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BIODOT . . .

is the leading supplier of systems for the research, development and manufacture of diagnostic tests. Its Mission is to enable, inspire and educate scientists to commercialize their R&D ideas through to manufactured product. Using its core competencies in low volume non-contact and contact dispensing, and technology transfer services, BioDot has developed a range of equipment for the research and development, and manufacture of biochips.

With a commitment to fully understanding our customer requirements, BioDot's personnel have a genuine wish to help you develop your research ideas. Our sales teams are highly trained in providing expert advice in both process and material handling needs. They are backed by strong support from teams of applications scientists and service engineers.

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Bringing Manufacturing Strength to the Laboratory

BIOCHIPS



An alternative to pin gridding, the most common means of achieving high-density arrays, is to use BioJet Plus or Scienion Piezo for a non contact dispense. Show below are array examples achievable using BioJet Plus or Scienion Piezo technology, each with decreasing center-to-center spacing from left to right.



Shown below are arrays of 10 x 10 drops, and a 1.0 mm center-to-center spacing (array density is 100 drops/cm2). The pattern was created in a two step process. The first step was dispensing sub-pattern A to each location, followed by dispensing the complementary sub-pattern B to each location.



Using BioJet Plus or Scienion Piezo, non-contact arraying can be completed on glass slides, membranes or in microtiter plates.

MORE ON BIOCHIPS . . .

"A Single Nucleotide Polymorphism, or SNP is a single base, point, genetic change, or variation, that can occur within a person's DNA sequence. The genetic code is specified by the four nucleotide "letters" A (adenine), C (cytosine), T (thymine), and G (guanine). SNP variation occurs when a single nucleotide, such as an A, replaces one of the other three nucleotide letters - C, G, or T^{" 1}. Specifically, the apparent benign genetic change represents a deviation from the "normal" or known, common sequence for a particular gene.

SNPs that appear in the promoter region, coding region, or at exon/intron boundaries may result in altered transcriptional regulation, altered



TURN THINKING

amino acid sequence in the gene product, and altered mRNA editing (splicing), respectively. Investigating the frequency and phenotypic correlates with known SNPs harbors the potential to



discover specific genes that are responsible for predisposition for disease risk, as well as offers value in forensics research and population genetics. Many efforts to use SNP's for understanding genetic variability are now ongoing. High Throughput laboratories are undergoing research to map SNP's for disease diagnosis, pharmacogenomics, and agricultural genetics. Several institutions have exceeded runs of 100,000,000 wells per year. Given the increasing focus on SNP technology, there is an immediate need to increase throughput using robotic automation and to reduce reagent costs with nanoliter dispensing.

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Although specific methods and analytical approaches vary, there are common processes for which BioJet Plus, an innovative low volume dispenser can be successfully integrated. "Essentially all assay platforms for known SNPs exploit nucleic acid mismatch hybridization chemistry and/or single-base extension chemistry to identify the SNP(s) under investigation"^{2,3,4}.

As described in the flowchart below, BioJet Plus can be used for non-contact dispensing into a microtiter plate and MALDI target spotting.



Sequenom, Third Wave, and Applied BioSystems are some of the companies offering a variety products and techniques to support SNP Analysis. Each technique requires different dispense patterns and protocols. BioJet Plus Technology has been used with these widely recognized protocols to increase throughput and reduce the costs of reagents per well. Dispensed patterns to plates can be in interwoven matrices or in four distinct quadrants. An interwoven matrix allows for the four common reagents to be dispensed into wells A1, A2, B1, B2, Using this pattern in a 384 well plate, and four BioJet Plus channels, the entire plate can be filled in less than 30 seconds. Likewise by dispensing reagents into four distinct quadrants allows for 12 x 8 block of wells to be dispensed in less than 30 seconds. To increase throughput, additional BioJet Plus channels can be added, as multiples of eight.

References:

- 1. http://www.ncbi.nlm.nih.gov/About/primer/snps.html
- Kwok, PY (2001) Methods for genotyping single nucleotide polymorphisms. Annu Rev Genomics Hum Genet 2:235-258.
- Shi, MM (2001) Enabling large-scale pharmacogenetic studies by high-throughput mutation detection and genotyping technologies. Clin Chem 47:164-172.
- Kwok, PY (2000) High-throughput genotyping assay approaches. Pharmacogenomics 1: 95-100.

