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Opportunity Assessment
Prepared for NASA Jet Propulsion Laboratory

NPOs 30158, 30338, 30562, 30563: Piezoelectric Microvalves

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Executive Summary

Background

NASA Jet Propulsion Laboratory (JPL) requested National Technology Transfer Center (NTTC) to perform an Opportunity Assessment for four closely related inventions:

- NPO-30158, Normally closed, sealing enhanced MEMS-based micro valve with a piezoelectric stack actuator.
- NPO-30338, Micro valve for high-pressure applications.
- NPO-30562, An improved design of micro valve actuated by miniaturized piezoelectric stack for high-pressure liquid system applications.
- NPO-30563, A high stroke micro valve actuated by miniaturized piezoelectric bender actuator for miniaturized liquid systems with particulates.

The information technical and market-based judgments presented in this report are based on the invention disclosures received from JPL and on materials discovered in secondary research. NTTC reported its preliminary findings in a Technology and Market Overview previously submitted to JPL.

JPL provided the New Technology Reports and accompanying attachments for the four subject technologies as input to the study.

JPL seeks partners to support further development of its microvalve technologies. A technology and market overview conducted by NTTC determined that the technology was viable and recommended further investigation to identify potential partners. Thus the goal of this opportunity assessment is to identify and qualify companies active in the application areas identified in the overview.

Findings

- The subject technologies are a novel approach to fabrication of microvalves. Their technical capabilities provide leak-tight and high pressure capabilities not possessed by other technologies.
- Due to a lack in the public domain of specifications of the microvalve needs of the various potential applications, the identification of candidate companies was done pursuant to the applications suggested by the inventor.
- The microvalve industry is now in its second generation of development. Many of the first-generation concepts proved to be too impractical or too costly for successful commercial application.
- The subject technology is an enabling technology for some emerging microfluidics markets. Specific technical requirements for each market application need to be identified and compared with the subject technologies' potential capabilities.
- Initial markets for the subject technologies include: precision gas and chemical flow control for the semiconductor manufacturing market, precision dispensing for the life sciences market, and microvalves for the micro total analysis system market.

- Companies that may be interested in the subject technology include: major valve manufacturers, microvalve manufacturers, microfluidic components and systems manufacturers, and fabricators of microfluidic components.
- A search of available patents and patent applications indicates that the subject technologies currently do not have patent protection.

Recommendations

NTTC recommends that NASA establish an Intellectual Property (IP) position, through patent applications or non-disclosure agreements, prior to disclosing information about the subject technology. After the IP position has been established, then multiple field-of-use joint development partnerships or licenses be pursued using a tiered contact approach in the following applications:

- Gas and chemical flow control for semiconductor manufacturing market
- Precision dispensing for the life sciences market
- Microvalves for the micro total analysis system market.

Partnership candidates are listed in Appendix A, with contact information.

In the event that partnerships and/or licensing are to be pursued, only U.S. owned companies or companies having significant manufacturing presence in the U.S. are to be approached. The client would need to determine whether the U.S. manufacturing presence of multinational companies is sufficient to allow partnering for technology transfer purposes.

NOTE: NTTC ADVISES THE CLIENT TO PLACE IN THE FEDERAL REGISTER A NOTICE OF INTENT TO LICENSE THIS TECHNOLOGY AS REQUIRED BY 35 U.S.C. 209(e) IF A LICENSING ALTERNATIVE IS TO BE PURSUED.

Technology Overview

Background and Methodology

The technical portion of this opportunity assessment had as its initial goal to summarize the capabilities of the subject technologies and determine their capability to meet the requirements of various applications in which microvalves are or may be needed, for the purpose of limiting the list of companies who might need microvalve technology to those most likely to need the specific capabilities of the subject technologies. In the pursuit of this goal it was determined that there is a lack of information in the public domain that addresses the technical requirements of the various applications for microvalves, making it impractical to make accurate determinations of the suitability of any type of microvalve for specific applications. Consequently, the technical section of this opportunity assessment will focus on reviewing the capabilities and limitations of the subject technologies in comparison to other types of microvalves.

Description of the Subject Technology

Microvalves are small devices that stop or control the flow of a fluid. They typically have physical dimensions of less than a centimeter. Valves may be either active (where the state of the valve is controlled by an external stimulus) or passive (such as a check valve where the state of the valve is determined by the flow of the fluid). The subject technologies are active microvalves whose output can be controlled by how much voltage is applied to the valve actuator.

The four subject technologies are all designs for fabricating a microvalve using MEMS processing and all are closely related, the most recent two being practical improvements on the oldest two. The four subject technologies share in common the following:

- Fabricated in part by MEMS processes – the piezoelectric actuator is separately constructed and then is bonded to the rest of the valve body, which is fabricated using MEMS processes.
- Design featuring use of applied pressure to increase the sealing force.
- Design optimized for high-pressure operation.
- Narrow-edge, multiple concentric circles valve seat design and soft material valve body design to minimize leakage otherwise caused by particulates.
- Microvalve is normally off.
- Piezoelectric actuation which inherently provides:
    a. Fast response times – less than 50 milliseconds.
    b. Low-power operation – 3 milliwatts at DC operation; 100 milliwatts at 100 cycles per second.
    c. Flow control – valve opening controlled by voltage applied to actuator.

The oldest of the subject technologies (NPO-30158 – Normally closed, sealing-enhanced MEMS-based micro valve with a piezoelectric stack actuator, 20 February 2001) provides a design of the valve seat that minimizes leaks at high pressure.

The second oldest (NPO-30338 – A micro valve for high pressure applications, 1 August 2001) is merely an update of the oldest, disclosing some of the progress in the earlier design and, specifically, disclosing a new valve seat design that reduces leakage. These two microvalves are designed for use with gases.

The third technology (NPO-30562 – An improved design of micro valve actuated by miniaturized piezoelectric stack for high pressure liquid system applications, 25 February 2002) is optimized for low-flow, high-pressure liquid applications and the fourth is optimized for moderate-pressure, higher flow liquid applications or for liquid flow with larger particulates. This technology refines the design of the piezoelectric stack actuator such that it may be bonded to other elements of the system using MEMS manufacturing techniques, enhancing its value by enabling low-cost manufacturing of large numbers of integrated systems. The piezoelectric actuator is operated in longitudinal contraction mode (d_{31} mode). This permits the actuator to be electrically isolated from the liquid without placing a dielectric coating on the actuator. This technology also claims the use of a microneedle-type flow channel to connect the valve with external components such as flow test systems.

The fourth (NPO-30563 – A high-stroke microvalve actuated by a miniaturized piezoelectric bender actuator for miniaturized liquid systems with particulates, 25 February 2002) discloses a different design for the piezoelectric actuator that provides larger strokes for the valve (~15 microns) to allow use with fluids containing suspended particles whose diameter is as large as 10 microns. The bender actuator also is smaller than the stack actuator but generates significantly less force.

Thus the bender actuator is not suitable for high-pressure microthruster applications but would be a preferred design for other applications requiring higher flow rates or for liquids containing suspended particles. Lower pressure microthrusters have recently been designed. In addition, the moderate-pressure, higher-stroke, larger-opening design of the bender actuator is typically more suitable for the other applications noted below.

Technical Merit

Stage of Development

The valves optimized for gas flow (NPO-30158 and NPO-30358) are at NASA Technology Readiness Level (TRL) 4 (component and/or breadboard validation in laboratory environment). The liquid flow versions (NPO-30562 and NPO-30563) are at TRL 2 (technology concept and/or application formulated).

