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Perspectives on 21st Century Technology: The Nano-BIO-Info Convergence

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I. Introduction

Three converging 21st Century technologies will materially change how we live, how well we live, and above all, how long we live. Some of these technologies are bearing low-hanging fruit right now; others involve benefits that will be ready to drop in a decade or so. Still another group of blessings will accrue primarily to your great grandchildren. The three converging technologies in question are nanotechnology, biotechnology and information technology (see Chart 1).

Nanotechnology operates in the realm of the incredibly small. It is not to be confused with the older, more widely known, top-down approach called miniaturization. Nanotech devices and materials are ordinarily built from the bottom-up, one molecule or even one atom at a time. Nanotechnology involves the measurement, manipulation and fabrication of objects of size from one nanometer to about 100 nanometers. A nanometer is one billionth of a meter. My thumb is about 10 million nanometers wide. If we could shrink a mare to one nanometer in height, her newborn colt would be about one atom high. As we will see, the size and shape of nano-particles account for a large number of their highly useful applications. One particularly important property is that in the nanoworld, as we move to the nanoscale the surface area of material increases relative to volume, and at the nanoscale soft material can become ultra-strong. Insulators can be made conductive. Opaque materials can become transparent. Eventually scientists expect that they will even be able to manipulate the inner workings of molecules yielding applications not yet imagined.

Biotechnology enfolds innovations in biomedicine, agriculture and now even new innovations in information technology. It has become tightly interlaced both with nanotechnology and information technology generally. The information technology revolution that brought the age of computing now promises to combine with nanotechnology to yield another new age of quantum computing.

The effects of convergence of these technologies will be far-reaching, with potential social and economic benefits that are very, very large. However, these technologies also carry future societal risks and perils. Time constraints, however, dictate that I focus today primarily upon the promise, not the perils of these converging technologies.

II. Some of the Future is Already Here

Sir Arthur C. Clarke was a scientific visionary who conceived in 1945 the idea of orbiting earth satellites. He was also a widely read author of such science fiction as 2001: A Space Odyssey. Not long before his death in 2010, he left us with this thought: "Any sufficiently advanced technology is indistinguishable from magic." To illustrate his insight, I share with you some recent technological developments in nanotechnology that until now were found only in Science fiction, not Science itself.

These include:

1) Cloaking devices to make an object invisible.

2) Harnessing of anti-matter.

3) Detection of medical problems before external symptoms appear.

4) Cyborg Tissue.

Fruitful combinations of nano-bio- and information technology are yielding some astonishing "Star Trek moments" even now.

1) Cloaking Devices

Scientists now realize that Einstein's idea of curved space-time might someday provide invisible cloaks using curved space to hide objects (Science, Jan. 2, 2009). Armed with this idea, nanotechnologists have shown that a shell composed of certain nanoparticles can reroute light around an object in the way that water streams around a boulder. As a result, the object becomes invisible, in at least one direction. And, in 2010 scientists in Germany and Britain reported the realization of a 3-dimensional invisibility cloak (Science, April 16, 2010).

In a related discovery, researchers at Rice University have applied the light bending properties of nanoparticles called Nanocups to make 3-D nanoantennas that may result in very sharp gains in the efficiency of solar panels. And as Prof. Naomi Halas says, "The most interesting application of nanocups is something we haven't thought of yet."

2) Antimatter

The legendary physicist, Paul Dirac won the 1953 Nobel Prize in Physics for his discovery of anti-matter. In 2011, researchers at my own university – Rice – detected the heaviest antimatter particle yet discovered: the antimatter partner of the helium nucleus, the anti-matter particle in the hydrogen nucleus having been found in 2008. While the extreme scarcity of antimatter remains one of the greatest mysteries in physics, recent discoveries allow the use of properties of anti-matter in medical imaging. And greater knowledge of properties of antimatter may change technology in ways we cannot fathom at present.

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CHART 1
Technological Linkages Nano-Bio-Info Convergence

