NANOMEDICINE AND MEDICAL NANOROBOTICS

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Summary

Nanomedicine is the process of diagnosing, treating, and preventing disease and traumatic injury, of relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body.

In the relatively near term, nanomedicine can address many important medical problems by using nanoscale-structured materials and simple nanodevices that can be manufactured today, including the interaction of nanostructured materials with biological systems.

In the mid-term, biotechnology will make possible even more remarkable advances in molecular medicine and biobotics, including microbiological biorobots or engineered organisms. In the longer term, perhaps 10-20 years from today, the earliest molecular machine systems and nanorobots may join the medical armamentarium, finally giving physicians the most potent tools imaginable to conquer human disease, ill-health, and aging.

1. Nanotechnology and Nanomedicine

Annual U.S. federal funding for nanotechnology R&D exceeded $500 million in 2002 reaching $849 million in FY 2004 and could approach $1 billion in next year's budget. The European Commission has set aside 1.3 billion euros for nanotechnology research during 2003-2006, with annual nanotechnology investment worldwide reaching approximately $3 billion in 2003. The worldwide market for nanoscale devices and molecular modelling should grow 28%/year, rising from $406 million in 2002 to $1.37 billion in 2007, with a 35%/year growth rate in revenues from biomedical nanoscale devices.

In December 2002 the U.S. National Institutes of Health announced a 4-year program for nanoscience and nanotechnology in medicine. Burgeoning interest in the medical applications of nanotechnology has led to the emergence of a new field called nanomedicine. Most broadly, nanomedicine is the process of diagnosing, treating, and preventing disease and traumatic injury, of relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body. The NIH Roadmap's new Nanomedicine Initiatives, first released in late 2003, "envision that this cutting-edge area of research will begin yielding medical benefits as early as 10 years from now" and will begin with "establishing a handful of Nanomedicine Centers...staffed by a highly interdisciplinary scientific crew including biologists, physicians, mathematicians, engineers and computer scientists...gathering extensive information about how molecular machines are built" who will also develop "a new kind of vocabulary – lexicon – to define biological parts and processes in engineering terms". Even state-funded programs have begun, such as New York's Alliance for Nanomedical Technologies.

In the relatively near term, over the next 5 years, nanomedicine can address many important medical problems by using nanoscale-structured materials and simple nanodevices that can be manufactured today (Section 2). This includes the interaction of nanostructured materials with biological systems. Over the next 5-10 years, biotechnology will make possible even more remarkable advances in molecular medicine and biobotics – microbiological robots or engineered organisms (Section 3). In the longer term, perhaps 10-20 years from today, the earliest molecular machine systems and nanorobots may join the medical armamentarium, finally giving physicians the most potent tools imaginable to conquer human disease, ill-health, and aging (Section 4).

2. Medical Nanomaterials and Nanodevices

2.1. Nanopores

Perhaps one of the simplest medical nanomaterials is a surface perforated with holes, or nanopores. In 1997 Desai and Ferrari created what could be considered one of the earliest therapeutically useful nanomedical devices, employing bulk micromachining to fabricate tiny cell-containing chambers within single crystalline silicon wafers. The chambers interface with the surrounding biological environment through polycrystalline silicon filter membranes which are micromachined to present a high density of uniform

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nanopores as small as 20 nanometers in diameter. These pores are large enough to allow small molecules such as oxygen, glucose, and insulin to pass, but are small enough to impede the passage of much larger immune system molecules such as immunoglobulins and graft-borne virus particles. Safely ensconced behind this artificial barrier, immunoisolated encapsulated rat pancreatic cells may receive nutrients and remain healthy for weeks, secreting insulin back out through the pores while the immune system remains unaware of the foreign cells which it would normally attack and reject. Microcapsules containing replacement islets of Langerhans cells – most likely easily-harvested piglet islet cells – could be implanted beneath the skin of some diabetes patients.[16] This could temporarily restore the body's delicate glucose control feedback loop without the need for powerful immunosuppressants that can leave the patient at serious risk for infection. Supplying encapsulated new cells to the body could also be a valuable way to treat other enzyme or hormone deficiency diseases, including encapsulated neurons which could be implanted in the brain and then be electrically stimulated to release neurotransmitters, possibly as part of a future treatment for Alzheimer's or Parkinson's diseases.

The flow of materials through nanopores can also be externally regulated. The first artificial voltage-gated molecular nanosieve was fabricated by Martin and colleagues in 1995. Martin's membrane contains an array of cylindrical gold nanotubules with inside diameters as small as 1.6 nanometers. When the tubules are positively charged, positive ions are excluded and only negative ions are transported through the membrane. When the membrane receives a negative voltage, only positive ions can pass. Future similar nanodevices may combine voltage gating with pore size, shape, and charge constraints to achieve precise control of ion transport with significant molecular specificity. Martin's recent efforts have been directed at immobilizing biochemical molecular-recognition agents such as enzymes, antibodies, other proteins and DNA inside the nanotubes as active biological nanosensors, to perform drug separations, and to allow selected biocatalysis. Others are investigating synthetic nanopore ion pumps, voltage-gated nanopores embedded in artificial membranes, and an ion channel switch biosensor that detects changes in chemical concentration of $\sim 10^{-18}$. Molecular dynamics theoretical studies of viscosity and diffusion through nanopores are in progress.

Finally, Daniel Branton's team at Harvard University has conducted an ongoing series of experiments using an electric field to drive a variety of RNA and DNA polymers through the central nanopore of an alpha-hemolysin protein channel mounted in a lipid bilayer similar to the outer membrane of a living cell. By 1998, Branton had shown that the nanopore could be used to rapidly discriminate between pyrimidine and purine segments (the two types of nucleotide bases) along a single RNA molecule. In 2000, the scientists demonstrated the ability to distinguish between DNA chains of similar length and composition that differ only in base pair sequence. Current research is directed toward reliably fabricating pores with specific diameters and repeatable geometries at high precision, understanding the unzipping of double-stranded DNA as one strand is pulled through the pore and the recognition of folded DNA molecules passing through the pore, experiments with new 3-10 nm silicon-nitride nanopores, and investigating the benefits of adding electrically conducting electrodes to pores to improve longitudinal resolution "possibly to the single-base level for DNA".Nanopore-based DNA-sequencing devices could allow per-pore read rates potentially up to 1000

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bases per second, possibly eventually providing a low-cost high-throughput method for very rapid genome sequencing.

2.2. Artificial Binding Sites and Molecular Imprinting

Another early goal of nanomedicine is to study how biological molecular receptors work, and then to build artificial binding sites on a made-to-order basis to achieve specific medical results. Molecular imprinting is an existing technique in which a cocktail of functionalized monomers interacts reversibly with a target molecule using only noncovalent forces. The complex is then cross-linked and polymerized in a casting procedure, leaving behind a polymer with recognition sites complementary to the target molecule in both shape and functionality. Each such site constitutes an induced molecular "memory," capable of selectively binding the target species. In one experiment involving an amino acid derivative target, one artificial binding site per (3.8 nm) polymer block was created. Chiral separations, enzymatic transition state activity, and high receptor affinities have been demonstrated.

Molecularly imprinted polymers could be medically useful in clinical applications such as controlled drug release, drug monitoring devices, quick biochemical separations and assays, recognition elements in biosensors and chemosensors, and biological and receptor mimics including artificial antibodies (plastibodies) or biomimicking enzymes (plastizymes). But molecularly imprinted polymers have limitations, such as incomplete template removal, broad guest affinities and selectivities, and slow mass transfer. Imprinting inside dendrimers (Section 2.7) may allow quantitative template removal, nearly homogeneous binding sites, solubility in common organic solvents, and amenability to the incorporation of other functional groups.

2.3. Quantum Dots and Nanocrystals

Fluorescent tags are commonplace in medicine and biology, found in everything from HIV tests to experiments that image the inner functions of cells. But different dye molecules must be used for each color, color-matched lasers are needed to get each dye to fluoresce, and dye colors tend to bleed together and fade quickly after one use. "Quantum dot" nanocrystals have none of these shortcomings. These dots are tiny particles measuring only a few nanometers across, about the same size as a protein molecule or a short sequence of DNA. They come in a nearly unlimited palette of sharply-defined colors which can be customized by changing particle size or composition. Particles can be excited to fluorescence with white light, can be linked to biomolecules to form long-lived sensitive probes to identify specific compounds up to a thousand times brighter than conventional dyes used in many biological tests, and can track biological events by simultaneously tagging each biological component (e.g., different proteins or DNA sequences) with nanodots of a specific color.

Quantum Dot Corp. (www.qdots.com), the manufacturer, believes this kind of flexibility could offer a cheap and easy way to screen a blood sample for the presence of a number of different viruses at the same time. It could also give physicians a fast diagnostic tool to detect, say, the presence of a particular set of proteins that strongly indicates a person is having a heart attack or to detect known cellular cancer markers.

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On the research front, the ability to simultaneously tag multiple biomolecules both on and inside cells could allow scientists to watch the complex cellular changes and events associated with disease, providing valuable clues for the development of future pharmaceuticals and therapeutics. Quantum dots are useful for studying genes, proteins and drug targets in single cells, tissue specimens, and living animals. Quantum dots are being investigated as chemical sensors, for cancer cell detection, gene expression studies, gene mapping and DNA microarray analysis, immunocytochemical probes, intracellular organelle markers, live cell labeling, medical diagnostics and drug screening, SNP (Single Nucleotide Polymorphism) genotyping, vascular imaging and many other applications. Quantum dot physics has been studied theoretically and computationally using time-dependent density functional theory and other methods.

Researchers from Northwestern University and Argonne National Laboratory have created a hybrid "nanodevice" composed of 4.5-nm nanocrystals of biocompatible titanium dioxide semiconductor covalently attached with snippets of oligonucleotide DNA. Experiments showed that these nanocomposites not only retain the intrinsic photocatalytic capacity of TiO_2 and the bioactivity of the oligonucleotide DNA, but more importantly also possess the unique property of a light-inducible nucleic acid endonuclease (separating when exposed to light or x-rays). For example, researchers would attach to the semiconductor scaffolding a strand of DNA that matches a defective gene within a cell, then introduce the nanoparticle into the cell nucleus where the attached DNA binds with its defective complementary DNA strand, whereupon exposure of the bound nanoparticle to light or x-rays snips off the defective gene. Other molecules besides oligonucleotides can be attached to the titanium dioxide scaffolding, such as navigational peptides or proteins, which, like viral vectors, can help the nanoparticles home in on the cell nucleus. This simple nanocrystal nanodevice might one day be used to target defective genes that play a role in cancer, neurological disease and other conditions, though testing in a laboratory model is at least two years away.

