

Nanomanufacturing: Application of Nanotechnology in Manufacturing Industries

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Abstract

Advances in nanoscale science have led to the development of new materials and techniques which are affecting production capabilities in a number of manufacturing industries. We look at key features of advances made possible by nanoscale science that are relevant to manufacturing capabilities, and examine how these capabilities are being employed in six industries – semiconductors, solar cells, rechargeable batteries, lighting, display and healthcare.

Introduction

Differences in technological capabilities are at the core of differences in economic development across regions and countries. Governments across the globe spend massive amounts in support of research and development to maintain technological competitiveness. A commonly held view of technological change pictures long term technological cycles, each cycle stemming from a revolutionary new scientific advance. In this view, the industrial derivatives of the scientific advance ripples through different sectors in the economy, improving the production techniques and sparking innovation in each of them. Such fundamental scientific advances, and their industrial applications, are often referred to as General Purpose Technologies, to capture the range of their impact across different sectors in the economy. Gordon¹ suggests that there were three such technological waves over the last several centuries of industrialization. The steam engine and railroad revolution spanning 1750 to 1830 forms the first, the electricity revolution during 1870-1900 the second, and the information technology revolution from 1960s to present day forms the third. This paper examines the impact of a fundamental scientific advance, nanotechnology, and the characteristics that make it likely to be a General Purpose Technology with ability to substantially change production techniques in a wide swathe of industries, and constitute a fourth industrial revolution.

The fundamental scientific advance here is the ability to observe and manipulate matter at the scale of individual atoms and molecules. Since typical atomic diameter is less than 1 nanometer², science at this scale has aptly been named as nanoscale science. Scientists had long predicted that the ability to

¹ Gordon, Robert J. "Is U.S. Economic Growth Over? Faltering Innovation Confronts the Six Headwinds." The National Bureau of Economic Research (2012): NBER Working Paper No. 18315 (2012)

² Sharma, Shatendra. "The Size of Atoms." Atomic and Nuclear Physics. 1st ed. New Delhi: Pearson, 2008. 17. Print.

manipulate matter at the nanoscale would open up a treasure trove of industrial possibilities. In the first clearly documented reference to nanoscale science, Feynman 1959³ predicted a never ending series of scientific and industrial advances once the ability was obtained. In the 1980s, a series^{4,5} of advances in microscopy gave rise to powerful tools for imaging, measuring and manipulating matter at the nanoscale. The focus of this paper is on the application of nanotechnology enabled production techniques to manufacturing industries. While there are numerous industries that would be affected, the impacts of these techniques in a subset of industries are examined below. Before proceeding to discuss the impact on individual industries, the next section summarizes the general ideas behind why advances in nanoscale techniques can have the ability to affect manufacturing operations.

Nanomanufacturing

There are two characteristics of being able to manipulate objects at the atomic or molecular level that lend a distinct advantage from a manufacturing perspective, and enable a set of production techniques often collectively referred to as nanomanufacturing. First, by using materials at the nanoscale level one can increase the surface area for the same weight of material used, which can be very valuable for some manufacturing operations. For example, many chemical reactions occur at surfaces, and hence a given material will be much more reactive in nanoscale particulate form than in the form of larger particles. Second, at the nanoscale level quantum effects arise, which do not have much impact when dealing with larger sized objects. Quantum effects arise from the dual particle and wave like behavior of energy and matter. The manufacturing importance of these quantum effects stem from the fact that these affect the electrical, magnetic and optical properties of materials. By exploiting these quantum effects one can create materials that combine desirable properties, strength with lightness (in airplane frames), conductivity without overheating⁶ (in integrated circuits) etc. These two characteristics of nanotechnology affect manufacturing through the development of new materials and new fabrication processes, as described below.

Material Synthesis – Using nanomanufacturing techniques, new materials, loosely defined to include compounds and devices, can be synthesized with desirable properties. These new materials can be nanoscale in one dimension (like very thin films, layers and surfaces) or nanoscale in two dimensions (nanowires and nanotubes) or nanoscale in three dimensions (nanoparticles). This plethora of new nanoscale surfaces, wires and particles are anticipated to find wide use in many manufacturing industries, some of which are explored below.

Fabrication - Ability to manipulate matter at the nanoscale level gives rise to new capabilities for traditional fabrication processes used in manufacturing - like deposition and lithography. An age old industrial technique is the process of depositing one material, like paint, on another. With new

³ Feynman, Richard P. "Plenty of Room at the Bottom." American Physical Society, USA, Pasadena. Dec. 1959. Talk.

⁴ G. Binnig and H. Rohrer, Scanning Tunneling Microscopy, 30.4 IBM JOURNAL OF RESEARCH AND DEVELOPMENT 355 (1986)

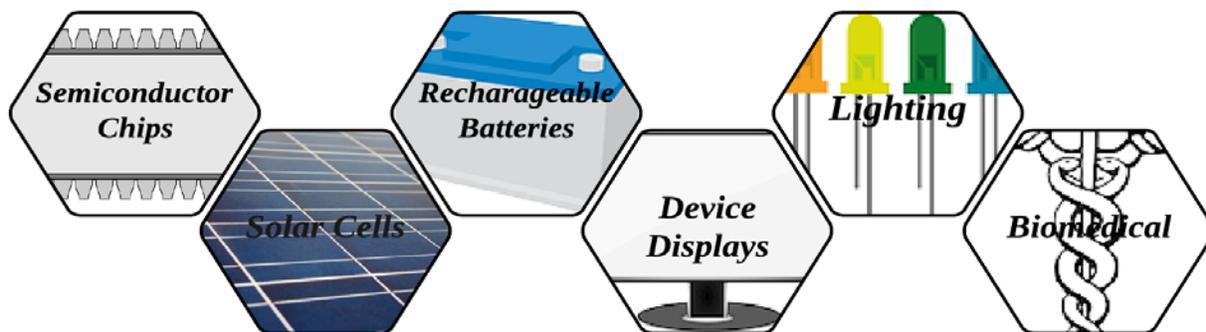
⁵ G. Binnig and C. F. Quate, Atomic Force Microscope, 56.9 PHYSICAL REVIEW LETTERS 930 (1986)

⁶ Baringhaus, J. et al., Exceptional ballistic transport in epitaxial graphene nanoribbons, 506 NATURE 349 (2014)

nanomanufacturing processes, like Atomic Layer Deposition, thin films of nanometer thickness can be deposited on substrates, a very valuable capability for the manufacture of semiconductor devices and optical coatings. Similarly, new nanolithography techniques allows for the fabrication of nanoscale structures by the transfer of a pattern to a photosensitive⁷ material by selective exposure to a radiation source such as light, ions or electrons.⁸

For the industrial techniques like deposition and lithography mentioned above, nanoscale manipulation of matter offers advances that are fundamentally incremental, the ability to deposit finer and finer layers or make smaller and smaller electronic devices. These incremental advances are often said to constitute a ‘top-down’ approach, in that these advances increase the capabilities of macro scale techniques. Yet perhaps the real contribution of nanomanufacturing would be in a very different and revolutionary way, by making products by assembling them ‘bottom-up’ from the individual atoms. This technique, called Self-Assembly, envisions nanoscale building blocks like nanoparticles, nanowires and nanotubes that can be made to self-assemble into desired objects under appropriate conditions⁹.

