Synthetic Biology for Space Exploration

# Introduction: The Challenges of Space Settlement

On December 11, 2017, President Trump issued Space Policy Directive 1, which outlined new long-term exploration goals for the United States government’s human spaceflight programs. It stated, “the United States will lead the return of humans to the Moon for long-term exploration and utilization, followed by human missions to Mars and other destinations.”[[1]](#footnote-1) To realize a goal of long-term utilization, humans will have to go beyond short expeditions to the Moon or Mars and begin constructing infrastructures and systems that will allow for permanent human presences in space.

One of the most challenging aspects of long-duration space operations will be creating an outpost that is as self-sufficient as possible. Shipments of important materials from Earth will likely be difficult and cost-prohibitive. The more that a permanent human outpost can rely on itself to meet material needs, the less strain will be placed on the Earth-outpost supply lines. An illustrative example is provided by the physical constraints on spaceflight – every kilogram of payload delivered to Mars will require the launch of 99 kilograms of fuel.[[2]](#footnote-2) Ideally, a space outpost will tend as much as possible towards “material closure.”[[3]](#footnote-3) Material closure, as an ideal, means that an outpost would neither take in matter from its surroundings nor emit waste elsewhere. Although perfect material closure is probably not possible, it is a useful design principle for space outposts.

Life support systems, the creation of a maximally independent biosphere capable of sustaining human life, will be key in a space outpost. This is a significant undertaking – on Earth, chemical elements such as carbon, nitrogen, oxygen, phosphorous, and sulfur are all continually exchanged between the atmosphere, lithosphere, and the biosphere in complicated, self-regulated flows that make life possible. Recreating systems to serve as substitutes on a distant world is a tall order. The biosphere created must be able to sustain life of many different complexities ranging from microbes to plants to, most importantly, the human inhabitants of the outpost. Unlike on Earth, where chemicals can take thousands of years to go through the biogeochemical cycles and large quantities are stored in the oceans and crust, an isolated, artificial biosphere must operate with relatively fast cycles and small reservoirs.2 For an example of what can go wrong, one need look no further than the experience of Biosphere 2 in the 1990s, an attempt to construct a self-contained biosphere that ultimately failed for a variety of reasons. One key factor is that oxygen within Biosphere 2 fell to 14% of the atmosphere (from 21% on Earth generally) due to the presence of excessive photosynthetic bacteria in the soils.[[4]](#footnote-4) Clearly small oversights can wreck the careful balance of a biosphere.

Beyond life-support, a space outpost’s self-sufficiency also relies on it being able to meet its own material needs as much as possible. Modern industrial and chemical practices rely on a vast, often globalized supply chain that will be difficult to extend to an interplanetary range, especially during early stages of an interplanetary outpost. Therefore, alternate means of manufacturing will need to be developed. This is especially true for a few important sectors: materials, medicines, and useful organic chemicals. Materials will be required to replace, repair, and expand on-site facilities, possibly with 3D-printing technology. Medicines will be required to treat any number of difficult-to-foresee medical problems that could arise in crew members, especially for long-term missions. Useful organic chemicals such as solvents or reagents may be in conducting scientific work in space, one of the most prominent drivers of early exploration.

In all of these cases, a main thrust of the program ought to be emphasizing flexible, general-purpose solutions. New capabilities will be needed as the mission continues and new needs arise. The need for adaptability can come from both accidental and deliberate shifts. Accidental shifts may be required by unforeseen circumstances, for instance, as in Biosphere 2, the ecological system may require adjustments that were not prepared for. Deliberate shifts occur as missions continue, lasting months and years: goals and therefore requirements may be changed and therefore an outpost’s needs will change along with them.

# Synthetic Biology and Space Exploration

## What is Synthetic Biology?

Synthetic biology is “the design and construction of new biological systems not found in nature.”[[5]](#footnote-5) As a science, it seeks to understand biology from the bottom up by constructing new biological systems to gain insight into how naturally occurring systems work and function. As a discipline of engineering, it creates the basis for a new sector of biotechnology focused on construction. Rather than move genetic material or functionality from one organism to another, synthetic biologists construct *sui generis* systems that perform functions no natural organism does, or perform natural functions through entirely new pathways.

