Adding *Life* to the nanotechnology

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Abstract: A confluence of nanobiotechnology and nanofabrication technology gives birth to a new class of engineering which adds life to the silicon world. Such hybrid machines of molecular motors snuggled in silicon matrix are expected to bring a great revolution in the fields of health- and space- management.

Key words: nanomotors; bionanotechnology; nanofabricationtechnology; microelectro mechanical system.

A confluence of biology and engineering gives birth to a hitherto unknown hybrid field

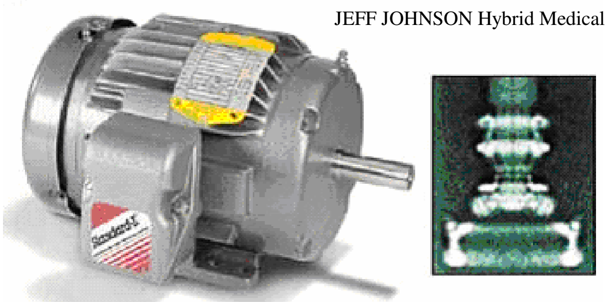
The Creator of the Universe has never kept things in secret it seems. He created men and material on this Earth and left the workshop open for us to learn. Since then millions of years passed for man to come out from the shy of procreation. He has evolved and reached maturity enough to peep through the nano-slit of the cellular body and started wondering about the tools and process operate inside of him. Now man attained enough skill to employ such devices for his own artifacts. The tools and devices that make tiny cells to live a life is the treasure hunt for him. To this effect what happens in current years is the integration of the hitherto known 'nanobiotechnology' & 'nanofabrication technology'. A confluence of such scientific advancements grows into a new branch of subject field which can be named as **nanochimeric engineering (NE)**, for our convenience. We can also define **NE** as fabrication of tools and devices involving organic/inorganic component integrated with nanobiomolecules. Hence **NE** is centered on integrating **two** components: one from the non-living world and another derived from the living world. In this backdrop, we can continue the remaining part of our discussion.

The Cellular processes are driven by molecular motors. The Creator has kept many motors inside of our every body cell to drive the life process

Akin to many machines, cells too are inbuilt with motors that help carry out our essential physiological life process. Some motors are fixed below the cilia or flagella which make bacterial cell or sperm to propel. A rotary motor fixed in the membrane of a bacterium turns a shaft and superficially resembles an electric motor. The flagellar motor does not use electric current; instead it uses up ATP to bring certain changes in the shape of the molecules and make the protein shaft revolve.

Some energy spinning motors churn out the energy rich adenosine triphosphate (ATP) by gluing ADP and iP. Another group of motors carry cargoes at the expense of ATP and are responsible for intracellular traffic. They can shuttle between different organelles or cellular compartments. In extreme cases they make trips as lengthy as half a meter along the axons of nerve cells. To facilitate the traffic movements, the cells are equipped with rail like ropes in cytoplasm on which most of the motor proteins navigate. They also act like cellular muscle and impart 3-D structure to the animal cells. These

Conventional electric motor has close resemblance to the molecular motors (right side) that propel the flagella in a bacterium



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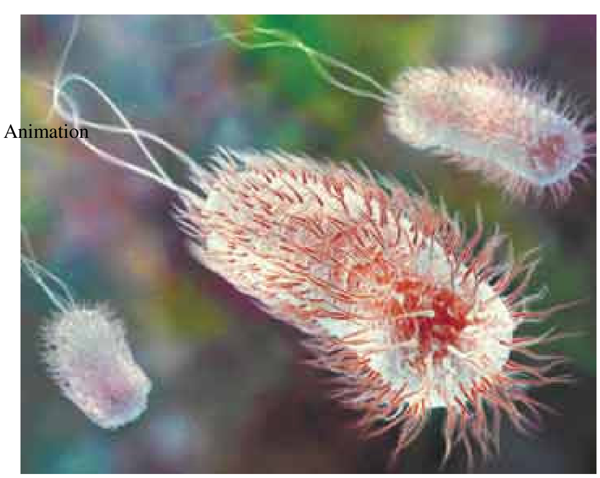
JEFF JOHNSON Hybrid Medical Animation

