Chemical and Biological Sensors

Crossroads 2020

Timothy M. Swager, tswager@mit.edu

Why Chemical Sensors?

State of the Art Analytical Lab

- Dedicated Facility
- High Capital Costs
- Need for Skilled Technical Support

Chemical Sensors

- Relatively Inexpensive
- Portable/Field Deployable
- Distributed Sensors can Provide Spatial/Temporal Data
- Minimal Technical Training for Users

Chemical Sensors: Features and Limitations

General Feature/Definition: Enabled by Molecules/Materials

Materials Technology (Transduction) Makes for Inexpensive Hardware

Spectroscopic Methods (Hybrids Paired with Materials)

Can be Information Rich and Uniquely Identify Analytes

Devices Often Have Fixed Sampling Chambers That Can Foul (e.g. Mass Spec)

Often More Expensive with Limited Portability

Receptor/Materials Based Methods

Often Limited by Chemical Selectivity

Can be Prone to Drift (Changing Baselines)

Can be Extremely Inexpensive

Often Can Have a Consumable (Refreshable) Interface with the Sample

Multimodal Sensing with Spectroscopic Methods is Possible

Expanding Markets

Environmental Monitoring
- Distributed Sensors for Identification Non-Point Sources

Wearable Sensors
- Occupational Safety in Manufacturing, Research, Hazmat
- Individuals Interested in Personal Exposure

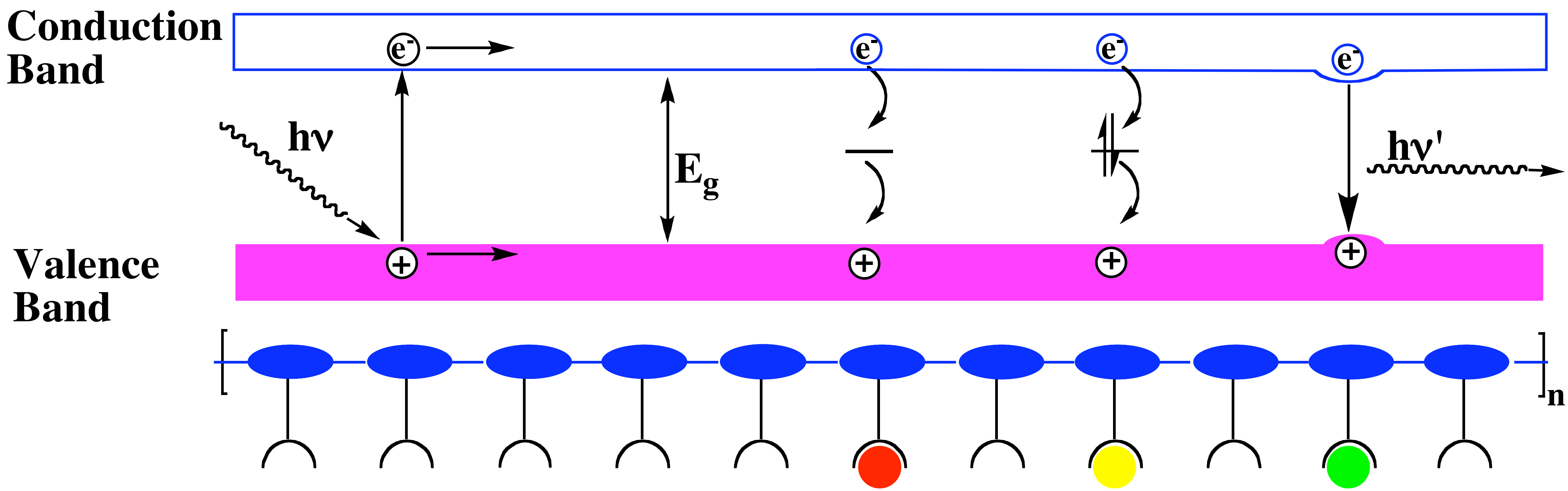
Building Controls
- Integrated Distributed Air Quality Sensors

Biotech/Manufacturing
- Process Controls

Medical Diagnostics
- Home Screening/Clinic

Food and Ag
- Distribution
- Production- Greenhouses
- Personal Testing of Food

Amplification by Energy Migration in Electronic Polymers



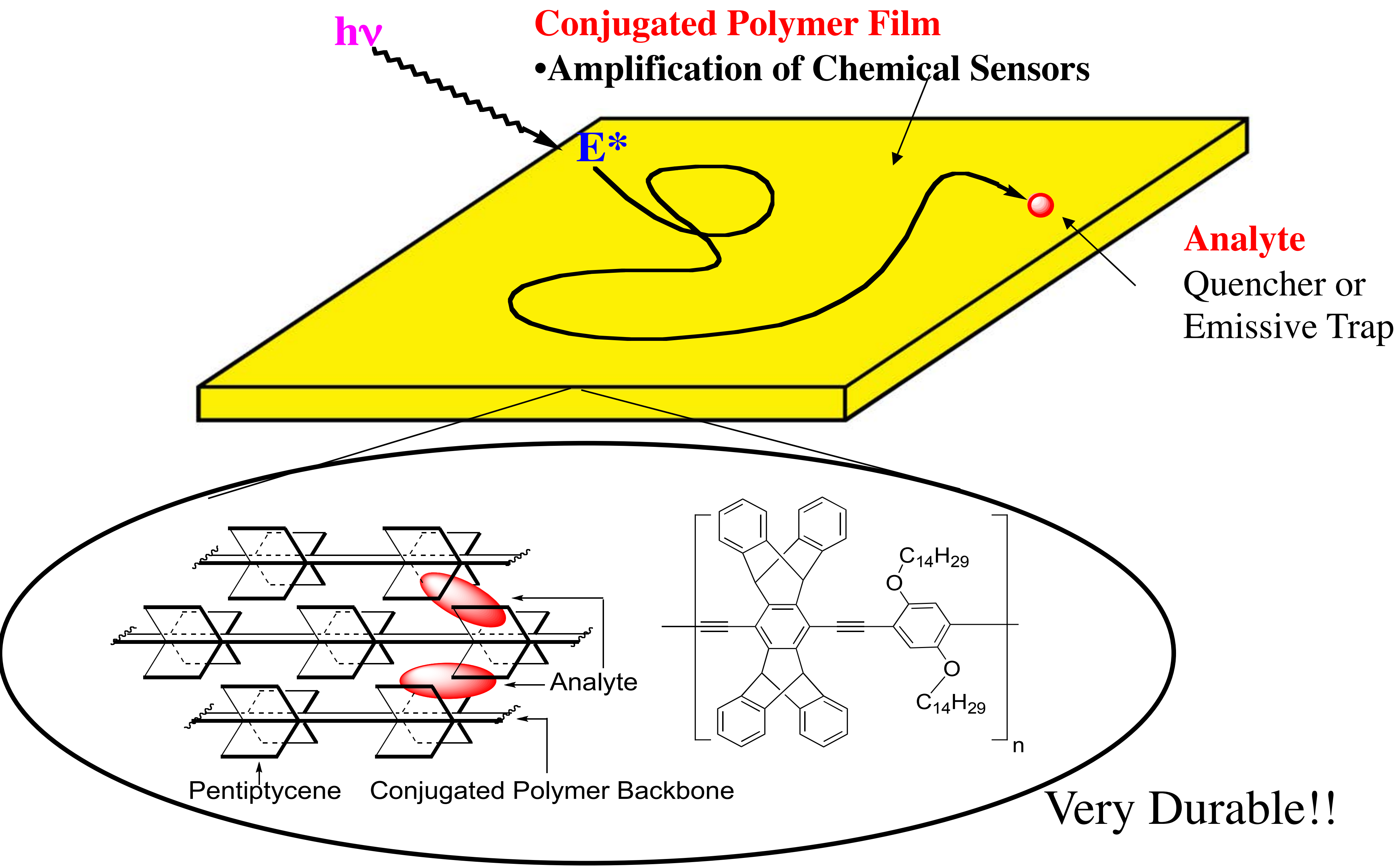
Excitations migrate along the polymer backbone and are quenched when they encounter an acceptor.

J. Am. Chem. Soc. **1995**, *117*, 12593

Accts. Chem. Res. **1998**, 31, 201-7

- "Conjugated Polymer-Based Sensory Materials" *Chem. Rev.* **2000**, 100, 2537-2574.
- "Chemical Sensors Based on Amplifying Fluorescent Conjugated Polymers" *Chem. Rev.* **2007**, *107*, 1339 - 1386.

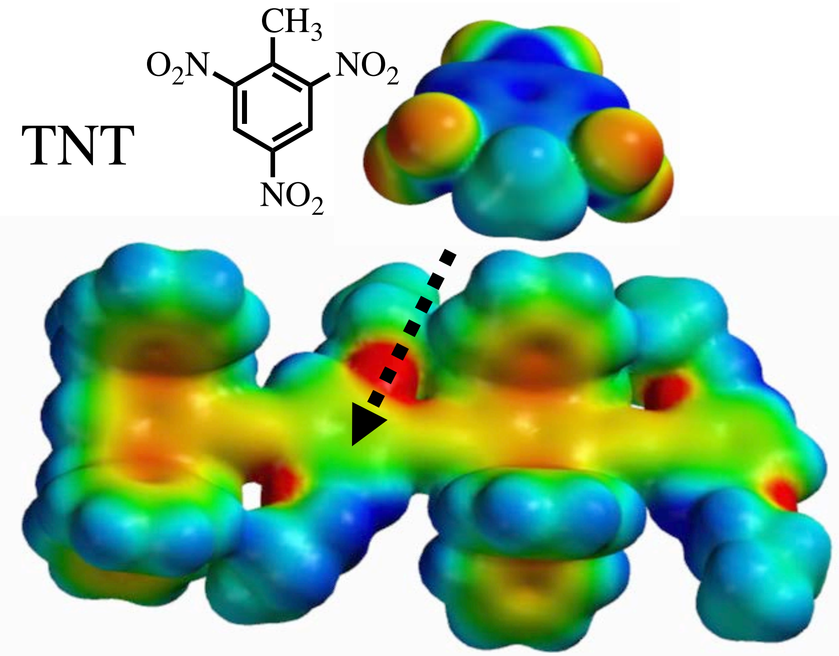
Going 3D: Sensory Polymer Films



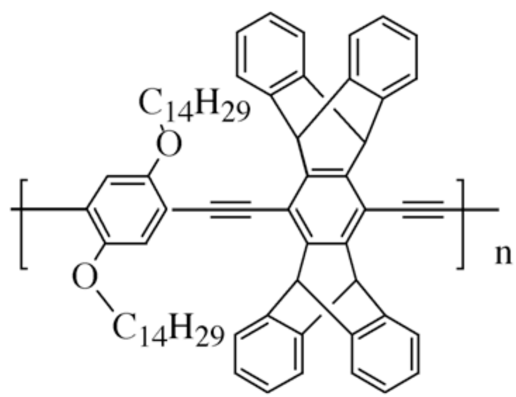
Very Durable!!

Yang, J.-S.; Swager, T. M. *J. Am. Chem. Soc.* **1998**, 120, 5321-5322.

Amplifying Polymers For Explosives Detection

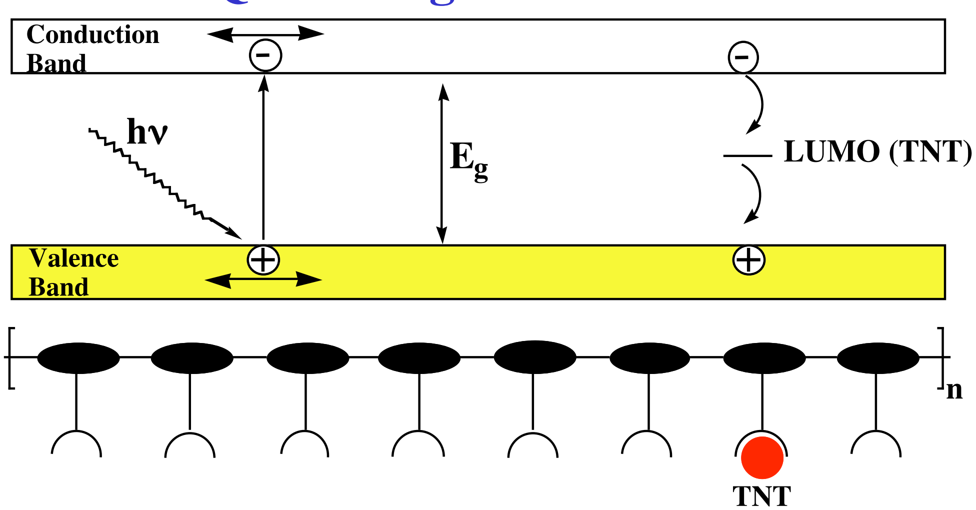


Nitroaromatics Are Ubiquitous in Explosives
TNT has only a 5-8 ppb Vapor Pressure

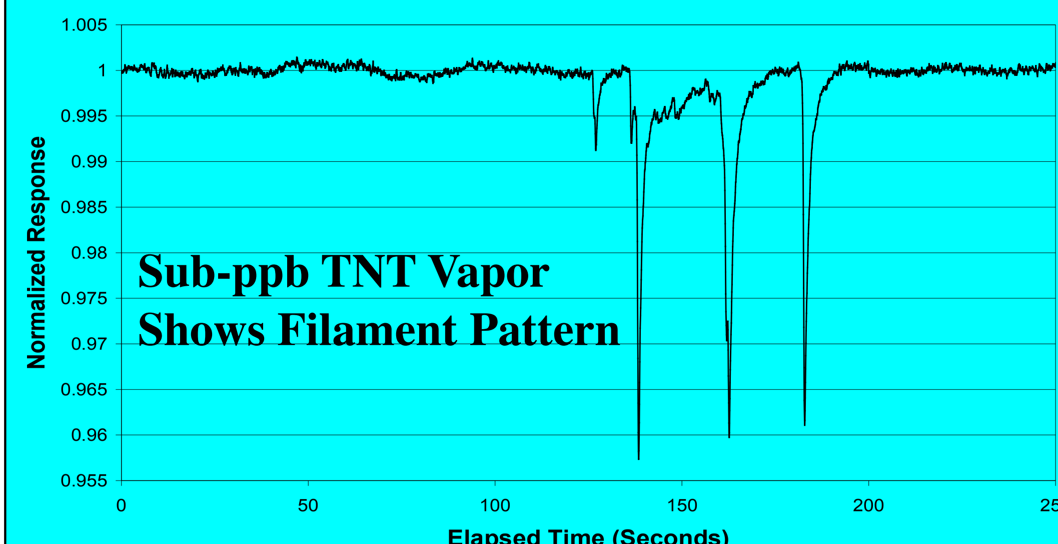


MIT Polymers Are the Basis of the FLIR Fido Detectors

Quenching Mechanism



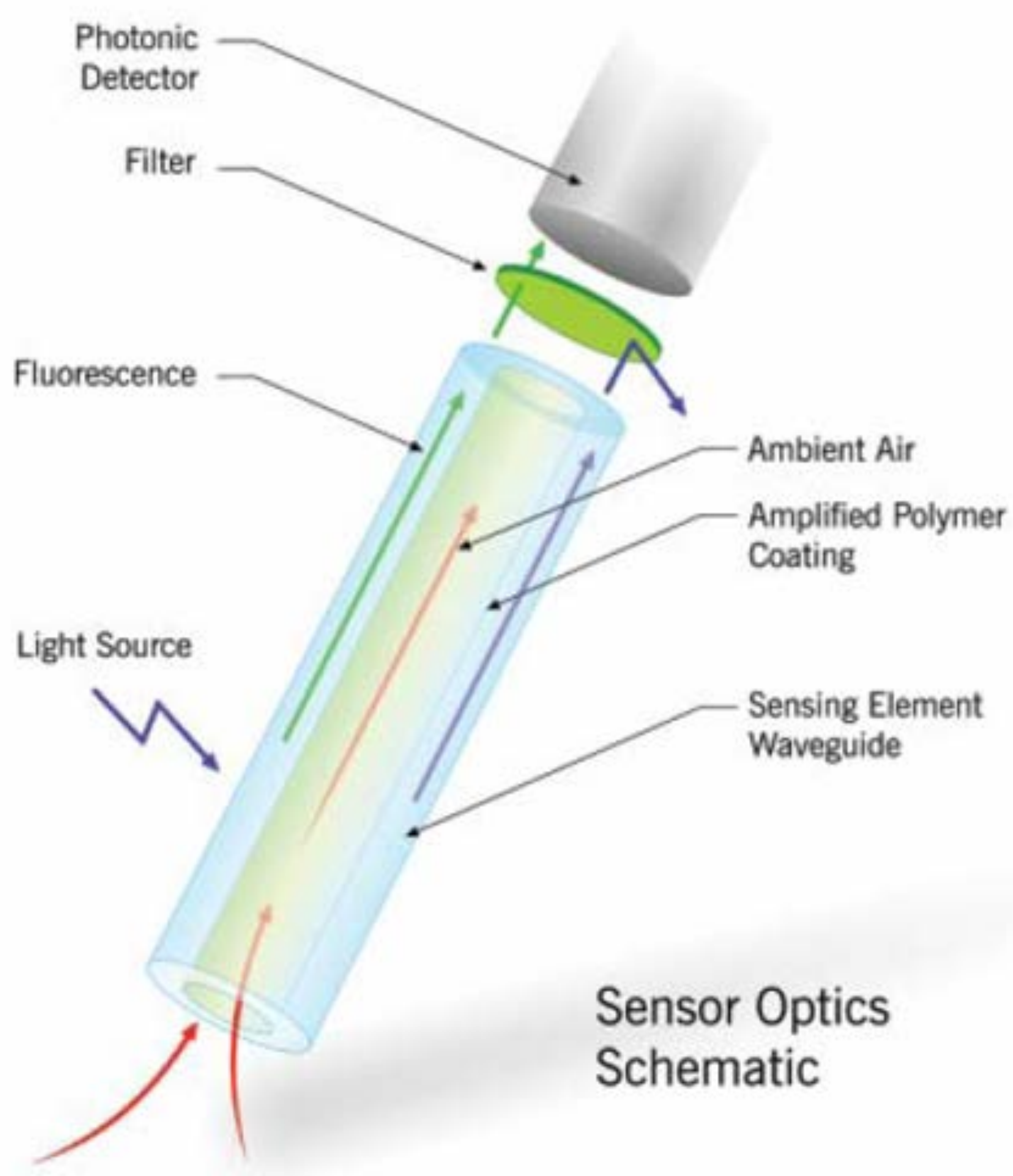
2-Meter Standoff Detection of TNT Demo-Blocks

