A Mathematical Model
for Hydrocephalus

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Abstract

Hydrocephalus is a pathological condition of the brain, which is most commonly observed with infants, but can also be acquired at a later age. It is characterised by an abnormal accumulation of cerebrospinal fluid (CSF) inside the brain ventricles, accompanied by a considerable deformation of the surrounding brain tissue. Building on existing models, this work puts forward a mechanical model for the disease, based on quasi-steady, linearly poroelastic mechanisms. The model incorporates a strain dependence of the brain’s permeability and also takes into account possible CSF absorption or production in the brain parenchyma, which leads to novel ideas about the development of different hydrocephalus types.

The mechanisms are examined in three different geometries: a spherically symmetric, one-dimensional geometry, a cylindrically symmetric, two-dimensional geometry, and a three-dimensional geometry without any symmetry. Analytic as well as numerical methods are used to solve the model equations, yielding qualitative and quantitative predictions for the development and treatment of hydrocephalus. The thesis concludes with some notes about the use of finite deformation elasticity in poroelastic hydrocephalus models.
Contents

1 Introduction ........................................... 1
   1.1 Pathology of hydrocephalus ....................... 1
   1.2 Aim of mathematical research .................... 2
   1.3 Modelling hydrocephalus .......................... 3

2 Model assumptions and mechanisms ................. 4
   2.1 Geometry ........................................ 4
   2.2 Quasi-steady state ................................ 5
   2.3 Poroelastic mechanisms ........................... 5
   2.4 Fluid mechanisms .................................. 6

3 Governing equations ................................ 8
   3.1 Displacement ..................................... 8
   3.2 Pressure ......................................... 9
   3.3 Boundary condition at the skull ................ 9
   3.4 Boundary condition at the ventricle wall ....... 10
   3.5 Polar coordinates ................................ 11
       3.5.1 Cylindrically symmetric geometry .......... 11
       3.5.2 Spherically symmetric geometry ............ 13

4 Nondimensionalisation ................................ 14

5 Solution methods .................................... 17
   5.1 One-dimensional geometry ........................ 17
   5.2 Two-dimensional geometry ........................ 19
   5.3 Three-dimensional geometry ...................... 20
6 Results
6.1 Spherically symmetric simulations ...................... 24
   6.1.1 Implications of a strain-dependent permeability ...... 24
6.1.2 Source or sink in the parenchyma, NPH and BIH .......... 27
6.1.3 Possible vascular effects, compliance .................. 30
   6.1.4 Shunt treatment .................................. 32
   6.1.5 Infantile hydrocephalus .......................... 33
6.2 Cylindrically symmetric simulations .................... 35
   6.2.1 Ventricle shape .................................. 35
   6.2.2 Loose connection to the skull ......................... 39
   6.2.3 Hydrostatic pressure ................................ 40
   6.2.4 Damage measures .................................. 41
6.3 Three-dimensional simulations ............................ 43
   6.3.1 Two lateral ventricles ............................. 43

7 Note on the use of more complex elastic constitutive laws 46
7.1 Linear finite deformation elasticity ........................ 47
7.2 Blatz-Ko hyperelasticity ................................ 48
7.3 Results ................................................. 49

8 Conclusions .............................................. 50

A Appendix ............................................... 52
A.1 One-dimensional analytic solution ........................ 52
A.2 FEM for the two-dimensional geometry .................... 54
A.3 FEM for the three-dimensional geometry .................. 56
A.4 Existence of solutions in a rectangular geometry ........ 59
A.5 Constitutive law for the brain compliance ................ 62
A.6 Stress equilibrium of a spherical membrane ............... 64
A.7 Model extension to hydrostatic pressure .................. 64
A.8 Stresses, strains and constitutive laws ................... 66
A.9 Poroelasticity for finite deformation .................... 68

Bibliography .............................................. 70
Chapter 1

Introduction

A brief description of the relevant brain anatomy and the pathology of hydrocephalus will be followed by a note on the expectations laid on mathematical research in this area. Afterwards, a short chronology of hydrocephalus models will be given, as well as an outline of the thesis structure.

1.1 Pathology of hydrocephalus

At the centre of the human brain there is a system of cavities, the so-called ventricular system (Fig. 1.1). In a healthy brain a water-like liquid, known as cerebrospinal fluid (CSF), is produced inside the left and right lateral ventricles. This fluid then successively flows through the third ventricle, the aqueduct (a long thin canal), and the fourth ventricle. It finally leaves the ventricular system, partly flowing down the spinal cord and partly filling the gap between brain and skull—or more precisely between pia mater, the epithelium covering the brain surface, and the arachnoid membrane, which is, together with the dura mater, firmly attached to the skull. From there the CSF is absorbed into the sinuses of the dura mater, which form a part of the venous system.

The role of CSF has not yet been unravelled entirely. It is sometimes ascribed a transport function for nutrients, messengers, and waste products around the brain. Most importantly, however, it stabilises the brain mechanically via the compensation of gravity by buoyant force [19].

In a hydrocephalic brain some ventricles accumulate so much CSF that they are highly dilated, pushing the brain tissue aside (Fig. 1.2). This is often accompanied by increased fluid content or oedema in the adjacent parenchyma. There is a variety of causes for CSF accumulation in the ventricles, among which a blockage of CSF circulation is the most common, e.g. an obstruction of the aqueduct by a tumor or a
cyst. In principle, hydrocephalus can occur due to an obstruction of the normal CSF pathway or due to abnormalities in CSF production or absorption.

1.2 Aim of mathematical research

The interest of mathematicians in the disease arouse about three decades ago, when neurosurgeons hoped to gain more understanding of the pathogenesis with the help of physical models. Despite these thirty years of research, a breakthrough has never been reached, and many issues remain unclear. Therefore, the predominant objective of mathematics in this area still consists in providing a mathematical model explaining the disease consistently in all (or most of) its facets. The subordinate, but practically more relevant aim is to develop a model which, albeit not explanatory, yields accurate predictions for the state of the brain during development of hydrocephalus or its treatment—information that can be used by physicians to optimise therapies.
1.3 Modelling hydrocephalus

The first hydrocephalus models in the early 1970s were compartment models without any spatial component, relating the CSF pressure $p$ to the intracranial CSF volume $v$ with the help of a compliance $c(p) = \frac{\partial v}{\partial p}$ — a critical review is given by Tenti et al. [26, 27]. Soon it became clear that a spatially varying pressure distribution might be essential to the development of hydrocephalus and that a proper model requires a biphasic approach: Hakim et al. [8, 9] put forward the idea of a sponge-like brain tissue with CSF flowing through it in 1976, which paved the way to a new generation of models based on poroelasticity (also known as consolidation theory in soil mechanics). In 1987 Nagashima et al. [18] proposed such a model and numerically computed pressure and strain in a two-dimensional geometrical approximation of the brain. However, they used highly simplified boundary conditions, and parts of the model are ambiguous—especially the use of Poisson’s ratio. Much more recently (1996), Kaczmarek et al. [10] examined hydrocephalus in a much simpler, cylindrical geometry using nonlinear poroelasticity; yet, their results lie outside physiological ranges. Three years later Levine [13] examined normal pressure hydrocephalus (NPH) and introduced the idea of CSF absorption in the parenchyma, while Sivaloganathan, Tenti et al. developed a linearly poroelastic [28] as well as a viscoelastic hydrocephalus model, in which the pulsatile nature of the intracranial pressure is included [22, 23].

Most models have been hampered by poor knowledge of the physical parameters of the brain, whose determination is by all means nontrivial. Only the reassessment of elastic parameters by Taylor et al. [25] finally allowed Smillie et al. [24] to construct a one-dimensional, linearly poroelastic model with elaborate boundary conditions that yields predictions within a physiological range.

Building on this basic model, the thesis puts forward and examines several extensions, some of which have already been proposed whereas others represent new possible concepts for the development of hydrocephalus. First, the involved mechanisms are introduced, and the governing equations are derived. After a nondimensionalisation, the methods of solution (numerical and analytical) are specified, and the effects of the model mechanisms are examined in geometries of different complexity. Finally—not directly included into the basic model due to a lack of adequate constitutive laws—the role of finite deformation elasticity is explained, and ways are shown to include more complicated elastic constitutive laws.
Chapter 2

Model assumptions and mechanisms

There are basically two routes for CSF to flow from the production site in the inner ventricles to the subarachnoid space near the skull where it is absorbed into the bloodstream. The normal flow path leads through the system of aqueduct and fourth ventricle. If this is blocked, produced CSF is forced through the brain tissue (where it may already be partly absorbed) before it reaches the skull. In the following we shall summarise the basic assumptions and poroelastic mechanisms involved.

2.1 Geometry

The model shall be implemented in geometries of three different complexities (Fig. 2.1). The simplest geometry, suggested by Hakim et al. [9], is spherically symmetric. The brain is approximated as a ball of radius $c$ with a concentric spherical ventricle of radius $a$ inside, justified by the more or less spherical shape of the human cranium and of the dilated ventricles in some cases of hydrocephalus. The only spatial variable is the radius $r$, reducing the model to one dimension in space. The virtue of such simplicity lies in the gain of explanatory power: Due to an eased analysis, effects of the basic mechanisms can readily be seen. Furthermore, analytic solutions for special cases provide a benchmark for simulations in two- and three-dimensional geometries.

At least two space dimensions are required to examine effects of more complex ventricle shapes or hydrostatic pressure differences in the brain. The geometry can be kept simple by using cylindrical symmetry: The brain is still approximated as a sphere, whereas the ventricles are cylindrically symmetric with the ventricle wall being specified by a function $f$ of the zenith angle $\theta$ (compare Fig. 2.1):

$$r = f(\theta)$$

(2.1)

This form is simple, yet flexible enough to allow for quite complex (e.g. non-convex) ventricle shapes.
Finally, we shall also implement the model in a three-dimensional geometry with no symmetry requirement. This allows to investigate effects of a non-spherical brain shape, but is predominantly intended to pave the way for simulations in highly accurate model geometries which are most valuable for their predictory power. Only results from an accurate three-dimensional geometry can quantitatively be compared to other models or reality. Of course, such models also require precise anatomical and physical data.

In all three geometries the system of aqueduct and fourth ventricle is modelled as a thin tube of notional diameter $d$ and notional length $L$, connecting the outside of the brain with the inner ventricles, but having no effect on the local deformation.

The lack of data about differences in the physical properties between white and grey matter ([20]) motivated Smillie et al. [24] to take the same values for both tissues in their careful parameter estimation. Hence, we shall initially not distinguish between white and grey matter, keeping in mind that different brain compartments can in principle be assigned different material parameters during numerical simulations.

## 2.2 Quasi-steady state

Since the evolution of hydrocephalus happens at a timescale of days and weeks [9], all inertial terms are considered negligible in the following. The brain is assumed to be in instantaneous response to all pressure and fluid volume changes; the state of the brain is regarded as quasi-static. The only slow time dependence will later appear in a boundary condition including the production and drainage of CSF.

## 2.3 Poroelastic mechanisms

Although there is evidence that the mechanical properties of brain tissue vary spatially and directionally, these variations have not yet been quantified, which justifies an approximation of the brain tissue as an isotropic, homogenous material. The brain’s porosity and perfusion by CSF suggest the application of consolidation theory as introduced by Biot [4] and used by various authors to model hydrocephalus [10, 18, 25, 28].
The poroelastic mechanism can be described by a pair of conservation and constitutive laws. The conservation of momentum is expressed as stress equilibrium. As mentioned before, inertial terms are neglected, as well as body forces since the brain floats in a liquid of almost equal density (CSF). Hence, the conservation law takes the form of three coupled PDEs in the components of the Cauchy stress tensor $\sigma$:

$$\frac{\partial \sigma_{ij}}{\partial x_j} = 0,$$  \hspace{1cm} (2.2)

using Einstein’s summation convention and Cartesian coordinates $x_1, x_2, x_3$.

The constitutive law relies on Terzaghi’s principle that the stress in the brain partly consists of the so-called effective stress of the solid matrix and partly of the pressure of the fluid flowing through, according to

$$\sigma = \sigma_{\text{eff}} - \alpha p \delta,$$  \hspace{1cm} (2.3)

where $\alpha$ is the Biot-Willis parameter and $\delta$ the identity tensor, ensuring that the pressure has no influence on shear stresses. The effective stress is taken to obey Hooke’s law, although biological tissue is known for its nonlinear behaviour—especially for large strains. However, there are no adequate constitutive laws available, and most researchers use linearised elasticity not only in hydrocephalus models, but also in the field of neurosurgery, where the deformations are of similar order [7, 10, 18, 24, 25, 28]. Hence, equation (2.3) changes to

$$\sigma_{ij} = 2G\varepsilon_{ij} + \lambda \varepsilon_{kk} \delta_{ij} - \alpha p \delta_{ij},$$  \hspace{1cm} (2.4)

with the strain tensor $\varepsilon$, Lamé constants $G$ and $\lambda$, and the Kronecker delta $\delta_{ij}$.

Finally, to relate strain and brain deformation, we define the brain displacement $u$ (i.e. each material point $x$ is displaced to $x + u(x)$) and the strain tensor by

$$\varepsilon_{ij} = \frac{1}{2} \left( \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right).$$  \hspace{1cm} (2.5)

2.4 Fluid mechanisms

Observations are that CSF secretion in the inner ventricles happens at a constant, pressure independent rate $Q_p \approx 500 \text{ml/day}$ [19]. CSF, mainly composed of water, is incompressible so that its mass conservation can be expressed in the form

$$\nabla \cdot \mathbf{v} = s,$$  \hspace{1cm} (2.6)

where $\mathbf{v}$ is the fluid velocity and $s$ represents a source ($s > 0$) or a sink ($s < 0$).
If all the produced fluid enters the brain parenchyma at the ventricle wall \( r = a \), the filtration velocity at \( r = a \) is \( U = \frac{Q_a}{4\pi a^3} \). Hence, using the kinematic viscosity \( \mu / \rho \) and the average pore size \( b \) from Table 4.1, the Reynolds number is given by

\[
Re = \frac{U \rho b}{\mu} = \frac{Q_p \rho b}{4\pi a^2 \mu} \approx 10^{-4} \ll 1,
\]

which justifies the assumption of Darcy flow, i.e. the fluid velocity is proportional to the pressure gradient \( \nabla p \) with the permeability \( k \) and viscosity \( \mu \) as coefficients:

\[
v = -\frac{k}{\mu} \nabla p
\]  

(2.7)

The permeability intuitively must be a function of the strain—a volume reduction will lead to a smaller pore size, which in turn lowers the permeability. Kaczmarek et al. [10] propose the relation \( \frac{1}{k} = \frac{1}{k_0} (1 - Me) \) as a small strain approximation of

\[
k = k_0 e^{Me}
\]  

(2.8)

with the total strain or dilation \( \varepsilon \) defined as

\[
\varepsilon = \varepsilon_u = \nabla \cdot \mathbf{u}.
\]  

(2.9)

However, we shall use the fully nonlinear form (2.8).

As long as the system of aqueduct and fourth ventricle is open, CSF will run through it. Again, if all the produced fluid flows through the tube at velocity \( U = \frac{4Q_a}{\pi d^2} \), the Reynolds number is

\[
Re = \frac{U \rho L}{\mu} = \frac{4Q_p \rho L}{\pi d^2 \mu} \approx 36 \ll 2000.
\]

This justifies the assumption of Poiseuille flow for which the flow rate \( Q \) is given by

\[
Q = \frac{\pi d^4}{128\mu L} (p_v - p_s),
\]  

(2.10)

\( p_v \) and \( p_s \) being the ventricular and the subarachnoid pressure, respectively.

A rough estimate of the proportions between CSF seepage through the brain tissue via Darcy flow and flow through the aqueduct can be obtained by approximating

\[
\frac{Q_{\text{tissue}}}{Q_{\text{aqueduct}}} \sim \frac{4\pi a^2 k_0 \rho b}{128\mu L} \frac{p_v - p_s}{c - a} \sim \frac{512 k_0 a^2 L}{d^4 c},
\]  

(2.11)

which is about \( 1.8 \times 10^{-5} \) with the parameters from Table 4.1 for a healthy brain.

Finally, the CSF absorption into the bloodstream near the skull is proportional to the pressure difference between subarachnoid and blood pressure \( p_s \) and \( p_b \), i.e. the absorption rate \( Q \) obeys

\[
Q = \frac{p_s - p_b}{\mu R}
\]  

(2.12)

with \( R \) being a constant resistance.
Chapter 3

Governing equations

The previously described mechanisms can be condensed into one PDE in the CSF pressure $p$ and three coupled PDEs in the brain displacement $\mathbf{u}$. These four second order equations are complemented by four boundary conditions at each boundary of the domain, i.e. at the skull and at the ventricle walls. For the two- and one-dimensional geometry, the governing equations reduce to three PDEs respectively two ODEs, when expressed in polar coordinates.

### 3.1 Displacement

In order to obtain a system of differential equations in the displacement, we first express the strain tensor in terms of $\mathbf{u}$ by substituting (2.5) into (2.4)

$$\sigma_{ij} = G \left( \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right) + (\lambda \nabla \cdot \mathbf{u} - \alpha p) \delta_{ij}$$

(3.1)

and then use this in the stress equilibrium (2.2):

$$0 = \frac{\partial}{\partial x_j} \left[ G \left( \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right) + (\lambda \nabla \cdot \mathbf{u} - \alpha p) \delta_{ij} \right] = G \nabla^2 u_i + (G + \lambda) \frac{\partial}{\partial x_i} (\nabla \cdot \mathbf{u}) - \alpha \frac{\partial p}{\partial x_i}$$

Writing $x, y, z$ for $x_1, x_2, x_3$ and defining the three displacement components as

$$\mathbf{u} = (u_1, u_2, u_3)^T = (u, v, w)^T$$

we can express the stress equilibrium (with the help of (2.9)) in form of three coupled PDEs:

$$\begin{align*}
0 &= G \nabla^2 u + (G + \lambda) \frac{\partial u}{\partial x} - \alpha \frac{\partial p}{\partial x} \\
0 &= G \nabla^2 v + (G + \lambda) \frac{\partial v}{\partial y} - \alpha \frac{\partial p}{\partial y} \\
0 &= G \nabla^2 w + (G + \lambda) \frac{\partial w}{\partial z} - \alpha \frac{\partial p}{\partial z}
\end{align*}$$

(3.2)
3.2 Pressure

The nonlinear permeability (2.8) together with Darcy’s law (2.7) substituted into the mass conservation (2.6) yields the PDE in the pressure:

\[ \nabla \cdot \left[ k_0 e^{\lambda e} \nabla p \right] = -\rho_s. \]  (3.3)

Note that there are two different possible interpretations of this equation, and we shall use both (we shall always explicitly make clear how the PDE is to be understood in each case). Interpreted one way, the derivatives are taken in the undeformed brain configuration, as if the brain shape would not change. This is consistent with the use of small strain elasticity, which usually implies a negligible difference between deformed and undeformed state. However, although we use the methods of linearised elasticity, the displacements will be relatively large so that for simulations it is more appropriate to interpret equation (3.3) in the deformed brain configuration. The first interpretation shall thus only serve the purpose of obtaining a one-dimensional analytical solution, e.g. to benchmark numerical schemes.

3.3 Boundary condition at the skull

As mentioned above, four boundary conditions are required at each boundary of the brain. Concerning the displacement at the skull, we may assume

\[ u = v = w = 0, \]  (3.4)

i.e. the outer surface of the brain is fixed and cannot move. The justification comes from the meningeal structure: A dense system of short strands extends from the arachnoid membrane, which together with the duramatter is firmly attached to the skull, to the pia mater, which forms the brain surface. This enables free CSF flow in the space between pia mater and arachnoid membrane, but at the same time fixes the brain to the skull. Of course, condition (3.4) does not apply to infants, where the skull’s flexibility allows an outward brain displacement, a characteristic feature of infantile hydrocephalus. For adults, though, the skull may be treated as rigid.

The fourth condition represents a balance of flow rates. The amount of fluid flowing to the skull through the aqueduct according to (2.10) plus the amount which leaks from the brain tissue must equal the absorption rate (2.12) into the blood stream:

\[ \frac{p_s - p_h}{\mu R} = \frac{\pi q^4}{128 \mu L} (p_v - p_s) + \oint_S \left( -\frac{k}{\mu} \nabla p \right) \cdot \mathbf{n} dS, \]  (3.5)
where the last term is a surface integral over the outer brain surface $S$ with unit outward normal $\mathbf{n}$. The ventricular pressure $p_v$ is the pressure at the other boundary; $p_s$ is the pressure at the skull and is constant around the brain:

$$p = p_s = \text{const. on } S.$$  

Finally, the blood pressure $p_b$ is assumed not to vary with time, neglecting the pulsatile nature of the circulatory system.

