A Poroelastic-Viscoelastic Limit for Modeling Brain Biomechanics

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ABSTRACT

The brain, a mixture of neural and glia cells, vasculature, and cerebrospinal fluid (CSF), is one of the most complex organs in the human body. To understand brain responses to traumatic injuries and diseases of the central nervous system it is necessary to develop accurate mathematical models and corresponding computer simulations which can predict brain biomechanics and help design better diagnostic and therapeutic protocols. So far brain tissue has been modeled as either a poroelastic mixture saturated by CSF or as a (visco)-elastic solid. However, it is not obvious which model is more appropriate when investigating brain mechanics under certain physiological and pathological conditions. In this paper we study brain’s mechanics by using a Kelvin-Voight (KV) model for a one-phase viscoelastic solid and a Kelvin-Voight-Maxwell-Biot (KVMB) model for a two-phase (solid and fluid) mixture, and explore the limit between these two models. To account for brain’s evolving microstructure, we replace in the equations of motion the classic integer order time derivatives by Caputo fractional order derivatives and thus introduce corresponding fractional KV and KVMB models. As in soil mechanics we use the displacements of the solid phase in the classic (fractional) KVMB model and respectively of the classic (fractional) KV model to define a poroelastic-viscoelastic limit. Our results show that when the CSF and brain tissue in the classic (fractional) KVMB model have similar speeds, then the model is indistinguishable from its equivalent classic (fractional) KV model.

INTRODUCTION

Brain tissue is a biomaterial made of interconnected networks of blood vessels, neuronal and glia cells immersed in cerebrospinal fluid (CSF). Recent experimental observations show that brain’s vasculature behaves as a non-linear elastic solid [1], while brain’s cells respond to mechanical loading like linear viscoelastic solids [2]. In healthy state, CSF is a colorless liquid made of 99% water, few lipids and proteins, and no blood cells [3], and thus it can be modelled as an incompressible Newtonian fluid. Therefore, the brain tissue can be viewed as a viscoelastic sponge [4]. There are two main approaches that have been used to study brain mechanics. The first one treats the brain as a viscoelastic material [5-6], while in the second approach the brain is a porous, linearly elastic solid with Newtonian fluid-filled pores [7-8]. However, it is not obvious which of these two modelling approaches is more appropriate when studying brain mechanics under certain physiological and pathological conditions.

In this paper we follow the technique proposed in [9] to define a poroelastic-viscoelastic limit for modeling brain mechanics. To account for brain’s evolving microstructure, we will use equivalent fractional Kelvin-Voight (KV) and fractional Kelvin-Voight-Maxwell-Biot (KVMB) models where the time derivatives in the equations of motion are represented by Caputo fractional order derivatives. We start by proposing a novel fractional KVMB model where the brain is a poroelastic mixture made of two phases: 1).
CSF, an incompressible Newtonian fluid, and 2). networks of vasculature and brain cells which are assumed to be one incompressible, linear elastic solid. The model links the dynamic viscosity of CSF, the permeability and tortuosity of brain. The motion in the fractional KVMB model is described by a system of fractional order linear differential equations whose solutions can be found by using the generalization of the eigenvalue method proposed by [10]. These eigenvalues are then used to build an equivalent fractional KV model where the brain is seen as a one-phase viscoelastic solid. The motion in the fractional KVMB model is described by a system of fractional order linear differential equations whose solution can be found by using the generalization of the eigenvalue method proposed by [10]. These eigenvalues are then used to build an equivalent fractional KV model where the brain is seen as a one-phase viscoelastic solid. The classic KV and KVMB models can be easily obtained from their fractional counterparts by simply letting the fractional order of the temporal derivative be equal to unity.

**FRACTIONAL KV AND KVMB MODELS**

In the KV model (Fig.1a) the mass of viscoelastic material $m$ is attached to a spring element of spring constant $k_{KV}$ and dashpot element of viscosity $\eta_{KV}$ connected in parallel. In the KVMB model (Fig.1b) the two phases of the mixture are represented by two masses: $m_s$, the mass of the elastic solid frame, and $m_f$, the mass of the pore fluid. These masses are connected in series to a spring element of spring constant $k_{KVMB}$ and a dashpot of viscosity $\eta_{KVMB}$ caused by frictional losses resulting from the relative motion between the fluid and the frame. Fractional KV and KVMB models are obtained by replacing the first order time derivative in the classic KV and KVMB models by the Caputo fractional order derivative of order $0<\alpha<1$ whose definition for a generic function $f(t)$ is [6]:

$$D^\alpha f(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t \frac{df(s)}{ds} (t-s)^{\alpha-1} ds.$$  

