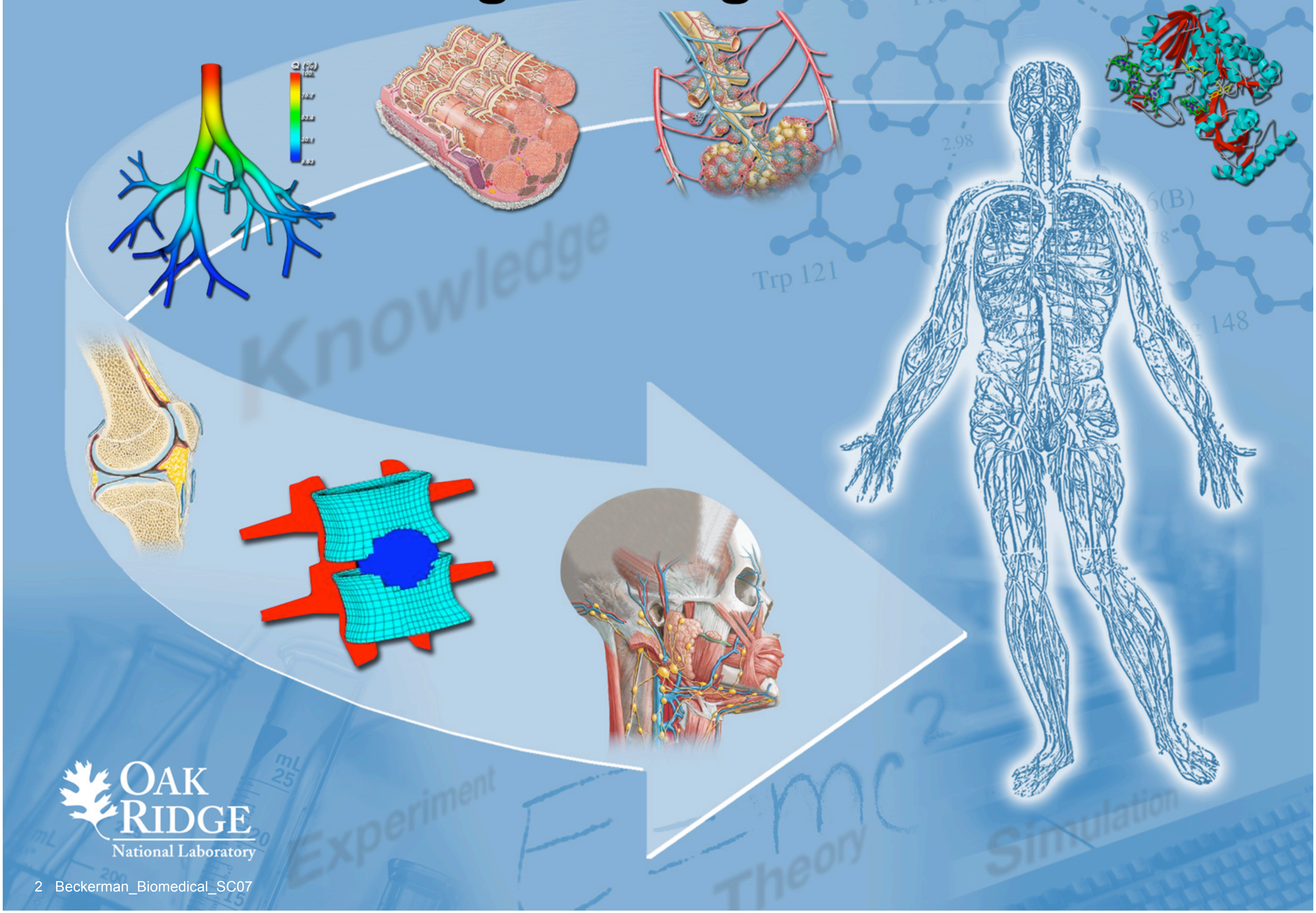
Biomedical Engineering and Biomedical Informatics