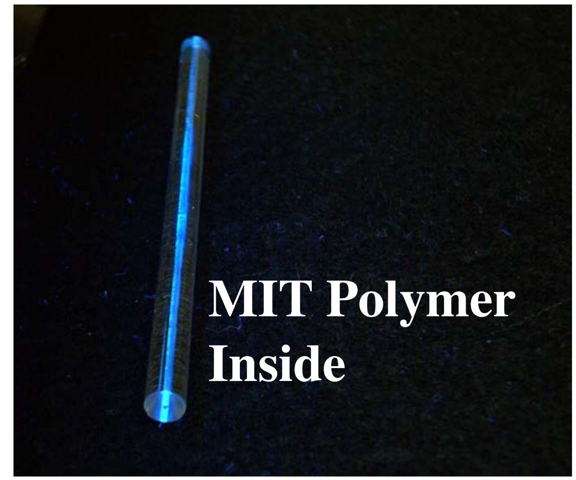


Data Courtesy of Mark Fisher, FLIR Systems

Courtesy of FLIR Systems

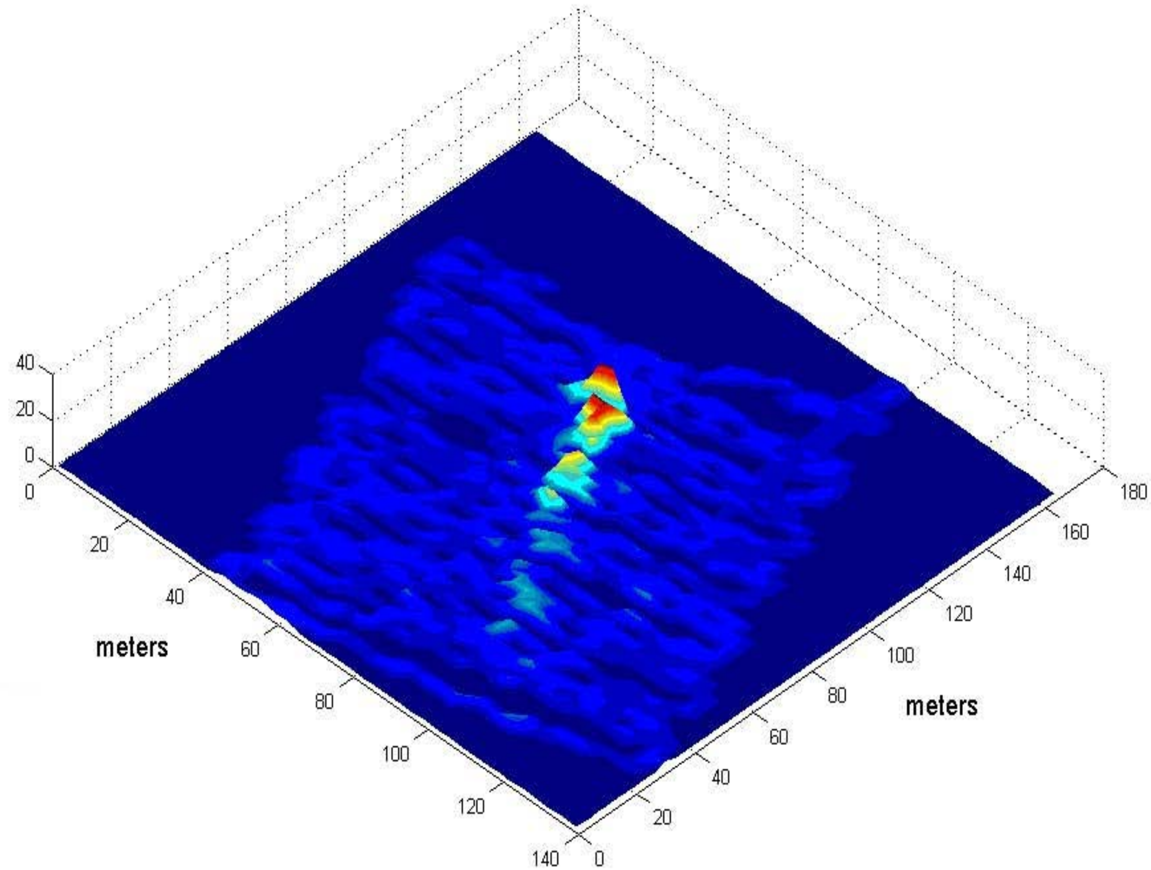
Single-Channel Fido Schematic





TNT Plume Tracing by Underwater Autonomous Vehicles

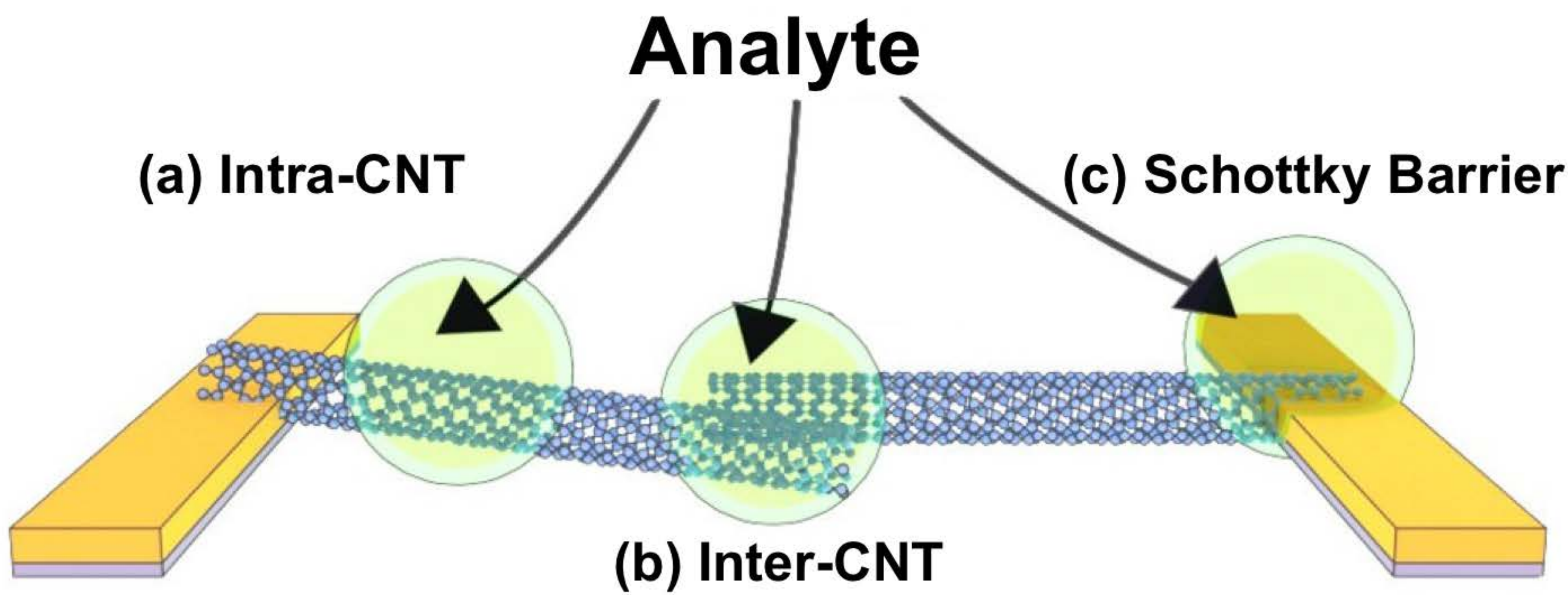
FLIR SYSTEMS



GPS Tracking of ppb TNT in Pacific Ocean

Carbon Nanotube Sensing Mechanisms

Chemiresistor/Chemicapacitance Responses are Often the Result of a Complex Mixture of Mechanisms

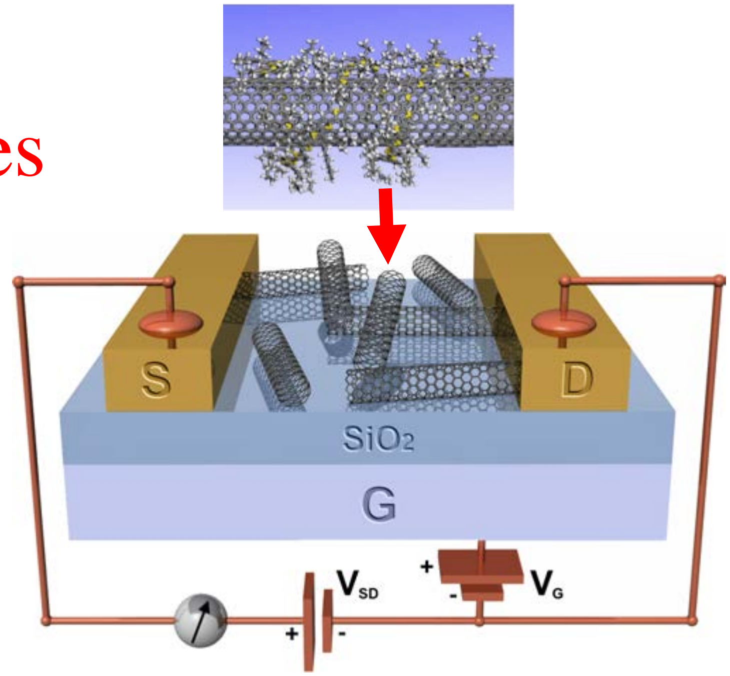


Schröder, V.; Savagatrup, S.; He, M.; Lin, S.; Swager, T. M. "Carbon Nanotube Chemical Sensors" *Chem. Rev.* **2019**, *119*, 599-663.

CNT Chemiresistors

Intrinsic Advantages of Chemiresistors

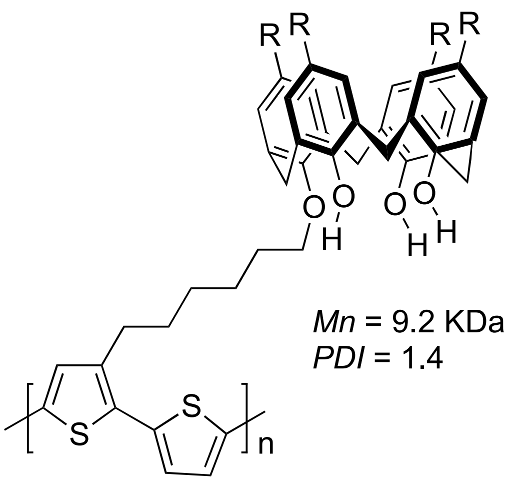
- Low Power/Cost
- Small Footprint
- Wireless Network

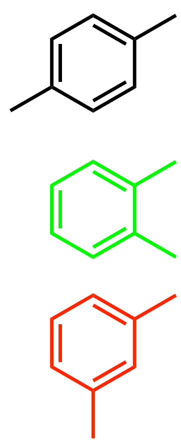


Technical Needs

- High Sensitivity
- **Selectivity**
- Minimize Drift

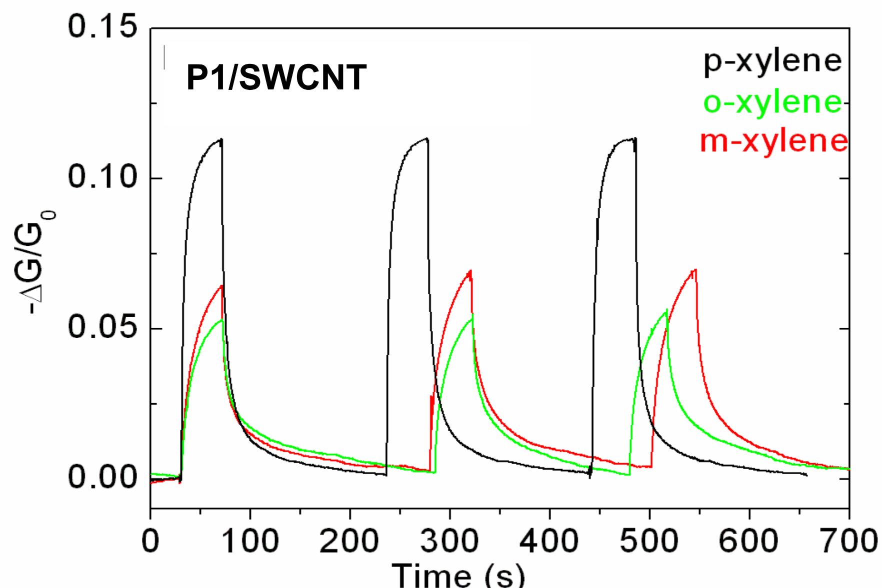
Polymer Wrapper/Receptor





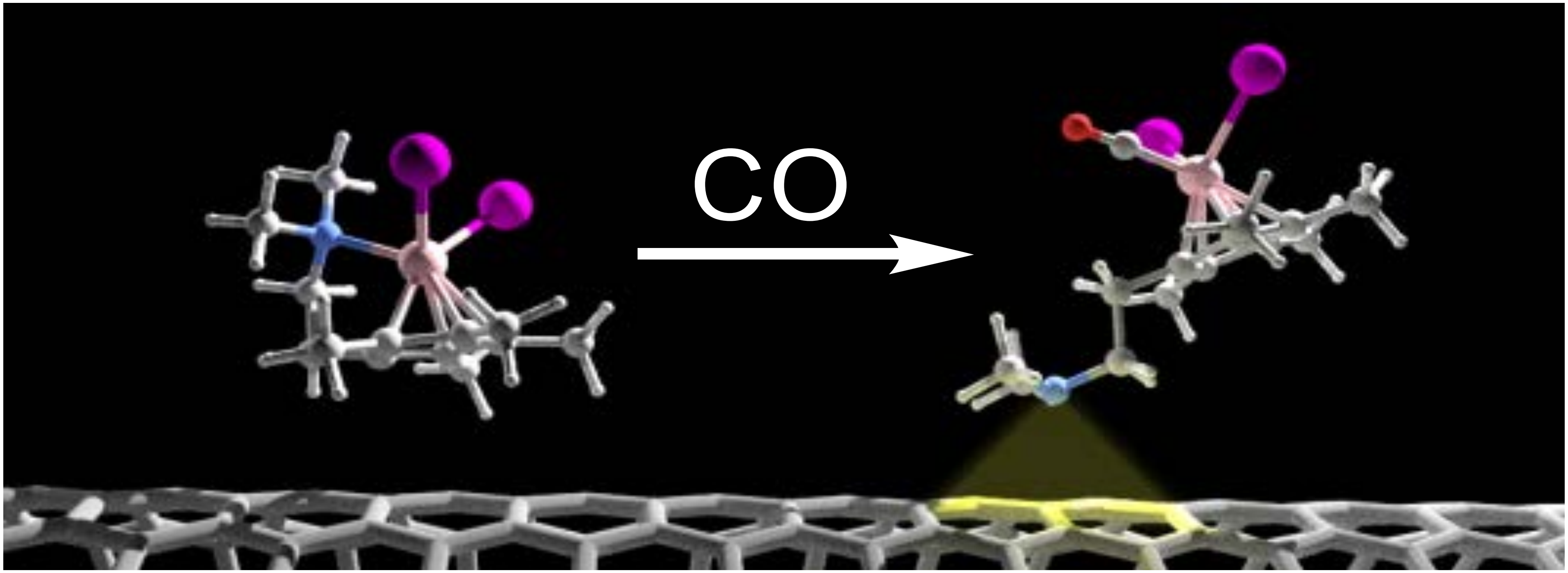
Binds in Calixarene

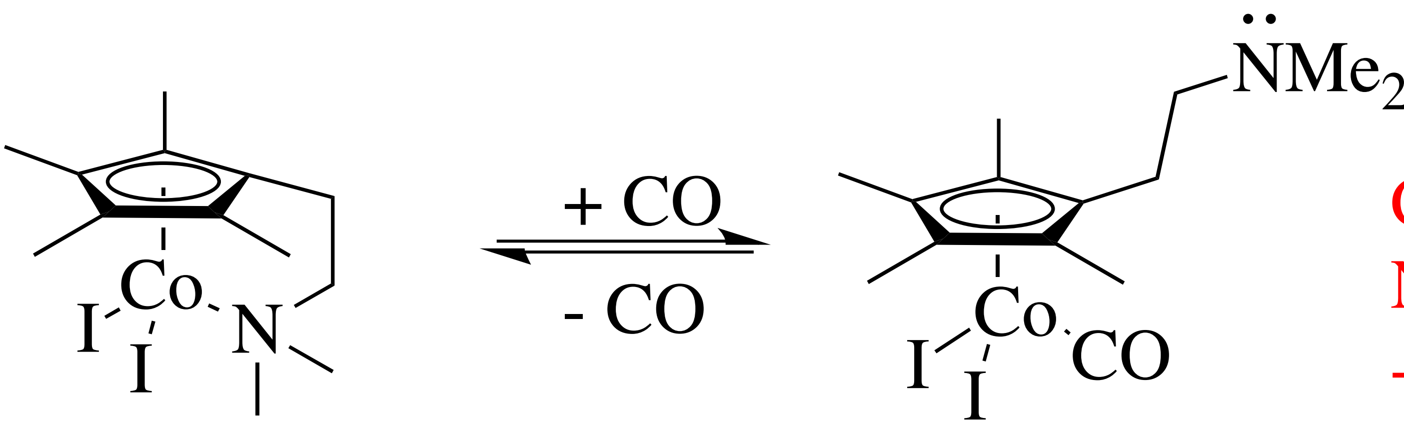
To Wide for Strong Binding



Wang, Yang, Swager *Angew. Chem. Int. Ed.*, ***2008*, *47*, *8394-8396***

Triggered Amine Release

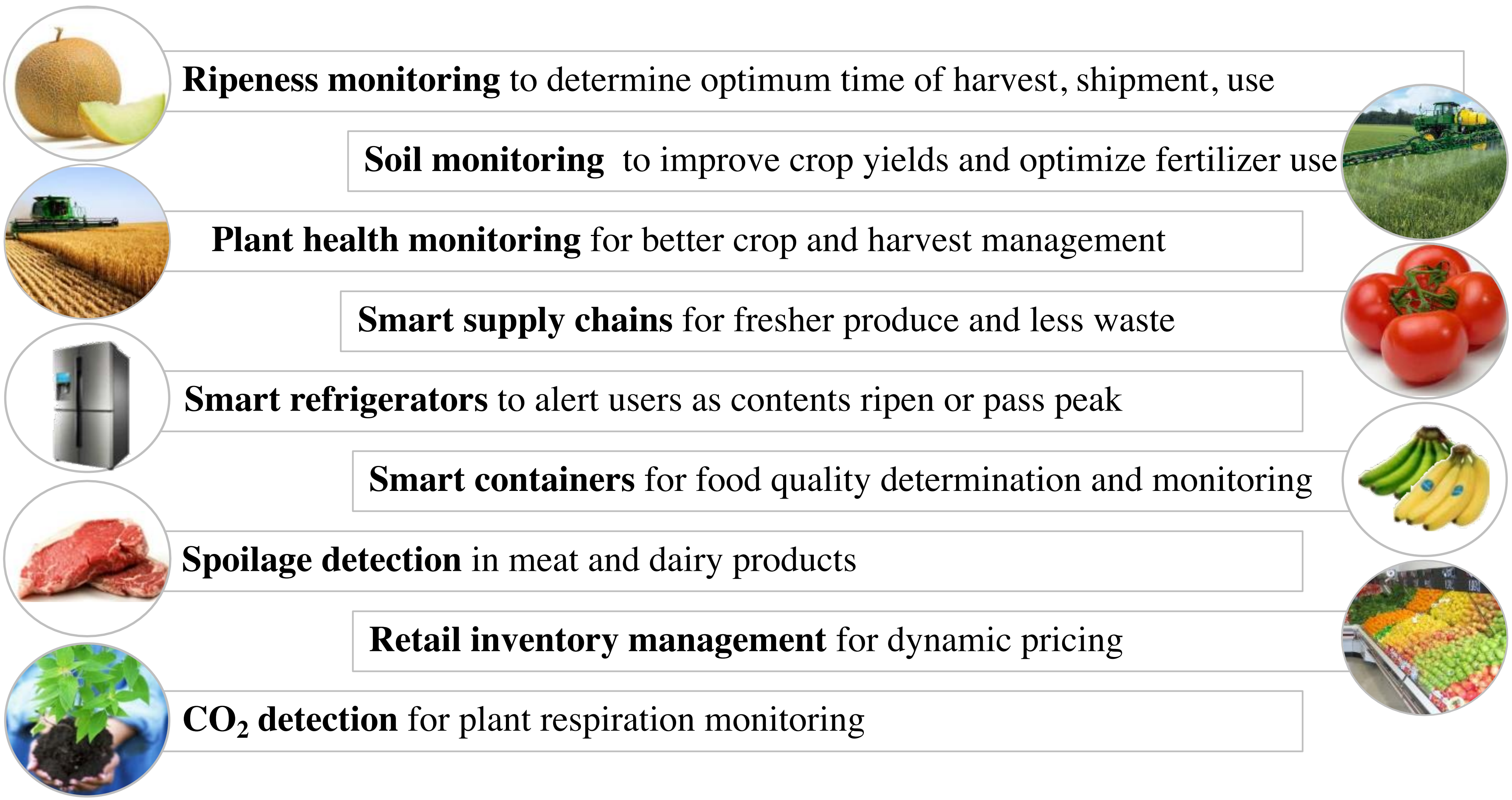




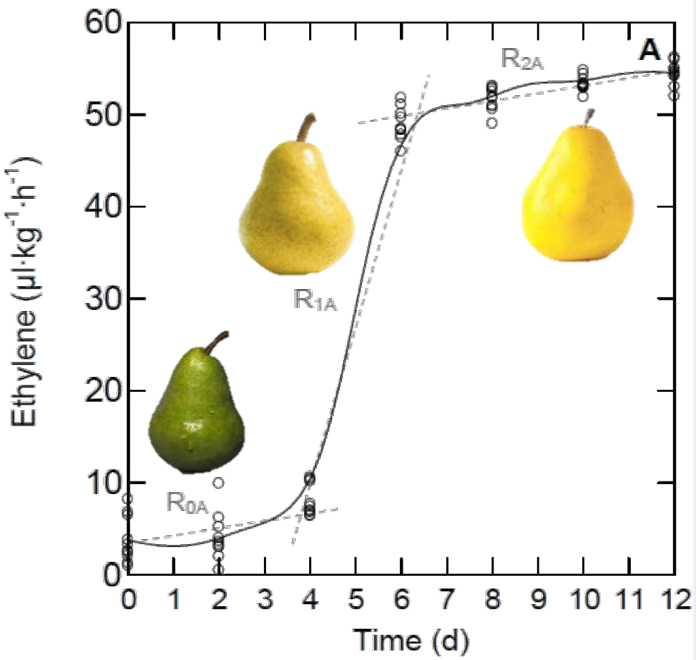
Charge Transfer to the Nanotube Reduces the + Carriers (Holes)

Liu, S. F.; Lin, S.; Swager, T. M. *ACS Sensors* **2016**, *1*, 354-357
Jutzi, P.; Kristen, M.; Dahlhaus, J.; Neumann, B.; Stammler, H.-G. *Organometallics* **1993**, *12*, 2980–2985.

