Human Adaptation to Deep Space Environment: An Evolutionary Perspective of the Foreseen Interplanetary Exploration

François Criscuolo, Cédric Sueur, Audrey Bergouignan

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François Criscuolo*, Cédric Sueur, Audrey Bergouignan*

Université de Strasbourg, CNRS, IPHC, UMR 7178, Strasbourg, France

*Authors for correspondence (audrey.bergouignan@iphc.cnrs.fr, francois.criscuolo@iphc.cnrs.fr)

Long-term and deep space exploration is a prevailing dream that is becoming a reality. Is that so? The answer to this question depends on how the main actors of space exploration, i.e. politicians, scientists and engineers, define "long-term" and the ultimate goals of the current space programs. Presently, long-term refers to few months or years, which is equivalent to the time necessary for a manned mission to reach another planet and return to Earth. Such a space mission is a tremendous scientific challenge associated with multidisciplinary issues spanning from technology [1] to medicine biology [2], social and psychological science [3]. It has been a priority of the main westernized societies that has attracted the brightest and most innovative scientific minds since World War II. At first the stakes were mainly political in order to demonstrate to other countries power and strength. It progressively became a scientific motivation to uncover the secrets of the Universe and life's origin, and potentially to find traces of distant life. More recently, a desire to colonize space and exploit resources on other planets has emerged as a new dream. Although the journey to Mars is still a prospective and travelling in deep space a further elusive goal [4], one can question the ultimate implications of deep space exploration over the long-term.

This perspective requires subscribing to a new paradigm that no longer sees "long-term" as months or years but rather as time in an evolutionary context. This further means that instead of thinking about the physiological and psychological response of the human body to the space environment, we must consider the adaptations that will be naturally selected by this extreme environment. The long-term objective may then be to provide humanity an access to space shelters (*i.e.* spaceships or exoplanets) in order to survive the Sun's death.

Going into deep space should therefore also concern evolutionary biology/ecology research fields. Including evolutionary concepts to better assess the long-term challenges imposed by the human presence in space could open up new perspectives for imagining how successive generations of humans will cope with the environmental conditions of space. Such a question belongs to the research field of evolutionary biology, which essentially tackles how evolution resolves previous challenges imposed to life on Earth. We believe this question easily extends to how evolution will help a human population adapt to an environment drastically different from the present on Earth. In fact, evolution through natural selection has led to the emergence of species that can live in extreme environment. Some prokaryotic microorganism (*e.g.* bacteria), crabs and fishes can inhabit extreme environments like boiling waters and/or live under high environmental pressure. Some Vertebrates (mammals and birds) can also live when facing ambient temperatures of -40°C or sustaining highly demanding physical activities at an altitude above 7000 m. Such a questioning on the evolutionary mechanisms and environmental limits of living beings was actually, although not presented as in the present perspective, recognized by the NASA Astrobiology Roadmap as one of the scientific objectives to be addressed [5].

Presently, research in space life science mainly focuses on understanding the physiological adaptations to the space environment, *i.e.* physiological responses to microgravity and radiation, and to a lesser extent to the loss of nycthemeral cycles, exposure to extreme temperatures or hypercapnic conditions present in the ISS. The goal is to assess the impact of these changes on health and consequently on the safety and survival of the crew members. It is now well known that microgravity leads to a myriad of body alterations including bone and muscle mass loss, cardiovascular deconditioning, impaired exercise capacity, immune-deficiency and alterations of peripheral metabolism [6-8]. To prevent the development of these physiological modifications during spaceflights international space agencies have put a lot of effort into the development of countermeasures. Countermeasure programs essentially consist in nutritional and pharmacological treatments, exercise training protocols, vibrations and low body negative pressure used separately or in combination [2]. Adaptations to the space environment are often referred to as maladaptations when they are in fact physiological responses to a new environment with different physical characteristics. What is commonly considered maladaptive is a physiological trait that deviates from an optimal response shaped by natural selection in the terrestrial environmental conditions, but not an inability to adapt to space environment. A first provisional response to such a challenge could be to artificially modify human physiology to allow human life to thrive in the unique space environment. One could imagine that synthetic molecules could be developed to prevent short-term physiological alterations. This could be a promising avenue for space research on human adaptation [9], if long-term administration of synthetic molecules does not trigger additional medical issues over the long-term. The different approaches developed by the field of synthetic biology [10], such as genetic engineering or synthetic molecules redefining the main physiological pathways, could theoretically provide biological tools for a short-term adaptation to multiple challenges imposed by spaceflight. However apart from the obvious ethical issues of human design, the start of a new human lineage is not, in our opinion, a definitive solution. Such pre-adaptation to space will be based on our current knowledge of astronaut's health problems (*e.g.* bone and muscle loss), which may not be the main factors limiting the long-term survival of humans in space. Furthermore, exposing these humans designed for living in deep space does not preclude human physiology to pursue evolutionary process through selection. Nevertheless, synthetic biology offers interesting opportunities. It could be used to either investigate synthetic genetic systems that can neutralize evolution of key genes, or to send synthetic entities capable of evolution into deep space and thus ensure space observation, analysis or pioneering tasks [10].

