SurFACTS in Biomaterials

Winter 2007 Volume 12 Issue 1

BioInterface Draws Large Crowd
Will Return to California in October

The Surfaces In Biomaterials Foundation's annual BioInterface Workshop & Symposium received a warm reception in San Mateo, CA, Dec. 4-6 where 120 surface science professionals gathered for serious discussion as well as renewed business and personal contacts.

First up on the agenda was the Workshop on Dec. 4 that delved into the Delivery of Therapeutic Biologics. Chaired by Joe Chinn of SurModics, the Workshop began with an overview of traditional drug-eluting biomaterials by Kishore Udipi from Medtronic, followed by an overview of biologic delivery systems by Paul Burke of Amgen. The Workshop also featured speakers from Abbott Vascular, SurModics, Pharmanet and the University of California.

The Applied Technology Workshops completed the afternoon program with presentations from Evans Analytical Group, Hysitron, Spire Biomedical and Integument Technologies. The opening day wrapped up with keynote speaker Alan Hoffman from the University of Washington and a discussion of PEGylated Surfaces.

The Symposium officially kicked off on Tuesday, Dec. 5 with a welcome from Foundation president Dan Ammon from Bausch & Lomb. Presentations explored

BioInterface Continued on Page 2

On My Microscopic Soapbox Part II

By Steven Goodman
Editor

I have previously discussed how microscopy is arguably the most critical single "tool" for the analysis of biomaterials and biomaterial-based devices. As stated previously, only with microscopy can we determine the structure of our devices, and the 2D and 3D relationships between these devices and materials they are made from with the biological systems that they interact with. Simply put, most of the tissues and all of the cells and proteins are much too small to be seen with the naked eye, not to mention the polymer coatings, drugs, and the applied and inadvertent textures on the surfaces of the devices we produce. However, it is all too easy to fool oneself with microscopes. In my consulting as well as in my reviewing of submitted papers and grant proposals, I often see confusion and real problems in the application, interpretation, and even the presentation of microscope images.

On page 4 of this issue is an article by Klaus Wormuth (SurModics Inc.) and Greg Haugstad (University of

From the Editor Continued on Page 6

What's Inside

BioInterface Continued from Page 1

Frontiers in Tissue Imaging, reviewing both neurovascular and biointerfacial aspects of tissue engineering applications. Tuesday's program concluded with the lively and popular Rump Session that examined Therapies of the Future: Tissue-Based or Device-Based. Jim Brauker from Dexcom took the device side and Gail Naughton from San Diego State University took the tissue side.

Surfaces Past President Dann Ammon

The "Rump" Session refers to a debate in a "rumpus room" atmosphere that is somewhat less formal than other presentations or discussions. It was decided by the board to refer to this component of the Symposium in the future as "Point-Counterpoint" to be more specific.)

Keynote speaker Alan Hoffman

Day 2 of the Symposium kicked off with the Student Poster Session. Six students presented their best ideas for review and consideration. Brian Murphy from Wayne State University was deemed to have the best presentation of the group and he received the $500 check from the Foundation.

The Symposium explored peripheral vascular and orthopaedics for the morning sessions. Robert Ward received the Excellence in Surface Science Award at the luncheon as a highlight of the event. Ward's career in biomaterials began in the 1970s when his early work included the development of the silicone-modified polyurethane used in the first clinical intra-aortic balloon pump.

Attendees had ample time to review exhibits

The conference wrapped up with the Invention Symposium Wednesday afternoon that allowed representatives of new or emerging companies to present their products or services.

Surfaces board members, past and present, left to right: Dave Sogard, Larry Salvati, Victoria Carr-Brendel, Carl Turnquist, Dan Ammon, Lise Duran, Joe Chinn, Dn Hook

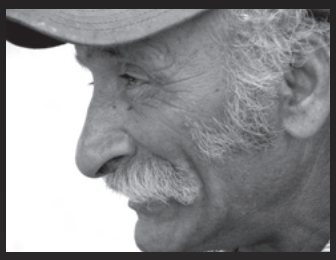
Mark your calendars for Oct. 29-31 for the BioInterface 2007 Workshop and Symposium. The board of directors made a decision in early January to return to the same site to build on the success of 2006. Carl Turnquist of Genzyme is the chair of the 2007 Symposium and Dave Sogard of Boston Scientific will chair the Workshop. Please forward your ideas and your willingness to help to either Carl or Dave. Or send them to Bill Monn at the Surfaces offices and he will forward the information.

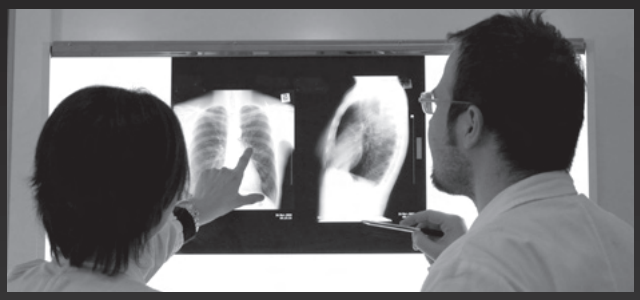
SurFACTS in Biomaterials is the official publication of the foundation and is dedicated to serving industrial engineers, research scientists, and academicians working in the field of biomaterials, biomedical devices, or diagnostic research.

FDA Updates Its Statement On Coronary Drug-Eluting Stents

By Phil Triolo, PhD, RAC

As communicated in the Fall 2006 issue of SurFACTS, the FDA issued a statement on coronary drug-eluting stents (DES) relating to data indicating that there is a small, but significant increase in very late stent thrombosis in patients treated with currently approved DES. Because the Agency did not have sufficient information to make recommendations on the use of DES, it convened a public panel meeting of external scientific experts to thoroughly review all available data and recommend what actions would be appropriate.



The Circulatory System Devices Advisory Panel met on Dec. 7 and 8, 2006, in an effort to fully characterize the risks, timing and incidence of DES thrombosis. Panel members included cardiologists, cardiovascular surgeons DES manufacturers, and biostatisticians.

The relevance of this meeting and the conclusions reached to the combination product community cannot be overemphasized. DES, like them or not, are the "flagship" products of the industry. Any results that seriously question their safety or efficacy cannot be taken lightly, as these results may affect how the public, investors, and regulatory agencies, view, fund, and review devices that incorporate medicinal substances.

The stated purposes of the meeting were:

(1) To provide a forum for the presentation of clinical data relevant to the issue of DES thrombosis (both when DES are used according to their label and in more complex patients beyond their labeled indication) and

(2) To address the appropriate duration of antiplatelet therapy (aspirin plus clopidogrel) in DES patients.

The main conclusions and recommendations of the Panel regarding DES when the devices are used in accordance with their approved indications are that both FDA-approved DES are "associated with a small increase in stent thrombosis compared to bare metal stents that emerge 1 year post-stent implantation. However, based on the data available, this increased risk of stent thrombosis was not associated with an increased risk of death or myocardial infarction (MI) compared to bare metal stents [BMS]. This finding may be due to (1) an insufficient number of patients in currently available studies; or (2) an increase in deaths or MIs was offset by a reduction in events associated with in-stent restenosis and additional revascularization procedures."

FDA Update Continued on Page 13

Understanding Biomaterial Surfaces via Atomic Force Microscopy

By Klaus Wormuth, Ph.D, Director of Characterization Sciences, SurModics, Inc.
Greg Haugstad, University of Minnesota, Institute of Technology Characterization Facility

The Surfaces in Biomaterials Foundation provides a forum for research which fosters understanding of the "biointerface," the interface between biomaterials and human tissue. On the biomaterials side of the biointerface, questions arise as to which properties of synthetic material surfaces most influence biocompatibility. Better measurement of the physical and chemical morphology of the outer surfaces of biomaterials remains an active research area. Currently, no all-in-one "Ginzu Surface-o-Meter" exists which combines high nano-scale spatial resolution with high chemical and physical property specificity. For understanding of the chemistry of polymeric surfaces, the surface-specific methods of x-ray photoelectron spectroscopy (XPS), time-of-flight SIMS (ToF-SIMS) remain the most commonly applied methods. However, low spatial resolution limits imaging applications of XPS, and the significantly better imaging resolution of ToF-SIMS only approaches the nanoscale (~100 nanometers). See the last issue of *SurFacts* for the latest in ToF-SIMS research.

On the other hand, atomic force microscopy (AFM) probes surfaces with a resolution of about one nanometer. Rather than probe surface chemistry with ion beams as done in XPS and ToF-SIMS, AFM rasters a sharp tip attached to a flexible cantilever over a surface, maintaining constant force between tip and surface through a feedback mechanism. Actually, AFM refers to a whole collection of "scanning probe" microscopies (SPM) which measure a wide variety of tip-surface interactions: mechanical, friction, magnetic, electrical and thermal effects. For example, so-called "chemical force microscopy" measures the interaction of chemically modified tips with surfaces in order to map surface chemical heterogeneities.

