



Nanomanufacturing @ NSF

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Civil, Mechanical and Manufacturing Innovation Division
Engineering Directorate
National Science Foundation
Alexandria, VA

2018 AFOSR Biophysics Program Review, Arlington, VA, April 18, 2018

Outline



- NSF / ENG / CMMI
- Nanomanufacturing
- Bio-nanomanufacturing

National Science Foundation



France Cordova
Director

Mission

- *The NSF Act of 1950 (PL 81-507): To promote the progress of science; to advance the national health, prosperity and welfare; to secure the national defense; and for other purposes*

Vision

- *A Nation that creates and exploits new concepts in science and engineering and provides global leadership in research and education*



- ~4% of Federal R&D
- ~44% of non-medical R&D at US Universities

2019 Budgets:

- NSF \$7.5B; NIH \$34.8B; DOE \$5.4B

What's new?

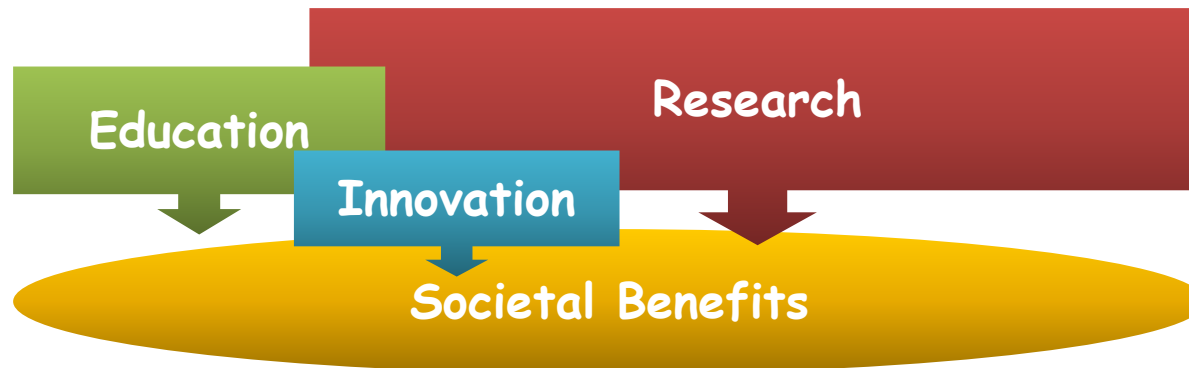




Supporting these ideas will push forward the frontiers of U.S. research and provide innovative approaches to solve some of the most pressing problems the world faces, as well as lead to discoveries not yet known

Vision

- Invest in engineering research and education to foster innovations for the benefit of society



Dawn Tilbury
Assistant Director,
ENG

ENG Initiatives and Priorities Address National Interests

- Innovations at the Nexus of Food, Energy, and Water Systems (INFEWS)
- Risk and Resilience
- Clean Energy Technology
- Cyber-Enabled Materials, Manufacturing, and Smart Systems (CEMMSS)
 - Advanced Manufacturing; MGI; Robotics; CPS

- Smart and Connected Communities
- National Nanotechnology Initiative (NNI)
- Understanding the Brain (BRAIN Initiative)
- National Strategic Computing Initiative
- Innovation Corps (I-Corps™)
- Inclusion across the Nation of Communities of Learners of Underrepresented Discoverers in Engineering and Science (INCLUDES)

Goal

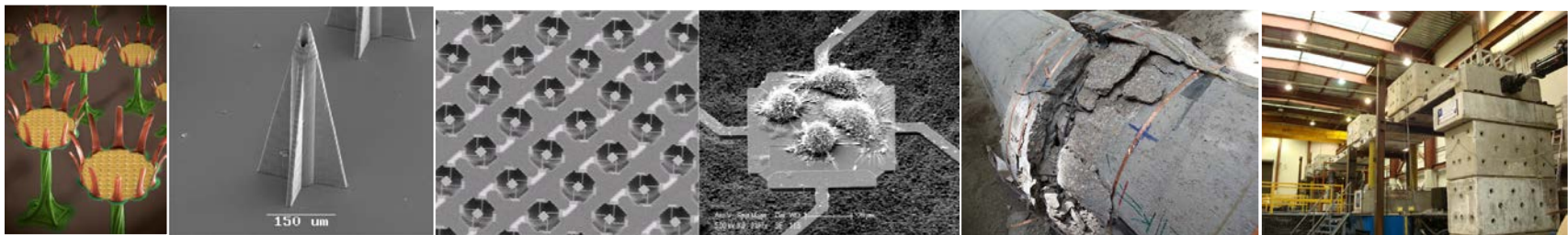
- *Enabling the frontiers of civil, mechanical and manufacturing research at all scales*

