Synthetic Biology for Space Exploration: Promises and Societal Implications

Chapter · January 2016

DOI: 10.1007/978-3-319-21088-9_4

5 authors, including:

Cyprien Verseux
University of Rome Tor Verg...

Lynn Rothschild
NASA

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Cyprien N. Verseux, Ivan G. Paulino-Lima, Mickael Baqué, Daniela Billi and Lynn J. Rothschild

1 Introduction

Can humanity develop sustainable and autonomous colonies beyond Earth? We landed humans on the Moon during the Apollo program and now, thanks to recent technological advances, sending humans to Mars is a realistic medium-term goal (e.g., Horneck et al. 2006). Several projects designed for this purpose are currently under development. In 1990, Mars Direct, a project initiated by Robert Zubrin (then engineer at Martin Marietta), was designed to bring humans to Mars in a decade (Baker and Zubrin 1990; Zubrin and Wagner 1996). NASA aims at having technologies ready to land humans on Mars in the mid-2030s[1] and, even though many unknowns remain in the agency's plans, its deep space crew capsule successfully made its first in-space test on December 5 2014.[2] Space Exploration Technologies Corporation (SpaceX) targets 2026, and its CEO Elon Musk will unveil his Mars

[1]http://www.nasa.gov/content/nasas-human-path-to-mars. Accessed 15 Mar 2015.
[2]http://www.nasa.gov/press/2014/december/nasa-s-new-orion-spacecraft-completes-first-spaceflight-test. Accessed 15 Mar 2015.

C.N. Verseux (✉) · M. Baqué · D. Billi
Department of Biology, University Tor Vergata, Rome, Italy
e-mail: cyprien.verseux@gmail.com

C.N. Verseux
NASA EAP Associate, NASA Ames Research Center, Moffett Field, CA, USA

I.G. Paulino-Lima
NASA Ames Research Center, Moffett Field, CA, USA

L.J. Rothschild
NASA Ames Research Center, Earth Sciences Division, Moffett Field, CA, USA
e-mail: lynn.j.rothschild@nasa.gov

K. Hagen et al. (eds.), *Ambivalences of Creating Life*, Ethics of Science and Technology Assessment 45, DOI 10.1007/978-3-319-21088-9_4

colonization plans by the end of 2015.[3] Mars One, a private company aiming at sending humans to Mars in a one-way mission, targets 2027 and is in the process of selecting crewmembers.[4] These might fail to meet their announced deadlines, or at all; postponing and cancelling is common in space missions. But other Mars colonization projects and private spaceflight companies are emerging, who can benefit from the advances of their predecessors. Your direct descendants may walk on red dust and contemplate a blue sunset. And going beyond Mars is likely to be possible in the more distant future. But there is a big gap between short-term missions and permanent colonies: the longer you stay and the farther you go, the less you can depend on Earth.

Indeed, launch costs do not allow realistic plans for a continuous resupply of colonies beyond the Moon. Let's take food as an example. If all food is to come from Earth, and assuming the easiest option of providing shelf-stable, pre-packaged food similar to provisions of the International Space Station, about 1.8 kg per day and per crewmember should be sent (Allen et al. 2003). Adding the needed vehicle and fuel weight to carry the food, and assuming a 10:1 vehicle-to-payload ratio (Hoffman and Kaplan 1997), a 1000-day food supply for a crew of six would add more than 108 metric tons to the initial mass of the transit vehicle. Worse, these figures are largely under the food minimum needed for a healthy diet: even though shelf-stable items are convenient due to their reduced need for storage facilities and contamination risks, a diet composed exclusively of this type of food would be nutritionally incomplete and thus not adequate in the long term. Given the technical challenges and costs associated with leaving Earth and landing on planetary bodies (e.g., in the order of $300,000 per kg sent to Mars, according to Massa et al. 2007), sending all consumables needed to sustain crews is unrealistic in the long term.

Thus, the time we can stay in remote settlements will depend on our ability to be independent of Earth. This can be achieved by relying on resources found on site, through an approach referred to as in situ resource utilization (ISRU). ISRU can partially rely on physicochemical processing but some necessary products such as high-protein food can currently not be produced or recycled without biological processing (Drysdale et al. 2003; Montague et al. 2012). Besides, many components of physicochemical life support systems are heavy, bulky, consume large amounts of energy and require high temperatures for processes to occur. Even in the case where physicochemical processes are the backbone of life support systems, these could be complemented by biological ones. Besides, overlapping functions would provide a safe redundancy.

Microorganisms, in particular, could be extremely useful. Humans have been consuming and otherwise using microorganism-produced resources on Earth throughout their history: oxygen produced by cyanobacteria and eukaryotic microalgae, food and drinks as edible microorganisms and fermented products (e.g.,

[3] http://www.huffingtonpost.com/2015/01/06/elon-musk-mars-colony_n_6423026.html. Accessed 15 Mar 2015.

[4] http://www.mars-one.com. Accessed 15 Mar 2015.

wine and yoghurt), drugs, various chemicals, biomaterials, biofuels, mined metals and so on. We also rely on them for many critical processes such as, for instance, waste recycling. So, why not use microorganisms to cover our daily needs in space and on foreign planetary bodies as we do on Earth? Here is the beginning of an answer: because all organisms we currently know have evolved on Earth and are not adapted to most environments found beyond it. First, most substrates they usually rely on are absent. If we need to bring from Earth all starting compounds needed for microbial processes to occur there, we slightly move the mass problem but certainly not fix it. As an example, the mass of metabolic consumables needed to sustain a crew of six during a 1000-day Mars mission using the European life support system MELiSSA (Godia et al. 2002) has been estimated to be about 30 metric tons, hygiene water not included (Langhoff et al. 2011). Then, the conditions found outside Earth are generally extremely harsh to all known microorganisms, and reproducing Earth-like conditions within a large volume and surface would be extremely costly.

A solution could be to use synthetic biology to increase the fitness of, and to confer new functions to, the organisms in extraterrestrial outposts. Given its potential for enabling space exploration, synthetic biology has aroused NASA's interest (Cumbers and Rothschild 2010; Langhoff et al. 2011; Menezes et al. 2014). In this paper, a brief overview of the possible applications of synthetic biology within extraterrestrial outposts is given (efforts were done to keep it general and easy to understand by interdisciplinary readers) and the resulting impacts on our society are briefly discussed. Focus is here given to Mars, as it is very likely to be the first planet beyond Earth where autonomous outposts are established, but the general ideas apply to other destinations. The Moon could also have been taken as an example, but Mars colonization was preferred to illustrate the concepts outlined below as (i) travel time, costs and difficulty, as well as scientific work that could potentially be conducted (e.g., search for life) justify the establishment of permanent human outposts there, (ii) since it is much farther from Earth than the Moon and has a higher gravity, sending supplies would be more expensive and challenging, increasing the need for exploiting on-site resources instead, and (iii) key resources for biological systems (e.g., water, carbon dioxide and dinitrogen) are widely available on-site. A consideration about the use of synthetic biology for ascribing value to lunar resources can be found elsewhere (Montague et al. 2012).

