

14th International Conference

Biodetection Technologies 2009

Technological Responses to
Biological Threats

June 25-26, 2009
Baltimore, MD USA

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14th International Conference

Biodetection Technologies 2009

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June 25-26, 2009

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Biodetection Technologies 2009

CONFERENCE AGENDA

June 25-26, 2009

Thursday, June 25, 2009

8:00 *Registration, Exhibit Viewing/Poster Setup, Coffee and Pastries*

8:50 **Organizer's Welcome and Opening Remarks**

9:00 **KEY NOTE ADDRESS**

Ultra-Rapid, Low-Complexity Bio-Analyzers

Dennis L. Polla, PhD, Program Manager, Defense Advanced Research Projects Agency (DARPA);

John C. Carrano, PhD, President, Carrano Consulting, LLC; and

Susan Barker, PhD, Senior Scientist, System Planning Corporation

The strategic landscape for biological testing is undergoing a truly disruptive transformation spanning a broad and diverse spectrum of applications from testing in the physician's office to screening for diseases in the developing world to environmental sensing of acts of bio-terrorism. The principal drivers for this dramatic paradigm shift are reducing costs, lowering mortality rates, reducing morbidity, and improving national security. In vitro diagnostics testing is largely done today at major, centralized laboratories owing to the efficiencies associated with high-throughput, semi-automated testing. While the current model affords some pragmatic benefits, the future trends call for a radically new diagnostic solution that is portable, multiplexed, fast, inexpensive, and yet still clinically accurate. We believe the single greatest challenge for realizing pragmatic biological sensors and diagnostic instruments is the development of efficient (in terms of SWAP-C), safe, and simple technologies for the acquisition, preparation, and processing of samples. We refer to this goal as "automation for portability" or as "front-end automation". Up till now, much effort, expense, and research has gone into the development of exciting, novel new detection modalities, but this is only one part of the overall total system solution; largely neglected has been the automation of the front-end. In this talk we will present concepts for automation for portability that DARPA would like to develop in collaboration with industry, academia, and national laboratories.

9:30 **Overview of Biological Simulants Used For Biodetection Trials & Evaluations**

Guilhem Larigauderie, PhD, Technical Expert in Biology, DGA/French Ministry of Defense, France

The comparison of existing and emerging biodefense technologies and systems requires performing trials with calibrated, non-hazardous and easily manipulated simulant bio-agents. Relevant surrogates for bacteria, viruses and toxins have to be used to cover the biological diversity, including the physical properties of biothreat agents. We developed molecular tools to detect and quantify a new harmlessness model, the *Cydia pomonella* granulovirus (baculovirus), simulating large enveloped and double-stranded DNA poxviruses.

10:00 **Single Domain Antibodies for Biothreat Detection**

George Anderson, PhD, Research Chemist, Center for Bio/Molecular Science and Engineering, U.S. Naval Research Laboratory

Single domain antibodies (sdAb) are heavy chain only variable domains cloned from camelids. We have isolated and characterized sdAb towards biothreat agents including *ricin* and *botulinum A* complex. They are able to bind target with both high affinity and specificity. Most are capable of refolding after heat denaturation, recovering their secondary structure and binding activity. They function well as capture and tracer reagents in both ELISA and fluid array immunoassays.

10:30 *Networking Refreshment Break, Exhibit/Poster Viewing*

USE OF NANOTECHNOLOGY

11:00 **Portable Electronic Nucleic Acid Detection**

Michael Connolly, PhD, Integrated Nano-Technologies, LLC

INT is developing a field portable system for rapid and accurate identification of infectious agents. The system is a novel sensor which electronically detects nucleic acid sequences in a sample. No amplification is required. INT's approach utilizes nano-scale metallized DNA wires to provide a sensor that can detect a single molecule. A microfluidic system has been developed to deliver all reagents to the sensor in a small manufacturable disposable cartridge.

11:30 **A Nanofluidic System for Rapid, Quantitative Multi-Pathogen Detection in One or More Samples Simultaneously**

Colin Brenan, PhD, CTO and Senior Vice President, BioTrove Inc.

We have developed a nanofluidic system (OpenArray®) combining the precision and accuracy of real-time quantitative PCR (qPCR) in a high density array format capable of rapid, quantitative detection of multiple pathogens in one or more specimens simultaneously. The functional independence of each assay in the panel simplifies assay design and validation and provides a high degree of flexibility in selecting the assay number that provides optimal information content. System miniaturization and passive nanofluidics simplifies user workflow and makes for a robust, reliable and reproducible detection system. We will report on the system design, its function and its application to bacterial and viral identification and quantification in environmental and clinical specimens.