Despite the power of AFM to resolve nano-forces over nano-regions, accurate interpretation of the signal generated as the tip interacts with a material surface remains challenging. Even the interpretation of a "simple" image of the topography (height) of a compliant surface could present problems: AFM applies a finite force which could compress soft surface features. Also, AFM tips exhibit a finite radius of curvature (~10 nm), and so sharp features might appear smeared, especially if imaged too fast for the tip to conform to the surface. In "contact mode" imaging the tip drags across the surface, and if the applied force becomes too high, surface scratching results. Intermittent contact modes, in which the AFM tip "taps" the surface (at frequencies up to 300+ kHz) minimize the time of tip-surface contact, and thus minimize the chance for permanent distortion of soft material surfaces.

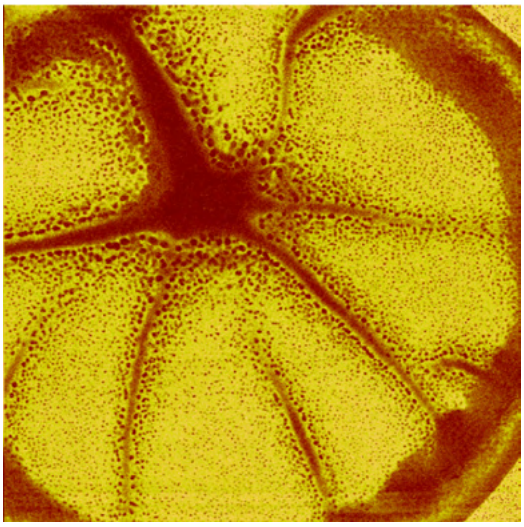


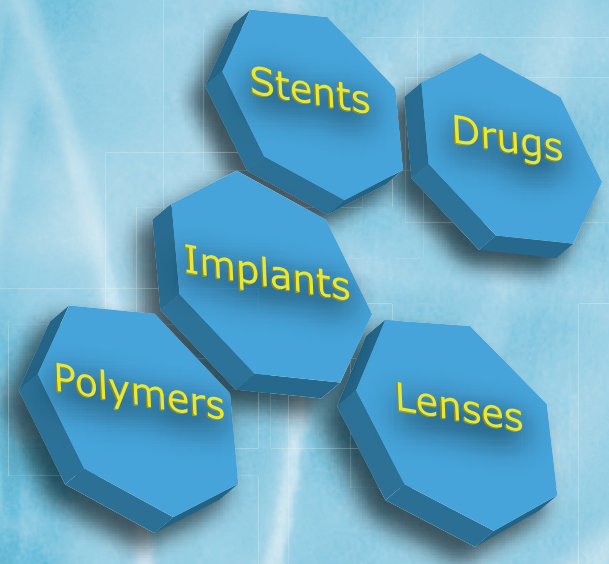
Figure 1: AFM Image of Dried Droplet of Drug/Polymer Mixture

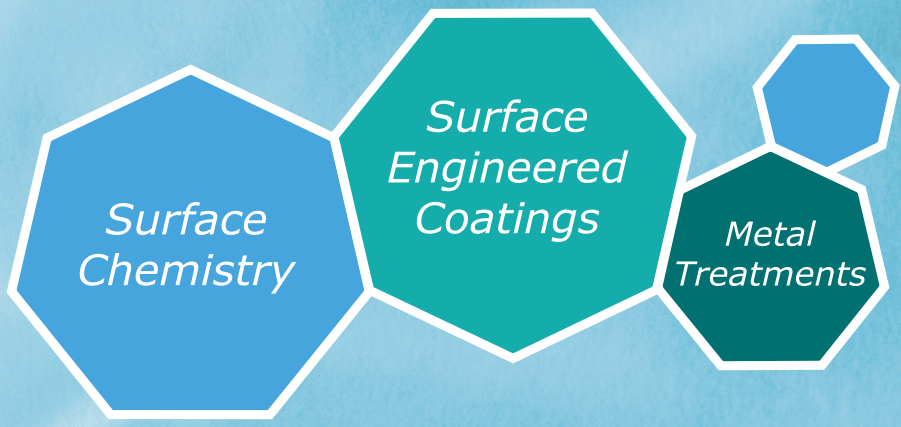
However, the ability of AFM to sensitively probe the compliance of surfaces presents a powerful tool for deciphering surface chemistry. Intermittent contact modes such as the "pulsed force mode" press-in and retract the tip from the surface while time-resolving each part of the cycle at every pixel in an image, sensing all the forces which might drive AFM tip-surface interactions: capillary forces due to thin condensed water layers, electrostatic forces due to surface charges, van der Waals repulsive forces due to tip-sample dipole-dipole attractions, polymer steric forces due to solvated polymer chains, adhesive forces due to tip-sample sticking, and viscoelastic forces due to material compliance. Note that by increasing the applied force, the AFM tip probes deeper into a surface: by comparing images generated with varying applied force, any thin surface films present become visible.

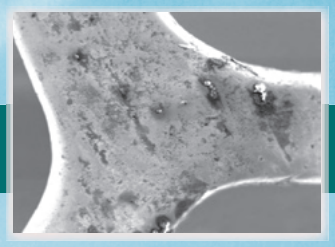
Research challenges remain in conversion of the AFM force signal into chemically specific information. Oftentimes, prior knowledge of the sample or measurements on simpler mixtures of ingredients provide the keys for unlocking complex AFM signals. For example, in an effort to better understand drug delivery coatings, spray droplets of a drug/polymer mixture deposited on a glass slide were probed with AFM. An AFM image of the "stiffness" of the coating shows dark (low stiffness) regions which likely correspond to viscoelastic polymer, and brighter (high stiffness) regions which likely correspond to hard amorphous drug (Figure 1: imaged area 50 x 50 microns). Thus, if interpreted properly, AFM yields information on surface chemical properties with nanoscale resolution.

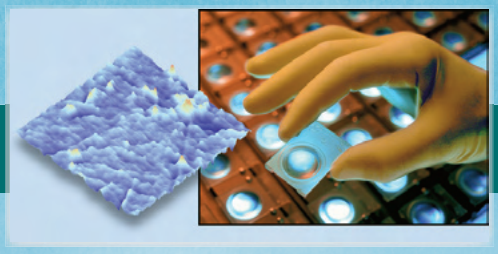
BioMaterials
BioDevices
BioSurfaces

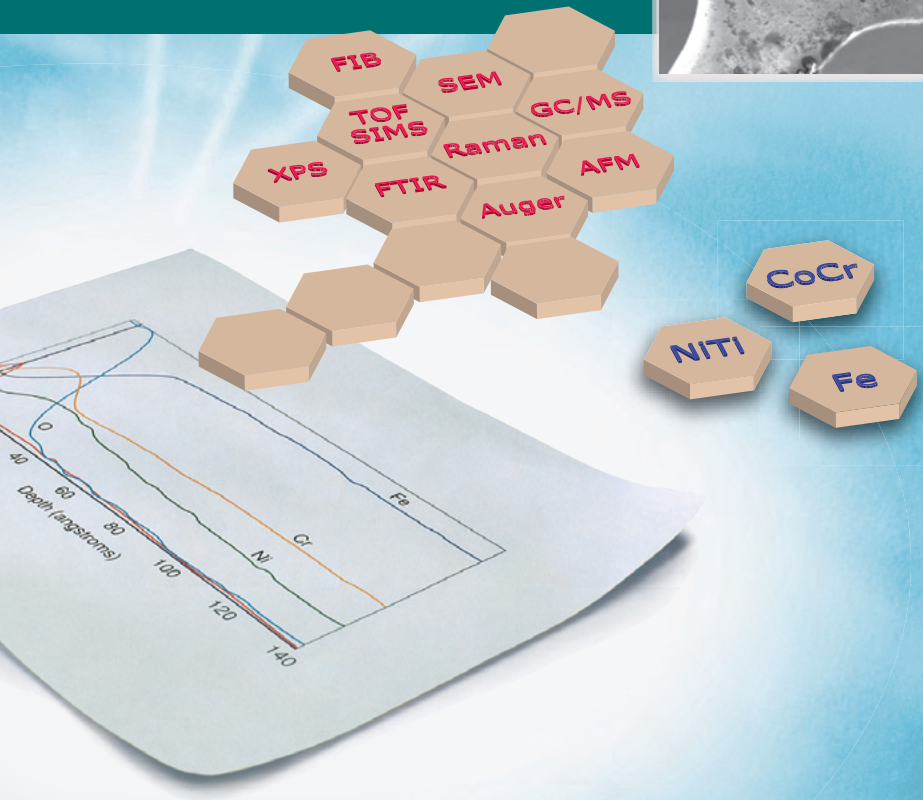
Specialists in Materials Characterization











Providing state-of-the-art Surface Analysis at each stage of the product life cycle. We work with our customers to provide answers to problems, not just data. Modern Instruments, Experienced Analysts and Knowledge in BioSurfaces. Rely on Evans Analytical Group*.

