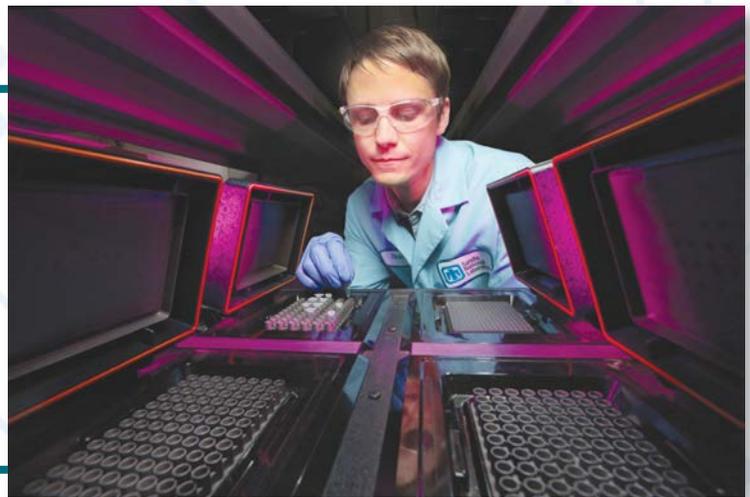
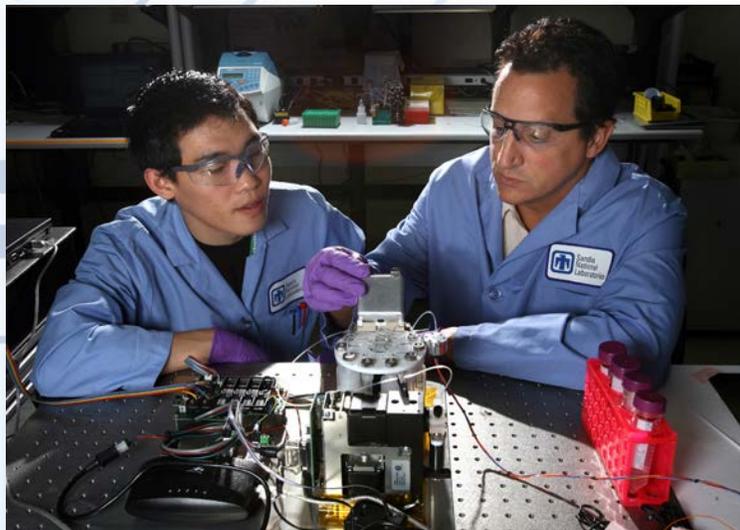


Microfluidics Issue

SANDIA'S INNOVATION MARKETPLACE

A Quarterly Update of Available Technologies for Industry



November 2016 • Vol 3, Issue 4

Welcome to Sandia National Laboratories' Intellectual Property Magazine

Sandia's Innovation Marketplace is a quarterly magazine published by Sandia National Laboratories. This publication highlights exceptional opportunities for licensing Sandia's intellectual property, including patents, copyrights (generally software), trademarks, and mask works. Listings within should not be construed as an offer to license technology. All licenses are subject to negotiation and availability of the intellectual property for licensing. This publication is intended for indications of interest only.

Why Work with Sandia?

Leverage World-Class Technology and Research

For more than 60 years, Sandia has delivered essential science and technology to resolve the nation's most challenging security issues. A strong science, technology, and engineering foundation enables Sandia's mission through a capable research staff working at the forefront of innovation, collaborative research with universities and companies, and discretionary research projects with significant potential impact.

The Best and Brightest

In keeping with our vision to be the nation's premier science and engineering laboratory for national security and technology innovation, we recruit the best and the brightest, equip them with world-class research tools and facilities, and provide opportunities to collaborate with technical experts from many different scientific disciplines. The excitement and importance of our work, an exemplary work environment, partnerships with academia, industry, and government, and our record of historic contributions help us attract exceptional staff. Our employees are recognized by their professional peers for their outstanding contributions.



CONTACT US

To discuss licensing opportunities, please send inquiries to: ip@sandia.gov
Or for more information, visit our website: <https://ip.sandia.gov>

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Over 20 Years of Experience

Sandia National Laboratories has been working on the forefront of microfluidics device development for over twenty years. Our researchers have vigorously probed the physics of microfluidic transport and developed high performance transport-based microfluidic and nanofluidic systems. Sandia has an extensive microfluidic patent portfolio consisting of over 100 granted US patents and over 200 patent applications filed. We are actively seeking commercial partners interested in licensing opportunities to build upon these technologies and components developed at Sandia.

Goal: Inexpensively manufacture miniaturized devices for use in national security applications and broaden availability to consumers to test water or immediate environment. Better detectors for airborne toxins, rapid DNA analyzers for crime scene investigators, and new pharmaceutical testers for drug development are among the possible future uses of microfluidic devices.

Lab-on-a-Chip

Early research in lab-on-a-chip technology led the way for further advances in microfluidic device development here at the Labs. Miniaturizing sensing technologies allowed researchers to develop portable diagnostic devices that could test for trace amounts of chemicals using microsensors. Lab-on-a-chip technology was later integrated into Sandia's MicroChemLab™ and other portable diagnostic devices. Advances in chip performance allowed researchers to design better components to create a design for better, faster, cheaper chemical/biological analysis.