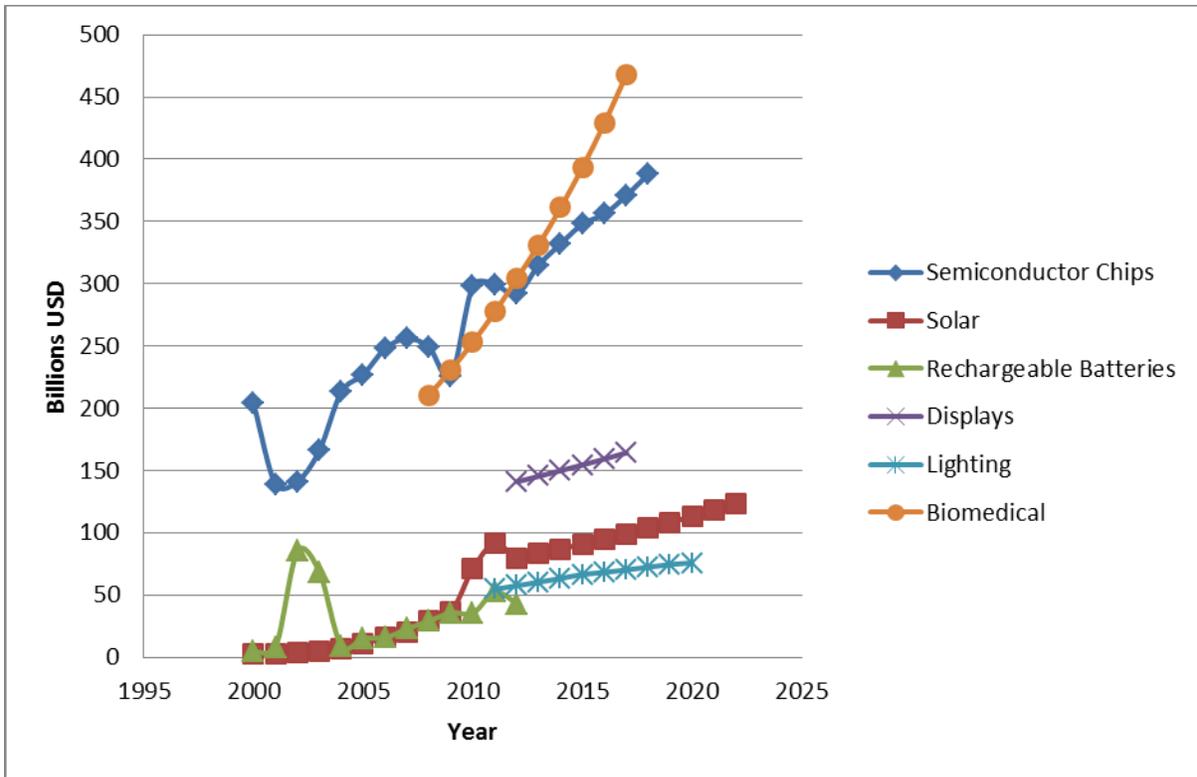
In what follows, the application of these new nanoscale materials and fabrication techniques will be described for six manufacturing industries: Semiconductor chips, Solar cells, Rechargeable batteries, Display devices, Lighting and Biomedical Healthcare.



⁷ A photosensitive material is that which experiences a physical property change(s) when exposed to a radiative source e.g. UV light.

⁸ Selectively exposing a photosensitive material to radiation (e.g. by masking some of the radiation) the pattern of the radiation on the material is transferred to the material exposed, as the properties of the exposed and unexposed regions differ. "Lithography." *Lithography*. MEMSnet, n.d. Web. 21 Apr. 2014. <<https://www.memsnet.org/mems/processes/lithography.html>>.

⁹ Roger, Whatmore W., *Nanotechnology: Big Prospects for Small Engineering*, 9 INGENIA 28 (2001)



The sizes of the Semiconductor, Solar, Rechargeable Battery, Device Display, Lighting & Biomedical industries over the years along with projections.¹⁰

¹⁰ Sources of industry data: Semiconductor - World Semiconductor Trade Statistics (WSTS) '00-'12, Gartner, Inc. '13-'18; Solar - CleanEdge; Rechargeable Battery - Gale Company Intelligence Database (Storage battery manufacturing); Device Display - MarketsandMarkets (Nov '12 SE1382); Lighting - McKinsey 2012 ('11-'16 = 5% cagr; '16-'20 = 3% cagr); Biomedical - MarketLine (August '13) - Biotechnology: World Market Overview (Market size, Segmentation and Trends Analysis); Authors' analysis

Nanomanufacturing in Select Industries

Semiconductor Industry

A number of recent studies have provided strong evidence that technological progress in the semiconductor industry has been a big driver of productivity growth and improvements in living standards in the U.S.^{11,12} The semiconductor industry has grown from a few thousand dollar industry in 1950 to an industry with sales in the hundreds of billions of dollars. The key dimension of technological progress in the industry is the size of the transistor, a switch which is the basic electronic component used in semiconductors. The central story of the industry has been the relentless drive towards smaller transistors (see Figure 1b). Smaller transistors confer two benefits, more of them can be put on a given area, and smaller transistors switch faster. This march towards smaller transistors has decreased the key dimension of transistors from 10,000 nanometers in 1970 to 22 nanometers in 2012. Advances in nanomanufacturing techniques for deposition, etching and lithography have been the key enablers of this miniaturization of transistors. The effect of this miniaturization has been a spectacular increase in quality of semiconductor chips, or correspondingly a decline in quality adjusted cost of producing the chips. Figure 1a shows decrease in price per bit of Dynamic Random Access Memory (DRAM) chips, the commonly used storage device in personal computers.

