HIGHLIGHT

Macromolecules at Surfaces: Research Challenges and Opportunities from Tribology to Biology

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ABSTRACT: A comprehensive review of ongoing and recommended research directions concerning the structure, dynamics, and interfacial activity of synthetic and naturally occurring macromolecules at the solid–liquid interface is presented. Many new developments stem from the ability to target new size regimes of 1–100 nm. These rapid developments are reviewed critically with respect to chemical synthesis, processing, structural characterization, dynamic processes, and theoretical and computational analysis. The common problems shared by flat and particulate surfaces are emphasized. A broad spectrum of material properties are discussed, from the control of interfacial friction between surfaces in moving contact, to the mechanical strength and durability of the interfaces in hybrid materials, to optical and electronic properties. Future research opportunities are identified that involve (1) the emergence of nanoscale material properties, (2) polymer-assisted nanostructures, and (3) the crossroads between interfacial science and biological and bioinspired applications. J Polym Sci Part B: Polym Phys 41: 2755–2793, 2003

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INTRODUCTION

Research on macromolecules at interfaces is in a state of active growth and exciting development. This stems, above all, from an increasing recognition of the importance of macromolecular science and technology over a range of length scales and timescales spanning the molecular to the macroscopic and their impact on many vital needs of society. It is also driven by the unprecedented availability of new tools for chemical synthesis, physical characterization, and theoretical analysis, which are leading to rapidly expanding scientific understanding.

This review is the product of a study panel commissioned by the U.S. Department of Energy Council on Materials to critically assess the research needs and opportunities in this area. An international panel was convened with representatives from universities, national laboratories, and industry. In this review, we emphasize developments since 1988, when a previously convened study panel published an influential report on this subject.[1] Many of the developments since that time stem from the ability to target new size regimes of 1–100 nm. To restrict the scope of this review, we decided not to cover important issues related to the interfaces in immiscible polymer blends.[2–4] We focus on needs and opportunities in the following emerging areas:

- The emergence of nanoscale material properties. Properties ranging from chain structure and thermodynamics to chemical reactivity are found to change as polymers are confined within geometries whose characteristic dimensions approach molecular dimensions.
- Polymer-assisted nanostructures and functional surfaces. These developments are possible because of the conjunction of new synthetic capabilities, processing methods, and even self-assembly paradigms.
- The crossroads between interfacial science and biological and bioinspired applications. Opportunities for high-payoff advances are evident when one considers the cross-fertilization between the physical sciences and the biological sciences.
- New directions in instrumentation and national instrumentation facilities. Newly available research infrastructure is making possible much of the current research agenda. Recommendations are presented for new infrastructure facilities.

These areas address an array of open questions. Developing a fundamental understanding of the structure, dynamics, chemical reactivity, and electronic and photonic response of macromolecular interfaces and how they are modified by the presence of strong driving fields, such as shear, electricity, and magnetism, is a central theme. Then there are major puzzles concerning the characteristic rates and mechanisms of molecular diffusion. The dynamics are surely anisotropic: there is one rate of diffusion for molecules crawling in the plane of the surface, and there is another rate of diffusion for traffic between the surface and spaces farther away (although one can speculate that the second process may facilitate the first). What is the impact on the kinetics of subsequent phase transformations and on heterogeneous nucleation versus homogeneous nucleation? How does the density of thin films compare to that in the bulk state?

How do these facts affect the mechanical response of a polymer-based coating? How is chemical reactivity modified in confined geometries? How are electrical signals and mechanical forces transmitted through a heterogeneous surface microstructure? These and many other questions need to be addressed. We are now in the position of synthesizing molecular surfaces whose chemical and topographical makeup can be tailored and characterized reliably. This sets the stage for the pursuit of a broad new agenda of fundamental scientific questions.

Polymer chain conformations at an interface always differ from the bulk. Now there are rich new applications pertaining to the self-assembly of multifunctional polymers, polymers impregnated with inorganic nanoparticles, and the interaction between synthetic biomedical devices and the natural biological environment. It had been a great limitation that, until recently, there were few laboratory methods capable of either reliably producing or characterizing lateral variations of chemical composition and topography on a surface. There are many relevant length scales, from 1 nm to the continuum limit. It is exciting to see new capabilities in this direction come online. Another great limitation in the past was an artificial distinction between flat and particulate surfaces. This was unfortunate because it discouraged cross-fertilization between different research communities. The same holds true for the restrictive distinction between physical and biomedical sciences. We emphasize the common elements that underlie seemingly disparate problems or disciplines.

Beyond the immediate scientific and practical motivations for studying these systems are the larger energy, health, technological, and environmental consequences of these issues. Questions of lubrication, coating, corrosion, and stabilization of colloidal particles, such as ceramics and metal particles, are obvious when one considers the control of interfacial interactions by the placement of macromolecules at surfaces. Health-related issues, such as the sequestration of DNA for gene therapy and the manipulation of protein assemblies for the treatment of diseases such as cystic fibrosis, arise in surprisingly similar fashion. Questions concerning flow processing to form desired shapes, the welding of polymer interfaces, and membrane technologies arise when one considers more complex fluids, and they raise fascinating issues of controlling the coupling between adjacent phases when they are driven far from an equilibrated state. Currently relevant ideas of the templating of metal and ceramic microstructures onto polymer-assisted self-assembled microstructures arise similarly. Still other questions involve fluids in situations in which the surface-to-volume ratio is high (e.g., catalysis, filtration, and chromatography). Without wishing to minimize the differences between these areas, we can certainly say that they share common themes.

In discussing the science agenda of this report, the panel was impressed by the potential for breakthrough technologies that might be enabled by its successful pursuit. Among the examples of major enabled technologies whose success depends on the successful resolution of the issues raised here are the following:

- The creation of nanotube-based composite materials that are light-weight but maintain their strength.
- The development of gene therapy methods that can greatly facilitate the cure of debilitating diseases such as cancer and genetic diseases.
- The creation of three-dimensional (3D) replicated materials that can have arbitrarily defined 3D geometries, enabling innovations in the emerging field of nanotechnology.
- The creation of organic-based devices (light emitting) and molecular computers whose storage capacity and speed will circumvent the limitations currently faced by silicon-based technology.

Although this list is by no means exhaustive, it provides a few illustrative examples in which the research could have profound consequences. It must be stressed that these developments cannot occur without the concurrent development of enabling methodologies, including the synthesis, characterization, and modeling of these nanoscale situations. In our discussion, we categorize our focus topics into two groups. Areas in which there is considerable current research and prospects for future development are discussed in two parts, one emphasizing existing knowledge and the other stressing potential research areas. In contrast, areas deemed as mature or just evolving are discussed in a single section.

2. CURRENT RESEARCH AND FUTURE OPPORTUNITIES

The primary research activities related to the surface and interfacial behavior of synthetic and biological polymers, which are relevant from a fundamental and application perspective, have been broadly classified into 10 different focus groups in this report (Table 1). These groupings are somewhat arbitrary because these topics share commonalities, both in the tools necessary to probe the underlying physics and because the scientific issues underpinning these physical situations and their applications are closely related. For example, we describe the current understanding of chain structure in thin films in one section, but this information is clearly critically important to understanding the dy-

Table 1. Interrelations between Different Focus Areas

Section	Research Area	Related sections	Representative Applications
2.1	Macromolecules at liquid interfaces, and tribology	2.2, 2.3, 2.7	Friction, wear, drug delivery, blood flow, sharkskin defects in extruded samples
2.2	Chain structure and phase transformations in thin polymer films	2.2, 2.3, 2.4, 2.5, 2.7	Superreflective coatings, sensors and actuators, controlled patterning of the air surface
2.3	Thin-film mobility and chain dynamics	2.1–2.7, 2.9	T_g's of thin films and mechanical properties as functions of thickness
2.4	Nanostructured interfaces	2.6	Creation of nanowires, applications to photonic crystals
2.5	Hybrid polymer–inorganic systems	2.2, 2.3, 2.7	Polymer–clay nanocomposites
2.6	Photonic and electronic applications of thin and confined polymers	2.2, 2.3	Molecular electronics, creation of photonic crystals
2.7	Modeling issues	2.1–2.7, 2.9	Creation of multiscale modeling techniques to bridge hierarchical time and length scales, ability to control the structure and function on a nanometer scale
2.8	Synthetic issues	2.1–2.7	Ability to control the structure and function on a nanometer scale
2.9	Biological and bioinspired issues	2.1–2.8	Health, drug delivery
2.10	Infrastructure issues	2.1–2.9	Efficient use of scarce resources

namics of chains, which is relevant to the mechanical properties of thin polymer layers, such as in nanocomposites. Similarly, we have chosen to stress the importance of synthesis, modeling, and infrastructure issues in separate sections, and in those sections, we describe additional developments that are required to advance the current state of this field

2.1 Macromolecules at Liquid Interfaces and Tribology

Macromolecules at liquid interfaces are ubiquitous in nature and technology. For instance, many colloidal suspensions could not be dispersed or be stable if macromolecules were not present to provide steric repulsion against particle–particle attraction. This mechanism is employed in features as diverse as the stabilization of particles in paints, of additives in motor oils, and of fat globules in milk. Likewise, the surfaces of biocompatible materials must be inert with respect to proteins contained in the organism.

2.1.1 Conformational States of Macromolecules at Solid–Liquid Interfaces

Present Research Status. A vast amount of theoretical effort has been devoted to the description of polymer conformations in the equilibrium state. This provides the fundamental information needed to predict the surface–surface potential energy describing the interaction of two surfaces (as in colloidal problems) or between the surface and an adjoining fluid.[5] In addition, it has become of interest to understand the manner and kinetics with which macromolecules form attachments with a surface, the nature of exchange (if any) between the solution and the adsorbed state, and the dependence of these issues on variables such as the concentration, solvent quality, pH, and ionic strength.[6–9]

The particular case of polymer brushes has been the focus of much experimental and theoretical work during the last 15 years. Unlike the case of statistically adsorbed homopolymers, the conformations of polymer brushes equilibrate rapidly, and the complicating issues of heterogeneity and history dependence, which are very often inherent in the adsorption of homopolymers and proteins, are consequently avoided.[10–12] Much is known about the concentration profile of neutral polymer brush chains in the direction perpendicular to the surfaces, the force between two surfaces covered with brushes as they approach each other, and the very small tangential forces necessary to shear these layers past each other. Newer efforts have focused on corresponding phenomena for charged polymer brushes, and significant progress is currently being achieved.[13,14] Another current emphasis has been on the direct synthesis of polymer brushes from

substrates for the creation of layers with 3D control over the structure.

Long-Term Prospectus. Experimental methods are appearing that provide direct information on the segmental density distribution within the surface layer. However, these methods lack lateral resolution and, consequently, only provide an average of the surface conformations as a function of distance from the surface. On the theoretical side, the importance of surface heterogeneities is attracting attention, in part because of the potential in advancing the understanding of specific surface recognition, but experiments have not yet entirely kept pace with theory and simulation in this area.

The role of solvent quality in brush structure has been studied in detail theoretically but not yet in sufficient detail experimentally, despite scattered studies.[15–17] When the solvent changes from good to poor, a pinned mushroom structure has been suggested for brushes of intermediate grafting density.[18] Although the role of varying solvent quality on the z-dependent concentration profile has been studied and some atomic force microscopy (AFM) studies have appeared that detail pinned micelle structures, little quantitative information is available regarding this pinned analogue of a phase transition. A proper understanding of the structure of the pinned micelles and the thermodynamics of this phase transition may hold the key to unlocking a doorway to self-assembled ordered arrays of nanostructures on a surface.

2.1.2 Dynamic Interactions of Macromolecular Surfaces with Their Environments

Achieving sufficient lateral resolution in an experiment to probe surface chain conformations poses a significant experimental challenge, partly because small distances are necessarily involved and partly because in many of the most interesting systems, surface chains are buried beneath bulk phases and not exposed to air or vacuum. In addition to equilibrium energetics of polymer chains at surfaces, kinetic processes play a key role. One must consider not only well-documented equilibrium forces characteristic of polymers at interfaces (osmotic, bridging, and electrostatic) but also the characteristic timescales of motions and relaxations, as measured by viscoelasticity and rheology. This bears directly on the steric stabilization of colloidal-sized particles at the rapid encounter rates engendered by Brownian motion and possibly also membrane–membrane biophysical interactions, adhesion, and tribology. There is also some relevance to polymer chain dynamics in filled rubbers and phase-separated block copolymer microstructures. In each of these cases, the forces sustained when the two brush-laden surfaces interact arise only in part from the equilibrium potential of the interaction that can be calculated from statistical mechanical considerations of equilibrium free energy. A major additional component consists of time-dependent, frequency-dependent relaxations of chains within the interface, that is, the rheology of the interface.

Present Research Status. Dynamic aspects are more problematic than equilibrium, in part because of the paucity of experimental and theoretical methods with the capacity to probe time-dependent changes in systems with so many degrees of freedom as well as high-energy barriers between local free-energy minima. One approach used recently is to study the exchange dynamics between the adsorbed state and free solution.[6–8] This, however, is limited to long times, minutes to hours, and is insensitive to single chains. Evanescent wave light scattering is also used to study collective rearrangements that give rise to fluctuations on the order of the optical wavelengths.[19,20] Still other approaches involve nuclear magnetic resonance (NMR) and electron spin resonance.[5] These methods have the advantage of probing more rapid relaxations characteristic of individual polymer chains during the time that they reside in the adsorbed state. However, interpretation is generally model-dependent, and these methods do not give direct, quantitative dynamic information such as the characteristic times for translational or rotational motion of individual segments within adsorbed chains.

For a time, it seemed self-evident that segmental mobility in the liquid state must be faster near a nonadsorbing surface than in the bulk. There is ample simulation evidence in favor of such an idea[21,22] because random coils orient preferentially parallel to a solid boundary for steric reasons.[22] Attractive forces between polymer segments and the surface, and surface corrugation, might, of course, retard motion because of altered chain conformations, that is, multiple points of contact of the chain with the surface-limiting adsorption–desorption events. There is copious evidence from experiments[23,24] and many computer simulations of the qualitative effect. However, even this conclusion turns out to be controversial. The glass-transition temperature (T_g) may be depressed in the same systems in which near-surface diffusion is observed to be retarded.[23,24] Controversies concerning the glass transition in thin polymer films typify the difficulty, at the current state of understanding, of generalizing about even an attractive case when different chemical systems are compared.[25–29]

The diffusion of molecules within monolayers at a surface is potentially a simpler starting point. The related question of protein diffusion within lipid membranes at submonolayer coverage has been studied exhaustively.[30–32] The question asked in this field is how center-of-mass

diffusion scales with concentration in the monolayer. Reasonable agreement has been found with theories that model the molecule as a compact-shaped, solid object. These models also seem to describe the scaling of the diffusion coefficient with the surface concentration when flexible polymers are spread at submonolayer coverage at the water–air interface.[33]

Consider now the surface diffusion of flexible chains. Does a chain of N repeat units diffuse as N independent objects? If not, how are they correlated? Computer simulations of Carmesin and Kremer[34] for a two-dimensional (2D) solution found no evidence of strong correlations for dilute chains in the absence of hydrodynamic interactions; the center-of-mass diffusion coefficient (D) was found to scale as $D \sim N^{-1}$ (Rouse behavior). The pioneering experiments of Maier and Rädler[35,36] on the diffusion of DNA, a cationic polymer on an anionic fluid lipid membrane, also found $D \sim N^{-1}$, the prediction of the Rouse model without hydrodynamic interactions. These experiments focused on stiff DNA chains, long enough to visualize in an optical microscope, having statistical segments such that the molecular conformations obeyed random walk statistics with excluded volume. The Coulombic interactions responsible for binding the chain to the surface are inherently long-range. It is worth asking whether a system dominated by short-range interactions, as expected for nonpolar polymers, would behave similarly. Second, because the lipid membrane used as a surface in those experiments was in the fluid phase, the surface that the DNA experienced may have been effectively flat on the relevant timescale. However, the limited available experiments concerning diffusion on a solid (rather than fluid) surface and using uncharged (rather than charged) flexible polymers show a different dependence of the rate of lateral transport, $D \sim N^{-3/2}$ (N is the degree of polymerization).[37,38]

Long-Term Prospectus. Intramolecular conformations, and even the local density of polymers in solution and the melt, may be anisotropic in the directions parallel and normal to a surface and may vary with the distance normal to that surface. The structure and dynamics may be further influenced by interfacial interactions and by the topographical and chemical heterogeneity of the surface itself. Benchmark computer simulations for a single adsorbed chain on a corrugated surface with and without hydrodynamic interactions would also be very valuable. With the rapidly expanding technological developments in computer power, simulations of such a problem with an explicit solvent may soon be feasible. On the experimental side, there is a good chance of advances in understanding single-molecule dynamics coming from fluorescence experiments.

2.1.3 Friction and Lubrication: Tribology

A macroscopic observation such as lubricated friction has tremendous practical relevance but is so complex that its origin has been traditionally deemed to be too complex for scientific understanding. This situation is changing rapidly as a result of advances in molecular tribology.

