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AES NEWSLETTER

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The Gaylord Hotel/Convention Center in Nashville will be a delightful venue for the AES meeting on Nov 9-12, 2009

We're looking forward to seeing everyone soon at the 2009 annual AES meeting to be held as Topical 3 of the American Institute of Chemical Engineers meeting in Nashville. The AES will have approximately 80 presentations in sessions spanning 4 days plus a poster session. The location for the Monday and Tuesday AES presentation sessions is Canal A, with the Wednesday and Thursday sessions being held in Canal D, all at the Gaylord Opryland Hotel. See the enclosed program grid for details. The poster session will be held from 6-8 pm on Tuesday, November 10 at Ryman Hall B1/B2 in the Hotel. Details will be emailed to the poster presenters soon. Please attend the annual business meeting on Wednesday, November 11 at 6:00 pm.(meeting room will be announced). Ideas for session topics for next year will be welcome at the business meeting, as will volunteers to help with various items. Don't forget to sign up for the annual AES banquet that will follow the business meeting at 7:30 pm at the Ristorante Volare in the Gaylord Hotel. The banquet speaker, Fred Stohl, will tell us about the history of the Oak Ridge National Laboratory.

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AES 2009 Meeting Co-Chairs

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Our traditionally strong meetings, with sessions strengthened by invited plenary speakers discussing state-of-the-art topics, would simply not be possible without help from our supporters. Their donations are greatly appreciated.

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An Introduction to Semantic Technology

By Robert Stevenson, Editor of Separation Science for International Scientific Communications, Inc.

Excel has become the *de facto* data management application of the sciences, and much of the rest of the scholarly universe. If Excel is too small, then one scales up to larger enterprise-wide or even global knowledge management systems from IBM, Oracle, etc. For the sciences, data management with Excel is becoming less useful as the file sizes increase, or files age. The latter is particularly a problem when it is necessary to make a change, such as adding new columns or rows to include new measurements. This problem is worse when one wants to compare results from one data file with that from another with different organization. Cutting and pasting sometimes works but these operations are seldom documented so that others can follow and verify them.

This is the background for a new programming and data management paradigm called the semantic web (SW). The semantic web relies on a series of three element statements (called triples) that allow the user to attach two descriptors to the data. These provide origin and context to the value or operation. Triples are used in a variety of ways to interconnect operations as well as data points. The overall language is called RDF which stands for Resource Description Framework. A variety of RDF extensions are available to assist the programmer in performing complex operations.

RDF uses structured statements that incorporate three independent, individual fields (object, subject, predicate) e.g., a thing, and how it is related to another thing. A triple can be simply described as three URIs. A URI (Uniform Resource Identifier) is a Web identifier: like the strings starting with "http:" or "ftp:" that you often find on the World Wide Web, analogous to URL (Uniform Resource Locator which locates individual web pages). The first URI defines the thing itself (for instance, a gene). After this URI comes a second field, which may be another URI or one of a set of well defined operations including identification, creator, etc. This one describes the relationship. The third field is the data, which can be numeric value or text. By stacking these statements into a string, one can create machine readable language that is much more complex, flexible and powerful than an Excel spread sheet. The down side is that each data point is composed of a triple that is considerably larger than the bits coding an Excel cell value. However, the fantastic growth in computer speed makes the entire process acceptably fast. See Jeffrey Pollack's book "Semantic Web for Dummies" (Wiley, 2009) for more information about the unique lexicon, history and power of the SW.

The attraction of the SW is its ability to open the deep web to an individual or an organization like the AES. Only about 10% of the information on the web can be accessed with current search engines such as Google and Bing that use proximity technology to rank the responses to a search query. Specific uses of the semantic web were described at the June 09 Semantic Technology Conference in San Jose, CA.

Cambridge Semantics (CS, Cambridge, MA) adopted Excel as the human interface for the semantic web, and then back filled the triples behind the screen. For example, data silos are each organized and maintained by a different scientist. Sometimes, he/she is working alone, and other times, as a member of a multidisciplinary group. Either way, the data is not useful unless collaborators can access it.

Collaboration involves sharing data and documents via email and accessing shared files on a common file/web server. The scientist provided the original context, history and indexing but it was often impractical for collaborators to find and reuse the data without significant effort and risk of error. Data created by instruments is also difficult to reuse outside of the original sheet. CS recognized that Microsoft's Excel is widely utilized by scientists and engineers to generate data sheets, so they didn't need to create and validate a new human interface. In two years they moved from experimental to marketable software that destroys the boundaries between data silos. The CS staff is confident that a novice can achieve first results in less than one week using their packages.

