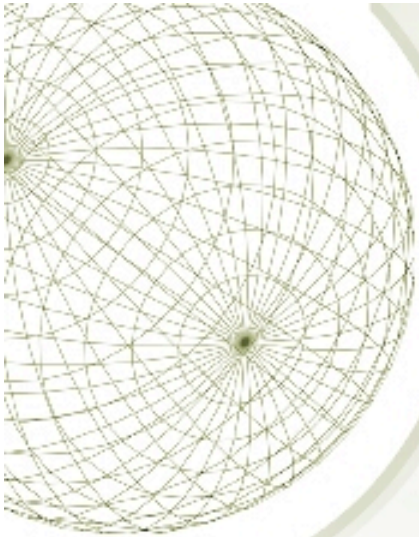


Multiscale Modeling

Peter T. Cummings

John R. Hall Professor of Chemical and Biomolecular Engineering
Vanderbilt University

and

Principal Scientist, Center for Nanophase Materials Sciences
Oak Ridge National Laboratory

Presentation to

IMAG (Interagency Modeling and Analysis Group) and the MSM (Multi-scale Modeling Consortium

June 10, 2008

Outline

- Introduction to SBE&S study
- Multiscale modeling findings
- Other findings on biology
- Conclusions

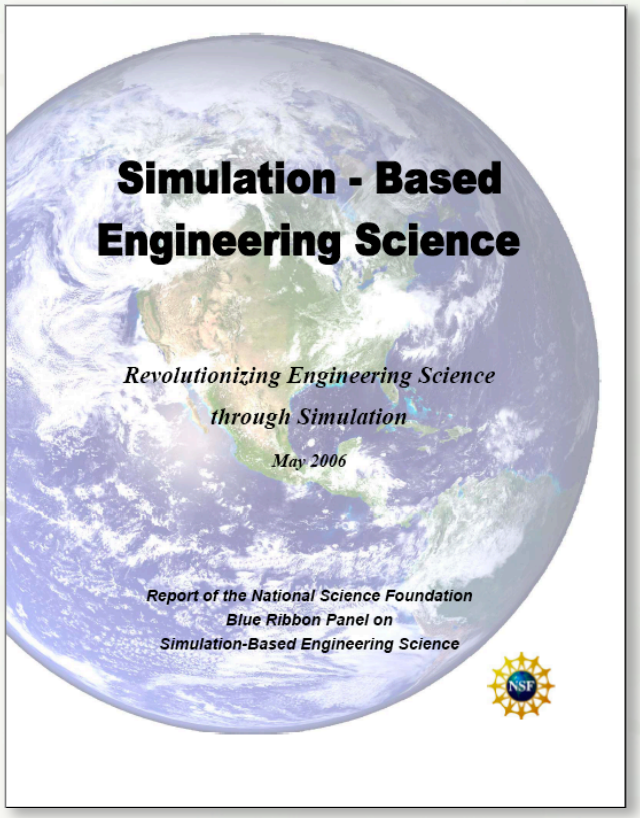
My Background

- Computational Biology
  - Cell-based mathematical modeling of bacterial motility and chemotaxis
    - Cellular dynamics of motility and chemotaxis on motility in bulk and in porous media
  - Cell-based mathematical modeling of cancer invasion
    - Anderson hybrid model
    - Off-lattice CGMD model
    - Migration experiments
  - Modeling of a low-cost high-throughput genomic sequencing device (molecular dynamics, MD)
  - Binding of DNA to C_{60} buckyballs (MD)

- **The International Assessment of Research and Development in Simulation-Based Engineering and Science (SBE&S) is co-sponsored by the**
  - *National Science Foundation (NSF)*
  - *Department of Energy (DoE)*
  - *Department of Defense (DoD)*
  - *National Institutes of Health (NIH)*
  - *National Institute of Biomedical Imaging and Bioengineering (NIBIB)*
  - *National Aeronautics and Space Administration (NASA)*
  - *National Institute of Standards and Technology (NIST)*
- **WTEC is the leading organization in the U.S. that performs international technology assessments via expert review**
  - *WTEC has conducted over 60 such studies since 1989*

Previous SBES study

- Our study builds upon previous efforts:
  - Workshops run by NSF Engineering Directorate
  - NSF Blue Ribbon Panel report chaired by J. Tinsley Oden, May 2006 - lays out intellectual arguments for SBES
  - SBES broadened to SBE&S
  - & many previous reports on computational science



http://www.nsf.gov/pubs/reports/sbes_final_report.pdf

SBE&S - A National Priority

- "The Promise: Advances in mathematical modeling, in computational algorithms, in the speed of computers, and in the science and technology of data intensive computing, have brought **the field of computer simulation to the threshold of a new era**, an era in which unprecedented improvements in the health, security, productivity, and competitiveness of our nation may be possible. A host of **critical technologies are on the horizon** that cannot be understood, developed, or utilized without simulation methods."

--From Oden report

SBE&S: Why now?

- A tipping point in SBE&S
  - Computer simulation is more pervasive today, and having more impact, than ever before - *hardly a field untouched*
  - Fields are being transformed by simulation
  - Reached a useful level of predictiveness; complements traditional pillars of science
  - “Flattening world” of computer simulation that will continue to flatten - *everyone can do it*
  - Disruptive multicore technology likely to be transformative for SBE&S

SBE&S: Why now?

- Simulation is key to scientific discovery and engineering innovation.
  - The toughest scientific and technological problems facing society today are **complex and messy**, and their solution requires a **partnership among experiment, theory and simulation**, working across disciplines.
  - Recent reports argue **our nation is at risk at losing of its competitive edge**. Our continued capability as a nation to lead in simulation-based discovery and innovation is key to our ability to compete in the 21st century.

