BioMEMS and Electrophoresis in 2006: Review of the 23rd Annual Meeting of the American Electrophoresis Society

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The 23rd Annual Meeting of the American Electrophoresis Society (AES) was held at the San Francisco Hilton in San Francisco, California on 12–17 November 2006. This year's meeting featured a look toward the future, with an emphasis on theoretical and experimental advances in miniaturization of BioMEMS, electrokinetics, and proteomics technologies. A total of 13 sessions accommodating 71 presentations and 18 posters were held in conjunction with the Annual Meeting of the American Institute of Chemical Engineers (AIChE). This review and corresponding special issue of *Biomicrofluidics* provide a sampling of some of the exciting research presented at the conference. © *2007 American Institute of Physics.*
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I. INTRODUCTION

The American Electrophoresis Society (www.aesociety.org) is an organization dedicated to promoting research aimed at advancing fundamental knowledge and developing new technologies in all areas of electrokinetics and electrophoresis.[1] This is the 6th year that AES has organized a program of focused topical symposia devoted to Biological Micro Electro Mechanical Systems (BioMEMS) held in conjunction with the much larger Annual Meeting of the American Institute of Chemical Engineers (AIChE).[2] This union has proven to be highly beneficial for both organizations as research in microfluidics and electrokinetics by chemical engineers has skyrocketed over the last decade. During this time chemical engineers have taken a leading role in research involving microfluidics and electrokinetics, particularly at the biological interface, by adapting their extensive knowledge of transport phenomena to the microscale. By bringing AES's diverse membership consisting of biologists, biochemists, and molecular geneticists from both academia and industry, together with the chemical engineering community, the AES symposia offer a truly unique forum to spur cross-disciplinary interactions, avid discussions, and new scientific collaborations.

The sessions in this year's symposia were organized along two main themes: work focusing on BioMEMS and microfluidics applications, and work focusing on developments in electrokinetics and electrophoresis. Within the BioMEMS and Microfluidics focus, five sessions were held: Biomedical Diagnostics; Sensing, Detection, and Integration; Novel Applications; Proteome Analysis; and Cell and Biomolecule Analysis. Four sessions focused on Advances in Electrokinetics and Electrophoresis including Particles and Biomolecules; DNA Applications; Fundamentals and Advances in Capillary Electrophoresis (CE); and Microdevice Technology for Genomic Analysis. Experts from around the world came to learn from each other and present their progress. Advances in microanalytical systems were featured along with advances in electrokinetics; chemical, electrochemical, and optical in-line sensor technology; and novel low concentration detection in capillary electrophoresis systems. This meeting features some of the most focused programming in the area of electrokinetics for microscale applications.

Abstracts of all talks can be obtained by accessing the AIChE Conferences webpage[2] directly, or through the AES site.[1] Extended abstracts are available for a subset of the contributions and can be obtained by purchasing the proceedings from AIChE. Descriptions of each society, current news, and information on future conferences are available on the respective websites.

II. INTEREST AND INVOLVEMENT OF INDUSTRY

The AES strategically partners itself with industrial researchers. This is evident through the contributions of the industrially-aligned session chairs featuring cutting edge results from industry. These perspectives enhance the breadth of technical content in the meeting and provide unique networking opportunities for attendees. Further, AES is extensively supported by industrial sponsors including CBS Scientific, Danisco Genencor, GE Healthcare, Kendrick Labs, Inc., Nonlinear Dynamics, Proctor & Gamble, Perkin Elmer, and Syngene. This balance between academia and industry is demonstrated in the featured plenary speakers.

III. FEDERAL FUNDING AGENCY INVOLVEMENT

A cornerstone of the 2006 program was funding provided by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) at the National Institutes of Health (NIH) to support 20 graduate student and postdoctoral research presenters. These awards play an instrumental role in helping prepare the next generation of scientists and researchers to tackle problems in cutting edge electrokinetics and biomicrofluidics. To further increase the visibility of these contributors, their papers were highlighted in meeting pamphlets and were the select oral presentations invited to contribute to the poster session. Throughout this meeting review paper, NIH Expense Grant Awardees are identified with an asterisk (*) next to their name.

