SurFACTS in Biomaterials

September-October 2011 | Volume 16 Issue 3

Goodbye From Steven Goodman

By Steven Goodman, Exiting Executive Editor of SurFACTS

It is with regret that I have stepped aside as the Executive Editor of SurFACTS after nearly 6 years. This was a difficult decision since I greatly enjoy educating and learning with the biomaterials science and business community. However, due to increasing professional demands it has become difficult to devote the time that that this position deserves and requires. My stepping aside, of course, has the benefit that a new energetic Executive Editor with new ideas has agreed to come on board:

This is my welcome to Joe McGonigle of SurModics.

While I will no longer be your editor, I will remain actively involved with the Surfaces in Biomaterials Foundation. I greatly look forward to attending BioInterface 2011 this coming October, where I will co-chair the Characterization of Biomaterials session and present a paper on a novel highly surface sensitive Imaging IR methodology. I expect to continue being active in future meetings, and with providing analytical microscopy services to the medical device and drug release industry. In fact, a major reason for stepping aside is that my firm's consulting services on pharma and biomaterials analysis has substantially increased.

While I regret stepping aside, I must admit that I look forward to sitting back and just reading future issues of SurFACTS.

Inside this Issue

Hello and Welcome from Joe McGonigle

By Joe McGonigle, Ph.D., SurModics, Inc.
Incoming SurFACTS Executive Editor

Thanks to Steven for the welcome and also a very large thanks for his many years of hard work as Executive Editor. I am excited to be coming on board as the new Executive Editor and am looking forward to continuing to improve the quality and value of the newsletter.

As a quick introduction, I am currently a scientist in the Research group at SurModics, Inc. in Eden Prairie, Minnesota. I have a Ph.D. in Bioengineering from the University of Washington with a broad background in biomaterials, drug delivery, vascular biology and gene therapy which I'm hoping will serve me well in dealing with the diverse interests of the biomaterials community.

I would like to use this editorial section today to discuss some of the changes we are planning to improve the usefulness and content quality of SurFACTS. The most important change will be to move towards using more original content provided through contributions from Surfaces in Biomaterials Foundation members. In order to make this change we will need help from members both to provide content as well as give feedback on what is working and what is not. I encourage all readers to contact me with articles, ideas or criticisms and we'll be sending out email reminders soliciting contributions for upcoming editions of SurFACTS.

In addition to more original content, we are adding a calendar of upcoming events in the biomaterials field which will be published in each of issue of SurFACTS and the Surfaces website. Again, here I'll make a plug for member support in letting us know about any events that will be of interest to readers. On a related front, I'd like to steer folks to the Surfaces in Biomaterials Foundation Group on LinkedIn which also provides a good source of information on events as well as job and networking opportunities.

I will be attending BioInterface in October and am eager to meet Surfaces members in person. I'd love to hear additional suggestions on improvements to SurFACTS and will also be seeking volunteers to help put those changes into place.

Members are encouraged to submit articles for future editions of SurFACTS. Please e-mail your story (with all appropriate figures and graphics) to Staff Editor Cody Zwiefelhofer at codyz@ewald.com for consideration in a future issue. Deadlines for upcoming issues are posted on surfaces.org.

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.

Analysis of Metals in Biological Matrices Using Inductively Coupled Plasma/Mass Spectrometry (ICP/MS)

By Wendy Fleming and Bill Katz, Katz Analytical Services

The use of implanted materials can be seen throughout the history of man with early discoveries of bone embedded implants linked to the Mayan civilization over 1,350 years ago. Excavations of these Mayan burial sites in Honduras unearthed fragments of tooth shaped shell pieces placed into the mandible dating from about 600 AD.

More recently, beginning in the 1930s, we started seeing more sophisticated implants as artificial hips became more common with the use of steel and chrome joints.

Today, metallic implants are used in many clinical applications with examples including:

1. Bone and Joint Replacement — about one million patients worldwide are treated annually for replacement hip and knee joints.
2. Dental Implants — a titanium "root" is introduced into the jaw bone where the superstructure of the tooth is then built.
3. Maxillo and Cranial/Facial Treatment — artificial parts may be required to restore the ability to speak or eat, as well as for cosmetic appearance.
4. Cardiovascular Devices — includes devices such as pacemakers and defibrillators, replacement heart valves, and intra-vascular stents.

