Learning for Life Lecture Series, Northwestern University
November 2, 2022

Speakers

Dr. Chad A. Mirkin is the Director of the International Institute for Nanotechnology and the George B. Rathmann Prof. of Chemistry, Prof. of Chemical and Biological Engineering, Prof. of Biomedical Engineering, Prof. of Materials Science & Engineering, and Prof. of Medicine at Northwestern University. He is a chemist and a world-renowned nanoscience expert, who is known for his discovery and development of spherical nucleic acids (SNAs) and SNA-based biodetection and therapeutic schemes, the invention of Dip-Pen Nanolithography (DPN) and related cantilever-free nanopatterning methodologies, On-Wire Lithography (OWL), Co-Axial Lithography (COAL), and contributions to supramolecular chemistry and nanoparticle synthesis. He is the author of over 825 manuscripts and over 1,200 patent applications worldwide (over 393 issued), and the founder of multiple companies, including AuraSense, Exicure, TERA-print, and Azul 3D. Mirkin has been recognized for his accomplishments with over 230 national and international awards. These recently include the Kabiller Prize in Nanoscience and Nanomedicine, the SCI Perkin Medal, Friendship Award, Nano Research Award, and AAAS Philip Hauge Abelson Award. Mirkin served as a Member of the President's Council of Advisors on Science & Technology (Obama Administration) for eight years, and he is one of very few scientists to be elected to all three US National Academies (Medicine, Science, and Engineering). Dr. Mirkin holds a B.S. degree from Dickinson College and a Ph.D. degree in Chemistry from the Penn. State University.

Dr. Omar Farha is the Charles E. and Emma H. Morrison Professor in Chemistry at Northwestern University and an Executive Editor for ACS Applied Materials & Interfaces. Dr. Farha's research seeks to solve exciting problems in chemistry and materials science ranging from energy and environment related applications to challenges in national defense by employing atomically precise functional materials. By exploiting the modular nature of metal–organic frameworks (MOFs) and porous organic polymers (POPs), his group works to fundamentally understand the role of three-dimensional architecture in modifying a material's function for applications in gas storage and separation, catalysis, water remediation and detoxification of chemical warfare agent simulants. His research is widely recognized with awards such as the Kuwait Prize, from the Japanese Society of Coordination Chemistry, the Royal Society of Chemistry and the American Chemical Society. Based on his research, Prof. Farha co-founded NuMat Technologies, the first company to commercialize a system-level product enabled by Metal-Organic Framework Materials.

Moderator

Lisa Dhar is the Interim Executive Director of the Querrey InQbation Lab, Northwestern's new incubator for research-based entrepreneurship and a faculty member with the Farley Center for Entrepreneurship and Innovation. She was co-founder and vice president of InPhase Technologies, a company spun out of Bell Laboratories, Lucent Technologies. Prior to joining Northwestern, she was the Senior Associate Director of the Office of Technology Management at the University of Illinois at Urbana-Champaign. Lisa has served on the National Academies' Assessment Panel on Materials Science and Engineering at the National Institute of Standards and Technology (NIST) and on the Advisory Board for University of Colorado's Women in Engineering. Lisa holds a PhD in Physical Chemistry from the Massachusetts Institute of Technology and a BS in Chemistry from the University of Chicago.

30 Years of Innovation in Nanotechnology

Dr. Chad Mirkin

This talk will provide an overview of the field of modern nanotechnology. About 25 years ago, the then President of Northwestern, Henry Bienen, endorsed and made possible the founding of the International Institute of Nanotechnology (IIN), a prescient "bet" at a seminal time for the field, as the technologies and tools that have propelled nanotechnology were just emerging. The IIN is now the largest institute for nanotechnology in the world and an important example of how basic science lays the foundation for impactful technology development.

<u>Background information:</u>

- Nanotechnology is based on the phenomenon that any bulk material, when shrunk down will exhibit many interesting and often useful properties. These new properties are the basis for applications in a wide range of fields from devices, energy, medicine, to sustainability. We'll focus first on advancements in medicine.

- In the development of new types of pharmaceuticals, structure matters. Structures determine the maximum potency of drugs as seen in the modalities of small molecule drugs or biologics such as monoclonal antibodies. However, until recently, structure was not so central to vaccine science.

- Recent vaccines are a movement towards nanotherapeutics. The recent Pfizer and Moderna vaccines are examples of tiny structures that carry a component of the virus that elicits an immune response. These mRNA vaccines rely on **central dogma** of biology in which through the process of transcription, DNA sends out mRNA which leads to the synthesis of proteins.

- Current mRNA vaccines rely on synthetically made mRNA encased in fat globules known as lipid particles which causes are body to produce the spike protein <u>associated</u> with the virus (not the virus!). The body mounts an immune response, giving us short-term immunity. Unlike traditional vaccines, there is no use of the live or weakened virus. Packaging on the nanoscale was instrumental to this technology.

<u>Spherical Nucleic Acids (SNAs)</u>

- Another such structure comes from the Mirkin lab at Northwestern. Research began in the 1990s with the aim of building artificial forms of matter. Tiny particles were modified with short strands of DNA, strands that tend to be sticky and could facilitate the building of new types of matter. Along the way, the value of these structures as artificial forms of DNA (**Spherical Nucleic Acids, SNA**) was realized.