The National Academies summarizes the impact of synthetic biology by contrasting it with other approaches to biotechnology. Synthetic biology has at its core the principles of “abstraction, modularization, standardization, decoupling, and modeling.”[[6]](#footnote-6) These principles allow for much easier development of new biotechnologies, because the low-level elements can be naturally combined into functional units that are themselves built into progressively larger systems. Thus, high-level design can occur independently from the low-level details, just as computer programming allows a software designer to focus on the highest-level logic rather than the intricacies of hardware operation. This approach makes synthetic biology potentially much more powerful, flexible, and extensible than earlier paradigms of biotechnology.

## The State of the Art and the Future in Synthetic Biology

 Thus far, the main targets for synthetic biology have been the creation of new genetic circuits and capabilities in *E. Coli* and strains of yeast. (The use of yeast is unsurprising considering that humans have been using yeast to perform chemistry – fermentation – for millennia.) On the horizon, synthetic biologists have also discussed the possibilities of building multicellular, complex organisms, or perhaps communities of several engineered microorganisms, but the technical capability is far from routine engineering of these more complicated organisms.[[7]](#footnote-7)

 A major point of interest in synthetic biology is the creation of entirely new organisms from “scratch.” The development of artificial cells along these lines has been an active area of research for years, but there are not yet self-replicating, self-maintaining artificial cells.[[8]](#footnote-8) A similar approach is to attempt to strip down natural cells to as few functions as possible, as was done by scientists at the Venter Institute in 2010 when they developed a new microorganism containing only 473 genes.[[9]](#footnote-9) Such cells are not viable outside of their laboratory environments.

 Going forward, many believe that the future of synthetic biology research lies in the creation of platform technologies, those that are specifically intended to create the basis for future technological development. These “platform technologies” will then be applicable to a broad range of areas of technological development.[[10]](#footnote-10) One example of a platform technology would be well-characterized host cells that serve as chassis for engineered capabilities. Again, an analogy with software development is helpful here. Software development became much easier once tools like compilers allowed humans to work on more abstract levels, trusting the already-constructed platforms to translate their instructions into low-level machine code. The development of platform technologies for synthetic biology will allow for faster development along standardized lines, thus enhancing the ability for one research group to build on the work of another.

## Synthetic Biology for Space Outposts

 Synthetic biology is extremely well-suited to address many of the challenges we outlined earlier for a space outpost.[[11]](#footnote-11) This is because of two different characteristics of the field: first of all, synthetic biology has applications in precisely the places that space outposts will need new capabilities, and second, the characteristics of synthetic biology as a manufacturing platform line up well with the needs of an outpost.

 Earlier, we identified materials, medicine, and industrial chemicals as serious manufacturing challenges to a space outpost. A radical change in the production of materials has been identified by the National Academy of Engineering as one of the most promising applications of synthetic biology.[[12]](#footnote-12) The production of pharmaceuticals through synthetic biology has already passed from speculation into commercial reality – a precursor chemical for anti-malarial drugs, artemisin, can now be produced in *E. Coli* and yeast. This artemisin has already entered the commercial market and is competitive with traditional supplies.[[13]](#footnote-13) Although anti-malarial drugs will hopefully not be required on space outposts, this proof of concept suggests that complicated pharmaceutical molecules can be produced via synthetic biology. In the future, synthetic biology could be used to produce pharmaceutical molecules directly within the body, targeting them precisely.[[14]](#footnote-14) Many companies are already attempting to use synthetic biology to develop important industrial chemical such as rubber and biofuels, food chemicals like sugar, and even antibiotics and other medicines.[[15]](#footnote-15),[[16]](#footnote-16)

Current synthetic biology applications are often pitched towards the generation of biofuels, which can generate fuel from organic waste. On Earth, this often serves as a climate or environmental benefit, allowing waste products to be used instead of discarded. In space, these benefits become much more immediate, as any waste product that cannot be recycled or reused represents a gap that must be patched by some input to the system. Thus, the sustainability motivation behind synthetic biology applications aligns precisely with the needs of space outposts. Finally, we note that there is incredible possibility of flexibility in synthetic biology. The “manufacturing facility” for synthetic biology could be potentially reduced to some growth medium which is common to many different application organisms and starter cultures for which could be easy to distribute to outposts in a way that chemical precursors or industrial facilities would not be. In addition, there is significant hope (see next section) that a common, open-source foundation can be laid for synthetic biology going forward. In this eventuality, it is possible that nearly any desired organism could be synthesized from a few pieces of equipment. Already, researchers have demonstrated the creation of a “digital-biological converter” which allows the information specifying a particular biological component to be directly synthesized.[[17]](#footnote-17) This combination of broad power, natural sustainability, and immense flexibility makes synthetic biology a natural fit for space outposts.

