Module-4

Biodevice and Application:-

Introduction

Bio-nanotechnology is a science that site at the convergence of nanotechnology and biology. The field applies the tools of nanotechnology to biological problems, creating specialized applications. Concepts that are enhanced through nanobiology include: nanodevices (such as biological machines), nanoparticles, and nanoscale phenomena that occurs within the discipline of nanotechnology. This technical approach to biology allows scientists to imagine and create systems that can be used for biological research.

The most important objectives that are frequently found in nanobiology involve applying nanotools to relevant medical/biological problems and refining these applications. Developing new tools, such as peptoid nanosheets, for medical and biological purposes is another primary objective in nanotechnology. The imaging of native biomolecules, biological membranes, and tissues is also major topic for the nanobiology research. Other topics concerning nanobiology include the use of cantilever array sensors and application of nanophotonics for manipulating molecular processes in living cells.

Bio-Nanostructures

Nanostructure refer to materials that have the relevant dimensions of internal structure defined at the nanometer scale. These materials have unique physical properties that are distinctly different from bulk materials. Biological systems are almost entirely driven by self-assembly. Self-assembly is a process by which molecules spontaneously assemble into some structure or molecular machine under the appropriate conditions and adopt a defined arrangement in space. It requires no tools to move and orient components. Selective binding between matching surfaces is uniquely defined with attractive forces between components that prevail random connections. It is an essential process for many of the key activities for living cells. These include the formation of protein and nucleic acid complexes necessary to protein, RNA, and DNA synthesis and degradation, formation of plasma membrane etc. Biological molecules forming these systems range from nuclei acids, polypeptides and polysaccharides. They can even be regulated by multiple chemical and biological stimuli. fiber forming proteins are fundamental building blocks of life. They play an essential role in motality (Flagellin), elasticity (elastin, collagen), scaffolding (actin), stabilization (keratins) and protection of the cells, tissues and organisms (spider and insect silks). They also form a tight stable

structure that has the tendency to self-assemble. These proteins are widely used in many medical and technical applications.

Therefore biological systems offer many different molecules (peptides, nucleic acids, polysaccharides) that can be used to form bionanostructures / bionanomaterials. By the regulation of assembly of these components, the smart bionanostructures / bionanomaterials are only a step away. Polysaccharides, such as cellulose represent the majority of biomass, however nucleic acids are the most easy to modify and synthesize. Polypeptides seems to represent the best balance of structural and functional versatility, and allow ample possibility of modifications so it is no wonder that most of the natural nanomachines and also dynamic structural elements are made of polypeptide. Natural polymers are all candidates for the components of self-assembled bionanostructures.

Nanofibers:-

Nanofibers are fibers with diameters in the nanometer range. Nanofibers can be generated from different polymers and hence have different physical properties and application potentials. Examples of natural polymers include collagen, cellulose, silk ~~for~~ fibroin, keratin, gelatin and polysaccharides such as chitosan and alginate. Polymer chains are connected via covalent bonds. The diameters of nanofibers depend on the ~~pp~~ type of polymer

used and the method of production. All polymer nanofibers are unique for their large surface area-to-volume ratio, high porosity, appreciable mechanical strength, and flexibility in functionalization compared to their microfiber counterparts.

Collagen is one of the long, fibrous structural proteins whose functions are quite different from those of globular protein, such as enzymes. Tough bundles of collagen called collagen fibers are a major component of the extracellular matrix that supports most tissues and gives cells structure from the outside, but collagen is also found inside certain cells. Collagen has great tensile strength, and is the main component of fascia, cartilage, bone, and fibrous tissues like ligaments, tendons, and skin.

It is the main structural protein in the extracellular space in the various connective tissues in animal bodies. As the main component of connective tissues, it is the most abundant protein in mammals, making 25% to 35% of the whole-body protein content. Collagen consists of amino acids wound together to form triple-helices to form of elongate fibrils. Along with elastin and soft keratin, it is responsible for skin strength and elasticity, and its degradation leads to wrinkles that accompany aging. It strengthens blood vessels and plays a role in

tissue development. It is present in the cornea and lens of the eye in crystalline form. It has a wide variety of applications, from food to medical. For instance, it is used in cosmetic surgery and burn surgery. It is widely used in the form of collagen casings for sausages, which are also used in the manufacture of musical strings.

Cellulose is a straight chain polymer: unlike starch, no coiling or branching occurs, and the molecule adopts an extended and rather stiff rod-like conformation, aided by the equitorial conformation of the glucose residues. The multiple hydroxy group on the glucose from one chain form hydrogen bonds with oxygen atoms on the same or on a neighbor chain, holding the chains firmly together side-by-side and forming microfibrils with high tensile strength. This confers tensile strength in cell walls, where cellulose microfibrils are meshed into a polysaccharide matrix.

Fibroin is an insoluble protein present in silk created by spiders, the larvae of Bombyx mori, other moth genera such as Antheraea, Cricula, Samia and Gonometa, and numerous other insects. Silk in its raw state consists of two main proteins, sericin and fibroin, with a glue-like layer of antiparallel beta sheets.

Its primary structure mainly consists of the recurrent amino acidsequence (Gly-Ser-Gly-Ala-Gly-Ala). The high glycin (and to a lesser extent, alanine) content allows for ~~tight~~ packing of the sheets, which contributes to silk's rigid structure and tensile strength. A combination of stiffness and toughness make it a material with applications in ~~several~~ several areas, including biomedicine and ~~textile~~ manufacture.

Keratin is one of a family of fibrous structural protein. It is the key structural material making up hair, horns, claws, hooves, and the outer layer of human skin. Keratin is also the protein that protects epithelial cells from damage or stress. Keratin is extremly insoluble in water and organic solvents. Keratin monomers assemble into bundles to form intermediate filaments, which are tough and form strong unmineralized epidermal appendages found in reptiles, birds, amphibians and mammals. The only ~~o~~ the biological matter know to approximate the toughness of keratinized tissue is chitin.

Gelatin is an irreversibley hydrolyzed form of collagen, wherein the hydrolysis results in the reduction of protein fibrils into

smaller peptides, which will have broad molecular weight ranges associated with physical and chemical methods of denaturation, based on the process of hydrolysis. It is a translucent, colorless, brittle (when dry), flavorless food ingredient that is derived from collagen obtained from various animal body parts. It is commonly used as a gelling agent in food, medications, drug and vitamin capsules, photographic films and papers, and cosmetics.

Chitosan is a linear polysaccharide composed of randomly distributed α-(1→4)-linked D-glucosamine (deacetylated unit) and N-acetyl-D-glucosamine (acetylated unit). It is produced commercially by deacetylation of chitin, which is the structural element in the exoskeleton of crustaceans (such as crabs and shrimp) and cell walls of fungi. It has a number of commercial and possible biomedical uses. It can be used in agriculture as a seed treatment and biopesticide, in winemaking as a fining agent, in industry as a self-healing polyurethane point coating. In medicine, it is useful in bandages to reduce bleeding and as an antibacterial agent, also be used to help deliver drugs through the skin. Other uses of chitosan that have been researched include use as a soluble dietary fiber.

Alginic acid, also called algin or alginate, is a polysaccharide distributed widely in the cell walls of brown algae, where through binging with water it forms a viscous gum. It is also a significant component of the biofilms produced by the bacterium Pseudomonas aeruginosa, the major pathogen in cystic fibrosis, that confer it a high resistance to antibiotics and killing by macrophages. Its colour ranges from white to yellowish-brown. It is sold in filamentous granular or powdered forms.

Production of Biological Nanofibre by Self-assembly.

The self-assembly technique is used to generate peptide nanofibers and peptide amphiphiles. The method was inspired by the natural folding process of amino acid residues to form proteins with unique three-dimensional structures. The self-assembly process of peptide nanofibers involves various driving forces such as hydrophobic interactions, electrostatic forces, hydrogen bonding and van der Waals force and is influenced by external conditions such as ionic strength and pH.

Applications of Nanofibers

1. Medicine:-

Applications described below represented the main areas of nanofiber utilization in healthcare. Many other medical applications can benefit from the favorable properties of nanofiber materials as well. Nanofibers for medical purposes can be spun from biodegradable polymers and allows various additives that bring intended functionality. Moreover the structure and size (close to human cell dimension) of ananofibers can be controlled, thus optimized for tissue engineering research.

2. Drug delivery:-

Nanofiber membrane from biopolymers can be used as a bioactive material or drug carrier. Active pharmaceutical ingredients can be incorporated into the nanofibers they naturally show the fast release of drugs. As a result nanofibers provide significant bioavailability improvement, especially for poorly soluble drugs.

3. Wound healing:-

Nanofiber layers produced from biopolymers (chitosan, gelatine, collagen, polykaprolakton, etc., or combinations of these materials) can be used as a wound dressing for significant support of the wound healing process. On the basis of results realized from in vitro and in vivo experiments, nanofiber materials have shown significant benifits. When using nanofiber material on contaminated

wounds, it is possible to add antibacterial material and drugs to the nanofiber structure.

A. Tissue engineering:-

Nanofiber materials made from biopolymers (collagen, polylactic acid, polycaprolactone etc.) are possible substrates for growing cells. With the mechanical and structural properties of the nanofiber material, it is possible to prepare scaffolds which are suitable for implanting by different types of cells. Nanofiber substrates effectively support cell proliferation and enable tissue replacement prepared from a patient's cells. During the preparation of nanofiber scaffolds, it is possible to incorporate different bioactive materials, for example, growth factor, and eventually other drugs such as an immunosuppressant.

Nanotubes:-

Cyclic peptides form nanotubes:-

Reza Ghadiri has designed a modular concept for the self-assembly of nanotubes. He uses cyclic peptides that are perfectly designed to stack on top of one another. The peptide groups in their circular molecules have hydrogen bonding groups facing up and down from the plane of the circle, forming hydrogen bonds that glue one ring to its neighbours.

circles are made from amino acids with all the side chains face radially out from the centre of the circle, leaving a ~~smooth~~ smooth channel through the centre.

When these rings are created from Leucine and tryptophan amino acids, the resultant nanotubes have a carbon-rich outer surface. These rings assemble into nanotubes that span lipid membranes. By choice of the size of the ring, the diameter of the channel can be tunned. A circle of 8 amino acids form a channel of about 0.45 nm diameter. When synthesized, these formed effective channels for metal ions but blocked passage of larger molecules. A slightly larger ring of 10 amino acids has a channel of about 0.9 nm. Those nanotubes have been shown to allow the passage of glucose.

"Smart" bionanotubes: Santa Barbara have developed "smart" bio-nanotubes with open or closed ends - that could be developed ~~Form~~ drug or gene delivery applications. Lipid protein nanotubes made of microtubule protein (made of tubulin protein subunits that is coated by a lipid bilayer which in turn is coated by tubulin protein rings or spirals. By controlling the relative amount of lipid and protein it is possible to switch between two states of nanotubes with either open ends or closed ends with lipid caps, a process which forms the basis for controlled chemical and drug encapsulation

and release. A top view of the nanotubes and a magnified region is shown on the right.

The nanotubes are "smart" because in the future they could be designed to encapsulate and then open up to deliver a drug or gene in a particular location in the body. The scientist found that by manipulating the electrical charges of lipid bilayer membranes and microtubules from cells, they could create open or closed-nanotubes, or nanoscale capsules.

Nanocellulose:-

Nanocellulose is a term referring to nano-structured cellulose. It is a light solid substance obtained from plant matter which comprises nanosized cellulose fibrils. This new material is a pseudo-plastic and possesses the property of specific kinds of fluids or gels that are generally thick in normal conditions. The lateral dimensions of nanocellulose range from 5 to 20 nm, and the longitudinal dimension ranges from a few 10's of nanometers to several microns. These nanocellulose may be either cellulose nanocrystal (CNC or NCC), cellulose nanofibers (CNF) also called microfibrillated cellulose (MFC), or bacterial nanocellulose, which refers to nano-structured cellulose produced by bacteria.

Production of Nanocellulose

Nanocellulose, which is also called cellulose nanofibers (CNF), microfibrillated cellulose (MFC) or cellulose nanocrystal (CNC), can be prepared from any cellulose source material, but woodpulp is normally used.

Nanocellulose is generally produced from wood pulp using the following steps.

1) Remove non-cellulose impurities from the wood pulp using a homogenizer. The high pressure homogenizers used in the production process helps delaminate the cell walls of the fibers and separate the nanosized fibrils. This process consumes very large amounts of energy and values over 30 MWh/tonne are not uncommon.
2) Separate the cellulose fibers by beating the mixture gently.
3) Allow the fibers to form a thick paste of needle-like crystals or a spaghetti-like structure of cellulose fibrils.
4) The thick paste that is obtained can be shaped and readily used to laminate surfaces.