These implants are constructed from various metals each having unique physical properties for specific applications. Common implant materials include stainless steel, cobalt-chromium alloys, titanium and titanium alloys, gold, and tantalum.

Despite the wide application of metal implants, concerns regarding corrosion and wear resulting in the production of metal ions and debris is a growing issue. While the specific effect of these metallic contaminants is a topic of current study, researchers have suggested that these species may enter the cell, disrupting inter-cellular processes causing alteration of the immune system and hypersensitivity. Others have raised concerns about chromosomal damage, chronic inflammation, necrosis of bone marrow, and carcinogenic effects.

Clearly, release and accumulation of metal debris/ions is a potential problem requiring further study. But, how does one quantitatively analyze such species at low levels in tissue, blood, and urine?

Inductively coupled plasma-mass spectrometry (ICP-MS) is an extremely sensitive method of determining metals. With proper sample preparation and low blank dissolution techniques, ICP-MS can provide analyses of solutions from parts per billion (ppb or ng/mL) to parts per trillion (ppt or pg/mL) levels in a variety of matrices including blood, tissue, urine, and many other biological matrices.

What sets this technique apart from other elemental analyses including atomic absorption and optical emission techniques is speed, sensitivity, precision, a wide dynamic range, ability to perform simultaneous multi-elemental analysis, and the capability to do isotopic comparison. The highly sensitive detection capability is essential when determining trace level metals from implants in biological fluids and tissue, making this technique favored above all others for this application.

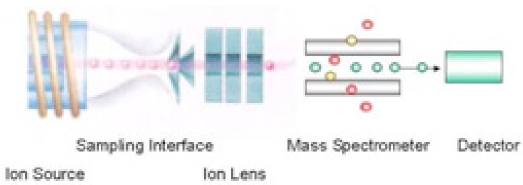


Figure 1: a schematic representation of an ICP-MS.

With ICP-MS, as illustrated in Figure 1, the sample is introduced into the argon plasma as an aerosol from the nebulizer. Once the aerosol is introduced, it is completely desolvated and the elements in the aerosol are converted into gaseous atoms and then positively ionized. These ions are then focused by a series of lenses and separated with a quadrupole mass spectrometer with respect to their mass to charge ratio with subsequent detection by an electron multiplier.

Data are only as good as the sample; therefore, selecting the correct sample preparation technique is essential to obtaining quality data. There are a variety of sample

Metal Analysis Continued on Page 4

Artificial Collagen-Based Wound-Care Tissue Promotes Vascular Growth

May 27, 2011 • By Qmed

Scientists from Cornell University (Ithaca, NY) have developed an artificial wound-care tissue that promotes vascular growth. The new material could encourage healthy skin to invade the wound area, hasten healing, and reduce the need for surgery.

Known as a dermal template, the material was engineered in the lab of Abraham Stroock, an associate professor of chemical and biomolecular engineering and member of the Kavli Institute for Nanoscale Science, in collaboration with Jason A. Spector, assistant professor of surgery at Weill Cornell Medical College.

Measuring about the size of a dime and exhibiting the consistency of tofu, the template is made from Type 1 collagen, a biocompatible material that contains no living cells, thus reducing concerns about immune system response and rejection. The material promotes the in-growth of a vascular system to the wounded area by providing a template for growth of both skin tissue and blood vessels.

The template was fabricated using tools at the Cornell NanoScale Science and Technology Facility to contain networks of microchannels that promote and direct the growth of healthy tissue into wound sites. While dermal templates have been created previously, current versions do not efficaciously encourage growth of healthy tissue because they lack the microchannels developed by the Cornell researchers. A key finding of the study is that the healing process responds strongly to the geometry of the microchannels within the collagen because they guide healthy tissue and vessels to grow toward the wound in an organized and rapid manner.

Metal Analysis Continued from Page 3

preparation techniques specific to biological matrices to choose from that will dissolve the elements of interest into solution: closed vessel microwave digestion, acid digestion, sample ashing, and chemical chelation. Having a good understanding of the chemistry of the sample matrix and the element(s) of interest is the best approach to selecting the sample preparation technique.

