Computer Modeling of Diffuse Axonal Injury Mechanisms

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Abstract— *We investigate numerically which properties of the human brain cause Diffuse Axonal Injuries (DAI) to appear in a scattered and pointwise manner near the gray/white matter boundary, mostly in the white matter. These simulations are based on our dually-nonlinear, viscoelastic, fluid Traumatic Brain Injury model, which includes a nonlinear stress/strain relation. We simulate rotational accelerations and decelerations of a human head that replicate realistic traumatic scenarios. The rotational loads are quantified by our Brain Injury Criterion, which extends the translational Head Injury Criterion to arbitrary head motions. Our simulations show that: (i) DAI occurrences near the gray/white matter boundary can be explained by the difference in the gray and the white matter's shear modulus values, (ii) the scattered/pointwise DAI character can be attributed to the nonlinear fluid aspect of the brain tissue, and (iii) the scattering of DAI deeper in the white matter appears to be caused by the complicated shape of the brain. Our results also show that the nonlinear stress/strain relation plays a secondary role in shaping basic DAI features.*

Keywords: computer modeling, diffuse brain injury, nonuniform shear modulus, nonlinearity

1. Introduction

The most 'mysterious' kind of Traumatic Brain Injuries (TBI) are Diffuse Axonal Injuries (DAI). DAI predominantly appear during abrupt head rotations [1], [2]. However, despite many experimental and numerical studies, the way DAI are created in the brain matter is still not well understood. In particular, the following main characteristics of DAI require explanation [3]:

- The injuries are highly localized, i.e., some neurons are affected while their close neighbors are not.
- The injuries are randomly scattered, mostly in the white matter along its boundary with the gray matter.

In his initial studies with a nonlinear fluid TBI model, one of the co-authors investigated implications of the difference in the shear moduli between the gray matter and the white matter on the propagation of shear waves in human brain tissue. The results of a simulated *idealized instant* motion of two-layer brain tissue indicated that the different shear moduli could explain some features of DAI [4]. More recent studies have shown that the nonlinear stress/strain relation in brain tissue should also be taken into account when modeling scenarios leading to brain trauma [5].

In this paper, we present results of a systematic study of possible mechanism of DAI. The computer simulations are based on our new viscoelastic dually-nonlinear TBI model that includes a nonlinear fluid term as well as a nonlinear stress/strain relation derived from experimental data. Our new model uses a brain facsimile that reflects the *realistic general shape* of a human brain. The gray matter and the meninges are represented as thin layers that follow the skull's shape. We focus on simulating rotational accelerations and decelerations of a human head that recreate *realistic* dynamic conditions leading to severe brain trauma, e.g., a forceful helmet-to-helmet hit during a football game.

2. Dually-nonlinear TBI model

Our computational TBI model is rooted in the biophysical approach that describes the brain dynamics based on the viscoelasticity theory—the brain is injured when the strain field, created in the brain by shear waves due to the head motion, assumes sufficiently high values. To model the dynamic evolution of this strain field, we use the following system of nonlinear Partial Differential Equations (PDEs):

$$\frac{D\mathbf{v}}{Dt} = -\nabla\tilde{\mathrm{p}} + \triangle(s^2\mathbf{u} + \nu\,\mathbf{v}), \quad \frac{D\mathbf{u}}{Dt} = \mathbf{v}, \quad \nabla\cdot\mathbf{v} = 0. \tag{1}$$

Here, $D/Dt \equiv \partial/\partial t + (\mathbf{v}\cdot\nabla)$ is the nonlinear Lie (material) derivative, where $\mathbf{v}(\mathbf{x},t) \equiv (\mathrm{v}_1(\mathbf{x},t), \mathrm{v}_2(\mathbf{x},t), \mathrm{v}_3(\mathbf{x},t))$ with $\mathbf{x} \equiv (x_1, x_2, x_3)$ denotes the brain matter velocity vector field evaluated at time t in an external coordinate system; $\mathbf{u}(\mathbf{x},t)$ is the corresponding displacement vector field; $\tilde{\mathrm{p}}(\mathbf{x},t)$ denotes the generalized pressure term consisting of the density normalized pressure and the hydrostatic compression term; $s(\mathbf{x},t)$ describes the brain's shear wave phase velocity; and ν is the brain's kinematic viscosity.