12:00 **Dynamically Adjustable Nanopores for Nanoparticle Detection: Virology and Biosensing Applications**

Hans van der Voorn, Executive Chairman, Izon Science Ltd, New Zealand

Izon has patented a resizable nanopore technology for rapid

Biodetection Technologies 2009

CONFERENCE AGENDA

June 25-26, 2009

nanoparticle detection and analysis. The nanopores can be dynamically adjusted in real time enabling optimization of the aperture size for the particle set of interest. A significant application of this technology platform is in the field of virology. Material will be presented showing the application of this technology for detection of a range of nano-sized particles, both biological and synthetic, from 800nm to 12nm. Current developments of the Izon instrumentation will be described including the ability to accurately quantify viruses, and potential characterisation and identification of virus particles through size and shape attributes. Applications utilising antibody conjugated nanoparticles to identify viruses, and other approaches, will also be discussed.

12:30 *Luncheon Sponsored by Knowledge Foundation Technology Commercialization Alliance Membership Program*

POINT-OF-CARE DIAGNOSTICS

2:00 **A Handheld Confocal Fluorescence Scanner for Sensitive Point of Care Diagnostics**

Reinhold Wimberger-Friedl, PhD, Principal Scientist, Dept Molecular Diagnostics, Philips Research, The Netherlands

At Philips Research we have developed a handheld confocal scanner for sensitive fluorescence detection. The system is based on low cost optical components derived from optical storage technology. It has autofocus capabilities and single fluorophore sensitivity. Confocal scanning allows real time detection of the binding of labeled biomolecules due to background suppression. Sub-picomolar sensitivity is demonstrated with several target proteins, such as CRP and TNI under non optimized assay conditions in a few microliters of *serum*. The scanning autofocus system allows flexible multiplexing and does not require alignment. For point of care immunoassays we have developed an all plastic, capillary driven microfluidic cartridge with on-board reagents. In this way we can provide a low cost, versatile and robust platform for the diagnostic market.

2:30 **Development of the BioSeeq-Clinical System, Providing "Sample in, answer out" PCR Testing Capability for Point-of-Care Diagnosis**

John W. Czajka, PhD, MBA, Director Technology Development, Smiths Detection Diagnostics

Smiths Detection Diagnostics is currently developing the BioSeeq-Clinical System for the identification of hospital associated infections. The system utilizes a single-use sample preparation consumable that is driven by the BioSeeq instrument, providing true "Sample in, answer out" capability. A highly multiplexed LATE-PCR assay for MRSA is currently being developed and evaluated for use with the BioSeeq-Clinical System for pre-admission screening in hospitals.

3:00 **Intelligent Wound Management: In-situ Sensors to Detect Infection**
Duncan Sharp, PhD, Research Associate, Nottingham Trent University, United Kingdom

The development of a prototype sensor suitable for assessing wound integrity to alert the patient or clinicians to the onset of bacterial colonization by key organisms is described. Based on a multilayer laminate fabrication process, mass production of identical yet inherently disposable sensors suitable for direct incorporation within conventional wound dressings can be readily achieved. The design characteristics and application to the intelligent management of problematic burn wounds are described.

3:30 *Networking Refreshment Break, Exhibit/Poster Viewing*

4:00 **A Novel CMOS Biosensor Technology for Measuring Affinity Reactions**

Filip Frederix, PhD, Program Manager Biosensors, NXP, Belgium

Novel/complex biosensor technologies often lack the ability to be produced at low cost which hampers their commercialization changes. Classical diagnostic technologies (e.g. ELISA) use low cost plastic consumables and reagents. However, such technologies do not give an answer to the needs of the future in-vitro diagnostics with sensitive, multi-parameter point-of-care systems. Therefore, NXP developed a novel electronic biosensor technology, based on copper nanoelectrodes, which can be mass produced by standard CMOS processing at low cost. This biosensor can ultimately lead to massive parallel single molecule detection.

4:30 **Aluminum Oxide Based Sensors for Medical Applications**

Luis Moreno-Hagelsieb, PhD, Researcher, SENSOI, Université Catholique de Louvain, Belgium

In medical applications, simple, low cost and low consumption devices are required. In our laboratory aluminum oxide interdigitated capacitors have been developed and successfully tested on DNA hybridization test on HIV and cancer (TP-53), as well as on bacteria and humidity or condensation (coupled to a wireless breathing monitoring system), all of them showing comparable results to the state of the art using existing standard biological protocols procedures that open new opportunities for Medical Applications.