Applications

The non-aerospace applications listed in the New Technology Reports for gas (NPO-30158 and NPO-30358) or liquid (NPO-30562 and NPO-30563) flow microvalves include the following:

- Semiconductor manufacturing – precision control of chemical gas flow. For application in semiconductor processing, MEMS-based systems are predicted to make "dramatic changes in semiconductor processing" (Henning et al. 1998). Specifically, Henning states that there is a need for a low-flow mass controller built of modules including normally closed, low leak-rate shut-off valves. The subject technologies, particularly NPO-30338, meet this requirement.
- Biological and chemical monitoring systems (miniature chemical labs/lab-on-a-chip or micro total analysis systems) for in-situ analysis (e.g., for detection of biological and chemical weapons or other pollutants). In these applications "molecules rather than electrons flow through labyrinths of tiny channels and chambers outfitted with valves, filters and pumps" (ORNL undated). The performance of the subject technology should make it a good candidate for the valves that control the flow of these molecules.
- LIGA gas chromatograph/mass spectrometer. LIGA is a German-invented process combining x-ray lithography, electroforming, and molding to produce parts of high precision. The subject technologies are compatible with LIGA and could be used in the microfluidics that feeds samples into the gas chromatograph/mass spectrometer.
- Miniature dosing systems – Miniature dosing pumps are used for pumping flavorings, chemical reagents, solvents, inks, dyes, and cleaning agents. The subject technology provides microvalves that could be used with these materials for precise dosing. Reference was also found to miniature dosing systems for implantation in veins.
- Micro cooler – Development of fluid micro coolers for cooling electronics is underway at several locations including Microflux, Inc., Stanford University (AFRL 2002), the University of California at Berkeley (Kirshberg, Liepman and Yerkes 1999), and Universiteit Twente (ter Brake 1999). All are developing MEMS-based fluid systems. Microvalves will be needed for temperature control and integration with other subsystems.
- Miniature liquid sample collector – Microvalves will have application in microfluidic devices to sample a variety of substances. OraSure is partnered with the University of Pennsylvania to develop a microfluidic sampler for oral fluid diagnostics (OraSure 2003). Sandia National Laboratories and Harvard Thermal Inc. collaborated to develop a microhotplate for a microfluidic sample collector to submit concentrated analyte to a gas chromatograph. (Mamginell 1999).
- Micro-fuel cell/bioreactor – Miniaturized fuel cells are being touted for the power supply for portable electronics. The National Research Council of Canada – Institute for Fuel Cell Innovation has developed a piezoceramic microvalve for use in micro fuel cells (Rahbari 2004).

- DNA sequencing and cell sorting. In her PhD research at the California Institute of Technology, Anne Fu developed a microfluidic cell sorter using microvalves (Fu 2002). The approach replaced electrokinetic-driven flow with pneumatic actuation control. A review of several papers on miniaturizing DNA sequencing found no references to a need for valves. However, it is speculated that microvalves may be needed for integration of a DNA sequencer with other modules of a fully integrated system.
- Fluidic MEMS in general – wherever a precise amount of fluid is required. The characteristics of an application that should consider the subject technologies for its microvalves include:
    - Needs or uses an external supply of pressure to move the fluid (50-1000 psi).
    - The microvalves are needed as part of a control system (active control as opposed to passive check valves).
    - Needs microvalve off when no voltage is applied.
    - Microvalve must be leak tight (5×10^{-3} sccm at 800 psi for gas microvalve).
    - Maximum flow rate less than 52 sccm at inlet pressure of 300 psi.
    - Needs precise control (valve actuation speed of 50 Hz).
    - Needs small valve size (0.1 cm^3).
    - For use with liquids, particulates whose size is less than 10 microns may be present
    - Low power draw (0.1 W at 100 Hz)

Technical Advantages

Performance

In comparison with non-piezoelectric microvalves and conventionally machined miniature valves, all four-subject technologies provide the following general performance advantages:

- Operates over a wide range of pressures – most existing applications for microvalves function at 50 psia or less – the subject technologies are capable of much higher pressures. Microfluidic devices require high pressure to move fluids through narrow microchannels at reasonable flow rates.
- Repetition rates of 100 Hz or greater – fast compared to thermo-mechanical actuators. The subject technology is comparable in speed to electrostatic actuators but provides much greater actuation force.
- Low leakage rates via enhanced sealing design especially at high pressure (5×10^{-3} sccm at 800 psi). Many other microvalve technologies have comparatively high rates of leakage.
- Valve seat of multiple narrow edge rings to enhance sealing and reduce leak rates.

- The narrow edge of the valve seat reduces the number of particulates that get trapped between valve seat and boss. The multiple rings prevent leaking by providing redundancy so that a leak in one seal ring does not permit the entire valve to leak.
- Valve boss coated with flexible elastomer to enhance sealing by permitting particulates to embed in the elastomer – a feature that further increases the resistance to leakage.
- 10-15 micron valve opening, enabling flow of 10 micron suspended particulates (NPO-30563 only). A design compromise to provide greater flow rates where high-pressure resistance is not required.
- Low-power operation – 0.1 W at 100 Hz. Power consumption is lower than for shape memory alloy and thermopneumatic actuation.
- Small size and weight – valve body on the order of 0.1 cm^3.

In comparison with other piezoelectric microvalves the valve seat design of the subject technologies provides greater resistance to leaking, with or without particulates in the flow.

Manufacturing Process

The subject technologies are fabricated by bonding custom-designed piezoelectric actuators (either stack or bending) onto micromachined silicon formed via MEMS processing. This leads to the low power and small size noted earlier. The most challenging part is bonding the piezoelectric actuator to the rest of the valve body, which is fabricated using MEMS processing. The alignment must be very precise in all three dimensions for the valve to function properly and the pin that performs the sealing must lift up and then reseat properly as the actuator is turned on and then off. Tests indicate success of the concept, and laboratory results prove feasibility.

Technical Advantages for Commercialization

For semiconductor processing, as noted earlier, a need exists for normally closed gas microvalves to control the flow of dry-etch gases. Such a microvalve could be a component of pressure-based mass flow controllers, vacuum leak-rate shut-off valves, and pressure regulators (Henning et al. 1998a). Of all the applications herein listed, this appears to be the area where the subject technology has greatest advantage over other microvalves and alternative methods.

For application to lab-on-a-chip and micro total analysis systems, the most significant advantage of the subject technologies is its low leak rate at high pressures. Forcing liquids through microchannels at reasonable rates requires high pressure, and most competing technologies have not demonstrated acceptable leak rates.

In the area of chemical and biological monitoring systems for both medical and environmental applications, the need exists in lab-on-a-chip and micro total analysis systems for microvalves to collect, direct, or dispense minute quantities of liquids from point to point within the chip, e.g., mixing test sample liquids with reagents. Included in the functions that will be reduced to lab-on-a-chip are mass spectroscopy, polymerase chain reaction, DNA sequencing, Southern blots, 2-D gel separations, ELISA assays, chromatography, and flow cytography (Graham 2002).

The subject technologies, particularly NPO-30563, will meet the precision flow control criterion and thus should be a good candidate for these applications.

For medical applications such as DNA sequencing and cell sorting, particulates on the order of 5-10 microns are present in the flow. The valve seat and boss design of NPO-30563 specifically accommodates such particles by making it difficult for them to stick on the valve seat and create leak paths.

For general microfluidic commercialization purposes, the most significant of the subject technologies' advantages are the combination of the low-power operation, the small size, and the lower cost associated with partial fabrication using established MEMS processes, although the actuator must still be made using traditional machining processes. The low power permits longer battery life or a smaller battery for battery-operated applications. MEMS processing, which enables low-cost production and small size, has advantage in many applications. The bender actuator of NPO-30563, which increases stroke to permit higher flow rate and larger particulates, will be the specific design of greatest interest to commercial markets.

Technical Limitations

Performance

The subject technologies are limited in flow rate by the relatively small stroke that is possible with piezoelectric actuators. The bender actuator of NPO-30563 is designed to improve the valve stroke to 10 microns at supply pressures of 50 psi, but sacrifices maximum pressure capability to achieve higher stroke. Lower-pressure operation may lead to higher leak rates, since the pressure of the source fluid is used to increase the sealing force. A piezoelectric bender actuator provides a larger displacement and lower force than piezoelectric stack actuators.