Overall Scope/Objectives of Study

- Gather key data needed to assess:
  - where the next big breakthroughs are likely to come from, and in what;
  - where US is leading, trailing, or in danger of losing leadership in SBE&S;
  - where critical investments in SBE&S are needed to maintain or gain US leadership, and how those investments will impact R&D and innovation capabilities in strategic areas for US.
- Provide sufficient analysis and guidance to inform and shape development of multi-agency federal initiative in SBE&S
- Findings, not recommendations

Structure of Study

- **Primary thematic areas**
  - *Materials*
  - *Life sciences and medicine*
  - *Energy and sustainability*
- **Core cross-cutting issues**
  - *Next-generation algorithms and high performance computing*
  - *Multiscale simulation*
  - *Simulation software*
  - *Validation, verification, and quantifying uncertainty*
  - *Engineering systems*
  - *Big data and data-driven simulations*
  - *Education and training*
  - *Funding, organization, and collaboration*

The SBE&S Study Team

Panelists

Sharon Glotzer (Chair)	*University of Michigan*
Sangtae Kim, NAE (Vice Chair)	*Purdue University*
Peter Cummings	*Vanderbilt University & ORNL*
Abhi Deshmukh	*Texas A&M University*
Martin Head-Gordon	*University of California Berkeley*
George Karniadakis	*Brown University*
Linda Petzold, NAE	*University of California Santa Barbara*
Celeste Sagui	*North Carolina State University*
Masanobu Shinozuka, NAE	*University of California Irvine*

Advisors

- Tomas Diaz de la Rubia, Lawrence Livermore National Lab
- Jack Dongarra, University of Tennessee/ORNL
- James Duderstadt, University of Michigan
- David Shaw, D. E. Shaw & Co. & Columbia Univ.
- Gil Omenn, University of Michigan
- J. Tinsley Oden, University of Texas, Austin
- Martin Wortman, Texas A&M

Study Timeline

- Kickoff meeting: 10 July 2007
- Baseline workshop: 1-2 November 2007
- Visit to Asia: 3-7 December 2007
- Visit to Europe: 25-29 February 2008
- **Final workshop: 25 April 2008**
- Final report: Fall 2008

- *Research Directions Workshop in Fall 2008*

Sites Visited in China – December 2007

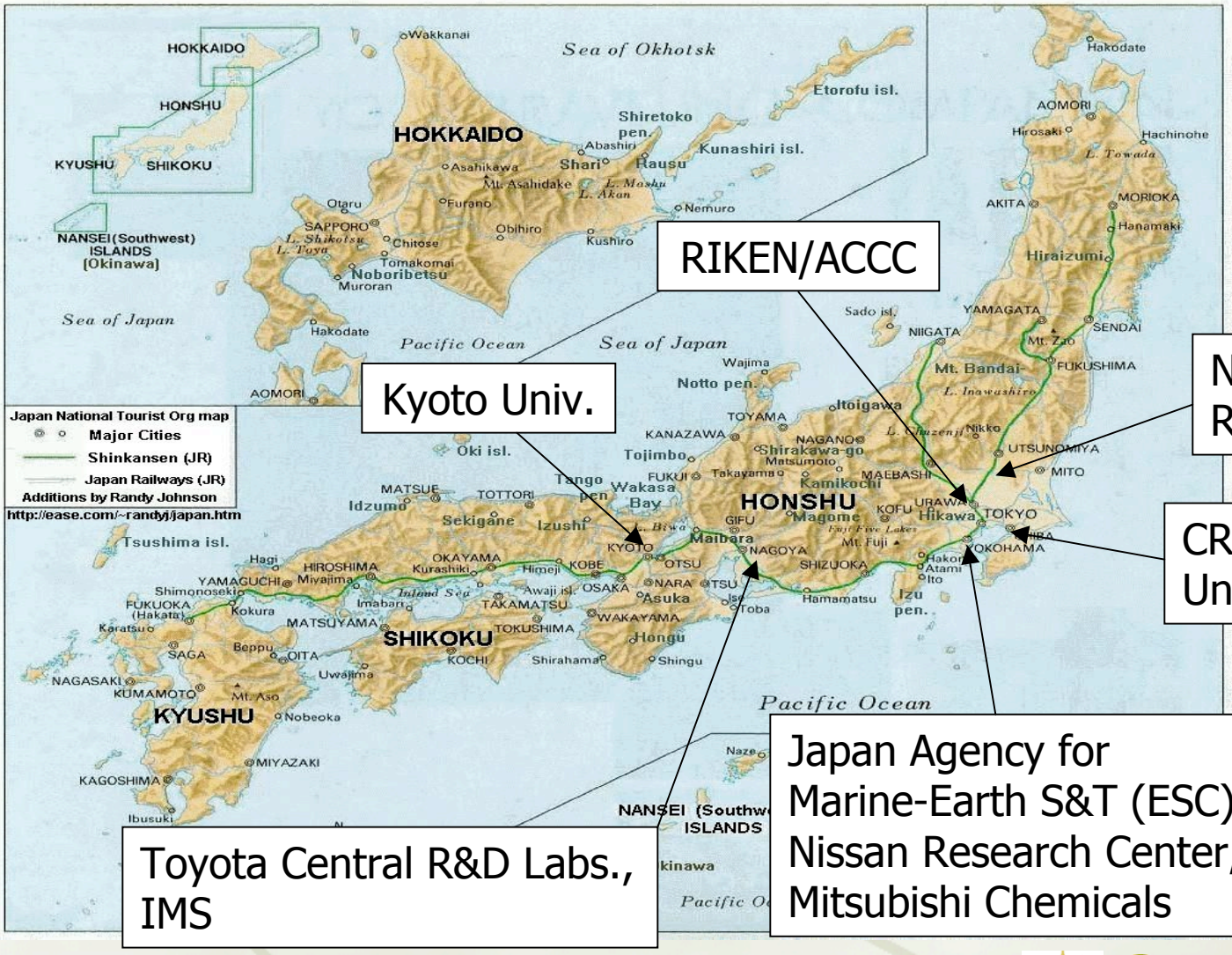
Peking Univ./CCSE, Tsinghua Univ./DEM, ICCAS, ICMSEC/CAS, IPE/CAS,

Dalian Univ. of Technology

SSC, Shanghai Univ., Fudan Univ.

http://www.lonelyplanet.com/maps/asia/china/

Sites Visited in Japan – December 2007



RIKEN/ACCC

Kyoto Univ.

