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Using a Simulated Electrical Equivalence Model to Understand Intracranial Pulsatility.

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Abstract

An electrical equivalence circuit was initially presented by Thacker et al [1] in 2004, and validated through the acquisition of phase contrast magnetic resonance imaging (PC-MRI) [2]. Attempts to estimate model parameters on a per-subject basis found problems with stability, so ultimately only average parameters were determined for a group of normal subjects. A number of these parameters were well defined in this validation whilst others still proved problematic. However, the model was sufficient to make a prediction of the jugular waveform [3].

Given the above observations it was decided to attempt to understand the source of the parameter instability via simulation. An AC circuit simulator [4] is used to demonstrate that the overall flow processes seen in PC-MRI can be replicated by this circuit and that flow pulsatilities shown are possible given the well-defined parameters.

In order to build the simulation circuit additional components are required to those originally estimated from MR data. The simulation has been used to determine appropriate values for these new components which set appropriate analogous mean input pressures and pulsatilities. Plausible values, consistent with general biological behaviour, are also now provided for the poorly defined parameters. Once this is done it is possible to predict mean and pulsatility pressures for different compartments of the anatomy, including brain tissue. Pressures within the brain (both mean and pulsatility) are shown to be significantly smaller than input pressures, and to have a heavy dependence on the ratio and absolute values of inflow impedance to outflow impedance. Increasing the impedance of the spinal sub-arachnoid space results in increased pressure pulsatility. The mean pressure in the brain is shown to be significantly larger than that in the CSF.

The model is successful in explaining parameter estimation instabilities, and an extension to account for the internal carotid and vertebrobasilar networks separately is proposed.

Introduction

It is widely accepted that the peak pressure of blood entering the skull is reduced during its passage through the arteries in order to prevent damage to the brain. The peak to peak difference (pulsatility) of the flow is thought to be greatly reduced through a significant resistance to blood entering the brain to provide a constant flow of blood through the brain. This resistance causes an enlargement of the arteries in the cranial sub-arachnoid space thereby displacing a volume of cerebrospinal fluid (CSF). Although the skull is considered to be a rigid casing, there is a compliant spinal sub-arachnoid space into which CSF may flow. The blood and CSF are each considered as incompressible and as such a volume of CSF which equals the increased volume of the arteries, must either leave the rigid skull, or displace the blood in the veins. It is thought that a combination of the two exists, with the movement of CSF out of the skull into the compliant spinal sub-arachnoid space being the dominant mechanism.

The medical community have concluded that the ability to measure intracranial pressure is vital to improving treatment of traumatic brain injury, and neuro-degenerative diseases. Unfortunately a reliable method of making such a measurement has not been made available clinically. Phase contrast magnetic resonance imaging (PCMRI) is able to quantify the flow (and flow pulsatility) of fluids (blood and CSF) in the skull. The skull can be approximated as a rigid casing, meaning that flows (mean and pulsatility) must relate to pressures (mean and pulsatility). Abnormalities in both mean pressures, and pressure pulsatilities within the skull have been linked with neuro-degenerative illnesses, and processes associated with traumatic brain injuries. It is clear that the ability to obtain accurate measurements of intracranial pressures would enable greater understanding of abnormal behaviours, thereby enabling improved treatment and/or more accurate prognoses.

The relationship between flows and pressures can be quantified by modelling the impedances to flows, and compliance of boundaries. A popular method of doing this in the literature is via an equivalent electrical circuit model. The periodicity of the alternating current (AC) circuit approximates the flow pulsatility, whilst applying a direct current (DC) bias allows the mean flow to be set. The voltage of the electrical circuit provides an analogy to pressure.

One such model provided by Thacker and colleagues is of particular interest. Theoretically, using this model, both the mean intracranial pressure, and the pressure pulsatility throughout the skull can be estimated non-

invasively. **Until now, it has not been independently verified, meaning that the general biological behaviour expected for the estimated parameters have not been confirmed. Also difficulties seen when attempting to estimate parameters were never fully understood. For example, parameter estimations were not possible for individuals, and instead a population was required to provide better stability. Also, three of parameters were never well defined for the population. For these reasons a circuit simulator [4] is used to verify the well-defined parameters, and to gain understanding as to why other parameters could not be well estimated.**

Background Literature

A number of these models can be seen in literature including an early model of pressures along the cerebrovascular bed made use of a Starling resistor [6]. In effect this model consists of a tube running through a box which transports fluid from one side of the box to the other representing the transport of blood through the skull. The box itself is rigid and filled with fluid which is representative of the cerebrospinal fluid (CSF). Increasing the amount of fluid in the box demonstrates the effect of increasing CSF pressure. This demonstrated the fact that increasing CSF pressure has no effect on blood flow or pressure until the CSF pressure exceeds the venous outflow pressure. Once this occurs, the outflow pressure and flow are shown to decrease with increasing CSF pressure, whilst the inflow pressure increases. This work was extended by Zagzoule and colleagues in a mathematical model, which hoped to describe the pressures and associated pressure pulsatilities in a number of cerebral blood vessels [19].

In 1987 Takemae and colleagues created the expanded on the work by done by Chopp in creating a model which split the intracranial bloodflow into three components (arteries, arterioles and capillaries, and veins) [7]. This also included a compliance of the CSF space, stating that it would become zero if Monro-Kellie were to be strictly true. The analogies of electrical components to biological features were well defined, and the model was created and simulated using estimated values. A seven compartment (arteries, brain, capillaries, veins, venous sinus, jugular bulb, CSF) model was later presented by Karni et al [8]. This involved the argument that the three volumes (blood, brain, and CSF) are linearly compressible with an increase in one volume invoking a corresponding decrease in another volume. Although the outputs of the model showed promise, the complexity does not allow for biological verification.

A year later Ursino presented his first model, which comprised of four subsections (Cerebral arterial, CSF production and absorption, cerebral venous, and craniospinal dynamics) to create a full description of ICP dynamics [9]. The model was verified against literature for a number of conditions in a second paper [10] which related biological effects to alterations in model parameters. This became a very popular model, leading Ursino to conduct further research in the field. This involved refinement and verification until 1997, when he noted that such complex models are extremely limited in their clinical usefulness [11] whilst presenting a simplified model. Ursino noted that this simple model was unable to assess intracranial pressure pulsatility (ICPP), but in the same year he reported that the model is effective in some clinical situations [12]. This highlights the usefulness of simpler models.

The Ursino models are all computational, with the outputs compared against literature, or collected data; parameters are not calculated using real patient data. In the year 2000, a simple four compartment (veins, arteries, CSF and body) model was proposed by Stevens and Ladkin, with an emphasis on intracranial compliances [13]. A number of curves are explained and reproduced, but with no biological verification. As with the models presented by Ursino, this includes a CSF production mechanism (assume this goes to zero at equilibrium), as well as an infusion mechanism to allow simulation of bolus injection. In 2003 Ladkin presented a complex 16 compartment model, which described circulations in both the head and body [14]. There is no way to fully validate such a model, rendering it clinically useless. This led to the simplification of the model through the deletion of the majority of the body components being presented with the aim of studying steady state ICP [15]. This was further simplified in 2007 by uniting the CSF spaces, but the addition of CSF bulk flows into two of the compartments were imposed which has never been explicitly validated [16]. Stevens went on to add the CSF production component to a number of models in order to study the failure of the CSF production absorption equilibrium. Tain returned to the use of a simple model in 2011 to assess craniospinal compliance [17]. Here they use a simple lumped RC component (cranial) in parallel with an LRC component (spinal canal), which they cite from previous work [18].

