Perspectives on Hibernation Applied to Manned Space Exploration

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Abstract

An overview of current thinking at the European Space Agency into the implications of a human hibernation system for manned space exploration is presented. The overview begins with a brief discussion of why hypometabolic stasis in humans would be, from a resource-driven perspective, desirable in a manned deep space voyage scenario, taking a a reference a manned mission to Mars. We then review the nature of the deep space mission environment, with particular regards to physiological effects on the human organism. The overlapping areas between the likely physiological effects of hibernation and the space environment are then briefly discussed. The fundamental parameters within which a human hibernation system would have to operate, imposed by the nature of the space environment, are defined, and general requirements and directions for possible strategies are considered. In summary, it is understood that achievement of the goal of human hibernation within a terrestrial setting will in itself require an enormous research effort. Hibernation in space, with the increases in the complexity of the problem caused by the nature of the environment, will be substantially more difficult to achieve, both from a physiological and systems perspective; a huge multidisciplinary effort covering a multitude of different specialisms will be required. However, the realisation of human hibernation for space travel would have very considerable benefits for human presence in space.

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Introduction

Hibernation is a common tactic within the natural world for creatures that wish to survive in an environment where the normal pace of life is not possible or practical. The length of hibernation is dependent upon the periodicity of the environmental change that requires it; hibernation is normally based around seasonal variation, and therefore normally has an annual periodicity. However, longer term suspension of life is observable, for example in the case of seeds, which commonly can remain in the dormant phase for several years or more until the right environmental conditions prevail.

This suspension of life takes its most extreme form at the microbial level; on April 20, 1967, the unmanned lunar lander Surveyor 3 landed near Oceanus Procellarum on the surface of the moon, and on departure left behind a camera. Two-and-a-half years later, on November 20, 1969, Apollo 12 astronauts Pete Conrad and Alan Bean recovered the camera. When the camera was examined back on Earth they found specimens of *Streptococcus mitis* that were still alive. Because of the precautions the astronauts had taken, it was known that the germs were inside the camera when it was retrieved, so they must have been there before the Surveyor 3 was launched; these bacteria had survived for 31 months in the vacuum of the moon's atmosphere. More recently US researchers have claimed revival of bacteria that have been in suspended animation for 250 million years [Adam, 2000], with important consequences for panspermic theories, and the ability of life to travel the vast distances between planets and perhaps even solar systems.

If mankind is to attempt to travel the kinds of distances involved for interstellar travel, without recourse to exotic propulsion, journey times will be of the order of possibly thousands of years or more. In these instances, some means of suspending or drastically reducing the normal processes of life would be desirable in order to make the journey feasible through reducing the load on the Life Support System (LSS) of the vessel. Journeys of a shorter length such as those to destinations within our solar system would perhaps require a less severe strategy, involving a degree of suspension closer to that of seasonal hibernators on Earth, which is characterised by a suppression but not complete suspension of biological processes. It is this type of hibernation that is the focus of this report.

Motivation

One of the long-term (30 year time horizon) goals of the European Space Agency at present is a manned mission to Mars, currently being pursued under the Aurora program []. Such a mission would involve an outward flight time of the order of 6 to 9 months, a short stay in orbit and on the surface of Mars, followed by a journey of comparable duration to the outward flight for the voyage home. During these two voyages, the Life Support System (hereafter LSS) would have to fulfill a number of requirements in order to maintain the crew (see table 1).

Life Support Area	Purpose
Atmosphere Management	Atmosphere composition control, temperature and humidity control, pressure control, atmosphere regeneration, contamination control, ventilation
Water Management	Provision of potable and hygienic water, recovery and processing of waste water
Food Production and Storage	Provision and, potentially, production of food
Waste Management	Collection, storage, and processing of human waste and refuse
Crew Safety	Fire detection and suppression, radiation shielding
Crew Psychology	Maintenance of crew mental health

Table 1 - the requirements placed on the Main Areas of Life Support (adapted from [Eckart, 1996]).

Resource demands on the LSS during fulfillment of these requirements would be enormous, requiring either very large amounts of resources (approximately 30 tonnes for consumable water alone for a 6-man crew over 200 days with 10% loop closure) or an extremely high degree of LSS loop closure (expressable as a simple percentage of the resources that are reused). Even with a closure of 90%, water requirements are estimated to be of the order of 10 tonnes for a 6-man crew over 200 days. Furthermore, the journey to Mars would challenge the ability of the astronauts to live and work for an extended period of time in an enclosed environment [Nicogossian et al., 1987]. The unique psychological nature of the situation will impose significant psychological pressures on the crew, as they voyage to a destination that, when it recently passed as close to the Earth for 50,000 years was still 55.76 million kilometers away. Just six months ago, Mars was about five times that distance (for discussion of the psychological issues pertaining to long-term space missions, see [Rosnet et al., 1998] and [Kanas, 1998]). Psychological requirements of the crew would have to be engineered into the design of the spacecraft, necessitating the construction of leisure facilities, which would involve considerable additional mass and volume penalties.

In order to reduce the resource requirements and burden on the LSS during both the outward and return flights of a such a mission, it would therefore be desirable to reduce consumption of resources to a minimum, and try to minimise or avoid any deleterious psychological effects (whilst still maintaining crew health and effectiveness at acceptable levels). Between establishment of the interplanetary trajectory (exit from earth orbit) and insertion into Mars orbit, complete automation is not an unreasonable goal for a well-designed spacecraft. If this were the case, the mission requirement for crew activity during this period would collapse to zero, introducing the possibility of some form of hypermetabolic stasis (hereafter HS), by which both the physical and psychological requirements of the crew could be minimised. Induction of a state similar to hibernation observed in certain animals, characterised by a huge reduction in activity, with a concomitant reduction in resource consumption, would reduce drastically the requirements imposed on the LSS in virtually every area (see table 1). This is with the possible exception of crew safety, where some augmentation could be necessary to compensate for the inability of dormant astronauts to respond to threatening anomalous events such as solar flares.