Present Research Status. The short-range structure of a fluid becomes perturbed near a solid surface with important consequences. For example, density oscillations in the direction normal to the surface result in oscillatory forces that resist the approach of two surfaces in a liquid medium. This is understood in principle and has been analyzed theoretically,[39] but there exist at present no direct measurements of the collective structure factor, $S(\mathbf{Q})$ (where $\mathbf{Q}$ denotes the wavevector), to give quantitative information analogous to the radial distribution profile that is characteristic of bulk fluids. Measurements have been restricted to the liquid–vapor interface,[40,41] the physics of which are quite different because there is no atomic structure in the phase that adjoins the liquid and because the geometrical restriction is so soft. Recent measurements go beyond this to measure the short-range structures of small-molecule liquids[42] and polymers[43] against a single solid surface and recently of small-molecule fluids confined to molecularly thin spacings between two surfaces.[44] Measurements are beginning to appear concerning aqueous fluids.[45] This has impeded our understanding of confined fluids rather severely, especially because of the unknown and controversial degree to which $S(\mathbf{Q})$ of a fluid develops anisotropy near a solid surface.[45–50] From the standpoint of macroscopic friction measurements, many recent studies on model systems have concerned friction between atomically smooth solid surfaces separated by molecularly thin liquids.[47]

Another emerging issue is the boundary condition when a flowing fluid meets a solid boundary. For many years, it has been observed that there is no compelling argument to justify the standard no-slip boundary condition of textbook continuum hydrodynamics, which states that a fluid at a solid surface has no relative velocity to it.[51,52] No-slip, for example, explains why large particles are easy to remove by blowing past a surface, but small particles not. Similarly, readers who wash dishes will have noticed that it is difficult to remove all the soap just by running water; a washcloth is needed for effective cleaning. Why? There are two schools of microscopic explanation. The traditional explanation is that because most surfaces are rough, the viscous dissipation as the fluid flows past surface irregularities brings it to rest, regardless of how weakly or strongly molecules are attracted to the surface.[53–55] More recently, this has been

challenged by accumulating evidence that, if molecularly smooth surfaces are wet only partially by the moving fluid, hydrodynamic models work better when one uses instead partial-slip boundary conditions.[56–65] Then, the main issue is whether fluid molecules attract the surface or the fluid more strongly. Recently, hydrodynamic forces were compared for the flow of Newtonian fluids past surfaces of variable roughness but similar poorly wetted surface chemistry. The critical shear stress and shear rate at which deviations from predictions using the no-slip boundary condition occurred increased nearly exponentially with increasing roughness and diverged at a root-mean-square roughness of approximately 6 nm. This suggests that local intermolecular interactions dominate when the surface is very smooth but roughness dominates otherwise.[66] This quantified the limits of both ideas but failed to give direct microscopic information about the physical mechanism underlying slip. Other experiments and theories involve the slip of polymer melts and solutions as they flow past solid surfaces,[67–71] this being a vital issue in polymer processing. The extent of drag reduction (which appears as apparent slip) can be controlled by the addition of surfactants.[70,72,73] Furthermore, other related work involves the creation of durable biological implants to replace joints (e.g., hip and knee joints) in the human body.[74,75] Polymer model systems have been used to address this biolubrication issue.[76–78]

Long-Term Prospectus. Hairy surfaces—polymer chains tethered to surfaces in a liquid environment—present complex physical problems decidedly different from hard, rigid surfaces, as illustrated in Figure 1. There are at least two questions at hand: the influence of the surface texture on the flow of a Newtonian liquid and flow-induced deformations of polymer conformations at the surface.[12,79–82] The presence of the polymer renormalizes the location of the solid surface to a new location, the actual solid surface plus the hydrodynamic radius of the surface-tethered polymer, as long as the fluid on the surface of the renormalized moving body moves at the same rate as that body.[83,84] (Another limiting case, the near-field situation, occurs if the polymer-laden surfaces are so close together that the chain conformations overlap. Then, the flow of the solvent through these chains is akin to the flow of the solvent through a porous medium,[85,86] albeit one whose structure can adjust to flow.[83]) This has an evident bearing on understanding a variety of physical situations in which a fluid flows past polymer-laden surfaces at a rapid rate. Not only is this particularly important to the dispersion and aggregation of colloidal particles in foods, paints, and other filled systems, but it is also relevant to the flow of water past ships and fish,[87] microfluidic devices,[88] and fluid flow in biological organs, such as the kidney.[89]

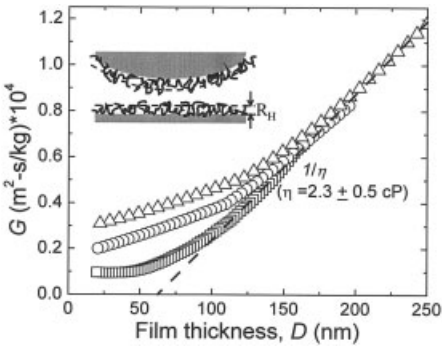


Figure 1. End-attached poly(vinyl pyridine)–polybutadiene diblock copolymers in tetradecane were placed at variable spacings larger than twice the layer thickness within a modified surface-force apparatus, and the hydrodynamic forces due to the flow of the solvent past these layers were measured as a function of the surface spacing, pumping frequency, and pumping velocity (the product of the frequency and amplitude). When the flow rate was lower than a critical level, the findings agreed with a simple hydrodynamic picture in which the solvent appeared to flow past surfaces of defined spacing, the solid–solid spacing being less twice the hydrodynamic radius (R_H). When the flow rate exceeded a critical level, the magnitude of the hydrodynamic forces became up to an order of magnitude less than could be described by flow past a layer of thickness R_H and the stick boundary condition at that layer. In this plot, the reciprocal of the hydrodynamic forces ($G = 6\pi R^2 \nu_{peak}/F_{H,peak} = D - 2R_H/\eta$) is plotted for a 2.6-Hz oscillation at different amplitudes: (□) 0.6, (○) 1, and (△) 2 nm. The reciprocal of the slope at a large film thickness yielded the known viscosity of the flowing solvent ($\eta = 2.3 \pm 0.5$ cP at 25 °C). The intercept gave $2R_H$, the hydrodynamic layer thickness of an adsorbed or grafted polymer. The insets shows an image of the experimental configuration. (From Y. Zhu and S. Granick, Macromolecules, 2002, 35, 4658, adapted by permission.)

The numerous outstanding questions include the following: (1) How does the fluid avoid the development of prohibitively high forces when rapidly driven far from equilibrium? It seems clear that there is no single mechanism and that solutions to this problem will bring the field into closer contact with emerging questions of polymer processing and, more generally, the boundary conditions for fluid flow over a surface. (2) If we now move out of steady-state conditions, how does a soft fluid respond to a high-amplitude, short-lived change in the pressure, deformation rate, or compression? (3) No one yet really knows whether a general theory of surfaces in sliding contact is possible. The flow of confined fluids is very much like granular materials such as sand, powder, and colloidal particles. Too often the models are system-specific, but common responses strongly suggest more universality, which could reflect the fact that high-density, short-range packing and dynamic rearrangements of

structure by instability are interrelated. Can we predict, from theory rather than empiricism, what makes lubricant molecules of one chemical structure more effective in lowering friction forces than those of another?

2.2 Chain Structure and Phase Transformations in Thin Polymer Films

The study of phase transformations in thin polymer films is driven by their relevance to a variety of current and potential applications. For example, the phase separation of a thin binary polymer mixture leads to the nanostructuring of the film surface, and the lateral size and height can be varied.[90] Although this patterning of the surface affects the specular reflectivity of light, that is, its gloss, the size and lateral ordering of these surface features are random. Topographies generated from polymer mixtures have already been used as antireflection coatings, for example. When the local curvature is extremely high, the effects are not yet understood clearly. For example, the phase separation of protein mixtures within lipid bilayers influences the behavior of cells; strong local curvature can lead to the budding of the cell wall, a step critical to cell division.

To date, most experiments on thin films of synthetic polymers yield z-dependent concentration profiles, although a few provide limited chemical information laterally. However, no information is generally available on the lateral structure and thermodynamics of polymer chains in confined geometries. This is due primarily to the small sample volumes inherent in the structures and the lack of appropriate characterization tools. Similarly, most theoretical models assume lateral homogeneity, and so we cannot assess the importance of these issues to system thermodynamics. We discuss the current status of the field and also focus on directions in which fruitful advances are anticipated with the proper availability of experimental and theoretical tools.

2.2.1 Chain Conformation in Confined Geometries

Present Research Status. The conformation of polymer chains in confined geometries is important, for example, in the design of thin, polymer-based superreflective coatings. The modification of chain conformation on confinement can affect the birefringence and crucially degrade the reflectivity. Similarly, separation schemes, such as gel permeation chromatography, are driven by the free-energy loss associated with the confinement of long polymer chains in porous hosts. Although much theoretical work has been done in this area, little is known experimentally about the conformations adopted by polymer chains in these restricted environments.

When a polymer melt is confined into a planar thin film of a thickness comparable to the bulk radius of gyration of the chains (R_g), the chains are strongly squeezed along the confinement direction. What is less obvious is the conformation assumed by the chains parallel to the surfaces (i.e., in the x–y plane). Many past theories and simulations have suggested that chain conformation remains Gaussian in this direction and that the chain dimensions parallel to the surfaces are perturbed by less than 10%, even when the thickness (L) is less than R_g.[91,92] These reflected Gaussian ideas, which afford considerable simplification in theoretical analyses, are important because they form the underpinnings of our understanding of polymer behavior in confined geometries. However, the small sample volume of a thin film, typically 10^4 to 10^5 times smaller than a bulk sample, makes these experiments strongly noise-limited.[93] Recent small-angle neutron scattering (SANS) data on planar films as thin as $L \sim 10$ nm, which have measured chain dimensions in the x–y plane for isotopic polymer mixtures far from phase separation, show that the chains retain their unperturbed Gaussian conformations in the direction parallel to the surfaces even when L is less than R_g.[94] These results lend significant credence to reflected Gaussian ideas and form a solid basis from which we can understand the behavior of polymer materials in thin films.

Long-Term Prospectus. Although the simplest question of the in-plane chain conformation has been studied, the corresponding information along the confinement direction cannot be explored by traditional methods such as SANS because of the presence of the concentration profile in this direction. This is an important issue that remains to be elucidated. Similarly, the size of melt chains in more confined environments, such as lines and dots, which are relevant to nanolithography, remains to be studied. Finally, we note that current studies of the conformation of polymer chains in porous hosts, which are relevant to separation schemes, yield results that are strongly affected by the random orientation of pores in a typical medium such as Vycor. The availability of hosts with spatially ordered pores can help to alleviate this concern and to obtain predictive insights into commercial separation schemes.

2.2.2 Liquid–Liquid Phase Separation in Thin Polymer Films

Present Research Status. The last 5 years have seen considerable improvements in the understanding of phase transitions in thin films. The major experimental finding in this area, later complemented by simple theories, is that the air surface of relatively thin films (with a thickness of $L < 300$ nm) becomes macroscopically rough.[90] This result has been empirically known in the

paint industry for close to 50 years, in which it is recognized that the gloss (i.e., the specular reflectivity of light) of the air surface can be dramatically reduced by the phase separation in a thin coating. An important point is that these rough elements are random in size and distribution over the surface. Studies of thin-film phase transitions on chemically patterned surfaces and on surfaces patterned by buffing[95] show that the resulting structures can be confined to lie along lines determined by the patterning of the underlying substrate. Manipulating the size, order, and orientation more precisely through the control of the interactions remains open. Developing routes by which phase transformations can be directed, that is, forced into well-defined, ordered, and orientationally directed patterns without the use of external fields, will be a breakthrough for many future applications.

A related question is the effect of size reduction on the actual phase diagram when geometric constraints and surface segregation can markedly alter the behavior. This has been a theoretical focus in the last decade, and the general prediction is large shifts in a phase diagram on confinement; that is, measurable shifts are predicted even for films of a thickness of $L > 100R_g$. Although Chen and Reich[96] first studied this problem using light scattering over 20 years ago, more recent experiments have yielded conflicting results. Results from AFM, light scattering, neutron reflectivity (NR), and SANS have effectively shown no change in the phase diagram even for films as thin as $L = 50$ nm.[90,96,97] In other cases, 10–50 K shifts in the phase diagram have been seen even for relatively thick films ($L > 200$ nm). The underlying physics and thermodynamics giving rise to these differences are unresolved.

Long-Term Prospectus. A promising idea for applications is to control the sizes and lateral ordering of the nanostructures that form at the air surface of the coatings. There are many opportunities in both synthetic and biomolecular systems that are opened once such control is attained. With synthetic polymers, although chemical patterning or buffing has been used to generate lines of these structures, little control exists within these lines. Advances are needed to achieve control over the sizes and 2D order of the patterned surfaces. There are intriguing related issues in the field of biomacromolecules, such as shape transformations of lipid bilayers within living cells. Membrane proteins with asymmetry between the hydrophilic and hydrophobic portions tend to preferentially aggregate within the membrane, causing a local curvature of the bilayer. Such phenomena may logically lead to the budding of cells. Indeed, the role of phase separation of the proteins in a lipid bilayer, and the importance of the nonequilibrium nature of this phenomenon, are issues that could be fruitfully addressed by careful studies of model polymer mixtures in the presence of flexible boundaries.

2.2.3 Microphase Separation of a Block Copolymer in Thin Films

When a block copolymer is confined into a thin film, the chemical dissimilarity between the blocks results in a preferential segregation of one block to the interface. This preferential interfacial segregation interacts with the connectivity of the blocks and orients the copolymer morphology parallel to the surface. Although this orientation persists only over a few layers for diblock copolymers in the disordered state, the orientations can propagate many lattice periods away from the surface when the block copolymer is ordered. Two important questions arise here: the first is the role of the film thickness on the order–disorder transition (ODT) in thin films. This issue has been studied through a combination of SANS and NR, and it has been found that the ODT only shifts by 5–10 K even for very thin films. The second question that has been addressed in some detail concerns the factors governing the orientation of block copolymers, that is, parallel to the surfaces, as discussed previously, versus perpendicular to the surfaces. The two ways of obtaining a perpendicular orientation of the lamellae are to use very thin films or to modify the surface interactions, such as through the use of random copolymers, to effectively neutralize the surface preference for any given block. We do not discuss these issues further because they have been extensively investigated and discussed in the current literature. We expect that these nanostructures will be of great relevance in the creation of porous media consisting of ordered pores and in the synthesis of nanowires with well-defined diameters and chemical structures. These issues are discussed later.

2.2.4 Crystallization in Thin Polymer Films

The crystallization of polymers in thin films is relevant to predicting their mechanical and electrical response, which are empirically known to vary strongly with L. The utility of these films as sensors and actuators thus varies strongly with the film thickness. Similarly, poly(vinylidene fluoride)-based polymers are finding increasing use in photonic applications. Their thin films could impact the creation of polymer-based photonic crystals; a polymer can form the pattern around which inorganics can be assembled, and then the polymer is typically burned out. Concerning crystallinity in thin films, little else is well established either theoretically or experimentally. We expect this area to become of increasing importance.

2.2.5 Combinatorial Materials Science For Polymer Thin Films and Coatings

The success of combinatorial and high-throughput methods in pharmaceutical research has received increasing attention for the discovery and synthesis of new inorganic materials, catalysts, and organic polymers.[98–101] Combinatorial methods can also allow the rapid scanning of the parameter space to make fundamental measurements and develop physical models. Both the industrial processing and fundamental research on polymeric coatings and thin films involve an inherently unlimited combination of systems parameters, including the composition, temperature, and pressure. Hence, combinatorial methods are well suited for characterizing these materials.

One major limitation in extending the techniques used to create combinatorial libraries of inorganic materials (samples containing thousands of compositions or other processing variables) has been that vapor-phase deposition is not applicable to polymers. In addition, most of the measurement techniques traditionally used to characterize films have been developed for one-sample/one-measurement use, and they require extensive modification for high-throughput screening. However, techniques have been recently demonstrated for depositing polymer film libraries that employ continuous gradients of thickness, composition, surface energy, and temperature.[98–100] Each library, about the size of a standard microscope slide, contains between 1000 and 3000 differentiable conditions within the parameter space. These techniques have been applied to characterizing several fundamental phenomena of dewetting, phase separation, and block copolymer coatings and thin films by automation of the measurements. This produces high-throughput screening in far less time than conventional methods. Furthermore, not only do these methods produce a large amount of data with a broad range of parameter values, they also provide the characterization of the kinetics and processing. Although it continues to be necessary to validate each new combinatorial method by comparison with existing processing methods, the potential is clear for this approach to address new questions not addressable, or not so efficiently addressable, otherwise.

