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AES Newsletter

Electrophoresis takes many forms: see the AES collage at the Austin Meeting, Nov. 7-11, 2004

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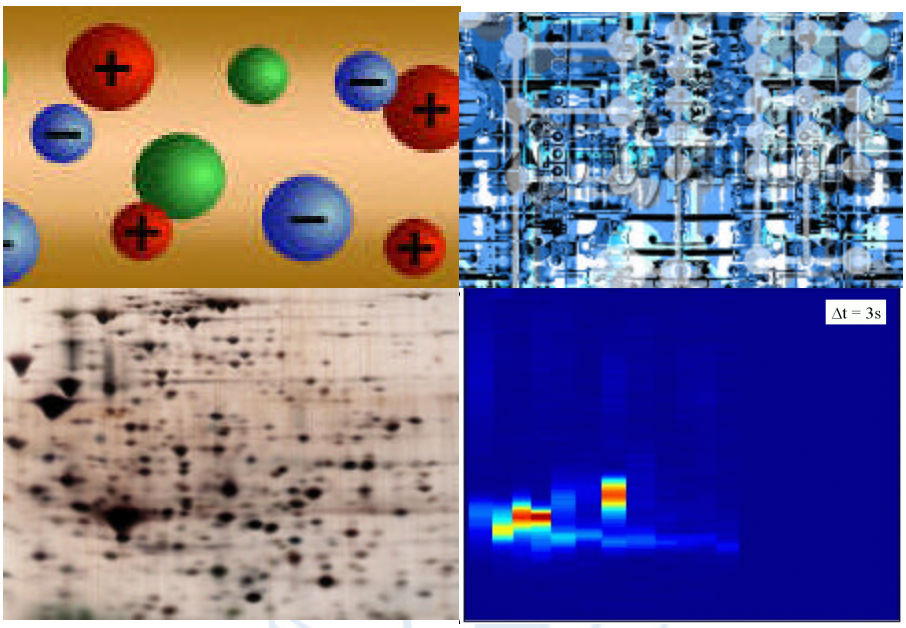

The many faces of electrophoretic separations (clockwise from top left): charge separation representation, microfluidic chip, gel-like plots constructed from CCD images collected during 2D separations, 2DE gel.

Many thanks to our Sponsors for contributions funding the 2004 meeting.

Bio-Rad Labs

CBS Scientific

GE Healthcare

Genencor International

Nonlinear Dynamics

Proteome Systems

Scimagix

Syngene

Our traditionally strong meetings, with sessions chaired by invited plenary speakers discussing state-of-the-art topics, would simply not be possible without funding from sponsors. These donations are greatly appreciated.

Final Run-through:

We're down to the wire and the meeting is looking very good. Annelise Barron, the Meeting Organizer, along with the Session Chairs and Vice-chairs have done a terrific job, as you will see.

Electrophoresis has developed over the past 20 years from theoretical origins to numerous applied systems. Many will be presented at the Austin meeting. Monday the entire day's focus will be on the exploding area of proteomics. Tuesday morning we will be treated to two exciting plenary talks, by Dr. Ronald Pethig, speaking on Micro-Dielectrophoresis and by Dr.Walter Blackstock, speaking on Cell Maps. Tuesday afternoon there will be thought-provoking bioinformatics sessions on transcriptomics and on proteomics, followed by the Poster Reception at 5:30 - 7:30 p.m. Wednesday the cutting edge topic of microfluidic chips is addressed in three intense sessions: biomedical applications, proteome analysis, and genomic assays. The Society banquet in the evening will provide a culinary breather. Only two sessions will be held on Thursday but they're good ones, including topics of microfluidics analysis of biomolecules and electrokinetics/ microfluidics combinations. See you there!

Nancy Kendrick
Outgoing President

Dave Garfin
President Elect

2DE proteomics problems: an overview and specific case

University of Texas Medical Branch, NHLBI Proteomics Center

The Joy and Pain of 2D Gel Electrophoresis - an overview: Two-dimensional gel electrophoresis (2DGE) technology has been in place for some 30 years and, although it has been a valuable technique, researchers commonly remark that 2DGE is technically challenging and difficult to employ. So, if 2DGE is so fraught with difficulties, how is it that it has survived for so long? The answer lies in the benefit of comparative analysis of globally characterized protein expression from two or more biological sources. As a separation technique, 2DGE is unsurpassed in its powers of numerical resolution. Moreover, its ability to represent complex mixtures of many thousands of proteins in a single gel, or more appropriately, in a single picture remains unchallenged. Furthermore, the current renaissance in the application of 2DGE in biology is due to the marriage of its separation power with new mass spectrometry technologies, and the availability of genomic DNA sequences. No other technique is capable of describing a complete experiment comparatively gauging the global expression of proteins from two or more sources as efficiently as 2DGE. That is the joy of 2DGE.