Life Support Area	Purpose	Effect of HS
Atmosphere Management	Atmosphere composition control, temperature and humidity control, pressure control, atmosphere regeneration, contamination control, ventilation	Reduced heating requirement, reduced regeneration requirement
Water Management	Provision of potable and hygienic water, recovery and processing of waste water	Reduced drastically
Food Production and Storage	Provision and, potentially, production of food	Reduced Drastically
Waste Management	Collection, storage, and processing of human waste and refuse	Reduced Drastically
Crew Safety	Fire detection and suppression, radiation shielding	Augmented?
Crew Psychology	Maintenance of crew mental health	Reduced Drastically

Table 1 – The effect of HS on the requirements placed on the Main Areas of Life Support (adapted from [Eckart, 1996]).

1.1.1 The Space Environment and Space Medicine

In order to approach the problem of inducing hypometabolic stasis in space (likely to be a physiologically complex and stressful process), the existing effects of the space environment on the human organism must be appreciated. The human space environment (a typical environment aboard a spacecraft or space station away from Earth orbit) imposes several different stressors on the human organism. These can be identified as the following:

- Isolation
- Altered social interactions
- Confinement
- Reduce afferent flow in the CNS
- Hypokinesia
- Removal of circadian cues
- Increased radiation
- Micro-gravity

Because these factors are all present, it is very difficult to isolate and quantify the degree to which different stressors are responsible for the observed physiological and behavioural changes associated with spaceflight. Many physiological changes observed in subjects during microgravity experiments (full stressor range) are similar to those observed in bed-rest studies (due to hypokinesia but also psychological stressors), which in turn have physiological effects partially similar to those observed during confinement and isolation studies (psychological stressors only). Figure 4.1 shows the partitioning of stressors between these three main types of study conducted.

<table>
<tr><td>Isolation</td><td></td><td></td><td rowspan="3">Confinement Studies</td><td rowspan="5">Bed-Rest Studies</td><td rowspan="8">Space Environment Studies</td></tr>
<tr><td>Altered Social Interactions</td><td></td><td></td></tr>
<tr><td>Confinement</td><td></td><td></td></tr>
<tr><td colspan="4">Reduced Afferent flow in CNS</td></tr>
<tr><td colspan="4">Hypokinesia</td></tr>
<tr><td colspan="5">Removal of circadian cues</td></tr>
<tr><td colspan="5">Increased Radiation</td></tr>
<tr><td colspan="5">Micro-gravity</td></tr>
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Figure 4.1 – Space environment stressors and their spread across studies

Investigation of the psychological stressors associated with the space environment has been conducted through isolation studies such as the EXEMSI study [Maillet et al., 1996]. These have produced effects such as, for example, loss of body weight [Gunga et al., 1996], and the same pattern of changes in parameters such as blood volume and regulating hormones renin and aldosterone as bed rest [Husson et al., 1996]. Confinement also has a major effect on the immune system of both animals and humans, principally through an increase in stress response [Husson et al., 1996]. Hypokinesia and reduced afferent flow in the CNS have been investigated through bed-rest studies, such as [Ishizaki et al., 2002]. Additionally, the use of 'tilt-down' bed-rest studies has allowed investigation of some of the physiological effects that accompany microgravity (principally body fluid redistribution [Zorbas et al., 2000]).

Microgravity is the principle stressor in the human space environment. Animal and plant physiology is a tuned response to the huge diversity of environments present on the earth, with environmental differences encompassing ranges of temperature, water supply, pressure and so forth. However, gravity is effectively constant over the entire range of terrestrial environments (and has been so over the entire evolutionary period of life on Earth). It is therefore readily apparent that the constant presence of gravity during the evolution of life on earth has influenced and indeed largely dictated a substantial fraction of the evolved physiological strategies and mechanisms that biological agents use in order to survive. This influence extends from the macro-scale physiological adaptation of large muscle groups, the musculo-skeletal system, motor adaptation, through to the cellular and molecular level, where gravitic field fluid dynamics (buoyancy, convection, sedimentation, hydrostatic pressure) have ordered the structure and mechanisms of life at a cellular level (for example plants require positional cues from gravity in order to direct growth, both at a macro and cellular level [Sievers & Hensel, 1990].). All life forms are predominantly composed of liquids, and employ surfaces to isolate their different constituents and facilitate/mediate the enormous number of biochemical reactions that are essential to support life [Seibert et al., 2001]. With this in mind, it is obvious that a change in the magnitude or removal of gravitation will have a substantial effect on biological systems.

Nevertheless, mature terrestrial animals appear to have regulatory mechanisms available for adaptation to moderate changes in gravity, which are the same mechanisms used to adapt to changing gravitational loading caused by, for example, weight gain [Jones et al., 1991]. Evidence exists, for example, of adaptive increases and decreases in skeletal mass in response to respective increases and decreases in loading and unloading.

In addition to microgravity, the ionising radiation environment of interplanetary space is a source of danger to astronaut health. The radiation environment is principally composed of galactic cosmic rays (protons, alpha particles, HZEs) and are very difficult to shield against. Additional radiation load is provided by solar particle events (solar flares) composed mainly of protons and helium ions. However, particulate energy of solar flares is much less than that of cosmic radiation (typically less than 1 GeV/nucleon [Wilson et al., 2001]), and so shielding is more effective. Nevertheless, secondary particle production can be important in higher energy events. GCR radiation can however be fragmented by the shielding, and the GCRs and their products can penetrate further into the shielding and expose the astronaut. [Curtis et al., 1998] estimates that over a three year journey to Mars at solar minimum, between 40 and 50% of neural cells in certain critical areas (retina, hippocampus, thalamus) will be traversed by a particle with a Z greater than or equal to 15. Ionising radiation can act both directly and indirectly to promote carcinogenesis and oncogenesis. Direct impact of nuclear or electromagnetic radiation can produce physical lesions in DNA; indirectly, radiation effects on the cell structure may be equally important, through the production of intracellular electrophiles and reactive oxygen species (ROS) [Stanford, 1999], which can cause genetic damage themselves, by causing nucleotides to cross link each other.

