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A fully dynamic multi-compartmental poroelastic system: Application to aqueductal stenosis

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ABSTRACT

This study proposes the implementation of a fully dynamic four-network poroelastic model which is underpinned by multiple-network poroelastic theory (MPET), in order to account for the effects of varying stages of aqueductal stenosis and atresia during acute hydrocephalus. The innovation of the fully dynamic MPET implementation is that it avoids the commonplace assumption of quasi-steady behaviour; instead, it incorporates all transient terms in the casting of the equations and in the numerical solution of the resulting discrete system.

It was observed that the application of mild stenosis allows for a constant value of amalgamated ventricular displacement in under 2.4 h, whereas the application of a severe stenosis delays this settlement to approximately 10 h. A completely blocked aqueduct does not show a clear sign of reaching a steady ventricular displacement after 24 h. The increasing ventricular pressure (complemented with ventriculomegaly) during severe stenosis is causing the trans-parenchymal tissue region to respond, and this coping mechanism is most attenuated at the regions closest to the skull and the ventricles. After 9 h, the parenchymal tissue shows to be coping well with the additional pressure burden, since both ventriculomegaly and ventricular CSF (cerebrospinal fluid) pressure show small increases between 9 and 24 h. Localised swelling in the periventricular region could also be observed through CSF fluid content, whilst dilation results showed stretch and compression of cortical tissue adjacent to the ventricles and skull.

1. Introduction

1.1. Hydrocephalus

Hydrocephalus can be described as the abnormal accumulation of Cerebrospinal fluid (CSF) within the brain (Tully and Ventikos, 2011; Rekate, 2009; Thompson, 2009; Stagno et al., 2013). Hydrocephalus is classified as obstructive when the point of CSF blockage or distinct lesion lies within the ventricular system and hinders flow before it enters the subarachnoid space (Corns and Martin, 2012). If this is not the case, it is generally known as communicating hydrocephalus.

1.2. Aqueductal stenosis

Cinalli et al. (2010) describe the aqueduct as a curved conduit around 15 mm in length and up to 3 mm in width, with concavity towards the base of the skull and a highly variable cross section, where there is a shape transition from triangular (cranial orifice), oval in the central area and finally resembles an inverted "U" at the level of the inferior colliculi (Jellinger, 1986). The interior lumen of the Sylvian aqueduct is lined with ependymal cells (Bruni, 1998). This cell layer however, is not confined to being unicellular, and in some cases ependymal cells may even be absent from the lining of the aqueduct. These denuded areas pose a problem since they may lead to the bridging of the canal via an overproduction of glial fibrils.

Mass lesions (from tumours or vascular malformaitons) may aid in the stenosis/atresia of the aqueduct of Sylvius. In addition, histopathological classifications of "nontumoral aqueduct anomalies" have been confirmed as *Stenosis*, *Forking*, *Septum formation* and *Gliotic stenosis* (Cinalli, 2010; Russel, 1949; Spennato et al., 2013). During stenosis, the aqueduct is forced to narrow and the ependymal lining of the lumen remains intact. Gliotic stenosis may be considered an acquired condition and is characterised by the occlusion of the aqueduct due to an overproduction of glial fibres or the creation of multiple channels that lack an evident ependymal lining (Cinalli, 2010).

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1.3. Modelling aqueductal stenosis using poroelasticity

There are numerous works in the literature that have utilised a poroelastic approach in modelling parenchymal tissue (Kaczmarek et al., 1997; Levine, 1999, 2000; Smillie et al., 2005; Shahim et al., 2012; Tully and Ventikos, 2009, 2011; Vardakis et al., 2013a). Considering aqueductal stenosis or atresia whilst modelling the brain as a poroelastic medium in the manner outlined in this work (excluding any CFD coupling) yields a narrower selection of relevant work (Smillie et al., 2005; Sobey and Wirth, 2006).

In this manuscript, we investigate the effect of artificially imposed aqueductal stenosis and atresia using a novel application of a one dimensional, fully dynamic multiple-network poroelastic (MPET) formulation. The MPET formulation allows the tracking of the parenchymal matrix displacement (relative to a reference position), which assimilates the pore pressures of the respective fluid networks. Once the methodology has been described, some results based on aqueductal stenosis follow, along with the interpretation of these results.

2. Methods

In this section, we outline the definition of the MPET framework that is used to model parenchymal tissue, along with its adaptation to the cerebral environment. We then proceed with outlining the spherical representation of the cerebral environment that dictates the nature of the 1D MPET model. Boundary conditions are then discussed, along with justification of the poroelastic constants.

