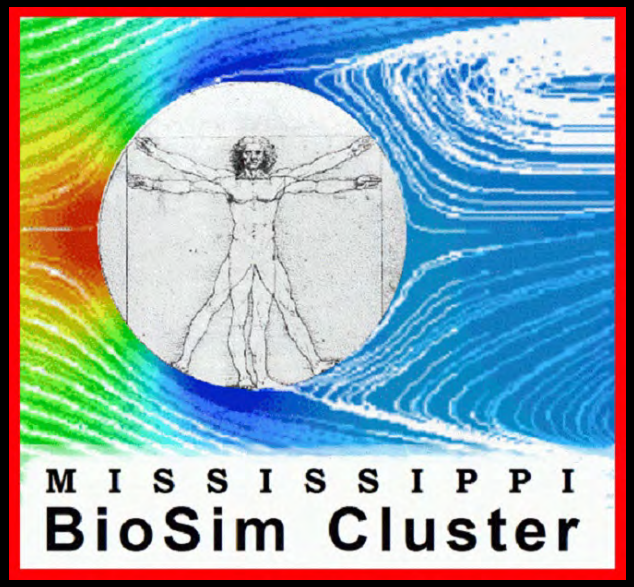
Research Area: BioSim

Multi-Scale Simulation Framework for Biological Systems



University Participants:

Mississippi State University

Jackson State University

University of Mississippi Medical Center

Senior Personnel

Shahrouz Aliabadi, JSU
Mohammed Ali, JSU (Seed Grant Collaborator)

Greg Burgreen, MSU
David Thompson, MSU
Keisha Walters, MSU
Keith Walters, MSU

Thomas Coleman, UMMC
Robert Hester, UMMC
Radu Iliescu, UMMC

BioSim Cluster Long-Term Goals

1. Develop nationally recognized and respected multi-institutional programs of excellence in biosystem simulation.
2. Develop nationally recognized expertise in multi-scale modeling for biological simulations.
3. Develop accurate models of physiological behavior and apply those models to realistic biosystem problems having clinical significance.

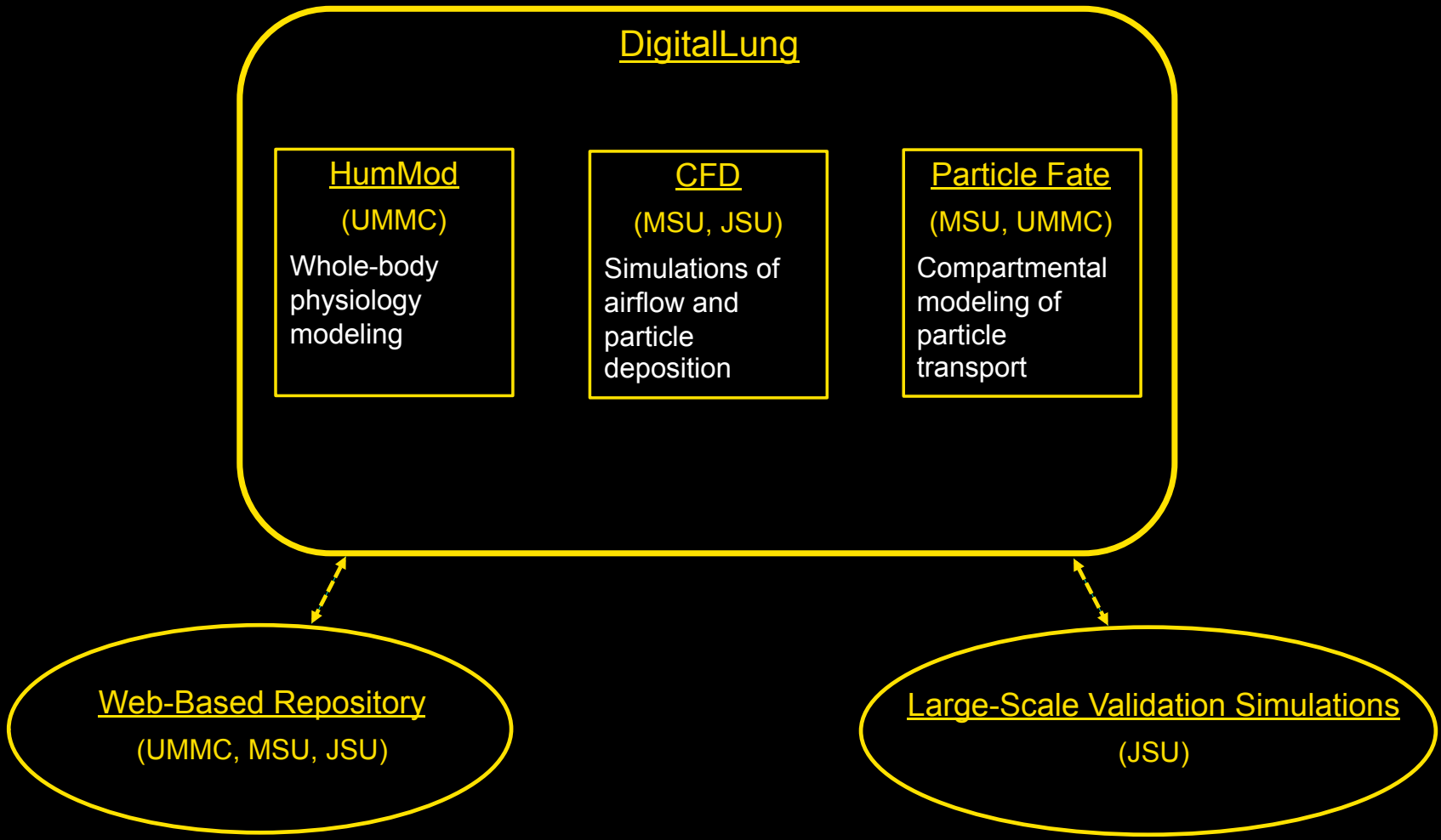
Objectives of Current RII

1. Establish new intra- and inter-institutional teaming arrangements among investigators from multiple disciplines, with a focus on computational modeling and biological systems, and strengthen existing collaborations.
2. Develop a multi-scale simulation framework for investigating human biological processes that integrates multiple simulation and modeling methods into a single analysis tool.
3. Develop and enhance cyber-infrastructure tools for coordination of research activities and for dissemination of results and newly developed software tools to be used for research, education, and training.

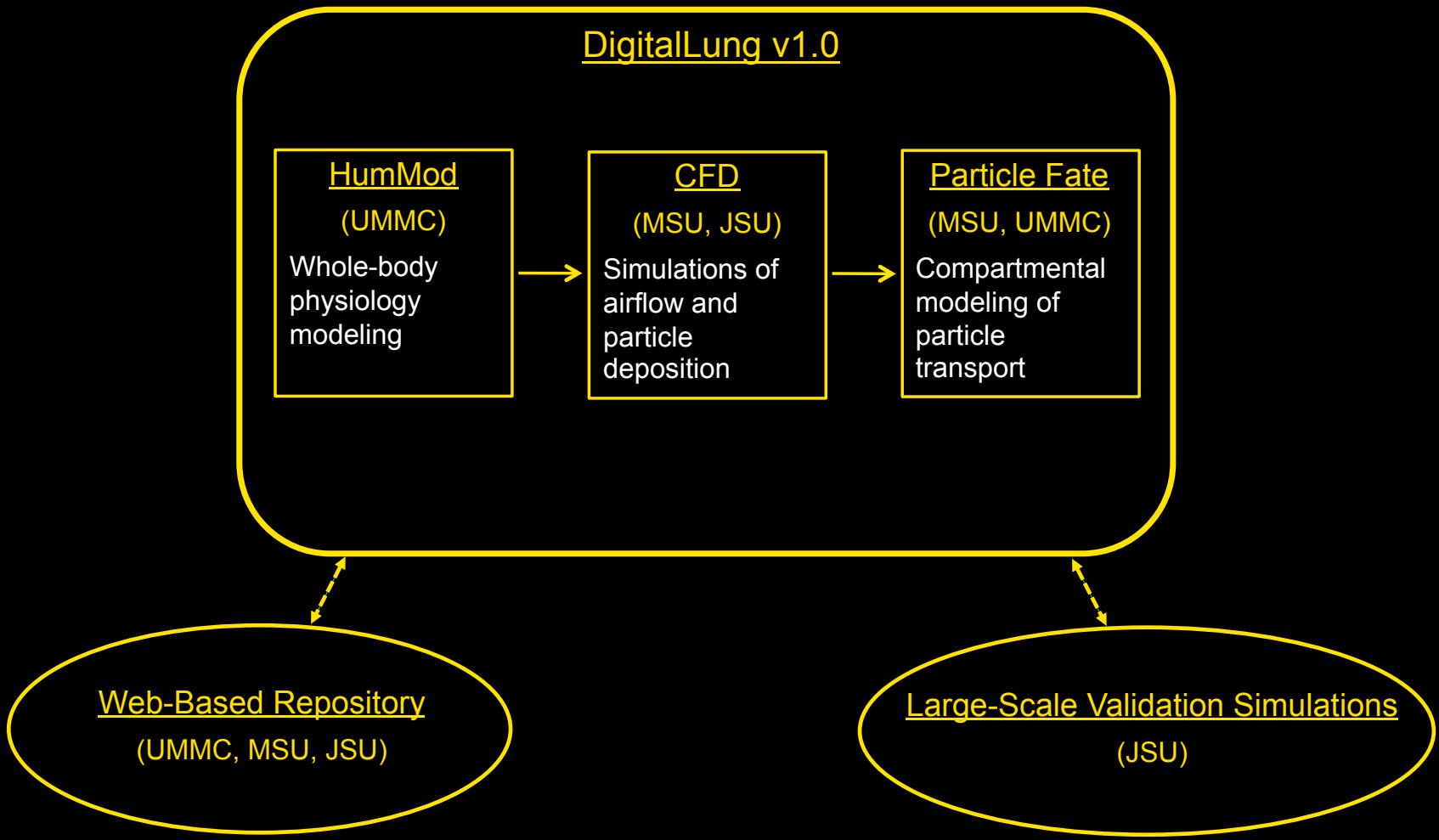
Technical Approach

1. Driven by directed research
   - Real-world applications should actively drive our basic research.
2. Focus on interdisciplinary research
   - Combine High Performance Computing (HPC) results with desktop-based results (multi-architectural)
   - Combine high-fidelity simulations at *structure to organ* level with macro-scale models at *system to organism* level (multi-scale)
3. Initial application of multi-scale methodology: DigitalLung
   - Predictive modeling of particle inhalation, deposition, and physiological impact
   - Multilevel Integrative Model of Human Physiology
   - Fluid Dynamics Simulation of Lung Respiration and Meso-Scale Particle/Aerosol Deposition
   - Compartmental Modeling of Post-Deposition Particle/Chemical Fate

