FORESIGHT NANOTECH INSTITUTE
Advancing Beneficial Nanotechnology

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Foresight Nanotech Update

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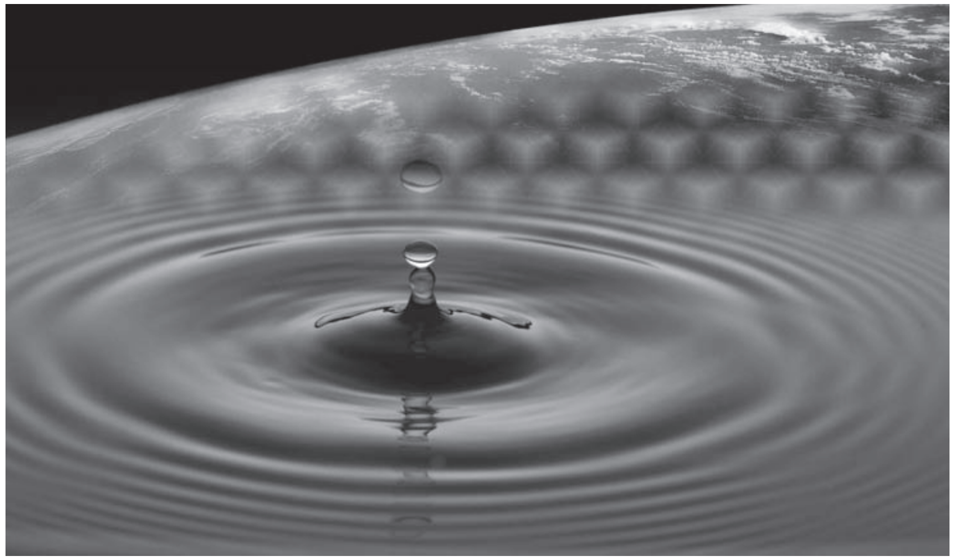


Good for people. Good for the planet.

Foresight Nanotech Institute was founded 20 years ago to prepare society for nanotechnology. A central theme to our activities has been the continued belief that nanotechnology can be a powerful force to improve the health and well being of people and the planet.

Today, nanotechnology is no longer an idea. Nanotechnology has become a fundamental force that will offer major rewards for humanity in fields ranging from biotech to energy.

It has been a year since we launched the new Foresight and created the Foresight Nanotechnology Challenges as a communication platform. Many of our members have expressed the desire for us to focus more on nanotechnology and the environment. With this in mind, we have changed Challenge #4 to Healing and Preserving the Environment.

Foresight Nanotechnology Challenges:

1. **Meeting global energy needs with clean solutions**
2. **Providing abundant clean water globally**
3. **Increasing the health and longevity of human life**
4. **Healing and preserving the earth**
5. **Making powerful information technology available everywhere**
6. **Enabling the development of space**

Focus on Challenge #2:
Providing abundant clean water globally

In this issue of Foresight Nanotech Update, we have invited experts to offer their ideas on how nanotechnology will affect filtration and desalination in the future. Clean water is a major challenge and its availability impacts the health and well being of all people.

We have also identified companies that are currently working on nanotechnology research and products that may provide solutions to this challenge. We hope you find this issue of the Foresight Nanotech Update informative.

Water & Nanotechnology Experts Q&A: Richard Skaggs and Glen Fryxell

Battelle / Pacific Northwest National Laboratory

"Nanotech will provide more effective alternatives to treatment of challenging contaminants such as arsenic, perchlorate, and mercury."

Richard L. Skaggs
Natural Resources Division Manager
Battelle / Pacific Northwest National Laboratory

1. When do you think we will begin to see clean water applications of nanotech being used?

One key example of nanotech already in use is nanofiltration membranes.

Nanofiltration is a form of filtration wherein membranes preferentially separate different fluids or ions. Nanofiltration uses partially permeable membranes to perform the separation, but the membrane's pores are typically much larger than the pores used in reverse osmosis membranes.

At Battelle, we have recently licensed our SAMMSTM (Self-Assembled Monolayers on Mesoporous Supports) technology for use in a broad range of water treatment applications that could range from treatment of industrial wastewater to drinking water.

2. How soon we will see the impact of nanotechnology in traditional water filtration and treatment?

In the area of membrane filtration it is already having an impact, particularly as pre-treatment to reverse osmosis desalination. As cost effective, engineered forms of emerging nanotechnologies are developed they will be applied first to challenging treatment problems such as arsenic removal.

3. Traditional water filtration is fairly costly and relatively effective, how would nanotechnology change the consequences?

Nanotech will provide more effective alternatives to treatment of challenging contaminants such as arsenic, perchlorate, and mercury. As we become increasingly aware of how certain contaminants can have an impact on human and environmental health, even at trace levels, it becomes increasingly important to be able to monitor and remove these contaminants at lower and lower levels. Traditional filtration/flocculation/precipitations methodologies are effective at higher concentrations, and less effective at these trace levels. New nanotech approaches are much more effective at the lower concentrations, and they also contribute to the monitoring/measurement needs as well. Traditional filtration methods can't do this.

4. What are the anticipated downsides of nanotechnology applications toward water filtration?

Initially, it will be development of engineered forms that can be cost-effectively retrofitted to conventional engineered treatment systems.

5. What do you anticipate as the upsides of nanotechnology water filtration?

Nanotechnology will provide alternatives to conventional treatment to address treatment of challenging contaminants, reduction of water treatment residuals, and achievement of new regulatory standards that are beyond the capability of conventional treatment. Nanotech will also provide new capabilities in terms of analytical measurements, thereby enhancing our ability to monitor key environmental contaminants, especially at the trace level. We can't devise an effective strategy to remove something if we don't know it's there.

6. Do you see nanotechnology making clean water available globally to the point where conflict over water may lessen?

Nanotechnolgy will certainly make previously unusable water sources available such as brackish water, sea water, and wastewater, in effect increasing the available water supply. By making clean water more available, one might hope that potential conflict over water would be reduced.

7. If you were in the office pool, which nanotech clean water solution would you put your money on to make the biggest impact in the future?

Membranes for cost-effective desalination can have a global impact.

8. In context with your current work, how do you see it impacting clean water in the future?

Self-assembled monolayers on mesoporous supports (SAMMSTM) is a versatile technology that can address a number of water contamination problems. Currently we are focused on mercury treatment, but envision applications to other contaminants such as arsenic, chromate, lead, cadmium and perchlorate.

"Nanotech will also provide new capabilities in terms of analytical measurements, thereby enhancing our ability to monitor key environmental contaminants, especially at the trace level."

Glen Fryxell
Scientist
Battelle / Pacific Northwest National Laboratory

SAMMS has also proven to be effective for preconcentration for analytical applications, increasing sensitivity by as much as 6 orders of magnitude.