Once it is completely separated from the wood pulp, the nanocellulose is in a water suspension. At this stage, care should be taken to prevent the formation of rough clumps in cases when the cellulose fibers stick together as the material dries. Processes have already been developed that allows nanocellulose to dry without the formation of rough clumps and also prevent the cellulose fibrils from sticking together and enable

the cellulose fibers to retain their mechanical properties.

Cellulose nanowhisker are rodlike highly crystalline particles (relative crystallinity index above 75%) with a rectangular cross section. They are formed by the acid hydrolysis of native cellulose fibers commonly using sulfuric or hydrochloric acid. Amorphous section of native cellulose are hydrolysed and after careful timing, crystalline sections can be retrieved from the acid solution by centrifugation and washing. Their dimensions depend on the native cellulose source material, and hydrolysis time and temperature.

Structure of Nanocellulose

Dimension and Crystallinity :-

The ultrastructure of nanocellulose derived from various sources has been extensively studied. Techniques such as transmission electron microscopy (TEM), scanning electron microscopy (SEM), atomic force microscopy (AFM), wide angle X-ray scattering (WAXS), small incidence angle X-ray diffraction and solid state ^{13}C cross-polarization magic angle spinning (CP/MAS), nuclear magnetic resonance (NMR) and spectroscopy have been used to characterize typically dried nanocellulose morphology.

Pulp chemistry has a significant influence on nanocellulose microstructure. Carboxymethylation increases the number of charged groups on the fibril surfaces, making the fibrils easier to liberate and results in smaller and more uniform fibril widths (5-15 nm) compared to enzymatically pre-treated nanocellulose,

where the fibril widths were 10-30 nm. The degree of crystallinity and crystal structure of nanocellulose exhibits cellulose crystal organization and the degree of crystallinity is uncharged by the preparation of the nanocellulose. ~~Typically~~ Typical values for the degree of crystallinity were around 63%. However, the lateral dimensions of nanocellulose range from 5 to 20nm, and the longitudinal dimension ranges a few 10's of nanometers to several microns.

Properties of Nanocellulose

Nanocellulose is lightweight, electrically conductive, and even stronger than steel. The crystalline form is transparent, and gas impermeable.

The properties of nanocellulose are listed below -

Viscosity :- The high viscosity at low nanocellulose concentrations makes nanocellulose very interesting as a non-caloric stabilizer and gellant in food applications, the major field explored by the early investigators.

Nanocellulose gels are also highly shear thinning (the viscosity is lost upon introduction of the shear forces). The shear-thinning behaviour is particularly useful in a range of different coating applications.

Mechanical Properties :-

Crystalline cellulose has interesting mechanical properties for use in material applications. Its ~~tensil~~ tensil strength is about 500 MPa, similar to that of aluminium. Its stiffness

is about 140-220 GPa, comparable with that of Kevlar and better than that of glass fibers, both of which are used commercially to reinforce plastics. films made from nanocellulose have high strength (over 200 MPa), high stiffness (around 20 GPa) and high strain (12%). Its strength/weight ratio is 8 times that of stainless steel.

Barrier Properties:- In semi-crystalline polymers, the crystalline regions are considered to be gas impermeable Due to relatively high crystallinity, in combination with the ability of the nanofibers to form a dense network held together by strong inter-fibrillar bonds (high cohesive energy density), it has been suggested that nanocellulose might act as a barrier material.

Foams:- Nanocellulose can also be used to make aerogels/foams, either homogeneously or in composite formulations. Nanocellulose-based foams are being studied for packaging applications in order to replace polystyrene-based foams. The magnetic cellulose foam may allow for a number of novel applications of nanocellulose and the first remotely actuated magnetic super sponges absorbing 1 gram of water within a 60 mg cellulose aerogel foam were reported. Notably, these highly porous foam (>98% air) can be compressed into strong magnetic

nanopapers, which may find use as functional membranes in various applications. It is highly absorbent when used as a basis for aerogels or foams.

Surface modification:- The surface modification of nanocellulose displays a high concentration of hydroxyl groups at the surface which can be reacted. However, hydrogen bonding strongly affects the reactivity of the surface hydroxyl groups. In addition, impurities at the surface of nanocellulose such as glucosidic and lignin fragments need to be removed before surface modification to obtain acceptable reproducibility between different batches.

Safety aspects:- Processing of nanocellulose does not cause significant exposure to fine particles during friction grinding or spray drying. No evidence of inflammatory effects or cytotoxicity on mouse or human macrophages can be observed after exposure to nanocellulose. The results of toxicity studies suggest that nanocellulose is no cytotoxic and does not cause an effects in inflammatory system in macrophages.

Applications of Nanocellulose:-

Nanocellulose with its lightweight, high strength and transparent properties is of great interest for many applications in a wide variety of areas. The material that is of immense significance in the ongoing commercialization of nanotechnologies, and researchers and industrials are analyzing and exploring new manufacturing process and applications for nanocellulose. Some of the key applications of nanocellulose are:-

Paper and paperboard :-

There is potential of nanocellulose applications in the area of paper and paperboard manufacture. Nanocellulose are expected to enhance the fiber-fiber bond strength and hence, have a strong reinforcement effect on paper materials. Nanocellulose may be useful as a barrier in grease-proof type of papers and as a wet-end additive to enhance retention, dry and wet strength in commodity type of paper and board products. It has been shown that applying CNF as a coating material on the surface of paper and paperboard improves the barrier properties, especially air resistance, It also enhances the structure properties of paperboards (smother surface).

Nanocellulose can be used to prepare flexible and optically transparent paper for electronic devices. It is recyclable, compatible with biological objects, and easily degrades when disposed of.

Composite

Nanocellulose makes an interesting material for reinforing plastics. ~~Nanometeri~~ Nanocellulose has been reported to improve the mechanical properties of, for example, thermosetting resins, starch based matrixes, soy protein, rubber latex, poly(lactide). The composite applications may be for use as coatings and films, paints, foams, packaging.

Food

Nanocellulose can be used as a low calorie replacement for today's carbohydrate additives used as ~~thickness~~ thickeners, flavour carriers and suspension stabilizers in a wide variety of food products and is useful for producing filling, crushes, chips, wafers, soups, gravies, puddings etc. The food applications were early recognised as a highly interesting application field for nanocellulose due to rheological behaviour of the nanocellulose gel.

Hygiene and Absorbent Products:

Applications in this field include: super water absorbent material (e.g., for incontinence pads materials), nanocellulose used together with super absorbent polymers, nanocellulose in tissue, non-woven products or absorbent structures and as antimicrobial films.

Emulsion and Dispersion:

Nanocellulose has numerous applications as a food additive, and in the general area of emulsion and dispersion applications in other fields. Oil in water applications were early recognized. Early investigators has explored the area of non-settling suspensions for pumping sand, coal as well as paints and drilling muds.

Oil recovery:-

Hydrocarbon Fracturing of oil-bearing formations is a potentially interesting and largescale applications. Nanocellulose has been suggested for use in oil recovery applications as a fracturing fluid. Drilling muds based on nanocellulose have also been suggested.

Medical, cosmetic and pharmaceutical

The use of nanocellulose in cosmetics and pharmaceuticals was also early recognized. A wide range of high-end applications have been suggested.

- Freeze-dried nanocellulose aerogels used in sanitary napkins, tampons, diapers or as wound dressing.
- The use of nanocellulose as a composite coating agent in cosmetics e.g., for hair, eyelashes, eyebrows or nails.
- A dry solid nanocellulose composition in the form of tablets. For treating intestinal disorders.
- Nanocellulose films for screening of biological compounds and nucleic acid encoding biological compound.
- Nanocellulose in compositions of a photoreactive noxious substance purging agent.
- Elastic cryo-structured gels for potential biomedical and biotechnological application.
- Matrix for 3D cell culture.

Other Applications:-

- As a highly scattering material for ultra-white coating.
- Active the dissolution of cellulose in different solvents.
- Regenerated cellulose products, such as fibers films, cellulose derivatives
- Tobacco filter additive.
- Organometallic modified nanocellulose in battery separators.
- Loud-speaker membranes
- Lightweight body armour & ballistic glass.

Biological Nanomachines

A number of nanomachines are working inside the human body. They are made by living cells developed by the process of evolution. They are selected to perform their tasks in a very specific environment and are subject~~ed~~ to the unfamiliar forces imposed by the enviornment. These nanomachines work in many processes of life - eating, breathing, growing and repairing, sensing danger and responding to it and producing.

The biological nanomachines are the ~~th~~ true nanomachines which are built to nanoscale specifications with each atom precisely placed and connected to its neighbours. Many of the nanomachines still

perform their atom sized functions even after they are isolated, purified if the environment is not too harsh. They do not have to sequestered safely inside the cell. Each one is of a self-sufficient molecular machine.

For example, Natural digestive enzymes like pepsin and lysozyme are so tough that they can be added to laundry detergents to digest away strains. Amaylases are used on an industrial scale to convert powdry starch into sweet corn syrup. Similarly, the DNA manipulating nanomachines are now available commercially.

Some of the characteristics of these machines are —

- Gravity and inertia are negligible at the nanoscale.
- Nanomachines show Atomic granularity.
- Thermal motion is significant force at the nanoscale
- They require a water environment
- Most natural nanomachines are composed of protein.

Ribosomes :-

The Ribosomes is a complex molecular machine, found within all living cells, that serves as the site of biological protein synthesis (translation). Ribosomes link amino acids together in the order specified by messenger RNA (mRNA) molecules. Ribosomes consist of two major components: the small ribosomal subunits (blue), which read the RNA, and the large subunits (red), which join amino acids to form a polypeptide chain. Each subunit comprises one or more ribosomal RNA (rRNA) molecules and a variety of ribosomal protein (r-protein). The ribosomes and associated molecules are also known as the translational apparatus.

Ribosomes from bacteria, archaea and eukaryotes in the three-domain system, resemble each other to a remarkable degree, evidence of a common origin. They differ in their size, sequence, structure, and the ratio of protein to RNA. The differences in structure allow some ~~additional~~ antibiotics to kill bacteria by inhibiting their ribosomes, while leaving human ribosomes unaffected. In bacteria and archaea, more than one ribosome may move along a single mRNA chain at one time, each "reading" its sequence and produced from ~~mich~~ mitochondrial genes, and functionally

resemble many features of those in bacteria, reflecting the likely evolutionary origin of mitochondria.

Ribosome Location:-

Ribosome are classified as two types, "free" or membrane-bound". free and membrane-bound ribosomes differ only in their spatial distribution, they are identical in structure. Whether the ribosome exists in a free or membrane-bound state depends on the presence of an ER-targeting signal sequence on the protein being synthesized, so an individual ribosome might be membrane-bound when it is making one protein, but free in the cytosol when it makes another protein.

Ribosomes are sometimes referred to as organelles; but the use of the term organelle is often restricted to describing sub-cellular components that include a phospholipid membrane, which ribosomes, being entirely particulate, do not. For this reason, ribosomes may sometimes be described as "non-membranous organelles."

Free ribosomes

Free ribosomes can move about anywhere in the cytosol, but are excluded from the cell nucleus and other organelles. Protein that are formed from free ribosomes are released into the cytosol and used within the cell. Since the cytosol contain high concentrations of glutathione and is, therefore, a reducing environment, proteins containing disulfide bonds, which are formed from oxidized cysteine residues, cannot be produced within it.

Membrane-bound ribosomes:-

When a ribosome begins to synthesize protein that are needed in some organelles, the ribosome making this protein can become "membrane-bound". In eukaryotic cells this happens in a region of the endoplasmic reticulum (ER) called the "rough ER". The newly produced polypeptide chains are inserted directly into the ER by the ribosome undertaking vectoral synthesis and are then transported to their destination, through the secretory pathway. Bound ribosomes usually produce proteins that are used within the plasma membrane or are expelled from the cell via exocytosis.

Ribosome biogenesis: -

In bacterial cells, ribosomes are synthesized in the cytoplasm through the transcription of multiple ribosomal gene operons. In eukaryotes, the process takes place both in the cell cytoplasm and in the nucleolus, which is a region within the cell nucleus. The assembly process involves the coordinated function of over 200 protein in the synthesis and processing of the four rRNA, as well as assembly of those rRNA with ribosomal protein.

Origin: -

The ribosome may have first originated in an RNA world, appearing as a self-replicating complex that only later evolved the ability to synthesize proteins when amino acids began to appear. Studies suggest that ancient ribosomes constructed solely of rRNA could have developed the ability to synthesize peptide bonds. In addition, evidence strongly points to ancient ribosomes as self-replicating complexes, where the rRNA in the ribosomes had informational, structural, and catalytic purposes because it could have coded for tRNAs and proteins

~~needed~~ needed for ribosomal self-replication. Hypothetical cellular organisms with self-replicating RNA but without DNA are called ribocytes.