For more details call 408 530-3500, visit WWW.EAGLABS.COM or email info@eaglabs.com

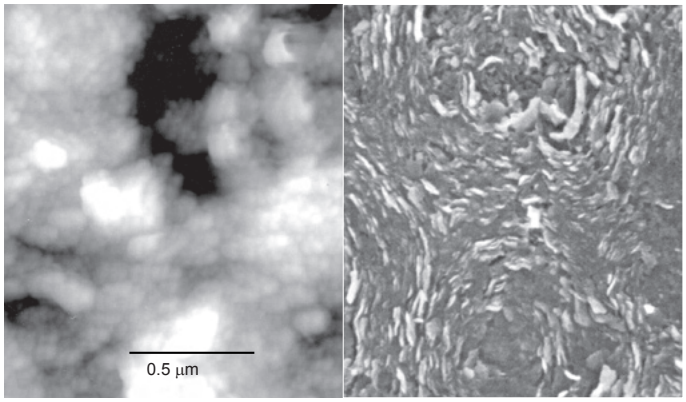
*Formerly known as: Charles Evans & Assoc. and Evans East

EAG℠
Evans Analytical Group

Rely on the Experts

From the Editor Continued From Page 1

Minnesota) that discusses one of the most misused and misunderstood imaging analytical instruments, the Atomic Force Microscope. I highly recommend that you read this brief article to better understand the limitations and some of the capabilities of this powerful analytical instrument. When asked about the utility of the AFM in seminars, I generally reply that the AFM is an excellent tool for imaging and measuring the topography of flat surfaces. The internal contraction in this last sentence is made on purpose: As briefly discussed in the article, the finite size and dimension of the measuring probe (the AFM tip) limits its ability to evaluate pits or deep areas within specimens, as well as to accurately measure many lateral features. Hence a rough surface cannot be adequately imaged using AFM. An example from my own work shows this quite clearly. These images show the texture of a leaflet from a commercial "highly polished" mechanical heart valve made from pyrolytic carbon. The same leaflet was examined with AFM and with low voltage high resolution SEM. The difference in these two images is startling. While one might be tempted to state that in this case the AFM is not useful, that would be incorrect. The AFM much more readily provides very accurate measurement of heights (albeit with poor measures of depths), and the AFM can be used to measure some mechanical or physical properties that cannot be obtained in any other way. The lesson is not to readily trust images obtained with only one instrument or method.



AFM (left) and high resolution low voltage SEM image (right) of a pyrolytic carbon heart leaflet. Both images are at the same magnification.

A second aspect to consider is the presentation of microscope images. Due to confidentiality, I cannot show you any of the numerous examples I have seen of improperly presented and processed microscope images. I believe most of these were simple mistakes or oversights, but others appear to be borderline, or even egregious, fraud. An example of this includes manuscripts and proposals where two images are shown of two different experimental conditions, such as cells on different materials or two different surface coatings. I can't tell you how often I see such side-by-side micrographs at two different magnifications. How can the reviewer or reader, or even the author, make a fair comparison? Come on—Don't fool yourself and don't try to fool others. While I see this all too often, I don't think this is done on purpose. I suspect that a student or technician simply obtained images without careful instructions or did not consider that comparisons would be made.

Perhaps the most troubling examples I have had the pleasure to "review" were where two very different magnification SEM images were provided of the same object. However one was labeled as belonging to "Condition A" while the second was labeled as coming from "Condition B." One could even see the rectangular raster pattern on the low magnification Condition A image that was created by the high magnification Condition B image. More troubling areas of concern are where the images are "Photoshopped" in some way or another. This can be a bit of a grey area since image contrast, brightness and sometimes other parameters may need to be adjusted to see what it is you are looking for and to show others. My opinion is that:

1) such adjustments should be minimal,
2) should be applied equally to all images where comparisons are made, and
3) if you are uncomfortable in making the data interpretation, than you've probably gone too far in altering the presentation.

The overriding rule is, "Don't fool yourself and don't try to fool others."

Nano Hemostat Solution

By Duda Markovic, Ph.D, Research & Development Manager, Dexcom

Blood clots are produced after injury, but take 1 or 2 minutes to form. Dealing with serious blood loss, on the other hand, requires the use of mechanical or thermal intervention that can cause secondary tissue damage, while chemical agents that induce clotting or constriction of the veins may lead to a negative immune response.

A liquid containing protein fragments has quickly stopped bleeding in rodents, researchers from the Massachusetts Institute of Technology and Hong Kong University reported in the October issue of *Journal of Nanomedicine* (R G Ellis-Behnke et al., J. Nano. 2006, DOI: 10.1016/j.nano.2006.08.001)

Nano Hemostat Solution (NHS-1) is applied directly to the wound as a liquid or gel, and can lead to complete haemostasis within 15 seconds (compared to 90 seconds in the cauterized control sample).

When the liquid is applied to open wounds in brain, liver, skin, spinal cord and intestinal tissues of hamsters and rats, the peptides assemble into a "nanoscale protective barrier gel" that seals the cut.

The exact mechanism of the solutions' action is not fully understood, but the researchers are confident that it does not act as a clotting agent.The solution is non-toxic and non-immunogenic, and breaks down naturally into simple amino acids that the body can use in the healing process.

The authors suggest that biodegradable liquid could be very useful to surgeons since up to half of the time during a surgical procedure is spent addressing the control of bleeding. In addition, less blood reduces the need for transfusions. In addition, patients will suffer less secondary damage in tissue from bleeding.

Ohio Hospital to Partner with Medical Product Startups

Hospital venture aims to develop new products

By Cheryl Powell

Akron General Medical Center wants to become a birthplace for new medical products and treatments.

The nonprofit hospital recently launched its Technology Transfer, Commercialization and Innovation Office, a venture that will allow the hospital to partner with startup companies trying to bring new medical products to market.

The concept allows Akron General to capitalize on its patient care and research expertise, as well as the animal research capabilities of its Kenneth Calhoun Research Lab, said Dr. James M. Dougherty, chairman of Medical Education and Research.

The hospital will be able to provide entrepreneurs with office space, as well as advice from practicing doctors and access to research facilities and equipment, Dougherty said.

These and other services enable startup medical companies to test their ideas and develop products that ultimately could be used by patients, he said.

``What we end up with is an integrative research initiative that goes from bench to bedside,'' said Robert Anthony, manager of the new office.

Several firms have expressed interest in partnering with Akron General, but no deals have been finalized yet, Anthony said.

The terms of the deals will vary from project to project, Anthony said. But the contracts could include paying Akron General for services or offering the hospital an equity stake in the ventures being developed.

Eventually, Dougherty said, the office could be spun off as a for-profit arm of the hospital.

Akron General is launching its technology transfer initiative as city leaders are trying to promote biotechnology and medical development.

Last year, the city established a biomedical corridor to encourage investments in medical developments near the downtown hospitals.

Recently, representatives from 15 Israeli companies specializing in medical information technology visited with local hospital, university and government officials to look for investment opportunities in Northeast Ohio.

The visit was a follow-up to a trade mission to Israel last year by Akron Mayor Don Plusquellic and representatives from 21 public and private Akron-area institutions.

Other area hospitals also have launched their own initiatives to get a share of the emerging biomedical market.

In 2003, Summa Health System started its Summa Enterprise Group, a for-profit entrepreneurial subsidiary focused primarily on developing helpful services to market to hospitals in the region and nationwide.

Summa also is a partner in BioEnterprise, a Northeast Ohio consortium that supports and recruits bioscience startup companies.

Likewise, Akron Children's Hospital is working with its doctors and other researchers who want to test innovative ideas for new treatments and medical products through its Akron Children's Research Center, said Maryan Mathis, administrative director for the center.

Akron General's goal is to partner with other area hospitals and universities to attract biomedical investment and development in the region, Dougherty said.

``The days of being able to do everything by yourself are over,'' he said. ``We absolutely would... be willing to talk to anybody who feels that they can add a level of expertise to the companies that would come through our technology transfer office.''

Medtronic CEO Signals Interest in Acquisitions

The chief executive of Medtronic Inc. said January 8, the medical device maker will look for ways to expand into new areas of growth, signaling the potential for strategic acquisitions.

Medtronic Chairman and Chief Executive Art Collins said the company, which makes treatments for ailments ranging from heart disease to diabetes and neurological and spinal disorders, can meet its goals through organic growth. But it is also seeking new opportunities for expansion.

"The good news is, we believe we are fortunate in operating in a number of growth segments, that if we execute correctly, we can reach our growth objectives without any major acquisitions," Collins told the JPMorgan Healthcare Conference, which was webcast.

"Having said that, I think that it's clear over the next year to three years that we will be looking at, how do we prepare for and expand into several additional growth platforms going forward?" Collins said.

Medtronic in December said it expects annual sales growth, for the company as a whole, of 8 percent to 12 percent in fiscal 2007 and 11 percent to 14 percent in fiscal 2008. Its internal target for compound annual revenue growth over five years is just over 14 percent.

The company in December announced plans to spin off its external defibrillator unit in order to focus on higher-growth treatments. Medtronic, the world's largest maker of implantable cardioverter defibrillators, struggled last year with a slowdown in demand for those devices following rival Guidant Corp.'s series of high-profile product recalls. Medtronic cut its fiscal 2007 and 2008 earnings and revenue forecasts in August.

But in November, Medtronic said its ICD business accelerated as it took market share from competitors, contributing to a higher-than-expected fiscal second-quarter profit.