2.4. Fullerenes and Nanotubes

Soluble derivatives of fullerenes such as C_{60} have shown great utility as pharmaceutical agents. These derivatives, many already in clinical trials (www.csixty.com), have good biocompatibility and low toxicity even at relatively high dosages. Fullerene compounds may serve as antiviral agents (most notably against HIV,[5] where they have also been investigated computationally), antibacterial agents (*E. coli*,[62] *Streptococcus*, *Mycobacterium tuberculosis*, etc.), photodynamic antitumor and anticancer therapies, antioxidants and anti-apoptosis agents which may include treatments for amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease) and Parkinson's disease. Single-walled and multi-walled carbon nanotubes are being investigated as biosensors, for example to detect glucose, ethanol, hydrogen peroxide, selected proteins such as immunoglobulins, and as an electrochemical DNA hybridization biosensor.

2.5. Nanoshells and Magnetic Nanoprobes

Halas and West at Rice University in Houston have developed a platform for nanoscale drug delivery called the nanoshell. Unlike carbon fullerenes, the slightly larger nanoshells are dielectric-metal nanospheres with a core of silica and a gold coating,

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whose optical resonance is a function of the relative size of the constituent layers. The nanoshells are embedded in a drug-containing tumor-targeted hydrogel polymer and injected into the body. The shells circulate through the body until they accumulate near tumor cells. When heated with an infrared laser, the nanoshells (each slightly larger than a polio virus) selectively absorb the IR frequencies, melt the polymer and release their drug payload at a specific site. Nanoshells offer advantages over traditional cancer treatments: earlier detection, more detailed imaging, fast noninvasive imaging, and integrated detection and treatment. This technique could also prove useful in treating diabetes. Instead of taking an injection of insulin, a patient would use a ballpoint-pen-size infrared laser to heat the skin where the nanoshell polymer had been injected. The heat from nanoshells would cause the polymer to release a pulse of insulin. Unlike injections, which are taken several times a day, the nanoshell-polymer system could remain in the body for months.

Nanospectra Biosciences (www.nanospectra.com), a private company started by Halas and West, is developing commercial applications of nanoshell technology. Nanospectra is conducting animal studies at the MD Anderson Cancer Center at the University of Texas, specifically targeting micrometastases, tiny aggregates of cancer cells too small for surgeons to find and remove with a scalpel. The company hopes to start clinical trials for the cancer treatment by 2004 and for the insulin-delivery system by 2006. In mid-2003, Rice researchers announced the development of a point-of-care whole blood immunoassay using antibody-nanoparticle conjugates of gold nanoshells. Varying the thickness of the metal shell allow precise tuning of the color of light to which the nanoshells respond; near-infrared light penetrates whole blood very well, so it is an optimal wavelength for whole blood immunoassay.[79] Successful detection of sub-nanogram-per-milliliter quantities of immunoglobulins was achieved in saline, serum, and whole blood in 10-30 minutes.[78]

An alternative approach pursued by Triton BioSystems (www.tritonbiosystems.com) is to bond iron nanoparticles and monoclonal antibodies into nanobioprobes about 40 nanometers long. The chemically inert probes are injected and circulate inside the body, whereupon the antibodies selectively bind to tumor cell membranes. Once the tumor (whether visible or micrometastases) is covered with bioprobes after several hours, a magnetic field generated from a portable alternating magnetic field machine (similar to a miniaturized MRI machine) heats the iron particles to more than 170 degrees, killing the tumor cells in a few seconds. Once the cells are destroyed, the body's excretion system removes cellular residue and nanoparticles alike. Test subjects feel no pain from the heat generated. Triton BioSystems plans to start designing human tests and ask the FDA for permission to begin human clinical trials in 2006.

Mirkin's group at Northwestern University uses magnetic microparticle probes coated with target protein-binding antibodies plus 13-nm nanoparticle probes with a similar coating but including a unique hybridized "bar-code" DNA sequence as an ultrasensitive method for detecting protein analytes such as prostate-specific antigen (PSA). After the target protein in the test sample is captured by the microparticles, magnetic separation of the complexed microparticle probes and PSA is followed by dehybridization of the bar-code oligonucleotides on the nanoparticle probe surface, allowing the determination of the presence of PSA by identifying the bar-code sequence

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released from the nanoparticle probe. Using polymerase chain reaction on the oligonucleotide bar codes allows PSA to be detected at 3 attomolar concentration, about a million times more sensitive than comparable clinically accepted conventional assays for detecting the same protein target.

2.6. Targeted Nanoparticles and Smart Drugs

Multisegment gold/nickel nanorods are being explored by Leong's group at Johns Hopkins School of Medicine as tissue-targeted carriers for gene delivery into cells that "can simultaneously bind compacted DNA plasmids and targeting ligands in a spatially defined manner" and allow "precise control of composition, size and multifunctionality of the gene-delivery system." The nanorods are electrodeposited into the cylindrical 100 nm diameter pores of an alumina membrane, joining a 100 nm length gold segment and a 100 nm length nickel segment. After the alumina template is etched away, the nanorods are functionalized by attaching DNA plasmids to the nickel segments and transferrin, a cell-targeting protein, to the gold segments, using molecular linkages that selectively bind to only one metal and thus impart biofunctionality to the nanorods in a spatially defined manner. Leong notes that extra segments could be added to the nanorods, for example to bind additional biofunctionalities such as an endosomolytic agent, or magnetic segments could be added to allow manipulating the nanorods with an external magnetic field.

Targeted radioimmunotherapeutic agents include the FDA-approved "cancer smart bombs" that deliver tumor-killing radioactive yttrium (Zevalin) or iodine (Bexxar) attached to a lymphoma-targeted (anti-CD20) antibody Other antibody-linked agents are being investigated such as the alpha-emitting actinium-based "nanogenerator" molecules that use internalizing monoclonal antibodies to penetrate the cell and have been shown, in vitro, to specifically kill leukemia, lymphoma, breast, ovarian, neuroblastoma, and prostate cancer cells at becquerel (picocurie) levels, with promising preliminary results against advanced ovarian cancer in mice. However, drug specificity is still no better than the targeting accuracy of the chosen antibody, and there is significant mistargeting, leading to unwanted side effects.

Enzyme-activated drugs, first developed in the 1980s and still under active investigation, separate the targeting and activation functions. For instance, an antibody-directed enzyme-triggered prodrug cancer therapy is being developed by researchers at the University of Gottingen in Germany. This targeted drug molecule turns lethal only when it reaches cancer cells while remaining harmless inside healthy cells. In tests, mice previously implanted with human tumors are given an activating targeted enzyme that sticks only to human tumor cells, mostly ignoring healthy mouse cells. Then the antitumor molecule is injected. In its activated state, this fungal-derived antibiotic molecule is a highly-strained ring of three carbon atoms that is apt to burst open, becoming a reactive molecule that wreaks havoc among the nucleic acid molecules essential for normal cell function. But the molecule is injected as a prodrug – an antibiotic lacking the strained ring and with a sugar safety-catch. Once the sugar is clipped off by the previously positioned targeted enzyme, the drug molecule rearranges itself into a three-atom ring, becoming lethally active. Notes chemist Philip Ball: "The selectivity of the damage still depends on antibody's ability to hook onto the right cells,

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and on the absence of other enzymes in the body that also activate the prodrug."

A further improvement in enzyme-activated drugs are "smart drugs" that become medically active only in specific circumstances and in an inherently localized manner. Yoshihisa Suzuki at Kyoto University has designed a novel drug molecule that releases antibiotic only in the presence of an infection. Suzuki started with the common antibiotic molecule gentamicin and bound it to a hydrogel using a newly developed peptide linker. The linker can be cleaved by a proteinase enzyme manufactured by *Pseudomonas aeruginosa*, a Gram-negative bacillus that causes inflammation and urinary tract infection, folliculitis, and otitis externa in humans. Tests on rats show that when the hydrogel is applied to a wound site, the antibiotic is not released if no *P. aeruginosa* bacteria are present. But if any bacteria of this type are present, then the proteolytic enzyme that the microbes naturally produce cleaves the linker and the gentamicin is released, killing the bacteria. "If the proteinase specific to each bacterium [species] can be used for the signal," wrote Suzuki, "different spectra of antibiotics could be released from the same dressing material, depending on the strain of bacterium." In subsequent work an alternative antibiotic release system triggered by thrombin activity, which accompanies *Staphylococcus aureus* wound infections, was successfully tested as a high-specificity stimulus-responsive controlled drug release system. Other stimulus-responsive "smart" hydrogels are being studied, including a hydrogel-composite membrane co-loaded with insulin and glucose oxidase enzyme that exhibits a twofold increase in insulin release rate when immersed in glucose solution, demonstrating "chemically stimulated controlled release" and "the potential of such systems to function as a chemically-synthesized artificial pancreas.

Nanoparticles with an even greater range of action are being developed by Raoul Kopelman's group at the University of Michigan. Their current goal is the development of novel molecular nanodevices for the early detection and therapy of brain cancer, using silica-coated iron oxide nanoparticles with a biocompatible polyethylene glycol coating. The miniscule size of the particles – 20-200 nanometers – should allow them to penetrate into areas of the brain that would otherwise be severely damaged by invasive surgery. The particles are attached to a cancer cell antibody or other tracer molecule that adheres to cancer cells, and are affixed with a nanopacket of contrast agent that makes the particles highly visible during magnetic resonance imaging (MRI). The particles also enhance the killing effect during the subsequent laser irradiation of brain tissue, concentrating the destructive effect only on sick cells unlike traditional chemotherapy and radiation which kills cancerous cells but also destroys healthy cells. Nanoparticles allow MRI to see a few small brain tumor cells as small as 50 microns – depending on the cancer type, tumor cells can range from 5-50 microns each and may grow in locations separate from the tumor site, hence are sometimes not visible to surgeons. Fei Yan, a postdoc in Kopelman's lab, is working on these nanodevices, called the Dynamic Nano-Platform (Figure 1), now being commercialized as therapeutic "nanosomes" under license to Molecular Therapeutics (www.moleculartherapeutics.com). According to the company, "the nanosome platform provides the core technology with interchangeable components that provide ultimate flexibility in targeting, imaging and treatment of cancer and cardiovascular disease indications."