PDE system (1) generalizes the linear solid Kelvin-Voigt (K-V) model (successfully used to develop a DAI criterion [6]) by introducing *two* nonlinear terms $s(\mathbf{x},t)$ and $\mathbf{v}\cdot\nabla$, and the term $\tilde{\mathrm{p}}(\mathbf{x},t)$ that is necessary in such a case cf. [4].

The material derivative allows us to model the nonlinear fluid (gel-like) aspect of the brain tissue, whereas $s(\mathbf{x},t)$ describes how the brain matter stiffens under larger deformations, i.e., how the shear wave velocity increases with the strain. Experiments imply that this relation is linear only for small strains [5], [7] and that it can be approximated by an exponential function for larger strains [8].

Thus, we model the stress/strain relation by $s(\mathbf{x},t) \equiv c(\mathbf{x})\exp(qP(\mathbf{x},t)))$, where $c(\mathbf{x}) \equiv \sqrt{G(\mathbf{x})/\delta(\mathbf{x})}$ denotes the basic shear wave velocity in the absence of strain ($G(\mathbf{x})$ and $\delta(\mathbf{x})$ are the brain matter shear modulus and density, respectively), and $P(\mathbf{x},t)$ describes the time evolution of the spatial distribution of the maximum strain. For strains larger than 50%, we assume that $s(\mathbf{x},t)$ smoothly becomes proportional to the basic shear wave velocity $c(\mathbf{x})$.

Experiments, cf. [5], [8]-[10], imply that:

- the basic wave velocity in the white matter is $c_w \approx$1m/s and c_g in the gray matter is up to 4 times larger,
- the coefficient q determining the stress/strain relation is within the range $0.4 \leq q \leq 2.5$, and
- the brain's viscosity ν equals approximately 0.013m^2/s.

3. Simulation setup and display method

We simulate sideways head rotations about a fixed vertical axis through the brain's center of mass and forward or backward head rotations about horizontal axes located at the brain's center of mass, the neck, and the abdomen. Keeping the axes fixed allows us to solve PDEs in separate horizontal or sagittal 2D brain cross sections, which simplifies the analysis and presentation of the results.

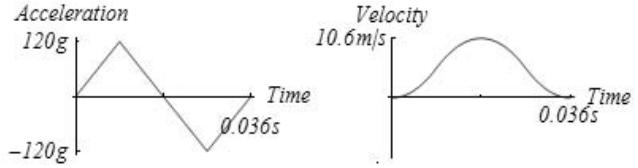
We show the effects of head rotations in a form of time snapshots presenting (in horizontal and sagittal brain cross sections) the distribution of:

- the vector field $\mathbf{V}(\mathbf{x},t)$ describing the brain matter velocity relative to the skull,
- this relative velocity's magnitude $|\mathbf{V}(\mathbf{x},t)|$,
- and the values $P(\mathbf{x},t)$ of the maximum strain in the white and the gray matter as well as in the meninges.

To better present the character of the brain matter oscillations, we depict the vector field $\mathbf{V}$ in form of curved vectors [11]. The dark to light shading of the curved vectors indicates the motion's direction. Animated 'movies' built from the snapshots of various head rotations are available at our website: http://www.funiosoft.com/brain/.

The average (around the skull's perimeter) tangential acceleration loads we apply are quantified by the value of our universal Brain Injury Criterion BIC_{1000T}, where T is the load's duration [12]. It means that the average power per unit mass transmitted from the skull to the vicinity of the considered 2D brain cross section is equal to the average power transmitted to this vicinity under the translational load corresponding to the Head Injury Criterion HIC_{1000T} successfully used by the automotive industry to determine critical loads [13], [14].

The results presented are obtained using the following triangularly shaped acceleration/deceleration load characterized by the critical value BIC_{36}=1000:



Under this tangential load, the sideways rotations of about 110^o replicate, e.g., a blow to a boxer's head, whereas similar forward or backward rotations simulate a head motion, e.g., during a car accident.

