An Integrated Big Data Framework Utilizing Stream Computing to Support Real-Time Clinical Decision-Making in the Field of Space Medicine

By

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Chair of Examining Committee	Dr. Manon Lemonde
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The above committee determined that the thesis is acceptable in form and content and that a satisfactory knowledge of the field covered by the thesis was demonstrated by the candidate during an oral examination. A signed copy of the Certificate of Approval is available from the School of Graduate and Postdoctoral Studies.

Abstract

Space exploration continues to be one of greatest endeavours of humankind. As manned space exploration extends to deep space, destinations such as the Moon and Mars, technological improvements and scientific advancements are in order, so as to enable safe prolonged human presence in space. Existing challenges of medical care delivery in space need to be addressed, while the meaningful and practical use of the acquired data will enable greater understanding of the impact of space travel on humans. This thesis proposes a novel wholistic approach to the human-technology ecosystem, enabling integration of the various components to address existing challenges of fragmented, retrospective discontinuous file-base data acquisition, in-batch data processing, extensive data down-sampling and an enormous amount of data loss. It presents an innovative solution to support proactive prognostics, diagnostics and health management, while providing the necessary tools to support action-taking and informed decision-making within the field of space medicine.

Keywords: *clinical decision support system; space medicine; big data; adaption-based assessment; human-technology systems;*

Author’s Declaration

I hereby declare that this thesis consists of original work of which I have authored. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Statement of Contributions

I hereby certify that I am the sole author for Chapters 1, 2, 3 and 4, which were written under the supervision of Dr. Carolyn McGregor. Chapters 1, 4, and 8 and have not been published or submitted for publication. I have used standard referencing practices to acknowledge ideas, research techniques, or other materials that belong to others. Furthermore, I hereby certify that I am the sole source of the creative works and/or inventive knowledge described in this thesis.

This thesis consists in part of ten manuscripts written for publication.

Part of the work described in Chapter 2 has been published as:

> **Prysyazhnyuk, A.**, and McGregor C., 2020. Space as an Extreme Environment or "Galactic Adventures – Exploring the limits of human mind and body, one planet at a time", Engineering and Medicine in Extreme Environments, Springer, 2020, in press.
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> **Prysyazhnyuk, A.**, and McGregor C., 2020. Physiological monitoring in space from first manned missions to the future on mars. 42nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society in conjunction with the 43rd Annual Conference of the Canadian Medical and Biological Engineering Society. Montreal, Quebec, July 20-24, 2020.

Part of the work described in Chapter 3 has been published as:

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Part of the work described in Chapter 5 has been published as:

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The research studies presented in Chapters 6 and 7 have been conducted at the Institute of Biomedical Problems of the Russian Academy of Sciences (IBMP RAS) in Moscow, Russia. I was responsible for the analysis of the collected data.

Part of the work described in Chapter 6 has been published as:

Orlov, O., McGregor, C., Baevsky, R., Chernikova, A., **Prysyazhnyuk, A.**, Rusanov, V., "Perspective Use of the Technologies for Big Data Analysis in Manned Space Flights on the International Space Station", 68th International Astronautical Congress (IAC 2017), Adelaide, Australia, 25-29 September 2017.

Prysyazhnyuk, A., McGregor, C., Baevsky, R., Chernikova, A., Luchitskaya, E., Rusanov, V., 2017, "Big Data Analytics for Enhanced Clinical Decision Support Systems during Spaceflight", IEEE 1st Life Science Conference, Sydney, Australia, 13-15 Dec, 4 pages.

Prysyazhnyuk, A., McGregor, C., 2018, "Spatio-Temporal Visualization of Big Data Analytics During Spaceflight", 69th International Astronautical Congress, Bremen, Germany, 1 to 5 October 2018, 10 pages.

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Prysyazhnyuk, A., McGregor, C., Bersenev, E.I., & Slonov, A.V. (2018). Investigation of Adaptation Mechanisms During Five-Day Dry Immersion Utilizing Big-Data Analytics. *2018 IEEE Life Sciences Conference (LSC)*, 247-250.

Prysyazhnyuk, A., McGregor, C., Chernikova, A., Rusanov, V., 2019, "A sliding window real-time processing approach for analysis of heart rate variability during spaceflight" 70th International Astronautical Congress, Washington, D.C, USA, 21-25 October 2019, 11 pages.

Dedication

I dedicate this thesis to my loving family, who have tirelessly supported and encouraged me through every step of the way. I am wholeheartedly grateful for all the sacrifices you have had to make to enable me to pursue my Masters. Your endless love, patience, encouragement and support have made this journey possible.

A special thank you to my mother for her love and support. You have instilled the tireless work ethic and determination in me. You have always encouraged me to set my goals high and be determined and persistent on my path to achieving them.

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"Education is for improving the lives of others and for leaving your community and world better than you found it." – Marian Wright Edelman

This journey started for me in 2015 when one of my former supervisors, Dr. Roman Baevsky introduced me to the captivating field of space medicine. I was incredibly fortunate to have learned about the foundations of space medicine from Dr. Roman Baevsky, who was the pioneer of space cardiology and has participated in the first animal and manned space flights. Dear Roman Markovich, your contribution to my education and career journey has been invaluable and I am so deeply honoured to have known you.

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Publications Related to this Thesis

1. Orlov, O., McGregor, C., Baevsky, R., Chernikova, A., **Prysyazhnyuk, A.**, Rusanov, V., "Perspective Use of the Technologies for Big Data Analysis in Manned Space Flights on the International Space Station", 68th International Astronautical Congress (IAC 2017), Adelaide, Australia, 25-29 September 2017.
2. Slonov, A. V., Baevsky, R. M., Rukavishnikov, I. ., Amirova, L. ., McGregor, C., **Zhmurchak, A.**, & Bersenev, E. Y. 2017, "Analysis of Body Posture Changing, Painfulness, Regulation of the Heart and Breath during night Sleep in Experiment with a 5-Day Dry Immersion", 9th International Symposium on Neurocardiology (NEUROCARD 2017). Belgrade, Serbia.
3. **Prysyazhnyuk, A.**, McGregor, C., Baevsky, R., Chernikova, A., Luchitskaya, E., Rusanov, V., 2017, "Big Data Analytics for Enhanced Clinical Decision Support Systems during Spaceflight", IEEE 1st Life Science Conference, Sydney, Australia, 13-15 Dec, 4 pages.
4. **Prysyazhnyuk, A**., McGregor, C., 2018, "Spatio-Temporal Visualization of Big Data Analytics During Spaceflight", 69th International Astronautical Congress, Bremen, Germany, 1 to 5 October 2018, 10 pages.
5. **Prysyazhnyuk, A.,** McGregor, C., Bersenev, E.I., & Slonov, A.V. (2018). Investigation of Adaptation Mechanisms During Five-Day Dry Immersion Utilizing Big-Data Analytics. *2018 IEEE Life Sciences Conference (LSC)*, 247-250.
6. **Prysyazhnyuk, A.**, McGregor, C., Chernikova, A., Rusanov, V., 2019, "A sliding window real-time processing approach for analysis of heart rate variability during spaceflight" 70th International Astronautical Congress, Washington, D.C, USA, 21-25 October 2019, 11 pages.
7. **Prysyazhnyuk, A.**, and McGregor C., 2020. Space as an Extreme Environment or "Galactic Adventures – Exploring the limits of human mind and body, one planet at a time", Engineering and Medicine in Extreme Environments, Springer, 2020, in press.
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9. **Prysyazhnyuk, A.**, and McGregor C., 2020. Physiological monitoring in space from first manned missions to the future on mars. 42nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society in conjunction with the 43rd Annual Conference of the Canadian Medical and Biological Engineering Society. Montreal, Quebec, July 20-24, 2020.
10. **Prysyazhnyuk, A.**, and McGregor C., 2020. A wholistic approach to assessment of adaptation and resilience during spaceflight, 71st International Astronautical Congress, CyberSpace Edition.

Table of Contents

List of Figures

List of Tables

Chapter 1 - Introduction

1.1 Overview

This thesis proposes a novel big data framework that utilizes a stream computing approach, the enormous potential value of which has remained in its infancy in the field of space medicine to-date. The concept of big data is used to describe data in terms of three V's, it's volume, velocity and variety. The proposed framework introduces a novel paradigm change that recognizes the dynamic nature of the data that can be effectively leveraged through stream computing, to create a harmonious human-technology system. It has great potential to support the development of an autonomous medical decision support system and contribute to action-taking and evidence-based clinical decision making within the field of space medicine.

The proposed framework extends the existing Artemis, big data analytics platform, by incorporating multi-source multi-variate data, including medical history, non-medical data, physiological data, clinical observations and personal assessments. It presents an integrated framework architecture to support multi-variate data throughout all of the stages of its lifecycle, beginning with the data collection, all the way through to data reporting and storage within the context of space medicine. The proposed framework identifies the necessary modifications and extensions to a conceptual Advanced Crew Medical System (ACMS) Space Medicine Decision Support System (SMDSS) architecture, as outlined by the Canadian Space Agency, and the Artemis platform. It supports real-time capability of health and wellness analytics, adaption-based analytics, activity and environmental analytics, all while ensuring continuity of data acquisition, processing and storage. It further recognizes that novel space medicine systems must be dynamic, provide real-time functionality and be able to integrate inputs from a variety of data sources, and as such, contribute to a valid, reliable and practical use of technologies to support successful manned space exploration. Limited research opportunities during space missions necessitate the use of ground-based analog environments, to test new technologies developed for space-use, and to investigate the various effects of spaceflight environments and their impact on human health and performance. As such, the instantiations of the proposed framework will be demonstrated within the context of two ground-based studies, namely the "Luna-2015" study conducted at the NEK isolation habitation facility in Moscow, Russia and the "Dry Immersion" study conducted in immersion baths at the Institute of Biomedical Problems, Moscow, Russia. Within the two ground-based studies various components of the spaceflight environment have been simulated and their effect on human health and well-being were assessed. A commercial grade "Cosmocard" Holter-style ECG monitoring device has been used for data acquisition, the device, currently in use for cosmonaut health monitoring within the Russian segment of the ISS. Electrocardiogram (ECG) recordings were scheduled and discontinuous. The near real-time functionality, characterized by a minimal latency between data acquisition and processing, of the proposed analytics will be demonstrated within the context of adaption-based analytics. The adaption-based analytics utilize Baevsky's functional health state algorithm, in order to assess how human body adapts to the various conditions of spaceflight environment [1, 2]. The functional health state algorithm utilizes an electrocardiogram signal recording from which the various features of heart rate variability are extracted, to assess adaption capacity of the human body. This research presents a re-modelled functional health state assessment algorithm that has been re-engineered as a MATLAB instance, to be integrated as a stream-graph, in the future, within the Online Analytics component of the proposed framework.

This thesis proposes a novel wholistic approach to the human-technology ecosystem, enabling integration of the various components to address existing challenges of fragmented, retrospective discontinuous file-base data acquisition, in-batch data processing, extensive data down-sampling and an enormous amount of data loss. It presents an innovative solution to support proactive prognostics, diagnostics and health management, while provide the necessary tools to support action-taking and informed decision-making within the field of space medicine.

1. 2 Background

Emerging scientific and technological advancements continue to re-define the landscape of space medicine, while extending the boundaries of human presence beyond Low-Earth Orbit (LEO) [3]. Provision of medical care in space remains an active area of knowledge discovery, fostering dynamic international collaborations [1]. Preservation of health and sustainability of human performance during space missions remains the paramount priority for space agencies, due to an increasing number of planned exploratory-class missions beyond LEO [3, 4]. Exploratory-class missions to the Moon, Mars and potentially asteroids present new risks, such as increased distance and duration, lack of or delays in communication, isolation, increased radiation exposure and higher probability of onset of medical contingencies [3]. Medical contingencies may present as psychological and/or physiological implications that can have significant impact on astronaut's health and performance. Compromised behavioural and health performance of an astronaut has a profound impact on the outcome of the mission and threaten safety of the entire crew.

The spaceflight environment inflicts a significant level of stress on the human body, approbating the capability of adaptation mechanisms to withstand physiological and psychological changes, while preserving homeostasis and maintaining a healthy level of performance [5]. Deconditioning of human body systems has been extensively studied in terrestrial simulation environments and during space missions of various durations. The underlying etiology of the most commonly reported medical contingencies associated with musculoskeletal and cardiovascular deconditioning, neurosensory disturbances, immunological and metabolic changes is well understood, while early diagnosis and timely intervention necessitate further investigation [6].

Increasing scientific evidence suggests that deconditioning of body systems is attributed to the processes of maladaptation, closely associated with changes in the dynamics of heart rate variability parameters [1]. Heart rate variability patterns and behaviours have been extensively studied in prior research and strong scientific evidence suggests that it is an effective indicator of the overall performance of the human body [1, 2]. As a result, the functional health state algorithm, also known as the wellness algorithm, has been developed on the principles of stepwise discriminative heart rate variability analysis, used to assess the level of wellness of Russian cosmonauts on the International Space Station to-date [1, 2, 7].

Space, by its nature, is a unique extreme environment, in which provision of medical care is greatly constrained by physical space, availability of resources, limited on-board medical expertise and intermittent communication with terrestrial mission control centres, all of which will become even more aggravated as humans embark on exploratory-class missions beyond LEO [1, 3]. Noteworthy, the Crew Medical Officer (CMO) is the ultimate source of on-board medical expertise. The medical expertise of the CMO exceeds that of an ordinary astronaut, by an additional 80 hours of general medical training [8]. CMO is trained to handle most commonly reported medical emergencies, while anything outside the scope of the CMO's expertise relies on telehealth support from terrestrial mission control centres (MCC) [3, 8]. MCC provide extensive medical support via telemetry during mitigation of medical incidents and emergencies that occur aboard the spacecraft or during extra-vehicular activities. It is important to note that under some life-threatening circumstances missions can be aborted and the crew can safely return to Earth. However, the operational requirements and logistics of unplanned return to Earth from exploration-class missions would be extremely complex, if at all possible. As such, ongoing efforts are made to improve the CMO's clinical decision capacity aboard the spacecraft, which is of utmost significance for missions beyond LEO, where communication with terrestrial MCC's will be delayed and limited, if at all possible. However, existing physiological monitoring practices on the ISS are only able to support scheduled, discontinuous data acquisition and fragmented retrospective analytics, imposing a significant risk on timely intervention and preservation of astronaut's health [7].

Health informatics, big data analytics in particular, is a promising field of science that is capable of addressing the challenges associated with space travel beyond LEO, serving as a toolkit for the design of new space medicine clinical decision support systems (SMDSS) [9]. It has the capacity to improve onboard physiological monitoring, provide essential decision-making tools to the

CMO and inform the development of autonomous, comprehensive and reliable SMDSS, all of which will contribute to efficient management of medical contingencies during space travel.

The clinical decision support system (CDSS) can be described as an information technology system that offers person-specific information in such a way as to provide situation-specific information represented in a clinical context of interest. More specifically, CDSS can be described in term of five main functionalities, "*provide the right information, to the right person, in the right format, through the right channel, at the right point in workflow to improve health and health care decisions and outcomes*" [10]. A subset of CDSS is Space Medicine Decision Support which is unique because of the nature of spaceflight environments, characterized by physical space constraints, communication delays and strict guidelines governing the availability and usability of diagnostic modalities in-flight. Space medicine decision support system architectures can be described in terms of four main components, including data acquisition, data transmission, analytics and results presentation, each of which will be briefly described in the sections to follows.

Design and implementation of new space biomedical monitoring modalities and technologies has been challenging, due to strict space exploration specifications, outlined by Martin *et al.*, as "*lightweight, miniaturized, portable, wireless, reusable, ruggedized, non- or minimally-invasive, user-friendly, scalable and flexible in their use*" [3]. Other factors that have to be taken into account in the design and selection of biomedical monitoring modalities include battery life, data acquisition, transfer and storage processes and minimal interference with astronaut's day-to-day operations [11]. The necessary steps are then taken to ensure the integrity of the acquired physiological signal is maintained, while interferences and noise levels are kept at a minimum [11]. Once the device has demonstrated compliance with space exploration requirements it is subjected to extensive terrestrial testing to validate its effectiveness and compliance with space exploration protocols, while demonstrating its day-to-day operability. Data transmission to terrestrial Mission Control Centres mostly relies on two-way telemetry downlinks, supporting intermediate and partitioned data transmission [12]. The complete datasets are transferred via a portable memory device, such as the Flash drive, upon return to Earth. The usability and applicability of such communication would be greatly impacted by missions of longer distance and duration. Exploration-class missions are expected to have significant communication delays, which will render existing medical decision support systems impractical, should an emergency situation arise. Highlighting the need for development of an autonomous medical decision support system that would have the capacity to provide real-time feedback.

Space Medicine Decision Support has conventionally been limited to retrospective functionality, due to the inaccessibility of the data during the mission attributed to the lack of appropriate onboard information systems. Retrospective data analyses have also been subjected to the use of a complex of software applications, contributing to data smoothing and averaging that continues to contribute to a significant amount of data loss [1, 13].

Over the years, various data visualization techniques have been explored to enhance display and interpretation of the acquired results. More specifically, physiological data has been visualized in accordance with the desired data type and format, utilizing one of the four main methods, such as the metaphoric, graph-based, object-based and/or tabular displays [7]. All of the aforementioned methods have failed to support interactive functionality, focusing on short-term static visualization of the data. As such, trajectory of changes, especially during longitudinal physiological monitoring has been challenging, if at all possible [7, 14].

Emerging technology for data acquisition, transmission and analysis presents an enormous potential for clinical discovery and continuous physiological monitoring, empowering timely physiological data acquisition, real-time analytics, efficient management of medical contingencies and preservation of the crew's health and performance [7, 14]. It has the potential to overcome existing challenges associated with data accessibility, data loss and impracticality of existing on-board medical systems due to retrospective data analytics methods and techniques. As such, the proposed framework offers insight into real-time functionality of the human body in the absence and presence of gravitational forces, which has great applicability on Earth, in remote and extreme terrestrial environments, as well as aimed at individuals living and/or working under conditions of chronic stress.

1.3 Research Motivations

The challenge of provision of medical care in space is attributed to the inability of crew medical officers to leverage complete physiological data to enable early detection monitoring and inform the management of medical contingencies during space mission. Existing methods are confined by limited resources, scheduled and discontinuous data acquisition and retrospective, fragmented data analytics, all of which contribute to significant data loss and delayed detection of onset of deleterious effects imposed by conditions of spaceflight [1, 15]. The latency in development of harmonious human-technology systems has rendered most of the acquired data impractical, strongly emphasizing the need for a paradigm change.

It should be noted that the data acquisition component of the proposed framework has been limited by existing in-flight biomedical monitoring modalities approved for use onboard the spacecraft. Existing in-flight biomedical monitoring devices have been limited to record and store Holter-style monitoring devices, such as “Cosmocard”. The introduction of novel wearable smart garments, such as the Bio-Monitor, also known as Astroskin, remain at the early stages of implementation and at the time of terrestrial simulation studies were not yet approved for use aboard the International Space Station [16].

The existing Crew Health Care System (CHeCS) on the ISS is fragmented, utilizing a reactive health management approach and very limited prognostic and diagnostic capacity. It is further challenged by the retrospective discontinuous file-base data acquisition, in-batch data processing, extensive data down-sampling, an enormous amount of data loss and lack of real-time feedback mechanisms. As such, imposing significant limitations on the ability to support health, wellness and adaption-based analytics.

Adaptation is a dynamic entity, which actively responds to changes in external and internal stimuli [13]. Adaptation mechanisms foster interactive functionality of body systems in an attempt to (re)establish an equilibrium, also known as, homeostasis, and preserve health. Existing methods rely on fragmented data acquisition, which is then stored and retrospectively analyzed. Retrospective data analysis methods are applied upon return to Earth, to derive average hourly readings, which are later averaged to produce a single reading for the entire day that is used to establish astronaut's functional health level. However, critical dynamics in heart rate variability parameters are often overlooked, which may be the basis of early onset of maladaptation, preventing timely introduction of the necessary countermeasures [1, 13]. As a result, this necessitates a more comprehensive approach that would enable real-time data acquisition and processing to allow for timely interventions during the same spaceflight, minimizing the risk of illness and contributing to preservation of health and occupational performance of the entire crew. As such, the proposed framework presents potential to support scheduled and ad-hoc continuous and discontinuous data acquisition. It has the capacity to support multi-variate, multi-source data integration to enhance understanding of observed clinically-significant physiological patterns. The proposed framework can support multi-modal data analytics, including real-time, near real-time or retrospective analyses of the acquired data, which can be fully customizable, so as to meet the mission-specific objectives. It further demonstrates the capacity to generate results in a form of interactive dashboards, contributing to practicality and usability of the acquired data during the same mission. Overall, it presents potential to support timely, effective and proactive health management, while enhancing prognostic and diagnostic capacity aboard the spacecraft.

1.4 Research Aims and Objectives

The primary aim of this research is to propose a wholistic, integrated big data framework, utilizing a data lifecycle approach, so as to develop an innovative solution to support proactive prognostics, diagnostics and health management. This will provide the necessary tools to support action-taking and informed decision-making within the field of space medicine. The proposed framework aims to address existing challenges of fragmented and discontinuous data acquisition, transmission and processing. In addition, the aim of this research is to support real-time analytics to further enhance medical capacity and autonomy aboard the spacecraft.

This thesis proposes the following four hypotheses:

1. *That a big data framework can be designed to support the development of space medicine clinical decision support systems to assess astronaut's health and adaption to conditions of spaceflight in-real time.*
2. *That the proposed framework can be instantiated through the extension of an existing big data analytics platform.*
3. *That the application of the framework and instantiation can be demonstrated with adaption-based analytics, namely the functional health state assessment, in near real-time and real-time environments.*
4. *That an alternative data processing approach, namely the sliding-window analysis can be instantiated to enhance the adaptation-based analytics.*

1.5 Research Contributions

The knowledge presented within this thesis includes contributions to the fields of health informatics, computer science and space medicine, more specifically:

Health Informatics:

- Design of a wholistic, integrated big data framework demonstrates potential to support the development of space medicine clinical decision support system. The proposed framework extends the Artemis, big data platform to support acquisition and processing of multi-source, multi-variate data. More specifically, the proposed framework has the capacity to acquire, integrate and process data streams and file-based packets of data.

Computer Science:

- The potential of the proposed framework to support real-time online health analytics is demonstrated through instantiation of the functional health state algorithm as a MATLAB instance, to enable near real-time and real-time functionality of prior retrospective file-based in-batch data processing method.

Space Medicine:

- The potential of the proposed framework to support the development of an autonomous space medicine clinical decision support system is demonstrated through application and instantiation of the framework within the context of two ethically approved ground-based clinical research studies. The capability of the proposed framework to support multi-modal adaption-based assessment demonstrates potential to support early detection monitoring and contribute to improved health outcomes in-flight.

The application of the contributions is demonstrated within the context of two terrestrial analog studies "Luna-2015" and "Dry Immersion 2016" performed at the NEK ground-based analogue facility at the Institute of Biomedical Problems of the Russian Academy of Sciences in Moscow, Russia.

1.6 Research Methodology

The constructive research methodology was used as a framework for the research design presented in this thesis. The constructive research methodology was first introduced in accounting and management, but later demonstrated potential to inform the design and development of practically relevant solutions in various fields of science. The idea of constructive research is based on the principle of identifying a practically relevant problem that has both a theoretical and practical research potential [17]. Core elements of successful constructive research study design include practical relevance, practical functioning, theory connection and theoretical contribution [18]. This research methodology was strategically chosen to bridge the gap in operational requirements of medical care delivery in space, while enhancing the prognostic and diagnostic medical capacity aboard the spacecraft. Table 1-1 details the phases of constructive research methodology that were undertaken in the design and development of the proposed solution for real-time adaption assessment in spaceflight environment.

Table 1-1. Constructive research methodology

Phase	Constructive Research	Spaceflight Adaption Assessment Constructive Research
1	Find a practically relevant problem that also has a research potential.	Can a space medicine clinical decision support system be designed using big data analytics to assess astronaut's adaptation to conditions of spaceflight in-real time?
2	Obtain a general and comprehensive understanding of the topic.	A comprehensive review of various aspects of human space travel has been completed to provide an overview of environmental, medical and bioethical challenges of manned space exploration. Technological considerations of biomedical monitoring modalities and their operational limitations associated with space flight environment have been reviewed. Future medical system considerations have been assessed on the basis of existing terrestrial methods and techniques, the enormous potential of which has not been leveraged by the field of space medicine to-date. More specifically, the concepts of big data, stream computing and data life cycle approaches were explored. The limitations of existing approaches were used to inform the design of the future space medicine clinical decision support system. Theoretical foundations of the various stressors and their impact on human health and performance have been reviewed in order to assess the concept of health and its norm as it pertains to space flight environment. The method of functional health state assessment has been identified as a scientifically valid and extensively approbated technique to support adaption-based assessment during spaceflight. The functional health state assessment has demonstrated capacity to detect transitional states, as the human body transitions from the state of physiological norm towards maladaptive state or development of pathology.
3	Innovate (i.e., construct a solution idea)	This research presents an innovative solution for real-time assessment of adaption to conditions of spaceflight, utilizing a big data artificial intelligence platform. This research presents a framework to support seamless real-time data acquisition, transmission and processing with the ability to generate results and provide feedback in-flight, as opposed to existing retrospective methods and techniques. It further demonstrates the capability

		inform clinical decision making aboard the spacecraft to preserve health and well-being of the crew.
4	Demonstrate feasibility of the solution.	The feasibility of the proposed methodology is demonstrated within the context of two ground-based analog studies, “Luna 2015” and “Dry Immersion 2016” the ethical approval for which has been granted by the Ontario Tech University Research Ethics Board under REB# 15-047 Integration of Russian Cosmonaut Monitoring with Artemis and Artemis Cloud.
5	Show the theoretical connections and the practical research contribution of the solution concept.	The practicality and usability of the proposed framework is demonstrated through its instantiation within an extended Artemis platform, within the context of two ground-based case studies, Luna-2015 and Dry Immersion 2016. The instantiation of the proposed framework addresses existing challenges of enormous data loss and impracticality of existing medical monitoring systems aboard the spacecraft.
6	Examine generalizability of the solution.	The proposed research methodology and instantiated platform demonstrate great potential for both space and terrestrial application. It has great potential to support adaption assessment in various extreme environments, including high altitude pilots, divers, first responders, tactical operators and many other ground-based occupations exposed to hazardous environments and highly stressful occupational conditions.

1.7 Thesis Structure:

This thesis is structured as follows. Chapter 1 serves as an introduction into spaceflight environment and some of the challenges of medical care delivery in space. It highlights existing information technology challenges and limitations, and presents an overview of an innovative approaches presented in this thesis. Chapter 2 provides an in-depth review of space as an extreme environment, its hazards and implications on human health and occupational performance. It presents an overview of past and present biomedical challenges, as well as considerations for future medical care systems tailored to unique conditions of spaceflight environment. Chapter 3 presents information systems theory, identifying existing limitations of systems architecture and describing an artificial intelligence big data analytics platform, Artemis, used within this thesis. Chapter 4 details the theoretical background of functional health state algorithm. Chapter 5 presents the proposed framework. Chapters 6 and 7 demonstrate the application of the contributions presented in this thesis within ground-based analog studies, "Luna 2015" and "Dry Immersion 2016" respectively. Chapter 8 concludes this thesis by outlining limitations of presented research work and identifying future research directions and considerations.

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Chapter 2 - Literature Review

"***…no risk in the long run, ever prevented the humankind from trying to satisfy his unquenchable thirst for knowledge. Therefore, as witnessed by history, neither ethical boundary nor health risks will likely impede the man's race to an endless progress***" – Bizzari *et al.* [1].

Over the past century revolutionary advancements have been made within the field of science and technology enabling the human race to explore other habitats within the solar system and marking the beginning of the era of human space exploration. Human curiosity has been fueled by many "firsts" of the 19th century, including the first manned spaceflight, landing on the Moon, first extravehicular activity, in-orbit crew transfer and the launch of the first space station [2]. There were many failures and successes that have led to a significant number of breakthroughs, resulting in the establishment of the International Space Station (ISS) and international space programs.

Space exploration sparked innovation within the fields of science, technology, engineering and mathematics (STEM) on Earth and in outer space. Manned space exploration provided a deeper understanding of the concept of health and how the human body responds to various environmental stimuli. It has verified human capacity to live and work in outer space habitats for extended periods of time, while preserving optimal health and occupational performance [3]. Advancements in the field of space medicine have led to the betterment of health outcomes both on Earth and in outer space.

This literature review chapter discusses the various implications of human space travel. The literature review begins with an introduction to space as an extreme environment, identifying environmental risks that astronauts are exposed to during spaceflight. Following is the review of medical aspects of manned space exploration, including the various physiological and psychological effects the human body endures in, highlighting the sex- and gender-based differences in adaptation to conditions of spaceflight. Subsequently, technological considerations of medical care in space are presented, with the focus on past and present biomedical challenges and future medical system considerations. Also, this literature review briefly considers the bioethical challenges of manned space exploration and the process of “acceptable” health risks assessment and mitigation.

Manned space exploration occurs in a tightly embedded environment, where the interplay of the various environmental factors has a profound effect on human health and the methods utilized for its assessment. The design of a clinical decision support system necessitates understanding of the risks and challenges endured during manned space travel as whole, rather than a sum of its individual components. Integration of the environmental and health challenges, supplemented with bioethical considerations and technological limitations provide an in-depth understanding of the needs that the future clinical decision support system will have to address in a meaningful and practical way. As a result, this literature review provided motivation for the first research hypothesis.

