Physiological and Biological Changes in Space

Microgravity Lessons and Lunar Discovery

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What ISS taught us about biology under altered gravity

- ISS is a unique laboratory for scientific discovery
- Eliminates gravity-driven processes (buoyancy, convection)
- Critical for human space exploration and sustainability of future missions
- ISS ≠ Moon
    - Shielded radiation
    - Continuous crew presence
    - Frequent resupply

Case Studies: Biological Systems and Physiological Change in Space

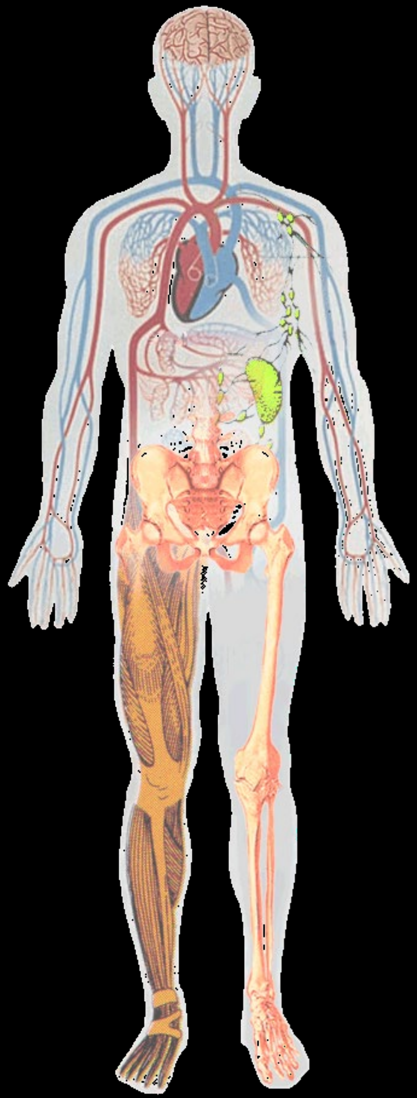
- Human physiological monitoring during spaceflight
- Molecular profiling of cells, microbes, and human samples
- Environmental and microbial sensing in closed habitats
- Synthetic Biology and Biomanufacturing

Human physiological monitoring during spaceflight and altered gravitational environments

Human Physiology: Response to Spaceflight

Humans experience a
spectrum of adaptations
in flight and postflight

Balance disorders
Cardiovascular
deconditioning
Decreased immune function
Muscle atrophy
Bone loss



- Neurovestibular
- Cardiovascular
- Bone/Muscle
- Increased CO2
- Immunology
- Nutrition
- Waste
- Radiation