Sensing for Food and Agriculture



Importance of Gases in Food/Ag



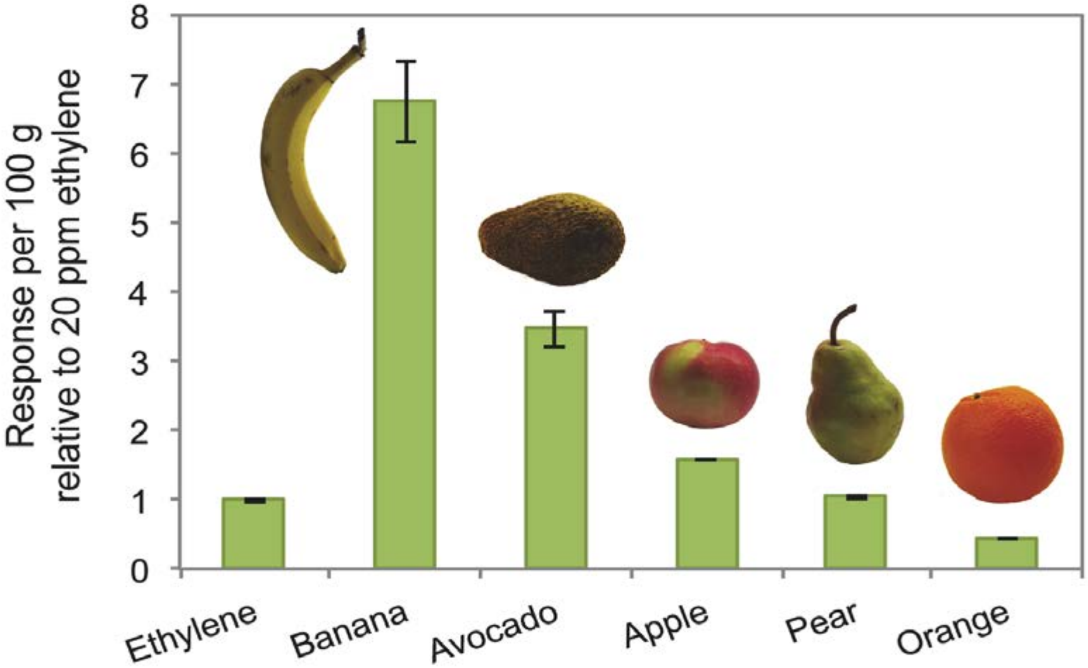
Ethylene emission increases close to peak ripeness

Ethylene:
- **Given off by produce during ripening** (15+ climacteric fruits, e.g. avocado, banana, apple, mango)
- **Induces ripening** (35+ fruits, vegetables, and flowers respond to ethylene)
- **Indicator of plant health** (can be combined with measurement of other gases)

Amines:
- **Indicator of meat/fish spoilage**

Ammonia:
- Soil **nutrient level monitoring**

Detection of Ethylene Emissions from Fruit

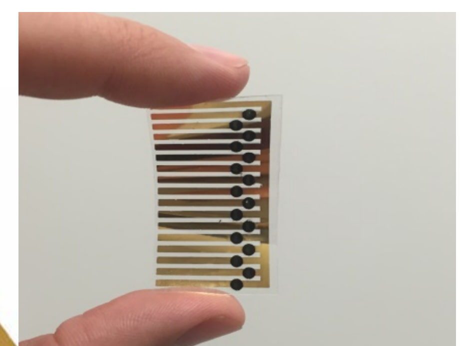


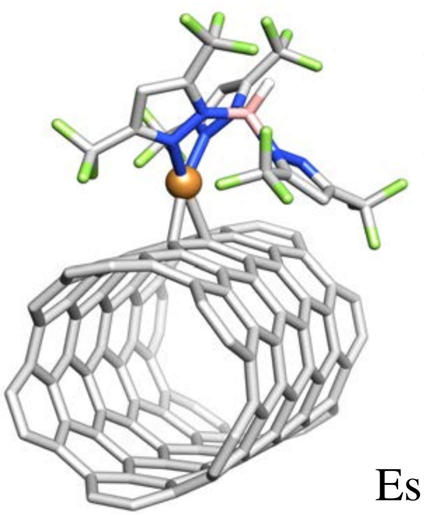
Relative response of **[Cu]**-SWNT devices to 100 g of fruit relative to the response to 20 ppm ethylene

Carbon Nanotube Chemiresistors

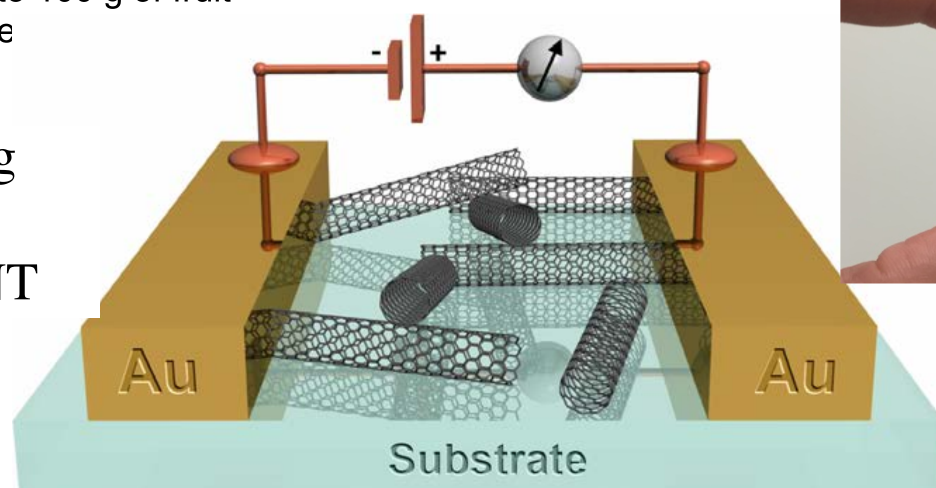
- **Plug and Play:** variable resistor read-out
- **Array-Capable:** 80+ analytes demonstrated
- **Miniature:** 1-2 mm^2 per sensor element
- **Low cost:** replaceable sensor chips
- **Disposable:** paper, plastic, or glass substrates
- **Simple Fabrication:** screen- or inkjet-printing

Sensors on Plastic





Ethylene Binding Metal Complex Bound to SWCNT

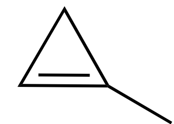


Esser, B.; Schnorr, J. M.; Swager, T. M. *Angew. Chem. Int. Ed.* **2012**, *51*, 5752-5756.

Real-Time Ethylene and 1-MCP Sensors for Apple Cold Storage Rooms

Pilot Product Deployed at 100 Locations in 5 Countries

AgroFresh



1-methylcycloprop-1-ene

FOR IMMEDIATE RELEASE

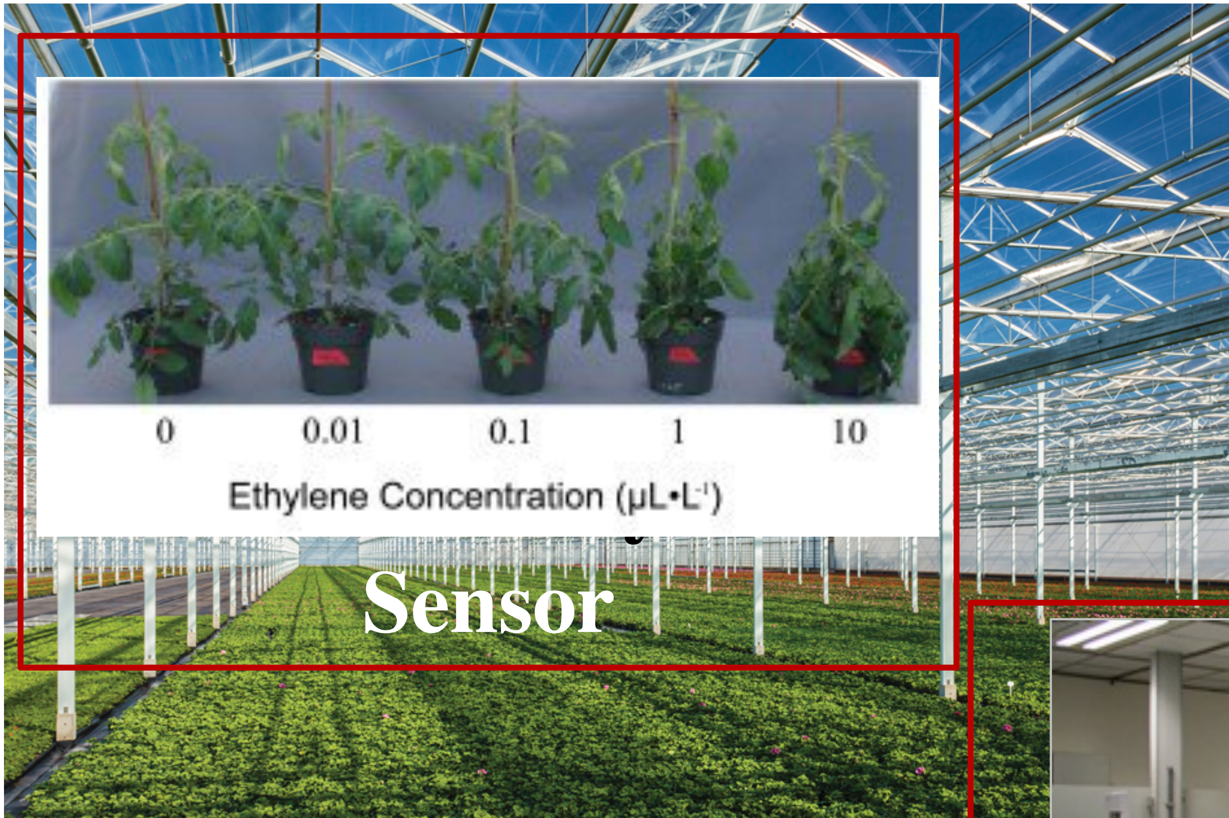
AgroFresh Introduces Novel Sensor Technology

New sensors pair with SmartFresh™ technology to provide unparalleled peace of mind to storage room operators

PHILADELPHIA, Sept. 7, 2016 – AgroFresh Solutions, Inc. (NASDAQ: AGFS) and C_2Sense, Inc. have co-developed proprietary sensors to monitor ethylene and 1-methylcyclopropene (1-MCP), the active ingredient in patented SmartFresh™ post-harvest technology. The sensors are designed to deliver real-time information for better insights into the condition of fruit in refrigerated and controlled atmosphere (CA) storage rooms.

Apple Cold Storage Facilities: $1M in Each Room

Protecting Plants in Greenhouses

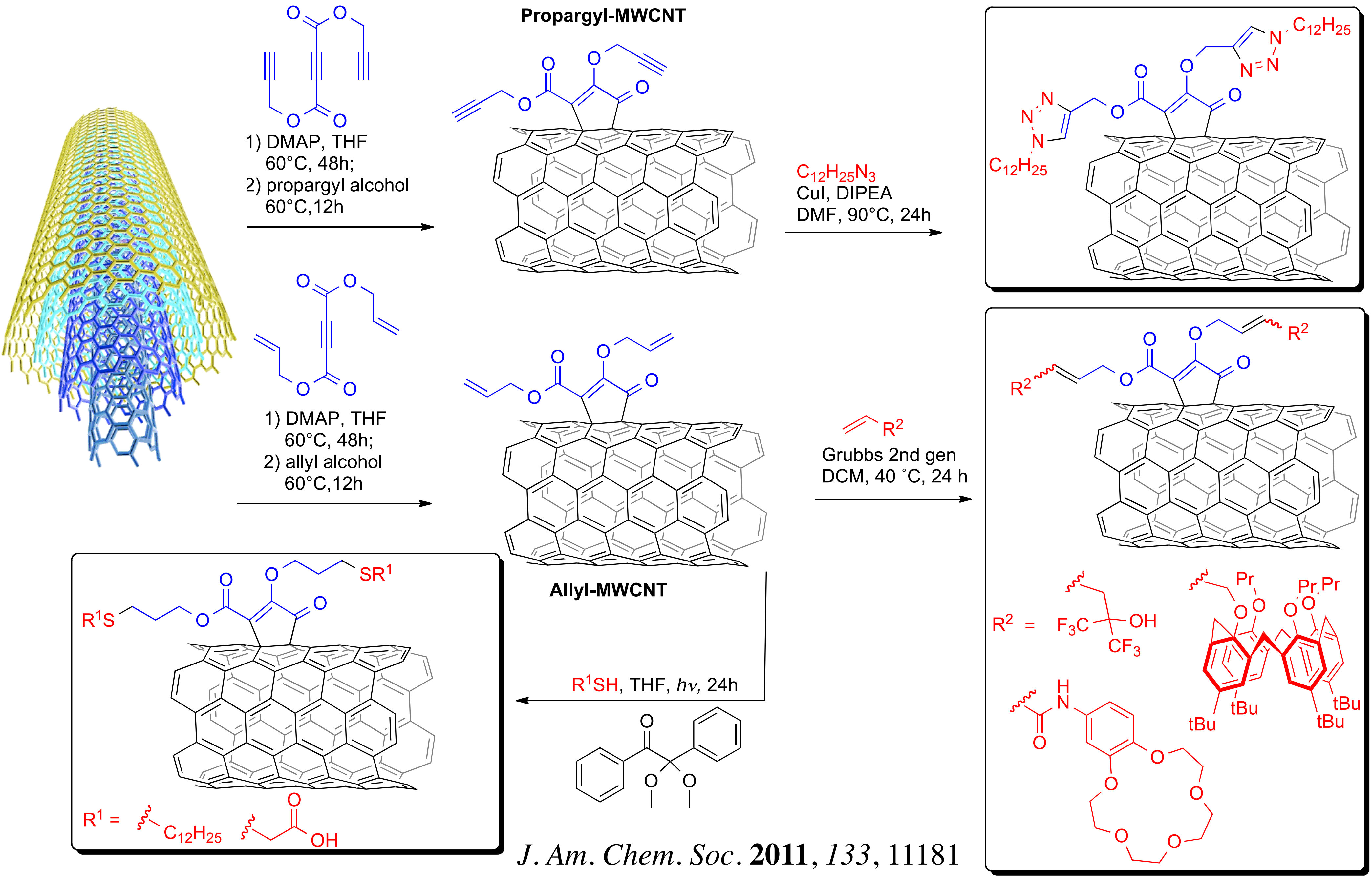


Ethylene:

- Given off by produce during ripening
- Induces ripening/spoilage

Sensor

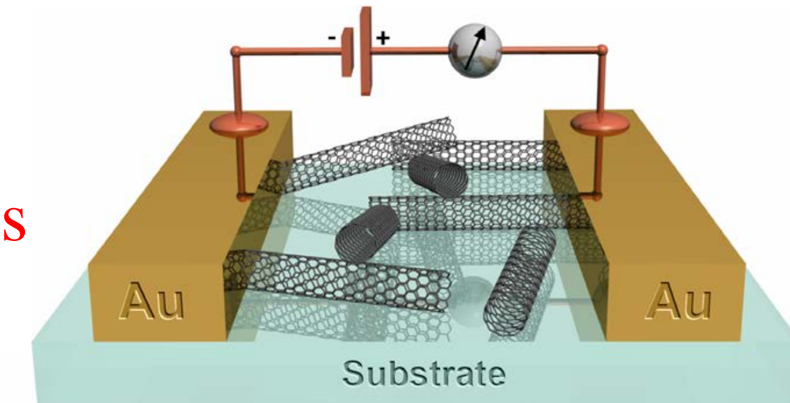
Functionalization of MWCNTs



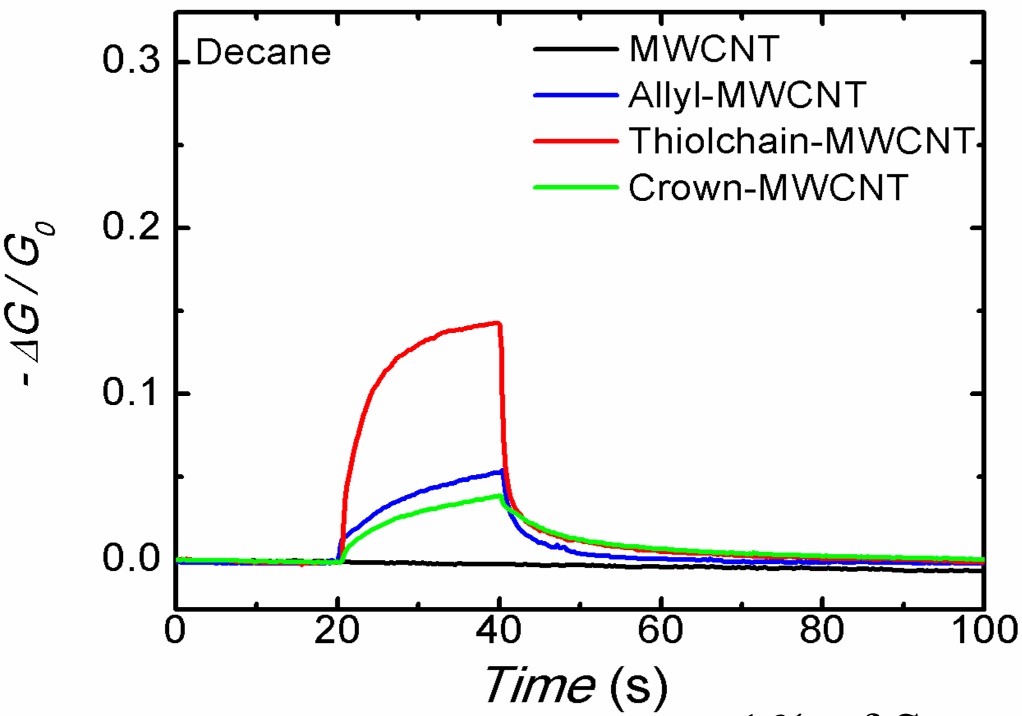
J. Am. Chem. Soc. **2011**, *133*, 11181