2.1. Multiple-network poroelastic formulation

The classical form of Biot's consolidation model (Biot, 1941) is described for an isotropic and incompressible solid matrix and homogenous porous medium. For a simple poroelastic medium to be defined, an equilibrium equation is needed to define elastic deformation and Darcy's law is used to model fluid flow. Finally, mass conservation is also required. Biologically, the quadruple MPET system is derived by accommodating a high pressure arterial network (a), lower pressure arteriole/capillary network (c), interstitial fluid (ISF)/CSF network (e) and finally a venous network (v) (Tully and Ventikos, 2011). One may cast equations to be solved for the mean displacement of particles forming the solid matrix, $\mathbf{u}$, and the scalar pore pressures of the extended multicompartmental porous medium (p^a, p^c, p^e, p^v) which is defined through multiple-network poroelastic theory (MPET). A general MPET derivation will now follow.

The stress–strain relationship for a solid is re-written in the form reminiscent of Rice and Cleary (1976), which makes use of Lamé's constants (G, λ), and subsequently extended to multiple-porosity poroelasticity:

$$\sigma_{ij} = 2G\epsilon_{ij} + \lambda\epsilon_{kk}\delta_{ij} - \sum_{A=a,e,c,v} \alpha^A p^A \delta_{ij} \tag{1}$$

In the above equation, the Biot–Willis coefficient α can be interpreted from both a microscopic and macroscopic perspective. The global version of the Biot–Willis parameter allows for Eq. (1) to be interpreted as the weighted average contribution of each fluid network to the constitutive effective stress of the multiple-network system. The range of values for the global Biot–Willis coefficient is $\alpha[0, 1]$.

Darcy's Law is extended to take into account all of the fluid networks, hence:

$$\boldsymbol{q}_A = -\frac{k_A}{\mu_A}\left(\nabla p^A\right), \quad A = a, e, c, v \tag{2}$$

The first governing equation of motion for a unit volume within the MPET framework is given by:

$$\sigma_{ij,j} + \left[\sum_{A=a,e,c,v} (n^A(\rho^A - \rho_s) + \rho_s)\right](b_i - \ddot{u}_i) - \sum_{A=a,e,c,v} \rho^A\left(\dot{w}_i^A + w_j^A w_{i,j}^A\right) = 0 \tag{3}$$

$\sigma_{ij,j}$ is the stress within the solid matrix. The convention will be made to align a positive value of this stress with a tension. u_i describes the mean displacement of elements forming the solid matrix, w_i is the ratio of fluid flow to cross sectional area and $\sum_{a=1}^{A} n^a\rho^a + (1-n)\rho_s$ is the total density of the system, ρ_s is the solid density and $\sum_{a=1}^{A} n^a$ is the total porosity of all the individual fluid networks. Finally, b_i is the body force per unit mass.

The second governing equation of motion is that defining the momentum of each individual fluid network:

$$p_i^A - R_i^A - \rho^A(b_i - \ddot{u}_i) - \frac{\rho^A}{n^A}\left(\dot{w}_i^A + w_j^A w_{i,j}^A\right) = 0 \tag{4}$$

In the above, R_i^a is the viscous drag force utilising Darcy's seepage law (Zienkiewicz et al., 1999).

Flow conservation for the fluid phase is given by:

$$S_\varepsilon^A \dot{p}^A + \alpha^A \dot{\varepsilon}_{ii} + w_{i,i}^A + \frac{1}{\rho^A}\dot{\rho}^A = \sum_{A=a,e,c,v} \overbrace{\omega_{ij}\left(p_j - p_i\right)}^{\hat{s}_{ij}} \tag{5}$$

$\dot{\varepsilon}_{ii}$ is the rate of change of the strain within the solid matrix, α^A is the Biot parameter of the fluid network in question and finally the right hand side possesses either source ($\hat{s}_{ij} > 0$) or sink ($\hat{s}_{ij} < 0$) densities and $\boldsymbol{q}$ represents the fluid flux vector. From Eq. (5), the fluid phase continuity equations include the sum of all compartmental fluxes ($\hat{s}_{ij}$), from network j to i. Here, the transfer is considered to be driven by a hydrostatic pressure gradient, whilst ω_{ij} is the transfer coefficient scaling the flow from network j to network i.

Eliminating w_i^A from Eq. (4) as in Tully and Ventikos (2011), one may then focus on the primary variables $\mathbf{u}$ and p. Utilising Darcy's seepage law (Zienkiewicz et al., 1999) and Eq. (4), one obtains:

$$w_i^A = k_{ij}^A p_i^A - k_{ij}^A \rho^A (b_j - \ddot{u}_j) \tag{6}$$

k_{ij}^A defines the anisotropic permeability coefficient. If isotropy is sought, this value is replaced by a single k^A constant (which is assumed in this manuscript). Substituting Eq. (6) to into Eq. (5), one obtains:

$$S_\varepsilon^a \dot{p}^a + \alpha^a \dot{\varepsilon}_{ii} + \left[k_{ij}^a p_i^a - k_{ij}^a \rho^a (b_j - \ddot{u}_j)\right] - \sum_{A=a,e,c,v} \hat{s}_{ij} = 0 \tag{7}$$