Designing Components for Faster, More Efficient Devices

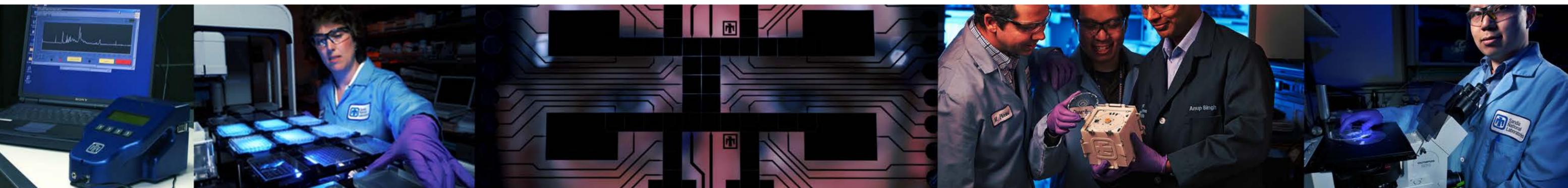
Sandia's extensive fabrication capabilities continue to enable further development of novel microfluidic devices. Sandia possesses the ability to design and fabricate complicated flow channels with embedded electrodes in glass, patterned monolithic porous polymers and post arrays within channels, and to employ deep reactive-ion etching, embossing, casting, and micro-injection molding to produce state-of-the-art microsystems with previously unachievable capabilities. Research is ongoing to explore a variety of manufacturing methods to improve performance and expand capabilities.

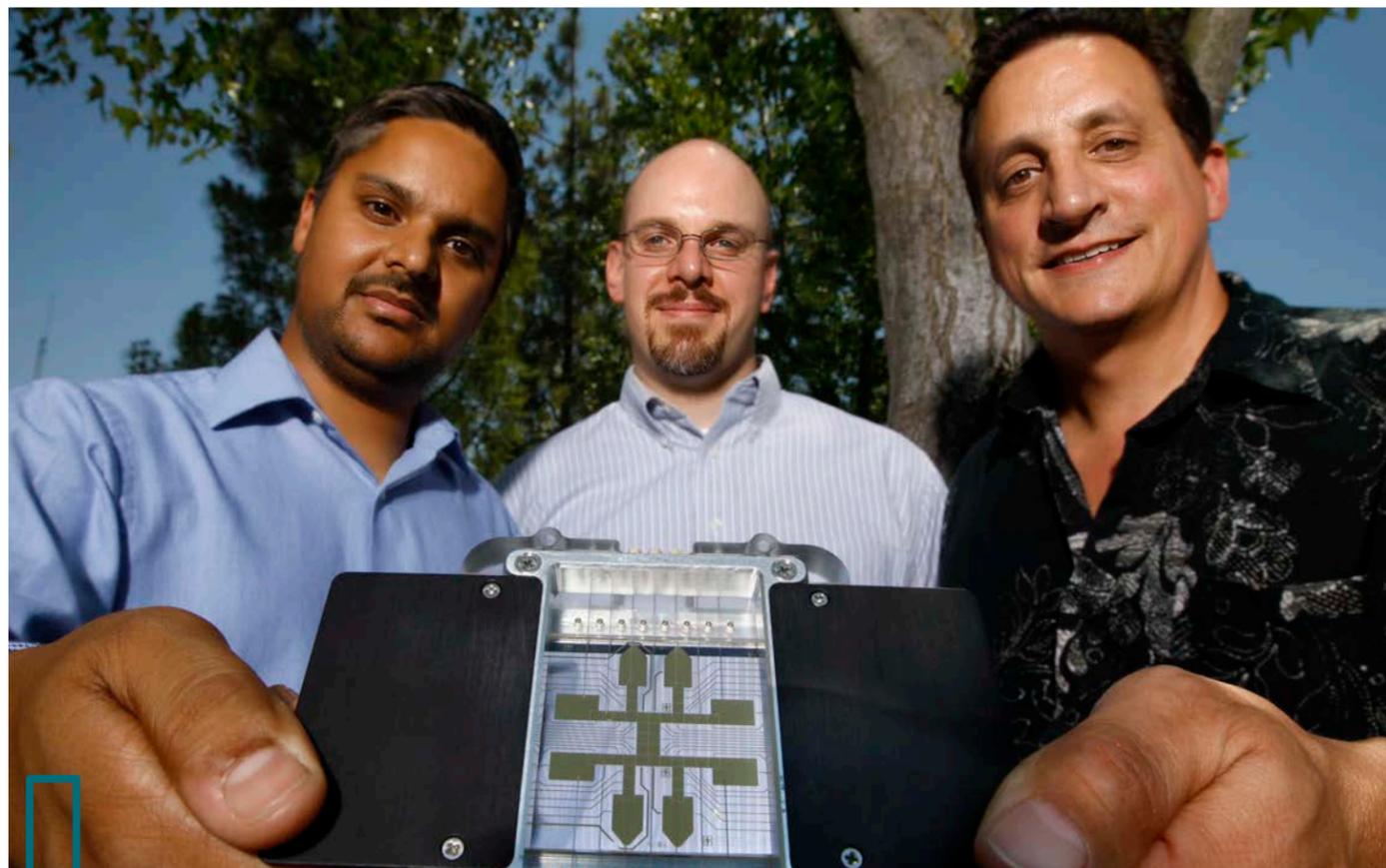
Multidisciplinary Approach

Sandia's ability to form and optimize multidisciplinary teams is a key enabler behind many of our high-impact solutions to the nation's most pressing security challenges. In keeping with this tradition, Sandia bioscientists work closely with experts in other science and engineering fields to expand capabilities for biological exploration. Drawing on their combined knowledge and ideas, teams work to translate their understanding into developing next-generation chemical and biological testing devices that push the limits of what is possible. **Explore some of the novel capabilities behind our powerful solutions.**