The actuation voltage (150 VDC) to achieve the high stroke and flow rate is significantly higher than that needed for operation of semiconductor electronics.

The operating pressure range is too low for microfluidic liquid chromatography, where pressures on the order of 10,000 psi are envisioned to speed analysis.

Manufacturing Process

The actuator is made by traditional machining processes and must be bonded to the rest of the valve, which is made using MEMS processes.

Technical Barriers to Commercialization

The primary technical barrier to commercialization is competing technology. The field of microvalve development is crowded with competitors and different approaches, many of which have not been successful. According to Michael J. Felton, editor of *Analytical Chemistry*, "Microfabricated valves were once expected to open the floodgates for development of labs on chips; they have not, but the second-generation devices are finally making it outside academia." (Felton 2003).

As described in the Technology and Market Overview previously, several others are working to develop piezoelectrically actuated microvalves. Likewise, other methods of actuation are being developed for the same applications that are listed as being appropriate for the subject technologies. Some use electrokinetic methods to move liquids through microchannels. Electrokinetic pumping eliminates the need for valves to control the flow. Similarly, the use of passive check valves with pumps competes with the method of generating a pressure and using active valves to control the flow.

And some applications for which microvalves were originally seen as perfect are now handled in other ways (Felton 2003).

The competing technologies for control in microfluidics include:

- Other piezoelectric MEMS microvalves.
- Other methods of MEMS microvalve actuation (electrostatic, electromagnetic (solenoid), thermopneumatic, shape memory alloys, bimetallic).
- Passive valves (pumps with check valves).
- Non-mechanical pumping (electrokinetic or electroosmotic).

Given the wide range of approaches, each with its own advantages and disadvantages, and with little published on the technical requirements of each application, it is not clear at this point which technology will be superior for each application.

Technical Findings

- The subject technologies are a novel approach to fabrication of microvalves. Their technical capabilities provide leak-tight and high-pressure capabilities not possessed by other technologies.
- Due to a lack in the public domain of specifications of the microvalve needs of the various potential applications, the identification of candidate companies was done pursuant to the applications suggested by the inventor.
- The microvalve industry is now in its second generation of development. Many of the first generation concepts proved to be too impractical or too costly for successful commercial application.
- A search of available patents and patent applications indicates that the subject technologies currently do not have patent protection.

Market Assessment

Introduction

The prior NTTC Technology and Market Overview report on the subject technologies identified a number of microvalve applications and manufacturers but did not evaluate them for partnership potential. The purpose of this Market Assessment is to identify companies that would be expected to have the greatest interest in further developing or licensing the subject microvalve technology.

Market Structure

The microfluidics marketplace is populated by vendors on at least three levels:

- Microvalve manufacturers.
- Microfluidic subsystems manufacturers, e.g., of precision dispensers.
- Systems vendors employing microfluidic components, e.g., for laboratory automation systems.

Both microvalve and microfluidics systems manufacturers supply broad fields of application, including:

- Precision gas or fluid (chemical) flow control for semiconductor manufacturing processes, particularly mass flow control for dry etch equipment.
- Precision dispensing (micro-dosing) for the life sciences market, particularly for the high-density microarray market.
- Biological and chemical monitoring and analysis micro-systems such as micro gas chromatographs.

Considerations

- The subject technology is potentially enabling for some emerging microfluidics markets. For example, the high-density microarray market has been limited by the precision of the dispensing apparatus. Piezo-jet technology currently in use has limited chip density to features greater than 100 microns. The subject technology may provide a solution capable of reducing the feature size.
- So-called valveless or virtual valves are under development for certain medical microfluidic applications. These should be considered competing methods rather than potential applications for the subject technologies.

Company information is provided in Appendix A. Appendix B provides inventor interview information.

Potential Partners/Licensees:

Companies listed in Appendix A have been selected according to the following criteria.

- Microvalve and valve manufacturers—companies whose valves are incorporated into the final products of other equipment manufacturers for a variety of markets.
    - Microvalve companies specifically have experience with microvalves and have a limited line of valves.
    - Major valve companies have extensive lines of valves that may include micro-sized valves and are expected to have microvalve development resources available. Valves currently are supplied to multiple equipment markets. Trends in markets such as chemical and gas analysis equipment would require these valve manufacturers to further miniaturize current valves in order to maintain customers shifting to emerging microequipment markets.
- Microfluidic components and systems manufacturers, primarily for the life-sciences market, which manufacture a variety of microfluidic processing and analysis equipment and may be able to use smaller microvalves than are currently available. Such a company might either make its own microvalve or specify microvalve requirements to valve manufacturers. Companies that have pursued valveless microfluidics technologies have not been included unless they appear to also have a need for an active valve.
- Semiconductor dry-etch system manufacturers are companies that currently manufacture dry etch equipment that will need to have more precise gas flow control for MEMS and nanotechnology manufacturing. The company may either make its own valve or specify valve requirements to valve manufacturers.
- Additionally, emerging fabricators of micro-sized components that may serve as central points to enable for microvalve and microsystem production. Funds are likely to be limited and project dependent.

Potential partnership candidates have been determined by reviewing market applications, past valve manufacturing experience, supply chain interrelationships, expertise in microfluidics and components, and a combination of these criteria. The companies selected have the ability to make valves or microvalves that may be used in the companies' own products or in OEM's products. These companies also have the ability to further develop the subject technologies for specific applications, though available resources vary.

Several tiers of candidates have been identified in terms of likelihood of interest and expected timing of opportunity.

Tier 1 – More Immediate Opportunities for Specific Applications

Companies that earlier have expressed interest in the technology.

- Applied Materials, Inc. – a leader in semiconductor production equipment.
- Redwood MicroSystems, Inc. – a leader in microvalves for mass flow controllers for instrumentation makers such as Rosemount Analytical (now part of Emerson Process Control).

Leaders in microarray spotting technology:

- Affymetrix, Inc. – a leader in microarray technologies with an extensive intellectual property portfolio.
- Amersham BioSciences Corp. – a market leader that recently bought miniaturization and dispensing technologies from Molecular Dynamics and Motorola. Motorola was using Packard Bioscience's piezoelectric dispensing technology.
- Applera Corporation, Applied Biosystems Group – competes against Affymetrix's technology and appears to have the Packard Bioscience dispensing technology.

Leaders in microfluidics that have been working with instrumentation companies:

- Caliper Life Sciences Inc. – a recognized leader in the microfluidics and lab-on-a-chip fields with interest in both valve and valveless technologies. Microarrays, molecular diagnostics, and polymerase chain reaction are targeted applications. Caliper partners with most of the major pharmaceutical and biotechnology companies as well as dispensing system companies such as Titertek.
- Eksigent Technologies Llc – develops novel classes of microfluidic devices that are likely to need microvalves for integration with other devices, particularly for Beckman Coulter instruments.
- Kloehn, Inc. – develops and makes microdispenser valves for many major analytical instrumentation and industrial application companies.
- Micronics, Inc. – develops and has extensive license rights to micropumps and valves, and partners with Beckman Coulter and Honeywell.
- Tecan Systems, Inc. – makes nanopipetting systems—piezoelectric dispensing systems for laboratory automation.
- The Lee Company – makes micro- and nano-dispensing valves

Instrumentation companies that have been working with microfluidics companies:

- Agilent Technologies, Inc., Life Sciences and Chemical Analysis Business Group, Agilent Ventures, Agilent Labs (with Caliper) – makes gas and liquid chromatography systems for lab automation. The company's microarray deposition technology does not allow densities sufficient for high-density microarrays, leaving a potential opening for the subject technology.
- Beckman Coulter (with Micronics and Eksigent).
- Honeywell International (with Micronics) – the company's mesopump technology uses low power, larger, electrostatically-actuated silicon microvalves for portable flow cytometry.

