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BIOINFORMATICS SYMPOSIUM OF THE ANALYTICAL DIVISON OF THE AMERICAN CHEMICAL SOCIETY MEETING

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On March 28, 2000 the Bioinformatics Symposium was held at the ACS National Meeting in San Francisco. In this symposium we brought together analytical chemists who were developing novel techniques to generate information on genomes, proteomes, or cells with informatics experts who were developing data mining and modeling algorithms and software. The goal of the symposium was to highlight the role and opportunity for analytical chemistry research in the informatics revolution that is changing the face of biological research.
The following presentations were given:

- "Trends, opportunities, and challenges in bioinformatics" by J.C. Wooley (UC-San Diego)
- "Integrative Bioinformatics: bridging the chasm between genomics and cell biology" by R.D. Phair (Bioinformatics, Inc.)
- "Profiling signal-transduction networks in single mammaliam cells" by N.L. Allbritton (UC-Irvine)
- "Integrated software tools for functional genomics" by T. Ferrin
- "Bioinformatics in the chemical process industry" by L.D. Rothman (Dow)
- "Past, present, and future of the protein data bank as an enabling resource" by H.M. Berman (Rutgers U.)
- "Analyzing genetic variations by mass spectrometry" by L.M. Smith (U. Wisconsin)
- "Signal transduction in insulin secretion: An opportunity for bioinformatics" by R.T. Kennedy (U. Florida)
- "Integrated view of bioinformatics for both genomics and proteomics" by W.S. Hancock (ThermoFinnigan)

Several themes emerged from this series of talks. The tools for genomics and proteomics are highly generalized and quite sophisticated for analyzing sequence data. Such data/data analysis tools are rapidly becoming an indispensable tool for the pharmaceutical and biotechnology industry. While DNA sequencing technology is now quite robust and well-developed, analysis of genetic variations, proteomes, and cellular biochemistry still requires considerable research to generate information at the level need for a bioinformatics approach. Cellular data requires both temporal and spatial resolution to be of use.

We estimate that over 200 people were in attendance for each talk. Based on the strong attendance throughout the day and the extensive discussions that resulted after each talk, the symposium was considered highly successful.

219th BOOK OF ABSTRACTS

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ACS National Meeting
March 26-30, 2000

ABSTRACTS OF PAPERS

Part 1

219th ACS National Meeting
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March 26-30, 2000

American Chemical Society

DIVISION OF ANALYTICAL CHEMISTRY ABSTRACTS

219th ACS National Meeting

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T. R. Williams, Program Chair

disposability obviates carryover and contamination problems. Applications in drug screening and genetic analysis, where the use of electrophoretic separations is a key to effective performance, will be described.

171.
HIGH-ASPECT RATIO MICROMACHINING IN PLASTICS: A LOGICAL CHOICE FOR THE FABRICATION OF DNA ANALYSIS DEVICES. *Stephen A. Soper, Kevin Kelly, Robin McCarley, Sean Ford, Shize Qi, Scott McWhorter, Gloria Thomas, Suzzane Lassiter, Alyssa Henry, and Yun Wang. Louisiana State University, Baton Rouge, LA 70803, steve.soper@chemserv.chem.lsu.edu*

LIGA micro-machining can be used to produce mold inserts with very high aspect ratios to fabricate microstructures (HARMs) with small dimensions and relatively large heights (or depths). For example, using LIGA, narrow channels (~10-20 mm) with large depths (50-100 mm) can easily be machined to perform fluidic-type functions. In addition, these HARM inserts can be used to produce microchips in various types of plastics using either hot embossing or injection molding. We have initiated work on fabricating microchips in polymethylmethacrylate (PMMA) for electrophoresis-based applications specifically targeted toward analyzing DNAs. Due to the fact that deep channels with narrow widths can be fabricated, fluidic interconnects to the chip can be made using conventional capillary tubes with minimal unswept volumes for convenient sampling from titer wells containing sequencing or genetic samples. In our presentation, we will discuss the fabrication of PMMA microchips using LIGA processing, the assembly of PMMA devices and also, material properties of PMMA. We will also discuss robust surface modification procedures in PMMA to alter the electroosmotic properties of the material. Finally, we will discuss results using multi-channel devices for high throughput sequencing and/or genetic analyses.