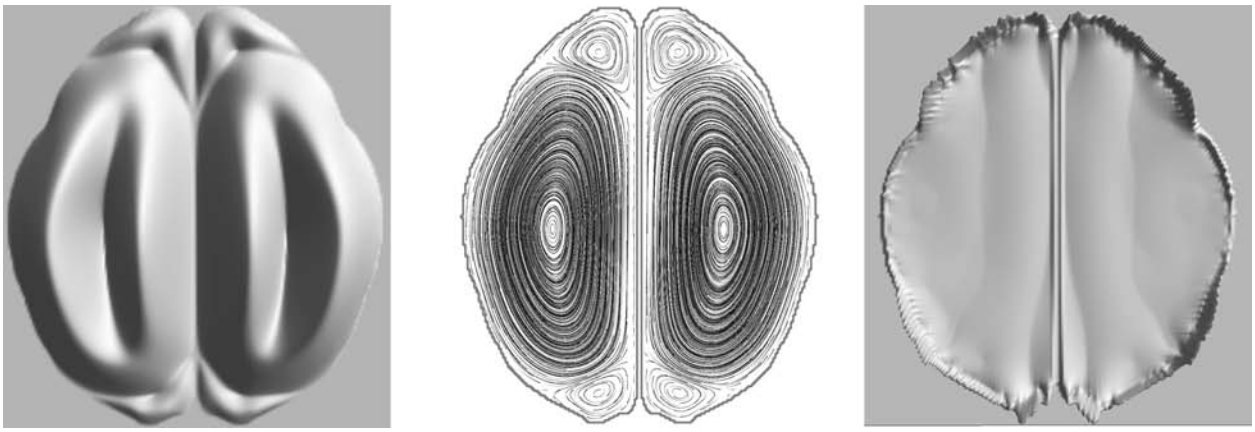
4. The role of a nonuniform shear modulus and brain geometry

We have previously shown that the brain's geometry influences the character of traumatic brain oscillations [11], [15]. To separate the role played by the brain geometry in shaping DAI features from the role of the difference in the gray and white matter shear moduli and the role of the brain's nonlinear properties, we first simulate rotations of the brain with a uniform or nonuniform shear modulus using the linear K-V TBI model.

Fig. 1 (resp. 2) shows the velocity and the maximum strain distributions at time t = 0.025s in a horizontal brain cross section (separated by the falx cerebri) with a uniform (resp. nonuniform) shear modulus during a counterclockwise sideways rotation of the head.

In a case of a uniform shear modulus with $c_g = c_w$ = 1m/s, the velocity magnitude $|\mathbf{V}|$ is distributed quite smoothly with $|\mathbf{V}|_{max} \approx$ 0.6m/s, Fig. 1 left panel, even where the skull's shape creates (at the top and bottom of the cross section) secondary vortices with 'opposite' oscillations than those appearing in the major two vortices, Fig. 1 middle panel. Consequently, high strain magnitudes appear only in the meninges, where the transfer of energy between the skull and the brain takes place, Fig. 1 right panel.

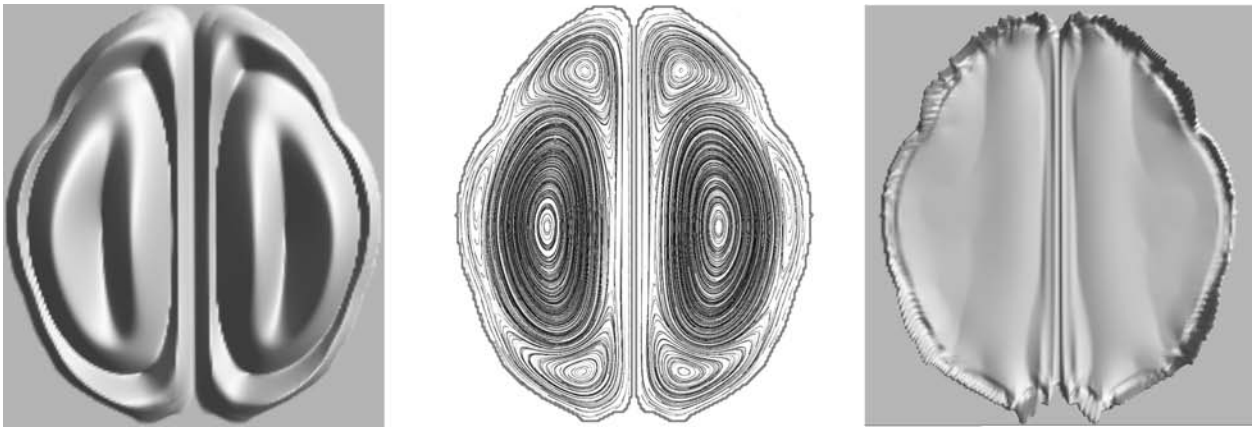
In a case of a nonuniform shear modulus with c_g = 1.75m/s and c_w = 1m/s, the gray matter tends to oscillate along the skull and the falx cerebri in the opposite direction than the white matter, Fig. 2 middle panel. This leads to very steep changes in magnitudes $|\mathbf{V}|$ at the gray/white matter boundary, Fig. 2 left panel, and hence to high strain values there, Fig. 2 right panel. The largest strain values exceed 30%, which suffices to severely damage neurons [6], [16]-[18], most likely due to a chemical imbalance [19], [20].



