BIOMATERIALS
FORUM
SOCIETY FOR BIOMATERIALS

October - December 2003 • Volume 25, Issue 3

Drug Delivery
Special Interest Group

Society Announces Symposium on Biomaterials in Regenerative Medicine

Membership:
Innovative Ideas for Growth

Biomaterials Forum, the official news magazine of the Society For Biomaterials, is published quarterly to serve the biomaterials community. Society members receive *Biomaterials Forum* as a benefit of membership. Non-members may subscribe to the magazine at the annual rate of $48. For subscription information, or membership inquiries, contact the Membership Department at the Society office (e-mail: info@biomaterials.org) or visit the Society's Web site, www.biomaterials.org.

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FORUM

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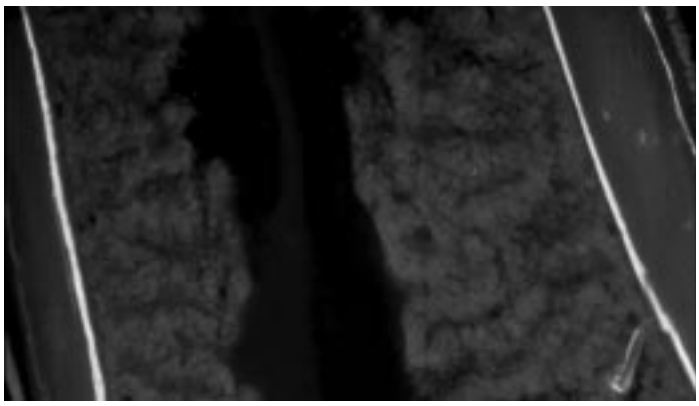
Features



Histological section of balb/c mice bone after injection of HPMA copolymer-FITC conjugate with alendronate as targeting moiety. Endosteum and periosteum of diaphyseal shaft labeled. (Photo courtesy of Prof. Jindrich Kopecek, University of Utah)

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Biomaterials Community

From the Editor

By Martine LaBerge, Executive Editor

A New Editorial Calendar and Procedure for *Biomaterials Forum*

Great changes are on the way for *Biomaterials Forum*. In 2004, issues will be published quarterly—the 1st Quarter issue appearing in January 2004 with a revised editorial calendar. A focus will be particularly given on member, industrial, government, and academic news and the magazine will continue to feature Special Interest Groups in addition to articles of interest to the members of the Society for Biomaterials.

In an effort to enhance communication between the Society and its members, the members of the Board will periodically use *Biomaterials Forum* as a communication tool. In response to the pledge made by President Nicholas Peppas to increase membership in the Society and dissemination of the field of biomaterials science and engineering, every issue of *Biomaterials Forum* will target member benefits.

The 2004 editorial calendar has been developed to enhance communication with members and present technology and research that will mark the field of biomaterials science and engineering in the future. The editorial calendar for next year can be found at www.biomaterials.org/publications/calendar.htm.

The 2004 annual buyer's guide will appear in the 1st Quarter issue. Also, in addition to quarterly issues, the Society's Web site will present "Biomaterials Forum Live," where hot news will be found.

All members are encouraged and pledged to participate as contributors to *Biomaterials Forum*. Suggestions for the new look of Forum are also highly sought. All comments and submissions should be sent directly to the Executive Editor or the Contributing News Editors.

Biomaterials scientists and engineers are recognized for their teamwork skills. The success of *Biomaterials Forum* and its content are a reflection of teamwork, a challenge that all members should help to address.

The Editorial Board of *Biomaterials Forum* looks forward to being the voice of the membership.

Membership

Innovative Ideas for Growth

By Richard Gemeinhart, Membership Committee Chair

The Membership Committee of the Society For Biomaterials has been charged by President Nicholas Peppas with increasing the membership as well as identifying methods of retention of current members. The committee chair did not hesitate to accept the challenge given by Dr. Peppas, and put together a committee that represented all members of the Society. This committee has been active in identifying both problems that may hinder the growth of the Society as well as several potential solutions to these problems.

A professional society is only as strong as its members. Currently, there are several issues noted by the committee that could be improved in the membership process. The committee has been in place for several months and has been given a free reign to suggest any ideas (radical or simple) that could potentially increase the membership, increase participation, and increase retention of members. This committee has seriously considered many aspects of the membership process and several issues have repeatedly been encountered. The committee made a formal report of all issues at the 2003 fall Council meeting of the Society; however, a few of these issues are being reported here with the hope that this will prompt those who are not a part of the Membership Committee to contribute ideas.

The first issue that has been discussed repeatedly is the membership "benefit" of reducing the cost of attending the annual meeting. The committee as a whole holds the annual meeting as a major "benefit" of the Society. During the last several years, the cost to attend the meeting has been lower for nonmembers ($555 early registration) than for members when the cost of membership ($580 early registration plus dues) is included. Other benefits do exist—journals subscription, *Biomaterials Forum*, SIG membership—that are not accounted for in this argument; however, many potential new members view the meeting as the major Society benefit. These other benefits will not be overlooked by the committee and will be addressed in the coming months.

Several non-members questioned at the last annual meeting of the Society in Reno noted that they did not join the Society because it would have increased the cost of the meeting. The amount was not significant, but when the meeting is considered the main benefit of membership, the amount is significant enough to discourage those who are not familiar with the other benefits of the Society from joining. Three suggestions have been proposed: (1) increase the cost for non-members, (2) decrease the cost for members, and (3) combine option one or two with membership for the following year. The third option would automatically admit those attending their first meeting to apply for membership for one year. There are some potential problems with this third option that will need to be examined to allow this to be a viable alternative. This issue is one of the main ones needing to be addressed and will be presented to the Council. Another suggestion that has been proposed is to use members as recruiters for the Society. Our Society has the strength of an active membership, and members can best benefit the Society by contacting their colleagues and collaborators. The Membership Committee asks that members encourage their collaborators, friends, and colleagues to join the Society and attend annual meetings. If each member can successfully promote joining the Society to one colleague, the Society will double in size. This is a lofty goal, but it will not take a monumental effort to accomplish. Individual members attend other meetings and visit other institutions; this time can be used to mention that the work has been presented at Society For Biomaterials meetings and that there are many other researchers presenting data that may also be of interest to those individuals. If it is known that excellent science is presented at our annual meetings the demand to attend will increase.

The final issue believed to be fundamental to the future membership of the Society For Biomaterials is student membership. Students are the future of the Society; an approximately 20 percent retention of students, as is observed currently, is not acceptable. Several suggestions have been made, although none are ready for implementation. The one suggestion that should be proposed is the increase in student chapter participation. When the Society gives an opportunity for student participation, the students remember this and are more willing to give back to the Society in the future. Experience and outside observation suggests that this concept is viable. Promoting the Society to students will benefit the Society in the long run by initiating students into the Society at an early stage and allowing them to see the benefits of joining the Society in the future. Other suggestions are ready to be proposed, however, these are in early stages of development.

The Membership Committee has been active in trying to find creative ways to increase membership while not losing the focus of the Society. The committee is more than willing to accept ideas from anyone, and strongly encourages any member who has an idea to submit it to a committee member, particularly the committee chair, Richard Gemeinhart (rag@uic.edu). Other members of the committee are Carmelita Frondoza, Lance Kam, Margaret Kayo, Alan S. Litsky, Philip Messersmith, John Ricci, and Tim Topoleski. The committee sincerely welcomes any input from members to better represent their needs.

From the President

A new year in the history of the Society For Biomaterials is ready to start, a year of challenges, but also great opportunities. As president of the Society, I want to make sure that we will all focus on the solution of important problems and the implementation of new ideas for our Society.

Indeed, both the field of biomaterials and the Society are at a pivotal point in their history. While certain types of biomaterials continue to be used in successful applications such as hip replacement and intraocular lenses, the demand for sophisticated materials and specialty applications has grown. We all realize that biologists and molecular engineers need to work together if we are to collect the fruits and the promise of nanotechnology and molecular engineering. In this changing biomaterials world, combinatorial methods, molecular design, understanding of materials/protein and materials/cell interactions, and appreciation of biological mechanisms associated with the biomaterials' function have become important subjects for new research and for development of superior medical products. At the same time, the changing financial conditions in our industry, as well as the stringent regulatory requirements, have made all of us more appreciative of the need to better understand the function of biomaterials in physiological and biological environments.

It is time for the Society to address this changing world of biomaterials by attracting new members from the broader biological and engineering community, by providing more services in the form of specialized conferences, tutorial meetings, and special publications, and by consulting with the Food and Drug Administration and other organizations about improved regulatory conditions. As I mentioned in my talk at the Reno meeting in May, it is important that we set the foundations for these new opportunities in our field. Our Society must be in the forefront of this effort.

Since May, I have appointed new subcommittees, or working groups, and I have asked current Society committees to examine the following initiatives in relation to our future:

- Significant increase of membership by simplifying the procedures of engineers, scientists or clinicians to become Society members effortlessly without jeopardizing the standards that our Society has set for membership.
- Organization of specialized meetings, smaller conferences, and tutorial meetings.
- Publication of focused publications on subjects of current scientific, technical, business or regulatory interest.
- Significant enhancement of the Society's reserve fund.
- Creation of the SFB Foundation with the goal to form an endowment that will fund important new projects that will impact our field.