172.
POLYMERIC MICROFLUIDIC SYSTEMS WITH INTEGRATED ELECTROCHEMICAL DETECTION FOR DNA ANALYSIS. *Werner G. Kuhr, Sara Brazill, C Brandon Davis, Binayak Roy, and Joan Stuart. Department of Chemistry, University of California, Riverside, CA 92521, fax: 909-787-4713, werner.kuhr@ucr.edu*

A PDMS microfluidic chip has been developed which allows for the direct detection of several distinct DNA targets present in a sample. Electrochemical detection of DNA is accomplished with integrated electrodes in very small volumes. The DNA sample can be labelled with an electroactive tag and separated in a sieving buffer with capillary electrophoresis for DNA sequencing. Alternatively, DNA hybridization probes can be attached in the microchannels on the chip via a biotin/avidin linkage. Following hybridization of the target, an alkaline buffer is introduced to the channel to dehybridize the double-stranded DNA and flush the target downstream to a copper electrode. The dehybridized DNA is then detected electrochemically. Integrating the detector and the sensing probes on the microfluidic chip allows for an inexpensive and easily fabricated biosensor device for the precise recognition and subsequent detection of a specific complimentary DNA target for diagnosis and genetic screening.

173.
MICROSYSTEMS FOR CHEMICAL ANALYSIS. *Scott D. Collins, Carlos Gonzalez, Kin Yan, and Rosemary L. Smith. Department of Electrical Engineering / MicroInstruments and Systems Laboratory, University of California, One Shields Ave, Davis, CA 95616, fax: 530-758-8103, collins@ece.ucdavis.edu*

Presented here is a basic overview of the current state of microsystem development for chemical analysis. More specifically, the overview highlights three specific microsystems recently developed at MISL, and their fabrication, function, characterization, and limitations to chemical analysis will be discussed. The three microsystems include: 1). A surface plasmon resonance microinstrument (SPR). The SPR not only provides generic detection for HPLC or affinity chromatography, but provides simultaneous chemical analysis of the effluent. The small size of the detector, 1cm × 2cm × 0.5cm, also allows use as a stand-alone sensor for remote or biologically hostile areas. 2). A miniature Fourier Transform Spectrometer (FTS) predicated on the Michelson interferometric with a resolution of <0.1cm-1. Because of its small size, 10cm × 5cm × 1.5cm, the FTS is extremely portable and may be used as a automated sensor to monitor virtually any desired set of preprogrammed chemical signatures through the use of standard pattern recognition algorithms or appended to the output of any chemical separation system for analysis. 3). A modular electrophoretic separation microsystem for the massively parallel separation and analysis of combinatorial chemistry products. (http://ece.ucdavis.edu/misl/Homepage.htm).

174.
HPLC COLUMN TECHNOLOGIES IN THE NEW MILLENNIUM. *Ronald Majors, AL*

Abstract text not available.

175.
PROSPECTS IN CAPILLARY-ELECTRAL CHROMATOGRAPHY. *Zsabag Horvath, B/A, MO*

Abstract text not available.

176.
SEPARATING MICROBES IN THE MANNER OF MOLECULES. *Daniel Armstrong, University of Missouri, Rolla, MO 65401, fax: 573-341-6033*

Abstract text not available.

177.
FAST SOLVATING GAS CHROMATOGRAPHY FOR CHIRAL SEPARATION. *Milton Lee, Analytical Chemistry, University of Utah, UT, fax: (801) 378-5474, milton_lee@byu.edu*

Abstract text not available.

178.
PROGRESS AND PROSPECTS FOR SEPARATION OF POLYMER SYSTEMS. *R. Tijssen, University of Amsterdam Netherlands*

Abstract text not available

179.
STRUCTURE IN THE DEVELOPMENT OF AFFINITY CHROMATOGRAPHY. *Robert Wixom, University of Missouri, M121 Med. Sci. Building, Columbia, MO 65212*

Abstract text not available.

