The Center for Biological and Environmental Nanotechnology (CBEN)

Annual Report to the National Science Foundation (NSF)

Report Year: 2002
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3. Project Summary

The Center for Biological and Environmental Nanotechnology, or CBEN, aims to discover and develop nanomaterials that enable new medical and environmental technologies. This mission is inspired by the fact that nanomaterials interact with and control biological systems in ways completely distinct from bulk substances. Located at Rice University, CBEN engages in collaborative, interdisciplinary research activities with over twenty participants from ten departments. An understanding of the wet/dry interface between nanomaterials (and biomolecules), complex aqueous systems, and ultimately the environment is necessary for intelligent material design, and nanoscience efforts in CBEN are directed toward these goals. This knowledge supports engineering efforts to integrate nanomaterials into systems that solve outstanding problems in environmental and biological engineering. CBEN’s centerwide programs develop the technical workforce of the future, ensure efficient transfer of CBEN research into the marketplace, and communicate the implications of CBEN research to media professionals and policymakers.

CBEN has many diverse research accomplishments this year – ranging from a novel photothermal treatment for cancer to new porous materials for water purification (Section 8). West and Halas have developed nanoshell colloidal materials which absorb strongly in the near-infrared; these systems are small enough to access tumors deep in the body where they can be targeted to destroy abnormal cells. Such enabling technology is now incorporated into systems-level testbeds that consider the activity of these bio-nanoconjugates in animals. Another research highlight is the discovery of near-infrared emission from single-walled carbon nanotubes (SWNT) by Weisman and Smalley. This work, reported in Science, has far-reaching implications for bio-nanosystems applications. Already, CBEN researchers are working with experts from the Texas Medical Center to use nanotube fluorescence in medical imaging applications and have recently demonstrated in-vitro imaging from nanotube labeled cells.

The broader impacts of CBEN programs are substantial. Teacher training initiatives for ninth grade science have already engaged over thirty local Houston and south Texas teachers with CBEN members. The innovative imagery of Nanokids™, developed by CBEN organic chemist Tour, is now being piloted in the Houston school district. Through these and other K-12 outreach efforts CBEN has in a relatively short time had impact on hundreds of teachers and students. Over fifty undergraduate and graduate students are involved in CBEN research projects and a greater number benefit from the many new courses offered at Rice as a result of CBEN’s programs. CBEN has good participation of underrepresented minorities in its faculty and student populations as compared to national averages, and is implementing strategies to improve diversity centerwide. Finally, CBEN has become an important information source for journalists and policymakers alike as nanotechnology’s negative press has increased. Through these knowledge transfer activities, CBEN has reached thousands of people through popular articles and has informed lawmakers’ work on pending legislation that codifies the national nanotechnology initiative.
### 4. Quantifiable Outputs

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* Printed, In Press, Submitted

** Implemented, Under Development

*** Implemented, Under Development. CBEN is contributing to two of the three new Sloan Professional Masters programs under development at Rice, the Nanoscale Physics program, and the Environmental Decision Making program

**** Cumulative total reflects only printed/implemented.
5. Mission and Broader Impact

CBEN’s mission is to discover and develop nanomaterials that enable new medical and environmental technologies. This mission is accomplished by the following:

- **Fundamental examination of the ‘wet/dry’ interface** between nanomaterials, complex aqueous systems, and ultimately our environment (Theme 1).
- **Engineering research** that focuses on integrating nanomaterials into systems that solve problems in environmental and biological engineering (Themes 2, 3).
- **Educational programs that develop teachers, students, and citizens** who are well informed and enthusiastic about nanotechnology.
- **Innovative knowledge transfer activities** that recognize the importance of communicating nanotechnology facts to media, policymakers, and the general public.

These efforts are inspired by the observation that because of their small size and unique properties, nanomaterials can interact with and control biological systems in entirely new ways. Our research exploits these novel capabilities to develop innovative biomedical and environmental technologies. To ensure that our technologies flourish, our outreach addresses broader issues such as technology transfer, public acceptance of nanotechnology, and workforce training.

In our center’s first eighteen months, we have achieved many diverse research accomplishments ranging from a novel photothermal treatment for cancer to new porous materials for water purification (refer to Section 8.0). **West and Halas** have developed nanoshell colloidal materials which absorb strongly in the near-infrared; these systems are small enough to access tumors deep in the body where they can be targeted to destroy abnormal cells. Such enabling technology is leading to more systems-level testbeds that consider the activity of these bio-nanoconjugates in animals. **Wiesner, Barron, and Colvin** have reported new types of membrane architectures for filtration based around template-assisted chemistries. With morphologies spanning multiple length scales (nanometers to micrometers), such architectures are an important step toward generating water purification systems that are resistant to surface fouling. Other research highlights include the discovery of near-infrared emission from single-walled carbon nanotubes (SWNT) by **Weisman and Smalley**. This work reported in *Science* has far-reaching implications for bio-nanosystems. Already, CBEN researchers are working with experts from the Texas Medical Center to use nanotube fluorescence in medical imaging applications and have recently demonstrated *in-vitro* imaging from nanotube labeled cells.

CBEN has made significant progress in developing scientifically literate students and teachers at the K-12 level; a focus on this younger generation is essential for the long-term development of a technical workforce. Much of our work here is aimed at increasing the quality and quantity of scientifically literate students and teachers at the pre-college level and is described in Section 9. Our ninth grade science program develops better teachers through a CBEN organized content class, CBEN summer fellowships, and a sabbatical for curriculum development. We have worked with over thirty local Houston teachers to date, and also created more concentrated classes for rural and minority communities in south Texas. CBEN also reaches out directly to students using the innovative imagery of Nanokids™; this effort, led by CBEN organic chemist **Tour**, takes advantage of the visual appeal of animated molecules to...
teach the concepts of nanoscience and engineering. Our local school district is currently piloting Nanokids™ content in its middle school classrooms using CBEN sponsored materials. Through these and other K-12 outreach efforts CBEN has, in a relatively short time, had impact on hundreds of teachers and students (refer to Section 9).

Near-term, it is vital that CBEN train the next generation of nanotechnologists to sustain and grow the industries spawned by our center’s efforts. Over fifty undergraduate and graduate students are involved in CBEN research projects and a greater number benefit from the many new courses offered at Rice as a result of CBEN’s programs. Our nanotechnology curriculum has taken on new directions with Rice’s Sloan Master’s programs in both nanotechnology and environmental decision-making.

We strive to increase diversity in all of our training programs. Our K-12 educational outreach programs serve the largely minority Houston and Laredo school districts; the majority of our participants are underrepresented minorities. CBEN’s graduate student population is nearly half female, which far exceeds the national average in science and engineering. CBEN is making good progress in increasing the representation of minorities in both its faculty and student populations (refer to Table 4 and section 9.6). However, realizing our long-term goals for center diversity requires our sustained attention over many years. CBEN’s summer undergraduate research program is the centerpiece of this effort, and we are pleased that our recruiting efforts this year resulted in a class that is nearly entirely underrepresented minorities.

Our knowledge transfer activities include outreach to both established and new companies. We have begun an industrial affiliates program this year and developed technology transfer agreements suitable for both our administration and interested partners. However, like biotechnology, nanotechnology is developing primarily in high-risk, high-payoff start-up companies associated with academic intellectual property. We prepare our students for this by offering a graduate level course in entrepreneurial management. In this course, PhD scientists and engineers work with MBAs to develop business plans. We also sponsor forums to expose business experts to CBEN investment opportunities. This model has proven successful in attracting the interest of the business community. Over five hundred people have attended CBEN forums where new business ideas from Rice faculty were presented. This year, two companies have been founded by CBEN faculty at least in part because of CBEN support of both research and academic entrepreneurship.

Finally, we have invested in knowledge transfer activities far beyond the scope of a traditional center. The increasing public concerns with the dangers of nanotechnology and our research on the implications of nanotechnology motivated us to develop media and governmental outreach as a cornerstone of our strategic plan. (See Sections 10.1 and 10.2.) Various CBEN members now interact almost weekly with media and policymakers; in a coordinated strategy we inform them and the public about nanotechnology and inject hard data into the emotional debate on ‘risks.’ Our position as a center has been essential here, as it gives us access to a wide set of research data both from CBEN and around the world. Our message on the management of risk in emerging technologies, like nanotechnology, has been widely disseminated in talks, media interviews, and congressional hearings.
6. Nuggets

6.1. Carbon Nanotube Fingerprints

Researchers have predicted carbon nanotube-based molecular electronics, nanodevices, and other applications for some time, but have been hampered by the wide range of tube types present in typical samples. Researchers Bruce Weisman and Richard Smalley at Rice University’s Center for Biological and Environmental Nanotechnology have discovered that not only do carbon nanotubes emit light, or fluoresce, under the right conditions, but that this light is also a fingerprint for each nanotube. They demonstrated that typical samples have over thirty types of tubes, each emitting a different wavelength of near-infrared light. Because most of our bodies are transparent to near-infrared light, this fluorescence could have important medical applications. In Figure 6.1, each peak corresponds to a single nanotube type absorbing and emitting a different pair of light wavelengths.

![Figure 6.1 Profile of nanotube absorption and emission](image1)

6.2. Cooking Cancer with Nanoparticles

Imagine killing cancer cells by zapping them, and only them, with a laser. Researchers Jennifer West and Naomi Halas at Rice University’s Center for Biological and Environmental Engineering are finding ways to do just that, by injecting miniscule particles of gold-coated glass, known as gold nanoshells, into tumors. These nanoshells absorb a particular kind of light, known as near-infrared light, which is invisible to the eye and passes straight through the soft tissues in our bodies without problems. When such light from an invisible laser is absorbed, it makes the nanoshells heat up, killing the cells nearby. Dr. West is currently finding ways to ‘target’ the nanoshells, or attach a molecule that will stick only to cancer. That way, the nanoshells could be injected into the body, and would only come to rest at tumors, which can then be cooked away. In the figure, a mouse’s hindquarters are shown; the blue regions are tumors with high local temperatures. This NSF sponsored research has recently been awarded a multimillion dollar NIH grant to take photothermal ablation therapy into animal testing.

![Figure 6.2 Temperature profile of mouse hind-quarters irradiated with nIR light across two tumors with injected nanoshells](image2)
6.3. Fullerenes Accumulate in Living Systems

Although the self-replicating nano-robots of Michael Crichton’s “Prey” may be science fiction, real nanotechnology resulting from much simpler nanoparticles is being developed worldwide. Researchers at Rice University’s Center for Biological and Environmental Nanotechnology are trying to determine what, if anything, they will do to the living things they interact with. The first nanoparticle studied, buckminsterfullerene or \( \text{C}_{60} \), is the soccer-ball shaped carbon molecule whose discovery at Rice University won the 1996 Nobel Prize in Chemistry. \( \text{C}_{60} \) accumulated in all three organisms examined, \( \text{E. coli} \) bacteria, white rot fungus, and redworms. Some toxicity was observed for a colloidal form of \( \text{C}_{60} \), making the molecule an interesting antimicrobial agent.

Figure 6.3 \( \text{C}_{60} \) and \( \text{E. Fetida} \). Right-hand image from http://www.sarep.ucdavis.edu/worms/image5.htm
7. Strategic Research Plan

7.1. Executive Summary

CBEN discovers and develops nanomaterials to enable new medical and environmental technologies. Nanotechnologies generally have great potential to revolutionize how we treat disease and clean our environment. CBEN focuses on those technologies that use chemically prepared, soluble nanomaterials. These materials are the same size as naturally occurring biomolecules, and can be designed for specific functions in biological and environmental systems. Successful applications require fine manipulation of the interface between inorganic nanostructures (the dry side) and biological systems (the wet side). CBEN has termed this the ‘wet/dry interface’ and its control is the organizing theme of all of CBEN’s science and engineering research.

Though unified intellectually by the wet/dry interface, our research programs are oriented toward tangible technological outcomes, or engineered systems. These are:

- Nanoparticles that detect and treat disease
- Effective, high performance water purification systems
- Sustainable manufacturing systems for nanoparticle production

Each of these goals carries substantial technical challenges specific to its particular objectives that are addressed in CBEN’s environmental (Theme 3) and bioengineering (Theme 2) thrust areas. We have also identified roadblocks to these technologies that lie outside of their disciplines. These are the development of sustainable manufacturing methods for nanoparticles and the public acceptance of nanotechnology and nanomaterials. We address the first roadblock in the third systems objective, which cuts across CBEN. The second roadblock is not entirely technical, but as has become recently apparent, remains a critical issue to address. For this reason, we retain both a strong research effort on toxicological and environmental studies of nanomaterials as well as a substantial commitment to educating the public about the real versus perceived risks of nanotechnology.

Every year, CBEN members participate in workshops to draft a strategic plan, the text of which follows this summary. This document serves to provide guidance to members when developing and reporting on projects, as well as to introduce interested partners to the goals and operations of CBEN. Finally, it highlights emerging technical needs in the center. The prominent conclusions of this year’s discussion:

- CBEN will be driven by 2-3 engineered systems that may evolve over time.
- CBEN is dedicated to developing nanomaterials responsibly, with an understanding of their environmental risks.
- Structural characterization of the wet/dry interface is a growing need across CBEN and new members with relevant skills should be incorporated into existing programs.
7.2. CBEN Organization

Research in CBEN is organized into distinct but highly interrelated projects. (refer to section 8 for a diagram) We strongly select for interdisciplinary teams of at least two and more typically three and four investigators. These groups work on problems that can be grounded in fundamental science, focused on enabling technologies, or a combination of the two. In all cases they must be related to the engineering systems goals as articulated in this plan for CBEN.

All projects in CBEN have strong interactions with other efforts in the center. However, for management reasons we group efforts roughly based on their objective: Theme 1 for materials development, manufacturing, and fundamental science, Theme 2 for bioengineering oriented projects and Theme 3 for environmental engineering efforts. Also, CBEN has evolved a number of common objectives that are apparent in distinct engineering efforts. For example, in many projects the need to produce water-soluble and stable nanoparticles of various types is a major goal. These cross-cutting themes are highlighted every year in the annual report to encourage work on the topic and to develop strong connections between projects.

7.3. Systems-level Goals

Systems-level goals play an important role in CBEN: they prioritize the research efforts and provide a longer term framework for all projects. They are ambitious and at the early stages of CBEN it is unlikely that all participants will be working directly on a systems-level goal. Still, all enabling technologies and fundamental science in CBEN are directed from considerations of these tangible outcomes. Center members and project leaders can articulate clearly how and when their work will be used in developing engineered systems.

CBEN has picked three systems-level goals from among the multitude of possible ways to use nanomaterials in biological and environmental engineering. The third is both an enabling technology for all other systems goals, as well as an engineered system itself.

1. Nanoparticles that detect and treat disease. Nanoparticles can be three-dimensional biomaterials whose small size permits them to access regions of the body not available to conventional devices. We explore a variety of particle types, detection and treatment schemes. Drug delivery, photothermal cancer treatments and imaging contrast agents (magnetic, optical, etc.) are some examples where soluble nanoparticles play a key role.

2. Effective, high performance water purification systems. Nanoscale materials, whether they are porous membranes or catalytic particles, can offer the means to remove and remediate contaminants from water. We support projects that build multifunctionality into materials which address specific and relevant challenges (for example, arsenic removal) in water purification.

3. Sustainable manufacturing systems for nanoparticle production. It is critical to consider ways to make nanostructures that are practical, scalable, green, and cost-effective. Projects that seek to address one of the three elements of sustainability (economic, environmental and social) are encouraged by CBEN. This aim is both an enabling technology for all other systems goals, as well as an engineered system itself.
7.4. CBEN’s Three-Plane Chart

In keeping with the engineering research center’s model for center organization, CBEN’s efforts can be described with a three plane chart, as shown below. All critical needs for CBEN as well as potential roadblocks to our systems engineering goals were considered in order to develop the research tasks. These were then organized based on whether they involved fundamental science, enabling technology, or systems engineering (specific planes). Because of our focus on soluble nanostructures, our systems engineering efforts share many enabling

![Three-Plane Chart](image-url)

Figure 7.1 Schematic Three-Plane Chart
The following is a more complete list of all research tasks:

1. NPs with tunable, strong near-infrared absorption/scattering/emission
2. Conjugation strategies for coupling NPs to water-soluble coatings
3. Localized heating of tissue due to near-infrared absorption from NPs
4. Biocompatible coatings that minimize non-specific adsorption/aggregation
5. Staged batch reactors for high yield formation of NPs
6. Characterization methods for bio-nanoconjugate orientation, stoichiometry, and activity
7. Bioavailability of NPs in extracellular matrix
8. Soluble and stable (physically and chemically) NPs in biological fluids
9. Bioconjugation strategies for coupling inorganic particles to proteins
10. Controlled NP aggregates with tunable pore size and thickness
11. NPs with efficient photogeneration of OH radicals/catalytic sites for dehydrogenation
12. Predictive models for NP formation processes in batch reactions
13. New characterization methods for rapid evaluation of NP quality
14. Understanding of bioavailability, fate and transport of NPs in living organisms
15. Understanding of bioactivity of bio-nanoconjugates
16. Light delivery system for efficient illumination of tissue with near-infrared light
17. NPs that efficiently clear from the body
18. Models for crystallization in nanoscale solids
19. Online characterization methods for rapid analysis of NP quality
20. Toxicological understanding of select nanoparticles
21. Integrated therapeutic process for laser tissue welding
22. NPs that effectively target particular cells in vivo with high selectivity
23. NPs with tunable, large permanent magnetic dipole moments
24. Separation schemes for NP size, aspect ratio and surface chemistry
25. Feedback controlled reactors for optimizing NP quality
26. Integrated therapeutic process for targeted photothermal cancer therapy
27. Imaging system for near-infrared detection
28. NPs that sorb target contaminants with high selectivity
29. Water purification systems based on ultra- and nanofiltration membranes
30. Light delivery methods for photothermal and photoactivated remediation
31. Fast and efficient methods for separating NPs for solvent recycling
32. Integrated system for bioimaging using NP-scattered near-infrared light
33. Integrated system for bioimaging using NP-emitted near-infrared light
34. Magnetic separation systems for treatment of arsenic and pesticides in water
35. Systems for simultaneous pumping and treatment of contaminated groundwater
36. Continuous flow reactors with automated separation and analysis schemes
8. Research Accomplishments and Plans

Summary of research organization and objectives

Nature provides us with breathtaking examples of elegant and functional nanosystems. From magnetic bacteria that sense the earth’s magnetic field using nanosized bar magnets, to the nanoparticle-mediated transport of inorganic material in wastewater, the world around us is filled with examples of nanomaterials in action. These examples illustrate that the interaction between nanosystems and biosystems can be a strong and important one, a lesson that nanoscientists are just beginning to explore in the design of artificial, chemically prepared nano-biosystems. Our Center’s research seeks to understand and ultimately manipulate this interaction, which we term the wet/dry interface, as it manifests over a wide range of length scales, ranging from biomolecules to the earth’s environment.

CBEN’s research program is oriented towards specific engineered systems that exemplify how nano-biosystems can be used to solve real world problems. One systems goal is the development of hybrid bio-nanomaterials that can detect and ultimately treat disease. In Theme 2, CBEN researchers under the direction of theme leader Dr. West pursue both near-term enabling technologies and as well as longer term testbeds (e.g. animal studies) for using nanomaterials to solve problems in bioengineering. A second engineered system goal is the development of more efficient and higher performance water treatment systems. This research is carried out in Theme 3 and is led by theme leader Dr. Joe Hughes. By exploiting state-of-the-art nanochemistry these projects demonstrate that nanomaterials can revolutionize how we treat water and remediate its waste. Themes 2 and 3 share several cross-cutting projects that seek to address major roadblocks to nanomaterial commercialization- namely their manufacturing and the characterization of their environmental and health effects. While grounded in different engineering disciplines (biological and environmental), these two theme areas also share many of the same fundamental science needs. Center projects in Theme 1 address these basic questions in chemistry, physics and biology by studying bio-nano interactions over multiple length scales and systems.
While we divide the research into themes for easier management, our engineered systems have multiple interaction points and share numerous enabling technologies. For example, researchers in Theme 1 provide researchers in Themes 2 and 3 with new varieties of nanomaterials for desired applications. Our recently discovered near-infrared emitting SWNT are examples of recently applied medical materials. Also while our engineered systems plan is diverse as it must be for such a high-risk technology area, we have carefully chosen our portfolio to have overlapping near-term objectives. For example work on solvating nanoparticles (Theme 1) is complemented by work on nanoparticle surface chemistry, aggregation, and contaminant adsorption in the cross-cutting environmental impact project (Theme 3). Nanobiosystems developed in Themes 1 and 2 may also find application in environmental measurements (Theme 3); this year, magnetic nanocrystals developed for a medical application are now being evaluated for their use in magnetically driven water treatment.

Summary of major research accomplishments

The overwhelming majority of CBEN projects are “new start” collaborations, in which investigators had no prior collaborative work. In light of this fact, our existing research output (see section 4, Table 1) and the indicators for our future performance (e.g. talks, presentations) are very encouraging. Our research highlights include:

- Single-walled carbon nanotube (SWNT) fluorescence has been identified from water-solubilized, individualized tubes. Each semiconducting nanotube present in the samples is identifiable by distinct excitation/emission wavelength pairs, allowing for the first time bulk-scale characterization of nanotube samples with respect to tube type. The fluorescence is observed in the near-infrared region of the spectrum, squarely within the region of maximum transmittance of biological tissues. This makes SWNTs highly attractive candidates for fluorescence contrast agents in medical imaging applications.

- Metal nanoshells – nanoparticles with tunable optical absorption and scattering characteristics – are being developed into a targeted cancer thermal ablation therapy. Localized heat generation in biological tissues, sufficient to induce cell death, has been demonstrated upon near-infrared irradiation in vitro and in vivo. Initial studies indicate particle clearance through the liver.

- Fullerenes are observed to bioaccumulate in three model systems, *E. coli* bacteria, *E. fetida* roundworms, and *P. chrysosporium* white rot fungus. In the most dramatic case, *E. fetida* concentrated fullerenes laced in the soil by a factor of 21 (final tissue concentration vs. initial soil concentration) over the course of five days. Toxicity was seen only in one fullerene sample preparation of *E.coli*, where fullerenes are thought to be aggregated colloids.
8.1. Theme 1: Nanoscience at the Wet/Dry Interface

Nature is filled with examples of intricate carbon-based machinery optimized to perform complex chemical, physical, and biological processes. If these biosystems can be harnessed to promote nanoscale synthesis and assembly, the resulting “wet nanoscience” will transform both nanochemistry and biology. This approach was established just five years ago when DNA was used to assemble nanostructures; since then, biological materials have proven increasingly useful to solve nanoscience problems, and bio-nanomaterials have been used extensively to study biology. These striking applications attracted our center’s scientists to fundamental questions concerning how inorganic nanomaterials and biological systems interact. Nanomaterials are, in most cases, foreign materials in biology. How they affect biochemical and cellular processes is a crucial question for the rational design of hybrid nano-biosystems, the topic of Theme 2 as well as for developing a complete picture of their environmental impact. In this theme area, the research approaches these issues from diverse biological viewpoints so that together we can develop a view of how nanomaterials fit within the study of living organisms.

Over the past eighteen months projects in this theme area, which with one exception are ‘new-start’ collaborations, have been remarkably productive. New methods for forming and purifying bio-nanoconjugates have been demonstrated in the bionanoconjugate project, and these tools are rapidly transitioning to a broader base of materials. The near-infrared emission from SWNT (refer to Section 8.1.3) was reported in two separate publications in Science magazine.

Table 8.2.1 Theme 1 research allocations

<table>
<thead>
<tr>
<th>Project</th>
<th>Leader</th>
<th>Investigators (name, dept.)</th>
<th>Disciplines Involved</th>
<th>Number of Current Investigators Disciplines Students and Post-docs</th>
<th>Current Year Budget</th>
<th>Proposed Budget</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.1.1</td>
<td>Colvin</td>
<td>Matthews, Biochemistry</td>
<td>Inorganic Chemistry, Biochemistry, Biology</td>
<td>3</td>
<td>$165,741</td>
<td>$94,933</td>
</tr>
<tr>
<td>8.1.2</td>
<td>Hafner</td>
<td>Natelson, Physics</td>
<td>Physics, Biology</td>
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<td>$90,947</td>
<td>$36,665</td>
</tr>
<tr>
<td>8.1.3</td>
<td>Weisman</td>
<td>Smalley, Chemistry</td>
<td>Chemistry, Biology, Physics, Bioengineering</td>
<td>4</td>
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<td>$209,526</td>
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<tr>
<td>8.1.4</td>
<td>Ma</td>
<td>Smalley, Chemistry</td>
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<td>$37,709</td>
</tr>
<tr>
<td>8.1.5</td>
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<td>Yakobson, Materials Science</td>
<td>Chemistry, Physics</td>
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<tr>
<td>8.1.6</td>
<td>Wong</td>
<td>Zygourakis, Chemical Engineering</td>
<td>Chemistry, Chemical Engineering</td>
<td>4</td>
<td>$340,805</td>
<td>$143,476</td>
</tr>
</tbody>
</table>

Totals | $830,992 | $562,111 |

1Investigators listed in bold have joined the project, and investigators listed in italics have left it. The Y02 budget figures include any carry-forward from Y01 due to startup delays. Budgetary information includes both NSF and matching funds, and includes overhead.

2For convenience, compound department titles have been shortened to the most appropriate component. For example, the Department of Physics and Astronomy is listed simply as ‘Physics’.

3Due to late hires in Y01, the operating budget for Y02 in this project contained a significant amount of carry-forward. The average annual budget for Y01 and Y01 is $101,116.

4Y02 funding for this project was requested by the principal investigator to be deferred to Y03, and that request was honored. Note total funding for the project diminished 48% in Y03.

5Dedicated laboratory space was not allocated to this project until Y02, so the Y02 budget contains a great deal of project start-up carry-forward. Primarily earmarked for equipment, the average annual budget for Y01 and Y02 is $174,027.

6Some projects cross theme-area boundaries; they are listed and described only once, but their budgetary information is split equally between the two or three theme area totals. Personnel are listed only in the theme in which the projects are described. The project, "Biomedical Apps. of SWNTs," is in the process of transitioning from Theme 1 to Theme 2, so its Y03 budgetary information is split equally between the Theme 1 total and the Theme 2 total. Similarly, the project, "Environmental Exposure Routes," is split equally between Themes 1 and 3 for all three years, and the projects, "Nanomanufacturing," and "Nanotoxicology," are split across all three theme areas.
Over the next year we expect this work to expand both in Theme 1 as the theoretical efforts for treating SWNT photonics and solubility are developed, as well as into the engineered systems of Theme 2. New partnerships with the Texas Medical Center (Nagahvi) have allowed the recently discovered photonic properties of SWNT to be quickly transitioned into biomedical research laboratories as was always the intention of Theme 1 research efforts. The most significant change to this theme area over the next year is integration of two structural biologists into ongoing projects. As all participants have recognized, further development of nano-biosystems for all of CBEN’s research will require more informative and rapid characterization of the bio-nanointerface. Dr. Jane Tao, an expert in cryo-electronmicroscopy and Dr. Kevin MacKenzie, specialist in solution state NMR of biomolecules, are now focusing on the problem of characterizing nano-bioconjugates.
8.1.1. Activity of Bionanoconjugates (Colvin, Matthews, Tao, MacKenzie)

**Overview**

This project seeks to characterize the effect that covalent conjugation to nanoparticles has on biomolecular function. Since many engineered systems under development within CBEN rely on exploitation of the function of the biocomponent of a bionanoconjugate, a thorough and general understanding of this effect is central to the center’s mission. As a starting point, we have chosen to focus work on a well-characterized biochemical system, the lactose repressor (LacI) protein from *E.coli*. Work over the past year has developed new chemical coupling schemes for tethering, exploited protein engineering to position nanoparticle/protein contacts, and discovered analytical ultracentrifugation as a new tool for characterizing and purifying these materials. We will extend and optimize these new attachment schemes over the next year, will increase our focus on bionanoconjugate characterization, and will include a team member with expertise in cryo-electron microscopy (Tao) and a team member with expertise in nuclear magnetic resonance spectroscopy (MacKenzie). With control over the LacR system in hand our team will transfer the chemistry, characterization and separation schemes to a broader class of biomolecular recognition processes, including calmodulin, antibody-antigen interactions, and cell surface recognition.

**Results**

**Aim 1: Forming gold nanocrystals suitable for conjugation chemistry.**

Several challenges are associated with developing nanocrystals for bioconjugation. First, particles must be stable in the high ionic strength buffers needed for biomolecular activity. Second, non-specific binding should be minimized where possible. Unprotected crystals (UPCs) exhibited nonspecific binding to LacI, as evinced by a lack of aggregation of the UPCs but a blockage of LacI function based on DNA binding analysis. Monolayer protected gold nanocrystals (MPCs) were coated with bifunctional ligands that covalently attach to the nanocrystals and can then link to the LacI. Because of the more straightforward nanoconjugation, DNA was attached first using literature methods. Efforts to optimize this conjugation protocol are ongoing.