Presented by

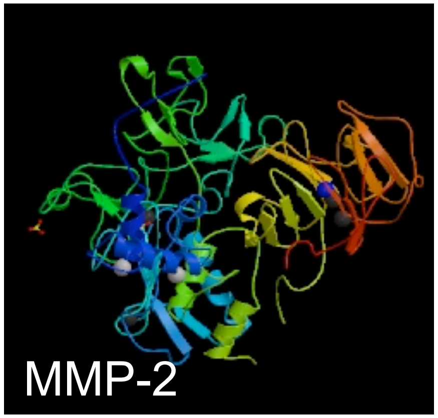
Barbara Beckerman

Modeling and Simulation Group
Computational Sciences and Engineering

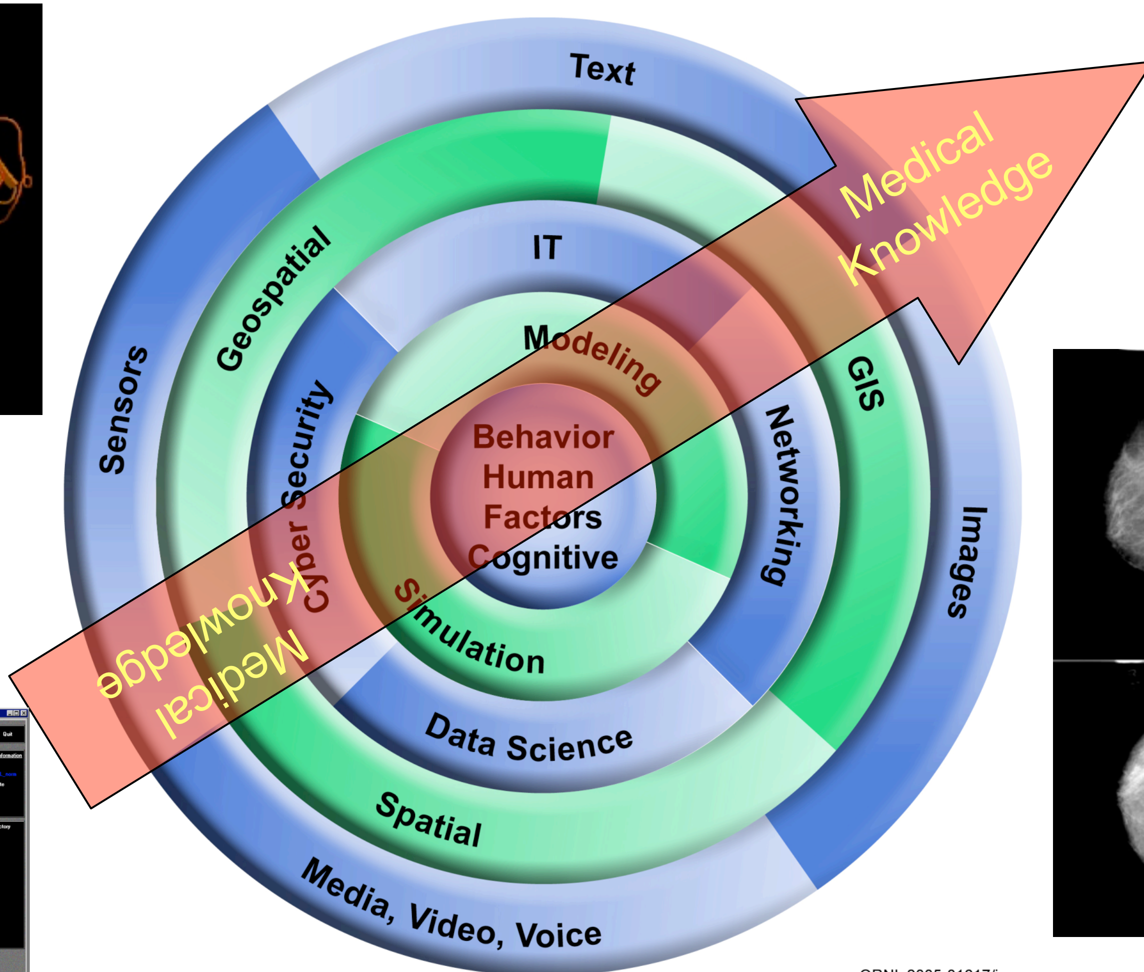
Biomedical engineering and informatics



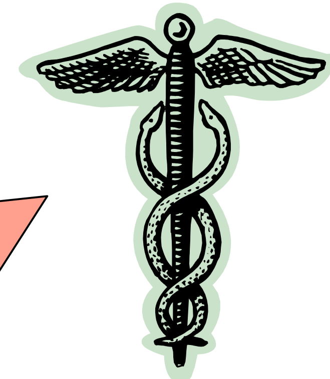
CSED knowledge discovery focus

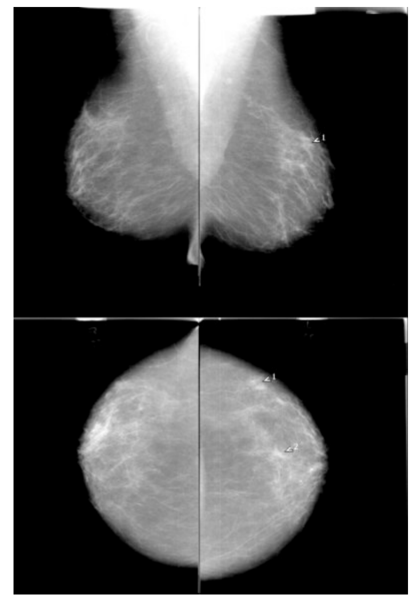


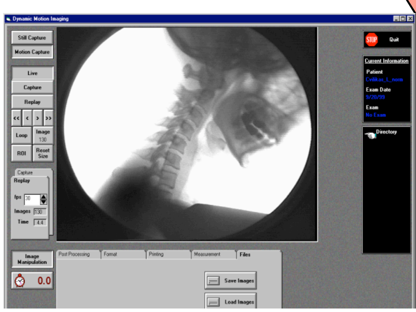
Dynamic Knowledge Discovery



ORNL 2005-01617/jcn







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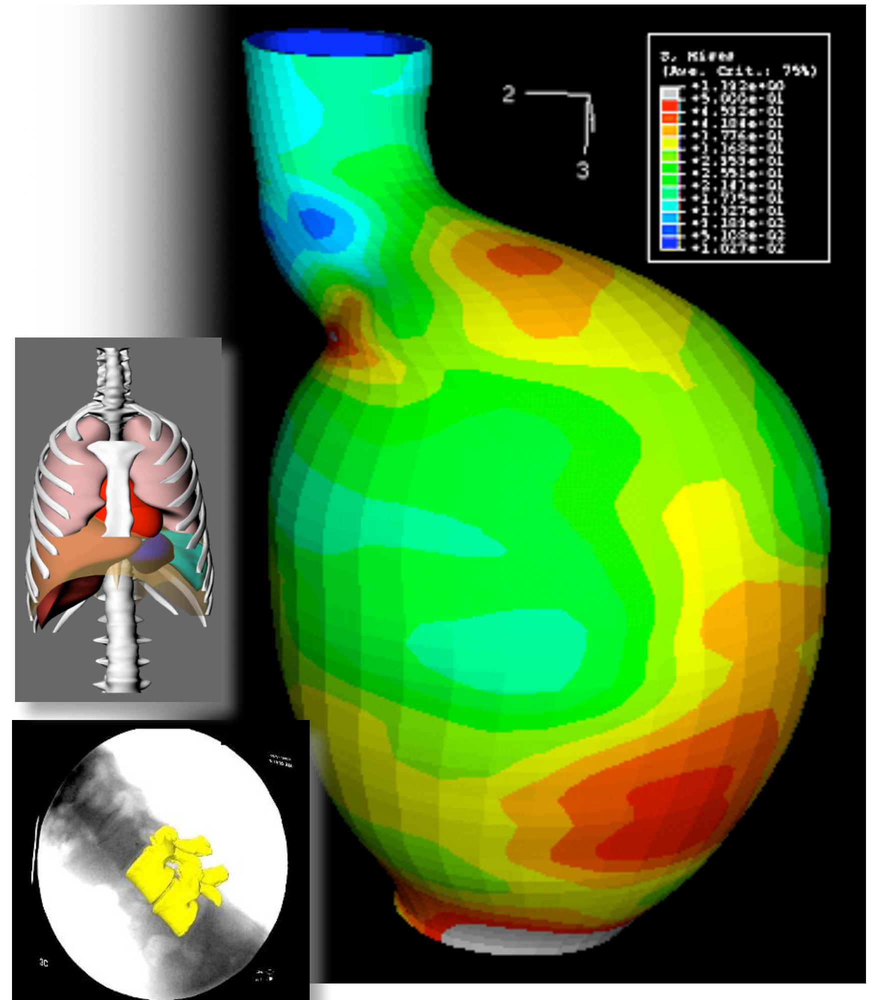
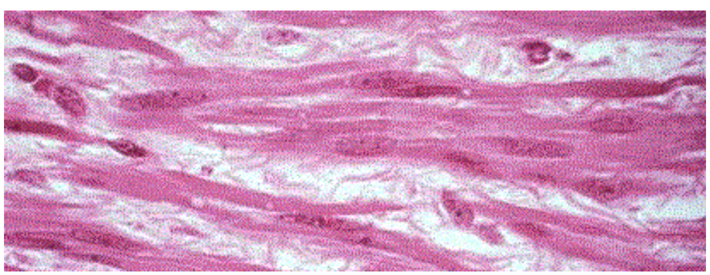
Biomedical engineering and biomedical informatics research at ORNL

- Biokinetic and biotransport modeling
- Three-dimensional organ and tissue modeling using CT or other imagery (pulmonary, arterial, musculoskeletal)
- Prediction of outcomes based on biomedical models
- Knowledge discovery and intelligent agents for data mining and analysis
- Integration of models at multiple temporal and spatial scales
- Computer environments (data repositories, search tools, visualization, etc.) in support of biomedical and medical applications
- Biomedical informatics and telemedicine
- Musculoskeletal Research

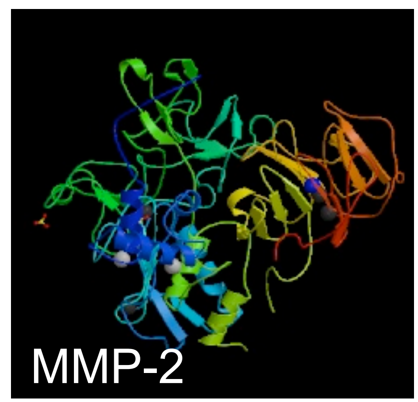


Vascular research at ORNL

- Predicting abdominal aortic aneurysm (AAA) rupture from CT scans
- AAA endoleak experimental and computational studies
- Improving bifurcated AAA geometry models
- Model of MMP-2 & MMP-9 enzyme kinetics involved in vascular disease
- Developing predictive, inductive, mechanistic, and statistical models of vascular pathologies.

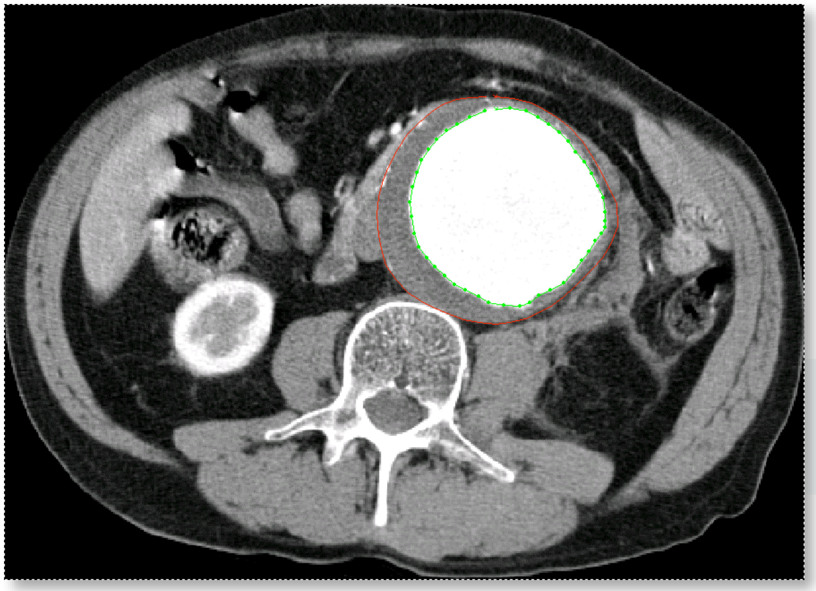


Vascular smooth muscle cells



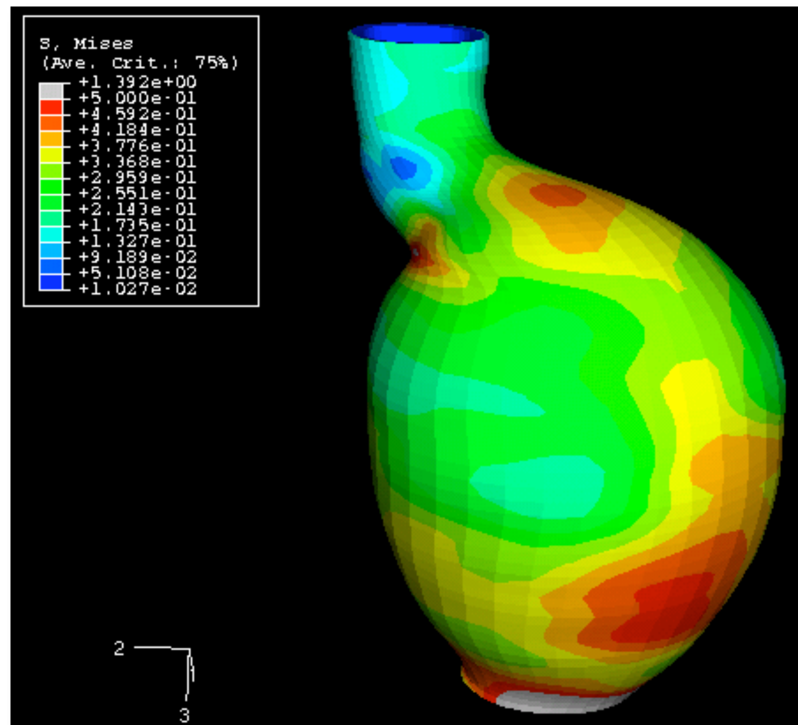
Matrix metalloproteinase enzyme

Finite-element AAA models predict location of rupture



- CT scans utilized to construct geometrical model of AAA.
- Numerical simulations give wall mechanical stress distribution.
- Predict AAA rupture site from stress distribution.

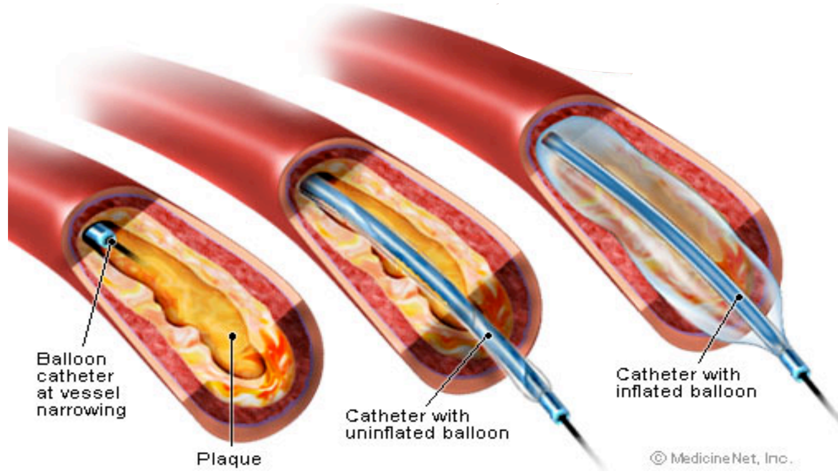
- Collaboration with UT Graduate School of Medicine Department of Surgery and Vascular Research Lab.



