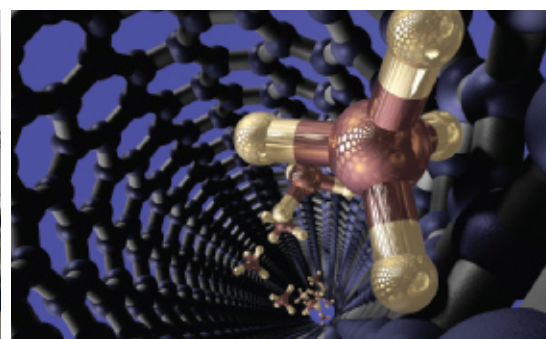
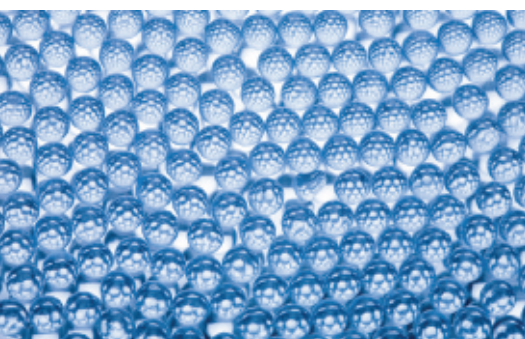


# Nanoscience: Tiny Players Make Huge Strides for Technology, Medicine and Everyday Life



*A white paper reporting on the rapidly developing area of nanoscience and nanochemistry and the possibilities they pose for improving our health, lives and the world around us.*



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# Nanoscience: Tiny Players Make Huge Strides for Medicine, Technology, and Everyday Life

## TABLE OF CONTENTS

<b>Executive Summary . . . . .</b>	<b>2</b>
<b>I. Nanotechnology Teams Up with Medicine to Fight Disease . . . . .</b>	<b>3</b>
<b>Nanomaterial-based therapeutics reach the clinic . . . . .</b>	<b>3</b>
<b>Nanomedicine research at the pre-clinical stage . . . . .</b>	<b>5</b>
<b>Nanomaterials for diagnostics, sensing, and imaging . . . . .</b>	<b>7</b>
<b>Doing it all: Theranostics both diagnose and treat disease . . . . .</b>	<b>9</b>
<b>Other applications of nanotechnology in medicine . . . . .</b>	<b>11</b>
<b>II. Making Strides for Energy and the Environment . . . . .</b>	<b>12</b>
<b>Nanomaterials may open the way to new energy sources. . . . .</b>	<b>12</b>
<b>Nanostructures clean up water . . . . .</b>	<b>12</b>
<b>Nanoparticles help locate oil in reservoirs . . . . .</b>	<b>13</b>
<b>III. Engineering Stronger, Cleaner Construction Materials with Nanotechnology . . . . .</b>	<b>14</b>
<b>IV. Nanotechnology Supports Basic Chemical Research . . . . .</b>	<b>15</b>
<b>V. Smaller is Better: Nanotechnology's Role in Shrinking Electronics . . . . .</b>	<b>17</b>
<b>VI. The Untapped Potential of Nanomaterials . . . . .</b>	<b>19</b>
<b>DNA nanotechnology . . . . .</b>	<b>20</b>
<b>Proteins and bionanotechnology . . . . .</b>	<b>21</b>
<b>Molecular machines. . . . .</b>	<b>21</b>
<b>VII. Nanomaterials in the Environment: Health and Safety Concerns . . . . .</b>	<b>22</b>
<b>VIII. Conclusions: The Future of Nanoscience . . . . .</b>	<b>25</b>
<b>IX. References . . . . .</b>	<b>25</b>

## ABOUT THIS REPORT

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## Executive Summary

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Technological advances over the past several decades have paved the way for researchers to study life at the nanoscale.<sup>1</sup> Long before the term “nanotechnology” was coined, acclaimed physicist Richard Feynman gave a talk, titled “There’s Plenty of Room at the Bottom,” at a 1959 meeting of the American Physical Society. He spoke of a time when scientists would be able to control matter on the level of atoms and molecules.<sup>2</sup> Two decades passed, then the development of the scanning tunneling microscope allowed researchers to catch their first glimpse of individual atoms, ushering in the era of modern nanoscience and nanotechnology.<sup>1</sup>

At the nanoscale, many materials exhibit enhanced physical, chemical, optical, and mechanical properties. Humans have been using nanoscale materials for centuries without knowing it; for example, stained glass windows get their color from nano-sized particles of gold and silver.<sup>1</sup> Nanomaterials come in a variety of “flavors,” including nanoparticles, nanotubes, and molecular machines based on synthetic molecules or biopolymers. Scientists have already demonstrated the utility of nanomaterials in applications ranging from personalized cancer treatments to stronger buildings and everyday products, such as sunscreen and cosmetics. Many proponents believe we have just begun to scratch the surface of what nanoscience can accomplish for society. But as progress in nanotechnology gives way to a growing number of nano-based commercial products, researchers are recognizing the crucial importance of assessing the impact of nanomaterials on human health and the environment and making strides toward improving safety.

Nanoscience is a rapidly developing multi-disciplinary research area, and every step toward a deeper understanding of the workings of the nanoscale seems to uncover new questions and obstacles. Continued success in the field will depend on the combined efforts of chemists, materials scientists, biologists, engineers, and biomedical researchers. Chemists have an important role to play in the synthesis and characterization of nanomaterials and the development of new applications, as well as in the investigation of ways to minimize toxicity and improve safety.

This report will present numerous examples of the ways nanotechnology is making an impact on diverse industries and fields, including medicine, energy, construction, basic chemical research, electronics, and commercial products for everyday use. The examples included are representative of recent progress in the field, with emphasis placed on the role chemists are playing to push the boundaries of nanoscience.

## I. Nanotechnology Teams Up with Medicine to Fight Disease

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The field of nanomedicine brings together chemists, biologists, pharmacists, engineers, and medical researchers, with the common goal of exploiting the unique properties of nanomaterials to develop improved therapeutics and diagnostics.

One of the goals of nanomedicine is to improve on or complement current therapeutic approaches. Nanoscience research teams are working on developing nanoparticle-based anti-cancer drugs that deliver cytotoxic compounds specifically to diseased cells.<sup>3</sup>

Some are working to create new drugs, while others are teaming up nanomaterials with already-existing drugs to achieve better outcomes.<sup>4</sup> Many believe nano-based therapeutics will be capable of combating traditionally tough-to-treat ailments by taking advantage of all that the nanoscale has to offer. But drug treatments cannot fulfill their role in fighting disease without reliable diagnostic tools, so another major nanoscience research effort is focused on developing nanomaterials into improved imaging, biosensing, and diagnostic tools. Still others are designing nanomaterials that wear many hats and can both diagnose and treat a disease at once.

Since the earliest days of nanotechnology developments for medical applications, scientists have envisioned that nanomaterials could help improve outcomes and reduce side effects during the treatment of cancer and other diseases. The goal is to kill diseased cells while causing minimal damage to healthy tissue. The problem is that traditional approaches to treating cancer, which include the surgical removal of the tumor or a dose of radiation or an anti-cancer compound, often damage and kill both cancerous and healthy cells. Although sometimes successful, these therapies come with their share of painful side effects.<sup>4</sup>

Nanoscience researchers are working to develop improved treatments by getting nanoparticles straight to diseased cells, where they can unload their toxic cargo, silence genes to stop tumor growth, or heat up with the help of light and kill cancerous cells from the inside out.<sup>3</sup> Some nanoparticle-based therapies have made it to the market and to clinical settings, although much work still remains in the early stages.<sup>4</sup>

### **NANOMATERIAL-BASED THERAPEUTICS REACH THE CLINIC**

Nanoparticle-based drugs have been on the market for almost two decades, starting in 1995 with Doxil, which contains the drug doxorubicin encapsulated in a liposome or a vesicle made from a lipid bilayer. The drug was initially approved for treating AIDS-related Kaposi's sarcoma, and later for treating ovarian cancer. Another drug, Abraxane (approved in 2005), is composed of protein-based nanoparticles loaded up with paclitaxel, a drug that treats several types of cancer.<sup>4</sup>

These early examples, despite being successful, are simple nanoformulations that don't take advantage of all that working on the nanoscale has to offer, experts say.<sup>4</sup> For example, chemical modifications to nanomaterial surfaces can help increase cellular uptake, the high surface area-to-volume ratio can be exploited to enable delivery of large payloads, coating particles with targeting ligands can help direct them specifically to diseased cells, and nanoparticle composition can be tailored to control the location and rate of drug release. Simply stated, there is much room for growth in nanomedicine and many avenues for continued exploration.

