Human spaceflight alterations: a journey from experiments to computational modeling

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Missione Spazio: come orbitano corpo e mente
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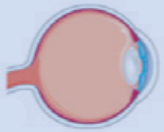
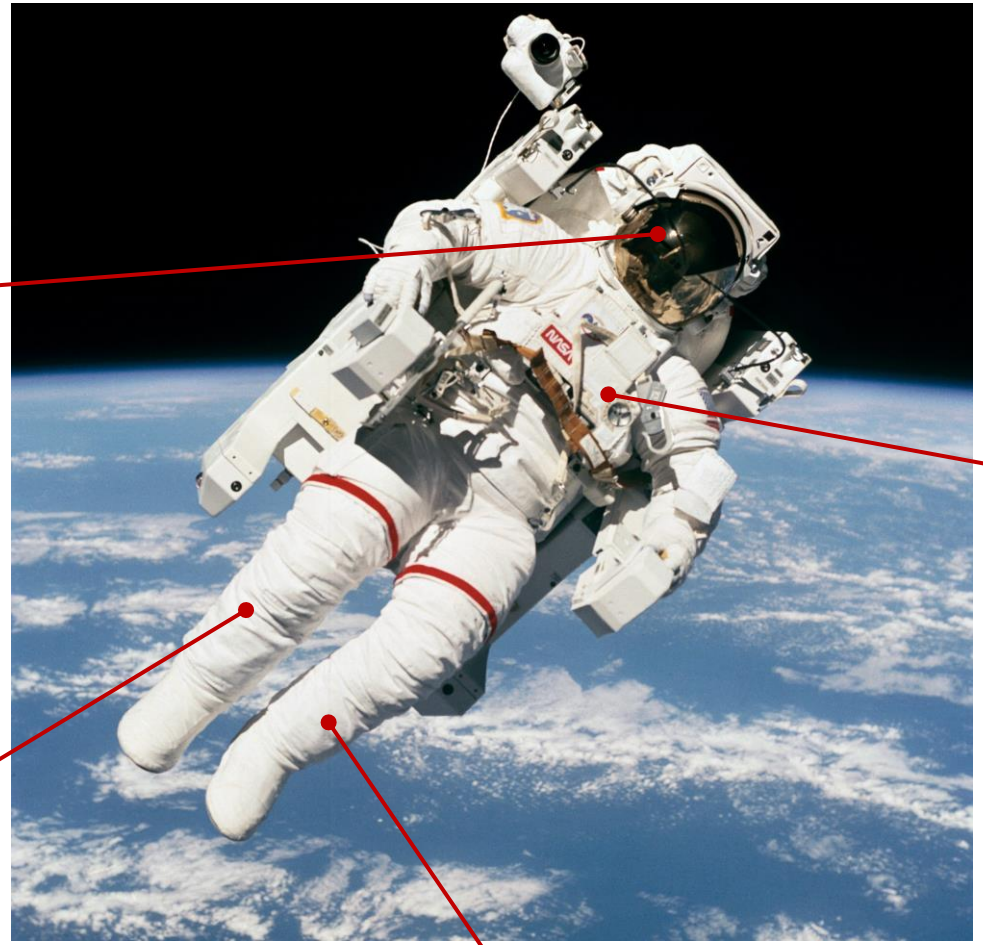
Background and Outline

- Space flight: extreme environment for human life with continuous exposure to **gravity changes** (*micro*- to *hypergravity*) and cosmic radiation
- **Space physiology** and **medicine**: understand the role of gravity in life processes and guarantee the health and welfare of the astronauts and space travelers
- Human spaceflight is a unique and irreplaceable laboratory for increasing our knowledge in physiology and medicine → 0g partial adjustment point
- Space technology is a 9:1 economic multiplier → huge impact on immobilization and aging-related pathologies on Earth
- Overview of spaceflight-induced human alterations, with ground-based analogs and countermeasures
- Combining *in silico-in vivo* framework: a 0D-3D **cardiovascular digital twin for spaceflight applications**

Physiology alterations associated to human space flight

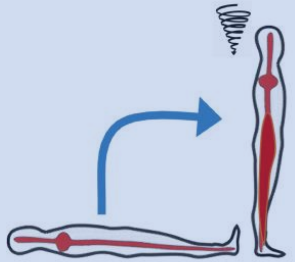
Neuro-vestibular system
Space motion sickness and Spaceflight-associated neuro-ocular syndrome (SANS)

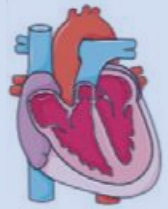




Muscular system
Muscle atrophy

Cardiovascular system
Cardiovascular deconditioning (fluid shift from lower to upper body, reduced exercise capacity and autonomic response, blood volume reduction, and cardiac atrophy) and Orthostatic intolerance