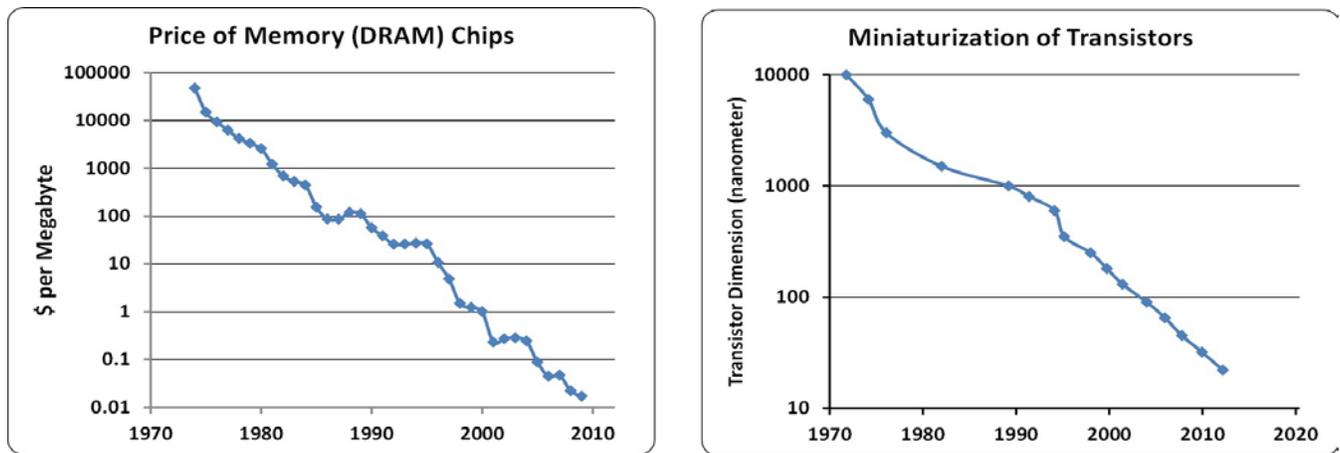


Figure 1: Reduction in price of DRAM memory chips over time Figure 1a (figure on left) driven by continual decrease in size of transistors Figure 1b (figure on right)

¹¹ Jorgenson, Dale W., Information Technology and the U.S. Economy, 91.1 AMERICAN ECONOMIC REVIEW 1 (2001)

¹² Byrne, David, Steven Oliner, and Dan Sichel, Is the Information Technology Revolution Over?, 25 INTERNATIONAL PRODUCTIVITY MONITOR 20 (2013)

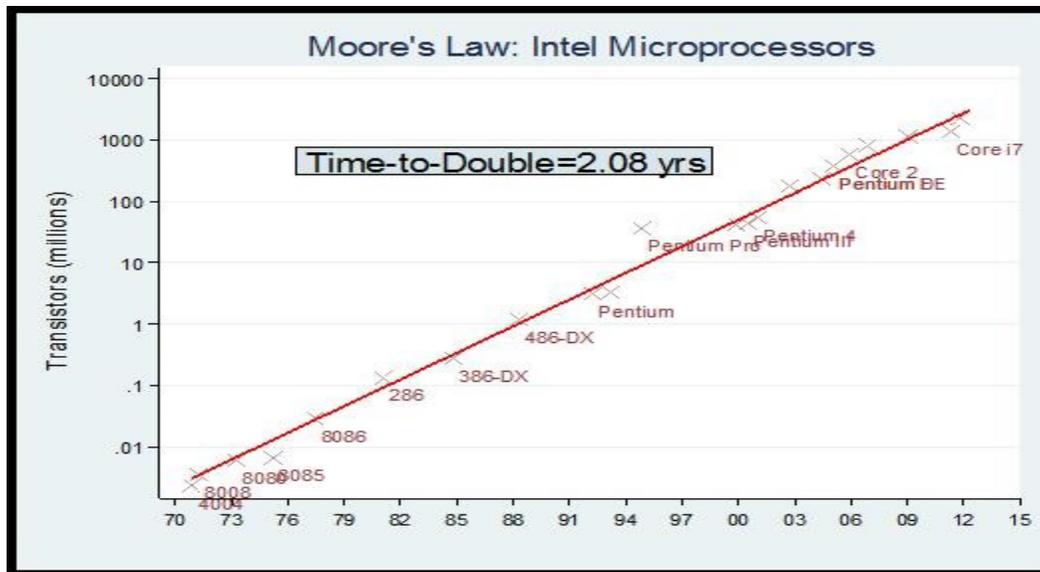


Figure 2: Increase in Transistors per Chip (Moore's Law)

Further improvements in manufacturing techniques are needed to continue on the path of miniaturization and/or improvement.^{13,14} New materials synthesized using nanoscale techniques, like Carbon Nanotubes, will take the place of silicon transistors in future semiconductor chips.¹⁵ Carbon Nanotubes (CNT) have a nanoscale structure that can theoretically be closely packed together and display very striking electrical properties. A rudimentary computer based completely on CNT transistors has been made by researchers at IBM.¹⁶ Recently, researchers have also used nanomanufacturing techniques to build semiconductor chips out of graphene.¹⁷ Silicon nanowires, with diameters close to 1 nanometer, are also being actively considered to build the future generation of tiny transistors (known as “gate-all-around” transistors) for semiconductor chips.¹⁸

Solar Industry

Increasing electricity generation through solar photovoltaic cells is a major thrust of efforts to combat global warming. At present however, electricity from photovoltaics (PV) constitute a very small fraction of the world electricity production. The cost of generating electricity from solar PV systems has fallen over time. A major factor behind this decline has been the continual decrease in the price of solar panels (also called solar modules), the principal component in PV systems (Figure 3a). These declines have

¹³ Bauer, Harald, PhD, Jan Veira, MBA, and Florian Weig, PhD. "Moore's Law: Repeal or Renewal?" McKinsey & Company. Dec. 2013. Web. 27 May 2014.

¹⁴ Ahmed, Khaled, and Klaus Schuegraf. "Transistor Wars." Transistor Wars: Rival Architectures Face off in a Bid to Keep Moore's Law Alive. IEEE Spectrum, 28 Oct. 2011. Web. 04 Apr. 2014.

¹⁵ Courtland, Rachel. "First Computer Made From Carbon Nanotubes Debuts." IEEE Spectrum, 25 Sept. 2013. Web. 04 Apr. 2014. <<http://spectrum.ieee.org/tech-talk/semiconductors/devices/first-computer-made-from-carbon-nanotubes-debuts>>.