Courtesy of Mike Barratt

Radiation biology: ISS vs Lunar

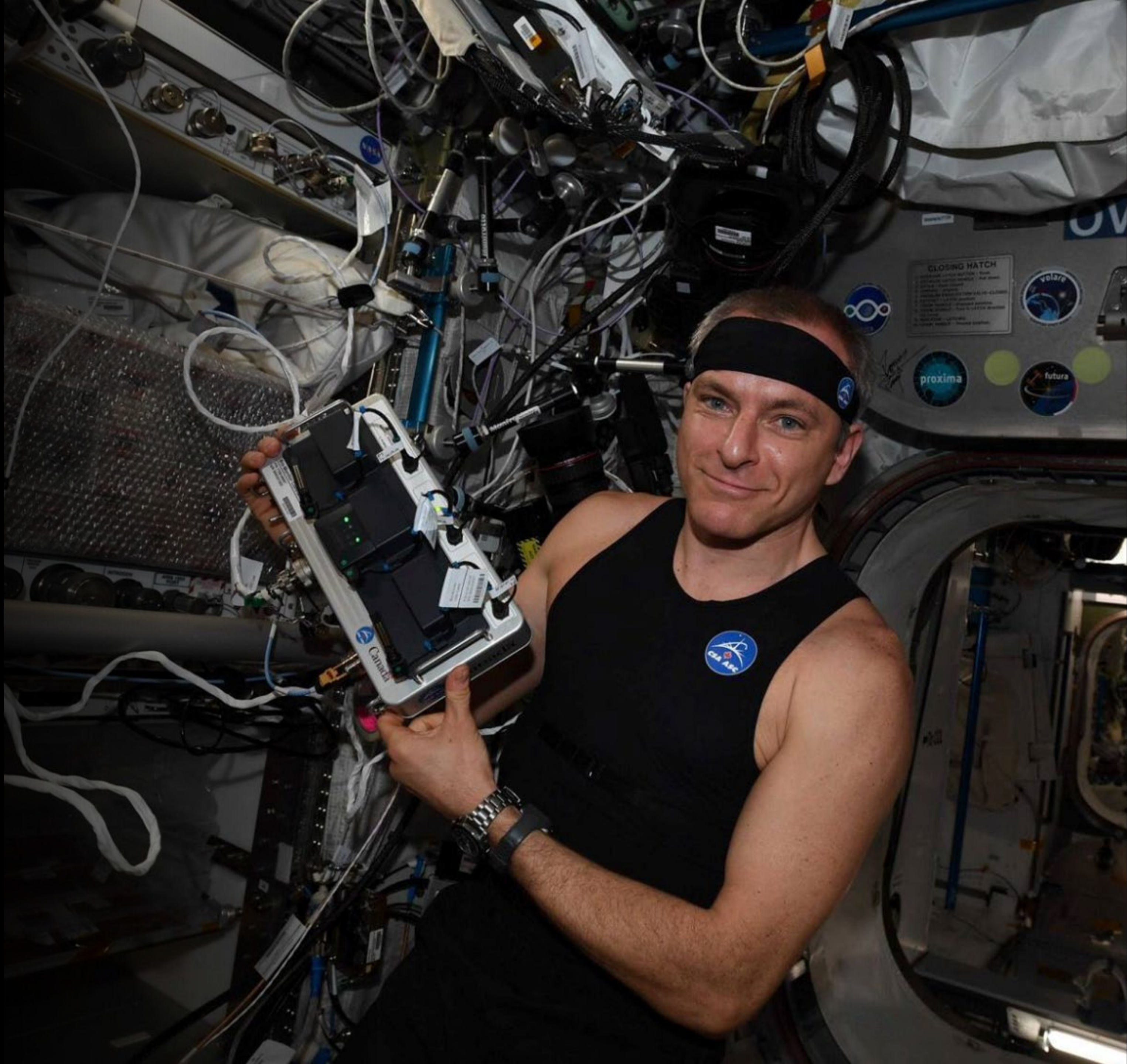
- What We Know from ISS
  - Space radiation induces DNA damage and persistent gene expression changes
  - Alterations observed across immune, cardiovascular, and cellular repair pathways
  - Omics approaches (e.g., GeneLab, Twins Study lineage) enable system-level insight
- What Changes on the Lunar surface
  - Continuous radiation exposure beyond Earth's magnetosphere
  - Different radiation quality and particle spectra than low Earth orbit
- What We Do Not Yet Know
  - Longitudinal molecular and cellular responses in lunar-relevant radiation environments
  - Variability, persistence, and reversibility of genomic and epigenomic changes
  - Interaction of radiation with partial gravity, dust, and other lunar stressors

Characterizing the Human Health Risk for Lunar Missions

- We do not yet understand the magnitude, nature, or operational risk profile of biological alterations in sustained partial gravity, nor the emergence of new lunar-specific risks absent in low Earth orbit
  - ISS data reveal biological vulnerability, not lunar risk envelopes
  - Apollo data is limited and pre-molecular biology era
  - Partial gravity may mitigate some changes and exacerbate others
  - Risk is defined by severity, variability, and interaction with lunar stressors

Future of Human Health Monitoring in Space

- Wearable sensors
- Human-centered design, transparent systems
- Remote monitoring
- Integrated diagnostics
- EVA recovery
- Sleep, radiation exposure, fatigue



