THESEUS Report Summary

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Final Report Summary - THESEUS (Towards human exploration of space: a European strategy)

Executive summary:

When preparing for human space exploration in the solar system, past space missions in Earth orbit have demonstrated that human beings can survive and work in space for long durations. However, there are pending technological, medical and psychological issues to be solved before adventuring in longer duration space missions (protection against ionising radiation, psychological issues, behaviour and performance, prevention of bone loss). Furthermore technological breakthroughs, e.g. in life support systems and recycling technologies are required to reduce the costs of these expeditions to acceptable levels. Solving these issues will need scientific and technological breakthroughs of interest for clinical and industrial applications and also allow identifying the relevance of these questions to health applications on Earth. Despite many existing European Space Agency (ESA) or National Aeronautics and Space Administration (NASA) studies, up to now Europe did not have a roadmap approved by the European scientific communities. The THESEUS coordination action filled this gap and developed an integrated life sciences research roadmap enabling European human space exploration in synergy with the ESA strategy, taking advantage of the expertise available in Europe and identifying the potential of non-space applications and dual research and development.

Over 120 international experts joined 14 thematic Expert groups (EGs) set up by the project to identify knowledge gaps and future scientific priorities. THESEUS EGs covered the whole spectrum of human spaceflight-related science and were grouped in five clusters focused on integrated physiology, psychology and human-machine systems, space radiation, habitat management and health care.

With additional inputs received via an online consultation addressed to the scientific community at large, THESEUS EGs identified a set of 99 scientific key issues. At the core of THESEUS concept, Key Issues can be defined as high priority disciplinary scientific topics or methodology issues representing challenges or opportunities for human space exploration, requiring further attention in the future. While identifying and detailing the importance of each Key Issue for human space exploration, EGs also addressed and highlighted their relevance to major Earth Based societal challenges.

The findings and recommendations from EGs were discussed during an integration workshop held in June 2011. This event recommended that the THESEUS roadmap is structured around three themes:
1. an integrated view of adaptation to the space environment;
2. an integrated view of countermeasures to multiple stressors; and
3. an integrated view on tools and methods.

The THESEUS roadmap and EGs reports were officially launched in March 2012 and are available on THESEUS website.

Space agencies and governments are currently jointly discussing their plans for space exploring, and any research roadmap
enabling human exploration of these targets should be incorporated in these plans in order to ensure their relevance. In this context, taking into consideration THESEUS' results and recommendation would ensure that basic and applied research priorities, as defined by the relevant communities, are addressed in a consistent and upstream manner by these agencies and governments in the future.

Project context and objectives:

Today, the exploration of space remains one of the most stimulating and exciting areas of scientific research and technological development. One of the objectives for the next decades is to create, and then implement, a long-term plan for the robotic and human exploration of the solar system, with near-Earth objects, Moon and Mars as first targets. To undertake such future scenarios require major efforts of global and interdisciplinary cooperation of scientific, industrial and legislative parties.

In 2007 the European Space Sciences Committee of the European Science Foundation (ESSC-ESF) was asked by ESA to organise a consultation in Europe's planetary research community and come up with a science-driven scenario for Europe's exploration programme. In its report, the steering committee concluded that:

'Europe's exploration programme should focus on targets that can ultimately be reached by humans...The role of humans as a unique tool in conducting research on the Moon and on Mars must be assessed in further detail... Since Europe Exploration programme's ultimate goal is to send humans to Mars in the longer term, research on humans in a space environment must be strengthened. Beyond the necessary on-going and planned biological research and human presence on, e.g. the International Space Station (ISS) or in Antarctica, opportunities to this end might also arise in the context of an international lunar exploration programme. ESA needs to ensure the continuity of the necessary expertise in the longer-term by supporting the relevant groups.

Hence the goal set up by the relevant science communities in Europe pointed to the need to pave the way for future human exploration of the solar system, starting with missions in low-Earth Orbit on the ISS, and continuing on to Mars with the necessary intermediary steps, i.e. the Moon and / or near-Earth objects.

A vital stepping stone for the preparation of this human space exploration is ESA's 'European life and physical sciences in space' (ELIPS) programme which was evaluated by ESF in February 2008 for its accomplishments, through a broad user consultation. The report from this consultation looks in detail at various disciplinary aspects of ELIPS. In the areas that are most relevant to human space exploration, i.e. physiology and psychology, the report recommended that:

Physiology research programmes should be based upon three principal pillars, namely fundamental science, applied science, exploration-driven science. There was a further recommendation that the following themes should be superimposed upon this three pillar foundation:

- radiation;
- human performance;
- microbial safety;
- systems homeostasis and adaptation;
- life-support systems;
- and countermeasures.

These themes therefore represent the disciplines that should be studied in preparation of future human spaceflight. The physiology recommendations included the fact that a better understanding of partial gravity environments / artificial gravity should be obtained.
In the area of psychology, the community felt that more research in the following areas was needed in the longer term:

i) research on, and development of, effective training tools in order to prepare crews for exploratory missions;

ii) research on, and development of, effective support tools in order to provide the best possible psychological in-flight support of crews during exploratory missions:

iiia) establish countermeasures for monitoring and dealing with social problems and individual stress reactions;

iiib) establish countermeasures for reducing the impact of boredom and monotony on performance and psychological health;

iii) research on safety management in space organisations.

These findings and recommendations led scientists and relevant institutions to propose an activity aimed at answering these challenges.

Past space missions in Earth orbit have demonstrated that humans can survive and work in space for durations of up to several months. However, there are pending technological, medical and psychological issues to be solved before adventuring in longer duration space missions, such as those envisioned in the space exploration programme. For example, prevention of bone loss, protection against ionising radiation, psychological issues, impaired behaviour and performance after long duration space travel, are the main limiting factors for a manned mission to Mars. Furthermore technological breakthroughs, for instance in life support systems and recycling technologies, are required to reduce the costs of these expeditions to acceptable levels. Solving these issues will need scientific and technological breakthroughs, which will also be of interest for clinical and industrial applications.