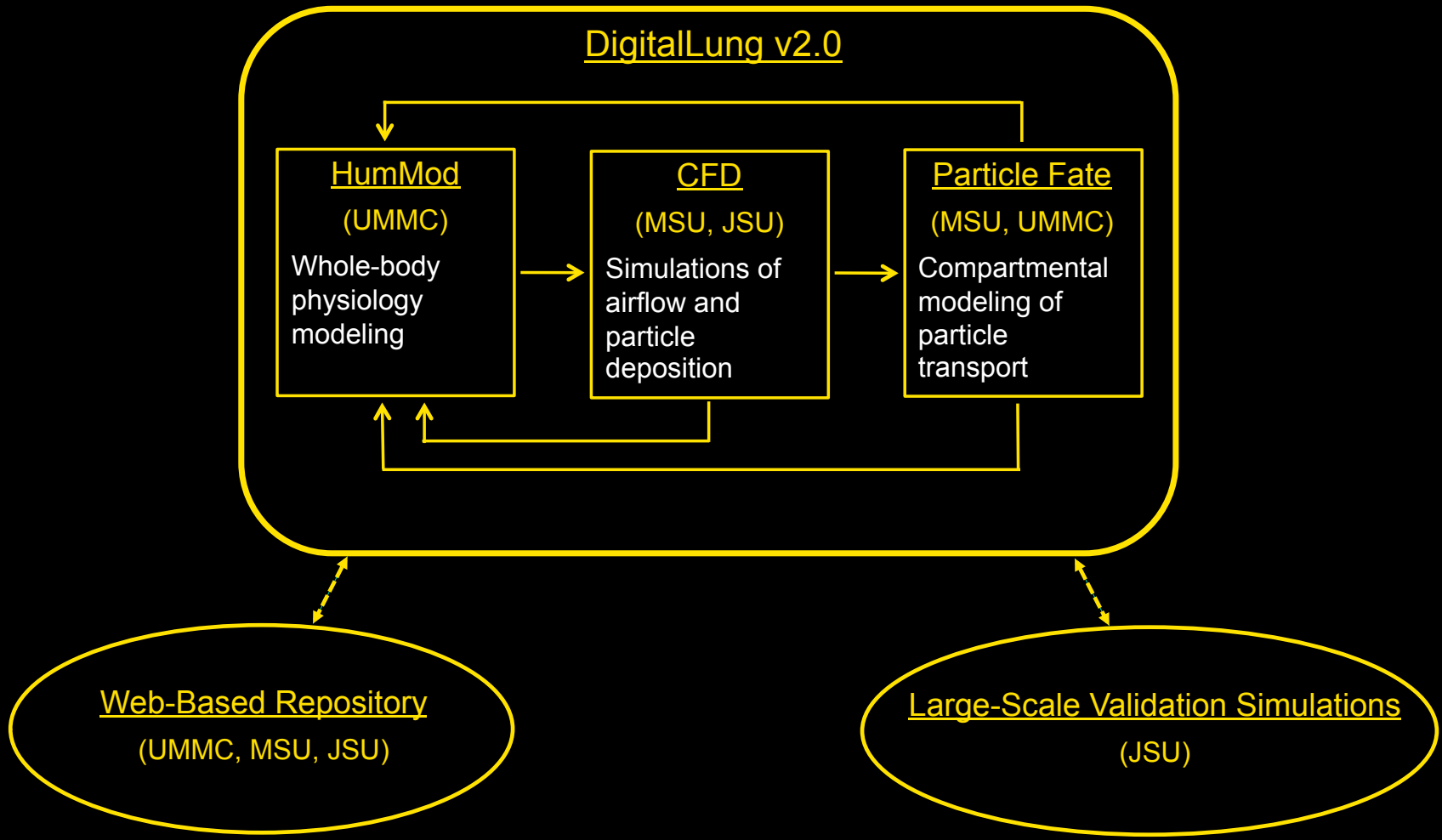
Technical Organization



Technical Organization



Technical Organization



Technical Organization

Cross-Cutting Research Activities

Summary of 2009-2010 Accomplishments

1. Eight (8) archival publications arising directly out of the EPSCoR project
2. Four (4) conference proceedings papers and/or posters arising directly out of the EPSCoR project
3. Seven (7) presentations at conferences and workshops on EPSCoR activities
4. Ten (10) proposals submitted totaling $19.1 M
5. One (1) proposal awarded totaling $800K
6. Eight (8) graduate students and research associates supported
7. Nine (9) undergraduate researchers supported

BioSim Highlights

- David Thompson (MSU) and Keisha Walters (MSU) were inducted into the Bagley College of Engineering Academy of Distinguished Teachers.
- David Thompson is vice-chair (chair elect) of the American Institute of Aeronautics and Astronautics Meshing, Visualization, and Computational Environments Technical Committee
- Keith Walters is vice-chair (chair elect) of the American Society of Mechanical Engineers Fluids Applications and Systems Technical Committee
- Greg Burgreen (MSU) will be a speaker in the upcoming NIH/FDA/NSF sponsored Workshop on Computer Methods for Cardiovascular Devices
- Keith and Keisha Walters to present paper on EPSCoR funded outreach activities at the American Society of Engineering Educators national conference, June 2010.
- Robert Hester (UMMC) was selected as Chair of the Cardiovascular Section of the American Physiological Society
- Shahrouz Aliabadi (JSU) is organizer and scientific committee member of Parallel CFD Conference in Taiwan, May 2010.
- A PhD graduate of the EPSCoR program (Bela Soni, MSU) is currently employed as a Post-Doctoral Research Associate at the Northrop Grumman Center at JSU.

DigitalLung Research Components

Automated Geometry and Mesh Generation of the Bronchopulmonary Tree

Realistic Geometrical Modeling of Upper Lung Airways

Air Flow and Particle Deposition (CFD) Simulations in Bronchial Airways

Reduced Geometry Modeling (CFD) of Lower Lung Airways

Efficient Parallel Algorithms for Large-Scale CFD Lung Flow Simulations

Eulerian Particle Phase Modeling for Tracheobronchial Flows

Compartmental Modeling of Lung Clearance and Retention

Experimental Characterization of Aerosol/Tissue Interactions

Modeling Electrostatic Forces in CFD Simulations of Particle Deposition

HumMod Integrated Whole-Body Physiology Modeling

DigitalLung Research Components

Automated Geometry and Mesh Generation of the Bronchopulmonary Tree

Realistic Geometrical Modeling of Upper Lung Airways

Air Flow and Particle Deposition (CFD) Simulations in Bronchial Airways

Reduced Geometry Modeling (CFD) of Lower Lung Airways

Efficient Parallel Algorithms for Large-Scale CFD Lung Flow Simulations

Eulerian Particle Phase Modeling for Tracheobronchial Flows

Compartmental Modeling of Lung Clearance and Retention

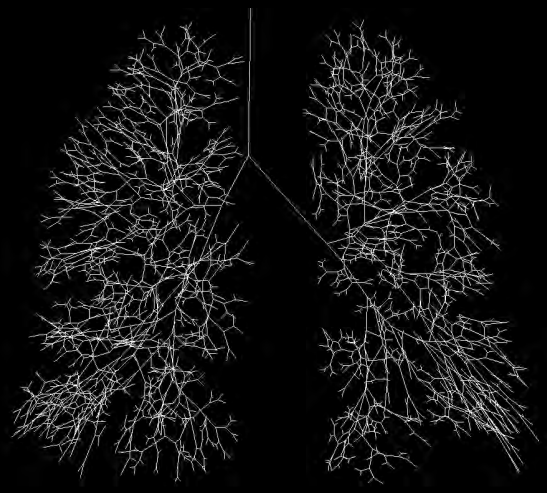
Experimental Characterization of Aerosol/Tissue Interactions

Modeling Electrostatic Forces in CFD Simulations of Particle Deposition

HumMod Integrated Whole-Body Physiology Modeling

Automated Geometry and Mesh Generation of the Bronchopulmonary Tree (MSU)

Key Senior Personnel:
Greg Burgreen, MSU
David Thompson, MSU
Keith Walters, MSU



Objective/Overview:
Develop software approaches to automatically extract and mesh the human lung airways from bronchial branches to the terminal alveoli.

We are seeking NIH funding to extend this project to accommodate dynamic volume changes of the airways to more accurately mimic physiologically realistic dilatation-driven flow in the lungs.

Technical Collaboration:
The modeling of this project will closely link to the MSU and JSU CFD lung airflow projects. Key physiological respiration rates will derive from the UMMC HumMod macro-scale modeling effort. The dynamic volume extension of this project will be critical to the MSU particle deposition efforts.