Generally, exposure to the space environment induces two types of response:

- Adaptive – neuromotor adjustments, occur as the body compensates for the lack of gravitational pull and or stimuli, and taper off as the body adapts to microgravity [Nicogossian, 2001]

- Pathophysiological – disuse osteoporosis or chromosomal damage from radiation exposure arise as space environment induced changes to the body proceed.

In the case of humans hibernating in space, some of the stressors will effectively be obviated (see table 4.1).

Space Environment Stressor	Obviated by hibernation	Exsacerbated by hibernation	Unaffected by hibernation
Micro-gravity			X
Increased Radiation			X
Reduced afferent flow		X	
Hypokinesia (reduced muscle use)		X	
Removal of circadian cues	X		
Confinement	X		
Isolation	X		
Altered Social Interactions	X		

Table 4.1 – interactions between hibernation and space environment stressors

In the hibernation instance, the psychological stressors are effectively obviated, since the hibernating subject is not awake to worry about his or her situation. This can extend to the circadian cue stressor, since circadian cueing is mediated in humans by photonic sensing. However, in hibernation, afferent flow through the nervous system is likely to collapse to effectively zero; this might have several physiologically (and particular neurologically) undesirable effects. In addition to this the degree of hypokinesia experienced will be increased, again with muscle use effectively collapsing to zero; this is likely to increase the atrophic effects on muscles. The microgravity and radiation effects are obviously left unchanged.

In this very short review, the effect of the space environment (the stressors not obviated by hibernation) on the human physiology is summarised. The gross effects are divided into the main functional systems of the human body. Areas of physiology important in space environment are different to those in hibernation. These are:

- Cardio-vascular systems
- Musculo-skeletal systems
- Neuro-vestibular systems
- Immuno-endocrine and haemological systems

Additionally, a short review of cellular effects of microgravity (underpinning many of the macro-effects of microgravity) is given.

1.1.2 Cardiopulmonary Function

The microgravity effects of spaceflight on human cardio-vascular functions have many features in common with those incurred by bed-rest or immersion. Primary amongst these effects is the redistribution of body fluids under the influence of the abolition of the normally present gravitic hydrostatic pressure gradient. This results in a net movement of body fluids towards the thoraco-cephalic regions in the absence of hydrostatic pressure [Guell et al., 1990], in turn initiating a series of reactive responses in the cardiovascular system and other organs (mediated by the high pressure carotid baroreceptors located in the neck and mid-body receptors located in the aorta, and low pressure – atria and veins. [Gaffney, 1987]). Primary among these responses is a decrease in total blood volume (hypovolemia). This produces changes in functions such as neuro-endocrine mechanisms (section 4.3) through which fluid and electrolyte regulation by the kidneys are also affected. For example, water salt regulation by the antidiuretic hormone ADH (a major regulator of body fluid osmolality) is impaired [Ivanova et al., 1989]. Potassium, sodium and calcium loss proceeds through urine. Changes to blood biochemistry also occur in the form of increased GOT, GPT, amylase activity, glucose and cholesterol activity, haemoglobin, HDL cholesterol, and a loss of glycogen stores [Markin et al., 1998].

The size of the heart decreases in reaction to microgravity, and impaired cardiac performance is present in the form of reduced filling volume (i.e. impairment of mechanical and electrical function). As the space-flight duration progresses, growth in cardiac contractility, and changes in the autonomic regulation the heart are observed [Baevsky et al., 1998]. Upon return to a gravitational environment, the adaptive process is reversed, and heart rate increases to maintain cardiac output, blood pooling occurs in the lower body, and the hypovolemic response that occurred in microgravity leads to decreased cerebral flow and hence orthostatic intolerance.

The lung is particularly sensitive to changes in gravitational load. Gravity causes gradient-dependent changes in perfusion and ventilation, leading to regional variations in ventilation-perfusion relationships and gas exchange. The removal of gravity can therefore be expected to induce changes in many aspects of pulmonary function, and this is indeed the case. Lung capacity decreases in microgravity, and is thought to be at least partially caused by pulmonary interstitial edema, a consequence of the body fluid redistribution towards the torso, and weakening of the respiratory muscles [Venturoli et al., 1998].

1.1.3 Musculo-Skeletal Function

Prolonged exposure to microgravitic conditions leads to both progressive muscle atrophy and loss of bone mass [Riley, 1999]. The atrophic response of muscle can be graded, with atrophy occurring the most in slow extensors, then fast extensors, and finally fast flexors. The atrophy takes the form of a loss of muscle protein (mediated by changes in prostoglandin release [Stein, 1999]), with a loss of contractile proteins relative to cytoplasmic proteins. The myofibrillar protein content goes down [Harlow et al., 2001]), and there is a reduction of cross-sectional area of slow-twitch fibres, and specific changes in enzyme activity [Girten et al., 1991], accompanied by a partial transformation of slow-twitch into fast twitch fibres (the percentage of fibres expressing fast MHC isoforms increases in unloaded slow-twitch muscle). The muscle metabolism shifts in the glycolytic (metabolic breakdown of glucose and other sugars that releases energy in the form of ATP) direction, through increased activity of glycolytic enzymes, elevated storage of glycogen, and disappearance of peripheral mitochondria. There is a corresponding decrease in ability to function oxidatively, increasing muscle susceptibility to oxidative stress. The loss of specific components from the muscle leads to an increase in urinary nitrogen, creatinine kinase, phosphorous and amino acids. It is also hypothesised that loss of afferent neural influence also plays a part in the muscle atrophy process [Ohira et al., 2002].