IV. PLENARY SESSION

The AES Annual Meeting opened with a plenary session highlighting the diverse interests of all members. Both the theoretical and practical development of electrophoretic and electrokinetic technologies were featured, including molecular-scale electrophoresis, electrokinetic phenomena in nanocapillaries, development of commercially available microfluidic chip technologies, and tracking evolution through genome-wide analysis. After opening remarks from the meeting organizers, Professor Paul W. Bohn from the University of Notre Dame spoke on mass-limited chemical analysis at the nanoscale. The emerging area of nanofluidics opens up opportunities and challenges due to small amounts of toxins being detected (femto/picograms in zepto or attoliters of volume). The Bohn group has utilized nanocapillary array membranes to selectively control motion of charged molecules between two crossed channels in a three-dimensional configuration. The phenomena observed are different than that at larger scales because the radius of nanocapillaries are the same order of magnitude as the length of the Debye layer extended out from the charged walls. Controlled nanofluidic mass transfer between the channels is achieved by controlling an applied electrical bias. This impacts the polarity and density of the immobile nanopore surface charge, which differs relative to the microfluidic channels. The result is a switchable fluid volume across the nanocapillary array membrane capable of separating enantiomers. A complete review of this group's findings is included in the AES 2006 special issue.[3] The second plenary speaker, Dr. Robin H. Liu of CombiMatrix Corporation in Mukiteo, WA highlighted one of their products, a microarray-based chip capable of automatic multistage sample processing and fluid handling. The fully integrated DNA analysis device consists of microfluidic plastic cartridges seamlessly integrated with microfluidic components such as electrochemical pumps, bubbling micromixers, and check valves. CombiMatrix has also "developed a unique electrochemical detection based ElectraSense microarray platform, which eliminates the need for an expensive and sensitive laser-based optical system and fluorescent reagents."

Another plenary talk in the BioMEMS area was "UltraFast Electrophoresis at the Nanoscale using Atomic Force Microscopy" by National Academy of Engineering member, Dr. H. Kumar Wickramasinghe, who was at the IBM Almaden Research Center prior to becoming The Henry Samueli Endowed Chair at University of California, Irvine. This work was also featured in the AES Spring 2006 Newsletter.[4] This work demonstrates an innovative adaptation of electrophoresis that involves harnessing an electric field imposed parallel to an atomic force microscope (AFM) tip. The DNA fragments to be separated are first electrokinetically collected at the base of the AFM cantilever, then released by a periodically reversing the electric field applied between the cantilever and substrate. Since the DNA fragments display a size-dependent mobility as they travel along the length of the AFM tip, desired fragment sizes can be transferred from the tip to the substrate by tuning the frequency at which the electric field is reversed. The speed of such manipulations has the potential to allow selective separations that are faster than current capillary electrophoresis systems.

Lawrence I. Grossman from Wayne State University concluded the plenary session with an enthralling talk about the next generation of computational analysis capabilities and their implications in the construction of advanced genomic databases. His group has developed an "on-line, automated analytic tool that (1) extracts orthologous protein coding nucleotide sequences from public databases; (2) generates in-frame multiple alignments, and (3) performs inferential statistical tests of natural selection." The technique was applied to a section of DNA sequences coding for mitochondrial ATP synthase in primates and other mammals. The similarities and differences were compiled and tracked from a molecular evolution perspective. Mutations that were either favorable or unfavorable were tracked through time (by means of aligning with an evolutionary tree). This work reinforces the knowledge that can be obtained on a secondary level from genomic sequencing via electrophoresis.