Emerging developers or fabricators of a range of microcomponents, though companies are small and resources appear to be limited:

- CytoPlex BioSciences – designs and fabricates novel microdevices and wants to miniaturize complex labs for use in doctors' offices, consumer homes, and point of care facilities

- Nanostream, Inc. – microfluidic technology used in high-throughput systems and micro parallel liquid chromatography with prior technology sold to Motorola
- Very Small Technologies – an emerging MEMS and nanotechnology fabrication company that claims to be setting a new industry standard for building microsystems

Emerging microvalve companies in other application areas such as active flow control and that have experience obtaining third-party funding (such as SBIR grants):

- Alumina Micro LLC – silicon microvalve developed with funding from the Advanced Technology Program of the National Institute of Standards and Technology.
- iACTIVE Corporation – low power, pneumatic array of electrostatically actuated microvalves developed on an SBIR with the U.S. Air Force originally for active flow control, being applied to refreshable braille displays.

Tier 2 – Mid-term Opportunities Likely to Require More Time to Develop Technologically

Companies that make miniature valves or precision dispensers and that want to adapt product lines to include microvalves for next generation instrumentation:

- Nordson Corporation, Life Sciences Venture, EFD, Inc., and March Plasma Systems – the company makes precision dispensing equipment for pharmaceutical, genetic research, drugs, proteins, and plasma etching.
- Parker Hannifin Corporation, Parker Life Sciences Division and Veriflow Division – makes microvalves for microarray spotting and for critical gas and liquid flow for semiconductor fabrication.
- PerkinElmer, Life and Analytical Sciences and Fluid Sciences – the company had a piezoelectric dispensing system from Packard Bioscience and may need an improved technology. Modular surface mount gas delivery systems for semiconductor industry have mass gas flow controllers.

Semiconductor dry etch system manufacturers that need increased precision for fluid or gas delivery during a variety of product manufacturing:

- Advanced Energy Industries, Inc. – a standard for digital mass flow controllers.
- Celerity Group, Inc., former Unit Instruments – digital mass flow controllers.
- Speedline Technologies, Inc. – precision deposition systems.

Leaders in microfluidics who may be interested in an alternate approach for other applications:

- Fluidigm Corporation – the company's valveless technology approach still has obstacles to overcome.
- TiNi Alloy Company – developed shape memory alloy and might be interested in further developing another technology, but funds are uncertain.

Genetic analysis system developers that are recognized leaders, but that are struggling with financial losses:

- Cepheid – claims state-of-the-art microfluidic and microelectronic technologies for genetic analysis, biothreat, and life sciences markets.
- Ciphergen Biosystems, Inc. – an emerging leader in biomarker, drug target discovery, and assay development.

Tier 3 – Longer term Development Applications

Companies that are in the early development stage of microfluidics but do not currently compete in the life sciences market:

- Intel Corporation, Intel Research, Precision Biology – researching novel applications of large-scale networks of sensors and actuators using nanotechnologies to bridge technologies from multiple disciplines to create new life science markets

Other Companies Considered but Unlikely to Be Interested

Moog Inc., Marotta Controls, Inc., Kaiser Marquardt (now part of General Dynamics Corporation), and VACCO Industries were considered as potential partners because they had expressed interest in the subject technology in the past, but were eliminated from consideration as a result of correspondence with the inventor. These companies had an interest specifically in micro-propulsion applications and have since found other solutions.

Recommendations

NTTC recommends that NASA establish an Intellectual Property (IP) position, through patent applications or non-disclosure agreements, prior to disclosing information about the subject technology. After the IP position has been established, then multiple field-of-use joint development partnerships or licenses be pursued using a tiered contact approach in the following applications:

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Note: NTTC advises the client to place in the Federal Register a notice of intent to license this technology as required by 35 U.S.C. 209(E) if a licensing alternative is to be pursued.

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Appendix A: Company Information

Companies are listed here in six categories, with contact information:

- Microvalve manufacturers
- Major valve manufacturers with extensive product lines
- Manufacturers of microfluidic components and systems
- Semiconductor dry etch system manufacturers
- Developers and fabricators of microfluidic components
- Microvalve companies with other technologies

Microvalve Manufacturers

Micronics, Inc.

Address:
8463 154th Avenue NE, Building F
Redmond, WA 98052

Phone: 425-895-9197
Fax: 425-895-1183
Web site: http://www.micronics.net

Sales (2003): Private
Employees (2003): Private

Product Focus:

Micronics has developed or obtained exclusive, worldwide license rights to 33 issued patents on the use of laminar flow diffusion in microchannels, microcytometry, and micro pumps and valves. More than 40 patent applications are pending. Micronics makes thin film laminate-based lab cards for applications such as immunoassays, nucleic acid assays, protein crystallography and DNA sequencing. The company is participating in projects for DoD, NIH, and others that require state-of-the-art assay miniaturization in a disposable lab card format. Micronics also provides expertise in micro pumps and valving interface with macro instrumentation.

Beckman Coulter has a non-exclusive right to Micronics intellectual property for flow cytometry. Honeywell and Micronics are co-developing a wristwatch-sized blood cell monitoring device under the DARPA BioFlips program.

Redwood MicroSystems, Inc.

Address:
959 Hamilton Avenue
Menlo Park, CA 94025-1431

Phone: 650-617-1200

Fax: 650-326-1899
Web site: http://www.redwoodmicro.com

Sales (2002): $1.0 million
Employees (2002): 20

Product Focus:

Redwood MicroSystems, Inc. makes silicon microvalves, microvalve-based pressure regulators, and mass flow controllers. Redwood's Fluistor™ Microvalve is used for proportional control of gas flow rates from microliters per minute to liters per minute and is the only commercially available normally closed microvalve that handles pressures up to 100 psig and flow rates of 1.5 liters per minute of nitrogen at 20 psid. The valve chip measures 6 mm x 6 mm x 2 mm. The Fluistor microvalve is also used in Rosemount Analytical (now part of Emerson Process Control) GCX gas chromatograph transmitters.

In 2002, the NTTC received an inquiry from the company regarding "Improvements in a Piezoelectrically Actuated Microvalve," NPO-30338, an earlier version of the subject technology. Redwood licensed microvalve technology from Stanford University.

Tecan Systems, Inc.

Address:
2450 Zanker Road
San Jose, CA 95131

Phone: 408-953-3100
Fax: 408-953-3107
Web site: http://www.cavro.com, http://www.tecan.com

Sales (2003): $25.0 million
Employees (2003): 107

Product Focus:

Tecan Systems, Inc., formerly Cavro Scientific Instruments, Inc., makes products that include highly precise liquid dispensing systems for laboratory automation. The Cavro brand syringe pumps and valves are used in end-products manufactured by lab automation and liquid handling OEMs. Tecan has developed a series of products for assay miniaturization. The company believes that miniaturization of laboratory processes will be a key factor in reducing costs, improving throughput and reducing use of precious samples and compounds such as used in molecular diagnostics. Tecan's NPS Nano Pipetting System is a piezoelectric dispensing tip that can handle between 0.5 nanoliter and 10 microliter amounts. Tecan's disposable LabCD™ is a miniaturization platform for a variety of assays.

The Lee Company

Address:
2 Pettipaug Road

Westbrook, CT 06498-0424

Phone: 860-399-6281
Fax: 860-399-2270
Web site: http://www.theleeco.com

Sales (2003): $79.9 million
Employees (2003): 550

Product Focus:

The Lee Company has pioneered the development of miniature precision fluid control components. Lee manufactures miniature hydraulic valves, restrictors, safety screens, solenoid valves, dispense pumps, and manifold systems. Products are used in medical and scientific instrumentation, inkjet printing, and the aerospace and automotive industries.

