The case for biotech on Mars

The stepwise application of biotechnology will be instrumental to addressing four key challenges of Martian settlement.

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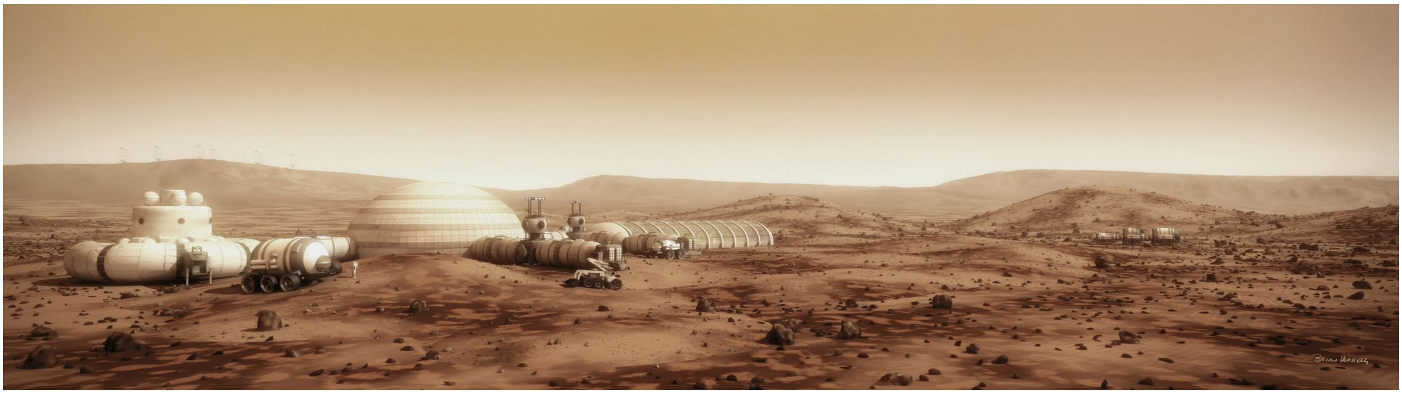
Human exploration of Mars is one of the major scientific and technological endeavors of our time. It will enable the discovery and settlement of another world while galvanizing the development of technologies to promote human flourishing on Earth. Work is underway to demonstrate that crewed missions to Mars are possible sooner and more cheaply than previously believed. This has underscored the critical need for advanced life support systems to enable such missions. How to support life—human, plant and microbial—on Mars is thus our central focus in this Comment. We lay out actionable biotechnological strategies to pursue a sustained human presence on Mars. We then argue why biotech is uniquely suited to address multiple crewed-mission needs and lay out how its flexibility enables progressive, stepwise integration into traditional life support systems over time.

Preparing for Mars

Since the Apollo era, travel to Mars has been viewed as the next major step for human spaceflight[1]. Recent milestones in space engineering have placed us within arms' reach of its surface[2]—but we lack any system for providing extended life support once we arrive. In the aggregate, Mars offers a promising array of conditions for sustainable habitation: its proximity allows relatively tractable mission and resupply times; its equatorial temperatures are similar to those of a continental winter (although the average equatorial temperature is −14 °C, given the lack of windchill, it will feel closer to 1 °C)[3]; it contains water in surface and underground reservoirs[4,5]; its atmosphere contains life-essential elements in accessible forms; its regolith has the remaining elements needed for life[6]; and its rotational period can likely maintain essential human and plant circadian rhythms with sunlight (annual solar irradiance at the equator is ~120 W/m^2—roughly equivalent to that of Northern Europe—and a Martian day lasts 24 h and 37 min)[7,8]. Until recently, the possibility of humans traveling to Mars has been overshadowed by the technological, political and financial immensity of the endeavor (as seen in the timelines and budgets of NASA's Constellation Program and Space Launch System)[9–13]. But today, advances across diverse disciplines put Mars in sight for human exploration and settlement in the near future.

