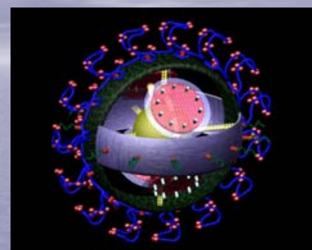

BIO-NANO-MACHINES FOR SPACE APPLICATIONS

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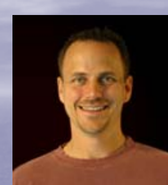

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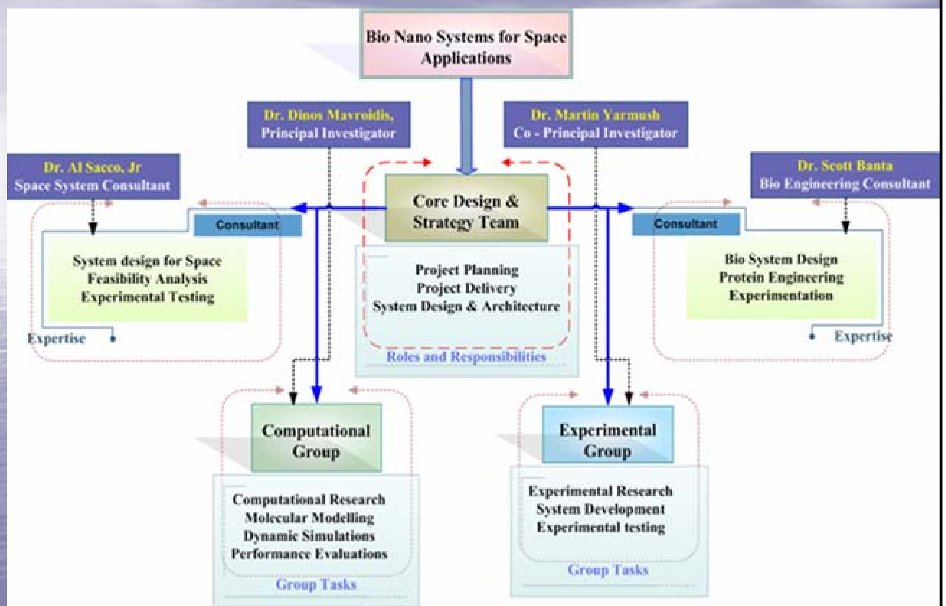
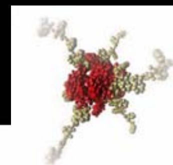


Introduction and Objectives

- Identify and study computationally and experimentally protein and DNA configurations that can be used as bio-nano-machine components
- Design two macro-scale devices with important space application that will be using bio-nano-component assemblies:
  - ***The Networked TerraXplorer*** (NTXp)
  - ***All Terrain Astronaut Bio-Nano Gears*** (ATB)

The Concept



- **Nanorobots** would constitute any ***"smart"*** structure capable of *actuation, sensing, signaling, information processing, intelligence, and swarm behavior* at nano scale.

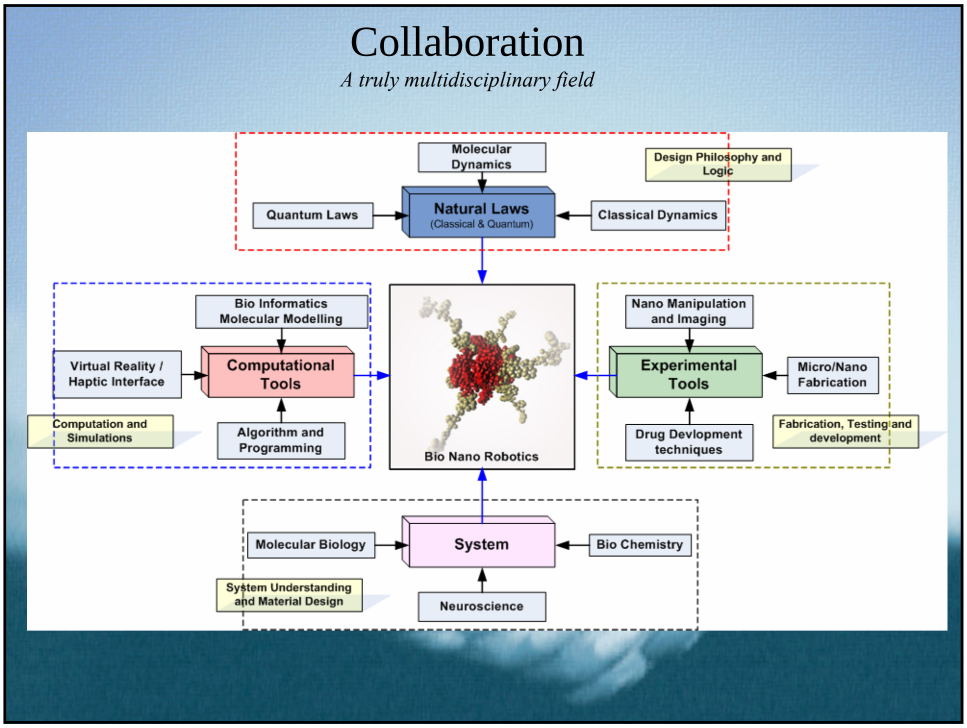
- ***Bio* nanorobots** – Nanorobots designed (and inspired) by harnessing properties of biological materials (peptides, DNAs), their designs and functionalities. These are inspired not only by nature but machines too.

