

ON MECHANISMS OF DIFFUSE AXONAL INJURIES

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INTRODUCTION

One of the main directions in mathematical modeling of brain injuries assumes that brain matter can be treated as a viscoelastic solid. In particular, Ljung [1] develops such a model; hereinafter the Voigt model (cf. [2]). The main mechanistic feature of this Voigt model consists of shear waves whose propagation and damping are governed by a set of linear differential equations. These equations may be viewed as a linearization of the Navier-Stokes equations describing incompressible fluids, see e.g. [3], and are sometimes referred to as Kelvin-Voigt equations [1]. Following [2], we shall refer to them simply as Voigt equations; reserving Kelvin's name for a model where an additional damping term is introduced.

Thanks to Ljung [1], there are known analytic solutions of the Voigt equations in some particular three-dimensional cases with a rotational symmetry (rotating cylinder, half-cylinder and sphere). These solutions indicate that during a typical accident scenario, the physical characteristics of human brain tissue allow the propagation of shear waves that induce relative displacements of the brain tissue up to 50%. Since veins are prone to rupture when stretched by 50% [4,5], and some experiments [6] suggest that stretching axons by 10-15% can lead to ion imbalances in the axons and consequently to their death, such displacements of brain tissue provide a potential explanation of some forms of traumatic brain injury. In fact, Margulies and Thibault [7] proposed a criterion for Diffuse Axonal Injuries (DAI) that is based, in part, on Ljung's results related to the effective stretching of axons. The Voigt equations have been further investigated (see [8,9] and the references therein) to more accurately model potential mechanisms of brain hematomas and DAI.

Recent experiments [10] indicate that ion imbalances in axons are not observed even when axons are stretched by 85% that contrasts with the results reported in [6]. Embracing these data leads to an intrinsic inconsistency in continuing to use the Voigt equations for modeling DAI. Indeed, the derivation of the Voigt equations is based on the assumption that the displacements of a continuous physical medium are small (Hook's law) [3]. Even the 50% relative displacement found in the Voigt model (that has been proposed as a

causal mechanism for hematomas) is "too large" for justifying assumptions used to derive the Voigt equations. Moreover, microscopic studies show the following three features of DAI: 1) a highly localized character of damages, i.e., some portions of neurons are affected while the other portions as well as close neighbors of damaged neurons are not; 2) such pointwise damages are scattered over larger regions, most commonly in the white matter; and 3) the injured cells are often concentrated along the border between the gray and white matter.

The Voigt model is unable to explain these observed characteristics of brain injuries. Similarly, a great majority of the criteria for brain injuries predicts only under which external (physical) circumstances such injuries may occur while specifying no detailed internal features or locations of the injuries.

A NONLINEAR MODEL

The brain tissue contains approximately 80% water. Therefore it is reasonable to generalize the Voigt model by considering a version of the Navier-Stokes equations that describes an incompressible viscoelastic fluid. This approach allows us to investigate, in a more consistent way than the Voigt model, how large relative displacements of brain tissue can cause brain injuries.

More importantly, the shear module of brain tissue induces shear waves whose phase speed is comparable with the speed of the flow of the brain tissue induced typically in accidents (1m/s). Consequently, nonlinear phenomena such as steepening of the wave fronts and their turbulent breaking could explain both the pointwise and scattered character of DAI.

Finally, recent experiments [11,12] show that there exists an essential difference in phase speed of shear waves in the gray and white matter. Namely, the phase speed in the white matter is measured to be approximately 1m/s whereas in the gray matter it appears to be 2 or even 4 times larger. Thus a 1m/s flow of the gray matter (induced e.g. by a rotation of a human head in an accident) might cause no damage in that layer of the brain tissue (because it is much slower than the speed of shear waves in the gray matter). However, the

propagation of this flow into the white matter (that takes place due to the $0.01\text{m}^2/\text{s}$ viscosity of the brain tissue) can lead to a flow that is faster than the phase speed of shear waves in the white matter, resulting in nonlinear phenomena described above. Consequently, brain damage might likely appear near the border between the gray and white matter as has been reported in clinical studies.

NUMERICAL MODEL AND RESULTS

To numerically solve our system of nonlinear differential equations we adapted the numerical model developed at the National Center for Atmospheric Research in Boulder, Colorado. Namely, we extended for our needs the semi-Lagrangian/Eulerian atmospheric fluid code EULAG that has been broadly documented in the literature (see, e.g., [13,14,15] and the references therein). EULAG solves the anelastic equations of motion in the standard, nonorthogonal terrain-following coordinates. This feature is especially important since it allows to take into account the asymmetric shape of the human skull as well as the complicated geometry of some internal structures such as the falx cerebri. The numerical model was validated against the analytic solutions obtained by Ljung [16].

Initially our numerical simulations were primarily devoted to studying the flow of homogeneous brain tissue contained in an infinite elliptic cylinder of 'bigger' radius $R=0.1\text{m}$ rotated along its axes with various tangential velocities ($0.5\text{-}3\text{m/s}$). Some of these results are documented in [16]. The numerical simulations clearly show that in our nonlinear model even a minor violation of rotational symmetry (eccentricity) may lead (within hundreds of milliseconds) to a turbulent flow if the tangential velocity of rotation is sufficiently large (3m/s). Similar results are observed when an inner obstacle simulating the shape of the falx cerebri is introduced.

The most revealing results are from the numerical simulations of a rotating elliptic cylinder which contains a two-layer medium with physical characteristics corresponding to the gray and white matter. Namely, the asymmetry of the ellipse leads to solutions that exhibit four regions of highly localized spikes in relative displacement which occur at the border between the gray and white matter. Figure 1 depicts (in elliptic coordinates ρ, θ) the operator norm N of the Jacoby matrix of the displacement (derivatives with respect to spatial variables) at the time 0.01s , for a cross-section of the elliptic cylinder with $R=0.01\text{m}$ and the eccentricity 0.87 , rotated for 0.05s with the tangential velocity 1.35m/s .

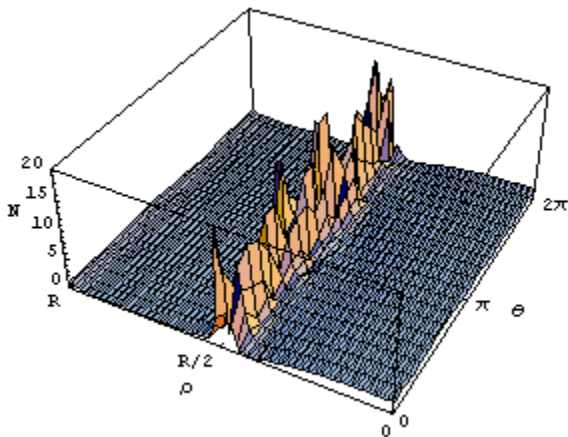


Figure 1. Norm at $t=0.01\text{s}$ for the 0.05s rotation with the tangential velocity 1.35m/s . Wave speeds: in the gray matter 1.8m/s - in the white matter 0.9m/s .

This and other numerical simulations show that scattered 'singularities' appear at the border between the gray and white matter very quickly even if: 1) the forced rotation is very short, and 2) the rotation speed of the cylinder induces a flow in the gray matter whose speed is smaller than speed of shear waves in the gray matter but comparable with, or larger than, the speed of shear waves in the white matter. Thus our results strongly suggest that nonlinear effects combined with the very complicated geometry of the brain/skull structure may be responsible for the scattered and highly localized character of Diffuse Axonal Injuries as well as for the fact that these injuries tend to appear at the border of the gray and white matter.

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