### 3.4 Boundary condition at the ventricle wall

As at the skull, the CSF pressure is the same all over the ventricle wall $\mathcal{V}$:

$$p = p_v = \text{const. on } \mathcal{V}$$  

For continuity of stresses, this pressure, exerted by the CSF inside the ventricles on the ventricle wall, must balance the poroelastic stress in the brain tissue. Hence, denoting the unit outward normal to the ventricle wall by $\mathbf{n}$,

$$-p_v \mathbf{n} = \mathbf{\sigma} \cdot \mathbf{n} \text{ on } \mathcal{V}.$$  

The convention of tensile stresses being positive accounts for the negative sign. This vector equation already comprises three boundary conditions and can be expressed in terms of the deformation with the help of (2.4):

$$(\alpha - 1)p_v \mathbf{n} = 2G\varepsilon \cdot \mathbf{n} + \lambda \epsilon \mathbf{n}$$

The last boundary condition relates the change of ventricle volume to CSF production and drainage and thus introduces a time dependence into the system. The change in ventricle volume $\dot{V}$ must equal the ventricular CSF production $Q_p$ less the drainage (2.10) through the aqueduct, less amounts $S(p_v)$ that might be drained during treatment, and less the flow rate into the brain parenchyma:

$$\dot{V} = Q_p - \frac{\pi d^4}{128\mu L} (p_v - p_h) - S(p_v) - \int_\mathcal{V} \left( \frac{k}{\mu} \nabla p \right) \cdot \mathbf{n} \, dS$$  

The last term again is a surface integral over the ventricle wall $\mathcal{V}$ with unit outward normal $\mathbf{n}$. Treatment will be specified later, in particular the functional form of $S(p_v)$. Condition (3.10) already suggests that the striking physiological phenomenon of a pressure independent CSF production $Q_p$ is crucial to the evolution of hydrocephalus.
3.5 Polar coordinates

In the one- and two-dimensional geometry we can reduce the complexity of the governing equations by introducing polar coordinates \( r > 0, \theta \in (0, \pi), \) and \( \varphi \in (0, 2\pi) \) (Fig. 3.1). Let \( \sigma_{rr}, \sigma_{\theta \theta}, \) and \( \sigma_{\varphi \varphi} \) be the normal stresses along the spherical basis vectors \( e_r, e_\theta, \) and \( e_\varphi, \) and let \( \sigma_{r \theta}, \sigma_{r \varphi}, \) and \( \sigma_{\theta \varphi} \) be the shear stresses. The stress equilibrium (2.2) in polar coordinates can be found in standard references [2]:

\[
\begin{align*}
0 &= \frac{2\sigma_{rr} + \cot \theta \sigma_{\theta \theta} - \sigma_{\varphi \varphi}}{r} + \frac{\partial \sigma_{rr}}{\partial r} + \frac{\partial \sigma_{rr}}{\partial \theta} + \frac{1}{r} \frac{\partial \sigma_{r \theta}}{\partial \theta} + \frac{\sigma_{r \theta}}{r} + \frac{1}{r \sin \theta} \frac{\partial \sigma_{r \varphi}}{\partial \varphi}, \\
0 &= \frac{3\sigma_{rr} + \cot \theta \sigma_{\theta \theta} - \sigma_{\varphi \varphi}}{r} + \frac{\partial \sigma_{\theta \theta}}{\partial r} + \frac{\partial \sigma_{\theta \theta}}{\partial \theta} + \frac{1}{r} \frac{\partial \sigma_{r \theta}}{\partial \theta} + \frac{\sigma_{r \theta}}{r} + \frac{1}{r \sin \theta} \frac{\partial \sigma_{\theta \varphi}}{\partial \varphi}, \\
0 &= \frac{2 \cot \theta \sigma_{\varphi \varphi} + 3\sigma_{rr}}{r} + \frac{\partial \sigma_{\varphi \varphi}}{\partial r} + \frac{\partial \sigma_{\varphi \varphi}}{\partial \theta} + \frac{1}{r \sin \theta} \frac{\partial \sigma_{\varphi \varphi}}{\partial \varphi}
\end{align*}
\]

(3.11)

The constitutive equation of linear poroelasticity (2.4) still holds with \( i, j \in \{r, \theta, \varphi\} \) instead of \( i, j \in \{1, 2, 3\}, \) since the orthonormal basis vector set is just rotated. Let us denote the components of the displacement vector along \( e_r, e_\theta, \) and \( e_\varphi \) by \( u, v, \) and \( w \) (for simplicity we use the same notation as for the three-dimensional geometry in the Cartesian coordinate system). Then the strains are given by

\[
\begin{align*}
\varepsilon_{rr} &= \frac{\partial u}{\partial r}, \quad \varepsilon_{r \theta} = \frac{1}{r} \frac{\partial u}{\partial \theta} + \frac{u}{r}, \\
\varepsilon_{r \varphi} &= \frac{1}{2} \left[ \frac{\partial u}{\partial r} - \frac{w}{r} + \frac{1}{r \sin \theta} \frac{\partial w}{\partial \phi} \right], \\
\varepsilon_{\theta \theta} &= \frac{1}{2} \left[ \frac{\partial u}{\partial \theta} - \frac{u}{r} + \frac{1}{r \sin \theta} \frac{\partial u}{\partial \phi} \right], \\
\varepsilon_{\theta \varphi} &= \frac{1}{2} \left[ \frac{\partial u}{\partial \theta} - \frac{u}{r} + \frac{1}{r \sin \theta} \frac{\partial u}{\partial \phi} \right], \\
\varepsilon_{\varphi \varphi} &= \frac{1}{2} \left[ \frac{\partial u}{\partial \varphi} + \frac{w}{r} + \frac{1}{r \sin \theta} \frac{\partial w}{\partial \phi} \right], \\
\varepsilon_r &= \frac{1}{2} \left[ \frac{\partial v}{\partial r} - \frac{v}{r} + \frac{1}{r \sin \theta} \frac{\partial v}{\partial \phi} \right], \\
\varepsilon_{\theta \varphi} &= \frac{1}{2} \left[ \frac{\partial v}{\partial \theta} - \frac{v}{r} + \frac{1}{r \sin \theta} \frac{\partial v}{\partial \phi} \right], \\
\varepsilon_{\varphi \varphi} &= \frac{1}{2} \left[ \frac{\partial v}{\partial \varphi} + \frac{w}{r} + \frac{1}{r \sin \theta} \frac{\partial w}{\partial \phi} \right].
\end{align*}
\]

(3.12)

3.5.1 Cylindrically symmetric geometry

In the two-dimensional case the symmetry around the z-axis implies that the displacement component \( w \) in \( \varphi \)-direction and all derivatives with respect to \( \varphi \) are zero. Hence, we can substitute the strains into the stresses (2.4) and obtain

\[
\begin{align*}
\sigma_{rr} &= 2G \frac{\partial u}{\partial r} + \lambda \varepsilon - \alpha p, \\
\sigma_{r \theta} &= 2G \left[ \frac{\partial \theta}{\partial \theta} + \frac{u}{r} \right] + \lambda \varepsilon - \alpha p, \\
\sigma_{r \varphi} &= 2G \left[ \frac{\partial \theta}{\partial \theta} + \frac{u}{r} \right] + \lambda \varepsilon - \alpha p, \\
\sigma_{\theta \theta} &= 2G \left[ \frac{\partial \theta}{\partial \theta} + \frac{u}{r} \right] + \lambda \varepsilon - \alpha p, \\
\sigma_{\theta \varphi} &= 2G \left[ \frac{\partial \theta}{\partial \theta} + \frac{u}{r} \right] + \lambda \varepsilon - \alpha p, \\
\sigma_{\varphi \varphi} &= 2G \left[ \frac{\partial \theta}{\partial \theta} + \frac{u}{r} \right] + \lambda \varepsilon - \alpha p,
\end{align*}
\]

(3.13)

where the volume dilation \( \varepsilon = \varepsilon_{rr} + \varepsilon_{\theta \theta} + \varepsilon_{\varphi \varphi} \) is shorthand for

\[
\varepsilon = \frac{\partial u}{\partial r} + \frac{2u}{r} + \frac{1}{r} \frac{\partial v}{\partial \theta} + \frac{\cot \theta v}{r}
\]

(3.14)
This reduces the stress equilibrium in polar coordinates to two differential equations in the unknowns \( u \) and \( v \) (the third equation is trivially true), which can algebraically be transformed into the two displacement PDEs for cylindrical symmetry,

\[
0 = -\frac{\partial p}{\partial r} + (\lambda+G) \frac{\partial^2 u}{\partial r^2} + \frac{\lambda+G}{r} \frac{\partial^2 u}{\partial \theta^2} + \frac{G}{r} \frac{\partial^2 u}{\partial \phi^2} + \frac{G}{r^2} \frac{\partial^2 u}{\partial \theta \partial \phi} + \frac{\lambda+G}{r^2} \frac{\partial^2 v}{\partial \theta^2} - \frac{2(\lambda+2G)}{r^2} \frac{\partial p}{\partial \theta} - \frac{(\lambda+3G) \cos \theta}{r^2} \frac{\partial^2 u}{\partial \theta^2} - \frac{2(\lambda+2G)}{r^2} \frac{\partial p}{\partial \theta} - \frac{(\lambda+3G) \cos \theta}{r^2} \frac{\partial^2 v}{\partial \theta^2} - \frac{2(\lambda+2G)}{r^2} \frac{\partial p}{\partial \theta} - \frac{(\lambda+3G) \cos \theta}{r^2} \frac{\partial^2 v}{\partial \theta^2}.
\]

(3.15)

The pressure PDE is found by writing \( \nabla p = \left( \frac{\partial p}{\partial r}, \frac{1}{r} \frac{\partial p}{\partial \theta}, 0 \right)^T \) and then expressing (3.3) in polar coordinates:

\[
\frac{1}{r^2} \frac{\partial}{\partial r} \left[ r^2 k_0 e^{Me} \frac{\partial p}{\partial r} \right] + \frac{1}{r \sin \theta} \frac{\partial}{\partial \theta} \left[ \frac{\sin \theta}{r} k_0 e^{Me} \frac{\partial p}{\partial \theta} \right] = -\mu s
\]

(3.16)

Again, derivatives may either be taken in the deformed or undeformed configuration.

The skull boundary conditions (3.4) and (3.5) stay the same—for a numerical computation it is convenient not to transform the integral in the latter equation into an integral in \( r \) and \( \theta \). The same holds for the ventricle condition (3.10). However, we shall express boundary condition (3.9) in polar coordinates. To obtain the unit outward normal \( n \) in terms of \( e_r \), \( e_\theta \), and \( e_\phi \), we define the ventricle wall (2.1) as a surface in the Cartesian coordinate system,

\[
g(x, y, z) := r - f(\theta) = 0,
\]

(3.17)

so that the outward normal can be expressed as follows:

\[
n = \frac{\nabla g}{\| \nabla g \|} = \left( \frac{\partial g}{\partial r} e_r + \frac{1}{r \sin \theta} \frac{\partial g}{\partial \phi} e_\phi + \frac{1}{r \sin \theta} \frac{\partial g}{\partial \phi} e_\phi \right) = \frac{e_r - \frac{f(\theta)}{r} e_\theta}{\sqrt{1 + \frac{f'(\theta)^2}{r^2}}} = \frac{f(\theta) e_r - f'(\theta) e_\theta}{\sqrt{f^2(\theta) + f'^2(\theta)}}
\]

(3.18)

Multiplying both sides of (3.8) with \( \sqrt{f^2(\theta) + f'^2(\theta)} \), the condition in polar coordinates becomes

\[
-p_v \begin{pmatrix} f \\ -f' \end{pmatrix} = \begin{pmatrix} \sigma_{rr} & \sigma_{r\theta} & 0 \\ \sigma_{r\theta} & \sigma_{\theta\theta} & 0 \\ 0 & 0 & \sigma_{\phi\phi} \end{pmatrix} \begin{pmatrix} f \\ -f' \end{pmatrix},
\]

(3.19)

which (after substituting the stresses in) can be transformed into the two equations

\[
\begin{align*}
(\alpha-1)p_v &= (\lambda+2G) \frac{\partial u}{\partial r} - \frac{\lambda+G}{r} \frac{\partial^2 u}{\partial \theta^2} + \frac{\lambda+G}{r^2} \frac{\partial^2 u}{\partial \phi^2} + \frac{G}{r^2} \frac{\partial^2 u}{\partial \theta \partial \phi} + \frac{\lambda+G}{r^2} \frac{\partial^2 v}{\partial \theta^2} - \frac{2(\lambda+2G)}{r^2} \frac{\partial p}{\partial \theta} - \frac{(\lambda+3G) \cos \theta}{r^2} \frac{\partial^2 u}{\partial \theta^2} - \frac{2(\lambda+2G)}{r^2} \frac{\partial p}{\partial \theta} - \frac{(\lambda+3G) \cos \theta}{r^2} \frac{\partial^2 v}{\partial \theta^2} - \frac{2(\lambda+2G)}{r^2} \frac{\partial p}{\partial \theta} - \frac{(\lambda+3G) \cos \theta}{r^2} \frac{\partial^2 v}{\partial \theta^2},

\frac{\partial p}{\partial \theta} &= -\lambda \frac{f'}{f} \frac{\partial u}{\partial r} + \frac{\lambda}{r} \frac{\partial^2 u}{\partial \theta^2} + \frac{\lambda}{r^2} \frac{\partial^2 u}{\partial \phi^2} + \frac{G}{r^2} \frac{\partial^2 u}{\partial \theta \partial \phi} - (\lambda+\lambda)(\lambda+2G) \frac{\partial p}{\partial \theta} - (\lambda+\lambda)(\lambda+3G) \cos \theta \frac{\partial^2 u}{\partial \theta^2} - (\lambda+\lambda)(\lambda+3G) \cos \theta \frac{\partial^2 v}{\partial \theta^2} - (\lambda+\lambda)(\lambda+3G) \cos \theta \frac{\partial^2 v}{\partial \theta^2}.
\end{align*}
\]

(3.20)

Since the domain of computation in the \( r-\theta \)-plane exhibits two additional artificial boundaries at \( \theta = 0 \) and \( \theta = \pi \) (Fig.3.2), we have to define further boundary conditions there. For symmetry reasons we assume on both boundaries

\[
v = \frac{\partial u}{\partial \theta} = \frac{\partial p}{\partial \theta} = 0.
\]

(3.21)
3.5.2 Spherically symmetric geometry

For the one-dimensional, spherically symmetric geometry, also the displacement component \(v\) and all derivatives in \(\theta\)-direction are zero so that the system of governing equations (3.15) and (3.16) reduces to two ODEs in \(u, p,\) and \(r:\)

\[
(\lambda + 2G) \left[ \frac{\partial^2 u}{\partial r^2} + \frac{2}{r} \frac{\partial u}{\partial r} - \frac{2u}{r^2} \right] - \alpha \frac{\partial p}{\partial r} = 0
\]

\[
\frac{1}{r^2} \frac{\partial}{\partial r} \left[ r^2 k_{\theta e} \frac{\partial p}{\partial r} \right] = -\mu s
\]

Although the radius \(r\) is the only spatial variable, we use partial derivatives since \(u\) and \(p\) also depend on the time \(t.\) The boundary conditions become at the skull

\[
u = 0 \quad \text{at } r = c,
\]

\[
\frac{p - p_b}{\mu R} = \frac{\pi d^4}{128\mu L} (p_v - p) - 4\pi r^2 k_{\theta e} \frac{\partial p}{\partial r} \quad \text{at } r = c,
\]

where the ventricle pressure \(p_v\) is \(p|_{r=a+u(a)}\) or \(p|_{r=a},\) depending on whether the pressure is computed in the deformed or undeformed configuration. At the ventricle wall conditions (3.20) and (3.10) become with \(v = f' = \frac{\partial}{\partial \theta} = 0\)

\[
(\alpha - 1) p_v = (\lambda + 2G) \frac{\partial u}{\partial r} + 2\lambda \frac{u}{r} \quad \text{at } r = a,
\]

\[
\frac{d}{dt} \left[ \frac{4}{3} \pi (a + u(a))^3 \right] = Q_p - \frac{\pi d^4}{128\mu L} (p - p_s) - S(p) + 4\pi r^2 k_{\theta e} \frac{\partial p}{\partial r}
\]

at \(r = a\) if the pressure is computed in the undeformed configuration, and at \(r = a + u(a)\) otherwise. The skull pressure is given by \(p_s = p|_{r=c}.\)

Alternatively we shall add boundary conditions for the special case of no source or sink in the parenchyma and a reached steady state (i.e. \(\vec{V} = 0).\) Then the venous system near the skull absorbs exactly that amount of CSF which is produced inside the ventricles so that (3.27) may be replaced by

\[
\frac{p|_{r=e} - p_b}{\mu R} = Q_p.
\]
Chapter 4

Nondimensionalisation

First, we choose to nondimensionalise all lengths with respect to $c$, the brain radius of the spherically and cylindrically symmetric geometry:

$$x, y, z, r, u, v, w, f(\theta) \sim c, \quad V \sim c^3$$ (4.1)

The time scale $\hat{t}$ shall be the time to fill the cranial volume with CSF at constant production rate $Q_p$,

$$t \sim \hat{t} = \frac{4\pi c^3}{3Q_p}, \quad s \sim \hat{t}^{-1}. \quad (4.2)$$

Let us denote the ventricular aspect ratio $\frac{a}{c}$ by $\eta$. An adequate pressure scale $\hat{p}$ is determined by Darcy’s law. Whereas the pressure for flow through a porous wall will basically decrease linearly with depth, the pressure during flow from the middle to the outside of a porous ball will behave like $\frac{1}{r}$. Therefore, in the brain we have approximately

$$p \approx p_{\text{skull}} + \frac{a}{c-a} \left( \frac{c}{r} - 1 \right) \hat{p} \quad (4.3)$$

and according to Darcy’s law the fluid velocity

$$W \approx \frac{k_0 \partial p}{\mu \partial r} \approx \frac{k_0}{\mu} \frac{ac}{c-a} \frac{1}{r^2} \hat{p}. \quad (4.4)$$

Hence, the time for CSF flow from the ventricles to the skull can be approximated by

$$\hat{t} \approx \int_a^c \frac{dr}{W} = \left[ \frac{\mu c - a r^3}{k_0 ac \hat{p}} \right]_a^c = \frac{\mu (c - a) (c^3 - a^3)}{3k_0 ac \hat{p}} \approx \frac{\mu c^4}{3k_0 ac \hat{p}}, \quad (4.5)$$

which (denoting the nondimensional pressure by $p^*$) suggests to scale the pressure by

$$p = p_b + \hat{p}^*, \quad \hat{p} = \frac{1}{3} \frac{\mu c^4}{k_0 ac \hat{t}} = \frac{Q_p \mu}{4\pi k_0 a}, \quad (4.6)$$
Let us define the dimensionless parameters

$$\hat{\alpha} = \frac{\alpha \hat{p}}{G} = \frac{\alpha Q_p \mu}{G \pi k_0 a}, \quad \gamma = \frac{\pi d^4 \hat{p}}{128 \mu L Q_p} = \frac{d^4}{312 L k_0 a}, \quad \delta = \frac{\hat{p}}{Q_p R \mu} = \frac{1}{4 \pi k_0 a R}.$$  (4.7)

Then, noting $\frac{x - G}{G} = \frac{1}{1 - 2\nu}$ with $\nu$ being the undrained Poisson's ratio of the solid brain matrix, the system of governing equations (3.2) and (3.3) with boundary conditions (3.4), (3.5), (3.9), and (3.10) in nondimensional variables (asterisks dropped) is

$$\nabla^2 u_i + \frac{1}{1 - 2\nu} \frac{\partial \epsilon}{\partial x_i} = \hat{\alpha} \frac{\partial p}{\partial x_i},$$  (4.8)

$$\nabla_i [e^{M_e} \nabla p] = -3\eta_s,$$  (4.9)

$$u = v = w = 0 \quad \text{on} \ S,$$  (4.10)

$$\delta p_s = \gamma (p_v - p_s) - \frac{1}{4 \pi \eta} \int_S e^{M_e} \frac{\partial p}{\partial n} dS,$$  (4.11)

$$\frac{\alpha - 1}{\alpha} \left( \frac{\alpha p_b}{G} + \hat{\alpha} p_v \right) n = 2\nu \cdot n + \frac{2\nu}{1 - 2\nu} \epsilon \cdot n \quad \text{on} \ V,$$  (4.12)

$$\frac{3}{4\pi} \hat{V} = 1 - \gamma (p_v - p_s) - \frac{S(p_v)}{Q_p} + \frac{1}{4 \pi \eta} \int_V e^{M_e} \frac{\partial p}{\partial n} dS.$$  (4.13)