5:00 **Selected Oral Poster Highlights/Concluding Discussion**

5:30 *End of Day One*

Biodetection Technologies 2009

CONFERENCE AGENDA

June 25-26, 2009

Friday, June 26, 2009

8:15 *Exhibit Viewing/Poster Setup, Coffee and Pastries*

BIOINFORMATICS FOR BIODEFENSE

9:00 **RIGEL: A Bioinformatics System for Biodefense**

Willy A. Valdivia-Granda, PhD, CEO, Orion Integrated Biosciences Inc.

In this talk we present an integrated approach for the development of standardized and interoperable diagnostics, detection and surveillance systems. Our approach in the recognition of bacterial and viral biothreats will be discussed.

OPTICS BASED SINGLE MOLECULE DETECTION

9:30 **Role of Non-Linear Optics in Meeting the Challenges of Near-Single Molecule/Organism Detection**

H. James Harmon, PhD, Professor of Physics; Director, Center for Sensors and Sensor Technology, Oklahoma State University

The ability to detect chem/bio analytes at sub-pM levels in 10 seconds or less utilizes several aspects of "non-linear optics" and/or quantum effects including: (1) Multiple photon absorbance; (2) 'Up-conversion'; (3) Minimizing self-quenching; (4) Absorbance enhancement of evanescent wave transmission in waveguides; (5) Alteration of analyte symmetry and extinction coefficient; (6) Alteration of excited state lifetimes; (7) Quantum confinement (not limited to just 'quantum dots'); and (8) Multiple exciton generation (carrier multiplication). Understanding the role of these aspects is crucial to decreasing the LOD of detection using any form of EM radiation and can increase sensitivity by several orders of magnitude compared to "linear optic" effects.

10:00 **Optical Mapping: A Novel Single Molecule System for Microbial Comparative Genomics and Identification**

Trevor Wagner, PhD, Field Applications Scientist, OpGen, Inc.

Rapid identification of bacteria is important to biodefense. Current methods typically require pure cultures thereby lengthening the time to identification or requiring prior knowledge of the organism to choose the appropriate test. In contrast, Optical Mapping can provide rapid identification of organisms in mixed cultures without prior information or PCR amplification. Optical Mapping is a *de novo* technology allowing for the detection of genetic variation including rearrangements, indels, and other genetic modifications across the entire genome not detected by other methods.

10:30 *Networking Refreshment Break, Exhibit/Poster Viewing*

FLUORESCENCE BASED DETECTION

11:00 **The Veritide Ceeker™: A Close Look at the Function and Performance of this Handheld Bacterial Spore Detector**

Lou Reinisch, PhD, Principal Scientist, Veritide Ltd., New Zealand

Veritide Limited has created a portable, battery operated spore detector that uses a combination of photochemistry and fluorescence to non-destructively determine if a white powder contains bacterial spores. This detector, the Ceeker™, is simple to use, requires less than 10 minutes to identify a sample and can be fully decontaminated. There are hundreds of white powders that have been used as hoax substances for bacterial spores. We have tested the Ceeker™ on more than 150 different hoax substances multiple times and find that it has impressive sensitivity (fraction of true positives accurately identified) and specificity (fraction of the true negatives accurately identified) for bacterial spores. The Ceeker™ identifies the dipicolinic acid that is unique to bacterial spores to discriminate against a wide array of hoax compounds. This presentation will discuss the theory of operation for the Ceeker™, how the detector is used, and the results of several thousands of tests.

11:30 **Detection of Airborne Bio-Particles Using 2P Intrinsic Fluorescence and Aerodynamic Diameter**

Jorge E. Gonzalez, PhD, President, Caribbean Biotechnologies, Inc.

We describe the development of an airborne bio-particles monitoring technique and system for real time field detection and identification using 2-photon intrinsic fluorescence excitation combined with the aerodynamic diameter of airborne particles. The intrinsic fluorescence of environmental bioaerosols such as bacteria, fungus, and viruses provide a high degree of specificity given the high energy levels required to induce fluorescence with 2-photons, and the required degree of beam focus of the light source.

ELECTROACTIVE POLYMERS BASED INTELLIGENT SENSORS

12:00 **Intelligent Sensors for Pathogen Detection and Identification**

Yanxiu Zhou, PhD, President, Y&Z Innovation LLC; and

Kalle Levon, PhD, Professor, Dept of Chemical and Biological Sciences, Polytechnic Institute of New York University

The human system interacts with the environment via a range of polymeric sensors that allow us to smell, see, taste, touch and hear by converting physical and chemical stimuli into electric impulses that transmit along the nervous system.