Next year is the right year for us to address these activities. Since we do not have a major Society meeting in the United States in 2004 (because of the World Biomaterials Congress in Sydney), we are given the opportunity to concentrate our efforts towards a re-evaluation of the goals of our Society. We hope this new vision, and associated mission and metrics, will lead us to a revitalized and exciting organization that will be a true leader, not only in our field, but in the broader area of biomedical engineering and sciences. In this effort, I am most fortunate to have the support of a dedicated Board enjoying the sage advice of our two past Society presidents, Stuart Goodman and Jim Burns. Both of them set goals that have led to significant changes in our Society already. Our Board is fortunate to have the extremely capable contributions of three financial wizards—Anne Meyer, Mauli Agrawal, and Lynne Jones—whose imaginative ideas and contributions will lead to an improved, balanced budget and to new ideas about additional revenue for the Society. Finally, your Member-at-large, Jennifer West, is your voice on the Board, but also a scientist extremely knowledgeable about the future directions of biomaterials science.

This past year, I had the pleasure to work on a Board that was directed by, Jim Burns. Jim and the Board undertook the weighty task of selecting a management office for our society and directing the whole transition process. Jim has been an exceptional leader who has taught us all to be fiscally responsible, scientifically innovative, and responsive to the needs of our members. I hope to continue his legacy and I thank him for everything that he has done for our Society.

I hope all of you will feel free to send me your ideas about improvement of our organization, our services, and our future initiatives. Be bold in your ideas. As Andre Gide (Nobel laureate, literature 1947) stated, "one cannot discover new lands without leaving the shore for a long time." We are clearly at the beginning of a long journey that will make our Society richer in ideas, more diverse, and the place to be for biomedical research and information.

Nicholas A. Peppas, President

Regional Workshop on Tissue Engineering and Biomaterials Introduced

The Torch

By Karen J.L. Burg and Ann E. Schmierer

The Southeast Workshop on Tissue Engineering and Biomaterials is a newly organized annual event, beginning in 2004 at Clemson University, and conducted at a different southeastern location each year. The mission of the workshop is to foster collaborations between southeastern universities that are involved in biomaterials research and tissue engineering, to establish an educational workshop that will travel to participating university campuses, to provide a forum to showcase faculty and student research, and to establish liaison activities with local and international companies interested in biomaterials and tissue engineering. Baxter BioSurgery will be a sponsor for the first Southeast Workshop.

The inaugural 2004 event will be held at Clemson University in Clemson, S.C., January 29-30. The target audience will be students and faculty from southeastern research universities, as well as individuals from industry. The 2004 workshop will commence with keynote speaker, Dr. Ioannis Yannas, professor of mechanical engineering at MIT, and a member of the National Academy of Sciences and the Institute of Medicine. Dr. Yannas will discuss the genesis of tissue engineering and the contribution of biomaterials to this field. A poster session and reception open to all participants will be held on the evening preceding the day-long workshop. The program will highlight the evolution of various forms of biomaterials in tissue engineering applications, exploring the use of natural and synthetic biomaterials in the context of tissue engineering. The second day of the workshop will consist of 20-minute podium presentations provided by senior faculty, junior faculty, and students from the participating universities and companies.

This annual workshop will provide an opportunity to establish connections within universities as well as other regional universities and companies, with a new host site for each workshop. The workshop will follow a similar program format (poster, keynote, and podium sessions), designed by the host institution. The Georgia Tech/Emory Center for the Engineering of Living Tissues and the Department of Bioengineering at Clemson University will be co-anchor institutions to ensure the continuation of this program and assist the workshop host institutions.

For more information on the Clemson workshop, or information about serving as a host institution, please contact Dr. Ann Schmierer at ann.schmierer@ibb.gatech.edu, (404) 385-2259, or Dr. Karen Burg, kburg@clemson.edu, (864) 656-6462, or visit the workshop Web site at www.ces.clemson.edu/bio.

Education and Professional Development Committee:

Pursuing Development of Resources for Researchers and Students

The Torch

By Martine LaBerge, Executive Editor

The 2003-2004 Education and Professional Development Committee is building on past efforts to develop educational and professional development resources for members of the Society. Educational resources being developed include a video library, a listing of textbooks and course syllabi for teaching biomaterials, and negotiating for additional text/reference book discounts. The video library project is being spearheaded by Jeff Karp at the University of Toronto, Canada. He currently has collected 15 videos from biomaterial companies, including Cook Inc., Biorthex Inc., Biomet Inc., Carbomedics Inc., and Straumann covering topics such as hernia repair, lumbar fusion, total joint repair, heart valve replacement, and dental implant placement and craniofacial reconstruction. It is anticipated that the library will be made available to Society members for use in educational and training activities through the Society's Web site. Additional videos are welcome and may be sent to Jeff by contacting him at jeff.karp@utoronto.ca. Resources for teaching biomaterials, including textbooks, course syllabi, and student projects, are also being collected and organized in conjunction with the video library.

For professional development, the committee is working to facilitate the posting of positions wanted and positions available for members and biomaterial companies and institutions on the Society's Web site. Additionally, a series of articles is being developed especially for students and young investigators that highlights professional skills and strategies for succeeding in a biomaterials science and engineering career.

Additional information will be made available as the Web site for the library, teaching, and career development is pursued. Members are also encouraged to contact Joel D. Bumgardner (jbumgard@abe.msstate.edu) with educational and professional development matters, information, or resources to be considered by the committee.

Education and Professional Development Committee: Joel D. Bumgardner, Chair, Alan Litsky, Kay C. Dee, W. John Kao, Fred Schoen, Liisa Kuhn, Lisa Friis, Jeff Karp, Josh Lovekamp, and Steve Echard (SFB executive director).

Activities of the Liaison Committee

By Joachim Kohn

According to the bylaws, the Liaison Committee "shall consider, advise, and make recommendations to the Council with respect to all aspects of the relationships between the corporation and other technical and professional societies." The bylaws indicate that the founders of the Society envisioned the Liaison Committee to take an active role in shaping the interactions between societies and organizations of relevance to the field of biomaterials. Accordingly, the Liaison Committee has been involved in creating joint programming activities with other professional societies at various symposia and conferences. However, this is not the only area of activity. One member of the Liaison Committee, appointed by the president, serves as a special liaison between the Society and other standards-making organizations on matters affecting the development and establishment of standards relating to, or associated with, biomaterials. This special liaison person currently is Dr. Mutlu Karakelle from Alcon Research, Ltd. Finally, the committee interacts with the International Union of Societies for Biomaterials Science and Engineering (IUS-BSE). The main function of the IUS-BSE is to facilitate the World Biomaterial Congresses that take place every four years. To ensure continuity of representation from one World Congress to the next, the bylaws stipulate that the chairperson of the Liaison Committee shall be appointed to serve a four-year term. The current chairperson is Joachim Kohn. He was appointed in 2000 at the World Biomaterials Congress in Hawaii and will complete his term at the 2004 World Biomaterials Congress in Sydney, Australia. Martine LaBerge is the second U.S. representative to the IUS-BSE and also serves on the Liaison Committee.

The Liaison Committee has been active in fostering collaboration between the societies and organizations that relate to the focus and mission of the Society For Biomaterials. In fact, this is a good time to collaborate, as many organizations are feeling the impact of a slowing economy, reduced business travel, and reduced global stability. Since 2001, the Liaison Committee has reached out to the American Association of Pharmaceutical Scientists (AAPS), the Controlled Release Society (CRS), the American Vacuum Society (AVS), AIMBE, Wound Healing Society, Tissue Engineering Society, Pittsburgh Tissue Engineering Initiative (PTEI), and several other organizations to arrange for joint symposia and programming activities that were of interest to our membership. Bozena Michniak was particularly active in arranging for such joint activities. Prof. Michniak used her key positions within the pharmaceutics and drug delivery (PDD) section of the AAPS and her contacts as editor of the CRS newsletter to set up, among many other events, the Joint Symposium on "Intelligent Biomaterials for Protein Delivery, Molecular Imprinting, and Micropatterning" at the CRS annual meeting in Seoul, Korea, June 20-25, 2002, with Dr. Nick Peppas as invited plenary speaker. This past year, James Hickman took the lead in coordinating a jointly sponsored session between the Society For Biomaterials and the Biomaterials Interfaces Division of the AVS at the AVS annual meeting held November 3-8, 2002, in Denver, Colo. Although there are no plans to hold a similar joint session at this year's AVS meeting, Robert Latour will explore this possibility for next year.

Recently, the Liaison Committee's discussions with the leadership of other professional societies led to an attempt to increase the level of cooperation between the societies by creating events that involve the sharing of risks and fiscal benefits through partnering in events that are truly "jointly administered." A first such event is planned between the Society For Biomaterials and the Tissue Engineering Society in 2006. By working together, the societies hope to reduce the number of conferences, workshops, and symposia that overlap in content and tend to compete unnecessarily for a limited amount of travel funds.

Taking the level of cooperation a step further, the Liaison Committee is exploring Dr. Karakelle's far-reaching proposal to create the "Associated Societies for Biomedical Science and Engineering" so a potential member can pay only one single membership fee for access to programs and benefits provided by all participating Societies. The association would work much like the partnerships among airlines, where the members of one airline's frequent flyer program can participate in the programs provided by other partnering airlines. Dr. Karakelle's proposal is based on the recognition that the dynamic and multidisciplinary nature of the biomedical sciences is increasingly requiring a closer communication and collaboration platform between the different scientific disciplines and the many societies that operate under the general umbrella of biomedical science and engineering. Many scientists and engineers from the biomedical industry would like to participate in more than one society, but company policies tend to limit the number of professional memberships and the number of trips to scientific meetings. Likewise, academicians suffer from a chronic shortage of travel funds and would greatly benefit from a closer collaboration among the various societies. As an additional benefit, the concept of the "Associated Societies" could result in an overall increase in membership for all the participating societies.

