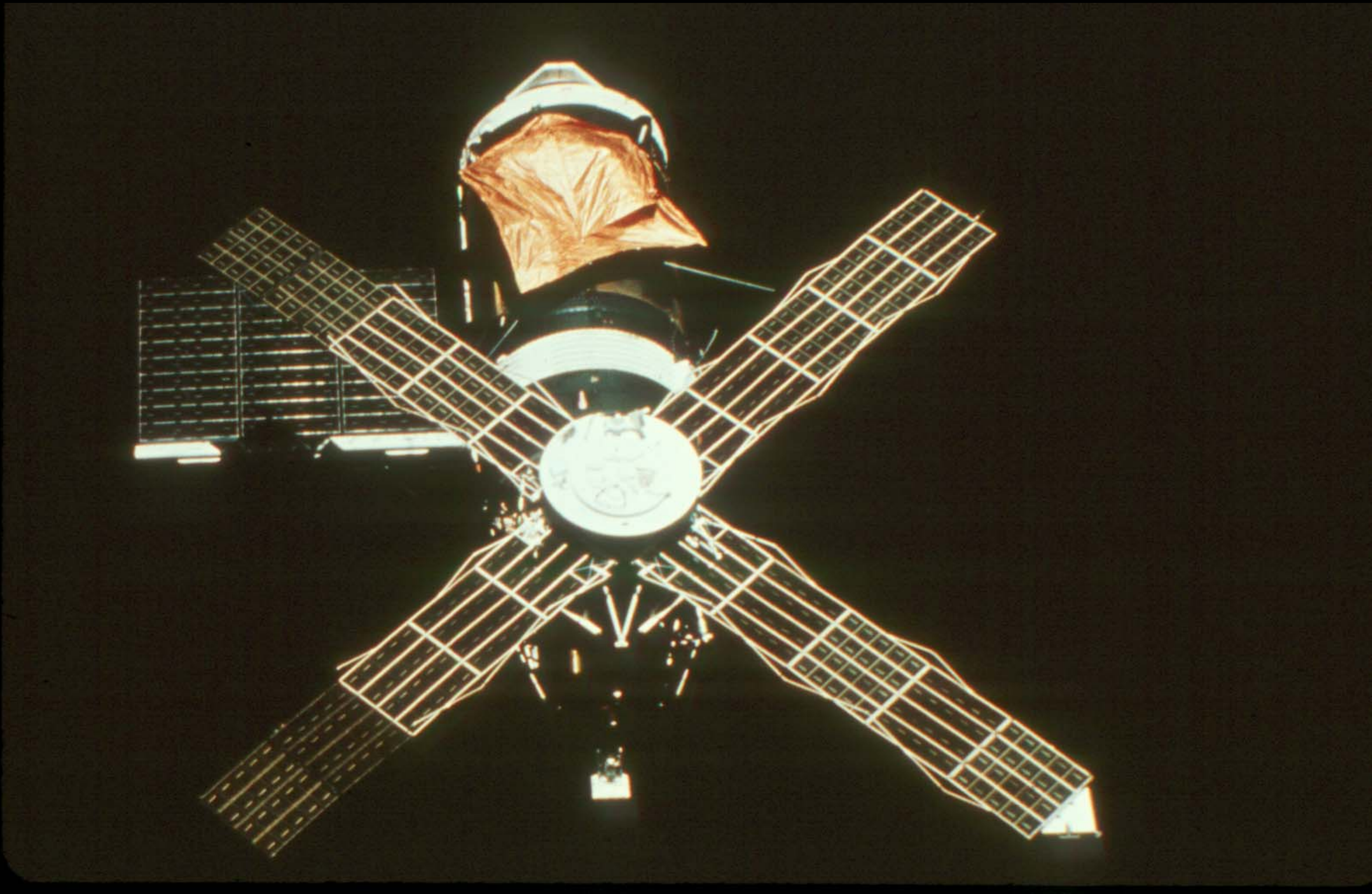
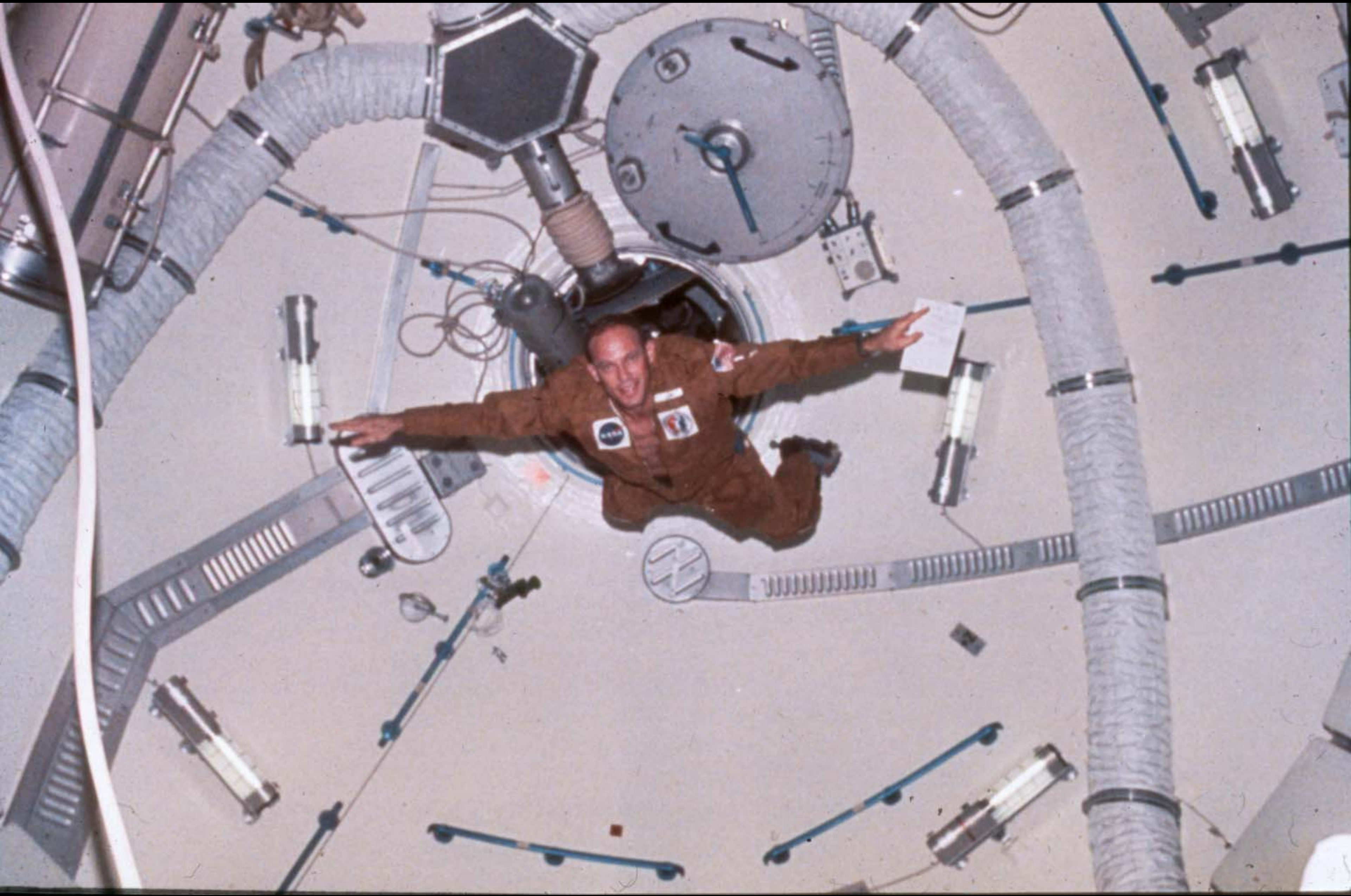
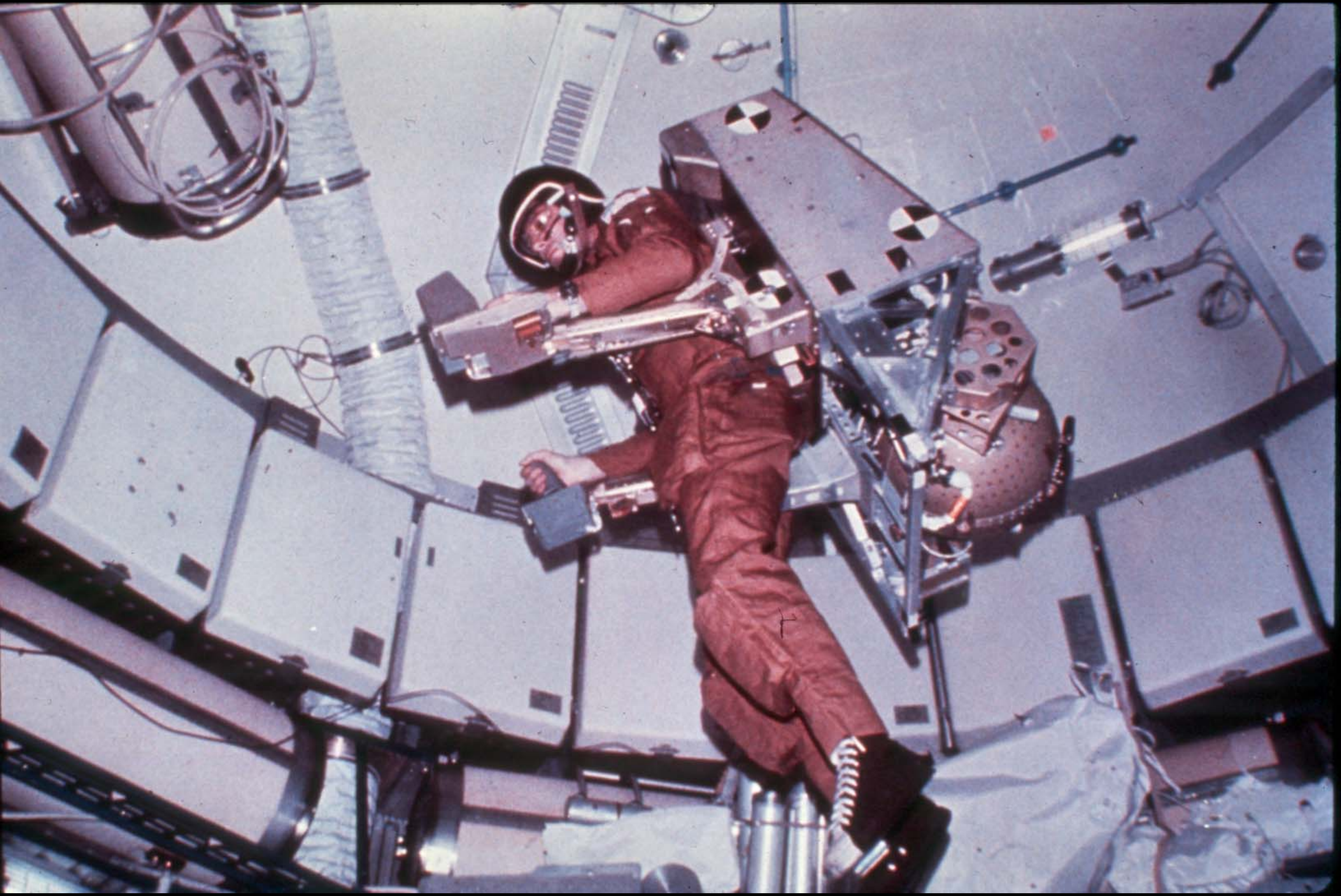
# The Digital Human

