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Advancing terrestrial health: lessons from space

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Driving innovation in medicine through quantum biology

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(Eds.)

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ADVANCING TERRESTRIAL HEALTH:

LESSONS FROM SPACE

Introduction: Are mitochondria trapping humans on Earth? The role of stress, optimal health and non-chemical homeostasis

Professor Alistair Nunn

The Guy Foundation and University of Westminster

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Life on Earth took a very long time to evolve. However, after some 4 billion years, one species finally managed to develop technology to a point where it could get "off planet". Once modern science and technology got going, humans went from their first tentative hops in a powered heavier than air machine in 1903, to putting the first man in space in 1961, to one on the moon in 1969, and a fully occupied orbiting space station in 1971. In 2023, there are now two orbiting manned spacecraft, the International Space Station and the Tiangong CSS. Moreover, plans are being made to build permanently occupied outposts on the moon, as well as for a human exploration of Mars. Although the technology doesn't exist yet, many would love to expand manned flights to the other planets/moons/asteroids in our solar system, and onward to the nearest stars and beyond. In evolutionary terms, this jump happened in a blink of the eye – far shorter than any standard evolution could take place – especially for a complex species like humans. This suggests, unless we are prepared to do some drastic genetic engineering, we will need to take our home environment with us.

The plethora of science fiction novels, and their popularity, testify to humankind's urge to expand. However, quite apart from the technological propulsion issues, keeping humans and other living organisms in optimal health in space might be more of a challenge than previously thought. Alas, even the healthiest of astronauts, and most are very fit, quickly develop physiological, metabolic and cognitive problems once they go into orbit. This "dyshomeostasis" is hardly surprising, as we witness something similar on Earth by simply living a poor lifestyle, which seems to lead to an accelerated ageing phenotype; space is vastly more hostile than simply eating too much and being sedentary.

Much like the craft they build, humans have a “flight envelope”, which evolved and helped us survive under a very specific set of environmental conditions. It didn’t evolve to endure space. And much like the black box in most commercial and military aircraft and spacecraft, it seems that modern complex life also has a “black box” organelle, a canary in the metabolic coalmine if you will, that may well be telling us what is going wrong when complex life goes into space. This is the mitochondrion. Similarly, like modern technology, it is becoming apparent that organelles such as the mitochondrion may also be using significant quantum effects to function, which may explain life’s sensitivity to electromagnetic fields and might suggest some dependency on them. We may need to heed this last point when going beyond Earth’s magnetic fields and circadian prompts, and quite possibly, gravity as well. Thus, not only do we need to consider the importance of “non-chemical homeostasis” in optimal health on Earth, but also in space. The problem is perhaps highlighted as we are still a long way from understanding the “hard” questions, such as the origins of life, consciousness, ageing, and things like cancer, indeed, we even struggle with a definition of life, which perhaps hinders our search for it beyond Earth. In short, for humans to expand beyond their own planet we are going to have to understand ageing and health, which is a problem we still have not fully cracked on Earth.

Human health on Earth is of course a big subject and has not been resolved. For example, some estimates have put the global cost of obesity at more than $2 trillion per year; in the USA, this could be as much as $850 billion, which dwarfs the funding that NASA gets at some $20-30 billion. We have previously suggested that this could, as a human allegory and in keeping with the space theme, explain Fermi’s paradox: once any advanced race develops technology, it changes its environment to make life easier, so removing the very environmental stress factors that helped it evolve; the result – sky high healthcare costs. Not only might this reduce a species overall intelligence, as obesity through inflammation worsens cognition, but it reduces healthy and absolute life expectancy. Simply put, ET may not be visiting us any time soon because they cannot afford to as they spent their GDP on healthcare. It seems less about ET phoning home and more about phoning the gym. The truth is that although average life expectancies have improved due to better hygiene, food and shelter, healthy life expectancy has not, which is leading to morbidity expansion; many people are not living anywhere as long as they could be, and they spend a higher percentage of their lives in ill health.