**Aim 2: To create and purify a LacI mutant, T334C, for specific binding and develop suitable assays.**

A mutant protein with cysteine at Threonine 334 for oriented reaction was designed that allows for precise positioning of LacI onto the nanocrystal surface. The O₁ DNA binding curves for T334C and wild type LacI show that the mutant protein has very slightly diminished affinity for operator compared to wild type LacI (2 x 10⁻¹¹) and remains sensitive to inducersugar. Stoichiometric binding curves demonstrate that purified T334C has DNA binding activity ≥ 90%.

**Aim 3: To conjugate unprotected (UPCs) and monolayer protected gold nanocrystals (MPCs) to T334C and characterize the products.**

The general scheme for conjugation and a to scale image of the particles are shown in Figure 8.3. Since these nanocrystals are unstable in standard potassium phosphate buffer, different conditions suitable for both protein and nanocrystal were developed. The optimal T334C
concentration for conjugation to nanocrystals was determined to be a monomer to nanocrystal ratio of 25 to 1.

We have found that analytical ultracentrifugation determines the relative amounts and stoichiometries of nanoparticle bioconjugates much more precisely and generally than gel electrophoresis. Sedimentation velocity experiments of free T334C, free nanocrystal and a conjugation reaction demonstrate clearly that the nanocrystals sediment rapidly, the free protein sediments very slowly, and the nanoconjugates demonstrate intermediate behavior. This method will be applied to assess the conjugates for dispersity and may be modified to fractionate the nanoconjugates.

Aim 4: To assay LacI-gold nanocrystal conjugates for operator DNA affinity.

Binding assays of nanoconjugates showed that a measure of specific operator affinity was retained when bound to gold nanocrystals. The nanocrystals appear to interact nonspecifically with the DNA binding domain, precluding DNA binding for native LacI. This was verified by binding assays in the presence of 10 mM DTT to inhibit nanocrystal/cysteine interactions. The results demonstrate that conjugation occurs between LacI and nanocrystals and that DNA binding activity of the protein is diminished by non-specific conjugation.

Plans
A. Characterization of LacI conjugated to gold nanoparticles.

1. Establishing and characterizing the optimal mode of conjugation. We will investigate whether LacI interacts with the nanoparticles in fully folded a denatured/partially denatured form. We will utilize nanocrystals with a more stable monolayer that are being developed in the Colvin Lab. We will develop analytical ultracentrifugation for bionanoconjugate separations, ultimately, to be combined with mass spectrometry and force microscopy, with an early focus on determining the extent of conjugation for both T334C and WT/UPC conjugation reactions. Separation of particles from nanoconjugates will be attempted by phosphocellulose chromatography and size exclusion chromatography (see 8.1.6).

2. Electron microscopy characterization. The most straightforward application of EM will be to provide direct visualization of LacI bionanoconjugates bound to DNA strands. We will use palindromic DNA with the operator sequences embedded in the center to define a reference for...
this visualization. It may also be possible to complete a reconstruction of LacR-gold nanoconjugates; recently, cryo-TEM was used to generate a reconstruction of a virus-gold nanocrystal conjugate. If the bionanoconjugates are purified, and if the linkages between protein and particles are relatively short, then topographic images of the overall structure of bionanoconjugates could be developed. We aim to use this system as a standard to develop methodologies for cryo-TEM that can be widely applied to the challenging problem of bionanoconjugate characterization.

3. **Nuclear magnetic resonance characterization.** The structure and dynamics of specific LacI bionanoconjugates will be characterized by solution NMR spectroscopy if effective concentrations of 50 µM LacI can be obtained. Initial work will focus on 15N-labeled LacI, and pulse sequences optimized for large molecules that tumble slowly (TROSY) will be employed. Since these methods work best at ultra high magnetic fields, the use of the 800 MHz NMR instrument to be installed at Rice will be critical; limited concentration of sample will probably necessitate use of a cryoprobe. Comparison with free LacI will allow us to identify regions of the protein whose structure or backbone dynamics have been altered by conjugation to the nanoparticle. We will also identify the structural changes associated with binding to DNA and inducer sugar, and any influence of the nanocrystals on these processes.

**B. Characterization of LacO-nanoparticle conjugates**

We will characterize the influence of conjugation on LacI binding affinity and allosteric response by nitrocellulose filter binding assay by utilizing a 40-60 bp double-stranded DNA where the linkage reaction is performed under gold particle excess and the DNA-conjugate is radiolabeled.

**C. Determining the effect of nanoparticle/biomolecule composition on behavior**

Palladium will be the initial point of comparison, as it a strong affinity for imidazole moieties, and a poly-histidine extension can be added to the C-terminus of LacI dimer for conjugation. Comparison of the behavior to gold systems will indicate whether particle type or conjugation chemistry is the most critical factor influencing functional properties of the protein.

Other well-characterized monomeric proteins (e.g. lysozyme or ribonuclease) will be examined to compare the effects of conjugation on their structure and function. Particular attention will be paid to calmodulin.
8.1.2. Imaging Biological Charge Distributions (Hafner, Natelson)

Overview

This project aims to develop new modes of scanning probe microscopy to measure charge distribution and charge dynamics in biological systems at the nanometer scale, and to apply these methods to the development of biological nanosensors. Current charge density mapping techniques by atomic force microscopy (AFM) in fluid environments measure force curves at every pixel, requiring an hour-long scan for only a 64x64 pixel image, as compared to 2 minutes for a topographical image at 256x256 pixel resolution. This work has developed “lift mode” charge mapping, simultaneously measuring topography and charge electrostatic interactions in a single scan, dramatically improving resolution and speed. This technique was applied to cationic supported lipid bilayers and to DNA samples imaged in fluid. Over the next year, this project’s focus on sensing will be redirected towards general characterization problems of relevance to CBEN.

Results

Biomolecular imaging

DNA was chosen for study over the initial choice of F-actin, whose non-covalent bonds make the conditions under which actin remains fibrillized rather specific, limiting the approaches available to bind F-actin sufficiently for imaging in fluid. Fortunately, the ionic transport concept only relies on a linear biomolecule with a large charge density. F-actin had been chosen simply because it is the system in which the ionic currents were first observed. Rather than chemically fixing the filaments to make them more stable, the focus switched to DNA, which is also a highly charged linear biomolecule, but is much more stable and more extensively studied by AFM. λDNA was deposited and imaged in fluid on mica and silicon substrates, as shown in the figure below, bottom.

The new characterization methods developed for this project will also be applicable to supported lipid bilayer membrane technology. Supported lipid bilayers were formed by the fusion of small unilamellar vesicles (SUVs) prepared by extrusion through a polycarbonate filter. When imaged in fluid, the supported membranes form submicron scale islands of lipids on the surface, with the expected 6 nm height based on the thickness of a lipid bilayer.

Charge Mapping

One of the new characterization techniques under developed for this project is surface charge density mapping through electrostatic forces between the tip and sample. By employing "lift mode" AFM, higher resolution and higher speed mapping has been accomplished than previous methods. In lift mode, the tip scans each line of the image twice. On the first pass it measures the topography as usual. On the second pass the feedback loop is turned off and the tip repeats the topographic scan at a constant lift height. During the lift scan the cantilever deflection

![Figure 8.1.5 Bottom: λDNA imaged in fluid on mica (600 nm scan).](image)
is measured, which is proportional to the tip-sample force. The force between a spherical tip and planar surface in electrolyte solution from DLVO theory is:

$$F(z) = \frac{4\pi R \lambda \sigma_t \sigma_s}{\varepsilon} e^{-z/\lambda}$$

where $z$ is the tip-sample separation, $R$ is the tip radius of curvature, $\lambda$ is the Debye length, $\sigma_t$ is the tip surface charge density, $\sigma_s$ is the sample surface charge density, and $\varepsilon$ is the dielectric constant of the medium. Assuming the tip geometry and charge density remain constant, the force varies linearly with the sample charge density, so the deflection signal recorded during lift mode is linearly proportional to the sample charge density. Lift mode charge mapping was first tested on cationic supported lipid bilayers consisting of mixtures of 80% 1,2-Dioleoyl-3-Trimethylammonium-Propane (DOTAP) and 20% 1,2-Dioleoyl-sn-Glycero-3-Phosphocholine (DOPC). As shown in the figure, the negatively charged tip shows a downward attractive deflection over the positively charged DOTAP, as expected.

Charge mapping was also applied to DNA samples imaged in fluid in an attempt to observe its charge density and to see if it attracts loosely bound counterions as does a charged 2D surface. The figure to the left shows the topographic image of DNA on the left and the lift mode charge map on the right. A faint repulsive cantilever deflection can be seen to follow the DNA contour. This is the expected result considering that the DNA is negatively charged as well as the tip. To test if the interaction follows DLVO theory, which would imply a counterion cloud around its surface, the lift mode signal (proportional to the tip-sample force) was imaged at several tip-sample separations. The plot of force versus separation displays a clear exponential decay, implying that the DNA charge is attracting counterions.

![Figure 8.1.6](image_url) Left: Topographic image of supported DOPC/DOTAP lipid bilayers on mica. Right: Charge density map over the supported.

![Figure 8.1.7](image_url) Top left: Topographic image of DNA. Top right: charge density map over DNA with a 5nm lift. Both images are 600 nm scans. Bottom: plot of tip deflection as a function of tip-sample separation.
8.1.3. Biomedical Applications of SWNT (Weisman, Smalley, Tao, Hauge, Naghavi)

Overview
This project seeks to develop an in vivo fluorescence imaging system using single-walled carbon nanotubes (SWNT) as the contrast agents. Optical biomedical imaging systems frequently suffer from absorption of the light by tissues, dramatically reducing the observed contrast. Few organic fluorophores emit light at the long wavelengths that afford highest tissue transparency, and there are heavy-atom toxicity risks associated with many inorganic emitters. A groundbreaking result from this project over the last year was the discovery that SWNT fluoresce strongly in the near-infrared region of the spectrum, the wavelength range of maximum transparency in biological tissues, and far beyond the accessible region of organic fluorophores. As part of this work, we have developed a technique for separating surfactant-dispersed SWNT that are individuals from those that are bundled, and have mapped the 2-D excitation/emission spectrum features onto individual nanotube types, which until now were indistinguishable in bulk samples. Planned work includes preparation and characterization of biologically relevant SWNT samples, solubilized by bio-compatible surfactants and/or covalently linked to targeting biochemicals that have high affinity for selected tissue. These samples will then be studied optically ex situ and in biological samples. A sensitive non-imaging system will be developed to detect and quantify fluorescence from trace concentrations of SWNT in tissues, and a fluorescence microscopy system will be developed to image SWNT in cell and tissue samples. Over the past year, this project has resulted in two papers in Science, one invention disclosure, and many presentations.

Results
The original goal of this project was to study the optical spectroscopy of single-walled carbon nanotubes (SWNT). Each possible SWNT structure can be conceptually generated by rolling a graphene sheet into one of a finite set of seamless tubes, each denoted by a unique set of indices (n,m). The values of n and m determine the nanotube’s diameter and chiral angle. Real-world samples of SWNT contain a wide variety of tube structures and lengths. Although length should have very little influence on nanotube electronic properties, those properties will vary strongly with (n,m) structure, with 1/3 of the tubes metallic and 2/3 semiconducting. Optical spectroscopy can probe allowed transitions for these species between the sharp maxima in electronic state density that arise from quasi-one dimensionality and are known as van Hove singularities, producing a distinct absorption for each tube type.

Until recently, however, optical spectra of nanotube samples have displayed only broad absorptions that could not reveal transitions of individual tube types. In a recent breakthrough in our project, a method was developed for processing mixtures of nanotubes so as to obtain aqueous samples highly enriched in unbundled SWNT individually surrounded by a micelle-like adsorbed surfactant phase. Such samples show strikingly sharp absorption spectra in the near-infrared and visible regions. Second, we discovered that samples containing individual semiconducting nanotubes in surfactant suspensions emit near-infrared band-gap fluorescence.
This discovery provides a powerful new tool for studies of nanotube electronic structure and also opens the door to several important applications.

We have carefully measured two-dimensional excitation-emission spectra using a near-IR enabled spectrofluorometer, revealing dramatically well-resolved features arising from more than thirty distinct semiconducting nanotube species. Through a challenging and complex process of pattern analysis supplemented by measurements of resonance Raman spectra, we were able to identify the specific (n,m) species responsible for 33 sets of van Hove optical transitions. Our findings provide unprecedented, precise experimental values for electronic transition energies in semiconducting SWNT. The results are not in adequate agreement with current theories of nanotube electronic structure, presenting a challenge and an experimental benchmark for the refinement of nanotube theory.

An important analytical application follows immediately from our deciphering of nanotube optical spectra. By measuring fluorescence intensities for combinations of excitation and emission wavelengths known to correspond to various semiconducting (n,m) species, one can readily deduce the relative concentrations of these species in an arbitrary sample of nanotubes. This approach offers a sensitive, rapid, non-destructive, and species-selective method for nanotube analysis. It will surely prove useful for monitoring the products of nanotube generators and for guiding the development of methods to separate nanotubes by diameter, chiral angle, or specific structure. It also seems clear that near-IR fluorescence will prove to be the most sensitive and selective method for detecting nanotubes in complex environmental or biological surroundings.

**Plans**

Sudden cardiovascular events and our inability to predict and prevent them remain the leading cause of loss of human lives in many countries, soon in the whole world. Unlike most other diseases where the presence of illness is revealed by signs and symptoms, in more than 50% of heart attack victims the first symptom is sudden death. In the past decade the field of cardiology has witnessed a major paradigm shift. Discovery of vulnerable plaque has shed light on our understanding of the underlying cause of heart attack. The long term erroneous perception that described heart attack as an ultimate result of progressive atherosclerotic narrowing of coronary arteries that clinically presented by restricted blood flow and ischemia is no longer supported. We now know that heart attack and sudden cardiac death are caused by a blood clot superimposed on ruptured vulnerable plaques that results in sudden occlusion of coronary arteries.

Figure 8.1.9 Bulk-phase determination of SWNT diameter and chirality distribution.
Non-invasive diagnosis of vulnerable plaque utilizing electromagnetic spectral properties without contrast enhancement has been attempted. However, due to the physical location, size and composition of vulnerable plaques, there is a need to develop nanoparticle contrast enhancement agents that can be taken up by activated immune cells in these plaques and then reveal their presence.

Early results from a collaboration between Rice University and the Texas Heart Institute strongly suggest that single-walled carbon nanotubes can be excellent candidates for developing such contrast agents. The natural near-infrared properties of these tubes along with their extremely small size allow them to localize in small plaques. It is our intention to study the interaction of these nanotubes with monocytes and macrophages that comprise the majority of cellular components of vulnerable plaques.

This project is intended to support the development of two engineered systems:

1. A combination of hardware and methodology for detecting, quantifying, and imaging fluorescent SWNT in biological specimens, enabling essential toxicological studies.

2. A compact, low-cost device for non-invasive, non-ionizing medical diagnosis using fluorescence detection from SWNT that have been targeted to tissues of clinical interest.

We will pursue two sub-projects in parallel, each building on our unique expertise in the production and spectroscopy of nanotubes. The first involves preparation and characterization of biologically relevant SWNT. In this effort, we will prepare SWNT using the HiPco method, process them to generate nanotubes with desired length distributions, and solubilize them using a variety of bio-compatible surfactants. Samples will also be prepared for covalent linkage reactions intended to form nanotube bioconjugates having high affinity for selected tissues.

The second sub-project comprises optical studies using the SWNT samples described above. We will use absorption and fluorescence spectra to characterize the diameters and chiralities of nanotubes in the samples. Fluorescence spectra and quantum yields will be measured for nanotubes of different lengths in surfactant suspensions and in samples of blood and other tissues. A sensitive non-imaging system will be developed to detect and quantify fluorescence from trace concentrations of SWNT in tissues. Using fluorescence intensities as an assay, we will add nanotubes to whole blood and determine how they partition among different components. We will also develop NIR fluorescence microscopy to image SWNT in cells and tissue samples. Finally, we will assess the near-IR fluorescent properties of SWNT bio-conjugates.
8.1.4. SWNT Modeling in Micelles (Ma, Smalley)

Overview

This project aims to develop a working, fundamental-level understanding of the interactions of carbon-based nanomaterials, such as the fullerenes and nanotubes, with aqueous systems of biological interest, such as pure water, lipid membranes, nucleic acids, and proteins. Over the long term, this understanding will aid in the development of engineered bionanoconjugates. In the nearer term, we are developing an understanding of the interfacial dynamic, thermodynamic, and mechanical properties of bio-nano systems at different spatial and temporal resolutions. Molecular dynamics (MD) studies on water surrounding and inside single-walled carbon nanotubes (SWNT) revealed a remarkably ordered, ice-like structure to the interior water molecules, consisting of helical ice-sheets in a perfectly hydrogen-bonded network. MD simulations of C_{60} inside a fullerene-specific antibody elucidated the interactions between the binding site and the carbon cage. Work will continue to model the environment of a SWNT in a surfactant coating.

Results

Interfacial Interactions of Nanotubes with Water Molecules

Carbon nanotubes are generally hydrophobic, so the dynamical and structural properties of surrounding water molecules are expected to differ greatly from those of bulk water. We have carried out molecular dynamics (MD) simulations of segments of pristine SWNT of different sizes submerged in a periodic hexagonal prism of water under physiological conditions (300K and 1 atm). Segments of SWNT with a length of 20 Å and indices of (n,n) were studied (n=5,6,7,8,9,10,15).

We found that the (5,5) tube (6.75 Å in diameter) is too small to accommodate any water molecules inside, and the behavior of the water molecules inside the (15,15) tube (20.26 Å in diameter) is similar to that of bulk water, but that tubes of intermediate sizes exhibit a highly-ordered arrangement of enclosed water molecules. They tend exist 3 Å away from the wall, and strikingly, along the central axis there is a much lower water density. We also observed unconventional water trajectories along the inner wall of the tubes. For example, there are a total of six columns of water molecules inside the (9,9) tube (12.16 Å in diameter) forming a perfectly hydrogen-bonded network. The water sheet appears to be very stable in the simulations. Only occasionally do individual water molecules migrate from the sheet and result in a rapidly resealed defect. Similarly, the simulations of tubes of various sizes show that the (6,6) tube (8.11 Å in diameter) can accommodate a single hydrogen-bonded chain of water, the (7,7) tube (9.46 Å in diameter) a three-column water network, the (8,8) tube (10.81 Å in diameter) a four-column water network, and the (10,10) tube (13.51 Å in diameter) a seven-column water network. The effect of accounting for the polarizability of the SWNT was examined by a high level ab initio quantum mechanical calculation on the complex formed by a segment of (6,6) tube and the single file of water molecules. The geometry optimization calculation showed that the single file water inside the (6,6) tube is stable in the isolated tube-water complex, verifying that it is a reasonable approximation to omit the SWNT polarizability.
The behavior of water molecules inside the hydrophobic nanotubes is of great interest for biological applications. For example, there are growing lines of evidence suggesting that the transmembrane channels such as $K^{+}$-channels and water channels all have a pore lined with hydrophobic residues. Such a ‘greasy’ pore is believed to be important for facilitating efficient axial passage of small ions or water molecules without getting ‘stuck’ to the walls. The lengths of the nanotube segments simulated here are in general comparable with those of the hydrophobic pores in transmembrane channels. This creates a possibility of using segments of nanotubes as cell transmembrane channels or pores. Moreover, the extremely ordered hydrogen-bonded water network inside the tubes is intriguing given that many proton conducting membrane channels use a continuously hydrogen-bonded water column acting in a concerted fashion for proton translocation.

**Interfacial Interactions of Buckyball C$_{60}$ with a Fullerene-specific Antibody**

Molecular dynamics simulations of an antibody-buckyball complex demonstrated that a single C$_{60}$ molecule can be readily accommodated in the suggested binding site of the antibody. The ball inside the binding site undergoes a small relative translational motion, but a significant rotational motion with no favored axis of rotation. About 17% of the surface of the ball is solvent exposed throughout the simulation, with the antibody covering the remaining surface, which could be utilized for additional functionalization.

Figure 8.14 shows the ball in the binding site surrounded mostly by hydrophobic amino-acid sidechains, revealing shape complementarity of the antibody pocket and the fullerene and rich interactions between the ball and the aromatic sidechains of the antibody, including triple $\pi$-stacking and weak hydrogen-bonding.

**Plans**

Future work will investigate solubilized SWNT systems, similar to those in use in the project described in section 8.3.3.
8.1.5. Fullerene/SWNT Theory (Scuseria, Yakobson)

Overview

Theory and computations of DOS (density of states) with the focus on van Hove singularities have been performed in order to predict optical signatures of single-walled carbon nanotubes (SWNT) and compare with ongoing within CBEN absorption and fluorescence spectroscopy. The advantages of a novel hybrid-functional have been demonstrated, permitting us to achieve very good agreement with available experimental DOS measurements. Based on this progress, an initial study of defects in tubular structures has begun.

Results

The electronic structure of individual single wall carbon nanotubes (SWNT) is currently the focus of considerable theoretical and experimental interest. In SWNT, a small change in atomic structure (diameter and/or chiral angle) may produce significant changes in electronic properties of the tube. Tight binding calculations predict that SWNTs with indices \((n, m)\) such that \(2n+m/3=k\) (where \(k\) is an integer) should be metals, whereas for \(k\) non-integer, the tubes should be semiconductors. It has also been shown that the energy difference between the first two van-Hove singularities (VHS), which reflect the one-dimensional (1D) band structure of the tubes and appear as sharp peaks in the density of states (DOS), is a smooth function of the tube diameter. The Tight Binding (TB) model has been widely used in theoretical studies of SWNTs, and while recent experiments have confirmed its general theoretical predictions about the shape and positions of van Hove singularities, fine effects are not reproduced by these TB models. Detailed study of the spectral features has been directed towards higher-accuracy density functional theory (DFT) based calculations, and towards more realistic account for the ever-present structural imperfections and defects in the nanotubes.

In this work, we have carried out a systematic comparison of experimental and theoretical DOS of individual nanotubes with different diameters and chiral angles using for the first time hybrid functionals, \(i.e.,\) those that contain a portion of exact HF exchange. We have calculated the optimized geometries and electronic structures of a number of zigzag, armchair, and chiral SWNTs using the development version of the Gaussian suite of programs, which allows for DFT calculations with periodic boundary conditions and geometry optimizations using analytic energy gradients.

![Density of states calculations for a (10,0) SWNT by three techniques.](image)

Figure 8.1.14 Density of states calculations for a (10,0) SWNT by three techniques.
**Plans**

Detailed study of the spectral features will be directed towards higher-accuracy density functional theory (DFT) based calculations, and towards more realistic account for the ever-present structural imperfections and defects in the nanotubes (see figure as an example). In this work, we will continue the systematic comparison of experimental and theoretical DOS of individual nanotubes with different diameters and chiral angles using hybrid functionals. Particular emphasis will be placed on a systematic study of the optical manifestations (signatures) of the series of possible defects: mono- and di-vacancies (missing carbon atoms), Stone-Wales defects 5/7/7/5, individual split dislocation 5/7 (in both cases 3 possible orientations must be considered as their effect on DOS is different). Due to employed periodic boundary conditions important artificial effect must be accounted for – finite size L of the supercell, equivalent to a high (1/L) concentration of defects.

A direct extension of defect@nanotube DOS calculation can include the analysis of attached chemical groups, from monoatomic (-F, -H) to larger (-CH₃, -C₆H₅Cl etc.), as chemical-functionalization and spectroscopic data increases in experimental work.

![Figure 8.1.15 Effect of defects on density of states.](image-url)
8.1.6. Nanomanufacturing (Wong, Zygourakis, Pasquali, Colvin, Mantzaris, West)

Overview

The nanomanufacturing facility addresses two distinct and universal challenges faced by CBEN engineers: the production of large amounts (> 10 grams) of nanomaterials for testing and the need for ongoing, sometimes incremental, improvements in nanomaterial design. While academic nanochemistry groups are eager to generate new materials for demonstration purposes, most are less motivated to expend resources on scale-up and material optimization after the fact. CBEN recognized this cultural barrier early on, and provided for funds to equip and maintain a separate laboratory space devoted to solving these problems. Nanomanufacturing was scaled back due to budgetary constraints in the first year, and has only started to function in the middle of this year as Rice made a 1000 square foot synthesis lab available. In this brief period, nanomanufacturing staff have developed new ways to form metal nanoshells in collaboration with CBEN industrial partners as well as generated water soluble magnetic nanocrystals for sorption studies in Theme 3. Additionally, chromatographic methods for characterizing and separating nanocrystals have been developed, and quantitative modeling of the nanocrystallization reactions is now underway. These two enabling technologies are the first steps towards the engineering systems goal of sustainable, high-yield nanoparticle production processes.

Results

i) Thin nanoshells. Nanomanufacturing is available to all CBEN participants and members are encouraged to nominate informally materials development projects that are too limited for a full project. In the past six months, nanomanufacturing staff have worked with West and colleagues at Nanospectra Biosciences to generate nanoshells with very thin (d < 5 nm) coatings. The challenge is to keep nanoshell absorption in the transparency range of tissue (~1000 nm), while shrinking the overall size of the particle to less than 100 nm. For cores of 40 nm diameter, this requires an even shell coating of less than 5 nm. Such materials are straightforward to prepare but required significant changes to existing nanoshell formulations; silica spheres from Nissan were first coated with thiol (-SH) functionalities using standard literature methods and their concentrations verified with Ellman’s reagent. Then very small gold nanocrystals prepared via standard reactions in organic solvents were coupled to their surfaces.

ii) Magnetic nanocrystals. One outstanding problem for environmental engineers worldwide has been the efficient removal of arsenic from water. Hughes and Tomson suggested iron oxide membranes or particles as sorbents given the strong and specific interactions between arsenic and iron minerals. A new professor on the Rice campus, Laibinis, also suggested that monodisperse magnetic nanocrystals would improve magnetic separation processes currently limited by poorly controlled particles. Nanomanufacturing has optimized a recently reported preparation of nanoscale magnetite and developed surface coatings that allow these particles to be stabilized in water. These materials will be incorporated into nanoshell interiors for applications suggested by colleagues from the Texas Medical Center (Naghavi). Additionally, this effort has enabled a new direction within Theme 3 that is resonant with its overall systems engineering needs (see section 8.3.5).

iii) Chromatographic separation of nanoparticles. Long-term, nanomanufacturing aims to develop manufacturing systems that produce nanoparticles in high-yield, at low cost and with minimal impact on the environment. An important component of this plan is the need for on-
line nanoparticle characterization tools, as well as separation methods that allow solvent from these reactions to be recovered and reused. Nanomanufacturing (Colvin) has developed new methods for applying chromatography to solve these problems. Size-exclusion chromatography (SEC) allows for the rapid sizing and separation of particles based on their hydrodynamic radius; while it is widely used in biological separations both in the lab and industrial scale, its application in nanochemistry is virtually unknown. We have developed SEC recycling methods similar to those used for polymers to separate populations of particles that differ by only 5% in their diameter. Additionally, we demonstrated for the first time how SEC can be used to separate semiconductor quantum dots under 10 nm in diameter. These milestones are critical to the progress of our effort in nanomanufacturing of particles; moreover, the methods developed here find immediate application to the challenges associated with purifying nanobioconjugates in Theme 1.

iv) Population balance modeling of nanoparticle growth. Population balance models are often applied to complex kinetics for problems ranging from biological cell proliferation to crystal growth. We have adapted this tool to the special case of the growth kinetics of semiconductor nanocrystals. A simple population balance model is the starting point for our analysis (Mantzaris) and we incorporate classical particle growth equations into this framework (Pasquali, Zygourakis). While the details are beyond the scope of this brief report, the result is a model that relates the size distribution of a nanocrystal population to the key reactor parameters, such as temperature and monomer concentration.

Plans
Over the next year nanomanufacturing will continue to take on materials development projects as time and interest will allow. The post-doctoral staff of nanomanufacturing has become adept at switching quickly between projects and project managers, and with the new lab fully equipped by the end of summer it should be even easier to meet the ongoing materials development needs. We anticipate the nanochemists Wong, Colvin and Barron to be the most likely advisors for these projects.

Nanomanufacturing has a longer term systems goal to generate sustainable, high-yield nanoparticle production processes using the most advanced methods in chemical engineering reactor design. This is a key enabling technology for all engineered systems in CBEN. To do this requires a fundamental understanding of the kinetics of nanoparticle (NP) formation and the effects of reactor design and fluid flow on NP properties. Over the next year we will design a novel NP reactor to collect particle growth data, to model the evolution of particle growth and population, and to use this information to optimize the production of high quality NPs. We target CdSe quantum dots as the model NP system initially because the strong correlation of particle size and optical spectra allows us to monitor reactions quantitatively. Chromatographic methods described earlier will be used in later years to extend models to other materials that lack size dependent optical signatures.

Current preparation methods for CdSe NPs are carried out in small reactor vessels batch-wise, and are difficult to scale up for large-scale production. Using larger vessels will not necessarily lead to larger amounts of NPs due to increased difficulty in maintaining uniform temperature and precursor concentrations within the vessel. For the same reasons, the NPs may be lower quality (e.g. particle sizes and shapes are less uniform). Running the NP synthesis
reactions in multiple, identical reactor vessels is not a viable solution, either. Whereas the high quality of the NPs could be ensured, such a scale-up approach is labor-intensive, has high capital costs, and would still yield batch-to-batch variations in NP properties. This approach would also exacerbate the current NP preparation problems of large solvent use and high energy costs.