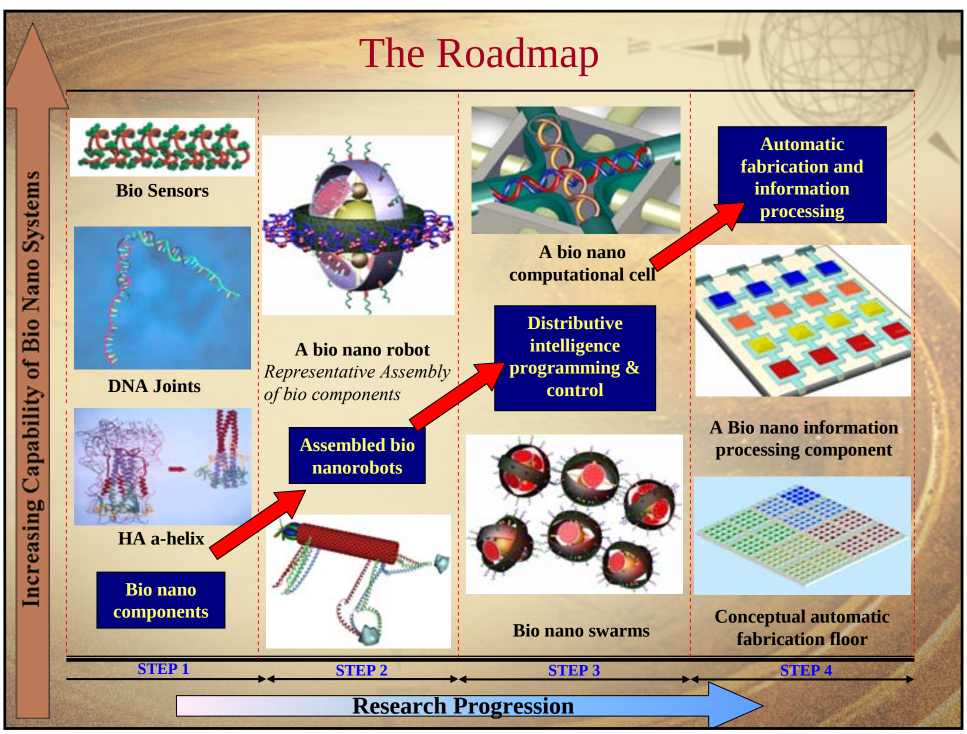
Motivation

The motivation behind research in the field of bio nanorobots

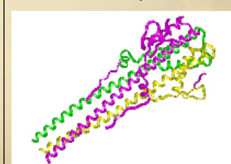
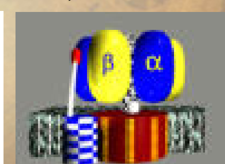
Why *bio*?

- Several properties and functionalities *(self replication, healing, adaptability, life, intelligence)* exhibited by the nature *(these materials)* which are very desirable.
- Many mechanisms and machines (*biochemical*) associated with these materials are reversible and highly efficient *(ATP synthase).*
- Their diversity and availability.
- The applications – how nature which is made of up molecular machines translate it into macro application *(see the figure)* and hence an open source for innovative applications.
- Novel way of influencing nano world with these components – *a possible industry enabler*

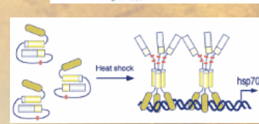

Collaboration
A truly multidisciplinary field
Molecular Dynamics
Design Philosophy and Logic
Quantum Laws
Natural Laws
(Classical & Quantum)
Classical Dynamics
Bio Informatics Molecular Modelling
Virtual Reality / Haptic Interface
Computational Tools
Computation and Simulations
Algorithm and Programming
Bio Nano Robotics
Nano Manipulation and Imaging
Experimental Tools
Micro/Nano Fabrication
Drug Devlopment techniques
Fabrication, Testing and development
Molecular Biology
System
Bio Chemistry
System Understanding and Material Design
Neuroscience


The Roadmap
Increasing Capability of Bio Nano Systems
Bio Sensors
DNA Joints
HA a-helix
Bio nano components
A bio nano robot
Representative Assembly of bio components
Assembled bio nanorobots
A bio nano computational cell
Distributive intelligence programming & control
Bio nano swarms
Automatic fabrication and information processing
A Bio nano information processing component
Conceptual automatic fabrication floor
STEP 1
STEP 2
STEP 3
STEP 4
Research Progression

Macro-Nano Equivalence

Structural Elements	
Metal, Plastic Polymer	DNA, Nanotubes  
Actuators	
Electric Motors, Pneumatic Actuators, Smart Materials, Batteries, etc.	ATPase, VPL Motor, DNA  

