Nanosensors:

Transitioning Nanosensors from the laboratory to the marketplace: Challenges and Lessons learned

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Center for Advanced Sensors
& Environmental Systems

Science –to –Technology (S_2T)

- A vast amount of nanosensors have been developed, tried and tested
  - biosensors
  - electrochemical capacitors
  - batteries, fuel cells, novel membrane systems and many more
- There are many roadblocks in bridging the gap between academic research and the market place

Highlights

- Operational definitions
  - Category 1 nanosensor
  - Category 2 nanosensor
- Case studies-
  - *Ultra-sensitive Portable Capillary Sensor* (U-PAC™)
  - CeO_2, Fe_2O_3, TiO_2, ZnO, and fullerenes
- Testbeds and performance metrics
- Bridging the gap
  - a proposal for moving forward

How do you bridge the gap between research and commercialization?

Answer the two key questions of successful innovation:

- Can you make a product?
- Can you get anyone to buy it?

Trivia Questions

- Who was:
- The first innovator of electrochemist instruments?
- The person who founded Shockley Semiconductor Laboratory creating Silicon Valley and electronics innovation?

Answer

- **Arnold Orville Beckman** (April 10, 1900 – May 18, 2004) was an American chemist who founded Beckman Instruments based on his 1934 invention of the pH meter, a device for measuring acidity. He also funded the first transistor company, thus giving rise to Silicon Valley.

Beckman’s pH meter

Beckman's first pH meter - predecessor of Model G.
This is a picture of original model made in 1934 and patented.
Picture courtesy of Beckman Coulter, Inc

Model G pH meter.
Device was closed in wooden box 12" wide by 8" deep by 9" high. - was hardly portable, weighting almost 8 kilograms.

“maybe you want to call it entrepreneurship or invention, I don’t know. But anyway, I thought, well, heck, lets make a complete instrument then. Get rid of the stuff spread on the desktop and make it a compact unit”.

Nanosensor Classification

- Type 1 Nanosensors:

  Nanotechnology-enabled sensors or sensors that are themselves nanoscale or have nanoscale materials or components

- Type 2 Nanosensors:

  Nanoproperty-quantifiable sensors that are used to measure nanoscale properties

Sadik et al, Journal of Environmental Monitoring, 11, 25, ***2009***

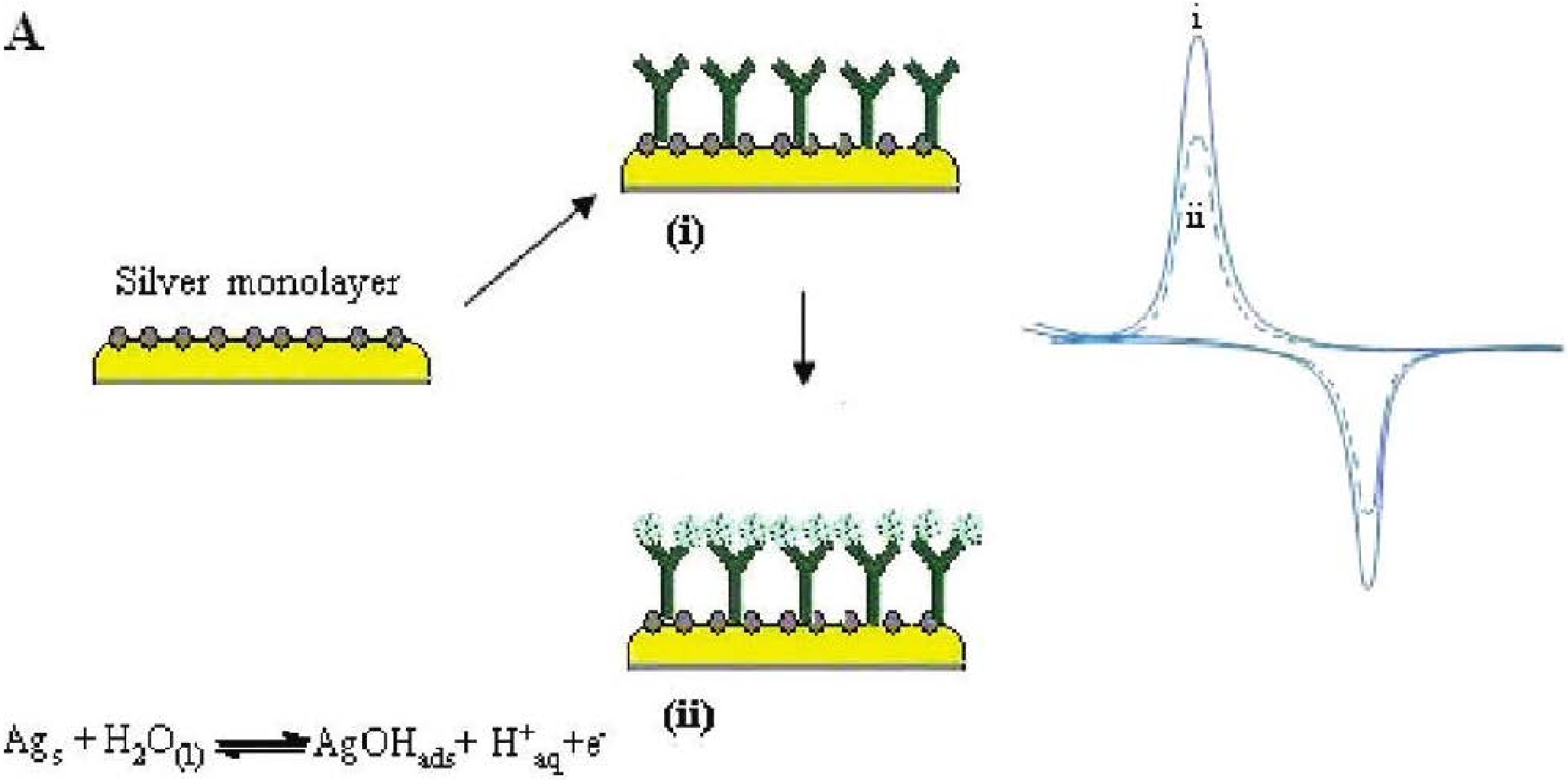
http://www.epa.gov/osa/pdfs/nanotech/epa-nanotechnology-whitepaper-0207.pdf