Which of course raises the question, what is health and how do we define it? Is it simply a lack of disease, or a failure of homeostasis, and can we even measure it, and critically, can we stimulate it? What we do know is that humans have, like most other species a genetically determined lifespan that evolved to fit a niche. However, within this environmental "Goldilocks" zone, we also know that it can be modified, and one of the key factors that controls this is a biological process called "hormesis", which is encapsulated by the phrase: "what doesn't kill you makes you strong, smarter, and longer lived". It is in effect a biphasic adaptive response to stress that all life displays, and is derivable from adaptive thermodynamics and quantum mechanics, and fits well with the description of life as a far from equilibrium self-organising and replicating dissipating system. As Schrödinger put it, life is a piece of negentropy. The key warning shot here, of course, is that this also means that individuals, and species, are entirely disposable in the process of life's adaption to change to fulfil entropy's ultimate conclusion – heat death of the Universe. Death is a natural consequence of life and is intimately linked into a biological process that tries to repair damage, inflammation and thus ageing, which is described by the term "inflammaging".

One definition of living in optimal health is that an organism exhibits a high level of metabolic flexibility and reserve, in effect, robustness, and this seems to require a certain amount of the right kind of stress to stimulate its maintenance, for instance, exercise, occasional calorie restriction, and a diet with plant material containing phenolic compounds. The most recent example of this is reflected by the populations most at risk of SARs-CoV-2; being aerobically fit and not obese is protective. Central to this is the mitochondrion, which is multifunctional and is involved in just about every system in the cell and is a major sensor to environmental changes. It doesn't just harness energy, but is key in ion and redox homeostasis, anabolite production, life and death, immunity and inflammation, and thus, of course, ageing. It senses changes to the plasma membrane, the endoplasmic reticulum, the nucleus, and perhaps most critical of all in relation to space, the cytoskeleton where the concept of "tensegrity" is key as life evolved under 1 x g. A healthy mitochondrial system is very good at resisting oxidative stress and controlling inflammation and changes in the environment.

Any environmental change will thus alter, potentially, protein structure and thus the flow of electrons and other ions. One could thus envision the concept of the "smart quantum mitochondrion", where any change in electron flow alters redox, and thus, reactive oxygen species (ROS) production. Key here is that the mitochondrial metabolism can be traced all the way back to the most likely place where life evolved, the alkaline thermal vent, and some of the key components, such as the iron sulphides and aromatic compounds, which, if combined with the importance of chemiosmosis and the flow of hydrogen ions linked to movement of electrons, indicates that charge flow, and thus electric fields, were an integral part of life's origins. When considering life, it therefore isn't just about "conventional" biochemistry, but electrodynamics and fields. Maybe acknowledging the concept of "field homeostasis" will help us improve medicine and the concept of optimal health – and it may well be important in keeping people healthy in space.

So how do the concepts of hormesis, optimal health and non-chemical homeostasis help us with space travel? One aspect is that it may help determine whether the metabolic changes we see in astronauts are adaptive or pathological – life will try and compensate if it can, but outside of its metabolic flight envelope, without natural selection through genetics, it likely becomes pathological. For instance, humans can adapt, to some degree, to varying levels of pressure and oxygen, much as they can to gravity, radiation and temperature, and even changes in diet. But if they venture into an environment too far outside their flight envelope, they may not be able to adjust, as they do not have the software, or the hardware to adapt. We evolved to exist in a "Goldilocks" zone. Hormesis can expand the flight envelope, but only to a certain degree; we can train to run faster, or hold our breath for longer, for instance – but we cannot survive without oxygen. But feed us too much and stop us exercising, and our ageing rate accelerates; feed us too little and over exercise us, and we succumb. Evidence is, based on the effects on mitochondria, that orbiting the Earth also does the same thing. In contrast, prokaryotes do seem to be able to adjust to space, although even they seem to display some problems – but they are far simpler and can rapidly evolve. Thus, in some respects, being multicellular with complex cytoskeletons and mitochondria does make us a bit more susceptible. The "tensegrity-mitochondrial" system in space may be pushed beyond its design specification.

In this symposium we brought together scientists from several different disciplines – some of which may not necessarily be immediately thought of when thinking about space health. A lack of gravity is clearly important, as is a different spectrum and intensity of radiation, but it may also be likely that changes in, or indeed, the lack of Earth's magnetic field, its oscillations, as well as gravitational wobbling could also be something that life is sensitive to, and possibly reliant on for optimal health. In effect, life is *slaved* to the Earth's gravitational and electromagnetic signature, which, after all, was pivotal in the form life took at the very beginning. We are in "step-lock" with it. Out is space, we may be out of step.

