Self-Assembly and Crystallization in Nanoscale Confinement

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ABSTRACT: This supplement has supported a graduate student from Dr. Guangzhao Mao's research group at Wayne State University, Ms. Jenifer Blacklock, to conduct research in Dr. Helmuth Möhwald's research group at Max Planck Institute of Colloids and Interfaces in Potsdam Germany. Dr. Mao's research focuses on the nanoconfinement effect on molecular self-assembly, which impacts molecular electronics, drug delivery, and high-throughput screening. The central hypothesis of the project is when the confinement size is less than the critical nucleus size, the confinement will alter the self-assembled structure. Blacklock conducted a three-month research study in summer 2007 to encapsulate aspirin in the layer-by-layer (LbL) thin films with chemical heterogeneity mimicking the lipid bilayer. She utilized the unique characterization facilities at the host institution for the study of drug permeability in the thin films. Aspirin was shown to diffuse into the DMPC bilayer supported on the LbL thin films. The thin film structure was studied by quartz crystal microbalance. In addition, Ms. Blacklock conducted experiments with regards to the controlled release of DNA from the LbL thin films. The controlled release was accomplished by the use of disulfide-containing reducible polycations. It was determined that DNA release was altered by the presence of a top DMPC bilayer. This part of the work was conducted with ellipsometry, neutron scattering as well as the quartz crystal microbalance

INTRODUCTION

This project is an international collaboration between Wayne State University and Max Planck Institute of Colloids and Interfaces. Dr. Mao's research focuses on the nanoscale confinement effect on the molecule's ability to self-organize[1]. The size effect on molecular crystallization has emerged as a critical issue in a wide range of industrial sectors. For example, drug capsules are known to affect a drug's solid-state form and therefore its circulating half-life and bioavailability. Surface patterns and defects approaching the critical nucleus size will also influence the charge transport properties of thin film microelectronic devices. As the integrated fluidic patterns in high-throughput crystallization screening become increasingly sophisticated, it is essential to understand how fluid channel geometry and size at nanoscale affect the crystallization processes. The central hypotheses of the project are 1) when the confinement size is greater than the critical nucleus diameter, site-specific crystallization will occur whose shape, size, and distribution are dictated by the pattern; and 2) when the confinement size is less than the critical size, the pattern will either prohibit nucleation or trap precritical clusters. The research has begun with simple lipophilic benzoic acids (e.g. aspirin) as the nucleating agents and lipid/alkane bilayers as the confining media.

Encapsulation studies are conducted in collaboration with Prof. Möhwald at Max Planck Institute of Colloids and Interfaces, whose group pioneered the LbL thin film and microcapsule technologies[2]. They offer expertise and methods that are critical to the success of the project. The IREE supplement allowed the student to take up the initiative in the ongoing collaboration, to collect data using instruments unavailable at home, to be exposed to the research atmosphere at a leading international research institution, and to establish personal contacts with foreign partners.

Ms. Blacklock has benefited from her first visit to the host institution. She has learned new thin film characterization methods including quartz crystal microbalance, neutron scattering techniques, and X-ray refraction. During her stay she also obtained data that will contribute to her Ph.D. thesis; established valuable contacts at the early stage of her career; and will likely incorporate her new data into a future publication and continue to keep the collaboratin strong between Wayne State University and Max Planck Institute. Her background is currently working with localized gene and drug therapy techniques[3] and this work will become a charpter in her Ph.D. thesis.

Prof. Möhwald is the Head of the Interface Department at the Max Planck Institute of Colloids and Interfaces. He is among the top three most cited scientists in both physics and chemistry in Germany. He has developed many interfacial characterization techniques including fluorescence microscopy and neutron scattering used worldwide. Most importantly with regards to Ms. Blacklock's research, is that he has pioneered the LbL thin film and capsule research with a wide range of application interests.

IREE travelers (Detroit, MI to Berlin, Germany)
Jenifer Blacklock: 04/28-08/03/2007
Guangzhao Mao: 05/21-28/2007.

Research Activities and Accomplishments of the International Cooperation

During this international experience, the program of research is in the realm of interfacial engineering and transport phenomena. The specific topic of the research is on self-assembly in nanoconfinement. This project provides a fundamental understanding of the crystallization processes used widely in industry for material separation and purification. It also impacts technologies requiring site-specific crystallization with nanoscale precision such as drug encapsulation, molecular electronic circuitry, and high-throughput crystallization screening. The international training aspect of the project prepares the US students to better cope with the increasingly global research environment. The graduate students have gained research experiences by working with researchers from one of the leading research institutions in the world – the Max Planck Institute of Colloids and Interfaces. The project addresses an issue at the heart of nanotechnology, how to make better materials out of a few molecules at a time. The method to capture a few molecules is the spontaneous assembly of long-chain amphiphilic molecules. The self-assembly method generates reliable patterns with size much below the typical limit of 50 nm by the lithographical methods. This new size range will be used to vary crystallinity within a nanoparticle made of a few molecules.

