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Molecular and Multiscale Modeling in Chemical Engineering – Current View and Future Perspectives

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Recent Developments Towards Commercialization of Solid Oxide Fuel Cells

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Research in Bioengineering and Nanotechnology

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Modular Materials by Self-Assembly

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Structure, Dynamics and Thermodynamics in Complex Systems: Theoretical Challenges and Opportunities

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Perspective

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Introduction

A brief overview is presented of molecular and multiscale modeling in modern chemical engineering. Three examples, taken from the recent literature, are used to illustrate the role of modeling in emerging areas of technology. The first is concerned with design of liquid-crystal based biosensors. The second is concerned with flow of DNA through microfluidic devices. The third addresses the use of guided self-assembly and block copolymers for nanolithographic processes. Each of these examples shows, in its own manner, how modeling and mathematical analysis of molecular level processes will continue to provide a unifying theme for research and development.

As one tries to think about fields of research where chemical engineers have had an impact, mathematical modeling across multiple length and timescales is one of the main subjects that comes to mind. In fact, one could even say that modeling and analysis have shaped much of the identity of the chemical engineering discipline. The early work of Amundson, Aris and coworkers on reactors, for example, provided the basis for the development of process modeling and changed the entire chemical industry. The work of Bird, Stewart and Lightfoot, provided the analytical framework for analysis of macroscopic transport processes in terms of molecular concepts. The same is true of the work of Prausnitz and coworkers, who pioneered molecular-based models for prediction of fluid-phase equilibria and the thermodynamic properties of fluid mixtures encountered in complex industrial processes.

Long regarded as a purely mathematical subject, molecular and multiscale modeling is most relevant for its physical significance. Chemical engineering is entering a new era, characterized by unprecedented control over chemical reactions, as well as product molecular architecture, conformations and morphology. It is entering an era of molecular processing and manufacturing, in which single-molecule experiments are becoming routine, and complex miniature processes are beginning to be commercialized for a number of applications. These experiments and processes not only benefit from modeling, but in some cases must be interpreted or implemented through a concerted modeling effort. As their complexity increases, so will the need for modeling and analysis. Chemical engineers are particularly well-suited to developing the necessary modeling framework for molecular processing and manufacturing; it requires an understanding of chemistry, molecules and reactions, a firm mathematical foundation, and an intimate knowledge of thermodynamics and transport phenomena. The following examples, taken from several recent applications, illustrate these points in some detail.

Development of Sensors

Recently, Abbott and coworkers[3] have developed a remarkably simple and effective sensing mechanism, based on the ability of liquid crystals to form defects. The principle of operation of a liquid-crystal based biosensor is illustrated in Figures 1 and 2. A surface is decorated with molecules that exhibit a strong affinity for a specific protein or virus. The topography of the surface (e.g., grooves) is such that a thin film of liquid crystal molecules adopts a uniform, defect-free orientation. When the surface is exposed to the protein or virus of interest, however, these are bound at the interface, thereby destroying the order of the liquid crystal and giving rise to optical signatures that can be detected by simple polarized light.[3] The source of the optical texture seen in Figure 2 is the formation of defects in the liquid crystal in the immediate vicinity of the particle (a protein or a virus) at the surface. At equilibrium, the characteristic dimensions of the defect around an isolated particle are comparable to the dimensions of the particle (Figure 1). In the images shown in Figure 2, however, the length of the defects is microscopic. So the question that arises is: why do such complex patterns arise, and can one interpret them quantitatively to infer surface concentrations and other properties of interest? Furthermore, can theory be used to improve or optimize the design of sensors for effective detection of dangerous pathogens?