The members of the Liaison Committee welcome the comments and feedback of our membership. Please feel free to contact the Liaison Committee members: Joachim Kohn, chair, (kohn@rutchem.rutgers.edu), Mutlu Karakelle (mutlu.karakelle@AlconLabs.com), Martine LaBerge (laberge@clemson.edu), Robert A. Latour Jr. (latourr@clemson.edu), and Bozena B. Michniak (michnibb@umdnj.edu).

Society Announces the Symposium on Biomaterials in Regenerative Medicine

By Michael V. Sefton, University of Toronto, on behalf of the Organizing Committee

The Advent of Combination Products • October 16 - 18, 2004, Philadephia

Once upon a time, life for a biomaterials scientist was simple. He (or the rare she) could focus on an understanding of materials science and select the best material for an implant. As long as nothing untoward happened in the body, approval by the regulatory authorities would soon be forthcoming. And soon hip implants, intraocular lenses, vascular grafts, sutures and a wide variety of very useful and important devices were available.

But now, new fields such as tissue engineering and regenerative medicine have been developed and are resulting in combination products that push the frontiers of materials science and biology. Materials science know-how is no longer enough, and integrating biology is discussed as much as material properties. Materials are now carriers for drugs (drug delivery systems), DNA (vectors), or cells (scaffolds). Some have immobilized peptides to enable cell adhesion or migration, some are degradable by hydrolysis or by specific enzyme action. Some contain bioactive agents (e.g. heparin, thrombomodulin) to prevent coagulation or platelet activation, while others incorporate bioactive groups to enhance osteoconduction.

Regenerative Medicine promises to enable the regeneration of irreplaceable tissues, to create an unlimited supply of organs for transplantation, and new therapies to allow the elderly to lead active, healthy and productive lives. But to realize this promise, one must overcome numerous regulatory and business challenges. These are most apparent in the way the therapeutic world has been divided into devices, drugs and biologicals. Now, coronary stents combine metals, polymer coatings and drugs, while tissue constructs combine biomaterials and living cells. These combination products are challenging everyone—from the laboratory bench to the regulatory authorities, from manufacturers to clinicians.

It was once sufficient to show that the material had no effect (i.e., it was inert) in order to get the blessing of the regulatory authorities. Now, it is the presence of an effect and a significant one that needs to be regulated. The Food and Drug Administration has established an Office of Combination Products (www.fda.gov/oc/combination) to deal with these products, and every indication suggests that it is not long before these products are the norm.

Biomaterials are central to many of these combination products and the Society For Biomaterials is organizing a two-day symposium to enhance our understanding of the scientific, commercial and regulatory issues. This is being planned as a terrific opportunity for students (especially those who may not have a chance to go to Australia) to present their research at the frontiers of biomaterials and to learn what is happening throughout the world of biomaterials. The meeting is also being planned with the interests of our industrial members in mind, who will learn more about the issues of translating discoveries into commercial or clinical reality. Furthermore, this will be an opportunity for all to network with both emerging and established leaders.

The meeting has been organized to emphasize the underlying scientific and regulatory problems that transcend specific clinical applications. Thus, sessions will focus on the variety of interactions materials have with drugs, cells, or the host that underlie all applications. Nonetheless, there are still many opportunities to present specific developments in the context of frontiers in biomaterials.

Later this fall, a call for papers will be distributed widely. That call will highlight the following topics around which the meeting will be structured:

Frontiers in Combination Products
- Combination products in specific clinical areas (e.g., neural cardiovascular, orthopaedic, ophthalmic, etc.)
- Biology of regeneration, repair, healing
- Nanotechnology in regenerative medicine
- Regulatory issues associated with combination products

Novel Materials
- Synthesis strategies of nanostructures
- Self-assembled nanostructures and materials
- Active protein-biopolymer nanodevices
- Biomimetic materials

Material-Cell Interactions
- Biomaterial and soluble/insoluble cues for cell phenotype
- Stem and progenitor cell delivery in regenerative medicine

Material-Drug/DNA Interactions
- Materials for DNA delivery
- Drug/DNA/material interactions
- Drug delivery systems in regenerative medicine
- Material processing strategies to preserve protein/DNA structure/function

Materials and Endocytosis

Host Response
- Validation of biological models
- In vitro/in vivo/clinical correlations
- Materials as agonists of biological response
- Functional integration of combination products

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Scaffold Structure and Cell Function Through Multimodal Imaging and Quantitative Visualization

By Joy P. Dunkers and Marcus T. Cicerone

Tissue engineered medical products (TEMPs) are often three-dimensional (3D) hybrid materials consisting of a porous scaffold upon which the tissue is grown. While it is generally understood that a complex interaction of many variables influences the success of TEMPs, the precise nature of these interactions has yet to be worked out in many instances. A significant difficulty in furthering the understanding of the interaction between these factors and cell behavior is the lack of a high-resolution imaging technique that can penetrate deeply and nondestructively into the scaffold. An approach that uses advanced optical imaging to noninvasively monitor the developing tissue was developed. However, before any assessment of the tissue viability can be made, the volumes of imaging data must be rigorously analyzed. Therefore, an equally important component of this effort is image visualization and quantification. Progress in these areas is summarized below.

MULTIMODAL IMAGING

An instrument that can gather information on a TEMP using multiple imaging modalities was constructed. This means that each channel of imaging data provides different but complimentary information. Optical coherence microscopy (OCM) was chosen as the technique to image scaffold, cell, and tissue structure because of its unique combination of high resolution (^{a}1 μm) and high sensitivity (> 100 dB). OCM is an interferometric technique that uses both confocal and coherence gating mechanisms for stray light rejection, rendering it comparable in resolution to laser scanning confocal microscopy but far superior in imaging depth. Confocal fluorescence microscopy (CFM) was added to the

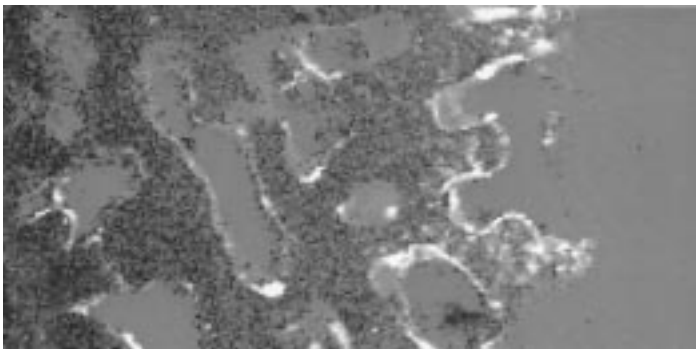

Figure 1: Image of merged and registered OCM and CFM images of the cultured PCL scaffold at 145 _m below the surface.

OCM to collect information on cell function using traditional cell-staining techniques. In the collinear instrument, volumetric images of cell and scaffold structure were collected using the OCM channel and cell function using the CFM channel. Each channel is then overlayed in the rendered image for maximal insight. Figure 1 displays merged and registered OCM and CFM images 145 μm below the surface of a TEMP. The TEMP consists of a volume fraction of 50 percent poly(ε-caprolactone) (PCL) scaffold that was cultured with fetal chick osteoblasts for 10 weeks and stained with a nuclear stain. In Figure 1, the regions of low OCM signal are red (pores), high OCM signal are black (scaffold), and regions of high CFM signal are yellow (cells). CFM complements OCM by allowing us to positively identify stained tissues at more shallow depths. Once identified, OCM allows us to discriminate these tissues from scaffold, and thus view them at a greater depth. This will form the basis of structure-property relationships for TEMPs based on microscopic characterization of scaffold properties and concomitant cellular responses.

QUANTITATIVE VISUALIZATION

Quantification of scaffold properties must be performed to establish scaffold structure and cell function relationships and to optimize scaffold design. One goal is to design an approach that is valid with any pore structure. Figure 2 displays a volumetric view of the PCL scaffold images collected using X-ray computed tomography. In this figure, the pores are colored in red and the scaffold in green.

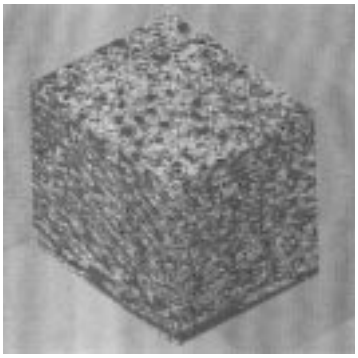

Figure 2: X-ray computed tomographic reconstruction of a PCL based scaffold. Dimensions: 1.0 mm on each side.

From viewing this image, one gets a qualitative sense of the need for such an approach. Heterogeneity in the microstructure is exhibited by the difference in pore size, shape and anisotropy as seen on the different faces of the volume. Pore volume, size distribution, tortuosity, and connectivity are metrics of interest for the scaffold microstructure. An example of the type of information gleaned from the imaging data is shown on page 20. Figure 3 displays the pore size as measured by the chord length distribution function (CLDF). The CLDF is the probability of finding a chord of length l between x and x + dx entirely in one phase. Chords are defined as the segments formed by the intersection of lines with the interface between two phases.