Surface Science & Art

New! Homometallic™ Nanostructured Coatings

New! MetoCeramic™ Wear-resistant Coatings

New! IonGuard-Focus™ Surface Treatment

New! NanoTite™ Hydroxyapatite Coatings

SPI-Polymer™

SPI-Ceramic™

SPI-Argent™

SPI-Sight™

IonGuard®

SPI-Met™

IonTite™

spire Biomedical

FDA Registered

ISO 13485:2003

See us at BioInterface 2006

For customized solutions for your surface modification needs, contact rdinfo@spirecorp.com

Spire Biomedical, Inc., One Patriots Park, Bedford, MA 01730-2396 781-275-6000 1-800-510-4815 www.spirebiomedical.com

BioInterface 2007: October 29-31

BioInterface 2007 is the annual technical conference of the Surfaces in Biomaterials Foundation. This year's Workshop and Symposium will be held October 29 through October 31 in San Mateo, CA. The first day (Monday) is our Workshop. Our technical program follows on Tuesday and Wednesday with topics of current interest. My committee is currently developing a program covering the Surface Characterization, Tissue Engineering, Biodegradable Polymers, Neurovascular Devices, Drug Elution Devices, Nanotechnology and Orthopedic areas. Wednesday includes our highlight Award presentation luncheon honoring a distinguished Biomaterials pioneer. Please visit www.surfaces.org for details and updates.

New Board of Directors Elected

The new board of directors for the Surfaces in Biomaterials Foundation has officially started its term with Vicky Carr-Brendel, Boston Scientific, moving into the position of President. Dan Ammon, Bausch & Lomb, transitioned from President to Past President of the Foundation. Ammon also accepted the post of chair of the Membership Committee.

Carl Turnquist, chair of BioInterface Symposium, joined the board and was elected President-Elect. Turnquist has agreed to chair the Symposium again in 2007. Dave Sogard, joined the board from Boston Scientific-Cardiovascular in the position of Vice President. In this position he will chair the Workshop for the annual Surfaces conference.

Klaus Wormuth, SurModics, was elected to the position of Secretary and Larry Salvati, DePuy, was elected Treasurer.

Members of the Surfaces in Biomaterials Foundation are encouraged to contribute their ideas to the board, especially in regard to the annual Workshop and Symposium. Greater involvement makes a stronger association. Board members' contact information is listed here. Members always are encouraged to contact Bill Monn at the Foundation's offices if they need information or would like to get more involved.

President
Victoria Carr-Brendel
Boston Scientific
2710 Orchard Scientific
San Jose, CA 95134
Telephone (408) 895-3548
Facsimile (408) 895-2216

President-Elect
Carl Turnquist
Genzyme
PO Box 9322
Framingham, MA 01701-9322
Telephone (617) 591-5540

Secretary
Klaus Wormuth, Ph.D.
SurModics, Inc.
Regenerative Technologies
9924 West 74th Street
Eden Prairie, MN 55344
Telephone (952) 947-8652
Facsimile (952) 829-2743

Treasurer
Lawrence Salvati
DePuy Orthopaedics
700 Orthopaedic Dr
Warsaw, IN 46581-0988
PO Box 30450
Telephone (574) 372-7159

Vice President
Dave Sogard
Boston Scientific, Cardiovascular
5905 Nathan Lane
MS-P33
Plymouth, MN 55442
Telephone (763) 694-3009
Facsimile (763) 694-6940

Past President
Dan Ammon
Bausch & Lomb
1400 North Goodman Street
Rochester, NY 14609-0450
Telephone (585) 338-8387
Facsimile 585) 338-0042

Executive Director
Bill Monn
Surfaces in Biomaterials Foundation
1000 Westgate Dr
Suite 252
St. Paul, MN 55114
Telephone (651) 290-6295
Facsimile (651) 290-2266

Volunteers Wanted:

If you would like to contribute your talents to the Surfaces in Biomaterials Foundation, we'd love to have you. Let us know if you'd like to help with membership recruitment, writing or editing articles for the SurFACTS newsletter, adding content and interest to the Web site or other areas where your talents could be put to good use. If interested please contact Bill Monn at billm@ewald.com or call 651-290-6295.

Sustained and Controlled Delivery of Therapeutic Proteins:

A Novel Polysaccharide Matrix System

By Stephen J. Chudzik, Research Fellow, and Laura M. Patrick, Program Manager, Eureka Technologies, both of SurModics, Inc., Eden Prairie, Minnesota USA

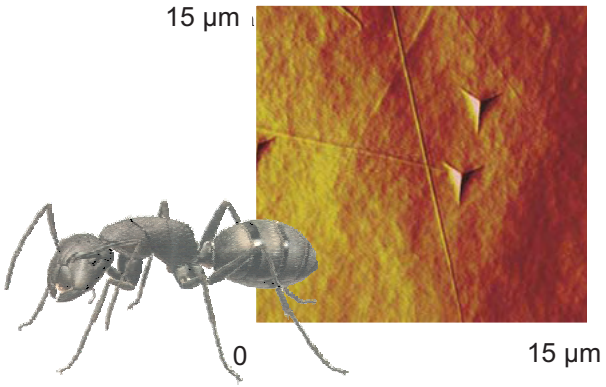
The use of proteins as therapeutic agents has been actively pursued since insulin, thyroid hormones and coagulation Factor VIII were made commercially available in the early part of the 20th century. Currently, approximately 200 protein or peptide agents have been approved by the FDA as treatments for a variety of human diseases and conditions, including agents from various sources. The modern techniques of genomic and proteomic screening provide methods that can rapidly identify new protein drug candidates. However, it remains challenging to develop delivery technologies that can deliver an active biologic agent to the site where it is needed in therapeutically relevant concentrations; and ideally, for an extended period of time.

Proteins Continued on Page 14

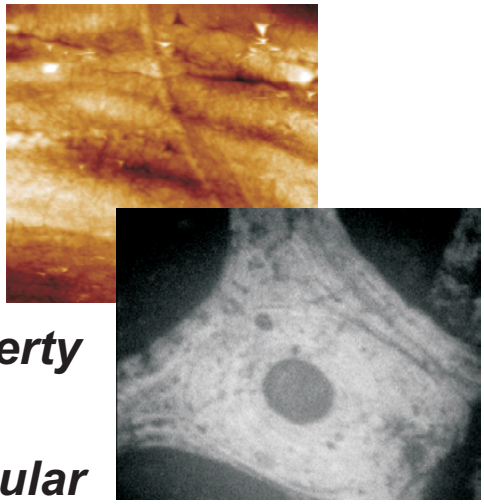
Nano Testing for Natural & Artificial Structures

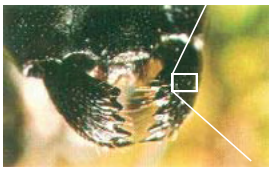
Hard or Soft Materials
Nanomechanical Testing Delivers Results

Hardness of ant mandible



Nanoindentation of the lamellar structure of trabecular bone

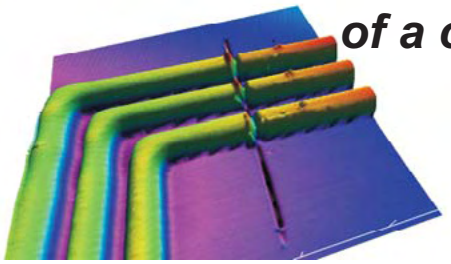




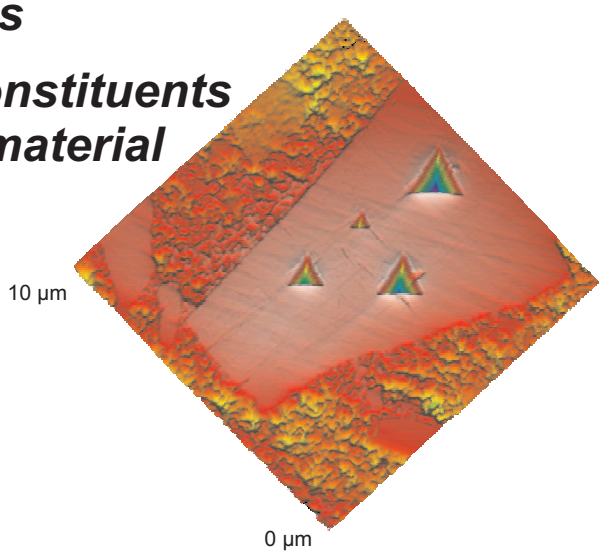
Determine structure-property relationships

Test specimens with irregular geometries

Probe individual constituents of a composite material



Scratch and indents on a MEMS structure



Mechanical properties of individual particles embedded in a matrix

Nanomechanical Test Instruments

Hysitron, Inc.

For more information please visit our website at www.hysitron.com

Engineering the Biomolecule and the Biomatrix

By Duda Markovic, Ph.D, Research & Development Manager, Dexcom

Sam Stupp and colleages at Northwestern University believe their synthetic molecules could lead to regeneration of bodily tissue. They have designed novel bioactive scaffold biomaterials, materials that can act as artificial extracellular matrices. These materials present specific ligands on their surfaces for cell receptors or membranes. These cell-material interactions could promote the regeneration of tissues such as bone, cartilage, blood vessels, nerves, and many others. Relying on certain parameters of the platform strategy, the investigators search for relevant biological knowledge about proteins, functions, and structures from different sources and incorporate it into their matrix technology. They then customize the information for specific organs and tissues.

The latest fruit of the efforts of Samuel Stupp and his co-workers is using the biopolymer heparin and a nanofiber scaffold to develop a novel nanostructure that promotes blood vessel growth. (Nano Lett., DOI: 10.1021/nl0613555).