Biodetection Technologies 2009

June 25-26, 2009

CONFERENCE AGENDA

Conducting polymers are good candidates for such purpose that their electroactive polymer chains can be used to immobilize recognition ligands to interact with target analytes and transfer the recognition process into electrical signal, and no labeling process needed. Here we mimic nature by attaching pathogen recognition elements onto electroactive polyaniline backbone to develop intelligent sensors to identify and detect biological warfare agent: *anthracis* spores. The pathogen recognition elements, such as peptides, were covalently bond to polyaniline chain and formed an interpolymer. The resulting intelligent sensor system has been used to real-time detect bacterial spores with high sensitivity and low limit of detection, it can be used to detect a few spores within minutes.

12:30 *Lunch on Your Own*

WATER PROTECTION AND MONITORING APPLICATIONS

2:00 **Automated Real-Time On-Line Measurement of Bacteria in Water Using Multi-Angle Light Scattering Techniques**

John A. Adams, PhD, Chief Scientist Sensor Products, JMAR Technologies, Inc.

JMAR's BioSentry water-monitoring system utilizes multi-angle light scattering (MALS) to detect and classify microorganisms through continuous slip-stream analysis. MALS enables the generation of a species-specific light-scattering pattern. As a microbe passes through the detection area, the pattern is captured by a photo detector and classified using proprietary algorithms (based on size, shape and morphology) in real-time. BioSentry is able to detect the presence of microbes (e.g. *E. coli*) down to 600 organisms/ml, compared with conventional water sensors (e.g. turbidity, particle counters, chlorine residual measurements) which had a detection minimum of 25,000 organisms/ml.

2:30 **Ultrasensitive Biosensor for Monitoring of Trace Amounts of Biological Macromolecules**

Bo Mattiasson, PhD, Professor, Dept of Biotechnology, Lund University, Sweden

Design of ultrasensitive assays makes it possible to analyse samples with very low content of the analyte. Often one does not need the sensitivity per se, but due to the good sensitivity it is possible to dilute the sample thereby reducing matrix-effects on the analysis. A capacitive biosensor has been developed that has a sensitivity surpassing those of most other biosensors. Thus, *cholera* toxin has been detected in buffer solutions at concentrations in the range 10^{-19} to 10^{-20} moles per liter. When spiking a natural water from a local river with a lot of suspended material, it was possible to quantify the toxin down to 10^{-18} moles per liter. The assay is relatively simple. It has been used for detection of a range of macromolecules, e.g. bacterial toxins and DNA. Quantification of virus particles is ongoing. Most of the assays have been on discrete samples, but continuous monitoring is also possible. When the sensor surface is saturated, one will then have to

regenerate it. This can be done by dissociating the bound material from the sensor surface, or by using disposable electrodes. The capacitive biosensor serves the need to detect primary indicators of presence of bacteria. PCR will be used to demonstrate the presence by quantifying the DNA. This means that these two techniques complement each other. The biosensor in its present configuration is of a typical lab-design, but a new version being developed is more adopted to field applications.

3:00 **Early Warning of Microbiological Contamination of Water**

Yuliya Shakalisava, PhD, Research Fellow, Chemical Sciences - Adaptive Sensors Group, Dublin City University, Ireland

Microbial contamination of public water resources represents serious health risk. Monitoring of microbial water quality rely on culture growth methods and require at least 18-24 hours for analysis. This is not acceptable in cases where immediate action has to be taken. The presented work evaluates several strategies for utilizing surrogate measurements of water quality, such as turbidity, particle size and video sensing, as early warning systems for microbiological contamination, using parallel cell-based measurements for reference measurements. Results from initial field studies will be presented, along with a discussion on potential strategies for maximizing the usefulness of the surrogate approaches, in particular, through minimization of false positives and false negatives.

3:30 *Networking Refreshment Break, Exhibit/Poster Viewing*

ISSUES OF FIELD TESTING AND RESULTS INTERPRETATION

3:45 **Five Questions to Answer before Implementing Biological Field Testing**
Speaker to be confirmed

Following the Anthrax Letters, a demand for field identification of biological agents led to a plethora of commercially developed assays to fulfill this perceived need. This presentation will outline questions participants should ask before deciding to implement field tests to detect or identify biological agents. Using the tools presented, participants can develop answers enabling them to determine if a field test is likely to be reliable and appropriately useful, justify costly investments, integrate field decisions concerning when and when not to do field testing, coordinate field testing with outside agency requirements, and provide a sound basis for interpreting results.

4:15 **Selected Oral Poster Highlights/Concluding Discussion**

4:45 **Summary, Concluding Remarks**

5:00 *End of Conference*

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