# The Goal

**An accurate simulation of the human body from molecules to cells, tissues, organ systems and the entire body.**

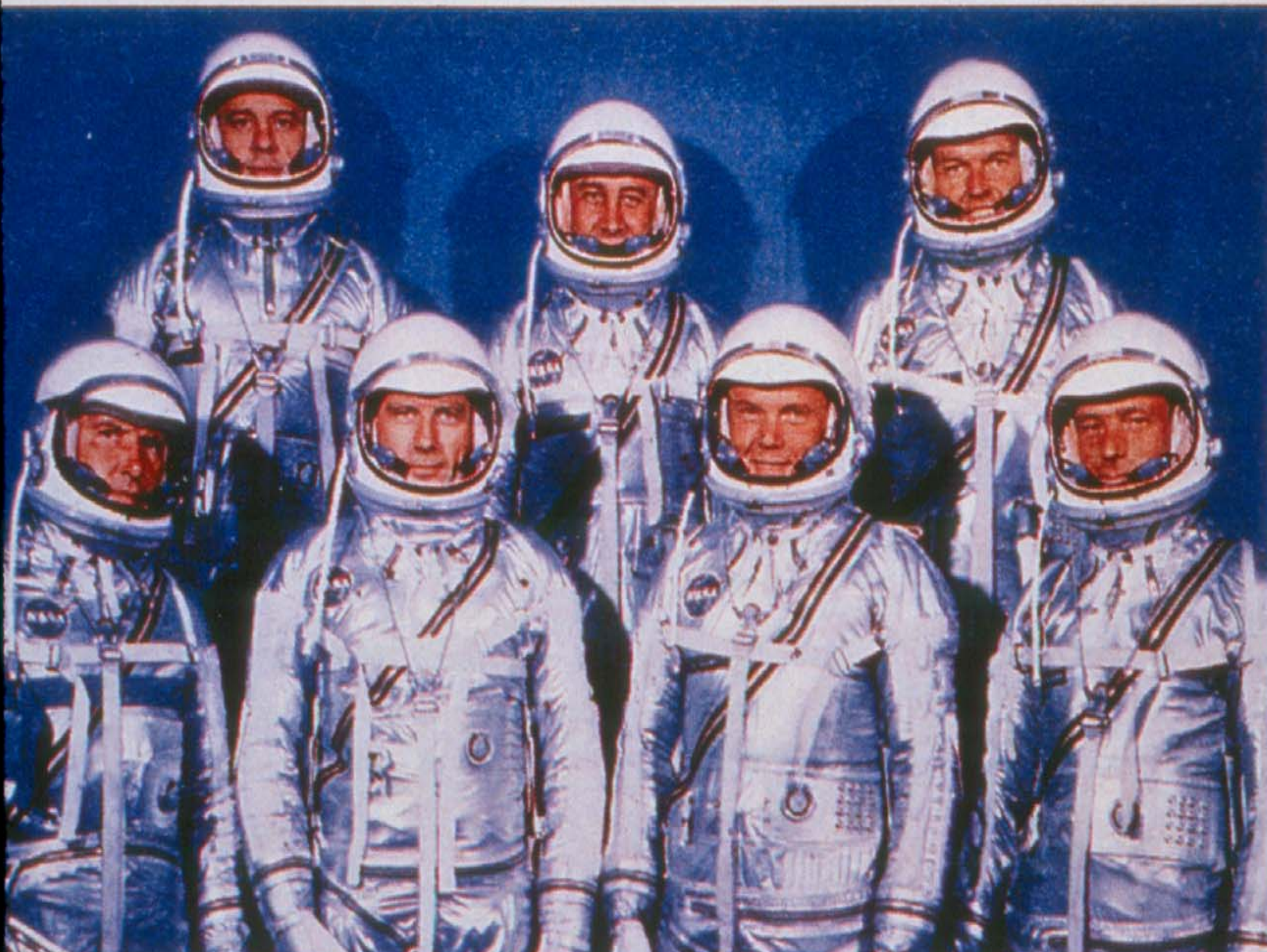




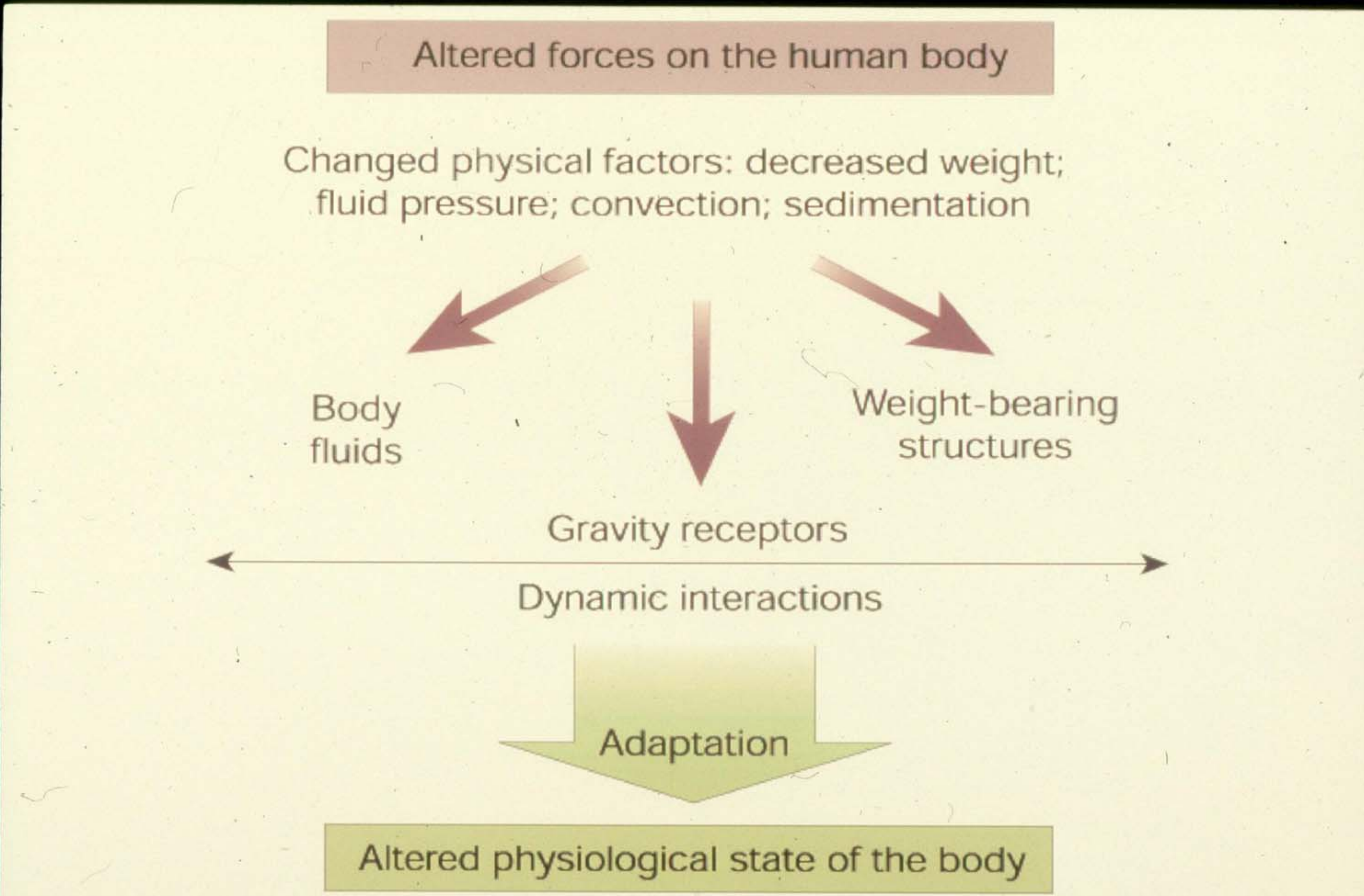


Gravity is not just a good idea

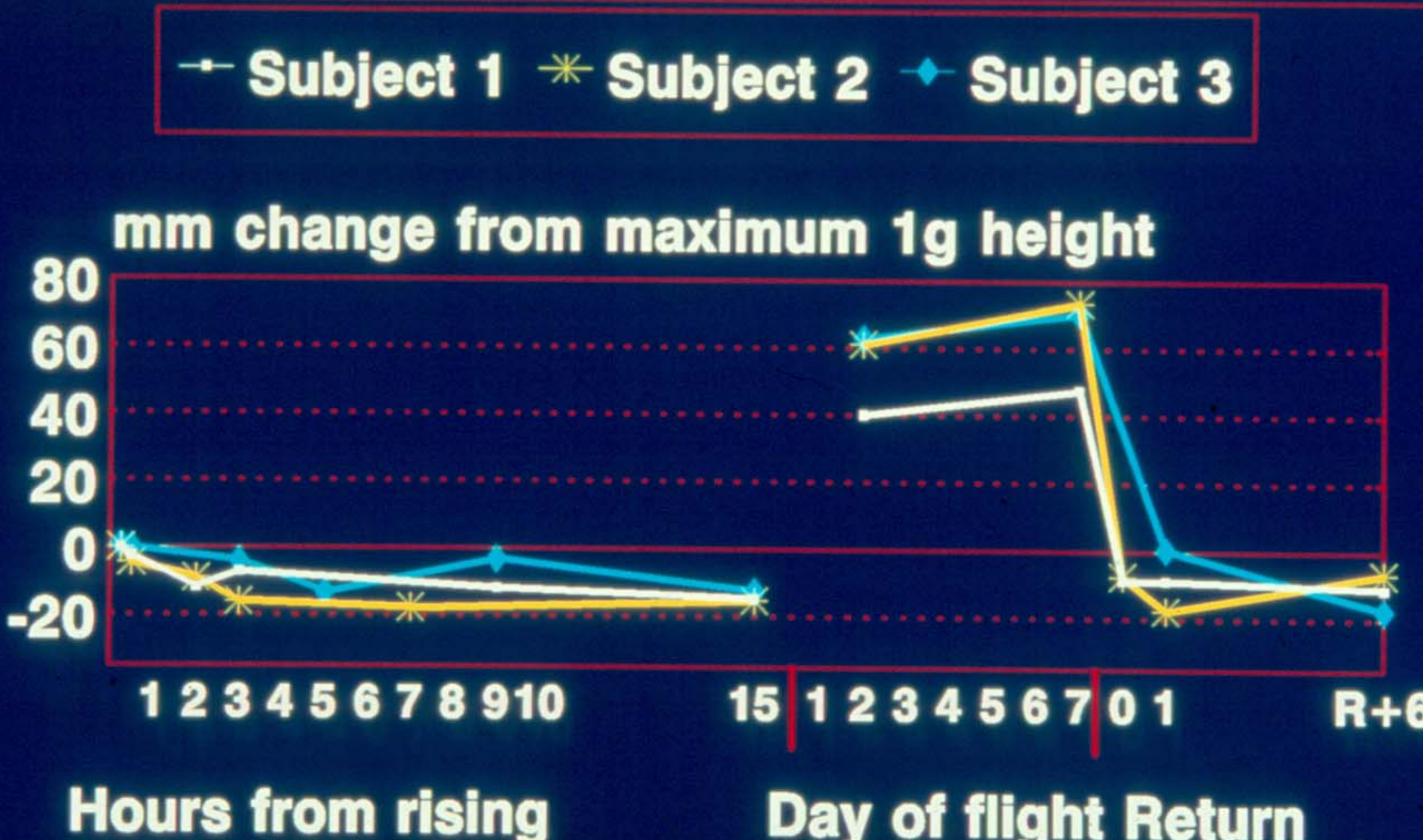
It's the LAW

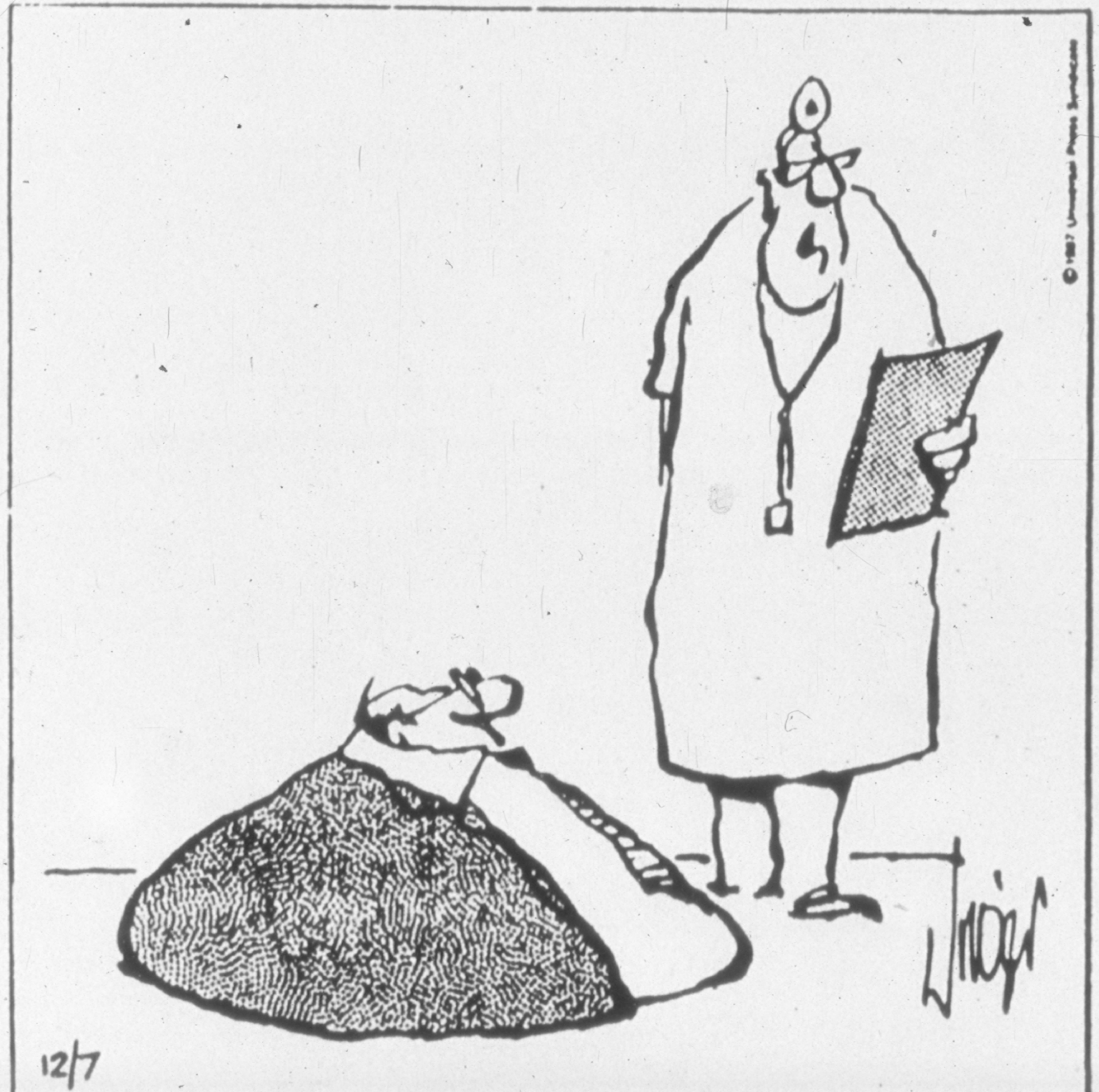


The original Mercury astronauts, selected in 1959. Front, l-r: Walter M. Schirra Jr., Donald "Deke" Slayton, John H. Glenn Jr. and M. Scott Carpenter. Rear, l-r: Alan B. Shepard Jr., Virgil I. "Gus" Grissom and L. Gordon Cooper Jr.

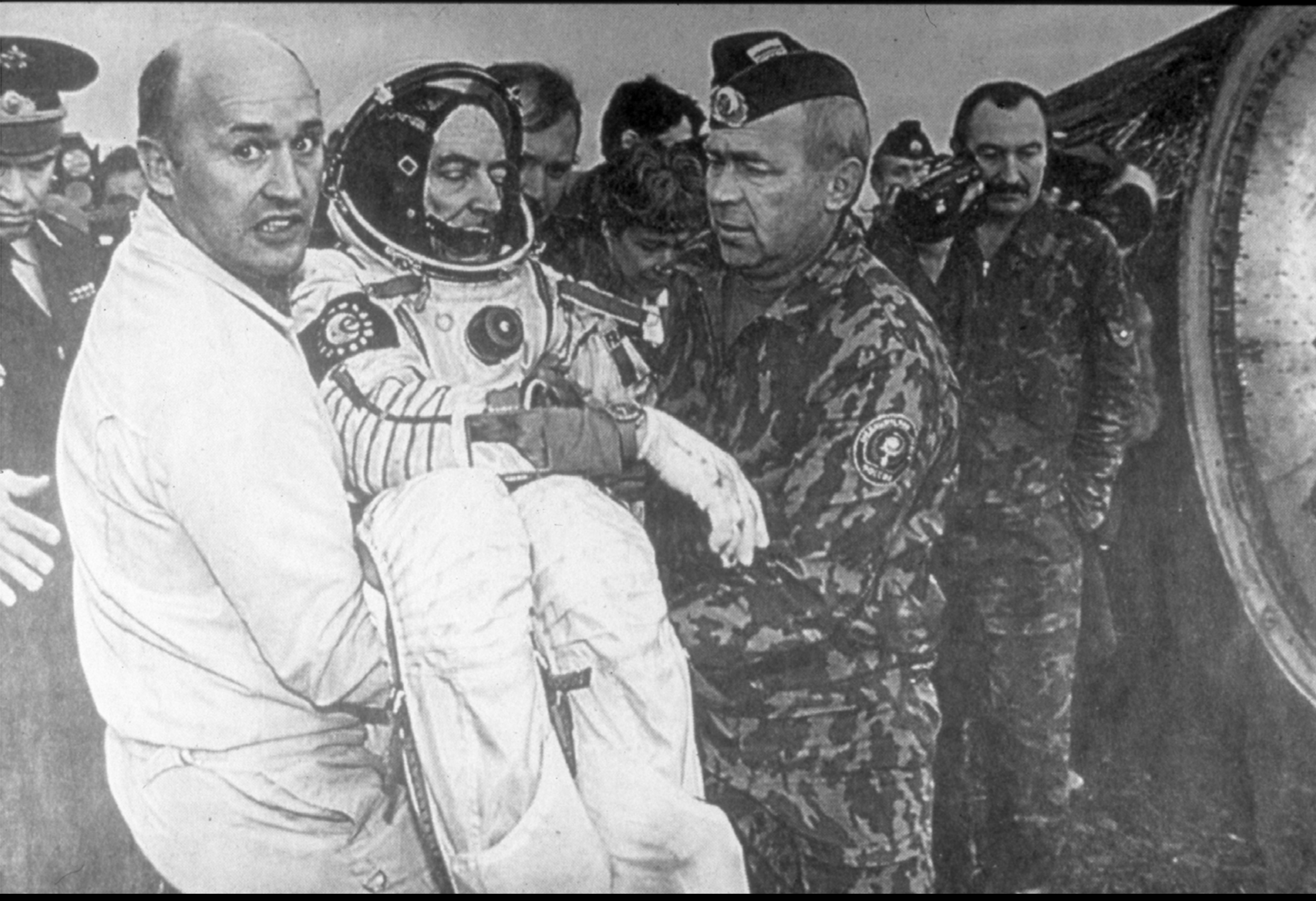

Altered forces on the human body
Changed physical factors: decreased weight; fluid pressure; convection; sedimentation
Body fluids
Weight-bearing structures
Gravity receptors
Dynamic interactions
Adaptation
Altered physiological state of the body