Areas of Interest

- **Advanced Manufacturing:** advances in manufacturing and materials processing, with emphases on efficiency, economy, sustainability and scalability
- **Mechanics and Engineering Materials:** understanding the properties and use of materials in engineered and natural systems
- **Resilient and Sustainable Infrastructures:** innovation to advance resilience and sustainability of civil infrastructure and distributed infrastructure networks
- **Operations, Design and Dynamic Systems:** decision-making aspects of engineering, including design, control, optimization and systems science



Deborah Goodings
Division Director



Nanoscale to Infrastructure Scale Research

CMMI Organization and Programs



Division Director
Deborah Goodings
Deputy Director
Mary Tony

**Interdisciplinary and
Cross-Divisional Activities**
Bruce Kramer

Integrative Activities
Jo Culbertson

Advanced Manufacturing (AM)

**Materials Engineering
and Processing (MEP)**

*Thomas Kuech, Alexis Lewis,
Vacant*

**Manufacturing Machines
and Equipment (MME)**

*Steven Schmid,
Bridgid Mullany*

NanoManufacturing (NM)

*Khershed Cooper,
Bridgid Mullany*

**CyberManufacturing
Systems (CM)**

Bruce Kramer

Mechanics and Engineering Materials (MEM)

**Mechanics of Materials
and Structures (MOMS)**

*Kara Peters
Siddiq Qidwai*

**Biomechanics and
Mechanobiology (BMMB)**

David Fyhrie

**Leading Engineering for
America's Prosperity, Health
and Infrastructure (LEAP HI)**

Bruce Kramer

Resilient and Sustainable Infrastructures (RSI)

**Civil Infrastructure
Systems (CIS)**

Cynthia Chen

**Engineering for Civil
Infrastructure (ECI)**

*Richard Fragaszy,
Grace Hsuan, Joy Pauschke*

**Humans, Disasters and
Built Environment
(HDBE)**

Robin Dillon-Merrill

**Natural Hazards Engineering
Research Infrastructure
(NHERI)**

Joy Pauschke

Operations, Design and Dynamical Systems (ODDS)

**Mind, Machine and Motor
Nexus (M3X)**

Robert Scheidt

**Engineering Design and
Systems Engineering (EDSE)**

Richard Malak

**Dynamics, Control and
System Diagnostics (DCSD)**

*Jorden Berg, Atul Kelkar,
Irina Dolinskaya*

Operations Engineering (OE)

*Georgia-Ann Klutke,
Irina Dolinskaya*



Leading Engineering for America's Prosperity, Health, and Infrastructure (LEAP HI)

- research goals are NOT achievable through small, short-term projects
- engineers take a visible, leadership role
- research has broad societal impacts
- incorporate knowledge and methods not normally included in CMMI proposals
- emphasis on planning and coordination
- emphasis on communicating results broadly