To enable long-duration human presence in space it is required to identify:

(i) the constraints and conditions imposed on humans by the space environment;

(ii) the physiological and psychological risks of long duration space flight on humans. Knowing these constraints and risks will allow:

(iii) to formulate the protection, support and countermeasures that the space habitat needs to provide for humans to survive in this space environment.

In the United States, NASA has developed a plan for its future exploration programme, the human research roadmap and its associated programme. In Europe, ESA supported several preliminary studies enabling the definition of priorities to prepare interplanetary manned exploration missions, such as the HUMEX, FIPES and MARTECHCARE studies. ESA also developed an important ground programme to validate countermeasures through bed rest studies and use of artificial gravity applied in a short-arm centrifuge. However, before THESEUS, Europe had no roadmap including an action plan approved by the European scientific (disciplinary) communities. There was therefore a need for a Europe-wide strategy, relying on ESA programmes and supported through the European Commission (EC)’s Framework Programme (FP), integrating the expertise of non-ESA Member States. This strategy, developed through THESEUS identifies the commonalities with other research fields and technological areas, both space and non-space related.

The goal of THESEUS was to develop an integrated life sciences research roadmap enabling European human space exploration, in synergy with the ESA strategy and the objectives of the EC’s FP, taking advantage of the expertise available in Europe and identifying the potential of non-space applications.

This goal could be captured through a series of three objectives, performed essentially in sequence:

Objective 1: identify disciplinary research priorities.

Objective 2: focus on fields with high terrestrial application potential.

Objective 3: build a European network as the core of this strategy.
THESEUS brought together experts to identify the constraints and risks associated to human spaceflight and formulated the research and technological developments needed to enable long-duration human spaceflight in the future. The THESEUS experts were gathered in 14 disciplinary EGs involving 123 experts.

Finally, since any human exploration initiative can only be conceived as a well-coordinated series of programmes at the international level, the issue of international cooperation and coordination with other nations, agencies and programmes was central in the establishment of the THESEUS roadmap. Space agencies (under the ISECG umbrella) and government (within the Lucca process) are currently jointly discussing their plans for exploring the Moon and Mars, the THESEUS key issues and roadmap will represent clear and strong inputs to these processes. Taking into consideration the THESEUS Key Issues will ensure that basic and applied research priorities, as defined by the relevant disciplinary communities, are addressed in a consistent and upstream manner by these agencies and countries.

It was crucial that relevant space agencies are represented as observers in the course of the THESEUS development. ESA, CNES (France), the Japanese Space Agency (JAXA), and NASA were observers in this coordinated action. Having the right impact on science policy-makers was also an important item that the THESEUS consortium members were eager to address properly. To this end, discussions took place with the European Space Policy Institute (ESPI) based in Vienna, and it was agreed that ESPI would contribute to the project, as an associated partner.

Project results:

1. Project structure and work logic

As mentioned above, the ultimate goal of THESEUS was to develop an integrated life sciences research roadmap enabling European human space exploration, in synergy with the ESA strategy and the objectives of the EC’s FP, taking advantage of the expertise available in Europe and identifying the potential of non-space applications and dual research and development.

In order to reach this ambitious objective, THESEUS relied on the expertise of 123 international investigators involved in 14 EGs. The project's progresses were sequenced in six main steps that resulted in the identification of disciplinary research priorities and the consolidation and promotion of an integrated strategic roadmap.

Step 1: The launch conference (Milestone 1 - Addressed through WP8)

Three months after the official start of the project, all 14 EGs were invited to attend the launch conference; this event was structured around plenary sessions and parallel meetings of the EGs. The objective was to identify a set of key research challenges / questions that need to be addressed in priority to enable human exploration in the next 10-15 years and to design onmine surveys that would allow to gather inputs on these points.

Step 2: Website, publications and visual identity (Milestone 2 - Addressed through WP7)

The project website (www.theseus-eu.org) did not only present the project and its progress, it also provides highlights on its outcomes and findings. A particular attention was given to providing concise summaries of the EGs reports. The project website naturally disseminated information but it was also a key element of the priority identification exercise as it hosted the various online consultations aimed at gathering the inputs form the scientific community.

Within a few weeks after the start of the project, a promotional leaflet, providing key information on the project objectives and process was published and widely disseminated within the networks of the various actors of the project. Regular newsletters (twice a year), providing information on the project have been issued and are available on the website for download.
Step 3: Online consultation and first draft of EG reports (Milestones 3 to 7 - Addressed through WP1, WP2, WP3, WP4 and WP5)

Because it was of crucial importance to open the science priority setting to the relevant European scientific community at large, the project launched a broad online community consultation on the draft Key Issues identified during the launch conference. This consultation was promoted by all the actors of the project via their respective networks and 169 submissions (of which 149 from non-EG members) were submitted. Work Package leaders compiled the inputs received and forwarded them to the members of the EGs.

Step 4: Second meetings of the EGs (Milestones 8 to 12 - Addressed through WP1, WP2, WP3, WP4 and WP5)

At Month 10 (October 2010), a second set of workshops was organised where EGs met in clusters (by WP). During these meetings, EGs considered and analysed the information gathered via the consultation. They also identified the important points expressed and additional experts were invited to support the groups when deemed necessary. Finally, they identified and agreed on the key issues to be put forward in their report.

Step 5: Integration workshop (Milestones 13 - Addressed through WP6)

This step was a crucial milestone of the project as it was instrumental in synthesising the findings, recommendations and outputs of the individual EGs.

At Month 18 (23-24 June 2011), the integration of the different EGs' reports was organised during a workshop with the chairs and rapporteurs of each EG, the Steering Committee of the project and some selected additional experts. Following this event, and in accordance with the recommendations expressed at this occasion, the consortium progressed towards the definition of the THESEUS roadmap.