In the first talk, I provided an overview of how we, as a species, could view optimal health from the concepts of hormesis and quantum mitochondrion, and the importance of fields, and maybe acknowledge that as we have not sorted out our own Earth-bound health, we still have a lot to learn about how to move medicine forward on Earth, let alone space. In the second talk Afshin Beheshti, using data from astronauts and NASA, as well as other agencies, made it clear that mitochondria certainly do become dysfunctional pretty quickly, even in low Earth orbit. In the third talk, Michal Cifra summarised just how important electric fields are in biology, which led into the fourth talk by Mike Levin indicating that morphogenetic fields are part and parcel of how organisms define their shape and are key in regeneration – and how we need to learn the software language which determines this. In the fifth talk Betony Adams gave an overview of magnetic fields and raised the prospect that biology could well be using quantum spin, which as Wendy Beane indicated in the sixth talk, could be very much part of redox homeostasis – which is fundamental to life. In the seventh talk, Steve Thorne outlined a theory that life isn't just dependent on a fixed gravitational field but could also be influenced by gravitational oscillations due to the Earth's rotation and the effects of the moon. Unfortunately, Aenor Sawyer who was scheduled to give the last talk of the day on the physiological effects of microgravity was unable to attend, so I stepped in and summarised some of the effects, which are very extensive indeed. Microgravity seems to affect detrimentally just about every system in the body – ranging from the more obvious, such as muscle and the cardiovascular system, to the less obvious, such as the skin, gut microbiota and eyesight. Critically, we can see the effects all the way down from macro to micro levels, the latter for instance, in the massive changes to cellular structure that would be predicted by removing gravity and its effects on the cytoskeleton, which through multiple pathways would greatly affect basic cell homeostasis, including mitochondrial function – and could involve sensing by the "quantum underground". Whether or not our current biological genotype/phenotype can adapt to slow down the ageing effects is simply not known.

Overall, it seems clear that there is still a great deal to learn about life and what it means to live in "optimal health", not only on Earth, but also beyond its birthplace. The most startling conclusion is that unless we can mimic Earth's signature in space, astronauts are very likely to develop an accelerated ageing syndrome – adaption becomes pathological. Evidence is hinting that reproduction may also be compromised. For instance, it might be predicted from the relationship between mitochondria and the cytoskeleton that a lack of gravity, and changes in magnetic fields, would affect development, let alone the effects of excessive "space" radiation. It will therefore be key to do a lot more experimentation to unravel what is happening and why.

It is likely, as we now know, that humans can to some extent, even with the current technology, adapt to some degree, but most data are limited to a very few, very fit and healthy people who have spent less than a year in low Earth orbit where they are protected to some degree from the worst ravages of space radiation, and likely, are still influenced by the Earth's gravitational and magnetic fields. We also simply do not have large enough datasets on those that have been in space; this is partly due to low "n" numbers. For instance, depending on definitions, less than 650 people have been into space – and far fewer have spent more than a few weeks. This lack of knowledge has probably also been due to a lack of a coordinated long-term study, and pivotal experiments, such as nullifying microgravity by say, living in a rotating habitat. Beyond Earth's protective blanket, in deep space, where people could be for years, the environment is likely to push the human metabolic flight envelope well outside of its boundaries. It is likely that the weak gravity on other planets/moons will compensate to some degree, but the emerging evidence suggests that field-based homeostasis, and an associated quantum underground to life, indicates we need to embrace less explored biological avenues.

The overall question behind this symposium was "are humans trapped on Earth?". Clearly in the short term the answer is not, but in the longer term, and for people not trained to the athletic levels that most astronauts are, being in space for any significant time may well result in an age-accelerating metabolic dyshomeostasis. There is thus a great opportunity for a two-way flow of information; sub-optimal health on Earth may tell us a lot about disease in space, and vice versa.

Professor Alistair Nunn

Director of Science, The Guy Foundation and Visiting Professor at University of Westminster