NIMS/CMSC, RICS/AIST

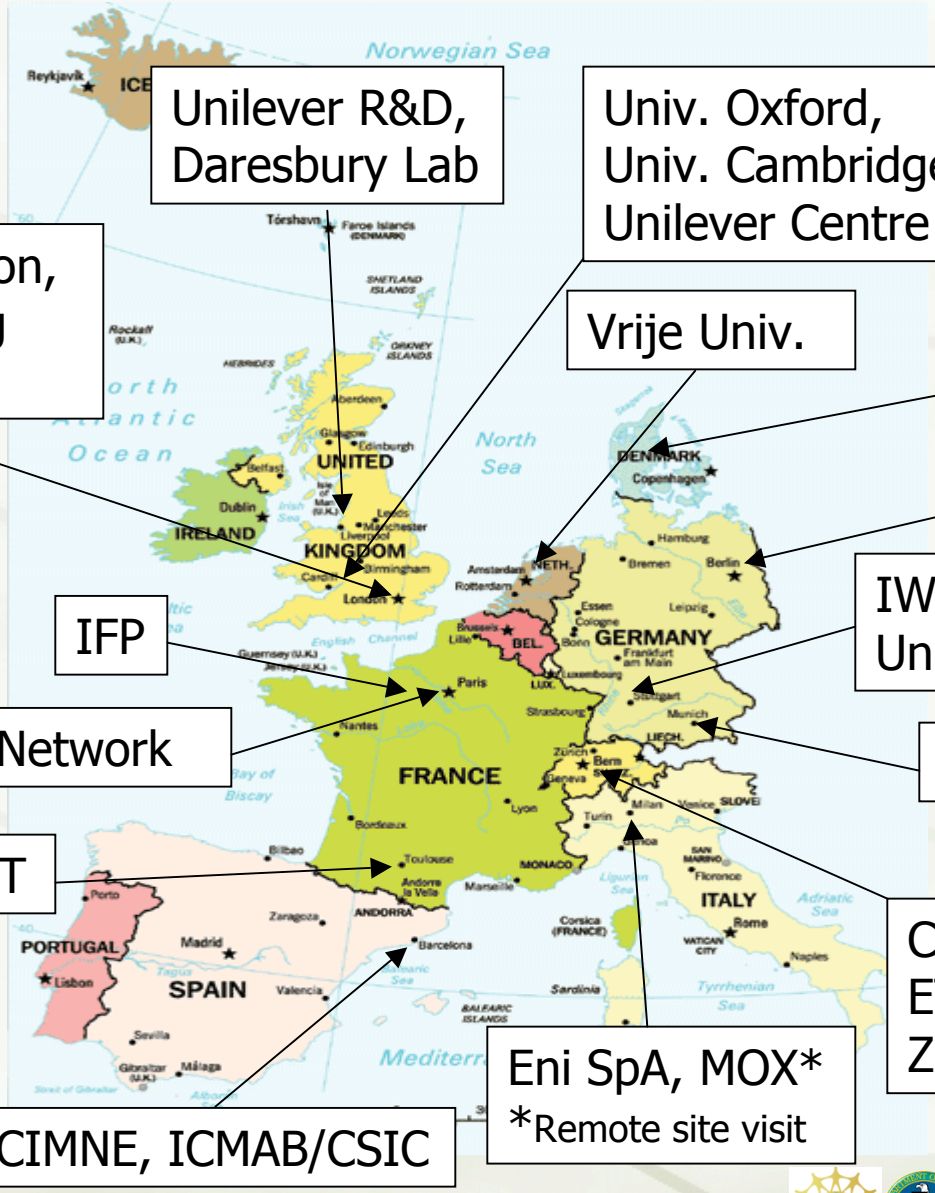
CRIEPI, SBI, Univ. Tokyo

Japan Agency for Marine-Earth S&T (ESC), Nissan Research Center, Mitsubishi Chemicals

Toyota Central R&D Labs., IMS

http://www.ease.com/~randyj/japanmap.htm

Sites Visited in Europe – February 2008



Unilever R&D, Daresbury Lab

Univ. Oxford, Univ. Cambridge, Unilever Centre

Univ. College London, The Thomas Young Centre

Vrije Univ.

DTU

ZIB

IFP

IWM,BASF, ITTPE, Univ. Karlsruhe

Paris Simulation Network

Tech. Univ. Munich

IMFT, ENSEEIHT, IRIT

CERN, EPFL/IACS, ETH, IBM, Univ. Zürich

Eni SpA, MOX*

*Remote site visit

CIMNE, ICMAB/CSIC

http://www.europeetravel.com/maps/western-europe-map.htm

57 sites, 36 in Europe

Threats to US leadership in SBE&S

- Many countries now have and use HPC
- Japan and Germany have world-class resources, faculty and students and are committed to sustained investment in HPC and SBE&S
- Despite US DOE lab leadership in applied HPC algorithms, fundamental algorithm development in US lags
- US invented and first used multicore technology in computers, but we are not training next generation of simulators to use it
- Community code development projects much stronger in EU, with national strategies and long-term support.
- Many of the most popular codes developed outside US; some cannot be used by our defense labs, and we are not developing our own

Threats to US leadership in SBE&S (continued)

- US lead slim in integration of UQ, V&V for “atoms to enterprise’
- The transition from physical systems modeling to social-scale engineered systems in US lags behind the Japanese
- Many of the best students from Latin America, China, elsewhere in SBE&S now going to EU instead of US, and we’re not growing enough of our own.
- All but the top academic institutions report increasing difficulty in finding qualified/interested SBE&S students.