# IML-1
## Photographically Measured Height Data

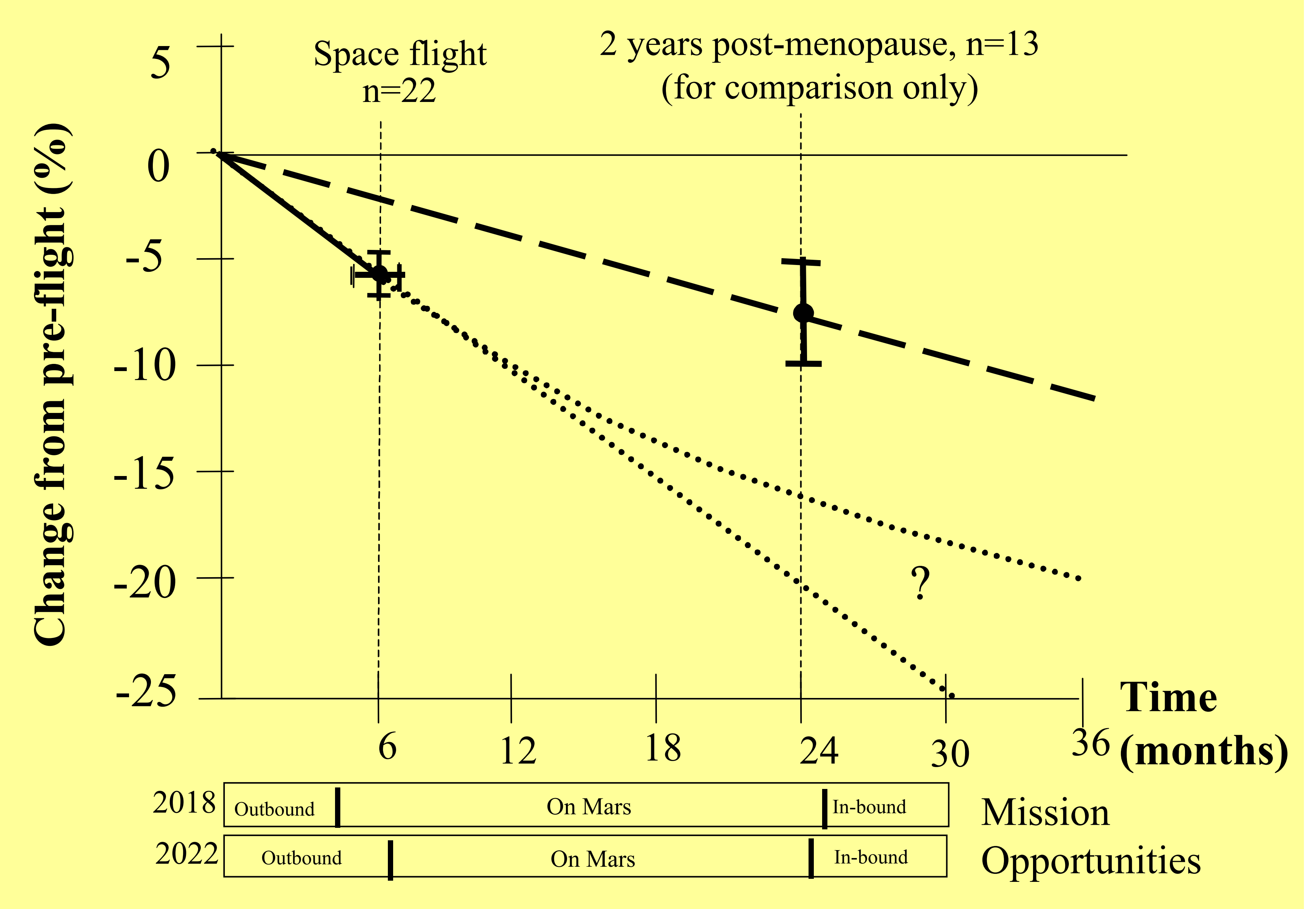




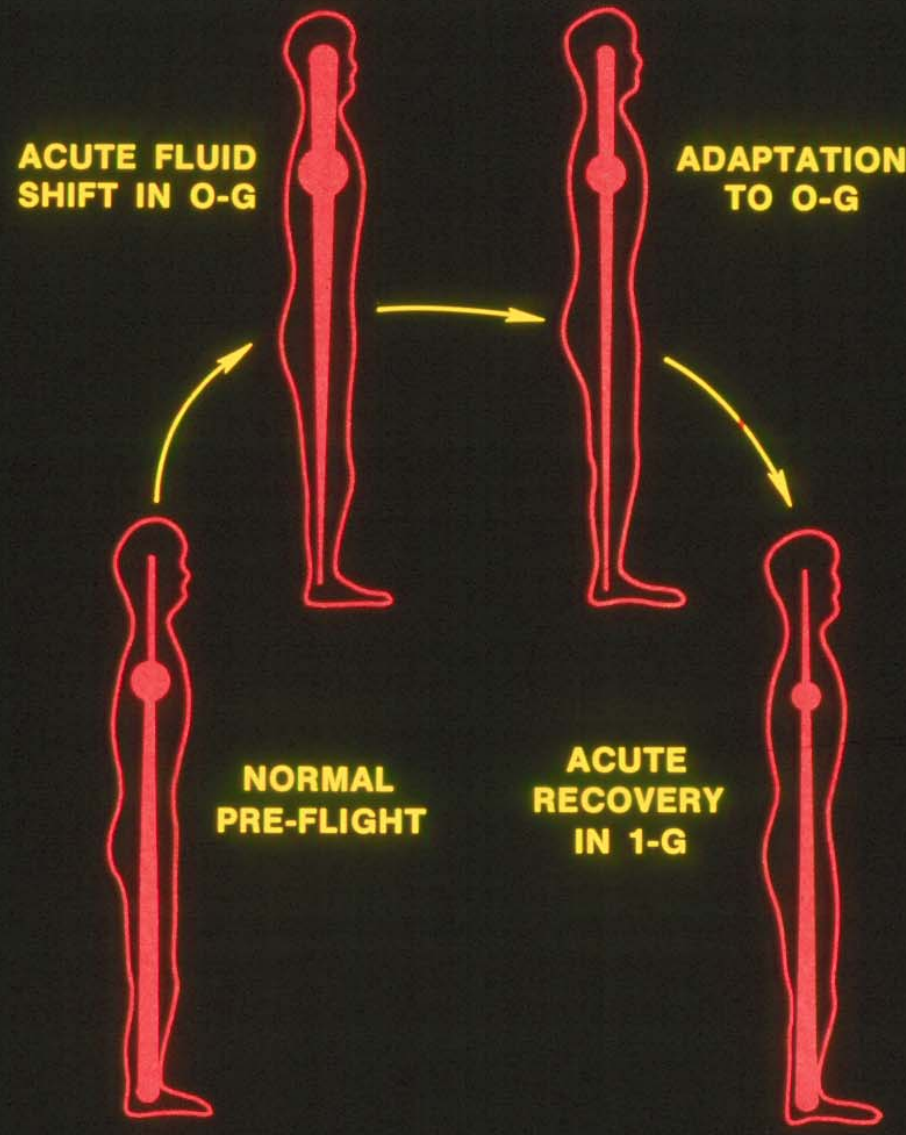
"Your skeletal structure can't support your weight anymore."

