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Development of a New Prebreathe Protocol for Future Spacecraft Atmospheres

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Zusammenfassung

Da die astronautische Weltraumforschung sich zum Ziel gesetzt hat, über die niedrige Erdumlaufbahn hinaus zu gehen und Langzeitmissionen zum Mond und zum Mars durchzuführen, wird die Notwendigkeit einer schnelleren und effizienteren Vorbereitung auf Außenbordaktivitäten (EVA) immer wichtiger.

Die derzeit auf der Internationalen Raumstation (ISS) angewandten Voratmungsverfahren können bis zu vier Stunden dauern, was sie für häufige oder Notfall-EVAs in zukünftigen außerirdischen Umgebungen unpraktisch und nicht nachhaltig macht. Um schnellere und sicherere Operationen zu ermöglichen und Dekompressionskrankheiten zu vermeiden, müssen neue Voratmungsprotokolle untersucht und entwickelt werden.

Daher untersucht diese Arbeit die physiologischen Prozesse im menschlichen Körper, die zu Dekompressionskrankheiten führen, und erforscht neue Möglichkeiten, um die derzeitigen langen Vorbereitungen zu verkürzen. Das bestehende menschliche Modell in der MATLAB-Umgebung Virtual Habitat (V-HAB), genannt Detailed Human, wurde um Stickstoffauflösungsprozesse erweitert. Mit diesem aktualisierten Modell wurden verschiedene Simulationen durchgeführt, um die Auswirkungen von Kabinendruck, atmosphärischer Zusammensetzung und körperlicher Aktivität auf die Denitrogenisierung zu analysieren.

Die Ergebnisse zeigen, dass spezifische und optimierte Kombinationen von atmosphärischen Eigenschaften und Trainingsprofilen die Voratmungsprotokolle erheblich verkürzen und gleichzeitig die Sicherheit der Besatzung gewährleisten können. Diese Erkenntnisse ebnen den Weg für die Entwicklung effizienterer Voratmungsprotokolle, die auf schnellere und flexiblere EVA-Einsätze für zukünftige Erkundungsmissionen zugeschnitten sind.

Abstract

As human space exploration sets its goal to venture beyond low Earth orbit, toward long-duration missions to the Moon and Mars, the need for faster and more efficient Extravehicular activity (EVA) preparation becomes increasingly critical.

Current prebreathe procedures used on the International Space Station (ISS) can last up to four hours, making them impractical and unsustainable for frequent or emergency EVAs in future extraterrestrial environments. In order to enable faster and safer operations, as well as to avoid decompression sickness, new prebreathe protocols need to be studied and developed.

Therefore, this thesis investigates the physiological processes in the human body that lead to decompression sickness, and explores new options to mitigate the current long preparations. The existing human model in the MATLAB-environment Virtual Habitat (V-HAB), called Detailed Human, was expanded to also include Nitrogen dissolution processes. Using this updated model, different simulations were performed to analyze the effects of cabin pressure, atmospheric composition, and physical activity on denitrogenation.

Results show that specific and optimized combinations of atmospherics characteristics and exercise profiles can significantly shorten prebreathe protocols while assuring crew safety. These findings pave the way for the development of more efficient prebreathe protocols tailored for faster and more flexible EVA operations for future exploration missions.

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Abbreviations

CEVIS	Cycle Ergometer with vibration isolation and Stabilization
CO_2	Carbon Dioxide
DCS	Decompression sickness
ECLSS	Environmental Control and Life Support System
EMU	Extravehicular Mobility Unit
EVA	Extravehicular Activity
ExMes	Extract Merge Processor
F2F	Flow to Flow
H_2	Hydrogen
ISLE	In-Suit Light Exercise
LSS	Life Support System
Manip	Manipulators
N_2	Nitrogen
NASA	National Aeronautics and Space Administration
O_2	Oxygen
P2P	Phase to Phase
V-HAB	Virtual Habitat
VGE	Venous Gas Emboli

1 Introduction

1.1 Motivation

Nowadays, the boundaries of space exploration are expanding at an accelerating pace, and with them the need to design spacecrafts to safely accommodate the crew. In order to accomplish further and longer missions, it is crucial to meet astronauts needs, which become more demanding as the complexity of the journey increases.

Among these, decompression sickness (DCS) is a concern that cannot be overlooked.

This phenomenon occurs when the human body sustains an abrupt change in the surrounding pressure environment, going form a greater pressure value to a lower one. This sudden decompression causes N_2 bubbles to form in both the blood and tissues, with consequential side effects ranging from pain in the joints to death. This behavior is dictated by the difference between the ambient pressure and the inert gas pressure, with the latter being higher.

DCS is very common within divers and astronauts carrying out Extra Vehicular Activity (EVA), which this work will focus on.

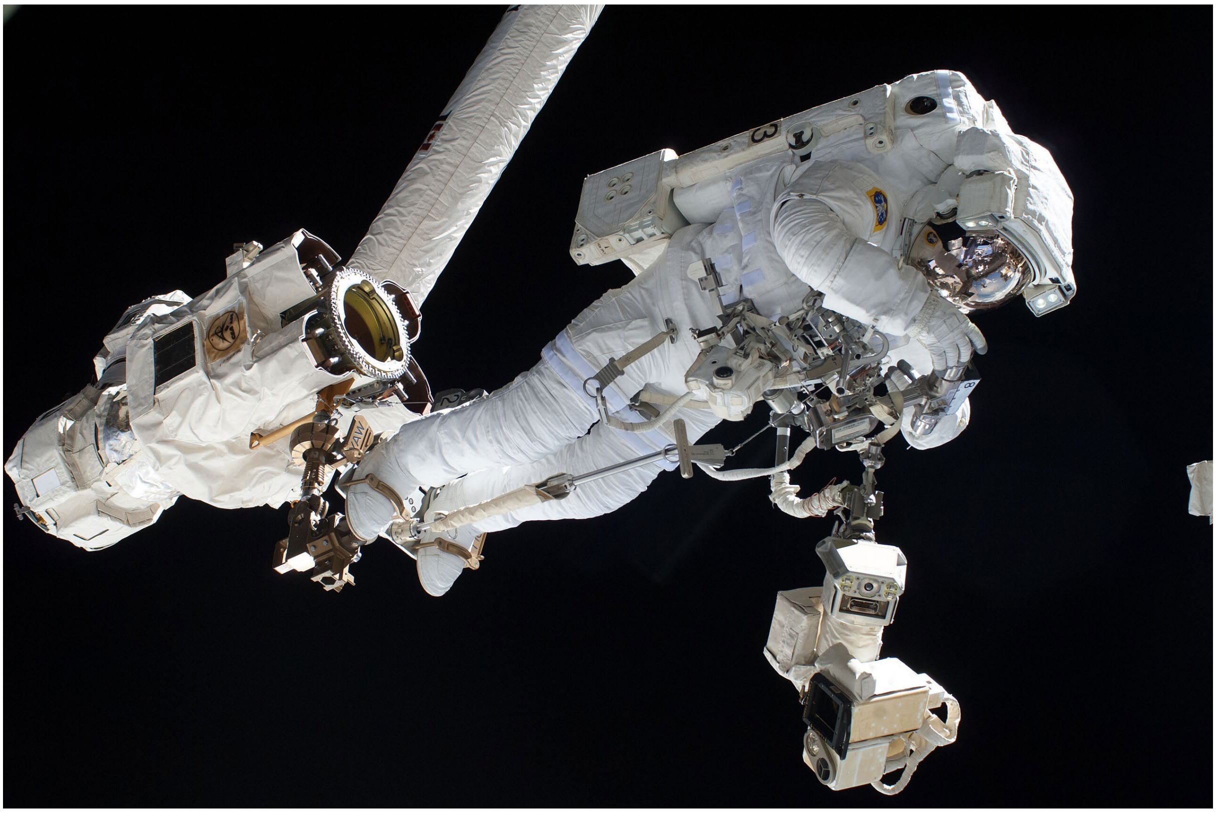

Figure 1. Astronaut Luca Parmitano during an Extravehicular Activity [1]

In its current configuration, the International Space Station (ISS) is designed with an atmosphere very similar to the terrestrial one at sea level (1 atm or 101.3 kPa). On the other hand, to conduct an EVA, it is mandatory to use the Extravehicular Mobile Unit (EMU), a spacesuit specifically designed with a pressure of 29.6 kPa.

As the pressure difference is large (0.7 bar) and the change from one environment to the other needs to happen gradually, it is necessary to implement prebreathe protocols.

Prebreathe protocols are procedures by which denitrogenation is facilitated through various means, such as different atmospheric composition, physical exercise, and length of exposure time, as longer durations result in a more complete N_2 washout.

Since the beginning of crewed missions, N_2 washout has been addressed with different levels of technical detail. Some shorter missions opted for a 100% O_2 atmosphere for their whole duration, while others started implementing more refined prebreathe protocols.

Every mission presents its own specific characteristics, to which different prebreathe protocols may apply. For example, regarding ISS procedures, these protocols may take up to 4 hours.

The duration of prebreathe protocols represents a critical factor for the future of space exploration. In scenarios such as lunar habitats, Martian settlements, or extended missions [2], astronauts will face increasingly frequent EVAs, making shorter preparation times essential for timely interventions.

This is the reason why the main objective of this thesis is to design a shorter, but still effective, protocol to be implemented in future crewed missions, by analyzing existing prebreathe protocols and the respective factors that contribute to their duration.

Numerous protocols have been analyzed and implemented, and much more are being studied. DCS is a wide known phenomenon, especially within divers and astronauts. Prebreathe protocols, on the other hand, remain a topic that is still being actively researched, since in diving only decompression stops are implemented: divers stop on their ascent to prevent the formation of N_2 bubbles.

Astronauts, however, require more detailed procedures which have been improving during the years: in the early missions 100% O_2 atmospheres were implemented. This atmosphere is the best solution to eliminate N_2 from the human system, but poses other issues such as flammability and challenges related to o O_2 partial pressure.

Nowadays prebreathe protocols are the outcome of the combination of different factors, such as atmosphere composition, environment pressure and physical exercise. These different variables are being studied in order to optimize the protocols for greater safety and shorter times.

In this work, by using the MATLAB based programme V-HAB, the variables and their interaction will be analyzed with the goal of designing a shorter and more efficient prebreathe protocol.

1.2 Goals

To conduct and carry out this work, various approaches have been taken into account.

Firstly, a throughout literary research has proved fundamental to better understand DCS issue and all its consequences. Relevant literature was consulted to define a comprehensive baseline of human physiology and DCS. Afterwards past and present prebreathe protocols were analyzed, to obtain information about which factors contribute to their optimization, or what restrictions and constrictions regarding their use may exist.

Secondly, gaining knowledge about the MATLAB based programme V-HAB (Virtual-Habitat) was a mandatory asset. Through introduction tutorials and external resources, a sufficient understanding of the program was acquired, which was necessary to be able to model and edit the code.

The successive step was the implementation of N_2 in the code. V-HAB is a programming environment in which it is possible to study and simulate life support systems and their effect on the human body. In fact, in the MATLAB class structures a modeled *Detailed Human* can be found, including the main physiological processes of interest for the space environment. However, in the existing code, only processes regarding CO_2 and O2 were implemented, neglecting the effects of N_2 in the body.

For this reason, N_2 needed to be added to the *Detailed Human* model. In order to do so, more research was necessary: it was essential to find the most accurate mathematical model to represent DCS. After this model was chosen, the equation needed to be implemented in the V-HAB code and be modified to be consistent with the rest of the procedures.

Subsequently, once the code had been optimized, existing prebreathe protocols were implemented and compared to the code in order to verify the used equation and to prove the effectiveness of the code.

Lastly, considering the impacting parameters, a time optimized prebreathe protocol has been designed.

1.3 Methods

The focus of this study is on better understanding DCS and its effects and limitations on the human body, and the designing of a shorter, but efficient, prebreathe protocol. While more details can be found in the other chapters of this work, in this section the adopted methodology is presented.

A literature review was conducted using technical reports, academic volumes, scientific databases, and existing studies on human physiology, DCS and N_2 processes. This provided a theoretical background, which allowed to form model assumptions and parameterizations.

To simulate N_2 elimination, the current V-HAB code, which initially included only O_2 and CO_2, was modified to incorporate N_2 as well. These modifications allowed the model to account for N_2 behavior and processes in order to study the risk of DCS and better design a new prebreathe protocol.

Finally, model validation and calibration were performed by comparison with experimental and published data, in order to ensure reliable predictions while providing valid grounds to explore new prebreathe scenarios.

1.4 General thesis overview

In this section every step of the work conducted is outlined and explained as follow.

In Chapter 1 the problem that motivated this work is outlined, followed by a brief overview of the state of the art, the goals set to accomplish and the methods implemented.

In the following chapter a more detailed explanation of DCS can be found. Afterwards, various past and present prebreathe protocols are presented, with a deeper focus on the ones currently in use. Moreover, the chapter highlights the factors that contribute to the duration of the protocols.

An extensive overview of the Virtual Habitat (V-HAB) code is given in Chapter 3. This MATLAB-based simulation system is the foundation of the modeling work presented in this thesis. In this chapter the program is presented and explained, along with its functionalities that are of interest for this work.

In the next chapter, Chapter 4, an immersive description of the process of modeling N_2 is stated. Here the chosen models are listed and the equations explained. Moreover their implementation in the MATLAB environment and the necessary modifications are presented.

Chapter 5 presents the procedures of validating existing prebreathe protocols to ensure the proper functioning of the code and its consistency with real-life conditions. Subsequently new protocols have been tested, and a duration optimized one is described.

Lastly, in Chapter 6 final considerations are drawn. An analysis of the work is conducted and the final results are compared with the initial objectives to investigate if the initial goals have been met. Additionally, limitations and possible future research are outlined.

2 Theoretical background

In this section a detailed explanation of DCS is given, followed by description and analysis of existing prebreathe protocols.

2.1 Overview of Decompression Sickness

Decompression sickness (DCS) is a medical condition caused by the formation of N_2 bubbles in the blood and tissues, that occurs mostly during diving and EVAs.

N_2 is an inert gas which is widely present in the blood and tissues, as it constitutes about 78% of the air that humans inhale. In normal conditions, N_2 is inhaled and exhaled, without having any effect in the human metabolism, but settling in the blood and tissues. When the environment pressure decreases rapidly, the partial pressure of the dissolved gas in the body exceeds the surrounding one. Because of the rapidity of the change, N_2 is not able to diffuse out gradually, but it will form bubbles in an effort to leave the solution and restore the pressure equilibrium.

The bubbles released in the bloodstream can be the cause of various symptoms, which range from mild ones, like numbness and joint pain, to more severe ones, including death.

It is possible to differentiate two different types of DCS and related side effects:

- *Type I DCS*, often called 'the bends', is less severe and it is characterized by musculoskeletal pain and cutaneous symptoms. Common manifestations include joint pain, single extremity tingling or numbness, itching and mild rashes. In general, the symptoms for this type of DCS can build in intensity but do not result in fatal or serious outcomes.
- *Type II DCS* is considered more serious and can be life threatening. Three different categories of Type II DCS exists:
    - *Central DCS*, occurs when N_2 bubbles are present in the arterial blood stream and reach the brain, with the possibility of causing arterial gas embolism;
    - *Pulmonary DCS*, a very rare type, it happens when N_2 bubbles are found in the lungs and compromise their correct functioning. Symptoms may result in dry cough, chest pain and dyspnea;
    - *Neurological DCS*, takes place when N_2 bubbles affect the nervous system. Consequences can include paresthesia, muscle weakness, difficulties walking and physical coordination, paralysis or mental confusion [3].

The seriousness of DCS, especially Type II, lies not only in all the diverse symptoms that may arise, but also in the rate of manifestation. In fact, they can develop quickly or slowly, and build up over several hours. If the first symptoms are weakness and fatigue, which are very common and expected outcomes during strenuous physical activities such as EVAs, the seriousness of the situation may be overlooked until more severe symptoms arise, threatening the astronaut's health and life. For these reasons, even if some treatments exist, it is necessary to prevent DCS.