Introduction to The Guy Foundation

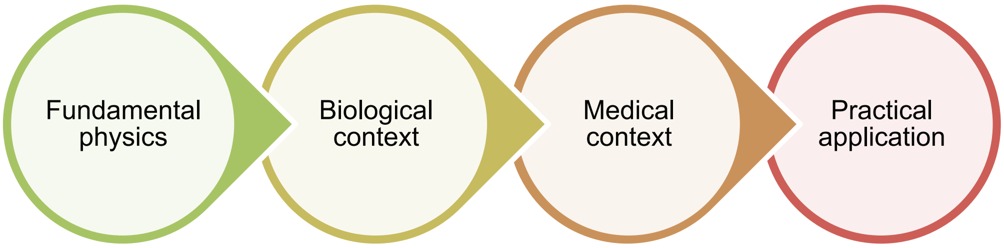
Professor Geoffrey Guy

Founder and Chairman, The Guy Foundation

The Guy Foundation aims to support and promote the investigation of quantum effects in biology, with the aim of improving our understanding of disease and thus medicine. Our belief is that significant quantum effects may well have been essential for life to get going, but also enabled it to grow in complexity by amplifying these effects both in space and time. All living systems depend on iron-sulphur compounds that display interesting tunnelling properties, which could be enhanced by the addition of proteins and chromophoric molecules. These molecules were all created by well understood geochemical/interstellar chemical processes long before life began, which coupled with established thermodynamic mathematical principles involving self-organisation of dissipative structures in energy gradients, do provide the basis of a starting point for life. In short, if significant quantum effects are part of life, the failure to maintain this state probably plays a role in disease and thus, the ageing process, and, of course, medicine.

The pioneers of thermodynamics and quantum physics, and – over the years – scientists, embracing many different disciplines, have discussed the possibility that biology could be using significant quantum effects. Some, such as Roger Penrose, have even gone as far as suggesting it could explain consciousness itself, which, even today, is still far from being understood. In fact, with time, despite the 20th century optimism that by the 21st century mankind would have found cures for cancer and many other diseases, and possibly even for ageing itself, a deeper understanding of life seems to be still out of reach. It could be even further away as emerging global obesity appears to be *shortening* both a healthy and absolute life expectancy, which is resulting in spiralling health care costs across the planet. Despite mankind's emerging technical mastery of nature, we still have a very long way to go in terms of truly understanding it.

The Guy Foundation thus leads and supports quantum biological and related research with the ultimate aim of advancing the development of new medical diagnostics and therapeutics. The Foundation believes this advancement can be achieved in a number of ways, which is reflected by the cross-section of scientists who join us for our online symposia as well as the research we fund. Our approach is summarised as encompassing research from bench to bedside.



Our priorities encompass the spectrum of theoretical, experimental, and practical advances. Understanding the fundamental physics (e.g., quantum mechanics, electrodynamics, thermodynamics) is important. More specifically we aim to understand this physics within the biological and physiological contexts, with the emphasis on furthering the study of medicine. Overall, we would like to see this knowledge translated and applied in new diagnostics and therapeutics.

The Foundation therefore aims to provide a platform and a forum for upstream push through and downstream pull through of the understanding of the role of quantum effects in biology in health and disease. With an emphasis on building a research community to further investigate these interests, The Guy Foundation operates in a spirit of collaboration rather than straightforward grant funding, to advance the course of useful knowledge towards the mainstream and bring it to the attention of more conventional funders. We aim to do this in various ways. For instance, by curating a programme of scientific meetings and publications that incorporates the diverse aspects of the field and facilitates engagement from scientists across relevant disciplines; as well as by identifying what we see as research priorities and building a network of interested scientists through the funding of collaborative projects to accelerate relevant high-quality scientific research.

Professor Geoffrey Guy MB BS, LRCP MRCS, LMSSA, DipPharmMed, BSc, DSc

Founder and Chairman of the Board of Trustees, The Guy Foundation

Abstract Proceedings

These are abstracts of an online symposium held on 1 February 2023, hosted by The Guy Foundation.

They have been written by the speakers and have not been formally peer-reviewed. We hope you enjoy them; video recordings are available on the Foundation's website **www.theguyfoundation.org**.