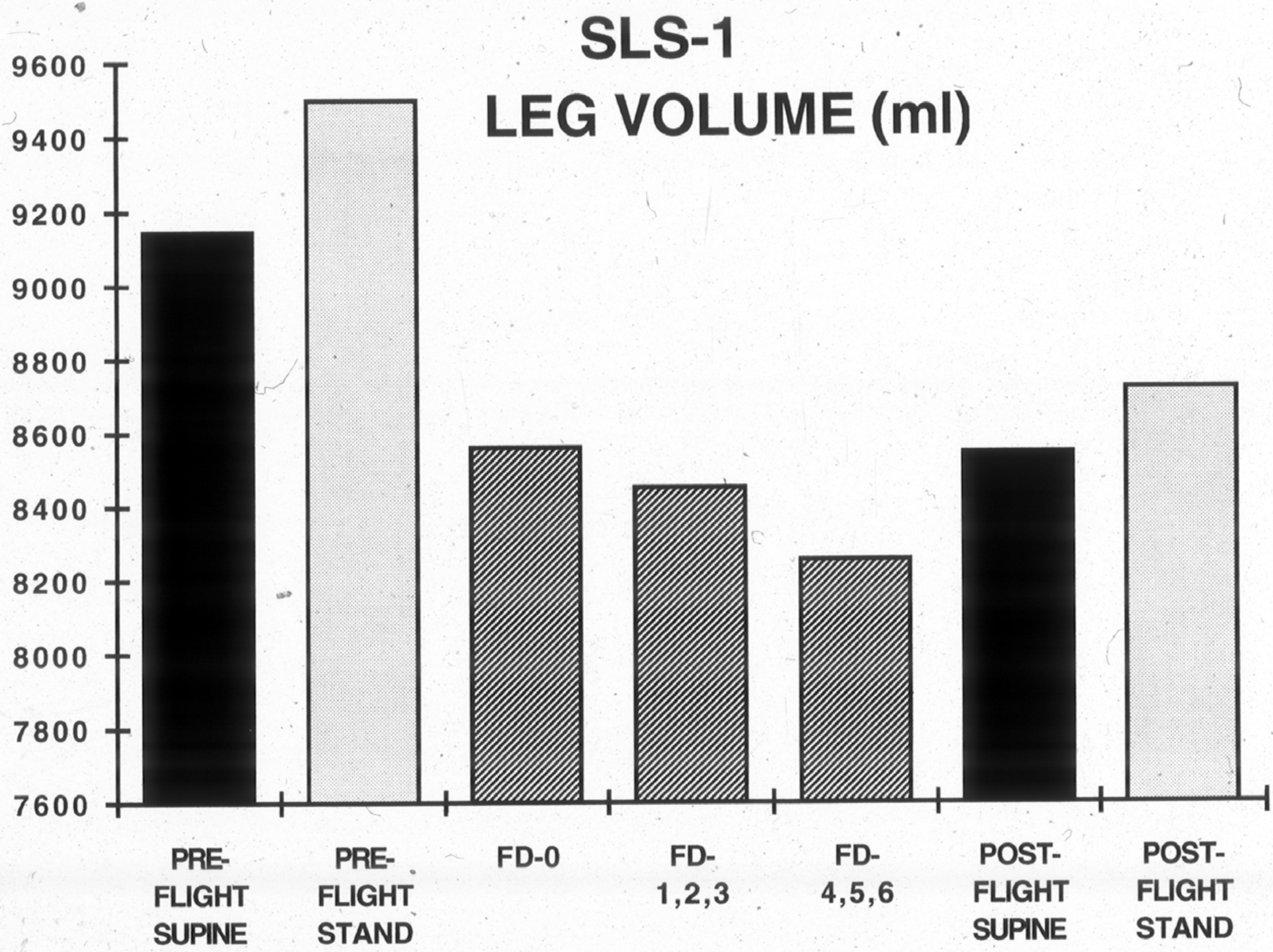


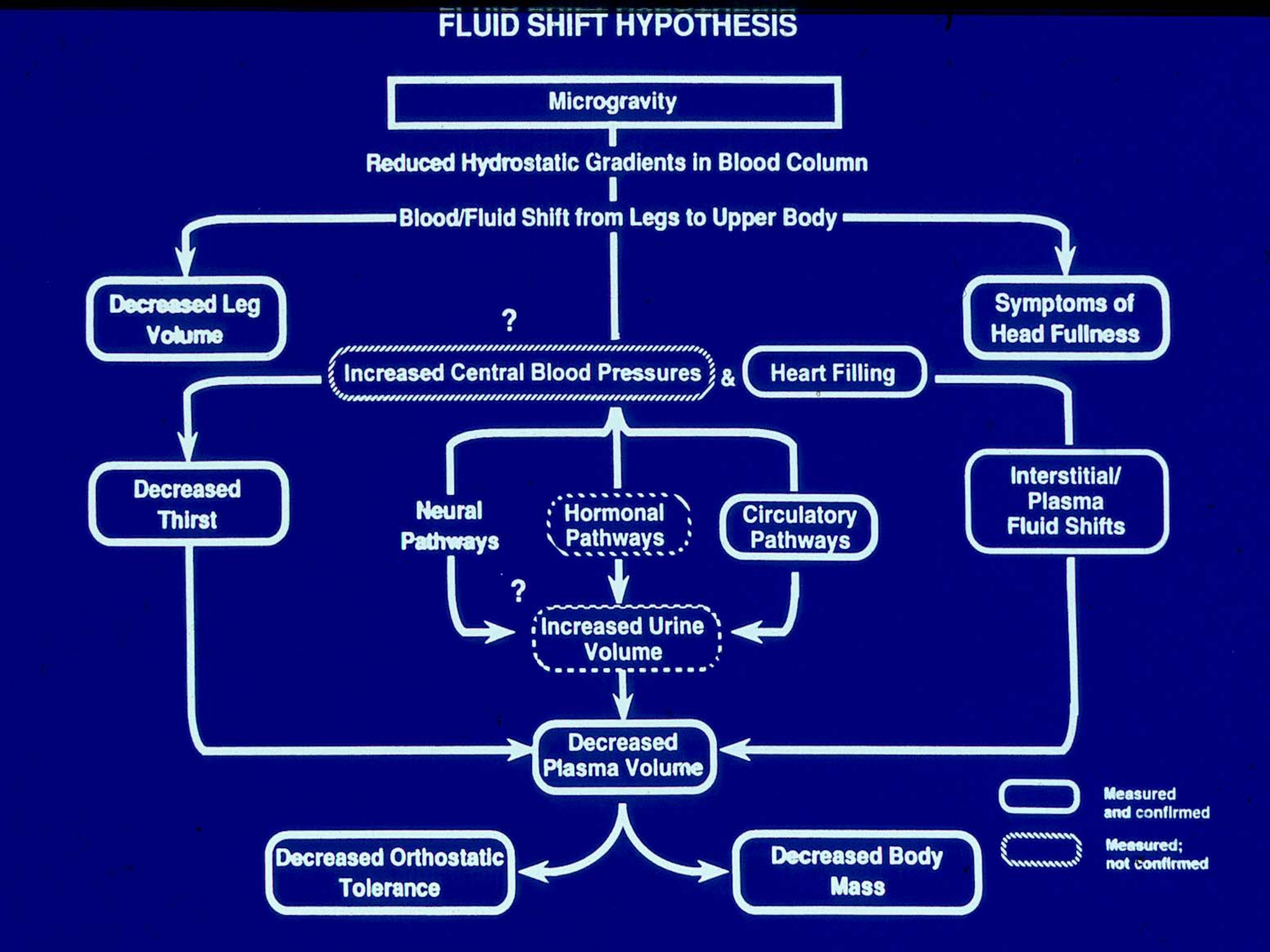
# Bone Integrity in Weightlessness

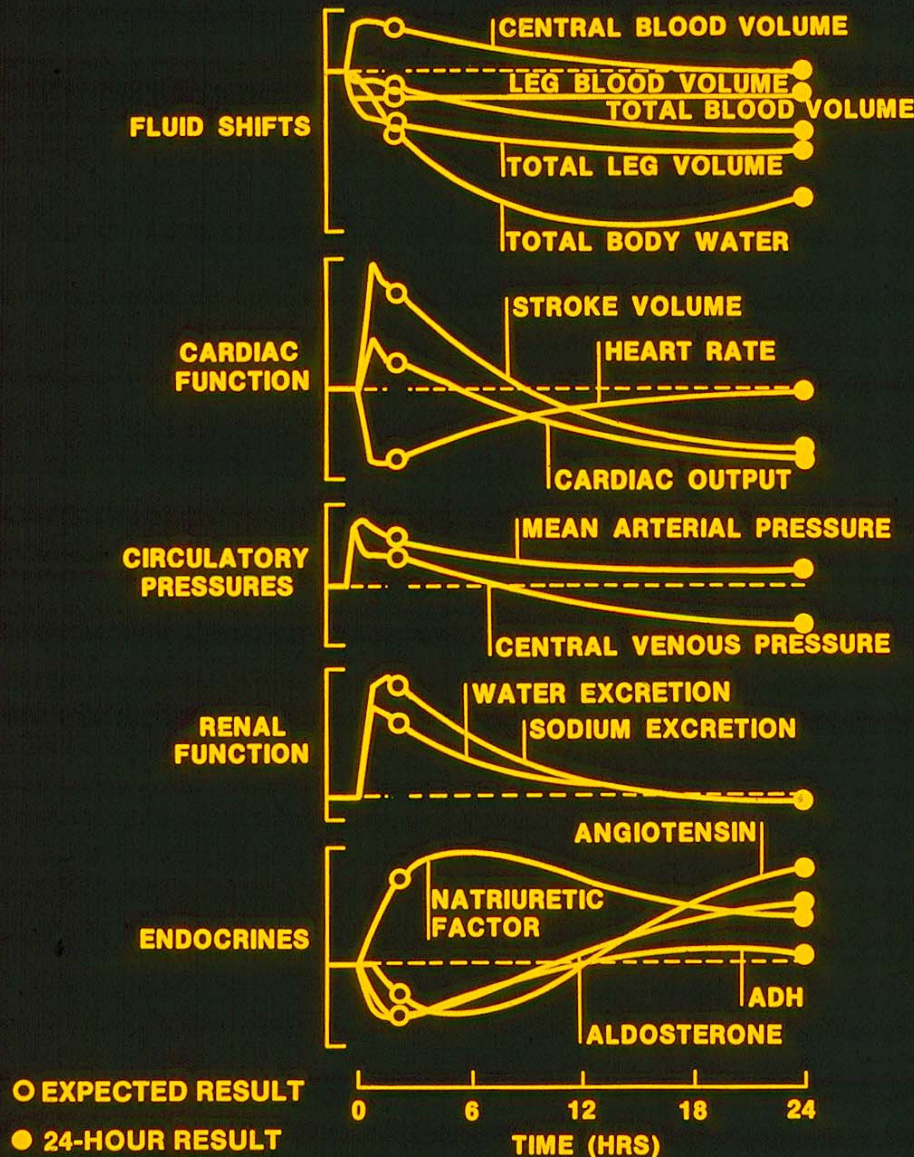


# FLUID SHIFT RESPONSE TO WEIGHTLESS EXPOSURE



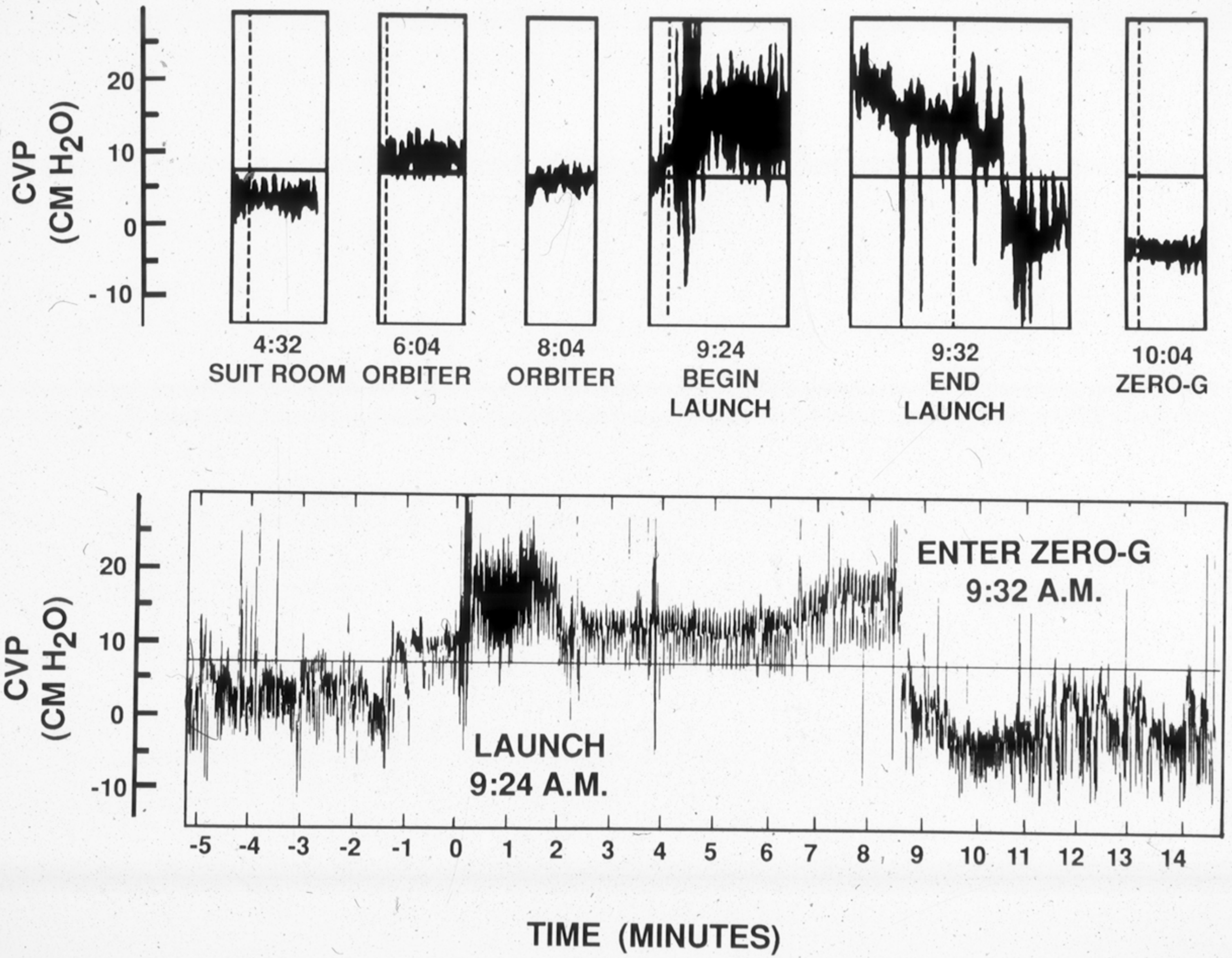

SLS-1
LEG VOLUME (ml)
9600
9400
9200
9000
8800
8600
8400
8200
8000
7800
7600
PRE-FLIGHT SUPINE
PRE-FLIGHT STAND
FD-0
FD-1,2,3
FD-4,5,6
POST-FLIGHT SUPINE
POST-FLIGHT STAND


FLUID SHIFT HYPOTHESIS
Microgravity
Reduced Hydrostatic Gradients in Blood Column
Blood/Fluid Shift from Legs to Upper Body
Decreased Leg Volume
Symptoms of Head Fullness
?
Increased Central Blood Pressures
&
Heart Filling
Decreased Thirst
Neural Pathways
Hormonal Pathways
Circulatory Pathways
Interstitial/ Plasma Fluid Shifts
?
Increased Urine Volume
Decreased Plasma Volume
Measured and confirmed
Measured; not confirmed
Decreased Orthostatic Tolerance
Decreased Body Mass



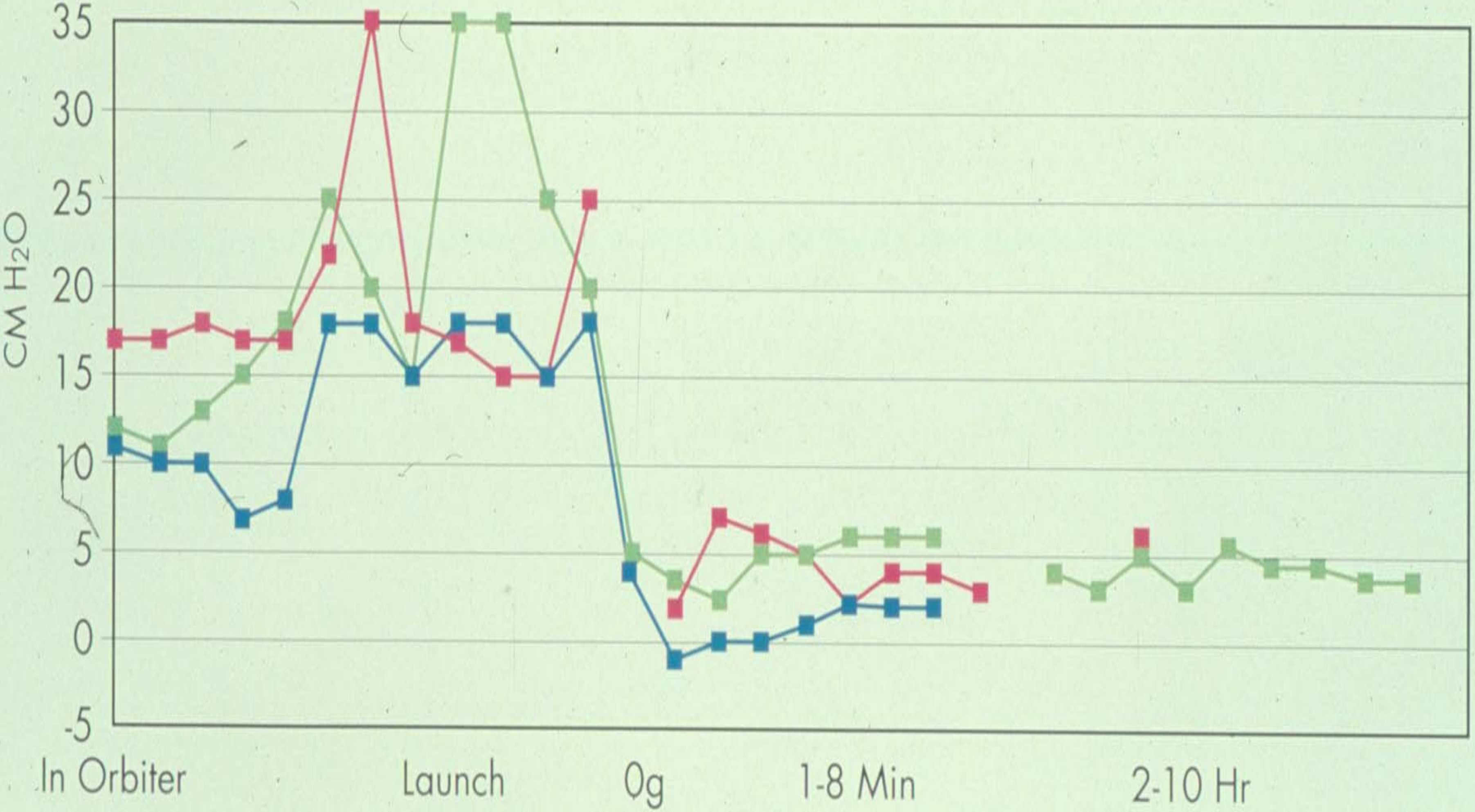

SIMULATION OF HEAD DOWN TILT (-6°)