A. Part I: BioMEMS and microfluidics

1. Biomedical diagnostics

Emerging breakthroughs in BioMEMS and microfluidics were highlighted in four sessions: biomedical diagnostics; sensing, detection, and integration; novel applications; proteome analysis; and cell and biomolecule analysis. Biomedical diagnostics encompassed a wide variety of analytical microdevices focused at novel ways to monitor and screen for medical ailments in a compact, versatile, inexpensive, and rapid format. These devices are made possible by ongoing research in the areas of sample introduction, preparation, electrokinetic transport of biofluids, development of quantitative detection sensors, and the incorporation of genomic and proteomic biomarkers. Contributions to this session featured novel microanalytical tools focused at the cellular and molecular level including development and fabrication of innovative devices; novel biofluid separators and purifiers; nanoviscometers, isotachophoretic applications, polymerase chain reaction (PCR), and electroporation. Specifically Shramik Sengupta* from the Chang group at Notre Dame discussed, "A continuous microfluidic blood/plasma separation unit with electrokinetic stirring and cross-flow." Exciting work on a nanoliter viscometer was presented by Nimisha Srivastava,* a newly graduated member of the Burns' group at the University of Michigan. This fully automated device was calibrated with polymeric fluids alongside biofluids and would be useful for detecting cardiovascular diseases or type 2 diabetes, which are characterized by changes in blood viscosity. Charles Park, from Caliper Life Sciences spoke about a novel application of isotachophoresis, which improved the quality of microchip immunodiagnostic assays. Malgorzata Witek from Soper's group at Louisiana State University featured photoactivated polycarbonate microfluidic devices capable of DNA purification from whole cell lysates. A unique electroporation method utilizing DC fields and constricting channels was explored by Angie Wang* of Purdue University in order to deliver DNA into mammalian cells. Real time chip-based PCR was accomplished via electrochemistry means by I.-Ming Hsing at the Hong Kong University of Science and Technology. This microdevice was touted to have the ability to carry out electrochemistry-based real time PCR, which could rival fluorescence-based chips for point-of-care diagnostic applications.

2. Sensing, detection, and integration

This intriguing session, chaired by Chang Lu and Joseph Irudayaraj, focused on microscale and nanoscale devices for the detection and manipulation of biological cells and molecules. Contributions dealt with micro/nanoscale immunosensors, electrochemical sensors, actuators, and various spectroscopic or separation tools on an integrated microchip format. An overview talk given by Hsueh-Chia Chang on his research group's accomplishments was entitled, "Rapid pathogen detection with integrated AC electrokinetic devices." This work is further featured in a paper in this AES special issue.[5] Due to potential incompatibilities between surfaces intended for micropatterning and the chemical or thermal process steps associated with standard microfabrication, Kyung Eun Sung from the University of Michigan discussed a pattern transfer technique that could even be used to create three-dimensional structures. Nicholas Lynn* from Colorado State University patterned proteins using static microfluidic patterning and flow focused microfluidic patterning; applications include sensing motifs within BioMEMS. Field-effect-transistor flow control and electrostatic response of charged dye molecules were studied in nanofluidic channels by Youn-Jin Oh. Timothy Leong* held the audience mesmerized as he discussed the assembly of nanoliter sized, 3-D metallic containers with controlled surface porosity. The containers were fabricated laying flat on the surface and folded into a three-dimensional cube or other shape using elastic "hinges." Data showing the controlled release of dyes were demonstrated in this work. The final contributor to this session was Devesh Srivastava* who discussed fabrication of biomimetic interfaces that include nanostructured fullerenes and carbon nanotubes in order to tailor performance for limited bioelectronic applications.

3. Novel applications

Additional novel applications in the life sciences were highlighted in this session. For example, Neil Crews* explained their work at the University of Utah involving PCR microchips with two unique characteristics. First, they could perform a 22 cycle amplification in 200 seconds. In addition, they were fabricated with Xurography, which takes less than 45 minutes total processing time. Streamlining DNA analysis using gel preloaded microchips was further explored by Yi-Je Juang at Ohio State. Chang Lu's group presented additional results on the medium osmolarity dependence of their DC electroporation apparatus. A unique contribution by Atul M. Doke involved the use of a CANARY (cellular analysis and notification of antigens risks and yields) biosensor in order to detect pathogens. Of concern was modeling the binding and dissociation rate coefficients by single- or a dual-fractal analysis. Exciting experimental results presented by Diana Hou* showed that pathogens can be rapidly concentrated ($<$15 min) to produce strong surface-enhanced Raman signals from a dilute 0.2 ml sample as featured in a paper in this issue.[5] In order to provide an immunological barrier around transplanted cells, Dawei Luo's work involves cell encapsulation. This encapsulation technique has been optimized using hydrodynamic flows in a microfluidic device.