Threats to US leadership in SBE&S (China)

- Not currently a strong US competitor in SBE&S, but their "footprint" in SBE&S is changing rapidly.
- Strategic change towards innovation, and recognition by industry and State that innovation requires simulation
- Recognition of need to train new generation of "computationally-savvy" students, and new large-scale programs at the Ministry of Education to do this
- Overall non-uniform quality of SBE&S research, but high quality examples on par with EU and US
- China contributes 13% of the world's output in simulation papers, second to the US at 27% and growing (although they still publish in lower impact journals and are overall cited less frequently).

Threats to US leadership in SBE&S (Germany)

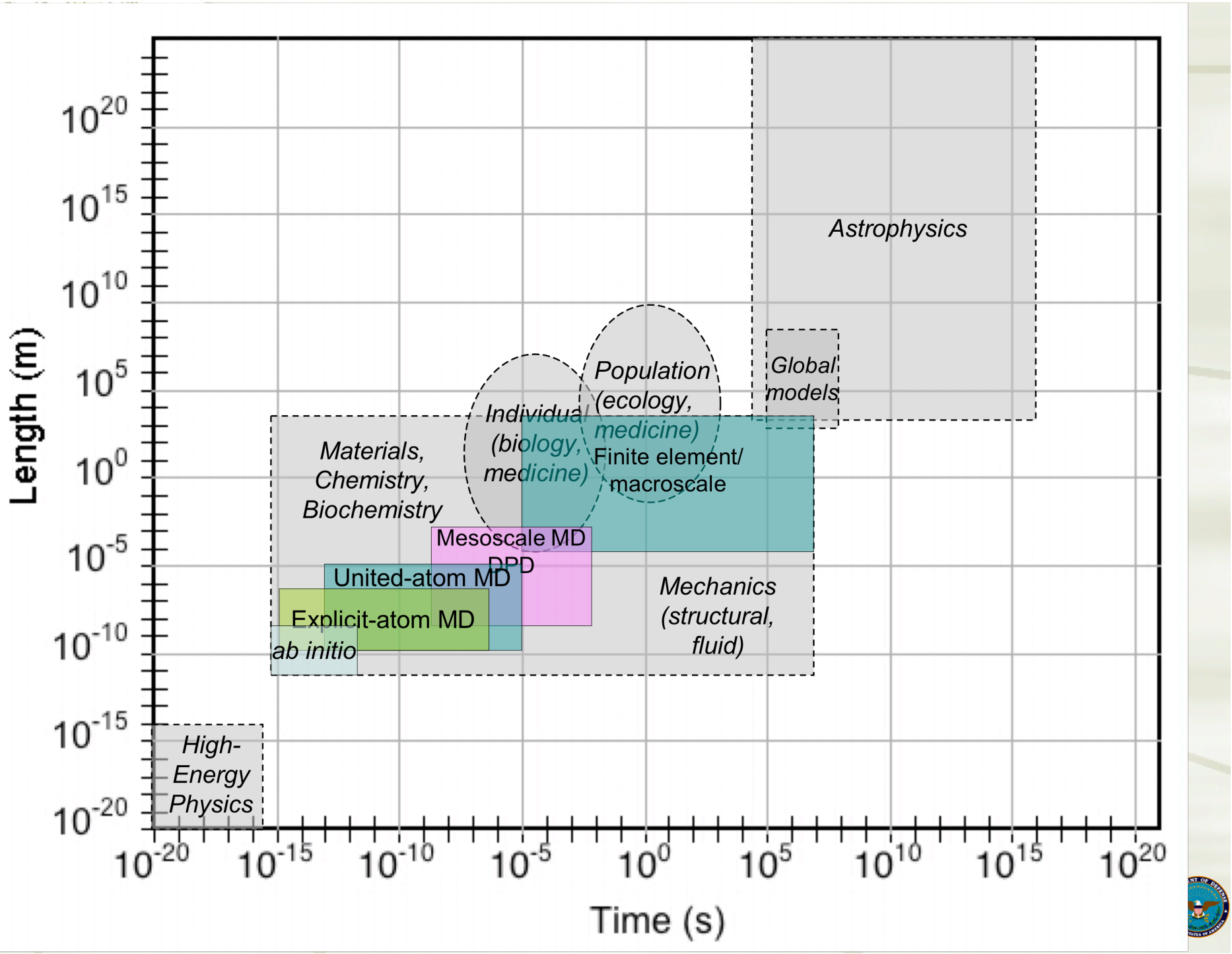
- Vigorous new initiatives in SBE&S and commitment.
- Longtime strengths in molecular, polymer, structural materials, catalyst & process simulation
- Increased commitment to SBE&S through industry and government partnerships
- Restructuring of universities (centers, curricula, industry/faculty)
- Sustained commitment to HPC infrastructure and “big iron”
- Distinctive mechanism for code development support at supercomputer centers
- DFG initiatives (Priority Program Initiative by white papers - $3B/6yr each year)

Outline

- Introduction to SBE&S study
- Multiscale modeling findings
- Other findings on biology
- Conclusions