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The system is in this case inherently multiscale. It requires an understanding of defect dynamics and energetics at scales ranging from a few nanometers to hundreds of microns. At the smallest length scales, one can examine the nature of the defects that arise around an individual nanoscale particle in a liquid crystal through molecular simulations. The image in Figure 1 shows a representative configuration from a Monte Carlo simulation of a nanoscale particle suspended in a liquid crystal [1]. In this case, liquid crystal molecules are represented as ellipsoidal particles, and the system exhibits a nematic phase. In this particular case, for perpendicular or "homeotropic" anchoring of liquid crystal molecules at the nanoparticle surface, a "Saturn ring" defect appears around the particle. One of the important pieces of information provided by multiscale modeling has been to reveal the nature of defects around small particles as a function of size. For a given particle size and a given liquid crystal, simulations also provide a characteristic length and energy for the defect, and material properties for the liquid crystal (e.g., "Frank" elasticity constants) which are subsequently used as input for mesoscopic theories capable of describing the structure and dynamics of a nanoparticle-laden nematic system.[1]

The structure of the liquid crystal can be described in terms of a position-dependent order parameter tensor. A scalar order parameter, which typically varies between zero and unity, provides a measure of the local order in the nematic phase; it is relatively large (e.g., 0.7) for a nematic domain, and it is relatively small (e.g., 0.1) for a disordered domain. Near a defect, the orientation of the liquid crystal changes abruptly and the order parameter is small. The evolution of the order parameter can be described by relatively simple transport equations[7]. Figure 2 shows side views of the predicted texture of the liquid crystal between two plates onto which several nanoparticles have been adsorbed. [5] The grayscale color provides a measure of the order in the system. At elevated temperatures (in the isotropic phase of the liquid crystal) the system is isotropic, as evidenced by the existence of numerous small domains of varying color. As the temperature is suddenly quenched and the system is allowed to enter a nematic phase, defects attract and annihilate each other, in a process aimed at lowering the elastic free energy of the system. At equilibrium, the system eventually adopts a uniform orientation. Beyond a critical concentration of particles at the surface, however, the system attains a metastable state consisting of trapped defects that cannot relax (Figure 2).[5] These defects propagate throughout the system, and are ultimately responsible for the texture observed in optical micrographs.

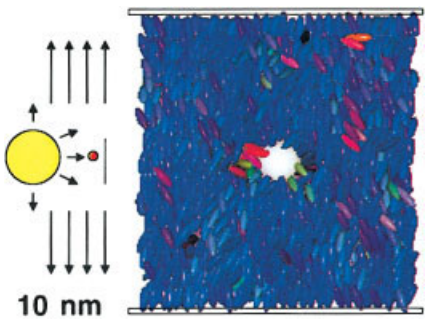

Figure 1. Monte Carlo simulation of a nanoparticle suspended in a nematic liquid crystal.[1]

Liquid crystal molecules are represented as ellipsoids. The anchoring conditions are such that liquid crystal molecules adopt an orientation perpendicular to the surface of the particle and to the two confining walls (shown in red). These anchoring conditions give rise to the formation of a "Saturn Ring" defect, where the orientation of the liquid crystal changes abruptly. The core of the defect is denoted by a red circle in the schematic representation on the left; the arrows represent the average orientation of the liquid crystal.

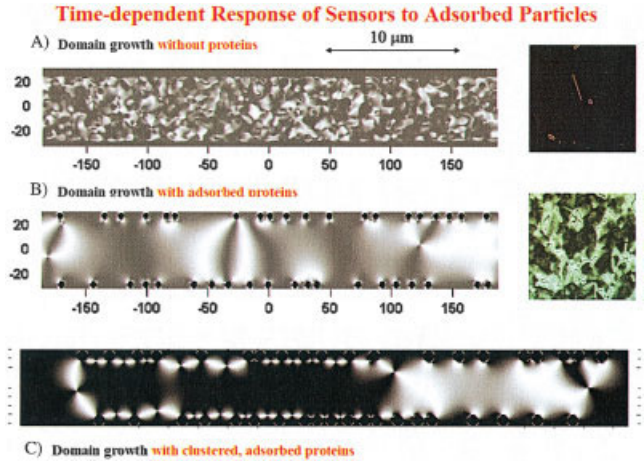

Figure 2. Side view of a liquid crystal based biosensor: The liquid crystal is confined between two surfaces.