Category 1 Nanosensors

- Hundreds of research articles using nanomaterials for chemical & biosensors have been published. There are dozens of reviews available which partly deal with use of nanomaterials for electrochemical nanobiosensors
    - Nanoparticles
    - Nanowires
    - Nanoneedles
    - Nanosheets
    - Nanotubes
    - Nanorods

Biosensors & Bioelectronics, **24, 2749-2765, 2009**.

Metal-Enhanced Electrochemical Detection (MED)



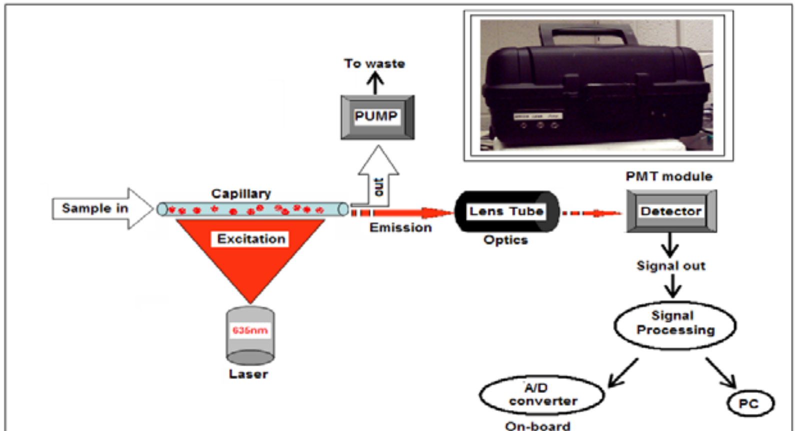
$$Ag_s + H_2O_{(l)} \rightleftharpoons AgOH_{ads} + H^+_{aq} + e^-$$

Kowino I., Agarwal R., Sadik O. A., Langmuir 19, 4344-4350, 2003

UPAC Biosensor

SUNY-Binghamton scientists and engineers have developed a portable, fully autonomous, and remotely operated sensing device, called Ultra-Sensitive Portable Capillary Sensor (U-PAC™)

1. Sadik. O., Karasinski, J, "Ultra-Sensitive, Portable Capillary Sensor", U.S. Patent No. 8,414,844 B2, April 9, 2013.
2. Sadik. O., Karasinski, J, "Ultra-Sensitive, Portable Capillary Sensor", U.S. Patent No. 7,708,944, May 5, 2010.
3. Sadik, O., Wang Q., Blythe, P., US Provisional Application No. 32291/1310 (RB-347), "Capillary Biosenso and its Method of Use", April 19, 2010
5. *Analytical Chemistry*, 74,713-719, **2002**
6. Guide 101-10, March **2007**, US Department of Homeland Security, Preparedness Directorate, Office of Grants and Training Systems Support Division, Washington DC.



UPAC instrument

Bench-top System (Developed by Sadik Group in conjunction with the Naval Research Lab[1,2])

- Use proven immobilization and fluorescent chemistry to study and optimize the capillary geometry

1. Ligler F., Breimer M., Golfen J., Sadik O. A. Anal Chem., 74., 713, 2002
2. Breimer M., Gelfand G., Sadik O. A., Biosens. Bioelectronics, 14, 779, 2003
3. Sadik O. A., Karasinski J., U.S. Patent No. 7,708,944"Ultra-Sensitive, Portable Capillary Sensor, May 5, 2010.