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MIT's *Technology Review* Recognizes Biomaterial Scientists and Engineers

By Martine LaBerge and Nicholcas A. Peppas

Technology Review, MIT's Magazine of Innovation, announced its third class of innovators 35-years-old or younger whose technologies have a profound impact on today's world. Nominees are recognized for their contributions in transforming the nature of technology in industries such as biotechnology, computing, energy, medicine, manufacturing, nanotechnology, telecommunications, and transportation. The TR100, chosen by the editors of *Technology Review* and an elite panel of judges, consists of 100 individuals 35-years-old or younger who have been selected for their innovative work. The field of biomaterials science and engineering has been emphasized by *Technology Review* through its biomedicine and biotechnology, and nanotechnology lists. Achievers and leaders in their field, these individuals have a common goal to improve patient care. Their technology, often the result of extensive basic science and engineering work, has also been recognized by peer-reviewed funding and publications, and highlighted at national meetings of the Society For Biomaterials, among others. Among these innovations, biomaterials science and engineering is emphasized by:

- Guillermo Ameer, Northwestern University, who synthesizes polymers for the replacement of damaged heart and lung tissue and rebuilding of blood vessels.

- Sangeeta Bhatia, University of California, San Diego, who uses microchip-manufacturing tools to develop artificial livers.

- Karen Burg, Clemson University, a member of the Publications Committee of the Society For Biomaterials, who engineered a minimally invasive process to rebuild tissue for breast cancer survivors consisting of tiny, degradable synthetic beads on which a patients' own fat cells can be cultivated. A degradable gel is used to help temporarily bind the beads and cells injected into the damaged tissue.

- Michael E. Gertner, University of California, San Francisco, who developed a process for coating stents with metallic films that carry drug molecules that can be released for up to six months.

- Justin Hanes Affiliation, Johns Hopkins University, who devised a way to make coated polymer particles porous to serve as drug-carrying vessels that are large enough to lower the odds of attack by the immune system. As the polymer degrades, insulin, growth hormones, or asthma medication can be released over time.

- Krishna Kumar, Tufts University, who improves the stability and effectiveness of protein-based drugs. Chemically altered segments of the proteins stiffens their structures and improves their stability. Proteins that can penetrate human cells, opening portals through the cell membranes to allow the passage of drug molecules, are fabricated.

- Erin Lavik, Yale University, who designed polymer scaffolds that mimic the architecture of a healthy spinal cord.

- Anthony Lowman, Drexel University, who created a novel method of shielding insulin inside polymer-based hydrogels. The hydrogels have pores that can hold insulin and open only in response to the high pH of the upper small intestine.

- Jennifer West, Rice University, Member-at-Large of the Society For Biomaterials, who synthesizes polymers that contain biological signaling molecules and molds the synthetic polymers into a blood-vessel-shaped template that is then seeded with live cells; by optimizing the polymers for different cell types in different regions of the template, the architecture of a natural vessel can be created.

- David M. Lynn, University of Wisconsin-Madison, who developed a process that could synthesize hundreds—or even thousands—of new polymers at once and screen their varying DNA-transferring capabilities.

- Balaji Narasimhan, Iowa State University, who devises time-release polymers to replace multiple vaccine injections by encapsulating vaccines in specially tailored biodegradable polymers, thereby maximizing immune response and making booster shots unnecessary.

Implants and medical devices are designed and intended to benefit patients. The past century pioneered implants, medical products, and devices and emphasized the role of biomaterials scientists and engineers as members of clinical teams. The 21st century promises to be even more exciting as the medical device industry observes an explosion of possibilities for the marketing of new ideas. The Society For Biomaterials congratulates the scientists and engineers cited on the TR100 for their legacy to the medical device industry.

Drug Delivery Special Interest Group News

By Corinne Bright and Brent Vernon

The Drug Delivery Special Interest Group (SIG) is comprised of more than one hundred members, roughly divided between academic and industrial affiliations. The goal of the Drug Delivery SIG is to: facilitate communication between industry, academic, and student members; provide timely information related to funding for drug delivery research; and provide information related to employment opportunities. This information will be disseminated via e-mail, a quarterly Drug Delivery SIG newsletter, and a dedicated Drug Delivery link on the Society for Biomaterials Web site. Student members are actively encouraged to participate in all aspects of SIG activities. The SIG has organized subcommittees to address issues related to drug delivery education at the undergraduate and graduate school levels; development of drug delivery standards (ISO, ASTM, AAMI); development of sessions, symposia, workshops, and tutorials; and to improve the quality of abstracts submitted for presentation at annual meetings. Active SIG members will review abstracts and moderate sessions at annual meetings.

Many Drug Delivery SIG members attended the Society's 29th Annual Meeting, making broad contributions in hydrogel, coating, stent, micro/mesosphere, and fiber-based drug delivery systems. Many SIG members also attended the 2003 Controlled Release Society (CRS) Annual Meeting Exposition in Glasgow, Scotland. Some of the contributors to this year's conferences are highlighted.

NO-generating Hydrogels for Prevention of Restenosis[1]

Arterial angioplasty, a common procedure to open occluded arteries, often injures the arterial wall, triggering endothelial denudation, smooth muscle cell (SMC) proliferation and migration, and platelet aggregation. In 30 percent to 40 percent of patients, neointima formation leads to restenosis. As a result, researchers are investigating methods to locally deliver therapeutic drugs to prevent re-occlusion. Nitric oxide (NO) is thought to act as an inhibitor of vascular lesion formation based on its capacity to inhibit platelet aggregation and SMC proliferation and migration. However, NO's short half-life and narrow therapeutic window preclude the drugs systemic administration. Dr. Jennifer West's group at Rice University has developed PEG-Cys-NO/PEG-diacrylate hydrogels that can be applied perivascularly and crosslinked *in situ* via interfacial photopolymerization to provide a local and sustained source of NO. *In vitro*, these NO-generating hydrogels have been shown to inhibit both SMC proliferation and platelet adhesion while promoting re-endothelialization. In an *in vivo* rat carotid balloon-injury model, PEG-Cys-NO/PEG-diacrylate hydrogels significantly reduced neointima formation compared to control PEG-diacrylate hydrogels. Fourteen days after vessel injury and hydrogel application, intimal thickness is reduced by approximately 82 percent and intimal-to-medial-area ratio is reduced by 78 percent. The hydrogels can be designed to release NO for periods of hours, days, or months. In this manner, the release properties can be tailored to generate an initial burst of NO post-injury followed by a sustained release of NO. Ultimately, these hydrogels can be incorporated into stents or vascular grafts. See Figure 1.

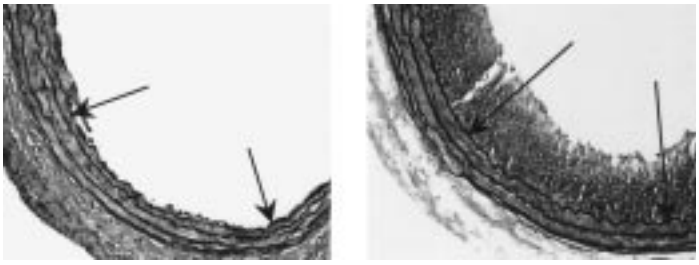

Figure 1. The perivascular application of NO-generating hydrogels significantly reduced neointima formation in the rat experimental balloon injury model as compared with control hydrogels. This figure shows histological sections of rat carotid arteries that were explanted 14 days after injury. Staining was by van Gieson elastin stain. Arrows indicate the position of the internal elastic lamina. On the left, PEG-CYS-NO treated vessel. On the right, control hydrogel treated vessel. In this vessel, all of the tissue above the internal elastic lamina is involved in the restenosis process. $p < 0.0002$ (Picture courtesy of Jennifer West, Rice University)

HA-drug composites for Analgesia[2]

Pro-drug conjugates have been demonstrated to favorably alter the therapeutic index of a drug by improving drug efficacy while reducing toxicity. Hyaluronic acid (HA) is a promising natural polymer for drug delivery because it is nontoxic, contains multiple sites for drug loading, and the polymers resorption rate can be controlled by the degree of crosslinking. Research led by Dr. Bob Miller and Dr. Michael Philbrook at Genzyme Corp. resulted in the development of a hyaluronic acid-based drug delivery system with a hydrolytically labile ester bond for the delivery of analgesic drugs. Morphine, codeine, and the narcotic-antagonist naloxone were conjugated to HA. The group demonstrated that by varying the functional group around the ester and the leaving group, the analgesic release rate could be controlled. For example, the presence of a methyl group reduced the release rate of codeine five-fold compared with an acryl group, providing sustained release of codeine *in vitro* for more than 60 days. The company has expanded this to the delivery of anesthetics with the similar goal of extending the half-life, increasing the duration of action, and eliminating the need for repeat dosing or indwelling catheters. At the recent CRS meeting, Genzyme demonstrated bupivacaine release from HA-bupivacaine depot for more than 100 hours *in vitro*. Furthermore, the HA-bupivacaine system has a half-life of 16 hours compared with a physical mixture of HA and bupivacaine with a half life of 0.4 hours. In an *in vivo* sciatic nerve model, rats were injected with bupivacaine tethered to hylan B, a crosslinked HA derivative. Rats showed an extended impairment of hind leg motor function compared to those injected with free bupivacaine and hylan B.