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Bibliography

Adamschik, M., M. Hinz, C. Maier, P. Schmid, H. Seliger, E.P. Hofer and E. Kohn, 2001 - , "Diamond micro system for bio-chemistry," Diam. Rel. Mater. 10, 722 – 730

Ahmad, A., S. Senapati, M.I. Khan, R. Kumar, R. Ramani, V. Srinivas and M. Sastry, 2003 - "Intracellular synthesis of gold nanoparticles by a novel alkalotolerant actinomycete, *Rhodococcus* species," Nanotechnology 14, 824 – 828

Akita, S., Y. Nakayama, S. Mizooka, T. Okawa, Y. Miyatake, S. Yamanaka, M. Tsuji and T. Nosaka,2001 - "Nanotweezers consisting of carbon nanotubes operating in an atomic force microscope," Appl. Phys. Lett. 79, 1691

Alberti, P., and J.-L. Mergny, 2003 - "DNA duplex-quadruplex exchange as the basis for a nanomolecular machine,"Proc. Natl. Acad. Sci. (USA) 100, 1569-1573 http://www.pnas.org/cgi/content/full/100/4/1569

Albrecht, T.R., S. Akamine, M.J. Zdeblick and C.F. Quate, 1990 - "Microfabrication of integrated scanning tunneling microscope," J. Vac. Sci. Technol. A 8, 317-318

"Alliance for Nanomedical Technologies," http://www.research.cornell.edu/anmt/

Arkin, A.P., 2001 - "Synthetic cell biology," Curr. Opin. Biotechnol. 12, 638 -644

Baker, Jr., J.R., A. Quintana, L. Piehler, M. Banazak-Holl, D. Tomalia, E. Raczka, 2001 - "The synthesis and testing of anti-cancer therapeutic nanodevices," Biomed. Microdevices 3, 61 – 69

Ball, P., 2002 - "Magic bullet homes in," Nature Science Update, 4 March 2002;

http://www.nature.com/nsu/020225/020225-14.html

Becker, R.S., J.A. Golovchenko and B.S. Swartzentruber, 1987 - "Atomic-scale surface modifications using a tunneling microscope," Nature 325, 419-421

Betley, T.A., J.A. Hessler, A. Mecke, M.M. Banaszak Holl, B. Orr, S. Uppuluri, D.A. Tomalia and J.R. Baker, Jr., 2002 - ., "Tapping mode atomic force microscopy investigation of poly(amidoamine) core-shell tecto(dendrimers) using carbon nanoprobes," Langmuir 18, 3127-3131

Bhatia, S.K. and D. Nicholson, 2003 - , "Hydrodynamic origin of diffusion in nanopores," Phys. Rev. Lett. 90, 016105

Blackledge, C., D.A. Engebretson and J.D. McDonald, 2000 - Langmuir 16, 8317

Boggild, P., T.M. Hansen, C. Tanasa and F. Grey, 2001 - , "Fabrication and actuation of customised nanotweezers with a 25 nm gap."Nanotechnology 12, 331 – 335

Bogunia-Kubik,K. and M. Sugisaka, 2002 - "From molecular biology to nanotechnology and nanomedicine," Biosystems 65, 123-138

Itoh, T., T. Ohashi and T. Suga, 1996 - "Piezoelectric cantilever array for multiprobe scanning force microscopy," 9th Intl. Conf. on MEMS , p. 451-455

Borchardt, P.E., R.R. Yuan, M. Miederer, M.R. McDevitt and D.A. Scheinberg,2003 -"Targeted actinium-225 in vivo generators for therapy of ovarian cancer," Cancer Res. 63, 5084 – 5090

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Bosi, S., T. Da Ros, S. Castellano, E. Banfi and M. Prato, 2000 - , "Antimycobacterial activity of ionic fullerene derivatives,"Bioorg. Med. Chem. Lett. 10, 1043-1045

Bowden, N., F. Arias, T. Deng and G.M. Whitesides, 2001 - "Self-assembly of microscale objects at a liquid/liquid interface through lateral capillary forces," Langmuir 17, 1757 – 1765

Brahim, S., D. Narinesingh and A. Guiseppi-Elie, 2002 - "Bio-smart hydrogels: co-joined molecular recognition and signal transduction in biosensor fabrication and drug delivery," Biosens. Bioelectron. 17, 973-981

Breen, T.I., J. Tien, S.R.J. Oliver, T. Hadzic and G.M. Whitesides, 1999 - "Design and self-assembly of open, regular, 3D mesostructures," Science 284, 948-951

Breivik, J., 2001 - "Self-organization of template-replicating polymers and the spontaneous rise of genetic information," Entropy 3, 273 - 279 http://www.mdpi.org/entropy/papers/e3040273.pdf

Brittain, S.T., O.J.A. Schueller, H. Wu, S. Whitesides and G.M. Whitesides, 2001 - "Microorigami: fabrication of small, three-dimensional, metallic structures," J. Phys. Chem. B 105, 347-350

Bruggemann, O. 2002 - Molecularly imprinted materials--receptors more durable than nature can provide Adv. Biochem. Eng. Biotechnol. 76, 127-163

Bullen, D., S. Chung, X. Wang, J. Zou, C. Liu and C. Mirkin, 2002 - "Development of parallel dip pen nanolithography probe arrays for high throughput nanolithography," Symposium LL: Rapid Prototyping Technologies, Materials Research Society Fall Meeting, 2-6 December 2002, Boston, MA, Proceedings of the MRS, Vol. 758; http://mass.micro.uiuc.edu/publications/papers/84.pdf

Cagin, T., A. Jaramillo-Botero, G. Gao, W.A. Goddard III, 1998 - Molecular Mechanics and Molecular DynamicsAnalysis of Drexler-Merkle Gears and Neon Pump Nanotechnology 9, 143 http://www.wag.caltech.edu/foresight/foresight_1.html

Cai, H., X. Cao, Y. Jiang, P. He and Y. Fang, 2003 - "Carbon nanotube-enhanced electrochemical DNA biosensor for DNA hybridization detection," Anal. Bioanal. Chem. 375, 287 -293

Carbone, A., and N.C. Seeman, 2002 - "Circuits and programmable self-assembling DNA structures," Proc. Natl. Acad. Sci. (USA) 99, 12577 – 12582

http://www.pnas.org/cgi/content/full/99/20/12577

Cello, J., A.V. Paul and E. Wimmer, 2002 - "Chemical synthesis of poliovirus cDNA: Generation of infectious virus in the absence of natural template," Science 297, 1016 - 1018; http://www.sciencemag.org/cgi/content/full/1072266/DC1

Cetin, O., K. Saitou, H. Nishigaki, S. Nishiwaki, T. Amago and N. Kikuchi, 2001 - ., "Modular structural component design using the first order analysis and decomposition-based assembly synthesis," Proc. 2001 ASME Intl. Mechanical Engineering Congress and Exposition, New York, 11-16 November 2001;

http://www-personal.engin.umich.edu/~kazu/papers/imece-01.pdf

Chan, W.C., D.J. Maxwell, X. Gao, R.E. Bailey, M. Han and S. Nie, 2002 - "Luminescent quantum dots for multiplexed biological detection and imaging,"Curr. Opin. Biotechnol. 13, 40-43

Chen, C.I., 1993 - *Introduction to Scanning Tunneling Microscopy*, Oxford University Press, Oxford

Chen, J., and N.C. Seeman, 1991 - "Synthesis from DNA of a molecule with the connectivity of a cube," Nature 350, 631-633

Chen, R.J., S. Bangsaruntip, K.A. Drouvalakis, N.W. Kam, M. Shim, Y. Li, W. Kim, P.J. Utz and H. Dai, 2003 - "Noncovalent functionalization of carbon nanotubes for highly specific electronic biosensors," Proc. Natl. Acad. Sci. (USA) 100, 4984-4989

Choi, C., 2002 - "Radio-controlled DNA act as gene switches," United Press International, 14 January 2002; http://www.mail-archive.com/ctrl@listserv.aol.com/msg85249.html

Choi, I.S., N. Bowden and G.M. Whitesides, 1999 - , "Macroscopic, hierarchical, two-dimensional self-assembly," Angew. Chem. Int. Ed. Engl. 38, 3078 - 3081.

Chrusch, D.D., B.W. Podaima and R. Gordon,2002 - "Cytobots: intracellular robotic

UNESCO – EOLSS SAMPLE CHAPTERS

micromanipulators," in *Conference Proceedings*, [W. Kinsner and A. Sebak (eds.)], 2002 IEEE Canadian Conf. on Electrical and Computer Engineering, 12-15 May 2002, IEEE, Winnipeg, Canada

http://www.umanitoba.ca/faculties/medicine/radiology/Dick_Gordon_papers/Chrusch,Podaima,Gordon2002

Clark, T.D., M. Boncheva, J.M. German, M. Weck and G.M. Whitesides, 2002 -, "Design of three dimensional, millimeter-scale models for molecular folding," J. Am. Chem. Soc. 124, 18 – 19

Clark, T.D., J. Tien, D.C. Duffy, K.E. Paul and G.M. Whitesides, 2001 - , "Self-assembly of 10-micron-sized objects into ordered three dimensional arrays," J. Am. Chem. Soc. 123, 7677-7682

Clark, T.D., R. Ferrigno, J. Tien, K.E. Paul and G.M. Whitesides,2002 - , "Template-directed self-assembly of 10-microm-sized hexagonal plates," J. Am. Chem. Soc. 124, 5419 – 5426

Collier, C.P., G. Mattersteig, E.W. Wong, Y. Luo, K. Beverly, J. Sampaio, F.M. Raymo, J.F. Stoddart and J.R. Heath, 2000 - , "A [2]Catenane-based solid state electronically reconfigurable switch," Science 289, 1172 – 1175

Cornell, B., V. Braach-Maksvytis, L. King, P. Osman, B. Raguse, L. Wieczorek and R. Pace, 1997 - "A biosensor that uses ion-channel switches," Nature 387, 580-583

Cramer, P., D.A. Bushnell and R.D. Kornberg, 2001 - "Structural basis of transcription: RNA polymerase II at 2.8 Angstrom resolution," Science 292, 1863- 1876

Cumings, J., A. Zettl, 2000 - Science 289, 602 (2000).