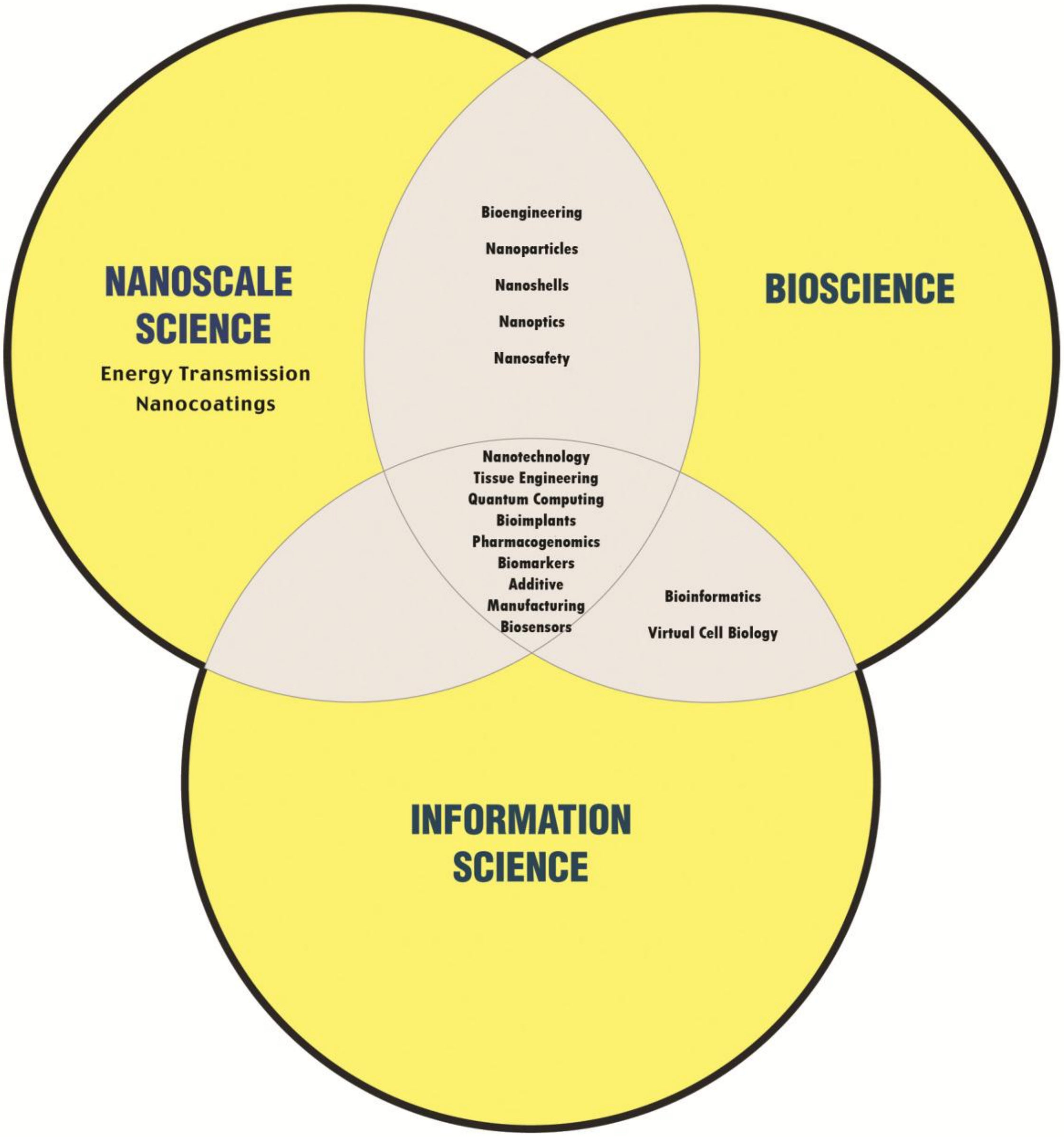

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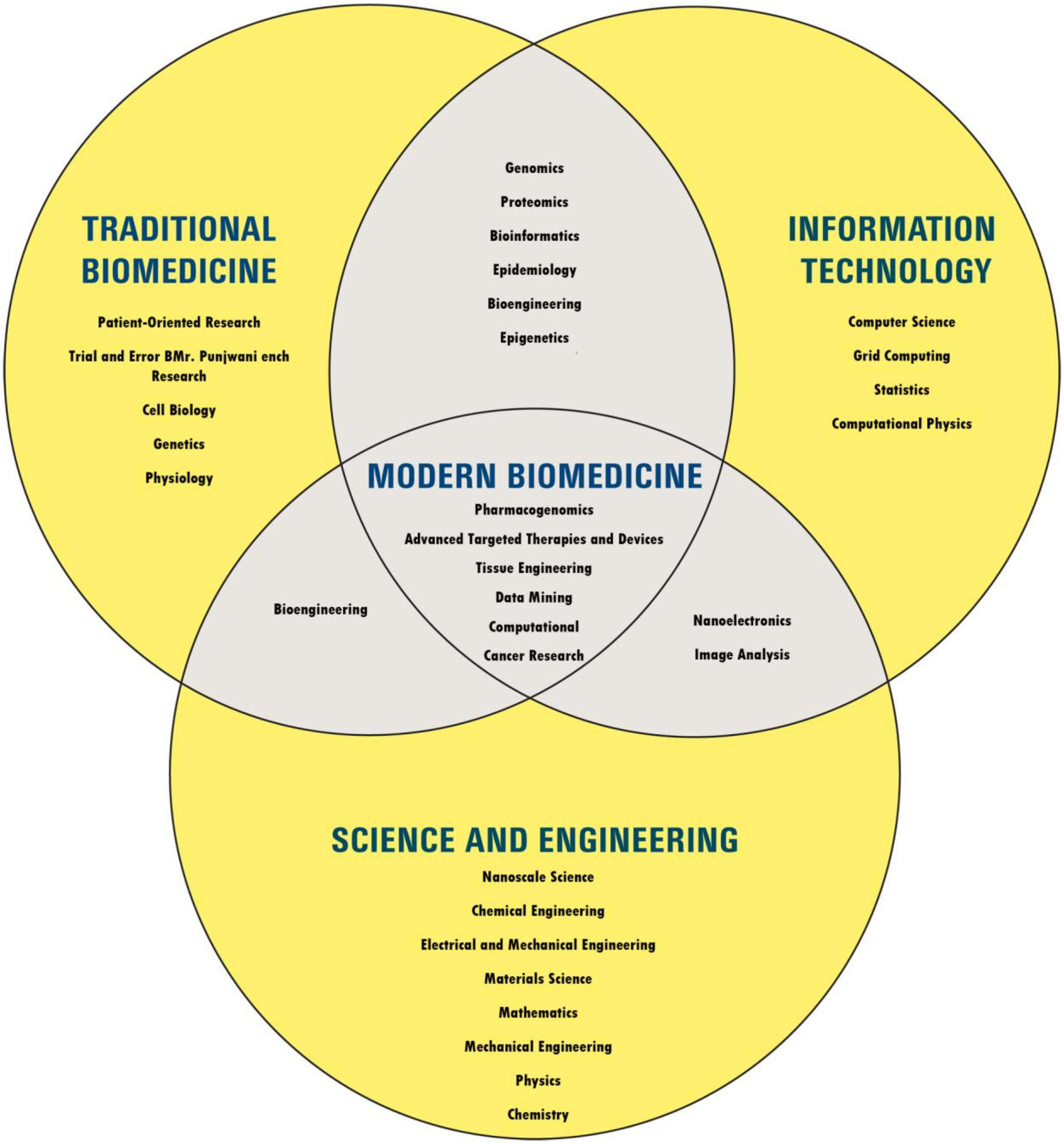
CHART 2
Modern Biomedicine and Some Nano-Bio-Info Interfaces