Potential Impacts

- Multiscale modeling is pervasive concern in SBE&S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Population (ecology, medicine)
Individual (biology, medicine)
Finite element/ macroscale
Materials, Chemistry, Biochemistry
Mesoscale MD
DPD
United-atom MD
Explicit-atom MD
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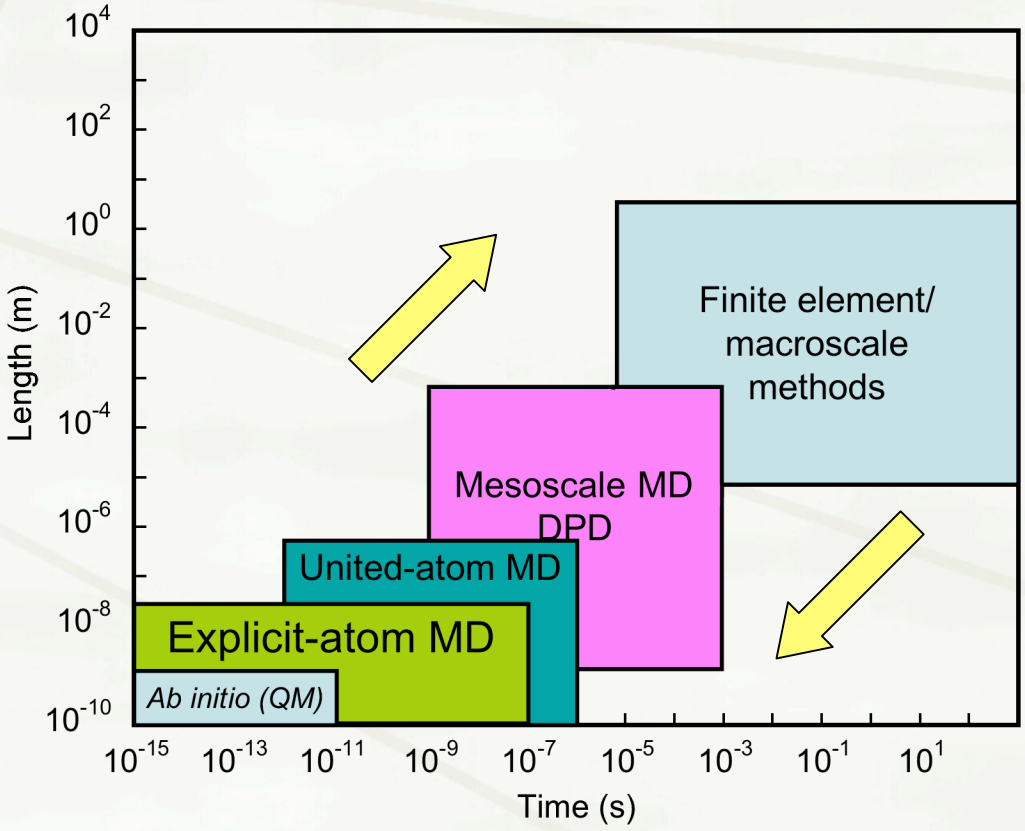
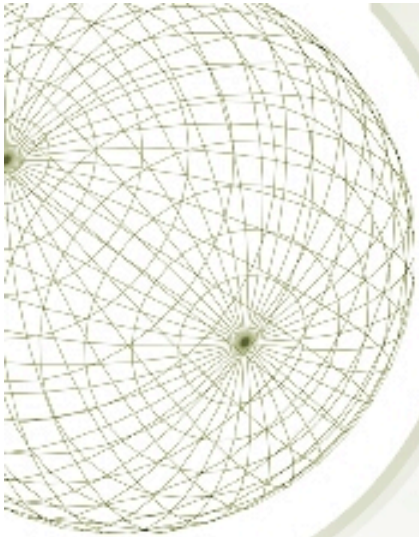
Multiscale in Materials





