# Computational Modeling and Image Processing of Biomedical Problems

Department of Mathematical Sciences
Michigan Technological University

June 15 $\sim$ 17, 2019

Welcome to the Copper Country Computational Modeling and Image Processing of Biomedical Problems symposium. This is an interdisciplinary conference dedicated to mathematical and computational aspects of biomedical imaging. It fosters knowledge transfer between the applied mathematics and imaging communities. Particularly, the conference offers a venue to initiate new connections between and across the traditional boundaries among mathematics, engineering, physics, and biomedical sciences, both within Michigan Tech and beyond.

Local organizing committee at Michigan Tech University:

| | |
|---|---|
| Mark S. Gockenbach | Department of Mathematical Sciences |
| Sean J. Kirkpatrick | Department of Biomedical Engineering |
| Jingfeng Jiang | Department of Biomedical Engineering |
| Zhengfu Xu | Department of Mathematical Sciences |

Here is the tentative schedule (Room: **Dow building #642**):

| Date | June 15th, Saturday | June 16th, Sunday | June 17th, Monday |
|---|---|---|---|
| 8:40 – 9:00 | *Opening Remark* | -- | -- |
| 9:00 – 9:40 | Guirong Liu | Nikhil Paliwal | Jeff Calder |
| 9:40 – 10:20 | Bryan P. Bednarz | Jian-Xun Wang | Yong Yang |
| 10:20 – 10:40 | *Coffee Break* | | |
| 10:40 – 11:20 | Li Wang | James C. Gee | Aditya Viswanathan |
| 11:20 – 12:00 | Student Poster Presentation | Yue Yu | Yuan Liu |
| 12:00 – 2:00 | *Lunch Break* | | |
| 2:00 – 2:40 | T. Douglas Mast | Local Tour Copper Harbor | Free Discussion |
| 2:40 – 3:20 | Wenrui Hao | | |
| 3:20 – 3:40 | *Coffee Break* | | |
| 3:40 – 4:20 | Mingchao Cai | | |
| 4:20 – 5:00 | Susanta Ghosh | | |
| 5:00 – 9:30 | *Conference Retreat* | | |

# Conference Program

## – Day 1: June 15, Saturday –

**9:00 AM ∼ 9:40 AM**

Prof. **Guirong Liu** Professor
Affiliation/Web: University of Cincinnati Email: liugr@uc.edu

**Title: Smoothed Finite Element Methods and Data for Effective Simulation of Biological Systems: Soft, Flidic, Interactive and Adaptation**

***Abstract***: *This talk provides an overview of computational methods that are physic-law and data based for the analysis of biological systems. The general formulations of meshfree and element-based methods will be briefed using strong, week and weakened weak (W2) formulations. Studies on the comparisons of W2 formulations with the strong and weak formulations will be presented. We will present a family of W2 models known as S-FEM developed in the recent years. Properties of this class of methods important for automation in computation will be discussed including, spatial and temporal stability and convergence, softening effects induced by various types of smoothing domains, upper bound properties leading to certified solutions, and insensitivity to the quality of mesh allowing effective uses of triangular/tetrahedral meshes, which are best suited for adaptive analyses. For fluid flow problems, the gradient smoothing methods (GSM) will be briefly introduced. Application examples will also be presented for simulating behavior of various biological, including red-blood cells, blood flows in micro-veins, bone tissue heeling process, bone remodeling, flying birds, etc.*

***Keywords***: FEM, S-FEM, GSM, FSI, numerical methods, blood flow, red blood cell, osseointegration, bone remodeling, bird fly, cardiovascular tissues

**9:40 AM ∼ 10:20 AM**

Prof. **Bryan P. Bednarz** Associate Professor
Affiliation/Web: University of Wisconsin-Madison Email: bbednarz2@wisc.edu