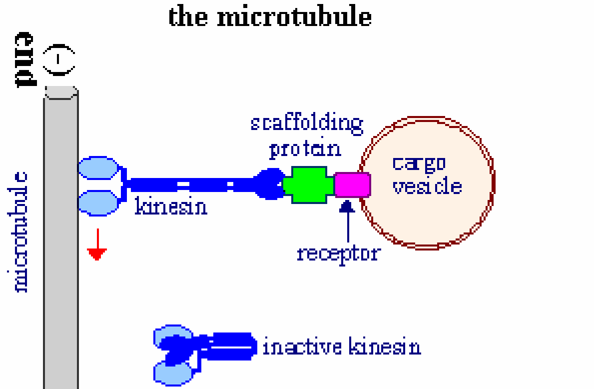


rails of variable length and thickness are very often direction specific. Thus motor driven movements inside the cell is effected by two molecular components: very thin rod-like **filaments**, which form a complex network of rails, and molecular **motors**, which move along those filaments and carry the cargo. When bound to the filaments (intracellular rails), the motors split and liberate the chemical energy locked within ATP for mechanical work. For all molecular motors, ATP is the biological fuel which is freely available throughout the cytoplasm.

Few well known molecular motors-Kinesins, Dynein & Myosin

Kinesins are group of motor proteins mostly function as rope-motors which move on microtubules. More than 12 different members have been identified. Each kinesin member transports a specific cargo and has molecular weight of 380,000. They move materials faster across the nerve cell ends with a velocity of about 3 µm/s thereby causing the transmission of nerve impulses in lightening speed. The

Kinesin transporting cargo along the microtubule



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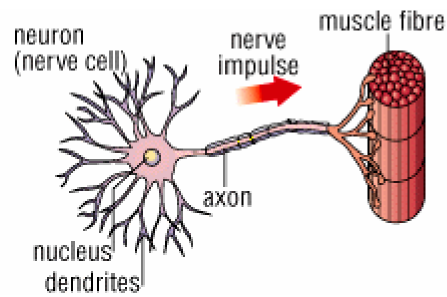
absolute value of this velocity is not very impressive, but relative to its size, the motor molecule moves very fast: indeed, on the macroscopic scale, its movement would correspond to an athlete who runs 200 meters in one second!

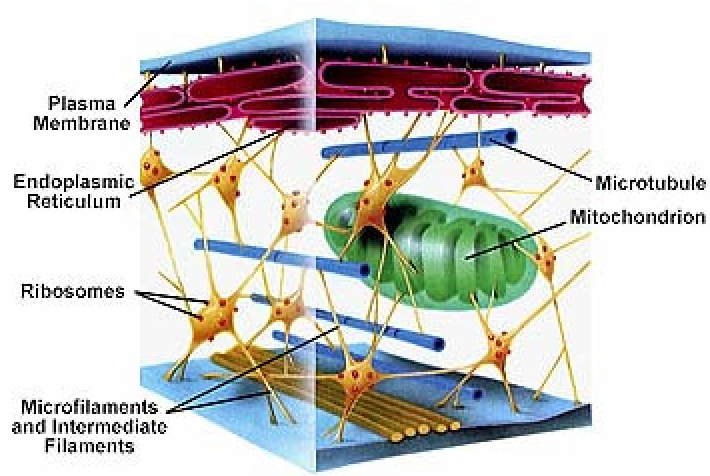
Cell division is aided by another protein motor known as **dynein**. They are relatively larger motor group with molecular weight of about 1,000,000. Dynein motors are also anchored on microtubule rails for movement. In fact, the anticancer drug Taxol works on a related approach of destroying the rails of the dynein motor -the microtubules! Dynein probably ferry chromosomes and other materials to the appropriate locations within a cell to facilitate cell division. Dynein motors are responsible for the propulsion of cilia and flagella (of bacteria/ sperm) too! In that process the energy locked in ATP molecule is used up.