The bone system is in a constant state of flux, with mineral deposition and reabsorption occurring constantly, mediated by osteoblast (mineral depositing) and osteoclast (mineral absorbing) cells. Cytoskeletal changes change the function of these osteocells, thereby disrupting bone deposition/reasborption. The primary response of the skeletal system to unloading in microgravity is a reduction in osteoblast activity. This is accompanied by a significant reduction of electrolytes in the bone (e.g. loss of calcium and phosphates), and a corresponding increase of electrolytes circulating in blood plasma [Zorbas et al., 2000]. There are changes in circulating hormones related to bone mass loss. Two hormones have been identified; PTH (parathyroid hormone) and 1, 25 D (vitamin D hormone). PTH induces mineral loss in bones by enhancing bone reabsorption. [Arnaud et al., 1990]. Calcium and electrolyte loss proceeds through both the urine and faeces, mediated by a kidney response similar to that causing ureal loss of muscular components [Stein, 1999]. The increased levels of plasma calcium also lead to an increased risk of renal kidney stone formation [Doty & Seagrave, 2000].

1.1.4 Neuro-Vestibular Function

Gravity is not only a constraint on limb movement, but an essential internally modelled reference for planning movements [Baroni et al., 2001]. Motor function disturbances occupy an important place in the complex of effects caused by prolonged exposures to microgravity [Kozlovskaya et al., 1991] and when humans are exposed to the conditions of space and gravity is removed a number of neurological disorders quickly become apparent. Space Adaptation Syndrome (SAS or 'space sickness') is the immediate short term (abating within 1 to 14 days) effect, caused by the mismatch between otolith organs and the visual proprioceptive inputs. The symptoms include headache, nausea and vomiting.

Microgravity has significant effects on the neuroplasticity of nervous system structures that respond to gravitational cues (i.e. principally the vestibular system, those parts of the brain that process gravity information, and the neural control of load-bearing muscles). Neurological changes specifically due to microgravity are thought to be due to a reduction in the afferent (incoming) traffic through the nervous system, which induces a reduction in activity in the pyramidal cells of the motor cortex [Vazquez, 1998]. This in turn is thought to produce two generalised responses:

1. Reactive synaptogenesis – attempt to compensate for lack of afferent flow through decoupling of vestocular input
2. Decrease of functional levels – decrease in protein content, decreased synthesis of neurotransmitters and neuropeptides, reduced nucleoi size.

The effect of the radiative environment of space on the neuronal system is also important. This has been investigated by studying the effect of heavy ion radiation on laboratory animals. Fe^{56} exposure in rats [Joseph et al., 1998] [Joseph et al., 2000]. Because Fe^{56} constitutes approximately 1-2% of GCRs, extrapolation from this suggest that possible radiation exposure of this magnitude could cause mission compromising motor and behavioural defects on long-term space missions. In particular, the Nigrostriatal system in the lower brain has been identified as a major centre for motor control, which is adversely affected by heavy ion radiation [LeBaron-Jacobs et al., 2003]. Two types of general effect are apparent in the nigrostriatal system: deficits in signal transduction and cell loss. Tissue loss in the dopaminergic system has also been identified as a result of exposure to heavy ions [Rabin et al., 2000]. Dopamine has important behavioural and motor control functions, and radiative effects of the dopaminergic system could have important behavioural consequences.

1.1.5 Hemo/Immume/Endocrine System

Hormones and the Endocrine system are the principal regulators of homeostasis, as well as mediating event-specific physiological responses (in tandem with the nervous system) such as the stress response. The Endocrine system is largely based upon feedback, so it is unsurprising that microgravity induces a range of hormonal responses. Hormonal regulation of bone turnover is upset by microgravity, and leads to the effects described in section 4.2. There are three hormones principal governors of bone regulation: parathyroid hormone (PTH), 1,25D and Calcitonin. Other hormones involved are Growth hormone (GH), Insulin (IRI) and IGF-1. PTH increases calcium absorption by gut, and counteracts calcium loss via the kidney. PTH also activates octeoclasts to dissolve bone mineral. 1,25 D is a strong promoter of calcium absorption, whilst calcitonin lowers circulating calcium levels by stimulating calcium excretion by the kidneys, and inhibiting osteoclast-dependent bone demineralisation. GH regulates collagen synthesis, and triggers IGF-1 production in liver.

Microgravity also causes a loss of red blood cell mass, accompanied by decrease in haemoglobin mass. Blood composition also changes in response to balance upsets in other areas of the body (for example, increased calcium content of plasma due to bone demineralisation).

There are various immunological responses during spaceflight. Studies have shown a reduced immune response due to decreased circulation of both T and B-lymphocytes. Lymphocytes exposed to spaceflight or altered gravity exhibit significant growth alteration and metabolic changes, and there is a decrease of mitogen-induced proliferative response of peripheral blood lymphocytes (decrease in lymphocyte blastogenesis), inhibited lymphocyte response, reduction in interferon production, and a reduction in interleukin-2 (interleukin-2 is a principle mediator of immune reactions) production and activity [Konstantinova et al., 1991]. The functional activity of T-helper cells decreases, and the cytotoxic activity of natural killers is decreased. The stress response, mediated through the hypothalamic-pituary-adrenal axis [Sonnenfeld, 1999], could have an important role in this immune response, due to the well-documented adverse effects of stress on immuno-response.

1.1.6 Cellular Function

It is well known that mechanical cell forces in a g-field are the result of two oppositely directed processes:

· Randomisation of the position of intracellular elements of different densities
· The tendency of intracellular elements to undergo sedimentation at various rates due to the influence of gravity.