We propose to develop a general methodology for the large-scale liquid-phase production of high-quality NPs using an approach chemical engineers have taken to processing both polymers and colloids. Our first task is the design of a reactor to continuously monitor the CdSe NP size and size distribution during particle growth in a batch reaction. This system will (a) collect reliable and reproducible particle size distribution data; (b) control and program the reaction temperatures during the nucleation and particle growth phases, and (c) implement various feed schedules. The few reported attempts to monitor CdSe growth dynamics during processing have been low-throughput and labor intensive, which limits the ability to develop accurate models of the process. In anticipation of the difficulties in relating other synthesis parameters to the NP characteristics due to batch-to-batch variations in CdSe NP synthesis, we will design a two-stage batch reactor in which the nucleation and NP growth steps are decoupled (see Figure 8.1.16). By separating the two steps into two sequential reactors, we can control both nucleation and growth (vis-à-vis temperature and residence time) independently of one another.

Our second task is to develop a rigorous mathematical modeling framework from the experimental data and extract particle growth kinetics to be fed back into optimization of reactor design and operation. Such models are standard in polymer processing, for example, but have never yet been applied to nanochemistry. We will feed these concentration-time data into a population balance model to extract kinetic parameters for this particle growth model. Our first model will be a simple one, which assumes a pseudo-steady-state for the monomer concentration in the bulk solution, and simultaneous addition of Cd and Se monomers to the growing particle surface. The kinetic information derived from inverse modeling will then be used to optimize the synthesis of CdSe NPs in the batch reactor, in terms of growth temperature.

The ultimate result of the proposed, highly interactive modeling/experimental studies will be a robust reactor system that will lead to high-throughput, high-quality formation of CdSe nanoparticles. Moreover, many of the mathematical/computational tools to be developed for this project will be readily available to other applications involving nanoparticle formation from colloidal synthesis routes i.e., the integrated modeling-simulation tools together with the various reactors will be an enabling technology for scaling up other NP growth processes.
8.2. Theme 2: Nanoparticles that Detect and Treat Disease (Nanobioengineering)

Table 8.2.1 Theme 2 research allocations

| Project | Leader$^1$ | Number of Investigators Disciplines Students Year Proposed Budget |
|----------|------------|--------------------------|--------------------------|--------------------------|
| 8.2.1 Nanostructures that Detect and Treat Disease | West, Bioengineering | Halas, Electrical Engineering | Bioengineering, Biochemistry, Inorganic Chemistry | 2 | $290,083 | $194,762 |
| 8.2.2 Nanostructures that Detect and Treat Disease | West, Bioengineering | Halas, Electrical Engineering | Bioengineering, Biochemistry, Inorganic Chemistry | 0 | $ - | $17,880 |
| 8.2.3 Nanostructures that Detect and Treat Disease | West, Bioengineering | Halas, Electrical Engineering | Bioengineering, Biochemistry, Inorganic Chemistry, Physics | 1 | $86,938 | $59,600 |
| 8.2.4 Nanostructures that Detect and Treat Disease | West, Bioengineering | Halas, Electrical Engineering | Bioengineering, Biochemistry, Inorganic Chemistry, Physics | 3 | $168,172 | $144,446 |
| 8.2.5 Nanostructures that Detect and Treat Disease | West, Bioengineering | Halas, Electrical Engineering | Bioengineering, Biochemistry, Inorganic Chemistry, Physics | 1 | $ - | $47,430 |

$^1$Investigators listed in bold have joined the project, and investigators listed in italics have left it. The Y02 budget figures include any carry-forward from Y01 due to startup delays. Budgetary information includes both NSF and matching funds, and includes overhead.

$^2$For convenience, compound department titles have been shortened to the most appropriate component. For example, the Department of Physics and Astronomy is listed simply as 'Physics'.

$^3$Some projects cross theme-area boundaries; they are listed and described only once, but their budgetary information is split equally between the two or three theme area totals. Personnel are listed only in the theme in which the projects are described. The project, "Biomedical Apps. of SWNTs," is in the process of transitioning from theme 1 to theme 2, so its Y03 budgetary information is split equally between the theme 1 total and the theme 2 total. Similarly the projects, "Nanomanufacturing," and "Nanotoxicology," are split across all three theme areas.

There may be no division of engineering that places greater constraints on materials performance and characteristics than bioengineering. Not only do biomaterials have to meet stringent requirements for specific applications, but they often also must be biocompatible. We believe that nanomaterials can provide solutions for many biomedical problems. Their extremely small size enables them to access a variety of biological environments; their size also endows them with valuable size dependent properties which can be exploited in applications. Finally, their large surface areas are platforms for engineering multifunctional systems capable of recognizing and responding to disease states.

The four projects in this area, in addition to the transitioning theme 1 project on SWNT near-infrared imaging, all reflect different approaches to the overall systems engineering goal of ‘nanoparticles that detect and treat disease’. Two complementary efforts (8.2.1 and 8.1.3) aim to apply nanoparticles to imaging of cancerous tumors as well as plaque inside of arteries. Beyond imaging, the strong and tunable near-infrared absorption of some nanoparticles can be used to heat tissue deep inside of animals using external light sources. The application of this enabling technology to cancer treatment, developed this year in CBEN research, is explored next year in a testbed project with animal studies. A related seed project (8.2.2) seeks to apply this basic enabling technology to a new problem in biomedical engineering, tissue welding. Project 8.2.4 uses nanoparticles to improve tissue replacement materials for disease treatment. This theme area is fortunate to have NIH funding available as leverage and this year projects 8.2.1 and 8.2.3 have received multimillion dollar NIH grants to supplement CBEN efforts in testbed development. As a result, additional funds were made available to fund a new project led by Paul Laibinis to explore better approaches to non-fouling coatings for bioactive nano-bioconjugates.
8.2.1. Nanoshell-based Cancer Therapy (West, Halas)

Overview
This project aims to develop a nanoshell-based thermal ablation therapy (NBTA) as a significant new therapeutic tool for the treatment of cancer. It is ideally applied to otherwise inoperable cancers where surgery is currently accompanied by a high probability of morbidity or mortality. Metal nanoshells, core-shell nanoparticles fabricated by growing a thin metal shell onto a dielectric nanoparticle (gold grown on silica, in this application), can be designed to absorb near-infrared light where human tissue is relatively transparent. NBTA utilizes metal nanoshells to convert externally applied near-infrared (nIR) light into localized heat to destroy cancer cells, minimizing damage to surrounding tissue and avoiding the long-term effects of radiation therapy or chemotherapy. Over the last reporting period, we have demonstrated localized generation of heat by nanoshells upon nIR light absorption, and have performed some initial clearance studies. This systems-level research plan includes a series of animal (mouse) studies to (i) further evaluate biodistribution and clearance of nanoshells in order to assess targeting efficacy and safety and (ii) ablate tumors and study survival of animals treated with NBTA therapy.

Results
Localized Generation of Heat by Nanoshells Upon nIR Light Absorption
The amount of heat generated upon nIR light absorption can be controlled by the nanoshell density, the light intensity, and the duration of illumination. These relationships have been explored in tissue phantoms using a fast phase gradient MRI technique to monitor temperature profiles during illumination. Further, heating is well localized to the vicinity of the nanoshells.

Initial studies have been conducted both in cell culture and in vivo to demonstrate that this localized heating phenomena can be used to destroy cancerous cells. HTB-30 cells (derived from human breast carcinoma) can be targeted with nanoshells bound to HER-2 antibodies, as shown above. After binding of nanoshells to these tumor-derived cells, we have used near infrared light (nIR, 821 nm) to induce nanoshell heating and thus cell ablation. Results from this in vitro ablation study indicate that while neither nanoshells alone nor the nIR light alone affect cell viability, the interaction of nIR light with cell-bound nanoshells destroyed all cells within the circular laser spot (see figure 8.2.2, next page).

Initial animal studies to investigate tumor ablation after nanoshell injection and nIR illumination have been conducted in NOD CB17-Prkd c SCIfi/J mice inoculated subcutaneously with the canine transmissible venereal tumor cell line. Two tumors were grown on each mouse to a tumor burden of 1 cm. Nanoshells were directly injected into tumors to evaluate heating and ablation at known and controlled nanoshell dosages; controls received saline injections. During nIR illumination (821 nm, 4 W/cm², 6 minutes illumination), temperature profiles were...
monitored via fast phase gradient MRI analysis. Temperatures sufficient for ablation could be achieved in nanoshell-treated tumors. Moreover, when both tumor sites were injected with nanoshells, heating occurred in both tumor sites during nIR exposure, while the intervening normal tissue was not affected by the illumination. Following light exposure (with or without nanoshell injection), tumors were excised and evaluated via gross pathology and histology. The region where ablation is evident corresponds to the region treated with nanoshells (verified by silver staining of histological sections) and heat generation (as determined by fast phase gradient MRI).

**Initial Clearance Studies**

Nanoshells have not demonstrated any adverse biological reactions in tissue culture or in mice. Initial results from an ongoing series of animal experiments have demonstrated that the Nanoshells are cleared through the liver, not the kidneys. We expect that gold Nanoshells have equivalent biocompatibility to gold colloid (i.e., highly compatible and non-toxic). Additional understanding of clearance mechanics is a goal of the proposed research and has many strong interactions with ongoing nanotoxicology studies (see project 8.3.6).

![Figure 8.2.2 Demonstration of cell destruction using nanoshells and nIR light. Left is with five minute exposure to nIR light only. Center is with nanoshells only. Right is with both nIR light for five minutes and nanoshells, and cell destruction is observed within the spot illuminated.](image)

**Plans**

Initial studies have focused on direct injection of nanoshells into tumor sites before infrared illumination. Ultimately, the goal is to administer nanoshells via intravenous injection, with accumulation of nanoshells within the tumor site due to the dense and leaky capillary networks and subsequent cellular-level targeting using antibodies or peptides conjugated to the nanoshell surfaces. In order to achieve the overall objectives of the project, this proposed research will focus on answering the following questions:

(A) The scientific literature indicates that a relatively high targeting efficiency can be achieved for nano-scale particulates simply as a result of the dense and leaky capillary networks in tumor clusters. What is the efficiency of targeting nanoshells by intravenous injection? Does antibody conjugation provide a further enhancement of targeting efficiency?

(B) Initial studies indicate that a high level of targeted heat can be applied using nanoshells. What are the optimal parameters for to apply sufficient heat with minimal damage to non-targeted tissue?

(C) Finally, what survival time improvement can be observed in relevant animal models?
Study 1: Evaluate tumor biodistribution uptake, and clearance kinetics

This task will provide baseline information for research in subsequent tasks in addition to answering critical questions. Variables affecting the biodistribution are likely to be the size of the particles and surface treatment of particles and this work will be strongly coordinated with ongoing efforts in theme 3, the nanotoxicology of particles (8.3.6). Nanoshells will be injected into mice intravenously and intramuscularly. At pre-determined time points, mice will be sacrificed by CO₂ asphyxiation following anesthesia with isoflurane. Tissue, urine, and fecal samples will be analyzed for the presence of nanoshells (based on the presence of gold) using neutron activation analysis, performed on a fee-for-service basis at Texas A&M University. In addition, any tissues that are found to contain nanoshells will be assessed histologically using silver stain and hematoxylin & eosin. Based on previous studies with similar gold colloid materials, the nanoshells are expected to accumulate in the liver and spleen and be cleared mainly in feces over a period of 14-21 days.

One objective of these studies is to evaluate the permeation of intravenously injected nanoshells into the tumor space. Based on the vascular permeability in the tumor region, nanoshells should escape from the vasculature and enter the tumor interstitium. The degree to which this occurs should depend upon the nanoshell size (30-150 nm) and the surface treatment (PEGylation or antibody conjugation).

Study 2: Survival of Tumor-bearing Mice Following NBTA Treatment

The efficacy of the NBTA therapy will be assessed in NOD CB17-Prkd c SCill/J mice inoculated with HTB-30 human breast carcinoma cells (one injection site per mouse). Anti-HER-2-PEG-conjugated nanoshells will be injected intravenously when tumors have reached 0.4 cm diameter. Control groups will receive PEGylated nanoshells without conjugated antibodies (to determine the efficacy of targeting) or no nanoshells. Based on results from above, nIR treatment will be initiated after sufficient circulation time to allow for tumor uptake and targeting of nanoshells. During illumination, thermal profiles will be continuously monitored using fast phase gradient MRI. If temperatures sufficient for ablation are not achieved, the illumination time, light intensity, or nanoshell dosage can be adjusted as needed. Following NBTA treatment, seven mice from the targeted treatment group and each of the control groups will be sacrificed by CO₂ asphyxiation after isoflurane anesthesia after 24 hr to assess the degree of thermal damage to the tissue by gross pathology and histology. In the remaining mice (14 per group), tumor size will be monitored as will survival. Mice will be euthanized when tumor size exceeds 1 cm. Survival times will be compared between the three groups.
8.2.2. Nanoshell Assisted Tissue Welding (West, Halas)

Overview

This project aims to develop nanoshells as an exogenous heat transfer agent for laser tissue welding. This procedure, the joining of two tissues by heat produced from absorption of light, has emerged as a commercially and clinically attractive strategy that offers a number of potential benefits over conventional closure methods (e.g., suturing) such as immediate fluid-tight sealing, improved wound healing, improved mechanical integrity, and speed of procedure. Currently, tissue welding is accomplished when laser light is absorbed by tissue components such as water or hemoglobin, producing sufficient heat to cause denaturation of collagens and other proteins with subsequent entanglement of adjacent protein chains. The laser light used in this traditional approach does not discriminate between the wound surface and other tissue. As a result, the success of laser tissue welding has been limited because of (1) the generation of superficial welds with poor mechanical integrity as a result of poor optical penetration and (2) excessive damage to adjacent tissues. Given these limitations, focus has turned to the investigation of exogenous materials to facilitate the transfer of heat to enable wound closure. Using metal nanoshells tuned to absorb light in the nIR water window offers a number of advantages over other tissue welding agents. This project, a new start for CBEN, will address the strength of welding that can be generated with this approach as well as the healing process that ensues.

Results

Despite this project being a new start for CBEN, some preliminary experiments have been performed. Figure 8.2.3 shows temperature profiles in muscle tissue after exposure to near infrared light in the absence or presence of Nanoshells. Significant heating was observed only when Nanoshells were injected into the tissue before laser irradiation. When Nanoshells were injected, temperatures sufficient to induce welding were achieved within several seconds of light application.

In an initial study, excised muscle tissue strips (chicken) were exposed to near-infrared light. Dilute Nanoshells in an aqueous suspension were applied with a pipette onto surfaces to be joined. When applied carefully, the Nanoshells tend to stick to the tissue via electrostatic attractions or gold-thiol bonding from native cysteine. The light from the diode laser was scanned over the junction between two adjacent tissue strips for 1 min. The Nanoshell-treated tissues were effectively and strongly joined (see figure 8.2.4) while tissues not treated with Nanoshells exhibited no welding whatsoever.

Additional welding experiments were performed using rat skin and chicken tendons, with similar success. In these studies, Nanoshells of increased concentration were suspended in a viscous solder media. Albumin, which has shown some promise as a solder material, was
employed in these experiments, but Nanoshells are expected to be compatible with other solder materials that could demonstrate superior results in the future.

We tested a series of concentrated aqueous Nanoshell solders in 20-50% (w/v) bovine serum albumin (BSA). After a small tendon or other piece of tissue was cut in half, a small amount of solder was applied on the surfaces to be reconnected. Only a small amount of solder was required. Various methods for deposition were investigated, including the use of a pipette and a cannula. The pieces of tissues were lined back up to their pre-cut orientation. A quick pass with the laser (5 sec/cm) on the solder seam served to make a preliminary bond. Then two long laser passes (15 sec/cm) were made at a 45° angle (relative to the first seam) aimed to penetrate to deeper solder locations and strengthen the bond. Welds of rat skin and chicken tendons made with this procedure appeared complete and had significant tensile strength when assessed qualitatively.

**Plans**

To investigate the feasibility of commercialization of this technology, the proposed research will have the following technical objectives:

1) Optimization of nanoshell and solder delivery and dosage with ex vivo tissue
2) Optimization of laser treatment for effective welding with minimal damage and mechanical testing of ex vivo welded tissue
3) Assessment of the mechanical integrity of tissue welds in a rat model

**Optimize Nanoshell and Solder Configurations**

In the first stage of the research we will evaluate the characteristics of various Nanoshell-solder materials based on physical characteristics including viscosity, absorption (heating) profile, and stability. Additionally, each solder will be evaluated in terms of the ability to minimize extraneous tissue damage.

A matrix of the relevant variables will be evaluated in terms of the essential physical parameters of the Nanoshell-solder materials: (i) sufficient viscosity to allow application to the wound of a thin layer without dispersion and (ii) the ability to produce sufficient heat to allow protein denaturation throughout the solder and into the wound edge at a low (1.5 W or less) laser power and within one minute of exposure.

Albumin and fibrinogen, having demonstrated the basic requirements of biocompatibility and the ability to act as a matrix for wound healing, will be tested. Two different concentrations of each solder will be prepared and evaluated in formulations that alter both Nanoshell concentration and pegylation (PEG coating). Additionally, at least two concentrations of
Nanoshells will be utilized in each solder. Nanoshells conjugated with PEG and without PEG will be utilized to evaluate stability and viscosity. The solutions will be examined to determine the heating rate at different laser powers and times.

Because several albumin and fibrinogen solders should meet the two basic criteria, the solders will be further tested to minimize superfluous tissue damage by reducing Nanoshell migration into surrounding tissues. In practice, a thin bead of solder will be applied to the surface of a sample of chicken muscle and then irradiated. Histology will be used on surrounding tissues, including hematoxylin and eosin staining which serves to increase the contrast on cellular walls and nuclei. Cellular damage will be appraised, and favor will be given to those solders which reach denaturation temperatures at the surface while minimizing damage away from the wound. Silver staining will be used to assess the migration of Nanoshells into the tissue. Mason's trichrome stain may also help distinguish undamaged from denatured collagen and help assess cellular damage.

**Ex Vivo Laser Welding and Assessment of Mechanical Integrity of Tissue Welds**

In this stage of the research we will evaluate the Nanoshell-solder configurations chosen from stage one in ex vivo welds. We will evaluate laser dosimetry and tensile strength for each of the configurations. The various Nanoshell-solder configurations, applied with needles or steel cannulas ranging from 30-gauge to 18-gauge, will be used to weld fresh, excised skin and tendons. The junction between the two tissue samples will be irradiated at 821 nm at powers ranging from 0.5 to 3.5 W/cm² for varying times while the temperatures in the tissues adjacent to the weld site are monitored via infrared thermal sensors or thermocouples. Immediately after welding, the tissue samples will be evaluated by pulling it to failure in an Instron tensile testing machine; the ultimate tensile strengths and moduli will be determined from the stress-strain diagrams.

**Investigation of Wound Healing Following Welding - In Vivo Laser Tissue Welding**

The purpose of the in vivo studies is to assess wound healing following Nanoshell-assisted laser tissue welding and provide preliminary information on biodistribution. A rat skin incision model will be employed for these experiments. Following isoflurane anesthesia, a 1 cm full thickness incision will be made in the dorsal skin. In control animals (n = 12), the incision will be sutured with continuous 4-0 Vicryl. In animals treated with laser tissue welding (n = 12), Nanoshells will be applied in the optimal manner as determined from the initial experiments. As above, 821 nm irradiation will then be applied using the optimized protocol (as determined from above experiments). Three animals from each treatment group will immediately be euthanized by CO₂ asphyxiation following isoflurane anesthesia. Tissue surrounding the incision site will be harvested and subjected to mechanical testing as described above. Wound sites in remaining animals will be photographed on a daily basis and analyzed by planimetry. At days 7, 14, and 28 rats will be euthanized and tissue surrounding the incision site will be harvested. One half will be processed for histological analysis. The other half of the tissue sample will immediately undergo mechanical testing as described above.
8.2.3. Nanomaterials for Imaging (Drezek, West, Halas)

Overview

This project aims to engineer nanoparticles to function as visible and near IR contrast agents for optical imaging. Optical technologies are ideally suited for in situ detection of precancers and early cancer, providing a rapid, inexpensive, and non-invasive means to image tissue in many organ sites, a vital need for tumor detection in organs such as the ovaries where detection is typically in late stages, reducing survival rates significantly. We believe scattering-based imaging techniques will significantly impact patient care in the future due to strong commercial appeal generated by the cost-effectiveness and portability of devices using these particular technologies, and their millionfold enhancement in optical extinction. The optical tunability, biocompatibility, and existing bioconjugation protocols make gold nanoshells our target of choice for developing these contrast agents. To date, a computational system for modeling scattered light propagation through dispersive materials has been developed and validated, initial experimental efforts to validate its results are underway, and preliminary optical contrast tomography (OCT) measurements have been taken.

Results

8.2.3.1.1 Computational Efforts

We have developed and validated a 3D finite-difference time-domain (FDTD) code using perfectly matched layer (PML) boundary conditions that is capable of modeling dispersive materials and is used to simulate light propagation through heterogeneous biological cells and tissue including tissue containing metal nanoshells.

To allow simulation over larger volumes than can be accommodated through pure FDTD approaches, we have developed a hybrid FDTD/Monte Carlo model of light propagation through tissue which we are using to optimize optical system design for detection of nanoshell and nanoemitters based optical contrast agents.
**Experimental/Feasibility Studies**

We have built a simple goniometer (scattered intensity vs angle) so that we can compare the measured scattering properties of nanoshells we produce against theory. We are in the process of making and characterizing scattering nanoshells optimized for both our initial cell studies (visible wavelengths due to the silicon detector we will use) and initial animal studies (near IR wavelengths optimized for optical coherence tomography). We have begun development of well-characterized non-biological scattering and absorbing phantoms which we will use in assessing optical contrast achievable through the use of nanoshell contrast agents. Preliminary OCT measurements indicate nanoshells can significantly enhance scattering with minimal degradation in image quality due to absorption effects. We have conducted a series of immunostaining studies using the OVCA420 and OVCA433 cell lines to identify cell surface antigens that are either tumor specific or overexpressed in epithelial tumors for proof of concept nanoparticle imaging experiments.

**Plans**

*Our project is comprised of the following specific technical objectives:*

1. We will design and fabricate novel nanoshell contrast agents optimized for imaging via confocal reflectance microscopy and optical coherence tomography. We will demonstrate that the nanoshells can be specifically targeted to molecular markers of disease.

2. In order to provide a rational approach to engineering nanoparticles for optimal optical contrast, we will continue development of computational tools to simulate the interaction of light with tissue containing nanoparticles.

3. We will develop phantoms to systematically study optical contrast achievable as a function of the physical properties of the engineered contrast agents, the concentration of the agents, and the optical properties of the tissue.

4. We will validate the nanoshells as imaging contrast agents in models including normal cells from primary culture and epithelial tumor epithelial cell-lines, three-dimensional organotypic tissue phantoms, and metabolically active fresh tissue slice models.

5. We will test nanoshells as contrast agents for optical imaging using a subcutaneous mouse tumor model. We will first test non-targeted nanoshells for imaging relying on the increased permeability of tumor vasculature for differential uptake. We will then test molecular specific nanoshells. Based on the availability of an appropriate antibody and preliminary immunohistochemistry, our plan is to initially target EGFR while assessing whether tumor-to-background ratios are sufficient for imaging. If the tumor-to-background differential is not sufficient, we will consider alternative molecular targets with increased specificity.
Nanostructured Bone Replacements (Hartgerink, Mikos, Barron)

Overview

This project aims to develop engineered bone replacements utilizing supramolecular self-assembly and biomimetic mineralization to mimic native tissue, and nanoparticles for mechanical reinforcement. Tissue engineering (TE) is a relatively new area of medical research with a great deal of promise to replace damaged or diseased tissues with new ones that have been grown in vitro. The advantage of this approach over more traditional organ transplant therapies is that the recipient can often provide the cells required for the new tissue or organ which thereby eliminates problems associated with the lack of suitable donors and immune rejection of foreign material. During the last reporting period, polymer scaffolds have been reinforced by two types of ceramic nanoparticles, alumoxane and montmorillonite layered silicates (MLS), producing composites with improved mechanical properties. Future work on the original project direction will focus on developing better dispersion techniques for the reinforcing nanoparticle, adding extra functionality to promote bone regrowth to the particles, and evaluating cytotoxicity and soft-tissue responses to the materials. This last effort has strong ties to the nanotoxicology program (8.3.6) in theme 3. In a recently added sub-project aimed at mimicking the structure and properties of native bone, artificial collagen has been synthesized, purified, and characterized to serve as the building-blocks for directed self-assembly of an extended scaffolding network. Future work will include the self-assembly of the organic matrix component and biomimetic mineralization of the inorganic component.

Results

Poly(propylene fumarate)-based nanocomposites

We are focusing on two types of nanophase ceramics for reinforcement of polymeric networks of poly(propylene fumarate) (PPF) and the crosslinking agent poly(propylene fumarate)-diacrylate (PPF-DA): alumoxane and montmorillonite layered silicates (MLS). Two strategies were employed to incorporate these nanoparticles into the polymer matrix:

1) Activation of the particles by modifying their surfaces with acrylate functional groups so they can covalently bond with the polymer network during free radical crosslinking.

2) Attachment of a surfactant to the nanoparticle surface to improve their organophilicity and dispersion within the polymers.

Activated alumoxane nanoparticles were prepared in two reactions. First, molecules of lysine were affixed to the alumoxane surface by hydrothermal carboxylation. These lysine groups provided terminal amine sites for the subsequent attachment of acrylate functional groups by Schotten-Baumann acylation. Surfacted alumoxanes were synthesized by coating the particle surface with stearic acid via hydrothermal carboxylation. The alumoxane modifications were verified by solid state NMR and FTIR.

MLS particles were modified by free ion exchange with a choline. The activated and surfacted MLS were reacted with acryloyloxycholine and di(oleoyl)phosphatidylcholine, respectively. Modifications were characterized by solid state NMR, FTIR, and XRD.

Nanoparticles were delivered into the polymer phase by the solvent-dilution method at loadings of 1 wt%. The PPF/PPF-DA nanocomposite blend was then crosslinked into a solid
materials with the photoinitiator bis(2,4,6-trimethyl) phenylphosphine oxide (BAPO) and ultraviolet (UV) light. Specimens rods were prepared for 3-point bend testing (figure 8.2.7).

All nanocomposites showed improved flexural moduli compared to the unloaded (blank) PPF/PPF-DA networks. There was however a decrease in flexural strength in the alumoxane nanocomposites, probably due to the nanoparticles serving as discontinuities that can incite crack propagation. This behavior was not observed in the MLS nanocomposites because interface pinning of the polymer chains by the high aspect ratio silicates prevents crack propagation.

Composites with the surfacted nanoparticles imparted greater reinforcement than their activated counterparts. This was investigated further by visualizing the nanocomposite interfaces with ESEM. Large aggregates, in excess of 60 microns long, were seen within the matrix of the activated alumoxane nanocomposites. The surfacted alumoxane nanocomposites showed no resolvable particles, however the presence of alumoxanes within the polymer was confirmed by EDAX, indicating that a mesophase dispersion resulted in improved reinforcement of the material. Similar observations were seen in the MLS nanocomposites.

These results showed that PPF/PPF-DA networks can be strengthened by nanoparticle reinforcement. Surfactant modified nanoparticles demonstrated improved properties over activated nanoparticles because their enhanced organophilicity enabled mesophase dispersion within the matrix. The reinforcement of the activated particles was hindered by severe aggregation.

*Supramolecular self-assembly/biomimetic mineralization*

In this project, a recent addition to CBEN, the constituent peptide sequences of artificial collagen, which contain a large number of imino acids (proline and hydroxyproline), have been designed based on a staggered triple helical structure (see below for details), synthesized on an Advanced Chemtech APEX396 automated solid-phase peptide synthesizer, purified by reversed phase HPLC and characterized by MALDI-TOF mass spectrometry.
**Plans**

Poly(propylene fumarate)-based nanocomposites

In an effort to combine increased dispersability observed in the surfacted samples and the expected mechanical reinforcement resulting from direct cross-linking into the polymer matrix, we will doubly modify the nanoparticles in order to impart both functionality and organophilicity. These nanoparticles will be incorporated into the PPF/PPF-DA networks as previously described and the reinforcement will be evaluated by 3-point bend testing. Particle dispersion within the polymer matrix will be characterized by ESEM and EDAX.

We also plan to conduct a further modification by adsorbing calcium and phosphorus components onto the nanoparticle surfaces. It is hypothesized that the presence of these groups would impart biofunctionality to the nanocomposite, specifically the ability of the enhance osteoblast function and thus bone tissue growth on the material. This will first be investigated by in vitro culture of osteoblasts on these nanocomposites and will eventually lead to in vivo studies.

The cytotoxicity and in vivo bone and soft-tissue responses to the composites in their initial state and at various stages of degradation will also be examined.

**Supramolecular self-assembly/biomimetic mineralization**

With the successful synthesis of our self-assemblers we are now prepared to begin assessing their ability to assemble under physiological conditions. This assembly will be characterized by FT-IR, CD, and cryo-TEM as a function of pH and ionic concentration in order to optimize the formation of the desired triple-helical structure, designed through register alignment of amino acid sequences.

