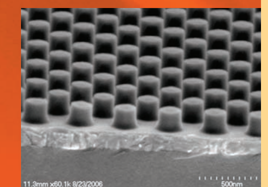
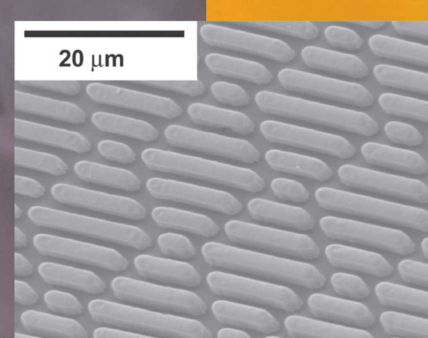
SOLVENTS AND PROCESSES

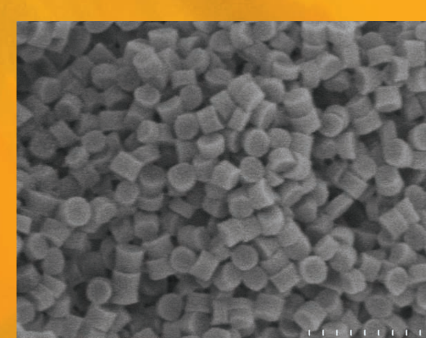
CENTER FOR ENVIRONMENTALLY RESPONSIBLE SOLVENTS AND PROCESSES CERSP



SOLVENT-FREE METHODS OF CHEMICAL SYNTHESIS LEAD TO CANCER THERAPIES, NCI CENTER

"Once you get scientists and engineers working in an interdisciplinary manner, you can't contain it," laughs Joseph DeSimone, director of the Center for Environmentally Responsible Solvents and Processes (CERSP) and the William R. Kenan, Jr. Distinguished Professor of Chemistry and Chemical Engineering at the University of North Carolina, at Chapel Hill (UNC-CH).





"Things have evolved certainly beyond the original scope of our center. Starting off with a focus on sustainability and green chemistry has led us into new cancer therapies and imaging agents," says DeSimone.

CERSP's initial goal was to establish the scientific fundamentals necessary to enable liquid and supercritical CO_2 and solvent-free processes to replace aqueous and organic solvents in a large number of key processes in our nation's manufacturing sector.

More than 30 billion pounds of organic and halogenated solvents are used worldwide each year as manufacturing process aids, cleaning agents, and dispersants. Considerably more water is used and contaminated in related processes.

In the future, manufacturing and service industries must work to avoid the production, use, and subsequent release into the environment of contaminated water, volatile organic solvents, chlorofluorocarbons, and other noxious pollutants.

CERSP is a multi-disciplinary effort with participants from five academic centers and two national laboratories: UNC-CH, North Carolina State University, North Carolina A&T University, University of Texas at Austin and the Georgia Institute of Technology.

CERSP codirector Ruben Carbonell points out that many companies are focusing today on finding alternatives to fluorinated surfactants that break down into a compound called perfluorooctanoic acid, or C8, which accumulates in the body and may pose a health threat. Center researcher Keith Johnston and colleagues are looking at alternative surfactants that have different chemical structures that won't bio-accumulate and have good surfactant properties.

The manufacture of Teflon™ is a case in point. The conventional process uses a C8 surfactant to make an emulsion. An alternate synthesis, developed in the center, doesn't require any surfactants, says Carbonell. It's done completely in CO_2.

The process has been commercialized. "There's a DuPont plant in Fayetteville, North Carolina that makes Teflon™ in carbon dioxide. The technology, developed in DeSimone's lab, was licensed by DuPont several years ago," says Carbonell. One of the advantages is a smaller environmental footprint. "There are no surfactants at all—it's just the monomer reacting in the presence of carbon dioxide. The particles grow, and when you reduce the pressure, the particles fall out of solution, completely dry and with no surfactant," says Carbonell. "And the process should be cheaper because there's no need to evaporate water at the end of the process. One of the major energy consumption points in making any polymer, but particularly Teflon-based materials, is that they're made in aqueous solvents or aqueous-organic emulsions. If you make it in CO_2 and depressurize, the polymer powder comes out completely dry. And the CO_2 is recycled for use."

