Cell Scale to Macroscale Integration

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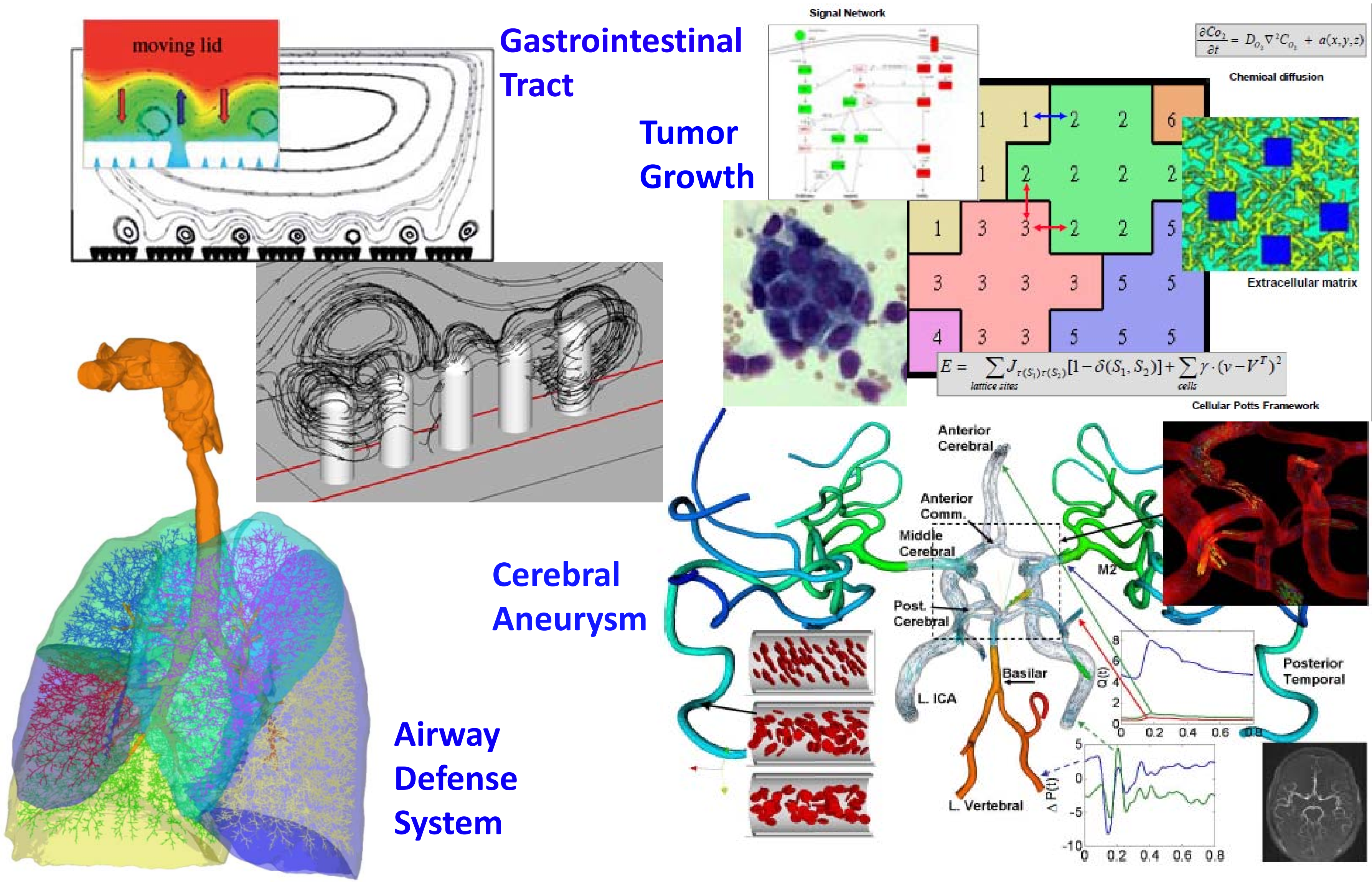

Model Integration

Scale	Macroscale to extra-cellular level								Mesoscale cellular level	Microscale intracellular level
Methods	Global	Local	Fluid		Solid		Fluid-Structure Interaction		Collective structural behavior	Biochemical signaling pathways
Geometry	Organ scale	Part of organ	Subject-specific prediction	General predictions	Subject-specific predictions	General predictions	1 way coupling	2 way coupling		
Lung	3D3D, 3D1D	3D	FEM		FEM		Image Registration	FEM	cell culture experiment	x
Blood	3D1D	3D	FEM		FEM			FEM	DPD	
GI tract (gut)	2D 3D LBM, organ scale	2D 3D LBM		LBM			x			
Tumor	x	x		x	x	x		x	MC, rule	Boolean, rule-based

Recommendations

- **Education:**

  To achieve a better integrative Physiome, we recommend that NIH sponsor short courses/summer workshops offered through NIH sponsored centers and leading institutions.

- **Imaging and Geometric Modeling:**

  To understand structure-function relationship at all levels, we need to improve the accuracy of imaging, image analysis and geometric modeling of structure, and to quantify the uncertainty of geometric models and its effect on function. We recommend that NIH promote study of image-based morphology at the organ and tissue functional levels, and the integration of imaging data into modeling strategies.

- **Transport within Biofluid Flow Simulation:**

  Transport within biological fluid flows occurs over an extremely wide range of scales and with complexity that includes critical interactions at the cellular level and transport at the molecular level within continuum level bulk flow. We recommend that emphasis be directed at the accuracy of bio fluid flow simulation at different scales and that empirical and approximate modeling strategies be progressively replaced by more exact methods grounded in the laws of physics and with the lowest reasonable level of parameterization.

- **Tissue Properties and Multiscale Tissue Mechanics:**

  Quantitative experimental measurements of cell and tissue level behaviors and properties are needed to establish baseline model parameters and to validate simulation results. These properties are important in modeling fluid-structure interaction for stress transmission and for neuromuscular controls. We recommend that NIH encourage and support the development of new methods for quantifying tissue properties and modeling multiscale tissue mechanics that can address *in vivo* as well as *in vitro* response.

- **Uncertainty Quantification:**

  We recommend that NIH emphasize the quantification of uncertainties in tissue and fluid properties, geometrical modeling, model parameterization, constitutive laws, or model boundary condition, and the impact of such uncertainties in multiscale and multiphysics integration.

Goals and Tasks

- **Publication**: Special issues on multiscale modeling in high-quality, high-impact archival journals, e.g. *Journal of Computational Physics*.
- **Conference**: Joint IMAG MSM and Euro Virtual Physiological Human (VPH) meeting (2011).
- **Collaboration**: Promote collaborations between WG members (through grant applications) to build a more integrative model toward Physiome.