CHAPTER 1

INTRODUCTION TO NANOTECHNOLOGY

1.1 Introduction

Technology is generally regarded as the utilization or application of science to benefit society. Nanotechnology is an emerging technology, which is no longer just a vision for the future as it was generally seen at the end of 20th century. Instead, nanotechnology is a ubiquitous technology with a potential to impact on every aspect of modern human civilization. An incredibly diverse range of areas will be affected, such as agriculture, communication, energy generation/transmission, computers, environmental monitoring, food manufacturing/processing, health care, personal care, space travel, robotics, but probably the biggest impact will be in medical technology(1).

In general, nanotechnology is acknowledged to represent a new frontier in science and technology of the 21st century. One may argue, however, that nanotechnology is not as contemporary as it seems to be. Although the word nanotechnology is relatively new, the “natural version” of nanotechnology was already in pole position with procreation of life itself thousands of millions of years ago. Fig 1.1 shows the scale of things in nanometer and more. All natural materials and systems establish their foundation at the nano scale. Basically, the biological building blocks of life are nano-entities that possess unique properties determined by the size, folding, and patterns at nanoscale. Fig 1.2 shows the genetic material of deoxyribonucleic acid (DNA). It is composed of four nucleotide bases in sizes ranging in the sub-nano meter scale,
and the diameter of the double helix structure of DNA is in the nano metre range. The same is true for proteins and cell membranes which consist of lipids and proteins (2).

Manufacturing “non-natural” nano materials faces many challenges, often requiring a specific approach. Miniaturization has been applied quite successfully for some decades now. This “top-down” approach has traditionally been used in the fabrication of electronics in the semiconductor technology industry. Fig 1.3 shows top down approach used in semiconductors. However, nanotechnology is more than miniaturization alone. In order to explore the full potential of nanotechnology a new paradigm has to be set. This is accomplished by a “bottom-up” approach building structures from more basic materials. Self-assembly is a bottom-up technique that attracts much attention. In fact, this concept is not new. Biological systems are built predominantly using self-assembly. What is new is the enhanced ability to “externally” or “specifically” or “intentionally” control the structure at the nano scale and manufacture new materials such as nano tubes, nano wires, and nano capsules as shown in Fig 1.4(a) and Fig 1.4(b) (3,4). Nano materials are difficult to maintain as individual particles. One reason for this is their marked propensity to agglomerate because agglomeration reduces the enormous surface area in relation to the volume of the nano material, which is energetically unfavorable (5).

Appropriate “bottom-up” approaches and applying precision surface engineering may overcome agglomeration. Nevertheless, nanotechnology
offers very interesting possibilities of developing new innovative products for many areas of daily life, some of which have already been realised.

Also the field of medical technology has already started to benefit from the progress in nanotechnology. Many revolutionary applications, such as novel sensing technologies, surface modifications, and implant technologies are currently being developed (6, 7). Probably the most significant impacts of nanotechnology will be at the biomaterials/living tissue interface and the non-biological/cell interface, e.g. human-machine (for example retinal prosthesis).

Whether a prosthetic implant is accepted or rejected, whether a drug is effective or whether living tissue will regenerate are all questions which could be approached at the nanometer scale. Interfacing materials with human biology/physiology is one of the exciting new frontiers of nanotechnology in the field of medical applications. Nanotechnology will definitely be a strategic branch for science and engineering during the coming century. It will fundamentally restructure the technologies currently used for manufacturing, medicine, communication, computation, transportation and many other application areas. The term "nanotechnology" was first defined by Tokyo Science University, Norio Taniguchi in 1974 paper (8). "Nano-technology' mainly consists of the processing of, separation, consolidation, and deformation of materials by one atom or one molecule.

Nanotechnology and nano science got a boost in the early 1980s with two major developments: the birth of cluster science and the invention of the scanning tunneling microscope (STM). This development led to the discovery
of fullerenes in 1985. As practiced at Rice University, there are three distinct nanotechnologies.

"Wet" nanotechnology

It is the study of biological systems that exist primarily in a water environment. The functional nanometer-scale structures of interest here are genetic material, membranes, enzymes and other cellular components. The success of this nanotechnology is amply demonstrated by the existence of living organisms whose form, function, and evolution are governed by the interactions of nanometer-scale structures. Fig 1.5 shows the DNA tetrahedron made of nucleic acids.