Several cellular processes, such as growth rates, signalling pathways and gene expression are modified when placed under conditions of micro-g. [Maccarone et al, 2002]. There is significant alteration in cell proliferation rates, cell growth, differentiation, metabolism, membrane properties, secretory capacity, and electrolyte concentration. Within the cytoskeleton (which maintains cell shape, provides mechanical support, coordinates cell movement, maintains proper spatial position of organelles along with other functions), both microtubule and microfibrill growth is gravity dependent, and affected in micro-gravity. Weightlessness also induces other effects such as for example reductions in antioxidant enzymes, and significant increases in lipid peroxidation [Girten et al., 1989].

1.1.7 System–Level Issues

A group hibernaculum could be used if individual sensitivity to environmental parameters was sufficiently low, but consideration of the likely requirements for environmental and therapeutic control to be tailored to each specific hibernator indicates that there would probably be a separate hibernaculum for each astronaut.

It is envisaged that hibernation would occur over transit periods in which there are just minor course-corrective manoeuvres. Therefore, the force environment of the hibernator is held virtually constant. In-transit course corrections for deep space missions are likely to be achieved using low thrust propulsion (and this would probably be the preferred case due to requirements for propulsive efficiency), with accelerative loads of the order of 0.01 ms^{-2}. Such small loads would be unlikely to upset the hibernation state, but would still need to be transmitted to the hibernator in an acceptable manner. One possible solution for the system without artificial gravity could be straps that could be used to 'suspend' the astronaut at the centre of the hibernaculum, in contact with the astronaut through loose bands.

If artificial gravity were employed to obviate problems with micro-gravity, there would be problems associated with prolonged immobility of the astronaut in a gravitic environment. For example, bed sores (decubitus ulcers) form when a person is sitting or lying in one position for too long, and are caused by sustained pressure on one area, leading to reduced blood flow to the skin and subdermal tissues, and subsequent damage. Possible solutions to this are use of electrostimulus or another mechanism (perhaps behavioural) to effect periodic (or as necessary) postural change.

1.1.7.1 Control of the hibernation

The hibernating human is likely to require continuous external monitoring and modification of their condition, through administration of pharmaceutical compounds, regulation of environmental parameters etc. Minimally, this would require a range of monitoring equipment and an agent (a nurse) to interpret and act upon the information acquired in a timely manner. However, even on Earth with ready access to human nurse agents, the time-span associated with hibernation (for example coma patients) precludes the constant and direct involvement of a human agent. In the case of a vessel travelling through space for an extended period of time, one or more crew members could conceivably remain awake, in order to monitor and control the condition of the remaining hibernating astronauts. However, this would significantly obviate the resource saving gained from the hibernation tactic, as well as introduce potential psychological issues due to the reduced *effective* crew size (including possible situation-specific psychological responses such as resentment towards the hibernators).

For intra-solar system missions, where communication delays between the vessel and Earth would be of the order of 30 minutes, relay of medical monitoring information to Earth, decision making and then relay of the decisions back to the spacecraft for implementation would be possible, but would be dependent upon the time-scale of possible adverse effects and problems during the hibernation process (as well as a very robust communication link with no down-time).

Looking to examples of reactive timescales in ordinary medicine applied to patients in a vegetative state (intensive care, coma) we see that, although a nurse is not continuously involved in monitoring the patient, medical staff are available to administer reactive measures in response to alarms from monitoring equipment in a matter of minutes, if not less. Thus in-situ monitoring and control of the hibernative state is required, and therefore so is an automated AI agent.

An AI agent (the agent paradigm includes all types of AI implementation, neural nets, expert systems etc.) can be defined as an entity capable of carrying out goals, perceiving and acting autonomously. The key concepts are therefore autonomous operation, i.e. the ability to carry out certain functions without help from other agents, and community, where within the agent cooperates with other agents (in this the ground segment) to some degree to synergistically achieve high level goals [Hayes, 1999].

Agent technology is already finding increasing application within health care in functions such as coordinating distributed data, maintaining autonomy of collaborating participants, scheduling and monitoring [Nealon et al., 2000]. Examples of agent technology specifically applied to patient monitoring and administration include GUARDIAN [Larsson et al., 1998], which monitors and diagnoses intensive-care patients recovering from heart surgery. The GUARDIAN potentially has the ability to operate independently, but is aimed at supplementing human agents in diagnostic decision-making. Work has also been performed on using neural networks as intelligent agents for medical diagnosis [Cohen & Hudson, 2002].

As previously outlined, the tasks of the agent would involve automated monitoring of the hibernator and environmental parameters, and automated control actions such as therapeutic drug delivery and environmental regulation. These task responsibilities would cover not just maintenance of hypometabolic stasis, but also perhaps initiation and termination of the bout, through the administration of chemical or environmental cues (depending on the mechanics of the hibernation strategy, and the task division between the hibernator and the agent).

Although an in-situ agent on onboard the spacecraft would provide immediate short-term monitoring and control, this would not preclude longer-term supplementary decision-making provided through a link with a ground station. This would probably be necessary anyway because the agent would be unlikely to have the ability to maintain the hibernative state independently. Task-division between ground station and agent would be dependent upon agent sophistication, and the time-scale of control (longer term decisions would be taken by the ground station, based on longer time-scale information).