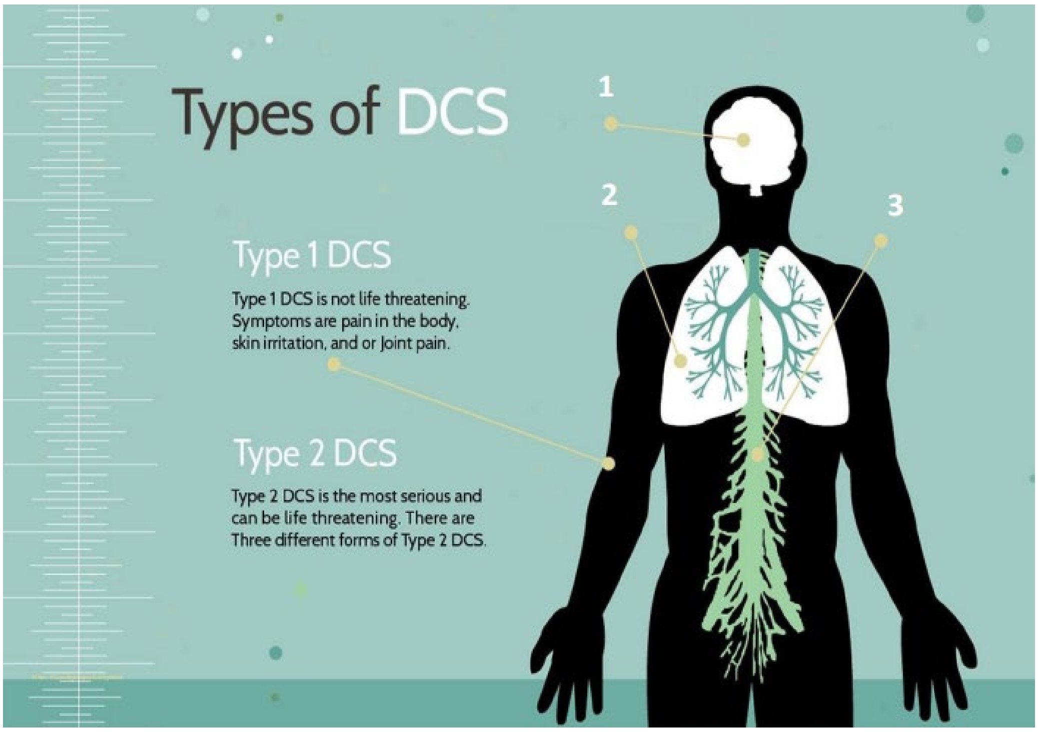

Figure 2. Types of Decompression Sickness [4]

In general, two conditions are necessary for DCS to develop: the first is inert gas supersaturation, defined as the partial pressure of a gas being greater than the ambient pressure, and the second is the presence of a bubble nuclei (or micronuclei) from which the gas can evolve into a gas bubble.

Following these requirements, DCS could be prevented either by acting upon the pressure difference in the environments, or by hindering the transformation of tissue micronuclei into gas bubbles. However, the most effective way to counter DCS, is proven to be the reduction of the pressure difference.

The pressure difference can be decreased either by reducing the partial pressure of N_2 in the cabin or by increasing the pressure in the in suit. In the first instance, appropriate adjustments need to be made regarding the composition of the cabin atmosphere, whilst in the second case new spacesuits should be designed.

Both these remedies have their own limits, which will be explained in detail in Section 2.3. Let it be noted, however, that these countermeasures are not sufficient on their own and, combined with the difficulty of diagnosing early DCS symptoms, it is therefore mandatory to introduce prebreathe protocols to reduce the level of N_2 in the body.

2.2 Past and present prebreathe protocols

Prebreathe protocols are procedures that astronauts must undergo before any displacement that comprises the shift from a higher-pressure environment to a lower-pressure one, like performing EVAs.

As stated above, DCS is not easy to diagnose and overlooked symptoms may advance to severe conditions before timely intervention is possible, moreover treatment can only begin once the astronaut has terminated or aborted the EVA and returned to the habitat. It includes pure O_2 administration and recompression therapy with the goal of reducing the size of N_2 bubbles and eliminating the gas from the body. For these reasons prevention is preferred to treatment.

In some missions, like Mercury and Gemini, an atmosphere of 100% O_2 was constantly implemented, which did not require prebreathe protocols. However, for other missions, such as the Shuttle Program and especially the International Space Station, the composition of the atmosphere also included N_2, thus establishing the need for prebreathe protocols.

2.2.1 Shuttle Program

In the Space Shuttle program, two protocols were chosen for flight operations. These protocols resulted from hundreds decompression trials performed in the span of more than a decade. The two prebreathe protocols implemented, were based on the “R” value of 1.65, which represents the ratio between the N_2 tension in a 360-minute half-time tissue compartment and the spacesuit pressure [5].

The two protocols were outlined as follows:

- a 4-hour O_2 prebreathe performed while wearing a suit pressurized to 101.2 kPa;
- a staged decompression, comprehensive of:
    1. 1-hour O_2 prebreathe;
    2. depressurization of the cabin to 70.2 kPa with 26.5% O_2 for the whole crew. This was maintained for a minimum of 12 hours;
    3. additional 75 minutes of O_2 prebreathe in-suit for the EVA crewmembers. This time could be reduced based on the length of exposure to the 70.2 kPa cabin environment.

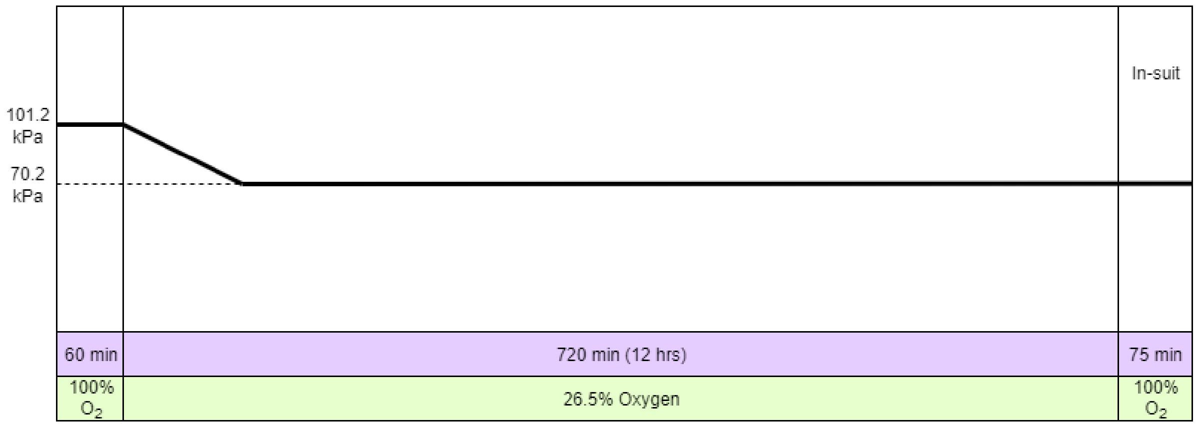

Figure 3. Staged Decompression Prebreathe Protocol Operational Timeline

As the Shuttle Program is over, this protocol is no longer being used. However the staged decompression approach has been adapted to other missions, such as the Polaris Dawn mission by SpaceX.

2.2.2 In-Suit Light Exercise Protocol

The In-Suit Light Exercise (ISLE) Protocol, was developed with the goal of reducing the length of prebreathe procedures. In particular, in this case, physical exercise was added, as it accelerates the rate of denitrogenation. It consists of:

1. 60 minutes of O_2 breathing followed by a depressurization to 70.2 kPa while performing light exercise ($5.8\frac{ml}{kg \cdot min}$, the value stating the ml of O_2 consumed per kg of weight per minute of exercise);
2. 30-minute suit donning at 70.2 kPa while breathing enriched air (26.5% of oxygen);
3. 50 minutes in-suit light activity ($6.8\frac{ml}{kg \cdot min}$) breathing O_2 while repressurization to 101.2 kPa;
4. 50 minutes rest while breathing O_2 [6].

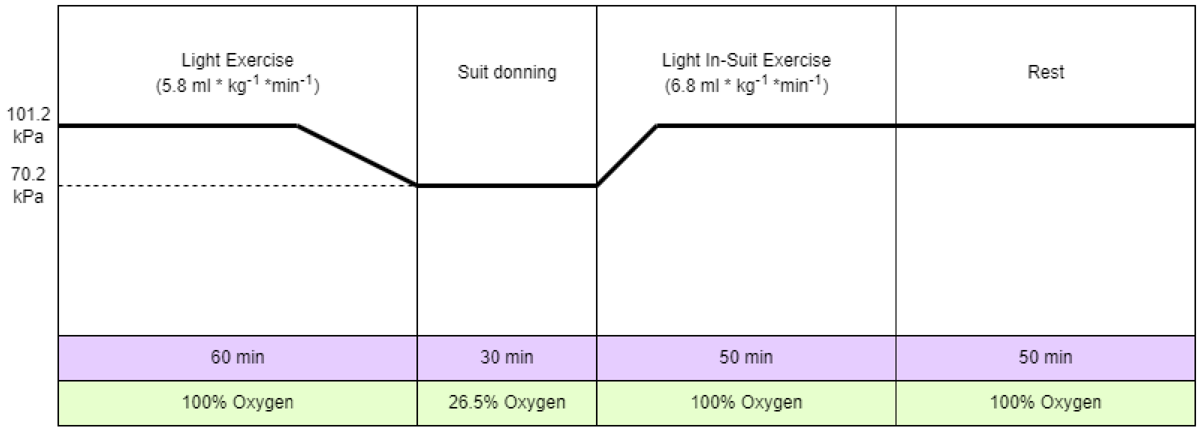

Figure 4. In-Suit Light Exercise Prebreathe Protocol Operational Timeline

This protocol is the current standard used on the ISS.

2.2.3 Campout Protocol

The campout protocol owes its name to the fact that, during this procedure, the two EVA astronauts “camp out” in the airlock. The complete protocol is composed of the following steps:

1. 8 hours and 40 minutes in the airlock at 70.2 kPa, breathing 26.5% O_2 the night before the EVA;
2. 70 minutes O_2 breathing with a mask at 101.2 kPa, while eating and using the restroom;
3. donning suits at 70.2 kPa while breathing 26.5% O_2;
4. 50 minutes of repressurization to 101.2 kPa and assistance from another astronaut before final pressurization to the vacuum of space [7].

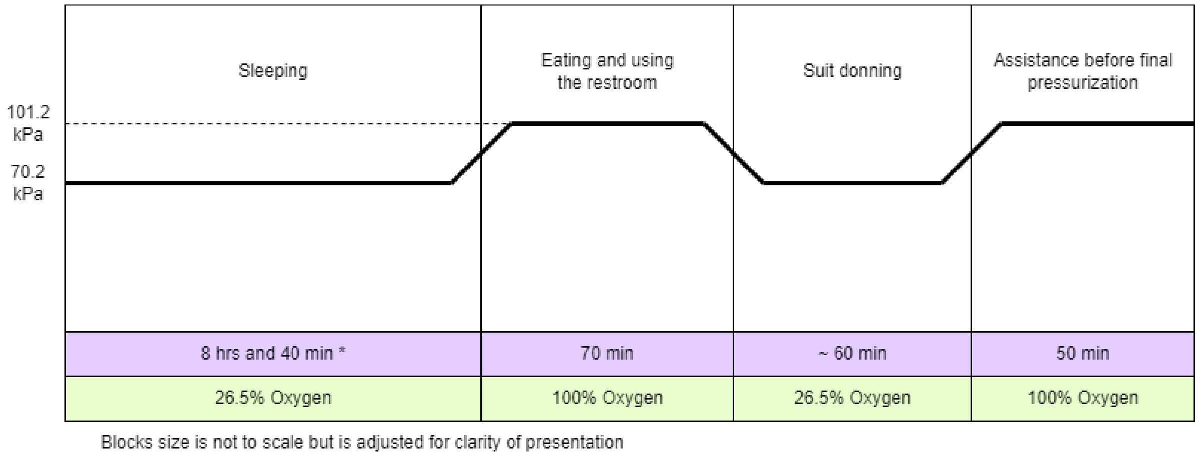

Figure 5. Campout Prebreathe Protocol Operational Timeline

This protocol has been used on the ISS and can still be implemented, but the ISLE protocol is the preferred one.

2.2.4 Cycle Ergometer with Vibration Isolation and Stabilization Protocol

The Cycle Ergometer with Vibration Isolation and Stabilization (CEVIS) is a protocol that begins before launch, and it is divided in different phases:

1. *preparation prior to launch*, astronauts perform a maximum O_2 uptake (VO_2 max) test on a leg ergometer. The protocol is designed based on the test results, and the workload is divided between 12% upper body and 88% lower body;
2. *prebreathe coupled with exercise*, breathing through a mask astronauts perform exercise at 75 bpm, starting at 37.5% VO_2 max and increasing to 50% VO_2 max, 62.5% VO_2 max and 75% VO_2 max for 7 minutes;
3. *final prebreathe*, astronauts breathe O_2 for 50 minutes while the airlock is depressurized to 70.2 kPa in a 30-minute period. During this period astronauts don their suit, and when O_2 is stabilized to 26.5%, they remove their mask and finish donning;
4. *suit check*, astronauts perform suit check and purge at 100% O_2;
5. *in-suit prebreathe*, this last phase begins with a 5-minute depressurization to 101.2 kPa and is followed by airlock and suit depressurization to 29.7kPa [7].

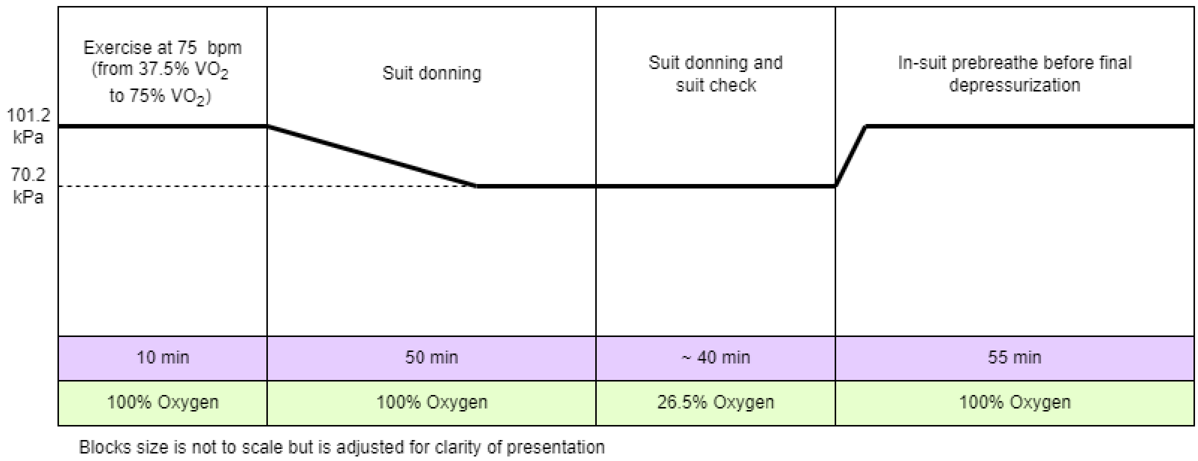

Figure 6. Cycle Ergometer with Vibration Isolation and Stabilization Prebreathe Protocol Operational Timeline

2.3 Factors that influence prebreathe protocol duration

As stated in Section 2.1, different methods exist to facilitate denitrogenation and thus reduce the risk of DCS. Prebreathe protocols account for a large share of the available solutions, but other contributing factors can also play an important role in reducing the duration needed to prepare for an EVA.

2.3.1 Cabin atmosphere

Since the risk of DCS is present when astronauts need to move from the higher-pressure environment of the cabin to the lower-pressure environment of the suit, manipulating the cabin atmosphere can be one method to facilitate N_2 wash out.

Some atmospheres from past and present missions are shown below.

Program	Cabin Pressure [kPa]	Cabin Oxygen Concentration [%]	EVA Suit Pressure [kPa]	EVA O_2 Prebreathe Time [min]	EVA Prebreathe Conditions
Mercury	34.5	100	-	-	-
Gemini/Apollo	34.5	100	25.8	0	-
Skylab	34.5	70	25.8	0	-
Shuttle	70.3	26.5	29.6	40	In-suit (after 36 hours at 70.3 kPa)
	101.3	21	29.6	240	In-suit
ISS/US	101.3	21	29.6	120-140	Mask and in-suit; staged w/ exercise
				240	In-suit
Salyut, Mir, ISS/Russian	101.3	21	40.0	30	In-suit

Table 1. Historical and current mission atmospheres with eventual prebreathe protocol conditions [8]

The two key aspects to considerate for the optimization of the cabin atmosphere are the ambient pressure and the percentage of O_2 in gas mixture.

On one hand, decreasing the cabin pressure results in less pressure difference to the suit pressure, which could lead to shorter prebreathe protocols. In some cases, if the cabin pressure is reduced accordingly and the suit pressure is high enough, prebreathe protocols may not be necessary at all, as was the case during the Mercury and Gemini missions, as can be seen in Table 1.

On the other hand, a lower cabin pressure could pose health risks for the astronauts, such as hypoxia and other possible long-term effects of living at hypobaric environments that at present remain unknown. Moreover, appliances and equipment functioning might have to be re-evaluated as they are designed for a specific environment and can be subjected to failures or outgassing.

A higher concentration of O_2 in the atmosphere leads to a faster denitrogenation, contributing to short prebreathe protocols. The main problem this solution poses, is the flammability risk. In fact, during ISS and Shuttle programs, the maximum limit for O_2 concentration was 30%. One blatant yet dreadful example is the Apollo 1 disaster. During a pre-flight ground test, while the crew was in the sealed and pressurized capsule, a fire broke out likely from a damaged wiring. The electrical spark ignited combustible materials found in the command module, and the fired spread almost instantaneously due to the pure O_2 and high-pressure atmosphere, resulting in a tragic fatal incident for the astronauts [8].

In future missions, if atmospheres with higher O_2 concentration will be considered, it will be mandatory to undergo significant testing to determine material suitability [9].

In Figure 7 it is possible to observe the physiological limits the pressure and O_2 concentration pose to humans, and the acceptable values for atmospheric composition. Furthermore, historical missions and their atmospheres are labeled.