Construction of ontologies for a particular application is a key step in utilizing the power of the SW. Ontologies are relationships between data and context distilled from triples above. One of the most powerful and simplest to understand is logical inference of equality (If A=B, and B=C, then A=C). This was illustrated during a tutorial session hosted by Dr. Ivan Herman of the World Wide Web Consortium. His case in point was describing a book that had been written in both English and French. First he constructed a set of triples that described the original novel, including author, publisher, ISBN, Date, etc. Then he did the same for the French translation. These were converted to a graph that linked the various properties such as title, author etc. Upon linking the sets many relationships are tied together using logical inference. The French words were thus related and indeed translated into English (and vice versa) since they had a common node. These relationships can be strengthened by adding specific extra statements that "glue" or confirm apparent relationships.

Dr. Pollock pointed out a common misconception that all data needs to be converted to RDF. This is simply untrue. One can make a few conversational triples or links, and the SW then works with the non RDF data using the SW logic elements.

In early 2009, I'd heard several fleeting references to using SW technology in the life sciences. A poster by Dr. Erich Gombocz and Zack Rhoades of IO Informatics (Berkeley, CA) titled "Predictive Toxicology: Applied Semantics with major implications towards safer drugs" addressed this area. Toxicology is a major concern for drug developers. Firms could save a lot of money and time if they could predict a compound's toxicity in silico rather than in cultured cells followed by lab animals followed by clinical trials. A huge amount of data already exists, but there is little coherence since it was gathered over decades by different individuals using different techniques and descriptions.

The test program involved administering a single dose of selected hepatic toxicant to four rats and sampling fluids from the liver, serum and urine at 0, 6, 24, and 48 hrs later. Assays included a panel of 1603 metabolites (using LC-MS) and 31096 transcript probes.

First, a large data set of toxicological responses in rats was created using ontology graphing to force coherence from the diverse legacy data. The analytical results were analyzed and correlated with principle component analysis (PCA). The results were que-

ried against the database. The query results were displayed in a semantic map that facilitated exploring causal relationships. This led to identification of pathway enzymes encoded by the genes that were responding to the dose, a key step in predicting toxicology. Listing the enzymes led to creation of a combinatorial biomarker profile that correlated and then predicted structure-activity relationships (SARs). These were subsequently used as a biological model to predict the toxicological risk profile of potential compounds even before they had been synthesized.

The Semantic Technology 2009 Conference, is billed as industry's largest conference on semantic technologies. It attracted almost 600 scientists plus another 200 professionals from vendors to the Fairmont Hotel in San Jose, CA in June, 2009. This was the fifth meeting in the series, which started as a small intimate group five years ago that met in the Fairmont Hotel in San Francisco. The meeting then was mostly about the vision; today, it has expanded to case histories showing a huge variety of applications. I expect that in five years, the SW technology will have largely replaced today's search technology, but changes will be invisible to the vast majority of the users. It is tantalizing to think that this methodology might be useful for linking microdevice inventors with each other for the purpose of collaboration and also to avoid duplication. It might also serve to connect end users with inventors.

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Microchip Electrophoresis: Tremendous Progress, Even Greater Potential

By Victor Ugaz, Texas A&M University, Department of Chemical Engineering.

Electrophoresis continues to be one of the most versatile and robust techniques available for analysis of multicomponent samples ranging from small molecules, to DNA, to proteins. These features, combined with relatively straightforward design and operation, have in turn helped to make electrophoresis a central component in the development of miniaturized systems for chemical and biochemical analysis. In fact, CE-based analytical systems provided among the first successful demonstrations of microfluidic technology in the early 1990s. Some of the most important considerations in the design and construction of microchip-based electrophoresis systems include the materials and processes used to construct them, how samples are injected into the device, the choice of sieving gel matrix (if needed), and how the separated analytes are detected. Here we briefly survey how research in these key areas continues to improve and expand the capabilities of miniaturized electrophoresis systems.

In terms of construction, most electrophoresis microchips are fabricated using some combination of silicon, glass, or polymeric substrates. A microchannel network is typically imprinted or etched into one substrate, then bonded to a second flat substrate to create a sealed enclosure. Glass substrates have been widely studied owing to similarities with the capillaries employed in conventional CE systems. This has also made it possible to draw upon the results of past work aimed at development of robust coating procedures to neutralize surface charges. But plastic-based devices have not been as widely studied, and the magnitude and reproducibility of the resulting electroosmotic flow effects can be challenging to precisely control because they are highly sensitive to surface chemistry and buffer *p*H. Ongoing research in this area is critical to the successful operation of these devices.