Step 6: Final conference (M14 - Addressed through WP6)

This step represented an important opportunity to report in front of the THESEUS community and relevant stakeholders and to disseminate the project results.

At month 27 (15 March 2012), the final conference aimed at presenting all the outcomes, findings and recommendations for the project and in particular its roadmap was held in Paris, France. This successful event, gathered 65 stakeholders from various space agencies and members of the community built-up through the project. The roadmap and the disciplinary findings were very well received and acknowledged as being a valuable step towards a more integrated approach to human spaceflight.

2. The 99 THESEUS Key Issues

Key issues are at the core of the THESEUS concept; key issues can be fined as high priority disciplinary scientific topics or methodology issues representing challenges or opportunities for human space exploration, requiring further attention in the future. In identifying key issues, the THESEUS EGs considered the challenges imposed by the most demanding space exploration scenario proposed in the first steps of the THESEUS project, this led the groups to study knowledge gaps to be filled and methodological approach required to implement a long duration mission to Mars (in the range of 500 days). At the occasion of the first meetings EG identified a preliminary set of 112 key issues (for all groups). These key issues were detailed in the online surveys and the scientific community at large was invited to comment on them. Considering the 123 experts from the EGs and the contribution received from an additional 149 scientists through the online consultation, THESEUS KI and roadmap development involved more than 270 investigators across the world.

Taking into consideration the inputs received, following further discussions during their second meeting and further exchange, EG refined the number of KI to 99. Most EGs presented and detailed each KI around six axes:
relevance for space exploration;
Earth benefits and applications;
brief review of latest developments;
knowledge gaps and research needs;
proposed investigations and recommendations;
transdisciplinary aspects.

The 99 key issues are listed below details can be found in the individual EG reports (compiled in Cluster reports).

Cluster 1: Integrated systems physiology

EG1.1: Bones and muscles
- sex-based differences in the preservation of musculoskeletal tissue during space flight;
- effects of micro-gravity on musculoskeletal injuries and healing processes (ligaments and tendons, bone fracture, back pain);
- role of genetics in musculoskeletal performance, preposition to injury and overall adaptation to micro-gravity;
- biomechanics and impact of partial gravity on the musculoskeletal system;
- effects of radiation exposure experienced during space flight on the musculoskeletal system;
- ground-based human studies;
- ground-based animal studies;
- optimise countermeasure efficiency and utilise an integrated physiology approach.

EG1.2: Heart, lungs and kidneys
- What are the inflight alterations in cardiac structure and function?
- What is the influence of spaceflight on structure and function of blood vessels?
- What level of cardiovascular function loss is acceptable and what type and quantity of exercise is necessary to ensure that this loss is not exceeded?
- What are the risks associated with exposure to extraterrestrial dust?
- What are the roles of diet and bone demineralisation on kidney stone formation and can we predict the risk of kidney stones?

EG1.3: Immunology
- Identification and quantification of stress factors and their impact on the immune system.
- Are immune system development, response and regulation as efficient in space (ISS / Moon / Mars) as on Earth?
- Consequences of long duration (1 year) missions on the degree of immune-suppression.
- Consequences of ‘chronic' immune changes during and after long-duration mission on disease.
- Effect of Lunar or Mars dusts, habitat environment and other chemicals on immune performance.
- Are the observed stress-dependent virus reactivation patterns linked to cancer development?
- Interaction between immune system and other stress-sensitive systems.
- Definition and testing of (immune targeted) countermeasures.

EG1.4: Neurophysiology
- impacts of spaceflight on the senses;
- impacts of spaceflight on sensorimotor performance;
- impacts of neurophysiological changes on spaceflight-induced decrements in neuro-behavioural performance;
- countermeasure strategies to minimise the risks associated with neurophysiological changes during and after g transitions;
- understand the role of gravity in the development of the nervous system.

EG1.5: Nutrition and metabolism
- the in-flight negative energy balance;
- feeding behaviour;
- metabolic stress;
- micronutrients deficiency;
- alterations of gut microflora;
- hydro-electrolytic imbalance.

Cluster 2: Psychology and human-machine systems

EG2.1: Group / team processes
- maintenance of team cohesion, wellbeing and performance;
- impact of reduced communication between crew and earth;
- managing intra-crew differences and conflicts;
- integral monitoring of crew and individual behaviour.

EG2.2: Human-machine interface
- design of human-automation system;
- adaptation to support operator state and mission goals;
- evolving, problem solving and updating during missions;
- simulation and virtual / augmented reality (SVAR);
- robots (HRI), agents (HAI) & human-robot-agent interaction (HRAI).

EG2.3: Skill maintenance
- risks for operational effectiveness from infrequent or non-use of skills;
- need for different training methods for the acquisition and maintenance of different types of skill;
- use of on-board top-up training to maintain and enhance skills;
- protection against effects of stressors on skill learning and effective long-term skilled performance;
- management of sleep and work / rest schedules to prevent skill impairment by sleepiness and fatigue.

Cluster 3: Space Radiation

EG3.1: Space radiation effects on humans
- What is the particle and dose rate dependency for acute effects?
- How is the sensitivity to acute effects modified by the space environment?
- What is the effectiveness of GCR at low doses for carcinogenesis?
- Is there a risk of CNS damage from low doses of GCR?
- Is there a risk of non-cancer late effects from low doses of GCR?
- Is there a risk of hereditary effects from low doses of GCR?
- How will multi-scale mechanistic-based modelling of space radiation improve risk estimates?
- How can radiation effects be effectively mitigated?