Molecular profiling of cells, microbes, and human samples

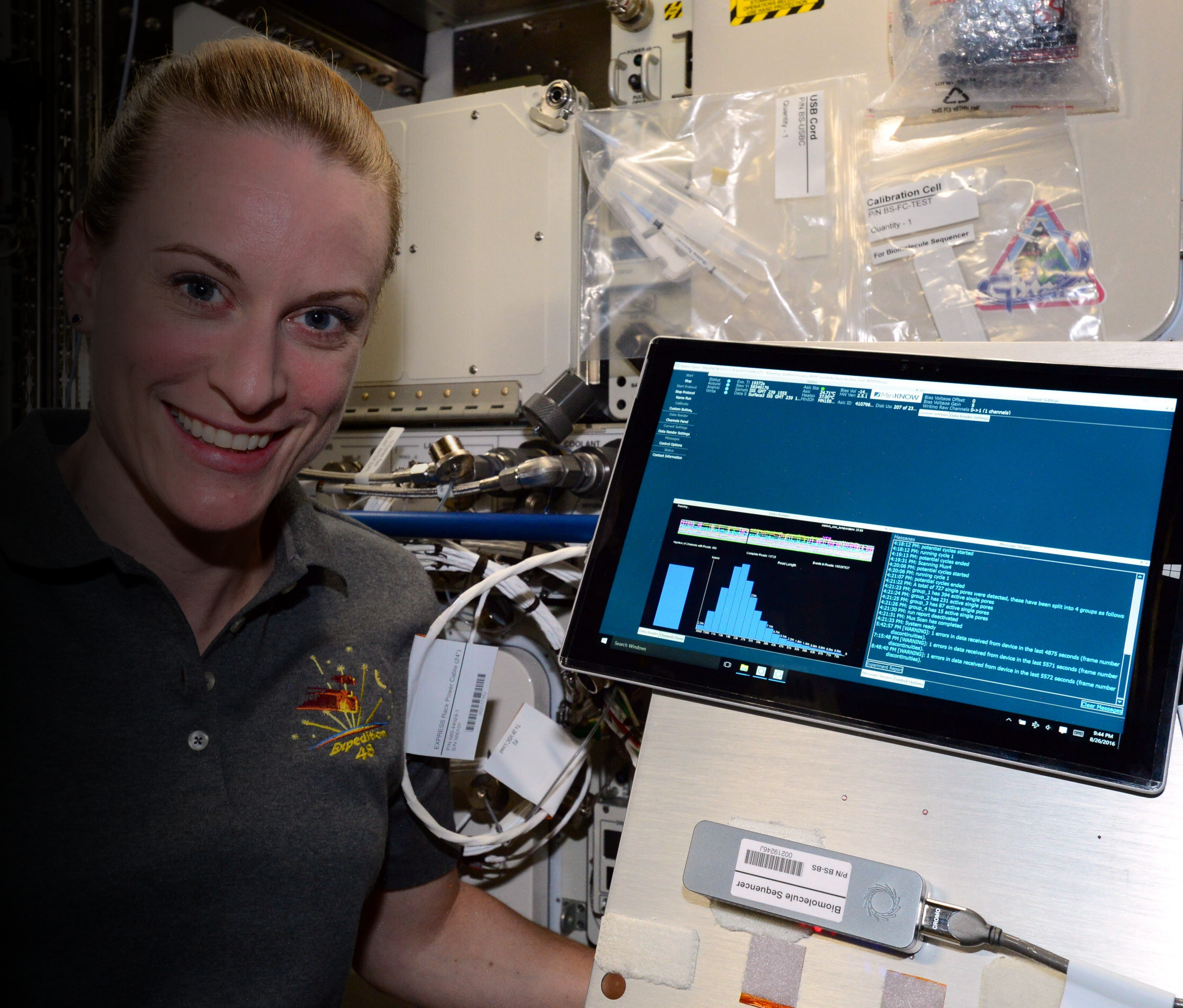
Key advances in the last decade:

- First DNA/RNA sequencing in space
- Real-time microbial and environmental profiling
- Long duration cell culture and organoid/tissue model systems
- Cell visualization and microscopy
- Longitudinal omics from the same biological samples
- Integration of molecular data with physiological measurements

Why do DNA/RNA sequencing in space?

- Microbial/environmental sensing
- Monitor human health and disease closer to real-time
- Increasing Earth-independence in future Moon-to-Mars missions
- Why is this important for lunar destinations?
  - Delayed Earth support
  - Surface dust and closed habitats
  - Longer autonomous operations
  - Planetary protection awareness

Nanopore DNA Sequencing and Genome Assembly on the ISS



- Castro-Wallace, S.L., Chiu, C.Y., John, K.K. *et al.* Nanopore DNA Sequencing and Genome Assembly on the International Space Station. *Sci Rep* **7**, 18022 (2017).