Researchers at Cerulean, a Cambridge, Mass.-based pharmaceutical company, are looking to nanotechnology to help revive drugs that failed in previous clinical trials, such as the chemotherapeutic agent camptothecin. The company has reformulated the drug, creating nanoparticles made of camptothecin entrapped in the hydrophobic core of tangled polymers. The new treatment, named CRLX101, made it to clinical trials for treating non-small-cell lung cancer, and initial tests revealed it may have fewer side effects than other treatments.<sup>4</sup>

Another platform involves the use of nanoparticles made of an amphiphilic copolymer, which can encapsulate hydrophobic drugs in their core and be tailored to present targeting ligands on their surface to help promote specific interactions with diseased cells. Since the particles are modular in nature, their properties can be tailored by building in different components to yield particles with the desired size, drug release profile, payload size, surface charge, and targeting ligand. One example of a nanotherapeutic based on this platform is BIND-014, which contains the chemotherapeutic docetaxel and made it to clinical trials for treating prostate cancer.<sup>4</sup>

Nanomedicine scientists and engineers are also looking to nanoparticles to encapsulate and extend the lifetime of small-molecule drugs or biomolecular cargo in the bloodstream. For example, researchers at Calando Pharmaceuticals have created a drug, known as CALAA-01, which is composed of nanoencapsulated polymer nanoparticles containing silencing RNA (siRNA). The nanoparticles form when linear polymer chains containing both positively charged regions and cyclodextrin moieties mix with siRNA. The complex helps prevent siRNA from being readily degraded in the bloodstream. Once taken up by a cancer cell, the siRNA silences a gene, causing the cell to shut down.<sup>4</sup>

Some nanoparticles themselves exhibit anti-cancer characteristics without the help of an anti-cancer compound. Clinical trials are underway for hafnium oxide nanocrystals that join forces with standard radiation treatment to kill cancer cells. The crystals, upon injection into the tumor site, help focus the force of radiation onto the diseased cells. This allows the use of lower doses of radiation to kill the cells, effectively minimizing harm to healthy tissues that are penetrated by X-rays traveling through the body to the tumor site.<sup>4</sup>

Another nanoparticle-based therapy in clinical trials involves particles which themselves serve as the anti-cancer agent. The gold nanoshells, known as AuroShells, get caught up in cancerous tissue without a specific targeting ligand because blood vessels that run through tumors are

inherently leaky – a phenomenon known as the enhanced permeability and retention (EPR) effect. After the particles accumulate in the tumor, light from a near-infrared laser causes them to heat up and destroy the tumor. Healthy tissues remain unscathed, and the particles themselves are inert, minimizing the risk of toxicity.<sup>4</sup> Researchers hope such photothermal therapies may one day help kill cancer cells that are particularly difficult to remove via surgery, such as those wrapped around nerve bundles and arteries,<sup>4</sup> or gliomas, which contain fingerlike projections throughout brain tissue.<sup>3</sup>

The Food & Drug Administration, which is responsible for reviewing applications for new drugs, including those that contain nanomaterials, received more than 150 applications for nanoparticle-based drugs as of September 2012.<sup>5</sup> The three largest contributors to nanotech-related drug applications submitted to the FDA are based on liposomes, nanoparticles, and nanocrystals, at 39, 27, and 14 percent, respectively. The largest class of nanotech-related drugs is being developed to target cancer, accounting for 38 percent, with treatments for pain and infection trailing at about 10 percent each. The majority of nanotech-related drug applications is being developed for intravenous administration (56 percent), followed by oral administration (23 percent). The data include 128 applications for investigational new drugs, which are typically filed before clinical testing, and 30 applications for new drugs that have been through clinical testing already.<sup>5</sup> Nanoparticle-based treatments that do not involve a pharmaceutical compound are not considered drugs, and were not included in this analysis.

The FDA review process is hampered by the lack of clear requirements for characterizing nanomaterials and reporting the data.<sup>5</sup> For example, nanoparticle size can affect product performance, such as bioavailability and dissolution, but the FDA does not currently have clear guidelines for how to report data on particle size and distribution. FDA scientists are performing research to better understand nanomaterials-based drug products and are conducting assessments to optimize and standardize the nanotech drug review process.<sup>5</sup>

To make it in a clinical setting, nanoparticle-based therapeutics must be stable in the body, circulate well, and have minimal interactions with healthy cells. To be appealing to physicians, it's not enough for the nanotherapeutics to fight the disease – they must do so better than existing therapies, with fewer side effects and lower toxicity.<sup>4</sup> These criteria present challenges that require the combined effort of researchers in diverse disciplines to overcome.

## **NANOMEDICINE RESEARCH AT THE PRE-CLINICAL STAGE**

The growing success of nanotechnology-based therapeutics in the clinical setting has coincided with the increasing popularity of nanomedicine as a research area in recent years. Thanks to nanoparticles, drugs that have dropped out of the development pipeline due to poor solubility may get a second chance. This is because nanoparticles have been found to boost drug solubility, and reformulating these previous drug failures with nanomaterials could give them a second chance at success in the clinical setting.<sup>6</sup> Solubility directly relates to bioavailability, or the ability of the drug to enter into circulation in its active form.

Nanoformulation technology is a growing field that some experts believe will increase the chances of getting lipophilic drug candidates with poor solubility onto the market.<sup>6</sup>

In nanoformulations research, scientists tether soluble compounds to nanoparticles or create nano-sized complexes of compounds and polymers to see if the new formulation results in greater bioavailability. Sometimes, a nanoparticle carrier is not needed to improve performance, but instead the compound itself is made into a nanostructure. In one example, researchers create a nanofoam out of the compound with the help of supercritical carbon dioxide. Others have used arrays of inorganic nanoparticles as “nanotemplates” to create a nanostructured material composed of the pure drug, while others have created molds to create pure drug nanoparticles in a variety of shapes. Scientists are also investigating the possibility of creating hybrid nanomaterials, composed of both the drug and a compound that helps create a nanostructured material. For example, one research team found that a hydrophobic drug can be coprecipitated with  $\text{CaCO}_3$  to create an intercalated nanostructure that is readily soluble in the human gut.<sup>6</sup> Some challenges in nanoformulations research include long processing times and quality-control issues. But efforts in the field create the possibility of giving low-solubility compounds with otherwise promising therapeutic potential a second chance at succeeding as drugs.<sup>6</sup>

In addition to boosting drug solubility to improve performance, nanomaterials can also serve as drug delivery vehicles that help carry therapeutic cargo to its destination in the body.<sup>3</sup> Researchers led by Sangeeta N. Bhatia at the Massachusetts Institute of Technology are investigating ways of pairing up different types of nanoparticles to find out if they have a greater therapeutic effect together. The team demonstrated the use of rod-shaped gold nanoparticles and drug-carrying liposomes to stop a growing tumor in its tracks. They first injected tumor-bearing mice with the gold nanorods and shined a near-infrared light on the tumors. The light caused the nanorods to heat up, damage the tumors’ blood vessels, and initiate the blood-clotting cascade. At that moment, they injected another type of particles – liposomes carrying the anti-cancer drug doxorubicin along with a peptide that binds to an enzyme involved in clotting. The liposomes hitched a ride on the clotting enzymes to the tumor site, where they accumulated at higher concentrations than regular liposomes alone could, and helped prevent tumor growth.<sup>7</sup>

Another research team at Johns Hopkins University is exploring ways to use chemistry to help nanoparticles make their way into brain tissue. They found that when nanoparticles as large as 114 nm are coated with the polymer polyethylene glycol (PEG), they gained the ability to penetrate and spread through brain tissue. Particles of that size were previously believed to be too large for accomplishing such a feat. The findings give researchers hope that nanoparticle-based drug delivery systems may one day be used to treat brain disease.<sup>8</sup>

An inevitable part of introducing foreign materials into biological fluids is the buildup of proteins and lipids onto the surface, creating what is known as a protein corona. This can often cause problems for nanoparticle-based drug delivery vehicles; one approach to combat



this issue is to chemically modify the particles to minimize the accumulation of unwanted biomolecules on them. But others have found a way to exploit the protein corona and actually use it to help get nanoparticles to their destination. A team of researchers from the University of Oxford and Scripps Research Institute modified quantum dots with a cholesterol-based molecule that they predicted would trigger the misfolding of a specific endogenous protein in the corona. The act of protein misfolding exposed binding sites that helped the particles get taken up specifically by certain types of immune cells, and the team proposes that different molecules could be used to help the particles get taken up by other types of cells.<sup>9</sup> A research team from the University of Pennsylvania has taken a slightly different approach: they coat nanoparticles with specific endogenous proteins that help them evade the immune response and deliver their lethal cargo to tumors.<sup>10</sup>