3) Lab-on-a-Chip

The convergence of nano-bio-info has yielded a chip that may transform the practice of medicine, partly by helping to diagnose medical problems before symptoms appear. This is discussed in greater detail later.

4) Cyborg Tissue

In September 2012, researchers announced the merging of nanoscale wires with human tissue. This is also discussed at greater length below.

III. Technological Change in Historical Perspective

For half a millennium, technology was central to growth and prosperity in the Roman Empire. For the foreseeable future, technological innovation will be the defining factor in economic growth.

Historical evidence old and new testifies to the technological prowess that underlay Roman prosperity and hegemony until the end of the fifth century A.D. The centuries after the fall of the western half of the empire were followed by economic retrogression and pervasive human misery culminating in The Dark Ages. There was almost no net growth in world population and zero growth in per capita income. Not coincidentally, this was also an era of technological stagnation in almost all fields except warfare.

Circumstances improved slightly from 1500 to 1800, as per capita income worldwide began to grow very slowly. Still even by the beginning of the 19th century, life for most humans everywhere was nasty, brutish, and above all, short. Then came the waves of technological innovations that ignited the industrial revolution. From 1820 to 1980 per capita income in the industrial West grew by 13-fold, owing primarily to the startling jump in productivity made possible by education and technical change.

The pace of technological change quickened measurably after 1980 as the electronic revolution began to supersede the industrial revolution. Then, the discovery of the double helix, carbon 60 (the buckeyball), and accelerated innovation in information science ushered in startling advancements in biology and nanoscale science. One telling illustration of recent progress in medical science: thirty years ago, a physician had only <u>one</u> reliable way to detect prostate cancer: the tip of his finger. And there was only one treatment: surgery, which was often ineffective. Now, using biomedical devices borne of the union of nanotechnology and information technology, the detection and successful treatment of this pervasive form of male cancer utilizes ultra advanced imaging and laser techniques unknown even a decade ago, with heartening gains in detection and improvements in survival rates.

The emerging coalescence of biotechnology, nanotechnology and information technology holds out prospects for economic and social benefits that could make those of the past half century appear pale by comparison. (See Chart 1) Note: I do not refer to breakthroughs that may be made "one day," but rather applications from science we <u>already</u> know, the fruits of discoveries already made.

Advances in molecular-level science furnish ample justification for this claim, not only in biology, but in nanoscale science and information science. Virtually all the molecular rungs on the chemical ladders of the human genome have been identified. So we now have an almost complete "parts list" for a human and some animals. Now science is learning how all the parts work together.

There is another, related, revolution going on at and below the molecular level, in information science and nanotechnology. This revolution capitalizes upon our growing understanding of the once forbidding world of quantum mechanics. This is enabling unexpected, rapid advances in quantum computing, which may endow laptops of year 2025 with more computing power than millions of today's super computers. The age of computing has been with us for only a quarter century. A new age of quantum computing may have begun in 2007, with the announcement of the world's first practical quantum computer (Economist, Feb. 17, 2007).

The biomedical implications of the ongoing marriage of computational sciences and nanotechnology are especially auspicious. In 25 years, powerful, ubiquitous microscopic computers may be used as implants as sensors to monitor our bodily systems, to forecast weather, etc. And of course, everything in nanotechnology goes on at the molecular or atomic level.

How can we best develop useful perspectives on the rapidly evolving, converging fields of biotechnology, information technology and nanotechnology? It helps to know that technological revolutions hardly ever proceed smoothly, but rather in unpredictable fits and starts.

This is partly because innovations must become widely diffused to have any significant economy-wide impact. This takes time. Steam, after all, brought significant economic benefits only decades after Watt improved Lycoming's steam engine. Biomedical examples abound. C-reactive proteins were found decades ago to indicate liver disease, but only now are they widely used as a marker for cardiovascular risk. Sonar was developed for submarines during WWII, but forty years passed before clinical ultrasound imaging was developed. Carlson found a way in

1938 to make an exact replica of a document, but it took 22 more years for his discovery to surface as the Xerox machine.

Technological advancement proceeds through many channels, sometimes involving disruptional displacement of markets, other times expansion of existing markets, and sometimes creation of entirely new markets. However it proceeds, the convergence of bio-nano-info clutch of technologies foreshadows a grand technological synthesis that will materially change the human condition.