2.3 Thin-Film Mobility and Dynamics

The drive to reduce the size scale of devices translates into feature sizes and film thicknesses that are tens of nanometers or less, that is, size scales approaching R_g of the polymer chains. With decreasing film thickness (L), not only will confinement effects be of importance, but the fraction of chains in contact with the surface will increase, amplifying the importance of interfacial interactions. As discussed previously, in the context of chain conformations, this raises fundamental questions about whether the mobility and relaxation processes of the polymer molecules are perturbed. These are not only of importance in the context of the basic physics of chain molecules but also have significant technological and practical impact. For example, the shape retention of nanoscopic structures made from a linear, amorphous polymer depends on the mobility of the chains. This is highly relevant to nanolithography. Similarly, the diffusion of chains into the galleries of clay sheets is critical to the formation of polymer-based nanocomposites. Experimental studies on chain dynamics in thin films are plagued by the absence of techniques for probing dynamics directly. As a result, indirect methods for deducing the role of confinement in dynamics, such as the measure of thermal expansion, have been used. This results in seemingly contradictory estimates of T_g in thin films by different methods, which are now only beginning to be resolved.[102] The development and application of experimental tools that directly measure dynamics will speed this resolution and lead to new insights.

2.3.1 Glass-Transition Phenomena in Thin Films

Present Research Status. Even the simplest situation, a linear homopolymer film on a solid substrate, has important open questions regarding T_g of the polymer either near the substrate or in the vicinity of the free surface of the film.[25,26,103,104] These issues have been of considerable interest because they form the basis for understanding the mechanical, rheological, and electrical response of thin polymer films, which is critical to applications. T_g is often estimated by the measurement of the thickness of the film as a function of temperature, but depending on the character of the substrate and the polymer, results show that T_g can either increase or decrease as the film becomes thinner. Although the specific attraction of the polymer to the substrate will clearly lead to a decrease in the mobility of the polymer, it is not yet possible to generalize from the available experiments in those cases in which the substrate interactions are balanced and in which polymers at a free (air or vacuum) surface are considered. The molecular orientation appears to persist even after long annealing times after casting, resulting in birefringence, and this suggests that films remain out of equilibrium even after long annealing. This effect may also contribute to reports of T_g shifts in thin films.

An important question, which has not been settled, is in what respect the experiments really measure a glass transition. Many techniques are invasive and probe distances well beyond the surface. Others rely on the measurement of an average property of the film, such as the thermal expansion coefficient, refractive index, or density. Still others rely on spectroscopic methods, such as

near-edge X-ray absorption spectroscopy (NEXAFS) and NMR, which provide direct measures of the surface relaxation. Other experiments such as positron annihilation, which measures the local density, or AFM, which measures the local mechanical response, also give contradictory results. Theories and simulations on this subject, which could shed considerable light on these issues, remain rather sketchy. Thus, many open issues need to be addressed before the mechanical properties of thin films can be predicted quantitatively.

Long-Term Prospectus. The development of noninvasive experimental methods, such as inelastic scattering, that can sense polymer mobility with a spatial resolution of 1 nm are key to advancing our understanding of this problem. In this context, the availability of high-radiation fluences at the Advanced Photon Source of the Argonne National Laboratory, the proposed Spallation Neutron Source under construction at the Oak Ridge National Laboratory, and enhancements to the neutron reactor sources at the National Institute of Standards and Technology and the Oak Ridge National Laboratory all offer the realistic possibility of delineating these dynamics at various levels of coarse graining. The relationship between the measured dynamics from such experiments and those observed in the variety of macroscopic experiments previously discussed also needs to be established to understand the apparently contradictory results reported in the literature. In this context, computer simulations can play a critical role because they can address all of these issues and help to resolve these controversies.

2.3.2 Diffusion in Thin Polymer Films

Present Research Focus. The measurement of the diffusion of polymers near surfaces and in thin films is another relevant measure of chain dynamics in confined geometries. These measurements could have a significant impact on the use of diblock copolymers for the creation of ordered templates, especially when annealing methods are used to create structures with few grain boundaries. A remarkable slowing of the diffusion normal to solid interfaces has been observed even at distances greater than $10R_g$ from the solid surface.[105,106] The decrease in D and even its dependence on the molecular weight (M) of the diffusing chain is a function of the character of the solid substrate. The lateral diffusion of polymers in thin films shows an equally surprising linear reduction in D as a function of the film thickness,[106] even when L is approximately $10R_g$. The influence of surface interactions on D over such large distances has yet to be explained by theoretical arguments.

Unusual results are also found for the diffusive lateral spreading of ultrathin films of polymers (polydimethylsiloxane, PDMS) on Si surfaces covered with a native oxide layer.[107] Changing the relative humidity changes the power-law dependence of D on the molecular weight of the monodisperse polymer (M) from $D \sim M^0$ at a relatively humidity (RH) of 98% to $D \sim M^{-0.6}$ at RH = 82% to $D \sim M^{-1}$ at RH = 40%. In all cases, D of a high-M polymer is decreased much more strongly by decreases in RH than D of a low-M polymer. Such diffusive spreading is technologically important for hard disk lubricants as well as the melt intercalation of polymers into the galleries of mica-type silicates to form nanocomposites. The universal behavior observed for diffusion in flexible polymer melts, in which the chemical architecture of the chain is only important in determining the values of parameters such as the entanglement molecular weight, will not be found for the mobility of chains in the melt near solid interfaces. Here the chemical details matter greatly, even determining the exponents of the scaling laws.

Long-Term Prospectus. A promising means of resolving these issues is to consider the diffusion of chain molecules on chemically patterned surfaces. One of the most attractive methods for doing this is to form self-assembled monolayers on the substrate. These layers can be applied by microcontact printing,[108] which allows access to pattern sizes in the 1-μm range. These have proved useful in templating the ordering of block copolymers[109] and, as discussed previously, in controlling the lateral phase separation of mixtures of homopolymers. However, the bonding of these monolayers is too weak to be useful in the 100–200 °C temperature range in which typical diffusion studies are conducted.[109,110] Some important steps have already been taken to alleviate these problems, such as living free-radical initiators, which can be bound to surfaces from which thick brushes can be grown.[111] If thick brushes are not required, a very attractive method is that of Prucker et al.,[112] in which a benzophenone silane is coupled to a surface and then covered with a layer of a polymer or copolymer. When the benzophenone is irradiated by ultraviolet light, it produces a bound free radical that reacts with the polymer or copolymer chains to graft them to the surface. Films with patterns approximately 20-nm-thick can be produced in this way.

2.3.3 Adhesion and Adhesion Promotion

Adhesion promoters or silane coupling agents are used to improve the interfacial adhesion between polymers and inorganic solids in applications ranging from composite materials to ink jet printers. Even though they have been used for over 40 years, adhesion promoter selection and optimization are still more art than science. As applied in practice, these are not monolayers but thin films of network polymers crosslinked after deposition by the

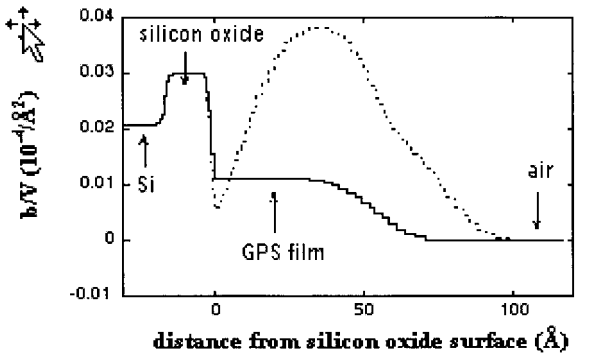


Figure 2. Best-fit scattering length density (SLD) profiles determined by NR (—) before and (–) after swelling with deuterated nitrobenzene vapor of a 5-nm-thick film of crosslinked GPS on an SiO_x native oxide layer on silicon. (From H. Yim et al., J Phys Chem B, 2002, 106, 2474, adapted by permission.)

condensation reaction of hydrolyzed Si—OH groups on the silane. It seems likely that the crosslinking reactions of such layers will be affected by the presence of both the substrate and air surfaces, but until recently, there was no way of determining the uniformity. However, because the density of crosslinks in the network affects the swelling by the vapor of a solvent and because such swelling can be sensed by NR if the solvent is deuterated, such measurements can now be made. Figure 2 shows the scattering length profile determined by NR before and after swelling with deuterated nitrobenzene vapor of a 5-nm-thick film of crosslinked (3-glycidoxypropyl)-trimethoxysilane (GPS) on an SiO_x native oxide layer on Si.[113] The swelling and scattering length density are very low at the SiO_x/GPS interface but are quite large in the center of the film before decreasing again at the air interface. As opposed to the almost zero swelling (and thus high crosslink density) at the SiO_x interface, the swelling in the center of the 5-nm-thick film corresponds to an extension ratio of the GPS network normal to the film of approximately 2.5. Such results have important implications for the failure of such layers, especially under combined conditions of high stress and humidity, and suggest a number of possible remedies now that the tools are available to measure the resultant microstructures.

2.4 Nanostructured Interfaces

The fabrication of thin organic films that possess nanoscopic patterns in the directions normal or parallel to a solid surface constitutes an emerging theme of modern materials science. Many of the systems discussed next involve the use of block copolymers, in which the self-organization of the amphiphilic polymer in the melt state provides a natural opportunity for introducing mesoscale ordering. Other systems involve layer-by-layer self-assembly from solutions of charged polymers and charged particles[114–120] and lateral phase separation of immiscible homopolymer systems.[98] An example of the capability to form single crystals in a block copolymer film is shown in Figure 3.

2.4.1 Homogeneous Interfaces

Present Research Status. The key to manipulating the orientation of the copolymer morphology in thin films is to control the interfacial interactions. A particularly simple way of achieving this control is anchoring a random copolymer to the interface, which consists of monomer units identical to those of the block copolymer. Through the variation of the fraction of the monomer units of each type in the random copolymer, interfacial interactions can be balanced, and the diblock microstructure will orient normal to the surface. This very simple, robust process has opened many potential applications. In the simple case of a cylindrical microdomain morphology, the thin film is essentially an array of nanocylinders oriented normal to the surface with an areal density that is dictated by the molecular weight of the copolymer. Areal densities in excess of 9×10^{11} cylinders/cm^2 are easily anchored. With standard lithographic procedures, one polymer is crosslinked, and the second is degraded. This produces an array of nanopores on the surface that can be used as templates for the transfer of patterns to the substrate, or as porous separation media after removal from the substrate. By chemical or electrochemical methods, the pores can be filled with metal, glass, or other inorganic materials, and this produces arrays of nanowires with exceptionally high aspect ratios.[121]

Long-Term Prospectus. Although arrays of nanoscopic structures have potential uses in many applications, certain applications require that each structure be addressable. This mandates that the lateral position of each element be precisely defined; that is, one hexagonal lattice defines the entire surface. On a homogeneous surface with balanced interfacial interactions, micrometer-sized grains consisting of arrays of well-ordered, hexagonally packed nanocylinders oriented normal to the film surface form. These grains are randomly oriented on the surface. With ultrathin films (one lattice period thick or less) of asymmetric diblocks having spherical[122] or cylindrical[123] microdomains, significant strides have been made toward the removal of all grain boundaries through various annealing procedures.

However, as the structures move from being 2D to 3D, such as cylinders or lamellae oriented normal to the surface, these coarsening processes alone are not sufficient. Rather, a field with an in-plane component will be

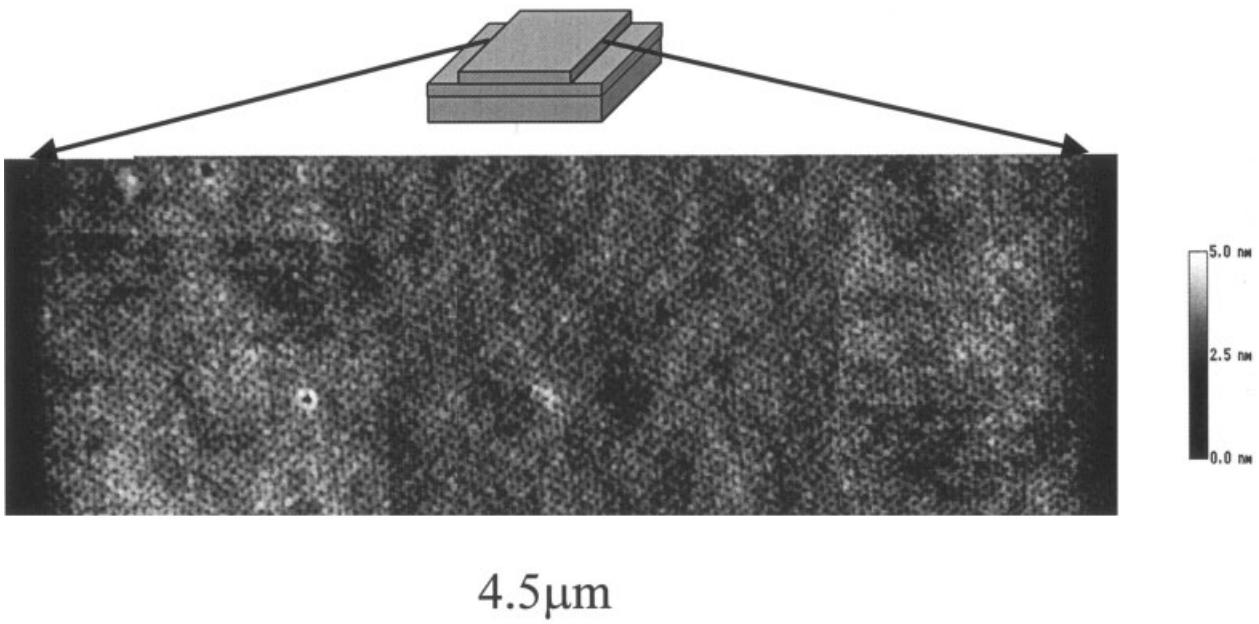


Figure 3. Scanning force micrograph of a spherical domain block copolymer film on top of an SiO_2 surface consisting of 30-nm-high mesas and wells. When the mesa (or well) edges are less than 5 mm apart, a single crystal of spherical domains is formed, templated by these edges.

necessary. Along these lines, several interesting possibilities are surfacing, including dip coating, which involves directed flow during casting; in-plane thermal gradients, which are akin to zone refinement; directed in-plane ordering from the mixed state; and lateral swelling gradients.

If the chemical modification of a surface is not possible, an alternative means of manipulating the orientation of the morphology in polymers is the use of an external field. The shear alignment of domains normal to substrates has not been achieved in thin films, but unconventional processing methods may hold promise in this area. For example, if the alignment is normal to the shear direction and to the vorticity direction, as has been seen in certain frequency ranges for lamellar diblock copolymer morphologies, unusual shear-directed reorientation may ensue. Although magnetic fields are quite attractive, the magnetic moments of most polymers are quite small, and the orientation is not efficient at the relatively low magnetic fields achievable in the laboratory. High magnetic fields at the National High Magnetic Field Facility may make such a possibility more attractive in block copolymer phases that have lower mobilities. Electric fields[121,124,125] have been found to be a very effective means of orienting the morphology in thin polymer films. For a multiphased system in which there is an anisotropy in the shape of the phases, the difference in the dielectric constants of the domains will force an orientation of the domains in the direction of the field lines. Because the field lines span the entire thickness of the sample, complete orientation of the morphology will result.

One limitation to the use of block copolymers for producing nanostructures is that size scales are limited. Achieving structures smaller than approximately 10 nm or larger than approximately 100 nm is quite difficult. The larger length scales are not accessible because of the slow kinetics of phase separation. Adding low-molecular-weight compounds to swell the copolymer provides one route to circumvent this. Alternatively, larger scale nanostructures can be assembled from monolayers of micellar solutions of block copolymers.[126] Just as the topology of the substrate can be useful in organizing block copolymer domains in thin molten films, topological features can be use to impose order on the solvent-swollen micelles. The assembly of gold dot structures from micellar solutions with such capillary forces was demonstrated by Moller et al.[127] Similar selective absorption and reduction of organometallic compounds in a given domain of a block copolymer film from supercritical CO_2 were also recently demonstrated by Watkins et al.[128]

Metal or other inorganic particles produced by chemical transformations in a block of a block copolymer can also serve as etch-resistant masks for pattern transfer. A separate possibility is to incorporate a metallorganic moiety directly into a block. For example, Manners et al.[129] demonstrated that ferrocenylsilanes can be poly-

merized by living methods to produce block copolymers with metal containing blocks, and Vancso et al.[130] showed that such blocks are some 60–80 times more resistant to reactive-ion etching than carbon backbone polymers.

Important advances are expected to come from developments in surface microanalysis techniques. It is evident that the technique of secondary-ion mass spectroscopy (SIMS) promises micrometer-size lateral resolution and that nuclear magnetic resonance/scanning probe microscopy (NMR/SPM) is already starting to map out the local chemical composition as scanning probes are rastered over solid surfaces.

2.4.2 Heterogeneous Surfaces

Present Research Status. Polymer nanostructures can also be prepared in which the interfacial interactions are laterally heterogeneous. Here, the surface will have a strong preferential affinity for one of the components over a predetermined distance and then abruptly change to be nonfavorable. Such interactions can be varied in a periodic manner with a characteristic wavelength (λ), be varied in a nonperiodic manner with a correlation length (ξ), or be random. In each case, the surface can act as a template for ordering polymers or for placing polymers into a highly nonequilibrium state. Commensurability between the natural length scale of the polymer and that presented by the surface is key.[131,132]

Long-Term Prospectus. Studies of this nature also represent an area in which combinatorial processes can be used effectively. In particular, by varying the conditions to prepare striped surfaces, we can prepare surfaces across which λ gradually increases. Thus, on one surface, L/λ can be varied from being much less to much greater than 1. By this route, an entire study requiring the preparation of numerous substrates with different periods could easily be reduced to one study on one substrate. For a process to be truly combinatorial, one needs a variation of two parameters in orthogonal directions on the surface. Consequently, in a direction normal to the gradient in the period, gradients in the temperature, solvent evaporation rate, added homopolymer, or even copolymer molecular weight could be imposed during preparation.