Scientists are also looking to nanotechnology to find alternatives to RNA interference agents, which help fight disease by controlling gene expression. Traditional siRNA-based drugs suffer from instability due to degradation by endogenous and pathogenic agents, but a new type of nanoparticle-based conjugates known as “nanozymes” hold promise for overcoming some of these challenges.<sup>11</sup> Nanozymes are made of gold nanoparticles presenting DNA and endonucleases, or enzymes capable of cleaving DNA-RNA complexes. The particles are capable of entering virus-infected cells, where the DNA binds to a target RNA strand, resulting in enzymatic cleavage of the RNA and subsequent reduction in expression of the protein it encodes. In this way, the nanozymes subdue viral replication without any noticeable side effects. Future challenges include nanozyme delivery to specific organs or cell types, perhaps with the addition of functionalities that help direct the conjugates to their desired destination.<sup>11</sup>

A recently developed approach to forming nano-sized vesicles, tubes, and disks for drug delivery and other applications involves the use of highly branched organic compounds known as Janus dendrimers. The amphiphilic dendrimer molecules self-assemble in water to form structural mimics of biological membranes known as dendrimersomes, which may have advantages over other types of synthetic vesicles such as liposomes and polymersomes because they are stable, uniform, and can be functionalized to present targeting ligands or accommodate guest molecules.<sup>12</sup>

## **NANOMATERIALS FOR DIAGNOSTICS, SENSING, AND IMAGING**

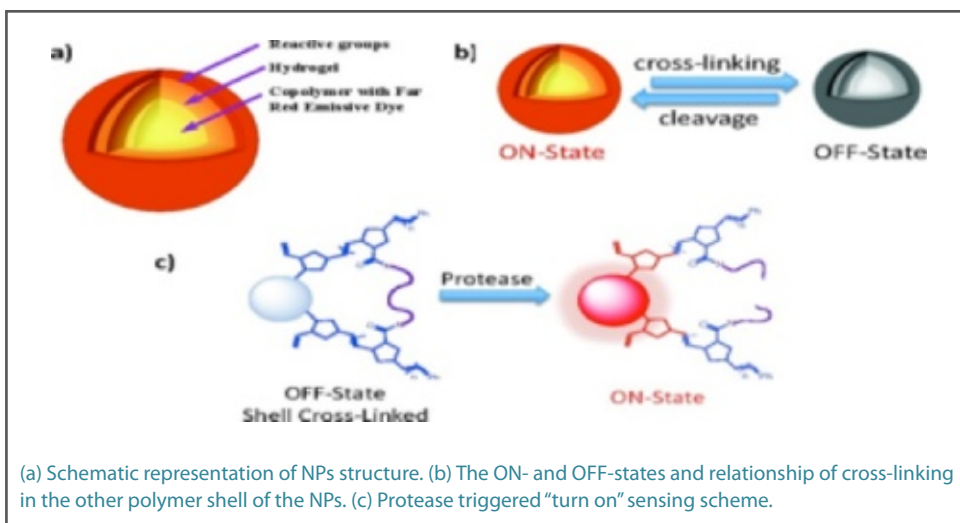
Without diagnostic tools, therapeutics would not be able to fulfill their role in combating disease. Researchers are looking to nanotechnology to develop more sensitive techniques for detecting biomarkers, which could help doctors diagnose diseases in the earliest stages when the chances of patient survival are the greatest.

Nanoparticles for diagnostic applications entered the scene more than a decade ago when researchers found that gold nanoparticles functionalized with antibodies, or with single-stranded DNA or RNA, could detect DNA or protein targets with much greater sensitivity



than the standard fluorescence-based techniques in use at the time. Nanoparticles' ability to scatter light enables them to detect target molecules with up to 100 times more sensitivity than traditional enzyme-linked immunosorbent assays in some cases.<sup>13</sup> Since then, numerous demonstrations of nanoparticles and other nanomaterials for sensing and diagnostic applications have been reported.

For example, Timothy M. Swager and Carlos Cordovilla of Massachusetts Institute of Technology recently reported a method for creating polymer-based nanoparticles that light up in the presence of a specific protease, which may one day serve as a sensing platform for detecting proteases present in the early stages of cancer. The polymers' light-emitting abilities are suppressed when they are wrapped up with a peptide composed of an amino acid sequence recognized by the protease. When the particles encounter the enzyme, the peptide is cleaved and the glowing polymers are released, signaling the enzyme's presence.<sup>14</sup>

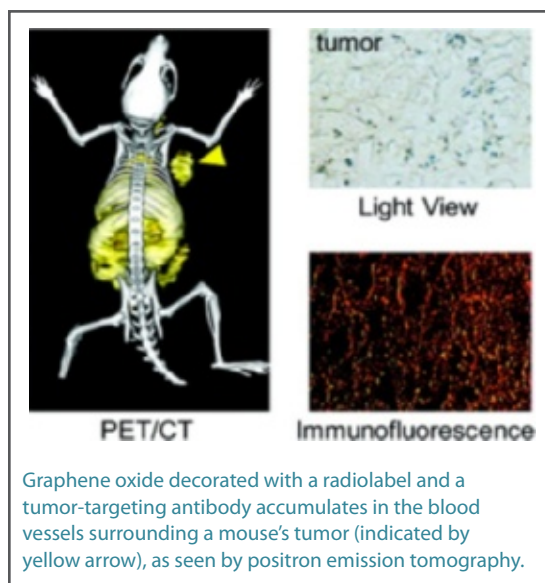


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Researchers from Stanford University have also looked to nanomaterials to develop tools that could help in both the detection and surgical removal of tumors. The team tagged gold rod-shaped nanoparticles with a near-infrared dye and injected them into mice with ovarian cancer. They found the tagged nanorods could be detected with photoacoustic imaging, which enables visualization of tumors buried deep within tissue, as well as with surface-enhanced Raman spectroscopy imaging, which can help ensure complete surgical removal of diseased tissues.<sup>15</sup> Imaging tumors with Raman spectroscopy is enabled by the enormous signal amplification that results from light interacting with gold or silver nanoparticles within the tissue; this method has the added advantage of providing chemical information and having multiplexing capabilities.<sup>16</sup>

Another research team from the University of Wisconsin School of Medicine & Public Health developed a graphene-based imaging agent for visualizing tumors in live mice. In their

approach, they coat tiny sheets of graphene oxide with a polymer chain. Some of the polymers were tagged with a radiolabel that enabled visualization with positron emission tomography, while others were functionalized with a tumor-targeting antibody to help guide the sheets to the tumor site.<sup>17</sup>



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Visualization capabilities of nanoparticles are also being exploited to enhance tumor imaging with magnetic resonance imaging (MRI). A research team from Seoul National University found iron oxide nanocubes cause certain types of tissue to light up during in vivo MRI, demonstrating the potential of the uniformly sized particles to serve as contrast-enhancing agents for imaging applications and lead to new tools for fields ranging from basic biology to clinical diagnostics and therapy. The nanocubes, made of ferri-magnetic magnetite, were found to outperform commercial and other experimental agents for imaging cells both in vitro and in vivo.<sup>18</sup>

Finally, a recent report shows the use of nanotechnology to detect cancer cells by looking at the composition of their ribonucleic acid (RNA). Christoph Gerber of the Swiss Nanoscience Institute of the University of Basel, along with coworkers, developed nano-sized mechanical sensors – tiny cantilevers that they found can distinguish healthy cells from cancerous ones. The technique is sensitive enough that the RNA does not require amplification or labeling to achieve a measureable signal.<sup>19</sup>

### DOING IT ALL: THERANOSTICS BOTH DIAGNOSE AND TREAT DISEASE

Researchers are exploring new ways to use nanoparticles and other nanomaterials to combine therapeutics and diagnostics into a single platform, known as “theranostics,” for fighting cancer and disease.<sup>3</sup> Although theranostic nanoparticles have not made it to clinical settings yet, promising results from preliminary research efforts have many experts optimistic that these novel particles could soon become a useful new addition to physicians’ toolboxes. Nanoparticles inherently have a high surface-to-volume ratio that enables them to carry a large payload. And due to their extremely small size, nanoparticles can enter into cells, where they can unload an imaging agent or therapeutic to help diagnose or treat the disease.