$|\mathbf{V}(\mathbf{x}, 0.025\text{s})|$ $\mathbf{V}(\mathbf{x}, 0.025\text{s})$ $P(\mathbf{x}, 0.025\text{s})$

Fig. 1

RELATIVE VELOCITY AND MAXIMUM STRAIN IN A HORIZONTAL CROSS SECTION DURING SIDEWAYS ROTATION ABOUT THE CENTER OF MASS; LINEAR KELVIN-VOIGT MODEL; UNIFORM SHEAR MODULUS: $c_g = c_w = 1$M/S.



$|\mathbf{V}(\mathbf{x}, 0.025\text{s})|$ $\mathbf{V}(\mathbf{x}, 0.025\text{s})$ $P(\mathbf{x}, 0.025\text{s})$

Fig. 2

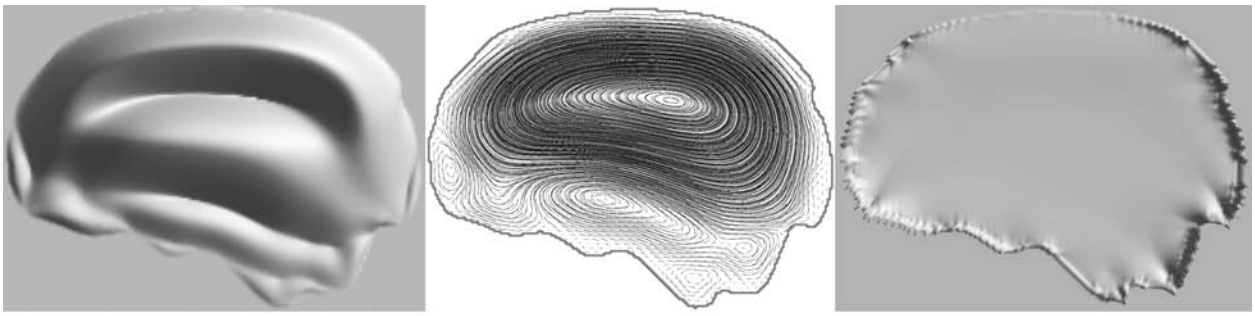
RELATIVE VELOCITY AND MAXIMUM STRAIN IN A HORIZONTAL CROSS SECTION DURING SIDEWAYS ROTATION ABOUT THE CENTER OF MASS; LINEAR KELVIN-VOIGT MODEL; NONUNIFORM SHEAR MODULUS: $c_g = 1.75$M/S, $c_w = 1$M/S. NOTE THE HIGH VALUES OF $|\mathbf{V}|$ AT THE GRAY/WHITE MATTER BOUNDARY IN THE LEFT PANEL, WHICH ARE THE RESULT OF THE 'OPPOSITE' OSCILLATIONS OF THE GRAY MATTER ALONG THE SKULL AND THE FALX CEREBRI WHEN $c_g > c_w$, MIDDLE PANEL. CONSEQUENTLY, HIGH STRAIN MAGNITUDES APPEAR ALONG THIS BOUNDARY, RIGHT PANEL, WHICH ARE NOT PRESENT IN FIG. 1.

Our simulation results of forward and backward head rotations further show that the brain's shape plays a major role in the localization of oscillatory vortices within the gray and the white matter.

Fig. 3 (resp. 4) on the next page depicts the relative velocity and the maximum strain distributions predicted by the linear K-V model in a sagittal cross section with a uniform (resp. nonuniform) shear modulus when the head is rotated forward about the neck.

In both cases, the shape and the position of the major oscillatory vortex reflects the general semi-circular shape of the upper part of the brain and the fact that the rotational axis is substantially lower than the brain's center of mass, Figs. 3 and 4 middle panels.