**Title: Multi-scale radiation transport modeling for radiopharmaceutical therapy**

***Abstract***: *Radiopharmaceutical therapy (RPT) is experiencing tremendous growth due to the incorporation of more radiopharmaceuticals into the armamentarium of oncologists in recent years. Novel targeting vectors are being paired with novel radioisotopes to more effectively target systemic disease. Accompanying this growth is a renewed interest in performing voxel-level dosimetry in patients to help guide clinical decision making and optimize therapeutic efficacy. Computational radiation dosimetry is known as a "radiation transport" problem, which describes the motion of particles in certain materials through an equation known as the Boltzmann transport equation. While a variety of methods have been used to solve the Boltzmann transport equation, the Monte Carlo (MC) method is considered the most accurate and versatile method for dosimetry problems and can be adapted to model any current and future radionuclide for therapy. Over the last several years, my lab has developed an advanced dosimetry platform called RAPID (Radiopharmaceutical Assessment Platform for Internal Dosimetry), which can perform Monte Carlo-based voxel-level dosimetry calculations for RPT. More recently, we have expanded the capabilities of the platform to perform simulations at cellular and sub-cellular scales. This talk will provide an overview of RAPID and discuss a variety pre-clinical and clinical problems for which RAPID is being used to address.*

**10:40 AM $\sim$ 11:20 AM**

Prof. **Li Wang** Assistant Professor
Affiliation/Web: University of Minnesota, Minneapolis Email: wang8818@umn.edu

**Title: Accurate front capturing schemes for tumor growth models**

***Abstract***: *We consider a class of tumor growth models under the combined effects of density-dependent pressure and cell multiplication. When the pressure-density relationship becomes highly nonlinear, it converges to a free boundary model as a singular limit. In particular, the constitutive law connecting pressure $p$ and density $\rho$ is $p(\rho) = \frac{m}{m-1}\rho^{m-1}$, when $m \gg 1$, the cell density $\rho$ may evolve its support due to a pressure-driven geometric motion with sharp interface along the boundary of its support. The nonlinearity and degeneracy in the diffusion bring great challenges in numerical simulations, let alone the capturing of the singular free boundary limit. We develop a numerical scheme based on a novel prediction-correction reformulation that can accurately approximate the front propagation even when the nonlinearity is extremely strong. We show that the semi-discrete scheme naturally connects to the free boundary limit equation as $m \to \infty$. With proper spacial discretization, the fully discrete scheme has improved stability, preserves positivity, and implements without nonlinear solvers.*

**11:20 AM $\sim$ 12:00 PM**

**Student Poster Presentations**

- Kevin Sunderland
- Ami Kling
- Sulin Wang
- David Rosen
- Ranit Karmakar
- Han Gao
- TBD

**12:00 PM $\sim$ 2:00 PM**

Lunch Break

**2:00 PM $\sim$ 2:40 PM**

Prof. **T. Douglas Mast** Professor
Affiliation/Web: University of Cincinnati Email: masttd@ucmail.uc.edu

**Title: Convolutional simulation of pulse-echo ultrasound imaging**

***Abstract***: *An efficient, powerful approach to numerical simulation of pulse-echo ultrasound images is presented. To account for diffraction effects, time-harmonic beam patterns of canonical ultrasound sources and receivers are computed by methods including exact series solutions for circular pistons and an extended Fresnel approximation for rectangularly symmetric apertures. Appropriate convolutions and inner products of computed transmit-receive beam products with 3D numerical tissue models directly simulate beamformed scan lines, which can be processed to yield B-mode and echo decorrelation images. Simulated echo decorrelation images of random media are shown to accurately estimate specified decoherence distributions that simulate heating effects in thermal ablation. To illustrate how this simulation approach enables design optimization for imaging devices and methods, effects on accuracy of decoherence estimates by 3D echo decorrelation imaging are analyzed for factors including scan configuration, correlation window size, simulated lesion size, and ensemble averaging.*

**2:40 PM ∼ 3:20 PM**

Prof. **Wenrui Hao** Assistant Professor
Affiliation/Web: Penn State University Email: wxh64@psu.edu