To help target nanoparticles specifically to diseased cells, researchers can coat them with antibodies that recognize proteins and receptors that are highly expressed on those cells. Once they arrive at the scene, some types of particles will unload their drug payload, while others can kill cells with heat – a technique known as photothermal therapy. Magnetic particles are

heated up with an alternating magnetic field, while gold nanoparticles heat up when electrons in the particles are caused to oscillate by light – a phenomenon known as surface plasmon resonance.<sup>3</sup>

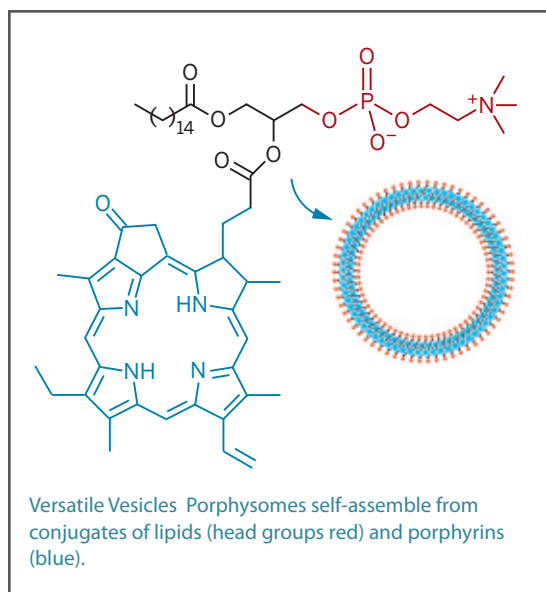
Gold nanoparticles, despite being expensive,<sup>3</sup> are attractive to researchers because of their biocompatibility and chemical stability.<sup>20</sup> In one report, researchers led by Younan Xia at Washington University in St. Louis used near-infrared light to heat up porous gold “nanocage” particles, which were coated with a heat-sensitive polymer that entrapped a cancer drug known as doxorubicin. The heat released the drug payload and helped kill cells from within.<sup>3</sup> Other researchers are looking to iron oxide, a more affordable material that, like gold, enables both imaging and therapy applications.<sup>3</sup> The ability to tune nanoparticles to absorb electromagnetic radiation in the UV, visible, or near-infrared regions requires an in-depth understanding of the optical and electronic properties of nanoparticles, which can be affected by their size, shape, and functionalization.<sup>16</sup>

A research team led by Gang Zheng at Canada’s Ontario Cancer Institute developed a method for creating nanovesicles that can do many things at once: target cancer cells, serve as a contrast agent for imaging, deliver a drug payload, and kill cancer cells with heat. These porphysomes, composed of lipids and a class of molecules known as porphyrins, exploit their intrinsic properties to accomplish these feats. Unlike organic drug delivery vehicles such as liposomes, which require labeling with a radioisotope or other contrast agent to allow visualization, porphysomes absorb enough near-infrared light to be used for in vivo imaging through tissue. As a bonus, the nanovesicles are enzymatically biodegradable and consequently less toxic than inorganic nanoparticles such as quantum dots.<sup>21</sup>

Researchers are also exploring the use of theranostics for delivering nucleic acid therapies. One team developed a method for creating polyplexes, composed of polymer complexes and

plasmid DNA or siRNA, to deliver DNA or RNA into cells for nucleic acid therapy. They found the complexes could be reliably produced at low cost and could be tagged with polymer beacons composed of a heavy metal to enable MRI.<sup>3</sup>

Some experts believe that photothermal therapy and other types of theranostics may one day help treat diseases that are difficult to combat with traditional therapies, as discussed above, since targeted nanoparticles that heat up with light or radiation could help kill the cancerous cells without the need for surgery.<sup>3</sup>



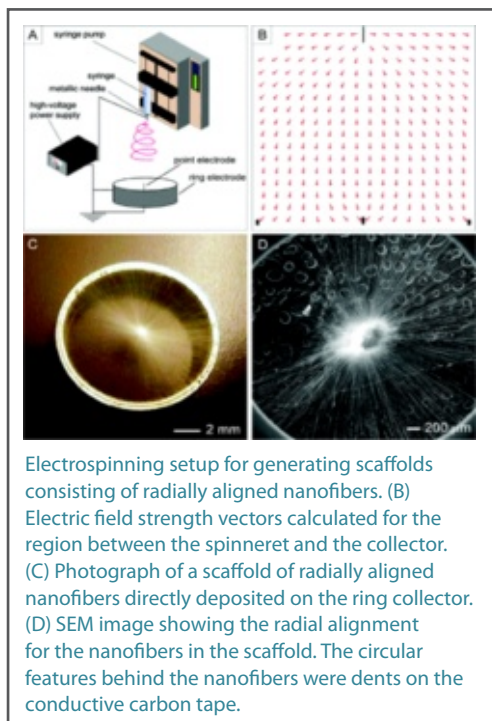
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Numerous obstacles must be overcome before theranostics find their way into clinical settings. One issue is that nanomaterial synthesis typically results in a range of particle sizes, number of targeting molecules and visualization tags, and payload size. Having a single platform bearing multiple items can also present challenges when it comes to determining optimal dosages. For example, the amount of theranostic material required to administer the ideal drug payload must not require higher-than-allowed levels of radioactive isotopes.<sup>3</sup> Traditional therapeutics and diagnostics made from small-molecule synthesis are typically exempt from these issues, and regulatory agencies are still in the process of setting standards for the approval of nanomaterials for human use.<sup>5</sup>

## OTHER APPLICATIONS OF NANOTECHNOLOGY IN MEDICINE

Researchers are also looking to nanotechnology to develop new approaches to cell therapy and other medical applications, ranging from treating alcohol intoxication to finding bacterial infection.

A research team at Washington University in St. Louis has found electrospun nanofiber scaffolds made of polymers to be promising candidates for applications in tissue regeneration. The scaffolds, composed of radially aligned nanofibers, help promote the growth of dural fibroblast cells, which make up the dura mater (the tissue surrounding the brain and spinal cord). Such substrates could replace or help promote growth of dura mater after neurosurgery, an alternative to the use of tissue grafts that are prone to adverse effects such as disease or rejection.<sup>22</sup>



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Another team led by Patrick C. H. Hsieh of Taiwan's Academia Sinica has demonstrated that peptide-based nanofiber scaffolds may one day be used to help repair heart tissue after a heart attack. The peptide nanofiber gel contains a protein that helps recruit healthy cells to the damaged tissue to speed up the repair.<sup>23</sup>

Nanomaterials may one day even help in treating alcohol intoxication. A method recently developed by researchers at the University of California in Los Angeles involves polymer nanocapsules that contain an enzyme pair that helps break down ethanol. The team found that the nanocapsules reduce rodents' blood alcohol levels when used either as a prophylactic or antidote to alcohol intoxication. The method has potential to be applied to encapsulating other classes of enzymes for different applications.<sup>24</sup>

Magnetic nanoparticles have also been found to help remove bacteria from blood. Researchers at Massachusetts Institute of Technology and Harvard Medical School coated magnetic particles with a complex that binds to anionic phospholipids, such as those present on the surfaces of bacteria. They then added them to bacteria-tainted cow blood and found that the nanoparticles helped pluck away the bacteria. This approach could be developed into a treatment for sepsis, a potentially life-threatening condition that involves the buildup of bacteria in the bloodstream.<sup>25</sup>

Although many nano-based medical research efforts remain in their early stages, several nanomaterials-based drugs have been on the market for years, such as the anti-cancer drugs Doxil and Abraxane. But as described above, there remains enormous untapped potential in the field of nanoscale medical technologies. Many challenges remain, ranging from scientific obstacles to regulatory hurdles, which will require the continued collaboration of researchers from diverse disciplines to overcome.

