IAA Study Group Status Report
September 28, 2005

Responsible Commission: Commission 2. Life Sciences

Study Number and Title: 2.1 Mathematical Modeling & Physiological Simulation: The Digital Astronaut/Cosmonaut

Short Study Description: The overall goal of this IAA Study Group is to develop an Academy-endorsed, community-based publishable report on the issues, problems and benefits of an international program to develop a mathematical modeling and simulation system focused on the physiological and medical problems of space travelers.

Progress in past six months:

- Held a Study Group Discussion Meeting on May 23, 2005 at the 15th Humans in Space Symposium in Graz, Austria. Attendees: R. White, R. Gerzer, J. McPhee, G. Fogleman, F. Kappel, J. Batzel, and M. Cabrera.
- Discussed the idea behind IAA Study Groups and the current Outline for the Study Group report. It was suggested that the report include a section on unsolved space problems worth solving and amenable to treatment using modeling.
- See detailed outline attached.

Website Study Information up to date? Not at this time, but updates will be made shortly. The membership is proposed to be increased slightly. The Schedule is modified slightly, but the basic study plan is unchanged.

Issues requiring resolution? None

Product Deliveries on Schedule?

Current Schedule:

- Report Outline — Completed
- Individual Contributions — December 2005
- First Review — January 2006
- Second Review — March 2006
- Final Report Submission to SAC — October 2006

Study Team Member Changes? Note: Complete contact information including email, tel. and fax must be provided for all additions. Only Members with complete contact information will be listed and receive formal appointment letters from the IAA Secretariat.)

Name of person providing Study Group Status (Study Group Chair or Co-Chair): R. J. White

Status Report Date: September 28, 2005

Please email the completed reports to Dr. Kasturirangan, krangan@nias.iisc.ernet.in and katkuri@isro.org, and Dick Kline, rlkline@cox.net. Then post it on your IAA Commission Website **no later than September 28, 2005.** ***Thank you!***

Study Team Membership Changes

Effectivity Date: October 2005

Discontinue: None

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The Digital Astronaut/Cosmonaut: Moving Space Biomedical Research Into The 21st Century

OUTLINE

I. Introduction

Comments:

- The report will be aimed at a general reader (non-specialist) and not at a biologist or modeler. For two examples of space-related writing aimed at different levels of non-specialists, see:
  - White, R. J. Weightlessness and the Human Body. *Sci. Am.* **279**:38-43 (1998).
  - White, R. J. & Averner, M. Humans in Space. *Nature* **409**:1115-1118 (2001).
- The Introduction should be the last section written and should summarize the purpose of the report and the main arguments supporting the use of modeling and simulation in space biomedical research.

II. Background

A. The Human in Space

Comments:

- This section should orient the reader to the environmental challenges that space travelers face and provide the rationale for serious study of the human in space as an intact organism.
- Two draft figures relating to this section are included in the associated FIGURES files:
  - The Human in Space: Environmental Challenges
  - Caring for the Human in Space

B. Modeling the Human in Space – A Brief History

Comments:

- This section should briefly tell the story of past modeling efforts related to human space flight. It is not intended that this section include a thorough review of previous work (see Srinivasan, R. S., Leonard, J. I. and White, R. J. Mathematical Modeling of Physiological States. *Space Biology and Medicine, Vol. III, Book 2* (ed. by Leach-Huntoon, C. S., Antipov, V. V. and Grigoriev, A. I.). AIAA, Washington, DC, 559-594, 1996 for a partial review). Rather, it should provide succinct highlights and a few success stories.
- The following draft figures relating to this section (probably more than we would use) are included in the associated FIGURES files:
  - Biomedical Modeling & Space Flight
  - The Whole-Body Algorithm: The Digital Astronaut of the 1970s

- Unlabeled – Guyton Flow Chart
- Structure of Long-Term Circulatory, Fluid & Electrolyte Model
- Short-Term Thermoregulatory Model
- Short-Term Respiratory Model
- Short-Term Cardiovascular Model

C. The Digital Human and Related Projects

Comments:

- This section should provide an overview of current activities in the community related to the Digital Astronaut.
- A draft figure relating to this section and to Section III.D is included in the associated FIGURES files:
  - The Digital Human & Related Systems (courtesy of J. Coolahan)

III. The Digital Astronaut

A. Definition

Comments:

- One definition that I have used in the past is: *The Digital Astronaut is an integrated, modular modeling and database system that enables the construction and utilization of important predictive simulations of the whole human body.* Of course, the definition should continue and describe the types of space-related and ground-analogue conditions that should be the focus of the system.
- The important points about this definition are:
  - that the Digital Astronaut is an integrated SYSTEM, not a single model,
  - that it includes, as an integral part, an associated biomedical database related to space flight and to important ground experimental analogues, and
  - that the system itself is modular.