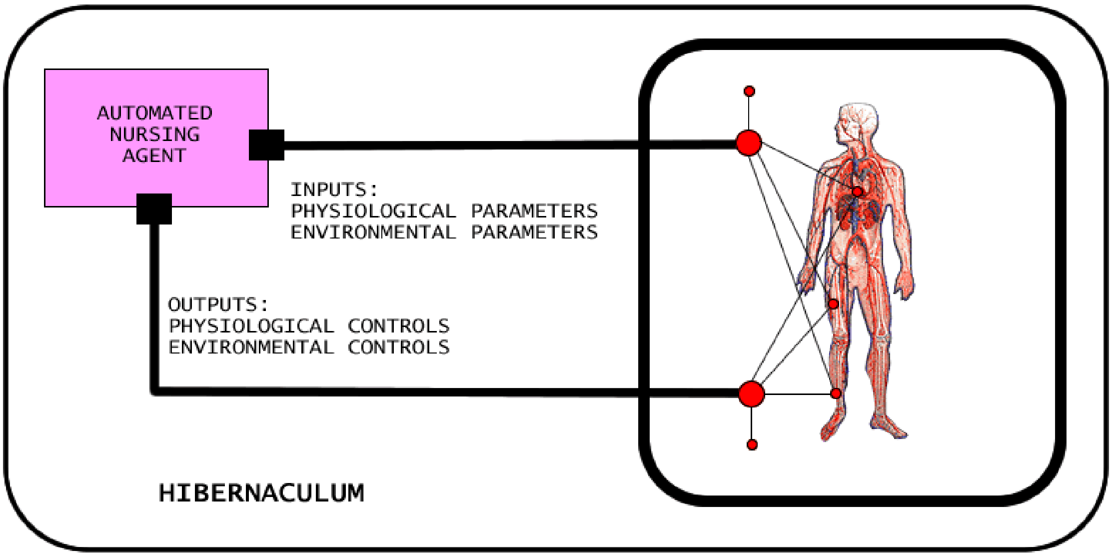

figure 5.1 – human hibernation system

1.1.7.2 Integration of hibernacula and with Ship-wide LSS

Integration of hypometabolic stasis with the LSS has a number of important consequences. Simple consideration of the principle characteristics of physical-chemical and bio regenerative LSS (table 5.1) indicates that a hypometabolic stasis system would be most suited to integration with a physical-chemical LSS. Food production (the principle advantage of a bio regenerative system) is not a requirement for hibernating crew, and in any case, crew maintenance of food production (an envisioned requisite for the foreseeable future) would be impossible. If the hibernation strategy adopted involved periodic arousal (in which case life support would have to be extended from the hibernaculum to a sufficient portion of the spacecraft to allow the crew to perform inter-bout activities), bio regenerative systems would have trouble providing the required environmental changes due to typically slow response times.

Physical-Chemical	Bio regenerative
Well understood, Compact, Low maintenance, Quick response times, Cannot replenish food stocks	Not well understood, Large volume, Power & maintenance intensive, Slow response time, Can provide food

Table 5.1 – principle characteristics of physical chemical and bioregerative life support systems

Any LLS would require complex control strategies that can maintain stable system performance and balance resources [Kortenkamp et al., 1998]. This requirement for dynamic response would be increased with the presence of hypometabolic stasis. The dynamic variability of the life support load would be increased, as for at least one extended period; the life support requirement on board the spacecraft will be reduced drastically. LSS function will then have to mirror (and to some degree anticipate) the physiological function of the hibernator as stasis is entered and exited.

1.1.8 ESA's Present Position

The European Space Agency Advanced Concepts Team [] has recognised the benefits of HS for manned deep space missions. However, the concept remains at present virtually completely unapproached, due to the enormous complexity and difficulty surrounding the problem. Whilst human hibernation in space travel has revealed itself to be a common feature in science fiction movies, practical approaches to the problem do not hithertoo exist.

The remit of the Advanced Concepts Team is to investigate the applicability of new technologies and concepts to European space exploration and utilisation. As such, initial definition and investigation of a concept such as human hibernation for space travel falls into our sphere of activity. In order to investigate advanced concepts such as this for which we do not possess internal expertise, an accelerated contracting mechanism called Ariadna [] has been constructed in order to allow small study contracts to be quickly awarded to external experts in areas where an initial investigation of a topic is required.

Upon hearing of the ESF workshop on Mammalian hibernation, and the nascent efforts to coordinate European hibernation research. Four initial pilot studies are therefore to be released on October ?? (see appendix 1). These studies are not clinical in nature, but are simply the application of existing knowledge to the problem, starting from identification of possible hibernation mechanisms, through to a first-order investigation of the effects of a human hibernation system at a systems level.

1.1.9 Summary

The achievement of human hibernation for deep space travel will be the result of a program of research that is likely to last decades. The fields of pharmacology, genetic engineering, environmental control, medical monitoring, AI and agent technology, radiation shielding, therapeutics, spacecraft engineering, life support and more will all be involved in the realisation of such a system. The wide range of fields that contribute suggests that making use of breakthrough technology that has been researched and developed independently will be a priority – for example, progress within AI medical monitoring (which is on going) within the next 10 years may well largely address the medical monitoring requirements of a space based human hibernation system.

In addition, certain features of the space borne hibernation problem will themselves have to be addressed through basic research. Experiments investigating the effect of factors of the space environment on hibernation mechanisms will have to be performed (for example hibernation experiments on the ISS), as will development and validation of other components of a space borne HSS, such as the agent technology required to oversee the hibernator.

Study Objectives

The objective of the study is to construct a roadmap detailing the required steps leading towards a human hibernation system for deep space travel. Of particular interest is the identification of research areas that are likely to contribute to space borne human hibernation, and the extent to which this Earth-based research can be applied to the problem. For example, there is on going research into mammalian hibernation, and other fields such as AI and medical agent technology that are mentioned above. Reapplication of the increasing quantity of knowledge from these disparate fields to space borne hibernation is a key issue, and the strategy to achieve this needs to be defined. The formulation of a such a strategic framework, taking into acount the realities of research, is therefore a fundamental goal of the study.

The study should also identify those technology areas that are specific to the space borne human hibernation problem, and therefore which require dedicated research. The study should formulate research and experimental plans that suggest how to address these areas.