Davidson, J., W. Kang, K. Holmes, A. Wisitsora-At, P. Taylor, V. Pulugurta, R. Venkatasubramanian and F. Wells, 2001 - "CVD diamond for components and emitters," Diam. Rel. Mater. 10, 1736-1742

Deamer, D.W. and M. Akeson, 2000 - "Nanopores and nucleic acids: prospects for ultrarapid sequencing," Trends Biotechnol. 18, 147-151

"Dendrimers, Tecto-Dendrimers, 3-D Dendrimers," Center for Biologic Nanotechnology, University of Michigan, 12 August 2003; http://nano.med.umich.edu/Dendrimers.html

Desai, T.A., W.H. Chu, J.K. Tu, G.M. Beattie, A. Hayek and M. Ferrari, 1998 - "Microfabricated immunoisolating biocapsules,"Biotechnol. Bioeng. 57, 118 -120

Diaz, D.J., J.E. Hudson, G.D. Storrier, H.D. Abruna, N. Sundararajan and C.K. Ober,2001 - Langmuir 17, 5932 – 5938

Dischler, B., and C. Wild (eds.), 1998 - *Low-Pressure Synthetic Diamond: Manufacturing and Applications*, Springer Verlag, New York

Dixon, K.L., 2003 - "The radiation biology of radioimmunotherapy," Nucl. Med. Commun. 24, 951-957

Douglas, T., M. Young, 2998 - "Host-guest encapsulation of materials by assembled virus protein cages," Nature 393, 152-155

Dowling, D.P., P.V. Kola, K. Donnelly and T.C. Kelly, 1997 - "Evaluation of diamond-like carbon-coated orthopaedic implants," Diam. Rel. Mat. 6, 390 – 393

Drexler, K.E., 1991 -, "Molecular tip arrays for molecular imaging and nanofabrication," J. Vac. Sci. Technol. B 9, 1394-1397

Drexler, K.E., 1992 - *Nanosystems: Molecular Machinery, Manufacturing, and Computation*, John Wiley & Sons, New York

Drexler, K.E., 1981 - "Molecular engineering: an approach to the development of general capabilities for molecular manipulation," Proc. Nat. Acad. Sci. (USA) 78, 5275-5278

Drexler, K.E., 1995 - "Introduction to nanotechnology," in *Prospects in Nanotechnology: Toward Molecular Manufacturing*, [M. Krummenacker and J. Lewis (eds.)], John Wiley & Sons, New York), p. 1.

Drexler, K.E., and R.C. Merkle, "Simple pump selective for neon"; http://www.imm.org/Parts/Parts1.html or http://www.imm.org/Images/pumpApartC.jpg

UNESCO – EOLSS SAMPLE CHAPTERS

Dubertret, B., P. Skourides, D.J. Norris, V. Noireaux, A.H. Brivanlou and A. Libchaber, 2002 - "In vivo imaging of quantum dots encapsulated in phospholipid micelles," Science 298, 1759-1761

Dugan, L.L., E. Lovett, S. Cuddihy, B. Ma, T.-S. Lin and D.W. Choi, 2000 - "Carboxyfullerenes as Neuroprotective Antioxidants," in *Fullerenes: Chemistry, Physics, and Technology*, [K.M. Kadish and R.S. Ruoff (eds.)], John Wiley and Sons, New York , p. 467.

Dzegilenko, F.N., D. Srivastava and S. Saini, 1998 - , "Simulations of carbon nanotube tip assisted mechano-chemical reactions on a diamond surface," Nanotechnology 9, 325 - 330;

http://www.nanology.ustc.edu.cn/chinese/.%5Cpdf%5Cna8404.pdf

Eastwood, M., D.A. McGrouther and R.A. Brown, 1998 - , "Fibroblast responses to mechanical forces," Proc. Inst. Mech. Eng. [H] 212, 85 -92

Eichman, J.D., A.U. Bielinska, J.F. Kukowska-Latallo and J.R. Baker, Jr.,2000 - "The use of PAMAM dendrimers for the efficient transfer of genetic material into cells," Pharm. Sci. Technol. Today 3, 232 – 245

Elowitz M.B., and S. Leibler, 2000 - A synthetic oscillatory network of transcriptional regulators," Nature 403, 335-338

Emerich, D.F. and C.G. Thanos, 2003 - "Nanotechnology and medicine," Expert Opin. Biol. Ther. 3, 655

Endy, D., L. You, J. Yin and I.J. Molineux, 2000 - "Computation, prediction, and experimental tests of fitness for bacteriophage T7 mutants with permuted genomes," Proc. Natl. Acad. Sci. (USA) 97, 5375 – 5380 http://www.pnas.org/cgi/content/full/97/10/5375

Endy, D., and R. Brent, 2001 - "Modelling cellular behavior," Nature 409, 391 -395

Ertl, S., M. Adamschik, P. Schmid, P. Gluche, A. Floter and E. Kohn, 2000 - Surface micromachined diamond microswitch," Diam. Rel. Mater. 9, 970 – 974

Evans, G.A., 2003 - "Method for the complete chemical synthesis and assembly of genes and genomes," United States Patent No. 6,521,427, Egea Biosciences, Inc., San Diego, CA, 18 February 2003.

Fearing, R.S., 1992 - "Micro structures and micro actuators for implementing sub-millimeter robots," in *Precision Sensors, Actuators and Systems*, [H.S. Tzou and T. Fukuda (eds.)], Kluwer Academic Publishers, Boston, MA, p. 39.

Feng, L., S.H. Park, J.H. Reif and H. Yan, 2003 - "A two-state DNA lattice switched by DNA nanoactuator," Angew. Chem. Intl. Ed. 42, 4342 – 4346

Fennimore, A.M., T. D. Yuzvinsky, Wei-Qiang Han, M. S. Fuhrer, J. Cumings and A. Zettl, 2003 - "Rotational actuators based on carbon nanotubes," Nature 424, 408 -410

Feynman, R.P., 1960 - "There's Plenty of Room at the Bottom," Eng. Sci. (CalTech) 23, 22 -36;

http://www.zyvex.com/nanotech/feynman.html

Fincher, E.F., L. Johannsen, L. Kapas, S. Takahashi and J.M. Krueger, 1996 - , "Microglia digest Staphylococcus aureus into low molecular weight biologically active compounds," Am. J. Physiol. 271, R149 – R 156

Freitas Jr.,R.A., 1999 - *Basic Capabilities.* In " *Nanomedicine", Volume* , Landes Bioscience, Georgetown, TX; http://www.nanomedicine.com/NMI.htm

Freitas Jr.R.A., J. 2000 - "Nanodentistry, Amer. Dent. Assoc. 131, 1559 -1566

http://www.rfreitas.com/Nano/Nanodentistry.htm

Freitas Jr.,R.A., 2003 – *Biocompatibility* In: " *Nanomedicine", Volume IIA:* , Landes Bioscience, Georgetown, TX, http://www.nanomedicine.com/NMIIA.htm

Freitas Jr..R.A., 2002 - The future of nanofabrication and molecular scale devices in nanomedicine," Stud. Health Technol. Inform. 80, 45-59

Freitas Jr. R.A., and W.P. Gilbreath (eds.), 1982 - *Advanced Automation for Space Missions*, NASA Conference Publication CP-2255, N83-15348, U.S. GPO, Washington, DC;

UNESCO – EOLSS SAMPLE CHAPTERS

http://www.islandone.org/MMSG/aasm/

Freitas Jr., R.A., and R.C. Merkle, 2004 - *Kinematic Self-Replicating Machines*, Landes Bioscience, Georgetown, TX; http://www.MolecularAssembler.com/KSRM.htm

Freitas Jr., R.A., 2000 -"Say Ah!" The Sciences 40, 26-31 http://www.foresight.org/Nanomedicine/SayAh/index.html

Freitas Jr., R.A., 1998 - "Exploratory design in medical nanotechnology: A mechanical artificial red cell," Artif. Cells, Blood Subst., and Immobil. Biotech. 26, 411-430; http://www.foresight.org/Nanomedicine/Respirocytes.html

Freitas Jr., R.A., 2001 - "Microbivores: Artificial mechanical phagocytes using digest and discharge protocol," Zyvex preprint, March 2001; http://www.rfreitas.com/Nano/Microbivores.htm

Freitas Jr., R.A., 2000 "Clottocytes: Artificial mechanical platelets," Foresight Update No. 41 . 9-11 ; http://www.imm.org/Reports/Rep018.html

Freitas Jr. R.A., and C.J. Phoenix,2002 - "Vasculoid: A personal nanomedical appliance to replace human blood," J. Evol. Technol. 11 ; http://www.jetpress.org/volume11/vasculoid.pdf

Fritz, J., M.K. Baller, H.P. Lang, H. Rothuizen, P. Vettiger, E. Meyer, H.-J. Guntherodt, C. Gerber and J.K. Gimzewski, 2000 - "Translating biomolecular recognition into nanomechanics," Science 288, 316-318 http://www.sciencemag.org/cgi/content/full/288/5464/316

Gao, X. and S. Nie, 2003 - "Molecular profiling of single cells and tissue specimens with quantum dots," Trends Biotechnol. 21, 371-373

Gao, X., W.C. Chan and S. Nie, 2002 - "Long-term multiple color imaging of live cells using quantum dot bioconjugates," J. Biomed. Opt. 7, 532-537

Gao, Y.F., and Z. Suo, 2003 - , "Guided self-assembly of molecular dipoles on a substrate surface," J. Appl. Phys. 93, 4276 ; http://beijing.princeton.edu/~yfgao/140.pdf

Gardner, T.S., C.R. Cantor and J.J. Collins, 2000 - "Construction of a genetic toggle switch in Escherichia coli," Nature 403, 339-342

Garoufalis, C.S., A.D. Zdetsis and S. Grimme, 2001 - , "High level ab initio calculations of the optical gap of small silicon quantum dots," Phys. Rev. Lett. 87, 276402

Gerion, D., W.J. Parak, S.C. Williams, D. Zanchet, C.M. Micheel and A.P. Alivisatos, 2002 - "Sorting fluorescent nanocrystals with DNA," J. Am. Chem. Soc. 124, 7070 – 7074

Gillis, J., 2002 - "Scientists planning to make new form of life," Washington Post, Thursday, 21 November 2002, p. A01; http://www.washingtonpost.com/ac2/wp-dyn?pagename=article&node=&contentId=A17496-2002Nov20

Gillitzer, E., D. Willits, M. Young and T. Douglas, Chem. Commun. (Camb.) 20, 2390 (2002).

Goddard III, W.A., T. Cagin and S.P. Walch, "Atomistic design and simulations of nanoscale machines and assembly," Computational Nanotechnology Project, Materials Simulation Center, California Institute of Technology, 1996; http://www.wag.caltech.edu/gallery/nano_comp.html

Goho, A.M., 2003 - "Life Made to Order: Efforts to create custom-made organisms – one DNA letter at a time – could yield new sources of energy or novel drugs," Technol. Rev. 106, 50 – 57

Gracias, D.H., J. Tien, T.L. Breen, C. Hsu and G.M. Whitesides, 2000 - "Forming electrical networks in three dimensions by self-assembly," Science 289, 1170 - 1172; http://people.bu.edu/jtien/Gracias_Sci_2000_289_1170.pdf

Gracias, D.H., V. Kavthekar, J.C. Love, K.E. Paul and G.M. Whitesides, 2002 - "Fabrication of micrometer-scale, patterned polyhedra by self-assembly," Adv. Mater. 14, 235 – 238

Griffith, S., 2002 - "Tools for designing programmatic self-assembling systems," 6.978 Final Paper, December 2002; http://www.swiss.ai.mit.edu/projects/amorphous/6.978/final-papers/saul-final.pdf

Haberzettl,C.A., 2002 - "Nanomedicine: destination or journey?" Nanotechnology

UNESCO – EOLSS SAMPLE CHAPTERS

13:R9-R13.