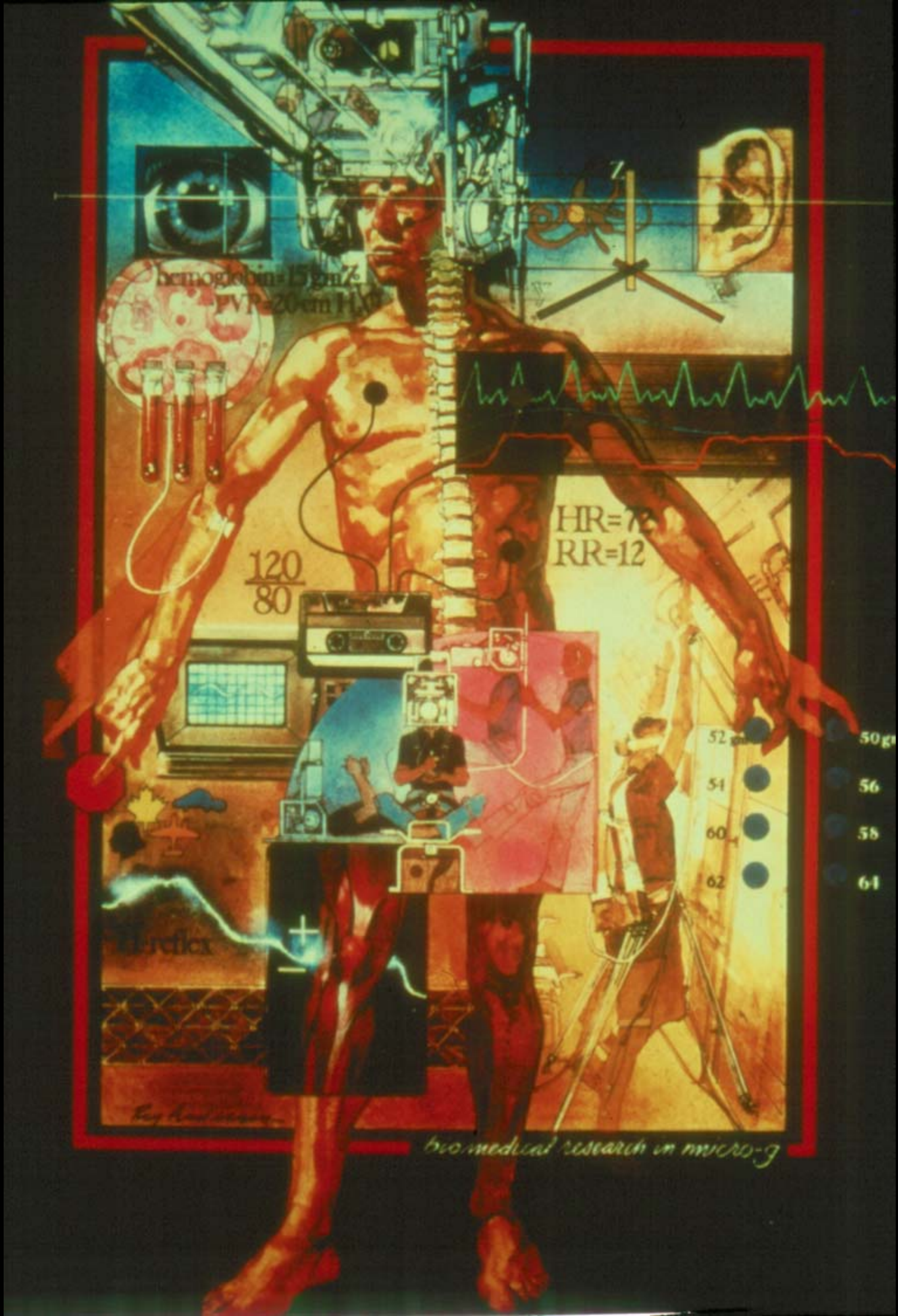

STS
40
304
40 STS MASH UNIT



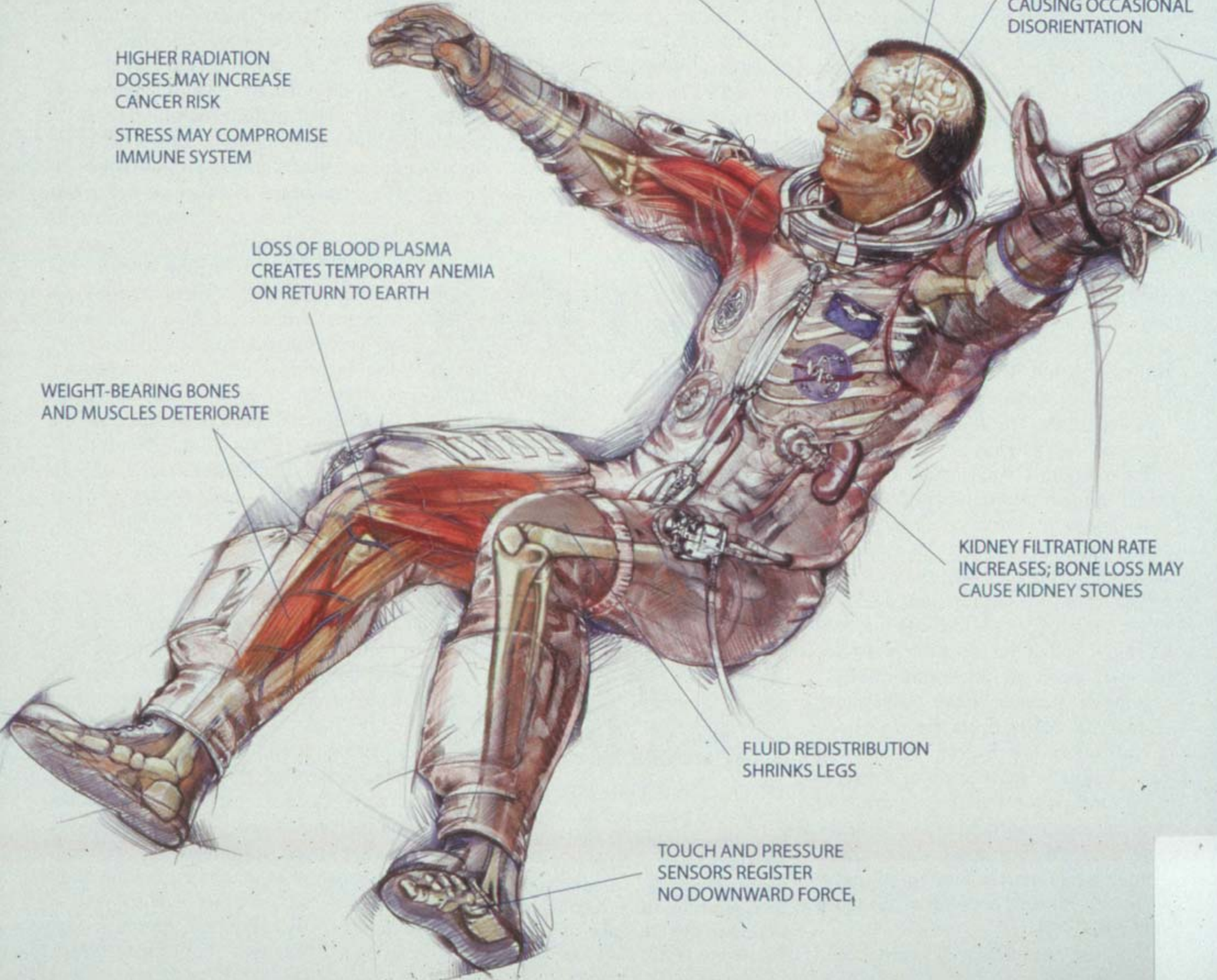
CVP
(CM $H_2O$)
20
10
0
- 10
4:32
SUIT ROOM
6:04
ORBITER
8:04
ORBITER
9:24
BEGIN
LAUNCH
9:32
END
LAUNCH
10:04
ZERO-G
CVP
(CM $H_2O$)
20
10
0
-10
ENTER ZERO-G
9:32 A.M.
LAUNCH
9:24 A.M.
-5
-4
-3
-2
-1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
TIME (MINUTES)

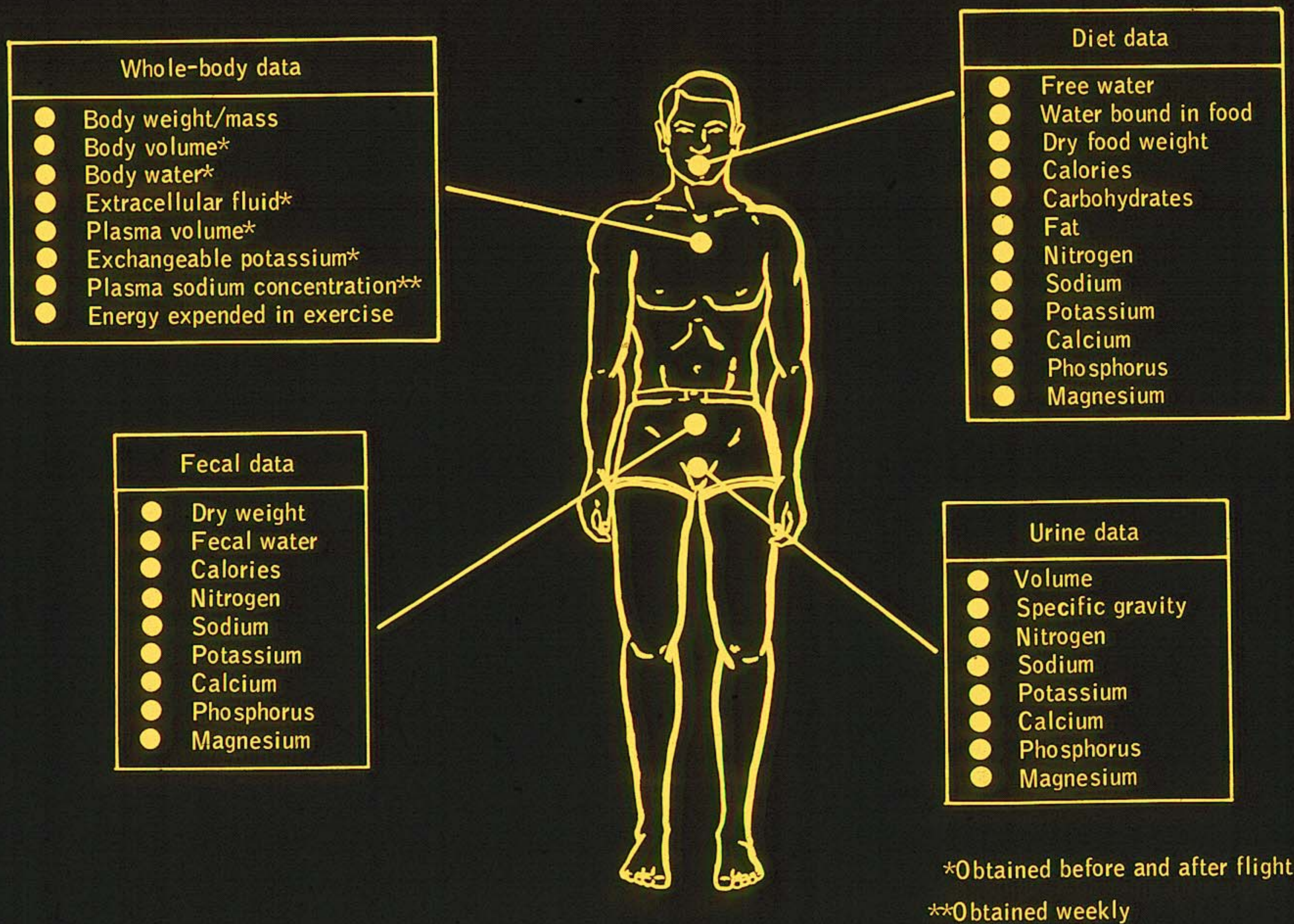
# Central Venous Pressure




HR=72
RR=12
120
80
52
54
60
62
50
56
58
64
biomedical research in micro-g

# The Effects of Space Travel on the Body






METABOLIC DATA FROM SKYLAB

# The Environment for Creating the Whole-body Algorithm

- Physiological deconditioning and dysfunction in astronauts returning from space
- Changes are highly dynamic and may lead to a new steady-state
- Changes lend themselves to interdisciplinary analysis and multi-system models
- A very large number of measurements were planned on Skylab. How do we integrate this data? How do we systematically keep track of all the hypotheses (and their implications) that might explain the data?

**Can a group of subsystem models and an integrated model simulate the human responses to space flight and assist in analyzing the Skylab data?**

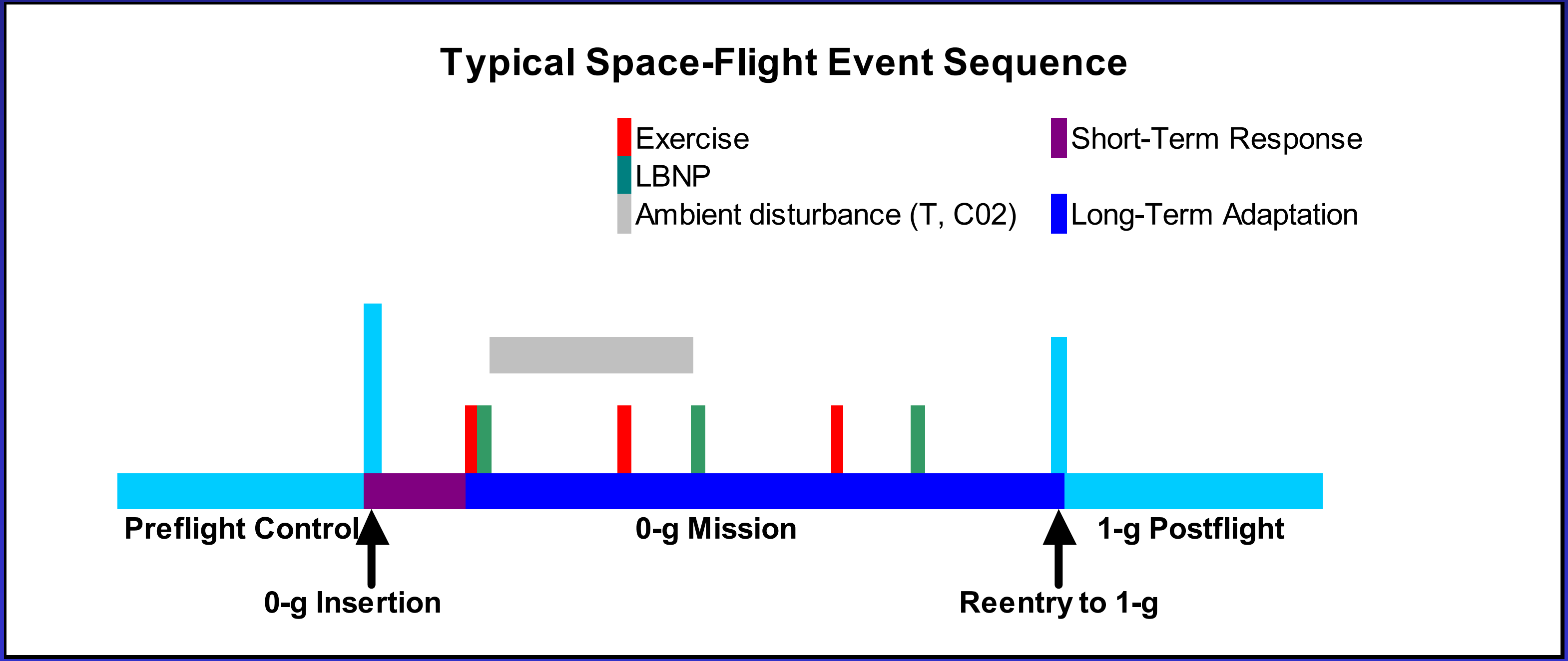
# Whole-Body Algorithm: Objectives

A) To provide a tool for evaluating hypotheses related to physiological adaptation to space flight

| | Principal Observations |
|---|---|
| Fluid-Electrolyte Regulation | • Headward fluid shifts<br>• Body mass decreases<br>• Loss of body fluids and electrolytes<br>• Dehydration and thirst |
| | |
| Blood Regulation | • Decreased red blood cell mass |
| | |
| Cardiovascular Regulation | • Orthostatic intolerance<br>• Reduced exercise capacity |

# Whole-Body Algorithm: Objectives

B) To provide a realistic end-to-end simulation of the major physiological events and biomedical tests of the Skylab mission



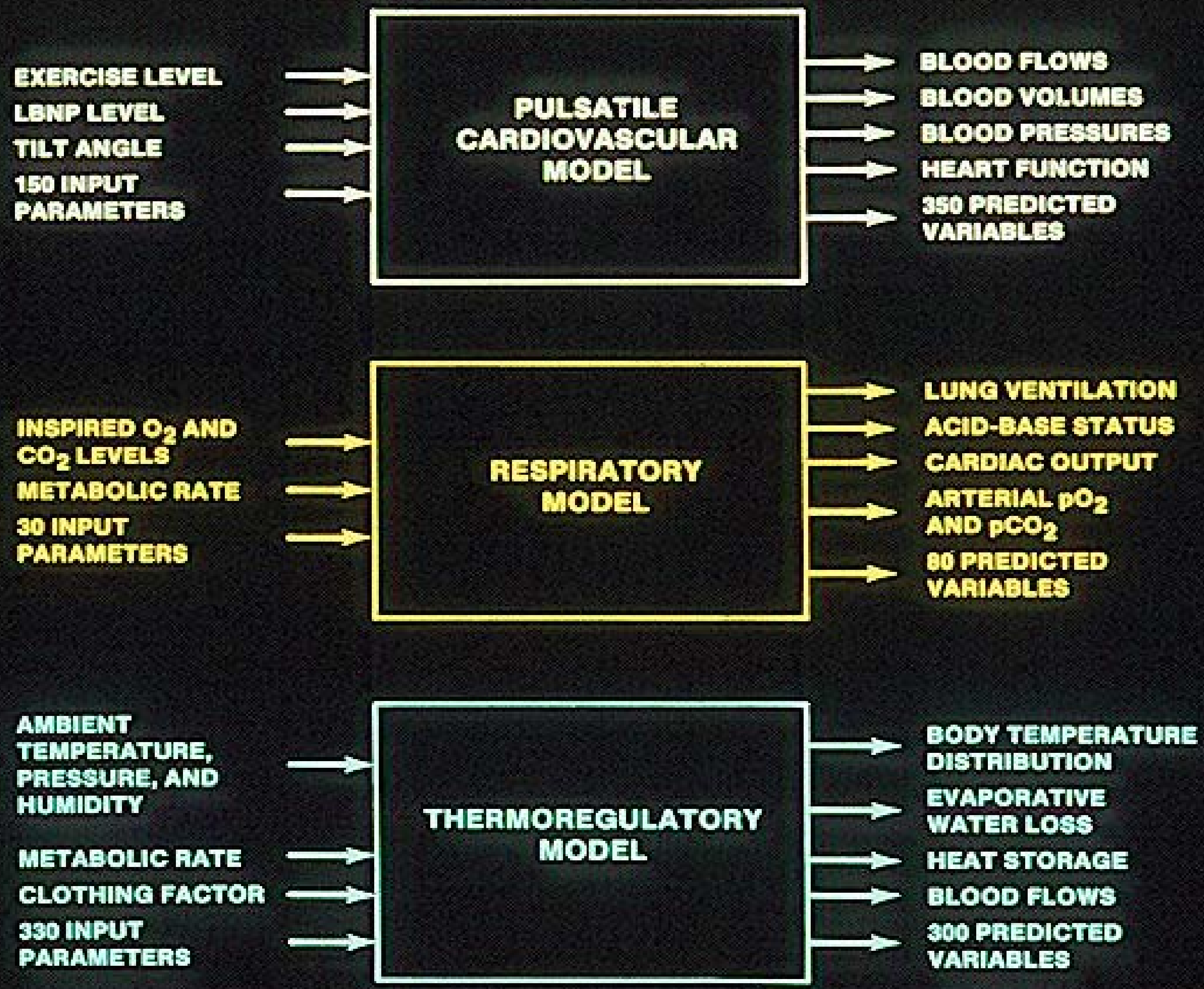
# Whole-body Algorithm: Design Requirements

