

11 Nanotechnology—In Relation to Bioinformatics

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INTRODUCTION

The first use of word “Nanotechnology” has been attributed to Norio Taniguchi in a paper published in 1974. Eric Drexler, in 1986, published book “Engines of Creation” in which he described his ideas of molecular nanotechnology used to build miniature machines and devices from the bottom up using self-assembly. Many scientists from mainstream disciplines—biology, chemistry or physics—will argue of course that they are and have been ‘doing’ nanotechnology for years and that it is nothing new. Indeed chemists play with atoms and molecules which are sub-nano and molecular biology deals with the understanding and application of biological nano-scale components. Nature has used nanotechnology and, in fact, it has taken millions of years to develop this by a process of evolution and natural selection. Nanotechnology is an emerging research field which promises to have a wide range of interesting applications. Nanotechnology encompasses all technology that aims to create nanometre-scaled structures or is able to address or manipulate matter at the nanometre level.

National Science and Technology Council (US) (2000) has defined Nanotechnology as: “Research and Technology development at the atomic, molecular, or macromolecular levels in the length of approximately 1-100 nm range, to provide fundamental understanding of phenomena and materials at the nanoscale, and to create and use structures, devices and systems that have novel properties and functions because of their small size. The novel and differentiating properties and functions are developed at a critical length scale of matter typically under 100 nm. Nanotechnology research and development includes integration of nanoscale structure into larger material components, systems, and architectures. Within these larger scale assemblies, the control and construction of their structures and component devices remain at the nanometer scale.”

DNA COMPUTING

DNA computing is just one of the many applied areas of nanotechnology published by Dan E. Linstedt in 2004. He described that DNA computing is the ability to drive computations, store data and retrieve data through the structure and use of DNA molecules. DNA computing requires understanding of the molecule. For example, molecules are made up of atoms; the atoms contain protons, neutrons and electrons. The molecule can be a combination of atoms such as water molecule (H_2O). The nanotechnology aspect involves the ability of man to alter and control the makeup of the atom within the molecule.

DNA computing takes strands of DNA with proteins, enzymes and program specific states in each molecule in the double helix strand. To begin with, the idea of DNA computing is similar to the action of DNA. One strand of DNA houses the 'RAM' or memory, the other strand is a backup (like Raid 0 + 1 on disk). The enzymes are the motors that copy, search, access, read/write the information into the DNA strands. When the DNA is put into an aqueous solution (like water), and the data is added, the data or information finds the appropriate DNA component to combine with and attaches itself. The data is usually in the form of a chemical solution with its own enzymes, providing motion or movement to the atoms. Once the atoms bind, they cannot be unbound without changing the environment. Changing the environment may mean making it "unfriendly" to the data; thus the enzymes uncouple the chemically bonded elements (data) and return it to its previous state.

DNA computing marks require understanding on the data sets and to generate "software" that programs specific information and knowledge of chemistry and biology. It is well-known that in general to search across one gram of DNA in an aqueous solution, it might take one to three seconds. The nano-structures constructed in experimental demonstrations consists of DNA crossover molecules that self assemble into large lattices that can execute computations as well as DNA molecules that reconfigure for possible use of motors.

DNA computing experiment proved that data can be stored, replicated, searched and retrieved from DNA structures. "DNA bases represented the information bits: ATCG (nucleotides) spaced every 0.35 nanometres along the DNA molecule, giving DNA a remarkable data density of nearly 18 mbits per inch". This provides hope for computing power. Each nucleotide can represent a bit. Not only does the bit type make differences, but the order or sequence as well. A "T" in a third position means something completely different than a "T" in the first position, leading to limitless possibilities for computation.

Furthermore, each of these nucleotides can be complemented by "S" and hybridized. In other words, they can produce double stranded DNA. For error correction this is very important. It gives the nano-computer a chance

to correct what should be a comparable equivalent (copy) of the data. Such is the way of Raid 0+1 disk arrays. For example, if there are four values per atom, each atom taking 0.35 microns across, this would be impressive for storage sizes. If we want to think about modeling the information, we must consider the first two-dimensional mode (2D) atoms with electrons; different atoms tied together through valence bonding, providing a surface area to the molecule and a chemical make up. The three-dimensional (3D) model allows for multiple twists of the atomic layers. Dan E. Linstedt in his document cited: compression and encryption algorithms have already been developed, tested and used in DNA computing. Terabyte-sized storage has already been reached and furthermore, quantum level parallel operations have also already been created, used and proven successful.

There have been similar reports of success from governments and research laboratories all over the world.