Macro-Nano Equivalence

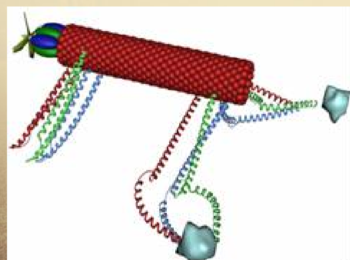
Sensors	
Light sensors, force sensors, position sensors, temperature sensors	Rhodopsin, Heat Shock Factor  
Joints	
Revolute, Prismatic, Spherical Joints etc.	DNA Nanodevices, Nanojoints 

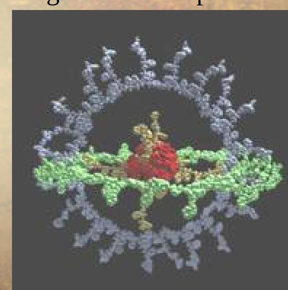
Assembled Bionano Robots

The assembly of functionally stable bionano components into complex assemblies.

Potential methodologies for assembling bio nano components:

Molecular docking method is very important for the design of nanorobotic systems. This method is utilized to fit two molecules together in 3D space



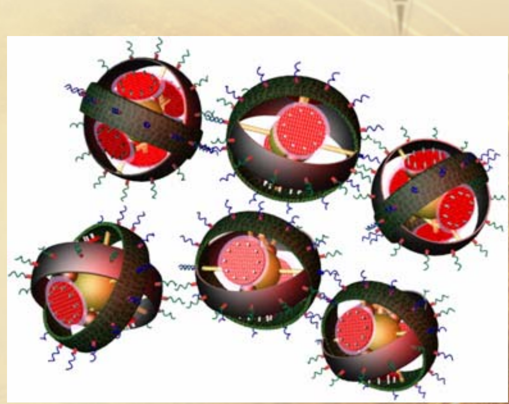


Distributive Intelligence, Programming & Control

Develop concepts that would enable collaboration among bionanorobots and hence development of "colonies".

i) Binding mechanism for swarm formations

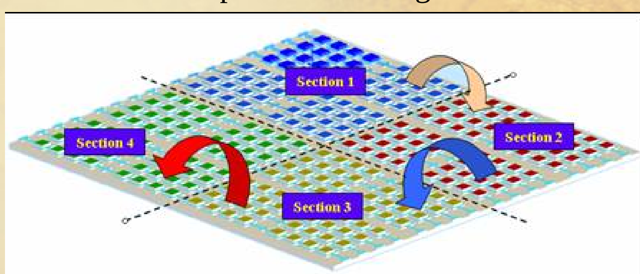
ii) Inter robotic signaling mechanisms, which would include molecular recognition of similar functioning nano robots and sustaining dedicated molecular connections.



Automatic Fabrication

Automatic fabrication methodologies of such bio-nano robots *in vivo* and *in vitro*.

Floor concept of assembling bionanorobot:



Different colors represent different functions in automatic fabrication mechanism. The arrows indicate the flow of components on the Floor layout. Section 1: Basic Stimuli storage – Control Expression; Section 2: Bio molecular component manufacturing (actuator / sensor); Section 3: Linking of bio-nano components; Section 4: Fabrication of Bio-nano robots (assemblage of linked bio-nano components)

Design Philosophy and Architecture

A. ***Modular Organization*** - Modular organization defines the fundamental rule and hierarchy for constructing a bio-nanorobotic system. Such construction is performed through *stable integration* of the individual *'bio-modules or components'*, which constitute the bio-nanorobot.

B. ***The Universal Template*** (Bio Nano STEM System) - The modular construction concept involves designing a universal template for bio-nano systems, which could be 'programmed and grown' into any possible Bio nano system in the domain of the materials used. This concept mimics the embryonic stem cells found in the human beings.

Design Philosophy and Architecture

C. ***Information Processing (Memory Storage and Programming)*** - Capability of information processing is one of the most novel features of the bio nano systems being discussed. The design of these systems would incorporate the various functionalities of bio materials, such as, reversibility and function dependence on conformational changes.

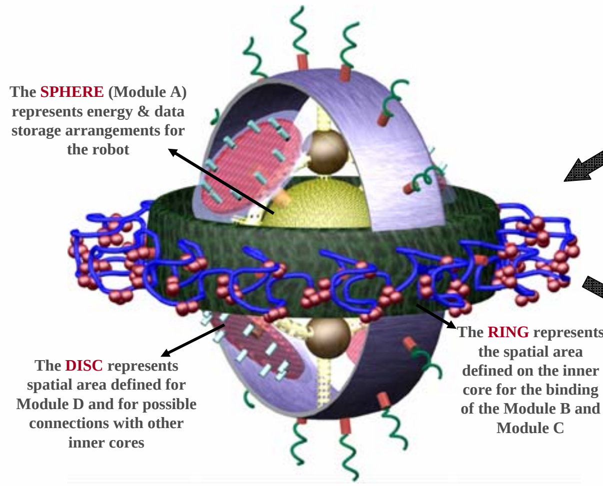
D. ***Bio Nano Intelligence*** - Integrating bio-nano information storage and programming capability with the functionality of growth and evolution, lays the foundation of Bio-nano intelligence.