Capability Highlights:

- Sample concentration & efficient delivery to sensor chip
- Methods for mass manufacturing
- Methods for multiple fluidic connections
- Ability to increase number of external components—allowing for increased applications





Automated Molecular Biology Platform



The advent of next generation DNA sequencing (NGS) technology represents a quantum leap in the field of genetic analysis: what once required a decade-long, multibillion dollar Human Genome Project can now be reproduced in 1-2 weeks time for less than \$5,000. Despite advances in sequencing technology, upstream library (sample) preparation protocols, which require numerous sample processing steps and hours of hands-on laboratory time, have not benefited from comparable increases in speed or efficiency. While automation of the library preparation process can help overcome this widely recognized bottleneck, current approaches rely on large and expensive pipetting robots designed for use in dedicated high-throughput sequencing facilities.

To fully realize the promise of next generation sequencing for more ubiquitous, individualized, decentralized applications such as personalized genomic medicine, point-of-care diagnostics, public health screening, and DNA forensics, technologies automating NGS sample preparation must also become more affordable and accessible. To address this need, Sandia has developed an Automated Molecular Biology (AMB) system enabling the cost-effective automation of complex protocols like NGS library preparation and other labor-intensive bioanalytical procedures and processes.

The heart of the AMB system is a unique droplet-based digital microfluidic (DMF) platform which functions as a central hub for the distribution and routing of samples and reagents. Digital

microfluidic technology uses electrostatic and electrowetting forces to manipulate microliter-scale droplets sandwiched between closely spaced, hydrophobically coated substrates patterned with individually addressable electrodes. These devices enable discrete droplet movement and droplet operations such as merging, splitting, mixing, and aliquotting to be performed at scales much smaller than what can be conventionally achieved. Our DMF platform functions as a sample distribution and reagent interface hub and fills a role equivalent to that of a pipetting robot in a high-throughput laboratory automation workflow, but at a fraction of the size, cost, and complexity.

The central innovation of our digital microfluidic platform was the development of a custom manifold frame providing self-aligning registration of top and bottom DMF substrates to achieve the precise tolerances required for reliable DMF operation. The open architecture of the frame enables access to the interior of the DMF device by in-plane transfer capillaries. This capillary interface allows liquid to be transferred to and from the DMF device with nanoliter precision using external syringe pumps, providing not only a method for coupling the DMF platform to external modules, but also the means to execute a variety of advanced on-platform operations including serial dilution, droplet subsampling, chaotic mixing, fraction collection and sorting, magnetic bead manipulations, and sample archiving. The Automated Molecular Biology system is completed by integrating this adaptable digital microfluidic platform, its high-voltage control electronics, supporting syringe pumps, and functional submodules with a PC-based user interface enabling coordinated control and script-based automation of all sample preparation operations.

Technical Snapshot

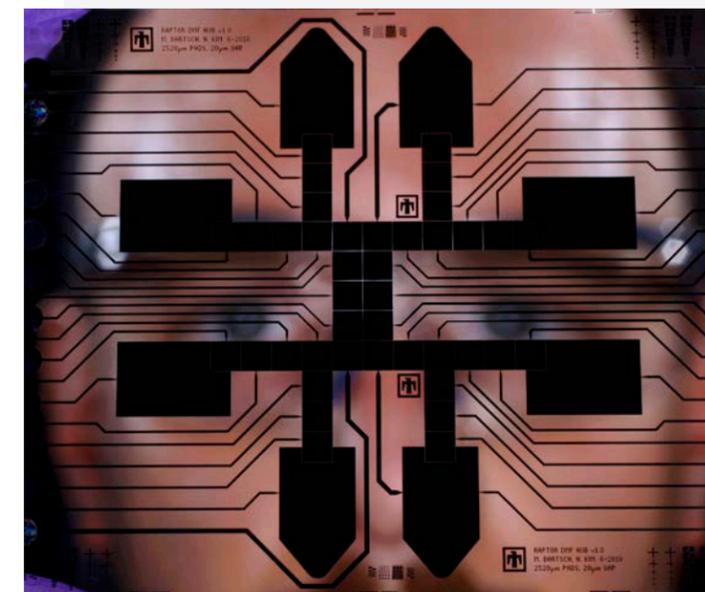
AMB functions as a router and separation and detection are almost always done off platform

Technical Benefits:

- Only microliter volumes are required for analysis
- Ease of sample preparation-fully integrated at a microscale all the steps necessary to automate and prepare DNA for sequencer
- A variety of diseases, infections, and intoxications can be diagnosed by switching antibody probes
- Designed for interconnectivity
- Operational flexibility

Key US Patents

8,940,147 Microfluidic hubs, systems, and methods for interface fluidic modules





MicroChemLab™

“Using the MicroChemLab™ will provide a way to bring the labs to the site and get results in a more timely manner.”
— Curtis Mowry, Principal Investigator, New Mexico MicroChemLab™ project

The MicroChemLab™ Bio Detector is a portable device for determining the presence of a target analyte and enabling fast microfluidic separations of biological samples with high sensitivity. The device miniaturizes bench-scale analyses using fabricated microchannels in a hand-held, low-power device. Many different separations

can be run simultaneously, and identification of the compound of interest is determined from unique retention-time signatures.