There are few if any studies in the literature that address the situation in which the surface heterogeneities are randomly arranged on a surface. Some studies exist on the bioactivity of surfaces, but these are qualitative in nature.[133] The manner in which a long-chain molecule having recognition sites distributed along its contour interacts with a surface on which the recognition sites are not periodic is an exceptionally challenging problem that is receiving considerable attention in several communities. Theoretical studies indicate that the conditions for recognition are quite stringent, in that the correlation of sites along the chain must closely match those on the surface.[134–136] On the experimental side, the challenges are numerous. Although the preparation of heterogeneous surfaces can be achieved in a variety of ways, the characterization of the lateral distribution of interacting sites on the surface is not straightforward. How does one characterize a truly random surface? Can one characterize heterogeneities on the segmental level? At present, there is no method that covers such small length scales. NMR/SPM has been proposed and is in development. Such scanning probe microscopy would revolutionize the characterization of nonconducting surfaces, allowing one, for example, to map the distribution of silanol groups on an SiO_2 substrate.

Paralleling this is, perhaps, an even more difficult problem, the sequencing or characterization of the monomer sequences along a chain. Through synthesis, sites can be placed along a chain so that the distribution is blocky, alternating, or random to different degrees. However, even in the simple case of a chain consisting only of two different monomers, how can one measure the sequence precisely? Synthetic polymers are fraught with irregularities of molecular weight and chemistry from chain to chain and with dispersities of both. This poses a daunting theoretical challenge. The characterization of such synthetic systems poses an even more challenging problem experimentally. Nonetheless, recognition between chains and surfaces is central in directing morphologies in thin films and, of course, indispensable in biomolecular structures and functions. In the future, the explicit sequencing of copolymers will grow in interest, as well as their characterization by explicit sequencing rather than merely (as at present) by average composition.

2.5 Hybrid Polymer–Inorganic Systems

The distinction between 3D macromolecules such as buckyballs and dendrimers and nanoparticles is only semantic. At very small size scales, the dividing line between nanoparticles and macromolecules blurs, and perhaps one should only focus on the 3D character of the material. Such small particles introduce a large surface area and can markedly alter the properties of the polymer.

Polymer–nanoparticle composites offer a range of interesting opportunities by combining the properties of the inorganics, such as magnetism, scratch resistance, or hardness, with the flexibility or melt processability of the polymers.[137] As a result, one can seriously contemplate scratch-free glasses, flexible magnets, and high-performance lightweight composites. These composite systems

are dominated by the behavior of polymers close to interfaces; for example, 10-nm silica particles have a surface area of approximately 300 m^2/g in direct contact with the polymer. A strongly coupled shell of the polymer on the nanoparticles holds the key to many applications.[138] Adsorbed polymers, for example, stabilize the dispersion of the particles, which simplifies both wet and dry powder processing, which is critical for the dispersion of the particles in polymer films and coatings. The adsorbed polymer layer also protects the particles from the environment and the environment from the particles. This is important for the application of nanoparticles in biosystems ranging from cancer therapy to cosmetics. However, particles take on stealth properties to become more stable against oxidation or phagocytosis. The selective adsorption of polymers on specific sites of a nanocrystal allows self-organization through programmed tensorial forces. The critical issues include making the nanoparticles in controlled ways, bringing them homogeneously into a polymer system, and spatially organizing the particles in space. Here we focus only on the first two topics for which interfacial issues are key.

2.5.1 Synthesis, Stabilization, and Compatibilization of Nanoparticles

Present Research Status. Amphiphilic macromolecules play a leading role. They control the interfacial energy of nanoparticles because their chemical structure can be selected to stabilize interfaces between materials with very different chemical natures, polarities, and cohesion energies in a manner that is more efficient than with a small-molecule surfactant. In principle, it is possible to blend polymers with ceramic and metallic nanoparticles. For example, the surfaces of gold nanoparticles can be covered by thiol groups (covalent binding), strong ligands (electron-pair donation and complexes), or polarizable units such as nitrile groups (dipole–dipole interaction), whereas other parts of the macromolecule provide compatibility with the solvent or the matrix. Very prominent examples of direct and meaningful applications of nanoparticle- or nanofiber-filled polymers are the green tire, in which the replacement of 10 wt % of the carbon particles by surface-engineered silica particles can provide a 10% savings in fuel consumption, and nanofiber-reinforced composites, which provide new lightweight materials for the next generation of cars and airplanes.

Long-Term Prospectus. There are a number of possibilities for the synthesis of such polymer–nanoparticle hybrids. For instance, particles can be generated in an already preformed polymer structure, that is, a micelle or an ordered block copolymer structure. In this way, excellent size control and high colloidal stability are obtained, as reviewed recently for amphiphilic block copolymers. Another illustrative example is the generation of Au nanoparticles and CdS nanodots within dendrimers, in which the functional polymer provides stabilization and particle size control and protects the nanoparticles from oxidation and fluorescence quenching.

Organic–inorganic nanocomposites can also be made by the covalent attachment of an initiator to the nanoparticle.[139] Such an approach is especially promising for the generation of polymer–clay nanocomposites in which the diffusion of the polymers into the gallery of the clay sheets is either prohibitively slow or the thermodynamics are easily nonfavorable.[140] Polymerization from initiating sites anchored to the clay particles is facilitated by the rapid diffusion of small molecules between the clay sheets to these reaction sites. This simple chemical route to exfoliation could lead to exquisite control over the structure and properties of the composite. A third promising possibility consists of tailored polymers that act as crystallization modifiers; that is, they control the nanoparticle size and polymer adsorption throughout the formation of a crystalline nanoparticle, as discussed later in more detail.

Buckyballs, dendrimers, and other model nanoparticle materials have been shown to modify the interfacial tension, interfacial viscosity, and interfacial elasticity of the polymers. Changes in the surface tension brought on by the nanoparticles will modify surface pattern formation in ultrathin films of blends and block copolymers, patterns in drying and heated polymer films (Marangoni patterns), patterns in mechanically agitated films (Faraday patterns), and spinodal patterns in dewetting thin polymer films. The physics underlying these phenomena will lead to the stabilization of polymer coatings by suppressing defects and controlling interfacial adhesion. Strong interfacial effects of the nanoparticles will reduce drag in both low Reynolds Number pipe flow and turbulent flow.[141] The control of flow instabilities and interfacial interactions during polymer processing are critical factors for eliminating shark skin and melt fracture. Nanoparticle additives should also provide control of the phase breakup of fluid threads (Taylor–Tomitika instabilities) and droplet spreading on solid substrates. Applications of associating nanoparticle additives relate to flammability suppression, droplet control in sprays, and droplet interfacial dynamics,[142] and the emulsification of polymer blends can be anticipated.

2.5.2 Vectorial Alignment of Nanoparticles and Nanofibers

Present Research Status. The interplay between the control of growth and the control of mutual interaction can be used to create structural composition. Examples in-

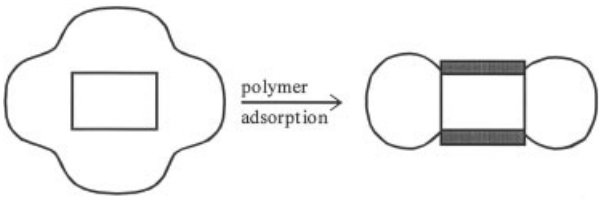


Figure 4. Scheme of vectorial crystal growth. The crystal field (van der Waals and dipole interactions) of a nanocomponent is shielded by the specific polymer adsorption, and objects with tensorial force fields or a heterogeneous distribution of polarity are obtained.

clude the generation of complex crystal morphologies (the control of crystal growth by specific adsorption) and superstructures by controlled adsorption interactions. One controls not only the shape of the building blocks but also the rules of self-assembly. For example, lead sulfite (PbS) nanorods have been grown from lead-containing surfactant assemblies in a polymer matrix.[143] The crystallization of barium sulfate from microemulsions results in extended crystalline nanofibers that align into superstructures.[144] The precipitation of barium chromate in the same surfactant system results in primary cuboids that further align to linear caterpillars or rectangular mosaics.[145]

Long-Term Prospectus. The high specificity of polymer adsorption onto distinct chemical patterns on particle surfaces with matching patterns within the polymer structure has tremendous potential in controlling and directing the growth of the particles. The scheme is illustrated in Figure 4. Such selective adsorption can occur with objects having nonspherical and noncylindrical symmetry, such as inorganic nanocrystals. Polymer adsorption at specific crystal faces not only blocks and stabilizes those surfaces but also modifies the colloidal interaction potential in a vectorial or tensorial fashion.

This is the potential base for encoded self-assembly due to programmed forces, that is, spontaneous self-organization into ordered nanostructures. The classical Derjaguin–Landau–Verwey–Overbeek potential, with the high symmetry and spatial degeneracy needed for mathematical simplicity, is broken; single tensorial components become adjustable by polymer adsorption, and left and right or up and down can be differentiated. Synthesis can be passive, not active. Self-assembling millistructures based on this premise have been fabricated already.[146] We believe that extension to the nanoscopic realm holds tremendous opportunity.[147–150]

Polymer adsorption influences a whole chain of kinetic growth and interaction processes, which finally result in complexity. The structures are sometimes beautiful, as illustrated in Figure 5, but they are also potentially very useful, with widespread applications for drugs, pigments, or fillers. It must also be kept in mind that these structured nanoparticles are closely related to a structured pore system, which is just the geometric inversion.

2.6 Photonic and Electronic Applications of Thin Films

The literature provides an exciting record of the accomplishments that are being made in the study of advanced polymeric materials with properties of interest for the fabrication of organic microelectronic and optoelectronic devices. The rapid growth of interest in these materials follows from the remarkable performance demonstrated by prototypes of one particular class of devices, organic light-emitting diodes.[151] These devices have demonstrated performance properties that compare very favorably with those of inorganic materials. The ability to tune emission profiles via rational molecular design provides a powerful technology-based driver. Functionalities that have received significant attention in the past several years include molecular conductors,[152] semiconductors,[153] unconventional superconductors,[154] optoelectronic materials,[155] photonic materials,[156] and responsive systems and microelectronic mechanical systems.[157]

Present Research Status. The fundamental properties of many types of devices based on macromolecular architectures depends sensitively on the structures and organization at the polymer interface. In organic thin-film transistors, for example, the device properties depend strongly on the transport characteristics manifested in a very narrow-channel region proximal to the gate electrode.[158] Similarly, molecular junction devices (e.g., res-

Figure 5. Alien flowers made on an electron microscopy grid from barium sulfate under polymer adsorption control (from the laboratory of M. Antonietti).

onant tunneling diodes) have performance properties that depend on barriers mediating charge injection at a metal electrode.[159] Charge injection can severely degrade molecules at the electrode interface. The interfaces of general interest in these systems are frequently buried within complex multilayer architectures. As a result, many of the complex issues of the chemistry and physics of these interfaces remain poorly defined.

Long-Term Prospectus. There is considerable overlap between the progress being made on systems that are based rigorously on macromolecular materials and those that use molecular constituents and assemblies. Frequently, issues related to processing and synthesis drive these selections. The lessons learned in molecular systems, however, provide significant synergy for studies of related macromolecular systems. These dualities are seen most clearly in the areas associated with optoelectronic systems. Light-emitting devices provide an excellent point of consideration. Optically stimulated emission and amplification have been seen in a wide variety of organic materials. The very high mobilities needed to generate stimulated emission via direct charge injection have limited material choices to molecular single crystals.[160] Thus, there is a considerable need to develop macromolecular materials and processing methods to fabricate microstructures with improved carrier mobilities. This will have a significant impact on the development of technologies based on organic thin-film transistors, as the latter has been restricted by the limited choices available for some carrier types, and on the microstructure of the material present in the active narrow-channel regions.[161] The dynamics of charge injection and trapping are also affected by the molecular structure of the semiconducting material and its structure in the regions that mediate the charge motion.[162]

A second area of opportunity concerns microelectronic mechanical systems and, more generally, actuators.[163] A significant motivation is the compatibility between devices based on organic materials and the conditions under which biological samples need to be handled. Electrochemically dopable polymers, for example, are suited for use as actuating microstructures that function in aqueous solutions, but the interface between the polymer and the aqueous solution has not seen enough attention.

Polypyrrole thin films are easily oxidized (doped) electrochemically, and the large volume change from the uptake of the balancing counterions provides a large figure of merit for mechanical motion. Inganas et al.[163] demonstrated the utility of this system as the basis for constructing biologically compatible actuators and microelectronic mechanical system structures. Given the sensitivity of such systems to the electrochemically mediated charge-transfer processes involved in charge injection and the sensitivity of the actuator time constant to the dynamics of ion uptake, the central role played by interfaces in these systems is evident. Insights gained from detailed studies of the dynamics associated with the various types of charge motion could help to direct the ideas used to generate new molecular designs. It is also clear that applications in biomicroelectronic mechanical systems will benefit from the integration of devices within microfluidic systems. Polymeric materials will clearly be central contributors to this end, given the ease of their synthesis, processing, and fabrication as useful thin-film microstructures.

An opportunity also exists to develop patterning methods that lift essential constraints of photolithography-based patterning, such as the need for planar substrates in conventional technologies, and open the door to printing on nonplanar surfaces. Costs are another consideration. Many of the most promising areas of application for devices based on macromolecular materials are those in which a dominant Si-based technology does not exist. Soft lithographic patterning methods have attracted significant attention as complimentary alternatives to photolithography-based patterning.[165] Polymeric materials are important elements in this new suite of patterning methods. The methods are also well suited to amplification via self-assembly. A notable example of the latter is illustrated by the directed deposition of polymeric resists via the patterning of transition-metal catalysts via microcontact printing, a prototypical soft lithography method.[166–168]

2.7 Modeling and Simulations

Present Research Agenda. Over the past 50 years, our theoretical understanding of polymers has grown tremendously through a combination of analytical approaches, from mean field theories and scaling arguments to field theoretical methods and numerical simulations. Combining these techniques has been valuable in understanding a wide range of problems, from the structure of dilute polymers to the dynamics of dense polymer melts. Many of the techniques that are important for bulk polymers, including self-consistent field and density functional theories and simulations, will continue to play important roles near surfaces. The level of detail incorporated into a polymer simulation depends on the particular question of interest and the computational resources available. It is critical to match the resources with the question. Otherwise, the simulations cannot give useful information.

A schematic illustration of the simulation methods suited to various time and length scales is shown in Figure 6. Conventional Monte Carlo and molecular dynam-

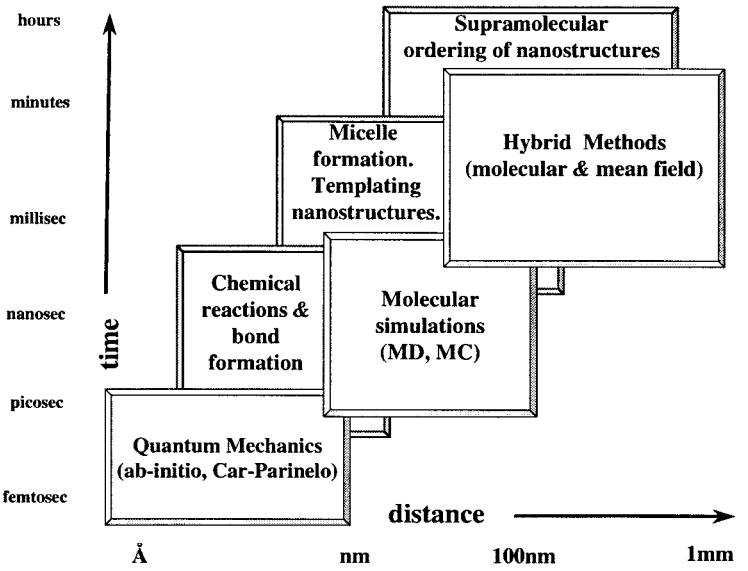


Figure 6. Schematic illustration of the vast span of length scales (angstroms to macroscopic) and timescales (femtoseconds to macroscopic), which present a challenge to realistic simulations. The simulation methods presently suited to the indicated span of length scales and timescales are shown.

ics simulations have been widely used to study the properties of polymers, both in the bulk and near surfaces.[164] Most of the previous work has been on simple coarse-grained models, either on a lattice or in the continuum. The advantage of this type of model is the computational speed. Because the interactions are usually short-range and bending and torsional interactions are usually neglected, it is possible to study polymers of relatively long-chain lengths (~400–10,000) for very long times. However, in the past few years, with the advent of teraflop computers and relatively inexpensive workstation clusters, there has been a greater emphasis on more realistic models of polymers, in which more atomistic detail is included. United atom models in which the CH_n moiety is modeled as a composite monomer have been successfully used to model the structure and dynamics of a number of polyolefins.[169–171] For water-soluble polymers, including biological molecules such as DNA and proteins, one much include the hydrogen atoms explicitly. Even though the basic time step in a molecular dynamics simulation for this case is quite small, approximately 1 fs, significant progress using models with this level of detail has occurred.[172] For example, a 100-ns molecular dynamics simulation of a system of a 100,000 polyethylene monomers takes a week on a 512-processor system for the united atom model. Including the hydrogen atoms explicitly would increase the time by at least a factor of 10. Although this is a very large simulation, it only begins to cover the time and length scales that are important. Thus, it is clear that even with the normal increases in computational processor speed, the range of time and length scales accessible in the next 5 to 10 years will allow us to explore only a portion of the temporal–spatial landscape by direct simulation. New techniques, which bridge this range of time and length scales, are clearly needed. For problems in which the dynamics are not important, Monte Carlo methods that exchange the monomer type or insert whole chains or parts of chains may be useful.[173] One promising technique[174] that could significantly speed up the simulations consists of finely discretized lattice models for Monte Carlo simulations for phase behavior and structure.