After determining the conditions under which these peptides will assemble into extended triple helical structures we will covalently capture the supramolecular fibrils by using the “native ligation” procedure, which allows the coupling of two or more unprotected peptides while in water, converting a relatively fragile supramolecular structure into a far more robust polymeric fibril. The resulting structure contains free thiol regularly distributed on the backbone which can be harnessed to attach a variety of chemical modifiers, such as drugs, chemical signals for cells, and growth factors.

The inorganic portion will be added after the self-assembly and covalent capture of the artificial collagen fibrils by biomimetic mineralization though phosphate groups attached super saturation and templating of calcium phosphide.
8.2.4. Anti-fouling Coatings (Laibinis, West, Barron, Wiesner)

Overview

In this new-start project, a method for modifying the surfaces of particles and membranes with locally-grown polymeric films is explored for altering the adsorptive properties of such nanostructured systems. Fouling, the formation of unwanted adherent thin films onto surfaces as a result largely of non-specific adsorption events, is a key problem facing the deployment of many engineered solid-state systems that present interfaces to the real world. Examples include the formation of scale and biofilms on inorganic surfaces used in remediation, clots and deposits formed on biomedical devices, and the fouling of sensors by the adsorption of biological and cellular materials. The approach is based on the use of a surface-initiated ring-opening metathesis polymerization reaction (s-ROMP) for generating anchored coatings to metal and oxide surfaces. Specifically, s-ROMP will be employed to generate brush-like polymer films of controlled thicknesses, compositions, and densities, where segments of the brush will contain side chains that are chemically reactive for the attachment of anti-fouling components. These films promise the incorporation of high local surface densities and complete coverage—key needs for overcoming unwanted non-specific adsorption events at interfaces with high surface areas—within nanoscale coatings. The use of molecular precursors to perform this surface modification affords particular advantages for introducing coatings along the walls of inner surfaces, such as those found in membranes and porous systems. We will focus on the growth of s-ROMP films from particles, membranes, and model flat surfaces employing norbornenyltrichlorosilane as monomer and oligo- and poly-(ethylene glycols) as surface modifiers. The use of these latter agents for both providing antifouling characteristics and introducing biomolecular recognition elements for targeting specified binding events will also be explored.

Plans

In 1991, Prime and Whitesides presented a landmark finding that surfaces presenting as little as 1-3 nm of a hydrogel-like material could provide antifouling characteristics against unwanted protein (and later cell) adsorption, if this material could be organized well and completely covered a surface. In their work, they employed self-assembled thiol-based monolayers on gold, where the tail group of the adsorbing alkanethiol included short oligomers of ethylene glycol or other uncharged hydrophilic species. Their key discovery—which has been widely adapted across hundreds of papers employing flat gold as substrate—is a result of the dense packing and completeness of coverage provided by the self-assembly of alkanethiols onto gold to form monolayer films. Transition of this monolayer approach to other substrates has been slow as the ease and ability to form complete monolayers on other substrates is must less than for gold surfaces. For example, we have explored the use of oligo(ethylene glycol)-terminated alkyltrichlorosilane reagents as a means to generate related monolayer films onto glass and other metal oxide surfaces and found that unwanted non-specific adsorption can be diminished, but not to the extent provided by the thiol-on-gold strategy.

![Figure 8.2.9 Mechanism of native peptide ligation.](image-url)
As a means to introduce highly dense, thin polymer films onto surfaces, we recently developed an application of the metal-catalyzed ring-opening metathesis polymerization (ROMP) reaction (schematically illustrated below)

that employs norbornenyl derivatives as monomers and builds on the work of Grubbs et al. who have developed a series of new highly stable, ruthenium-based catalysts for solution-phase ROMP reactions. As substrates, we employed gold surfaces modified with HS(CH₂)₁₁OH to expose hydroxyl groups or hydrated oxide surfaces on silicon wafers. Notable features of the s-ROMP reaction are an ability to control the thicknesses and compositions of grafted polymer films readily by selection of monomer, concentration, and reaction time. Thicknesses can be varied from a few nanometers to over a tenth of a micron. This room temperature reaction appears to be a living polymerization process, allowing construction of multiple polymer layers on surfaces. The tolerance of the ROMP reaction for a variety of chemical functionality provides the ability to generate s-ROMP films from various species and to incorporate sites along the polymer backbone for subsequent modification. This latter ability is a key enabling feature of the s-ROMP strategy for incorporating a high density of reactive functionality that can provide sites for the attachment of antifouling components to the coatings. ROMP has also been shown to be useful for forming polymer films on particles, but little has been done to explore the use of such films on particles as a way to introduce new physical properties.

The general approach to be developed by this proposal for generating antifouling coatings on the surfaces of particles and membranes by s-ROMP is schematically illustrated below:

The expansion beyond our past work on flat surfaces is to incorporate a subsequent chemical modification to the s-ROMP films, here using a side-chain functionality such as a SiCl₃ group (as pictured above) or functionalities such as acid chlorides (COCl) or isocyanates (NCO) that can be included on the norbornenyl monomer. These functionalities will provide reaction sites for the attachments of hydrophilic moieties such as oligo(ethylene glycol)s (OEGs) or carbohydrates. Additionally, the new directions will focus on curved and porous surfaces where we are likely to encounter new challenges for generating thin complete films. The basic approach is that the s-ROMP procedure will provide covalent anchoring to a support, a highly dense grafted polymer film as a result of growth occurring by monomer addition rather than direct polymer grafting, and large amounts of highly active functionality for derivatization. On the particle and membrane surfaces, a key feature is that the growing poly(norbornenyl) chains can
expand from its initial attachment point to cover a broader area of the surface. The use of a surface reaction employing monomers for polymer formation as opposed to the direct grafting of a preformed polymer to a surface insures the generation of thicker films with high packing densities. Control over reaction conditions provides an ability to tailor film thickness and site density for optimization of film properties.

Initial studies investigating this chemistry illustrated above on flat surfaces have shown success in terms of growing s-ROMP films from norbornenyl trichlorosilane as monomer, attaching oligo(ethylene glycol) (OEG) groups to the resulting poly(norbornenyl trichlorosilane) films, and generating films with antifouling characteristics toward proteins and some cells in limited studies. For flat surfaces (gold and glass), the molecular weight of the OEG group appears to play a key role in determining the level of OEG functionality that could be incorporated into the s-ROMP film and in the anti-fouling properties of the final films. Notably, antifouling properties have been observed on the flat surfaces for OEG layer thickness as little as 2 nm, suggesting that this approach may provide a means to introduce antifouling properties by very thin films. For particle and membrane surfaces, selection of OEG molecular weight and s-ROMP reaction conditions are anticipated to influence the antifouling properties of the coatings. Further, the shape, radius of curvature, and morphology of the substrate are expected to play key roles in the properties of these films on the particle and membrane surfaces, and the exploration of these fundamental relationships is a topic of interest in this research. The approach should be particularly useful for incorporating complete coatings on the inner surfaces of the membrane as it relies on the transport of molecular rather than polymeric species for producing the resulting polymeric antifouling coatings.

Based on our preliminary promising results on flat surfaces for introducing antifouling properties by s-ROMP, we expect that these films can be developed for use on porous and particle substrates and their properties tailored to provide requisite antifouling characteristics for CBEN’s targeted biomedical and environmental applications. s-ROMP will be developed by this proposal for producing antifouling coatings on the particles generated by Jennifer West’s group, the membranes being developed by Andrew Barron and Mark Wiesner and their groups, and made available for introducing antifouling characteristics broadly into the nanostructured materials being developed by others in CBEN. These functionalized hybrid systems will be specifically characterized in terms of their abilities to retard the non-specific adsorption of proteins, cells, and cellular debris as well as agents found in remediation that can induce fouling. Systems prepared by West, Barron, and Wiesner will be re-engineered as necessary (porosity, sizes, chemical composition) based on obtained results.

In addition to the antifouling properties to be introduced by this approach, the terminal hydroxyl units of the OEG groups also offer sites for the attachment of recognition elements onto the surfaces of these generally non-adsorbing materials. For directing recognition events useful in detection, diagnosis and general separations, a future direction that will be initially explored during the span of this proposal is to attach specific ligands and/or antibodies to these surfaces as a means to introduce one selective mode for adsorption/attachment on a material that offers a background surface that provides general avoidance of adsorption/attachment to other species. Such abilities to direct surface activity in these nano-engineered systems will be important for producing hybrid materials that can be individually tailored in terms of their bulk and surface properties.
8.3. Theme 3: Effective, High-Performance Water Purification Systems (Nanoenvironmental Engineering)

Table 8.3.1 Summary of research Theme 3 allocations

<table>
<thead>
<tr>
<th>Project</th>
<th>Leader*</th>
<th>Investigators (name, dept.)</th>
<th>Disciplines Involved</th>
<th>Number of Students and Post-docs</th>
<th>Current Year Budget</th>
<th>Proposed Budget</th>
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<tbody>
<tr>
<td>8.3.1 Nanostructured Membranes</td>
<td>Baron, Chemistry</td>
<td>Wiesner, Environmental Engineering</td>
<td>Inorganic Chemistry, Physical Chemistry, Environmental Engineering</td>
<td>2</td>
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<td>$95,478</td>
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<td>8.3.2 Template-based Membranes</td>
<td>Wiesner, Environmental Engineering</td>
<td>Colvin, Chemistry</td>
<td>Physical Chemistry, Inorganic Chemistry, Environmental Engineering</td>
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<td>$116,547</td>
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<td>8.3.3 Polymer Flow on Nanoscale</td>
<td>Pasquali, Chemical Engineering</td>
<td>Kolomensky, Chemistry</td>
<td>Physical Chemistry, Environmental Engineering</td>
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<td>$68,588</td>
<td>-</td>
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<td>8.3.4 Nanocatalysts for Pollutant Treatment</td>
<td>Wong, Chemical Engineering</td>
<td>Colvin, Chemistry</td>
<td>Inorganic Chemistry, Environmental Engineering</td>
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<td>8.3.5 Sorption of Contaminants</td>
<td>Tomson, Environmental Engineering</td>
<td>Colvin, Chemistry</td>
<td>Inorganic Chemistry, Environmental Engineering</td>
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<td>8.3.6 Nanotoxicology</td>
<td>Hughes, Environmental Engineering</td>
<td>West, Bioengineering</td>
<td>Chemistry, Biology, Biochemistry, Environmental Engineering</td>
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<td>8.3.7 Environmental Exposure Routes*</td>
<td>Hughes, Environmental Engineering</td>
<td>Wiesner, Environmental Engineering</td>
<td>Physical Chemistry, Environmental Engineering</td>
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<td></td>
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*Investigators listed in bold have joined the project, and investigators listed in italics have left it. The Y02 budget figures include any carry-forward from Y01 due to startup delays. Budgetary information includes both NSF and matching funds, and includes overhead.

1For convenience, compound department titles have been shortened to the most appropriate component. For example, the Department of Physics and Astronomy is listed simply as 'Physics'.

2Funding for this entire project area is contingent on CBEN's full budget request being honored.

3Some projects cross theme-area boundaries; they are listed and described only once, but their budgetary information is split equally between the two or three theme area totals. Personnel are listed only in the theme in which the projects are described. The project, "Environmental Exposure Routes," is split equally between themes 1 and 3 for all three years, and the projects, “Nanomanufacturing,” and “Nanotoxicology,” are split across all three theme areas.

Society faces significant challenges in the area of environmental technology; cheap, effective and ‘green’ ways to clean up our current environment are desperately needed. CBEN focuses on the broad problem of water purification; whether it is arsenic, pesticides or trichloroethylene (TCE) drinking water standards become more stringent even though methods for treating water, which have changed little in the last several decades, aren’t up to the task. Work in this theme aims at our engineered system goal of ‘effective, high performance water purification systems’ and uses nanoparticles of various types to shift the traditional paradigms for cleaning water.

The closely related projects, 8.3.1 and 8.3.2, develop membranes for water purification. The availability of potable water is of increasing concern both nationally and globally and membrane filtration is emerging as a general solution to this important environmental problem. Membranes remove finer contaminants, faster and at lower cost than traditional methods for water treatment, such as packed bed filters, sedimentation basins or secondary wastewater clarifiers. These advantages have spawned huge growth in the applications of membranes to waste separations, especially in the area of municipal water treatment. The most pressing issues are the development of non-fouling systems and more efficient and higher performance nanofiltration membranes. Projects 8.3.4 and 8.3.5 look at more targeted removal problems, particularly of arsenic and TCE in groundwater. Here, smart nanoparticles with catalytic functionality first sorb and then remediate these waste species; with the addition of Paul Laibinis, we can now use magnetic separation methods to ensure these nanomaterials are reusable. Taken together, these projects will provide new enabling membrane technology and smart nanosorbents that will be integrated into water treatment systems over the next decade.
Beyond our engineered systems work, it is equally important that we ensure nanotechnology does not exacerbate existing environmental problems. Our last two projects 8.3.6 and 8.3.7, which have been maintained at reduced funding levels, address directly this potential roadblock for all of CBEN’s engineered systems. Nanomaterials that are produced cleanly and with little adverse impact are important to more than just environmental activists; increasingly, the American public has become sensitive to the environmental costs of new technology. Consumers vote with their pocketbook as the food industry has discovered; sales of organic produce continue to skyrocket while many consumers reject genetically modified foods. Clearly, CBEN’s technical objectives will be greatly affected if environmental and health issues become entangled with public perception of nanotechnology. CBEN has made a concerted effort to develop an informed public as described in our knowledge transfer section, 10.1. However, the reality is that we have very little real information to provide on the topic of environmental and health impacts of nanomaterials.

We are requesting additional funds, approximately 10% of our total funding, in order to remedy this situation. As originally proposed, CBEN conceived of an ambitious plan for studying the societal and environmental impact of nanomaterials; after receiving a 37% budget reduction from the outset we had no choice but to make deep cuts in several programs. This topic reviewed very highly, and was clearly a unique feature of CBEN; however, since the effort was driven by a potential roadblock for nanotechnology rather than a specific engineered system it could not be funded at a high level. Over the past 18 months our investigators have worked with seed-level funding and two papers are currently under review and two are in preparation. We now understand much better what it will take to make progress on this important problem. In light of the intense public interest in this issue and the over one billion dollar federal investment in U.S. nanotechnology research, CBEN’s evaluation of the environmental impact of nanomaterials is timely and essential.

Our proposed funding increase, 10% or nearly $250,000, is targeted specifically at our work on environmental exposure and engineered nanomaterials (8.3.7). With their reduced funding, investigators Tomson and Wiesner have over the last eighteen months characterized the fate and transport of nanomaterials and their associated contaminants in aqueous systems. This work has required significant input from CBEN chemists and substantially new protocols for particle detection and characterization. For larger nanoparticles (d > 100 nm) Wiesner found that models for colloidal transport through porous media are applicable at this size range; however, smaller particles exhibit more unusual behavior that can be very sensitive to flow rates. In studies of contaminant sorption, Tomson found rather predictable sorption capacities for engineered nanocrystalline titania and fullerenes. However, fullerene aggregation in water leads to irreversible sorption of hydrophobic contaminants, a phenomena unique to these nanoscale materials. This increased funding will allow this project to progress from the seed stage; investigators will expand their studies to a wider range of nanomaterials, involve a geochemist with expertise in bioremediation of minerals and permit their projects to connect, for example by evaluating whether contaminant sorption onto fullerenes can enhance its bioaccumulation.
8.3.1. Nanostructured Membranes and their Applications (Barron, Wiesner)

Overview
This project aims to develop nanostructured ceramic membranes for environmental separations utilizing an environmentally benign pathway for ceramic fabrication. Membrane-based technologies play a unique and increasingly important role in pollution prevention, resource recovery and waste treatment activities. Due in large part to cost considerations, polymeric membranes have dominated these environmental separations applications. However, their use in separations involving aggressive materials such as many solvents, acids, bases, and oxidants may be limited by their tolerance to extreme conditions, whereas ceramic membranes are noted for their excellent mechanical strength and tolerance to pH, oxidant, biodegradation and temperature extremes. Work over the last year has resulted in a new process for the fabrication of iron oxide ultrafiltration membranes from ferroxane nanoparticles. The ferroxane fabrication process takes place in aqueous environment, does not involve the use of hazardous substances, and has low energy consumption due to the low firing temperature of the ceramic. Over the next year, we will develop casting and firing methods for making metal-oxane membranes, extend the characterization of ferroxane and alumoxane membranes, and perform comparative life-cycle assessments of metal-oxane and sol-gel processes for fabricating membranes. In the last year this project resulted in the formation of a new company, NewCyte Corporation.

Results
Alumoxane-derived membranes
Previous research by Wiesner and Barron has been aimed at understanding the control of ceramic porosity afforded by the use of carboxylic-acid surface-stabilized alumina nanoparticles (carboxylate-alumoxanes) as ceramic precursors. It was found that the pore size and pore distribution are influenced by the selection of the organic substituent on the nanoparticle surface, while the average pore sizes may be altered through either physical or chemical mixtures of two (or more) carboxylate-alumoxanes. Control over the alumina nanoparticles yields a significant improvement of the membrane performance over our prior results. The new alumoxane derived membranes have a molecular weight cut-off in the range of < 1,000 g.mol\(^{-1}\), and show good selectivity to a range of synthetic dyes. Further control over selectivity and flux of these ceramic membranes may be obtained by the use of doped alumina nanoparticles (Fe, Mn, and La) that result in the formation of the appropriate aluminate membranes. Of these, LaAlO\(_3\) shows the most promising results, with an increase in selectivity and increased flux as compared to the alumina analogue. Retention coefficients and flux values may also be altered by the chemical functionalization of the interior surface of the membranes by reacting the alumina surface with carboxylic acids. Asymmetric alumina ultrafiltration membranes with a hierarchical structure have been fabricated using carboxylic acid surface stabilized alumina nanoparticles (alumoxanes).
**Ferroxane-derived membranes**

Ceramic membranes are usually fabricated in layers: a substrate or support of large pore size gives mechanical strength; a thin layer of smaller pore size material act as an effective filtration layer. Substrates are fabricated from metal oxide powders pressed, extruded or slip cast and then sintered. Pores obtained with this method vary from 5 to 15 nm. Smaller pores sizes can be obtained by the sol-gel process. Although the sol-gel process yields an acceptable product, sensitive control of the process is required and the reagents used are not without environmental impact. Alternative processes have recently been proposed. The alumoxane route has already proved to be an environmentally benign alternative to ceramic membrane fabrication. The alumoxane nanoparticles are deposited on a substrate and converted to alumina upon sintering. Alumoxane derived membranes have an average pore size of 10 nm; the BET surface area is 120 m$^2$/g; and their molecular weight cut off is in the order of 40,000 daltons. We developed an analogous procedure for making ceramic membranes from iron-based nanoparticles; FeOOH and Fe$_2$O$_3$ are more resistant to acidic, corrosive and oxidant conditions than AlOOH and alumina, making them better candidates for PEM's, and opening the possibility of creating reactive membranes.

**Nanoparticle and Membrane Characterization**

A number of tools have been used to characterize these systems. The membranes are imaged with a scanning electron microscope (SEM) and an atomic force microscope (AFM) to study their topology. Porosity, surface area, pore volume and pore size distributions can be obtained from nitrogen adsorption/desorption isotherms.

Clean water flux measurements were conducted for membranes with one, two, and three coatings of ferroxane nanoparticles to investigate the effect of consecutive coating steps on membrane permeability. Rejection data (shown below) indicated that with the preparation conditions used in this work, two coatings of nanoparticles were necessary to effectively form a complete ceramic layer on top of the supports. The resistance of the membrane was calculated using Darcy’s law. The flow rate at a transmembrane pressure of 10 psi (0.69 x 10$^5$ Pa), the flux, membrane resistance and its inverse membrane permeability are indicated in Table 8.3.2. These values are dependent on the support material used and on the thickness of the ferroxane layer. The permeability can be improved by selecting a support with lower hydraulic resistance and reducing the thickness of the ferroxane film.

<table>
<thead>
<tr>
<th>Number of Coatings</th>
<th>Flow rate (ml/min)</th>
<th>Flux (m$^3$/m$^2$ * s)</th>
<th>Resistance (m$^2$)</th>
<th>Permeability (m$^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.71</td>
<td>9.02 * 10$^{-5}$</td>
<td>8.53 * 10$^{-1}$</td>
<td>1.16 * 10$^{-12}$</td>
</tr>
<tr>
<td>2</td>
<td>4.50</td>
<td>4.66 * 10$^{-5}$</td>
<td>1.66 * 10$^{-12}$</td>
<td>6.02 * 10$^{-15}$</td>
</tr>
<tr>
<td>3</td>
<td>3.93</td>
<td>4.07 * 10$^{-5}$</td>
<td>1.91 * 10$^{-14}$</td>
<td>5.28 * 10$^{-13}$</td>
</tr>
</tbody>
</table>

Table 8.3.2 Clean water flow rate, flux, membrane resistance and permeability of ferroxane-derived membranes for a transmembrane pressure of 10 psi (0.69 x 10$^5$ Pa) measured in dead end mode.
Molecular weight cut-off (MWCO) experiments were performed following the American Society for Testing and Materials (ASTM) Publication E 1393-90, using dextran as the test solution. Figure 8.3.2 shows a typical rejection curve of a ferroxane-derived membrane. The sharpness of the cut off is a consequence of the relatively narrow size distribution of the ferroxane nanoparticles. This MWCO corresponds to a diameter between 14.9 nm and 17.3 nm.

**Plans**

The proposed effort will yield the following results:

- The design of an alternative synthetic pathway to the fabrication of iron ceramic membranes in the ultra- and nanofiltration ranges which does not utilize toxic reagents or solvents.
- Development of methodologies for casting membranes as alternatives to present technologies to prevent or reduce environmental harm.
- Demonstration of the capabilities of ferroxane-derived iron oxides alone or doped with manganese as catalysts in Fenton’s type reactions for use in membrane reactors or configured as reactive membranes.
- A comparative life cycle assessment of the fabrication of ferroxane-derived ceramic membranes and membrane produced by the conventional sol-gel procedure.

With these ends in view, we propose an effort composed of the following 5 tasks:

1. Develop casting and firing methods for making metal-oxane membranes of variable formulations.
2. Create asymmetric ferroxane-derived membranes.
3. Characterize ferroxane and alumoxane membranes in terms of physical chemical properties, tolerance to extreme pH, temperature and oxidation regimes, with particular emphasis on their separation/reaction characteristics for targeted environmental pollutants, proton transfer, and their fouling behavior in treating aqueous streams.
4. Evaluate the potential for catalysis and adsorption or target compounds using ferroxane-derived membranes and powders with doped variations of metal-oxanes.
5. Comparative Life Cycle Assessments of the proposed and current (sol-gel) processes.
8.3.2. Template-Based Fabrication of Polymeric Membranes (Colvin, Wiesner)

Overview

This project exploits the latest advances in nanochemistry and membrane engineering to produce new kinds of efficient, anti-fouling ultrafiltration (UF) membranes for improved water treatment. ‘Templated’ membranes are formed using a sacrificial colloid to define pore size and architecture. The structures, which resemble a honeycomb in their most dense state, will have significantly lower operating pressures and improved rejection efficiency as compared to less porous conventional membranes. Additionally, we are using both computational and experimental techniques developed during the past year to form hierarchically structured membranes from colloidal deposits of varying density. This strategy, coupled with a new focus on anti-fouling polymers as membrane materials (Laibinis, 8.2.5), will lead to UF membranes with improved fouling resistance and lower operating pressures.

Results

We have pursued two separate strategies for controlling the spatial distribution of pores in membranes over the last year. This is a critical enabling technology for reaching the milestone of fouling resistant membranes. In the first strategy, colloidal silica was deposited in dense thin films on glass surfaces following methods developed in the Colvin lab. These opals were then templated into macroporous membranes of high strength and flexibility. We showed this year that it is possible with appropriate treatments to perform subsequent depositions of different sphere sizes onto silica crystals. Figure 8.3-3 shows such a macroporous film where smaller films formed dense packings on top of a stack of larger spheres. Such an asymmetric distribution of pores could be developed through multiple depositions, which take less than one day. While this method allows for great control over the average void size its porosity is limited to 70% due to the dense layer packing.

A second strategy leveraged the control over electrostatic and capillary forces that is gained by rational design of the surface chemistry/solvent interactions during deposition of the sacrificial colloid. Here, silica particles of sizes ranging from 50 nm to 300 nm have been deposited on glass slides through solvent evaporation. The deposits were imaged with SEM in order to observe the resulting morphologies. In all cases, the ethanol and pure water suspensions gave deposits with a uniform arrangement of particles that resembles the hexagonal packing of spheres as reported in the traditional depositions described above. The deposits formed from ethanol have slightly more ordered structures; this can be attributed to the difference of surface tension of the solvents; the decrease of surface tension in the case of ethanol facilitates the meniscus deformation, and increases the magnitude of the capillary interaction.
As the ionic strength of the solvent increases, as shown in the data below, the structure of the deposits become more open; the structures exhibited tree-like morphologies, with branches composed of clusters of particles grew from the relatively more compact arrangement of the first layers. We can use simple simulations of the statistics of particle deposition to help us understand these results.

![Figure 8.3.4](image1.png)  
Figure 8.3.4 Silica particle deposits on a vertical glass microslide. Particles have an average size of 305 nm. The suspensions were prepared with different solvents: a) ethanol; b) ultrapure water; c) aqueous solution 0.1 M IS.

![Figure 8.3.5](image2.png)  
Figure 8.3.5 Silica particle deposits on a vertical glass microslide. Particles have an average size of 244 nm. The suspensions were prepared with different solvents: a) ethanol; b) aqueous solution 0.15 M ionic strength; c) aqueous solution 1.5 M IS.

![Figure 8.3.6](image3.png)  
Figure 8.3.6 Silica particle deposits on a vertical glass microslide. Particles have an average size of 88 nm. The suspensions were prepared with different solvents: a) ultrapure water; b) aqueous solution 0.001 M ionic strength; c) aqueous solution 0.01 M IS.

**Plans**  
With an understanding of the templating process in hand, and methods to form macroporous polymers of controlled geometry this year we will move into membrane evaluation. The technical effort surrounds three distinct tasks:  

Research Theme 3
1. *Formation of template-directed porous polymers as ultrafiltration membranes.*

We hypothesize that a macroporous polymer will have higher permeability, larger fluxes and lower transmembrane pressures as compared to conventional UF systems. As a benchmark, we will form macroporous, hydrophilic acrylate polymer films .5 to 3 microns thick using controlled drying self-assembly methods developed in the Colvin group. We anticipate that the high porosity of these films will decrease the operating pressures by up to an order of magnitude, based on a simple, qualitative analysis. And following that analysis, from the Hagen-Poiseuille equation we see that to maintain a constant flux, as the size of pores is decreased, the thickness of the active separating portion of the membrane must also decrease in order to compensate for the increase in pressure exerted on the membrane. Thus, decreasing the pore size to the nanoscale would also require the creation of ultrathin membranes. Creating thin films is not challenging; however, handling these films is. This problem will be overcome by creating membranes with a graded microporous structure (asymmetric membranes), where the critical separation layer is only at one face of the membrane.

Finally, we will begin to use more practical polymers and surface coatings in our templating schemes, paying particular attention to the hydrophilicity and hydrophobicity, and to materials developed in CBEN for bioengineering applications (Laibinis). Further, these efforts in membrane materials development will be closely coordinated with ongoing work in the waste remediation arm of our water treatment group.

2. *Characterization of membranes*

Each film will be characterized for pore sizes, film thickness and most critically window sizes will be evaluated through (automated) statistical analysis of hundreds of scanning electron microscopy images. Wiesner will analyze the materials for thermomechanical properties, molecular weight cut-off, silting index, the plugging index, and fouling index or silt density index, the modified fouling index or membrane filtration index, permeance to water, transmembrane pressure, and flux.

3. *Methods for membrane casting*

A final goal for the future endeavors of this project will be to investigate methods allowing for the scale up of the current procedure to an industrial scale. While this is not a dominant goal for the next two years, we hope to carry out preliminary evaluations of several schemes so that we can focus more efficiently our efforts in the 2005-2007 grant cycle. The current templating procedure uses a controlled drying methodology to form thin and highly controlled deposits on vertical surfaces; while ideal for the research environment, and easily scaled to meter areas, the thinnest films form when the solvent evaporation is slow (days). We are seeking collaborations with industrial partners, primarily in the pigment industry, who have expertise in colloidal film-forming methodologies. Our application is attractive to these partners since it applies their knowledge in new markets.
8.3.3. Polymer Flow on the Nanoscale (Pasquali, Kolomeisky)

Overview

The dynamics of polymers in confined geometries is important in many biological, chemical and industrial processes (e.g., gene therapy, viral injection, drug delivery, ultrafiltration, separations), although from the fundamental point of view these phenomena are very complex because they bridge different length and time scales. The traditional approach to modeling these systems is typically centered on a single scale at a time. The long-term goal is to develop a theoretical description of polymer dynamics in confined geometries that accommodates biochemical specificity while spanning long time scales and large structural fluctuations. The first step toward this goal is to build the simplest phenomenological theories, then to supplement, improve, and expand them by using Molecular Dynamics, Brownian Dynamics, Monte Carlo simulations, and quantum chemical calculations.