DISPENSING TECHNOLOGIES

Contact Dispensing:

Front Line:

Front Line dispensing is ideal for printing lines on membranes and other substrates for BioChips. The technology couples a high resolution syringe pump with a microtube. During dispensing the microtube glides across the surface of the membrane or substrate to create a quantitative line. Multiple Front Line dispensers can be configured on one dispense head. The width of the line can be adjusted by increasing or decreasing the programmed volume of the line.



Silicon Pins:

The Silicon Microarray™ Printer fabricates highly precise microarrays at a fast rate

and low cost. Ultra high precision micromachining capabilities and the unique physical properties of single crystal silicon have been combined to create a contact printing technology.





Using the Parallel Synthesis Silicon Pins allows for a very dense array with reduced carryover. The Silicon Pins are also capable to aspirate from a 1536 well source plate and have no pre-spotting requirements.



sciFLEXARRAYER™:

The Scienion sciFLEXARRAYER piezo system is a non contact liquid handling and spotting system. The technology dispenses with a high dynamic volume range (picoliter to nanoliter) and can accurately aspirate and dispense aqueous and

organic solutions as well as living cells. Using piezo, spot volume can be changed as well as dispensing reagents on top of each other without contamination. Results can be analyzed with standard technology and give immediate results for optimal reaction parameters.





BioJet Plus[™]:

The proprietary BioJet Plus technology was developed for high speed dispensing. The technology involves (1) the coupling of a high speed micro solenoid valve with a high resolution syringe pump and (2) synchronization of the dispense system with the movements of the stage. The result is an extremely fast dispensing system which can deliver volumes from 20 nL to 4 μ L in a single drop. BioJet Plus can work in either an Aspirate/Dispense or Bulk Dispense modes.

Use BioJet Plus to dispense buffers, antibodies, enzymes or cells. BioJet Plus dispensing is independent of the substrate allowing flexible dispensing to microtiter plates, glass slides or membranes. BioJet Plus systems are available from compact R&D systems to complete integrated manufacturing modules.



BioJet Plus[™]

"HANDS ON" WORKSHOPS

BioDot conducts worldwide workshops and seminars on the technology of manufacturing of Rapid Tests. In these workshops, BioDot and its strategic partners bring together experts in the various disciplines of rapid assay technologies to provide the most up to date information possible.

The workshops are a mixture of lecture and laboratory to present both a "Classroom" and "Hands On" style.

Classroom Sessions

- Emerging Rapid Assays & Challenges to Development
- Classical Approach to Microarrays & Application Challenges
- Multiplex Detection of Proteinaceous Toxins in Food
- High Speed Interferometric Detection of Label-Free Immunoassays using Bio-Discs
- Antibodies: The Basis of a Good Rapid Assay
- Development, Validation, and Application of Antibody Arrays
- Polymer Based Visible Microarrays
- Next Generation Substrates
- Scalable Dispensing Technologies for Biochip Manufacturing
- High Throughput Laser Scanning Platforms for Arrays in Multiwell Plates
- EpiTags: The Scalable Approach to Quantitative Multiplex Immunoassays
- Adhesives and Tapes used with BioChip Devices



"Hands On" Sessions

- Protein Arraying with BioJet Plus using S. Pneumoniae
- Protein Arraying with sciFLEXARRAYER piezo
- Slide Processing and Development
- Adhesives Property and Evaluation
- Fluorescent Detection of Antibody and Spot Array
- Data Analysis

*Note: Agenda subject to change due to availablility of speaker.



Emerging Quantitative Rapid Assays Technologies

Location	Date
San Diego, CA	Oct. 2005
Taipei, TW	Nov. 2005
Tokyo, JP	Nov. 2005
Salt Lake City, UT	Mar. 2006
Beijing, CN	Apr. 2006
Shanghai, CN	Apr. 2006
Dublin, IE	Apr. 2006
Chicago, IL	Jul. 2006
Taipei, TW	Nov. 2006
Seoul, KR	Nov. 2006
Salt Lake City, UT	Mar. 2007
Amsterdam	May 2007
Shanghai	Jun. 2007
Shenzhen	Jun. 2007
San Diego, CA	Jul. 2007
San Diego, CA	Sep. 2007
Minneapolis, MN	Apr. 2008
Washington, DC	Jul. 2008
Brussels	Sep. 2008
San Diego, CA	Sep. 2008