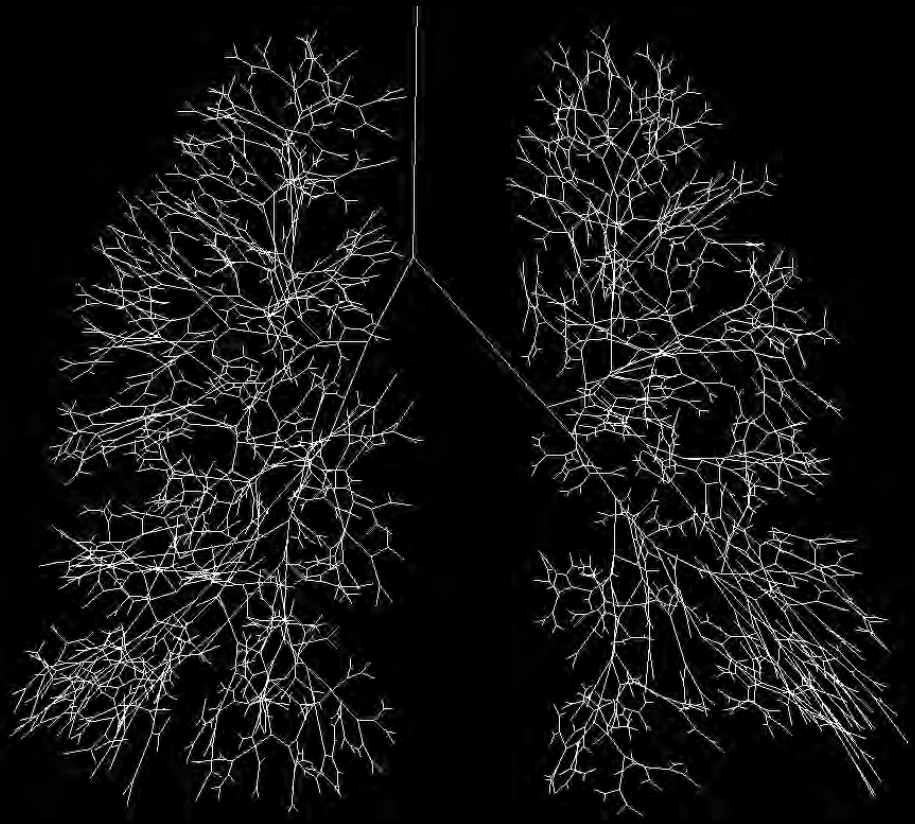
Automated Geometry and Mesh Generation

Skeletal data of lung branching structure forms the basis for our approach.

As initial data, the publically available data of Schmidt et al. (2004) provides 18 generations of bifurcation data.

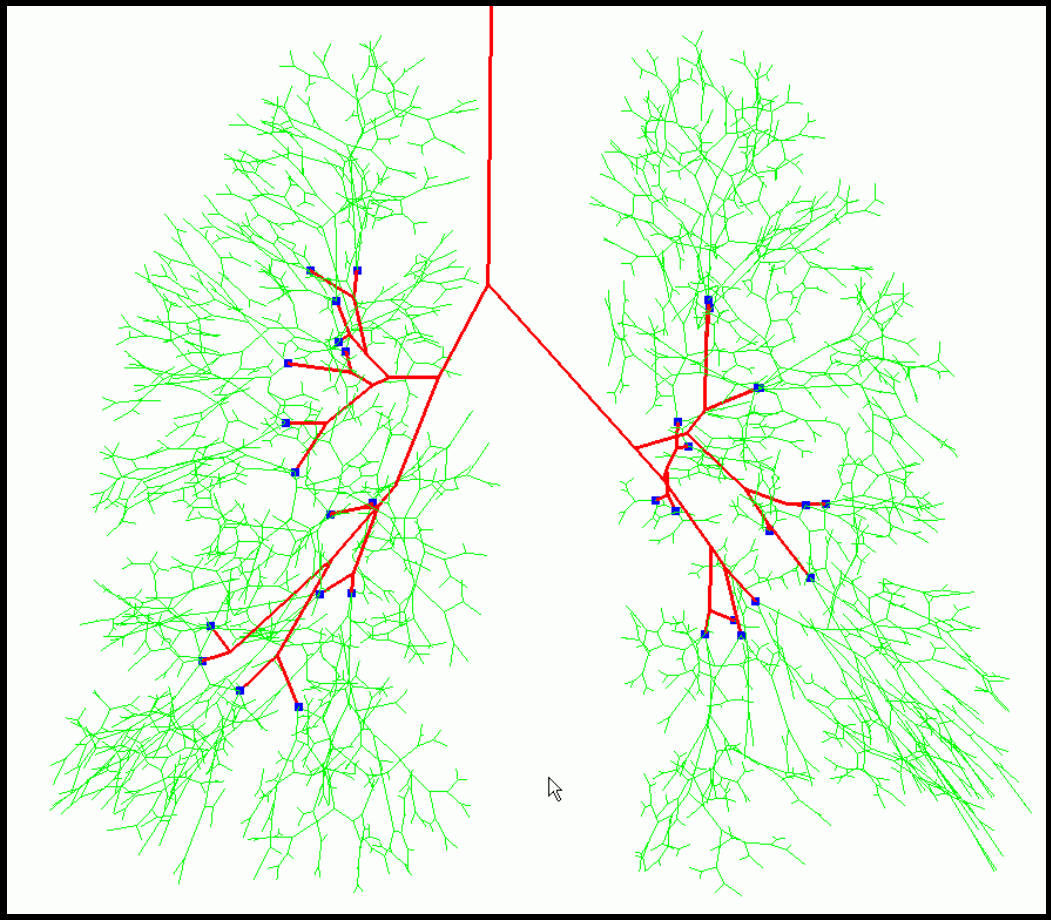
We choose only a small number of discrete airway paths to model using CFD, as opposed to modeling the full lung.

The extraction of selected pathway data should be as automated as possible.



Automated Geometry and Mesh Generation

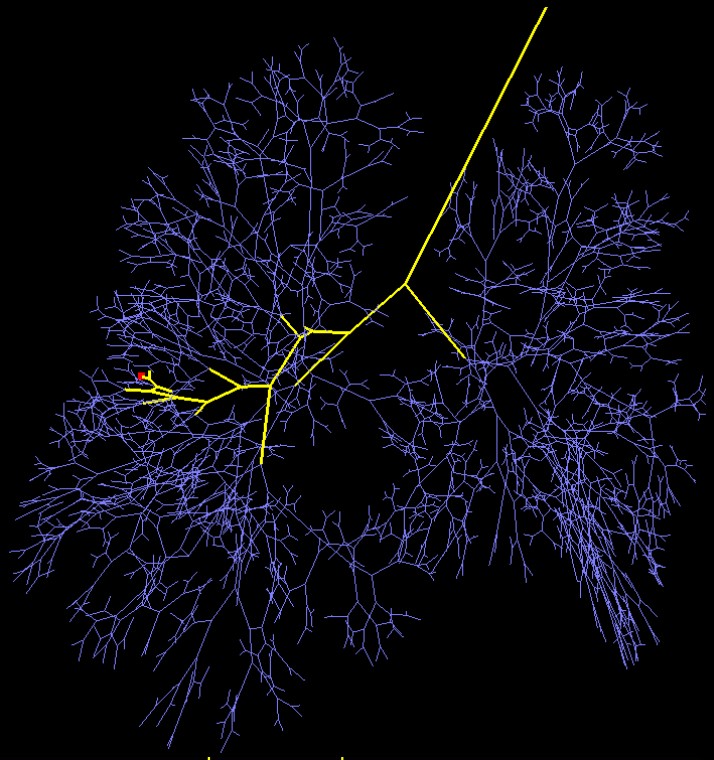
Schmidt lung data – automatic selection of all branches to generation 6

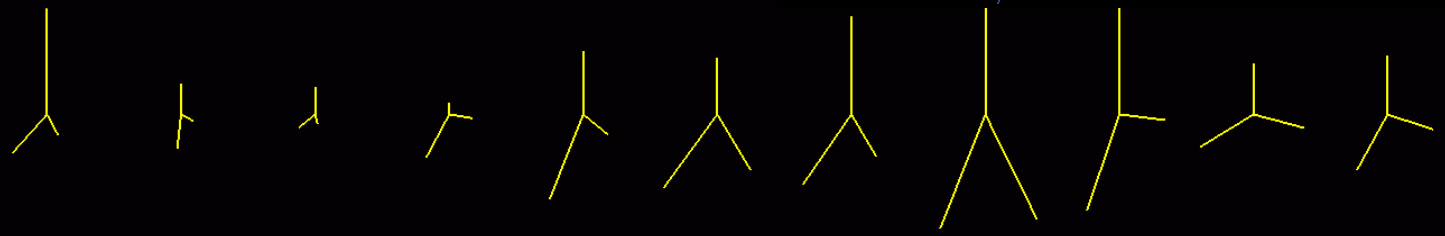


Automated Geometry and Mesh Generation

Schmidt lung data – one isolated airway and its constitutive unit bifurcations

The next step is to convert the isolated branches into a computational mesh for CFD analysis.