The nanofiber's basic building block is a peptide amphiphile that has a hydrocarbon chain on one end and a polypeptide designed to bind heparin on the other. In the presence of heparin, these chainlike molecules assemble into cylindrical fibers with the hydrocarbon chains at the core and the peptide-heparin complex at the surface. When combined with nanogram amounts of angiogenic growth factors (VEGF, FGF-2) that interact with heparin, the nanostructures stimulate extensive new blood vessel formation in vivo.

When the researchers injected a solution containing the amphiphiles into the corneas of mice–a standard model for testing new blood-vessel growth–the amphiphiles formed fibers that then prompted new blood vessels to grow.

To see whether the fibers could help animals recover from an actual injury, Stupp teamed up with Jon Lomasney, a molecular pharmacologist at Northwestern University Feinberg School of Medicine in Chicago, Illinois. The researchers induced heart attacks—and thus heart damage—in 20 mice. A half-hour later, they injected half of the mice with a solution containing their heparin-binding amphiphiles, while control animals received either an injection of growth factors alone or no treatment.

The growth factors quickly diffused away from the target area in the control animals. But in those given the amphiphiles, nanofibers assembled at the injury site and stayed put, drawing the body's own growth factors to the injury site. A month later, the team found that the hearts of the animals that received the amphiphiles pumped blood nearly as well as those of healthy animals. In contrast, the hearts of the control animals contracted about 50% less than normal. The same nanofibers also dramatically hastened wound healing in rabbits, the researchers reported last fall at a semiannual meeting of the American Chemical Society.

Stupp recently formed a company called Nanotope to help commercialize the technology.

Health Regulators Criticize L.A. Hospital for Bacteria Outbreak

Hospital staff did not properly clean medical instruments linked to a deadly bacterial outbreak at a medical center's neonatal intensive care unit, according to a report by state health regulators.

White Memorial Medical Center closed off its neonatal intensive care unit Dec. 4 following an outbreak of Pseudomonas aeruginosa that sickened five infants. Two of the babies are believed to have died as a result of the pathogen.

In a report, inspectors from the California Department of Health Services faulted hospital staff for not sterilizing laryngoscope blades, which are used to insert breathing tubes, in accordance with manufacturer's recommendations. The report said the respiratory therapy staff used soap, tap water and alcohol wipes to clean the blades.

White Memorial said in a statement the report "simply confirms the hospital's preliminary findings."

The neonatal care unit reopened to patients two weeks after the outbreak was identified, and the hospital said it has worked closely with county public health officials and outside experts. There have been no new infections, officials said.

Of the roughly two million hospital-acquired infections each year, about 10 percent are caused by P. aeruginosa. The germ is a common but potentially deadly bacterium, particularly to people with weak immune systems. It can be spread by health care workers, medical instruments, disinfectant solutions and food.

White Memorial also had briefly closed its pediatrics intensive care unit after discovering two children had tested positive for the germ. The unit was reopened after executives determined the bacterial strain that sickened the older children was not passed on by the same equipment that infected the five infants.

FDA Update Continued From Page 3

Further, "When compared to bare metal stents, DES are not associated with an increased rate of all-cause mortality. The concerns about thrombosis do not outweigh the benefits of DES compared to bare metal stents when DES are implanted within the limits of their approved indications for use. Larger and longer premarket clinical trials and longer follow-up for post-approval studies are needed, using uniform definitions of stent thrombosis and close attention paid to patient compliance with antiplatelet therapy."

The Panel also made recommendations on the broader off-label use of DES in patients with more complex patients and coronary lesions than those patients studied to support initial marketing approval, and on the duration of antiplatelet therapy, which, due, in part, to patient compliance and/or cost issues, is often prematurely discontinued. The FDA observed that at least 60% of current DES use is off-label.

The Society for Cardiovascular Angiography and Interventions (SCAI) subsequently published a clinical alert in its online journal, *Catheterization and Cardiovascular Interventions*. The alert includes a more detailed review of the data and clinical trial results that prompted the FDA to convene the Panel, and advice for DES and BMS use. The alert notes that the complications associated with off-label use of DES are more frequent than in the indicated population. The advice addresses patient selection, stent implantation techniques; dual antiplatelet therapies; medical-legal concerns; and further clinical studies. It is recommended reading, as it concisely addresses the clinical data that revealed the increase in very late stent thrombosis for DES over BMS, and identifies other clinical alerts that have been issued with respect to DES use, especially as they relate to antiplatelet therapy.

The FDA update concluded, "We will be working closely with the manufacturers of both approved DES and other DES still under study to incorporate appropriate modifications to labeling and changes to pre- and post-approval studies. Additionally, we will continue to work with professional societies, consumer organizations, and health care providers to provide physicians and patients with the most updated information as quickly as possible."

Let's all hope that clinicians heed their colleagues' advice; patients comply with their antiplatelet drug regimens; and postmarket studies continue to support a significant improvement in outcomes for DES over BMS, as a failure of these products to live up to their promise would represent a serious setback for the entire combination product industry.

Proteins Continued From Page 10

Delivery Strategies

- Injection: Injection is the current method of delivery for most protein drugs. Reducing injection frequency would be beneficial from the standpoints of compliance, efficacy, and economics.
- Inhalation: Proteins can be introduced into systemic circulation via inhalation through the lungs (pulmonary), or through the nasal cavity. Technologies in this area focus on permeation-enhancing excipients and bioadhesion enhancements.
- Oral: The successful oral delivery of protein therapeutics requires a delivery technology that overcomes the proteolytic degradation that occurs in the gastrointestinal system, and enhances the permeation of epithelial tissue barriers.
- Transdermal: An attractive concept due to the noninvasive nature of the therapy. The skin, however, is relatively impermeable to macromolecules, such as proteins.

Obstacles

In order for the delivery systems outlined above to be clinically successful, many shared obstacles need to be overcome, including:

- Dosing: A therapeutically meaningful amount of active protein must be delivered. In the case of a sustained delivery system, the active protein must be delivered for an extended period of time. Issues of bioavailability, potency, and clearance must be addressed.
- Manufacturability: The delivery system must be economical to produce. Proteins generally lack robustness and must be handled carefully. Sterilization is a significant issue for devices intended for sustained delivery of proteins.
- Stability: Proteins are susceptible to various forms of destabilizing events. The loss of protein tertiary structure can result in loss of activity and increased immunogenicity.

Sustained Delivery Technology: Delivering Proteins through Cross-Linked Polysaccharide Matrices

For many applications, a controlled and sustained delivery of active protein would be a very desirable feature. Technologies that are currently being investigated include micro/nanoparticles, implantable devices, and in situ-forming systems.

Materials

Natural and modified-natural polysaccharides have been widely used in pharmaceutical applications because they are generally recognized as being safe for human use. By covalently cross-linking polysaccharide chains, a permanent and controllable method of matrix formation is created. Some polysaccharides (e.g., starch) are degraded by physiological enzymes, while others (e.g., cellulose) are not degraded in the physiological environment.

To provide a sustained release of protein, the drug delivery system must possess a mechanism of controlled release as well as a means of stabilizing the protein. Therapeutic proteins can be incorporated into the natural polysaccharide matrix as it is being formed. The protein-containing matrix can be fabricated in a variety of implant configurations such as filaments, coils (Figure 1), scaffolds, or as a coating on a medical device without altering the biodegradation and drug compatibility features of the matrix. When implanted into the body, the matrix will enzymatically degrade from the surface inward. Entrained proteins are prevented from diffusion through the matrix, and are released only as the surface of the implant degrades. In vitro degradation and elution experiments have been conducted with this matrix.

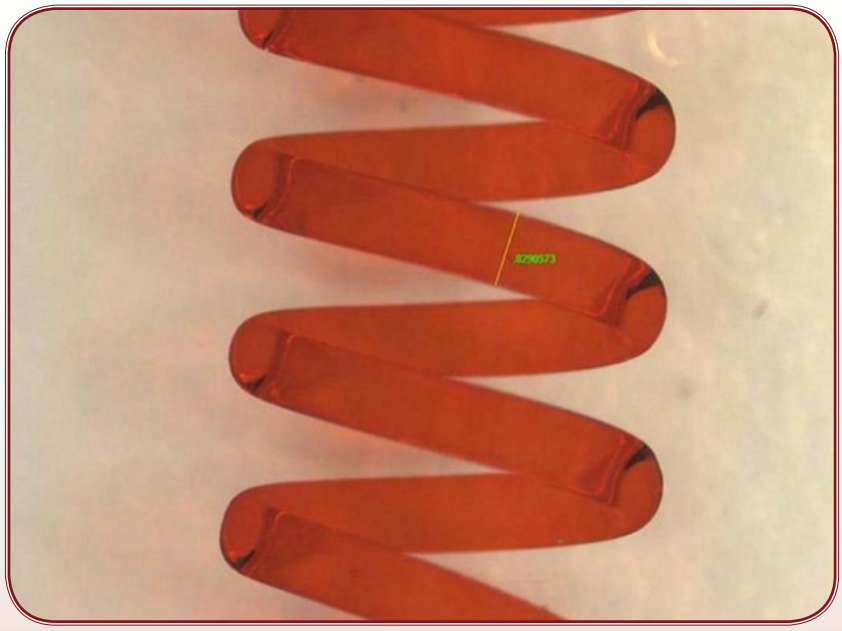


Figure 1. Coil made from the cross-linkable polysaccharide matrix. The cross-linkable polysaccharide has the ability to be formed into different shapes while maintaining the same biodegradation and elution properties.