Mitochondria and space - the data in a nutshell

Dr Afshin Beheshti

KBR at NASA Ames Research Center

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Determining the biological impact of spaceflight through novel approaches is essential to reduce the health risks to astronauts for long-term space missions. The current established health risks due to spaceflight are only reflecting known symptomatic and physiologic responses and do not reflect early onset of other potential diseases. There are many unknown variables which still need to be identified to fully understand the health impacts due to the environmental factors in space. Utilizing a public omics data repositor for space biology data (NASA GeneLab), a comprehensive multi-omics approach was implemented correlating transcriptomics, proteomics, metabolomics, and methylation analysis. We found that cells have stronger overall biological response than the tissues to spaceflight, with mitochondrial activity and innate immunity pathways being heavily impacted. NASA Twin Study results are consistent with a specific alteration in mitochondrial ATP production. In addition, when expanding this initial on other organisms (e.g., C. elegans, plants, etc.) we observe similar mitochondrial changes occurring during spaceflight. Our results indicate that the space environment can directly induce mitochondrial damage, with mitochondrial dysfunctions being a cause for chronic inflammation and both being involved in the development of metabolic disorders that cause changes in lipid metabolism. We also found biological changes occurring during spaceflight with cell cycle, circadian rhythm and olfactory activity pathways which can also influence and be influenced by alterations on mitochondrial activity. In addition, from our earlier work, we demonstrated a circulating microRNA (miRNA) signature that is present and involved with the general increased health risks during spaceflight that impacts mitochondrial function directly. From this work we demonstrated that this miRNA signature impacted the overall biology and health with both the microgravity and space radiation components of the space environment. We showed that this miRNA signature can be an optimal biomarker for health risk and also has potential to be utilized as a countermeasure to mitigate the damage caused by the space environment by utilizing a human 3D microvascular tissue model. By applying a novel self-delivery system to target 3 miRNAs (i.e. antagomirs) from our spaceflight miRNA signature impacting cardiovascular health risks, we were able to completely mitigate damage caused by exposure to simulated Galactic Cosmic Ray (GCR) irradiation. Here we further expand on the countermeasure experiments to uncover the specific novel biology involved with this countermeasure and *in vivo* experiments that demonstrates that these antagomirs rescue damage caused to certain organs due to both microgravity and space radiation. Specifically, the miRNAs rescued damage to the heart, immune suppression, and improved mitochondrial function that occurs during spaceflight in addition to other key biology. In addition, we have also observed with the 3D microvascular tissue model improved DNA double strand break repair machinery which can also contribute to improved recovery and protection against damage caused by space radiation. This work expands on our previous work and further uncovers how a potential minimally invasive countermeasure can be used to mitigate space environment effects and that mitochondrial dysfunction is a key driver in biological response to spaceflight and potentially can lead to health risks.

Overview of electric fields

Dr Michal Cifra

Czech Academy of Sciences

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Electric fields play an essential role in biological systems, from the local electric fields of biomolecules [1] to the electric potential of the cell membrane. Electric fields are intrinsic to biological cells and are critical for higher organisms' functioning, where they trigger muscle movement and information processing. In biology, electric fields are mostly studied for low frequencies, while exploring higher frequency ranges in radio frequency bands and gigahertz could reveal the potential role of electric fields in bio-electrics [2].

Interestingly, the Earth can be described by a global electric circuit: due to the Earth's conductive surface and ionosphere, which represents a capacitor, everything present in this environment and on Earth is permanently exposed to this electric field [3].

External electric fields of appropriate parameters can also have a significant impact on biology. At the molecular level, electric fields can cause structural and functional changes if the field strength is high enough [4]–[8]. For example, exposure to electric fields at the cellular level can lead to electrotaxis [9], electroporation [10] and higher frequencies can affect structures within the cell interior. In the field of bioelectronics and tissue stimulation [11], electric fields have been shown to stimulate tissue growth and regeneration [12]. Finally, there is evidence that cells can generate and respond to electric fields, potentially using them for communication [13]. This area of research is still controversial but presents many exciting opportunities for understanding how cells interact with each other [14], [15].

In conclusion, the lecture highlights the importance of electric fields in biology, ranging from biomolecules to organisms. Electric fields have been shown to have significant impacts on various biological systems and could potentially lead to new research opportunities in the field of high-frequency bioelectrics. Resources are available for those interested in learning more about this field [2], [16].

The abstract was generated using Chat-GPT based on the transcript of the lecture and author's modifications.

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Membrane potential and regeneration

Professor Mike Levin

Allen Discovery Centre, Tufts University

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Biology is fundamentally built on a multi-scale competency architecture: every level of organization is able to solve specific problems (physiological, transcriptional, morphological, behavioural) with various degrees of intelligence. One of the most interesting aspects, for evolutionary biology and biomedicine, is the ability of information to cross levels. How does metabolic activity at the subcellular level scale up to order on the tissue, organ, and whole-body levels, eventually becoming brain-directed behaviour? In this talk, I will describe developmental bioelectricity as a kind of cognitive glue: a set of information-processing mechanisms that enables scale-up of cellular activity into higher-order functions such as morphogenesis and eventually, brain-mediated cognition. I will describe some examples across birth defects, regeneration, and cancer of how this information-based approach can be used as a roadmap for discovery of biomedical interventions. Numerous powerful applications will become possible when we master the scaling of physiological homeostatic loops into higher order information structures that regulate health and disease. I will also discuss the results of an experiment in which we allowed planarian flatworms to regenerate on the International Space Station, which resulted in anatomical, behavioural, and microbiological changes in the worms that lasted for over a year after they were returned to Earth.