4. Proteome analysis

Amy E. Herr, Sandia National Labs, and Rajiv Bharadwaj, Caliper, organized a session on proteomic analysis in microfluidic platforms. Microfluidic technology holds the promise of enabling novel, more efficient, and higher throughput proteomic and genomic analyses in a low-power portable format. As products based on microfluidics are introduced commercially, the promise is becoming a reality. Papers on chip-based novel methods for proteomic analysis including sample preparation, electrokinetic approaches in 1-D and 2-D, and microfluidic interfaces with downstream analytical instrumentation spurred interesting discussions in this session. The session started with Bryan R. Fonslow's* (University of Minnesota) talk on microfree flow electrophoresis on a microchip. Optimization of the chip design produced 16 times greater linear velocities. Huanchun Cui* from the Ivory group at Washington State University spoke on a solid-state microvalve they have been perfecting which can reduce dispersion and sample loss in electrokinetic flows on microchips. Additional work was also done simulating and experimentally testing

nonlinear electrophoresis of proteins by the WSU group. This was followed by a theoretical examination of the hydrodynamic effects of channel morphology on electrophoretic transport by Rodrigo Hidalgo. The session closed with Robert Larsen's talk on development of an ELISA-based microblood analyzer to measure cardiac fatty acid binding protein. This could be accomplished in less than 10 min with ample sensitivity for acute myocardial infarction diagnosis.

5. Cell and biomolecule analysis

Electrophoresis continues to be an integral tool for the analysis of biomolecules in both basic biology and medicine due to the potential benefits in therapeutics and drug discovery. The adaptation of this technology to the microfluidic device format to probe chemical and biochemical responses at the cellular and subcellular levels was the focus of this session chaired by Anubhav Tripathi and Joshua I. Molho. An automated cell culturing system was the focus of Yuan Wen's* talk. Nutrient transport issues were addressed via microfluidic operations in order to maintain cells. Robert J. Meagher presented on behalf of Anup Singh's group regarding integrated approaches for purifying proteins between the cell culture and analysis steps. Results were presented on an aqueous two-phase extraction method. Sarah C. Heilshorn has been developing a microfluidic gradient generator that does not permit sheer stress because of that force's adverse effect on culturing primary neurons. Yong Yang demonstrated a novel approach to assembling polymeric micro/nanostructures in an aqueous environment in the presence of cells and biomolecules by using low-pressure carbon dioxide. The behavior of a free-living soil nematode—*C. elegans*—was studied in specially designed microfluidic chips by Hang Lu at GA Tech. The microfluidic platform offers an ideal platform to investigate responses to environmental stimuli under highly-controlled conditions. The session concluding with Paul Takhistov's work at Rutgers examining microelectrode-based systems for cell adhesion detection. This work is particularly useful for *in vivo* monitoring of biofilm properties.

The second half of the AES Symposia was dedicated to presentations on novel research results involving phenomena induced by electric fields. Three sessions were dedicated to subtopics in the broad areas of electrokinetics and electrophoresis including particles and biomolecules; DNA applications; and fundamentals. Capillary electrophoresis and the related microdevice technology utilizing capillary channels were highlighted in a dedicated session. A wide variety of topics were discussed during this portion of the symposia and included microfluidic networks and their applications (mixing, reaction, separations, or transport processes); complex particles and surfaces (nanoparticles, heterogeneous particles, biological cells, soft particles); electrokinetically-directed assembly; electrokinetic effects in nonpolar media; novel applications of electrokinetic phenomena (biosensors, displays, environmental, or chemical assays); and novel measurement techniques (electrophoretic mobility, charge nonuniformity, forces, electroacoustics, electro-optics).

B. Part II: Advances in electrokinetics and electrophoresis

1. Particles and biomolecules

Nimisha Srivastava and Victor Ugaz chaired a session dedicated to electrokinetic techniques for nanoparticle characterization and directed electronics assembly for applications ranging from micropumps/mixers to biosensors and DNA sequencing. The fundamental perspectives were covered by Docoslis and Godoy. The applied perspectives on state of the art electrokinetic techniques were highlighted by Hoggard, Ivory, Dulay, and Minerick. James Hoggard* opened the session by presenting data on dynamic aggregation and separation experiments in multiparticle systems under the influence of low frequency AC fields. Due to the independence of scale of isotachophoresis, it can handle mass loadings as small as picograms and focus pure proteins. Cornelius Ivory discussed theoretical and experimental findings supporting the use of isotachophoresis in multidimensional separations platforms. Maria Dulay from Richard Zare's group at Stanford presented on photopolymerized sol-gels for chemical analysis. This was followed by Adrienne Minerick's talk on targeted rupturing of the pathogenic bacterium *Vibrio parahaemolyticus* in dielectrophoretic fields. Aristides Docoslis spoke on electrokinetics system parameters that most effectively capture

