Synthetic Biology: Duct Tape for a Mars Mission

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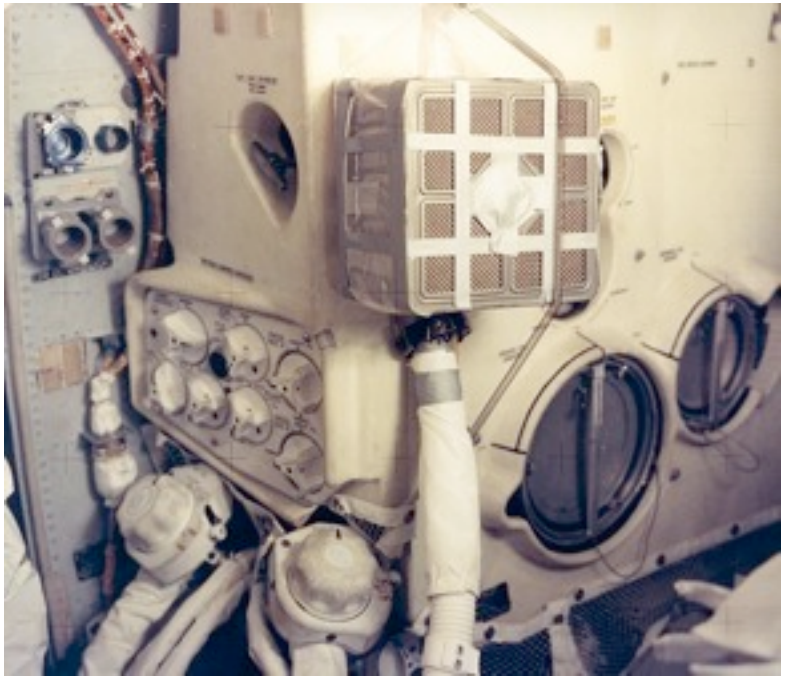
Respond to the Unexpected

- On a long term mission one should probably plan for the unexpected
  - To state the obvious: one cannot send spare parts to Mars quickly
- You can send information, so tools that convert that information into physical materials should be a part of any mission that involves long travel times
- Bring flexible, general use tools that will give you the ability to respond to new problems as they arise

Inspired by the Example of Apollo 13

- Give the earth-bound support team more to work with



So, Bring a Big Tool Kit

- DNA doesn't weigh much
  - 1,000,000 different genes, 30 grams, a few cubic inches
- So bring a large collection of genes
  - Enzymes, synthetic pathways
  - Regulatory networks
  - Sensors
  - Structural proteins
  - Antibody backbones
  - Human genes
  - Protein and mAb drugs
    - Non-exclusive license for use outside orbit may not cost much…

Design Here, Build There

- Distribute the on-board tool kit to the synthetic biology community, universities, companies, government labs
- When the unexpected happens, you can deploy a broad range of engineering resources to find a solution using the tool set available on the mission
- Transmit a recipe, build a new strain and voila!

Molecular Biology on Mars

- Bring a few simple pieces of equipment
- Design protocols for simplicity and "supportability"
- Manufacture reagents on site
- Use enzymatic DNA amplification to propagate parts
- Repurpose more complex analytical tools from other missions
  - Microscopes, cameras
  - Miniature mass spec
  - Biosensors?

Molecular Biology Equipment

- Re-useable pipets and plasticware
- Pocket Thermocycler (e.g., LavaAmp)
- Electroporator and cuvettes
- Incubator
- Gel box, light source, camera stand
- Low speed centrifuge
- Under 5 kg all in

Molecular Biology Reagents

- Develop protocols based on crude purification of enzymes and reagents
  - Thermostable enzymes produced in low temp strains
  - Bacterial strains engineered to produce dNTPs, etc.
  - Protocols based on cell lysates instead of purified enzymes
- Produce antibiotics using fermentation
- Agarose substitute from agriculture or fermentation
- Enzymatic methods to amplify primers
- Bring some low weight reagents (e.g., SYBRSafe)?