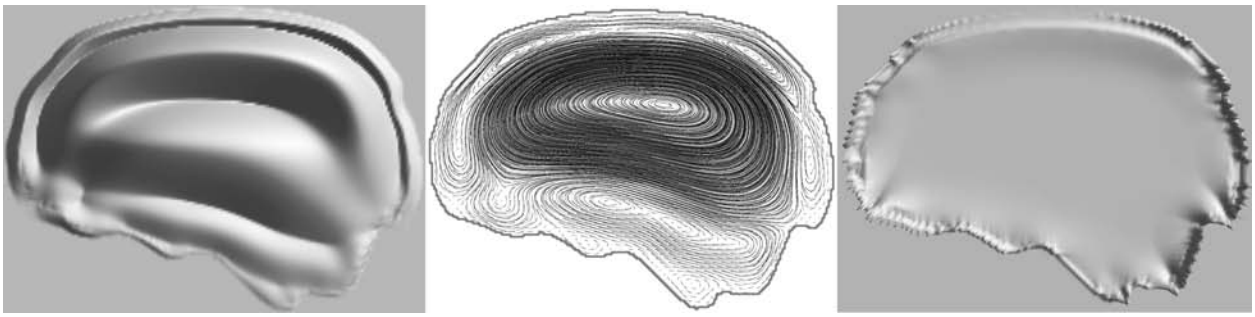
A head rotation about an axis located at the abdomen (not shown here) shifts the major vortex towards the top of the brain whereas a head rotation about the brain's center of mass pushes the position of the major vortex down.



$|\mathbf{V}(\mathbf{x}, 0.025\text{s})|$ $\mathbf{V}(\mathbf{x}, 0.025\text{s})$ $P(\mathbf{x}, 0.025\text{s})$

Fig. 3

RELATIVE VELOCITY AND MAXIMUM STRAIN IN A SAGITTAL CROSS SECTION DURING FORWARD ROTATION ABOUT THE NECK; LINEAR KELVIN-VOIGT MODEL; UNIFORM SHEAR MODULUS: $c_g = c_w = 1$M/S.



$|\mathbf{V}(\mathbf{x}, 0.025\text{s})|$ $\mathbf{V}(\mathbf{x}, 0.025\text{s})$ $P(\mathbf{x}, 0.025\text{s})$

Fig. 4

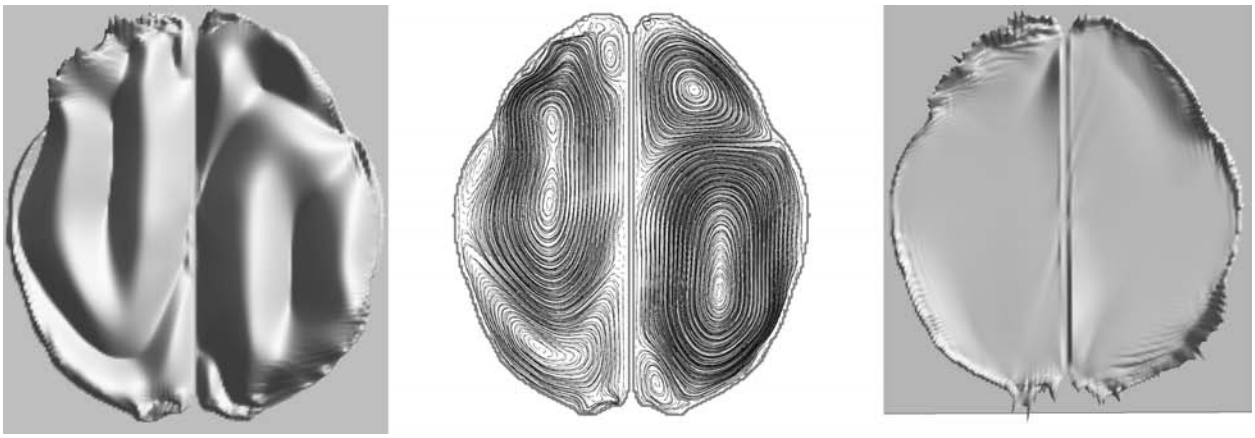
RELATIVE VELOCITY AND MAXIMUM STRAIN IN A SAGITTAL CROSS SECTION DURING FORWARD ROTATION ABOUT THE NECK; LINEAR KELVIN-VOIGT MODEL; NONUNIFORM SHEAR MODULUS: $c_g = 1.75$M/S, $c_w = 1$M/S. NOTE THE HIGH VALUES OF $|\mathbf{V}|$ AT THE GRAY/WHITE MATTER BOUNDARY IN THE LEFT PANEL, WHICH ARE THE RESULT OF THE 'OPPOSITE' OSCILLATIONS OF THE GRAY MATTER ALONG THE SKULL WHEN $c_g > c_w$, MIDDLE PANEL. CONSEQUENTLY, HIGH STRAIN MAGNITUDES APPEAR ALONG THE GRAY/WHITE MATTER BOUNDARY, RIGHT PANEL, WHICH ARE NOT PRESENT IN FIG. 3.