The commercial spaceflight industry has been the vanguard of this advancement, garnering several historic successes in the past three years: the first vertical landing of a suborbital rocket from space (November 2015), the first landing of a rocket that deployed a payload into orbit (December 2015) and the reuse of two first-stage booster rockets to launch the most powerful operational rocket into orbit (February 2018; second only to the now defunct Saturn V program). The first successful suborbital flight of a spaceplane designed for tourism occurred in December 2018, and test flights for the second stage of the SpaceX Super Heavy launch vehicle, *Starship*, are planned for 2020. Propelled by these and expected future[14] achievements, industry and governments are taking the first concerted steps toward a human presence on Mars. SpaceX has proposed an ambitious timeline that would bring crewed missions to the surface of Mars in 2025[14,15]. The US National Aeronautics and Space Agency (NASA) and Lockheed Martin have announced plans to create an orbiting Martian Space Station by 2028, as well as to send crews to the Martian moons by 2033 and the planet's surface in the 2040s. These efforts are concomitant with the announced plans of other national space agencies, including those of Russia (Roscosmos) and China (CNSA), to follow by mid-century.

Logistics and survivability research—crucial prerequisites for a Mars mission—have also recently made important strides. The results of the largest study on the health impacts of long-duration (>6 months) spaceflight, the NASA Twins Study[16], describe many effects of prolonged spaceflight on the human body.



An artist's impression of a future Mars colony. Credit: Bryan Versteeg/spacehabs.com

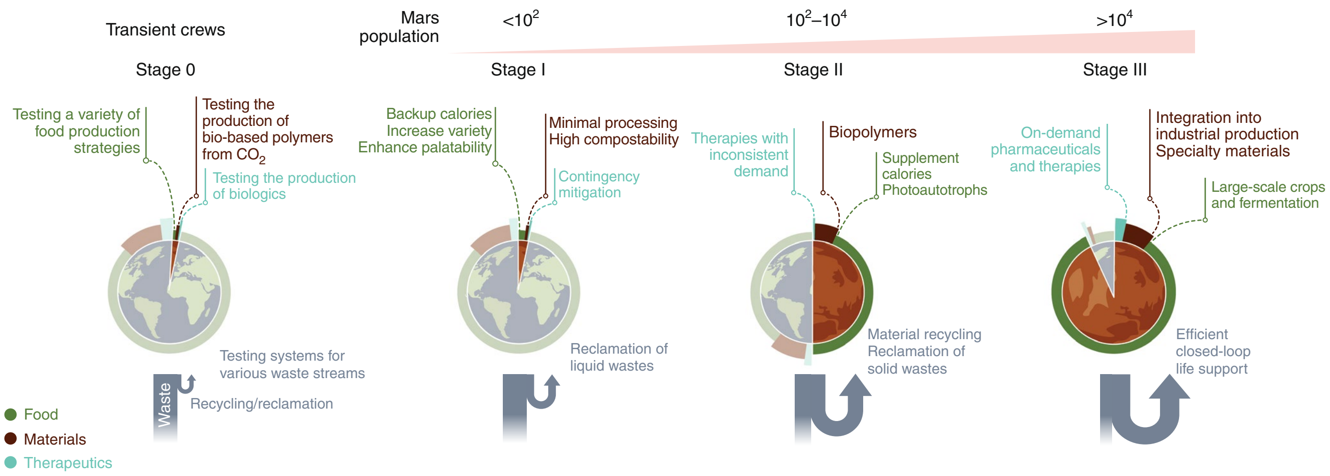


Fig. 1 | Incremental integration of biotechnology into Mars mission designs. As Mars becomes industrialized, biotech will adapt to differing demands. We focus on four primary applications: food, materials, therapeutics and waste reclamation. We envision each category playing an ever-increasing role in life support systems. Early missions will rely almost exclusively on stored cargo, with only a small-scale experimental contribution from biotech. As bioengineered solutions are vetted and optimized, crews will be able to rely more on them for core requirements. Eventually, biotech will play a prominent role in a self-sustaining Martian infrastructure.

Additional aspects of crew physical and mental health, inter-crew dynamics and mission logistics are also being studied on terrestrial Mars analog sites, follow-on one-year International Space Station (ISS) missions and the Mars-500 and HI-SEAS missions[17].

All of the above efforts indicate that crewed missions to Mars are imminent. However, human presence on Mars will still be limited by launch capacity from Earth, and as such, living off the land—via in situ resource utilization (ISRU)—will make the effort vastly more tractable and sustainable. By generating necessary supplies on site, ISRU minimizes the payload bottleneck while promoting independence, exploration and flexibility—all of which are required for long-term settlement.