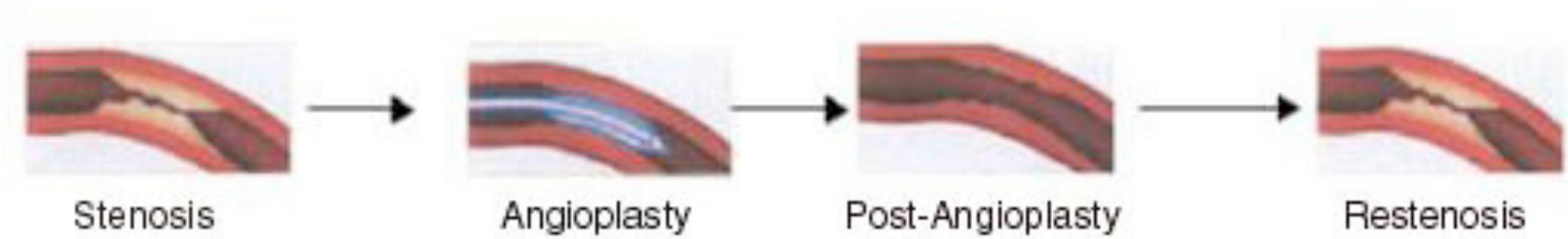
THE UNIVERSITY OF TENNESSEE MEDICAL CENTER

Specific medical problem: cardiovascular treatment may cause restenosis

- Atherosclerosis (hardening of arteries) results from plaque buildup
- Treated by balloon angioplasty with or without stent placement
- Vessel response can be intimal hyperplasia (IH) and/or restenosis



www.medicinenet.com/coronary_angioplasty/article.htm



www.utmem.edu/vascular/injury.lab.htm

Can we predict

- Who will be helped or harmed with balloon angioplasty?
- Does hormone replacement therapy affect outcome?

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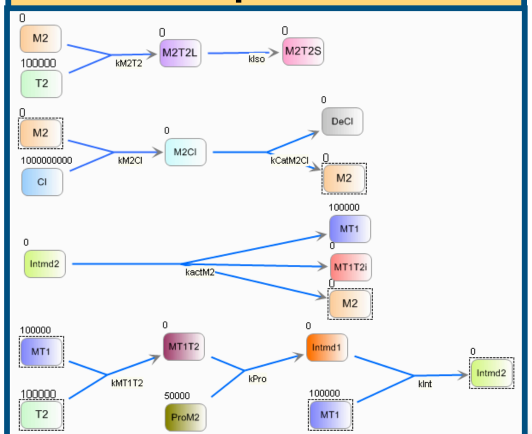
Long-term vision: Predictive modeling to support medical decision making

Hybrid model for predicting patient response



Treatment option 1

Treatment option 2

Treatment option 3

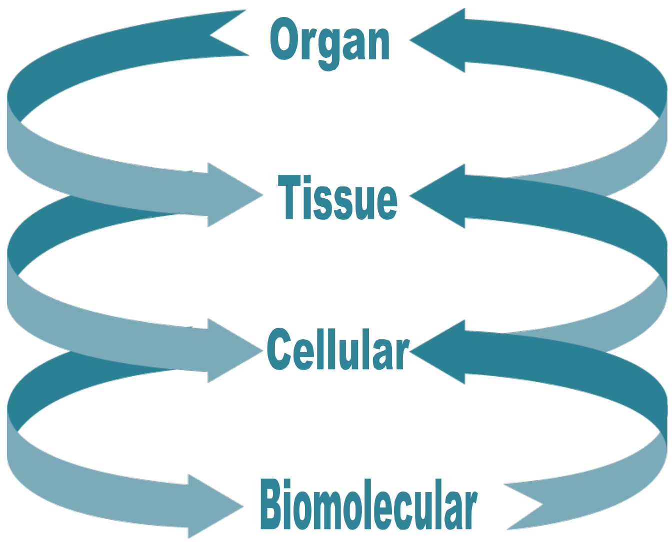
Hybrid model predicts option 2 has best outcome for patient

Predictive multi-scale modeling

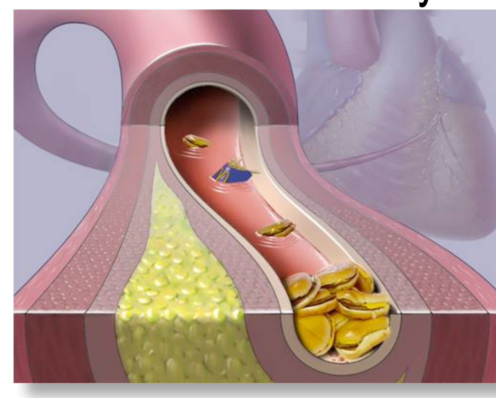
Goal: Predict migration of smooth muscle cells from media to intima due to inflammatory response after injury

Model for predicting vascular disease

- Spatial modeling of cell migration
- Diffusive and kinetic modeling of biochemicals
- Result: A multi-scale hybrid continuous-discrete predictive model for tissue pathology

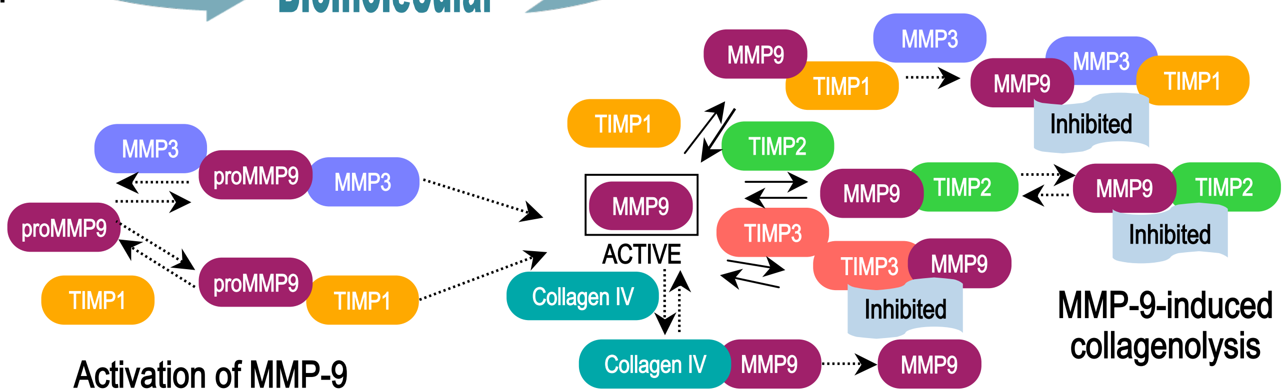


Atherosclerotic artery



R. Conway 2005,
zoologynews.blogfa.com/post-23.aspx

Matrix metalloproteinases (MMPs)



Activation of MMP-9

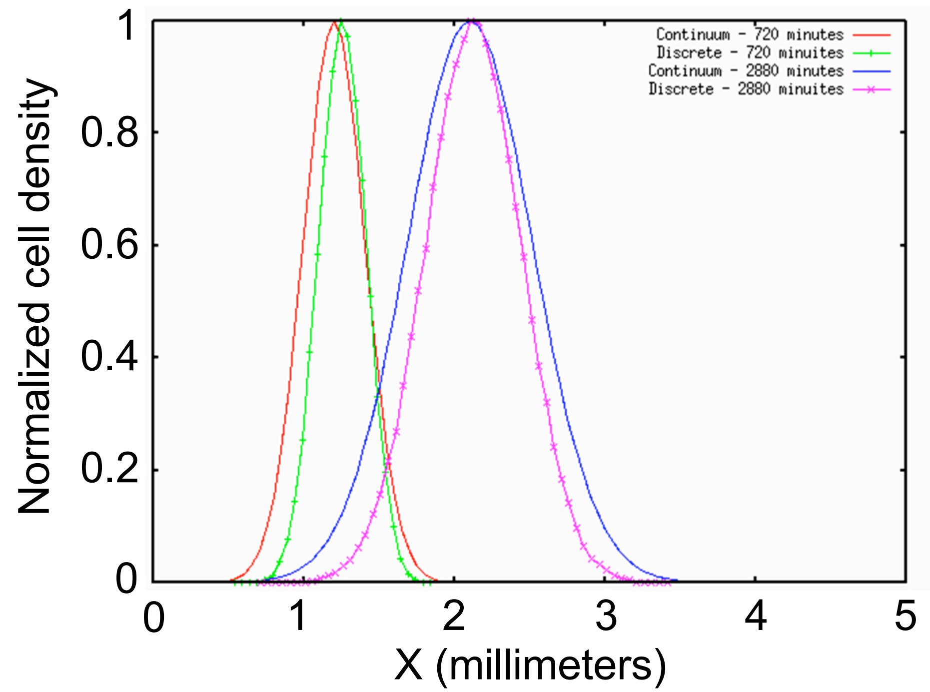
Inhibition of MMP-9

MMP-9-induced collagenolysis

Approach: Hybrid model to provide predictive capability for intimal hyperplasia

- **Discrete Model**
  for cell proliferation, phenotype change, and migration triggered by injury and biochemical response
- **Continuous Model**
  for biochemical inflammatory response to injury