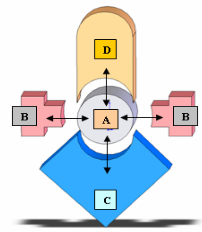
A. Modular Organization…

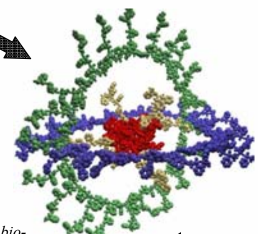
Functionality	Bio Nano Code	Capabilities Targeted	General Applications
Energy Storage and Carrier	E	Ability to store energy from various sources such as, Solar, chemical for future usage and for its own working	Supplies the energy required for the working of all the bio-chemical mechanisms of the proposed bio-nano-robotic systems
Mechanical	M	Ability to precisely move and orient other molecules or modules at nano scale. This includes ability to mechanically bind to various target objects, and carry them at desired location.	1. Carry moities and deliver them to the precise locations in correct orientations. 2. Move micro world objects with nano precision.
Input Sensing	S	Sensing capabilities in various domains such as, chemical, mechanical, visual, auditory, electrical, magnetic	Evaluation and discovery of target locations based on either chemical properties, temperature or others characteristics.
Signaling	G	Ability to amplify the sensory data and communicate with bio-systems or with the micro controllers. Capability to identify their locations through various trigger mechanisms such as fluorescence	Imaging for Medical applications or for imaging changes in Nano Structures
Information storage	F	Ability to store information collected by the sensory element. Behave similar to a read - write mechanism in computer field	1. Store the sensory data for future signaling or usage 2. Read the stored data to carry out programmed functions. 3. Back bone for the sensory bio-module 4. Store nano world phenomenon currently not observed with ease
Swarm Behavior	W	Exhibit binding capabilities with "similar" bio-nano robots so as to perform distributive sensing, intelligence and action (energy storage) functions	All the tasks to be performed by the bio-nano robots will be planned and programmed keeping in mind the swarm behavior and capabilities
Information Processing	I	Capability of following algorithms (Turing equivalent)	Programmable
Replication	R	Replicate themselves when required	1. Replicate by assembling raw components into nanorobots, and programming newly-made robot to form swarms that form automated fabricators. 2. Assemble particular bio-modules as per the demand of the situation, consistent with the Foresight Guidelines for safe replicator development [Foresight Institute, 2000]

Design Philosophy and Architecture

A. Modular Organization



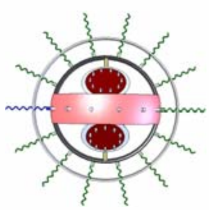




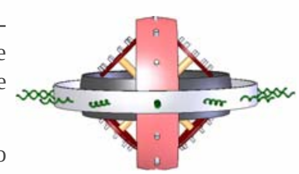
A Bio-Nano-Robotic Entity 'ABCD', where A, B, C and D are the various Bio Modules constituting the bio-nano-robot. In our case these bio modules would be set of stable configurations of various proteins and DNAs.

Design Philosophy and Architecture

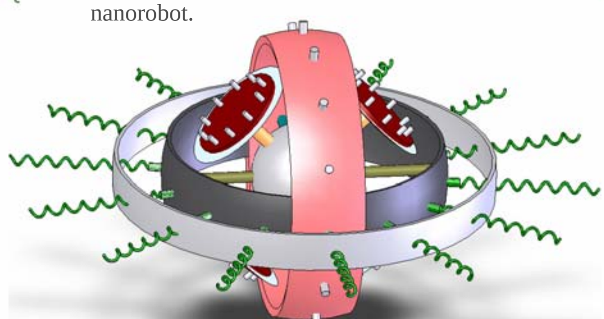
B. The Universal Template



A basic template which could be at run-time modified and subjected to have specific functionality is the goal of the bio nano STEM cells.



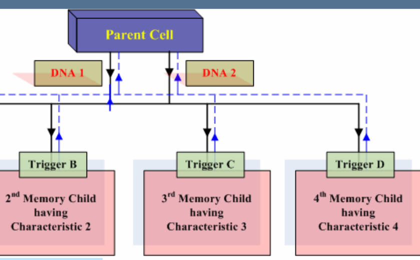
Sensing capability enhanced Bio nanorobot.

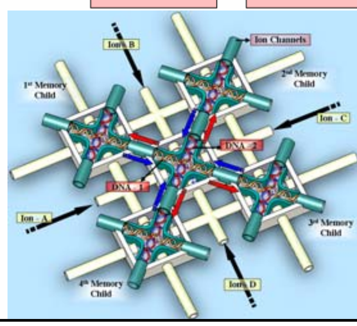


Design Philosophy and Architecture

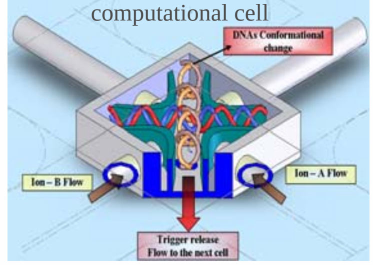
C. Memory Storage and Programming

A proposed model designed for memory storage capability at nano scale





Bio nano computational cell



C. Memory Storage and Programming

The working principle is illustrated in the following equations

$$IonA^{+} + (DNA_{1a} + DNA_{1b}) \underset{\text{fully reversible reaction}}{\overset{\text{Presence of a Field Gradient}}{\rightleftarrows}} (DNA_{1^{*}}) + Trg_{A}$$

$$IonB^{+} + (DNA_{1a} + DNA_{1b}) \underset{\text{fully reversible reaction}}{\overset{\text{Presence of a Field Gradient}}{\rightleftarrows}} (DNA_{1^{**}}) + Trg_{B}$$

