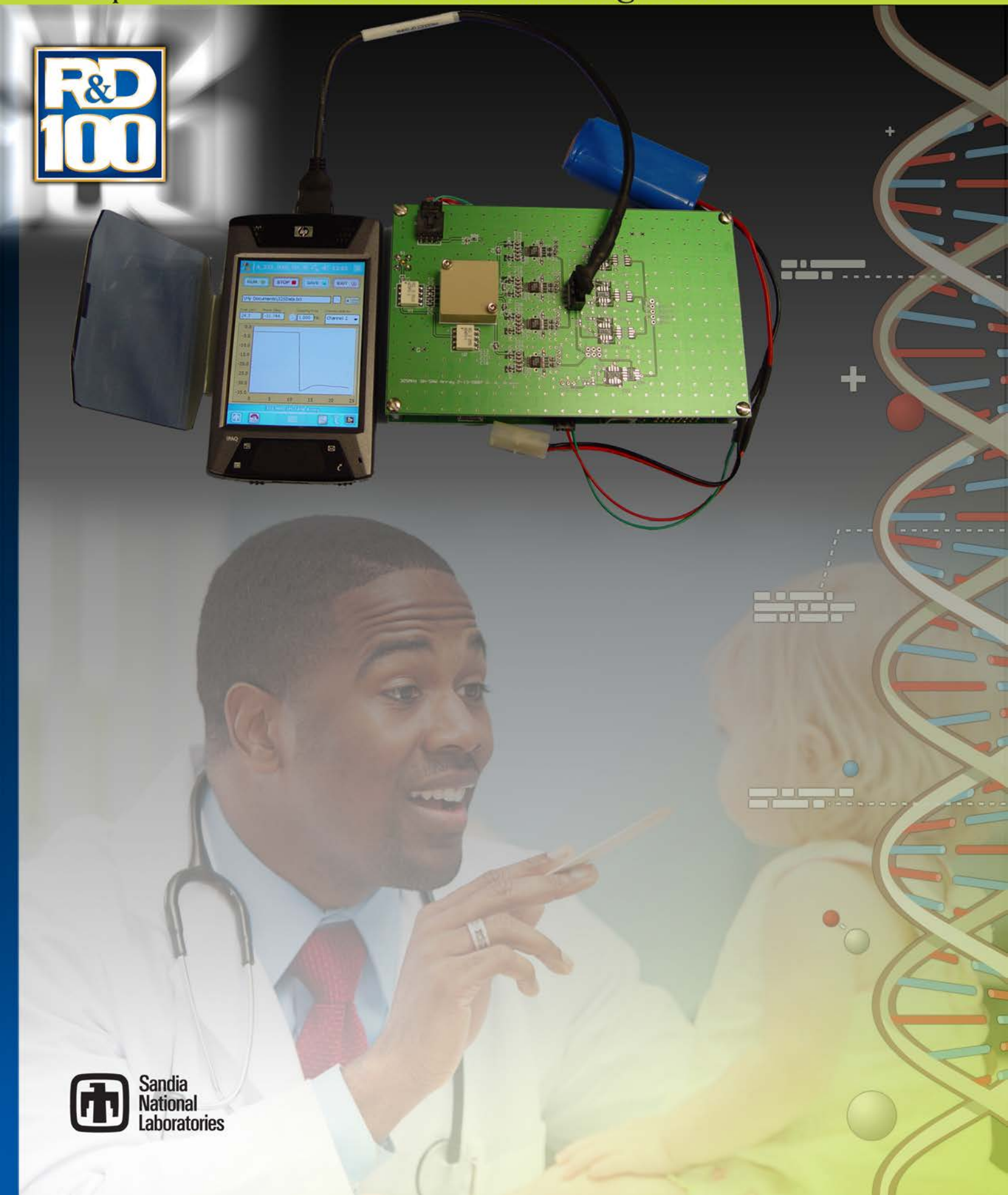
Acoustic Wave Biosensors 2010

Rapid Point-of-Care Medical Diagnostics



Sandia National Laboratories

Acoustic Wave Biosensors
Rapid Point-of-Care Medical Diagnostics

2010
R&D 100 Entry

Submitting Organization

Sandia National Laboratories
P.O. Box 5800
Albuquerque, NM 87185

Susan Brozik
Address: P.O. Box 5800, MS 0892
City/State: Albuquerque, NM
Zip/Postal Code: 87185
Country: USA
Phone: 505-844-5105
Fax: 505-845-8161
smbrozi@sandia.gov

Contact Person

Glenn Kubiak
Sandia National Laboratories
Director, Biological and Materials Science Center
Address: 7011 East Avenue, MS 9405
City/State: Livermore, CA
Zip/Postal Code: 94551
Country: USA
Phone: 925-294-3375
Fax: 925-294-3403
Email: **kubiak@sandia.gov**

Joint Entry

University of New Mexico Health Sciences Center
Address: 1 University of New Mexico
City/State: Albuquerque, NM
Zip/Postal Code: 87131
Country: USA
Contact Name: Richard Larson, MD, PhD
Phone: 505-272-6950
Fax: 505-272-5186
rlarson@salud.unm.edu

Product Name

Acoustic Wave Biosensors for Rapid Point-of-Care Medical Diagnostics

"The collaborative partnership of UNM and Sandia National Laboratories made the development of this sensor possible."

–Peter F. Bythrow, PhD
National MASINT Management Office
Defense Intelligence Agency

Acoustic Wave Biosensors
Rapid Point-of-Care Medical Diagnostics

2010

Brief Description

This technology is a handheld instrument that performs rapid, point-of-care medical diagnostic analyses of viruses, proteins, bacteria, and DNA with little or no sample preparation.

Product First Marketed or Available for Order

This technology became available for licensing in January 2009.

Inventors or Principal Developers

Developer Name: Susan Brozik, PhD
Position: Principal Member of Technical Staff
Organization: Sandia National Laboratories
Address: P.O. Box 5800, MS 0892
City/State: Albuquerque, NM
Zip/Postal Code: 87185
Country: USA
Phone: 505-844-5105
Fax: 505-845-8161
Email: smbrozi@sandia.gov

Developer Name: Darren Branch, PhD
Position: Principal Member of Technical Staff
Organization: Sandia National Laboratories
Address: P.O. Box 5800, MS 1425
City/State: Albuquerque, NM
Zip/Postal Code: 87185
Country: USA
Phone: 505-284-5843
Fax: 505-844-1198
Email: dwbranc@sandia.gov

Developer Name: David Wheeler, PhD
Position: Principal Member of Technical Staff
Organization: Sandia National Laboratories
Address: P.O. Box 5800, MS 0892
City/State: Albuquerque, NM
Zip/Postal Code: 87185
Country: USA
Phone: 505-844-6631
Fax: 505-845-8161
Email: drwheel@sandia.gov

Developer Name: Thayne Edwards, PhD
Position: Senior Member of Technical Staff
Organization: Sandia National Laboratories
Address: P.O. Box 5800, MS 0892
City/State: Albuquerque, NM
Zip/Postal Code: 87185
Country: USA
Phone: 505-845-0467
Fax: 505-845-8161
Email: tledwar@sandia.gov

Developer Name: Richard Larson, MD, PhD
Position: Vice President for Translational Research, Sr. Associate Dean for Research
Organization: UNM Health Science Center
Address: 1 University of New Mexico, MSC08 4640
City/State: Albuquerque, NM
Zip/Postal Code: 87131
Country: USA
Phone: 505-272-6950
Fax: 505-272-5186
Email: rlarson@salud.unm.edu

Developer Name: Brian Hjelle, MD, PhD
Position: Professor, School of Medicine, Pathology Department
Organization: UNM Health Sciences Center
Address: 1 University of New Mexico, MSC08 4640
City/State: Albuquerque, NM
Zip/Postal Code: 87131
Country: USA
Phone: 505-272-4814
Fax: 505-272-5186
Email: bhjelle@salud.unm.edu

Developer Name: David Brown, MS
Position: Health Sciences Research Specialist, School of Medicine, Pathology Department
Organization: UNM Health Sciences Center
Address: 1 University of New Mexico, MSC08 4640
City/State: Albuquerque, NM
Zip/Postal Code: 87131
Country: USA
Phone: 505-272-3506
Fax: 505-272-5186
Email: dcbrown@salud.unm.edu