The corresponding cylindrically symmetric PDEs (3.15) and (3.16) with boundary conditions (3.20) and (3.21) become

$$\begin{align*}
(1 - 2\nu) \frac{\partial^2 u}{\partial r^2} &+ \frac{1}{r} \frac{\partial}{\partial r} \left[ r^2 e^{M_e} \frac{\partial p}{\partial r} \right] + \frac{1}{r} \frac{\partial}{\partial \theta} \left[ \frac{\sin \theta}{r} e^{M_e} \frac{\partial p}{\partial \theta} \right] = -3\eta_s, \\
(1 - 2\nu) \frac{\partial^2 v}{\partial r^2} &+ \frac{1}{r} \frac{\partial}{\partial r} \left[ r^2 e^{M_e} \frac{\partial p}{\partial r} \right] + \frac{1}{r} \frac{\partial}{\partial \theta} \left[ \frac{\sin \theta}{r} e^{M_e} \frac{\partial p}{\partial \theta} \right] = -3\eta_s,
\end{align*}$$  (4.14)

$$\begin{align*}
\frac{\alpha - 1}{\alpha} \left( \frac{\alpha p_b}{G} + \hat{\alpha} p_v \right) &\frac{\partial}{\partial r} \left[ r^2 e^{M_e} \frac{\partial p}{\partial r} \right] + \frac{1}{r} \frac{\partial}{\partial \theta} \left[ \frac{\sin \theta}{r} e^{M_e} \frac{\partial p}{\partial \theta} \right] = -3\eta_s, \\
\frac{\alpha - 1}{\alpha} \left( \frac{\alpha p_b}{G} + \hat{\alpha} p_v \right) &\frac{\partial}{\partial r} \left[ r^2 e^{M_e} \frac{\partial p}{\partial r} \right] + \frac{1}{r} \frac{\partial}{\partial \theta} \left[ \frac{\sin \theta}{r} e^{M_e} \frac{\partial p}{\partial \theta} \right] = -3\eta_s,
\end{align*}$$  (4.15)

$$\begin{align*}
\frac{\alpha - 1}{\alpha} \left( \frac{\alpha p_b}{G} + \hat{\alpha} p_v \right) &\frac{\partial}{\partial r} \left[ r^2 e^{M_e} \frac{\partial p}{\partial r} \right] + \frac{1}{r} \frac{\partial}{\partial \theta} \left[ \frac{\sin \theta}{r} e^{M_e} \frac{\partial p}{\partial \theta} \right] = -3\eta_s, \\
\frac{\alpha - 1}{\alpha} \left( \frac{\alpha p_b}{G} + \hat{\alpha} p_v \right) &\frac{\partial}{\partial r} \left[ r^2 e^{M_e} \frac{\partial p}{\partial r} \right] + \frac{1}{r} \frac{\partial}{\partial \theta} \left[ \frac{\sin \theta}{r} e^{M_e} \frac{\partial p}{\partial \theta} \right] = -3\eta_s,
\end{align*}$$  (4.16)

where the remaining three boundary conditions stay in the form (4.10), (4.11), and (4.13). The corresponding spherically symmetric ODEs (3.22) and (3.23) become

$$\frac{\partial^2 u}{\partial r^2} + \frac{2 u}{r^2} + \frac{2 u}{r^2} = \frac{1 - 2\nu}{2(1 - \nu)} \hat{\alpha} \frac{\partial p}{\partial r},$$  (4.18)

$$\frac{1}{r^2} \frac{\partial}{\partial r} \left[ r^2 e^{M_e} \frac{\partial p}{\partial r} \right] = -3\eta_s.$$  (4.19)
while boundary conditions (3.24), (3.25), (3.26), and (3.27) change to

\[ u = 0 \quad \text{at} \ r = 1, \quad (4.20) \]

\[ \eta \delta p_s = \eta \gamma (p_v - p_s) - e^{M_e} \frac{\partial p}{\partial r} \bigg|_{r=1}, \quad (4.21) \]

\[ \frac{1 - 2\nu}{2(1 - \nu)} \frac{\alpha - 1}{\alpha} \left( \frac{\alpha p_b}{G} + \hat{\alpha} p_v \right) = \frac{\partial u}{\partial r} + \frac{\nu}{1 - \nu} \frac{2u}{r} \quad \text{at} \ r = \eta, \quad (4.22) \]

\[ \frac{d}{dt} \left( \eta + u(\eta) \right)^3 = 1 - \gamma (p_v - p_s) - \frac{S(p_v)}{Q_p} + \frac{t^2}{\eta} e^{M_e} \frac{\partial p}{\partial r} \bigg|_{r=\eta \text{ or } \eta + u(\eta)}. \quad (4.23) \]

As the alternative for (4.23) in the case of a steady state with \( s = 0 \), equation (3.28) becomes

\[ p_s = \delta^{-1}. \quad (4.24) \]

By default we shall use the parameter values (Tab. 4.1) from Smillie et al. [24], who performed a careful parameter estimation with reasonable results. Parameter \( M \) comes from Kaczmarek et al. [10]. It has to be stressed that up to the present a fully satisfactory determination of the poroelastic constants has not been achieved so that each value inevitably contains a considerable portion of uncertainty. We shall therefore also examine the sensitivity of results to the parameter estimates. With Table 4.1,

\[ \dot{t} \sim 7 \cdot 10^5 \text{s} \approx 8 \text{d}, \ \dot{p} \sim 1000 \text{Pa}, \ \hat{\alpha} \sim 4.5, \ \delta \sim 2, \ \gamma \sim \begin{cases} 0 & \text{blocked aqueduct,} \\ 1.7 \cdot 10^4 & \text{open aqueduct.} \end{cases} \]

The magnitude of \( \hat{\alpha} \) reflects the decisive influence of the pressure on the brain displacement, confirming the hypothesis that ventricle dilation can be caused by hydrocephalic pressure gradients. It is also obvious that in the case of an open aqueduct the Poiseuille flow term with \( \gamma \) by far outweighs all other terms; i.e. all CSF flows through the aqueduct, and equation (4.11) implies \( p_v \approx p_s \) (no transparenchymal pressure gradient).

<table>
<thead>
<tr>
<th>( a )</th>
<th>30 mm</th>
<th>( k_0 )</th>
<th>( 1.4 \times 10^{-14} \text{m}^2 )</th>
<th>( Q_p )</th>
<th>( 5.8 \times 10^{-9} \text{m}^3/\text{s} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( c )</td>
<td>100 mm</td>
<td>( \mu )</td>
<td>( 8.9 \times 10^{-4} \text{Pa s} )</td>
<td>( R )</td>
<td>( 8.5 \times 10^{13} \text{m}^{-3} )</td>
</tr>
<tr>
<td>( L )</td>
<td>70 mm</td>
<td>( G )</td>
<td>216 Pa</td>
<td>( p_b )</td>
<td>650 Pa</td>
</tr>
<tr>
<td>( d )</td>
<td>4 mm</td>
<td>( \lambda )</td>
<td>524 Pa</td>
<td>( M )</td>
<td>4.3</td>
</tr>
<tr>
<td>( \alpha, \beta )</td>
<td>1, 0.99</td>
<td>( \nu )</td>
<td>0.35</td>
<td>( b )</td>
<td>0.2 mm</td>
</tr>
</tbody>
</table>

Table 4.1: Standard parameter values.
Chapter 5

Solution methods

Except for some special cases in the spherically symmetric geometry, the solution to the governing equations is computed numerically in MATLAB using finite difference schemes in the one- and two-dimensional and finite element methods in the two- and three-dimensional geometry. The interconnection between pressure and displacement equation is treated by an iteration between both.

5.1 One-dimensional geometry

One of the objectives for the one-dimensional geometry is to obtain an analytic solution for simple special cases. Let the source $s$ in (4.19) be zero, and let us approximate the deformed brain tissue by the undeformed state, i.e. equations (4.18) and (4.19) both refer to the undeformed configuration. The solution to both ODEs is derived in appendix A.1:

\[
p = \frac{2(1-\nu)}{M(1-2\nu)\alpha} \ln \left( \frac{C_3}{r} + C_3 \right) - C_1, \tag{5.1}
\]

\[
u = \frac{1}{3Mr^2} \left( -(\frac{C_3}{\alpha})^2 + \frac{(\frac{C_3}{\alpha})^2}{2} + (\frac{C_3}{\alpha})^3 \ln(r) + (\frac{C_3}{\alpha})^3 \ln(\frac{1}{r} + \frac{C_3}{\alpha}) + r^3 \ln(\frac{C_3}{r} + C_3) \right) + \frac{C_4}{r^2}. \tag{5.2}
\]

$C_1$ to $C_4$ are integration constants to be determined by the boundary conditions.

In the case of a reached steady state for a completely obstructed aqueduct (boundary conditions (4.20) to (4.22), (4.24), and $\gamma = 0$) it is shown in appendix A.1 how to express $C_1$, $C_2$, and $C_4$ in terms of $C_3$. Furthermore, a condition $g(C_3) = 0$ for $C_3$ is derived, where $g$ is a monotonically increasing function. $C_3$ (and thus the other constants) is computed from this condition via a Newton iteration.

To obtain displacement and pressure distribution at a stage where the aqueduct is not fully blocked and the steady state is not yet reached, we use boundary conditions (4.20) to (4.22) and replace condition (4.24) by $p_s = p_c < \delta^{-1}$. This system of equations corresponds to that stage of the evolution or treatment of hydrocephalus,
where the subarachnoid pressure has just reached $p_c$. This time, appendix A.1 shows (for $\alpha = 1$) how to obtain $C_1$, $C_3$, and $C_4$ in terms of $C_2$, and how to derive a condition $h(C_2) = 0$, which again is solved via a Newton iteration.

To solve the system (4.18) to (4.23) in its entire complexity, we use a numerical scheme. Unlike before, the pressure shall now be computed in the deformed configuration, i.e. $r$ in (4.19), (4.21), and (4.23) is the deformed radius. At each time step we shall first solve for the pressure in the not yet updated configuration. The pressure is then used in the displacement computation, whose result serves to update $\epsilon$ and the domain of the pressure computation. This iteration is continued until pressure and displacement converge so that the next time step can be treated.

The interval $[\eta, 1]$ is subdivided by equispaced points $r_i = \eta + i \Delta r$, $i = 0, ..., m = \frac{1-\eta}{\Delta r}$. Derivatives in (4.18) are replaced by central differences on this mesh, i.e. defining the nodal approximations $U_i \approx u(r_i)$ and $P_i \approx p(r_i + u(r_i))$, the equation discretises to

$$U_{i-1} - 2U_i + U_{i+1} \over \Delta r^2 + \frac{2U_{i+1} - U_{i-1}}{2\Delta r} - \frac{2U_i}{r_i} \over r_i^2 = \frac{1 - 2\nu}{2(1 - \nu)} \over \Delta r \left( \alpha \frac{p_b}{G} + \alpha \tilde{P}_0 \right).$$

This at all internal nodes together with the discretised boundary conditions

$$U_m = 0$$

$$- \frac{U_1 - U_0}{\Delta r} + \frac{\nu}{1 - \nu} \frac{2U_0}{r_0} = \frac{1 - 2\nu}{2(1 - \nu)} \left( \alpha \frac{p_b}{G} + \alpha \tilde{P}_0 \right)$$

yields a tridiagonal $(m + 1)$ by $(m + 1)$ linear system in the unknowns $U_0$ to $U_m$, which can readily be solved. Then $\epsilon$ is computed for each node via central differences (one-sided differences at the boundaries). To compute the pressure, the domain of computation $[r_0 + U_0, r_m + U_m]$ is discretised as $\hat{r}_j = r_0 + U_0 + j\Delta \hat{r}$, $j = 0, ..., m = m = \frac{r_m + U_m - r_0 - U_0}{\Delta \hat{r}}$, and $\epsilon$ is linearly interpolated at each node $\hat{r}_{j+1/2} = \hat{r}_j + \Delta \hat{r}$. Now, central differences on the new mesh are applied to the pressure equation (4.19),

$$\left[ \hat{r}_{j+1/2}^2 e^{M_{\epsilon_j+1/2}} \hat{P}_{j+1/2} - \hat{P}_{j+1} \over \Delta \hat{r} - \hat{r}_{j-1/2}^2 e^{M_{\epsilon_j-1/2}} \hat{P}_{j-1/2} \right] \over \Delta \hat{r} = -3\eta s_j \hat{r}_j^2,$$

with boundary conditions

$$\eta \delta \hat{P}_m = \eta \gamma (\hat{P}_0 - \hat{P}_m) - e^{M_{\epsilon_m}} \hat{P}_{m-1} \over \Delta \hat{r},$$

$$3(\eta + U_0)^2 \over \Delta t = 1 - \gamma (\hat{P}_0 - \hat{P}_m) - \frac{S(\hat{P}_0)}{Q_p} + \frac{\hat{r}_0^2 e^{M_{\epsilon_0}} \hat{P}_1 - \hat{P}_0}{\eta}.$$

where $\bar{U}_0$ is the value of $\bar{U}_0$ at the last time step and uniform time steps $t_k = k \Delta t$ are used. This tridiagonal system for $\hat{P}_0, ..., \hat{P}_m$ is solved, and the values $\hat{P}_j$ are interpolated at the $r_i$ to obtain the $p_i$, which are then used in the next iteration for the displacement computation.
Figure 5.1: Discretisation of the domain of computation for \( m = 5, n = 6 \). The middle graph shows the triangulation for the pressure finite element scheme, the right one shows the mesh after the coordinate transform for the displacement computation.

5.2 Two-dimensional geometry

The cylindrically symmetric system is solved numerically. As before, at each time step an iteration between pressure and displacement equation is conducted, repeatedly updating the dilation \( \epsilon \) and the domain for the pressure computation until \( p, u \) and \( v \) converge. The pressure will be found via a finite element scheme, whereas a finite difference scheme is more convenient to compute the displacement.

The computational domain in the \( r-\theta \)-plane is divided into tetragons by equispaced points along some equispaced radii, i.e. for some \( m, n \in \mathbb{N} \) we use nodes \((r_{ij}, \theta_j)\) with \( \theta_j = j \frac{\pi}{n}, j = 0, \ldots, n \), and \( r_{ij} = f(\theta_j) + \frac{i-1-f(\theta_j)}{m}, i = 0, \ldots, m \) (Fig. 5.1). Each tetragon is divided into two triangles to obtain a triangulation for the pressure finite element scheme (different triangulations are compared later on). Then a coordinate transform maps \((r, \theta)\) onto \((\tilde{r}, \tilde{\theta}) = \left( \frac{r-f(\theta)}{1-f(\theta)}, \theta \right)\) to obtain a regular mesh for the displacement finite difference scheme (compare Fig. 5.1).

The weak formulation of the pressure equation \((4.15)\) with boundary conditions \((3.6), (3.7), \) and \((4.17)\) is derived in appendix A.2: If \( \mathcal{B} \) is the deformed brain domain in the \( r-\theta \)-plane, we seek \( p \in \{ g \in H^1(\mathcal{B}) | g \circ u(f(\theta), \theta) = p_\theta, g(1, \theta) = p_s \} \) such that

\[
\int_{\mathcal{B}} -\nabla_p q \cdot [Ap] + qb^T \nabla_p p drd\theta = \int_{\mathcal{B}} -3qsdrd\theta, \quad A = e^{Me} \begin{pmatrix} 1 & 0 \\ 0 & \frac{1}{r^m} \end{pmatrix}, \quad b = e^{Me} \begin{pmatrix} \frac{2}{\cos \theta} \\ \frac{2}{r^m} \end{pmatrix},
\]

for all \( q \in \{ g \in H^1(\mathcal{B}) | g \circ u(f(\theta), \theta) = g(1, \theta) = 0 \} \) (having abbreviated \((\frac{\partial}{\partial r}, \frac{\partial}{\partial \theta})^T = \nabla_p \)). Furthermore, on each triangle \( K \) the local load vector \( f_K \) and the local stiffness matrix \( A_K \) of the pressure computation are shown to be

\[
f_K = -3q \frac{\det(J)}{24} Q \begin{pmatrix} s_1 \\ s_2 \\ s_3 \end{pmatrix}, \quad Q = \begin{pmatrix} 2 & 1 & 1 \\ 1 & 2 & 1 \\ 1 & 1 & 2 \end{pmatrix},
\]

\[
A_K = -\det(J) D^T J^{-1} A_1 + A_2 + A_3 \frac{\det(J)}{6} J^{-T} D + \frac{\det(J)}{24} Q \begin{pmatrix} b_1^T \\ b_2^T \\ b_3^T \end{pmatrix} J^{-T} D, \quad D = \begin{pmatrix} -1 & 1 & 0 \\ -1 & 0 & 1 \end{pmatrix},
\]

where \( J \) represents the Jacobian of the coordinate transform from \( K \) to the standard reference element and \( s_1 \) to \( s_3 \), \( A_1 \) to \( A_3 \), and \( b_1 \) to \( b_3 \) are the source \( s \), the matrix \( A \), and the vector \( b \) at the triangle vertices.
After the assembly of global stiffness matrix and load vector, two rows and columns are added to implement conditions (3.6), (3.7), (4.11), and (4.13) for a steady state solution, which is also detailed in appendix A.2. To simulate the temporal evolution, the latter, time dependent condition is replaced by \( p_v = p_k, \ k = 0, \ldots, l \in \mathbb{N} \), where \( p_0 \) is the initial and \( p_l \) the final ventricle pressure, and the \( p_k \) are exponentially distributed pressure values in between. After solving the system for each ventricle pressure \( p_k \), \( \dot{V}_k \) at that pressure can be computed via (4.13) so that the time between the states with \( p_v = p_k \) and \( p_v = p_{k+1} \) can be approximated by \( t_{k+1} - t_k \approx \frac{2(V_{k+1} - V_k)}{V_{k+1} + V_{k+1}} \).

Concerning the displacement, the derivatives in the PDE (4.14) and boundary condition (4.12) are adjusted to the new coordinates:

\[
\begin{align*}
\frac{\partial}{\partial r} &= \frac{1}{1-f(\theta)} \frac{\partial}{\partial \tilde{r}}, \\
\frac{\partial}{\partial \theta} &= \frac{\partial}{\partial \tilde{\theta}} + \frac{r-1}{(1-f(\theta))^2} f'(\theta) \frac{\partial}{\partial \tilde{r}}, \\
\frac{\partial^2}{\partial \tilde{r}^2} &= (r-1) \frac{f''(\theta)}{(1-f(\theta))^3} \frac{\partial}{\partial \tilde{r}} + \frac{\partial^2}{\partial \tilde{\theta}^2} + 2 \frac{(r-1)^2 f''(\theta)}{(1-f(\theta))^4} \frac{\partial}{\partial \tilde{r} \partial \tilde{\theta}} + \frac{(r-1)^3 f''(\theta)}{(1-f(\theta))^5} \frac{\partial^2}{\partial \tilde{r}^2}, \\
\frac{\partial^2}{\partial \tilde{r} \partial \tilde{\theta}} &= \frac{1}{(1-f(\theta))^2} \frac{\partial}{\partial \tilde{r}} + \frac{1}{1-f(\theta)} \frac{\partial}{\partial \tilde{\theta}} + \frac{1}{(1-f(\theta))^3} f'(\theta) \frac{\partial^2}{\partial \tilde{r}^2}.
\end{align*}
\]

Since the mesh in \((\tilde{r}, \tilde{\theta})\) is regular, central finite differences are then used at each internal node and one-sided differences at the boundary to approximate the derivatives in \( \tilde{r} \) and \( \tilde{\theta} \). This yields a linear system (18-diagonal) to be solved for the \( U_{ij} \approx u(\tilde{r}_i, \tilde{\theta}_j) = u(r_{ij}, \theta_j) \) and \( V_{ij} \approx v(\tilde{r}_i, \tilde{\theta}_j) = v(r_{ij}, \theta_j) \). Finally, the dilation at each node is computed via the finite difference version of (3.14) so that it can be used for the pressure computation.

### 5.3 Three-dimensional geometry

In the three-dimensional geometry both, pressure and displacement, are computed by a finite element method. As in the two-dimensional case, the pressure equation is solved in the deformed brain, and at each time step we iterate between pressure and displacement computation until the values converge (a simultaneous solution would result in a too large linear system).

The mesh generation on the undeformed brain starts from a regular mesh on a ball of unit radius. In a second step, mesh points of the ventricle walls and the skull are added, whereas those inside the ventricles or beyond the skull are deleted. A Delaunay triangulation then covers the convex hull of all mesh points with tetrahedrons, of which the ones inside the ventricles are deleted. To reduce the computational effort, each node is given two binary bits in addition to its coordinates, encoding whether
it belongs to \( \mathcal{V} \) or \( \mathcal{S} \). After each iteration all nodes are shifted by the computed displacement to obtain the new mesh for the pressure computation.

In appendix A.3 the weak formulation for the pressure and displacement equations is derived and shown to be of the following form: Let \( \mathcal{V} \) be the deformed ventricle wall and \( \mathcal{B} \) the undeformed, \( \mathcal{B} \) the deformed brain. Seek \( p \) in the Sobolev space \( H^1(\mathcal{B}) \) with \( p|_\mathcal{S} = p_s \), \( p|_{\mathcal{V}} = p_v \), and \( u, v, w \in H^1(\mathcal{B}) \) with \( u = v = w = 0 \) on \( \mathcal{S} \) such that

\[
\int_{\mathcal{B}} \nabla q \cdot [e^{\mu_c} \nabla p] \, dx \, dy \, dz = \int_{\mathcal{B}} 3 \eta q s \, dx \, dy \, dz,
\]

\[
\int_{\mathcal{B}} \nabla O \cdot [A_u \nabla u + A_v \nabla v + A_w \nabla w] \, dx \, dy \, dz = - \int_{\mathcal{B}} \hat{\alpha} O \frac{\partial p}{\partial x} \, dx \, dy \, dz \int_{\mathcal{V}} O \frac{\alpha - 1}{\alpha} \left( \frac{\partial p}{\partial x} \right) n_1 \, dS,
\]

\[
\int_{\mathcal{B}} \nabla P \cdot [B_u \nabla u + B_v \nabla v + B_w \nabla w] \, dx \, dy \, dz = - \int_{\mathcal{B}} \hat{\alpha} P \frac{\partial p}{\partial y} \, dx \, dy \, dz \int_{\mathcal{V}} P \frac{\alpha - 1}{\alpha} \left( \frac{\partial p}{\partial y} \right) n_2 \, dS,
\]

\[
\int_{\mathcal{B}} \nabla Q \cdot [C_u \nabla u + C_v \nabla v + C_w \nabla w] \, dx \, dy \, dz = - \int_{\mathcal{B}} \hat{\alpha} Q \frac{\partial p}{\partial z} \, dx \, dy \, dz \int_{\mathcal{V}} Q \frac{\alpha - 1}{\alpha} \left( \frac{\partial p}{\partial z} \right) n_3 \, dS
\]

for all \( q \in H^1(\mathcal{B}) = \{ f \in H^1(\mathcal{B}) | f = 0 \) on \( \mathcal{S} \cup \mathcal{V} \} \) and \( O, P, Q \in H_{E_0}(\mathcal{B}) = \{ f \in H^1(\mathcal{B}) | f = 0 \) on \( \mathcal{S} \} \), where the matrices \( A_u \) to \( C_w \) are given in appendix A.3. The detailed finite element formulation is also described there; we shall only mention that the pressure conditions (3.6), (3.7), (4.11), and (4.13) are handled as in the two-dimensional case and that, once assembled, the displacement stiffness matrix stays the same (which saves a lot of computation time, since the displacement stiffness matrix is nine times as big as the pressure stiffness matrix).