"Halas wins innovator award in fight against breast cancer," Rice University Press Release, 9 July 2003; http://www.eurekalert.org/pub_releases/2003-07/ru-hwi070903.php

Hamad-Schifferli, K., J.J. Schwartz, A.T. Santos, S. Zhang and J.M. Jacobson, 2002 - "Remote electronic control of DNA hybridization through inductive coupling to an attached metal nanocrystal antenna," Nature 415, 152 – 156

http://www.nature.com/nlink/v415/n6868/abs/415152a_fs.html

Han, M., X. Gao, J.Z. Su and S. Nie, 2001 - , "Quantum-dot-tagged microbeads for multiplexed optical coding of biomolecules," Nat. Biotechnol. 19, 631-635

Hanaki, K., A. Momo, T. Oku, A. Komoto, S. Maenosono, Y. Yamaguchi and K. Yamamoto, 2003 - "Semiconductor quantum dot/albumin complex is a long-life and highly photostable endosome marker," Biochem. Biophys. Res. Commun. 302, 496-501

Hansen, K.M., H.F. Ji, G. Wu, R. Datar, R. Cote, A. Majumdar and T. Thundat, 2001 - "Cantilever-based optical deflection assay for discrimination of DNA single-nucleotide mismatches," Anal. Chem. 73, 1567-1571

Hirsch, L.R., J.B. Jackson, A.Lee, N.J. Halas and J.L. West, 2003 - , "A whole blood immunoassay using gold nanoshells," Anal. Chem. 75, 2377-2381

Hla, S.-W., and K.-H. Rieder, 2002 - "Engineering of single molecules with a scanning tunneling microscope tip,"Superlattices and Microstructures 31, 63 – 72

Hla, S.-W., and K.-H. Rieder, 2003 - "STM control of chemical reactions: Single-molecule synthesis," Ann. Rev. Phys. Chem. 54, 307 - 330; http://www.phy.ohiou.edu/~hla/HLA-annualreview.pdf

Ho, W., and H. Lee, 1999 - "Single bond formation and characterization with a scanning tunneling microscope," Science 286, 1719 - 1722; http://www.physics.uci.edu/~wilsonho/stm-iets.html

Hogg, T., 1999 - "Robust self-assembly using highly designable structures," Nanotechnology 10, 300 – 307

Hosokawa, K., I. Shimoyama and H. Miura, 1994 - "Dynamics of self-assembling systems: analogy with chemical kinetics," Artif. Life 1, 413 – 427

Huang, D., H. Uchida and M. Aono, 1994 - "Deposition and subsequent removal of single Si atoms on the Si(111)-7x7 surface by a scanning tunneling microscope," J. Vac. Sci. Technol. B 12, 2429-2433

Huang, T.J., W. Lu, H.-R. Tseng, B. Brough, A. Flood, B.-D. Yu, J.F. Stoddart and C.-M. Ho, 2003 - , "Molecular Shuttle Switching in Closely Packed Langmuir Films," 11th Foresight Conference on Molecular Nanotechnology, Palo Alto, CA, 9-12 October 2003; http://www.foresight.org/Conferences/MNT11/Abstracts/Huang/index.html

Huie, J.C., Smart 2003 - "Guided molecular self-assembly: a review of recent efforts," Mater. Struct. 12, 264 – 270

Ishiyama, K., K. I. Arai, M. Sendoh and A. Yamazaki, 2003 - "Spiral-type micro-machine for medical applications," J. Micromechatronics 2, 77-86

Jaiswal, J.K., H. Mattoussi, J.M. Mauro and S.M. Simon,2003 - "Long-term multiple color imaging of live cells using quantum dot bioconjugates," Nat. Biotechnol. 21, 47-51

Johnston, W.K., P.J. Unrau, M.S. Lawrence, M.E. Glasner and D.P. Bartel, 2001 - "RNA-catalyzed RNA polymerization: accurate and general RNA-templated primer extension," Science 292, 1319 – 1325

Kelly, M. 2003 - "Startups Seek Perfect Particles To Search And Destroy Cancer," Small Times, 18 April 2003; http://www.smalltimes.com/document_display.cfm?document_id=5867

Kelly, T.R., H. De Silva and R.A. Silva, 1999, "Unidirectional rotary motion in a molecular system," Nature 401,

pp 150 -152

UNESCO – EOLSS SAMPLE CHAPTERS

Kim, J.-W., A. Malshe and S. Tung, 2003, "Bio-inspired MEMS: A novel microfluidics system actuated by biological cell motors," Institute of Biological Engineering (IBE) Annual Meeting, Athens, GA

Kim, P., and C.M. Lieber, 1999 - "Nanotube nanotweezers," Science 286, 2148-250

Kirk, W.P., and M.A. Reed (eds.), 1992 - *Nanostructures and Mesoscopic Systems*, Academic Press, New York

Klarreich, E., 2003 - "Digital Cells: Computer circuits made of genes may soon program bacteria," Sci. News 163 (26 April 2003); http://www.sciencenews.org/20030426/bob11.asp

Klaus, T., R. Joerger, E. Olsson and C.G. Granqvist, 1999 - , "Silver-based crystalline nanoparticles, microbially fabricated,"Proc. Natl. Acad. Sci. (USA) 96, 13611 -13614

Klem, M.T., D. Willits, M. Young and T. Douglas, 2003 -"2-D array formation of genetically engineered viral cages on Au surfaces and imaging by atomic force microscopy," J. Am. Chem. Soc. 125, 10806

Kohn, E., M. Adamschik, P. Schmid, S. Ertl and A. Floter, 2001 -"Diamond electro-mechanical devices – technology and performance," Diam. Rel. Mater. 10, 1684 – 1691

Kondo, Y., M. Nojiri, Y. Hishikawa, E. Togawa, D. Romanovicz and R.M. Brown Jr.,2002 - "Biodirected epitaxial nanodeposition of polymers on oriented macromolecular templates," Proc. Natl. Acad. Sci. (USA) 99, 14008 - 14013 http://www.pnas.org/cgi/content/full/99/22/14008.

Kong, D., and J. Yin, 1995 - "Whole-virus vaccine development by continuous culture on a complementing host," Biotechnology (NY) 13, 583-586

Koumura, N., R.W. Zijlstra, R.A. van Delden, N. Harada and B.L. Feringa, 1999 - "Light-driven monodirectional molecular rotor," Nature 401, 152-155

Kowshik, M., N. Deshmukh, W. Vogel, J. Urban, S.K. Kulkarni and K.M. Paknikar, 2002 - "Microbial synthesis of semiconductor CdS nanoparticles, their characterization, and their use in the fabrication of an ideal diode," Biotechnol. Bioeng. 78, 583 – 588

Krauss, A.R., O. Auciello, D.M. Gruen, A. Jayatissa, A. Sumant, J. Tucket, D.C. Mancini, N. Moldovan, A. Erdemir, D. Ersoy, M.N. Gardos, H.G. Busmann, E.M. Meyer and M.Q. Ding, 2001 - "Ultrananocrystalline diamond thin films for MEMS and moving mechanical assembly devices," Diam. Rel. Mater. 10, 1952 – 1961

Kukowska-Latallo, J.F., A.U. Bielinska, J. Johnson, R. Spindler, D.A. Tomalia and J.R. Baker, Jr.1996 - . "Efficient transfer of genetic material into mammalian cells using Starburst polyamidoamine dendrimers,", Proc. Natl. Acad. Sci. (USA) 93, 4897 – 4902

Kukowska-Latallo, J.F., E. Raczka, A. Quintana, C. Chen, M. Rymaszewski and J.R. Baker, Jr., 2000 - "Intravascular and endobronchial DNA delivery to murine lung tissue using a novel, nonviral vector," Hum. Gene Ther. 11, 1385 -1395

Landers, J.J., Z. Cao, I. Lee, L.T. Piehler, P.P. Myc, A. Myc, T. Hamouda, A.T. Galecki and J.R. Baker, Jr., 2002 -, "Prevention of influenza pneumonitis by sialic acid-conjugated dendritic polymers," J. Infect. Dis. 186, 1222 – 1230

Lange, D., M. Zimmermann, C. Hagleitner, O. Brand and H. Baltes, 2001 - , "CMOS 10-cantilever array for constant-force parallel scanning AFM,"Technical Digest, Transducers '01, Vol. 2, p. 1074.

Lannoo, M., C. Delerue, G. Allan and Y.M. Niquet, 2003 - "Confinement effects and tunnelling through quantum dots," Philos. Transact. Ser. A Math Phys. Eng. Sci. 361, 259-272

Lee, I., B.D. Athey, A.W. Wetzel, A. Kar, W. Meixner and J.R. Baker, Jr., 2002 - "Structural molecular dynamics studies on therapeutically-applied polyamidoamine dendrimers: the effects of pH and surface derivatization group,"Macromolecules 35, 4510-4520

Lee, S.-W., C. Mao, C.E. Flynn and A.M. Belcher,2002 - , "Ordering of quantum dots using genetically engineered viruses," Science 296, 892 – 895

Lee, S.B. and C.R. Martin, 2002 - "Electromodulated molecular transport in gold-nanotube membranes," J. Am. Chem. Soc. 124, 11850 – 11851

Lee, S.B., D.T. Mitchell, L. Trofin, T.K. Nevanen, H. Soderlund and C.R. Martin, 2002 -"Antibody-

UNESCO – EOLSS SAMPLE CHAPTERS

based bio/nanotube membranes for enantiomeric drug separations," Science 296, 2198 -2200

Leigh, D.A., J.K.Y. Wong, F. Dehez and F. Zerbetto,2003 - "Unidirectional rotation in a mechanically interlocked molecular rotor," Nature 424, 174

Lent, C.S., B. Isaksen and M. Lieberman, 2003 - "Molecular quantum-dot cellular automata," J. Am. Chem. Soc. 125, 1056 -1063

Leoni, L. and T.A. Desai, 2001 - , "Nanoporous biocapsules for the encapsulation of insulinoma cells: biotransport and biocompatibility considerations," IEEE Trans. Biomed. Eng. 48, 1335-1341.

