

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

- [1] P. F. Antonietti, S. Giani, and P. Houston. hp-version composite Discontinuous Galerkin methods for elliptic problems on complicated domains. *SIAM J. Sci. Comput.*, 35(3):A1417–A1439 (2013)
- [2] M. Corti, F. Bonizzoni, P. F. Antonietti, Structure Preserving Polytopal Discontinuous Galerkin Methods for the Numerical Modeling of Neurodegenerative Diseases, *J. Sci. Comput.*, 100:39 (2024)
- [3] I. Fumagalli, M. Corti, N. Parolini, P. F. Antonietti, Polytopal discontinuous Galerkin discretization of brain multiphysics flow dynamics, *J. Comput. Phys.*, 513:113115 (2024)
- [4] C. B. Leimer Saglio, S. Pagani, P.F. Antonietti, A p -adaptive polytopal discontinuous Galerkin method for high-order approximation of brain electrophysiology, *Comput. Methods Appl. Mech. Eng.*, 446:118249 (2025)
- [5] V. Pederzoli, M. Corti, D. Riccobelli, P. F. Antonietti, A coupled mathematical and numerical model for protein spreading and tissue atrophy applied to Alzheimer's disease, *Comput. Methods Appl. Mech. Eng.*, 444:118118 (2025)