Results

Specifically, we have to date considered the translocation of biopolymers through nanopores. A polymer molecule moving across a nanopore faces a large entropic barrier due to the decrease in the number of available configurations for polymer segments. In order to overcome this barrier and to accelerate the motion of polymers, an external field or interaction is needed. In nature, the translocation of polymers is assisted by cooperative chemical interactions with various proteins. In chromatography, the forced flow of the solvent or an electric field gradient is used to enhance the transport of polymer molecules across confined regions.

Figure 8.3.7 Computational model of polymer flow through a finite-length nanopore.
8.3.4. Nanocatalysts for Remediation of Environmental Pollutants (Wong, Colvin, Hughes)

Overview
Chlorinated hydrocarbon compounds, such as trichloroethylene (TCE), are among the most prevalent contaminants in groundwater. Conventional technologies to remediate TCE involve the removal of the pollutant from groundwater through adsorption or air-stripping, but are slow and inefficient. A promising alternative uses palladium (Pd)-based catalysts and hydrogen gas to convert these compounds rapidly into hydrocarbons and hydrochloric acid, although the effect of catalyst structure on the reaction is currently under debate in the literature. Our objective is to gain a better understanding of how the size and structure of Pd nanoparticles (NPs) affects catalytic activity, through the synthesis of new Pd-based catalysts. To date, we have developed the methods to evaluate the catalytic performance in batch reactors and flow reactors, and began work on synthesizing Pd-based materials to be evaluated for TCE HDC. Future work includes two approaches in which nanoparticle-based materials are used in the catalytic treatment of organic contaminants in groundwater: bimetallic NPs for TCE treatment, and titanium oxide NPs for humic acid treatment. The metallic NPs will be extended to other chlorinated compounds and be subject to test-bed feasibility studies in the remediation of groundwater.

Results
For this newly-funded Y02 project, a preliminary batch reactor to evaluate the catalytic performance of Pd nanocrystals has been assembled and tested. The reactions are carried out in serum vials (160 mL) with a 0.71 liquid to headspace volume ratio. The serum bottle containing TCE saturated in water is charged with the catalyst and then sealed and purged with H₂/CO₂ (80%/20%, Tri-Gas) for 12 min. TCE is added and measurements begin 1 min later, in which the headspace is sampled and analyzed using a GC/FID.

As preliminary tests of the batch reactor, 2 types of Pd materials, Pd black and Pd/alumina, were studied for HDC of TCE. Acquired from Aldrich, Pd black is 99% pure Pd, with a measured surface area of 17 m² g⁻¹, and Pd/alumina contains 1 wt% Pd, with a surface area of 177 m² g⁻¹. The flask was charged with equal amounts of Pd, 0.002 g Pd black and 0.2 g Pd/alumina).

Figures 8.3.8 and 8.3.9 show the changes in TCE concentrations using Pd black and Pd/alumina, respectively. TCE was reduced to ethane with no intermediates detected in either case.
The mass balance was not closed in either case; adsorption onto the catalyst surface will be investigated. PCE, DCE, and VC were also completely reduced to ethane (data not shown), which suggests that intermediates such as DCE could have formed during TCE reaction but were short-lived.

**Plans**

*Bimetallic-based NP catalysts for the catalytic reduction of TCE in groundwater*

The hydrodechlorination (HDC) is preferred over the catalytic oxidation of chlorinated compounds, because the latter is more energy-intensive and can lead to the formation of hazardous by-products.

HDC catalysts can adsorb hydrogen gas dissociatively and can cleave the C-Cl bond hydrogenolytically. Pd metal is a particularly good HDC catalytic material, but it can be deactivated by adsorbed Cl atoms. An approach to improving the catalytic properties of Pd has been to synthesize supported Pd/metal alloys. Pd/Fe NPs have been prepared and studied for TCE HDC, but this material is not a true catalyst, since the Fe portion is consumed during the reaction. It was reported that Pd on silica and Pd/Ag on silica were active for the gas-phase conversion of 1,2-dichloroethane, but the latter catalyst was more selective to ethylene than ethane. While it biased the product distribution towards a less hydrogenated product, the Ag content was found to increase deactivation resistance.

We will build on our current studies on unsupported Pd nanoparticles and Pd supported catalysts, in which we are synthesizing bimetallic Pd-based NP catalysts with controlled compositions. Here, we propose to concentrate on synthesizing Pd/Ag (at different metal atom ratios) aluminas through the conventional impregnation method, and study their deactivation behavior for TCE HDC in water. The optimized catalyst will then be studied for resistance to poisoning by sulfites and sulfide anions.

The catalytic properties of bimetallics are highly dependent on the distribution of metal atoms within the nanoparticulate active site i.e., are the two metals homogeneously mixed on the atomic level or are they segregated into different metal domains. We propose to synthesize Pd/Ag NP catalysts with controlled distribution by modifying the colloidal metal chemistry of Murphy and co-workers. We will prepare homogeneously mixed Pd/Ag NPs with particle sizes < 10 nm through the reduction of a mixed metal salt solution. For NPs with anisotropic metal distribution, we will synthesize Pd-coated Ag NPs through a seeding process in which Ag NPs act as heterogeneous nucleation sites for Pd reduction. TCE HDC testing will be performed with these NPs in colloidal form; aggregated NPs can also be tested, but the reduced accessibility to the catalyst surface will be reflected as lower reaction rates.

*Titanium oxide NPs as photooxidation catalysts for humic acid treatment*

Titania is a photocatalyst that when exposed to sunlight, generates hydroxyl radicals capable of oxidizing a variety of toxic components in water. It has been widely applied to water treatment problems, including the removal of chlorinated hydrocarbons from water. Very recently, commercially available titania was shown to degrade humic acids in a variety of groundwater samples. By oxidizing humic acids to smaller and less ionic forms, membrane fouling in ultrafiltration schemes could be reduced significantly. If particle sizes can be reduced to below 5 nm, then it would be possible to use nanoscale particles as circulating protectants for
membrane water treatment processes; the methodology could ultimately be applied to even more selective and fouling-sensitive nanofiltration schemes.

Here, we will optimize the titania particles to make this process practical and efficient. Both the size and surface chemistry of titania NPs are critical for improving photocatalytic behavior. Nanoscale titania, for example, shows increasing photocatalytic behavior as its size becomes smaller. We have great expertise in hydrothermal and non-hydrolytic synthesis of nanocrystalline titania. Non-hydrolytic particles, in particular, exhibit distinctive surface chemistry due to the lack of Ti-OH functionality, and could have interesting adsorptive interactions with humic acid. They will be prepared in sizes ranging from 3 to 15 nanometers, and their adsorption properties with humic acid will be quantified and correlated to materials properties. Their photocatalytic efficiency under UV illumination will be evaluated using standard methods for humic acid quantification. This project spans both the catalytic and membrane development projects in CBEN, and once the basic characterization work is done, the fouling of commercial membranes in the presence and absence of photocatalytic protectants will be characterized.

Platinization of titania has been a routine method for forming supported catalysts, but only recently have its effects on the photocatalytic properties of titania been studied. Most critically, platinum can sensitize nanoscale titania particles for visible light absorption, making sunlight-driven processes a tenable option for photocatalytic treatments. Additionally, it can make far more selective the photocatalytic reactions of titania, which generally is non-selective due to the large oxidation potential of OH radicals. We will study these Pt/titania NP materials for humic acid photooxidation using visible light.

**Performance tests under realistic conditions for use in CBEN test bed facility**

Studies will be conducted at the bench-scale to assess the sustainability of catalysts, assess the factors that influence fouling, and monitor the rates of product formation. Initial studies will focus on the use of palladium catalysts for TCE reduction in groundwater. As shown in the progress report, we have demonstrated desired reactivity (TCE reduction to ethane) in a hydrogen atmosphere using simple batch tests. We will construct and optimize small flow-through column systems to mimic the transport of water through well bores. The column will contain a bed of supported nano-palladium and a syringe pump will be used to control the flow of water containing desired levels of hydrogen and TCE. Effluent samples will be monitored for reduced ethenes and ethane as will as hydrogen. By varying flows and concentrations of hydrogen and TCE we will establish the effective range of operating parameters specific to catalysts provided.

Subsequent studies with the most desirable catalysts will focus on the potential for catalyst fouling from sulfides (produced by naturally occurring sulfate reducing bacteria that grow on hydrogen) and the ability to restore activity through washing procedures (e.g., acid wash). We are well equipped to quantify volatile hydrocarbons (GC/MS, among others) and also have scintillation counting equipment for $^{14}$CO$_2$ production.
8.3.5. Sorption of Contaminants onto Engineered Nanomaterials (Tomson, Colvin, Laibinis)

Overview

The characterization of contaminant sorption onto nanoparticles is an important problem. Here, we study the process both for evaluating the environmental impact of nanomaterials as well as for developing improved sorbents for water treatment. Over the past year, we have evaluated the basic sorption properties of two classes of nanoparticles (titania and fullerenes). This data indicates that nanoscale materials can behave quite differently than their bulk counterparts; over the next two years we will generalize the conclusions of these early efforts by comparing the process on a wider selection of material types and evaluating sorption in the presence of natural organic matter. A new direction for this project is to also consider how coatings on particles can be used to both prevent as well as promote contaminant sorption. We include a new team member (Laibinis) with expertise in developing nanoparticle sorbents for separations. Our ultimate aim is to manipulate the sorption process so as to provide materials suitable for removing arsenic and other contaminants from drinking water.

Results

Two model nanomaterials were chosen as standards: fullerenes and nanoscale titania. They represent different extremes of material surfaces. C\textsubscript{60} is hydrophobic, and only about 1 nm in diameter; in solution it can take on a variety of forms ranging from isolated particles to aggregates of varying size. It is commercially available. Titania has an acidic oxide surface; it is quite hydrophilic and often charged, depending on its surface chemistry. Novel methods for forming nanoscale titania were developed for this project. The sorption of model contaminants, naphthalene for fullerenes and cadmium on nanotitania, was characterized by batch adsorption/desorption methods.

Adsorption/desorption of naphthalene to fullerene.

The main purpose of this study was to characterize the adsorption and desorption interaction of naphthalene, a model environmental organic pollutant, with fullerene surfaces, on which future study of environmental impact of nanomaterials can be based. Naphthalene is one of the most widely found contaminants in aquatic environments and therefore was chosen as a model adsorbent. Typical batch reactors were used to perform adsorption and desorption experiments. Adsorption and desorption of naphthalene on activated carbon, a common sorbent, was also studied as a reference for C\textsubscript{60}.

In the desorption study of the well dispersed C\textsubscript{60}, desorption of naphthalene from C\textsubscript{60} to aqueous solutions exhibited strong hysteresis, with only ca. 11\% of total naphthalene was desorbed after over 60 days. This is similar to the desorption of organic pollutants from soil where a dual equilibrium desorption model has been proposed. As the desorption partition coefficient in the irreversible component for C\textsubscript{60} matched that of a wide range of hydrophobic organic compounds with soil, similar mechanisms are probably active. We propose that C\textsubscript{60} forms clusters that rearrange to entrap naphthalene.

Adsorption of cadmium to nanoscale titania

Heavy metal contamination in natural environments has always been a great concern since heavy metals are toxic and non-biodegradable. Adsorption onto oxides has been found to be important for many heavy metals and may significantly affect their mobility in aquatic...
environments. Laboratory experiments have demonstrated that titanium oxides (TiO₂), are strong sorbents for heavy metals, and the surface and adsorptive properties of titanium oxide for various contaminants, have been studied in detail, including the adsorption behaviour of cadmium. These studies, however, were mostly conducted on large crystals.

Since nanomaterials frequently exhibit different physical, chemical and biological properties that may not be predictable from observations on larger-sized materials, we examined the adsorption of a typical priority pollutant, Cd²⁺, onto both nanoscale and large anatase crystals, in batch experiments. In contrast to C₆₀, the adsorption of cadmium on both large and nanoscale anatase appears to be completely reversible. At pH 6.1, on a per-mass basis, Cd²⁺ adsorption capacity to anatase was found to vary by a factor of ~12 among the different sized anatase samples, where stronger adsorption is observed with the nanoscale particles of higher surface area. The Cd²⁺ adsorption to the smallest nanocrystalline anatase is approximately ~150 times stronger on a per mass basis than to natural sediment, although the isotherms of five of the six samples overlap when normalized by surface area. We can interpret this data to mean that because of their high structural perfection, as compared to larger commercial anatase, nanocrystals are less adsorptive on a per surface area basis.

Plans
Over the next year this project will evolve away from its focus on characterizing nanoparticle sorption and move into providing enabling technologies for our engineered water treatment system. Like before, the work brings together the expertise of a materials chemist (Colvin) and an environmental engineer (Tomson); a new team member, a chemical engineer (Laibins), provides a new concept for nanoparticle separations. We envision that this work will ultimately lead to the development of nanosorbent libraries, where different mineral types and sizes would be used in combination. Some materials would be the active sorbents, while other would be added for flocculation, sweep, and recovery; these combination schemes will require basic physical-chemical characterization of nanocrystals, as well as systematic evaluation of the systems engineering of magnetic separation schemes.

The role of surface chemistry on nanoparticle sorption
Nanocrystalline oxides will be prepared using hydrothermal and non-hydrolytic methods developed in the Colvin lab. We will expand our materials base in this project to include zirconia, quartz and iron oxide so as to simulate mineral surfaces of varying properties. These oxides are also candidate materials for toxicological research. The materials will be characterized by a variety of methods to provide information about particle size, surface chemistry and composition. Arsenic and especially arsenic (III) is strongly associated with reduced sulfur species (this is probably the biochemical origin of arsenic toxicity); and therefore sulfur containing adsorbents and modified nanoparticles will be prepared and tested for selective arsenic removal.

One need emerging from nanomanufacturing concerns is for an easy and economical treatment to form benign, encapsulated nanoparticles with non-reactive surfaces. These particles will be effectively rendered inactive, and most suitable for disposal into the environment. We hypothesize that potato starches, biodegradable additives which are available in large quantities at low cost, will associate strongly with the mineral surfaces and block adsorption sites. Also, engineered biocompatible polymers, such as polyaspartic acid and polypyridilone will be tested.
The affinity of particles for these starches will be measured via HPLC and FTIR and the particle size by photon correlation spectroscopy (Wiesner).

We are equally interested in promoting the sorption of materials to nanoparticle surfaces. In this case nanoparticles will become intelligent sorbents for new approaches to water treatment. Our technical plan for this is described in the next section.

Magnetic Sorbents for Gettering Arsenic from Drinking Water

The challenge in developing sorbent technologies are 1) making the dispersed nanoparticles selective adsorbents able to remove ppb-levels of contaminants from natural water samples, and 2) removing the particles with attached contaminants from the solution. Both of these challenges will be addressed in this research.

Figure 8.3.10 Schematic representation arsenic removal from drinking water

The Colvin group has already prepared both magnetite and maghemite iron oxides following standard literature routes; recent developments in the formation of these materials now make it possible to create highly monodisperse, crystalline magnetic particles with tunable size. The permanent magnetic dipole moment of these particles should be optimal at diameters of ~12 nm; the effectiveness of the magnetic separation will scale directly with this value.

Iron oxide is well known for exhibiting strong and specific interactions with arsenic in water; indeed, macroscopic iron filings are one material used to remove arsenic from groundwater in India. However, the free surface of the iron oxide particles may exhibit poor solubility in water making it difficult to simultaneously engineer particles with free surface for sorption, as well as coatings for water solubility. If this is true, coated particles will be treated with polymers chosen for the ability to ion-exchange arsenic very selectively. Alternatively, larger 12 nm particles will be coated and decorated with smaller, uncoated 4 nm nanoparticles. The larger cores will optimize the magnetic separations, while the decorative 4 nm iron oxide will provide the active surface area for sorption. One advantage of working with iron oxide as a sorbent is that when treated with light, it is able to catalyze when illuminated the reduction of As(V) to the less toxic As(III) and thus can be recycled.
8.3.6. Nanotoxicology & Cell-Nanomaterial Interactions (Hughes, West, Colvin)

Overview

The bioaccumulation, toxicity, and biotransformation of nanomaterials are of great importance to nearly all projects in CBEN. In theme #2 this information controls whether nanoparticles will likely be used for in-vivo applications; in theme #3, the concentration of nanomaterials in the environment is of crucial importance in gauging the impact of these substances; biological processes will be central in defining the persistence and effects of nanomaterials in the environment. Fullerenes, while recently discovered, are produced sporadically by natural processes. Thus, contact between fullerenes and biological systems in the environment is an ongoing phenomenon that, to date, has not been extensively researched. This year, nanotoxicology funding has been directed primarily to Hughes for developing methodologies for studying how nanomaterials interact with bacteria, fungi and earthworms. In some cases these model nanomaterials were toxic to organisms and all apparently bioaccumulated. Moreover, preliminary data suggests the hydroxylation of fullerenes can occur naturally highlighting the importance of biotransformation processes in understanding nanomaterial fate and transport. Over the next year, West’s lab will begin biodistribution and cytotoxicity screens of standard CBEN materials such as nanoshells. Finally, Colvin is preparing quartz, iron oxide and titania nanocrystals for use in formal toxicology studies with partners in industry and government (Kevin Dreher, EPA). This work requires that particles be non-aggregated and stable in the complex tissue growth media, a challenge for most systems; much of the chemistry for these materials models that used in theme #1 project 8.1.1.

Results

It has been shown that due to their hydrophobicity, fullerenes can integrate into lipid bilayers and have the propensity to be retained in tissue (from research performed using eukaryotic systems examining medical applications of fullerenes). With regard to toxicity, it has been shown that C$_{60}$ and its derivatives have some mutagenic activity with Gram- negative and Gram-positive bacteria. Fullerenes can act as antimicrobial agents, although few studies have been performed to support this finding. Little information is available on the biotransformation of fullerenes. A number of enzymes capable of degrading macromolecular aromatic polymers such as lignin are thought to be capable of oxidizing C$_{60}$ to a hydroxylated form.

This report documents the progress of our investigation into the bioaccumulation, toxicity, and bio transformation of fullerenes in the environment. Bioaccumulation was investigated using prokaryotes (E. coli in liquid media) and eukaryotes (E. fetida in soil). Toxicity testing was primarily assayed with prokaryotes (E. coli) and to a lesser degree with other biotic experiments. An accepted model system to evaluate the potential for non-specific oxidation of fullerenes, namely Fenton’s reaction, was employed to test the possibility of fullerene biotransformation. This model provided positive results, therefore cell free enzyme systems and whole cell fungal systems were subsequently investigated.
Bioaccumulation

Three different suspensions of C$_{60}$ were prepared, as described elsewhere: a colloidal suspension in water with THF, a colloidal suspension in water using toluene addition, and micelles in water using PVP. Depending on the organism, different methods, the details of which are beyond this brief report, were used to introduce fullerenes into the growth medium and ultimately into the organism. The amount of fullerenes in the biological samples was assayed by a toluene extraction and HPLC. The extraction efficiency varies for each C$_{60}$ preparation (data not shown), but a considerable amount of C$_{60}$ is lost in all cases when compared to bacteria-free controls. The measurements are erratic but the trend of C$_{60}$ associating with organisms is consistent. The nature of this association could not be verified as the method used to separate the periplasmic fraction from the cells, leaving spheroplasts, yielded only about 10% spheroplasts. C$_{60}$ was found in the dried worm tissue at a concentration of 21.0 µg C$_{60}$/g dried tissue (0.002% dry weight as C$_{60}$). This is a positive indication that C$_{60}$ accumulates in earthworms. The worms, *E. fetida*, grew in the presence of C$_{60}$, up to 1 g C$_{60}$/kg of soil. The fungi, *P. chrysosporium*, also grew in the presence of C$_{60}$ (200mg/L). Otherwise, no other toxicity tests were performed thus far.

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<tr>
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<td>no</td>
<td>yes</td>
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</tr>
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</table>

Biotransformation

Fenton’s Reaction Stock solution of fullerene as C$_{60}$ dissolved in toluene (1g/L) was added to a 30% hydrogen peroxide (H$_2$O$_2$) solution. Ferric iron was added to the aqueous phase in the form of FeSO$_4$·7H$_2$O (Fisher Scientific) as a catalyst and stirred vigorously. Along with HPLC analysis, mass spectroscopy was performed using a FAB MALDI procedure, with results indicating products occurring with 16/17 mass shifts from the base 720 indicating a possible oxidation in the form of an epoxide and/or of hydroxyl addition (s). This confirms the possibility of biotransformation of C$_{60}$ provided the appropriate biological system exists.

The enzyme assays were performed with a manganese peroxidase from *Nematoloma frowardii*, as described elsewhere. These experiment suggest that the enzymatic transformation of C$_{60}$ is possible and warrants further in depth study. Fungal assay *Phanerochaete chrysosporium* (ATCC 24725) was grown in a liquid growth medium used to induce lignolysis (through nitrogen limitation). Based on the results from the Fenton’s reaction experiment, it is apparent that the C$_{60}$ structure can be oxidized in a manner similar to that found in fungal systems. There is evidence of bioaccumulation as C$_{60}$ associated with living fungi cell mass twice as much as with the dead cell control.
**Plans**

Studies in this area will focus on fullerenes, and primarily C\textsubscript{60}, and will address their interaction with living systems of interest in exposure assessment. Information from preliminary studies (from the Hughes lab and other groups) indicate that fullerenes interact with living systems in a variety of potentially important ways. Aqueous experiments with fullerenes are by their nature difficult due to the extreme hydrophobicity of fullerene molecules. As done previously, all proposed research described in this section will use forms of C\textsubscript{60} that can be wetted or solubilized in aqueous media. These include C\textsubscript{60} in the form of colloidal particles, in micelles, or as hydroxylated derivatives, depending on the objective of individual experiment. Additionally, with particle methodologies in hand work will begin to consider similar issues for other nanoscale materials such as nanoshells and nanocrystals (see project 8.2.1).

One hypothesis stemming from research to date is that once the C\textsubscript{60} is hydroxylated (by biochemical or abiotic means) it may possess a greater propensity for further biochemically mediated oxygen radical reactions due to the dramatic increase in water solubility following hydroxylation. This will be evaluated by using commercially available hydroxylated fullerenes through comparative rate studies using C\textsubscript{60} as a control. Studies of biouptake and bioconcentration will employ bacterial, fungal, and annelids assays. Initial bacterial studies show *E. coli* grown under anaerobic conditions take up underivatized fullerenes (C\textsubscript{60} as colloidal particles and in micelles). However, it was not clearly established how and where the fullerenes were incorporated into cells. (Interestingly, when uptake assays were conducted under aerobic conditions no growth was observed. Apparently, fullerenes may have bacteriocidal properties that vary with growth conditions.) To determine the location of fullerenes, bioaccumulation experiments will be performed and results characterized with careful separation of outer membrane, periplasm and spheroplast. Qualitative observations using SEM and/or TEM microscopy may also be employed.

Based on the positive results reported in the progress report regarding accumulation of C\textsubscript{60} in earthworms (*Eisenia fetida*) and fungi (*Phanaerochaete chrysosporium*), further experiments investigating the accumulation of C60 in eukaryotes will be performed. A matrix of experiments will be designed to explore the capacity of representative soil biota (fungi, earthworms, and possibly plants) to take up various forms of soluble C\textsubscript{60}. Parallel to the aforementioned bacterial studies, the location and toxicity of C\textsubscript{60} will be characterized. Dissections, membrane separations, tissue extractions, and microscopy will be used to determine the location of C\textsubscript{60} in the organisms. These studies will also consider the fullerene “form” in the uptake observed. This will include colloidal, surfactant wrapped, and soil associated forms (in collaboration with the Tomson Group and project 8.3.5). Also, experiments that evaluate the possible flow of fullerenes through the food chain are necessary. We propose introducing bacteria, which have accumulated fullerenes, to appropriate biota, such as protozoa, annelids, etc. and measuring the flux of fullerenes between living systems (biomagnification, which has been widely observed with xenobiotic hydrophobic compounds released into the environment).
8.3.7. Environmental Exposure Routes (Hughes, Wiesner, Tomson, Luttge)

Overview

The biological response of any organism to a chemical or nanomaterial is controlled by the “dose” to which it is exposed. When exposure results from environmental contamination the effective dose applied is controlled by a number of physical, chemical, and biological processes. In this continuing project, studies will be conducted to identify and quantify factors that will control the exposure of nanomaterials (in particular, those being developed and studied by the CBEN nanomanufacturing group) to receptors in the environment. To achieve proposed objectives, an interdisciplinary team works together to identify processes most important to nanomaterial fate and transport in environmental systems. As a result, it will be possible to generate predictive models of processes that translate “release to the environment” to the “dose experienced” by receptors. This research represents an essential component in the development of risk analysis tools needed to assure that the manufacturing and disposal of new nanomaterials do not result in adverse humans health effects or diminish ecosystem function. This project has resulted in the submission of two manuscripts, several oral presentations at national meetings, and one book chapter. Through its synergy with our media and government outreach, this work has lead to well over twenty oral presentations for its participants.

We note that the bioaccumulation and biotransformation studies of Hughes described in 8.3.6 are highly relevant to the goals of this project; while not described here in detail due to space limitations, this project will allow for the expansion of that effort to include new classes of nanomaterials and is described here. Additionally, we have added a geochemist Luttge to this project area. His experience with geobiochemical transformations of minerals, as well as his interferometric analysis system, will be crucial for characterizing the biological transformations of mineral particles.

This project is central to our mission and we are requesting a 10% increase in our budget to ensure that it gets completed. We have been forced because of the 37% budget reduction in year 1 to make very difficult choices in project funding. Through rollover funds from delayed hires in year 1, CBEN was able to maintain this project at reduced levels in year 2. However, these resources are not available in year 3 and without a modest budget increase ($246,050) CBEN cannot continue this project. It is highly unfortunate that our most visible project area is also the least connected to our engineered systems. Still the indirect connection is very strong in that adequate environmental impact work will be crucial to overcome problems with the public acceptance of nanotechnology. Such research is best completed in the context of a large center where interactions between nanomaterials and biosystems are addressed. Moreover, as we have demonstrated over the past year, the center provides critical resources for interpreting what can be controversial data for the wider public.

Results

i) Nanoparticle fate and transport (Wiesner)

In order to predict how fast and efficiently nanoparticles will move through water and soil it is crucial to understand their fundamental transport properties; for much larger colloids, there exist standard models which relate the macroscopic transport to factors such as particle size, surface chemistry, and soil conditions. Thus, if the models are valid (as they are for colloids > 1 µm) simple laboratory tests can provide a prediction of how a fixed concentration of
materials will move in time and space through soil environments. Our work to date has focused on how these models change when colloids drop below one micron.

Soils are usually modeled as porous media with various physio-chemical characteristics; to simulate the transport of particles through such materials we used a packed glass bead stationary matrix. Breakthrough curves which describe the relative particle concentrations transported in the bed were measured as a function of particle size:pore volume; we also completed zeta potential measurements to allow for variation of particle surface charge density with pH. The surface chemistry of particles is an essential characteristic for governing their mobility in porous media, and this complex factor is captured in most models as a sticking coefficient, or $\alpha_c$. Typical breakthrough curves for the particles considered, commercially available anatase and silica of sub-micron size, are shown in the figure.

These curves can be can be described in terms of a collision efficiency factor using Rajagopolan and Tien’s expression for the single collector efficiency. Using experimental C/Co values and theoretical collector efficiencies experimental $\alpha_c$ (or sticking coefficient) values have been calculated and are tabulated below. More sophisticated modeling of the fraction of influent particles remaining for the deposition phases in the absence of electrostatic effects have also been completed. This formulation captured the characteristics of the final deposition rate well for all particles except the smallest (57 nm) silica.

We have also begun to alter our flow and solution conditions so as to mimic the conditions of a sandy soil; at these lower filtration rates relative concentrations for anatase are lower than those for similar sized silica while at faster filtration anatase particles have breakthrough curves located above those of silica. Clearly aggregate stability is important in understanding nanoparticle transport, and it is likely that at high flow rate aggregates are broken down and thus less retained during transport through the filter bed.

<table>
<thead>
<tr>
<th>Kind of Nanoparticles</th>
<th>C/Co</th>
<th>C/Co</th>
<th>$\alpha_c$</th>
<th>$\alpha_c$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Us=0.02 cm/s</td>
<td>Us=0.136 cm/s</td>
<td>Us=0.02 cm/s</td>
<td>Us=0.136 cm/s</td>
</tr>
<tr>
<td>Silica 57 nm</td>
<td>0.969</td>
<td>0.963</td>
<td>0.005</td>
<td>0.020</td>
</tr>
<tr>
<td>Silica 57nm bis</td>
<td>0.970</td>
<td>0.986</td>
<td>0.004</td>
<td>0.007</td>
</tr>
<tr>
<td>Silica 135 nm</td>
<td>0.669</td>
<td>0.634</td>
<td>0.107</td>
<td>0.429</td>
</tr>
<tr>
<td>Silica 135 nm bis</td>
<td>0.670</td>
<td>0.609</td>
<td>0.107</td>
<td>0.466</td>
</tr>
<tr>
<td>Anatase 198 nm</td>
<td>0.551</td>
<td>0.736</td>
<td>0.203</td>
<td>0.372</td>
</tr>
<tr>
<td>Anatase 198 nm bis</td>
<td>0.557</td>
<td>0.731</td>
<td>0.199</td>
<td>0.379</td>
</tr>
</tbody>
</table>
ii) Nanoparticle-mediated transport of contaminants (Tomson)

The sorption capacity and behavior of both fullerenes and nanocrystalline titania were evaluated using model materials. As expected, due to the large surface areas of the nanoparticles, large amounts of contaminants were found to associate with the nanoparticles in solution. However, the overall surface reactivity on a per area basis was lower for highly crystalline nanoparticles as opposed to amorphous colloids. Finally, the sorption-desorption behavior of fullerenes indicated unusual aggregation and rearrangement of materials in the presence of organic contaminants. For more details on these experiments and results please refer to the project 8.3.5.