The secondary oscillatory vortices at the bottom of the sagittal cross section, Figs. 3 and 4 middle panels, appear regardless of whether the head is rotated about an axis located at the brain's center of mass, the neck, or the abdomen, i.e., they are created mainly due to the brain's geometry. The specific character of these oscillations changes essentially when the head is rotated backwards, which again highlights the role of the brain's geometry in the distribution of the strain values.

Similar to what we observed in sideways head rotations, in forward head rotations under the linear K-V model neither the major nor the secondary oscillatory vortices create very steep changes in the values of $|\mathbf{V}|$ in the brain interior and consequently they do not lead to high strain values there, Figs. 3 and 4 left and right panels.

When forward or backward head rotations are simulated assuming a nonuniform shear modulus, the results near the gray/white matter boundary are also similar to those obtained during sideways head rotations—the gray matter tends to oscillate in the opposite direction than the white matter, Fig. 4 middle panel. Hence, very steep changes in the velocity magnitudes are created near the gray/white matter boundary, Fig. 4 left panel, that result in high strain magnitudes there, Fig. 4 right panel.

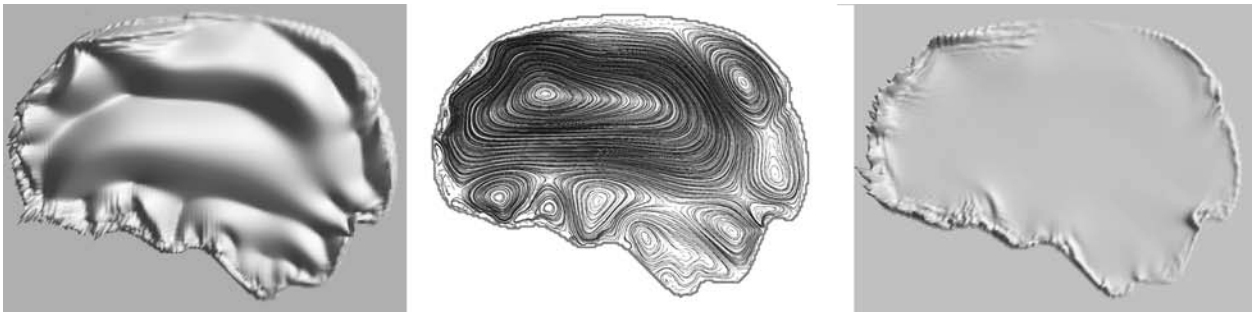
Although, according to the K-V model, the brain geometry substantially influences the character of the brain oscillations, it does not change the maximum velocity magnitude $|\mathbf{V}|_{max}$ and the largest maximum strain values, which are very similar during sideways, forward and backward rotations under the same load.



$|\mathbf{V}(\mathbf{x}, 0.025\text{s})|$ $\mathbf{V}(\mathbf{x}, 0.025\text{s})$ $P(\mathbf{x}, 0.025\text{s})$

Fig. 5

RELATIVE VELOCITY AND MAXIMUM STRAIN IN A HORIZONTAL CROSS SECTION DURING SIDEWAYS ROTATION ABOUT THE CENTER OF MASS; NONLINEAR FLUID MODEL; UNIFORM SHEAR MODULUS: $c_g = c_w = 1$M/S. NOTE THAT THE ASYMMETRIC OSCILLATIONS, MIDDLE PANEL, LEAD TO AN ASYMMETRIC SCATTERING OF THE HIGH STRAIN VALUES ALONG THE BRAIN'S PERIMETER, RIGHT PANEL.



$|\mathbf{V}(\mathbf{x}, 0.025\text{s})|$ $\mathbf{V}(\mathbf{x}, 0.025\text{s})$ $P(\mathbf{x}, 0.025\text{s})$

Fig. 6

RELATIVE VELOCITY AND MAXIMUM STRAIN IN A SAGITTAL CROSS SECTION DURING FORWARD ROTATION ABOUT THE NECK; NONLINEAR FLUID MODEL; UNIFORM SHEAR MODULUS: $c_g = c_w = 1$M/S. NOTE THE RANDOM SCATTERING OF OSCILLATORY VORTICES, MIDDLE PANEL, AND OF HIGH STRAIN VALUES, RIGHT PANEL, DUE TO THE BRAIN'S GEOMETRY.