Li, J., M. Gershow, D. Stein, E. Brandin and J.A. Golovchenko, 2003 - "DNA molecules and configurations in a solid-state nanopore microscope," Nature Mater. 2, 611 -615; http://mcb.harvard.edu/branton/LiGershowSteinOnlinePub.pdf

Li, J.J., and W. Tan, 2002 - "A single DNA molecule nanomotor," Nano Letters 2, 315-318

Lim, Y.T., S. Kim, A. Nakayama, N.E. Stott, M.G. Bawendi and J.V. Frangioni, 2003 - "Selection of quantum dot wavelengths for biomedical assays and imaging," Mol. Imaging 2, 50-64

Liu, H., J.J. Schmidt, G.D. Bachand, S.S. Rizk, L.L. Looger, H.W. Hellinga and C.D. Montemagno, 2002 -"Control of a biomolecular motor-powered nanodevice with an engineered chemical switch," Nat. Mater. 1, 173 – 177

Liu, J. T. Lee, B.L. Walsh, R.P. Andres, D.B. Janes, M.R. Melloch, J.M. Woodall and R. Reifenberger, 2000 - "Guided self-assembly of Au nanocluster arrays electronically coupled to semiconductor device layers," Appl. Phys.Lett. 77, 373 http://www.eng.yale.edu/reedlab/people/takhee/pdf//liu-APL00.pdf

Lomer, W.M., 1951 - "A dislocation reaction in the face-centered cubic lattice," Phil. Mag. 42, 1327 – 1331

Lutwyche, M.I., and Y. Wada, 1995 - , "Observation of a vacuum tunnel gap in a transmission electron microscope using a micromechanical tunneling microscope," Appl. Phys. Lett. 66, 2807 – 2809

Manalis, S.R., S.C. Minne and C.F. Quate, 1996 - "Atomic force microscopy for high speed imaging using cantilevers with an integrated actuator and sensor," Appl. Phys. Lett. 68, 871 – 673

Mann, D.J., J. Peng, R.A. Freitas Jr. and R.C. Merkle, 2004 - , "Theoretical Analysis of Diamond Mechanosynthesis. Part II. C_2 Mediated Growth of Diamond C(110) Surface via Si/Ge-Triadamantane Dimer Placement Tools," J. Comp. Theor. Nanosci. 1, 71

Mao, C., W. Sun, Z. Shen and N.C. Seeman, 1999 - "A nanomechanical device based on the B-Z transition of DNA," Nature 397, 144 – 146

Mao, C., C.E. Flynn, A. Hayhurst, R. Sweeney, J. Qi, G. Georgiou, B. Iverson and A.M. Belcher,2003 - "Viral assembly of oriented quantum dot nanowires,"Proc. Natl. Acad. Sci. (USA) 100, 6946 – 6951

Marcorin, G.L., T. Da Ros, S. Castellano, G. Stefancich, I. Bonin, S. Miertus and M. Prato, 2000 - "Design and synthesis of novel [60]fullerene derivatives as potential HIV aspartic protease inhibitors," Org. Lett. 2, 3955 – 3958

Martel, S., L.C. Olague, J.B.C. Ferrando, S. Riebel, T. Koker, J. Suurkivi, T. Fofonoff, M. Sherwood, R. Dyer and I. Hunter, 2001 - "General description of the wireless miniature NanoWalker robot designed for atomic-scale operations," Proc. SPIE: Microrobotics and Microassembly, Vol. 4568, SPIE, Newton, MA (2001), p. 231-240

Martin, C.R. and P. Kohli, 2003 - "The emerging field of nanotube biotechnology," Nature Rev. Drug Discov. 2, 29-37

McDevitt, M.R., D. Ma, L.T. Lai, J. Simon, P. Borchardt, R.K. Frank, K. Wu, V. Pellegrini, M.J. Curcio, M. Miederer, N.H. Bander and D.A. Scheinberg, 2001 -, "Tumor therapy with targeted atomic nanogenerators," Science 294, 1537 -1540

McMillan, B.A., C.D. Paavola, J. Howard, S.L. Chan, N.J. Zaluzec and J.D. Trent, 2002 - "Ordered nanoparticle arrays formed on engineered chaperonin protein templates," Nat. Mater. 1, 247-252

McNiven, M.A., H. Cao, K.R. Pitts and Y. Yoon, 2000 - "The dynamin family of mechanoenzymes: pinching in new places," Trends Biochem. Sci. 25, 115 – 120

UNESCO – EOLSS SAMPLE CHAPTERS

Medintz, I.L., A.R. Clapp, H. Mattoussi, E.R. Goldman, B. Fisher and J.M. Mauro, 2003 - "Self-assembled nanoscale biosensors based on quantum dot FRET donors," Nat. Mater. 2, 630 – 638

Meller, A., L. Nivon, E. Brandin, J. Golovchenko and D. Branton, 2000 - "Rapid nanopore discrimination between single polynucleotide molecules," Proc. Natl. Acad. Sci. (USA) 97, 1079-1084 ;

http://www.pnas.org/cgi/content/full/97/3/1079

"MEMS micromover," Agilent Technologies; http://www.labs.agilent.com/news/event/demos.html#6 and "Prototype: Micro-Mover," Technol. Rev. (June 2003); http://www.technologyreview.com/articles/prototype0603.asp

Merkle, R.C., 1997 - "A proposed 'metabolism' for a hydrocarbon assembler," Nanotechnology 8, 149-162 ; http://www.zyvex.com/nanotech/hydroCarbonMetabolism.html

Merkle, R.C., and R.A. Freitas Jr.,2003 - "Theoretical analysis of a carbon-carbon dimer placement tool for diamond mechanosynthesis," J. Nanosci. Nanotechnol. 3, 319

Meyyappan, M., H. Partridge and T.R. Govindan, "Nano and BioTechnology Research at NASA Ames," 17 December 2002; http://www.ipt.arc.nasa.gov/Graphics/nanotechresearch.pdf

"Microcantilever Arrays," Protiveris Corp. (2003);

http://www.protiveris.com/cantilever_tech/microcantileverarrays.html

Miller, S.A., K.L. Turner and N.C. MacDonald, 1997 - , "Microelectromechanical scanning probe instruments for array architectures,"Rev. Sci. Instrum. 68, 4155 – 4162

Minne, S.C., Ph. Flueckiger, H.T. Soh and C.F. Quate, 1995 - "Atomic force microscope lithography using amorphous silicon as a resist and advances in parallel operation J. Vac. Sci. Technol. B 13, 1380-1385

Minne, S.C., G. Yaralioglu, S.R. Manalis, J.D. Adams, J. Zesch, A. Atalar and C.F. Quate, 1998 - "Automated parallel high speed atomic force microscopy," Appl. Phys. Lett. 72, 2340 - 2342;

http://www.nano.unr.edu/adams/papers/auto_par.pdf

Mitchell, D.T., S.B. Lee, L. Trofin, N. Li, T.K. Nevanen, H. Soderlund and C.R. Martin, 2002 - "Smart nanotubes for bioseparations and biocatalysis," J. Am. Chem. Soc. 124, 11864 – 11865

Miyata, N. and T. Yamakoshi, 1997 - *:* Recent Advances in the Chemistry and Physics of Fullerenes and Related Materials ,in *Fullerenes, Chemistry, Physics and Technology* [K.M. Kadish and R.S. Ruoff (eds.)], Electrochemical Society, Pennington NJ), Vol. 5, p. 345.

Montemagno, C.D., and G.D. Bachand, 1999 - "Constructing nanomechanical devices powered by biomolecular motors,"Nanotechnology 10, 225 – 231

Montemagno, C.D., 2003 - Feynman Prize award lecture, 11th Foresight Conference on Molecular Nanotechnology, Palo Alto, CA, 9-12 October 2003.

"MR-Sub," NanoRobotics Laboratory, Ecole Polytechnique, Montreal, Canada (2003); http://www.nano.polymtl.ca/en/mrsub.html

Muller, W., H. Ringsdorf, E. Rump, G. Wildburg, X. Zhang, L. Angermaier, W. Knoll, M. Liley and J. Spinke, 1993 -, "Attempts to mimic docking processes of the immune system: recognition-induced formation of protein multilayers," Science 262, 1706 -1708

Mushegian, A.R., 1999 - "The minimal genome concept", Curr. Opin. Genet. Dev. 9, 709 -714

Nadeau, O.W., D.W. Gump, G.M. Hendricks and D.H. Meyer, 1992 - "Deposition of bismuth by Yersinia enterocolitica," Med. Microbiol. Immunol. (Berl.) 181, 145-152

Naik, R.R., S.J. Stringer, G. Agarwal, S.E. Jones and M.O. Stone, 2002 - "Biomimetic synthesis and patterning of silver nanoparticles," Nat. Mater. 1, 169-172

Nakanishi, H., O. Mazda, E. Satoh, H. Asada, H. Morioka, T. Kishida, M. Nakao, Y. Mizutani, A. Kawauchi, M. Kita, J. Imanishi and T. Miki, 2003 - "Nonviral genetic transfer of Fas ligand induced significant growth suppression and apoptotic tumor cell death in prostate cancer in vivo," Gene Ther. 10,

UNESCO – EOLSS SAMPLE CHAPTERS

434-442

Nam, J.-M., C.S. Thaxton and C.A. Mirkin, 2003 - "Nanoparticle-based bio-bar codes for the ultrasensitive detection of proteins," Science 301, 1884-1886

"Nanomedicine: grounds for optimism, and a call for papers," Lancet 362(30 August

2003):673; http://www.alphagalileo.org/nontextfiles/P_5258_14984_1.pdf

"Nanotechnology may help overcome current limitations of gene therapy," Northwestern University press release, 21 April 2003; http://www.scienceblog.com/community/article1507.html

National Nanotechnology Initiative: Research and Development FY 2002; http://www.nano.gov/2002budget.html

Neumann, J. von 1966 - *Theory of Self-Reproducing Automata*, [A.W. Burks (ed.)], University of Illinois Press, Urbana, IL

"NIH Roadmap: Nanomedicine," National Institutes of Health, 30 September 2003;

http://www.nihroadmap.nih.gov/nanomedicine/index.asp

Nishizawa, M., V.P. Menon and C.R. Martin, 1995 - "Metal nanotubule membranes with electrochemically switchable ion-transport selectivity," Science 268, 700-702

Noguchi,H., and M. Takasu, 2001 - , "Self-assembly of amphiphiles into vesicles: A Brownian dynamics simulation," Phys. Rev. E 64, 41913

Ogut, S., R. Burdick, Y. Saad and J.R. Chelikowsky, 2003 - "Ab initio calculations for large dielectric matrices of confined systems," Phys. Rev. Lett. 90, 127401

Okushi, H., Diam. 2001 - "High quality homoepitaxial CVD diamond for electronic devices," Rel. Mater. 10, 281-288

Oyabu, N., O. Custance, I. Yi, Y. Sugawara and S. Morita, 2003 - "Mechanical vertical manipulation of selected single atoms by soft nanoindentation using near contact atomic force microscopy," Phys. Rev. Lett. 90, 176102 http://link.aps.org/abstract/PRL/v90/e176102