1.1.10 Summary

To conclude, human hibernation for long-term space travel will make use of a wide variety of techniques, in a combination, which is currently unknown. The problem of is a good example of the type of systems engineering that will increasingly be required in the future; bringing together a very diverse range of fields that do not commonly sit together. In the human hibernation case these fields include pharmacology, genetic engineering, environmental control, medical monitoring, AI and agent technology, radiation shielding, therapeutics, spacecraft engineering, life support and more. Integrating these disparate disciplines in such a way as to successfully create a safe, effective and space-borne human hibernation system will be an enormous challenge. But, if realised, it will bring significant potential benefits to human travel in space.

Appendix: Human Hibernation Related Ariadna Proposals

1. Identification of Human Hibernation Relevant Mammalian Hibernation Mechanisms

Type of activity: Small Study (2 months, 15 KEUR)

The ability to induce a hypometabolic state within astronauts during long – term space voyages would have a considerable effect on Life Support System resource requirements.

Hibernators exist in every phylum, and the behavioural and physiological mechanisms that animals use to hibernate are as diverse as the animals themselves (for examples of general metabolism suppression, see [1,2]). Because of their phenotypical/genotypical similarity to humans (belonging to the *mammalia* class), mammalian hibernation mechanisms [3] are considered to hold the most promise in application to human hibernation. Within the class *mammalia* hibernators exist in the orders *Monotremata, Marsupialia, Primates, Insectivora, Chiroptera, Carnivora* and *Rodentia*. There exist many different behavioural and physiological mechanisms peculiar to specific species within these orders, but there also exists a wide range of common behaviour and mechanisms that characterise mammalian hibernators as a whole.

Study Objectives

The objective of the study is to perform a review of knowledge gained to date concerning the mechanisms used by mammalian hibernators (such as the ground squirrel *Spermophilus tridecemlineatus*) and winter sleepers (typified by the Brown bear *Ursus arctos*). The review should cover general hibernation strategies common to all hibernators and general mechanisms of winter sleepers as well. Example areas include strategies such as lipid accumulation (white and brown), hibernation cues (photocues etc.), hibernation induction trigger molecules, non-shivering thermogenesis, protein synthesis from ureal nitrogen, reversible phosphorylation, and the role of differential gene expression (this list is not comprehensive, and many more mechanisms should be explored). For every mechanism identified, the suitability/practicality of applying similar mechanisms to human hibernation should be explored and guaged (for example, pharmaceutical mimicry of HIT molecules, gene therapy to allow differential expression of relevant genes and more). Of particular interest is assessing the suitability of hibernation and winter sleep to human hibernation, and a principal result from the study should be a reasoned argument in favour of one of these principle mechanisms.

In summary the study objectives are:

- Review of currently identified mammalian hibernation and winter sleep mechanisms, and their suitability for application to human hibernation.

- Assessment of each mechanism's suitability to human hibernation, and a preliminary assessment of the research steps required.

References

[1] Storey, K. B., Storey, J. M. (1996). *Natural Freezing Survival in Animals.* Annual Review of Ecological Systems. Vol. 27, pp.365-386.

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[3] Boyer, B., Barnes, B. M. (1999). *Molecular and Metabolic Aspects of Mammalian Hibernation*. Bioscience, Vol. 49, No. 9.

2. Interactions between the Space Evironment and Possible Human Hibernation Mechanisms

Type of activity: Medium Study (4 months, 25 KEUR)

In order to approach the problem of inducing human hibernation in space (likely to be a physiologically complex and stressful process), the existing effects of the space environment on the human organism must be appreciated. The human deep space environment (a typical environment aboard a spacecraft or space station away from Earth orbit) imposes several different stressors on the human organism. These can be identified as the following [1,2]:

- Isolation
- Altered social interactions
- Confinement
- Reduce afferent flow in the CNS
- Hypokinesia
- Removal of circadian cues
- Increased radiation
- Micro-gravity

These stressors have a cumulatively very negative impact on the human physiology. Immediate effects predominantly upset homeostasis; these include blood volume redistribution, mismatch between otolith organs and the visual proprioceptive inputs (Space Adaptation Syndrome), and changes in lung perfusion and ventilation. Longer term effects include changes in blood composition, loss of muscle and bone mass (especially in load-bearing regions) including the heart, hormonal imbalances, immune response degredation, neuronal changes and more.

Study Objectives

The objective of the study is to assess the likely impact of the physiological effects of the space environment on the human hibernation mechanisms identified in xx/xxxx. Obviously, hibernation will obviate certain stressors such as the psychologically-based effects of isolation and altered social interactions (although the prospect of entering hibernation will itself have a pronounced psychological effect). Other stressors are likely to be worsened by a hibernating state, such as hypokinesia. Additionally, the therapeutic measures taken to induce/regulate hibernation on Earth may be unsuitable for a space borne hibernation system. For example, the kinetics of pharmaceutical compounds, and hence their effects (diffusion, onset, duration etc.) will be changed in the absence of gravity [3].

In summary the study objectives are:

- Assess the impact of the space environment on those hibernation mechanisms that have possible application to human hibernation, as identified in xx/xxxx.

References

[1] Sievers, A., Hensel, W. (1990). *Fundamentals of Space Biology*. Japan Scientific Societies Press and Springer-Verlag.

[2] Sonnenfeld, G. (1999). *Space Flight, Microgravity, Stress, and Immune Responses*. Advances in Space Research, Vol. 23, No. 12, pp.1945-1953.

[3] Cintron, N. M. Putcha, L., Vanderploeg, J. M. (1987). *Inflight Pharmokinetics of Acetaminophen in Saliva*. Results of the Life Sciences DSOs conducted aboard the Space Shuttle 1981 – 1986, p.19-23.

