Processes used by NASA's Digital Astronaut Project to vet Biomedical Models and Simulations

Lealem Mulugeta

DAP Project Scientist

mulugeta@dsls.usra.edu

lealem.mulugeta@nasa.gov

Multiscale Modeling (MSM) Consortium Meeting

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The Goal of this Presentation

- Initiate conversation on what the greater MSM community need to take into consideration in order to instill confidence in biomedical models and simulation for clinical and research application

- Input from the MSM community will be consolidated as a foundation to carry the conversations to the next step (e.g. propose common practices among MSM investigators and greater biomedical M&S community)

Overview of Digital Astronaut Project

- Novel operational conditions of space spaceflight pose health risks that are not well understood and perhaps unanticipated
- Advanced computational simulation environments can beneficially augment research to predict, assess and mitigate potential hazards to astronaut health
- NASA's Digital Astronaut Project (DAP), within the NASA Human Research Program, strives to achieve this goal
- NASA requires rigorous credibility assessment of computational tools intended for decision making that can impact astronauts' well-being

NASA Standard 7009

A comprehensive set of requirements and processes for developing and applying models and simulations, while ensuring appropriate verification, validation and credibility of the M&S results

Credibility Assessment Scale and Definitions

Level	Verification	Validation	Input Pedigree	Results Uncertainty	Results Robustness	Use History	M&S Management	People Qualifications
4	Numerical errors small for all important features.	Results agree with real-world data.	Input data agree with real-world data.	Non-deterministic & numerical analysis.	Sensitivity known for most parameters; key sensitivities identified.	De facto standard.	Continual process improvement.	Extensive experience in and use of recommended practices for this particular M&S.
3	Formal numerical error estimation.	Results agree with experimental data for problems of interest.	Input data agree with experimental data for problems of interest.	Non-deterministic analysis.	Sensitivity known for many parameters.	Previous predictions were later validated by mission data.	Predictable process.	Advanced degree or extensive M&S experience, and recommended practice knowledge.
2	Unit and regression testing of key features.	Results agree with experimental data or other M&S on unit problems.	Input data traceable to formal documentation.	Deterministic analysis or expert opinion.	Sensitivity known for a few parameters.	Used before for critical decisions.	Established process.	Formal M&S training and experience, and recommended practice training.
1	Conceptual and mathematical models verified.	Conceptual and mathematical models agree with simple referents.	Input data traceable to informal documentation.	Qualitative estimates.	Qualitative estimates.	Passes simple tests.	Managed process.	Engineering or science degree.
0	Insufficient evidence.	Insufficient evidence.	Insufficient evidence.	Insufficient evidence.	Insufficient evidence.	Insufficient evidence.	Insufficient evidence.	Insufficient evidence.
	M&S Development		M&S Operations			Supporting Evidence		

M&S Criticality and Risk Assessment

- How are the models and simulations (M&S) going to be used?
  - What are the decisions to be made?
  - Is it for research or clinical applications?
  - Do the M&S provide insight to guide decisions or are they the decision making tool?
  - Is there substantial data to strengthen confidence in the results?
- What is the impact on human health or the mission?

Must apply NASA-STD-7009

M&S Results Influence					
	5: Controlling				
	4: Significant		DAP - Reduced gravity		
	3: Moderate		DAP - Micro-gravity		
	2: Minor				
	1: Negligible				
		IV: Negligible	III: Moderate	II: Critical	I: Catastrophic
		Decision Consequence			

Selected Examples and Lessons Learned

1. Integrative Physiology for modeling and simulating the response of the "whole body" to spaceflight and induced perturbations (e.g. exercise and nutrition)

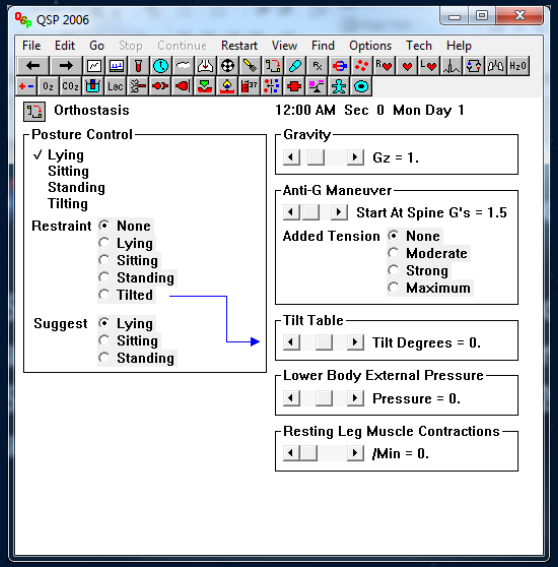
2. Exercise countermeasures modeling and simulation

