Microgravity Cell Biology

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Terrestrial Life and Microgravity

- As life evolved on earth a multiplicity of changes in physical and chemical factors invoked adaptations and participated in the complicated selection process
- For many factors there are clear examples of the role of changing physical forces in evolution
- A notable exception is gravity. It has been a constant 9.8 m/sec^2 for the ~4.8 billion years of the Earth's history
- Therefore, there is little or no genetic memory of life responding to force changes in the low gravity range
- It is likely that terrestrial life adapting to microgravity will reveal many novel mechanisms that will be helpful in biomedical research, commercialization, fundamental science, and space exploration

Unique aspects of μG

- No sedimentation
- Loss of gravity driven convection
- Decreased hydrodynamic shear
- No hydrostatic pressure gradient
- Mass transfer of nutrients and waste products approaches the rate of diffusion

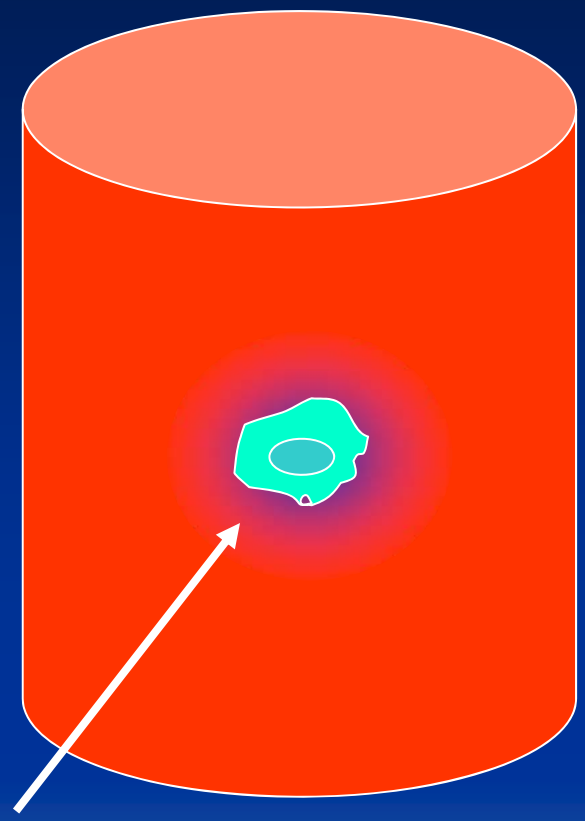
Cells in Microgravity

Theoretical Effects

- Absence of gravity driven convection
- Nutrient transfer limited to the rate of diffusion
- Cells become anoxic

Actual Effects

- They don't die
- There may be non gravity driven convections that facilitate mass transfer