Overview of magnetic fields

Betony Adams

University of KwaZulu-Natal

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A magnetic field might be described, very simply, as the space or region in which a magnetic force is experienced. Magnetism was first discovered as a property of certain materials, such as lodestones which are composed of naturally occurring magnetite. Magnetism in a material can be understood from the electronic structure of the material and the arrangement of magnetic moments. A magnetic field can also be induced by an electric current, or the movement of charge in a material. While electricity and magnetism were long thought of as separate phenomena, scientists such as Orsted and Faraday and Maxwell were instrumental in demonstrating, experimentally and theoretically, that they were related phenomena, which led to electromagnetism and the understanding of light as electromagnetic radiation. This was further developed in the context of quantum theory and particle physics. Magnetic fields are already instrumental to medical research in the context of magnetic resonance imaging (MRI) which fundamentally changed our ability to see inside the body. MRI exploits the property of 'spin' which is defined as an intrinsic angular momentum and is the property of matter that describes how a particle such as an electron behaves in a magnetic field. MRI techniques utilise strong magnetic fields but there is growing interest in the role that weak magnetic fields, such as the Earth's magnetic field, might play in biological systems. This interest has its roots in spin chemistry, which developed models such as the radical pair mechanism to explain how weak magnetic fields could change the outcome of chemical reactions through the manipulation of spin states. While this mechanism has predominantly been applied to the biological context of avian navigation, it is garnering interest in the medical context due to research indicating that magnetic fields might be used to manipulate reactive oxygen species (ROS) and concomitant biological outcomes, such as stem cell proliferation. The role that spin plays in biology has also come under the spotlight because of chirality. Chirality is a description of mirror symmetry, or handedness. Chirality is particularly interesting in the context of biology because of the fact that biological molecules such as amino acids have a distinct chirality rather than being a mix of both right and left chirality.

There is experimental evidence for weak magnetic field effects in both plants and animals. However progress in this has been slowed by the fact that these experiments give conflicting evidence and are unstandardised. While we should be concerned about changing magnetic fields in the context of space travel, this also might lend us some insight into health on earth. The earth's magnetic field varies by latitude, from approximately 30 to 70 µT. There are a number of diseases with latitude dependence. These include Multiple Sclerosis, Inflammatory Bowel Disease, infant spasms consistent with epileptogenesis, and even COVID-19. What is interesting about all these diseases is that they are inflammatory diseases. While there are other latitude dependent aspects to take into account such as light differences and vitamin D levels, could magnetic field differences contribute to differences in inflammation, with reactive oxygen species modulation being the underlying mechanism at play? What is clear is that further research into the role that magnetic fields play in living systems is important for both future human settlement in space as well as life and health on Earth.

Radical oxygen species (ROS) and stem cells

Professor Wendy Beane

Department of Biological Sciences, Western Michigan University

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Organisms live with the Earth's geomagnetic field, which averages 25-65 µT depending on where you stand. Numerous species, from bacteria to turtles to birds, have the ability to sense and respond to changes in this field, for example as migration cues. As humans spend more time in space, understanding how our physiology interacts with magnetic fields will be essential. Between planets there is no magnetic field to protect astronauts from cosmic radiation, and scientists have long researched methods to provide spacecraft with an artificial magnetic field. However, comparatively little research has been done on the potential harm (or benefits) from the magnetic fields themselves. Using the planarian regeneration model system, our data suggest that dividing cells are able to respond to changes in magnetic field strength due to corresponding changes in reactive oxygen species (ROS). At certain strengths (such as 200 µT) we see increased ROS accumulation at the wound site after injury, which in turn increase expression of genes that drive stem cell division, ultimately resulting in increased amounts of new tissue growth [1]. Conversely, we also found field strengths (such as 500 µT) that decreased ROS levels, inhibiting gene expression, stem cell expression, and regenerative growth [2]. These data suggest that the ability to respond to quantum changes (such as those induced by magnetic fields) may be a more common cellular characteristic than previously thought. In addition, the data indicate that much more research needs to be done into the cellular effects from specific magnetic field strengths across a broad range of conditions.