Performance Characteristics

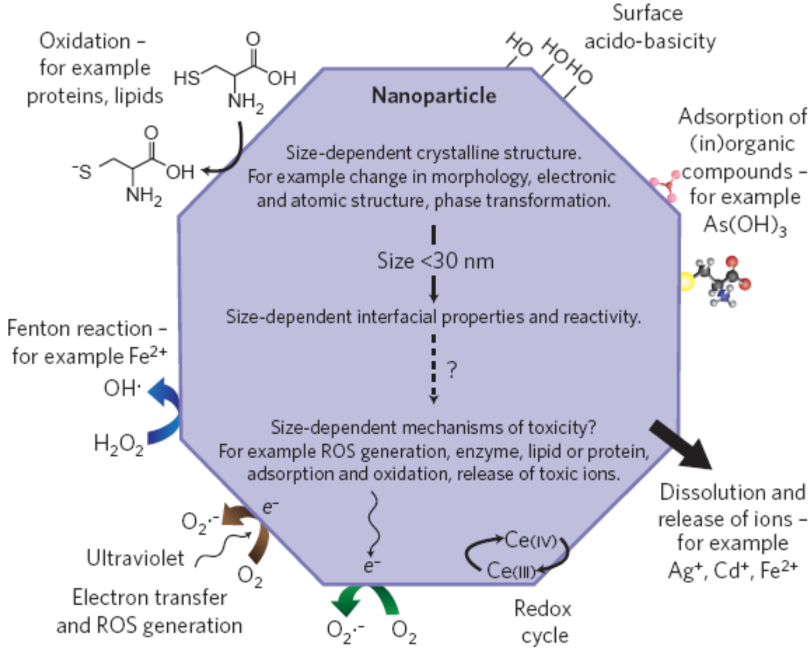
Technique	LOD	Response Time	Sample Preparation
UPAC Biosensor	112 spores/ml	30 min	Minimal
Standard ELISA	4269 spores/ml	6hrs	Extensive
Standard PCR	250 spores/ml	12 hrs	Extensive (PCR extraction)
Optical Leaky Clad waveguide biosensor	10,000 spores/ml	40 min	Autonomous
DOX	Qualitative	30 min	Minimal

Category-1:Nanoscale Properties

Few sensors exist to measure nanoscale properties including mechanical, electronic, photonic, and magnetic properties

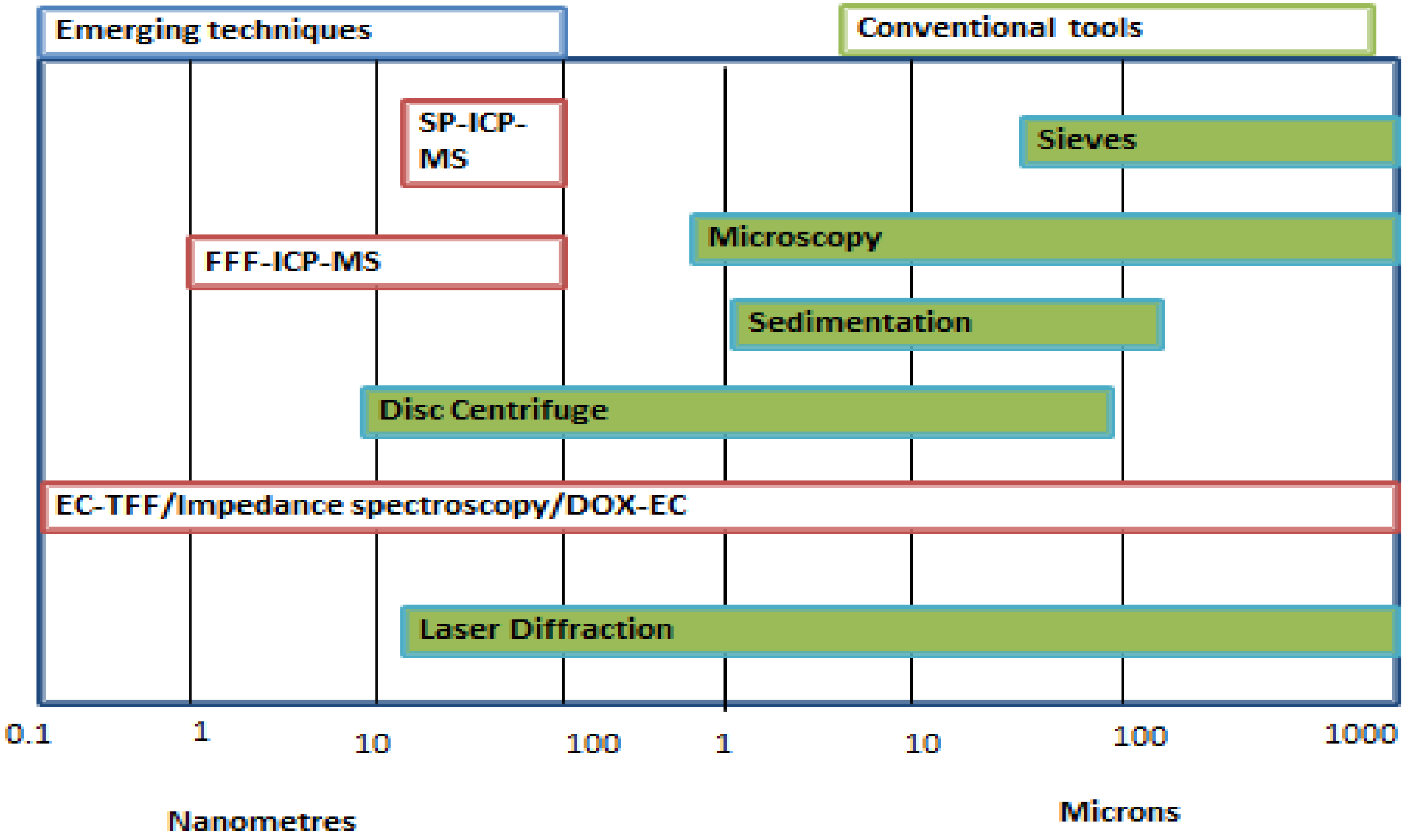
- ROS production

- **Characterization methods**
  - Not high-throughput
  - Not mass quantitative
- **Electron microscopy**
  - Size, shape, composition
- **Crystallinity**
  - XRD, XPS, Raman
- **Size in liquid**
  - DLS