Developer Name: Pam Hall, PhD
Position: Research Assistant Professor, Molecular Genetics Microbiology
Organization: UNM Health Sciences Center
Address: 1 University of New Mexico, MSC08 4660
City/State: Albuquerque, NM
Zip/Postal Code: 87131
Country: USA
Phone: 505-272-4210
Fax: 505-272-5186
Email: phall@salud.unm.edu

Acoustic Wave Biosensors
Rapid Point-of-Care Medical Diagnostics

2010

Developer Name: Marco Bisoffi, PhD
Position: Assistant Professor: Biochemistry Molecular Biology
Organization: UNM Health Sciences Center
Address: 1 University of New Mexico, MSC08 4670
City/State: Albuquerque, NM
Zip/Postal Code: 87131
Country: USA
Phone: 505 272-8157
Fax: 505-272-5186
Email: mbisoffi@salud.unm.edu

Product Price

Sandia National Laboratories (Sandia) and the University of New Mexico Health Sciences Center (UNM HSC) have entered into an agreement with Adaptive Methods, Inc., to grant the latter an exclusive license in the subject technology. Led by Adaptive Methods, Inc., the three organizations plan to commercialize the technology into a handheld device utilizing single-use disposable sensors, suitable for operation in a physician's office.

Anticipated pricing:

- Under $1000 for the base unit with standard Laptop/Desktop/PC interface and application software.
- Less than $50 per disposable sensor (test).

Patents or Patents Pending

US Patent Application #12/069284, February 8, 2008, DETECTION OF BIOAGENTS USING A SHEAR HORIZONTAL SURFACE ACOUSTIC WAVE BIOSENSOR, February 8, 2008, Larson, Hjelle, Hall, Brown, Bisoffi, Brozik, Branch, Edwards, and Wheeler.

Sandia National Laboratories

UNM | Health Sciences Center

Adaptive Methods

Acoustic Wave Biosensors
Rapid Point-of-Care Medical Diagnostics

2010

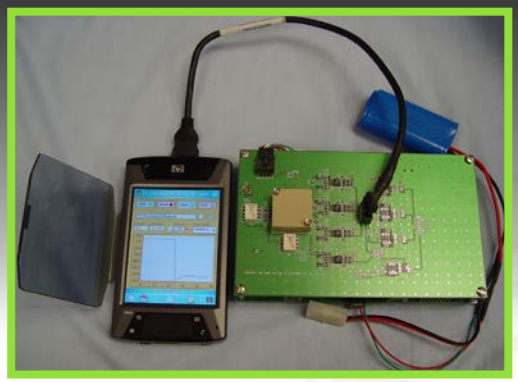


Figure 1: Acoustic wave biosensor instrument with PDA controller and rechargeable battery. Sensor arrays fit in the tan enclosure on the circuit board.

Product's Primary Function

What does it do? How does it do it?

We have developed a handheld, battery-powered, portable detection system that is capable of multiplex identification of a wide range of medically relevant pathogens and their biomolecular signatures—viruses, bacteria, proteins, and DNA—at clinically relevant levels. This detection occurs within minutes, not hours, at the point of care, whether that care is in a physician's office, a hospital bed, or at the scene of a biodefense or biomedical emergency. The Acoustic Wave Biosensor provides fast, low-cost diagnostic results with as good or better sensitivity than traditional techniques.

The technology is extremely versatile, useful in both biodefense applications and biomedical diagnostics. This system is capable of detecting biological pathogens in complex, real-world environmental samples such as air, water, food, and soil. The detection system employs Sandia's shear horizontal surface acoustic wave (SH-SAW) biosensor array functionalized with selective ligands—antibodies, peptides, or single-strand DNA, depending on the application. The SH-SAW sensor array acts as a miniature analytical balance, weighing the amount of pathogen bound to its surface by these ligands. One can think of the SH-SAW sensor as a spring with a small weight bouncing at one end, with the ligands serving as an adhesive layer covering the weight. As the pathogens stick to the surface, the weight on the spring increases, which causes the speed of the spring's bouncing to decrease. By measuring the speed of the bouncing, we can determine how much of the pathogen has been captured. What makes this a particularly useful sensor is that the SH-SAW can detect minute weight differences. In addition, the ligands are highly selective, capable of distinguishing between closely related pathogens.

Acoustic Wave Biosensors
Rapid Point-of-Care Medical Diagnostics

2010

The sensor array is packaged in a disposable plastic cartridge that is inserted by the user into the battery-powered electronics unit. In our current system, a drop of liquid—saliva, urine, or liquid extracted from a swab—is placed on the sensor input port. Due to the package design, surface tension draws the sample over the sensor, so no pumps or valves are required. The absence of pumps and valves makes the sensor much smaller, more reliable, less expensive to manufacture, and extends the operating time of the rechargeable batteries. System control, data analysis, and reporting are performed by a personal digital assistant (PDA). Multiplex detection of different targets, up to six with our latest design, or orthogonal detection of a single target, enhancing detection reliability, are both possible modes of operation. Advances in sensor design, made possible by Sandia's proprietary sensor design software, are key to our ability to identify viruses at clinically relevant levels at the point of care, setting us apart from competing technologies.

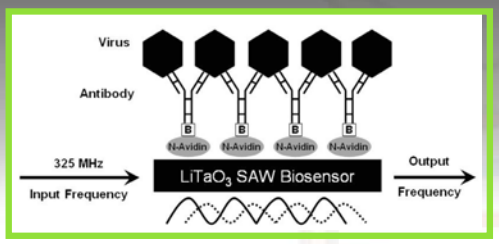


Figure 2 : Schematic of biosensor construction and function.

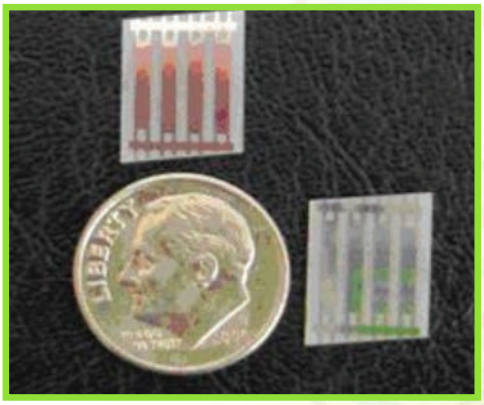


Figure 3: Acoustic wave biosensor arrays with four sensors per device.

Product's Competitors

Current approaches to the diagnostic detection of pathogens are relatively mature and have generated a wide range of products. However, competing approaches can be classified into several technological areas, including: bacterial cultures; viral cultures; polymerase chain reaction (PCR) for nucleic acid identification (genetic fingerprinting) of bacteria, viruses, and genetic disease; and enzyme immunoassays (EIA, both colorimetric and strip or swab assays) to detect pathogen protein signatures and protein toxins. Of these approaches, bacterial and viral[1] cultures, PCR[2], and colorimetric[3] EIA require the facilities in a regional medical laboratory and cannot be performed at the point of care. Strip enzyme immunoassays (SIA), also known as lateral flow immunoassays, do provide point-of-care diagnostic capability and are available from Silver Lake Research Corporation[4] and Oxoid, Ltd[5]. As shown in the following comparison matrix, no existing product matches ours in performance in a point-of-care-setting.

"Having a hand-held sensor that can rapidly detect a variety of analytes, including infectious agents, is critical to ensure the integrity of the blood supply and deliver pertinent care. This technology promises to deliver significant results in this area."

–Jessie Salk
President and CEO, Tricore Reference Laboratories

Comparison Matrix

Product/ Technology	Versatility	Size	Speed	Sensitivity	Specificity	Ease of Use	Unit Price	Cost per test
Acoustic Wave Biosensor	Virus, DNA, proteins, bacteria, spores	Handheld	Minutes	High: medically relevant	High	Simple, no additional reagents	$1,000 (estimate)	$50 (estimate)
Bacterial Culture	Bacteria	Laboratory	Days	Low	High	Extensive training, additional reagents	High: requires lab facility	$50–$500
Viral Culture	Virus	Laboratory	Days to Weeks	Low	High	Extensive training, additional reagents	High: requires lab facility	$50–$500
PCR	DNA	Tabletop	Hours	High	High	Careful sample prep, extensive training, expensive reagents	High: requires lab facility	$50–$500
Colorimetric EIA	Proteins	Tabletop	Minutes	Low	High	Extensive training, additional reagents	High: requires lab facility	$1–$10
SIA	Proteins	Handheld	Minutes	Low	Low	Simple	$0–$25	$1–$10

How Product Improves on Competition

As shown in the comparison matrix, no near-competitors exist for a handheld pathogen detector that enables a real-time diagnosis with little or no sample preparation. This conclusion is supported by market research performed by Adaptive Methods, Inc., the technology licensee, and by letters of support from physicians and the president of a regional medical reference laboratory (see Appendix B).