NANOENGINEERING BIOINFORMATICS

Engineering bioinformatics as a meaningful paradigm to complement modern nanotechnology has been examined by Lyshenski et al. (2003). They consider Bioinformatics as a coherent abstraction in devising, prototyping, design, optimization and analysis of complex nanosystems. Nano and microscale biological systems exist in nature in enormous variety and sophistication. They are applying complex biological patterns in order to devise, analyze and examine distinct systems. One cannot blindly copy biosystems due to the fact that many complex phenomena and effects have not been comprehended and system architectures and functionalities have not been fully examined. Typical examples include unsolved problems to comprehend the simplest Escherichia Coli (*E. coli*) and Salmonella typhimurium bacteria that integrate three dimensional biocircuitary, computing processing, networking nanobioelectronics, nanobiomotors, nanobiosensors, etc. Correspondingly, attention is also concentrated on devising novel paradigms in systematic synthesis through Bioinformatics with the ultimate objective to fabricate these systems applying nanotechnology. This will allow one to derive new operating principles examining functionality of different subsystems, researching novel structures, studying advanced architectures (topologies) and characterizing distinct systems, subsystems and devices reaching the nanoarchitectonics horizon. The scientist examines complex patterns in biosystems because superior system can be devised and designed through engineering Bioinformatics to achieve ultimate objective of engineering bioinformatics and system design. These are far-reaching frontiers of modern nanoscience and nanoengineering. The synergetic paradigm reported is demonstrated researching biosystems and coherently examining distinct nanostructures, complex and subsystems (Lyshenski et al., 2003).

NANOTECHNOLOGY - CANCER TREATMENT

Nanotechnology will complement genomic and proteomic research and accelerate the ability of scientist to prevent, detect and treat cancer. The onset of premalignant and malignant transformation will be detected at the molecular level long before the anatomic presence of a tumour is *discernible*. This will permit less drastic methods of elimination. A greater understanding of the human biology of cancer revealed from patients will complement and stimulate new laboratory investigations *in vitro* and *in silico*, linking delivery back to discovery in the continuum. Tomorrow's patients will know their susceptibility to cancer and the lifestyle factors needed to keep healthy. Molecular epidemiology and gene/environment interactions will help determine populations at risk. Emphasis on cancer biology will permit a systems approach to understand the cancer process. An integrated clinical trials system with a common bioinformatics grid will rapidly test and validate new strategies for early detection, prevention and prediction of cancer (Andrew & Eschenbach, 2004). The development of tools in genomics, proteomics, molecular imaging, bioinformatics, nanotechnology and other advanced technologies is a critical step.

BIOINFORMATICS, NANOTECHNOLOGY – DISINFECTANT FOR SEVERE ACUTE RESPIRATORY SYNDROME (SARS)

WHO, on March 12, 2003, issued a global alert on the outbreak of the epidemic – a new form of pneumonia-like disease with symptoms that are similar to those of the common flu. This illness is potentially fatal and highly contagious and had spread quickly to many parts of the world. Nevertheless, Severe Acute Respiratory Syndrome (SARS) was at one point a public health issue threatening large populations of the world.

Government research centres in Canada and the U.S. decoded the genome of the coronavirus which was proved to be the cause of SARS. The British Columbia Cancer Agency (BCCA) in Vancouver was the first to sequence the SARS genome on April 13, 2003, followed closely by the Center for Disease Control and prevention (CDC) of the US on April 14, 2003.

The sequence information itself does not provide a cure, but rather the test and diagnostics for this particular virus. The sequencing success was a combination of several events, serendipity being one of the most significant. The challenge was to produce a DNA copy of the virus's RNA genome to work with. After several days of effort, scientists managed to produce one millionth of a gram of the genetic material on April 6, 2003. To sequence the SARS genome, the genome was broken in manageable fragments. Within a week, all the fragments had been sequenced. Once started, the sequencing itself was "fairly routine". The sequenced genome fragments were then assembled into the complete genome in 12mers under UV light, electromer

pairs are created. The negative electrons and positive holes create very strong oxidizers, called hydroxide radical, even stronger than chlorine used as a sterilizer. When harmful substances stick to the positive holes, they are completely broken down into the carbon dioxide and other harmless compounds. As a disinfectant, the hydroxide radical can also inhibit the growth of bacteria.

Bacteria can be found all over the place and they multiply quickly. The idea is to have disinfectant agents, such as TiO_2 that will kill bacteria faster than they multiply to sustain cleanliness. For TiO_2 to be effective as a disinfectant, the size has to be in the nanometre (10^{-9} m) range. In this range, it has been shown that the effectiveness of TiO_2 as disinfectant can go as high as 70 - 99%. The problem that scientists have is that the cost to grind the substance increases with diminishing size. Many industries now use micrometre (10^{-6} m) range TiO_2 . Though much cheaper, the effect is drastically reduced.