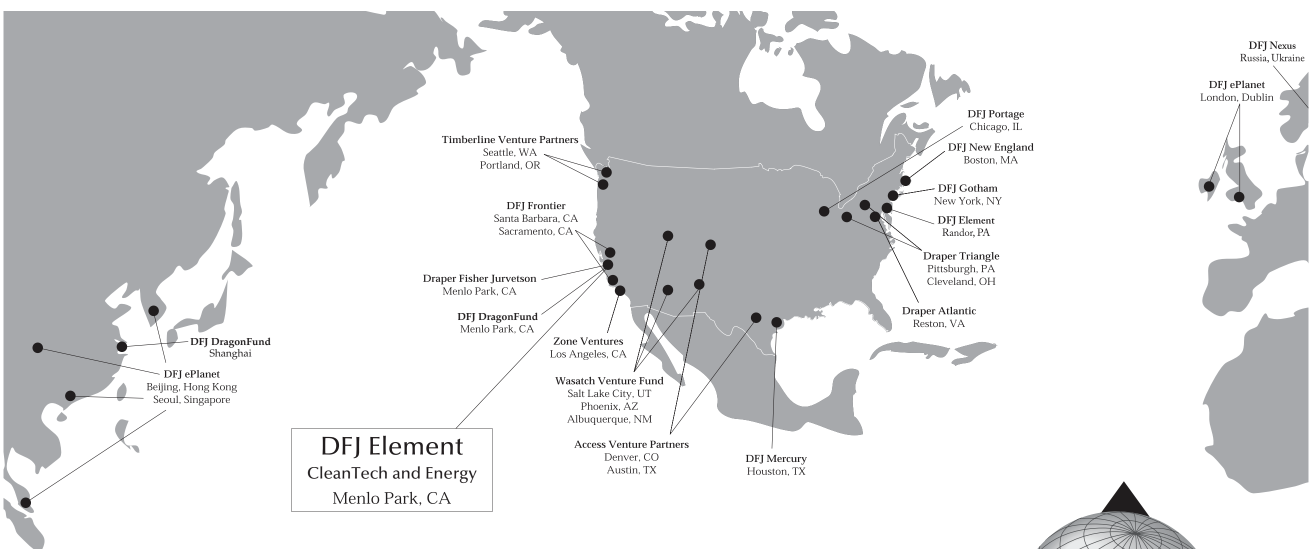
About Glen Fryxell, Ph.D

Glen Fryxell is a member of the Materials Chemistry and Surface Research Group within the Materials Division of ESTD, and has been a member of Materials since 1990. For the last 15 years, his research has focused on organic synthesis, surface chemistry, silane chemistry and the interfacial elaboration of self-assembled monolayers. He is a co-inventor of self-assembled monolayers on mesoporous supports (SAMMS) and has developed these materials for a wide variety of environmental applications, such as the sequestration of toxic heavy metals, radionuclides and oxometallate anions. Dr. Fryxell is named as inventor in 11 patents, and has over 100 publications and 60 invited presentations. He obtained his B. Sc. from the University of Texas in 1982, where he worked for two years in the laboratories of Prof. Marye Anne Fox studying the photochemistry of enolates and carbanions. His Ph. D. was awarded in 1986 from the University of North Carolina, where he worked with Prof. Paul J. Kropp studying the photochemistry of phenylthio ethers.

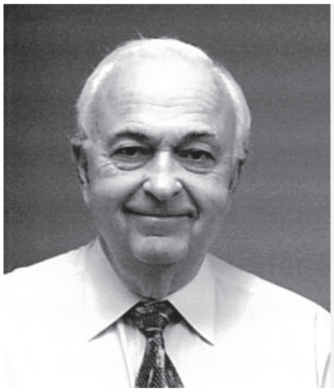
About Richard L. Skaggs, Ph.D., P.E.

Richard Skaggs leads the development and implementation of Pacific Northwest National Laboratory's (PNNL) water science and technology programs. Efforts encompass materials and process science, technology development and deployment, and commercialization of advanced fluid treatment and contaminant detection technologies to resolve emerging water quality and availability problems. Activities also include extension of adaptive management concepts to natural resources protection and restoration, water resources infrastructure planning, and adaptation to climate change and variability. He is a member of the Multi-Laboratory Energy-Water Nexus Committee focused on identifying science and technology needs to ensure U.S. water/energy resources sustainability. As a special assignment, Dr. Skaggs served as Chief Scientist working with the Mexico City Water Department to assess alternatives for ensuring the long-term sustainability of the City's water supply. Previously, he managed PNNL's Earth Systems Sciences Department and Geosciences Department. He was also the Vice President for Systems Engineering at U.S. Water L.L.C. He received his M.S. (1976) in Civil Engineering from Stanford University and Ph.D. (1995) in Civil Engineering from Arizona State University.

Pacific Northwest National Laboratory
http://www.pnl.gov/



Water & Nanotechnology Experts Q&A: Fred Tepper



"Generally nanotech solutions are more expensive than traditional methods, but the need for clean drinking water often trumps their higher cost."

Fred Tepper
President, Argonide

1. When do you think we will begin to see clean water applications of nanotech being used?

Nanotech has been used for some time for cleaning water. Good examples are the ultraporous and nanoporous membranes used in advanced municipal water treatment for filtering ultrafine particulates. The high pressure drop of such filters is typically circumvented by tangential filtration. In a broad sense one could describe granular activated carbon, a venerable product, as nano because a large amount of its adsorbing capability involves pores in the range of tens of nanometers.

2. How soon will we see the impact of nanotechnology in traditional water filtration and treatment?

Advanced treatment based on technology is continuously evolving. Polymeric fibers of about 300 nm diameter and ceramic filter media with 200 nm pore size are now being used for filtering particulates including bacteria from water. Nanosize (NanoCeram®) electropositive filters, with the capability for retaining nanosize particles, are entering the marketplace.

3. Traditional water filtration is fairly costly and relatively effective, how would nanotechnology change the consequences?

Traditional water treatment relies heavily on the use of chlorine but recently there have been several incidents where it was inadequate for sanitizing certain microbes such as Cryptosporidium, a protozoa (cyst) that is resistant to chlorine. A serious incident occurred in Milwaukee in 1993, when more than 100 people died and hundreds of thousands were sickened by Cryptosporidium in their municipal water. The EPA has since mandated that municipal water treatment plants must now filter their water to remove cysts. The concern about cysts has also expanded the use of home filters capable of removing cysts. The product range includes filters at the point of entry (POE) and point of use (POU) which is at or under the faucet, or in a pitcher filter. Nano based filters are better able to achieve the 99.95% filtration efficiency required to achieve certification for removal of cysts.

Viruses are responsible for about 40% of the gastrointestinal disease incidents, because many virus are also chlorine resistant. Unfortunately the technology for sampling water and assaying it for virus is not economically viable and is not routinely done. Once that is achieved, methods of treating water will be developed to assure complete removal of virus. Filtration via nano membranes and nano electropositive media virus will be preferred treatments.

Another downside of chlorination is that processing by products such as halomethanes are carcinogenic. Alternative sanitization processes include ozonation and ultraviolet treatment. Prefiltration upstream of oxidation or ultraviolet treatment improves the efficiency of these processes while minimizing the generation of halogenated by products. Sub-micron filters such as electropositive nano alumina are effective in reducing the organic carbon, minimizing the amount of halocarbon that would be formed.

4. What are the anticipated downsides of nanotechnology applications toward water filtration?

Generally nanotech solutions are more expensive than traditional methods, but the need for clean drinking water often trumps their higher cost.

5. What do you anticipate as the upsides of nanotechnology water filtration?

Nanofilters are being developed for improved filtration of pathogenic microbes, particularly those that are resistant to conventional treatment or are too small to be filtered by conventional depth filters. They are also effective as prefilters to prevent the fouling of reverse osmosis membranes. The latter are used on a large scale as in desalinization plants, in industrial settings and also in residences.

6. Do you see nanotechnology making clean water available globally to the point where conflict over water may lessen?

Population growth and the reduced availability of clean or economically cleanable water will continue to pinch and conflicts for drinking water will inevitably grow. Pundits have projected that conflicts over water will equal those over oil. Nano solutions will help to mitigate but not eliminate conflicts over diminishing supplies.

7. If you were in the office pool, which nanotech clean water solution would you put your money on to make the biggest impact in the future?

Hard to say, but I would bet on better desalinization membranes.

8. In context with your current work, how do you see it impacting clean water in the future?

Our group has developed a disposable electrostatic nano filter ("NanoCeram®") that can remove very small particles even at high flowrates. It is effective in filtering cysts, bacteria and even virus. It has a very high dirt holding capacity for colloidal matter, which would make it a superior candidate for protecting reverse osmosis membranes. As a prefilter, it enhances the efficiency of ultraviolet and ozone purification systems. Its applications include POU and POE filtration at the residence, and for filtering colloidal matter from industrial water. It can be used as a low cost sampler of virus for the purpose of assaying the virus content both upstream and downstream of municipal plants. It is also being developed for virus assays of seawater near shellfish beds. There are several government supported programs related to detecting biological weapons in municipal water systems, where the NanoCeram® filter is being used as a collector and concentrator of pathogenic microbes.

About Fred Tepper

Fred Tepper *founded Argonide in 1994. Headquartered in Pittsburgh, Pennsylvania, the company's mission is to develop and market new products based on nanotechnology. They have an international business perspective, with collaborative work in Italy, Japan, Singapore and in particular with Russian institutes active in nanotechnology.*

Fred is a former Vice President for the Mine Safety Appliance Company (MSA) of Pittsburgh, Pennsylvania. When he retired, he had almost 40 years with MSA, starting out as a chemist/materials scientist in respiratory filter development and water purification. In 1970 he was promoted to General Manager of the Catalyst Research Corp, where he led the team that developed the long life lithium pacemaker battery. He was promoted again to General Manager of the Instrument Division of MSA that included several additional profit centers including the Callery Chemical Company.

Argonide
http://www.argonide.com/index.htm

Water & Nanotechnology Experts Q&A: Gayle Pergamit

"Nanotechnology-based water filtration should be able to deliver completely pure water from any source at vastly reduced energy usage and lower total costs."