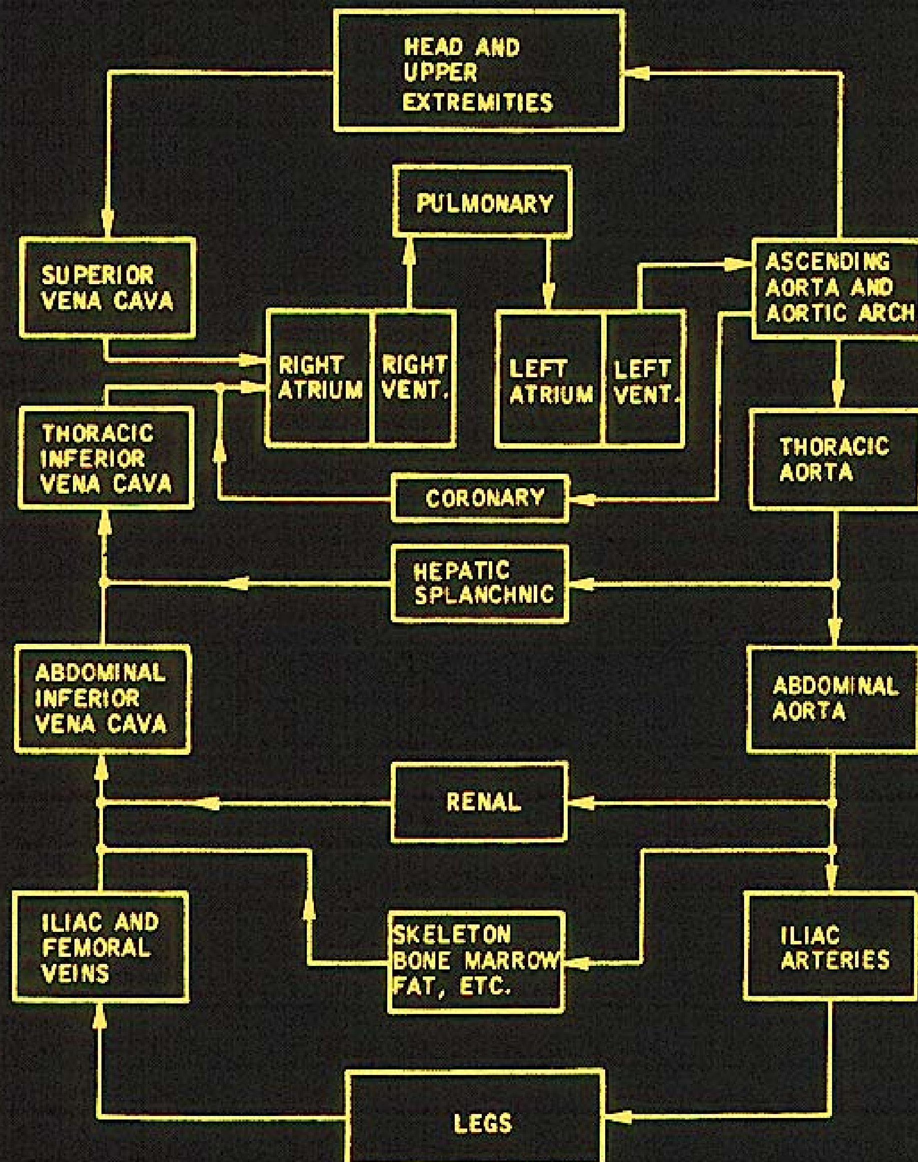
- Should include representations of the cardiovascular, respiratory, thermoregulatory, hematological, and fluid-electrolyte systems
- Models should be deterministic, mechanistic
- Dynamic capability to simulate both acute and long-term changes
- Specifically validated to simulate specific stress experiments used to evaluate the space-flight adaptation process

  -- LBNP --1-g tilt -- Supine and Erect bicycle ergometry -- Bed Rest

- Capability to simulate the environmental stresses which may influence the results of these experiments (temperature, humidity, $PP0_{2,}$, $PPCO_2$)
- Should include an automated database system of ground-based and Skylab measurements for validating and testing the models.

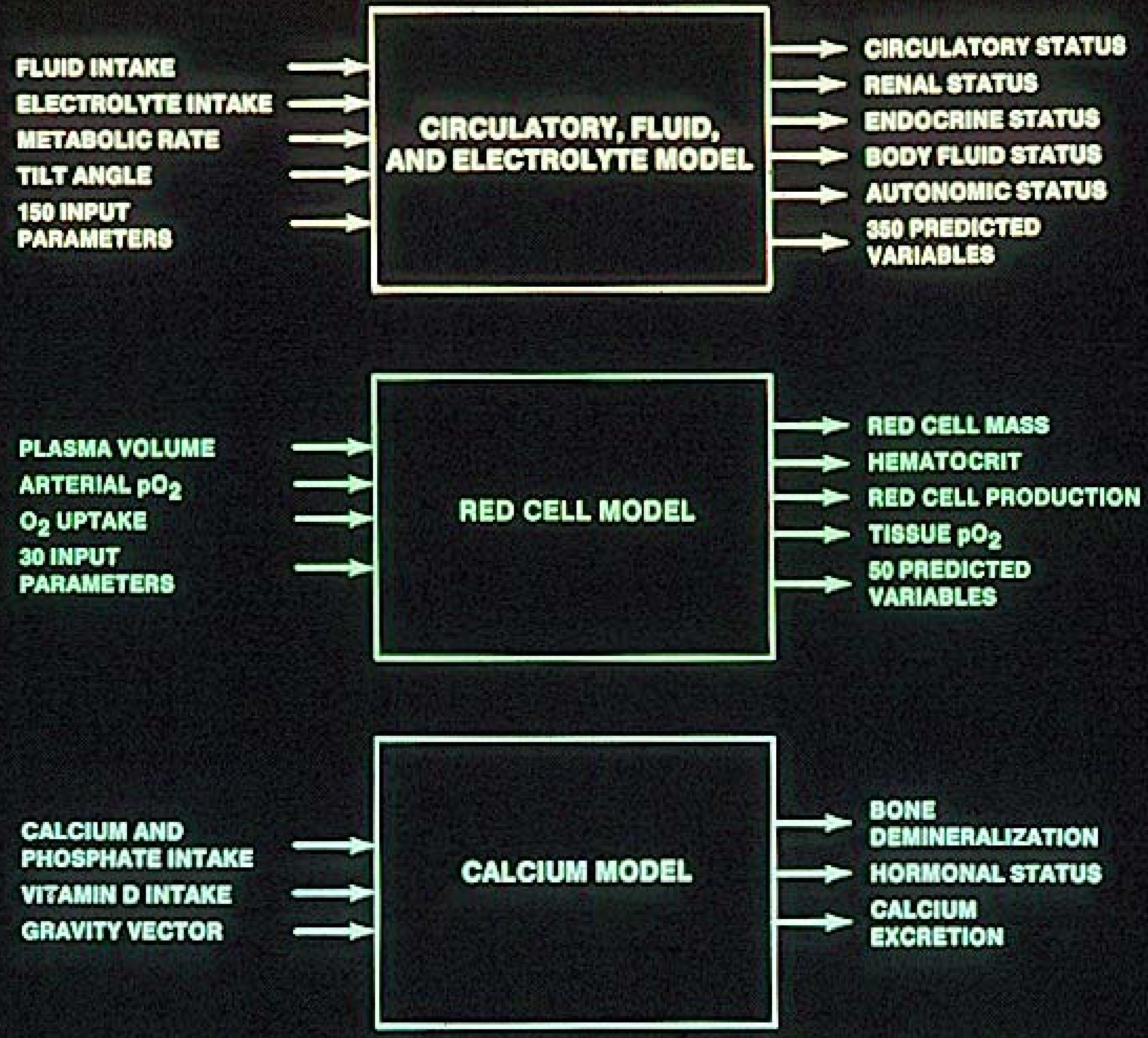
# MODELS FOR SIMULATING SHORT-TERM EVENTS