The process by which samples are injected into the separation channel is also vitally important. Injection of a non-concentrated and unfocused sample zone not only requires a long separation distance in order to distinguish each component, but the corresponding signal from each species may fall below the detectable range as the zones spread by diffusion. Injection of a concentrated and focused sample zone allows each component to be detected in a considerably shorter separation distance. A variety of schemes are possible, the majority of which involve a perpendicularly crossed T-shaped channel geometry where analytes are electrokinetically transported across the separation channel after which the voltage is switched such that only the sample volume at the intersection is injected. Other methods that have been explored include hydrodynamic injection, dielectrophoretic trapping, focusing at embedded membranes or microchannel-nanochannel intersections, and on-chip microelectrode arrays. Development of injection and pre-concentration technology, combined with improved interfaces with other on-chip and off-chip components are areas of active research.

A variety of sieving matrix formulations have been employed in electrophoresis microdevices, most notably in applications involving DNA and protein separations where analyte mobilities in free solution are either not size dependent or only weakly so. Polyacrylamide gels (both crosslinked and non-crosslinked) are widely used owing to favorable properties including optical transparency, electro-neutrality, and overall separation performance. More recent advances include development of thermoreversible gels that undergo a transition from gel-like to liquid-like behavior over a specific temperature range, and copolymers containing embedded chemical groups that associate to form a replaceable gel with properties resembling those of a crosslinked network. Many ongoing research efforts are focused on rational development of improved sieving gels capable of meeting the demanding requirements of the microdevice format.

Another critical component of electrophoresis microdevices is the ability to detect migration of the separated zones. Laser induced fluorescence methods have remained a workhorse, whereby fluorescently labeled species are illuminated by a laser that excites fluorophores conjugated with the migrating analytes. The resulting fluorescence signal is filtered to block background illumination from the excitation source and recorded using a photodetec-

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tor (e.g., CCD, photomultiplier tube). But a drawback of optical detection techniques is that they generally require an illumination source and photodetection components that in many cases contribute significantly to the overall size of the system. Non-optical detection techniques, particularly electrochemical methods, are currently being widely explored as a means of providing more compact device designs.

Recent advancements have resulted in the development of separation technologies offering capabilities beyond those found in adaptations of conventional electrophoresis techniques. A notable example is the use of micro- and nano-fabricated pillar arrays as separation matrix structures in place of polymer gels. These post arrays can be easily mass produced using micromachining technology and possess inherently uniform monodisperse two-dimensional pore morphologies. By manipulating the size, shape, and spacing of the pillars, separation properties can be tuned to make them compatible with a wide range of samples and analyte sizes. In addition, since the sieving structures are pre-fabricated inside the microchannel the gel loading process is eliminated. Ongoing research seeks to understand the detailed physics associated with collisions and interactions that occur between the migrating analytes and the array of obstacles, and how these interactions are responsible for introducing size dependent mobilities.

Considerable strides have been made since microfabricated electrophoresis devices were first developed in the early 1990s. Some of the challenges that remain to be addressed include reducing the cost of these devices, enhancing integration and improving the capability to interface with the external macroscale world, and developing miniaturized detection technology. Systematic fundamental studies are also important in order to provide a more complete understanding of the physics of electrophoresis in micro- and nano-scale environments. Future developments in these areas are likely to lay the foundation for a new generation of rapid, sensitive, and inexpensive instrumentation with separation performance exceeding that in many of the conventional benchtop-scale analytical systems available today.

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Results of AES 2009 Elections

Four positions were open for elections, Secretary and three Councilor seats, and an equal number of members have volunteered to run. The candidates are:

- ***Phil Beckett**, Senior Scientist, Proteomics Applications, GE Healthcare, Piscataway, NJ (Secretary).*
- ***Kevin Dorfman** , Assistant Professor, University of Minnesota, Department of Chemical Engineering and Materials Science, Minneapolis, MN (Councilor).*
- ***Blanca Lapizco**, Associate Professor of Biotechnology and Food Engineering, Tecnologico Monterrey, Mexico (Councilor).*
- ***Shramik Sengupta** Assistant Professor, Dept of Biological Engineering, University of Missouri, Columbia MO (Councilor).*

Our applicants, tapped by the council, are again of the highest caliber. They will assume office upon formal approval by the council at the Nashville meeting. Their biosketches and pictures will be provided in the January, 2010 newsletter.

Learn about Oak Ridge National Laboratory! Oak Ridge National Laboratory, a 2.5-hour drive from Nashville, is the home of the world's largest supercomputer as well as the Graphite Reactor, a building on the National Historic Register where in 1943 scientists developed the world's first production nuclear reactor for plutonium. Learn more about the history of ORNL from Fred Stohl, the AES Banquet speaker, on Wednesday evening, November 11.