2 Providing "Off the Land" Substrates for Microbial Growth

Does Mars contain the substrates we need for feeding microorganisms without sending materials from Earth? Obviously you won't find, waiting under a rock, bottled culture media as those used in laboratories to grow microbes. Yet, most elements needed to support life have been detected in the Martian soils and rocks,

including all the basic building blocks (C, H, O, N, P, S) and other elements needed in smaller amounts (Mg, Fe, Ca, Na, K, Mn, Cr, Ni, Mo, Cu, Zn…). There is gaseous carbon (in carbon dioxide but also, as recently evidenced, in methane—see Webster et al. 2015) and nitrogen in the atmosphere, and additional carbon atoms can be found in the CO_2 ice caps, in the surface and subsurface regolith (the loose soil that can be seen on photographs of Martian landscapes) due to exchange with the atmosphere, possibly in reservoirs formed when the atmosphere was thicker (Kurahashi-Nakamura and Tajika 2006). Fixed nitrogen compounds have also been detected (Ming et al. 2014), even though what exactly they are and whether or not they could be used by living organisms is not defined yet.

Thus, Martian rocks (Cockell 2014) and atmosphere seem to contain all the basic elements needed to support life. Water is also there: it has been detected in large amounts (Tokano 2005) as ice at the north polar ice cap, under the south carbon ice cap and in the subsurface at more temperate latitudes, as mineral hydration, and as vapor in the atmosphere, even though at low concentrations. It will also be a by-product of human metabolism and industrial activity. Solar energy is of course present. As Mars is approximately 1.5 AU from the Sun, the average radiation flux is 43 % that of Earth's.

So, while all needed elements are naturally present and some additional sources will come from human activity (Table 1), they are in a form that most organisms cannot use. In particular, many organisms—qualified as heterotrophic and including animals such as us humans, as well as most microorganisms—need organic compounds as carbon and energy sources, and their state and availability on Mars remain poorly known (Ming et al. 2014) but is likely low. Fixed nitrogen, such as nitrate (NO_3^-), ammonia (NH_3) and amino-acid chains (but not atmospheric nitrogen which is in the form of dinitrogen, N_2), is also needed for most organisms. The main limitation is consequently not the lack of life-supporting elements, but the

Table 1 Main sources of nutrients for cyanobacterium-based biological processes on mars

Source	Elements
Atmosphere[a]	CO_2, N_2
Soil, rocks[a]	P, S, Mg, Fe, Ca, Na, K, and metal micronutrients
Ice caps, subsurface ice, atmosphere, hydrated minerals[a]	H_2O
Solar radiation[a]	Energy for photosynthesis, heat
Human waste	Fixed N, organic material, CO_2, H_2O
Side effects of other artificial processes (fuel combustion, manufacturing…)	CO_2, H_2O
Cyanobacteria (fed with the above)	O_2, fixed N, organic material, metal nutrients

[a]Naturally present, independently of human activity

abilities of microorganisms to use them under the form they are encountered on Mars's surface.

That being said, not all microorganisms need organic compounds to grow; autotrophs such as cyanobacteria don't. Just like plants, cyanobacteria can photosynthesize—they use CO_2 and solar radiation as carbon and energy sources to produce their own organic material. In a nutrient desert such as Mars, this would give them a strong advantage over heterotrophic organisms. In addition, some can fix N_2, which like CO_2 is present in the Martian atmosphere. On top of this, some have the ability to extract and use nutrients from analogues of Martian rocks and have consequently been suggested as a basis for systems producing life-sustaining compounds from local resources (Brown et al. 2008; Brown 2008a, b). Most—if not all—nutrients needed to cover their needs could be directly provided from Mars's resources. Some cyanobacteria (e.g., *Anabaena cylindrica*) are capable of growing in distilled water containing only powdered Mars basalt analogues, under terrestrial atmosphere (Olsson-Francis and Cockell 2010a). Other studies showed that the growth of several species of cyanobacteria isolated from iron-depositing hot springs in Yellowstone National Park was stimulated by the presence of Martian soil analogues in culture media (Brown and Sarkisova 2008) and that a strain called *Nostoc* sp. HK-01 could grow on a Mars regolith stimulant for at least 140 days, without any other nutrient source besides atmospheric gas (Arai et al. 2008).

As cyanobacteria produce organic compounds, why not use them for feeding heterotrophic organisms? Cultures could be used after simply destroying the cyanobacterial cells; researchers have successfully used lysed cyanobacterial biomass as a substrate for ethanol-producing yeasts (Aikawa et al. 2013; Möllers et al. 2014). However, if we could harvest nutrients without killing cells, processes could be much more efficient. This could be achieved by having cyanobacteria release substrates in the extracellular medium, and this solution has been investigated in the Rothschild laboratory since the 2011 Brown-Stanford iGEM team engineered *Anabaena* PCC7120 to secrete sucrose.[5] Heterotrophic bacteria from a common soil species, *Bacillus subtilis*, were able to grow in filtered medium in which the engineered *Anabaena* had grown but no additional organic compounds were added (unpublished data). Previously, the cyanobacterial strain *Synechococcus elongatus* PCC7942 had been engineered to produce and secrete either glucose and fructose, or lactate, which then served as a substrate for growing the model bacterium *Escherichia coli* (Niederholtmeyer et al. 2010). Ammonium (NH_4^+; a fixed nitrogen compounds that can be used by most microorganisms) is naturally released by some cyanobacteria. The extracellular concentration of ammonia can reach more than 10 mM in cultures of *Anabaena* species relying on atmospheric nitrogen as a sole nitrogen source, without killing the cyanobacteria (Subramanian and Shanmugasundaram 1986). Ammonia becomes limiting only when at extremely low concentrations; for *Escherichia coli*, for instance, it is below a few µM (Kim et al. 2012), several orders of magnitudes below the above mentioned concentrations in

[5]http://2011.igem.org/Team:Brown-Stanford/PowerCell/Introduction. Accessed 6 Mar 2015.

cyanobacterial cultures. Then, cyanobacteria grown using Martian rocks as a substrate would release inorganic elements (Ca, Fe, K, Mg, Mn, etc.) into water, as shown in a study performed with terrestrial analogues of Martian basalt (Olsson-Francis and Cockell 2010a), making them available to species which cannot extract them from rocks. Taken as a whole, these studies suggest that using cyanobacteria to produce substrates for microorganisms from Martian resources (see Fig. 1) may be a viable option.

In addition to that of other microorganisms, cyanobacterial cultures could be used to support the growth of plants. Even though basalt is the dominant rock type in Martian regolith and weathered basalt can yield extremely productive soils on Earth (Dahlgren et al. 1993), regolith would probably need a physicochemical and/or biological treatment before it can be used as growth substrate for plants. Reasons for this include its poor water-holding properties (due to its low organic carbon contents), and that regolith nutrients are hardly available to plants (Cockell 2011; Maggi and Pallud 2010). Besides carbon, the soil will need to be enriched in other elements, including nitrogen, as most plants cannot fix atmospheric nitrogen (even though symbiotic nitrogen fixation occurs in some plants, mainly legumes, due to harboring specific bacteria in their tissues). It has already been proposed to

