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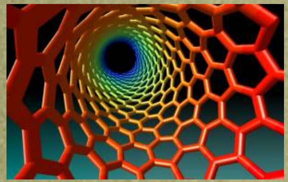


Bio → Nano → Space → Info → Lego

Best toy ever devised: SPACE LEGOS :D “Every piece has its purpose”

Experimental Data

Literature Data

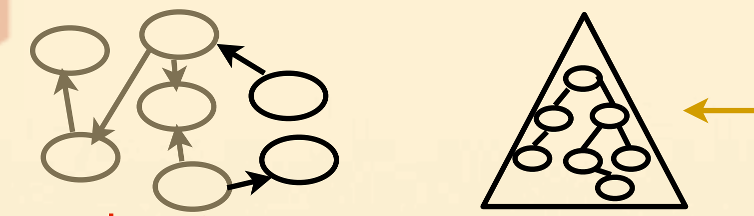
Parts Database:
Parts
Circuits
Modules

Based on the interchangeable part agenda initially led by the group from MIT (Registry of Standard Biological Parts)

Environments of Interest

Ontology-based NLP Data Integration

Automated scanning of the literature and curated management by experts



Bio-Nano-ISRU-Ontology

Computational Re-Design, Regularization, Data mining Search Optimization, Machine Learning, Clustering, Graph Algorithms

Visualization, Simulations, Modeling Tools

molecular motors: kinesin, myosin, dyneins, actin G to actin F, RNA polymerase on DNA tracks
enzymes: design of new functions by protein domain re-combination
molecular communication: cytokines
functional RNAs: ribozymes, RNAi, miRNA, siRNA, shRNA
energy production: ATPases (hydrolysis and mechanical), ATP synthase
molecular shredders: proteasomes
cell adhesion cadherin
fluorescent nano-sensors: dsRed, antifreeze proteins
cell-surface receptors
proteins storing metals: (in non-toxic form) ferritin magnetic nanoparticles
metabolism type: photosynthetic fixing CO2 cyanobactera
environmental properties: thermophilic, halophilic, ionizing radiation resistant
...

Chemical and physical properties of Parts in different Environments:

- ***Mechanical properties:*** pressure, elastic modulus, fracture toughness, wear resistance, fatigue resistance, and hardness.
- ***Electrical properties***
- ***Optical and photonic properties:*** light sensitivity, reactivity to electromagnetic and ionizing radiation, photoreactivity
- ***Magnetic properties***
- ***Chemical properties:*** acidity, alkalinity, salinity, oxidation and reduction characteristics, surface properties, hydrolysis and catalytic responses as well as differing hydrophobic, hydrophilic, or amphipathic surface properties
- ***Thermodynamic parameters:*** temperature, measures for enthalpies and free energies of formation of parts assemblies

Parts → Circuits → Modules → System

Environment

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Characteristics of Circuits for Space SynBio

respond to changes in the environment and to its internal state, searching out raw materials and energy, avoiding toxins, repairing damaged parts

Parts:

Circuits:

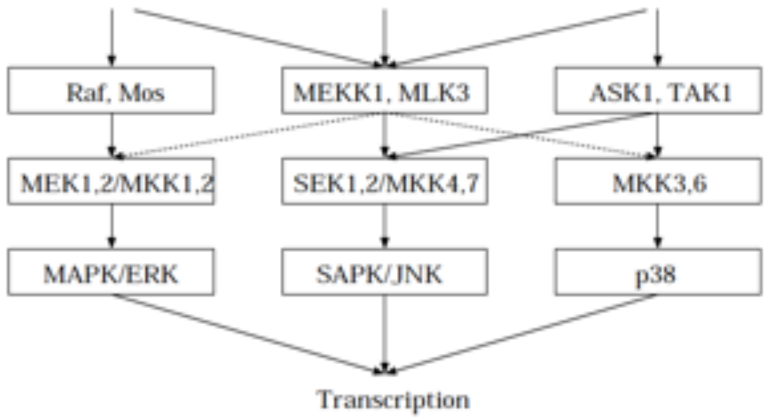


Figure 1.6 Redundancy in MAP kinase cascade

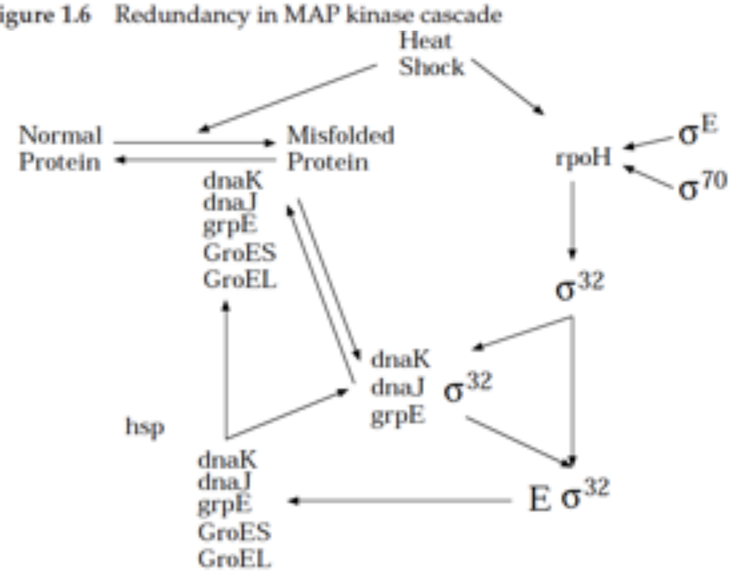
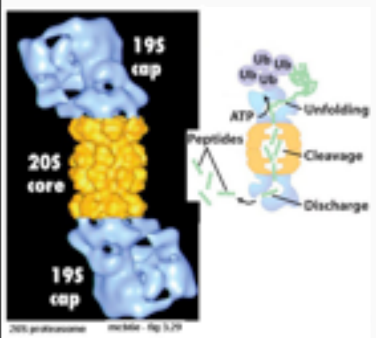


Figure 1.4 Heat shock response with feedforward and feedback control



Protein (RNA) design: promising source of new parts for synthetic biology. (1) rational design and (2) directed evolution methods. E. g. enzymes with non-natural functionalities (Jiang et al. 2008, Röthlisberger et al. 2008), design of new folds (Kuhlman et al. 2008) that can be used as scaffold for the design of new parts and also has allowed the construction of sensors for non-natural molecules (Looger et al. 2003).

Robustness since cells are noisier under stress

Redundancy via duplication of genes, existence of **homologous genes and circuits** improve reliability so that transcription of genes can be carried out even when only a small number of transcription factors are available.

Positive feedback loop to auto-regulate a gene to maintain its own expression level is an effective means of ensuring the trigger is not lost in the noise.

Adaptability to maintain flexibility

Feedback mechanisms to fit the environment: e.g. heat shock circuit- combined use of **feedforward** control and **feedback** control. The goal of the control system is to repair misfolding proteins by activating a heat shock protein (hsp), or to dissociate misfolding proteins by protease.

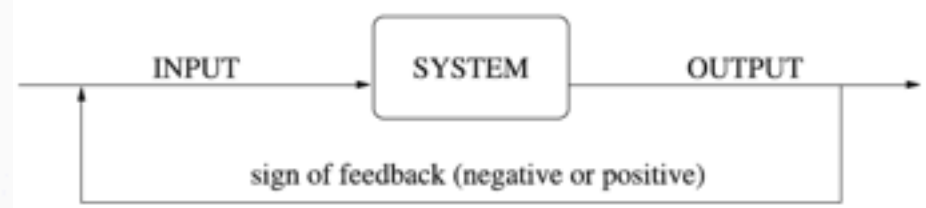


Fig. 1.2. Systems with feedback.

Duration of operation, control

Tunable internal links dials with graded control of activity

Diagnostic apparatus to inform us of errors that cannot be automatically corrected

An actuator system to carry out the repair or/and safe 'Kill' switch

Importance of orthogonality from native cell pathways

Segregate the resource-producing enzymes from the endogenous enzymes due to yields and toxicity (e.g. Chin et. al have engineered both messenger RNA and the ribosomes in *E. coli*.)

