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# Scrimmage Briefing Packet

NNI Nanosensor Manufacturing Workshop

# Nanoscrimmage Briefing Packet

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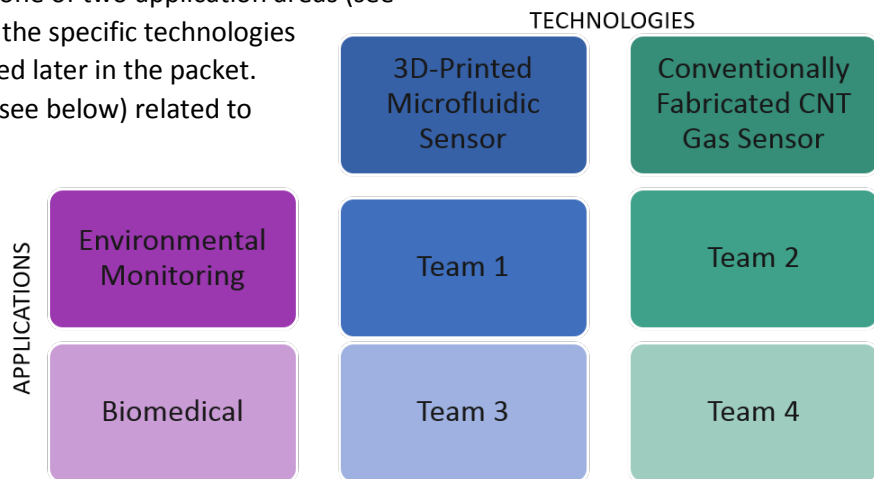
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## Nanoscrimage Overview

The second day of the NNI Nanosensor Manufacturing workshop<sup>1</sup> will include an interactive “scrimmage,” in which participants will walk through a hypothetical scenario of planning the scale-up or migration of a technology platform for wide distribution. The main findings from the scrimmage may be shared with the broader research and development community through a future webinar.

The workshop participants will be divided into four teams, and each team will address one of two hypothetical technologies and one of two application areas (see graphic). More information on the specific technologies and application areas is provided later in the packet.

Each group will discuss topics (see below) related to manufacturing its hypothetical technology for the specified application area. Market information and other relevant resources are provided in the packet for context.<sup>2</sup> Conversations should focus on the technological aspects of manufacturing quality control and scale-up.



- Primary Discussion Points
  - Factors impacting the reproducibility of the manufacturing method and final product
  - Factors to consider when choosing materials (e.g., cost, purity, source)
  - The plan for testing, including field/test conditions, regulatory requirements, scope, etc.
- Other Considerations
  - Factors impacting the scalability of the manufacturing method
  - Limitations in terms of raw materials and processing technologies
  - Manufacturing cost drivers for this technology
  - Remaining technical issues hindering commercialization of this technology
  - Factors that will influence the decision to manufacture in-house vs. contracting out
  - Life-cycle considerations (e.g., device or effluent disposal)
  - Major safety concerns for manufacturing the sensor
  - Other (please specify)

The morning will open with an introduction to the technologies and application scenarios, followed by brief presentations on select resources available for decision making on materials. Then the teams will meet for approximately two hours to discuss their scenarios. Representatives from a company that has commercialized a nanomaterials-based sensor will act as informal consultants and share insights from their experience with the scrimmage teams. Each group will then present its main findings, as well as

<sup>1</sup> The Nanosensor Manufacturing Workshop supports the goals of the [Nanotechnology for Sensors and Sensors for Nanotechnology Signature Initiative \(NSI\)](#).

<sup>2</sup> Note that the technologies and application areas addressed in the scrimmage are intended to be realistic, but not real. As such, some information provided in this packet is purely hypothetical and was invented specifically for this activity.

responses to the discussion points above. The day will wrap up with an open discussion to identify common themes and differences among the technologies and application areas.

## Technology Descriptions

### 3D-Printed Microfluidic Sensor (Teams 1 & 3)

This technology is based on a device design described in *Biomicrofluidics* **10**, 054113 (2016). The device consists of a 3D-printed microfluidic mixer with a 500  $\mu\text{m}$  channel diameter and ring-shaped channels (see Figure 1). Consistent sample introduction is ensured by using a “slot-in” sampling platform with  $\sim 20$   $\mu\text{L}$  wells, one well for the sample and a second well for the reagents. One minute after mixing has occurred, colorimetric analysis is performed using a cell phone camera and in-house app to determine analyte concentration. The sample is aligned with the camera lens using a 3D-printed chip housing.