Lee's Electro-Fluidic Systems family of products include the INKA™ Series high speed micro and nano-dispensing valves for use with inks, air, biological reagents, and other fluids.

Major Valve Manufacturers with Extensive Product Lines

Kloehn Ltd. USA (parent company is in Switzerland)

Address:
10000 Banburry Cross Drive
Las Vegas, NV 89144-6500

Phone: 702-243-7727
Fax: 702-243-6036
Web site: http://www.kloehn.com

Sales (2004): $15.0 million
Employees (2004): 100

Product Focus:

Kloehn Ltd. designs and makes liquid and gas tight micro-syringes, miniature inert shear valves, miniature solenoid valves, medical probes, needles, fittings, dispensing and processing devices. The company's integrated fluidic circuit platforms can have fluid channels less than 0.02" in cross section and can use valves, pumps, check-valves, liquid chambers, and filters. Miniature solenoid valves are used for blood chemistry analysis, drug discovery, DNA sequencing, liquid chromatography. Kloehn also makes micro-dispenser valves for inkjets and Geronimo valves for microfluidic dispensing and high-density manifolding applications.

The products are used in instruments for the analytical, clinical, diagnostic, medical, and industrial markets. Clients of Kloehn include companies such as Abbott Laboratories, Bayer Corporation, Beckman-Coulter, Dade Corporation, Tecan, Hewlett-Packard, Waters Corporation, Zymark Corporation, Affymetrix, Spark

Holland, PE Applied BioSystems, Agilent Technologies, Roche Instruments, and Mettler-Toledo.

Nordson Corporation, Advanced Technology Business Segment's Nordson Life Sciences Venture, EFD, Inc., March Plasma Systems, and Asymtek

Address:
28601 Clemens Road
Westlake, OH 44145

Phone: 440-892-1580
Fax: 440-892-9507
Web site: http://www.nordson.com

Sales (2004): $667.3 million
Employees (2004): 3,483

Product Focus:

Nordson Corporation produces precision dispensing equipment to apply adhesives, sealants and coatings to a broad range of consumer and industrial products during manufacturing operations.

In 2002, the Life Sciences Venture was formed to serve the pharmaceuticals industry, the medical and genetic research industry, and companies that make medical instruments, supplies, and disposables. Nordson expects to adapt existing technologies and develop new ones to help drive the biotech and medical device high technology markets. Some potential applications mentioned include fluid and powder dispensing and "hyper" surface cleaning systems.

EFD makes precision fluid dispensing systems that increase yields and transfer efficiency by enabling precise consistent application of adhesives, drugs, protein solutions, and other fluids used in medical devices. March Plasma Systems makes plasma etching equipment. Asymtek makes automated fluid dispensing systems.

Parker Hannifin Corporation, Parker Life Sciences Division and Veriflo Division

Address:
6035 Parkland Boulevard
Cleveland, OH 44124

Phone: 216-896-3000
Fax: 216-383-9414
Web site: http://www.parker.com

Sales (2004): $7.1 billion
Employees (2004): 46,787

Product Focus:

Parker Hannifin Corporation's Veriflo Division makes precision valves, regulators, surface mount components, and filters used to control and apply liquids and gases used in semiconductor fabrication. The Veriflo Division is part of the Instrumentation Group that specializes in critical gas and fluid flow components for process instrumentation, ultra-high-purity, medical, analytical, and biopharmaceutical applications.

The Parker Life Sciences Division worked with an OEM to develop a high-speed liquid handling system that met microarray spotting demands. Parker Life Sciences makes equipment ranging from miniature solenoid valves to highly integrated automation systems. The company's X-valve is touted to be the smallest valve on the planet and is less than 8 mm in width. Parker Life Sciences also makes miniature diaphragm pumps for portable medical and analytical instruments, gas monitors, and air samplers.

Manufacturers of Microfluidic Components and Systems

Affymetrix, Inc.

Address:
3380 Central Expressway
Santa Clara, CA 95051

Phone: 408-731-5000
Fax: 408-481-0422
Web site: http://www.affymetrix.com

Sales (2003): $300.8 million
Employees (2003): 871

Product Focus:

Affymetrix, Inc. makes GeneChip® oligonucleotide arrays, the instruments to process and analyze the arrays, and control and target labeling reagents for use with the arrays. The integrated GeneChip Instrument System is used for discovery research such as gene expression RNA analysis and DNA analysis.

Affymetrix' microarrays have used a photolithography-based manufacturing process to create chips that have 408,000 features. By scaling its feature size to 18 microns and reducing the number of probes per gene, it was theorized that Affymetrix could situate all of the estimated 100,000 human genes on just four chips as opposed to the competitions' 64 chips. Theoretical limitations have effectively limited feature sizes to 70 and 150 microns. Motorola, Agilent, and Dow Corning were considered to the major competitors. Affymetrix has a patent portfolio that has been considered to be so strong relative to the high-density market that a competitor who develops a manufacturing process conducive to production of high-density chips would need to obtain a license from Affymetrix (Dain Rauscher Wessels 2000).

Agilent Technologies, Inc., Life Sciences and Chemical Analysis Business Group

Address:
5301 Stevens Creek Boulevard
Santa Clara, CA 95051-7201

Phone: 650-752-5000
Fax: 650-752-5633
Web site: http://www.chem.agilent.com

Sales (2003): $1.1 billion
Employees (2003): 3,700

Product Focus:

The Life Sciences and Chemical Analysis business group of Agilent Technologies, Inc. makes gas chromatograph/mass spectrometer and liquid chromatograph/mass spectrometer systems that integrate and automate laboratory work. Products are used in the pharmaceutical, bioscience, environmental, and other industries. The business group also produces microarrays using the ink jet printing process of Hewlett-Packard. The technology is a scalable deposition technology but has a density cap determined by a feature size of approximately 70 microns. This density is too low for the high-density microarray market (Dain Rauscher Wessels 2000).

Agilent Labs is the central research organization for the company. Agilent Ventures is a business unit that is dedicated to investing globally in start-up or early-stage technology companies. The venture group invests in leading-edge technologies in the life sciences market and facilitates new technology development partnerships with Agilent.

Amersham BioSciences Corp. (subsidiary of General Electric Company)

Address:
800 Centennial Avenue
Piscataway, NJ 08855

Phone: 732-457-8000
Fax: 732-457-0557
Web site: http://amershambiosciences.com, http://www.motorola.com

Sales (2002): $1.0 billion
Employees (2002): 4,400

Product Focus:

Amersham Biosciences Corp. develops and manufactures integrated technology platforms for genomic and proteomic research, drug discovery and development, and biopharmaceutical manufacturing. Some of the products manufactured are the AKTA™ chromatography systems, MegaBACE™ automated high-throughput DNA analysis system, and Oligo Pilot II instrument/reagent systems for DNA synthesis.

In the past, Amersham obtained miniaturization and dispensing technologies from companies such as Molecular Dynamics, Inc. and Motorola Life Sciences. Based on a past history of developing and selling microtechnology to Motorola, Nanostream, Inc., may have a possible future microfluidics relationship with Amersham, however this is speculative.

The MegaBACE™ DNA sequencers that were used in the Human Genome Project were developed by Molecular Dynamics, Inc. In 1999, Molecular Dynamics was bought by APBiotech (formerly Amersham Pharmacia Biotech). Molecular Dynamics had teamed in 1994 on a long-term $63 million government funded project with Affymetrix to develop miniaturized DNA diagnostic systems. In 2001, Molecular Dynamics found a way to increase DNA sequence analysis systems.

