

Insulator Based Dielectrophoresis (iDEP): A Tool to Detect, Separate and Concentrate Aerosolized Biological Particles

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Biological Sensor Requirements



- **Requirements and Performance Measures:**

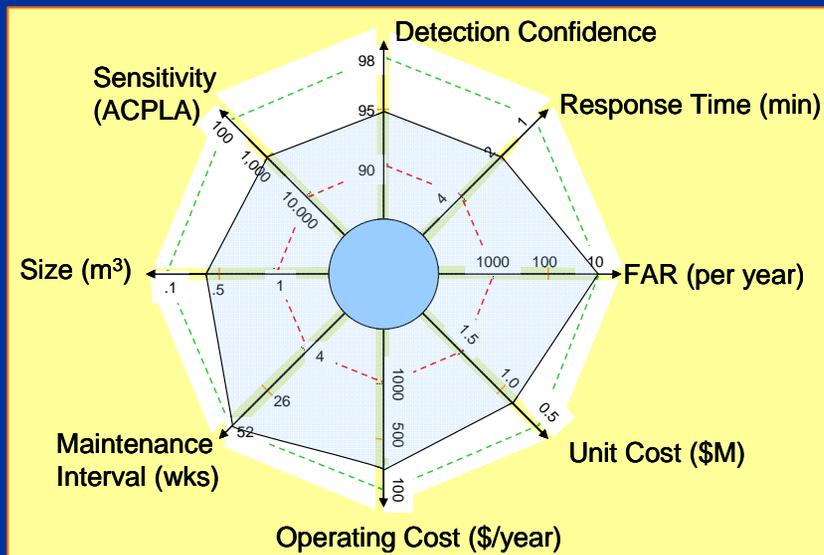
Affordability - Early detection - Low false alarm rate

- **Current Biological Detection System Deficiencies:**

Expensive - Hours/days for analysis - Sensitivity vs false alarm rate

- **Desirable Characteristics of Typical Detect-to-Warn Sensor:**

Spider Charts: metrics shown by length of legs

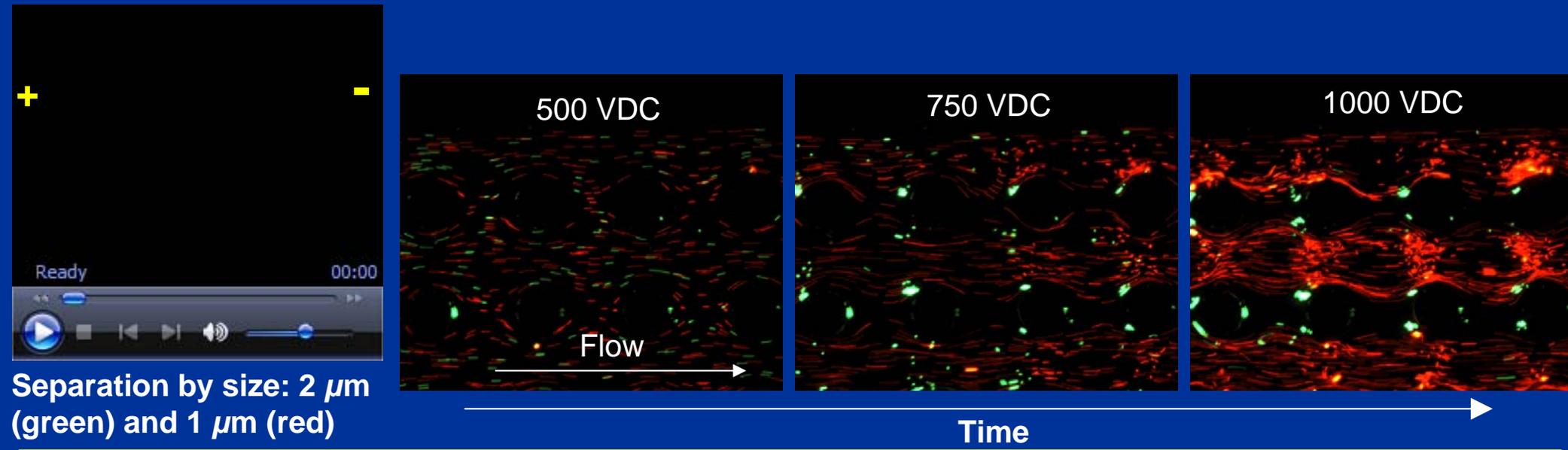


- **Ideal Biological Detection System:**

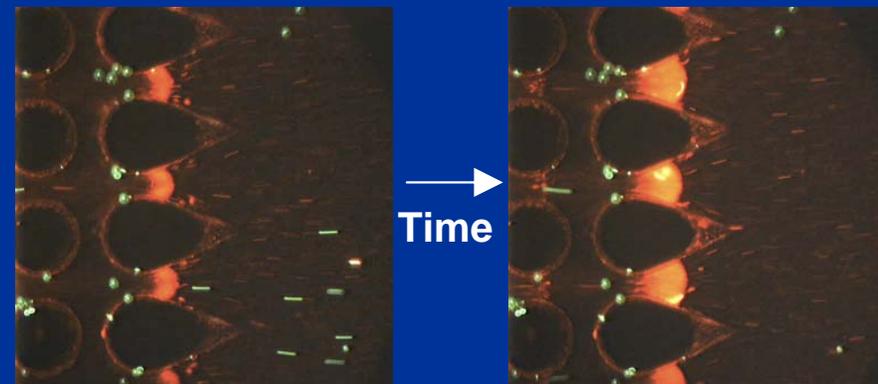
- Low cost, low consumables and simple operation
- Operational flexibility: Configurable as either detect-to-warn or as a detect-to-treat system
- Expensive bioassays may be used if inexpensive orthogonal triggers limit the number of times bioassays are run



Why an iDEP Approach?



Bacillus subtilis spores (red) trapped. $1\ \mu\text{m}$ polystyrene beads (green) pass.