Other technologies are either too slow or too large and complex to be used at the point of care, or they do not possess sufficient sensitivity or specificity to function as a reliable diagnostic tool. Bacterial cultures, viral cultures, and PCR, which are commonly used today, require personnel with specialized training to perform the tests, and hours-to-days to complete. Colorimetric EIA takes less time but still requires highly trained personnel. All these tests are performed in regional biomedical reference laboratories because the equipment requires a large capital investment. They cannot, therefore, be implemented at the point of care. At the other end of the technology spectrum, SIAs, similar to home pregnancy tests or home glucose tests, are small, low cost, and easy to use, but do not have sufficient sensitivity or specificity to identify pathogens at clinically relevant levels. For example, it is more efficacious to prescribe antibiotics for any patient presenting symptoms of a strep infection than to use the strep SIA due to its poor reliability. In comparison to technologies in commercial use today, our device will, for the ***first*** time, give medical staff the ability to identify a broad range of pathogens ***while the patient is in the office*** and therefore make an accurate and immediate diagnosis. This will allow, for example, a physician to distinguish between a bacterial and viral infection and to prescribe antibiotics only in instances where efficacy is assured.

Figure 4: Packaged biosensor arrays showing capillary filling from sample port above the array.

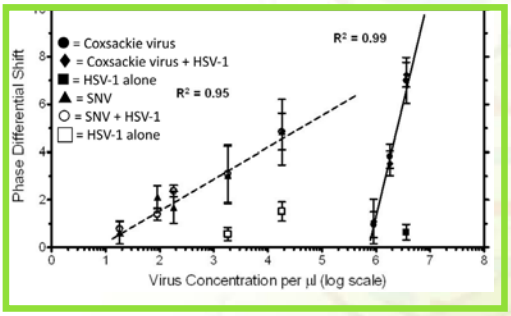


Figure 5: Selective detection of Coxsackie virus and Sin Nombre virus (SNV) in a background Herpes Simplex virus (HSV-1).

...our device will, for the first time, give medical staff the ability to identify a broad range of pathogens while the patient is in the office and therefore make an accurate and immediate diagnosis.

Acoustic Wave Biosensors
Rapid Point-of-Care Medical Diagnostics

2010

Product's Prinicpal Applications

The detection of biological pathogens is a critical need for medical diagnostics and for biodefense, but no solution yet exists that gives healthcare providers, first responders, and military personnel the ability to identify them at the point of care or in the field with the necessary sensitivity, specificity, and speed. Our technology addresses these needs in both medical diagnostic and biodefense applications. We have developed a handheld, battery-powered, portable, and rapid detection system capable of multiplex pathogen identification (e.g., viruses, bacteria, spores, proteins, and DNA) at clinically relevant levels within minutes at the point of use. Our system is capable of identifying pathogens in nasal and throat swabs, saliva, urine, and blood and can perform environmental detection in complex, real-world samples from water, air, soil, food, and surfaces. While our research[6, 7] has focused on the identification of viruses and bacteria on the Center of Disease Control and Prevention (CDC) Category A list of highly infectious pathogens[8], this system could, for example, allow a pediatrician to quickly determine whether a child's ear infection is caused by a virus or bacterium, eliminating the precautionary practice of antibiotic prescription when the actual cause is unknown.

Timely access to diagnostic test results is a significant healthcare issue in the United States and other developed countries. A 2006 study[9] indicates that over half of all patients in the United States experience long wait times for diagnostic tests, clinical records have been unavailable at the time of an appointment for over one-third of the patients, and one-fifth have had to repeat tests because results were unavailable. Other countries report similar statistics. Point-of-care diagnostic tests would eliminate these problems.

To perform biopathogen diagnostics with this point-of-care system, the user—a healthcare provider or emergency first-responder—selects a small (approximately 1 inch by 1 inch by 1/8 inch) plastic microfluidic sensor cartridge matched to the suspected pathogen and inserts it into the handheld instrument.

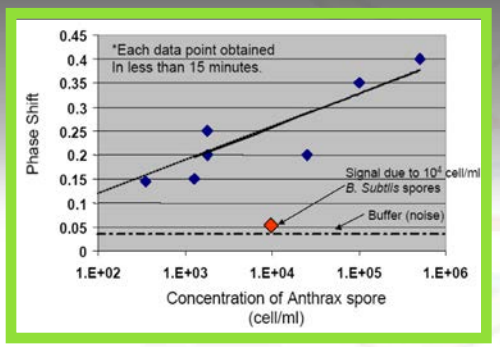


Figure 6: Selective detection of anthrax spore simulant in large background concentration of interferent.

The detection of biological pathogens is a critical need for medical diagnostics and for biodefense, but no solution yet exists that gives healthcare providers, first responders, and military personnel the ability to identify them at the point of care or in the field with the necessary sensitivity, specificity, and speed.

Our current cartridges detect up to three pathogens per cartridge, and our latest instrument design accepts two cartridges at a time. A single drop of the sample is placed on the cartridge's input port where capillary action will draw it onto the sensor, and again, no pumps or valves are required. Within minutes, the instrument's software, run on a PDA or laptop computer, analyzes the response of the sensor array, identifies the pathogen and its concentration, and displays the result for the user. Because the analysis requires very little power, the system can perform many analyses over the course of a day without having to recharge its batteries. The instrument can also be plugged into an outlet if electric power is available.

Other diagnostic measurements are frequently complicated by the sample preparation required to remove interferents—typically, confounding viruses, proteins, and bacteria that mask the pathogen of interest—prior to analysis. Testing has shown that our system can detect viruses and bacterial spores even in backgrounds of other microbes at much higher concentrations. We have also demonstrated that we can detect low levels of virus in real-world environmental samples, for example untreated river water and sewage treatment plant effluent, without any sample preparation. After sample introduction, our system requires no additional chemicals or reagents to complete the analysis, in contrast to some competing approaches. All chemicals needed to perform specific and sensitive detection are functionalized onto the sensor arrays during cartridge assembly. Without the need for sample preparation or additional reagents, our instrument is significantly simpler to operate, has a lower cost of ownership, and is truly field portable. Moreover, the training required to operate the instrument is minimized.

Even though this technology will greatly improve the speed and quality of healthcare in the United States and other developed nations, it will have a potentially greater impact on healthcare in developing countries, where access to medical diagnostic laboratories is limited or unavailable.

Even though this technology will greatly improve the speed and quality of healthcare in the United States and other developed nations, it will have a potentially greater impact on healthcare in developing countries, where access to medical diagnostic laboratories is limited or unavailable.

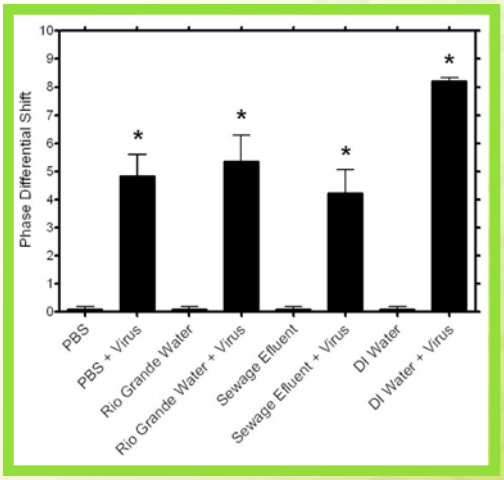


Figure 7: Detection of Sin Nombre virus (SNV) in laboratory water (PBS and DI), river water, and sewage plant effluent.

The benefits of providing diagnostic tests at the point of care will be greatly magnified when and where access to equivalent laboratory tests is restricted and the opportunity for follow-on medical intervention at a later date is impractical.