Zone of depletion

O_2 is depleted first

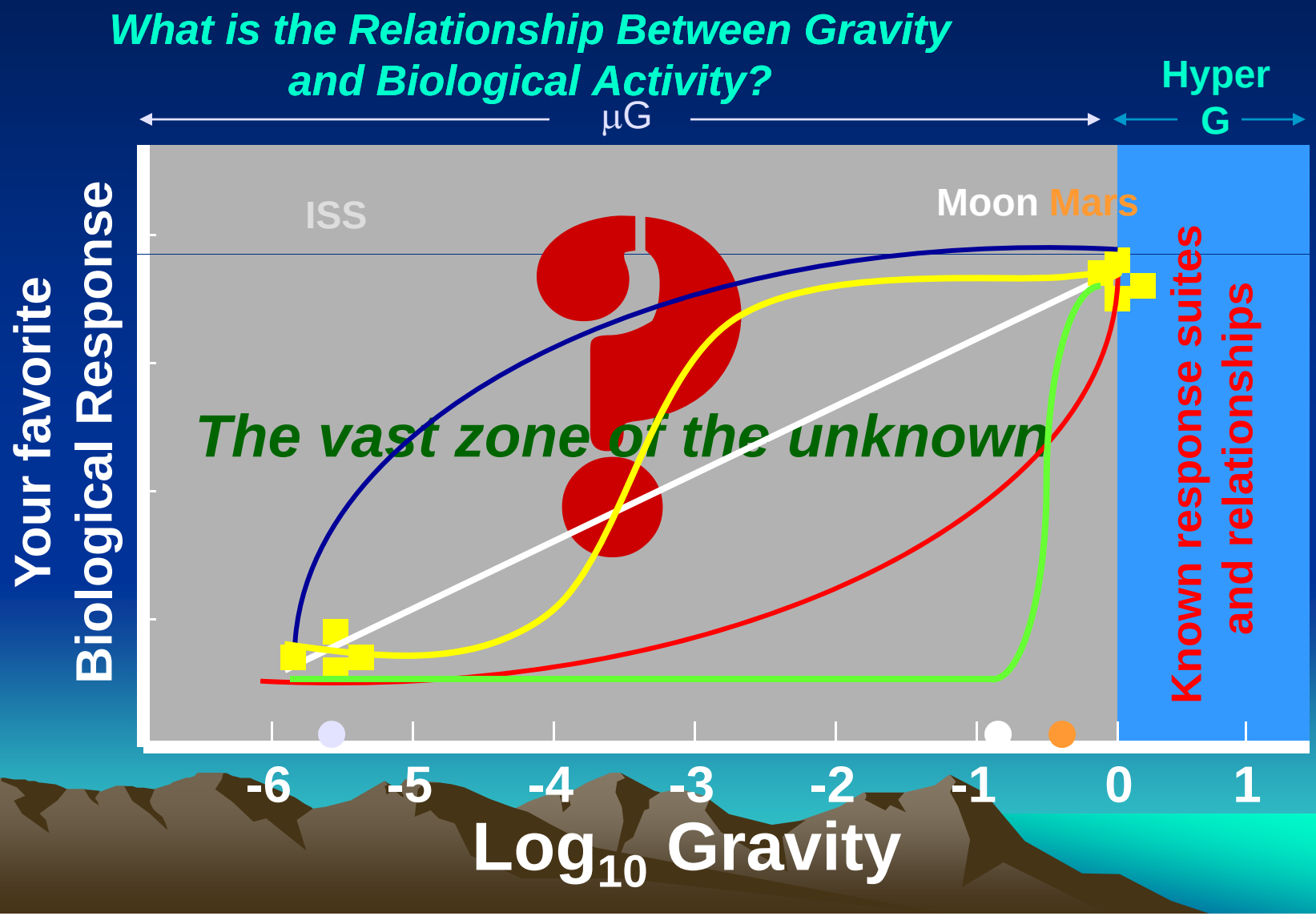
Glucose is second

Others follow

Fundamental Questions

- What is the basis of the response to microgravity?
  - Intrinsic response in the cell (gravisensor?)
  - Response to environmental changes induced by gravity
    - Reduction in Shear (hydrodynamic and mechanical)
    - Concomitant decrease in mass transfer
    - Reduced contact with container
    - No sedimentation
    - Other forces (attraction) take on a new dominance
- How is response different in microbial cells (that are bound by a cell wall) vs. eukaryotic/mammalian cells that do not have a cell wall?
- What is the threshold '*G*' necessary for normal function?
- How does microgravity change cell response thresholds to other stimuli (radiation, magnetic fields, shear, toxins, other chemicals)?
- How do the changes in individual cells relate to tissues, organs, and organisms?