Biological conversion, coalescing recent advances in the field with the inherent strengths of biology, must be a central component of ISRU on Mars. Earth's organisms represent billions of years of learning to transform raw materials into complex compounds; they also self-replicate, function in diverse environmental conditions and propagate stored information (as DNA or RNA). Breakthroughs in high-throughput DNA synthesis, multi-omics and bioinformatics have magnified our ability to construct new genetic and metabolic pathways, and the diversity of potential production organisms provides wide-ranging environmental tolerance. Bioproduction could add tremendous flexibility and versatility to missions: the universality of bioreactor infrastructure and the modularity of metabolic pathways enable ubiquitous inputs (for example, CH_3OH and CO_2) to yield diverse products. Furthermore, development of bioproduction strains can be done on Earth, requiring only the transmission of genetic sequences for synthesis and downstream production on Mars with no additional payload cost—a 'point-to-point biology' that would provide the Martian biotech infrastructure with an essential, inherent advantage. Through the above capabilities, biotech has been able to transform industries on Earth, and this power will be essential to establishing them on Mars.

In the following Comment, we explore how to leverage biology as a technology for Mars exploration by building on foundational analyses of this idea[18–20] and examining how we engineer biology on Earth for production and reclamation. Bioproduction accesses an unparalleled space of complex molecular products; its applications have ranged over millennia from mead-making to the production of recombinant insulin and novel biomaterials. Bioreclamation harnesses metabolism to transform harmful or wasted byproducts into safer, more useful forms; it has been a pillar of urban waste infrastructure for over a century.

With this background, we focus on four applications best suited for bioengineering on Mars: first, food production; second, materials development; third, therapeutics; and fourth, waste reclamation. Readers should note that we do not include energy-related applications of bioengineering, such as biofuels (for example, ethanol and methane), because these are not as well suited to the purpose as chemical systems currently in development (for example, Sabatier, reverse water–gas shift and solid-oxide electrolysis)[21]; see Fig. 1.

Biotech applied to food, materials, therapeutics and waste reclamation can be deployed incrementally within Mars habitats, enabling adaptive integration of bioengineering alongside established abiological processes for increasingly sustainable settlements. The early-stage mission applications of biotech will serve as backup systems; as their operation is vetted, biological processes will be given more central functions.

We do not believe that terrestrial microbes pose a major contamination risk[1]. Although it is possible that microorganisms brought to Mars could escape the controlled environment, such organisms would likely not be the first examples of microbial Earth–Mars contamination[22], nor would they have a high likelihood of survival when exposed to the Martian surface pressure, temperature, radiation and perchlorate content[23,24].

The opportunity to send humans to Mars—not only to explore, but to promote a long-term presence beyond Earth—is now a reality. Mars represents a technological crucible, which will drive the development of solutions that feed back to benefit some of Earth's most challenging problems as they enable Martian settlement. But to realize these benefits, we must build a more robust extraterrestrial biotech infrastructure. Technologies for space require extensive stress-testing for many years before deployment, and biotech can require even longer development timelines than hardware: for ISRU biotechnologies to be operational in time for near-term crewed Mars missions, we must expand development now.

Bioengineering and Martian resources

Long-term Martian settlements will require in situ production of supplies needed for human survival and planetary exploration. Everything from food and medicines to breathable air, industrial chemicals and building materials must eventually be produced on site. For products needed in large volumes or continuously, such as propellant and breathable air, bringing along well-established chemical processing equipment for ISRU is likely the best approach. However, for more complex consumables and for intermittent needs, bioproduction on Mars will be essential. We envision the development of this Martian bioproduction system within a staged progression of Martian settlement from total dependence on terrestrial resources to near-total independence from them. This progression is aligned with NASA's three-phase paradigm (Stage I, Earth-reliant; Stage II, proving ground; and Stage III, Earth-independent) of challenges on the journey to Mars[25]. Because of the challenges of accurate timeline prediction, we instead define the stages by population size (Fig. 1).

Our envisioned Martian bioproduction system would use common inputs and equipment, growing an entire library of production strains in a handful of shared fermenters. In examining the common inputs, we make the following assumptions about the early missions: first, they will be powered by photovoltaics (with progressive integration of nuclear reactors) and chemically fix N_2 and/or compress CO_2 from the atmosphere; second, they will extract accessible water from ice, the atmosphere, the regolith or subsurface liquid reservoirs[4,26–28]; and third, they will electrolyze water for oxygen and hydrogen.