2.1 Methodology

A PubMed digital library has been utilized to perform a systematic literature search on human health and its aspects within the spaceflight environment. The first search used the keywords “space mission medical care systems” and the second search used the terms “human health and performance during spaceflight”. Search results were not subjected to any date range constrains, to ensure that an evolution of medical care in space can be assessed. The first search returned twenty-seven articles. Abstract review resulted in removal of twenty-two articles, leaving five articles for inclusion in this review. The second search found three hundred and ten articles, which were filtered to include only human research, resulting in removal of one hundred seventy-four papers. Abstract review was completed on the remaining one hundred and thirty-six articles, of which eighty-two were removed and fifty-four were included in this review. A total of fifty-nine full-text articles were included in this literature review. The analyzed literature included a wide range of topics dealing with human health during space travel. The topics ranged from specifics of spaceflight environment, such as environmental, physiological and psychological effects on the human body. The bioethical challenges and considerations of space missions and definition of assessment of "acceptable" human health risks endured during space travel. Review of past and present biomedical challenges pertaining to health monitoring in space, their limitations and considerations for future health care during deep space exploration. Figure 2-1 schematically represents the literature review method that was undertaken.

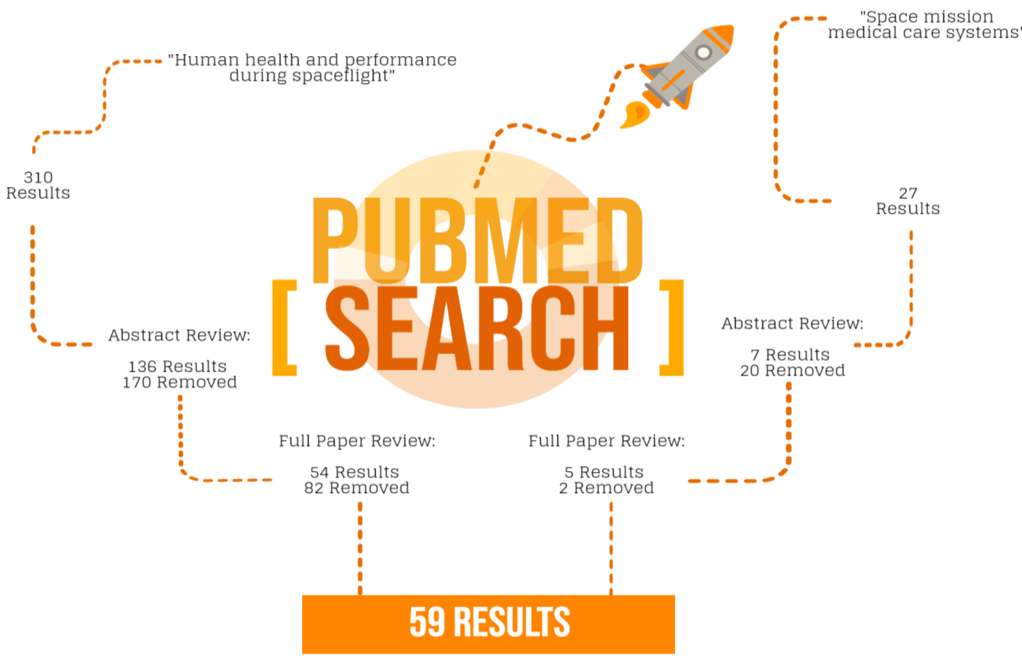

Figure 2-1. Literature Review Method

2.2 Space as an Extreme Environment

Space has always sounded futuristic, captivating the human mind about the endless possibilities that lie beyond the low Earth orbit. It has always sparked the curiosity of the human kind and motivated exploration of the solar system, but most importantly the exploration of the limits and possibilities of the human body and mind.

Hodkinson *et al.,* define spaceflight as the "*journey that takes place more than 100km above sea level*", the boundary also known as the Karman line. The Karman line has been internationally recognized as the margin above which the conventional aircraft is not effective due to insufficiently dense atmosphere [4]. In addition, the Karman line lies on the margin of Earth's protective magnetic field, beyond which the human body is exposed to harmful radiation, solar flares, space debris and many other environmental hazards [4].

The human spaceflight can be broadly classified into three categories, on the basis of travel distance, such as suborbital, low Earth orbit (LEO) and exploration class missions (i.e. Moon and Mars) [4]. Suborbital flights are short, lasting only a few hours, with minimal exposure to conditions of weightlessness that lasts only a few minutes and briefly affects the cardiorespiratory system. Low Earth Orbit (LEO) has been the main designation of human space exploration to-date, at an in-orbit altitude of 200-400km [4]. The implications of LEO manned exploration will be reviewed in great detail in sections to follow, as they form the foundations of the risks and challenges of human health and performance in space. Exploration-class missions are long distance, beyond low Earth orbit, to destinations such as Moon and Mars [4]. These missions are of much longer duration due to their remoteness from Earth and present vastly different risks and challenges, as opposed to majority of human manned space exploration experience known to-date.

The main themes of manned spaceflight implications identified in the literature review are summarized in Figure 2-2 and reviewed in detail in sections to follow. There are four main categories that can be defined, including environmental, medical, bioethical and technological implications of spaceflight environment. The environmental features of spaceflight environment include radiation, solar flares, weightlessness, isolation, confinement, cabin toxicology and closed-loop support systems. The medical implications include psychological and physiological manifestations of space-flight induced responses, supplemented with sex- and gender-based specifics of adaptation to conditions of the spaceflight environment. Technological considerations review the physical constraints imposed on the design and selection of appropriate onboard equipment. Bioethical considerations review the ethical principles governing the development of appropriate guidelines and policies to support manned space exploration.

The Low Earth Orbit is a unique habitat that has been the designation of choice for manned space exploration for over half a century. LEO houses the International Space Station that has been the first permanently inhabited human laboratory in outer space [2]. The hazards associated with the spaceflight environment encountered in LEO and beyond can be broadly classified into five categories, such as radiation exposure, isolation, remoteness from Earth, microgravity, and hostile closed-loop spacecraft environment.

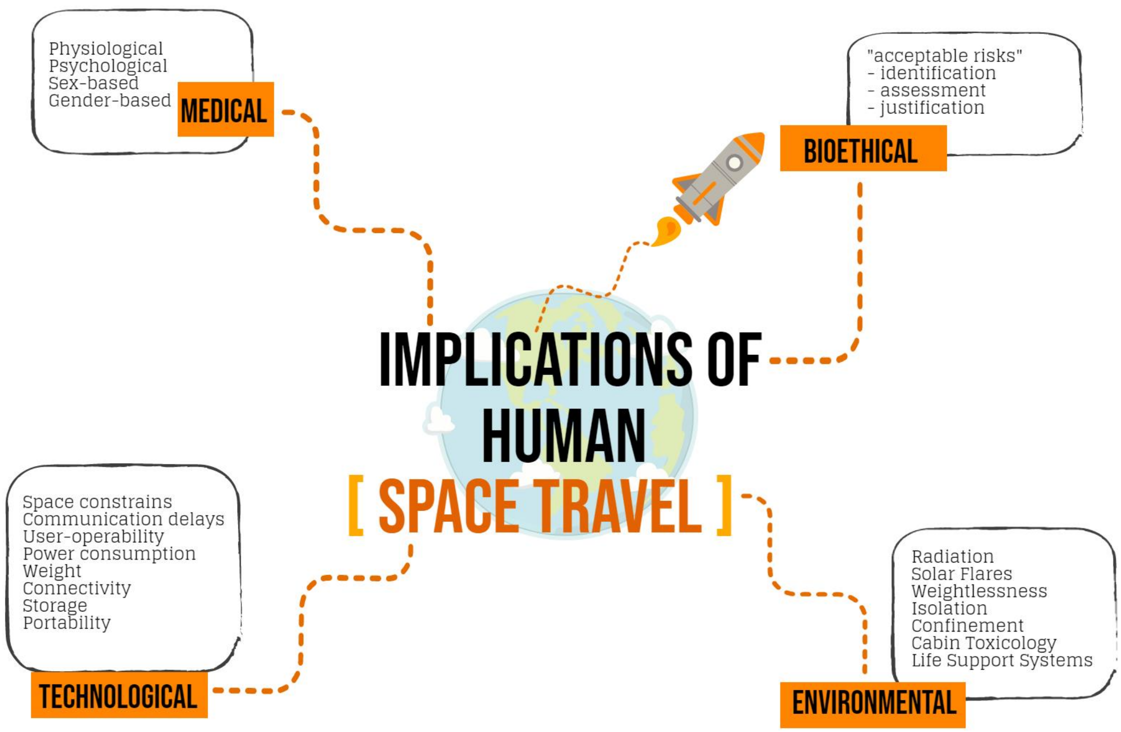

Figure 2-2. Summary of manned spaceflight implications.

2.2.1 Radiation

Space radiation is one of the main hazards that astronauts are exposed to. Space radiation can be described in terms of particle types, their energies, dose and quantity [5]. There are three main sources of radiation within the Low Earth Orbit, which are the low-energy protons and electrons found within the solar winds; Galactic Cosmic Rays (GCR) that consist of heavy-charged particles, and energetic photons emitted by the Sun in instances known as the Solar Particle Events (SPE) [4, 6]. The protective Earth's magnetic field and shielding within the International Space Station attenuates a significant amount of harmful radiation, enabling safe prolonged human presence within the low-Earth Orbit [6]. However, the exploration-class missions to deep space present significant human health risks associated with radiation exposure, which are expected to exceed the maximum acceptable radiation exposure thresholds [1, 5]. The prodromal effects of exposure to GCRs and SPEs can clinically manifest as fatigue, malaise, nausea and vomiting [6]. In addition, collisions of cosmic rays with spacecraft structures can produce neutrons and high energy charged particles that have detrimental effects on critical organ systems and cellular structure. Deep space exploration imposes significant risks of developing various radiation-induced pathological states, such as carcinogenesis, damage of the central nervous system, tissue degeneration and acute radiation disease [1]. As such, radiation exposure significantly contributes to increased morbidity and mortality rates [5]. Mitigation of radiation-educed effects necessitates development of strong and reliable radiation shields, especially as human space exploration extends to deep space, outside the Earth's protective magnetic field.

2.2.2 Isolation

Isolation and confinement are important features of spaceflight environment that profoundly influence behavioural and health performance, especially during long duration space missions [7]. Prolonged isolation gives rise to pronounced inter-individual differences, mood disturbances, interpersonal conflicts that arise within the crew, and between the crew members and the ground-based Mission Control Centre [8, 9]. It also contributes to increased level of experienced stress, leading to sleep disturbances, deficits in behavioural alertness, all of which result in overall physical exhaustion and contribute to onset of depressive emotional states [8, 9]. As such, isolation and confinement play a substantial role in team dynamics, physical and mental health, as well as occupational performance.

2.2.3 Remoteness

The distance from Earth is also an important multifaceted hazard, having biomedical, technological and operational implications, to name a few. Biomedical challenges can manifest as various physiological and psychological maladies known to man. Operational requirements and logistics of long-duration long-distance space missions place a significant psychological burden on the crew, greatly limiting ground-based support, should an emergency situation arise [1, 10]. In addition, increased distance from Earth introduces significant communication delays, emphasizing the need for enhanced medical and technical expertise aboard the spaceship [4].

2.2.4 Microgravity

Microgravity, also known as weightlessness, is associated with the environment where gravitational loading, experienced on Earth, is eliminated, resulting in onset of an array of physiological changes to help the body adapt to conditions of spaceflight [4]. Ongoing efforts are being made to design and develop effective countermeasure protocols so as to attenuate the deleterious effects of spaceflight environment. Clinical manifestation of physiological and psychological effects associated with conditions of microgravity will be described in detail in sections to follow.

2.2.5 Closed-loop Environment

Closed-loop environments within a spacecraft constitute an important environmental system that ensures habitability, safety and comfort of the crew during space exploration. The closed-loop system functions on the premise of a feedback mechanism, where the system's output regulates the amplitude of the input signal. Some examples of closed-loop systems aboard the spacecraft include environmental control, such as temperature, pressure, humidity, light levels, water quality, etc [4]. The nature of a closed-loop environmental system contributes to cabin toxicology and risk of microbial contamination, which in turn compromise the human immune system and as such, have direct health implications for the crew [11-13].

In summary, space is a hostile environment, having a profound effect on all organ systems, mental health, behavioural and occupational performance, detailed review of which is presented in sections to follow.

2.3 Implications of Spaceflight Environment on Human Health

2.3.1 Physiological Implications

Manned space exploration has demonstrated that human body is an undiscovered reservoir of limits and possibilities. It has a unique ability to adapt to challenging and potentially lethal environments [4]. While the human body and its functional processes heavily depend on Earth's gravitational forces for their performance, it has a unique ability to adapt to conditions of weightlessness, while preserve optimal health and performance. Next sections will review physiological spaceflight-induced responses according to the organ systems they affect, more specifically, the musculoskeletal, cardiovascular, immune and neurosensory systems, as well as the respective metabolic changes. It should be noted that clinical manifestation of spaceflight-induced responses is subjected to inter-individual differences and duration of the mission.

Musculoskeletal System

Musculoskeletal system is directly influenced by the lack of gravitational loading under conditions of spaceflight environment. Elimination of gravitational forces results in fluid redistribution and unloading, especially of lower limbs, resulting in a significant loss of muscle and bone mass, characterized by a dramatic decline in physical fitness and reduction in aerobic capacity [14-18]. Decrease in muscle mass, calf muscles and quadriceps in particular, is also supplemented with structural changes, characterized by the transition from slow-to-fast fibre types and decrease of tendon stiffness [16, 19]. As a result, substantial muscle atrophy is observed in postural muscles that are composed of high proportion of slow fibres [20]. Other factors contributing to orthostatic intolerance and muscle atrophy include a decrease in neural drive, astronaut's age, pre-flight level of fitness, nutritional status, and use of countermeasures in-flight [16, 20].

Spaceflight environment has a direct influence on nutritional status, resulting in lower dietary acid load that impacts the efficiency of bone resorption, further contributing to decrements in bone mineral density, imposing a greater fracture risk and onset of osteoporosis [21-23]. In addition, decrease in bone resorption leads to an increase of urinary calcium, further contributing to an increased risk of renal stone formation [22-24]. However, the severity of experienced musculoskeletal deconditioning varies depending on inter-individual differences and application of in-flight countermeasure protocols [25].

Cardiovascular System

Cardiovascular deconditioning manifests as a combination of physiological changes induced by elimination of gravitational forces and redistribution of bodily fluids towards the cranial area [4]. Rapid fluid redistribution results in facial oedema, accompanied by space motion sickness, characterized by nausea, pallor and vomiting [4]. The resulting fluid shift is perceived by the body as an increase in total circulating blood volume, triggering a cascade of compensatory reactions, also known as the process of cardiovascular autonomic adaptation [26]. As a result, spaceflight-induced cardiovascular deconditioning has been characterized by both structural and functional changes. Structural changes of the heart include decrease in size of the ventricles, decrease in the wall thickness of left ventricle and increase of cardiac sphericity [26, 27]. The functional changes of the heart are attributed to intravascular hypovolemia, which results from an increase of capillary permeability induced by the fluid redistribution [4, 28]. Increased capillary permeability contributes to the shift of intravascular fluids into extracellular spaces, resulting in reduction of plasma volume, which contributes to a decreased aerobic capacity [4, 16, 28]. Other functional changes pertaining to cardiac performance during spaceflight, include altered ventricular repolarization, characterized by a prolonged QT interval on the ECG recording, reduced contractile function, reduced sensitivity of baroreceptors, decreased stroke volume, altered blood flow and reduced vascular tone that further contribute to increased orthostatic intolerance [26, 29, 30, 31]. In addition, a decrease of the heart rate was reported during the early days of spaceflight, with characteristic tendency to increase with the progression of spaceflight duration.

Cardiovascular risks associated with spaceflight environment, include increased risk of cardiac arrhythmias, exacerbation of cardiac disease, autonomic/vascular dysfunction, orthostatic intolerance, reduced aerobic capacity and structural changes of the heart [27].

Immune System

Human health and performance in microgravity is directly affected by the immune system function. Several studies have identified immune system dysregulation associated with the nature of spacecraft environment, characterized by radiation exposure, increased risk of microbial contamination and cabin toxicology, as a by-product of closed-loop environmental systems [11]. All of which are supplemented by increased levels of experienced physiological and psychological stress, altered nutrition and desynchronized circadian rhythms [11]. Alterations in immune system function manifest on cellular level, with characteristic increase of granulocytes, decrease of lymphocytes, elevation of B cells and decrease of natural killer cells [4, 32]. Moreover, altered expression of key surface receptors and signal molecules was observed, the underlying mechanisms of which require further investigation. It has also been reported that astronauts on long-duration space missions have experienced a gradual increase in core body temperature by 1^0C, yet the effects of weightlessness on thermoregulation are still not understood [33].

Neurosensory System

Neurosensory disturbances have been well-documented in missions of varying durations, while their clinical manifestation significantly varied in onset, duration and severity of experienced symptoms. As such, spaceflight-influenced neurosensory disturbances will be reviewed in accordance with the sensory systems they affect. More specifically, visual, acoustic, olfactory, gustatory and peripheral sensory systems, supplemented with some general sensory experiences [34].

Space adaptation syndrome is among the first and most profound physiological effects experienced instantly upon exposure to spaceflight environment [4]. It affects between 60-80% of astronauts, with clinical manifestation of nausea, pallor and vomiting resulting from redistribution of bodily fluids in the cranial, upper body direction [4]. This neurosensory disturbance is short-term and its severity declines over a couple of days into the spaceflight.

Visual sensory system is impacted by numerous habitability specifics of the ISS, including illumination, lack of circadian variations, monotony, unusual visual perception of objects in weightlessness and lack of spatial cues [34]. Clinical manifestation of spaceflight-induced visual deprivation has been characterized by sleep disruptions [35], reduced sensorimotor and somatosensory control [36-38], impaired functional mobility [36], altered cortical activation patterns, reduced eye-head coordination [39], and structural ophthalmic changes [40].

Reduced sensorimotor control is associated with changes in posture control, locomotion and manual dexterity [36, 41, 42]. A decline in balance and mobility have been associated with neuroplastic changes that occur as a result of reduced sensory inputs, leading to altered brain region activation [36, 37, 43-45]. Modification in neural networks further contribute to a reduced spatial orientation and cognition, sensorimotor and somatosensory control, which impact higher cognitive functions, collectively planning, coordination and execution of voluntary movements [36, 37]. Moreover, spatial disorientation has been closely associated with altered cognitive performance, taking a toll on critical decision making, memory and other cognitive tasks [46]. Altered sensorimotor control also impacts eye-head coordination, which has been characterized by prolonged reaction and reduced vigilance during target acquisition, which has important implications during landing of the spacecraft, as astronauts are returning to Earth [39]. As such, various techniques have been explored to artificially upregulate vestibular inputs and attenuate the deleterious sensorimotor effects experienced during spaceflight [43, 44, 47].

Some astronauts have experienced a phenomenon, known as the astronaut ophthalmic syndrome. Astronaut ophthalmic syndrome can be characterized by ophthalmic changes in choroidal folds, optic disc edema, cotton-wool spots, globe-flattening and refraction changes

[40]. The aforementioned ophthalmic changes can cause visual disturbances and impact optic nerve or eye functionality [40].

Acoustic sensory system is influenced by the background equipment noise levels, restricted habitation modules and lack of privacy [34]. As a result, astronauts have consistently reported sleep issues, characterized by poor quality and decreased duration, accounting to a total of 6 hours in daily average sleep time [35, 38, 48]. The main factors contributing to decreased amount and quality of sleep are the cabin environment, work-rest schedule, circadian rhythm disruption and mental/physical discomfort [34]. Chronic sleep deprivation had numerous performance and health manifestations, including decreased alertness, cognition and operational performance, supplemented with emotional changes and overall decline of physical health [35].

Olfactory system deprivation is attributed to lack of familiar odours, waste removal processes and their respective scents, as well as specifics and limitations associated with personal hygiene aboard the spacecraft [34].

Gustatory system deprivation is attributed to a limited variety, type and quality of the available foods for consumption aboard the spacecraft [34]. Although, space food is specifically designed to support adequate nutritional requirements and to contribute to improved vitamin and mineral absorption by the body [49].

The spaceflight environment significantly impacts the peripheral sensory system through elimination of gravitational forces, acceleration, vibrations, temperature and humidity variations, poor air ventilation, monotony of tactile stimulations, and multi-system sensory deprivations [34, 38]. As such, numerous countermeasures continue to be developed to counter the deleterious effects of neurosensory disturbances and ease astronaut’s re-adaptation upon return to Earth.

Metabolic Changes

Spaceflight-induced fluid redistribution is perceived by the body as an increase in total circulating blood volume, which induces a cascade of compensatory metabolic changes [4, 26]. The induced metabolic changes contribute to reduction of plasma and extracellular fluid volume, altered vitamin, mineral and electrolyte balance [4]. The metabolic changes do not manifest as exclusive clinical symptoms, but rather contribute to multi-system deconditioning experienced during spaceflight.

2.3.2 Psychological Implications

Spaceflight environment in its nature is a hostile environment, prolonged exposure to which triggers numerous psychological and behavioural changes. Psychological implications of spaceflight environment are closely associated with physiological well-being and occupational performance, as such, some psychological aspects have been eluded to in prior sections. The most commonly reported psychological changes include mood disturbances [50], manifested as varying degrees of anxiousness [51], depression [8], anger and interpersonal conflictuality [34]. Further enhanced by decreased cohesiveness of the crew [34], altered team dynamics [9] and declining harmony of the crew [34]. As such, numerous countermeasures are being developed to foster a positive team environment and ensure a healthy work-life balance is maintained, contributing to an improved physical health and occupational performance [4, 34].

2.4 Gender and Sex-based Differences of Adaptation to Conditions of Spaceflight

To date, the impact of spaceflight environment on health, wellness and adaption, on the basis of biological sex and gender, has remained a limiting factor in the current body of literature [52]. Physiological and psychological changes associated with manned space exploration have predominantly been reported for male astronauts, and differences for the female population are not well understood [52, 53]. A gap in knowledge of spaceflight sex-based differences is further enhanced by disproportionate representation of biological sexes in existing astronaut cohorts, significant limitations of which are yet to be addressed [52]. As such, numerous initiatives have been launched in order to investigate sex-based differences in human adaptation to extreme environments, such as spaceflight [52].

Social determinants, such as educational level, field-expertise and marital status, had significant implications in sex-based differences in adaptation to conditions of spaceflight [52]. Extensive military experience has been reported for a substantial proportion of male astronauts, while the female astronauts had a higher number of doctoral degrees [52, 53].

Profound sex-based differences in behavioural responses to conditions of spaceflight have been observed in a number of ground-based analog studies [53]. It has been reported that females are more prone to develop anxiety disorders and functional impairment, while males are more prone to insomnia and weight loss during spaceflight [53]. In addition, sex-based differences were observed in coping strategies. More specifically, women demonstrated a more cooperative and supportive behaviour, while men tended to express anger, non-cooperation and conflict as a result of psychosocial isolation [53].

Physiological differences in sex-based adaptation to conditions of spaceflight are summarized in Figure 2-3. There were no significant differences reported in bone health between female and male population during spaceflight [54]. However, females were more prone to orthostatic intolerance post-space flight [52]. Females also suffered from a more pronounced cardiovascular deconditioning, attributed to a greater loss of plasma volume, reduced leg vascular resistance and a greater elevation of the heart rate in response to stressful stimuli [52]. As such, women reported a greater incidence and severity of space motion sickness.

Significant sex-based differences have been reported in neurosensory disturbances associated with spaceflight environment. Males were more prone to develop severe visual and acoustic impairments, further supplemented by decline in sensitivity to fine detail and increased reaction time for target acquisition [52]. On the contrary, females were more resistant to bacterial and viral infections, but once infected, had a greater risk of developing autoimmune disorders. In addition, women were more susceptible to radiation-induced pathologies, and as such had a significantly lower threshold of safe spaceflight duration [52].

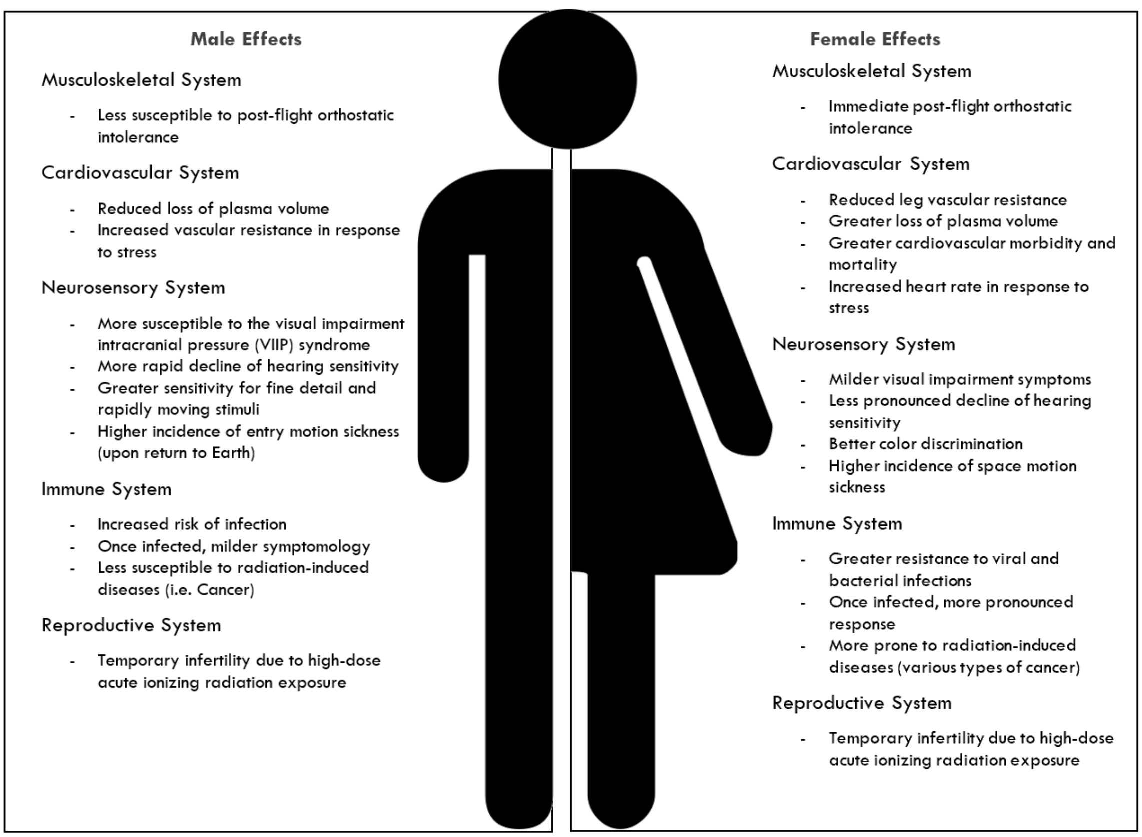

Figure 2-3. Biological sex differences in adaptation to conditions of spaceflight, created from [52].

2.5 Bioethical Challenges of Human Space Travel

The study of bioethics within the context of manned space exploration is of crucial significance. It is used to inform and establish health standards for long duration missions, where astronauts will be exposed to risks that are poorly characterized, uncertain and unforeseen [1]. As humankind embarks on deep space exploration, the bioethical challenges of manned spaceflight are expected to amplify, especially that operational and logistic requirements of emergency return to Earth are extremely complex, if at all possible.

Bioethics is a branch of philosophy that encompasses a system of morals or rules of behaviour that are concerned with human character and form the foundations of human conduct [55]. There are four main principles that are used to guide conduct, more specifically, beneficence, nonmaleficence, justice and autonomy. Beneficence, in principle, is the concept of promoting goodness, while non-maleficence is the requirement to do no harm [55]. The concept of justice is used to establish impartiality and integrity. Autonomy, is one of the core principles of biomedical ethics, which ensures that the person has the ability to determine his/her own destiny, and that their consent to do so is valid and voluntary [55].

The study of bioethics is concerned with the concept of “acceptable risk”, the magnitude of the possible harm and the probability of the harm actually happening [1, 55]. Numerous frameworks have been developed to enhance personal understanding of actions, the possibility and magnitude of harm produced by those actions and its various implications [55]. As such, space organizations and government officials have a fiduciary duty to provide astronauts with all available information pertaining to the risks and challenges of manned space exploration. The information should be presented in a meaningful, clear, inclusive, and effective manner so as to aid understanding of the material, to be able to make an informed, competent, voluntary, valid and full consent to participate [55]. As such, the various practices, including selection and training of astronauts are governed by the overarching bioethical principles, to enhance astronauts' ability to evaluate risks and estimate their ethical limits. It has been recognized that as the complexity of the task or activity increases or becomes more intrusive, the possibility of it being ethically unacceptable also increases. Although, the ethical acceptability of the activity increases as the number of involved people decreases, yet that raises another important question of what value can be placed on an individual life, discussion of which greatly exceeds the scope of this thesis.

In summary, the bioethical principles form the foundation of astronaut recruitment processes, including, selection and training, further enhanced by in-flight medical supports. To ensure autonomy and comprehensive understanding of health-related risks, future medical systems need to have an autonomous functionality and comprehensive capacity to inform and guide clinical decision making, especially when ground-based medical support will be limited, if at all possible.

2.6 Biomedical Challenges During Spaceflight

The deleterious physiological, psychological and behavioural effects of spaceflight environment on the human body, which have been covered in the prior sections, emphasize the need for a comprehensive pre-mission selection and in-flight health monitoring [56]. Increased distances and mission duration necessitate technological advancements to support adequate in-flight monitoring, to minimize possible health risks associated with deep space exploration. The objectives of in-flight monitoring can be summarized as "*the practice of all aspects of* *preventative medicine including screening, health care delivery, and maintaining human performance in the extreme environment of space and preserving the long-term health of space travellers*" [4].

Multiple diagnostic techniques have been developed for physiological monitoring of spaceflight induced deconditioning, an overview of which is summarized in Figure 2-4 [57]. The diagnostic techniques span across different medical fields, including haematology, nephrology, immunology, electrophysiology, microbiology and bone health assessments.

The nature of the space flight environment imposes fundamental biomedical challenges attributed to geographic isolation, habitation specifics, physical space constrains, logistics of healthcare delivery and patient retrieval [10]. Diagnostic devices for in-flight application are subjected to various physical limitations, including weight, volume, power consumption, connectivity, and operational specifics, which must be compatible with the environment of microgravity [57].