Plan

Fate and transport (Wiesner, Colvin, Smalley)

Task 1: Evaluate the factors that control transport of engineered nanocrystals in aquatic systems. Our results to date suggest that sub-micron colloids behave similarly to larger colloidal matter in terms of following basic models for particle transport. However, as suggested by the data on our very smallest commercially available particle, the small size and increased surface areas of particles well under 50 nm in diameter could lead to qualitatively different behavior as compared to larger particles. Additionally, as discovered in Tomson’s sorption work engineered nanocrystals (8.3.5), nanocrystals can have surface chemistries that are quite distinctive from comparable colloidal materials. We will perform experimental transport studies as described in our results section with the ultimate aim of generating a theoretical basis for predicting the attachment efficiency of very small nanoparticles as a function of particle and solution chemistry properties.

Task 2: Expand effort to include several nanoparticle types. To date this work has considered only commercially available colloids; this has allowed us to verify basic particle transport measurements to sizes well below a micron. However, we have always expected that the most unusual behavior will emerge as particles become truly nanoscopic, with sizes well under 10 nm. Next year we will expand our efforts to include fullerenes (both C60 and SWNT), nanocrystalline titania, alumoxane and fluorescent quantum dots of CdSe-ZnS. The biggest experimental challenge will be detection of particles in the flow stream (light scattering is not accurate for such small particles); by incorporating absorption and fluorescence detection methods we will be able to overcome this challenge for most materials.

Biotransformations of mineral surfaces (Hughes, Luttge)

Task 1: Biotransformations of mineral nanoparticles. Section 8.3.6 describes how fullerene materials undergo substantial chemical changes in response to biological systems such as bacteria and fungi. In this closely related project the Hughes group will expand their study of this problem by considering the changes in mineral nanoparticle composition and surface chemistry. Iron oxide nanocrystals, produced in the nanomanufacturing effort, provide a model system with controllable size and well defined surface chemistry. Additionally, these materials can be labeled with Fe$^{57}$ for easy detection above the naturally occurring iron backgrounds in biological systems. Moreover, because they are magnetic they can be easily separated from biological materials via magnetic fields.
Task 2: Characterization of biologically mediated changes on mineral and carbon surfaces. An outstanding question in biotransformation efforts is the molecular level processes giving rise to altered particle size and/or surface chemistry. Using vertical scanning interferometry, Luttge’s group will evaluate this problem on both HOPG graphite and model iron oxide surfaces using organisms studied in 8.3.6. Using an interferometric method pioneered in his laboratory Luttge can measure surface topography in-situ with angstrom resolution. Such data allows mechanisms for dissolution to be characterized and overall dissolution rates determined; the instrument also has the resolution to evaluate how single nanoparticles (d > 10 nm) dissolve under flow conditions with various biological species present. While focused on this project initially, the geochemistry perspective provided by Luttge will be essential to developing a full understanding of how nanoparticles interact with the ecosystem.

III) Nanoparticle-Facilitated Transport of Sorbed Contaminants (Tomson,Hughes)

Task 1: Expansion of studies of hysteretic sorption onto fullerenes. The unusual finding that aromatic molecules can become irreversibly sorbed to fullerenes in water suggests that aggregation creates internal compartments for hydrophobic materials. We will follow this work by characterizing the desorption resistant compartment in spike labeled experiments using fluorescent probes. These probes may also provide information about the chemical environment of these compartments by measuring the energy and dynamics of their emission.

Task 2: Integration of bioaccumulation and sorption experiments. Based on the sorption studies of Tomson, fullerenes have a high and irreversible capacity to sorb hydrocarbons, which would include contaminants like PAH, from water. Hughes has also shown that fullerenes bioaccumulate in various lower organisms. This project brings these results together, and will determine whether sorbents can be accumulated in biological organisms via their interactions with fullerenes.
9. Education and Human Resources

The goal of our educational outreach and human resource programs is to cultivate a future workforce experienced with using nanoscience and nanoengineering to solve problems in biological and environmental engineering. This objective necessarily echoes one of the primary missions of the NSF, namely training of the technical workforce of the future [1]. It also directly relates to our mission: CBEN’s technical objectives can only be realized if there are well-trained scientists and engineers to discover, develop and manage its nanotechnologies.

CBEN’s activities in this area address both long-term and short-term needs in workforce training. Short-term, the next generation of nanotechnologists will be drawn from current graduate and undergraduate students already in our pipeline. We strive to ensure our students are diverse, and have a substantial percentage (40%) of female graduate students. We also develop students with the right skills to be highly effective researchers. Our systems engineering focus and collaborative research environment train people who excel at working in large, interdisciplinary teams. Through its center programs CBEN also provides researchers with crucial oral and written communication skills, as well as broader perspectives on the economic, societal and governmental applications of their research.

Addressing the longer term challenge of workforce training requires programs that increase the number and quality of people entering the science and engineering pipeline. For this, CBEN has developed connections to our local school districts, businesses and community. We run eleven formal programs for such outreach activities; they are diverse and involve students as young as ten years old as well as laypeople over sixty. These efforts all exploit the capacity that nanotechnology has to spark a sense of wonder in students and adults alike. Like the space program, we find that nanotechnology is an ideal ‘hook’ for drawing people into science and technology.

CBEN’s educational outreach activities are coordinated by Dr. Kristen Kulinowski, Executive Director for Education and Public Policy. CBEN faculty members and students, however, contribute substantially to these programs, as is apparent in section 9.7, which provides a comprehensive listing of all educational outreach activities. The highlights of our program this year include:

- **Training for teachers of at-risk students** in the diverse Houston and United Independent School Districts (Laredo, TX).
- **Involvement of students from 9th grade through graduate school**, in research, classroom and outreach activities
- **Integration of CBEN research into education** by making links between nanotechnology and the Texas high school science curriculum
- **Development of NanoKids™ DVD** for proof-of-concept testing in middle school classrooms
9.1. **CBEN educational outreach and human resource programs**

**Continuing CBEN educational programs**

1. High school teacher professional development series
   a. Spring Content Course
   b. Summer Internship
   c. pH Model Lab Sabbatical
2. Integrated Physics and Chemistry (IPC) workshop for teachers from United Independent School District (Laredo, TX)
3. Summer academy for high school students (summer 2003)
4. NanoKids™ instructional materials development
5. Undergraduate nanotechnology curriculum development
6. Graduate nanotechnology curriculum development
7. Entrepreneurship education for graduate students
9. Bi-monthly graduate student networking and problem-solving lunches
11. Nanotechnology Research Experience for Undergraduates (summer 2003)

**New activities for 2003-2004**

1. NanoLand museum project with Houston Museum of Natural Science
2. Workshop on integrating nanotechnology into Advanced Placement® courses for attendees of the School of Continuing Studies Advanced Placement® Summer Institute

**Summary of participants in CBEN educational activities**

Total numbers of people who participated in a CBEN education program activity for the period February 1, 2002-March 15, 2003 are summarized in the table below.

<table>
<thead>
<tr>
<th>K-12 Teachers</th>
<th>K-12 Students</th>
<th>Undergraduate/Graduate Students</th>
<th>Community</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>237</td>
<td>928</td>
<td>410</td>
<td>330</td>
<td>1905*</td>
</tr>
</tbody>
</table>

*A participant may be double counted. For example, a graduate student may have taken multiple CBEN courses.

A complete listing of all CBEN educational activities with a breakdown of the number and type of people impacted by each can be found in the appendix following this narrative.
9.2. **K-12 Programs**

9.2.1. **High school teacher professional development series**

Our centerpiece K-12 educational outreach program focuses on ninth grade science teachers. We feel that by investing in high quality, long-term teacher training, our center’s investment is multiplied many times over. A single teacher will over a decade influence directly hundreds of students, and influence thousands of others through mentoring of other teachers.¹

We target ninth grade teachers, rather than the more sophisticated and educated advanced placement teachers, for several reasons unique to Houston and CBEN’s research focus. First, in Texas ninth grade science is an integrated physics and chemistry (IPC) class. The integrated subject content of this class makes it a natural place to use illustrative examples of our center’s research in the classroom. Also, there is an acute need for teacher training at this level. This class is often the first assignment given to young teachers. Most do not have extensive scientific training, yet are expected to succeed if they want to advance to courses that are more "desirable". This results in low teacher retention rates and poor student performance. Improvements made at this level will increase the pool of qualified and motivated students for the more advanced high school science classes.

These teacher-centered challenges are exacerbated by those faced by their students. Not surprisingly, there is a high dropout rate in high school in HISD; statistics from the United States Department of Education show that only 47% of those HISD students who entered 9th grade in 1994 graduated in 1998. As in most other large urban school districts, many HISD students face serious barriers to learning, including poverty (75.4% of students are on free/reduced lunch), migrancy (38.2% mobility rate), and language (26.5% have limited English proficiency). Additionally, investing our efforts in HISD impacts mostly underrepresented groups simply due to its diverse demographic makeup: 56% Hispanic, 31% African American, 10% White, and 3% Asian. [2]

The three phases of our program are:

- **Spring Content Course**: refreshes understanding of core science concepts and connects those concepts to ongoing nanotechnology research.

¹ Assuming one teacher has four classes per day with 30 students per class, this amounts to 1200 students in a decade.
• **Summer Internship**: reinforces science as a process by placing teachers in research laboratories.

• **pH Model Science Lab II**: a year-long sabbatical residency to introduce constructivist teaching techniques.

**CHEM 570: Spring Content Course**

This evening course has the dual goals of refreshing the teachers’ understanding of core physics and chemistry concepts, and connecting those core scientific concepts to ongoing nanotechnology research. For the first hour of each evening, basic science concepts are reviewed and extended. Dr. Kulinowski, the moderator, uses a variety of teaching formats that cover physics and chemistry while modeling active learning techniques. In the second hour of each class period a center researcher presents on their CBEN research and emphasizes a connection to the scientific concepts discussed in the first hour. For example, CBEN researcher Jianpeng Ma discussed molecular dynamics calculations of carbon nanotube interactions with water after the teachers received a basic lecture on Newton’s laws of motion. In the third hour, the teachers brainstorm about ideas for how to incorporate the research concepts into their classroom. The goal is to leave the teachers with tangible lessons, worksheets, activities, active-learning exercises, or other materials that incorporate center research concepts. Pre-test/post-test assessment from last year’s program demonstrated marked improvement in teacher’s knowledge of their IPC course content and an increased awareness of nanotechnology.

In its second offering, the course has an enrollment of eleven people: eight from HISD, one from the nearby Ft. Bend school district, one from a private middle school in Houston, and one from the educational division of NASA Johnson Space Center. With feedback from these pilot classes, we aim to reach a steady state enrollment of twenty teachers over the next two years.

**Summer Internships for Teachers**

We have tailored our summer program to the needs of 9th-grade Integrated Physics and Chemistry teachers. Rather than have teachers work on independent research, as is generally the case for a Research Experience for Teachers (NSF-RET) program, we use the center’s resources to focus instead on techniques for translating the center’s research methodology and results into a classroom setting. The goals of our summer internship program piloted in the summer of 2002 are to reinforce each teacher's sense of science as a process, to deepen each teacher's understanding of the achievements and potential of nanoscience, and to apply lessons learned from the content class to a research setting.

We do this by asking that our summer teachers create a lesson plan that explains the research of the host lab at a level appropriate for a high school teacher or student. Over the course of the four-week program, teachers spend four days per week observing and assisting in research, as well as interviewing lab personnel. On the fifth day of each week, the teachers meet together to share and discuss activities in their respective labs, review existing nanoscience and materials-science instructional resources, and develop a lesson that applies center science to at least one unit in IPC. The teachers’ understanding of nanoscience is demonstrated by the construction of a web page or course materials. High quality lessons will be posted on the CBEN website so other teachers can use them.
**pH Model Science Lab II: A sabbatical for teachers**

The final component of our teacher training program is a sabbatical for teachers in the year after their summer internship. This sabbatical is incorporated into our program because of the success that this approach has found in middle school science teacher training. This program, the Model Science Lab (MSL), was developed at Rice prior to CBEN and is an intense residency program in which eight middle school science teachers spend a sabbatical year in an inner city school studying and class-testing discovery-based approaches to science education. Tangible achievements of the MSL include an almost perfect teacher retention rate (95% after 11 years), the professionalization of a cadre of teachers who act as peer mentors, and the improvement in student test scores. The students of MSL teachers demonstrated greater improvement on both the state achievement test and on a pre/post modified NAEP (National Assessment of Educational Progress) test than students taught by control teachers in each of their schools. [3]

The pH Model Science Lab II, our 9th grade successor program to this successful 5th-8th-grade program, was piloted in the fall of 2002 with four teachers, three funded by our center and the fourth and the programmatic costs funded by the Cain Foundation. A host high school, Lee High School, provides a home for teachers as they develop curricula, and inquiry based demonstrations centered on nanotechnology. The four teachers for this pilot were selected from the participants in the summer internship program described above. In future years, further external funding will be sought to increase the complement of teachers to eight.

**9.2.2. Laredo/Rice IPC Teacher Training Workshop**

Leveraging the curriculum developed for CHEM 570, described above, the center developed an intensive 3-day workshop for teachers that was piloted last June for a set of 9th-grade IPC teachers from Laredo, TX. Even more than HISD the Laredo school district’s students suffer from serious barriers to learning (91.4% were categorized as economically disadvantaged in 2000). Since the district is located 160 miles from the nearest major metropolitan area, its teachers have only limited access to professional development opportunities. In addition to running the workshop, the center covered the travel expenses for eleven teachers to participate in the event. The center’s efforts in this program strongly target traditionally underrepresented minorities as 95% of the district’s student population is Hispanic. [4] We plan to expand this successful program by offering the summer 2003 workshop in conjunction with the Ellison Miles Geotechnology Institute in Dallas, TX. EMGI will offer use of their facilities and will recruit teachers from local school districts. CBEN will pay for interested Laredo teachers to travel to the EMGI and will provide all instructional materials and speakers. Response to the workshop
offered in June 2002 was so positive that in November 2002 the Laredo school district paid for a
group of 4 teachers to bring 48 high-school students to Rice. Executive director Kristen
Kulinowski arranged a daylong program of lectures on CBEN research, and tours of research
labs and the campus.

9.2.3. High-School Summer Academy (pilot to be offered June 2003)

Summer science experiences provide an excellent tool for discovery-based pedagogy at
the high school level. Further, the excitement and interest that can be generated in students by
vibrant fields such as nanotechnology and environmental science can dramatically increase the
effectiveness of such a teaching tool. We will use the cadre of informed and motivated teachers
from the HISD professional development series to draw high school students from
underrepresented groups into the research activities of the center. This process will begin with a
two-week Science Academy for promising 9th/10th grade students identified by MSL teachers.
Structuring the Academy as a science fair workshop in which students learn how to construct and
test a hypothesis will allow the process of scientific inquiry begun in the MSL intern's classroom
to continue. Dr. Mary McHale, a chemistry lecturer and water quality expert, is designing a
curriculum in which students analyze local water samples from various sources for impurities.
CBEN research into the role of nanotechnology in water purification will be integrated into the
academy.

At this age, students are at a pivotal time in the evolution of their career planning. If we
can continue to excite them about the process of scientific discovery, more of them may consider
studying science and engineering in college. Promising graduates of the Academy will be invited
back in subsequent summers to work in the research labs as assistants or on their own science
fair projects under the mentorship of a center researcher. The impact of student involvement in
center activities will be assessed through student interviews or surveys. Each student's progress
through high school and beyond will be tracked for the duration of the research grant. The center
will coordinate activities and work aggressively with Rice's Coordinator of Minority
Recruitment; their staff has been drawn from backgrounds similar to those of the minority
students we are targeting, and their mentorship will be important in developing minority student
relationships.

9.2.4. Nanokids™ Instructional Materials Development

Center member James Tour has synthesized organic molecules whose structures are
visually reminiscent of children. The NanoKids™ program is developing curricular materials
that introduce the nanoscale world through animated characters based on these molecules. [5]
The central theme of ‘atoms and molecules are our world’ emphasizes that most matter is made
up of atoms bonding together to form molecules, which form our environment and us. The
program is initially targeting the middle-school level, as that is the point in the normal science
curriculum where the concept of molecules is introduced.

The NanoKids™ program has completed its 20-minute proof-of-concept animation DVD. The
DVD has 46 built-in stop/returns to facilitate instruction, and is accompanied by an
electronic interactive student workbook, a teacher's study guide that includes background
material, lesson plans and supplementary activities, a parents' study guide, and a support website
with online assessment capabilities. The program will begin beta testing in selected middle
schools throughout the Houston Independent School District in September 2003, as well as three
independent schools in May 2003. Prior to the beta testing, CBEN will sponsor a four-hour workshop for participating teachers to facilitate use of the materials.

Formative evaluation is key to the NanoKids™ development process, and is in full swing through student, parent and teacher focus groups. Basic science teaching and learning techniques, character looks and qualities, interest-catching settings, and prospective music styles are under scrutiny by experts in the field and by those whom the project is meant to serve. In addition, NanoKids efforts are being leveraged in the museum project described in the next section.

9.2.5. Museum Project

CBEN is involved in an NSF Informal Science Education proposal to build a traveling museum exhibit, NanoLand, in conjunction with our sister NSEC at Columbia University, the Houston Museum of Natural Science and the Oregon Museum of Science and Industry. NanoLand is a large-scale immersion exhibit that takes visitors to “Nanoputian” dimensions, allowing them to experience the molecular world by walking through carbon nanotubes and interacting with DNA helices and their associated enzymes. The NanoKids will act as tour guides and scale bars throughout the exhibit. NanoKids creator James Tour is proposal PI and CBEN executive director Kristen Kulinowski is a co-PI on the proposal. Just prior to submitting this report, we learned that our preproposal had been accepted and a full proposal is under development.

9.3. Undergraduate Programs

Internal educational activities are intended to enhance the knowledge base and professional skills of our undergraduate and graduate students and post-docs. Our undergraduate educational development programs encompass a Nanotechnology Research Experience for Undergraduates program, new course development, and modification of existing courses.

9.3.1. Nanotechnology Undergraduate Research for Undergraduates (NREU)

Involving students in discovery-based scientific inquiry is the primary objective of our Nanotechnology Research Experience for Undergraduates (NREU) program, to be offered for the first time in the summer of 2003. This program is modeled after an existing REU program offered by the Rice Quantum Institute, in which undergraduates work on independent research projects in a Rice lab for 10 weeks and present their work at a conference held at the end of the summer. Our NREU program specifically targets a diverse group of students through recruitment trips at regional colleges and universities and at national meetings of professional organizations such as the National Society of Black Physicists. It is possible for advanced high school students from the Academy or MSL teacher’s classes to participate in this program. We also welcome incoming graduate students who arrive early to do research with a CBEN faculty member.

2 The name “Nanoputian” is derived from the inch-sized Lilliputians, the people of Lilliput, in Jonathan Swift’s classic, Gulliver’s Travels.
addition to providing a research experience, we will have weekly social events in which students can interact with one another and discuss any issues of importance to them regarding their career plans.

This NREU program is coordinated with Rice’s existing, exceptionally successful Alliances for Graduate Education and the Professoriate (AGEP) program. The AGEP summer undergraduate research program is specifically designed to give hands-on research experience to undergraduate students in the fields of math, engineering, science, and technology-related disciplines. This AGEP program is itself the successor of a highly effective Spend a Summer with a Scientist (SaS) program, which over its lifetime achieved an impressive 62% enrollment of its undergraduate participants in graduate school, of whom 88% were Hispanic or African American. For comparison, National Center for Educational Statistics demonstrate that less than 9% of Hispanics and African Americans who received baccalaureate degrees entered graduate school over the same period; the percentage is even lower in the specific fields covered by Rice’s SaS program. Recruitment for the summer 2003 program is underway. At the time of this report, we had received acceptances from four African-American females, two Caucasian females, and two Hispanic males.

9.3.2. Science Education for New Civic Engagements and Responsibilities (SENCER)

CBEN proposes a new undergraduate course for nonmajors on the societal implications of nanotechnology modeled after the SENCER program. (Kulinowski) SENCER, an NSF-funded initiative administered by the American Association of Colleges and Universities (AAC&U), robustly connects science and civic engagement by teaching “to” basic science “through” complex, contested, current public issues.[6] The current public debate over the benefits and risks of nanotechnology provides a timely platform on which to build a course that engages nonmajors in exploring this new field. Dr. Kulinowski will write and present a backgrounder paper on nanotechnology and its social context for the SENCER Summer Institute (SSI 2003) and will lead a campus effort to design a course to be offered in the 2004 academic year.

9.3.3. New Undergraduate Courses

For graduate and undergraduate education, CBEN’s vision is to create a series of interlocking courses in nanoscience and education. The planning for the start of this curriculum is already underway, and will leverage two new programs at Rice. One of these, the Sloan Professional Master’s program, has majors in Nanotechnology (physics) and Environmental Decision Making. The second, the Rice Connexions program to develop web-based materials, started in the Electrical Engineering department, provides staff and a web programming language well-suited for equation display and self-study. Many of the courses described in this section are also available to graduate students, and many of the courses described in the graduate section are also available to undergraduates.

The Chemistry Department at Rice currently offers its upper-division undergraduate lab courses in the format of half-semester or semester themed modules that integrate skills traditionally developed in separate courses. This format is intended to more closely simulate the systems-level focus that underlies many research projects, especially those spanning traditional divisions within a discipline. In an example of a current module, CHEM 373, students synthesize, separate, and characterize fullerenes using electrochemical and photophysical
techniques, thus integrating skills conventionally within the separate domains of organic, analytical, and physical chemistry laboratories. One new module was offered during the reporting year and another is under development.

- **NEW: CHEM 375 Advanced Module in Nanochemistry.** This new half-semester course, inspired entirely by CBEN research, introduces students to synthesis and structure of nanoparticles and their physical characterization. It was first offered in the Fall 2002 semester by Prof. Vicki Colvin and had an enrollment of nine students, which demonstrates strong student interest in the subject. It will be offered again in Fall 2003 and on a yearly basis thereafter.

- **PLANNED:** We are planning a semester module in environmental waste remediation using nanoscale titania for the spring of 2003. Melanie Thoms, a new instructor joining the Chemistry Department this summer, will work with Profs. Wong and Tomson to use the photooxidation of organic halides by nanoscale titania as a case study in the cost-benefit analysis of clean-up strategies for environmental science. This new course will be disseminated to the education community at national meetings such as Biennial Conference on Chemical Education and through publication in journals such as the *Journal of Chemical Education*.

In addition to these lab modules, Prof. Susanne Stemmer, who recently left Rice to take a position at UC Santa Barbara, offered a course with partial CBEN content in Spring 2002.

- **NEW: MSCI 415 Ceramic and Glasses.** This lecture class covered fundamentals of ceramic and glassy materials, including phase relations, theoretical properties, structure, bonding, and design. Nanoscale ceramics and glasses were topics of the course.

### 9.3.4. Undergraduate Courses Modified to include Center Content

Two pre-existing Rice University courses have been modified to include center research. In addition, some graduate level classes, described below, are available for advanced undergraduates. The modified undergraduate courses include:

- **BIOE 441: Advanced Bioengineering Laboratory.** This course is required of all seniors majoring in bioengineering. We have developed a module where students use metal nanoshells and their associated photothermal phenomena to induce tissue welding. Students learn about the nanostructured materials and optical interactions, and then also use this as an opportunity to use their skills in biomechanics to evaluate the efficacy of nanoparticle-assisted laser tissue welding. Piloted Spring 2003.

- **ENVI 401: Introduction to Environmental Chemistry.** Results of CBEN research included as appropriate examples of concepts discussed in class.

### 9.4. Graduate Programs

Our graduate educational development programs encompass new course development, modifications of existing courses, development of an entrepreneurship education program, outreach to Bremerhaven University of Applied Sciences, media training, and networking/troubleshooting lunches.
9.4.1. Networking and Skill Development Lunches

During the reporting year, we inaugurated a twice-monthly series of lunch meetings for graduate students and post-docs, during which information about Centerwide events is disseminated and one or two students give a brief overview of their research via an informal chalk talk. (Kulinowski, Ausman) These meetings aim to

- Increase interactions among students working on different CBEN projects;
- Provide an opportunity for open dialog about stumbling blocks encountered in the research lab;
- Inform graduate students about upcoming CBEN events;
- Provide opportunities to hone oral presentation skills.

In general, the PIs do not attend these lunches at the request of the students so as to provide a low pressure forum for discussing problems with research projects. When a student presents a research challenge, other students with whom he or she would not normally interact often ask questions or provide suggestions. Occasionally, a meeting is used to provide information on alternate careers, develop nontechnical skills, and discuss societal implications of nanotechnology research. In May 2003, we will offer a media training seminar during one of these meetings.

9.4.2. New Graduate Courses

There are very few interdisciplinary courses in nanoscience offered by universities at the graduate level. We feel the need for graduate education in this area is particularly pressing given our interest in integrating nanoscience into the broader research community. A two-semester course on nanostructures and nanotechnology, exploring the physics of structures and devices at the nanometer scale, was offered during the 2002-2003 academic year (Natelson) as was the first semester of a two-semester course in experimental techniques for physics (Hafner). CBEN, working in conjunction with the Sloan Nanotechnology Physics program, is also planning a two-semester lecture course in nanomaterials and nanoscience that will be team taught by several faculty, including Drs. Colvin, Natelson, and Hafner. This course will consist of interlocking modules covering topics in chemistry, physics, and materials science. This lecture course, to be augmented by materials developed with the Rice Connexions program, will be offered in the fall of 2004. Ultimately, we will produce a textbook and interactive web page that will serve as a resource for courses at other institutions. Non-center physics professor Alex Rimberg developed a course on characterization and fabrication at the nanoscale with CBEN content provided by Jason Hafner. A seminar course covering recent advances in nanoscale science and engineering is planned for 2004. In addition, interactive light propagation software designed for use in courses in biomedical optics will be developed and tested at Rice and then broadly disseminated to the optics community (Drezek). The software will allow students to explore (1) relationships between subcellular biochemical and morphological structure and light scattering using a 3D FDTD (finite-difference time domain) model to computationally solve Maxwell's curl equations and (2) relationships between tissue optical properties, fiber optic delivery and collection geometries, and remitted reflectance and fluorescence signals using a Monte Carlo model.
New course offered during the reporting period are:

- **NEW: CENG 630 Chemical Engineering of Nanostructured Materials.** This lecture class gives an overview of materials with structural features on the nanometer scale. General concepts of synthesis, characterization and applications are discussed, as are advances stemming from CBEN research and/or found in the recent literature.

- **NEW: PHYS 533 Nanostructure and Nanotechnology I.** This lecture class gives an overview of physics of structures and devices at the nanometer scale. After a review of solid state physics, topics include nanostructured materials, nanoelectronics, and nanomagnetism. Emphasis on relevance of nanophysics to current and future technologies.

- **NEW: PHYS 534 Nanostructure and Nanotechnology II.** Physics of structures and devices at the nanometer scale. Topics include nanomechanics, bionanotechnology, advanced sensors and photonics. Continuation of PHYS 533.

- **NEW: PHYS 537 Methods of Experimental Physics I** (Partial CBEN content) This two-semester course familiarizes students with basic experimental techniques that are common to all academic and industrial research laboratories. Topics include lab safety, mechanical design, computer-based data acquisition and experimental control, laboratory electronics, vacuum technology, optics, thermal measurement and control, cryogenics and charged particle optics.

### 9.4.3. Graduate Courses Modified

Several pre-existing Rice University courses have been modified to include center research. These include:

- **BIOE 531: Biomaterials Engineering.** A module has been added to this course focusing on nanostructured materials.

- **BIOE 572: Fundamentals of Systems Physiology.** A new semester project has been added in which students advise a mock venture capital firm about potential investments in novel bioengineering technology. Nanoengineered optical contrast agents are used as the sample technology in class.

- **BIOE 589: Computational Molecular Bioengineering.** Results of CBEN research included as appropriate examples of concepts discussed in class.

- **BIOE 620: Tissue Engineering:** A module has been added to this course focusing on nanostructured materials.

- **CENG 603: Rheology.** Results of CBEN research included as appropriate examples of concepts discussed in class.

- **ELEC 603 Nano-Optics.** This is a seminar-based course for seniors and graduate students where a variety of currently hot areas in subwavelength optics are studied. The main topics include: near field optics, microscopy and sensing, single molecule spectroscopy, nanoparticles and their optical properties, and photonic crystals and arrays.

- **ENVI 534: Transport Phenomena and Environmental Modeling.** Examples illustrating transport of nanoparticles in the environment have been introduced.

- **ENVI 550: Applied Water Chemistry.** Results of CBEN research included as appropriate examples of concepts discussed in class.
• **ENVI 635: Advanced Topics in Water.** Results of CBEN research included as appropriate examples of concepts discussed in class.