180.
TRENDS, OPPORTUNITIES, AND CHALLENGES IN BIOINFORMATICS. *John C. Wooley, Associate Vice Chancellor for Research, University of California, San Diego Supercomputer Center, 9500 Gilman Drive, MC 0505, La Jolla, CA 92093-0505, fax: 858-822-0948, jwooley@ucsd.edu*

In the "sequenced genomes era," often called beyond the genome, extraordinary challenges and opportunities await in determining the chemistry of protein-protein interactions and cellular networks, the architecture of supramolecular structures, and many other research areas necessary to describe the complexity of living systems. Data intensive computing environments and the need to use computer tools to turn biological data into knowledge—one definition of bioinformatics—will underpin future biochemical and biophysical investigations that will begin with the knowledge of the genome sequence for all major organisms used in molecular research, but will need to uncover the chemical mechanisms by which the gene products function. The success of molecular biology in understanding single-gene diseases is "a hard act to follow" as we move toward what appear to more typical multigene traits. What will such data look like? Biological data are characterized by hierarchical complexity and uniqueness (that is, the data are not reducible by symmetric or temporal considerations); this contrasts with the huge but highly redundant data sets from meteorology and astronomy. Due to the nature of the research and of living systems themselves, the database efforts as a whole can not be effectively

coordinated. As a consequence, biological data is also stored, managed, and manipulated as—in effect—a "cottage industry" with no standards of nomenclature or representation routinely used. Providing tools that allow individual users not just to access but to compute on multiple data resources is one of the major challenges of bioinformatics. Today, information science and computational science provide critical tools for biochemistry, from focusing experimental studies to providing discovery tools for insight that otherwise could not be obtained.

181.
INTEGRATIVE BIOINFORMATICS: BRIDGING THE CHASM BETWEEN GENOMICS AND CELL BIOLOGY. *Robert D. Phair, Bioinformatics Services, 12114 Gatewater Drive, Rockville, MD 20854, fax: 413-487-5098 rphair@bioinformaticsservices.com*

Twenty-first century analytical chemistry will produce a tidal wave of experimental data that will swamp our human abilities to comprehend and integrate information. These enormous databases will, however, also contain hidden keys to complex diseases. Bioinformatics aims to provide computational tools for extracting this vital information. Beginning with an overview of bioinformatics from the perspective of 30 years as a bench/computational biologist, I will define integrative bioinformatics as a set of tools for testing modern biology's cellular signaling diagrams by translating them into computer models consisting of large systems of differential equations, and then applying the experimental protocol. In this way we can know with precision what the diagram predicts, and we can compare these predictions to the experimental time-course data. This comparison, with the help of modern optimization techniques, provides a powerful quantitative test of the hypothesis represented by the signaling diagram. My examples will be from cell biology.

182.
PROFILING SIGNAL-TRANSDUCTION NETWORKS IN SINGLE MAMMALIAN CELLS. *Nancy L. Allbritton, Gavin D. Meredith, Christopher E. Sims, and Joseph S. Soughayer. Dept. of Physiology & Biophysics, University of California, Irvine, D380, Medical Sciences I, Center for Biomedical Engineering, Irvine, CA 92697, fax: 949-824-8540, nlallbri@uci.edu*

A central goal of genomics and proteomics is to catalog the biological molecules present in different organisms and cell types under various conditions. A greater challenge for accurate and comprehensive characterization, however, lies in determining the activities and functional relationships of the biological molecules, particularly the enzymes, as they occur within the complex cellular networks that comprise biological systems. To accomplish this task, new technologies must be developed to measure multiple chemical species within intact intracellular networks. We have demonstrated a new method for the simultaneous measurement of the activation of key regulatory enzymes in a single cell. This assay strategy should be broadly applicable to single-cell measurements of a broad range of enzymes, including kinases, phosphatases, proteases, and nucleases. New bioinformatic tools will need to be developed to describe and predict outputs from the signal transduction networks comprised of these enzymes. Multidisciplinary approaches will be required to unravel the complex signaling networks controlling cellular responses.