As amino acids gradually appeared in the RNA world under prebiotic conditions, their interactions with catalytic RNA would increase both the range and efficiency of function of catalytic RNA molecules. Thus, the driving force for the evolution of the ribosome from an ancient self-replicating machine into its current form as a translational machine may have been the selective pressure to incorporate proteins into the ribosome's self-replicating machines, so as to increase its capacity for self-replication.

Function:-

Ribosomes are minute particles consisting of RNA and associated proteins that function to synthesize proteins. Proteins are needed for many cellular functions such as repairing damage or directing ~~cellu~~ chemical processes. Ribosomes can be found floating with the cytoplasm or attached to the endoplasmic reticulum.

Ribosomes act as catalysis in two ~~extremly~~ extremely important biological processes called peptidyl transfer and peptidyl hydrolysis. The "PT center is for producing protein bonds during protein elongation".

Translation (genetics)

Ribosomes are the workplaces of protein biosynthesis, the process of translating mRNA into protein. The mRNA comprises a series of codons that dictate to the ribosome the sequence of the amino acids needed to make the protein. Using the mRNA as a template, the ribosome traverses each codon (3 nucleotides) of the mRNA, pairing it with the appropriate amino acid provided by an aminoacyl-tRNA. Aminoacyl-tRNA contains a complementary anticodon on one end and the appropriate amino acid on the other. For fast and accurate recognition of the appropriate tRNA, the ribosome utilizes large conformational changes. The small ribosomal subunit, typically bound to an aminoacyl-tRNA containing the amino acid methionine, binds to an AUG codon on the mRNA and recruits the large ribosomal subunit. The ribosome contains three RNA binding sites, designated A, P and E. The A-site binds an aminoacyl-tRNA, the P-site binds a peptidyl-tRNA (a tRNA bound to the peptide being synthesized), and the E-site (exit) binds a free tRNA before it

exit the ribosome. Protein synthesis begins at a start codon AUG near the 5'-end of the mRNA. mRNA binds to the P site of the ribosomes first. The ribosome is able to identify the start codon by use of the shine-Dalgarno sequence of the mRNA in prokaryotes and Kozak box in eukaryotes.

Although catalysis of the peptide bond involves the C2 hydroxyl of RNA's P-site adenosine in a protein shuttle mechanism, other steps in protein synthesis (such as translocation) are caused by changes in protein conformations. Since their catalytic core is made of RNA, ribosomes are classified as "ribozymes", and it is thought that they might be remnants of the RNA world.

In Fig-1, both ribosomal subunits (small and large) assemble at the start codon (towards the 5' end of the RNA). The ribosome uses RNA that matches the current codon (triplet) on the mRNA to append an amino acid to the polypeptide chain. This is done for each triplet on the RNA, while the ribosome moves towards the 3' end of the mRNA. Usually in bacterial cells, several ribosomes are working parallel on a single RNA, forming what is called a polyribosome or polysome.

Photosynthesis systems.

Photosynthesis systems are electronic scientific instruments designed for non-destructive measurement of photosynthetic rates in the field. Photosynthesis systems are commonly used in agronomic and environmental research, as well as studies of the global carbon cycle.

The main features of photosynthesis systems are

* Absolute and differential Non-dispersive Infrared Gas Analyser.
* System can be used for both open as well as closed system measurement technique.
* The only system available for 9 leaf chamber heads for different types of leaves.
* The chamber will be directly connected to the analyser, therefore very accurate and fast response.
* Uses Infrared non-contact type leaf temperature sensor, which is most accurate.

"Open" systems or 'closed' systems;-

There ~~two~~ are two distinct types of photosynthetic system; 'open' or 'closed'. This distinction refers to whether or not the atmosphere of the leaf-enclosing chamber is renewed during the measurement.

In an 'open system' air is continuously passed through the leaf chamber to maintain CO_2 in the leaf chamber at a steady concentration. The leaf to be analysed is placed in the Leaf chamber. The main consol supplies the chamber with air at a known rate with a known concentration of CO_2 and th_2O. The air is directed to over the leaf, ~~then~~ then the CO_2 and th_2O concentration of air leaving the chamber is determined. The out going air will have a lower CO_2 concentration and a higher th_2O concentration than the air entering the chamber. The rate of CO_2 uptake is used to assess the rate of photosynthetic carbon assimilation, while the rate of water loss is used to assess the rate of transpiration. Since CO_2 intake and th_2O release both occur through the stomata, high rates of CO_2 uptake are expected to coincide with high rates of transpiration. High rates of CO_2 uptake and th_2O loss indicates high stomatal conductance.

Because the atmosphere in renewed, 'open' system are not seriously affected by outward gas leakage and adsorption or absorption by the materials of the system.

In contrast, in a 'closed system' the same atmosphere is continuously measured over a period of time to establish rates of change in the parameters. The CO_2 concentration in the chamber is decreased, while the H_2O concentration increases. this is less tolerant to leakage and material adsorption.

How photosynthesis system function:-

Photosynthesis systems function by measuring gas exchange of leaves. Atmospheric carbon dioxide is taken up by leaves in the process of photosynthesis, where CO_2 is used to generate sugars in a molecular path way known as the Calvin cycle. This draw-down of CO_2 induces more atmospheric CO_2 to diffuse through stomata into the air spaces of the leaf. while stoma are open water vapor can easily diffuse out of plant tissues, a process known as transpiration. It is this exchange of CO_2 and water vapor that is measured as a proxy of photosynthetic rate.

The basic components of a photosynthetic system are the leaf chamber, infrared gas analyzer (IRGA), batteries and a console with keyboard, display and memory. Modern 'open system' photosynthesis systems also incorporate miniature disposal compressed gas cylinder and gas supply pipes. This is because external air has natural fluctuations in CO_2 and water vapor content, which can introduce measurment noise. Modern 'open system' photosynthesis systems

removes the CO_2 and water vapour by passage over soda lime and drierite, then add CO_2 at a controlled rate to give a stable CO_2 concentration. Some systems are also equipped with temperature control and a removable light unit, so the effect of these environmental variables can also be measured.

The leaf to be analysed is placed in the leaf chamber. The CO_2 concentration is measured by the infrared gas analyzer. The IRGA shines infrared light through a gas sample onto a detector. CO_2 in the sample absorbs energy, so the reduction in the level of energy that reaches the detector indicates the CO_2 concentration. Modern IRGA take account of the fact that H_2O absorbs energy at similar wavelengths as CO_2. Modern IRGAs may either dry the gas sample to a constant water content or incorporate both a CO_2 and a water vapour IRGA to asses the difference in CO_2 and water vapour concentrations in air between the chamber entrance and outlet.

The liquid crystal Display on the console displays measured and calculated data. The console may have a PC card slot. The stored data can be viewed on the LCD display, or sent to a PC. Some photosynthesis systems allow communication over the internet using standard internet communication protocols.

Modern photosynthesis systems may also be designed to measure ~~and calculated data. The console may have a PC~~ leaf temperature, chamber air temperature, PAR (photosynthetically active radiation), and atmospheric pressure. These systems may calculate water use efficiency (A/E), stomatal conductance (gs), intrinsic water use efficiency (A/gs), and sub-stomatal CO_2 concentration (Ci). Chamber and leaf temps are measured with a thermistor sensor. Some systems are also designed to control environmental conditions.

A simple and general equation for ~~photost~~ photosynthesis is:

$$CO_2 + H_2O + (\text{Light energy}) = C_6H_{12}O_6 + O_2$$

calculating photosynthetic rate and related parameters.

Calculations used in 'open system' systems:-

For CO_2 to diffuse into the leaf, stomata must be open, which permits the outward diffusion of water vapour. Therefore, the conductance of stomata influences both photosynthetic rate (A) and transpiration (E), and the usefulness of measuring A is enhanced by the simultaneous measurement of E. The internal CO_2 concentration (Ci) is also quantified, since Ci represents an indicator of the availability of the primary substrate (CO_2) for A.

A carbon assimilation is determined by measuring the rate at which the leaf assimilates CO_2. The change in CO_2 is calculated as CO_2 flowing into leaf chamber, in mol ~~co~~ mol CO, minus flowing out from leaf chamber, μmol mol^{-1}. The photosynthetic rate is differential water vapour concentration, mbar, multiplied by the flow of air into leaf chamber per square meter of leaf area, $mol\ s^{-1}\ m^{-2}$, divided by atmospheric pressure, in ~~mBar~~ mBar.

Calculation ~~of~~ used in 'closed system' systems

A leaf is placed in the leaf-chamber, with a known area of leaf enclosed. Once the chamber is closed, carbon dioxide concentration gradually declines. When the concentration decreases past a certain point a timer is started, and is stopped as the concentration passes at a second point. The difference between the concentrations gives the change in carbon-dioxide in ppm. Net photosynthetic rate in micro grams carbon-dioxides" is given by; $(V \times \rho \times 0.5 \times FSD \times 99.7)/t$. where V = the chamber volume in liters, ρ = the density of carbon dioxide in $mg \times cm^{-3}$, FSD = the ~~the~~ carbon dioxide concentration in ppm corresponding to the change in carbon-dioxide in the chamber, t = the time in seconds for the concentration to decrease by the set amount. Net photosynthesis per unit leaf area is derived by dividing net photosynthetic rate by the leaf area enclosed by the chamber.

Applications

* Since photosynthesis, transpiration and stomatal conductance are in integral part of basic plant physiology, estimates of these parameters can be used to investigate numerous aspects of plant biology. The plant-scientific community has generally accepted photosynthetic systems as reliable and accurate tools to assist research. There are numerous peer-reviewed articles in scintific Journals which have used a photosynthetic system. To illustrate the utility & diversity of applications of photosynthetic systems, ~~below~~

* The effect of CO_2 enrichment on the photosynthetic behavior of an endangered medicinal herb was investigated by a steam at Garhwal University, India Photosynthetic rate (A) was stimulated during the first 30 days, then significantly decreased. Transpiration rate (E) decreased significantly throughout the CO_2 enrichment, whereas stomatal conductance (g_s) significantly reduced initially. Overall, it was ~~conclu~~ concluded that the medicinally ~~important~~ important part of this plant showed increased growth.

* The dynamic responses of stomatal conductance (g_s) net photosynthesis (A) to a progressive drought in the ~~pota~~ poplar clone with contrasting drought tolerance. g_s and A were measured using a photosythetic system. Plants were either well-watered or drought preconditioned.

Protein Nanotechnology

Protein nanotechnology is an emerging field that is still defining itself. It embraces the intersection of protein science, which exists naturally at the nanoscale, and burgeoning field of nanotechology.

The protein structure also makes them suitable for forming functional biological materials as well as their ability to self-assemble. The resulting developments in protein-based nanotechnology include proteins being utilized as important elements in nanotechnology applications, along with applying nanodevices to the biological environment where proteins are contained.

Protein in Nanomachine Assembly :-

Protein are suitable for use in material development and for building nanoscale machines because they provide similar to roles in biology. The complex protein formations that occur in the biological environment include rings, tubes and cages, potential building blocks for nanomachines. Nanoscale component assembly is problematic because the small dimensions involved cause difficulty in manipulation. The utilization of proteins provides a solution

as they show natural affinity to other biomolecules and can spontaneously self-assemble. By engineering protein affinities, nanodevices can self-assemble when individual components are mixed. However, protein engineering has been hindered by the difficulty of designing specific self assembling proteins because of chemical ~~hetero~~ heterogeneity and the large scale surfaces required for protein-protein interaction.

A startegy for forming a controlled assembly of protein nanostructures was developed in 2015. Gold nanoparticles are employed as scaffolds allowing for directed interfacial interaction. A protein is then grafted onto the gold nanoparticles and assembly is performed through protein pair formation. The technique has the potential to be optimized for functional nanomaterial engineering as well as applications in biosensing and cell targeting.

Proteins as Nanowires for Biosensing

Nanowires are slender structures with a diameter at the nanoscale. Their application is not limited to the physical sciences with increasing use in the biosciences, particularly in biosensing studies. Biological structures such as DNA have previously been assessed as material for nanowires but there are questions about the inherent conductivity of DNA.

The advantages to the application of proteins for constructing nanowires include:

1. The natural occurrence of fibrous protein structures is particularly suited to the formation of self-assembled nanowires. Fibrous proteins also have greater stability than globular proteins.
2. The basic amino acid chain structure of proteins allows for the exploitation of amino acid chain chemistry, including as a base for metallic modification.
3. Genetic control of the primary sequence forming the amino acids provides further opportunity for increased functionalization.
4. Protein can be generated in large amounts and can provide a readily available source material.