![Graphs showing numerical experiments for the 1D-solver](image)

Figure 5.2: Numerical experiments for the 1D-solver: The maximum relative error of pressure \( p \) and displacement \( u \) decreases linearly with the mesh size \( \Delta r \), whereas computation time for both increases linearly. Also the pressure-displacement iteration converges linearly.

The numerical schemes for the one-, two-, and three-dimensional geometry are all first order accurate in that the error in pressure and displacement linearly depends on
Figure 5.3: Different meshes for the 2D pressure computation (with a spherical ventricle) and contour lines of the corresponding computation error. The first mesh exhibits a strong directional dependence.

the mesh size (see Fig. 5.2 to 5.5). The reason lies in the ventricle boundary conditions, which involve the first derivative. If instead Dirichlet conditions for pressure and displacement are implemented on all boundaries, the schemes become second order accurate (as expected for a 1D-solver with a second order truncation error and for the finite element methods with linear Lagrange elements).

The computation time for pressure and displacement in one and two dimensions is expected to increase linearly with the number $M$ of nodes, since the matrix assembly time is proportional to $M$ and the system matrix has a fixed number of non-zero diagonals so that the system can be solved in linear time. The 1D-solver roughly obeys this rule (with some fluctuations, Fig. 5.2). Also the 2D pressure computation time increases linearly with $M$ and therefore quadratically with the inverse of the maximum triangle diameter (Fig. 5.4). The displacement computation, however, takes longer. A close analysis reveals that MATLAB needs the additional time to reference the system matrix entries during the assembly. This increased referencing time only occurs for large sparse matrices and hence mainly affects the displacement computation whose system matrix is four times as big as the pressure system matrix. In three dimensions, where the matrices are even larger, the referencing time completely outweighs all other processes. Hence, computation time behaves like the sixth power of the inverse tetrahedron diameter (Fig. 5.5), although we would expect the ninth power: The solving time of the linear system increases cubically with the matrix size and thus with the number of nodes, which in turn increases cubically with decreasing tetrahedron diameter. However, this relation will only be seen for matrices larger than the ones in our simulations. For our three-dimensional simulations we will
Figure 5.4: Numerical experiments for the 2D-solver: The maximum relative error of pressure $p$ (for the three different meshes of Fig. 5.3) and radial displacement $u$ decreases linearly with the maximum triangle diameter $diam(\Delta)$, whereas computation time for the pressure increases quadratically and for the displacement almost cubically. The pressure-displacement iteration converges linearly.

usually use maximum tetrahedron diameters of around 0.15, which results in linear systems of the approximate order 15000 by 15000.

As can be seen in Figure 5.4, the different triangulations of Figure 5.3 for the 2D pressure computation are of similar accuracy. However, the second mesh is inconvenient to use in combination with a displacement finite difference solver on a regular mesh, and the first mesh produces an artificial asymmetry (the error is directionally dependent, Fig. 5.3). Hence, we shall use the third mesh throughout our simulations.

Figure 5.5: Numerical experiments for the 3D-solver: The maximum error of pressure $p$ and displacement $u$, $v$, and $w$ decreases linearly with the maximum tetrahedron diameter $diam(\Delta)$, whereas computation time for both is proportional to the sixth power of the inverse tetrahedron diameter. The pressure-displacement iteration converges linearly.
Chapter 6

Results

In this chapter we shall present the general model predictions for the evolution, the clinical picture, and the treatment of hydrocephalus. We shall furthermore examine the effect of various model extensions and the sensitivity to them, successively for the one-, two-, and three-dimensional geometry.

6.1 Spherically symmetric simulations

6.1.1 Implications of a strain-dependent permeability

Figure 6.1 compares the model results for a constant \( M = 0 \) and a strain-dependent permeability \( M = 4.3 \) in the case of a completely blocked aqueduct and no CSF production or absorption in the brain tissue. Both predictions exhibit a transparentcy-real pressure difference of ca. 400 Pa and a ventricle wall displacement of around 1 cm, which already lies well within physiological ranges despite the simple geometry. Pressure and displacement are a bit lower for the strain-dependent permeability than for \( M = 0 \). Whereas the pressure decreases with \( \frac{1}{r} \) for \( M = 0 \), the strain-dependence results in an almost linear pressure decrease, which can be ascribed to the spatial strain distribution: The tissue near the skull is compressed, resulting in a lower permeability and hence a steeper pressure gradient. Near the ventricles the tangential expansion produces a volume dilation which results in a higher permeability and thus a lower pressure gradient. The dilation also accounts for the increased fluid content \( \zeta \) near the ventricles, a symptom often observed in contrasted CT scans. The fluid velocity decreases with the square of the radius in both cases since no fluid vanishes in the parenchyma. In comparison with \( M = 0 \), the displacement for \( M = 4.3 \) has a more sigmoidal shape with the steepest gradient at the skull. The ventricle wall displacement is a bit lower with a ventricular aspect ratio of \( \frac{c}{d} \approx 2.7 \).
Figure 6.1: CSF pressure $p$, CSF velocity, fluid increment $\zeta$, radial displacement $u$, radial effective stress $\sigma_{rr}$, and tangential effective stress $\sigma_{\theta\varphi} = \sigma_{\varphi\varphi}$ throughout the brain parenchyma for $M = 0$ (solid line) and $M = 4.3$ (dotted line) in the case of a completely obstructed aqueduct. The displacement is plotted versus the undeformed radius $r$, while all other graphs use the deformed radius.

The sigmoidal shape of the displacement can be associated with an interesting feature of strain-dependent permeability. While the linear model by Smillie et al. [24] was always uniquely solvable, solutions with nonlinear permeability cease to exist for some cases: As explained in the previous chapter, the integration constants of the analytic solution (5.1)-(5.2) can (for $\alpha = 1$) be found by determining the zero of a monotonically increasing function $g$. However, in appendix A.1 this function is shown to have a lower limit (A.5) which—if positive—prevents a zero and hence a solution from existing. The limit value increases monotonically with $ME = M \frac{1-2\nu}{2(1-\nu)} \frac{\alpha Q_\mu \mu}{G^2 \pi \kappa_0}$, implying that there is e.g. an upper limit for $M$ or a lower limit for the permeability $k_0$, beyond which there are no solutions.

In appendix A.4, this phenomenon is briefly examined in a simple rectangular geometry, i.e. a CSF flux $q$ per unit area is assumed to penetrate a rectangular layer of brain tissue with thickness $c$, forced by a pressure gradient and causing a displacement. Also a CSF source $s$ within the brain tissue is included. It is shown that the flux $q$ is limited, no matter how large the pressure difference across the brain layer is:

$$q < \frac{(2G + \lambda)k_0}{M\mu c} - \frac{cs}{2} \tag{6.1}$$

Obviously, the maximum flux decreases with increasing $M$ and decreasing $k_0$. Also, it is reduced by a parenchyma source $s$. Appendix A.4 shows that if we try to force through a larger flux, the material becomes compressed so densely at the skull that its permeability decreases to zero and the brain tissue choke off. In the spherical geometry, this choking effect at the skull is reflected by the limit (A.5) being positive.
Figure 6.2: Simulation results for a completely blocked aqueduct and three different initial permeabilities $k_0 = 0.6 \times 10^{-14} \text{ m}^2$ (dashed line), $1.4 \times 10^{-14} \text{ m}^2$ (solid line), $2.1 \times 10^{-14} \text{ m}^2$ (dotted line).

Basically, the phenomenon can be observed for all kinds of strain-permeability relations as long as the permeability is allowed to decrease to zero. Experiments show that for our model the critical value for $k_0$, where—all other parameters unchanged—a solution ceases to exist, is around $5 \times 10^{-15} \text{ m}^2$ which lies in the range of values used in the literature [10]. This suggests that a choking effect might possibly appear at a fatal state of hydrocephalus. During our simulations, however, we have to ensure that we remain within the parameter ranges where a solution exists. (Note that if the aqueduct is still partly open, the integration constants in (5.1)-(5.2) are found by determining the zero of a different function $h$. This zero does always exist, signifying that fluid can always escape through the aqueduct so that there is always a solution, see appendix A.1.)

To complicate matters even further, the model behaviour is different for non-unit $\alpha$, also examined for a rectangular geometry in appendix A.4. Restricting ourselves to the case of no parenchyma production and absorption ($s = 0$), the flux $q$ which can be forced through the tissue is unlimited for $\alpha > 1$, hence there is always a unique solution to our model. However, if $\alpha < 1$, there is a maximum flux $q_{max} = \frac{\left(2G+\lambda\right)k_0}{\mu c} (1-\alpha)^{\frac{m \alpha}{\lambda}}$. If less CSF is produced and forced through the parenchyma, there are two solutions. The one which corresponds to the solution for $\alpha = 1$ is stable, the other one unstable (see appendix A.4).

Near the critical permeability the pressure rise in the ventricles is very sensitive to $k_0$, whereas the displacement does not change too much. Permeability values close to the critical one quickly result in exorbitant pressures. Figure 6.2 shows the simulation results for three different $k_0$; the lowest $k_0$ already causes a strong tissue compression (visible as a decreased fluid content) and a steep pressure gradient near the skull,
characteristic for a beginning choking effect. Different permeabilities of white and grey matter are discussed later in connection with normal pressure hydrocephalus. Finally, Figure 6.3 shows the development of hydrocephalus after a sudden aqueduct blockage to happen at a time scale of about one day.

6.1.2 Source or sink in the parenchyma, NPH and BIH

Normal pressure hydrocephalus (NPH) and benign intracranial hypertension (BIH) are two forms of hydrocephalus which have rarely been modelled effectively on a mechanical basis.\footnote{Levine proposes a model for BIH\cite{12} and NPH\cite{13}, but the latter fails to reproduce the symptoms.} While NPH is a condition where the ventricles are highly enlarged but the intraventricular pressure is normal, BIH can be regarded as the counterpart in that the intracranial pressure is strongly elevated but the ventricles are not dilated—in fact they often seem diminished and may be barely visible. Both conditions usually remain despite an open aqueduct.

Taking up Levine’s idea of CSF absorption in the brain tissue we shall propose the idea of a mechanism for NPH development relying on a CSF sink in the parenchyma: The lack of a pressure difference between ventricles and subarachnoid space suggests that both regions are communicating via an open aqueduct (compare Chapter 4). If now a parenchyma absorption is triggered by an injury or a tumor, CSF will flow from the ventricles into the tissue, causing an outwards displacement of the ventricle wall which would be observed as NPH.

The elevated pressure of BIH on the other hand will be modelled by a CSF overproduction in the parenchyma. Although it is well accepted that the main CSF production takes place within the ventricles, physicians believe that up to 25\%\cite{19} or even 50\% are produced in the surrounding tissue. The resistance to CSF absorption at the skull results in a pressure rise proportional to the overproduction, and the CSF flow from the brain tissue into the ventricles accounts for the slightly smaller ventricles. Additionally, this ventricle compression features a self-amplification: As the ventricle size decreases, the adjacent tissue is compressed, resulting in a smaller permeability and hence a further inward displacement.
Figure 6.4: Simulation results for a constant CSF sink of \( s = -1.4 \times 10^{-6} \text{s}^{-1} \) throughout the parenchyma and a grey matter permeability of \( k_0 = 1.4 \times 10^{-14} \text{m}^2 \) (dashed line), \( 1.4 \times 10^{-15} \text{m}^2 \) (solid line), and \( 1.4 \times 10^{-16} \text{m}^2 \) (dotted line).

Though both mechanisms work in principle, the predicted ventricle wall displacement is too small for NPH and BIH if the grey matter on the outside of the brain is not assumed to be less permeable than white matter. While some fluid enters or leaves the parenchyma at the ventricle wall, a much greater amount flows across the pia mater, the membrane surrounding the brain. This latter flow causes a displacement, partly undoing the displacement at the ventricle wall which is small anyway. By decreasing the permeability in a thin region near the skull the bulk of the CSF exchange will take place at the ventricles, hence having a more obvious effect. Furthermore, the reverse movement near the skull will be restricted to a thin region, which can only account for a minor compensation.

Figure 6.4 shows the final NPH steady state for a constant CSF sink \( s = -1.4 \times 10^{-6} \text{s}^{-1} \) in the parenchyma, i.e. altogether approximately the entire amount of CSF produced inside the ventricles is absorbed in the brain tissue. The experiment is conducted for three different permeabilities of grey matter: The same permeability as white matter (dashed line), the low permeability value used by Kaczmarek et al. [10] (dotted line), and a value in between (dashed line). In all three cases the pressure is the same in subarachnoid and ventricular space and achieves a minimum in the parenchyma. The ventricle wall is displaced most for the lowest grey matter permeability. The fluid content near the ventricle wall is elevated, agreeing well with the location of oedema in real hydrocephalus.

BIH is examined in Figure 6.5. Whereas the dotted line corresponds to no CSF production inside the brain tissue, the solid line represents the parenchyma producing as much as the ventricles, and the dashed line corresponds to the parenchyma producing half the amount. The ventricular pressure can be seen to rise up to 400 Pa.
relative to the state with no parenchyma production. While the fluid content inside the brain tissue increases, the areas near the skull and the ventricles are drained. It would be interesting to see whether this pattern can be observed on CT scans.

Until now there is no standard treatment for BIH. Draining the overproduced CSF via a ventricular shunt will relieve the pressure build-up but will leave the brain tissue distorted. If the hypothesis of a source in the parenchyma proves realistic, a shunt inserted into the brain tissue might be advantageous to remove the fluid excess where it is produced.

Another proposal for the development of NPH consists in an interruption of the regular CSF production in the parenchyma. Whereas in the normal state the ventricles would be slightly compressed (like in our BIH simulation), after the termination of parenchyma production they would return to a stress free state, in which they appear much larger. However, it remains unclear in what way the brain tissue is then negatively affected to account for the mental symptoms.

While CSF secretion in the brain tissue is likely to be pressure independent as the production inside the ventricles, an absorption in the parenchyma seems to be more realistic if pressure dependent. In his paper [13] Levine included such a mechanism. Basically, the sink $-s$ in (3.23) can be replaced by $\kappa(p - p_b)$, where $p_b$ is the blood pressure and $\kappa$ an absorption coefficient. A length scale $D$ of how deeply a fluid can penetrate the porous medium is given by $D = \sqrt{\frac{\kappa_0}{\mu \kappa}}$. Levine tried to model NPH as a combination of an obstructed aqueduct with an efficient ($D \approx 3$ mm) CSF absorption in the parenchyma. However, his model shows nearly no ventricle wall displacement and needs a blockage of the aqueduct, which is often not the case. An alternative suggestion would be to combine an impaired absorption near the skull with an open
Figure 6.6: Simulation results for a pressure dependent CSF absorption in the parenchyma \((D = 6\, \text{cm})\) and an impaired subarachnoid absorption \((R = 8.5 \times 10^{15} \, \text{m}^{-3})\). The same permeabilities of grey matter were used as in Figure 6.4.

aqueduct and a non-efficient parenchyma absorption (e.g. \(D \approx 6\, \text{cm}\)), which could be triggered by the high intracranial pressure after the decrease in subarachnoid absorption. The results are qualitatively the same as for a constant sink (compare Figures 6.4 and 6.6). The resistance to subarachnoid absorption has been increased by the factor 100 for the simulation in Figure 6.6. Subarachnoid and ventricular pressure lie around 1100 Pa, the same pressure as for no parenchyma absorption and normal subarachnoid resistance.

A precise measurement of the difference between white and grey matter permeability would be of great help to verify the previous suggestions. Even more important to verify or reject the modelling ideas would be a measurement of the pressure throughout the parenchyma, which has not been attempted yet. Especially a CSF source or sink in the brain tissue could be identified as a pressure maximum or minimum there.

### 6.1.3 Possible vascular effects, compliance

Following the ideas of Levine [13] the vascular system can be integrated into the model by changing the Biot-Willis parameter \(\alpha\): Using the bulk modulus \(K = \lambda + \frac{2G}{3}\) and Skempton’s coefficient \(\beta\), the increment of fluid content is given by

\[
\zeta = \alpha \epsilon + \frac{(1 - \alpha \beta) \alpha}{K \beta} p.
\]  

(6.2)

Obviously, for constant pressure \(p\) a dilation change \(\Delta \epsilon\) results in a fluid content change \(\Delta \zeta = \alpha \Delta \epsilon\) so that \(\alpha\) can be interpreted as the ratio of fluid content change to total volume change. If now a volume change \(\Delta \epsilon\) of the brain is not only accommodated by a change \(\Delta \zeta\) of CSF content but also a similar change \(\Delta \chi\) of blood content
in the brain vessels, \( \alpha = \frac{\Delta \rho}{\Delta c + \Delta \rho} \) is less than 1. For \( \alpha = 1 \) any volume change has no effect on the blood content but only on the CSF content of the brain. According to Levine, an accommodation of brain volume change by interstitial fluid and blood proportional to their volume portion corresponds to \( \alpha = 0.83 \).

In general, a decrease in \( \alpha \) below one has the effect of an overall increase in CSF content (compare Fig. 6.7 for the case of a completely blocked aqueduct) due to the pressure term in (6.2). Furthermore, the ventricle wall displacement is increased due to boundary condition (3.9): The ventricle pressure now acts like a force which has to be balanced by the solid matrix, whereas before it was completely balanced by the interstitial pressure. The pressure distribution, however, can be seen not to change much. This provides a further idea about the cause of NPH: If \( \alpha \) decreases while the aqueduct is open and the pressure is normal throughout the brain, then the ventricle walls are pushed outwards, resulting in a condition similar to NPH (Fig. 6.8). Radial and tangential stress are similar to the typical stress distribution within the wall of a high pressure tank.

A reduction in \( \alpha \) could be associated with an increase in the ratio of blood volume to interstitial volume (e.g. if the brain porosity decreases due to calcification at a high age or if the blood perfusion increases due to high blood pressure as found in [3]). This implies that concepts of treatment other than shunting would e.g. include methods to increase the interstitial fluid content. The idea of NPH being caused by a decrease in \( \alpha \) does not rely on an excess of CSF production or hampered absorption, but rather on a change of the brain properties, in particular of the compliance. The compliance \( C \) is the CSF volume pressure ratio \( \frac{\partial V}{\partial p} \) which forms the basis of the earliest hydrocephalus models. Its interpretation in the light of consolidation theory could refresh the interest.
Figure 6.8: Simulation results for an open aqueduct and $\alpha = 1$ (solid line), $\alpha = 0.8$ (dashed line), and $\alpha = 0.6$ (dotted line), representing a possible form of NPH.

In this parameter. In appendix A.5 the compliance is computed for our model to be

$$C = \frac{4}{3} \pi (c^3 - a^3) \frac{1 - \alpha}{K \alpha}$$

(6.3)

for physiological pressure ranges. This agrees well with the fact that $C$ is roughly pressure independent within a certain range of pressures [26].

### 6.1.4 Shunt treatment

The treatment of choice for hydrocephalus is the insertion of a shunt into the dilated ventricles, which drains the fluid build-up into the peritoneal area. To avoid overdrainage or backflow, the shunts incorporate a valve. As long as the ventricle pressure $p_v$ lies above blood pressure $p_b$ the valve is open, allowing a flow $S$ whose magnitude depends on the pressure difference $(p_v - p_b)$. Smillie et al. [24] proposed the relation

$$S(p_v) = \begin{cases} S_1(p_v - p_b) & \text{for } (p_v - p_b) > 0 \\ 0 & \text{for } (p_v - p_b) \leq 0 \end{cases}$$

(6.4)

for simple ball on a spring devices and for shunts with silicon diaphragm valves

$$S(p_v) = \begin{cases} S_2(p_v - p_b) + S_3(p_v - p_b)^2 & \text{for } (p_v - p_b) > 0 \\ 0 & \text{for } (p_v - p_b) \leq 0 \end{cases}$$

(6.5)

where for conventional shunts $S_1 = 1.25 \times 10^{-10} \text{m}^5/\text{Ns}$, $S_2 = 3.03 \times 10^{-11} \text{m}^5/\text{Ns}$, and $S_3 = 3.77 \times 10^{-14} \text{m}^7/\text{N}^2\text{s}$. For a blocked aqueduct, both shunts establish a stable steady state where the ventricular wall velocity $\frac{dv}{dt}$ is zero (compare the phase plot in Fig. 6.9). The linear shunt almost recovers the original brain shape completely, whereas the silicon diaphragm valve leaves a ventricle wall displacement of 3 to 4 mm. There is virtually no difference in the final state for a strain-dependent ($M > 0$) and
-independent \((M = 0)\) permeability since the strain nearly reduces to zero anyway. However, the time scale of recovery is faster for \(M > 0\) as it starts off with a smaller initial displacement (Fig. 6.9). For our model with \(M = 4.3\) shunting takes effect after about one hour for the ball on spring valve and one hour later for the silicon diaphragm.

### 6.1.5 Infantile hydrocephalus

In infants the cranial bones are not yet connected rigidly, but only held together by a fibrous material, the sutures. This allows the brain to grow, pushing the skull outside, until the brain reaches full size and the cranial bones are fused. As a consequence, hydrocephalus apparently pushes an infantile skull outside so that hydrocephalic children appear to have a strongly dilated head. Since there is very little data about the geometry and the mechanical properties of an infant’s skull, we shall only introduce a crude model of the cranium, which nevertheless captures the main aspects. Since the thickness of skull and scalp is small compared to the cranial radius, we may model both as one thin membrane across whose breadth all stresses are equally distributed.

