + \chi\phi_p(\mathbf{r})\,(1-\phi_p(\mathbf{r}))] \tag{3}$$

The first term represents the entropy of the system, where k is Boltzmann's constant and Ω is the degeneracy of the chain conformations on the lattice. The terms within the brackets represent the energetic contributions arising from the electrostatic and mixing interactions. We use eq 2 to obtain the degree of dissociation, α, of the acid groups located at $\mathbf{r}$. From $\alpha(\mathbf{r})$ and $\phi(\mathbf{r})$, we obtain the charge density, $\rho(\mathbf{r})$ (which includes charges from both the ions and counterions). The electrostatic field $\psi(\mathbf{r})$ is calculated from $\rho(\mathbf{r})$ through Poisson's law. The mixing interactions are incorporated through the Flory–Huggins approximation, where χ is the monomer–solvent interaction energy, and $\phi_p(\mathbf{r})$ is the polymer density distribution. An additional constraint on the system is that the lattice is fully occupied: for any layer in the lattice

$$\sum_i \phi_i(\mathbf{r}) = 1 \tag{4}$$

where the sum is over the different components in the system.

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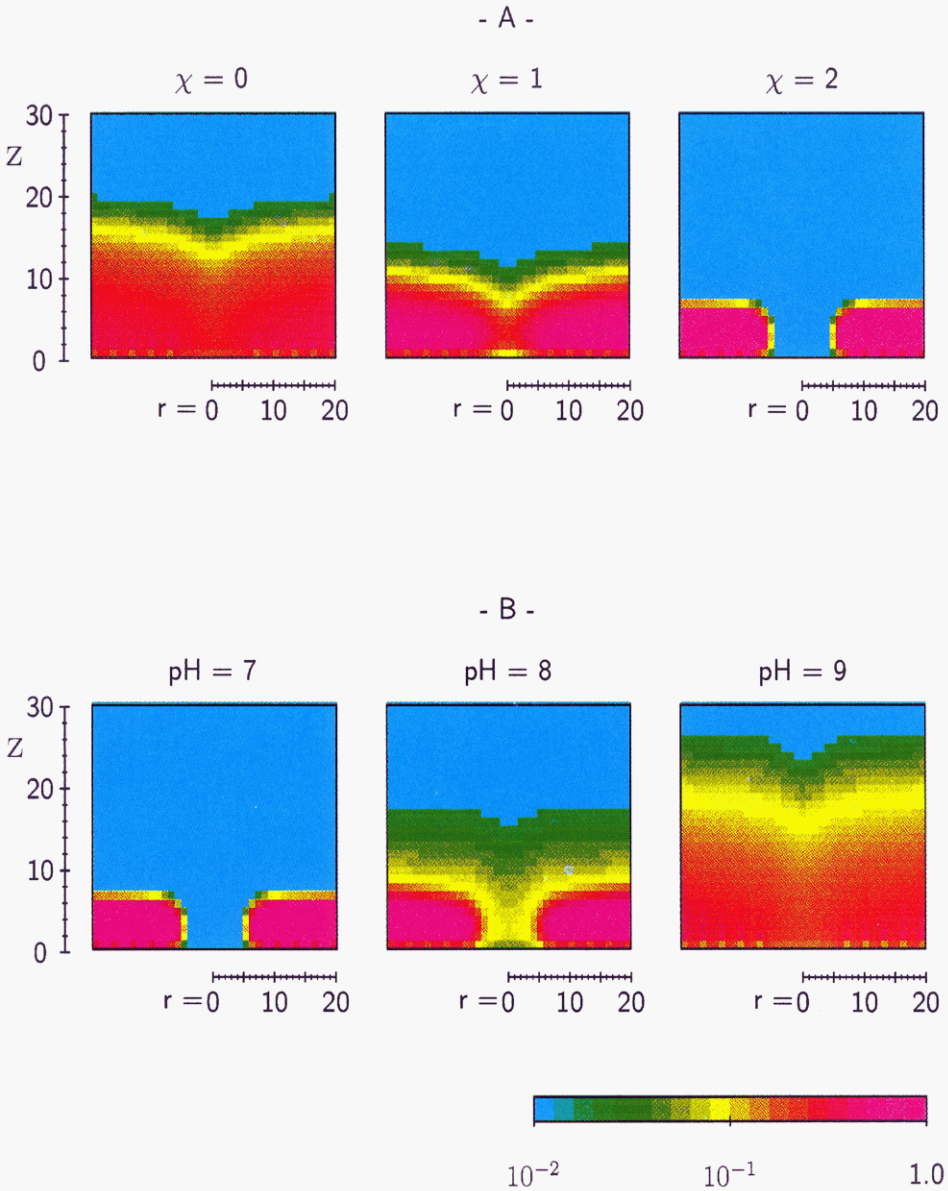