NASA's exploration atmosphere is set at 56.537kPa (8.2 psi) and 34% O_2 [10]. This atmospheric composition is the result of a trade-off considering risk of DCS, hypoxia and flammability, and it is a mission research profile used to study human physiology in spacecraft and surface habitats designed to support high-cadence EVAs.

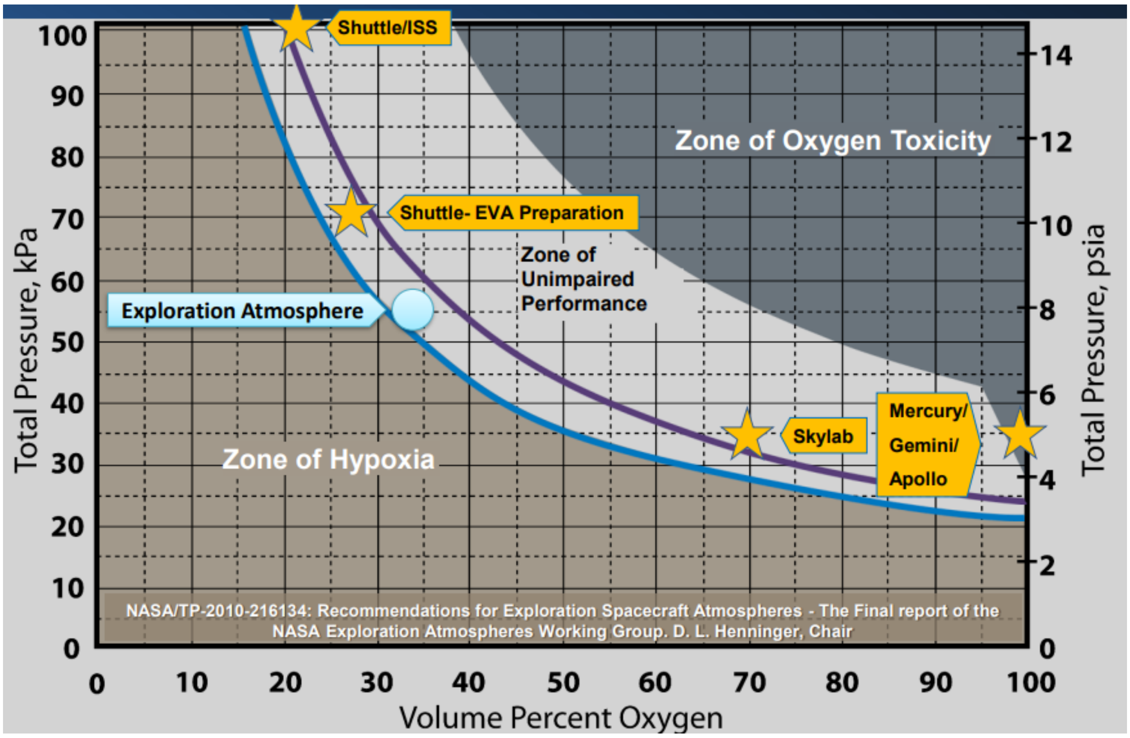

Figure 7. Atmospheric compositions and limits of historical and current missions, with physiological limits [10]

2.3.2 Suit pressure

Another possibility for shorter prebreathe protocols would be to increase the pressure of the suit used to carry out EVAs.

The reasons that spacesuits require a much lower pressure than terrestrial atmospheric pressure, typically around 30–40 kPa, are connected to mobility, safety and physiological limits.

The reduction in internal pressure is mostly motivated by the need to provide enough mobility for the astronaut, as higher pressures result in increased stiffness of the suit structure and joints, and a higher structural complexity, making it harder to manipulate and move the suit.

For this reason, the atmosphere of the suit is composed of 100% O_2, in order to maintain the partial pressure of O_2 high enough to avoid hypoxia, and to avoid unnecessary overall pressure increase caused by the addition of any other gas. Higher pressure would also result in risk of hyperoxia.

Considering physiological and engineering requirements, suit pressure presents upper and lower pressure limits:

- 24.1 kPa is a reasonable minimum based on health needs;
- 41.4 kPa is a reasonable operating maximum based on structural capability [10].

As of now, the EMU has a pressure of 29.7 kPa, a compromise to maximize mobility while providing enough O_2 to the astronaut.

2.3.3 Physical exercise

Despite studies being still ongoing and not complete, it is proven that physical exercise accelerates denitrogenation. During physical activity blood is redistributed towards more active tissues and muscles, thus improving perfusion.

Various experiments and tests have been performed to optimize exercise implementation in prebreathe protocols. While it is true that different types of activity results in more or less efficient denitrogenation, an optimal exercise has not yet been defined.

Nevertheless, some crucial information to select the exercise that best fit the protocols has been gathered:

- physical exercise during prebreathe protocols should always be kept to a light level, as EVAs are long and physical demanding activities;
- the best outcome is obtained if light activities are maintained throughout the whole duration of the prebreathe protocols;
- having a short but intense burst at the beginning (for example 10 minutes at 75% VO_2) can help shorten the prebreathe time [11]. The intense exercise should be performed throughout a short period, comparatively to the whole protocol: this ensure that enough time is left to recovery the spent energy.

3 Virtual-Habitat overview

In this chapter a detailed explanation of the Virtual Habitat (V-HAB) and its features will be given.

3.1 General features

V-HAB is a MATLAB-based simulation system developed to model and analyze life support systems in crewed habitats. It focuses mostly on dynamic behaviors, evaluating how temperature, pressure, human metabolic demands, gas, liquids and solid components interact and evolve over time in a specific closed environment.

The program is built using objected-oriented MATLAB structures, which means that the code is organized into classes and objects, which represents physical components and processes. Using this approach, the program turns out to be modular and reusable: it is possible to reuse different blocks, resulting in combining and connecting them in different scenarios to build the desired habitat simulation.

The basic V-HAB repository contains four directories:

- core, where the central V-HAB framework is located;
- lib, existing components, functions and tools can be found here;
- user, folder dedicated to user-specific simulations;
- data, simulation results and related data end up here.

To create the systems and subsystems that make up the habitat, it is necessary to introduce the key elements of V-HAB. These are explained below, and represent the fundamentals blocks to implement in order to design life support systems (LSS).

3.1.1 Stores and Phases

In the V-HAB environment, a store represents a physical container inside an LSS. This could be a cabin, a recipient for water supply or waste storage and so on. The basic functionality of stores is to contain matter, and for this to happen it is mandatory to introduce the phases as well. A phase defines the current matter state and in V-HAB there are four different types to choose from: solid, liquid, gas and mixture. In general different phases can be found in the same store, like in the case of modeling a tank with fuel and pressuring gas.

In order to add a store to the simulation, the following code must be used:

```
matter.store(this, 'StoreName', fVolume, tGeometryParams);
```

Where:

- 'this' indicates that the store is being added to the current simulation;
- 'StoreName' can be changed into the desired name representing the store;
- 'fVolume' defines the volume of the store. The volume must be large enough to accommodate all the phases present. In general liquids and solids are assumed incompressible, and therefore the volume of an eventual gas is calculated by the store by subtracting the volume of liquids and solids from the total volume;

- 'tGeometryParams' is an optional struct that can be added to provide more detailed information about the geometry of the store.

Stores created as above are empty, thus one or more phases need to be added. To do so the following string of code has to be implemented:

```
matter.phases.XXX(oStore, 'PhaseName', struct('Substance',fMass),
YYY);
```

Where:

- 'XXX' is specific for the type of phase desired, and should be replaced accordingly with solid, liquid, gas or mixture;
- 'oStore' needs to be replaced with the name of the store where the phase is contained;
- 'PhaseName' represents the name of the phase;
- 'struct('Substance', fMass)' is a struct where the type and mass of the phase should appear. In particular the name of the substance must be the same name saved in the matter table, and the mass should be expressed in kilograms. It is also possible to add more than one substance in the same struct. For example *struct('N2', 2, 'O2', 0.5)* corresponds to adding 2 kilograms of N_2 and 0.5 kilograms of O_2;
- 'YYY' contains specific additional information for the type of phase described.
    - Solid substances require an additional input to set the temperature of the phase in Kelvin;
    - Liquid phases need inputs to set the temperature and also the pressure;
    - For gas matters initial volume and temperature are defined. For this phase, the volume input will be overwritten by V-HAB once the remaining volume of the store is calculated. In most cases it is more ideal to define gas phases by their partial pressures instead of by their masses; this can be achieved by using helpers and expressing the partial pressure in Pascal. Moreover, flow and boundary phases can be defined, which refer to infinitesimal small and infinitely large volumes;
    - Mixture phases exist to compensate for impossible combinations, often characterized by substances of different phases. This phase allows for phase changes to occur and it requires inputs for the initial matter state, temperature, pressure and the absorber substance. However, this phase is not of interest for this work.

3.1.2 Branches

Branches are the structures that allow to move matter from one store to another. However, in V-HAB, the representation differs slightly from reality. A branch represents the physical link between two stores, but it needs to be associated with a solver, which implements a flow rate to allow the actual transfer from one store to the other. For this reason, a branch always requires a solver to go with. In general, different types of solvers can be applied in accordance with the requirements; this will be explained more in detail later on.

In order to move matter between stores, an additional element must be added, the Extract Merge Processor (ExMes). This element creates the necessary connection to add or remove matter to or from a phase, and it comes in four different types, one for each matter state: solid, liquid, gas and mixture. ExMes can be added either by implementing their own line of code or by defining them inside the branch definition.

Branches are defined as follow:

```
matter.branch(this, 'Store_1.ExMe_1', {}, 'Store_2.ExMe_2',
                        'Branch_Name');
```

Where:

- ‘Store_1.ExMe_1’ and ‘Store_2.ExMe_2’ need to be replaced with the name of the stores that are being connected and the names of the ExMes that are being used for the connection;
- { } could contain flow to flow processors, which represent components used to model the pipes, pumps and other parts;
- ‘Branch_Name’ indicates the name given to the branch.

As stated above, instead of ExMes, the path to a phase object can be written in the branch definition.

Once the branches are established, the corresponding solvers need to be defined. As previously mentioned, different types of solvers exist, and differ in the level of accuracy provided.

The simplest one is the manual solver, where it is possible to specify the flow rate to be applied. By leveraging the functionalities of this solver, it is also possible to implement mass transfer.

Another type of solver is the interval one, which calculates the flow rate considering the pressure difference within the branch. In particular, it works on the idea that the pressure difference is equal to the pressure losses in the branch.

The residual solver, on the other hand, automatically adjusts the flow rate so that the mass on the left boundary of the branch remains constant. For this reason only one residual solver can be connected to the same phase on its left side.

For flow phases, namely phases with infinitesimal small mass, a multibranch solver is implemented. In this solver a linear system of equations is solved, with the same operating principles as the internal solver. However this solver is of no interest for this work, and it will not be investigated further.

Lastly, a thermal solver must be added to every system that deals with thermal energy transport.

3.1.3 Processors

The term processors refers to all those components that modify the properties of matter, such as pressure, mass or temperature. Being this a very broad group of elements, more partition is needed:

- ExMes, which are described above;
- Phase to Phase (P2P) processors describe the transfer of mass between different phases that belong to the same store, like for example a gas

condensing. They model if and how much matter should be relocated from one phase to another;
- Flow to Flow (F2F) processors represent any addition that may be found in a physical plumbing system, like pumps, heat exchangers or other components that alter the properties of the matter flowing through a specific branch;
- Manipulators (manip), lastly, are used when there is the need to transform one substance into a completely different type, thus allowing to model chemical reactions.

3.1.4 Time Step

The time step, which controls the progression of the simulation, can be set differently for each component in the simulation, allowing for individual time steps. This usually depends on the type of solver that is being used or particular requirements implemented by the user. Moreover, in each simulation step stability conditions and user inputs are calculated, resulting in a more accurate, but slower, model when relevant changes are occurring, and a faster one when the system is found in a near steady state [12].

This feature is of specific importance for this work, as prebreathe protocols operate on a strict time schedule, and also because it allows to manage and control how efficient the protocol is at a precise instant.

Various prebreathe protocols, as it can be seen in Chapter 2.2, are characterized by changes in atmospheric composition and ambient pressure. By assigning an appropriate time step size, it is possible to study the variations in N_2 partial pressure and thus assess the progress of a specific prebreathe protocol, in order to validate it or adjusts its parameters to improve its effectiveness.

3.2 Existing code description

In the current state of the art, the V-HAB environment contains various MATLAB classes describing components useful to design an ECLSS. In particular they could be divided into three macro categories: electrical, matter and thermal, and inside each of these folders more elements can be found, like heat exchangers, O_2 generator assembly, conductors.

Since one of the main objectives of this research is to model DCS, it is therefore necessary to focus on the sections of code which are best suited to this purpose. In V-HAB two suitable models can be found: the "*Human*" and the "*Detailed Human*". Both sections of code represent the human body and its metabolic processes, however the *Detailed Human* is supplied with more details, hence the name. For this reason the latter has been chosen for this work. Its folder is situated inside the "matter" category, and it includes itself five subcategories, called "Layers", which are *Digestion*, *Metabolic*, *Respiration*, *Thermal* and *Water Balance*.

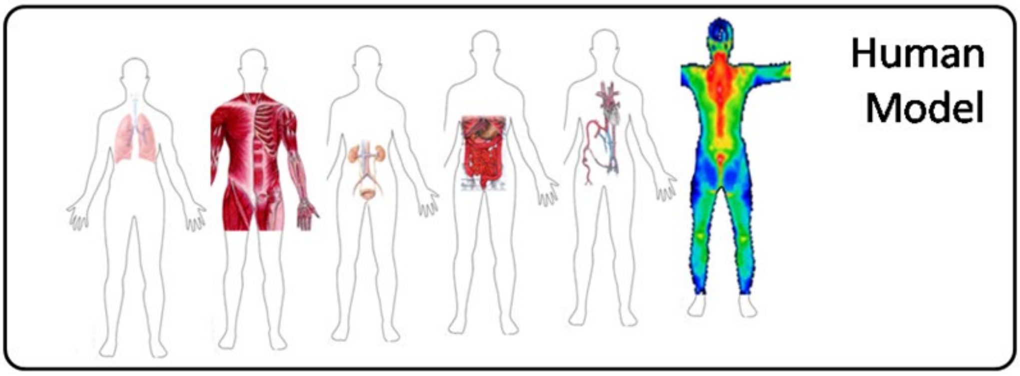

Figure 8. Representation of the five layers of the *Detailed Human*

Given that DCS mainly concerns the respiratory and the cardiovascular systems, the analysis focuses on the *Respiration* module, in which the behavior of these systems is modeled.

Below, in Figure 9, the path to reach the desired folder in V-HAB is highlighted with arrows.

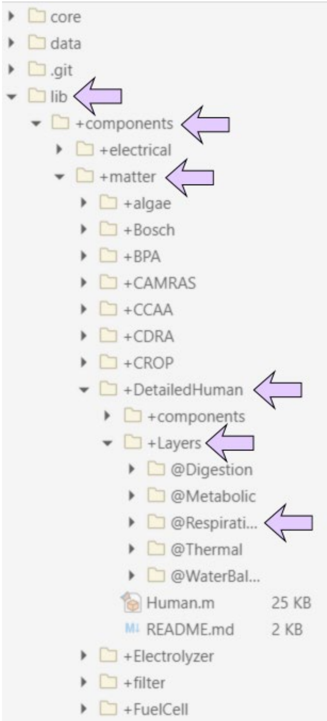

Figure 9. Virtual Habitat folders path for *Detailed Human* and *Respiration*

In the *Detailed Human* code all the information and values are taken from [13] and [14], unless stated otherwise.

The *Respiration* code provides the numerical and physiological simulation of the human respiratory system, as well as describing the interaction with the cardiovascular system. It models the dynamic exchange and circulation of O_2 and CO_2 between the brain, tissues, lungs and bloodstream, while simultaneously controlling ventilation and blood flow in response to feedback mechanisms. This allows for the reproduction of respiratory and circulatory behaviors under various conditions dictated by the environment or the human metabolism.

Throughout the code, different functions are defined, each of them having its specific role and scope. Among these, the most relevant for DCS modeling regard the calculation of blood concentration, gas partial pressure in the tissues, brain and blood, and rate of mass change.

The key functions involved are explained below:

- `calculateBloodPartialPressure()`, it calculates the updated partial pressures of O_2 and CO_2 in the blood, which correspond to the values of the current concentrations of the gases in the blood, given as an input. By using the concentrations in different part of the cardiovascular system, it is possible to calculate partial pressures in different areas, like for example the arteries, as it is done in the code;
- `calculateBloodConcentration()`, it evaluates the updated concentration of O_2 and CO_2, considering the actual values of the gases partial pressures, which are stated as the input. As well as in the previous case, it is possible to calculate blood concentration of different zones based on the parameters given. In the code this function is used to calculate blood concentration in the brain and in the tissues;

- `calculatePartialPressureTissue()`, it determines the partial pressure of O_2 and CO_2 for the respective tissue and the gases flow rates from the tissue to the blood stream. In the same way as the other functions, with this one it is possible to determine the partial pressures and flows based on the inputs given. In the code it is used for the variables related to the brain and to the tissues.