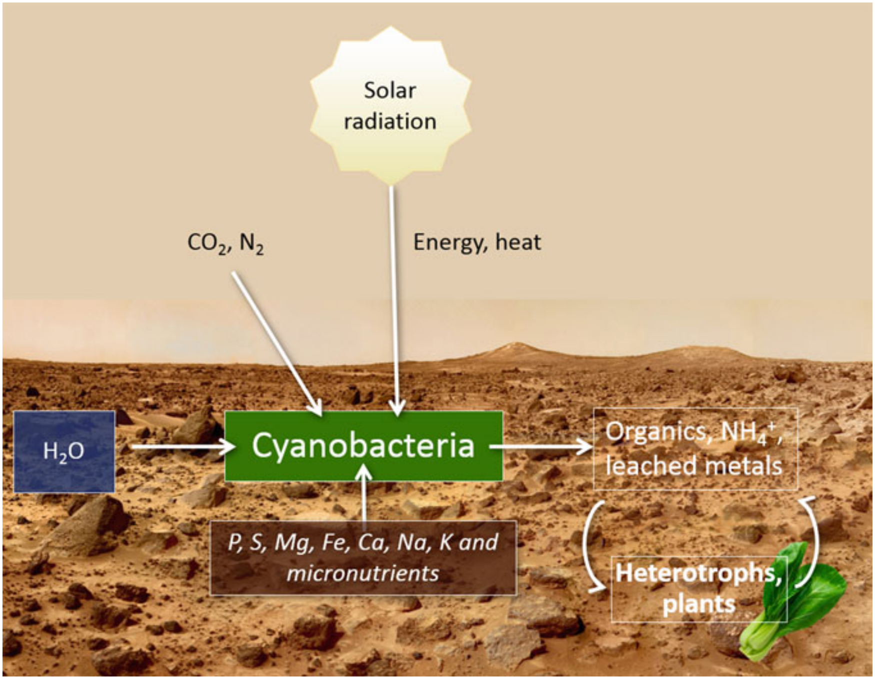

Fig. 1 Using cyanobacteria to process Martian resources into substrates for other organisms. Reproduced from Verseux et al. (2015) with permission from the editor of the International Journal of Astrobiology

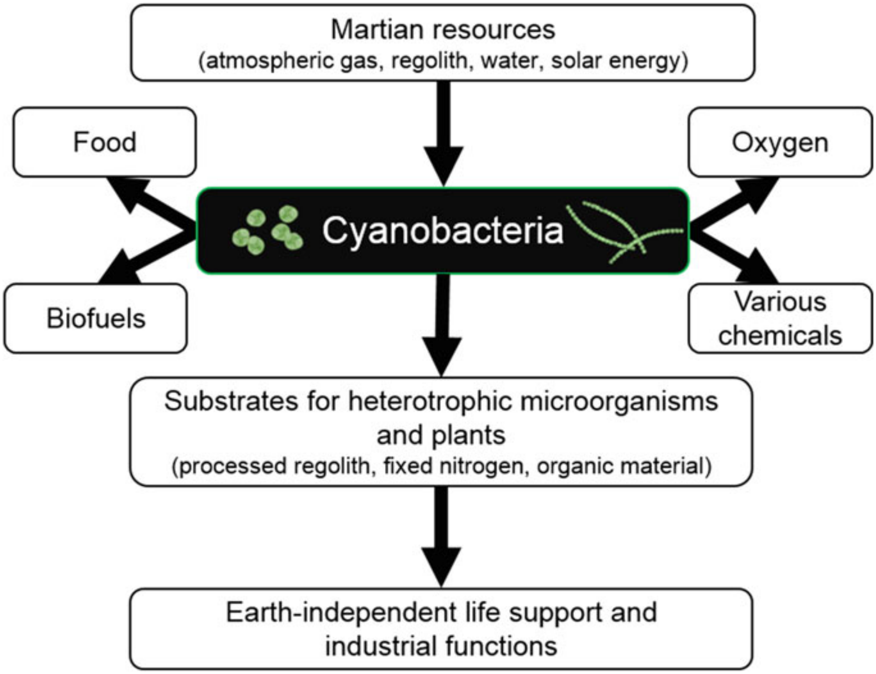

Fig. 2 Cyanobacteria as a link between Martian resources and on-site resource production systems—a simplified overview

use cyanobacteria to release chemical elements from extraterrestrial rocks to an aqueous phase, aimed at being incorporated in a substrate for hydroponic cultivation (Brown and Sarkisova 2008). In addition to these elements, fixed nitrogen and biomass resulting from cyanobacterial cultures could be used as substrates for plant cultivation, as a hydroponic substrate and/or to make a fertile soil.

More information about the potential of Mars-specific cyanobacterium-based biological life support systems (CyBLiSS) is given elsewhere (Verseux et al. 2015) and an overview is given in Fig. 2. The key point is that, thanks to their photosynthetic, rock leaching and nitrogen fixing abilities, cyanobacteria could be used for processing inorganic compounds found on Mars into a form that is available to other microorganisms and to plants. Additional nutrients could come from the recycling of human waste. Finally, if some micronutrients (e.g., some metal ions) could not be mined or biologically synthesized on site, bringing them from Earth would only add negligible mass to the initial payload, as they are needed in trace amounts only.

Why would synthetic biology be useful here? First, as illustrated above, cyanobacteria can be engineered to secrete organic substrates; proofs-of-concept have been done with the secretion of sucrose, lactate, glucose and fructose. Even though growth rates of the heterotrophic organisms were quite low due to low sugar yields,

these could be improved by increasing production rates or decreasing processing of targeted products by producing strains (in the work of Niederholtmeyer et al. 2010, produced sugars could be consumed by cyanobacteria, thereby decreasing their concentration in the extracellular medium). Cyanobacteria can also be genetically modified for ammonium secretion (Spiller et al. 1986). Second, synthetic biology can be used to increase the abilities of cyanobacteria to use and process Martian resources (see below), as well as the ability of other microorganisms to use resources produced by cyanobacteria.

3 Engineering Microbial "Mars Worthiness": Increasing Resistances and Abilities to Use On-Site Resources

The harsh environmental conditions faced directly on Mars's surface (see Table 2) do not allow any known microorganism to grow efficiently: there are low temperatures, low pressure (5–11 mbar) and a high UV flux including UV-C radiation. The atmosphere is mostly composed of carbon dioxide (95.3 %), little nitrogen (2.7 %) and even less oxygen (0.13 %), and low moisture. Because of the temperature, pressure and radiation issues, microbial cultures must be enclosed in an appropriate culture system, providing shielding and an environment suitable for metabolism and growth. Elaborated culture hardware providing Earth-like conditions could be suggested, but they would be highly energy consuming, very massive and consequently extremely costly to send to Mars (Lehto et al. 2006) even for small-scale cultures, and would have many possible causes of failure due to relying

Table 2 Environmental parameters on Mars and Earth surfaces

Parameter		Mars	Earth
Surface gravity		0.38*g*	1.00*g*
Mean surface temperature		−60 °C	+15 °C
Surface temperature range		−145 to +20 °C	−90 to +60 °C
Mean PAR photon flux		8.6×10^{19} photons m^{-2} s^{-1}	2.0×10^{20} photons m^{-2} s^{-1}
UV radiation spectral range		>190 nm	>300 nm
Atmospheric pressure		5–11 hPa	1013 hPa (mean at sea level)
Atmospheric composition (average)	N_2	0.189 hPa, 2.7 %	780 hPa, 78 %
	O_2	0.009 hPa, 0.13 %	210 hPa, 21 %
	CO_2	6.67 hPa, 95.3 %	0.38 hPa, 0.038 %
	Ar	0.112 hPa, 1.6 %	10.13 hPa, 1 %

Adapted from Kanervo et al. (2005) and Graham (2004), and reproduced from Verseux et al. (2015) with permission from the editor of the International Journal of Astrobiology

on complex technologies (that being said, the potential of ultimately creating many of these facilities with in situ resources is being explored in Rothschild's lab).

However, culture conditions do not have to be exactly as on Earth: microorganisms have specific ranges of tolerance for environmental factors. In particular, some thrive in extreme environments, including some deserts considered as Mars analogues due to radiation, rock composition, drought and extreme temperatures. Their resistance to conditions found on Mars's surface have been extensively studied, using low Earth orbit- and Earth-based simulations (e.g., Baqué et al. 2013; de Vera et al. 2013, 2014; Olsson-Francis and Cockell 2010b; Rothschild 1990).