This work

Models provided in the literature can generally be split into those which are too complex to be clinically useful, or those which are too simple to provide adequate information. The model provided by the Thacker group (Fig.1) is very similar to the one suggested by the Takemae group [7]. The major advancement is the estimation of parameters based on PC-MRI measurements. In addition, it is theoretically possible to provide estimates of ICP

Component	Biological analogy	Provided by [2]	Used in Model
R1	Impedance of arterial capillaries	1.0±0.025	1kΩ
R2	Impedance of cerebral aqueduct	Approximately zero	10Ω
R3	Impedance of venous capillaries	Approximately zero	10Ω
R4	Impedance of exit from skull		270Ω
R5	Impedance of arteries	$0.001\pm8\times1.8^{-3}$	10Ω
R6	Impedance of entry to skull		300Ω
R7	Impedance of spinal subarachnoid space		135Ω
C1	Elastic capacitance of arteries	Large	20Ω
C2	Elastic capacitance of ventricles	4.11±0.11	4.11μF
C3	Elastic capacitance of capillaries	$0\pm5\times10^{-3}$	5nF
C4	Elastic capacitance on veins	271.017±18	271μF
C5	Elastic capacitance of spinal subarachnoid space		540Ω

Table 1: Components of the circuit with their values and biological analogies

in the CSF, the bloodstream through the brain, and in the brain itself.

The original paper concerned itself with measurable intracranial flow dynamics, and the RC characteristics of neither the inflow or the spinal sub-arachnoid space were directly estimatable from these measurements. When building either a real circuit or a simulation, only the input voltage characteristics can be set. This leads to the requirement of inflow and outflow resistors (R6 and R4) in order to prevent "back-flow" and set appropriate input voltage (pressure) levels. Also, the complete circuit simulation requires a specification of the spinal impedance (R7). The impact of these parameters on mean pressure, and pressure pulsatility (peak to trough difference) mean that their parameterisation is crucial in making the simulation biologically useful. The additional information required to set these parameters comes here from nominal values for systolic and diastolic pressure and observed FM flow pulsatility. In clinical situations these values could be patient specific.

Method

Since the overall impedance of the circuit is frequency dependent, it would seem appropriate to provide the circuit with an AC input at 70 cycles per minute (1.17Hz) as an approximation to the average resting heart rate. Unfortunately this is awkward to simulate and would make the circuit impossible to build using practical circuit components should physical verification ever be required. Modelling the circuit at 70,000 cycles per minute (1.17kHz) moves the components into more practical ranges. The resistances were multiplied by 1000, and the capacitances were divided by the same amount to preserve the RC constant observed in the body (Table.1).

The input function was limited to being a sine wave by the simulator, but this was regarded as acceptable for verifying the output of the model. This also results in all current and voltage curves being simple shifted sine curves, allowing all parts of the circuit to be completely described by mean values and a peak to peak pulsatility. A DC bias was added to the AC component to provide an overall input voltage with a maximum value of 120V and a minimum value of 80V, to provide an input which maps to

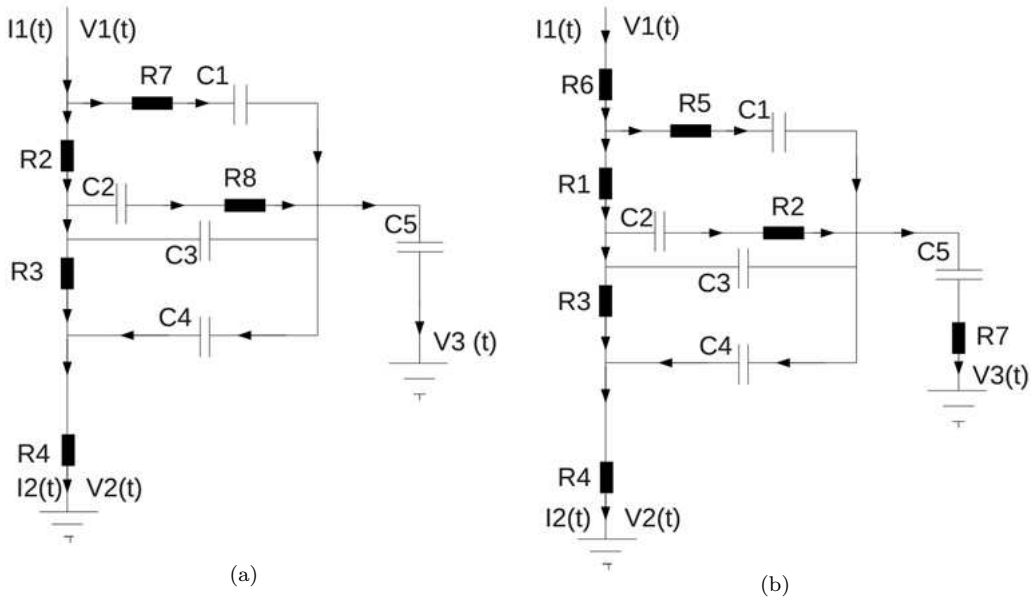


Figure 1: The electrical equivalence circuit proposed by Thacker A) original and B) expanded physical circuit.

the average resting arterial blood pressure of 120/80mmHg. Using the circuit simulator allowed the well-defined parameters to be replicated exactly, whilst the other parameters were estimated.

The high compliance expected of the spinal sub-arachnoid space (C5) means that the flow pulsatility through the FM would be expected to approximately equal to the input pulsatility. Instead only two thirds of the input pulsatility is observed to traverse the FM. Given the fact that there are only two paths through which the flow pulsatility can exit the skull, it follows that the ratio of the resistances of these two paths must be the inverse of the ratio of flow pulsatilities. It is therefore reasonable to assume that the resistance to flow into the spinal sub-arachnoid space (R7) should be half the value of the resistance to blood flowing out of the skull (R4). Once the ratio of input (R6) to output (R4) resistance was established as 10 to 9, the values of both were scaled to investigate the effect of scaling these resistances. The inflow resistor was set as 300Ω, the outflow resistor (R4) was set as 270Ω, and the spinal resistance was set as 135Ω. Having determined these as nominal values, an investigation into the effects of changing parameter values on mean flow and pressure and pulsitilies was undertaken. The aim here being to develop an understanding of the sensitivity of the model to parameter variation.

As the ability to estimate a parameter requires us to see changes in measured data values, sensitivity of flow pulsatilities to a parameter also implies the ability to make good parameter estimates. Whilst large increases in pressure pulsatility implies the possibility of stress induced tissue damage in analogous pathology.

Results

Increasing the outflow resistance increases the mean pressures and pressure pulsatilities with respect to the inflow, but has no effect on flows, or flow pulsatilities with respect to inflow. Similarly pressure increases with no associated normalised flow increases are observed upon increasing the resistances to inflow (R6), outflow (R4), and spinal sub-arachnoid space (R7).

Increasing the resistance to flow into the brain (R1) decreases pressure (mean and pulsatility) throughout the skull as well as the flow pulsatility in the CSF. The initial reduction followed by an increase in the CSF flow pulsatility through the cerebral aqueduct (CA) indicates flow pulsatility being transferred from the brain to CSF at low resistance to flow into the brain (R1), with the opposite being true at higher resistances. The resistance to the transfer of pulsatility from the arteries to the CSF (R5) decreases pressure pulsatilities throughout whilst decreasing the flow pulsatility in the CSF. In both cases pressure pulsatilities are indicated by CSF flow pulsatility. This is also true for the mean pressure in the case of the resistance to blood flow into the brain. In the case of the arterial compliance (C1), the opposite is true, with flow pulsatilities in the brain, CA, and CSF around the veins corresponding to an increase in pressure pulsatility throughout the skull. This provides a classic example of a one

