

Interagency Modeling and Analysis Group (IMAG)

Multiscale Modeling (MSM) Post-Award PI Consortium Meeting

Monday February 6, 2006

Stafford I, Room 375

NSF Campus

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Overall Intent of Solicitation

- To develop new methodologies that span across biological scales
- To develop multiscale methodologies applicable to biomedical, biological and behavioral research
- To develop methodologies within the local multidisciplinary team and within the larger Framework environment
- To further promote multiscale modeling through model sharing

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Categories by Science

- **Cardiovascular (ROOM 375)**
 - Baracos – tissue engineering
 - Bassingthwaighte – muscle physiology
 - Beard - metabolism
 - Cabrera - metabolism
 - McCulloch - physiology
 - Karniadakis - blood
 - Lin - lung
 - Kunz – lung
- **Biological (ROOM 120)**
 - Glazier - developmental
 - Shvartsman - developmental
 - Head-Gordon - signaling
 - Kamm - micromechanics
 - Ladd - actin
 - Ortoleva - microbial
 - Pierce - DNA
 - Schieber - polypeptides
 - Taufer - polypeptides
- **Other Systems (ROOM 380)**
 - Brain – Cai, Choe
 - Gastrointestinal - Brasseur
 - Musculoskeletal - Guess
 - Immunology - Kirschner
 - Cancer – Luebeck, Wilson

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Categories by Methods

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- **Finite Element Methods**
 - Barocas, Beard, Glazier, Kamm, Lin, McCulloch
- **Reduced model formulation, sys ID, integration across scales**
 - Bassingthwaite, Cabrera, Kunz, Pierce
- **Dynamic - ordinary and partial DE**
 - Beard, Cabrera, Glazier, Kirschner, McCulloch, Ortoleva, Shvartsman
- **Numerical Methods, fast algorithms, stochastic**
 - Brasseur, Cai, Glazier, Head-Gordon, Kamm, Kirschner, Karniadakis, Ladd, Luebeck, Pierce, Schieber, Shvartsman, Taufer, Wilson
- **Image processing**
 - Choe, Lin

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Existing Sharing Environments

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Cardiovascular

- www.physiome.org – model repository, CellML, JSim (Bassingthwaighte, Beard, McCulloch)
- Cell Modeling Database (Beard)
- NIH Center for Modeling Integrated Metabolic Systems (Cabrera)
- Adaptive finite element software platform (Barocas)
- PSU Exterior Communications Interface (Kunz)
- MPICH-G2/TeraGrid (Karniadakis)

Biological

- CompuCell3D (Glazier)
- Peer-to-peer (P2P) file sharing (Brasseur)
- CHARMM for molecular dynamics (Kamm)
- NUPACK (Nucleic Acid Package) www.nupack.org (Pierce)
- DAPLDS project and several other environments (Taufer)

Other Systems

- Musculoskeletal model databases (Guess)
- MIT website for Multiscale Modeling and Mechanobiology (Kamm)
- SIMBIOS – SIMTK (Larkin)

Desired Collaborative Environment

(question #1, {Page 12 of PDF})

- Communication, interaction, meetings
- Access, information distribution
 - Interactive, centralized website
 - model repository, documentation
 - tool repository for models
 - threaded online discussion
 - Grid resource
- Model validation
- Organization, oversight, modular, long-term maintenance, common formats
- Communication between groups of graduate students
- Special conferences, journal publications, collaborative proposals

Challenges for Multi-disciplinary Collaboration (question #5, {Page 14 of PDF})

- Starting the conversation, speaking the same language, using the same terminology, tools, mutual appreciation, break down cultural barriers
- Mutual understanding of relevant problems, goals and objectives
- Focus on synthesis rather than analysis to fill gaps in different domains
- Broaden expertise and knowledge of collaborators
- Different approaches (hypothesis-driven vs. analytic models)
- Engineers oversimplifying the biological system, biological phenomena across laboratories
- Mathematicians not eager to understand meaning of biological error, need to be familiar with experiments
- Biologist not eager to understand modeling process and meaning of equations, fear of mathematics
- Biologist focused on phenomena in local laboratory
- Extend collaborations beyond 3 years
- Lack of suitable trainees with multidisciplinary background
- Identifying biologists studying small RNAs with interesting hybridization kinetics
- Time commitment for developing mutual understanding
- Statistical description of structure versus deterministic description of structure

Challenges for Sharing Models

(question #3, {Page 13 of PDF})

- Model documentation
- Interoperability of coding languages, validated models
- Platform dependence
- Solutions
 - Standard data formats to archive and share models
 - CellML with FieldML
- Models are scale, science, goal specific
- Integrate models that are **modular**, flexible and user-friendly
- Framework for easy replication of results
- Patient and task-specific biomechanical models
- Different scientist working on same biological problem
- Culture of adopting standard code

Challenges for Linking Scales

(question #2, {Page 15 of PDF})

- Understanding mechanisms when bridging scales, rather than methods
- Good input data, reliable data translation from in vitro to in vivo
- Scales varying by orders of magnitude – stiff problems
- Composite models at the same level with common parameterization
- Reduced robustness of higher level models
- Biological, physical and mathematical reductions and integrations
- Dynamic effects affecting properties across scales (rigid vs. flexible, sampling issues)
- Integrated data collection across scales
- Identify bridging phenomena at each scale to integrate scales
- Common tools, common variables, integration of existing models
- Define geometric, spatial and time scale separations and their coupling
- Creation of discrete-continuous algorithms
- Visualizing results at multiple scales
- Small scale effects on long-time
- Small scale effects on large scales
- Automatic 3D meshes across scales
- Statistical issues across scales
- Available functional and structural data
- Efficiently mapping free energy landscapes

Challenges for Model Validation

(question #4, {Page 16 of PDF})

- Acquiring a good test case/problem, quantitative data of high reliability and variety
- Common definition of “validation”
- Variability of biological samples – in vivo measurements and in vivo testing
- Validation at one scale, not necessarily valid at other scales
- Validation for one phenomena, not necessarily valid with other phenomena
- Interactive data annotation environment, distributed and web-based
- Access to electronically available data
- Confirming simulation results that cannot be measured
- In vivo to in vitro translation for simulation and validation
- Computational scientists working at different scales should work on same biological problem
- Identify trends that distinguish physical pictures
- Acceptable standards and metrics for quantitative agreement, common validation tools
- Multidisciplinary collaboration
- Linking validation studies, validation experiments
- Differences between animal and human models and data acquisition
- Technology for single cell genome wide assays not available
- Expensive biological experiments
- Building multi-channel single-molecule fluorescence microscopy instruments
- Time intensive automated image analysis methods