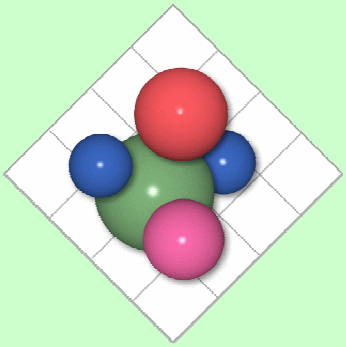


Center for Structured Organic Particulate Systems (C-SOPS)

Rutgers University (lead institution)

Building the fundamental science base for the rational design, development, and manufacturing of structured organic composite particulate products for the pharmaceutical, food, and agrochemical industries

A National Science Foundation Engineering Research Center since 2006

Partner Institutions:

- ***Purdue University***
- ***New Jersey Institute of Technology***
- ***University of Puerto Rico at Mayaguez***

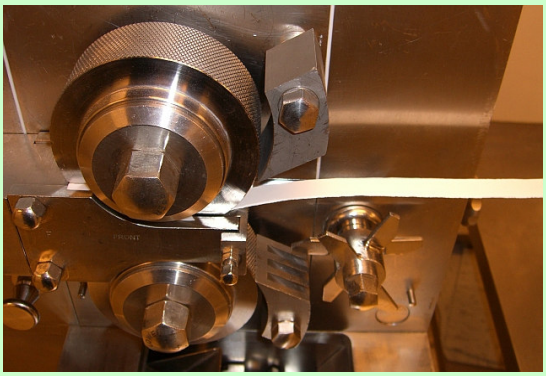
The impact of today's sophisticated drug discovery process in the improvement of human health is being seriously delimited by current pharmaceutical product development processes and manufacturing methods. The newsmagazine of the American Chemical Society has flatly stated that "…the pharmaceutical industry stands out as having particularly inefficient manufacturing operations." Manufacturing improvements are hampered by the lack of predictive scientific models for the structure and production of the complex, multi-component organic particulate systems which are the basis of modern drug delivery. The vision of the Center for Structured Organic Particulate Systems (C-SOPS) is to become the national focal point for science-based development of structured organic particle-based products and their manufacturing processes. By accomplishing this we will enhance the speed of drug development and the quality of the resultant medications, while reducing manufacturing costs.

Research

The C-SOPS is focusing on three thrust areas that will have maximum impact in mitigating the manufacturing inefficiencies cited above. Individual projects are developed to address scientific and engineering problems in each of those thrust areas.

*Thrust 1 (**Manufacturing Science**)* concentrates on developing the technologies needed to extend and integrate into the manufacturing arena the fundamental knowledge and rigorous models resulting from Thrusts 2 and 3. Thus, the major objectives are: (1) the development and implementation of advanced science-based sensor technologies for effective process monitoring (composition, state, etc.) in the manufacture of engineered composite particulate products; and (2) optimization of the performance of manufacturing processes through development and implementation of advanced model-based informatics, supervisory control strategies, and real-time optimization methodologies.

The topics addressed in *Thrust 2 (**Composite Synthesis and Characterization**)* are concerned with constructing composites from individual materials. The major targets are: (1) the development of methods for controlling the spatial structure of organic particulate composites; and (2) the development of multiscale simulation methods for the determination and optimization of structure-function-performance relationships.

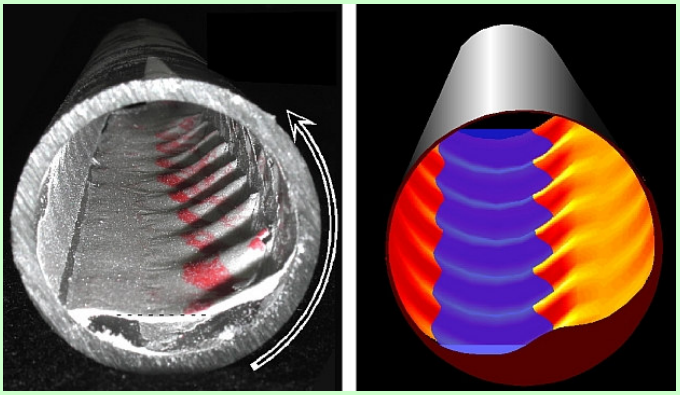


A fully instrumented roller compacter at Purdue Industrial Pharmacy Laboratory

*Thrust 3 **(Particle Formation and Functionalization)*** focuses on two major goals: (1) the development of new methods for controlled-size particle formation which can be effectively scaled to the manufacturing level; and (2) the control and optimization of physicochemical properties of materials (size, shape, stability, affinity to materials) through systematic functionalization. Both of these goals require the development of requisite characterization techniques for effective measurement of critical particle properties and for process monitoring.