Motorola had formed a life sciences business unit to focus on development and commercialization of DNA chip technology. Originally, Motorola had a cooperative agreement with Argonne National Laboratory and Packard Biosciences to develop a three-dimensional gelpad technology to support DNA probes on microarrays. Packard Biosciences moved forward with the technology in conjunction with the company's piezo-electric dispensing technology. The piezojet technology inherently limited chip density to between 3,000 and 5,000 features because the feature sizes were greater than 100 microns. Motorola was using Packard Biosciences' piezoelectric dispensing technology (Dain Rauscher Wessels 2000).

In 2002, Amersham bought Motorola's CodeLink™ bioarray business that was based on a unique patented manufacturing process that produced high-quality arrays. The CodeLink Human Whole Genome Bioarray has about 55,000 quality probes. Motorola exited the bioarray market, but retained the eSensor™ operation that had been purchased from Clinical Micro Sensors, Inc. which was founded by the current Nanostream CEO.

Applera Corporation, Applied Biosystems Group

Address:
301 Merritt 7
Norwalk, CT 06851

Phone: 203-840-2000
Fax: 203-762-6000
Web site: http://www.applera.com

Sales (2003): $ 1.7 billion
Employees: 4,540

Product Focus:

Applera Corporation consists of the Applied Biosystems Group and the Celera Genomics Group. The location of the Applied Biosystems group is the same as that of PerkinElmer's Applied Biosystems unit and appears to have been sold or spun out. The Applied Biosystems Group develops and markets instrument-based systems, consumable, software, and services for the life science industry and research community. These products are used to analyze nucleic acids, small molecules, and proteins for scientific discovery, new pharmaceutical development, and testing.

Applied Biosystems entered the microarray market in 2004, but produces oligos offline prior to microarray spotting as opposed to Affymetrix's possibly more advanced online approach. The human microarray capacity of the Applied Biosystems microarray is 27,868 genes as opposed to the targeted 100,000 genes on a single chip.

Caliper Life Sciences Inc.

Address:
68 Elm Street
Hopkinton, MA 01748

Phone: 508-435-9500
Fax: 508-435-3439
Web site: http://www.calipertech.com

Sales (2003): $ 49.4million
Employees: 454

Product Focus:

Caliper Life Sciences Inc. is a leader in lab-on-a-chip technologies that miniaturize, integrate, and automate many laboratory processes. Caliper has positioned itself as a leader in the life science tool market and is looking to new markets such as microarrays and molecular diagnostics. Caliper has advanced liquid handling and LabChip® technologies that are used to create leading edge tools that accelerate drug discovery. Caliper is looking to add more functions that cannot be done with capillary electrophoresis to the chips. Inline polymerase chain reaction has been targeted as the next chip application.

Caliper is a leader and an innovator in microfluidics platforms that include both valve and valveless technologies for microchips, automated liquid handling, high throughput screening applications, flow cytometry, and sample injection. The company's LibraryCard™ Reagent Array is used to analyze nanoliter sized drops of sample biological fluids. Caliper's Sciclone ALH3000 liquid handler (formerly Zymark's) used a multidrop dispenser made by Titertek.

Caliper's proprietary sipper chips are described as the "chip-to-world" interface that allows automated sampling from microtiter plates. Manufacture of Caliper's new sipper chips began late in 2003, but difficulties have been experienced in manufacturing both the chips and instruments. Key manufacturing supplies, components, and subassemblies, are purchased from single-source suppliers, including a German supplier, thus making Caliper dependent upon them.

The company works closely with most of the major pharmaceutical and biotech companies as well as instrument companies like Agilent Technologies. Caliper acquired Zymark Corporation in 2003. Partners of Caliper include: Agilent Technologies, Applied Biosystems of PE Corporation, Bacterial Barcodes, Inc., Beckman Coulter, Inc., Bio-Rad, Bio-Tek Instruments, Inc. of Lionheart Technologies, Inc., BMG Labtechnologies, Bruker, Cellomics, Eppendorf, Genomic Solutions, IGEN International, Inc., Labsystems, Molecular Devices, Packard Bioscience, PerkinElmer, Qiagen, Tecan, and Varian.

Cepheid

Address:
904 Caribbean Drive
Sunnyvale, CA 94089

Phone: 408-541-4191
Fax: 408-541-4192
Web site: http://www.cepheid.com

Sales (2003): $18.5 million
Employees: 178

Product Focus:

Cepheid develops, manufactures, and markets fully-integrated systems that perform genetic analysis, including DNA and RNA analysis, for the clinical genetic assessment, biothreat, and life sciences markets. The systems enable rapid, sophisticated genetic testing of organisms by automating complex manual laboratory procedures. Cepheid's systems are based on state-of-the-art microfluidic and microelectronic technologies. The company's focus is on rapid genetic testing that is important for the infectious disease, cancer and biothreat testing markets. Revenues increased in the first quarter of 2004 due to increased sales of GeneXpert modules and anthrax cartridges to Smiths Detection and Northrop Grumman, however a net loss of $4.1 million occurred.

Ciphergen Biosystems, Inc.

Address:
6611 Dumbarton Circle
Fremont, CA 94555

Phone: 510-505-2100
Fax: 510-505-2101
Web site: http://www.ciphergen.com

Sales (2003): $58.4 million
Employees (2003): 341

Product Focus:

Ciphergen develops, manufactures, and markets ProteinChip® systems that are used for clinical, research and process proteomics applications as well as a range of bioseparations media. The ProteinChip is interfaced to high-end quadrupole tandem mass spectrometers. Ciphergen is also combining chromatography with the ProteinChip for single-step on-chip purification and analysis.

Ciphergen works with customers to develop new products and applications. The company is emerging as a leader in biomarker and drug target discovery, assay development, and characterization.

Customers include pharmaceutical and biotechnology companies as well as government agencies, research institutions, and universities. Ciphergen's net loss fell to $7.5 million for the first quarter of 2004. It is unknown as to whether the company has other sources of development money.

Eksigent Technologies Llc

Address:
2021 Las Positas Court, Suite 161
Livermore, CA 94551-7304

Phone: 925-960-8869
Fax: 925-960-8867
Web site: http://www.eksigent.com

Sales (2003): $1.3 million
Employees (2003): 16

Product Focus:

Eksigent Technologies Llc develops and manufactures microscale systems for drug discovery, development, and drug delivery applications. Key technologies include microscale flow generation and control and microfabricated system integration. Eksigent combines these technologies to create novel classes of microfluidic devices that set new standards in throughput and sensitivity. These technologies are valveless, however integration with other devices probably needs microvalves.

Eksigent has a suite of microfluidic, or lab-on-a-chip, technology. Products include the NanoLC™ system for proteomics research, ExpressLC™ system for high throughput analytical HPLC, and EKPumps™ for drug delivery. The company is considered to be one of the top suppliers of nanoscale chromatography systems.

Beckman Coulter and Eksigent entered into a development collaboration and licensing agreement in 2001 to incorporate Eksigent's microfluidics technology into future Beckman Coulter instrument platforms.

Honeywell International

Address:
101 Columbia Road
P.O. Box 4000
Morristown, NJ 07962

Phone: 973-455-2000
Fax: 973-455-2096
Web site: http://www.honeywell.com

Sales (2004): $23.1 billion
Employees (2004): 108,000

Research Address:
12001 State Highway 55
Plymouth, MN 55441

Product Focus:

Honeywell has developed a portfolio of emerging technologies that includes microfluidic devices that measure, control or actuate, and deliver nanoliter and sub-nanoliter levels of fluids. The Mesopump technology uses low power, electrostatically-actuated silicon microvalves in gas and liquid pumps that use normally closed valves. The technology was developed in conjunction with Micronics under DARPA funding.

The system was developed for use in a portable flow cytometer. Other applications that are expected to exist include point-of-care medical microinstruments, highly parallel processing in drug discovery applications, micro-dosing systems for drug delivery, and on-line process monitoring in the food or chemical industries. The subject technology appears to be smaller than Honeywell's microvalve.