Practical Considerations of Development & Manufacture of Biochips

Location	Date
Oklahoma, OK	May 2006
Oklahoma, OK	Aug. 2006
Fairfax, VA	Sep. 2006
Salt Lake City, UT	Mar. 2007
Amsterdam	May 2007
Shanghai	Jun. 2007
Shenzhen	Jun. 2007
Philadelphia	Sep. 2007
San Diego, CA	Sep. 2007
Salt Lake City, UT	Mar. 2008
Minneapolis, MN	Apr. 2008
Shanghai	May 2008
Taipei	Jun. 2008
San Diego, CA	Jun. 2008
Washington, DC	Jul. 2008

PRODUCTS & OPTIONS. .

Dispensing Systems

Dispensing Platform Summary

	AD1500	AD3400	AD6000
PC Controller with AxSys™ Software	Yes	Yes	Yes
Maximum # BioJet Plus Pumps	4	32	96
Dispense Area	450 mm x 70 mm	495 mm x 300 mm	600 mm x 600 mm
Vacuum Pump(s) Needed	1	2	2
Additional Configuration Options:			
Ability to add on Contact Dispensing	Yes	Yes	Yes
Helium Degasser	Yes	Yes	Yes
In Line Degasser	Yes	Yes	Yes
Chilled Source Position	Yes	Yes	Yes
Ultrasonic Wash	No	Yes	Yes
Pre-Dispense Vision Systems (Horizontal Camera)	No	Yes	Yes
Alignment Vision Systems (Vertical Camera)	No	Yes	Yes
Shuttle Systems	No	Yes	Yes
Indexing Conveyor	No	No	Yes

AD1500

Research & Development System



PRODUCT DESCRIPTION

The AD1500 is a tabletop workstation designed for high speed aspirating and dispensing applications to glass slides, microtiter plates or membranes. Its compact footprint and up to four BioJet Plus Pumps make it ideal for a research laboratory to investigate new applications.

Both chemical and biological reagents can be dispensed using the proprietary BioJet technology. BioJet Plus couples the X-Y-Z motion control system with the high precision displacement capabilities of a syringe pump and the high-speed actuation of a microsolenoid valve. The three components synchronized together result in a precise, noncontact liquid handling system.

FEATURES AND BENEFITS

SPEED

- -"On the Fly" dispensing
- Non-Contact mode reduces wash time

FOOTPRINT

- Small design to accommodate research environment

MULTI-MODE DISPENSING

- Contact and Non-Contact dispensing capabilities
- Dispense to slides, microtiter plates, or membranes
- Aspirate and Dispense or Continuous Dispense operations

PERFORMANCE

- X-Y Table Speed 175 mm/second
- Minimum Aspirate Volume 1 µL
- Minimum Dispense Volume 20 nL
- Dynamic Dispense Range 20 nL - 250 µL
- Positioning Performance Stepper Motor Resolution = 1.3 µm
- Repeatability < ± 10 μm (95% Confidence)

SPECIFICATIONS

DIMENSIONS (L x W x H) 32" x 24" x 24"

WEIGHT 85 lbs (38.6 kg)

POWER REQUIREMENT 110/220 VAC; 50/60 Hz

VACUUM REQUIREMENT Vacuum Wash Station: 2.1 CFM (~60 CL)

DISPENSING SPECIFICATIONS

DISPENSE MODES Aspirate/Dispense (source to destination) Continuous (bulk reservoir to destination)

DISPENSE AREA 450 mm x 70 mm

DISPENSE TO DISPENSE PRECISION <10% CV at 50 nL, <7% CV at 100 nL; <4% CV at 500 nL

DISPENSE ACCURACY ±7% at 50 nL, ±5% at 100 nL

DISPENSE SPEED

Using 8 BioJet Plus channels, a 3 x 3 microtiter plate array completes in approximately 4 minutes

OPTIONS

UP TO 4 BIOJET PLUS DISPENSERS SILICON MICROARRAY PINS, PRINTHEAD, AND WASH STATION HUMIDITY CONTROL SUBSTRATE NEST Glass Slide, Microtiter Plate, or Membrane Hold Down

VACUUM PUMP HELIUM DEGASSER IN LINE DEGASSER



A 3 x 3 array dispensed into a 96 well microtiter plate



Close Up photo of an AD1500 configured with a 14 glass slide nest

AD3400

Development to Pilot Production System



PRODUCT DESCRIPTION

The AD3400 is a workstation that is suitable for R&D through to production levels. With its superior positional accuracy and speed, it is foreseeable to begin biochip projects on this system and then increase throughput using the same system. With a choice of 3 nests and mechanical shuttle, allows users the ability to interchange substrates and process biochips in a semi automated process.