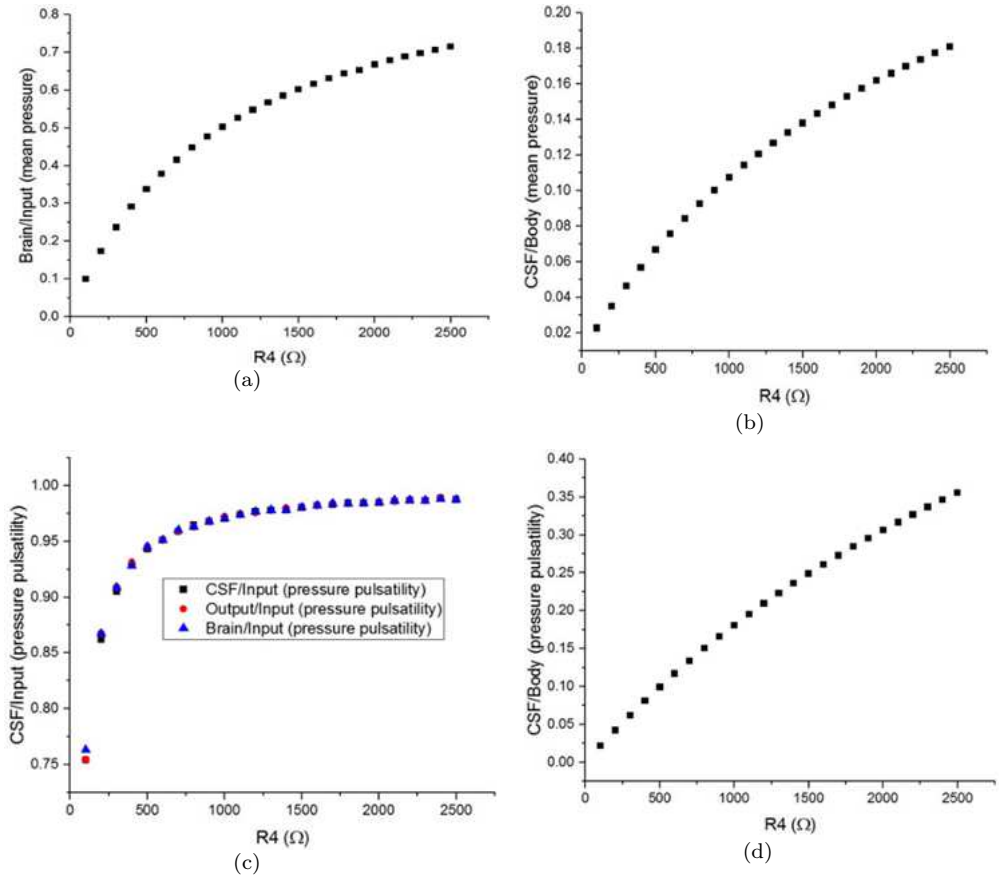


Figure 2: The effects of increasing R4, with the spinal resistance always being equal to R4/2, and all other parameters remaining constant. A) Mean pressure through the brain normalised to mean input pressure, B) Mean CSF pressure normalised to mean blood pressure in the body, C) Intracranial pressure pulsatilities normalised to input pressure pulsatility, and D) CSF pressure pulsatility normalised to blood pressure pulsatility in the body.

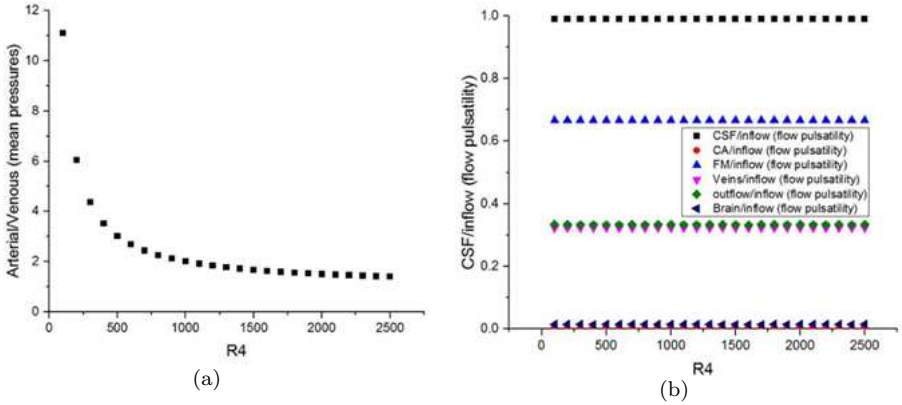


Figure 3: A) the effect of increasing R4 whilst keeping the input resistance constant on the arterial to venous pressure ratio, B) Graph demonstrating the fact that increasing R4 has no effect on flow pulsatilities

sided parameter, with no changes in flows or pressures occurring due to increasing compliance beyond around 20μF. The compliance of the spinal sub-arachnoid space (C5) provides a similarly one-sided effect, with flow pulsatilities no longer changing beyond 10μF, and the pressure pulsatilities no longer changing after around 60μF. Here though, the mean CSF pressure continues to decrease over a large range of compliances. Increasing the resistance to flow through the ventricles (R2) leads only to small differences in flow pulsatility, which have no observable effect on pressures, whereas increasing the compliance of the boundary between the brain and the ventricles (C2) increases the mean pressure in the CSF with associated changes in flow pulsatility. As the resistance to blood leaving the

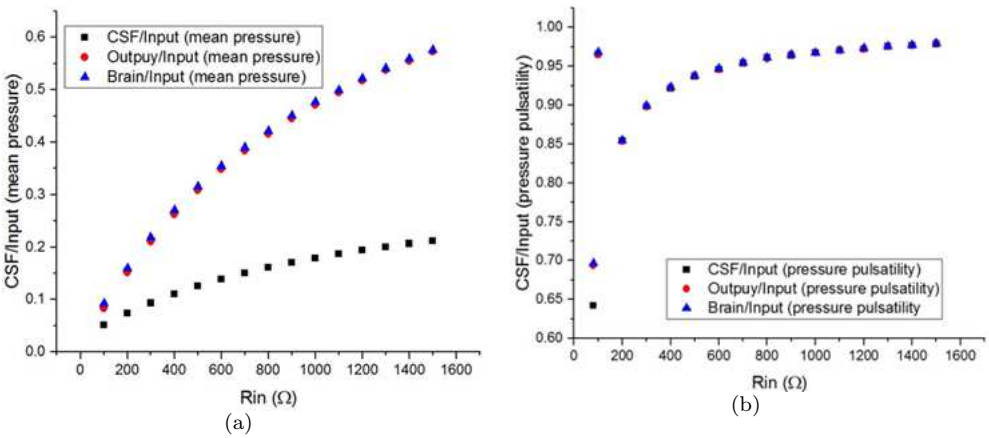


Figure 4: The effect of increasing both the infow resistance and R4 by a common factor on A) mean pressure normalised to input pressure, and B) pressure pulsatility normalised to input pressure pulsatility