183.
INTEGRATED SOFTWARE TOOLS FOR FUNCTIONAL GENOMICS. *Thomas Ferrin, Patricia Babbitt, Conrad Huang, and Teri Klein. Computer Graphics Laboratory, University of California, San Francisco, CA 94143-0446, fax: 415-502-1755, tef@cgl.ucsf.edu*

The successes of the genome projects have largely solved the problems of mapping, sequencing and annotation to produce the enormous volumes of information currently available. Now, in the post-genomic era, the tasks are both more difficult and diverse, requiring new theoretical constructs and technologies for turning this information into knowledge. For example, we currently have no unified theory for the prediction of function from sequence or structure. An effective solution to this problem requires the ability to compute with function, which is currently not possible. In recent research work at UCSF, we have begun to address this issue through development of new computational methods for integrating sequence and structural information to enable explicit mapping to function. This work includes designing, building, and integrating computational and visualization tools for constructing and manipulating protein superfamilies. This talk will describe some of these tools and how they might be extended to be useful for the entire genomic space.

184.
BIOINFORMATICS IN THE CHEMICAL-PROCESS INDUSTRY. *L. David Rothman, Dow Chemical Company, 1776 Building 2nd Floor, Midland, MI 48674, fax: 517-638-9707, ldrothman@dow.com*

Advances in analytical chemistry have enabled the production of massive amounts of gene and protein sequence and structure data. Analytical chemistry also provides a means to identify and measure metabolites to aid understanding organism metabolism. The chemical process industry has interest in sequence and metabolism data as a means to develop new products and raw materials. This presentation will discuss the interaction of analytical chemistry and computing science in the generation, management and interpretation of these data.

185.
PAST, PRESENT, AND FUTURE OF THE PROTEIN DATA BANK AS AN ENABLING RESOURCE. *Helen M. Berman[1], John Westbrook[1], Philip Bourne[2], Helge Weissig[2], Gary Gilliland[3], and T. N. Bhat[3]. (1) Department of Chemistry, Rutgers University, 610 Taylor Road, Piscataway, NJ 08854, fax: 732-445-4320, berman@rcsb.rutgers.edu, (2) San Diego Supercomputer Center, University of California, 9500 Gilman Drive, La Jolla, CA 92093, (3) National Institute of Standards and Technology, Gaithersburg, MD 20899*

The Protein Data Bank began as a flat file archive for the storage of information on biological macromolecular structures. As the technology for determining the structures of molecules improved the number of structures increased, as did the demand for information about these structures. Thus, it became imperative to develop a system that allowed for high throughput data processing and versatile access to the primary and derived data. A description of the system that is currently in place will be given as well as examples of the type of research that the PDB has enabled. A vision for the future of the PDB resource and how it is expected to interact with new initiatives in structural bioinformatics will be described.

186.
ANALYZING GENETIC VARIATIONS BY MASS SPECTROMETRY. *Lloyd M. Smith, Department of Chemistry, University of Wisconsin-Madison, 1101 University Avenue, Madison, WI 53706-1396, fax: 608-265-6780, smith@chem.wisc.edu*

In the last decade two powerful new tools for the mass spectrometric analysis of biomolecules have been developed, Matrix-Assisted Laser Desorption Mass Spectrometry (MALDI-MS), and Electrospray Ionization Mass Spectrometry (ESI-MS). The power of these methods lies in their ability to produce and mass analyze intact gas phase ions from very large molecules such as proteins and nucleic acids. The speed, accuracy, and sensitivity of the technologies make them well-suited to address a number of problems in genetic analysis, including the analysis of DNA sequence, genetic variations, and gene expression. Results in these areas will be presented, including recent work in which single nucleotide polymorphisms (SNPs) in genomic DNA may be analyzed without need for a prior PCR amplification step.