Already, researchers and space agencies are identifying synthetic biology as a promising future for on-site manufacturing on a space outpost.[[18]](#footnote-18) In a 2015 document outlining technological challenges and roadmaps for space exploration, NASA identified biosensing, bioluminescence, and biofuel production as likely solutions to engineering challenges encountered on missions to Mars.[[19]](#footnote-19) Another study looked specifically at the reduction in mass for a 916-day Mars mission enabled by synthetic biology manufacturing and estimated that the mass of fuel-production facilities could be reduced by 56%, the mass of food shipped reduced by 38%, the mass of a six-person habitat could reduced by 85% (by using bio-produced 3D printing materials), and the need for shipping out any significant store of common pharmaceuticals such as acetaminophen could be eliminated entirely.[[20]](#footnote-20)

## Recommendation 1: Bolster NASA Efforts in Synthetic Biospheres

 Little of the synthetic biology research currently conducted is directly pitched towards space. As a result, NASA may find itself unable to use synthetic biology technologies without significant modification. It may be easier to involve NASA directly so that space needs can be co-designed with other goals in synthetic biology. NASA ought to be brought in (possibly through the structure created from Recommendation 3) to the decision making process at agencies like NSF or NIH so that synthetic biology research develops in a way that maintains usefulness for space outposts.

 NASA should also be supplied with money specifically to investigate synthetic biology of self-contained biospheres, identify uses for existing synthetic biology, and direct future research into new capabilities.

## Planetary Protection

 For the foreseeable future, the primary aim of expeditions to other planets will be scientific. Studying Mars could teach us a great deal about the origins of life on Earth, the nature of the early solar system, and whether life exists, or has ever existed, on Mars itself. Each of these questions will be more difficult to study if the Martian environment is disrupted by human activity.

 Planetary Protection (PP) is the field of study concerned with minimizing biological impact on other planets.[[21]](#footnote-21) While there are ethical reasons to care about PP, such as our obligation not to interfere with natural ecosystems or pristine planetary environments, there are also serious practical ones. If we wish to learn from the chemical or microbial environment of Mars, we must not contaminate it. Such an obligation should be viewed as part of the obligation towards future scientists who will wish to study these environments.

 Synthetic biology systems for space exploration introduce several interesting wrinkles for planetary protection. Designing systems specifically to survive on other planets seems to greatly increase the risk of contamination far from the outpost itself. While any human outpost will have some effect on its surroundings, those outposts should still adhere to a philosophy of harm reduction.

 One place that synthetic biology changes significantly due to planetary protection concerns is the potential of artificial cells. On Earth, artificial cells’ minimalism makes them a low risk for escape – Earth’s biosphere has spent 4.5 billion years evolving to push out all competitors, so custom-purpose organisms without natural defenses are unlikely to spread far. Even in a report focused on biosecurity, the National Academies of Sciences, Engineering, and Medicine considered the risk of an artificial pathogen spreading as “a relatively low level of conern.” However, this may not be the case in space, where the ambient environment is qualitatively different. Biosafety and biosecurity in space will take on different characteristics and need to be considered separately from biosafety on Earth, because the systems being protected are different.

## Recommendation 2: Include Planetary Protection in NASA Efforts

 Since planetary protection overlaps with, but is not identical to, the biosafety and biosecurity conversations happening surrounding terrestrial synthetic biology, we ought to be developing an independent system of assessment for planetary protection. NASA should be provided with the necessary funds and personnel to develop a set of guidelines both for how missions should be conducted and how synthetic biology can be modified for a space environment in which forward contamination is a concern. This should result after a review of the goals of planetary protection in the context of long-term

# Building the Synthetic Biology We Need

 It’s clear that the possibilities offered by a synthetic biology approach to the space operations and outposts are extremely enticing. In this section we will examine what changes are needed on Earth to create a viable synthetic biology future in space.