## II. Making Strides for Energy and the Environment

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### **NANOMATERIALS MAY OPEN THE WAY TO NEW ENERGY SOURCES**

A new approach to solar cells, involving nanowires made from indium phosphide, has shown itself to have comparable efficiency with traditional flat solar cells. Nanowire array photovoltaics, which have previously struggled with low efficiencies, have the potential to be more cost-effective and environmentally friendly than traditional solar cell materials. The nanowire materials may also be developed for applications in photodetectors and other optoelectronic devices.<sup>26</sup>

For years, nanotech scientists and engineers have been working to develop new ways to use sunlight to convert water molecules into hydrogen for use in fuel cells. Nanoscience researchers at the University of Rochester recently developed a nanocrystal-based photocatalytic system that generates hydrogen gas from light and protons and lasts for at least two weeks – longer than any nanoparticle-based systems of its kind.<sup>27</sup> Another team led by John H. Golbeck of Pennsylvania State University has made a nanodevice out of proteins, molecular wires, and crosslinking agents; they found that the nanodevice produces hydrogen with a higher electron-transfer throughput than natural photosynthesis.<sup>28</sup>

### **NANOSTRUCTURES CLEAN UP WATER**

In the event of an accident at a nuclear facility, one potential danger is the release of radioactive ions, such as cesium and iodide, which are produced during uranium fission. Nanomaterials have shown promise for helping clean up water contaminated with radioactive waste. Researchers led by Huaiyong Zhu of Australia's Queensland University of Technology found that titanate nanotubes and nanofibers made from titanium dioxide are able to chemisorb or trap radioactive ions for safe disposal.<sup>29</sup>

## NANOPARTICLES HELP LOCATE OIL IN RESERVOIRS

Even after a well is considered tapped out, an estimated 30 to 70 percent of its oil is still underground, but the challenges to locating and retrieving that remaining oil are so significant that companies elect to move on and leave it behind. Oil companies and oil-field service providers have been looking to nanotechnology for help with retrieving that oil. Research is currently underway, funded by the Advanced Energy Consortium, to use nanotechnology to create a sensing element that can get into the reservoir and convey information to drillers about where precious fuel remains underground.<sup>30</sup>

One approach involves using superparamagnetic nanoparticles, such as those made from iron oxide, that can serve as contrast agents for the electromagnetic imaging of the reservoirs. Among the many chemical challenges that exist is the development of particle coatings to keep the particles from adsorbing to the reservoir's rock and clumping in the high-salt conditions. In contrast to nanoparticles for biomedical applications, which require material on the order of micrograms per application, oil and gas applications will require tons of material, so scaling up the fabrication process will also present a significant obstacle to overcome.<sup>30</sup>

## NANOTECHNOLOGY: FUNDING AND EXPECTATIONS

Nanotechnology has the potential to revolutionize our lives and the economy in the near future, much like the field of information technology has done over the past few decades.<sup>72</sup> In order to stay competitive in the worldwide nanotechnology marketplace, the U.S. government has committed to supporting nanotechnology research and development, with the creation of the National Nanotechnology Initiative (NNI). With 26 participating federal departments and agencies, the NNI coordinates funding for nanotechnology research and is one of the largest federal interagency research and development programs. The 2013 federal budget provides the NNI with \$1.8 billion, and the U.S. has invested a total of more than \$18 billion since 2001.

A 2008 survey estimates about 150,000 people in the U.S. and 400,000 people worldwide work in the area of nanotechnology. An estimated 2 million nanotechnology jobs in the U.S. will be available by 2020, according to a study funded by the National Science Foundation.<sup>73</sup>

### III. Engineering Stronger, Cleaner Construction Materials with Nanotechnology

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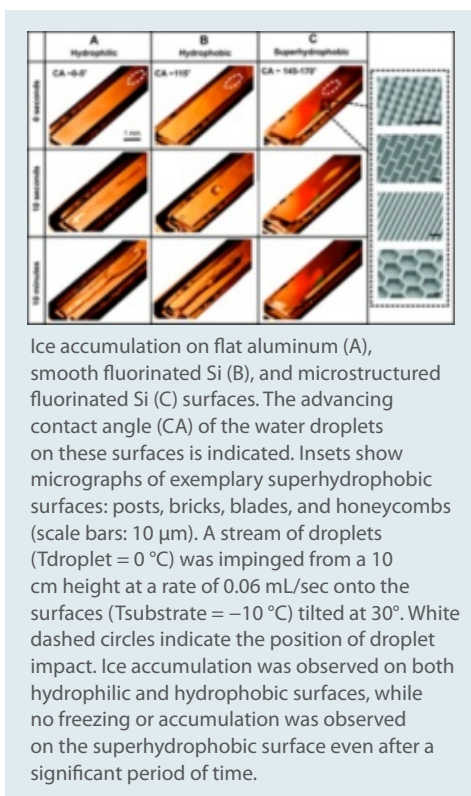
Nanoparticle-based materials that are stronger and cleaner than traditional materials are making appearances on the construction scene, but many commercial applications are still in their early stages. One example is nanostructured particles of titanium dioxide, which are used to make brighter, cleaner, and stronger building materials. The particles, when mixed with concrete, give the material a bright white hue. Not only do the materials start off white, but the nanoparticles help them stay that way, thanks to their ability to catalyze the oxidation of organic grime in the presence of UV light. Researchers have found a synergistic effect in the nanoparticle-concrete mixtures: the porous concrete causes pollutants to gather, and the nanoparticles help them decompose. The particles also clean the surrounding air, eating up smog with the same photocatalytic mechanism they use to self-clean. Companies developing construction titanium dioxide-based materials are working on boosting performance and lowering costs. For example, Italcementi, a company that sells cement containing a smog-eating nanostructured substance known as TX Active, has ongoing efforts to improve the material and make it more affordable.<sup>31</sup>

Researchers are also working on ways to use nanotechnology to make concrete less brittle, more sustainable, and faster hardening. Some groups are exploring the use of carbon nanotubes and nanofibers to make cement and concrete more resistant to cracking. Others have developed a way to use a by-product of coal production known as “fly ash” in place of cement, combining it with nanoparticulate silica to make more durable, faster-hardening concrete.<sup>31</sup>

Other applications at the intersection of nanotechnology and construction include improved façade paints, corrosion-resistant steel, and self-cleaning windows. Paint made with organic plastic polymer and nanoscale silica particles has improved water-repellent properties and resists both cracking in cold weather and getting tacky in hot weather. Steel made with alternating nanoscale layers of two different steel crystal forms has been shown to be more ductile, less prone to corrosion, and stronger. Glass coated with a thin, clear layer of titanium dioxide nanoparticles both photocatalyzes the oxidation of organic grime and makes the surface hydrophilic, causing water to run down it as a sheet and wash away dirt. Nanoscale coating of other materials, such as silica, silicon, or fluorine-doped tin oxide, can help regulate the amount of heat that comes through or escapes, reducing heating and cooling costs.<sup>31</sup>

Although not yet at the stage of commercial development, researchers have demonstrated nanostructured surfaces that help prevent supercooled water from freezing. This work may lead to the development of new ice-repelling materials for buildings, as well as airplanes, pipelines, and power lines.<sup>32</sup>





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Nanotech scientists and engineers expect future investigations will include the exploration of carbon nanotubes for making stronger, lighter materials, and the development of nanoscale sensors for detecting damage within a structure.<sup>33</sup> A recent report demonstrates the potential of such future applications: with the help of an infrared spectrometer, a nanotube-based paint reveals structural strain before the damage can be seen by the naked eye.<sup>33</sup>

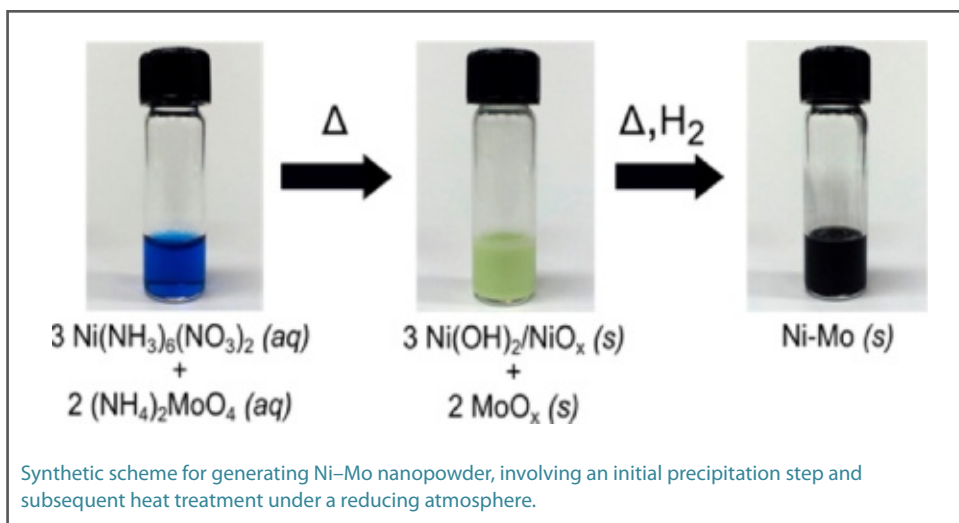
Despite the many attractive properties of nanomaterials for construction, the incorporation of nanoparticle-based building materials has been slowed by the higher costs compared to traditional materials, and by the fact that research funding for construction applications can be hard to come by. As nanomaterials become more popular at construction sites, concurrent investigations into the safety of these new materials will be essential to avoid adverse environmental and human health consequences.<sup>31</sup>

## IV. Nanotechnology Supports Basic Chemical Research

Beyond applications in medicine, industry, and everyday life, nanomaterials are helping support basic research efforts in chemical research labs. Chemists are among those taking advantage of nanoscale materials to help boost reaction rates, increase synthetic yields and purity, enhance chemical sensing capabilities, and gain better control over crystal growth. For example, a research team from China's University of Science & Technology have found that certain types of palladium nanocrystals can activate oxygen and catalyze oxidation reactions with organic compounds. The team found palladium nanocubes specifically could selectively catalyze the oxidation of glucose leading to the death of human cervical cancer cells, suggesting the particles' potential to both boost reaction rates and help in the fight against cancer.<sup>34</sup>

Others have found that synthesizing catalysts in the form of a nanopowder can help boost their catalytic activity. In one study, researchers from the California Institute of Technology created a nanopowder of a nickel-molybdenum catalyst that generates hydrogen from water.