3. Visual Impairment and Intracranial Pressure (VIIP)

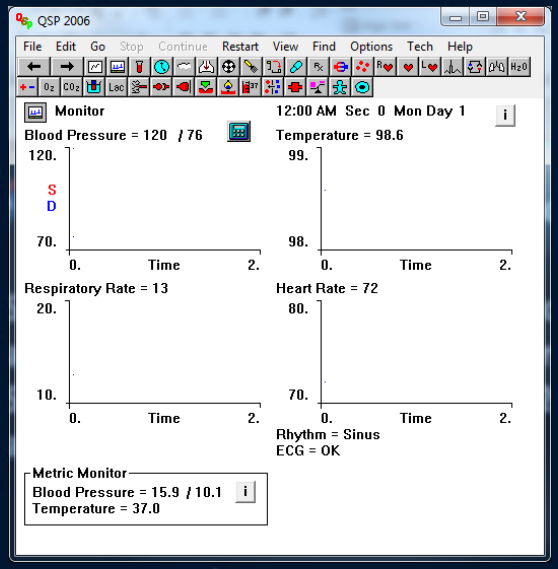
Integrative Physiology

- The University of Mississippi Medical Center's Quantitative Circulatory Physiology education model was adapted for space flight physiology
- The Guyton-Coleman model was substantially expanded to include over 4000 variables and equations (lumped-parameter model)
- The focus was on physiologic impacts of reduced gravity, analogue environments and nutrition on the cardiovascular system