Thus the equations of motion of the fractional KVMB model are:

$$D^\alpha \begin{pmatrix} u_s(t) \\ D^\alpha u_s(t) \\ D^\alpha u_f(t) \end{pmatrix} = A_{KVMB} \begin{pmatrix} u_s(t) \\ D^\alpha u_s(t) \\ D^\alpha u_f(t) \end{pmatrix},$$  

where $u_s(t)$, $D^\alpha u_s(t)$, $D^\alpha u_f(t)$ are the displacement and fractional speed of the solid phase, and respectively the fractional speed of the fluid, and:

$$A_{KVMB} = \begin{pmatrix} 0 & -k_{KVMB}/m_s & -\eta_{KVMB}/m_s \\ 0 & -\eta_{KVMB}/m_s & \eta_{KVMB}/m_s \\ 0 & \eta_{KVMB}/m_f & -\eta_{KVMB}/m_f \end{pmatrix}.$$  

According to theorem 4 in [10], the analytic solution of system (1) is given by:

$$\begin{pmatrix} u_s(t) \\ D^\alpha u_s(t) \\ D^\alpha u_f(t) \end{pmatrix} = B_{KVMB} \begin{pmatrix} E_\alpha(\gamma_1 t^\alpha) & 0 & 0 \\ 0 & E_\alpha(\gamma_2 t^\alpha) & 0 \\ 0 & 0 & E_\alpha(\gamma_3 t^\alpha) \end{pmatrix} B^{-1}_{KVMB} \begin{pmatrix} u_s(0) \\ D^\alpha u_s(0) \\ D^\alpha u_f(0) \end{pmatrix},$$  

where $\gamma_i$ are the eigenvalues of $A_{KVMB}$. 

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According to theorem 4 in [10], the analytic solution of system (1) is given by:
where $\gamma_i, i = 1, 2, 3$ are the eigenvalues of the matrix $A_{KVMB}$, the matrix $B_{KVMB}$ has its columns made of the corresponding eigenvectors, and the Mittag-Leffler function is by definition: $E_\alpha(z) = \sum_{j=0}^{\infty} \frac{z^j}{\Gamma(a+1)}$, $z \in \mathbb{C}$.

Fig.1. Schematics of (a) fractional KV and (b) fractional KVMB models. When $\alpha=1$ the models reduce to their corresponding classic representations.

If $\gamma_1, \gamma_2$ are the complex conjugate eigenvalues, then like in [9] we introduce the equivalent fractional KV model as follows:

$$\frac{k_{KV}}{m} = \gamma_1 \gamma_2, \quad \frac{\eta_{KV}}{m} = -(\gamma_1 + \gamma_2). \tag{3}$$

Then $\gamma_1, \gamma_2$ are the eigenvalues of the matrix $A_{KV} = \begin{pmatrix} 0 & 1 \\ -k_{KV}/m & -\eta_{KV}/m \end{pmatrix}$, and the displacement $u(t)$ and fractional speed $D^\alpha u(t)$ of the viscoelastic material are solutions of the system: $D^\alpha \begin{pmatrix} u(t) \\ D^\alpha u(t) \end{pmatrix} = A_{KV} \begin{pmatrix} u(t) \\ D^\alpha u(t) \end{pmatrix}$, and are given by [10]:

$$\begin{pmatrix} u(t) \\ D^\alpha u(t) \end{pmatrix} = B_{KV} \begin{pmatrix} E_\alpha(\gamma_1 t^\alpha) & 0 \\ 0 & E_\alpha(\gamma_2 t^\alpha) \end{pmatrix} B_{KV}^{-1} \begin{pmatrix} u(0) \\ D^\alpha u(0) \end{pmatrix}, \tag{4}$$

where the columns of the matrix $B_{KV}$ are the eigenvectors of matrix $A_{KV}$ corresponding to eigenvalues $\gamma_1, \gamma_2$.

We notice that when $\alpha = 1$, $D^1 f(t) = \frac{df(t)}{dt}$ and $E_1(z) = \exp(z)$, and thus the fractional KV and KVMB models reduce to the corresponding classic models and solutions (2) and (4) become the classic solutions given in [8].