The color provides a measure of its local orientation. In the absence of particles adsorbed at the surfaces, when the liquid crystal is quenched from a disordered (isotropic) state (Figure 2A), it enters a nematic phase and assumes a uniform orientation throughout the entire sensor (see micrograph to the right[3]). In the presence of particles at the surface, however, simulations indicate that the liquid crystal enters a metastable state.[5] Many defects are trapped; (B), giving rise to an optical signature that is detected through cross polars (see micrograph on the right). The results of calculations also show that the optical texture that emerges (as well as the dynamics of the system), are particularly sensitive to particular arrangements (e.g., clustering) of the nanoparticles on the surface,[5] as illustrated by (C).

Multiscale modeling, using the formalism described above, has revealed that liquid-crystal biosensors are particularly sensitive to the lateral organization of adsorbed nanoparticles.[5] Calculations have also shown that the dynamics of the liquid crystal sensor contain valuable information that could be used to discern the nature of the particles adsorbed on the substrate. These findings have motivated new experiments on patterned surfaces, in what constitutes a fruitful loop of analysis and discovery that will ultimately lead to better sensors, new devices, and new applications. Furthermore, as the complexity of sensors continues to increase,[7] so will the interplay between multiscale modeling and experiment. Some of the new sensing systems that are now being envisaged will include multiple phases, soft interfaces and surfactants. Their study will necessarily include elements of thermodynamics, transport phenomena and colloid science, and will raise multiple opportunities for research and discovery.

Development of Microfluidic Systems for Genetics Applications

Over the past decade, it has become increasingly clear that microfluidic-based analytical methods offer a number of ad-

vantages over traditional techniques. [8] Many of these advantages are associated with small sampling volumes and speed. The study of DNA structure and dynamics in microfluidic systems has received considerable attention, both from an experimental and a theoretical point of view. The ease with which microfluidic systems can be fabricated, and the development of sophisticated DNA manipulation techniques and imaging methods, have provided an unprecedented view of the dynamics of individual macromolecules. The need to interpret these experiments has instigated the development of simple and elegant molecular models of the structure and dynamics of DNA, in the bulk and under confinement.[9, 10] As discussed later, these models have in turn provided predictions that have fueled the development of novel microfluidic devices.

Long, double-stranded DNA molecules can be stretched out and adsorbed onto chemically modified surfaces. Restriction enzymes can be used to "cut" the molecule at specific locations, which can be detected with a fluorescence microscope. By using various restriction enzymes to cut the DNA at distinct locations, it is possible to generate a consensus map of large DNA molecules in a relatively short amount of time. This procedure provides the basis for what is known as "shotgun optical mapping"[11] and holds considerable promise for the fast and effective analysis of entire chromosomes. One of the bottlenecks in optical mapping is the stretching or elongation of DNA for subsequent analysis. One must elongate the molecule, which can measure more than a millimeter, and avoid overlaps with other DNA fragments on the surface that could generate ambiguous results. It turns out that microfluidic flows provide a particularly effective means for stretching and manipulating DNA. In order to understand how a flow field or an electrical field influences the conformation and dynamics of DNA, particularly near a surface, it is important to have a model capable of describing the motion of individual molecules. Most theoretical studies to date have adopted a "bead-spring" representation of DNA, in which "blobs" of DNA segments are connected by worm-like chain springs.[9] The solvent in which the DNA is immersed is represented by a hydrodynamic continuum. Figure 3 provides a representation of such a model. The corresponding equations of motion include forces arising from connector springs, from interactions between different beads, from interactions between the beads and surfaces, and from the friction generated by the solvent. The behavior of this model can be examined by means of Brownian dynamics simulations.[12] The parameters that appear in the various force expressions of the model can be determined from independent experimental measurements, including single-molecule pulling experiments (e.g., through an atomic force microscope) and diffusion experiments (e.g., using fluorescence microscopy).