Budget: \$1-2 million total for up to 5 years for projects

Letter of Intent: (1) Dec 15, 2017; (2) Jul 16, 2018

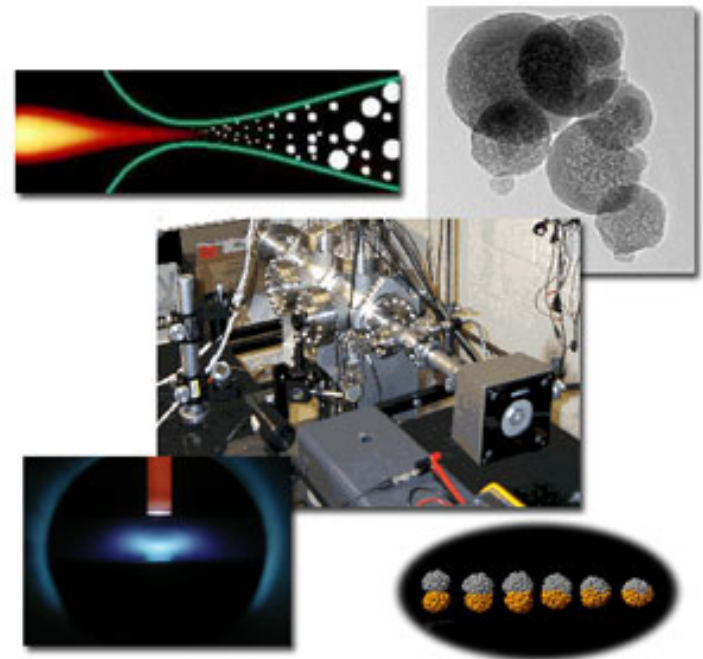
Full Proposal Submission: (1) Feb 5-20, 2018; (2) Sep 1-15, 2018

For more information contact Bruce Kramer, bkramer@nsf.gov

https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=505475

Definition: *Fabrication* of nano-scale building-blocks (nanomaterials, nanostructures), their *assembly* into higher-order structures, and the *integration* of these into larger scale systems with *manipulation and control at nano-scale*

- **Study** *techniques and methods* to manipulate and control matter at the nanoscale in 1-, 2-, and 3-dimensions, *reproducibly*
- **Nanoscale:** Approx. 1-100 nm, *a dimension – significant beneficial effect*
- **Processes:** Bottom-up (self- and directed-assembly); top-down (lithography, deposition, removal)
- **Integration:** Hierarchical / heterogeneous; Across: length scales, materials (0D, 1D, 2D), geometries, processes, functions



Nanomanufacturing @ NSF



NM (2002-present) - https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=13347

- Typical \$100-150K/yr; 3-years
- 1-investigator; Collaborative; GOALI
- *Fundamental research to enable and improve large-scale or customized manufacturing of nanomaterials, nanostructures, nanodevices and nanosystems*

SNM (2011-2016)/**SNM-IS** (2017)

- Max \$375K/yr; 4-years
- Inter-disciplinary; Collaborative; GOALI; Industry
- **SNM:** *Overcome scientific and engineering barriers that prevent production of useful nanomaterials, structures, devices and systems at an industrially relevant scale, reliably*
- **SNM-IS:** *Fundamental principles of scalable or customizable manufacturing for nano-based integrated systems towards eventual manufacture of useful nanotechnology products*

NSECs (2004-18)/**NERCs** (2013-present)

- \$4M/yr; 5 to 10-years
- Multi-institution; Industry; Labs
- **NSEC:** *Understand nanoscale processes, develop novel tools for measurement and manufacturing at nanoscale, develop novel concepts for high-rate processing of nanostructures and nanosystems, and scale-up of nanoscale processing methods*
- **NERC:** *Integrate engineering research and education with technological innovation*

Bridge gap between nanoscience discoveries and nanotechnology products

Examples of Scientific Barriers



- 3D printing methods are limited in printing *resolution and throughput*
- Moore's Law is in danger of ending because *difficulty and expense of approaches* that rely on using ever shorter wavelengths of light are becoming prohibitive
- Understanding *nucleation and growth* of nano-arrays under continuous flow conditions
- *Difficult to fabricate and assemble* 0D, 1D, 2D nanostructures over large areas and in 3D configurations
- Conventional 2D printing utilizes inks that require post-print processing and cannot fabricate sub-micron structures, which *limits the substrate and ink selection*
- Soft-lithographic contact printing relies on patterned elastomeric stamps and demands better *adhesive control* at the stamp-substrate interface