## Better Federal Coordination of Synthetic Biology

Thus far, US government support for synthetic biology research has been financially strong but still quite scattered. Federal funding for synthetic biology has risen to $140 million a year in the last decade, however, there is no overarching structure or governance within the government that coordinates these efforts.[[22]](#footnote-22) In addition, over two-thirds of the US funding for synthetic biology comes from DARPA and other Department of Defense sources, while only 0.02% of it comes from NASA.[[23]](#footnote-23) While the DoD research is valuable and will likely have spillover applications to the space setting, its focus on biosafety and biosecurity is not necessarily suited to the work required to develop synthetic biology for space outposts.

There is currently no federal-level coordinating body for synthetic biology. Such structures allow the government to keep track of the current research, develop technology roadmaps and forecasts, and provide a unified point of contact for industrial interests. As there is no such body right now, development of synthetic biology technologies is not coordinated across different agencies, which can lead to inefficiencies. A more unified governance structure and strategy would allow for less duplication of effort and better integration of research initiatives from different areas, for instance, both civilian and military.

## Recommendation 3: Creation of a Federal Coordinating Body

The U.S. government should create a centralized place for synthetic biology research coordination. The most obvious type of coordinating body that could be created would be a subcommittee of the National Science and Technology Committee under the Committee on Technology. Other subcommittees in this category include one on “Advanced Manufacturing” and one in nanotechnology, both of which are similar to synthetic biology in their ability to create technological and scientific change. Options may also include the creation of a permanent position in the Office of Science and Technology Policy, which would provide the executive branch with an institutional location for expertise in synthetic biology.

## Supporting the Open Biology Commons

 Since 2006, an organization called the BioBricks Foundation has been operating to encourage an open exchange of synthetic biology techniques.[[24]](#footnote-24) They endeavor to create a library of “BioBricks” which are individual biological “parts” intended to be interoperable. These are submitted by “Contributors” and can then be downloaded by “Users.” Contributors waive intellectual property rights to the parts they submit, while Users are expected to contribute their own advances back into the common space. This regime protects the freedom of users to create new works of synthetic biology without fearing that they will accidentally infringe on a patent.[[25]](#footnote-25) It also provides clarity: many who work in intellectual property law have become concerned that a confusing network of patent obligations creates an “anti-commons” in which innovation is discouraged by unclear rules.[[26]](#footnote-26) By contrast, an open ecosystem for intellectual property encourages collaboration. A collaborative environment further encourages the standardization of parts, which enables more thorough characterization and better design. This commitment to openness also dovetails with ongoing efforts in the US, EU, and worldwide towards “open science” which includes several directives from the Office of Science and Technology Policy. According to the National Academies, “The rationale for opening the methods and outcomes of research is strong, multifold, and increasingly accepted by scientific, engineering, and biomedical investigators.”[[27]](#footnote-27)

 An open source environment such as BioBricks could be very beneficial for future development of synthetic biology, by helping to realize the “platform technologies” discussed above. Just as software projects such as Python and Linux make up a commonly owned infrastructure from which commercial, protected software can be built, the same can be true for biotechnology.

 One obvious concern is whether, as the technology becomes more commercial, private companies will wish to contribute to the BioBricks commons. BioBricks does not use any kind of “copyleft” technique as some software projects do – there is no requirement that modifications or improvements on its properties be returned to the repository, and such improvements can be patented.23 This makes it somewhat “leaky.” However, the relevant example is again software. Software companies have made many contributions to open source projects since the movement began in the 1980s.[[28]](#footnote-28) Private companies benefit significantly when there is a substantial shared platform, since new workers are likely already familiar with the basic technical processes needed to create new products, an economic incentive known as the “alumni effect.”[[29]](#footnote-29) Companies also benefit when their own work is open-sourced because users themselves can diagnose issues and suggest bug fixes.