The more the organisms can withstand conditions found on site, the simpler the culture system can be. Besides, having resistant organisms would allow loss risk to be minimized (Cockell 2010; Olsson-Francis and Cockell 2010a), both during the journey (the organisms' tolerance to long periods of dehydration, possibly in a differentiated state such as spores or akinetes, would allow a safe and freezing-independent storage) and on site: high resistance to Martian surface conditions would provide safety in case of system malfunction during which cultures could be exposed to less attenuated conditions (e.g., desiccation, low pressure, high radiation levels, altered pH and sudden temperature shift), both when stored and grown.

Synthetic biology could be used to increase the resistance of microorganisms to Martian conditions, probably not enough to make them thrive at the surface but enough to reduce both hardware needs and risks of culture loss. A strategy could be to express genes from other organisms known to confer an advantage in coping with targeted stresses to increase microorganism's fitness under conditions found beyond Earth (Cumbers and Rothschild 2010). This approach has been successful in other contexts, mainly with *E. coli* (see, e.g., Billi et al. 2000; Ferrer et al. 2003; Gao et al. 2003, and the 2012 Stanford-Brown iGEM team[6]). Once specific genes have been shown to confer an advantage to the targeted stress when expressed in the microorganism, they can be improved using various computational and molecular biology tools and methods. This approach is becoming more and more efficient, with notably a sharp decrease in DNA synthesis cost, the improvement of automated gene assembly methods, knowledge gained from systems biology, and the development of biological computer aided design (BioCAD) and other computational tools.

While expressing genes from other organisms (or overexpressing genes from the organism itself) might confer a significant advantage in coping with some environmental stressors, this approach may not be suitable for resistance features that are highly multifactorial, each individual factor having a relatively weak impact. For instance, there is not a single factor that confers *Deinococcus radiodurans* (one of the most radioresistant known microorganism) its extreme radiation resistance, but a very wide combination of features including efficient DNA repair mechanisms, anti-oxidation defenses and specific morphological characteristics (e.g.,

[6]http://2012.igem.org/Team:Stanford-Brown/HellCell/Introduction. Accessed 6 Mar 2015.

Slade and Radman 2011). For such multifactorial features, dramatic changes in phenotype through computational genetic engineering are more challenging.

Instead, directed evolution provides an alternative approach that can allow complex modifications at an organismal level without an a priori knowledge of mechanisms. To accomplish this, a parental population is subjected to iterations of mutagenesis and artificial selection. Genetic diversity is created presumably at random, and the mutated population is subjected to selection for the best adapted progeny. To witness the power of selection to shape microbial populations, look no farther than the battle between microbes and antibiotics. Microbial evolution is the reason why doctors insist the patient comply fully with antibiotic regimens. If the antibiotic dosage fails to kill even a few infectious bacteria that happened to be more resistant than the others, they may proliferate and generate a new population of bacteria which will be more resistant than the previous one. Repeat the cycle and you'll need a different treatment.

In the laboratory, similar processes can be exploited to confer on organisms new or improved functions. The dynamics of directed evolution have been widely studied in the last decades and have been used successfully to increase organisms' specific properties (see, e.g., Conrad et al. 2011; Elena and Lenski 2003), including radiation resistance in bacteria (Ewing 1995; Goldman and Travisano 2011; Harris et al. 2009; Wassmann et al. 2010). One of the main issues when designing an optimization process based on directed evolution is the need for linking the optimized function (e.g., production of a compound of industrial interest) to the organism's fitness: strategies must be designed to make the cells of interest thrive while eliminating the others. When increasing resistance, the process is more straightforward: selection can be accomplished by applying increasing levels of the targeted stress and selecting survivors. Directed evolution can be improved by automation (de Crecy et al. 2009; Dykhuizen 1993; Grace et al. 2013; Marlière et al. 2011; Toprak et al. 2013) and recent methods such as, for instance, the so-called genome shuffling (Patnaik et al. 2002) and multiplex genome engineering (Wang et al. 2009).

Once a microbial production system is well established and automated, directed evolution to increase adaption to the Mars environment could be performed on Mars. It can be much faster to evolve organisms on-site than it is on Earth, provided screening methods and adequate organisms are available there (Way et al. 2011). Indeed, Earth-based simulations of some of the factors encountered on Mars (and their combination) are difficult, expensive and cannot faithfully reproduce all their effects.

Computational genetic engineering and directed evolution are not mutually exclusive, in fact, they can be used in combination (Rothschild 2010). Engineered organisms can be submitted to directed evolution for optimization and, conversely, data obtained from genome sequencing of evolved organisms (so as to understand what mutations are responsible for improved properties) can give gene targets for design. An example of strategy combining both is illustrated in Fig. 3. Briefly, natural and evolved gene libraries are generated using directed evolution followed by sequencing and/or comparative gene expression assays in the presence or

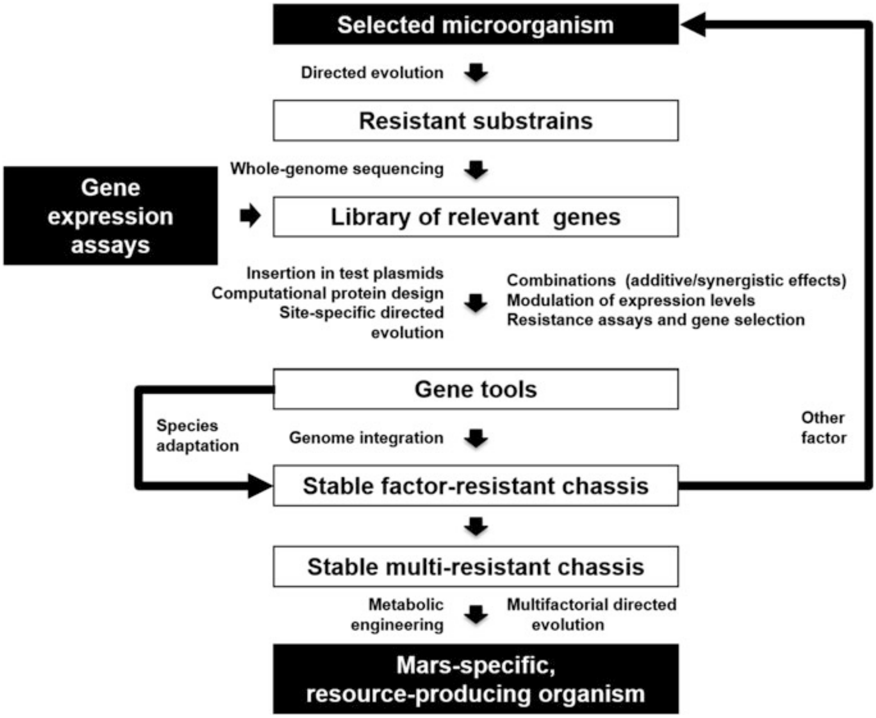

Fig. 3 Theoretical example of a synthetic biology-based strategy combining genetic engineering and directed evolution to improve the suitability of selected microorganisms for resource production in Martian outposts

absence of the environmental stressor. Genes selected for the properties they confer (e.g., metabolic pathway based on local resources or resistance to a target stress) are then engineered using synthetic biology to increase their impact. They are finally adapted to the target organism, the "chassis", which will be used for on-site resource production. Again, this scheme is an example and different workflows can be considered.