Comparison of cell densities produced by Continuum and discrete migration models



Hybrid modeling combines both into complete approach

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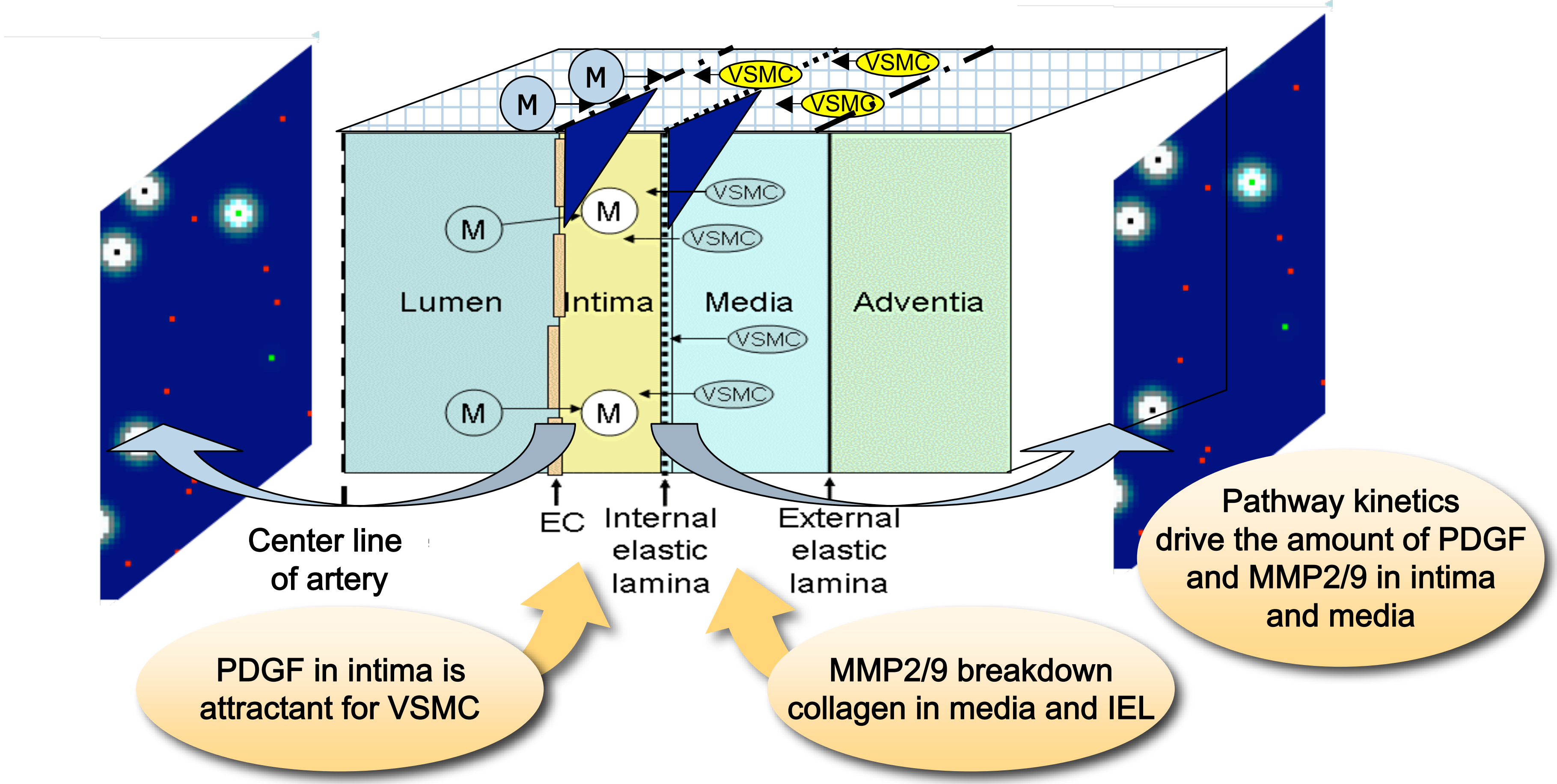
Schematic of hybrid model for intimal hyperplasia



- Build SMC proliferation/migration model
- Add monocyte migration and EC re-coverage
- Add detailed (low-level) enzyme kinetic models for degradation of collagen by MMPs in the media and IEL

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Computational modeling of *in vivo* vascular systems: Collaboration with UT Graduate School of Medicine

Mammalian models

Dorsal view

Ventral view

Thoracic and neck vasculature seen in the microCAT scanner using the vascular contrast agent Fenestra VC

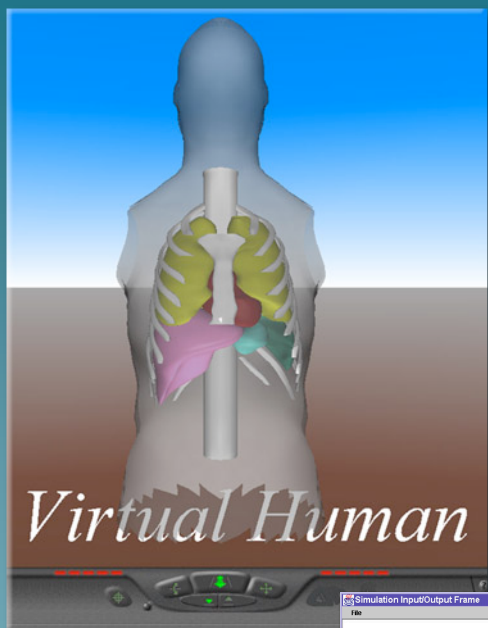
(Images courtesy of J. Wall, University of Tennessee Graduate School of Medicine)

Computational models

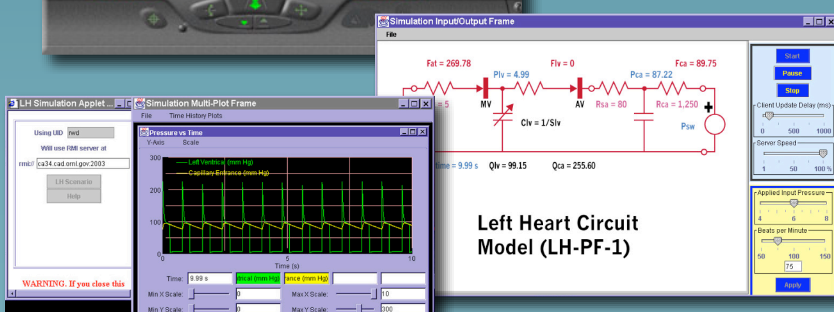
- Metrics for tissue anatomy
- Temporal measurement of lumenal diameter
- Imaging of vascular wall perturbations after injury due to balloon angioplasty
- Biological modeling and simulation environments (cellular, tissue, and multi-scale kinetics models)
- Discrete event simulations to predict results of vascular wall injury

Cardiovascular modeling environments

Integrate



- Models
- Computations
- Visualization
- Predictions



Connect

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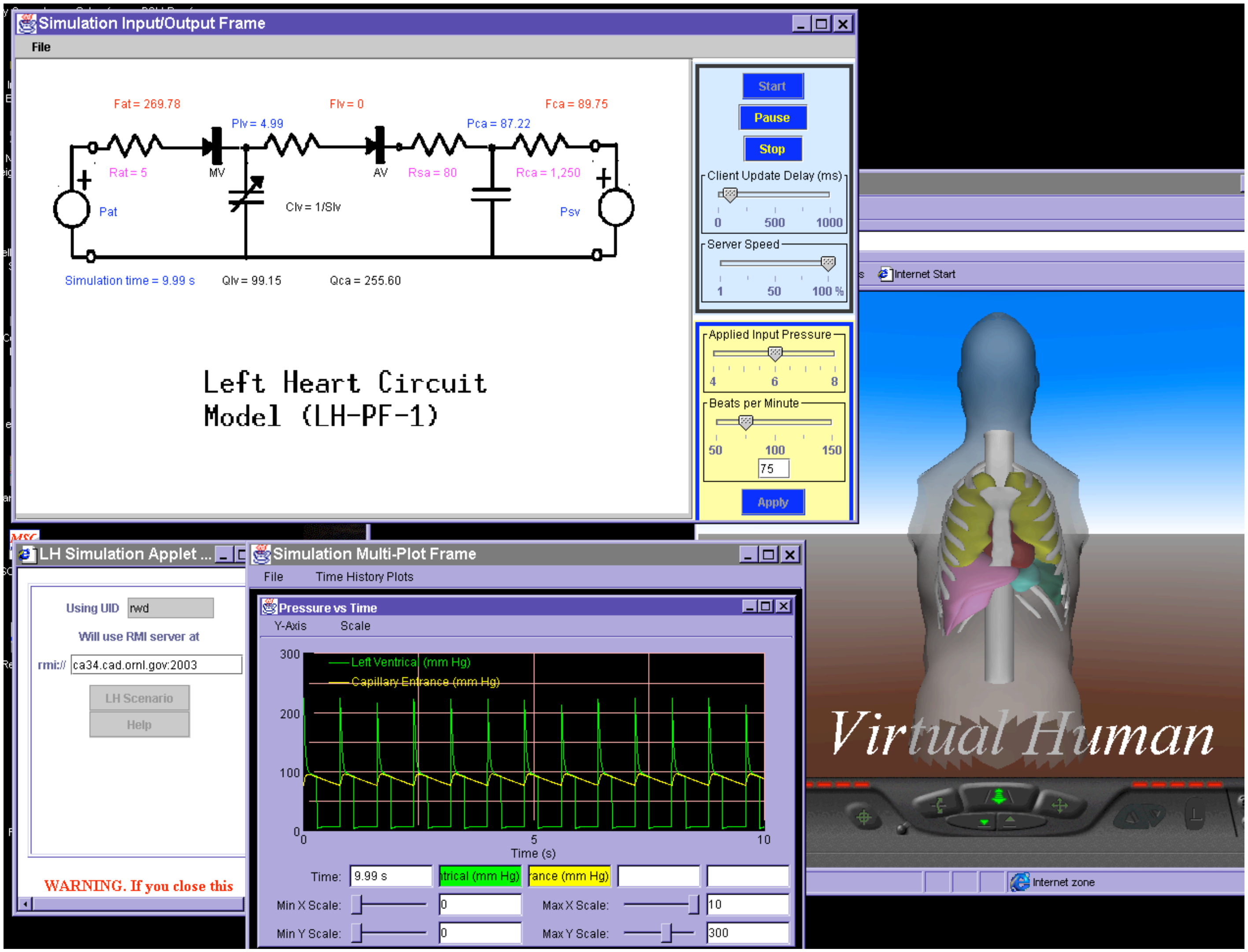
Virtual Human pioneered development of medical problem-solving environments