Multiscale in Biology

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NSF NASA NATIONAL INSTITUTES OF HEALTH NIBIB NIST

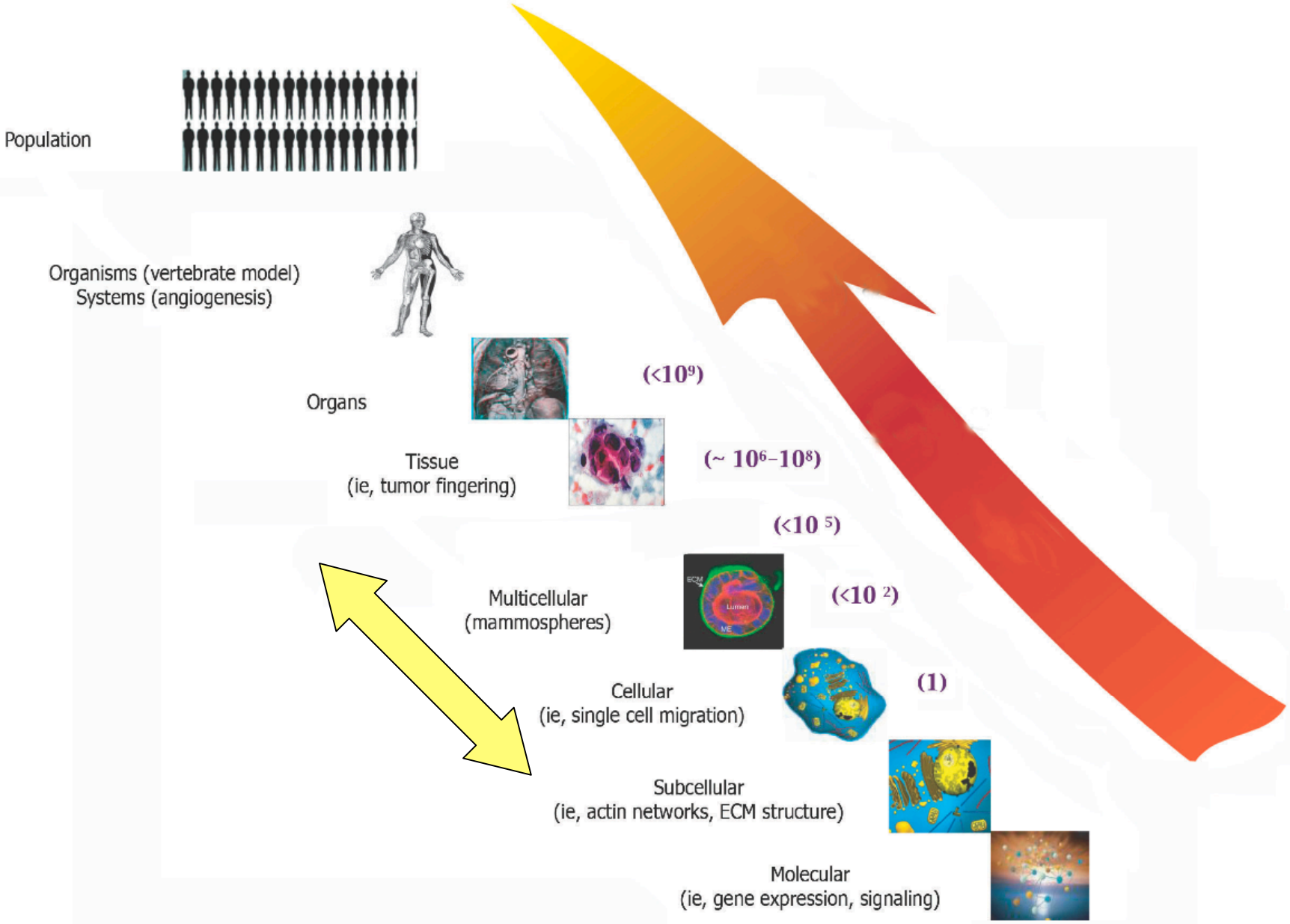


Image from Vito Quaranta

Potential Impacts

- True multiscale modeling….
  - Automatic upscaling (hard) and downscaling (harder)
  - General methods have been proposed
    - Homogenization theory, equation-free methods
  - Orders-of-magnitude time saving
  - Revolutionary
- ….remains holy grail of SBE&S
  - “Full physics” simulations

Research and Technology Areas

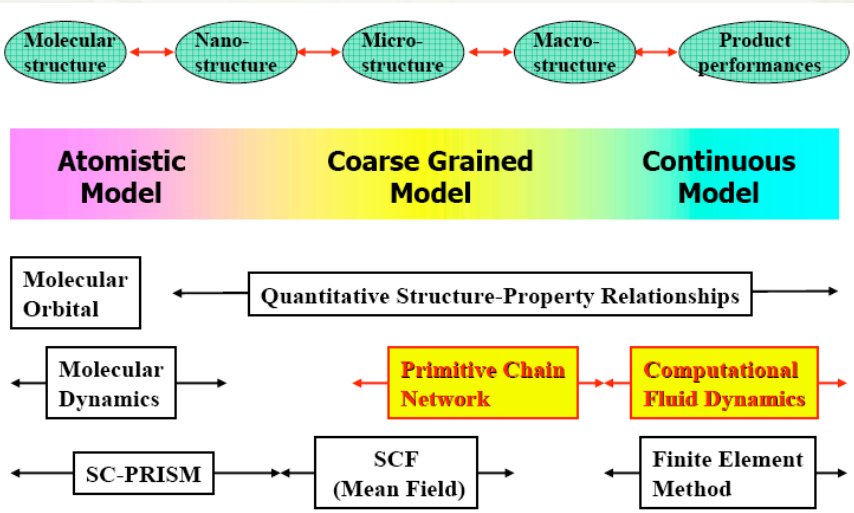
- Materials modeling
  - Crack propagation
  - Polymers
- Biology
- Energy
- Global climate
- Astrophysics
- Engineering design and operations
  - Smart manufacturing
    - "In the future, smart plants will be developed, designed, and operated using molecularly informed engineering."
    - Design and operations from global supply chain to molecule and vice versa

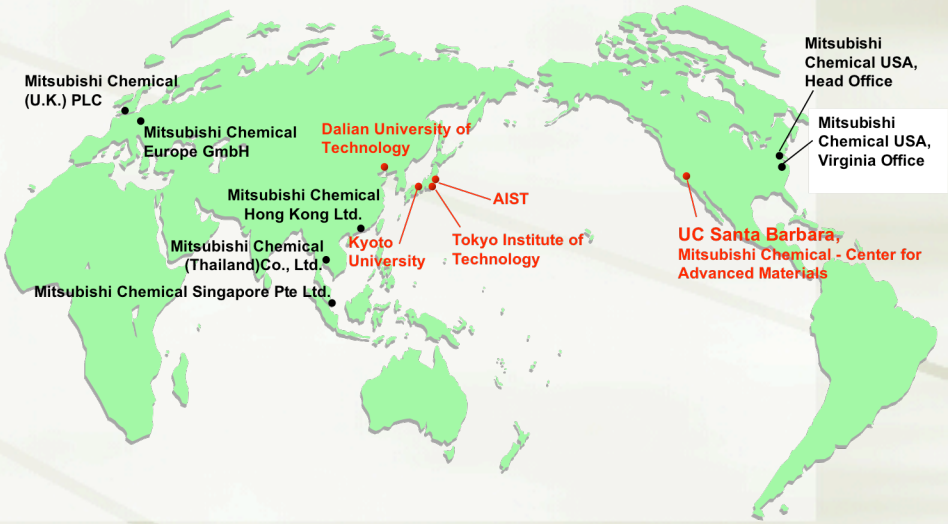
SBE&S Requirements

- Multiscale modeling
  - Cross-cutting enabling capability
- SBE&S needs
  - Standards for interoperability of codes (e.g., CAPE-OPEN)
  - New methodologies and validation/application of existing techniques
  - Multidisciplinary research teams
  - Development of MM frameworks
  - Training of students in use of MM frameworks

Regional Highlights - Japan

- Mitsubishi Chemical
  - Polymer modeling (beyond Doi project)
    - Multiscale model from atoms to CFD based on SC-PRISM