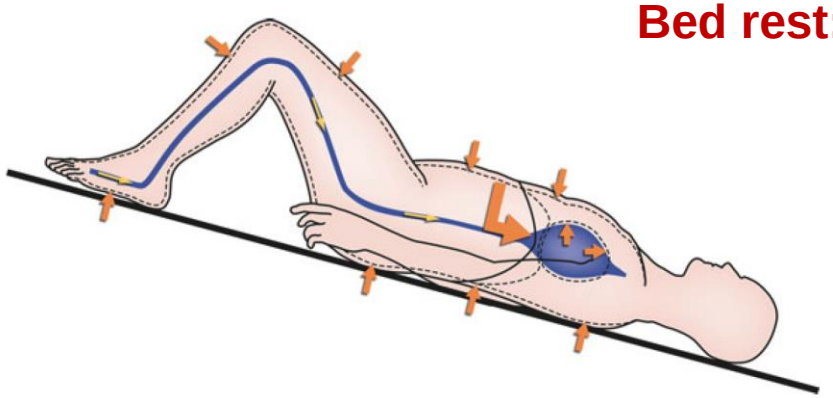


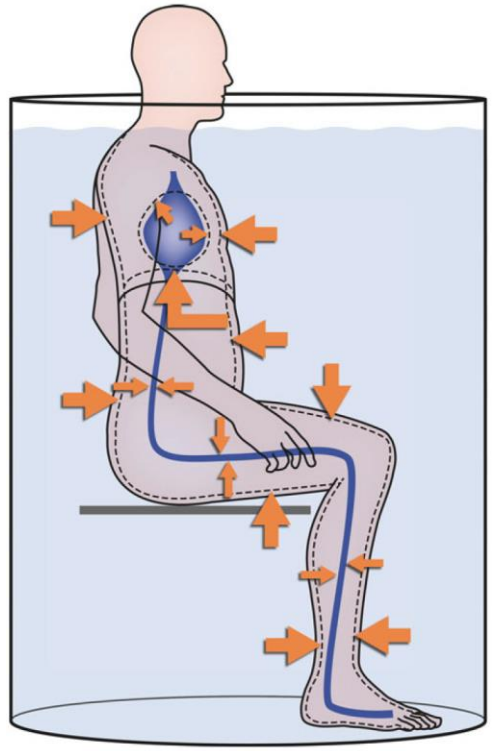


Skeletal system
Bone demineralization

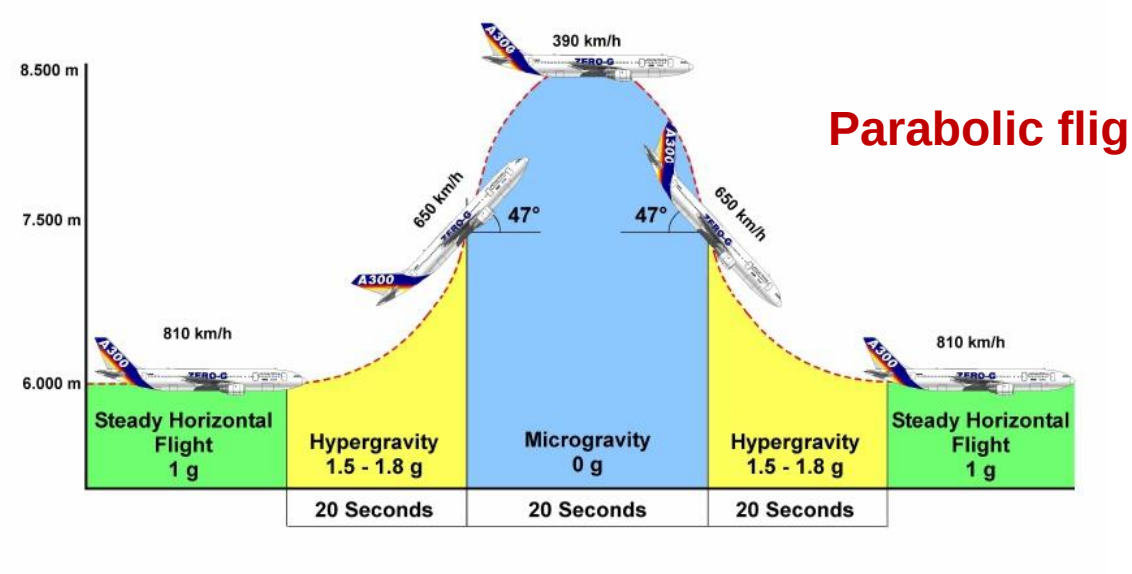
Ground-based analogs

Bed rest: -6° head down tilt

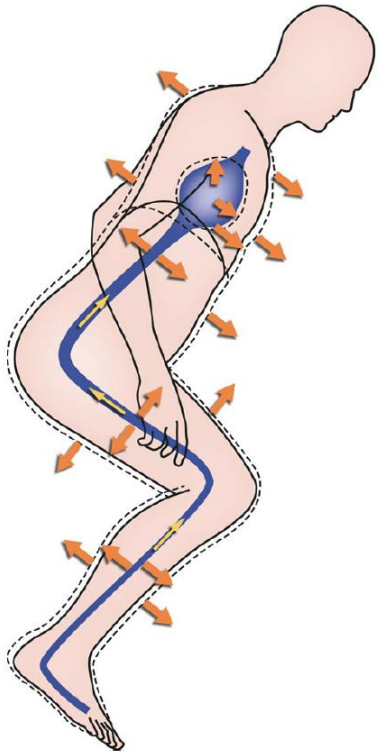




Water immersion



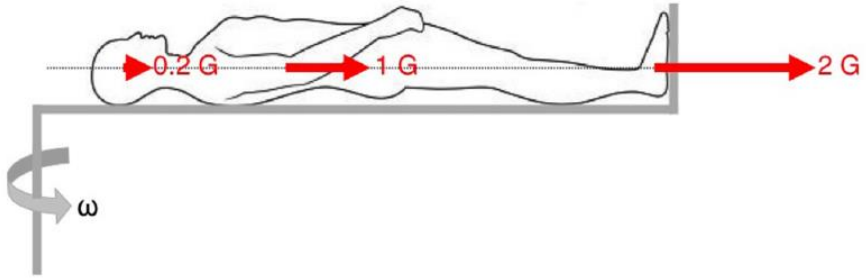
Parabolic flight



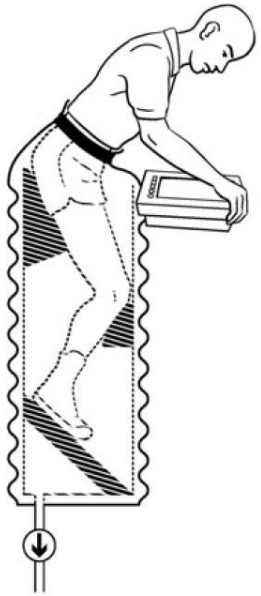
Inflight countermeasures

Exercise

Artificial gravity



Lower body negative pressure



Anti-0g suits and wearable devices

Combining *in silico-in vivo* framework: 0D-3D cardiovascular digital twin

0D-1D central-systemic cardiovascular model

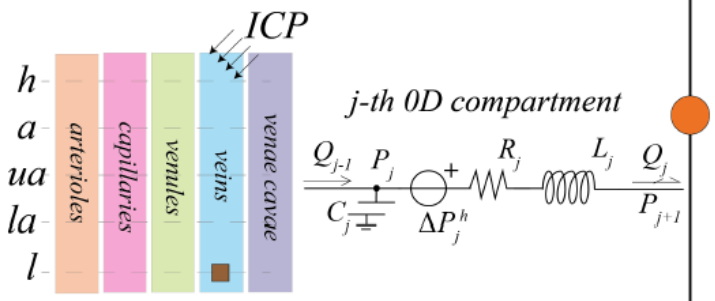
Short-term control and submodels

- arterial baroreflex
- cardiopulmonary reflex
- Drzewiecki's P-A (1D arteries)
- cerebral autoregulation
- Melchior's P-V (0D veins)