• **MSCI 614: Principles of Nanoscale Mechanics.** Results of CBEN research included as appropriate examples of concepts discussed in class.

9.4.4. **Entrepreneurship Education**

An important element of our strategic plan is the realization that in the future many of the most important industrial collaborations for our center members will involve small startup companies. Not only are they becoming a major employer of technical PhDs, but these businesses are also becoming the route by which high-risk technologies are developed. These trends are due in some part to the bull market of the mid- to late 1990's; however, a principle that has withstood the test of time is that breakthrough technology is best developed by small groups of highly skilled, risk-taking individuals. These companies, which often involve the inventors as owners and partners, have very different concerns than larger corporations and require more active involvement of inventors. Our entrepreneurship education programs are designed to prepare our students for these job opportunities and to forge strong relationships between the center and those corporations founded by our own members.

The entrepreneurial model for business development demands that inventors have access to the resources and talent of the business community. This requires that academics interact with business professionals, ideally in a forum to present their inventions. CBEN in collaboration with the Jones Graduate School of Management provides such opportunities. The *Rice Alliance for Technology and Entrepreneurship* is the centerpiece of the University's bold initiative that joins the resources of the Wiess School of Natural Sciences, Brown School of Engineering, and Jones Graduate School of Management together with other academic units and the Office of Technology Transfer. The mission of the Rice Alliance is to promote collaboration among university researchers and technology entrepreneurs, the outcome of which is the formation of new technology firms that bring to the marketplace innovative and useful products and services. In addition to the educational activities described below, our center is collaborating with the Rice Alliance on Innovation Forums, described in section 10.3 of this report.

**Entrepreneurship Education Workshop**

To start new companies, or to interact with existing startups, academic inventors must also have a rudimentary knowledge of business practices and language. We held a two-day workshop in Entrepreneurship Education for Researchers for professors, post-docs, and graduate students. This course on the commercialization of research discoveries in science and engineering was staffed by professors in Rice’s Jones Graduate School of Management and industry participants (e.g., local entrepreneurs and investors) involved in the Rice Alliance or as industrial affiliates. The center sponsored the attendance of its own members and promising junior nanoscience researchers at other academic institutions. Topics covered in this course include intellectual property, evaluation of business plans, negotiation skills, corporate governance in new ventures, common mistakes of entrepreneurs, and university incubators. The first of these workshops was held in conjunction with our first annual conference, in the fall of 2002.
Graduate Course in Entrepreneurship for Scientists and Engineers

In keeping with our focus on creating technical Ph.D.s well informed about career options, as well as our mission to enhance our members’ knowledge of business practices, we offer a year-long graduate course entitled "Entrepreneurship for Scientists and Engineers" which is co-taught by center faculty from the science, engineering and management schools. This class has already been developed for chemistry students with the support of the Coleman and Dreyfus Foundations. First semester topics include: venture financing, intellectual property (IP), market research and organization behavior. In the 2nd semester, science and management students work together in teams to perform extensive market and IP research for one or more center inventions, culminating in the creation of a business plan for commercializing a center innovation. Five students participated in the spring semester of this course in 2002, and eight participated in the course offered in Fall 2002.

- MGMT 750/CHEM750/MSCI 750: Entrepreneurial Management for Science and Engineering. Results of CBEN research included as appropriate examples of concepts discussed in class.
- MGMT 751/CHEM 751/MSCI 751: New Venture Creation for Science and Engineering. Results of CBEN research included as appropriate examples of concepts discussed in class.

9.4.5. Hochschule Bremerhaven University of Applied Sciences

A partnership with Hochschule Bremerhaven in Bremerhaven, Germany, is being developed, wherein two Masters-level students per year would visit Rice for six months to take classes and work on projects in the center’s nanomanufacturing research. This would help fulfill their degree requirements, and will provide extra applied-sciences help in scaling up nanomaterial syntheses. Implementing this outreach project is contingent upon acquiring external funding to support the students and the interest of the nanomanufacturing facility.

9.5. Community Programs

9.5.1. Continuing Studies Course for the Public

Many of our center's members are already involved in bringing the excitement of nanoscience to the public through a "Frontiers of Science" course offered by the School of Continuing Studies. This eight-week lecture course has been enormously popular with enrollments exceeding 80 attendees. In this reporting period, our center provided speakers and materials to continue and expand this very successful program through a course titled, “Nanotechnology: What's So Big About the Science of the Very Small?”.

9.6. Increasing the diversity in CBEN’s programs

CBEN is committed to increasing the number of traditionally underrepresented students choosing to study nanoscience and engineering. Its educational outreach programs are designed to draw these groups into center activities beginning with middle school students and teachers. Tables 3 (Section 9) and 4 (Section 12) present available diversity statistics on participants in CBEN’s outreach and research activities, respectively. This section highlights the key features with breakout tables.
First the good news. CBEN is doing well at training female graduate students, especially as compared with the national and Rice averages within the natural sciences and engineering. As shown in table 9.2, women comprise 45% of CBEN-funded graduate students. This is not surprising given the fact that women are well represented within the center leadership.

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBEN Graduate Students</td>
<td>55%</td>
</tr>
<tr>
<td>Benchmarks Rice</td>
<td>71%</td>
</tr>
<tr>
<td>National</td>
<td>68%</td>
</tr>
</tbody>
</table>

Includes only natural science and engineering students

CBEN is the only Engineering Research Center and the only Nanoscale Science and Engineering Center with a female director (Colvin). Two of the three theme leaders, Drs. Colvin and West, are women, as is Dean of the Wiess School of Natural Science and center researcher Dr. Kathy Matthews.

CBEN is also doing well at drawing underrepresented groups into its K-12 activities and is showing promise in its NREU program. (See Table 9.3.) The high school teachers who have participated in our three-phase training program and workshop draw heavily from the diverse populations of the Houston (56% Hispanic, 31% African American, 10% White, and 3% Asian) and United (95% Hispanic) ISDs.

Table 9.3 CBEN students and outreach participants by ethnic diversity

<table>
<thead>
<tr>
<th>NA</th>
<th>PI</th>
<th>AA</th>
<th>C</th>
<th>A</th>
<th>NP</th>
<th>Hispanic</th>
<th>Other non-US</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBEN Undergrad Students</td>
<td>0%</td>
<td>0%</td>
<td>8%</td>
<td>67%</td>
<td>8%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Benchmarks Rice</td>
<td>1%</td>
<td>0%</td>
<td>6%</td>
<td>52%</td>
<td>17%</td>
<td>10%</td>
<td>11%</td>
</tr>
<tr>
<td>National</td>
<td>1%</td>
<td>0%</td>
<td>6%</td>
<td>74%</td>
<td>11%</td>
<td>2%</td>
<td>6%</td>
</tr>
<tr>
<td>CBEN Outreach Participants</td>
<td>0%</td>
<td>10%</td>
<td>10%</td>
<td>16%</td>
<td>6%</td>
<td>10%</td>
<td>48%</td>
</tr>
<tr>
<td>Benchmarks HISD</td>
<td>0%</td>
<td>0%</td>
<td>31%</td>
<td>10%</td>
<td>3%</td>
<td>0%</td>
<td>56%</td>
</tr>
<tr>
<td>CBEN Graduate Students</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>48%</td>
<td>9%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Benchmarks Rice</td>
<td>0%</td>
<td>0%</td>
<td>2%</td>
<td>36%</td>
<td>6%</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>National</td>
<td>0%</td>
<td>0%</td>
<td>3%</td>
<td>51%</td>
<td>7%</td>
<td>4%</td>
<td>3%</td>
</tr>
</tbody>
</table>

NA = Native American; PI = Pacific Islander; AA = African American; C = Caucasian; A = Asian; NP = Not provided

Given the demography of the HISD student population we expect this diversity to be matched or exceeded in the high school student academy program. We launch our NREU program this summer and it appears that our targeted approach to recruitment, which includes visits to regional schools and national meetings of groups such as the National Society of Black Physicists has paid off. At the time of this report, we had received acceptances from four African-American females, two Caucasian females, and two Hispanic males. These students are not included in these tables this year, but will be included in next year’s annual report.
CBEN has developed a long-term strategy for improving our student diversity statistics; Table 9.3 shows our current participants with benchmarks to the university and national averages. While CBEN has good diversity representation when we count all affiliated CBEN graduate students, if we consider only our directly funded graduate students (as shown in Table 9.3) we find poor representation of minorities. However, our success at involving diverse undergraduate students in our research is a good sign that we can improve upon these statistics in the future.

Improvements in minority representation are not quickly achieved; for that reason we have a long-term plan for increasing the number of underrepresented students entering graduate school in science and engineering, whether at Rice or another institution. Our NREU program this year alone will provide eight students with invaluable research experience. Over time, by mentoring a diverse population of students in our NREU program, CBEN will expand the population of students interested in graduate school. Also, this year CBEN has worked with departments to improve their recruitment of graduate students generally. We have begun and will continue to reach out to the incoming graduate students from underrepresented groups by offering them financial support to do CBEN research and affiliation with the AGEP program (see Section 9.3.1) during the summer before they begin graduate work. This kind of support can reduce attrition caused by the often difficult adjustment to graduate work.

9.7. References Cited
# 9.8. Summary of CBEN Educational Outreach Activities

## Course for K-12 Teachers

<table>
<thead>
<tr>
<th>Teachers</th>
<th>Date</th>
<th>CBEN participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHEM 570</td>
<td>15 Spring</td>
<td>Ausman*, Harcombe, Ma, Wiesner, Stemmer, Dustin James (Tour staff scientist), Tomson, West, McHale, Virginia Davis (Pasquali grad student), Yakobson, Mikos, Colvin</td>
</tr>
<tr>
<td>CHEM 570</td>
<td>10 Spring</td>
<td>Kulinowski*, Colvin, West, Ma, James, Ausman, Lamminen (NanoKids), Drezek, Mikos, Hafner, Wiesner</td>
</tr>
</tbody>
</table>

*Indicates Course Leader

## Courses for Undergraduate Students

<table>
<thead>
<tr>
<th>Topic</th>
<th>Students</th>
<th>Date</th>
<th>New/Modified</th>
<th>CBEN participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIOE 441 Advanced Bioengineering Lab</td>
<td>11</td>
<td>Fall 2002</td>
<td>Modified</td>
<td>West, Drezek</td>
</tr>
<tr>
<td>CHEM 373 Fullerene Lab</td>
<td>17</td>
<td>Fall/Spring 2002</td>
<td>Existing</td>
<td>Weisman</td>
</tr>
<tr>
<td>CHEM 375 Nanochemistry Lab</td>
<td>9</td>
<td>Fall 2002</td>
<td>NEW</td>
<td>Colvin</td>
</tr>
<tr>
<td>ENVI 401 Intro Environmental Chemistry</td>
<td>16</td>
<td>Fall 2002</td>
<td>Modified</td>
<td>Tomson</td>
</tr>
<tr>
<td>MSCI 415 Ceramics and Glasses</td>
<td>11</td>
<td>Spring 2002</td>
<td>NEW</td>
<td>Stemmer</td>
</tr>
</tbody>
</table>

## Courses for Graduate and Advanced Undergraduate Students

<table>
<thead>
<tr>
<th>Topic</th>
<th>Students</th>
<th>Date</th>
<th>New/Modified</th>
<th>CBEN participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIOE 531 Biomaterials Engineering</td>
<td>31</td>
<td>Fall 2002</td>
<td>Modified</td>
<td>West, Mikos</td>
</tr>
<tr>
<td>BIOE 572 Fundamental of Systems Physiology</td>
<td>15</td>
<td>Spring 2003</td>
<td>Modified</td>
<td>Drezek</td>
</tr>
<tr>
<td>BIOE 589 Computational Molecular Bioengineering</td>
<td>8</td>
<td>Fall 2002</td>
<td>Modified</td>
<td>Ma</td>
</tr>
<tr>
<td>BIOE 620 Tissue Engineering</td>
<td>27/27</td>
<td>Spring 2002/2003</td>
<td>Modified</td>
<td>Mikos</td>
</tr>
<tr>
<td>CENG 603 Rheology</td>
<td>8</td>
<td>Fall 2002</td>
<td>Modified</td>
<td>Pasquali</td>
</tr>
<tr>
<td>CENG Chemical Engineering of</td>
<td>16/18</td>
<td>Spring</td>
<td>NEW</td>
<td>Wong</td>
</tr>
<tr>
<td>Course Code</td>
<td>Course Title</td>
<td>Students</td>
<td>Date</td>
<td>CBEN participants</td>
</tr>
<tr>
<td>-------------</td>
<td>--------------------------------------------------</td>
<td>----------</td>
<td>------------</td>
<td>--------------------------------------------</td>
</tr>
<tr>
<td>ELEC 603</td>
<td>Nano-Optics</td>
<td>8</td>
<td>Fall 2002</td>
<td>Modified Halas</td>
</tr>
<tr>
<td>ENVI 534</td>
<td>Transport Phenomena and Environmental Modeling</td>
<td>6</td>
<td>Fall 2002</td>
<td>Modified Wiesner</td>
</tr>
<tr>
<td>ENVI 550</td>
<td>Environmental Organic Chemistry</td>
<td>6</td>
<td>Spring 2003</td>
<td>Modified Tomson</td>
</tr>
<tr>
<td>ENVI 635</td>
<td>Advanced Topics in Water</td>
<td>3</td>
<td>Fall 2002</td>
<td>Modified Tomson</td>
</tr>
<tr>
<td>MGMT 750</td>
<td>Entrepreneurial Management for Science and Engineering</td>
<td>8</td>
<td>Fall 2002</td>
<td>Existing Barron</td>
</tr>
<tr>
<td>MGMT 751</td>
<td>New Venture Creation For Science and Engineering</td>
<td>5</td>
<td>Spring 2002</td>
<td>Existing Barron</td>
</tr>
<tr>
<td>PHYS 533</td>
<td>Nanostructure and Nanotechnology I</td>
<td>22</td>
<td>Fall 2002</td>
<td>NEW Natelson</td>
</tr>
<tr>
<td>PHYS 534</td>
<td>Nanostructure and Nanotechnology II</td>
<td>10</td>
<td>Spring 2003</td>
<td>NEW Natelson</td>
</tr>
<tr>
<td>PHYS 537</td>
<td>Methods of Experimental Physics I</td>
<td>20</td>
<td>Fall 2002</td>
<td>NEW Hafner, Killian (non-CBEN)</td>
</tr>
<tr>
<td>PHYS 539</td>
<td>Characterization and Fabrication at Nanometer Scale</td>
<td>10</td>
<td>Fall 2002</td>
<td>Modified Hafner</td>
</tr>
</tbody>
</table>

Courses for the Public or General Audiences

<table>
<thead>
<tr>
<th>Topic</th>
<th>Students</th>
<th>Date</th>
<th>CBEN participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rice Alumni Nanotechnology Basics</td>
<td>50</td>
<td>Feb 2002</td>
<td>Colvin</td>
</tr>
<tr>
<td>Rice Alumni Medical Applications of Nanotechnology</td>
<td>50</td>
<td>Feb 2003</td>
<td>Lee Hirsch (West grad student)</td>
</tr>
</tbody>
</table>
### Workshops and Campus Visits

<table>
<thead>
<tr>
<th>Audience</th>
<th>Topic</th>
<th>Teachers</th>
<th>Students</th>
<th>Date</th>
<th>CBEN participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>United ISD (Laredo TX) HS teachers</td>
<td>3-day accelerated version of CHEM 570</td>
<td>11</td>
<td>0</td>
<td>June 2002</td>
<td>Ausman, Virginia Davis (Pasquali), Kolomeisky, Mikos, Colvin, Harcombe, Wiesner, West</td>
</tr>
<tr>
<td>Entrepreneurship Education</td>
<td>Taking discoveries from the lab to the market</td>
<td>0</td>
<td>60</td>
<td>September 2002</td>
<td>Currall, other Jones School faculty</td>
</tr>
<tr>
<td>United ISD (Laredo TX) HS Students</td>
<td>Daylong campus visit, tours, talks on nanotechnology</td>
<td>4</td>
<td>48</td>
<td>November 2002</td>
<td>Kulinowski, Colvin, Natelson, Raj Wahi (Colvin grad student), Erik Haroz (Smalley undergrad) Tomson, Tour, Smalley, Drezek</td>
</tr>
</tbody>
</table>

### Lectures on Nanotechnology and Careers for K-12 Teachers and Students

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<tr>
<th>Lectures</th>
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<th>CBEN participants</th>
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<td>100</td>
<td>600</td>
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<td>Richard Smalley</td>
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<td>Future Problem Solvers—Spring ISD</td>
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<td>30</td>
<td>November 2002</td>
<td>Kevin Ausman</td>
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| Future Problem Solvers Mentors—  
| Spring ISD | 20 | 0 | November 2002 | Jason Hafner |
| National Honor Society Address  
| Duchesne Academy  
| (*Students and parents) | 0 | 100* | November 2002 | Kathy Matthews |
| Westfield HS | 1 | 30 | November 2002 | Kevin Ausman |
| Future Problem Solvers—Pearland ISD | 1 | 20 | January 2003 | Kristen Kulinowski |

**Lectures on Nanotechnology for Undergraduates, Graduate Students and Post-docs**

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**Lectures on Nanotechnology for the Public**

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</table>
10. Outreach and Knowledge Transfer

Should the public fear nanotechnology? Responding to that question has redefined “knowledge transfer” at CBEN this year. We believe our activities in this area are central to ensuring long-term public acceptance of nanomaterials and nanotechnologies, an issue highlighted in our strategic plan. This acceptance could be in jeopardy as nanotechnology’s “yuck index” rises, due both to the revival of old debates and the emergence of new controversies. As the only NSF center charged with assessing the environmental impact of nanomaterials, CBEN’s efforts have been thrust into the public spotlight. In response to the media barrage, we developed an aggressive communications strategy to introduce hard data into this emotional debate (See sections 10.1 and 10.2). As a result of these strategies, CBEN has become the primary academic source for journalists and policy makers concerned about the public perception of nanotechnology. Our outreach to these non-traditional communities will only increase over the next year as the first toxicology studies of nanomaterials become available.

More traditional knowledge transfer activities will continue as well. Our industrial outreach programs develop partnerships with large corporations as well as encourage the entrepreneurial activities of our faculty members (See sections 10.3, 10.4). We have a successful program in place to educate our researchers about issues related to transferring their discoveries to the marketplace. This includes an entrepreneurship workshop for academics, innovation forums, and courses for graduate students and post-docs. Many of these programs are described under educational outreach, in section 9.4.4. CBEN has also sponsored workshops and conferences in bio-nano-enviro topics for researchers and industrial partners, as described in section 10.5.

10.1. Outreach to media professionals

10.1.1. Highlights

- 171 mentions of CBEN in the popular press (over fifty media interviews)
- Feature articles in the magazines Technology Review and smalltimes (cover)
- Professional media training for several CBEN PIs and administrators in November 2002; future training planned for graduate students and post-docs
- CBEN hosting of three CASE Media Fellows in December 2002; future CASE Fellows include reporters from the New York Times and smalltimes
- Web page resource for journalists containing up-to-date information and links to prior articles

10.1.2. Motivation

The public will play a critical role in either accepting or rejecting commercialized nanotechnologies. One need only examine the backlash against genetically modified foods to see that shutting the public out of dialogs on technology risk can have disastrous consequences for the development of a nascent industry. CBEN seeks to avoid a hostile response to the fledgling nanotech industry by inviting the public to question and debate its potential impacts during these early stages. In an emerging area such as nanotechnology, the public mostly shapes its opinion around the information conveyed by the mass media; thus, in order to deal with issues...
of public acceptance of nanotechnology we must develop and disseminate a message in that arena. Public engagement in these debates is not only healthy for, but critical to, the future success of the nanotechnology enterprise. For all but the most eminent academic researchers, this kind of leadership is only possible under the aegis of a Center. We have developed a message, and taken steps to educate both journalists and nanotechnologists in the public policy of emerging technologies.

10.1.3. The public message

The recent backlash against nanotechnology provides an important context for our message development. An old and persistent discussion about nanotechnology is the ‘gray goo’ scenario, first posited 16 years ago by scientist and inventor Eric Drexler in his book *Engines of Creation* [7] and echoed in a recent article by Sun Microsystems’ CEO Bill Joy [8]. Briefly stated, the gray-goo scenario cautions that nanobots may uncontrollably self-replicate and eventually wipe out life on Earth. Michael Crichton’s recent novel, *Prey*, [9] essentially fictionalizes the gray-goo scenario by describing swarms of predatory, intelligent, organized nanobots that turn on their human creators. Most nanotechnologists agree that such nanobots are decades away, and the perceived fears are nowhere near being realized. More significant issues, relevant to CBEN, are the environmental concerns about nanomaterials. Early in 2002, ETC, an activist organization based in Canada, drew widespread attention from the media and policymakers for two reports that call for a moratorium on the production of new nanomaterials until regulatory bodies such as the Environmental Protection Agency and the Food and Drug Administration demonstrate they are benign. [10, 11]

While CBEN cannot speak for everyone in the center, much discussion and debate has gone into these questions of nanotechnology risks and what message, if any, CBEN should promote. As the only federally funded center with an emphasis on nanotechnology and the environment, we realized the importance of developing a documented policy position on these issues. Vicki Colvin’s recent testimony before the U.S. House Committee on Science, a copy of which can be found on our website, sums up CBEN’s position. In brief, we do not support a moratorium on nanotechnology development and do not believe the gray-goo scenario will come to pass. Nevertheless, we do believe that it is simplistic to assume that all nanotechnology will provide only beneficial impacts on society. The reality is that the consequences of a massive scaleup of nanotechnology research and development are unknown. Too little data on toxicology and environmental impact exist to make definitive statements about the benign nature of nanomaterials. CBEN has played a leading role in highlighting the need for more public support of such studies. Finally, questions about emerging technologies risks must be balanced by the known benefits. We argue that given the known advantages of nanotechnology, it is unwise to limit its development based on unknown and ill-defined risks.
10.1.4. Well-informed journalists and educational articles

We believe it is important to communicate our policy position widely so that stakeholders from the technical, legislative, regulatory, and public communities are kept well informed. CBEN was mentioned in the general print media at least 171 times between February 1, 2002 and March 15, 2003 in publications including the *New York Times*, *U.S. News and World Report*, *Nature*, *Houston Chronicle*, *smalltimes*, *Wired*, *Science News*, *Associated Press*, *Technology Review*, *United Press International*, *Foresight Update*, *Chemical and Engineering News*, *Yahoo News*, and *Physics Today*. Of these, 35 are unique items and 130 are reprints of a September 2002 Associated Press article on the benefits of nanotechnology to the environment. Of the unique items, 19 articles dealt with the growing controversy over the environmental and health impacts of nanotechnology. The others described CBEN research, CBEN’s role in nanotechnology business development, and CBEN personnel. In efforts to keep the nanotechnology and larger communities informed about the important policy issues facing the field, we have posted a website where links to many of these articles can be found: http://www.ruf.rice.edu/~cben/Media.shtml.

In addition, CBEN researchers met with three fellows of the Council for Advancement and Support of Education (CASE) in December 2002. Now in its twelfth year, the CASE Media Fellowship program offers opportunities for journalists to learn about new scientific and technological developments in depth from the researchers making the discoveries. Dan Vergano of *USA Today*, freelance journalist Stephen Leahy, who has written for *New Scientist* among many other publications, and Eric Berger of the *Houston Chronicle* spent two days at Rice learning about biomedical and environmental applications of nanotechnology. Though CBEN research was the focus of their Fellowship, their costs were not covered by CBEN funds but were borne by Rice University. We plan to host another group of CASE Fellows in May 2003 and have received commitments from Kenneth Chang (*New York Times*), Alex Witze (*Dallas Morning News*) and Candace Stuart (*smalltimes*).

10.1.5. Training and motivating researchers to interact with the media

The ultimate sources for science journalists are the researchers themselves; it is thus critical to equip our center members, students and faculty alike, with communication skills to prepare them for media interviews. Effective interaction with the media is a valuable skill for both faculty members and their students and post-docs as it enables them to better communicate the results of their research to the general public. Such situations can be very different from the more structured teaching environments familiar to academics. There is also the chance that interviews can be hostile, especially in the topical area of nanotechnology regulation. Several CBEN PIs and directors underwent a daylong media training session in November 2002 run by Susan Peterson Productions Inc. In May 2003, CBEN and the Rice Media Relations office will hold a media training seminar for graduate students and post-docs.

Equally important is motivating researchers to take time out of their busy schedules to interact with journalists. We find that most researchers are baffled about the public’s fears of nanotechnology, and skeptical that these concerns could influence the development of the area. Many of the policy talks given by CBEN representatives in this area use illustrative examples from other new technologies (e.g., the human genome project and genetically modified foods) to
show how public perception, and the media stories that influenced it, affected the direction of basic research in those areas.

10.2. Government Relations and Public Policy

While the media may influence public opinion of nanotechnology, it is also necessary to inform government leaders and public policymakers, who have more direct influence on its development. Think tanks, such as the Woodrow Wilson International Center for Scholars (WWIC), can bring policy issues to the attention of members of Congress and executive branch officials, who ultimately control both the amount of public funding of nanotechnology and the manner in which the funds are disbursed. CBEN has been proactive in communicating with these groups about the importance of continued research in basic nanotechnology as well as its societal impacts.

10.2.1. Highlights

- **Policy speech** given by Vicki Colvin at the Woodrow Wilson International Center for Scholars, Washington DC, November 2002: “Nanotechnology and the Environment”
- **ACS Symposium** organized by Vicki Colvin on “Health and Biological Effects of Nanomaterials”, March 2003

Government outreach has taken on a special meaning as both houses of the U.S. Congress debate new nanotechnology legislation. In February 2003, U.S. Representatives Sherwood Boehlert (NY-23) and Mike Honda (CA-15) introduced H.R. 766, *The Nanotechnology Research and Development Act of 2003*, which authorizes a federal nanotechnology research and development (R&D) program in statute thus assuring stable, long-term support. The bill also authorizes appropriations for nanotechnology R&D in those agencies within the Science Committee’s jurisdiction that currently participate in the National Nanotechnology Initiative. A companion bill, S. 189, has been introduced in the Senate by Senator Wyden and Senator Allen. H.R. 766 supports the President’s initiative but adds review and oversight mechanisms to assure that new funds are used in the most effective manner possible. The bill also addresses a number of the issues raised by the National Academy of Sciences and other outside experts. [12]

CBEN has been an important resource for Congressional staffers authoring this and related legislation; we have provided
information about CBEN’s nanotechnology research and policy positions. The three key CBEN personnel driving these efforts are Vicki Colvin, Kristen Kulinowski and Richard Smalley. Kulinowski responded to requests for information by Rep. Chris Bell (TX-25) regarding his amendment to H.R.238: The Energy Research, Development, Demonstration, and Commercial Application Act of 2003 which recommended that, insofar as possible, research on societal impacts be integrated with nanotechnology research and development in the Department of Energy. On April 2, 2003 the Science Committee adopted the Bell amendment. A similar amendment will likely be offered to H.R. 766. The Science Committee has shown its strong support for societal impacts research by including specific language in H.R. 766 and convening a special hearing on these provisions on April 9, 2003. Vicki Colvin testified at this hearing.

10.3. Entrepreneurship Promotion

We believe that, as with biotechnology, many of CBEN’s technologies will find commercialization through entrepreneurial ventures centered on our own academic inventions. We thus have several programs designed to enhance and improve academic-entrepreneurial activities. Many of these include educational efforts for graduate students and faculty that are described in section 9.4.4. Here we focus on the portion of our entrepreneur program that aims to develop new business.

10.3.1. Highlights

- **Two Nanotechnology Innovation Forums** held
- **Two start-up companies formed** by CBEN personnel

In this reporting period, CBEN, in partnership with the Rice Alliance for Technology and Entrepreneurship, held two Nanotechnology Innovation Forums. The Rice Alliance is a Rice community resource that, through its Innovation Concept Forums, brings together a talent pool of potential collaborators in entrepreneurship ventures. These include scientists and engineers with technical innovations at various stages of development, venture capitalists, investment bankers, local entrepreneurs, faculty members, recent MBA graduates, and students. These forums are structured around presentations by inventors, who receive feedback on their innovations and business plans from a panel of experts.

The first of these two Nanotechnology Innovation Forums was held on March 1, 2002. Keynote speaker Dr. Jack Gill, general partner of Vanguard Ventures, provided an update on the state of global ventures. Five business concepts or early-stage ventures were presented to an audience of 240. These presentations were:

- Tim Belton: Molecular Electronics Corporation – Commercializing Molecule-Based Electronic Devices
• Dr. Jennifer West: NanoSpectra BioSciences – Nanotechnology for Optical Therapeutics
• Dr. Mark Wiesner: Membrane Products Corporation – Nano-Structured Media for Environmental and Industrial Separation
• Dr. John Margrave: Designer Nanotubes – New Materials for Energy Storage and Unique Polymer Composites
• Dr. Michael Wong: NanoCapsules – Hollow Microspheres in Sixty Seconds

The second Forum was held on January 24, 2003, to a standing-room only crowd of nearly 250 attendees. Keynote speaker Warren Packard, Managing Director of Draper Fisher Jurvetson, discussed, “Heisenberg, Darwin, and the Science of the Very Small – Quantum Physics and Natural Selection Meet the Market.” Five business concepts or ventures were presented:

• Dr. Stephen Wilson: C Sixty Inc. – Fullerene Exploration and Exploitation
• Dr. Joe Hughes: Environmental Applications of Nanomaterials – the Use of Nano-Engineered Materials to Address Environmental Needs
• Dr. Felipe Chibante: Bucky USA – Marketing Carbon Nanomaterials
• Dr. Daniel Mittleman: PicoRisks – Making Your Risks Smaller than Nano
• Chris Coker: Oxane Materials – Nanostructured Membranes and Nanomaterials

Two of the companies listed above, NanoSpectra BioSciences and Oxane Materials (now called NewCyte), are ventures that resulted in part from CBEN-supported research.