We focus on local raw materials (C, O and N) because they comprise the majority of bacterial biomass: C (1): H (1.77): O (0.49): N (0.24): P, S, Mg, Cl, K ($\approx$0.1)[29]. For example, the elemental requirements for cells grown to $OD_{600} = 30$ in 500,000 liters are approximately seven tons of C, N and O in total and one ton of trace elements (such as P, S, Na, Mg, Cl, K and Ca)[30]. We assume that we will be able both to reclaim the majority of biomass and to supplement trace elements with bulk shipments, rather than extracting them from the regolith, in early stages.

We propose that atmospheric CO_2 and methanol, from the catalytic reduction of CO_2, will serve as common chemical and biological feedstocks[31]. Other feedstock components, such as phosphate, trace metals and additional fixed nitrogen, will be supplemented from Earth and reclaimed from waste. Eventually, these elements can be mined and refined from the regolith, but providing the equipment needed is impractical for the initial small-scale needs. With these assumptions, we discuss plausible modes of production based on current and emerging technologies, following a strategy in which each stage of implementation is meant to be additive, not displacive.

Food production. Food production is one of the most immediate uses of biotechnology on Mars[32,33]. Approximately five tons of food are required to sustain a crew of six on 3,000 calories per day for an ~500-day surface mission, with an additional eight to ten tons for transit and contingencies. Traditionally, in the interest of minimizing payload, dietary options for astronauts have favored calorically and nutritionally dense formulations over variety and palatability. For Mars missions, however, the sensory factors become critical due to their impact on psychological well-being. We see bioproduction as a mechanism to support both caloric and gustatory needs. We describe three stages of food biotech that will require progressively more complex infrastructure but will be capable of producing more varied and palatable foods to provide an increasing proportion of the crew's diet.

Although early missions will transport all food required for survival, engineered organisms, both microbial and vegetal, can supplement the core food supply and magnify future yields[34]. Because we do not envision animal husbandry—aside from insect farming[35]—becoming a major food source on Mars in the near term, engineered microbes are the best sources for essential micronutrients such as calcium, iron, vitamin B_{12}, zinc, iodine, omega-3 fatty acids, vitamin D and taurine)[36–39]. Recent advances in fermentative production of flavors, textures and foods can form the basis for new Mars-directed engineering efforts. Successful deployment will require the in-tandem development of organisms and fermenters for Martian conditions; the system must use CO_2 and CH_3OH as its sole carbon sources, accommodate unreliable solar irradiance and tolerate the potential presence of contaminants in water and regolith. To support this development, we propose scaling Martian food production in three stages: Stage I involves lithoautotrophic and heterotrophic fermentation; Stage II involves photoautotrophic fermentation and small-scale crop growth; and Stage III involves large-scale crop cultivation.

Stage I. Both methanol-using heterotrophic and CO_2-using lithoautotrophic fermentation will be used to complement the crew's diet and serve as an initial demonstration of Martian food production. Fermentation technologies also have the added benefit of shorter boot-up and production timelines (days to weeks) compared with the production of staple plant crops (weeks to months). Fermentation can be carried out in simple stir tanks or airlift reactors that use engineered organisms to produce complex carbohydrates and proteins[40,41].

Several suitable methylotrophic organisms, such as *Methylophilus methylotrophus* and *Pichia pastoris*, are already genetically characterized, industrially optimized and extensively deployed for large-scale production. Methylotrophic genes have also been heterologously expressed in model organisms such as *Escherichia coli* and *Bacillus subtilis*[41]. Such organisms can be engineered to produce a wealth of ingredients, including flavors, protein, organic acids, vitamins, fatty acids, gums, textures and polysaccharides[41]. Bioreactors with these organisms have very high process intensities, with a single 50-m^3 reactor able to produce as much protein as 25 acres of soybeans, with only a few days to the first harvest[42–44]. CO_2-using lithoautotrophs could similarly be engineered to couple their hydrogen oxidation and CO_2 fixation into oligosaccharides, protein and fatty acid production.

Maximizing yields in these microbial chassis and adapting the above organisms to Martian minimal medium remain key challenges. Initial applications can focus on small-scale sources of backup calories and on establishing benchmarks for subsequent larger-scale implementation. Demonstration of aero- and hydroponic systems to grow spices, herbs and greens would be explored in this stage[45].