Myosins are a class of motor protein which moves on microfilament. They are especially responsible for muscle movement. Its molecular weight is about 500K daltons and account for half of the protein present in the myofibrils that comprise muscle fibers. Body stiffness on death probably results from failure of myosin head to detach from microfilament due to non-availability of ATP which is essential for detachment. This state is called **rigor mortis.** Each



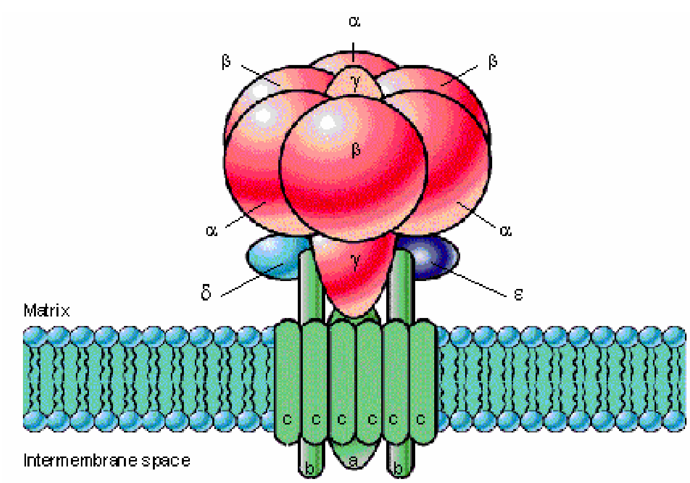
myosin molecule consumes about 10 ATP molecules per second as fuel.

All the 3 families of "Motor proteins" are mechanico-chemical enzymes involved in locomotion or transport by generating force and movement. While kinesin and Dynein require thicker rail (**microtubules** of 25 nm dia and made up of tubulin protein monomer), the Myosin motors need **microfilament** (in this case, the molecular rope is as thin as 4-6 nm dia; composed of actin protein monomers). The molecular rails are polar and have two different ends, a ‘plus’ end and a ‘minus’ end. In a cell,



these filaments are arranged in such a way that all ‘plus’ ends point into the same direction. Such an arrangement provides many parallel tracks for the molecular motors and, thus, represents a multi-lane highway in the nanoregime. The advantage of molecular motors is their availability in different sizes and varieties specific to different types of cargo. They are also directional specific. For an example, Kinesins and Dyneins motors move cargoes in opposite directions on a microtubular rail. **Kinesin** is a (+) end directed microtubule motor protein i.e., they move unidirectional on a molecular rope. Dynein is a (–) end directed motor protein. Such difference explains not only how movement of cargo is powered but also how the direction of movement is controlled. These variable characters of molecular motors in moving the cargo to evolve a flexible biomimetic model system with controlled parameters.

Another most studied motor is **ATPsynthase**. ATPsynthase is a ubiquitous enzyme found in every living organism. It is composed of a pair of bioengine: Fo-ATPase and F1-ATPase. The two generator-like motors

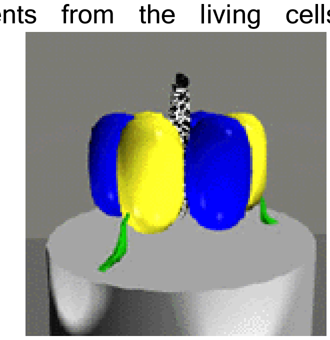


work together to produce ATP. Coupled through a single axle, one motor (Fo) that converts the cell's electrical energy into rotation, another one (F1) that converts rotation into ATP chemical synthesis. The 2 engines are again composed of different subunits (e.g., α,β,γ in F1-ATPase). ATPsynthase can also work in reverse, turning ATP into electrical energy. Cells typically use the energy of sun light or of food to generate an electrical potential by pumping protons that carry a positive charge across their cell membrane. The energy stored drives the protons back through Fo-ATPase enforcing rotation of the axle; the rotation in turn induces ATP synthesis in F1-ATPase. FoF1-ATP synthase is one of the largest molecular machines in biological cells

In nutshell, biological cell is a chemical workshop comprising the functional species *viz* IT storage (DNA), catalysts, sensors, structural elements, pumps, motors etc. Man understood this secret and tries to exploit the process and machinery for his own interest.