- DNA and RNA don't naturally enter cells which is the reason mRNA had to be packaged for delivery for vaccines. However, SNAs enter cells very efficiently providing a structure that goes into cells naturally and in large amounts.

- Vaccines provide an important example of translation with a focus on structure. Typical vaccines rely on **adjuvants** (immune stimulator) and **antigens** (targeting entity) which allow campaigns against infection or as vaccines, involving mixing and injecting through trial and error to look for a response. SNAs, on the other hand, enable the opportunity to structurally vary these entities to optimize response, the basis for rational vaccinology.

- We can construct an SNA using DNA as the adjuvant and peptides to target what we want to eradicate. In addition, the ability to use multiple targeting entities allow us flexibility with variants unlike the current mRNA vaccines. An SNA-based vaccine candidate for HPV-caused cancer shows tremendous promise in mouse models. The Mirkin lab is now building vaccines for a wide range of cancers. With the right type of peptide, they can build the vaccine. Using a similar platform, a vaccine for COVID was also built.

- SNAs also have applications in diagnostics. Using gold nanoparticles, an array-based method can facilitate rapid identification for markers of diseases such as hepatitis B, HIV, Ebola and many others. This technology is incorporated in Verigene® systems. Commercialized by the Northwestern startup Nanosphere, later acquired by Luminex, it is now used widely in hospitals for rapid detection of diseases.

- The overriding message is behind the translation of important technologies is basic science: the discovery of SNAs was back in 1996 and in-depth scientific understanding of these materials was necessary to facilitate the technological advances we see today.

Nanoprinting

- Another important Mirkin technology, Dip-Pen Nanolithography (DPN), was inspired by Atomic Force Microscopes (AFMs) which uses tiny tip-like structures to obtain topographical information on the nanoscale. DPN uses this tool to instead do chemistry – using the AFM-like tips to deliver chemicals and locally make surface patterns. The Mirkin lab parallelized the approach, putting 11 million tips onto a 2x2 cm chip, creating a powerful and massively parallel synthesis tool. These tools now produce **megalibraries**.

- These megalibraries enable extremely rapid, flexible materials synthesis and thereby rapid materials discovery. Human history has been and will continue to be defined by materials (stone age, bronze age, iron age, . . . silicon age, . . .) The ability to precisely control material combinations is extremely powerful. For example, taking just 4 of the 103 elements of the periodic table, there are over 2 million combinations. The architecture of megalibraries enables us to look at not only different combinations of materials but also the effect of size.

- As an example, each tip generates a tiny reactor, encompassing attoliters of volume (atto=10^{-18}) creating new combinations of materials. A typical run can create a megalibrary of which 90% are materials which have never existed before.

- Trial-and-error materials discovery can now be replaced by these megalibraries complemented with artificial intelligence/machine learning tools trained on the massive amounts of data resulting from the DPN-enabled approach.

- Materials discovery is now underway for catalysis, electronics, displays, energy, and many other fields. The Mirkin lab has teamed up with Northwestern computer scientists to provide artificial intelligence methods to investigate and push the materials genome in ways never before possible.

Nanotechnology for Water and Security

Dr. Omar Farha

The overall goal of the Farha lab is to improve quality of life through programmable chemistry which relies heavily on nanotechnology. Air and water issues are crisis level - - 1.8 billion people are living in water-stressed areas and 2.8 billion people live in areas with hazardous pollution levels. The receding water levels in Lake Mead is a dramatic example of our water crisis. The United Nations General Assembly has passed a resolution declaring that everyone on the planet has a right to a healthy environment. The Farha Lab is dedicated to finding technologies to help insure clean air, water, and a stable climate.

Background Information:

- New materials are sorely needed to help address our climate challenges. Our reliance on "old" materials such as activated charcoal will not help us manage the looming issues. Building complex structures to pursue complex tasks must be based on using simple materials put together in a systematic way. Can we create a platform of "nano-tinkertoys"?

- The Farha Lab has created synthetic method which mixes materials resulting in a single type of molecular structure – **metal organic frameworks (MOFs)**. The structures, characterized by nanocages of nanometer size, are formed in a rational, programmable way.

- These MOFs are similar to sponges – regeneratively useful but with preferred surfaces to which molecules like to stick. For example, 1 gram of a recently made MOF, unfolded, would have surface area larger that the field at Ryan Field!

- One area where these MOFs are useful is water harvesting. The Farha Lab along with Honeywell and NuMat, a startup spun out of the Farha Lab, has delivered to DARPA (Defense Advanced Research Projects Agency) a device that can produce 7L water/day, simply pulling water from the atmosphere.

- The Department of Energy has funded a multimillion-dollar project in the Farha Lab to build a carbon capture system which can take CO_2 from the atmosphere and produce useful chemicals.

- Additional examples are a nanomaterial coated sponge that can selectively absorb oil for oil spills and a collaboration with the Department of Defense, where the Farha Lab has created a material that can protect both biological and chemical threats.

- NuMat Technologies is currently scaling up this technology working with partners such as Patagonia and the Department of Defense.

- An interesting recent article in the Wall Street Journal on MOFs and highlighting NuMat is at These Tiny Ultra-Porous Crystals Could Transform Cancer Treatments and More - WSJ.