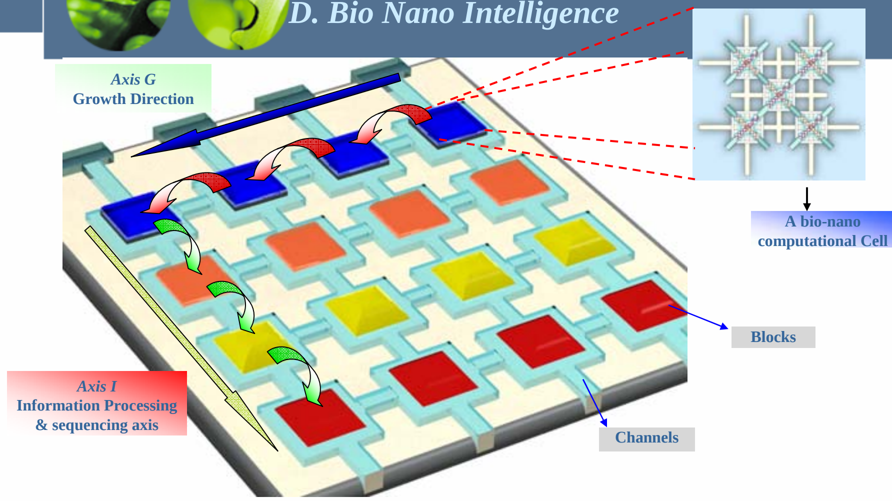
$$IonC^{+} + (DNA_{2a} + DNA_{2b}) \underset{\text{fully reversible reaction}}{\overset{\text{Presence of a Field Gradient}}{\rightleftarrows}} (DNA_{2^{*}}) + Trg_{C}$$

$$IonD^{+} + (DNA_{2a} + DNA_{2b}) \underset{\text{fully reversible reaction}}{\overset{\text{Presence of a Field Gradient}}{\rightleftarrows}} (DNA_{2^{**}}) + Trg_{D}$$

$$4\,Ions\,(Input) \underset{Generates}{\overset{Reacts\,With}{\rightleftarrows}} Bio\_Chemical\_Center \underset{Reacts\,With}{\overset{Generates}{\rightleftarrows}} 4\,Triggers$$

Design Philosophy and Architecture

D. Bio Nano Intelligence



A model is being proposed which describes programming, learning and hence evolving as one combination of events which can quantitatively describe intelligence. Ionic strength and their variations could be few of the important variables responsible for the behavior of a bio-nano robotic system.

D. Bio Nano Intelligence

- Axis I, is the axis where the information is filtered and various components are sequentially isolated and stored in the bio-nano computational cell. The stimuli obtained by activation of the first block, triggers a reaction, which activates the subsequent blocks along the Axis I.

- Axis G is the Growth Direction. Along this axis copy of the initial data is made. Once a row is finished along the Axis I, the Axis G elements are activated. And again the sequencing along the Axis I would start. A single stimulus could trigger multiple outputs through this mechanism. Axis G would also enable parallel computations, thereby accelerating the response to a given input. This is typical of an intelligent living system, where the past stimuli are responded to faster when they felt.

- Ion types could be related to the variations in behavior and Ion Concentration could be related to the intensity of the behavior of a bio-nano robotic system.

Control of Bionano Robotic Systems

Internal Control

Passive control **-** depends upon the mechanism of bio chemical sensing and selective binding of various bio molecules with various other elements.

Active control - 'active' control mechanism has to be designed for the nanorobots such that they can vary their behavior based on situations they are subjected to, similar to the way macro robots perform.

This requires the nanorobot to be programmable and have an ability for memory storage. Professor Ehud Shapiro's lab has devised a biomolecular computer which could be an excellent method.

External Control

This type of control mechanism employs affecting the dynamics of the nanorobot in its work environment through the application of external potential fields.

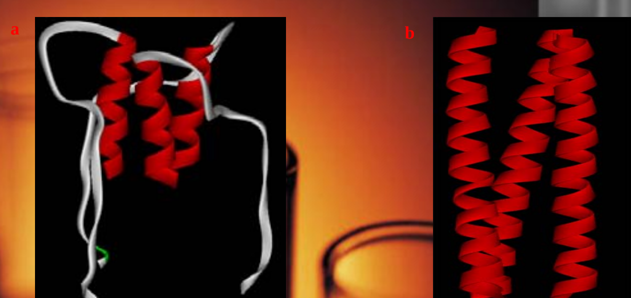
Researchers (Prof Sylvain Martel) are using MRI as an external control mechanism for guiding the nano particles.