Appendix A.6 shows that then the stress \(\sigma_{rr}\) exerted on the membrane from the inside (by brain and CSF) must equal \(-E_s(1 + \nu_s) \frac{2u(r=c)}{cr}\), where \(\nu_s\) is the Poisson’s ratio of the sutures and \(E_s\) their Young’s modulus times their thickness. Hence, boundary condition (3.24) can be replaced by

\[-E_s(1 + \nu_s) \frac{2u}{r^2} = (\lambda + 2\mu) \frac{\partial u}{\partial r} + \lambda \frac{2u}{r} - \alpha_p s \quad \text{at} \ r = c \quad (6.6)\]

with the nondimensional form

\[
\frac{E_s}{cG}(1 + \nu_s)u = \frac{\dot{\alpha}}{2}p_s - \frac{1 - \nu}{1 - \nu} \frac{\partial u}{\partial r} - \frac{2\nu}{1 - 2\nu}u \quad \text{at} \ r = 1. \quad (6.7)
\]

Margulies et al. [15] determined the Young’s modulus of infantile sutures as 171.5 MPa. Together with a thickness of 2 mm this would yield \(E_s = 343\) kN/m so that the nondimensional coefficient on the left hand side is \(\frac{E_s}{cG} \sim 16 \times 10^3\). This implies practically
Figure 6.10: Simulation results for infantile hydrocephalus with head enlargement for a blocked aqueduct (dotted line) and for an impaired subarachnoid absorption (dash-dot line, \( R = 1.7 \times 10^{14} \text{m}^{-3} \)). The solid and the dashed line represent the same simulations, only head enlargement is prevented, e.g. by compressive head wrapping.

\( u = 0 \) at the skull, hence no skull displacement. Obviously, a head enlargement must therefore be associated with stress induced growth\(^2\) at the sutures and cannot develop suddenly. This might explain why some cases of infantile hydrocephalus remain unnoticed until adolescence.

To obtain a more adequate boundary condition we note that the stress within the membrane is proportional to the pressure against it (see appendix A.6). Hence, instead of assuming that skull growth is induced by an excess stress within the membrane, we may just as well model it to be induced by the excess radial pressure of brain and CSF against the skull. In a healthy person, the skull only has to bear a subarachnoid pressure of \( p_n = p_b + \mu R Q_p \). Hence, the suture growth provoked by hydrocephalus stops as soon as the radial stress of brain and CSF against the skull reaches this value, i.e. when

\[
(\lambda + 2G) \frac{\partial u}{\partial r} + \lambda \frac{2u}{r} - \alpha p_s = -p_n \quad \text{at } r = c \tag{6.8}
\]

or dimensionless

\[
2(1 - \nu) \frac{\partial u}{1 - 2\nu} + \frac{4\nu}{1 - 2\nu} u - \dot{\alpha} p = -\frac{p_n}{G} \quad \text{at } r = 1. \tag{6.9}
\]

Figure 6.10 shows the head enlargement for the two most frequent cases of infantile hydrocephalus, an aqueductal stenosis (blocked aqueduct) and an impaired subarachnoid CSF absorption. The skull displacement of some millimeters to centimeters

\(^2\)Hakim et al.\cite{9} propose that the head enlargement is balanced by the tangential stresses in dura mater and scalp. However, this seems unlikely considering that the sutures alone are strong enough to prevent any sudden head enlargement.
seems realistic. In both cases we can see high stresses in the solid brain matrix, all tensile in nature and stronger than for adults. Consequently we may infer that the brain is more affected in infants. Also, a treatment like compressive head wrapping would decrease stresses and strains (compare Fig. 6.10) and thus might provide a bit of relief if a shunt insertion is not feasible.

### 6.2 Cylindrically symmetric simulations

#### 6.2.1 Ventricle shape

The consensus is that quantitatively accurate predictions for hydrocephalus require precise geometrical modelling of ventricles and brain. However, here we are more concerned with the qualitative effect of different ventricle shapes, for example on the fluid distribution, on the location of oedema, on the intracranial pressure, or on the ventricle distortion. For this purpose we shall conduct experiments on a mixture of four different ventricle shapes, displayed in Figure 6.11 and given mnemonic names. The ellipsoid serves to examine differences between ventricle wall areas of different convexity, the “peanut” shape features a slight constriction at its centre, the cross-like shape (remember that this description only refers to the cross-section; the three-dimensional ventricle shape rather resembles two hollow cones) will reveal differences between strongly convex and concave areas, and finally the more moderate, bone-like shape is reminiscent of ventricle images on CT scans.

We shall first examine the case of an obstructed aqueduct, in which a CSF flow through the parenchyma causes the tissue distortion. As can be seen in Figure 6.12, a remarkable feature of the ventricle dilation is that the ventricle walls seem to be shifted outwards almost uniformly; there seem to be no regions which bulge out significantly more than others, irrespective of the used ventricle geometry. In different words, as a good first approximation the distorted ventricle shape can be obtained by displacing each point on the ventricle wall by the same amount normal to the surface. This fact agrees with observation and has led to phenomenological models [21], where the normal velocity of the ventricle wall during evolution or treatment of hydrocephalus is assumed to be constant all over the ventricle walls.
Figure 6.12: Distribution of pressure (upper row), fluid velocity (middle), and fluid content (lower row) for a blocked aqueduct. The distribution is given in the deformed brain configuration; the inner line in the first row shows the original ventricle shape. In these and later contour plots light areas correspond to higher values.

As expected, the pressure decreases almost linearly from the high ventricular to the lower subarachnoid pressure, just like in the one-dimensional simulations. However, especially the “cross”- and “bone”-shape reveal that in highly concave ventricle wall regions, where brain tissue is literally surrounded by fluid-filled cavities, the pressure gradient approaches zero; these regions nearly have a constant pressure close to the ventricular pressure. The ventricular pressure itself is of the same magnitude as in the one-dimensional case (see Tab. 6.1). The relatively small differences between the ventricle shapes are related to the different minimum distances between ventricles and subarachnoid space and to the overall change in permeability. Even if the ventricle size is scaled to an initial volume of 25 ml, the pressure only changes a bit (Tab. 6.2).

<table>
<thead>
<tr>
<th></th>
<th>“ellipsoid”</th>
<th>“peanut”</th>
<th>“cross”</th>
<th>“bone”</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_0$</td>
<td>37.7 ml</td>
<td>91.8 ml</td>
<td>255.5 ml</td>
<td>59.3 ml</td>
</tr>
<tr>
<td>$V$</td>
<td>99.3 ml</td>
<td>197.1 ml</td>
<td>428.5 ml</td>
<td>139.2 ml</td>
</tr>
<tr>
<td>$p_e$</td>
<td>1479 Pa</td>
<td>1439 Pa</td>
<td>1363 Pa</td>
<td>1447 Pa</td>
</tr>
</tbody>
</table>

Table 6.1: Undeformed and deformed ventricle volume, and ventricular pressure for a blocked aqueduct.

The fluid content is increased in regions of highly convex ventricle walls, in particular for the “cross”- and “bone”-shape. This is a manifestation of the strong volume dilation in these areas: As the ventricles enlarge, the tissue near the convex ventricle walls is stretched tangentially so much that the minor radial compression is overcompensated. This increases the porous space and thus the fluid content. More concave
regions on the other hand get squeezed with a decreased fluid content, e.g. the constriction in the “peanut”-, “cross”-, and “bone”-shape. This characteristic distribution of fluid content corresponds very well to the location of oedema in hydrocephalic brains, which form especially at the strongly convex so-called ventricular horns.

Also the fluid velocity can be seen to be the highest near the protuberances, owing partly to the stronger dilation and hence higher permeability in those regions and partly to the shorter distance to the subarachnoid space and thus steeper pressure gradient.

In order to get an impression of whether a changed compliance or a CSF source or sink in the brain tissue provide adequate explanations of NPH and BIH, we shall conduct the same experiments which we did in one dimension for the different cylindrically symmetric geometries. The resulting two-dimensional graphs can then intuitively be compared to CT scans.

The results for CSF absorption and production in the brain tissue are shown in Figures 6.13 and 6.14. The pressure within the parenchyma is lower, respectively higher than in the ventricles and subarachnoid space. Whereas the fluid content is increased near convex ventricle walls for NPH, the opposite happens for the BIH simulation: The fluid content decreases in these regions. In particular the BIH simulation for the “bone”-geometry results in almost slit ventricles, matching very well

<table>
<thead>
<tr>
<th></th>
<th>“ellipsoid”</th>
<th>“peanut”</th>
<th>“cross”</th>
<th>“bone”</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V$</td>
<td>71.0 ml</td>
<td>71.5 ml</td>
<td>69.8 ml</td>
<td>70.7 ml</td>
</tr>
<tr>
<td>$p_v$</td>
<td>1498 Pa</td>
<td>1504 Pa</td>
<td>1490 Pa</td>
<td>1489 Pa</td>
</tr>
</tbody>
</table>

Table 6.2: Deformed ventricle volume and ventricular pressure for a blocked aqueduct, where the ventricle geometries are all scaled to have an initial volume of 25 ml.
the description of barely visible ventricles.

The simulation result for a changed brain compliance ($\alpha < 1$) with an open aqueduct, which might be connected with NPH, is illustrated in Figure 6.15. There is a qualitative difference in the ventricle distortion to the situation of a blocked aqueduct, but $\alpha = 1$. Regions of concave ventricle walls bulge out significantly more than others; the ventricles tend towards a rather spherical shape. This phenomenon becomes clear remembering that the ventricular pressure now acts as a mere force on the ventricle wall. Areas further away from the skull hence appear softer, because there is more material to compress. The fluid content is still slightly increased in convex and decreased in concave regions, but much less pronounced than in the blocked aqueduct case. If both mechanisms—a parenchyma sink and a raised compliance—can account for NPH, then the different ventricle shape and the more evenly distributed fluid content may help to distinguish the two different types of hydrocephalus.

The ventricle volume almost changes linearly with $\alpha$; if all shapes start off at the same undeformed volume, the deformed ventricle volume is nearly independent of the ventricle shape (Tab. 6.3 and 6.4).

<table>
<thead>
<tr>
<th>$\alpha$</th>
<th>&quot;ellipsoid&quot;</th>
<th>&quot;peanut&quot;</th>
<th>&quot;cross&quot;</th>
<th>&quot;bone&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9</td>
<td>58.6 ml</td>
<td>135.3 ml</td>
<td>363.0 ml</td>
<td>91.2 ml</td>
</tr>
<tr>
<td>0.8</td>
<td>84.9 ml</td>
<td>189.1 ml</td>
<td>487.0 ml</td>
<td>129.5 ml</td>
</tr>
<tr>
<td>0.7</td>
<td>116.8 ml</td>
<td>254.3 ml</td>
<td>628.4 ml</td>
<td>174.5 ml</td>
</tr>
</tbody>
</table>

Table 6.3: Deformed ventricle volume for different $\alpha$.

The time scales of development and of shunt treatment basically only depend on the initial and the final ventricle volume. This is plausible, since e.g. equation (3.10) shows that the initial slope $\dot{V}$ of ventricle volume per time is $Q_p$ for a sudden blockage.
Figure 6.15: Distribution of fluid content for an open aqueduct and $\alpha = 0.7$. The inner line represents the undeformed ventricle shape.

Figure 6.16: Ventricle volume versus time for a sudden blockage of the aqueduct (dashed line: “ellipsoid”; dotted line: “peanut”; dash-dot line: “cross”; solid line: “bone”; solid line with dots: spherical ventricle). The right graph represents the time evolution if all shapes are scaled to an undeformed volume of 25 ml.

of the aqueduct, irrespective of the ventricle shape. Figures 6.16 and 6.17 show the time evolution for scaled and not scaled ventricle sizes.

<table>
<thead>
<tr>
<th>$\alpha$</th>
<th>“ellipsoid”</th>
<th>“peanut”</th>
<th>“cross”</th>
<th>“bone”</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9</td>
<td>39.3 ml</td>
<td>39.1 ml</td>
<td>39.2 ml</td>
<td>40.0 ml</td>
</tr>
<tr>
<td>0.8</td>
<td>57.5 ml</td>
<td>57.0 ml</td>
<td>56.8 ml</td>
<td>58.1 ml</td>
</tr>
<tr>
<td>0.7</td>
<td>79.9 ml</td>
<td>79.1 ml</td>
<td>78.2 ml</td>
<td>79.7 ml</td>
</tr>
</tbody>
</table>

Table 6.4: Deformed ventricle volume for different $\alpha$, where the ventricle geometry is scaled so that the initial volume is 25 ml.

6.2.2 Loose connection to the skull

So far we have always assumed the brain displacement at the skull to be zero, justified by the strands connecting pia mater and arachnoid membrane. If these strands are long enough to allow for movement of the brain or if they are torn, the brain might be displaced tangentially to the skull (a radial outward movement is still impossible). Hence, we replace the skull boundary condition of zero tangential displacement $v = 0$ by zero shear stress $\sigma_{\tau \theta} = 0$; i.e.

$$0 = \sigma_{\tau \theta} = G \left( \frac{\partial v}{\partial r} + \frac{1}{r} \frac{\partial u}{\partial \theta} - \frac{v}{r} \right)$$  \hspace{1cm} (6.10)

The shear stress might be non-zero due to friction so that we might overestimate the tangential displacement.
or dimensionless
\[ 0 = \frac{\partial v}{\partial r} + \frac{1}{r} \frac{\partial u}{\partial \theta} - \frac{v}{r}. \]  

(6.11)

However, the numerical simulation reveals the insignificance of that change. Table 6.5 shows the maximum tangential displacement at the skull to be half a millimeter and less in the steady state, even for quite irregular ventricle shapes. Furthermore, there is no macroscopic difference in final ventricle shape and pressure distribution so that an approximation of zero displacement at the skull proves to be adequate.

<table>
<thead>
<tr>
<th>“ellipsoid”</th>
<th>“peanut”</th>
<th>“cross”</th>
<th>“bone”</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.37 mm</td>
<td>0.38 mm</td>
<td>0.48 mm</td>
<td>0.52 mm</td>
</tr>
</tbody>
</table>

Table 6.5: Tangential displacement at the skull.

### 6.2.3 Hydrostatic pressure

Comparing the simulated pressure difference between ventricles and subarachnoid space for a blocked aqueduct with the pressure difference between different locations of the brain due to a different water column at these points, we notice that the latter, “hydrostatic” differences lie around 1 to 2 kPa and are thus higher than the pressure differences of some hundred Pa we have been looking at until now. Including hydrostatic pressure into our model might therefore show a major effect. However, an introduction of hydrostatic pressure must inevitably be accompanied by the introduction of body forces into the stress equilibrium (since hydrostatic pressure is just a manifestation of these), and appendix A.7 shows that for \( \alpha = 1 \) both extensions compensate each other. Hence, the model solution does not change except for a superimposed hydrostatic pressure component.

For \( \alpha < 1 \) the behaviour is different, though (compare appendix A.7): The effect of the pressure is restricted by \( \alpha \) so that the hydrostatic component can no longer bear the full amount of body forces, resulting in an overall downward displacement of brain and ventricles. Furthermore, simulations show that the volume dilation above
Figure 6.18: Distorted ventricle shapes for open (dotted line) and blocked aqueduct (solid line), where the simulation included hydrostatic pressure. The dashed line represents the vertical z-axis (which is also the axis of symmetry). The upper row is for $\alpha = 0.9$, the lower row for $\alpha = 0.8$. The original shapes of a sphere, the “peanut”, a disk-like shape, and the “cross” can be seen to be distorted downwards.

the ventricles is quite high, causing an increase of fluid content and of fluid flow (due to the higher permeability) in that region.

Figure 6.18 shows the displacement for $\alpha = 0.9$ and $\alpha = 0.8$ with different initial ventricle shapes. It is quite obvious that CT scans of the ventricles will differ for different postures of the patient. There might also be implications for the positioning of the head during surgical procedures and for the most advantageous location of a shunt.

6.2.4 Damage measures

The mental symptoms of hydrocephalus can only be entirely understood if we are able to localise precisely the damage in the brain. Unfortunately, the appropriate measures of tissue damage are still unknown. In the following we shall briefly compare several damage indicators, some of which are frequently used in the literature.

Three material failure theories are most commonly used in engineering science: Rankine theory assumes that material failure is caused by the maximum principal stress (which is the maximum eigenvalue of the stress tensor $\sigma$). Since tensile stresses within the brain are presumably borne by nerve fibres along the direction of the stresses, an application of this theory to hydrocephalus would hypothesise that dysfunctions are evoked by abnormally stretched nerve axons. In Tresca theory the shear stress is responsible for material damage. This idea is used for hydrocephalus models by several authors ([3, 13, 24]), who associate shear stresses with demyelination of nerve axons. According to Mohr’s circle we obtain the maximum shear stress as half the difference between the maximum and minimum eigenvalue of $\sigma$. Finally, von
Mises-Hencky theory makes use of an energetically equivalent unidirectional stress
\[ \sigma_c = \frac{1}{\sqrt{2}} \sqrt{(\sigma_1 - \sigma_2)^2 + (\sigma_1 - \sigma_3)^2 + (\sigma_2 - \sigma_3)^2}, \]
where \( \sigma_1, \sigma_2, \) and \( \sigma_3 \) are the eigenvalues of \( \sigma. \)

It also seems plausible that only the shear stresses \( \sigma_{r\theta} \) and \( \sigma_{r\phi} \) might cause major
damage: Although we assume isotropy for the poroelastic brain properties, we may
suspect anisotropy concerning tissue damage; since most nerve axons follow a more
or less radial direction, tangential shear stresses could cut them off.

A further, often proposed index of tissue damage ([13, 24]) is the increment \( \zeta \)
of fluid content (6.2), indicating a tissue dilation and visible in form of oedema in
the white matter. Interstitial fluid pressure on the other hand is less likely to be of
great relevance, considering the strong symptoms of NPH despite normal pressure.
Nevertheless we shall include it into our comparison.

As can be seen in Figure 6.19, all introduced indicators predict tissue damage to
be concentrated in the periventricular white matter. While the interstitial pressure
appears to affect the parenchyma uniformly around the ventricle walls, all other
measures show a more differentiated picture. Whereas Rankine, Tresca, and von
Mises-Hencky theory only differ negligibly and all predict more damage in regions
of concave ventricle walls, the fluid content is increased most in regions of highly
convex ventricle walls. A fourth, qualitatively different result is obtained from the
assumption of the tangential shear stress causing damage: Here those regions are
most affected, where the ventricle walls are almost parallel to the radial nerve fibres.

An autopsy of hydrocephalic brains could be used to obtain information about the
qualitative damage distribution around the ventricles. This information could then
be used to determine which of the suggested damage indicators is most appropriate.
6.3 Three-dimensional simulations

6.3.1 Two lateral ventricles

For our three-dimensional simulations we are no longer limited in the choice of the ventricle and brain geometry. However, because of the long computation time we shall not implement too realistic shapes, but rather restrict ourselves to incorporate some characteristic features of the brain anatomy which we were not able to reproduce before.

The first extension concerns the arrangement of ventricles. Instead of one single representative ventricle we shall approximate both lateral ventricles by two bent ellipsoids (Fig. 6.20). The second geometrical improvement consists in representing the brain as a sphere whose bottom is cut off. The bottom plane forms the interface between brain and subjacent soft tissue; the brain is not attached to the skull in that region. Therefore we shall conduct two different simulations, first assuming that the brain bottom is fixed, and then letting it move as freely as the ventricle walls.

For the fixed brain bottom and a blocked aqueduct the ventricles appear to enlarge almost uniformly at all points, just like for the cylindrically symmetric geometries. However, the displacement towards each other is a little bit smaller, associated with the lack of a pressure gradient between both ventricles. The ventricular pressure of 1426 Pa is similar to the results of the one- and two-dimensional simulations; the ventricular volume almost doubles from 76 to 129 ml.

For a loose lower brain surface the tissue is generally more displaced downwards, stretching the ventricles vertically. The displacement of the brain bottom lies around 1.7 cm. Again, the ventricle volume almost doubles to 133 ml in the final configuration. The ventricular pressure of 1345 Pa is quite low; due to the free movement of the brain bottom the tissue can be stretched more and acquires a higher permeability which in turn results in a lower pressure. Of course, in reality the brain bottom is neither
Figure 6.21: Distribution of pressure (upper row) and fluid content (lower row) for the geometry with two bent ventricles. The graphs are cross-sections at three different heights. In the lower row the ventricles are shaded to make the increased fluid content around them more evident. Light areas correspond to higher pressure or fluid content values.

Figure 6.22: The undeformed geometry and the deformed ventricles in case of a blocked aqueduct. The used mesh contains 12196 nodes and 66876 tetrahedrons.

fixed nor can it move freely; hence, the real behaviour is expected to lie in between both results. A more accurate analysis would also include the tissue below the brain.

Figure 6.21 shows the distribution of pressure and fluid content in transversal cross-sections through the brain. The resemblance to real CT-scans is impressive.

Our final simulation tries to imitate the C-shaped form of the lateral ventricles (Fig. 6.22). Furthermore, the brain is modelled as a flattened ellipsoid with the semi-axes taken from [14]. This time the initial ventricular volume of 25 ml is closer to the normal value of about 23 to 25 ml [19].