187.
SIGNAL TRANSDUCTION IN INSULIN SECRETION: AN OPPORTUNITY FOR BIOINFORMATICS. *Robert T. Kennedy, Chemistry, University of Florida, P.O. Box 117200, Gainesville, FL 32611-7200, rtkenn@chem.ufl.edu*

Defects in insulin secretion are associated with Type II diabetes, therefore a greater understanding of the biochemical mechanisms underlying insulin secretion are of great significance. It is accepted that glucose metabolism by beta-cells of the pancreas is transduced into insulin secretion by a series of biochemical and biophysical events. In this talk, we describe how novel

microsensors, fluorescence microscopy, and gene-knockout technology have been used to unravel some of the chemical events involved in insulin secretion at the single cell level. It is demonstrated that multiple signal transduction pathways may interact resulting in a process that requires extensive use of bioinformatics to develop an appropriate model.

188.
INTEGRATED VIEW OF BIOINFORMATICS FOR BOTH GENOMICS AND PROTEOMICS. *William S. Hancock, Agilent Laboratories, 3500 Deer Creek Road, MS26U-6, Palo Alto, CA 94304-1126, fax: 650-857-2860, william_hancock@agilent.com*

The relationship of functional genomics to proteomics will be a key issue in the post-genome era. Functional genomics will be based on the study of the transcription/translation process and thus is a measure of the functionality of a given genome. The term proteome has been introduced to define the full complement of proteins in a cell and thus requires description of the localization, concentration and multi-subunit associations of each of these proteins. Another requirement is the definition of the post-translational modifications such as glycosylation, phosphorylation and sulfation as well as the incorporation of lipid components. These modifications often play a key role in the activity, localization and turnover of an individual protein species. Such measurements have become even more challenging with the recent revolution in sequencing of the human genome that will result in the discovery of several hundred novel protein sequences of unknown function. Thus the field of proteomics will require the development of a new set of analytical tools that allow the resolution and characterization of complex sets of protein mixtures in a high throughput manner. This presentation will describe the development of new instrumentation aimed at this challenge, such as high efficiency separations coupled with mass spectrometry. The presentation will also focus on strategies for integration of both genomic and proteomic data in the context of the biological system.

189.
CHARACTERIZATION OF MODERN AUTOMOTIVE FINISHES BY FOURIER-TRANSFORM MASS SPECTROMETRY. *William J. Simonsick, Jr, DuPont Performance Coatings, DuPont Marshall Research and Development Laboratory, Marshall R & D Laboratory, 3401 Grays Ferry Ave, Philadelphia, PA 19146, fax: 215-539-6087, william.j.simonsick@usa.dupont.com*

The chemistry of automotive coatings has undergone tremendous changes over the past twenty years in response to environmental pressures to reduce the volatile organic content (VOC) and an increase in consumer expectations for appearance and durability of the finish. Furthermore, the use of organic pigments is increasing in today's coatings due to environmental, health, and durability issues. Significant overlap now exists between the molecular weights of modern coating components and the mass range amenable to Fourier transform mass spectrometry (FTMS). One popular approach to lowering the VOC is the use of high solids (70%) low-molecular-weight (<5000 Daltons) enamels.1 However, structural imperfections in the organic molecules used in high solids formulations have a more profound impact on final properties than do imperfections in their low solids high-molecular-weight predecessors, therefore sophisticated analytical techniques are required. For polymers, soft ionization methods using CO2 laser desorption or electrospray ionization afford both the chain length distribution and the chemical composition at every chain length. Gel permeation chromatography can be coupled to FTMS through an electrospray ionization interface to characterize telechelic polymers.2 Using quadrupolar axialization and collisional cooling, high resolutions are possible for end group determinations. Tandem MS studies performed on polymer molecular ions provide information about the specific architecture and functionality location. Using CO2 laser desorption molecular ions are furnished for organic pigments contained in cross-linked colorcoats.