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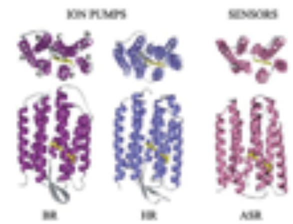
BioNanoInfoLego for Space, Future work

Biology is plastic to accommodate unfamiliar materials from the inorganic world

Reliance solely on biological elements limits problem solving capacities, need to interface with nanotechnology

Bridging Bio-Nano (biotic/abiotic) interfaces for space ISRU: Evolve (design) useful pluggable catalogs of polymers and crystals, including specificity for photosynthesis, energy production, bio-mining, and bio-production

e.g. search for light-sensitive or mechanically-sensitive and piezo components



Current Advances:

1) **Bio-glue for assembling inorganic nanocrystals: immune system antibodies** and genetically engineered polypeptides able to recognize and bind to **fullerenes**, **carbon nanotubes**, variety of **crystal surfaces** (GaN,ZnS,CdS,Fe_3O_4,$CaCO_3$), and **metals** (e.g. gold).

Near-term milestones:
(1) attaching targeted molecules or functional groups to nanostructures for ISRU
(2) Injecting signal information or energy into the cell as electrical potential, gradient transport, ion exchange mechanism (via nano-structures)
(3) Developing controllable robust interfaces for bio-based ISRU manufacturing techniques in the extremophile cell

2) **Proteins that produce mechanical motion in the cell have been used *in vitro* to transport nanoscale objects in a directional manner:** propelling protein filaments **(microtubules) down lithographically defined tracks**. Enzyme ATP synthase, a membrane protein with a 'head' that rotates as it converts ADP to ATP (or vice versa), **can be used as a molecular motor to drive rotary motion at the nanoscale** (Soong *et al*).

Near-term milestones:
developing controllable robust interfaces for bio-based ISRU transport in space environments

3) **Viruses employed for nanowires/ nanotube synthesis:** virions (viruses rendered inert by the removal of their genome) used as templates for moulding inorganic. Recognition peptides was added to the surfaces of **M13 bacteriophag**e so that they bound ZnS or CdS, acting as templates for the **synthesis of polynanocrystalline nanowires** (Mao *et al*). Similar modifications to the **tubular protein sheath of the tobacco mosaic virus** so that it can bind metal ions such as cobalt, potentially enabling the virus to **template magnetic nanowires and nanotubes** (Francis *et al)*.

Near-term milestones:
developing virions for cyanobacteria for ISRU nanowires and nanotube production

4) **Biomolecules can be immobilized in membrane-mimetic nano environments:** bacterial rhodopsin (Meier *et al*), photosystem I (Zhang *et al)* and other membrane proteins retain their integrity and function when immobilized in thin, robust films of crosslinked copolymers with a hydrophilic–hydrophobic–hydrophilic sandwich structure, mimicking the environment of lipid membranes. **BR** was used to actively pump protons against a pH gradient and thereby to reduce hydrogen ion leakage across the proton exchange membrane of a **fuel cell** (Ho *et al*)
Photosystem I assembly and pigment molecules can effect light-activated electron transport, with applications in **photovoltaic technology**.

Near-term milestones:
(1) biomimetically simulating cell function by arraying cell motors, bioenergetics,
or subcellular molecular assemblies on organic scaffolds.
(2) develop fuel cells using BR and Photosystem I and other proteins in vitro in extremophile

Goal - new syn-bio-nano technologies for ISRU:
- controlled self-organization and swarm-forming behavior of cells for mining, production, transport, terraforming
- controlled self-replication
- easy self-diagnostic
- bio-nano information processing and programmability
- bio-nanorobots - actuation, sensing, signaling (sensory targets water, oxides, minerals, can self-replicate when target is detected)