Again, the ventricular volume doubles to 50 ml as the ventricles enlarge almost uniformly. Also the ventricle pressure of 1440 Pa lies in the range found by the one- and two-dimensional simulations.
Figure 6.23: Distribution of pressure (upper row) and fluid content (lower row) for the geometry with C-shaped ventricles. The graphs are cross-sections along slightly tilted planes at three different heights. In the lower row the ventricles are shaded to make the increased fluid content around them more evident.
Chapter 7

Note on the use of more complex elastic constitutive laws

In our hydrocephalus model we made use of linear elasticity despite the fact that biological tissue is well-known for its nonlinear stress-strain relations, in particular for large deformations. Although it seems plausible that our results qualitatively and to a certain degree also quantitatively remain valid, there will soon be no way around modelling the brain matrix as a nonlinear material to obtain more accurate predictions.

The use of finite deformation theory and nonlinear elasticity has often been advocated [13, 18, 24, 28], but never fully been attempted (Miller et al. [25] seem to implement a linear finite deformation constitutive law in their numerical simulation, and Kaczmarek et al. [10] use a superposition of small linear steps\(^1\)).

One reason for this discrepancy certainly is the absence of appropriate poroelastic constitutive laws. This situation seems to be associated with indecision about what an appropriate form of constitutive law would be. There are viscoelastic and hyperelastic models for brain tissue [11, 16, 17, 25], but they view the brain as a material composed of only one constituent and cannot be applied in a biphasic approach. In the following we shall introduce a simple way to combine the familiar concepts of consolidation theory and hyperelasticity, including an example of a constitutive law.

Since the correct use of different stress and strain notions is essential to finite deformation theory, a short summary of the used terms and definitions is given in appendix A.8. There it is also shown how the Lagrange stress relates to the deformation gradient via a strain energy function for hyperelastic materials.

----

\(^1\)Their incremental loading technique actually seems unnecessary, since it only prevents the development of artificial stresses due to rigid rotations. In their cylindrical geometry, however, such rotations do not occur.
The idea of how to include finite deformation elasticity into consolidation theory is simply to replace the small strain approximation of the effective stress, \(2G\varepsilon_{ij} + \lambda\varepsilon_{kk} \delta_{ij}\), in the poroelastic constitutive relation (2.4) by any finite deformation constitutive law, e.g., a hyperelastic one. The new poroelastic law can then be expressed in the Lagrangean description, i.e., in terms of stresses and strains measured in the undeformed configuration, and the equilibrium of stresses in the Lagrangean description then yields a set of differential equations which can be solved for the deformation. The details are given in appendix A.9, as well as the verification that this approach is consistent with the thermodynamic interpretation of poroelasticity.

The advantages of this procedure lie in its simplicity and in the fact that existing forms of constitutive laws for the solid constituent can be used. Nevertheless, we do hope that soon complete poroelastic constitutive laws of the brain are found, e.g., by specifying the Gibbs free energy \(G\) for brain tissue (see appendix A.9).

As an example, we shall now implement linear finite deformation elasticity and afterwards Blatz-Ko hyperelasticity into the spherically symmetric hydrocephalus model.

### 7.1 Linear finite deformation elasticity

Although the linear finite deformation constitutive law in Kirchhoff stress \(S\) and Lagrange strain \(E\),

\[
S_{ij} = 2GE_{ij} + \lambda E_{kk} \delta_{ij},
\]

is as inappropriate as linearised elasticity and is only meant to remedy the disadvantage of linearised elasticity that rigid rotations produce stresses, we shall use it as an example of a finite deformation constitutive law. According to appendix A.9, the corresponding poroelastic law (with \(I\) being the identity matrix) is

\[
S = 2GE + \lambda \text{tr}(E) I - \alpha p \text{det}(F) F^{-1} F^{-\text{T}}.
\]

As usual, let the brain displacement be \(u(r)\). Let \(\mathbf{F}\) be the deformation gradient in Cartesian coordinates and \(Q = (\mathbf{e}_r, \mathbf{e}_\theta, \mathbf{e}_\phi)\) be the rotation matrix for the coordinate transform into spherical polar coordinates. Then the deformation gradient \(F\) in polar coordinates is given by

\[
F = Q^T \mathbf{F} Q = \begin{pmatrix}
1 + \frac{\partial u}{\partial r} & 0 & 0
0 & \frac{r + u(r)}{r} & 0
0 & 0 & \frac{r + u(r)}{r}
\end{pmatrix}.
\]
It is now trivial to obtain the Lagrange strain \( E = \frac{1}{2} (F^T F - I) \), the Kirchhoff stress \( S = 2GE + \lambda \text{tr}(E) I - \alpha p \det(F) F^{-1} F^{-T} \), and the Lagrange stress \( T = SF^T \). Finally, expressing the equilibrium (A.33) for spherical symmetry, 
\[
\frac{\partial T_{rr}}{\partial r} + \frac{1}{r} (2T_{rr} - T_{\theta \theta} - T_{\varphi \varphi}) = 0, \tag{7.4}
\]
yields a nonlinear differential equation in \( u \) and \( p \). Boundary conditions (3.24) and (3.26) become
\[
u = 0 \quad \text{at} \quad r = c, \tag{7.5}
\]
\[-p_v = \sigma_{rr} = \frac{1}{\det(F)} (FT)_{rr} = \frac{r^2}{(r + u(r))^2} T_{rr} \quad \text{at} \quad r = a. \tag{7.6}
\]
(Remember that the entries of \( T \) depend on \( u \) and \( p \)). This has to be solved together with the pressure ODE (3.23) and boundary conditions (3.25) and (3.27). However, since the use of finite deformation theory implies that the pressure should be computed in the deformed configuration (i.e. unlike before we do not have the option to compute the pressure in the undeformed state of the brain), we shall rewrite the pressure equations such that \( r \) is the undeformed radius: Each \( r \) must be replaced by \( r + u(r) \), and \( \frac{\partial}{\partial r} \) becomes \( \frac{1}{1+u(r)} \frac{\partial}{\partial r} =: \frac{1}{1+u(r)} \frac{\partial}{\partial r} \). Hence equations (3.23), (3.25), and (3.27) change to
\[
\frac{1}{(r+u(r))^2} \frac{1}{1+u(r)} \frac{\partial}{\partial r} \left[ \frac{(r+u(r))^2}{1+u(r)} k_0 e^{\frac{M_0}{\mu}} \frac{\partial p}{\partial r} \right] = -\mu \sigma, \tag{7.7}
\]
\[
\frac{p_v - p_b}{\mu R} = -\frac{\pi d^4}{128 \mu L} (p_v - p_b) - 4 \pi c^2 k_0 e^{\frac{M_0}{\mu(1+u(c)} \frac{\partial p}{\partial r} \quad \text{at} \quad r = c, \tag{7.8}
\]
\[
\frac{d}{dr} \left[ \frac{4}{3} \pi (a + u(a))^3 \right] = Q_p - \frac{\pi d^4}{128 \mu L} (p_v - p_b) - S(p_v) + 4 \pi (a + u(a))^2 \frac{k_0 e^{\frac{M_0}{\mu(1+u(a)}} \frac{\partial p}{\partial r}. \tag{7.9}
\]

### 7.2 Blatz-Ko hyperelasticity

As an example for a hyperelastic constitutive law we shall use a simplified Blatz-Ko relation. The Blatz-Ko model was originally developed for rubber foams and hence provides an adequate concept of modelling brain tissue, because the foam is also porous and the base material is—like nerve cells—incompressible. So far it has only rarely been used for biological tissue, though, e.g. to model tumor cells [1]. The simplified strain energy function is given by
\[
W = \frac{G}{2} \left[ \frac{J_2}{J_3} + 2\sqrt{J_3} - 5 \right], \tag{7.10}
\]
where \( G \) is the shear modulus of the material and \( J_2 \) and \( J_3 \) are strain invariants (compare appendix A.8). Hence, the poroelastic Lagrange stress is given by
\[
T = D_{kr} W - \alpha p \det(F) F^{-1} \quad \text{with} \quad (D_{kr} W)_{ij} = \frac{\partial W}{\partial F_{ji}}. \tag{7.11}
\]
Figure 7.1: Pressure, displacement, and fluid increment for a blocked aqueduct, using a linear finite deformation model (solid line) and a Blatz-Ko model (dotted line). For the linear model we had to take $M = 0$ for a solution to exist.

To obtain a differential equation in $u$ and $p$, we first have to express $J_2$ and $J_3$ in terms of the deformation gradient entries $F_{ij}$. Then we need to compute the Lagrange stress tensor via the above equation in terms of the $F_{ij}$, and finally we have to substitute the $F_{ij}$ by the expressions from (7.3). The stress equilibrium (7.4) then yields the desired differential equation, which has to be solved along with equations (7.5) to (7.9).

### 7.3 Results

For a numerical scheme the derivatives of $u$ and $p$ in the stress equilibrium and (7.7) are replaced by central differences on a regular grid $r_i = a + \frac{e-n}{m}, i = 0, \ldots, m \in \mathbb{N}$. For boundary conditions (7.5), (7.6), (7.8), and (7.9) one-sided differences are used. As a result we obtain a system of $2m + 2$ nonlinear algebraic equations in the nodal values $U_i$ and $P_i$ of $u$ and $p$. After rewriting the equations such that their right hand side is zero, the system is solved via a Newton iteration. If the corresponding variable vector has the form $(U_0, P_0, \ldots, U_m, P_m)$, the Jacobi matrix (computed at each step of the Newton iteration) is hexadiagonal, and the linear system to be solved at each iteration can be treated by the Thomas algorithm in linear time.

Figure 7.1 shows the results obtained for linear finite deformation and the Blatz-Ko model. Both simulations are done for the steady state of a blocked aqueduct. The solution for linear finite deformation does however not include a strain dependence of the permeability (otherwise problems occur concerning the existence of solutions, compare Section 6.1.1). Pressure and displacement distribution in both cases are very similar to the results of linear elasticity. A detailed analysis is not appropriate, since the used constitutive laws only serve to illustrate the modelling procedure.
Chapter 8

Conclusions

In this work, the three major refinements with respect to earlier poroelastic hydrocephalus models are the use of a fully nonlinear, strain-dependent permeability, the incorporation of a CSF source or sink in the brain parenchyma, and the model development for three space dimensions without any geometrical constraints (though novel ideas about mechanisms of the evolution of hydrocephalus were introduced in a one- and two-dimensional geometry to reduce geometric side effects to a minimum). Also, a way has been suggested to include nonlinear elasticity, which has often been postulated but never been attempted. However, due to a lack of adequate elastic constitutive laws the basic model uses linearised elasticity.

The model has been applied to examine widely-accepted mechanisms for the evolution of hydrocephalus (e.g. CSF flow through the brain tissue after a blockage of the aqueduct), but also to present novel ideas of involved processes, most importantly an overproduction or overdrainage of CSF in the brain parenchyma. In each of the contexts the hydrocephalic symptoms such as dilated ventricles, oedema, or increased intracranial pressure could be explained by mechanical means, and predictions were obtained about the distribution of physical variables (pressure, stresses, fluid velocity, fluid content, etc.) throughout the brain. Also, an altered brain compliance, which is a parameter used in early hydrocephalus models and still measured by physicians, has been linked with a change in poroelastic parameters.

In addition to the basic processes, various supplementary features have been examined, e.g. a flexible skull in infantile hydrocephalus, shunt treatment, and the influence of hydrostatic pressure. The concept of investigating the model on three different complexity levels (one to three space dimensions) has proven advantageous as for each case the geometry of adequate complexity could be chosen.

Despite several decades of hydrocephalus research we still have not left the stage of understanding the causes and pathogenesis. Therefore, as for most hydrocephalus
models, rather than having direct implications, this model should stimulate experiments and measurements to verify the proposed mechanisms. Extremely helpful in separating out misguided theories would be a measurement of pressure and displacement throughout the brain, which has not been attempted so far. It seems likely that there is not a single route for the development of hydrocephalus but that instead several factors might act together, making hydrocephalus rather a syndrome than a disease.

Another important task is the experimental determination of a nonlinear, compressible elastic constitutive law for brain tissue which can be used in poroelastic models. An incorporation of nonlinear elasticity represents a major step towards highly accurate models which might finally be used by physicians to simulate treatment or development of hydrocephalus for each individual patient and thus to optimise therapies.

There is lots of further work to be done: Possible model extensions include an ependymal membrane as ventricle wall, a detailed incorporation of blood vessels, an improvement of geometrical accuracy together with an implementation of the different functional brain regions, pulsation from heartbeat and breathing, the incorporation of bone growth models for infantile hydrocephalus, or micro-scale models for the detailed processes of CSF production and absorption (which still are unrevealed), just to name a few.

We can still hope that a broad comprehension of the disease will soon be achieved and result in better and safer treatment, making life easier for hydrocephalic patients.
Appendix A

A.1 One-dimensional analytic solution

If $s = 0$ and $E$ is short for $\frac{1 - 2\nu}{2(1 - \nu)}$, equations (4.18) and (4.19) multiplied with $r^2$ can be integrated,

$$
\frac{\partial u}{\partial r} + \frac{2u}{r} = E(p + C_1), \tag{A.1}
$$

$$
r^2 \exp \left[ M \left( \frac{\partial u}{\partial r} + \frac{2u}{r} \right) \right] \frac{\partial p}{\partial r} = -\frac{C_2}{ME}, \tag{A.2}
$$

with constants $C_1 \in \mathbb{R}$ and $C_2 > 0$ since the pressure derivative will be negative due to the elevated ventricular pressure. Substituting (A.1) into (A.2) yields

$$
r^2 \exp [ME(p + C_1)] \frac{\partial p}{\partial r} = -\frac{C_2}{ME} \Leftrightarrow \exp [ME(p + C_1)] ME \frac{\partial p}{\partial r} = -\frac{C_2}{r^2}.
$$

Upon integration,

$$
\exp [ME(p + C_1)] = \frac{C_2}{r} + C_3,
$$

where we need $C_3 > -C_2$ for the equation to be well defined for all $\eta \leq r \leq 1$. Hence, the pressure is

$$
p = \frac{1}{ME} \ln \left[ \frac{C_2}{r} + C_3 \right] - C_1. \tag{A.3}
$$

Using this in (A.1), multiplying both sides with $r^2$, and then integrating yields $u$:

$$
r^2 u = \frac{1}{3M} \left( -(\frac{C_2}{C_3})^2 r + (\frac{C_2}{C_3})^2 \ln(r) + (\frac{C_2}{C_3})^3 \ln(\frac{1}{r} + \frac{C_2}{C_3}) + r^3 \ln(\frac{C_2}{r} + C_3) \right) + C_4. \tag{A.4}
$$

For the steady state and a completely blocked aqueduct (conditions (4.20) to (4.22), (4.24), and $\gamma = 0$), equations (4.20) and (4.24) immediately yield

$$
C_4 = \frac{1}{3M} \left( \left( \frac{C_2}{C_3} \right)^2 - \frac{1}{2} \left( \frac{C_2}{C_3} \right)^3 \ln \left( 1 + \frac{C_2}{C_3} \right) - \frac{C_2}{C_3} \ln \left( 1 + \frac{C_2}{C_3} \right) - \ln(C_2 + C_3) \right),
$$

$$
C_1 = \frac{1}{ME} \ln(C_2 + C_3) - \delta^{-1}.
$$
\(C_2\) for \(\gamma = 0\) can be obtained from (4.21):

\[
\eta \delta^{-1} = -e^{ME\left(\frac{1}{\delta}\ln(C_2 + C_3) - C_1 + C_1\right)} \frac{1}{ME} \left[\frac{C_2}{1} + C_3\right]^{-1} - \frac{C_2}{12} \Leftrightarrow C_2 = ME\eta.
\]

\(u, p, C_1, C_2,\) and \(C_4\) substituted into (4.22) yield a condition

\[
g(C_3) = 0,
\]

where \(g\) is defined on \(C_3 \in [-ME\eta, \infty]\). For \(\alpha = 1\) the function is concave and monotonically increasing, having the limit

\[
2\eta + 2\ln(ME\eta) + 2\ln(1 - \eta) + \eta^2 - \frac{\eta^3}{2} \ln(ME(1 - \eta)) - \frac{3}{2(2\nu - 1)} \eta^3 \ln(ME(1 - \eta)) - 3 \quad (A.5)
\]

as \(C_3 \to -ME\eta\) and diverging to infinity as \(C_3 \to \infty\). As long as limit (A.5) is negative, there is a solution which can be found via a Newton iteration.

If the steady state is not yet reached and the aqueduct is still partly open \((\gamma \neq 0)\), we can use boundary conditions (4.20) to (4.22) and \(p_s = p_c < \delta^{-1}\) to compute pressure and displacement for a state where the skull pressure is \(p_c\). (The volume change at this stage can then be computed via (4.23)). \(C_4\) has the same form as before, but \(C_1\) changes to

\[
C_1 = \frac{1}{ME} \ln(C_2 + C_3) - p_c.
\]

Furthermore, condition (4.21) can be solved for \(C_3\):

\[
C_3 = -\frac{C_2}{\eta} \exp\left(\frac{ME\delta p_c - C_2}{\gamma}\right) \frac{\eta - 1}{\eta} \exp\left(\frac{ME\delta p_c - C_3}{\gamma}\right) - 1
\]

Substituting \(u, p, C_1, C_3,\) and \(C_4\) back into (4.22) yields a condition

\[
h(C_2) = 0,
\]

where (for the case \(\alpha = 1\)) the function \(h\) is defined for \(C_2 \in [0, ME\eta\delta p_c]\) with \(\lim_{C_2 \to 0} h(C_2) = -\infty\) and \(\lim_{C_2 \to ME\eta\delta p_c} h(C_2) = \infty\). A Newton iteration then gives the zero and hence all needed constants.
A.2  FEM for the two-dimensional geometry

Let the deformed brain domain in the $r$-$\theta$-plane be denoted by $\tilde{B}$ and the boundary at $\theta = 0, \pi$ by $\tilde{\Gamma}$. Equation (4.15) can be expressed in the form

$$\nabla_p \cdot \begin{pmatrix} e^{M_r} & 0 \\ 0 & e^{M_\theta} \frac{r}{r^2} \end{pmatrix} \nabla_p p + \begin{pmatrix} \frac{\partial \beta_r}{\partial r} \\ \frac{\partial \beta_\theta}{\partial \theta} \end{pmatrix} \nabla_p p = -3\eta_s,$$

where $\nabla_p$ is shorthand for the gradient in polar coordinates, $\nabla_p = (\frac{\partial}{\partial r}, \frac{\partial}{\partial \theta})^T$. By multiplying the equation with $q \in H^1_{\tilde{E}_0}(\tilde{B}) = \{g \in H^1(\tilde{B}) | g \circ \mathbf{u}\{f(\theta), \theta) = g(1, \theta) = 0\}$ and integrating by parts we obtain

$$\int_{\tilde{B}} -\nabla_p q \cdot [A \nabla_p p] + q b^T \nabla p d\theta d\theta + \int_{\tilde{\Gamma}} q A \nabla_p p \cdot \mathbf{n} d\mathbf{r} = \int_{\tilde{B}} -3\eta q \delta d\theta d\theta,$$

where $\mathbf{n}$ is the unit outward normal, i.e. $n = (0, -1)^T$ at $\theta = 0$ and $\mathbf{n} = (0, 1)^T$ at $\theta = \pi$. Furthermore, due to (4.17) the integral on $\tilde{\Gamma}$ vanishes so that we seek $p \in H^1_{\tilde{E}}(\tilde{B}) = \{g \in H^1(\tilde{B}) | g \circ \mathbf{u}\{f(\theta), \theta) = p_v, g(1, \theta) = p_1\}$ such that

$$\int_{\tilde{B}} -\nabla_p q \cdot [A \nabla_p p] + q b^T \nabla p d\theta d\theta = \int_{\tilde{B}} -3\eta q \delta d\theta d\theta \quad \forall q \in H^1_{\tilde{E}_0}(\tilde{B}).$$

On each triangle $K$ the functions $p$ and $q$ are approximated as linear. Let the triangle nodes be numbered from 1 to 3 and let the corresponding coordinates and function values be denoted by $r_1, r_2, \ldots$. Let $J$ be the Jacobian of the coordinate transform from $K$ to the standard reference element:

$$J = \begin{pmatrix} \begin{pmatrix} -1 & 1 & 0 \\ -1 & 0 & 1 \end{pmatrix} \cdot \begin{pmatrix} r_1 \\ r_2 \\ r_3 \end{pmatrix} \end{pmatrix}^T \begin{pmatrix} r_1 & \theta_1 \\ r_2 & \theta_2 \\ r_3 & \theta_3 \end{pmatrix}.$$

Then the (constant) gradient of any linear function $m$ can be expressed as

$$\nabla_p m = J^{-T} D \begin{pmatrix} m_1 \\ m_2 \\ m_3 \end{pmatrix}.$$

Hence, using the trapezium rule on $K$, we obtain

$$\int_K \nabla_p q \cdot [A \nabla_p p] d\theta d\theta = \nabla_p q \cdot [\int_K A d\theta d\theta \nabla_p p] = \begin{pmatrix} q_1 \\ q_2 \\ q_3 \end{pmatrix}^T D^T J^{-1} \begin{pmatrix} \det(J) \frac{A_1 + A_2 + A_3}{6} J^{-T} D \begin{pmatrix} p_1 \\ p_2 \\ p_3 \end{pmatrix} \end{pmatrix}.$$
Furthermore, interpolating $b$ and $s$ linearly on $K$,

$$
\int_{K} q b^T \nabla p \, \text{d}r \text{d}\theta = \int_{K} q b^T \text{d}r \text{d}\theta \nabla p = \frac{\text{det}(J)}{24} \begin{pmatrix}
q_1 & q_2 & q_3
\end{pmatrix}^T \begin{pmatrix}
2 & 1 & 1 \\
1 & 2 & 1 \\
1 & 1 & 2
\end{pmatrix} \begin{pmatrix}
b_1^T \\
b_2^T \\
b_3^T
\end{pmatrix} J^{-T} D \begin{pmatrix}
p_1 \\
p_2 \\
p_3
\end{pmatrix},
$$

$$
\int_{K} q s \text{d}r \text{d}\theta = \frac{\text{det}(J)}{24} \begin{pmatrix}
q_1 & q_2 & q_3
\end{pmatrix}^T \begin{pmatrix}
s_1 \\
s_2 \\
s_3
\end{pmatrix}.
$$