References

[1] For a discussion of viral cultures, see http://www.lhsc.on.ca/lab/MICRO/virology/vir_cult.htm viral culture

[2] Diagnostic PCR is performed by SABiosciences, http://www.sabiosciences.com/RTPCR.php

[3] Colorimetric EIA systems are manufactured by Quansys Bioscienses, http://www.quansysbio.com/

[4] Watersafe Test Kits, http://xthw5.tabx9.servertrust.com/

[5] Remel Xpect, http://www.oxoid.com/uk/blue/press/press.asp?art=Y&arch=&pRef=PR0363&c=UK&lang=EN

[6] D. W. Branch and S. M. Brozik, Low-level detection of a *Bacillus anthracis* simulant using Love-wave biosensors on 36°YX $LiTaO_3$, Biosensors and Bioelectronics 19 (2004) 849 – 859; see also Appendix D

[7] M. Bisoffi et al., Detection of viral bioagents using a shear horizontal surface acoustic wave biosensor, Biosensors and Bioelectronics 23 (2008) 1397 – 1403; see also Appendix E

[8] Center of Disease Control and Prevention (CDC) Category A; available at http://www.bt.cdc.gov/agent/agentlist-category.asp

[9] On The Front Lines Of Care: Primary Care Doctors' Office Systems, Experiences, And Views In Seven Countries, C. Schoen et al., Health Affairs, 25, w555 – w571 (2006); available at http://content.healthaffairs.org/cgi/content/full/25/6/w555?ijkey=3YyH7yDwrJSoc&keytype=ref&siteid=healthaff, see Appendices F, G, and H

Other Applications

In addition to pathogen detection for medical diagnostics and biodefense, our system's ability to detect DNA will someday allow us to identify an individual's propensity to inherited diseases, including some cancers. We have made initial steps by demonstrating the ability to identify DNA associated with the BRCA gene, a genetic marker for breast cancer susceptibility. In the future, with this capability in a physician's office, a patient can be informed of disease risk without having to return for a follow-up visit, minimizing emotional stress associated with the delay and reducing healthcare costs. This ability to identify specific genetic characteristics will also improve treatment outcomes because it will permit physicians and patients to tailor treatment to complement the patient's individual genetic makeup, accelerating the era of truly personalized medicine.

One unique application that is currently being studied under a grant from the National Institutes of Health (see Letter of Support from Gerald Kost, MD, Appendix B) is field testing of blood prior to transfusion. In the wake of a natural disaster or other emergency, existing blood supplies can be exhausted, requiring transfusions from local volunteers. Without a functioning blood bank, there is no way to guarantee the safety of the donated blood. With this biosensor technology, it will be possible to screen donated blood in the field for a wide range of bacterial and viral pathogens.

The acoustic wave biosensor technology could have a significant potential impact in the area of food safety. The ability to rapidly screen for pathogens such as *E. coli* at meat packing plants and even in supermarkets could prevent thousands of hospitalizations, significantly more cases of infection that don't result in hospitalization, and a large number of deaths every year.

...our system's ability to detect DNA allows us to identify an individual's propensity to inherited diseases, including some cancers.

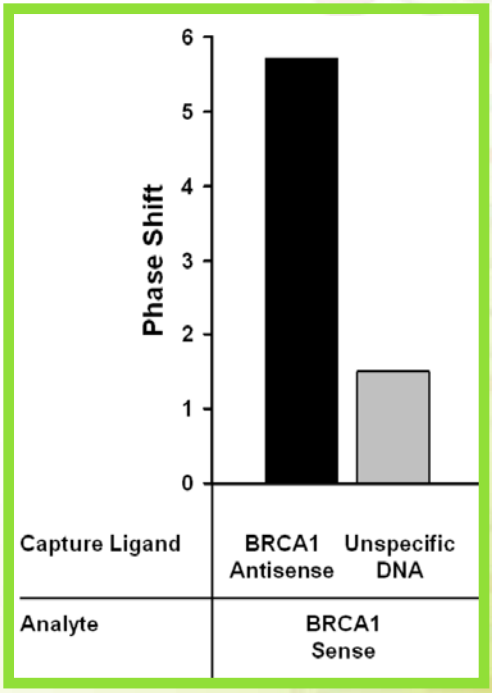


Figure 8: Detection of breast cancer DNA marker, BRCA-1, using acoustic wave biosensor.

Acoustic Wave Biosensors
Rapid Point-of-Care Medical Diagnostics

2010

Summary

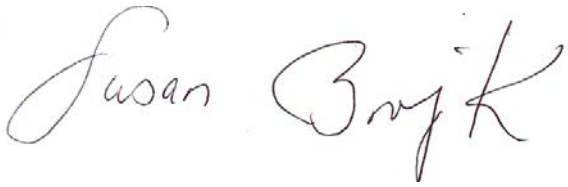
The ability to perform multiple medical diagnostic tests for infectious and disease-causing pathogens, at the point of care and at lower cost than with the current diagnostic technologies, will dramatically improve the quality of healthcare in both the developed and developing world. Physicians will be able to determine treatments more rapidly and more accurately while patients will benefit from better outcomes, less uncertainty, and fewer follow-up appointments. In high-consequence applications such as medical emergencies and biodefense, rapid and accurate testing can literally be the difference between life and death. And as genetic indicators of disease and treatment are better understood, this technology will allow primary-care physicians to optimize medical interventions to best fit the individual patient.

"During disasters, such as Hurricane Katrina and the Haitian earthquake, it is critical to have point-of-care instruments that are handheld, portable, battery-operated, and reliable for the detection of a variety of infectious agents."

–Gerald Kost, MD, PhD
Director, UC Davis–LLNL
POC Technologies Center
Department of Pathology
and Laboratory Medicine

AFFIRMATION

By uploading this form to R&D Magazine's website you affirm that all information submitted as a part of, or supplemental to, this entry is a fair and accurate representation of this product.



Susan Brozik

Appendices

Appendix A: Letter of Support from Adaptive Methods, Inc.

ADAPTIVE METHODS

15825 Shady Grove Road, Suite 135 ■ Rockville, MD 20850 ■ ph 301-840-9722 ■ fax 301-975-1067

Editor
R&D Magazine

Advantage Business Media
100 Enterprise Drive
Suite 600, Box 912
Rockaway NJ 07866-0912

Re: R&D 100 Awards

To whom it may concern,

Adaptive Methods recently entered into a partnership to commercialize a revolutionary biosensor technology co-developed by scientists at Sandia National Labs and the Health Sciences Center at the University of New Mexico, and the subject of this nomination for an R&D 100 Award. Prior to entering into this partnership, our due diligence indicated that this technology had the potential to substantially advance the way infectious diseases are diagnosed and treated, to the great benefit of not only patients, but of society as a whole. This device will enable medical staff to diagnose viral and bacterial infections immediately and specifically, thereby ensuring that treatment is timely and appropriate. The ability to confirm a viral infection by itself will help in medicine's battle to curtail the worsening problem of over-prescription of antibiotics. With this device, relief can come faster and lives can be saved as it shortens the time to confirmed diagnoses of infection, from days to minutes. Further, in a situation where transfusions are urgently needed and screened blood is not available, we can envision applying the technology to test donated blood for HIV, Hepatitis, etc., on site and in real time.

Adaptive Methods also sees great promise in the subject technology's potential application to food safety and bio-defense. The technology's inherent speed lends itself to just-in-time testing at all points in the food processing and distribution chain, potentially reducing the likelihood that tainted food ever reaches the public. Just the same, the technology's inherent sensitivity can be harnessed by the military, government agencies, and first responders to detect bio-agents in extremely low concentrations before a population can become infected.

We at Adaptive Methods enthusiastically support this nomination for an R&D 100 Award for 2010.