**Title: Harness computational modeling to biomedical data**

***Abstract***: *Progress in understanding disease processes based on the availability of data about individual patients has the potential to greatly improve medical treatments by personalizing them known as precision medicine. Computational modeling has been used as a data-driven predictive tool for precision medicine. This talk will present several examples of computational modeling on cardiovascular disease and Alzheimer's disease. All of them are based on analysis of biomedical imaging data by using the computational modeling approach which integrates an understanding of the relevant individual variability of physiology with efficient computational data driven algorithms.*

**3:40 PM ∼ 4:20 PM**

Prof. **Mingchao Cai** Assistant Professor
Affiliation/Web: Morgan State University Email: cmchao2005@gmail.com

**Title: Parameter Robust Algorithms for Biot Model with Applications in Brain Edema Simulation**

***Abstract***: *Several algorithms are developed for Biot model. In the first algorithm, stabilized Finite Elements are applied to discretize the model. We propose some preconditioners to solve the resulting saddle point systems. It is proved that the condition number of the preconditioned system is independent of mesh size and physics parameters. In the second algorithm, by introducing an intermediate variable, we obtain a multiphysics reformulation of the model. A coupled algorithm and a decoupled algorithm are then designed to solve the problem. We show that the algorithms can achieve optimal approximation order and are parameter robust. Numerical simulations of brain edema under different settings are reported.*

**Joint work with:** Guoliang Jv and Jingzhi Li at Southern University of Science and Technology.

**4:20 PM ∼ 5:00 PM**

Prof. **Susanta Ghosh** Assistant Professor
Affiliation/Web: Michigan Technological University Email: susantag@mtu.edu

**Title: An Error in Constitutive Equations Approach for Elasticity Imaging using Ultrasound Data**

***Abstract***: *Ultrasound-based elasticity imaging modalities are very attractive due to their innocuous nature, low-cost and portability. However, computational inverse problem approaches face several major challenges when ultrasound data is used: uni-directionality of measured displacements, planar acquisitions, lack of boundary information, and noise, among others. In this talk, we will present our recent progress in developing computational inverse problem techniques that effectively address these challenges. To this end, we have developed a PDE-constrained optimization approach based on the minimization of an error in constitutive equations functional augmented with a least squares data misfit term. Through variational arguments, we demonstrate that the current framework allows naturally for problems in which boundary conditions are partially or completely unknown, making it a very suitable candidate for ultrasound-based elasticity imaging. We will present inversion results using both simulated and experimental ultrasound data. In our synthetic data cases, finite element computations were polluted using noise that emulates the ultrasound-tracking process. We will also present reconstructions obtained from laboratory phantoms in which bulk waves were excited using the radiation force of ultrasound and tracking of the propagating waves was performed using the*

*same ultrasound transducer.*
*Our results indicate that our proposed framework could be effectively coupled with current ultrasound imaging techniques to produce accurate reconstructions of mechanical fields. Furthermore, our results highlight the potential of our approach to be employed in clinical settings.*
**Joint work with:** Susanta Ghosh, Manuel I. Diaz, Zilong Zou, Mark L. Palmeri, Mahdi Bayat, Mostafa Fatemi, and Wilkins Aquino

## – Day 2: June 16, Sunday –

**9:00 AM ∼ 9:40 AM**

**Nikhil Paliwal** PhD Candidate
Affiliation/Web: University at Buffalo Email: npaliwal@buffalo.edu

**Title: Predicting Clinical Outcome of Intracranial Aneurysms treated with Flow Diverters using CFD and Machine Learning**

***Abstract***: ***Background and purpose***: *Flow diverters (FDs) aim to induce stasis in the aneurysmal sac, enabling thrombosis and eventual obliteration of the IA. FD-treated aneurysms with persistent blood-flow leave patients at persistent risks of rupture and thromboembolic complications*[1]*. To enable a priori prediction of FD-treatment outcome, we developed a computational workflow that included aneurysmal geometry assessment, FD-modeling and computational fluid dynamic (CFD) simulations to obtain relevant parameters, which were used to train machine-learning algorithms*[2]*. In this study, we applied the computational workflow to aneurysm patients treated using FDs from our center to generate predictive models. Furthermore, we also investigated the impact of different features (geometrical, FD-related and pre- and post-treatment hemodynamics) in outcome prediction of FD-treated IAs.*