The proposed research intends to monitor and control self-assembly and crystallization of lipophilic benzoic acids in the structured hydrophobic interior of lipid bilayers. Lipid molecules self-assemble into bilayer nanopatterns on graphite and normal bilayers on oxidized silicon from solution and a variety of self-assembled “molecular” templates using a variety of amphiphiles (Figure 1 and Figure 2). The more soluble lipophilic benzoic acids co-adsorb, self-assemble, and crystallize preferentially in the hydrophobic interior of the bilayer upon reaching their solubility limit. The nucleation behavior of benzoic acids is studied when the confinement length is varied in the vicinity of the critical nucleus diameter. Encapsulation studies are conducted using LbL capsules with chemical heterogeneity mimicking the lipid bilayer. The aims of the research are 1) to monitor nucleation and early stages of crystallization, and 2) to control the solid-state form using nanoconfinement.

The Mao group has produced nanopatterns based molecular self-assembly (Figure 1). The confinement imposed by the DMPE lipid nanopattern has been found to alter the adsorption and nucleation behavior of the drug aspirin (Figure 2). During Ms. Blacklock’s three-month stay she was able to successfully finish her tasks, which included learning new techniques for analysing thin films, and presented a seminar at the end of her work for the entire department at Max Planck Instititue of Colloids and Interfaces. Ms. Blacklock started her research project abroad by learning the quartz crystal microbalance (Figure 3) technique. She started regular meetings with Prof. Möhwald and Dr. Rumen Krastev, who supervised her upon arrival. She presented her findings in a one-hour talk to the Interface Department in the last week. In addition to the quartz microcrystal balance, she also learned x-ray refraction and confocal laser microscopy (Figure 4) from other staff scientists at the Institute. She traveled with Dr. Krastev’s group to the synchrotron laboratory in Switzerland to conduct neutron scattering experiments on her samples. Dr. Mao visited the Institute and met with

Blacklock, Möhwald, and Krastev to discuss research progress. During this time, new ideas were formulated based on initial findings and new experiments were planned for further understanding and for future publication.

Experimental studies of nucleation steps in nanoconfinement are necessary for a better understanding of structural and morphological transitions undergone by discrete molecular clusters en route to the critical nucleus and the final crystal structure. Surface patterns can potentially control crystal morphology, crystallographic orientation, and their spatial distribution simultaneously, which until now remains a challenge. Nanoconfinement promises to stabilize metastable structures that are commensurate with the pattern, and enables the observation of stepwise cluster transformations during nucleation when the pattern size is near the critical dimension. The choice of the confinement size at the critical dimension fills a void in template-directed crystallization. Template-directed crystallization has focused predominantly on inorganic crystals and size range beyond 100 nm. The epitaxial templates are crystalline layers themselves, which then are matched with the dimensional and stereochemical needs of the guest crystalline plane. Unlike the epitaxy, the proposed method does not require a prior knowledge of the guest crystal structure but rather that guest molecules discriminate among heterogeneous surface (or medium) structures.

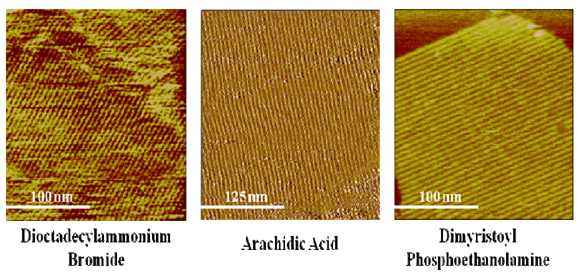

Figure 1. Nanopattern by self-assembly. Alkyl amphiphiles self-assemble into a crystalline stripe phase due to epitaxy between the alkyl chain and graphite lattice. The amphiphilic pattern exhibits an undulating chemical field whose wavelength is equal to the bilayer width. The pattern exposes the cross-section of bilayer lamellae for direct AFM observation of molecular recognition by drug or biomolecules.