Man spies on the Creator; the biological nano machines to takeover the silicon world

As discussed above, living systems contain a wide variety of nanomachines including motors, shafts and valves. Membrane bound ion-channels behave as valves which selectively permit the entry of ions and molecules. Now engineers utilize some of the parts of the cell e.g., the nano motors for a possible applications in nanoscale devices that could perform a sequence of repetitive movements such as rotations, vibrations, translocations along tracks, linear contractions, etc. The energy requirement for these motions hitherto comes from enzyme-catalyzed ATP reactions. Efforts have already been made in isolating both motors and filaments from the living cells to construct biomimetic transport systems. How these machines could be functionally useful outside their native environment is going to be seen in future. Since ATP production is a chemical reaction, there should not be a problem to make the fuel available outside the cellular condition.

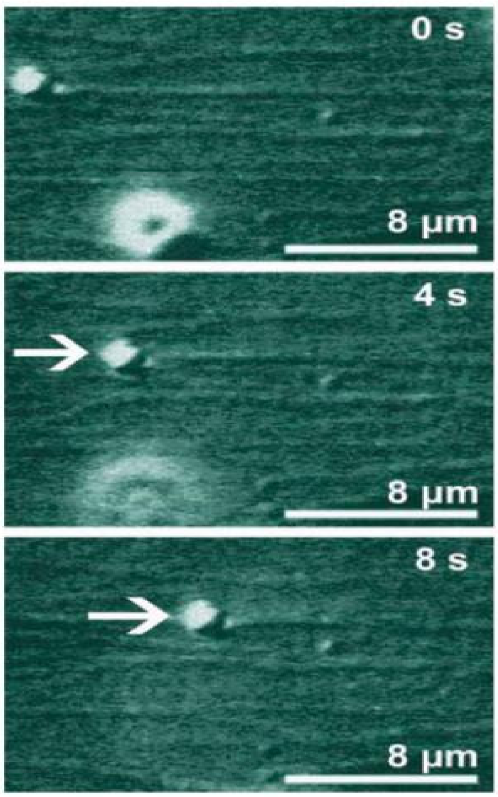


A new class of hybrid machines is the blending of biological motors & artificial matrix

Though many such molecular motors have been working around for eons in natural system, they were incredibly small that we unable to use them for anything. Moreover we didn't know how to connect these interfaces between electronic, mechanical, and biological systems. Connecting artificial nanotechnology to biological systems is a topic of great interest. Only very recently has the size scale of nanofabricated inorganic mechanical devices approached a dimension that could conceivably be compatible with the force production and dimensions of molecular motors. In fact, man has succeeded in creating the chimerical nano-motor with **F_1-ATPase**.

Researchers (Carlo Montemagno et al.) from Cornell University found a method to connect a biological motor to a tiny metal propeller. The 11-nanometer-square biological motor is anchored on a 200-nanometer nickel post, and sports a 750-nanometer-long nickel propeller. The whole device is several times smaller than a red blood cell, which is 5,000 nanometers across. The tiny bits of metal were produced using microelectromechanical systems (MEMS) processes. This hybrid nanomechanical device is capable of generating a force >100 pN which is among the greatest of any known molecular motor. It has a calculated no-load rotational velocity of 17 r.p.s., and a diameter of less than 12 nm. One turn of the motor produces about 120 piconewtons per nanometer. One newton is about the force of the weight of an apple and a piconewton is one trillionth of that force. The energy released from the three ATP molecules needed to rotate the motor once is actually 240 piconewtons per nanometer, giving the motor a 50 percent efficiency rate. It is envisaged that F_1-ATPase motors will pump fluids and open and close valves in microfluidic devices, and provide mechanical drives for a new class of nanomechanical devices (refer *Nanotechnology* **10** (1999) 225-231 for more details).