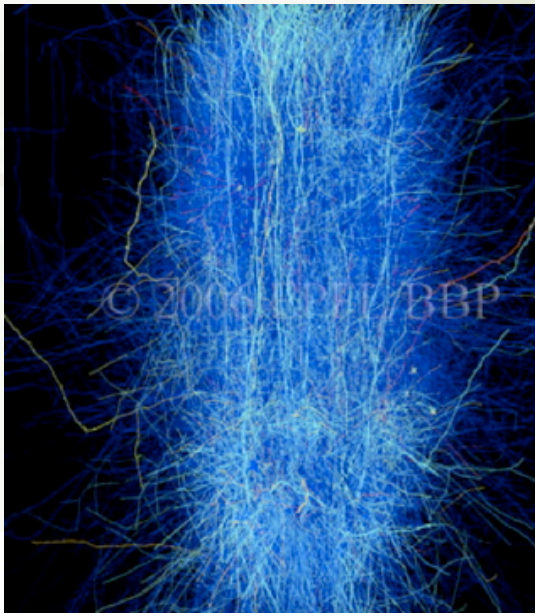
Regional Highlights - Europe

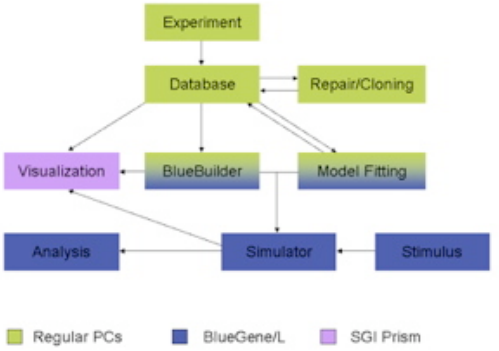
- Mike Payne, Materials, Cambridge
  - Crack propagation in graphene sheets
    - Example of multiscale in specific problem domain

QuickTime™ and a
decompressor
are needed to see this picture.

Regional Highlights - Europe

- École Polytechnique Fédérale de Lausanne (EPFL) Blue Brain Project with IBM
  - 3D replica of brain cerebral neocortex
    - Cellular infrastructure constructed from experimental data
    - Electrophysiological interactions
    - 10,000 neurons of 340 different types; 30 million connections
    - First cellular-level neocortical column
  - 35 research/development personnel
  - IBM Blue Gene





Findings

- Multiscale modeling is exceptionally important but has long way to go
- Examples exist within narrow disciplinary boundaries
  - E.g., crack propagation within materials
- Attempts to develop general strategies have not succeeded
- Industry attempts to do this because they must
  - Lack of standards-based interoperability of codes is major impediment
    - Cited by several companies

How does the U.S. compare?

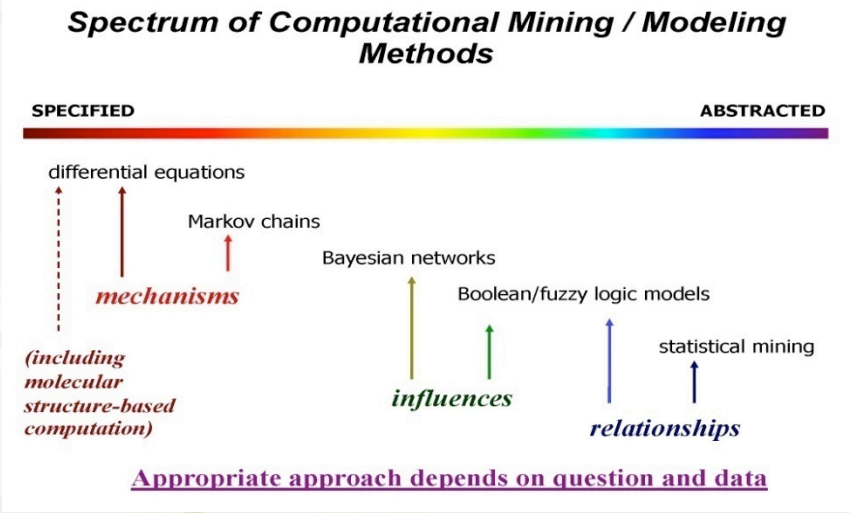
- U.S. research is on par with Japan and Europe
  - However, U.S. research is distributed, lacks focus and integration
  - Japanese and European approach is to fund large interdisciplinary teams
    - Japan: Large industrial component (Doi project)
    - Europe: 35-person EPFL/IBM project
- Petascale and exascale computing are needed to validate multiscale approaches
  - Can anyone get petascale resources for validation of MM approach?
- Tradition of interdisciplinary collaboration leading to community software is much stronger in Europe and Japan than in the U.S.
  - MM may be solved, and MM frameworks developed, outside the U.S.

Outline

- Introduction to SBE&S study
- Multiscale modeling findings
- Other findings on SBE&S in biology
  - Linda Petzold
- Conclusions

SBE&S

- Large, focused multidisciplinary teams: iteration between model and experiment
- Integrated community-wide software infrastructure: SBML, SBGN, Cell Designer, Copasi, …
- High-performance simulation at scales ranging from molecular dynamics to PDEs, and at levels of complexity ranging from Boolean to discrete stochastic and multiscale



Multiscale models and techniques in systems biology *(D. Lauffenburger)*

SBE&S

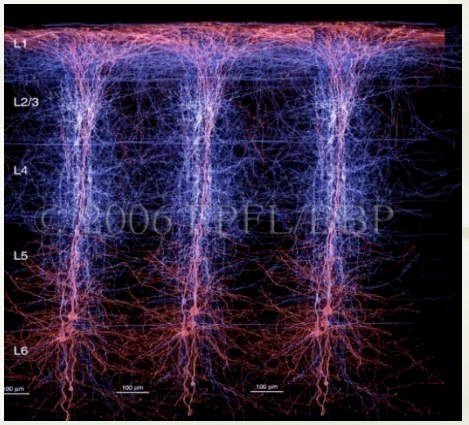
- Data: data provenance, heterogeneous data, analysis of data, network inference from data
- Sensitivity, uncertainty, model invalidation: biodata is notoriously noisy and imprecise – what can we conclude or not conclude about the mechanism?
- High performance computing: scalable algorithms for multicore architectures – petascale will enable MD simulation of macromolecules on millisecond timescale
- Visualization: massive data and relationships, network behavior of 10,000 neurons
- Appropriately trained students