Method of Action

Protein is trapped in the matrix and is released only when surface degradation occurs. Since the matrix is only degraded enzymatically and not through simple hydrolysis, the elution rate can be finely tuned by controlling the cross-linking density of the material. The chemistry ensures that the device degrades completely, which allows for the complete release of protein while maintaining structural integrity and preventing the matrix from falling apart into particulates (Figure 2).

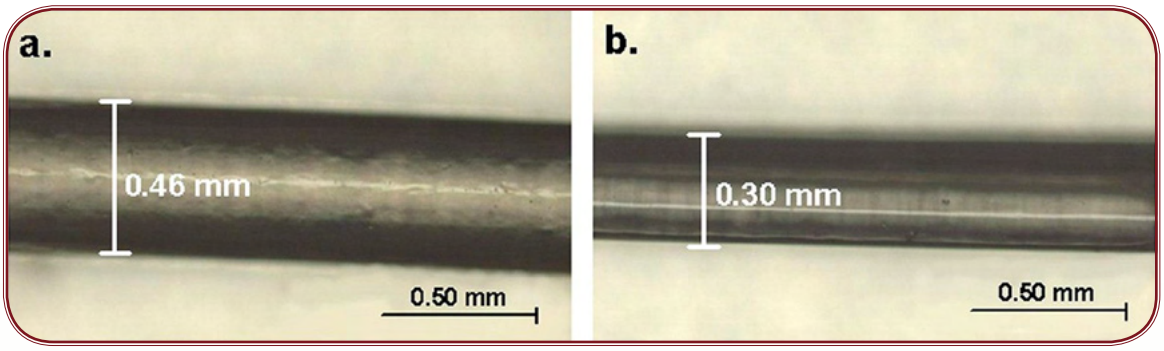


Figure 2. Degradation of the matrix: Photographs of filaments fabricated of the cross-linked polysaccharide. Figure 3a (left) shows a device after 58 days in phosphate buffered saline (PBS) with no measurable degradation. Figure 3b (right) shows an equivalently constructed filament after 58 days in PBS solution containing a physiologic concentration of amylase. Controlled surface erosion of the filament in amylase is evident.

Elution Control

By varying the cross-link density of the matrix, the elution profiles of proteins of varying sizes and molecular weights can be manipulated. Figure 3 shows the elution of IgG protein (MW ~ 150 kDa), and Figure 4 shows the elution of a F(ab) protein (MW ~ 50 kDa) from various matrix formulations. In both instances the matrix can be modified to vary the elution profile. Figure 4 shows that different formulations of the polymers deliver the same antibody fragment at various tunable rates, from 0.1 µg/day to 10 µg/day.

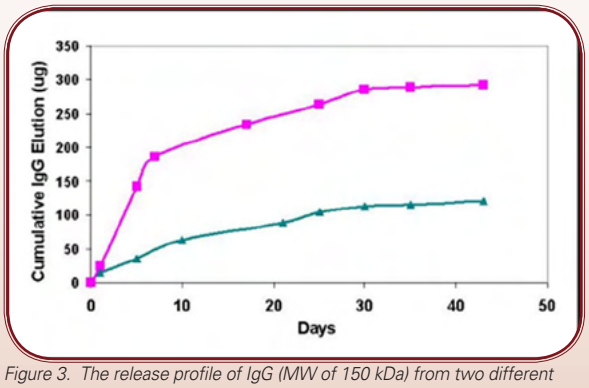


Figure 3. The release profile of IgG (MW of 150 kDa) from two different formulations of the cross-linkable polysaccharide matrix.

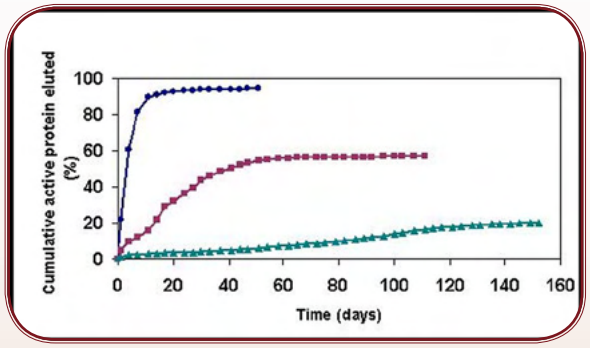


Figure 4. Three different formulations of the cross-linkable polysaccharide matrix elute active F(ab) fragments at three different rates, as detected by ELISA.

Stabilization

The advantage of using an enzymatically degradable polysaccharide as protein delivery matrix is that its natural breakdown products are mono- and di-saccharides, which are known to stabilize proteins. Another advantage of this system is that the protein is never exposed to harsh mechanical stress, organic solvents, or solvent/aqueous interfaces during matrix formation. In vitro experiments have shown that this polysaccharide matrix can stabilize active protein in physiological conditions for at least 6 months, while retaining 90% activity, as measured by ELISA.

Conclusion

Cross-linked polysaccharide matrices are ideal for delivering biomacromolecules. They provide a method for controlling the elution rate of proteins and as a means of stabilizing the entrained proteins when implanted. The natural polysaccharides are degraded by enzymatic digestion at the surface of the matrix, which allows for a tunable system that can meet the delivery needs of therapeutic protein regimens.

For More Information Contact:
Laura Patrick
SurModics, Inc.
9924 West 74th Street
Eden Prairie, MN 55344 USA
T: 952-947-8625
E: lpatrick@surmodics.com

Medical Device Stocks: A Healthy Outlook

S&P thinks the group's long-term fundamentals are positive and features Medtronic and Stryker among its top picks

by Sam Stovall

While flipping through the rolling 12-month relative strength charts for the nearly 140 subindustry indexes in the S&P Composite 1500 Index (consisting of the S&P 500, S&P MidCap 400 and S&P SmallCap 600 indexes), the S&P Health Care Equipment subindustry index chart popped out at me as a long-term turnaround candidate.

During 2006, the S&P Health Care Equipment index rose 3.4%, vs. a 13.3% advance for the S&P Composite 1500 index. The subindustry's relative strength, despite still being below one standard deviation from its mean, has improved ever so slightly and has broken above its moving average. Take a look at the accompanying chart. As a reminder, the jagged blue line represents the subindustry index's rolling 52-week price performance as compared with the 52-week performance for the S&P 1500.

52-Week Relative Strength—Health Care Equipment

Any point above 100 indicates market outperformance over the prior year, while points below 100 indicate market underperformance. The red line is a rolling 39-week moving average, while the two green bands indicate one standard deviation above and below the subindustry index's 17-year mean relative strength.

No Blockbusters on Horizon

Robert Gold covers this group for S&P, and he shares my interest in this subindustry. His fundamental outlook on the health-care equipment subindustry is positive, and he believes that early signs of a rebound in the implantable defibrillator market, combined with ongoing strength in the cardiology, diabetes, pain management, orthopedics, and oncology markets will help drive accelerating sales growth during 2007.

Gold remains concerned about a lack of blockbuster new product introductions anticipated for 2007, but he believes several important products may be launched during 2008 and 2009. In addition, he thinks merger-and-acquisition activity will continue to rise in 2007, providing some support to stock valuations and creating more powerful global competitors in categories such as orthopedics, vision care, interventional cardiology, and oncology.

S&P estimates that 2007 revenues will rise by about 11% to 12%, as improved pricing in orthopedics joins with slowing growth in the interventional cardiology category, particularly regarding drug-eluting coronary stents, which have, in Gold's view, saturated the market in the U.S. He continues to anticipate a rebound in the implantable defibrillator markets in 2007, and thinks growth will persist in the spinal surgery, pain management, robotic surgery, diagnostic imaging, and diabetes management product areas.

Strong in the Knees

Gold also looks for strong gains in the cosmetic surgery categories, with particular strength projected in the facial-aesthetics and breast-augmentation segments, although a weaker-than-expected level of consumer confidence in the U.S. could negatively affect demand for plastic surgery.

In orthopedics, S&P expects protracted strength in the knee-joint-replacement market in 2007, reflecting favorable global demographics and technological innovation. Gold sees spinal repair, including artificial discs, as another strong industry area. Although a broad investigation by the Justice Dept. into orthopedic-device pricing could result in additional headline risk for these stocks, Gold thinks the underlying fundamental drivers remain solid and anticipates that merger-and-acquisition activity will remain strong into 2007.

S&P sees positive longer-term fundamentals, including growing global demand for quality health care, an aging population, and rising R&D outlays, leading to a steady flow of new diagnostic and therapeutic products in areas such as cardiology, orthopedics, oncology, and minimally invasive surgery.

So there you have it. From both a fundamental and momentum standpoint, we believe the S&P Health Care Equipment group will begin to outperform the overall market over the

Stocks Continued on Page 23

Thank You to Our Members!

ANGIOTECH Pharmaceuticals, Inc.

AST PRODUCTS, INC.