The study of the potential effects of metals accumulation is currently a topic of investigation in many laboratories. While much of the work to date is considered preliminary in scope, various research groups have published results in different types of animal models.

One such study is from J.L. Woodman at Rush-Presbyterian-St Luke's Medical Center (*Journal of Orthopaedic Research* 1:421-430, Raven Press, New York, 1984) where the effects of titanium, aluminum, and vanadium implants were studied in baboons. In a study of seven living baboons, they reported higher titanium levels in urine from an implanted animal as compared with the control, 14 ng/ml of titanium versus 2 ng/ml in the control animal. No differences in either the aluminum or vanadium concentrations were noted. In the same study analyzing the serum, they find significantly higher aluminum in the implant animal as compared with the control, 472 ng/ml and 264 ng/ml, respectively and neither titanium nor vanadium serum levels increased.

While the topic of metals accumulation is currently receiving significant attention, clearly more work is required before the long-term clinical effects are fully understood. Because of the potential biological impact low metal levels can have, ICP-MS is certainly a technique that will provide the sensitivity and accuracy required for such investigations.

Surface Science Calendar of Events

ESB 2011, 24th European Conference on Biomaterials: The Annual Conference of the European Society for Biomaterials
Sept. 4-9, 2011
Dublin, Ireland
http://www.esb2011.org/

Biomedical Engineering Society (BMES) 2011 Annual Meeting
October 12–15, 2011
Hartford, Connecticut
http://www.bmes.org/aws/BMES/pt/sp/meetings

BIOINTERFACE 2011

Surfaces in Biomaterials Foundation Annual BioInterface Meeting
October 24-26, 2011
Bloomington, MN
http://surfaces.org/cde.cfm?event=331217

BIOINTERFACE 2011

Workshop on Tissue Reactions to Medical Devices
October 27, 8:30am - Noon
University of Minnesota, Minneapolis, MN
http://surfaces.org/cde.cfm?event=360357

- Biomaterials: Inflammatory Response and the Foreign Body Reaction
  James M. Anderson, Case Western Reserve University
- Molecular Characterization of Tissue-Biomaterial Interactions
  Themis Kyriakides, Yale University
- Interconnections between Innate and Adaptive Immunity in Response to Combination Devices
  Julia Babensee, Georgia Institute of Technology

Medical Design and Manufacturing (MD&M) Minneapolis
November 2-3, 2011
Minneapolis, MN
http://www.canontradeshows.com/expo/minn11/

BioFuture 2011: Young European Biomaterial Scientists Designing a View for the Future
November 16-18, 2011
Het Pand, Ghent, Belgium
http://www.pbm.UGent.be

Transcatheter Cardiovascular Therapeutics (TCT) 2011
November 7-11, 2011
San Francisco, CA
http://www.tctconference.com/

Innovations in Cardiovascular Interventions (ICI) Meeting 2011
December 4-6, 2011
Tel Aviv, Israel
http://www.icimeeting.com/

TERMIS-NA 2011: Scaffolds in Tissue Engineering: Bridging Matrix Biology and Biomaterials Science
December 11-14, 2011
Houston, TX
http://www.termis.org/na2011/

6th International Symposium on Surface Science
December 11-15, 2011
Tokyo, Japan
http://www.sssj.org/isss6/

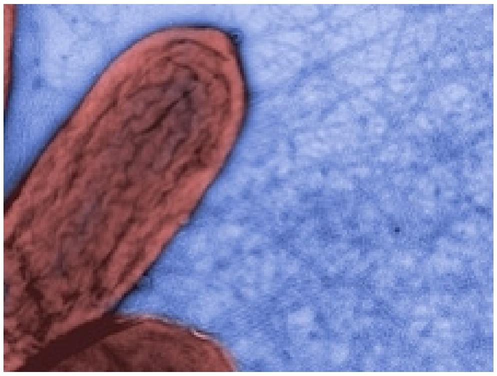
Medical Device and Manufacturing West (MD&M West)
Feb 13-16, 2012
Anaheim, CA
http://www.canontradeshows.com/expo/west11/

EuroPCR 2012
May 15-18, 2012
Paris, France
http://www.europcr.com/page/europcr/9-course-concept.html

UMass Amherst Research Team Discovers New Conducting Properties of Bacteria-Produced Nanowires

August 7, 2011 • By Janet Lathrop, UMass Amherst

The discovery of a fundamental, previously unknown property of microbial nanowires in the bacterium Geobacter sulfurreducens that allows electron transport across long distances could revolutionize nanotechnology and bioelectronics, says a team of physicists and microbiologists at the University of Massachusetts Amherst.