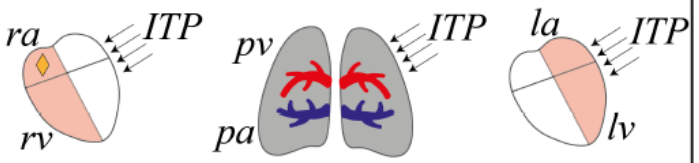
0D coronary microcirculation

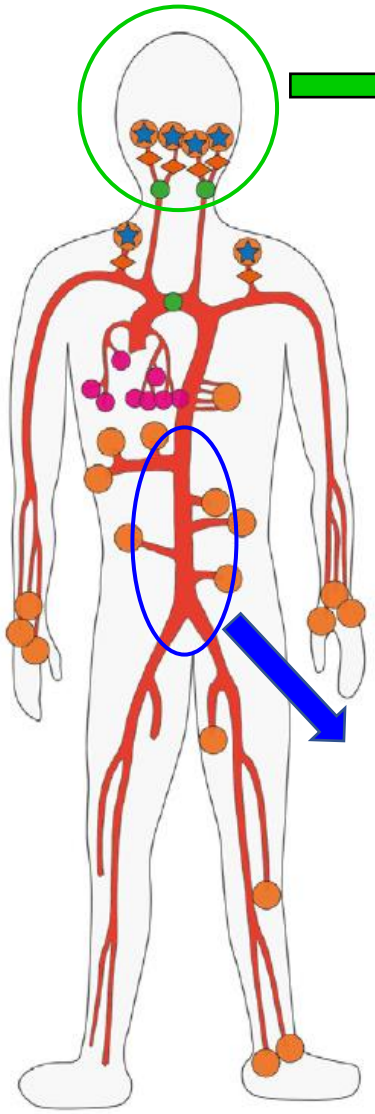
coronary myocardial layers — IMP

0D peripheral microcirculation and venous return

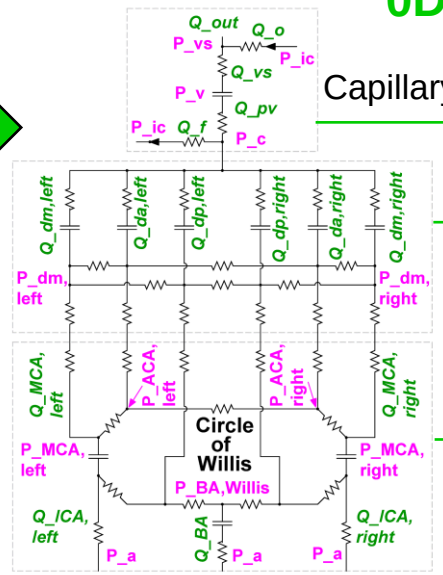


0D cardiopulmonary circulation





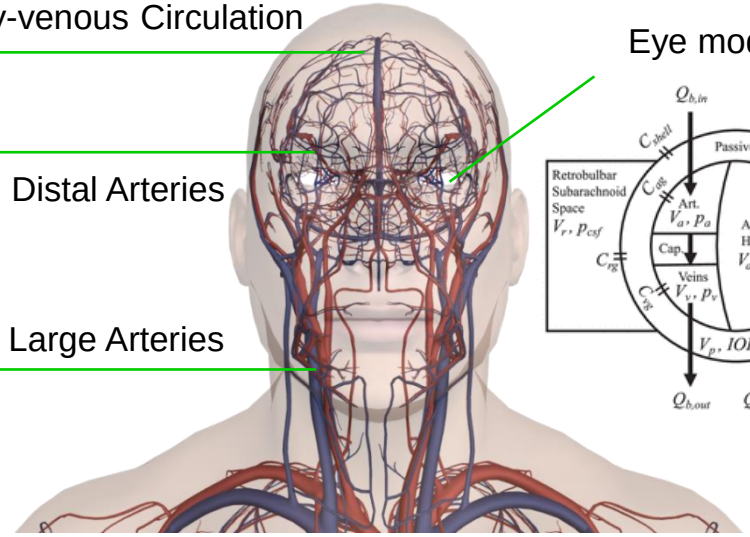