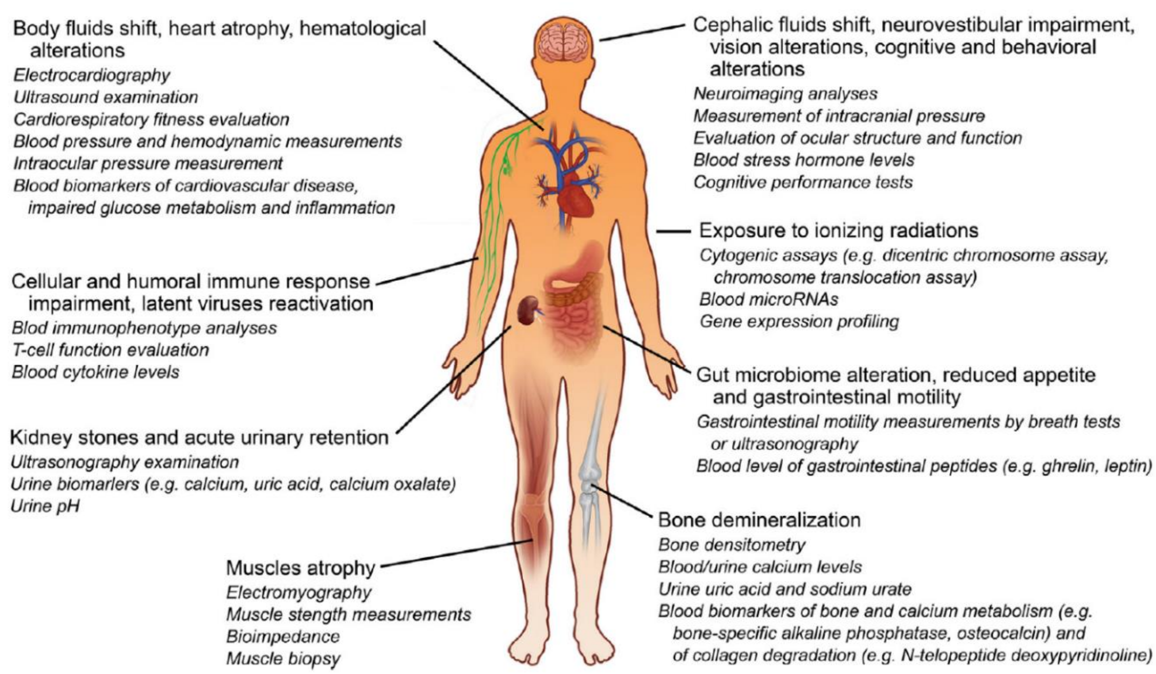

Figure 2-4. Space flight induced deconditioning and techniques for its monitoring from [57].

An existing healthcare system on the ISS is known as the Crew Healthcare System (CHeCS), which consists of three main components, namely the environmental health system, health maintenance system and the countermeasures system [58, 59]. The generic architecture of CHeCS and its subsystems constitute data acquisition, data processing, data storage, telecommunication links and limited decision-making capabilities [10]. Current telemedicine capabilities are able to support limited physiologic data transfer from the ISS to terrestrial Mission Control Centres, while the future deep-space exploration and expected communication delays will significantly impair this functionality [1, 57-59]. An additional component, known as the Crew Return Vehicle (CRV) is docked at the ISS to support retrieval of deconditioned crew members. It has the capacity to provide basic life support to one incapacitated crew member [58]. Meanwhile, patient retrieval on exploration-class mission will present significant challenges, the logistics and operational requirements of which will be complex and significantly delayed, if at all possible [59]. As such, further emphasizing the need for a comprehensive onboard medical system that would be able to prevent prognostics, diagnostics and health management in-flight.

Over the years, aerospace community, including astronauts and military pilots have expressed lack of interest and compliance with continuous health monitoring in-flight. Existing biomedical monitoring modalities have hindered the execution of occupational tasks or simply have proven to be impractical, emphasizing the urgent need for a paradigm change in an in-flight medical monitoring [46].

NASA has recognized that a multi-tier medical prevention and intervention approach should be undertaken in order to develop an enhanced medical capacity to support exploration-class missions [59]. The major components of the multi-tier medical system are meant to provide 3 categories of care, namely:

1) Advanced Life Support
2) Transitional Care
3) Ambulatory Care

Moreover, Streinkraus *et al.*, have outlined a number of preconditions of future medical monitoring systems that must be met in order to support interplanetary travel and support in-flight medical monitoring compliance. The novel health monitoring modalities must be "*dynamic, provide real-time information and use valid, reliable and practical technologies*", while the diagnostic algorithms should be capable to support in-flight medical data availability [7, 46].

2.7 Conclusion

This literature review chapter discussed the various implications of human space travel. It reviewed the environmental, physiological and psychological hazards associated with manned space exploration. It demonstrated the interplay of environmental factors and their effect on human health and performance. It further identified the dynamicity of human organ systems and the cascade of compensatory reactions that are triggered to support homeostasis and prevent onset of disease or pathology. The various components of health monitoring systems in space, along with the operational challenges and limitations have been reviewed. More specifically, it was revealed that the various data types and sources, including personal assessments and sensor data from Environmental Systems, Countermeasure System and Crew Healthcare System are fragmented, contributing to impracticality of the systems to support proactive rather than reactive health management in-flight. Furthermore, the various systems in-flight continue to be used as individual components, rather than a wholistic system that could detect stressor and task-specific response of organ system and help alleviate the deleterious health effects experienced during spaceflight. As such, the limitations of existing systems have motivated the work presented in this thesis. More specifically, the various systems components, including medical, environmental and activity data have been identified as fundamental inputs that should be integrated in order to support wholistic health assessment in-flight. Additionally, the current data processing approaches do not support meaningful use of the acquired physiological data, which necessitates a paradigm change. As such, this chapter identified the importance of real-time in-flight health monitoring, emphasizing an urgent need in development of a comprehensive, autonomous medical decision support system, the framework of which is proposed within this thesis.

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Chapter 3 – Information Systems

This chapter presents the foundations of the information systems theory in order to support the generation of the first hypothesis of this thesis. It provides a brief introduction into the field of big data, the benefits of which have not been leveraged by the field of space medicine to-date, further motivating the work proposed within the context of this thesis. This chapter concludes with an overview of an artificial intelligence big data analytics platform, known as Artemis, that is used as the foundation of the methodological framework proposed within this thesis.

3.1 Information Systems Theory

Information is an endless reservoir of knowledge, used to study and explain the various phenomena and aspects of interactions within oneself and the outside environment. Information is generated in various formats from a vast number of sources, necessitating a structured and systematic approach for its acquisition, integration and processing. As such, information systems form the foundation of an effective interaction between the various types and sources of information, by providing a structured mechanism for defining "*a set of interactions exchanging information capable of integrating them into common units*" [1]. Since the early 1960's, systems theory has been used to solve many challenges faced by the humankind [2]. However, the systems approach experienced many failures due to the inability to establish a harmonious system, in which human and technology could coexist [2].

The technology improvements continued to expand human capacity to generate information, yet the latency in development of appropriate systems has hindered the ability to effectively acquire, manage and leverage the enormous amount of data that was produced. As a result, very little data has been practically used [3]. It wasn't until the concept of big data evolved that organizations have realized the potential of artificial intelligence and machine learning tools, to support timely and efficient management of information.

3.2 Big Data

The concept of big data has evolved between 2001 and 2008 in the computer science industry, where the concept of big data was defined in terms of three 'V's" namely, its velocity, variety and volume [3]. The human body is a dynamic entity that generates an enormous amount of data, also referred to as data volume, at a very high rate, knows as data velocity. The variety of physiological data corresponds to the various types of data that is being produced and the ways or rather formats in which it can be captured. For instance, the activity of cardiovascular system can be assessed on the basis of electrical activity of the heart, which is captured as an electrocardiogram signal recording. Typically, the electrocardiogram sampling frequency for an adult population is set at 250Hz, equivalent to 250 readings per second [4]. As such, the concept of big data has the capacity to describe the data in terms of its variety, velocity and volume, which has been slowly adopted within the healthcare field and yet remains at its infancy in other fields of science and technology.

The healthcare environment has been generating "*an immense volume, variety and velocity of data across a wide range of healthcare networks*" [3]. The clinical nature of healthcare data has effectively demonstrated the pitfalls and impracticality of existing information systems and the enormous potential of big data to support evidence-based clinical decision making and inform action taking, which has not been leveraged to its full potential to-date. The concept of big data forms the foundations of the data lifecycle framework, that supports data throughout all of its stages, including capture, aggregation, analytics, information exploration and data governance, detailed review of which is presented in [3]. Several studies have demonstrated the potential and utility of big data to benefit the development of autonomous medical decision-support systems within the field of space medicine, and enable actionable use of data during space missions. The clinical decision support system (CDSS) can be briefly described in terms of five main functionalities. More specifically," it *provides the right information, to the right person, in the right format, through the right channel, at the right point in workflow to improve health and health care decisions and outcomes*" [5].

3.3 The Canadian Space Agency Medical Information Systems Architecture

In 2016, the Canadian Space Agency issued a Request for Information, highlighting an existing need in development of an appropriate information system, to develop medical capacity aboard the spacecraft and support medical autonomy for the crew on long-range missions [6]. The issued Request for Information provided a conceptual diagram for an information systems architecture and an overarching set of requirements that would support the development of the Advanced Crew Medical System (ACMS) Space Medicine Decision Support System (SMDSS). The conceptual diagram of the ACMS architecture is presented in Figure 3-1.

The proposed ACMS framework revealed three main architectural layers, namely the Input, Data Processing and Handling, and the Output. The Input layer included the various data types and sources available for medical assessments pre-, during and post-spaceflight. The proposed architecture presented an innovative wholistic approach to healthcare assessment within the context of spaceflight environment. More specifically, the data types included the medical history, non medical data, including environmental and activity data; medical device data, supplemented with clinical observations and personal assessments. The data sources ranged between the various interfaces, including onboard medical system interface that has different user access controls for the crew and the crew medical officer, the sensor interface and its respective hardware/software interfaces. All of which were meant to embed the various data into an electronic medical record (EMR) database, which would prepare the data for consumption by the space medicine decision support system (SMDSS), within the data handling and processing component. The proposed SMDSS consists of a Decision Engine and two data warehouses, namely the medical knowledge database (MKD) and the ACMS Operations and Maintenance Database. The Decision Engine would analyze the data according to the type of required intervention, such as the prognostic health management or diagnostics and medical treatment intervention, the results of which will be generated within an output component. The output architectural layer included the information such as the astronaut medical telemetry and health status, diagnosis, recommended treatment or countermeasures, data archiving suitable for research and medical consumables management. While the proposed conceptual ACMS architecture provided a wholistic approach to health assessments in space, through integration of the various types and sources of information, it has had some fundamental limitations [7]. More specifically, the conceptual ACMS architecture has not introduced the concept of big data and streaming analytics, as well as lacks the real-time feedback functionality of derived health analytics, further contributing to impracticality of the generated medical data [7]. As such, the limitations of the conceptual ACMS architecture have served as the motivation for the development of an integrated methodological framework, presented within this thesis. The proposed framework utilizes an innovative big data approach, developed as a series of extensions to an existing Artemis platform, an overview of which is presented in sections to follow.

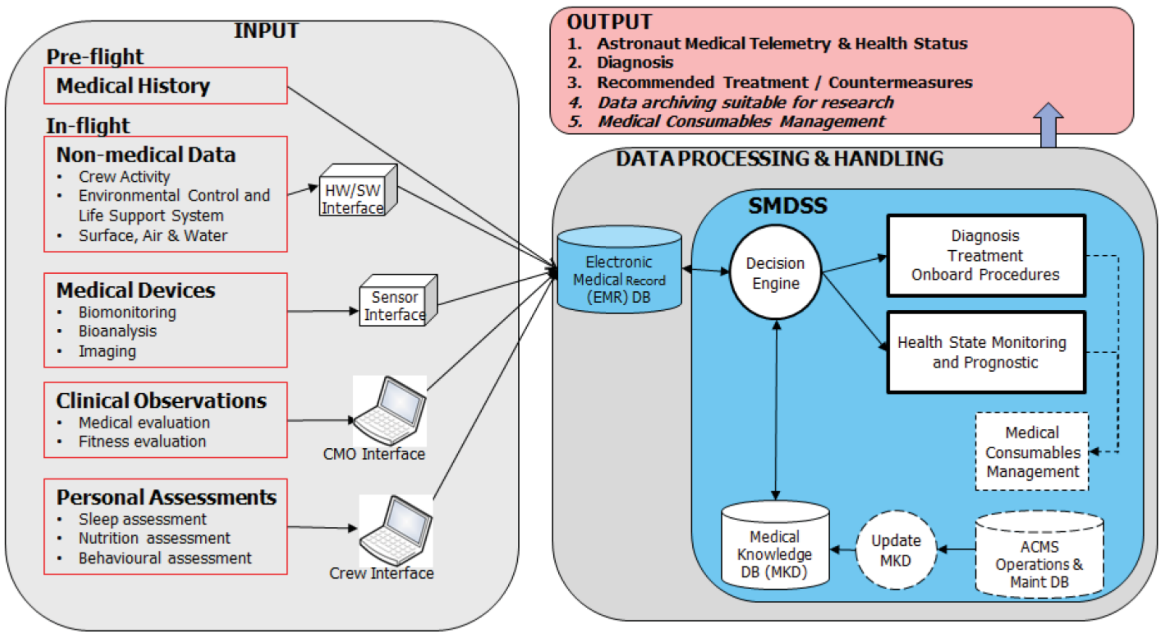

Figure 3-1. Conceptual diagram of the ACMS SMDSS architecture [6].

3.4 ARTEMIS

This section introduces Artemis, an artificial intelligence big data analytics platform that is extended in this thesis. The Artemis platform has previously been proposed by McGregor for concurrent multi-stream, multi-patient, multi-diagnosis temporal analysis in real-time environment [8]. Artemis in an international award-winning healthcare platform that has demonstrated a strong track-record of autonomous, remote and complex monitoring of various physiological and environmental data within numerous populations, including neonates, tactical operators, first responders, serious gamers and astronauts [8-11].

Artemis is provisioned as a cloud-based health analytics as-a-service platform that has the capacity to support autonomous and remote monitoring of physiological, environmental and activity data. The Artemis framework is made up of eight core components, including data collection, data acquisition, data transmission, online analytics, data persistency, knowledge discovery, (re)deployment and results presentation, schematically represented in Figure 3-2.

The data collection component enables concurrent acquisition of multi-variate temporal data, including physiological waveforms, numeric data streams and any other type of relevant clinical information that can include diagnostic imaging and haematologic results [8, 12]. It has the capacity to support data acquisition from various biomedical monitoring devices, including critical care bedside patient monitors, store and record Holter-style monitoring devices and wearable smart garments, such as the Bio-Monitor, Zephyr BioHarness monitoring system and many others [8, 11].

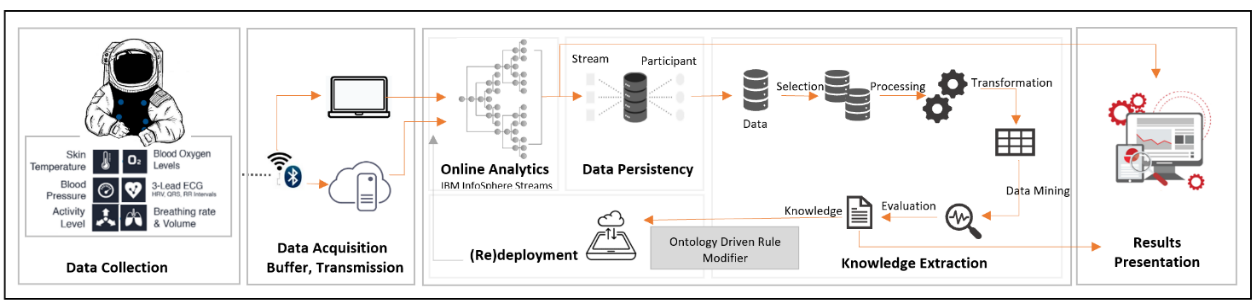

Figure 3-2. Artemis architecture for online health analytics during spaceflight [12].

The Artemis platform supports multimodal data acquisition, including wired (ethernet, serial and USB) and wireless (WiFi and Bluetooth) modes of data collection device connectivity [8]. Its Data Acquisition component is tailored to acquire high-frequency, high-fidelity, large volume and velocity real-time biomedical device data. It has built-in data buffering mechanisms to support temporary storage of data as it is being transmitted from data collection device to a local and/or cloud-based instance of Artemis platform. It should be noted that cloud-based instances of the Artemis platform are deployed at the Centre for Advanced Computing (CAC) based at Queen's University in Kingston, Ontario, Canada.

The Online Analytics component of the Artemis platform utilizes IBM InfoSphere Streams, a leading data integration tool that supports various data manipulation jobs, including data extraction, transformation, storage, etc. [8, 12, 14]. The Online Analytics component of the Artemis platform supports real-time concurrent operation of multiple algorithms, which are written in a streams programming language, also referred to as the stream graphs [12]. Stream graphs are specifically designed to analyze the incoming streams of physiological data and look for identifiable patterns that are associated with onset of various pathophysiologies and manifestation of clinical symptoms. The raw and derived analytics are stored within a cloud-based instance of the Artemis platform [14].

The Data Persistency component of the platform utilizes IBM DB2 knowledge centre. DB2 is a leading database warehouse that provides advanced data management capabilities, ensuring high performance, continuous data availability and reliability, as well as advanced data governance and storage [8, 15].

The Knowledge Extraction component of the Artemis platform utilizes McGregor's patented Service-Based Multi-Dimensional Temporal Data Mining ($STDM^n_0$) method, described in greater detail in [16]. The $STDM^n_0$ method incorporates extensive data manipulations, including data selection, optional cleaning, processing, transformation, data mining, evaluation and knowledge extraction. This component is tailored to support real-time data processing as well as retrospective clinical discovery. It has the capacity to analyze incoming data and look for new observable patterns in physiological data that can be indicative of early onset of medical conditions or states.

The Deployment component of the Artemis platform uses an ontology-driven rule modifier. It offers the ability to deploy new algorithms or redeploy refined versions of existing algorithms to support detection of new clinically significant temporal features discovered in knowledge discovery component of the platform [8, 12].

The Results presentation component of the Artemis platform is constantly refined to respond to innovative approaches for visualization and dynamic presentation of streaming data analytics. The latest iterations of results presentation component of the Artemis platform utilize an off-the-shelf visualization product, known as Microsoft Power BI [17]. Power BI offers advanced visualization tools to create interactive dashboards of real-time streaming analytics with minimal latency period between the time data is received and visualized.

Overall, the Artemis platform is a state-of-the-art computing paradigm that has the potential to support complex health analytics in extreme environments and critical care facilities. Its framework has been specifically designed to support autonomous, remote functionality that would be well-suited for clinical decision support systems aboard the spacecraft, especially for exploratory-class missions where there will be significant communication delays and extremely limited ground-based medical support. However, the Artemis platform has several limitations, as it has been designed specifically for processing of physiological data streams, and as such, is incompatible with existing technologies used for physiological monitoring in-flight.

3.5 Conclusion

This chapter presented the foundations of the information systems theory in order to inform the development of the framework proposed within this thesis. Novel terrestrial approaches, such as big data and stream computing, which have shown the potential in Earth-based applications, yet have not been introduced in the field of space medicine to-date, have been reviewed within this chapter. The fundamental challenges and limitations of existing information system architectures, hindering practical and meaningful in-flight instantiation have been used as motivations of the work proposed within this thesis. More specifically, the conceptual ACMS SMDSS architecture and prior Artemis research have been used as the foundation of the framework proposed within this thesis. The various data types identified by the ACMS SMDSS architecture have been recognized as essential inputs required for a wholistic in-flight health assessment, while a number of architectural limitations have been revealed. More specifically, lack of real-time data processing approaches and feedback functionality of derived analytics continue to contribute to impracticality of the acquired medical data. As such, it was recognized that ACMS SMDSS and Artemis architectures can be merged, with an introduction of a number of extensions, to support the development of an autonomous, comprehensive clinical decision support system. The proposed extensions to the Artemis platform would address incompatibility with existing technologies used for physiological data acquisition in-flight. More specifically, the Artemis platform needs to be extended to support acquisition the various data types and sources, including structured, unstructured and semi-structured data types. It needs to include a middleware data capture component that will support multi-modal data acquisition, such as wired and wireless, while enable data routing, and queueing mechanisms in accordance with the data format (i.e. streaming, file-based). Additionally, the Artemis platform needs to be extended to support integration of relevant streaming data and file-based packets of data to enable real-time wholistic in-flight health assessments. Further to that, novel methods have to be explored to enable interactive data visualization and preparation of multifunctional dashboards to support meaningful use of the acquired data in-flight.

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Chapter 4 – The Functional Health State Algorithm

This chapter presents the prior art methodology developed by the Russian Institute of Biomedical Problems for wellness and adaption-based assessments relating to spaceflight induced psychological and physiological responses. The selected methodology has extensive theoretical base, the validity of which has been demonstrated through a substantial track record of terrestrial and space applications. The selected methodology is deeply rooted in the study of health and how it changes in response to the various stimuli within the context of spaceflight environment. It further recognizes that human body dynamically responds to stress, which triggers a cascade of compensatory reactions of regulatory mechanisms that can be detected at the early stages of transition from the state of physiological norm towards maladaptation and development of pathology. As such, it has the potential to support early detection monitoring and contribute to preservation of health during space flight. Theoretical foundations of the health, wellness and adaption-based assessment method are presented within this chapter, highlighting the challenges and limitations of existing data processing methods, which motivate the re-engineering of the functional health state algorithm and its instantiation within the methodological framework presented in this thesis.

4.1 The concept of health and its norm in space medicine

Over the centuries, numerous schools of thought hypothesized what health was. The early definitions of health viewed it merely from a medical model perspective, where it was defined exclusively as an absence of disease [1]. Over the years, the model of health was revised, as health organizations and government authorities came to realization that there were additional indicators of health, beyond those of physical well-being. It was then, that mental well-being and the social determinants of health were included in the definition, taking on a more holistic approach to health. Subsequently, World Health Organization (WHO) defined health as "*a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity*" [1]. This definition viewed health as a static state that can be achieved. It was further expanded to move away from a static model of health towards a more dynamic model, where health is viewed as "*a resource of everyday life, not the objective of living*" [2]. It was the concept that viewed health as a resource of physical, personal and social capacities, all of which are essential in determining the quality of life [2]. Over the years, schools of public health have started to move away from the concept of population health towards a patient-centred approach, leading to realization that health is highly contextualized for each individual in their own way. While the concept of health has been coined to reflect major determinants of health on Earth, its definition had to be revisited as humans embarked on the journey of space exploration. The concept of health and its norm required a vastly different criteria to be met for those living on Earth and completing missions to LEO and beyond [3].

Human space exploration has led to realization that terrestrial and space medicine have fundamentally different objectives and challenges [3]. The general population on Earth spans across the entire continuum of health and disease, while astronauts are among the "healthiest" of that population. The focus of terrestrial medicine is deeply rooted in diagnosis and treatment of pathological states and medical conditions. On the contrary, the main objectives of space medicine are to preserve health and well-being through introduction of prophylactic measures and protocols to maintain a steady state of bodily systems, also known as homeostasis, and preserve adaptive capabilities of the human body and mind [3]. Astronauts are required to undergo rigorous screening and medical examination protocols to ensure minimal potential medical impact on future missions, which could pose life-threatening risks to an individual and an entire crew, while threaten success of the mission and safe return to Earth [4]. As such, the concept of health and its norm in space medicine can be considered in accordance with the main determinants of health, including physical, mental and social well-being, the main aspects of which have been covered in detail in Chapter 2 and briefly summarized here. The main requirement of physical health in space consists of adequate and efficient adaptability and resilience of bodily systems, so as to effectively respond to changing physical, environmental, and psychological stimuli and minimize the deleterious effects imposed by space flight environment [3, 5]. Behavioural health and performance are essential in maintaining cognitive performance, critical decision making and emotional stability, directly impacting overall health and occupational performance. Lastly, social well-being is vital for success of the mission, significantly impacting the dynamics of interpersonal communication, harmony and cohesiveness of the crew, contributing to a positive environment [6, 7].

4.2 Theoretical foundations of functional health states and their classification

The study of adaptation and its underlying biological and psychological mechanisms dates back to the early nineteenth century, when the term "General Adaptation Syndrome" was first coined by "the father of stress" Hans Selye. Selye was the first to identify stress as an underlying factor of nonspecific pathology. He recognized that chronic exposure to stress triggers complex physiological and psychological responses that contribute to the "*faulty adaptation or adjustment to the environment*" and are clinically manifested as "*many of the most common maladies of man*" [8]. This ideology was further supported by Crookshank, who stipulated that "*while health comprised successful adaptation to the environment, disease constituted a dissociation of functional unity, or maladjustment due to failure or incompleteness of adaptive response*" [8]. As such, it was then recognized that the etiology of general adaptation syndrome consisted of a dynamic multifaceted response to stress, which included an alarm phase, followed by resistance to change, which finally resulted in exhaustion in countering the stressor. This ideology was challenged by many scientists and researchers from a broad range of scientific fields.

Baevsky, as one of the pioneers of space medicine, the division of space cardiology in particular, was the first to recognize the prominent potential of stress and adaption research in space and its ground-based analogs. It was an ideal environment to study an interplay of environmental, physiological and psychological factors in healthy people, in a confined, isolated and controlled environment. His extensive research on Earth and in space has led to development of a unique methodology for the assessment of health and adaptive capacity of the human body, further referred to as the functional health state assessment, the conceptual model of which is schematically represented in Figure 4-1. Baevsky's conceptual model of health assessment further confirmed that health is a dynamic entity that necessitates an effective and timely interplay of adaptive and regulatory mechanisms in order to maintain homeostasis and to preserve an optimal level of health. As denoted in Figure 4-1, the level of health, also referred to as the adaptive capacity of the body is subjected to environmental conditions, interindividual and age-related differences, type and duration of experienced stress, level of performance of the main functional systems, in additional to the level of functional reserves of regulatory mechanisms and the state of energy metabolism.

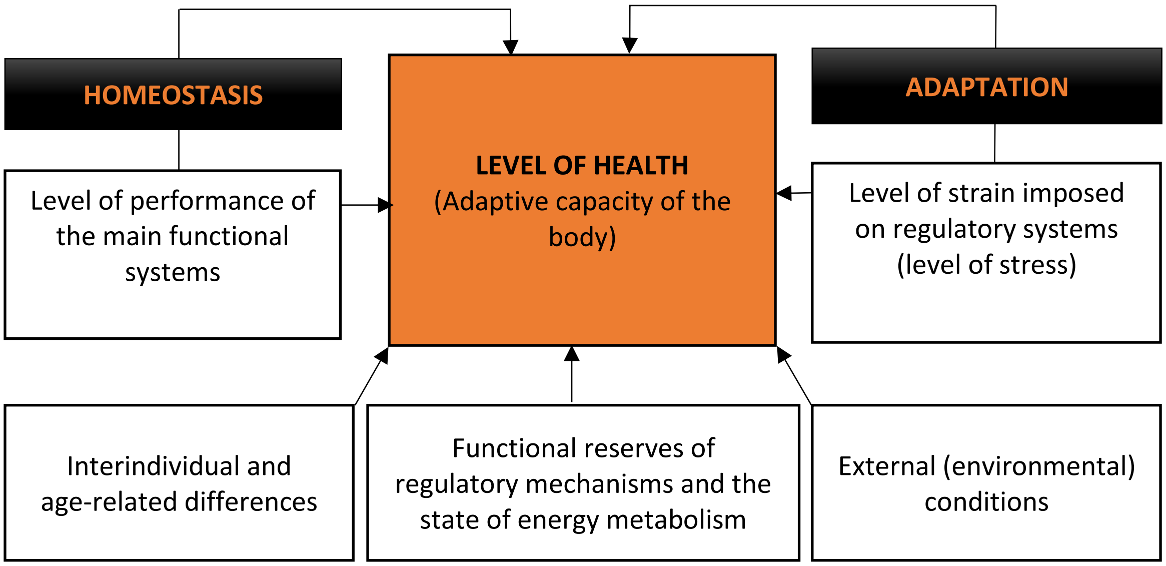

Figure 4-1. Conceptual model of health assessment from [9].

As becomes apparent from the conceptual model represented in Figure 4-1, the functional health state methodology is based on the principles of Selye's general adaptation syndrome. It recognizes that health is a dynamic entity and that transition from health to disease is a gradual process that can be described in terms of transitional health states, supported by changes in adaptive capacity of functional systems. As such, Baevsky's model of functional health states identified four main functional states, which are the state of physiological norm, prenosological state, premorbid state and the state of pathology, the onset of which is dependent on the inter-relationship between three main factors, which can be summarized in a simple mathematical equation:

Level of Health = Functional Reserves (FR) * Systems Tension (ST) [9]

where, the systems tension is the most informative parameter in classification of the level of health. Systems tension serves as the most dynamic indicator of regulatory systems activity, which enables an in-depth assessment of activation of various components of regulatory mechanisms. It can be measured by a relatively simple method of heart rate variability analysis, which has been widely used for evaluation of the activity of autonomic nervous system in response to stressful stimuli [9].

Decades of research in the fields of space and terrestrial medicine have validated the method of heart rate variability analysis to indicate changes in activity of regulatory mechanisms and adaption capacity that can be further deduced to determine the level of health, mathematical model of which is presented in sections to follow [3, 10].