The device prototypes were fabricated with a laptop-sized 3D printer (D3 ProJet 1200), which has a 30  $\mu\text{m}$  pixel resolution. Microfluidic design that enabled effective mixing of reagents and samples without an external power source was achieved by performing 3D computational fluid dynamic simulations of potential configurations using commercially available software. A force balance between the capillary force (dependent on the surface tension and channel diameter) and frictional force (dependent on the dynamic viscosity of the fluid, wetted length, flow velocity, and fluid density) determines the auto-mixing flow rate. Successful auto-mixing depends on well-matched channel, surface, and fluid properties.

The printer feedstock consists of 2 weight percent of 75 nm silica spheres dispersed in VisiJet FTX Clear resin—triethylene glycol diacrylate, sobornyl methacrylate, and 2% photoinitiator phenylbis (2,4,6-trimethylbenzoyl)-phosphine oxide. Devices were printed per the vendor’s instructions, cleaned using isopropyl alcohol, and blown dry with compressed air. Each device was printed in 10 minutes at a cost of \$0.50. Ethylene glycol chemistry was used to develop a hydrophilic surface. The devices were soaked in a solution of 1.82M potassium hydroxide (KOH) in pure ethylene glycol (Sigma-Aldrich; anhydrous, 99.8%) at 55°C for 2 hours. After the ethylene glycol treatment, the devices are stable for several days when stored in water.

### Conventionally Fabricated CNT Gas Sensor (Teams 2 & 4)

This technology is based on a sensor array design described in *Sensors* **16**, 1163 (2016). The 32-sensor array (see Figure 2) is made with four different sensing materials (carboxylic single-walled carbon nanotubes [SWCNTs], sulfonated SWCNTs, hydroxyl-functionalized SWCNTs, and polyaniline) to achieve selective discrimination using pattern recognition. The resistance of each sensing material will uniquely change in response an analyte, changing the resistance of that particular material and resulting in a unique response pattern for different analytes. Each sensor consists of an interdigitated electrode that is coated

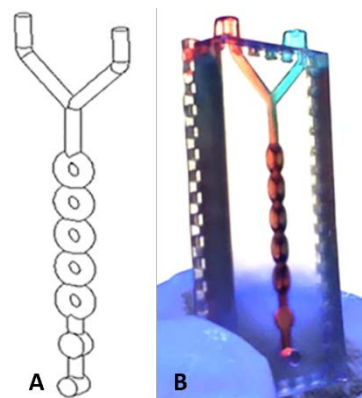


Figure 1. (A) CAD design of microfluidic channel and (B) photo of 3D-printed, 3D-structured micromixer showing efficient mixing within 1 second using colored dye solutions. Images from *Biomicrofluidics* **10**, 054113 (2016).



Figure 2. Phone sensor module, including 32 sensors and a microfan. Image from *Sensors* **16**, 1163 (2016).

with one of the four sensing materials. The sensor array communicates with a smartphone, which is used for data acquisition, storage, and processing, via Bluetooth.

Single-walled carbon nanotubes were purchased from Helix Material Solutions (Richardson, TX, USA). Chemical modification of SWCNTs was performed by acid treatment to obtain carboxylic SWCNTs and sulfonated SWCNTs. The SWCNTs were acid refluxed at 120°C for about 4 hours to allow sufficient time for reaction and achieve a high level of carboxylic functionalization. Carbon nanotubes were also functionalized using potassium hydroxide to obtain hydroxyl (OH) functionalized SWCNTs. These functionalization processes increase the surface activity and enable easier interaction with the target gases. The functionalized nanotubes were then dispersed in a solvent and sonicated for 2 hours. Polyaniline base was protonated using strong hydrochloric acid to obtain a polyaniline salt. The green precipitate was filtered, washed with distilled water, and dried in a vacuum oven for 3 hours at 40°C. The sensing materials were deposited and pipetted across interdigitated electrodes, which were fabricated using standard lithographic techniques and included a 120 µm finger gap. Each device can be fabricated in 1.5 days for \$2/device.

### Application Areas

#### Team 1: Measuring arsenic in well water

Team 1 will develop and manufacture the 3D-printed microfluidic sensor for measuring arsenic levels in well water. Water samples will be mixed with a solution of citrate-stabilized gold nanoparticles (AuNPs). The AuNPs will aggregate in the presence of As(III), causing the solution to shift from red to blue at concentrations of As(III) above 0.01 parts per million (ppm). The U.S. EPA's Maximum Contaminant Level for arsenic is 0.010 mg/L or parts per million. The size of the market for arsenic sensors is estimated to be 2 million units per year, and the average cost of current, commercially available technologies is \$15 per unit.