0D cerebrovascular-ocular model



Capillary-venous Circulation

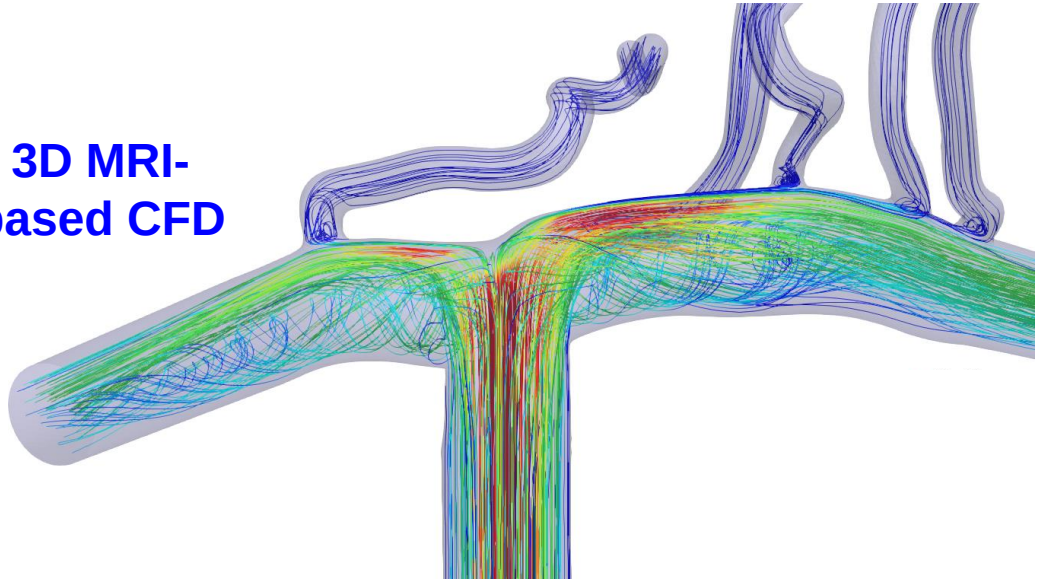
Distal Arteries

Large Arteries

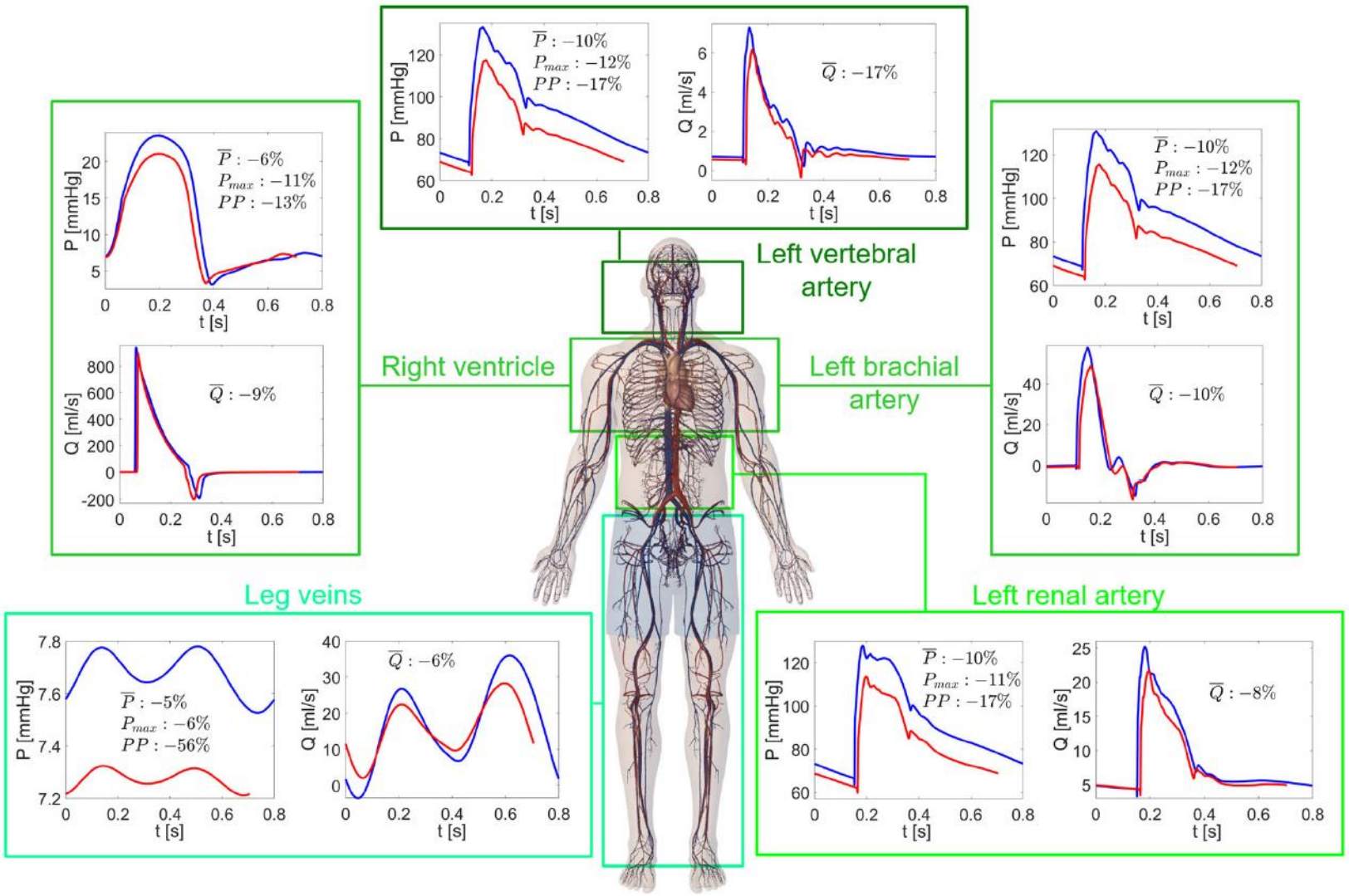


Eye model

3D MRI-based CFD



Cardiovascular deconditioning during long-term spaceflight



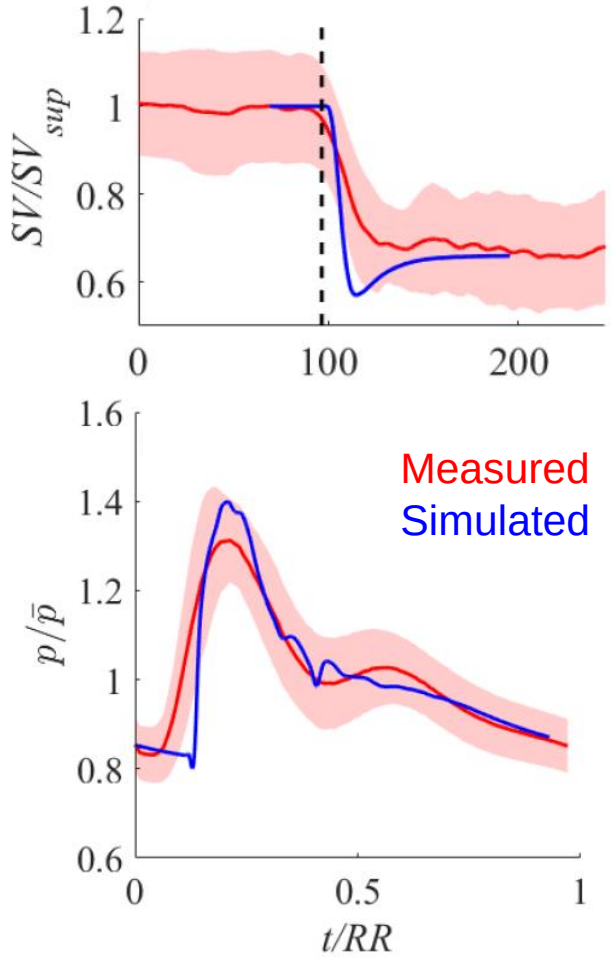