Sincerely,

Mark Meister
Vice President
Adaptive Methods

Appendix B: Letters of Support from Physicians

UNM HEALTH SCIENCES CENTER

OFFICE OF THE EXECUTIVE VICE PRESIDENT FOR HEALTH SCIENCES CENTER AND DEAN OF THE SCHOOL OF MEDICINE

March 3, 2010

TO: Editor, R&D Magazine

RE: R&D 100 Awards Nominee, "Ligand-based sensor for rapid pathogen-detection"

I wish to express my strong enthusiasm and support of this technology for the R&D 100 Award. This biosensor was developed initially for the detection of anthrax and was subsequently modified for the detection of category A virus hemoraghic fever-causing agents. In its original design, the sensor required little or no pre-processing of water-based or clinical specimens. It would allow first responders to determine if a material presented an infectious risk within minutes of its arrival. This project was recognized by the Defense Intelligence Agency's Chief Scientist Award for its contribution to national defense in 2006.

This project could not have been developed without the collaboration of the University of New Mexico and Sandia National Laboratories. The University was critical in bringing together basic scientists and clinical investigators to partner with the engineers at Sandia to develop and validate this instrument. Beyond the original intelligence applications, it has recently been adapted to medical diagnostic applications. Earlier this year the sensor was adapted at UNM for the diagnosis of HIV-1 and-2, and Hepatitis B and C in blood samples so that rapid evaluation of blood products from donors could occur. During catastrophic events such as what recently happened in Haiti, emergent blood products for transfusion were not available, and testing for that blood product is difficult since transportation of the test sample to a distant site may not be practical. Using this detector, blood donors could be tested and, if free of infection, their blood rapidly used for transfusion. After the initial few weeks of the onset of the catastrophic event, there is then a need for disaster hospitals to have reliable instrumentation that does not depend on electricity. This sensor is also easily adapted to the detection of a variety of infectious diseases. During the latter phase of recovery from a catastrophic event, it is critical to have a battery-powered, hand-held instrument such as this sensor for the detection of microorganisms.

Overall, this technology has great promise for both intelligence and medical diagnostic applications. We are proud that this collaboration between Sandia National Laboratories and the University of New Mexico Health Science Center has been so productive. We look forward to the benefits it will bring to the state of New Mexico and the United States.

Sincerely,

Paul B. Roth, MD, FACEP
Executive Vice President for Health Sciences
Dean, School of Medicine

Appendix B: Letters of Support from Physicians

UNM SCHOOL of MEDICINE

Department of Emergency Medicine

March 3, 2010

Editor
R&D Magazine

RE: R&D 100 Awards

To Whom It May Concern:

I am currently the department chair of the Emergency Medicine and the director emeritus of our Center for Disaster Medicine. I wish to convey my strong support for this technology for the R&D 100 Award. As an experienced leader in disaster medicine, I can attest to the potential impact of this technology in disaster scenarios. In these scenarios there is an acute phase lasting a few weeks in which numerous trauma victims need medical attention. During this phase, having a device such as this can be critical in helping assure that blood prepared for transfusion does not carry an infectious disease.

After the first several weeks of a disaster, it is then important that reliable instruments are available. It is common in many disaster scenarios to have disruptions of municipal infrastructure to include the loss of electricity and potable water. As a result, traditional laboratory instruments will be out of commission and having a small battery-operated instrument that can operate in austere environments can allow health care professional the opportunity to provide standard medical care.

An equally important disaster employment of this device is its potential intelligence applications. It rapidly detects bioagents such as anthrax, and subsequently modified, the platform for detection of Category A virus hemorrhagic fever causing agents such as Dengue, Andes, and LCM viruses. This project was recognized with the Defense Intelligence Agency's Chief Scientist Award for its contribution to national defense.

This device is a huge step forward benefiting both medicine and defense in emergency situations, providing disaster control assistance worldwide.

Sincerely,

Michael Richards, MD, MPA
Chair, Department of Emergency Medicine

Appendix B: Letters of Support from Physicians

DEFENSE INTELLIGENCE AGENCY

WASHINGTON, D.C. 20340-5100

2 March, 2010

Editor, R&D Magazine
Re: R&D 100 Awards Nominee,
"Ligand-based sensor for rapid pathogen-detection"

Ladies and Gentlemen,

In my role as director of the National Consortium for MASINT Research (NCMR), I enthusiastically support the nomination of this technology for the R&D 100 Award. Initially, my office funded the UNM development of a ligand-based sensor for rapid detection of bioagents such as anthrax. Subsequently, we supported a modified platform for detection of Category A virus hemorrhagic fever causing agents such as Dengue, Andes, and LCM viruses. This unique sensor requires little or no pre-processing of water-based or clinical specimens. The sensor provides an accurate result in less than two minutes; and is easily adaptable to the detection of other viral agents. This project was recognized with the Defense Intelligence Agency's Chief Scientist Award for its contribution to national defense. The collaborative partnership of UNM and Sandia National Laboratories made the development of this sensor possible. UNM was the glue in bringing together basic scientists, engineers, and clinical investigators to develop and validate this highly successful instrument.

Although this detector has significant intelligence applications, it is readily adaptable to medical diagnostic applications. Earlier this year the sensor was adapted at UNM for diagnosis of IIV-1 and -2, and Hepatitis B and C in blood samples so that rapid evaluation of blood products from donors could occur. During catastrophic events such as Hurricane Katrina, emergent blood products for transfusion were not available and testing of that blood product is difficult since transportation of the test sample to a distant site may not be practical. Using this detector blood product could be shown to be acceptable for blood transfusion, and trauma victims could receive blood product.

This project, under Dr. Larson's leadership, received funding as part of a U54 grant from NIAID with University of California-Davis. Again, by facilitating a broad array of investigators to work together and by providing the necessary resources for testing, the CTSC was critical to this effort. Finally, I have recently re-directed NCMR funds so that UNM investigators can rapidly adapt this sensor to the detection of 2009 H1N1 "Swine Flu."

In addition to the flagship project that I described above, the NCMR program has also worked closely with UNM and provided funding to support their interactions with both Los Alamos and Sandia National laboratories in other areas such as laser design and nanotechnology for non-invasive imaging and diagnostics. The NCMR program and the Defense Intelligence Agency

Appendix B: Letters of Support from Physicians

have promoted interactions between the national laboratories in New Mexico and the UNM CTSC. We are proud that their collaborations have been so productive and will continue to benefit the citizens of New Mexico and the United States.

Sincerely,

Peter F. Bythrow, PhD

Chief Scientist
National MASINT Management Office
Defense Intelligence Agency
Bldg 6000, Bolling AFB
Washington, DC 20340

Appendix B: Letters of Support from Physicians

UC DAVIS - LLNL POINT-OF-CARE TECHNOLOGIES CENTER
Critical - Emergency - Disaster Care

Gerald J. Kost, MD, PhD, MS, FACB
Director, UC Davis-LLNL POC Technologies Center
Pathology and Laboratory Medicine
3455 Tupper Hall, School of Medicine
University of California, Davis, CA, USA 95616
PHONE: 530-752-4702 FAX: 530-752-4548
Email: poctcenter@ucdavis.edu
Website: www.ucdmc.ucdavis.edu/pathology/poctcenter

March 4, 2010

Editor, R&D Magazine
Advantage Business Media
100 Enterprise Drive, Suite 600, Box 912
Rockaway, NJ 07866-0912

Re: R&D 100 Awards Nominee, "Ligand-Based Sensor for Rapid Pathogen-Detection"

Dear Editor,

As Director of the UC Davis-Lawrence Livermore National Laboratory Point-of-Care Technologies Center, I would like to express my strong support for the nomination of Surface Acoustic Wave biosensor (SAWB) technology for the R&D 100 Award.

The POC Technologies Center, funded by a National Institutes of Biomedical Imaging and Bioengineering (NIBIB) U54 award, focuses on advancing critical-emergency-disaster care by developing novel point-of-care technologies for rapid multiplex pathogen detection.

In April 2009, the Center awarded Dr. Richard Larson, Principal Investigator, and his SAWB project, selectively chosen for its significance in making safe donor blood available during emergencies and disasters, a 2-year $300,000 NIH U54 exploratory grant.

During disasters, such as Hurricane Katrina and the Haitian earthquake, it is critical to have point-of-care instruments that are handheld, portable, battery-operated, and reliable for the detection of a variety of infectious agents. During that time period, rapid transfusion of blood products that have low probability of communicating infection is necessary to reduce the risk of disease and to ensure repletion in acute blood loss.

The SAWB shows promising results. Initial pilot data generated with the technology indicate that it can detect HIV-1/2 and hepatitis B and C. We are pleased that we have been able to support such a successful technology to date and will continue to assist Dr. Larson in its further development over the next year.