Pandit-Taskar, N., P.A. Hamlin, S. Reyes, S.M. Larson and C.R. Divgi, 2003 - "New strategies in radioimmunotherapy for lymphoma,"Curr. Oncol. Rep. 5, 364 – 371

Paunesku, T., T. Rajh, G. Wiederrecht, J. Maser, S. Vogt, N. Stojicevic, M. Protic, B. Lai, J. Oryhon, M. Thurnauer and G. Woloschak, 2003 - "Biology of TiO2-oligonucleotide nanocomposites," Nat. Mater. 2, 343 -346

Park, S.J., A.A. Lazarides, C.A. Mirkin and R.L. Letsinger, 2001 - "Directed assembly of periodic materials from protein and oligonucleotide-modified nanoparticle building blocks," Angew. Chem. Int. Ed. Engl. 40, 2909-2912

Pearson, H., 2003- "Construction bugs find tiny work," Nature Science Update, 11 July 2003; http://www.nature.com/nsu/030707/030707-9.html

Peng, J., R.A. Freitas Jr. and R.C. Merkle, 2004 - "Theoretical Analysis of Diamond Mechanosynthesis. Part I. Stability of C_2 Mediated Growth of Nanocrystalline Diamond C(110) Surface," J. Comp. Theor. Nanosci. 1, 62

Penrose, L.S., 1959 -"Self-reproducing machines," Sci. Amer. 200, 105 – 114

Pozhar, L.A., E.P. Kontar and M.Z. Hu, 2002 - "Transport properties of nanosystems: viscosity of nanofluids confined in slit nanopores," J. Nanosci. Nanotechnol. 2, 209-227

Ptashne, M., 1996 - *A Genetic Switch: Phage (Lambda) and Higher Organisms*, Blackwell Science, Inc., Boston, MA

Quintana, A., E. Raczka, L. Piehler, I. Lee, A. Myc, I. Majoros, A.K. Patri, T. Thomas, J. Mule and J.R. Baker, Jr., 2002 - "Design and function of a dendrimer-based therapeutic nanodevice targeted to tumor cells through the folate receptor," Pharm. Res. 19, 1310-1316

"RB-162 Biomedical Applications of Nanoscale Devices," Business Communications Company, Inc., 25

UNESCO – EOLSS SAMPLE CHAPTERS

Van Zant Street, Norwalk, CT 06855, August 2003; http://www.bccresearch.com/editors/RB-162.html

Reed, M.A., and T. Lee (eds.), 2003 - *Molecular Nanoelectronics*, American Scientific Publishers, Stevenson Ranch, CA

Requicha, A.A.G., 1999 - "Massively parallel nanorobotics for lithography and data storage," Intl. J. Robotics Res. 18, 344 – 350

http://www-lmr.usc.edu/~lmr/publications/ijrr98/

Reuter, J.D., A. Myc, M.M. Hayes, Z. Gan, R. Roy, D. Qin, R. Yin, L.T. Piehler, R. Esfand, D.A. Tomalia and J.R. Baker, Jr., 1999 - "Inhibition of viral adhesion and Rietman, E.A., 2001 - *Molecular Engineering of Nanosystems*, AIP Series, Springer-Verlag, New York

"Rice makes first rapid, sensitive whole-blood immunoassay," Rice University Press Release, 22 July 2003; http://www.eurekalert.org/pub_releases/2003-07/ru-rmf072203.php

Rietman, E.A., 2001 - *Molecular Engineering of Nanosystems*, AIP Series, Springer-Verlag, New York

Roco, M.C. 2004, "National Nanotechnology Investment in the FY2004 Budget Request," AAAS Report XXVIII: Research & Development FY2004; http://www.aaas.org/spp/rd/04pch25.htm

Rosenthal, A.M., 2002 - "Viral Workhorses," Scientific American online, 2 September 2002; http://www.sciam.com/article.cfm?articleID=000005F3-393F-1D6E-90FB809EC5880000

Rothemund, P.W.K., and E. Winfree, 2000 - "The program-size complexity of self-assembled squares," Proc. 32nd Annual ACM Symp. On Theory of Computing, ACM, New York (2000), p. 459.

Rothemund, P.W.K., 2000 - "Using lateral capillary forces to compute by self-assembly," Proc. Natl. Acad. Sci. (USA) 97, 984 – 989

"Rutgers to create ultra-tiny 'bio-nano' motors under National Science Foundation grant," Rutgers University, 24 September 2003; http://ur.rutgers.edu/medrel/viewArticle.html?ArticleID=3467

Saitou, K., 1999 - "Conformational switching in self-assembling mechanical systems," IEEE Trans. Robotics and Automation 15, 510 http://www-personal.engin.umich.edu/~kazu/papers/tra-99.pdf

Salem, A.K., P.C. Searson and K.W. Leong, 2003 - "Multifunctional nanorods for gene delivery," Nat. Mater. 2, 668 – 671

Salling, C.T., and M.G. Lagally, 1994 - , "Fabrication of atomic-scale structures on Si(001) surfaces," Science 265, 502 – 506

Sample, I., 2001 -"Small Visions, Grand Designs," New Sci. 172, 30-35

Sauer-Budge, A.F., J.A. Nyamwanda, D.K. Lubensky and D. Branton, 2003 - "Unzipping kinetics of double-stranded DNA in a nanopore," Phys. Rev. Lett. 90, 238101-1 – 238101-4;

http://mcb.harvard.edu/branton/Sauer-BudgePhysicalReviewLetters.pdf

Scheibel, T., R. Parthasarathy, G. Sawicki, X.-M. Lin, H. Jaeger and S. Lindquist, 2003 - "Conducting nanowires built by controlled self-assembly of amyloid fibers and selective metal deposition," Proc. Natl. Acad. Sci. (USA) 100, 4527 – 4532

Schinazi, R.F., R. Sijbesma, G. Srdanov, C.L. Hill and F. Wudl, 1993 - "Synthesis and virucidal activity of a water-soluble, configurationally stable, derivatized C60 fullerene," Antimicrob. Agents Chemother. 37, 1707-1710

Schliwa , M., and G. Woehlke, 2003 - "Molecular motors," Nature 422, 759-765

Schmidt, J. 2003 - Development of Biomimetic Devices using Membrane Proteins," 11th Foresight Conference on Molecular Nanotechnology, Palo Alto, CA, 9-12 October 2003;

http://www.foresight.org/Conferences/MNT11/Abstracts/Schmidt/index.html

Schmidt, J.J., and C.D. Montemagno, 2002 - "Using machines in cells," Drug Discovery Today 7, 500 – 503

Schuler,D., and R.B. Frankel, 1999 - "Bacterial magnetosomes: microbiology, biomineralization and

UNESCO – EOLSS SAMPLE CHAPTERS

biotechnological applications," Appl. Microbiol. Biotechnol. 52, 464 – 473

Seeman, N.C., 1999 - "DNA engineering and its application to nanotechnology," Trends Biotechnol. 17, 437-443

Seeman, N.C., 1998 - "New Motifs in DNA Nanotechnology," Nanotechnology 9, 257 – 273

Sershen, S.R., S.L. Westcott, N.J. Halas and J.L. West, 2000 - "Temperature-sensitive polymer-nanoshell composite for photothermally modulated drug delivery," J. Biomed. Mater. Res. 51, 293-298

Service, R.F., 2002 - "Biology offers nanotechs a helping hand," Science 298, 2322 – 2323;

http://www.sciencemag.org/cgi/content/full/298/5602/2322?etoc

Service, R.F., 2001 - Nanoscientists look to the future," Science 294, 1448-1449

http://www.cs.cmu.edu/~msitti/science.pdf

Sharke, P., 2001 - "Hybrid NEMS," Mech. Eng. 123, 42 (February 2001);

http://www.memagazine.org/backissues/feb01/features/nems/nems.html

Shi,H. and B.D. Ratner, 2000 - "Template recognition of protein-imprinted polymer surfaces," J. Biomed. Mater. Res. 49, 1-11

Shu, D., and P. Guo, 2003 - "A viral RNA that binds ATP and contains a motif similar to an ATP-binding aptamer from SELEX," J. Biol. Chem. 278, 7119 – 7124

Siwy, Z. and A. Fulinski, 2002 - "Fabrication of a Synthetic Nanopore Ion Pump," Phys. Rev. Lett. 89, 198103

Skidmore, G.D., E. Parker, M. Ellis, N. Sarkar and R. Merkle, 2001 - "Exponential assembly," Nanotechnology 12, 316-321; http://www.foresight.org/Conferences/MNT8/Papers/Skidmore/index.html

Smela, E., O. Inganas and I. Lundstrom, 1995 - "Controlled folding of micrometer-size structures," Science 268, 1735 – 1738

Smith, S.S., 2001 - "A self-assembling nanoscale camshaft: Implications for nanoscale materials and devices constructed from proteins and nucleic acids," Nano Lett. 1, 51-56

Soong, R.K., G.D. Bachand, H.P. Neves, A.G. Olkhovets, H.G. Craighead and C.D. Montemagno, 2000 - , "Powering an inorganic nanodevice with a biomolecular motor," Science 290, 1555-1558

Sotiropoulou, S. and N.A. Chaniotakis, 2003 - "Carbon nanotube array-based biosensor," Anal. Bioanal. Chem. 375, 103 -105

Sparks, H., 2002 - "How Miniature Radiation Detectors Will Keep Astronauts Safe in Deep Space," SPACE.com, 17 July 2002; http://www.space.com/businesstechnology/technology/radiation_nanobots_020717.html

Srinivasan, U., D. Liepmann and R.T. Howe, 2001 - "Microstructure to substrate self-assembly using capillary forces," J. Microelectromechanical Syst. 10, 17-24

http://www.me.berkeley.edu/~liepmann/assets/Thara-selfassembly.JMEMS.pdf

Steinle, E.D., D.T. Mitchell, M. Wirtz, S.B. Lee, V.Y. Young and C.R. Martin, 2002 - "Ion-channel mimetic micropore and nanotube membrane sensors," Anal. Chem. 74, 2416-2422

Stikeman, A., 2002 - "Nanobiotech Makes the Diagnosis," Technol. Rev. 105 (2002);

http://www.techreview.com/articles/stikeman0502.asp

Storm, A.J., J.H. Chen, X.S. Ling, H.W. Zandbergen and C. Dekker, 2003 - Nat. Mater. 2, 537 (2003).