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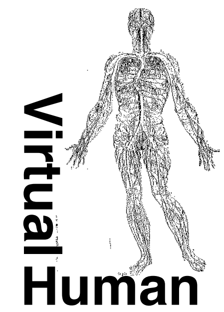
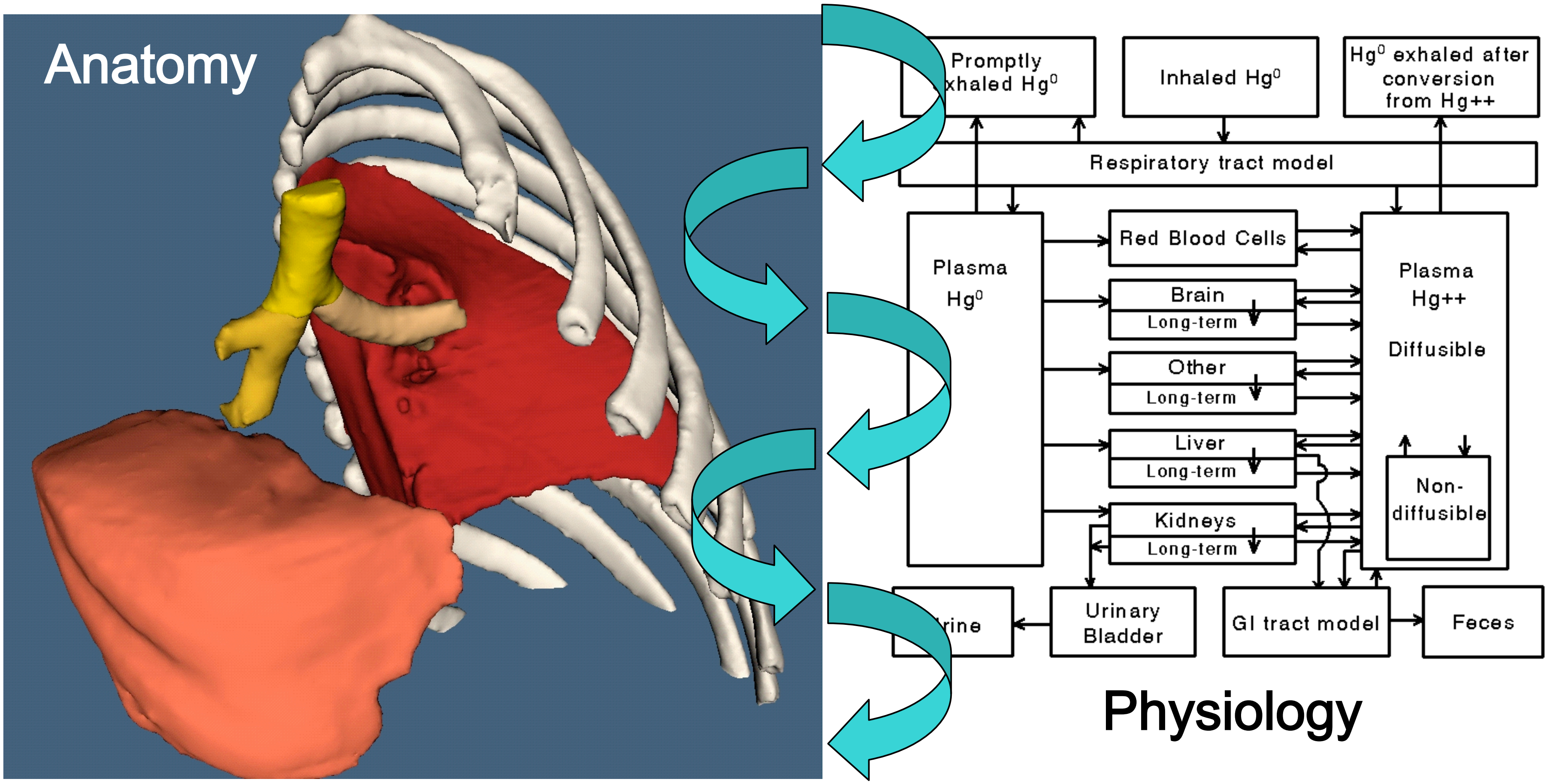
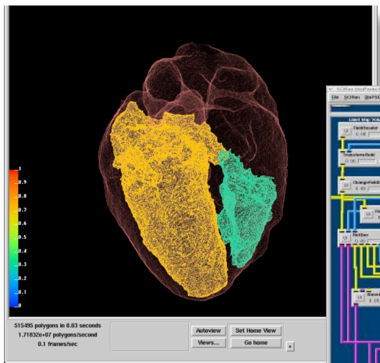
Virtual Human—Bringing together anatomy and physiology



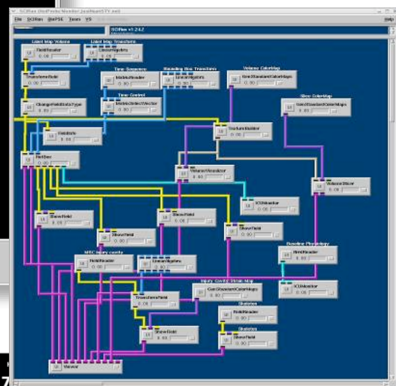


ORNL HotBox integrates all the DARPA Virtual Soldier windows

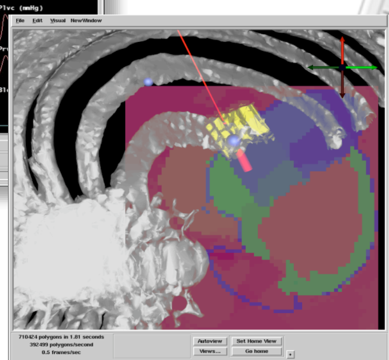
Predicted location of wound



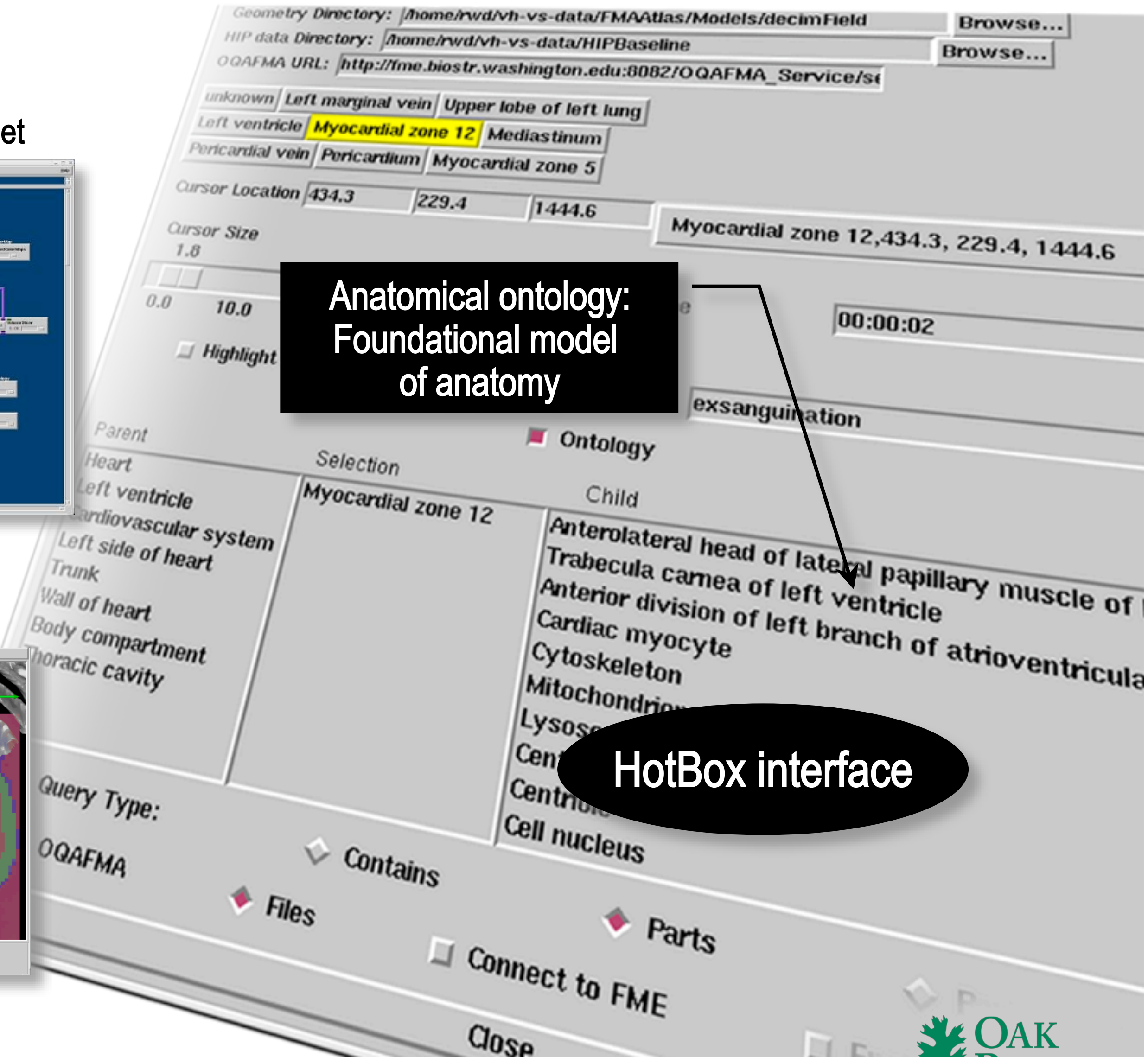
SCIRun Net



Physiology display



Geometry window with thorax model



Joint ORNL/UT Center for Musculoskeletal Research

Center for Musculoskeletal Research

- Joint Center
  - Oak Ridge National Laboratory
  - University of Tennessee
- Focused on biomedical research
  - Musculoskeletal Research
  - Orthopaedic Research
- Researchers and surgeons: As a team
- Richard D. Komistek, Ph.D.—Director