Chemists are interested in nickel-based catalysts because they are more cost-effective and have comparable activity compared to traditional noble-metal electrocatalysts. Now, with the ability to create them in the form of a nanopowder, the catalyst is more easily processed and can be studied in better detail.<sup>35</sup>



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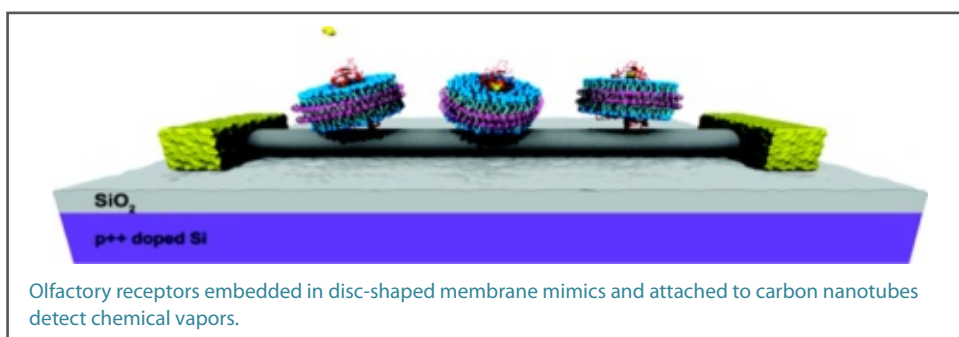
Scientists have also found that immobilizing catalysts within nanotubes can improve their activity. Platinum is a well-known catalyst for asymmetric hydrogenation in organic chemistry. Researchers at the Dailan Institute of Chemical Physics in China demonstrated that, when platinum nanoparticles are adsorbed onto the interior of carbon nanotubes rather than onto the outside, the nanotubes drive asymmetric hydrogenations more effectively – both faster and with greater enantiomeric excess.<sup>36</sup>

Nanomaterials are also having an impact in the world of chemical sensing and analysis. Researchers have found that carbon nanotubes deposited onto the surface of gold electrodes can be used to detect ethylene (a compound that signals fruit ripeness) by transmitting a signal proportional to the amount of the chemical present. These low-cost, carbon nanotube-based sensors may one day replace more expensive analytical techniques, such as gas chromatography and mass spectrometry, for monitoring fruit freshness.<sup>37</sup>

Carbon nanotubes, when paired up with enzymes in a field-effect transistor, can also be used to electronically monitor the enzymes' movements over long time periods, as demonstrated by researchers from the University of California, Irvine.<sup>38</sup> This is something that's challenging to do with traditional fluorescence techniques for enzyme monitoring because photobleaching can reduce the observable signal over time.

Inspired by the sniffing abilities of the mammalian nose, researchers at the University of Pennsylvania developed a method for tethering olfactory receptors, which detect chemical vapors, to carbon nanotubes. These odor-detecting nanotube transistors act like a synthetic

nose, producing an electrical current when in the presence of a vapor stream that contains different odorant molecules. The device contained three different olfactory receptors, while a mammalian nose contains hundreds. Future work is needed to increase the sensor's complexity, to make the devices stable for longer periods, and to achieve higher levels of sensitivity.<sup>39</sup>



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When it comes to growing crystals in solution, one of the difficulties scientists encounter is controlling the resulting crystal size. Recently, Northwestern University's Bartosz A. Grzybowski and coworkers found that when nanoparticles with opposite charges are mixed together and added to a solution of a salt or molecule, they adsorb onto the surface of the microcrystals and help slow down the crystal growth process. With these nanoparticles, the team found they could control the final size of the crystals by altering the pH of the solution and the ratio of the nanoparticle concentration to the concentration of the salt or molecule.<sup>40</sup>

Thanks to advances in nanoscale imaging, scientists can also watch nanocrystals as they grow, at a resolution that was not previously possible – down to the sub-nanometer level. The technology has enabled researchers to learn, for example, that nanosized particles grow into larger crystals by undergoing subtle reorientations that cause their lattices to become aligned.<sup>41</sup>

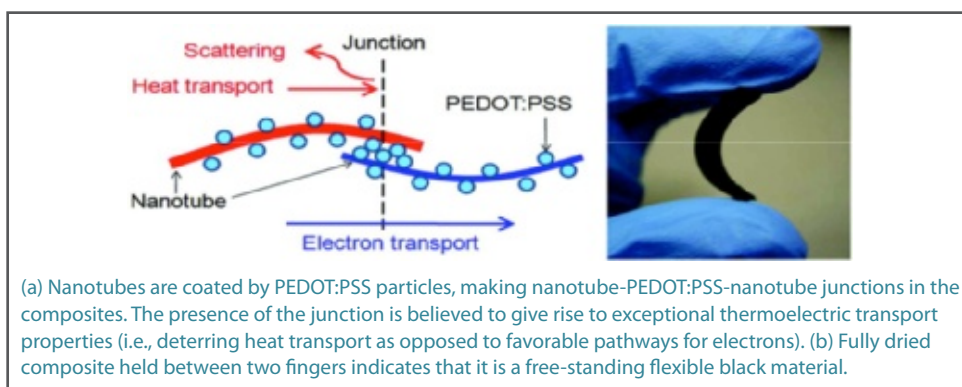
## V. Smaller is Better: Nanotechnology's Role in Shrinking Electronics

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For more than a decade, scientists and engineers have sought to incorporate carbon nanotubes, or CNTs, into electronic circuits.<sup>42</sup> Early on, the primary challenge was identified to be finding a way to separate out the useful semiconducting tubes from the troublesome metallic ones, in order to build reliable circuits. The first demonstration of CNT electronics was accomplished when researchers found a way to selectively decompose the metallic tubes, leaving behind semiconducting nanotubes and creating an array of CNT-based transistors. That report and many others that followed gave researchers hope that CNT electronics would soon replace silicon-based electronics, whose component sizes are limited by what lithographic patterning techniques can achieve.<sup>42</sup>

Although this dream has not yet become reality, researchers still hold out hope and say chemists have a role to play in overcoming the obstacles that stand in the way. The biggest challenge, experts say, is creating a scalable and reliable method for the production of high-purity semiconducting nanotubes.<sup>42</sup> This is no small feat: high-performance logic applications, which will require billions of transistors integrated on a chip, need metallic CNT impurities to be less than 0.0001 percent, but statistical analyses indicate that 33 percent of all CNTs are metallic.<sup>43</sup>

Some researchers are hoping that teaming up CNTs with other types of nanomaterials will help improve outcomes. One team from Texas A&M University used CNTs combined with organic polymers to make flexible thermoelectric materials. These flexible materials, which are also nontoxic, light-weight and low-cost, may one day replace brittle inorganic materials that are currently used in applications such as commercial solid-state cooling and conversion of waste water to electric power.<sup>44</sup>