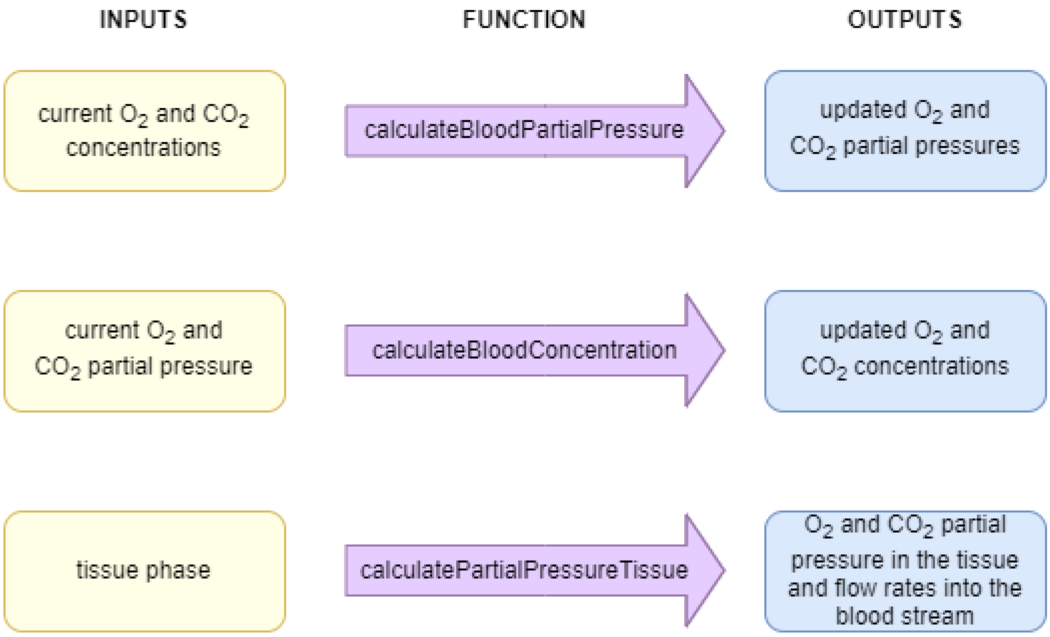

Figure 10. Key *Respiration* functions summarized with respective inputs and outputs

Despite these functions being the core of the *Respiration* class, some modifications are needed in order to model DCS. The main issue lies in the fact that the original model only accounts for O_2 and CO_2, in that they are the main gases which take part in the human metabolic reactions. In fact, even though N_2 makes up for almost 80% of the air we breathe, it remains an inert gas: it does not participate in biological processes within the human body. Moreover, humans exhaled the same amount of N_2 that is inhaled, in contrast with the behavior of O_2 and CO_2, which are absorbed or released based on physiological needs.

However, the addition of N_2 is fundamental to study DCS and its effects, and it needs to be implemented in the code. More than this the *Detailed Human* requires to be inserted in a setting, like a cabin atmosphere, in order for the code to be executed; for this reason, an environment is modeled. This will be better explained in Section 3.3 and Chapter 4.

3.3 Required modifications and additions to the code

As stated above, N_2 and its processes are not implemented in the original *Respiration* code. The modifications need to be realized with some forethought considering the different metabolic role of N_2 compared to O_2 and CO_2.

The addition of N_2 in the code requires a thorough redesign of the internal logic. It is in fact necessary that the inclusion of a new gas will not compromise the balance of the equations and the already existing calculations. The general behavior of the model needs to remain stable.

Given that these adjustments involve different computational and structural updates, the specific changes will be described in more detail in the following chapter. However, it is necessary to highlight the importance of maintaining a reliable and cohesive code.

4 Nitrogen Modeling

In this chapter the human respiration process is described in more detail to provide a better understanding of the physiological mechanisms involved, and to support the mathematical approaches implemented. The models are then presented and analyzed.

4.1 Respiration process and Nitrogen addition

When humans inhale, O_2 and N_2 enter the body and the bloodstream. O_2 binds to the hemoglobin inside red blood cells and it is diffused and delivered to tissues and organs where it is needed for cellular respiration. N_2 is also diffused in the bloodstream and tissues, but has no role in metabolic processes.

During exhalation, CO_2 is expelled as a waste gas. In this process CO_2 is collected by the blood and it is carried outside of the body. In the course of this procedure N_2 is expelled as well. [15]

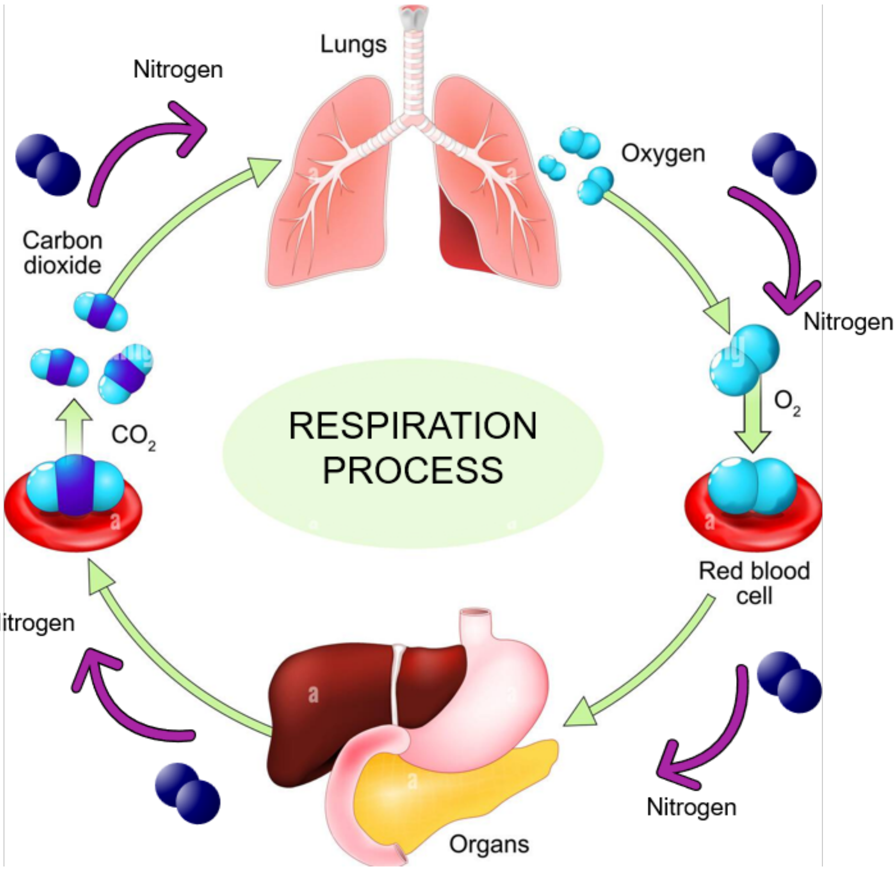

Figure 11. Scheme of the respiration process and difference between CO_2 and O_2 metabolic processes and N_2 inert behavior [16]

The risk N_2 poses by being an inert gas, which would correspond to DCS, arises when the pressure between the body and the outside environment changes rapidly. It has no correlations to other metabolic processes that take place during respiration.

Because of physiological and metabolic differences, the respiration process requires different models in the code for O_2 and CO_2, and for N_2.

N_2 partial pressure and concentration were added, both as an input and as an output, in the equations mentioned in Section 3.2. Where possible, the same models used for O_2 and CO_2 were copied, but this was very rarely the case.

The main variable used to evaluate the level of N_2 in the body is its partial pressure. This choice is derived from the level of detail already implemented in the existing code and by the equations analyzed to model N_2 dynamics. By considering the partial pressure it is possible to define a threshold below which the risk of DCS is minimal. For this work the maximum acceptable N_2 partial pressure value has been set between 100 and 200 mmHg. This value is not a universal threshold that guarantees no occurrence of DCS however, during the MATLAB analysis it resulted as a common value at which most simulations would end. This can be better seen in Section 5.1, but most simulated protocols resulted in a final N_2 partial pressure value lower than 10 kPa, which roughly equates to 75 mmHg. Given the possible uncertainties and approximations of the models, a slightly higher value has been chosen.

It is to be noted that this value is not a universal limit under which DCS will absolutely not happen, nor is the evaluation method a perfect approach. In fact, DCS is a very complex phenomenon that is still under investigation, and it depends on numerous factors which are not unique, as they vary among individuals according to their physiological characteristics. More than this, more approaches are being studied as to which is the best model to evaluate the risk of DCS. [11] This aspect is discussed in greater detail in Chapter 6.

Regarding the technique implemented for this work, other aspects need to be explained.

As in the code both the partial pressure of the gases in the tissues and in the brain are calculated, it is necessary to determine which value is compared to the threshold, in order for the model to be conservative. As explained in Section 2.1, one of the most dangerous types of DCS is Central DCS, which happens in the bloodstream and brain. However, the equations used to model N_2, which are explained below in Section 4.2 and 4.3, are more accurate for the tissue partial pressure and, in addition to this, the perfusion of N_2 in the brain is higher than the one in the tissues, meaning that the pressure equilibrium can be reached faster. For this reason, the choice of considering the N_2 partial pressure in the tissues has been made, selecting a more conservative threshold value. [17]

Moreover, another consideration regarding N_2 modeling needs to be addressed. As stated more than once throughout this work, denitrogenation is influenced by diverse factors. For this reason, two different equations have been implemented, which are labeled “static” and “dynamic”. The static equation refers to fixed values determined by the surrounding environment, such as ambient pressure, O_2 concentration and time of exposure, while the dynamic equation refers to values that vary according the intensity of physical activity. It has to be noted that these labels are introduced here for convenience and do not correspond to standard definitions.

Lastly, it is necessary to add the *Detailed Human* code to an environment, in order for it to run and perform analysis. Since at this stage of the work no particular requirements needed to be fulfilled with regards to the setting, the *Detailed Human* was added to the environment built during the initial part of the V-HAB study, which is presented in Figure 12.

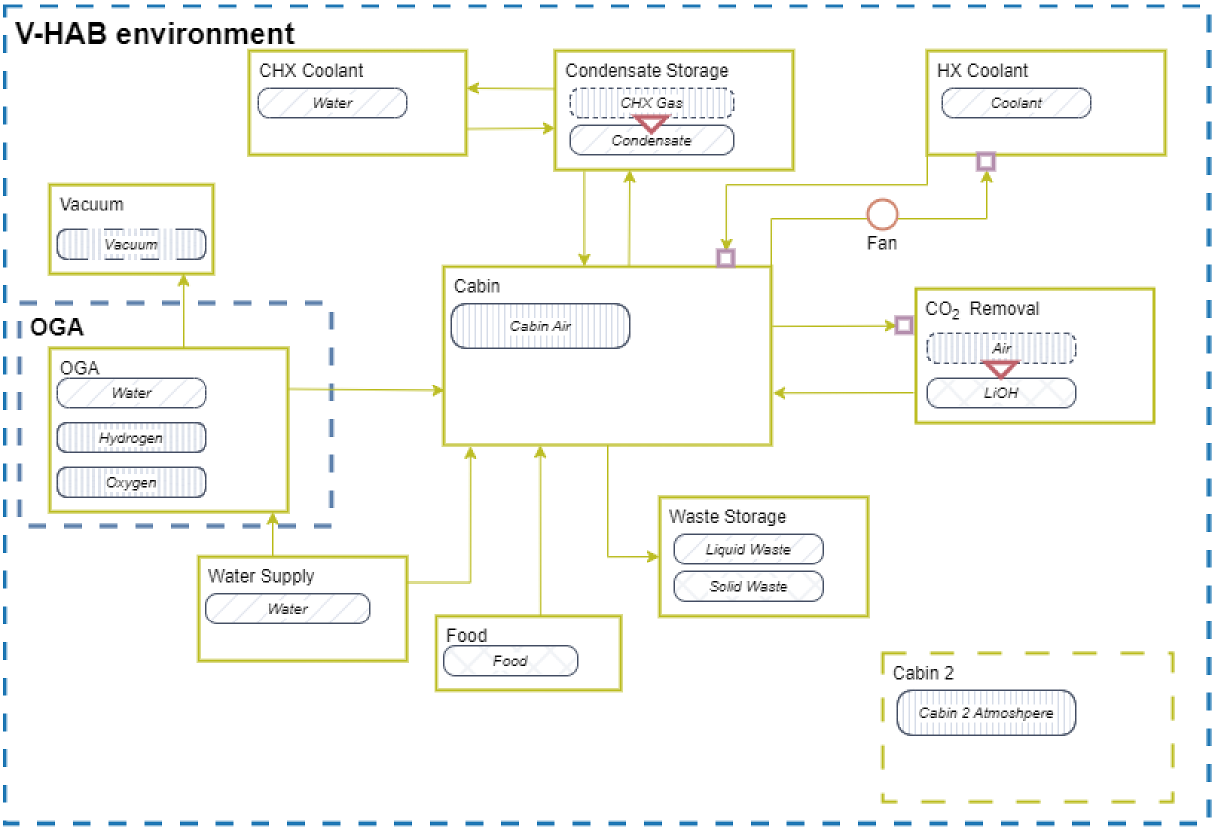

Figure 12. Virtual Habitat environment built in order to implement and analyze the *Detailed Human*

It is to be reminded, however, that some prebreathe protocols require for the astronauts to undergo different atmosphere compositions. This was achieved by adding different stores (see Paragraph 3.1.1) with the necessary characteristics, and by moving the humans from one place to the other with the adequate V-HAB function. In Figure 12 this is represented by “Cabin 2”, which indicates one or more eventual cabins that can be added to the environment with the scope of simulating different prebreathe protocol conditions.

4.2 Static approach - The Bühlmann model

This model was developed by Swiss physician Dr. Albert Alois Bühlmann by means of hyperbaric chamber experiments, and it was used to create decompression tables for divers, which would allow them to plan the depth and duration of dives as well as the decompression stops.

Unless stated otherwise, all the information and values regarding this model are taken from Dr. Bühlmann's *Decompression – Decompression Sickness* [17] and [18].

As already explained during this work, both astronauts and divers are at risk of experiencing DCS, as they transition from an environment at higher pressure to one at lower pressure: for astronauts this means moving from the ISS to the EMU, and for divers from deeper sea levels to shallower ones.

For divers, actual prebreathe protocols don't really exist, but they are required to perform decompressions stops while reaching the surface from a dive. For this reason, different methods and techniques have been implemented to allow divers to know the correct duration and depth to carry out the stops at in order to avoid DCS.

Even though the water environment for divers and the space environment for astronauts, as well as the magnitude of pressure they experience, are very different, the underlying physical principles show notable similarities which allow to look at diving mathematical methods to model DCS for astronauts. However, this resulted in several models to be discarded because they required some parameters that could not be converted, such as water temperature, depth reached, ascent and descent rates and more. In addition, some equations were completely unsuitable as they would not sustain pressure values lower than the ambient one.

4.2.1 Definition of the model

Amidst various model, the Bühlmann one resulted the most appropriate fit for this research. Before diving deep into the model, a brief overview on tissue saturation and desaturation is required.

As already explained, when a person is at a certain pressure for a significant amount of time, the different tissues of the body are saturated and the absorption and off-gassing of N_2 is balanced. In general, the speed of saturation of a given tissue is proportionate to the size of its blood supply, which varies depending on the weight of the tissue and its working status. In particular blood supply, and so N_2 absorption, is increased with the expansion of the blood vessels, which occurs during physical exercise.

When the ambient pressure is reduced, the tissues are supersaturated with N_2, which is released from the blood into the lungs. As it is known by now, if the change in pressure is too rapid, bubbles can be formed thus leading to DCS.

Dr. Bühlmann, in his model ZH-L16, was able to establish how much supersaturation the tissues can tolerate without injury. To better represent the effect of N_2, the model separates the human body in 16 different compartments, based on their assigned half-time. The half-time represents the required time for the difference between the current inert gas pressure in a tissue and its equilibrium pressure with the surrounding environment to be halved.

The half-time of each compartment mostly depends on its blood perfusion rate, which indicates how fast blood circulates through that tissue. In particular, tissues which present rich blood supply (like brain or muscles) are characterized by short half-times, which translate to them taking up and releasing inert gas rapidly. On the contrary, tissues with poor bloody supply (like fat or connective tissue) have long half-times, resulting in slower gas exchange.

The half time values, which are directly connected to blood supply and N_2 absorption, are used to determine the amount of inert gas partial pressure that a tissue can safely tolerate. It comes naturally that tissue with higher blood supply, and short half-times, can withstand higher levels of supersaturation and vice versa.

The division of compartments is as follows, where "overlapping" indicates that the slowest tissue of the group has a longer half-time than the fastest tissue of the following slower group:

- 1-4: fast tissue like the central nervous system and the spine;
- 5-11: the skin (overlapping);
- 9-12: the muscles (overlapping);
- 13-16: slow tissues like the limbs, ligaments, cartilage and bones (overlapping).