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Overview of oscillating gravitational fields

Steve Thorne

The Copernican Project

View the video recording **here**

Travelling into space subjects all functional molecules, enzymes, and electrochemical processes within our metabolic pathways to an unfamiliar set of inertial strains. While we tend to forget about our state of motion when looking through a microscope, all living organisms on Earth's surface are being spun through three major gravitational potentials and made to wobble around a co-orbiting barycenter at nearly Mach 88 each day. Our inertial state possesses natural kinetic and potential energy cycles that define the low-energy baseline states which underlie all electrochemical exchange.

Perhaps then, it should not be surprising that when astronauts venture into orbit around the Earth – bringing their same chemical compositions with them – significant fundamental metabolic changes occur, including oxidative stress, DNA damage, mitochondrial dysregulation, epigenetic changes, telomere length alterations, and microbiome shifts. While some of these affects are attributable to radiation, the most fundamental non-chemical stimuli they are subjected to is found in the shift in the astronaut's inertial state.

Interestingly, there are correlations between energy exchange at the basal level of our metabolism suggesting that our inertial state may have played an important evolutionary role in sculpting biomolecular structures into functional states that would deliver improved coherence with the natural strain cycles inherent to our orbital motion. Basal Metabolic Rates, ATP hydrolysis energy, and the mean mass-specific metabolic energy rates in over 3000 species on Earth each roughly correlate with the daily change in gravitation potential energy experienced when oscillating in the frame of the sun. Perhaps even more intriguing is that these correlations suggest that basal metabolic energy exchange may adhere to Clausius' Virial Theorem which serves as the basis for many thermodynamic relationships and applies to all complex quantum, electromagnetic, and gravitational interactions.

In this talk we will review these correlations and outline a set of experiments that will search for evidence of this bio-inertial coupling.

Microgravity and its effect of human physiology – a metabolic “coffin corner” in space?

Professor Alistair Nunn

The Guy Foundation and University of Westminster

View the video recording **here**

The problem with space is that life evolved at 1 x g. Without technology, or a very large asteroid impact, life was never likely to leave Earth. Extended periods of microgravity have not been crystalised into the metabolic flight envelope of life, although short periods of weightlessness have, as falling can result in far worse, and often, life-limiting outcomes – especially for big heavy organisms. Astronauts develop a whole range of problems: they get motion sickness, they lose muscle and bone mass, their cardiovascular systems become less robust, they lose proprioceptive function, their eyesight deteriorates, they get upset gastrointestinal systems and experience massive fluid distribution changes leading to “moon face”. To boot, they also get cognitive problems, and their skin becomes more friable. This is also mirrored at the cellular level, as they develop metabolic, inflammatory and epigenetic changes that are associated with mitochondrial dysfunction. Some of these do correct with time back on Earth, but not all, and it is not known due to the limited number of people who have been in space, and limited studies, how long they may last. In short, although a lack of gravity is not the only problem, as there are also potential issues with excess radiation, and changes in magnetic fields and circadian rhythms, it is probably the major one. For instance, gravity can be viewed as a hormetin, as it is a stress that induces adaption, and requires energy to maintain structure. At the intracellular level, a key component of any modern eukaryotic cell is its cytoskeleton, which becomes very important when you are multicellular. Key in this is the design principle of “tensegrity”, where a discontinuous set of compression elements is opposed and balanced by continuous tensile force, creating an internal prestress that stabilises the structure. Biology has thus evolved highly complex “gravisensors”, as well as “matrisomes”, which contain multiple proteins in supramolecular complexes, which sense any change in the cytoskeleton and thus the external and intracellular environments, and relay adaptive signals – both internally and beyond the cell. These enable rapid degradation or rebuilding of the cell architecture. This might suggest that a loss of gravity might result in pathological degradation as the system tries to adapt, not only affecting cell adhesion and migration, as it induces oxidative stress and apoptosis, but potentially inhibiting wound healing and activating the acute phase inflammatory response. A key nexus in this is the mitochondrion, as it interacts with the cytoskeleton in multiple ways, for instance via tubulin and the voltage dependent anion channel 1 (VDAC1), both supporting its maintenance and being moved around the cell by it. This integration could also extend to field homeostasis; mitochondria generate huge electric fields, and it is well known that external electric fields modulate mitochondrial interaction with the cytoskeleton. As mitochondria are key in modulating adaption to stress, it is possible that zero gravity is beyond their adaptive envelope, resulting in pathology, but it might suggest the periodic hypergravity may compensate – or even the low levels of gravity found say, on the moon or Mars. This would explain why exercise is so important in space, as it is a key mitochondrial stimulus that via mitokines, does stimulate the rest of the body, although it doesn't completely compensate. Lessons for medicine here, both on Earth and in space. So, at the most fundamental level, a lack of gravity removes a major stress stimulus that normally informs a complex biological structure how to behave. It is well outside its flight envelope – much like an aircraft going below its stall speed, or exceeding velocity never exceed (VNE). As every pilot knows, due to decreasing air density, as an aircraft climbs higher, its flight envelope narrows, eventually reaching "coffin corner" – as its stall speed gets close to its VNE; how narrow is this for humans in space and what is the maximum gravitational "altitude"?