Bausch & Lomb

Boston Scientific
Delivering what's next.

CarboMedics
A SORIN GROUP COMPANY

carmeda
A SUBSIDIARY OF W. L. GORE & ASSOCIATES

DePuy
a Johnson & Johnson company

EAG
Evans Analytical Group

genzyme

GORE
Creative Technologies Worldwide

HYSITRON, INC.
Nanomechanical Test Instruments

Integument
Integument Technologies, Inc.

MDEC
Medical Device Evaluation Center

Medtronic
When Life Depends on Medical Technology

Physical Electronics
a division of ULVAC-PHI

PLASMA TECHNOLOGY SYSTEMS

spire
Biomedical

Surface Solutions
Laboratories Incorporated

SurModics

THE UNIVERSITY OF ARIZONA
BIOMEDICAL ENGINEERING

THE UNIVERSITY OF MINNESOTA

UWEB
University of Washington Biomaterials Group

Drugmakers' 'Arms Race' Might Spur Biotechnology Deals

By Angela Zimm

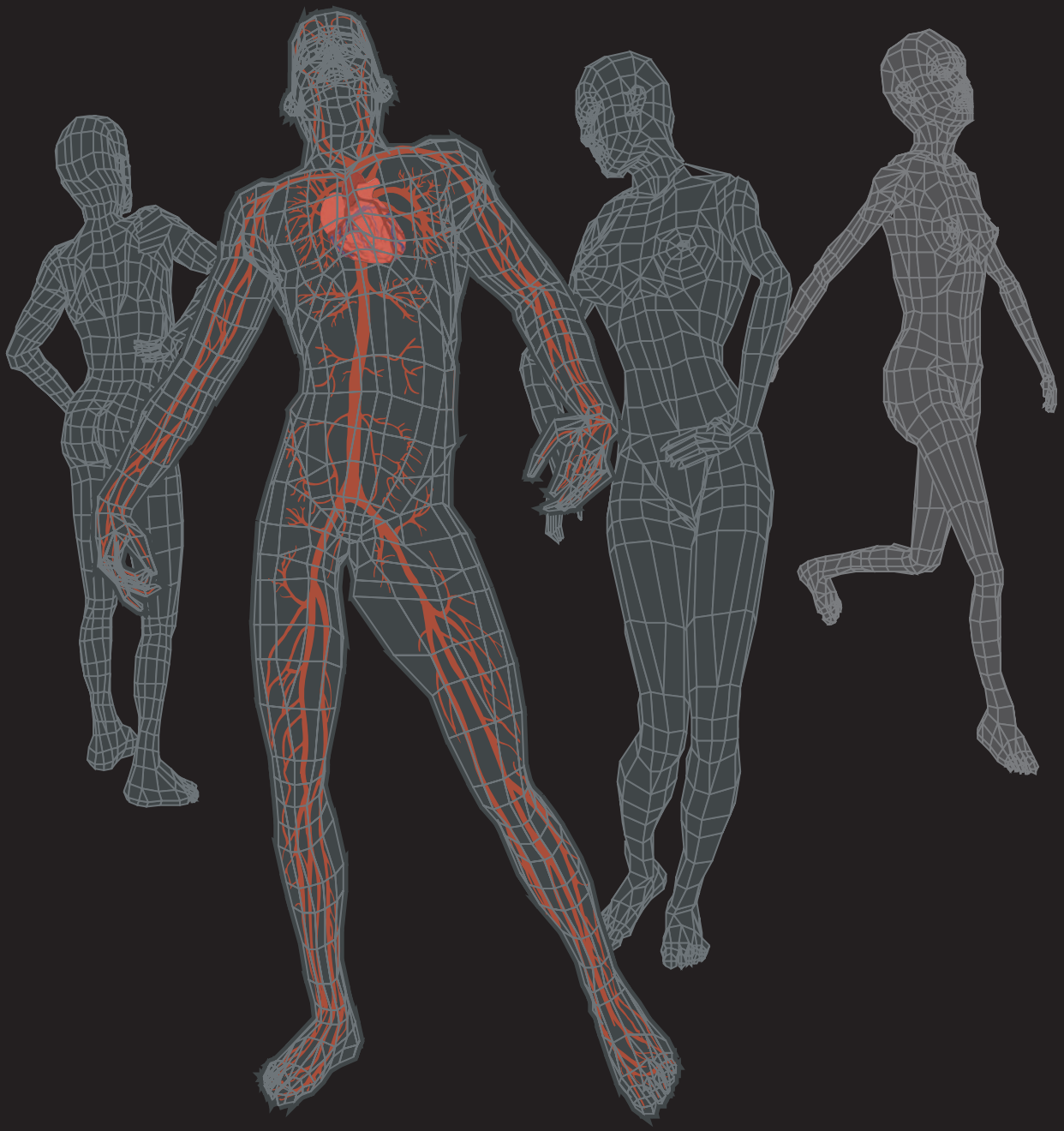
Vincent Aita of Kilkenny Capital Management says he picks biotechnology stocks on their potential as takeover targets. The strategy is paying off.

The number of biotech deals, including acquisitions and product alliances, rose 32 percent to 232 last year, according to data compiled by Bloomberg. At least four of Aita's holdings, including Serono SA and Kos Pharmaceuticals Inc., were bought by bigger drugmakers. Aita, who manages about $200 million in health stocks, is betting there will be even more transactions in 2007.

``There is an escalating arms race,'' Aita said in an interview at the JPMorgan Healthcare Conference this week in San Francisco. ``There are more deals to be had.''

Pfizer Inc., the world's largest pharmaceuticals maker, and Merck & Co. may buy biotech companies to make up for a scarcity of experimental medicines and expiring patents for best-selling products. On the shopping list are companies with experimental compounds as well as those with new drug-development science and technologies, investors at the conference said.

Arms Race Continued on Page 20



Working in partnership with physicians for over 50 years to bring the benefits of biomedical technology to patients around the world.

Medtronic

Alleviating Pain · Restoring Health · Extending Life

Arms Race Continued From Page 18

Last year the number of biotech deals in North America, including company acquisitions and joint ventures, increased from 175 in 2005, and the average premium rose to 33 percent from 23 percent, based on Bloomberg data.

Upward Trend

More transactions and higher premiums are likely this year, according to analysts, investors and company executives interviewed recently at the San Francisco conference, the annual meeting where buyers and sellers gather to make deals. About 7,000 people packed hallways and conference rooms at the Westin St. Francis Hotel to hear presentations from 310 companies.

``Premiums are going up,'' JPMorgan analyst Geoffrey Meacham said in an interview. ``You're seeing a lot of bidding wars.''

Driving the trend are big pharmaceutical companies with billions in cash that need new drugs to ensure growth. New York-based Pfizer may lose almost half of its $51 billion in 2005 sales as a result of competition from generic drugmakers to products with expiring patents. Pfizer, with $30 billion, has entered at least six research partnerships since November. Two transactions for which a value was disclosed totaled a combined $450 million.

Merck's Deals

Merck, the fourth-largest U.S. drugmaker, may lose $3 billion in sales this year from its top-selling Zocor cholesterol pill because of generic competition. It signed 35 transactions last year, including the $1.1 billion million purchase of San Francisco-based Sirna Therapeutics Inc., which is developing drugs based on blocking genes involved in disease.

Whitehouse Station, New Jersey-based Merck aims to become ``the best biotechnology company,'' Chief Executive Officer Richard Clark said in an interview. Merck's biotech deals totaled $1.4 billion in 2006.

``It's science and technology and potential companies —we're looking at all ends of the spectrum,'' Clark said. ``Obviously, it's competitive.''

Eli Lilly & Co., which is offering $2.28 billion to buy its biotech partner Icos Corp., is spending $1.5 billion this decade on building its own biotechnology operations.

``The price of poker has definitely gone up,'' said John Lechleiter, Indianapolis-based Lilly's president and chief operating officer, at the conference. ``There are too few good assets and too many bidders.''

Amgen Inc., the world's biggest biotechnology company, and Biogen Idec Inc. also are considering acquisitions and alliances.

Biogen

Biogen since May has bought three companies with a combined value exceeding $270 million to reduce reliance on its biggest product, the multiple sclerosis treatment Avonex. The Cambridge, Massachusetts-based company recently agreed to pay as much as $120 million for closely held Syntonix Pharmaceuticals, adding experimental treatments for hemophilia.

Merck's shares rose 53 cents, or 1.2 percent, to $44.79 at the close of New York Stock Exchange composite trading. Pfizer added 18 cents to $26.64, and Lilly increased 37 cents to $52.60. Amgen jumped $1.36, or 1.9 percent, to $73.27 in Nasdaq Stock Market composite trading, and Biogen rose 53 cents, or 1 percent, to $50.97.

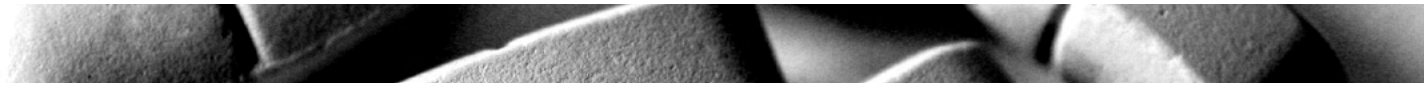
`Most Active'

The pace of acquisitions ``is the most active in our history,'' Biogen CEO James Mullen told investors in a presentation at the conference. There were 10 announced company acquisitions last year, up from 8 in 2005, JPMorgan analyst Meacham said in a Jan. 5 investment report.