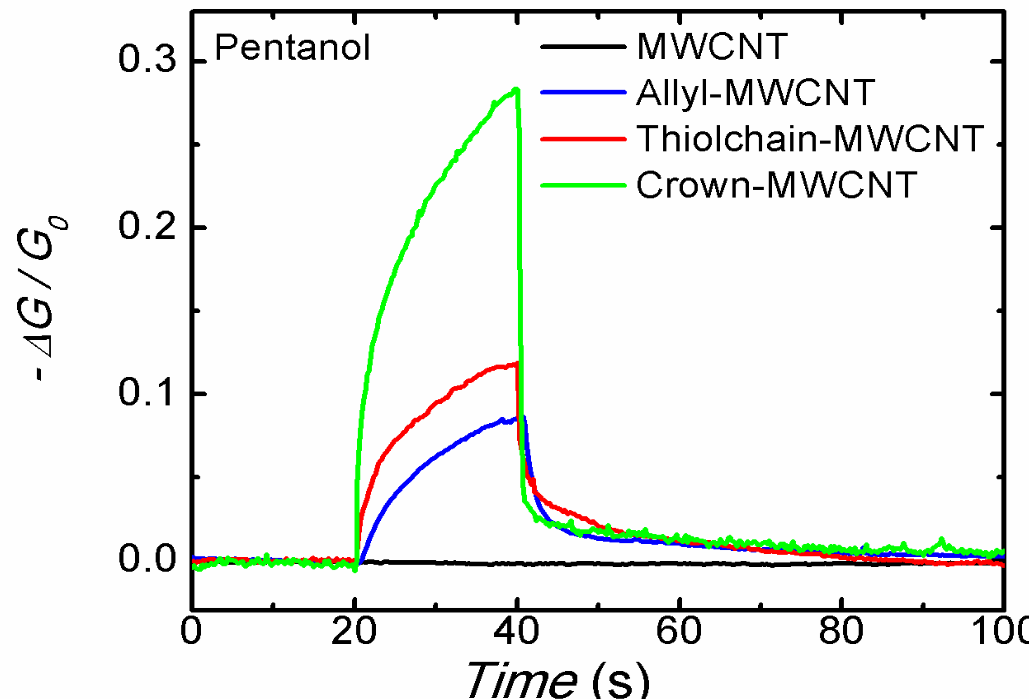
Raw Data From the Sensors

Pristine MWCNTs
Exhibit Small Responses



Reduction in
Conductance
From Increased
CNT Spacing



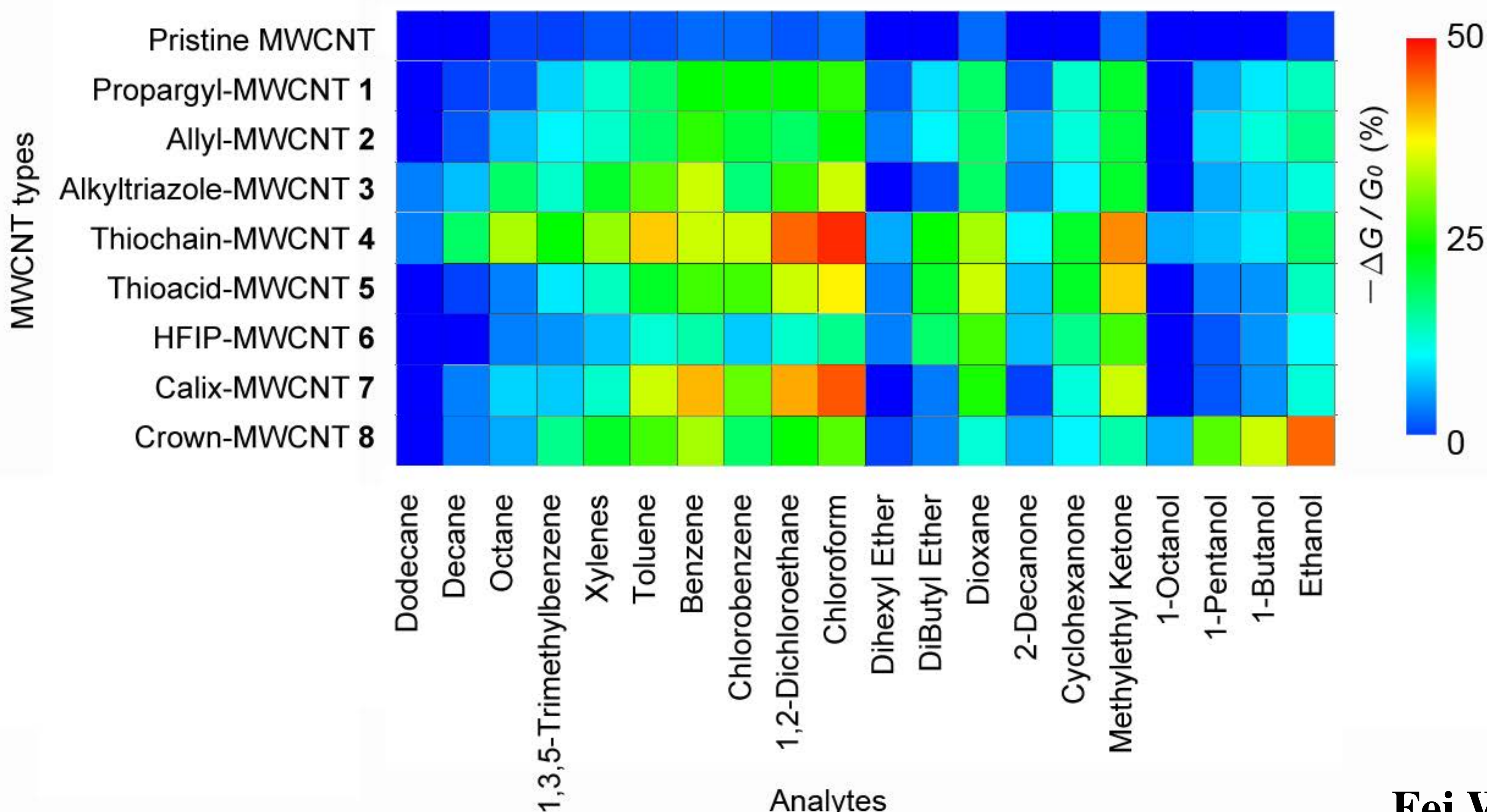


1% of Saturated Vapor
Bias Voltage (0.05 V)

Fei Wang

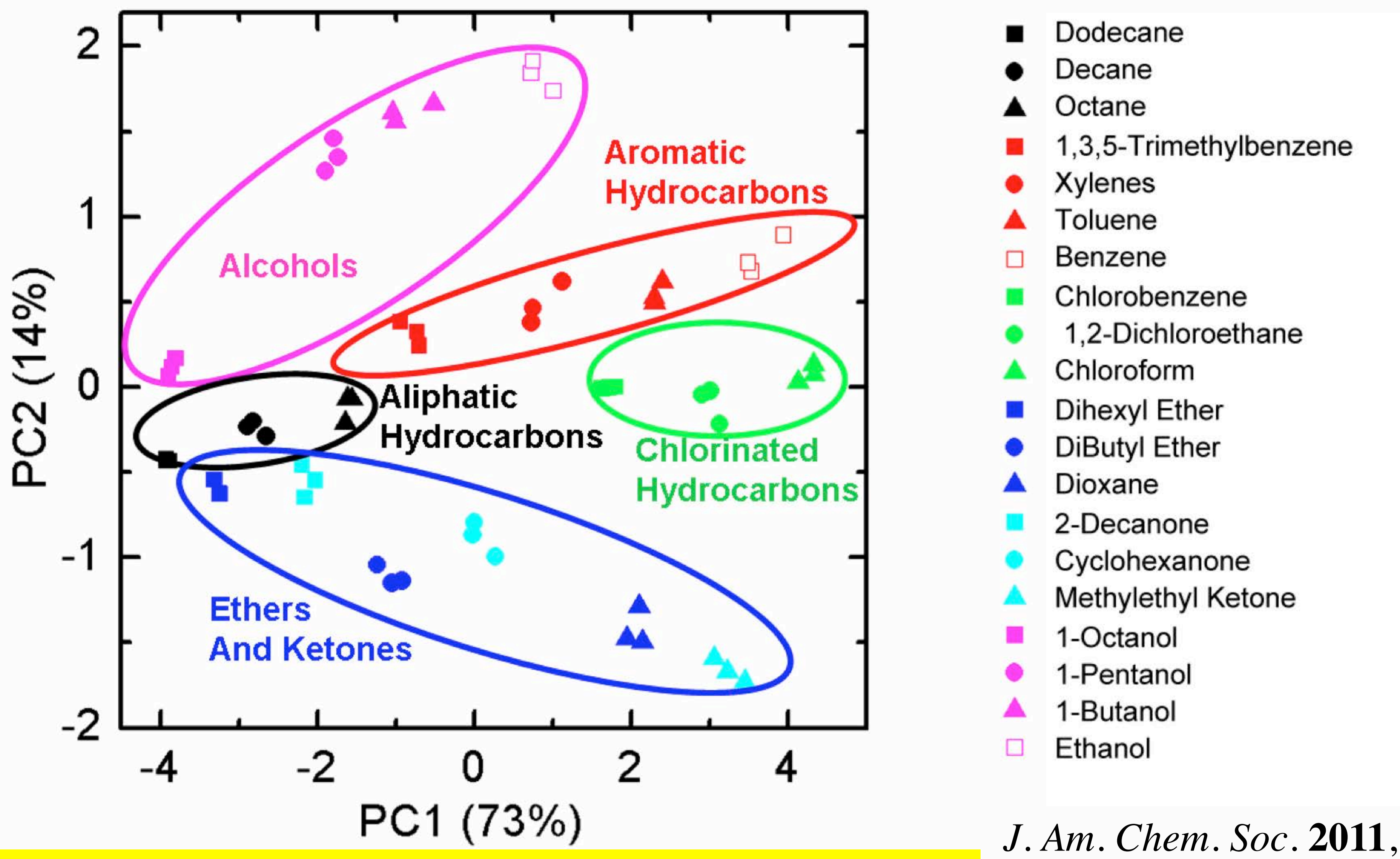
Response Matrix

- Functionalization Increases Sensing Responses
- Diverse Functional Groups Lead to Cross-Sensitive Responses



Fei Wang

Principal Component Analysis



J. Am. Chem. Soc. **2011**, *133*, 11181–11193

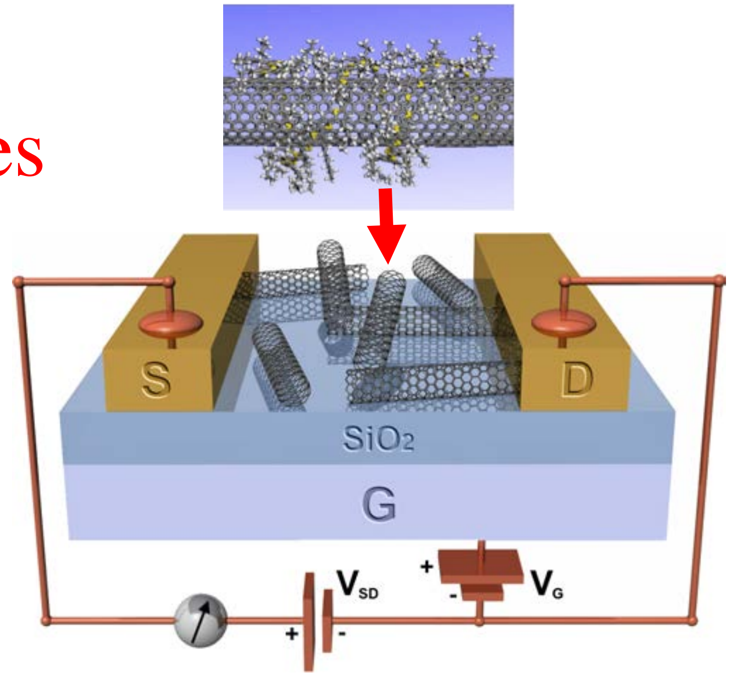
- **23 chemicals are well separated**
- **100% Accuracy in Classification with 60 Trials**
- **Overlaps are result of chemical similarities**

Fei Wang

CNT Chemiresistors

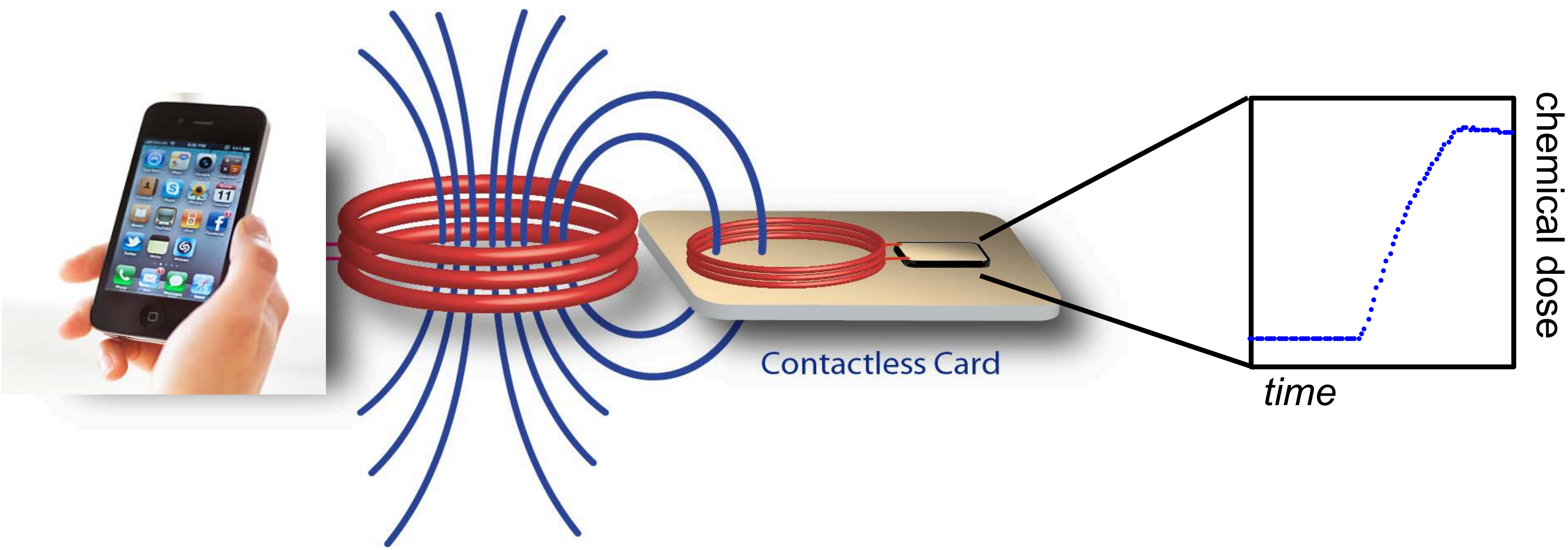
Intrinsic Advantages of Chemiresistors

Low Power/Cost
Small Footprint
Wireless Network

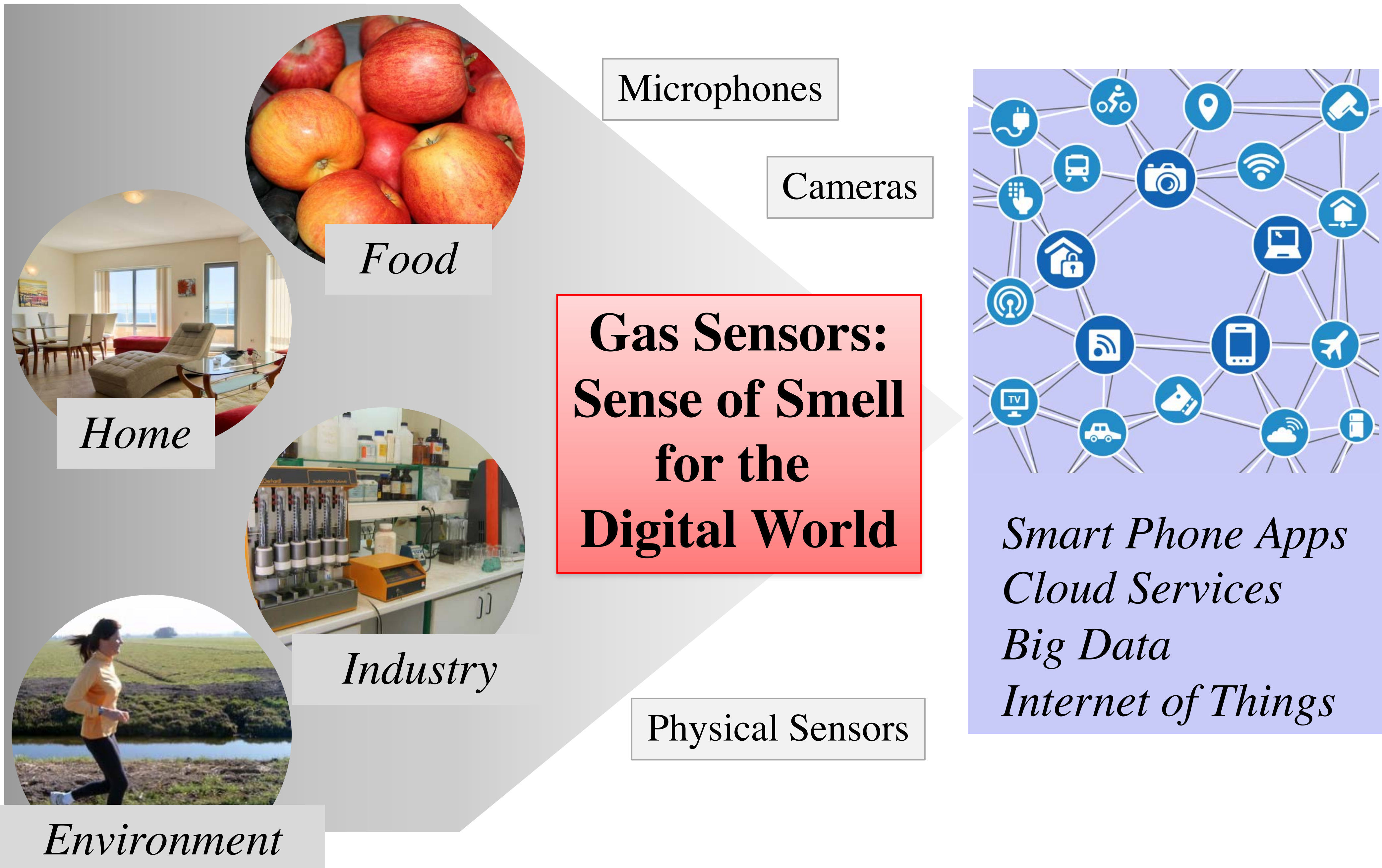


Technical Needs

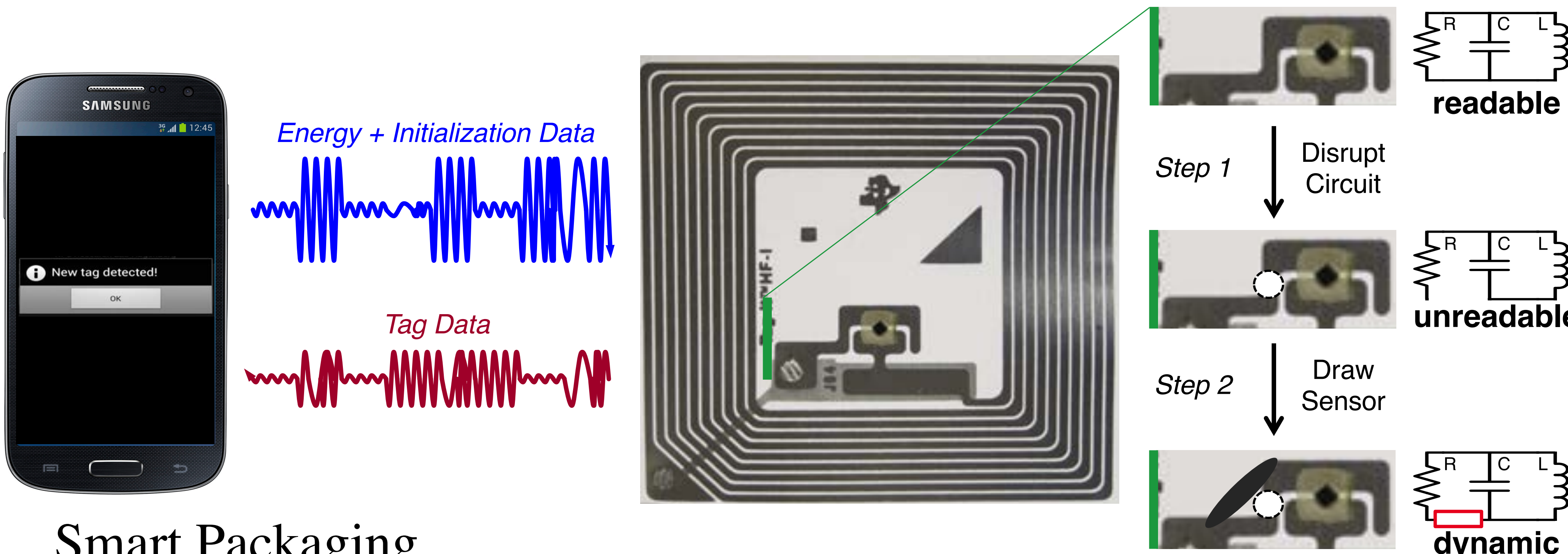
High Sensitivity
Selectivity
No Calibration



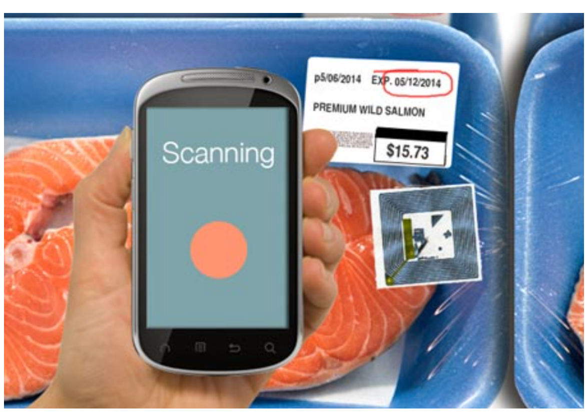
A Sense of Smell for the Digital World



Smartphone Sensing: Ultra-Low Power Wireless Sensors



Smart Packaging



Sensor Tags are Inductively Powered and Read by Smartphones

$$f_0 = \frac{1}{2\pi}\sqrt{\frac{1}{LC} - \left(\frac{R}{L}\right)^2}$$

Azzarelli, J. M., Mirica, K. A., Ravnsbæk, J. B.; Swager, T. M. *Proc. Nat. Acad. Sci.* **2014**, *111*, 18162-18166.