Stage II. The second stage focuses on introducing photoautotrophs to synthesize food. With increasing investment in Martian infrastructure, more complex bioreactors can be deployed to grow green algae rich in carbohydrates, fatty acids and protein[46]. Several well-developed terrestrial examples of algal industrialization exist, such as *Arthrospira platensis* for food or commercial algal biofuels[47]. On Earth, the high capital costs of building reactors and supplying high concentrations of CO_2 for optimal production are commercially challenging.

On Mars, however, this challenge becomes an advantage: the CO_2-rich atmosphere can be enclosed and pressurized for algal growth. As photoautotrophic growth is scaled to meet more nutritional requirements of the crew, maintaining reliable production despite the weaker Martian sunlight and planet-engulfing dust storms will be a key challenge, requiring surface testing of several reactor designs. We do not anticipate using natural sunlight as an energy source for photoautotrophs at these stages because it alone is insufficient for growth: once solar photons have passed through greenhouse materials, photoautotrophs would receive around 17 mol $m^{-2}sol^{-1}$—up to fourfold less than their typical minimal requirements[35,48]. Thus, at this stage, photosynthetic organisms would be grown in photobioreactors or growth chambers with optimized artificial lighting.

For longer habitation, the psychological benefits of having living plants and familiar foods are substantial[49]. Much of the infrastructure required for cultivating algae can be adapted for plants, and the two may be introduced on similar time scales. On Earth, hydroponic crop growth is already well developed, with many crops competing commercially with soil-grown agricultural plants.

Stage III. Growing crops directly in minimally processed Martian regolith is a late-stage goal; there are clearly disadvantages of relying on plants for food in the early stages of colonization, including the minimal natural light, long boot-up times, large footprint, inefficient conversion of sunlight to biomass, poor genetic tractability and low caloric density. We envision large-scale crop production to be most feasible once there is a robust infrastructure in place on Mars[35].

Following photoautotroph and hydroponic plant growth in controlled environments, crews can begin soil-based cultivation of nutritionally rich terrestrial plants, such as soybeans, potatoes and peanuts. Such farming processes will require the largest initial infrastructure and generate the lowest yield of food per unit area. They will also require more time to first harvest compared with the aforementioned alternatives. Given Mars's lower insolation, prolonged sun-blocking dust storms, different inorganic nutrient profiles and potential soil toxicants, growing non-engineered terrestrial plants may be challenging, even in otherwise ideal greenhouse conditions. As mentioned above, supplemental light will be required to grow staple crops, the energy demands of which will likely only be manageable at the later stages of settlement growth[35]. Engineered microbes could be used to condition the regolith for crop growth by minimizing toxicants, enriching for specific nutrients and decomposing wastes for fertilizers[7].

Materials production. Settlements will require a variety of materials sourced on and off planet. Determining the set of essential materials is an ongoing project that could draw inspiration from remote military bases, submarines, and arctic and Mars analog research stations. Here, we focus primarily on materials that can be sourced from CO_2. Although materials manufactured from the regolith will likely be components of building structures, the regolith's suitability for most other applications is limited, given its limited transparency, biodegradability and plasticity[50].

Plastics (transparent and non-transparent) are extremely versatile and will likely comprise a substantial portion of Mars mission materials[51]. Some plastics can be made chemically with established processes: ethylene to polyethylene[52], methanol to olefins[53] and transparent poly(methyl methacrylate)[54]. However, the reclamation of these materials will require energy and specific infrastructure. Both chemical and biological processes will require off-planet supplies, and each will have their own advantages and disadvantages. Chemical processes can be highly efficient, with high productivity, but may be energy intensive and require consistent resupply of exotic catalysts. Biological processes require comparatively lower energy inputs but are likely to have higher water demands with lower yields and production rates, and also may require trace elements from Earth. A key advantage of biological processes is that they can generate complex materials that existing chemical processes cannot produce. Their applications for ISRU will have to be determined by weighing these characteristics and determining which technology is best suited for the task. Bio-based materials will be an important class due to their general reclaimability through biological mechanisms. When produced microbially, these materials are highly versatile and tailorable with minimal changes to fermentation technology[51]. Examples of Martian infrastructure that can be built on bioplastics include aquaponics[55–57], wastewater treatment[58] and materials that will only be needed temporarily.

Martian plastics will be produced from local CO_2 and ideally reclaimed by life support—two roles for which microbes are well suited. They can produce and decompose a variety of polymers with thermoplastic properties (such as polylactide (PLA) or polyhydroxyalkanoates (PHAs))[59], as well as a diverse set of polysaccharide-based polymers (such as cellulose, chitin and starch)[60,61].