DigitalLung Research Components

Automated Geometry and Mesh Generation of the Bronchopulmonary Tree

Realistic Geometrical Modeling of Upper Lung Airways

Air Flow and Particle Deposition (CFD) Simulations in Bronchial Airways

Reduced Geometry Modeling (CFD) of Lower Lung Airways

Efficient Parallel Algorithms for Large-Scale CFD Lung Flow Simulations

Eulerian Particle Phase Modeling for Tracheobronchial Flows

Compartmental Modeling of Lung Clearance and Retention

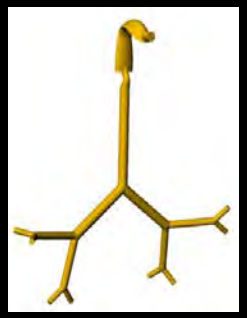
Experimental Characterization of Aerosol/Tissue Interactions

Modeling Electrostatic Forces in CFD Simulations of Particle Deposition

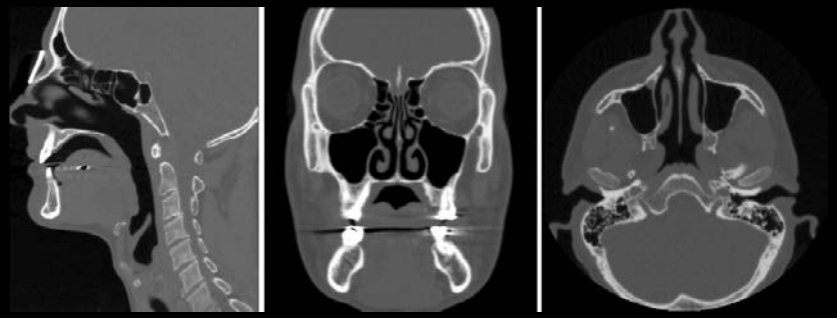
HumMod Integrated Whole-Body Physiology Modeling

Computational Modeling of Realistic Upper Lung Airways (MSU)

Key Senior Personnel:
David Thompson, MSU
Greg Burgreen, MSU
Keith Walters, MSU



Notional upper airway model



Sample CT data of nasal and oral airways.
From *IEEE Trans Vis Comput Graph*. 2009 Nov-Dec;15 (6):1407-14

Objective/Overview:

Develop realistic models of the upper airways for use in high-fidelity simulations of flow and particulate transport .

While only minimal particle deposition occurs in the upper airways, previous efforts using idealized geometries have demonstrated the importance of correct flow partitioning on particle deposition in subsequent generations. We will employ realistic geometrical representations of the upper airways along with advanced turbulence models for coupled flow and particle motion (multi-phase) simulations.

Technical Collaboration:
This output from this model will provide representative input conditions for the *Reduced Geometry Lower Airway Model.*

Geometrical Models for Upper Airway

Approach

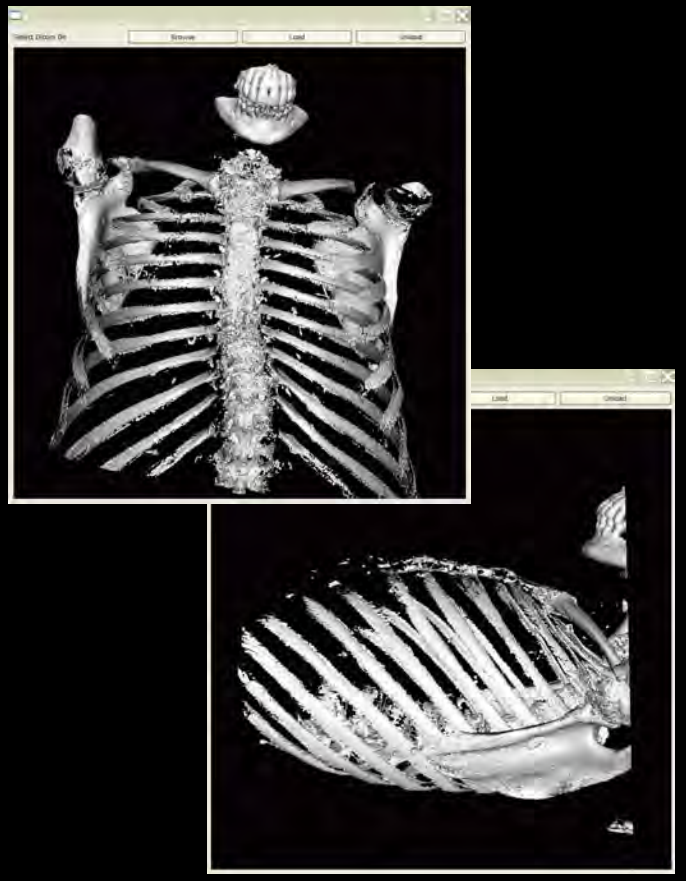
High-resolution CT-scan of upper airways including orotracheal region and glottis will be obtained from Premier Imaging, Starkville

Thresholding operations are used to change or identify pixel values to extract internal coherent physiological structures.

Status

An imaging protocol has been prepared and is pending IRB approval from MSU.

Currently evaluating commercial software packages



Extraction of bone structures from sample CT data

DigitalLung Research Components

Automated Geometry and Mesh Generation of the Bronchopulmonary Tree

Realistic Geometrical Modeling of Upper Lung Airways

Air Flow and Particle Deposition (CFD) Simulations in Bronchial Airways

Reduced Geometry Modeling (CFD) of Lower Lung Airways

Efficient Parallel Algorithms for Large-Scale CFD Lung Flow Simulations

Eulerian Particle Phase Modeling for Tracheobronchial Flows

Compartmental Modeling of Lung Clearance and Retention

Experimental Characterization of Aerosol/Tissue Interactions

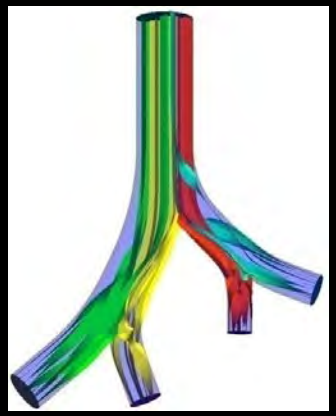
Modeling Electrostatic Forces in CFD Simulations of Particle Deposition

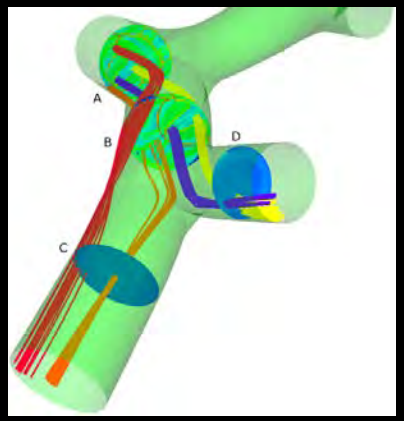
HumMod Integrated Whole-Body Physiology Modeling

Air Flow and Particle Deposition Simulations in Bronchial Airways (MSU, JSU)

Key Senior Personnel:
David Thompson, MSU
Keith Walters, MSU
Shahrouz Aliabadi, JSU

Other Key Personnel:
Bela Soni, JSU





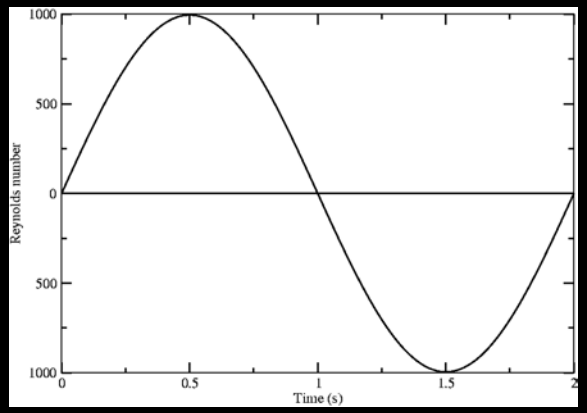
Objective/Overview:
Establish the level of complexity needed to simulate aerosol deposition dynamics in the meso-scale structures of the human lungs.

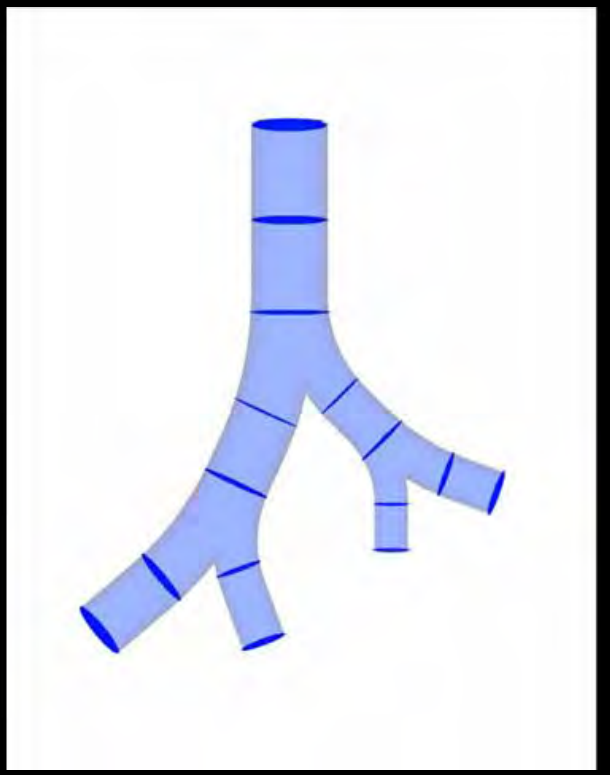
Overall simulation methodology employs computational representation of complex geometry, high resolution unstructured mesh capability, state-of-the art high-resolution computational flow solvers, coupled flow and particle motion (multi-phase) simulation.

Technical Collaboration:
Dr. Soni, a December 2009 PhD graduate at MSU, is continuing to contribute to the project as a post-doctoral researcher at JSU.