Best regards,,

Gerald J. Kost

Gerald Kost, MD, PhD
Director, UC Davis-LLNL POC Technologies Center
Department of Pathology and Laboratory Medicine

Appendix B: Letters of Support from Physicians

1001 Woodward Place NE
Albuquerque, NM 87102
www.tricore.org

TRICORE
REFERENCE LABORATORIES

Main: 505-938-8888
Toll Free: 800-245-3296
Fax: 505-938-8977

March 1, 2010

Editor
R&D Magazine

Re: R&D 100 Awards

Dear Gentlemen and Ladies:

This point-of-care testing instrument promises to have significant impact on medical care in the areas of disaster medicine, standard point-of-care testing, pandemic control, and for first responders. Accordingly, the biosensor has my strongest support for the R&D 100 Award.

This hand-held sensor developed by Sandia National Laboratories and the University of New Mexico team will have broad applicability in disaster situations. Having a hand-held sensor that can rapidly detect a variety of analytes, including infectious agents, is critical to ensure the integrity of the blood supply and deliver pertinent care. This technology promises to deliver significant results in this area.

During normal medical care, a point-of-care testing instrument such as this biosensor will also have great impact on pandemic control and the application of accurate therapy. For instance, the ability to rapidly and germanely prescribe antibiotics in a physician's office will dramatically decrease costs. This instrument requires little pre-processing and can make a diagnosis of a viral infection within a few minutes in a doctor's office.

Finally, this technology is of considerable import for first responders and forensic analysis. In catastrophic situations it is critical to assess whether material found at the site is infectious. This instrument will allow for rapid assessment of whether white powder or other substrates are dangerous.

In all, I wish to convey that this hand-held technology requiring little pre-processing of water-based or clinical specimens; providing a result in less than two minutes; and easily adaptable to the detection of other viral and bacterial agents has the potential to have dramatic impact on the practice of medicine. I am pleased that such technology has been developed in New Mexico and look forward to participating in further testing of this instrument as it moves toward FDA approval.

Sincerely,

Jessie Salk
President & CEO

Appendix C: Patent Application

DETECTION OF BIOAGENTS USING A SHEAR HORIZONTAL SURFACE ACOUSTIC WAVE BIOSENSOR, February 8, 2008, Larson, Hjelle, Hall, Brown, Bisoffi, Brozik, Branch, Edwards, Wheeler.

COLEMAN SUDOL SAPONE, P.C.
PATENT, TRADEMARK AND COPYRIGHT MATTERS

714 COLORADO AVENUE
BRIDGEPORT, CT 06605-1601
PHONE: (203) 366-3560
FAX: (203) 335-6779
E-MAIL: COSUD@EROLS.COM

EXPRESS MAIL No.: **EV 757371250 US** Deposited: **February 8, 2008**
I hereby certify that this correspondence is being deposited with the United States Postal Service, "Express Mail Post Office to Addressee" service under 37 CFR 1.10, on the date indicated above and is addressed to: COMMISSIONER FOR PATENTS, P.O. Box 1450, Alexandria, VA 22313-1450.

Curtis L. Schrandt

COMMISSIONER FOR PATENTS
Alexandria, VA 22313-1450

Docket No: N12-109US

Sir:

Transmitted herewith for filing is the patent application in the name(s) of: **LARSON, Richard S.; HJELLE, Brian; HALL, Pam R.; BROWN, David C.; BISOFFI, Marco; BROZIK, Susan M.; BRANCH, Darren W.; EDWARDS, Thayne L.; and WHEELER, David**

FOR: **DETECTION OF BIOAGENTS USING A SHEAR HORIZONTAL SURFACE ACOUSTIC WAVE BIOSENSOR**

ENCLOSED ARE:
(1) Application Data Sheet;
(2) Specification (pages 1-32), Claims (pages 33-37/ 29 claims) & Abstract (page 38);
(3) Drawing Sheets (7 pp); and
(4) Preliminary Amendment.

Note(s): Large entity status applies to this application.

THE FILING FEE HAS BEEN CALCULATED AS SHOWN BELOW:

	Claims Filed		Extra		~~SMALL ENTITY~~	or	LARGE ENTITY
Basic Fee					$ 155.00		$ 310.00
Search Fee					$ 255.00		$ 510.00
Examination Fee					$ 105.00		$ 210.00
Total Claims	29	- 20 =	9	x $ 25.=	$		x $ 50.= $ 225.00
Indep. Claims	4	- 03 =	1	x $105.=	$		x $210.= $ 210.00
( ) Multiple Dependent Claim(s) Presented:				+ $185.=			+ $370.= $
( ) Appl'n Size Fee (add'l 50pp over 100pp):				+ $130.= $			+ $260.= $
Total Filing Fee:					$		$
Assignment recordation fee ($ 40.00):					$		$
CHECK ENCLOSED:					$		$1465.00

The Commissioner is hereby authorized to charge payment of all fees associated with the filing and prosecution othis application, but not limited to: (X) Any patent application processing fees under 37 CFR 1.17;
(X) Any filing fees under 37 CFR 1.16 for the presentation of extra claims;
and credit any overpayment to Deposit Account No. **04-0838.** A duplicate copy of this sheet is enclosed.

Respectfully submitted,

Dated: February 8, 2008

Henry D. Coleman, Reg. No. 32,559
R. Neil Sudol, Reg. No. 31,669
William J. Sapone, Reg. No 32,518

Enclosures

Appendix D: Journal Article (excerpt)

Low-level Detection of a *Bacillus anthracis* Simulant Using Love-wave Biosensors on 36°YXLiTaO$_3$

ELSEVIER

Available online at www.sciencedirect.com
SCIENCE DIRECT®

Biosensors and Bioelectronics 19 (2004) 849–859

BIOSENSORS & BIOELECTRONICS

www.elsevier.com/locate/bios

Low-level detection of a *Bacillus anthracis* simulant using Love-wave biosensors on 36°YX LiTaO$_3$

Darren W. Branch*, Susan M. Brozik[1]

Sandia National Laboratories, P.O. Box 5800, MS-0892, Albuquerque, NM 87185-0892, USA

Received 6 March 2003; received in revised form 29 July 2003; accepted 22 August 2003

Abstract

We present an acoustic Love-wave biosensor for detection of the *Bacillus anthracis* simulant, *Bacillus thuringiensis* at or below inhalational infectious levels. The present work is an experimental study of 36°YX cut LiTaO$_3$ based Love-wave devices for detection of pathogenic spores in aqueous conditions. Given that the detection limit (D_l) of Love-wave-based sensors is a strong function of the overlying waveguide, two waveguide materials have been investigated, which are polyimide and polystyrene. To determine the mass sensitivity of Love-wave sensor, bovine serum albumin (BSA) protein was injected into the Love-wave test cell while recording the magnitude and phase shift across each sensor. Polyimide had the lowest mass detection limit with an estimated value of 1.0–2.0 ng/cm^2, as compared to polystyrene where $D_l = 2.0$ ng/cm^2. Suitable chemistries were used to orient antibodies on the Love-wave sensor using protein G. The thickness of each biofilm was measured using ellipsometry from which the surface concentrations were calculated. The monoclonal antibody BD8 with a high degree of selectivity for anthrax spores was used to capture the non-pathogenic simulant *B. thuringiensis* B8 spores. *Bacillus subtilis* spores were used as a negative control to determine whether significant non-specific binding would occur. Spore aliquots were prepared using an optical counting method, which permitted removal of background particles for consistent sample preparation. This work demonstrates that Love-wave biosensors are promising for low-level detection for whole-cell biological pathogens.
© 2003 Elsevier B.V. All rights reserved.

Keywords: SH-SAW; Love-wave; Spores; *Bacillus anthracis*; Biosensor

1. Introduction

Surface acoustic wave (SAW) sensors have been routinely applied in the fields of chemical and biological sensing. In these devices an acoustic wave is launched from an interdigital transducer (IDT) on the piezoelectric substrate either as a surface acoustic wave or a bulk acoustic wave (BAW). The device may operate as a resonator or delay line, responding to any shift in mechanical and electrical properties of the contacting media. When the device is configured as a delay line, the detection is through changes in velocity. Given that the acoustic energy is confined near a thin surface region of the substrate, SAWs are highly sensitive to surface perturbation of the propagating medium. The boundary conditions at the solid or liquid interface govern the wave amplitude and velocity, allowing the surface wave device to operate as mass or viscosity sensor. For this reason, SAWs are suitable for detecting changes in surface mass (Du et al., 1996; Gizeli, 1997; Harding et al., 1997) and viscosity (Campitelli et al., 1998; Jakoby and Vellekoop, 1998a,b; Yamazaki et al., 2000).