Long-Term Prospectus. As shown in the previous discussions, the range of length scales and timescales that are important in understanding polymers near surfaces is large. As an example, consider the surfactant-mediated synthesis of nanomaterials. Although the elementary reaction typically occurs on the length scale of molecular entities, that is, nanometers in size, what governs the properties are not only the ordering at these length scales but also the supramolecular ordering at the micrometer to millimeter length scales. To understand and develop improved synthetic methods for producing nanostructured materials, the theoretical tools to be used must cover a hierarchy of length scales and timescales that range from the microscopic to the mesoscopic to the macroscopic. The current state of the art in this area is not close to accessing the many orders of time and length scales that are necessary to quantitatively understand these situations. In fact, this issue of covering a multiple of time and length scales is critical to each of the areas

discussed in this report. Here we briefly review some of the theoretical and modeling approaches used to study polymers at surfaces and interfaces, and we suggest areas for future research.

Atomistic simulations are limited in their predictive capability by the quality of the interatomic potentials. Because of the large number of atoms needed to simulate even the simplest polymeric systems, full quantum-level simulations are impractical, although on small systems they are useful for testing new potentials. Thus, for modeling polymers, either in the bulk or near a surface or interface, we must rely at some level on empirical classical potentials. In the past few years, there has been considerable effort in developing reliable interatomic potentials for a wide range of polymeric materials, including polyolefins,[175,176] poly(dimethylsiloxane),[177] and poly(ethylene oxide).[178] However, little work has been done on developing interatomic potentials to describe one of these polymers near a surface of a nonpolymeric material, such as a ceramic or metal oxide. To obtain a fundamental understanding of the chemical bonding between dissimilar materials, such as a polymer and an oxide, we must first develop reliable potentials. In the past, different groups have worked on these different classes of materials. A challenge for the future is to bring these communities together to develop robust interatomic potentials, which can be used to model polymers at surfaces. Improved potentials will be valuable in a variety of simulations of polymers at surfaces and interfaces.

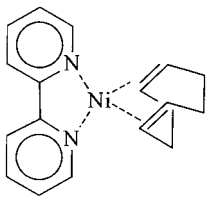
In many problems, both explicit atom models and coarse-grained simulations are required to make significant progress. Examples in which a combined approach is critical to success include the properties of polymer nanocomposites, polymer adhesion, and the mobility and transport of thin films. Some issues for these systems, particularly those related to local chemical bonding and local structures near the interface, can only be described within the context of a detailed atomistic model. In these simulations, as discussed later, one needs accurate interatomic potentials. Other aspects can only be addressed by higher level coarse-grained or even continuum models. For example, polymers are tough adhesives because they can dissipate large amounts of energy. However, the relaxation times of this dissipation are well beyond atomistic simulations. Coarse-grained simulations of this type will be very valuable in determining the fundamental fracture mechanics at a polymer–surface interface, including the formation and propagation of cracks in polymeric materials. Large-scale molecular dynamics simulations will also be of value for relating the properties of polymer composites to the size, density, aspect ratio, and elastic properties of the added filler particles. Flow at moving boundaries, the spreading of liquids on polymer surfaces, polymer extrusion, polymer diffusion in porous media, and diblock ordering near patterned surfaces and in the presence of particles are examples of areas in which, because of the long length scales and timescales, coarse-grained modeling is more suitable than explicit atom models. It is not that these problems do not have issues for which explicit atom simulations are of interest, but with present and near-term computational resources, larger scale simulations have the potential for much greater impact.

In addition to molecular-level simulations, one can also apply analytical methods to studying polymers at surfaces. The most widely known is self-consistent field theory.[5] This is a mature methodology, which has had a wide impact on our understanding of polymers at surfaces, including the structures of diblock copolymers near patterned surfaces and in the presence of particles.[179] Density functional theory[180] has been applied in some cases but still needs further development for studying polymers near complex surfaces. Other techniques[181] can also play a role. Although it has been often discussed in the past, there is still no methodology bridging the range of length scales and timescales shown in the figure. Except for some limited success with explicit atom simulations used to determine the parameters for coarse-grained models, bridging the length scales and timescales still remains a major challenge.

Another problem with polymer–surface and polymer–polymer simulations that has not received much attention is how to construct the initial state without one's available computational resources being exhausted. Consider, for example, if one wanted to study, using molecular-level simulations, how diblock copolymers strengthen a polymer–polymer interface. One would like to study the coverage and chain-length dependence of the work of adhesion. However, there is no good procedure at present to generate a reliable molecular representation of the polymers at the interface, which can be used as a starting state for pulling the surfaces apart. In this and many other problems of interest, the construction of an equilibrated starting state for molecular-level simulations is a major obstacle.

2.8 Synthetic Considerations

From a synthetic viewpoint, the common theme underlying all of these rapidly emerging areas is the importance of interfacial chemistry and molecular structure. To enable the continued development of these fields, and to permit the emergence of new directions, we must understand and control the molecular interactions that underpin these interfacial properties. The ability to prepare well-defined and tailor-made macromolecules with precise control over the structure, architecture, and placement of functional groups is key to these efforts.



BipyNi(COD), 1

Figure 7. Well-defined organonickel initiators (**1**) that allow for the controlled living polymerization of NCAs into complex polypeptide sequences and architectures. This enhances ability to prepare well-defined block copolypeptides.

Present Research Status. Significantly, a renaissance has occurred over the last 5–10 years in the area of synthetic polymer chemistry, which has the potential to act as a catalyst for the future development of interfacial science. Techniques have been developed and refined that now permit the preparation of functionalized macromolecules with a degree of control that would have been impossible, or prohibitively difficult, until recently. Not only does this permit the significantly increased availability of known materials, it also allows previously unknown structures and functionalized macromolecules to be prepared that may open up further opportunities.

Long-Term Prospectus. Some examples of major advances in polymer chemistry are the development of new approaches to poly(amino acids) structures using either single-site organometallic catalysts or the use of recombinant DNA techniques to prepare unnatural poly(peptides) with defined sequences and potential structures and functions. Deming[182–184] exploited transition-metal chemistry to produce synthetic block copolypeptide materials with precise control over the comonomer sequence and composition and polymer molecular weight. Until now, the lack of well-defined synthetic polypeptides has limited their use in interfacial and material applications; however, the ability to prepare well-defined block copolypeptides significantly increases their potential as biomolecular materials. As shown in Figure 7, well-defined organonickel initiators (**1**) allow for the controlled living polymerization of α-amino acid-*N*-carboxyanhydrides (NCAs) into complex polypeptide sequences and architectures.

The potential for these block poly(peptides) to act as interfacial agents in the environmentally benign preparation of organized silica structures under biomimetic conditions has recently been demonstrated and reveals the potential for these biocompatible synthetic macromolecules. In this case, the synthetic block copolypeptides hydrolyze and condense the silica precursor, tetraethoxysilane, at the ambient temperature and pH. This copolymer not only catalyzes silica formation but also self-assembles into superstructures that direct the formation of the silica into ordered morphologies (e.g., mesoporous spheres and columns).[185] The mimicking of naturally occurring adhesives by designer polypeptides is also an area of potential impact.[186,187]

Even more precisely defined artificial poly(peptides) can be prepared with the novel concept of applying recombinant methods to polymer synthesis.[188] In this approach, the techniques of genetic manipulation and protein biosynthesis are applied to the preparation of polymers with precisely defined molecular weights, compositions, sequences, and stereochemistries. Because these structures are as well-defined as other naturally occurring proteins, synthetic proteins that resemble telechelic polymers, block copolymers, ionomers, and so forth can now be prepared and examined for their activity as network precursors, membranes, surface layers, and catalysts.[189,190]

The area of single-site catalysis has also led to recent developments in the polymerization of strained olefins (ring-opening metathesis polymerization),[191] biodegradable lactides and lactones,[192] and olefin monomers.[193] The attractive aspects of these studies is that the defined nature of the catalyst allows the possibility of controlling the chain ends, stereochemistry, and molecular weight. In fact, many of these systems are living in nature, offering a significant advantage over traditional techniques, which yield poorly defined materials, and this new ability to control the polymer structure and composition allows the indirect control of interfacial properties. The use of organocatalytic methods to control the ring-opening polymerization of a variety of cyclic monomers also offers significant potential because it is a metal-free process, with the reactivity of a small-molecule catalyst, such as an *N*-heterocyclic carbene, being easily modified.[194]

A similar renaissance has occurred in traditional radical polymerizations by the development of living free-radical polymerizations. The three current techniques—nitroxide-mediated,[195,196] atom transfer,[197,198] and radical addition and fragmentation[199]—are complimentary and permit the design of functionalized, vinyl-based homopolymers and copolymers with a degree of control that was not possible previously. The compatibility of living free-radical procedures with a variety of functional groups and the use of functionalized initiators allow the synthesis of telechelic and chain-end-functionalized macromolecules with extremely high fidelity. Functionalized block copolymers can also be prepared from both vinyl monomers or a combination of vinyl and nonvinylic units in which the functional groups are inserted at various points throughout one or both blocks, at chain

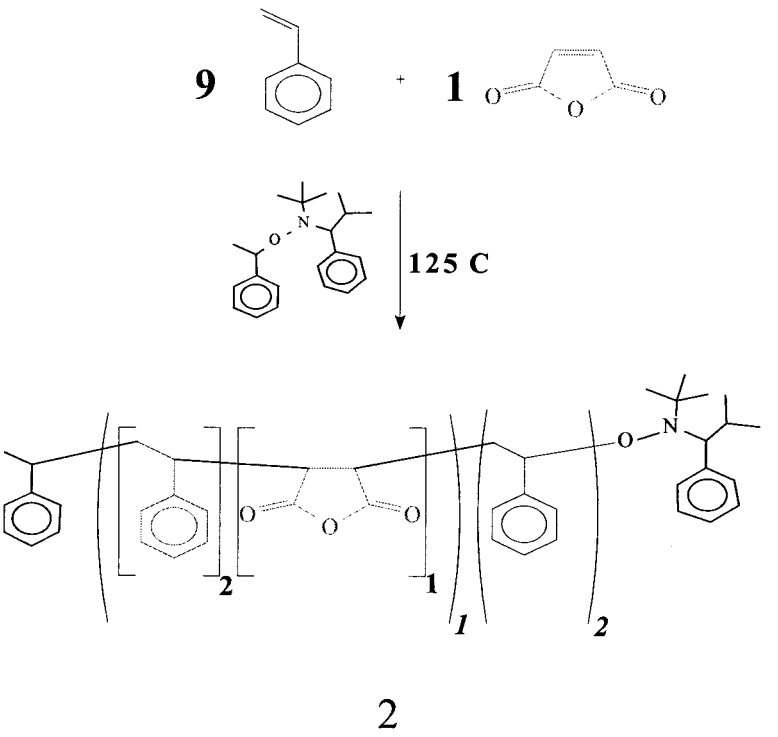


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Figure 8. Pseudoblock copolymers prepared in a single step from mixtures of styrene and maleic anhydride are examples of gradient-type macromolecular structures. For instance, a 9:1 mixture of styrene and maleic anhydride gives a tapered block copolymer (**2**) in which the relative incorporation of maleic anhydride varies from near-alternating at the start of the polymer chain to essentially a pure polystyrene block at the end of the polymer chain.

ends, or at the junction between blocks. The latter are particularly interesting for the covalent linking of self-assembled nanostructures. A similar approach was exploited by Wooley and coworkers[200,201] in the design of functionalized nanoparticles from block copolymers. Such structures are being targeted for applications as wide-ranging as drug delivery, encapsulation technologies, coatings, pollutant removal systems, catalysis, and composites. The 3D structures of these assemblies, coupled with their layered structures, create interesting issues related to chain diffusion and structural reorganization in polymer assemblies and at constrained polymer interfaces.

It should also be appreciated that living free-radical procedures permit the synthesis of previously unknown copolymers. Perfect examples of these are gradient or random block copolymers. As their name implies, gradient copolymers are characterized by a tapered structure in which the monomer composition varies in a controlled fashion from one end of the molecule to the other.[202] Various gradients are possible, and the versatility of living free-radical procedures allows control of the gradient by the exploitation of different monomer reactivity ratios or metered addition techniques. Extreme examples of this gradient-type structure are pseudo-block copolymers prepared in a single step from mixtures of styrene and maleic anhydride. For example, a 9:1 mixture of styrene and maleic anhydride gives a tapered block copolymer (**2**) in which the relative incorporation of maleic anhydride varies from near-alternating at the start of the polymer chain to essentially a pure polystyrene block at the end of the polymer chain (Fig. 8).[203] Although similar in concept, random block copolymers bear a greater resemblance to traditional block copolymers, in that there are two discrete blocks, the main difference being that one or more of these blocks are composed of a random copolymer segment. An excellent example of the synthesis and application of these materials is the preparation of a functionalized random block copolymer (**4**). An initial random copolymer of methyl acrylate and glycidyl methacrylate (**3**) is prepared by nitroxide-mediated living free-radical polymerization and then used to initiate the polymerization of isoprene, which leads to **4** (Fig. 9).[204] The design of these macromolecules incorporates a random block that is not only miscible with thermosetting epoxies but also can undergo a reaction leading to covalent linking between the copolymer microstructure and the crosslinked epoxy resin. The poly-

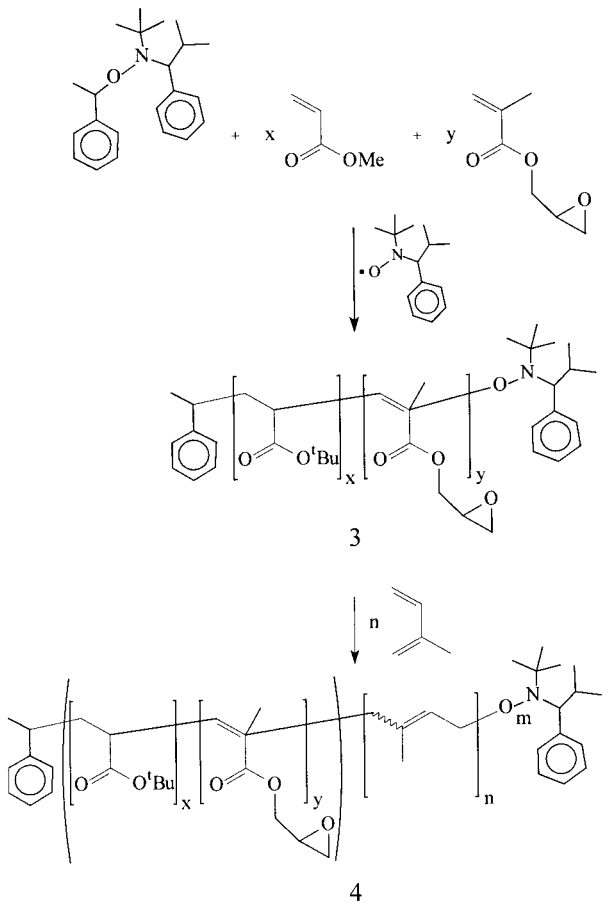

Figure 9. Random block copolymers bear a greater resemblance to traditional block copolymers, in that there are two discrete blocks, with at least one being composed of a random copolymer segment. An excellent example of the synthesis and application of these materials is the preparation of the functionalized block copolymer **4**. An initial random copolymer of methyl acrylate and glycidyl methacrylate (**3**) can be prepared by nitroxide-mediated living free-radical polymerization and used to initiate the polymerization of isoprene, which leads to **4**.

isoprene block is immiscible and, therefore, drives the formation of a nanoscopic phase-separated structure and leads to the modification of the physical and mechanical properties of the thermosetting epoxy.

An important feature of all of the novel structures that can be prepared by living free-radical procedures is the synthetic ease with which these materials can be prepared. This not only opens up their availability to a much wider range of researchers instead of a few specialist groups, but it also permits these materials to be prepared in large quantities. Because the rigorous purification of the monomers is not required and inert and oxygen- and moisture-free reaction conditions are unnecessary, hundreds of grams of these novel functionalized block copolymers can now be routinely prepared in a laboratory setting. For random and gradient copolymers, it should also be appreciated that the composition of polymer chains within a sample does not vary significantly. This is unlike traditional free-radical systems in which the chains produced early in the polymerization may be structurally very different from those produced later in the reaction. Such well-defined and functionalized copolymers have the potential to significantly affect areas that rely on interfacial interactions and properties, such as lubrication, adhesion, and compatibilization.