Of particular interest would be to increase resistance to long-term dehydration (for storage, as cells enter a state in which they do not need to be fed, and resting stages are often more resistant to environmental extremes), to radiation (ionizing radiation and UV radiation, especially for photosynthetic microorganisms due to the need to access radiation from other parts of the solar spectrum; that being said, ionizing radiation is not extremely high when compared to microorganisms' resistance and UV can easily be blocked or filtered), to a wide range of temperatures, to low pressures, to large and brutal shifts in these parameters (in case of system failure), and to combinations of them. Then, tolerance to a wide range of physicochemical parameters (e.g., high and low pH, presence of oxidative species) would allow constraints on culture conditions to be relaxed.

The growth-permissive limits of most of these factors have been widely studied, even though little is known about their combined effects (Harrison et al. 2013), both regarding the limits and the involved mechanisms. However, metabolism under low pressure remains poorly described and should be characterized and increased, as using a pressure as close as possible to Mars's ambient pressure (about 7–11 hPa, with seasonal variations; Earth's is about 1013 hPa) would greatly lower construction weight and cost of culture systems due to minimizing the need for reinforcing the structures to withstand inside/outside pressure differences, and minimize the risk of the leakage of organic matter (Lehto et al. 2006). Some methane-producing microorganisms have been shown to maintain low but detectable methane production, and thus metabolic activity, at 50 hPa of pressure (Kral et al. 2011) and a few bacteria have shown growth under 7 hPa of CO_2-enriched anoxic atmospheres (Nicholson et al. 2013; Schuerger et al. 2013). However, these abilities are uncommon: a wide range of microorganisms are unable to grow on semisolid medium at pressures below 25 hPa of ambient air (Nicholson et al. 2010). On the other hand, the lowest pressures at which biological niches are naturally present on Earth is about 330 hPa (at the top of the Mount Everest), way above Mars's surface pressure of about 10 hPa (Fajardo-Cavazos et al. 2012), and selective pressure on coping with such low pressures is virtually non-existent for current terrestrial microorganisms. The full potential for growth at low pressures is probably far from being reached. Thus, there might be much room for improvement by artificially evolving microorganisms to grow faster under low (and to grow at lower) pressures. Consistently, adaptation to low pressure has been shown possible with *Bacillus subtilis*: after cultivation at 5 kPa for 1000 generations, one isolate showed an increased fitness at this pressure (Nicholson et al. 2010). It should however be noted that a physical limitation to the pressure range that can be used at growth-permissive temperatures comes from the need to maintain a liquid phase.

Besides resistance, increasing the abilities of microorganisms—especially cyanobacteria if they are used for processing raw resources—to use resources found on Mars's surface would allow yields to be increased, while relaxing culture constraints and the need for materials imported from Earth. In particular, increasing their abilities to leach rocks and to get most of their nutrients from these within a wide range of pH, and to fix molecular nitrogen at low partial pressure, would be highly beneficial. In that case, genetic engineering might be more efficient than it is for increasing their resistance. Some clues have been given regarding the engineering of microorganisms with increased bioleaching abilities (Cockell 2011). However, even though metabolomics has made great advances in the last decade and synthetic biology strongly benefits from it (see for instance Ellis and Goodacre 2012 and Lee 2012), the complex interactions occurring in cells are still hard to predict and model, and whole-cell scaled directed evolution will here again be very useful. In that case, selection can be done by cyclically growing microorganisms and diluting them, in presence of the target nutrient source, and letting the fastest-growing mutants become dominant.

Culture conditions in human outposts on Mars should thus result from a compromise between conditions that provide enough support for microbial metabolism

while minimizing costs, initial mass, energy consumption and reliance on materials sent from the Earth. Synthetic biology can be used to push this compromise towards the most sustainable solution, while decreasing risks of losing cultures—what could have terrible consequences if humans rely on them—and increasing yields of the processes by increasing microorganisms' abilities to use on-site resources.

4 Roles of Engineered Organisms in Martian Outposts

Once microorganisms can be grown on Mars, what can they be used for? The most obvious applications will be basic life support functions. Various bioregenerative life support systems (BLSS) based on microorganisms and/or plants have been proposed (and some are under development) for recycling gas, liquid and solid wastes, thereby extending their usage, during beyond-Earth missions (e.g., Drysdale et al. 2004; Giacomelli et al. 2012; Gitelson et al. 2003; Godia et al. 2002; Lobascio et al. 2007; Nelson et al. 2010), including within lunar and Martian outposts (e.g., Blüm et al. 1994; Gitelson 1992; Nelson et al. 2010; Tikhomirov et al. 2007). The most advanced BLSS projects under design depend heavily on materials imported from Earth (even though a recently patented theoretical physicochemical/biological resource production system relies on Martian resources; see Cao et al. 2014). In spite of the potential of some of them to lead to extremely helpful systems in various space mission scenarios, they are consequently not suitable for autonomous, long-term human bases on Mars. Their limitations come, first, from the fact that their running time without resupply is limited by the decreasing amount of materials cycling in the system: recycling cannot reach 100 % efficiency and some losses are unavoidable (for quantitative information regarding the theoretical recycling efficiencies of MELiSSA, see for instance Poughon et al. 2009). Second, they cannot be expanded since the mass of cycling components is at most equal to their initial mass. Currently developed BLSS technologies consequently need regular re-supply of all materials from the ground, which is unrealistic when targeting Mars because of the high costs and high risks of delivery failure. Third, their power consumption is generally high and they represent a large volume and initial mass.

As outlined in the above sections, BLSS could be linked to resources found on site using selected—and possibly genetically enhanced—cyanobacteria. This would allow them to become sustainable, expandable (as new material would enter the loop, processes could be scaled up) and to dramatically decrease the mass of the payload to be sent from Earth. The first point (sustainability) is particularly critical: a permanent human presence on Mars requires colonies that are autonomous.

BLSS could be further improved by the introduction of engineered microorganisms, provided they are genetically stable over the long term. They could perform the functions they are selected for faster and using fewer resources. The system could also be simplified by reducing the number of organisms performing a given set of functions, by increasing organisms' versatility. A smaller set of

compartments could thus be used, thereby reducing the variety of resource requirements and the set of possible failure causes.

Another dramatic simplification could be the minimization of the role of plants which, among other drawbacks, are much less efficient than cyanobacteria (which could also perform photosynthesis-related tasks) regarding surface, CO_2 and mineral use (Langhoff et al. 2011; Way et al. 2011), are much more sensitive to environmental conditions, require more manpower, are harder to genetically engineer, take more time to regrow in case of accidental loss (Kanervo et al. 2005; Lehto et al. 2007), are less manageable (Horneck et al. 2003) and contain inedible and hard-to-recycle parts (Hendrickx and Mergeay 2007). The most critical role of plants in BLSS is oxygen and food production, which can also be performed by cyanobacteria (e.g., Hendrickx et al. 2006; Lehto et al. 2006).

However, even though some edible cyanobacterial species such as *Arthrospira* spp. have excellent nutraceutical properties (e.g., Henrikson 2009), they can currently not be used as a staple food due to their unpleasant and unvaried taste, lack of vitamin C and possibly essential oils, and low carbohydrate/protein ratios. These limitations could be addressed using synthetic biology (Way et al. 2011). First, taste, smell and color molecules have already been, or could be, expressed in bacteria. Then, modifying the sugar, protein and lipid ratios, as well as introducing essential molecules (e.g., vitamin C) could be achieved using metabolic engineering and, more generally, nutraceutical properties could be improved by genetic engineering. Preliminary work has been done in this direction; for instance, mutant strains of *A. platensis* have been selected that contained higher contents than the wild-type in essential amino acids, phycobiliproteins and carotenoids, among other nutrients (Brown 2008b). Cyanobacteria could also be used for food complementation without being directly eaten: they can be engineered to secrete nutritional compounds, so used culture media could be harvested without lysing cells and added to food (Way et al. 2011). Besides, as mentioned above, the possibility of engineering cyanobacteria to produce and secrete sugars has already been demonstrated. The use of plants could thus be restrained to applications where no large amounts are needed and where they could be grown within habitats (thus relieving the need for large-scale areas under highly controlled parameters): ornament and horticulture—which have beneficial psychological impact on crewmembers (Allen 1991)—and occasional provision of comfort food.