EG3.2: Radiation dosimetry
- experimental determination of radiation field parameters;
- modelling of radiation environments;
- space weather forecast;
- transport codes;
- shielding;
- individual radiation exposures;
Cluster 4: Habitat management

EG4.1: Microbiological quality control of the indoor environment in space
- define correct upper and lower thresholds for indoor environmental quality control of air, water, food and surfaces in space habitats;
- develop efficient materials and methods to prevent environmental microbial contamination in space;
- develop adequate environmental contamination monitoring (prediction, detection, identification) systems for use in space;
- develop materials and methods to mitigate environmental microbial contamination and its harmful effects in space;
- acquire better knowledge on microbial community (microbial ecosystem) dynamics and microbial cell evolution over time in confined manned habitats in space.

EG4.2: Life Support: management and regeneration of air, water and food
- Develop and adopt common metrics for evaluation of different Life support system (LSS) architectures, technologies, and their evolution;
- develop model-based regenerative Life Support via a system level approach;
- further develop Life Support subsystems and components for long-duration space flight and planetary surface mission phases;
- improve autonomy of LSS via monitoring and control;
- improve LSS robustness, reliability, availability, maintainability, safety, acceptability in long-term integrated operations;
- screen and develop high performance materials for LSS;
- develop and demonstrate capabilities to exploit resources available on other planets (in-situ resource utilisation or ISRU) for life support;
- improve LSS architecture to increase habitability.

Cluster 5: Health Care

EG5.1: Space medicine
- Insufficient control of infectious diseases potentially exacerbated by on-board micro-organism mutations, drug inefficiencies and drug resistance - Provide an on-board available means to deal with the risk of infectious disease.
- The acute risk to health from radiation exposure, in particular solar flares - Provide on-board physical and / or pharmacological countermeasures and / or protection.
- Dietary and nutrition-related space flight disorders and complaints - Provide on-board countermeasures.
- Sub-optimal physical countermeasure hardware for health maintenance - Identify and provide improved solutions to current bone and muscle loss countermeasures;
- Insufficient on-board medical imaging hardware - Provide on-board means to maintain medical risks at an acceptable level.
- Insufficient on-board smart sensors / smart devices for health monitoring and medical diagnostics - Provide on-board means to maintain medical risks at an acceptable level.
- Insufficient on-board expert systems / decision support systems for medical diagnostics - Provide on-board means to maintain medical risk at an acceptable level.
- Insufficient on-board drugs for medical / surgical procedures - Provide the capability to offer sufficient drugs and appropriate procedures to maintain on-board medical risks at an acceptable level.
- Insufficient on-board equipment to make sufficient medical procedures available for appropriate health care delivery - Provide on-board capability to maintain medical risks at an acceptable level.
- Insufficient on-board surgical techniques and devices (e.g. endoscopic procedures, restraint systems) - Provide sufficient on-board surgical techniques and devices to maintain medical risks at an acceptable level.
- Insufficient provision of virtual reality training systems / human patient simulators - Provide on-board capability to maintain
medical risks at an acceptable level during human exploration missions.

- Lack of provision of appropriate medical curricula for physician astronauts - Provide capability to achieve and maintain physician skill sets and knowledge to maintain medical risks at an 'acceptable' level during human exploration missions.
- Lack of provision of methods to define the minimum on-board medical infrastructure needed to maintain medical risks at an 'acceptable' level during human exploration missions.
- What triage decisions and medical capability limitations shall be acceptable during human exploration missions?
- What criteria shall be accepted for the medical selection of astronaut crews for human exploration missions?
- What psychological criteria shall be used for the medical selection of astronaut crews for human exploration missions?

EG5.2: Medication in space
- Is there evidence supporting changes in drug efficacy in-flight.
- Which systems / pathways are operationally important for human spaceflight and why?
- What classes of drugs should be studied as a priority to sustain the health and performance of astronauts during spaceflight?
- Which drugs may have what important unwanted effects? What classes of drugs should be studied to prevent toxicity and risk issues during human spaceflight? What are the important drug interactions that should be avoided?
- What pre-flight or in-flight tests should be conducted to avoid or assess possible side effects such as allergic reactions, problems from pharmacogenetics or influences on performance?
- What tests should be conducted to assess the possible influences of medication on pre-flight and in-flight performance and sleep quality?
- It is important to know whether the pharmacokinetics of various drugs in space is altered. What pharmacokinetic changes in what classes of drugs have the most important clinical impact in space?
- What evidence exists of pharmacodynamics changes resulting from posture and physical (in)activity seen in clinical studies (bed ridden patients, sedentary people)?
- What models should be used to study pharmacodynamics?

3. Definition of the THESEUS roadmap

THESEUS roadmap is a high level strategic science policy document that provides an overarching framework to implement the recommendations and KI put forward by the EG. Developing this document, involved going from detailed disciplinary considerations (ranging from the maintenance of skills to nutrition) to an integrated approach that allowed to address individual interest while identifying cross cutting aspects.

Definition of the roadmap was based on five pillars:
- the reports from the EGs and the 99 key issues (detailed above);
- the integration workshop and the discussions held at this occasion;
- a detailed background analysis of key issues and their interactions;
- the actual roadmap development.

THESEUS integration workshop

The integration workshop was held at the International Space University (Illkirch-Graffenstaden, France) on 23-24 June 2011. This meeting was targeted towards chairs and rapporteurs of the EGs as well as members of the steering committee and selected additional experts and was attended by 39 participants.

The objectives of this event was to present the main outcomes from each EG to representatives from all other EGs in plenary sessions, and to identify the issues that cut across a significant (if not all) part of the THESEUS spectrum. The latter was mostly achieved during splinter group discussion sessions.
The discussions and recommendations from this event did not so much focus on specific common research themes but rather addressed the general approach and overall structure of the roadmap, thereby more strongly emphasising the challenge imposed by the synthesis of all the output from the EGs. From this, the workshop called for a deeper and systematic analysis of the findings expressed by the THESEUS experts with a strong emphasis on identifying interactions between key issues and between EGs. The main recommendations arising from the integration workshop were therefore:

- to structure, as much as possible, the roadmap around three themes, namely: an integrated view of adaptation to the space environment (in particular the combined effect of multiple stressors), an integrated view of countermeasures to multiple stressors (in particular interaction between different countermeasures), and an integrated view on (enabling / required) tools and methods;
- to systematically identify and investigate the elements driving the interactions between the 99 key issues identified by the EGs and between the EGs;
- to produce matrices providing cross-comparisons of issues of common interest between stressors and countermeasures methods.