Regional Highlights - Japan

- Kitano Lab (Systems Biology). Kitano is widely regarded as the 'father of systems biology'. Research plan focuses on development of experimental and software infrastructure to accelerate development of the research field
  - Systems Biology Markup Language (SBML) (together with Caltech)
  - Systems Biology Graphical Notation (SBGN)
  - Web 2.0 Biology
  - Connection with Riken next-generation supercomputer effort
  - Funding model: Funded for 10 years, $2 million per year, noncompetitive 'men in black' grant

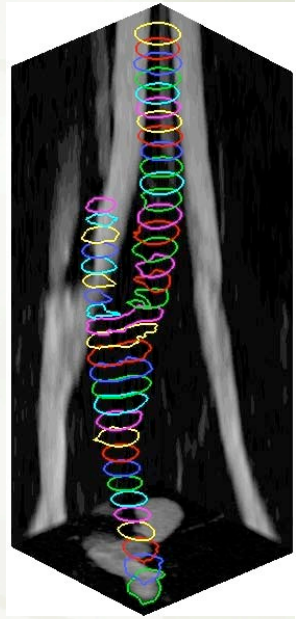
Regional Highlights - Europe

- EPFL Blue Brain Project (EPFL/IBM, Henry Markram). Digital 3D replica of the brain, models in full experimental detail the cellular infrastructure and electrophysiological interactions within the cerebral neocortex.
  - 10,000 neurons of 340 different types; 30 million connections - orders of magnitude larger and in more detail than state of the art in U.S.
  - Development of annotated database of experimental results is a major focus
  - Impressive visualization
  - 35 research/development personnel



Regional Highlights - Europe

- EPFL (Quarteroni). Multifaceted program, strong connections to industry.
  - Models and methods for local drug delivery from nano/microstructured materials : controlled drug delivery with application to drug-eluting stents. Mechanical analysis, analysis of drug release, characterization of material properties
  - Computational fluid dynamics in the cardiovascular system. Multiscale, fluid-structure interaction.



"…Europe is currently acknowledged to be the world leader in a number of aspects of the Virtual Physiological Human, and we hope that by taking heed of the roadmap, European research can gain additional momentum to improve this position further."
(letter from Europhysiome leaders to EU)

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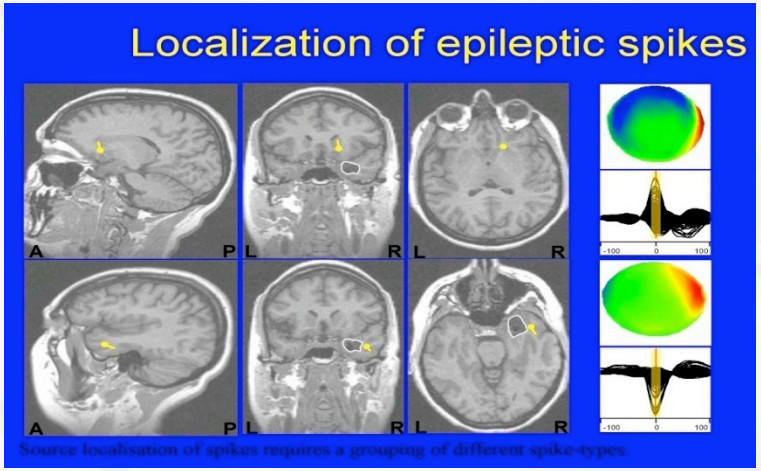
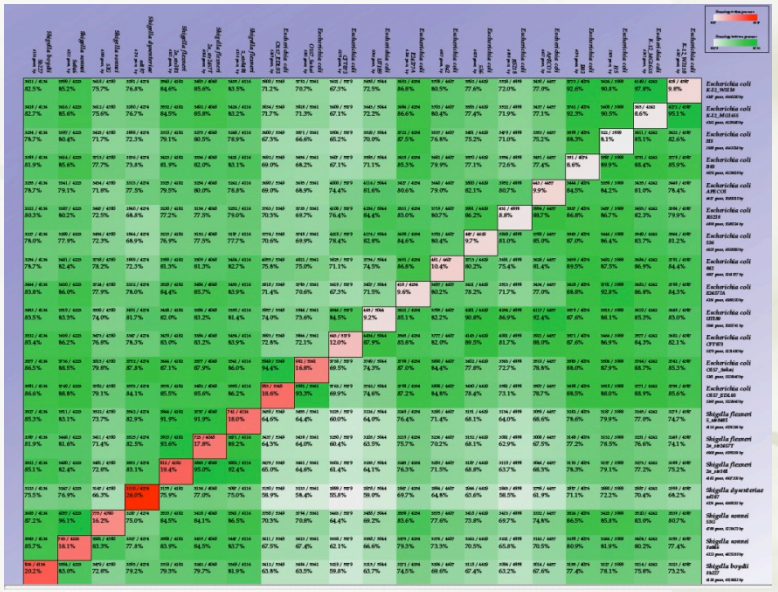
Regional Highlights - Europe

- Vrije Universitat Amsterdam.
  - Systems biology (Westerhoff, Bakker). 'To cure a disease, we must cure the network'.
    - Silicon Cell effort – makes computer replicas of chemical pathways available on the web for in silico experimentation
    - Network-based drug design
  - Brain imaging (J. C. deMunck) EEG and fMRI



Regional Highlights - Europe

- Center for Biological Sequence Analysis (CBS), TU Denmark
  - One of the largest bioinformatics centers in EU
  - Strong teaching component, many courses, some transmitted real-time over Internet
  - Highly popular suite of WWW servers and bioinformatics codes (>2 million visits per month)
  - Strong publications, citations



Outline

- Introduction to SBE&S study
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- Conclusions

Conclusions

- Multiscale modeling
  - Broadly important in SBE&S
  - Cross-cutting across all disciplines
  - Large investment by our research competitors
    - Large integrative group projects with long-term ambitious goals

Acknowledgments

- SBE&S panel members
  - Particularly
    - Sharon Glotzer (overview slides)
    - Linda Petzold (biology)