Materials and Structures

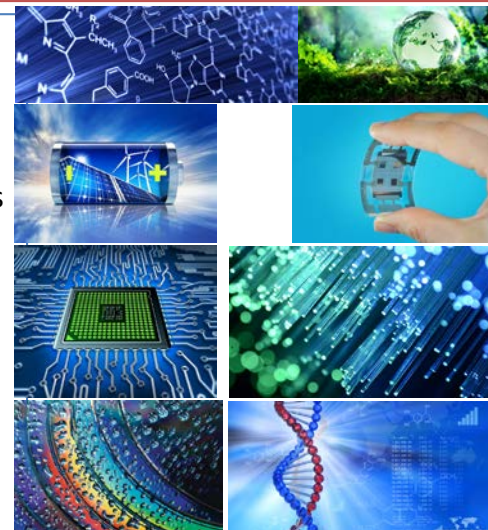
- **C-based:** CNT, Graphene, Bucky-tape, CNT Fibers, Cellulosic
- **0D:** Nanoparticles, QDs, Core-shell, Janus, Hierarchical, Composite
- **1D:** Nanowires, Nanopillars, Nanotubes, Nanofibers
- **2D:** MoS₂, BN, TMDs
- **3D:** Nanoporous, Aerogels, Arrays, Patterns
- **Material Systems:** Metals, Ceramics, Polymers, Organics, Composites

Processes and Methods

- **Chemical/Thermal:** Combustion, Plasma, Hydrothermal, Drawing, Etching
- **Vapor-based:** CVD, PVD, PECVD, Laser CVD, ALD, MLD
- **Fluid/Solution-based:** Coating, Casting, Colloids, Electrospray, Electrophoresis, Electrospinning, Electroetching, Microfluidics, Microreactors, Ink-jet Printing
- **Lithography/Patterning:** BCPs, AFM, DPN, NIL, PLD, Laser Writing, E-beam, Ion-beam
- **Assembly:** Self, Directed (chemical, magnetic, acoustic), Molecular
- **Bio-assisted:** DNA, Virus, Protein, Peptides, Diatoms
- **Mechanical:** Exfoliation, Nanomachining, Ball-milling
- **3D Nanomanufacturing:** 3D Printing, Holographic Lithography, MacEtch

Applications

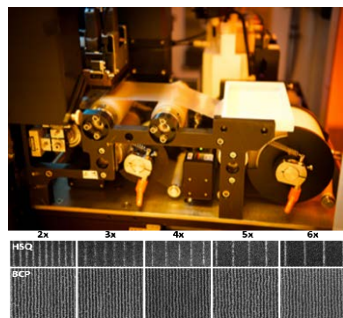
- **Environmental:** Water/Air Purification, Analytical Separation
- **Chemical:** Catalysis, Gas Storage
- **Energy:** Storage, Conversion, Harvesting, Batteries, Supercapacitors, PVs, Solar Cells, Fuel Cells
- **Electronics:** ICs, Flexible, Storage Memory, 3D Devices, TFTs, EM-Shielding
- **Optoelectronics/Photonics:** Imaging, Waveguides, Displays, Lighting, Metamaterials
- **Sensors:** Biological, Chemical, Multiplexed
- **Structural:** High-Strength, Light-Weighting, Packaging
- **Biomedical:** Implants, Tissue Scaffolds, Diagnostics, Therapeutics, Drugs, Probes
- **Sheets/Wires:** Fibers, Cables, Filters, Membranes, Textiles, Paper, Fabric, Nonwovens



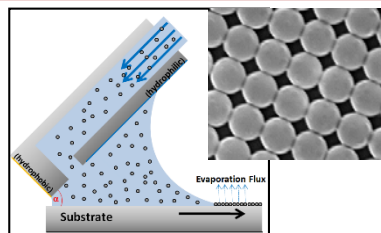


- **Continuous Roll-to-Roll Processes, Top-down/Bottom-up Processes**
 - Processes: Printing, Imprinting, Self-assembly, Deposition, Coating, Lamination
 - Examples: Printing of nanoparticles, forming of CNT Bucky paper, and convective deposition of self-assembled nanoparticles
- **Parallel, Large-area Top-down or Bottom-up Processes**
 - Processes: Lithography, Direct-write, Directed- and Self-assembly
 - Example: Optical lithography using parallel nanoantennae arrays
- **Parallel, Large-area 3D Nanofabrication**
 - Processes: 2-Photon Polymerization, Nanoimprinting and Self-assembly, Strain Eng.
 - Example: Projection SLA and DW of 3D heterogeneous biological scaffolds
- **Continuous or Parallel Reaction Synthesis/Fluidics Techniques**
 - Processes: Microreactor, Microfluidic, Hydrothermal synthesis, Chemical synthesis, Plasma, Electrospray, Electrospinning, Fiber-drawing
 - Example: Grow quantum dots and core-shell nanoparticles in colloids or solutions
- **Large-area Bio-enabled Nanofabrication**
 - Process: Templating using DNA
 - Example: Molecular self-assembly of atomically-precise, defect-free DNA patterns