Lapizco-Encinas, B. H.; Simmons, B.A., et al. , Anal. Chem. 2004, 76, 1571-1579

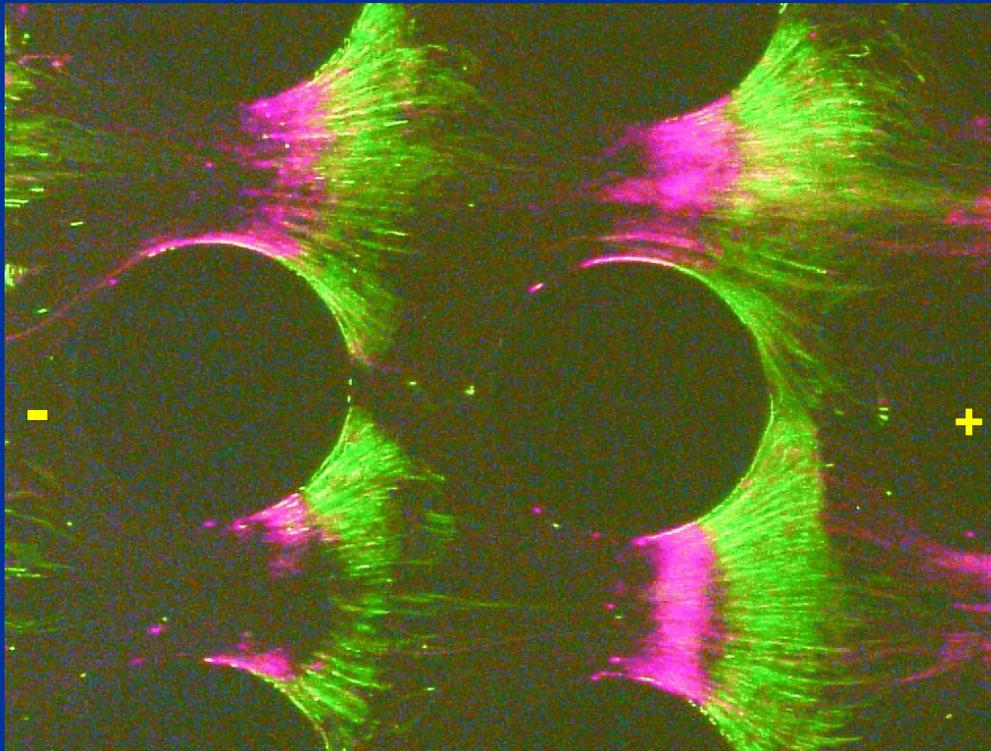
iDEP Selectively Traps Particles and May be Used as a Trigger



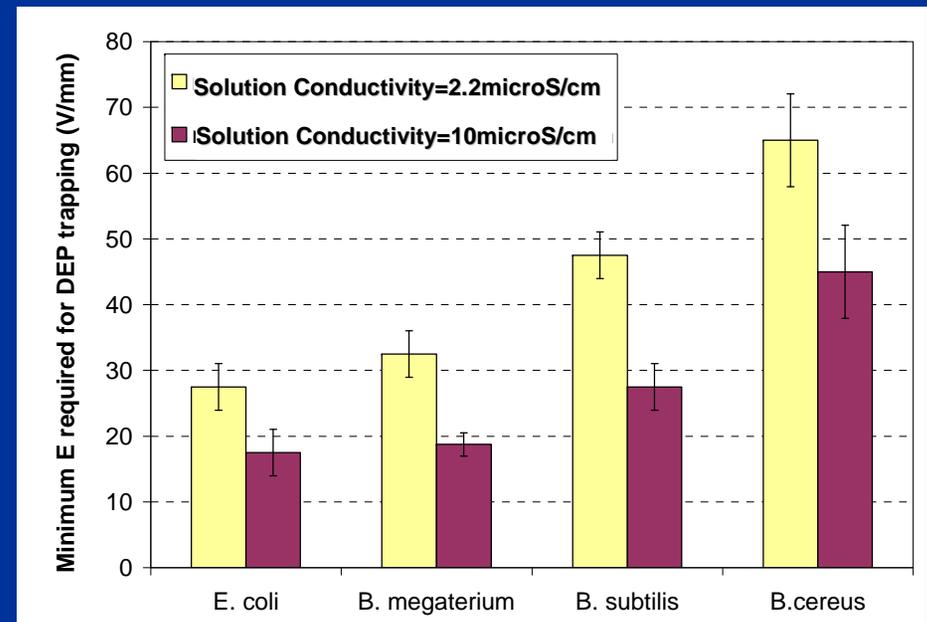
iDEP Can Concentrate Bacteria Selectively



- iDEP Separation of Live *B. subtilis* and *B. cereus* (similar bacteria)
- Mechanism: Different Size and Shape
- Also Separated *E. coli*, *B. cereus*, *B. subtilis*, *B. megaterium*, *B. subtilis* spores, TMV virus, and polystyrene particles of various sizes



Selectively trapping *B. cereus* (green)
while passing *B. subtilis* (red)



E. coli < *B. megaterium* < *B. subtilis* < *B. cereus*

Lapizco-Encinas, B. H.; Simmons, B.A., et al. ,
Electrophoresis 2004, 25,1695-1704.



iDEP is a Physically Selective Phenomenon



- **DEP: Motion of Conductive Object Toward (away from) High Electric Field**

- Along electric field gradients
- Nonlinear in the applied electric field

- **DEP Force Proportional to:**

- Particle volume
- Conductivity + polarizability difference between particle and liquid