Expansion of In Situ Sequencing Capabilities on ISS

Established capabilities:

- DNA, direct RNA, and cDNA sequencing in microgravity
- Culture-dependent and culture-independent microbial identification
- Environmental microbial profiling of surfaces and water systems
- Genetic manipulation and detection in spaceflight conditions

Castro-Wallace *et al.* 2017, Burton *et al.* 2020, Stahl-Rommel *et al.* 2021, Nguyen *et al.* 2023, Nguyen et al 2023

Large-Scale Microbial Mapping in a Space Habitat

- Large-scale, spatially resolved sampling across the ISS interior
- Culture-independent profiling of surfaces
- Integration of microbial and chemical measurements across locations
- Mapping of microbial distributions driven by habitat use patterns
- This approach provides a foundation for biological mapping of sustained lunar surface habitats

803 surface samples
>31 million 16S sequences
3.7 billion metagenomic reads
21,000 chemical features

Cell

CellPress

The International Space Station has a unique and extreme microbial and chemical environment driven by use patterns

Sequencing as a Key Capability for Lunar Surface Biology

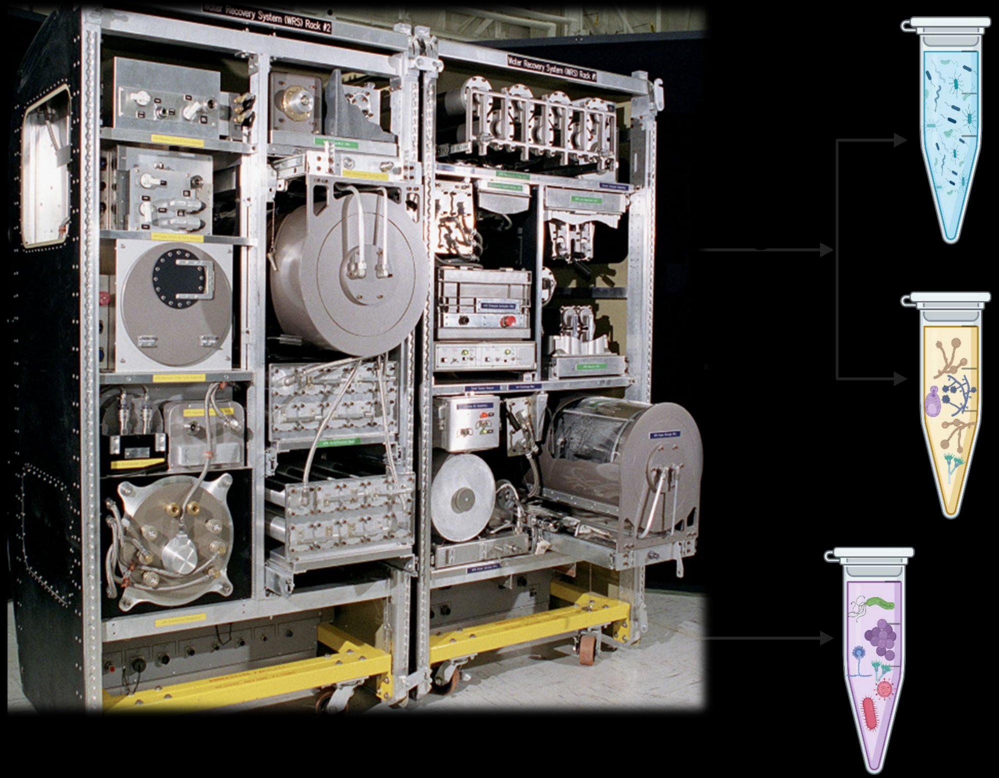
- Crew health monitoring with delayed Earth contact and high performance loads
- Environmental monitoring (air, water, surfaces, radiation)
- Planetary protection and contamination awareness
- Technologies that advance lunar biological discovery
  - Automated sample preparation, minimal crew time
  - Miniaturization and modularity
  - Machine learning with large-scale data sets

Gravity-Dependent Forces Shape Biological Structure and Function

- Gravity-dependent forces regulate tissue structure and function
  - Buoyancy, shear, and sedimentation shape cell organization
- Microgravity findings demonstrate force sensitivity
  - Enhanced organoid self-organization and lumen formation
  - Improved vascular sprouting under reduced shear
  - Altered extracellular matrix assembly (collagen, fibrin, alginate)
  - Bioprinting without structural collapse or sagging
- Relevance for the Moon
  - Partial gravity will reintroduce mechanical forces at different magnitudes
  - Biological systems in lunar gravity are a regime we have never studied
  - New steady states, altered tissue mechanics, or unexpected failure modes may emerge