"Dry" nanotechnology

It is derived from surface science and physical chemistry, focuses on fabrication of structures in carbon (for example, fullerenes and nano tubes), silicon, and other inorganic materials. Unlike the "wet" technology, "dry" techniques admit use of metals and semiconductors. The active conduction electrons of these materials make them too reactive to operate in a "wet" environment, but these same electrons provide the physical properties that make "dry" nanostructures promising as electronic, magnetic, and optical devices. Another objective is to develop "dry" structures that possess some of the same attributes of the self-assembly that the wet ones exhibit. Protein based nanotubes potentially capable of self organization and replication is shown in Fig 1.6.
Computational nanotechnology

It permits the modeling and simulation of complex nanometer-scale structures. A molecular bearing designed using computational nanotechnology is shown in the Fig 1.7. The predictive and analytical power of computation is critical to success in nanotechnology: nature required several hundred million years to evolve a functional "wet" nanotechnology; the insight provided by computation should allow us to reduce the development time of a working "dry" nanotechnology to a few decades, and it will have a major impact on the "wet" side as well. These three nanotechnologies are highly interdependent. The major advances in each have often come from application of techniques or adaptation of information from one or both of the others.

1.2 Nanotechnology and Antibacterial effect

Most of the natural processes also take place in the nanometer scale regime. Therefore, a confluence of nanotechnology and biology can address several biomedical problems, and can revolutionize the field of health and medicine (9). Nanotechnology is currently employed as a tool to explore the darkest avenues of medical sciences in several ways like imaging (10), sensing (11), targeted drug delivery (12) and gene delivery systems (13) and artificial implants (14). The new age drugs are nanoparticles of polymers, metals or ceramics, which can combat conditions like cancer (15) and fight human pathogens like bacteria (16-20).

The development of new resistant strains of bacteria to current antibiotics (21) has become a serious problem in public health; therefore, there
is a strong incentive to develop new bactericides. Bacteria have different membrane structures which allow a general classification of them as Gram-negative or Gram positive. The structural differences lie in the organization of a key component of the membrane, peptidoglycan. Gram negative bacteria exhibit only a thin peptidoglycan layer between the cytoplasmic membrane and the outer membrane(22), in contrast, Gram-positive bacteria lack the outer membrane but have a peptidoglycan layer of about 30 nm thick (23). Silver has long been known to exhibit a strong toxicity to a wide range of microorganisms (24), for this reason silver-based compounds have been used extensively in many bactericidal applications (25,26). Silver compounds have also been used in the medical field to treat burns and a variety of infections (27). Several salts of silver and their derivatives are commercially employed as antimicrobial agents (28). Commendable efforts have been made to explore this property using electron microscopy, which has revealed size dependent interaction of silver nanoparticles with bacteria. Nanoparticles of silver have thus been studied as a medium for antibiotic delivery (29), and to synthesize composites for use as disinfecting filters (30) and coating materials (31). However, the bactericidal property of these nanoparticles depends on their stability in the growth medium, since this imparts greater retention time for bacterium– nanoparticle interaction. There lies a strong challenge in preparing nanoparticles of silver stable enough to significantly restrict bacterial growth.

Large number of researchers carried out research on both antibiotic resistant (ampicillin- resistant) and nonresistant strains of gram-negative (Escherichia coli) and a non-resistant strain of gram-positive bacteria (Staphylococcus aureus). A multi-drug resistant strain of gram-negative
(Salmonella typhus, resistant to chloramphenicol, amoxycilin and trimethoprim) bacteria was also subjected to analysis to examine the antibacterial effect of the nanoparticles (32). Efforts have been made to understand the underlying molecular mechanism of such antimicrobial actions.

1.3 Importance of nano silver

Silver (Ag) is a transition metal element having atomic number-47 and atomic mass-107.87. The medicinal uses of silver have been documented since 1000 B.C. Silver is a health additive in traditional Chinese and Indian Ayurvedic medicine (33). Its action as an antibiotic comes from the fact that it is a non-selective toxic "biocide." Silver based antimicrobial biocides are used as wood preservatives. In water usage, silver and copper based disinfectants are used in hospitals and hotels distribution systems to control infectious agents (for example, Legionella).