According to Bühlmann and the ZH-L16 model, the saturation and desaturation of the various compartments can be calculated with the following equation:

$$p_{Tig}(t_e) = p_{Tig}(t_0) + \left[p_{ig} - p_{Tig}(t_0)\right] \cdot \left[1 - 2^{-t_e/t_{1/2}}\right]$$

where:

- $p_{Tig}(t_e)$ represents the pressure of N_2, in the tissue, at the end of exposure;
- $p_{Tig}(t_0)$ corresponds to the pressure of N_2, in the tissue, at the beginning of exposure;
- p_{ig} indicates the pressure of N_2 in the breathing mix;
- t_e stands for the duration of exposure in minutes;
- $t_{1/2}$ is the half-time in minutes.

It is to be noted that this equation is only valid for constant pressure, meaning that the human would stay the whole time at the same pressure during a prebreathe protocol, which is not the case as the pressure needs to be lowered. For this reason it is possible to split the prebreathe protocol into smaller sections, so that each of them maintains the same pressure and it is then possible to apply the equation.

The half-time stated by the ZH-L16 model are shown in Table 2.

Number of compartment	$t_{1/2}$ [min]
1	4.0
2	8.0
3	12.5
4	18.5
5	27.0
6	38.3
7	54.3
8	77.0
9	109.0
10	146.0
11	187.0
12	239.0
13	305.0
14	390.0
15	498.0
16	635.0

Table 2. Half-times of compartments according to ZH-L16 [17]

4.2.2 Implementation in the Virtual-Habitat

As explained in section 4.1, the equation of the ZH-L16 model has been added to the `calculatePartialPressureTissue()` function in the *Respiration* class in V-HAB. Because the compartments of the model do not exactly represent a specific part of the human body, a compromise needed to be found to choose the more suitable half-time for the tissues. Considering both the division of Bühlmann's compartments and different MATLAB analysis, a reasonable value has been decided at $t_{1/2} = 45\ min$.

In Figure 13 a visual example of the different behavior of compartments during a 4-hour long prebreathe protocol while breathing 100% O_2 can be found.

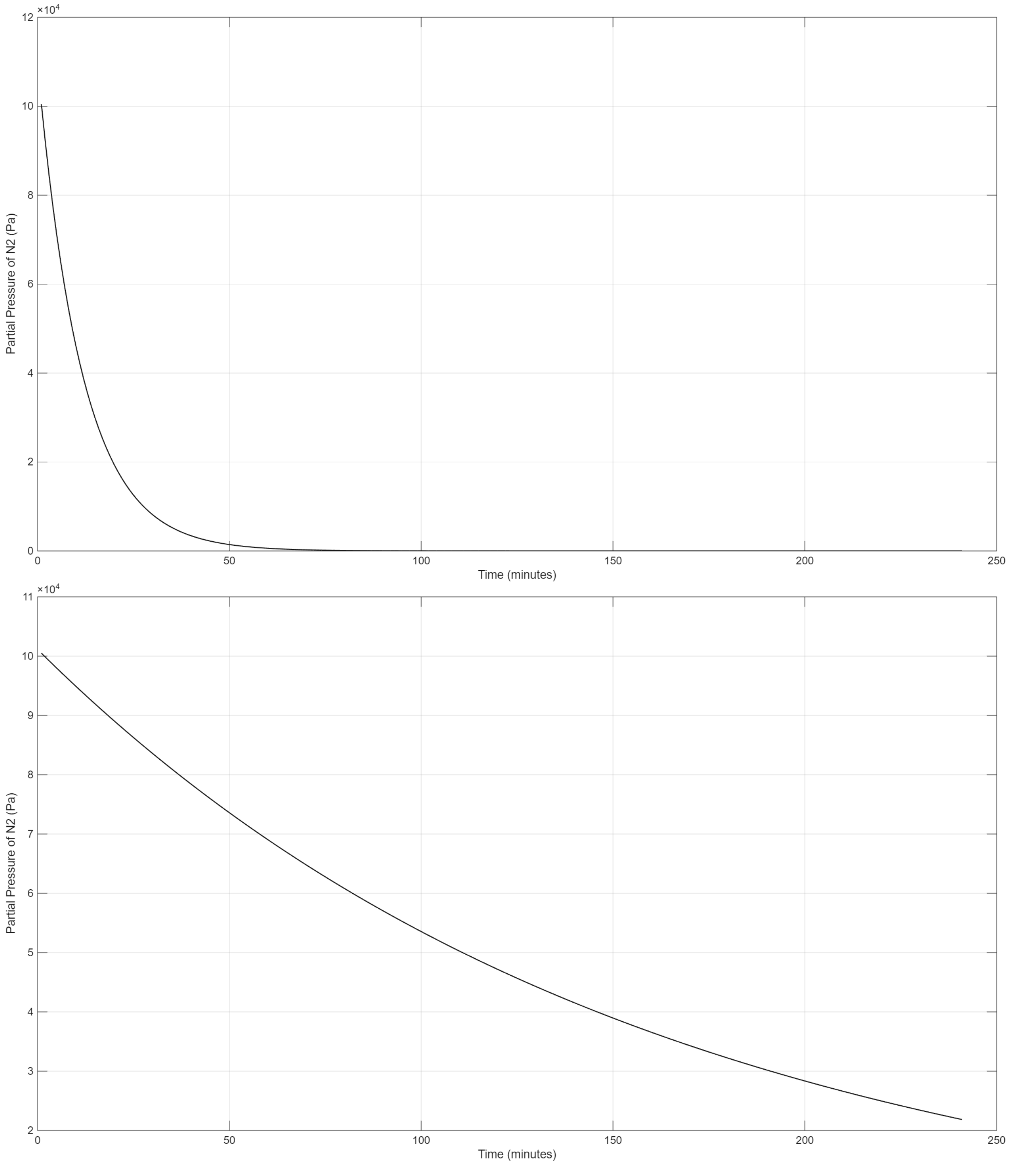

Figure 13. N_2 partial pressure trends for compartment 2 with $t_{1/2} = 8\ min$ and for compartment 9 with $t_{1/2} = 109\ min$

From the graphs in Figure 13 the difference in denitrogenation duration, between a compartment characterized by a short half-time and another characterized by a longer one, can be clearly seen. As explained before, short half-times correspond to higher blood supply and, consequently, faster inert gas exchange rates. Because of this, for faster tissues (meaning tissues with short half-times) a shorter prebreathe protocol would be sufficient to exhale enough N_2 to avoid the risk of DCS.

However, the human body is composed of diverse tissues, each of them characterized by its own perfusion rate. It then would not be a conservative approach to only consider compartment paired with short half-times for these analyses.

Lastly, to also implement N_2 calculations in the other two *Respiration* functions `calculateBloodPartialPressure()calculateBloodConcentration()`, Henry's law was used, which states that the amount of dissolved gas in a liquid is directly proportional to its partial pressure.

$$C = k \cdot p$$

Where:

- *C* is the concentration of the gas;
- *k* represents Henry's law constant and is set at $k = 6.10 \cdot 10^{-4}\, mol/L \cdot atm$ for N_2;
- *p* states the partial pressure of the gas.

As explained in Section 4.1, it was not possible to implement the same equations used for O_2 and CO_2 because the metabolic processes of the gases in the body are different, and also because the existing code in V-HAB is derived from analysis and experiments carried out specifically for only O_2 and CO_2.

As the values of N_2 partial pressure and concentration, resulting from the two aforementioned *Respiration* functions, are only used in the code and not compared with the limit threshold for DCS, it was possible to introduce Henry's law. However, it has to be noted that this represents a simplification which will be discussed in more detail in Chapter 6.

4.3 Dynamic approach

Physical exercise is one of the main variables which contributes in shortening prebreathe protocols. As also stated before, metabolically active tissues present higher blood perfusion, which is directly connected to a faster N_2 washout.

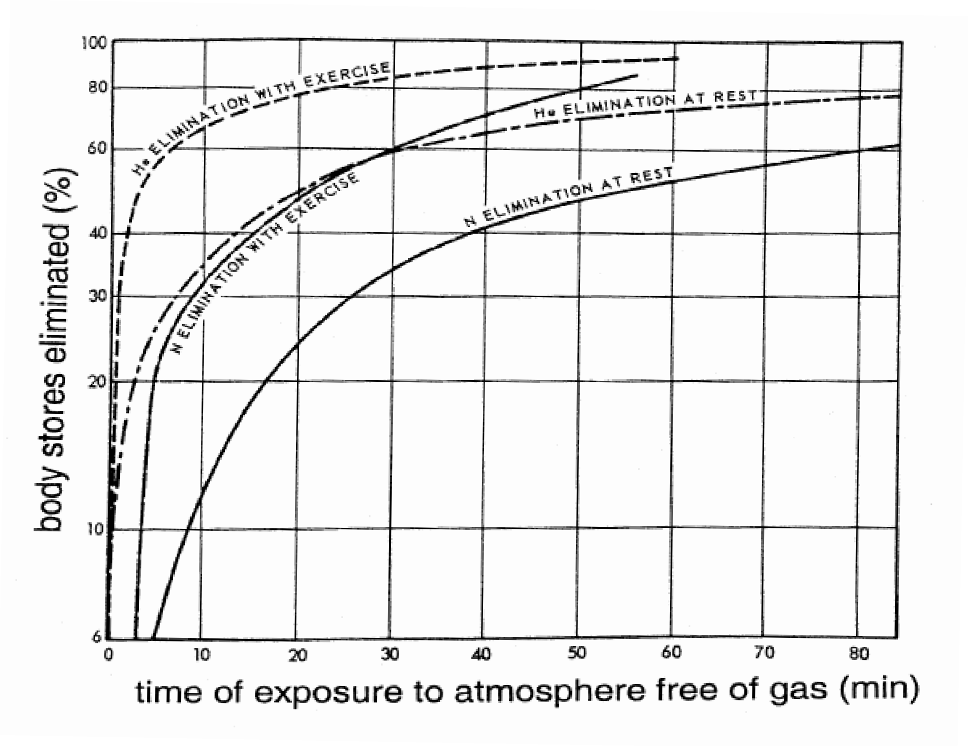

Figure 14. Difference in Nitrogen elimination depending on exercise in prebreathe protocols [11]

In this section the implementation of physical exercise as a factor in calculating the variation of N_2 partial pressure in V-HAB is presented. Unless stated otherwise, all information is derived from [11]. In this work a probability model to compute the decrease of N_2 partial pressure in the tissues, given specifics about exercise during prebreathe protocols, is illustrated.

4.3.1 Definition of the model

In order to quantify the effectiveness of exercise during prebreathe, two approaches can be used, either measuring the quantity of N_2 removed, or quantifying the incidence decrease of DCS and venous gas emboli (VGE) during subsequent exposure. Nonetheless, some aspects are yet to be clarified, such as which type of exercise would result in the most efficient prebreathe protocol, or if physical activity may pose any contraindications, and if so which ones.

These questions will be better explored in the Chapter 6, but this section is focused on the description and analysis of the mathematical model implemented.

To interrelate exercise with denitrogenation, this model implements VO_2 in the calculation. This value represents the volume of O_2 consumed during physical activity, per kg of weight per minute of exercise, and it is expressed in $\frac{ml}{kg \cdot min}$. In particular, the model equation requires the percentage of the maximum value of VO_2 (VO_2 max) reached during a particular exercise. So, for example, if the VO_2 max achievable by a person corresponds to 40 $\frac{ml}{kg \cdot min}$, and during a physical protocol the person reaches an O_2 consumption peak of 10 $\frac{ml}{kg \cdot min}$, then the VO_2 percentage during that exercise would be equal to $VO_2\ percentage = \frac{10}{40} \cdot 100 = 25\%$. In general, the maximum VO_2 value that a person can achieve depends on various factors like age, gender, body weight and heart rate.

In order to account for the metabolic activity, the equation used to describe the model is the following:

$$p_{tN_2}(t_e) = p_{tN_2}(t_0) + [\left(p_a(t_0) - p_{tN_2}(t_0)\right) \cdot (1 - e^{-k \cdot t_e})]$$

Where:

- $p_{tN_2}(t_e)$ is the partial pressure of N_2 in the tissue, at the end of the exercise;
- $p_{tN_2}(t_0)$ is the partial pressure of N_2 in the tissue, at the beginning of the exercise;
- $p_a(t_0)$ is the partial pressure of N_2 in the environment, at the beginning of the exercise;
- k is the tissue rate constant, which will be discussed in Section 4.3.2;
- t_e is the duration of the exercise in minutes.

4.3.2 Definition of the tissue rate constant *k*

'*k*' is the tissue rate constant and binds the partial pressure of N_2 in the tissue with the VO_2 for the duration of a specific exercise. According to the model, three different equations can be used to define the best relationship between *k* and VO_2.

4.3.2.1 Linear relationship k_1

The hypothesis is that exercise reduces DCS risk in proportion to exercise.

$$k_1 = (\lambda_1 * VO_2) + 0.0019254$$

Where:

- λ_1 is a slope term that is estimated by trial and error;
- VO_2 is the percentage consumption of O_2.

In this case the best-fit could be a linear relationship between *k* and VO_2, so that an incremental change in VO_2 results in an incremental change in the tissue rate constant.

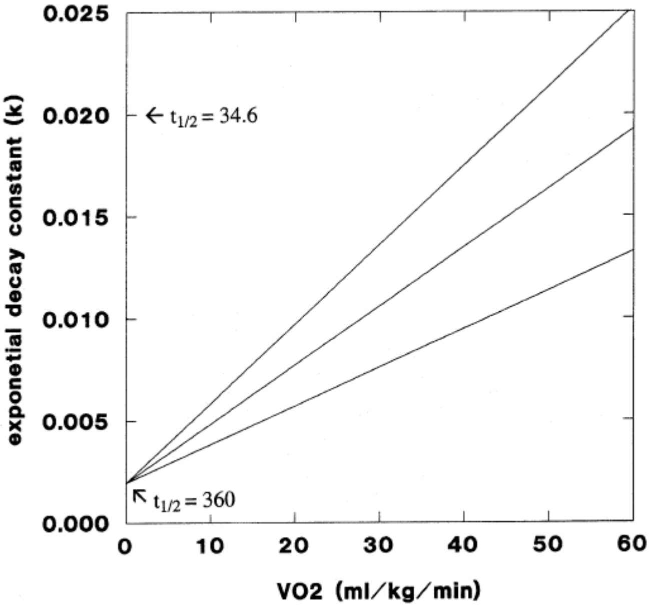

Figure 15. Linear relationship between *k* and VO_2 as estimated by [11]

4.3.2.2 Nonlinear relationship k_2

The hypothesis is that little extra exercise does not dramatically reduce DCS risk, but high exercise is important.

$$k_2 = (1 - e^{-\lambda_2 \cdot VO_2})/519.37$$

Where:

- λ_2 is a slope term that is estimated by trial and error;
- VO_2 is the percentage consumption of O_2.

In this case the best-fit may not be a linear relationship between *k* and VO_2, so that light exercise is less beneficial than heavy exercise.

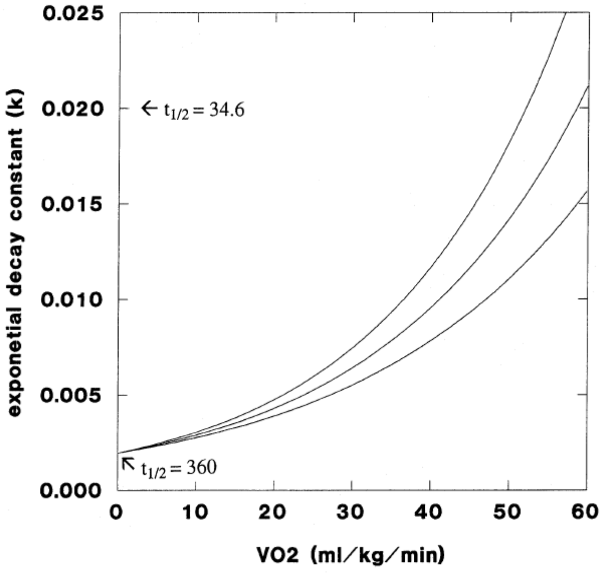

Figure 16. Nonlinear relationship between *k* and VO_2 as estimated by [11]

4.3.2.3 Nonlinear relationship *k_3*

The hypothesis is that little extra exercise dramatically reduces DCS risk.

$$k_3 = \left[\frac{\left(1 - e^{-\lambda_3 \cdot VO_2}\right)}{51.937}\right] + 0.0019254$$

Where:

- λ_3 is a slope term that is estimated by trial and error;
- VO_2 is the percentage consumption of O_2.

In this case the best-fit could be a nonlinear relationship such that light exercise produces a substantial reduction in denitrogenation, while progressively heavier exercise yields diminishing returns.