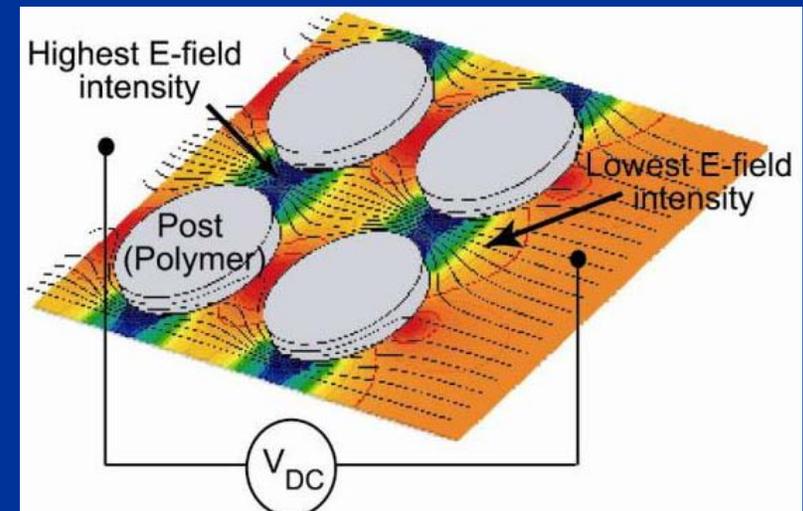
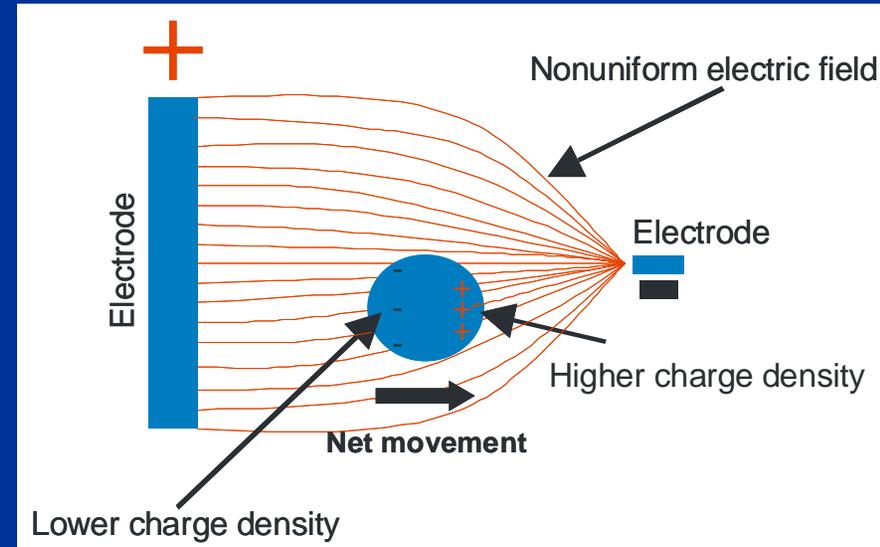
$$F_{DEP} = 2\pi\epsilon_0\epsilon_m r^3 \operatorname{Re}\{f(\tilde{\sigma}_p, \tilde{\sigma}_m)\} \nabla E^2$$

$$\text{For Vdc, } f(\sigma_p, \sigma_m) = (\sigma_p - \sigma_m) / (\sigma_p + 2\sigma_m)$$

Sabounchi, P.; Morales, A.M. et al. Biomed Microdevices, 2008, 10, 661–670.

- **DEP Force depend on:**

- Conductivity of the particle, σ_p
- Conductivity of the medium, σ_m
- Size of the particle, r



iDEP Uses Insulating Post Features to Shape E-field



iDEP with Pressure Driven Flow



- Large Sample Volumes Must be Processed for Many Clinical Applications
- Only Pressure Driven Flow can Process Such Volumes

$$m \frac{du_{particle}}{dt} = -\gamma(u_{particle} - U) + \sum F$$

$$u_{particle} = U + \mu_{EK} E + \mu_{DEP} \nabla(E \cdot E)$$

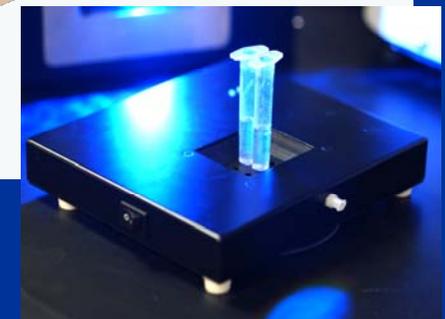
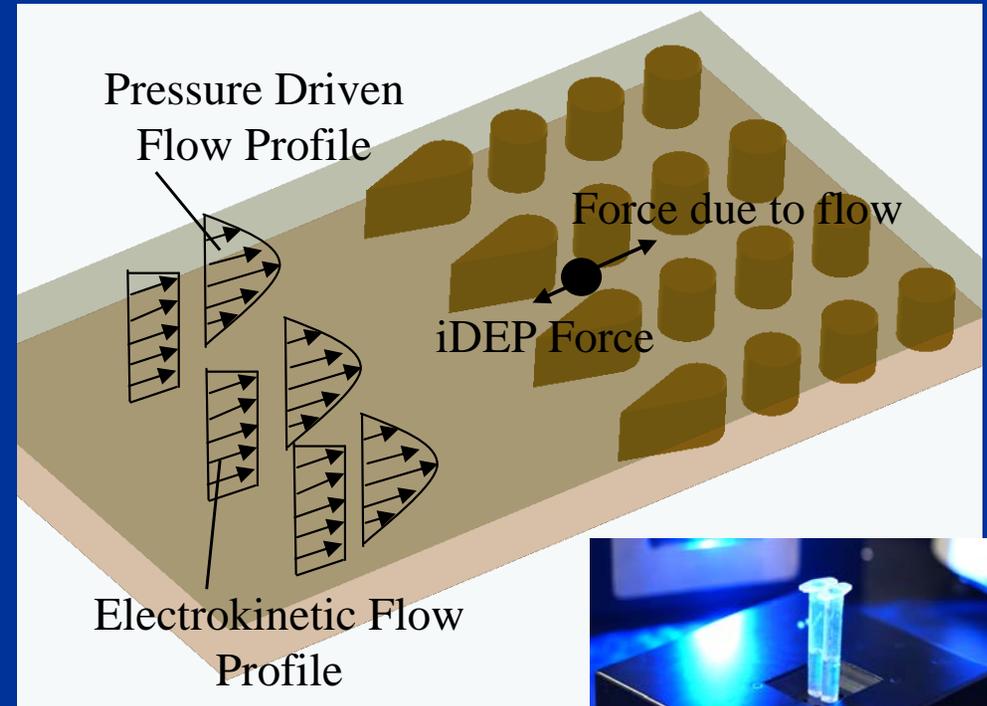
Fluid Flow

Electrokinetic
Velocity

Dielectrophoretic
Velocity

- Potential Attributes of Biological Sensor Incorporating iDEP:

- Affordability: iDEP trigger for bioassay
- Early Detection: Response within seconds of turning on
- Low False Alarm Rate: Orthogonal iDEP trigger



**A Significant Amount of Work
Done in the Lab.**

What Will it Take to Field iDEP?