Biosensing involves ~~the act~~ the detection of biological and chemical molecules at the nanoscale through signal transduction. It is therefore advantageous to develop signal transduction pathways in the same scale. Protein and peptides have been used to create a biosensing device through the modification of

electrodes to create a porous nanowire. A protein enzyme is immobilized onto the protein nanotube or nanofiber via cross-linking molecules. This structure is then attached to an electrode. The biosensing device formed is capable of applications such as glucose sensing, by the covalent bonding of glucose oxidase to the protein nanotube complex. The employment of this technology is particularly important in diabetes management.

DNA Nanotechnology

DNA nanotechnology is the design and manufacture of artificial nucleic acid structures for technological uses. In this field, nucleic acids are used as non-biological engineering materials for nanotechnology rather than as the carriers of genetic information in living cells. Researchers in the field have created static structures such as two- and three-dimensional crystal lattices, nanotubes, polyhedra, and arbitrary shapes, and functional devices such as molecular machines and DNA computers. The field is beginning to be used as a tool to solve basic science problems in structural biology and biophysics, including applications in X-ray crystallography and nuclear magnet

resonance spectroscopy of proteins to determine structures. Potential applications in molecular scale electronics and nanomedicine are also being investigated.

The conceptual fundation for DNA nanotechnology was first laid out by Nadrian Seeman in the early 1980's, and field began to attract widespread interest in the mid-2000s. This use of nucleic acids is enabled by their strict base pairing rules, which cause only portions of strands with complementary base sequences to bind together to form strong, rigid double helix structures. This allows for the rational design of base sequences that will selectively assemble to form complex target structures with precisely controlled nanoscale features. Several assembly methods are used to make these structures, including tile-based structures that assemble from smaller structures, folding structures using the DNA origami method, and dynamically reconfigurable structures using strand displacement methods. The field's name specifically references DNA, but the same principles have been used with other types of nucleic acids as well, leading to the occasional use of the alternative name nucleic acid nanotechnology.

Fundamental concepts

These four strands associate into a DNA four-arm junction because this structure maximizes the number of correct base pairs, with A matched to T and C matched to G fig-1 shows for a more realistic model of the four-arm junction showing its tertiary structure.

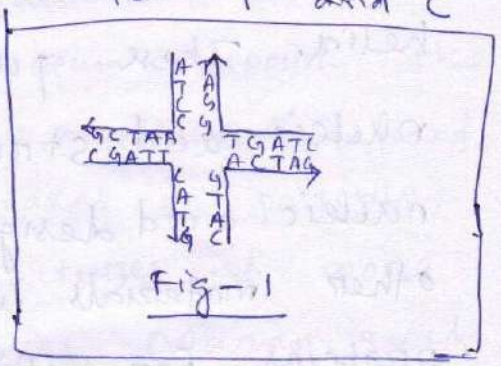
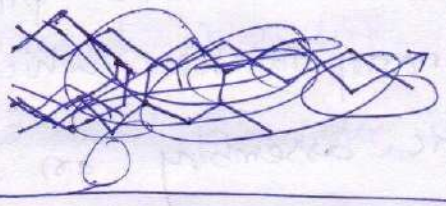


Fig-1

This double-crossover (DX) supramolecular complex consists of five DNA single strands that form two double-helical domains, on the top and the bottom in the fig-2. there are two crossover points where the strands cross from one domain into the other.



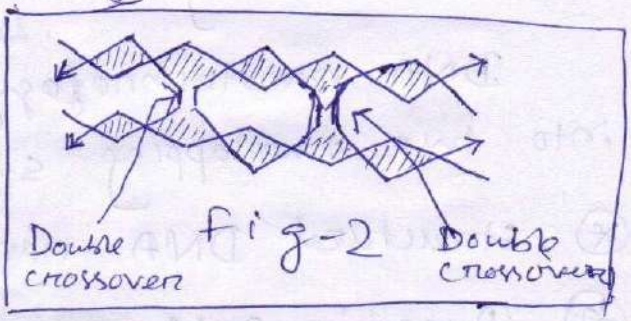


fig-2

DNA nanotechnology, specifically, is an example of bottom-up molecular self-assembly, in which molecular components spontaneously

organize into stable structures; the particular form of these structures is induced by physical and chemical properties of the components selected by the designers. The component materials are ~~stand~~ strands of nucleic acids such as DNA; these strands are often synthetic and almost always used outside the context of a living cell. DNA is well-suited to nanoscale construction because the binding between two ~~nuc~~ nucleic acid strands depends on simple base pairing rules which are well understood, and form the specific nanoscale structures of the nucleic acid double helix. These qualities make the assembly of nucleic acid structures easy to control through nucleic acid design. This property is absent in other materials used in nanotechnology, including proteins, for which protein design is very difficult, and nanoparticles, which lack the capability for specific assembly on their own.

DNA nanotechnology is sometimes divided into two overlapping subfields.

- Structural DNA nanotechnology
- Dynamic DNA nanotechnology

Structural DNA nanotechology, sometimes abbreviated as SDN, focuses on synthesizing

and characterizing nucleic acid complexes and materials ~~where~~ that assemble into a static, equilibrium and state. On the other hand, dynamic DNA nanotechnology focuses on complexes with useful non-equilibrium behavior such as the ability to reconfigure based on a chemical or physical stimulus. Some complexes, such as nucleic acid nanomechanical devices, combine features of both the structural and dynamic subfields.

Structural DNA nanotechnology

Structural DNA nanotechnology, sometimes abbreviated as SDN, focuses on synthesizing and characterizing nucleic acid complexes and materials where the assembly has a static, equilibrium endpoint. The nucleic acid double helix has a robust, defined three-dimensional geometry that makes it possible to predict and design the structures of more complicated nucleic acid complexes. Many such structures have been created, including two and three-dimensional structures, and periodic, aperiodic, and discrete structures.

Extended lattices

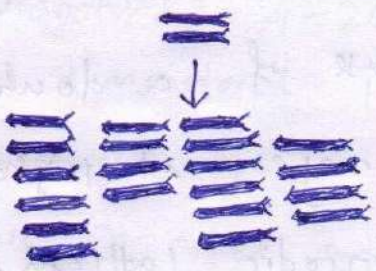


fig-a- The assembly of a DX-array.

In fig-a each bar represents a double-helical domain of DNA, with the shapes representing complementary sticky ends, The DX complex at top will combine with other DX complexes into the two-dimensional array shown at bottom.

Small nucleic acid complexes can be equipped with sticky ends and combined into larger two-dimensional periodic lattices containing a specific tessellated pattern of the individual molecular tiles. The earliest example of this used double-crossover (DX) complexes as the basic tiles, each containing four sticky ends designed with sequences that caused the DX units to combine into periodic two-dimensional flat sheets that are essentially rigid two-dimensional crystals of DNA. Two-dimensional arrays have been made from other motifs as well, including the holiday junction rhombus lattice and various DX-based arrays making use of a double-cohesion scheme. The top two images at right show examples of tile-based periodic lattices.

Two-dimensional arrays can be made to exhibit aperiodic structures whose assembly implements a specific algorithm, exhibiting one form of DNA computing. The DX tiles can have their sticky end sequences chosen so that they act as Wang tiles, allowing them to perform computation. A DX array whose assembly encodes an XOR operation has been demonstrated; this allows the DNA array to implement a cellular automation that generates a fractal known as the Sierpinski gasket. The third image at right shows this type of array. Another system has the function of a binary counter, displaying a representation of increasing binary numbers as it grows. These results show that computation can be incorporated into the assembly of DNA arrays.

DX arrays have been made to form ~~hollow~~ hollow nanotubes 4-20 nm in diameter, essentially two dimensional lattices which curve back upon themselves. These DNA nanotubes are somewhat similar in size and shape to carbon nanotubes, and while they lack the electrical conductance of carbon nanotubes, DNA nanotubes

uses a lattice of curved DX tiles that curls around itself and closes into a tube. In an alternative method that allows the circumference to be specified in a simple, modular fashion using single-stranded tiles, the rigidity of the tube is an emergent property.

Discrete structure: -

Nanostructures of arbitrary, non-regular shapes are usually made using the DNA ~~origi~~ origami method. These structures consists of a long, natural virus strand as a "scaffold", which is made to fold into the desired shape by computationally designed short "staple" strands. This method has the advantages of being easy to design, as the base sequence is predetermined by the scaffold strand sequence, and not requiring high strand purity and accurate stoichiometry, as most other DNA nanotechnology methods do. DNA origamic was first demonstrated for two-dimensional shapes, such as a smiley face, a coarse map of the Western Hemisphere, and the Mona Lisa painting. Solid- three-dimensional structures can be made by using parallel DNA

helices arranged in a honeycomb pattern, and structures with two-dimensional faces can be made to fold into a hollow overall three-dimensional shape, akin to a ~~cardbox~~ cardboard box. These can be programmed to open the reveal or release a molecular cargo in response to stimulus, making them potentially useful as programmable molecular cages.

Dynamic DNA nanotechnology

Dynamic DNA nanotechnology often makes use of toehold-mediated strand displacement reactions. In this example, the red strand binds to the single stranded toehold- region on the green strand (region 1), and then in a branch migration process across ~~reg~~ region 2, the blue strand is displaced and freed from the complex. Reactions like these are used to dynamically reconfigure or assemble nucleic acid nanostructures. In addition, the red and blue strands can be used as signals in a molecular logic gate.

Dynamic DNA nanotechnology focuses on forming nucleic acid systems with designed dynamic functionalities related to their overall structures, such as computation and mechanical motion. There is some overlap between structural and dynamic DNA nanotechnology, as structures can be ~~to~~ made to form dynamically in the first place.

Application

DNA nanotechnology provides one of the few ways to form designed, complex structures with precise control over nanoscale features. The field is beginning to see application to solve basic science problems in structural biology and biophysics. The earliest such application envisaged for the field, and one still in development, is in crystallography, where molecules that are difficult to crystallize in isolation could be arranged within a three-dimensional nucleic acid lattice, allowing determination of their structure. Another application is the use of DNA origami rods to replace liquid crystals in residual dipolar couplingexperiments in protein NMR spectroscopy; using DNA origami is advantageous because, unlike liquid crystals, they are tolerant of the detergents needs to suspend membrane protein in solution DNA walkers have been used as nanoscale assembly lines to move nanoparticles and direct chemical synthesis. further, DNA origami structures have aided in the biophysical studies of enzyme function and protein folding.

The assembly of a nucleic acid structure could be used to template the assembly of a molecular electronic elements such as molecular wires, providing a method for nanometer-scale control of the placement and overall architecture of the device analogous to a molecular breadboard.

There are potential applications for DNA nanotechnology in nanomedicine, making use of its ability to perform computation in a biocompatible format to make "smart drugs" for targeted drug delivery. One such system being investigated uses a hollow DNA box containing proteins that induce apoptosis, or cell death, that will only open when in proximity to a cancer cell.

Design

DNA nanostructures must be rationally designed so that individual nucleic acid ~~strand~~ strands will assemble into the desired structures. This processes usually begins with specification of a desired target structure or function. Then, the overall secondary structure of the target complex is determined, specifying the arrangement of nucleic acid strands within the structure, and which portions of those strands should be bound to each other.

The last step is the primary structure design, which is the specification of the actual base sequence of each nucleic acid strand.

Structural design:-

The first step in designing a nucleic acid nanostructure is to decide how a given structure should be represented by a specific arrangement of nucleic acid strand. This design step determines the secondary structure, or the positions of the base pairs that hold the individual strands together in the desired shape. Several approaches have been demonstrated:

(*) **Tile-based structures:-** This approach breaks the target structure into smaller units with strong binding between the strands contained in each unit, and weaker interaction between the units. It is often used to make periodic lattices, but can also be used to implement algorithmic self-assembly, making them a platform for DNA computing. This was the dominant design strategy used from the mid 1990s until the mid-2000s, when the DNA origami methodology was developed.

(*) Folding structures:- An alternative to the tile-based approach, folding approaches make the nanostructure from one long strand, which can either have a designed sequence that folds due to its interactions with itself, or it can be folded into the desired shape by using shorter, "staple" strands. This latter method is called DNA origami, which allows forming nanoscale two- and three-dimensional shapes.

(*) Dynamic assembly:- This approach directly controls the kinetics of DNA self-assembly, specifying all of the intermediate steps in the reaction mechanism in addition to the final product. This is done using starting materials which adopt a hairpin structure, these then assemble into the final ~~for~~ conformation in a cascade reaction, in a specific order. This approach has the advantage of proceeding isothermally, at a constant temperature. This is in contrast to the thermodynamic approaches, which require a thermal annealing step where a temperature change is required to trigger the assembly and favor proper formation of the desired structure.