Bioproduction of basic materials, including PLA, PHA and thermoplastic starch, has been demonstrated at industrial scale on Earth, whereas more complex polymers are still limited to laboratory scale[62]. Recent advancements have led to the bioproduction of various animal-free materials, such as silk and leather[63]. For commercial applications on Earth, adoption of microbially produced materials is largely limited by their low productivity and high cost as compared to petrochemical or farmed-animal sources. On Mars, the lack of petrochemicals, abundant energy and animals may promote the use of these biological routes for material production. Bioengineered materials from microbes also provide unique flexibility, as material properties can be tuned genetically. Regardless of the application, materials selected for bioproduction should require minimal equipment for manufacturing and downstream processing (DSP), integrate into reclamation systems and contribute to medium and fertilizer production by introducing low-abundance elements (for example, N or P) after use. Materials will eventually be produced from local Martian resources, but from the beginning, the priority will be on recycling the majority of complex molecules into the life-support system. This reframing of manufacturing and use will require a strong emphasis on sustainability and scarcity mitigation—ideally feeding back to Earth to promote more sustainable industries. As for food production, we envisage materials production from living organisms occurring in three distinct stages.

Stage I. As with food production, early missions will not have the infrastructure for substantial material manufacturing, but small-scale demonstrations of production, isolation, polymerization and testing on the surface will be essential to the use of microbially derived materials during later missions. Furthermore, bioengineering will play an important role in developing reclaimable packaging. By sending supplies—such as packaging and filaments for additive manufacturing—made of degradable plastics, we can minimize waste and pursue regenerative life support from the start. The lack of petrochemicals on Mars will drive ongoing development of alternative routes to plastic synthesis and efficient waste reclamation systems to retain reduced carbon. Ultimately, this strategy may have the potential to return knowledge and inform strategies to improve the sustainability of plastics on Earth.

Stage II. Microbially produced materials made by optimized strains can be selected and developed for a wide variety of potential applications, such as expanding habitats and greenhouses. In this stage, the materials established in stage I will start to be manufactured on site. Strains and their products will be selected to effectively share DSP unit operations across different materials and allow conversion of purified monomers to finished plastics with minimal additional equipment.

Stage III. As the need for production volume and efficiency increases, a substantial manufacturing infrastructure will be developed that relies substantially on Martian resources, with large-scale ore mining, smelting plants, foundries and tooling shops for a variety of applications. At this stage, bulk plastic will be produced chemically in dedicated high-volume chemical manufacturing plants, with low-volume, flexible bioproduction efficiently providing numerous specialty products.

Therapeutics production. Any long-term mission requires planning for crew health maintenance[64]. During a Mars mission, an emergency return or resupply from Earth will be impossible. Safeguarding the physical and mental health of the crew therefore demands a plan for long-term therapeutic self-sufficiency, with in situ production playing an increasing role in later missions. Here again, we outline a staged approach to bringing a Mars colony to an advanced therapeutics production capacity.

Stage I. The entire complement of therapeutics required by astronauts will likely be included in cargo, with substantial radiation shielding to prevent the degradation of therapeutic agents en route. Any initial in situ therapeutic bioproduction would be limited to basic recombinant biologics or small molecules in bacterial chasses to supplement these stocks as a contingency reserve, as well as to support process development for future missions.

Stage II. Bioproduction of some therapeutic compounds on Earth will enable the development of a streamlined process pipeline for later mission stages. Therapeutics already made through bioproduction include insulin[65], opioids[66] and some antibiotic precursors[67].

Radioprotective therapeutics could prove especially important to our ability to develop a sustained human presence on Mars, as current NASA estimates indicate that the combined radiation exposure of a Mars mission will likely meet or exceed the lifetime radiation limit for astronauts[68]. Current radiation estimates of galactic cosmic rays and solar energetic particles from the Curiosity rover indicate that a 500-day mission on Mars and two 180-day transits would still be within the acceptable (albeit elevated) range of risk for astronauts, totaling 1.01 Sievert (Sv)[69,70]. Estimates suggest that approximately three meters of regolith shielding is sufficient to reduce the radiation risk to Earth-like levels (1.8 mSv/year, for example, in the Swiss Alps). Astronauts accumulate 160 mSv on a six-month mission on the ISS and up to 6 Sv over their career[71]. In addition to therapies for systemic symptoms of acute radiation exposure, such as filgrastim[72], several promising natural products may protect biomolecules from radiation damage or induce cellular repair processes[69]. At this stage, bioproduction would be a good candidate for a subset of medicines with short shelf lives and inconsistent demand, such as erythropoietin, antimicrobials and biologics for radioprotection.

