A Pulsatile Cerebrospinal Fluid Model for Hydrocephalus

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Workshop on Brain Biomechanics:
Mathematical Modelling of Hydrocephalus and Syringomyelia
Centre for Mathematical Medicine
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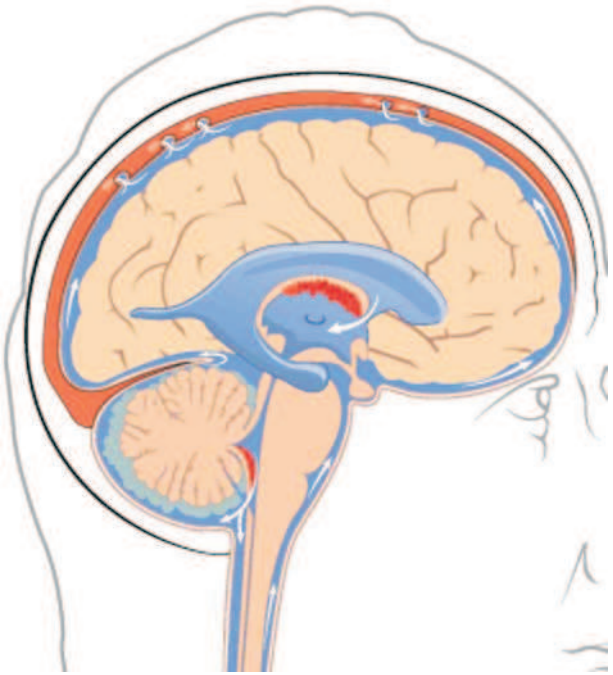
Collaborators

This work was done in collaboration with

- Prof. S. Sivaloganathan
- Prof. G. Tenti
- Dr. J.M. Drake
- Dr. A. Jea,

and was supported by NSERC.



[Medtronic, Inc. 2007]

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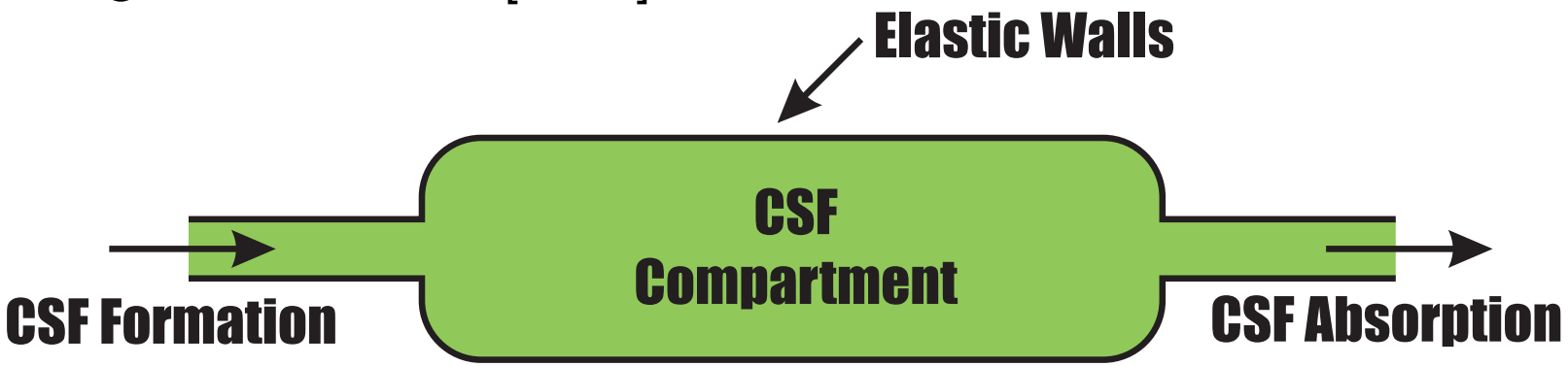
- Recent research by Egnor et al. [2001] and others suggest that CSF pulsations may be an important factor in the pathogenesis of hydrocephalus.
- The goal is to determine if these pulsations are mechanically relevant to the development of hydrocephalus.
- My tools include a one-compartment CSF model and a poroelastic thick-walled cylinder brain parenchyma model.
- The poroelastic model provides a time- and space-dependent analysis of the pulsations which demonstrate the mechanical effects the pulsations have on the parenchyma.