Orthostasis and Bed rest controls



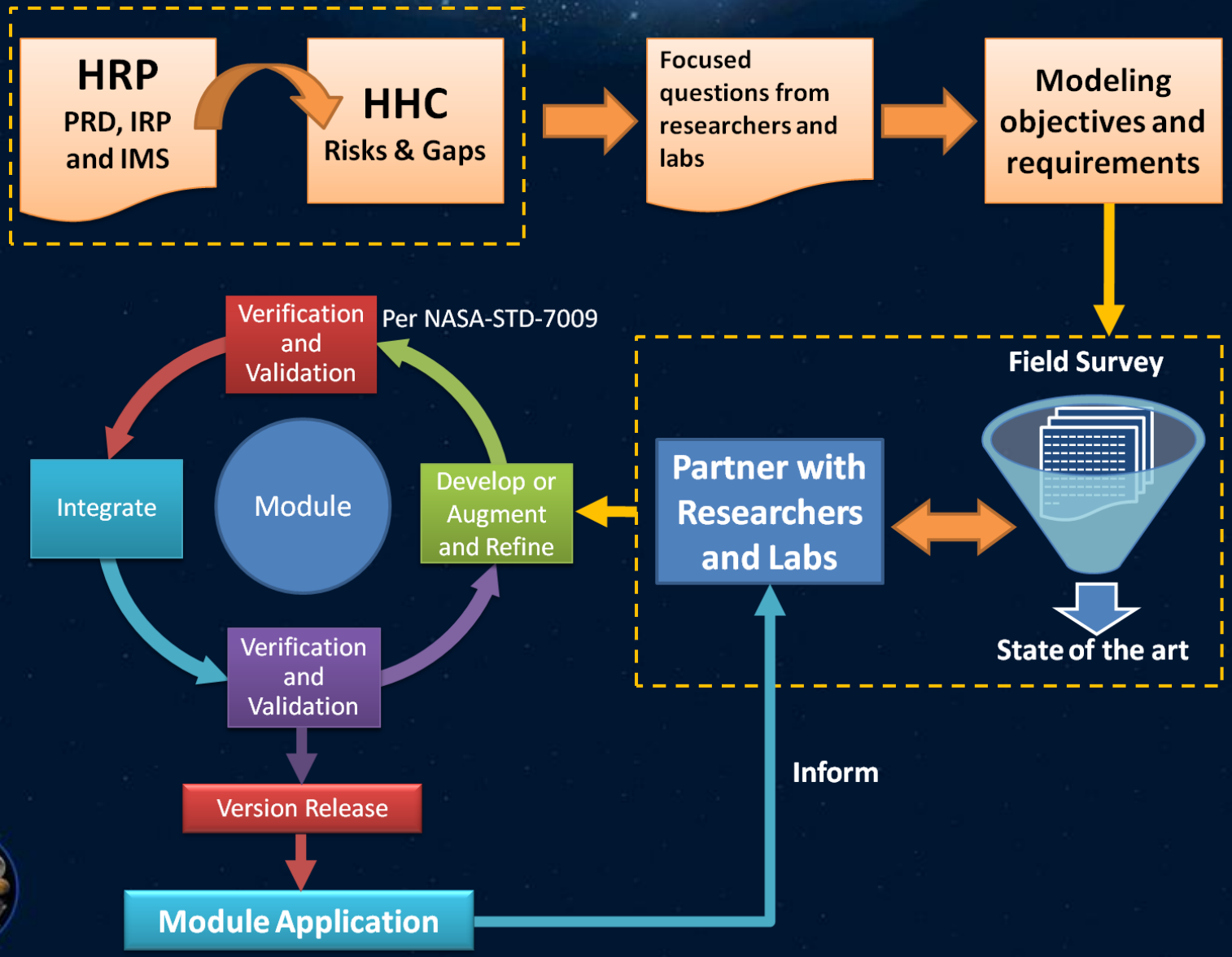
Monitor for basic vitals



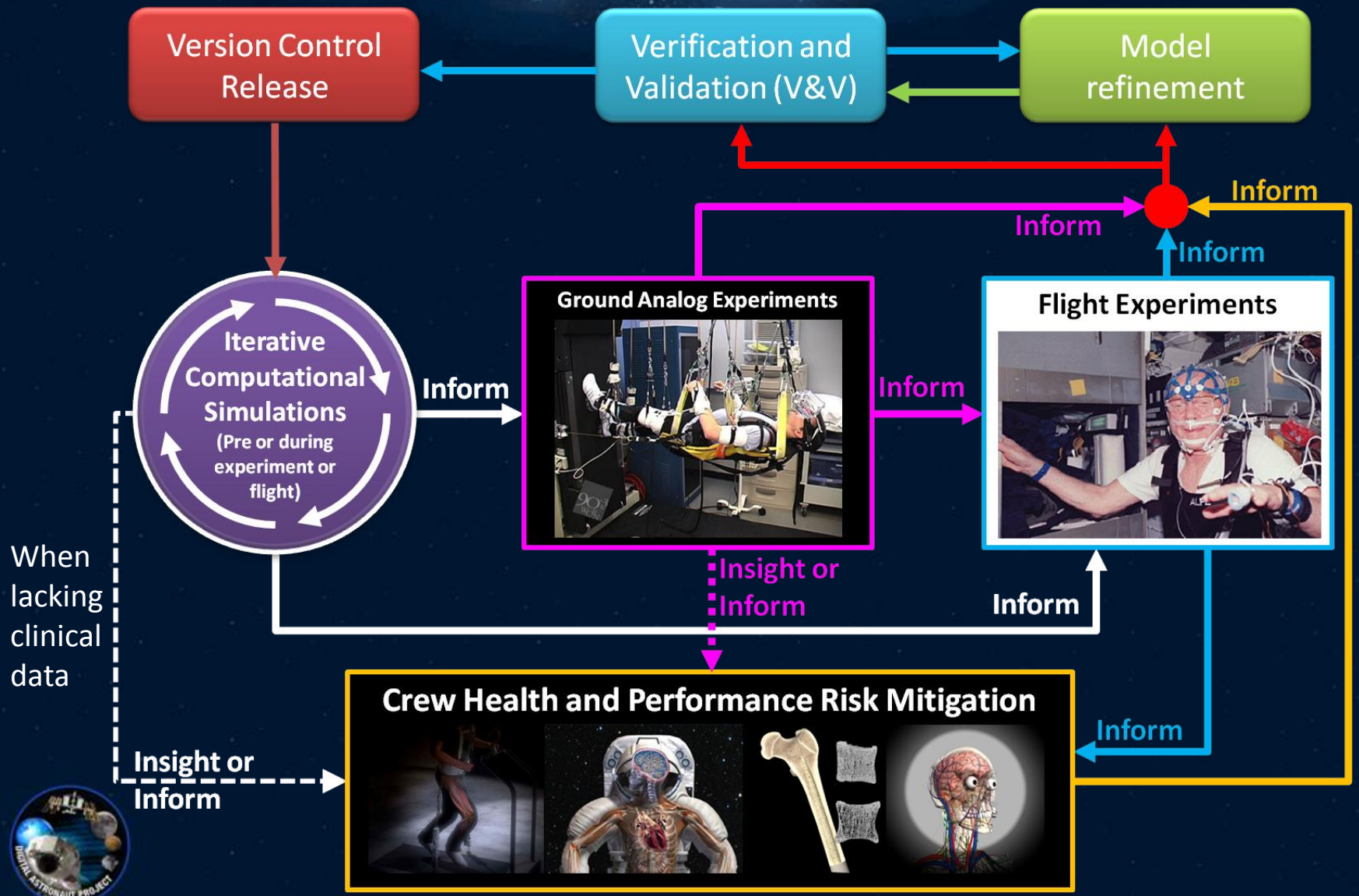
Process for Vetting Integrative Physiology Model

