Expert Review of Proteomics

ISSN: 1478-9450 (Print) 1744-8387 (Online) Journal homepage: informahealthcare.com/journals/ieru20

25th Annual Meeting of the American Electrophoresis Society

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To cite this article: David E Garfin (2009) 25th Annual Meeting of the American Electrophoresis Society, Expert Review of Proteomics, 6:3, 239-241, DOI: 10.1586/epr.09.18

To link to this article: https://doi.org/10.1586/epr.09.18

Published online: 09 Jan 2014.

EXPERT REVIEWS

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Expert Rev. Proteomics 6(3), 239–241 (2009)

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25th Annual Meeting of the American Electrophoresis Society

Philadelphia, PA, USA, 17–20 November 2008

Presentations at the 2008 meeting of the American Electrophoresis Society dealt with many aspects of this key separation technology. In total, there were 65 technical talks and 13 posters in a 4-day meeting. The proteomics technical talks described applications of 1D and 2D gel electrophoresis, capillary electrophoresis and microscale platforms. Some new platforms may find use in future proteomics research.

Electrophoresis has always been an integral part of proteomics. Researchers working with 2D gels realized the value of massively parallel analyses of proteins. On the other hand, the advent of proteomics spurred activities in electrophoretic methodologies that might otherwise have been slower to develop. Although there is a great desire to replace gel electrophoresis with more automatable techniques, gel electrophoresis in one form or another is still a vital tool in protein and nucleic acid research. Nevertheless, the basic platforms for electrophoretic separations have not changed significantly since their introductions.

Of all the groups working on the development of new electrophoretic methodologies, the largest is probably the chemical engineers. The reason for this is owing to the fact that this discipline is based on separation technologies. Thus, for the past 8 years, The American Electrophoresis Society (AES) [101], whose interests are in all forms of electrophoretic and electrokinetic separations, has partnered with the American Institute of Chemical Engineers (AIChE) [102] in order to facilitate interactions between biochemists, chemists, physical chemists and engineers working in the proteomic field. The AES annual meeting is now an integral part of the (much larger) annual AIChE meeting. Significantly, the 2008 meeting was a milestone for both organizations. It was the AES's 25th annual meeting and also the 100th anniversary meeting of AIChE. The meeting was held in mid-November 2008, in Philadelphia (PA, USA). The AES portion was organized by Shashi Murthy (Northeastern University, MA, USA) and Jonathan Posner (Arizona State University, AZ, USA). The portion of the AES meeting devoted specifically to proteomics included 14 talks. BioMEMS, microfluidics and electrokinetics completed the rest of the 4-day meeting. This article is only concerned with the proteomic aspects of the meeting.

Engineers, whose training is largely in chemical and mathematical concepts, have taken it upon themselves to learn basic proteomics and genomics. They do this either by teaming up with *bona fide* biochemistry or molecular biology laboratories or by digging in on their own and learning the intricacies of protein and nucleic separations and even some of the biology involved. Biologists provide the in-depth knowledge of biology, as well as being knowledgeable on the relevant separation techniques, so the pairing of the two disciplines is synergistic.

At the AES meetings, presentations describing 'standard' electrophoretic methods are mingled with specialized presentations on such topics as electrokinetic theories and the motions of macromolecules undergoing electrophoresis. Many presentations at the 2008 AES meeting dealt with different microdevices that are being developed for separating and analyzing cells, proteins and nucleic acids. These devices meet with varying degrees of success because they are typically plagued by resolution that is too

 10.1586/EPR.09.18 ISSN 1478-9450

low for research work. Nonetheless, some current configurations may find use in process development, quality control and diagnostic applications.

In this reporter's opinion, no matter how sophisticated microchanneling becomes, micro-/nano-devices will never universally replace polyacrylamide gel slabs for research separations. This is because, at this time, it is not possible to duplicate the resolution for proteins obtainable in macroscale gel slabs with miniature devices (nucleic acids can be adequately resolved in small channels). A large part of poor protein resolution in small dimensions is due to the lack of sieving materials compared with polyacrylamide gels. Polyacrylamide gel is particularly well suited for protein separations:

- Pore sizes are comparable to protein sizes so that the gels act as 3D sieves;
- Pore sizes of polyacrylamide gels can be matched to differing protein size ranges – including pore-size gradients;
- Polyacrylamide gels are hydrophilic and electrically neutral (when fresh);
- Polyacrylamide does not bind proteins (when fresh);
- Polyacrylamide gels can withstand denaturing conditions;
- Polyacrylamide gels are transparent to wavelengths above approximately 250 nm.

No other material fits this bill. Nevertheless, there are drawbacks to the use of polyacrylamide gels, especially in miniature devices. Since the polymerization reaction is exothermic, it is hard to cast bubble-free gels, which puts limitations on commercialization of gel-filled microchannel devices. In the common basic buffers, polyacrylamide gels deteriorate with time, becoming negatively charged. Polyacrylamide gels are opaque at the wavelength of the peptide bond (~210 nm), which limits detection methods, especially at the short path lengths in miniature devices. So, for research purposes, slab gels would appear to be with us for the foreseeable future. As indicated, however, in applications where high resolution is not required, miniature devices with or without gels will have a role to play in the future.