Stage III. As the bioproduction and DSP infrastructure available to Mars missions matures, in situ production will come to serve as a primary source of frequently used therapeutics. We envisage that a mature pharmaceutical production pipeline would also enable on-demand or emergency production of specific niche medications from a library of microbial stocks as the need arises[73].

The lack of DSP infrastructure on Mars is an important limitation for the bioproduction of therapeutics. For stages I and II, however, we posit that the purity standards for some therapeutics need not necessarily meet stringent US Food and Drug Administration requirements for them to be functional. Innovations in streamlined DSP design with small footprints have shown tremendous potential to enable facile, on-demand bioproduction of therapeutics[74]. Such parallel advancement of inexpensive and portable DSP solutions for therapeutics would also immensely benefit Earth applications in low-resource contexts[65,75–79].

Reclamation applications. On Earth, we commonly use anaerobic digestion for wastewater and sewage treatment with concurrent biogas and fertilizer production. On Mars, developing waste reclamation methods will be integral to closing the life-support loop. Waste recycling will provide ready sources of essential elements (such as N, P and S) in bioavailable forms that would otherwise be prohibitively difficult to extract from the environment during initial missions. For example, in the case of N, urea and other N-rich molecules will be converted to ammonia through chemical or biological means to return N to its bioavailable form. NASA currently lists bodily and organic waste, respiratory waste and material inorganic waste as central capability gaps[80]—which we propose to address, at least in part, through biotechnological means. Among these, the application of biological reclamation to organic waste, particularly urine and solid organic waste, is the closest to realization, given Earth's existing wastewater treatment and reclamation infrastructure. As for other applications, we lay out below a three-staged approach for how bioengineering would be used to meet reclamation and remediation goals.

Stage I. An initial focus for bioreclamation should be on processing urine. Urine has high concentrations of bioavailable nutrients, is chemically simpler and more homogeneous than solid waste, and is easily captured as a separate waste stream. Filtration, adsorption and distillation are well-established methods for water recovery and will likely be employed, but currently the leftover brine (concentrated urine) is normally discarded[81]. However, this brine contains nitrogen that can be converted to ammonia and used for microbial feedstocks and plant fertilizers. Unprocessed urine has been used as an agricultural fertilizer for millennia, and the bioreclamation of urine as a microbial feedstock also shows promise[82]. For example, when cultures of *A. platensis*—a cyanobacterium commonly known as spirulina and used as a dietary supplement—were grown on urine feedstock, their production of nutrients and proteins did not differ substantially from those of cultures grown on standard media. Although further engineering is needed to address potential inhibition of culture growth from secondary metabolites as well as to tune microbial metabolisms to the crew's urine composition on a Mars diet[83], urine bioreclamation through the fermentation modes described here could provide a viable supplement to defined, transported media for growing microbes.

Stage II. As bioreclamation technology advances, reclamation systems can be adopted to begin to process solid organic waste. This process is more challenging, given the greater heterogeneity of human fecal, food and plant waste streams. Although there have been substantial efforts to catalog the composition and capabilities of activated sludge[84], systematic design principles and rational engineering of such systems remain ongoing. Centralization of microbial community data to study community dynamics and develop design principles can contribute to the rational design of microbial community inoculants for a wide variety of organic waste feedstocks[84]. Given the likely complexity of solid organic waste streams overall, it may be necessary to deliver a repository of microbial species or activated sludge samples to Mars.

Stage III. As a long-term goal, engineered microbes will be used to improve the efficiency and capacity of existing reclamation systems. Overall, utilization of more complex material waste streams, such as organic waste, packaging or chemicals, may benefit substantially from metabolic engineering of organisms delivered in a custom and on-demand combination of spatially linked microbial consortia (SLMC)[85]. SLMC designs spatially separate organisms into bioreactor modules optimized for individual species or small communities while allowing the flow of medium through each module, enabling the maintenance of optimal reaction conditions for each individual organism or community and the transfer of intermediate metabolites from one bioreactor to the next. Simultaneously, metabolic engineering techniques[86] enable the optimization of multiple biodegradation or biosynthesis pathways across organisms and reduce metabolic load on a single engineered organism[87]. Through the union of genetic engineering and SLMC, we may develop custom microbial communities for on-demand bioreclamation and materials production from changing waste streams. Biological processes offer advantages in their ability to form robust communities in variable conditions, operate at or near ambient conditions and produce fewer hazardous byproducts[81].