- Reduction of cardiac work, oxygen consumption, contractility indexes, central mean and pulse pressures
- Exercise tolerance like an untrained sedentary person
- Significant waveform alterations at the capillary-venous level

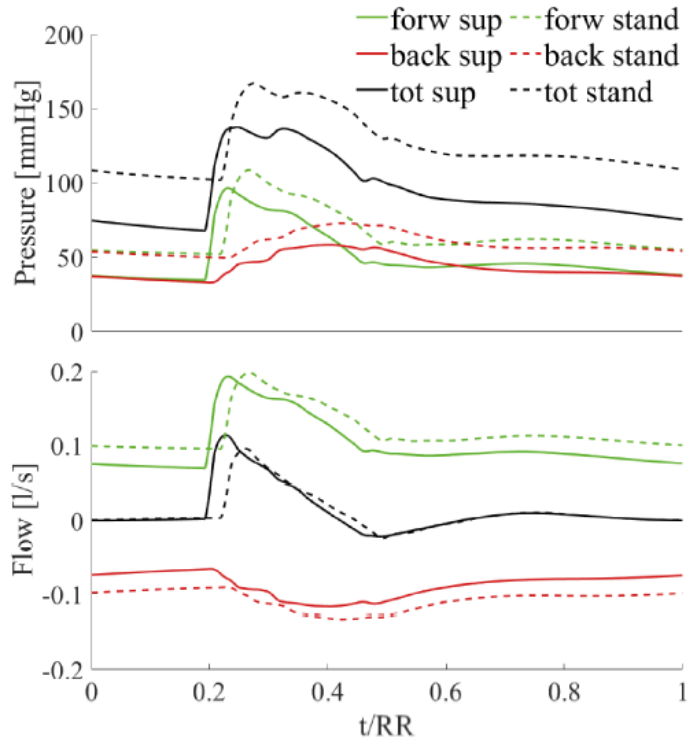
Gallo et al., njp Microgravity 2020

Short term orthostatic stress: head-up tilt (HUT)