Gayle Pergamit
Cofounder and CEO, Agua Via

1. When do you think we will begin to see clean water applications of nanotech being used?

If the definition of "nanotech" focuses mainly on activity in the nanometer size regime – bulk materials in size ranges below 100 nanometers – then we are seeing things being done today, and they do bring benefits.

If you are talking about more advanced applications – things that will profoundly impact the world's water crisis – those will probably debut in the next few years.

2. How soon we will see the impact of nanotechnology in traditional water filtration and treatment?

When you're talking about the really advanced stuff, the Department of the Interior has said that the US will actually run out of water by 2020……..so it's a good bet that solutions will be pushed into the market place well before then. Our own timetables have us in the market in well under 5 years with advanced technology which meets the strong definition of nanotechnology: materials designed and built with atom by atom precision.

3. Traditional water filtration is fairly costly and relatively effective, how would nanotechnology change the consequences?

Nanotechnology, whether applied to purification, desalination or other problems such as water lost in canals during transit, has the potential to provide the purest water people have ever had, while dropping the costs to affordable levels even by the developing world.

Over the last century, engineers have worked long, hard and creatively to improve the quality and bring down the cost of both traditional water filtration and desalination. However, even with these improvements, desalination still costs 6 to 10 more than water purification. This puts it out of reach for all but the wealthiest countries with an urgent need.

By replacing traditional, filtration technologies with ultra-thin materials (1-5 nanometers thick), the energy required for desalination – and therefore the cost – will bring desalinating water to the same as today's cost for purifying fresh water.

If those ultra-thin, low energy materials are also built with atomic precision, then we will see solutions that deliver ultrapure water – no matter how contaminated the source water. This means purer and less expensive water than traditional technologies can deliver.

In the US, we have had centuries of abundant, cheap groundwater. Most of that water has either required relatively little in the way of purification, or we were blissfully unaware of the substances – such as arsenic – which needed to be removed.

At present, even in the G8 countries, it is too expensive to test and treat all water for all possible problems. The traditional method is to wait until a problem emerges -- death or disease among significant numbers of the population – to draw attention to a potential problem with a water supply. Then that particular problem is tracked down and fixed. However, even in the US, most small water systems can't afford the level of purification they need to deal with the endemic problems of Lamblia (giardia), Cryptosporidium and arsenic. If small US communities can't afford adequate purification, the implications for developing nations are grim.

Nanotechnology-based applications could change this. They should have the ability to:

- Provide completely pure water – without previous testing needed to see which contaminants needed removing
- Drop the cost sufficiently that even the poorest communities or poorest individuals could have that completely pure water
- Cost effectively open up new sources of water supply – whether from desalinating water or by cleaning up heavily polluted water cost effectively

(Continued on page 6)

- Provide strong pollution control and cleanup both by preventing pollutants from entering water streams, and being low cost enough to enable environmental cleanup

4. What are the anticipated downsides of nanotechnology applications toward water filtration?

The downsides would come, as usual, from lapses of wisdom. The two major potential downsides are the issues of waste disposal and possibility of negative environmental impacts by expanding human habitats.

Why waste disposal? Let's say you are desalinating a saline aquifer hundreds of miles inland. You are pumping the water to the surface and removing the salt. How are you disposing of the salt? Or, if you are cleaning up water polluted by cyanide from mining operations, how are you disposing of the cyanide? The San Francisco Bay is polluted by mercury leaching from mine tailings left by Gold Rush miners in 1849. Instead of extracting gold, now we will be extracting valuable water. How is the waste – the arsenic, boron, salt, mercury, MBTE -- disposed of?

The second downside is the potential for extending negative environmental impacts on land. Once pure and inexpensive water is abundant, people will be able to cost effectively colonize habitats which are today uninhabited. What will be the environmental impact of this expansion? The negative scenario may be versions of how the Amazon rain forest is being lost to expanded cattle ranching. The positive version of this scenario is where abundant water and appropriate reforestation repairs environments, such as North Africa, which humans have turned into deserts.

5. What do you anticipate as the upsides of nanotechnology water filtration?

Nanotechnology-based water filtration should be able to deliver completely pure water from any source at vastly reduced energy usage and lower total costs.

It should end the World Water crisis. It would provide abundant pure water at costs which even the Developing World could afford. In the Developing World, pure water for drinking and hygiene would eliminate the #1 killer: the many varieties of water borne disease. By providing cheap water for agricultural irrigation, Developing World farmers can multiply their productivity. Cheap water is the basis for ending starvation and increasing their prosperity.

Today, G8 countries like Australia are already carrying the heavy cost of desalination because their fresh water aquifers are depleted. As things stand today, the rest of the world – the US included – will all follow. Expensive water impacts the cost of growing all food, and the cost of all manufacturing. Nanotechnology-based filtration will end that scenario, and we'll avoid going through economic shock as prices for food and goods soar if water becomes scarce.

It should stop the worldwide depletion of aquifers, and even make possible aquifer recharge and habitat restoration. It should allow us to cost effectively correct many of humanity's previous mistakes by helping clean up pollution, curtail new pollutants from entering the environment, and provide the basis for much habitat restoration.

6. Do you see nanotechnology making clean water available globally to the point where conflict over water may lessen?

Former Secretary of State George Shulz, an advisor to Agua Via, is specifically focused on this possibility for nanotech filtration. Secretary Shulz has spent decades looking for workable low cost desalination technology and other water technologies for their potential for bringing about peace or forestalling war in many nations. Stopping water wars is clearly one of the expected outcomes of nanotechnology derived products. Desalinating ocean water or the salt water aquifers which unlie most continents means abundant water is readily at hand to most nations. Cost effective desalination would end water scarcity and therefore most water conflicts.

7. If you were in the office pool, which nanotech clean water solution would you put your money on to make the biggest impact in the future?

I have put my money on a clean water solution that I think will make the tremendous impact you're talking about.

At Agua Via, we're building water purification, water remediation (pollution cleanup) and desalination filtration systems based on using a one-atomic layer thick nanomembrane (.05nm). At one atomic layer thick, this membrane offers no impedance to flow, so you're operating at the lowest energy thermodynamically possible. One implication is that in a rural setting without power – typical in the developing world – a filtration cartridge at the bottom of a tube with a 27" head of water is sufficient to purify water and potentially eliminate all chemical or biologic hazards.

For desalination systems, for example, this ultra thin membrane would offer 2/3rds of the potential energy cost reduction, and overall cost reductions of up to 33% based on energy savings alone. Eliminating high pressure pumps, energy recovery systems (little wasted energy to recover), certain pretreatment systems, reduction of backflushing and other maintenance costs may produce additional savings bringing a total reduction of approximately 60% under current desalination costs. This would bring the cost of desalination into the realm of affordability, even for developing nations.

We've been working to the rigorous definition of "complete control at the atomic scale," and – not at all surprisingly – found that it provides unprecedented benefits in such areas as exquisite filtration specificity, high filtration performance, low energy requirements, non-fouling in the face of multiple complex water feedstocks and the other criteria needed to be an ideal solution to water purification and desalination needs. With complete control over the structure of each pore, the nanomembrane is designed and built to provide only the desired end product – usually either potable water (water plus earth salts), or water that is completely salt free.

8. In context with your current work, how do you see it impacting clean water in the future?

We had the dimensions of the problems involved in the World Water Crisis in mind when we formed Agua Via and began work. We expect this technology to play a significant role in bringing the maximum benefits of clean water and desalinated water to fruition. We designed from the very beginning to provide ultra-pure water at the lowest energy, maintenance, educational and dollar cost possible

– which is what's needed to address issues like water in developing countries or strong pollution cleanup. We think we will see these nanomembranes effective at making clean water affordable to all.

The simplicity, long life, low cost, ease of use, high reliability, low maintenance and high effectiveness of these systems means that they should be useful in a wide range of applications where size and energy are critical, including rural or remote use. We think you will see this technology configured to the wide range of physical circumstances under which desalination, purification or remediation must be performed: point of use solutions for home or individuals in the field, mobile systems, and city-sized systems in industrial, recreational, emergency, commercial, medical, agricultural, and municipal settings as well as rural settings with no power sources available.