Environmental and microbial sensing in closed habitats

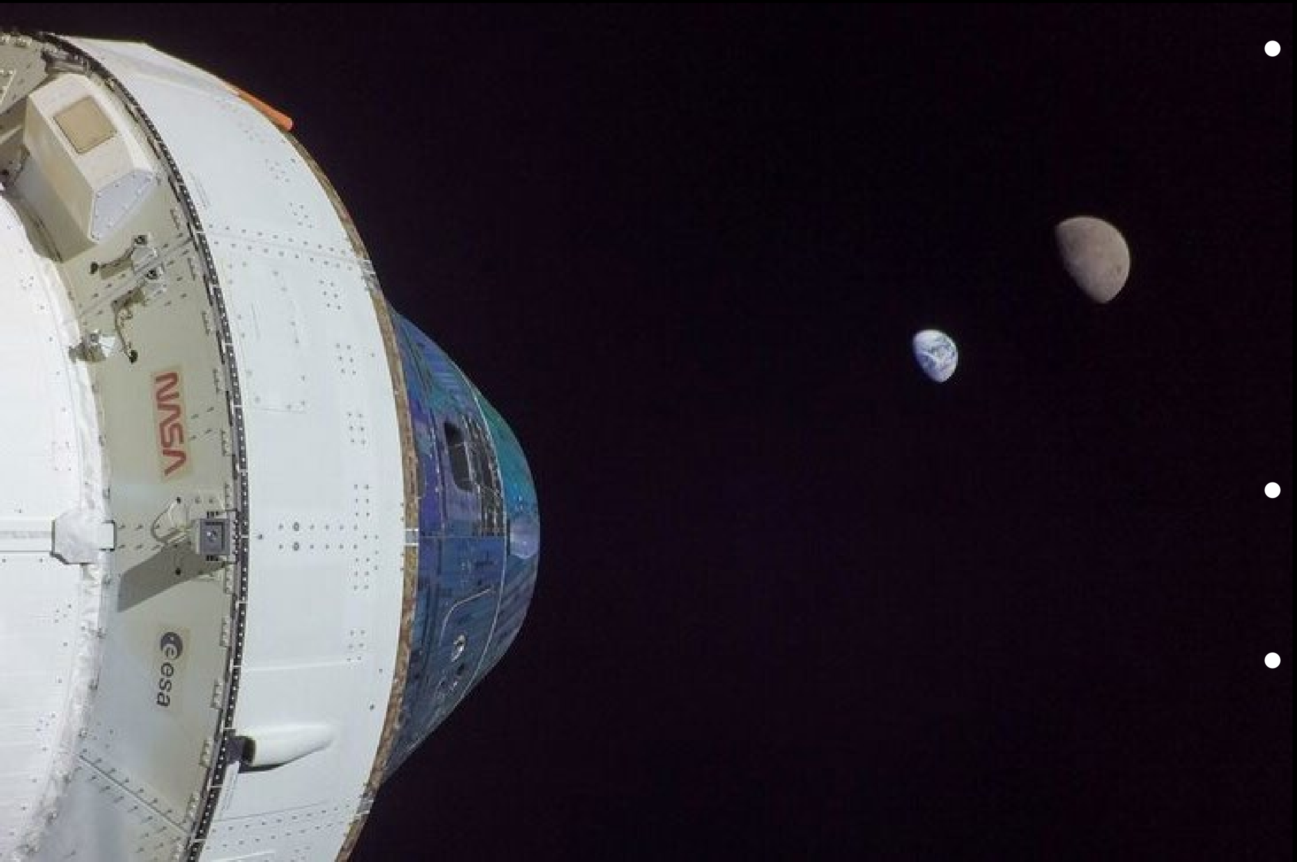
- 97% closed loop efficiency for the water system
- The ISS wastewater tank has minimal microbial control, and we do not regularly sample for species identification
- Metagenomic methods for spacecraft water system monitoring
- Other in situ sensors that could provide health and status of water system



Every molecule counts on the way to the Moon!