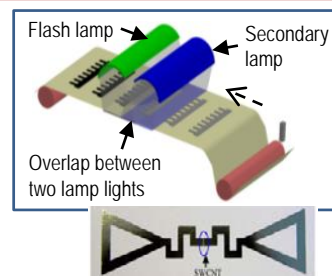
Examples of Scale-up Approaches



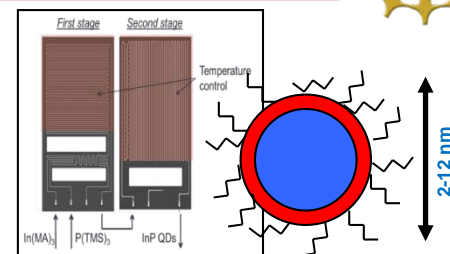
Roll-to-roll NAnopatterning
(SV Sreenivasan, UT-Austin)



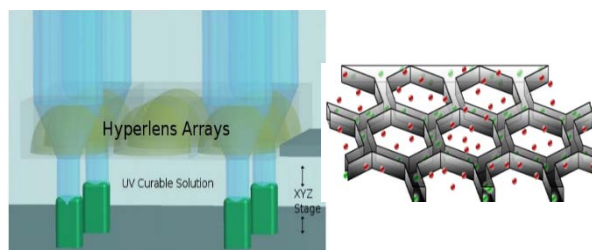
Vibration-assisted Convective Deposition
(James Gilchrist, Lehigh)



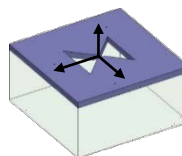
R2R/Flash-Sinter Metal Patterning
(Chih-hung Chang, Oregon State)



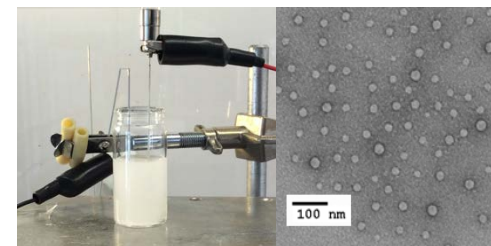
Microfluidic Reactor for QDs
(Klavs Jensen, MIT)



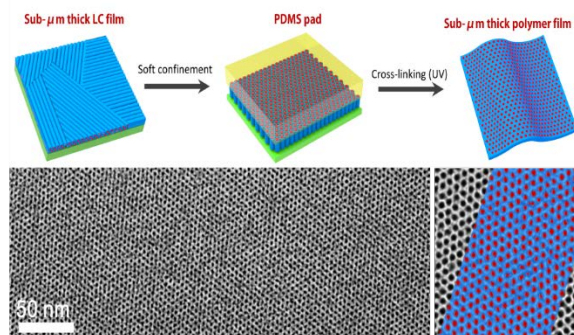
3D Printing of Biomimetic Scaffold
(Shaochen Chen, UC-San Diego)



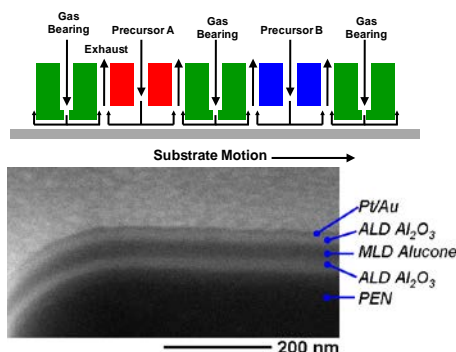
Parallel Bow-tie Antenna Array Patterning
(Xianfan Xu, Purdue)



Micellar Electrspray of Nanocomposite
(Jessica Winter, OSU)



Field-directed Aligned Nanoporous Films
(Chinedum Osuji, Yale)



Multi-layer Roll-to-Roll ALD/MLD
(Yung-Cheng Lee, U of Colorado-Boulder)



What is it?

