

**A MECHANO-ELECTROCHEMICAL MODEL OF BRAIN
NEURO-MECHANICS:
APPLICATION TO NORMAL PRESSURE HYDROCEPHALUS**

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Abstract. Normal pressure hydrocephalus (NPH) is a neurological condition that occurs in adults usually older than sixty years, characterized by an excessive accumulation of cerebrospinal fluid in the brain ventricles in the absence of an elevated intracranial pressure. Although the first description of this disease has been given in 1965 by Hakim and Adams, the progress in improving the diagnosis and treatment outcome of NPH has been slow due mainly to the fact that the causes of NPH continue to remain unknown in most of the cases. The few existing biomechanical models of NPH existing in the literature are based on the bulk flow theory which requires an increased intracranial pressure and thus fail to properly explain the onset of NPH. The aim of the present paper is to formulate the first neuro-mechanical model that will couple the electro-chemical and mechanical properties of the brain. We assume that the brain tissue is a charged hydrated soft tissue made of a solid phase, an interstitial fluid phase and an ion phase with (for now) two monovalent ion species. Using our model, we will show that NPH could be caused by a change in the concentrations of Na^+ and Cl^- in the ventricular cerebrospinal fluid in the absence of an elevated intracranial pressure.

Key words. brain neuro-mechanics, triphasic model, normal pressure hydrocephalus, brain swelling

1. Introduction

Normal pressure hydrocephalus (NPH) is a serious neurological disorder characterized by gait disturbance, mental deterioration and urinary incontinence in patients with enlarged cerebral ventricles in the absence of increased intracranial pressure [1, 2]. NPH is predominantly found in adults over 60 years of age and is often missed or misdiagnosed because many conditions affecting older individuals can mimic the symptom profile of NPH, including Parkinson's disease, Alzheimer's disease, metabolic and psychiatric disorders, endocrine dysfunction, infections, trauma, vascular and neurodegenerative disorders [4]. In most of the cases, the cause of NPH is unknown.

Recent estimates of NPH incidence range from 50,000 to 375,000 people in the United States, with the higher figure more likely to be correct [3]. In 2002, the U.S. Census Bureau estimated that there were nearly 60 million people age 55 or older living in the United States. Average life expectancy was approximately 77 years in 2001, according to the National Center for Health Statistics, Centers for Disease Control and Prevention [5]. Since average life expectancy is expected to continue to increase, the number of diagnosed cases of NPH and the associated treatment costs will continue to grow, as well.

The efforts in treatment have been principally through the diversion of the ventricular cerebrospinal fluid (CSF) flow. Within limits, the dilation of the ventricles

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can be reversed by a surgical placement of a shunt in the brain to drain excess CSF into the abdomen where it can be absorbed. The extent of improvement after neurosurgical shunt procedures varies greatly: 45%-65% of patients respond positively [6, 7, 8], while morbidity is about 40%-50% [6, 8, 9]. Therefore, there is an urgent need for a proper selection of patients who may benefit by a shunt operation.

In order to design better diagnostic and treatment protocols for NPH, we need to develop realistic biomechanical models of the brain for the numerical simulation of NPH. The few existing models presented in the engineering literature on NPH are based on the hydrodynamics of CSF which tends to accumulate in the brain ventricular system during the development of NPH (in a healthy brain, the CSF circulates continuously between the ventricles, the site of CSF production, and the subarachnoid space, the site of CSF absorption) [10]-[20]. All these models are based on the bulk flow theory: the driving force of the CSF bulk flow is the CSF pressure at the production site being higher than the pressure at the absorption site. In this theory, the enlargement of the ventricles during the development of hydrocephalus is due to an increased intracranial pressure. However, NPH is incompatible with the bulk flow theory since in the case of NPH the ventricles dilate without an increase of the CSF pressure [21]. Recently, Levine [22] postulated that there exists an abnormal but very small gradient of static pressure across the cerebral mantle that should be sufficient to produce the ventricular dilatation of NPH. Although this is an attractive theory, it has very limited medical applicability since there are no instruments sensitive enough to measure such small abnormal gradients. Finally, none of the published biomechanical models of NPH incorporates any relevant clinical information about abnormal electro-chemical processes taking place during the development of NPH [23, 24].

The aim of the present paper is to formulate the first neuro-mechanical model that will couple the electro-chemical and mechanical properties of the brain. We assume that the brain tissue is a charged hydrated soft tissue made of three phases: an intrinsically incompressible, porous-permeable, charged solid phase that includes the extracellular matrix and brain cells; an intrinsically incompressible, interstitial fluid phase that models the extracellular fluid; and an ion phase with, for now, only two monovalent ion species anion (-) and cation (+). In addition, there exist negatively charged groups on the solid phase called fixed charges since they are much less mobile than the freely mobile ions dissolved in the fluid phase. The existence of such fixed charges in the brain tissue has been proved experimentally by Erkin et al [33]. The solid phase and the ion phase are electrically charged, while the fluid phase and the tissue as a whole are electrically neutral. A schematic picture of the structure of the triphasic brain tissue is shown in Figure 1.

So far, the triphasic mechano-electrochemical theory has been applied successfully to model the mechanics of the articular cartilage [25]-[28]. In a series of conference papers [31, 32], we have shown some promising preliminary results on NPH using the above mentioned triphasic model for the brain, and very recently a similar model has been used to analyze brain tissue swelling (cerebral oedema) due to traumatic brain injury or stroke [33].