Friction is of particular interest to this discussion in that it provides the "link" between the explicit, molecular representation of DNA and the more coarse-grained (continuum) representation of the solvent. The motion of a bead i creates a disturbance of the solvent which propagates and is felt by bead j at a distance r. Such solvent-mediated interactions are referred to as hydrodynamic interactions,[13] and are relatively long-ranged. As has become apparent in recent years, hydrodynamic interactions dictate multiple aspects of the behavior of DNA in microfluidic devices,[10] ranging from the scaling of diffusion with molecular weight to the migration away from a surface in the presence of shear forces.

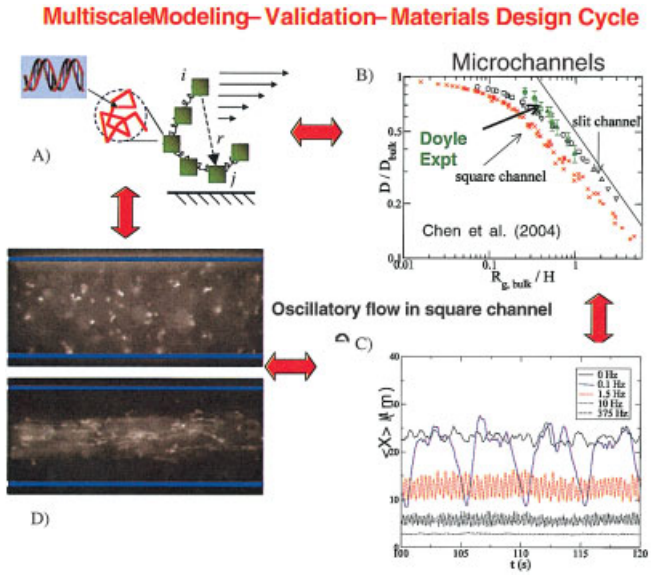

Figure 3. (A) Coarse-grained model for double-stranded DNA in solution.

Each bead represents a collection of many base pairs and multiple persistence lengths. Each red "segment" represents a persistence length. Adjacent beads on the molecule are connected by worm-like chain springs. All beads undergo hydrodynamic interactions, which are meant to capture the solvent-mediated effect that the motion of bead i has on the motion of bead j when separated by a distance r; (B) diffusion coefficients of DNA in square or slit channels. The crosses and open symbols show results of simulations. The green symbols show experimental data;[4] (C) predicted degree of stretching of DNA molecules undergoing oscillatory flow in a square channel, and (D) images showing the stretching and segregation of DNA molecules at equilibrium (top image), and undergoing oscillatory flow in a square channel (bottom figure, courtesy of Dr. Schwarz).

As the conformation of the molecule fluctuates under the influence of Brownian forces, hydrodynamic interactions also fluctuate. The numerical evaluation of fluctuating hydrodynamic interactions is particularly demanding and, until recently, was not readily possible. In recent years, however, new algorithms and faster computers have permitted simulations with full blown hydrodynamic interactions. Figure 3 shows predictions for the diffusion coefficient of DNA molecules in square channels and in slit pores.[4] The diffusion coefficient of confined DNA is much lower than that in the bulk. It is interesting to point out that calculations based on a model parametrization pertaining to bulk solutions yield results for confined DNA that are in excellent agreement with experiment.[4] This agreement suggests that the model can be used with some level of confidence to design microfluidic processes. This provides an interesting example of "scale down" that should be contrasted with the "scaleup" work that has traditionally occupied the process industry.