¹⁶ Shulaker, Max M., Gage Hills, Nishant Patil, Hai Wei, Hong-Yu Chen, H.-S. Philip Wong and Subhasish Mitra, Carbon Nanotube Computer, 501.7468 Nature 526 (2013)

¹⁷ Takahashi, Dean. "So Long Silicon? IBM Scientists Build Experimental Graphene-based Semiconductor Chip." VentureBeat, 30 Jan. 2014. Web. 04 Apr. 2014. <<http://venturebeat.com/2014/01/30/ibm-scientists-builds-experimental-graphene-based-semiconductor-chip/>>.

¹⁸ Cress, C. D., and S. Datta, Nanoscale Transistors--Just Around the Gate?, 341.6142 SCIENCE 140 (2013)

brought the price of solar generated electricity closer to the price of electricity generated from conventional sources, but a gap still remains. The solar industry is actively exploring new nanomaterials and nanoscale fabrication techniques to further reduce the cost of solar panels and increase their efficiency.¹⁹

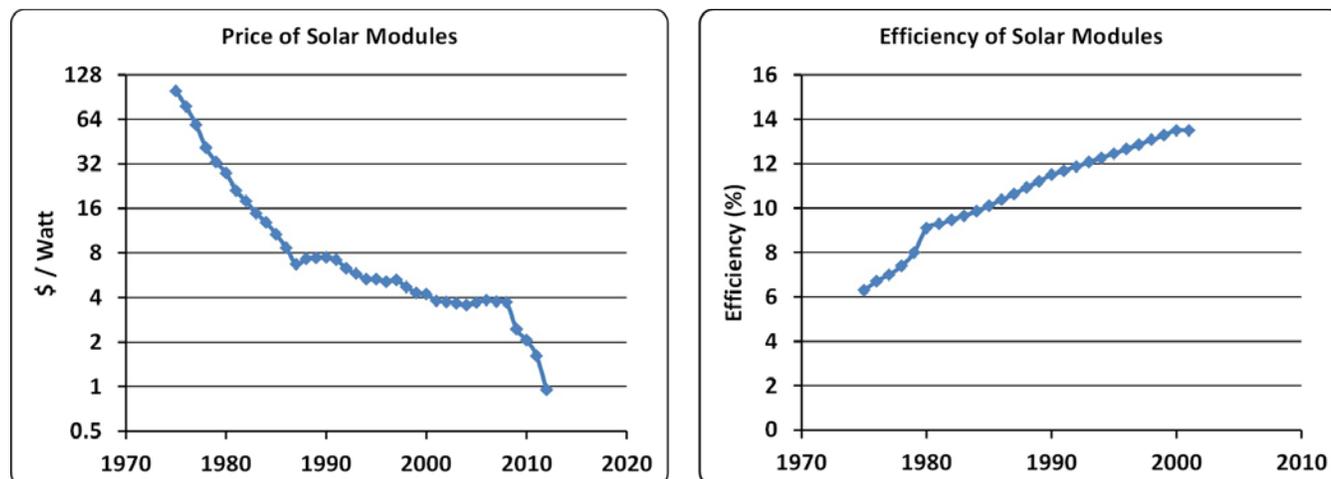


Figure 3: Reduction in price of solar modules over time Figure 3a (figure on left) driven in large part by continual increase in light-to-electricity conversion efficiency Figure 3b (figure on right)

Studies on nanoscale devices have shown promising results to increase conversion efficiency.²⁰ Single wall carbon nanotubes (SWNTs) can form ideal p-n junction diode showing photovoltaic effect.²¹ SWNTs possess a wide range of direct bandgaps matching the solar spectrum, strong photoabsorption, high carrier mobility and reduced carrier transport scattering, all of which make them ideal as PV material. Another promising technology in the next generation of thin-film solar cells are organo-lead halide perovskite solar cells, whose efficiencies have increased from a few percent to more than 15 percent in the last few years. Recent studies have shown promise in decreasing the cost of these synthetically produced organic polymers by using inorganic hole conductors of copper iodide.²² Experimental research in polymer solar cells have shown that cells which are more than 65% transparent to the human eye (possible use in windows and other energy scavenging scenarios) can produce

¹⁹ Solar cell efficiency is the ratio of electrical output to the energy from sunlight incident upon the surface of the cell. While there is loss of power due to generation inefficiencies the overwhelming dependence of overall module efficiency is upon the initial capture and conversion of sunlight to electricity by the photovoltaic effect.

²⁰ Li, Zhongrui, Vasyl P. Kunets, Viney Saini, Yang Xu, Enkeleda Dervishi, Gregory J. Salamo, Alexandru R. Biris, and Alexandru S. Biris, SOCl[sub 2] Enhanced Photovoltaic Conversion of Single Wall Carbon Nanotube/n-silicon Heterojunctions, 93.24 APPLIED PHYSICS LETTERS 243117 (2008)

²¹ Lee, Ji Ung, Photovoltaic Effect in Ideal Carbon Nanotube Diodes, 87.7 APPLIED PHYSICS LETTERS 073101 (2005)

²² Christians, Jeffrey A., Raymond C. M. Fung, and Prashant V. Kamat, An Inorganic Hole Conductor for Organo-Lead Halide Perovskite Solar Cells. Improved Hole Conductivity with Copper Iodide, 136.2 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY 758 (2014)

electricity.²³ The modest near 3% efficiency is just scratching the surface of theoretical limits of up to 37% efficiency.²⁴

The contribution of nanomanufacturing in the solar industry has not only been in the production of new photovoltaic materials, but also in improving the manufacturing techniques used in current manufacture of solar cells. For example, advancements in the use of ultra-precision tools (very fine diamond saws) help to tackle the very real problem of kerf loss when cutting solar cells into individual modules. This has a direct impact on curbing costs. Over the past several years, material usage for silicon cells has been reduced significantly from around 16 grams/Watt to 6 grams/Watt²⁵.