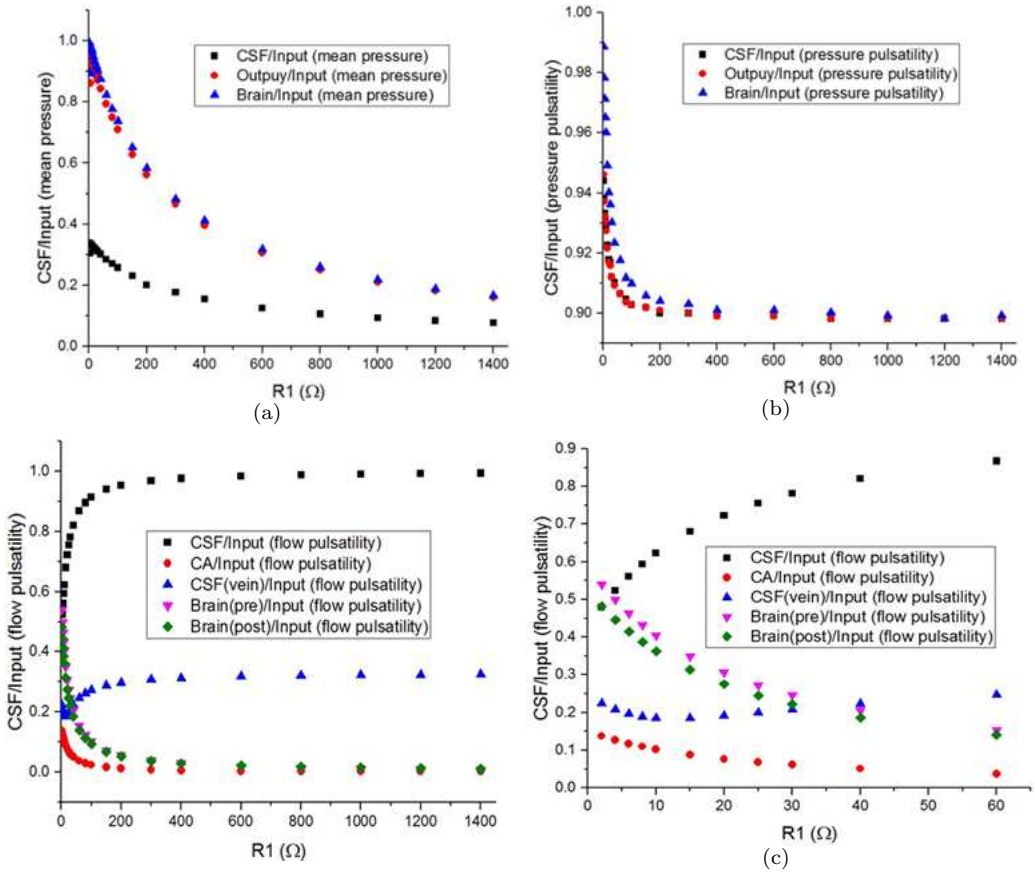
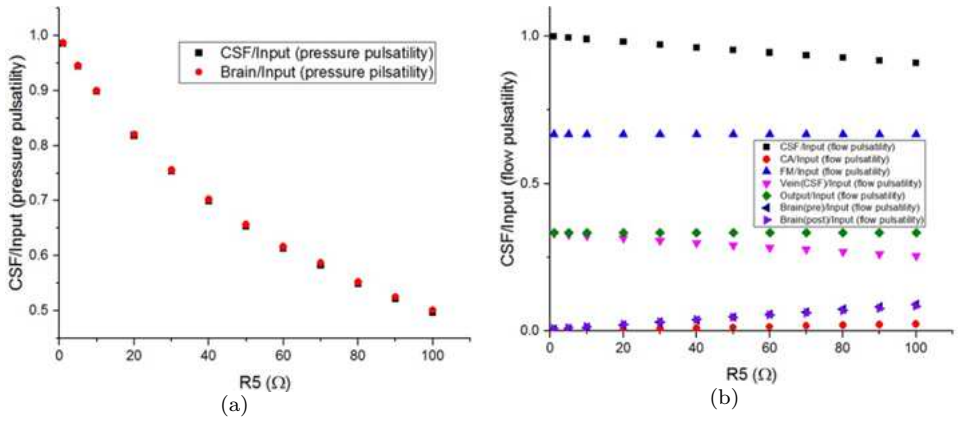


Figure 5: The effect of increasing R1 whilst keeping all other parameters constant on A)mean intracranial pressures normalised to input pressure, B) pressure pulsatility normalised to input pressure pulsatility, and C) and D) flow pulsatility normalised to inflow pulsatility

brain (R3) increases, the mean pressure in the brain decreases, forcing a change in the direction of flow pulsatility transfer leading to decreased flow pulsatility in the brain, with increased pulsatility in the CSF through the CA. The resistance to flow into the spinal sub-arachnoid space (R7) is the only parameter to have a significant effect on the pulsatility in the FM. The consequence of this reduction is an increase in the pressure pulsatility everywhere in the skull.

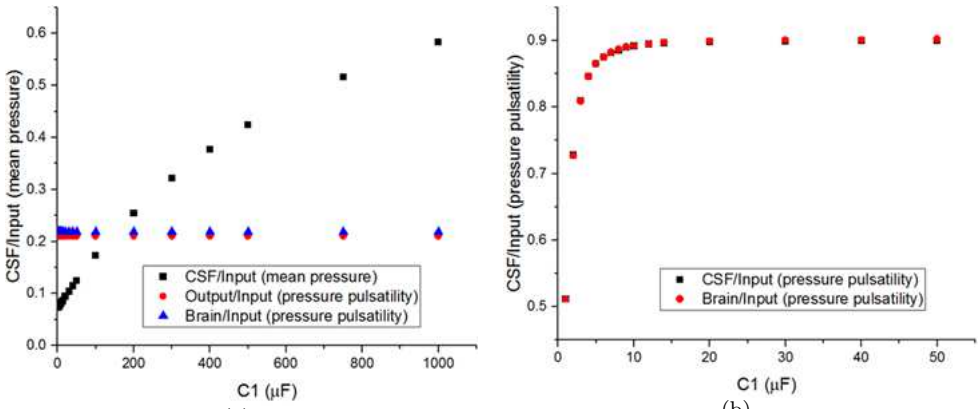
	Pressure pulsatility	Mean pressure	Flow pulsatility
CSF	Increase: R4, Rspine Decrease: R1, R3, R5, C4 Decrease followed by increase: C5	Increase: R4, C1, C2, C4 Decrease: R1, R3, C5	Increase: R1, C4 Decrease: R5
CSF (vein)	Increase: R4, Rspine Decrease: R1, R5 Decrease followed by increase: C5	Increase: R4 Decrease: R1	Increase: R3, Rspine, C2, C4, C4 Decrease: R1, R2, R5, C1, C5 Decrease followed by increase: R1
FM			Increase: C5 Decrease: Rspine
CA			Increase: R5, C2, Decrease: R1, R2, C1, C4, C5 Decrease followed by increase: R3, R3, Rspine
Brain (pre)	Increase: R4, Rspine Decrease: R1, R5, C4 Decrease followed by increase: C5	Increase: R4 Decrease: R1, R3	Increase: R5, Decrease: R1, R3, C1, C5
Brain (Post)	Increase: R3, R4, Rspine Decrease: R1, R5, C4 Decrease followed by increase: C5	Increase: R3, R4 Decrease: C4, R1	Increase: R5, Rspine Decrease: R1, R3, C1, C4, C5 Increase followed by decrease: R2, C2
Outflow	Increase: R4, Rspine Decrease: R1, R3, R5, C4 Decrease followed by increase: C5	Increase: Decrease: R1	Increase: Rspine Decrease: C5

Table 2: Summary of how altering parameters changes different behaviours within the skull



(a) (b)

Figure 6: The effect of increasing R5 whilst keeping all other parameters constant on A) intracranial pressure pulsatility normalised to input pressure pulsatility, and B) intracranial flow pulsatility normalised to inflow pulsatility



(a) (b)

Figure 7: The effect of increasing C1 whilst keeping all other parameters constant on A) mean intracranial pressures normalised to input pressure, and B) intracranial pressure pulsatilities normalised to input pressure pulsatility

Discussion

Equivalent electrical circuits have become a common way of constructing analogue models of biological systems. They are valid up to a point, specifically we must assume that all pressure changes with pressure compartments are instantaneously communicated. Voltages are set in accordance with the velocity of electrons, which is a sizeable fraction of the speed of light. As pressure moves at the speed of sound this is a relatively good approximation for most flow circuits. However, blood does not move this quickly, so the blood or CSF flow leaving an anatomical region may be delayed relative to the input. This can prove problematic at flow junctions. In the circuit considered here the main departure of the equivalent electrical circuit would be where blood exits brain tissue. At this point blood has been delayed by typically 6-10 seconds in comparison to the pressure wave induced in the CSF pool by the arteries. As a consequence the pressure wave induce by the CSF on the veins may be out of phase with the output flow. However, if output pulsatility from the brain is negligible, it will make little difference to the computed output. If we needed to take better account of this it would be necessary to include a delay somewhere in the model.