***Materials and methods***: *Between 2011 and 2018, FD-treated sidewall aneurysms located at the internal carotid artery, with 6-month clinical follow-up and pre-treatment 3D-digital subtraction angiographic image available were enrolled. Based on their clinical outcome, aneurysms were divided into two groups: occluded (successful, with complete aneurysmal occlusion) or residual (unsuccessful, with residual contrast filling at the aneurysmal neck/dome). For each case, we computed a total of 16 features: 6 geometrical (G), 2 FD-related (D) and 8 pre- and post-treatment hemodynamic features (U* and T*, respectively). Cases were then normalized and randomized into a 3:1 ratio in training and testing cohorts. Three neural network (NN) models were trained using following features: (1) geometry, pre- treatment hemodynamics, FD-related and post-treatment hemodynamics (GU*DT*), (2) geometry, pre-treatment hemodynamics and FD-related (GU*D), (3) geometry and pre-treatment hemodynamics (GU*) and (4) geometry (G). To compare performance of the models, ROC curves and prediction accuracies on the training and testing cohorts, respectively, were assessed.*

***Results***: *One-hundred-five aneurysms in 98 patients were included in this study: 80 occluded and 25 residual at 6-month follow-up. Seventy-nine aneurysms (60 occluded, 19 residual) were included in the training cohort and 26 aneurysms (20 occluded, 6 residual) were included in the testing cohort. ROC analysis on the training cohort showed that models GU*DT*, GU*D, GU* and G had similar AUC values of 0.86, 0.86, 0.78 and 0.84, respectively. However, in terms of outcome prediction on the independent testing cohort, GU*DT* had the highest accuracy (92.31%), followed by GU*D and GU*(80.77%) and G(73.08%) models. These results suggest that even though all models showed similar performance in the training cohort, superior performance of model trained using all the features (GU*DT*) suggests that post-treatment hemodynamics is a huge contributor in classifying occluded cases from the residual ones. This might also suggest that post-treatment hemodynamics play a critical role in healing after FD-treatment. Conclusions: Our computational workflow predicts the outcome of FD-treated aneurysms with 92.31% accuracy. Models trained using all features, including geometry, FD-related, and pre- and post- treatment hemodynamics outperformed other models in predicting the outcome of FD-treated IAs.*

***References***:

[1] Siddiqui et al., Journal of Neurosurgery, 2012.
[2] Paliwal et al., Neurosurgical Focus, 2018.

**9:40 AM ∼ 10:20 AM**

Prof. **Jian-Xun Wang** Assistant Professor
Affiliation/Web: University of Notre Dame Email: jwang33@nd.edu

**Title: Surrogate Modeling for Blood Flow Simulations Based on Physics-Constrained, Label-Free Deep Learning**

***Abstract***: *Computational fluid dynamics (CFD) modeling has become an indispensable tool in hemodynamics for predicting blood flow patterns and hemodynamic forces, which are critical for understanding the physiological mechanisms of cardiovascular diseases. On the other hand, however, CFD simulations are usually computationally expensive, particularly for flows with complex arterial geometry and/or considering fluid-structure coupling. Such drawback largely limits its real-time applications for supporting clinicians in their decisions and poses great challenges to many-query analysis, including uncertainty quantification, parameter estimation, and optimization problems arising in cardiovascular modeling. Therefore, there is a strong need to develop efficient surrogates for cardiovascular flow simulations.*

*Deep learning (DL) has shown new promises for surrogate modeling due to its capability of handling strong nonlinearity and high dimensionality. However, the off-the-shelf DL algorithms, success of which heavily relies on large-scale training data, fail to operate in the small data regime. Unfortunately, labeled data are often sparse in surrogate modeling since each data point in the parameter space requires an expensive CFD simulation. In this work, we provide a physics-constrained DL approach for surrogate modeling of fluid flows not relying on any simulation data. Specifically, a structured deep neural network (DNN) architecture is devised to enforce the boundary conditions, and the governing PDEs (i.e., Navier-Stokes equations) are incorporated in the loss function for the DNN training. Numerical experiments are conducted on a number of internal flow cases relevant to cardiovascular flow applications, and the uncertainties in fluid properties and domain geometry are considered. The numerical results show that the DL-propagated uncertainties have a favorable agreement with those propagated through the principled CFD simulations, which demonstrate the merits of the proposed method.*