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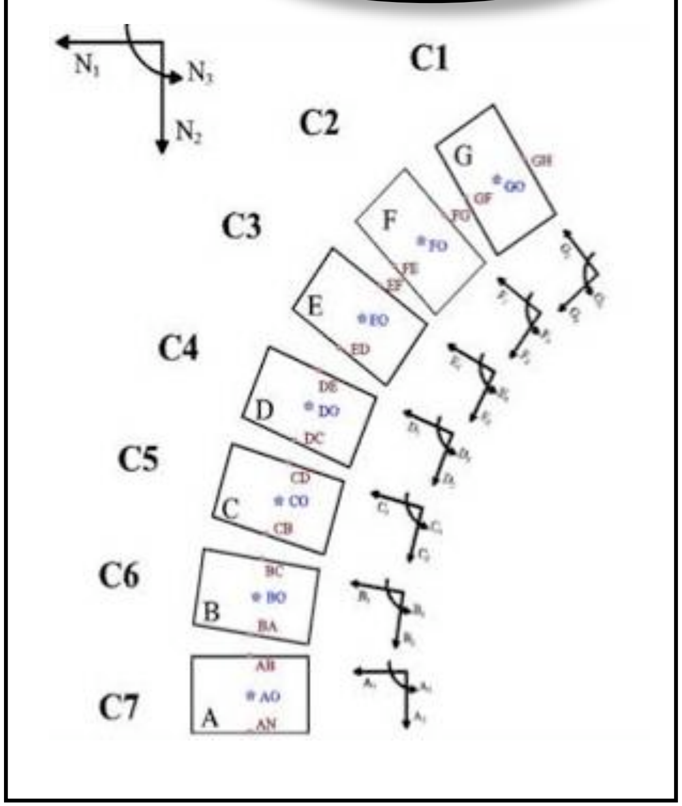
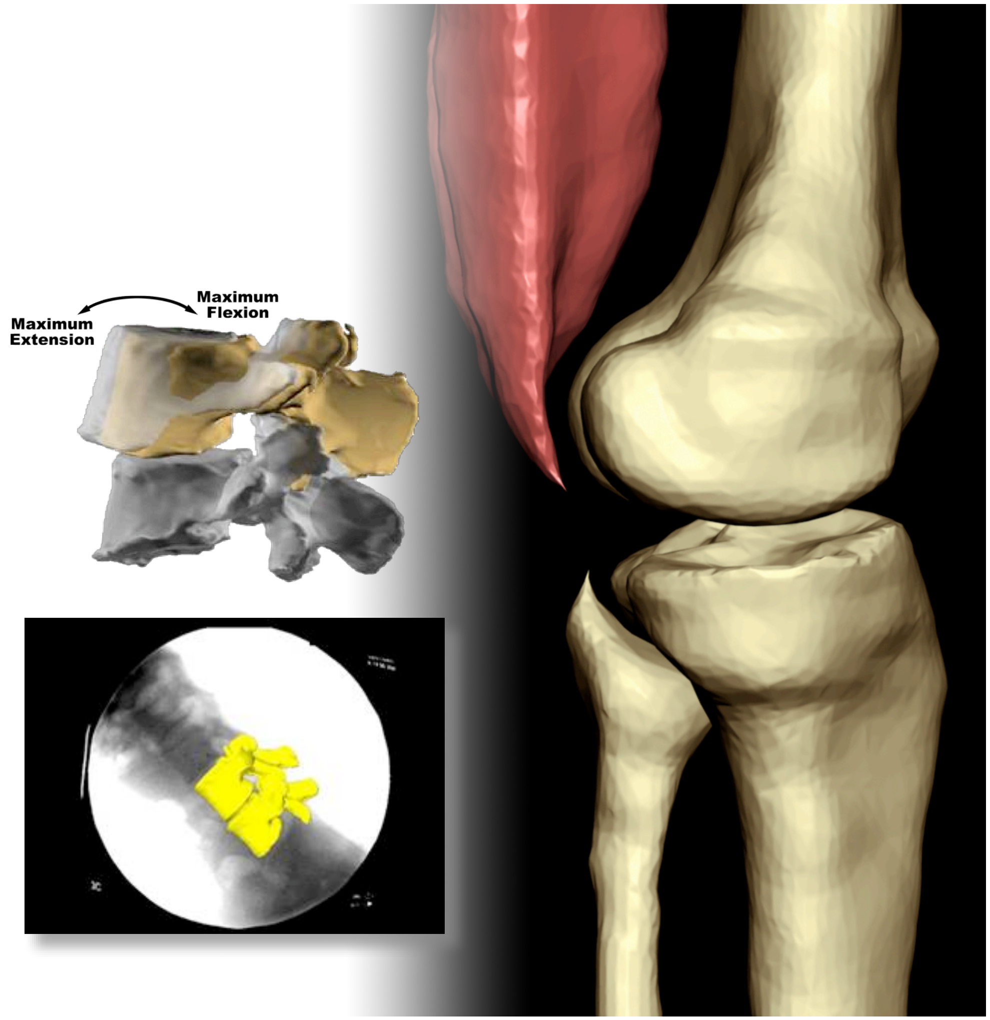
Orthopedics research at UTK/ORNL
Dynamic and kinematic models of motion for knees, hips, and spine

Cervical Spine Dynamic Model





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Mathematical model

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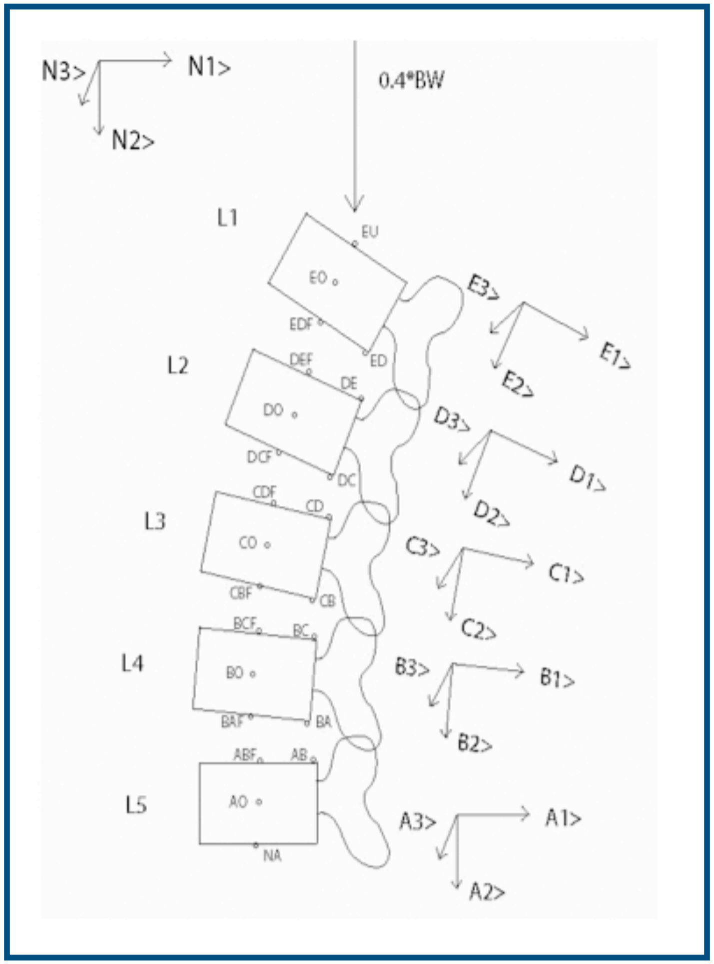

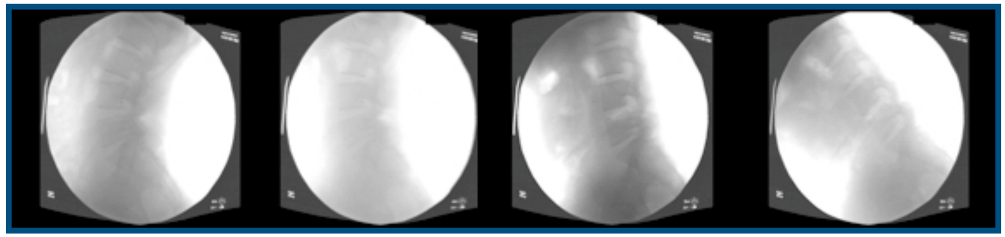

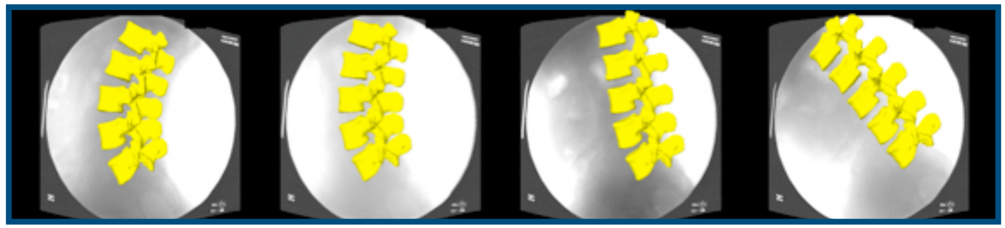

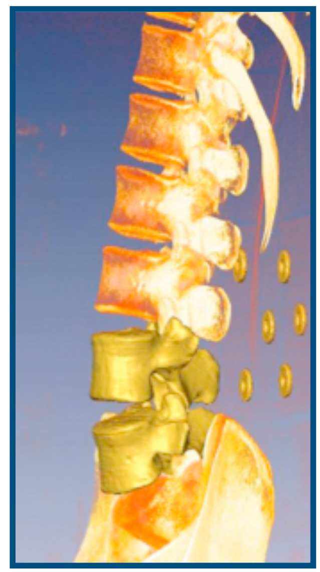

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Biomedical Engineering Program:
Innovative tools for *in vivo* computational prediction of lumbar stresses

- NIH/National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) 1R01AR05582-01A1
- Value: ~$1.7 million, four years, beginning September 2007
- Interdisciplinary team: ORNL (lead institution), University of Tennessee, Vanderbilt University
- PI: Richard Komistek, Ph.D. (ORNL/UT CMR)
- Co-PIs:
  - Mohamed Mahfouz, Ph.D. (ORNL/UT CMR)
  - Joseph Cheng, M.D. (Vanderbilt)
- ORNL researchers: B. Beckerman, P. Nukala, R. Ward

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Specific aims

Develop an accurate computational methodology that could eventually be used to predict *in vivo* contact stress at the bearing surface interfaces, ligament forces that provide constraint, and muscle forces (and tendons) of the vertical bodies of the lower back. This model would allow for assessment of surgical outcomes in terms of reduction of pain after fusion or disc replacement surgery.