4.3 Mathematical Modeling of Functional Health States

The method of mathematical modelling of human functional health states is based on heart rate variability analysis, which utilize recordings of raw electrocardiogram (ECG) signal. ECG signal represents the electrical activity of the heart, which can be characterized in terms of waves, segments and intervals, schematically represented in Figure 4-2. A normal ECG pattern is composed of 5 waves, denoted as P, Q, R, S, and T, each of which is responsible for a particular electrical event within the cardiac cycle [11, 12]. P wave represents the initial bursts of electrical activity that trigger an action potential, and induce depolarization and contraction of the atria. Subsequently, the wave of depolarization propagates through the AV node (Q wave), down the septum toward the apex of the heart and along the outside walls towards the top of the heart (R wave), which results in contraction of the ventricles (S wave) [11, 12]. Overall, QRS complex reflects the progressive wave of ventricular depolarization, while the T wave represents its repolarization [12]. Atrial repolarization is not depicted within electrocardiogram, as its electrical activity is weak and overlaps with the QRS complex [11]. It should also be noted that ECG wave can be reflected both above and below the baseline, depending on the charge of the electrode that the wave is moving towards. Thus, if the net movement is towards the positive electrode it will point upward and if it's towards the negative electrode it will be directed downward, below the baseline [12].

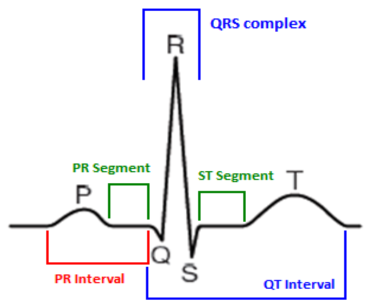

Figure 4-2. Electrocardiogram waves, segments and intervals.

As such, the method of mathematical modelling of functional health states utilizes the electrocardiogram signal to identify and extract R-R cardio-intervals that are further subjected to statistical, geometric and frequency-domain analyses.

Statistical Analysis:

Statistical analyses of the heart rhythm include computation of a range of variables that enable characterization of the number, type and duration of the observed cardio-intervals. Once the RR intervals are defined, they are subjected to filtering and artifact removal to produce the normal-normal (NN) intervals. As a part of statistical analysis, heart rate (HR), maximum interval in the NN array (Mx), minimum interval in the NN array (Mn), difference between Mx and Mn (MxDMn), and pNN50, number of successive RR intervals that differ by more than 50ms, are derived. Once the statistical features of the heart rate variability have been extracted, a cubic spline interpolation of the NN interval array is performed to generate an evenly sampled signal that is subjected to additional statistical, spectral and geometric analyses.

Geometric Analyses:

Geometric analyses are performed on an evenly sampled NN interval array, which is used to generate a histogram. The histogram ranges are defined as 50ms segments, representing the time series values between 300ms to 1700ms. There is a total of 28 bins generated within the histogram, supplemented with the respective number of samples that fall under each specified range. The range with the maximum number of samples is recorded, and represents the mode (Mo), also known as the most frequently occurring cardio-interval. Subsequently, the amplitude of the mode (AMo) is computed to determine the percentage proportion of the most commonly occurring cardio-intervals within an NN interval array. The generated geometric features of the HRV, such as the MxDMn, Mo and AMo are used to calculate the stress index (SI), summarized in the following mathematical equation:

$$SI = \frac{AM_0}{2 \times M_0 \times MxDMn}$$

Frequency-Domain Analysis:

The frequency-domain analyses are performed on an evenly sampled NN interval array to generate multiple frequency domain features of the HRV spectrum, including the total spectral power (TP), and the various frequency bands, including high (HF), low (LF) and very-low (VLF), which are represented in hertz (Hz) and as a percentage of the total spectral power. The Fast Fourier Transform algorithm is used to convert the signal from its original temporal domain form to its respective representation as a frequency domain signal. The total power spectrum of the array is computed by squaring the result of the Fourier transform algorithm, which is subsequently normalized to the length of the array. The highest frequency component is defined as the portion of the power spectrum within the range of 0.15Hz and 4.0Hz. The aforementioned two frequencies are used to determined the low and high bins of the power spectrum.

Mathematical Modelling of Functional Health States

As the method of heart rate variability analysis gained popularity in terrestrial and space medicine research, the need for an effective methodology to support assessment of the level of health or rather adaptive capacity of the human body was recognized. Baevsky and Chernikova explored the use of multiple mathematical models, including stepwise discriminant function analysis and correlation regression analysis to identify which model is the most suitable for differentiation of health and its transitional states prior to onset of pathology [9, 13].

Stepwise discriminant function analysis methodology is based on the principle of establishing a linear function of variables that are the most informative in separating or rather discriminating the data of interest into known groups or categories [14]. The stepwise classification of such variables is based on assignment of weights, also known as discriminant coefficients, so as to reflect the interrelationship between the variables to meet the criteria of the established conditions.

Correlation-regression analysis methodology is based on the principle of establishing and quantifying the direction and magnitude of linear association between dependent and independent variables.

Extensive research has demonstrated the efficacy of the stepwise discriminant function analysis to identify two canonical variables, each of which can be considered as independent parameters of health [9, 13]. The two canonical variables L_1 and L_2, generalized equations of which are presented below, are collectively known as the functional health state algorithm.

$$L_1 = 0.112HR + 1.006SI + 0.047pNN50 + 0.086HF$$

$$L_2 = 0.140HR + 0.165SI + 1.293pNN50 + 0.623HF$$

The functional health state algorithm can be described in terms of two canonical variables L_1 and L_2 each of which represents a weighted interrelationship between the most informative parameters of heart rate variability, including the mean heart rate (HR), stress index (SI), pNN50 and high frequency spectral power. HRV parameters in each of the equations have assigned weights to reflect their dynamic interrelationship and distinguish changes in adaptive capacity and activity of regulatory mechanisms. As such, the highest weight in the first equation is attributed to stress index (SI), which enables L_1 to serve as an independent parameter of systems tensions. In the second equation, the highest weight is assigned to pNN50, enabling L_2 to represent the functional reserve capacity of bodily systems. Once the two canonical variables, L_1 and L_2, are computed they are used as coordinates to establish a phase plane of functional states, schematically represented in Figure 4-3.

L_1 and L_2 values within the phase plane of coordinates are established in such a way that four main functional states can be identified, including the state of physiological norm in the lower right quadrant, intermediate (prenosological) state in the upper right, premorbid state in upper left and the state of pathology in the lower left quadrant. Classification of functional states is established in such a way that transitional states are associated with the same level of systems tension, yet different availability of functional reserves. While prenosological state represents an optimal functionality of regulatory systems and adequate availability of functional reserves, premorbid state is characterized by depleted functional reserves and increased risk of maladaptation. Similarly, the state of physiological norm is associated with high performance of regulatory mechanisms and high amount of functional reserves, while the state of pathology results in exhaustion of functional reserves and onset of maladaptive response, clinically manifested as disease or pathology [10].

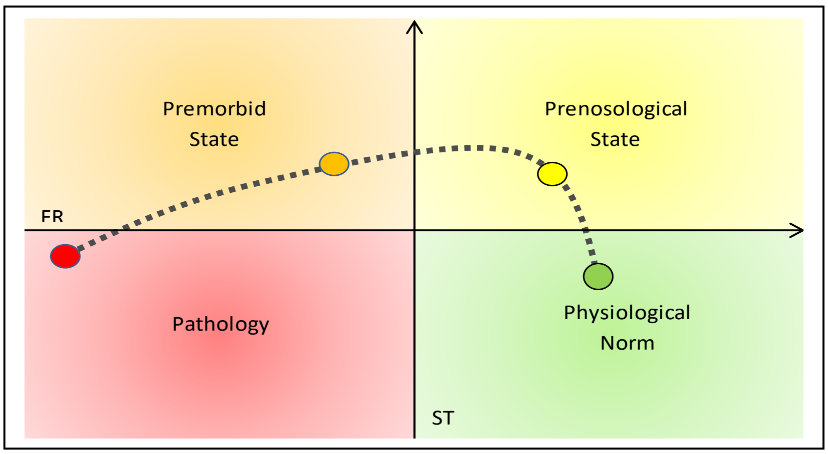

Figure 4-3. Phase plane of functional health state coordinates [15].

Historically, the computation of functional health states has been performed retrospectively, in accordance with the information systems architecture outlined in Figure 4-4 [16]. Figure 4-4 represents an existing architecture of information systems used to acquire ECG data aboard the ISS and subsequent data transfer, processing and analytics. ECG data acquisition remains scheduled and discontinuous, while the data transfer to terrestrial Mission Control Centre typically occurs post-spaceflight. Terrestrial sub-system of data processing includes a complex of software applications, each of which performs a particular type of data manipulation jobs, corresponding to temporal, spectral and geometric analysis of heart rate variability features [16].

Once the canonical variables, L_1 and L_2, have been computed on the basis of 5-minute windows of data, representing a sample collected at the frequency of 500 readings/second, they were traditionally represented as hourly or daily averages, resulting in significant data smoothing and averaging, further contributing to an enormous amount of data loss.

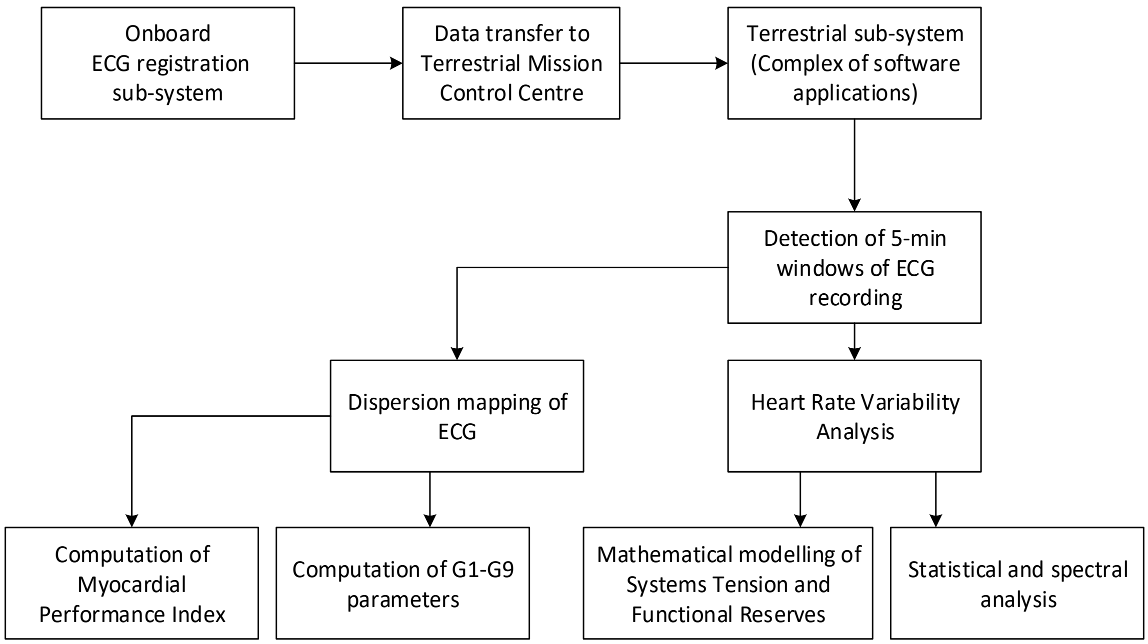

Figure 4-4. Existing Information Systems architecture on International Space Station (ISS) and at terrestrial Mission Control Centre recreated from [16].

It is important to note that the processing of the heart rate variability, as part of the functional health state computation, followed the traditional data processing approach. More specifically, a time tuple has been generated for every 5-minute interval, starting at time 0:00-4:59min, 5:00-9:59min, 10:00-14:59min and so on. This data sampling approach presents a fundamental limitation in the ability to de-trend the HRV signal and identify the authentic cause of the observed physiological response, as well as eliminate the potential effect of co-founding factors, such as noise or artefacts. As such, the functional health assessment necessitates exploration of novel approaches to support the validity of the established functional health state estimates and to minimize the risk of potential error, so as to enhance the capability to support early detection monitoring and contribute to improved health outcomes during space flight.

4.4 Conclusion:

Existing retrospective and discontinuous data acquisition and processing techniques continue to contribute to an enormous amount of data loss, all while being highly impractical for use during the mission. As such, the limitations of existing methods served as the primary motivation of the work presented in this thesis and detailed in chapters to follow. Innovative computing methods and techniques have been explored so as to enable creation of an integrated framework to support data throughout its entire life cycle. Furthermore, utilization of big data and stream computing approaches to support near real-time or real-time computation of functional health states has been proposed to improve usability of the acquired physiological data and to effectively support clinical-decision making during spaceflight.

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Chapter 5 – Methodology

This chapter proposes a novel framework that extends the existing Artemis, big data analytics platform, to provide an integrated framework architecture to support data throughout all of the stages of its lifecycle, beginning with the data collection, all the way through to data reporting and storage within the context of space medicine. The proposed framework addresses existing challenges of retrospective discontinuous file-base data acquisition, in-batch data processing and extensive data down-sampling. It is aligned with the core principles of the Advanced Crew Medical System (ACMS) and Space Medicine Decision Support System (SMDSS) architecture, as outlined by the Canadian Space Agency in [1]. The proposed framework identifies the necessary modifications and extensions to existing ACMS SMDSS architecture and the Artemis platform, in order to support real-time capability of health and wellness analytics, adaption-based analytics, activity and environmental analytics, all while ensure continuity of data acquisition, processing and storage.

An enormous amount of data is being generated every second aboard the International Space Station, while its invaluable potential is not being leveraged due to the lack of appropriate information systems to support the lifecycle of the data. Lack of continuity in data collection, integration, processing and storage presents significant challenges for practicality and usability of the acquired data, as well as contributes to a vast amount of data loss. The proposed framework addresses existing challenges through an integrated architecture framework to support data throughout all of the stages of its lifecycle, beginning with the data collection, all the way through to data reporting and storage.

The proposed architecture of big data analytics framework is made up of eight core components, which are the data collection, data capture, data integration, data persistency, online analytics, knowledge extraction, (re)deployment and results presentation, schematically represented in Figure 5-1 and detailed in sections to follow. The architectural components that have been adopted from prior Artemis research include, Data Persistency, Knowledge Discovery, (Re)deployment, Online Analytics and the real-time streaming adaptive API of the Data Integration component. Extensions of the Artemis platform within the proposed big data framework presented in this thesis include Data Collection, Middleware Data Capture and Results Presentation components. In addition, the prior Data Integration component is extended by introduction of a message sub-flow to enable integration of file-based packets of data with relevant streaming data. Further to that, adaption-based analytics within the Online Analytics component are extended through instantiation of multi-modal adaption-based assessment presented in this thesis. As such, the proposed framework addresses existing limitations of information systems and presents great potential to support autonomous clinical decision-making during spaceflight.

5.1 Data Collection

The data collection component is an essential data hub that represents the heterogeneity of data types and sources that are of relevance within the context of spaceflight environment. The multiple data types can be grouped into three main categories, including structured, semi-structured and unstructured data. Structured, semi-structured and unstructured data have

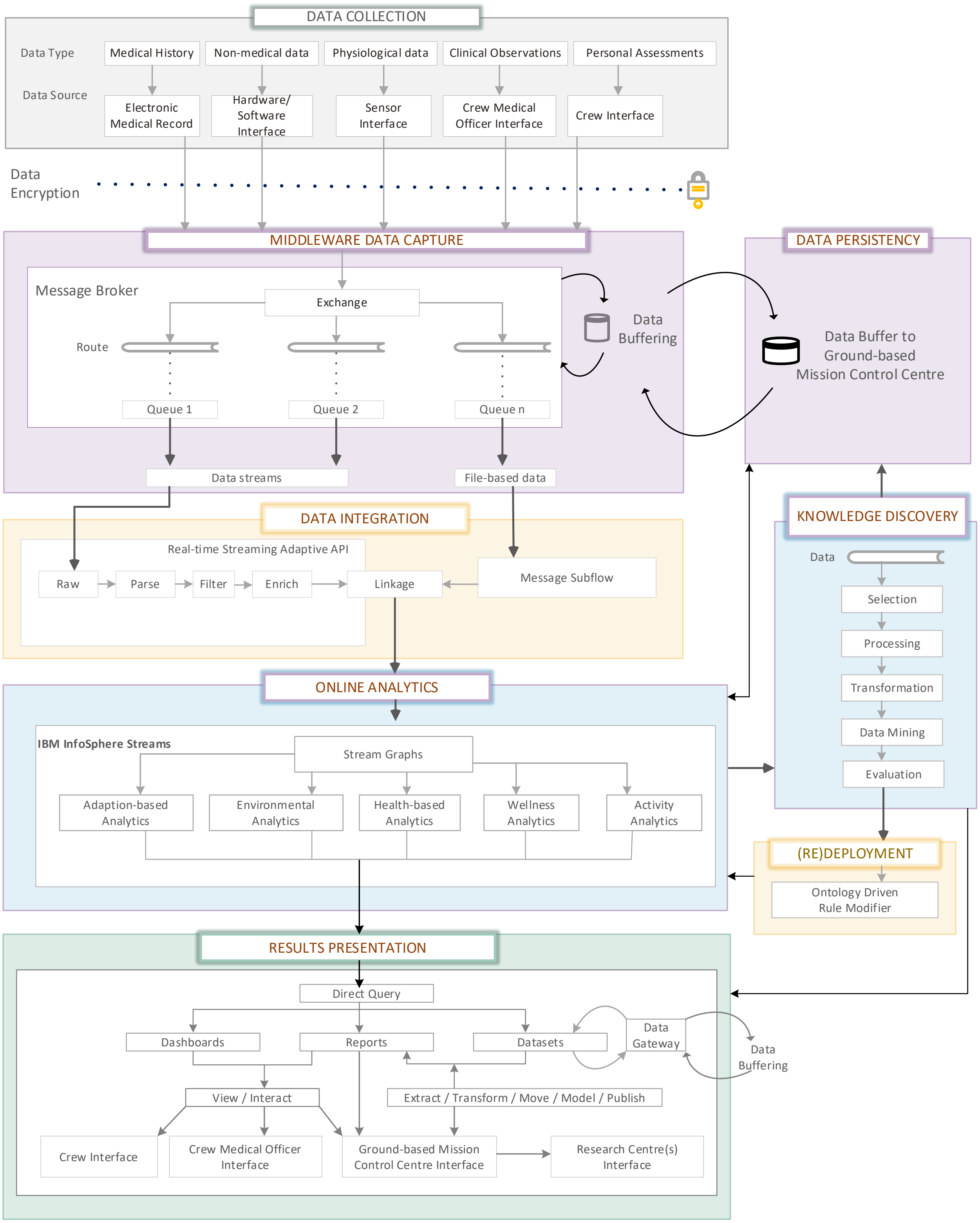

Figure 5-1. The proposed framework of health analytics as a service aboard the ISS.

different properties, which significantly impact data acquisition, transmission, integration and analytics capabilities. Structured data includes pre-flight medical history, non-medical data, such as the crew activity data, environmental control and life support systems data and medical, vital signs data. Clinical observations and personal assessments constitute semi-structured data logs, while diagnostic imaging represents an unstructured data type. The various data types are acquired from a collection of multiple data sources, including Electronic Medical Records (EMRs), Hardware/Software Interfaces for environmental and activity data, biomedical sensors and onboard medical systems. An onboard medical system consists of two interfaces, namely the crew and crew medical officer interface that significantly differ in user access control properties and settings.

Structured data can typically be generated as a continuous stream of data, representing an unbounded dataset that can be processed as the data is being acquired. As the data is being produced and captured by the multiple data sources, it is subjected to multi-tier data security and encryption protocols prior to arriving at the middleware data capture component of the proposed architecture framework. Semi-structured and unstructured data types are generally produced as file-based packets of data, as such, the data collection has to be completed in order to initiate file transfer and processing.

5.2 Middleware Data Capture

The middleware data capture component supports multi-modal data acquisition, including wired and wireless connectivity, and constitutes of a message broker engine and a data buffering mechanism. A message broker serves as an intermediary between the data producer and consumer. As the data messages are arriving through the data pipeline, they are being routed through a series of interdependent protocols that queue the data either directly or through a pre-defined number of topics and/or filters, in order to deliver specific message formats to its consumers. As outlined in Figure 5-1, the message broker generates separate queues of streaming data and file-based packets of data in preparation for the data integration. The data buffering mechanism is tightly coupled with the message broker engine, ensuring temporary storage of all incoming data, as it is being processed through the messaging protocols. Other benefits of an integrated data buffering mechanisms include fault tolerance and data persistency, ensuring that no data is being lost in the event of unplanned or planned outages of downstream components. It should be noted that data buffering to ground-based Mission Control Centres is also supported, when connection to do so is available.

5.3 Data Integration

The data integration component utilizes the previously proposed real-time streaming adaptive application programming interface (API), proposed by Inibhunu *et al.,* represented in Figure 5-2 and detailed in [2].

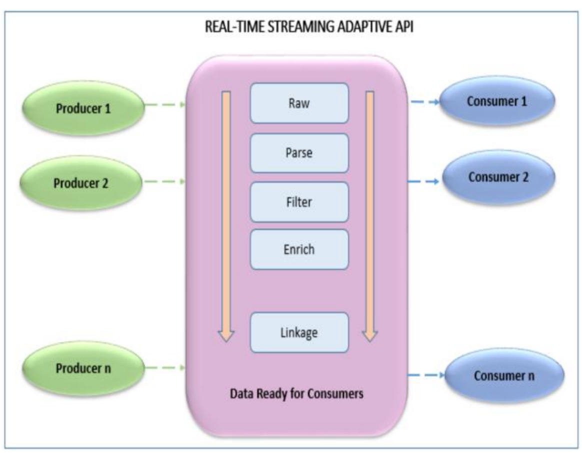

Figure 5-2. Real-time streaming adaptive API from [2].

The real time streaming adaptive API consists of a series of modules that process raw incoming data streams and prepare them for consumption by other processes. This collection of data processing modules is based on a massively parallel processing paradigm that support concurrent processing of multiple streams of data. The real-time streaming API is further enhanced in the proposed architecture framework by an introduction of a message sub-flow to support integration and linkage of file-based packets of data with relevant streaming data. The message sub flow has the capacity to be configured using specific properties. Once the linkage of data within the data integration component has completed, the data is published and ready to be consumed by the Online Analytics component.

5.4 Online Analytics

Similarly, to the Artemis framework and platform, the Online Analytics component of the architecture utilizes the IBM InfoSphere streams software platform that supports various data manipulation jobs on heterogeneous data flows, offering valuable insights with minimal latency period. It supports real-time concurrent operation of multiple algorithms, which are written in a streams programming language, also referred to as the stream graphs. The stream graphs of interest within the context of diagnostics, prognostics and health management during spaceflight include multiple health analytics, utilizing environmental, activity, adaptation, wellness and health data. It is important to note that the Online Analytics component is tightly-coupled with the data persistency component, ensuring that the raw data and derived analytics are being stored within the local data warehouse, as well as transmitted to the terrestrial Mission Control Centre, when connection to do so is available. Specifics of the online analytics component are demonstrated as an instantiation of adaption, health and wellness analytics within the context of two ground-based case studies “Luna-2015” and “Dry Immersion-2016”, in Chapters 6 and 7 respectively.

5.5 Knowledge Discovery

The Knowledge Discovery component is adapted from the existing Artemis platform to support real-time and retrospective clinical discovery of new insights within the data streams. It utilizes McGregor’s patented Service-Based Multi-Dimensional Temporal Data Mining ($STDM^n_0$) method that involves a complex of data manipulations, including selection, processing, transformation, data mining and evaluation, to help discover early signs of transitional health states or onset of medical contingencies. Once the new clinical algorithms have been validated or existing ones have been modified, they can be instantiated within the Online Analytics component of the proposed architecture framework during the same space flight through the (re)deployment component.

5.6 (re) Deployment

The (re)Deployment component utilizes an ontology-driven rule modifier, which supports updates to existing clinical algorithms or the creation and deployment of new stream graphs within the Online Analytics components of the proposed framework.

5.7 Results Presentation

The Results Presentation component of the proposed architecture framework utilizes the data visualization application programming interface that supports ingestion of heterogeneous types of data and performs various data management jobs. The direct query functionality allows for interactive import and integration of data from multiple data sources that are further used to aggregate data, consolidate new datasets, generate reports and prepare interactive dashboards. Imported and derived datasets are continuously stored through the data buffering mechanisms in local and cloud-based data warehouses. The final dashboards and reports have different interfaces, depending on the end-user account control settings. The Crew Interface includes only authorized crew-member specific data, which has limited view and interact functionality. The crew medical officer interface has elevated privileges in user access control, as such CMO can view the reports for the entire crew, as well as for each of individual crew members. The most privileges in user access control settings are granted to the Ground-based Mission Control Centres who have the capacity to perform various data manipulations, including extraction, transformation, moving, modelling and publishing. Lastly, there is also a potential for development of a Research Centre Interface that can have de-identified encrypted consented data to support research activities.

A demonstration of this framework within the context of ground-based isolation and confinement study is contained in Chapter 6 and Dry Immersion study in Chapter 7.

References:

1. RFI regarding the Advanced Crew Medical System (ACMS) Space Medicine Decision Support System (SMDSS). (2016). Retrieved 12 March 2020, from https://buyandsell.gc.ca/cds/public/2016/07/21/ce21b3d9c1ab2b55122a526b38eea330/ABES.PROD.PW_MTB.B545.E13964.EBSU000.PDF
2. Inibhunu, C., Jalali, R., Doyle, I., McGregor, C., (2019). Adaptive API for Real-Time Streaming Analytics as a Service in 41st Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), pp:3472-3477. doi:10.1109/EMBC.2019.8856602

Chapter 6 – Case Study – Luna 2015

This chapter presents the instantiation of the big data analytics framework described in Chapter 5, within the context of ground-based study, Luna-2015, in which a mathematical model for functional health states is re-engineered as an instance within MATLAB environment to demonstrate its potential to support near real-time or real-time functionality within Artemis, big data analytics platform. This enables the second and third hypotheses of this thesis to be addressed.

The study, namely the "Luna 2015", was the first of its kind all-female crew retrospective ground-based isolation and confinement study performed in the IBMP Ground-Based Experimental Complex / Nazemnyy eksperimental'nyy kompleks (NEK) isolated habitation facility in Moscow, Russia. The six study participants were healthy female volunteers between the ages of 30±5 years old, with an average height of 163cm and mean weight of 58.5kg. The overarching goal of the research focused on investigation of physiological and psychological effects of the all-female crew on a seven-day simulated flight around the Moon. There were several research studies performed by multiple research teams in association with the Luna 2015 isolation experiment. The research presented in this chapter was the subject of a study that was reviewed and approved by the IBMP Research Ethics Board, and the Ontario Tech University Research Ethics Board under REB# 15-047 Integration of Russian Cosmonaut Monitoring with Artemis and Artemis Cloud. This research has been supported by the Canada Research Chairs program (#950-203427 and #950-225945) and the Canadian Foundation for Innovation (#203427).

The experimental architecture framework, along with the modifications to existing adaption-based analytics, also known as the functional health state assessment, to support real-time functionality are schematically represented in Figure 6-1 and will be detailed in sections to follow.

6. 1 Data Collection

Data collection modalities aboard the International Space Station (ISS) are extremely limited due to physical constrains and specifics of spaceflight environment, which are difficult to address due to stringent regulatory guidelines and protocols governing the use of specific biomedical monitoring modalities aboard the ISS. As such, the proposed framework will describe the architectural changes that are required to support data acquisition from existing biomedical monitoring modalities, such as the Cosmocard, commercial-grade Holter-style ECG monitoring device that functions as a record and store device.

Physiological data within the context of Luna 2015 case study was acquired with a commercial grade “Cosmocard” Holter-style ECG monitoring device, currently in use for cosmonaut health monitoring within the Russian segment of the ISS. Electrocardiogram (ECG) recordings were scheduled and discontinuous. ECG-recordings spanned over the period of 24-hours and were collected for half of the crew on the second, forth and sixth day of the study, and similarly on the third, fifth and seventh day of the study for the remainder of the crew. ECG sampling rate was set to 500 samples/second. Following each instance of data collection, the Cosmocard device was docked for wire-based data acquisition and transmission to occur. Study participants followed the ISS data handling protocol, which required for the collected data to be stored locally on a PC, and saved on a USB flash drive to transfer to the research team for subsequent retrospective data processing and analysis. The outlined data collection approach presented fundamental

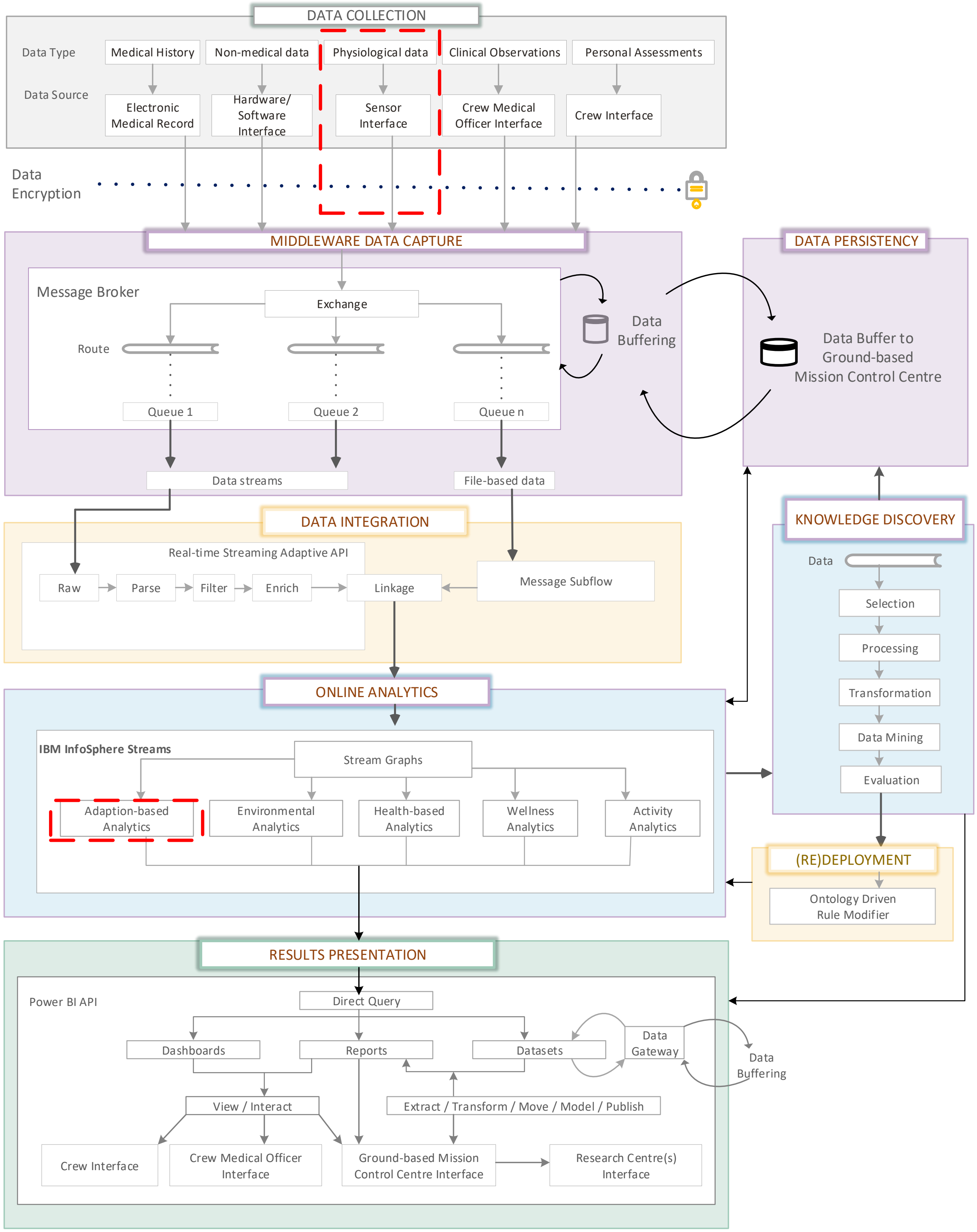

Figure 6-1. The instantiation of the proposed framework within the context of Luna-2015.

limitations to the approbation of the middleware data capture and data integration components of the proposed framework, detailed in Figure 6-1. The red boxes within Figure 6-1 identify the data type and source, namely physiological data acquired from a sensor interface, approbated in instantiation of the proposed framework within the context of Luna 2015 case study. Additionally, near real-time functionality of the online health analytics has been demonstrated through instantiation and application of adaption-based analytics.