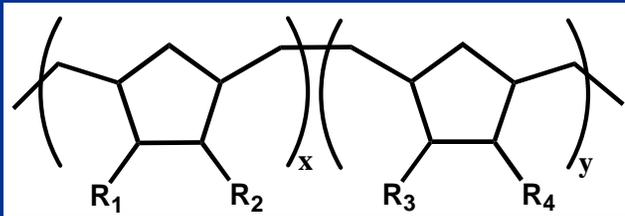


Micro-molded iDEP Zeonor Chips

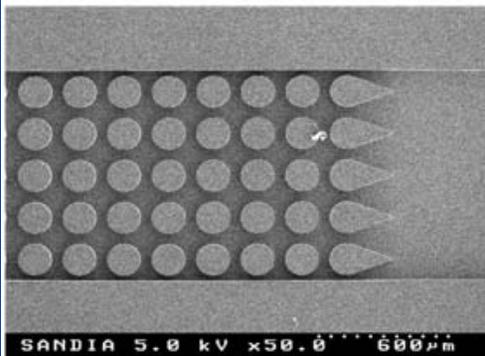
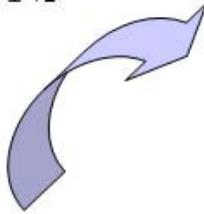


• Polymer iDEP Chips:

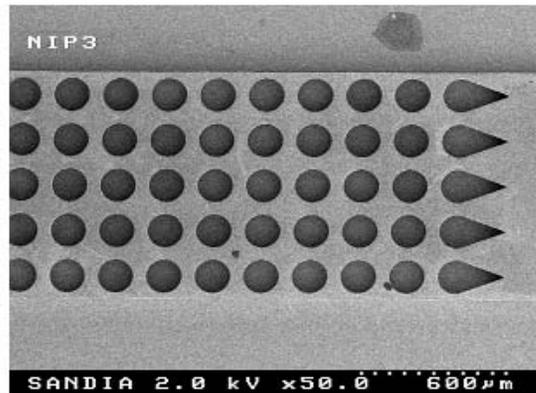
- Low Cost & Ease of Manufacture
- Amenable to Large Scale Production



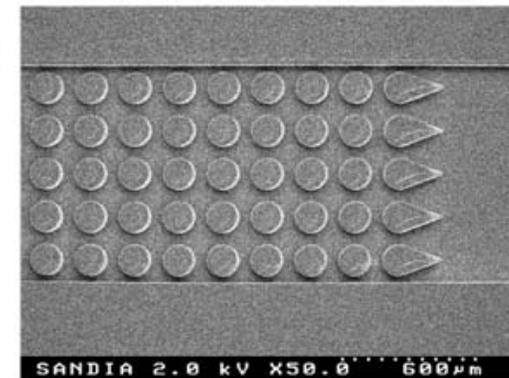
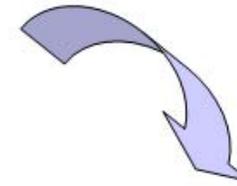
Electroplate Ni Stamp



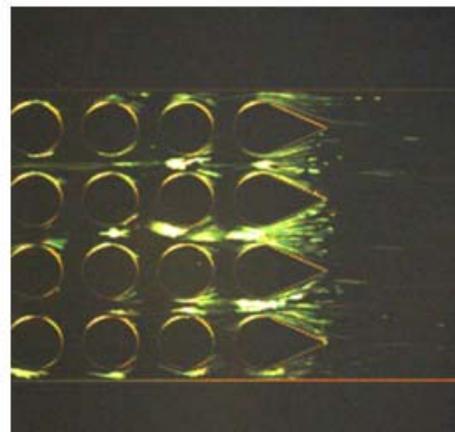
Fabricate Master from Mask (glass, silicon)



Replicate Features into Z1060r Through Injection Molding/Hot Embossing



Bond Chips to Lids and Test

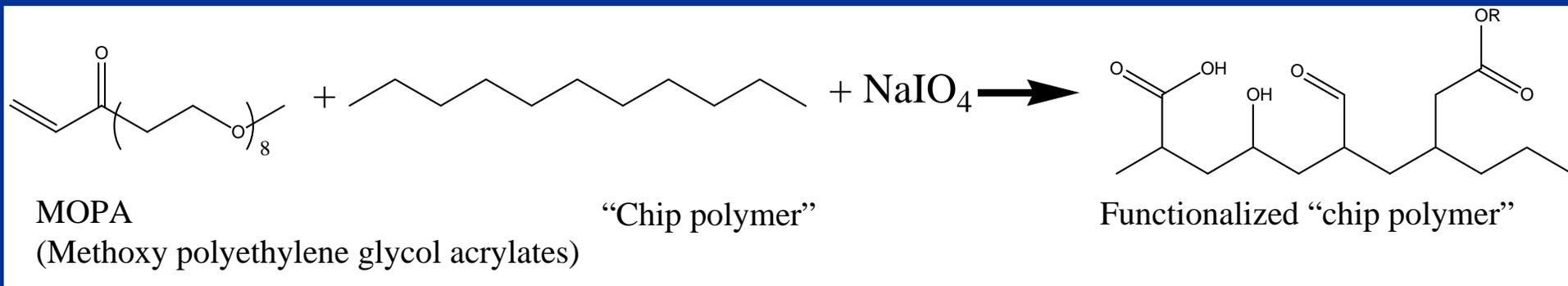




Chip Surface and Buffer Chemistry Is Critical



- **Surface & buffer chemistry enable repeatable trapping with pressure driven flow**

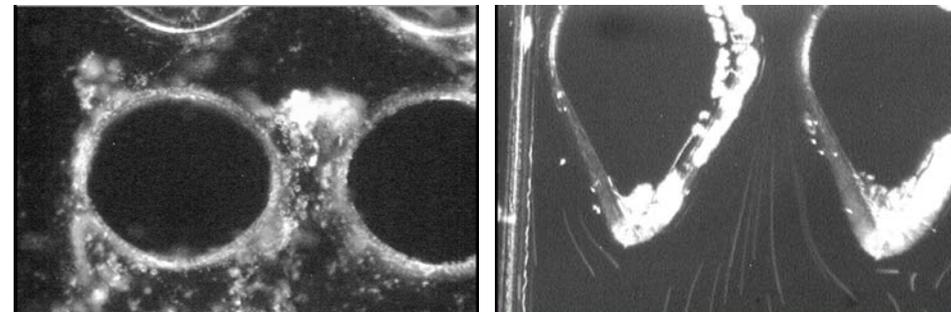


- **MOPA Treatment Lowers Contact angle, $90 \pm 2^\circ$ w/o MOPA vs $65 \pm 4^\circ$ w/ MOPA**