Designed for the rapid detection of proteins, the MicroChemLab™ has been used to identify biotoxins such as ricin, staphylococcal enterotoxin B, and

botulinum toxin; its capability has been extended in combination with innovative, automated sample preparation technology to enable the identification of viruses and bacteria. Parallel analysis channels provide highly accurate detection at nanomolar sensitivities with a low false alarm probability.

MicroChemLab™ consists of a preconcentrator unit that samples and collects analytes from an inlet gas sample stream and ejects them on command into the separation stage. The separation stage consists of a thin silicon nitride membrane supporting a patterned metal film heating element. The preconcentrator film is tailored to capture analytes of interest while allowing interferences to pass by. The suspended membrane structure of the preconcentrator gives it an extremely low heat capacity, which allows for very rapid heating. The application of a current pulse to the heater causes the film layer to heat rapidly and uniformly; this thermally desorbs the collected analytes in a narrow concentrated chemical pulse.

Built-in lasers and photodiodes read results in each channel. Its internal microprocessor then analyzes results. The microprocessor is easily programmed to detect certain analytes through a digital interface. An electrokinetic pump produces high pressure and significant fluid flow rates to route liquids through injection and separation without moving parts.

Originally developed for homeland security and defense applications, MicroChemLab™ has potential applications in a variety of different fields including: air and water quality, medical diagnostics, biotechnology, and industrial process controls.

Technical Snapshot

Method of separation: Gas chromatograph

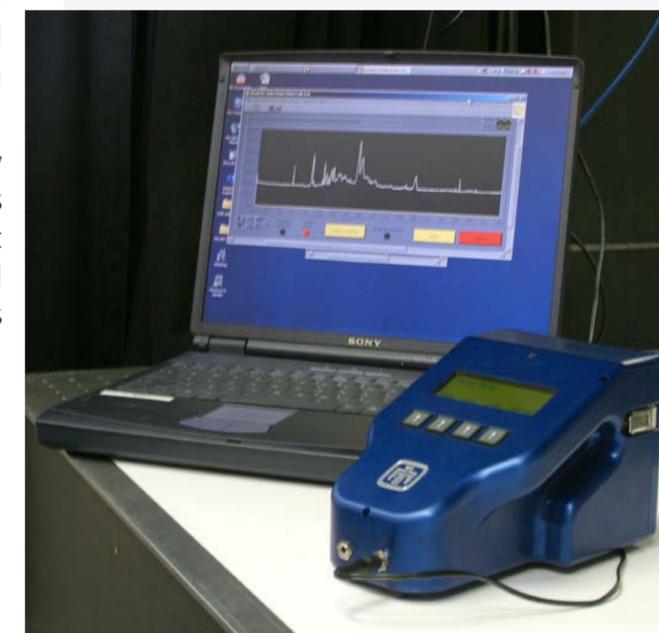
Method of detection: Chemically selective surface acoustic wave array or laser-induced fluorescence

Technical Benefits:

- Portable and easy to use
- Low power consumption
- Rapid analyses
- Highly accurate detection at nanomolar sensitivities
- Low false alarm rate

Key US Patents

7,012,342 Low Power, scalable multichannel high voltage controller





SpinDx™

SpinDx™ uses an innovative technique for conducting simultaneous multiplexed immunoassays and white blood cell counts from a single finger prick of blood (20-40 µL) with less than 15 minutes from sample to answer. Our technique is based on centrifugal microfluidics, or “lab-on-a-disk” technology, which uses centrifugal forces to manipulate samples and reagents through microfluidic channels implanted on disks that are of the same size as a standard CD or DVD.

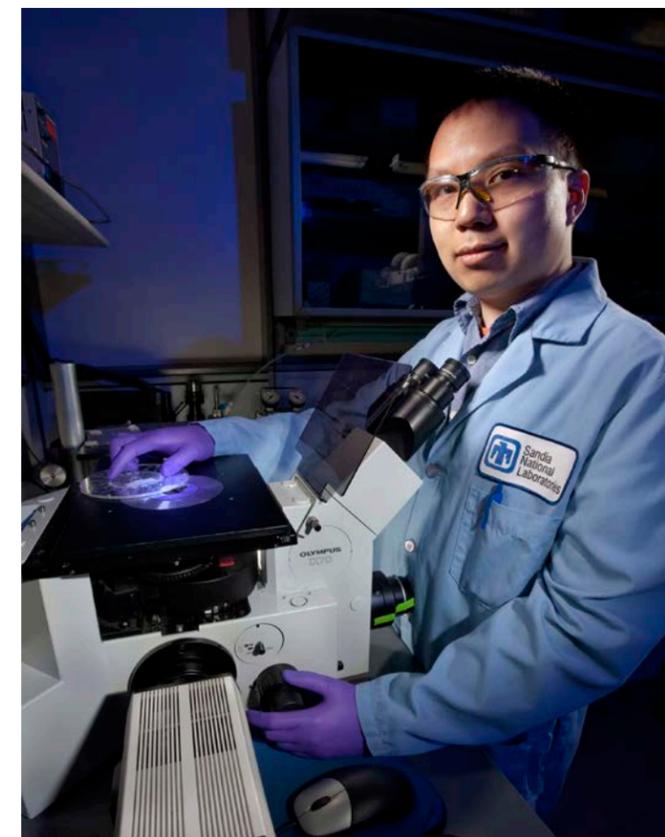
The fully-integrated, portable SpinDx™ prototype was developed as a user-friendly sample in,

answer out functionality. The system uses a touchscreen control pad for assay operation and result dissemination. Samples are self-collected and loaded onto the device using standard capillary collection tubes. Miniaturized fluorescence optics are used for detection. Optional wireless data transmission can be added for remote and point-of-care testing applications.