For sensing in liquid environments, however, there is a strong radiation loss for longitudinal bulk modes such as Rayleigh surface waves and most Lamb-wave modes (Jakoby and Vellekoop, 1998a,b). Surface waves with displacements normal to the surface generate compression waves, which dissipate wave energy in the liquid. For this reason, acoustic waves that have the particle displacement parallel to the device surface and normal to the wave propagation direction are essential. These waves, referred to as shear horizontal (SH) waves, will propagate without coupling acoustic energy into the liquid. SH type acoustic waves include thickness shear modes (TSM), acoustic plate modes (APM), surface skimming bulk waves (SSBW), Love-waves, leaky surface acoustic waves (LSAW), and Bleustein–Gulyaev (BG) waves (Nakamura et al., 1978).

* Corresponding author. Tel.: +1-505-284-5843; fax: +1-505-845-8161.
E-mail addresses: dwbranc@sandia.gov (D.W. Branch), smbrozi@sandia.gov (S.M. Brozik).
[1] Tel.: +1-505-844-5105; fax: +1-505-845-8161.

0956-5663/$ – see front matter © 2003 Elsevier B.V. All rights reserved.
doi:10.1016/j.bios.2003.08.020

Appendix E: UNM/Sandia National Laboratories Viral Detection Journal Article (excerpt)

Detection of Viral Bioagents Using a Shear Horizontal Surface Acoustic Wave Biosensor

ELSEVIER

Available online at www.sciencedirect.com
ScienceDirect

Biosensors and Bioelectronics 23 (2008) 1397–1403

BIOSENSORS & BIOELECTRONICS

www.elsevier.com/locate/bios

Detection of viral bioagents using a shear horizontal surface acoustic wave biosensor

M. Bisoffi [a,*], B. Hjelle [b], D.C. Brown [b], D.W. Branch [c], T.L. Edwards [c], S.M. Brozik [c], V.S. Bondu-Hawkins [b], R.S. Larson [b]

[a] *Department of Biochemistry and Molecular Biology, The University of New Mexico School of Medicine, Albuquerque, NM, USA*
[b] *Department of Pathology, The University of New Mexico School of Medicine, Albuquerque, NM, USA*
[c] *Sandia National Laboratories, Albuquerque, NM, USA*

Received 19 July 2007; received in revised form 15 November 2007; accepted 11 December 2007
Available online 3 January 2008

Abstract

Viruses are of high medical and biodefense concern and their detection at concentrations well below the threshold necessary to cause health hazards continues to be a challenge with respect to sensitivity, specificity, and selectivity. Ideally, assays for accurate and real time detection of viral agents would not necessitate any pre-processing of the analyte, which would make them applicable for example to bodily fluids (blood, sputum) and man-made as well as naturally occurring bodies of water (pools, rivers). We describe herein a robust biosensor that combines the sensitivity of surface acoustic waves (SAW) generated at a frequency of 325 MHz with the specificity provided by antibodies for the detection of viral agents. A lithium tantalate-based SAW transducer with silicon dioxide waveguide sensor platform featuring three test and one reference delay lines was used to adsorb antibodies directed against either Coxsackie virus B4 or the category A bioagent Sin Nombre virus (SNV), a member of the genus Hantavirus, family *Bunyaviridae*, negative-stranded RNA viruses. Rapid detection (within seconds) of increasing concentrations of viral particles was linear over a range of order of magnitude for both viruses, although the sensor was approximately 5×10^5-fold more sensitive for the detection of SNV. For both pathogens, the sensor's selectivity for its target was not compromised by the presence of confounding Herpes Simplex virus type 1. The biosensor was able to detect SNV at doses lower than the load of virus typically found in a human patient suffering from hantavirus cardiopulmonary syndrome (HCPS). Further, in a proof-of-principle real world application, the SAW biosensor was capable to selectively detect SNV agents in complex solutions, such as naturally occurring bodies of water (river, sewage effluent) without analyte pre-processing. This is the first study that reports on the detection of viral agents using an antibody-based SAW biosensor that has the potential to be used as a hand-held and self-contained device for rapid viral detection in the field.
© 2007 Elsevier B.V. All rights reserved.

Keywords: SAW; Biosensor; Antibody; Virus; Category A bioagent; Hantavirus

1. Introduction

Recently, there has been a heightened interest in developing rapid and reliable methods of detection of micro-organisms involved in bioterrorism, food poisoning, and clinical problems. Biosensors are devices under intense development to achieve these goals and a number of different types of transduction modes are currently investigated, including electrochemical, optical, thermal, and acoustic (Deisingh and Thompson, 2004). Shear horizontal surface acoustic wave (SH-SAW) devices that are based on horizontally polarized surface shear waves (HPSSW) enable label-free, sensitive and cost-effective detection of biomolecules in real time and have been used for the detection of bacteria and viral DNA (Berkenpas et al., 2006; Branch and Brozik, 2004; Moll et al., 2007). A SAW device typically has a planar electrode structure consisting of a piezoelectric substrate containing inter-digital transducers (IDTs) (Branch and Brozik, 2004). An often used substrate compound that meets many of the required conditions for successful HPSSW generation is lithium tantalate ($LiTaO_3$) (Branch and Brozik, 2004; Martin et al., 2004). Applying an alternating voltage via the IDTs at high frequency (typically from 80 to 400 MHz), HPSSW

* Corresponding author at: Department of Biochemistry and Molecular Biology, University of New Mexico School of Medicine, MSC08 4670, 1 University of New Mexico, Albuquerque, NM 87131, USA. Tel.: +1 505 2728157; fax: +1 505 2726587.
E-mail address: mbisoffi@salud.unm.edu (M. Bisoffi).

0956-5663/$ – see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.bios.2007.12.016

Appendix F: Physicians Survey Results, Exhibit 5 (from Ref.8)

Access Experiences and Office Hours among Primary Care Physicians in Seven Counties, 2006

EXHIBIT 5
Access Experiences And Office Hours Among Primary Care Physicians In Seven Countries, 2006

	AUS (%)	CAN (%)	GER (%)	NET (%)	NZ (%)	UK (%)	US (%)
Office hours							
Does your practice have office hours to see patients at the following times?							
Some early morning hours (before 8:30 a.m.)	43[b,c,d,e,f]	27[c,d,e,f,g]	80[d,e,f,g]	85[e,f,g]	37	33[g]	40
Some evening hours (after 6:00 p.m.)	52[c,d,e,f,g]	48[c,d,e,f,g]	74[d,e,f,g]	4[e,f,g]	38	39	38
Some weekend hours	76[b,c,d,e,f,g]	38[c,d,f,g]	24[d,e,f,g]	2[e,f,g]	39[f,g]	5[g]	47
None of these	14[b,c,e,f,g]	34[c,d,f]	7[d,e,f,g]	13[e,f,g]	34[f]	40[g]	29
Does your practice have an arrangement where patients can be seen by a doctor or nurse if needed, when the practice is closed, not including ER? (percent yes)	81[b,c,d,e,f,g]	47[c,d,e,f,g]	76[d,e,f,g]	95[e,f,g]	90[g]	87[g]	40
How often do you think your patients experience the following?							
Difficulty paying for prescriptions							
Often	15[b,c,d,e,g]	24[d,f,g]	23[d,f,g]	7[e,f,g]	27[f,g]	13[g]	51
Sometimes	64[b,c,d,f,g]	56[c,e,f,g]	35[d,e,f,g]	55[f,g]	62[f,g]	48	43
Rarely/never	21[c,d,e,f,g]	18[c,d,e,f,g]	42[d,e,g]	36[e,g]	11[f,g]	39[g]	5
Difficulty paying for care other than prescriptions							
Often	27[c,d,e,f,g]	25[c,d,e,f,g]	35[d,f,g]	12[e,g]	39[f]	14[g]	42
Sometimes	59[b,c,f,g]	51[c,d]	36[d,e,f,g]	61[e,f,g]	54	50	51
Rarely/never	14[b,c,d,e,f,g]	22[c,e,f,g]	29[e,f,g]	26[e,f,g]	7[f]	35[g]	7
Long waiting times for diagnostic tests							
Often	6[b,d,e,f,g]	51[c,d,e,f,g]	8[d,e,f]	26[f,g]	28[f,g]	57[g]	9
Sometimes	39[c,d,e]	39[c,d,e]	16[d,e,f,g]	49[f,g]	53[f,g]	36[g]	42
Rarely/never	55[b,c,d,e,f,g]	9[c,d,e,f,g]	76[d,e,f,g]	23[f,g]	19[f,g]	6[g]	48
Long waiting times for elective surgery or hospital care							
Often	69[c,d,e,f,g]	70[c,d,e,f,g]	9[d,e,f]	51[e,f,g]	85[f,g]	62[g]	9
Sometimes	26[d,e,f,g]	24[d,e,f,g]	27[d,e,f,g]	42[e,f,g]	14[f,g]	35	34
Rarely/never	4[c,e,g]	4[c,e,g]	66[d,e,f,g]	7[e,f,g]	1[f,g]	2[g]	56