- **Background Buffer pH Adjusted to 8 While Keeping Conductivity Low**

- **Compatible with TWEEN used in Aerosol Sample Collector**

Without MOPA



With MOPA

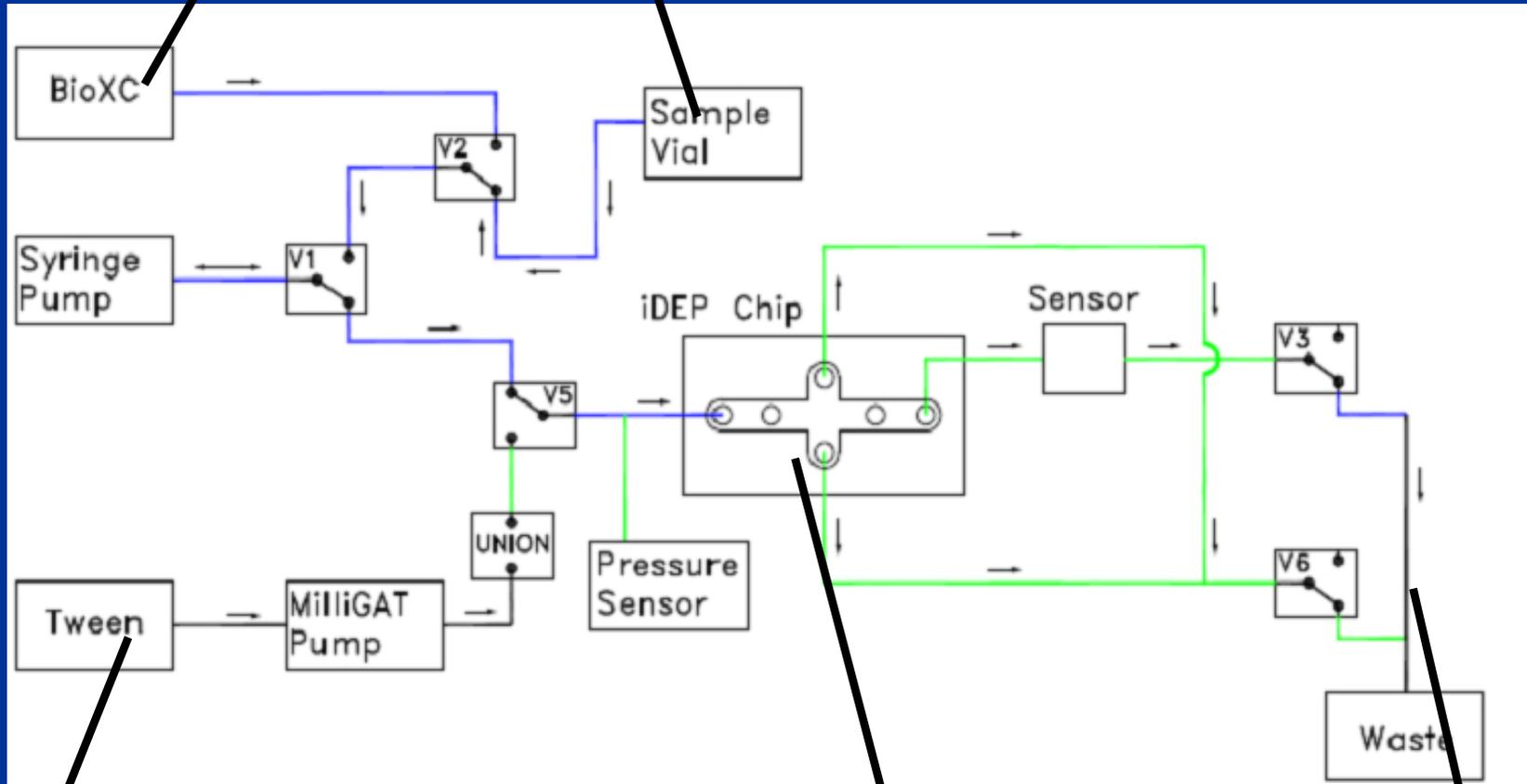




System Layout and Architecture



Aerosol Collector Test Sample



Background Buffer

iDEP Chip

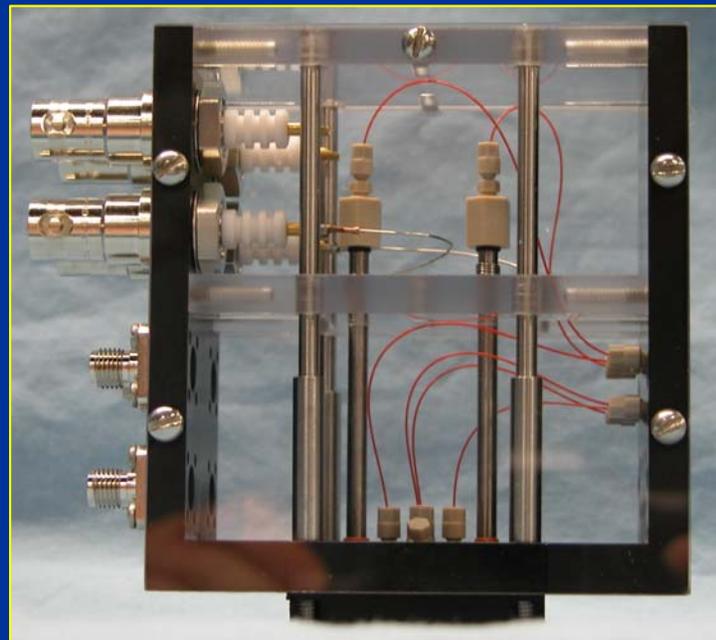
Waste Manifold



Robust Automated iDEP System



- **Designed a Robust System Capable of Operating in the Field**
- **Both Software & Hardware were Simplified and Optimized with Reliability and Safety in Mind**
- **Prototype Field Test Unit Fabricated, Integrated and Tested**