The proprietary BioJet Plus technology was developed for high speed dispensing. The technology involves (1) the coupling of a high speed micro solenoid valve with a high resolution syringe pump and (2) synchronization of the dispense system with the movements of the stage. The result is an extremely fast dispensing system which can deliver volumes non contact from 20 nL to 4 μ L in a single dispensed drop.

BioJet Plus allows for flexible biochip development by dispensing to a glass slide, microtiter plate or membrane material.

FEATURES AND BENEFITS

FLEXIBILITY

- Incorporate multi dispensing technologies
- Aspirate and Dispense Capability
- Bulk Dispense Capability

ACCURACY

- High resolution X-Y-Z positioning

UPGRADEABLE

- Suitable to add components for batch production mode
- -Ability to add contact and non-contact dispensing options
- -Ability to add vision capabilities

PERFORMANCE

X-Y-Z Speed 250 mm/second

- Minimum Aspirate Volume 1 µL
- Minimum Dispense Volume 20 nL

Dynamic Dispense Range 20 nL - 250 µL

Positioning Performance Stepper Motor Resolution = 1.3 µm

Repeatability < ± 10 µm (95% Confidence)

SPECIFICATIONS

DIMENSIONS (L x W x H) 1219 mm x 762 mm x 1000 mm (48" x 30" x 39.5")

WEIGHT

500 lbs (227 kg)

POWER REQUIREMENT 110/220 VAC; 50/60 Hz

VACUUM REQUIREMENT Vacuum Wash Station: 2.1 CFM (~60 CL)

DISPENSING SPECIFICATIONS

DISPENSE MODES Aspirate/Dispense (source to destination) Continuous (bulk reservoir to destination)

DISPENSE AREA 495 mm x 300 mm

DISPENSE TO DISPENSE PRECISION <10% CV at 50 nL, <7% CV at 100 nL; <4% CV at 500 nL

VALVE TO VALVE PRECISION <10% average CV at 100 nL (8 valves)

DISPENSE ACCURACY ±7% at 50 nL, ±5% at 100 nL

DISPENSE SPEED 20 seconds to fill a 1536 well plate with 500 nL/well (8 channels)

Note: All specifications are based on total experiment cv's, which include drop to drop plate filling (where applicable) and plate reader cv's.

OPTIONS

UP TO 32 BIOJET PLUS PUMPS AIRJET DISPENSING SYRINGE DISPENSING FRONT LINE DISPENSING PIN DISPENSING HUMIDITY CONTROL SUBSTRATE NEST Glass Slide, Microtiter Plate, or Membrane

VACUUM PUMP HELIUM DEGASSER IN LINE DEGASSER ULTRASONIC WASH STATION BARCODE READER VISION SYSTEM



AD3400 System configured with four BioJet Plus Dispensers

AD6000

Production Biochip System



PRODUCT DESCRIPTION

The AD6000 is a workstation designed for high throughput biochip manufacturing. Vision inspection (CCD camera), and barcode reading, can be configured on the AD6000 for verification of substrate positioning and reagent spot dispensing.

BioJet Plus proprietary non contact dispensing technology, links high resolution syringe pump liquid displacement with micro-solenoid actuated valve, controlling drop ejections. BioJet Plus synchronizes all parameters to achieve "on the fly" dispensing at very high speeds without compromising drop positional accuracy.