Premiums over the market price of traded shares also are rising. They ranged from 21 percent for Swiss drugmaker Actelion Ltd.'s purchase of Cotherix Inc., a U.S. biotechnology company, to 170 percent for AnorMed Inc., which Genzyme Corp. took over in a bidding war with rival Millennium Pharmaceuticals Inc.

``Last year saw the first hostile bid by a biotechnology company,'' in the Genzyme takeover of AnorMed, said Steven Burrill, CEO of Burrill & Co., a life-sciences investment adviser in San Francisco.

``Premiums are running 50 percent to 100 percent, which



means the market is undervaluing the stocks," Burrill said. Biotechnology companies raised $20 billion in partnership deals last year, up from $17 billion in 2005, according to Burrill.

Companies already aligned with bigger drugmakers through partnerships are likely takeover targets, said Kilkenny's Aita.

Amgen

Last year Amgen purchased its partner, Abgenix Inc., to gain control of the cancer drug Vectibix. Genentech Inc., the world's No. 2 biotechnology company, agreed to buy its partner Tanox Inc. in November, gaining the asthma medication Xolair. The $919 million transaction was the first acquisition in Genentech's history.

Biotech companies in partnerships that may be takeover targets include Onyx Pharmaceuticals Inc., which co-markets the Nexavar kidney cancer drug with Bayer AG, and New River Pharmaceuticals Inc., which sold rights to its hyperactivity treatment to London-based Shire Plc, Aita said. Onyx shares rose 24 cents, or 2 percent, to $12.22 at the close of Nasdaq Stock Market trading. New River fell 37 cents to $55.76.

Others include BioMarin Pharmaceutical Inc., which shares a rare-disease drug with Genzyme, and Millennium, which co-markets its Velcade cancer drug with Johnson & Johnson. BioMarin shares gained 33 cents, or 1.9 percent, to $17.67 and Millennium rose 21 cents, or 1.9 percent, to $11.46.

`You don't often see biotechnology companies selling out of weakness," Aita said. ``Partnering and M&A have been the lifeblood of the industry. Consolidation isn't going away."

Inflammation-Fighting Drug Fails in Heart Trial

An inflammation-fighting drug has failed to improve the survival of people who had stents implanted after suffering a heart attack, researchers report.

But the idea of fighting inflammation to help such patients remains alive, said Dr. Christopher B. Granger, associate professor of medicine and director of the cardiac care unit at Duke University, a member of the team that tested the drug, pexelizumab, in a large-scale study.

"I think most of us believe, and I do, that there still is promise for the general approach, but this particular drug did not turn out to be effective," Granger said.

The drug had shown promise in some earlier trials, he said. In one study, "it reduced some of the markers of inflammation, such as C-reactive protein and interleukin-6, and that reduction in markers appeared to be associated with better clinical outcomes," Granger said.

But in the larger study, reported in the Jan. 3 issue of the *Journal of the American Medical Association*, use of pexelizumab made no difference.

The trial included 5,745 people treated for acute ST-elevation myocardial infarction -- a certain pattern on an electrocardiogram following a heart attack. All had stents implanted after undergoing artery-opening angioplasty. Half were given pexelizumab before angioplasty and for 24 hours afterward; the other half got a placebo, an inactive substance.

The 30-day death rate was almost identical for the two groups—3.92 percent for those getting a placebo, 4.06 percent for those getting the drug. The numbers were similar for the combination of death, cardiac shock or heart failure in the following 30 days—9.19 percent for placebo, and 8.99 percent with pexelizumab.

Other inflammation-fighting drugs are being investigated, Granger said, "and there are also others that have failed."

The general idea, he said, is to "inhibit inflammation and improve the metabolic health of the cell."

But the problem is that "inflammation is a nonspecific response, and there are so many redundant pathways for it that coming up with a specific treatment is difficult," Granger said.

Dr. Paul W. Armstrong is professor of medicine at the University of Alberta, in Edmonton, Canada, and lead author of the report. He said, "The science of this [behind the study] remains very attractive. We know that inflammation is an important player in heart attack and acute coronary conditions caused by narrowing. Reducing inflammation is desirable. The challenge is how you make it happen in the clinic."

Still, Armstrong said, "there are other agents and other approaches" to reducing inflammation. He described the study result as "obviously disappointing," but added that "in some ways, it opens the field to other pretenders to the throne."

Wanted: Members

To be leaders in the surface science community

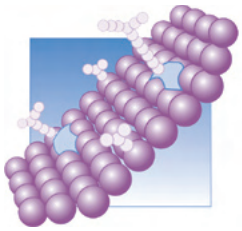
- Join a forum that fosters discussion and sharing of surface and interfacial information
- Have your voice heard and your interests represented within the surface science and biomedical community
- Help shape workshops and symposia that further the world-wide education of surface science
- Promote understanding of interfacial issues common to researchers, bio-medical engineers and material scientists.

Benefits of Membership:

- Discounted registration at BioInterface, the annual symposium of the Surfaces in Biomaterials Foundation.
- Your logo and a link to your Web site in the member directory on the official Web site of the Foundation, www.surfaces.org.
- Complimentary full page ad in surFACTS, the Foundation's newsletter and discounts on all advertising.

Join the Foundation that connects the academic, industrial, and regulatory committees within the surface science/biomedical communities!

Visit the Foundation at www.surfaces.org for a membership application or call 651-290-6267.



Surfaces in *Biomaterials* Foundation

Meeting/Conference/Trade Show Calendar

Meeting/Conference/Trade Show	Place	Dates	Web Address
(AIMBE) American Institute for Biomedical Engineering	Feb 27 - Mar 1	Washington D.C.	http://www.aimbe.org/content/index.php?pid=180
MEDTEC Stuttgart	Feb 27 - Mar 1	Stuttgart	http://www.devicelink.com/expo/medtec07
Society of Interventional Radiology SCVIR (now SIR)	Mar 1-6	Seattle	http://www.sirmeeting.org/index.cfm?fuseaction=Custom.Content&MenuID=1000&CFID=287208&CFTOKEN=73019835
Academy of Osseointegration (AO)	Mar 8-10	San Antonio	http://www.osseo.org/
American College of Cardiology	Mar 24-27	New Orleans	http://acc07.acc.org/
Drug Delivery 2007	Apr 9-11	San Francisco	http://www.arrowheadpublishers.com/DrugDeliveryConference.html
Am. Assoc. of Neruological Surgeons (AANS)	Apr 14-19	Washington DC	http://www.aans.org/annual/2007/default.asp
The Design of Medical Devices Conference 2007	Apr 17-19	Minneapolis	www.me.umn.edu/dmd
Society for Biomaterials	Apr 18-21	Chicago, IL	www.biomaterials.org
AIChE Annual Meeting - Spring National Meeting	Apr 22-26	Houston Hilton Houston, TX	http://www.aiche.org/Conferences/SpringMeeting/index.aspx
Pharma MedDevice 2007	Apr 24-26	Javits Center New York	http://www.pharmameddevice.com/App/homepage.cfm?moduleid=3155&appname=100485
American Association for Thoracic Surgery (AATS)	May 5-9	Washington DC	www.aats.org
ARVO (Association for Research in Vision and Ophthalmology) Annual Meeting	May 6-10	Fort Lauderdale	https://www.arvo.org/EWEB/startpage.aspx?site=AM_2007
American Urological Association (AUA)	May 19-24	Anaheim	www.auanet.org
BioInterface 2007	**Oct 29-31**	**San Mateo, CA**	**www.surfaces.org**

Stocks Continued From Page 16

longer term. S&P's 5-STARS (strong buy) picks in the group are Medtronic (MDT) and Stryker (SYK).

Industry Momentum List Update

For regular readers of the Sector Watch column, here is this week's list of the industries in the S&P 1500 with Relative Strength Rankings of "5" (price performances in the past 12 months that were among the top 10% of the industries in the S&P 1500), along with a stock that has the highest S&P STARS (tie goes to the issue with the largest market value).

Industry	Company	S&P STARS Rank	Price (1/12/07)
Apparel, Accessories & Luxury Goods	Coach (COH)	5	$46
Broadcasting & Cable TV	Comcast (CMCSA)	4	$44
Casinos & Gaming	Harrah's Entertainment (HET)	3	$83
Department Stores	Federated Dept. Stores (FD)	4	$39
Diversified Metals & Mining	Freeport McMoRan (FCX)	4	$55
Integrated Telecom. Svcs	CenturyTel (CTL)	3	$44
Investment Banking & Brokerage	Merrill Lynch (MER)	5	$97
IT Consulting & Other Svcs	SRA Intl. (SRX)	5	$28
Metal & Glass Containers	Ball Corp. (BLL)	4	$45
Motorcycle Manufacturers	Harley-Davidson (HOG)	3	$73
Movies & Entertainment	Disney (Walt) (DIS)	5	$35
Steel	Carpenter Technology (CRS)	4	$104
Tires & Rubber	Goodyear Tire & Rubber (GT)	3	$25