## Recommendation 4: Support Open Synthetic Biology

 One major threat to open synthetic biology is that broad or foundational patents granted to one corporation could be used to stifle or control the market in the future. To prevent this, the government should establish a body that will monitor the patent landscape. Under the Bayh-Dole Act, the government has broad “march-in” rights to force the licensing of patents which it has invoked or threatened to invoke in the past to prevent patent abuse in pharmaceuticals or to ensure military access to technologies. As synthetic biology is likely to be a critical technology, the government should work aggressively to ensure that patent holders behave responsibly.

 From a space perspective, there are several reasons to favor an open development environment for synthetic biology. One of the great potential benefits of synthetic biology as a manufacturing platform in space is its flexibility: a large number of needs may be met from the same base equipment needed to synthesize and grow organisms. However, this benefit would be curtailed if different organisms and biological parts cease to be interoperable and common. Openness also allows for easier innovation, meaning that if a space outpost is actively trying to engineer its biosphere as new problems arise, it will be easier for many contributors to design potential solutions, bringing to bear the full knowledge base of synthetic biology on a problem.

 There are several outstanding problems in the world of open biotechnology. First is the development of the baseline technical standards, such as common languages for the description of biological parts and their construction. Second, the BioBricks commons must be protected from patent trolls and investigate means to prevent too much of the intellectual property it represents from “leaking” out of the public domain. (These last two can be potentially combined, as standards-setting can be an important part of managing an intellectual property environment.[[30]](#footnote-30)) Finally, broad patents with significant downstream effects could potentially lead to monopoly effects in the synthetic biology sector, preventing a widespread, open commons from taking root. The government has broad overview of patent rights that can be deployed in this context.[[31]](#footnote-31)

## Recommendation 5: Create Interoperable Biotechnology Standards

 Organizations like NIH should partner with NIST to develop a common language for synthetic biology. In addition, the government should integrate these standards into its ongoing “Open Science” initiatives. In addition to sharing data openly and making the results of publicly-funded research publicly-available, working synthetic biology innovations into a common platform and aligning with industry standards should be a precondition of public funding.

# Conclusions

 Over the next few decades, human exploration of space will continue. While the lessons learned from both previous expeditions (Apollo) and long-term space living (International Space Station) will undoubtedly prove useful, long-term space habitation requires a degree of self-sufficiency we have not yet been able to demonstrate. Ultimately, it requires the creation of a new biosphere that will be minimally dependent on inputs from Earth. As this will need to be an actively-managed system that is capable of producing everything astronauts will need to live on a deep space outpost. For the synthetic biosphere, synthetic biology is a natural choice.

 However, for synthetic biology to realize this goal, we will need to build a cohesive, shared environment for the tools and designs of the field. This will require building a new framework for intellectual property law in the biotech sector and funding the creation of technical standards. Only by ensuring an open ecosystem can we realize the great gains, both on Earth and in space, which can be realized by synthetic biology.