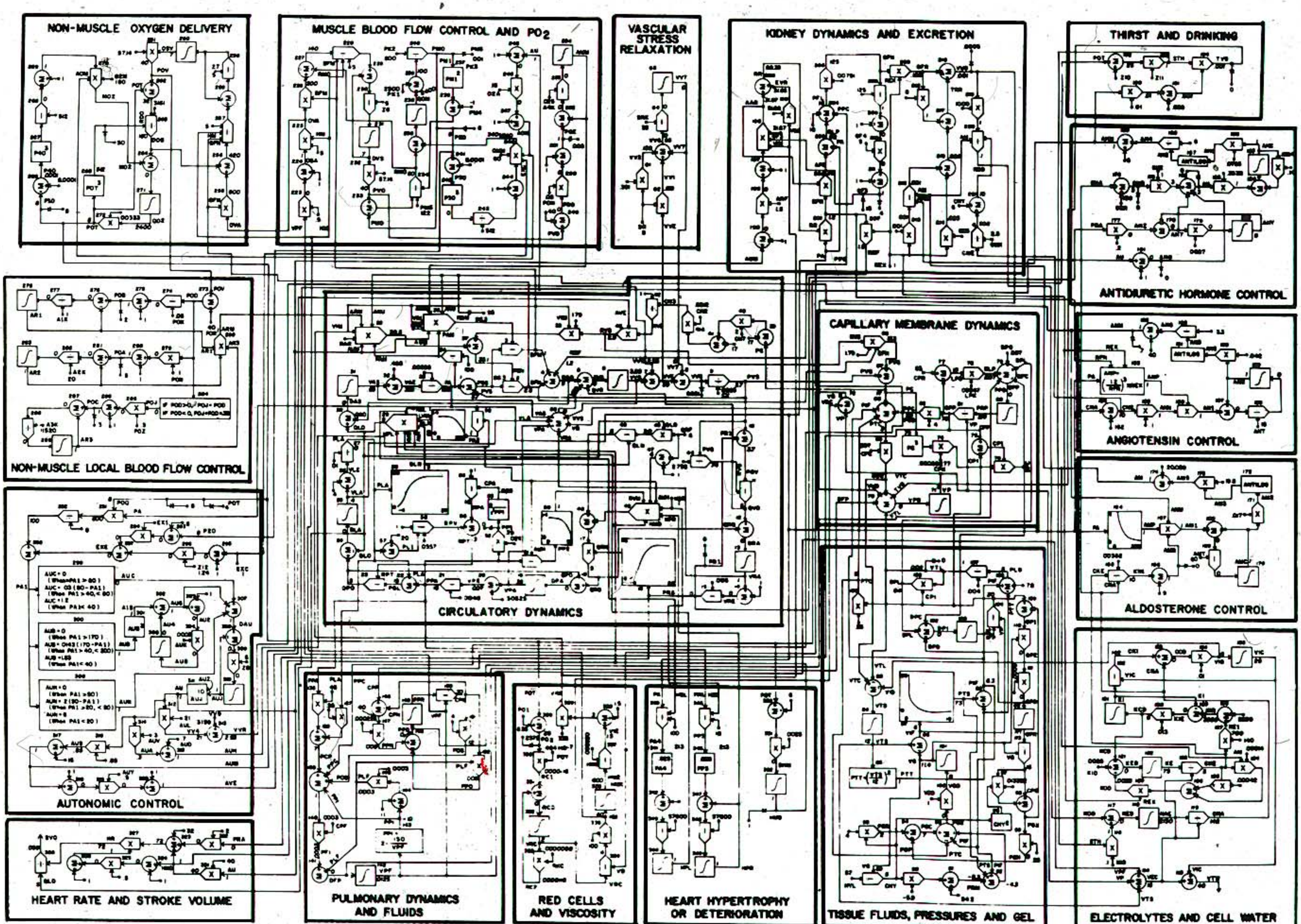




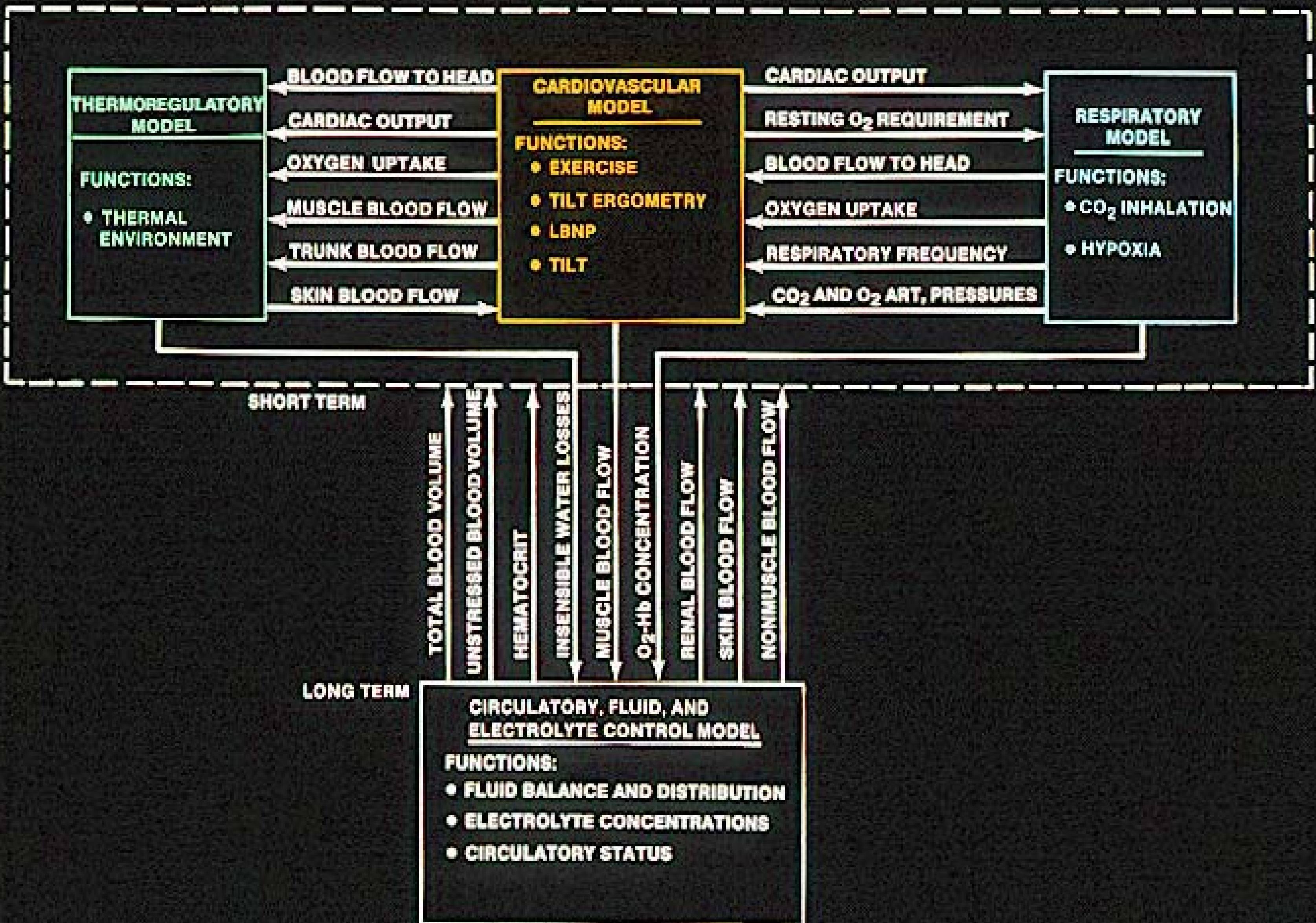

CIRCULATORY MODEL BLOCK DIAGRAM

# MODELS FOR SIMULATING LONG-TERM EVENTS

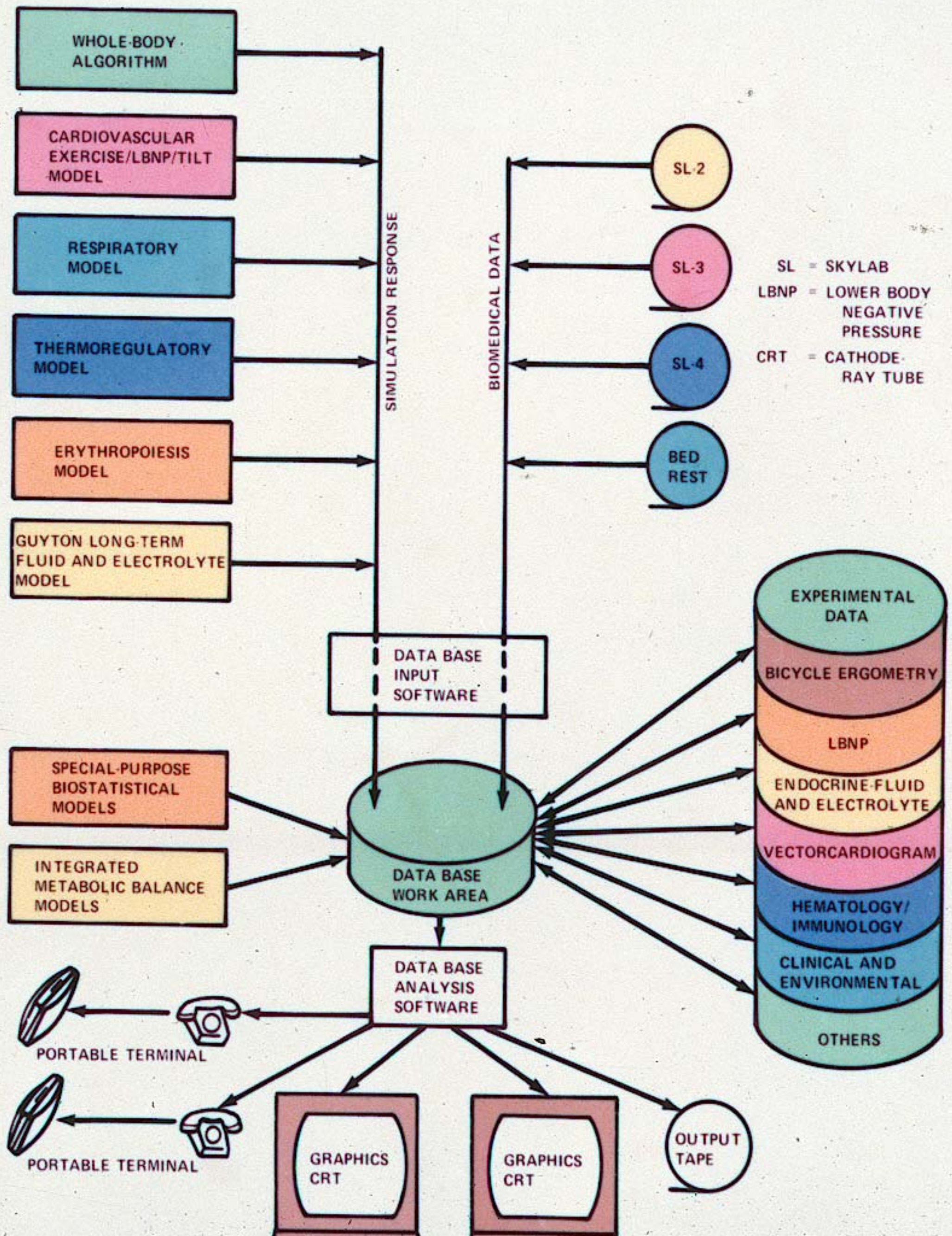



NON-MUSCLE OXYGEN DELIVERY
MUSCLE BLOOD FLOW CONTROL AND PO2
VASCULAR STRESS RELAXATION
KIDNEY DYNAMICS AND EXCRETION
THIRST AND DRINKING
ANTIDIURETIC HORMONE CONTROL
NON-MUSCLE LOCAL BLOOD FLOW CONTROL
CAPILLARY MEMBRANE DYNAMICS
ANGIOTENSIN CONTROL
CIRCULATORY DYNAMICS
ALDOSTERONE CONTROL
AUTONOMIC CONTROL
HEART RATE AND STROKE VOLUME
PULMONARY DYNAMICS AND FLUIDS
RED CELLS AND VISCOSITY
HEART HYPERTROPHY OR DETERIORATION
TISSUE FLUIDS, PRESSURES AND GEL
ELECTROLYTES AND CELL WATER