First, let us consider nanotechnology in isolation.

IV. Nanotechnology- Wet and Dry

Nanotechnology

Nanotechnology has been heavily hyped, with some excessive claims. Still, it seems safe to say in 2012 that never before in history has one technology been so filled with promise, nor so potentially powerful, nor has any technological revolution happened as quickly. At the nanoscale, the boundaries separating traditional scientific and engineering disciplines become blurred to the point of non-existence. Therefore nanotechnology must draw on many fields: physics, chemistry, mathematics, biology, computer science, engineering and clinical science. Much of nanoscale science and its growing applications are situated on the borderline or below the familiar world of classical physics and the spooky realm of quantum mechanics. To begin to understand the forbidding world of quantum mechanics, one must accept as an article of faith that which can be shown mathematically: that a sub-atomic particle can be in two places at once. Two electrons, for example, establish a kind of telepathic link that transcends space and time.

This is called quantum entanglement, long understood to apply in the inorganic world and now perhaps in biological systems.

Research focused on the nanoscale has uncovered new phenomenon that display properties of matter never before observed. Consider that the properties of matter change when taken down to nanosize. If the material in aluminum can be reduced to 25 nanometer size it would become pyrophoric, and explode spontaneously. Another manifestation: quantum dots two nanometers wide have different properties than those six nanometers wide: the former glows in blue light, the latter shines in red.

Nanoscientists and/or nanotechnologists work in either "wet" or "dry" nanofields. The dry, waterless side points toward valuable applications in energy efficiency and materials science, owing to the fact that some forms of carbon nanotubes are far stronger than steel, at one-sixth the weight as conductive as copper by volume and much better by weight.[1] The "wet side" (discussed in greater detail below), centers on study of biological systems that exist in a water environment such as human cells. And since everything that goes on in a human cell is nanotechnology, some go so far as to assert that most of 21^{st} century biotechnology is a subset of wet nanotechnology.

Generally, nanotechnology applications are growing quite rapidly in the energy industry. Nanotechnology is being deployed to remove contaminants from the huge amounts of produced water that results from hydraulic fracturing of oil bearing formations (see paper #2).

[1] I note in passing that there are some quite unusual applications on the dry side, including Nano-ice, invented in Iceland, appropriately enough, in 2001. The process uses nanoparticles that eliminate the airpockets so detrimental to conventional freezing techniques. As a bonus, Nano-ice uses 90% less refrigerant and 70% less power than today's ice-making machines. (Reference).

- Nanomaterials such as graphene oxide are available to treated produced water for radioactive contamination. This can occur when oil wells pierce uranium bearing formations, such as the Chattanooga shale.

- Scientists at Rice University have developed a nanoparticle that absorbs 100% of its weight in carbons, and can therefore be used for CO_2 capture.

- Another group of scientist there have developed a sponge made of carbon nanotubes to soak up oil spills, in cold or warm water (see Hashim et. al. Scientific Reports, Vol 2, Article #363, April 13, 2012).

- Other nanotech applications already in use in the energy industry include the use of nano-coatings to sharply reduce corrosion in casings and pipes in oil and gas wells, as well as nanocoatings to strengthen downhole materials subject to very high temperature and very heavy stress. One scientist at Rice is developing a nanocoating corrosion inhibitor that promises not only to be very effective, but at $3.50 per pound inexpensive as well.

- Nanoscale proppants are already being used to improve recovery of oil and gas from wells where hydraulic fracturing has been utilized. Proppants literally “prop open” fissures in rock so that oil and gas may more readily flow. The proppants in this case are nano-sized ceramic spheres with special density properties.

- Among important dry-side applications include those being developed at my own university merits mention: Nanowires for transmission and conservation of energy.

Composed of billions of carbon nanotubes, this nanowire is known as Armchair Quantum Wire (AQW). Research on this innovation has been underway for seven years, and is now attracting attention of business enterprises in the U.S. and elsewhere.

The AQW resembles chicken wire all rolled up, but it is a high strength wire made from pure carbon. One AQW would be about one to two centimeters thick, consisting of billions of single-walled carbon nanotubes (SWCNT), one of the members of a family of nanotubes measuring about two nanometers across.

Not only is the AQW stronger than steel, but at one-<u>sixth</u> the weight of steel it has up to ten times better tensile strength than other composite wires. Thus, it could support itself as a high-tension, high voltage cable. (Hartley, Medlock, 2011).

Here are but a few of the implications:

- Potential savings of as much as in of the energy cost of electricity, as transmission losses due to resistance are reduced.
- Usage of nanowires could increase the efficacy of <u>renewable</u> energy sources:
    - For <u>wind</u>, it would help end the stranding of capacity because of insufficient transmission capacity.
    - <u>Solar</u> energy from the desert could now be profitably transmitted to large urban areas.

<u>More Recent Discoveries – Dry Side</u>

New breakthroughs on the dry side of nanotechnology are reported each month. I present to you just four of these discoveries that have emerged just recently.

1. Strain Paint, Self-Healing Paint

Of the many other potential applications of carbon nanotubes in energy, construction materials, clothing and body armor, one of the most fascinating is "strain paint" that can reveal weakness in metal structures. Researchers at University of Strathclyde, in Scotland and Rice University in Houston have developed carbon nanotube paint that can identify microscopic faults arising from stress or fatigue in materials in buildings, bridges and aircraft. The Rice version of strain paint is a varnish like substance which displays fluorescence in infrared light. Each nanotube in the paint would undergo equivalent strain as the surface is painted. A handheld infrared spectrometers reads out the degree of strain in the structure.