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Special Interest Groups Revitalized at Reno Meeting

By Elaine Duncan

An initiative spanning more than six months culminated at the 2003 Annual Meeting in Reno with an "ALL SIG Meeting." Representatives from each Special Interest Group (SIG) reported on the objectives and major programs supported by their group and shared some of their frustrations and needs for future growth. Clearly, all SIGs share a common goal of growth for the Society and opportunities for their members. Prior to the ALL SIG meeting, SIG officers and various Council members participated in a review of how the SIGs were structured and the impediments to their continued development. This article will review some of those findings and resultant recommendations, as well as summarize some of the key points made during the ALL SIG meeting.

To better facilitate SIG use of the Society Web site, the SIG council representative, Elaine Duncan, has been appointed temporary Web site editor to work with the editor of *Biomaterials Forum*, Martine LaBerge, and the publications chair, Jack Ricci, to help the SIGs have a voice in Web site content and format. This activity has been delayed to give Association Headquarters Inc., the Society's new management company, time to settle in. But, the first planning meeting has been scheduled. Please send any and all ideas for SIG Web site content to Elaine at the e-mail address at the end of this article.

Budgeting methods for SIG operations have been simplified. However, the re-engineering initiative identified the need of SIGs to have a method of developing "enterprise." This year, the SIGs will work closely with the secretary-treasurer and secretary-treasurer-elect to develop a format for presentation and review of SIG enterprise. The Society's financial structure, particularly for active membership, continues to restrain the Society's operating budget. As improvements are made at that level, it is hoped the constraints on SIGs will likewise improve.

Student recognitions directly awarded by SIGs have been suspended. Instead, each SIG that would like to redevelop student recognitions is asked to work with the Awards and Nominations Committee on ways to develop a presence in the existing student award program or in alternative programs for consideration. Administration of awards directly from each SIG had become unwieldy.

The standards subcommittee chair of the Materials and Devices Council Committee, Gina Malczewski (gina.malczewski@dowcorning.com), encouraged SIG members to volunteer in their area of expertise to review and recommend voting on international standards.

Revisions to the bylaws now permit election of SIG officers by mail or electronic ballot. Details on the system will be announced later in the year. It is anticipated that the next SIG officer elections will be conducted using remote ballots because the annual meeting will be held in conjunction with the 7th World Biomaterials Congress in Sydney, Australia.

Although the re-engineering initiative did not result in any immediate changes in SIG organization, it is clear that continuing assessment of how SIGs interface with Council and the Board, particularly on budget and meeting planning, is in order. SIGs continue to struggle between reliance on the Society for funding and approval of activities, and self-reliance in the implementation of initiatives and the need for grass-roots, fast-paced response to current events. This is fertile ground for fruit.

Because of the World Congress, it is anticipated that SIGs may not have sufficient membership for quorum meetings in 2004. For that reason, one time period will be allocated to SIG business meetings (time and date to be announced). As an alternative, each SIG is encouraged to use their prerogative to hold a meeting in conjunction with other meeting venues on their topic, or to hold a student day at a convenient university. Individual SIG initiative ideas will be a major topic of discussion as the season gets underway.

As a recruitment tool for each SIG, the program chair for each SIG was encouraged to review the author names for presentations and posters against the SIG membership list and invite nonmembers to join the SIG representing that topic at the meeting. In the past, student member retention has been notoriously low. Each SIG active member is encouraged to "adopt a student" as a "SIG-Buddy" from the group to foster membership retention. Respective SIG secretary-treasurers can be contacted for potential contacts.

Any SIG secretary-treasurer that has not formally presented minutes of their meeting is encouraged to do so. The meetings in Reno were held simultaneously. Although it was inconvenient for members in more than one SIG, it was a necessity at this meeting due to timing and objectives for the meetings. Future annual meetings (but not the World Congress in Sydney) should be planned with enough foresight to permit the Program Committee sufficient time for scheduling SIG meetings at respectable hours of the day without conflict with presentations.

The Biomolecular SIG has been terminated effective second council meeting at Reno in April 2003, in accordance with provisions in the bylaws. The SIG failed to have a quorum meeting for a second year, the membership had reached the marginal level for active members, and no active member came forward to act as pro-tem officer during the probation period. Members who had paid their dues to this SIG have been contacted and offered a membership in any other SIG. Anyone not responding has been assigned to the Tissue Engineering SIG, but contacting the Society office and requesting an alternative assignment for the remainder of the year can change this.

The coming year will be an opportunity for SIGs to develop through cross-collaboration. SIG chairs will be asked to rotate

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New Jersey Biomaterials Consortium

The Rutgers-based New Jersey Center for Biomaterials (CBM) has received a five-year, $5.1 million grant from the National Institute for Biomedical Imaging and Bioengineering of the National Institutes of Health (NIH). The award will support the establishment of a national biotechnology center, formally designated as "Integrated Technologies for Polymeric Biomaterials" (RESBIO).

"This is the first of more than 60 NIH-funded national biotechnology resources across the nation to be located in New Jersey," said Joachim Kohn, CBM director and Board of Governors Professor of Chemistry and Chemical Biology at Rutgers, The State University of New Jersey. CBM is a cooperative research initiative sponsored by Rutgers, the University of Medicine and Dentistry of New Jersey (UMDNJ), and New Jersey Institute of Technology (NJIT).

"The RESBIO program will foster multidisciplinary investigations that integrate chemical, biological and materials research with the goal of supplying biomedical engineers with the biomaterials and devices that will enable new kinds of therapies," Kohn said. "This will involve developing key biomaterials research capabilities such as materials design, chemical synthesis, processing, fabrication, and biological and clinical evaluation."

The new therapies will include implanted and degradable drug delivery systems and tissue engineering scaffolds. The NIH-supported research will employ leading-edge equipment to be shared by all RESBIO scientists—researchers drawn from Rutgers and other participating institutions.

Through outreach, visiting scientists, workshops, and reports at conferences, RESBIO staff will promote collaborative projects with investigators across the country, including basic studies of the healing response, novel polymer tissue engineering implants, and the development of polymers for drug and gene delivery.

Expert research teams from RESBIO laboratories will be a resource for investigators nationwide facing polymer materials-related problems. Researchers will be able to bring samples to RESBIO experts who can conduct tests, fabricate shapes, create images, and perform technical services using their advanced equipment. Technical service areas will include parallel polymer synthesis (simultaneously creating multiple materials), multiphoton confocal microscopy imaging (the latest development in infrared imaging technology), polymer processing, and electron microscopy. Active communication and training programs will ensure the greatest impact of and access to RESBIO resources.

RESBIO will provide links to four New Jersey universities with federally funded centers (Rutgers, UMDNJ, NJIT, and Stevens Institute of Technology) and to individual collaborators and affiliated institutions nationwide. For further information, contact admin@njbiomaterials.org or see www.njbiomaterials.org.

By Cher H. Davis and Michael J. Fasolka

NIST Combinatorial Methods Center:

A Partner in Accelerating Materials Research

The NIST Combinatorial Methods Center (NCMC)—now in its second year—has attracted 16 member partners from industry and government. Since its inception, the NCMC has tailored its research and outreach towards current and emerging industrial needs in C&HT methods. As part of its FY2003 outreach, the NCMC organized three workshops. The first, NCMC-2, was held Oct. 7-8, 2002, at NIST. NCMC-2 related NCMC-developed C&HT measurement methods for mechanical properties and adhesion (including SIEBIMM). In addition, the NCMC-2 program included a plenary symposium, facilities tours, and a panel discussion that revealed industrial needs for a focused project in HT Interfacial Tension Measurements (now launched, see www.nist.gov/combi).

Two additional workshops were aimed at initiating NCMC actions in C&HT informatics. Needs in the field were gleaned at the NCMC Combinatorial Informatics industrial symposium held in conjunction with a Knowledge Foundation Meeting Feb. 19, 2003, in San Jose, Calif. Analysis of industry concerns indicated two areas that presented a NIST role. First, industry requires examples of how to integrate automated fabrication instruments, characterization devices, and analysis routines into a database-centered informatics system suitable for C&HT research. Second, interoperability barriers hamper informatics system development. In particular, the lack of a common data interchange format greatly complicates the integration of devices from disparate vendor sources into a coherent C&HT system.

In response to these needs, the NCMC is building a model C&HT informatics system in its laboratory facilities. Constructed with open-source code, the NCMC system provides transparent examples of informatics infrastructure. In addition, the NCMC endeavors to help create data interchange format standards for the C&HT materials research community. Both efforts were highlighted at NCMC-3: Combinatorial Informatics, held at NIST May 22-23, 2003. This workshop outlined issues in C&HT informatics and several NIST XML-based interchange formats relevant to materials research. NCMC-3 culminated with the formation of the Combinatorial Materials Research Data Standards (CMRDS) Working Group—a first success towards establishing data standards for the C&HT materials community. Ten NCMC-3 attendees volunteered to serve on CMRDS committees, which are aimed at identifying opportunities (e.g. XML) and at defining components for a data interchange format. For details, see the CMRDS Web site at http://polymers.msel.nist.gov/combi/cmrds.html.