Closing note and a call to action

Professor Geoffrey Guy

The vision of space exploration and settlement is a compelling one. However, as has been made very clear by the various presentations outlined in this Proceedings, the short and long term health risks associated with extra-terrestrial travel have been critically underdeveloped. Given The Guy Foundation's interest in advancing the frontiers of medicine, this symposium was conceived as a way to explore what lessons might be learnt from the study of physiology in the specific context of space. In terrestrial medicine, one approach to the investigation and understanding of chronic illness is to focus on an example in which this disease is acute, to foster, as it were, 'acute' research. In a similar manner, space travel and the health of astronauts exposed to space conditions, provides good models of accelerated physiological processes such as ageing and adaption. Which aspects of human physiology – the microbiome for example – are flexible to environmental perturbation, and which are not.

The symposium took a field-based angle in its approach, focusing on the role that electric, magnetic and gravitational fields might play in physiology. While it is very unclear what novel pathogens might exist in space and on other planets, it is more certain that the fields that biological systems will be exposed in these contexts will be different to Earth's. This then seems an appropriate departure point to discuss how human health will weather space travel. At the same time, the attention paid to fundamental physics in the biological context is also of relevance to terrestrial health and medical innovation. Much of the research around space health has been in the context of radiation. Whereas on Earth the geomagnetic field offers protection from cosmic radiation, astronauts will have to contend with more intense radiation. In the progress of medicine, non-chemical interventions have also focused to a large extent on radiation. But radiation is only one aspect of electromagnetic interaction in biology. There is now growing evidence that electric and magnetic fields play more of a role in biological systems than has previously been thought. Progress made in understanding the physical, rather than only chemical, mechanisms that underpin biological organisms – as well as how these interact – will thus advance both health in space and on Earth.

That radiation is central to most space health research as well as medical physics seems more than coincidental. Both face similar challenges in investigating, for example, the role that magnetic fields may play in biological systems: the proposed fields are too weak to have an effect; some element of alarmism is associated with the subject; there is a lack of consistent, convincing data. In response to this it would seem essential that a foundation of crucial experiments is put in place, an objective that we hope to foster with this symposium. From the data presented in the presentations it is clear that the physiological impact of space travel on the health of astronauts has not yet been properly calculated. The rapid progression of, and public interest given, the technologies associated with visiting space appear to have far outstripped our understanding of the effects that space will have on those piloting these technologies. Indeed, the development and funding of these carefully engineered vehicles seems decades ahead of our understanding of how to – healthily – fill them with humans.

With this in mind, we hope this Proceedings might serve as a call to action. We invite the symposium participants, as well as other interested researchers, to send us their suggestions on the key questions that need to be addressed and what they consider to be the integral studies or experiments that should be done in this area. To discern the impact of space travel on human health, as a precursor to any understanding of how space exploration may be modified to optimise astronauts' health, our objectives will include mapping the exact environment in which life evolved and consideration of the ways in which this environment varies in different destinations in space, and other factors such as the stresses and strains associated with getting there.

We will establish a working group that is necessarily interdisciplinary, comprising space scientists, researchers active in quantum biology, particularly with respect to mitochondria, and experts in subjects such as electromagnetism and gravitation. We will consider the suggestions we receive and formulate recommendations which we will publish in due course.

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