- Develop and implement innovative kinematic tools that can be used as input data for computational models
- Apply innovative computational modeling tools to more accurately determine the *in vivo* forces and torques on the spine
- Develop a constitutive model for computational modeling of intervertebral discs
- Develop computational models for *in vivo* analysis of the lumbar spine structure
- Create a methodology for data correlation and assessment that can be used by clinicians to diagnose pain associated with the lumbar spine and the location of the pain

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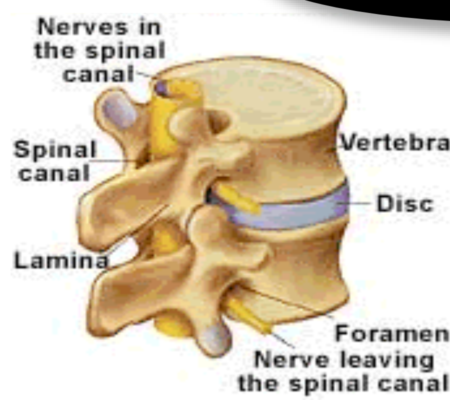
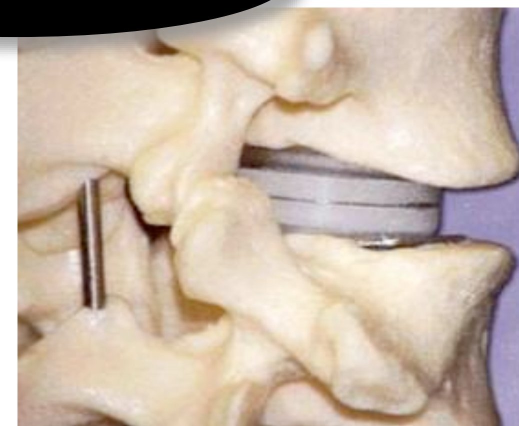
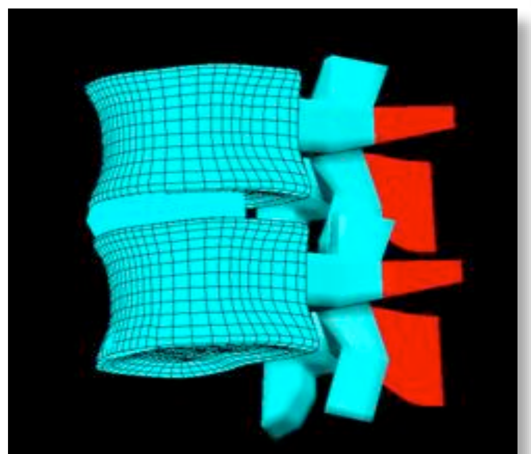
Computational modeling of pre- and post-operative lumbar spine system

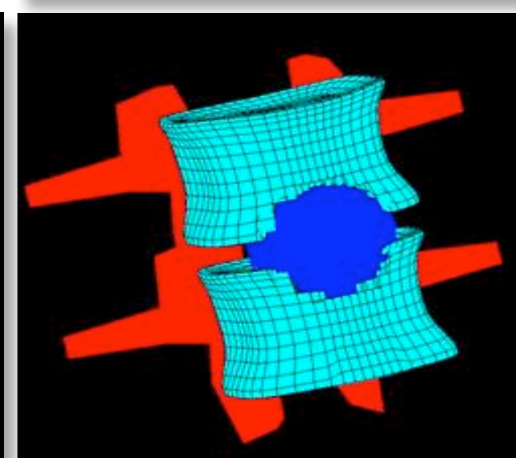
- *In vivo* imaging and analysis of lumbar spine system (Komistek, Mahfouz)
- Finite-element mesh models of the spine (Nukala)
- Constitutive modeling of intervertebral discs (Nukala)

Two vertebrae and a disc









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Biomedical Applications for the Next-Generation Internet (NIH/NLM)*

*Funded by National Library of Medicine – NLM-N01-LM-0-1-3512 and LM-0018-01 (1998–2003);
PI—Mitch Schnall, University of Pennsylvania; Co-PI/Technical Director —B. Beckerman, Oak Ridge

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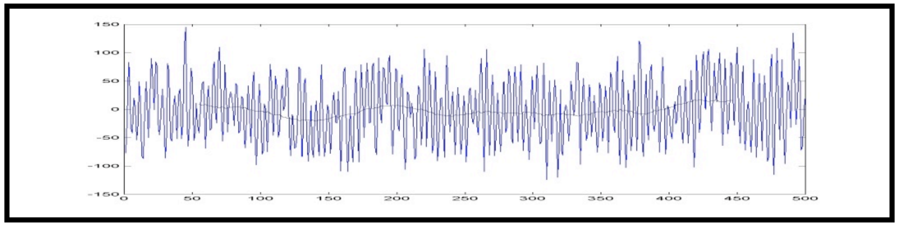
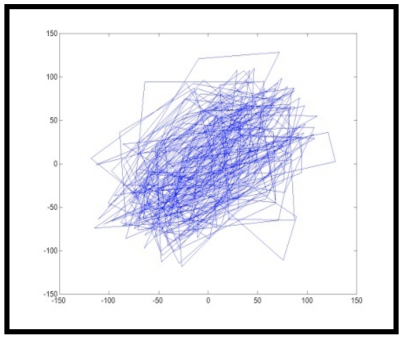
Time serial data: Medical diagnosis and event forewarning

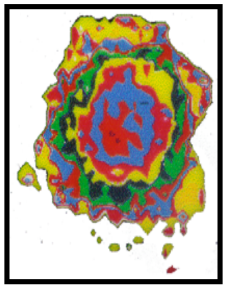


EEG data describing epileptic seizure

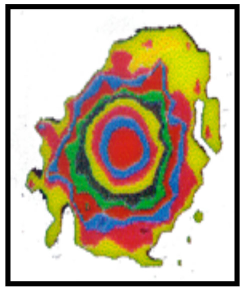


Phase space

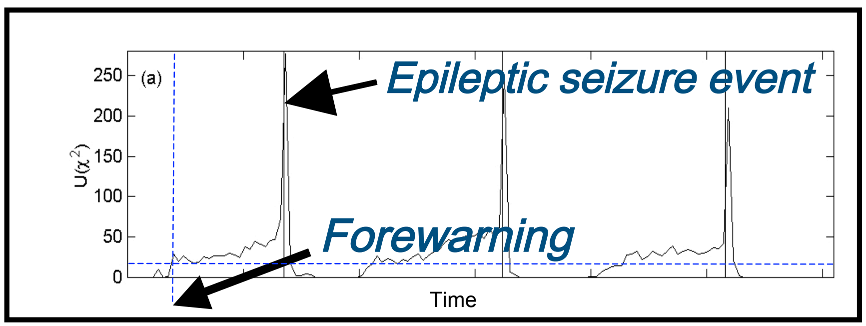
Normal

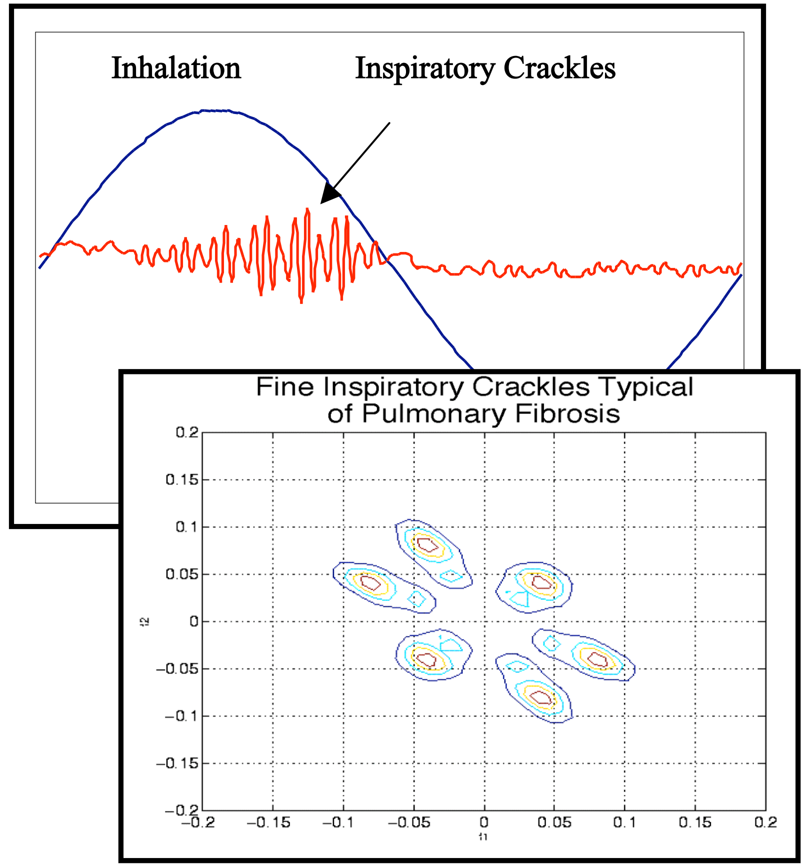


Preseizure



PS distribution function





MSG classified pulmonary fibrosis using inspiratory crackles and higher order spectral analysis