FY2004 promises sustained effort and new directions from the NCMC. NCMC-4: Polymer Formulations, held Oct. 6-7, 2003, featured C&HT measurement strategies for complex fluids and sessions dedicated to the Interfacial Tension Focused Project and the CMRDS Working Group. Moreover, new focused projects in formulations and adhesion will be launched. In addition, a new NCMC effort in nanotechnology will create reference substrates designed to test and calibrate advanced scanning probe microscopy measurements. For more information on these efforts and other NCMC programs, see www.nist.gov/combi.

NCMC Members (*New in FY2003)

3M	Exxon Mobil Research
Air Force Research Lab	Honeywell International
Accelrys Inc.*	ICI/National Starch & Chemicals
Air Products & Chemicals	Michelin*
Akzo Nobel	PPG Industries*
BASF	Procter & Gamble
Bayer Polymers	Rhodia
Dow Chemical Company*	Symyx Technologies*

Contributors and collaborators are A. Karim, W. Zhang, K.L. Beers, C. Stafford, A. Forster, H.J. Walls, J.T. Cabral, A.I. Norman, D.H.A. Chiche, E.J. Amis (Polymers Division, NIST). For more information, please contact chdavis@nist.gov or mfasolka@nist.gov.

Tooth, Heal Thyself

Government News
By John A.Tesk

Dentists beware: Teeth soon may be smart enough to fix themselves

"Smart materials" invented at the National Institute of Standards and Technology (NIST) that stimulate repair of defective teeth soon may be available. Laboratory studies show that these composites, made of amorphous (loosely structured) calcium phosphate embedded in polymers, can promote re-growth of natural tooth structures efficiently.

In the presence of saliva-like solutions, the material releases calcium and phosphate ions, forming a crystalline calcium phosphate similar to the mineral found naturally in teeth and bone. Developed through a long-standing partnership between NIST and the American Dental Association (ADA), these bioactive, biocompatible materials are described by ADA's Drago Skrtic and NIST's Joseph Antonucci and Edward Eanes in a recent issue of the NIST *Journal of Research*. Plans are being made for clinical trials. Initial applications include adhesive cements that minimize the decay that often occurs under orthodontic braces. The material also can be used as an anticavity liner underneath conventional fillings and possibly in root canal therapy.

NIST and ADA scientists continue to enhance the material's physicochemical and mechanical properties and remineralizing behavior, thereby extending its dental and even orthopedic applications. For example, the researchers found that adding silica and zirconia to the material during processing stabilizes the amorphous calcium phosphate against premature internal formation of crystals, thereby achieving sustained release of calcium and phosphate over a longer period of time. This work is funded through a grant from the National Institute of Dental and Craniofacial Research. For more information, contact joseph.antonucci@nist.gov, (301) 975-6794.

Miniature Mix-ups to Speed Materials Research

Government News
By John A.Tesk

A new National Institute of Standards and Technology (NIST) project aims to stir up materials research by adapting "lab-on-a-chip" technology to mix and evaluate experimental concoctions at a rapid clip, hastening improvements in products ranging from paints to shampoos to plastics.

Initially, researchers at the NIST Combinatorial Methods Center (NCMC) and several of the NCMC's company members plan to rev up the search for new or better emulsions—often-complex formulations that are the basis for U.S. product markets totaling more than $50 billion. They will start by deciphering interactions at the interfaces (inter-facial tension) between the various components that make up these viscous mixtures and are key to their performance. Now, efforts to improve paints, shampoos and other emulsions tend to be time-consuming, trial-and-error exercises. But with tiny "lab-on-chip" devices, much of the process can be automated, permitting rapid, systematic testing of new material formulations.

The project will extend the capabilities of so-called microfluidic systems—tiny, channel-lined devices now used regularly for medical testing. In DNA chips, for example, droplets of genetic material are routed through networks of tiny wells, each one set up for a particular diagnostic test. Material formulations, however, typically contain components—from solvents to different-sized particles—that do not readily mix and circulate through these minute plumbing systems, explains NIST research chemist Kate Beers.

To accommodate these differences, NCMC researchers, led by Kalman Migler, have designed and tested credit-card-sized prototypes tailored for viscous materials research. Features include mixers, pumps, reservoirs and computer control of the flow of sample droplets through a network of millimeter-wide channels. Mixture properties will be characterized with real-time image measurement techniques that NIST is developing with an eye on many application areas. For more information, contact kalman.migler@nist.gov, (301) 975-4876.

Deciphering How Arteries Contribute to Hypertension

By Cher H. Davis and Michael J. Fasolka

National Institute of Standards and Technology (NIST) scientists are taking their knowledge of mechanical tensile strength tests in metals and composites and applying it to medical research problems.

Physicians long have known that babies born with congenital heart defects at higher altitudes have an increased risk of developing complications, such as pulmonary hypertension. Could there be some way to trick the arterial walls so that they wouldn't stiffen under increased blood pressure?

Working with the Children's Hospital and University of Colorado Health Sciences Center in Denver, NIST researchers have used rat arteries—both normal and hypertensive—supplied by the university center and placed them in a mechanical stress tester. The tester holds a small disc-shaped sample of the arterial tissue that is slowly stretched by pumping a special liquid against the back of the disc. The pressure of the liquid causes a bubble to form on the front of the disc. The shape of the resulting bubble helps the researchers determine details about the tissues' elasticity, strength, stiffness, and other properties.

"Hypertensive tissue should be stiffer, so we will get less inflation with the same amount of pressure," says NIST materials reliability researcher Elizabeth Drexler. "What we want to know is what it is in the artery that causes it to stiffen. Is it more collagen? Is it the smooth muscle cells? Perhaps we could give the muscle cell a signal not to produce more collagen." So far they have studied 20 rat arteries and plan to study 20 more, along with some calf arteries. A preliminary report that verifies their test method appears in the May/June issue of the NIST *Journal of Research*.

For more information, contact Elizabeth Drexler at drexler@boulder.nist.gov, (303) 497-5350.

Drug Delivery...

(Continued from page 10)

Bimodal Soy Protein Drug Delivery Systems[3]

Multimodal drug release systems are emerging to better mimic natural drug release profiles. Dr. António Cunha's group at University of Minho has been investigating novel approaches to the design of bilayered systems based on soy protein thermoplastics. The goal of this work was to design a core layer that functions as a drug depot with an external skin layer that restricts early drug diffusion. During the compounding/extrusion of the soy protein, the polymer was loaded with the bioactive drug, theophylline (SID). Axisymmetrical dumbbell-like skin/core specimens approximately 1.5 mm in diameter were co-injection molded to form an SI skin surrounding an SID core. The bilayer system provides more sustained release of theophylline compared with a single layered device for more than 500 minutes. The duration of drug release can be controlled by the degree of crosslinking of the layers as well as the addition of ceramic fillers.

Bone-Targeted Drug Delivery System[4]

In bone diseases such as osteoporosis, Paget's disease, and bone cancer, the normal balance between bone resorption and remodeling is disrupted. While many therapeutic drugs have been identified for the treatment of these diseases, poor tissue targeting has hampered their clinical application. In an effort to increase the bioavailability of the drug in the bone, Dr. Dong Wang, Dr. Scott Miller, and Dr. Jindrich Kopecek of the University of Utah conjugated HPMA copolymer to FITC, a model drug, and either D-aspartic acid (D-Asp) or alendronate to render the polymer osteotropic. In an *in vitro* study presented at the 30th Annual Meeting of the Controlled Release Society, the polymers conjugated to the targeting moieties demonstrated stronger binding to hydroxyapatite, while the control polymer without the moiety showed only minimal binding. Twenty-four hours after intravenous injection of the bone-targeted polymers into balb/c mice, the P-alendronate-FITC and P-D-Asp-FITC showed strong fluorescent staining in bone as compared with control animals injected with P-FITC. The preliminary data hold promise for the bone-specific delivery of therapeutic agents with minimal side effects. The group is also working on a variety of HPMA-drug conjugates for the improvement of cancer chemotherapy.

1. *Lipke, E.A., et al. in Society for Biomaterials 29th Annual Meeting. 2003. Reno, NV.*
2. *Gianolio, D.A., et al. in Controlled Release Society 30th Annual Meeting. 2003. Glasgow, Scotland.*
3. *Vaz, C.M., et al. in Society for Biomaterials 29th Annual Meeting. 2003.*
4. *Wang, D., et al. in Controlled Release Society 30th Annual Meeting. 2003. Glasgow, Scotland.*

Kurve Technology, Inc. (Bothell, Wash.) announced the formation of a development partnership with **Medel** S.p.A. (Parma, Italy). Medel, the world leader in the manufacturing of aerosol therapy devices, will provide design services and prototype production. Once relegated to treating topical medical conditions such as allergic rhinitis and sinusitis, nasal drug delivery is now gaining global attention for treating a wide range of topical and systemic medical conditions from migraine headaches to cardiovascular disease. Nasal drug delivery offers the advantages of painless delivery, rapid drug absorption, and potentially fewer side effects than traditional drug delivery methods. Kurve's device is the only known nasal drug delivery device that has consistently penetrated the paranasal sinuses. Preliminary clinical results indicate that Kurve's controlled particle dispersion technology can apply liquid-based pharmaceuticals far deeper into the nasal cavity than traditional nasal drug delivery devices. Coverage of the nasal mucosa and depth of drug penetration are two important elements of effective and efficient intranasal pharmaceutical treatments.