Assemble Pathways from an Onboard Library

- PCR amplification from pure samples or low-complexity pools (e.g., 100 genes/pool)
- Recombinational cloning into appropriate vectors
- Transform using electroporation into E. coli
- Bacterial conjugation to transfer into appropriate strains or into a plant

Bring Diversity for Engineering

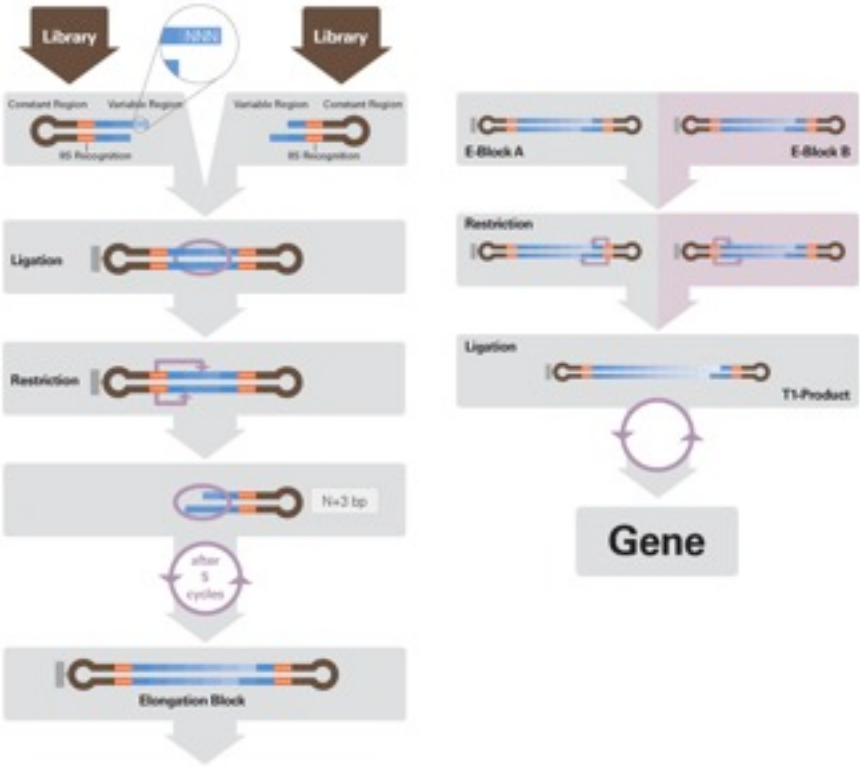
- Include a wide variety of enzymes and all possible variants of these
  - E.g., a few thousand enzymes and a few thousand single amino acid variants of each
  - Store in pools, recover using PCR
- Engineer genes for easy recombination
- Use this kit to select functions here
- Mix and match to build new functionality there

De Novo Gene Synthesis?

- The upside is access to any DNA sequence
  - But, it requires more infrastructure
- Chemical synthesis of oligonucleotides requires a set of reagents that are unstable and difficult to produce
- Generally feasible only within a functioning industrial base
  - Probably more trouble than it is worth until there is a broad industrial base

Enzymatic Gene Synthesis

- Enzymatic method based on libraries of pre-built oligos might be viable



R&D

- Self-supporting protocols
  - Isolate all the reagents you need using the on-board kit
  - Repurpose available materials
- Appropriate fermentation equipment and protocols
  - Somewhere between making beer in a garbage can and single-use pharmaceutical methods
- Robust, small instruments
- Production strains for mission materials
- Build the 1,000,000 gene kit

Duct Tape For Mars

- On site production of supplies will save weight and "pay for" the cost of molecular biology and fermentation capabilities
- Adding a diverse tool set to the mission would add little weight and complexity but could be invaluable
- Start now with research to provide these tools