Rechargeable Battery Industry

The proliferation of portable electronics and the demand for environmentally friendly power sources have created need for lightweight, more robust rechargeable batteries. Although there has been improvement in energy density of rechargeable batteries made with Lithium-Ion technology, (Figure 4), there is much to be done to enable mass commercialization of products, , like electric vehicles, that use these batteries. Many companies are experimenting with batteries where the anode, cathode and electrolyte are made with nanomaterials. Coating the electrodes with nanoparticles increase their surface area, allowing more current to flow, hence increasing the power available from a battery and reducing the time required to recharge the battery. Many new battery technologies like Non-aqueous lithium-oxygen (Li-O₂) can store energy at densities that can rival that of gasoline. A drawback of these promising high energy density battery technologies are their low recharging efficiencies. The application of catalytic ruthenium oxide (RuO₂) nanoparticles can significantly increase the recharging efficiency.²⁶ Use of lithium-oxygen batteries eliminates the need for cathodes made of heavy metal oxide conventionally used in lithium-ion batteries, and lets lithium react directly with atmospheric oxygen on cathodes made from light, porous materials such as CNTs. Improvement of lithium-ion batteries with the use of germanium nanowires coated with silicon has also shown promise.²⁷

²³ Lunt, Richard R., and Vladimir Bulovic, Transparent, Near-infrared Organic Photovoltaic Solar Cells for Window and Energy-scavenging Applications, 98.11 APPLIED PHYSICS LETTERS 113305 (2011)

²⁴ Lunt, Richard R., Theoretical Limits for Visibly Transparent Photovoltaics, 101.4 APPLIED PHYSICS LETTERS 043902 (2012)

²⁵ "Photovoltaics Report." FRAUNHOFER INSTITUTE FOR SOLAR ENERGY SYSTEMS ISE: pg.7. Fraunhofer Institute, 7 Nov. 2013. Web. <<http://www.ise.fraunhofer.de/en/downloads-englisch/pdf-files-englisch/photovoltaics-report-slides.pdf>>.

²⁶ Yilmaz, Eda, Chihiro Yogi, Keisuke Yamanaka Yamanaka, Toshiaki Ohta Ohta, and Hye Ryung Byon, Promoting Formation of Noncrystalline Li₂O₂ in the Li-O₂ Battery with RuO₂ Nanoparticles, 13.10 NANO LETTERS 4679 (2013)

²⁷ Liu, Yang, Xiao Hua Liu, Binh-Minh Nguyen, Jinkyong Yoo, John P. Sullivan, S. Tom Picraux, Jian Yu Huang, and Shadi A. Dayeh, Tailoring Lithiation Behavior by Interface and Bandgap Engineering at the Nanoscale, 13.10 NANO LETTERS 4876 (2013)

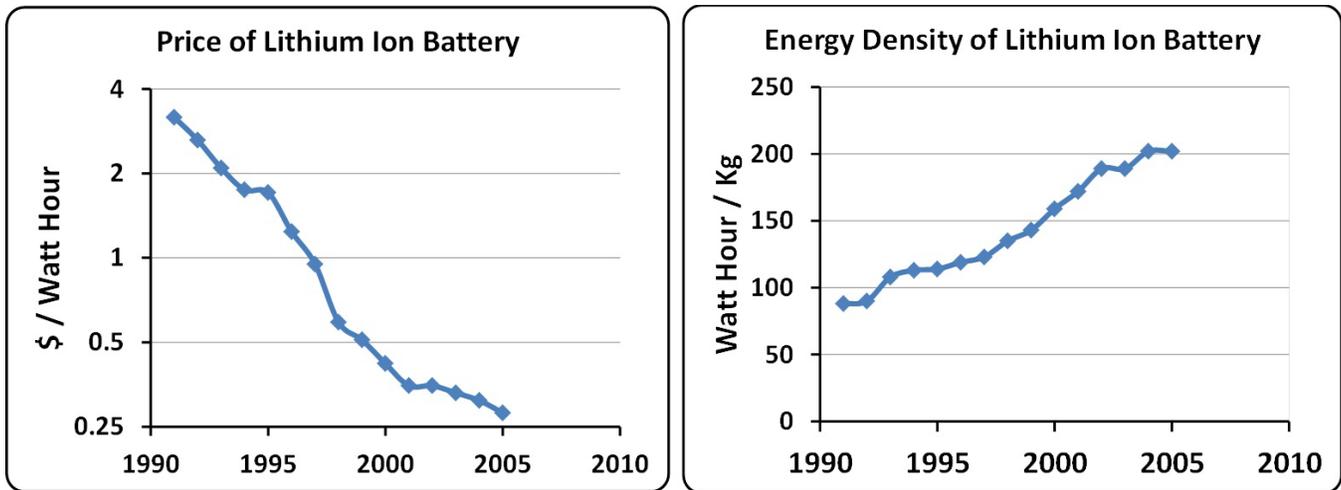


Figure 4: Reduction in Li-Ion Battery price over time Figure 4a (figure on left) driven by continual increase in energy density Figure 4b (figure on right)

Display Industry

New nanomaterials are finding widespread application in the large market for high-definition widescreen flat panel displays. Nanocrystalline zinc selenide, zinc sulphide, cadmium sulphide and lead telluride synthesized by sol-gel techniques²⁸ are candidates for the next generation of light-emitting phosphors.²⁹ Doping liquid crystals (LCs) with single³⁰ and multi-walled³¹ CNTs have shown significant improvements in response rates to applied electric fields i.e. the LCs are shown to be faster, eliminating more of the time delay in visual formation. CNTs are being investigated for low voltage field-emission displays; their strength, sharpness, conductivity and inertness make them potentially very efficient and long-lasting emitters.

The capability of Quantum dots³² to translate and adjust a spectrum of light makes them a good candidate for advancement in liquid crystal displays (LCD). Distinct from the conventionally used phosphor materials, quantum dots can be made to translate short-wave length light to any color within the visible light spectrum. Virtually any current technology using LCDs (smartphones, TVs, etc.) can be viewed with better clarity by remixing white light into red, green and blue components. Adaptive

²⁸ A process for making ceramic and glass materials, involving the transition from a liquid 'sol' phase to a solid 'gel' phase.

²⁹ Dowling, Ann et al, Nanoscience and Nanotechnologies: Opportunities and Uncertainties. London: Royal Society, 2004. Nanotechnology and Nanoscience. The Royal Society & The Royal Academy of Engineering Science Policy Section, July 2004 <<http://www.nanotec.org.uk/finalReport.htm>>.