The recommendations from the integration workshop were taken on-board by the THESEUS consortium.

Detailed background analysis of key issues and their interactions

This analysis involved identifying keywords of relevance for each Key Issue as presented on the EG Reports, this led a total of approximately 1,300 of keywords identified. In a second pass, these keywords were screened to provide a more homogeneous list, i.e. similar terms were grouped into a more comprehensive denomination, for instance, ‘monotony’ was retained both for ‘monotony’ and ‘boredom’.

From the list of keywords attached to each Key Issue and EGs and the commonalities between pairs of key issues and EGs, it was possible to create interaction matrices.

In addition to the ability to visualise interactions across elements in a matrix form, this method also allowed for the identification of concepts and issues that cut across the THESEUS scope, i.e. present an interest for a significant part of the THESEUS research domains. Six of the most transversal concepts are listed below by alphabetical order:

- Contamination
This mainly emerges from the EG on habitat management and design, but contamination (microbial and Lunar / Martian material) is also of relevance for integrated physiology issues, including the cardiovascular system, immunology, nutritional issues, digestion, infections and sterilisation.

- Individual factors
Investigating the mechanisms behind why and how individuals respond differently to the conditions of spaceflight by various means (e.g. psychological assessments, genetic and medical screening) has been pointed out several times by THESEUS EGs. This issue is relevant to develop a better understanding of human adaptation to spaceflight and could also be considered in the selection of astronauts and crew composition. While it is challenged by ethical issues, genetic predisposition seems to be a topic of increasing interest.

- Molecular and cell biology; genetics
This theme deals with every aspect of cellular and molecular mechanisms involved in various reactions to stressors at large. It is omnipresent: bones and muscles, genetics, immunology, contamination, radiation effects on cells etc. There was no explicit EG to deal with these mechanisms in THESEUS.

- Monitoring and modelling
Intelligent, integrated, synchronised monitoring of physiological and psychological systems together with the environment (e.g. radiation, habitat) are mandatory and will be extremely valuable to feed integrated models.

- Integrated countermeasures
Countermeasures must be approached in an interdisciplinary manner, firstly, because astronaut time is very constrained, and secondly because a comprehensive approach is much more efficient than the sum of local solutions. All dimensions need to be taken into account.

- Radiation effects
Negative radiation effects represent one of the most critical showstoppers for long-term spaceflight. Particles from mixed radiation sources are abundant in space, and conventional shielding by thickening the habitat is extremely challenging. Active shielding, forecasting events, and determining acceptable doses are all important aspects in protecting a crew from danger. Also, understanding the interaction of radiation with physiological systems is critical. Monitoring these events is of prime importance as well to feed prediction models.

This quantitative analysis of the EG reports allows to provide new insight and rational elements (matrixes as well as the list of overarching keywords and issues) that represented key integrated inputs to the development of the THESEUS roadmap.

Following third recommendations from the integration workshop, THESEUS consortium developed two matrixes intended to show interactions between human systems and (i) stressors experienced in during space exploration missions, (ii) countermeasure to mitigate the effects of these stressors, as well as (iii) the interactions between countermeasures and stressors.

This analysis required first reviewing and listing the stressors and countermeasures mentioned in the EG reports as well as filling the matrixes with the interactions mentioned in these reports.

Roadmap development and finalisation
The detailed analyses presented above were performed by early October 2010, opening the way for the roadmap development step. The resulting roadmap is structured around the three themes put forward by the Integration workshop and put forwards nine recommendations (more details are provided in the roadmap):

Theme 1: Develop an integrated view of human adaptation to the space environment
- Recommendation 1: Perform a detailed, integrated survey, define and quantify the multiple environmental stressors during human space exploration missions, and assess their potential hazards to humans, both individually and in combinations.
- Recommendation 2: Perform an integrated survey and identify interactive human adaptations to the complex environments of space exploration in order to assess the risks to astronauts and develop efficient countermeasures for their mitigation.
- Recommendation 3: Perform an inventory of personalised exposures and responses to the complex environments of space exploration with regard to gender-based differences, genetic disposition and other individual characteristics.
- Recommendation 4: Perform an integrated risk assessment for human exploration missions combining the risks from exposures to multiple-stressor environments, the interactive adaptations to these stressors, and from personalised responses. This should be the base for quantifying acceptable risks for astronauts during exploration missions.

Theme 2: Develop an integrated view of countermeasures to multiple stressors
- Recommendation 5: Mitigation strategies against certain adverse effects expected from environmental stressors should be implemented during the planning phase of a space exploration mission, e.g. by designing appropriate habitats, developing training methods and providing appropriate countermeasures with the mission scenarios and timelines.
- Recommendation 6: Develop optimised countermeasure procedures and programmes that integrate human body functions as well as inter-individual variability, and take into account the possible interactions between different countermeasures. To achieve this, ground-based analogue facilities need to be developed for animal and human studies addressing system-level questions.

Theme 3: Develop an integrated view of tools and methods

- Recommendation 7: Develop standardised protocols and procedures for studies on integrative human adaptation to the conditions of space during exploration missions and the development of efficient countermeasures.
- Recommendation 8: Set-up a database of results from ground and space-based integrative human research based on standardised protocols and procedures including the exertion of countermeasures. A data management and distribution system should be established in coordination with major European stakeholders (especially ESA and EC) to make these data accessible to the scientific community. Protocols should be established for disclosure of anonymous crew health data to qualified researchers.
- Recommendation 9: Utilise mathematical, physical, biological and neurocognitive modelling to understand and anticipate various risks to astronauts associated with exploration missions and for applying means to reduce them to an acceptable level.