Fois et al., Front. Physiol. 2022

Fois et al., Royal Soc. Open Sci. 2023

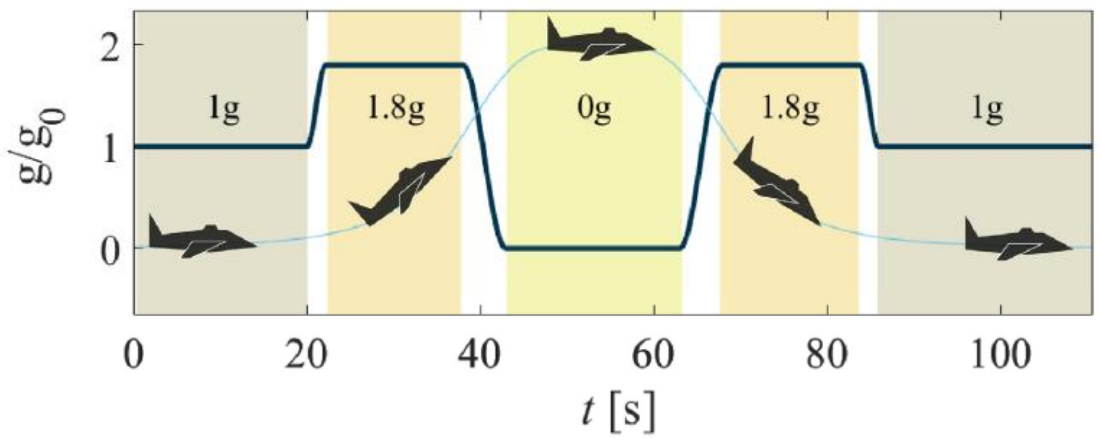




- Arterial wave dynamics adaptation and preservation

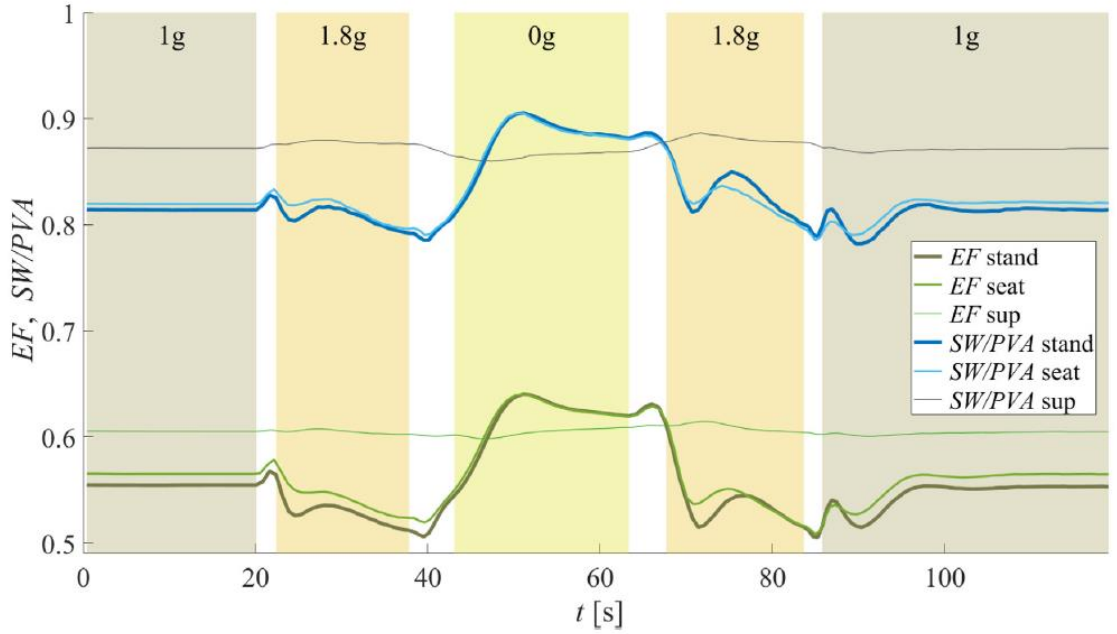
- Increase of mean arterial pressure and HR, decrease of SV and CO
- Transient dynamics not symmetric between HUT and HDT, strong tilting rate influence