Data processing and analysis followed IBMP's retrospective in-batch file-based processing approach in combination with the initial trial of functional health state algorithm instantiated within MATLAB environment, represented in Figure 6-2, further alterations of which will be integrated as an IBM Infosphere Stream instance within the Online Analytics component of the proposed framework.

6.2 Instantiation of Adaption-Based Analytics within MATLAB:

The Cosmocard data acquisition device produces two file formats for each instance of data acquisition, in a form of .dat and .hea files. These are binary files which can not be accessed directly through various programming languages, and as such, require an open-source waveform-database (WFDB) package, which serves as a toolbox for reading, writing and processing the various types of waveform physiological data, an electrocardiogram signal, in particular. The various steps involved in reading and processing of an ECG signal to enable instantiation of the functional health state algorithm within the MATLAB environment are described below and summarized in Figure 6-2.

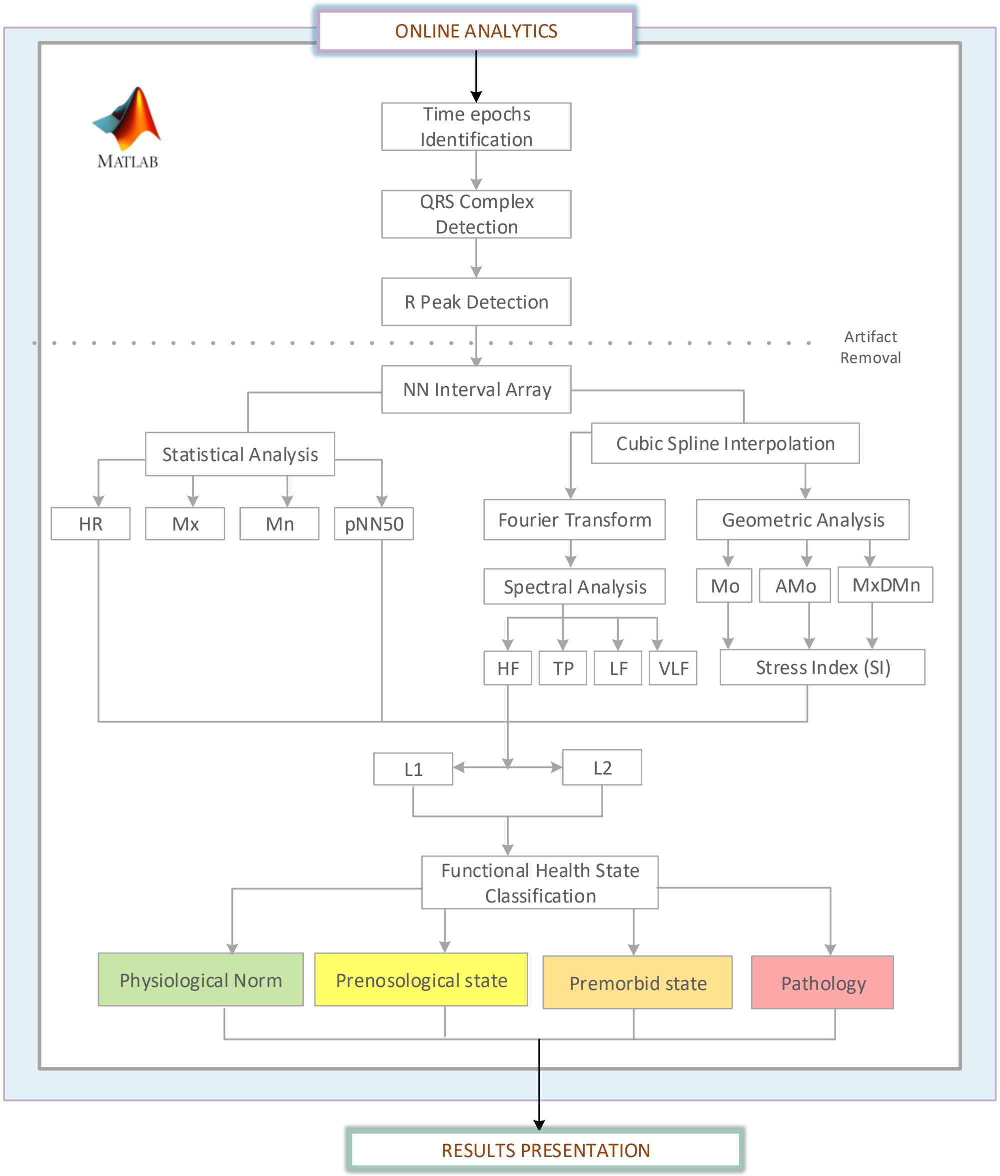

Figure 6-2. Functional health state as an instance within MATLAB environment.

6.2.1 QRS complex and R-peak Detection

The initial processing step of an ECG signal involves identification of time epochs, used to determine the beginning of each of the 5-minute windows of data, in the format <timestamp, ecg_value>. Once the temporal parameters of the signal have been established, the QRS complex and R peak detection begins. QRS complexes are detected by the wfdb detector algorithm, which is still relatively new and yet remains unpublished. The output of the R-peak detection algorithm is a list of time values where an R-peak was detected, which is subsequently used to generate an R-peak array in the format <timestamp, value>. Subsequently, the RR intervals are calculated by comparing the running difference in time between consecutive R-peaks, the output of which is an RR interval array in the format <timestamp, value>. The resulting RR interval array is subjected to initial pre-processing and filtering. The pre-processing and filtering of the ECG signal results in removal of

1) any RR interval less than 240ms;
2) any RR interval more than 2000ms;
3) any RR interval that differs from the mean by more than six standard deviations
4) any RR interval that differs from the last "correct" interval by more than 30%
5) the three smallest RR intervals
6) the three largest RR intervals.

The resulting array of RR intervals is ready for concurrent statistical analytics. It should be noted that this RR interval array can interchangeably be referred to as the NN interval array, representing the "normal" RR intervals free of artifacts.

6.2.2 The Functional Health State Canonical Variables Computation

The various geometric, statistical and spectral features of the heart rate variability, have been computed according to the previously established protocol, detailed in Chapter 4 and further used to compute the two canonical variables, L_1 and L_2, which form the foundation of the functional health state algorithm. The generalized equations of L_1 and L_2 are summarized below:

$$L_1 = 0.112HR + 1.006SI + 0.047pNN50 + 0.086HF$$

$$L_2 = 0.140HR + 0.165SI + 1.293pNN50 + 0.623HF$$

where, HR is the heart rate, SI is the stress index, pNN50 is the number of NN intervals differing by more than 50ms and the HF represents the high frequency band of the total spectral power. It should also be noted that HF and pNN50 are represented as a percentage in the L_1 and L_2 calculations. The resulting array of L_1 and L_2 values is ready for subsequent results presentation and visualization of the phase plane of functional health states.

6. 3 Results Presentation

The Results Presentation component of the demonstrated methodological framework within the context of Luna-2015 case study utilized the Microsoft Power BI application programming interface, further denoted as the Power BI API. Power BI API is a comprehensive platform that supports ingestion of heterogeneous types of data and performs various data management jobs. Power BI application programming interface was of particular interest, as it has the capacity to create interactive displays that can demonstrate the dynamicity of adaption mechanisms and identify the causal effect by analyzing the temporal aspect of the visualized heart rate variability features, combined with activity logs or any other relevant type and form of data. The Power BI API has the capacity to support data buffering of imported and derived datasets, both locally and on a pre-defined cloud-based instance of data warehouse. The various types of interfaces defined within the proposed framework, more specifically, crew interface, crew medical officer interface, ground-based Mission Control Centre interface and research centre interface have not been tested as part of this concept demonstration but can easily be created and customized to meet the mission-specific objectives.

6.4 Comparison of the Traditional Method vs Proposed MATLAB Instantiation of the Algorithm

The physiological data acquired with the Cosmocard data acquisition device, during Luna-2015 experiment, was analysed utilizing two implementations of the functional health state algorithm, namely the traditional computation approach, utilizing a complex of software applications, and the proposed MATLAB instantiation of the algorithm. The L_1 and L_2 values were calculated for every 5-minute sample and aggregated on an hourly basis over each 24-hour dataset to produce hourly L_1 and L_2 averages. The results of the comparison between the two implementations of the functional health state algorithm are summarized in a series of tables and figures to follow, generated per each study participant, and supplemented with the respective means and standard deviations.

Table 6-1 summarizes the frequency of each data collection instance, as the respective date and assigned day number, for each of the study participants. As such, subsequent results for each of the study participants will be reported using the day number (i.e. Day 1, 2, 3) for each instance of data collection.

Table 6-1. Data collection instances for each of the study participants during Luna-2015.

Subject	Day 1	Day 2	Day 3
1	29.10.2015	31.10.2015	02.11.2015
2	30.10.2015	01.11.2015	03.11.2015
3	30.10.2015	01.11.2015	03.11.2015
4	29.10.2015	31.10.2015	02.11.2015
5	29.10.2015	31.10.2015	02.11.2015
6	30.10.2015	01.11.2015	03.11.2015

The efficacy of the proposed MATLAB instantiation of the functional health state algorithm has been demonstrated within a series of tables (Table 6-2 through 6-7), located in the appendix. The tables summarized the results for Subjects 1 through 6, as hourly averages of L_1 and L_2 values, where L1 and L2 values represent the traditional instantiation and the L1_1 and L2_1 values represent the proposed MATLAB instantiation of the functional health state assessment. The means and standard deviation, comparing the two instantiations of the algorithm, were computed on the hourly-basis for L_1 and L_2 values and integrated within the tables. Daily averages of L_1 and L_2 values represented as means and standard deviations of the two instantiations were summarized in Figure 6-3. The computed L_1 and L_2 values for Subjects 1 through 5 were statistically significant and accurate, supported by a low standard deviation. The minor variance observed between the values was attributed to the specifics of QRS complex and R-peak detection algorithms of the respective instance of the functional health state assessment.

The reported results for Subject 6 introduced a great level of variance due the poor quality of the raw ECG signal, supported by high values of standard deviation. Traditional instance of the functional health state algorithm has excluded numerous segments of the raw ECG signal due to the inability to define the RR intervals and remove excessive noise and artifacts. While the MATLAB instantiation was able to perform a better QRS complex and R-peak detection, the variance in the computed L_1 and L_2 values remained. Further investigation and comparison of the various heart rate variability indices produced as a result of geometric, statistical and spectral analysis, revealed a significant variance within the geometric features of the heart rate variability. As such, the geometric feature variance and its respective assigned “weight” within L_1 calculation explained the large discrepancy in L_1 values. The L_2 values within the Table 6-7, Subject 6 were

Figure 6-3. Comparison of the efficacy of algorithm instantiation.

not affected as much, due to a much smaller weight of stress index within the L_2 equation. Overall, the proposed instantiation of the functional health state algorithm as a MATLAB instance has demonstrated great potential to support adaption-based analytics, while provide statistically significant accuracy and validity of the produced results. Further iterations of the proposed algorithm would necessitate improvement of the QRS complex detection algorithm. The QRS complex detection algorithm utilized in the proposed MATLAB instantiation algorithm was a part of an open-source toolkit and has not been released publicly yet. The review of the QRS complex detection algorithm of the traditional approach has not been possible either, due to propriety reasons.

6.5 Results Visualization and Physiological Significance

The dynamicity of adaption mechanisms throughout varying stages of the Luna-2015 case study for Subjects 1 through 6 is represented in a series of Figures provided below. The functional health states are presented as aggregated hourly values for each 24-hour dataset computed by two instances of the functional health state algorithm. The traditional instantiation is denoted by the day number (i.e. Day 1, 2, 3), while the proposed MATLAB instantiation is denoted by the day numbed supplemented with "new" (i.e. Day 1 (new), Day 2 (new), Day 3(new)).

The presented findings support the claim that HRV indices are effective indicators of cardiovascular system function and adaptation mechanisms. As depicted in Figures 6-4 and 6-5, the dynamics of vegetative regulatory mechanisms change in relation to various mission-specific tasks or time of the day. As becomes apparent, the degree of systems tension (L_1) changes significantly over the course of the experiment, in particular during nighttime (not visualized) but summarized within Tables presented in the appendix. This finding is consistent with the resting phase of regulatory mechanisms, at nighttime, that is also associated with replenishment of functional reserves. The level of functional reserves (L_2) varies insignificantly throughout the various stages of the study, as the study participants remain within the state of physiological norm or on the verge of prenosological state. An in-depth understanding of these dynamics presents great potential for early detection monitoring and development of personalized countermeasure protocols, so as to minimize the deleterious effects associated with conditions of spaceflight.

During this experiment, as is the case on the ISS, logs were captured reflecting workload and identifying specific tasks at any given point in time. As such, there is a potential to supplement physiological data with mission-specific tasks with the aim of developing targeted personalized stressor/resilience matrices.

A more dynamic presentation of the results is possible with utilization of Power BI interface, to enhance understanding of physiological processes and provision of medical care onboard the International Space Station. The proposed system enables live view of the results on the phase plane of functional states and enables provision of evidence-based clinical decision making aboard the spacecraft. It is important to note that the interactive visualizations, demonstrating the proposed functionality, could not be presented as static figures within this chapter.

This chapter has demonstrated that the proposed framework instantiated within the context of the ground-based Luna 2015 case study addresses the existing challenges of retrospective analysis of file-based packets of data and the tremendous data down-sampling that occurs during traditional processing of functional health state assessment. Moreover, this case study was able to demonstrate the ability of the proposed instantiation of the functional health state algorithm to generate the required heart rate variability indices, used for computation of L_1 and L_2 tuples and provide a more dynamic solution for data reporting and visualization. In so doing, this chapter has addressed the second and third hypotheses of this thesis.

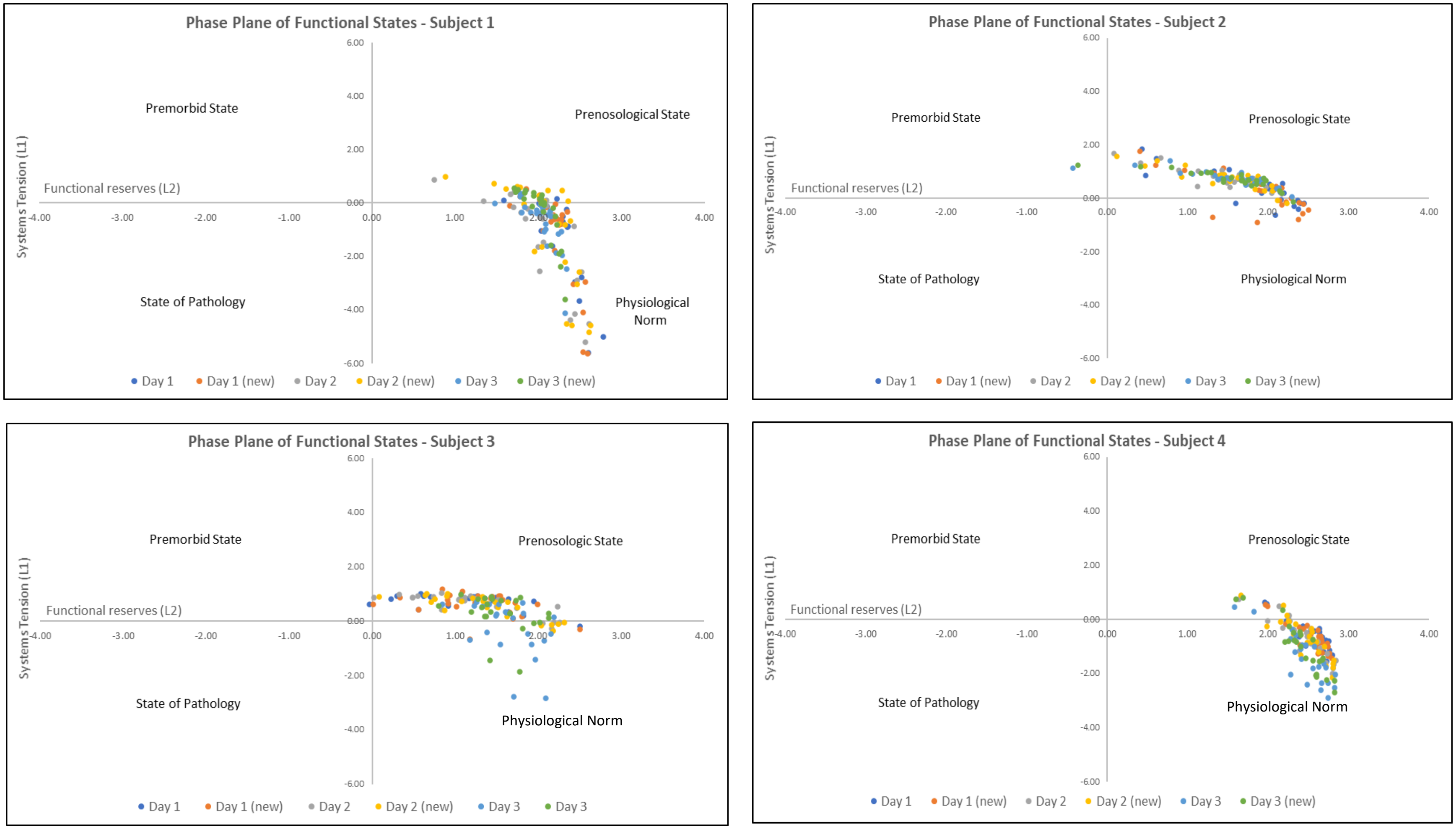

Figure 6-4. Phase plane of functional states for Subjects 1-4 during Luna 2015.

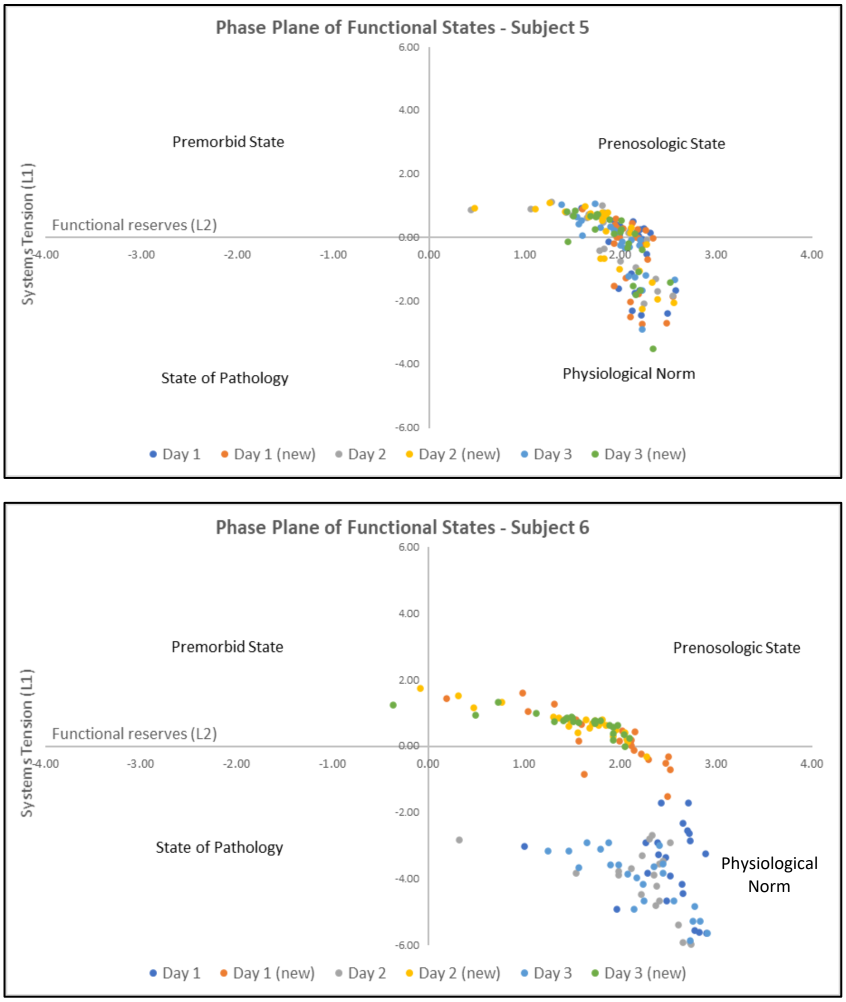

Figure 6-5. Phase plane of functional states for Subjects 5-6 during Luna 2015.

Chapter 7 – Case Study – Dry Immersion 2016

This chapter presents the instantiation of the big data analytics framework described in Chapter 5 and attestation of adaption-based analytics, namely the functional health state assessment, within the context of ground-based study "Dry Immersion 2016". The detailed description of methodology used to re-engineer the functional health state algorithm as an instance within MATLAB environment has been provided in Chapter 6. This enables the second and third hypotheses of this thesis to be addressed by a further case study than that presented in Chapter 6.

This chapter also presents an overview of the Dry Immersion method, which hasn't been widely used outside of its founder region, the Russian Federation.

The Dry Immersion 2016 case study has been conducted at the Institute of Biomedical Problems of the Russian Academy of Sciences in Moscow, Russia. The overarching purpose of the study was to utilize the method of Dry Immersion (DI) to model conditions of weightlessness and its respective physiological effects, so as to enhance the understanding of the triggers, timelines and outcomes of the short-term exposure to conditions of spaceflight environment. The twelve study participants were healthy male volunteers between the ages of 29±2 years old, with an average height of 177 ±1cm and weight of 70.2±2.6kg. The study cohort was further assigned into two groups, the control (age 24±1 y. o.; height 178±1cm, weight 68.3±4.2kg) and experimental (age 34±2 y. o.; height 177±1cm, weight 72.2±3.4kg) group, each of which had a total of six study participants. The experimental group wore an axial loading suit, known as "Penguin" for a total of 4 hours per day. The "Penguin" suit was used to apply differential axial loads on the various parts of the body. The degree of loading was determined on an individual-basis in accordance with the guidelines established for the International Space Station.

A 5- day dry immersion study utilized two single-person dry immersion baths. There was a total of 6 rotations of study participants. Tap water was used to fill the immersion baths that were thermoregulated at 33^{0}C. A waterproof elastic fabric was used as a barrier between the water and the skin of the study participants. The head-out depth supine immersion of the study subjects was selected for the purpose of the study. The study participants remained relatively motionless with limited ability to exit the baths for a daily average of 10-15 minutes to perform personal hygiene. Study participants remained under 24-hour surveillance throughout the entire duration of their 5-day dry immersion. The study's main objectives were acquisition of new scientific information and approbation of methods and technologies designed for space experiments on the ISS. There were several research studies performed by multiple research teams in association with the Dry Immersion experiment. The research presented in this chapter was the subject of a study that was reviewed and approved by the IBMP Research Ethics Board (Protocol #432), and the Ontario Tech University Research Ethics Board under REB# 15-047 Integration of Russian Cosmonaut Monitoring with Artemis and Artemis Cloud. This research has been supported by the Canada Research Chairs program (#950-203427 and #950-225945) and the Canadian Foundation for Innovation (#203427).

7.1 Overview of the Water Immersion Method

The method of water immersion dates back to the early 1970's, when it was first developed as a ground-based analog of weightlessness by the Russian scientists, K.B. Shulzhenko and I.F. Vil-

Vil’ams [1, 2]. Over the last half a century, the method of water immersion has been widely used in Russia, with consistently scheduled biannual experiments at the Institute of Biomedical Problems of the Russian Academy of Sciences. However, the usability of the method outside of its founder region has been extremely limited, with only a few reported studies in India and Austria [1]. In addition, the European Space Agency has only recently issued a call to explore the method of dry immersion and validate its efficacy in modeling spaceflight induced deconditioning [3]. The lack of literature available to the English-speaking community has been the primary factor contributing to the limited exposure of the water immersion method to a global scientific community. As such, this chapter begins with a brief overview of the water immersion method, detailed description of which is available in [1].

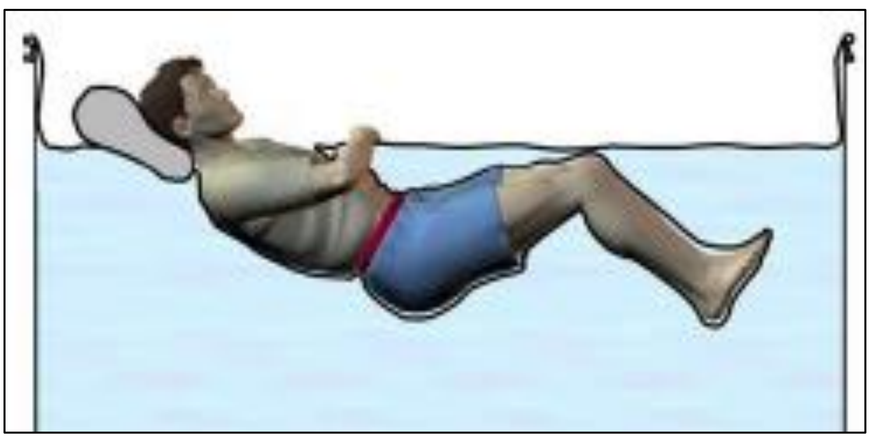

Figure 7-1. Dry Immersion (DI) method adopted from [2].

The method of water immersion can be classified into two main types, namely the “wet” and “dry”, determined on the basis of the study duration. The method of wet immersion represents immersion with direct skin-water exposure, the maximum duration of which does not exceed 6-12 hours, due to immanent risk of development of skin macerations and other skin-related complications [1]. On the contrary, the method of dry immersion utilizes a thin elastic waterproof fabric to create a water-skin barrier, schematically represented in Figure 7-1.

It is important to note that the size of the fabric greatly exceeds the size of the immersion bath, creating the effect of “supportlessness” and enabling execution of studies of much longer duration [1]. To-date, the longest reported dry immersion study lasted 56 days [1].

In Russia, single-person immersion baths are utilized for the experiments. The baths are filled with thermoneutral tap water (32.5-34.5^{0}C), which can be adjusted to subject’s preference, within the specified temperature limits, and remain thermoregulated for the duration of the immersion [1, 2]. There are four main variations of the dry immersion, categorized on the basis of the position and depth of subject immersion. More specifically, the position of immersion can be supine or sitting, while the depth can range from head-out to head and upper chest out [1]. The specific variations of position and depth of immersion are determined on the basis of study objectives, with the ability to mimic greater spaceflight-induced responses by head-out immersion [1]. It is important to note that some limited activity is permitted throughout the duration of the immersion. More specifically, subjects are permitted to exit the baths for a daily average of 10-15 minutes to perform personal hygiene. In addition, study participants have hands atop, enabling them to eat, do computer work or upper-body countermeasure protocols [1].

To-date, the method of dry immersion has demonstrated its effectiveness in triggering weightlessness-induced physiological deconditioning in a relatively short period of time, typically ranging between 3-7 days [1, 2]. It has proven effective in investigations of electrolyte balance, cardiorespiratory changes, muscular deconditioning and the adaptive responses of the various organ systems [1]. Meanwhile, the study cohorts have predominantly been limited to male participants, and as such gender- and sex-based stratification of the results has not been available [1]. Although, ESA is organizing the first all-female dry immersion experiment, which is scheduled to take place at the end of 2020 at MEDES facility in Toulouse, France [3].

7.2 Data Collection

Physiological data acquisition, the electrocardiogram recordings in particular, were performed with the use of commercial Holter-style ECG monitoring device “Cosmocard” during the Dry Immersion 2016 experiment. ECG sampling rate was set to 500 samples/second. The ECG recordings were scheduled and discontinuous. The data collection was performed on the daily-basis, exclusively at night time, beginning between 20:00-22:00 and finishing between 7:00-8:00 the next day. The temporal specifics of each data collection instance are summarized in Figure 7-2.