An alternative is to look at the short-term human physiological response to space in an evolutionary context. We should consider three possibilities when analysing the unhealthy output of exposition to microgravity. First, not everything in evolution is adaptive and some of the genetic and phenotypic traits we observe are the result from the best of misuse strategies. There are many examples in evolution showing that behaviours, reproductive tactics, or phenotypes originated from genetic conflicts or life-history trade-offs, which precludes organisms from being perfectly adapted to their environment [11]. Thus, it can be considered that humans may never optimally adapt to the space environment. Second, the responses of the human body to the space environment may reflect the short-term mismatch between the rapid and drastic changes in environmental conditions, and the concomitant modifications in human physiology (*i.e.* phenotypic plasticity). However, plasticity is not adaptation, and the evolution of human traits may require a much longer time-scale (*i.e.* thousands of years at least) to adapt to space conditions. Again, the synthetic biology may putatively accelerate the adaptation process. However, we know that the extent of bone or body mass loss widely varies among astronauts, some showing dramatic variations in their pre- and post-flight values, while others do not [12]. This means that there are genotypes and phenotypes within the human population that may offer some degree of short-term resistance to space environment. In evolutionary biology, this corresponds to the concept of reaction norms, *i.e.* the ability for the same genotype to produce different phenotypes under the influence of the environment. We can envisage that the directional selection conducted so far, based on short-term benefits and comprehensive rules of astronaut's safety, experience and productivity, prevented us from screening the whole distribution of human phenotypes/phenotypic plasticity that best matches with rapid exposition to living conditions in space. The recent rise of private companies (*e.g.* SpaceX, Blue Origin) that aim to open spaceflight to private passengers, *i.e.* individuals not selected on the basis of strict physical/cognitive performance, could provide an experimental window to test a wider range of human phenotypes in response to the space environment. Thirdly, we could also consider that the short-term responses observed so far in astronauts belong to an adaptation process in the evolutionary sense, *i.e.* long-term changes that will promote the selection of genetic and phenotypic variations of individuals associated with higher rate of reproductive success in space. We have already seen that these changes are slow in humans for various reasons including the diploid genome, our developmental constrains, and our pace-of-life. As a conclusion, fast changing variables (i.e. what is currently called human space adaptations) may be indicative or not about long-term adaptability (i.e. evolutionary human adaptation). The answer to this question will be unveiled when the impact of short-term adaptations on human fitness will be tested. With this in mind, we can enter into an evolutionary vision of the study of space biology applied to human biology, which has been surprisingly lacking over the past years [13].