A related application is self-healing paint. Nanomaterials have been developed for use as self-healing coatings for metals. Also, nanomaterials are being used as anti-barnacle coatings for ships hulls, with obvious implications for ship speed and energy conservation.

2. Nanofibers

Nanoparticles are already in widespread use in the clothing industry, for example to repel water and prevent stains. Now, a small amount of nanotube sheets has been developed that can be used to produce porous multifunctional yarns that are weavable, flexible and durable, and which also allow energy storage. This technology can be utilized to make yarns of superconductors, lithium-ion battery materials and catalytic nanofibers for fuel cells (Science, Jan. 7, 2011).

3. Nanomaterials with Viscoelastic Properties

A) <u>High Temperature Rubber</u>

One of the remarkable properties of carbon nanotubes is their viscoelastic behavior over a wide temperature range. (<u>Science</u>, Dec. 3, 2010). An example of a viscous item is honey. Viscoelasticity, among other properties, enables a material to dissipate energy, and also reversibly deform through elasticity (like a rubber band). Viscoelasticity is what allows polymer foam earplugs to adapt to any ear channel. Several other types of materials, such as amorphous polymers and a few metallic alloys exhibit viscoelasticity.

Materials made from carbon nanotubes display a very special type of viscoelasticity. Unlike rubber, which deforms permanently under very high temperatures, a mixture of several types of nanotubes (SWNT, DWNT, TWNT) yields a material that can recover its original shape after exposure to a very wide range of temperatures (as high as 1400°C for some mixtures and 300°C for others). (Reference coming).

These nanotube rubbers may soon be incorporated in such uses as wrinkle-free textiles, viscoelastic shoes and even in space vehicles that are constantly exposed to a very wide range of variable temperatures.

B) <u>Visoelaticity Sponges</u>

A scientist at Rice University has developed a nanomaterial made of carbon nanotubes doped with boron that can be utilized as a super-absorber of oil spills. The sponge repels water, but strongly attracts oil. It has an important property that makes it useful in Artic as well as warm waters it displays temperature invariant visoelasticity. Even in Artic waters the oil can be easily extracted from the sponge, which can be reused (see Hashim et. al. Scientific Reports, Vol 2, Article #363, April 13, 2012)

4. Graphenes

Andre Geim and Konstantin Novoselov were awarded the 2010 Nobel Prize in physics for their 2004 discovery of graphene, a carbon material that has the thickness of one atom. In the past eight years, the properties of graphene has been utilized to make possible major advances not only in electronic but other technologies as well. (Science, Oct. 8, 2010). The most important property of graphene is its two-dimensional nature. Because of this property, electrons in graphene travel through it as if they had no mass (much like photons).

Graphene exhibits unusual and sometimes antithetical or even paradoxical behavior. It is flexible like rubber, but is stronger than diamonds. It is transparent like glass but conducts electricity like metal. New uses of graphene are announced almost monthly. They are already utilized in touch screens. Researchers at IBM have made ultrafast transistors from graphene. It may prove useful in sequencing DNA.

In any case, it is apparent that the "dry" side of nanotechnology is thriving.

V. Biotechnology and the Bio-Nano Interface

Investments made a century ago in biomedical research allowed conquest of many diseases, including yellow fever, smallpox and tuberculosis. These investments are still paying off handsomely today. Tomorrow's biomedicine holds out the promise of benefits that were inconceivable a few decades ago. (See Chart 2) Fifty-four years have passed since Watson and Crick discovered the double helix. Since then, advances in genomics and related sciences have transformed biology from a discipline centering upon the passive study of life to one allowing the active alteration of life, almost at will.

We have seen that, the "wet" side of nanotech centers on the study of biological systems that exist in a water environment such as human cells. Since everything that goes on in a human cell is nanotechnology, some go so far as to assert that most of 21st century biotechnology is a subset of wet nanotechnology. The biomedical uses of Carbon 60, the first fullerene, stem from its special properties. (Carbon 60 was discovered at Rice in 1985 by Rick Smalley, Bob Curl and Harold Kroto. All were awarded the 1996 Nobel Prize in chemistry).

Smalley called the fullerene "God's molecule" because of its amazing and useful properties. Fullerenes are very, very small – about one nanometer wide. Second, their surfaces are thought to be particularly well suited for attaching therapeutic compounds. One promising anti-AIDS application capitalizes on three features of Carbon 60: very small size, its ability to carry chemicals to deliver drugs to specifically targeted sites, and its unique shape that facilitates binding with cells infected with HIV.

The increasingly ubiquitous carbon nanotube also holds out great promise in biomedicine. Nanowires made of nanotubes can be employed to detect infinitesimally small concentrations of pathogens. On the West Coast, nanotechnology is being used to sniff out infinitesimally small concentrations of protein leaking from cancer cells. A group of scientists in N.Y. in 2008 developed a virus-eating nanoparticle that could, among other things neutralize the virus in Avian flu. (Reference coming).