Finally, Eq. (1) is combined with Eq. (3), and ignoring the fluid acceleration relative to the solid and the convective terms of this acceleration, one obtains the final system:

$$\nabla\cdot\boldsymbol{\sigma} - \sum_{A=a,e,c,v} \alpha^A \nabla p^A + \rho_S(\mathbf{b} - \ddot{\mathbf{u}}) = 0$$
$$S_\varepsilon^A \dot{p}^A + \alpha^A \dot{\boldsymbol{\varepsilon}} + \nabla\cdot\left[k^A\cdot\rho^A(\mathbf{b} - \ddot{\mathbf{u}}) - k^A\cdot\nabla p^A\right] - \sum_{A=a,e,c,v} \hat{s}_{ij} = 0 \tag{8a – b}$$

2.2. Adaptation to the cerebral environment

The first stage of adapting an MPET modelling framework to describe the transfer of fluid through the brain parenchyma, is to postulate the overall formation of the MPET network. In this work, the solid porous matrix represents the *tissue* in the brain parenchyma, whilst the communicating fluid phases that will be taken into account are: arterial blood (a), arteriole/capillary blood (c), venous blood (v) and the CSF/ISF (e) space, i.e. four networks (Tully and Ventikos, 2011). Representing the $\Sigma\omega_{ij}(p^j\text{-}p^i)$ terms on the right hand side of Eq. (4) as $\hat{s}_{ij}$, the field Eqs. (5) and (6) for the four compartment MPET model are as follows:

$$\left[G\nabla^2\mathbf{u} + \left(\frac{G}{1-2\nu}\right)\nabla(\nabla\cdot\mathbf{u}) - \alpha^a\nabla p^a - \alpha^c\nabla p^c - \alpha^e\nabla p^e - \alpha^v\nabla p^v\right] = \rho^s\frac{\partial^2\mathbf{u}}{\partial t^2}$$
$$\frac{\partial}{\partial t}(S_\varepsilon^a p^a + \alpha^a\nabla\cdot\mathbf{u}) - \left[\frac{k_a}{\mu_a}\nabla^2 p^a + |\hat{s}_{a\to c}|\right] = \frac{k_a\rho^a}{\mu_a}\frac{\partial^2}{\partial t^2}(\nabla\cdot\mathbf{u})$$
$$\frac{\partial}{\partial t}(S_\varepsilon^c p^c + \alpha^c\nabla\cdot\mathbf{u}) - \left[\frac{k_c}{\mu_c}\nabla^2 p^c - |\hat{s}_{a\to c}| + |\hat{s}_{c\to e}| + |\hat{s}_{c\to v}|\right] = \frac{k_c\rho^c}{\mu_c}\frac{\partial^2}{\partial t^2}(\nabla\cdot\mathbf{u})$$
$$\frac{\partial}{\partial t}(S_\varepsilon^e p^e + \alpha^e\nabla\cdot\mathbf{u}) - \left[\frac{k_e}{\mu_e}\nabla^2 p^e - |\hat{s}_{c\to e}| + |\hat{s}_{e\to v}|\right] = \frac{k_e\rho^e}{\mu_e}\frac{\partial^2}{\partial t^2}(\nabla\cdot\mathbf{u})$$
$$\frac{\partial}{\partial t}(S_\varepsilon^v p^v + \alpha^v\nabla\cdot\mathbf{u}) - \left[\frac{k_v}{\mu_v}\nabla^2 p^v - |\hat{s}_{c\to v}| - |\hat{s}_{e\to v}|\right] = \frac{k_v\rho^v}{\mu_v}\frac{\partial^2}{\partial t^2}(\nabla\cdot\mathbf{u}) \tag{9a–e}$$

In the above equation, the S_ε term is the inverse of the specific storage (a measure of the released fluid volume per unit pressure in the control volume) at constant strain for each fluid compartment.

The transfer of fluid between four fluid networks is required to obey the law of continuity for the entire system, and so directionality between fluid compartments must be accurately specified. Fig. 1a provides a summary of the directional fluid restrictions placed. It is noted that the current MPET template takes into account the physiological relationship between CSF and ISF best represented in the recent literature (Iliff et al., 2012). It has been shown that CSF and ISF are in continuous exchange. The convective influx of CSF along the periarterial space facilitates this process. The *glymphatic system* recently discovered best portrays this macroscopic process, which also takes into account strategically located Aquaporin-4 channels. In previous work by the same authors (Vardakis et al., 2013b), this aquaporin channel was taken into account by a very simple functional relationship which varied the base permeability of the CSF compartment in the MPET system. In this work, the permeability of the CSF/ISF compartment keeps a constant value (see Table 1). The latter four equations are applied to the pressure gradients of the deformed brain configuration, whereas the stress equilibrium Eq. (9a) combines