It is far from incongruous to think that space and evolution are linked. Going past the billions of generations that separate us from the very first living being that appeared on Earth 4.5 billion years ago, and go back up one more generation, one can feel what the thinness of the presence and absence of life. In a similar vein, the Panspermia theory of Richter and Arrhenius was proposed more than a century ago hypothesizing that some forms of life, resistant to space stressors such as outer space or radiations, might have the ability to spread from planets to planets [14,15]. There is now experimental evidence showing that some life forms such as bacteria or tardigrades may survive exposure to space [16-19]. This actually opens up exciting avenues of research for human adaptation to space. Two of them have already been assessed because they have short-term implications. First, microgravity through genomic and phenotypic adaptation may enhance the population growth rate of certain bacteria as well as their virulence or resistance to antibiotics[19-22]. This has conducted researchers to study how the host-pathogen relationships can be accordingly modified [23]. The second (and still related to the former) concerns changes in the microbiome (*i.e.* the many microorganisms living in the human host) during exposure to microgravity and radiation. The diversity of microbiotes decreases after a spaceflight, which can weaken some healthy functions such as immunity [24]. By consequence, maintaining the microbiome during long-duration spaceflight is a major health challenge for astronauts. These changes may be due to (i) a direct causal effect of microgravity on the bacterial populations of the microbiome, or (ii) an indirect effect of spaceflight environment on the host (*i.e.* astronauts) physiology, such as stress or change in the quality of the diet [25]. These modifications in population composition may reflect intimate changes in the gene expression of bacteria [26], pointing out mechanisms of phenotypic plasticity and norms of reactions to space that need to be better understood. What would be the long-term output of having two entities intimately linked physically and physiologically but evolving at very different rates in response to the space environment? It is likely that natural selection will promote a remodelling of the microbiome towards a composition better associated with the greater reproduction success of its host, integrating the prevailing environmental constrains. This means that we cannot interpret, so far, the observed modification of the microbiome as an alteration of an optimal situation, which has evolved under different conditions on Earth. The temptation to explore the biological engineering of the microbiome [27] to establish the evolutionary stability of bacterial populations is interesting. However, we cannot extrapolate that this will provide the human host with a more suitable phenotype over generations of space travellers. Furthermore, the rate of change of the microbiome in humans is likely to be accelerated by our social nature as a species. As suggested by long-term simulation of living conditions in space [28], changes in the microbiome composition are partially driven by social interactions. Sociality matters for long-term space travels [29] ; for obvious reasons, it is already taken into account when selecting members for a space mission. As the microbiome influences individual behaviour *via* the gut-brain connection [30], it also has evolutionary consequences for the space adaptation of human beings. In addition, because highly deleterious parasitic organisms favour host-to-host transmission, limiting horizontal transmission between space mission members may be a key factor when considering generations of humans who are slowly developing new host-pathogen relationships. This should be taken into account in studies aimed at resolving infection diseases in deep space. Apart from isolating each person from the other, impinging horizontal transmission is a challenging strategy to implement given the operational capabilities of space shuttles. In conclusion, the rapid and low rates of evolutionary under space conditions apply to cells and whole-organism [31]. The adaptation of cells to gravity may or may not favour the adaptation of individuals (*i.e.* promote reproductive success in space), and we need more long-term data to fully understand the meaning of the short-terms dynamics of single cells response to the space environment.