Prof. Weihong Tan in University of Florida has made a "nanomotor" out of DNA bit. The motor was so small that hundreds of thousands of them could fit on a pin head. They curl up and extend like an inchworm. Osaka University in Japan has already working on incorporating similar DNA motors in biosensors to detect a very specific piece of DNA that may be the root-cause for a disease. As we are aware, DNA (deoxyribonucleic acid) is the celebrated biomolecule which holds the genetic record for most living beings. It exists in pair of twisted rope. During cell division, its double-helix structure duplicates so that each daughter DNA strands identical to parent DNA strands born out. When being separated from the complementary strands, DNA molecules also have the capacity to seek and pair with its identical partner. Researchers tap this property when synthesizing new DNA molecules for motors. Like all motors, nanomotors need power. DNA is useful because it gets its energy through ATP (chemical energy) as opposed to traditional sources such as electricity: also DNA can participate in biological activities.



Three snapshots showing the transport of a micrometer bead (white arrow) at 0, 4, and 8 seconds. The bead is pulled by molecular motors, which are invisible, along immobilized filaments on a matix. All filaments are aligned in such a way that their 'plus' ends point to the right and form a multi-lane highway in the nanoregime. The bead moves about 8 micrometers in 8 seconds; during this time, each motor makes about 800 steps (Image: Max Planck Institute of Colloids and Interfaces).

Researchers from Delft University of Technology's Kavli Institute of Nanoscience have discovered how to use the motors of biological cells in extremely small channels on a chip. Based on this, they built a transport system that uses electrical charges to direct the molecules individually. Molecular bio-motors, such as the enzyme kinesin, can walk in small steps (of 8 nanometers) with a load of material along the microtubule-networks within a cell. Fascinated by these biological motors, the researchers are expediting appropriate methods to ride kinesin-motors on microtubule rails in an electrically directed transport system that is made by the researchers using nano-fabrication techniques.

Molecular switches tailor biological & silicon worlds together

A major advancement in harnessing the biological motors in artificial devices is the incorporation of suitable control switch. Through Mol-Switch project (at Portsmouth University), scientists now found a way to connect biological world with the silicon world of electronic signals. The molecular switch can act as an actuator for the nano-scale world. The nano-scale actuator can supply and transmits a measured amount of energy for the operation of another mechanism or system. It can be a simple mechanical device, converting various forms of energy to rotating or linear mechanical energy. Or it can convert mechanical action into an electrical signal. It works both ways. They have created a molecular switch that could play a key role in thousands of nanotech applications. When the biological motor is working, there are specific sensors which emit electrons. The biological element of the device starts with a DNA molecule fixed to the floor of the microfluidic channel. This strand is held upright, like a string held up by a weather balloon, by anchoring the floating end of the DNA strand to a magnetic bead, itself held up under the influence of magnetism. A specific type of protein, called a Restriction-Modification enzyme, provides one of the DNA motors. The novelty of this type of DNA motor is that it will bind site specifically based on base sequence. So one can control exactly where the motor is placed on the vertical DNA strand. The motor is attached to the strand at the specific sequence of bases and fed by ATP as fuel for the motor. The motor then pulls the upright DNA strand through it until it reaches the magnetic bead, like a winch lowering a weather balloon. A Hall-Effect sensor can read the vertical movement of the magnetic bead as 'on' or 'off'.

In nutshell, man destines to harness the biological nano motors, valves and shafts that can work under his control outside the natural system. Molecular machines self-replicate and hence they can be made cheap in vast quantities; it is for the engineer to snuggle them harmoniously with the silicon world. Biomimetic systems based on molecular motors and filaments have immense application in bionanotechnology, pharmacology, and medicine. It can be a promising approach to evolve drug delivery systems that utilize the motor transport within human cells, and motile components for nanoscale manufacturing. In long term, we should also be able to construct 'smart' biomimetic systems which can repair human body free from diseases including cancer cells. A nanoscale submarine with dimensions of only a few billionths of a meter, could find immense use in medicine by navigating through the blood, seeking out destroy diseased cells. **Nanochimeric engineering** can also bring significant changes in aeronautical and space management.