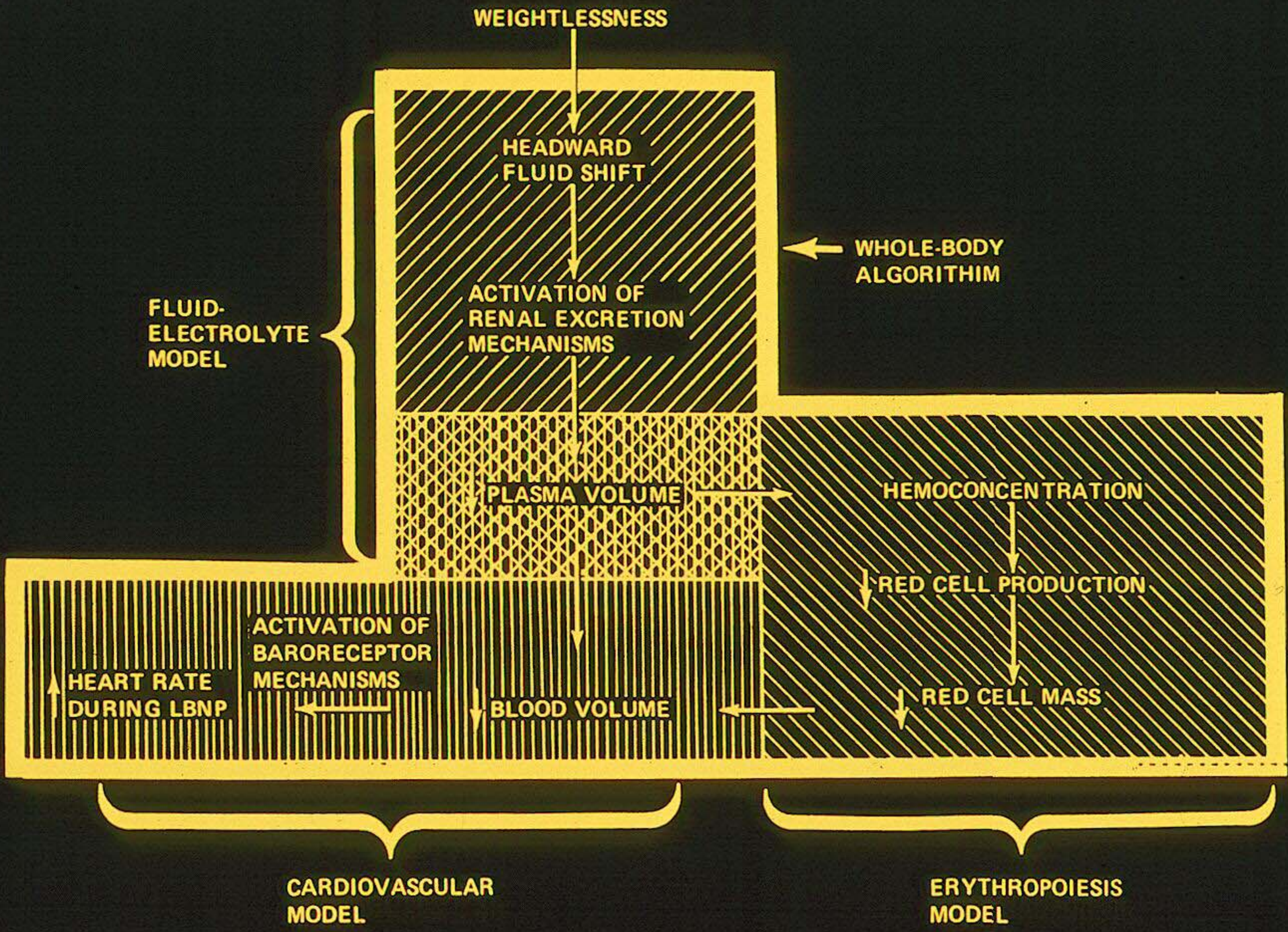
# WHOLE-BODY ALGORITHM



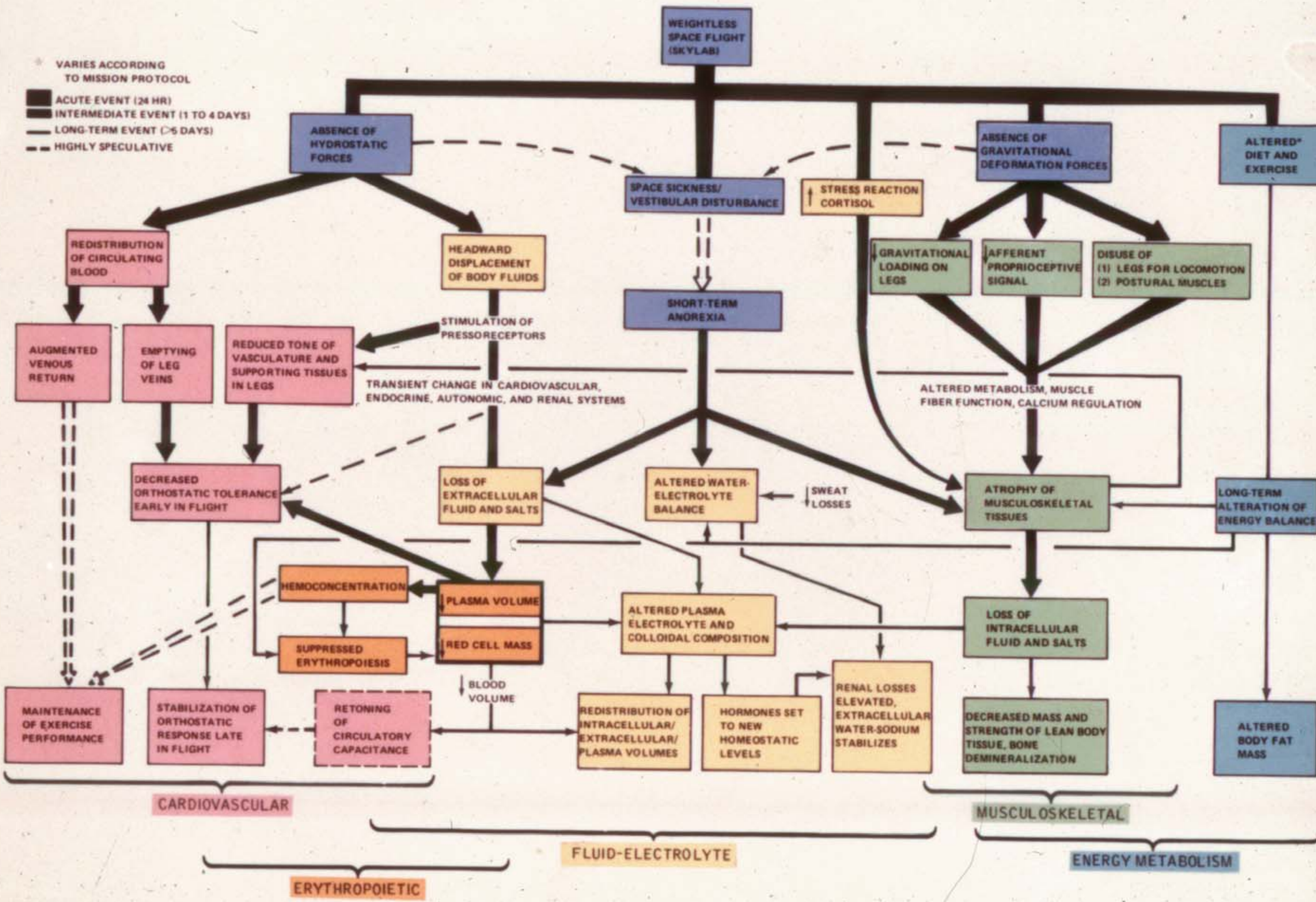
# SKYLAB INTEGRATED MEDICAL DATA ANALYSIS SYSTEM



# USE OF MODELS TO STUDY SPACEFLIGHT PHYSIOLOGY



# INTEGRATED HYPOTHESIS OF PHYSIOLOGICAL ADAPTATION TO PROLONGED SPACE FLIGHT



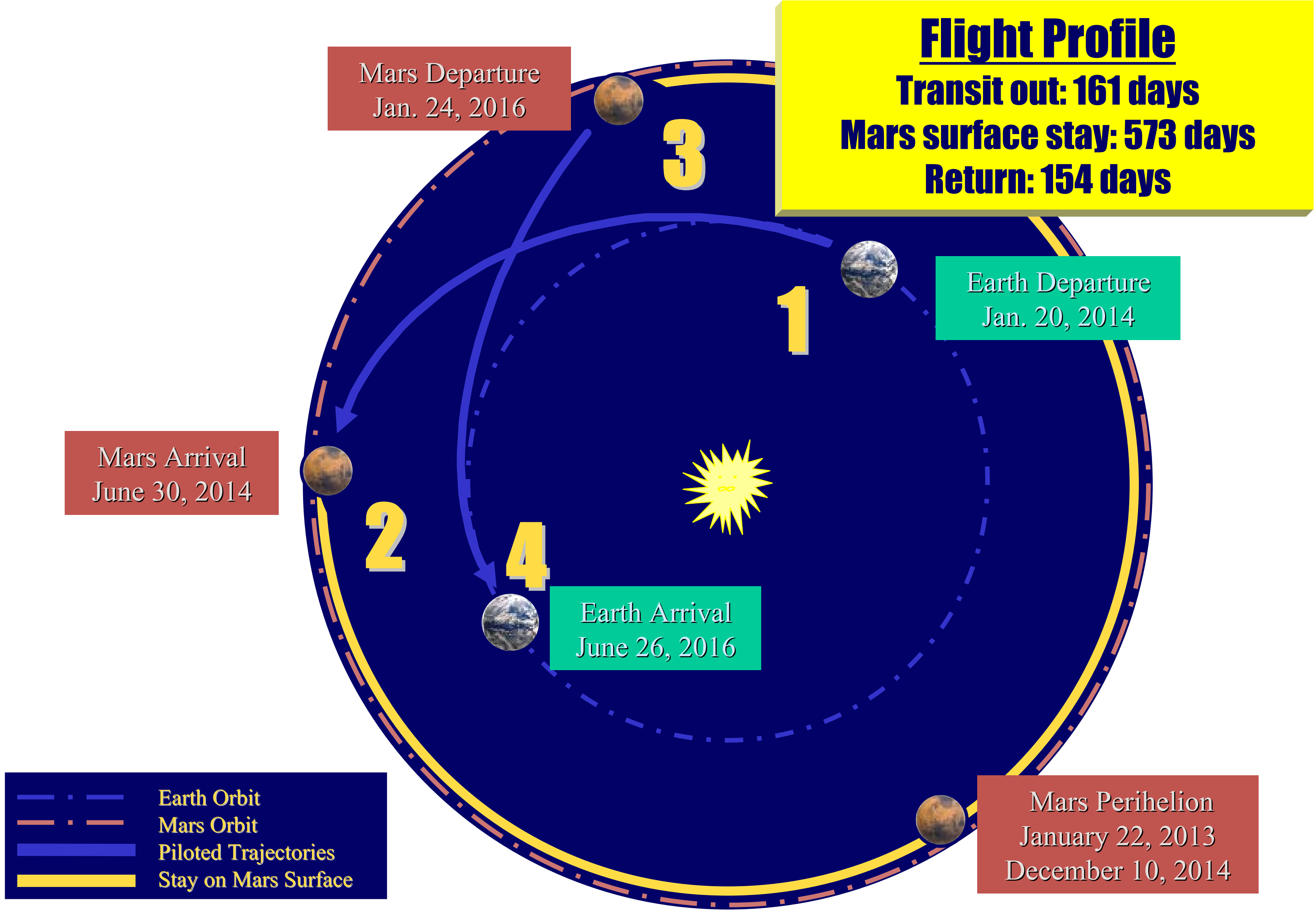
# Overall Contribution of WBA

- First time a physiological model of this scope was created
- Proven operational capability of end-to-end simulation of long-term adaptation of space flight accounting for short-term experiment and environmental stresses
- Models for simulating short-term events was a significant start on a multi-system (cardio-thermo-pulmonary) exercise model
- WBA provided a central repository for collecting hypotheses for a diverse group of physiological changes due to the microgravity environment

NATIONAL SPACE BIOMEDICAL RESEARCH INSTITUTE

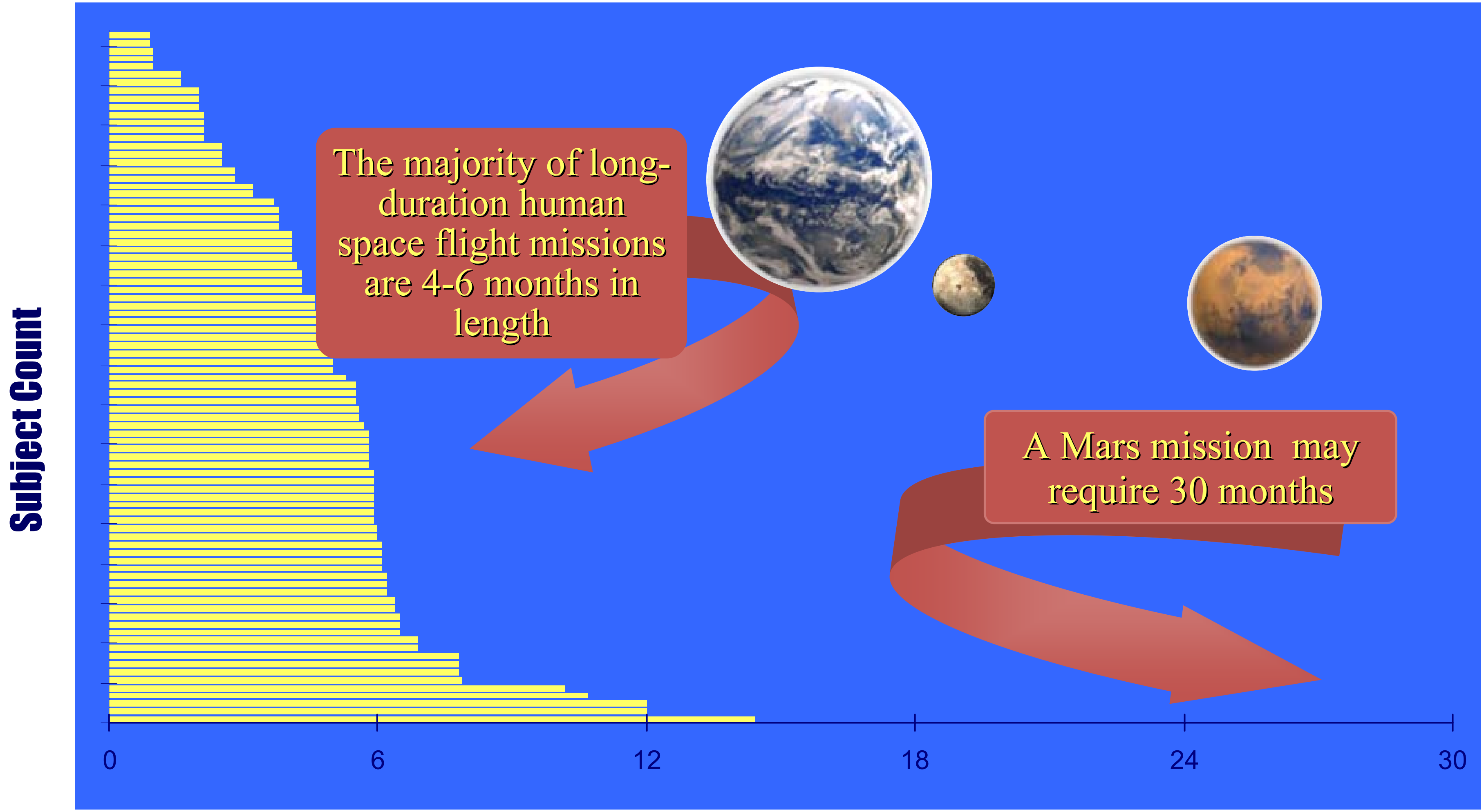
NSBRI

# 2014 Mars Design Reference Mission Scenario (typical)



# Human Space Flight Experience

## (Includes flights longer than 30 days as of January 1998)




**Flight Duration (months)**

# Impacts of Extended Weightlessness

Physical tolerance of stresses during aerobraking, landing, and launch phases, and strenuous surface activities

### Bone loss

- no documented end-point or adapted state
- countermeasures in work on ground but not yet flight tested

### Cardiovascular alterations

- pharmacological treatments for autonomic insufficiency

### Muscle atrophy

- resistive exercise under evaluation

### Neurovestibular adaptations

- vehicle modifications, including centrifuge
- may require auto-land capability

# Space Medicine Issues

## Reports of illness and injury during space flight

### Incidence Common (>50%)

- skin rash, irritation
- foreign body
- eye irritation, corneal abrasion
- headache, backache, congestion
- gastrointestinal disturbance
- cut, scrape, bruise
- musculoskeletal strain, sprain
- fatigue, sleep disturbance
- space motion sickness
- post-landing orthostatic intolerance
- post-landing neurovestibular symptoms

**Conceptualization of crew healthcare & exercise facilities**

### Incidence Uncertain

- infectious disease
- cardiac dysrhythmia, trauma, burn
- toxic exposure
- psychological stress, illness
- kidney stones
- pneumonitis
- urinary tract infection
- spinal disc disease
- unplanned radiation exposure

Data from R. Billica, Jan. 8, 1998

artwork from Constance Adams and Kris Kennedy for the JSC TransHab Team

# In Flight Medical Events STS-1 through STS-89

- 498 of 508 (98%) crew members reported medical events (excludes space motion sickness)
- 1867 separate events reported (1613 men, 254 women)
- 141 (7.6%) events due to injury

Data courtesy of NASA HQ: R Williams MD, NASA JSC: D Williams MD, S Pool MD, R Billica MD, T Marshburn MD

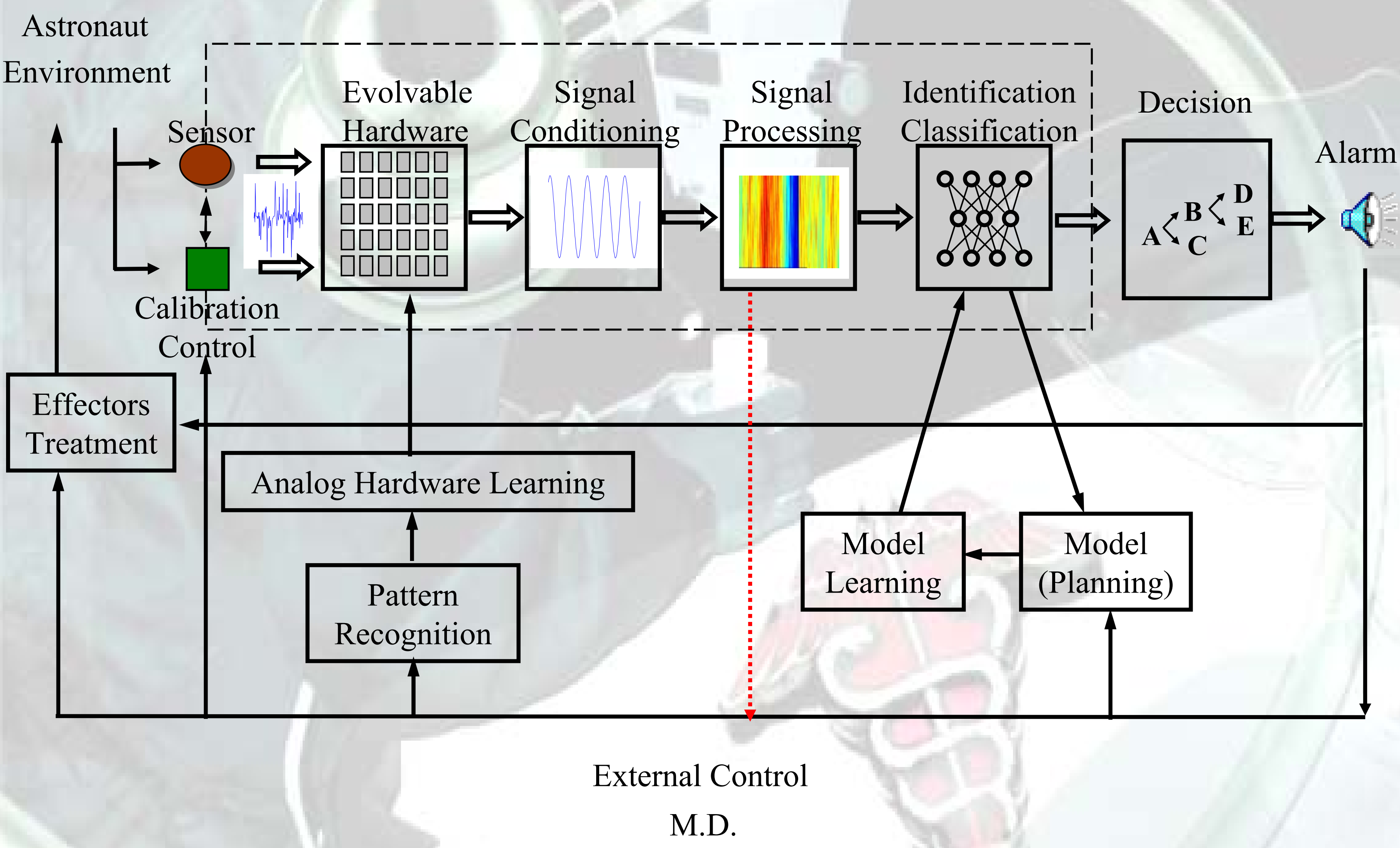
# Medical Risk

- Estimulated risk of <u>significant</u> event (= ER visit or hospitalization) on ISS = 1-3 events per annum

<u>Previous Experience</u>

- Two cosmonauts evacuated
- 44 med evacs in 10 yr. of Polaris fleet operations
- Antarctic experience with breast CA
- Increased risks for long space flight duration & older crew

# Prototypical Smart Medical System



# The Digital Human

# The Goal

An accurate simulation of the human body from molecules to cells, tissues, organ systems and the entire body.

# Applications:

- Aid research by tying together large amounts of information available about biological systems
  - -- gene expression
  - -- cell models
  - -- organ models
  - -- identify research needs

- Improve Education and Training at All Levels
  - -- Reduce the gap between classroom and practice
  - -- Make learning more efficient, more compelling
  - -- Reduce error rates through simulation-based training
  - -- Improve medical certification and accreditation (test more sophisticated skills)

# Applications (cont.)

- Assist biomimetics (computing, assembly)

- Improve the Practice of Medicine
  - Design and test medical devices and procedures
  - Tissue engineering
  - Artificial organs and prostheses
  - Help doctors and nurses communicate with patients
  - Provide a "body-double" for each patient, to individualize diagnosis and therapy
  - Eventually predict  the response of the human body to new therapies

- Simulated human surrogates: vehicle safety, environmental exposure, effects of extreme environments, ergonomics, …

# Why Now?

- State-of-the-art in experimental data ready to support increasingly complex simulations.
- State-of-the-art in information science (and hardware advances) ready to make shared development and interoperable objects a useful tool.
- Many non-interoperable approaches underway, but flexibility remains.

# We can agree that:

- Understanding biological systems is the most ambitious enterprise ever undertaken
- Understanding these systems mean mastering breathtaking complexity at all levels (there will be no unified field theory)

# *Therefore:*

- **The work must involve collaboration of a large and diverse research community**
- **Information technology will play an essential role in making sense out of this complexity AND in allowing groups to work collaboratively**

# Essential Tasks

- **A *technical architecture* for sharing simulation components and allowing interoperability of biomedical models**
- **A *collaborative, open source environment* for model design, communication, development and validation**

# Obstacles

**Biomedical Research community:**

- Concern that models go beyond empirical data
- Shortage of proven results
- Concern that IT researchers will waste precious research funds on irrelevant frolics yielding no short or long-term benefits
- Misunderstanding/underestimation of the potential of IT research

# Obstacles

**IT Research community:**

- Poor articulation of the power of IT methods (appear to have solutions looking for problems)
- Underestimate the problem
- Over promising in the past

**Everyone:**

- Fear and Loathing of burdensome, rapidly obsolete standards, endless committee meetings chaired by the most boring people in the field, commissars of compliance…
- Protection of intellectual property, protection of investment

# Why is this so hard?

- Several false starts & competing approaches
- Enormous complexity
- Limited data
- Many disciplines must work together (biomedical, computer science, engineering..)
- No 800 pound gorilla

# Next Steps?

- Create a wide open-source community supported by all federal funding agencies (carrot not stick) and an acceptable management system
- Develop a framework built around biological fundamentals (structures, messages)
  - encourage new work built to this framework
  - use the framework to define wrappers that allow interoperation of existing models and components

# Next Steps?

- Launch working groups in specific areas (heart ..). Pick leaders (champions) to jump start each area
- Federal agencies encourage cooperation and invest in essential tasks (coordination, building and testing kernels)
- Each agency play to its strengths (NIH is the logical leader)

# In Conclusion…

- Simulations will be supported on a massive scale because they are an essential. An intentional community would make the process vastly more efficient and more resistant to error
- The task won't be easy, and it won't be done quickly
- It must be the work of many hands!