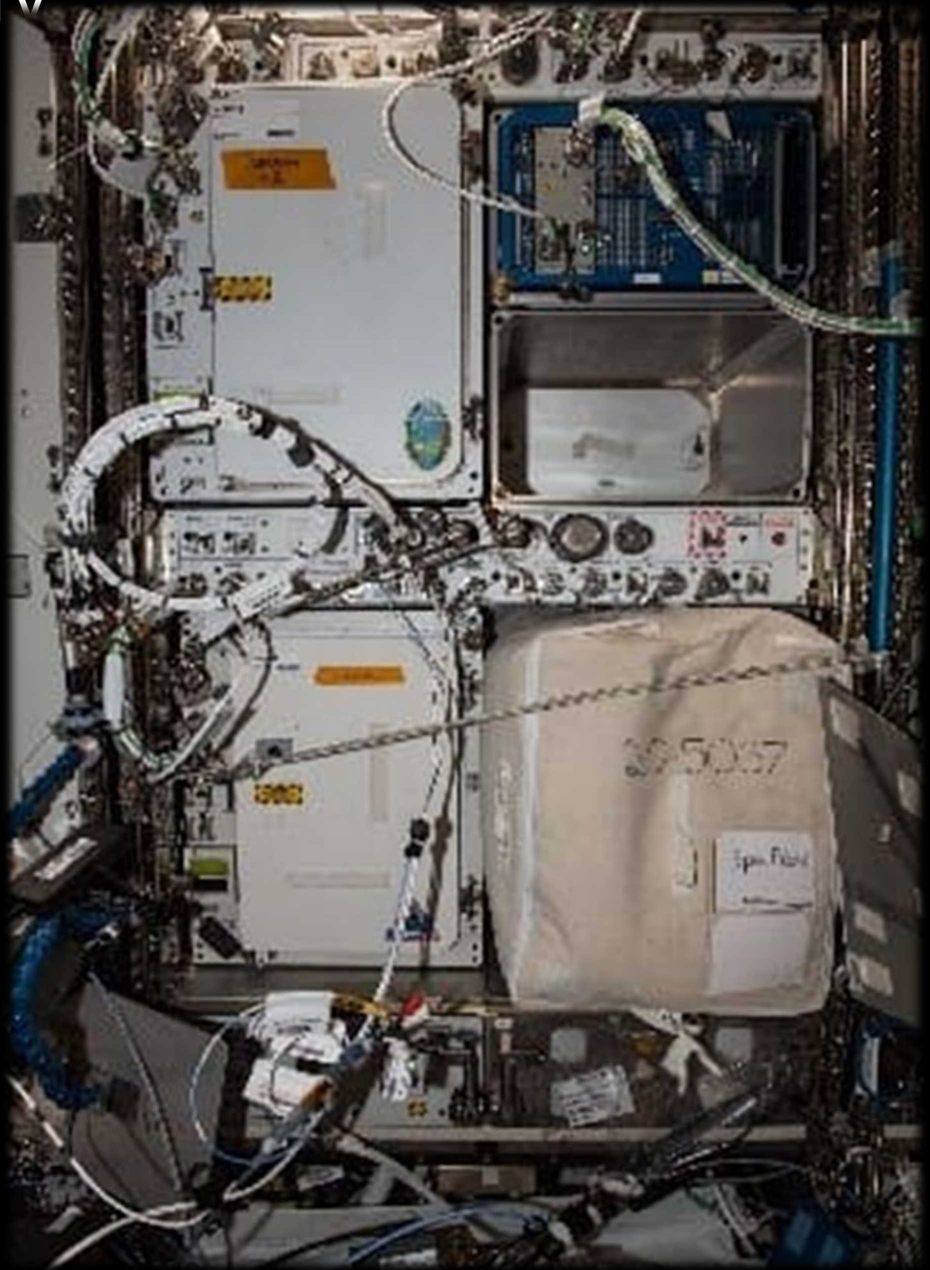
Synthetic Biology and Biomanufacturing

- Lunar surface logistics constraints
- Focus: on demand production of food, materials, pharmaceuticals, sensors, fuel, lubricants
- Building environmental control and life support technology from the ground up
  - Interfacing living and mechanical systems
  - Environmental sensors embedded in systems
- In situ resource utilization, reduced reliance on Earth-based resupply chains
- Consumables recycling/re-purposing
  - Reduction of waste footprint