Intel Corporation, Intel Research, Precision Biology research team

Address:
2200 Mission College Boulevard
Santa Clara, CA 95052

Phone: 408-765-8080
Fax: 408-765-9904
Web site: http://www.intel.com/research/exploratory/precision_biology.htm

Sales (2004): $30.1 billion
Employees (2004): 80,500

Product Focus:

The Precision Biology research team, headed by Andy Berlin, within Intel Corporation has a goal to combine Intel's nanotechnologies with aspects of biology and medicine to make it possible to use microchips in fundamentally new ways. Dr. Berlin's research interests are in creating novel applications of large-scale networks of sensors and actuators that require bridging technologies from multiple disciplines. He has served as a member of the Governing Council of the MEMS Industry Group.

A research fellow at Gartner Dataquest thinks that Intel could drive development of DNA sequencing systems for diagnostics and silicon implants for activities such as monitoring the body's health. Intel is hoping to create new markets for the company in the life sciences arena, but expects that at least three years will be needed to determine any success.

Intel recognizes that Aclara BioSciences and Caliper Technologies are developing labs-on-a-chip for biologists doing basic science, but differentiates its goal as putting such tools into the hands of doctors for treating patients.

The team has demonstrated ability to use microfluidics to isolate and interact with molecules, but needs to arrange for biological molecules to move single file across a microchip so that arrays of Intel's devices can detect and learn about the molecules.

PerkinElmer, Life and Analytical Sciences business segment (includes Packard Bioscience)

Address:
45 William Street
Wellesley, MA 02481

Phone: 781-237-5100
Fax: 781-431-4255
Web site: http://www.perkinelmer.com, http://www.las.perkinelmer.com

Sales (2003): $1.5 billion
Employees (2003): 10,000

Product Focus:

PerkinElmer, Inc., Life and Analytical Sciences business segment provides drug discovery, genetic screening, and chemical analysis tools and instrumentation as well as reagents and consumables. Some product categories include assay platforms, chromatography, high throughput screening, lab automation, microarrays, and proteomics.

Packard Bioscience is included in the Life and Analytical Sciences segment of PerkinElmer. Packard's piezojet technology had limited chip density of microarrays. See Amersham description notes. It is uncertain whether the former PerkinElmer Applied Biosystems location in California was sold to or spun off as Applera's Applied Biosystems group and what technology PerkinElmer retained or replaced possibly through a partnership with Caliper Life Sciences.

The company competes in the semiconductor industry through the Fluid Sciences business segment. PerkinElmer's components and assemblies enable existing process equipment technologies and support future directions. The company's vision is to be the world leader in design, production, and application of high precision sealing products for semiconductor wafer processing, ultra-high vacuum processing, and modular surface mount gas delivery systems.

Semiconductor Dry Etch System Manufacturers

Advanced Energy Industries, Inc.

Address:
1625 Sharp Point Drive
Fort Collins, CO 80525

Phone: 970-221-4670
Fax: 970-221-5583
Web site: http://www.advanced-energy.com

Sales (2004): $262.4 million
Employees (2004): 1,347

Product Focus:

Advanced Energy Industries, Inc. designs and manufactures components and subsystems for vacuum process systems used in the manufacture of semiconductors, data storage products, and flat panel displays. Microprocessor controlled digital mass flow controllers for fluid or gas delivery are made by the company. Advanced Energy's Aera digital mass flow controller has been selected as default standard by one of the Japanese semiconductor manufacturers for use in 300mm high-density plasma chemical vapor deposition applications. The Aera MFCs have also been selected as retrofits on poly etch systems. The company is still experiencing a loss, however, the semiconductor capital equipment market is gaining momentum.

Applied Materials, Inc.

Address:
3050 Bowers Avenue
P. O. Box 58039
Santa Clara, CA 95052

Phone: 408-727-5555
Fax: 408-748-9943
Web site: http://www.appliedmaterials.com

Sales (2003): $4.5 billion
Employees (2003): 12,050

Product Focus:

Applied Materials, Inc. develops, manufactures, sells, and services integrated circuit fabrication equipment for the semiconductor industry. Applied manufactures systems for most of the primary steps in the chip fabrication process, including plasma etching. The Etec Systems, Inc. subsidiary makes systems that generate, etch, measure and inspect circuit patterns on masks in the photolithography process.

Applied is the world's largest maker of semiconductor production equipment. Top customers of Applied include: Intel, Samsung Electronics, Advanced Micro Devices, and Motorola.

Applied Materials had expressed interest in the past to the inventor regarding the subject technology.

Celerity Group, Inc. part of Kinetics Systems, Inc., (formerly Unit Instruments, Inc.)

Address:
1463 Centre Pointe Drive
Milpitas, CA 95035

Phone: 408-946-3100
Fax: 408-935-7481
Web site: http://www.celerity.net

Former Unit Instruments, Inc. location
22600 Savi Ranch Parkway
Yorba Linda, CA 92887

Phone: 714-921-2640
Fax: 714-921-0636
Web site: http://www.unit.com

Product Focus:

Celerity Group, Inc. designs and produces high performance gas and chemical delivery process modules that are integral in the manufacture of semiconductors, flat panel display equipment, magnetic and optical storage media, microsystems equipment, and fiber optic cable manufacturers. Celerity's digital mass flow controllers use the company's MultiFlo™ technology.

The former Unit Instruments, Inc. location designs, manufactures, and markets mass flow controllers, high purity gas isolation boxes, gas panels and valve manifold boxes. These products are used in the semiconductor wafer manufacturing process to measure and control the flow of process gases.

Speedline Technologies, Inc.

Address:
16 Forge Park
Franklin, MA 02038-3157

Phone: 508-520-6999
Fax: 508-520-2288
Web site: http://www.speedlinetech.com

Sales (2003): $250.0 million
Employees (2003): 400

Product Focus:

Speedline Technologies, Inc. manufactures precision deposition systems that include stencil and screen printers, dispensers, reflow soldering, wave soldering and cleaning equipment for the printed circuit boards and other substrates used in the electronics industry. Speedline is a leader in providing MEMS manufacturing-related expertise in printing, dispensing, curing, and laser soldering processes.

Camalot™ dispensing units are used to dispense underfill materials, fine pitch printing materials, solder paste, adhesives, fluxes, conductive epoxies, and encapsulants.

Developers and Fabricators of Microfluidic Components

Cytoplex BioSciences Inc.

Address:
2401 Merced Street
San Leandro, CA 94577-4228

Phone: 214-868-9101
Web site: http://www.cytoplex.com

Sales: Not Available
Employees: 7

Product Focus:

Cytoplex BioSciences considers itself to be the pioneer of NanoBio, where novel microdevices and nanoengineered materials are used for innovative solutions in the life science, medical, and process industries. The company has expertise in semiconductor materials design, materials processing, device fabrication, and application to different areas of the industries that require processing (sorting and delivery) and detection of biochemicals. Cytoplex expects to eventually miniaturize complex labs as disposable single-use low-cost units for doctor's offices, consumer homes, and point-of-care facilities.

Nanostream, Inc.

Address:
580 Sierra Madre Villa
Pasadena, CA 91107

Phone: 626-351-8200
Fax: 626-351-8201
Web site: http://www.nanostream.com

Sales (2003): NA
Employees (2003): NA

Product Focus:

Nanostream provides high-throughput microfluidic analytical systems to drug discovery and development companies. The company's Veloce™ system provides micro parallel liquid chromatography and uses microfluidic Brio™ cartridges. Nanostream states that new product offerings present opportunities for funded collaboration to accelerate development and has raised $34.7 million to date.