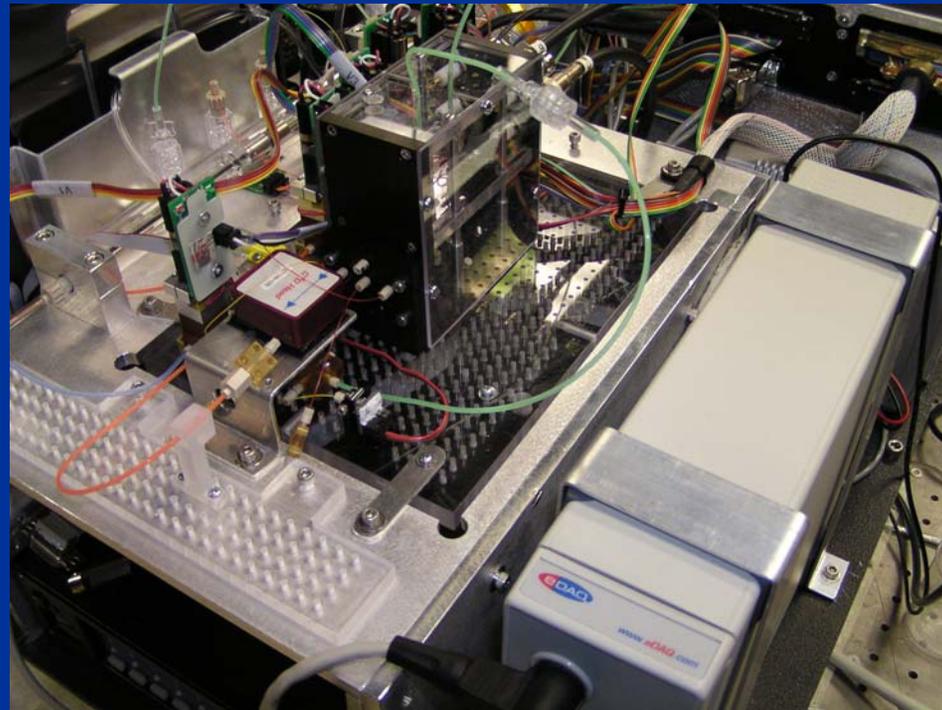
Modular iDEP chip holder



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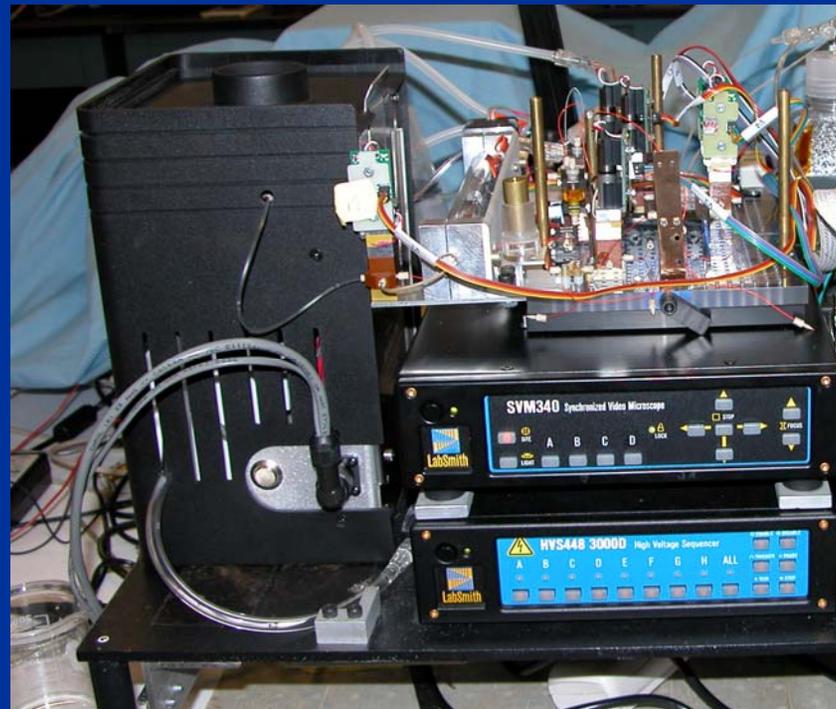
Commercial microfluidic connectors



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Electronics, HVS, and aerosol collector integrated



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Rack mountable packaging



Robust Automated iDEP System



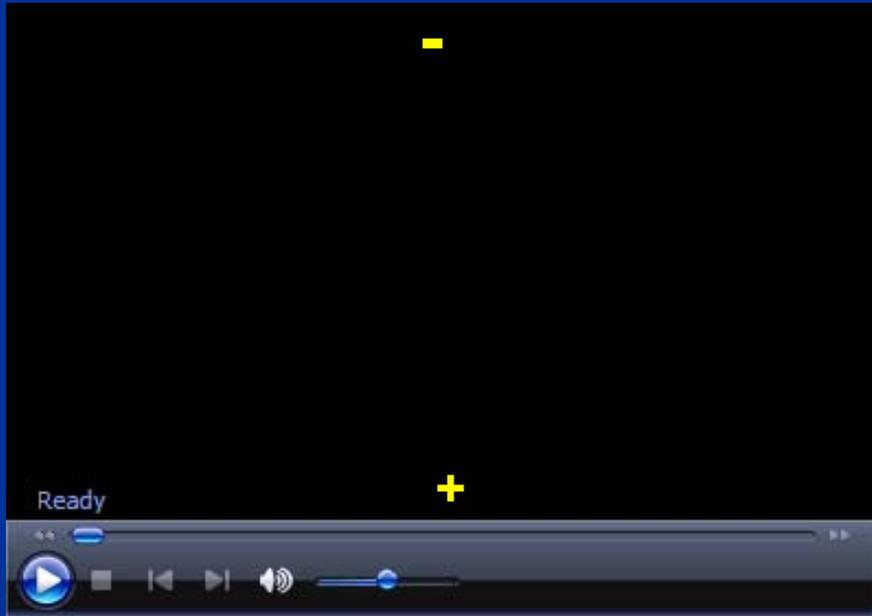
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Command	Time	MilligAT	Syringe	Valve 1	Valve 2	Valve 3	Valve 4	Valve 5	Valve 6	Imped.	H.V.	Collector
Valve	5.000	0.000	0.000	Red	Red	Red	Red	Red	Red	OFF	A 100.000	OFF
Syringe	6.000	0.000	-100.000	Red	Red	Red	Red	Red	Red	OFF	A 100.000	OFF
MilligAT	3.000	0.000	0.000	Red	Red	Red	Red	Red	Red	OFF	A 100.000	OFF
Valve	0.000	0.000	0.000	Red	Red	Red	Red	Red	Red	OFF	A 0.000	OFF