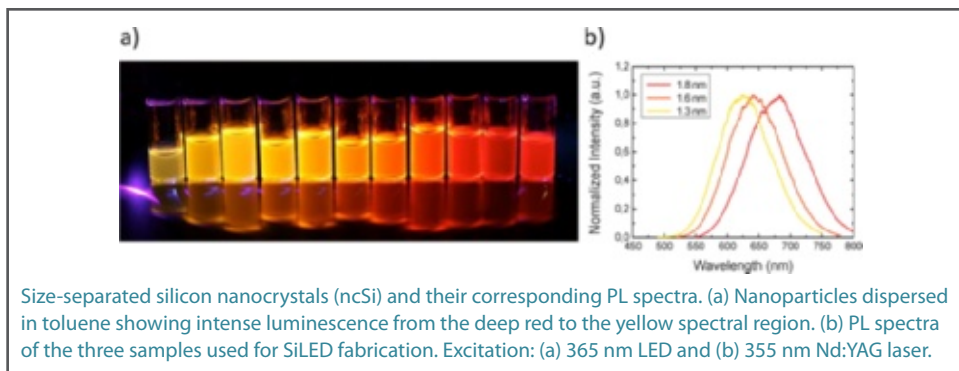


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In 2012, scientists at IBM reported using a chemical self-assembly process to pattern CNTs onto a silicon wafer. Using the new method, the team created hybrid silicon-CNT chips with more than 10,000 transistors that outperformed switches made from other materials.<sup>45</sup> Others are using CNTs as a starting material for creating nanoribbons of graphene, which have unique electronic properties and hold promise for applications ranging from electronic devices to composite materials and tissue regeneration.<sup>46</sup> A plethora of other nanomaterials are also coming onto the electronics scene, including nanowires, nanocrystals, and variations of carbon nanotubes in the form of fibers and yarn. In the hopes of achieving greater computing power than what is attainable with silicon-based devices, researchers have looked to polymer nanowires. One team used the wires to create extremely small electrical circuits, using a technique known as “chemical soldering” to link the nanowires to single molecules with the help of a scanning tunneling microscope (STM) tip.<sup>47</sup>

Nanoscience researchers are hoping advances in nanomaterials science may result in safer materials that can replace the toxic metals in devices such as computers and television

display screens. Semiconducting inorganic nanocrystals, known as quantum dots, are typically made with heavy metals, and they have qualities that make them ideal candidates for light-emitting diodes, such as those used in computers and televisions. A recent report from researchers at the University of Toronto and Germany's Karlsruhe Institute of Technology shows that silicon quantum dots glow in different shades of red, orange, and yellow, depending on their size, and that they could be a safer alternative to metal-based nanocrystals. More work is needed to improve the efficiency of the silicon-based devices at converting electricity into light, and to create smaller particle sizes that will enable the fabrication of devices in additional colors, such as green and blue.<sup>48</sup>



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Carbon nanotubes have been found to be capable of some heavy lifting – even carrying up to 100,000 times their own weight - when created in the form of a yarn with a solid wax filler. Ray H. Baughman of the University of Texas, Dallas and coworkers demonstrated the use of nanotube yarns in an electrically activated catapult.<sup>49</sup> Another team found that spinning nanotube fibers can result in extremely thin threads that can carry objects one million times their weight while conducting electricity. The fibers could one day be used in aerospace electronics and long-range power transmission applications.<sup>50</sup>

## VI. The Untapped Potential of Nanomaterials

While nanoscience researchers in many fields begin with the end goal in mind (such as creating a better drug, or developing a more powerful transistor), others set out with a more exploratory mindset. Researchers in the latter camp, although they may have some ideas about where their work will ultimately make an impact, seek to create nanomaterials with new and interesting properties with the confidence that, in time, they will find a research question to answer or a technological obstacle to overcome.

Nanostructures composed of biomolecules and molecular machines made from synthetic molecules are among the nano-players whose applications scientists are just beginning to discover. But the unique properties and capabilities of these structures have many scientists

optimistic about the impact they will have in applications ranging from basic biological studies to nanomedicine and electronics.

## DNA NANOTECHNOLOGY

Among the up-and-coming nanoscience research areas is the field of DNA nanotechnology, where nature's information storage molecules are used as the building blocks for nano-sized patterns and objects. Although much of the work in the field remains at the exploratory level, several demonstrations of functional DNA nanostructures highlight the potential of the tiny structures to lead to the development of advanced functional materials and other commercially viable applications.<sup>51</sup> Several properties make DNA an ideal molecule to work with, such as its predictability, stability, and versatility. Researchers can be confident that a strand with a certain sequence of nucleic acids will pair up with a complementary strand to form a DNA double helix. DNA can also be modified relatively easily and is durable and stable over time.<sup>51</sup>

In 2006, nanostructures known as DNA origami made their first appearance in the research literature, when a team led by Caltech's Paul W. K. Rothemund demonstrated the creation of memorable shapes such as smiley faces and three-dimensional polyhedrons.<sup>51</sup> The structures are fabricated through the self-assembly of a long strand of bacteriophage DNA, which is about 7,000 nucleotides long, with shorter "staple" strands of DNA, whose sequences are selected in such a way that yields the desired structure. Although visually appealing, clear applications of the structures were not apparent at the time.

Since those initial reports, research teams have demonstrated a handful of practical DNA-origami-based devices. One example is a membrane pore that controls the passage of ions.<sup>52</sup> The nanopore, modeled after the bacterial ion channel  $\alpha$ -hemolysin, self-assembles within a lipid membrane, and may one day be developed into an antimicrobial agent, drug delivery vehicle, or molecular device for sensing purposes.

In another study, Harvard Medical School's George M. Church and coworkers demonstrated the creation of a nanoscale robot that delivers deadly drugs specifically to cancer cells.<sup>53</sup> The DNA nanobot carries the therapeutic payload inside a hexagonal barrel tethered to DNA aptamers, which serve to both hold the barrel together and direct the structure to cancer cells. Researchers hope targeted delivery of cancer drugs to diseased cells with nanobots will help lower toxicity and side effects of cancer therapy, but DNA-based therapeutics will first need to prove they can hold up inside a living organism and be more effective than current treatments. Other examples of functional DNA-based devices include a DNA nanochip for performing single-molecule studies on a DNA-binding enzyme, a DNA nanopore for controlling the passage of macromolecules, and a DNA nanostructure that controls gene transcription.<sup>54</sup>

DNA origami technology is powerful, and more applications will come with time, experts say.<sup>51</sup> The ability to create tiny biopolymer-based structures with great precision could lead to the creation of nanodevices for studying other biological molecules, help answer basic questions

about how molecules and cells are arranged on the nanoscale, and shed light on the forces that are involved in their interaction with one another. Nanoscale objects may also be developed into drug delivery vehicles or devices that mimic organisms' way of catalyzing chemical reactions in sequence to create complex molecules.<sup>55</sup>

Among the challenges of working with DNA is the difficulty to obtain high yields with high quality. Additionally, while DNA nanostructures are typically created in solution, many applications will require precise positioning of the structures onto a surface.<sup>51</sup> This challenge has led one research team to look to computers for help.<sup>56</sup> The researchers created nanoscale drawings using a DNA canvas, which were designed to leave holes in predetermined shapes that could then be filled by other DNA strands. This modular approach can create nanostructures faster than DNA origami and other DNA sculpting methods.

## PROTEINS AND BIONANOTECHNOLOGY

DNA is the biomolecule of choice for some researchers, who appreciate its stability and predictability. But others are looking to proteins, which they argue are structurally and functionally even more versatile than DNA or RNA, since there are 20 amino acids to choose from to build proteins, compared with DNA's four nucleic acid building blocks.<sup>56</sup>

Working with proteins comes with its own set of challenges, most notably the difficulty in predicting what structure will result from a given protein sequence. Compared with DNA nanotechnology, protein bionanotechnology is in its infancy, and there are far more examples of nanoscale objects made from DNA than from proteins. But two back-to-back demonstrations of protein-based nanoscale containers reported in 2012 highlight the potential of proteins to make an impact in the field of bionanotechnology.<sup>56</sup> One research team demonstrated the first self-assembling synthetic nano-container made of protein subunits, and another team developed a computational program capable of predicting which protein sequences might yield a cage structure, and then demonstrated the creation of two of these predicted structures.

## MOLECULAR MACHINES

Single-molecule machines, once considered to be a far-fetched idea, have become a reality in recent years. Researchers have now shown they can create molecular motors powered by light, chemical reactions, or electricity.<sup>57</sup> Molecules known as chemical nanoswitches and nanofuses can undergo reversible or irreversible chemical reactions when hit with electricity.<sup>58</sup> Inspired by biological molecular machines that exhibit modular design and dynamic assembly, other researchers have designed and synthesized molecular shuttles made from mechanically interlocking molecules.<sup>59</sup>

In another example, a team led by Ben L. Feringa from the University of Groningen, present a nanocar, a single-molecule device that "drives" across a copper surface at extremely low temperatures (7 Kelvin, or about -447 degrees Fahrenheit) powered by electrons that come from



the tip of an STM.<sup>60</sup> Previous reported nanocars moved randomly or required an STM tip to drag them along, but this molecular machine was shown to move in a single direction thanks to the molecule's stereochemistry. Future work will involve achieving movement under ambient conditions, introducing cargo, and using light to drive the nanocar.