It was important to link each of these nine recommendations with the 99 key issues identified by EGs in order to demonstrate how they would support addressing these important topics. To this end, five tables (one by cluster) crossing recommendations with key issues have been produced (detailed in the THESEUS roadmap).

In addition to these nine rather detailed recommendations, the THESEUS roadmap puts forward an overarching recommendation that clearly calls for more integration in future research programmes.

Overarching recommendation:
Structure human exploration-enabling research around the themes and recommendations put forward by THESEUS, using the phased approach defined by the roadmap exercise. Programmes should be coordinated and implemented at the European level and consider direct funding, networking and exchange of knowledge as well as optimised utilisation of European research infrastructures. In this context, targeted calls and dedicated research solicitation would allow medium to long-term consistency in the process.

4. Earth benefits and application

In addition, THESEUS key issues and proposed approach definitely has some relevance for societal challenges down on Earth in particular when considering health, demographic change and wellbeing as well as Inclusive, innovative and secure societies. For each EG, the most relevant aspects for Earth concerns have been listed and highlighted. These issues are presented and detailed in the part dealing with potential impact below.

Potential impact:

The main impact THESEUS could have lies in the remit of the international space exploration landscape and the current processes considering a coordinated international initiative in the field. In this context, THESEUS provides a very valuable set of well identified research topics together with an overarching approach to address them. This strategic information and operational approach would allow streamlining the research effort required to enable human space exploration beyond LEO. However, while research activities are clearly identified in the cluster reports, this impact on space exploration programmes is set in the longer term and only focusses on space activities. In the context of EC's FP and the Commission's interest in addressing Earth-based challenges, it seems important to demonstrate the potential impact that THESEUS' proposed research
could have on the societies.

While THESEUS as such will not have a direct societal impact, by and large, the issues and problems that humans face during missions in low-Earth orbit and beyond share commonalities and applications with issues on Earth. However, the relative importance of these issues can vary dramatically. For example, the ability to predict space weather or the reliability of life support systems are critical issues for exploration missions beyond low-Earth orbit while also representing opportunities to significantly improve Earth-based systems and operation without immediate risk to loss of life.

Following this idea, it must also be acknowledged that most of the research relevant to considering THESEUS key issues is not performed only in the context of space activities. Therefore it is crucial that space exploration-related research is continuously linked with and aware of wider research activities and that in addition to spin-offs, potential spin-in research activities are identified and exploited. This is, for instance, the case for research on improving and optimising Human-Robot interactions. This field has many applications on Earth, and it is more likely that space activities will benefit from research performed on Earth than the other way around.

However, it has to be emphasised that while some topics are intensively investigated on Earth, space exploration provides very specific conditions in terms of environments, technical constraints as well as operational and safety requirements. These specificities allow consideration of scientific and technological topics with a different angle, eventually bringing added value to Earth applications. The issue of miniaturisation of diagnostics and health monitoring equipment provides a good example of such added value.

The most salient Earth application potentials of space exploration-enabling research identified through the THESEUS project are presented below.

**Integrated Systems Physiology**
Research on integrated systems physiology aims at maintaining crew health during and after missions and ensuring that crew members are in the required physical condition to perform their tasks. Therefore, this area of research is highly relevant to health issues on Earth and is strongly related to current societal challenges such as ageing.

**Bones and muscles**
The strongest translational potential of musculoskeletal research for spaceflight is the study of age-related osteoporosis and sarcopenia. Although ageing and spaceflight may involve changes in morphology and function by fundamentally different cellular and molecular pathways, they share a common feature of adaptation to changing levels in strain. Thus, studying musculoskeletal system adaptation to microgravity, and re-adaptation to 1-g parallels the context of age-related atrophy of bone and muscle tissue. Bed rest studies separate the effect of disuse from those associated with co-morbidities, both in the context of fracture healing and in atrophy due to prolonged hospital stays.

**Heart, Lungs and Kidneys**
Heart disease is a leading cause of death in the terrestrial population, prompting significant research efforts in the domain. During space flight, a healthy population (astronauts and cosmonauts) experience significant and rapid degradation of cardiovascular performance. This provides the potential to utilise space-based research to help understand the factors that lead to cardiovascular disease on Earth.

Additionally, many people are exposed to dusty environments in the workplace, and particulate matter in the environment is a known health risk to urban populations. Further, many drugs are now delivered in aerosol form, and so a comprehensive understanding of the deposition and subsequent clearance of deposited particles is of considerable importance in both areas.

**Immunology**
Understanding stress-related immune challenges in space is highly relevant to the understanding of the biology of cancer immunology, the balance of inflammation and endogenous mechanisms to control it, and the lack of control (autoimmunity / allergies) in young and ageing population on Earth.

The functions of the immune system can be affected in response to environmental / living conditions, and chronic and acute stress conditions can result in a further parallel interaction between the immune system and other organ systems. As an example, stress causes neurophysiologic responses and hormone liberation which can modulate inflammation but also promote bone resorption.

Neurophysiology

Spatial disorientation and situational awareness issues are responsible for up to a quarter of all civil aviation accidents. Diminished manual flying skills during visual flight piloting is an increasing problem, especially for search and rescue helicopter pilots required to fly with diminished visual cues. A better understanding of the mechanisms underlying disorientation as well as development of physical aids (e.g. tactile situational awareness system) and countermeasures developed to aid space travellers might also be useful for commercial and military aviation.

The altered gravity environments available during spaceflight offers an additional platform to study basic neurophysiology of dexterous manipulation (eye hand coordination), balance and locomotion and vehicle control. Research in these domains can provide knowledge that serves to help patients with vestibular, neurological, and motor control problems, as well as the elderly. Knowledge gained from studying the training and rehabilitation protocols developed for use with astronauts can be transferred directly to patients with specific lesions or disorders requiring retraining or rehabilitation.