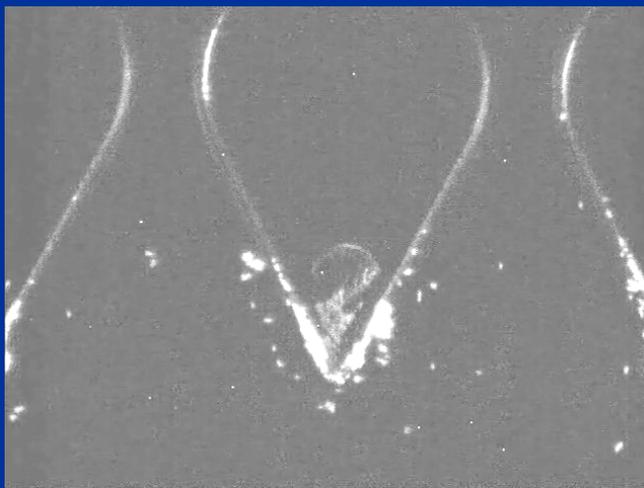
Dedicated control and data logging software



Sample Automated iDEP Run



Fluorescently labeled
2 μm polymer beads
(10^6 particles/ml)



Free Flow (0 V)



Trapping (1600 V)



Release (0 V)

Time



Fluorescence Detector is Immune to iDEP Artifacts

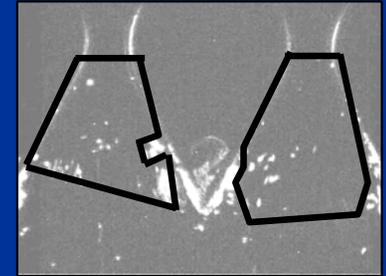
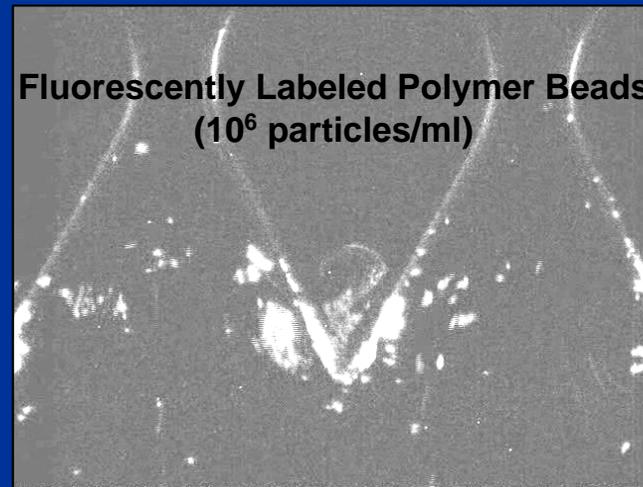


- **Off-chip, Capillary-based Conductivity and Absorbance Detectors are Affected by iDEP-trapping Related Artifacts**

- **Fluorescence Detection not Affected by Artifacts. On-chip Fluorescence Detection Senses:**

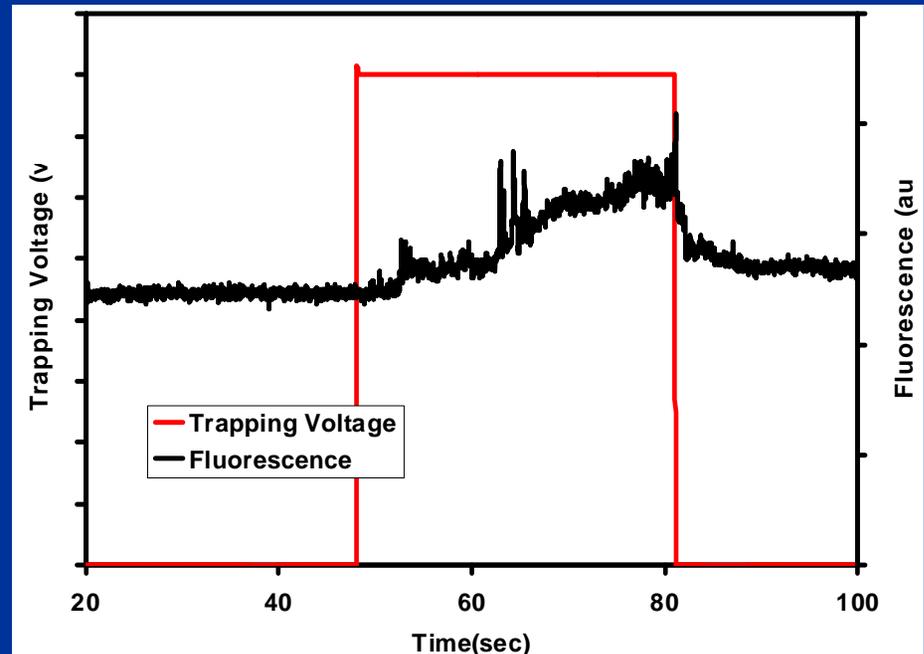
- Trapping & concentration between posts
- Trapped particles shortly after trapping voltage is turned on
- System response in seconds
- Biological particles by detecting native fluorescence