Results of the analysis of 34-week data from a randomized, multicenter, masked and controlled clinical trial designed to assess the safety and efficacy of the Retisert™ intravitreal implant for the treatment of noninfectious posterior uveitis showed that the uveitis recurrence rate was statistically lower in those eyes with the Retisert implant (2.9 percent) compared with the recurrence rate in the fellow eyes (43.7 percent). There also was a statistically significant improvement in visual acuity in the implant eyes and a reduced use of systemic corticosteroid and/or immunosuppressive therapy. The most common adverse events at 34-week included cataract progression and increased intraocular pressure. The implant, developed by **Bausch & Lomb** Inc., is a tiny drug reservoir designed to deliver sustained and consistent levels of the steroid fluocinolone acetonide directly to the back of the eye for up to three years. There is currently no approved treatment for noninfectious posterior uveitis, a sight-threatening disease afflicting an estimated 800,000 people worldwide.

A chemical called PIB was able to cross the blood-brain barrier and bind to the amyloid plaques in the brains of mice with Alzheimer's, which allowed researchers to diagnose the disease by detecting the chemical. Researchers studied the brain tissue through a hole in the skulls of the mice, using a multiphoton microscope that shows such minute tissues. Currently, Alzheimer's sometimes is indicated by symptoms, but a definite diagnosis can be made only after death. The new test under development in Pittsburgh and in Uppsala, Sweden, could offer the hope of early diagnosis and perhaps better treatment if it works as well in people as in animals. The ability to diagnose the disease in its early stages would be important, because it would allow any new therapy to be started before much damage had been done. While medicine has no current therapy for Alzheimer's, approaches from drugs to a vaccine are being studied.

Nymox Pharmaceutical Corp. (St. Laurent, Quebec) announced that newly discovered spherotoxin molecules represent an important breakthrough in the company's quest for effective Alzheimer therapeutics. According to Nymox scientists, spherotoxin molecules are released by bursting spherons in the aging brain, contributing significantly to the cell death and symptoms characteristic of Alzheimer's. Spherons are dense aggregates of protein found in the brains of everyone from age one. Researchers have found that as we grow older, spherons enlarge until they can no longer be contained in their brain cells. They eventually burst, creating senile plaques and setting off cellular damage and biochemical changes that are instrumental to the symptoms of Alzheimer's disease. A team of scientists at The Scripps Research Institute (TSRI) has identified more than 50 previously unknown proteins and associates several of them with rare human muscle and nerve degeneration diseases. The team used a technique called subtractive proteomics to identify 62 new proteins in the inner nuclear membrane of the human cell. The team demonstrated that 23 of these proteins are linked with strong probability to 14 rare muscle-wasting diseases such as congenital muscular dystrophy, Limb-Girdle muscular dystrophy, and spinal muscular atrophy, and several forms of the neurodegenerative Charcot-Marie-Tooth disease. Knowing the proteins that may cause or contribute to these diseases is a first step in the long process of looking for ways to detect, prevent, or treat them. This study has the potential to clarify a significant number of the more than 300 human dystrophies for which a causative gene has not been identified. A signal that triggers half the stem cells in the developing brain to commit suicide at a stage where their survival will likely do more harm than good has been identified by researchers at the Medical College of Georgia and the University of Georgia. The researchers have found that the lipid ceramide and the protein PAR-4—each already implicated for playing a role in cell death—become deadly partners inside a dividing stem cell in the developing mouse brain. They have documented increasing levels of ceramide in both resulting daughter cells while its death partner, PAR-4, gets handed off to only half the cells. The other half destined to survive are handed instead a protein called nestin. Nestin-bearing cells will develop into neural cells such as our neurons or astrocytes or other cells.

DakoCytomation Denmark acquired intellectual property rights for the Helicobacter pylori (H. pylori) test, including antibodies detecting the bacteria, from **Connex** GmbH. The test for H. pylori is part of DakoCytomation's diagnostic product portfolio. If a H. pylori infection is left undetected and, therefore, untreated, it can lead to stomach ulcers and in some instances, stomach cancer. Early, accurate diagnosis of infection allows the administration of appropriate antibiotic therapy and a full recovery by the patient. It is estimated that at least 10 percent of the Western population is infected with H. pylori, whereas 1 percent have symptoms, and 0.1 percent develop cell changes that can lead to stomach cancer.

Curis, Inc. (Cambridge, Mass.) announced that a medical research group at Saint Elizabeth's Medical Center in Boston has demonstrated that a key signaling pathway, controlled by the Hedgehog protein, plays a crucial role in promoting the development of new blood vessels following tissue injury (deprivation of oxygen). The research points to potential therapeutic applications for the Hedgehog pathway in the treatment of a variety of vascular (blood vessel) disorders. Curis has recently developed drug-like small molecules that can either turn the Hedgehog pathway on or off. This strongly positions Curis in terms of developing drug candidates for disorders where one would want either to promote new blood vessel development, as in certain cardiovascular diseases, or where one would want to halt inappropriate blood vessel development, such as for macular degeneration or certain forms of cancer.

Zimmer Holdings Inc. (Warsaw, Ind.) confirmed Sept. 19, 2003, that it held just under 99 percent of the shares in Swiss orthopedics company, **Centerpulse** AG, following its $3.4 billion offer. Definitive results of shareholder acceptances published in Swiss newspapers said combined with Zimmer's acquisition of InCentive Capital AG's stake in Centerpulse, Zimmer had 98.85 percent of Centerpulse's stock and voting rights. InCentive was

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Society Announces...

(Continued from page 7)

- Minimally and noninvasive assessment

Translation from Discovery to Development (An industry forum)

In addition to posters and oral presentations, a number of keynote speakers will be invited to 'anchor' these presentations. Speakers will include representatives from industry and the FDA, as well as leading scientists who will speak to topics ranging from drug-eluting stents to fundamentals of regeneration and the relationship to inflammation and wound healing.

The symposium will be held October 16-18, 2004, immediately after the annual meeting of the Biomedical Engineering Society (BMES) in Philadelphia. The last few years have seen the growth of bioengineering programs across the country, with biomaterials increasingly being seen as a critical part within the larger context of bioengineering. This symposium will enhance the collaboration between the Society and its sister scientific and professional societies where there is great synergy to be gained by both groups. The Symposium will be a separate meeting (separate registration, sorry!), but all efforts will be made for members of the Society to significantly benefit from this collaboration. The Organizing Committee expects that this effort will set an example that can be built on for the future.

Organizing Committee: Julia Babensee, Gerry Llanos, Tony Lowman, Bill Tawil, Kim Woodhouse, and Ben Wu.

Special Interest Groups Revitalized...

(Continued from page 11)

on a rep's advisory group to help foster swifter communication on issues of a timely nature. The Web site will become a more open forum for all SIGs to communicate to membership and their own members. Because of the unreliable nature of e-mail listing, SIGs will be encouraged to communicate with members through various media. Future initiatives will include cross-SIG committees working to improve the abstract review process with the program chair and cooperative ventures with other organizations and SIGs. Industrial relations will be an area where SIGs will be encouraged to help the Society and each other to broaden the outreach to the biomaterials industry. Continued development of multiple database initiatives will involve many members from various groups. Videos, bibliographies, literature reviews and the like are only a few of the innovative programs underway by SIG members.

Although SIGs have been a vital part of the Society for nearly a decade, this internal structure is still resilient, flexible and strong. Great things are expected from SIGs in the coming year; new energies have been found through the collective work of the officers, appointed task-masters, reporters and members. For more information on the SIGs, please visit the Society's Web site at www.biomaterials.org or e-mail ncan@paladinmedical.com.

Bioengineering and Bioinformatics Summer Institutes Held at Clemson University and Penn State University

By Martine LaBerge

To help increase the number of young people considering careers in bioengineering and bioinformatics at the graduate level and beyond, two federal funding agencies—the National Science Foundation and the National Institutes of Health—have established the Bioengineering and Bioinformatics Summer Institutes (BBSI) Program (http://bbsi.eeicom.com). The aim of this program is to provide students majoring in fields other than bioengineering with interdisciplinary bioengineering or bioinformatics research and education experiences. The Institutes consist of programs that extend across one, or in some cases, two summers. They combine for-credit coursework and research seminars with hands-on research mentored by leading faculty in the field. Nine sites have been selected for the program, and the field of biomaterials science and engineering is the focus at two sites: Clemson University and Penn State University.

The Summer Institutes reach broadly into the national student talent pool to attract a diverse group of U.S. citizens and permanent residents to careers in bioengineering or bioinformatics, with special emphasis on ensuring the participation of women, under-represented minorities, and persons with disabilities in the program. Students are paid a stipend while attending. The Summer Institutes, which were open to junior/senior undergraduates and, in most cases, first-year graduate students from the host university or other institutions, were held for the first time this past summer. Seventeen students completed the Penn State Summer Institute in Biomaterials and Bionanotechnology, which was focused on the understanding of fabrication techniques and materials knowledge on the micro- and nano-level. Students also learned how this knowledge can be used to better understand biological systems and design materials to better interact with these systems. Biomimetics, biomaterials, nanotechnology/microtechnology, bioengineering, and applications with biological systems were emphasized.

Clemson's Institute in Biomaterials Science and Engineering also enrolled 17 students from physics, nursing, biochemistry, mechanical engineering, electrical engineering, mathematics, and biological sciences for its 10-week program focused on medical devices. Lectures on biomaterials, clinical failure, medical device design, implantology, imaging, and other related topics were included in the curriculum, along with hands-on workshops on nanotechnology, cell printing, histopathology, microscopy, mechanical testing, and cell culture. The Institute concluded with the BBSI annual symposium on Innovative Biomaterials held August 8, 2003. The symposium featured Dr. Buddy Ratner, member and past-president of the Society For Biomaterials, as keynote speaker.