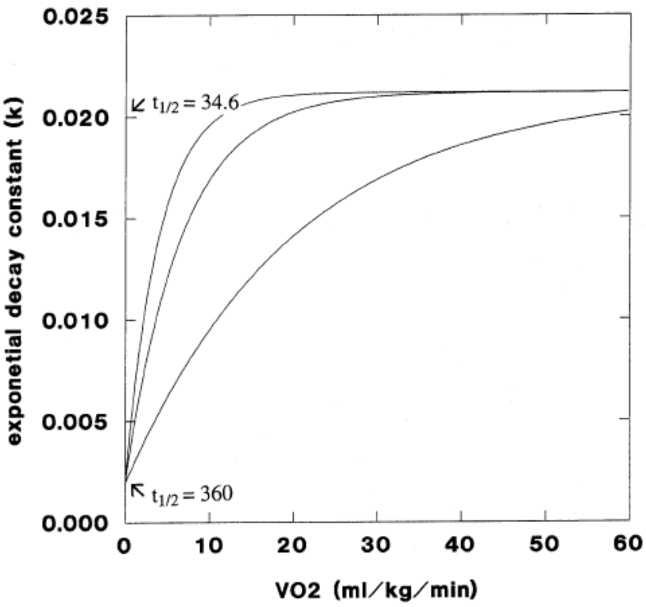

Figure 17. Nonlinear relationship between *k* and VO_2 as estimated by [11]

In general, *k* could also be defined as $k = \frac{0.693}{t_{1/2}}$, where $t_{1/2}$ is the half time of the compartment. This definition does not include VO_2, but it is used regardless to calculate the value of λ. In fact, in [11], λ is estimated through physical tests, not feasible in the circumstances of this work.

Because of this reason, an approximation was needed, and the value of λ is found by replacing $k = \frac{0.693}{t_{1/2}}$ in the chosen equation (k_1, k_2 or k_3) and by implementing the value of VO_2 percentage corresponding to the current prebreathe protocol.

4.3.3 Implementation in the Virtual-Habitat

Since the equation from [11] regards the partial pressure of N_2, it was added in the *Respiration* class, inside the `calculatePartialPressureTissue()` function. This posed a problem since another equation to calculate N_2 partial pressure was already present (Bühlmann's equation).

In reality the effect of physical exercise on denitrogenation has to be considered on top of the already present effect caused by the environment. In the code, however, the implementation of the equations was slightly different. Since each protocol is divided into multiple phases, for every phase only one equation was implemented: Bühlmann’s one if no exercise was practiced, or the dynamic approach one if exercise was performed.

5 Development and analysis

In this chapter the results of the analysis are presented, with comments and further explanations where needed.

5.1 Model Validation

In this section all the prebreathe protocols outlined in Section 2.2 are validated, to prove the efficiency of the code. before analyzing each protocol and its results, it is important to reiterate what expressed in Section 4.1 regarding N_2 threshold. According to approximations and various considerations, that can be read in the paragraphs aforementioned, a safe value for residual N_2 partial pressure was chosen at 100-200 mmHg (13 – 27 kPa). This value is not a concrete and universal limit, but only a threshold decided for this work as N_2 partial pressure is the main variable used to evaluate the risk of DCS. In reality an effective measure of residual N_2 partial pressure in the astronauts does not exist as other factors, like bubble formation probability, are take into account. Therefore, it is not possible to compare the results of the analysis of this work with real-life values, but only with the threshold value selected for this work, which was nonetheless chosen based on the estimates and considerations discussed above.

5.1.1 Shuttle Program

In the Shuttle Program, two different protocols were performed:

1. 4-hour O_2 prebreathe

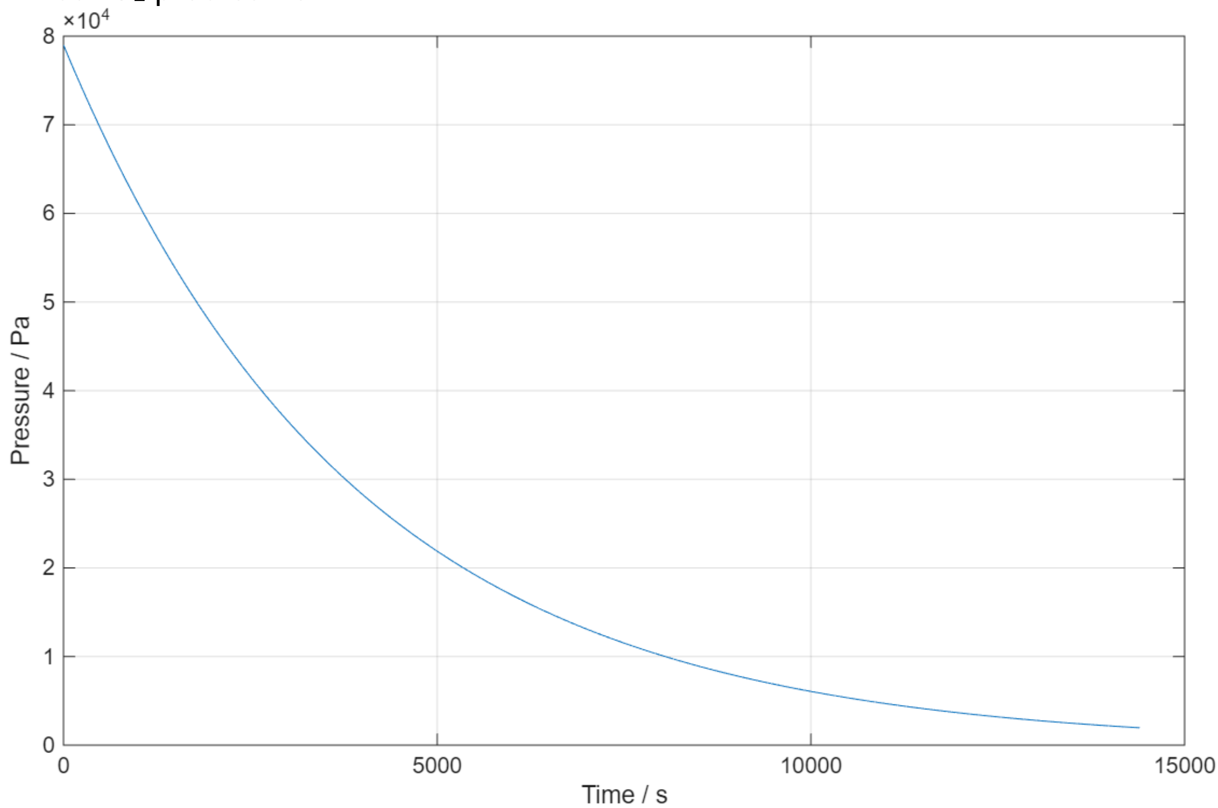

Figure 18. N_2 tissue partial pressure trend for a 4-hour prebreathe protocol in a 100% O_2 atmosphere at an ambient pressure of 101.2 kPa

2. Staged decompression

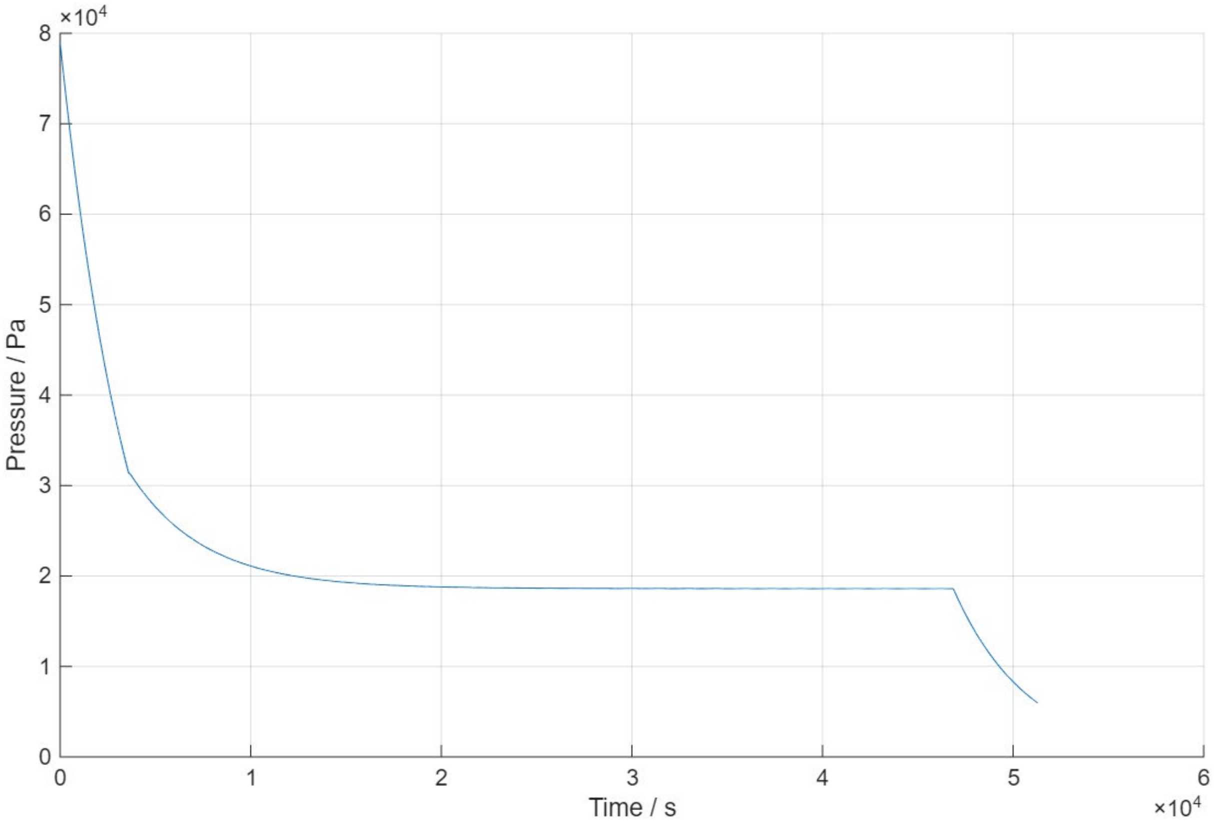

Figure 19. N_2 tissue partial pressure trend for the Staged Decompression prebreathe protocol

In the graphs in Figure 18 and Figure 19, the trend of the N_2 partial pressure in the tissues can be observed. It can be seen how the model was validated as the pressure decreased during the protocol reaching and since falling below the target threshold of 100-200 mmHg. In both these protocols no exercise is performed, so only the Bühlmann's equation was implemented.

5.1.2 In-Suit Light Exercise Protocol

In this prebreathe protocol, two different exercise phases are present, while the other two phases are carried out during rest. Before analyzing the graphs, some explanations are needed.

As stated in Section 4.3, to implement the dynamic approach equation, the percentage of VO_2 max is needed. However, in this case, that value was not available, as the only information regarding exercise intensity was the VO_2 at which the physical activity took place, but not the percentage related to VO_2 peak. Furthermore, as already explained, the maximum VO_2 achievable by a person is not a fixed number, but it depends on the own physical characteristics of the person and it is evaluable only by physical tests. For these reasons a VO_2 max percentage was estimated, considering the fact that the type of exercise is labeled as 'light exercise', and the average percentage of VO_2 max for that kind of exercise, which is below 40%. Moreover, the value of VO_2 consumed during the ISLE protocol, lies toward the lower end of the 'light exercise' range for the average adult, and thus can be approximated using lower, corresponding percentages [19].

The two different phases of exercise presented different values, which were approximated as follow:

- $5.8 \frac{ml}{kg \cdot min}$ to 20% VO_2 max;
- $6.8 \frac{ml}{kg \cdot min}$ to 25% VO_2 max.

Additionally, the linear relationship for the tissue rate constant described in Section 4.3.2.1 was selected for all exercise phases. This choice was dictated by two main reasons: for one, it is a linear relationship which correlates exercise and denitrogenation in a more direct way, even if less accurate, and secondly it resulted as the best-fit for this case scenario following different analyses. It has to be noted that this choice is strictly relative to the case of this work, and it could vary if associated with a modified code or a different approach to the problem.

Below, in Figure 20 and Figure 21, the N_2 tissue partial pressure trends can be observed, both including and excluding exercise.

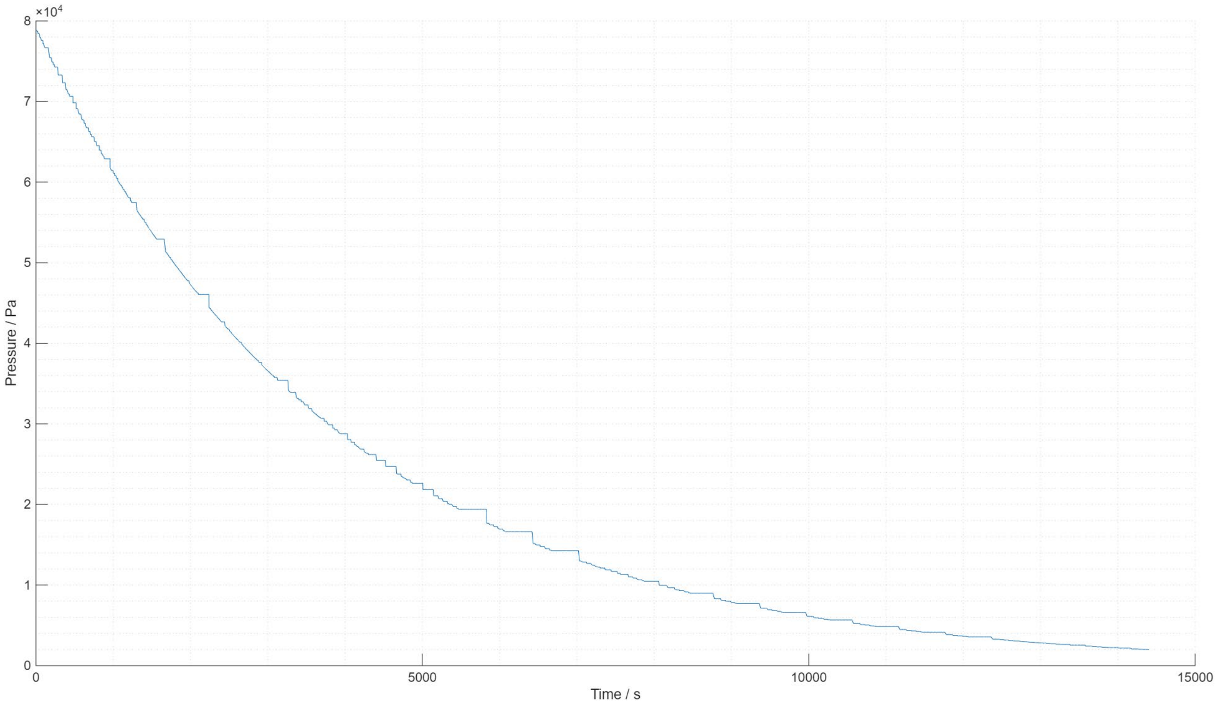

Figure 20. N_2 tissue partial pressure trend for ISLE prebreathe protocol without considering physical exercise

In the graph of Figure 20 the curve of N_2 tissue partial pressure is presented. This first result did not take into account the physical exercise and the whole simulation was run only implementing Bühlmann’s equation. It can clearly be seen how the N_2 partial pressure decreases over time upon reaching and falling below the limit value.

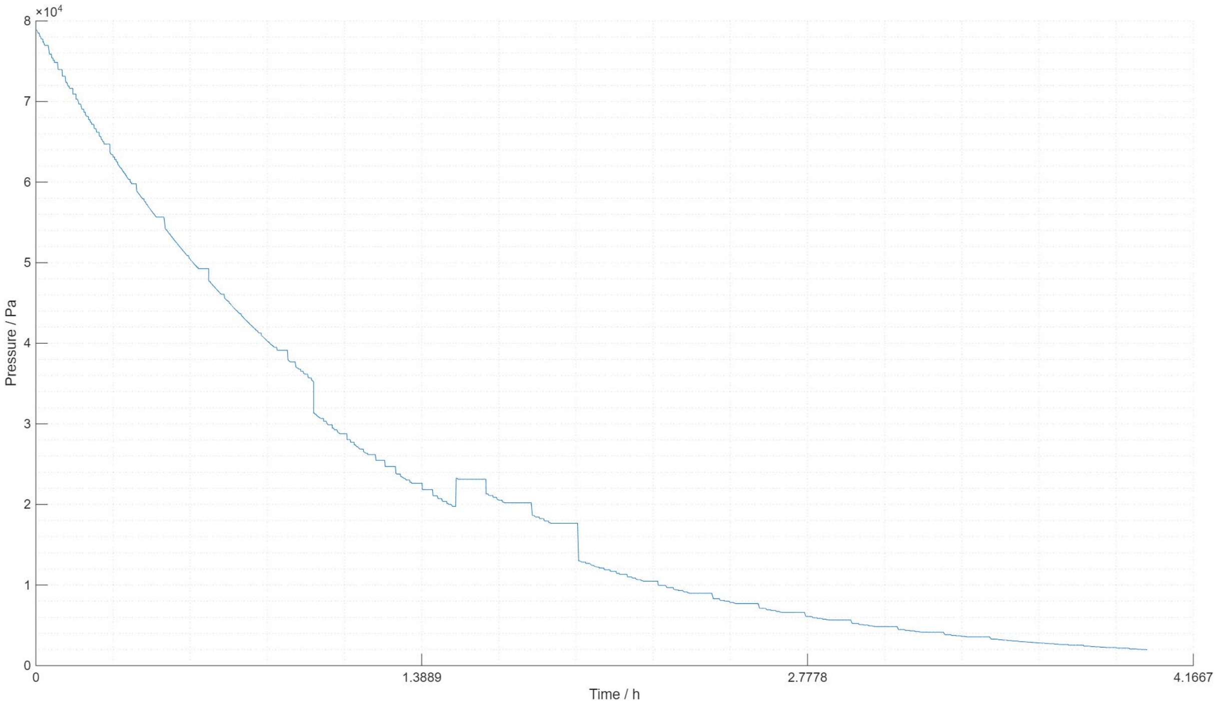

Figure 21. N_2 tissue partial pressure trend for ISLE prebreathe protocol considering physical exercise

In Figure 21, the trend of N_2 tissue partial pressure during the ISLE prebreathe protocol is presented. In this second case, physical exercise was considered and the code simulated both the Bühlmann's equation and the physical exercise equation.