The One-Compartment CSF Model

This is an extension of the one-compartment model described in Sivaloganathan et al. [1998].



By the principle of conservation of mass, assuming CSF to be incompressible, the governing equation can be written as:

$$\begin{pmatrix} \text{rate of volume} \\ \text{change in time} \end{pmatrix} = \begin{pmatrix} \text{rate of CSF} \\ \text{formation} \end{pmatrix} - \begin{pmatrix} \text{rate of CSF} \\ \text{absorption} \end{pmatrix}. \quad (1)$$

The One-Compartment CSF Model

Since intracranial volume depends on pressure,

$$V(t) = V(P(t)),$$

and in mathematics we write,

$$\left(\begin{array}{c} \text{rate of volume} \\ \text{change in time} \end{array} \right) = \frac{\mathrm{d}V}{\mathrm{d}t} = \frac{\mathrm{d}V}{\mathrm{d}P}\frac{\mathrm{d}P}{\mathrm{d}t} = C(P)\frac{\mathrm{d}P}{\mathrm{d}t}, \qquad (2)$$

where $C(P)$ is the compliance function.

The One-Compartment CSF Model

The rate of CSF formation is assumed to be in the following form:

$$\begin{pmatrix} \text{rate of CSF} \\ \text{formation} \end{pmatrix} = \begin{pmatrix} \text{constant rate of} \\ \text{CSF formation} \end{pmatrix} + \begin{pmatrix} \text{pulsatile rate of} \\ \text{CSF formation} \end{pmatrix}$$
$$= \quad I_f^{(e)} + a\sin^2(\omega t), \tag{3}$$

where a is the displacement of CSF due to blood flow and ω is the angular frequency of the heart beat.

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Finally, experimental evidence has shown that

$$\begin{pmatrix} \text{rate of CSF} \\ \text{absorption} \end{pmatrix} = \frac{1}{R_a}(P(t) - P_{ss}), \tag{4}$$

where R_a is the resistance to CSF flow and P_{ss} is the sagittal sinus pressure.

The One-Compartment CSF Model

Putting all of this together gives a differential equation describing the pressure in the CSF model:

$$C(P)\frac{\mathrm{d}P}{\mathrm{d}t} + \frac{1}{R_a}(P(t) - P_{ss}) = I_f^{(e)} + a\sin^2(\omega t). \qquad (5)$$

I will consider two cases:

1. the simple case, when compliance is constant: $C(P) = C_0$, and
2. when compliance fits the experimental data: $C(P) = \frac{1}{kP}$.

Case 1. CSF Model with Constant Compliance

The differential equation

$$C_0 \frac{\mathrm{d}P}{\mathrm{d}t} + \frac{1}{R_a}(P(t) - P_{ss}) = I_f^{(e)} + a\sin^2(\omega t), \tag{6}$$

together with the initial condition $P(t=0) = P_0$, has the solution

$$\begin{aligned} P(t) = &\left(P_0 - R_a I_f^{(e)} - P_{ss} - \frac{aR_a 4\omega^2\tau_0^2}{2(1+4\omega^2\tau_0^2)} \right) e^{-\frac{t}{\tau_0}} \\ &+ \left(R_a I_f^{(e)} + P_{ss} + \frac{1}{2}aR_a - \frac{aR_a}{2\sqrt{1+4\omega^2\tau_0^2}} \right) \\ &+ \frac{aR_a}{\sqrt{1+4\omega^2\tau_0^2}} \sin^2\left(\omega t - \frac{1}{2}\tan^{-1}(2\omega\tau_0) \right), \end{aligned} \tag{7}$$

where $\tau_0 = C_0 R_a$ is the characteristic time.