Also promising are efforts underway at Rice and nearby M.D. Anderson Cancer Center involving other types of nanoparticles: gold nanoshells. These are biocompatible devices with a gold surface adhered to a silica core. At about 100 nanometers in diameter, they easily pass through the circulatory system. The optical properties of nanoshells may prove extremely useful in both diagnosis and treatment. They are treated with a fluorescent dye inserted into the body, and delivered to sites of individual tumors by virtue of antibodies attached to them. They are struck by a harmless near-infrared light and heated up to 55 centigrade, enough to destroy cancer cells, while leaving unharmed healthy cells.

A very serious problem in chemotherapy cancer treatment has been that in injections of even the most potent anti-cancer drugs, very few of the drug molecules hit their target – perhaps 1 in 100,000. Some are filtered out by the liver, others by blood vessels. As a result, the drugs have to be administered in very high doses, often with devastating side effects from toxicity. But Scientists in the Houston Alliance for Nanohealth are now devising 3 stage nanorockets to deliver efficiently drug particles in far greater numbers to tumors with far less side effects. This is a rifle shot on cancer rather than a shotgun blast.[2]

Other approaches to efficacious drug delivery using nanotechnology has been the development of nano-bubbles by clinicians at Houston's M.D. Anderson Cancer Center together with faculty at Rice and Baylor Medicine. This process uses light-gathering nanoparticles to transform laser energy into plasmonic nano-bubbles (M.D. Anderson, Bulletin, April 16, 2012).

This approach delivers cancer drugs or other therapeutic cargo at the level of the single cell. The researchers have found the delivering very strong chemotherapy drugs with nano-bubbles was up to 30 times more deadly to cancer cells than traditional drug treatment.

[2] The 3-stage nanocarrier is injected into the bloodstream. The first stage seeks out the abnormal blood vessels around a tumor. As the first stage degrades, it releases the second: nanoparticles that burrow through the vessel to open a pathway for the medication to kill the cancer cells.

Also, the treatment required one tenth the clinical dose, thereby reducing harmful side effects.[3] Finally, conventional wisdom has long held that quantum entanglements did not apply to biological systems. But recent research now suggests that entanglement may be essential for the vital biological process, photosynthesis (See Sarovar, Ishizaki, et. al, "Quantum Entanglement in Photosynthetic Light-Harvesting Complexes," Nature Physics 6, 462–467 (2010). Also, birds are apparently endowed with a magnetism sensitive molecule that serves as a compass. Last year, researchers found that within that molecule, electrons remain entangled 10 to 100 times longer than the formulas of physics predict (Scientific American, November 2009). So, entanglement seems to be present also in large, warm systems including living organisms. Could entanglement then become a major focus in biomedicine? (See also Gauger, Rieper, et. al "Sustained Quantum Coherence and Entanglement in the Avian Compass," Physical Review Letters, Vol. 106, Issue 4, Jan. 2011).

Wet Nanotechnology: New Findings

Several new research findings in wet nanotechnology have been reported in the past year. In the interests of time, only a few will be discussed at some length.

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[3] See the following papers:
Biomaterials. 2012 Jul; 33(21):5441-50. Epub 2012 Apr 20.
"Cell-specific transmembrane injection of molecular cargo with gold nanoparticle-generated transient plasmonic nanobubbles," Lukianova-Hleb EY, Wagner DS, Brenner MK, Lapotko DO. Source: Department of Biochemistry and Cell Biology, Rice University, Houston, TX 77005, USA.

Biomaterials. 2012 Feb;33(6):1821-6. Epub 2011 Dec 2.
"Plasmonic nanobubble-enhanced endosomal escape processes for selective and guided intracellular delivery of chemotherapy to drug-resistant cancer cells," Lukianova-Hleb EY, Belyanin A, Kashinath S, Wu X, Lapotko DO. Source: Department of Biochemistry and Cell Biology, Rice University, Houston, TX 77005, USA.

Journal Article Advanced Materials (impact factor: 8.38). 03/2012; 24(28):3831-7. DOI:10.1002/adma.201103550
"Plasmonic nanobubbles enhance efficacy and selectivity of chemotherapy against drug-resistant cancer cells," Ekaterina Y Lukianova-Hleb, Xiaoyang Ren, Joseph A Zasadzinski, Xiangwei Wu, Dmitri O Lapotko. Source: Department of Biochemistry and Cell Biology, Rice University, Houston, TX 77005, USA.

Nanoparticles to Limit Brain Damage

Researchers at Rice University are developing a nanoparticle that could vastly improve the treatment of brain injury victims and also stroke victims.

In traumatic brain injury, cells release an excessive volume of reactive oxygen species (ROS) that into the blood ROS are notorious superoxides (toxic free radicals) that can cause heavy damage to the circulatory system resulting in sharply reduced blood flow to the brain.

The nanoparticle PEG-HCC (combined polyethylene glycol-hydrophilic carbon clusters) is a very effective anti-oxidant. Its power to neutralize ROS molecules became evident only during nanotoxicity studies of the nanoparticle (the particle has yet to show any earmarks of toxicity). An infusion of the nanoparticle stabilizes blood flow in brain trauma events. If over the next five years it proves out, the particle could be extremely valuable in saving lives after an earthquake, a severe gunshot wound or a collapse of a building.