(Auffan et al., 2009)

Conventional and emerging tools for charactering engineered nanoparticles

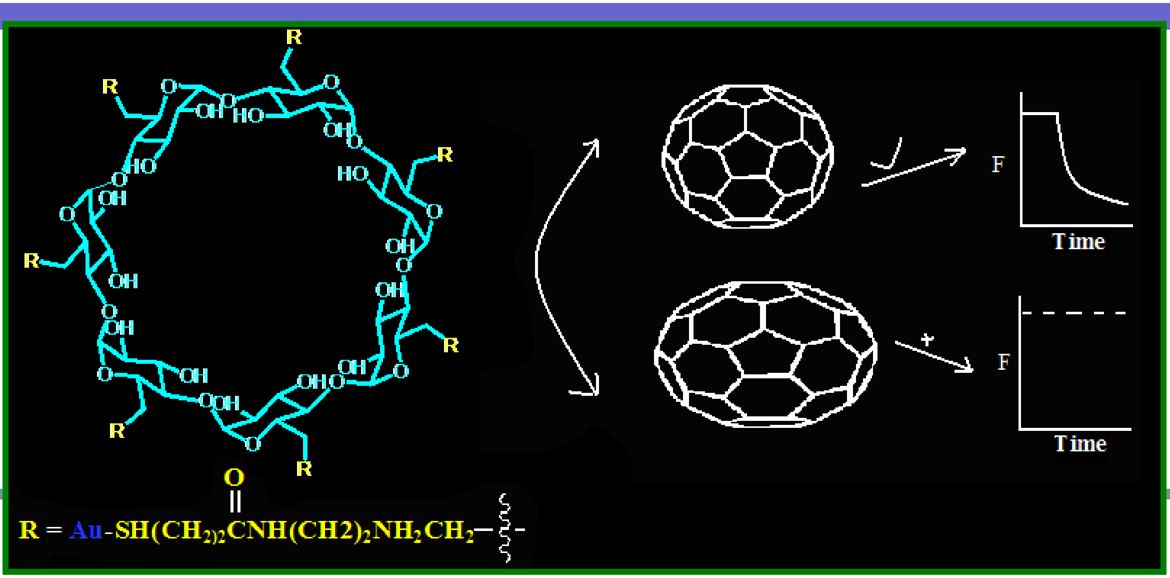


SP-ICP-MS= Single Particle Inductively Coupled Mass Spectrometer, FFF-ICP-MS=Fluid Flow Fractionation Inductively Coupled Mass Spectrometer, EC-TFF=Electro-Chemical Tangential Fluid Flow, DOX-EC=Dissolved oxygen Sensor coupled with Electrochemical technique, DLS= Dynamic Light Scattering.

Category 2:

Size-exclusive Nanosensors for Quantitative Analysis of Fullerenes

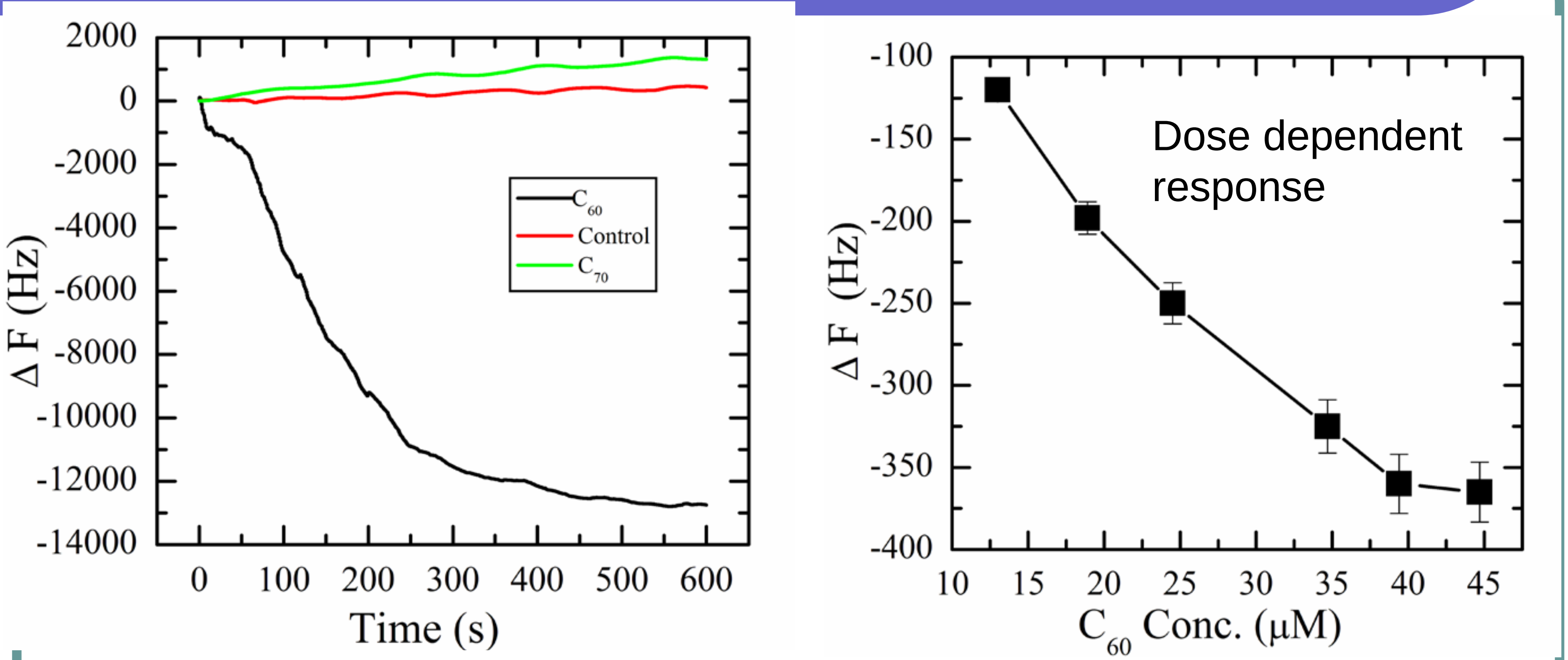
SADIK et al, ES&T 2011, 45, 5294 – 5294



A single-use quantity of cosmetic (0.5 g) may contain up to 0.6 µg of C_{60} and demonstrates a pathway for human exposure to engineered fullerenes

Benn et al., Environ. Poll. (2011)

Nanosensor Responses

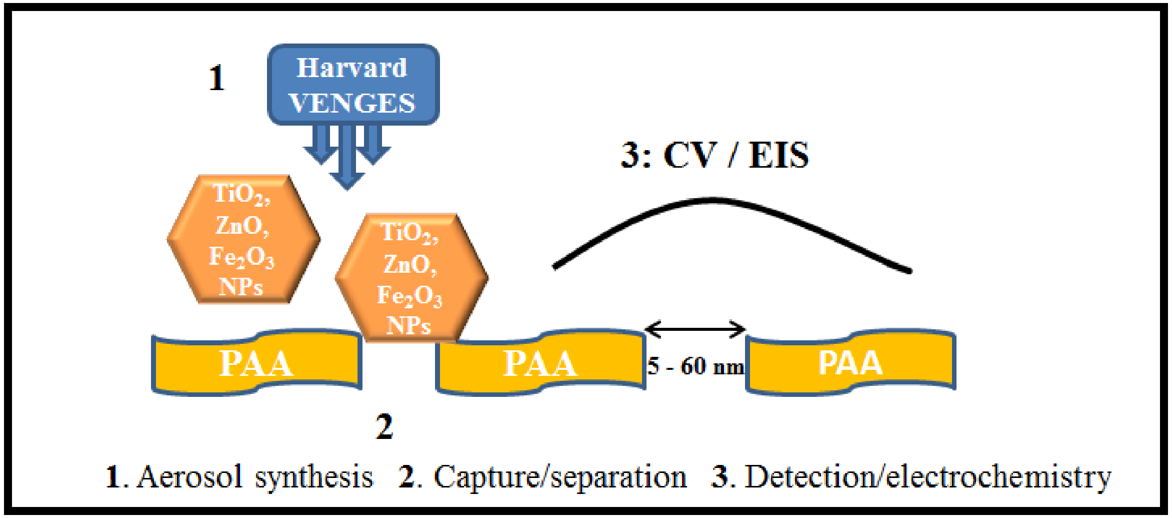


- Active sensing electrode surface area of 0.196 $cm^{2,}$ an equivalent of 2.02 $x10^{12}$ *beta*-CDs should fit on the QCM sensor
- At low concentrations, the ratio *of beta*-CD/C_{60} molecules was ~ 1.12 C_{60}/cavity which, is consistent with the host-guest chemistry of *beta*-CD-C_{60} 1:1 inclusion chemistry

ES&T 2011, 45, 5294 – 5294.

Category 2:

Capture and Detection of Aerosol Nanoparticles using Poly (amic) acid, Phase-inverted Membranes