The addition of an inflow resistor (R6) and spinal resistor (R7) were required to complete the circuit. The inflow resistor prevents back-flow, and is justified because that blood pressure in the skull is significantly reduced compared to that in the body, and the existence of anatomical features such as the carotid syphon. This resistor was part of the original model proposed by Thacker, but was not estimable from available data at the time. The resistance of the spinal sub-arachnoid space (R7) is the only parameter which has a significant effect on the flow through the foramen magnum assuming that the compliance of the spinal sub-arachnoid space (C5) is reasonably large. The resistance of the spinal sub-arachnoid space was added to account for the ratio between the inflow pulsatility

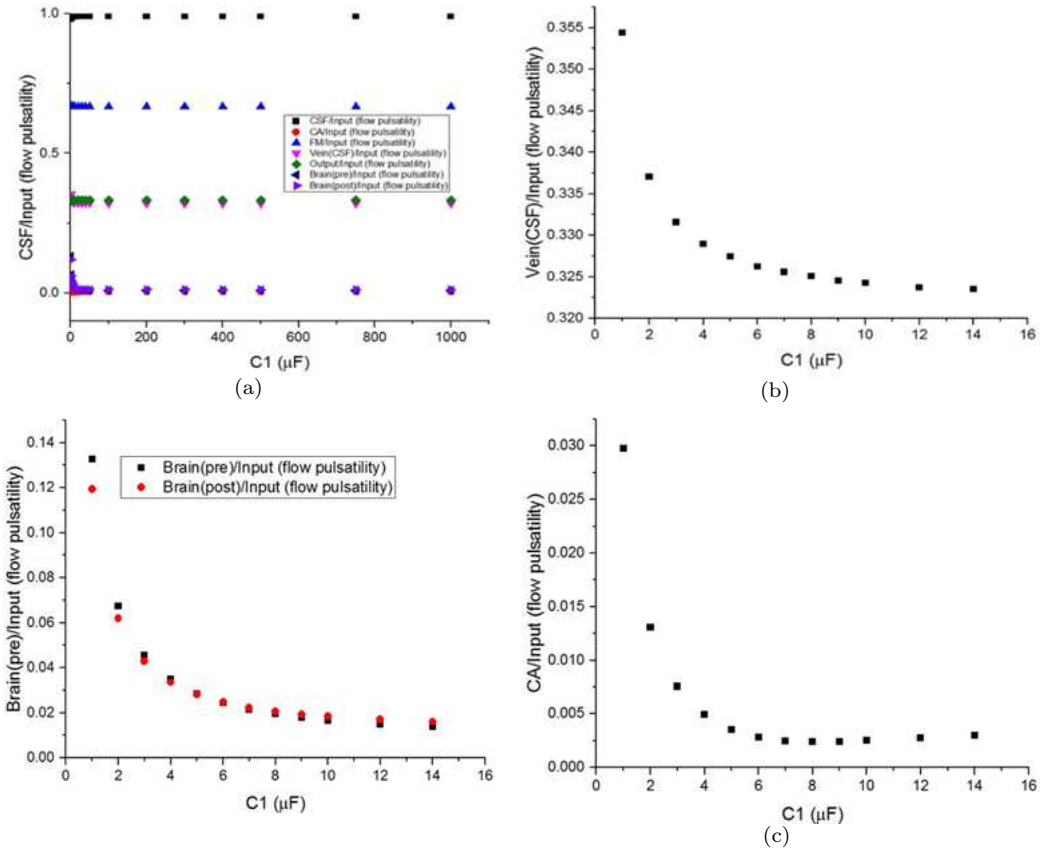


Figure 8: The effect of increasing C1 on A) Intracranial flow pulsatilities normalised to inflow pulsatility, B) flow pulsatility in the CSF space around the veins normalised to inflow pulsatility, C) flow pulsatility the brain normalised to inflow pulsatility, and D) flow pulsatility through the cerebral aqueduct normalised to inflow pulsatility

and the flow pulsatility through the FM. This resistance is likely to be a combination of viscous effects given the small aperture size, and resistances due to forces in the body. Unfortunately, the consequence of this additional resistance is increased pressure pulsatility throughout the skull (i.e. biologically a lower pressure pulsatility is better for the brain). It should be noted that the skull is not an entirely rigid casing, with soft anatomical features such as eyes limits the accuracy of this model.

With the addition of these two components, the circuit simulator was able to reproduce the flow pulsatility ratios derived from the MRI data of the population. The compliance of the capillaries (C3) is so small compared with the rest of the components that no observable effects arise from altering the value. Given this fact, it is reasonable to fix the value of this parameter. A number of parameters were found to be one sided with the flow pulsatilities being non-responsive beyond 20μ F for the arterial compliance (C1), and 4μ F for the compliance of the spinal sub-arachnoid space (C5). This lack of responsiveness is also observed when the resistance to flow through the ventricles exceeds 400Ω, but such a situation is unlikely to occur given that this value is estimated to be small.

Both the resistance to flow through the ventricles (R2) and resistance to flow out of the brain (R3) were poorly defined as being approximately zero. The only PC-MRI flow measurement to be affected by changes in these parameters is the flow pulsatility of CSF through the CA. Given accurate estimations of all other parameters, and very good data, this measurement should be able to identify the values of these two parameters more accurately, although there may be two possible solutions due to the turning point in CA flow pulsatility associated with the resistance to flow exiting the brain (R3).

The major CSF mean pressure alterations seem to be due to the arterial compliance (C1), and the compliance of the spinal sub-arachnoid space (C5). It seems clear that increasing CSF pressure would, in the first instance indicate a more rigid spinal sub-arachnoid space, or less rigid arterial input. Unfortunately flow pulsatilities are not affected by the arterial compliance (C1) beyond 20μ F, or the compliance of the spinal sub-arachnoid space (C5) beyond 4μ F. Increasing the compliance of the boundary between the brain and ventricles (C2) also increases the mean CSF pressure. Increasing the resistances to the flow of fluids exiting the skull increases the pressure pulsatility everywhere in the skull. This indicates that a blockage in any of these pathways would increase pressure pulsatility