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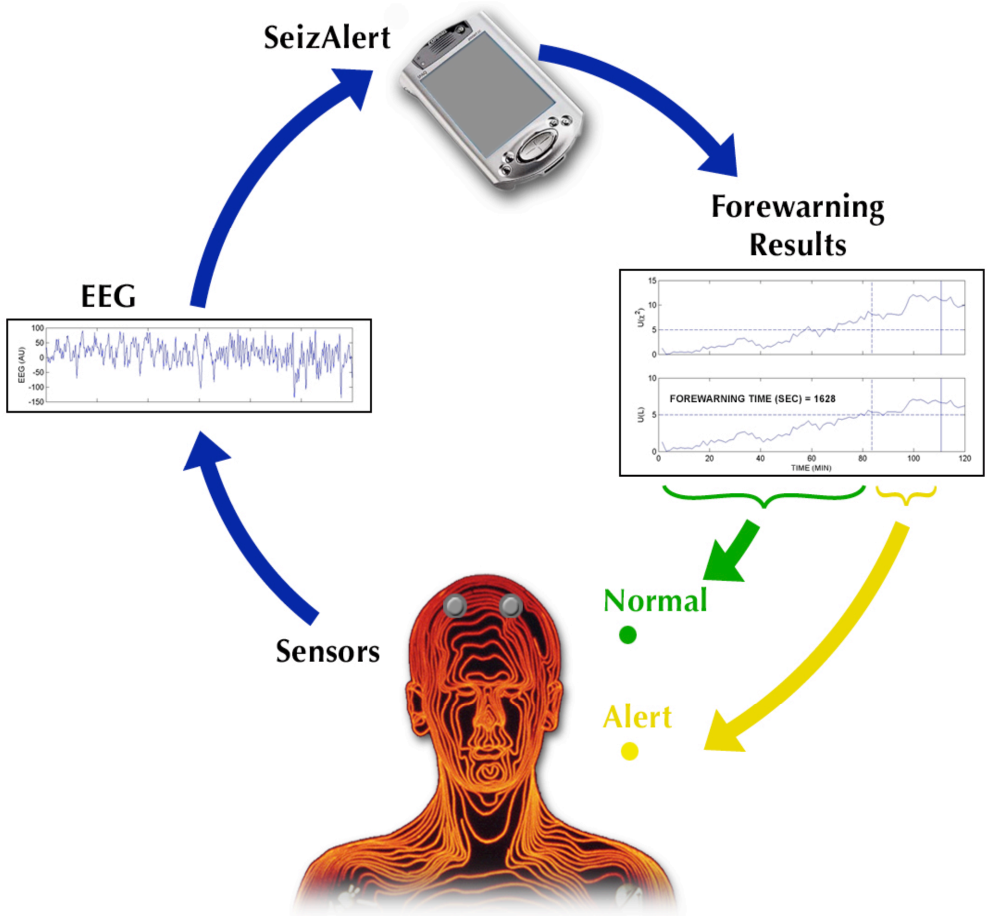
Seizalert on PDA: 2005 R&D 100 award*

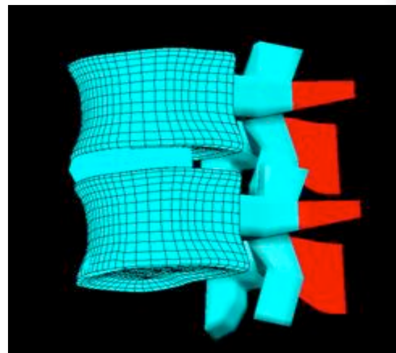


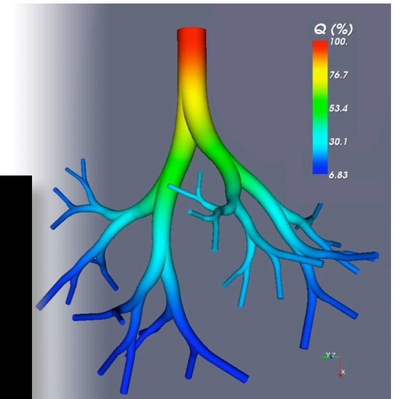
- Non-linear analysis approach predicts onset of epileptic seizure
- Implemented in software on a PDA or wearable device to alert wearer to occurrence of seizure
- Protected by five patents and two pending
- Licensed to Hercules Development Corporation

*Hively, Protopopescu, Munro, Kruse (2005)

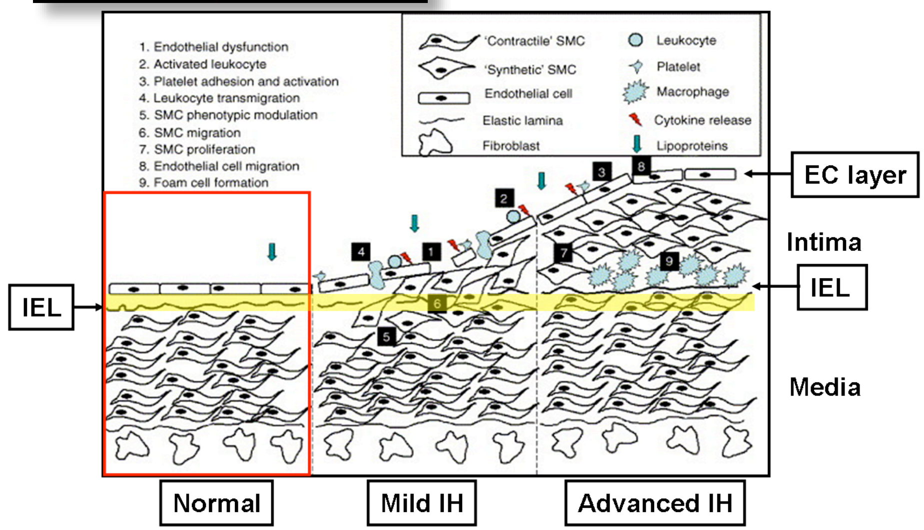
Summary of biomedical problem-solving

- Intimal hyperplasia
- Abdominal aneurysms
- Prediction of wounds, wound healing
- Data repositories
- Parallel computations
- Computational tools for toxicants
- Agent technologies
- Ontologies and informatics





www.erc.montana.edu/biofilmbook/MODULE_07/Mod07_S04-4_Blue.htm

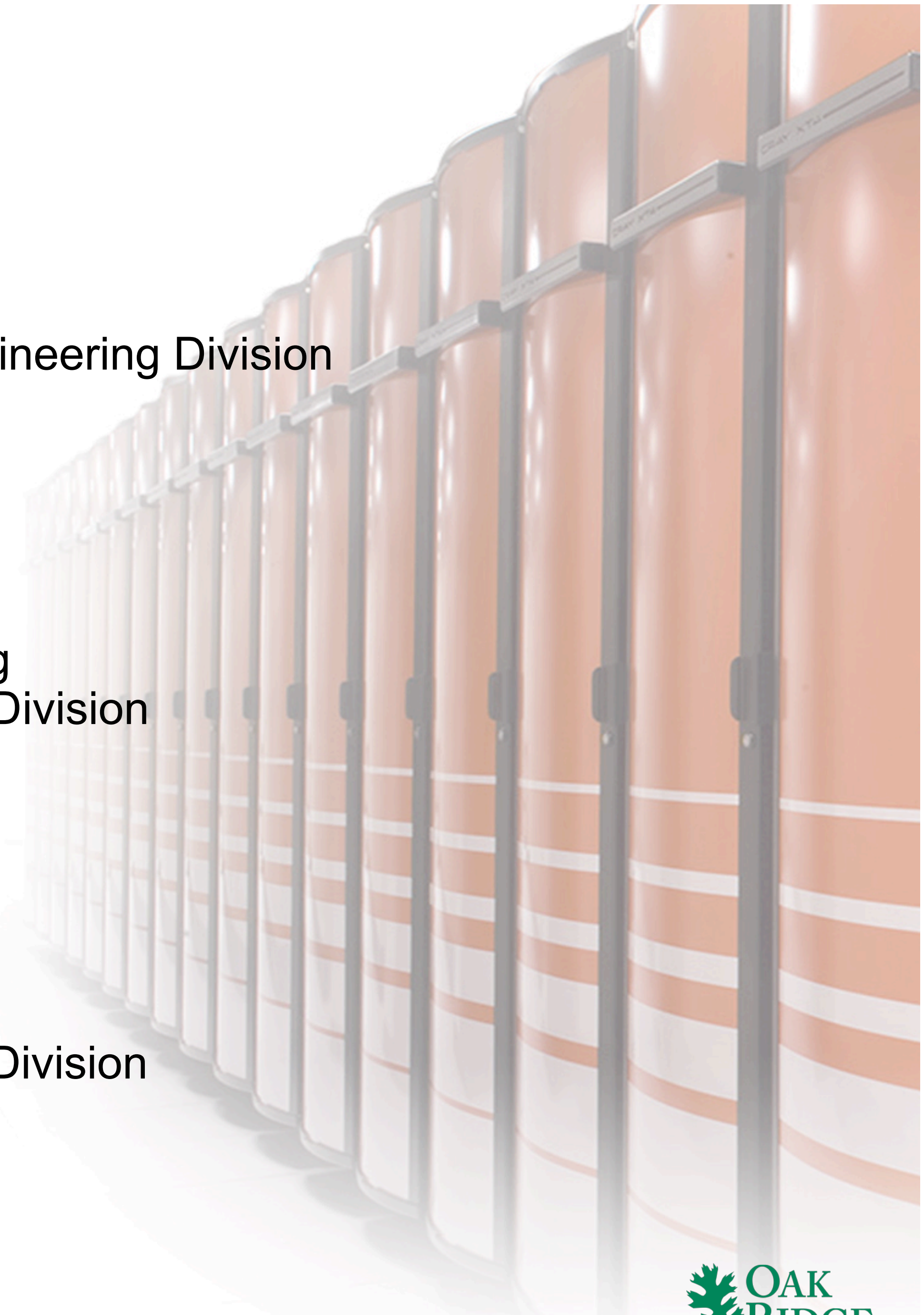


Adapted from: B. E. Rolfe, N. F. Worth NF, C. J. World CJ, J. H. Campbell, G. R. Campbell, “Rho and Vascular Disease”, Atherosclerosis 183 (1): 1-16 NOV 2005

Future directions

- Wound healing
- Bone biology
- Tissue engineering
- Biomedical imaging (cellular and systems biology, 3-D microscopy, in vivo imaging to support computational model development)
- Women's health (biomedical informatics)
- Non-linear dynamics and analysis (pulmonary medicine, sleep disorders, brain functions)
- Visualizations of complex biomedical problems

Contacts



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