Dosimeter Tags: Readable or Unreadable

readable

or

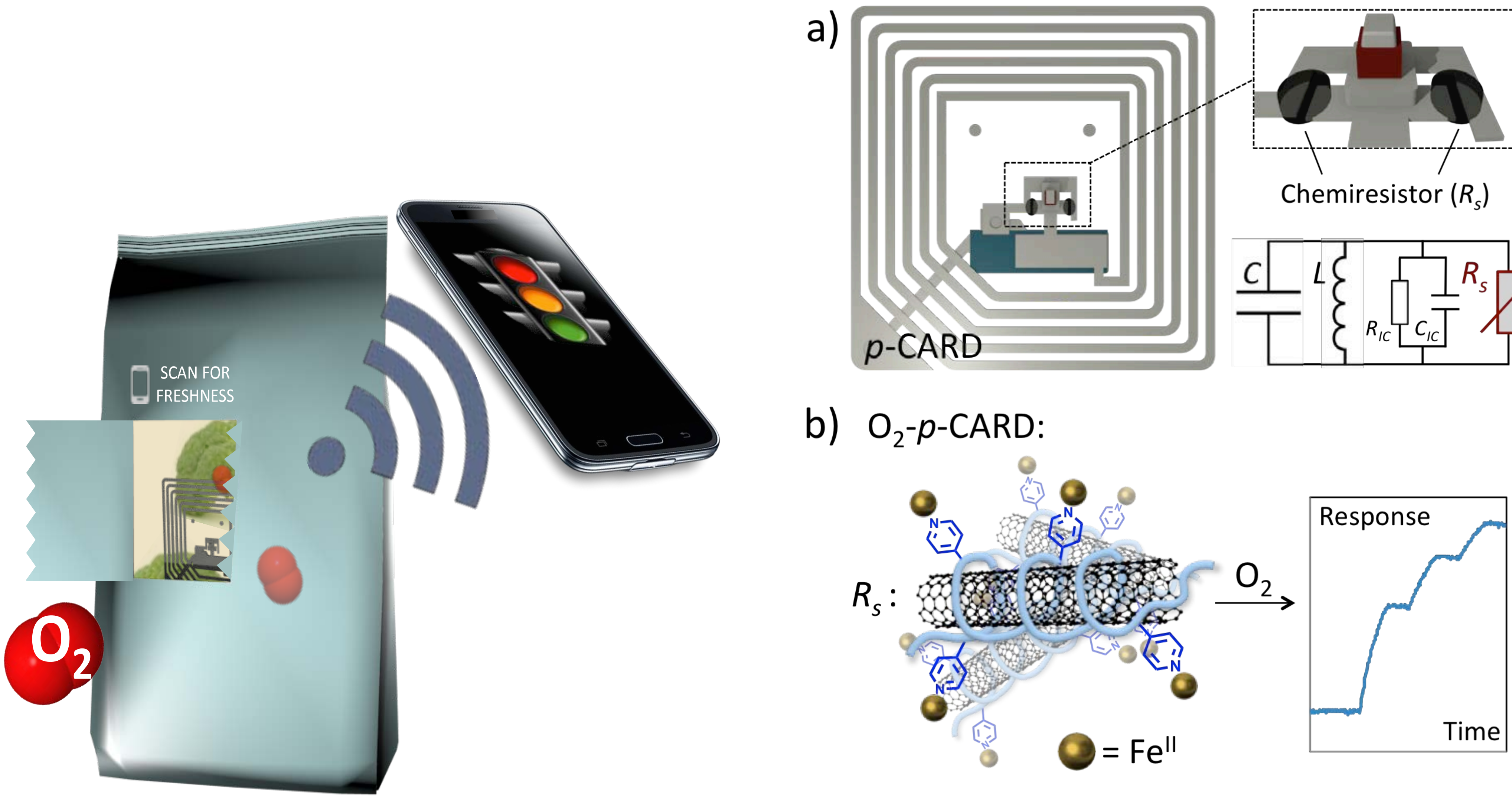
unreadable

Sensor Tags For Explosives Detection

[redacted]

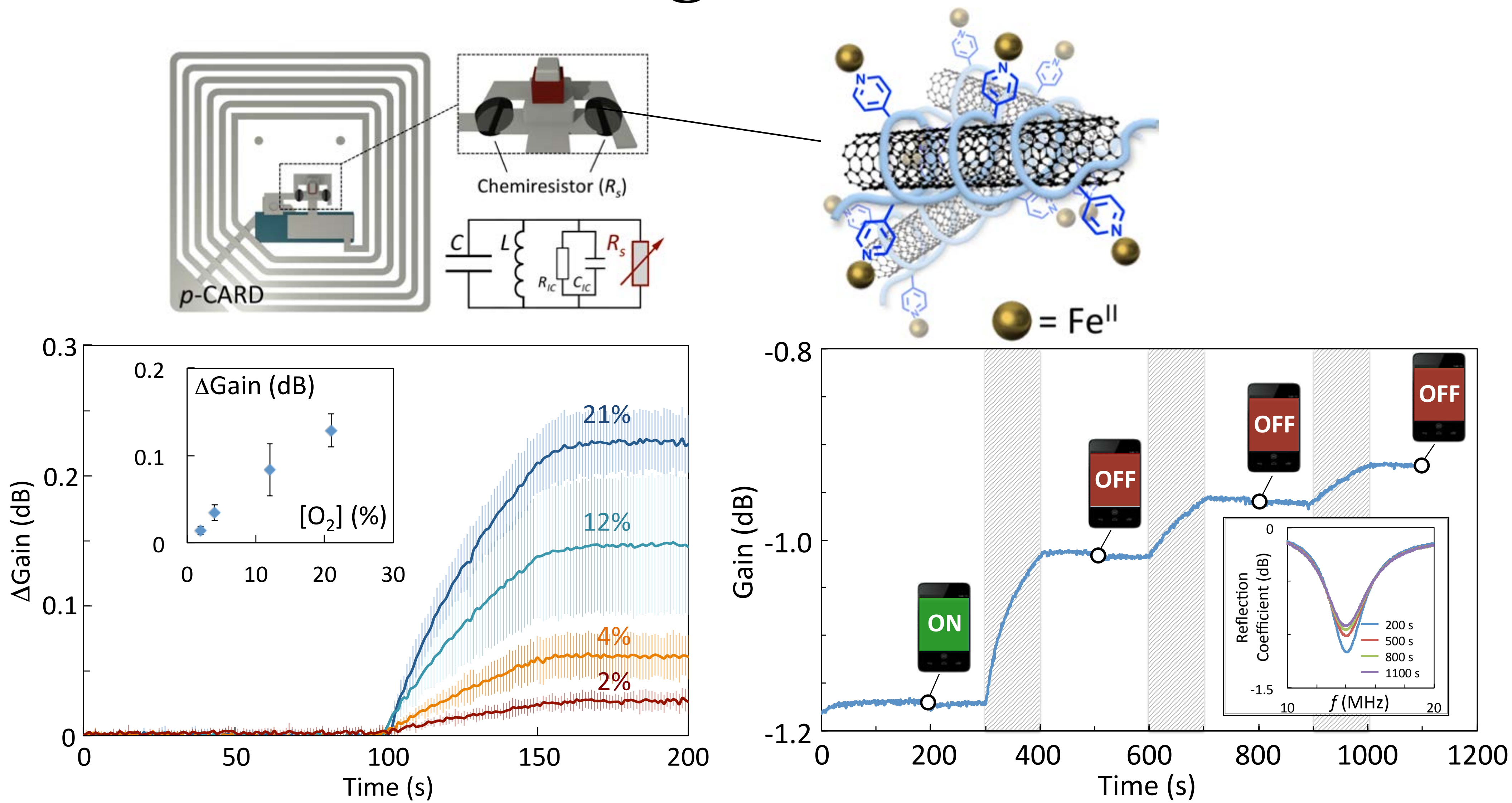
Azzarelli, J. M., Mirica, K. A., Ravnsbæk, J. B.; Swager, T. M. "Wireless Gas Detection with a Smartphone via RF Communication" *Proc. Nat. Acad. Sci.* **2014**, *111*, 18162-18166.

Food Packaging:
Non-Line-of-Sight Detection of Freshness



Zhu, R.; Desroches, M.; Yoon, B.; Swager, T. M. *ACS Sensors*, **2017**, *2*, 1044-1050.

Passive RFID Tag Sensors and Smart Phone Digital Readout

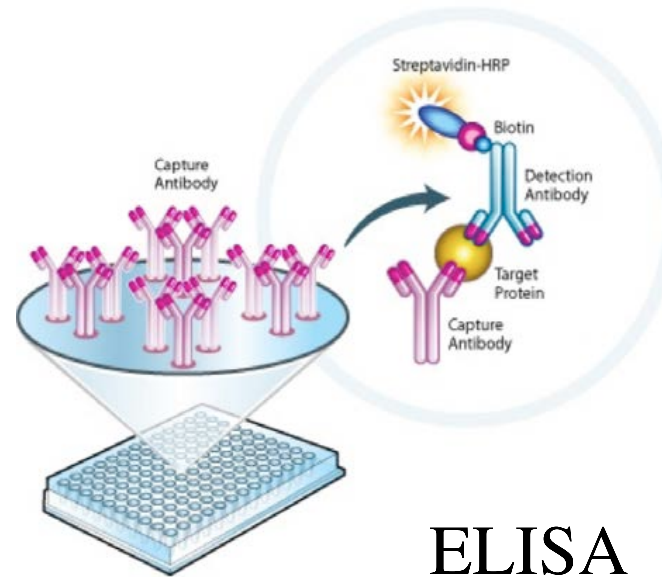


Zhu, R.; Desroches, M.; Yoon, B.; Swager, T. M. *ACS Sensors*, **2017**, *2*, 1044-1050.

Biosensors and Medical Diagnostics

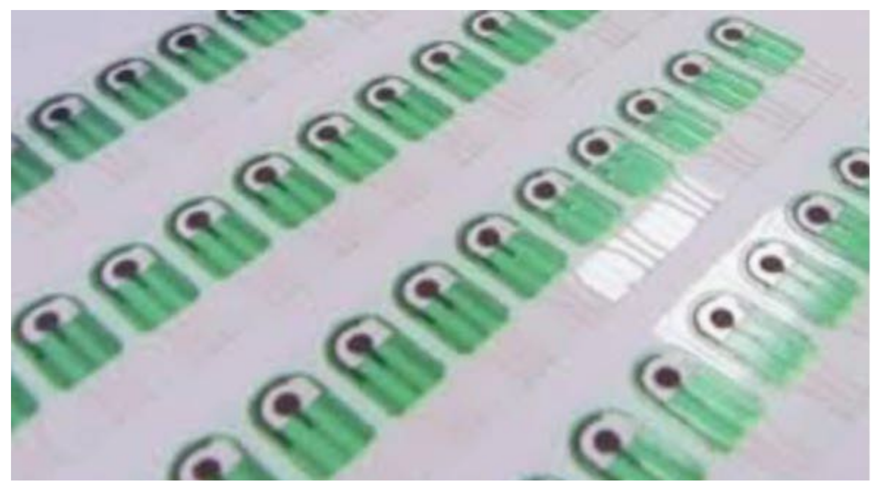
Diagnostics at Hospital -> Clinic -> Home
Telehealth, Geolocation, Disease Surveillance, Contact Tracing
ELISA, PCR, LFA, Electrochemical

- Specificity and Accuracy are Critical
- Fidelity Requires that Protein/Antibody Presentation Should Emulate Nature



ELISA

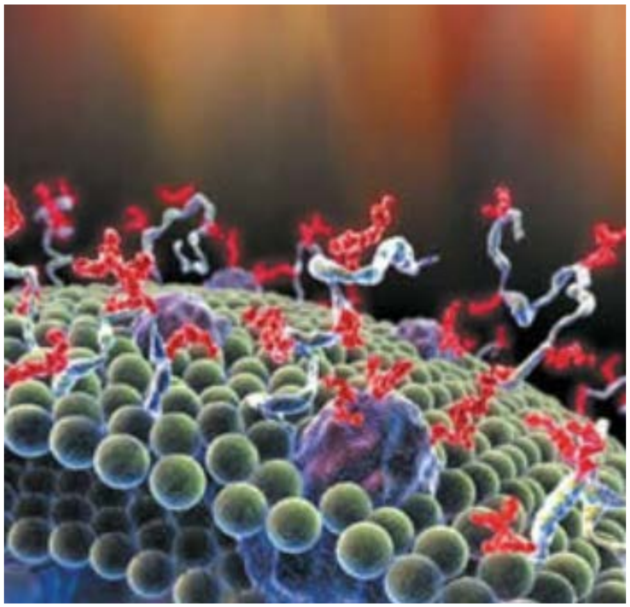
Lateral Flow Assay



Electrochemical

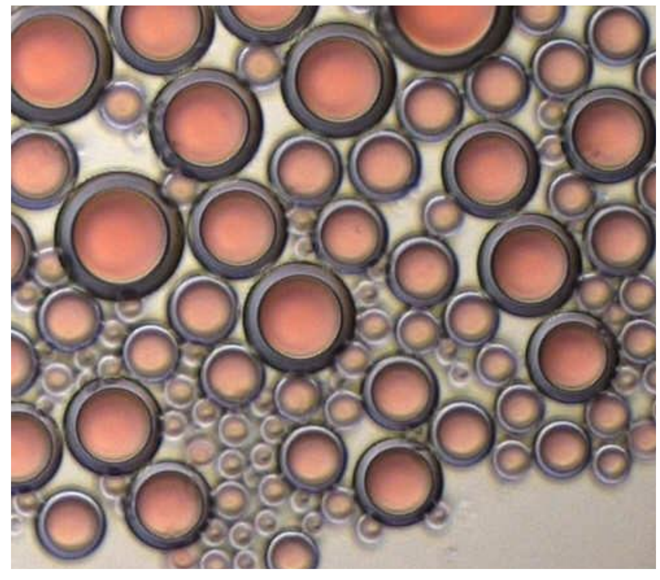
Bio-Sensing with Dynamic Colloids

Inspiration from Biology



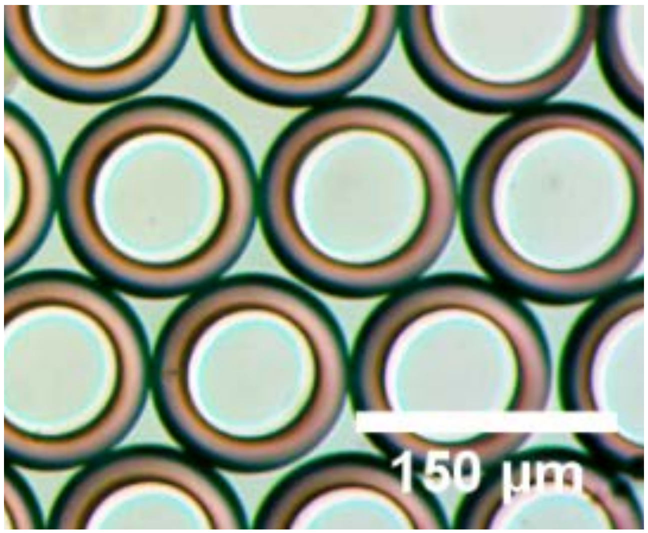
Cells have Reactive
Surfaces and Multiple
Internal Compartments

Droplets w/ Multiple Phases

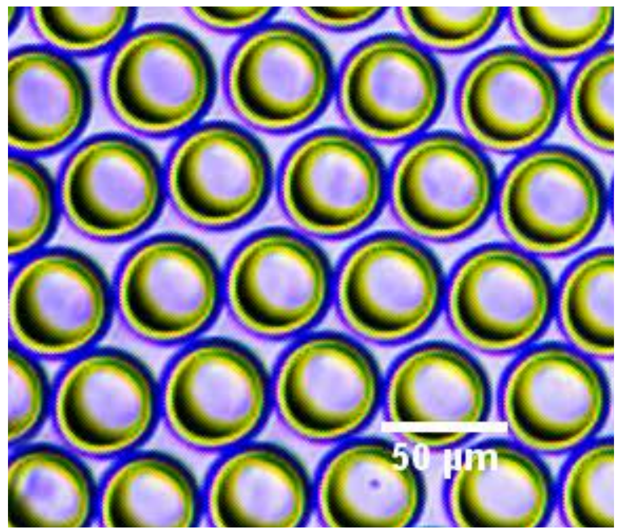


(**Fluorous**/Organic/Water)
(Silicone/Organic/Water)
(**Fluorous**/Silicone/Organic/Water)
Mechanical/Interfacial Properties
Well Matched to Living Cells

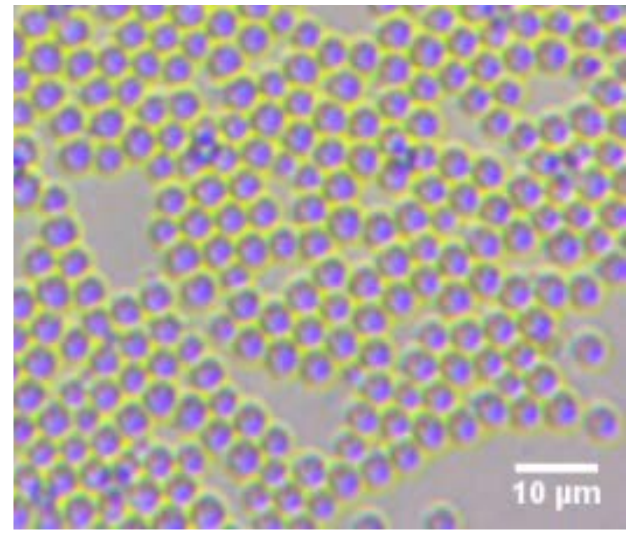
Our Methods Using Microfludic Chips



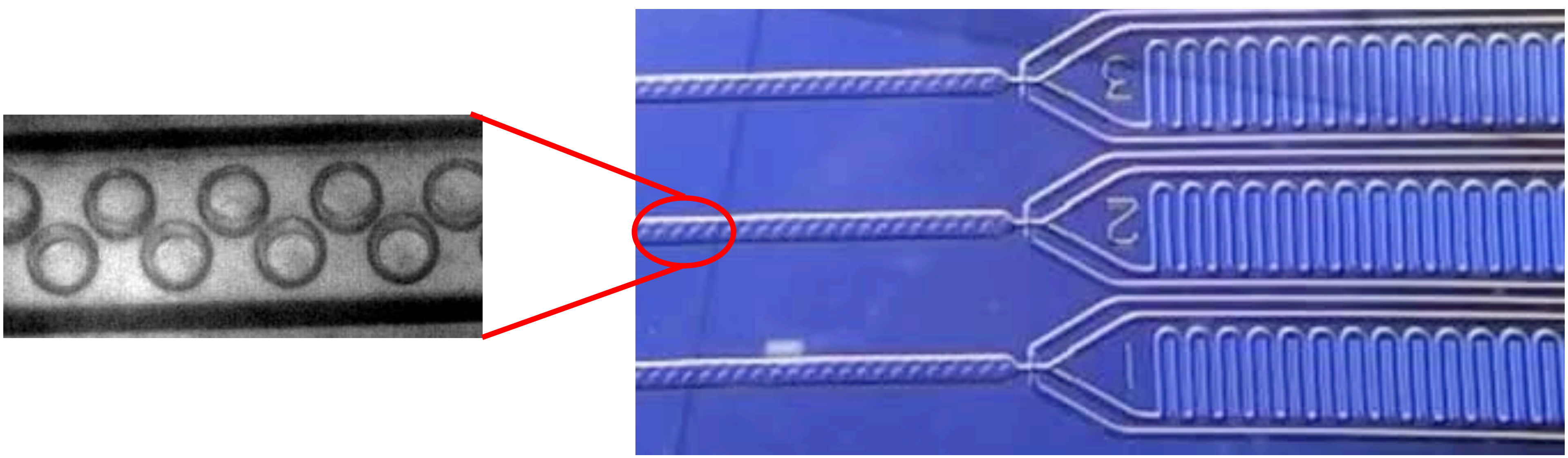
$Diameter = 118.9 \pm 3.7\ \mu m$



$Diameter = 41.8 \pm 2.5\ \mu m$

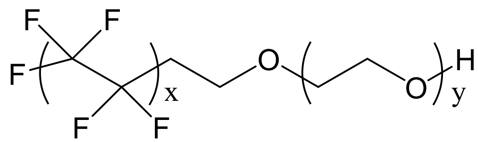


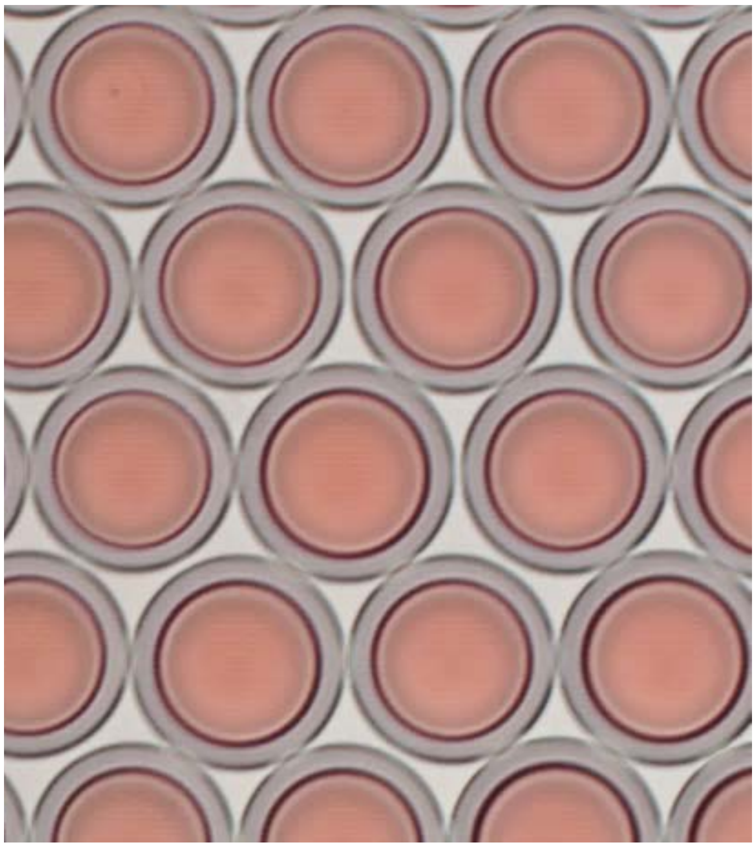
$Diameter = 5.5 \pm 0.68\ \mu m$



Hydrocarbon and Fluorinated Surfactants

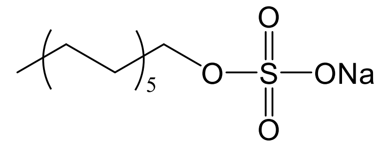
Fluorosurfactant (Zonyl FS-300)