1. <https://www.whitehouse.gov/presidential-actions/presidential-memorandum-reinvigorating-americas-human-space-exploration-program/> [↑](#footnote-ref-1)
2. Larson WJ, Wertz JR (eds). 1999. *Space mission analysis and design*, 3rd edn. El Segundo, CA: Microcosm Press. [↑](#footnote-ref-2)
3. M. Nelson et al., “Key ecological challenges for closed systems facilities” *Advances in Space Research* 52 (2013) 86–96 [↑](#footnote-ref-3)
4. Severinghouse, Jeffrey P. et al, Eos, Vol. 75, No. 3, January 18, 1994 [↑](#footnote-ref-4)
5. Schmidt, et al., *Synthetic Biology: the technoscience and its societal consequences.* [↑](#footnote-ref-5)
6. National Academy of Engineering and National Research Council, *Positioning Synthetic Biology to Meet the Challenges of the 21st Century: Summary Report of a Six Academies Symposium Series*. 2013. [↑](#footnote-ref-6)
7. Ceroni, Francesca, and Tom Ellis. "The challenges facing synthetic biology in eukaryotes." Nature Reviews Molecular Cell Biology, 2018. [↑](#footnote-ref-7)
8. Noireaux, Vincent, Yusuke T. Maeda, and Albert Libchaber. " Development of an artificial cell, from self-organization to computation and self-reproduction." PNAS 108, no. 9 (2011): 3473-3480. [↑](#footnote-ref-8)
9. Hutchinson III, Clyde A. et al. “Design and synthesis of a minimal bacterial genome.” *Science* Vol 351, 6280 (2016). [↑](#footnote-ref-9)
10. Kitney, Richard, and Paul Freemont. "Synthetic biology – the state of play." *FEBS Letters* 586 (2012). [↑](#footnote-ref-10)
11. Menezes AA, Montague MG, Cumbers J, Hogan JA, Arkin AP. 2015 “Grand challenges in space synthetic biology.” *J. R. Soc. Interface* 12 [↑](#footnote-ref-11)
12. National Academies of Sciences, Engineering, and Medicine. *Biodefense in the Age of Synthetic Biology.* Washington, DC: National Academies Press, 2018. [↑](#footnote-ref-12)
13. Paddon, Chris J., and Jay D. Keasling. "Semi-synthetic artemisinin: a model for the use of synthetic biology in pharmaceutical development." *Nature Reviews Microbiology* 12 (2014) [↑](#footnote-ref-13)
14. Álvarez B, Fernández LÁ. Sustainable therapies by engineered bacteria. *Microbial Biotechnology*. 2017;10(5):1057-1061. doi:10.1111/1751-7915.12778. [↑](#footnote-ref-14)
15. <https://www.bio.org/articles/current-uses-synthetic-biology-renewable-chemicals-pharmaceuticals-and-biofuels> [↑](#footnote-ref-15)
16. Khalil, Ahmad S, and James J. Collins. "Synthetic biology: applications come of age." *Nature Reviews Genetics* 11 (2010) [↑](#footnote-ref-16)
17. Boles, Kent S. et al. “Digital-to-biological converter for on-demand production of biologic.” *Nature Biotechnology* 35, 672–675 (2017) [↑](#footnote-ref-17)
18. Menezes AA, Montague MG, Cumbers J, Hogan JA, Arkin AP. 2015 “Grand challenges in space synthetic biology.” *J. R. Soc. Interface* 12 [↑](#footnote-ref-18)
19. *2015 NASA Technology Roadmaps TA 7: Human Exploration Destination Systems* [↑](#footnote-ref-19)
20. Menezes AA, Cumbers J, Hogan JA, Arkin AP. 2015 “Towards synthetic

biological approaches to resource utilization on space missions”. *J. R. Soc. Interface* 12: 20140715. [↑](#footnote-ref-20)
21. A. Frick et al., “Overview of current capabilities and research and technology developments for planetary protection” *Advances in Space Research* (2014) [↑](#footnote-ref-21)
22. Si T.; Zhao, H. “A brief overview of synthetic biology research programs and roadmap studies in the United States.” *Synthetic and Systems Biotechnology* 1 (2016) [↑](#footnote-ref-22)
23. The Wilson Center Synthetic Biology Project, “U.S. Trends in Synthetic Biology Research Funding.” September 2015. [↑](#footnote-ref-23)
24. <https://biobricks.org/biobricks-history/> [↑](#footnote-ref-24)
25. Hilgartner, Stephen. "Novel constitutions? New regimes of openness in synthetic biology." *BioSocieties* 7, no. 2 (2012) [↑](#footnote-ref-25)
26. Schmidt, et al., *Synthetic Biology: the technoscience and its societal consequences.* [↑](#footnote-ref-26)
27. National Academies of Sciences, Engineering, and Medicine. 2018. *Open Science by Design: Realizing a Vision for 21st Century Research*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/25116>. [↑](#footnote-ref-27)
28. Bitzer, J and Schroder, Phillip J.H. *The Economics of Open Source Software*. Elsevier 2006. [↑](#footnote-ref-28)
29. Lerner, Josh, and Jean Triole. "The Simple Economics of Open Source." *Journal of Industrial Economics* 52 (2002): 197-234. [↑](#footnote-ref-29)
30. Fitzpatrick, Ethan R. “Open Source Synthetic Biology: Problems and Solutions” 2013. *Law School Student Scholarship*. [↑](#footnote-ref-30)
31. Kapczynski, A. and Kesselheim, AS. “‘Government Patent Use’: A Legal Approach To Reducing Drug Spending.” *Health Affairs* 35 (5). May 2016. [↑](#footnote-ref-31)