Detection is achieved with a novel bead sedimentation immunoassay scheme. The sample is mixed on-disk with a detection cocktail consisting of a) capture beads coated with antibodies specific

for the target(s) of interest, and b) detection antibodies labeled with a fluorescent tag, which will be bound to the capture bead in the presence of the corresponding antigen. Following incubation, the beads are removed from the sample via sedimentation by washing the beads to remove any interferences as the beads stack at the end of the channel. The fluorescent signal of the resulting bead pellet is used to quantify the analyte present. Single channel multiplexing is achieved using beads of different size/density for individual targets.

SpinDx™ was developed to be faster, less expensive, and more versatile than similar diagnostics tools. It was designed to handle a wide range of substance viscosity, allowing for expansion into a variety of different applications such as food safety. SpinDx™ has the potential to be a useful tool in a variety of different applications.



Technical Snapshot

Method of separation: Centrifugal microfluidics

Method of detection: Sedimentation immunoassay scheme

Technological Benefits:

- Less than 15 minutes sample-to answer
- Less than 20µL whole blood input (finger puncture)
- Inexpensive disk fabrication with pre-loaded reagents for off-the-shelf processing
- Multiplexed immunoassays- up to 64 parallel assays from a single sample
- Leukocyte counts/differentials combined with proteomic detection
- Based on well-established principles requiring unsophisticated instrumentation
- Custom applications: assay disks developed for certain testing areas
- Easy-to-use: does not require specialized training for operation

Key US Patents

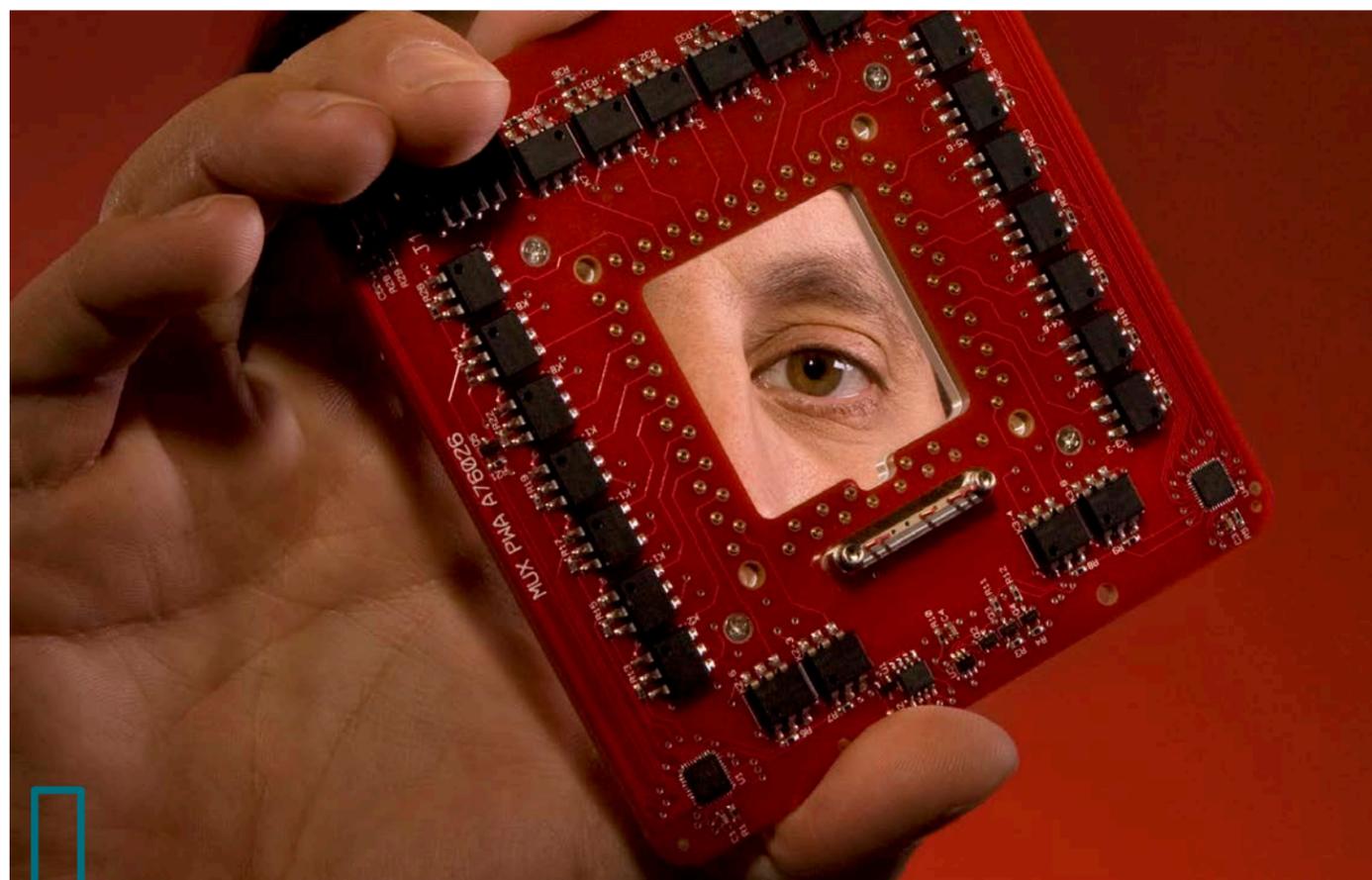
9,186,668 Microfluidic devices, systems, and methods for quantifying particles using centrifugal force