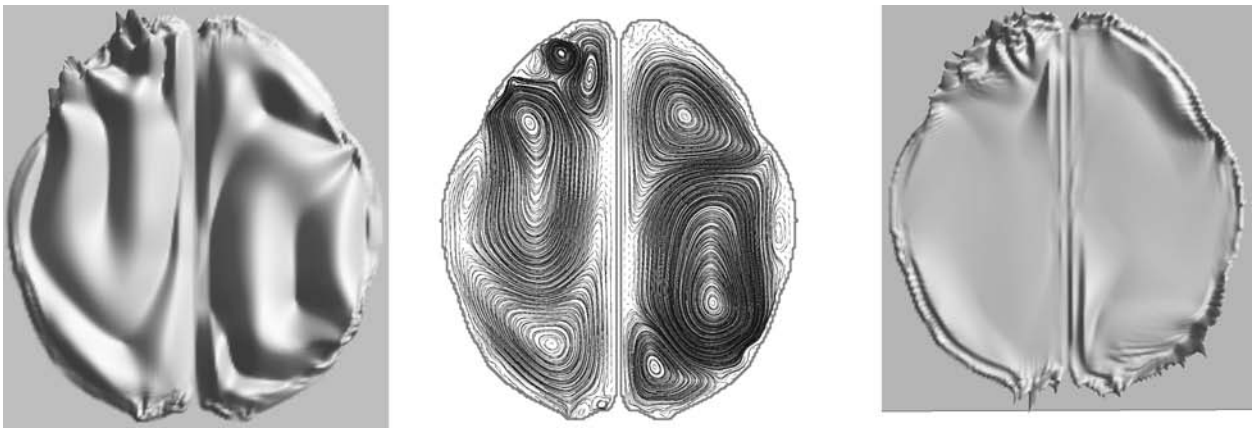
5. The role of the brain's fluidity

Replacing the linear temporal derivative in the Kelvin-Voigt model with the nonlinear material derivative allows us to reflect the fluid (gel-like) nature of the brain. This nonlinear fluid (N-F) model predicts more complicated oscillatory patterns than the linear K-V model, even when a uniform shear modulus is assumed, cf. middle panels of Figs. 1 and 5 as well as of Figs. 3 and 6.

In particular, the sideways rotations under the N-F model create asymmetric oscillatory patterns in the brain hemispheres, Fig. 5 middle panel, which is not the case under the K-V model. Thus, the localization of injuries can strongly depend on the rotational direction.

Similarly, the forward head rotations under the N-F model create multiple localized vortices in the back and the bottom of the brain, Fig. 6 middle panel, which are not predicted by the K-V model. The number of these vortices increases when the rotational axis is moved down to the abdomen and decreases when it is moved up to the brain's center of mass.

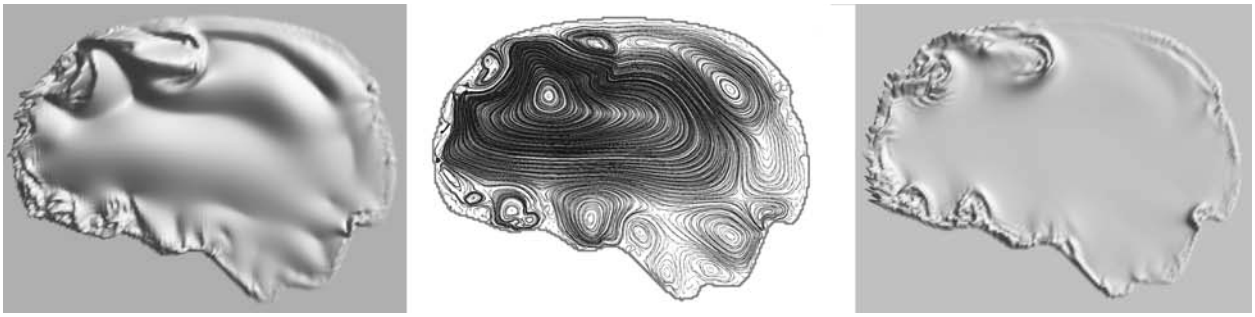
Moreover, under the N-F model with a uniform shear modulus, the value of $|\mathbf{V}|_{max}$ is up to three times higher than in the K-V model, and steep changes in the velocity magnitudes appear also at the brain's perimeter, Figs. 5 and 6 left panels. This leads to scattered high strain magnitudes near the brain's perimeter, which are not predicted by the K-V model, Figs. 5 and 6 right panels.