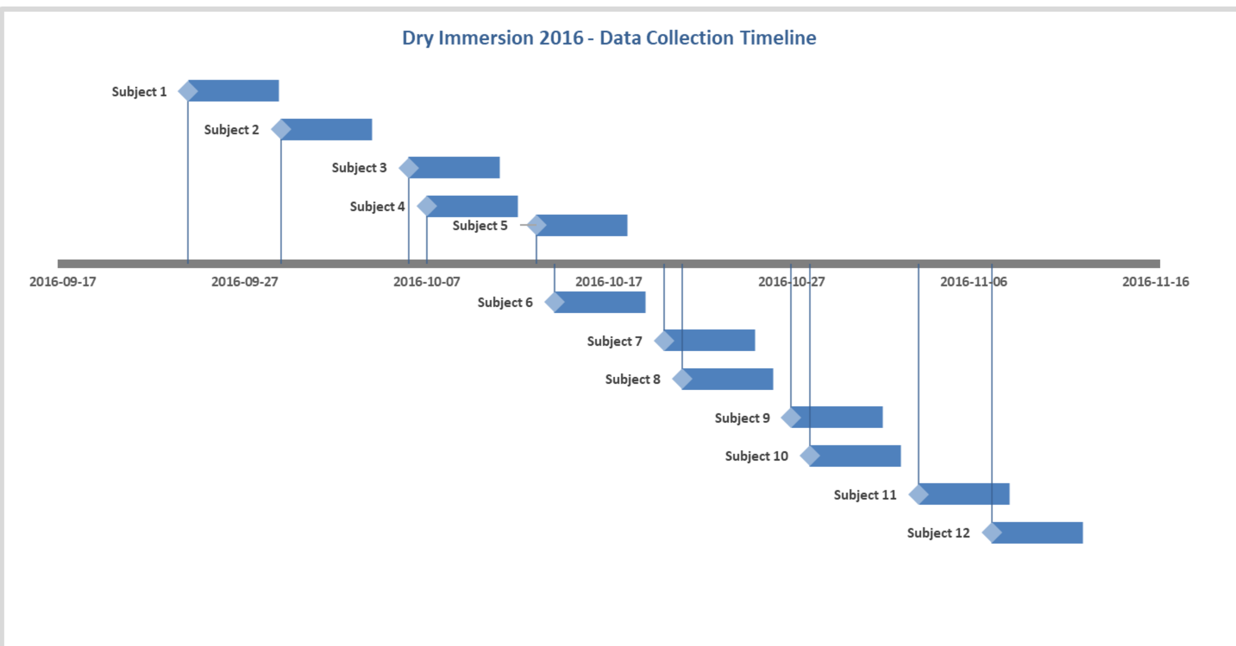

Figure 7-2. Dry Immersion 2016 data collection timeline.

It should be noted that every even subject number (i.e. 2, 4, 6, 8, 10, 12) represents control group, while odd numbers (i.e. 1, 3, 5, 7, 9, 11) correspond to the experimental group. Following each instance of data collection, the Cosmocard device was docked for wire-based data acquisition and transmission to occur. The local research team stored the collected data locally on a PC and did some preliminary data pre-processing. Preliminary data pre-processing included conversion of the original *.ecg file formats into *.hea and *.dat file formats. The re-formatted data files were subsequently uploaded onto a cloud-based drive to transfer to the international research teams for retrospective data processing and analysis. The outlined data collection approach presented fundamental limitations to the approbation of the middleware data capture and data integration components of the framework proposed within this thesis.

7.3 Adaption-Based Analytics

The adaption-based analytics of the acquired ECG recordings were performed by attestation of the re-engineered functional health state algorithm as an instance within MATLAB environment, detailed description of which is available in Chapter 6. The extraction of the various HRV features, including the percentage of high frequency power (HF), number of successive NN intervals differing by more than 50 milliseconds (pNN50), heart rate (HR) and stress index (SI) were performed on 5-minute tuples of data. The acquired HRV features were used for computation of L_1 and L_2 canonical variables on 5-minute tuples of data and further aggregated into hourly averages.

The cross-reference of the acquired hourly averages of L_1 and L_2 canonical variables for two instantiations of the functional health state algorithm, namely the traditional approach that utilizes a complex of software applications and the proposed instantiation as an instance within MATLAB environment were performed on Subject 1. The cross-referenced hourly averages of L_1 and L_2 canonical variables, along with the respective means and standard deviations were summarized hourly on the daily basis, detailed in Tables 7-1 through 7-5, located in the appendix. Within the Tables, L1 and L2 corresponds to the traditional computation approach, while L1_1 and L2_1 corresponds to the MATLAB instantiation of the functional health state algorithm. Figure 7-3 represents the hourly summaries of means and standard deviations for L_1 and L_2 of the two algorithm instantiations, where the respective days are abbreviated as D1 for Day 1, D2 for Day 2 and so on.

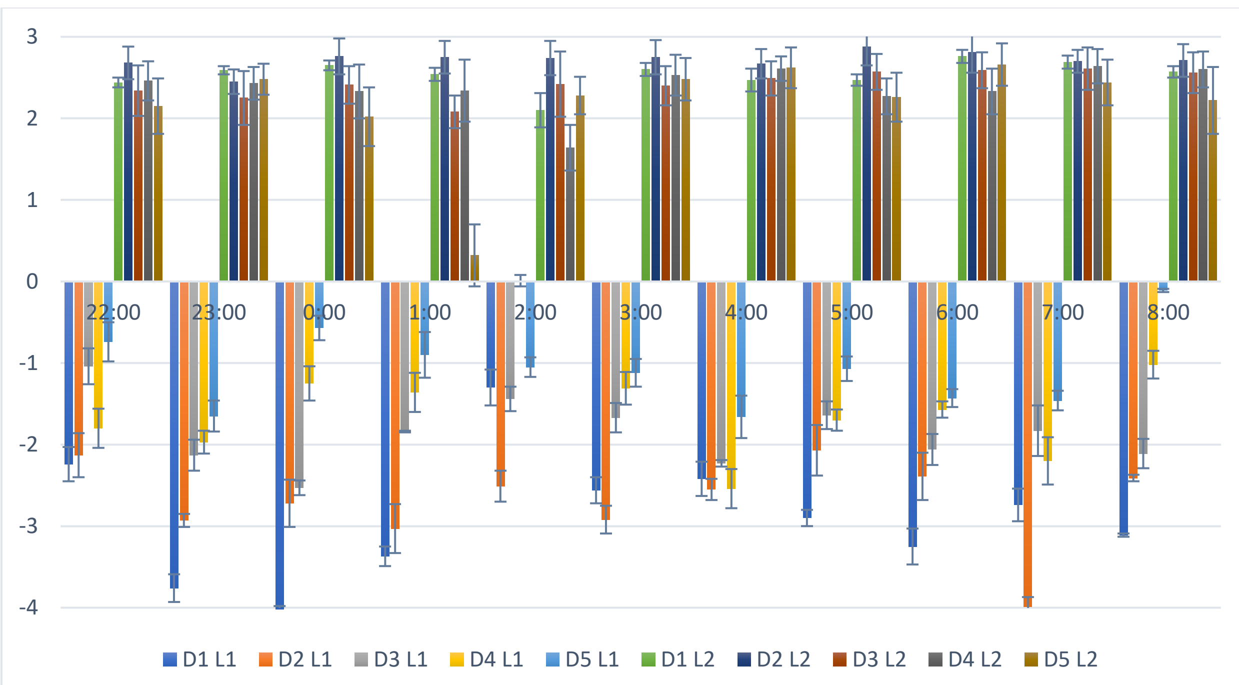

Figure 7-3. Hourly summaries of L1 and L2 means and standard deviation for Subject 1 during DI 2016.

The computed L_1 and L_2 values for Subject 1 throughout the duration of the immersion (Day 1-5) were statistically significant and accurate, supported by a low standard deviation. The minor variance observed between the values was attributed to the specifics of QRS complex and R-peak detection algorithms of the respective instance of the functional health state assessment.

7.4 Results Presentation

The dynamicity of adaption mechanisms throughout varying stages of the Dry Immersion 2016 case study for Subjects 1 through 12 are represented in a series of Figures provided below. The functional health states are presented as aggregated hourly values for each instance of data collection computed with the MATLAB instance of the functional health state algorithm. As becomes apparent from Figures 7-4 through 7-6, there is a lot of intra- and inter-individual variations in the level of experienced systems tension (L_1) throughout the various stages of the Dry Immersion 2016 experiment. Some of the variance in the L_1 is attributed to the "noise", also referred to as the artifacts within the raw ECG signals. It has been reported that some technical issues were experienced during the execution of the experiment, resulting in equipment malfunction and/or detachment of electrodes due to an increased level of humidity within the research facility. As such, records for Subject 7 Day 1, Subject 9 Day 5 and Subject 11 Days 1, 2 have been affected.

The poor quality of the aforementioned raw ECG signals has led to failure of the MATLAB code due to inability to read segments of the respective files. As such, manual investigation has been completed to identify the malfunctioning sections of the signal, which have been removed to enable the analysis of the remaining sample file. More specifically, the first twenty 5-minutes tuple of data have been excluded from Subject 7 Day 1, ten 5-minute tuples of data were excluded from Subject 9 Day 6 and fifteen 5-minute tuples of data were excluded from Subject 11 Days 1 and 2. The poor quality of the initial segments of the data corresponded to the initial

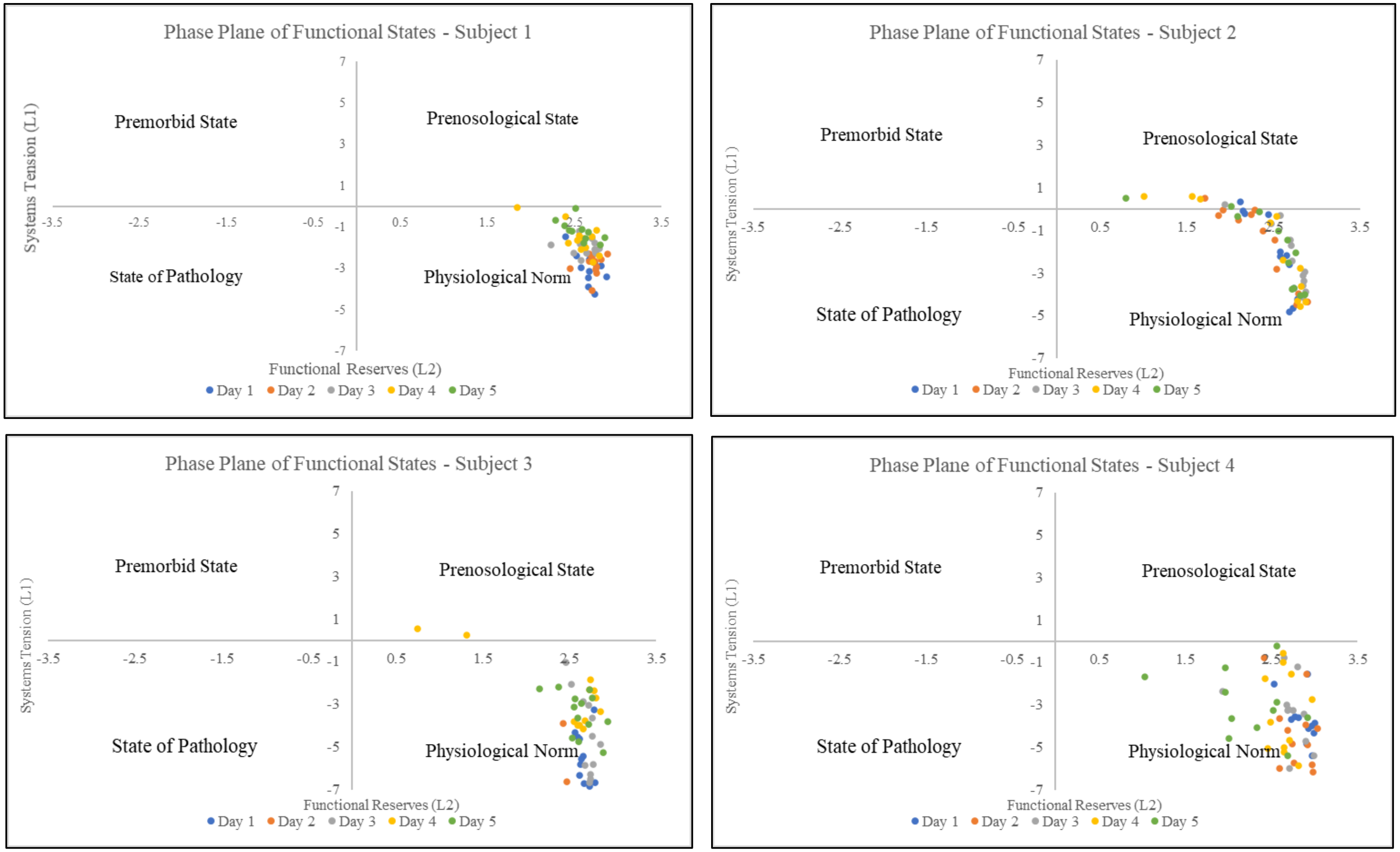

Figure 7-4. Phase plane of functional states for Subjects 1-4 for the duration of DI study.

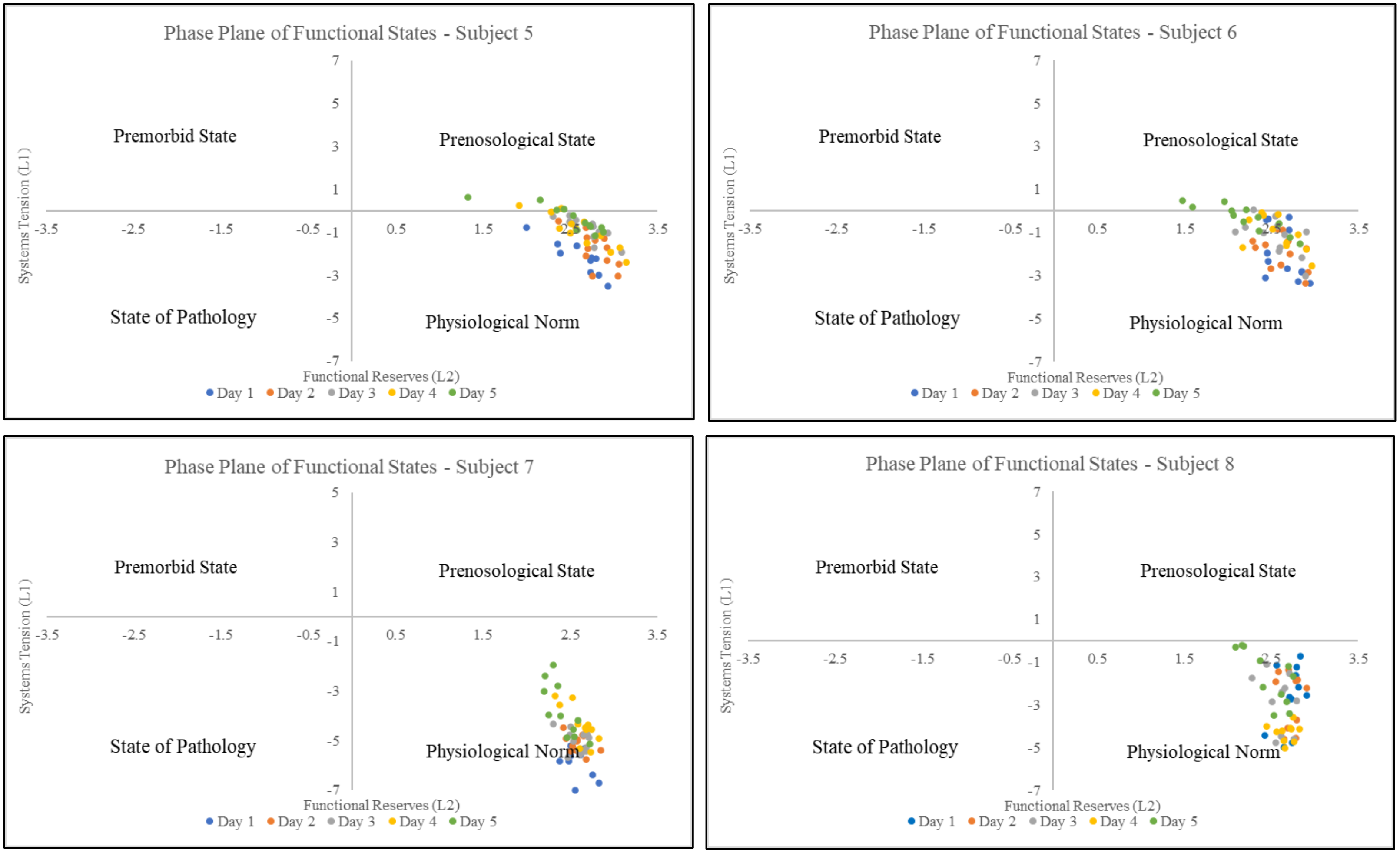

Figure 7-5. Phase plane of functional states for Subjects 5-8 for the duration of DI study.

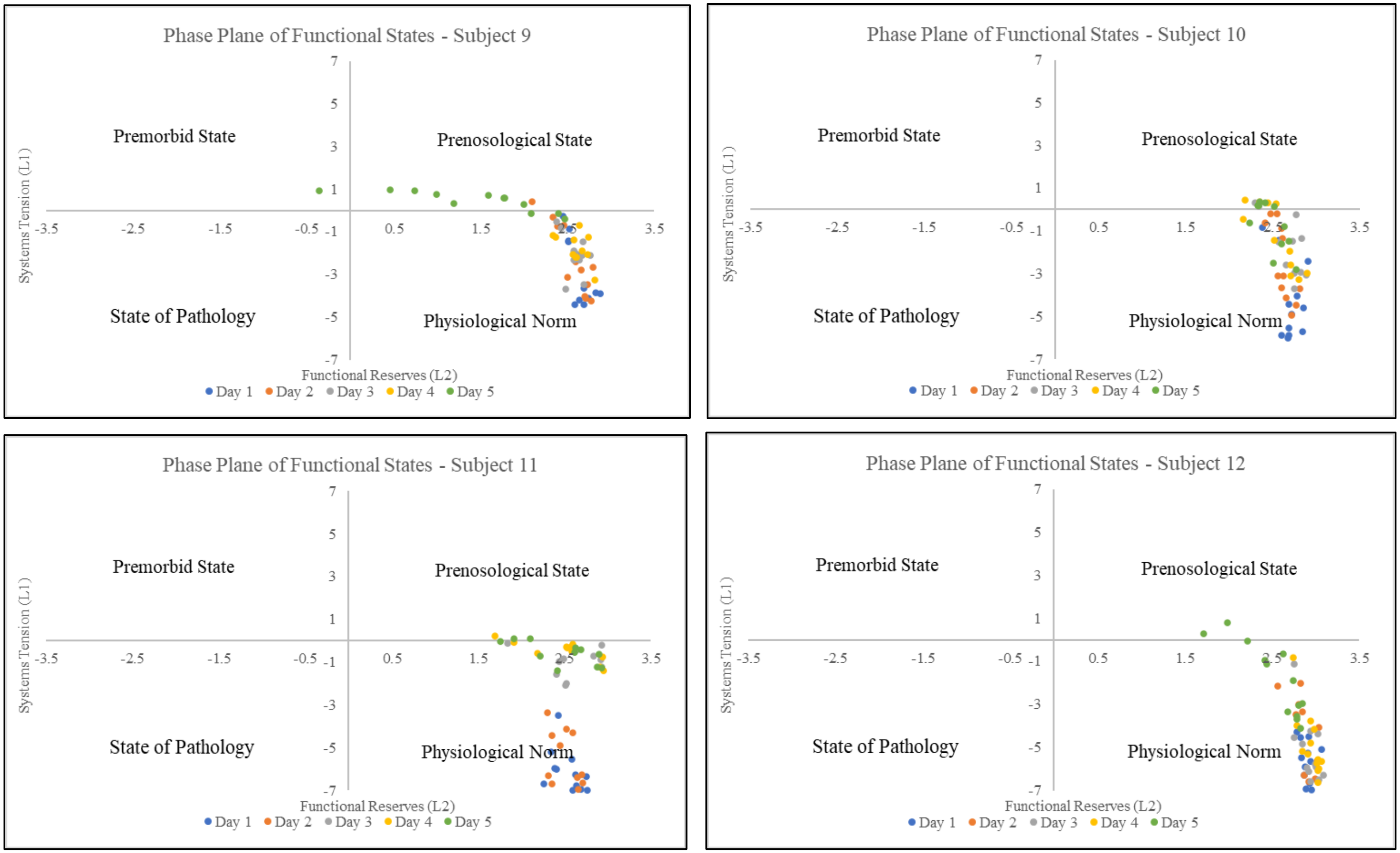

Figure 7-6. Phase plane of functional states for Subjects 9-12 for the duration of DI study.

set-up time, which may have resulted in improper placement of the electrodes that has been fixed once the issue was recognized.

The level of functional reserves (L_2) varies insignificantly throughout the various stages of the study, as the study participants remain within the state of physiological norm or on the verge of prenosological state. An in-depth understanding of these dynamics presents great potential for early detection monitoring and development of personalized countermeasure protocols, so as to minimize the deleterious effects associated with conditions of spaceflight.

Significant stress index variations, corresponding to the geometric features of the HRV signal, have been observed over the course of the experiment, suggesting an increased sympathetic activity of regulatory mechanisms [2, 4]. Prior research has established an association between stress index variations and onset of painful stimuli that can be attributed to discomfort, back and abdominal pain, typically reported in weightless [2]. Detailed analysis of the various HRV features are beyond the scope of the work presented in this thesis. However, the proposed integrated big data framework utilizing stream computing demonstrates an enormous potential to support health, wellness, activity and adaption-based analytics so as to improve understanding of weightlessness induced deconditioning, such as that modelled within Dry Immersion experiment.

7.5 Sliding-Window Analysis

The heart rate variability analysis performed with re-engineered functional health state algorithm, as an instance within MATLAB environment, on 5-minute tuples of data have been presented in prior section. The traditional heart rate variability data processing approach has been utilized. More specifically, a time tuple has been generated for every 5-minute interval, starting at time 0:00-4:59min, 5:00-9:59min, 10:00-14:59min and so on, schematically represented in Figure 7-7.

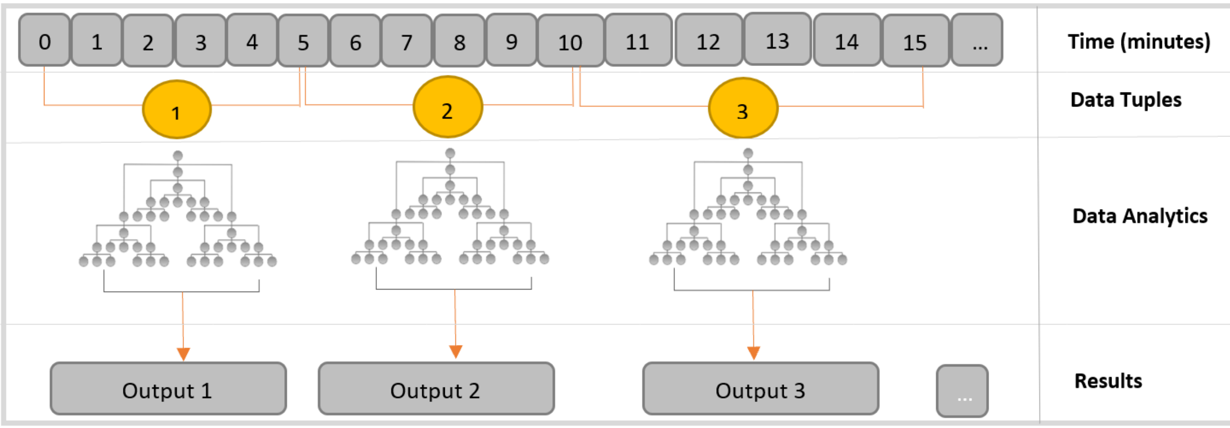

Figure 7-7. Schematic representation of traditional HRV data processing approach [4].

The various heart rate variability features, schematically represented as grey dots within the figure, have been calculated and subsequently aggregated into bins representative of the average value observed within the specified 5-minute interval, denoted as Output 1, 2, 3 and so on. Conventionally, the acquired 5-minute values are further aggregated as single hourly or daily values to indicate the activity of regulatory mechanisms and their respective compensatory processes. This approach has been widely used since the early days of manned space exploration and has demonstrated effectiveness in providing valuable physiological information [4]. However, a number of limitations of the traditional HRV data processing approach have been identified, which are of high relevance for in-flight health monitoring. More specifically, in-flight physiological data availability is subjected to the limitations of biomedical monitoring modalities, environmental factors (i.e. humidity, fluid dynamics, etc) and demanding astronaut schedules, all of which contributed to relatively short-term, discontinuous data acquisition. As such, the acquired physiological datasets greatly limit in-depth health, wellness and adaption-based analytics, emphasizing an urgent need for a paradigm change.

A novel method of sliding-window approach for heart rate variability analysis is proposed to overcome the existing challenge of limited size physiological datasets available for health, wellness and adaption-based analytics. The proposed approach enables generation of larger arrays of physiological data, utilizing the limited sample sizes that are currently available. Figure 7-8 provides a schematic representation of the proposed sliding-window approach for heart rate variability analysis.

The grey squares numbered 1-10 represent 1-minute time windows. Contrary to the traditional data processing approach, the 5-minute data tuples are generated at time 0:00-4:59, 01:00-05:59, 02:00-06:59, 03:00-07:59, 04:00-08:59, 05:00-09:59 and so on, denoted by coloured circles numbered 1-6 within the Figure 7-8. The grey dots correspond to geometric, statistical and frequency-domain analysis of the HRV for each of the 5-minute data tuples, while the Output bins provide aggregated 5-minute summaries of HRV features for the data tuple of interest. As such, the proposed approach demonstrates the capacity to increase the available sample size by generating more data points, within the same, relative short period of time. Increased sample size contributes to improved quality and greater stability of numerical estimates, and enhanced applicability of parametric criteria [4]. Furthermore, it has the capacity to support additional statistical analysis, such as the cross-correlation analysis, which are not possible with conventional data processing approach. In addition, larger array of physiological data has great potential to support fault tolerance and a more in-depth analysis, supporting de-trending of the

HRV to ensure that the observed physiological patterns are reflective of compensatory processes, rather than attributed to external noise or artefacts.

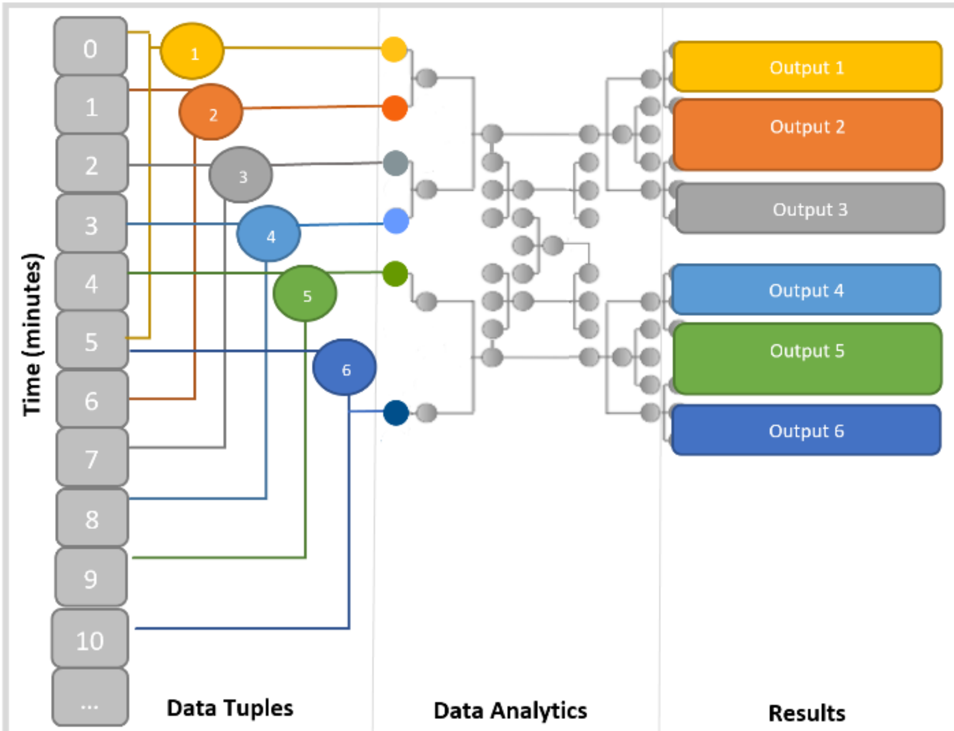

Figure 7-8. Schematic representation of real-time sliding window analysis of heart rate variability [4].

The preliminary protype of the proposed sliding-window approach for heart rate variability analysis is demonstrated on Subject 1 for the entire duration of the Dry Immersion experiment, represented in Figure 7-9. Figure 7-9 displays the phase plane of functional states as 5-minute aggregates of the corresponding L1 and L2 values. The dynamicity of regulatory mechanisms becomes apparent between each of the calculated data tuple, further demonstrating the great potential of the proposed approach to identify unstable states and establish relationships between possible triggers of produced physiological responses. As such, a sliding window approach has the capacity support early detection monitoring and discovery of new clinically significant physiological patterns, both retrospectively or in real-time. Further attestation of the proposed sliding-window approach along with modified time windows will be the subject of future studies. Once validated, the proposed approach of sliding window analysis will be deployed within Online Analytics component of the integrated big data framework, proposed within this thesis, to support both real-time and retrospective analytics.