New surfactants in development at the center are now of interest to companies wanting to do tertiary oil recovery using carbon dioxide, Carbonell adds. One of the ways of getting more oil out of the ground is to inject high pressure carbon dioxide into spent oil fields, using detergents to reduce the surface tension that's holding the oil globules inside the rock. For this purpose, surfactants that are soluble in carbon dioxide are needed. "One thing leads to another and then this problem of oil recovery that was not of any interest at all when the center began is now of great interest," notes Carbonell. Agility seems to be a recurring theme at CERSP. Carbonell notes: "We've been able to transform ourselves pretty readily."

Green Chemistry Pays Dividends for Research on Cancer Therapy

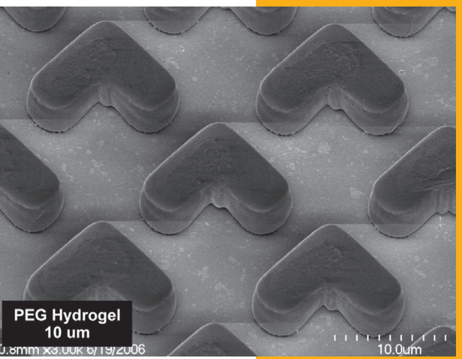
"What's curious—what has evolved—is that research on solvent-free methods has led to a new technology for making cancer therapeutics that we didn't anticipate," says DeSimone. It has led to us landing one of the eight centers of nanotechnology excellence funded by the National Cancer Institute, a $24-million center. It just shows the unbounded opportunities that happen when you get a bunch of good people together from different disciplines that are open-minded."

Initially, CERSP researchers were using carbon dioxide as a solvent-free method for making new fluoropolymers. They made some new materials that turned out to be excellent molding materials. The method called PRINT™—Particle Replication in Non-wetting Templates, was published in July 2005 issue of the *Journal of the American Chemical Society*.

The process begins with a liquid fluoropolymer that can wet surfaces very well. It is poured into a master and irradiated to make an array of tiny molds, not unlike a little ice cube tray, which can be used subsequently for mass production of particles of uniform size and shape, creating features of nanometer size.

The breakthrough came when they realized these particles could be used in medicine. "We use these particles as basically a 'delivery truck' for therapeutics and imaging contrast agents," says DeSimone. "Because it's such a gentle technique—we're just molding—we can easily paint the particles with targeting ligands, like monoclonal antibodies. And so now we have particles that can have on the surface an antibody and in the interior have a therapeutic. We're beginning to develop the tools and methods for scale-up and we've now molded particles and done our first pharmacokinetic studies in mice to see the biodistribution of these organic carriers," says DeSimone. □

STARTUP COMPANY



LIQUIDIA MAKES NANO-ENGINEERED PRODUCTS FOR LIFE SCIENCES, ENERGY, AND MATERIALS SECTORS

Joseph DeSimone and his colleagues from CERSP at the University of North Carolina at Chapel Hill have created a startup company called Liquidia Technologies based upon the PRINT™ nanoscale molding process, targeting applications in the life sciences, energy, and materials sectors.

Founded in 2004, Liquidia is working to precisely design and manufacture micro- and nano-structures in bulk, with particle sizes ranging from tens of nanometers to tens of microns. These structures may take multiple forms, including particles and patterned films.

Liquidia has partnerships with several major corporations to provide gram quantities of material for prototyping and feasibility studies. Examples include supplying particles that might become part of a medical device or an active layer in a display, and making fuel cell membranes or active layers in photovoltaic devices.

The company has grown to 24 people as of spring 2007 and has raised a total of $25 million, says co-founder and senior scientist Ginger Denison Rothrock, a former graduate student at CERSP. Located in Research Triangle Park and currently squeezed into 4,000 sq ft—"quite cramped but loving it"—the company is scheduled to move into a 17,000-sq-ft facility in August 2007.

In the life sciences, Liquidia is using the PRINT™ process to make particles containing therapeutic drugs that may be used to deliver medicine to a target site and gradually release it. The PRINT process gives precise control over particle size, shape, composition, modulus, and surface properties. According to the company, "Liquidia is the only company in the world that can independently tailor these variables simultaneously in the creation of engineered drug therapies." Rothrock notes that discussions are underway with three major pharmaceutical companies for prototyping projects.