The ability to prepare tailored catalysts and initiators also permits the controlled placements of these species at the interfaces and surfaces of a variety of substrates. This is a strategy with significant promise in areas as diverse as biomolecular recognition and nanocomposites.[205,206] Initiating molecules can be specifically placed and patterned on surfaces such as silicon wafers, glass slides, and gold. Not only does this permit the growth of polymer brushes to thicknesses approaching a micrometer, orders of magnitude thicker than can be obtained with traditional coupling technologies, but the living nature of the polymerization process permits the structures of these covalently constrained polymer chains to be accurately controlled. This leads to numerous exciting possibilities at the solid–liquid interface. For example, Brittain and coworkers[207,208] demonstrated the reversible formation of nanostructures from polystyrene-*b*-methyl methacrylate block copolymers on the exposure of these brushes to different solvents. The initiating sites, or the polymer brushes that are formed, can also be patterned with traditional lithographic or contact printing techniques.[209–211] This leads to chemically and topologically differentiated surfaces, the interactions of which with external agents, such as solvents or biomolecules, can be controlled and manipulated. It should also be recognized that in comparison with self-assembled monolayers, the polymer brush environment is a pseudo-3D space and that the availability of functional groups along the backbones of the polymer chains that comprise the brush is significantly enhanced not only numerically but also in terms of chemical availability. The incorporation of functional groups into the polymer brush also allows recognition sites for biomolecules to be incorporated into the structure or for the preparation of neutral surfaces. The neutrality of the surface can be in terms of cell adhesion, biocompatibility, or the interaction of block copolymers. Russell and coworkers[121,124] exploited these chemically neutral surfaces in the manipulation of the block copolymer morphology for the preparation of nanostructures.

The use of templated or adaptive syntheses to control the formation of nanoscale objects will also benefit from the development of new block copolymers. As discussed later, Colvin elucidated a suite of strategies for the fab-

rication of nanoscopic materials based on templated approaches. Similar strategies have been employed by researchers at IBM for the fabrication of nanoporous materials. In fact, a major issue in the fabrication of microelectronic devices is the development of ultralow-K (dielectric constant) dielectric materials with dielectric constants of less than 2.0. Such materials are critical for insulating the smaller and smaller wires and transistors planned for the next generation of microelectronics. Unfortunately, materials with these characteristics, which are compatible with microelectronic processing, are not known, and the only presently recognized solution to this commercially important issue is the incorporation of nanoscopic pores into a suitable matrix material. The chemistry, dimensional stability, and mechanical properties of these nanometer-sized pores, prepared by a templating approach, are critical to their performance in actual devices. A major synthetic challenge in this general area is to also understand the nature of the buried interfaces and surfaces in these templated materials. By accurately determining the number and location of the surface functionality, we will be able to quantify for the first time the extent of reaction at interfaces and to gain a greater understanding of the molecular structure of the interface. The stability of nanometer-sized pores, the formation of templates based on molecular and macromolecular recognition, and the fabrication of self-healing devices are all critically dependent on these issues.

In a related technology, photolithography is only now approaching sizes (50–100 nm) for which major interfacial issues are becoming critical for continued development. The dimensional stability of fabricated features 50–100 nm in size, merely an order of magnitude greater than R_g of the chains that comprise the structures, is influenced by interfacial issues such as T_g, the chain mobility at the surfaces, and the mechanical properties of thin polymer films.

Although the previous discussion is mainly directed toward the discussion of linear macromolecular systems, it must be appreciated that the rapid growth in synthetic capabilities also permits the preparation of branched macromolecules for use in interfacial systems. Even though they require greater study, preliminary results for branched macromolecules such as dendrimers and hyperbranched, star, and graft polymers do suggest that their interfacial behavior differs significantly from that of linear polymer of the same chemistry, and this may offer distinct advantages in applications. For example, the greater availability of chain-end-functional groups permits the stronger adhesion of interactions between a functionalized dendrimer and a surface than the corresponding linear polymers, and this is due to entropic considerations. Other property differences, such as a lack of entanglements in dendrimers, decreased crystallinity, and a compact 3D shape, may all be exploited to give materials with superior performance at the solid–liquid interface.[212,213]

Future Issues for Synthetic Capabilities. The recent advances in controlled polymer synthesis through the design of new living techniques will continue unabated. At the same time, these techniques provide an exciting springboard for future developments in the preparation of tailor-made materials for interfacial applications. A major driver in developing new synthetic techniques and optimizing present strategies will be the application of combinatorial and high-throughput techniques. Long the province of the pharmaceutical industry, similar themes emerging in material science have the potential to revolutionize the identification of new initiators, both heterogeneous and homogeneous, for polymerization and the optimization of polymerization conditions. In concert with these advances is the challenge of developing high-throughput characterization techniques for determining the structure and properties of thousands of different polymer samples that may be prepared in a single day in the near future.

The facile nature of many of these new polymerization techniques also opens up the fascinating possibility of manufacturing automated polymer synthesis machines. In analogy with automated peptide synthesizers, reservoirs with the appropriate initiator and monomers would be loaded into the machine, and under computer control, the required amounts would be fed into a reactor in the correct sequence; if required, intermediate purification steps could also be performed between the growth of each block. Not only would this greatly enhance the availability of well-defined polymeric materials, it would also increase synthetic reproducibility.

The ultimate goal of many of these new synthetic developments is to prepare synthetic polymers with a degree of control matching that of well-defined biological macromolecules. Although this may be a Herculean and potentially impossible task, the ability to have precise control over the monomer sequence, the placement of branches and intrachain crosslinks, the stereochemistry, the molecular weight, and so forth should have profound effects on a multitude of physical properties critical to nanotechnology and interfacial issues. Additionally, the ability to prepare single, functionalized macromolecules may open up entirely new areas of research, such as synthetic polymer folding, macromolecular electronics, and receptor–sensor systems.

2.9 Biological and Bioinspired Systems

Tools developed in the physical sciences to measure and manipulate macromolecular interfaces are increasingly

being applied to medical problems. In this section, we review recent advances in applying interfacial science to biomedical problems, with an emphasis on developing technologies that allow new views of how biological materials are assembled as well as synthetic methods that seek to mimic strategies of nature. The limited space of this article does not allow a review of more mature topics such as the use of macromolecular scaffolds for tissue engineering.

2.9.1 Detection of Biopolymers

The detection of biopolymers is important for pathogen detection (biosensors) and for developing medical diagnostic tools. Many ways are being used and developed for these purposes. Although all these ways offer scientific and engineering challenges, a method that is being explored in several laboratories may be of particular relevance to researchers engaged in studying macromolecular interfaces.

The basic experimental platform is an AFM cantilever. A probe biopolymer is adsorbed on one side of the cantilever. The cantilever is then exposed to a solution containing the target biopolymer. The binding of probe and target macromolecules at this interface can lead to a force that results in cantilever deflection. The deflection can be measured with optical methods. If one understands how cantilever deflection depends on the nature of the biopolymer binding, this phenomenon can be exploited in high-throughput detection applications with microarrays of AFM cantilevers that contain adsorbed probe molecules of various types. Understanding how biopolymer binding generates interfacial forces presents an opportunity for scientists engaged in understanding macromolecular interfaces.

An example of work along these lines that is particularly relevant to issues that are currently topics of investigation in the polymer physics community is presented by recent experimental studies of cantilever deflection resulting from DNA hybridization. Single-stranded DNA molecules are end-thiolated and adsorbed on one side of an AFM cantilever that is coated with gold. This causes a downward deflection of the cantilever. When this cantilever is exposed to a solution containing complementary DNA strands, hybridization occurs, and this leads to the formation of double-stranded DNA. This leads to an upward deflection of the cantilever. This is considered to be rather counterintuitive. What is the origin of this behavior? A simple explanation[214] involves ideas taken directly from studies of polymer brushes, a field developed by scientists engaged in studying synthetic macromolecules at interfaces. Basically, conformational entropy is shown to be an important player in determining the free energies that lead to cantilever deflection upon biopolymer binding in this case. Many questions, particularly those involving protein–protein binding and the resultant interfacial forces, remain.

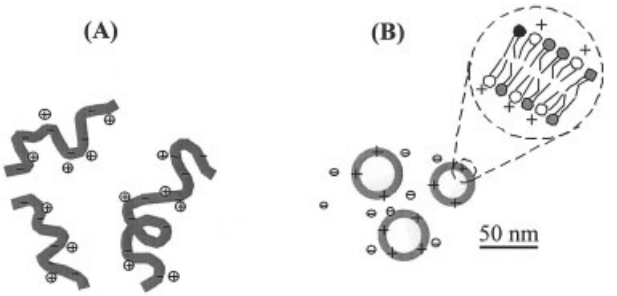

Figure 10. (A) Linear DNA with cationic counterions condensed on the backbone because of Manning condensation and (B) CLs (spherical membranes or vesicles) containing a bilayer of a mixture of cationic and neutral lipids.

2.9.2 Biological Polyelectrolyte Complexes

DNA chains dissolved in solution are known to give rise to a rich variety of condensed and liquid-crystalline phases at high concentrations.[215,216] Recently, there has been a flurry of experimental work on understanding the materials that are formed when DNA chains are mixed with oppositely charged cationic lipids. From a biomedical point of view, cationic liposomes (CLs; or vesicles) are empirically known to be carriers of genes (i.e., sections of DNA) in synthetic gene delivery applications.[217–222] The surge in research activity to develop synthetic gene delivery systems for therapeutic applications is due, in part, to their nonimmunogenicity, but it also exists because the single largest advantage of nonviral methods over viral methods for gene delivery is the potential of transferring extremely large pieces of DNA into cells. This was demonstrated when partial fractions of approximately 1,000,000 base pairs of artificial human chromosomes were recently transferred into cells with CLs as vectors, although extremely inefficiently (Fig. 10).

It is only recently that we have begun to experimentally discover the new types of liquid-crystalline self-assembled structures in these new materials that are currently used in clinical applications.[223–231] We describe recent work on the self-assembled structures of CL–DNA complexes by the quantitative techniques of synchrotron X-ray diffraction. Distinct structures have been discovered, including a multilamellar structure with alternating lipid bilayers and DNA monolayers,[223–226,228] an inverted hexagonal structure with DNA coated by cationic lipid monolayers and arranged on a 2D lattice,[227] and lamellar phases containing polypeptides and filamentous cytoskeletal proteins.[228] We expect that future studies will show that the mecha-

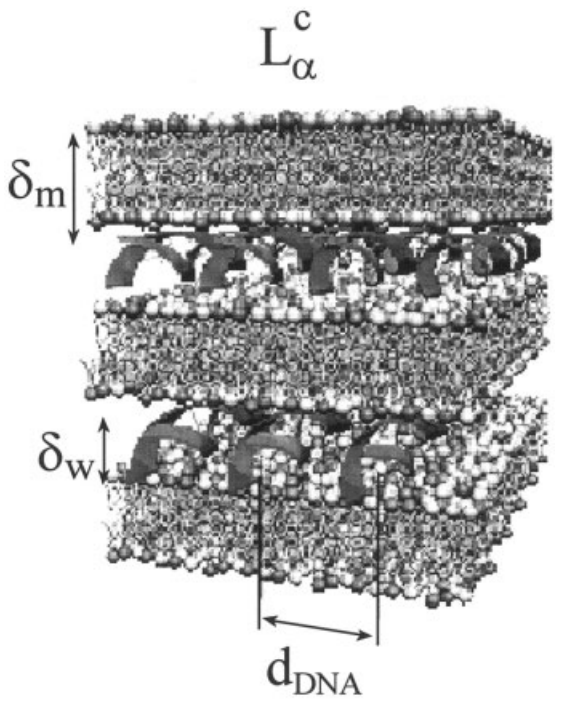

Figure 11. Schematic of the lamellar $L_\alpha{}^C$ phase with alternating lipid bilayers and DNA monolayers of CL–DNA complexes. The interlayer spacing is $d = \delta_w + \delta_m$.

nisms of gene release from CL–DNA complexes leading to expression in the cell are dependent on the precise structural nature of the self-assemblies and their interactions with endogenous biomolecules. As we describe later, recent quantitative synchrotron X-ray scattering.[223,224] and line-shape analysis[225,226] have shown that linear DNA confined between bilayers forms an expanding one-dimensional (1D) lattice of chains. Thus, this phase consists of a novel 2D smectic phase resulting from long-range electrostatic repulsions. The CL–DNA complex is a new hybrid phase of matter in which the DNA chains form a 2D smectic phase of finite size coupled to a 3D smectic lamellar phase of lipids, as shown in Figure 11.

The structure and thermodynamic stability of these CL–DNA complexes have also been the subject of much recent theoretical work.[232–238] Analytical and numerical studies of DNA–DNA interactions bound between membranes show the existence of a novel long-range repulsive electrostatic interaction.[234–236] Theoretical work on CL–DNA complexes has also led to the realization of a variety of novel new phases of matter in DNA–lipid complexes.[237,238] In particular, a novel new sliding columnar phase, which remains to be discovered experimentally, is found where the positional coherence between DNA molecules in adjacent layers is lost without the destruction of the orientational coherence of the chains from layer to layer. This new phase would be a remarkable new phase of matter if it exists, and it would share many fascinating similarities with flux lattices in superconductors.

From a biophysical perspective, it is important to explore the phase behavior of DNA in two dimensions as a tractable experimental and theoretical system for understanding DNA condensation. The mechanisms of DNA condensation *in vivo* (i.e., packing in a small space) are poorly understood.[239] DNA condensation and decondensation, which happen, for example, during the cell cycle in eukaryotic cells, involve different types of oppositely charged polyamines, peptides, and proteins (e.g., histones), in which the nonspecific electrostatic interactions are clearly important. In bacteria, which are the simplest cell types, it is thought that multivalent cationic polyamine molecules (spermine and spermidine) are responsible for DNA condensation in the 3D space of the cell cytoplasm. Recent experiments have led to a novel new finding: attractive interactions were observed between DNA chains adsorbed between membranes in the presence of divalent cations, leading to a 2D DNA condensed phase.[240] The importance of the observation lies in the fact that *in vitro* in 3D, DNA solutions containing divalent cations exhibit the usual repulsive interactions, with no hint of attractive interactions. Thus, it appears that the strength of the attractive Coulombic interactions between similarly charged polyelectrolyte rods is a strong function of either the dimension in which the rods reside or the effects of confinement.

From a completely different biomaterial perspective, there is at present a large effort directed at producing miniaturized nanoscale materials with applications in diverse technological areas. Specific examples include miniaturized materials for chemical and drug encapsulation and controlled release, sensors, separations, and nanoscale and microscale wires for electronic and magnetic applications. An equally exciting area is the development of components for micromachines, such as nanoscale conduits for connecting and flowing chemicals between nanoscale compartments. Micromachines are to be used in applications such as noninvasive drug delivery and diagnostics *in vivo* or in the design of microscopic robots for exploration in hostile environments (e.g., the ocean floors, with high pressures and extreme temperatures).

Recent advances in several technological areas should enable future research in this area. First, there is now a large body of knowledge regarding the nature of intermolecular interactions and structures of biomolecular self-assembly in lipids, proteins (G-actin and tubulin), and DNA/cationic lipid complexes. Second, the recent development toward producing ever smaller structures in the microelectronic industry has led to unprecedented

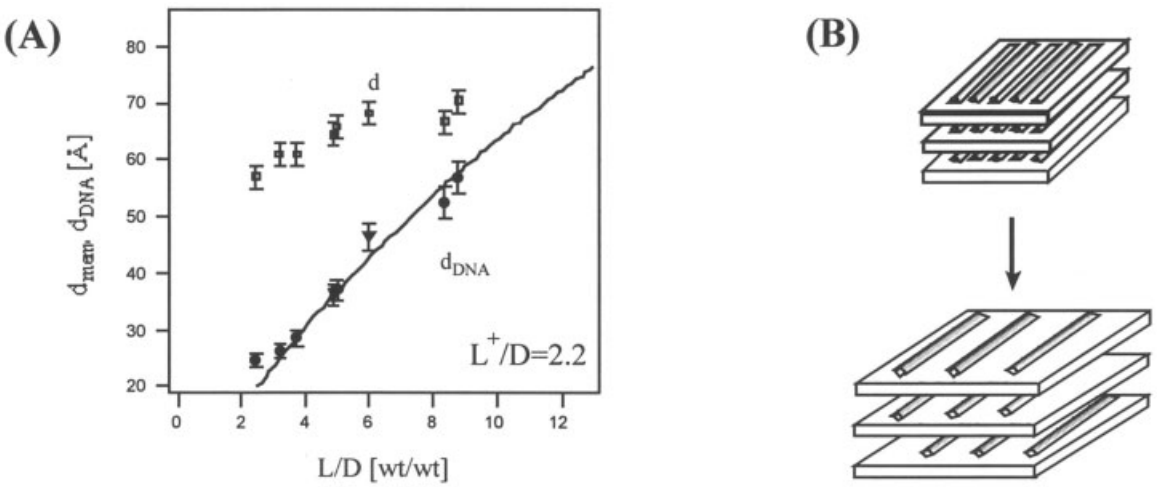

Figure 12. (A) d_{DNA} and d in the L_α^c phase (Fig. 2) plotted as functions of the lipid/DNA (L/D; w/w) ratio at an isoelectric point of 2.2 for the DOTAP/DNA complex. d_{DNA} expands from 24.5 to 57.1 Å. The solid line through the data is the prediction of a packing calculation in which the DNA chains form a space-filling 1D lattice. (B) Schematic of DNA–membrane multilayers showing an increase in the distance between DNA chains as the membrane charge density is reduced (as Φ_{DOPC} increases) at the isoelectric point. (From J. O. Raedler et al., Science, 1997, 275, 810; J. O. Raedler et al., Langmuir, 1998, 14, 4272; and I. Koltover et al., Science, 1998, 281, 78, adapted by permission.)

levels of control over pattern formation on semiconducting surfaces. Methods of electron lithography and reactive-ion etching exist that can produce nanoscale structures. As we describe later, these two approaches, when combined, can lead to the development of miniaturized materials. As will also become evident, an absolute requirement for success is a coherent effort using a broad spectrum of methodologies, particularly in microfabrication and nanofabrication techniques, in biomolecular self-assembling and synthesis methods, and in the manipulation and purification of biological molecules with modern biological methods.