- *Harnessing biology or nature, using living cells directly, borrowed, or taken as inspiration*
- Biomimetics: Use of bio-inspired concepts, functions and principles of operation
- Bio-enabled: Use of biological species such as DNA, virus, protein, bacteria, etc. to design and make new materials, structures and devices with nanoscale precision and architectures
- Nano-enabled: Use of nanomaterials or nano-scale processes to make useful biological constructs such as cells, proteins, etc.

Why interest?

- The benefits of using these enablers are programmability, precision of placement, specificity, adaptivity, ambient temperature processing, energy-efficient synthesis, ..., *all with nanoscale manipulation and control*

Bio-nanomanufacturing Concepts



- **Nano-biomachines, Nanorobots, Nanomotors, Nano-bioreactors.** Investigate design concepts, nanomanufacturing approaches and manipulation strategies for nano-biosystems. Nano-biosystems are built of organic, inorganic and biomaterials using top-down lithography and bottom-up assembly processes. *Applications are early medical diagnosis, targeted drug delivery, disease monitoring, micro-surgery, tissue repair, as well as in sensing, catalysis and environmental remediation*
- **DNA-enabled Nanofabrication.** Fabricate single molecule nanostructures that are progressively built up from small molecule components and self-assembled into complex, multi-dimensional nanocomponents. Understand fabrication of arbitrary and robust nanostructures using directed self-assembly of DNA origami shapes onto lithographically-patterned binding sites. This allows the reliable positioning of single molecules or nanoparticles at precise locations within nanofabricated devices. *Applications are data storage and membranes*
- **Single Molecule Patterning with Microtubules:** Understand biopen charging with bioink, bioink assembly properties, and control of amounts for writing individually or in parallel. Use in writing with organic and inorganic materials such as QDs and nanotubes. *Applications are drug screening and electronic system miniaturization*
- **Cell Reprogramming:** Investigate microfluidic approach to synthesize and manufacture novel polymeric nanoparticles for efficient gene delivery. Understand nanoparticle quality's influence on rate of cell reprogramming to produce desired types of a patient's cells with high yield. *Technology could accelerate clinical and pharmaceutical uses of patient-matched cells*
- **Nanoscale Drug Carriers:** Enable drug designers to tailor the delivery of therapeutic compounds to specific tissues or cells, and optimize the uptake of drugs into those cells. Transition of liposomal nanomedicines from the lab to the clinic requires nanomanufacturing scale-up. This is done through continuous-flow microfluidic system, resulting in nanoparticle self-assembly, passive and active drug loading, nanoparticle functionalization, and drug purification and concentration. *Application is drug delivery*
- **Nanostructured Bio-assemblies:** Study bioactive nanostructures for low-cost devices with appropriate detection sensitivity and selectivity for home and point-of-care diagnosis. Study large-scale manufacturing of functional nanostructured bio-assemblies on flexible and inexpensive substrates such as paper and plastic using 3D printing. *Applications include responsive materials for wearable bio-sensing devices, flexible bioelectronics, and functional contact lenses*
- **Protein-based Bio-nanomanufacturing:** Nature does an excellent job of reproducibly making complex metal and semiconductor nanomaterials. This biological inspiration of microbial metal nanoparticle fabrication is used to generate bio-nanomanufacturing platforms. Biological organisms utilize proteins and peptides to produce individual metal nanoparticles at room temperature without organic solvents as a method to deal with metal-ion toxicity in the biological cell. This bio-detoxification process produces uniform and spherical nanoparticles. Understand biological programming mechanism for control of size, shape, and purity of the nanoparticles
- **Virus-based Nanomanufacturing:** Research is focused on devising scalable and in-solution synthetic methods for the production of bio-nanoparticle assemblies with high yields, and involving fewer synthetic and purification steps, while maintaining high-precision nanostructuring. Plant virus-based nanoparticles are produced through genetic engineering and scalable molecular farming. Sphere- and tube-like bio-nanoparticles are used for solution-based chemical and colloidal synthesis with chemical functionalization carried out in situ. Janus-type nanoparticles, when functionalized with appropriate ligands or ions, have possible *applications in healthcare, sensors, display optics, energy conversion, and data storage devices*

Bio-nanomanufacturing Projects



SNM: Electronically Controlled Surface Assembly of DNA Nanostructures – *William Goddard, California Institute of Technology*