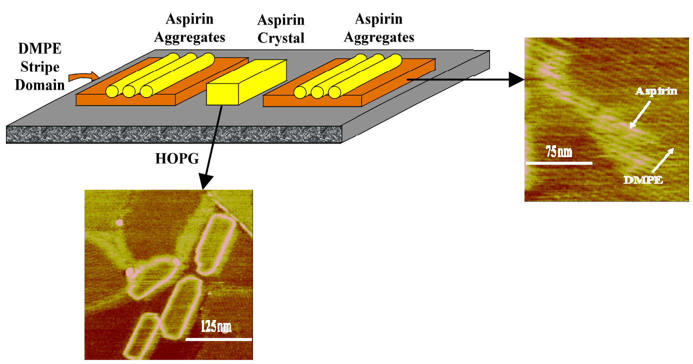

Figure 2. Crystallization on nanopatterns. It is shown that aspirin molecules adsorb only along the hydrophobic interior giving rise to dimer rods in registry with the DMPE template. It can also be seen that DMPE bilayer confinement inhibits aspirin crystallization by preventing its critical nucleus formation.

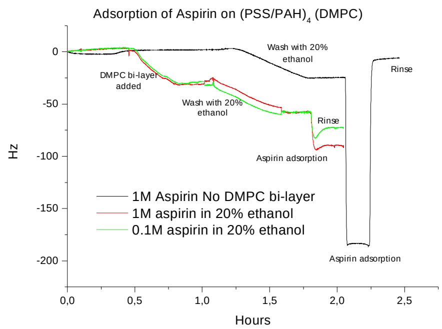

Figure 3. Quartz crystal microbalance was used to study the incorporation of aspirin in the DMPC bilayer supported on the LbL thin films.

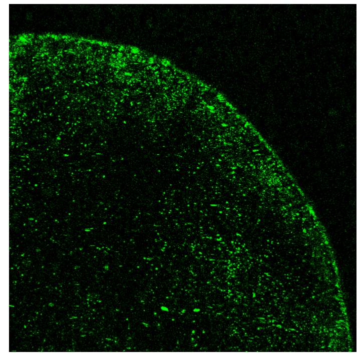

Figure 4. Confocal microscopy was used to study model hydrophobic perylene crystalized within the LbL films.

Broader Impacts of the International Travel

The supplement award promoted diversity because it provided international research opportunity of a female student to pursue a career in one of the STEM fields. The supplement expanded the original scope of the current award by utilizing the expertise and experimental methods that are unavailable at the home institution.

Prior to the travel, the communications and exchanges have been limited to the senior scientists. The travel leveraged the existing relationship and allowed the student to take up the initiative in the ongoing collaboration. She continues to collaborate with the German researchers by sending more samples to be tested, exchanging research ideas, and co-authoring papers.

Ms. Blacklock is a U.S. citizen. She interacted closely with researchers at the host institution. She was able to learn German even though the common language at the Institute is English. She was fully integrated into the group while there. She was able to incorporate new methods and new ideas into her Ph.D. thesis and is considering a postdoctoral research position in a foreign institution.

Discussion and Summary

The IREE funding allowed Ms. Blacklock to strengthen Wayne State University's collaboration with Max Planck Institute of Colloids and Interfaces, a leading institute which will help carve ideas enabling the project to continue to flourish. Without programs such as IREE, it would be hard for young scientists to become diversified in their fields. The contribution that Ms. Blacklock was able to give to the researchers at Max Planck Institute and vise versa is information that will continue to prosper in the future. The most significant accomplishments of the IREE program include 1) data collection on the proposed project using instruments unavailable at home; 2) personal contacts with staff scientists and graduate students; and 3) immersion in global research environment.

Although this program is nearly ideal for the kind of research project that the PI is doing, there are some additional recommendations that could benefit the program in the future. These include; a more clear agenda and participation of the supported researchers at the IREE conference and to have all students present their findings at the conference.

Acknowledgements

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BRIEF BIOGRAPHIES OF RESEARCHERS

Guangzhao Mao received the B.Sc. degree in Chemistry from Nanjing University (P. R. China) in 1988. She received her Ph.D. degree in Chemical Engineering from University of Minnesota in 1994. Following a 9-month post-doctoral research in Materials Science at University of Minnesota in the Department of Chemical Engineering and Materials Science, she joined the Department of Chemical Engineering and Materials Science, Wayne State University as an Assistant Professor. She was promoted to Associate Professor in 2001 and Full Professor in 2007. Her research interests include templated crystallization, nanoparticle thin films, and non-viral gene delivery systems.

Jenifer Blacklock received the B.Sc. degrees in Manufacturing Engineering and in Engineering Management from Miami University Ohio. She obtained her M.Sc. degree in Biomedical Engineering from Wayne State University with a M.Sc. thesis on “Layer-by-Layer Assembly for Controlled Release” in May 2006. She is currently a Ph.D. student at Wayne State University.