We hope this technology will play a major role in addressing the world water crisis in roles including:

- Purification applications, ranging from high purity semiconductor and medical uses through home drinking water
- Remediation of both waste water and polluted ground water
- Desalination applications, including both sea water and brackish water

About Gayle Pergamit

Gayle Pergamit is cofounder and CEO of Agua Via. Ms. Pergamit has focused on business development in the disruptive technologies which have characterized the San Francisco Bay Area . Ms Pergamit cofounded AMiX, which pioneered the e-commerce business models which underlie E-Bay and Priceline. She taught analysis and communication skills at Stanford University Graduate School of Business, and has co-authored two books: one on the subject of nanotechnology co-written with Dr. K. Eric Drexler, founder of the field of nanotechnology, and Christine Peterson. Ms. Pergamit was previously named by the publication "Microtimes" as one of Silicon Valley's Most Influential People. She can be reached at gayle@aguavia.com.

Nanotechnology & Clean Water

Filtration Companies

** Note: This is not a comprehensive list nor suggestions for investment purposes.*

Foresight Nanotech Institute has identified a small selection of companies doing nanotechnology research that may eventually help solve Foresight Nanotechnology Challenge # 2: Providing abundant clean water globally.

Argonide

http://www.argonide.com/

Headquartered: Sanford, Florida, USA
CEO: Fred Tepper
Technology focus: Argonide's NanoCeram® filter is a highly electropositive alumina fiber only 2 nanometers in diameter, that attracts and retains bacteria, viruses, DNA, silica particles, organic matter, and metals. "Filters fabricated from such fibers are capable of removing greater than 99.999% (5 logs) of bacteria and Cryptosporidium protozoa and greater than 99.99999% of virus. These filters are capable of providing a continuous flow of sterilized drinking water without using excessive pressure."
Product: NanoCeram® Pleated Fiber Cartridges have wide applications in chemical, microelectronic, and pharmaceutical manufacture, and for cleansing drinking water.
Recent news: The NanoCeram® Superfilter, which is able to extract bacteria, cysts, turbidity and even viruses from water, got the 2005 Hall of Fame award from the Space Foundation.

Aquamarijn Micro Filtration BV

http://www.microfiltration.nl/index.php

Headquartered: Zutphen, Netherlands
Technology focus: Microsieve Filtration membranes are produced using silicon micromachining technology and have low flow resistance because the membrane thickness is often smaller than the membrane pore size. The potential for rapid detection of micro-organisms and particles present in liquids leads to applications in the beverage industry and in water treatment. They also find use in biotechnology for sterilization and critical cell separations.
Product: The Microsieve® Micro Filtration membrane features defined pores in a ceramic membrane with a controllable pore size that can range from 100 nm to 100 μm, and is available with customer specific inorganic or organic coatings to give specially functionalized membranes.
Recent news: Aquamarijn Micro Filtration BV founder Cees van Rijn was a runner-up for the Innovator category of the Best of Small Tech Awards, Nov. 2004.

Biophiltre, LLC / Agua Via, LLC

Headquartered: Burlingame, California, USA
Technology focus: A novel platform technology for fabricating materials to atomic precision is used to make porous monomolecular membranes with orifices that can be designed with precisely controlled shape, size, charge, and surface characteristics so as to reject specific solute molecules. Because the membrane is so thin, it provides no resistance to flow, thus allowing rapid very low energy filtration. Smart Membrane™ and Smart Pores™ technology is being developed for water purification and desalination, and as a wearable 'artificial kidney' to treat kidney failure.

Emembrane

http://www.emembrane.com/

Headquartered: Providence, Rhode Island, USA
CEO: William Lee, Ph.D.
Technology focus: "The Company's proprietary platform technology is nano-grafting of combinatorial polymer brushes. This technology can impart on existing materials and membranes new & multiple functions." The grafted polymers densely cover and extend from the membrane surface, and can add any of a wide variety of chemical functions to the surface, giving it properties optimized for specific applications. Applications under development include removal of bacteria, viruses, proteins, toxic gases, and heavy metal ions.

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Water Experts Q & A: Kevin McGovern

"The future of nanowater will be an international phenomenon. Alliances will be key and the process will be simultaneously evolutionary and revolutionary."

Kevin McGovern
Chairman and CEO
McGovern Capital LLC

1. When do you think we will begin to see clean water applications of nanotech being used?

Nanotechnology is currently being used in some water filtration products, but it is not yet commercially viable on a large scale.

2. How soon will we see the impact of nanotechnology in traditional water filtration and treatment?

I really believe that water filtration solutions employing advanced nanotechnology filtration systems are only a few years away. At this time there are a lot of pilot studies happening. There will be a great deal of product tweaking. I think global solutions based on these studies will take one to five years to begin rollout.

Once you start with the rollouts there will be the huge task of distributing to and educating the markets. This is going to be missionary/social marketing style work because there will be different products for different situations. The products will need to be highly adaptable to a variety of water filtration situations.

3. Traditional water filtration is fairly costly and relatively effective, how would nanotechnology change the consequences?

Nanotech is one of the hottest sectors in water filtration. It should eventually bring relatively inexpensive, mobile and easily distributed solutions. The cost of water filtration, hopefully, at point of use, will decrease and become easier as the market solutions become more prevalent. Because of its ability to get down to the lowest levels to comprehensively intercept and kill both bacteria and viruses, nanoscience will have a huge impact.

4. What are the anticipated downsides of nanotechnology applications toward water filtration?

We are just learning about the incredible challenges that are presented in our goal to bring clean water to the world. Some of these challenges are market driven such as what to charge for the units, and how to educate the consumer. Also, how do we reach the consumer in undeveloped areas and get them to agree to use the product? In this case, I believe it will be social marketing to the women not the men that need to be educated. They need to be persuaded that the technology is not scary and that they need to use this product for the health of their families.

We need to convince them that their current traditions are not healthy in the long term. We will have to work closely with the locally knowledgeable companies, multinational NGO's, governments, and other organizations to make this an effective project.

This is how distribution can be tackled. Begin at the base of the pyramid of influence by starting with people who are the influencers in their society. Have the doctors use the filters in hospitals. When the schools see that the hospitals are using the filters, they will begin using them in their facilities as well. Once a mother sees the filter being used at the school, she will be more open to use the filter at home.

Price point will also be a challenge. How to provide this to 4 billion people and leave them with a little change in their pockets? Also, the time between swapping out filters needs to be sufficient so they can continue to buy the filter, and keep having clean water.

Another intrinsic challenge will be flow rate. We will need to separate out impurities and pathogens at a rapid enough rate to be viable for commercial use.

Additional issues are knock offs and security. Counterfeit devices might look the same but it might not work and then you encounter real health concerns. Then there is the security of knowing that a filter is working. The product may wear down and not show that it is being effective.

There has to be some means of monitoring the product to make sure it continues to work.

Some of these challenges are being addressed now in pilot research programs, but when these and others are met and tweaked the roll out is going to be revolutionary in my opinion.

5. What do you anticipate as the upsides of nanotechnology water filtration?

From a technical standpoint nanotechnology is the logical solution because of the filtration challenges. The size of the items we are filtering out of water range from small pathogens to big protozoa to level 20-30 nanometers. Poliovirus is smaller than 20-30. Nanotech is going to be the area that best separates out all of the microbiological solutions.

The users of the filters need to know that the pathogens are eliminated and killed rather than separated out. There needs to be a way created to monitor filter effectiveness.

6. If you were in the office pool, which nanotech clean water solution would you put your money on to make the biggest impact in the future?

We need solutions for both household (fresh) water and salt water. Personally I know more about point of use household solutions and believe that we will see our first wave of commercial products in this space. This will serve the vast majority of those who inhabit the urban and periurban markets.

However, the world is 97% salt water. That is water we must use for development and health, I think nanotechnology has a real shot at being part of that solution as well.

7. Do you see nanotechnology making clean water available globally to the point where conflict over water may lessen?

The global consumption of water is doubling every 20 years. Undoubtedly there will be conflicts even as filtration technology becomes more prevalent.

8. Any additional thoughts about nanotechnology and water filtration?

Everything needs to come together and work just right because this is a life and death situation.

Water-related diseases kill millions of people each year. About 2.3 billion people in the world suffer from diseases that are linked to water. Some 6,000 children die every day from diseases associated with lack of access to safe drinking water and proper hygiene.

The future of nanowater will be an international phenomenon. Alliances will be key and the process will be simultaneously evolutionary and revolutionary.

About Kevin McGovern

Kevin McGovern (kevin@kevinmcgovern.com)is the Chairman and CEO of McGovern Capital LLC, which provides Intellectual Property Rights Strategy, and originates, structures and implements capital formation, joint ventures and business alliances.