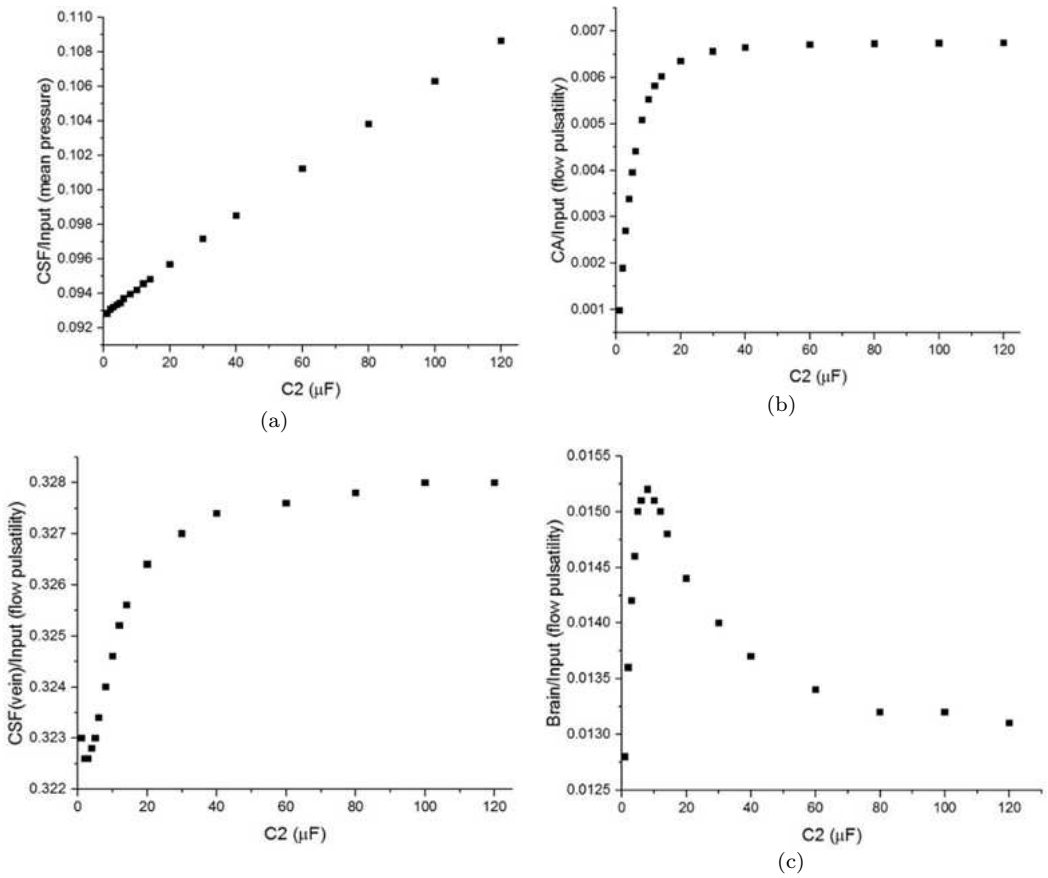


Figure 9: The effect of increasing C2 whilst keeping all other parameters constant on A) mean CSF pressure normalised to input pressure, B) flow pulsatility through the cerebral aqueduct normalised to inflow pulsatility, C) flow pulsatility in the CSF around the veins normalised to inflow pulsatility, and flow pulsatility through the brain normalised to inflow pulsatility.

leading to brain damage. The results indicate that high resistance to blood entering the brain is essential to the reduction of flow pulsatility within the brain, and pressure pulsatility throughout the skull. Pressure pulsatility remains approximately constant throughout the skull, whilst the mean pressures change significantly from one component to another. Increasing the compliance of the boundary between the brain and ventricles (C2) increases the mean CSF pressure. As should be expected, increasing the resistance to blood leaving the brain (R3) leads to an increased mean pressure in the brain.

Significant increases in CSF pressure do not have observable effects on the pressures of the blood through the brain. When the pressures in the blood are higher than those in the CSF this can be accepted logically, and it agrees with previous literature [5]. This trend is seen to continue when the CSF pressure becomes greater than the pressure of the blood through the brain. This is not a major concern, as Chopp indicated that the increasing CSF pressure would increase the pressure in the blood through venous collapse, and this is reproduced by an increase in the resistance to the outflow of blood from the brain (R3).

The pressure pulsatility to mean pressure ratio of both the blood entering the skull, and the blood leaving the skull can be tuned according to both absolute values and ratios of the inflow (R6), outflow (R4), and spinal (R7) resistances to some degree. The ratio of pressure pulsatility to mean pressure exiting the skull can be made equal to that in the body when the inflow resistance (R6) is 500 Ω, the outflow resistance (R4) is 450Ω, and the resistance of the spinal sub-arachnoid (R7) space is 225Ω. It should be noted that the pressure pulsatility to mean pressure ratio through the brain is also approximately equal to that in the body. The pressure pulsatility entering the skull at these values corresponds to a voltage of 9.7V, and this value is only decreased by approximately 6%. The mean pressures are greatly reduced everywhere, with the mean pressure in the brain being approximately 29% of that in the blood entering the skull. It is important to note that although the mean pressure of the blood entering the skull had decreased by approximately 21% (from 100V to 79.34V), the pressure pulsatility had decreased by over 75% (from 40V to 9.7V). This indicates that the reduction of pressure pulsatility is dependent almost entirely on the absolute values and ratios of the inflow resistance, and the two outflow resistances. It is likely that the overall

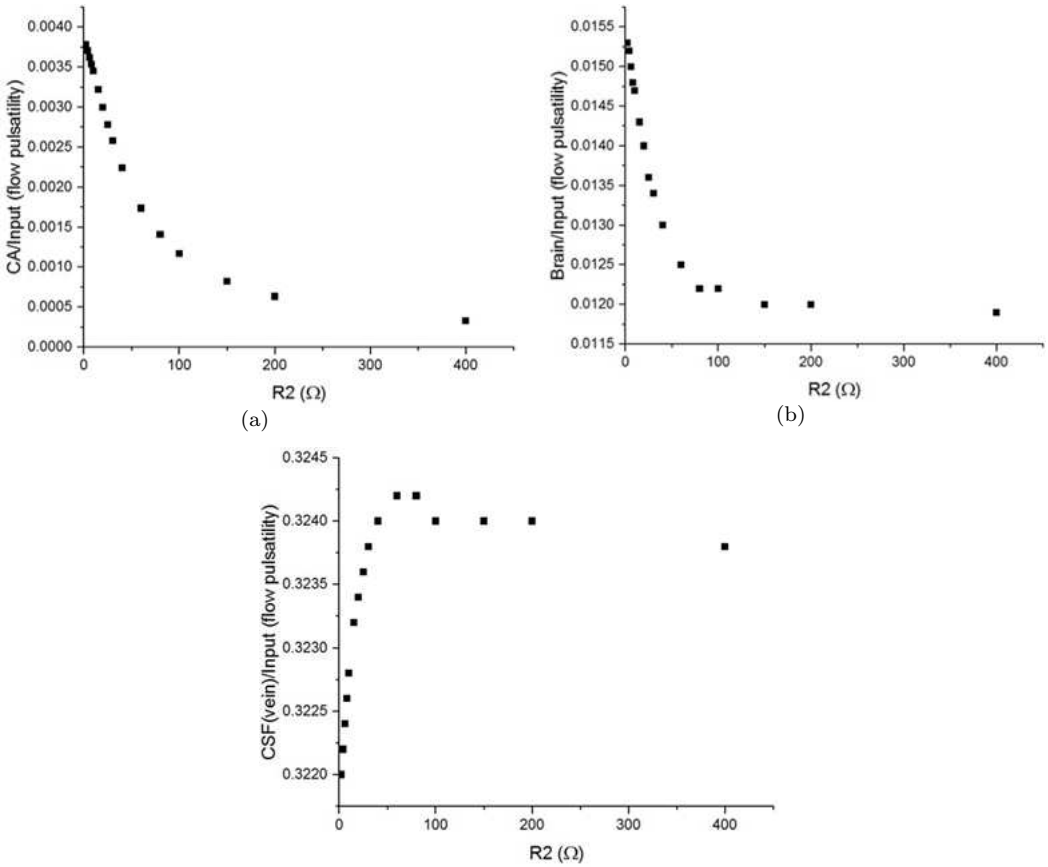


Figure 10: The effect of increasing R2 whilst keeping all other parameters constant on intracranial flow pulsatilities normalised to inflow pulsatility. A) through the cerebral aqueduct, B) through the brain, and C) in the CSF around the veins

impedance is important. The reduction of mean pressure has a greater dependence on the individual intracranial model parameters.

The model demonstrated that the mean pressure changes in the brain are significantly greater than that in the CSF for most values of parameters. Pressure pulsatility changes are global, whereas mean pressure changes differ significantly from one component to another.

The model has the ability to obtain an absolute measurement of pressure (mean and pulsatility) on an individual basis since the input pressure and frequency can be set according to the individuals resting heart rate and blood pressure measured using standard methods. The use of the model is limited to people with a reasonably steady heart rate and blood pressure. This is because the model is based on a stable input, as well as the fact that the quality of the PC-MRI data being dependent on this.

The model is effective, but does not fully describe the biology. It fails to address the fact that the anterior of the brain is supplied by the internal carotid arteries, and the posterior of the brain is supplied by the vertebral arteries which unite to become the basilar artery. A new model was created motivated by the theory that the brain exists as two semi-independent fluid dynamics systems. The model was briefly assessed to confirm that the additions do not need to alter the behaviour of the initial model. Further to this, it was found that the blood pressure through the vertebrobasilar component of the brain may be different to that of the internal carotid component, whilst the communicating CSF pools must have the same pressure. The model demonstrates that the pressure pulsatility in both areas of the brain will be equivalent, but that the mean pressures may be different. This should allow the relationship of the compliances of the two components of the brain to be better understood.