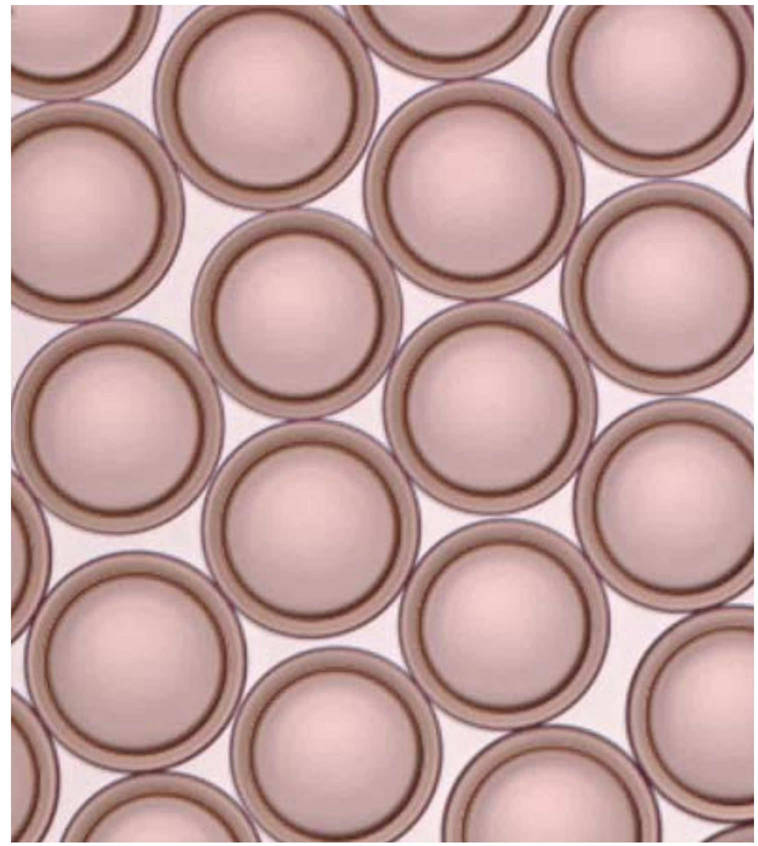




H/F/W
Fluorous Outside

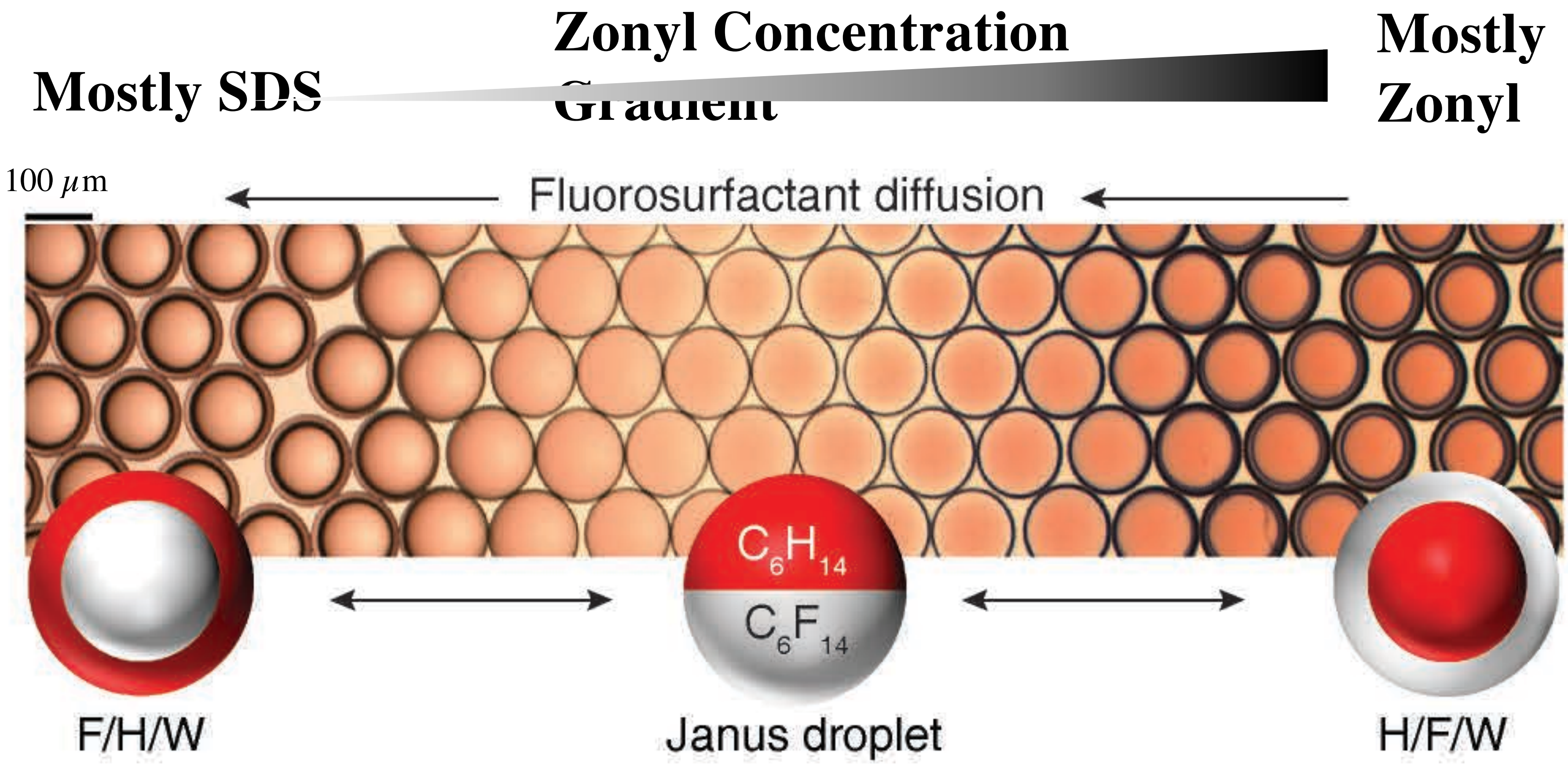
Sodium Dodecyl Sulfate, SDS





F/H/W
Hydrocarbon Outside

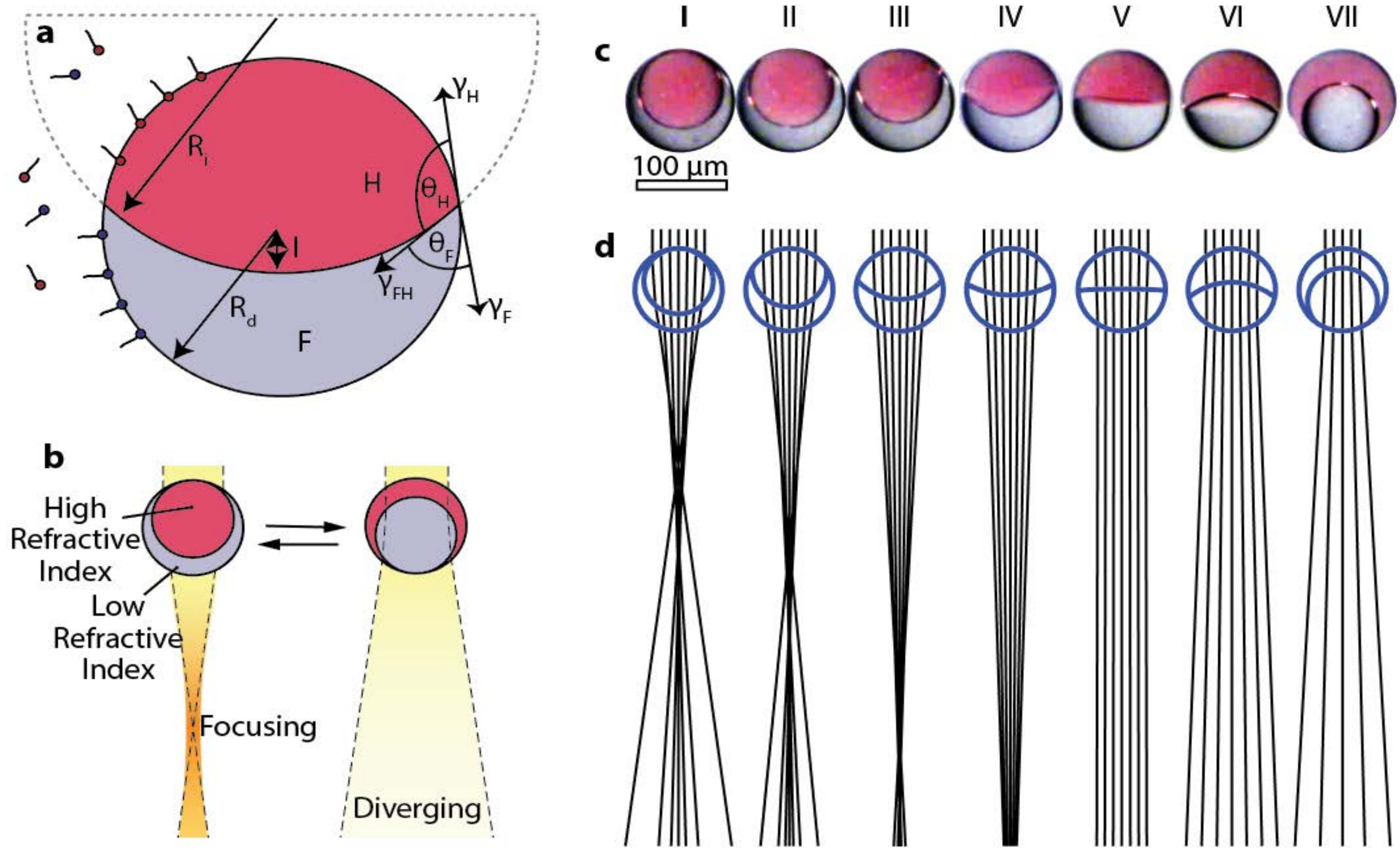
Droplets Morph in Response to Changes in Balance of Surfactant Concentrations



"Dynamically Reconfigurable Complex Emulsions via Tunable Interfacial Tensions" *Nature*, **2015**, *518*, 520-524.

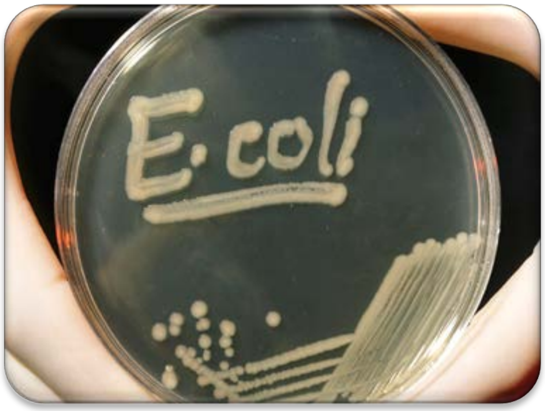
Lauren Zarzar

Fluorocarbon/Hydrocarbon Emulsions Behave as a Dynamic Lens



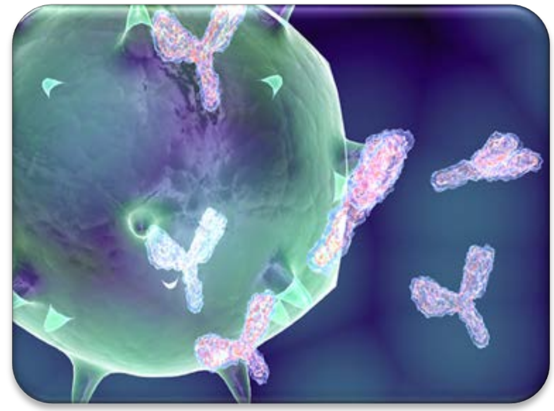
Nagelberg, S.; Zarzar, L. D.; Nicholas, D.; Subramanian, K.; Kalow, K. A.; Sresht, V.; Blankschtein, D.; Barbastathis, G. Kreysing, M.; Swager, T. M.; Kolle, M. “Reconfigurable and Responsive Droplet-based Compound Micro-Lenses” *Nature Comm*. **2017**, DOI: 10.1038/ncomms14673

Foodborne Pathogen Detection Methods



Microorganism Culturing

PCR and DNA Hybridization



Antibody-Based

These popular methods are reliable but require expensive equipment, long analysis times, and user training making them not ideal for rapid, on-site analysis at food production plants

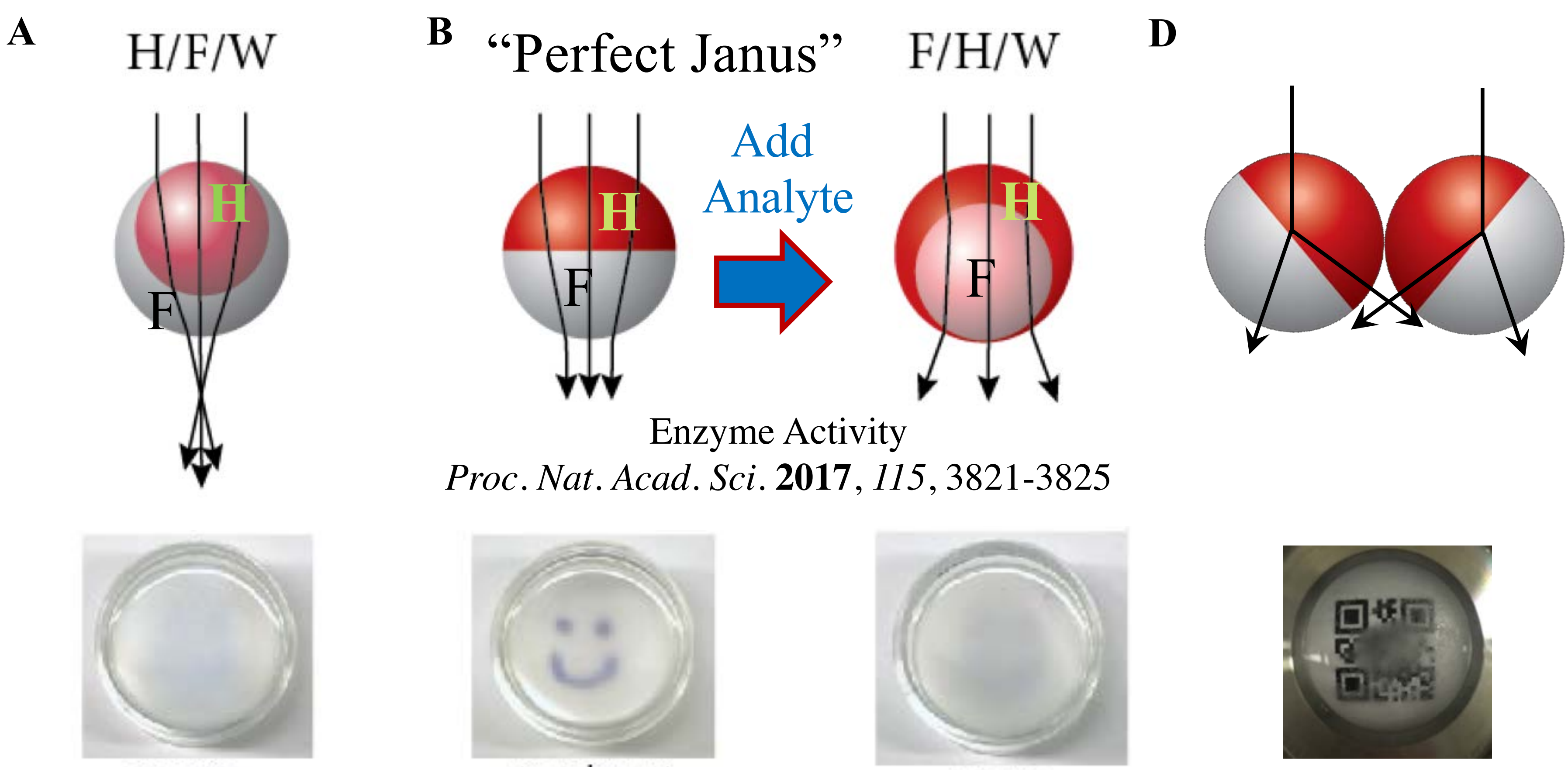
Sensors: Transforming or Tilting the "Invisible" Janus Droplet

Aqueous Phase, h_1 =1.33

Organic Phase, h_2 >1.33
Heptane: h_2= 1.3876

Fluorous Phase, h_3 <1.33
FC770: h_3 = 1.27

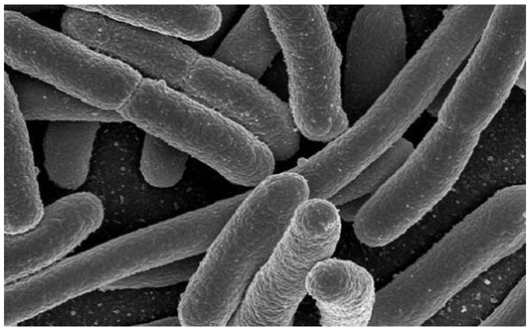
$h_1/h_2 = h_3/h_1$ For "Perfect" Case (0.960 ≈ 0.953 is Close Enough)



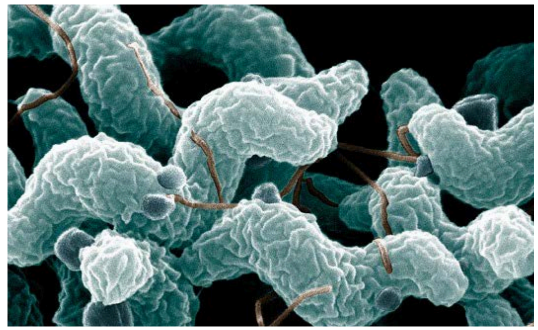
Enzyme Activity
Proc. Nat. Acad. Sci. **2017**, *115*, 3821-3825

Looking down through a field of droplets forming a layer between the image below and the camera above.