- **Chip Holder Design Becomes Complex**



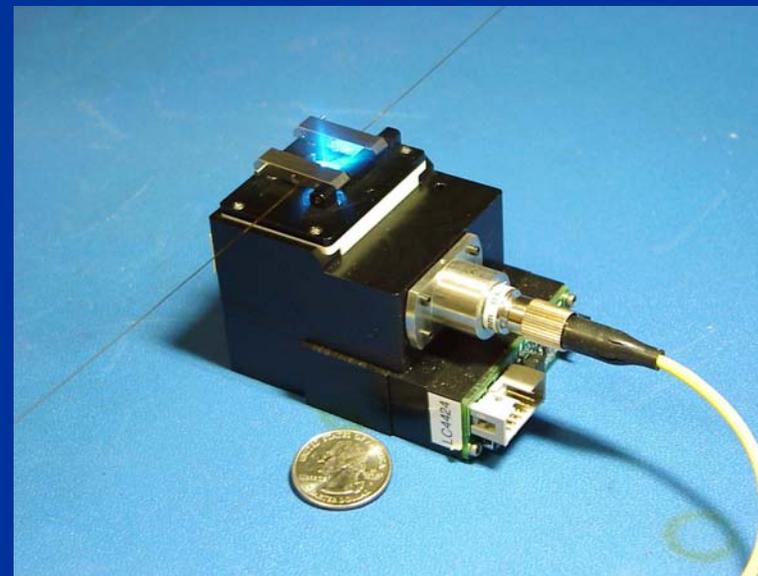
Fluorescence Analysis Areas

Fluorescence Imaging





- These LIF Detectors Have Been Used for Many Years Both in the Lab and in the Field at Various Locations
- The Detector Units were Developed to be Miniature, Rugged, & Consume Little Power
- They Measure Approximately 2.5 X 3 X 2 in, require 5.3 volts, < 100 milliamps, Excluding the Laser Source
- Detector has been used with 405, 488, 532, 635, and 650 nm Excitation Sources



Off-Chip Miniaturized Laser Induced Fluorescence Detector Unit

Renzi, R. et al, Anal. Chem., 2005, 77(2), pp 435–441

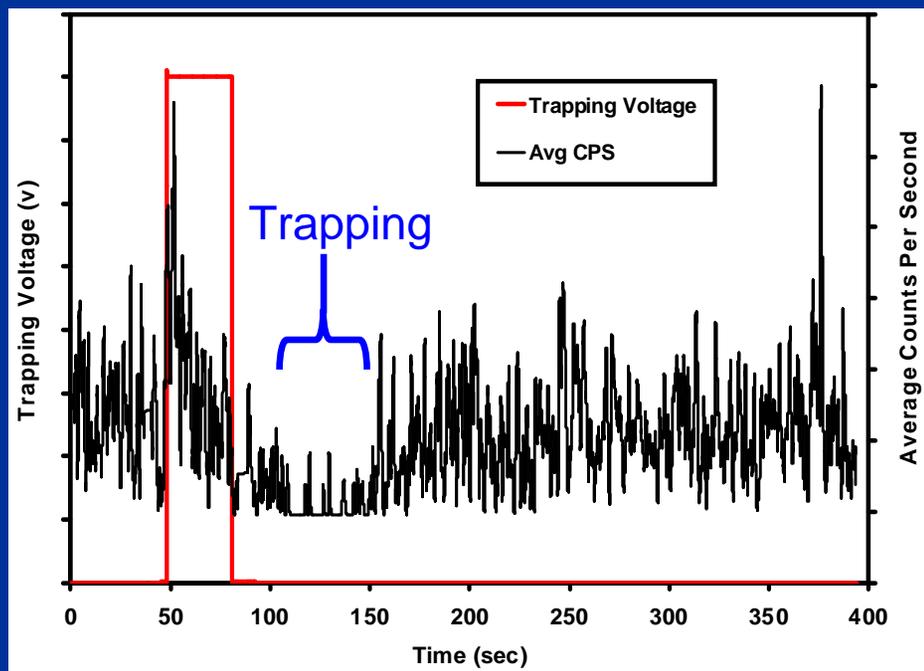
Embedded Capillary Fluorescence Provides Real-Time Detection



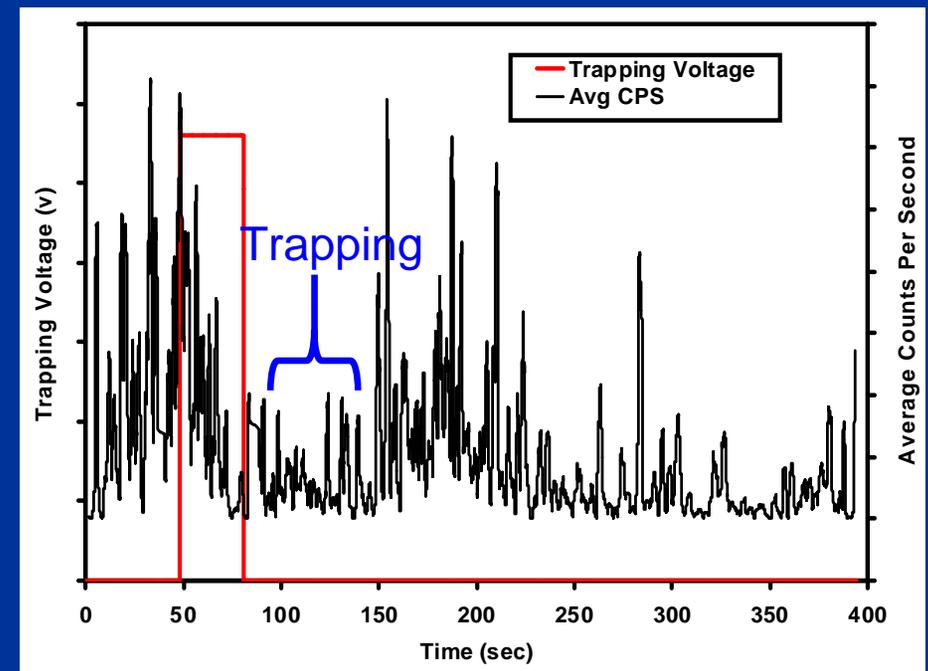
Fluorescence Indicates Trapping and Release



- No Redesign of Chip Holder Needed
- Fluorescence CPS Changes as Soon as Trapping Starts
- Trapping is Seen a Minute after Voltage is Applied vs Concentration!
- A Slight Delay is Introduced by Locating Sensor Off-chip



Fluorescently Labeled Polymer Beads
(10^6 particles/ml)



Fluorescently Labeled *Bacillus atrophaeus*
(10^6 particles/ml)



- **iDEP Has Several Features and Can:**
 - Selectively trap and concentrate particles
 - Be used as a trigger in a cost effective, fast biodetector
- **Automated, Prototype iDEP Field Unit has been Built, Integrated and Tested**
- **Embedded Fluorescence Detection has been shown to Sense Trapping and Concentration in < 1 minute After Applying iDEP Voltage**



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