Like in [9], we say that the equivalent fractional KVMB and KV models are similar (mapped or indistinguishable) if the displacement history of the solid phase in the fractional KVMB model is very close to the displacement history in the fractional KV model. We introduce the following similarity metric [9]: $\theta = \arccos \left( \frac{u_s^T u_m}{|u_s|_2 |u_m|_2} \right)$, where $|.|_2$ is the $L^2$-norm and $\cdot$ is the inner product in the $L^2$ space. If $\theta < 5^\circ$ then the two models are said to be mapped [9].
RESULTS

We apply the above models to the study of brain mechanics. For simplicity, we assume that a brain volume of $V = 1400 \text{ cm}^3$ fills a circular cylinder of height $L = 10 \text{ cm}$. Thus the radius of the cylinder is $R = 6.67 \text{ cm}$, and the cross-sectional area is $A = 140 \text{ cm}^2$. Brain parameters required by the fractional KVMB model are found as follows. From in vivo estimates done using magnetic resonance elastography, brain shear modulus is $\mu_s = 14 \text{ kPa}$ [11]. Then the spring constant of brain is calculated using the following formula [9]: $k_{KVMB} = \frac{\mu_s A}{L}$. The viscosity of the KVMB dashpot is given by [9]: $\eta_{KVMB} = \frac{32\mu_{CSF}\lambda \varphi V}{d^2}$, where the viscosity of CSF is $\mu_{CSF} = 0.01 \text{ g/(cm s)}$, the tortuosity of the healthy brain is $\lambda = 1.6$ [12], brain’s porosity is estimated from measurements of the volume of glymphatic CSF in the Virchow-Robin perivascular space [13] and is $\varphi = 0.1$, and the average diameter of brain pore is $d = 40 \text{ nm}$ [14]. Lastly, the masses of the solid skeleton and the CSF within brain are given by: $m_s = \rho_s (1 - \varphi) V$, $m_f = \rho_{CSF} \varphi V$, where the true densities of the brain and the glymphatic CSF are $\rho_s = 1.05 \frac{\text{g}}{\text{cm}^3}$, and respectively $\rho_{CSF} = 1 \frac{\text{g}}{\text{cm}^3}$.

Fig. 2: Damping ratio of the equivalent fractional KV model vs pore diameter (mm).

Fig. 3: Speed of the equivalent fractional KV model and speed of the solid phase of the fractional KVMB model vs time (s) for $\alpha = 1$ (top) and for $\alpha = 0.90$ (bottom). The pore diameter is 40 nm.
We calculate the parameters of the equivalent fractional KV model and compare the solutions (2) and (4) for the initial condition: 
\[
\begin{pmatrix}
  u_s(0) \\
  D^{\alpha}u_s(0) \\
  D^{\alpha}u_f(0)
\end{pmatrix} = \begin{pmatrix} 0 \\ 1 \\ 0 \end{pmatrix},
\]
and for \(\alpha = 0.90\) and \(\alpha = 1\). In addition, the variations of the damping ratio of the equivalent KV model: 
\[
|\gamma_1 + \gamma_2| / (2\sqrt{\gamma_1 \gamma_2})
\]
separate the region where the brain acts as a KV viscoelastic material from the region where the brain is a KVMB poroelastic mixture. In Fig.2 we see that for pore diameters below 1.5 mm the brain behaves viscoelastic, while for pore diameters larger than 1.5 mm the brain acts as a poroelastic mixture. Since the average pore diameter in a healthy adult brain is about 40 nm, it appears that healthy brain is a viscoelastic material. However, certain diseases and/or age could enlarge brain’s pores and in these cases the brain might be modelled as a poroelastic mixture.

![Graph](image)

**Fig. 4**: Speeds of the solid and fluid phases of the fractional KVMB model vs time (s) for \(\alpha = 1\) (top) and for \(\alpha = 0.90\) (bottom). The pore diameter is 40 nm.

The calculated values of the similarity metric for the two values of \(\alpha\) are much smaller than 5° which means that the equivalent fractional KV and KVMB models are indistinguishable as it can be seen in Figs. 3 and 4. We also notice from Figs. 3 and 4 that when \(\alpha = 1\) the speeds oscillate, while when \(\alpha = 0.90\) the speeds attenuate quickly. This observed attenuation might be due to the presence of dynamic microstructure.

**CONCLUSION**

In this paper we studied brain biomechanics using equivalent fractional KV and KVMB models and concluded that for a healthy adult brain the two models are indistinguishable. In our future work we plan to investigate more sensitive similarity metrics and perform a detailed analysis of the physical parameters of these two models.
REFERENCES