Figure 2. SCF polymer density profiles along r. (The calculation was performed in cylindrical coordinates; the density profiles are for a cross section through the center of the cylinder.) The color bar indicates the correspondence between color and the value of the density being plotted. Note that blue represents the lowest density, while pink denotes the highest. The pK_a of the system was held fixed at 7, and the salt concentration was fixed at 50 mM. In A, the pH was held fixed at 7 and χ is increased from 0 (athermal solvent) to 2 (poor solvent). In B, χ is held fixed at 2 and the pH is increased from 7 to 9.

The aim of the calculation is to find the density distribution that minimizes this free energy. Expressions (2)–(4) form a system of coupled equations that are solved self-consistently. The general numerical procedure for solving these equations can be found in refs 7 and 8. As we noted above, the calculation was performed in two dimensions (using cylindrical coordinates); thus, the segment densities explicitly depend on both the z and r directions.

We start our investigation by fixing the pH of the solution at 7 and varying the solvent quality. (The pK_a of the solution is held fixed at 7.) The nature of the solvent will dominate the properties of the brush at pH $\leq$ 7, where the chains are effectively neutral. Figure 2A shows the results of varying χ, the monomer–solvent interaction energy. At χ = 0, which represents an athermal solvent, there is no repulsion between the monomer and solvent molecules; consequently, the polymers dip into the well, effectively covering the hole. The location of the chains over the hole is entropically favored, since these segments are less constrained than in the more crowded brush. In effect, entropic factors dominate the behavior of the chains in this regime.

Increasing χ reduces the quality of the solvent and introduces a monomer–solvent repulsion. In order to avoid the energetically unfavorable interactions in a poor solvent, the grafted chains stretch away from the hole and extend toward the monomers in the brush. Here, energetic effects dominate the behavior of the chains and the channel remains intact and well-defined. It is also clear from Figure 2A that the monomer–solvent repulsion causes the grafted chains to collapse and, consequently, the layer becomes more compressed. This observation is consistent with earlier findings on uniformly grafted chains in poor solvents.[9,10]

The effect of solvent quality on the conformation of neutral chains that line a channel can also be determined through Monte Carlo simulations. The advantage of the simulations is that the computer graphics allow us to explicitly visualize the chain conformations. Furthermore, they provide an independent means of testing our results from the SCF calculations. In our simulations, the grafted

polymers are modeled as self-avoiding random-walk chains that are anchored to the surface at one end. The bond fluctuation method was implemented for the motion of the chains.[11] The quality of the solvent is controlled through the monomer–monomer interactions. A good or athermal solvent is modeled by setting the monomer–monomer interactions to zero, while the effect of a poor solvent is introduced through a monomer–monomer attraction.[12] The Metropolis algorithm[13] is used to determine whether monomer moves are accepted. In particular, moves that reduce the energy of the system are accepted with unit probability and moves that increase the energy of the system are weighted by the probability $\exp(-\Delta E/kT)$. The parameter ΔE is the change in energy associated with the movement of the monomer, k is Boltzmann's constant, and T is temperature. Figure 3 shows the conformations of the chains from the Monte Carlo simulations. The results confirm our finding from the SCF calculations: in a good or athermal solvent, the chains dip into the well and close the channel, while in a poor solvent, the polymers shrink away from the solvent-rich region, leaving the channel open. (The results also show agreement with recent theoretical[14,15] and computational[12,16] studies that predict grafted chains self-associate in the presence of a poor solvent.)

While a poor solvent at neutral pH causes the channel or pore to open, the SCF calculations predict that increasing the pH (while keeping χ fixed) causes the channel to close. This behavior is shown in Figure 2B. As the pH is increased beyond 7, the equilibrium in eq 1 is shifted to the right. In other words, the degree of dissociation increases and the chains become negatively charged. Now the densely grafted chains experience an electrostatic repulsion that drives the polymers to lie as far apart as possible. Consequently, the chains are driven into the poor solvent above the well and the channel is closed.