³⁰ Lu, Shin-Ying, and Liang-Chy Chien, Carbon Nanotube Doped Liquid Crystal OCB Cells: Physical and Electro-optical Properties, 16.17 OPTICS EXPRESS 12777 (2008)

³¹ Basu, Rajratan, Effect of Carbon Nanotubes on the Field-induced Nematic Switching, 103.24 APPLIED PHYSICS LETTERS 241906 (2013)

³² Nanometer scale semiconductor crystallites (i.e. nanocrystals) which three dimensionally confines the electron-hole pair. Reed, M., J. Randall, R. Aggarwal, R. Matyi, T. Moore, and A. Wetsel, Observation of Discrete Electronic States in a Zero-dimensional Semiconductor Nanostructure, 60.6 PHYSICAL REVIEW LETTERS 535 (1988)

adjustments for replacing existing LCD manufacturing processes, in the form of Quantum Dot Enhancement Films (QDEF), are already available.³³

Another promising application of nanomaterials is in zinc-oxide (ZnO) nanowire LEDs, whose emission intensity is dependent on the local strain put on them (for example, from a finger). The technology offers a better method to force imaging and could spur new techniques for man-machine interfaces. Resolution and response rates in these will be much improved when compared to touchscreens and other pressure sensor technologies.³⁴

Lighting Industry

Current lighting devices consume much energy and often have aesthetically and environmentally displeasing attributes (noisy, poor color profile, contain mercury, etc.), but semiconductor light-emitting diodes (LEDs) consume much less energy and are free of many of these attributes. Since its invention in 1960s LEDs were until recently confined to niche applications like indicator lights. But recent advances in LEDs have enabled them to penetrate the general lighting market. Lighting with LEDs – generally known as Solid State Lighting (SSL) – promise not just lower lifetime cost and energy consumption, but also integration with electronics to facilitate new lighting designs and applications.³⁵ A number of studies point to the possibility that LEDs will displace most of traditional lighting sources like incandescent lamps and compact fluorescent lamps (CFL).³⁶ The evolution of technology in LEDs follows a trend that has come to be known as Haitz Law (Figure 5), the cost per lumen falls by a factor of 10 each decade while the luminous flux increases by a factor of 20; lumen being the unit of luminous flux, the amount of visible light emitted by a source.

³³ Chen, Jian, Veeral Hardev, and Jeff Yurek, Quantum Dot Displays: Giving LCDs a Competitive Edge through Color, 29.1 INFORMATION DISPLAY 12 (2013)

³⁴ Pan, Caofeng, Lin Dong, Guang Zhu, Simiao Niu, Ruomeng Yu, Qing Yang, Ying Liu, and Zhong Lin Wang, High-resolution Electroluminescent Imaging of Pressure Distribution Using a Piezoelectric Nanowire LED Array, 7.9 NATURE PHOTONICS 752 (2013)

³⁵ Haitz, Roland, and Jeffrey Y. Tsao, Solid-state Lighting: 'The Case' 10 Years after and Future Prospects, 208.1 PHYSICA STATUS SOLIDI (A) 17 (2011)

³⁶ Tsao, Jeffrey Y., Michael E. Coltrin, Mary H. Crawford, and Jerry A. Simmons. "Solid-State Lighting: An Integrated Human Factors, Technology, and Economic Perspective, 98.7 PROCEEDINGS OF THE IEEE 1162 (2010)

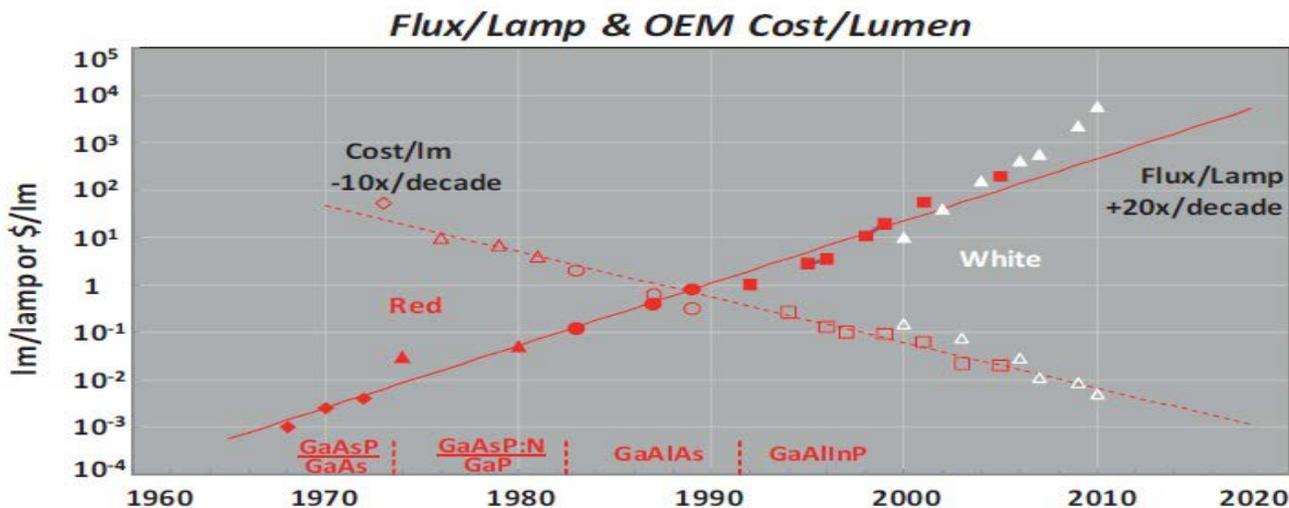


Figure 5: Chronological development of the performance (lm/lamp) and cost (\$/lm) for commercially available red and phosphor - converted (PC) white LEDs (Source: Haitz and Tsao, 2011)

One of the quality issues with LEDs is that they give off azure traces. A solution to this problem is to use Field-induced polymer electroluminescent (FIPEL)³⁷, which use nanoengineered polymer matrices to convert the charge into light, and gives off soft white light without azure traces. The technology has also been shown to be free of the undesirable hum that fluorescent tubes produce. This lighting solution is much more efficient than compact fluorescent (CFL) bulbs and on par with LEDs, but these bulbs won't shatter and contaminate a home like CFLs nor emit a bluish light like LED counterparts.³⁸ Another new technology is quantum dot³⁹ light emitting diodes (QD-LEDs), which has strong emission control and a straightforward manufacturing process. Although this technology currently suffers from drops in efficiency at high currents, new manufacturing approaches promise to mitigate this problem.⁴⁰ Organic LEDs (OLEDs), which are thinner, more flexible (and therefore can be printed) and have faster response times. Although they are currently expensive, replacing the indium-tin oxide (ITO) electrodes in these with graphene has shown much promise towards decreasing costs and increasing performance.⁴¹

Biomedical Industry

Total healthcare costs make up a sizeable chunk of the gross domestic product (GDP) of most countries. Nowhere is this more evident than in the USA where healthcare costs have been at or above 17% of

³⁷ A low power, electroluminescent light source composed of three layers of moldable light-emitting polymer blended with a small amount of carbon nanotubes glow when an alternating current is passed through them.