A Nanoparticle Trojan Horse

We noted that nanorockets are one approach to problem of debilitating side effects of very high doses in cancer chemotherapy where the drugs are as toxic to healthy cells as well as cancer cells. Another is a nanoparticle developed at Caltech (Science, Oct. 15, 2010) that effectively tricks tumor cells into allowing toxins to penetrate cell walls and only then release the cancer toxins to kill the cancer. The nanoparticles are doped with a drug toxic to cancer (paclitaxel) and used to ferry the toxin to the cancer cell. Nanoparticles are able to accomplish this, because they can be designed to optimize multiple functions:

- To destroy cancer cells
- Be soluble in water in order be transported by the circulatory system
- Able to target the tumor cells and neutralize the cancer cell's defenses
- Shield normal cells from the toxin being delivered

This treatment is in the middle of clinical trials, and is but one of almost a dozen clinical trials of nanoparticle drugs in the U.S., while more than 50 companies are developing nanoparticle-based drugs to diagnose and treat cancer. (Science, Oct, 2010).

Other innovations arising from wet nanotechnology include nanocoatings called Anhydide to de-icing agents, with obvious application in operations of airlines.

VI. The Biotechnology-Information Technology Interface

Increasingly scientific terminology from computer science is entering the vocabulary of life scientists. And, research on computers made from biological components is now well advanced. This is understandable, since in their own ways, biological cells display computational and communicative attributes. Instead of software, we could call this the "wetware" of molecular biology. It is clear that biology is increasingly an information science. Both fields deal with information processing. In the case of IT, the information is electronic. In the case of biology, biochemical information is processed. Decoding the human genome would have been impossible without the advanced computational technology now at our disposal. Visualize your genes as your own customized software, containing recipes, or codes, for complex proteins that tell the cells in your body what to do, and how and when to do it.

And consider the amazing properties of the human chromosome. Each cell contains in the cell nucleus 46 strands of the double helix. If the strands in just one cell nucleus could be uncoiled, they would together measure 1.8 meters. Think of the truly massive amount of information that can be encoded along this length. The human genome project revealed at least 30 thousand genes and at least 300.000 proteins. The recently concluded ENCODE project, discussed below, reveals much more. To more fully understand how all these genes work together requires computing capacity for beyond what was thought possible even a decade ago. The rapid increase in the speed, and the extraordinary fall in costs of analyzing genomic data has made mathematical, statistical and computer methods the handmaiden of advances in biomedical research, diagnosis and therapy. And when quantum computing becomes cost-effective, the implications for biotechnology could open up unknown horizons.

Another fruitful implication in the bio-info interface is found computational cancer research. Clinicians stress that cancer is not a hundred different diseases, but rather many thousands of different diseases. At least five mutations may be required to create a cancer cell, each drawn from a repertoire of several hundred genes. So, there is an overwhelming number of possible combinations and permutations of cancer-causing mutations and they vary according to individuals' genetic and epigenetic endowments. This problem that can be addressed only by clinicians working with biomathematicians, bioengineers, computational scientists, and biostatisticians. To illustrate, such a group at Cornell has created devices that rapidly identify mutations that cause tumors, thereby allowing more targeted, individualized therapies. Elsewhere, Israeli scientists in 2008 developed a DNA computer. This biological computer under certain conditions could release cancer-fighting drugs.

Also, our growing understanding of how human cells communicate with one another has led to totally new perspectives on cancer. Researchers in Cambridge (MA) have found that stroma, or non-cancer cells that host tumors, have a continuous dialogue with cancer cells inside the tumor. The signals they send may cause cancer cells to become more aggressive and then metastasize.

New approaches at the intersection of biotechnology and information technology also have wide applicability to the mainstay of 20th century biotechnology: new pharmaceutical products. For the 21st century, the difference will be that more and more pharmaceutical innovations will be IT based. In the future perhaps the most profitable strategy for drug companies would be to make lifelong customers of people who are rarely ill, owing to the efficacy of customized medical treatment developed from the new field of pharmacogenomics. This will allow the personalization of much of medical treatments, eventually replacing traditional therapy based on the outmoded premise that "one drug fits all".

Pharmacogenomics deals with the genetic basis underlying variable drug response in different individuals. It also relies on the study of sequence variations in genes thought to affect drug response: It looks at the entire genome, enabling not only the identification of variant genes governing different drug responses across patients, but also those genes that affect susceptibility to disease, allowing new insights into disease prevention as well as enhancing prospects for individualized application of drug therapy.

The potential for truly revolutionary work in the bio-info space has been greatly magnified by the September 2012 announcement of the results of the multi-year $180 million project called ENCODE. Previously, scientists believed that 22,000 genes underpin the "blueprint of human biology." But these 20,000 were only 2% of the human genome. ENCODE examines the other 80%, and came to the startling conclusion that what was once believed to be "junk DNA" is not only biochemically active, but contains about 40,000 regulators to help activate or silence genes. ENCODE results provide insights that will lead to new ways to diagnose and treat diseases.

VII. The Nano-Info Interface

Much of the interface of IT with the other two technologies is found in discoveries and applications involving biotechnology.

But one recent innovation in the nano-info sphere stands out.

The nano-info interface has yielded "additive" manufacturing, which now allows electronics and other goods to be printed on a wide variety of surfaces, an innovation which may possibly revolutionize the way many goods are produced (Economist, April 21, 2012, Special Report: "A Third Industrial Revolution). The process uses 3-D printers, which utilize "inks" or powders with electrical properties. The printers build up solid objects out of materials, one layer at a time. Already, additive manufacturing systems are already used to make car parts, transducers in small scanners, jewelry, hammers, lampshades and customized artificial limbs. They are also used to print sensors on military armor, and to make a plastic water tanks using embedded electronics to measure how full it is, and to turn pumps on and off.