Conclusions

We have highlighted four areas in which biotech and bioengineering can make major contributions along the human trajectory to Mars in the near, medium and long term. We chose our four application areas by focusing on the unique strengths of living matter, avoiding the use of biotech for its own sake. With that focus, we described solutions built around plausible—not merely possible—biology. Our examples show how biotech has a substantial opportunity to provide essential nutrients, develop novel material pathways, mitigate unexpected medical risks and reclaim waste. We close by highlighting potential benefits of these technologies for terrestrial life and suggesting specific ways to advance the field of bioengineering in non-terrestrial applications.

Technology development for space exploration has been closely associated with advances on Earth throughout the history of human spaceflight. Space programs have been instrumental in spurring the development of a multitude of technologies, from satellite imaging and LASIK eye surgery to charge-coupled devices (CCD) and global positioning system (GPS) signal correction[88]. These technologies emerged from the need to meet essential challenges in daunting environments. Although biotech is well suited for many Martian applications, the planet's inhospitable nature and distance critically require that crew have redundant, adaptable systems to handle unforeseen situations and emergencies with almost complete independence. This capability maps to the analogous terrestrial challenge of rapidly developing countermeasures to mitigate novel threats. In addition to acute needs, Mars presents major chronic constraints by rewriting the cost functions of common materials. The high cost of payload mass, for example, may drive the development of self-replicating, space-efficient and self-sufficient technologies. The crucible of Mars will push us to innovate immediately on resource-constrained challenges that echo the own impending resource crises on Earth.

But we do not set out to explore space solely for the ancillary benefits. Space exploration is a singular achievement for humanity and essential for its long-term survival. The difficulty of the task itself has inspired many to excel in ways no other challenge could. Mars is the next most important frontier of this exploration. For those who want to contribute their bioengineering expertise to the effort, many opportunities are available: products and materials can be developed for their anticipated dual-purpose terrestrial and Martian applications; Mars-analog habitat missions require expansion and innovation to vet new technological pipelines; meetings that bring together domain experts in space exploration and biology enable interdisciplinary collaboration, communication and learning to spark innovation in the field—particularly the work of the Center for the Utilization of Biological Engineering in Space (CUBES) and the Mars Exploration Program Analysis Group (MEPAG)[62,89]; and, crucially, the development of functional full-scale bioregenerative life-support systems must be fully tested on Earth. A key prerequisite is a comprehensive plan of how the myriad systems will be most efficiently integrated—such as we have outlined in this Comment.

The path forward is formidable, with countless challenges we cannot yet address. But by carefully selecting initial focus areas and expanding our efforts today, we can grow the edges of our knowledge, bringing solutions to these problems—and a Martian future—within reach. ❐

Editor's Note: This article has been peer-reviewed.

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https://doi.org/10.1038/s41587-020-0485-4

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Acknowledgements

Viriditas was a workshop organized in October 2018 at Ginkgo Bioworks by S.N.N., M.Y.W. and others to nucleate the development of a biotechnology roadmap for Mars missions. All article authors attended the event, and the conceptual framework that emerged from it was the basis for this article. The authors thank the co-organizers, sponsors, presenters and other attendees for their contribution to these ideas. The authors also thank J. Cumbers, C. Agapakis, C. Da Cunha, A. Robinson-Mosher and R. Howe for editing and guidance. S.N.N. thanks the Harvard Climate Change Solutions Fund for support. C.E.M. thanks WorldQuant, NASA (NNX14AH50G, NNX17AB26G) and TRISH (NNX16AO69A:0107, NNX16AO69A:0061).

Author contributions

S.N.N., M.Y.W., N.M., V.N. and M.Z. wrote the manuscript, and L.H., C.E.M., M.M., P.A.S., M.S., J.S. and D.B.T provided edits. All authors contributed to its conception.

Competing interests

M.Y.W., L.H., M.M. and M.S. are employees of Ginkgo Bioworks, a Boston-based company that makes and sells engineered organisms.