³⁸ Chen, Yonghua, Gregory M. Smith, Eamon Loughman, Yuan Li, Wanyi Nie, and David L. Carroll, Effect of Multi-walled Carbon Nanotubes on Electron Injection and Charge Generation in AC Field-induced Polymer Electroluminescence, 14.1 ORGANIC ELECTRONICS 8 (2013)

³⁹ Global Quantum Dot Industry size is projected to increase from 316 million USD in 2013 to 5 billion USD by 2020 Naidu, Shreyas, and Priyanka Gotsurve, Global Quantum Dot (QD) Market - Global Analysis, Growth, Trends, Opportunities, Size, Share and Forecast through 2020, Rep. no. SE 14141. Allied Market Research, Apr. 2014

⁴⁰ Bae, Wan Ki, Young-Shin Park, Jaehoon Lim, Donggu Lee, Lazaro A. Padilha, Hunter Mcdaniel, Istvan Robel, Changhee Lee, Jeffrey M. Pietryga, and Victor I. Klimov, Controlling the Influence of Auger Recombination on the Performance of Quantum-dot Light-emitting Diodes, 4.2661 NATURE COMMUNICATIONS (2013)

⁴¹ Wu, Junbo, Mukul Agrawal, Héctor A. Becerril, Zhenan Bao, Zunfeng Liu, Yongsheng Chen, and Peter Peumans, Organic Light-Emitting Diodes on Solution-Processed Graphene Transparent Electrodes, 4.1 ACS NANO 43 (2010)

GDP for the past several years and are on an upward trend⁴². Possibilities for nanotechnology in the realm of healthcare are immense, in everything from limb replacement to cancer treatment. Here we explore innovations underway in three subcategories in healthcare – drug delivery, gene therapy, and diagnostics.

Drug Delivery:

Drug delivery is being revolutionized by drug devices made using nanofabrication techniques.⁴³ For example, Nanodiamonds (NDs)⁴⁴ can be used for controlled release of medicine into the body. With this timed technology, long periods' worth of medication can be implanted on to the affected area at once. In cancer treatment, clusters of NDs can be used to surround drugs ensuring that they remain separated from healthy cells, preventing unnecessary damage. Once reaching the intended targets, the medications are released into the cancer cells, and the excess diamonds do not induce the conventional inflammation in cells.⁴⁵ They can also be used for adsorption purposes, and can draw undesirable and poisonous compounds out of the body or from open wounds.⁴⁶ For example, modified nanodiamonds have shown to adsorb away the toxic microscopic fungi aflatoxin at very high rates.⁴⁷ Nanogels⁴⁸ – cross-linked spherical hydrogel particles that have nanoscale (typically 20-250 nm) dimensions – have numerous properties that make them particularly appealing for biomedical applications including drug delivery. Nanogels have been used to create more effective biodegradable drug delivery agents that can offer better implementation of therapeutics.⁴⁹ Another application of nanomanufacturing techniques has been in the use of thin-films for drug delivery. A film constructed using hydrophilic polymers can quickly dissolve on the intended adsorbing surface like skin, bringing the drug to the general circulation. This provides for a less intrusive and pain free method of drug intake. Nanostructured thin film polymer devices have shown to provide zero-order kinetic release, which offers a means to control release rate as well as payload of the device.⁵⁰ Thin film delivery materials are available for medications to treat the harsh side effects of chemotherapy and opioid addiction⁵¹ or even dementia caused by Alzheimer's⁵².

⁴² "Health Expenditure, Total (% of GDP)." Data. The World Bank, Web. 07 June 2014.

<<http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS>>.

⁴³ Kam, Kimberly R., and Tejal A. Desai, Nano- and Microfabrication for Overcoming Drug Delivery Challenges, 1.14 JOURNAL OF MATERIALS CHEMISTRY B 1878 (2013)

⁴⁴ Also called ultradispersed diamond (UDD), is diamond that originates from a detonation. When an oxygen-deficient explosive mixture of TNT/RDX is detonated in a closed chamber, diamond particles with a diameter of ~5 nm are formed at the front of detonation wave in time of several microseconds.

⁴⁵ Chow, E. K., X.-Q. Zhang, M. Chen, R. Lam, E. Robinson, H. Huang, D. Schaffer, E. Osawa, A. Goga, and D. Ho., Nanodiamond Therapeutic Delivery Agents Mediate Enhanced Chemoresistant Tumor Treatment, 3.73 SCIENCE TRANSLATIONAL MEDICINE 73ra21 (2011)

⁴⁶ Puzyr, A.p., A.v. Baron, K.v. Purtov, E.v. Bortnikov, N.n. Skobelev, O.a. Mogilnaya, and V.s. Bondar, Nanodiamonds with Novel Properties: A Biological Study, 16.12 DIAMOND AND RELATED MATERIALS 2124 (2007)

⁴⁷ Puzyr', A. P., K. V. Purtov, O. A. Shenderova, M. Luo, D. W. Brenner, and V. S. Bondar, The Adsorption of Aflatoxin B1 by Detonation-synthesis Nanodiamonds, 417.1 DOKLADY BIOCHEMISTRY AND BIOPHYSICS 299 (2007)

⁴⁸ They have excellent biocompatibility, high water content, tunable sizes, large surface area for multivalent bioconjugation, and abundant space to accommodate bioactives such as drugs and live cells.

⁴⁹ Jiang, Yanjiao, Jing Chen, Chao Deng, Erik J. Suuronen, and Zhiyuan Zhong, Click Hydrogels, Microgels and Nanogels: Emerging Platforms for Drug Delivery and Tissue Engineering, 35.18 BIOMATERIALS 4969 (2014)

⁵⁰ Bernardis, Daniel A., Kevin D. Lance, Natalie A. Ciaccio, and Tejal A. Desai, Nanostructured Thin Film Polymer Devices for Constant-Rate Protein Delivery, 12.10 NANO LETTERS 5355 (2012)

⁵¹ MonosolRx - <http://www.monosolrx.com/index.htm>

Gene Therapy:

Nanomanufacturing techniques have also given a big boost to gene therapy. The idea behind gene therapy is to inject alien genetic material, packaged in carriers known as vectors, into targeted cells in order to correct the workings of deviant genes or to bestow biological ability not present previously. Gold nanoparticles and multifunctional nanorods have been shown to be excellent vectors, several times more efficient in delivery than the conventional viral methods. Use of NDs, however, has been shown to be almost two orders of magnitude more efficient at optimal conditions.⁵³