It can be seen how the different phases of the protocol are more obvious here. In particular, exercise occurs in the first phase (0 to 3600s) and third phase (5400 to 8400s). In these periods the curve of N_2 reaches higher values compared to the one where exercise is not considered. Although this may seem like a mistake, it has to be reminded that denitronegation favored by physical activity only occurs on top of the one caused by the environment. This in particular is not perfectly considered when only one equation is used for each phase of the protocol. Therefore, the results can be considered acceptable under this approximation.

Lastly, it can be observed that the end value of N_2 partial pressure is very similar to the one found in Figure 20. The reason for this also lies in the nature of the equations used. Bühlmann's equation only considers a handful of parameters among which is the partial pressure of N_2 in the atmosphere. Being that the ambient conditions don't vary during the transition from the third phase to the last (at 8400s), the equation is calculating the same values in both cases, with and without exercise. To better explain this is necessary to remember that the last two phases of the protocol happen under the same cabin conditions, which correspond to a 100% O_2 atmosphere. The Bühlmann's equation, which is used to model the last phase as there is no exercise performed, requires as input the atmospheric values, the N_2 tissue partial pressure at the beginning of the phase, and the time of exposure. In this specific scenario only the N_2 partial pressure differs between the simulation with exercise and the one without, because at the end of the third phase (and thus beginning of the last) the value is calculated with two different equations (Bühlmann's one if no exercise is performed, and dynamic approach one if it is performed). Because of this reason, the trend of the

N_2 partial is very similar in both the simulated cases. This, again, is a limitation to the code, but it can be considered a useful preliminary estimate.

5.1.3 Campout Protocol

In this protocol as well, no exercise is performed, so the only equations implemented is the Bühlmann's equation. This prebreathe protocol lasts almost 12 hours, so it is expected for the curve to reach a plateau. Nonetheless, in the graph in Figure 22, it is possible to see how the N_2 partial pressure decreases over time reaching a final value of about 52 kPa. This value is not as low as the desired threshold but, it being a very conservative goal and not a physical proven limit, it is possible to state that the results are more than acceptable. In fact, the final value is more than halved compared to the initial value of N_2 partial pressure and it can be considered low enough to significantly reduce the risk of DCS.

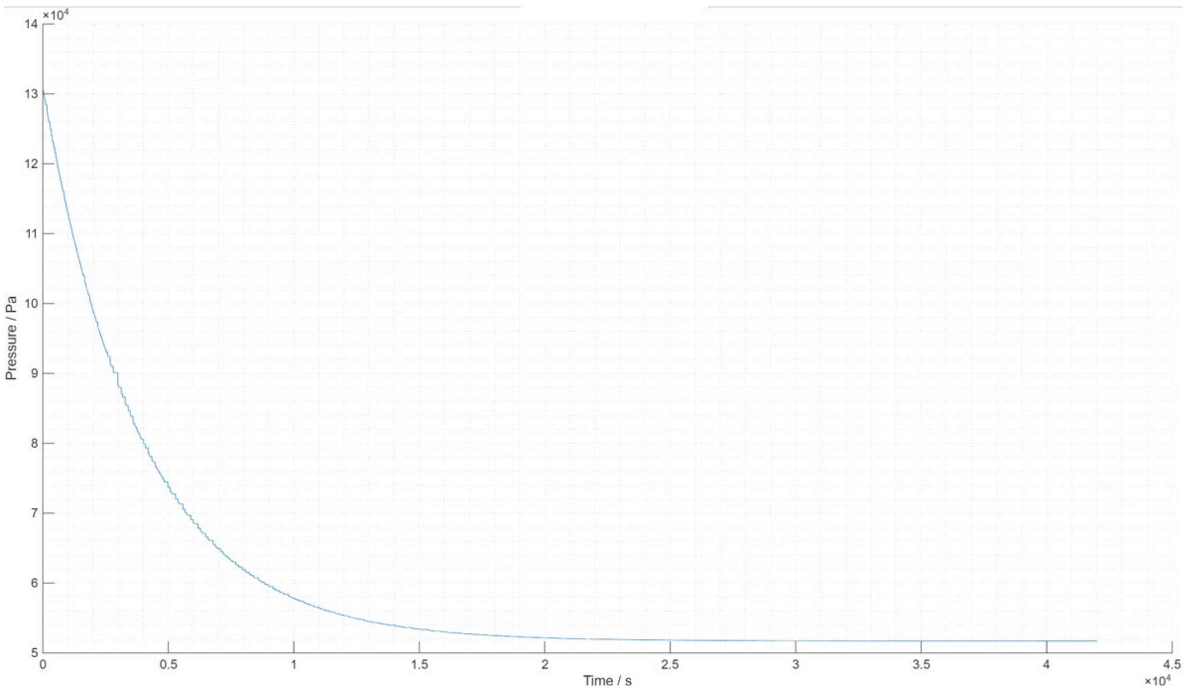

Figure 22. N_2 tissue partial pressure trend for the Campout prebreathe protocol

5.1.4 Cycle Ergometer with Vibration Isolation and Stabilization

This prebreathe protocol is characterized by an initial period of exercise which lasts 10 minutes. During this phase the intensity of the exercise is incremented from 37.5% VO_2 max to 75% VO_2 max. Since the percentage values are given directly, it was possible to implement the correct values without approximations.

Below, in Figure 23, it is possible to observe the trend of N_2 tissue partial pressure. The curve decreases well below the threshold value, and it is possible to observe a vertical decrement at 600s, which corresponds to the end of the 10-minute exercise period. This is caused by the implementation of the dynamic approach equation instead of the Bühlmann's one. The same considerations and observations made in Section 5.1.2 for the exercise implementation apply here.

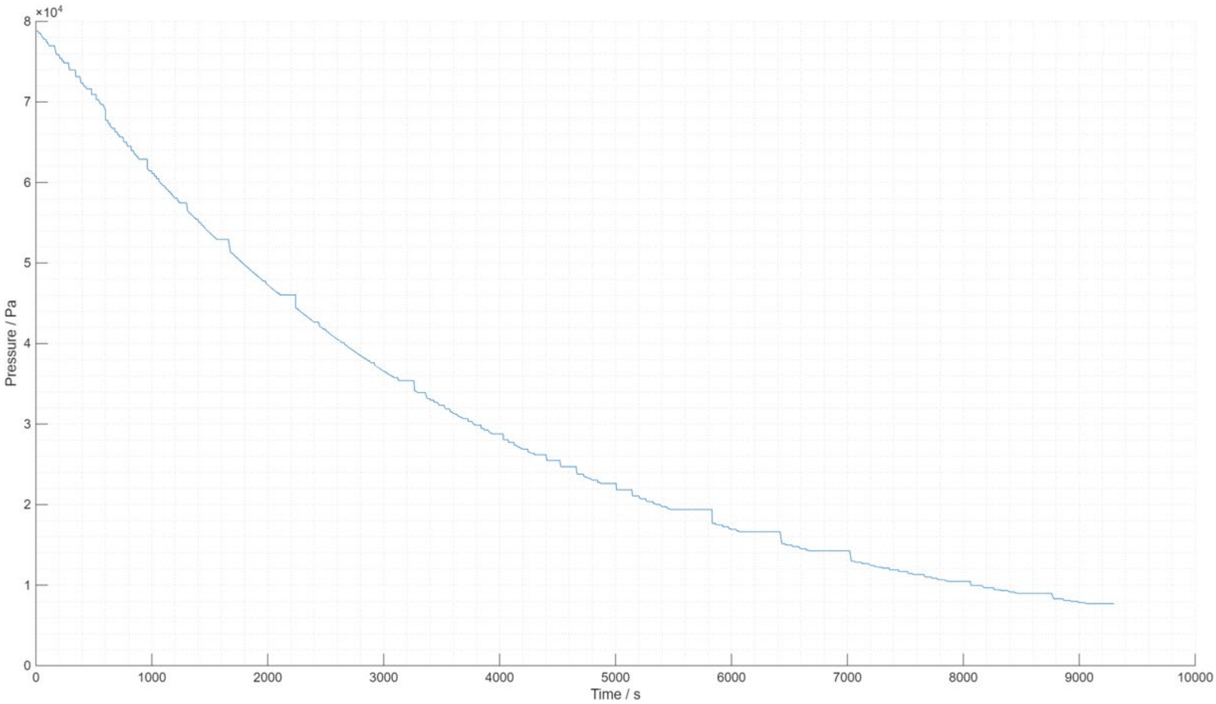

Figure 23. N_2 tissue partial pressure trend for the Cycle Ergometer with Vibration Isolation and Stabilization prebreathe protocol

5.2 Design and simulation of a new prebreathe protocol

To design a shorter prebreathe protocol, a trial-and-error approach was followed. The choices made are grounded in the assumption that the parameters exerting the greatest influence on prebreathe protocols are cabin atmosphere and physical exercise, as explained in Section 2.3. However, in the aforementioned section, suit pressure is also stated as an influencing parameter. Although it being true, it also stands that suit pressure is not implemented in the V-HAB code. The reasoning behind this lies in the fact that suit pressure is relevant when comparing the difference between N_2 partial pressure in the body and the pressure in the suit at the moment of donning. The lower this value is, the lower the risk of DCS happening.

Although the design process involved iterative trial-and-error, it was informed and refined based on the insights derived from the conducted analyses. For this reason, a few considerations need to be addressed.

Firstly, from the V-HAB produced graphs of existing protocols, it resulted that the cabin atmosphere was the most influential factor. In particular, prebreathe protocols or their phases in which the atmosphere was composed of 100% O_2, were characterized by a faster denitrogenation.

Another observation, even if already outlined, regards physical exercise. Even high intensity physical activity had a less steep N_2 partial pressure curve. In addition to this, physical exercise during the prebreathe protocol is advised to be of light intensity and not to prolonged in duration, in order to have enough energy to handle long and exhausting EVAs. However, as also seen in the CEVIS protocol, high intensity exercise may be allowed if it is performed at the beginning of the protocol and only for a very short period of time, so that the astronauts have time to recover from the endeavor.

Lastly, in order to reduce the duration of the protocol, a compromise needed to be reached for the final value of N_2 tissue partial pressure. Considering the maximum reachable operating suit pressure to be around 40 kPa (Section 2.3.2), a final value of N_2 partial pressure around 40 – 50 kPa (300 – 375 mmHg) can be considered acceptable, especially considering this simulation to be a preliminary study. It has to be noted that the Suit pressure value of 40 kPa does not refer to the EMU, but to the higher limit reachable considering structural and physical limitations. Additionally, as stated more than once throughout this work, it is not possible to determine a specific value for residual N_2 partial pressure at the end of a prebreathe protocol. The value needs to be lower enough to avoid N_2 supersaturation and bubbles formation, but no universal number exists, as it depends on the physiological features of each astronaut, probabilistic models and compartments half-time. Considering a N_2 partial pressure of about 40 kPa, the pressure difference between the body and the suit would be much smaller than considering the value of N_2 partial pressure before the prebreathe protocol, and the risk of DCS much smaller.

Another starting point for the design of a new prebreathe protocol was the decision of considering the NASA's exploration atmosphere, which is set at 56.537kPa (8.2 psi) and 34% O_2 [10]. This decision was dictated by the fact that this atmospheric composition is a trade-off specifically studied for future missions characterized by more frequent EVAs.

During the design process, different combinations of the main factors were implemented, with the objective to both achieve the most efficient protocol and provide different alternatives. Below the three best outcomes are explained.

5.2.1 New Prebreathe Protocol I

The first protocol presented is the longest of the three, but also the most simple.

The main aim of this protocol was to demonstrate how the standalone Exploration Atmosphere impacts the denitrogenation duration. This simulation has a duration of 90 minutes, which is a shorter time compared to already existing protocols, but there still remains a significant period of preparation before being able to perform any EVAs.

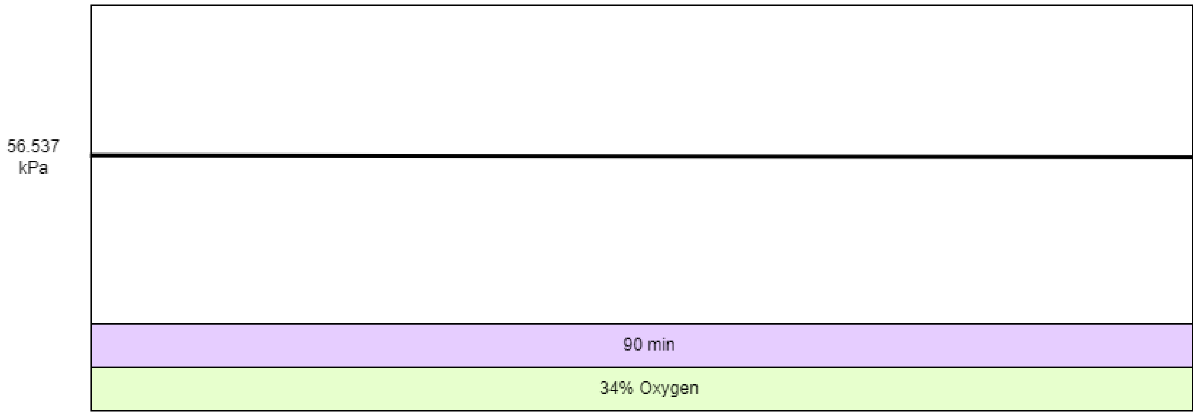

Figure 24. New Protocol I Operational Timeline

Below in Figure 25 the N_2 tissue partial pressure trend can be observed. After 90 minutes the N_2 partial pressure has reached a value of 45 kPa, which can be considered more than acceptable according to the observation made in Section 5.2. Moreover, if the NASA's Exploration Atmosphere is implemented in future spacecrafts or extraterrestrial villages, astronauts may be constantly living in this atmospheric condition, thus experiencing passive N_2 washout.

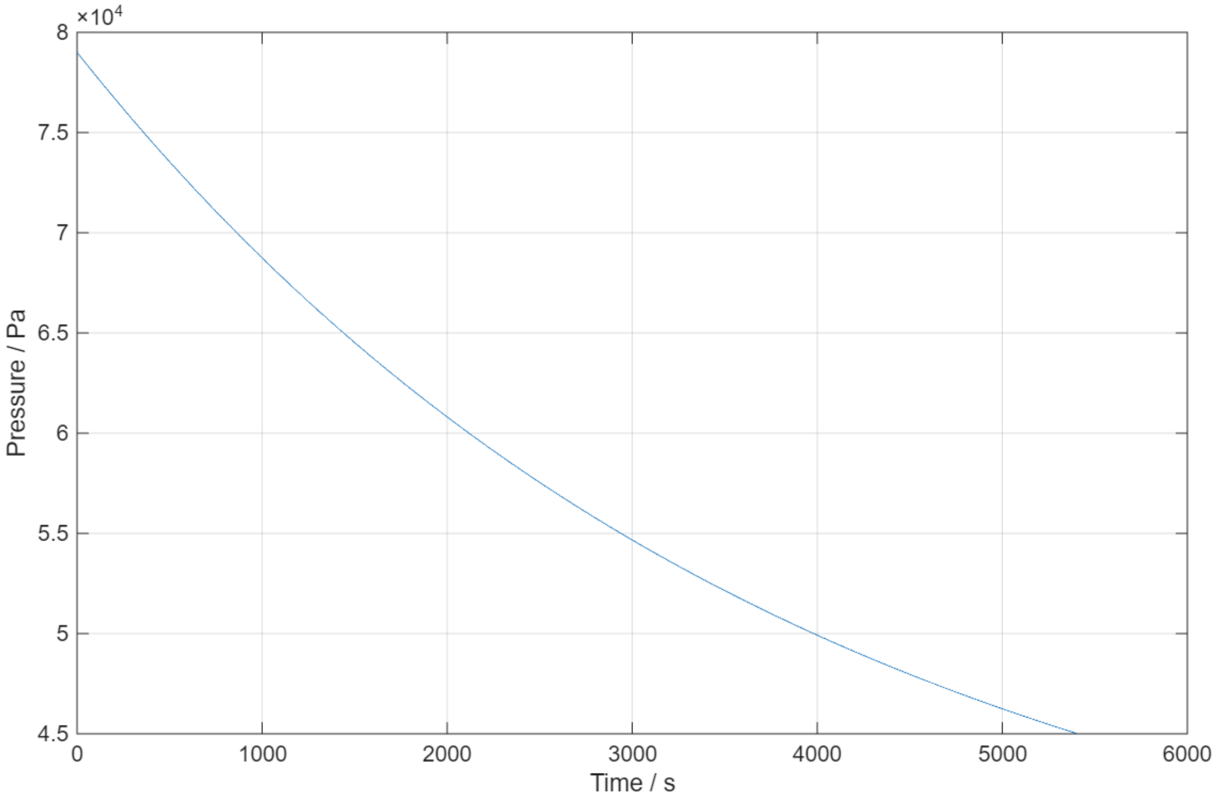

Figure 25. N_2 tissue partial pressure trend for the New Prebreathe I protocol

5.2.2 New Prebreathe Protocol II

The second protocol outlined lasts 1 hour and is divided into two phases. In the first one the atmosphere is set as the NASA's Exploration one, while in the second phase the atmosphere is composed of 100% O_2, with the addition of light exercise (25% VO_2 max).