Mr. McGovern is Co-Chairman of Angstrom publishing, which jointly publishes the Nanotech Report with Forbes.

In the field of nanotechnology, McGovern Capital is one of three owners of the largest manufacturer and worldwide seller of carbon filters for water and air purification. They also have various other nanotech investments in water-related companies, personal care, life sciences and products produced in emerging countries.

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GE Water & Process Technologies

http://www.gewater.com/index.jsp

Headquartered: Trevose, Pennsylvania, USA
Technology focus: GE Water & Process Technologies is part of GE Infratstructure, which is one of General Electric Company's primary businesses. Among their large repertoire of products for water, waste water, and process systems solutions to provide industrial, agricultural, and potable water are products for nanofiltration, a process that uses membranes to separate water from sugars, divalent salts, bacteria, proteins, particles, dyes, and other constituents that have a molecular weight greater than 1000 daltons. The membranes are manufactured from porous polymers made from proprietary resins. Some membranes have charged or chemically active surfaces to increase separation specificity.
Product: The DS-5 nanofiltration membrane allows water and monovalent ions such as NaCl to pass through the membrane but retains and concentrates organic constituents.
Recent news: In a press release dated March 14, 2006, GE announced plans to acquire Zenon Environmental, a pioneer in the use of ultrafiltration for water and waste water treatment, in a transaction valued at US $656 million.

Seldon Laboratories

http://www.seldontechnologies.com/

Headquarters: Windsor, Vermont
CEO: Alan Cummings
Technology Focus: Seldon has developed an exciting new technology that reliably removes micro-organisms from fluids, without the use of heat, ultra-violet radiation, chemicals, contact time, or significant pressure. This technology has been the primary focus of the company's efforts to date and is now ready for large-scale production. Seldon has delivered prototype portable purification systems to the United States Air Force for testing, and has a program for the manufacture, marketing, and distribution of a series of product applications in its subsidiary, Seldon Water Technologies, Inc.

Product: Seldon's product has the following attributes: provides reliably clean water, free of bacteria and virus, effective against all microorganisms in water, does not require high pressure, environmentally benign and simple to operate and requires little maintenance.

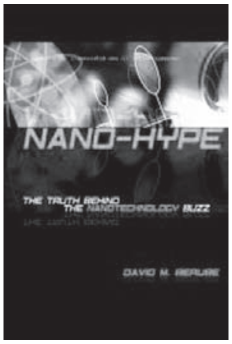
The product takes advantage of the most recent advances in nanotechnology to create a "kill zone" capable of destroying all shapes and all types of bacteria and virus, as well as other pathogenic microbes such as the common Cryptosporidium parvum and Giardia lamblia.

Book Review

Nano-Hype: The Truth Behind the Nanotechnology Buzz

by David M. Berube

Book Review by James Lewis Ph.D



Nano-Hype: The Truth Behind the Nanotechnology Buzz
by David M. Berube
Hardcover: 521 pages
Prometheus Books (Dec. 30, 2005)
ISBN: 1591023513

Author's blog:
http://nanohype.blogspot.com/

(Note: The copy read for this review was an uncorrected advance reading copy containing numerous minor errors, presumably corrected in the published book.)

David Berube, a professor of communication studies within the Department of English at the University of South Carolina, a Member of the USC Nanocenter, and a recipient of a National Science Foundation grant, has written a detailed and extensively referenced account of controversy, policy, and the role of government in the development of nanotechnology. His theme is the extensive misinformation that has accumulated as a result of hyperbole on the part of both those who advocate for and those who warn against. His declared goal is to separate the realistic prospects from the hype. A secondary goal is to describe how nanotechnology has been communicated.

Nano-Hype is enlightening but incomplete. Berube's presentation is both deep and broad. The many and complex debates and discussions that have accompanied the emergence of nanotechnology from the realm of theorists, futurists, and experimental scientists into the arenas of government, business, and public perceptions are clearly described, explored, and referenced. Even those who have followed the field closely are likely to learn several new things in each chapter. Those who are new to the topic will be more or less easily initiated into the complexities of the issues.

Prof. Berube succeeds in describing how nanotechnology has been communicated to diverse audiences. However, the effort to distinguish hype from reality is less successful. Potential exaggerations from various sources are flagged, and most of the debates are described in detail. There are clear guidelines presented that identify whether a statement is indeed hype, or merely sounds fantastic because reality will bring radical change. Prof. Berube makes an excellent start in framing the arguments and the participation by consumers, citizens, and commentators in guiding nanotechnology development, but he provides limited guidance to making sense of the issues. Useful insights are presented, but it usually remains unclear whether a given example represents hype or not.

A brief introduction to the agencies through which the US federal government supports science and technology development makes clear that the government's decision to adopt an initiative to encourage nanotechnology (NNI, the National Nanotechnology Initiative, which was institutionalized in 2003 via the 21st Century Nanotechnology Research and Development Act) was exceptional. Prof. Berube establishes his contention that the success of the NNI is jeopardized by the potential of a public backlash fueled by unrealistic perceptions about nanotechnology. He then proceeds to analyze current discussions by describing in detail the individuals, organizations, initiatives, and controversies that have defined public discussion. The sources seem current to about mid-2004.

Prof. Berube begins, of course, with Richard Feynman and concludes that Feynman was trying to probe the limits to knowledge—not instigate a research agenda. In contrast, K. Eric Drexler's description of nanotechnology was clearly meant to inspire a research program, and in the process it inspired two controversies. First, Richard Smalley, a prominent scientist working on aspects of nanotechnology, declared Drexler's proposals for atomically precise manufacturing infeasible. The second controversy, which grabbed public attention when Drexler's warning that improperly designed self-replicating molecular manufacturing systems could reduce the biosphere to "the gray goo concept." This concept was seized upon by respected computer scientist Bill Joy to argue in a widely noted essay that nanotechnology was too dangerous to develop and should be "relinquished".

Berube's account of these debates is balanced, and he does not hazard an opinion on who is correct. He does make the very useful point that much confusion in the public arena has arisen because of these controversies between nanotechnology that will take decades to implement with the technology that exists today in the laboratory.

"Professor Berube succeeds in describing how nanotechnology has been communicated to diverse audiences. However, the effort to distinguish hype from reality is less successful. Potential exaggerations from various sources are flagged and most debates are described in some detail, but no clean guidelines are presented for identifying whether a statement is indeed hype, or merely sounds fantastic because reality will bring radical change."

Berube seems to agree with several other quoted sources that simply denying the feasibility of molecular manufacturing is not an adequate response to Drexler's vision. A better course is to show that the consequences of molecular manufacturing are manageable and still distant.

The two controversies are, however, merely the intellectual framework for what Prof. Berube considers the engines driving the nanotechnology movement—government, industry, and capital markets. These are the subject of the large majority of the book, and there is probably no better place to get an overview of these topics. Special attention is given to SEIN (Societal and Ethical Implication of Nanotechnology, an area of inquiry mandated by US nanotechnology funding legislation), a topic of Prof. Berube's research.

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Detailed consideration is given to a half dozen individuals who have played prominent roles in the government or industry support for nanotechnology, Neal Lane, early backer of NNI at NSF and then Pres. Clinton's advisor and Mikhail Roco, the senior advisor on nanotechnology at NSF and instrumental in launching NNI. In the private sector: Josh Wolfe, of Lux Capital, whose Annual Nanotechnology Report is highly regarded; Steve Jurvetson, of Draper Fisher Jurvetson, a pioneer in funding nanotechnology-related startups; Charlie Harris, of Harris & Harris Group, a publicly held business development group. Other chapters focus on US and foreign government initiatives to support nanotechnology development, government and private reports, and business sectors. A chapter on non-governmental organizations profiles the Foresight Nanotech Institute and the Center for Responsible Nanotechnology as proponents of nanotechnology. He also mentions the ETC Group as an opponent most insistent on stopping research in applied nanoscience. Greenpeace Environmental Trust is a temperate, reasoned opponent focusing on the dangers of nanomaterials, but rejecting a moratorium.

Chapters on societal and ethical issues in nanotechnology recount the damage done to the biotechnology industry by ignoring public opposition to genetically modified organisms, and how some of the same individuals and groups active in the anti-GMO movement threaten to create an anti-nanotechnology movement based upon fears of health and environmental dangers from nanoparticles and other nanomaterials. In response, there is widespread agreement in industry and government on the need for more research on how nanomaterials affect health and the environment, leading to the requirement for SEIN research funding.