Diagnostics

In the realm of diagnostics, advances in nanotechnology have enabled lab-on-a-chip (LOC) technology, where many laboratory functions are implemented on a single chip. This technology will enable advanced lab functions with extremely small fluid volumes. The numerous applications include speedy blood examinations during the initial outbreak of disease, improved nutrition safety screenings, and point-of-care testing systems invaluable in tackling global health challenges.⁵⁴ Nanomanufacturing techniques are also contributing immensely to the emerging field of diagnostics using genome sequencing. The Human Genome Project⁵⁵, which formally began in the late 1990s, has led to discovery of genes associated with diseases at an exponential rate (Figure 6). During the last three decades, the speed of sequencing a genome has increased by over 780,000 times. As the trend continues, a \$1,000 USD sequencing system, which can finish reading of 3 billion human genomes in a timeframe of less than an hour, could be readily available to most doctors.⁵⁶ The promising work on nanoscale pores (nanopores)⁵⁷ aims to bring the cost down to the more ambitious target of \$100USD. Nanopores are versatile single-molecule sensors that can be used for the label-free detection and structural analysis of biological polymers such as DNA, RNA, polypeptides, and DNA–protein complexes in solution. They are used to essentially sieve and “unfold” the DNA strand to a linear configuration in conjunction with electromechanical measurement apparatuses that allow for the extraction of molecular properties.⁵⁸ These diagnostic procedures will provide much more efficient and effective healthcare.⁵⁹

⁵² Applied Pharma Research - <http://www.apr.ch/site/licence/index.htm#licence/>

⁵³ Zhang, Xue-Qing, Mark Chen, Robert Lam, Xiaoyang Xu, Eiji Osawa, and Dean Ho, Polymer-Functionalized Nanodiamond Platforms as Vehicles for Gene Delivery, 3.9 ACS NANO 2609 (2009)

⁵⁴ Yager, Paul, Thayne Edwards, Elain Fu, Kristen Helton, Kjell Nelson, Milton R. Tam, and Bernhard H. Weigl, Microfluidic Diagnostic Technologies for Global Public Health, 442.7101 NATURE 412 (2006)

⁵⁵ An international scientific research project with the goal of determining the sequence of chemical base pairs (which make up human DNA) and identifying & mapping all of the genes of the human genome from both a physical and functional standpoint.

<http://www.genome.gov/10001772>

⁵⁶ Chang, Yu-Sang and Lee, Jinsoo and Jung, Yun-Seok, Are Technology Improvement Rates of Knowledge Industries Following Moore’s Law?: An Empirical Study of Microprocessor, Mobile Cellular, and Genome Sequencing Technologies (October 2012). KDI School of Public Policy and Management Working Paper No. 12-04. Available at SOCIAL SCIENCE RESEARCH NETWORK: <http://dx.doi.org/10.2139/ssrn.2017413>

⁵⁷ Genia Corporation - <http://www.geniachip.com/technology/>

⁵⁸ Ivanov, Aleksandar P., Emanuele Instuli, Catriona M. Mcgilvery, Geoff Baldwin, David W. McComb, Tim Albrecht, and Joshua B. Edelman, DNA Tunneling Detector Embedded in a Nanopore, 11.1 NANO LETTERS 279 (2011)

⁵⁹ Emilien, G, Impact of Genomics on Drug Discovery and Clinical Medicine, 93.7 QJM 391 (2000)

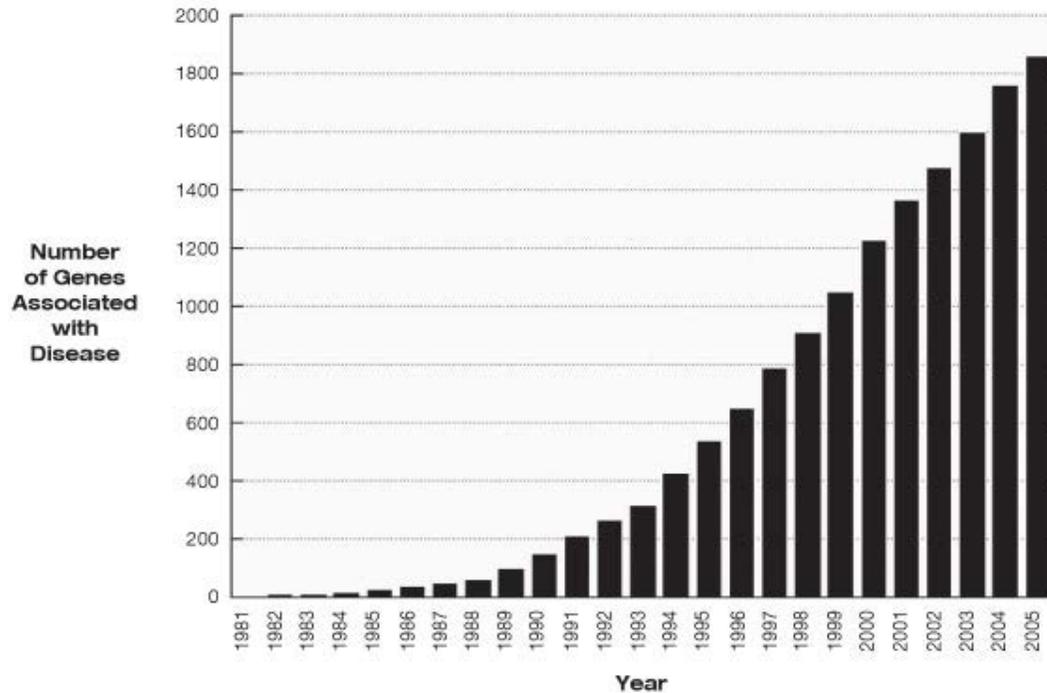


Figure 6: Cumulative Pace of Disease Gene Discovery 1981-2005 (Source: Online Mendelian Inheritance of Man, OMIM. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Balitmore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD). url:<http://www.ncbi.nlm.nih.gov/omim/>)

Conclusion

Advances in nanoscale science in the last few decades have opened up the possibility of using many new materials and process in manufacturing, some of which have already made their way to the factory floor. These nanomanufacturing techniques have improved production efficiency in many industries. Established industries, like the semiconductor industry, are relying on the breakthroughs in nanomanufacturing to continue on their technical trajectories, while emerging industries like the solar industry are looking toward innovations in nanomanufacturing to increase commercial viability of products. While the improvements offered by the nanomanufacturing techniques until now has essentially been incremental, new manufacturing techniques like self-assembly promise to alter the nature of manufacturing all together. Whether it is in renewable energy or new drug delivery systems, the application of nanomanufacturing techniques will enable technical and commercial viability of many promising products.