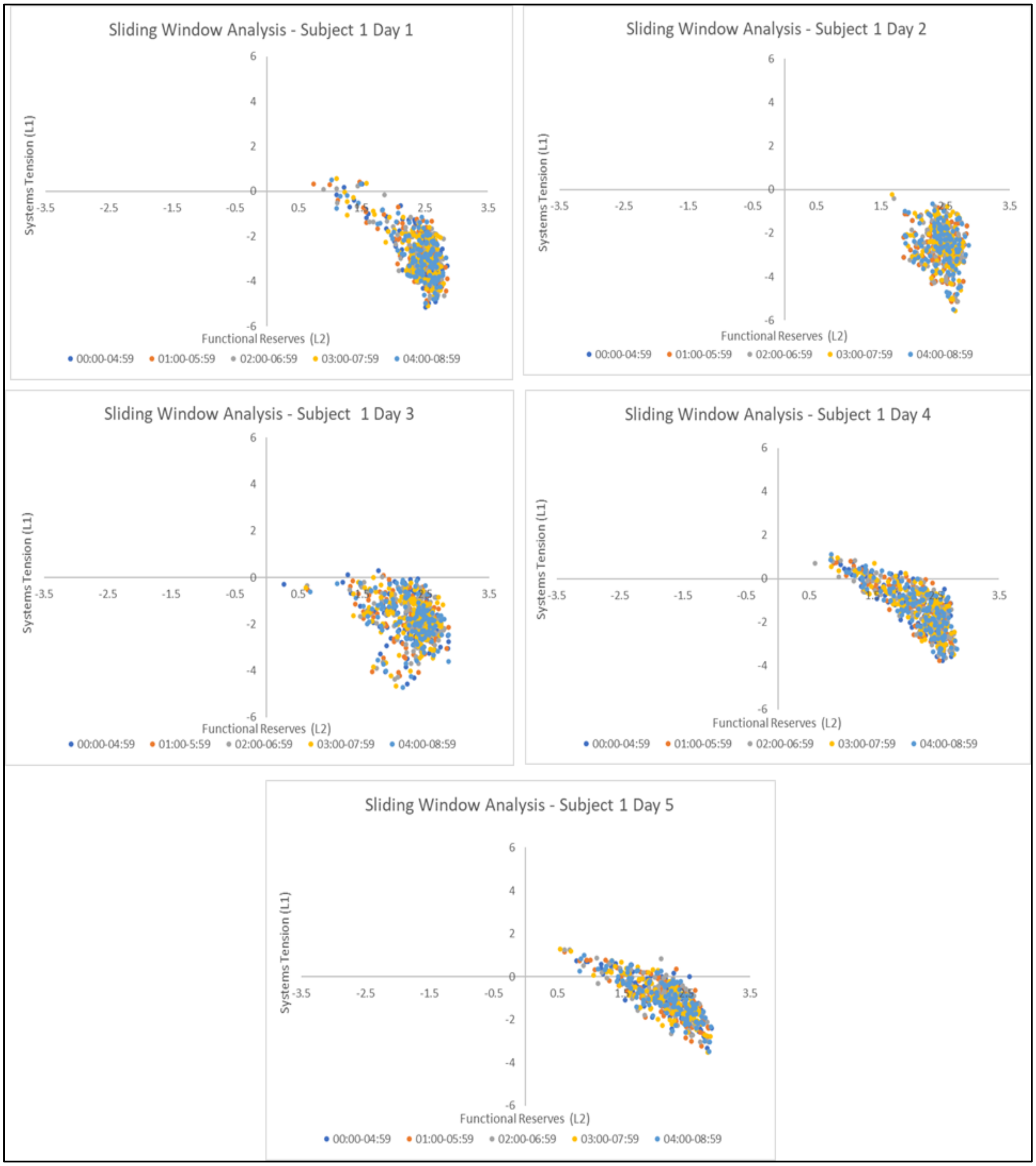

Figure 7-9. Instantiation of sliding window analysis within the context of DI study.

7.6 Conclusion

This chapter has demonstrated that the proposed framework can be instantiated within a big data analytics platform, clinical application of which has been demonstrated within the context of ground-based study Dry Immersion 2016. In so doing, this chapter has addressed the second and third hypotheses of this thesis in addition to what was presented in chapter 6. This chapter further validated the efficacy and accuracy of the re-engineered functional health state algorithm, as an instance within MATLAB environment, to support near real-time adaption-based analytics. Furthermore, this chapter has revealed the challenges of limited physiological datasets, emphasizing the need for a paradigm change, to support in-depth analytics and generate larger arrays of physiological data within the given datasets. As such, a novel method of a sliding-window approach for heart rate variability analytics has been proposed. The preliminary instantiations of the proposed sliding-window approach have been demonstrated within the context of ground-based Dry Immersion 2016 study. The proposed approach has demonstrated capacity to support generation of larger arrays of physiological data and de-trending of the HRV, in order to reveal stressor-induced physiological responses and contribute to isolation of external noise and artefact-induced responses. As such, it has great potential to support early detection monitoring and discovery of clinically significant physiological patterns.

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3. ESA Int. 2020. *Research Announcements*. [online] Available at: http://www.esa.int/Science_Exploration/Human_and_Robotic_Exploration/Research/Research_Announcements?t=3. [Accessed 15 May 2020].
4. Prysyazhnyuk, A., McGregor, C., Chernikova, A., Rusanov, V., 2019, A sliding-window real-time processing approach for analysis of heart rate variability during spaceflight. 70th International Astronautical Congress Proceedings, Washington, D.C., USA, 21-25 October, 2019.

Chapter 8 - Conclusion

8.1 Summary

Technological and scientific advancements continue to enable safe prolonged human presence in space, while extending the boundaries of manned exploration from low-Earth orbit into deep space. As humankind prepares to embark on exploration-class missions, to the Moon and Mars, mission objectives, risks and challenges become more complex and vastly different from majority of human manned space exploration experience known to-date. The potential health risks associated with deep space exploration are expected to amplify, the mitigation of which would necessitate complex and autonomous in-flight medical capacity, which has not been available to-date. The literature review within Chapter 2 of this thesis identified the implications of spaceflight-induced health deconditioning and its respective in-flight diagnostic monitoring modalities and their limitations. More specifically:

1) Space flight induced deconditioning affects mental, physical and social well-being.
2) Existing biomedical monitoring modalities are impractical and inconvenient.
3) Physiological data acquisition is file-based, limited and discontinuous.
4) Data processing approaches are fragmented and retrospective, resulting in extensive data down-sampling, smoothing and an enormous amount of data loss.
5) Significant amount of biomedical data remains unused.

As such, it was concluded that there is an urgent need in development of innovative solutions to enhance medical capacity in-flight and enable the paradigm change from reactive to proactive prognostics, diagnostics and health management during deep space exploration.

The limitations exposed by literature review in current space medicine in-flight health monitoring practices resulted in the following hypothesis for this thesis:

1. *That a big data framework can be designed to support the development of space medicine clinical decision support systems to assess astronaut's health and adaption to conditions of spaceflight in-real time.*
2. *That the proposed framework can be instantiated through the extension of an existing big data analytics platform.*
3. *That the application of the framework and instantiation can be demonstrated with adaption-based analytics, namely the functional health state assessment, in near real-time and real-time environments.*
4. *That an alternative data processing approach, namely the sliding-window analysis can be instantiated to enhance the adaptation-based analytics.*

The foundations of information technology systems and conceptual model of clinical decision-support systems architecture within the context of space medicine have been introduced in Chapter 3. This chapter further identified the novel approaches, such as big data and stream computing, which have an enormous potential to support autonomous health monitoring in-flight that have not been leveraged within the context of space medicine to-date. Chapter 4 described the implications of space flight environment on human health, and how the concept of norm differs on Earth and in outer space. It further introduced the method of adaption-based assessment that has been used retrospectively to assess health and wellness of Russian cosmonauts aboard the ISS. Chapter 5 proposed the big data framework, utilizing stream computing, to support real-time clinical decision making within the context of space medicine. The proposed framework incorporated the core principles of Advanced Crew Medical System (ACMS) Space Medicine Decision Support System (SMDSS) as outlined by the Canadian Space Agency, and further extended the existing Artemis, big data analytics platform. The proposed framework adapted the data lifecycle approach to address limitations of existing information systems. The embedded data lifecycle approach ensured that the framework can support the data throughout all of its stages, beginning with data acquisition, collection, processing and storage. This approach presented great potential to minimize the enormous loss of data that occurs when a complex of software applications is used to perform the various data processing jobs, resulting in data averaging and smoothing in each processing step.

The proposed big data framework presented in this thesis is made up of eight core components, which are the data collection, data capture, data integration, data persistency, online analytics, knowledge discovery, (re)deployment and results presentation. The proposed framework extends the type and amount of available data sources to include structured (medical, environmental and activity data), unstructured (diagnostic imaging) and semi-structured (clinical observations and personal assessments) data types. It further introduces the middleware data capture component to support multi-modal data acquisition, such as wired and wireless, and enable structured data routing and queueing, in accordance with the data format (i.e. streaming, file-based), supplemented with data buffering mechanisms. An extension to the data integration component has been proposed by introduction of a message sub-flow, to support integration and linkage of file-based packets of data with relevant streaming data. The results presentation component has been extended to include an interactive data visualization application programming interface. The proposed result presentation component has the capacity to support preparation of interactive dashboards with multi-interface functionality, established on the basis of end-user account control settings and mission objectives.

The instantiation of the proposed framework within extended Artemis platform has been demonstrated within the context of two ground-based studies, namely the “Luna 2015” and “Dry Immersion 2016”, presented in Chapter 6 and Chapter 7 respectively. The demonstration of the proposed framework within the context of ground-based studies has introduced modifications to existing adaption-based analytics. The conventional adaption-based assessment, namely the functional health state algorithm, has been re-engineered as a MATLAB instance to support near real-time and real-time analytics. Further to that, a prototype of a sliding-window approach for heart rate variability analysis has been proposed. Instantiations of re-engineered functional health state assessment and introduction of a sliding-window approach present novel methods for real-time big data analytics during spaceflight, further demonstrating capacity for remote autonomous functionality and clinical discovery, as well as improved health outcomes.

The clinical significance of the proposed framework within the context of two ethically approved terrestrial analog studies, Luna-2015 and Dry Immersion 2016, has supported the earlier findings of the dynamic nature of human organ systems and their regulatory mechanisms. It has further demonstrated that the dynamics of regulatory mechanisms, signifying adaptive capacity of the human body, change throughout the duration of the experiment in response to task-specific activities or the respective periods of the circadian rhythm, associated with specific activity of organ systems. The instantiation of the proposed framework further revealed the importance of assessment of each 5-minute interval, while the introduction of the sliding-window approach demonstrated great potential to support de-trending of the HRV to establish causal relationships between a particular stressor and the produced physiological response. As such, the application and instantiation of the proposed framework and multi-modal adaption-based analytics demonstrate great potential to enhance early detection monitoring and inform clinical decision making in-flight. Thereby, contributing to practical and meaningful use of physiological data to support proactive prognostics, diagnostics and health management during space flight.

8.2 Research Contributions

The research area contributions to knowledge within this thesis are, specifically:

Health Informatics:

- Design of a wholistic, integrated big data framework to support the development of an autonomous clinical decision support system in the field of space medicine.
- Design extensions to the existing big data platform to support acquisition and processing of multivariate data types. Enable integration of relevant file-based data packets and physiological data streams.

Computer Science:

- Demonstrate the potential of real-time online health analytics by re-engineering retrospective file-based in-batch adaption-based data processing method to enable automation of adaption assessment and support near real-time and real-time functionality.

Space Medicine:

- Demonstrate the potential of proposed framework to enhance practicality and usability of the acquired data and capacity to support improved health outcomes within the context of ethically approved ground-based clinical research studies.

8.3 Limitations and Future Work

Existing in-flight biomedical monitoring modalities present a significant limitation to approbation of the proposed framework. More specifically, the commercial-grade Holter-style ECG monitoring device utilized for physiological data collection within the Russian segment of the ISS, as well as in ground-based studies, namely the Luna-2015 and Dry-Immersion 2016, functions as a record and store device. As such, the data collection instance has to complete before the device can be docked for wire-based data transmission and subsequent data processing to occur. The outlined data collection approach presented fundamental limitations in approbation of the middleware data capture and data integration components of the proposed framework. In addition, technical issues with "Cosmocard" device have been reported during the Dry Immersion experiment, attributing to increased level of humidity during the execution of the research study. The wire-based attachment to electrodes also contributed to increased levels of external "noise" and artefacts, compromising the quality of the produced ECG signal. As such, the use of alternative wireless data acquisition devices needs to be considered. The ability of the data collection device to support wireless data transmission would contribute to practicality and feasibility of continuous health monitoring in-flight.

Another limitation that impacted the approbation of the proposed framework was the instantiation of the re-engineered adaption-based analytics within the Online Analytics component of the Artemis platform. The Online Analytics components utilizes IBM InfoSphere Streams, within which various clinical algorithms are deployed as stream graphs, written in streams programming language. The stream computing approach has a number of differences in computation of statistical, geometric and frequency-domain analytics as opposed to conventional data processing approaches utilized by various programming languages. The fundamental differences have been identified in frequency-domain component of the adaption-based assessment, which will necessitate further exploratory research to support the development of functional health state streams graph. Further to that, instantiation of a sliding window approach for heart rate variability analytics will be the focus of future studies, within which the data tuple size will be decreased.

The end-to-end attestation of the proposed framework will be the subject of future studies, so as to demonstrate its potential as an autonomous clinical decision support system in space medicine. It will further demonstrate its capacity to support real-time health analytics, clinical discovery and improve early detection of maladaptive responses during spaceflight.

8.4 Concluding Remarks

The work presented in this thesis has recognized the importance of information systems in the provision of health services in space. This thesis presented an integrated big data framework, utilizing stream computing, to support real-time clinical decision-making during spaceflight. It integrated novel big data, stream computing and data lifecycle approaches to support the development of a comprehensive, autonomous space medicine clinical decision-support system. The proposed framework has been demonstrated within the context of two ground-based studies that have been ethically approved. The research findings reported within this thesis have demonstrated the enormous potential of the proposed framework to support real-time health, wellness and adaption-based analytics during spaceflight. While the proposed framework has been demonstrated within the context of space medicine, it has a great potential to benefit global communities on Earth, ranging from remote communities to individuals working and or living under conditions of chronic environmental stress.

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Appendix

Table 6-2. Hourly summaries of L1 and L2 for Subject 1 during Luna 2015.

	Day 1								Day 2								Day 3							
Time	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2
10 AM	-0.02	0.13	0.05	0.10	2.01	2.01	2.01	0.0	-0.58	0.26	-0.16	0.59	1.84	2.01	1.92	0.12	-0.27	0.17	-0.05	0.31	1.98	2.01	1.99	0.02
11 AM	-0.90	-0.55	-0.73	0.25	2.35	2.17	2.26	0.1	-2.54	-2.20	-2.37	0.24	2.02	2.31	2.16	0.21	-0.78	0.37	-0.20	0.82	2.08	1.94	2.01	0.10
12 PM	-0.86	-0.70	-0.78	0.12	2.36	2.15	2.25	0.1	-5.21	-4.83	-5.02	0.27	2.56	2.60	2.58	0.03	-0.29	-0.06	-0.18	0.16	2.14	2.07	2.11	0.05
1 PM	0.29	0.25	0.27	0.02	1.78	1.78	1.78	0.0	-0.11	0.08	-0.02	0.13	2.09	2.07	2.08	0.02	-1.16	-0.19	-0.68	0.68	2.24	2.17	2.21	0.05
2 PM	-1.05	-1.05	-1.05	0.00	2.03	2.06	2.04	0.0	-0.17	0.58	0.20	0.53	1.70	1.78	1.74	0.06	-0.08	0.00	-0.04	0.06	2.02	2.07	2.04	0.03
3 PM	-0.55	-0.59	-0.57	0.02	2.19	2.22	2.20	0.0	0.42	0.52	0.47	0.07	1.71	1.61	1.66	0.07	0.36	0.42	0.39	0.04	1.78	1.73	1.75	0.04
4 PM	0.15	-0.04	0.06	0.14	2.22	2.20	2.21	0.0	0.11	0.48	0.29	0.26	2.10	2.11	2.10	0.01	-0.51	-0.33	-0.42	0.13	2.15	2.06	2.11	0.06
5 PM	-0.25	-0.34	-0.29	0.06	2.33	2.35	2.34	0.0	-0.36	0.46	0.05	0.58	1.79	2.28	2.03	0.35	-4.12	-3.61	-3.86	0.36	2.32	2.32	2.32	0.00
6 PM	-0.65	-0.61	-0.63	0.03	2.26	2.27	2.26	0.0	-0.42	0.07	-0.18	0.35	2.15	2.35	2.25	0.14	-0.38	0.38	0.00	0.54	1.97	1.83	1.90	0.10
7 PM	-0.65	-0.78	-0.71	0.09	2.27	2.27	2.27	0.0	-0.86	-0.68	-0.77	0.13	2.43	2.38	2.40	0.04	0.23	0.55	0.39	0.22	1.78	1.71	1.74	0.05
8 PM	-0.71	-0.82	-0.77	0.08	2.29	2.25	2.27	0.0	-0.53	-0.03	-0.28	0.35	2.01	2.04	2.02	0.01	-1.06	-0.01	-0.54	0.74	2.07	2.03	2.05	0.03
9 PM	-0.62	-0.60	-0.61	0.01	2.17	2.18	2.17	0.0	0.33	0.61	0.47	0.20	1.66	1.74	1.70	0.06	-0.19	0.16	-0.02	0.25	2.05	2.04	2.04	0.01
10 PM	-0.50	-0.45	-0.47	0.03	2.29	2.28	2.29	0.0	-0.20	-0.04	-0.12	0.12	1.87	1.82	1.85	0.04	-0.36	0.28	-0.04	0.45	1.91	1.94	1.92	0.02
11 PM	-0.47	-0.44	-0.46	0.02	2.17	2.18	2.18	0.0	0.87	0.98	0.92	0.08	0.74	0.88	0.81	0.10	-0.37	0.16	-0.11	0.37	1.80	1.82	1.81	0.02
12 AM	-0.13	-0.16	-0.15	0.02	2.10	2.09	2.10	0.0	-1.48	-1.63	-1.55	0.11	2.06	2.04	2.05	0.01	-0.39	-0.13	-0.26	0.18	2.02	1.93	1.98	0.07
1 AM	0.09	-0.11	-0.01	0.15	1.59	1.65	1.62	0.0	-1.63	-1.80	-1.71	0.12	2.00	1.95	1.97	0.03	-2.48	-2.38	-2.43	0.07	2.34	2.27	2.30	0.05
2 AM	-1.61	-1.79	-1.70	0.13	2.17	2.19	2.18	0.0	-4.15	-4.59	-4.37	0.31	2.43	2.40	2.42	0.02	-0.43	-0.51	-0.47	0.05	2.11	2.20	2.16	0.06
3 AM	-2.95	-3.04	-3.00	0.06	2.44	2.41	2.43	0.0	-4.51	-4.58	-4.55	0.05	2.60	2.62	2.61	0.01	-1.96	-1.90	-1.93	0.04	2.28	2.25	2.27	0.02
4 AM	-5.00	-5.58	-5.29	0.41	2.78	2.53	2.66	0.2	-2.89	-3.02	-2.96	0.09	2.46	2.46	2.46	0.00	-1.62	-1.57	-1.60	0.04	2.10	2.15	2.12	0.03
5 AM	-2.79	-2.95	-2.87	0.11	2.51	2.56	2.54	0.0	-4.38	-4.53	-4.45	0.10	2.38	2.34	2.36	0.03	-1.08	-0.82	-0.95	0.18	2.27	2.22	2.24	0.04
6 AM	-5.61	-5.64	-5.62	0.02	2.59	2.59	2.59	0.0	-2.58	-2.59	-2.58	0.01	2.52	2.49	2.50	0.02	-1.88	-1.82	-1.85	0.04	2.21	2.28	2.24	0.04
7 AM	-3.67	-4.08	-3.87	0.29	2.49	2.53	2.51	0.0	-0.59	-0.81	-0.70	0.15	2.05	2.32	2.18	0.19	-0.16	0.47	0.16	0.45	1.83	1.84	1.84	0.01
8 AM	0.22	0.30	0.26	0.06	2.03	2.01	2.02	0.0	-0.31	-0.77	-0.54	0.33	2.05	2.25	2.15	0.14	-0.99	0.50	-0.24	1.06	2.08	1.75	1.92	0.23
9 AM	0.49	0.52	0.50	0.02	1.85	1.85	1.85	0.0	0.07	0.74	0.40	0.48	1.34	1.47	1.40	0.09	-0.02	0.30	0.14	0.23	1.47	2.04	1.76	0.40

Legend: traditional approach represented as (L1, L2) and the new instantiation of the algorithm denoted as (L1_1 and L1_2).

Table 6-3. Hourly summaries of L1 and L2 for Subject 2 during Luna 2015.

	Day 1								Day 2								Day 3							
Time	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2
10 AM	0.36	-0.08	0.14	0.31	2.02	2.14	2.08	0.09	0.83	0.89	0.86	0.04	1.31	1.42	1.36	0.07	0.95	0.87	0.91	0.06	1.67	1.67	1.67	0
11 AM	0.20	-0.14	0.03	0.24	2.19	2.22	2.21	0.02	0.70	0.67	0.69	0.03	1.82	1.92	1.87	0.07	0.60	0.52	0.56	0.06	1.91	1.93	1.92	0.02
12 PM	-0.30	-0.80	-0.55	0.35	2.32	2.38	2.35	0.04	0.20	-0.09	0.05	0.21	2.05	2.12	2.08	0.05	0.05	-0.15	-0.05	0.14	2.29	2.31	2.30	0.01
1 PM	-0.64	-0.89	-0.77	0.18	2.09	1.86	1.98	0.16	0.17	-0.20	-0.01	0.26	2.17	2.23	2.20	0.05	0.72	0.73	0.72	0.01	1.37	1.45	1.41	0.05
2 PM	0.71	0.75	0.73	0.03	1.45	1.51	1.48	0.04	0.74	0.84	0.79	0.07	1.68	1.75	1.71	0.05	0.77	0.78	0.78	0.01	1.49	1.55	1.52	0.04
3 PM	0.61	0.53	0.57	0.06	1.73	1.91	1.82	0.13	0.56	0.61	0.59	0.04	1.78	1.81	1.80	0.02	0.72	0.73	0.72	0.01	1.91	1.94	1.93	0.02
4 PM	-0.20	-0.71	-0.45	0.36	1.60	1.31	1.45	0.20	0.52	0.33	0.42	0.13	1.77	1.84	1.80	0.05	0.73	0.60	0.67	0.09	1.41	1.44	1.43	0.02
5 PM	0.34	0.44	0.39	0.07	2.04	2.10	2.07	0.04	0.40	0.63	0.52	0.17	1.52	1.52	1.52	0.00	0.69	0.59	0.64	0.07	1.67	1.71	1.69	0.03
6 PM	-0.19	-0.17	-0.18	0.01	2.40	2.38	2.39	0.02	0.59	0.78	0.69	0.13	1.57	1.62	1.60	0.03	0.36	0.28	0.32	0.05	2.11	2.14	2.12	0.02
7 PM	-0.19	-0.43	-0.31	0.17	2.45	2.50	2.47	0.04	0.58	0.81	0.69	0.16	1.49	1.55	1.52	0.04	0.56	0.54	0.55	0.02	1.83	1.85	1.84	0.02
8 PM	-0.06	-0.24	-0.15	0.13	2.16	2.17	2.16	0.00	0.69	0.85	0.77	0.11	1.38	1.39	1.38	0.01	0.90	0.94	0.92	0.02	1.06	1.17	1.11	0.08
9 PM	-0.08	-0.22	-0.15	0.10	2.36	2.44	2.40	0.05	0.76	0.82	0.79	0.05	1.81	1.87	1.84	0.04	0.73	0.66	0.70	0.05	1.80	1.85	1.82	0.04
10 PM	-0.42	-0.58	-0.50	0.11	2.38	2.43	2.40	0.04	0.72	0.71	0.72	0.01	1.62	1.77	1.69	0.10	0.67	0.67	0.67	0.00	1.97	1.98	1.97	0.01
11 PM	0.20	0.30	0.25	0.07	1.91	1.89	1.90	0.02	0.60	0.28	0.44	0.23	1.74	1.95	1.85	0.15	0.49	0.46	0.48	0.02	1.72	1.79	1.76	0.05
12 AM	0.23	0.01	0.12	0.15	2.15	2.29	2.22	0.10	0.41	0.28	0.35	0.09	1.97	2.05	2.01	0.06	0.38	0.20	0.29	0.13	2.13	2.17	2.15	0.03
1 AM	1.47	1.25	1.36	0.16	0.61	0.61	0.61	0.00	1.04	0.80	0.92	0.17	0.89	0.92	0.91	0.02	1.41	1.14	1.28	0.18	0.78	0.79	0.79	0.01
2 AM	1.85	1.75	1.80	0.07	0.43	0.41	0.42	0.02	1.68	1.58	1.63	0.07	0.09	0.12	0.10	0.02	1.14	1.24	1.19	0.08	-0.43	-0.37	-0.40	0.04
3 AM	1.06	1.13	1.09	0.05	1.51	1.45	1.48	0.05	1.51	1.41	1.46	0.07	0.66	0.62	0.64	0.03	1.25	1.18	1.21	0.05	0.34	0.41	0.38	0.05
4 AM	0.86	0.89	0.87	0.02	1.43	1.45	1.44	0.02	1.03	1.23	1.13	0.14	1.13	0.96	1.05	0.12	0.86	0.95	0.91	0.07	1.34	1.29	1.31	0.03
5 AM	1.01	0.93	0.97	0.06	1.33	1.33	1.33	0.00	1.05	0.87	0.96	0.13	1.43	1.45	1.44	0.02	0.99	0.98	0.98	0.01	1.23	1.25	1.24	0.01
6 AM	0.56	0.38	0.47	0.13	2.18	2.17	2.17	0.01	1.32	1.21	1.27	0.08	0.42	0.47	0.44	0.04	0.68	0.69	0.69	0.00	1.74	1.76	1.75	0.02
7 AM	0.37	0.30	0.33	0.05	2.01	2.07	2.04	0.04	0.88	0.65	0.77	0.16	1.64	1.68	1.66	0.03	0.78	0.68	0.73	0.08	1.67	1.68	1.67	0.01
8 AM	0.52	0.28	0.40	0.17	2.02	1.91	1.97	0.07	0.57	0.46	0.52	0.08	1.92	2.04	1.98	0.08	0.70	0.66	0.68	0.03	1.52	1.66	1.59	0.1
9 AM	0.85	1.04	0.94	0.13	0.47	0.96	0.71	0.34	0.43	0.56	0.49	0.09	1.12	1.31	1.21	0.13	0.94	0.93	0.93	0.01	0.91	1.04	0.97	0.09

Legend: traditional approach represented as (L1, L2) and the new instantiation of the algorithm denoted as (L1_1 and L1_2).

Table 6-4. Hourly summaries of L1 and L2 for Subject 3 during Luna 2015.

	Day 1								Day 2								Day 3							
Time	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2
10 AM	0.81	0.86	0.83	0.04	0.22	0.33	0.28	0.08	0.97	1.00	0.99	0.02	0.32	0.66	0.49	0.24	-0.68	0.35	-0.17	0.72	1.17	1.19	1.18	0.01
11 AM	0.93	-0.67	0.13	1.13	0.62	1.17	0.90	0.39	0.87	0.95	0.91	0.06	0.48	0.64	0.56	0.11	-0.41	0.17	-0.12	0.41	1.38	1.35	1.37	0.02
12 PM	0.92	0.55	0.73	0.26	0.30	1.02	0.66	0.51	0.92	0.70	0.81	0.15	0.55	0.71	0.63	0.11	-0.73	-0.05	-0.39	0.48	2.07	2.01	2.04	0.04
1 PM	0.85	0.89	0.87	0.02	1.35	1.44	1.40	0.06	0.78	0.69	0.73	0.06	1.52	1.63	1.57	0.08	-0.87	0.19	-0.34	0.75	1.54	1.38	1.46	0.12
2 PM	0.90	0.92	0.91	0.01	1.22	1.27	1.24	0.04	0.84	0.84	0.84	0.00	1.23	1.21	1.22	0.02	0.56	0.99	0.78	0.30	1.23	1.07	1.15	0.11
3 PM	0.93	0.84	0.89	0.06	1.27	1.43	1.35	0.11	0.87	0.82	0.84	0.03	0.49	0.75	0.62	0.19	0.62	0.90	0.76	0.20	1.52	1.43	1.48	0.06
4 PM	0.93	0.97	0.95	0.02	0.62	0.93	0.77	0.22	0.81	0.50	0.66	0.22	1.05	1.38	1.21	0.24	0.67	0.87	0.77	0.14	1.81	1.78	1.79	0.02
5 PM	0.91	1.10	1.01	0.14	0.70	1.09	0.89	0.28	0.80	0.73	0.76	0.05	1.04	1.08	1.06	0.03	0.28	0.77	0.53	0.34	1.82	1.73	1.77	0.06
6 PM	0.83	0.92	0.88	0.06	1.52	1.54	1.53	0.01	0.92	0.66	0.79	0.19	1.18	1.39	1.28	0.14	-0.87	0.29	-0.29	0.82	1.92	1.66	1.79	0.18
7 PM	0.81	0.68	0.74	0.09	1.64	1.72	1.68	0.05	0.75	0.17	0.46	0.41	1.11	1.62	1.37	0.36	0.70	0.82	0.76	0.09	1.26	1.28	1.27	0.02
8 PM	0.86	0.10	0.48	0.54	1.48	1.69	1.59	0.15	0.86	0.71	0.79	0.11	1.11	1.48	1.30	0.26	0.25	0.62	0.44	0.26	1.50	1.38	1.44	0.08
9 PM	0.84	0.67	0.76	0.12	1.17	1.23	1.20	0.05	1.03	1.02	1.02	0.01	0.83	0.91	0.87	0.05	0.62	0.84	0.73	0.16	1.40	1.36	1.38	0.03
10 PM	0.83	0.90	0.86	0.05	1.44	1.44	1.44	0.00	0.88	0.90	0.89	0.02	0.02	0.08	0.05	0.04	0.34	0.77	0.56	0.31	1.60	1.55	1.58	0.04
11 PM	0.86	0.91	0.89	0.04	1.44	1.53	1.49	0.06	0.90	0.93	0.92	0.03	0.73	0.89	0.81	0.11	0.19	0.82	0.51	0.44	1.49	1.44	1.46	0.03
12 AM	0.66	0.79	0.72	0.09	0.92	0.91	0.91	0.01	0.84	0.90	0.87	0.05	1.21	1.32	1.27	0.08	-1.41	-0.07	-0.74	0.95	1.96	1.95	1.96	0.01
1 AM	0.58	0.65	0.61	0.05	0.91	0.91	0.91	0.00	0.49	0.50	0.49	0.01	1.74	1.75	1.75	0.01	0.54	0.51	0.53	0.02	1.32	1.32	1.32	0.00
2 AM	0.62	0.63	0.62	0.01	-0.03	0.01	-0.01	0.03	0.53	0.51	0.52	0.02	1.50	1.51	1.51	0.01	0.61	0.55	0.58	0.04	0.84	0.79	0.82	0.03
3 AM	0.44	0.42	0.43	0.01	0.56	0.55	0.56	0.01	0.42	0.40	0.41	0.02	0.83	0.87	0.85	0.03	0.32	0.35	0.33	0.02	1.61	1.42	1.52	0.14
4 AM	0.20	0.17	0.19	0.03	1.82	1.80	1.81	0.01	-0.27	-0.37	-0.32	0.07	2.16	2.17	2.16	0.01	-0.45	0.13	-0.16	0.41	2.15	2.12	2.14	0.02
5 AM	0.35	0.31	0.33	0.03	1.64	1.66	1.65	0.01	-0.05	-0.12	-0.09	0.05	2.19	2.16	2.18	0.02	0.14	0.29	0.22	0.10	2.18	2.13	2.16	0.04
6 AM	-0.19	-0.30	-0.25	0.08	2.50	2.50	2.50	0.00	-0.07	-0.16	-0.12	0.06	2.05	2.04	2.04	0.01	0.12	0.28	0.20	0.11	1.69	1.66	1.67	0.02
7 AM	0.73	0.62	0.68	0.08	1.94	1.99	1.97	0.03	-0.05	-0.12	-0.08	0.05	2.26	2.24	2.25	0.01	-0.47	-0.28	-0.37	0.13	1.87	1.81	1.84	0.04
8 AM	0.76	0.78	0.77	0.01	1.45	1.57	1.51	0.08	0.53	-0.04	0.25	0.40	2.24	2.31	2.27	0.05	-2.85	-1.86	-2.36	0.70	2.09	1.77	1.93	0.22
9 AM	1.02	1.18	1.10	0.12	0.58	0.84	0.71	0.19	0.79	0.73	0.76	0.04	1.10	1.33	1.22	0.17	-2.79	-1.44	-2.11	0.96	1.70	1.41	1.56	0.20

Legend: traditional approach represented as (L1, L2) and the new instantiation of the algorithm denoted as (L1_1 and L1_2).