viral particles. Parameters included applied voltage, frequency, medium conductivity, medium permittivity, and electrode spacing and showed that AC fields produce more rapid capture of particles. Jasna Godoy's work in Arce's group utilized a spatial-averaging method in combination with the solute species continuity equation to derive analytical expressions for effective dispersion coefficient and effective convective velocity in electroadvective flows. This work illucidates fundamental forces determining optimal separation times within microcapillary channels.

2. DNA applications

DNA sequencing has long been a grounding pilar of electrokinetic techniques. Victor Ugaz and Jayne Wu chaired this session on DNA related analysis, which continues to play a leading role in this field. Cornelius Ivory opened the session with his group's work into simultaneous 2-D electrofocusing that could one day replace labor intensive 2-D-PAGE (polyacrylamide gel electrophoresis) techniques. Patrick Doyle from MIT spoke about their theoretical investigations into size-separation of large DNA molecules around posts in microchambers. For sufficiently strong impacts, a coiled polymer hooks around the obstacle and unwinds into a hairpin configuration. Microfluidic post arrays were further explored with Kevin Dorfman's (University of Minnesota) analytically solvable continuous-time random walk modelling DNA/post collisions in a moderate electric field. Zheng Chen* from the University of Michigan has been using confocal laser scanning microscopy to investigate electrophoretic migration of DNA in the x, y, and z dimensions in microchannels. Intriguingly, it was observed that DNA migration appears to be preferentially directed toward the walls of the microchannel for fragment sizes above a certain threshold. Nancy Stellwagen's careful work on DNA fragments containing closely spaced A-tracks elucidated that A-tracts preferentially bind monovalent counterions, reducing their effective net charge. On average, the effective charge of each DNA fragment is reduced by approximately one-half charge unit per A-tract. In the concluding talk, Jean-Roland Pascault* presented on using DC induced mixing to enhance DNA hybridizations, which would improve analysis rates in genetic analysis chips.

3. Fundamentals

Electrokinetics involves the use of electrical fields and electrical forces (between surfaces and particles) to produce a motion of particles within either a fluid, porous, or fibrous medium. Within this framework, a detailed analysis of particle-to-particle electrostatic forces, the experimental measurements of their magnitude, and computer-based simulation approaches are relevant for the advancement of processes and technology involving electrokinetic principles. Pedro Arce and Mario Oyanader organized this session that opened with Prakhar Prakash's talk on electro-osmotic pumping. These electro-osmotic pumps were designed using inorganic membranes made of 99.99% silica or alumina; smaller pore sizes were able to produce larger velocities at lower voltages. Jillian Newton spoke about proteomic differences between aggregated and unaggregated bacillus cereus, a gram-positive, toxigenic bacterium, which readily forms biofilms. 2-D electrophoresis, in triplicate with narrow range (pH 4-7) isoelectric focusing strips and 10% SDS-PAGE gels were used to perform the analysis. Dynamic field gradient focusing was scrutinized by Jeffrey Burke* in order to optimize the separation and concentration of charged analytes. Earle Stellwagen used capillary electrophoresis to examine monovalent cations with small nucleotides and single and double-stranded DNA oligomers. Nonlinear mobility plots were presented when the cation was Tris, Li, Na, or K. The authors suggested that this means AMP, ADP, ATP, and double-stranded DNAs bind these cations. Ryan O'Hara systematically probed the role of orthogonal fields in order to effectively improve separations. This theoretical work utilized an area-averaging technique in an electrokinetic Couette-based device. To conclude the session, Debashis Dutta presented his work on electrokinetic transport of charged analytes through nanofluidic channels. The mathematical description of this transport process was based on the Gouy-Chapman picture for the Debye layer around the channel walls.

