Uncovering the Secrets of the Glymphatic System and Implications for Neurodegenerative Disease: A Computational Medicine Approach

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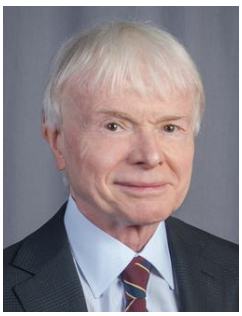

Abstract: An estimated 6.5 million Americans suffer from neurodegenerative diseases such as Alzheimer's Disease (AD) that result in progressive degeneration and death of nerve cells (neurons) impairing movement and/or mental functioning. In spite of monumental research efforts and numerous clinical trials, no successful treatment has emerged that can cure or retard the course of the disease.

It has long been held that the brain has no lymphatic drainage to remove metabolites and neurotoxins that enter the brain. However, evidence to the contrary has mounted, and in the last few years it has been shown that there is after all a mechanism for vascular exudate drainage from the intracranial compartment via the exterior aspect of major cerebral vessels and blended with cerebral and spinal fluid (CSF). This CSF drainage mechanism has been dubbed the *glymphatic system*.

Currently, there exists no comprehensive 3D subject-specific modeling framework geared toward providing a macro level understanding of glymphatic transport of molecules, proteins and nanoparticles. The paucity of research in this area may be attributed in part to the challenges associated with creating geometrically authentic 3D models of the complex cerebrovasculature network necessary for delineating CSF flow pathways, and then functionally coupling them to glymphatic transport processes in the brain parenchyma. There is also a dearth of relevant modeling of transport mechanisms with existing quantitative published data that can be used to verify simulation results and model assumptions. The objective of the research is to develop an integrated tool set of physiologically accurate flow modeling and experimental techniques to realistically describe glymphatic transport.