Unsteady Ventilation

Model unsteady ventilation as imposed mass flow boundary at inlet (for inhale) and exits (for exhale)





Sine-wave form of temporal variation of flow rate at inlet(s)
- Period of breathing cycle - 2 seconds

Inhale cycle
- Inlet (parent tube): parabolic velocity profile
- Outlets (third-generation): static pressure

Exhale cycle
- Inlets (third-generation): parabolic velocity profiles
- Outlet (parent tube): static pressure

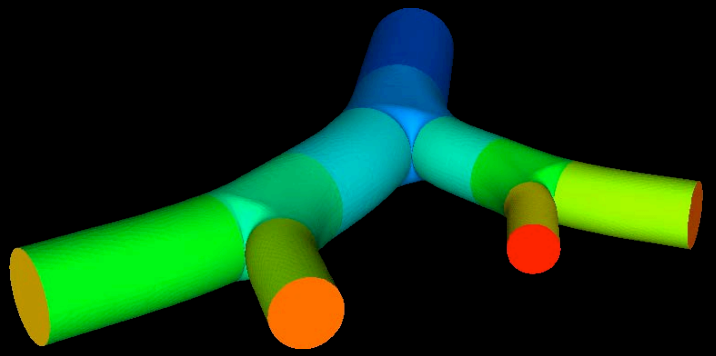
Unsteady Deposition Results

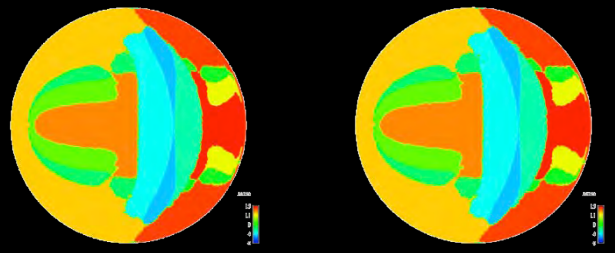
Considered several different particle release times to demonstrate effects of unsteadiness and flow rate on particle deposition

1. Minimal effect of unsteadiness for particle release at peak flow rate. More effect at off-peak release times.
2. Significant effect of initial particle velocity, which is related to instantaneous flow rate. Flow rate is increasing at t=0.3s and decreasing at t=0.7s.
3. Particle release at times in which the flow rate is the same (t=0.3s and 0.7s) show different deposition patterns due to secondary flows in third generation branches.
4. Only minimal effects due to exhalation *unless* more generations are included

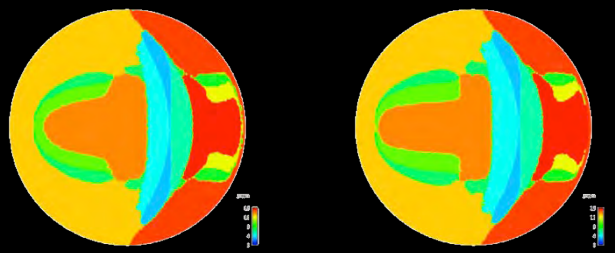
Significance:

These results demonstrate that, if unsteady ventilation is to be considered, the time of particle release (relative to the breathing cycle) is a key parameter.





steady *unsteady – t_r=0.5s*



unsteady – t_r=0.3s *unsteady – t_r=0.7s*

Particle destination maps – planar geometry

DigitalLung Research Components

Automated Geometry and Mesh Generation of the Bronchopulmonary Tree

Realistic Geometrical Modeling of Upper Lung Airways

Air Flow and Particle Deposition (CFD) Simulations in Bronchial Airways

Reduced Geometry Modeling (CFD) of Lower Lung Airways

Efficient Parallel Algorithms for Large-Scale CFD Lung Flow Simulations

Eulerian Particle Phase Modeling for Tracheobronchial Flows

Compartmental Modeling of Lung Clearance and Retention

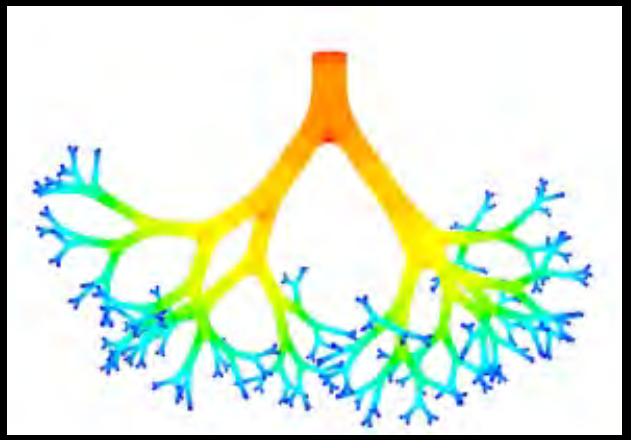
Experimental Characterization of Aerosol/Tissue Interactions

Modeling Electrostatic Forces in CFD Simulations of Particle Deposition

HumMod Integrated Whole-Body Physiology Modeling

Large-Scale CFD Simulations of Airflow in the Bronchopulmonary Tree (MSU, UMMC)

Key Senior Personnel:
Keith Walters, MSU
David Thompson, MSU
Greg Burgreen, MSU
Robert Hester, UMMC



Objective/Overview:
Develop computational simulation methodologies that effectively model large-scale sections of the bronchopulmonary tree, up to and including simulations of the entire lung airway.

Current strategies in the literature use three-dimensional Navier-Stokes simulation of the larger airways coupled with simple empirical or one-dimensional models for the smaller (pulmonary) regions. The approach developed here utilizes a flow path ensemble (FPE) comprised of several distinct pathways, and stochastically coupled boundary conditions to accurately reproduce a virtual geometry for the large-scale system.

Technical Collaboration:
The flow in the lung airway is strongly coupled across all scales. Large-scale simulation techniques will allow the detailed, high-resolution particle deposition simulations to be effectively coupled with the high-level integrative model of human physiology.

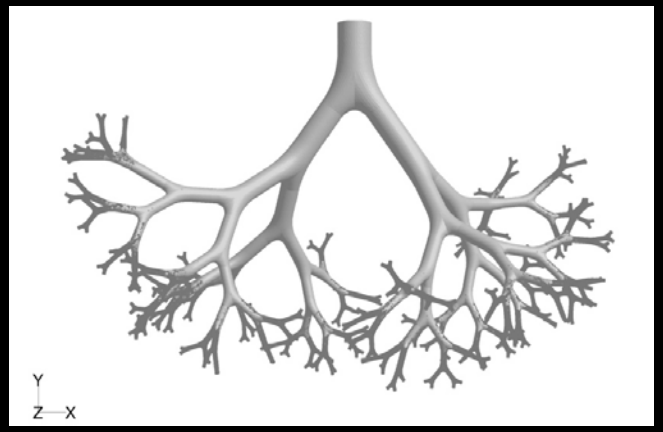
Flow Path Ensemble Method

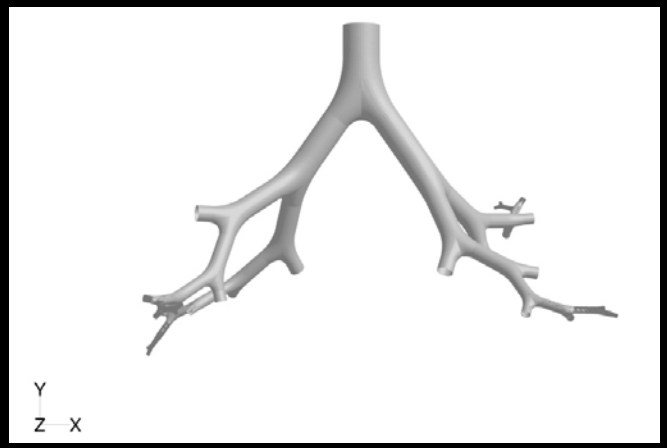
Finite number of distinct flow paths are retained in order to provide three-dimensional model representation at all scales

- Small airways represented using symmetric, non-planar branching generations

Boundary conditions at "cut segments" are obtained from equivalent locations in the resolved flowpaths and applied randomly

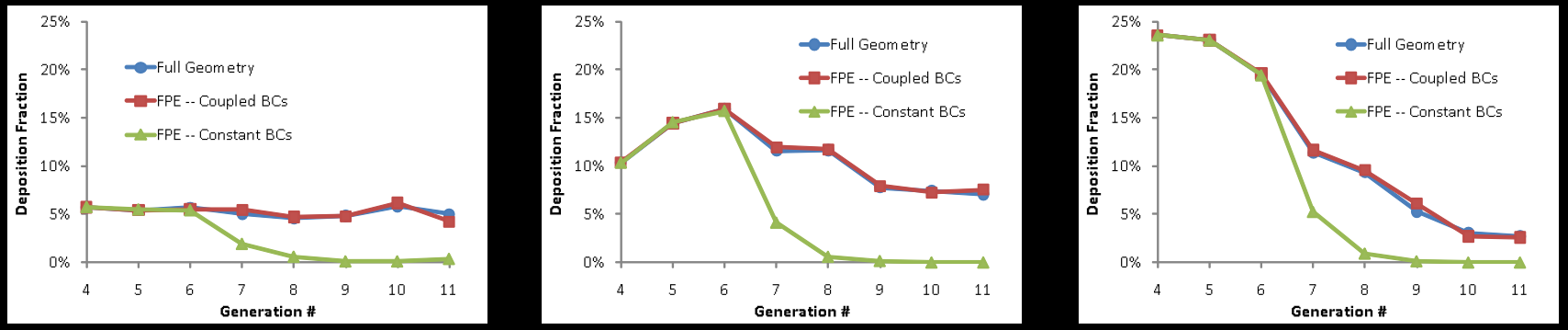
- Result is a "virtual geometry" in which the small scales are well represented provided a sufficient numbers of flow paths are retained





Flow Path Ensemble Method

Flow and deposition simulations were performed using the new FPE method with four retained flow paths, and were compared to equivalent simulations with a fully resolved geometry. The FPE simulations resulted in a computational savings (CPU and memory) of over 90%.