The CEO of Nanostream invented the core microfluidic technology of the company and co-founded four technology companies including Clinical Micro Sensors that was acquired by Motorola in 1999. The VP of Technology was responsible for designing, fabricating, and testing microelectronics devices at TRW, Inc., Space and Electronics Group. The VP Product Development has experience in pioneering complex life science products and has guided the high throughput microfluidic analytical systems development for Nanostream.

The Board of Directors has an array of experience with life science related companies such as Bayer Corporation, Pfizer, Inc., Waters Corporation, Hewlett-Packard's Bioscience Products, and Lilly Ventures.

Very Small Technologies, Inc.

Address:
Long Island Business and Technology Center
3500 Sunrise Highway, Suite T210H
Great River, NY 11739

Phone: 631-297-8004
Web site: http://www.verysmalltech.com

Sales: $7.0 million
Employees: 7

Product Focus:

Very Small Technologies, Inc. is an emerging MEMS and nanotechnology fabrication company. The company uses an approach to manufacturing microsystems that is expected to become the basis of a new industry infrastructure for building a wide range of microsystems.

Microvalve Companies with Other Technologies

Alumina Micro LLC

Address:
1971 Midway Lane, Suite J
Bellingham, WA 98226

Phone: 360-734-8220
Fax: NA
Web site: http://www.aluminamicro.com

Sales: NA
Employees: 6

Product Focus:

Alumina Micro LLC received funding from the Advanced Technology Program of the National Institute of Standards and Technologies to develop a novel MEMS silicon chip microvalve technology for controlling the flow of liquids, mists, and gases at high pressures and flow rates for automotive industry applications. Air conditioning systems could be integrated into windows, personal cooling systems could be enabled for soldiers, gas flow control, satellite control, transmission control, biotechnology, and drug research and development are some of the envisioned areas of future application. The project duration was from July 2002 to September 2004 with funds of $2 million.

Cofounders of the company worked for Harrison Radiator Division, now Delfi, of General Motors and CalSonic, a joint venture between GM and a Nissan supplier. The technology they developed equalizes pressure across the valve rather than pushing against the pressure like mechanical valves do. The valve technology is called MicroSTAQ® and is an intelligent fluid control microsystem.

Fluidigm Corporation

Address:
7100 Shoreline Court
South San Francisco, CA 94080

Phone: 650-266-6000
Fax: 650-871-7152
Web site: http://www.fluidigm.com

Sales (2003): $9.5 million
Employees (2003): 65

Product Focus:

Fluidigm Corporation's vision is to develop, deliver, and support the world's most efficient life-science systems, using the company's revolutionary integrated fluidic circuits (IFCs). The Nanoflex™ electrostrictive, electrostatic membranes are used to function like valves but have no moving parts. The microvalves are used in microarrays that annually increase in IFC valve density and complexity. Some difficulties have been experienced regarding Nanoflex membrane interaction with some fluids.

The Nanoflex technology is based on technology developed by Stephen Quake at California Institute of Technology. Fluidigm's patent portfolio includes five patents and 60 pending patents, that include technologies licensed from Caltech, Harvard, and Los Alamos National Laboratory.

iACTIVE Corporation (subsidiary of Orbital Research, Inc.)

Address:
4415 Euclid Avenue, Suite 510
Cleveland, OH 44103-3733

Phone: 216-432-0661
Fax: 216-649-0347
Web site: http://www.iACTIVcorp.com

Sales (2003): $2.4 million (Orbital)
Employees (2003): 15 (Orbital)

Product Focus:

iACTIVE Corporation was spun out of Orbital Research, Inc. to take advantage of MEMS microvalve technology developed by Orbital. iACTIVE's pneumatic, electrostatically actuated MEMS microvalves arranged in arrays replace piezoelectric actuators and are used to inflate bladders of air to form the points of Braille characters. Orbital has been dependent on government funding through the Small Business Innovative Research program and the U.S. Air Force.

The microvalve technology came about through the company's design of innovative flow control systems to enhance aerodynamic performance of air vehicles. Orbital is also collaborating with Lockheed Martin and General Dynamics to commercialize the active flow control systems technology.

The company is currently seeking early stage funding of between $850,000 and $1,250,000 for 2004-2005 and will need another $2.0 million for 2005-2006 for manufacturing and marketing microvalves into the aerospace market.

TiNi Alloy Company

Address:
1619 Neptune Drive
San Leandro, CA 94577-3162

Phone: 510-483-9676
Fax: 510-483-1309
Web site: http://www.tinialloy.com

Sales (2002): $1.4 million
Employees (2002): 9

Product Focus:

TiNi Alloy Company specializes in thin shape memory titanium nickel alloys (SMA) and microvalves. In the past, TiNi has received SBIR contracts from the Missile Defense Agency with the intent of improving field emitter display characteristics for flat-panel displays. The thin-film SMA devices also serve as spacers between the two panels, however, the out-of-plane actuators have a one-time only deployment. The company continues to refine techniques for creating microactuators using thin-film SMA and is focused on applications in the MEMS marketplace.

The company's microvalves have been powered by 50-150 milliamps and displace a poppet more than 100 microns. Similarly the technology could be applied as a micropump to move gas or liquid between chambers.

TiNi Alloy has also been the recipient of NIH, NSF, and DARPA funding. The company creates intellectual property and licenses it. The facility is devoted primarily to laboratory space and cleanroom equipment to fabricate MEMS devices.

Clients and grantors of TiNi include government agencies that include DARPA, NASA, NIH, NSF, USAF, USN, and MDA as well as the Department of Education. Commercial contracts have been with Delphi division of General Motors for fuel injectors, Ford Motor Company for electrical connectors, Johnson&Johnson for implantable medical systems, and SMART Therapeutics for intravascular devices. Licenses for limited fields of use have been issued to The Lee Company and TiNi Aerospace.

Appendix B: Inventor Interview

Inventor: Dr. Eui-Hyeok Yang
Date: August 10, 2004

This interview was conducted by e-mail.

Q. *What improvements have been made since the New Technology Reports were written?*

A. The microvalve has been fabricated and characterized in laboratory environment. Ultra-low leak operation has been achieved at very high inlet pressure. Updated feature is described in the attached paper.

Q. What is the current readiness level of the technology? Has the second generation of the technology been developed?

A. It is at TRL 3~4. The second generation development is on hold due to funding situation. It is unlikely it can be continued unless some follow-on funding is provided.

Q. Has the power consumption at 100 Hz been reduced to several microwatts?

A. The DC power consumption is ~3 mW and the power consumption at 100Hz is on the order of 100mW.

Q. What liquid flow rates are possible? (Only gas flow rates are mentioned in the NTRs.)

A. The high-pressure valve is for gas flow control. There is another version of the microvalve that can do liquid, but it is at TRL 2 or lower 3.

Q. Are you working with anyone at either Cal Tech or elsewhere on non-aerospace applications? If so, what applications?

A. Not at this point.

Q. HPLC applications were found that require 5000-15000 psi. Can the technology handle those pressures?

A. Gas version may hold the higher pressure if the packaging technology is provided.

Q. Moog, Lee, Marotta Scientific, and Kaiser Marquardt (now General Dynamics) were mentioned in the NTRs -- Are or were any of these companies interested in pursuing your technology?

A. They are rather competitors since, especially, Moog pursued similar type of application (micropropulsion). JPL microvalve has advantage in power consumption over SOA technologies.

Q. Are there any companies that you know are interested or likely to be interested in your technology? If so, which companies and for what types of applications?

A. There were some companies who expressed their interest. They include Applied Materials and VACCO. But, VACCO is not likely to be interested in collaboration now, since they might developed [sic] their own PZT type valves.

Q. Are there any companies that you particularly would like to have contacted?

A. Rather than companies that produce valve, it should be some companies that will use microvalves.

Q. The NTRs also mentioned possible collaborations with researchers at the University of California, Berkeley and the University of Southern California. Were any collaborations formed? If so, what type of collaborations occurred?

A. No.

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