- Selected parameters of interest and compared literature results to simulation results (BP, HB, CO, SV, LV mass, etc)
  - Spaceflight experimental results
  - Bed rest analog results
  - Reproduce previously published simulation results
- Recruited external subject matter experts from around the world to beta test
- Lessons learned:
  - V&V and credibility assessment for problem of interest needs to be an integral part of initial development
  - Clear fidelity levels/threshold must be set for problem of interest
  - Focused M&S development for specific questions can have higher return
  - Modularized approach can further facilitate this process

DAP's M&S Development and Implementation Process



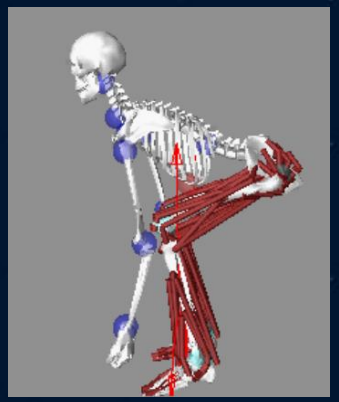
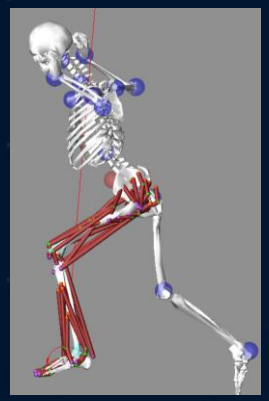
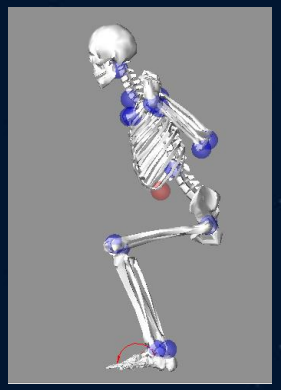
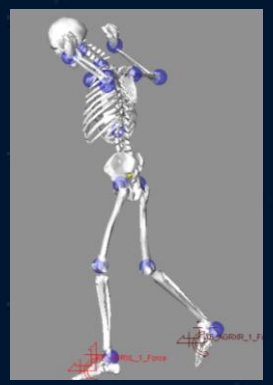
DAP's M&S Development and Implementation Process (cont'd)



Exercise Modeling with the Advanced Resistive Exercise Device (ARED)