Predicted fraction of particles deposited in each lung airway generation (numbers 4-11) for three different particle diameters.

DigitalLung Research Components

Automated Geometry and Mesh Generation of the Bronchopulmonary Tree

Realistic Geometrical Modeling of Upper Lung Airways

Air Flow and Particle Deposition (CFD) Simulations in Bronchial Airways

Reduced Geometry Modeling (CFD) of Lower Lung Airways

Efficient Parallel Algorithms for Large-Scale CFD Lung Flow Simulations

Eulerian Particle Phase Modeling for Tracheobronchial Flows

Compartmental Modeling of Lung Clearance and Retention

Experimental Characterization of Aerosol/Tissue Interactions

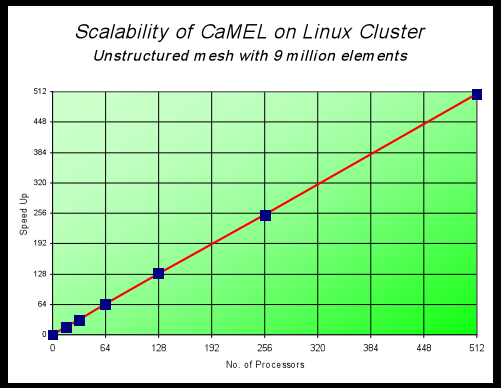
Modeling Electrostatic Forces in CFD Simulations of Particle Deposition

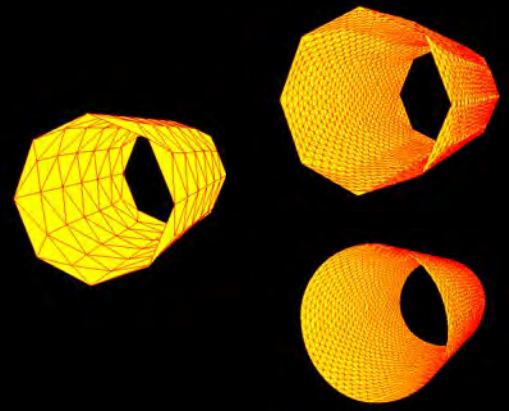
HumMod Integrated Whole-Body Physiology Modeling

Advanced Algorithm Development (JSU, MSU)

Key Senior Personnel:
Shahrouz Aliabadi, JSU
Keith Walters, MSU

Other Key Personnel:
Bela Soni, JSU





Objective/Overview:
Develop numerical algorithms and solver technology for next-generation HPC simulations of biological systems.

This effort addresses fundamental issues of computational simulation technology that are especially critical for biological systems, including advanced code development (CaMEL code, JSU), numerical schemes for multi-phase flows, and high-order representations of complex geometries.

Technical Collaboration:
The algorithmic tools developed as part of this effort will be used to perform high resolution, large-scale simulations, the results of which will serve to validate the reduced geometry methods being integrated into DigitalLung.

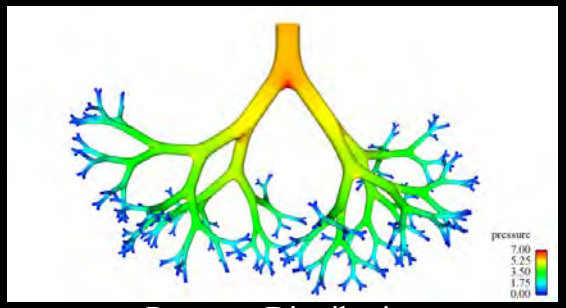
Lung Airflow Simulation Results

Airflow simulations were performed for the eight generation, fully resolved geometry shown above.

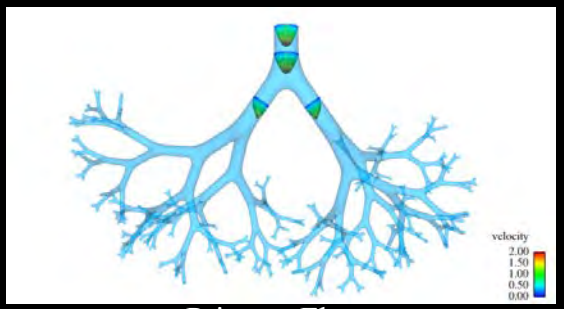
CaMEL code	
Number of nodes	19989857
Number of elements	113960558
Reynolds number	319
Time-step	0.01
Number of time-steps	1000
Processors	256
Overall CPU time	45 hrs

Significance:

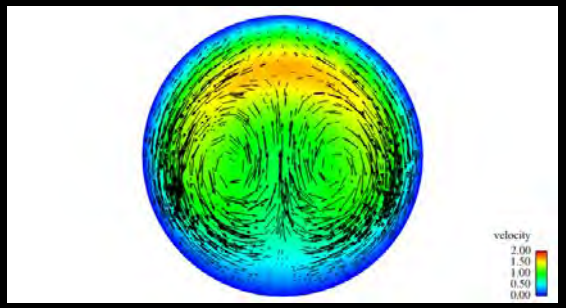
These results demonstrate that efficient, highly parallelized simulation of large-scale geometries is possible using the CaMEL solver. Fully resolved results obtained using CaMEL will be used to validate the reduced geometry modeling techniques for full lung simulation.



Pressure Distribution



Primary Flow



Secondary Flow

DigitalLung Research Components

Automated Geometry and Mesh Generation of the Bronchopulmonary Tree

Realistic Geometrical Modeling of Upper Lung Airways

Air Flow and Particle Deposition (CFD) Simulations in Bronchial Airways

Reduced Geometry Modeling (CFD) of Lower Lung Airways

Efficient Parallel Algorithms for Large-Scale CFD Lung Flow Simulations

Eulerian Particle Phase Modeling for Tracheobronchial Flows

Compartmental Modeling of Lung Clearance and Retention

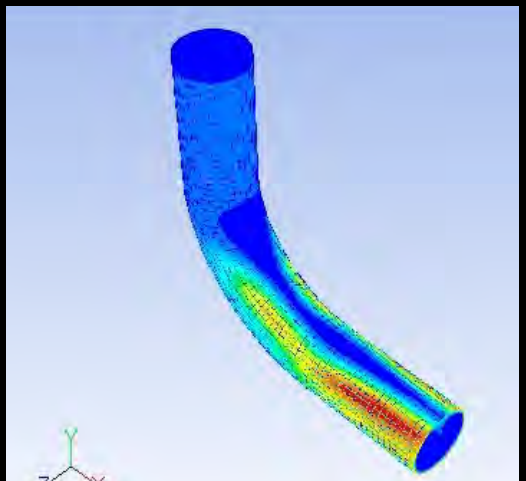
Experimental Characterization of Aerosol/Tissue Interactions

Modeling Electrostatic Forces in CFD Simulations of Particle Deposition

HumMod Integrated Whole-Body Physiology Modeling

Eulerian Particle Phase Modeling for Tracheobronchial Flows (MSU)

Key Senior Personnel:
Keisha Walters, MSU
Keith Walters, MSU



Particle Phase Concentration

Objective/Overview:
Develop an Eulerian particle transport model for gas-solid and gas-liquid multi-phase flow in trachebronchial geometries.

Computation solutions for an initial model have been obtained for a simple geometry. This 90-degree bend will serve as a test case as additional forces are added into the model, such as particle-particle and particle-fluid interactions, size, density, and heterogeneous inlet concentrations.

Technical Collaboration:
The mathematical models and simulations are being generated jointly by researchers in the Dave C. Swalm School of Chemical Engineering and SimCenter of MSU. Location-specific particulate impact patterns will be predicted and used as an input to the compartmental model.

DigitalLung Research Components

Automated Geometry and Mesh Generation of the Bronchopulmonary Tree

Realistic Geometrical Modeling of Upper Lung Airways

Air Flow and Particle Deposition (CFD) Simulations in Bronchial Airways

Reduced Geometry Modeling (CFD) of Lower Lung Airways

Efficient Parallel Algorithms for Large-Scale CFD Lung Flow Simulations

Eulerian Particle Phase Modeling for Tracheobronchial Flows

Compartmental Modeling of Lung Clearance and Retention

Experimental Characterization of Aerosol/Tissue Interactions

Modeling Electrostatic Forces in CFD Simulations of Particle Deposition

HumMod Integrated Whole-Body Physiology Modeling

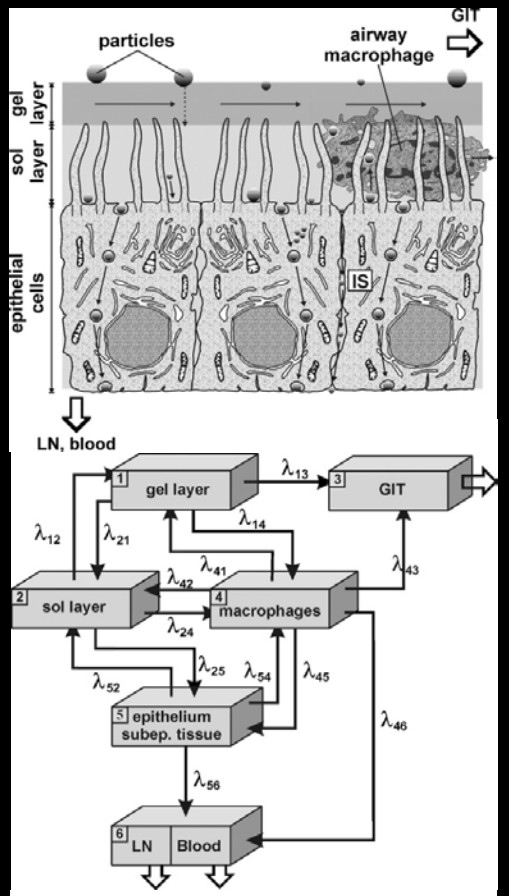
Compartmental Modeling of Lung Clearance and Retention (MSU, UMMC)

Key Senior Personnel:
Keisha Walters, MSU
Keith Walters, MSU
Robert Hester, UMMC

Objective/Overview:
Particle impact alone does not determine deposition and deposition position is not the final step in determining ultimate fate. The clearance and retention of inhaled particulates must be modeled to quantify residence time and cellular uptake, and to serve as an input to assess physiological impact.