B. Goal

Comments:

- This needs to be developed carefully, taking into account the international community of scientists that might be interested in participating in this activity and of the difficulties of carrying out a project of this type with such a distributed group.

C. Approach

Comments:

- The approach needs to be developed in conjunction with the goal defined above. It may be that we will need to have an international workshop to converge on the goal and approach (and on ways to handle the difficulties below). That might be feasible.

D. Difficulties

- Foundational (unified ontology, modeling methods, computational methods, community training, …)
- Structural Integration (whole body, organs, tissues, …)
- Functional Integration (coupled physiological subsystems)
- Data Integration (representation, archiving, utilization, standardization, …)

Comments:

- It is important to recognize these (and other) difficulties and to have a strategy to deal with them.

E. Benefits

- Space Research Community – Strengthens hypothesis development & testing and enables multidisciplinary team research to be more effective
- Engineers & Managers – Mission biomedical risk reduction through improved understanding of human systems and improved planning
- Physicians – Improved medical care through rapid access to all available data & additional capability of realistically testing therapies prior to use in space
- General Health Care Benefits (training, remote care, …)
- Unsolved Problems in Space Physiology

Comments:

- The benefits are very important to describe clearly. Otherwise, this kind of difficult project will not find the support it needs to actually be initiated.
- A draft figure relating to this section is included in the associated FIGURES files:
  - The Digital Astronaut System: A Few Benefits

IV. International Cooperation

Comments:

- The important role of international cooperation in a project such as this one should be presented so that it is clear to the reader why such cooperation is valuable (essential).

V. Summary and Conclusion

VI. Bibliography

Comments:

- Some references that I have found useful are included on the next few pages. The list is both personal and by no means complete.

Draft Bibliography & Assorted Useful References

Baldwin, K.M. Effect of spaceflight on the functional, biochemical, and metabolic properties of skeletal muscle. *Med Sci Sports Exerc.* **28**:983-987 (1996).

Bassingthwaigthe, J. B. Strategies for the physiome project. *Ann Biomed Eng* **28**:1043-1058 (2002).

Buckey, J.C., Lane, L.D., Levine, B.D., Watenpaugh, D.E., Wright, S.J., Moore, W.E., Gaffney, F.A. & Blomqvist, C.G. Orthostatic intolerance following spaceflight. *J Appl Physiol.* **81**:7-18 (1996).

Blomqvist, C. G. & Stone, H. L. Cardiovascular adjustments to gravitational stress. In: *Handbook of Physiology, Section 2: The Cardiovascular System* (eds Shepherd, J. T. and Abboud, F. M.) 1025-1063 (American Physiological Society, Bethesda, 1983).

Bock, G. & Goode, J. A. (eds) *'In Silico' Simulation of Biological Processes* (Wiley, Chichester, 2002).

Boyd, C. A. R. & Noble, D. (eds) *The Logic of Life: The Challenge of Integrative Physiology* (Oxford University Press, Oxford, 1993).

Clément, G. *Fundamentals of Space Medicine* (Kluwer Academic Publishers, Dordrecht, 2003).

Crampin, E. J., Smith, N. P. & Hunter, P. J. Multi-scale modelling and the iups physiome project. *J Mol Histol* **35**(7):707-14 (2004).

Crampin, E. J., Halstead, M., Hunter, P., Nielsen, P., Noble, D., Smith, N. & Tawhai, M. Computational physiology and the physiome project. *Exp Physiol* **89**(1): 1-26 (2004).

Czeisler, C.A. & Khalsa, S.B. The human circadian timing system and sleep-wake regulation. In *Principles and Practice of Sleep Medicine. 3rd ed.* (eds Kryger, M.H., Roth, T. & Dement, W.C.) 353-375 (W.B. Saunders, Philadelphia, 2000).