**Joint work with:** Luning Sun, Han Gao.

**10:40 AM ∼ 11:20 AM**

Prof. **James C. Gee** Associate Professor
Affiliation/Web: University of Pennsylvania Email: gee@upenn.edu

**Title: Modern Analytics for Medical Imaging Studies**

***Abstract***: *Contemporary imaging scientists typically collect a wealth of measurements on relatively few subjects. Studies are therefore usually underpowered. There is a need for automated tools that are able to identify a reduced set of multidimensional salient features that drive the biological mechanisms of disease, function and development. This talk will discuss methods for computing the features and statistical comparisons commonly needed by population studies in medical imaging.*

**11:20 AM ∼ 12:00 PM**

Prof. **Yue Yu** Assistant Professor
Affiliation/Web: Lehigh University Email: yuy214@lehigh.edu

**Title: A Multiscale/Multiphysics Coupling Framework for Heart Valve Damage**

***Abstract***: *Bioprosthetic heart valves (BHVs) are the most popular artificial replacements for diseased valves that mimic the structure of native valves. However, the life span of BHVs remains limited to 10-15 years, and the mechanisms that underlie BHVs failure remain poorly understood. Therefore, developing a unifying mathematical framework which captures material*

*damage phenomena in the fluid-structure interaction environment would be extremely valuable for studying BHVs failure. Specifically, in this framework the computational domain is composed of three subregions: the fluid (blood) , the fracture structure (damaged BHVs) modeled by the recently developed nonlocal (peridynamics) theory, and the undamaged thin structure (undamaged BHVs). These three subregions are numerically coupled to each other with proper interface boundary conditions.*

*In this talk, I will introduce two sub-problems and the corresponding numerical methods we have developed for this multiscale/multiphysics framework. In the first problem the coupling strategy for fluid and thin structure is investigated. This problem presents unique challenge due to the large deformation of BHV leaflets, which causes dramatic changes in the fluid subdomain geometry and difficulties on the traditional conforming coupling methods. To overcome the challenge, the immersogemetric method was developed where the fluid and thin structure are discretized separately and coupled through penalty forces. To ensure the capability of the developed method in modeling BHVs, we have verified and validated this method. The second problem focuses on the local-nonlocal interface condition which plays a critical role in the fluid—peridynamics coupling framework. In the nonlocal models the loading boundary conditions should be defined in a nonlocal way, namely, on a region with non-zero volume outside the surface, while in fluid—structure interfaces the hydrodynamic loadings from the fluid side are typically provided on a sharp co-dimension one surface. To overcome this challenge, we have proposed a new nonlocal Neumann-type boundary condition which provides an approximation of physical boundary conditions on a sharp surface, with an optimal asymptotic convergence rate to the local counter part. Based on this new boundary condition, we have developed a fluid—peridynamics coupling framework without overlapping regions.*

**12:00 PM $\sim$ 2:00 PM**

Lunch Break

**2:00 PM $\sim$ 5:00 PM**

Local Tour to Copper Harbor, MI

## – Day 3: June 17, Monday –

**9:00 AM ∼ 9:40 AM**

Prof. **Jeff Calder** Assistant Professor
Affiliation/Web: University of Minnesota, Minneapolis Email: jcalder@umn.edu

**Title: Computation of integral invariants for geometry processing with applications to analysis of broken bone fragments**