Another vital resource of human bases will be energy. Solar, wind and nuclear energy are potential sources of on-site (or durable) energy, and these could be complemented by biofuels produced on Mars for, for instance, powering vehicles. Microorganisms are well studied as biofuel producers. Some species studied for their abilities to generate biofuel precursors are heterotrophic and could have organic substrates generated by phototrophic microorganisms: for instance, yeasts are efficient ethanol producers and, even though usually relying on plant agricultural products as a carbon feedstock, cyanobacterial biomass (Aikawa et al. 2013; Möllers et al. 2014) or sugars secreted by cyanobacteria could be used as a substrate generated on-site. However, cyanobacteria could also be used to directly convert solar energy into biofuels, without relying on organic precursors: they can produce

various energetic compounds such as alkanes and lipids (see for instance Quintana et al. 2011) and dihydrogen (Raksajit et al. 2012), which can in turn be used for reducing locally available CO_2 to hydrocarbons to produce fuel (Hepp et al. 1993). For both heterotrophic and autotrophic microorganisms, microbial engineering using synthetic biology tools and methods for producing energetic biofuel precursors which are not naturally produced by the hosts, as well as for increasing yields, is a very active field boosting an increasing number of achievements (e.g., Ducat et al. 2011; Hallenbeck 2012; Peralta-Yahya et al. 2012; Radakovits et al. 2010; Zhang et al. 2011).

Engineered microorganisms could also be used for producing a pipeline of drugs on-site. In addition to the antibiotics, therapeutic peptides, antioxidants and other nutraceutical compounds that they naturally produce, microorganisms can be engineered to contain new metabolic pathways leading to the production of various drugs. The most famous example is the production in yeast and bacteria of a direct precursor of artemisinin, an antimalarial drug (Martin et al. 2003; Ro et al. 2006), but much more is to come (see, e.g., Folcher and Fussenegger 2012; Ruder et al. 2011; Weber and Fussenegger 2011).

Then, once all basic physiological requirements are covered (through BLSS processes, and drug and energy production), engineered microorganisms can be used for sustaining industrial processes. Metals could be extracted from Martian rocks by bioleaching: microorganisms are used on Earth to extract metals of industrial interest (e.g., copper and gold) from rocks, and their use on Mars to mine basalt and potential ores has been suggested, as well as ways of engineering microorganisms to increase their abilities to extract (and possibly sort) elements of interest (Cockell 2010, 2011). Extracted elements could be used within many chemical and manufacturing processes such as carbon dioxide cracking, electroplating, production of alloys and manufacturing of solar cells (see Cockell 2011; Dalton and Roberto 2008). Engineered microorganisms could also be used for producing or improving building materials such as bioplastics (Hempel et al. 2011; Osanai et al. 2014) and concrete-like materials (de Muynck et al. 2010; Jonkers et al. 2010).

This paper focuses on applications considered as realistic (even though ambitious) in the short- to medium-term (based on currently available techniques and past successes) and avoids reliance on too tentative speculations on the development of our biological engineering abilities. However, with the advances of synthetic biology, new methods for the improvement of biological strains will likely appear. One can for instance imagine changing the chemical composition of DNA (something that begins to be possible; see, e.g., Marlière et al. 2011) to make it less prone to radiation-induced lesion, or even synthesizing an artificial organism gathering the most relevant features from several microbes, leading to optimized metabolic abilities and outstanding resistance to the Martian environment. A byproduct of the development of such technologies will probably be the wish to use them for ecopoiesis by, for instance, increasing the abilities of selected microorganisms to spread on Mars's surface, to dissolve carbonates for thickening the atmosphere and to produce large amounts of oxygen (Thomas et al. 2006). The implications of such a

choice, as well as whether it is desirable or not, are beyond the scope of this paper. Modifications of multicellular organisms can also be thought of: plants, but also animals—including humans (and/or their microbiomes)—could be engineered to increase their fitness under extraterrestrial environments (Langhoff et al. 2011).

Even on a shorter term, many other applications of synthetic biology can be considered in human extraterrestrial outposts. Some are similar to what is expected on Earth (see, e.g., Khalil and Collins 2010 and Church et al. 2014 for examples of potential future applications), but many biotechnologies will probably be specific to space exploration. Indeed, some processes will benefit from synthetic biology there whereas they can be more economically performed by other means on Earth, for example by chemical methods, by using the natural host or by simply harvesting rather than producing the targeted compounds. Besides, metabolic pathways might differ: some substrates that are cheap and abundant on Earth will be extremely hard to provide on Mars. The key point here is that once organic substrates can be obtained from on-site resources (e.g., using cyanobacteria) and that microorganisms can be grown on Mars at low costs (e.g., due to genetically increased resistance), metabolic engineering opens the way to a wide range of potential applications.

There is still a long way to go: the brief overview given above doesn't reflect the work needed to overcome the obstacles lying between us and functional systems. Even though techniques are developed that allow efficient engineering of resistance and metabolic features, the increase in resistance needed to make a significant difference in extraterrestrial environments (e.g., the Martian surface) are huge, and engineering efficient processes for a wide range of products starting from Martian resources is currently at the edge of our abilities. Other tasks unrelated to synthetic biology must be conducted, such as selecting the most promising organisms according to their relevance for biological processes in Martian bases, thoroughly characterizing them to identify a compromise between, on one side, minimal requirements (radiation shielding, atmospheric composition and pressure, gravity, nutrient supply etc.) required for efficient growth and metabolism in planetary bases and, on the other side, conditions that can be provided on site (e.g., low atmospheric pressure composed of CO_2 and N_2) at minimal cost, designing a culture hardware that can provide these conditions directly on Mars's surface, linking the mentioned systems to full BLSS, and extensively testing all the components of the system to demonstrate its operational capability. However, the pace at which our abilities in synthetic biology increase make the design of suitable organisms reasonably achievable in the short- to medium-term; the other tasks are engineering or strategy issues, which are not obviously insurmountable given enough effort is dedicated to them. First manned missions to Mars will likely be short-duration (a few years) missions, and for these astronauts can rely on resources imported from Earth. These missions will be an opportunity to test BLSS technologies on-site while back-up resources are available. As our confidence in BLSS—and in life support technologies in general—increases, longer-duration missions can be planned where our dependency on local resources supplants that on imported materials.

In summary, naturally evolved cyanobacteria or those engineered for increased resistance and abilities to use in situ resources could be used for processing on-site materials and turning them into forms available to other microorganisms. From this basis, synthetic biology could open the way to a wide range of applications including the production of vital resources, energy, drugs, building materials, industrial reagents and comfort goods—all starting from resources found on site. Other potential applications of synthetic biology for space exploration (including modifications to non-microorganisms) are discussed elsewhere (Cumbers and Rothschild 2010; Langhoff et al. 2011; Menezes et al. 2014; Montague et al. 2012). Combined with physicochemical technologies (both completing each other and providing a safe redundancy for vital processes), synthetic biology can thus lead to the development of complex, Earth-independent human bases on Mars and beyond.