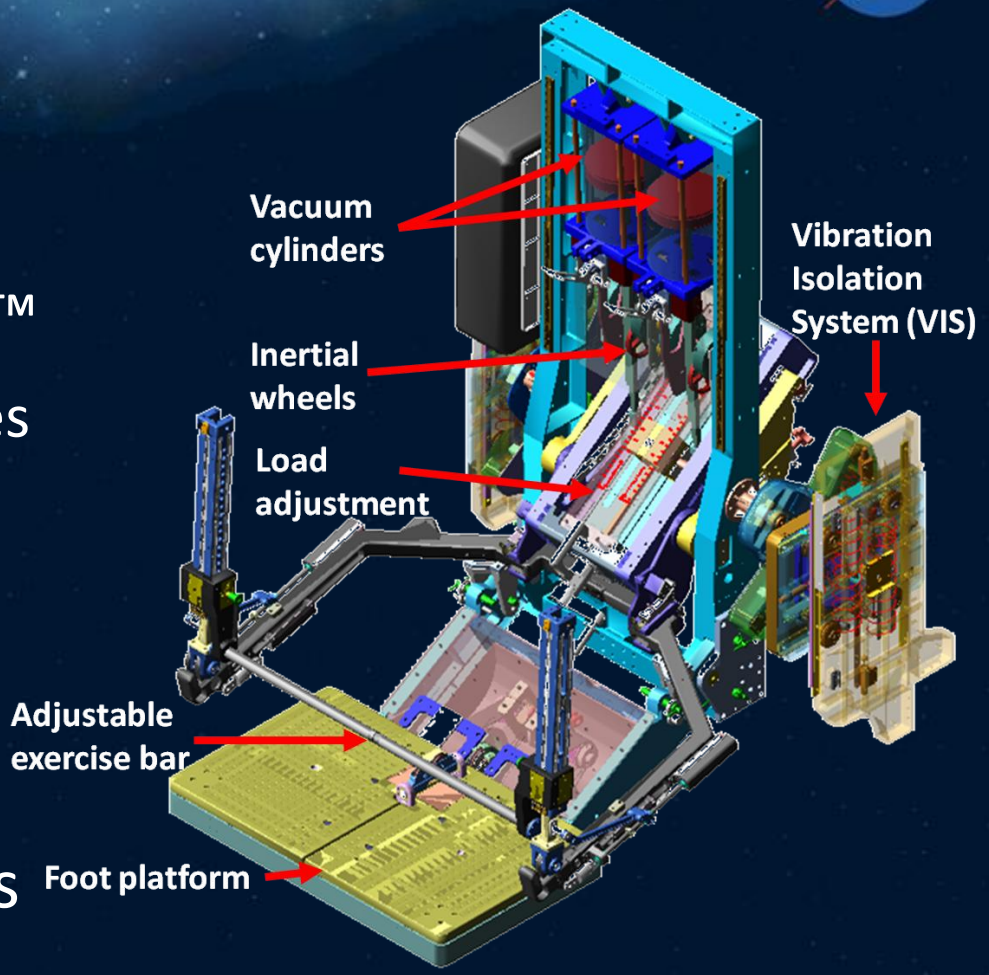
ARED Exercise Models

- Developed with LifeMOD™ using motion capture data acquired on the ARED ground unit at JSC

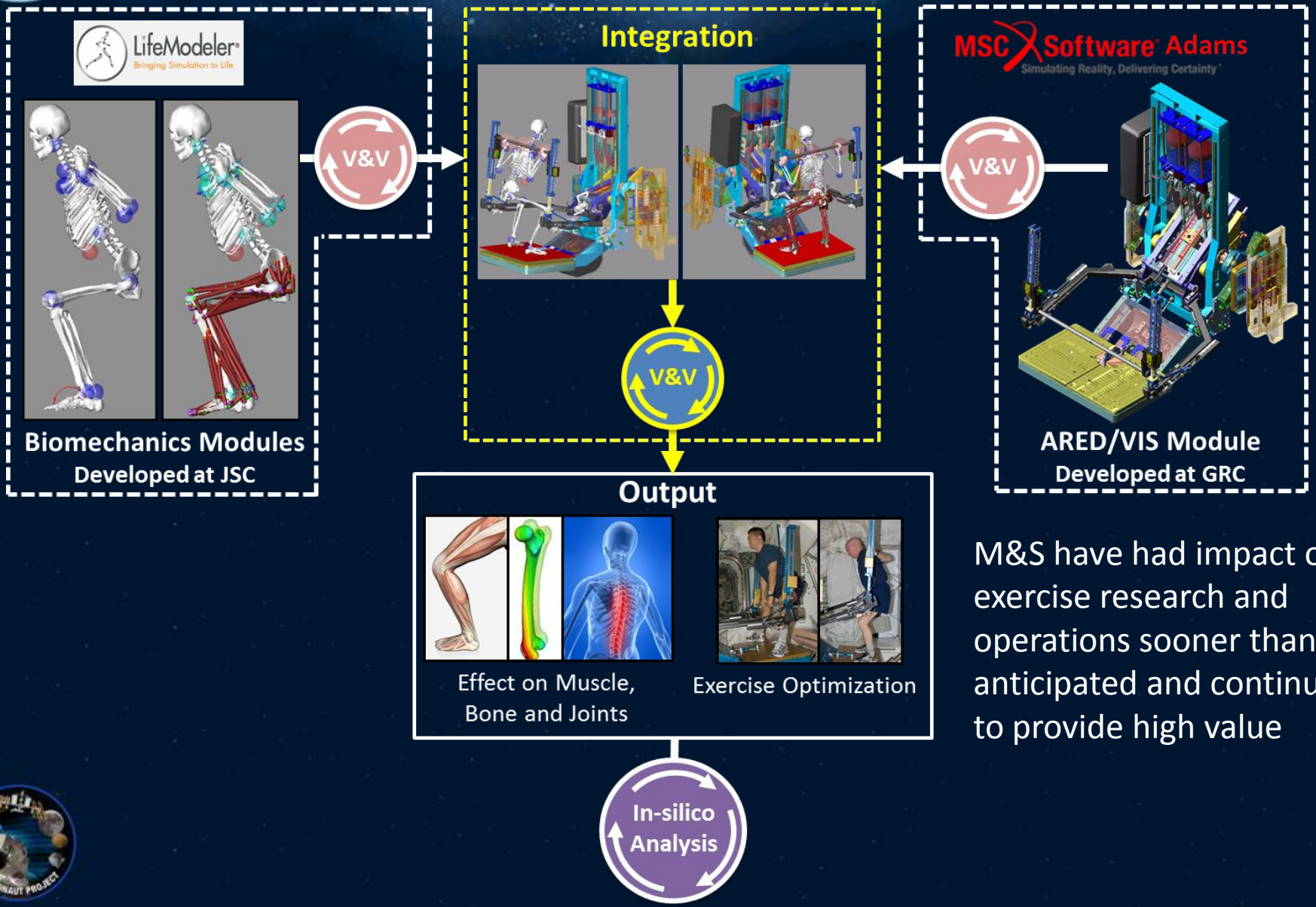
	Dead lift	Normal Squat	Single-leg squat
Muscle Module			
Joint Module			