An MRI system is capable of generating variable magnetic field gradients which can exert force on the nanorobot in the three dimensions and hence control its movement and orientation. But this method has some limitations on very accurate precision of the control.

Experimental and Computational Methods

- *Molecular modelling techniques in sync with extensive experimentations would form the basis for designing these bio-nano systems.*

- *Protein based linear motor, Viral protein linear (VPL) motor. VPL motor changes its conformation due to a change in its pH. This change in conformation gives rise to forces and linear displacements. It is a 36 amino acid peptide from the hemagglutinin protein of the influenza virus. This 36 amino acid peptide is termed Loop-36.*



VPL Motor at ***(a) neutral*** *and* ***(b) acidic*** *pH. a) Front view of the partially α-helical triple stranded coiled coil. VPL motor is in the closed conformation; b) VPL Motor in the open conformation. The random coil regions (white) are converted into well defined helices and an extension occurs at lower pH*

Experimental and Computational Methods

• To begin predictions of the dynamic performance of the peptide (i.e. energy and force calculation) we are performing Molecular Dynamics (MD) Simulations that are based on the calculation of the free energy that is released during the transition from native to fusogenic state, using the MD software CHARMM.

• Other then the Loop-36 our computational and experimental group are focusing on peptides which don't require high energy molecules and had been shown to undergo substantial conformational variations following changes in their environment. RTX β-Roll and Elastin are at the center of focus of our research.

• Our group is integrating these efforts with Virtual Reality based design techniques. Haptic interface is under construction which would help us evaluate in real-time the forces and its variations of the various molecules. In the next step we will integrate the experimental and computational process by making a peptide-AFM-Phantom-VMD-NAMD system.

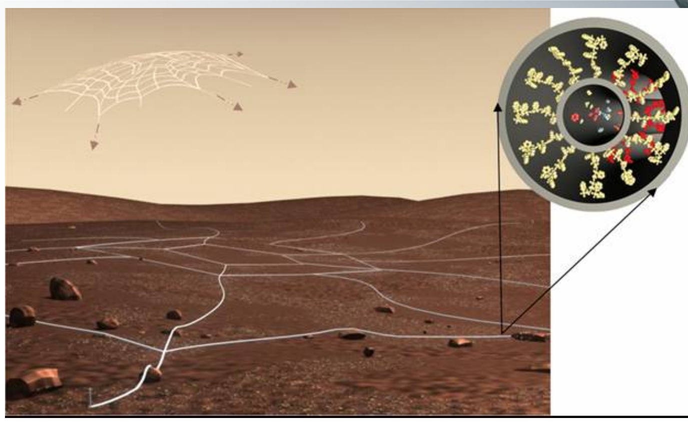
Space Applications

Our current research is focused on two main space based applications:

- Networked TerraXplorers *(NTXp)*
  - Mapping and sensing of vast planetary terrains
- All Terrain Astronaut Bionano Gears *(ATB)*
  - Enhanced health management and protection system for astronauts

Networked TerraXplorers (NTXp)

Mapping of vast planetary terrains



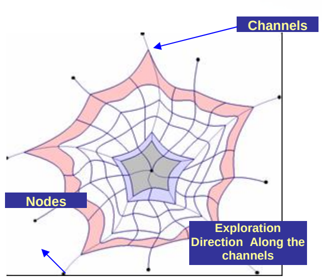
A realistic scenario where the Networked TerraXplorers (NTXp) are employed. These meshes would be launched through the parachute and these would be spread open on the target surface. These NTXps could be launched in large quantities (hundreds) and hence the target terrain could be thoroughly mapped and sensed. A single NTXp could run into miles and when integrated with other NTXPs could cover a vast terrain.

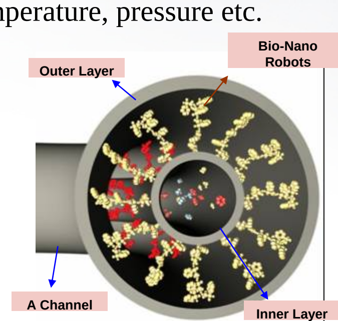
Networked TerraXplorers (NTXp)

Mapping of vast planetary terrains

Principle of Operation

The bio-nano robots will move inside the channels of the network and would have 'limited' window of interaction, through special valves with the outside environment. They will interact with the outside terrain and chemically sense the presence of water or other targeted resources / minerals. The micro channel would be designed in various layers, making it ready for the harsh conditions on the planetary surface, such as: Radiations, Temperature, pressure etc.