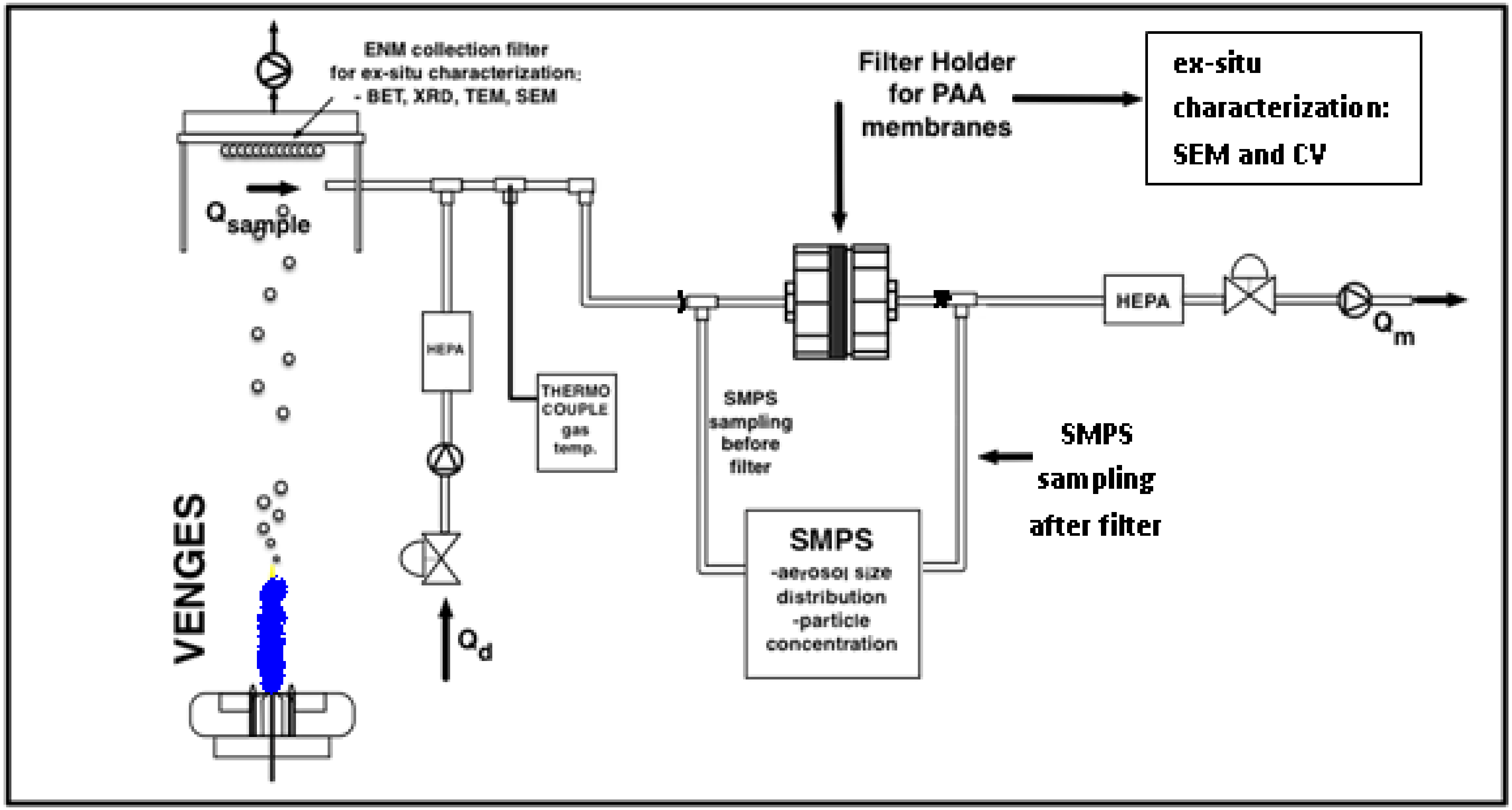
1. Aerosol synthesis **2**. Capture/separation **3**. Detection/electrochemistry

[1]SUNY-BINGHAMTON, NY

[2] HARVARD SCHOOL OF PUBLIC HEALTH, MA, Sadik, Demokritou et al, J. Hazardous Materials, 2014(In press), Nanoletters 2014