Daunton, N.G. Adaptation of the vestibular system to microgravity. In *Handbook of Physiology: Section 4: Environmental Physiology* (eds Fregly, M.J. & Blatteis, C.M.) 765-783 (American Physiological Society, New York, 1996).

Dickinson, C. J. *A Computer Model of Human Respiration* (University Park Press, Baltimore, 1977).

Edgerton, V.R. & Roy, R.R. Neuromuscular adaptations to actual and simulated spaceflight. In *Handbook of Physiology: Section 4: Environmental Physiology* (eds Fregly, M.J. & Blatteis, C.M.) 721-763 (American Physiological Society, New York, 1996).

Fitts, R.H., Riley, D.R., & Widrick, J.J. Physiology of a microgravity environment: invited review: Microgravity and skeletal muscle. *J Appl Physiol* **89**:823-839 (2000).

Fitzjerrell, D. G., White, R. J. & Croston, R. C. Cardiovascular modeling: simulating the human response to exercise, lower body negative pressure, zero gravity, and clinical conditions. In *Advances in Cardiovascular Physics, Vol. 5 (Part 1)* (ed. by D. N. Ghista) 195-229, (S. Karger, Basel, 1983).

Fritsch-Yelle, J.M., Leuenberger, U.A., D'Aunno, D.S., Rossum, A.C., Brown, T.E., Wood, M.L., Josephson, M.E. & Goldberger, A.G. An episode of ventricular tachycardia during long-duration spaceflight. *Am. J. Cardiol.* **81**(11):1391-1392 (1998).

Gmünder, F.K. & Cogoli, A. Effect of spaceflight in lymphocyte function and immunity. In *Handbook of Physiology: Section 4: Environmental Physiology* (eds Fregly, M.J. & Blatteis, C.M.) 799-814 (American Physiological Society, New York, 1996).

Grodins, F. S. *Control Theory and Biological Systems* (Columbia University Press, New York, 1963).

Gündel, A., Polyakov, V.V. & Zulley, J. The alteration of human sleep and circadian rhythms during spaceflight. *J. Sleep Res.* **6**:1-8 (1997).

Guyton, A. C., Coleman, T. C. & Granger, H. J. Circulation: Overall Regulation. *Ann. Rev. Physiol.* **34**:13-46 (1972).

Held, T., Shim, E. B., Kamm, R. D. & Mark, R. G. Computational modeling of cardiovascular response to orthostatic stress. *J Appl Physiol* **92**:1239-1254 (2002).

Hoppensteadt, F. C. & Peskin, C. S. *Mathematics in Medicine and the Life Sciences* (Springer-Verlag, New York, 1992).

Hunter, P. J. The iups physiome project: A framework for computational physiology. *Prog Biophys Mol Biol* **85**(2-3):551-69 (2004).

Hunter, P., Robbins, P. & Noble, D. The iups human physiome project. *Pflugers Arch* **445**(1):1-9 (2002).

Hunter, P. J., Nielsen, P. M. & Bullivant, D. The iups physiome project. In *'In Silico' Simulation of Biological Processes* (eds Bock, G. & Goode, J. A.) **247**:207-17, discussion 217-21 & 244-52 (Wiley, Chichester, 2002).

Hunter, P. J. & Borg, T. K. Integration from proteins to organs: The physiome project. *Nat Rev Mol Cell Biol* **4**(3):237-43 (2003).

Hunter, P., Smith, N., Fernandez, J. & Tawhai, M. Integration from proteins to organs: The iups physiome project. *Mech Ageing Dev* **126**(1):187-92 (2005).

Kanas, N. Psychiatric issues affecting long duration space missions. *Aviat Space Environ Med* **69**:1211-1216 (1998).

Kanas, N. & Manzey, D. *Space Psychology and Psychiatry* (Kluwer Academic Publishers, Dordrecht, 2003).

Keener, J. & Sneyd, J. *Mathematical Physiology* (Springer-Verlag, New York, 1998).

Khoo, M. C. K. *Physiological Control Systems* (Wiley, New York, 2000).