This decision might be a bit controversial as physical activity is performed at the end of the prebreathe protocol, but it also has to be noted how in the first 40 minutes astronauts are exposed to an environment that could typify most, if not all, future spacecrafts.

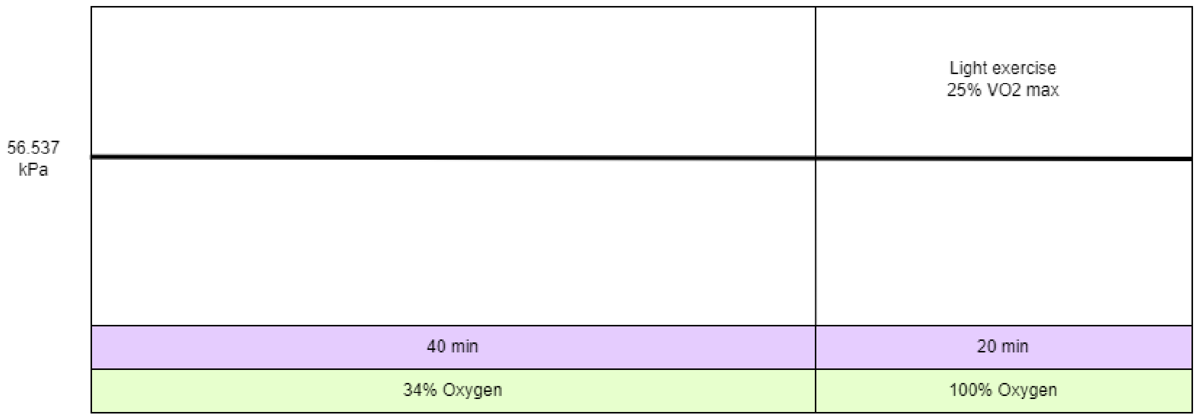

Figure 26. New Protocol II Operational Timeline

In Figure 27 the N_2 tissue partial pressure trend for the New Prebreathe Protocol II can be observed, with a final value of N_2 partial pressure between 40 and 45 kPa, which can be considered largely acceptable considering the assumptions made.

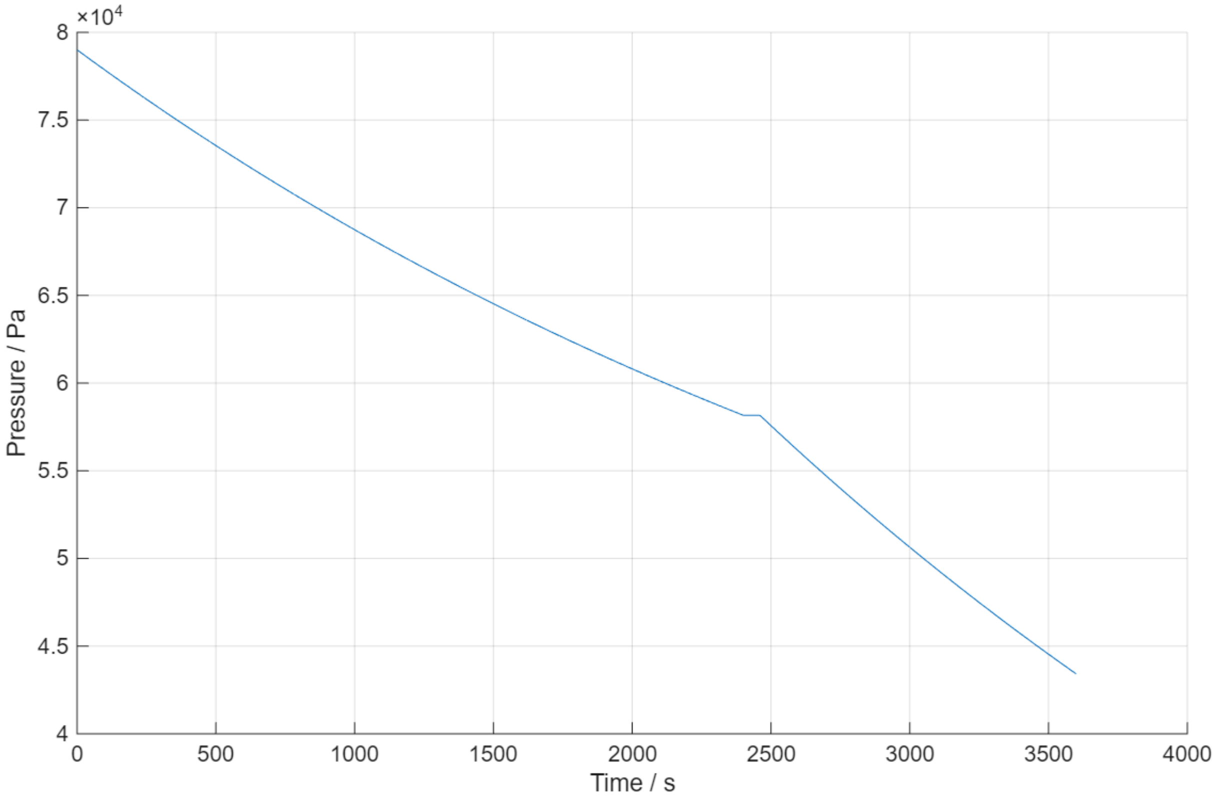

Figure 27. N_2 tissue partial pressure trend for the New Prebreathe II protocol

5.2.3 New Prebreathe Protocol III

The last prebreathe protocol presented, aimed to combine the NASA's Exploration Atmosphere, and the typical 100% O_2 environment implemented during other prebreathe protocols, which has proven to be very effective.

The duration of this protocol is the same as Protocol II, with 1 hour of running time. During the first 10 minutes the atmosphere is set as the NASA's Exploration one, while for the remaining 50 minutes it is switched to a 100% O_2 atmosphere.

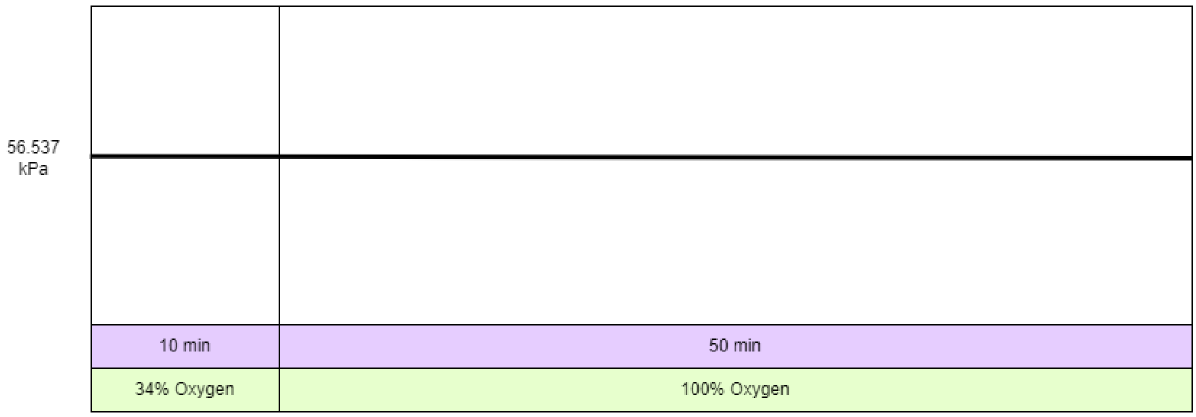

Figure 28. New Protocol III Operational Timeline

In Figure 29 the N_2 tissue partial pressure trend for the New Prebreathe Protocol III is shown. In this case the final value of N_2 tissue partial pressure reaches just below 35 kPa, which is lower than the value for Protocol I and II.

This result may seem preferable to the ones obtained for Protocol I and II, however it has to be noted that a dedicated environment is needed to implement the 100% O_2 atmosphere. The requirement may pose additional structural and technical measures and thus complicate the realization.

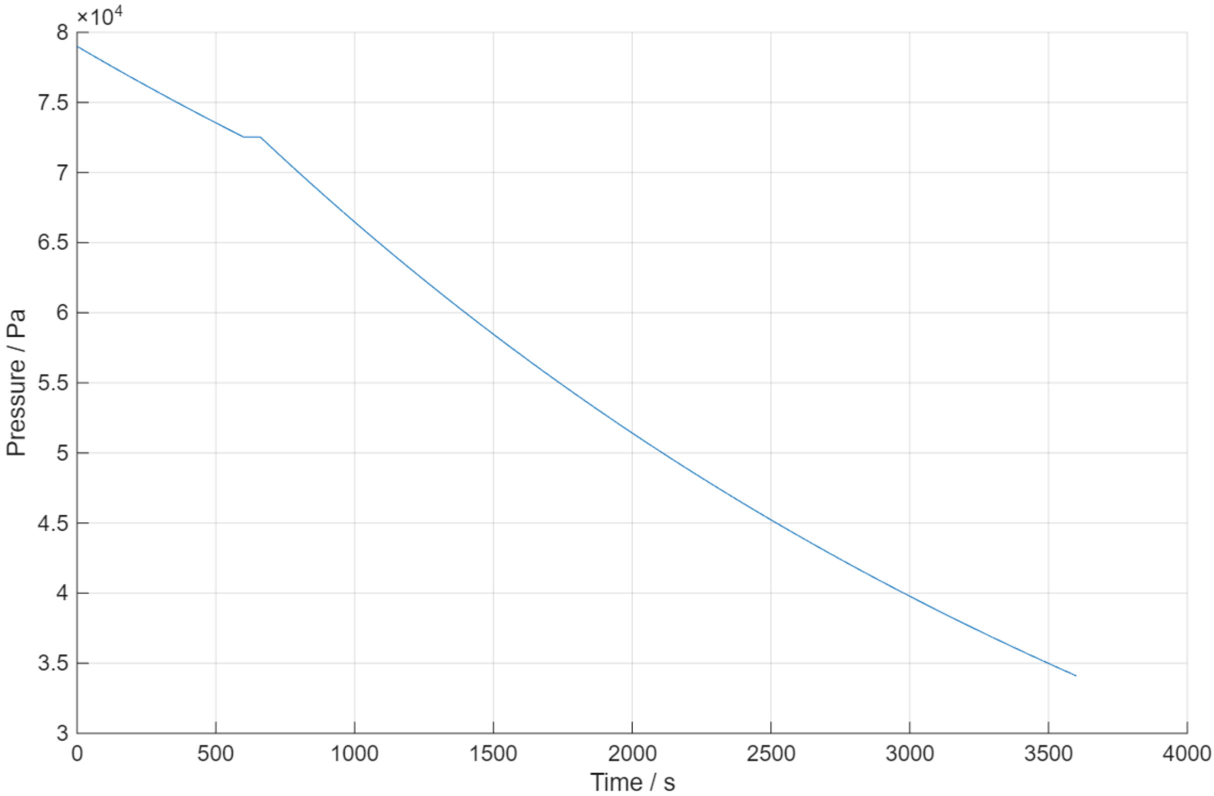

Figure 29. N_2 tissue partial pressure trend for the New Prebreathe III protocol

5.3 Comparison with current standards

The new prebreathe protocols outlined in Section 5.2 have been designed and analyzed considering current standards and physical and technical limitations.

The NASA's Exploration Atmosphere has been selected after a careful and throughout trade-off study fit into the safety limits for DCS, hypoxia and flammability. More information can be found at [10] and [20].

The 100% O_2 atmosphere is a typical set-up for prebreathe protocols, thus it can be implemented in these scenarios as well. However, it may require for specific technical and structural requirements, in order to prevent outgassing or other possible failures.

All three protocols reached the goal value, but they clearly demonstrated how different factors combinations lead to different outcomes. Although the final values of N_2 resulted higher than the ones calculated for the existing protocols, it has to be remembered that all of the New Protocols began in the NASA's Exploration Atmosphere. If these atmospheric conditions are implemented in future spacecrafts or extraterrestrial villages, astronauts will be constantly living in an environment that naturally enhances N_2 washout, allowing for it to happen even when they are performing other activities.

Below in Table 3 the three New Prebreathe Protocols are compared.

New Prebreathe Protocol	Duration [min]	NASA's Exploration Atmosphere	100% O_2 atmosphere	Exercise	Final N_2 Partial Pressure value [kPa]
I	90	Yes	No	No	4.5
II	60	Yes	Yes	Yes	4.3
III	60	yes	Yes	No	3.4

Table 3. Comparison of the New Prebreathe Protocols

The New Prebreathe Protocol III reaches the lowest value of N_2 partial pressure, which indicates the lower risk of DCS. However, it also requires for a dedicated set-up to simulate a 100% O_2 atmosphere. The New Prebreathe Protocol I presents the highest final value of N_2 partial pressure, however it can be considered a passive protocol, as astronauts are already living in an environment set to the NASA's exploration atmosphere, and it could lead to lower N_2 partial pressure values if astronauts are exposed to this environment for prolonged periods of time. Lastly, the New Prebreathe Protocol II reaches a middle value of N_2 partial pressure, but it also implements physical activity. As exercise is proven to fasten denitronegation, and the code provides an approximate representation of the behavior, it could be the best choice out of the three. However, this consideration should be backed by ulterior analysis and physical testing.

Overall, the New Prebreathe Protocols allow for shorter preparation times, both because the combination of variables accelerates denitronegation and because astronauts will live and work in environments that already match the NASA's exploration atmosphere. In fact, astronaut participating in long-duration missions, will already be accustomed with the planned atmospheric conditions, as NASA's exploration atmosphere is expected to become the standard for extraterrestrial habitats.

6 Conclusions and future perspectives

This work aimed to develop a new prebreathe protocol by implementing N_2 processes in the V-HAB model of the human body, with the objective of decreasing the risk of DCS during EVAs.

Throughout this thesis, a comprehensive study of the physiological and metabolic processes of human respiration was presented, with the objective of better determining the differences between the role of O_2 and CO_2, and N_2. Additionally existing prebreathe protocols and factors that influence their duration have been explored, focusing on how different variables affect denitrogenation and DCS risk.

Successively computational models to describe these mechanisms were developed and implemented in V-HAB, allowing to modeling the existing prebreathe protocols and successfully validating the models to ensure their applicability to new scenarios as well.

Relying on the newly created MATLAB code, multiple variables combinations were investigated to design a new prebreathe protocol, resulting in three most-efficient options.

The new prebreathe protocols allow for adaptable solutions and remain consistent with physiological and structural standards, while offering a foundation for the optimization of prebreathe protocols for future spacecraft atmospheres.

Being this a preliminary study, some aspects may be improved and optimized in future revisions. The areas in which enhancements may take place, fall into two main categories: physical and code related. The first one regards how biological and physiological parameters are interpreted and analyzed, while the second one is associated with possible refinements of the MATLAB code.

6.1.1 Physical limitations

The main physical limitation lies in the fact that the parameter chosen to establish the risk of DCS is N_2 partial pressure. Although this decision remains highly suitable for the study conducted and for the type of MATLAB code used in the V-HAB environment, there is no universal consensus that it constitutes the optimal variable for accurately characterizing DCS risk.

In [11] the parameter chosen to establish the risk of DCS are VGE. VGE represents the bubbles of N_2 that forms in the blood when rapid decompression takes place and the dissolved gas comes out of the blood too quickly. The detection of VGE is a direct indicator for N_2 supersaturation. Moreover, the quantity and size of VGE are correlated with the risk of DCS: an increased bubble load is directly related to an increased risk of DCS.

This approach would require for a dedicated code, which can take into account bubble formation, dimension and number. For this reason, the choice of analyzing N_2 partial pressure remains appropriate for this scenario.

6.1.2 Code limitations

The implementation in the code is characterized by some assumptions and approximations that could be optimized in future revisions of this work.

Firstly, in the two *Respiration* functions that do not calculate tissue partial pressure, `calculateBloodPartialPressure()calculateBloodConcentration()`, Henry's Law was implemented for N_2. While the latter is a valid and correct formula, it carries simplifications in describing blood behavior. In this particular work it was accepted as it was needed for the overall code, but not employes in the evaluation of the tissue partial pressure.

The most beneficial improvement aims at making the code applicable to any scenario. At the moment the main equations (Bühlmann's and the dynamic approach one) are automatically updated during the simulations, obtaining as input the new values as the code progresses. However, the settling of the environment still remains a manual process. Each protocol must be implemented individually in the code, including its phases and the timing of transitions of the human between environments. Even though this process does not require too much time, it still undermines the purpose of V-HAB, which is supposed to be a device to be used interchangeably to build LSSs with different characteristics.

Lastly, regardless of beneficial improvements, this work and code functions as a preliminary tool to better understand the dynamics of prebreathe protocols and the role that various parameters play in their reliability and duration.

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