Testbeds have been developed to validate the results, models, and predictions emanating from the individual projects. Each test bed allows integration and optimization of the separate projects into a complete manufacturing process for a different product form—tablet, drop, or strip film. The projects and testbeds are evolving as the center develops.

The continuous dry tableting testbed, for example, sequentially integrates the operations of powder mixing, compaction, and tablet formation. These operations are themselves complex phenomena and involve aspects of powder flow, powder cohesion, powder coating, compression, crystal strength, deformation, and fracture. In order to have the broadest impact and applicability, projects addressing these issues are grounded in experiments but then go on to develop predictive models of the phenomena involved. To build a complete process line, on-line sensors and instruments must be developed. These must be integrated with process controllers which will enable the required degree of manufacturing uniformity.



Sedimentation pattern of fine granule suspension during slow rotation (left). A computer simulation is on the right.

Finally, test methods must be adapted or developed which will assure appropriate product performance. Each aspect of the testbed is being addressed on the project level and has been incorporated into an appropriate research effort.

The same overall approach is being applied in the other testbeds. Moreover, the domain knowledge developed on the project level can be applied in most cases to more than one testbed.

Our overarching plan is to replace the empirical methods currently utilized in the pharmaceutical and related industries with a predictive framework for science-based product and process development for Structured Organic Composite Particulates. As the science and technology that the C-SOPS develops is adopted into industrial practice, boundaries will be pushed beyond the scope of the models we develop. This will drive the need to expand or re-define projects to develop more highly refined models which provide accurate predictions over a wider range of conditions.

Education

The education vision and goals of our Center are to:

- Educate students who will be effective engineers and leaders in the manufacturing and research operations of the pharmaceutical and allied industries of the Center
- Train students for roles in education and in the agencies involved in regulating food and drug manufacturing operations
- Bring the new Center research discoveries in engineered organic composite systems to enrich the existing engineering curricula at both the undergraduate and graduate levels
- Develop educational programs for industrial practitioners and foster alliances with industry in the education and outreach activities of the center
- Design and promote experiential programs and pedagogical material for K-12 outreach, recognizing diverse student and teacher backgrounds
- Develop a suite of modular educational units for use by the various Center partners in formats that allow for efficient web-based dissemination.

The programs include elements for K-12, undergraduates, graduate students, and current industrial practitioners.

Precollege: One program includes K-12 outreach in the form of mobile laboratory and hands-on learning modules that are brought to middle school classrooms using the Rutgers Science Explorer bus. Another effort is aimed at outreach to middle and high school teachers through a summer Research Experiences for Teachers (RET) program. Middle and high school teachers will have hands-on involvement in the research program of a C-SOPS laboratory. This will be followed by their working with ERC faculty to develop simplified teaching modules which they can take back to their classrooms. Finally, precollege activities for high school juniors are planned through the New Jersey Governor's School for Engineering at Rutgers University.

Undergraduate and Graduate: All of the ERC research projects provide hands-on opportunities for education of undergraduate and graduate students. They work in project teams with faculty, other students, and very often ERC participants from other disciplines and from partner schools. In addition to the graduate programs in the typical engineering disciplines, all of the institutions have plans for or active Master of Engineering or MS programs specifically oriented toward pharmaceutical manufacturing or pharmaceutical science. We also work closely with our outreach partner school, City College of New York (CCNY), to provide support to their undergraduate students engaged in research relevant to the ERC.

Professional Education is an ongoing issue that is being addressed by the development of 1-credit modules for flexible instruction. The module content makes up a digital library and web-based access will allow industrial members restricted use of these materials.