Ginger Denison Rothrock, former graduate student at CERSP and co-founder of Liquidia

THE SCIENCE HOUSE

The convergence of three forces in North Carolina has resulted in a resounding success for K12 education that has reached thousands of teachers and their students. The ingredients: CERSP, The Science House, and a new required course for high school students in the state of North Carolina.

By coincidence, just about the time that CERSP was getting started, North Carolina adopted a new course on earth and environmental science that was required for graduation from high schools in the state. It was a brand new course: the curriculum had been written but the teachers were not trained to teach it and there were very few resources linked to the curriculum.

Enter The Science House, a K12 outreach program of the College of Physical and Mathematical Sciences at North Carolina State University. The Science House organizes curriculum projects, student camps, and science enrichment programs, and it develops teacher training programs reaching a few thousand teachers a year. It is led by physicist David Haase in conjunction with 12 full-time education staff involving five offices across the state of North Carolina.

With the adoption of the new course and the formation of a center on environmentally responsible solvents and processes, the players saw an opportunity that linked a real need in North Carolina schools and the general idea of green chemistry that featured prominently in the NSF Science and Technology Center (STC).

Experts from The Science House partnered with CERSP faculty to help determine which core topics in the STC should be developed for K12 outreach. They developed a lab book and distributed it to earth and environmental science teachers with a guide that showed how those materials linked to the North Carolina and Texas curricula.

Haase emphasizes the value of this kind of partnership and notes, "We'd like to do this for more centers."

The materials were distributed to some 4,000 teachers in North Carolina and Texas. They prepare teachers to teach the lab program and show them how to do the labs. "Some of the lab equipment vendors partnered with us," says Haase, "so that the teachers would walk away not only with the laboratory manual but also some materials they could use in their own classrooms."

The STC provides about $150,000 per year to The Science House, which in total is has an annual budget of about $1 million per year.

Center: Physics professor David G. Haase (left,) director, and Mary Louise Bellamy of The Science House at North Carolina State University

A CONVERSATION WITH THE DIRECTORS

Joe DeSimone & Ruben Carbonell

One of the characteristics that distinguish CERSP is its leadership in center management. "We were able to get our center up and launched very quickly," says center director Joe DeSimone. He identified the tools and brought in the infrastructure to facilitate the startup process, with a codirector and a deputy director to form a team of three leading the center.

"Once you get through the launch phase—which is a heck of a lot of work," he laughs, "almost like a startup company—and you get everyone marching in one direction, then it's actually a little easier sailing. Then you just have great people doing fabulous science—and nothing speaks more clearly than their science."

An executive coach was brought in to help the team members analyze and characterize their different thinking styles. The idea came from DeSimone's entrepreneurial background, gained by launching startup companies. The coach educated the team on different communication and working styles and how to use those tools to engage with others.

DeSimone's style is to engage in blue sky brainstorming to identify options and then to focus in on the research targets with great intensity. "We've been expansive in our thinking to consider what could be done, and then we narrow in on it and come to closure."

The center recently has gone through another cycle of this process by means of workshops to identify new directions to see where the team could apply its expertise in a new arena. "We're morphing, we're looking at life sciences, alternative energy and power sectors, green chemistry, innovation, and entrepreneurship—looking at ways for the center to continue to be sustainable."

CERSP director Joseph DeSimone

CERSP co-director Ruben Carbonell

CERSP co-director Ruben Carbonell points to the complementary skills sets in the management team as a key factor for success. "Joe is a creative chemist, I'm a detail-oriented engineer," he laughs. "That's been a complementary set of skills."

Deputy director Everett Baucom has brought extensive industry experience to the team, which has allowed the directors to focus on research issues.

Carbonell reflects upon the benefits to faculty of participating in the center: "Those who have been with the center since 1999 have learned the advantages of doing collaborative work. One of the legacies of the STC is that faculty become better trained in a sense because they see the bigger picture, beyond the normal confines of their discipline. And as a result of that, they become leaders themselves.

"I can see among my younger colleagues that, after seven or eight years of being with us, they're now becoming the leads in new proposals that involve centers. That's been interesting to watch. They have a better appreciation of what it takes to run them, and of what they can do compared to single investigator work. They become, then, a source of new ideas for other faculty. That's not a legacy that maybe NSF counts, per se—obviously it's a difficult thing to quantify. We're struggling with how to report that. But it's an interesting observation."

SOLVENTS AND PROCESSES