One interesting prediction of multiscale calculations has been that shear forces induce the migration of DNA away from the surfaces of a confining channel or a slit pore.[10] For many years, the existence of such migration effects (and their direction) has been a subject of considerable controversy. Only now is a coherent picture of macromolecule migration in microfluidic devices beginning to emerge. As the flow rate (or "Weissenberg" number) increases, the segregation of DNA to the

center of the channel becomes increasingly pronounced. Furthermore, longer DNA molecules are pushed away from the surface more effectively than shorter ones, thereby providing a mechanism for separation according to molecular weight. The results of simulations have led to the conception and design of a system for "levitating" and immobilizing DNA in microfluidic flows. In what is referred to as the "microfluidic washer", DNA molecules are subject to an oscillatory flow (see Figure 3). If the frequency of the oscillatory flow is comparable to the longest relaxation time of the DNA, molecules can be induced to migrate to the center of the channel and remain there. These predictions are in quantitative agreement with experiments, and are already providing much needed insights for design of novel gene mapping systems.[14]

As useful and insightful as past work on DNA has been, numerous exciting applications require that more detailed models of DNA be developed. Applications involving the translocation of DNA through molecular pores, for example, will have to consider the detailed chemistry of DNA, and the effects of electrostatic interactions. Applications involving the ligation of distinct DNA strands will also require a more refined description than that depicted in Figure 3. There are also numerous opportunities involving multiple components, including proteins, liquid crystals, or nanoparticles.

Nanopatterning and Guided Self Assembly

In its relentless drive to produce smaller electronic circuits, the semiconductor industry has devised remarkably ingenious processes to assemble functional systems with critical dimensions on the order of a hundred nanometers. Lithography has been one of the workhorses of this industry. A series of lithography steps, sometimes as many as 20 or 30, can account for up to 70% of the cost of a printed circuit. There is considerable interest in exploring new nanofabrication routes capable of mass producing patterned structures at the scale of nanometers, hopefully at a fraction of the cost of current lithographic processes. Guided self-assembly is gradually emerging as a viable alternative for fabrication of electronic devices. One possibility is to combine existing fabrication techniques with materials capable of self-assembly to create functional devices. In recent years, it has become apparent that block copolymers offer considerable promise in that regard. Here, we consider the self assembly of diblock copolymers on patterned surfaces.

As illustrated in Figure 4, the overall goal of the process is to have the morphology of the block copolymer follow as faithfully as possible the pattern that is drawn on the surface. If, for example, it were possible to guide and register lamellae along a surface pattern, one could subsequently etch one of the blocks away for further processing. Whether this works or not depends on multiple variables, including the commensurability of the surface pattern (L_s), and the characteristic period of the diblock copolymer lamellar phase, L_0. It depends on the nature of the polymer-surface and polymer-air interactions, and on the characteristics of the polymer (e.g., molecular weight and persistence length of each block). Figure 4 shows a the multiple morphologies that can arise in a thin diblock copolymer film on a stripe-patterned surface.[2] Depending on the mismatch p between L_0 and L_s, and the thickness of the film D, the morphology can range from a "checker board" pattern, to lamellae oriented parallel to the surface, to lamellae oriented perpendicular to the surface. In this particular example, Monte Carlo simulations of diblock copolymer molecules on a lattice are used to indentify the various possible morphologies corresponding to a specific system. Distinct phase boundaries and a phase diagram can then be constructed by using these morphologies in mean field calculations. Each color in the diagram corresponds to a different morphology. As can be seen in Figure 4, the desired morphology (III_s) of perpendicular lamellae aligned with the surface pattern can be obtained in the vicinity of $p = 1$, and for film thicknesses as large as $6L_0$. Figure 4 also shows results of recent experiments on PMMA-Polystyrene diblock copolymers.[6] The system exhibits perfect order over relatively large areas, and offers exciting possibilities for the application of guided self-assembly in litho-