Still others, inspired by naturally occurring protein motors such as those that shuttle cargo throughout cells and pull chromatin apart during cell division, have been working to create molecules that can “walk” along a surface.<sup>61</sup> The earliest efforts used DNA to make a synthetic walking motor; more recently, tinier small-molecule-based motors have been reported. Molecular walkers can be powered by using interfering DNA strands, the pH of a solution, or light that switches the stereochemistry of a molecule to create motion.<sup>62</sup> Strolling molecules that accomplish a specific job are fairly new to the scene. In 2010, researchers led by New York University's Nadrian C. Seeman presented a DNA-based walker that could carry gold nanoparticles, and another team led by David R. Liu of Harvard University demonstrated a DNA walker capable of performing basic synthetic chemistry reactions.

One of the greatest challenges with molecular walkers is gaining control over the molecules' directionality. At the molecular level, Brownian motion acts as a powerful force threatening to literally sweep walking molecules off their feet, dislodging them from the surface into solution. As continued progress is made, molecular machines may one day serve as components in molecular devices for applications including nanoscale electronics, nanomechanical devices, and nanomedicine.

## VII. Nanomaterials in the Environment: Health and Safety Concerns

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Nanomaterials have become increasingly popular in consumer products over the past decade; more than 1,000 products containing nanomaterials are now on the market, according to a 2011 report in *Chemical & Engineering News*. Nanomaterials have made their way into numerous commercial products used in everyday life, including sunscreen, food packaging and cosmetics.<sup>63</sup> A nonprofit corporate accountability group is concerned over the use of nanomaterials in food products without the data to demonstrate their safety,<sup>64</sup> and concern from both consumers and scientists has grown over both the short- and long-term effects of nanomaterials on human health and the environment.<sup>63</sup> Researchers have found that not only can nanomaterials be transferred between organisms, they can increase in concentration as they move up the food chain – a process known as biomagnification.<sup>65</sup> Scientists believe biomagnification is the result of organisms' inefficient excretion of the foreign substances, and that it will vary for different types of nanoparticles, depending on their physicochemical properties, such as their hydrophobicity or whether they tend to aggregate into clusters. The presence of alumina nanoparticles also promotes the transfer of genes encoding antibiotic resistance between bacterial cells. Bacteria

are capable of transferring genes without the help of the particles, but the particles boost the transfer rate by up to a factor of 200, prompting concerns about the increasing use of nanomaterials in commercial products.<sup>66</sup>

Other studies have found nanomaterials can have a negative effect on fish reproduction.<sup>63</sup> Today's chemical safety standards are based on acute toxicity levels, but some experts are concerned that chronic exposure to low levels of nanomaterials can have worse, cascading effects on aquatic life than one-time exposures to high levels.<sup>63</sup>

In mammalian cells, polystyrene nanoparticles, which are generally nontoxic, have been found to disrupt cell membranes and cause increased iron uptake. In the same study, Cornell University's Michael L. Shuler and colleagues found that acute nanoparticle exposure resulted in less iron uptake in chickens than chronic exposure or no exposure.<sup>67</sup>

Nanoparticles have been shown to be able to cross the placental barrier in pregnant mice, and to cause neurological damage to offspring. But more recent studies have also found that upon injection, certain nanoparticles can cause pregnancy complications in mice, including smaller uteruses and fetuses. Nanoparticle size and composition seemed to play a role in whether the complications were observed. For example, functionalizing particles with carboxyl or amine groups abolished the negative effects of the otherwise troublesome particles.<sup>68</sup> Chemists are working to address some of the concerns over nanoparticle safety by exploring the effect of surface functionalization on toxicity. Previous studies had found that carbon nanotube fibers trigger a toxic response in mice similar to that caused by asbestos, but researchers have found a way to render asbestos-like nanotube bundles harmless by modifying the surface to present hydrophilic chains with a terminal amino group. They presume the reduced toxicity is the result of the particles remaining better dispersed due to their surface chemical properties.<sup>69</sup>

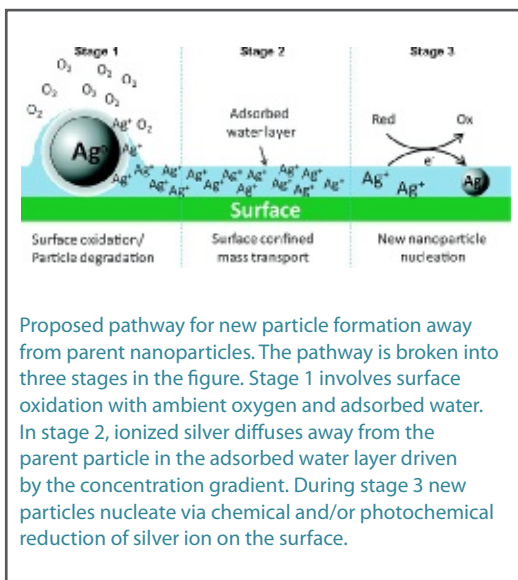
## NANOTECHNOLOGY IN EVERYDAY LIFE

Over the years, nanomaterials have made their way into numerous consumer products. Nanoparticles in sunscreen, cosmetics, and other personal care products absorb harmful UV rays to minimize skin damage from UV exposure. Silver nanoparticles in food packaging serve as antibacterial agents to help keep food fresh for longer. Nanoscale hydrogels enable diapers to hold more liquid and keep babies' bottoms dry. Nanotechnology provides eyeglasses with a thin protective anti-fog layer that also makes them easier to clean. The website for The Project of Emerging Nanotechnologies (<http://www.nanotechproject.org/inventories/consumer/>) provides a searchable inventory of nanotechnology-based consumer products on the market.<sup>74</sup>

In recent years, sunscreens made with zinc or titanium dioxide particles have become more common, because they tend to last longer and be less irritating to sensitive skin than traditional sunscreens made from UV-absorbing organic molecules. One unfortunate downside to initial formulations was the pasty white appearance that resulted from the inorganic particles' ability to scatter not only UV, but also visible light. Newer formulations have turned to smaller, nano-sized particles, which scatter less and are more transparent. But concerns over the ability of inorganic nanoparticles to generate free radicals that can damage skin, as well as pass through skin and possibly enter into the bloodstream, have come to the attention of toxicologists and some consumer groups. A recent surge of studies have focused on scrutinizing the safety of these newer sunscreen formulations.<sup>75</sup>

The Food & Drug Administration does not currently require companies to specify the kinds of nanoparticles in their products. In April 2012, the FDA released guidelines encouraging companies to label products, such as food packaging and sunscreen, with information about the nanoscale materials they contain, but the agency denied a petition from a consumer advocacy group to require both labeling and safety testing prior to the release of nanoparticle-based products onto the market.<sup>76</sup>

Such studies on the effects of physicochemical properties on nanomaterial safety have led a team from the University of California, Los Angeles, to create a model for predicting nanoparticle toxicity by just knowing the particles' water solubility and electronic properties. The model involves semiconducting metal oxide nanoparticles, such as those used in fuel cells and electronics.<sup>70</sup>



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But other researchers believe that more work needs to be done before conclusions can be made about the safety of nanomaterials in the food chain, especially since most studies have looked at the effect of nanomaterials at levels much higher than what is expected in nature. Some in this camp suspect that people have been exposed to incidental metal nanoparticles in the environment for millennia without noticeable harm. A team of chemists from Dune Sciences and the University of Oregon recently performed an analytical study that supports this idea. They found that under certain conditions, both synthetic metal nanoparticles and macroscale metal objects slough off ions, which then combine to yield the new particles. The

study involved the use of advanced analytical instrumentation, including electron microscopy and scanning probe microscopy, to directly observe the weathering of both silver and copper materials.<sup>71</sup>

Funding for nanotechnology safety research increased from \$34.8 million to \$117 million between 2005 and 2011, but technological developments are still currently outpacing the research on their safety.<sup>63</sup>

## VIII. Conclusions: The Future of Nanoscience

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As research in nanoscience and nanotechnology presses on, the world can expect to see ever-smaller electronic devices, new approaches to combating cancer and disease, more advanced tools for biomedical imaging, and a surge of new commercial products and technologies that impact everyday life. Studies on the impact of nanomaterials on human health and the environment are increasingly important as more companies look to nanotechnology to boost their product performance. Chemists will continue to play a central role in making nanomaterials more effective, affordable, scalable, and safer for their widespread applications.

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