Silver together with copper, is commonly used to inhibit bacterial and fungal growth in chicken farms and in post harvested cleaning of oysters. Silver used to sterilize recycled water aboard the MIR space station and on the NASA space shuttle (34). Microdyn (colloidal silver in gelatin) is sold in supermarkets to disinfect salad vegetables and drinking water. Johnson Mathey Chemicals (Nottingham, UK) developed an inorganic composite (immobilized slow-release silver product) for use as a preservative in cosmetics, toiletries, and similar retail hygiene-sensitive products (35).

In Japan, a new compound (Amenitop, silica gel microspheres containing a silver-thiosulfate complex) is mixed into plastics for lasting
antibacterial protection. Silver halide is often incorporated into prescription eye
glasses for reversible “photo chromatic” protection, as it decreases transmitted
visible light. Silver resistance is important to monitor because modern
technology has developed a wide range of products that depend on silver as a
key microbial component. In the late 1970s, Robert O. Becker discovered that
silver ions promote bone growth and kill surrounding bacteria. Silver kills
some 650 different disease organisms. Silver based topical dressing has been
widely used as a treatment for infections in burns, open wounds and chronic
ulcers. The Silver nanoparticles and Ag+ carriers can be beneficial in delayed
diabetic wound healing as diabetic wounds are affected by many secondary
infections. These nanoparticles can help the diabetic patients in early wound
healing with minimal scars (36). Silver nitrate is still a common antimicrobial
used in the treatment of chronic wounds (37).

**Colloidal Silver**

Scientists have discovered that the body's most important fluids are
colloidal in nature: suspended ultra-fine particles. Blood, for example, carries
nutrition and oxygen to the body cells. This led to studies with colloidal silver
(electrical silver atoms). An electro-colloidal process, which is known to be the
best method, is used for manufacturing the colloidal silver. Colloidal silver
appears to be a powerful, natural antibiotic and preventative against infections
(38). Acting as a catalyst, it reportedly disables the enzyme that one celled
bacteria, viruses and fungi need for their oxygen metabolism. They suffocate
without corresponding harm occurring to human enzymes or parts of the
human body chemistry. The result is the destruction of disease-causing organisms in the body and in the food.

The bactericidal effect of silver ions on micro-organisms is very well known however; the bactericidal mechanism is only partially understood. It has been proposed that ionic silver strongly interacts with thiol groups of vital enzymes and inactivates them (39). Experimental evidence suggests that DNA loses its replication ability once the bacteria have been treated with silver ions. Other studies have shown evidence of structural changes in the cell membrane as well as the formation of small electron-dense granules formed by silver and sulfur (40). Silver ions have been demonstrated to be useful and effective in bactericidal applications, but due to the unique properties of nanoparticles nanotechnology presents a reasonable alternative for development of new bactericides. Metal particles in the nanometer size range exhibit physical properties that are different from both the ion and the bulk material. This makes them exhibit remarkable properties such as increased catalytic activity due to morphologies with highly active facets (41-45). Several electron microscopy techniques can be applied to study the mechanism by which silver nanoparticles interact with these bacteria. We can use high angle annular dark field (HAADF) and scanning transmission electron microscopy (STEM), to develop a novel sample preparation to avoid the use of heavy metal based compounds.

1.4 Health and safety implications from nanoparticles

Nano pollution is a generic name for all waste generated by nano devices or during the nano materials manufacturing process. This kind of waste
may be very dangerous because of its size. It can float in air and might easily penetrate animal and plant cells causing unknown effects. Most human-made nanoparticles do not appear in nature, so living organisms may not have appropriate means to deal with nano waste.