Their findings reported in the Aug. 7 advance online issue of *Nature Nanotechnology* may one day lead to cheaper, nontoxic nanomaterials for biosensors and solid state electronics that interface with biological systems.

Lead microbiologist Derek Lovley with physicists Mark Tuominen, Nikhil Malvankar and colleagues, say networks of bacterial filaments, known as microbial nanowires because they conduct electrons along their length, can move charges as efficiently as synthetic organic metallic nanostructures, and they do it over remarkable distances, thousands of times the bacterium's length.

Networks of microbial nanowires coursing through biofilms, which are cohesive aggregates of billions of cells, give this biological material conductivity comparable to that found in synthetic conducting polymers, which are used commonly in the electronics industry.

Lovley says, "The ability of protein filaments to conduct electrons in this way is a paradigm shift in biology and has ramifications for our understanding of natural microbial processes as well as practical implications for environmental clean-up and the development of renewable energy sources."

The discovery represents a fundamental change in understanding of biofilms, Malvankar adds. "In this species, the biofilm contains proteins that behave like a metal, conducting electrons over a very long distance, basically as far as you can extend the biofilm."

Tuominen, the lead physicist, adds, "This discovery not only puts forward an important new principle in biology but in materials science. We can now investigate a range of new conducting nanomaterials that are living, naturally occurring, nontoxic, easier to produce and less costly than man-made. They may even allow us to use electronics in water and moist environments. It opens exciting opportunities for biological and energy applications that were not possible before."

The researchers report that this is the first time metallic-like conduction of electrical charge along a protein filament has been observed. It was previously thought that such conduction would require a mechanism involving a series of other proteins known as cytochromes, with electrons making short hops from cytochrome to cytochrome. By contrast, the UMass Amherst team has demonstrated long-range conduction in the absence of cytochromes. The Geobacter filaments function like a true wire.

In nature, Geobacter use their microbial nanowires to transfer electrons onto iron oxides, natural rust-like minerals in soil, that for Geobacter serve the same function as oxygen does for humans. "What Geobacter can do with its nanowires is akin to breathing through a snorkel that's 10 kilometers long," says Malvankar.

The UMass Amherst group had proposed in a 2005 paper in *Nature* that Geobacter's nanowires might represent a fundamental new property in biology, but they didn't have a mechanism, so were met with considerable skepticism. To continue experimenting, Lovley and colleagues took advantage of the fact that in the laboratory Geobacter will grow on electrodes, which replace the iron oxides. On electrodes, the bacteria produce thick, electrically conductive biofilms. In a series of studies with genetically modified strains, the researchers found

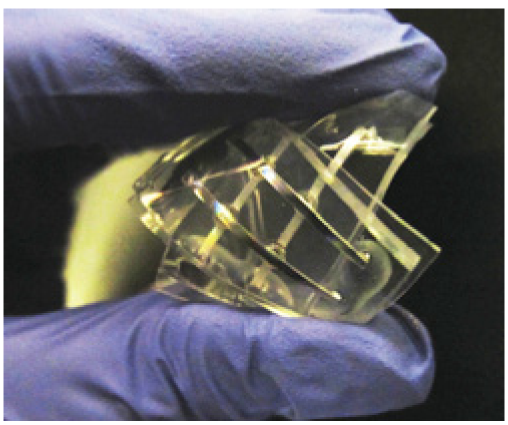
Bacteria-Produced Nanowires Continued on Page 9

Soft Memory Device May Lead to Biocompatible Electronics

August 16, 2011 • By Jamie Hartford, MDDI News

Researchers at North Carolina State University (NC State, Raleigh) have created a soft memory device that thrives in wet environments and could someday lead to new biocompatible electronics.

"We've made a memory device completely out of soft materials, gels that are literally like Jell-O," says Michael Dickey, assistant professor of chemical and biomolecular engineering at NC State and coauthor of a study on the devices.