2.9.2.a DNA–Lipid Complexes. Recent synchrotron studies[223,224] of CL–DNA complexes, in which the CLs consist of mixtures of the neutral lipid dioleoyl phosphatidylcholine (DOPC) and the cationic lipid dioleoyl trimethylammonium propane (DOTAP), have revealed that the structure is different from the hypothesized bead-on-string structure originally proposed by Felgner et al.[222] for CL–DNA complexes in their seminal article, picturing a DNA strand decorated with distinctly attached CLs (refer to Fig. 10). The addition of linear λ-phage DNA to CLs induces a transition from liposomes to collapsed condensates in the form of optically birefringent liquid-crystalline globules approximately 1 μm in size.

Small-angle-X-ray diffraction (SA-XRD) experiments[223,224] have revealed a novel self-assembled structure for the condensed globules consisting of mixtures of CLs and DNA. The data are consistent with a complete topological rearrangement of the liposomes and DNA into a multilayer structure with DNA intercalated between the bilayers (denoted L_α^c; Fig. 11). The membrane thickness and water gap are denoted δ_m and δ_w, respectively, with d ($\delta_m + \delta_w$) being the interlayer spacing (Fig. 11). The average thickness of the water gap, $\delta_w = d - \delta_m = 57$ Å $- 33$ Å $= 24$ Å ± 1 Å, is just sufficient to accommodate one monolayer of B-DNA (diameter ≈ 20 Å), including a hydration shell.[223,224] Additionally, SA-XRD data reveal a DNA–DNA correlation peak that allows one to measure the DNA interaxial spacing (d_{DNA}) with very high precision (Fig. 11). Figure 12(A) plots d and d_{DNA} as a function of L/D (where L, which is equal to $L^+ + L^0$, is the total lipid by weight, L^+ represents DOTAP, L^0 represents DOPC, and D is the total DNA by weight). The observed behavior is depicted schematically in Figure 12(B), which shows that as we add the neutral lipid (at the isoelectric point, $L^+/D = 2.2$) and, therefore, expand the total cationic surface, we expect the DNA chains to also expand and increase their interaxial spacing. The solid line in Figure 12(A) is derived from a simple geometric packing relationship, $d_{DNA} = (A_D/\delta_m)(\rho_D/\rho_L)(L/D)$, which equates the membrane charge density with the anionic charge density (resulting from linear DNA chains spaced d apart) and is only valid at the isoelectric point, at which there is no excess lipid or DNA coexisting with the complex.[223,224]

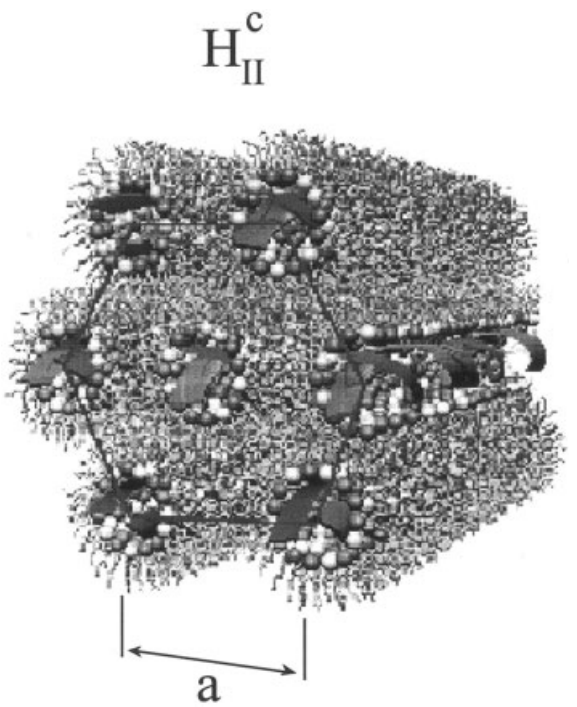

Figure 13. Schematic of the inverted hexagonal H_{II}^{C} phase (cylinders consisting of DNA coated with a lipid monolayer arranged on a hexagonal lattice) of CL–DNA complexes.

Here, $\rho_D = 1.7$ (g/cc) and $\rho_L = 1.07$ (g/cc) denote the densities of the DNA and lipid, respectively; $\delta_{m\ is}$ the membrane thickness; and A_D is the DNA area $\{A_D = \mathrm{Wt}(\lambda)/[\rho_D L(\lambda)] = 186\ \text{Å}^2$, Wt(λ) = weight of λ-DNA $= 31.5 \times 10^6/(6.022 \times 10^{23})$ g, and $L(\lambda)$ = contour length of λ-DNA = 48502 × 3.4 Å}. The agreement between the packing relationship (solid line) and the data over the measured interaxial distance from 24.55 to 57.1 Å [Fig. 12(A)] is quite remarkable given the fact that there are no adjustable parameters. The observation of a variation in the DNA interaxial distance as a function of *L/D* ratio in multilayers [Fig. 12(A)] unambiguously demonstrates that X-ray diffraction directly probes the DNA behavior in multilayer assemblies.[223,224] From the line widths of the DNA peaks, the 1D lattice of the DNA chains is found to consist of domains extending to 10 near neighboring chains.[225,226] Thus, the DNA chains form a finite-sized 1D ordered array adsorbed between 2D membranes; that is, a finite-sized 2D smectic phase of matter. On larger length scales, the lattice would melt into a 2D nematic phase of chains on account of dislocations.

A transition has been reported from L_α^C to the inverted hexagonal H_{II}^C (Fig. 13) structure in CL–DNA complexes containing DOTAP and the lipid dioleoyl phosphatidylethanolamine (DOPE) as a function of increasing volume fraction Φ_{DOPE}.[228] The transition can be understood by the observation that, in contrast to the neutral lipid DOPC and the cationic lipid DOTAP, which have cylindrical molecular shapes and tend to describe interfaces with a natural curvature of 0 (curvature $C_0^{DOTAP,DOPC}$ = 1/radius of curvature $R_0^{DOTAP,DOPC} = 0$), DOPE is cone-shaped, and this gives rise to an interface with a negative curvature ($C_0^{DOPE} = 1/R_0^{DOPE} < 0$). Thus, the natural curvature of the monolayer mixture of DOTAP and DOPE is driven negative with $C_0 = 1/R_0 = \Phi_{DOPE}\ C_0^{DOPE}$. Hence, as a function of increasing Φ_{DOPE}, we expect a transition to the H_{II}^C phase favored by the elastic free energy, as the data indicate (Fig. 13).

2.9.2.b Biomolecular Materials Self-Assembled on Microscale and Nanoscale Patterned Surfaces. For the realization of confinement-induced new phases, methods have been developed for producing and characterizing biomolecular materials self-assembled on patterned surfaces.[241] These patterned surfaces are produced with optical and electron-beam lithography and wet (HF) or dry (reactive-ion) etching methods for the fabrication of features tens of micrometers to about 100 nm in size. Channel depths may be as small as 2 nm and as large as 5 to 10 times deeper than the width, but in typical cases, the depth is about 1.5 μm. These are envisioned to be used for structural studies of biomolecules mixed in micrometer- and submicrometer-scale microchannel structures as substrate matrices for confining, orienting, and guiding the growth direction of the self-assemblies.

With recently developed methods, the patterned surfaces are typically modified so that the valleys (grooves) are hydrophilic, whereas the top surfaces are hydrophobic. In this manner, the charged membrane/polyelectrolyte biopolymer complexes remain inside the grooves, with the confining walls designed to be either attractive or repulsive (Fig. 14).

Highly oriented biomolecules can be prepared with microchannels as substrates.[241] Preparing highly oriented samples is crucial to many studies investigating the structures of biological macromolecules with optical microscopy and X-ray diffraction. The most common methods used presently include orienting these samples in magnetic field, capillary flow, and shear apparatus. The results obtained with DNA and microtubules demonstrate that the microfluidic channel arrays are very effective substrates for aligning these biological macromolecules. However, because of the finite thickness and width of the samples, which is set by the channel depth and width, it would be difficult to extract a sufficient signal with conventional X-ray diffraction methods. Current efforts toward developing X-ray microdiffraction methods with a focus size smaller than the channel width should be ideally suited for structural investigations with microchannel arrays.

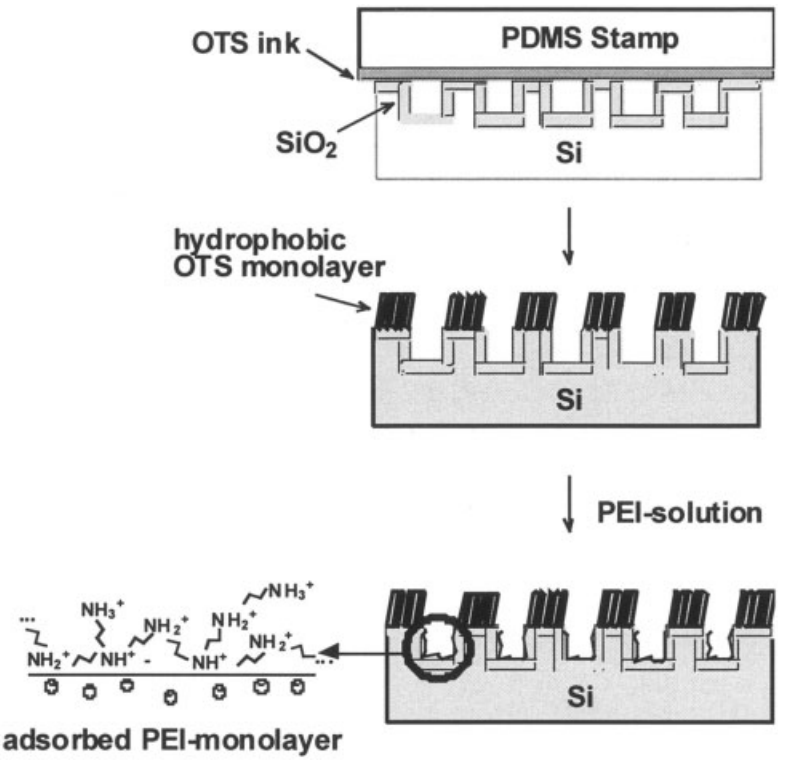

Figure 14. Surface modification procedure used to create wetting contrast in the channels. The treated channels are hydrophobic on the top and hydrophilic inside, and this facilitates the loading and processing of biomaterials in the channels. (From T. Pfohl et al., Langmuir, 2001, 17, 5343, adapted by permission.)

2.9.2.c Future Research Prospectus. One important new direction of research from scientific and technological perspectives involves the alignment of the biological polymer in the aforementioned biopolymer–membrane complexes. Biopolymers such as DNA, F-actin, and microtubules all pertain to these questions. We expect the persistence length to be a critical parameter in achieving oriented biopolymers in biopolymer–membrane complexes. The biopolymer should exhibit orientational order when the persistence length exceeds the width of the confining microchannels. Thus, the choice of biopolymers with different persistence lengths (1000 Å for DNA, 2–5 μm for F-action, and much larger for microtubules) should lead to a test of this idea. These experiments should lead to the possibility of observing new phases and, in particular, a novel confinement-induced sliding columnar phase predicted by a recent theory in which the biopolymers are orientationally locked (but positionally disordered) from layer to layer. Future microdiffraction X-ray studies (using either Bragg–Fresnel lenses or transmission zone-plate focusing optics) of samples oriented because of confinement in microchannels will allow an independent measurement of the critical persistence length (κ_c) and will open up a novel way of determining the persistence length of surface-adsorbed polyelectrolytes.

Aside from the structural biophysical studies, oriented multilamellar structures would have many important technological applications. These oriented biopolymer–multilamellar structures confined in microchannels may result in nanoscale materials. In recent experiments on unoriented bulk samples, it has been found that divalent electrolyte counterions common in biological cells (Ca^{2+}, Mg^{2+}, and Mn^{2+}) can condense anionic DNA molecules confined to 2D cationic surfaces.[240] DNA-condensing agents *in vivo* include cationic histones and the polyamines spermidine and spermine with sufficiently high valences (Z) of 3 or greater. *In vitro* studies show that electrostatic forces between DNA chains in bulk aqueous solutions containing divalent counterions remain purely repulsive and that DNA condensation requires a counterion valence of $Z \geq 3$. In striking contrast to the bulk behavior, synchrotron X-ray diffraction and optical absorption experiments show that above a critical divalent counterion concentration, the electrostatic forces between DNA chains adsorbed on surfaces of cationic membranes reverse from repulsive to attractive and lead to a chain collapse transition into a condensed phase of

DNA tethered by divalent counterions.[240] This demonstrates the importance of spatial dimensionality to intermolecular interactions in which nonspecific counterion-induced electrostatic attractions between the like charged polyelectrolytes overwhelm the electrostatic repulsions on a surface for $Z = 2$. This new phase, with a 1D counterion liquid trapped between DNA chains at a density of 0.63 counterions per DNA base pair, represents the most compact state of DNA on a surface *in vitro* and suggests applications in high-density storage and the retrieval of genetic information.

2.9.3 Macromolecular Interfacial Science in Biology and Biomedical Applications

Surfaces formed by both planar structure such as lipid bilayers and linear polymers such as those of the cytoskeleton and extracellular matrix are increasingly recognized as reactive surfaces where reactions differing from those in bulk solution are facilitated and where mutations or defects in protein folding can have devastating consequences in human disease.

2.9.3.a Diseases Related to Abnormal Interfaces Produced by Mutated or Inappropriately Presented Biopolymers. Some aspects of human pathology are based on polymer self-assembly and surface interactions that cannot be understood solely from the structure of the individual polypeptides involved. The assembly and interactions of these biological structures can be addressed by methods developed for surface studies in synthetic systems to provide data not forthcoming from traditional methods of biochemistry, cell biology, and genetics.

The pathology associated with a number of diseases, including Alzheimer's disease, other amyloid neuropathies, and sickle cell disease, is related to the properties of self-assembled biopolymers that form as the result of some mutation, either in the polypeptide that forms the polymer or in the precursor protein, that allow inappropriate protein processing. Although in some cases the genetic mutation associated with the disease is known, its relation to the pathological effects is usually not. Therefore, treatment and prevention methods are directed at elucidating and reversing the process of self-assembly of these protein polymers or their association with cellular membranes and other surfaces. For example, the self-assembly of the abnormal β-amyloid polypeptide associated with Alzheimer's disease,[242,243] infectious prions,[244] or sickle cell hemoglobin[245,246] is fundamentally similar to the self-assembly of a collection of nanoscale colloidal particles and has features distinct from the traditional lock-and-key specificity characterizing traditionally studied biochemical interactions. For example, a self-assembly and a secondary structure are induced when peptides characteristic of amyloid deposits are exposed to an air–water interface.[247,248] Typically, such abnormal self-assembled structures have diameters of approximately 10 nm and micrometer-scale lengths, and so they lend themselves to the structural characterizations of macromolecular assemblies in nonbiological systems. Significant recent progress from physicochemical studies using spectroscopy, scattering, and other methods provides a model for how similar self-assembling pathological structures form and thus suggests therapeutic strategies for preventing their pathological consequences.

Cystic fibrosis provides another example of the direct relationship of macromolecular interactions with human pathology. Although the genetic mutation responsible for this disease resides in an ion channel, until a gene-replacement therapy is devised to prevent the onset of the disease, treatment will be largely directed at the dissolution of the abnormally thick lung airway fluid formed as a result of bacterial infections characterizing this malady. In large part, the abnormal rheology of cystic fibrosis sputum is related to the presence of actin filaments[249] and DNA[250] within the muco–polysaccharide network of normal airway fluid, and therapies directed at the dissolution of these abnormal polymers are largely motivated by concepts of polyelectrolyte physics.[250] A recent advance is the realization that the polyelectrolyte natures of both DNA and actin play a central role in the formation of the large bundled aggregates of these filaments in cystic fibrosis sputum,[251] and the electrostatics of this crowded environment can have devastating effects on the sequestration of oppositely charged antimicrobial peptides that are inactivated in the disease. In this context, understanding the coarse-grained features of these biopolymers may be at least as important as elucidating their molecular structures in devising useful therapies.