Short of the intense manual effort, and lack of promise for success, its pain is felt when quantifying the observed differences in two or more albeit beautifully separated samples. One is struck with the horror that there is no way to be absolutely sure that proteins faithfully extracted from tissues or cells have transferred quantitatively from the first dimension gel to the second dimension gel. Nor can one be absolutely sure that the mobility differences observed in the second dimension between two possibly related spots are not due to variations in gel polymerization, run-times, field strengths, temperatures, state of reduction/aggregation, artifactual protein modification, etc. Aside from these artifactual influences, another source of variation that truly requires attention is the impact of genetic variation associated with some samples. Many proteins exhibit polymorphisms that require characterization prior to differential analysis by 2DGE of two or more protein expression states. If that isn't enough one can add to the list of woes the lack of dynamic range and linearity in detection systems routinely used in 2DGE.

Given these issues, newcomers to the field of proteomics may legitimately ask whether it is worthwhile to invest in 2DGE technology or wait for new replacement technologies to develop. In our opinion 2DGE still remains a gold standard of proteomics for protein separation and there is much to be gained from its application, albeit with some struggling. Undoubtedly, the comparison of the global expression pattern of a reference proteome to an affected proteome can lead to novel insights into the fundamental biochemical pathology of disease, or the pathway of cellular differentiation, or the mechanisms by which cells communicate with each other and interact with their environment, or even perhaps the biochemical basis of human thought and behavior. That is the hope and promise of differential proteomics.

John E. Wiktorowicz Alex Kurosky

UTMB, NHLBI Proteomics Center

Fox Chase Cancer Center

Specific Problems (email): Linking 2D gel results with microarray results is an important approach but problematic. Dealing with protein isoforms costs considerable time. The arrays and proteomics data sets have few overlaps so we limit ourselves to the spots that are changing by each technology. The less interesting genes have lots of overlaps. Of the overlaps for interesting genes, some say the same thing, so they do not get challenged initially. The different overlaps get Western blotted, which is when we find out about isoform problems. For our big 2D projects, we identify all possible polypeptide spots. However, for other experiments, we have missed non-changing isoforms of interesting proteins because we only identified the changing polypeptide spots. Now we've switched to identifying all visible spots within about 5 spot lengths around any spot that is changing, in an attempt to be exhaustive in finding isoforms. If there is a stronger spot near an interesting spot, we must rule out that the stronger spot is an isoform by mass spectrometry or else do a 2D Western blot. We also compare theoretical PI and mass with the observed PI and mass to rule out proteolysis. When no higher intensity isoform of a changing spot is found after exhaustive hunting, then transcriptional control becomes more enticing. At that point, we bring in quantitative real-time PCR. The hope is that a validated RT-PCR assay for the expression of a given protein will extend the proteomics investigation to biopsy samples and paraffin blocks. The latter techniques provide the larger sample size necessary for statistically significant conclusions.

Proteomics is a lot of work.

Tony Yeung,
Fox Chase Cancer Ctr

Results of Councilor Elections

The Presidency automatically shifts this year from Nancy Kendrick, who becomes Past President, to Dave Garfin, who becomes the new President. Three positions were open for elections, the Vice Presidency and two Councilors seats and three members volunteered to run, so voting is unnecessary. We are once again lucky that our applicants, tapped by the council, are of the highest caliber. Their statements are below. They will be formally approved at the November meeting.

AES Vice President:

Dr. L. Scott Rodkey, Professor of Pathology University of Texas -Houston Medical School

My research has included electrophoresis as a central theme since graduate school. Of my 77 publications, 29 directly involve electrophoresis as a major or sole component of the work. Further, I have five US patents and one Swedish patent for electrophoresis technologies. My current NIH grant support is for a basic research project in electrophoresis technology. In partnership with the University of Texas, I established a company to commercialize technology developed in my laboratory. As AES Vice President, I will use my experience in both academia and in technology development and transfer to further the goals of the Society. These goals will be served best by combining the best minds in academia with the best in the biotechnology industry to foster communication within these disciplines for their mutual benefit. The AES should maintain and expand its participation in ICES to better serve the needs of all members. It should work for continual improvement of content in the journal *Electrophoresis* by recruiting high quality reviewers and soliciting high quality papers from members and non-members alike. Continued and expanded efforts to actively engage both new and established biotechnology companies for support of AES activities that can benefit all should be pursued by the Council. I support expanding the AES newsletter and website to help serve the increasingly diverse needs of our members and would solicit member input into the effort. Additional efforts to increase our member base should be part of the Council agenda. As Vice President, I pledge to vote on issues for the best interests of all constituents of the Society and will actively seek input from the very best minds whenever I feel that specific issues coming to Council would benefit from outside guidance and input.

Dr. Scott Rodkey, New Vice President

Adrienne Minerick, AES Councilor 2004 - 2007

Adrienne R. Minerick is currently an Assistant Professor and Director of the Medical micro-Device Engineering Research Laboratory (M.D. - ERL) in the Dave C. Swalm School of Chemical Engineering at Mississippi State University. She obtained a B.S. in chemical engineering in 1998 from Michigan Technological University followed by an M.S. and Ph.D. in 2003 from the Department of Chemical and Biomolecular Engineering at the University of Notre Dame under the direction of Prof. Hsueh Chia Chang. Dr. Minerick joined the faculty at MSU in August of 2003, recently earned the 2004 Ralph E. Powe Junior Faculty Award from Oak Ridge Associated Universities, and has also been invited to participate in the National Academies 2004 Keck Futures Initiative. With her work in medical diagnostic microfluidics and physiological blood flow dynamics, Dr. Minerick has published articles in the journal *Electrophoresis* on linear and nonlinear microdevice electrokinetics. Her research interests currently focus on dielectrophoretic manipulation and characterization of erythrocytes, food borne pathogens, and sickle cells.