With generations of humans travelling into deep space, the selection of individuals with the greatest reproductive success in this specific environment must be top priority when considering human adaptation to the space environment. This has evolutionary consequences as well as obvious ethical issues [32]. We would like to highlight here key points relating to reproductive success, methodological or theoretical, both placed in the context of evolutionary theory. First, investigating adaptation in an evolutionary perspective calls for studies at the population level, because it will decipher the nature of the phenotype associated with the highest breeding success during spaceflight. This is the most powerful way to assess how organisms, as a species over generations, will succeed surviving the space environment. Previous studies in bacteria subjected to microgravity have revealed interesting evolutionary patterns. The bacterial populations exposed to microgravity display increased growth rates suggesting specific adaptations that lead them to overtake the cultures of their terrestrial siblings[22]. Ranging from the differential expression of genes and proteins, alternative splicing [33] or genome size reduction may explain, among other possibilities, the higher growth yields of space-exposed bacteria. The ultimate costs in terms of persistence of these mutants/phenotypes in the long-term remain to be established. Nevertheless, by reproduction we mean sexual reproduction (*i.e.* with male and female gametes) and not asexual reproduction (*i.e.* like most bacteria). The reason is simple: the evolution of humans in the space environment will never return to asexual reproduction. This is due to developmental constrains inherited from the history of human evolution based on the sequential expression of genes inherited from the father and mother during embryonic growth. In this line, how developmental constraints restrain evolution under microgravity is in itself an interesting topic because phenomena like blastula development is partly governed by gravity [34]. Then, we need to use sexually reproducing animal models, place them in microgravity and/or space radiation, and record the short-term changes in pre and post-natal growth patterns, as well as their genomic and phenotypic changes over generations. By allowing the population to evolve and establish these changes in gene frequencies associated with high reproductive success, we can identify key genes and alleles for space adaptations. Second, adopting an evolutionary view of human adaptation to space will bring us beyond purely medical aspects of human reproduction in microgravity [35]. Because sexual reproduction encompasses processes such as genetic conflict, mate selection and social constrains, we need to integrate specific traits of human biology and evolution into future experiments. For instance, the kin selection theory [36] has yielded important implications for our understanding of sexual reproduction and evolution of cooperation. Among these, the mother-father conflict is driving the expression of developmental genes, which are involved in the way the foetus will manipulate the mother's investment in reproduction, the outcome being a gain in foetal mass. Males found a benefice in driving genes promoting mass and survival of the offspring, while females have to found the best trade-off between the cost of their reproduction and their survival and chances to reproduce again. The way in which the expression of these genes is altered by the space environment is likely to have tremendous consequences on the evolution of human population over generations. For example, theories are emerging on the relationship between the mother-father conflict and mental illness in offspring [37]. Whether autism or schizophrenia prevalence may differ in space-based human population compared to Earth-based human population, considering parents-conflict or changes in the microbiome [38] has important predictive value.

Beyond the purely technological challenges, the question of the human presence in deep space turns first of all into philosophical questioning. For most of us, the rational of human space exploration is primarily related to high-value, near-term technological spinoffs or the economic promises of soon-to-be accessible natural resources. The growing share of private companies involved in spaceflight often justifies their activities by the extensive possibilities of exploiting minerals and metals, and thus being able to address the ecological crisis on Earth. Others also invoke exploitation of space resources as a way of reducing the environmental cost of human activities on Earth, reconciling the words sustainable and economic development for future human generations [39].

As we have seen so far, reflection on deep space travel brings us to address ethical and philosophical questions such as human engineering [40], and the selection of phenotypes or genotypes of the terrestrial inhabitants with the highest fitness. It further raises important questions about the future of sub-populations of astronauts derived from humans after generations living in space, and the relationship between human populations that will likely differ in their phenotype (and because evolution has to deal with contingency, evolution of different populations are likely to differ), but also in the way they view humanity's place in the cosmos. Astronauts have reported a shift in their relationship with Earth after a spaceflight. They specifically report that viewing the Earth from outer space increased their appreciation of its inestimable value and fragility [41]. As developed over the past 30 years by Frank White in his Hypothesis of the Cosma, a cognitive shift in awareness towards Earth, named as the overview effect, will likely occur in the mind of deep space travellers.

Every evolutionary biologist has had to face criticism of his/her scientific questions. The lack of immediate deliverables applicable to short-term objectives is often cited in evaluations. This is due to a misunderstanding of the goals of evolutionary biology. Studying the short-term physiological adaptations to microgravity and the long-term consequences of living in the space environment using an evolutionary perspective is not incompatible; both approaches are highly informative and relevant. However, we subscribe to the view that understanding the genomic, physiological and behavioural mechanisms underlying adaptations to new and contrasted environmental conditions must be placed in the light of evolution. Evolutionary biology is a field that attempts to understand a simple equation, *i.e.* how evolution actually finds a solution to an ecological problem. This is the question that life space science has tried to address: how do humans adapt to the space environment? By bringing current space research into the realm of evolutionary biology, we could generate new paradigms that will help humans to cope with deep space travelling. We are now entering a very exciting era during which such a question may be addressed.

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Author contributions

FC wrote a first text, which was thereafter extensively drafted by AB, and further commented by CS.

Competing interests

The authors declare no competing interests.

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