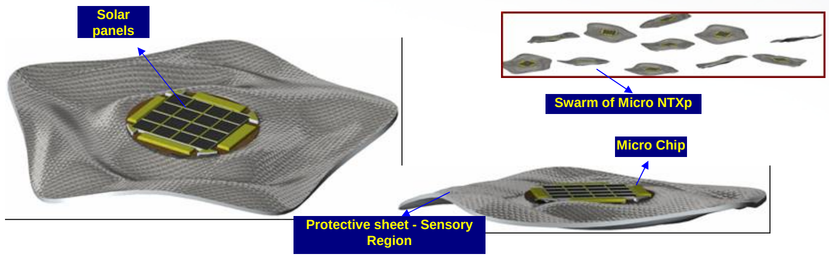




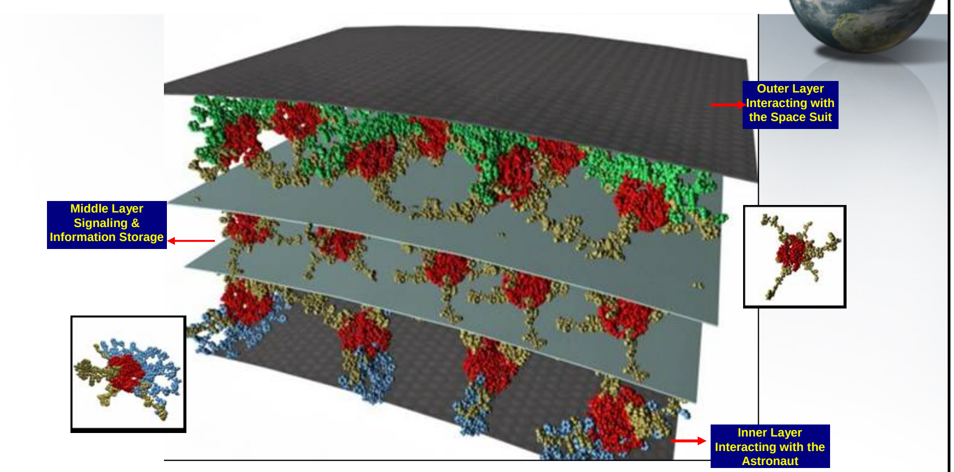
Micro Networked TerraXplorers (NTXp)

Mapping of vast planetary terrains

- Micro Networked TerraXplorers, is the extension of the NTXp concept. In this concept, the bio-nano robots would perform sensory function, but the signaling function would be performed by the "communication microchip" integrated with the bio-nano system. This microchip would signal the data gathered to the central receiver. This Micro NTXp would be very small in size (few mms or smaller) and could be sprayed from the air borne rover or orbiter to the desired location. These devices would form a sensory network amongst them and would act in collaborative and distributive way.



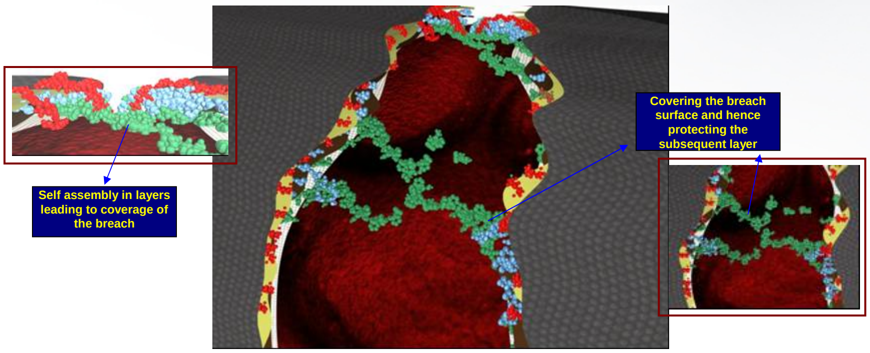
The All Terrain Bionano (ATB) *Gears for Astronauts*



The layered concept of the ATB gears. Shown are three layers for the ATB gears. The inner layer would be in contact with the human body and the outer layer would be responsible of sensing the outer environment. The middle layer would be responsible for communicating, signaling and drug delivery.

The All Terrain Bionano (ATB) *Gears for Astronauts*

Breach sealing mechanism: The mechanism of covering breach by the ATB gear is shown. The bio-nano robots would flow through various layers and bind amongst themselves and form a cover. Self assembly of the bionano robots is one of the properties employed for such mechanism.



Identification of Space Requirements

- Work environment – Targeting ***Mars environment***
- ***Temperature***
  - Maximum of around 20° C (68° F) and minimum of -140° C (-220° F)
- ***Pressure***
  - As low as 6.8 millibars (the average pressure of the Earth is 1000 millibars)
- ***Radiations***
  - ultraviolet (UV) radiations is the main source of radiations
  - between the wavelengths of 190 and 300 nm
- ***Sensory targets*** in space – water, oxides, minerals…what else!