Industrial Collaboration/ Technology Transfer

From the earliest planning stages, the C-SOPS has developed a multi-faceted program for fostering academic-industrial interactions. As one component, a system of tiered membership levels allows for industrial financial support of the center. More importantly, active industrial input and participation has helped to guide program development and execution. A steering committee, composed of the academic leadership and representatives of Tier 1 member companies, provides input on priorities and strategic advice on research goals, evaluates proposed projects, and recommends funding levels. All member companies, forming an Industrial Advisory Board (IAB), participate in the program evaluation and provide valuable tactical advice on project implementation. Industrial partners also provide technical mentors who actually work as part of the project team.

Industrial partners include end-use manufacturers such as pharmaceutical, nutraceutical, and food producers who employ similar manufacturing technologies and are held back by the same lack of predictive models. In addition, equipment and software suppliers to these manufacturers have joined the Center and are providing important input from their perspectives.

The US Food and Drug Administration regulates the products and manufacturing processes of many of our member companies. It is thus extremely important for the FDA to learn about and provide input into the development of new production methods; the FDA participates actively in our Center as a member of the IAB.

Center members enjoy a royalty-free license for in-house use of any of the technology developed by the ERC. Although information is relayed via formal reports, the technology is best learned at the earliest possible stage by our industrial partners participating in our project reviews and in the research projects themselves. This greatly facilitates the transfer of technology to their organizations.

Tablet manufacturing at the cGMP facility of the Chao Center for Industrial Pharmacy at Purdue University.

Facilities

The Center currently uses a total of approximately 17,000 sq. ft. of laboratory space, distributed across the partner schools. Another 20,000 sq. ft. has been committed and is available for expansion. Each partner, in addition to general laboratory and office space, provides specialized facilities and equipment.

At Rutgers, a separate Laboratory for Drug Delivery provides the capability for advanced *in vitro* testing of the delivery and absorption of drugs from composites, using cell or tissue models. Animal testing facilities are also available. The ERC administrative staff is housed in office space in the Department of Chemical and Biochemical Engineering.

The Chao Center at Purdue University has an 11,000 sq. ft. educational cGMP facility for manufacturing clinical trial and small-scale commercial materials. Purdue is also home to the Envision Center for Data Perceptualization, an NSF-funded virtual reality theater that can provide an effective means to communicate complex research results.

In addition to a well-equipped pharmaceutical engineering laboratory, the New Jersey Institute of Technology (NJIT) maintains world-class facilities for particle formation and characterization, both critical for the work of the ERC.

Due to Puerto Rico's role in manufacturing pharmaceuticals (60 plants), there is strong demand there for a multi-purpose research and training pilot facility. The University of Puerto Rico at Mayaguez (UPR-M) has planned and identified funding for an 11,500 sq. ft. facility. The facility will house primarily laboratories both for research and instruction, but also will contain warehouse, analysis, and classroom areas. Completion is expected in the summer of 2008.

Center Configuration, Leadership, Team Structure

C-SOPS is a multi-university consortium consisting of Rutgers, Purdue, NJIT, and UPRM. The Center Director is based at Rutgers and the Deputy Director at Purdue. Each location has a site leader who is responsible for the administration at that site. Project leaders are drawn from all four sites, and almost all project teams have at least one participant from each location.

Currently, about 40 faculty members representing 8 scientific and engineering disciplines participate in the work of the project teams.

Center Headquarters

Center for Structured Organic Particulates
Rutgers University
98 Brett Road
Piscataway, NJ 08854
Tel (732) 445-6278 • Fax (732) 445-6758
Homepage: www.ercforsops.rutgers.edu

Center Director: Dr. Fernando Muzzio
(732) 445-3557 • fjmuzzio@yahoo.com

Deputy Director:
Dr. Gintaras (Rex) Reklaitis, Purdue
(765) 494-9662 • reklaiti@ecn.purdue.edu

Administrative Director / Business Manager
Ms. Charanjeet Kaur
(732) 445-6709 • ckaur@rci.rutgers.edu

Industrial Liaison Officer
Dr. Eric Erenrich
(732) 445-6711 • eric.erenrich@rutgers.edu

Program Coordinator / Office Manager:
Ms. Ursula Wolf
(732) 445-6278 • uwolf@rci.rutgers.edu