The book concludes with three topics. A survey of current efforts to regulate nanotechnology is followed by a rather detailed look at Zyvex, a company founded to implement molecular manufacturing, but successfully re-focused to provide tools and materials for current nanoscience and technology. Lastly, efforts are introduced by the NSF to go beyond current nanoscience and promote the convergence at the nanometer scale of research and development in nanotechnology, biotechnology, information technology, and cognitive science.

Exactly where the hype is in all of this remains unclear. Prof. Berube at various points decries predictions made by government and business boosters of nanotechnology. He worries that the economic benefits of nanotechnology, particularly in creating new jobs, is oversold. He is concerned that proponents invoke US nationalism too much, and place too much emphasis on fears that the US is falling behind global competitors. Perhaps most of all, he worries that SEIN is merely a public relations tool, a way to manage public perceptions, rather than a genuine effort at difficult dialogue. All of these are very important issues, but what is realistic and what is hype, how do we identify the real problems, and how do we develop wise policy to deal with them?

Maximizing Benefits, Minimizing Downsides from Nanotechnology

By Christine L. Peterson

"With economic and social benefits expected to be so strong, we can be confident that increasingly-advanced nanodevices and systems will indeed be built. Not surprisingly, technologies this powerful also have potential downsides that look just as likely to occur."

As Foresight enters its twentieth anniversary year, it's a good time to do an overview of the challenges we now face in our goal of maximizing the benefits and minimizing the downsides of nanotechnology.

The field of nanotech is usually defined so broadly today that it seems to include most expected physical technologies of serious interest. To make progress in guiding it, it helps to divide the field up into stages. My favorite categories for this are: materials, devices, and systems —a roughly chronological order. These will overlap in time, with materials continuing to be important as devices arrive, and both materials and devices playing central roles in advanced nanosystems. Some of our challenges have already started now, in the early days of nanomaterials, while others will kick in only later as devices and systems are developed.

Our goal of advancing beneficial nanotechnologies faces at least three hindrances currently: a complex and confusing patent situation favoring large firms, the so-called "Valley of Death," and — in the U.S. — export controls.

There is serious concern that patents being issued in this area (as well as others) are overly broad and even in direct conflict with similar patents. Ask a patent attorney about this problem and you'll be told that "it will all get worked out in court, or more likely by out-of-court settlement, once there are enough profits to be worth suing over." This is a fine answer from their viewpoint, but won't do from the perspective of an entrepreneur with a small legal budget. To see the magnitude of the problem, check out how many carbon nanotube-related patents have been issued, and then try to figure out whose should in theory hold up, and who has the financial resources to enforce their legitimate claims. If you can't do it in a reasonable period of time, neither can prospective funders of small firms. This creates a bias against entrepreneurship, the source of a great deal of technical innovation. Countries heavily dependent on small-firm innovation, especially the U.S., should take note.

Another patent issue in the U.S. is caused by the Bayh-Dole Act, which assigns patent rights arising from federally-funded research to the universities at which the work is done. U.S. universities have become so focused on these prospective sources of income that negotiating licenses is getting very time-consuming — two years, in one recent case — leading companies to look outside the U.S. for universities to work with.

The second challenge, the "Valley of Death," is a worldwide issue. Once a new technological discovery is made, it needs to somehow make the leap from discovery to product prototype, plus fundable business plan. This is a huge jump, and finding funds for this highly speculative work is often very difficult. Angel investors are still feeling burned from the dot-com bust, and the U.S.'s DARPA is refocusing on near-term projects for which there is perceived to be an immediate defense need.

A third issue already impacting nanomaterials work in the U.S. is export controls. Evidently it is quite hard to know at the time of investment whether a proposed nanomaterial will be approved for export or not. This makes the size of the market much more uncertain, and this must be having a chilling effect on investment in U.S. nanoproducts. Investors may feel that it is safer to make their nanotech investments in a country that is not so restrictive, or at least clearer in its export rules.

Separate from the above concerns is the topic of last issue's column: the potential for accidental negative effects on health and the environment. This area is already getting substantial and growing attention, in particular from the non-profit/for-profit team of Environmental Defense and DuPont, as well as from the Wilson Center's Project on Emerging Nanotechnologies. These and other groups should eventually succeed in their push for improved safety testing and regulation: see, for example, their February 14, 2006, letter to the U.S. House and Senate Appropriations Committees, co-signed by Foresight (http://www.foresight.org/nanodot/?p=2166). This near-term concern — about toxicity of nanomaterials — is not fundamentally different from problems our society has faced before from toxic chemicals, and should be addressable in similar ways.

All of the above big tasks start to look small when we consider the more difficult issues raised by later nanotechnologies: first devices and later molecular nanosystems.

Before launching into those, it's worth reviewing the immense benefits expected from these stages of nanotech. At the top of most lists are medical applications, ranging from ever-improving cancer treatments to, someday, the ability to repair molecules inside cells. The software needed to control such tools will be very hard to write, but the payoff will be so huge that, eventually, we'll get it done. In the Q&A session after a recent talk at Wharton's Emerging Technologies event I was asked about the potential of nanomedicine. I said that it's hard to think of a disease that couldn't be treated with tools this precise.

The other huge application area for advanced molecular nanosystems will be the ability to produce First World standards of living

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for all without damaging the environment — in fact, while repairing the damage already done. You'll see the phrase "zero-waste manufacturing" used: building our products without throwing leftover molecules into the air or water. (Of course, there will always be some waste heat; nanotech can't get around thermodynamics.) To those of us who care deeply about the biosphere, this prospect of productive nanosystems — producing our products in a super-clean fashion with molecular-scale control — is greatly inspiring.

With economic and social benefits expected to be so strong, we can be confident that increasingly-advanced nanodevices and systems will indeed be built. Not surprisingly, technologies this powerful also have potential downsides that look just as likely to occur.

The first such issue, clearly on the way already, is nanosurveillance: the sensing of chemical information in the environment and attaching that information to individual humans producing it. Nanoscale sensors could also be useful in recording more traditional forms of information, such as audio and video, and in fact a new nanotech development enabling a no-flash, low-light video camera has just been announced in Korea. But it is the recording of chemical information which will be truly new, like having specialized dog noses throughout the environment, detecting and reporting molecules associated with each person. Most obvious is DNA, but this should also include other chemicals which would indicate what a person has been eating, say, or smoking. A recent report indicated that dogs can be trained to sense molecules that indicate a person has a particular form of cancer, and whatever a dog's nose can sense, an artificial nanosensor will also be able to sense. With such tools as widely available as video cameras are today, our ideas of personal privacy will need to evolve — and our laws may need to evolve as well — in a world of greatly increased transparency.

Transparency and openness have their obvious downsides for a society as privacy-oriented as, say, the U.S., but they have their benefits as well. Already today we're seeing a gradual increase in the destruction that can be done by one mentally-ill person or small, angry groups. As technology advances, this potential destruction increases far beyond what is possible today. I think we have some time before nanotechnologies are used to make new weapons of mass destruction, but sooner or later, this will happen. It's probably not helpful at this stage to publicly describe in detail what these would be like, so when asked by the media, I just suggest that they could be like today's chemical weapons, but individually targetable. That's bad enough to make the point.

What's needed in such a world is really excellent non-proliferation and arms control techniques, which would have to be based on an ability to detect nanoscale weapons. At any given time, the detection abilities of the "good guys" — define this how you choose — will need to exceed the construction abilities of the "bad guys." Fortunately, in my view, there are more good guys than bad guys overall, so we have a chance of success in this project if the good guys work together.

So there you have it: a brief sketch of the challenges to come for those of us working to maximize the benefits and minimize the downsides of nanotechnology. It's a lot to take on, but in my experience, once you start working on these big, challenging goals, you find such excellent allies that it's a joy to keep going. We at Foresight greatly appreciate the support of our members as we push forward toward a world of clean, beneficial nanotechnologies.

Christine Peterson *is co-founder and VP Public Policy of Foresight Nanotech Institute. Contact her at foresight@foresight.org.*

International Technology Roadmap for Productive Nanosystems

The working group team of world-class scientists, engineers, business leaders and academics met in early-March 2006. Hosted by our partner, Battelle, at their Oakridge facility in Tennessee the group is well on the way to developing a roadmap that will accelerate the development of molecular machines. The group met again in June at another Battelle facility, Brookhaven National Labs, in New York.

Current emphasis is on four pathways to atomically precise manufacturing. The Roadmap will also address the enabling technologies related to each pathway.