SOURCE: Commonwealth Fund International Health Policy Survey of Primary Care Physicians, 2006.

NOTES: Reading from left to right starting with Australia (AUS), the letter indicates significant differences with the country or countries to the right, as indicated ($p < .05$). For unweighted N, see Exhibit 1.

[b] Different from Canada.
[c] Different from Germany.
[d] Different from the Netherlands.
[e] Different from New Zealand.
[f] Different from the United Kingdom.
[g] Different from the United States.

Appendix G: Physicians Survey Results, Exhibit 3 (from Ref.8) v

Coordination of Care: Primary Care Physicians' Reports on Experiences in Seven Counties, 2006

EXHIBIT 3
Coordination Of Care: Primary Care Physicians' Reports On Experiences In Seven Countries, 2006

	AUS (%)	CAN (%)	GER (%)	NET (%)	NZ (%)	UK (%)	US (%)
During the past 12 months, how often have your patients experienced the following?							
Problems because care was not well coordinated across multiple sites or providers							
Often	5[f]	5[f]	5[f]	5[f]	4[f]	15[g]	5
Sometimes	35[b,c,d,e,f]	41[c,f,g]	16[d,e,f,g]	41[f,g]	45[g]	50[g]	32
Rarely/never	60[b,c,d,e,f]	51[c,f,g]	78[d,e,f,g]	52[f,g]	51[f,g]	34[g]	60
A patient's medical record/clinical information was not available at the time of scheduled visit							
Often	4[b,d,f,g]	10[c,d,e]	3[d,f,g]	1[f,g]	2[g]	7[e]	8
Sometimes	24[b,c,d,g]	31[c,d,e]	8[d,e,f,g]	15[e,f,g]	25[g]	29	32
Rarely/never	72[b,c,d,f,g]	56[c,d,e,f]	89[d,e,f,g]	83[e,f,g]	72[f,g]	64[g]	58
Tests or procedures had to be repeated because findings were unavailable							
Often	1[b,d,f]	3[c,d,e]	1[d,f]	<1[f,g]	1[f]	3	2
Sometimes	9[b,c,d,e,f,g]	17[c,d,f]	3[d,e,f,g]	7[e,f,g]	13[f]	24[g]	14
Rarely/never	89[b,c,d,e,f,g]	78[c,d,e]	95[e,f,g]	92[e,f,g]	86[f]	73[g]	82
When you refer a patient to another doctor, for what percentage of patients do you get information back about the results of the referral?							
Almost all	76[b,c,d,e,g]	62[c,e,f,g]	68[d,e,f,g]	61[e,f,g]	82[f,g]	75[g]	37
Most	19[d,e,g]	22[d,e,f,g]	21[d,e,f,g]	35[e,f]	14[g]	18[g]	33
About half or fewer	5[b,c,g]	15[d,e,f,g]	11[d,e,f,g]	4[g]	3[f,g]	7[g]	28
After patient has been discharged, how long does it take to receive a full discharge report from the hospital?							
Less than 48 hours	10[b,c,d,e,f,g]	3[e,g]	4[e,g]	5[e,g]	29[f,g]	4[g]	14
2–4 days	21[b,c,d,f,g]	6[e,f,g]	7[e,g]	7[e,g]	19[f,g]	10[g]	25
5–14 days	40[b,c,e,f,g]	28[c,d,f,g]	35	35	34	34	34
15 days or more, or rarely receive a full report	28[b,c,d,e,f,g]	58[c,d,e,g]	53[e,g]	48	18[f,g]	52	23
15–30 days	16	33	37	40	13	36	11
More than 30 days or rarely receive full report	12	25	16	9	5	18	12

SOURCE: Commonwealth Fund International Health Policy Survey of Primary Care Physicians, 2006.
NOTES: Reading from left to right starting with Australia (AUS), the letter indicates significant differences with the country or countries to the right, as indicated ($p < .05$). For unweighted N, see Exhibit 1.
[b] Different from Canada.
[c] Different from Germany.
[d] Different from the Netherlands.
[e] Different from New Zealand.
[f] Different from the United Kingdom.
[g] Different from the United States.

Appendix H: ***On The Front Lines Of Care: Primary Care Doctors' Office Systems, Experiences, And Views In Seven Countries, C. Schoen et al., Health Affairs***

On The Front Lines Of Care: Primary Care Doctors' Office Systems, Experiences, And Views In Seven Countries, C. Schoen et al., Health Affairs, 25, w555 – w571 (2006); available at http://content.healthaffairs.org/cgi/content/full/25/6/w555?ijkey= 3YyH7yDwrJSoc&keytype=ref&siteid=healthaff

On The Front Lines Of Care: Primary Care Doctors' Office Systems, Experiences, And Views In Seven Countries

Country variations in primary care practices indicate opportunities to learn to improve outcomes and efficiency.

by Cathy Schoen, Robin Osborn, Phuong Trang Huynh, Michelle Doty, Jordon Peugh, and Kinga Zapert

ABSTRACT: This 2006 survey of primary care physicians in Australia, Canada, Germany, New Zealand, the Netherlands, the United Kingdom, and the United States reveals striking differences in elements of practice systems that underpin quality and efficiency. Wide gaps exist between leading and lagging countries in clinical information systems and payment incentives. U.S. physicians are among the least likely to have extensive clinical information systems or incentives targeted on quality and the most likely to report that their patients have difficulty paying for care. Disease management capacity varies widely. Overall, findings highlight the importance of nationwide policies: Policy changes in the United States could lead to improved performance. [*Health Affairs* 25 (2006): w555–w571 (published online 2 November 2006; 10.1377/hlthaff.25.w555)]

PRIMARY CARE PHYSICIANS ARE ON THE front lines of care, providing first contact and preventive and ongoing essential care. Even in the United States, with its highly specialized physician workforce, primary care doctors account for the majority of patient visits for common conditions and are the doctors patients typically name when asked if they have a regular source of care.[1] Moreover, U.S. patients value having a "medical home" that serves as an ongoing source of care and helps coordinate care.[2] Increasingly, countries are instituting policies to hold primary care practices accountable for managing chronic conditions and meeting clinical standards. These include financial incentives and primary care practice redesign, with an emphasis on information technology (IT) and teams to support effective, safe, patient-centered, coordinated, and efficient care.

Cathy Schoen (cs@cmwf.org) is senior vice president, research and evaluation, at the Commonwealth Fund in New York City. Robin Osborn is vice president and Phuong Trang Huynh, associate director, international health policy and practice; Michelle Doty is associate director of research. Jordon Peugh is research director and Kinga Zapert, a vice president, at Harris Interactive, also in New York City.

DOI 10.1377/hlthaff.25.w555 ©2006 *Project HOPE–The People-to-People Health Foundation, Inc.*

Sandia National Laboratories is a multi-program laboratory operated by Sandia Corporation, a wholly owned subsidiary of Lockheed Martin company, for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000. SAND2010-2304P. Designed by the Sandia Creative Group.
(505) 284-3181. SP•144947•04/10