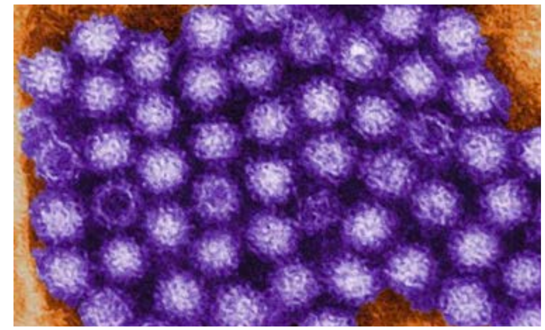
Orthogonal Carbohydrate Binding Interactions of Foodborne Pathogens



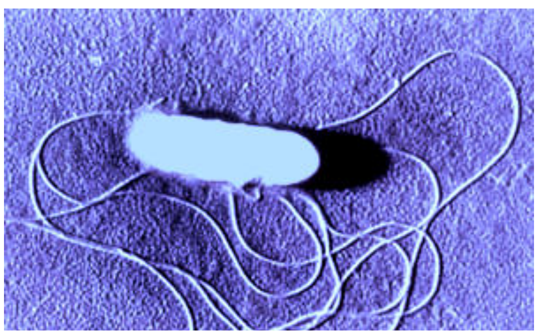
E. coli
(Man, Gb3)



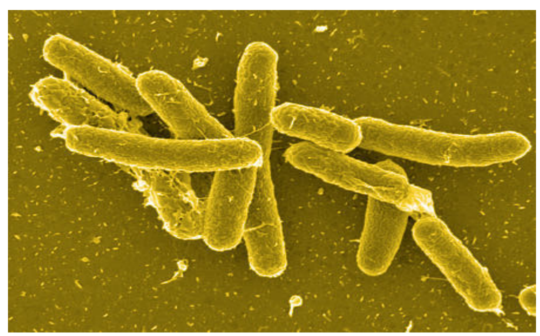
Campylobacter jejuni
(Fuc)



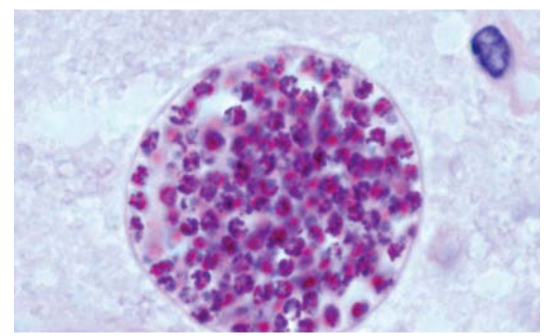
Norovirus
(Histo-blood group antigens)



Listeria monocytogenes
(GlcN, FucN)

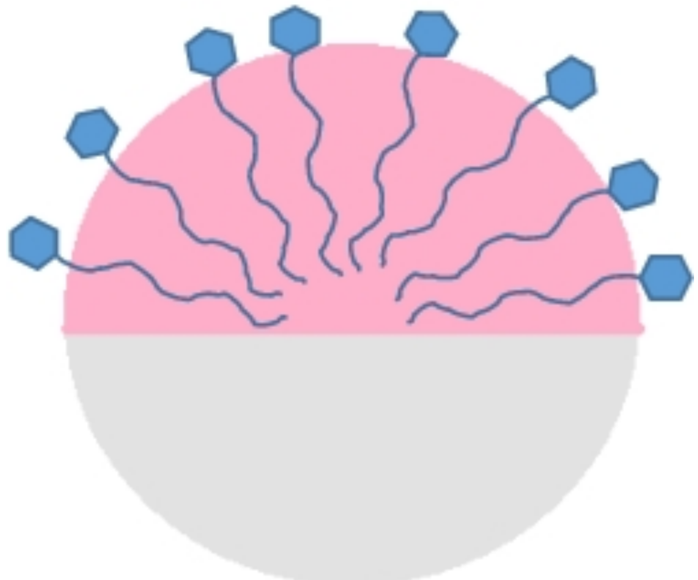


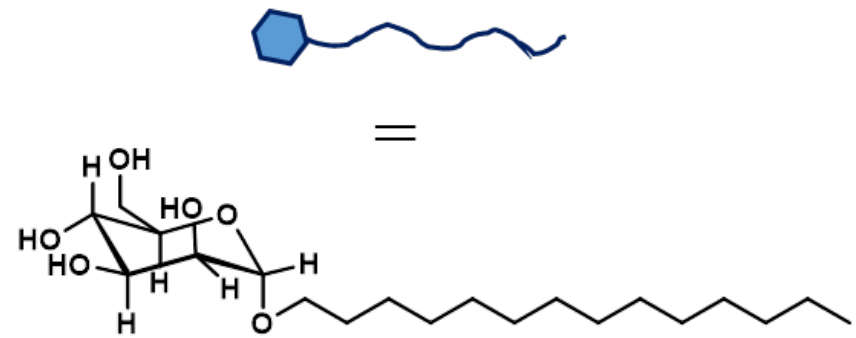
Salmonella enterica
(Man, Fuc)



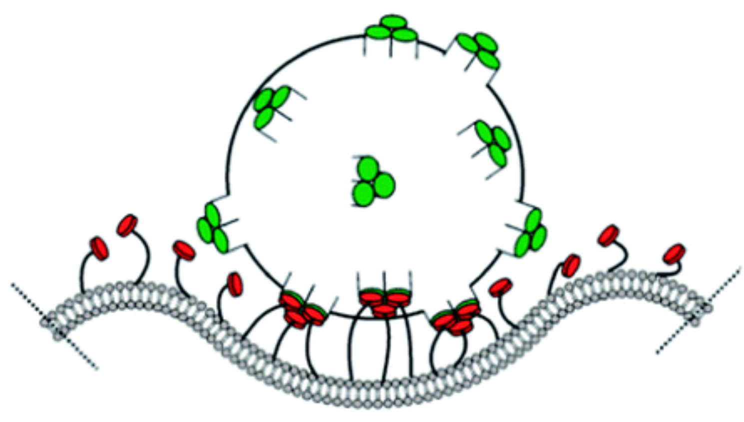
Toxoplasma gondii
(Neu5Ac, Sulfated Glycans)

Carbohydrate-Substituted Liquid Colloidal Particles

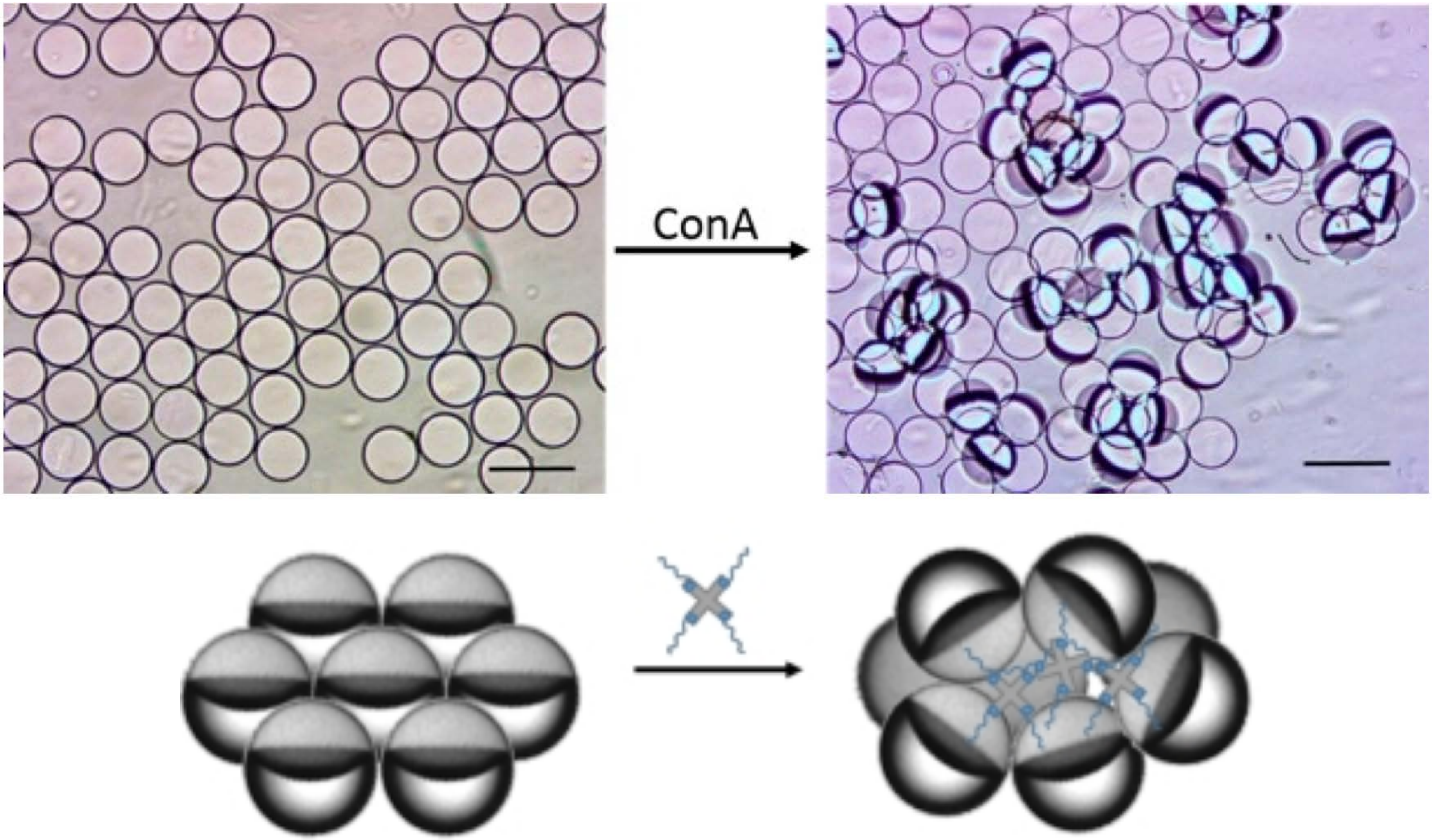




The continuous layer of carbohydrate ligands displayed on the droplet surface simulates multiple binding interactions



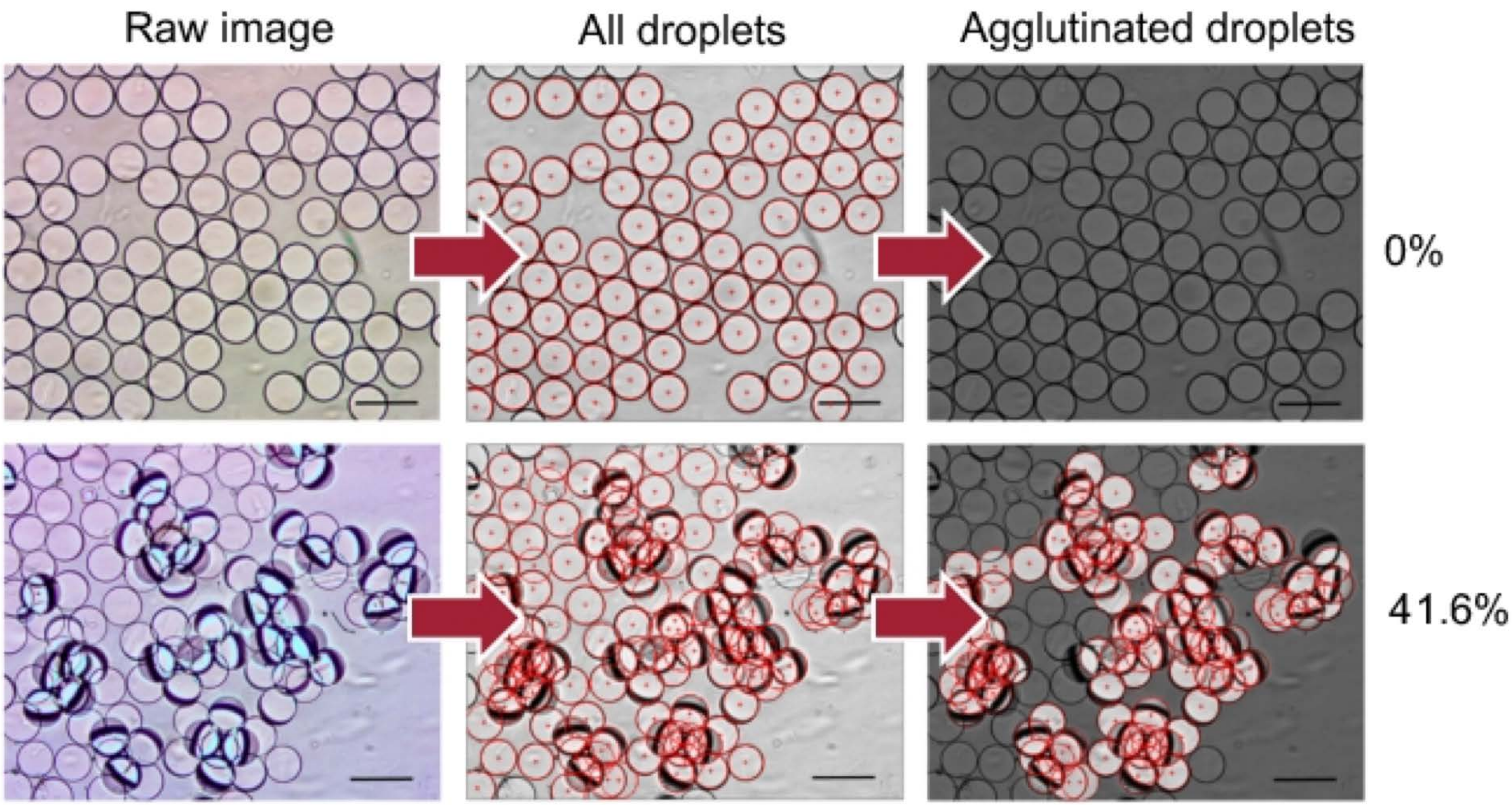
Detection of *E. Coli* Mimic: ConA



Binding of carbohydrate-substituted droplets to ConA leads to agglutination, which causes the solution to become opaque

Qifan Zhang

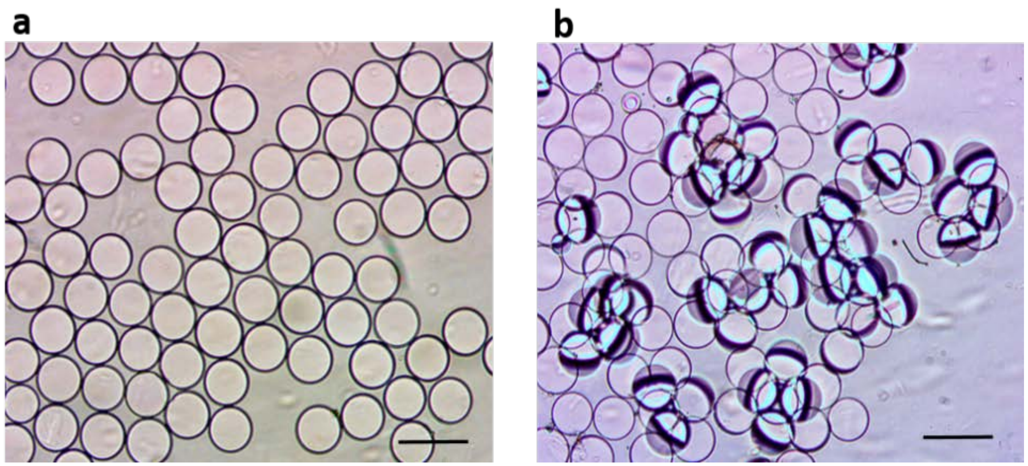
Computational Analysis of Agglutinated Droplets Provides Quantitative Data



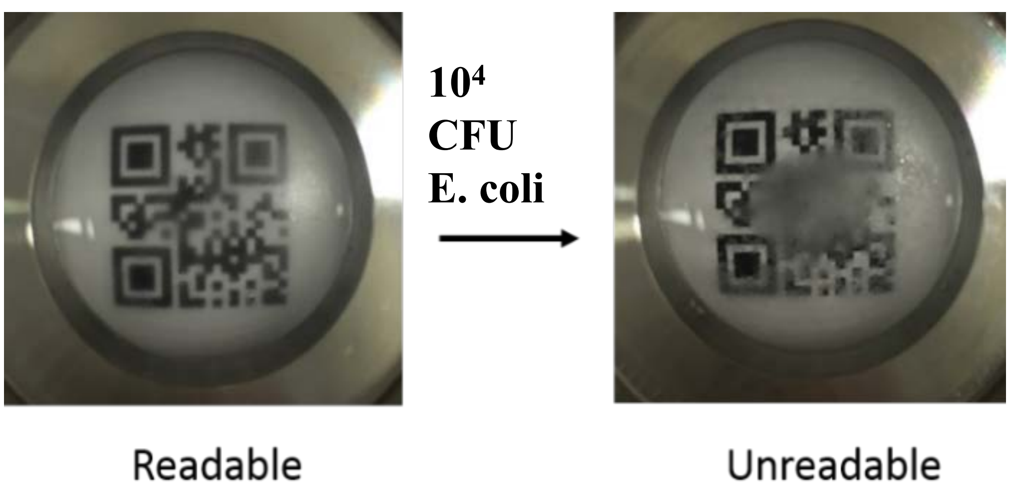
- Searches for overlapping droplets
- Calculate the intensity and the area covered by agglutination

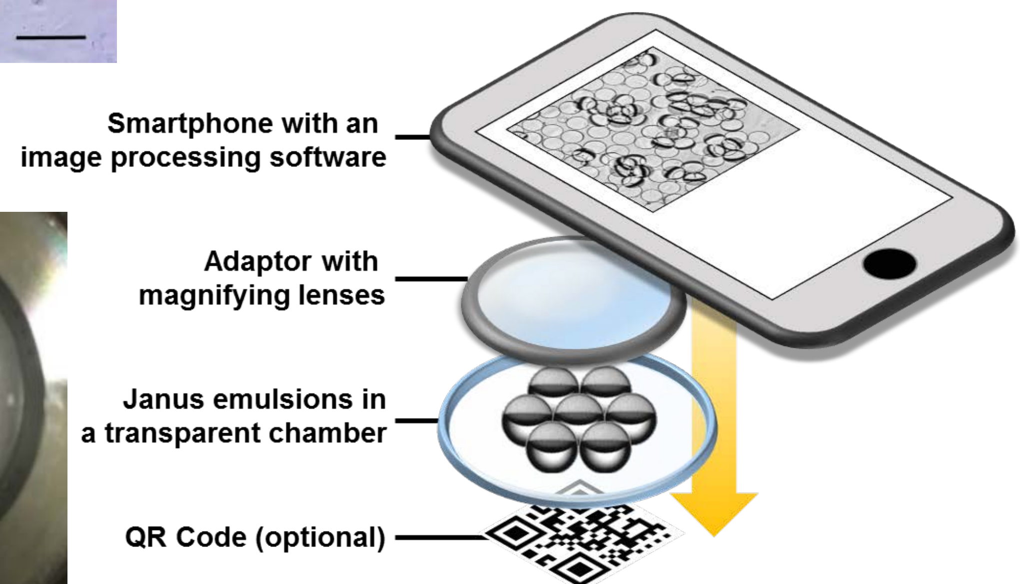
Suchol Savagatrup, Qifan Z

Binary or Quantitative Analysis of *E. coli*



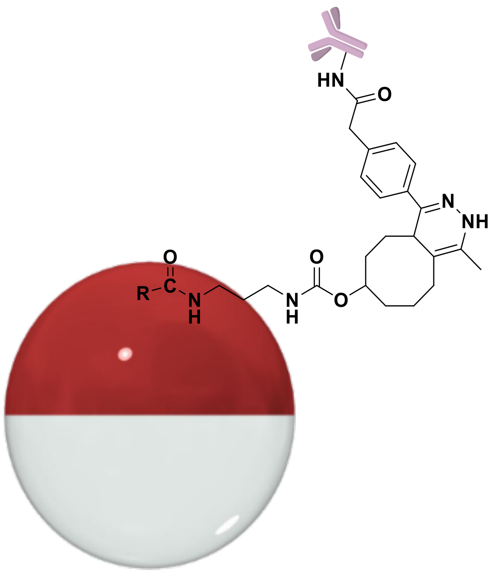
Quick Evaluation with Time and Location Data