Hence, the integral equation on $K$ can be expressed as

$$
\begin{pmatrix}
q_1 \\
q_2 \\
q_3
\end{pmatrix}^T A_K \begin{pmatrix}
p_1 \\
p_2 \\
p_3
\end{pmatrix} = \begin{pmatrix}
q_1 \\
q_2 \\
q_3
\end{pmatrix}^T f_K
$$

with the local load vector $f_K = -3\eta \frac{\text{det}(J)}{24} Q \begin{pmatrix}
s_1 \\
s_2 \\
s_3
\end{pmatrix}$ and the local stiffness matrix

$$
A_K = -\text{det}(J) D^T J^{-1} \frac{A_1 + A_2 + A_3}{6} J^{-T} D + \frac{\text{det}(J)}{24} Q \begin{pmatrix}
b_1^T \\
b_2^T \\
b_3^T
\end{pmatrix} J^{-T} D.
$$

After the assembly of global stiffness matrix and load vector, two rows and columns are added to the system of equations to implement the pressure boundary conditions. A constant ventricle pressure (3.7) and a constant skull pressure (3.6) are ensured by replacing each stiffness matrix row belonging to a ventricle node by $(0, ..., 0, 1, 0, ..., -1, 0)$ and each row belonging to a skull node by $(0, ..., 0, 1, 0, ..., 0, -1)$, i.e. the last column corresponds to $p_s$ and the one before to $p_v$. The corresponding load vector entries have to be zero. Boundary conditions (4.11) and (4.13) are implemented in Cartesian coordinates (which is easier than first transforming them into polar coordinates). The integral over $\mathcal{V}$ is subdivided into $n$ parts each of which belongs to one ventricle element $K_v$. The ventricle wall area associated with $K_v$ is generated by rotating the ventricle edge around the axis of cylindrical symmetry. This area is then multiplied with the (constant) integrand $e^{Mf} \frac{\partial p_v}{\partial n}$, where $\epsilon$ is averaged over the triangle edge. More detailed, if the Cartesian coordinates for each node are defined as $(x, z) = (r \sin \theta, r \cos \theta)$ and for each ventricle triangle $K_v$ the Jacobian to the standard reference element is defined by

$$
J = D \begin{pmatrix}
x_1 & z_1 \\
x_2 & z_2 \\
x_3 & z_3
\end{pmatrix},
$$

55
then

\[
\frac{\partial p}{\partial n} = \nabla p \cdot n = n^T J^{-T} D \begin{pmatrix} p_1 \\ p_2 \\ p_3 \end{pmatrix} = \begin{pmatrix} x_{v2} - x_{v1} \\ z_{v2} - z_{v1} \\ x_{v1} - x_{v2} \end{pmatrix}^T J^{-T} D \begin{pmatrix} p_1 \\ p_2 \\ p_3 \end{pmatrix},
\]

where \((x_{v1}, z_{v1})\) and \((x_{v2}, z_{v2})\) are the vertices of the ventricle edge. The rotation area of that edge around the \(z\)-axis can be obtained as the difference between the mantle surface area of two cones with heights \(x_{v1}\frac{z_{v2} - z_{v1}}{x_{v1} - x_{v2}}\) and \(x_{v2}\frac{z_{v2} - z_{v1}}{x_{v1} - x_{v2}}\) and opening angle \(2 \arctan \frac{z_{v1} - z_{v2}}{x_{v2} - x_{v1}}\).

\[
\text{area}_K = \pi (x_{v1} + x_{v2}) \sqrt{(z_{v2} - z_{v1})^2 + (x_{v2} - x_{v1})^2}
\]

The integral in (4.13) replaced by \(\sum_K \text{area}_K e^{\mu \text{area}_K} \frac{\partial p}{\partial n}\) yields a linear equation in the pressure values of all ventricle elements, which is taken to form the last row of stiffness matrix and load vector. The row before is formed by applying the same procedure to condition (4.11).

### A.3 FEM for the three-dimensional geometry

Denoting the undeformed and deformed brain tissue by \(\mathcal{B}\) and \(\bar{\mathcal{B}}\) and further the deformed ventricle wall by \(\hat{\mathcal{V}}\), we can multiply the pressure equation (4.9) with \(q \in H^1_0(\bar{\mathcal{B}}) = \{f \in H^1(\bar{\mathcal{B}}) | f = 0 \text{ on } \mathcal{S} \cup \hat{\mathcal{V}}\}\) and then integrate by parts:

\[
\int_{\bar{\mathcal{B}}} \nabla q \cdot [e^{\mu \mathbb{E}} \nabla p] \, dx \, dy \, dz = \int_{\bar{\mathcal{B}}} 3\eta q \sigma \, dx \, dy \, dz
\]

Hence, we have to find a function \(p \in H^1(\bar{\mathcal{B}})\), which satisfies this equation for all \(q \in H^1_0(\bar{\mathcal{B}})\) and furthermore the Dirichlet conditions \(p = p_0\) on \(\mathcal{S}\) and \(p = p_v\) on \(\hat{\mathcal{V}}\).

Regarding the displacement, let us define the matrices \(M_{ij} \in \mathbb{R}^{3 \times 3}, i, j = 1, 2, 3\), by

\[
(M_{ij})_{kl} = \delta_{ij} \delta_{kl} + \delta_{il} \delta_{jk} + \frac{2\nu}{1 - 2\nu} \delta_{ik} \delta_{jl}.
\]

For the sake of legibility we replace the index \(j = 1, 2, 3\) by \(j = u, v, w\) and rename the matrices \(M_{ij}, M_{2j}, M_{3j}\) as \(A_j, B_j,\) and \(C_j\). Then we can rewrite equations (4.8):

\[
\nabla \cdot [A_u \nabla u] + \nabla \cdot [A_v \nabla v] + \nabla \cdot [A_w \nabla w] = \hat{\lambda} \frac{\partial p}{\partial x}
\]

\[
\nabla \cdot [B_u \nabla u] + \nabla \cdot [B_v \nabla v] + \nabla \cdot [B_w \nabla w] = \hat{\lambda} \frac{\partial p}{\partial y}
\]

\[
\nabla \cdot [C_u \nabla u] + \nabla \cdot [C_v \nabla v] + \nabla \cdot [C_w \nabla w] = \hat{\lambda} \frac{\partial p}{\partial z}
\]

56
Now let \( O, P, Q \in H^1_{\partial_0}(\mathcal{B}) = \{ f \in H^1(\mathcal{B}) \mid f = 0 \text{ on } \mathcal{S}\} \) multiply the first, second, and third equation and integrate by parts on \( \mathcal{B} \):

\[
\int_{\partial \mathcal{B}} \nabla O \cdot [A_u \nabla u + A_v \nabla v + A_w \nabla w] \, dS = -\int_{\partial \mathcal{B}} \nabla O \cdot \frac{\partial p}{\partial x} \, dS \frac{\partial p}{\partial y} \, dS - \int_{\partial \mathcal{B}} \nabla O \cdot \frac{\partial p}{\partial z} \, dS \frac{\partial p}{\partial y} \, dS.
\]

Noting that \([A_u \nabla u + A_v \nabla v + A_w \nabla w], n, [B_u \nabla u + B_v \nabla v + B_w \nabla w], n, \text{ and } [C_u \nabla u + C_v \nabla v + C_w \nabla w], n\) are the first, second, and third vector component of the right hand side of (4.12) we obtain the weak formulation: Find \( u, v, \text{ and } w \in H^1_{\partial_0}(\mathcal{B}) \) such that for all \( O, P, Q \in H^1_{\partial_0}(\mathcal{B}) \)

\[
\int_{\partial \mathcal{B}} \nabla O \cdot [A_u \nabla u + A_v \nabla v + A_w \nabla w] \, dS = -\int_{\partial \mathcal{B}} \nabla O \cdot \frac{\partial p}{\partial x} \, dS \frac{\partial p}{\partial y} \, dS - \int_{\partial \mathcal{B}} \nabla O \cdot \frac{\partial p}{\partial z} \, dS \frac{\partial p}{\partial y} \, dS.
\]

For a finite element method, the functions \( p, u, v, w, q, O, P, \text{ and } Q \) are approximated linearly on each tetrahedron element \( K \). Let the nodes of \( K \) be numbered from 1 to 4 in a mathematically positive orientation, and let the corresponding coordinates and function values be \( x_1, x_2, \text{ etc.} \) Let us denote the Jacobian of the coordinate transform from \( K \) to the standard reference tetrahedron by \( J \),

\[
J = \begin{bmatrix}
-1 & 1 & 0 & 0 \\
-1 & 0 & 1 & 0 \\
-1 & 0 & 0 & 1 \\
\end{bmatrix}
\]

Then the (constant) gradient of any linear function \( m \) on \( K \) can be expressed as

\[
\nabla m = J^{-T} D \begin{pmatrix} m_1 \\ \vdots \\ m_4 \end{pmatrix}
\]

Using the dilation \( \epsilon_K \) from the displacement computation and the volume \( \frac{1}{6} \det(J) \) of \( K \) we obtain

\[
\int_K \nabla q \cdot [e^{M_K} \nabla p] \, dV = \frac{\det(J)}{6} e^{M_K} [J^{-T} D \begin{pmatrix} q_1 \\ \vdots \\ q_4 \end{pmatrix}]^T J^{-T} D \begin{pmatrix} p_1 \\ \vdots \\ p_4 \end{pmatrix}
\]

57
Each tetrahedron $K$ is assigned a constant source $s_K$ so that with the trapezium rule

$$\int_K qsdx dydz = s_K \det(J) \frac{q_1 + q_2 + q_3 + q_4}{24}.$$ 

Hence, using the local stiffness matrix $A_K = \frac{\det(J)}{6} e M e T J^{-1} J^{-T} D$ and the local load vector $f_K = 3\eta s_K \frac{\det(J)}{24} (1, 1, 1, 1)^T$, the pressure integral equation can be expressed as

$$\begin{pmatrix}
  q_1 \\
  \vdots \\
  q_4
\end{pmatrix}^T A_K
\begin{pmatrix}
  p_1 \\
  \vdots \\
  p_4
\end{pmatrix} =
\begin{pmatrix}
  q_1 \\
  \vdots \\
  q_4
\end{pmatrix}^T f_K.$$

After the assembly of global stiffness matrix and load vector two more rows and columns are added to implement the pressure boundary conditions (as was done in the two-dimensional case). Again, the integrals in (4.11) and (4.13) are subdivided into the portions of each ventricle and skull tetrahedron $K$,

$$area \cdot e^{M e K} n^T J^{-T} D \begin{pmatrix}
  p_1 \\
  \vdots \\
  p_4
\end{pmatrix},$$

where the surface area of the ventricle or skull face is half the norm of the cross product of two flanking edges, and the unit outward normal $n$ is the cross product divided by its norm. Hence, conditions (4.11) and (4.13) become two linear equations in the pressure values of all ventricle and skull elements, which are taken to form the last two rows of global stiffness matrix and load vector. Again, this only represents the steady state case computation; the time dependence is treated as in the two-dimensional case.

Each triple of displacement integral equations on $K$ can be written in the form

$$\begin{pmatrix}
  O_1 \\
  P_1 \\
  Q_1 \\
  \vdots \\
  O_4 \\
  P_4 \\
  Q_4
\end{pmatrix}^T A_K
\begin{pmatrix}
  u_1 \\
  v_1 \\
  w_1 \\
  \vdots \\
  u_4 \\
  v_4 \\
  w_4
\end{pmatrix} =
\begin{pmatrix}
  O_1 \\
  P_1 \\
  Q_1 \\
  \vdots \\
  O_4 \\
  P_4 \\
  Q_4
\end{pmatrix}^T f_K,$$

where $A_K$ is the local stiffness matrix and $f_K$ the local load vector. Furthermore,

$$\int_K \nabla O \cdot [A_u \nabla u + A_v \nabla v + A_w \nabla w] dx dy dz = volume(K) \nabla O \cdot [A_u \nabla u + A_v \nabla v + A_w \nabla w].$$

58
\[
\begin{align*}
\varrho & = \frac{\det[J]}{6}[J^{-T} D \begin{pmatrix}
O_1 \\
\vdots \\
O_4
\end{pmatrix}]^T [A_u J^{-T} D \begin{pmatrix}
u_1 \\
\vdots \\
u_4
\end{pmatrix} + A_v J^{-T} D \begin{pmatrix}
u_1 \\
\vdots \\
u_4
\end{pmatrix} + A_w J^{-T} D \begin{pmatrix}
u_1 \\
\vdots \\
u_4
\end{pmatrix}]
\end{align*}
\]
and similarly for the other two equations. Hence, if we use the standard value \(\alpha = 1\) (so that the surface integrals in the weak formulation vanish; the generalisation to a different \(\alpha\) is simple) and define the row and column indices \(i_O = i_u = [1,4,7,10],\)
\(i_P = i_v = [2,5,8,11],\) and \(i_Q = i_w = [3,6,9,12],\) it follows that
\[
\begin{align*}
A_K (i_O, i_j) &= \frac{\det[J]}{6} D^T J^{-1} A_j J^{-T} D, \\
A_K (i_P, i_j) &= \frac{\det[J]}{6} D^T J^{-1} B_j J^{-T} D, \\
A_K (i_Q, i_j) &= \frac{\det[J]}{6} D^T J^{-1} C_j J^{-T} D,
\end{align*}
\]
where \(j\) stands for \(u,v,w.\) Similarly, using the trapezoid rule,
\[
\int_K \hat{\varrho} \frac{\partial p}{\partial x} \, dx \, dy \, dz = \hat{\varrho}(1,0,0) \nabla p \int_K \varrho \, dx \, dy \, dz = \hat{\varrho}(1,0,0) J^{-T} D \begin{pmatrix}
p_1 \\
\vdots \\
p_4
\end{pmatrix} \frac{\det[J]}{24} J^{2+2+3+4}.
\]
and analogously for the other two equations so that
\[
\begin{align*}
f_K (i_O) &= -\hat{\varrho}(1,0,0) J^{-T} D (p_1, \ldots, p_4)^T \frac{\det[J]}{24}, \\
f_K (i_P) &= -\hat{\varrho}(0,1,0) J^{-T} D (p_1, \ldots, p_4)^T \frac{\det[J]}{24}, \\
f_K (i_Q) &= -\hat{\varrho}(0,0,1) J^{-T} D (p_1, \ldots, p_4)^T \frac{\det[J]}{24}.
\end{align*}
\]
After the assembly of global stiffness matrix and load vector, the rows corresponding to skull nodes are replaced by the equations \(u = 0, v = 0,\) and \(w = 0\) to satisfy the Dirichlet boundary condition. Finally, after solving the linear system, the (on each element \(K\) constant) dilation \(\epsilon\) is computed via
\[
\begin{align*}
\epsilon &= \frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} + \frac{\partial w}{\partial z} = \text{tr} \begin{bmatrix}
J^{-T} D
\end{bmatrix} \begin{pmatrix}
\vdots \\
\vdots \\
\vdots
\end{pmatrix}
\end{align*}
\]
so that it can be used by the next iteration.

### A.4 Existence of solutions in a rectangular geometry

For an easier analysis the existence of solutions can be examined in a rectangular geometry to avoid the algebraic complication by the spherical geometry. Let our porous medium be a rectangular layer of thickness \(c,\) fixed at one end and free at the other. Let a fluid flux \(q_0\) be applied at the free end, resulting in a pressure distribution
\( \dot{p}p(x) \) and a displacement \( cu(x) \), where \( 0 \leq x \leq 1 \) is nondimensional distance through the material and \( \dot{p} \) is a pressure scale. Let a time scale be given by \( \dot{t} = \frac{\mu \dot{p}}{k_0} \). In this case the dilation is given by

\[
e(x) = \frac{du}{dx},
\]

(A.6)

The equivalent to the nondimensional differential equations (4.18) and (4.19) is

\[
\frac{d^2u}{dx^2} = E \frac{dp}{dx}, \quad E = \frac{\alpha \dot{p}}{2G + \lambda},
\]

(A.7)

\[
\frac{d}{dx} \left[ e^{\mu \epsilon} \frac{dp}{dx} \right] = -s.
\]

(A.8)

The nondimensional boundary conditions can be written as

\[
u(1) = 0,
\]

(A.9)

\[
p(1) = 0,
\]

(A.10)

\[
\left. \frac{du}{dx} \right|_{x=0} = E \frac{\alpha - 1}{\alpha} p(0),
\]

(A.11)

\[
\left. e^{\mu \epsilon(0)} \frac{dp}{dx} \right|_{x=0} = -\frac{\mu \dot{q}_0}{k_0 \dot{p}},
\]

where \( q_0 \) is the flux per unit area and corresponds to the ventricle production \( Q_p \). The pressure scale \( \dot{p} = \mu \dot{q}_0 / k_0 \) changes the last condition to

\[
\left. e^{\mu \epsilon(0)} \frac{dp}{dx} \right|_{x=0} = -1.
\]

(A.12)

However, instead of solving this system we shall look at the inverse problem of solving (A.7) to (A.11) together with the fourth boundary condition

\[
p(0) = p_0
\]

(A.13)

and try to find the corresponding flux \( q_0 \). Let us start with \( \alpha = 1 \) to simplify (A.11).

Integration of (A.8) yields with a nondimensional flux \( q \) as integration constant

\[
\left. e^{\mu \epsilon} \frac{dp}{dx} \right|_{x=0} = -q - s x,
\]

(A.14)

which can then be used to rewrite (A.7) as

\[
\left. e^{\mu \epsilon} \frac{de}{dx} \right|_{x=0} = -E q - E s x
\]

This can be integrated using (A.11),

\[
e^{\mu \epsilon} = 1 - E M q x - E M s \frac{p^2}{2}
\]

(A.15)
\[ u(x) = \frac{1}{M} \int_1^x \log(1 - EMq\xi - EMS\alpha) \, d\xi. \]

Now using (A.15), equation (A.14) can be solved for \( p \):

\[
p = \frac{1}{E} \log \left( \frac{2 - EM(2q + s\xi)}{2 - EM(2q + s)} \right) + \frac{2q(1 - M)}{\sqrt{[EMq]^2 + 2EMS}} \left[ \text{atanh} \frac{-EM(s + q)}{\sqrt{[EMq]^2 + 2EMS}} - \text{atanh} \frac{-EM(s + q)}{\sqrt{[EMq]^2 + 2EMS}} \right]
\]

This has a real value for all \( 0 \leq x \leq 1 \) as long as \( q < q_{\text{max}} = \frac{1}{EM} - \frac{s}{2} \). Furthermore, as \( p_0 \to \infty, q \to q_{\text{max}}, \) i.e. no matter how large a pressure difference is applied, the flux through the matrix is limited by \( q_{\text{max}} \). If a greater flux is applied, there is no solution. Also, the stronger the source \( s \), the smaller is the amount of fluid that can enter the material. In dimensional terms, the maximum flux is given by

\[
\frac{c}{t} \left( \frac{1}{EM} - \frac{s\xi}{2} \right) = \frac{k_0(2G + \lambda)}{\alpha\mu CM} - \frac{cs}{2} = \frac{k_0(2G + \lambda)}{\mu CM} - \frac{cs}{2},
\]

and it is obvious that a too large \( M \) or too small \( k_0 \) can reduce this limit below \( q_0 \) so that there is no solution of (A.7) to (A.12). The physical interpretation is provided by a choking effect: As \( q \to q_{\text{max}} = \frac{1}{EM} - \frac{s}{2}, \epsilon(1) \to -\infty \). Hence, the permeability \( k_0e^{ME} \) decreases to zero at the fixed end, and no flux can get through. (In fact, a dilation \( \epsilon \) of negative infinity means interpenetration of matter and is unphysical. However, there is a flux \( q_{\text{max}} < q_{\text{max}} \) at which \( \epsilon(1) \) becomes -1, signifying material compression to zero volume and thus vanishing of the pore space. Then no flux can pass through so that in principle the choking effect still remains.)