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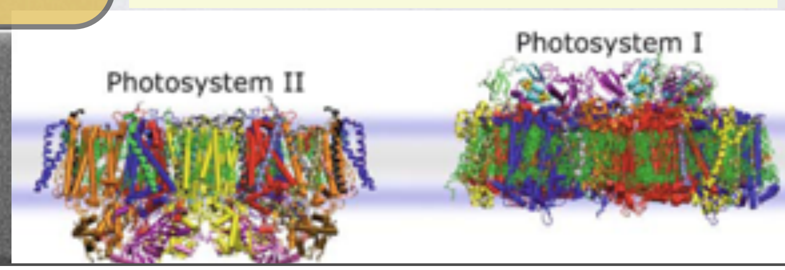


Examples of Opportunities and Challenges for synthetic biology in Space

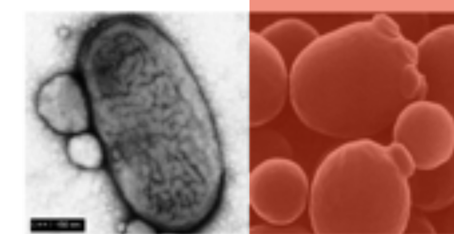
Photosynthesis has immense appeal for the closed cycle capture of energy from the Sun in forms**. Re-engineering biological photosynthesis for greater efficiency**, maximizing metabolic flux through specific biosynthetic pathways.

Fuel, Oxygen, Water, Food producing cell compartments (e.g. use fluorolipids – fatty acidlike molecules that contain a fluorocarbon chain in place of a hydrocarbon chain)

Design **cyanobacteria to efficiently repair its DNA** (resulting in great resistance to radiation) similar to Deinococcus

Design "Minimal genome" (chassis) or artificial protocells for space – eliminate genes that can lead to large mutations and genome re-arrangements in response to stress etc (space conditions)

Enzyme Solar Cells (e.g. Bacterial Rhodopsin)



Research on **non-biological photosynthesis** (where "photosynthesis" might include bio-inspired physical and chemical reactions or more straightforward photochemical or photothermal processes that generate fuels or store energy)

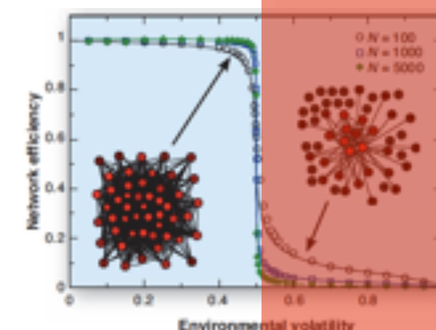
Bio-solar voltaic
Microbial fuel cells

Piezoelectric proteins

Bio-nano information processing and programmability

Freeze-dry, heat and radiation withstanding spore formation in cyanobacteria

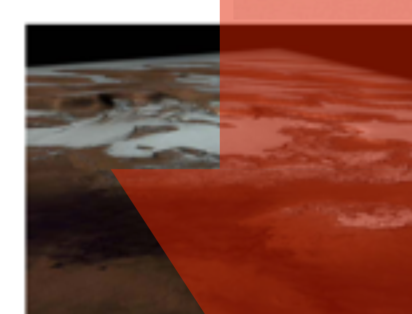
Directed evolution via adaptation in selected environment, the optimization of genetic constructs with the estimation of mutation sites or via *in silico* evolution causing the needed phase-transition for:
1) greater efficiency photosynthesis 2) maximizing metabolic flux 3) creation of orthogonal genetic and protein codes in extremophiles as chassis for space conditions



Develop **bacteria consortia** for ISRU mining/ production, **ability to compartmentalize** different biosynthetic reactions in different cells that are chemically incompatible with each other to perform in sequential reaction steps

Easy self-diagnostic

Microbe Solar Cells/Community-Solar Panel (e.g. Rhodobacter/Geobacter)



Controlled swarm-forming behavior of cells for mining, production, transport, terraforming

Controlled self-replication

In situ cell video-surveilance

Bio-nanorobots - actuation, sensing, signaling (sensory targets water, oxides, minerals, can self-replicate when target is detected)

Nano-tube radio control: re-design cell circuits to allow the use of a laser or radio-waves to communicate with each other