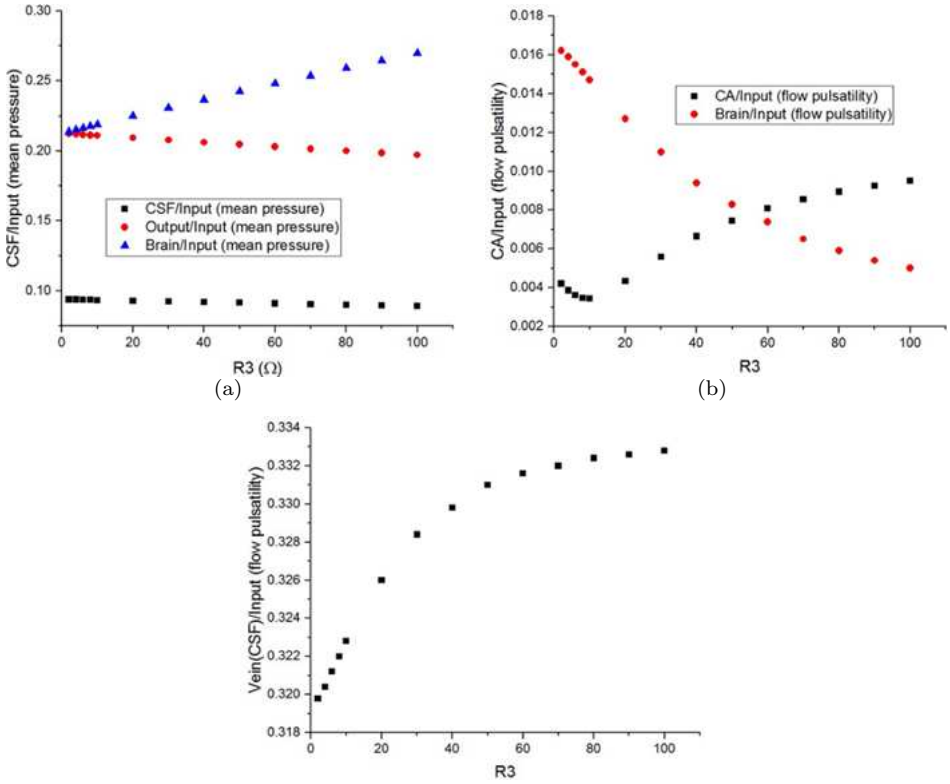


Figure 11: The effect of increasing R3 whilst keeping all other parameters constant on A) mean intracranial pressures normalised to input pressure, B) the flow pulsatilities through the brain and cerebral aqueduct normalised to inflow pulsatility, and C) the flow pulsatility in the CSF around the veins normalised to inflow pulsatility

Conclusion

The circuit simulator demonstrated that the parameters identified through model fitting to PC-MRI data could generate physically plausible flow and pressure behaviours. The addition of a spinal sub-arachnoid space resistance (R7) of approximately half the value of the outflow resistance (R4), and an inflow resistor (R6) were required to enable the model to be turned into an electrical circuit.

The capillary compliance is extremely small, and as such may be set as a constant value in future analysis. One sided effects (as seen in the original work) only really cause difficulty in assessing the arterial compliance (C1) in that any value beyond 20μ F cannot be observed through alterations in flow pulsatilities. Knowing how this mechanism originates, and on which parameters, should allow us to develop strategies for dealing with it appropriately when estimating parameters.

The flow pulsatility through the brain given the expected parameters is negligible (a few percent) compared to the flow pulsatility entering the skull. This makes a delay parameter (see discussion) necessary in normal subjects. The model therefore predicts a significantly reduces pressure stress on brain tissue for normal subjects. Approximately 1/3 of the flow pulsatility is transferred to the venous outflow, whilst 2/3 is dissipated via the spinal sub-arachnoid space. It is this mechanism which makes the model parameters estimable using PC-MRI data.

The resistances to the flow of blood into (R6), and out of (R4) the skull have a significant effect on mean pressure and pressure pulsatility with no effect on flow pulsatility. The compliance of the spinal sub-arachnoid space (C5) only affects the mean pressure of the CSF over a large range of values. Pressure pulsatility is affected everywhere in the skull up to a value of approximately 60μF by the compliance of the spinal sub-arachnoid space (C5), but the flow pulsatilities are only observed to change up to a value of 4μF. This is likely to cause issues when assessing patients where the spinal sub-arachnoid space is less compliant than it should be.

The resistance to flow in the spinal sub-arachnoid space is well defined in terms of the flow pulsatility through the FM. The use of a large resistance to flow pulsatility into the spinal sub-arachnoid space (R7) limits the reduction of pressure pulsatility. It is likely that other mechanisms exist to dissipate pressure pulsatility such as the fact that the skull cannot be represented as an entirely rigid casing. These effects are currently unquantifiable.

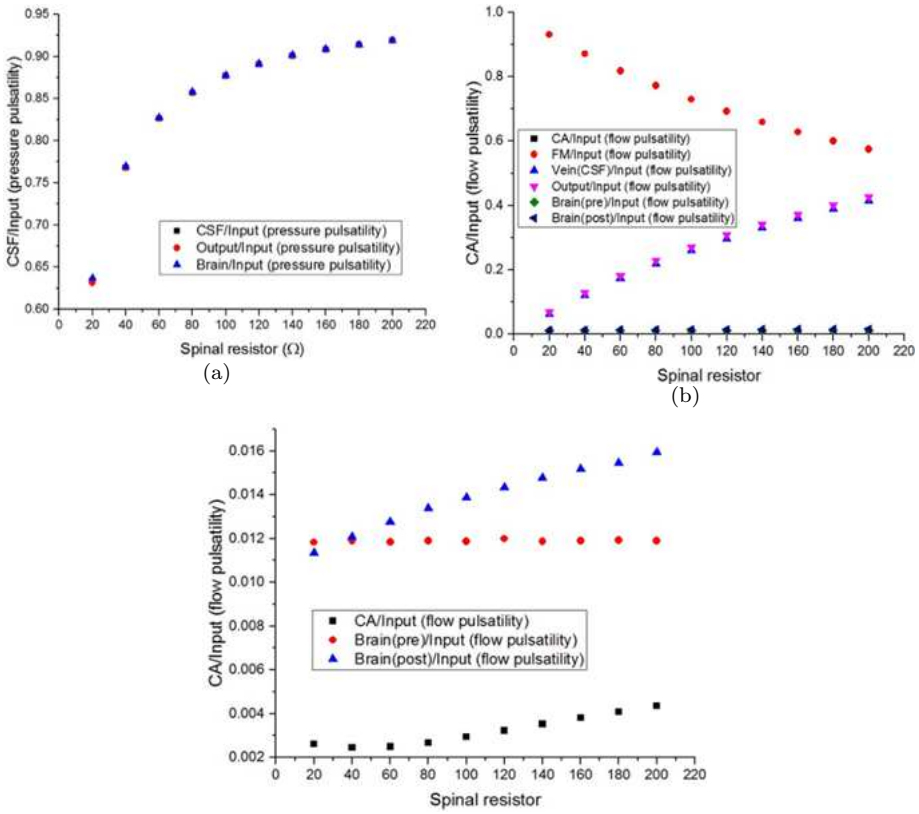


Figure 12: The effect of increasing the resistance to the spinal sub-arachnoid space on A) intracranial pressure pulsatilities normalised to input pressure pulsatility, B) and C) intracranial flow pulsatilities normalised to inflow pulsatility