Building upon compartmental models from the literature, particle fate upon impact with the mucus layer will be sorted as clearance via the gastro-intestinal tract or exhalation and deposition at/to alveolar surfaces, macro-phages, interstitial spaces, lymph nodes, and olfactory and upper airways regions. Future efforts will include the experimental determination of particle diffusion rates, aggregation potentials, and lift-off using synthetic mucus, endothelium, and saliva solutions.

Technical Collaboration:
Transport models will provide location-specific particulate deposition patterns and that will serve as an input to the compartmental model. The compartmental model will tie together flow and physiology modeling.



Sturm, R. Computers in Biology and Medicine 37 (2007) 680 – 690.

DigitalLung Research Components

Automated Geometry and Mesh Generation of the Bronchopulmonary Tree

Realistic Geometrical Modeling of Upper Lung Airways

Air Flow and Particle Deposition (CFD) Simulations in Bronchial Airways

Reduced Geometry Modeling (CFD) of Lower Lung Airways

Efficient Parallel Algorithms for Large-Scale CFD Lung Flow Simulations

Eulerian Particle Phase Modeling for Tracheobronchial Flows

Compartmental Modeling of Lung Clearance and Retention

Experimental Characterization of Aerosol/Tissue Interactions

Modeling Electrostatic Forces in CFD Simulations of Particle Deposition

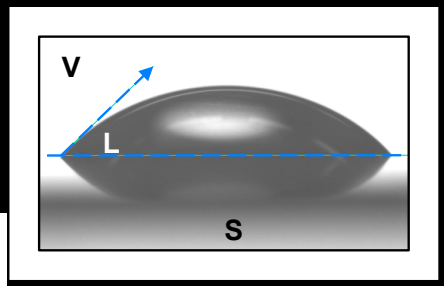
HumMod Integrated Whole-Body Physiology Modeling

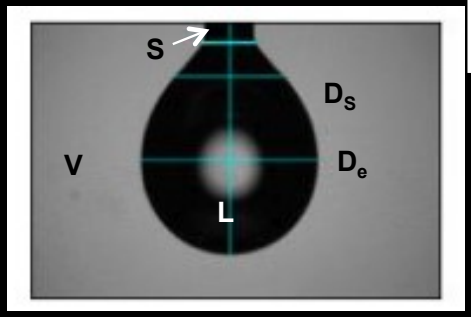
Experimental Characterization of Aerosol/Tissue Interactions (MSU)

Key Senior Personnel:
Keisha Walters, MSU

Objective/Overview:
The goal of this project is to measure and model the interactions of lung tissue and droplets of drug solution used in aerosol therapeutics. Interfacial tensions and contact angles of drug-doped solutions are obtained using pendant and static contact angle measurements. Bovine and rabbit lung tissue, three artificial saliva solutions, and several drugs (theophylline, KI, albuterol) have been tested. Increased concentrations ranges, alternate drugs (e.g., fluticasone/salmeterol), artificial mucus, viscosities, and alternate saliva formulations will be used to fill a database of liquid-solid interaction parameters.

Technical Collaboration:
Liquid-solid interaction parameters will be used in the compartmental and Eulerian flow modeling efforts to more accurately describe the interface between the aerosol droplets And biological surfaces.





DigitalLung Research Components

Automated Geometry and Mesh Generation of the Bronchopulmonary Tree

Realistic Geometrical Modeling of Upper Lung Airways

Air Flow and Particle Deposition (CFD) Simulations in Bronchial Airways

Reduced Geometry Modeling (CFD) of Lower Lung Airways

Efficient Parallel Algorithms for Large-Scale CFD Lung Flow Simulations

Eulerian Particle Phase Modeling for Tracheobronchial Flows

Compartmental Modeling of Lung Clearance and Retention

Experimental Characterization of Aerosol/Tissue Interactions

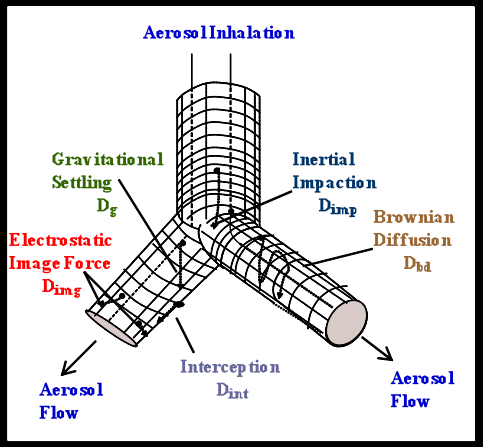
Modeling Electrostatic Forces in CFD Simulations of Particle Deposition

HumMod Integrated Whole-Body Physiology Modeling

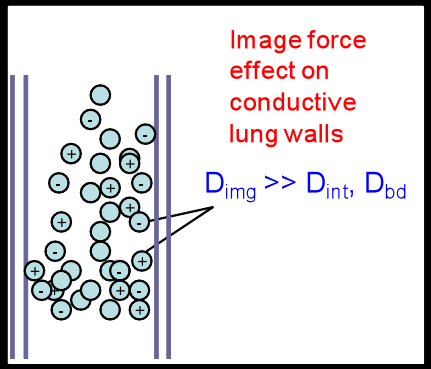
Modeling Electrostatic Forces in CFD Simulations of Particle Deposition (JSU, MSU)

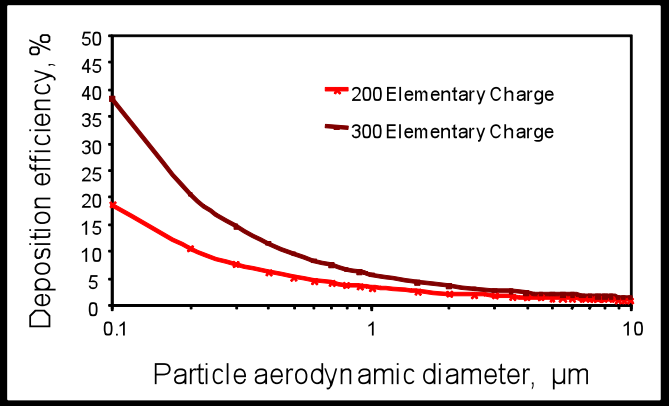
Key Senior Personnel:
Mohammed Ali, JSU
Keith Walters, MSU

Objective/Overview:
The effect of forces other than aerodynamic drag impact the transport and deposition of particles in the lung. One important force is the electrostatic image force between the particle and the airway wall. The objective of this effort is to develop mathematical models for image forces and implement them into CFD models of lung airway dynamics.



Technical Collaboration:
The image force models developed at JSU will be implemented directly into the general purpose CFD tools that form part of the multiscale DigitalLung modeling framework.