4. Advances in CE and microdevice technology for genomic analysis

As demonstrated in other AES sessions, microfluidic-based DNA and protein separation systems are beginning to emerge from the research laboratory and appear as commercially available products for use in a variety of genomic analysis applications. If sufficient miniaturization can be achieved, these microfabricated systems will enjoy a tremendous cost advantage over today's conventional macroscale systems, thereby ensuring a central role in future genomic analysis efforts such as the ambitious goal of sequencing a genome for $1,000 or less. Strategies to develop improved sieving media based on a variety of polymeric and nonpolymeric materials incorporating uniform and reproducible microstructures promise to generate tremendous improvements in the achievable level of separation performance. In addition, separation matrices composed of nanofabricated structures constructed directly on the surfaces of silicon, glass, and plastic substrates offer exciting possibilities in terms of exerting precise control over pore size and sieving properties. Malgorzata Witek of LSU organized this session, which took off with Christopher Fredlake's* talk, "How is it possible to sequence 600 bases of DNA in 6.5 minutes? The central role of carefully engineered polymer networks and coatings in microchip electrophoresis." Annelise Barron's group at Northwestern has made significant contributions to the field with carefully engineered polymer and matrix networks for high throughput DNA sequencing. Victor Ugaz then presented his group's work to develop new techniques based on mechanical rheometry, thermal analysis, and electron microscopy to quantify both the average pore size and the pore size distribution in hydrogel networks. These are important parameters that are generally challenging to predict due to relatively complex polymerization kinetics, while conventional experimental efforts to characterize these parameters are hampered by the mechanical fragility of most hydrogels. Robert Meagher, a recent graduate from Barron's group, spoke about End-Labeled Free-Solution Electrophoresis (ELFSE) in which each DNA molecule in a mixture is conjugated to a polymeric "drag-tag" that modifies the properties of the DNA. The featured drag-tags were a significant improvement over previous drag-tags and push ELFSE closer to the theoretically possible rapid separations with long read lengths. Rondedrick Sinville* of Soper's group presented on microchip electrophoretic separations of low abundance mutations, which are masked in normal genomic DNA sequences. The background signals were reduced sufficiently that the mutations can be used as biomarkers for early detection or monitoring of disease progression. High-performance glass capillary electrophoresis microchips were developed by Adam T. Woolley, by using a phase-changing sacrificial layer technique that enables easy solvent bonding of the glass microchips. Lastly, Mario Oyanader spoke about "Optimal separation times with an orthogonal electrical field in a cylindrical capillary."

V. POSTER SESSION

A poster session and reception were also held in order to stimulate further interactions and in-depth discussions among all participants. Original contributions as well as poster versions of select oral presentations were included in the 2006 session. Three experts in the field independently judged the posters and their results compiled. Five awards were given: First Place was to Bryan R. Fonslow* for his work on "Fabrication, optimization, and application of a microfree flow electrophoresis microfluidic chip." Second Place was to Bin Cao* for a well-conducted study on "Proteome analysis of pseudomonas putida during biodegradation of high concentration of benzoate: Activation of the meta pathway and physiological responses." A third place certificate was awarded for "Sequencing 600 Bases of DNA in 6.5 min," an interesting body of work by Chris Fredlake*, under the direction of Annelise Barron. Lastly, two honorable mention awards were earned by Prashant Daggolu* and Diana Hou* for their work on dielectrophoretic blood typing and bioparticle detection by microspiral flow, respectively.

VI. CONCLUSION

The union of the American Electrophoresis Society and the American Institute of Chemical Engineers provides an outstanding example of the benefits of providing a climate conducive toward interdisciplinary interactions in advancing the development of BioMEMS and electrokinetic related technologies. The results of these interactions are evident in a series of Symposia that represent some of the most highly-focused bodies of knowledge in the area of electrokinetics for microscale applications. AES is committed to continuing its efforts to offer future high-quality programming in these areas. Abstracts of all talks mentioned herein are available via AIChE's Conferences webpage[2] directly, or through the AES site.[1] Extended abstracts are available for purchase for a subset of the contributions.

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[1] American Electrophoresis Society website: http://www.aesociety.org/ (viewed 10 March 2007).
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