(*) Sequence design:-

After any of the above approaches are used to design the secondary structures of a target complex, an actual sequence of nucleotides that will form into the desired structure must be devised. Nucleic acid design is the process of assigning a specific nucleic acid base sequence to each of a structure's constituent strands so that they will associate into a desired conformation. Most methods have the goal of designing sequences so that the target structure has the lowest energy, and is thus the most ~~thermally~~ thermodynamically favorable, while incorrectly assembled structures have higher energies and are thus disfavored. This is done either through simple, faster heuristic method such as sequence symmetry minimization, or by using a full nearest neighbor thermodynamic model, which is more accurate but slower and more computational intensive. Geometric models are used to examine tertiary structure of the nanostructures and to ensure that the complexes are not overly strained.

Nano Robot and its Application:-

~~Nanotechnology~~

Nanorobotics is an emerging technology field creating machines or robots whose components are at or near the scale of a nanometer. More specifically, nanorobotics (as opposed to microrobotics) refers to the nanotechnology engineering discipline of designing and building nanorobots, with devices ranging in size from 0.1-10 micrometres and constructed of nanoscale or molecular components. The terms nanobot, nanoid, nanite, nanomachine or nanomite have also been used to describe such devices currently under research and development.

~~Nanorobotics Theory:-~~

Application of Nanorobotics (Nanobots)

Nano robots can be used in different application areas such as medicine and space technology. Nowadays, these nanorobots play a crucial role in the field of Bio-Medicine, particularly for the treatment of cancer, cerebral Aneurysm, removal of Kidney Stones, elimination of defected parts in the DNA structure, and for some other treatments that need utmost support to save human lives.

Nanorobotics in surgery:-

Surgical nanorobots are introduced into the human body through vascular systems and other cavities. Surgical nanorobots act as semi-autonomus

on-site surgeon inside the human body and are programmed or directed by a human surgeon. This programmed surgical nanorobot performs various functions like searching for pathogens, and then diagnosis and correction of lesions by nano-minipulation synchronized by an on-board computer while conserving and contacting with the supervisory surgeon through coded ultrasound signals.

Nowadays, the earlier forms of cellular nano-surgery are being explored. For example, a micropipette rapidly vibrating at a frequency of 100 Hz micropipette comparatively less than 1 micron tip diameter is used to cut dendrits from single neurons. This process is not ought to damage the cell capability

2. Diagnosis and Testing :-

Medical nanorobots are used for the purpose of diagnosis, testing and monitoring of micro-organisms, tissues and cells in the blood stream. These nanorobots are capable of noting down the record, and report some vital signs such as temperature, pressure and immune system's parameters of different parts of the human body continuously.

3. Nanorobotics in Gene Therapy:-

Nanorobots are also applicable in treating genetic diseases, by relating the molecular structures of DNA and protein in the cell. The modifications and irregularities in the DNA and protein sequences are then corrected. The chromosomal replacement therapy is very efficient, compared to the cell repair. An assembled repair vessel is inbuilt in the human body to perform the maintenance of genetics by floating inside the nucleus of a cell.

Supercoil of DNA when enlarged within its lower pair of robotics arms, the nanomachine pulls the strand which is unwounded for analysis, meanwhile the upper arms detach the proteins from the chain. The information which is stored in the large nanocomputer's data base is placed outside the nucleus and compared ~~the~~ with the molecular structures of both DNA and proteins that are connected through communication link to cell repair ship. Abnormalities found in the structures are corrected, and the proteins reattached to the Deoxy Nucelic Acid chain once again reforms into their original form.

4. Nanorobots in Cancer Detection and Treatment:-

The current stages of medical technologies and therapy tools are used for the succesful treatment of cancer. The important aspect to

to achieve a successful treatment is based on the improvement of efficient drug delivery to decrease the side-effects from the chemotherapy.

Nanorobots with embedded chemical bio-sensors are used for detecting the tumor cells in early stages of cancer development inside a patient's body. Nanosensors are also utilized to find the intensity of E-cadherin signals.

5. Nanodentistry is one of the topmost applications as nanorobots help in different processes involved in dentistry. These nanorobots are helpful in desensitizing tooth, oral anesthesia, straightening of irregular set of teeth and improvement of the teeth durability, major tooth repairs and improvement of appearance of teeth etc.

6. Nanorobots can also be used as ancillary devices for processing defferent chemical reactions in the affected organs. These robots are also useful for monitoring and controlling the glucose levels in diabetic patients.

Nanocapsule :-

Nanocapsule is a nanoparticle comprised of nontoxic, natural or synthetic polymer, lipid or other type of shell that enclosing its inner cavity or content core in which the drug is plaied. They have attracted great interest, because of the protective coating, which are usually pyrophoric and easily oxidized and delay the release of active ingredients. The typical size of the nanocapsule used for various applications ranges from 10 - 1000 nm. Nanocapsules have many uses, including promising medical applications for drug delivery, food enhancement, nutraceuticals, and for self-healing materials. The benefits of encapsulation methods are for protection of these substances to protect in the adverse environment, for controlled release, and for precision targeting. Nanocapsules can potentially be used as MRI-guided nanorobots or nanobots, although challenges remain.

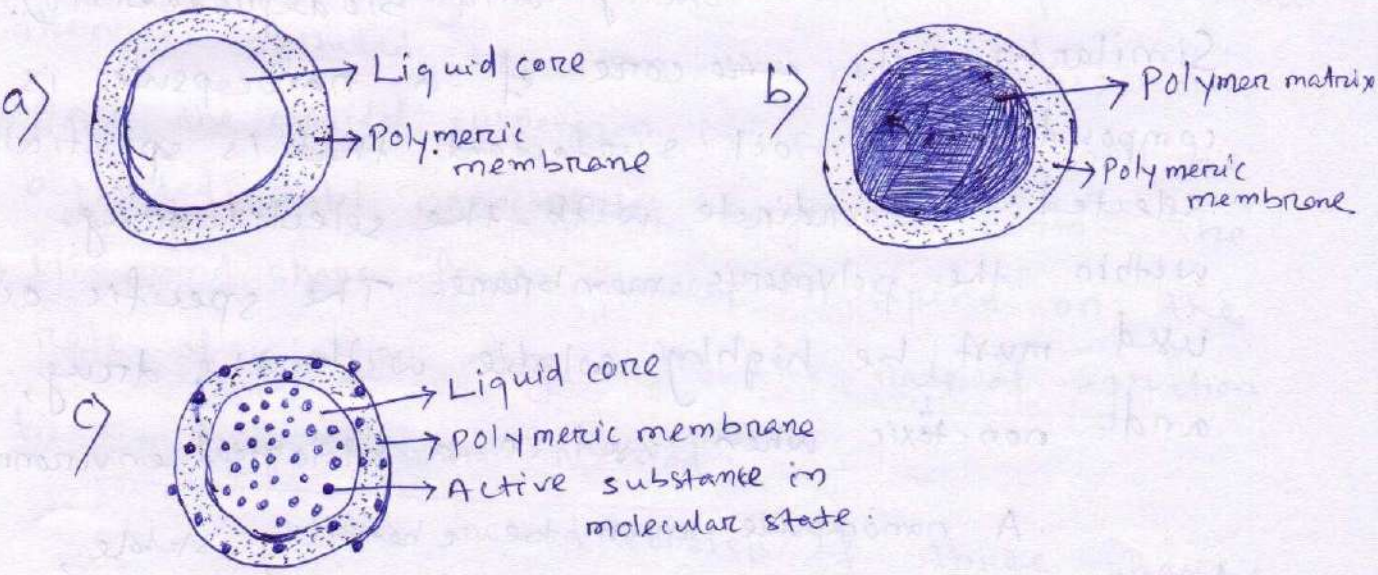


Figure :- Polymer based nanocapsule

Description :-

A nanocapsule is usually a hollow spherical particle made up of polymers or phospholipids (in this case it is called a liposome or a nanosome) containing a low-molecular substance inside. The shell of a nanocapsule may be fabricated from other materials, such as hydroxyapatite or calcium silicate, as well as from specifically organised DNA molecules. Poly-ε-caprolactone (PCL), poly(lactide) (PLA), and ~~poly~~ poly (lactide-co-glicolide) (PLGA) are typical polymers used in nanocapsule formation. As synthetic polymers have proven to be more pure and reproducible when compared naturally occuring polymers, they are often preferred for the construction nanocapsules. However, some natural occuring polymers such as chitosan, gelatin, and albumine are used in some drug delivering nanocapsules. Polysaccharids and saccharides are also used due to their non-toxicity and biodegradebility. Similarly, the ~~core~~ core of a nanocapsule is composed of an oil surfactant that is specifically selected to coordinate with the selected drug within the polymeric membrane. The specific oil used must be highly soluble with the drug, and non-toxic when used in a biological environment.

A nanocapsule must be chemically stable, bioactive, biocompatible and capable of protecting the encapsulated materials against undesirable effects, such as dissolution in liquids. The maximum

size of a nanocapsule is usually 100 nm, and a microsapsule - 600 nm. Nanocapsule have a high penetration capability and may penetrate even such "closed" areas of a body as the brain.

Processing :-

The encapsulation processes depend on the physio-chemical properties of the core material, the wall material, and the required size. The most common ways to produce nanocapsules are nanoprecipitation, emulsion-diffusion, and solvent evaporation.

a) Nanoprecipitation Method :

The nanoprecipitation method is also termed as solvent displacement method. In this method nanocapsules are formed by creating a colloidal suspension between two separate phases. The organic phase consists of a solution and a mixture of organic solvents. The aqueous phase consists of a ~~mas~~ mixture of non-solvents that forms a surface film. The organic phase is slowly injected in the aqueous phase which then is agitated to form the colloidal suspension. Once the colloidal suspension is formed it will be agitated until nanocapsules begin to form. The size and shape of the nanocapsule depend on the rate of injection along with the rate of agitation

b) Emulsion diffusion Method :-

This method consists of three phases : organic, aqueous, and dilution phase. In this method the organic phase is added to the aqueous phase

under conditions of high agitation which form an emulsion. During this process water is added to the emulsion which causes the solvent to diffuse. The result of this emulsion-diffusion is nanocapsule formation.

c) Solvent evaporation Method:-

It is another effective method to prepare nanocapsules. In this process, single or double emulsions are formed from solvents and are used to formulate a nanoparticle suspension. High speed homogeneization or ultrasonication is used to form small particle size in the nanoparticle suspension. Once the suspension is stable, the solvents are evaporated using either continuous magnetic stirring at room temperature, or by reducing the ambient pressure.

Processing issues and Solutions:-

Nanocapsules tend to aggregate and become unstable. Thus, substances within capsules can leak. To control the instability, nanocapsules can be dried either through spray drying or freeze drying (lyophilization).

Spray drying:- Solutions are sprayed into a drying medium. This method is more widely used in the food industry and used for encapsulation of many food products as flavors, minerals, colors, and vitamins. This method makes nanocapsules

more stable, and increases shelf-life of foods.

Freeze-drying :- This process involves dehydration of materials that are heat-sensitive. Unlike spray drying, water is removed through the sublimation process, without changing the structure or shape of the nanoparticles. Freeze-drying involves four states: Freezing, primary drying, secondary drying, and storage. Because of the multiple stages involved, this method is considered to demand more energy and time.

Properties of Nanocapsules:-

a) Absorbability :- Aspect ratio affects the ability of the nanocapsule to penetrate ~~to~~ tumor cells. Low aspect ratios (spherical capsules) tend to penetrate cells more easily than high aspect ratios (rod-shaped capsules).

b) Structure :- The nanosized structure of nanocapsules allows permeating through basal membranes, which makes them effective carriers of medicine in biological systems. The specific processing of nanocapsules gives them unique properties in how they release drugs in certain situations. Generally, there are three physico-chemical release mechanisms that are used to release the drug or medicine from the polymeric shell of the nanocapsule.

c) Delivery :-

1. Hydration and diffusion :- In this release mechanism the nanocapsule will swell due to the effects of hydration. Once the nanocapsule has swollen to a

point where it stretches, the polymeric membrane will allow for diffusion of the drug through the polymeric membrane and into the biological system.

2. Enzymatic reaction: - The polymer shell must be first selected to coordinate with the enzymes produced by the human body to produced and enzymatic reaction. This reaction will cause a rupture in the polymeric membrane which allows the drug to be dispersed into the system.

3. Dissociation of the Drug: - The drug dissociates from the swelled nanocapsule and diffuses out into the rest of the cell.

Other delivery Methods: - Substance delivery in medical use —

Near-infrared Light - Drug release is triggered from heat. The infrared technology can be absorbed deep in the body, turn to heat. The heat-sensitive material, particularly a polymer shell that swells upon heating, collapses. The action of deflating is what releases the drug.

Magnetic Fields: - Magnetic bars of millimeter-scale are embedded in poly(vinyl alcohol). The magnetic field within the bars is alternated, which results in the change of shape and ultimate collapse of the nanocapsules. The change in the structure then triggers the drug release.