Roadmap Pathways:

1. Self-directed manipulation
2. Machining (Feynman approach)
3. Bio Synthesomes
4. Chemistry and Materials Science

The Roadmap committee is on schedule to release the Executive Summary of the Roadmap in Spring 2007. For information about sponsoring the Roadmap, contact Jillian Elliott at jillian@foresight.org

"The International Technology Roadmap for Productive Nanosystems will provide a view of the pathways and enabling technologies in a way that will help industries, companies and even individuals plan the nanotechnology work they want to do."

Jillian Elliott, President, Foresight Nanotech Institute

Definition of Productive Nanosystems

Productive Nanosystems are functional systems that make atomically precise structures, components, and devices under programmable control.

Why Care About Nanotechnology?

By Mauro Ferrari, Ph.D.

"It is very important for the general public to understand that nanotech can really help provide major breakthroughs in medicine."

Why care about nanotechnology?

Nanotechnology is changing the way medicine is practiced, and will continue to do so. The clinical practices of the future will increasingly differ from what is standard today. It will not be too many more years before the makeover is complete.

The major changes will be reliance on early detection of disease rather than intervention. The practices will be localized, minimally invasive, and personalized therapies instead of the massively invasive, routinely all-too-damaging approaches that medicine today must take as recourse. This is especially true of cancer and cardiovascular diseases, but the changes will diffuse throughout medicine.

Let's be clear about the fact that nanotechnology alone cannot do any of the above - but nanotechnology will be a necessary component of the revolution if it is placed at the service of medicine, and fully integrated with the more traditional disciplines of biomedical research and clinical practice.

Why is nanotechnology important for the general public to understand?

Nanotechnology suffers from a unique ill: The same word is used to refer to science fiction stories, and to a set of scientific disciplines that are very real, and so deeply ingrained in the science world that there have already been awarded several Nobel prizes in the last fifteen years.

Referring in particular to medicine, every time I give a talk to medical scientists and clinicians I am delighted to remind them that nanotechnology has been in the clinic for ten years – and that they themselves in all likelihood have used it, by any other name, or have some nanotech-based device in their laboratories. This helps break down the perception barrier, and opens up communications and the possibilities for interactions at the service of the community of healthcare recipients.

It is very important for the general public to understand that nanotech can really help provide major breakthroughs in medicine. As with everything in medicine, extreme care must be exercised to make sure that the medical benefits of nanotherapies will exceed potential collateral damage - but then again, I think it would be very hard, in any circumstances, to develop nanotherapies that reach the undesired toxicity level of the chemotherapies we use in the cancer clinic every day on millions of Americans!

As demonstrated by recent polls, the general public is rightfully mindful of the potential environmental impact of nanotech – and we all should be. I am not an expert on the environmental impact of industrial products in general, but for what pertains to medical grade nanomedicines I am comforted by the fact that there are very stringent safety and efficacy tests that medicines (nano or not) must go through to be approved for market use, and that nanomedicines like all chemotherapeuticals and most medicines must follow very stringent rules on their handling and disposition. Plus, the very volumes and dosages are so small, that I am very optimistic that the medical nanorevolution will take place without undesired environmental effects.

Again, as shown by the Pew Charitable Foundation/Woodrow Wilson report, I am comforted that the general public views favorably the applications of nanotech to medicine, and is less concerned about undesired effects the more they know about it. I think these are the objectives we must collectively strive for: Full understanding by the general public of the benefits and potentials, and the ability for all together - scientists and non-scientists - to make the right decisions about priorities of investment and intervention.

What are your research goals?

I am active in four general areas, each of which has multiple sub-disciplinary components, but are mostly based on a combination of silicon nanotechnology, mathematical modeling, and molecular biology:

1. **Targeted therapeutics.** The idea is to make sure that the very toxic drugs that are used, for instance against cancer, reach the desired cancer target in large concentrations, once they are injected in the bloodstream, and then discharge their action without damaging healthy tissues. By contrast, what is current practice in oncology today, without any nano, is to inject somewhere between 10,000 and 100,000 parts of very toxic drugs to have only one part reach the cancer. The problem of targeting is very, very difficult and requires multiple functions onboard of the therapeutic agent – this is just perfect for nanotech – actually, I do not think there is any other way.
2. **Releasing drugs from wearable implants at desired time-release profiles.** It is not only a matter of getting the drug to the right place – we must also be able to mimic what the body does when it is healthy: release agents at the time when they are needed. Think diabetes: The solution is not to flood the body with insulin at all times (which would be rapidly deadly), but to have insulin available when needed, or most efficacious. Why should cancer therapy or intervention against say infectious diseases be any different? They aren't: tailoring the right release profile to the need is always an improvement. The problem has been so far that the only way to do time-release has been to connect to an IV line in a hospital room – clearly a suboptimal strategy.

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3. **Early diagnostics.** The best way to fight cancer, for instance, is to catch in its precursor or early stages, when it is easier to treat. It often takes 10-15 years for a mass of deranged cells to grow to the point when it is clinically detectable, and then it is often too late. It seems to me that with improved technology platforms it should be possible to monitor everyone and catch these clusters of deranged cells - we have a tremendously long time window to pick them up! In particular, I am convinced that early detection and mass screening of the general population will arise from blood tests - in particular examining the serum proteome. In view of the immense complexity and diversity of the protein population within blood, again I see no way to do it unless we employ nanotechnology platforms. Our approach is to use nanotextured surfaces in combination with mass spectrometry to identify protein profiles that are telling of something untoward going on.
4. **We also have a program to help secure quantitative information from breast cancer tissue biopsies,** and use the information to guide in the selection of the therapeutic regime to follow, in particular for what pertains to the wonderful new drug Herceptin. This is an example of personalized, molecular medicine meeting nanotech.

How is your research relevant to the general public?

We try not to do anything unless there is a clear path from the lab to benefits for the community at large. Obviously this does not guarantee that we always succeed – don't I wish that were the case!!! – it is just an indication of the driver for all of our work.

In the context of your research, how do you see it impacting the future?

We hope to reach the clinic with all four lines of work. More importantly, though, we hope SOMEBODY reaches the clinic successfully addressing the problems we are working on. We lose one person a minute to cancer in the USA, 20 a minute worldwide. I frankly don't much care who gets there first – we will all contribute a little bit, perhaps some more than others, but not by that much. Many readers of this article will witness a world where cancer is no longer a sentence to suffering and death for anyone. The key preoccupation must only be getting there as quick as possible, right?

Mauro Ferrari, Ph.D *is a Professor of Biomedical Engineering and Internal Medicine at The Ohio State University*

http://www.ibgp.org/faculty/profilepage.asp?ID=303

Research Review

By James Lewis, Ph.D

Treatment of cancer with RNA nanotechnology

Songchuan Guo, Nuska Tschammer, Sulma Mohammed and Peixuan Guo, "Specific Delivery of Therapeutic RNAs to Cancer Cells via the Dimerization Mechanism of phi29 Motor pRNA", Human Gene Therapy 16:1097–1109, Sept. 2005.

Peixuan Guo of Purdue University and his colleagues proved some years ago that a novel RNA (pRNA) drives the powerful molecular motor that packages the DNA of the bacterial virus phi29. Since then they have steadily developed the potential of RNA structures that mimic pRNA to act as nanodevices useful for gene and drug delivery to treat cancers and viral diseases. pRNA-like structures designed with complementary loops fit together like bricks to make larger structures. Others have shown that RNA molecules can be evolved in a test tube to bind to specific target molecules (such RNA molecules are called aptamers), and that RNA, as well as protein, molecules can be enzymes. Some of these ribozymes, as well as an additional class of RNA molecules called small interfering RNA (siRNA), can have potent therapeutic effects by silencing the expression of specific genes – if they can be introduced into the right cells.

"Human cancer cells (a line derived from a nasopharyngeal epidermal carcinoma) were treated either with the dimer or with controls lacking either folate or functional siRNA, and then injected into a strain of immunodeficient mice in which human tumors will grow. No tumors formed when the cancer cells had been treated with the dimer. Many steps obviously remain to make pRNA nanostructures into a robust therapy for cancer, but this work makes a very promising beginning."