ARED Hardware Model

- High fidelity dynamics model of ARED/VIS developed in MSC Adams™
  - Mass and inertial properties
  - Friction forces
  - Gas laws
- Currently allows for simulation of bar exercises only



ARED Exercise Modeling and Implementation Process



M&S have had impact on exercise research and operations sooner than anticipated and continue to provide high value

Microgravity Induced Visual Impairment and Intracranial Pressure (VIIP)

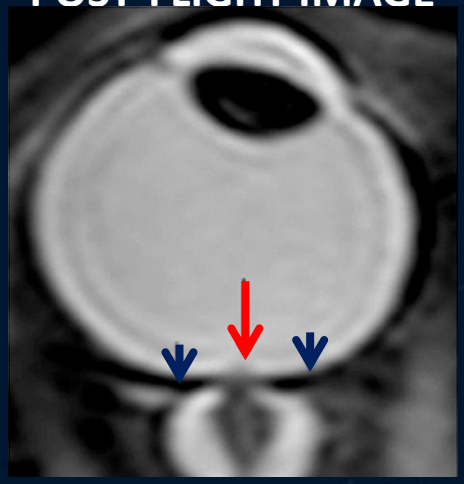
A significant number of spaceflight crewmembers have returned with permanent ophthalmic changes.

There is no definitive explanation for the changes, but the DAP seeks answers through an integrated modeling approach