SNM: DNA-Directed Self Assembly of Nanoscale Integrated Circuits – *Jason Slinker, University of Texas at Dallas*

SNM: Atomically Precise, Defect Free, DNA Masks with Embedded Metrology – *William Hughes, Boise State University*

SNM: Scalable Cell-free Protein Manufacturing via NanoClay-DNA (NanoCD) Microdonuts -- *Dan Luo, Cornell University*

NM: Collaborative Research: Large-Scale Nanomanufacturing of Well-Positioned and Highly Aligned DNA Wires from a Capillary Bridge -- *Zhiqun Lin, Iowa State University and Lei Zhu, Case Western Reserve University*

CAREER: DNA-templated Assembly of Nanoscale Circuit Interconnects -- *Rebecca Schulman, Johns Hopkins University*

NM: Casting Inorganic Nanostructure Arrays with 3D DNA Crystal Molds -- *Peng Yin, Harvard University*

NM: Scalable Nanomanufacturing and Supra-Assembly of Virus-Hybrid Janus Bionanoparticles -- *Nicole Steinmetz, Case Western Reserve University*

NM: Understanding DNA-Graphene Interaction Towards Scalable Nanomanufacturing -- *Jong Hyun Choi, Purdue University*

NM: Highly Parallel Synthesis of Nanostructures Inside Crystalline Protein Scaffolds – *Christopher Snow, Colorado State University*

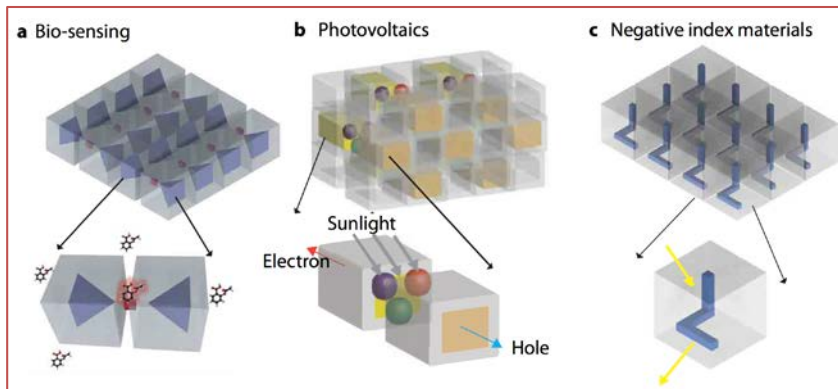
NM: Integrated Nanochannel and Nanopore Architecture for Studying Translocation Dynamics of DNA -- *MinJun Kim, Drexel University*

NM: Scalable Nanomanufacturing of Cyclic Peptide-Based Nanorobots for In Vivo Sensing -- *MingJun Zhang, Ohio State University*

Examples

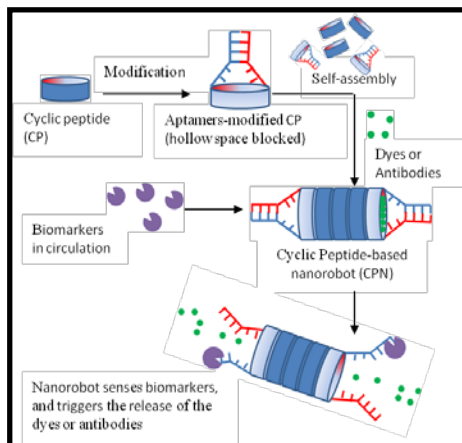


NM: Casting Inorganic Nanostructure Arrays with 3D DNA Crystal Molds - Peng Yin, Harvard



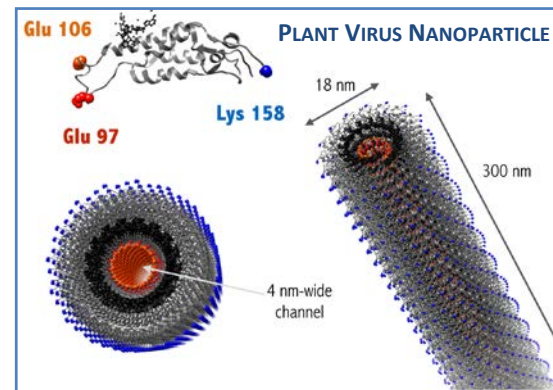
Casting growth: sub-25 nm digital fabrication of 3D metal nanoparticles at sub-5 nm resolution