The smaller a particle, the greater its surface area to volume ratio and the higher its chemical reactivity and biological activity. The greater chemical reactivity of nano materials results in increased production of reactive oxygen species (ROS), including free radicals. ROS production has been found in a diverse range of nanomaterials including carbon fullerenes, carbon nanotubes and nanoparticle metal oxides. ROS and free radical production is one of the primary mechanisms of nanoparticle toxicity; it may result in oxidative stress, inflammation, and consequent damage to proteins, membranes and DNA. Nanomaterials have proved toxic to human tissue and cell cultures, resulting in increased oxidative stress, inflammatory cytokine production and cell death (46). Unlike larger particles, nanomaterials may be taken up by cell mitochondria (47) and the cell nucleus (48, 49). Studies demonstrate the potential for nanomaterials to cause DNA mutation and induce major structural damage to mitochondria, even resulting in cell death (50). Size is therefore a key factor in determining the potential toxicity of a particle. However it is not the only important factor. Other properties of nanomaterials that influence toxicity include: chemical composition, shape, surface structure, surface charge, aggregation and solubility, and the presence or absence of functional groups of other chemicals (51).
Significant environmental, health, and safety issues might arise with development in nanotechnology since some negative effects of nanoparticles in our environment might be overlooked. However nature itself creates all kinds of nano objects, so probable dangers are not due to the nanoscale alone, but due to the fact that previously non-toxic materials can become harmful when ingested or inhaled as nanoparticles. Social risks related to nanotechnology development include the possibility of military applications of nanotechnology in biological warfare, chemical warfare, ammunitions and armaments and even as implants for soldier "enhancement." Enhanced surveillance capabilities through nano-sensors are also of concern to privacy rights advocates. In discussing issues related to nanotechnology, the acronym NELSI is used to signify nanotechnology's ethical, legal, and social implications.

Silver nanoparticles exhibit a broad size distribution and morphologies with highly reactive facets. The major mechanism through which silver nanoparticles manifested antibacterial properties is by anchoring to and penetrating the bacterial cell wall, and modulating cellular signaling by dephosphorylating putative key peptide substrates on tyrosine residues.

The antibacterial effect of nanoparticles is independent of acquisition of resistance by the bacteria against antibiotics. However, further studies must be conducted to verify if the bacteria develop resistance towards the nanoparticles and also to examine cytotoxicity (52, 53) of nanoparticles towards human cells before proposing their therapeutic use.
1.5 Medical Nano technology

Medical and healthcare textiles are a rapidly growing part of the textile industry. This growth is attributed to the continuous improvements and innovations that have been made in both textile technology and medical procedures. These medical and healthcare textiles have been engineered to have particular properties, such as good strength, flexibility, and sometimes moisture and air permeability, for medical and surgical applications. Recently, electrospun polymer nanofibers have attracted a great deal of attention for use in medical and healthcare textiles. The nanofiber webs have unique properties, such as a high surface area-to-volume ratio, small pore sizes, high porosity, etc. Nano fibers of various diameters are shown in the Fig 1.8(a) and 1.8(b). In particular, drug impregnated nanofibers are very effective for topical drug administration and wound healing because of their high surface area-to-volume ratio. The drugs can be released at various rates and profiles based on the nano fiber, morphology and the drug content. On the other hand, silver (Ag) ions and Ag compounds have been widely used in various biomedical fields, such as wound dressing materials, body wall repairs, augmentation devices, tissue scaffolds, antimicrobial filters, and so forth. Microorganisms with resistance to the antimicrobial activity of Ag are exceedingly rare. Yang et al. (54) first prepared ultrafine poly acrylonitrile (PAN) fibers containing Ag nanoparticles via electrospinning. Son et al. (55) prepared ultra-fine cellulose acetate (CA) fibers containing Ag nanoparticles by Electrospinning a CA solution containing small amounts of silver nitrate (AgNO₃) and subsequent photo reduction. They revealed that very small amounts of AgNO₃ (>0.05 wt %) were needed to endow the ultra-fine CA fibers with very strong
antibacterial properties. Furthermore, this process does not need any tedious processing such as precipitation re-dissolution and long photo reduction.

Nano medicine is now within the realm of reality, though there is some concern about the safety of nanoparticles introduced in the human body. Research is in progress to address this issue. Examples of medical devices utilising nanotechnology, which are already on the market are surgical tools with enhanced properties, such as nano-sized contrast agents for molecular imaging, bone replacement materials constructed from nano structured materials, pacemakers and hearing aids of reduced size and increased power, lab-on-a-chip devices for in vitro diagnostics, wound dressings containing nanocrystalline silver particles, micro cantilevers, and micro needle-based systems for minimally invasive drug administration. Over the next ten to twenty years nanotechnology may fundamentally transform science, technology, and society offering a significant opportunity to enhance human health in novel ways, especially by enabling early disease detection and diagnosis, as well as precise and effective therapy tailored to the patient.
REFERENCES

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