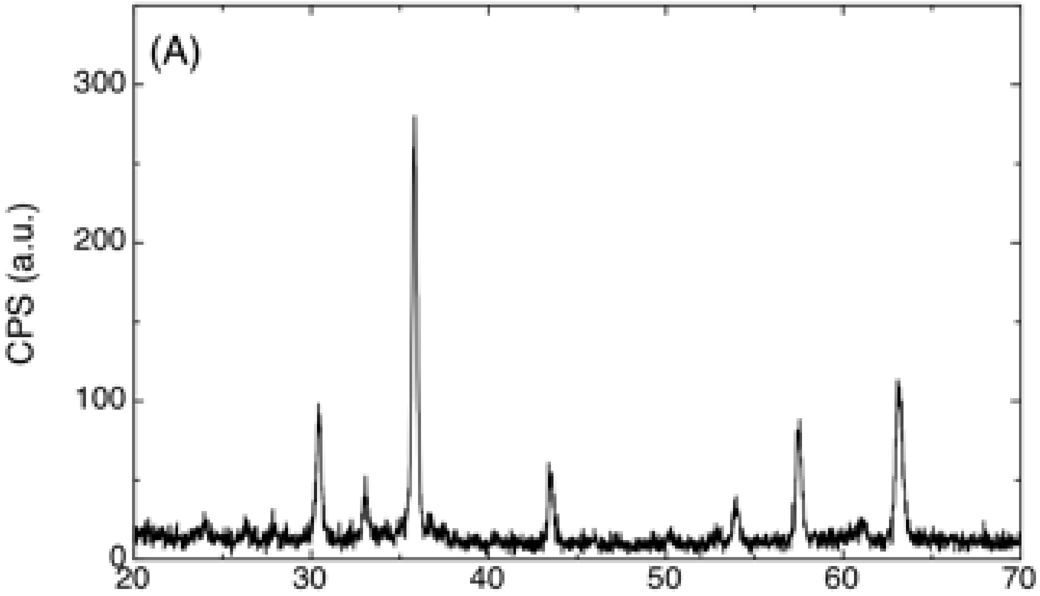
Harvard’s VENGES

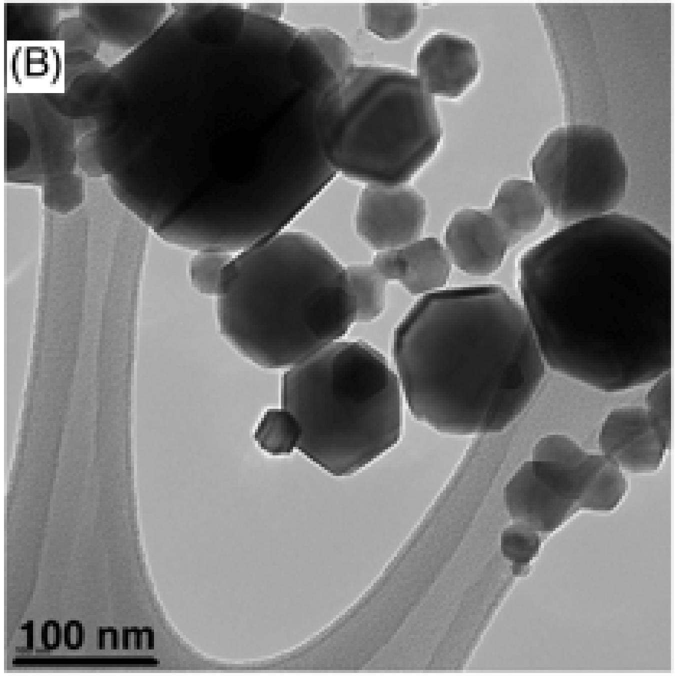
New Platform for pulmonary and cardiovascular toxicological characterization of inhaled ENMs