Nutrition and metabolism

The nutritional questions related to bioastronautics research are very relevant to multiple Earth-based related health issues. The potential spin-offs are interesting from a technical point of view and also have great clinical importance. Such spinoffs encompass the increasing burden of modern chronic diseases, in which the adoption of sedentary behaviour plays a central role (i.e. the metabolic syndrome, insulin resistance, dyslipidemia, type 2 diabetes mellitus, atherosclerosis, etc.).

Psychology and human-machine systems

Activities performed in space are set in a very specific and peculiar environment: crew members experience continuous confinement, isolation (including potential communication delay), a hazardous external environment as well as noise, cultural differences and dependency on other crew members. Additionally, crew are at the forefront of very costly and complex endeavours imposing equally complex tasks and procedures. In this very stressful environment, performance of astronauts has to be maintained at an appropriate level.

Similar environments can be found on Earth, notably in Antarctic stations but also with oil platforms, nuclear power plants, weather stations, military units stationed in foreign countries as well as crisis / rescue situations (e.g. fire-fighting, post-earthquake rescue operations). Knowledge gained through space exploration is highly relevant to operations in these specific settings.

Group / team processes

A defining characteristic of space missions is that humans operate primarily as a team, yet, they also have individual needs, preferences, skills and personalities. Crews sometimes operate explicitly as teams (with common task goals) and sometimes as separate individuals within a group (with personal goals). These roles, however, can overlap and effective inter-personal interactions between crew members are critical to overall mission success.

Developing methods and tools to monitor and maintain team cohesion, well-being and performance as well as the impact of reduced communication and intra-crew differences and conflict will benefit teams that have to work in stressful and high-risk
environments on Earth.

Human-machine interface
Space applications place extraordinary levels of reliance on technology and may drive advances in human-robot and human-agent collaborative work, interaction modalities, and concepts for interaction that involves shared physical proximity and high criticality applications.

Many current and planned work environments on Earth involve personnel interacting with increasingly automated systems. Two examples include the programme for transformation of the air traffic management system to accommodate higher levels traffic more efficiently (NextGen in the US and SESAR in Europe), and the increasing use of unmanned vehicles and robots by the military. Research on effective human-automation design will yield benefits for system efficiency and safety in these and other domains.

Skill maintenance
Research in the field of skill maintenance has a large significance for Earth applications where naturally long breaks occur between situations requiring the use of specific skills. There is an obvious relevance for safety critical systems (e.g. nuclear power plants, chemical plants, oil platforms or refineries, hospitals and commercial aviation). Also, there are numerous complex work situations such as in process control operations, the military, aviation, and civil protection services where skills have to be maintained over long time periods and which may rarely be called upon. For some situations it may be ethically impossible to train staff under real conditions, and therefore trained in real conditions. A particularly relevant example is when emergency rescue or disaster teams are required, or in medical emergencies when highly skilled team members are required, but the situations rarely occur.

Space Radiation
Radiation levels in space pose a major challenge for human exploration activities and are currently a showstopper for a human mission to Mars. Any knowledge gain in this domain is of high relevance on Earth, especially when considering particle therapy and protection from high dose exposures for individuals and electronic systems.

Radiation effects on humans
A better understanding of the acute and stochastic effects of radiation on humans is not only essential to future human spaceflight, but will also give insights into the impact of particle therapy used on Earth. Further research will determine particle therapy's impact not only healthy neighbouring tissue but also in the context of secondary tumours and non-cancer effects of radiation exposure.

New knowledge in the field of countermeasures could have a potentially high impact on mitigating the side effects from particle therapies, radiological accidents and terrorism.

Radiation dosimetry
Improved description of the radiation environment in space, as well as a larger degree of confidence obtained by models and simulations through optimised testing against measurements will have significant value for several terrestrial activities such as: (i) monitoring and improving the reliability of spacecraft electronics, for example terrestrial and satellite telecommunication and navigation systems (GPS, mobile communication, Galileo etc.), (ii) monitoring aircraft crew exposure, (iii) understanding failures rates in aircraft electronics; iv) improving hadron therapy and nuclear medicine, (iv) developing climate models.

Additionally, proper forecasting of solar events is an important part of the more general issue of radiation source modelling. Possible Earth applications are therefore very similar to those mentioned for the previous point. These will focus on minimising radiation driven electronic failures, avoiding potential damage to power grids, pipelines, aircraft electronics and
navigation, but also on radiation protection for occupational exposure (commercial and military flights, first responders).

Habitat management
Management of complex systems is a major challenge of the 21st century. Process engineering (based on chemical engineering principles) and systems engineering (based on a hierarchical approach of control of interacting subsystems) are the clues for modern developments of industrial processes, whatever the size or functionality. When developing and installing a rationale for a specific purpose, such as life support systems for space applications (especially systems including living organisms), the methodology and approach used will be completely transferable to other applications. Controllability, modularity and reliability requirements for life support systems are excellent examples of future developments in modern industrial technology. Applications to any environmental process are straight-forward.

Microbial quality control of the indoor environment in Space
The development of early detection and warning systems for environmental contamination and pollution has common interests for space and Earth applications. Such autonomous systems could be used to assure healthy environments in housing and working buildings, in hospitals for fast screening of incoming patients (carrier state), for the prevention of nosocomial infections in public areas and public transport, and in pandemic control in the case of natural catastrophes.

Potential medical applications are ample, including on-site infection detection and diagnosis. In addition, such systems will be of interest for continuous quality monitoring of air, water, surfaces and products in production facilities in the food and pharmaceutical industries.

In space vehicles, only a 'simplified' microbial community is able to develop (the only source is the humans, without interaction with plants, soil, animals). Space research could give a better understanding of microbial community dynamics under environmental conditions, which could be of interest for more complex Earth communities. A database of indicator organisms for expected / dominant microbial populations in confined habitats is also relevant for indoor environmental air quality control in housing and buildings on Earth in general, or for specific applications such as treatment of immune-depressed patients in hospital.