An Important Question in Space Cell Biology



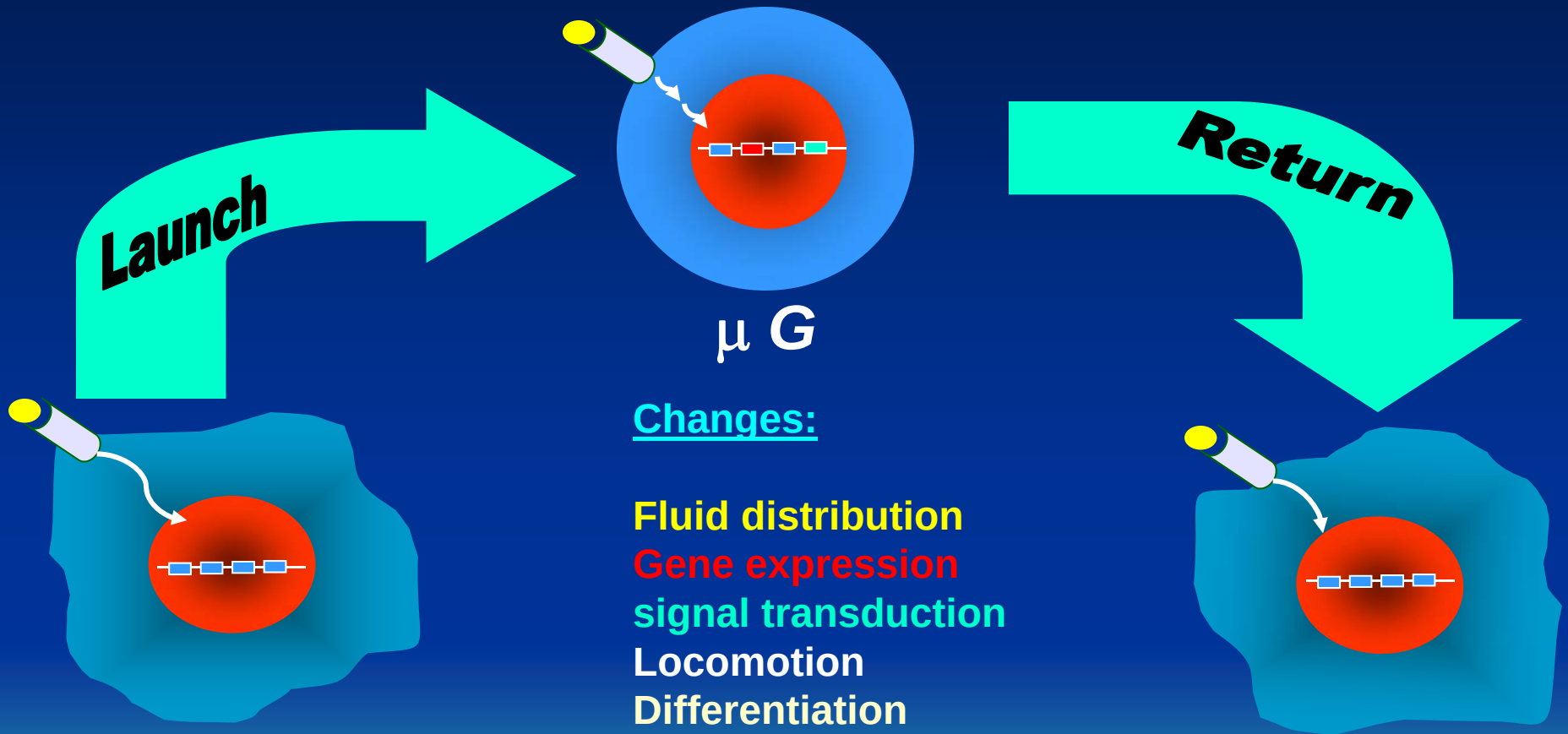
Implementation Questions to Address

- How to conduct focused programs of investigation in space?
- What are the appropriate analogs for μG to use for ground based preparation for space experiments?
- What are the controls that maximize the opportunity to ascribe a biological phenomenon to the influence of μG?

Theories regarding cells in microgravity

1. Microgravity Induced Environment Changes
2. Shape Change
3. Asymmetric Distribution in Mass
4. Loss of Hydrostatic Pressure Gradient
5. Cell force transducers, e.g., mechano-sensitive channels and the primary cilium