Short term ground-based analogs: parabolic flight

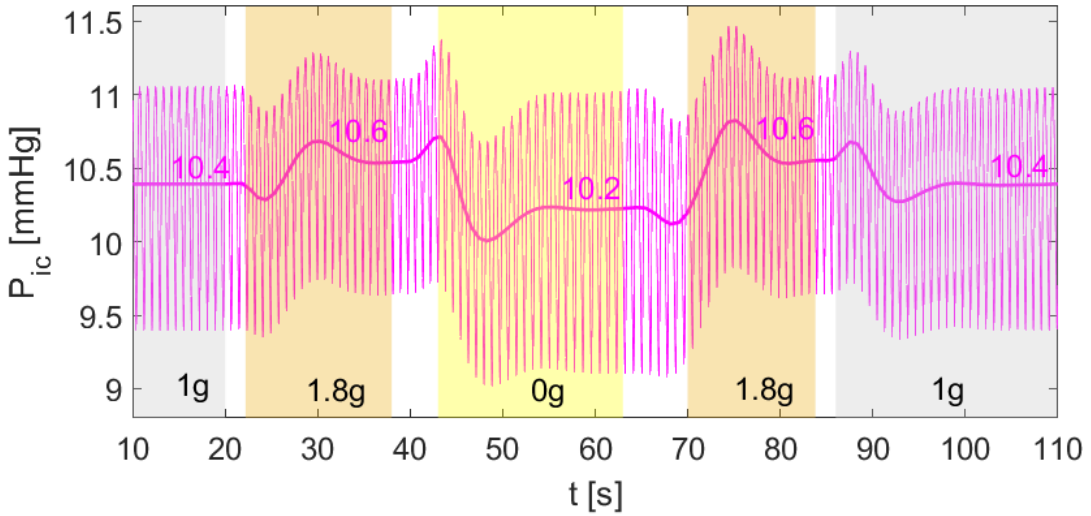


Fois et al., Acta Astronaut. 2022

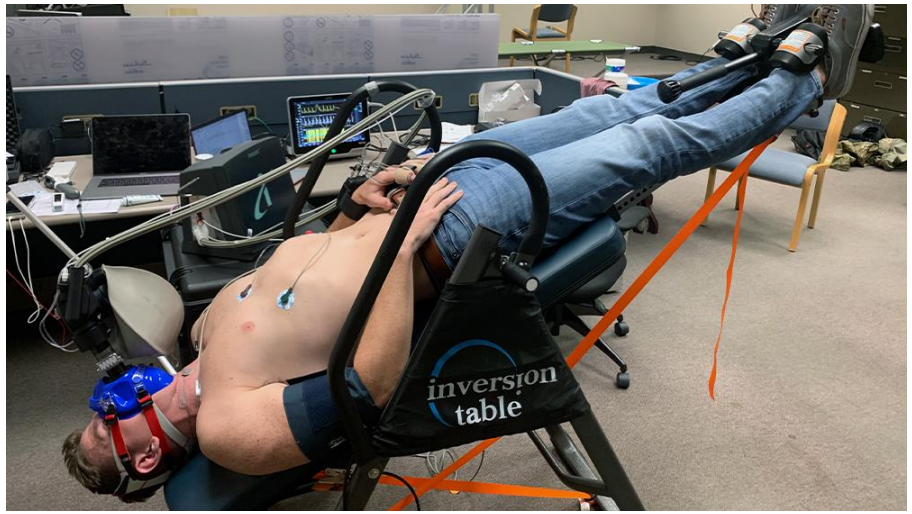
Scarsoglio et al., Acta Astronaut. 2023

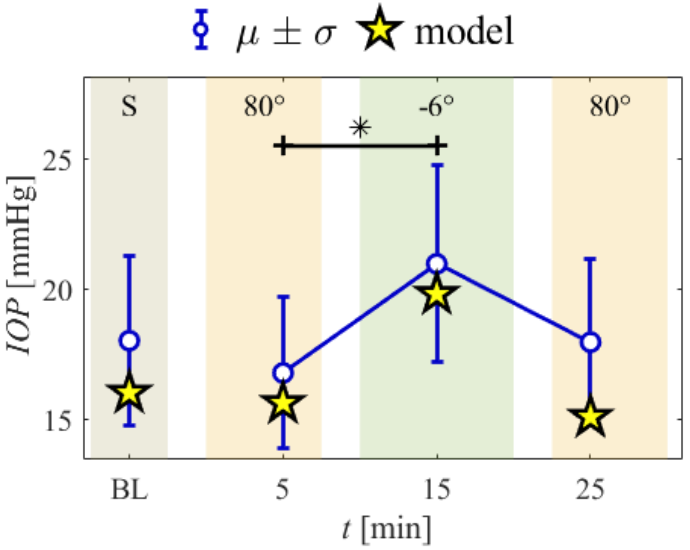


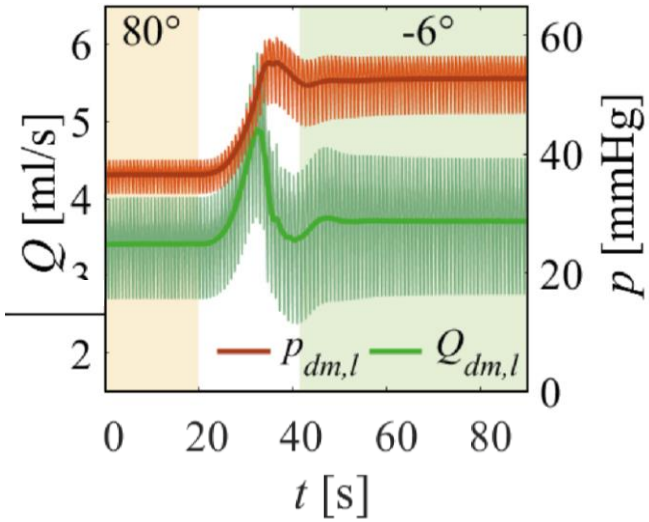
- Central aortic pressure, cardiac work and oxygen consumption indexes influenced by gravity and posture variations
- Improved cardiac efficiency in microgravity, while worsened in hypergravity
- Increased hemodynamic pulsatility in the 0g cerebral microcirculation (intracranial pressure, cerebrospinal fluid circulation, cerebral blood flow)