The advent of additive manufacturing has more general implications. Some believe it will drastically alter the way we view manufacturing. For one thing, additive manufacturing enables companies to produce locally without the need for holding large inventories. It will allow companies to avoid some of the costs of shipping raw materials and components in and shipping products out, over long distances. Therefore additive manufacturing will surely lower transportation costs in manufacturing. Some (Magnus, Financial Times, September 14, 2012) maintain that it will lower all costs of production, including those for capital and labor.

IV. The Grand Interface: Nano-Bio-Info

Consider that in 1970 the fabrication of a single transistor cost about 10 cents. The first Intel computer chip had 2300 transistors. This chip used 10,000 nanometer wide technology. The Intel Xeon processor uses 130 nanometer technology; the chips of 2008 required 65 nanometer technology. These developments are driving down rapidly the costs of storage capacities and sequencing. In 1990 the cost of sequencing only one base pair of genes was about $10. Today the cost is less than one penny per pair. I leave it to you to imagine the future implications for preventive medicine.

The marriage of nano-bio and info technology is making deep inroads in detection and diagnosis of cancer, cardiac disease and severe traumatic injury. Researchers at Rice, M.D. Anderson and UTHSC have devised an inexpensive diagnostic bio-nano chip that has been quite effective in detecting both malignant and pre-malignant oral cancer and other diseases. With the chip, invasive, painful biopsies are not needed. Results are ready on the spot not days later, and the cost is affordable.

This chip is one of the growing number of biomarkers under development in nanomedicine. At present it is being tested to detect heart attacks using saliva, with heartening results thus far. The chip works by deciphering body fluids such as saliva and blood, to reveal unique chemical and biological constituents, and changes in them.

Tissue engineering, a field born less than 2 decades ago, is an excellent example of the grand interface. Traditional biomedical engineering used metals, polymers and ceramics to construct temporary or permanent replacements of body parts that interact minimally with surrounding tissue. I have one of those in my foot. These replacement parts often promote infections, wear out, and loosen with time. Tissue engineers take exactly the opposite approach: they design biologically active materials that interact extensively with adjacent tissues in order to facilitate the regeneration process. Blending materials and concepts from nanotechnology and information technology into biotechnology, the new field has begun to yield products for repair of damaged tissue. Skin for burn patients is already available from first generation tissue engineering. Tissue engineering more generally promises to allow fabrication of a range of spare human parts to replace diseased or spent ones, or even to improve functions of healthy tissue. Tissue engineering targets include bone, cartilage, blood substitutes and organ replacements.

Already, scientists at Wake Forest University have grown gall bladders on artificial "scaffolds" of water soluble material. Seven patients have these new bladders, and they are still working. (The Economist, February 20, 2010), while physicians in Europe have implanted lab-grown tracheas. In Japan several children are living with tissue-engineered cardiac blood vessels (Science, Aug. 2011).

The second generation of tissue engineering is already upon us. Progress in rebuilding complex organs such as lungs will be difficult, but is no longer the stuff or science fiction. Tissue engineers, harnessing properties of intercellular communication, have even begun to induce *in vivo* heart muscle regeneration. If they are successful, it may be possible to generate muscle for a "cardiac muscle patch." (Science, February 12, 2010).

One new innovation in tissue engineering marries nanowires with human cells. In Sept. 2012 scientists from Harvard, MIT and other Boston-area universities announced the creation of Cyborg-like tissue, where a network of nanowires containing electrodes that will enable physicians to monitor changes in human tissue at levels not imagined before.

The third generation of tissue engineering is almost at hand. By 2020, engineers might deploy self-assembling nano-electronic components to create 3-D circuits to improve the tissue compatibility of implants. Especially promising are plans to print organs using inkjet technology to imprint stem cells. Scientists and engineers are adapting tissue engineering to deal with a multitude of medical problems such as kidney failure, atherosclerosis, spinal cord injuries, inflammations, age-related diseases, and osteoporosis. It now seems that there are only a few parts of the body that cannot be ultimately replaced with bio-artificial replications of body parts.

VIII. Conclusion

Nanotechnology will surely revolutionize energy and materials science. The potential for truly staggering applications of biotechnology as augmented by nano and information technology is also in little doubt. Whether much of this potential will be soon realized is, however, yet unclear. Financial constraints on transfer of innovations based on these technologies are loosening, but legal and regulatory constraints loom much larger than in past technological revolutions. In the U.S. the Food and Drug Administration has become increasingly risk-adverse in approving new genetic and nanotech treatments in medicine. And no one knows what the next session of congress will bring.

From genomics, biotechnology has already provided us with a complete parts list for humans. As a result of advances in wet nanotechnology and information technology, tissue engineering promises to provide widely available, inexpensive, and reliable spare parts for humans. If we can find ways to resolve ethical – and perhaps moral – issues raised by our fast-expanding capacities in these converging technologies, their economic and social impacts could be as profound and as positive as that wrought by any previous revolution in human history.

Even ten years ago, much of what we have discussed today seemed impossible. What can we say about that? I began with a quote from Arthur C. Clarke. I close with another example of his pithy wisdom: “The only way to discover the limits to the possible is to venture a little past them – to the impossible.”