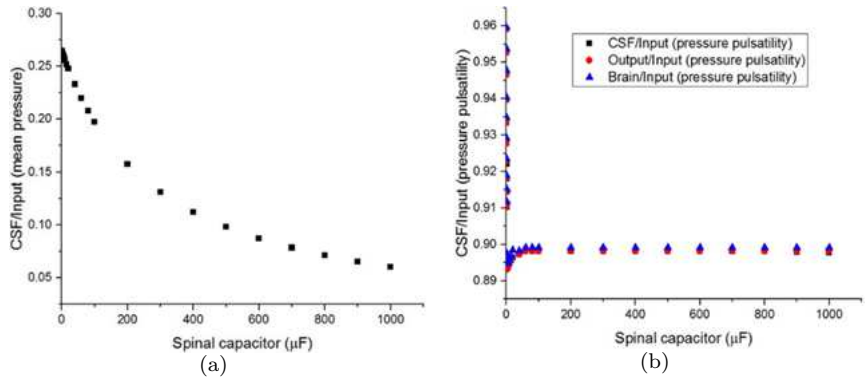


Figure 13: The effect of increasing the capacitance of the spinal sub-arachnoid space (C5) on A) the mean CSF pressure normalised to input pressure, and B) intracranial pressure pulsatilities with respect to input pressure pulsatility

The model demonstrates the possibility to estimate the mean pressures and pressure pulsatilities in the skull for individual patients. The ratio of systole and diastole pressures that are present in the body can be observed exiting the skull. The success of the model is dependent on the ability to obtain sufficient, high quality data to accurately describe all parameters of the model.

The model is effective in normal subjects, but it would need to extended in order to describe some pathologies, to account for the fact that the anterior part of the brain is supplied by the internal carotid system, and the posterior part of the brain is supplied by the vertebrobasilar system.

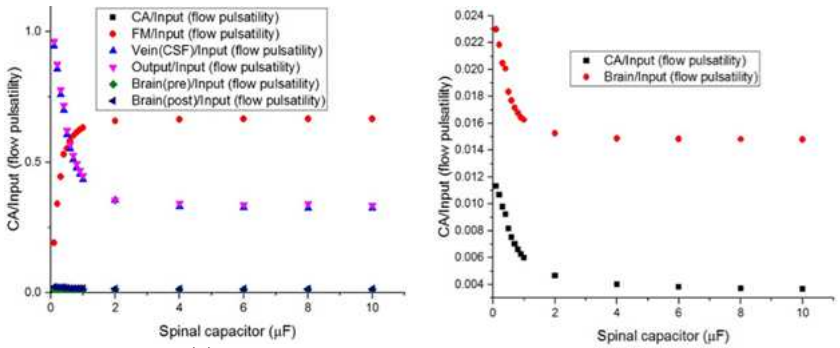


Figure 14: The effect of increasing the capacitance of the spinal sub-arachnoid space (C5) on intracranial flow pulsatilities normalised to the inflow pulsatility

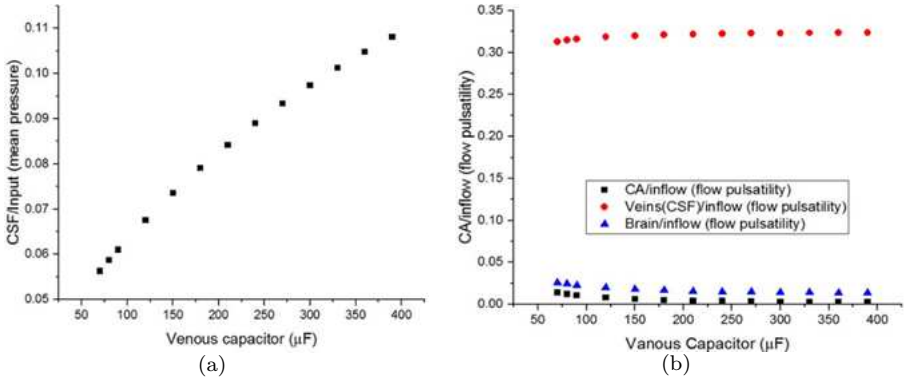


Figure 15: The effect of increasing the venous capacitor (C4) whilst all other parameters remain constant on A) mean CSF pressure normalised to input pressure, B) intracranial flow pulsatilities normalised to inflow pulsatility

References

[1] Thacker, N. A., et al. "An Electrical Equivalence Model for CSF Pulsatility." Tina memo, 2003-004, 2004.

[2] Kim, J., Thacker, N. A., Bromiley, S.J., Payne, J., and Jackson, A., "A Simple Electrical Equivalence Model of Intracranial Cerebrospinal Fluid Pulsatility: Design and Validation in Healthy Normals" Tina memo, 2006-003, 2006.

[3] Kim, J., Bromiley, S.J., Thacker, N.A., and Jackson, A., "Prediction of the Jugular Waveform using a Model of Cerebrospinal Fluid Dynamics

[4] http://falstad.com/circuit/

[5] Raboel, P. H., et al. "Intracranial pressure monitoring: invasive versus non-invasive methodsa review." Critical care research and practice 2012 (2012).

[6] Chopp, Michael, Harold D. Portnoy, and Craig Branch. "Hydraulic model of the cerebrovascular bed: an aid to understanding the volume-pressure test." Neurosurgery 13.1 (1983): 5-11.

[7] Takemae, Tadashi, et al. "A simulation study of intracranial pressure increment using an electrical circuit model of cerebral circulation." Biomedical Engineering, IEEE Transactions on 12 (1987): 958-962.

[8] Karni, Z., et al. "Quasi-steady-state compartmental model of intracranial fluid dynamics." Medical and Biological Engineering and Computing 25.2 (1987): 167-172.

[9] Ursino, Mauro. "A mathematical study of human intracranial hydrodynamics part 1the cerebrospinal fluid pulse pressure." Annals of biomedical engineering 16.4 (1988): 379-401.

[10] Ursino, Mauro. "A mathematical study of human intracranial hydrodynamics Part 2Simulation of clinical tests." Annals of biomedical engineering 16.4 (1988): 403-416.

[11] Ursino, Mauro, and Carlo Alberto Lodi. "A simple mathematical model of the interaction between intracranial pressure and cerebral hemodynamics." Journal of Applied Physiology 82.4 (1997): 1256-1269.

[12] Ursino, M., et al. "Intracranial pressure dynamics in patients with acute brain damage." Journal of Applied Physiology 82.4 (1997): 1270-1282.

[13] Stevens, S. A., and W. D. Lakin. "Local compliance effects on the global pressure-volume relationship in models of intracranial pressure dynamics." Mathematical and Computer Modelling of Dynamical Systems 6.4 (2000): 445-465.

[14] Lakin, William D., et al. "A whole-body mathematical model for intracranial pressure dynamics." Journal of mathematical biology 46.4 (2003): 347-383.

[15] Stevens, Scott A., William D. Lakin, and Paul L. Penar. "Modeling steady-state intracranial pressures in supine, head-down tilt and microgravity conditions." Aviation, space, and environmental medicine 76.4 (2005): 329-338.

[16] Stevens, Scott A., et al. "Idiopathic intracranial hypertension and transverse sinus stenosis: a modelling study." Mathematical Medicine and Biology 24.1 (2007): 85-109.

[17] Tain, RongWen, et al. "Determination of craniospinal canal compliance distribution by MRI: Methodology and early application in idiopathic intracranial hypertension." Journal of Magnetic Resonance Imaging 34.6 (2011): 1397-1404

[18] Tain, Rong-Wen, and Noam Alperin. "Noninvasive intracranial compliance from MRI-based measurements of transcranial blood and CSF flows: indirect versus direct approach." Biomedical Engineering, IEEE Transactions on 56.3 (2009): 544-551.

[19] Zagzoule, Mokhtar, and Jean-Pierre Marc-Vergnes. "A global mathematical model of the cerebral circulation in man." Journal of biomechanics 19.12 (1986): 1015-1022.