To complicate matters even further, the behaviour is different for non-unit \( \alpha \). Restricting ourselves to the case \( s = 0 \), equation (A.15) becomes

\[
e^{ME} = \Gamma - EMq, \quad \Gamma = e^{EMq_0}, \quad (A.16)
\]

\[
\Rightarrow \quad u(x) = \frac{1}{EM^2q} [(\Gamma - EMq) \log(\Gamma - EMq) + EMq - (\Gamma - EMq) \log(\Gamma - EMq) - EMq],
\]

and equation (A.14) solved for \( p \) is

\[
p = \frac{1}{EM} \log \left( \frac{\Gamma - EMq}{\Gamma - EMq} \right). \quad (A.17)
\]

Now (A.13) implies

\[
q = \frac{\Gamma}{EM}(1 - e^{-EMq_0}).
\]

As before, for unit \( \alpha \) the flux \( q \) is limited by \( \frac{1}{EM} \), and condition (A.12) can only be satisfied if this is greater than or equal to one. For \( \alpha > 1 \), \( q \) monotonically goes to infinity as \( p_0 \) does, hence there is always a unique solution to condition (A.12).
However, if $\alpha < 1$, $q$ has a maximum $q_{\text{max}} = \frac{\alpha}{E_M} (1 - \alpha)^{\frac{1-\alpha}{\alpha}}$ at $p_0 = -\frac{1}{E_M} \log(1 - \alpha)$. Hence again, there is a limiting flux, but below this flux there are two solutions. The one which corresponds to the solution for $\alpha = 1$ is stable, the other one unstable as the following analysis shows: The time dependent equivalent of (4.13), substituting (A.12), is given by

$$e^{M_\text{c}(x=0)} \frac{\partial p}{\partial x}|_{x=0} = -(1 - \frac{\partial u_0}{\partial t}),$$

(A.18)

where $u_0 = u(x = 0)$ is the ventricle wall displacement. In words, the produced fluid can either enter the porous material or stay outside, causing the ventricle wall to shift. Now (A.17) inserted into the definition of $\Gamma$ in (A.16) yields

$$\Gamma = \left( \frac{\Gamma}{\Gamma - EMq} \right)^{\frac{1}{\alpha - 1}} \Leftrightarrow \Gamma - \Gamma \frac{1}{\Gamma - EMq} = EMq.$$

For $\alpha$ near 1 the solutions to this can be approximated by $\Gamma_1 = 1$ (which corresponds to the case $\alpha = 1$) and $\Gamma_2 = EMq$. This yields

$$u_0 = \frac{\log(1 - EMq)}{EM^2q} + \frac{1}{M} [1 - \log(1 - EMq)], \quad \Gamma \approx \Gamma_1,$$

$$u_0 = \frac{1}{M} [1 - \log(EMq)], \quad \Gamma \approx \Gamma_2.$$

Replacing $q = 1 - \frac{\partial u_0}{\partial t} = 1 - \dot{u}_0$ ((A.14) inserted into (A.18)) and differentiating $u_0$ with respect to $\dot{u}_0$ yields

$$\frac{\partial u_0}{\partial \dot{u}_0} = \frac{\log(1 - EM) + EM}{EM^2} < 0, \quad \Gamma \approx \Gamma_1,$$

$$\frac{\partial u_0}{\partial \dot{u}_0} = \frac{1}{M} > 0, \quad \Gamma \approx \Gamma_2.$$

Therefore, the first steady state solution is stable, whereas the second one is unstable.

### A.5 Constitutive law for the brain compliance

The compliance $C$ of the brain is defined as the ratio of a change in the fluid content $V$ to a change in the pressure $p$ [27]:

$$C = \frac{\partial V}{\partial p}$$

It is usually measured by conducting a CSF bolus injection into one of the fluid-filled spaces of the craniospinal system under continuous recording of the pressure. We shall compute $C$ in terms of the pressure and our poroelastic constants.
Let us assume an open aqueduct and hence $p \equiv \text{const.}$ throughout the brain. Then the displacement ODE (3.22) can be integrated twice to obtain

$$u = \frac{C_1}{3} r + \frac{C_2}{r^2}$$

for integration constants $C_1$ and $C_2$. It is trivial to solve boundary conditions (3.24) and (3.26) for $C_1$ and $C_2$:

$$C_1 = 3\xi p, \quad \xi = \frac{a-1}{3a+2G+4G\left(\frac{a}{2}\right)} = \frac{a-1}{3a+4G\left(\frac{a}{2}\right)}$$

$$C_2 = -c^3\xi p$$

$$\Rightarrow \quad u = \xi pc \left[ \frac{r}{r} - \left( \frac{r}{c} \right)^{-2} \right]$$

Volume dilation and fluid increment follow from (3.14) and (6.2):

$$\epsilon = 3\xi p, \quad \zeta = \alpha (3\xi + \frac{1-\alpha\beta}{K\beta} \alpha) p$$

The total CSF fluid increment $V$ is composed of the ventricle volume increase and the interstitial fluid increment integrated over the tissue:

$$V = \frac{4}{3} \pi \left[ (a + u(a))^{3} - a^{3} \right] + \xi \frac{4}{3} \pi (c^{3} - a^{3})$$

$$= \frac{4}{3} \pi (c^{3} - a^{3}) \left[ -3\xi p + 3 \frac{\xi p^2}{\alpha} (c^{3} - a^{3}) - \frac{\xi p^{3}}{\alpha} (c^{3} - a^{3})^{2} + 3 \alpha \xi p + \frac{1-\alpha\beta}{K\beta} \alpha \right]$$

Upon differentiating with respect to $p$ we obtain the compliance

$$C = \frac{4}{3} \pi (c^{3} - a^{3}) \left[ 3\xi \left( \alpha - \left[ 1 + \xi p \left( 1 - \left( \frac{a}{c} \right)^{3} \right) \right] \right)^2 + \frac{1-\alpha\beta}{K\beta} \alpha \right]$$

However, this predicts a negative value for $|\xi p| \gg 1$, which is an artefact of integrating the small strain dilation $\epsilon$ over the brain volume. If we instead assume that for constant pressure $p$ a ventricle volume change $\Delta V$ results in the amount $\alpha \Delta V$ of CSF being squeezed out, the total volume increment is given by

$$V = \Delta V (1 - \alpha) + \frac{4}{3} \pi (c^{3} - a^{3}) \frac{1-\alpha\beta}{K\beta} \alpha p$$

$$= \frac{4}{3} \pi (c^{3} - a^{3}) \left[ (-3\xi p + 3 \frac{\xi p^2}{\alpha} (c^{3} - a^{3}) - \frac{\xi p^{3}}{\alpha} (c^{3} - a^{3})^{2} (1 - \alpha) + \frac{1-\alpha\beta}{K\beta} \alpha \right] .$$

Hence, the compliance becomes

$$C = \frac{\partial V}{\partial p} = \frac{4}{3} \pi (c^{3} - a^{3}) \left[ 3\xi (\alpha - 1) \left( 1 + \xi p \left( 1 - \left( \frac{a}{c} \right)^{3} \right) \right)^2 + \frac{1-\alpha\beta}{K\beta} \alpha \right] .$$

If we assume a saturated brain ($\beta = 1$) and pressures up to $p = 10$ kPa ($|\xi p| \ll 1$), this reduces to

$$C = \frac{4}{3} \pi (c^{3} - a^{3}) \left[ 3\xi (\alpha - 1) + \frac{1-\alpha}{K} \alpha \right] = \frac{4}{3} \pi (c^{3} - a^{3}) \left[ \frac{(\alpha-1)^2}{K+\frac{G}{2G}(\frac{a}{2})^3} + \frac{1-\alpha}{K} \alpha \right] \approx \frac{4}{3} \pi (c^{3} - a^{3}) \frac{1-\alpha}{K} \alpha .$$
A.6 Stress equilibrium of a spherical membrane

To model an infantile, non-rigid skull we use a membrane model since the skull is very thin compared to the cranial radius. Let a pressure $p = -\sigma$ be applied on the inside of a thin spherical membrane, in which the stresses may be assumed to be equally distributed over the membrane thickness. According to Figure A.1 the stress $-\sigma$ integrated over the infinitesimal area $(rd\varphi)^2$ has to be balanced by the force $s$ per unit length on the rim of the small square, i.e. by $4(rd\varphi) \cdot \sin\frac{d\varphi}{2}s$. Hence, approximating $\sin\frac{d\varphi}{2} = \frac{d\varphi}{2}$ for infinitesimal $d\varphi$ we have

$$-\sigma(rd\varphi)^2 = 4r\frac{d\varphi^2}{2}s \Leftrightarrow s = \frac{-r\sigma}{2}. \quad (A.19)$$

Furthermore, for a two-dimensional membrane the strains $\varepsilon_1$ and $\varepsilon_2$ in the two orthogonal directions 1 and 2 are related to the stresses $s_1$ and $s_2$ by

$$\varepsilon_1 = \frac{1}{E_s} s_1 - \nu_s\varepsilon_2, \quad \varepsilon_2 = \frac{1}{E_s} s_2 - \nu_s\varepsilon_1,$$

where $\nu_s$ is Poisson’s ratio of the material, and $E_s$ is the Young’s modulus times the membrane thickness. For our spherically symmetric membrane, $\varepsilon_1 = \varepsilon_2 = \varepsilon$ and $s_1 = s_2 = s$. Furthermore, if the membrane is displaced outwards by $u$, the tangential strain is given by $\varepsilon = \frac{u}{r}$ and hence

$$s = s_1 = E_s(\varepsilon_1 + \nu_s\varepsilon_2) = E_s(1 + \nu_s)\varepsilon = E_s(1 + \nu_s)\frac{u}{r}.$$

Now (A.19) yields the relation between stress $\sigma$ and displacement $u$:

$$\sigma = -E_s(1 + \nu_s)\frac{2u}{r^2}.$$

A.7 Model extension to hydrostatic pressure

The generalisation of Darcy’s law to incorporate the hydrostatic pressure component $p_h = -\rho g z$ (assuming the $z$-axis to be vertically upwards and denoting gravity by $g$
and fluid density by $\rho$) states that the fluid velocity is given by

$$\mathbf{v} = -\frac{k}{\mu} \nabla (p - p_h) = -\frac{k}{\mu} \nabla (p + \rho g z), \quad (A.20)$$

Hence, the pressure differential equation (3.3) changes to

$$\nabla \cdot [k_0 e^{\mu t} \nabla (p + \rho g z)] = -\mu s \quad \Leftrightarrow \quad \nabla \cdot [k_0 e^{\mu t} \nabla p] + k_0 \rho g \frac{\partial}{\partial z} [e^{\mu t}] = -\mu s. \quad (A.21)$$

The displacement differential equation (3.2) also has to be changed, since the consideration of hydrostatic pressure inherently implies the introduction of body forces. Brain tissue and CSF may well be approximated to be of the same density so that the specific body forces are given by $-\rho g \mathbf{e}_z$. Therefore, (3.2) changes to

$$G \nabla^2 u_i + (G + \lambda) \frac{\partial \epsilon}{\partial x_i} - \alpha \frac{\partial p}{\partial x_i} = \rho g \delta_{i3}. \quad (A.22)$$

Analogously, boundary conditions (3.4) to (3.10) become

$$p = p_s - \rho g z \text{ on } S, \quad (A.23)$$

$$p = p_v - \rho g z \text{ on } V, \quad (A.24)$$

$$u = v = w = 0, \quad (A.25)$$

$$\frac{p_s - p_b}{\mu R} = \frac{\pi d^4}{128 \mu L} (p_v - p_s) + \oint_S -\frac{k}{\mu} \nabla (p + \rho g z). \mathbf{n} dS, \quad (A.26)$$

$$\frac{(\alpha - 1) p n}{n} = 2G \varepsilon \cdot n + \lambda n \text{ on } V, \quad (A.27)$$

$$\dot{V} = Q_p - \frac{\pi d^4}{128 \mu L} (p_v - p_s) - S(p_v) - \oint_V -\frac{k}{\mu} \nabla (p + \rho g z). \mathbf{n} dS, \quad (A.28)$$

where $p_s$ and $p_v$ now represent an average subarachnoid and ventricular pressure.

Obviously, in the case $\alpha = 1$ the introduction of the variable $\bar{p} := p + \rho g z$ (i.e. the pressure without its hydrostatic component) recovers the old set of equations. Hence, we obtain the same solution as without hydrostatic pressure, only the hydrostatic component $-\rho g z$ is superimposed on the pressure.

For $\alpha < 1$ the behaviour is different, though: The hydrostatic pressure gradient in equation (A.22) does no longer bear the full amount of body forces, which results in a downward displacement of the material. Furthermore, the hydrostatic pressure component in the ventricle boundary condition (A.27) acts as an additional force, which is smaller in the upper parts and larger in the lower parts of the ventricles and hence amplifies the overall downward movement.
For the cylindrically symmetric case, the governing equations have to be changed in the same way as shown above for the fully three-dimensional geometry: The pressure \( p \) has to be replaced by \( p + \rho g r \cos \theta \) (pressure without hydrostatic component), and the body forces in \( r \)- and \( \theta \)-direction, \(-\rho g \cos \theta \) and \( \rho g \sin \theta \) respectively, have to be implemented in equation (3.15).

### A.8 Stresses, strains and constitutive laws

We shall only give a brief summary of the stress and strain notions used, a derivation can be found e.g. in [6].

The deformation of a body \( \mathcal{B} \) can be described as an injective mapping of each of its points \( \mathbf{x} = (x_1, x_2, x_3) \) onto a point \( \mathbf{y} = (y_1, y_2, y_3) \). The differential of \( \mathbf{y} \) with respect to \( \mathbf{x} \) is called the deformation gradient

\[
F = \left( \frac{\partial y_i}{\partial x_j} \right)_{ij}.
\]

In the deformed state, stresses within the body can be interpreted as forces exerted on a notional plane inside the material. At each point they can be expressed as a second order tensor, the Cauchy stress or real stress \( \sigma \), whose entries are the limits of forces per area exerted on the walls of an infinitesimal cube in the deformed body. Conservation of angular momentum implies that the shear stresses (and thus also \( \sigma \)) are symmetric.

Since the Cauchy stress is only defined in the (not yet known) deformed state, it is convenient to define notional stresses in the undeformed state, which are mathematically consistently related to the Cauchy stress. Such stresses can then be used for computations. The Lagrange stress tensor or first Piola-Kirchhoff stress tensor is given by

\[
T = \det(F) F^{-1} \sigma,
\]

whereas the Kirchhoff or second Piola-Kirchhoff stress tensor is defined as

\[
S = \det(F) F^{-1} \sigma F^{-T} = TF^{-T}.
\]

Note that \( T \) generally is not symmetric while \( S \) always is.

The corresponding notions of strain have to be chosen conjugate to the stress definition, i.e. such that their product yields work. The strain definition in the deformed state, conjugate to the Cauchy stress, is called Almansi or Euler-Almansi strain,

\[
e = \frac{1}{2}(I - B^{-1}),
\]
where $B = FF^T$ is the left Cauchy-Green strain tensor. The conjugate to Kirchhoff stress is the Lagrange or Green-Lagrange strain,

$$E = \frac{1}{2}(C - I), \quad \text{(A.32)}$$

where $C = F^T F$ is the right Cauchy-Green strain tensor. In the limit $F \to I$, i.e. for small deformations, Almansi and Lagrange strain equal the linearised strain $\varepsilon$, which is defined by (2.5) and which we used so far.

Conservation of linear momentum (neglecting body forces or acceleration terms) yields the well-known stress equilibrium, in tensor notation

$$\frac{\partial \sigma_{ij}}{\partial y_j} = 0.$$  

This can be shown to be equivalent to

$$\frac{\partial T_{ji}}{\partial x_j} = 0 \quad \text{or} \quad \frac{\partial}{\partial x_j}[(SF^{T})_{ji}] = 0. \quad \text{(A.33)}$$

These equations, combined with a constitutive law relating stress and strain, form a set of differential equation in the undeformed configuration, which can be solved to determine the deformation of the body.

Finally, the volume dilation $\varepsilon$, used in (2.8), has to be generalised to

$$\varepsilon = \det(F) - 1. \quad \text{(A.34)}$$

The simplest possible constitutive relation between Kirchhoff stress and Almansi strain takes a linear form similar to (2.4) (only without the fluid component, which will be dealt with later):

$$S_{ij} = 2GE_{ij} + \lambda E_{kk} \delta_{ij}. \quad \text{(A.35)}$$

It can be seen as a generalisation of the linearised version with Cauchy stress and linearised strain, in which rigid rotations do not lead to stresses. However, this relation is only valid for small strains.

The use of hyperelastic models with a strain energy function is more sophisticated and widely used in the field of biomechanics. A material is called hyperelastic, if there is a strain energy function $W(J_1, J_2, J_3)$ in the strain invariants $J_1, J_2, J_3$ such that

$$T_{ij} = \frac{\partial W}{\partial F_{ji}} = (D_{F^T}W)_{ij}, \quad \text{(A.36)}$$

where the strain invariants are defined as

$$J_1 = \text{tr}(B), \quad J_2 = \frac{1}{2}[J_1^2 - \text{tr}(B^2)], \quad J_3 = \det(B).$$

67
Alternatively, we may use the relation between Almansi strain and Kirchhoff stress,

\[ S_{ij} = \frac{\partial W}{\partial E_{ij}} = (D_F W)_{ij}, \quad (A.37) \]

which is equivalent because of equation (A.30) or rather \( T = S F^T \):

\[ T_{ij} = \frac{\partial W}{\partial F_{ji}} = \frac{\partial W}{\partial E_{\alpha\beta}} \frac{\partial E_{\alpha\beta}}{\partial F_{ji}} = S_{\alpha\beta} \left[ \frac{1}{2} F_{j\beta} \delta_{i\alpha} + \frac{1}{2} F_{j\alpha} \delta_{i\beta} \right] = \frac{1}{2} (S_{j\beta} F_{j\beta} + S_{\alpha\beta} F_{\alpha\beta}) = S_{i\alpha} F_{jm}, \]

where the last step follows from \( S^T = S \).

### A.9 Poroelasticity for finite deformation

Linear poroelasticity or consolidation theory as introduced by Biot [4] is a phenomenological theory in so far as it is based on the observation that stresses in a porous, fluid-filled material are partly exerted by the solid skeleton (so-called effective stress) and partly by the fluid pressure, which bears a portion of the normal stresses, but not of the shear stresses. The influence of the fluid pressure is then simply weighted by a parameter \( \alpha \) (the Biot-Willis parameter), whereas the effective stress is determined by the linear, small strain constitutive law of the drained solid skeleton. These steps are subsumed in the phenomenological law (2.4).

This idea has a natural extension to finite deformation theory. Using the definitions and notations of appendix A.8, we may assume that in the deformed configuration of a porous material the real Cauchy stress \( \sigma \) still is carried partly by the solid skeleton (effective stress) and partly by the fluid pressure \( p \). As before, the pressure may only have an effect on normal stresses, and its influence is weighted by a parameter \( \alpha \). For the effective stress, however, we may this time choose any adequate constitutive law of the solid matrix, e.g.–a hyperelastic one. Hence, in the deformed configuration we have

\[ \sigma_{ij} = \sigma_{ij}^{\text{eff}} - \alpha p \delta_{ij}, \]

which can be multiplied with \( \det(F) F^{-1} \) from the left to give

\[ T = T^{\text{eff}} - \alpha p \det(F) F^{-1} \quad \text{or alternatively} \quad S = S^{\text{eff}} - \alpha p \det(F) F^{-1} F^{-\top}, \]

where \( T^{\text{eff}} \) or \( S^{\text{eff}} \) may e.g.–be expressed via (A.35), (A.36), or (A.37). This formulation is very convenient since existing constitutive laws for the solid skeleton may be used. The stress equilibrium (A.33) now again yields a differential equation to be solved for the deformation.
What still remains to do, though, is to verify the consistency of the above approach with the thermodynamic derivation of poroelastic theory, as for example found in [5]: We may assume the existence of Gibbs free energy $G$ for a porous, fluid-filled material as a function of the Green-Lagrange strain $E$, the interstitial fluid pressure $p$, and the temperature $\theta$. Then Kirchhoff stress $S$, porosity $\Phi$, and entropy $S_E$ are given by

$$S = \frac{\partial G}{\partial E}, \quad \Phi = -\frac{\partial G}{\partial p}, \quad S_E = -\frac{\partial G}{\partial \theta}.$$  

Disregarding the influence of temperature, let us assume there is a strain energy function $W(E)$ which represents the energy stored in the drained solid skeleton. Furthermore, we note that the change of porosity $\Delta \Phi$ corresponds to the fluid increment (6.2). Thus,

$$\Phi = \Phi_0 + \Delta \Phi \quad \text{with} \quad \Delta \Phi = \alpha \varepsilon + \frac{(1 - \alpha \beta)\alpha}{K \beta} p,$$

where the volume dilation $\varepsilon$ is given by (A.34). Then the Gibbs free energy takes the form

$$G = W(E) - p\Phi_0 - \alpha p \varepsilon - \frac{1}{K \beta} \frac{\alpha \beta}{2} p^2,$$

and indeed, $-\frac{\partial G}{\partial p} = \Phi_0 + \alpha \varepsilon + \frac{(1 - \alpha \beta)\alpha}{K \beta} p = \Phi_0 + \Delta \Phi = \Phi$ and

$$T = \frac{SF^T}{p} = \frac{\frac{\partial G}{\partial E} F^T}{p} = \frac{\frac{\partial G}{\partial E} \frac{\partial F}{\partial E} p}{p} = \frac{\partial G}{\partial p} = T^{\text{eff}} - \alpha p \frac{\partial}{\partial p} [\text{det}(F)] = T^{\text{eff}} - \alpha p \text{det}(F) F^{-1},$$

which is exactly what the phenomenological approach predicted.

As mentioned before, the advantages of the phenomenological formulation lie in its simplicity and in the fact that existing constitutive laws for the solid constituent can be used. Nevertheless we do hope that soon complete poroelastic constitutive laws of the brain are found (also including a nonlinear form of (A.38)), e.g. by specifying the Gibbs free energy $G$.

For the sake of completeness we shall finally show how to obtain linear consolidation theory from thermodynamics. Again we assume the form

$$G = W(E) - p\Phi_0 - \alpha p \varepsilon - \frac{1}{K \beta} \frac{\alpha \beta}{2} p^2,$$

but this time we use small strain approximations $E \approx \varepsilon$ and $\varepsilon \approx \varepsilon_{II}$. Then

$$\sigma \approx S = \frac{\partial G}{\partial E} \approx \frac{\partial G}{\partial \varepsilon} \approx \frac{\partial W}{\partial \varepsilon} - \alpha p \delta,$$

where $\delta$ is the identity. If now $\frac{\partial W}{\partial \varepsilon}$ is linearised for a homogeneous, isotropic material, we obtain relation (2.4).
Bibliography