5 Societal Implications of Extraterrestrial Human Colonies Relying on Synthetic Biology

The societal ramifications of synthetic biology are being discussed intensely and at the highest levels worldwide. For example, in the US, the first report released by the Presidential Commission for the Study of Bio-ethical Issues was focused on synthetic biology (Presidential Commission for the Study of Bioethical Issues 2010). This report identified five guiding principles: (1) public beneficence, (2) responsible stewardship, (3) intellectual freedom and responsibility, (4) democratic deliberation, and (5) justice and fairness. Neither these principles nor the abundant discussion of the topic in other fora will be detailed here; some aspects are covered in other contributions to this book. Here, we rather focus on issues arising from the use of synthetic biology in support of human space colonization. Some are simply related to the fact that the former is fostered, thereby raising issues related to space exploration itself. Conversely, others come from the stimulation of synthetic biology by its application to the space sector. Finally, very specific issues are raised by the potential development of human colonies beyond Earth that rely on modified organisms.

As humans settle in destinations beyond Earth, a number of social, ethical and psychological concerns arise. There are those who doubt that investment should be made in space exploration: why should resources be spent on such a futuristic plan when there are problems to be solved on Earth?[7] But investment in space exploration is… an investment. Even a very rough assessment of the long-term economic benefits of colonizing new worlds would deserve a dedicated paper, but an interesting analogy can be made with colonization of America in the 17th century, or

[7]See for instance R. Hanbury-Tenison’s opinion in E&T Magazine (Issue 10, October 2011, p. 28), also available at http://eandt.theiet.org/magazine/2011/10/debate.cfm. Accessed 12 Mar 2015.

Australia in the 19th century.[8] Thinking of money spent in space as a net loss for other concerns on Earth can be compared to misevaluations of the value of these settlements by European governments, which now appear as absurd (Zubrin 1995). On the shorter term, economic benefits can be assessed based on past experience. Measuring economic returns from investment in the space sector is a complex task given that, to be accurate, one should take into account technologies indirectly derived from space innovations, and even technologies created by inventors inspired to pursue a career in science or engineering by space exploration. However, economic returns can be estimated from results of technology transfers; the "Space Economy" was assessed at $180 billion in 2005 by the U.S. Space Foundation.[9]

That being said, benefits brought by space exploration are not best described in economic terms. One of the most commonly mentioned arguments in favor of becoming a multi-planet species is the risk of large-scale disasters such as an asteroid impact, which justifies the development of our ability to reach and settle on other planetary bodies (see for instance Baum 2010; Matheny 2007). As pointed out in a talk at NASA's Goddard Space Flight Center by Michael Griffin, then NASA Administrator, "[t]he history of life on Earth is the history of extinction events, and human expansion into the Solar System is, in the end, fundamentally about the survival of the species" (Griffin 2006, p. 24). On a less extreme side, our everyday life has been greatly enhanced by technological advances brought by the Space Age.[10] It has led the development of a wide range of technologies such as telecommunications, GPS, weather prediction, large-scale environmental analyses, and disaster prediction and monitoring. To these can be added those that come indirectly from the space industry, such as artificial hearts and other medical improvements, innovations in the automotive and home industries, or land mine removal devices (see, e.g., Dick and Launius 2009; ESA and IAA 2005). Imagine our modern society bereft of the contributions derived from space exploration! And many more benefits are expected in the future, including our reliance on clean energies, breakthroughs in transport technologies, low gravity manufacturing, mining in space, increased knowledge of the universe, space tourism and stimulating challenge. In addition, humans have always been explorers, venturing forth out of Africa and beyond. They have a primal wish to discover new lands, which drives inspiration, creativity and discoveries. This sense of curiosity of what is beyond results in a sense of wonder and belonging to the greater spirit and purpose of humanity as a whole.

[8]This analogy here refers to economic aspects only and do not represent the authors' opinions on other elements of past colonization such as, for example, the way indigenous people were treated.

[9]http://www.nasa.gov/pdf/189537main_mg_space_economy_20070917.pdf. Accessed 13 Mar 2015.

[10]An analogy can be made with the military sector, which also leads to technological innovations due to the urgent need for technological advances (see for instance Perani 1997). Whether space exploration objectives are preferable to military ones as driving force for innovation is left to the reader's judgement.

The philosophical impacts of space exploration have been less tangible but no less momentous: space exploration humbles us by increasing our knowledge of the universe. It also fosters collaborations and forges agreements among countries, and attracts youth into careers in science and technology. More subtle consequences can also be expected. Space exploration may for instance shift our frame of reference from Earth to the solar system or even to the universe, which is likely to change radically our vision of our planet of origin and of the importance of preserving it. Different scenarios can be expected, which are not necessarily exclusive and may vary among individuals. One possible outcome is a decrease in Earth's perceived value—it would, after all, be just one of the places where we can live—but the opposite is also possible: by contrast to Mars and other planetary bodies, Earth may appear as incredibly hospitable and rich in diversity. Space exploration may also increase our awareness of how vulnerable Earth is, switching the status of global disasters from an abstract concept to a concrete risk, thereby fostering environmental protection policies and individual sustainable behaviors. It is also likely to affect the perception people have of "home"; a good model to predict such reactions can be drawn from emigrants' experience on Earth. People living outside their country generally develop a sense of belonging at a broader scale, defining themselves according to their nationality rather than, for instance, their city. Few people think of themselves as earthlings; what would be the consequences of such an extended sense of belonging? What effects would it have on global decisions? Would people consider interests at a larger scale? Then, adapting organisms to conditions previously considered as inhabitable extends the limits of what we consider as being the envelope for life. Such an artificial adaptation shows that this envelope's limits are not defined by life's absolute potential but rather by the limited evolutionary constraints in presence of which terrestrial life was shaped. The vision we have of the uniqueness of Earth as a life nursery and harbor may be affected, which may encounter resistance from people whose religious beliefs or worldviews are incompatible with it. Similar but more extreme reactions can be expected if space exploration leads us to the discovery of life beyond Earth (Connell et al. 1999; Race et al. 2012).

Outposts on Mars and other planetary bodies may also create a diversity of new cultures and sociopolitical forms. Their development will be facilitated by the freedom and self-reliance of pioneers, by the current lack of legislative framework on site and by the lack of means of remotely enforcing laws. New forms of society may emerge as an adaptive response to local environments and living conditions. They may take an original form, as created in unusual contexts and driven by isolated people sharing very specific traits such as, for instance, high intellectual abilities and a passion for science and engineering. Analogies can be found in human history. One of the most obvious examples comes from the first steps of America's colonization by Europeans: a relatively small number of people, gathered in a remote environment which was original to them, and sharing strong features such as a taste for novelty, a high adaptability and a project-rather than people-oriented mind gave rise to a society with a set of values differing from that of their countries of origin. With the colonization of another planetary body,

remoteness, novelty of the environment and strength of the shared features will be pushed to an extreme.