Dr. Adrienne Minerick, New AES Councilor

Victor Ugaz, AES Councilor 2004 - 2007

I am pleased to receive your consideration for the position of AES Councilor. I have been an Assistant Professor of Chemical Engineering at Texas A&M University since January 2003. My academic background includes B.S. and M.S. degrees in Aerospace Engineering from the University of Texas at Austin, a Ph.D. in Chemical Engineering from Northwestern, and 3 years of postdoctoral research at the University of Michigan in the laboratory of Prof. Mark Burns.

One of my primary research interests involves the study of DNA migration and transport in microfabricated electrophoresis systems. The aim of this work is to address the critical need that exists for the development of advanced technology to enable genomic analysis and DNA sequencing to be performed (i) with significantly higher throughput, and (ii) at significantly lower cost than is attainable with current systems. Microfluidic systems offer an exciting platform for achieving these advancements in separation performance that will ultimately make it feasible for genomic information to become an integral part of routine medical diagnostic protocols. As an AES Councilor, I will work to promote efforts in these emerging areas to help ensure that electrophoresis remains at the forefront of modern genomic analysis technology.

Dr. Victor Ugaz, New AES Councilor

Contact: Joan

Joan Stevenson

Executive Director

The Electrophoresis Society

3338 Carlyle Terrace

Electrophoresis past, present and future

Current Slate of Officers for 2005

President: David Garfin, Ph.D., 2DE Consultant (11/04 - 11/06)
Past President: Nancy Kendrick, Ph.D., Kendrick Labs Inc. (11/04 - 11-06)
Vice President: Scott Rodkey, Ph.D., University of Texas (11/04 - 11/06)
Secretary: Jasmine Gray, Ph.D., GE Healthcare (11/02 - 11/05)
Treasurer: Lawrence Grossman, Ph.D., Wayne State University (11/03 - 11/05)
Councilor: Pedro Arce, Ph.D., Tennessee Technological University (11/02 - 11/05)
Councilor: Alfred Gaertner, Ph.D., Genencor International (11/02 - 11/05)
Councilor: Adrienne Minnerick, Ph.D., Mississippi State University (11/04 - 11/07)
Councilor: Nancy Stellwagen, Ph.D., University of Iowa (11/02 - 11/05)
Councilor: Robert Stevenson, Ph.D., Abacus Group (11/03 - 11/06)
Councilor: Victor Ugaz, Ph.D., Texas A & M University (11/04 - 11/07)

Since much of the meeting this year revolves around microfluidic devices it seems useful to include basic information about microfluidics for AES members not in that field. Later on more complex issues can be discussed. The following information was taken from the web page of Dr. Paul Yager, University of Seattle. The references cited in the article below are listed on his web page:
http://faculty.washington.edu/yagerp/microfluidicstutorial/basicconcepts/basicconcepts.htm

Basic Microfluidic Concepts

A microfluidic device can be identified by the fact that it has one or more channels with at least one dimension less than 1 mm. Common fluids used in microfluidic devices include whole blood samples, bacterial cell suspensions, protein or antibody solutions and various buffers. Microfluidic devices can be used to obtain a variety of interesting measurements including molecular diffusion coefficients [1,2], fluid viscosity [3], pH [4,5], chemical binding coefficients [1] and enzyme reaction kinetics [6-8}. Other applications for microfluidic devices include capillary electrophoresis [9], isoelectric focusing [5,10,11], immunoassays [12-15], flow cytometry [16], sample injection of proteins for analysis via mass spectrometry [17-19], PCR amplification [20-22], DNA analysis [23-26], cell manipulation [27], cell separation [28], cell patterning [29,30] and chemical gradient formation [31,32]. Many of these applications have utility for clinical diagnostics [33,34].

Included with this newsletter are a program grid showing the schedule for AES talks, 2 drink coupons for the poster reception, and a page showing abstracts of talks that aren't on the AIChE website or in the program.

The use of microfluidic devices to conduct biomedical research and create clinically useful technologies has a number of significant advantages. First, because the volume of fluids within these channels is very small, usually several nanoliters, the amount of reagents and analytes used is quite small. This is especially significant for expensive reagents. The fabrications techniques used to construct microfluidic devices, discussed in more depth later, are relatively inexpensive and are very amenable both to highly elaborate, multiplexed devices and also to mass production. In a manner similar to that for microelectronics, microfluidic technologies enable the fabrication of highly integrated devices for performing several different functions on the same substrate chip. One of the long term goals in the field of microfluidics is to create integrated, portable clinical diagnostic devices for home and bedside use, thereby eliminating time consuming laboratory analysis procedures.

Don 't forget to see the Austin Bat Bridge!