8,945,914 Devices, systems, and methods for conducting sandwich assays using sedimentation

9,244,065 Systems, devices, and methods for agglutination assays using sedimentation

8,962,346 Devices, systems, and methods for conducting assays with improved sensitivity using sedimentation

“In doctor’s offices, time is money. Patients have become accustomed to an initial visit, some tests, samples that are sent off to a far-away lab, a wait of a week or more for results, more tests and charges every step of the way. With SpinDx™ you can see results before you even leave the office.”
—Anup Singh, Director Biological & Engineering Sciences



RapiDx™

“Toxins are often only present in the blood in trace amounts that disappear, by tissue uptake for example, so there is a limited window of time in which to detect them. Rapid detection offers a better prognosis for those exposed, as therapeutics are most effective within the first day or two after exposure.”
—Duane Lindner, Director Homeland Security & Defense Systems

The Rapid Automated Point-of-Care System (RapiDx™) developed by Sandia is a portable diagnostic instrument that can measure biomarkers linked to injury, disease, or infection. RapiDx™ is an ideal instrument for point-of-care diagnostics of disease and toxin detection in health clinics and in the field, allowing medical professionals the ability to treat ailments and diseases quickly.

Built on Sandia's advancements in lab-on-a-chip technologies, RapiDx™ requires mere microliters

of a sample to measure protein signatures. With RapiDx™, drawing tubes of blood is no longer required. Samples can be collected and analyzed at the point of care, thereby enabling low-cost, rapid diagnoses during an office visit. RapiDx™ can also be used to address bioterrorism threats. If a crowd is exposed to dangerous biotoxins, potentially exposed persons can be triaged rapidly with RapiDx™. Timely treatment—critical in such an event—also conserves valuable health resources (e.g., hospital beds, prophylactic supplies).

The heart of the device is a microfluidic chip that, in a few short minutes, concentrates and separates biological components of blood, saliva, or other bodily fluids prior to sensitive (low- to sub-picomolar detection limit) laser-induced fluorescence detection of the fractionated components using only a few microliters of the biological sample. The microfluidic chip houses microchannels that are 20-40 micrometers deep, 100 micrometers wide, and a few centimeters long (similar in scale to human hair). Multiple biomarkers (up to 64) are screened simultaneously by radially positioning multiple individual assay configurations within the microfluidic chip. The chip is integrated with miniaturized electronics, optical elements, fluid-handling components, and data acquisition software to provide a portable, self-contained device.

Numerous sample manipulation steps are required to complete detailed proteomic analyses. Seamless integration of these steps—sample preparation, mixing, and biomarker identification—is made possible using cast-in-place nanoporous polymeric gels fabricated within the microchannels using a photopolymerization process adapted from the semiconductor industry. Gel photopolymerization is a rapid, light-induced reaction that converts a liquid monomer into a solid polymer gel. Advantages of this process include the ability to confine the polymerization reaction to localized regions of the microchannels, and the ability to customize the gel properties by varying the composition of the monomer solution. Seamless integration of all functions required for biomarker identification, as described here, significantly improves the sensitivity of the system and also eliminates precious sample loss that can plague conventional biomarker detection methods.

Technical Snapshot

Method of separation: Cast-in-place nanoporous polymeric gels within microchannels

Method of detection: Gel photopolymerization

Technical Benefits:

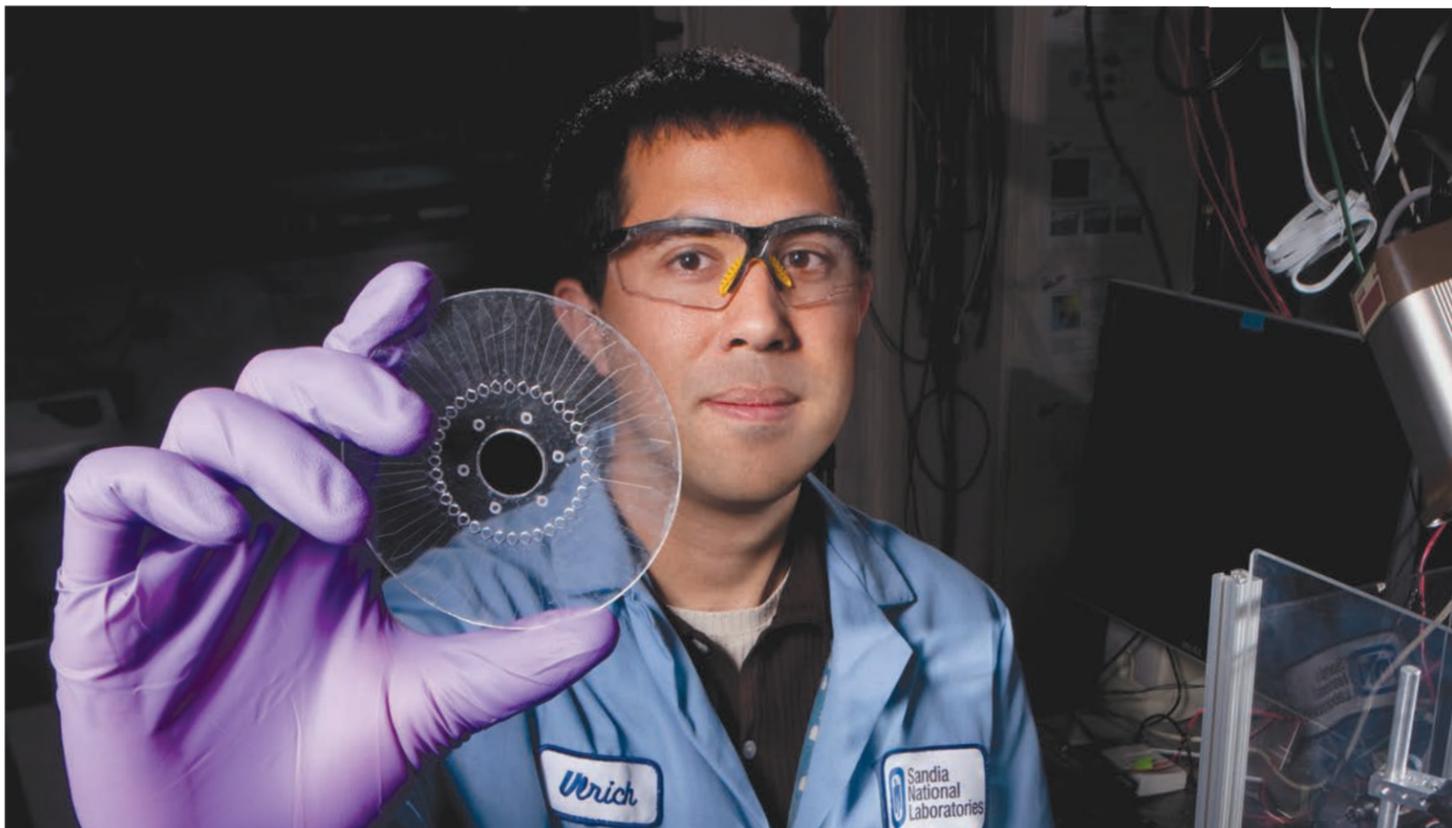
- Only microliter volumes (e.g., a small droplet of saliva or blood) are required for analysis
- Multiplex: A panel of up to 64 analytes can be analyzed simultaneously for accurate assessment
- A full panel of analytes can be measured within 10 minutes. Results can be obtained during a routine clinical visit
- Low-abundance markers and trace amounts of deadly toxins can be detected by sample preconcentration
- RapiDx™ is adjustable over several orders of magnitude by timing each preconcentration step
- Portable and easy to use
- Low cost
- A variety of diseases, infections, and intoxications can be diagnosed by switching antibody probes

Key US Patents

8,961,766 Microchannel gel electrophoretic separation systems and methods for preparing and using

9,201,069 Devices, systems, and methods for microscale isoelectric fractionation

8,728,290 Microfluidic device having an immobilized pH gradient and PAGE gels for protein separation and analysis



Sandia National Laboratories has been working on the forefront of microfluidics device and component development for over twenty years and has amassed a sizable patent portfolio, a portion of which is now available for licensing as a bundle of 50+ patents for one simple fee. To further Sandia's goal of disseminating and transferring taxpayer-funded technology into the private sector, this bundle is offered for non-exclusive licensing with an up-front fee of \$25,000 and nominal periodic maintenance fees.

The inventions, devices, and methods comprising this intellectual property bundle were primarily developed in support of Sandia's national security mission in chemical and biological defense, and as such, reflect an emphasis on compact, portable form factors and the low power and high reliability needed for extended field deployment. These bundled patents largely fall under three broad categories: chip-based devices and diagnostics, microfluidic interconnects and interfaces, and materials and fabrication methods. Licensed together, the contents of the bundle represent a broad-based suite of building blocks offering particular benefit to applications including laboratory automation, chemical and biological sample preparation and purification, separation science, analytical chemistry instrumentation, material synthesis, system integration, and biomedical diagnostics.

Bundled patents include a number of capillary microfluidic valves and fittings, a unique digital microfluidic interface, methods for producing axisymmetric coaxial flow fields in a chip-based format.

Also featured are interconnect devices which offer several components that can act as manifolds, check valves, or ultra-high pressure pumps. These can be used to construct devices that change the flow rate of the material and sample to detection units—including laser induced fluorescence, mass spectroscopy detectors, and flow cytometry. The fabrication materials and technologies allow the connections between microfluidic devices and external components while increasing the number of functional components that can be connected to a microfluidic device.

Sandia National Laboratories does not sell its products and relies on licenses like this to commercialize its technology into unique devices that reflect an emphasis on portability and reliability.