Synthetic biology could, as discussed in this paper, become a powerful tool for human space colonization; it could thereby hasten the benefits mentioned above. If this scenario occurs, it will also lead to the reverse: space exploration will become a driving force for synthetic biology. Little in human history has been such a powerful drive for science and technological breakthroughs as space exploration. In the past 60 years, technologies were developed that we didn't imagine before and would certainly not have expected in such a close future. If the next part of the story relies on synthetic biology, a wealth of game-changing innovations is to be expected in this field. The establishment of human colonies relying to a large extent on modified organisms will require dramatic advances in synthetic biology, as permanent access to many compounds taken for granted on Earth will depend on our ability to generate them on site. With the additional constraints to generate them from a limited set of starting compounds (on-site resources) and possibly under unusual environmental conditions, the limits of synthetic biology (noteworthy metabolic engineering) will have to be pushed to a new level. Its miniaturization and automation will likely be extensively improved as well, due to the need for minimizing mass and manpower requirements in space missions. Space synthetic biology will likely inspire a new generation of biologists, as the space race inspired many physicists and engineers, providing the brainpower needed to support this innovation wave.

By enhancing the pace of achievements in synthetic biology, space exploration can greatly speed the consequences—promises and perils—expected to come from the former. These range from extrapolations by media of talks from synthetic biology public figures, such as Craig Venter and George Church, where all plagues are cured by drugs produced by chemically synthesized microbes and all cars are powered by eco-friendly fuels, to apocalyptical "green goo" scenarios where the world ends after bioterrorists lose control of their creations. There is however a continuum of more plausible scenarios in-between these fantasized extremes, with society-impacting breakthroughs and catastrophes that can realistically be foreseen in the relatively short term. These are largely discussed elsewhere (see for instance Aldrich et al. 2008 and other chapters of this book) and won't be detailed here.

Unexpected applications can also arise on Earth from the fact that synthetic biology is specifically driven by space exploration. Extensive effort is made by space-related institutions to ensure that the developed technologies are transferred to the civil world; in the case of space synthetic biology, what does this imply? Our abilities to design organisms able to grow under modified environmental conditions will increase the efficiency of microorganism-dependent industrial processes which are often limited by the absence of microorganisms that can efficiently catalyze the appropriate chemistry under conditions (e.g., high temperature, high concentration of a reagent or product and specific pH) needed to optimize the process, and relax the need for providing energy-consuming culture conditions. In other words, pushing the bounds of terrestrial life can result in economic benefits, as the more hardy synthetic biology-enhanced life forms may be able to improve, or even

revolutionize, the bio-based manufacturing sector. Then, tools and methods developed to engineer the production of specific compounds starting from a very limited and constrained set of substrates could both decrease costs (starting from cheap substrates) and valorize specific products (starting from waste or troublesome compounds, such as glycerol which is largely generated as a by-product of the biofuel industry—see Pagliaro and Rossi 2010). Industrial processes could be more easily combined so that the end product of one becomes the substrate of another, creating a balanced "ecosystem" of biotechnological processes. In addition, transferring to Earth our abilities to design biological systems to live "off the land" in harsh environments and relying on a minimal set of resources could bring much more inspirational applications: generating resources in agriculturally poor countries. Rocky deserts could start to be considered as fertile lands, gathering all elements needed to sustain prospering human civilizations and to generate valuable resources.

The public's opinion of synthetic biology might also be fundamentally altered by its use as a tool in space pioneering. On Earth, practical applications of synthetic biology are often challenged by the public's opinion. Whether the benefits of a given use justify the perceived risks is not always clear and varies according to each individual's values. On other planetary bodies, however, alternatives are often not available and the use of synthetic biology may turn from being a luxury to being a necessity. For instance, a healthy diet can be obtained by traditional agriculture methods on Earth but is unlikely to be entirely produced on Mars without engineering organisms to produce some needed nutrients while relying on local resources. Besides, much of the opposition to synthetic biology is driven by fear of potential negative consequences, be they rational or not. Opposition may thus be reduced if applications are carried on far from Earth, making feared consequences much less likely to affect the layman. The public image of synthetic biologists might also change. Currently, it is mostly based on a very limited number of publicized researchers, and synthetic biologists are sometimes depicted as narcissistic scientists working not for the benefit of the society or for knowledge, but to feel empowered or for "playing God". In the context of space exploration, this image may switch to that of pragmatic scientists doing the necessary to support the expansion and long-lastingness of our species.[11]

There is, however, a major concern raised by the use of synthetic biology in space: contaminating extraterrestrial bodies with terrestrial life. This could jeopardize the search for potential extraterrestrial life and life precursors, extinct or extant. Measures should be taken to evaluate the planetary protection-associated risks of BLSS such as those described above (in addition to those of human-associated microbiomes and microbes present on all imported materials; see for instance McKay and Davis 1989, DeVincenzi 1992, and Debus and Arnould 2008) and strategies should be developed to mitigate them. Current international

[11]That being said, the possibility of this being seen as "playing God" cannot be ruled out.

treaties and policies related to planetary protection[12] provide a basis, even though requirements need to be extended to be relevant for manned missions (Horneck 2008). This risk is present even when synthetic biology is out of the equation, but increasing the abilities of microorganisms to withstand the explored environments increases the risk of contamination in case of microorganisms' accidental release. Issues associated with a targeted release of microorganisms, as could be considered for geoengineering, won't be discussed here; first, because the concepts mentioned in this paper assume that used organisms are contained and will not be purposely released and, second, because the ethics of implanting terrestrial life on other planetary bodies, Mars in particular, have been extensively discussed elsewhere (see for instance McKay and Marinova 2001).

6 Conclusion

Advances in applied physics allow us to go farther and farther from the Earth, with NASA's Voyager 1 spacecraft entering interstellar space on 25 August 2012; advances in applied biology can allow us to settle elsewhere in our solar system. Synthetic biology can increase our abilities to live "off the land" on other planetary bodies, thereby increasing our abilities to colonize them, to learn about them and to develop along the way technologies finding applications in our everyday lives. Ultimately, mastering the design of organisms capable of producing life-support resources from local substrates can be a key step in the path leading humans to become a multi-planetary species.

Conversely, using synthetic biology as a tool for space exploration can increase dramatically the development of the former, due to the resulting need for innovation and more generally to the technology drive of the space sector. The development of human colonies depending heavily on synthetic biology for survival and comfort would create an urging need for new discoveries and engineering work in this field. This can bring to a closer future the foreseen consequences—be they greatly beneficial, catastrophic or barely noticeable to the layman—of synthetic biology on Earth.

Besides, in addition to issues raised by the development of both fields independently, the possibly synergistic impacts of both becoming a multi-planetary species and of relying on extensively modified life forms are unprecedented and hard to predict. These can be economical, technological but also philosophical and psychological: how will our vision of our importance in the universe, of the preciousness of Earth and of the value of life be affected? And how will that translate into our everyday lives?

The path we have started to follow can dramatically affect the evolution of our society. Decisions should be taken well ahead of time to ensure that where we are going is not being defined only by what we *can* do, but by what we *decide* to be a desirable future.

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[12]See for instance http://planetaryprotection.nasa.gov/documents/. Accessed 6 Mar 2105.

Acknowledgements The authors are grateful to those who made possible the TASynBio Summer School where this book chapter was presented: the organizers Kristin Hagen, Margret Engelhard and Georg Toepfer, the attendees for their insightful comments and friendly conversations, and the funding body: the German Federal Ministry of Education and Research. They are thankful to the editors, whose comments and suggestions lead to significant improvements to the manuscript. They also thank the Italian Space Agency for supporting the BIOMEX_Cyano and BOSS_Cyano experiments. This work was supported by IGPL's appointment to the NASA Postdoctoral Program at NASA Ames Research Center, administered by Oak Ridge Associated Universities through a contract with NASA, and by CV's appointment to the NASA Education Associates Program managed by the Universities Space Research Association. Therefore the authors are also greatly thankful to the then Center Director S. Pete Worden.

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