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State-of-the-Art Modeling and Simulation of the Brain's Response to Mechanical Loads

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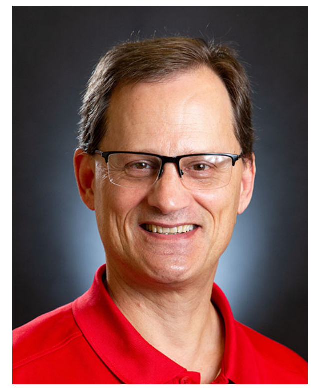
Traumatic Brain Injuries (TBI) are one of the most common yet least understood injuries to the human body. In the United States in 2013, an estimated 2.8 million hospital emergency department visits, hospitalizations, and deaths were TBI-related, contributing to nearly one-third of all injury-related deaths.[16] TBIs can occur because of many different types of events: falls, motor vehicle crashes, and impacts against or from an object, such as in sports and recreational activities. Sports-related concussions are also prevalent, with conservative estimates ranging from 1.6 to 3.8 million cases per year in the United States.[8] While TBI is a major public health concern for the general population, it is also a prominent factor in the injuries and deaths of warfighters.[15] Over 310,000 TBI cases were reported during Operation Iraqi Freedom and Operation Enduring Freedom.[5]

Biomechanics has long played a role in TBI research in our quest to study the mechanisms that transform impacts to the head into gross deformation of the brain, to localized straining of neuronal tissue and axons, and ultimately to neurological dysfunction. The first biomechanical models of TBI were physical surrogates developed by Holbourn in 1943 to investigate the strain distribution of the brain when the head suddenly accelerated from a blow.[6] Since then, modern brain injury research has moved towards computational approaches to understand the mechanisms associated with TBI at many different length scales and loading conditions. In fact, recent advances in the fields of neuroimaging, neuropathology, epidemiology, and experimental testing have enabled a rapid progression in the capability and fidelity of the models used today to understand the complex responses of the brain under different types of loading.

This special edition of the Annals of Biomedical Engineering focuses on the state-of-the-art of modeling and simulation methods related to traumatic brain injuries arising from mechanical loads. In this issue, fourteen articles are written by some of the world's leaders on this topic. In essence, the papers herein push the envelope of modeling the different aspects of how TBI might occur. This issue features research spanning a range of boundary conditions, from low-rate non-injurious motions of the head to high-rate impacts caused by the head's exposure to blast waves. Novel techniques are developed within these pages, and new analyses are presented that expand our knowledge of what happens when the head is impacted. The work in this issue builds on many years of research on the biomechanics of TBI and lays a foundation for future advances that will allow us to understand the brain better.

Different computational methods have been used over the years with a recent push towards higher fidelity simulations. Two review papers are presented herein that cover the history of modeling and simulation of TBI. Madhukar and Ostoja-Starzewski provide an in-depth background on the current state of the field for brain tissue modeling and describe a variety of finite element models of the human brain used in the literature for the study of TBI.[10] Giudice *et al.* focus primarily on a review of the numer-



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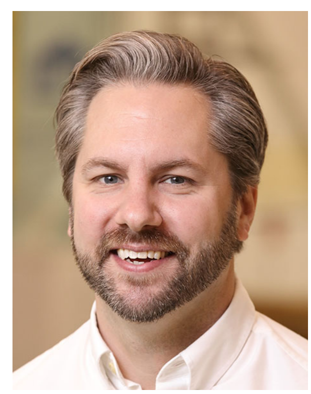
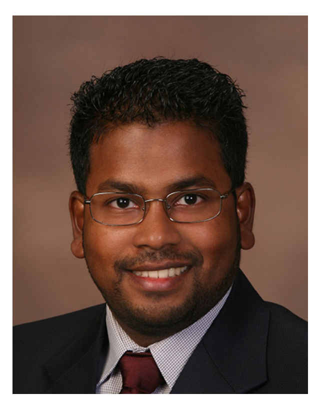


Matthew B. Panzer



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ical methods and meshing approaches currently used in finite element modeling of TBI and demonstrate that substantial sensitivities of the human brain model parameters affect the results.[3] Both review articles provide insight into how the science of TBI modeling and simulation has evolved over the years, highlighting the challenges that exist, and future directions this field is heading.