FEATURES AND BENEFITS

ACCURACY

- High resolution X-Y-Z overhead gantry for precise motion control
- Programmed parameters guarantee repeatability

MULTI-MODE DISPENSING

- Contact and Non-Contact dispensing capabilities
- Dispense to slides, microtiter plates, or membranes
- Aspirate and Dispense or Continuous Dispense operations
- Ability to Configure Both Non Contact and Contact Dispensing

FLEXIBLE

- Suitable for Slide, Plate, or Membrane Materials

PERFORMANCE

X-Y Table Speed 250 mm/second

Minimum Aspirate Volume 1 µL

Minimum Dispense Volume 20 nL

Dynamic Dispense Range 20 nL - 250 µL

Positioning Performance Stepper Motor Resolution = 1.3 μm

Repeatability < ± 10 µm (95% Confidence)

SPECIFICATIONS

DIMENSIONS (L x W x H) 122 cm x 113 cm x 170 cm (48" x 44.5" x 67")

WEIGHT

800 lbs (364 kg)

POWER REQUIREMENT 110/220 VAC; 50/60 Hz

VACUUM REQUIREMENT Vacuum Wash Station: 2.1 CFM (~60 CL)

DISPENSING SPECIFICATIONS

DISPENSE MODES Aspirate/Dispense (source to destination) Continuous (bulk reservoir to destination)

DISPENSE AREA 600 mm x 600 mm

DISPENSE TO DISPENSE PRECISION <10% CV at 50 nL, <7% CV at 100 nL; <4% CV at 500 nL

VALVE TO VALVE PRECISION <10% average CV at 100 nL (8 valves)

DISPENSE ACCURACY ±7% at 50 nL, ±5% at 100 nL

DISPENSE SPEED 20 seconds to fill a 1536 well plate with 500 nL/well (8 channels)

Note: All specifications are based on total experiment cv.s, which include drop to drop plate filling (where applicable) and plate reader cv.s.

OPTIONS

UP TO 96 BIOJET PLUS PUMPS AIRJET DISPENSING SYRINGE DISPENSING FRONT LINE DISPENSING PIN DISPENSING HUMIDITY CONTROL SUBSTRATE NEST Glass Slide, Microtiter Plate, or Membrane VACUUM PUMP HELIUM DEGASSER IN LINE DEGASSER ULTRASONIC WASH STATION BARCODE READER VISION SYSTEMS DUAL SHUTTLE

Scienion sciFLEXARRAYER™



PRODUCT DESCRIPTION

The sciFLEXARRAYER Piezo dispenser is a non contact system that dispenses with a high dynamic volume range. The sciFLEXARRAYER is available in three formats (the s3, s5, and s11) and comes with up to eight chemically inert dispense nozzles. The s3, s5 and s11 can accurately aspirate and dispense aqueous and organic solutions as well as living cells.

The sciFLEXARRAYER dispenser includes a low volume wash station and an ultrasonic cleaning function for the glass nozzles. A high resolution optical drop control system can be configured onto either the s3, s5 or the s11 sciFLEXARRAYER platforms.

Either the s3, s5 or the s11 can be configured for a broad range of substrates from glass slides, microtiter plates, MALDI-MS sample plates, chambered glass slides, membranes and HTA[™] Formats.

FEATURES AND BENEFITS

NON CONTACT DISPENSING

- Transfer Volume is not Affected by the Substrate
- Highly Reproducible
- -"Free-Fly" of droplets allows dispensing liquids into small cavities

FAST

-> 1000 drops/s -Efficient Mixing of Reagents

SOFTWARE

-Flexible and Easy Design of Chip Layout -Set up of Individual User Profiles

PERFORMANCE

Piezo Dispensing Non Contact Drop on Demand

Dispense Frequency 1-2000 Hz

Minimal Dispense Volume 150 pL (PDC 50) 300 pL (PDC 70) 500 pL (PDC 90)

Minimal Sample Update 0.5 0 1 μL

X-Y Motion < 5 μm

Z Motion < 10 µm

SPECIFICATIONS

DIMENSIONS (L x W x H)

s3: 85 cm x 83 cm x 65 cm

s5: 83 cm x 58 cm x 60 cm

s11: 135 cm x 58 cm x 60 cm

CAPACITY

s3: 3 Mirotiter Plates or 18 slides (portrait position), or 12 slides (landscape position)

S5: 5 Mitrotiter Plates or 30 slides (portrait position), or 20 slides (landscape position)

S11: 11 Mitrotiter Plates or 66 slides (portrait position), or 44 slides (landscape position)