***Abstract***: *Geometric invariants have a long history in shape analysis and processing, with differential invariants such as mean and Gauss curvature of surfaces playing key roles in early developments. More recently, integral invariants have been proposed that are less sensitive to noise. The focus of this talk is the spherical volume invariant, which is an integral invariant that measures the volume of the intersection of a sphere with the interior of an object. We will present an efficient method for computing the spherical volume invariant via a (hypersingular) surface integral, which can be computed analytically on a triangulated mesh. This work arose from a project to classify and reassemble broken bone fragments in an archaeological context, and we will briefly discuss applications to detecting fracture edges on fragments, and classifying fragments based on agent of breakage.* **Joint work with:** Riley O'Neill (University of St Thomas), Katrina Yezzi-Woodley (Anthropology, UMN), Peter Olver (Mathematics, UMN), Pedro Angulo-Umana, Bo Hessburg, and Jacob Elafandi (Mathematics, UMN).

**9:40 AM ∼ 10:20 AM**

Prof. **Yong Yang**
Affiliation/Web: Postdoc in ERDC-CHL Email: wacyyang@gmail.com

**Title: Using continuous finite element methods to solve FSI problems**Postdoc

***Abstract***: *The fluid-structure interaction (FSI) problems can be used to model many phenomenons, such as water-ship interaction, wind-bridge interaction, or red cell in the blood flow and so on. In this talk, I will present three algorithms of using continuous finite element method to solve FSI problems. Those three algorithms are the immersed boundary method, the shifted boundary method, and the pseudo-penalty method. I will show some results of benchmark tests and focus on the difference between those three methods. The immersed boundary method behaves better although our implementation looks like just the combination of several usual techniques. One application is the motion and deformation of cells flowing in the channel. I will show some numerical results on this problem and compare to the results in the literature.*

**10:40 AM ∼ 11:20 AM**

Prof. **Aditya Viswanathan** Assistant Professor
Affiliation/Web: University of Michigan - Dearborn Email: adityavv@umich.edu

**Title: Phaseless Imaging: Fast Algorithms, Recovery Guarantees, and Applications to Bio-Imaging**

***Abstract***: *The underlying physics of certain imaging modalities - such as x-ray crystallography and (Fourier) ptychography - requires the recovery of a signal from phaseless (or magnitude-only) measurements. This problem, commonly referred to as Phase Retrieval, is a challenging (and non-linear) inverse problem since the phase encapsulates a significant amount of structure in the underlying signal. In this talk, we discuss a framework for solving the phase retrieval problem from local (spectrogram-type) measurements. We summarize a recently introduced fast (essentially linear-time) and robust phase retrieval algorithm based on the Wigner deconvolution approach. The Wigner deconvolution procedure relates the autocorrelation of the unknown signal to the acquired measurements through Fourier transforms. An eigenvector based angular*

*synchronization algorithm can subsequently be utilized to recover individual phase information from these autocorrelation estimates. Theoretical recovery guarantees, numerical results, as well as applications to biomedical imaging will be discussed.*

**11:20 AM ∼ 12:00 PM**

Prof. **Yuan Liu** Assistant Professor
Affiliation/Web: Mississippi State University Email: yl686@msstate.edu

**Title: Krylov implicit integration factor discontinuous Galerkin methods on sparse grids for pattern formation**

***Abstract***: *Reaction diffusion system are most commonly used mathematical models for pattern formation in computational biology. In this talk, we will discuss a class of Krylov implicit integration factor (IIF) discontinuous Galerkin (DG) methods on sparse grids to solve reaction-diffusion equations on high spatial dimensions. The key ingredient of spatial DG discretization is the multiwavelet bases on nested sparse grids, which can significantly reduce the numbers of degrees of freedom. To deal with the stiffness of the DG spatial operator in discretizing reaction-diffusion equations, we apply the efficient IIF time discretization methods, which are a class of exponential integrators. Krylov subspace approximations are used to evaluate the large size matrix exponentials resulting from IIF schemes for solving PDEs on high spatial dimensions.*

**12:00 PM ∼ 2:00 PM**

Lunch Break

**2:00 PM ∼ 2:40 PM**

Prof.
Affiliation/Web: Email:

**Title:**

***Abstract***:

**2:40 PM ∼ 3:20 PM**

Prof.
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