3. Experimental Roadmap Definition for realisation of Human Hibernation for Deep Space Travel

Type of activity: Medium Study (4 months, 25 KEUR)

The achievement of human hibernation for deep space travel will be the result of a program of research that is likely to last decades. The fields of pharmacology, genetic engineering, environmental control, medical monitoring, AI and agent technology, radiation shielding, therapeutics, spacecraft engineering, life support and more will all be involved in the realisation of such a system. The wide range of fields that contribute suggests that making use of breakthrough technology that has been researched and developed independently will be a priority – for example, progress within AI medical monitoring (which is on going) within the next 10 years may well largely address the medical monitoring requirements of a space based human hibernation system.

In addition, certain features of the space borne hibernation problem will themselves have to be addressed through basic research. Experiments investigating the effect of factors of the space environment on hibernation mechanisms will have to be performed (for example hibernation experiments on the ISS), as will development and validation of other components of a space borne HSS, such as the agent technology required to oversee the hibernator.

Study Objectives

The objective of the study is to construct a roadmap detailing the required steps leading towards a human hibernation system for deep space travel. Of particular interest is the identification of those existing research areas that are likely to contribute to space borne human hibernation (but are not directly concerned with hibernation *in space*), and the extent to which this Earth-based research can be applied to the problem. For example, there is on going research into mammalian hibernation, and other fields such as AI and medical agent technology that are mentioned above. Reapplication of the increasing quantity of knowledge from these disparate fields to space borne hibernation is a key issue, and the strategy to achieve this needs to be defined. The formulation of a such a strategic framework, taking into acount the realities of research, is therefore a fundamental goal of the study.

The study should also identify those areas of research that are specific to the space borne human hibernation problem, and therefore which require dedicated research. The study should formulate research and experimental plans that suggest how to address these areas.

In summary the study objectives are:

- construct a roadmap detailing the required steps leading towards a human hibernation system for deep space travel

- identification of research areas that are likely to contribute to space borne human hibernation, and the extent to which this Earth-based research can be applied to the problem

- identify those research areas that are specific to the space borne human hibernation problem, and therefore which require dedicated research, and formulate research and experimental plans that suggest how to address these areas.

4. Hibernaculum Definition and Integration within a Deep Space Mission

Type of activity: Large Study (6 months, 35 KEUR)

As the time to enter hibernation approaches, all hibernators and winter sleepers select a specially chosen or constructed place within which to hibernate, termed the *hibernaculum*. For example, alpine marmots (*marmota marmota*) retreat in family groups into their hibernacula during late September, closing the entrance with a plug constructed out of stones, clay and faeces. Examples of hibernacula are diverse and include caves, tree bowls, buildings etc. However, all these locations are related in that they provide some measure of environmental protection and regulation that is conducive to the hibernation process.

The hibernating astronaut will also require a regulated, protective environment within which to hibernate. The hibernaculum will probably provide additional radiative shielding to the dormant astronaut, as well as mechanisms for transferring accelerations from ship manoeuvres to the astronaut in an acceptable manner. The form and function of this hibernaculum will depend on the hibernation mechanisms employed. Essentially definable by the extent to which the ability to hibernate has been internalised by the astronaut; The likely requirement will be for extensive physiological parameter monitoring and pharmaceutical delivery systems and environmental parameter monitoring and dynamic control. This level of sophistication will necessitate some form of AI agent (a nurse) to oversee the wellbeing of the hibernator.

The integration of the hibernaculum within a deep space mission will also have important system-level consequences for the design of the mission, particularly for the Life Support System (LSS). The hibernaculae of the hibernators are likely to be small, enclosed and environmentally independent regions of the ship; during hibernation, the wider LSS of the ship will largely be dormant. The correct mixture of integration/partitioning of the hibernaculum and ship-wide LSS systems is not yet known. Simple consideration of the principle characteristics of physical-chemical and bio regenerative LSS indicates that a hypometabolic stasis system would be most suited to integration with a physical-chemical LSS. Food production (the principle advantage of a bio regenerative system) is not a requirement for hibernating crew, and in any case, crew maintenance of food production (an envisioned requisite for the foreseeable future) would be impossible. If the hibernation strategy adopted involved periodic arousal (in which case life support would have to be extended from the hibernaculum to a sufficient portion of the spacecraft to allow the crew to perform inter-hibernation bout activities), bio regenerative systems would have trouble providing the required environmental changes due to typically slow response times.

Any LLS would require complex control strategies that can maintain stable system performance and balance resources [1]. This requirement for dynamic response would be increased with the presence of hypometabolic stasis. The dynamic variability of the life support load would be increased, as for at least one extended period; the life support requirement on board the spacecraft will be reduced drastically. LSS function will then have to mirror (and to some degree anticipate) the physiological function of the hibernator as stasis is entered and exited.

Study Objectives

Taking as a reference a manned Mars mission, the objective of the study is to perform a first iteration definition of one or more hibernaculae designs, based on the results from xx/xxxx, xx/xxxx and xx/xxxx. Form and function, resource requirements, radiation shielding, and AI nurse issues should also be addressed.

Once the requirements of the hibernaculum have been defined, study of the integration of the hibernaculum within a mission context will be performed. In the main this will focus on integration issues with the ship-wide LSS, but should address all systemic issues, such as management of accelerative loads. Of particular interest is the suitability of PC and Bio-regenerative LSS systems, dynamic response as hibernation is entered and exited, and other issues.

In summary the study objectives are:

- perform a first iteration definition of one or more hibernaculae designs, based on the results from 1, 2 and 3

- study of the integration of the hibernaculum within a mission context, paying particular attention to the interaction between the LSS and the hibernation system.

References

[1] Kortenkamp, D., Bonasso, R. P. (2001). *Distributed, Autonomous Control of Space Habitats*. IEEE 0-7803-6599-2/01.

References