Ultrasound :- Another option of drug release is through ultrasound, which is a "longitudinal pressure wave". The ultrasound can either be low-frequency, or LFUS, (between ~20 and ~100 KHz) or high-frequency, HFUS, (>1 MHz). Transdermal delivery (sonophoresis) is enhanced through LFUS, which then further allows the drug to be released. Since the wave of HFUS is higher, success of drug delivery has been demonstrated through the form of bubbles. The bubbles within the capsule are formed and collapsed due to the higher temperature of the wave.

Applications of Nanocapsules :-

i) Cancer :- Water-soluble polymer shells are being created to deliver a protein, apoptin, into cancer cells. The protein goes into the nucleus of the cancer cells while leaving healthy cells alone, unlike other conventional therapies as gene therapies and chemotherapy. The capsules are 100 nm in size.

Through active targeting, the nanocapsules form ligand that binds to malignant cells for cell delivery. This method is especially beneficial for those drugs that are not as permeable through the cell membrane, and where tissues are diseased, the nanoparticles are able to bond easier with the malignant cells.

ii) Food usage:- Nanocapsulation in foods involves the changing of textures, flavorings, colorings and stability in shelf-life.

Nutraceuticals: Nutraceuticals are substances that are placed in food to enhance nutrition. The increased bioavailability of these substances is relative to the size of the nanocarrier. The smaller the nanocarrier, the better the delivery properties and the solubility of the nutraceuticals; the nanocarrier is able to enter the bloodstream easier if smaller.

iii) Self-healing material:-

For materials such as components in microelectronics, polymeric coatings and adhesives, nanocapsules can reduce damage caused by high loads. The healing of cracks within these materials is alleviated by dispersing nanocapsules within the polymer. The healing substances include dicyclopentadiene (DCPD), which is prepared on site within the material by sonication. The nanocapsulated materials is first emulsified within the host materials by creating an oil-in-water self-healing epoxy. The emulsified material is then agitated within the host material to form particles which then bond to the host material.

Nanosomes :-

Nanosomes are nanoparticles that imitate the phospho-lipids that make up the cell membrane, the intercellular substance and the content of our ~~eto~~ cells. Nanosomes consist of one row of water heads and one row of ~~fitty~~ fatty tails. They were originally developed for the medical field to deliver drugs to the blood system and are now used in the cosmetic industry because of their excellent transportation capabilities. They are an excellent delivery system because as well as being able to penetrate deep into the skin, they can resist the cells defence systems but can nonetheless influence cell processes. Once having penetrated into the skin they can integrate themselves into larger molecules. Just as with Liposomes they should only be used in ~~the~~ and with products that do not contain chemical preservatives, chemical sunscreens, animal derivatives, fragrance and colorants as ~~these~~ these unwelcome elements will also be transported into the skin by the nanosomes and may cause dermatities, allergies, aging, hormonal disturbances, acne and even cancer.

A prior knowledge about lipid, phospholipid, cell ~~and~~ membrane, liposome is required to know the correct composition and structure of nanosome

Lipids

Lipids are a group of chemical compounds (such as oils and waxes) which occur in living organisms and are only sparingly soluble in water.

Phospholipids

Phospholipids are a special group of lipids containing phosphate. phospholipids are the building blocks of liposomes and cell membranes. Your skin, like the rest of your body, is composed of cells whose membranes must be healthy and strong in order for it to function properly. Phospholipids make this possible.

What do phospholipids have to do with cell membranes?

Lipids in general are hydrophobic, also called non-polar, this means they cannot be dissolved it water. However, the phosphate group in phospholipids is hydrophilic, also called polar, phospholipids can be dissolved in water. phospholipids are major building blocks of some natatrally-occuring structures such as cell membranes and some manufatured structures such as liposomes and Nanosomes. The major groups of phospholipids are:

- phosphatidycholine (PC)
- sphingomyelin (SM)
- Other phospholipids (OP)

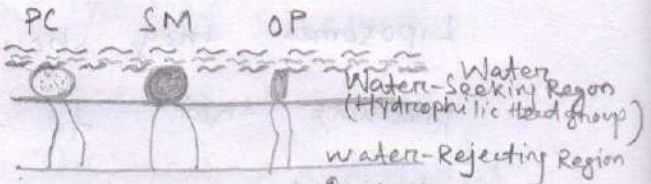


fig- Phospholipids

When phospholipids are immersed in water they arrange themselves so that their hydrophilic region point towards the water and their hydrophobic regions point away from the water. This's unique structure of phospholipids making them simultaneously hydrophilic and hydrophobic, is the key to their ability to organize as a double layer (bilayer formation) when immersed in water. The interaction and rejection forces between phospholipids and water cause ~~phopho~~

phospholipids to organize themselves as bilayers.

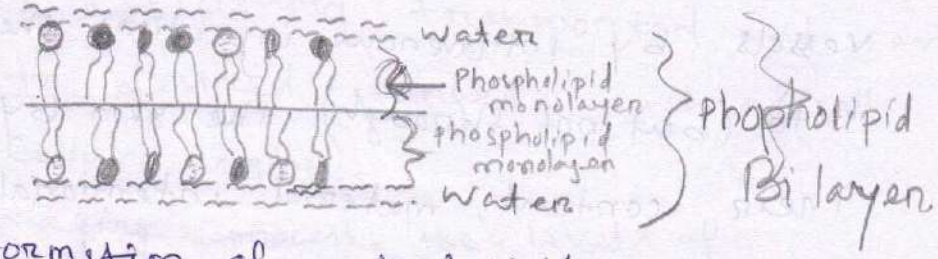


fig- Formation of a phopholipid bilayer structure.

Liposomes :-

Liposomes are small lipid-based bodies. Phospholipids are the core structure in the formation of Liposomes and cell membranes. phospholipid bilayers forming into a liposome or a cell membrane. ~~can be seen in the~~ Nanosomes can encapsulated and transport water-soluble ingredients in their polar cavity and oil-soluble ingredients in their hydrophobic cavity. Nanosomes can contain and mobilize water-soluble materials as well as oil-soluble materials in specific cavities inside themselves.

The very small, single-bilayer Nanosomes differ from large liposomes in some major ways. They are constructed from the highest possible quality of ingredients and they are created using a special technique. The material used to create Nanosomes has an extremely high percentage of phosphatidycholine (PC), one of the essential components of cell membranes. The process of creating Nanosomes requires subjecting large, multiple-layer liposomes to ultrasonic energy. This process is very long, extremely delicate, and is done in small batches.

Nanosomes can easily penetrate into small blood vessels by intravenous injection; they can also penetrate into (but not through) the skin by topical application. Their content, material intentionally entrapped inside them, is efficiently trasported and ~~be~~ can be delivered to desired targets such as cells.

Nanosomes with high-purity PC not only deliver encapsulated ingredients to cells but ~~ad~~ also deliver cell's own ~~buil~~ building block, phosphatidyl-choline (PC) itself. This unique feature of high-purity PC Nanosomes ~~re~~renders them the most powerful tool avilable for combating cellular aging.

Very ~~single~~ small, single-bilayer vesicles (Nanosomes) are very difficult to make, so Nanosomes are created in a speci~~l~~ way. The process of creating Nanosomes requires subjecting large, multiple-layer liposomes to ultrasonic energy. This process is very long, extremely delicate, and is done is small batches. Nanosomes can easily penetrate into small blood vessels by intravenous injection; they can also ~~penetrate~~ penetrate into (but not through) the skin by topical application.

Their content, material intentionally entrapped inside them, is efficiently transported and can be delivered to desired targets such as cells.

The Process of Cellular Aging :-

During the aging process, the level of phosphatidylcoline (PC) in cell membrane is diminished and the level of sphingomyelin (SM) increases.

The Process of Cellular Rejuvention

A Fresh Nanosomes made with very high content (over 90%) of PC is approaches an old cell membrane. The aging cell membrane has lost many of its "good" PC molecules (represented by the phospholipids with blue head groups) which have been replaced by "bad" SM molecules. ~~(represented by the phospholipids with~~

The Nanosomes and the aging cell membrane begin moving toward a New Equilibrium, a process in which molecules from the cell membrane will be exchanged with molecules from the Nanosomes. The bad SM molecule from the aging cell is being pulled out from the cell membrane, and the good PC molecules is being pulled out of the Nanosome. The SM molecule originating in the aging cell attempts to achieve equilibrium by reaching towards the Nanosomes. The PC molecule originating in the Nanosome attempts to reach equilibrium by moving toward the

aging cell membrane. The molecule exchanged between the Nanosome and the cell membrane are being repositioned in their respective new destinations.

Application of Nanosomes serum creates an environment in which many Nanosome are available. The large number of Nanosomes provides a very large surface area relative to the surface area of the aging cell membranes, ensuring that there is material available for use in achieving a new equilibrium. The end process provides a cell that has replenished with PC molecules and cleaned of SM molecules. The Nanosomes at this stage carry and discard the old chemical and physical image of the cell.

MEDIBOTS

A microrobot is a miniaturized, sophisticated machine designed to perform a specific task or tasks repeatedly and with precision. Microrobots typically have dimensions ranging from a fraction of a millimeter up to several millimeters. In general, a microrobot is just a bit larger than a nanobot, which is created on the nanoscale. Microrobots are usually visible, whereas some nanobots are not immediately visible to the human eye.

Modern technology has allowed engineers to put computer components into extremly small robots, which are used in many industries for different purposes. One example in medicine is "medibots", a microrobot which assist with clinical goals such as diagnostics or surgeries. Scientists have acknowledged the many potential uses of microrobots in the medical and health care industry. Because of their small size, microrobots can be placed inside the body for diagnostic or biopsy purposes, replacing very invasive tubes such as an endoscope.

Medibots are the world's smallest surgeons :-

Advances in robotics could revolutionize healthcare, pushing the limits of what surgeons can achieve, from worm-inspired capsules to crawl through your gut, and systems swallowed in pieces that assemble themselves inside the body, to surgical robots that will soon be ready to embark on a fantastic voyage through our bodies, homing in on the part that's ~~ai~~ ailing and fixing it from the inside.

A medibot allows a surgeon sitting at a control desk, to operate it for surgery in a manner that has several advantages over conventional method. In near future the surgeons will include tiny robots that enter out bodies and do their work from the inside, with no need to open patients up or knock them out.

While nanobots that swim through the blood are still in the realm of fantasy, several groups are developing devices a few millimetres in size. The first generation of "mini-medibots" may infiltrate our bodies through our ears, eyes and lungs, to deliver drugs, take tissue samples or install medical devices.

An innovative concept for the fabrication of dual action microrobots capable of performing single cell microsurgery along with a site directed drug delivery feature is also designed. These multi action plant derived biocompatible 'medibots' can play a pivotal role in understanding microtomotor interactions at the cellular level, aiming toward the destruction of harmful cells (like cancer) among others in living systems.

Artificial Pancreas :-

The pancreas is an organ in the body that secretes several hormones, including insulin and glucagon, as well as digestive enzymes that help break down food. Insulin helps cells in the body take up glucose (sugar) from the blood to use for energy, which lowers blood glucose levels. Glucagon causes the liver to release stored glucose, which raise blood glucose levels. The abnormalities in the blood glucose level raises to diabetes which are of mainly: Type 1 diabetes occurs when the pancreas produces little or none of the insulin needed to regulate blood glucose, and Type-2 diabetes ~~occurs~~ occurs when the pancreas does not produce enough insulin or the body becomes resistant to the insulin that is present.

Patients with type 1 diabetes and some patients with type 2 diabetes inject insulin, and occasionally glucagon, to regulate their blood glucose, which is critical to lower their risk of long-term complications such as blindness, kidney failure and cardiovascular ~~dis~~ disease.

When managing diabetes, many patients must vigilantly test blood glucose with a glucose ~~meter~~ meter, calculate insulin doses, and administer necessary insulin doses with a needle or insulin infusion pump to lower blood glucose. Glucagon may be injected in an emergency to treat severe low blood glucose. Some patients benefit from additional monitoring with a continuous glucose monitoring system.

Artificial Pancreas

The artifical pancreas is a man-made technology to help people with diabetes automatically control their blood glucose level by providing the substitute endocrine functionality of a healthy pancreas. An artificial pancreas is a man-made device that is designed to release insulin in response to changing blood glucose levels in a similar way to a human pancreas. Artificial pancreas system are being studied as a possible treatment option for people with type 1 diabetes and Type 2 diabetes. This system measured blood sugar levels using a continuous glucose monitor (CGM) and transmits this information

to an insulin pump that calculates and releases the required amount of insulin into the body, just as the pancreas does in people without diabetes.

How artifical pancreas device system work together?