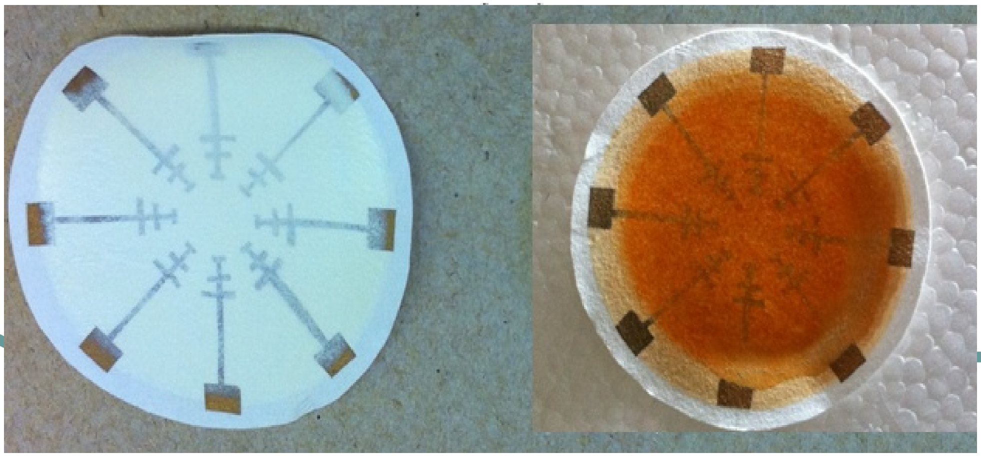


Nanotoxicology, 2011; Early Online, 1–11

Surface Characterization





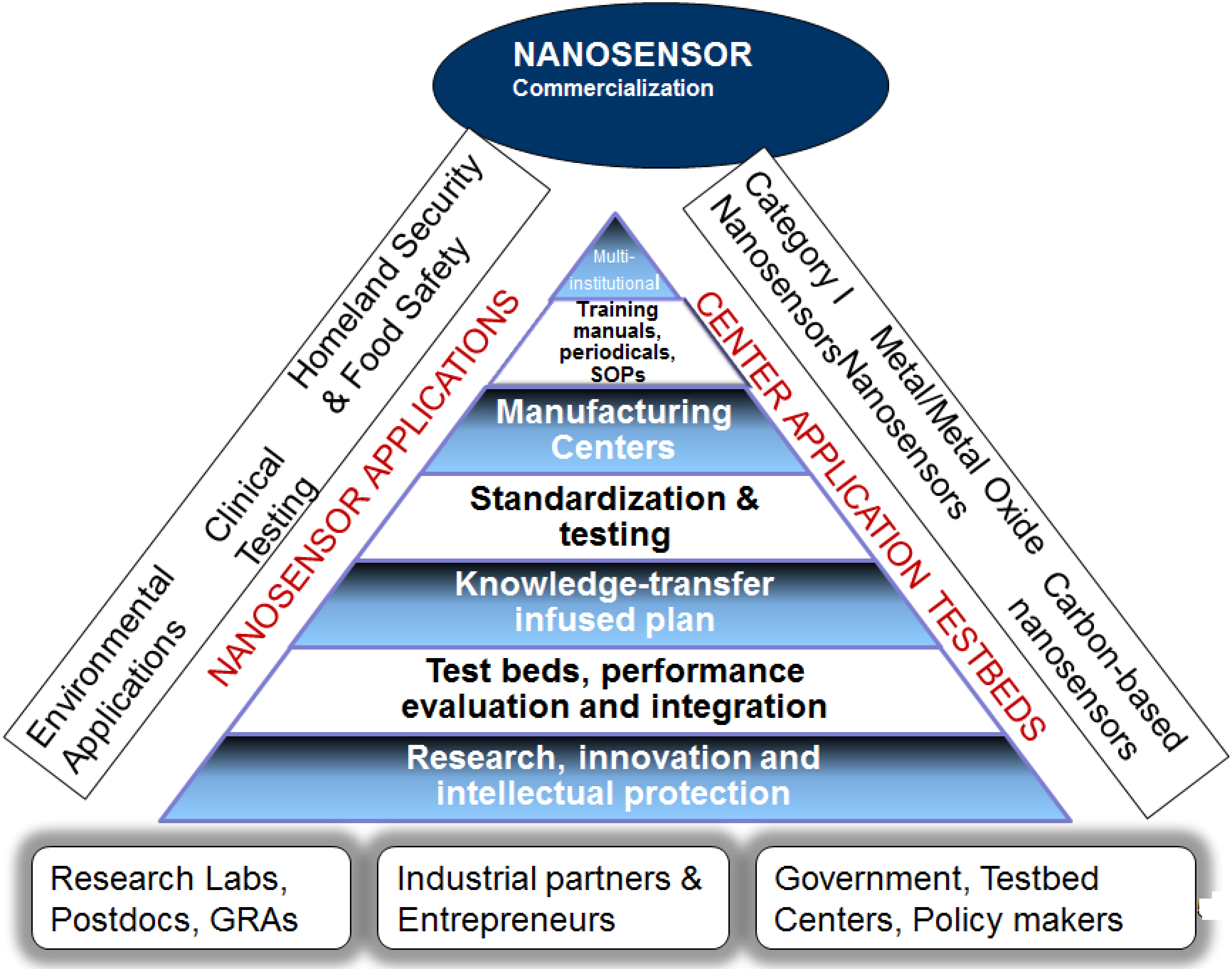


Proposal for Going Forward

- Develop the necessary calibration and validation tools
- Develop SRMs and the analytical quality control tools
- Develop acceptable standards testbeds & charactization centers

Overcoming Present Challenges

- **Develop acceptable SRMs**
  - **Depends on testbeds**
- **Calibration/validation tools**
- **Standardization and Testing Centers**
- **Develop training manuals & SOPs**
- **Define measures of success**



NANOSENSOR
Commercialization

Homeland Security & Food Safety

Clinical Testing

Environmental Applications

NANOSENSOR APPLICATIONS

Category I Nanosensors

Metal/Metal Oxide Nanosensors

Carbon-based nanosensors

CENTER APPLICATION TESTBEDS

Multi-institutional

Training manuals, periodicals, SOPs

Manufacturing Centers

Standardization & testing

Knowledge-transfer infused plan

Test beds, performance evaluation and integration

Research, innovation and intellectual protection

Research Labs, Postdocs, GRAs

Industrial partners & Entrepreneurs

Government, Testbed Centers, Policy makers

Test beds depend on the application

- **Health**
- **Food**
- **Pharmaceutical**
- **Process**
- **Environmental**
- **Defense & Security**

Testbed Specifications

- Environmental sensor should be sensitive, specific, provide fast response, must be reliable, flexible and capable of rapid and direct detection of toxic compounds.
- Additionally, there should be no need for sample preparation steps when analyzing environmental matrices or point-of-care biomedical samples.
- The sensor should be capable of convenient signal processing that will allow immediate remedial actions to be taken after detection

Environmental and Clinical Requirements

- **Precision, accuracy, measurement range, total error**
- **Interference**
- **Reference**
- **Response time**
- **Calibration**
- **Manufacturing**
- **Single use Vs. multi-use**

Nanosensor Performance Metrics-EPA QA/QC

- Data quality parameters
  - Precision, accuracy, LOD, robustness etc
- Method Determination
  - Method positive control, matrix spike, negative control(buffers, blanks, reagent water)
- Frequency
  - With every field sample, 1/batch or 20 samples, 10% of field samples, all standards, blanks, samples
- Quality objective & Comparability
  - % RSD, MDL, intended use of data
- Designated Analytical Levels.

- Sadik et. al, *Journal of Environmental Monitoring*, 6,513-522, **2004;** US-EPA (1995) and revisions. *Test Methods for Evaluating Solid Waste & Emergency Response,* Washington DC.

Performance Metrics

- Experimental variables should be defined
  - Sensitivity should be defined
  - Selectivity and reliability (false positives and false negatives) should be assessed using SOPs.
  - Optimization of experimental variables influencing sensor selectivity and sensitivity as well as the transfer to manufacturing platforms.
- Comparable to standard EPA, AOAC or FDA methods.

Conclusions -Needs of the Community)

- Manufacturing must produce stable sensors with uniform and non-distortable signals across sensing area
- Sensor layers must be mounted with a suitable transducer that does not distort them
- Unpreventable calibration errors in the devices must be reduced to an acceptable level
- Developing QC for the sensor industry requires the collaboration between the manufacturing, government, and research laboratories