190.
DETECTION AND CHARACTERIZATION OF INDIVIDUAL SUBMICRON PARTICLES BY LASER MASS SPECTROMETRY. *William D. Reents, Zhaozhu Ge, J. Eric Bower, Mark Morris, and Sanjay Patel. Bell Labs, Lucent Technologies, Murray Hill, NJ 07974*

Real-time detection and elemental characterization of particles using a single particle analyzer, the Particle Blaster, is described. This technique contrasts with typical off-line elemental analyses which provide results after a significant time lag, thus losing real time feedback or short term changes in particle characteristics. Ions are produced from individual particles by laser atomization/ ionization and then analyzed with a time-of-flight mass spectrometer. The ion/mass signals provide information on the complete elemental composition of each particle as well as the particle's size. This technique has been applied to detection of particles in a semiconductor process tool under normal operating conditions (plasma on, 8 mTorr pressure) as well as preformed particles (silica, alumina, polystyrene) in aqueous solutions. Both major and minor elements are detected in each particle, typically to 100 ppm levels.

191.
MEASURING ADSORPTION AND MONOLAYER FORMATION AT LIQUID INTERFACES BY VIBRATIONAL SUM-FREQUENCY SPECTROSCOPY. *Geraldine L. Richmond, Dept. of Chemistry, University of Oregon, Eugene, OR 97403, fax: 541-346-5859*

Using vibrational spectroscopy to study adsorption at liquid surfaces is challenging, particularly if one wants to measure the surface properties with monolayer sensitivity. Nevertheless such measurements are important as liquid/air and liquid/liquid interfaces play a central role in a wide variety of physical, chemical and biological processes in our everyday lives. In this talk I will summarize some of our recent experiments that measure the vibrational spectroscopy of surface molecules at air/water and organic/water interfaces during monolayer formation. The spectroscopic technique employed in making these measurements is vibrational sum frequency spectroscopy (VSFS). The talk will summarize recent results that we have obtained in measuring the molecular structure of surfactants at liquid/air and liquid/liquid interfaces and the accompanying change in hydrogen bonding of water in the surface region. All of the studies described provide unique information about these interfaces, factors that control adsorption and monolayer formation and differences between the structure and adsorption at air/water and organic/water interfaces.

192.
USE OF MESOPOROUS SILICA IN CHIRAL HPLC. *Christopher C. Landry, Andrew G. Eklund, Sara T. Jull, and Karl W. Gallis. Department of Chemistry, University of Vermont, Cook Physical Sciences Building, Burlington, VT 05405, cclandry@zoo.uvm.edu*

Porous silica is commonly used as a matrix for chromatographic separations. The surface areas of commercially available chromatographic grade silicas are generally less than 500 m^2/g. Mesoporous silica, which can have a surface area in excess of 1500 m^2/g, is expected to provide superior separating ability. Mesoporous silica is prepared by a micelle-templated sol-gel process which produces pore diameters adjustable between 20 and 300 Å with narrow pore size distribution. The mesoporous surface can be modified by bonding various organic groups to the surface to affect separation of various species. We have performed achiral separations using a variety of mesoporous stationary phases, with excellent results in terms of resolution and efficiency. Commercially available chiral stationary phases (CSPs) often are expensive, and are not always effective in separating enantiomeric mixtures. In this investigation, a variety of CSPs using mesoporous silica were developed. Several β-cyclodextrin-bonded CSPs were shown to effectively separate enantiomeric mixtures of amines as well as other molecules.

193.
GOLD PARTICLES AS TEMPLATES FOR THE SYNTHESIS OF HOLLOW POLYMER CAPSULES: CONTROL OF CAPSULE DIMENSIONS AND GUEST ENCAPSULATION. *Stella M Marinakos and Daniel L Feldheim. Department of Chemistry, North Carolina State University, Campus Box 8204, Raleigh, NC 27695-8204, fax: 919-515-8909, emmarina@eos.ncsu.edu*

Colloidal gold is used as a template for synthesizing hollow poly(pyrrole) and poly(N-methylpyrrole) nanocapsules with excellent control over shell thickness and core diameter. Diffusion rates of the gold etch solution [0.1M KCN/ 0.001M $K_3Fe(CN)_6$] were found to depend on the oxidation state of the polymer. The gold particle is also shown to be useful in delivering molecules into the core of the capsule, allowing this procedure to be used as a method of encapsulation.