1. Continuous Glucose Monitor (CGM) :- A CGM provides a steady stream of information that reflects the patient's blood glucose levels. A sensor placed under the patient's skin measures ~~patient's blood glucose levels. A sensor~~ the glucose in the fluid around the cells which is associated with blood glucose levels. A small transmitter sends information to a receiver A CGM continuously displays both an estimate of blood glucose levels and their direction and rate of change of these estimates.

⊛ Blood Glucose Device (BGD) :- Currently, to get the most accurate estimates of blood glucose possible from a CGM, the patient needs to periodically calibrate the CGM using a blood glucose measurement from a BGD; therefore, the BGD still plays a critical role in the proper management of patients with a APDS. However, over time, we anticipate that improved CGM performance may do away with the need for periodic blood glucose check with a BGD.

2. Control Algorith :- A control algorithm is a software embedded in an external processor (controller) that receives information from the CGM and performs a series of mathematical calculations. Used on these calculations, the controller sends dosing instructions to the infusion pump. The control algorithm can be run on any number of devices including an insulin pump, computer or cellular phone. The FDA does not require the control algorithm to reside on the insulin pump.

3. Insulin pump:- Based on the instructions sent by the controller, an infusion pump adjusts the insulin delivery to the tissue under the skin.

4. The patient:- The patient is an important part of Artificial pancreas Delivery system. The concentration of glucose circulating in the patient's blood is constantly changing. It is affected by the patient's diet, activity level, and how his or her body metabolizes insulin and other substances.

Types of Artifical Pancreas systems :-

There are three main artifical pancreas systems being worked on by researchers :-

* Closed-loop artificial pancreas
* Bionic pancreas
* Implanted artifical pancreas

a) Close-loop artificial pancreas:-

The most widely tested artificial pancreas is a "closed-loop insulin delivery system', also referred to as a closed loop artificial pancreas. It is made up of an externally worn insulin pump which communicates wirelessly to a CGM worn as a patch on the skin. The CGM measures blood sugar levels and the results is fed into a small computer which calculates how much insulin needs to be delivered by the insulin pump. The dose is then delivered into the body, completing the cycle.

b) Bionic Pancreas:-

In 2015 the world was introduced to the iLet, a bionic pancreas that could help people with type-1 diabetes manage the condition solely through the device.

The bionic pancreas, developed by Dr Edward Damiano's Beta bionics firm, automatically controls blood glucose levels, comprising two insulin pumps which deliver and insulin & and glucagon respectively.

The pump connect with an iphone app via Bluetooth enabling communication between the devices that helps calculate the required doses needed. Automated dosing decisions about insulin and glucagon are made every five minutes based on updated continuous glucose monitor (CGM) readings

c) Implanted artifical pancreas :-

The implantable insulin delivery device contains a gel that responds to changes in blood glucose levels. When blood glucose levels are elevated, the gel enables a higher rate of insulin to be released; during lower sugar levels, the gel decreases the amount of insulin it releases. The implantable system could be refilled with insulin on a regular basis.

Artificial Muscle :-

Artificial muscle is a generic term used for actuators, materials or devices that mimic natural muscle and can reversibly contract, expand, or rotate within one component due to an external stimulus (such as voltage, current, pressure or temperature). The three basic actuation responses - contraction, expansion, and rotation - can be combined together within a single component to produce other types of motions (e.g., bending by contracting one side of the material while expanding the other side). ~~Gener~~ Conventional motors and pneumatic linear or rotary actuators do not qualify as artificial muscles, because there is more than one component involved in the actuation.

Due to their high flexibility, versatility and power-to-weight ratio compared with traditional rigid actuators, artificial muscles have the potential to be a highly disruptive emerging technology. Though currently in limited use the technology may have wide future application in industry, medicine, robotics and many other fields.

Types of Artificial Muscle :-

~~Art~~ Artificial muscles can be divided into three major groups based on their actuation mechanism.

1. Electric Field actuation

a) Electroactive Polymers :-

Electroactive polymers (EAPs) are polymers that can be actuated through the application of electric fields. Currently, the most prominent EAPs include

piezoelectric polymers, dielectric actuators (DEAs), electrostrictive graft elastomers, liquid crystal elastomers (LCE) and ferroelectric polymers. While these EAPs can be made to bend, their low capacities for torque motion currently limit their usefulness as artificial muscles. Moreover, without an accepted standard material for creating EAP devices, commercialization has remained impractical. However, significant progress has been made in EAP technology since the 1990s.

b) Ion-based actuation :-

Ionic EAPs are polymers that can be actuated through the diffusion of ions in an electrolyte solution (in addition to the application of electric fields). Current examples of ionic electroactive polymers include polyelectrode gels, ionomeric polymers metallic composites (IPMC), conductive polymers and electrorheological fluids (ERF). In 2011, it was demonstrated that twisted carbon nanotubes could also be actuated by applying an electric field.

C) Electric Power actuation :-

Twisted and coiled polymer (TCP) muscles also known as supercoiled polymer (SCP) are coiled polymer that can be actuated by electric power. ATCP muscle look like a helical spring. TCP muscles are usually made from silver coated Nylon. TCP muscle can also made from other electrical conductance coat such as gold. TCP muscles should be under a load to keep

the muscle extended. The electrical energy transforms to thermal energy due to electrical resistance, which is known as Joule heating, Ohmic heating, and resistive heating. As the temperature of the TCP muscle increases by Joule heating, the polymer contracts and it causes the muscle contraction.

2. Pneumatic actuation :-

Pneumatic artificial muscles (PAMs) operate by filling a pneumatic bladder with pressurized air. Upon applying pressure to the bladder, isotropic volume expansion occurs, but is confined by braided wires the encircle the bladder, translating the volume expansion to a linear contraction along the axis of the actuator. PAMs can be classified by their operation and design; namely PAMs feature pneumatic of hydraulic operation, overpressure or underpressure operation, braided/netted or embedded membranes and stretching membranes or rearranging membranes. Among the most commonly used PAMs today is a cylindrically braided muscle known as the McKibben Muscle, which was first developed by J. L. McKibben in the 1950s.

3. Thermal actuation

a) Fishing line —

* Artificial muscles constructed from ordinary fishing line and sewing thread can lift 100 times more weight and generate 100 times more power than

a human muscle of the same length and weight.

- Artificial muscles based on fishing line already cost orders of magnitude less (per pound) than shape-memory alloy or carbon nanotube yarn; but currently have relatively poor efficiency.
- Individual macromolecules are aligned with the fiber in commercially available polymer fibers. By winding them into coils, researchers make artificial muscles that contract a speed similar to human muscles.
- A (untwisted) polymer fiber, such as polyethelene fishing line or nylon sewing thread unlike most materials, shortens when heated up to about 4% for a 250 K increase in temp. By twisting the fiber and winding the twisted fiber into a coil, heating causes the coil to tighten up and shorten by up to 49%. Researchers found another way to wind the coil such that heating causes the coil to lengthen by 69%.
- One application of thermally-activated artificial muscles is to automatically open and close windows, responding to temperature without using any power.
- Tiny artificial muscles composed of twisted carbon nanotubes filled with paraffin are 200 times stronger than human muscles

b. Shape- memory alloy :-

Shape-memory alloys (SMAs), liquid crystalline elastomers, and metallic alloys that can be deformed and then returned to their original shape when exposed to heat, can function as artificial muscles. Thermal actuator-based artificial muscles offer heat resistance, impact resistance, low density, high fatigue strength, and large force generation during shape changes. In 2012, a new class of electric field-activated, ~~electro~~ electrolyte-free artificial muscles called "twisted yarn actuators" were demonstrated, based on the thermal expansion of a seondary material within the muscle's conductive twisted structure. It has also been demonstrated that a coiled vanadium dioxide ribbon can twist and untwist at a peak torsional speed of 200,000 rpm.

Control Systems

1. Voltage control :-

The twisted and coiled polymer (TCP) muscles can be modeled by first-order linear time-invariant state spaces when input is electrical voltage, with accuracy more than 8.5%. Therefore, A TCP muscles can be easily controlled by a digital PID controller. A fuzzy controller can be used to speed up the PID controller.

2. EAP control :-

EAPs offer lower weight, faster response, higher power density and quieter operation when

compared to traditional actuators. Both electric and ionic EAPs are primarily actuated using feedback control loops, better known as closed-loop systems.

3. Pneumatic control:-

Currently there are two types of ~~Pneumat~~ pneumatic artificial muscles (PAMs).

a) Single bladder surrounded by a braided sleeve:-

Pneumatic artificial muscles, while lightweight and inexpensive, pose a particularly difficult control problem as they are both highly nonlinear and have properties, such as temperature, that fluctuate significantly over time. PAMs generally consist of rubber and plastic components. As these parts come into contact with each other during actuation, the PAM's temperature increases, ultimately leading to permanent changes in the structure of the artificial muscle over time.

b) Double bladder:-

This actuator consists of an external membrane with an ~~ext~~ internal flexible membrane dividing the interior of the muscle into two portions. A tendon is secured to the membrane, and exist the muscle through a sleeve so that the tendon can contract into the muscle. A tube allows air into the internal bladder, which then rolls out into the external bladder. A key advantage of this type of pneumatic muscle is that there is no potentially frictive movement of the bladder against an outer sleeve.

~~4. Thermal control~~

Applications of Artificial muscle :-

Artificial muscle technologies have wide potential applications in biomimetic machines, including robots, industrial actuators and powered exoskeletons. EAP-based artificial muscles offers a combination of light weight, low power requirements, resilience and agility for locomotion and manipulation. Future EAP devices will have applications in aerospace, automative industry, medicine, robotics, articulation mechanisms, entertainment, animation, toys, clothing, haptic and tactile interface, noise control, transducers, power generators, and smart structures.

Pneumatic artificial muscles also offer greater flexibility, controllability and lightness compared to conventional pneumatic cylinders. Most PAM applications involve the utilization of McKibben-like muscles. Thermal actuators such as SMAs have various military, medical, safety, and robotic applications, and could furthermore be used to generate energy through mechanical shape changes.

Nanoclinic For Gene Delivery and Photodynamic Therapy:-

Gene delivery is the process of introducing foreign genetic material, such as DNA or RNA, into host cells. Genetic material must reach the nucleus of the host cell to induce gene expression. Successful gene delivery requires the ~~foreig~~ foreign genetic material to remain stable within the host cell and can either integrate into the genome or replicate independently of it. This requires foreign DNA to be synthesized as part of a vector, which is designed to enter the desired host cell and deliver the transgene to that cell's genome. Vectors utilized as the method for gene delivery can be divided into two categories, recombinant viruses and synthetic vectors (viral and non-viral).

In complex multicellular eukaryotes, if the transgene is incorporated into the host's germline cells, the resulting host cell can pass the transgene to its progeny. If the transgene is incorporated into somatic cells, the transgene will stay with the somatic cell line, and thus its host organism.

Gene delivery is a necessary step in gene therapy for the introduction or silencing of a gene to promote a therapeutic outcome in patients and also has applications in the genetic modification of crops. There are many different methods of gene delivery for various types of cells and tissues.

Gene therapy is used to treat a monogenic hereditary or acquired disease by the introduction of therapeutic genes through two types of vectors, integrative or non-integrative. Integrative vectors are safe modified viral vectors that enable a therapeutic transgene to be transferred to the genome of the target cell. With non-integrative vectors, the therapeutic transgene is not stable expressed in the target cell.

Two different gene therapy strategies.

Gene Therapy Strategies :-

During the seventies, an important advance was made in the field of molecular biology with the discovery of restriction enzymes. These proteins were able to cut fragments of DNA and enabled researchers to cut and past the fragments as required. These new findings established the basis for gene transference and genetic modification of the cell genome. The first human trail of gene transfer was carried out in the late 1980s, although its objective was merely to gene-mark the target cells.

The First sucess in gene therapy was obtained in Italy in a clinical trail that was carried out on children suffering from X chromosome-linked severe combined immuno deficiency (SCID-X). These patients have a deficiency of the gene coding for the gamma

chain, an indispensable protein in the development of T and B lymphocytes, leading them to suffer from life threatening infections. The disease was known as the "bubble boy disease" after a boy with X-linked SCID who lived for 12 years in a plastic, germ-free bubble during the 1980s. The therapeutic transgene was introduced into bone marrow stem cells ex vivo using a modified gamma retroviral vector. These modified cells were then infused into the patients. After a few months, the patients became immunompetent, demonstreting that the therapy can constitute a definitive cure.

Gene Therapy and Nanoparticles

Succesful gene therapy depends on two important aspects.

(1) Efficient safe delivery of genes to the target cell in vitro and in vivo. To achieve this goal, it is necessary to improve trasduction efficiency, viral titer when using viral gene therapy, or transfection efficiency when using nuclei acids.