There have been technologies developed along this line to deliver one of these ingredients at an extremely low concentration to create a powerful hospital grade disinfectant that is non-hazardous and environmentally safe (Lim, 2003). One particular product line, employing unique nano-emulsive technology, is reported to be able to reduce the spread of a broad range of diseases caused by microorganisms including E. coli, Salmonella, Listeria, Staph, Strep, Pseudomonas, MRSA, VRE, Norwonk-like Virus, Influenza A, Hepatitis B and C.

Another product has been developed using proprietary technology to create a nanoemulsion. The nanoemulsion can be sprayed, smeared on clothing, vehicles, people or anything that has been exposed to slew of deadly substances. It can also be rubbed on the skin, eaten or put into beverages like orange juice, and used in the water of a hot tub. The working principle is that the nano-bubbles contain energy that is stored as surface tension. The energy is released when bubbles coalesce, thus zapping the contaminant. The hurdle is that a huge amount of energy is needed to make the nanoemulsion, with bubbles of sizes smaller than bacteria and viruses.

The major concern is that opportunists might seize the scope arising from the market for cheap prevention kits, disinfectant substances, and sterilizing systems that are of dubious effectiveness. The risk is that the public may lower their guard under the false impression that they are fully protected. Note that all the products, if they are effective, are good only for preventing, disinfecting or detecting infectious agents; they do not offer cure, yet.

Nanomedicine

Nanomedicine has been described as the process of diagnosing, treating and preventing disease and traumatic injury, relieving pain and preserving and

improving human health, using molecular tools and molecular knowledge of the human body. In short, nanomedicine is the application of nanotechnology to medicine (NSTC, 2000).

Nanomedicine is a large area and includes nanoparticles that act as biological mimetics, ‘nanomachines’, nanofibres and polymeric nanoconstructs as biomaterials, and nanoscale fabrication-based devices, sensors and laboratory diagnostics. Research into the delivery and targeting of pharmaceuticals, therapeutic and diagnostic agents using nanosized particles is the forefront of nanomedicine (NSTC, 2000). Freitas (2005) gave a partial taxonomy of nanomedicine technologies which was broken down into 18 classes (Table 1) and 96 sub-classes. This shows the potential application of nanotechnology in medicine.

Table 1: Nanomedicine Technologies – Main Classes

Raw nanomaterials	DNA manipulation, sequencing, diagnostics	Molecular medicine
Nanostructured materials	Tools and diagnostics	Artificial enzymes and enzyme control
Artificial binding sites	Intracellular devices	Nanotherapeutics
Control of surfaces	Bio MEMS	Synthetic biology and early nanodevices
Nanopores	Biological research	Biotechnology and biorobotics
Cell simulations and cell diagnostics	Drug delivery	Nanorobotics

NANOTECHNOLOGY IN DRUG DELIVERY

Nanotechnologists generate great excitement in the field of drug development and drug delivery. In fact, many are already used to treat patients. Indeed, since 1990, many drugs referred to as nano-therapeutics have been approved as products for clinical use. Most are anticancer drugs i.e. liposomes (e.g. Daunoxome), polymer coated liposomes (Doxil, Caclyx), polymeric drugs (copaxone), antibodies (Heraptin, Avastin) and antibody conjugates (mylotars), polymer protein conjugates (Oncaspar, Neulasta) and largely, a nanoparticles containing paclitaxel (Abraxane). These are nano-scale and commonly multicomponent constructs and can be viewed as the first nanomedicines to be used as clinical benefits. These nanomedicines are not really new. Many of these concepts e.g. antibody conjugates, liposomes, nanoparticles and polymer-conjugates were developed in the 1970s. However, significant funding has been given over to the research and development of Nanotechnologies that have great potential to contribute to medicine in the short and longer time. Today nanotechnology and nanoscience approaches to

particle design and formulations are beginning to expand the market for many drugs and are forming the basis for a very profitable niche within the pharma industry, wherein some predicted benefits are hyped (Moghimi et al., 2005).

However, examples in the scientific literature which demonstrate the potential and the reason for excitement surrounding nanomedicine are overwhelming. The reader is referred to the reviews (Freitas, 2005; Moghimi et al., 2005).

Today, nanomedicine has branched out in hundreds of different directions, but the core concept remains that ability to structure materials and devices at the molecular scale can bring enormous immediate benefits in the research and practice of medicine. It has been proposed that miniaturization of medical tools will provide more accurate, more controllable, more versatile, more reliable, cheaper and faster approaches to enhancing the quality of human life.

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