Identifying Biocomponents for Space

In general there is a ***positive correlation*** between the degree of stability (such as thermophilicity) of the source organism and the degree of stability (thermostability) of both their intracellular and extracellular proteins. Hence we are studying various micro organisms which exist in the extreme conditions and further isolating various bio components to be used as:

i. Sensors
ii. Actuators and manipulators
iii. Signaling
iv. Information Processing

Extreme Micro Organisms

Eukaryotes in Extreme Environments	**Definition**	**Operating Regime**	**Name of the Organisms**
Thermophiles	Micro organisms which can exist at higher temperatures	The range is pretty broad. The limit of life is expected to be around 140 degree centigrades.	1. *Cyanidium caldarium* - its optimal growth temperature was 45ºC and the maximum temperature at which growth occurred was 57ºC. 2. Cells like the archaean Pyrococcus grow above 100ºC.
Psychrophiles	Micro organisms which can exist at colder temperatures	Water is the solvent for life and must be present in a liquid state for growth to occur. This sets a practical lower limit for growth slightly below 0ºC.	*Cold Shock protein* - CspA a major cold shock protein of E Coli. *Cold-acclimation protein (CAPs)*- a second group of protein that are involved in the low-temperature growth of psychrophilic bacteria and yeasts. *(Pseudomonas syringae)* Ice-nucleating proteins forms ice crystals on leaves and flowers (-2 to -5 C). *(Pseudomonas, Erwinia, Xanthomonas)*
Acidophiles	Mico organisms which can exist in acidic environment (pH 3 or less). The internal pH of acidophiles has been measured between 5 to 7 C.	Less than pH of 3.	*T. ferrooxidans, Acontium cylatium, Cephalosporium spp., and Trichosporon cerebriae*

Extreme Micro Organisms

Alkalophiles	A micro organism whose optimum rate of growth is observed at least two pH units above neutrality or above 9 pH.	9 - 11 pH	*Spirulina, B. alcalophilus*
Xerophiles	A micro organism which can survive in driest environments.		*Metallogenium, Pedomicrobium,* and *lichens such as Rhizocarpon geographicum, Aspicilia cinerea , Caloplaca saxicola*
Radiation resistant organisms	Which can sustain ionizing radiations	When exposed to 1.5 million rads of ionizing radiation (a dose 3000 times higher than would kill organisms from microbes to humans), Deinococcus repaired the damage to its shattered DNA in a matter of hours.	*1. Deinococcus radiodurans 2. Halobacterium* - a master of the complex art of DNA repair. This bacteria has survived normally-lethal doses of ultraviolet radiation (UV), extreme dryness, and even the vacuum of space. Evolving to cope with a salty lifestyle could explain why Halobacterium is so good at surviving radiation and other ravages.

Biocomponents for Space Applications

Sensors

i. Biosensors based on metal binding proteins such as Phytochelatins and metallothioneins (MTs).

ii. Heat Shock Factor

iii. Elastin

Structural modules *(membrane or static structure construction)*

i. S-Layer proteins - these are the single most abundant polypeptide species in the thermophilic archaeobacterial.

ii. Tetraether lipids

Biocomponents for Space Applications

Information Processing module

i. DNA or protein arrays

ii. Molecular switches – sensitive to certain parameters, such as, light, receptor proteins.

Some of the thermally stable enzymes

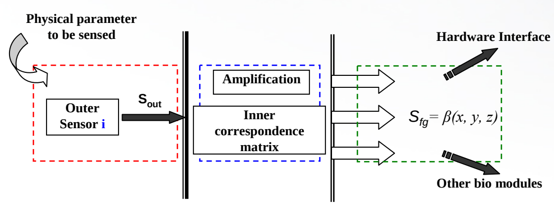
Enzyme	Organism
Pullulanase	Pyrococcus furiosus
RNA Polymerase	Thermoplasma acidophilum Sulfolobus acidocaldarius Thermoproteus tenax Desulfurococcus mucosus
Succinate thiokinase	Thermoplasma acidophilum
Sulphur oxygenase	Acidianus brierleyi
Topoisomerase I	Sulfolobus acidocaldarius
Transglucosylase	Desulfurococcus mucosus

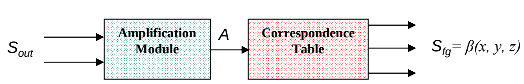
Sensor – Signal Dynamics

$S^i_{in} \to \{f, g ...\}$ is the signal generated per bio sensor

$S_{out} = p\{\sum_{1}^{n} (a_i f, b_i g)\}$ the net output signal from the Outer sensory system

The initially sensed physical parameter (say temperature) which was sensed by two parameters (f, g) is now corresponded to three signaling parameters (x, y, z) defined by function β.

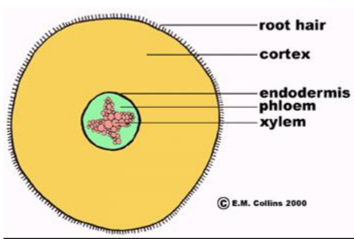


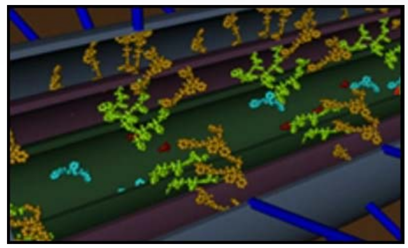


System Level Design of NTXp

Three tier skin design for the NTXp

1. The thermal insulating and pressure sustaining layer of the NTXp (shown in black).
2. Exchange layer of the NTXp (shown in blue). This is responsible for the exchange of particles of the parameter information from the outer layer to the inner sensing layer.
3. Inner sensing layer of the NTXp, which is responsible for the actual sensing. From this layer the actual sensory modules of the NTXp would be attached.





Animation of NTXp

Acknowledgments

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