Cerebrospinal Fluid Mechanics and Its Coupling to Cerebrovascular Dynamics

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Abstract
Cerebrospinal fluid (CSF) is not stagnant but displays fascinating oscillatory flow patterns inside the ventricular system and reversing fluid exchange between the cranial vault and spinal compartment. This review provides an overview of the current knowledge of pulsatile CSF motion. Observations contradicting classical views about its bulk production and clearance are highlighted. A clinical account of diseases of abnormal CSF flow dynamics, including hydrocephalus, syringomyelia, Chiari malformation type 1, and pseudotumor cerebri, is also given. We survey medical imaging modalities used to observe intracranial dynamics in vivo. Additionally, we assess the state of the art in predictive models of CSF dynamics. The discussion addresses open questions regarding CSF dynamics as they relate to the understanding and management of diseases.
1. INTRODUCTION

Cerebrospinal fluid (CSF) fills the cerebral ventricles as well as the cranial and spinal subarachnoid spaces (SAS). An anatomical overview of the CSF-filled spaces is given in Figure 1. The enclosed fluid body is not static but exhibits pulsatile motion inside the ventricular system, and between the cranial vault and spinal compartments, superimposed by bulk flow due to fresh production and final clearance into the venous systems. The pulsatile pattern is essential to normal brain function, and several diseases manifest disturbances of CSF flow dynamics.

Recent efforts in the scientific and clinical communities aim at precisely quantifying critical parameters of normal intracranial dynamics as well as detecting characteristic deviations in diseases. Of special relevance is the intracranial pressure (ICP), which can be measured only invasively. Additionally, CSF flow velocities, brain motion, and deformations within the cranial and spinal compartments can be acquired noninvasively. In vivo medical imaging is providing an unprecedented window into intracranial and spinal dynamics. Image data help to precisely delineate patient-specific anatomical spaces, characterize blood and CSF flow, and trace the biodistribution of pharmacological drugs transported rapidly by pulsating CSF. Because in vivo imaging often provides only point measurements, researchers and clinical practitioners are forced to hypothesize about the biomechanical interactions between central nervous system (CNS) compartments. Unfortunately, conceptual ideas without quantitative verification have so far not solidified our understanding of brain disease enough to improve patient care.

Quantitative models are needed to provide hard predictions in support of new insights about the fluid dynamics of blood and CSF in the CNS. Judging by the growing body of publications reviewed in this article, mathematical modeling has already garnered the attention of the neurological surgery and neuroscience communities. There appears to be a growing consensus about the important role mathematical models can play for better interpretation of in vivo data acquired at multiple length scales and locations.

Mathematical models can be characterized by two extreme cases. In black box models, measurements are fitted against algebraic functions without considering the conservation principles that govern the flow. These black box models represent data but do not elucidate or interpret the physics of the transport phenomena. Although black box models reproduce data trends with high precision, they offer little insight into the functional role between parameters. Conversely, mechanistic models are rooted in fundamental conservation laws of mass, momentum, and chemical species. An increasingly important role is played by image-guided computational fluid dynamics (CFD), which can simulate patient-specific scenarios for direct comparison to measurements in vivo (Linninger 2012). We advocate here the opinion that it is key for CFD models to avoid domains or limiting boundary conditions that diminish the rigorous computations to mere data fitting, but that they should explore novel hypotheses that account for the dynamic interaction between central nervous system compartments.

Figure 1

Anatomical diagram of the main structures in the central nervous system. The entire spinal and cranial space is shown on the left. (a) Detail of the cranial SAS (light blue), the four ventricular spaces (blue), and brain parenchyma (pink). Also shown is the location of the choroid plexus (green) inside the ventricles and arachnoid villi (red) at the superior most aspect of the cranial space. (b) Magnification of the cortical surface illustrating the penetrating arterioles, surrounding perivascular space, underlying pia mater and glia limitans. Panel b adapted from Iadecola & Nedergaard (2007) and Louveau et al. (2015). (c) Depiction of the spinal SAS at the lower thoracic region, T8–T12. The spinal cord is colored in yellow. Nerve roots protrude from the spinal cord and exit the dura membrane (gray envelope). Arachnoid trabeculae (dark blue) are microscopic features below the threshold for imaging but are illustrated here for context. (d) An axial plane highlighting the orientation of nerve roots (yellow) at the thoracic T10 inside the spinal SAS (blue). (e) An axial plane of the spinal SAS and spinal cord structures: spinal cord gray matter (dark yellow) and white matter (yellow). The three meningeal layers dura (brown), arachnoid (dark blue), and pia membrane (purple) are indicated. Arachnoid trabeculae are shown as thin dark blue lines. Abbreviations: CSF, cerebrospinal fluid; SAS, subarachnoid spaces.