Table 6-5. Hourly summaries of L1 and L2 for Subject 4 during Luna 2015.

	Day 1								Day 2								Day 3							
Time	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2
10 AM	-0.39	-0.96	-0.67	0.40	2.53	2.40	2.46	0.10	-0.42	-0.16	-0.29	0.18	2.33	2.34	2.33	0.01	-2.04	-0.82	-1.43	0.87	2.28	2.25	2.26	0.02
11 AM	-1.24	-1.25	-1.24	0.01	2.64	2.62	2.63	0.01	-1.61	-1.71	-1.66	0.07	2.72	2.72	2.72	0.00	-2.42	-1.44	-1.93	0.69	2.49	2.47	2.48	0.01
12 PM	-1.20	-1.23	-1.21	0.02	2.69	2.67	2.68	0.01	-1.82	-1.64	-1.73	0.12	2.81	2.80	2.81	0.00	-2.36	-2.04	-2.20	0.22	2.67	2.60	2.63	0.05
1 PM	-0.25	-0.34	-0.30	0.06	2.43	2.44	2.44	0.01	-0.88	-0.84	-0.86	0.03	2.53	2.54	2.53	0.00	-1.45	-0.83	-1.14	0.44	2.41	2.21	2.31	0.14
2 PM	-0.79	-0.90	-0.84	0.07	2.75	2.73	2.74	0.01	0.74	0.89	0.81	0.11	1.64	1.66	1.65	0.02	0.29	0.80	0.54	0.36	1.82	1.69	1.76	0.09
3 PM	-0.60	-0.85	-0.72	0.18	2.65	2.67	2.66	0.02	0.14	0.14	0.14	0.00	2.26	2.23	2.24	0.02	0.47	0.75	0.61	0.20	1.58	1.60	1.59	0.01
4 PM	-0.65	-0.76	-0.70	0.08	2.67	2.66	2.67	0.01	-0.06	-0.09	-0.08	0.02	2.27	2.26	2.26	0.01	-1.10	-0.46	-0.78	0.45	2.40	2.39	2.40	0.01
5 PM	-0.25	-0.28	-0.26	0.02	2.43	2.39	2.41	0.03	-0.83	-0.85	-0.84	0.01	2.61	2.60	2.61	0.01	-2.89	-2.08	-2.48	0.58	2.74	2.59	2.67	0.11
6 PM	-0.47	-0.63	-0.55	0.11	2.63	2.62	2.63	0.01	-1.07	-1.20	-1.13	0.09	2.65	2.63	2.64	0.02	-1.77	-1.45	-1.61	0.23	2.72	2.68	2.70	0.03
7 PM	-0.44	-0.54	-0.49	0.07	2.57	2.53	2.55	0.03	-1.51	-1.52	-1.51	0.00	2.84	2.82	2.83	0.02	-1.19	-0.27	-0.73	0.66	2.33	2.26	2.30	0.05
8 PM	-0.74	-0.90	-0.82	0.11	2.63	2.63	2.63	0.00	-0.36	-0.46	-0.41	0.07	2.53	2.55	2.54	0.01	-0.96	-0.58	-0.77	0.27	2.42	2.40	2.41	0.01
9 PM	-0.44	-0.50	-0.47	0.04	2.55	2.54	2.54	0.00	-0.48	-0.34	-0.41	0.10	2.47	2.53	2.50	0.04	-1.00	-0.75	-0.87	0.18	2.57	2.55	2.56	0.01
10 PM	-0.34	-0.62	-0.48	0.20	2.63	2.65	2.64	0.01	-0.74	-0.64	-0.69	0.07	2.55	2.51	2.53	0.03	-1.76	-1.54	-1.65	0.16	2.62	2.64	2.63	0.01
11 PM	-1.15	-1.27	-1.21	0.09	2.77	2.76	2.76	0.00	-1.25	-0.99	-1.12	0.18	2.73	2.70	2.72	0.02	-2.61	-2.13	-2.37	0.34	2.65	2.60	2.63	0.04
12 AM	-0.49	-0.40	-0.44	0.06	2.64	2.62	2.63	0.01	-0.63	-0.85	-0.74	0.16	2.48	2.49	2.48	0.00	-1.80	-1.52	-1.66	0.20	2.56	2.56	2.56	0.00
1 AM	0.64	0.55	0.60	0.06	1.96	1.97	1.96	0.01	-0.06	-0.25	-0.15	0.14	1.99	1.98	1.99	0.01	-0.58	-0.77	-0.67	0.14	2.34	2.33	2.33	0.01
2 AM	0.58	0.49	0.54	0.06	1.98	1.99	1.99	0.01	-1.18	-1.31	-1.24	0.09	2.39	2.40	2.39	0.01	-0.74	-0.83	-0.79	0.06	2.33	2.35	2.34	0.01
3 AM	-0.64	-0.58	-0.61	0.05	2.39	2.40	2.40	0.01	-1.67	-1.77	-1.72	0.07	2.81	2.81	2.81	0.00	-0.37	-0.49	-0.43	0.08	2.29	2.31	2.30	0.01
4 AM	-0.05	-0.19	-0.12	0.10	2.23	2.22	2.22	0.01	-0.37	-0.54	-0.46	0.12	2.31	2.31	2.31	0.00	-2.52	-2.68	-2.60	0.11	2.82	2.83	2.83	0.00
5 AM	-1.32	-1.44	-1.38	0.09	2.80	2.79	2.79	0.01	-2.00	-2.15	-2.08	0.10	2.80	2.79	2.79	0.00	-0.96	-1.00	-0.98	0.03	2.46	2.41	2.43	0.04
6 AM	-0.78	-0.99	-0.88	0.15	2.72	2.75	2.73	0.02	-0.95	-0.86	-0.90	0.06	2.57	2.49	2.53	0.06	-2.04	-2.25	-2.15	0.15	2.83	2.82	2.83	0.01
7 AM	-1.56	-1.35	-1.46	0.15	2.73	2.74	2.74	0.01	-0.32	-0.09	-0.21	0.16	2.18	2.16	2.17	0.02	-2.35	-2.23	-2.29	0.08	2.75	2.72	2.74	0.02
8 AM	-1.20	-1.02	-1.11	0.13	2.68	2.61	2.64	0.05	0.04	-0.06	-0.01	0.08	2.25	2.25	2.25	0.00	-1.63	-1.50	-1.57	0.09	2.69	2.67	2.68	0.01
9 AM	-0.98	-0.23	-0.60	0.53	2.46	2.49	2.48	0.02	0.49	0.52	0.50	0.02	2.14	2.19	2.17	0.04	-0.71	0.35	-0.18	0.75	2.28	2.18	2.23	0.07

Legend: traditional approach represented as (L1, L2) and the new instantiation of the algorithm denoted as (L1_1 and L1_2).

Table 6-6. Hourly summaries of L1 and L2 for Subject 5 during Luna 2015.

	Day 1								Day 2								Day 3							
Time	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2
10 AM	0.40	0.39	0.39	0.01	1.96	1.94	1.95	0.01	0.70	0.98	0.84	0.20	1.50	1.63	1.56	0.09	0.31	0.25	0.28	0.05	1.79	1.73	1.76	0.04
11 AM	-0.15	-0.19	-0.17	0.03	1.87	1.93	1.90	0.04	0.79	0.80	0.79	0.01	1.83	1.81	1.82	0.01	-0.25	0.18	-0.03	0.30	2.00	2.00	2.00	0.00
12 PM	0.05	-0.03	0.01	0.06	2.19	2.19	2.19	0.00	0.15	0.14	0.15	0.01	2.08	2.10	2.09	0.02	-0.07	0.11	0.02	0.13	2.20	2.14	2.17	0.04
1 PM	0.91	0.90	0.91	0.01	1.59	1.60	1.60	0.01	0.61	0.65	0.63	0.03	1.65	1.67	1.66	0.01	-0.14	-0.39	-0.26	0.18	2.02	2.22	2.12	0.15
2 PM	0.06	0.02	0.04	0.03	1.97	1.96	1.96	0.01	0.91	0.89	0.90	0.01	1.07	1.11	1.09	0.03	0.64	0.66	0.65	0.02	1.54	1.51	1.52	0.02
3 PM	0.09	0.01	0.05	0.06	1.99	1.99	1.99	0.00	0.87	0.92	0.90	0.04	0.44	0.47	0.46	0.02	1.03	0.85	0.94	0.12	1.39	1.52	1.45	0.10
4 PM	0.52	0.44	0.48	0.06	2.12	2.12	2.12	0.00	0.73	0.75	0.74	0.02	1.66	1.69	1.67	0.02	-0.09	0.13	0.02	0.15	2.11	1.93	2.02	0.13
5 PM	0.17	0.01	0.09	0.11	2.17	2.16	2.16	0.00	0.47	0.20	0.33	0.19	1.82	1.84	1.83	0.01	1.07	0.74	0.91	0.23	1.73	1.76	1.75	0.02
6 PM	0.30	0.31	0.31	0.00	1.93	1.96	1.94	0.02	0.27	0.32	0.30	0.04	2.10	2.11	2.11	0.01	0.43	0.67	0.55	0.17	1.56	1.69	1.62	0.09
7 PM	0.26	0.26	0.26	0.00	2.20	2.17	2.19	0.02	-0.08	-0.21	-0.15	0.09	2.27	2.27	2.27	0.00	0.54	0.83	0.68	0.20	1.59	1.44	1.52	0.11
8 PM	0.28	0.23	0.26	0.04	2.24	2.26	2.25	0.02	0.69	0.71	0.70	0.01	1.76	1.78	1.77	0.01	0.18	0.74	0.46	0.40	1.97	1.75	1.86	0.15
9 PM	0.53	0.58	0.55	0.03	1.93	1.95	1.94	0.01	0.74	0.53	0.63	0.15	1.82	1.81	1.81	0.00	0.16	0.57	0.37	0.29	1.94	1.88	1.91	0.04
10 PM	-0.51	-0.69	-0.60	0.13	2.27	2.28	2.27	0.01	1.00	0.79	0.90	0.15	1.81	1.87	1.84	0.04	-0.31	0.25	-0.03	0.40	2.09	2.00	2.04	0.06
11 PM	-0.06	-0.20	-0.13	0.10	2.22	2.24	2.23	0.02	-0.41	-0.66	-0.54	0.18	1.78	1.79	1.78	0.01	-1.19	-1.07	-1.13	0.08	2.26	2.19	2.22	0.05
12 AM	-1.13	-1.28	-1.20	0.11	2.11	2.05	2.08	0.05	-0.35	-0.67	-0.51	0.23	1.82	1.82	1.82	0.00	-2.90	-3.49	-3.20	0.42	2.22	2.33	2.28	0.08
1 AM	-1.60	-1.53	-1.57	0.05	1.98	1.93	1.96	0.04	-0.75	-0.99	-0.87	0.17	2.00	1.99	2.00	0.00	-1.23	-1.82	-1.53	0.41	2.08	2.15	2.12	0.05
2 AM	-1.65	-1.78	-1.72	0.09	2.20	2.18	2.19	0.01	-1.31	-1.42	-1.36	0.08	2.36	2.32	2.34	0.03	0.06	-0.13	-0.04	0.13	1.60	1.45	1.52	0.10
3 AM	-2.45	-2.72	-2.58	0.19	2.21	2.23	2.22	0.01	-1.83	-2.06	-1.95	0.16	2.55	2.55	2.55	0.00	-1.33	-1.40	-1.37	0.05	2.56	2.51	2.54	0.03
4 AM	-2.32	-2.50	-2.41	0.13	2.12	2.10	2.11	0.01	-2.09	-2.26	-2.17	0.12	2.24	2.23	2.24	0.01	-1.24	-1.53	-1.38	0.20	2.14	2.13	2.14	0.01
5 AM	-1.75	-2.02	-1.89	0.19	2.15	2.10	2.13	0.03	-1.69	-1.95	-1.82	0.18	2.39	2.38	2.38	0.00	-1.66	-1.65	-1.66	0.01	2.22	2.21	2.21	0.01
6 AM	-2.40	-2.69	-2.55	0.21	2.48	2.48	2.48	0.00	-0.93	-1.05	-0.99	0.09	2.16	2.19	2.18	0.02	-0.32	-0.32	-0.32	0.00	2.05	2.07	2.06	0.02
7 AM	-1.66	-1.85	-1.76	0.13	2.58	2.55	2.56	0.02	0.66	0.69	0.67	0.02	1.77	1.85	1.81	0.06	0.22	0.55	0.39	0.23	1.93	2.01	1.97	0.05
8 AM	0.16	-0.01	0.07	0.12	2.31	2.34	2.32	0.02	0.79	0.82	0.81	0.02	1.43	1.42	1.43	0.01	0.33	0.64	0.49	0.22	1.89	1.74	1.82	0.11
9 AM	0.35	0.28	0.31	0.06	2.00	2.03	2.01	0.02	1.12	1.10	1.11	0.02	1.28	1.26	1.27	0.01	-0.25	-0.20	-0.23	0.04	2.20	2.08	2.14	0.08

Legend: traditional approach represented as (L1, L2) and the new instantiation of the algorithm denoted as (L1_1 and L1_2).

Table 6-7. Hourly summaries of L1 and L2 for Subject 6 during Luna 2015.

	Day 1								Day 2								Day 3							
Time	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2	L1	L1_1	Mean_L1	SD_L1	L2	L2_1	Mean_L2	SD_L2
10 AM	-2.91	0.01	-1.45	2.06	2.27	2.11	2.19	0.11	-4.48	0.85	-1.82	3.77	2.21	1.36	1.79	0.61	-2.91	0.76	-1.08	2.59	1.65	1.41	1.53	0.17
11 AM	-3.35	-0.39	-1.87	2.10	2.47	2.29	2.38	0.13	-5.93	0.72	-2.60	4.70	2.65	1.81	2.23	0.60	-3.16	1.00	-1.08	2.94	1.24	1.12	1.18	0.09
12 PM	-4.66	-1.51	-3.08	2.22	2.48	2.49	2.49	0.01	-2.82	0.21	-1.31	2.14	0.32	2.06	1.19	1.23	-3.66	0.77	-1.45	3.13	1.57	1.79	1.68	0.16
1 PM	-4.43	0.14	-2.14	3.24	2.65	1.57	2.11	0.77	-3.84	-0.32	-2.08	2.49	1.53	2.27	1.90	0.52	-3.16	0.24	-1.46	2.40	1.46	2.09	1.78	0.44
2 PM	-2.85	0.66	-1.10	2.49	2.73	1.59	2.16	0.80	-3.88	0.63	-1.63	3.19	2.35	1.85	2.10	0.35	-2.90	-0.01	-1.45	2.04	1.88	2.05	1.97	0.12
3 PM	-2.90	0.68	-1.11	2.53	2.39	1.75	2.07	0.45	-4.68	0.62	-2.03	3.75	2.41	1.77	2.09	0.45	-4.68	0.85	-1.92	3.90	2.24	1.44	1.84	0.57
4 PM	-3.93	-0.86	-2.39	2.17	2.52	1.62	2.07	0.64	-3.77	0.31	-1.73	2.88	1.98	1.92	1.95	0.04	-4.16	0.75	-1.70	3.47	2.24	1.73	1.98	0.36
5 PM	-3.83	0.46	-1.69	3.03	2.28	2.02	2.15	0.19	-3.29	0.83	-1.23	2.91	2.23	1.46	1.85	0.54	-4.90	0.59	-2.16	3.88	2.14	1.93	2.03	0.15
6 PM	-4.91	-0.30	-2.61	3.26	1.96	2.50	2.23	0.38	-4.81	0.56	-2.13	3.80	2.37	1.68	2.02	0.49	-3.59	0.74	-1.42	3.06	1.98	1.31	1.64	0.47
7 PM	-3.03	-0.71	-1.87	1.64	1.00	2.52	1.76	1.08	-4.22	0.80	-1.71	3.55	2.38	1.64	2.01	0.52	-3.82	0.39	-1.72	2.98	2.44	1.93	2.18	0.37
8 PM	-4.15	0.17	-1.99	3.06	2.64	2.11	2.38	0.38	-2.80	0.89	-0.96	2.61	2.30	1.30	1.80	0.71	-3.86	0.34	-1.76	2.97	2.07	2.04	2.06	0.02
9 PM	-3.28	-0.52	-1.90	1.95	2.40	2.47	2.43	0.05	-2.70	0.79	-0.95	2.46	2.33	1.81	2.07	0.37	-3.54	0.73	-1.40	3.02	2.45	1.51	1.98	0.66
10 PM	-2.32	-0.23	-1.27	1.48	2.65	2.21	2.43	0.31	-2.91	0.70	-1.10	2.55	2.52	1.71	2.11	0.58	-2.99	0.88	-1.06	2.74	2.40	1.49	1.94	0.65
11 PM	-2.56	0.16	-1.20	1.93	2.70	1.99	2.34	0.50	-3.56	0.49	-1.53	2.86	2.41	1.96	2.18	0.32	-3.64	0.63	-1.51	3.02	2.35	1.88	2.12	0.33
12 AM	-2.63	0.14	-1.25	1.95	2.71	2.10	2.41	0.43	-3.70	0.14	-1.78	2.71	2.12	2.07	2.09	0.03	-3.96	0.64	-1.66	3.25	2.17	1.97	2.07	0.14
1 AM	-5.56	1.43	-2.07	4.94	2.78	0.19	1.48	1.83	-7.37	0.42	-3.48	5.51	2.90	1.56	2.23	0.95	-4.84	0.17	-2.33	3.54	2.77	1.92	2.35	0.60
2 AM	-6.61	1.62	-2.50	5.82	3.00	0.98	1.99	1.43	-5.91	1.73	-2.09	5.41	2.72	-0.09	1.32	1.99	-5.28	0.76	-2.26	4.27	2.75	1.73	2.24	0.72
3 AM	-5.64	1.28	-2.18	4.89	2.90	1.31	2.10	1.12	-6.00	1.51	-2.24	5.31	2.63	0.31	1.47	1.64	-4.67	0.92	-1.87	3.96	2.56	0.48	1.52	1.47
4 AM	-6.93	0.81	-3.06	5.47	2.85	1.41	2.13	1.02	-6.73	1.32	-2.71	5.69	2.72	0.77	1.74	1.38	-5.86	1.26	-2.30	5.03	2.73	-0.37	1.18	2.19
5 AM	-6.39	0.80	-2.80	5.08	2.86	1.54	2.20	0.93	-5.98	0.78	-2.60	4.78	2.73	1.73	2.23	0.71	-6.04	1.32	-2.36	5.20	2.83	0.73	1.78	1.49
6 AM	-5.62	0.42	-2.60	4.27	2.82	2.15	2.49	0.47	-6.61	1.17	-2.72	5.50	2.82	0.47	1.64	1.66	-5.27	0.83	-2.22	4.31	2.83	1.43	2.13	0.99
7 AM	-3.24	-0.11	-1.68	2.21	2.89	2.14	2.52	0.53	-5.40	0.78	-2.31	4.37	2.60	1.48	2.04	0.79	-5.65	0.86	-2.40	4.60	2.91	1.50	2.20	0.99
8 AM	-1.71	0.79	-0.46	1.77	2.70	1.52	2.11	0.84	-3.47	0.40	-1.54	2.74	2.45	2.04	2.24	0.29	-3.57	0.72	-1.43	3.03	1.90	1.57	1.73	0.23
9 AM	-1.70	1.06	-0.32	1.95	2.42	1.04	1.73	0.98	-3.89	0.59	-1.65	3.17	1.98	1.46	1.72	0.36	-3.11	0.69	-1.21	2.69	1.79	1.73	1.76	0.04

Legend: traditional approach represented as (L1, L2) and the new instantiation of the algorithm denoted as (L1_1 and L1_2).

Disclaimer: The ECG signal record for Subject 6 has been heavily contaminated with noise and artifacts, contributing to a poor quality of the signal and further impacting the quality and validity of data analysis

Table 7-1. Hourly summaries of L_1 and L_2 values for Subject 1 Day 1 during DI 2016.

Time	L1	L1_1	Mean L1	SD L1	L2	L2_1	Mean L2	SD L2
9 PM	-2.09	-2.39	-2.24	0.21	2.36	2.52	2.44	0.06
10 PM	-3.64	-3.88	-3.76	0.17	2.52	2.66	2.59	0.05
11 PM	-4.03	-4.24	-4.13	0.15	2.56	2.73	2.65	0.06
12 AM	-3.29	-3.46	-3.37	0.12	2.42	2.66	2.54	0.08
1 AM	-1.15	-1.46	-1.30	0.22	1.81	2.40	2.10	0.21
2 AM	-2.45	-2.67	-2.56	0.16	2.50	2.71	2.60	0.08
3 AM	-2.27	-2.56	-2.42	0.21	2.27	2.68	2.47	0.14
4 AM	-2.82	-2.97	-2.90	0.10	2.37	2.58	2.47	0.07
5 AM	-3.09	-3.41	-3.25	0.22	2.65	2.87	2.76	0.08
6 AM	-2.60	-2.88	-2.74	0.20	2.58	2.81	2.69	0.08
7 AM	-3.10	-3.13	-3.11	0.02	2.46	2.67	2.57	0.07
8 AM	-2.23	-2.74	-2.48	0.36	2.57	2.74	2.66	0.06

Legend: L1 and L2 corresponds to the traditional computation approach, while L1_1 and L2_1 corresponds to the MATLAB instantiation of the functional health state algorithm.

Table 7-2. Hourly summaries of L_1 and L_2 values for Subject 1 Day 2 during DI 2016.

Time	L1	L1_1	Mean L1	SD	L2	L2_1	Mean L2	SD L2
10 PM	-1.93	-2.32	-2.13	0.27	2.39	2.68	2.54	0.20
11 PM	-2.88	-2.99	-2.93	0.08	2.23	2.45	2.34	0.15
12 AM	-2.51	-2.92	-2.72	0.29	2.45	2.76	2.60	0.22
1 AM	-2.82	-3.24	-3.03	0.30	2.47	2.75	2.61	0.20
2 AM	-2.37	-2.64	-2.51	0.19	2.44	2.74	2.59	0.21
3 AM	-2.81	-3.04	-2.92	0.17	2.46	2.75	2.60	0.21
4 AM	-2.46	-2.65	-2.55	0.13	2.42	2.67	2.55	0.18
5 AM	-1.86	-2.29	-2.07	0.31	2.56	2.88	2.72	0.23
6 AM	-2.18	-2.59	-2.39	0.29	2.46	2.81	2.63	0.25
7 AM	-3.91	-4.07	-3.99	0.12	2.51	2.70	2.60	0.14
8 AM	-2.39	-2.44	-2.41	0.04	2.43	2.71	2.57	0.20

Legend: L1 and L2 corresponds to the traditional computation approach, while L1_1 and L2_1 corresponds to the MATLAB instantiation of the functional health state algorithm.

Table 7-3. Hourly summaries of L_1 and L_2 values for Subject 1 Day 3 during DI 2016.

Time	L1	L1_1	Mean L1	SD L1	L2	L2_1	Mean L2	SD L2
9 PM	-0.88	-1.20	-1.04	0.22	2.12	2.55	2.34	0.31
10 PM	-2.00	-2.26	-2.13	0.19	2.02	2.49	2.25	0.33
11 PM	-2.46	-2.60	-2.53	0.09	2.25	2.57	2.41	0.23
12 AM	-1.83	-1.85	-1.84	0.01	1.94	2.23	2.08	0.20
1 AM	-1.34	-1.55	-1.44	0.15	2.13	2.70	2.42	0.40
2 AM	-1.54	-1.79	-1.67	0.18	2.23	2.57	2.40	0.24
3 AM	-2.20	-2.26	-2.23	0.04	2.34	2.64	2.49	0.21
4 AM	-1.52	-1.76	-1.64	0.17	2.42	2.73	2.57	0.22
5 AM	-1.93	-2.19	-2.06	0.19	2.44	2.75	2.59	0.22
6 AM	-1.61	-2.04	-1.83	0.31	2.43	2.79	2.61	0.26
7 AM	-1.99	-2.24	-2.11	0.18	2.39	2.74	2.56	0.25
8 AM	-1.60	-2.09	-1.85	0.34	2.46	2.74	2.60	0.20

Legend: L1 and L2 corresponds to the traditional computation approach, while L1_1 and L2_1 corresponds to the MATLAB instantiation of the functional health state algorithm.

Table 7-4. Hourly summaries of L_1 and L_2 values for Subject 1 Day 4 during DI 2016.

Time	L1	L1_1	Mean L1	SD L1	L2	L2_2	Mean L2	SD L2
9 PM	-1.63	-1.97	-1.80	0.24	2.30	2.63	2.46	0.24
10 PM	-1.87	-2.06	-1.97	0.14	2.29	2.57	2.43	0.20
11 PM	-1.10	-1.40	-1.25	0.21	2.09	2.56	2.33	0.33
12 AM	-1.19	-1.53	-1.36	0.24	2.07	2.61	2.34	0.38
1 AM	0.05	-0.04	0.01	0.07	1.44	1.84	1.64	0.28
2 AM	-1.17	-1.45	-1.31	0.20	2.35	2.70	2.53	0.25
3 AM	-2.37	-2.71	-2.54	0.24	2.50	2.72	2.61	0.15
4 AM	-1.61	-1.79	-1.70	0.13	2.12	2.43	2.27	0.22
5 AM	-1.50	-1.64	-1.57	0.10	2.13	2.53	2.33	0.28
6 AM	-1.99	-2.40	-2.20	0.29	2.50	2.79	2.64	0.21
7 AM	-0.90	-1.14	-1.02	0.17	2.44	2.75	2.60	0.22
8 AM	-0.44	-0.51	-0.48	0.05	2.03	2.40	2.21	0.27

Legend: L1 and L2 corresponds to the traditional computation approach, while L1_1 and L2_1 corresponds to the MATLAB instantiation of the functional health state algorithm.

Table 7-5. Hourly summaries of L_1 and L_2 values for Subject 1 Day 5 during DI 2016.

Time	L1	L1_1	Mean L1	SD L1	L2	L2_1	Mean L2	SD L2
10 PM	-0.57	-0.92	-0.74	0.24	1.91	2.39	2.15	0.34
11 PM	-1.52	-1.79	-1.65	0.19	2.34	2.61	2.48	0.19
12 AM	-0.47	-0.68	-0.57	0.15	1.77	2.28	2.02	0.36
1 AM	-0.70	-1.10	-0.90	0.28	2.04	2.59	2.32	0.38
2 AM	-0.97	-1.14	-1.05	0.12	2.12	2.44	2.28	0.23
3 AM	-1.00	-1.24	-1.12	0.17	2.30	2.66	2.48	0.26
4 AM	-1.48	-1.84	-1.66	0.26	2.44	2.80	2.62	0.25
5 AM	-0.96	-1.18	-1.07	0.15	2.05	2.47	2.26	0.30
6 AM	-1.35	-1.51	-1.43	0.11	2.48	2.85	2.66	0.26
7 AM	-1.37	-1.54	-1.46	0.12	2.24	2.63	2.44	0.28
8 AM	-0.13	-0.10	-0.11	0.02	1.93	2.51	2.22	0.41

Legend: L1 and L2 corresponds to the traditional computation approach, while L1_1 and L2_1 corresponds to the MATLAB instantiation of the functional health state algorithm.