In both programs, students conducted state-of-the-art biomaterials research projects. More information about the didactic and research activities and applications for the Clemson's Institute can be found at www.ces.clemson.edu/bio/bbsi/, and at www.bbsi.psu.edu for Penn State University.

From the Director

It is with great pleasure that I take this opportunity to address the membership of the Society For Biomaterials. A lot has taken place since July 1, 2003, when Association Headquarters Inc. began the day-to-day management of the Society. I would like to express my sincere gratitude to Nicholas Peppas, Anne Meyer, and Elaine Duncan for their help in the transition from the previous management company.

For those members who are not familiar with Association Headquarters, we are one of only a handful of association management companies dually accredited by both the American Society for Association Executives (ASAE) and the International Association of Association Management Companies (IAAMC). The IAAMC worked with the American National Standards Institute (ANSI) to develop a "Standard of Good Practices for the Association Management Industry." If you would like to learn more about this process, visit our Web site at www.associationheadquarters.com.

Although we are confident we will be able to provide the services necessary to help the Society grow and develop, we also recognize that the true ability to achieve success lies in the hands of your volunteer leadership. Earlier this month, I attended my first Board of Directors and Council Meetings. As a result of these meetings, the Society For Biomaterials staff has been given clear direction in the types of programs and services the membership is looking for during the coming months.

Points of discussion included:

- Redesigning and adding functionality to the Web site to make it the "source" for information and news about the biomaterials industry
- Maintaining regular contact with membership (e-mail updates) regarding issues that affect the Society
- Validating and verifying the membership database to ensure consistent and ongoing communication among the committees and special interest groups
- Evaluating and modifying membership procedures to allow flexibility and increase the ability to grow the membership
- Significantly increasing the society's reserves and instituting new ways to increase funding of Society programs and projects
- Continuing negations with journal publishers to allow flexibility in subscriptions to the journals, which will allow the society to continue to grow and develop
- Establishing collaboration with other technical societies for meetings and other activities
- Increasing student participation and maintaining their interest as they move into a post-doctoral career

I hope that as you see these changes taking place you will take the time to thank volunteers for their dedication on behalf of the Society. Our mission at Association Headquarters is, "To exceed our client partners' expectations daily...no exceptions." Please feel free to let us know how we can serve you better.

Respectfully,

Steven C. Echard, CAE
Executive Director

Scaffold Structure...

(Continued from page 8)

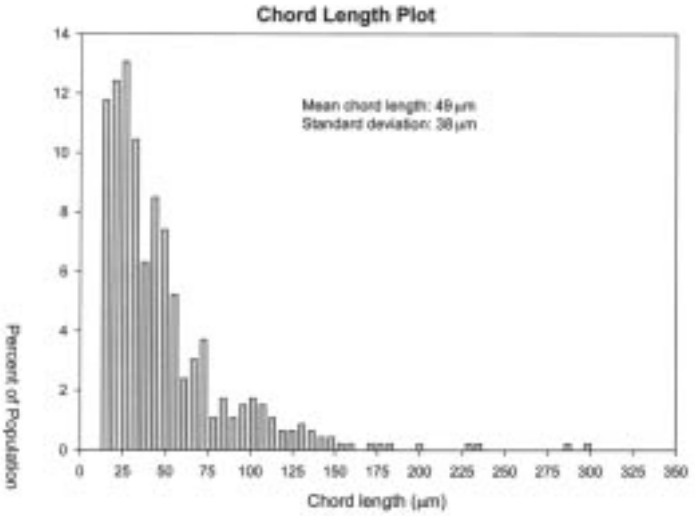

Figure 3: Example of a CLDF from one image plane in Figure 2.

Another important aspect of the effort to optimize scaffold design is the need to balance competing requirements. High porosity is required because of the need for cell migration, proliferation, and nutrient influx. However, the drive towards higher and higher pore volumes opposes the need for certain mechanical property requirements, especially in orthopedic applications. To this end, we are using 3D finite element analysis (FEA) to develop an analytical tool to predict the relationship between the effective properties and individual constituent properties of TEMPs based on real material images. This relationship, plus the analysis of the structural problem of interest, provides a means of optimizing the performance of

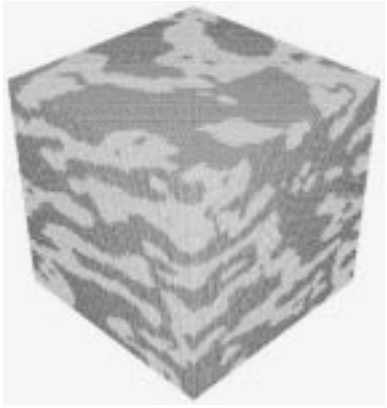

Figure 4: Finite element mesh of a subsection of scaffold shown in Figure 2. The dimension is 274 μm on each side.

TEMPs by varying individual constituent properties without conducting a variety of time-consuming experiments. Initially, the properties of interest are anisotropic elastic constants. Figure 4 displays a typical mesh of FEA based on a section of the PCL scaffold from Figure 2.

This work represents a systematic, integrated approach to the study of structure/function relationships and optimal design in TEMPs. Extracted metrics for the anisotropic scaffold microstructure and properties can be used to understand their influence on cell function, and on a larger scale, TEMP viability.

For more information on this topic, contact falandis@nist.gov or mchiang@nist.gov (Polymers Division, NIST). For information involving chemical imaging of TEMPs, contact marcus.cicerone@nist.gov and see the project page titled, "Coherent Anti-Stokes Raman Micro-spectroscopy (μ-CARS) for Understanding Tissue Growth in Scaffold Constructs," by M. Cicerone and T. Kee, given in http://polymers.nist.gov/annuals/2003/polymers2003.pdf.

Bio**Ink**

(Continued from page 16)

Centerpulse's largest single shareholder with 18.3 percent of the equity capital. The deal to create the world's biggest orthopedics group ended October 2. U.S.-based Zimmer's bid trumped an agreed offer for Centerpulse by Britain's **Smith & Nephew** Plc.

Roche has launched the AmpliChip CYP450 microarray, the company's first microarray for clinical applications, in the United States. The product enables clinical diagnostic laboratories to identify certain naturally occurring variations (called polymorphisms) in two genes, the CYP2D6 and CYP2C19, which play a major role in drug metabolism. These variations affect the rate at which an individual metabolizes many drugs used to treat cardiovascular disease, high blood pressure, depression, attention-deficit hyperactivity disorder, and more. Knowledge of these variations, when considered with other contributing factors, can help a physician select the best drug and set the right dose for a patient sooner, as well as avoid drugs that may cause the patient to suffer serious adverse reactions. Roche expects the AmpliChip CYP450 microarray-based assay to generate annual revenues of more than $100 million by 2008.

Community Calendar

Orthopaedic Research Society
50th Annual Meeting
March 7-10, 2004
Moscone West Convention Center,
Level 3
San Francisco, CA
www.ors.org

Australian Society for Biomaterials
7th Biomaterials World Congress
May 16-21, 2004
Sydney Convention and Exhibition
Centre
Sydney, Australia
612-9262-2277
biomaterials@tourhosts.com.au
www.tourhosts.com.au/biomaterials

Wound Healing Society
14th Annual Meeting & Exhibition
May 23-26, 2004
Sheraton Atlanta Hotel
Atlanta, GA
(763) 765-2377
www.woundheal.org

Regenerate 2004: Tissue Engineering the Human Body
June 9-12, 2004
Westin Seattle
Seattle, WA
(412) 235-5128
pcantini@ptei.org

Controlled Release Society
31st Annual Meeting & Exhibition
June 12-16, 2004
Hawaii Convention Center & Hilton
Hawaiian Village
Honululu, Hawaii
www.controlledrelease.org

AO Research Institute
ECM V: The Cell Biomaterial Reaction
June 28-30, 2004
Congress Centre
Davos, Switzerland
www.aofoundation.org

American Society for Bone and Mineral Research 26th Annual Meeting
October 1-5, 2004
Washington State Convention and
Trade Center
Seattle, WA
(202) 367-1161
asbmr@dc.sba.com
www.asbmr.org

BMES 2004 Annual Fall Meeting
October 13-16, 2004
Wyndham Franklin Plaza Hotel
Philadelphia, PA
(301) 459-1999
www.bmes.org

Society for Biomaterials Symposium on Biomaterials in Regenerative Medicine
October 16-18, 2004
Philadelphia, PA
www.biomaterials.org

Surfaces in Biomaterials Foundation Annual Symposium & Exhibition
October 27-29, 2004
Baltimore, MD
www.surfaces.org

Osteoarthritis Research Society International 2004 World Congress
December 2-5, 2004
Hyatt Regency Chicago
Chicago, IL
www.oarsi.org

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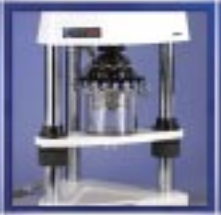
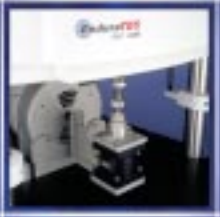


Multi-wire Fatigue Testing



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