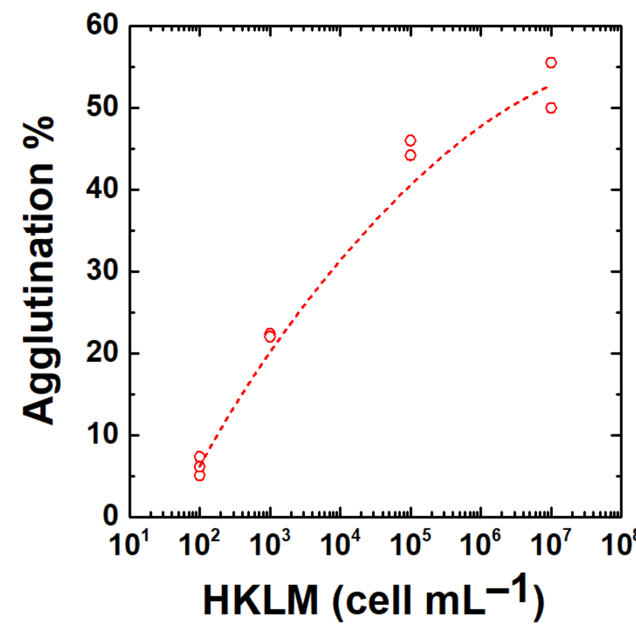


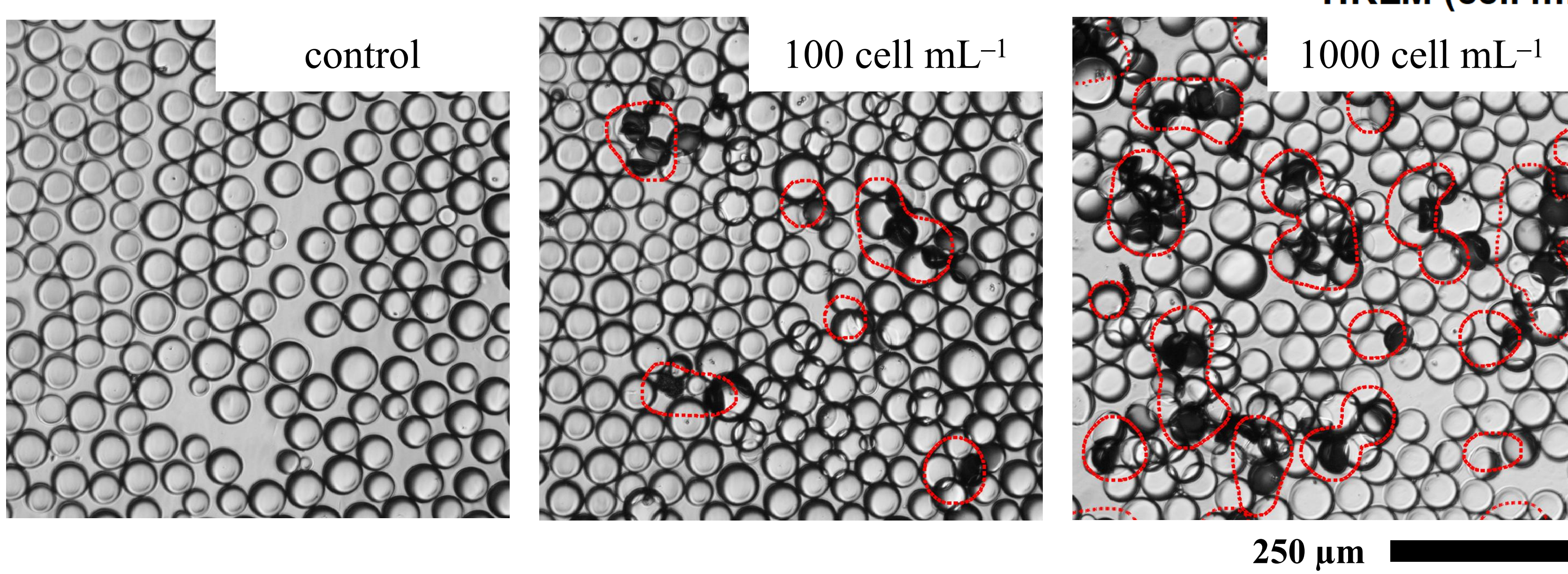
Zhang, Q.; Savagatrup, S.; Kaplonek, P.; Seeberger, P. H.; Swager, T. M. "Janus Emulsions for the Detection of Bacteria" *ACS Central*

Listeria Quantitation to Low CFUs



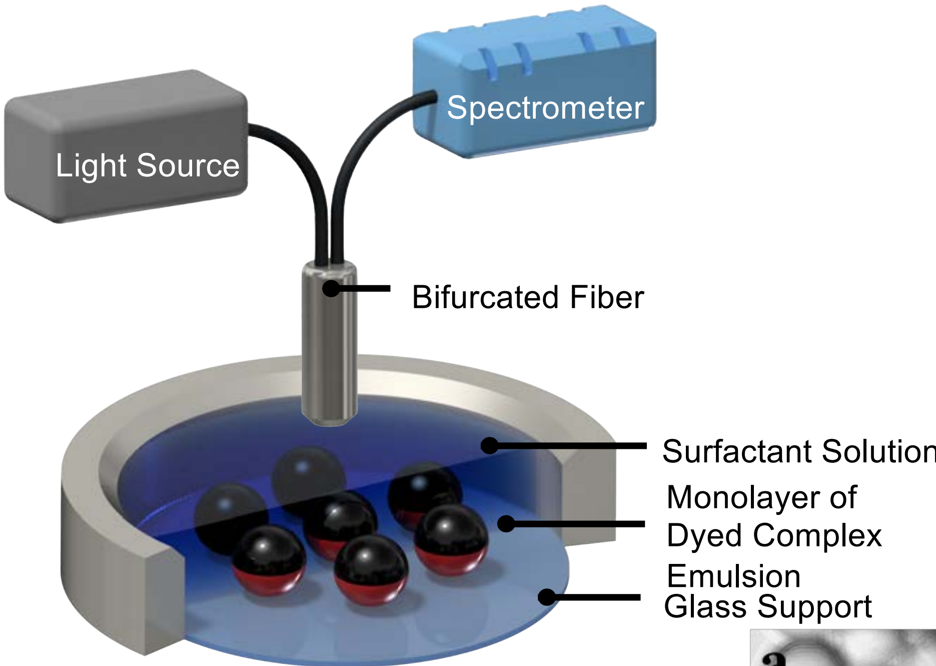
- Rapid Detection of Heat-Killed Listeria at Low Concentrations (100 cell mL^{-1})
- Transferal to Smart Phone Scheme
- Quantitative Analysis



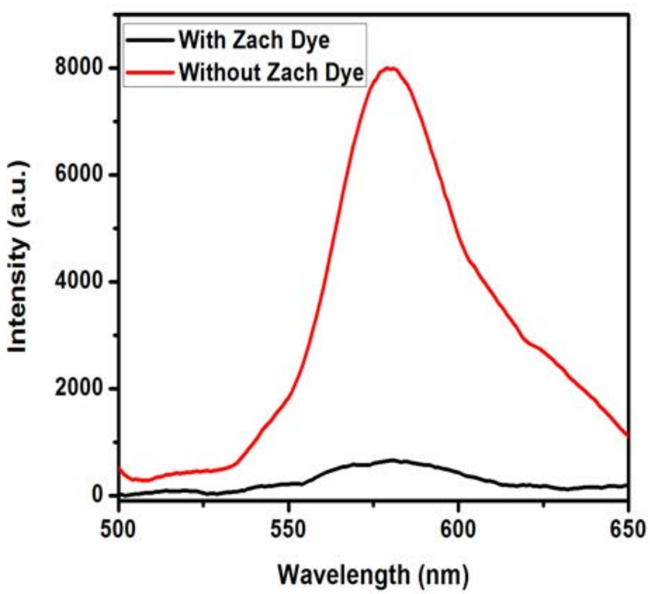


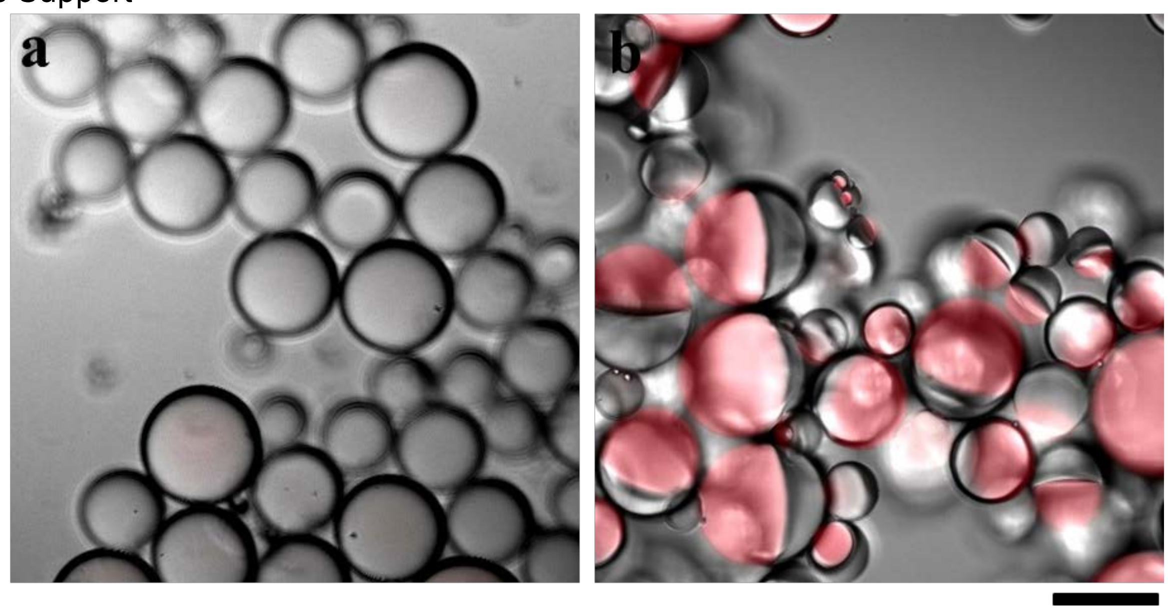
Suchol Savagatrup and Jie Li

Improved Agglutination System



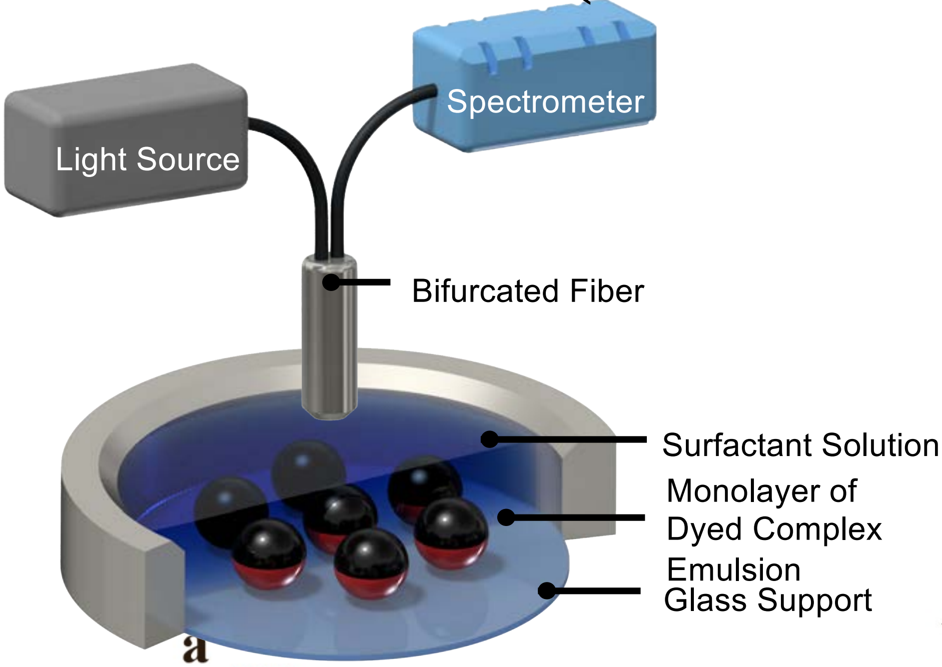
Filter/Emitter Combination Gives Superior Detection



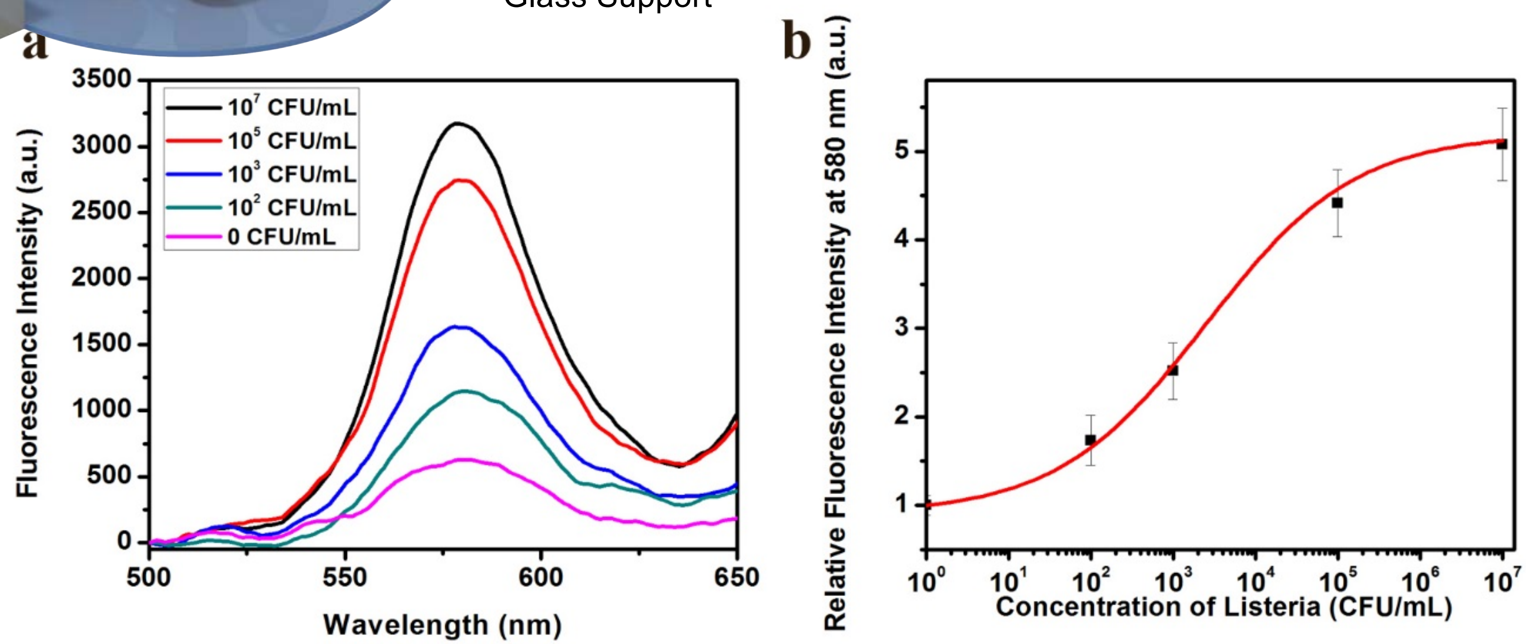


Jie Li. Zach Nelson. Kosuke

Improved Agglutination System (Batch Detection)



Filter/Emitter Combination Gives Superior Detection

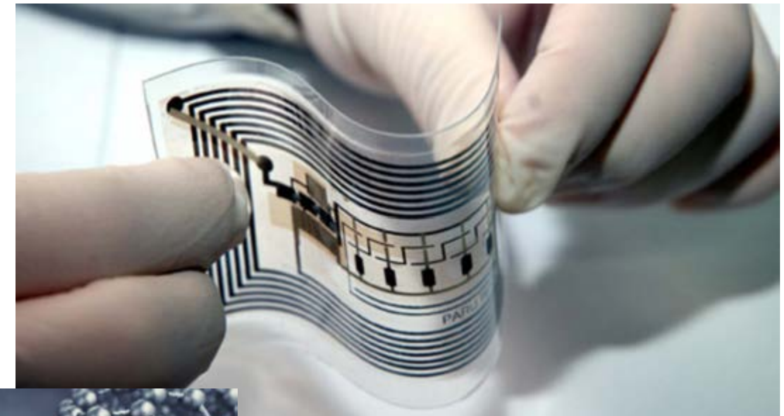


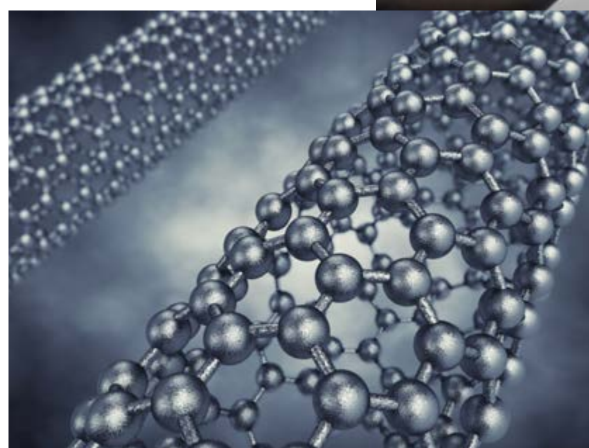
Jie Li

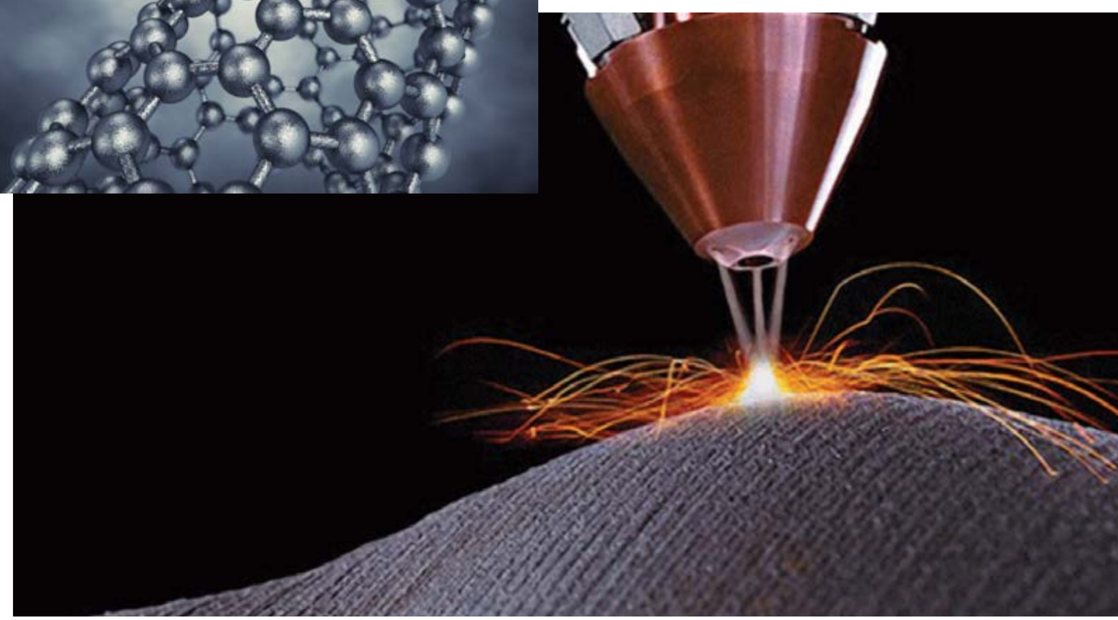
Chemical/Bio Sensors

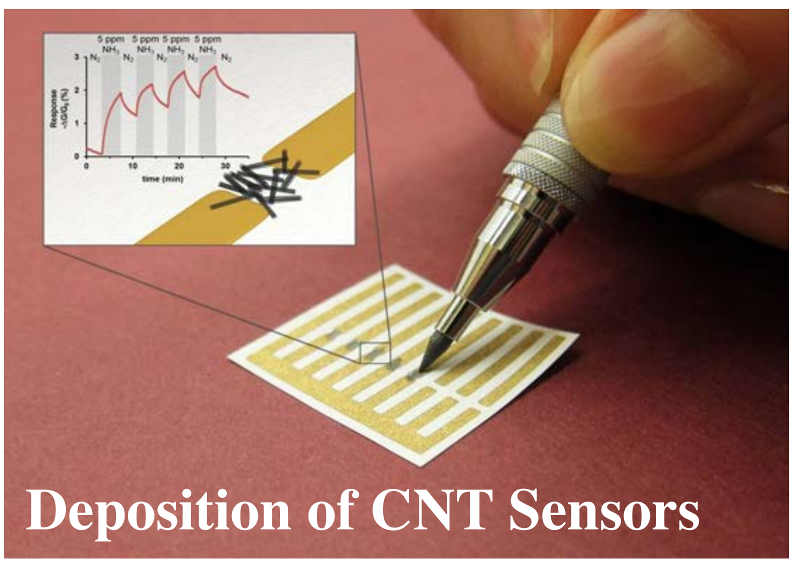
Rich with Opportunity:

Complex Materials
Inexpensive Hardware
IoT, Telehealth, Disease Surveillance
Nanomaterials
Printed Electronics
Additive Manufacturing









Key Points/Summary

- Transduction Materials Enable Inexpensive Chemical/Bio Sensors for Large Scale Applications
- Mechanisms of Chemical Selectivity are General and Transferable Between Transduction Materials
- Innovations in Manufacturing of Nanostructured Materials will Greatly Impact Commercialization
- Business Plans can be Developed that Leverage Present Methods and Expand into New Markets