#### Team 2: Measuring nitrogen dioxide in air

Team 2 will develop and manufacture the gas sensor array for measuring NO<sub>2</sub> levels in air. The U.S. EPA's National Ambient Air Quality Standard (NAAQS) for NO<sub>2</sub> is 100 parts per billion. The size of the market for NO<sub>2</sub> sensors is estimated to be 2 million units per year, and the average cost of current, commercially available technologies is \$15 per unit.

#### Team 3: Measuring a biomarker for pancreatic cancer in blood

Team 3 will develop and manufacture the 3D-printed microfluidic sensor for measuring a serum miRNA as a biomarker for pancreatic cancer in blood. AuNPs stabilized in a salt solution with probe hairpin DNA aggregate in the presence of target miRNA, which acts as an initiator for hybridization of the probe DNA hairpins and their consequent removal from the AuNP surface. A visible change in solution color from red to blue results. The size of the market for pancreatic cancer tests is estimated to be 100,000 tests per year, and the average cost of current, commercially available technologies is \$5,000 per test.

#### Team 4: Measuring a biomarker for lung cancer in breath

Team 4 will develop and manufacture the gas sensor array for measuring a panel of volatile organic chemicals in exhaled breath as a biomarker for lung cancer. The size of the market for lung cancer tests is estimated to be 100,000 tests per year, and the average cost of current, commercially available technologies is \$5,000 per test.

## Appendix A. Examples of Relevant Resources

- FDA Quality System (QS) Regulation/Medical Device Good Manufacturing Practices  
[www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/)
- MEMS Foundry Engagement Guide Wiki  
[memsfoundry.wikia.com/wiki/MEMS\\_Foundry\\_Engagement\\_Guide\\_Wiki](http://memsfoundry.wikia.com/wiki/MEMS_Foundry_Engagement_Guide_Wiki)
- EPA Air Sensor Toolbox: Resources and Funding  
[www.epa.gov/air-sensor-toolbox/air-sensor-toolbox-resources-and-funding](http://www.epa.gov/air-sensor-toolbox/air-sensor-toolbox-resources-and-funding)
- Regulatory Case Study for the Development of Nanotechnology-enabled *In Vitro* Diagnostic Devices  
[www.nano.gov/sites/default/files/sapsford\\_nsi\\_webinar\\_nov\\_2015\\_slides\\_with\\_captions\\_final.pdf](http://www.nano.gov/sites/default/files/sapsford_nsi_webinar_nov_2015_slides_with_captions_final.pdf)
- Sensors NSI web portal: Facilities  
[www.nano.gov/SensorsNSIPortal/Facilities](http://www.nano.gov/SensorsNSIPortal/Facilities)
- Sensors NSI web portal: Organizations  
[www.nano.gov/SensorsNSIPortal/SDOrganizations](http://www.nano.gov/SensorsNSIPortal/SDOrganizations)
- Sensors NSI web portal: Regulatory Guidance  
[www.nano.gov/SensorsNSIPortal/SDGuidance](http://www.nano.gov/SensorsNSIPortal/SDGuidance)
- Sensors NSI web portal: Standards  
[www.nano.gov/SensorsNSIPortal/SDStandards](http://www.nano.gov/SensorsNSIPortal/SDStandards)
- Sensors NSI web portal: Testing and Commercialization Support  
[www.nano.gov/SensorsNSIPortal/TestingCommercializationSupport](http://www.nano.gov/SensorsNSIPortal/TestingCommercializationSupport)

## Appendix B. Publications that Inspired the Scrimmage Technologies

K. Plevniak, M. Campbell, T. Myers, A. Hodges, M. He, [3D printed auto-mixing chip enables rapid smartphone diagnosis of anemia](#). *Biomicrofluidics* **10**, 054113 (2016).

A. Hannon, Y. Lu, J. Li, M. Meyyappan, [A Sensor array for the detection and discrimination of methane and other environmental pollutant gases](#). *Sensors* **16**, 1163 (2016).

P. Liu *et al.*, [Enzyme-free colorimetric detection of DNA by using gold nanoparticles and hybridization chain reaction amplification](#). *Anal. Chem.* **85**, 7689 (2013).

L. Gong *et al.*, [Colorimetric aggregation assay for arsenic\(III\) using gold nanoparticles](#). *Microchim. Acta* **184**, 1185 (2017).

X. Miao, X. Ning, Z. Li, Z. Cheng, [Sensitive detection of miRNA by using hybridization chain reaction coupled with positively charged gold nanoparticles](#). *Scientific Reports* **6**, 32358 (2016).