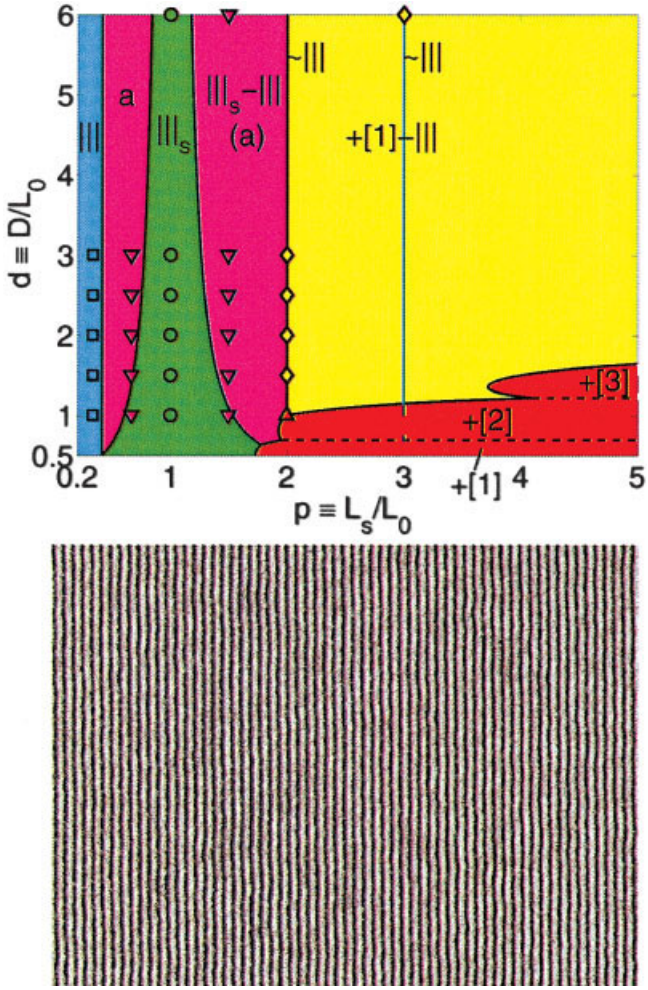

Figure 4. Morphology of thin symmetric di-block copolymer films on stripe-patterned surfaces predicted by Monte Carlo simulations (open symbols) and mean field theory (lines)[2].

L_s denotes the width of the pattern on the surface, L_0 denotes the characteristic lamellar period of the copolymer in the bulk lamellar phase, and D is the thickness of the films. The symbols on the figure denote different ordered phases of the block copolymer; the green region (III_s) corresponds to lamellae, perpendicular to the substrate, that follow the stripe pattern on the surface. The bottom figure shows an SEM image of a diblock styrene-PMMA copolymer on a patterned surface[6]. The polymer exhibits long-range order and perfect registration with the surface pattern.

graphic processes in which perfect order and registration are necessary. The natural question that arises now is whether block copolymers can be used for some of the more complex designs (e.g., lines that bend, circles, squares, etc.) that arise in electronics applications. Preliminary results are encouraging,[15] but this is only the beginning of what promises to be a fertile area of research and development.

More generally, it has become apparent that block copolymers exhibit a wide range of morphologies that could have interesting applications.[16] That range increases dramatically as the number of blocks and components increases. Modeling is needed not only to interpret the results of challenging characterization experiments, but also to identify novel phases and structures with particular applications in mind.

Perspectives

The case studies discussed earlier provide examples of what I called molecular processing and manufacturing. They serve to illustrate several points. The first is that molecular and multiscale modeling provides a unifying set of principles to understand and interpret the behavior of seemingly very different systems on common grounds. It provides a common language that enables practitioners of chemical engineering or soft-condensed matter physics to approach problems in areas as diverse as chemical sensing, microfluidics, genetics, or microfabrication. Without this language, it would be difficult to tackle such problems on a rational basis. Chemical engineering has traditionally benefited from concerted modeling and experimental activities, often within the same research group. The close interplay between modeling and experiment will continue to be critical, perhaps more than ever.

Second, as molecular processing and manufacturing gain acceptance, the demands on particular applications will undoubtedly increase. Molecular and multiscale modeling will be essential in meeting those demands.

Third, and most important, the limits of molecular processing and manufacturing, and therefore those of molecular and multiscale modelers, are set by the creativity of its practitioners. The chemical engineering discipline will flourish over the next decades to the extent that it is able to conceive, create, realize and develop new core technologies. Modeling can accelerate that process at multiple stages, but the fact remains that chemical engineers as a group must continue to identify promising applications to work on.

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