Life support: Management and regeneration of air, water and food
Today's major studies on environment issues and sustainability, e.g. in the field of industrial ecology, mainly focus on one requirement at a time (energy consumption, water consumption or any other). However, there is a need to approach systems with a much more integrated view, taking multiple requirements into account. Although the key criteria are not necessarily the same for space and Earth applications, the methodology and metrics used for space certainly could be valuable for Earth-based systems as well. As life support system complexity (required variety) is currently not known precisely, assessment methods and tooling will surely evolve. Assessment needs and methods have to have a simultaneous and continuous approach with life support system development and its increasing level of complexity. This completely matches the methods of integrating environmental concerns in industrial developments by finding innovative solutions to complicated environmental problems, as in the emerging domain of industrial ecology.

Closed-loop waste water recycling systems could be of interest for applications on boats and cruise ships, in remote hotels (eco-tourism), remote stations for exploration and / or exploitation of remote areas (e.g. Antarctica, desert). Derived from the MELISSA life support system, there have already been applications regarding grey water treatment for hotel complexes, e.g. The Dutch company IP-Star is currently implementing these applications. Furthermore, grey water treatment can be applied to major urban developments, especially new ones, laying the path for a more sustainable way of living on Earth.

Health care
Space medicine
With access to limited medical facilities and competencies on-board, space medicine requires that significant progress on diagnostic capability (e.g. imaging hardware, smart monitoring devices), and also on the ability to deliver appropriate health
care and surgery. Miniaturisation, automation and robotics as well as reliability of equipment and power efficiency are required to bring appropriate medical operation capabilities to spacecrafts. Furthermore, it is crucial that medical skills are maintained throughout long-duration missions in order to deal with the hopefully rare emergencies in the context of a Moon or Mars mission.

Drug effects
Research on the effects of spaceflight conditions (or analogues like bed-rest) on drug treatment, in particular pharmacokinetics, pharmacodynamics and side effects, will allow for a better understanding of the parameters that impact drug efficiency, and eventually improve the quality of medication on Earth.

Knowledge, experience and technological advances in these fields are highly relevant to the provision of medical care in remote and/or isolated conditions (e.g. polar stations, ships, submarines) and for rescue services through better equipment in ambulances. In addition to improving autonomy of some classes of patients, advances in individual health monitoring devices will also provide clear benefits in preventing diseases or attacks or easing the management of medical emergencies. Further, advances in telemedicine will provide the opportunity to improve the ability to diagnosis and possibly treat patients in remote areas on Earth.

Linking Space research to ‘Horizon 2020’
The numerous application potentials borne by space life sciences for the society can be articulated around, or at least linked to, the ‘Horizon 2020’ themes defined to support the ‘Europe 2020’ vision. While a full benefits assessment on these specific themes (together with an assessment of the European capacity) would require a significant effort and a dedicated survey, one can already identify how some Earth applications put forward through THESEUS relates to three of the ‘Horizon 2020’ themes:

Health, demographic change and wellbeing
- age-related osteoporosis and sarcopenia (integrated systems physiology);
- spaceflight-induced significant and rapid degradation of cardiovascular performance (integrated systems physiology);
- diseases related to sedentary behaviour (Integrated Systems Physiology);
- improved particle therapy and mitigation of adverse effects (radiation);
- protection from high dose exposures for individuals (accident, terrorism) (radiation);
- better diagnostic capability (e.g. imaging hardware, smart monitoring devices (health care);
- improved provision of medical care in remote and/or isolated conditions and for rescue services (health care).

Inclusive, innovative and secure societies
- air traffic management system, use of unmanned vehicles and robots (psychology and human-machine systems);
- safety critical systems (e.g. nuclear power plants, chemical plants), emergency rescue or disaster teams (psychology and human-machine systems);
- protection from high dose exposures for electronic systems (Radiation);
- early detection and warning systems for environmental contamination and pollution (habitat management).

Climate action, resource efficiency and raw materials
- closed-loop waste water recycling systems for ships, remote hotels and stations (Habitat Management);
- food security, sustainable agriculture, marine and maritime research and the bio economy;
- early detection and warning systems for environmental contamination and pollution (habitat management).

Dissemination activities
The primary targets of the THESEUS project in terms of dissemination were (i) space agencies and research council, in particular science policy manager in these institutions and (ii) the scientific community. The general public was not identified.
Dissemination and information about the project used three main vectors:

- Visual identity
As soon as the project started, the THESEUS office oversaw the definition of the project logo, promotional leaflet and graphic design. These are standards tools that allowed to give a 'corporate' identity to the project, all publications and presentations followed a similar layout, increasing the visibility of the project. This was particularly important for the cluster reports, the THESEUS roadmap and the four newsletters that constituted a coherent identifiable set of documents.

- Project website
The project website went online shortly after the kick-off conference. This platform:
i) provided a focal point for relevant project information for the experts involved in the project but also a wider audience;
ii) allowed to disseminate the project-related information and outputs;
iii) provide the technical framework of the community consultation and iv) provide a working area for the consortium and the EGs.
The website evolved over the project's lifetime accordingly to its developments, to suggestions received and to critical reviews from the steering committee. Between August 2010 (starting dates for the statistics) and March 2012, the project website has been visited by 1 900 unique visitors, on average 100 / month.

- Presentation at conferences
Besides direct involvement of experts in the THESEUS events and EGs, the main promotion vector for THESEUS was the presentation of the project in various scientific events and conferences, detailed list of presentation is provided in the part / table list of dissemination activities.

THESEUS was not a research project as such; therefore the project did not produce articles in peer-reviewed scientific journals. With all reports now finalised and published, the consortium is however committed to produce papers summarising the findings of the EGs and of the roadmap in scientific peer-reviewed journals.

List of websites: www.theseus-eu.org

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