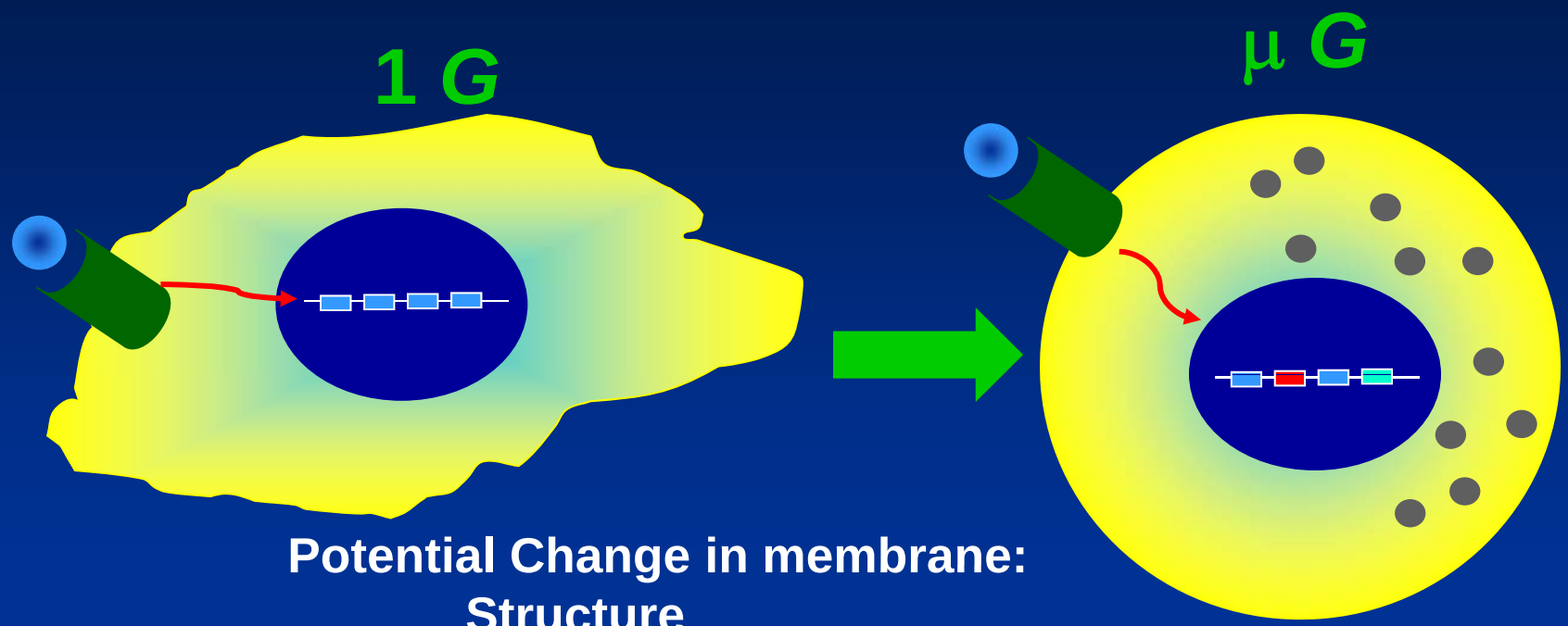
Animal Cells in Space



Changes:

Fluid distribution
Gene expression
signal transduction
Locomotion
Differentiation
Metabolism
Glycosylation
Cytoskeleton
Tissue morphogenesis

Theory of the Effect of μG on Mammalian Cells

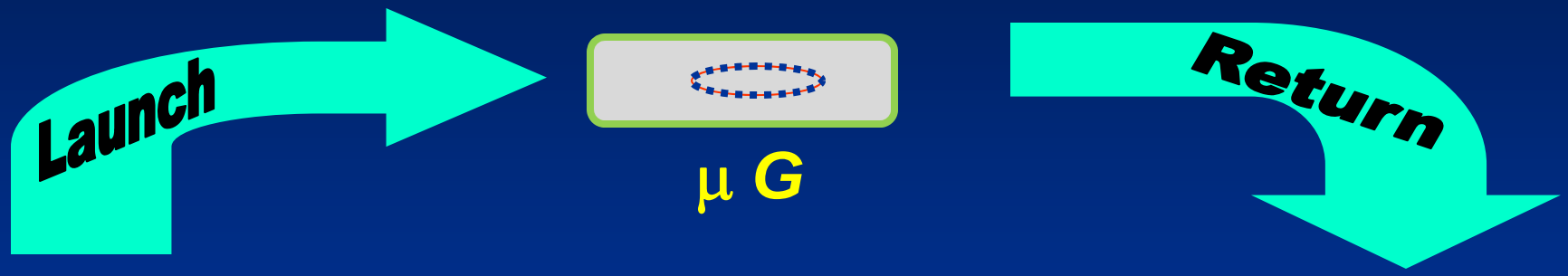


Potential Change in membrane:

- **Structure**
- **Composition**
- **Bi-leaflet organization**
- **Lipid rafts**
- **Association with the cytoskeleton**

Perhaps the 'forced' shape change induces a cascade of responses otherwise unrelated to μG

Bacteria in Space



Changes:

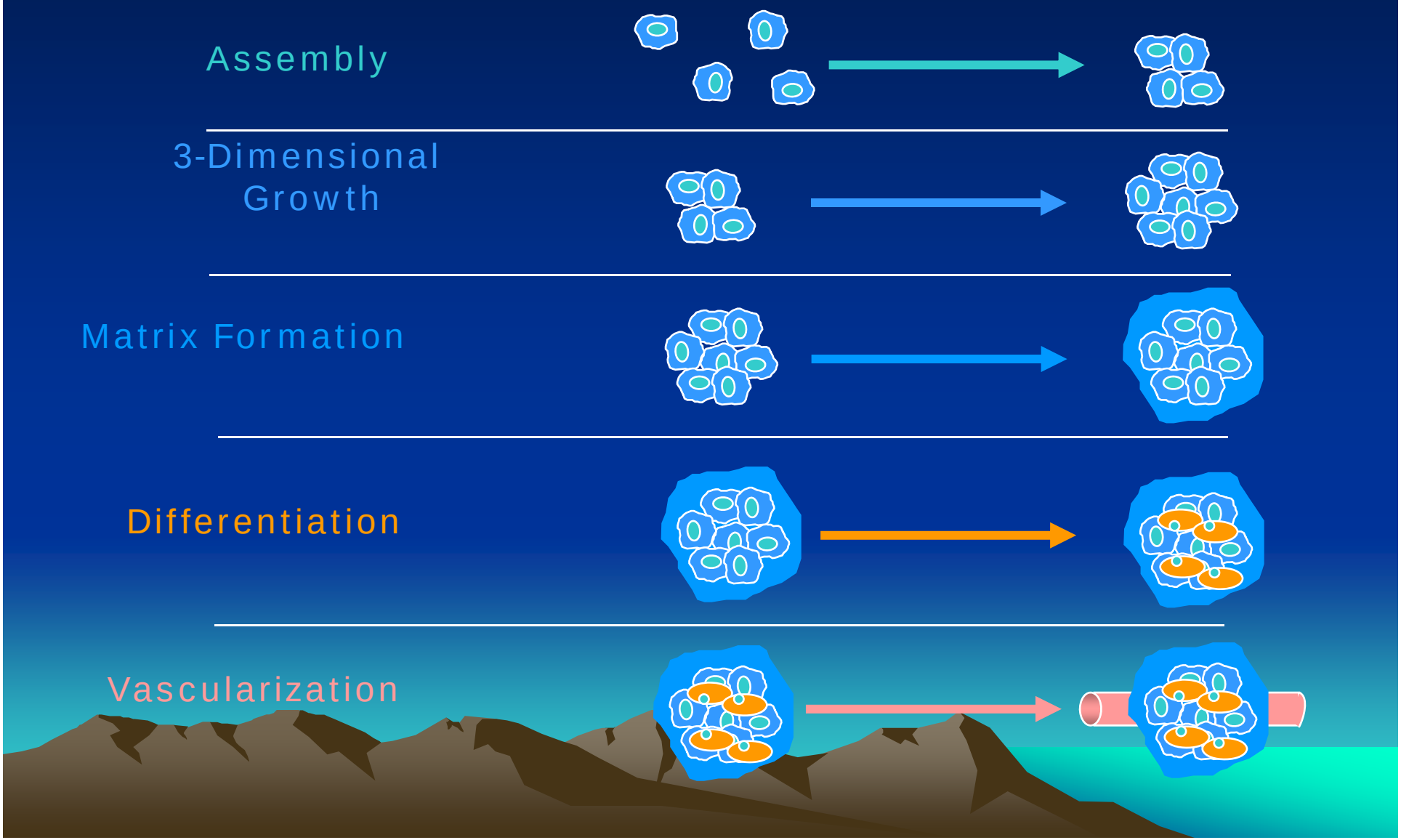
Bacillus spacecowboyum

1 G

Gene expression
Shift to secondary metabolism
Quorum sensing?
Virulence
Mechano-responsive mechanisms
Replication rates
Biofilm formation