In both of the examples cited, the cause of the disease is ultimately a mutation in a single DNA domain (cystic fibrosis) or multiple DNA domains (Alzheimer's) coding for a single protein or multiple proteins, respectively. Thus, until gene therapy reaches the state at which such defects are identified and reversed before the disease progresses, treatments will often be based on attempts to disassemble or at least block the growth of macromolecular aggregates when proteins on a nanometer scale dock in a highly specific but abnormal way to the growing aggregate. One challenge to interfacial science is to image such soft hydrated materials at a resolution now feasible for hard surfaces and so allow for the rational design of methods for blocking or altering these assemblies.

2.9.3.b Molecular Transmembrane Carriers and Timed-Release Particles. The last several years have provided a number of examples of membrane-permeating molecules that function in contrast to the generally valid rule that cell membranes are impermeable to charged or large hydrophilic molecules except in cases in which specific receptors are found. Several cationic amphiphilic peptides can cross the cell membrane without the need for an active transport system and without compromising the integrity of the lipid bilayer. The utility of such peptides in drug delivery is clear, but the mechanism by which these peptides function is not.

Time-controlled or cell-targeted drug delivery by the encapsulation of the drug in an artificial vesicle is a method decades old that has largely employed variants of the cell's own bilayer-forming molecules, phospholipids, to produce the carrier particle. Recently, vesicles formed from new artificial molecules such as block copolymers[252] or amphiphilic peptide derivatives[253] have also been suggested as promising and more versatile alternatives. Many new forms of microencapsulated particles that self-assemble on nanometer-scale templates, often by electrostatic interactions, are opening up a wide range of possibilities by which to target and release drugs under well-defined conditions.[254] Submicrometer-sized synthetic hollow-cage structures[255] and empty cell membranes[256] illustrate the variety of structures that may have utility in such delivery schemes.

2.9.3.c Cellular Interactions with Biological and Artificial Surfaces. The texture and viscoelasticity of surfaces on which cells grow can have as much effect on their growth and function as chemical signals delivered to the cell membrane of the nucleus. The rapid recent advances in this area have been facilitated by the availability of well-controlled surfaces and methods for characterizing their structure and rheology on a submicrometer scale. For example, the shape and motility of fibroblasts depend on the stiffness of underlying uniformly adhesive substrates,[257] and the growth rate and shape of the cells can be determined by the micropatterning of adhesive patterns on stiff inert substrates[258] as well as stiffness.[259] Such data suggest that chemical signals regulating growth, division, arrest, or programmed cell death may be augmented, diminished, or even reversed according to the stiffness of the underlying surface to which the cells are bound.

The top surface of a cell also has complex physiologically essential interactions with surrounding materials. For example, the response of endothelial cells lining the interior of blood vessels to changes in shear stress due to alterations of the blood flow is a major factor in the development of tissue damage related to arteriosclerosis, reperfusion injury, and other conditions. Understanding this regulation has been advanced by quantitative measurements of the surface topography, the fluid flow above the cell, and the surface elasticity. AFM has been especially valuable in defining some of these parameters, and much work has been directed at better elucidating how non-Newtonian fluids such as blood plasma flow over the complex surfaces of the underlying cell.[260] Here again, the ability to image soft materials on a nanometer scale will be important for future progress.

The intracellular membrane interface is somewhat simpler in the sense that the boundary between the surface and aqueous phase is smoother, although a rich texture and an electrostatic contour still shape the membrane curvature and disposition of peripherally bound proteins. In this area, key themes emerging from recent experiments are the importance of the lateral demixing of lipids into domains on the order of 10–1000 nm, which are variably called caveoli, lipid rafts, or corrals.[261,262] The concentration of certain lipids in these domains, such as highly anionic polyphosphoinositides,[263] is thought to recruit and activate enzymes and other proteins that initiate intracellular signals. A related effect is that finding the rate constants of some enzymes that phosphorylate or hydrolyze lipids in the membrane appear to depend strongly on the lateral demixing, curvature,[264] or surface pressure of the membrane[265] in which their substrates are packed and may be selectively recruited or activated at domain boundaries.

2.9.3.d Future Directions. Much of the progress in this field will be driven by technologies that extend to soft hydrated materials the same level of resolution and near-atomic-scale manipulation that is currently possible for hard materials.

One example of progress in the last few years is the application of AFM techniques, especially in the tapping mode, to biological materials. Both the structures on a nanometer scale and the forces on a nanonewton scale can now be accessed. As a result, ideas about DNA biochemistry and protein folding have been dramatically altered by data derived from this method.[266,267] The current limits of resolution will fall as this very new technology matures and is applied by a growing number of biochemists and cell biologists.

Other methods are also on track to enhance the study of biological surfaces. What is needed for the improved analyses of these structures is a better means of imaging fluorescence on a 1–10-nm scale, but also promising are methods of detecting nonfluorescence materials by techniques such as mass spectrometry. A resource for the development of this method for biological specimens is the National Resource for Imaging Mass Spectrometry at the Harvard Medical School recently funded by the National Institutes of Health.

Microrheological methods, particularly single and multiple particle tracking methods in which the high spatial (1-nm) and temporal (1-ms) resolution of the thermal motions of particles allows the measurements of elastic moduli, have been very rapidly expanded in the last few years.[268–270] Magnetic or retractile particles have been attached to membranes to probe effects at boundaries or embedded in cells or other biological gels to probe local viscoelasticity. The combination of micromanipulation and imaging made possible by optical and magnetic tweezers along with high-resolution light microscopy and AFM is sure to grow.

2.10 Infrastructure Issues

Instruments that are operated as national facilities are essential tools in the arsenal of modern scientific equipment. The continued support of these facilities is essential if the potentials outlined in this article are to be realized. These facilities provide the ability to execute experiments that are impossible to do in the laboratories of individual investigators. Although the maintenance of these facilities, both in terms of manpower and hardware, is necessary, these large facilities in fact enable innumerable single-investigator projects that would be impossible otherwise. As size scales shrink, these facilities provide essential tools for future progress.

2.10.1 Neutron Sources

The ability to substitute hydrogen with deuterium in many polymers provides a unique means of labeling chains without significantly altering the thermodynamics. This isotopic substitution, coupled with the availability of neutron scattering facilities and the deep penetrating power of neutrons, has provided a unique means of studying the behavior of polymer molecules. Although long held as a tool for investigating bulk samples, even with current sources, neutron scattering has been used to gain insight into ordering processes of copolymers and chain conformation in thin films. However, as the film thickness decreases, or if one is concerned only with chains at an interface, the total number of scatterers decreases and the signal-to-noise ratio presents severe limitations that can only be overcome by increased flux. Specular NR has emerged as a means of profiling polymer systems at surfaces and interfaces with a depth resolution of approximately 1 nm averaged over the coherence length of the neutron (typically micrometers). Increasing the incident neutron flux would enable experiments to be extended to high scattering vectors, for which the reflectivity is inherently low, and this is crucial as the film thickness or length scales of interest decrease. Enhanced incident flux would also enable real-time reflectivity measurements for probing dynamic processes, such as diffusion or adsorption. Aside from specular reflectivity, for which the diffraction vector is oriented normal to the surface, off-specular scattering, in which a component of the diffraction vector is placed in the plane of the film, provides a unique means of probing lateral correlations in density or composition. Currently, off-specular scattering is limited by incident flux and a quantitative interpretation of the data. Nonetheless, off-specular scattering represents an underused method of characterizing the behavior of polymers at interfaces. At angles below the critical angle, an evanescent neutron wave extends beyond the surface, penetrating several nanometers beyond the interface. The volume of scattering defined by the projection of the beam on the surface and the penetration depth is quite small, and so the number of scatterers is very small. Although neutron scattering from this volume would provide insight into the configuration of polymers at surfaces and interfaces, this grazing incidence neutron scattering technique has never been used to study polymers, primarily because of the limited, incident neutron flux.

Although neutrons provide may avenues for investigating the interfacial behavior of polymers, it is clear that the flux is a limitation. Current reactor sources are being pushed to their limits. Although advances will continue to be made with reactor sources, such as the ability to perform inelastic neutron scattering on thin films, or even with multiple wavelengths for reflectivity experiments, spallation neutron sources offer a beautiful complement to reactors. Unlike steady-state reactor sources, in which a single wavelength is selected from the distribution of neutron wavelengths provided by the source, pulsed spallation sources operate in a time-of-flight mode with a broad range of neutron wavelengths. In general, the time-averaged flux of reactor sources is greater than that for spallation sources, but the use of a broad wavelength spectrum of neutrons makes the effective flux of a spallation source comparable to that of a reactor source. With spallation sources, scattering over large ranges of scattering vectors can be obtained simultaneously. Currently, the Spallation Neutron Source, with potentially two target stations, is under construction at the Oak Ridge National Laboratory. This 1.4-MW source will provide the soft matter community with an unprecedented neutron flux on a sample. This source, which complements existing reactor sources, will enable many static near-surface and time-resolved experiments on polymers that are currently not possible. The development of spallation neutron sources and the upgrades to current reactor sources will markedly enhance our ability to probe the structure and configuration of polymers at interfaces in a noninvasive, rapid manner.

2.10.2 X-Ray Sources

Key enabling tools for much advanced research on interfaces are advanced synchrotron X-ray sources, such as the Advanced Photon Source at Argonne National Laboratory. These have rapidly become invaluable for structural determination. Researchers are starting to generate exciting new time-resolved information regarding the evolution of crystal structures and crystal–amorphous interfaces as polymers crystallize. Fluctuation correlation spectroscopy experiments[271–274] based on X-ray photon intensity correlation spectroscopy (PICS) are beginning to emerge. PICS uses coherent beams, in which the fluctuations of the speckle pattern in and out of the detector aperture are employed to study the time autocorrelation function of the scattered beam, thereby yielding information about the dynamics of the system within the probed volume. This is the analogue of dynamic light scattering but is capable of measuring the fluctuations on far shorter wavelengths. The method is intensity-limited because of the low coherent fraction of X-rays in the beam, but third-generation sources such as the advanced photon source (APS) offer an enormous gain in coherent beam intensity, making such experiments possible. PICS may be naturally applied to X-ray wave guides because the wave guide naturally provides an intense (and also completely coherent) flow of photons right in the region of the confined fluid. With X-ray fluorescence correlation spectroscopy (XCFS), the time correlation function of the fluorescence intensity from a particular set of atoms in a sample is measured as the number of these fluctuations in and out of the beam. This method has the advantage of being element-specific and can be used conveniently for elements with $Z > 19$, and it does not require coherent beams. However, the number of diffusing particles N must be small, as the fluctuation part of the intensity goes as $1/N$. In general, this requires microfocused X-ray beams and particles consisting of a large assembly of appropriately fluorescing atoms. XCFS is also something that can be used naturally in the X-ray wave guide geometry because, by its very nature, the number of particles in the thin film is small.

A generalization of XCFS using grazing-incidence reflection at a surface beneath a fluid to set up X-ray standing waves within the fluid can yield a direct measurement of $S(\mathbf{q},t)$, the intermediate scattering function, or the spatial Fourier transform of $S(\mathbf{q},t)$, that is, $\langle\rho(\mathbf{q},t)\rho(0,0)\rangle$, where $\mathbf{q}$ is the wavevector of the standing wave.

Similarly, coherent X-ray diffraction (CXD) occurs whenever a sample under investigation is smaller than the coherence of the X-ray beam used to measure it. With the availability of new third-generation synchrotron radiation sources, coherence lengths in the range of 10 (transverse) and 1 μm (longitudinal) are now available with sufficient flux to make such experiments practical. Thus, it is realistic to contemplate a situation in which an entire sample lies within the coherence volume and yet a measurable diffraction signal is still obtained. As an example of this usefulness, the symmetric part of the diffraction is given by the Fourier transform of the crystal shape, whereas the asymmetric part can be associated with the strain. Iterative Fourier transform methods can then be applied to reveal a 3D spatial image of the internal strain. The application of CXD to the imaging of strains within nanocrystals offers the possibility of revealing long- and short-range disorders in biocrystals (mosaicity, strain, and correlated and noncorrelated conformational and rotational disorders) and identifying growth conditions, processes, and stages responsible for these defects. Many other instances of the exciting possibilities opened up by X-ray microscopy can be imagined.

2.10.2.a NEXAFS Microscopy. Because the first demonstration of transmission NEXAFS microscopy in 1992,[275,276] X-ray microscopy has evolved into a quantitative analysis tool with an accuracy of a few percent at a spatial resolution of about 50 nm that is increasingly being used for the characterization of polymeric materials.[277] Soft X-ray synchrotron sources, such as the Advanced Light Source at Berkeley or the National Synchrotron Light Source at Brookhaven, provide the setting in which such microscopes can be realized. The combination of relatively high spatial resolution, low beam damage, and compositional sensitivity is unique. NEXAFS microscopy has been performed with a surface sensitivity of about 10 nm.[278,279] NEXAFS also depends on the orientation of bonds, and the resulting linear dichroism can be used to characterize the orientation of molecules or segments.[278,280,281] This combination makes NEXAFS microscopy an excellent complement to high-chemical-content microscopy, such as NMR, IR, and Raman, and high-spatial-resolution microscopes, such as various electron microscopes. So far, however, the number of application of NEXAFS microscopy in soft materials has been limited, although it has tremendous potential in providing information about polymer surface and interfaces.

Current NEXAFS microscopy capabilities are far from the fundamental limitations. For example, the far-field wavelength-limited spatial resolution for transmission instruments based on zone-plate optics is about 3 nm (for near-carbon K-edge energies), about an order of magnitude better than the resolution presently achieved. A spatial resolution of better than 10 nm appears to be possible with zone-plate-based microscopes. Even higher spatial resolution should be possible from surfaces with aberration-corrected X-ray photoemission electron mi-

croscopes. Theoretically, a lateral resolution of 0.5 nm is possible, and at present, X-ray photoemission electron microscopes with a 2-nm resolution are under construction.[282] If these microscopes achieve their full potential, they will constitute an important tool for the characterization of surfaces and interfaces.

2.10.3 SIMS

One of the great advances of the past 20 years has been the development of experimental methods for depth-profiling polymer films, particularly, but not exclusively, films with components or blocks labeled with deuterium. These techniques include forward recoil spectrometry, nuclear reaction analysis, dynamic SIMS, and NR. These methods are highly complementary, so that by the use of two or three of these on the same sample, a very complete picture of the composition versus depth of such films can be achieved down to the smallest length scales relevant for polymers. A major disadvantage is that this composition–depth profile is averaged over large lateral distances. This means that fundamental studies of the lateral patterning of films must now rely on chemical differences that can be sensed by electron optical means (transmission electron microscopy or low-voltage scanning electron microscopy)—this typically involves staining, which can often subtly alter the microstructure—or that can be sensed by scanning force microscopy after the ion milling of part of the structure. Typically, these methods involve either tedious sample preparation or analysis and require maintaining a registry when samples are moved back and forth from one instrument to another.

Ideally, one would be able to do both depth profiling and lateral composition imaging with the same instrument and with sensitivity for the lateral distribution of deuterium-labeled macromolecules. In principle, dynamic SIMS could provide such a capability—present instruments have a lateral resolution of about 10 μm—and it has excellent sensitivity for deuterium, easily detecting the natural isotopic abundance of ^{2}H in unlabeled polymers. The focusing of the primary ion beam and the mechanical stability of the instrument itself are what currently limit the lateral resolution of commercial machines. It seems likely that these limitations can be substantially improved. Already, the TOF-SIMS IV is being marketed, based on a Ga liquid metal gun, with a claimed lateral resolutions as good as 50 nm.

2.10.4 National Macromolecular Synthesis Facility

A key issue emerges when the chemical aspects of macromolecules at interfaces are considered. The central role of new materials in all future aspects of research and applications is immediately apparent. Surprisingly, this increased need for well-defined and functionalized macromolecules coincides with the focus on developing facile techniques for polymer synthesis. This presents an unique opportunity to make a far-reaching impact on this field, as well as countless others, by the establishment of a National Macromolecular Synthesis Facility. Ideally, such a facility would be associated with an existing national center, such as a National Nanofabrication Laboratory, and provide all materials, equipment, and expertise for the preparation of an exceedingly diverse range of functionalized macromolecules. The large number of groups that have an active interest in macromolecules at interfaces, but do not have access to synthesis techniques or expertise, would send students and researchers to the facility to prepare the required materials. The consequences of such a center would be profound. The availability of the latest materials, access to cutting-edge synthetic techniques and equipment, and the transference of knowledge and expertise would be maximized. As a result, the speed of discovery in all of these areas would be greatly accelerated. Additionally, the critical mass of such a center provides a perfect research arena for the development of novel tools for macromolecular fabrication, such as an automated polymer synthesizer and high-throughput apparatus. In turn, such in-house developed technology, as well as commercially available tools, would be available to visiting researchers because they may be prohibitively expensive for the vast majority of synthesis and physical research groups.

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