Special Licensing Opportunity: 50+ Microfluidic Patents for 1 Flat Fee of \$25,000.00

(patents included in bundle listed below)

US Patent #	Title
9,409,357	Devices, systems, and methods for microscale isoelectric fractionation
9,404,913	Micropores and methods of making and using thereof
9,190,736	Fabrication of small-scale structures with non-planar features
8,940,147	Microfluidic hubs, systems, and methods for interface fluidic modules
8,871,496	Methods, microfluidic devices, and systems for detection of an active enzymatic agent
8,808,588	Methods for integrating a functional component into a microfluidic device
8,703,058	Microfluidic devices and methods including porous polymer monoliths
8,563,325	Coaxial microreactor for particle synthesis
8,394,312	Method for forming polymerized microfluidic devices
8,163,254	Micromanifold assembly
8,047,829	Method for forming polymerized microfluidic devices
7,999,937	Microfluidic devices and methods for integrated flow cytometry
7,710,086	Modular high voltage power supply for chemical analysis

Click on patent numbers for more information

US Patent #	Title
7,625,474	Method for a microfluidic weaklink device
7,553,455	Micromanifold assembly
7,534,334	Apparatus and method for concentrating and filtering particles suspended in a fluid
7,527,977	Protein detection system
7,494,557	Method of using sacrificial materials for fabricating internal cavities in laminated dielectric structures
7,488,407	Castable three-dimensional stationary phase for electric field-driven applications
7,452,507	Portable apparatus for separating sample and detecting target analytes
7,400,119	Modular high voltage power supply for chemical analysis
7,390,377	Bonding thermoplastic polymers
7,384,526	High-pressure microhydraulic actuator
7,351,380	Microfluidic structures and methods for integrating a functional component into a microfluidic device
7,348,688	Low power, scalable multichannel high voltage controller
7,314,208	Apparatus and method for selectively channeling a fluid
7,246,524	MEMs fluidic actuator
7,182,371	Edge compression manifold apparatus
7,161,334	Modular high voltage power supply for chemical analysis
7,094,326	Electrodes for microfluidic applications
7,022,381	Method for producing high dielectric strength microvalves
7,012,342	Low power, scalable multichannel high voltage controller
7,004,198	Microfluidic interconnect
6,994,826	Method and apparatus for controlling cross contamination of microfluid channels

US Patent #	Title
6,988,402	Mobile monolithic polymer elements for flow control in microfluidic devices
6,952,962	Mobile monolithic polymer elements for flow control in microfluidic devices
6,846,399	Castable three-dimensional stationary phase for electric field-driven applications
6,833,068	Passive injection control for microfluidic systems
6,821,819	Method of packaging and assembling micro-fluidic device
6,797,187	Surface-micromachined microfluidic devices
6,782,746	Mobile monolithic polymer elements for flow control in microfluidic devices
6,772,513	Method for making electro-fluidic connections in microfluidic devices
6,770,182	Method for producing a thin sample band in a microchannel device
6,733,730	Method and apparatus for reducing sample dispersion in turns and junctions of microchannel systems
6,599,436	Formation of interconnections to microfluidic devices
6,548,895	Method of packaging of electro-microfluidic devices
6,537,437	Surface-micromachined microfluidic devices
6,443,179	Packaging of electro-microfluidic devices
6,428,666	Electrokinetic concentration of charged molecules
6,287,440	Method for eliminating gas blocking in electrokinetic pumping systems
6,277,257	Electrokinetic high pressure hydraulic system
6,210,986	Microfluidic channel fabrication method
6,019,882	Electrokinetic high pressure hydraulic system

For additional licensing opportunities, please contact: ip@sandia.gov

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Intellectual Property Creation & Licensing Practices

INTELLECTUAL PROPERTY CREATION

Sandia's intellectual property results primarily from R&D conducted for the government in the national security sector. Our laboratory collaborates with industry, leveraging different strengths to develop innovative technology. We perform internal R&D directed at the most challenging issues in national security, for which breakthroughs would provide exceptional value to government and industry. All totaled, Sandia has more than 1600 patents and 550 commercial copyrights, the bulk of which are available for licensing.

LICENSING SANDIA'S INTELLECTUAL PROPERTY

Sandia's intellectual property may be licensed for commercial use (internal or commercial sale), test and evaluation, or execution of a government contract. One may also secure an option on a future license. Example licenses include:

- Commercial Patent License
- Commercial Copyright License (software or design plans)
- Commercial Hybrid License (copyright and patent)
- Test and Evaluation License
- License Option
- Government Use Notice

Sandia is mandated by the Department of Energy to move its technology to the marketplace for the benefit of the U.S. economy. Given our national security focus, government is the primary customer for many Sandia licensees, but our technologies also find use in the industrial and consumer markets. Sandia issues licenses to companies ranging in size from start-ups to multinationals. Our qualification procedure considers a company's ability to bring a product to market as conveyed by their business plan, among other factors. The possibility to create a new company that can leverage our technology and achieve substantial growth remains an area of significant interest for Sandia.

Sandia's

INNOVATION MARKETPLACE

A QUARTERLY UPDATE OF AVAILABLE TECHNOLOGIES FOR INDUSTRY

To discuss licensing opportunities, please send inquiries to: ip@sandia.gov
Or for more information, visit our website: <https://ip.sandia.gov>

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