$|\mathbf{V}(\mathbf{x}, 0.025\text{s})|$ $\mathbf{V}(\mathbf{x}, 0.025\text{s})$ $P(\mathbf{x}, 0.025\text{s})$

Fig. 7

RELATIVE VELOCITY AND MAXIMUM STRAIN IN A HORIZONTAL CROSS SECTION DURING SIDEWAYS ROTATION ABOUT THE CENTER OF MASS; NONLINEAR FLUID MODEL; NONUNIFORM SHEAR MODULUS: c_g = 1.75M/S, c_w = 1M/S.



$|\mathbf{V}(\mathbf{x}, 0.025\text{s})|$ $\mathbf{V}(\mathbf{x}, 0.025\text{s})$ $P(\mathbf{x}, 0.025\text{s})$

Fig. 8

RELATIVE VELOCITY AND MAXIMUM STRAIN IN A SAGITTAL CROSS SECTION DURING FORWARD ROTATION ABOUT THE NECK; NONLINEAR FLUID MODEL; NONUNIFORM SHEAR MODULUS: c_g = 1.75M/S, c_w = 1M/S.

The introduction of a nonuniform shear modulus into our N-F model allows us to satisfactorily explain why Diffuse Axonal Injuries are highly localized and randomly scattered, mostly in the white matter along the boundary with the gray matter. Indeed, introducing a nonuniform shear modulus results in multiple oscillatory vortices that:

- are characterized by 1/3 higher values of the maximum velocity magnitudes $|\mathbf{V}|_{max}$ than in the case of a uniform shear modulus,
- create steep changes in $|\mathbf{V}|$ along the gray/white matter boundary as well as deeper in some regions of the white matter near this boundary, Figs. 7 and 8 left panels,
- are quite randomly scattered along the boundary between the gray and the white matter, Figs. 7 and 8 middle panels, and
- lead to localized very high strain magnitudes P that are also quite randomly scattered near the gray/white matter boundary as well as deeper inside the white matter, Figs. 7 and 8 right panels.

According to both the K-V and N-F models, the localization of high strain values depends essentially on whether the head is rotated forward or sideways. This outcome is consistent with results obtained by means of one of the most advanced finite element brain injury simulators SIMon [21].

However, the results of our simulations also imply that a specific type of traumatic head motion strongly influences the localization of high strain values. Thus, DAI localization can be quite different when the head is rotated forward or backward, about the brain's center of mass, the neck, or the abdomen, and counter-clockwise or clockwise.

6. The role of a nonlinear stress/strain relation

We have shown in our previous studies that including a nonlinear stress/strain relation with a high value of the parameter q into the K-V model with a uniform shear modulus has the following consequences [15]:

- during head rotations, it reduces strain magnitudes, especially near the skull, and
- after the forcing stops, it creates relatively higher strain magnitudes scattered within the white matter.

Our new simulations lead to similar results under the dually-nonlinear fluid (D-N-F) model with a nonlinear stress/strain relation and both uniform and nonuniform shear moduli. However, the increased strain magnitudes within the white matter due to the nonlinear stress/strain relation are smaller than the critical strain magnitudes appearing due to the nonuniform shear modulus and the brain geometry.

In fact, under the D-N-F model, a nonlinear stress/strain relation only slightly changes the spatial distribution of critical strain magnitudes appearing during head rotations and moderately increases the scattering of high strain magnitudes after the forcing stops. Thus, the nonlinear stress/strain relation seems to play a secondary role in shaping DAI features.

7. Conclusions

Simulations based on our dually nonlinear Traumatic Brain Injury model show that:

- the difference between the values of shear moduli in the gray and in the white matter can explain why Diffuse Axonal Injuries are primarily localized at the gray/white matter boundary,
- the nonlinear gel-like nature of the brain matter together with the complicated shape of the brain can explain the scattered random distribution and pointwise character of DAI, and
- the brain matter's nonlinear relation between stress and strain and the specific position of a fixed rotational axis influence DAI localization and may enhance the random scattered nature of neuronal injuries.

Because the brain's *general* shape and its fluidity already 'scatter' high strain values, one can expect the *convoluted* folding of the brain to cause further scattering of the localized high strain magnitudes along the gray/white matter boundary.

Moreover, since the position of the fixed rotational axis and the rotational direction significantly influence the localization of potential injury points, it is likely that a complicated head rotation about a *varying* axis will further 'randomize' the distribution of axonal injuries.

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