DigitalLung Research Components

Automated Geometry and Mesh Generation of the Bronchopulmonary Tree

Realistic Geometrical Modeling of Upper Lung Airways

Air Flow and Particle Deposition (CFD) Simulations in Bronchial Airways

Reduced Geometry Modeling (CFD) of Lower Lung Airways

Efficient Parallel Algorithms for Large-Scale CFD Lung Flow Simulations

Eulerian Particle Phase Modeling for Tracheobronchial Flows

Compartmental Modeling of Lung Clearance and Retention

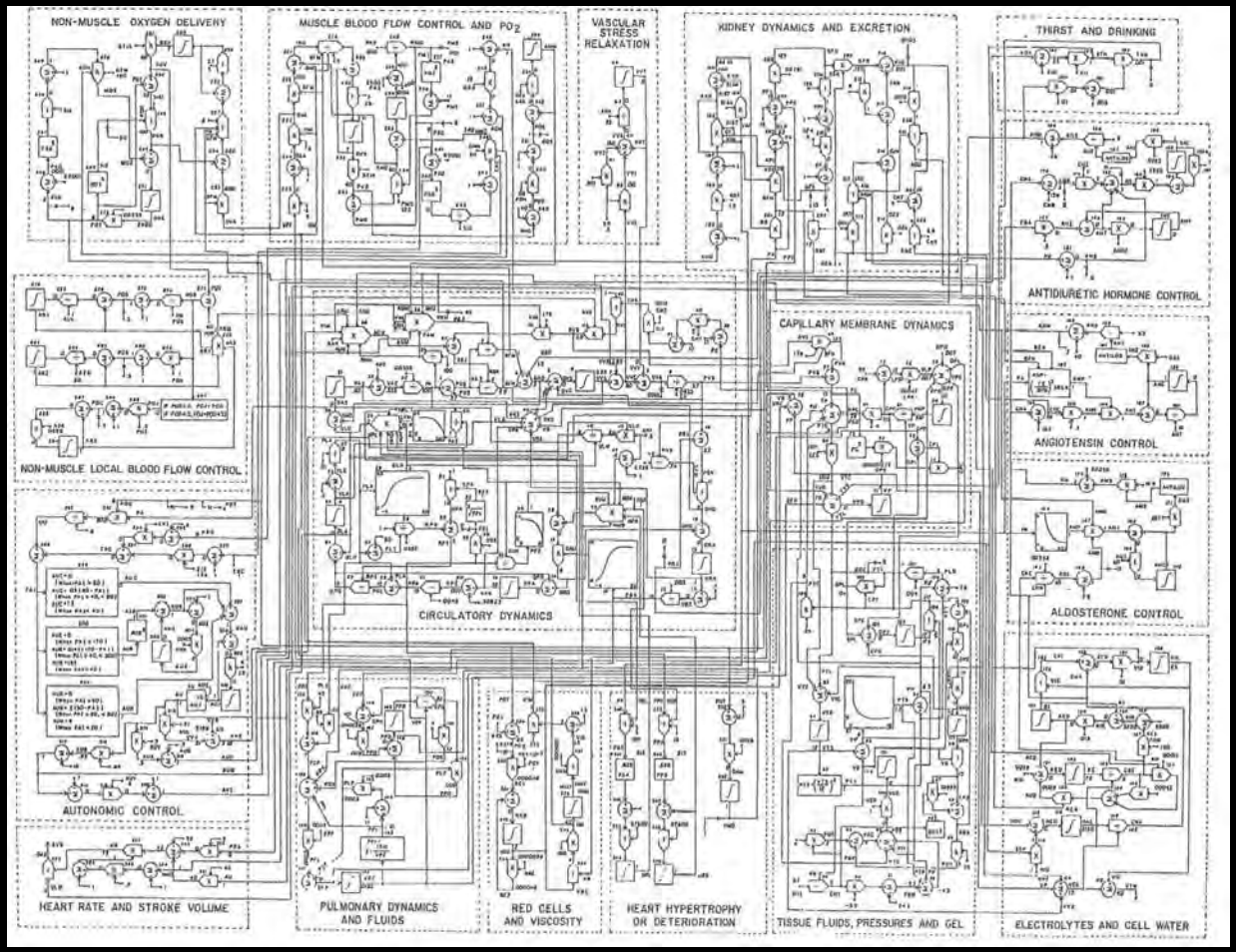
Experimental Characterization of Aerosol/Tissue Interactions

Modeling Electrostatic Forces in CFD Simulations of Particle Deposition

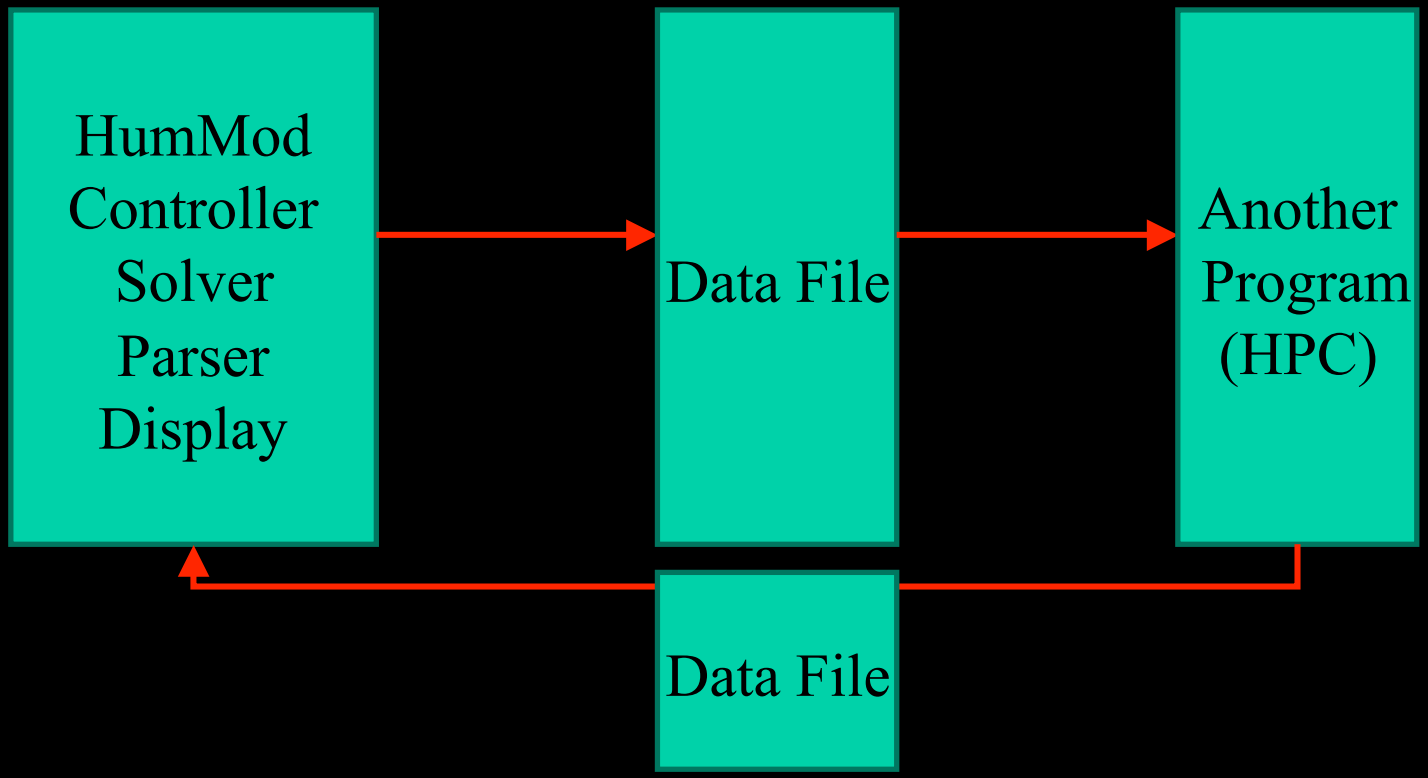
HumMod Integrated Whole-Body Physiology Modeling

QCP → QHP → DigitalHuman

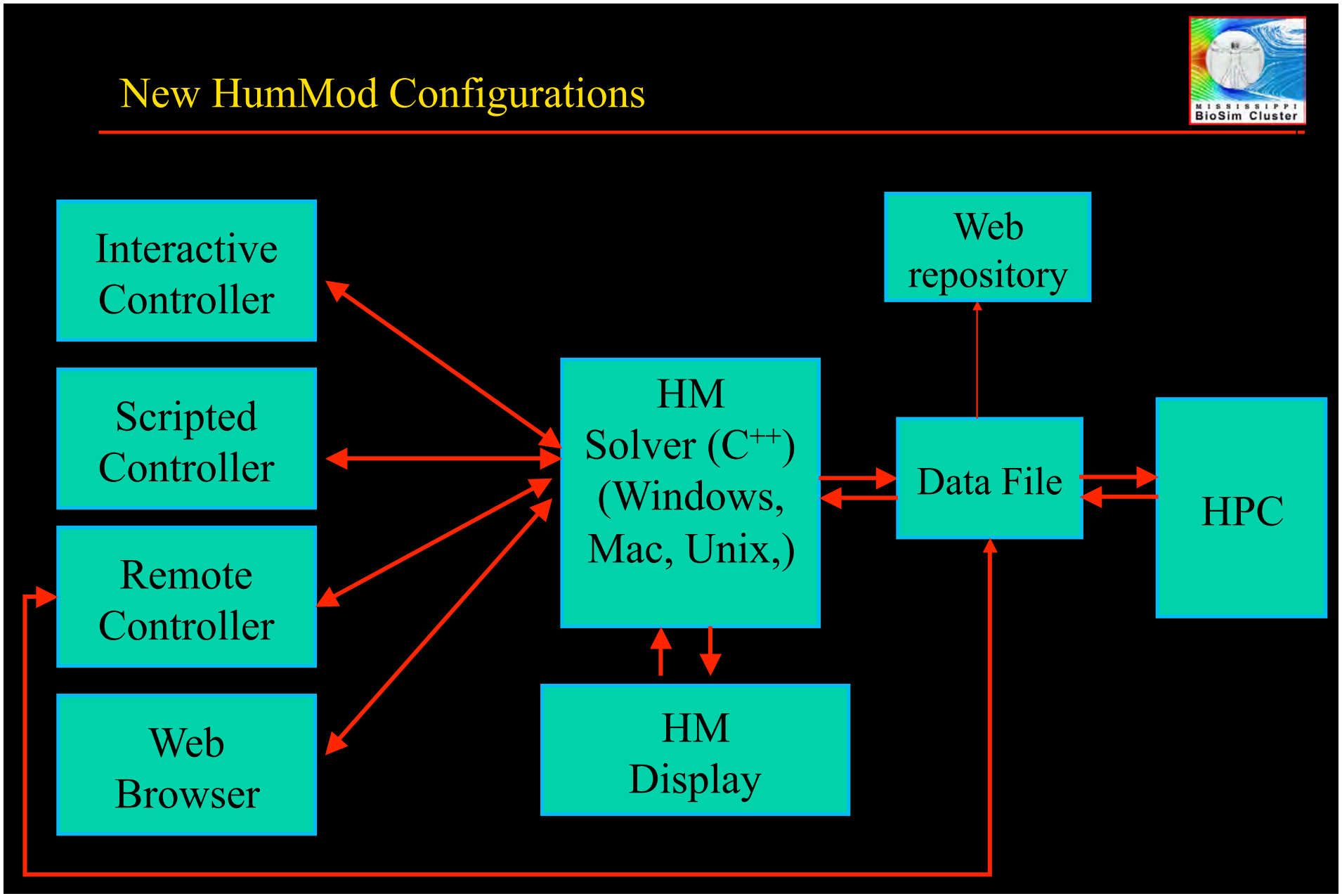
Model Navigator



Current Interaction with other software



New HumMod Configurations



Modular HumMod

Modular HumMod

Web Version of HumMod

Demonstration of Web version of HumMod

Questions?