10.4. Industrial Affiliates Program

10.4.1. Highlights

• Legal agreement for industrial partnerships approved by Rice Office of Technology Transfer
• Marketing strategy for industrial affiliates defined
• Over fifty industry visits by CBEN personnel

We have just begun to pursue relationships with established industries through our industrial affiliates programs. This program focuses on forming partnerships with companies interested in CBEN research or other activities. Much effort over the past year has gone into defining the boundaries of the academic-industrial partnerships. Most critically, we have authored, in partnership with the Rice Office of Technology Transfer, an agreement for sharing intellectual property with our industrial partners. Such a document was essential before starting recruitment for our affiliates program. We have also defined the benefits of our affiliates program in consultation with center members, Rice development officers and industrial partners. With five membership levels ranging from ‘advisor’ to ‘sponsor’, the program gives both us and our partner companies great flexibility in defining an appropriate relationship. CBEN members have been invited to visit several large corporations with the express purpose of exploring industrial partnerships; CBEN has also hosted numerous visits from interested industrial partners on the Rice campus (see tables in section 10.7).
10.5. Centerwide events

CBEN sponsors and co-sponsors numerous local and national events in order to disseminate center research, build relationships among its members, and increase the interactions of CBEN with other academic institutions. Our annual conference, Nanodays is held in the fall, and in 2002 featured talks from CBEN researchers and eight invited keynote speakers. Associated with this conference is the annual poster session for CBEN students. In 2003, Nanodays is slated to be held in October and will incorporate a meeting of the CBEN advisory board.

In December 2002, CBEN coordinated the NSF international workshop, “From Nanomaterials to Nanotechnology,” held in Boston, MA. Organized by CBEN director Dr. Vicki Colvin, this workshop brought together over 50 researchers from the United States and Europe to exchange information and ideas for collaborative proposals.

The ‘nano-vivo’ summit in early 2003 provided a forum for CBEN researchers to share their expertise and technologies with medical professionals from the nearby Texas Medical Center. In addition to these formal events, CBEN sponsors bimonthly meetings for its PIs to discuss ongoing research activities in addition to the graduate student meetings described in the educational outreach section 9.4.1.

10.6. References Cited

10.7. Summary of CBEN Knowledge Transfer and Outreach

Interactions with elected officials

<table>
<thead>
<tr>
<th>Event</th>
<th>Official or Hearing</th>
<th>Who</th>
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<tr>
<td>Briefing on CBEN research and policy positions</td>
<td>Senator Ron Wyden (OR) and U.S. Reps. Chris Bell, John Culberson (TX-07), Sheila Jackson Lee (TX-18), Mike Honda (CA-15), Washington DC</td>
<td>Kulinowski</td>
<td>Feb 2003</td>
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<td>Briefing on CBEN research and policy positions</td>
<td>Rep. Chris Bell, Rice University campus visit</td>
<td>Kulinowski, Smalley, Matthews, Burrus</td>
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Policy Symposia

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<td>“Health and Biological Effects of Nanomaterials”</td>
<td>225th National American Chemical Society Meeting, New Orleans LA</td>
<td>Colvin</td>
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<td>Inaugural Conference</td>
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Policy documents

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### Policy seminars on nanotechnology

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<td>“Environmental Impact of Nanomaterials”</td>
<td>NSF International Workshop on Societal Implications of Nanotechnology, Lecce Italy</td>
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<td>“Environmental Impact of Nanomaterials”</td>
<td>Environmental Protection Agency (EPA), Washington DC</td>
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<td>“The Environmental Implications of Nanotechnology”</td>
<td>NanoSpace 2002 Keynote Speech, Galveston TX</td>
<td>Ausman</td>
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<td>“CBEN”</td>
<td>Lord Sainsbury, Parliamentary Under Secretary of State for Science, United Kingdom, Rice University</td>
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<td>“The Environmental Implications of Nanotechnology”</td>
<td>Nanotech 2002, Houston TX</td>
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<td>“Nanotoxicology: What to Expect?”</td>
<td>EPA and National Institute for Environmental Health Sciences Meeting, Durham NC</td>
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<td>“CBEN”</td>
<td>British Nanomission, Rice University</td>
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<td>“Nanotechnology and Society: Avoiding the Wow to Yuck Trajectory”</td>
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<td>“Nanotechnology”</td>
<td>Colloquium on Science and Technology in Support of Army Transformation, Washington DC</td>
<td>Smalley</td>
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<td>“Nanotechnology, the Science and Technology Workforce, Energy and Prosperity”</td>
<td>President’s Council of Advisors on Science and Technology, Washington DC</td>
<td>Smalley</td>
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<td>Nanotechnology Innovation Forum I</td>
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<td>Greater Houston Partnership</td>
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<td>Nanotechnology Innovation Forum II</td>
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<td>Nanotechnology Colloquium Bi-weekly Discussion Group</td>
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**New Companies Started**

<table>
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<tbody>
<tr>
<td>NanoSpectra Biosciences</td>
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<tr>
<td>NewCyte</td>
<td>Wiesner, Barron</td>
</tr>
</tbody>
</table>
11. Shared Experimental Facilities

CBEN has strengthened the Rice infrastructure for nanoscience and engineering and leveraged its funding internally to create an organized facility for equipment management. Over the past sixteen months ~ $1.3M from CBEN matching monies has been expended on equipment in support of center research. These purchases build on an extensive set of instrumentation purchased since 1996 using $5M of private donor money given to Rice’s Center for Nanoscale Science and Technology (CNST). This equipment, along with the newer CBEN purchases, is housed in the CNST building. Completed in 1997 it has a three thousand square foot shared equipment space referred to as ‘the slab’ because of its low vibration characteristics. With these resources, CBEN has, through partnerships with other centers across Rice and the university’s administration, found a robust and lasting solution to the problem of shared equipment management. The highlights of our efforts towards building shared experimental equipment:

- **Strategic equipment purchases**, to address critical CBEN needs.
- **Stewardship of the shared equipment authority**, a faculty-run management organization for shared equipment across Rice.
- **Two PhD technical staff** for training and maintenance of shared equipment.

11.1. Existing equipment

Rice University laid the groundwork for our center’s experimental facilities with their 1993-6 fundraising campaign for nanoscience equipment. Our new nanoscience and technology building, Dell Butcher Hall, houses a state-of-the-art equipment room designed for vibrational and electrical isolation. Equipment located in this facility includes a Phillips environmental SEM, a JEOL electron beam lithography system, two Digital Instruments Atomic Force Microscopes, an Omicron low temperature UHV-STM, and a variety of smaller items such as sputter- and spin-coaters. Other instrumentation located elsewhere on campus and available for common use includes a JEOL 2010cx transmission electron microscope, a Nicolet FTIR microscope, a high-resolution X-ray diffractometer and an ISA Raman microscope. Additionally, the Texas Center for X-ray Crystallography is housed at Rice and manages two single-crystal, one powder, and one small-angle X-ray diffractometers.

11.2. Strategic equipment purchases

Approximately $1.3M of internal cost-sharing funds has been expended for CBEN equipment purchases. A new scanning electron microscope is now available to allow for the imaging of biological materials, and nanofiltration and bone replacement polymers. An upgrade to Rice’s ten-year old transmission electron microscope has made student training more effective. This upgrade retrofits the microscope with a digital camera and software for routine high-resolution imaging and makes hands-on demonstrations of microscope procedures much more effective. CBEN purchased two analytical instruments, atomic emission spectrometers, for the characterization of environmental processes of nanomaterials. CBEN also leveraged $433,377 of its equipment money with a SUR grant from IBM for a state-of-the-art parallel supercomputer with multiprocessor nodes running in shared-memory SEP configuration through high-speed switches (see section 18). Most of the parallel machines at Rice are obsolete or dedicated to specific groups. This facility supports both the memory applications (e.g. the PDE codes of Pasquali and Zygourakis), and the massively-parallel MPI codes (e.g. the molecular
dynamics codes of Ma and Yakobson and the quantum mechanical simulations of Scuseria and Yakobson). Finally, the balance of roughly $280,000 was used toward the purchase of a second transmission electron microscope. This system, which is also a JEOL 2010, has been optimized for use as a cryogenic TEM. **Dr. Jane Tao**, an assistant professor in biology and an expert in cryo-TEM, has been brought into CBEN to develop cryo-TEM for use in both theme 1 and 2 projects. This purchase addresses directly the critical need for better characterization of bio-nanoconjugates highlighted in our strategic plan.

### 11.3. Campus Initiative in Equipment Management: The SEA

The maintenance and management of shared equipment is a serious organizational challenge at any university; typically departments are the only entity given funds for such purposes, leaving shared equipment without any resources once the acquisition dollars have been spent. The obvious solution of levying user fees to offset maintenance costs brings up a different set of organizational concerns. For most shared equipment there is no clear authority in charge of setting and spending user fees, and there is no central administrative organization to keep records of equipment costs and to process and request user fees. University administrators are reluctant to cede control of such activities to independent faculty. These problems undermine the overall effectiveness and value of shared equipment in research.

In order to solve these institutional issues CBEN successfully advocated for Rice University to transfer control of all shared equipment, roughly twenty instruments across campus, to a faculty oversight committee. This has resulted in the formation of a new campus organization called the **Shared Equipment Authority (SEA)**. Chaired by center director, Dr. Vicki Colvin, SEA administers money raised from user fees on equipment, sets user fees on a quarterly basis, and makes recommendations concerning strategic instrument acquisitions. While SEA is denoted as a CBEN initiative in internal Rice documentation, its membership is not limited to CBEN participants. Bimonthly meetings throughout the fall and winter have tackled many important policy issues. A web page describing SEA and its current projects and instrument portfolio can be found at [http://www.sea.org](http://www.sea.org).

Last year SEA was successful at securing additional university funds to allow for the hiring of a dedicated administrator and technician, and increased funding for shared infrastructure is expected this year. These staff positions do not count as part of CBEN match monies, but they are leveraged from the investment CBEN has made in this critical area. With this new staff, SEA has implemented web-based management tools, including on-line manuals, sign-up sheets and checkout protocols which have been well received by the many CBEN students who rely on the instrumentation for their research.

An important issue for this organization is the strategy for cost recovery. SEA has projected that only 25% of the costs for shared equipment at Rice can be recovered by direct
billing of internal and external academic users if hourly fees are kept at the average nationwide values. SEA faculty are seeking federal monies to help sustain shared equipment infrastructure through proposals for the National Nanotechnology Infrastructure Network (NNIN). Also, SEA is working with Rice’s Office for Development to identify individuals and private foundations who would donate money for these purposes. The presence of a NSF center in nanotechnology is good leverage for this type of fundraising, and many of the same people who contributed to the highly successful nanocampaign in 1993-6 are being approached again. However, to maintain faculty confidence in SEA and its management, the university has agreed to maintain the technical staff positions associated with CBEN after the funding cycle of the center, and has committed to sustaining shared equipment infrastructure at Rice as needed.

We hope in the next year to increase the usage of all SEA instruments through a series of new training sessions that recognize the needs of ‘exploratory’ users. To address their issues, we are designing weekend workshops that illustrate how key instruments may be used to solve problems in certain disciplines. For example, Hafner will lead ‘Atomic Force Microscopy in Biology and Bioengineering’. A similar workshop in electron microscopy (Guo), and FTIR and Raman microscopy will also be developed. It is our intention that these workshops will motivate researchers to invest the time required to become independent and successful users. If instrument use can be doubled, then cost recovery through user fees will contribute to a larger fraction of maintenance costs.

11.4. Full-time staff for student training and equipment maintenance

Two permanent, full-time technical staff positions were hired during Y02 to oversee experimental equipment: microscopist Dr. Wenhua Guo and structural biologist Dr. Sean Moran. These staffers (See Figure 11-2) share responsibility for instrument maintenance, serve as the contact point for repairs, and offer training to students, post-doctoral associates, and visiting scientists. We have seen dramatic improvements in equipment usage as these staff people have helped students and post-docs use instruments more efficiently. Clearly, well-trained instrument users handle these expensive and sensitive instruments both more effectively and more frequently. For example, our TEM usage has increased from 80 hours a month to over 200 since Dr. Guo started managing and training users. Matching monies have also made available a system administrator for our investment in computational resources. This person is responsible for configuring the machine, adding users, doing periodic upgrades, maintaining a web page for the facility with information on the queuing system and software manuals, and delivering periodic training seminars for new users. In Y03 we anticipate that these staff positions will become fully shared with SEA in anticipation that their ultimate support will derive from university and not federal funds.
12. Personnel and Management

In the past eighteen months, CBEN has identified its entire staff and these personnel have begun active administration of the center’s outreach and research programs. CBEN has a physical home located between the engineering and natural science schools on the Rice campus. This 1154 square-foot space provides office space and meeting areas for CBEN staff.

While our management structure remains virtually identical to that outlined in our proposal, there have been several changes in personnel over the past twelve months. First, as was proposed and accepted during our last site visit, Dr. Vicki Colvin assumed directorship of the center in the fall of 2002. Dr. Rick Smalley maintains an active management role as founding director. Second, Dr. Mark Wiesner has accepted a position as director of the Rice Environment and Energy Systems Institute (EESI) and Dr. Joe Hughes is now theme leader for our environmental thrust. Finally, our executive director for education and public policy, Dr. Kristen Kulinowski, joined the center in September of 2002.

CBEN management is organized around four activities: strategic planning, resource allocation, assessment and operations.

### Figure 12.1 CBEN Management Structure

#### 12.1. Strategic Planning

The strategic planning process involves the entire center, and occurs every January. Our senior advisor, Dr. Neal Lane, and founding director, Dr. Rick Smalley, are important participants in this long-range planning process in that they work in collaboration with the director, Dr. Vicki Colvin, to write an initial draft of the strategic plan. Dr. Lane’s extensive past experience as White House science advisor and the Director of NSF provides an important
perspective for our planning process. As founding director of CBEN, Dr. Smalley has a long-range vision for the field of nanotechnology and the role of CBEN in its development. This year, the draft plan was modified and rewritten by center members in a series of four separate workshops held throughout January 2003. During these meetings, small groups of CBEN faculty critiqued the existing strategic plan and provided rewrites of the document. Their comments, and those of external reviewers (see next paragraph), were incorporated into the final document, which is presented in section 7.

CBEN also works actively to invite and incorporate feedback from external sources, including experts from academia, industry and government. This assessment process is used in several ways throughout the center. This year, for example, the external review board evaluated all proposals and reports submitted by PIs requesting funding for the next budget year. (See section 12.2.) Their comments were instrumental in the funding decisions for year three, and also for revisions to CBEN’s strategic plan. CBEN also is finalizing the composition of its external advisory board, chaired by Dr. Lane. Since Dr. Lane is not directly involved in the management or research organizations of CBEN, he can deliver an informed yet objective perspective about the center from within Rice University. The board will meet during our annual conference, Nanodays, to provide input on CBEN performance and future directions.

12.2. Resource Allocation

Director Dr. Vicki Colvin is responsible for leading the annual resource allocation and project evaluation processes. Research project evaluation begins by inviting existing project leaders to submit a progress report and future funding request; this year, CBEN also made a general announcement to all CBEN faculty that new project requests would be considered. Both new and continuing funding requests received substantive critiques from researchers outside of the center who comprised our external review board. Over twenty names for participants on this board were suggested by center members, but the executive directors were the only CBEN members aware of the identity of the final nine participants. External review comments were stripped of any identifying information and made available to project proposers and the internal review board which included theme leaders Drs. Colvin, West and Hughes. (Drs. Smalley and Colvin will appoint theme leaders annually based on the evolution of research and faculty availability and interest). The IRB is responsible for rank-ordering all proposals using the external review board’s comments as a guideline. A full description of our proposal process can be found at http://www.rice.edu/cben/JoinResearchers.shtml. Outreach projects underwent a similar internal review process, with future budget requests produced through the consensus of the executive directors for education and operations. Once the evaluations are completed, Dr. Colvin is responsible for the final resource allocation and annual budget proposal.

12.3. Assessment

In addition to producing a strategic plan, our long-term planning process continues as we develop concrete measures of center performance and establish targets for these performance indicators. In the summer of 2003, Drs. Smalley and Colvin, along with a working group of interested center members, will develop metrics for performance in CBEN. As CBEN matures the management will track carefully its performance using targets which address the number of interdisciplinary projects started, publications with multiple member authorship, students co-advised by members, industrial connections established, commercial ventures started, and the
impact of educational outreach programs. These quantitative goals will be balanced by more qualitative evaluations of member participation in extracurricular center activities and the visibility of the center in the academic and national community. The internal working group will also refine the criteria by which individual center research projects are evaluated. As a result of comments from last year’s working group, for example, projects were judged in our internal and external reviews by potential for relevance to the Center mission, potential for high impact, and probability of success, in that order.

12.4. Operations

The final function of CBEN management is day-to-day operations. The center has a number of responsibilities beyond its research activities, including center-wide programs, internal and external reporting, and industrial and educational outreach. After polling informally several engineering research centers CBEN determined that 10-15% of center funding should go towards these crucial functions, corresponding to 7 to 10 full-time personnel. The executive director for operations, Dr. Kevin Ausman, is responsible for developing industrial outreach programs, coordinating center-wide research activities (such as the annual conference, seminars, and research workshops), and serving as the contact point for NSF questions and reporting. Dr. Ausman’s efforts include active coordination of CBEN faculty to identify industrial affiliates and the development of center-industry partnerships. He works closely with the Rice Office of Technology Transfer. The executive director for education and public policy, Dr. Kristen Kulinowski, has responsibility for all educational and policy programming for the center. In addition, Dr. Kulinowski serves as the center’s communication director, translating center findings to the media, government and public at large. We would like to emphasize that naming a non-PI as director of center education does not reflect a lack of commitment to these outreach programs. All center faculty are required to make significant annual contributions to educational efforts, and many programs are lead by faculty. This kind of volunteerism, however, cannot replace the focus and effectiveness of a full-time professional dedicated to creating and nurturing our educational initiatives.

As originally proposed, CBEN also supports staff for general administrative purposes. Administrative director Jason Bradshaw is responsible for center-wide purchasing, accounts, and financial reporting; accountant/bookkeeper Janine Vails maintains records, tracks center expenses and handles travel reporting; receptionist Jerrie Johnson provides a daily presence in our offices, fielding phone calls and information requests; part-time secretary Todd Phillips, who is cost-shared by the Jones Graduate School of Management and located in their building, coordinates industrial programs such as the Rice Alliance Forums, the entrepreneurship workshops, and the annual center conference. Part-time undergraduate help during the school year is also available for specific project development. CBEN also supports two PhD-level technical positions for managing shared instrumentation. (Refer to section 11).
13. Publications and Patents

13.1. Publications

Primary CBEN Support


### 13.2 Patent Applications


### 13.3 Presentations


6. “Polymer Translocation through a Long Nanopore,” Anatoly Kolomeisky, *Department of Chemistry, Moscow State University, Moscow, Russia*, (December 2002).


24. “Structure-Resolved Absorption and Fluorescence Spectra of Carbon Nanotubes,” R. Bruce Weisman, *Department of Chemistry and Department of Physics, Oklahoma State University, Stillwater, Oklahoma,* (February 6, 2003).


45. “Nanotechnology Basics,” V.L. Colvin, *Rice Alumni School, Rice University, Houston, TX*, (February 16, 2002).

46. “Opals and Optics,” V.L. Colvin, *School of Continuing Studies, Rice University, Houston, TX*, (October 9, 2002).
14. Biographical Information

PAUL E. LAIBINIS

Biographical Sketch

EDUCATION
1985 S.B. (Chemical Engineering), Massachusetts Institute of Technology, Cambridge, MA.
1985 S.B. (Chemistry), Massachusetts Institute of Technology, Cambridge, MA.
1987 A.M. (Chemistry), Harvard University, Cambridge, MA.
1991 Ph.D. (Chemistry), Harvard University, Cambridge, MA.

PROFESSIONAL EXPERIENCE
2003 – present Associate Professor of Chemical Engineering, Rice University.
2001 – present Faculty Fellow, Molecular Engineering Programme, Singapore-MIT Alliance.
1999 – 2002 Associate Professor of Chemical Engineering, Massachusetts Institute of Technology.
1996 – 2002 Member, Center for Biomedical Engineering, Massachusetts Institute of Technology.
1994 – 1999 Assistant Professor of Chemical Engineering, Massachusetts Institute of Technology.

FIVE SIGNIFICANT PUBLICATIONS MOST RELATED TO PROPOSAL

FIVE SIGNIFICANT RECENT PUBLICATIONS
5. G. Kane Jennings, Tseh-Hwan Yong, Jeffrey C. Munro, and Paul E. Laibinis: “Structural Effects on the Protective Properties of Self-Assembled Monolayers Formed from Long-Chain
NIKOS V. MANTZARIS  
Ph.D., Assistant Professor in Chemical Engineering and Bioengineering, Rice University

PROFESSIONAL PREPARATION

- Diploma (M.S.), Chemical Engineering, National Technical University of Athens, Hellas-Greece, (1994)
- Ph.D., Chemical Engineering, University of Minnesota, (2000)
- Postdoctoral Associate, Mathematics, University of Minnesota, (01/2000-08/2001)

APPOINTMENTS

- Assistant Professor, Bioengineering Dept., Rice University (03/2003-)
- Assistant Professor, Chemical Engineering Dept., Rice University (09/2001-)
- Postdoctoral Associate, Dept. of Mathematics, University of Minnesota, (01/2000-08/2001)
- Graduate Research and Teaching Assistant, Dept. of Chemical Engineering and Material Science, University of Minnesota (09/1995-12/1999).

FIVE PUBLICATIONS CLOSELY RELATED TO THIS PROJECT


FIVE OTHER SIGNIFICANT PUBLICATIONS

Dr. Morteza Naghavi

Professional Preparation

**MD, Tehran University of Medical Sciences**

**Appointments**

1990-1996 Founder and Director, Cardiovascular Research Center, Tehran University of Medical Sciences

1996-1997 Founder and CEO, Rayavaran Research and Development Institute Inc., Tehran

1998-2000 Instructor of Medicine, Division of Cardiology, University of Texas Health Science Center at Houston

2000-Present Assistant Professor of Medicine, Division of Cardiology, University of Texas Health Science Center at Houston

2000-Present Director, Center for Vulnerable Plaque Research, Texas Heart Institute

2001 Co-Founder, Volcano Therapeutics Inc.

2001-Present Founder, Association for Eradication of Heart Attack - AEHA

**Publications**


2- Thermography Basket Catheter: In Vivo Measurement of the Temperature of Atherosclerotic Plaques for Detection of Vulnerable Plaques. (in press *Cardiovascular Catheterism*)

3- Superparamagnetic Iron Oxide–Based Method for Quantifying Recruitment of Monocytes to Mouse Atherosclerotic Lesions In Vivo Enhancement by Tissue Necrosis Factor-Alpha, Interleukin-1 Beta, and Interferon-Gamma (In press *Circulation*)


**Biographical Sketch** Andreas Lüttge

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### a. Professional Preparation

<table>
<thead>
<tr>
<th>Institution</th>
<th>Degree</th>
<th>Year</th>
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<tbody>
<tr>
<td>Technische Universität, Braunschweig, Germany</td>
<td>Vordiplom</td>
<td>1982</td>
</tr>
<tr>
<td>Eberhard-Karls-Universität, Tübingen, Germany</td>
<td>Diplom (= MS)</td>
<td>1985</td>
</tr>
<tr>
<td>Eberhard-Karls-Universität, Tübingen, Germany</td>
<td>Ph.D. (= Dr. rer. nat.)</td>
<td>1990</td>
</tr>
<tr>
<td>Eberhard-Karls-Universität, Tübingen, Germany</td>
<td>Habilitation</td>
<td>1995</td>
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### b. Appointments.

<table>
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<tr>
<th>Institution</th>
<th>Position</th>
<th>Years</th>
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</thead>
<tbody>
<tr>
<td>Rice University</td>
<td>Associate Professor</td>
<td>since 1999</td>
</tr>
<tr>
<td>Yale University</td>
<td>Associate Research Scientist</td>
<td>1997–1998</td>
</tr>
<tr>
<td>Yale University</td>
<td>Visiting Research Scientist</td>
<td>1995–1997</td>
</tr>
<tr>
<td>Univ. Tübingen</td>
<td>Wissenschaftlicher Assistent</td>
<td>1990–1995</td>
</tr>
<tr>
<td></td>
<td>(comparable an assistant professor position in the US)</td>
<td></td>
</tr>
<tr>
<td>Univ. Tübingen</td>
<td>Wissenschaftlicher Angestellter</td>
<td>1985–1990</td>
</tr>
<tr>
<td></td>
<td>(comparable a research scientist)</td>
<td></td>
</tr>
<tr>
<td>German Navy</td>
<td>Radio Operator (honorable discharge)</td>
<td>1977–1979</td>
</tr>
</tbody>
</table>

### c. Publications.

1. **(i)** 5 publications most closely related to the proposed project


2. **(ii)** 5 other significant publications


   Lasaga A.C., **Lüttge A.** (2003, in revision) A fundamental approach to mineral dissolution kinetics I. *American Mineralogist.*


Yizhi Jane Tao  
Assistant professor  
Department of Biochemistry and Cell Biology  
Rice University, MS140  
Houston, TX 77251  
Tel: 713-348-4910  
Email: ytao@rice.edu

**Education**

- **Peking University**  
  **Biophysics**  
  **B.Sc.**  
  **1988-1992**
- **Emory University**  
  **Physics**  
  **Ph.D. Program**  
  **1992-1994**
- **Purdue University**  
  **Biophysics**  
  **Ph.D.**  
  **1994-1999**
- **Harvard University/HHMI**  
  **Structural biology**  
  **Postdoctoral**  
  **1999-2002**

**Appointments**

- **2002-present**  
  Assistant professor, Dept. of Biochemistry and Cell Biology, Rice Univ.
- **1999-2002**  
  Postdoctoral associate, Dept. of Molecular and Cellular Biology, Harvard Univ./HHMI

**Publication**

**Recent publications related to the proposal:**


**Patent**


**Other significant publications**

KYRIACOS ZYGOURAKIS

Biographical Sketch

EDUCATION

1975 Dipl. Eng. (Chemical Engrg.), National Technical University, Athens, Greece.
1981 Ph.D., University of Minnesota (Major: Chemical Engrg.; Minor: Mathematics).

PROFESSIONAL EXPERIENCE

2001 – present A.J. Hartsook Professor in Chemical Engineering, Rice University.
1998 - present Chair, Chemical Engineering Department, Rice University.
1996 – present Professor of Bioengineering, Rice University.
1991 – present Professor, Chemical Engineering Department, Rice University.
1986 – 1991 Associate Professor, Chemical Engineering Department, Rice University.
1980 – 1986 Assistant Professor, Chemical Engineering Department, Rice University.

FIVE SIGNIFICANT RECENT PUBLICATIONS


SYNERGISTIC ACTIVITIES

Started a summer research program for undergraduates at Rice University. This program targets exceptional students who have just completed their first year of college, pairs them with a faculty mentor and places them in a chemical engineering research lab over the summer months. The program is funded by grants from Halliburton and the BP Amoco Foundation.
15. Honors and Awards

Rebekah Drezek
- 2003 HSEMB Outstanding Young Scientist
- 2003 Whitaker Young Investigator

Jason Hafner
- Beckman Young Investigator Award
- Petroleum Research Fund Starter Grant

Joseph B. Hughes
- Charles Duncan Award for Outstanding Academic Achievement, Rice University.
- ASCE Outstanding Professor Award, Rice University.
- Member: Chi Epsilon
- Chair: Science Advisory Committee, U.S. EPA West Coast Hazardous Substance Research Center.

Anatoly Kolomeisky
- NSF CAREER award (2002).

Jianpeng Ma
- Award for Distinguished Young Scholars Abroad, Chinese National Natural Science Foundation, P.R. China
- Faculty Early Career Development (CAREER) Award, National Science Foundation

Kathleen Matthews
- YWCA Outstanding Woman of Achievement in Medicine, Science, & Technology, 2002

Douglas Natelson
- Research Corp. Research Innovation Award.

Gustavo Scuseria
- 2002 Creativity Extension Award, Chemistry Division, National Science Foundation.
- 2002 Fellow of the American Physical Society.
- 2003 John Simon Guggenheim Fellow.

R. Bruce Weisman

Jennifer L. West
- Editor’s Choice in Science award; Hershel M. Rich Invention Award for patent on photothermal cancer therapy.

Michael Wong
- Recognized as one of the nation’s top young engineering researchers by the National Academy of Engineering (NAE).

Boris I. Yakobson
- Distinguished Faculty Associate at Brown College.