There were several presentations on work using traditional proteomics – namely gel electrophoresis and mass spectrometry. These studies employed various 'tricks of the trade' to dig deep into proteomes. Talks commonly employed various separation methods based on solubility, mobility, binding characteristics and density. Popular analytical tools, such as difference gel electrophoresis, isobaric tag for relative and absolute quantitation and western blotting, were utilized, as were novel labeling and analysis techniques.

For example, a total of 1037 membrane proteins (soluble and insoluble) from the thermoacidophilic archaeobacterium *Sulfolobus solfataricus* were found by Trong Khoa Pham from Phillip Wright's group at the University of Sheffield (UK) using iTRAQ tagging. Nancy Kendrick (Kendrick Laboratories, Inc., WI, USA) discussed western blotting approaches in studies of post-translational modifications. Tom Berkelman, from Bio-Rad Laboratories (CA, USA), spoke about the company's ProteoMiner™ protein-enrichment technology for the deep mining of proteomes.

Lydia A Finney (Argonne National Laboratories, IL, USA) has the unique opportunity of being able to routinely use the Advanced Photon Source at Argonne Laboratory for proteomic studies of metalloproteins. Synchrotron x-ray fluorescence is used to locate metal-containing proteins separated in nondenaturing gels. Julie C Liu (Purdue University, IN, USA) explained a method for the fluorescence tagging of newly synthesized proteins in mammalian cells by incorporation of noncanonical amino acid analogs, which are subsequently ligated to fluorescent dyes. Ugur Salli (Pennsylvania State University, PA, USA) developed a procedure for depleting histones from nuclear extracts by sedimentation at pH 4.5. Ke Xia (Rensselear Polytechnic Institute, NY, USA) described a relatively simple method for identifying kinetically stable proteins (i.e., proteins that resist unfolding and maintain the specific conformation important for activity) by running them first in a detergent-free gel and then in one containing sodium dodecyl sulfate.

An interesting microdevice was described by Yu-Wen Huang from Victor Ugas' group at Texas A&M University (TX, USA). It is a platform for the label-free detection of proteins, nucleic acids and other charged analytes. A closely spaced array of individually addressable electrodes is patterned along the floor of a microchannel. The electrode array can be activated to transport charged biomolecules and cause them to accumulate in localized zones. The concentrated biomolecules are visible under white-light illumination, probably because of light scattering from bubbles trapped within the concentrated zones.

Cornelius Ivory's group at Washington State University (DC, USA) is exploring alternative focusing mechanisms (alternative to isoelectric focusing). Bingwen Liu from that group described a novel nonlinear 2D electrophoresis system. With this capillary system, a first-dimension separation by isotachophoresis is followed by an isoelectric-focusing step. Isotachophoresis sharpens protein zones and concentrates low-abundance proteins, making this method ideal for feeding into an isoelectric-focusing step. At the macro level, Jeffrey M Burke from the Ivory group talked about dynamic-field-gradient focusing. This technique does not require analytes to be amphoteric, as in isoelectric focusing, but only that they have differing electrophoretic mobilities. Burke has been able to use this method to remove trace contaminants from desired molecules – an important task in pharmaceutical production.

Dielectrophoresis, a promising way of manipulating cells with nonuniform electric fields, has been receiving attention lately. Kaela M Leonard from Adrienne Minerick's laboratory at Mississippi State University (MS, USA) discussed the one-step dielectrophoretic rupturing of red blood cells with cell contents made available to an integrated diagnostic blood device incorporating separation, purification and analytical steps. Zachary R Gagnon (Notre Dame University, IN, USA) used dielectrophoresis to separate malaria-infected human red blood cells from their healthy counterpart and to separate live from dead yeast cells.

In total, 13 students presented posters on topics that included dielectrophoresis, electrokinetics and gel electrophoresis. Four prizes were awarded. First prize went to Javier L Baylon-Cardiel from Tecnológico de Monterrey (Mexico) for his poster on insulator-based dielectrophoresis. Nan Shi (Texas A&M University) took second prize with a poster on entropic trapping of DNA in gels. Third prize was won by Alice Jernigan from the University of Arkansas (AR, USA) for her poster on characterization of soil microbes by capillary electrophoresis. Finally, Aytug Gencoglu (Mississippi State University) received honorable mention for a poster on platinum electrodes subjected to dielectric fields.

Other highlights of the AES meeting were a field trip to Ian Blair's proteomics facility at the University of Pennsylvania (PA, USA) and a banquet speech by Phillip Westmoreland of the University of Massachusetts (MA, USA) and the US National Science Foundation on prospects for chemical engineering in the next 25 years.

The next AES/AIChE meeting will be held in Nashville (TN, USA), on 9–13 November 2009 [101,102]. Organizers are Anup Singh (Sandia National Laboratories, CA, USA) and Christa Hestekin (University of Arkansas). A full range of topics dealing with electrophoretic separations will be covered. The meeting is open to those interested in seeing state-of-the-art proteomics while, at the same time, learning about new tools that may be on the horizon.

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

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1 American Electrophoresis Society
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