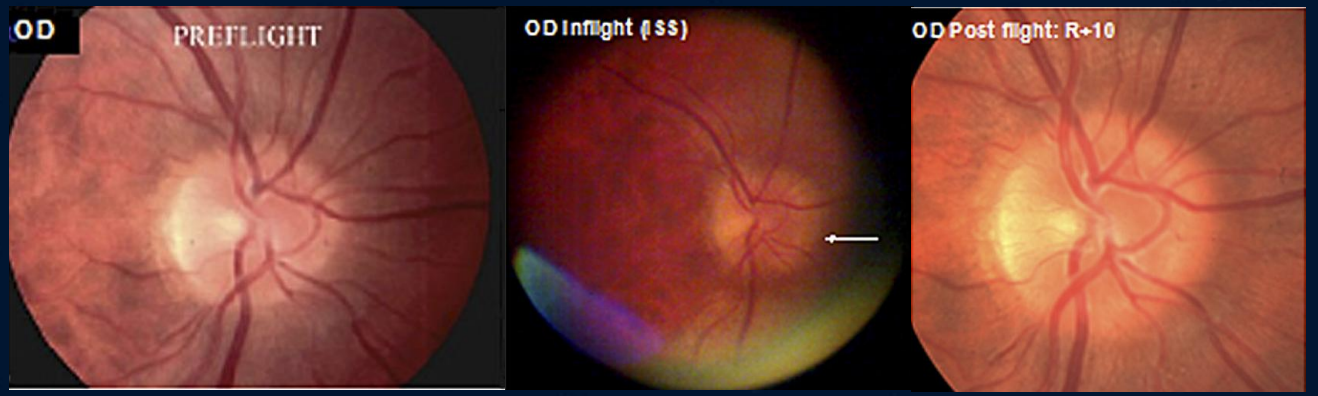
Observed changes

- Optic nerve sheath distension
- Optic disc edema
- Posterior globe flattening
- Choroidal folds
- Elevated post-flight CSF pressure
- Cotton wool spots
- Decreased IOP post-flight

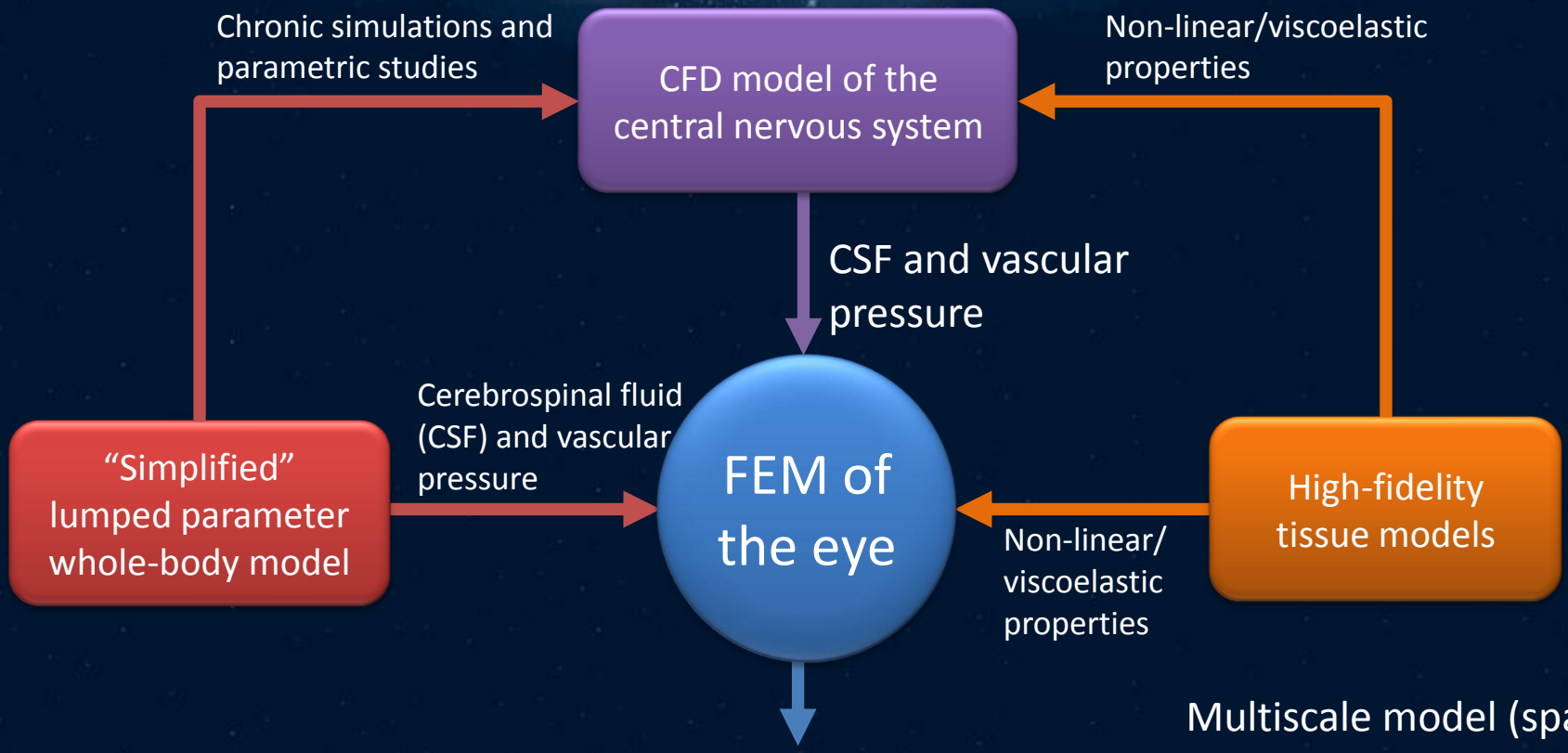
POST-FLIGHT IMAGE



PRE/IN/POST-FLIGHT IMAGING



Visual Impairment and Intracranial Pressure (VIIP) Conceptual Model



Ophthalmic changes

(Image Adapted from Google Body)