1 G

Microgravity Tissue Engineering



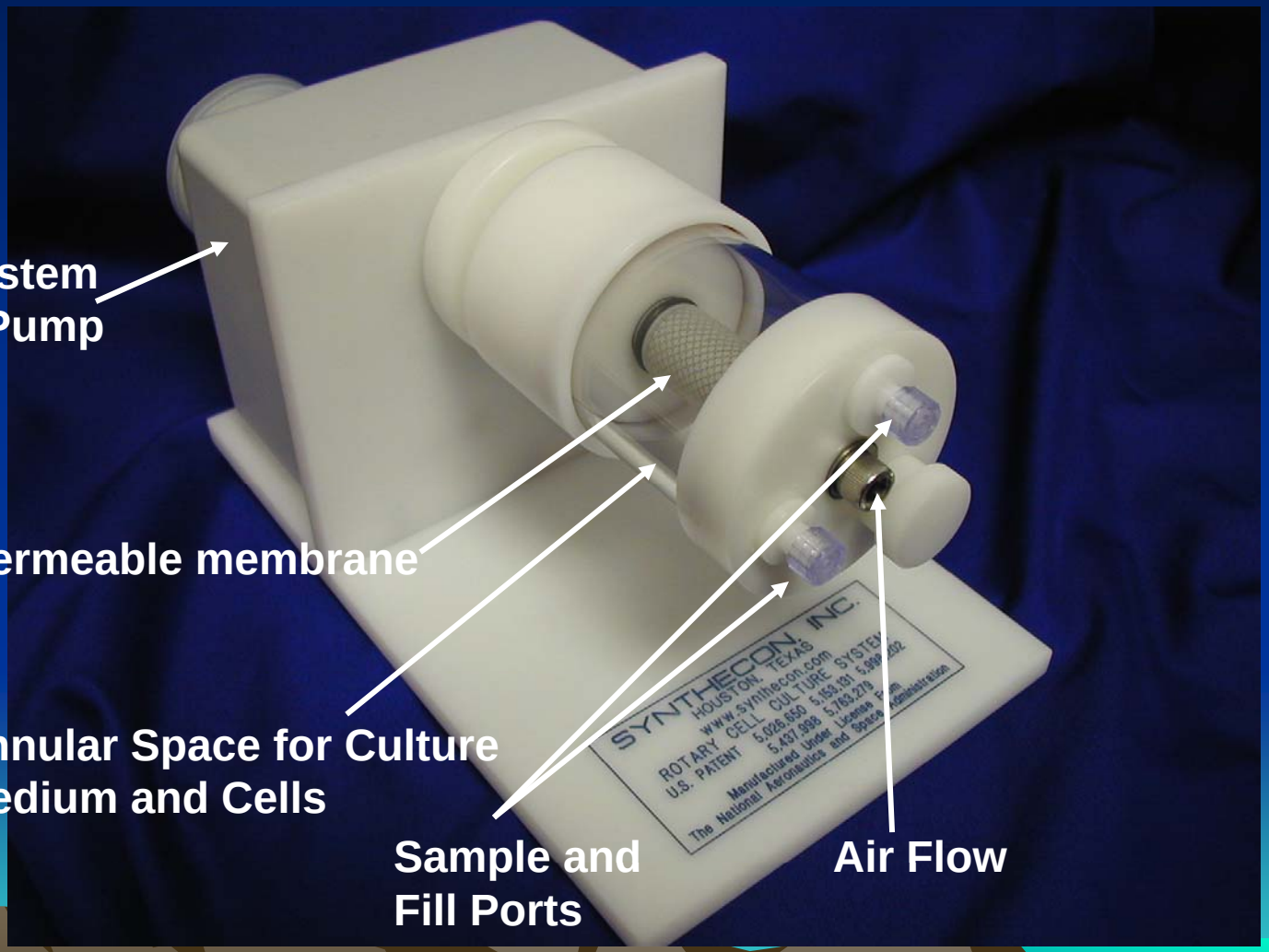
Some of the findings from space

- Decreased lymphocyte activation and cytokine synthesis- Cogoli A, Hughes-Fulford M, Sams C
- Decreased antibody secretion- Zimmerberg J
- Decreased lymphocyte locomotion- Pellis N
- Post-flight analysis of immune cells from rats- Chapes S
- Differentiation- Sytkowski A, Lelkes P, Duprat A
- Centriole complex of sea urchin embryos affected by space flight- Mitchell K
- Gene expression changes- Hammond T, Nickerson C
- Microbial virulence and sporulation- Nickerson C, Klaus, D
- Trans-membrane signaling- Cogoli A, Hughes-Fulford, M
- Cell surface expressions- Sonnenfeld G, Sams C
- Tissue engineering- Freed L, Jessup, J

Microgravity Cell Culture Analogs

- Clinostatic rotation
  - Solid body fluid rotation
  - Random positioning
- Magnetic levitation
  - Diamagnetic
  - Superconducting
- Neutral buoyancy
- Parabolic flight and drop towers

NASA Microgravity Analog Cell Culture System



Drive System and Air Pump

O_2/CO_2 permeable membrane

Annular Space for Culture Medium and Cells

Sample and Fill Ports

Air Flow

Manufactured by Synthecon, Inc.

Significance

- There is little doubt that cells respond decreased gravity environments.

- The mechanism of gravity induced responses in cells is unknown.

- Nevertheless, microgravity affords a unique tool to probe the underlying mechanisms in cell biology.

- We plan use of this tool in novel ways to increase our understanding of the role of gravity in life processes, to achieve goals in applied biological science and technology development, and to elucidate the long term effects of microgravity on terrestrial life.