Researchers can envision a "soft" memory device interfacing with neurons in the brain. Image courtesy of North Carolina State University.

The development came as the result of around two years of research. Dickey's team, which had been studying a liquid metal alloy of gallium and indium, collaborated with a team working under Orlin Velev, Invista professor in the NC State department of chemical and biomolecular engineering. Velev's team had been developing solar cells and diodes made from water-based gels.

"They were doing all this, but they were connecting them to the real world using rigid electrodes," Dickey says. "They were taking something that was really soft and making it not so soft. Our group was studying liquid metal, whose properties allow it to be molded into shapes other than spheres…We thought if you put those two things together, you could make something entirely soft."

The so-called mushy memory device creates the 0s and 1s of binary language using ions. The liquid metal alloy serves as an electrode. Positive and negative charges impact the thickness of an oxide layer, creating restive or conductive states accordingly.

"We're using materials that, in principle, could interface with things you find in biology—cells, enzymes, maybe even tissue," Dickey says. The memory device they created is both pliable and able to function in environments where conventional electronics could not. For instance, Dickey says student researchers working on the project even brought the device to one of their meetings in a bucket of water.

"Anyone who has worked on electronics knows that no one in their right mind would ever put a transistor or a cell phone or computer in water," Dickey says.

The researchers' long-term goals include possibilities such as integrating biological species into the gels and using them as sensors.

"The thing that would be easiest to imagine but hardest to pull off is using [the soft memory device] to interface with neurons in the brain," Dickey says. "But we have a long way to go before doing that."

Bacteria-Produced Nanowires Continued from Page 6

the metallic-like conductivity in the biofilm could be attributed to a network of nanowires spreading throughout the biofilm.

These special structures are tunable in a way not seen before, the UMass Amherst researchers found. Tuominen points out that it's well known in the nanotechnology community that artificial nanowire properties can be changed by altering their surroundings. Geobacter's natural approach is unique in allowing scientists to manipulate conducting properties by simply changing the temperature or regulating gene expression to create a new strain, for example. Malvankar adds that by introducing a third electrode, a biofilm can act like a biological transistor, able to be switched on or off by applying a voltage.

Another advantage Geobacter offers is its ability to produce natural materials that are more eco-friendly and quite a bit less expensive than man-made. Quite a few of today's nanotech materials are expensive to produce, many requiring rare elements, says Tuominen. Geobacter is a true natural alternative. "As someone who studies materials, I see the nanowires in this biofilm as a new material, one that just happens to be made by nature. It's exciting that it might bridge the gap between solid state electronics and biological systems. It is biocompatible in a way we haven't seen before."

Lovley quips, "We're basically making electronics out of vinegar. It can't get much cheaper or more 'green' than that."

Finally, this is a story about cross-disciplinary collaboration, which is much harder to accomplish than it sounds, Lovley says. "We were very lucky to have flexible funding from the Office of Naval Research, the Department of Energy and the National Science Foundation that allowed us to follow some hunches. Also, it took a physics doctoral student brave enough to come over to microbiology to work with something wet and slimy." That student, Nikhil Malvankar, now is a postdoctoral researcher who with Lovley and Tuominen will continue exploring what gives Geobacter's protein filaments their unique electrical properties.

Beneath the Surface: Surfaces Webinar Series Accepting Proposals and Sponsorships

Surface science/biomaterials professionals are invited to submit a proposal to present a 50-minute webinar on behalf of the Surfaces in Biomaterials Foundation. These presentations will bring together experts in biomaterials, implanted devices, biologicals, tissue engineering, and digital pathology to share new technologies and approaches to applied biological surface science. Surfaces in Biomaterials is looking for webinar presentations from members to share new technologies and approaches to the industry.

To submit a webinar proposal, please click here or visit http://surfaces.org/displayemailforms.cfm?emailformnbr=167106.

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The sponsor's logo and hotlink will also be embedded on the sponsored webinar's marketing communication. The sponsor will also receive a list of webinar attendees after webinar completion.

To sponsor an upcoming webinar, please click here or visit http://surfaces.org/displayemailforms.cfm?emailformnbr=165490.

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