Kofránek, J., Andrlík, M., Kripner, T., Mašek, J., & Velan, T. Simulation chips for GOLEM multimedia simulator of physiological functions. In *Simulation in the Health and Medical Sciences 2002* (eds Anderson, J. G. & Katzper, M.) 159-163 (Society for Computer Simulation International, San Diego, 2002).

Lackner, J.R. & DiZio, P. Human orientation and movement control in weightless and artificial gravity environments. *Exp. Brain Res* **130**:2-26 (2000).

Leach-Huntoon, C. S., Grigoriev, A. I. & Natochin, Y. V. *Fluid and Electrolyte Regulation in Spaceflight* (AAS, San Diego, 1998).

Levine, B.D., Zuckerman, J.H. & Pawelczyk, J.A. Cardiac atrophy after bed-rest deconditioning: a non-neural mechanism for orthostatic intolerance. *Circulation*, **96**(2):517-525 (1997).

McCulloch, A. D. Modeling the human cardiome in silico [editorial]. *J Nucl Cardiol* **7**(5):496-9 (2000).

McCulloch, A. D., Huber, G. Integrative biological modelling in silico. In *'In Silico' Simulation of Biological Processes* (eds Bock, G. & Goode, J. A.) **247**:4-25 (Wiley, Chichester, 2002).

Morey-Holton, E.R., Whalen, R.T., Arnaud, S.B. & Van Der Meulen, M.C. The skeleton and its adaptation to gravity. In *Handbook of Physiology: Section 4: Environmental Physiology* (eds Fregly, M.J. & Blatteis, C.M.) 691-719 (American Physiological Society, New York, 1996).

Murray, J. D. *Mathematical Biology I. An Introduction (3rd Ed)* (Springer-Verlag, New York, 2002).

Murray, J. D. *Mathematical Biology II. Spatial Models and Biomedical Applications (3rd Ed)* (Springer-Verlag, New York, 2003).

Nelson, G.A. Radiation in microgravity. In *Handbook of Physiology: Section 4: Environmental Physiology* (eds Fregly, M.J. & Blatteis, C.M.) 785-798 (American Physiological Society, New York, 1996).

Nicogossian, A., Huntoon, C. & Pool, S. (eds) *Space Physiology and Medicine. 3rd ed.* (Lea & Febiger, Philadelphia, 1994).

Ottesen, J. T., Olufsen, M. S. & Larsen, J. K. *Applied Mathematical Models in Human Physiology* (SIAM, Philadelphia, 2004).

Prisk, G. K., Paiva, M. & West, J. B. (eds) *Gravity and the Lung. Lessons From Microgravity* (Dekker, New York, 2001).

Reyes, C., Freeman-Perez, S. & Fritsch-Yelle, J. Orthostatic intolerance following short and long duration spaceflight. *FASEB J.* **13**:A1048 (1999).

Rideout, V. C. *Mathematical and Computer Modeling of Physiological Systems* (Prentice Hall, Englewood Cliffs, 1991).

Summers, R. L. & Coleman, T. G. Computer systems analysis of the cardiovascular mechanisms of reentry orthostasis in astronauts. *Comput Cardiol 2002* **29**:521-525 (2002).

Taylor, G.R. Overview of spaceflight immunology studies. *J. Leukoc. Biol.* **54**:179-188 (1993).

Wautenpaugh, D.E. & Hargens, A.R. The cardiovascular system in microgravity. In *Handbook of Physiology: Section 4: Environmental Physiology* (eds Fregly, M.J. & Blatteis, C.M.) 631-674 (American Physiological Society, New York, 1996).

White, R. J. Weightlessness and the human body. *Sci. Am.* **279**:38-43 (1998).

White, R. J. & Averner, M. Humans in space. *Nature* **409**:1115-1118 (2001).

White, R. J. & Blomqvist, C. G. Central venous pressure and cardiac function during spaceflight. *J. Appl. Physiol.* **85**:738-746 (1998). See also Chest volume and shape and intrapleural pressure in microgravity – reply. *J. Appl. Physiol.* **87**:1240-1241 (1999).

White, R. J., Leonard, J. I., Rummel, J. A. & Leach, C. S. A systems approach to the physiology of weightlessness. *J. Med. Systems* **6**:343-358 (1982).