(2) Effective monitoring of modified cells or modifying agents by ~~non-invasive~~ non-invasive imaging techniques. This will allow tracking of gene delivery and gene expression.

These aspects and others are being addressed in new approaches, one of which involves magnetic nanoparticles. On gene delivery, the nanoparticles used in MRI present important advantages over other imaging techniques, such as fluorescence, luminescence, or PET, which have been also used in gene therapy.

In the last few years, many people have reported the use of nanoparticles to complex and deliver viral vectors (e.g., adeno viruses, retroviruses) and nucleic acids, leading to the emergence of new approaches known as magnetofection and theranostics. Magnetofection is a viral and non-viral approach that uses super paramagnetic nano-particles to improve gene delivery under a magnetic field. Theranostics combines therapeutic with diagnostics and covers several fields, including personalized medicine, pharmacogenomics, and molecular imaging to develop efficient new targeted therapies with an adequate risk/benefit ratio. Furthermore, theranostics aims to monitor the response to treatment and to increase efficacy & safety.

Photodynamic Therapy:-

Photodynamic therapy (PDT) is a technique that was invented to treat skin cancers and ~~sun-damg~~ sun-damaged skin, which might one day turn cancerous (pre-cancers). In PDT, a special light activates a cream, which was applied to the lesion (affected area of skin). This treatment kills the abnormal cells in the skin.

PTD involves the use of a light-sensitive chemical (called a photosensitiser). This photo-sensitiser is, by itself, inactive. When light of a certain wavelength (usually red light) shines onto skin to which the photosensitiser was applied before, the photosensitiser is activated. This causes changes in the oxygen molecules within the sun-damaged skin cells. These "excited" oxygen molecules kill the abnormal cells. Only the area of skin exposed to the light source will be affected and inflamed. ~~ADTO~~ AFter

PTD can be used to treat various skin conditions including.

- Some types of basal cell ~~carci~~ carcinomas.
- Bowen's disease (in-situ squamous cell carcinoma), a pre-cancer.
- Actinic (solar) keratoses - early sun-damage, a pre-cancer.

Metal nanoparticles in PDT

Gold nanoparticles have been used in two ways in PDT: first, as drug-delivery platforms in a similar manner to other inorganic nanoparticles, which can be enhanced by an additional photothermal effect, second as surface plasmon-enhanced agents taking account of the nonlinear optical fields associated with very close distances to metal nanoparticles.

Photodynamic therapy is a unique treatment modality in which a systemically or locally administered photosensitizer is activated locally by irradiating the lesion site with light of a suitable wavelength and power through a specially designed light applicator. PDT offers various treatment options

in cancer management and has been used for localized superficial or endoluminal malignant and premalignant conditions. Its application has also been recently expanded to ~~soit~~ solid tumors. The antitumor efficacy of PDT might be enhanced through an effective immunoadjuvant to further expand its usefulness for a possible control of distant metastases. The non-invasive or minimally invasive nature of PDT also offers great promise in some non-malignant conditions in dermatology, ophthamology, and cardiology. Although photodynamic diagnostics (PDD) is beyond the scope of this article, it needs to be pointed out that compared to x-ray, ultrasound, MRI, and other tomographic techniques, contrasting and visualizing lesions by fluorescent markers provide an innovative; non-invasive and safer imaging technology. Some of the fluorescent photosensitizers (e.g., ALA)

discussed in this article have shown a selective absorption by malignant cells, and their fluorescent signals can be a powerful tool for diagnotic purpose. There is no doubt that the duel function nature of these photosensitizers will play an important role in future clinical photodynamics.

Nanoparticles in Cancer

Cancer is a class of diseases characterized by out-of-control cell growth. There are over 100 different types of cancer, and each is classified by the type of cell that is initially affected. A tumor cell is part of a tissue that is abnormally growing. It may be either malignant of benign in nature. Tumor cells are barically two types. Cancer harms the body when damaged cells divide uncontrollably to form lumps or masses of tissue called tumors. Cellular change takes place by the internal factors like hormones, immune conditions, inherited mutation etc and

external factors like chemicals, radiations, viruses, and lifestyle.

Let us consider melanoma for example, Melanoma, a form of skin cancer, is caused primarily by ultraviolet radiation from ~~sun~~ the Sun. To prevent we use a suspending a substance that either absorbs or scatters ultraviolet radiation in a thick emulsion (sun screen). But this emulsion is easily rubbed off and we need to apply periodically. An even bigger problem is that we leave openings during the application of emulsion due to macro-scale and micro-scale imperfections in our skin. So the UV radiation allows through dead layer of skin and causes wide damage. By using nanotechnology UV scattering substances like zinc oxide (ZnO) and titanium oxide (TiO_2) or UV absorbing

substances like octly methoxycinnamate and titanium oxide nanoparticles are ~~manuf~~ manufactured. These nanoparticles are targeted to skin cell surface proteins for an effective coat to prevent sunsceen.

Nanomaterials used for cancer diagnosis and treatment are - Nanoshells, Dendrimers, Quantum dots, Superparamagnetic Nanoparticles, Nanowires, Nanodiamods, Nanosponges.

Nanoshells :- One of new findings for nanoscale drug delivery in diagnosing and treating cancer are nanoshells - gold coated sillica. These nanoshells, set in a drug-containing tumor targeted hydrogel polymer, injected into the body, accumulate near ~~to~~ tumor cells. When heated with an infrared light, the nanoshells selectively absorbs a specific infrared frequency, melting the polymer and releasing the drug payload at a specific site. They are designed for specific targeting micrometastates, tiny aggregates of cancer cells too small to remove with a scalpel.

Dendrimers :-

Another nanoscale drug delivery system can be created with the use of dendrimers. Dendrimers is precisely constructed molecule built on the ~~nanoscale~~ nanoscale in a multistep process through up to ten generations and from 5 to 50 nm in scale. A dendrimer is typically symmetric around the core, and often adopts a spherical three-dimensional morphology. Drugs and recognition molecules can be attached to their ends or placed inside cavities within them.

Quantum Dots :-

When energy is applied to an atom, electrons are energised and move to a higher level. When the electron returns to its lower and stable state, this additional energy is emitted as light corresponding to a particular frequency. QDs work in

much the same way but a QD crystal acts as one very large atom. The energy source used to stimulate a QD is commonly Ultraviolet light. The frequency or color of light given off is not related to the material used in the quantum dot, but by the size of the QD. The dendritic multifunctional platform is ideal to combine various functions like imaging, targeting, and drug transfer into the cell. Quantum dots are semiconductors, the most commonly used cadmium selenide capped by zinc sulphide (CdSe/ZnS). The size of quntum dots ranges from 2 to 10 nm in diameter and these are composed of 10-50 atoms, containing electron-hole, pairs to discreate quantized energy.

Superparamagnetic Nanoparticles:

Iron oxide particles (Fe_3O_4) are treffered as magnetic nanoparticles and developed as superparamagnetic nanoparticles.

The size of the nanoparticles are less than 10 nm in diameter. These nanoparticles are having potential application in magnetic resonance imaging. Many reports revealed that superparamagnetic nanoparticles can be functionalized with other type of nanoparticle, so as to permit specific tumor targeting. These are also having importance in the use of magnetic fields to localized magnetic nanoparticles to targeted sites, a system known as magnetic drug targeting. Superparamagnetic nanoparticles can be modified by improving the solubility and specificity of iron oxide particles. Iron oxide nanoparticles can also be used in imaging techniques that can selectively image proliferating cells in vivo can provide critically important insights of tumor growth rate, degree of tumor angiogenesis,

~~of~~ angiogenesis, effectiveness of treatment and vigor normal cells.

Nanowires: Nanowires are nanoparticles with diameters of only a few nanometeres and extended lengths. Predictably, the length and ~~wid~~ width ratio is extremely large making them effectively one-dimensional structures. These are revolutionized innovative compounds these would be used to link together tiny components ~~to~~ into extremely small circuits. These nanowires are purported to have functions in monitoring brain electrical activity without having to use a brain probe and violating the brain parenchyma.

Nanodiamods: ~~Nanodiamods~~

Nanodiamonds:- Nanodiamonds are synthesized in 1962 by detonation and also can be prepared by covalent and non-covalent modification to absorb or graft a variety of functional groups and complex moieties, including proteins and DNA. ~~Thes~~ These are attractive agents for use in biological and medical applications

largely due to their greater biocompatibility than other carbon nanomaterials, stable photoluminescence, commercial availability and minimal cytotoxicity. Nanodiamonds can be used for cell labeling and tracing because they do not interrupt cell division or differentiation, have minimal cytotoxicity, and are easily functionalized with ~~other~~ proteins and other markers for targeting purposes. Nanodiamonds have successfully have been used as biomarkers or ~~tracers~~ to label or trace Hela cells, lung cancer cells, and murine fibroblasts.

Nanosponge: Nanosponge is like a three-dimensional network or scaffold. Its backbone is a long length of polymer and the size is of about virus. Nanosponge is mixed in solution with small molecules called cross-linkers that act like tiny seizing hooks ~~of~~ to tie up different parts of the polymer together. The net

effect of this arrangement is to form spherically shaped particles filled with cavities where drug molecules can be stored and then injected into the body. This tiny sponge circulates around the tumor cell until they encounter the surface to sustain releasing their drug cargo. Nanosponge is three to five times more effective at reducing tumor growth than direct injection. The targeted delivery systems of nanosponge have several basic advantages like, the drug is released at the tumor instead of circulating widely through the body, it is more effective for a given dosages. The nanosponge should have basic features such as fewer harmful side effects because smaller amounts of the drug will come into contact with healthy tissue.

BIONANOMOTORS :-

Nanobiomotors are tiny machines that utilize a primary energy source to do mechanical work. They are crucial to the sustenance of living systems, since they provide for biological motion, help direct cellular components to proper destinations, package DNA, contract muscles, and perform a variety of other functions. Biomotors exhibit a adversity of complex structures. Most have the same basic components, including a mechanical Frame (usually composed of proteins) with both moving

and static parts, powered by an energy supply. This energy is typically derived from the binding and hydrolysis of ATP, which lead to conformational changes in the motor protein, resulting in movement. Some motors use energy produced from ion gradients.

These motors are typically divided into categories based on the type of motion displayed: linear, rotary, and revolution motors. The action of revolution enables movement to be free of coiling and torque. Revolution motors have now solved many puzzles associated with viral DNA packing motor studies. They also have settled the discrepancies concerning the structure, stoichiometry, and functioning of DNA translocation motors. The rotation and revolution mechanisms can be distinguished by the size of channel: the channels of rotation motors are equal to or smaller than 2 nm, whereas channels of revolution motors are larger than 3 nm. Rotation motors use parallel threads that operate with a right-handed channel, while revolution motors use a left-handed channel to drive the right-handed DNA in an antiparallel arrangement.

Similarly, bionanomotors are miniscule protein machines that produce mechanical motion by converting an energy source into work. These biological motors are responsible for most form of motion in all life forms. Bionanomotors are essential in all aspects of crucial cellular processes critical to survival, such as mitosis, DNA replication, DNA repair, homologous recombination, Holliday junction resolution, RNA transcription, ATP synthesis, muscle contraction, viral genome packaging, and directional motality of cellular components to their destinations. Bionanomotors make possible the occurrence of otherwise thermodynamically unfavorable processes.

DNA Nanomotors:

Biological molecular motors, like myosin and kinesin, use the energy from the hydrolysis of ATP to initiate mechanical movements. These motors are essential molecular machines for movement in living organisms. Synthetic molecular motors which derive their operating concept from natural motors have been designed in a similar way using ATP as the energy source. Additionally, studies have been conducted on motors which use energy from the hydrolysis of the DNA backbone and DNA hybridisation. Innovations in synthetic chemistry and genetic engineering

enabled by nanotechnology are creating opportunities for scientist to create new motors which can complete a fully cycle of motion without external intervention. Although in the laboratory stage, some of the advances in the area are promising. Two models of molecular motors powered by DNA and RNA hydrolysis have been developed. In one model the cargo strand is hybridised into an anchorage. The track for the movement of the motor is made of identical single stranded anchorage attached to the double stranded backbone. Once it is hybridised, the enzymes contained in the cargo cut the anchorage, releasing a small fragment. This allows the cargo to stick to the next anchorage. The cargo can be then transferred fully to the next anchorage by a branch migration reaction. The cycle is repeated to complete the operation. In a second system a similar track was used to carry out the movement of the device. However, instead of the '10-23' catalytic enzyme used in the first motor, a recognition site in the cargo-anchorage duplex for a restriction enzyme was present.

Unidirectional motion was obtained by the destruction of the track once the motor have moved on. However, this reduces the potential use of these devices. The probability of the cargo moving out of the track can be reduced if the interaction between the cargo and anchorages are strong.