Studier, F.W., 1979 - "Relationships among different strains of T7 and among T7-related bacteriophages," Virology 95, 70-84

Stupp, S.I., V. LeBonheur, K. Walker, L.S. Li, K.E. Huggins, M. Keser and A. Amstutz, 1997 - Science 276, 384 – 389

Suzuki, Y., M. Tanihara, Y. Nishimura, K. Suzuki, Y. Kakimaru and Y. Shimizu, J. 1998 - "A new drug

UNESCO – EOLSS SAMPLE CHAPTERS

delivery system with controlled release of antibiotic only in the presence of infection," Biomed. Mater. Res. 42, 112-116

Tabata, Y., Y. Murakami and Y. Ikada, 1997 - "Photodynamic effect of polyethylene glycol-modified fullerene on tumor," Jpn. J. Cancer Res. 88, 1108-1116

Tabata, Y., Y. Murakami and Y. Ikada,1997 - "Antitumor effect of poly(ethylene glycol)-modified fullerene,"Fullerene Sci. Technol. 5, 989 – 1007

Tanihara, M., Y. Suzuki, Y. Nishimura, K. Suzuki, Y. Kakimaru and Y. Fukunishi, 1999 -"A novel microbial infection-responsive drug release system," J Pharm. Sci. 88, 510-514

Tao, S.L. and T.A. Desai, 2003 - "Microfabricated drug delivery systems: from particles to pores," Adv. Drug Deliv. Rev. 55, 315-318 .

Terfort,A. and G.M. Whitesides,1998 - "Self-assembly of an operating electrical circuit based on shape complementarity and the hydrophilic effect," Adv. Mater. 10, 470 – 471

Tien, J., T.L. Breen and G.M. Whitesides, 1998 - , "Crystallization of millimeter-scale objects with use of capillary forces," J. Am. Chem. Soc. 120, 12670 – 12671

Tien, J., A. Terfort and G.M. Whitesides, 1997 - "Microfabrication through electrostatic self-assembly," Langmuir 13, 5349 – 5355

Tietze, L.F. and T. Feuerstein, 2003 - , "Highly selective compounds for the antibody-directed enzyme prodrug therapy of cancer,"Aust. J. Chem. 56, 841-845

Tokumasu,F. and J. Dvorak, 2003 - , "Development and application of quantum dots for immunocytochemistry of human erythrocytes," J. Microsc. 211, 256-261

Tomalia, D.A., H.M. Brothers 2nd, L.T. Piehler, H.D. Durst and D.R. Swanson, 2002 - "Partial shell-filled core-shell tecto(dendrimers): a strategy to surface differentiated nano-clefts and cusps," Proc. Natl. Acad. Sci. (USA) 99, 5081-5087; http://www.pnas.org/cgi/content/full/99/8/5081

Tour, J.M., 2003 - *Molecular Electronics: Commercial Insights, Chemistry, Devices, Architecture and Programming*, World Scientific Pub. Co., Singapore

Tsao, N., P.P. Kanakamma, T.Y. Luh, C.K. Chou and H.Y. Lei, 1999 - , "Inhibition of Escherichia coli-induced meningitis by carboxyfullerence," Antimicrob. Agents Chemother. 43, 2273 -2277;

http://aac.asm.org/cgi/content/full/43/9/2273

Tsao, N., T.Y. Luh, C.K. Chou, J.J. Wu, Y.S. Lin and H.Y. Lei, 2001 - "Inhibition of group A streptococcus infection by carboxyfullerene," Antimicrob. Agents Chemother. 45, 1788-1793; http://aac.asm.org/cgi/content/full/45/6/1788

Turberfield, A.J., J.C. Mitchell, B. Yurke, A.P. Mills Jr., M.I. Blakey and F.C. Simmel, 2003 - "DNA fuel for free-running nanomachines," Phys. Rev. Lett. 90, 118102

Ulman, A., 1991 - *An Introduction to Ultrathin Organic Films, From Langmuir-Blodgett to Self-Assembly*, Academic Press, Boston

Vettiger, P., G. Cross, M. Despont, U. Drechsler, U. Duerig, B. Gotsmann, W. Haeberle, M. Lantz, H. Rothuizen, R. Stutz and G. Binnig, 2002 - "The Millipede – nanotechnology entering data storage," IEEE Trans. Nanotechnol. 1, 39-55; http://domino.research.ibm.com/Comm/bios.nsf/pages/millipede.html/$FILE/pv7201-preprint.pdf

Vincent, L., J. Varet, J.Y. Pille, H. Bompais, P. Opolon, A. Maksimenko, C. Malvy, M. Mirshahi, H. Lu, J.P. Vannier, C. Soria and H. Li, 2003 - , "Efficacy of dendrimer-mediated angiostatin and TIMP-2 gene delivery on inhibition of tumor growth and angiogenesis: in vitro and in vivo studies," Int. J. Cancer 105, 419 – 429

Walch, S.P., and R.C. Merkle, 1998 - "Theoretical studies of diamond mechanosynthesis reactions," Nanotechnology9,285-296;
http://www.iop.org/EJ/S/UNREG/T7WtMpSi4Oe3KKtSWopXsg/abstract/0957-4484/9/3/020

Walsh, P., A. Omeltchenko, R.K. Kalia, A. Nakano, P. Vashishta and S. Saini, 2003 - "Nanoindentation of silicon nitride: A multimillion-atom molecular dynamics study," Appl. Phys. Lett. 82, 118

UNESCO – EOLSS SAMPLE CHAPTERS

Walters, D.A., J.P. Cleveland, N.H. Thomson, P.K. Hansma, M.A. Wendman, G. Gurley and V. Elings,1996 - "Short cantilevers for atomic force microscopy," Rev. Sci. Instrum. 67, 3583 – 3590

Wang, J., and M. Musameh, 2003 - , "Carbon nanotube/teflon composite electrochemical sensors and biosensors," Anal. Chem. 75, 2075-2079

Wang, Q., T. Lin, L. Tang, J.E. Johnson and M.G. Finn, 2002 - , "Icosahedral virus particles as addressable nanoscale building blocks,"Angew. Chem. Int. Ed. 41, 459-462

Watanabe, H., C. Manabe, T. Shigematsu, K. Shimotani and M. Shimizu, 2001 - , "Single molecule DNA device measured with triple-probe atomic force microscope," Appl. Phys. Lett. 79, 2462

Watson, A., X. Wu and M. Bruchez, 2003 - "Lighting up cells with quantum dots, Biotechniques 34, 296-300

Weber, D.O., 1999 - "Nanomedicine," Health Forum J. 42, 32, 36-37

Weck, M., I.S. Choi, N.L. Jeon and G.M. Whitesides, 2000 - "Assembly of mesoscopic analogues of nucleic acids," J. Am. Chem. Soc. 122, 3546-3547

West, J.L., and N.J. Halas, 2000 - , "Applications of nanotechnology to biotechnology," Curr. Opin. Biotechnol. 11, 215-217

Whaley, S.R., D.S. English, E.L. Hu, P.F. Barbara and A.M. Belcher, 2000 - "Selection of peptides with semiconductor binding specificity for directed nanocrystal assembly," Nature 405, 665-668

Whitesides, G.M., J.P. Mathias and C. Seto, 1991 - "Molecular self-assembly and nanochemistry: A chemical strategy for the synthesis of nanostructures," Science 254, 1312 – 1319

Williamson, A.J., J.C. Grossman, R.Q. Hood, A. Puzder and G. Galli, 2002 - "Quantum Monte Carlo calculations of nanostructure optical gaps: application to silicon quantum dots," Phys. Rev. Lett. 89, 196803

Wu,, X., H. Liu, J. Liu, K.N. Haley, J.A. Treadway, J.P. Larson, N. Ge, F. Peale and M.P. Bruchez, 2003 -, "Immunofluorescent labeling of cancer marker Her2 and other cellular targets with semiconductor quantum dots," Nat. Biotechnol. 21, 41-46

Xu, H., F. Yan, E.E. Monson and R. Kopelman, 2003 - "Room-temperature preparation and characterization of poly(ethylene glycol)-coated silica nanoparticles for biomedical applications," J. Biomed. Mater. Res. 66A, 870-878

Xu, H., M.Y. Sha, E.Y. Wong, J. Uphoff, Y. Xu, J.A. Treadway, A. Truong, E. O'Brien, S. Asquith, M. Stubbins, N.K. Spurr, E.H. Lai and W. Mahoney, 2003 - "Multiplexed SNP genotyping using the Qbead system: a quantum dot-encoded microsphere-based assay," Nucleic Acids Res. 31, e43

Xu, G. and H.L. McLeod, 2001 - "Strategies for enzyme/prodrug cancer therapy," Clin. Cancer Res. 7, 3314 – 3324

Yamamoto, K., G. Shi, T. Zhou, F. Xu, J. Xu, T. Kato, J.Y. Jin and L. Jin, 2003 - "Study of carbon nanotubes-HRP modified electrode and its application for novel on-line biosensors Analyst 128, 249-254

Yan,, H., X. Zhang, Z. Shen and N.C. Seeman,2002 - "A robust DNA mechanical device controlled by hybridization topology," Nature 415, 62 – 65

Yang, X.M., R.D. Peters, P.F. Nealey, H.H. Solak and F. Cerrina, 2000 - , "Guided self-assembly of symmetric diblock copolymer films on chemically nanopatterned substrates," Macromolecules 33, 9575 – 9582

Yeh, H.J., J.S. Smith, 1994 - , "Fluidic self-assembly of GaAs microstructures on Si substrates," Sens. Mater. 6, 319 – 332

Yin, J., 1993 - "Evolution of bacteriophage T7 in a growing plaque," J. Bacteriol. 175, 1272 -1277

Yokobayashi, Y., R. Weiss and F.H. Arnold, 2002 -"Directed evolution of a genetic circuit," Proc. Natl. Acad. Sci. (USA) 99, 16587 - 16591 http://www.pnas.org/cgi/content/abstract/99/26/16587

Yoshikawa, M. 2001 - Molecularly imprinted polymeric membranes Bioseparation 10, 277-286

UNESCO – EOLSS SAMPLE CHAPTERS

Yurke, B., A.J. Turberfield, A.P. Mills, Jr., F.C. Simmel and J.L. Neumann, 2000 - , "A DNA-fuelled molecular machine made of DNA," Nature 406, 605 – 608

Zhang, Y., and N.C. Seeman, 1994 -"Construction of a DNA-Truncated Octahedron," J. Am. Chem. Soc. 116, 1661-1669

Zhu, Z., D.I. Schuster and M.E. Tuckerman, 2003 - "Molecular dynamics study of the connection between flap closing and binding of fullerene-based inhibitors of the HIV-1 protease," Biochemistry 42, 1326 – 1333

Zimmerman, S.C., M.S. Wendland, N.A. Rakow, I. Zharov and K.S. Suslick, 2002 - Synthetic hosts by monomolecular imprinting inside dendrimers Nature 418, 399-403.

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