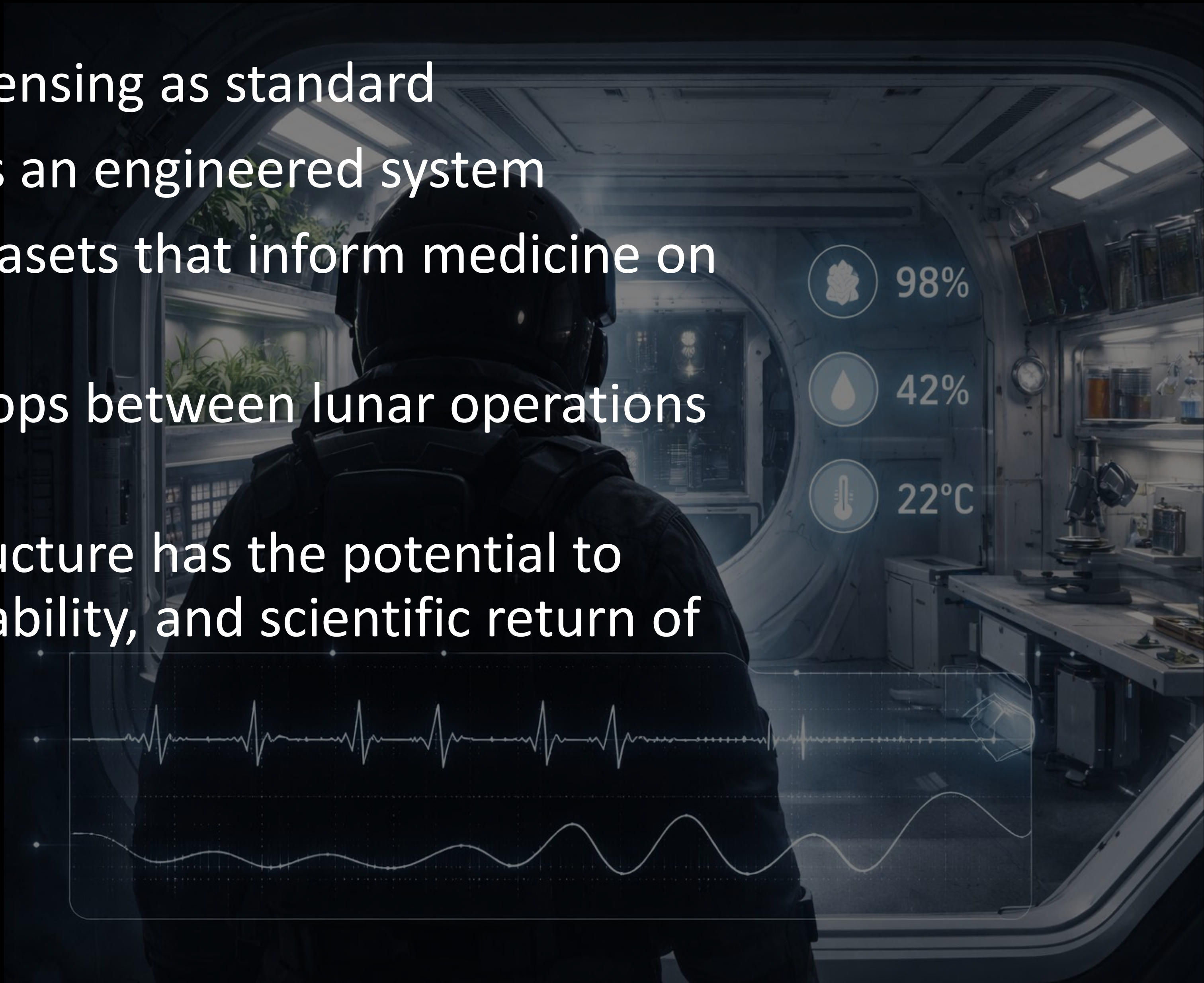
Gaps in Biological Infrastructure Today

- Limited availability of long-duration biological monitoring systems
- Limited autonomous diagnostics capability and hardware
- Limited integration of biological data architectures across missions
- Constraints on rapid iteration of biological hardware



Biology as an Operational Capability on the Moon

- Toward ontinuous biological sensing as standard
- Biology increasingly treated as an engineered system
- Lunar missions generating datasets that inform medicine on Earth
- Opportunities for feedback loops between lunar operations and biomedical innovation
- Integrating biology as infrastructure has the potential to strengthen the safety, sustainability, and scientific return of lunar exploration



What the Committee Should Take Away

1. What we learned:
   - ISS biology revealed how physiology responds to altered gravity
2. Why it matters scientifically:
   - Biological risk and performance must be characterized under sustained lunar conditions
   - The Moon enables discovery of partial-gravity biology
3. What must evolve operationally:
   - Lunar biology must be increasingly treated as infrastructure

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The International Space Station has a unique and extreme microbial and chemical environment driven by use patterns
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Questions?