CAPILLARY ORIFACE

- 50 m (PDC 50) 70 m (PDC 70) 90 m (PDC 90)
- **OPTIONS**

1-8 PIEZO DISPENSE CAPILLARIES HORIZONTAL PRE-DISPENSE VISION SYSTEM VERTICAL ALIGNMENT VISION SYSTEM INDEPENDENT, SECOND WASH STATION HUMIDITY CHAMBER HEPA FILTER VACUUM PUMP(S) HELIUM DEGASSER IN LINE DEGASSER CHASSIS









Ordering Information

AD1500	Dispense Options:	
	BioJet Plus Pump: BJP3000	
up to 4 BioJet Plus Pumps	Silicon Print Assembly	0005 4040
2 Microtiter Plate Positions or 7 Slide Nest or Vacuum Magnetic Hold-down Nest	(Printhead, pin, and wash station):	6035-A048
Integrated Wash/Vacuum Station	Nest Options:	Humidity Control:
Vacuum Pump	Plate Nest: 6001-A105	115 V: 6001-A110-01
Computer Controller	Slide Nest: 6001-A107	230 V: 6001-A110-02
	Vacuum Nest: 6001-A106	
AD3400	Dispense Options:	
	BioJet Plus Pump: BJP3000	
up to 32 BioJet Plus Pumps	Silicon Print Assembly	
9 Microtiter Plate Positions or 50 Slide Nest or Vacuum Magnetic Hold-down Nest	(Printhead, pin, and wash station):	6035-A048
Integrated Wash/Vacuum Station	Nest Options:	Humidity Control:
Vacuum Pump	Plate Nest: 6046-A041	115 V: 6001-A179-01
Computer Controller	Slide Nest: 6046-A042	230 V: 6001-A179-02
	Vacuum Nest: 6046-A043	
AD6000	Dispense Options:	
	BioJet Plus Pump: BJP3000	
up to 96 BioJet Plus Pumps	Silicon Print Assembly	
20 Microtiter Plate Positions or 100 Slide Nest or Vacuum Magnetic	(Printhead, pin, and wash station):	6035-A048
Hold-down Nest		
Integrated Wash/Vacuum Station	Nest Options:	Humidity Control:
Vacuum Pump(s)	Plate Nest: 6048-A011	115 V: 6001-A179-01
Computer Controller	Slide Nest: 6048-A012	230 V: 6001-A179-02
Humidity Chamber & Controller	Vacuum Nest: 6048-A013	
SCIEL EXARRAYERS	Dispense Ontions:	
	50 um Piezo Dispensers: 2100-00	11-04
s3	70 um Piezo Dispensers: 2100-00	11-01
Up to 8 Piezo Dispensers	80 µm Piezo Dispensers: 2100-00	11-02
3 Microtiter Plate Positions	90 µm Piezo Dispensers: 2100-00	11-03
Chemical Inert Wash Chamber		
Instrument Enclosure	Nest Options:	
Computer Controller	Chilled Source Plate: 2100-0026	
s5	Microscope with Black & White CC	D Camera: 2100-0006
up to 8 Piezo Dispensers	Microscope with color CCD Camer	a: 2100-0008
5 Microtiter Plate Positions		
Chemical Inert Wash Chamber	Humidity Control:	
Instrument Enclosure	Humidity Chamber: 2100-0005	
Computer Controller	HEPA Filter: 6028-A046-01	
s11		
up to 8 Piezo Dispensers		
11 Microtiter Plate Positions		
Unemical Inert Wash Unamber		

PRODUCTS & OPTIONS

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- - - - "Hands On" Workshops

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Ordering Information

The "Hands On" workshops are offered throughout the years at various geographic locations. Due to the "Hands On" format, attendance is limited to a set number of delegates.

Location	Date
Salt Lake City, UT	Mar. 2007
Amsterdam	May 2007
Shanghai	Jun. 2007
Shenzhen	Jun. 2007
San Diego, CA	Jul. 2007
San Diego, CA	Sep. 2007
Salt Lake City, UT	Mar. 2008
Minneapolis, MN	Apr. 2008
Amsterdam	May 2008
Taipei	Jun. 2008
Washington, DC	Jul. 2008
Brussels	Sep. 2008
San Diego, CA	Sep. 2008



To register for the next workshop, log on to www.biodot.com and download the registration form.