Multiscale model (spatial and temporal) consisting of several modules that will be vetted individually and after integration

The Takeaway

- The sooner M&S credibility assessment is integrated as part of the M&S development and implementation process, the sooner:
  - Researchers and decision makers gain confidence in M&S
  - The M&S can have positive impacts
- The sooner the end-user/customer is engaged to inform the M&S development and implementation process, the more likely the end product will have a higher impact
- Important to appropriately weight the different credibility assessment factors for the problem of interest and M&S type
- M&S should applied within their validation domain to maintain highest confidence in results

Questions?

For additional information about DAP

http://www.dsls.usra.edu/displays/digitalAstronaut.pdf

DAP Mission Statement

The DAP implements well-vetted computational models to predict and assess spaceflight health and performance risks, and enhance countermeasure development. The DAP aims to accomplish these goals by:

1. Partnering with subject matter experts to address Human Research Program (HRP) knowledge gaps and countermeasure development decisions
2. Modeling, simulating, and analyzing the physiologic responses to exposure to reduced gravity and analog environments
3. Providing timely input to mission architecture and operations decisions in areas where clinical data are lacking

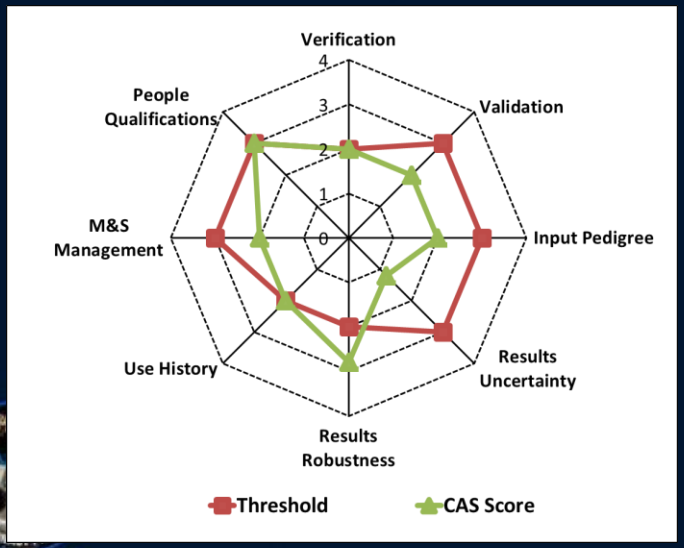
NASA-STD-7009 Background

- NASA M&S that impact on the crew or mission will be required to follow NASA-STD-7009, including biological models
- It was initially developed for engineering systems
- DAP and Integrated Medical Model (IMM) have adapted NASA-STD-7009 for biomedical models for clinical and research applications
- Given the highly comprehensive nature of the standard, DAP and IMM are working to establish a systematic process to apply it to vet M&S

Example of Credibility Scoring

	Credibility Assessment Scale (CAS) Factors	CAS Factor*		Technical Review*		CAS Score	Overall Score
		Threshold	Score	Threshold	Score		
1	Verification	2	2	3	2	2.0	1.2
2	Validation	3	2	3	2	2.0	
3	Input Pedigree	3	2	3	2	2.0	
4	Results Uncertainty	3	1	3	2	1.2	
5	Results Robustness	2	3	3	2	2.8	
6	Use History	2	2	N/A	N/A	2.0	
7	M&S Management	3	2	N/A	N/A	2.0	
8	People Qualifications	3	3	N/A	N/A	3.0	

* Maximum = 4; where 0=insufficient evidence and 4=highest fidelity/rigor achievable. Refer to NASA-STD-7009 Standard for Models and Simulations for detailed explanation.



Threshold: The required score agreed to by the end-user/customer and provider to achieve sufficient confidence in the M&S for intended use

CAS Score Legend
CAS Score > Threshold
Threshold ≥ CAS Score ≥ (Threshold-0.5)
(Threshold-0.5) > CAS Score ≥ (Threshold-1.0)
CAS Score < (Threshold-1.0)

M&S Validation and Application Domain