Modeling Human Brain Function and Pathways of Neurodegeneration

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Abstract

Neurodegenerative diseases (NDs) are complex disorders characterized by the progressive structural and functional deterioration of the brain. A common hallmark of many NDs is the accumulation of disease-specific misfolded and aggregated proteins, such as amyloid-beta and tau in Alzheimer's disease, alpha-synuclein in Parkinson's disease, and TDP-43 in Amyotrophic Lateral Sclerosis. In this presentation, we introduce a novel framework that integrates multiphysics and multiscale mathematical modeling, advanced discretization techniques, and computational learning paradigms to elucidate the mechanisms underlying neurodegeneration. The spatio-temporal dynamics of misfolded proteins are modelled using advanced conformational conversion systems discretized with high-order polytopal finite element methods [1, 2, 5]. Additionally, multiphysics mathematical models of cerebral waste-clearance dynamics, a critical factor influencing the onset and progression of NDs, are described, along with an analysis of how pathological processes associated with neurodegeneration may increase epileptiform activity [3, 4]. Finally, a computational learning framework is presented to infer latent disease states and predict personalized trajectories of ND progression from sparse, irregularly sampled, and multimodal clinical data. Extensive patient-specific numerical simulations are provided to validate the proposed methodological approach.

References

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