In particular, a number of articles in this issue have focused on developing new methods for modeling TBI based on current neuropathology and neuroimaging techniques. Horstemeyer *et al*. developed a new approach to modeling brain tissue, a mechanics-based brain damage framework that was able to correlate Chronic Traumatic Encephalopathy (CTE) pathology in deceased football players to the damage nucleation, growth, and coalescence mechanisms within the tissue model.[7] Garimella *et al*. and Wu *et al*. both developed new techniques for utilizing Diffusion Tensor Imaging (DTI) data to embed axonal tract information into existing finite element brain models.[2,19] These techniques improved the biofidelity of the models, but also allowed for better correspondence between TBI simulation of axonal strain and white matter changes in clinical TBI patients. Lu *et al*. utilized a different type of numerical technique, the material point method, to develop a model of the human brain that was validated against volunteer brain deformation data calculated from reconstructed magnetic resonance images.[9] Harris *et al*. used 2D planar human brain models to predict changes in brain anatomy during generalized and focused cerebral atrophy following a TBI.[4] Similarly, 2D planar models were used by Madouh and Ramesh to demonstrate the relative changes in strain distribution using a newly developed constitutive model for brain tissue that incorporates shear anisotropy.[11] All of the studies mentioned here are pushing the state-of-the-art of TBI modeling and simulation by incorporating the latest research from other fields, hereby building the advanced tools necessary for continued study of TBI mechanics.

Improving our understanding of TBI mechanics continues to generate interest in biomechanics, especially on the topic of relating external head impact conditions to TBI outcome or risk, which a number of studies herein are focused. Gabler *et al*., used a finite element model of the human head to determine the relationship between head kinematics and brain strain, and through this work developed a fast-solving metric that will provide an accurate assessment of TBI risk based on accelerometer data in a crash test dummy or wearable sensor.[1] Saboori and Walker performed a parametric study to provide insight on the strain amplitude and distribution within the brain to changes in magnitude and duration of a head impact and found a strong relationship between impact energy and brain deformation.[12] Singh and Cronin developed a multiscale approach to understanding how head kinematics and brain tissue response are influenced by different blast wave conditions, including tertiary blast effects because of head-to-ground contact.[14] All of these studies demonstrate the vital role that boundary conditions and head kinematics have on the potential for TBI.

This is also true for the cohort of papers in this issue that focuses on the brain's response to primary blast wave exposure in order to understand a problem that has plagued many veterans. Not only are these studies focused on understanding the mechanical response of the brain but are doing so under the complex boundary conditions associated with a primary blast wave impact on the head. Saunders *et al*. developed both a human and pig head model to study how brain tissue responses in one species correspond to brain tissue responses in another, with the goal of eventually linking preclinical injury model results to humans through correspondence rules.[13] Townsend *et al*. used a model of a rat brain exposed to a blast wave to study the sensitivity of intracranial pressure and brain tissue strain to changes in bulk and deviatoric brain tissue properties, which highlighted the need for more robust data to validate computational models of TBI.[17] A similar study was performed by Unnikrishnan *et al*., who used a rat brain model that had integrated cerebrovasculature to study the effects of including this type of neuroanatomy in the model.[18] The emergence of computational models of animal TBI is an indication of the eventual convergence between biomechanical modeling and simulation with the neuropathological and neuroimaging outcomes measured in preclinical models.

This concept of TBI models evolving with complementary fields within neurotrauma is found throughout this special issue from the microscopic level to the macroscopic level. As knowledge and capability continue to progress in the TBI research community, so too will the functionality and biofidelity of biomechanical TBI models. Advancements will be made with our enduring motivation to understand how the mechanics of the head cause TBI such that we may one day improve how we prevent, diagnose, treat, and rehabilitate this injury.

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