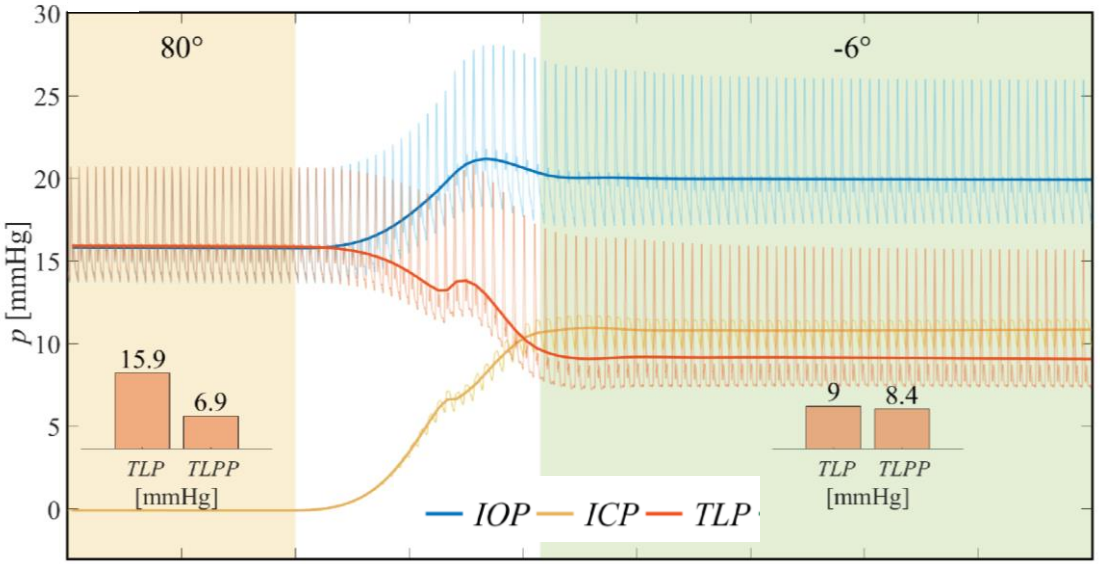


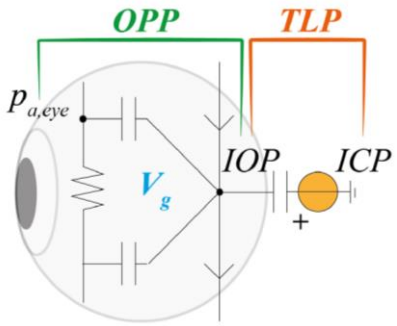
Short term ground-based analogs: -6° head down tilt (HDT)











- Increased pulsatility in the deep cerebral circulation
- Ocular translaminar pressure (TLP) decrease, ocular perfusion pressure (OPP) increase

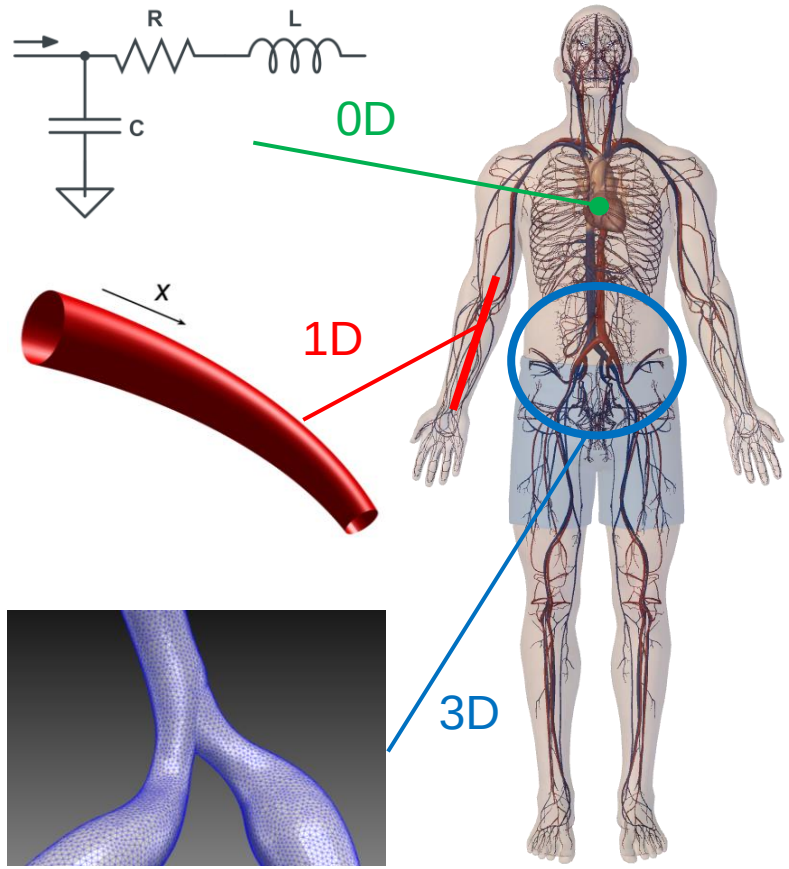
- Possible mechanisms (ocular globe deformation and edema formation) at the onset of SANS

Fois et al., njp Microgravity 2023

Next steps: ESA co-funded PhD project

Optimizing countermeasures against cardiovascular deconditioning and cerebral hemodynamics changes in long-term human spaceflights

Multiscale cardiovascular digital twin



Research Question

Solidifying the link between cerebral hemodynamics and neurovestibular dysfunctions in microgravity: which are the optimal countermeasures to face long-term human space missions?

Optimizing countermeasures

Open questions and future developments

- Mission length exceeding 1-year: amplification of already known reversible alterations or emergence of unrecognized irreversible changes and sustained pathologies (e.g., arrhythmias)?

- Will lengthy missions make space travelers unfit for return to a 1g environment (e.g., osteoporosis, cardiac atrophy, visual impairment)?

- Is 0g set-point (full physiological adjustment to space conditions of those born in space) reachable in the long-term?

- Current inflight countermeasures are not optimal: humans would not be operational after landing on Mars → Tested and validated countermeasures for longer missions are needed for each specific system

- Computational approach is a research frontier and can provide unique insights into weightlessness, since experimental data remain overall few, very expensive and difficult to obtain.

Thanks to all the team and sponsors

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