Our results indicate that, at values of pH $\leq$ 7, the mechanism that drives the opening of the channel is the lyophobic character of the polymers. At high pH, mutual repulsion between charged chains provides the mechanism for closing the channel. It is important to note that the polymer density at elevated pH is relatively uniform and diffuse throughout the system (see Figure 2B). Thus, above the well, the mass of polymers resembles a loose network or gel (as opposed to the high-density material in the brush at lower pH). Consequently, the overlapping chains would be more effective at preventing the diffusion of long or bulky molecules in or out of the hole than hindering the motion of small species or cations. Thus, our findings can be used to design devices that accept or release macromolecules at low to neutral pH but prevent their passage in high-pH solutions. In addition, the results can rationalize existing experimental data[4] that shows polyacids grafted to the surface of a porous membrane permit the passage of insulin at low pH (2.7) but inhibit the flow at a pH of 8.6.

Finally, we note that the width of the bare batch or channel will have a significant effect on the behavior of the system. Consider the case where the "bare batch" is comparable to the spacing between grafted chains in the brush. At low pH and poor solvent conditions, the collapsed layer will inhibit the flow of molecules in or out of the interface. At high pH, however, repulsion between the charged species causes the chains to become stretched. Molecules can now readily flow into and out of channels that lie between neighboring, stretched chains.[2] Thus, the pH dependence of the gating behavior can be tailored by varying the relative width of the channel. This phenomenon will be explored more fully in future work.

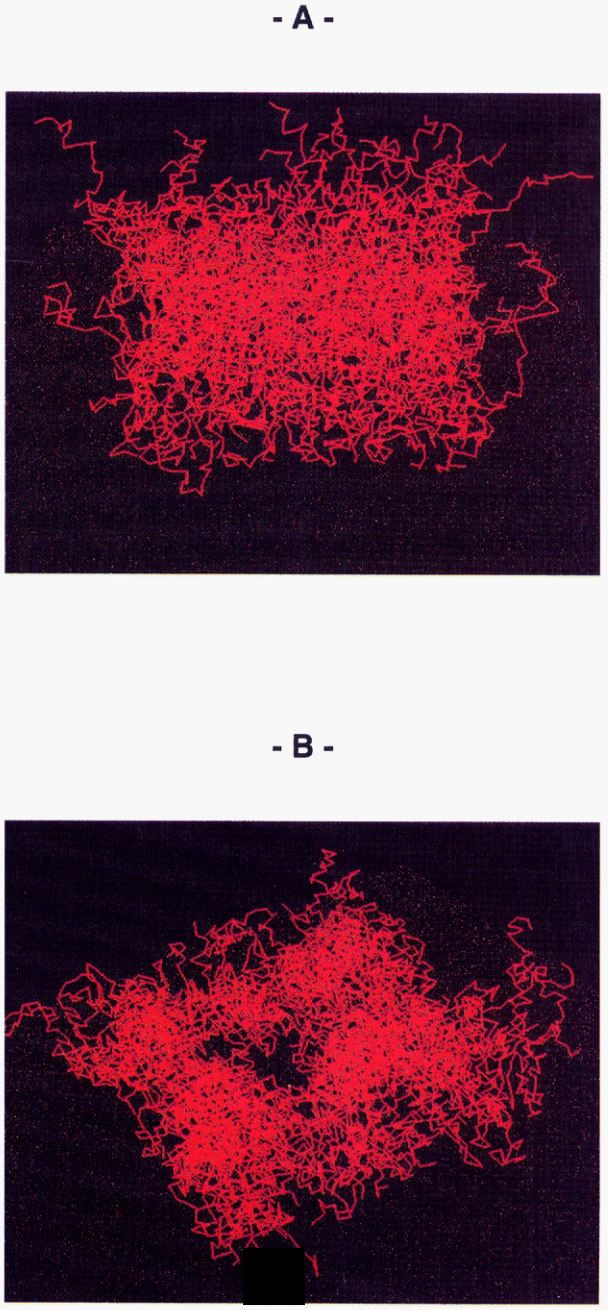

Figure 3. Snapshot from the Monte Carlo simulation showing the equilibrium conformation of the chains. The cubic lattice is 66 × 66 × 156 sites in size, the largest dimension being along the Z direction. Chains 36 segments in length are anchored onto the $Z = 1$ surface at a grafting density of 15%. The central, bare domain has dimensions of 20 × 20 sites. The simulation was run for 8×10^9 time steps. In A, the monomer–monomer interaction energy was set equal to 0, effectively modeling chains in a good solvent. The well is not visible since the chains extend over the bare domain, thereby closing the channel. In B, the monomer–monomer interaction energy was set equal to –0.7, which introduces an attractive interaction between the monomers and models the effect of a poor solvent. Now, the well is clearly visible.

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