A companion paper (Nano Lett., 5 (9), 1797 -1808, Sept., 2005) presents the incorporation of such therapeutic RNA molecules into 20-40 nm RNA nanostructures – small enough to enter cell membranes, but not so small as to be easily lost from circulation through the kidneys. Variants of pRNA were engineered to contain either an aptamer, an siRNA, or other small molecules, such as fluorescent dyes to visualize the nanostructure inside cells, or folate (folate receptors are over-expressed by most cancer cells, but generally absent in normal adult cells). Combinations of these variants were assembled three at a time to make 20 nm pRNA trimers, which were shown successful in introducing all three functions simultaneously into individual cells. Guo and his colleagues have shown that engineered pRNA molecules will also form hexamers, so it should be possible to co-deliver six-component therapy.

The Human Gene Therapy paper reports the biological effect of pRNA-based nanostructures upon cancer cells using 25-nm pRNA dimers (rod-shaped rather than the ring shaped trimers discussed above). One half of the dimer displayed folate and the other half included siRNA targeted to survivin, a protein found in most human cancer cells that prevents them from following the cell suicide program that abnormal cells otherwise follow. Human cancer cells (a line derived from a nasopharyngeal epidermal carcinoma) were treated either with the dimer or with controls lacking either folate or functional siRNA, and then injected into a strain of immunodeficient mice in which human tumors will grow. No tumors formed when the cancer cells had been treated with the dimer. Many steps obviously remain to make pRNA nanostructures into a robust therapy for cancer, but this work makes a very promising beginning.

Imaging proteins in real time to atomic precision

Elio A. Abbondanzieri, William J. Greenleaf, Joshua W. Shaevitz, Robert Landick & Steven M. Block "Direct observation of base-pair stepping by RNA polymerase", Nature 438, 460-465, 24 Nov 2005.

Steven Block of Stanford University and his colleagues have extended their pioneering research using optical traps (also called "optical tweezers") to study the nanoscale motions of single biomolecules, especially motor proteins, by developing an ultra-stable optical trapping system that can measure the motions of a single molecule to a precision of 0.1 nm – the diameter of a hydrogen atom.

Micromanipulation by optical traps uses an optical microscope to focus an infrared laser beam on a micron-scale bead of glass or polystyrene suspended in a liquid. As the light is refracted by the transparent bead, the conservation of momentum between the light beam and the bead creates a force that pushes the bead toward the focal point of the beam. If a bead is attached to the end of a motor protein or DNA molecule, the optical trap allows manipulation of the molecule and measurement of the movements of the molecule. Several factors limit the precision of the measurements that can be made. In a companion paper (Physical Review Letters 95, 208102, Nov. 2005), Block and his colleagues present a novel passive force-clamp technique that exploits a small region where the force does not change with displacement of the bead to achieve very high resolution position measurements.

In the Nature paper, the goal was to determine the motions of RNA polymerase (RNAP) as it steps along the DNA double helix joining together ribonuclotides to form an RNA copy of one DNA strand, a process called transcription. Resolving this process requires measuring the motion of a single RNAP molecule during each step to better than the 0.34 nm separating adjacent base pairs in the DNA helix. Previous single molecule measurements of motor proteins had succeeded because the steps were much larger, for example 8 nm for the protein kinesin. To measure the size of the steps during transcription, one section of the RNAP was attached to a 600-nm diameter polystyrene bead, and one end of the DNA template was attached to a 700-nm diameter bead, forming a bead – DNA–RNAP–bead dumbbell when the RNAP bound to the DNA. To increase the resolution of measurements, they implemented the passive force-clamp method of their PRL paper, and enclosed the optical elements external to the microscope in a helium atmosphere (because the refractive index of helium is lower than that of air, thus lowering

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random fluctuations of the laser beams.) They measured the displacement of one bead as the RNAP stepped along the DNA making an RNA segment, and found discrete steps averaging 0.37±0.6 nm. Detailed analysis of the data, including the effect of applied force on motion, gave the best fit with the hypothesis that RNAP moves along the DNA in one base pair-steps with each ribonuclotide added to the RNA. Further, the RNAP acts according to a brownian ratchet mechanism in which the incoming ribonucleotide fits into a secondary binding site before entering the RNAP active site.

New rigid, rapidly assembled DNA building blocks

R. P. Goodman, I. A. T. Schaap, C. F. Tardin, C. M. Erben, R. M. Berry, C. F. Schmidt, A. J. Turberfield "Rapid Chiral Assembly of Rigid DNA Building Blocks for Molecular Nanofabrication", Science 310, 1661-1665, 9 Dec. 2005.

Andrew Turberfield of Oxford University and his colleagues present a new method of assembling DNA building blocks for fabricating nanostructures. They designed a family of DNA tetrahedra to self assemble in a single step in a few seconds, producing a chirally pure product (only one of the two possible mirror image structures is made) in 95% yield. Tetrahedra can then be connected using programmable DNA linkers to form larger structures.

To construct the tetrahedra, four oligonucleotides were mixed together at 95C, and then cooled to 4C in 30 seconds so that complementary regions could pair to form the double helical edges. Each oligonucleotide runs around one face, and there is one unpaired base at each vertix. Two types of tetrahedra were made: (1) regular tetrahedra in which each edge is 20 base pairs (bp), and (2) several different irregular tetrahedra, such as one in which three 30-bp edges meet at one vertex and three 20-bp edges bound the opposite face. This irregular tetrahedron would be expected to be either 7.5 nm or 10.5 nm tall, depending on which size face is resting on the surface. Objects of both heights were visualized by atomic force microscopy (AFM).

The basic design was used to make nine different irregular tetrahedra, some with edges of three different sizes, or with single strand overhangs introduced into an edge to be used to link different tetrahedral building blocks together. With structurally rigid edges and chiral assembly, any given design will have a single strand overhang on one edge either face inside the tetrahedron, and thus be inaccessible for pairing, or face outside and thus be able to link two tetrahedra together. The confirmation of these predictions demonstrated that these building blocks are rigid enough that coordinates on any building block can be specified to almost atomic precision. Testing rigidity directly by crushing tetrahedra with an AFM tip showed that individual tetrahedra irreversibly deformed at loads between 70 and 200 pN. These building blocks for DNA nanotechnology thus have several advantages over earlier structures, including stiffness, purity, and ease of assembly.

Become a member of Foresight Nanotech Institute

Twenty years ago Foresight and our supporters had the vision and the belief that nanotechnology could be a powerful force to improve the health and well-being of people and the planet. Today, nanotechnology is no longer just an idea, it is a fundamental force that is reaping rewards for humanity in fields ranging from biotech to energy, and with Foresight helping to lead the way, we are on the pathway to developing productive nanosystems — molecular machine systems that build with atomic precision.

This vision is now becoming reality.

Since our earliest days, Foresight has been promoting an understanding of the beneficial uses of nanotechnology. Foresight was the first voice and today remains the leading public interest voice for nanotechnology. We hold technical conferences and numerous member gatherings to enhance understanding and create opportunities for like-minded individuals to share ideas and establish relationships. Today Foresight is even more active and we hope you will become to be a member of our team.

Over the last year Foresight has achieved important work, which wouldn't have been possible without our member support:

- **Foresight and Battelle launched an International Technology Roadmap for Productive Nanosystems.** With initial funding from the Waitt Family Foundation supporting a team of world-class scientists, engineers, business leaders and academics, we are on our way to developing a roadmap that will accelerate the development of molecular machines.
- **Re-launched and improved our web site,** where you can find even more information about nanotechnology, including a resource library that includes links and information about education, and jobs, and our popular blog Nanodot
- **Launched our weekly *News Digest,*** which provides the latest developments on nanotechnology and is read by 15,000 people in more than 125 countries each week.

We have updated our membership levels and benefits. These benefits provide exceptional value and recognize the important contribution our members make. With your help, we can continue to advance the field of nanotechnology.

We thank you for supporting the beneficial implementation of nanotechnology through Foresight. Please contact us any time with your requests, questions, and ideas for how Foresight can better further your goals for nanotechnology.

Foresight Nanotech Institute

The Foresight Update is a quarterly-publication for Foresight's participating and basic members. Foresight is a member driven organization and we thank you for your support.

We hope you enjoy this issue. Our next publication, Fall 2006, will be devoted to Foresight Nanotechnology Challenge #3: Increasing the health and longevity of human life.

Foresight Nanotech Institute would especially like to thank those who contributed to this issue on Nanotechnology and Clean Water.

Foresight Nanotech

Update

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If you find items relevant to Foresight's goal of preparing for future technologies, please forward them for possible coverage in Foresight Update, or submit them for posting at http://www.nanodot.org. Letters and opinion pieces will also be considered; submissions may be edited.

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