NM: Cyclic Peptide-based Nanorobots for *In Vivo* Sensing - Mingjun Zhang, Ohio State



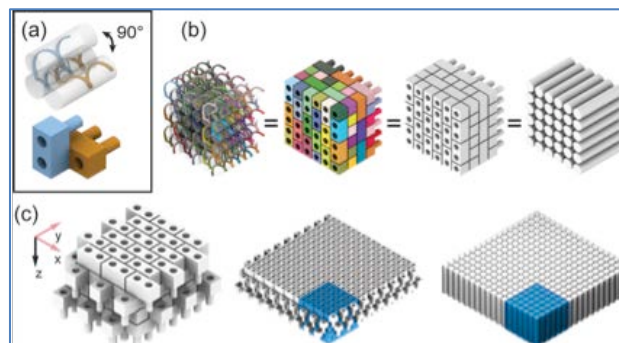
Applications: *In vivo* cancer cell targeting, imaging and monitoring drug delivery – deep tissue penetration for biomedical applications

NM: Scalable Nanomanufacturing and Supra-Assembly of Virus-Hybrid Janus Bionanoparticles - Nicole Steinmetz, Case Western



Applications: Drug Delivery, Prognosis

SNM: Atomically Precise, Defect Free, DNA Masks with Embedded Metrology - Will Hughes, Boise State



Design of complex DNA crystals using DNA bricks

Application: Random Access Memory

Bio-nanomanufacturing offers new capabilities and challenges



Capabilities

- DNA nanotechnology: Scaling nanoelectronics & optoelectronics below 5-nm technology node
 - emerging technology for volume nanomanufacturing
- Continuous, cell-free bioprocess to manufacture proteins and protein drugs

Challenges

- What are the barriers to *scale-up*?
- What are the possible disruptive *applications*?
- What are the *EHS challenges*?
- What will bio-nanomanufacturing platforms look like?
 - DNA Inside!

Biophysics can play a role



- Biophysics is the study of physical phenomena and physical processes in *living things*, on scales spanning molecules, cells, tissues and organisms
- Involves research into the *structure and dynamics of biomolecules*
- Fundamental principles that underlie *biomolecular interactions, regulation of biological function* at the atomic, near-atomic, and molecular levels
- Research at the interface of the *biological sciences* with the *physical, chemical, mathematical and engineering sciences*

Understand properties and behavior of biological species for their use in manufacturing or for their manufacture



Semiconductor Synthetic Biology for Information Processing and Storage Technologies (SemiSynBio) -- NSF and SRC

Vision:

- Future ultra-low-energy computing, storage and signal-processing systems can be built on principles derived from organic systems that are at the intersection of chemistry, biology, and engineering

Research

- Advancing basic research by exploring new *programmable models of computation*, communication, and memory based on synthetic biology;
- Enriching the knowledge base and addressing foundational questions at the *interface of biology and semiconductors*;
- Promoting the frontier of research in the design of new *bio-nano hybrid devices* based on sustainable materials, including carbon-based systems that test the physical size limit in transient electronics;
- Designing and fabricating hybrid semiconductor-biological microelectronic *systems based on living cells* for next-generation storage and information processing functionalities; and
- Integrating *scaling-up and manufacturing technologies* involving electronic and synthetic biology characterization instruments with computer-aided design (CAD)-like software tools.

<https://www.nsf.gov/pubs/2017/nsf17557/nsf17557.htm>



Designing and Engineering of Synthetic Cells and Cell Components (DESYN-C³)

- *Design of synthetic cells* will require convergence of chemical synthesis; self-assembly; process control; reaction engineering; mass transport; biomaterials science, biochemistry; molecular structure, dynamics and modeling
- Effort will require *advanced nanomanufacturing technologies*, such as DNA-enabled nanofabrication, to produce subsystems such as motors, actuators, reactors, etc.
- NSF Big Ideas: “Understanding the Rules of Life” and “Growing Convergent Research”

<https://www.nsf.gov/pubs/2018/nsf18071/nsf18071.jsp>



Thank you!

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