Case 1. CSF Model with Constant Compliance

Looking at the oscillating term, (remember $\tau_0 = C_0 R_a$)

$$\frac{aR_a}{\sqrt{1+4\omega^2\tau_0^2}} \sin^2\left(\omega t - \frac{1}{2}\tan^{-1}(2\omega\tau_0)\right),$$

- if $\frac{1}{C_0 R_a} << 2\omega$ then the resulting phase shift is $\frac{\pi}{4}$,
- if $\frac{1}{C_0 R_a} = 2\omega$ then the resulting phase shift is $\frac{\pi}{8}$, and
- if $\frac{1}{C_0 R_a} >> 2\omega$ then the resulting phase shift is 0,

i.e. the CSF pulsations are synchronous with the forcing.

Case 1. Simulations

Typical values of the parameters for a normal adult are [Shapiro et al. 1979]:

- $P_{ss} = 12.2$ mm Hg
- $R_a = 2.8$ mm Hg/ml/min
- $C_0 = 0.85$ ml/mm Hg.

Also chosen were

- $I_f^{(e)} = 0.35$ ml/min,
- $\omega = 140\pi$ rad/min, and
- $a = 2$ ml/min.

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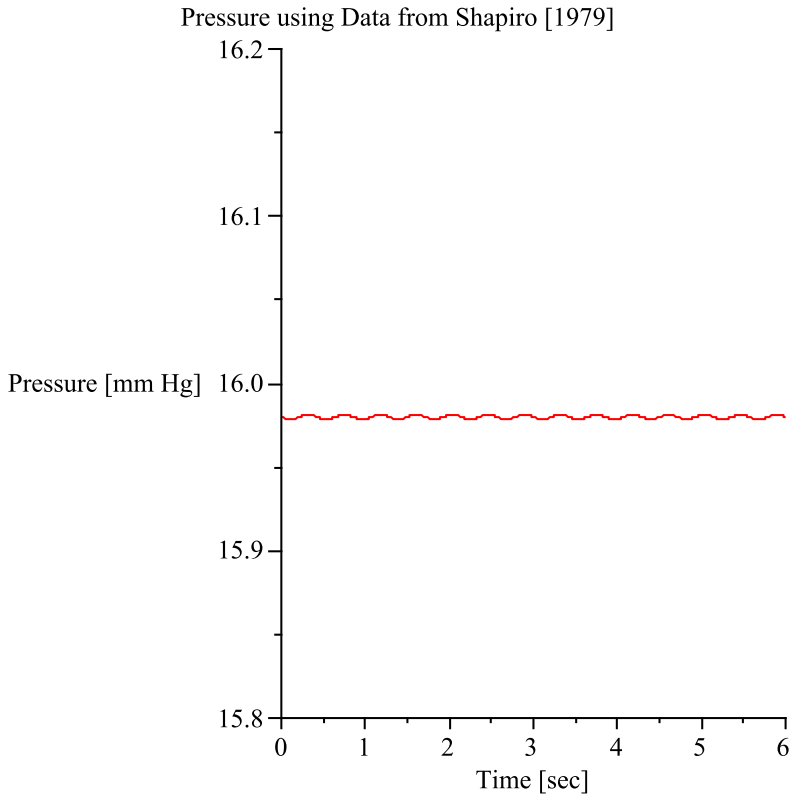
Using these values, the model predicts pressure pulsations that would not be visible on typical ICP measurements.



Case 1. Simulations

Using $I_f^{(e)} = 0.35$ ml/min,
$P_{ss} = 10$ mm Hg, and
$\omega = 140\pi$ rad/min, and
requiring that the:

- pressure pulsations have peak-to-peak amplitude of 5 mm Hg,
- mean CSF pressure is 13.5 mm Hg, and
- the phase shift is zero (i.e. synchrony exists)

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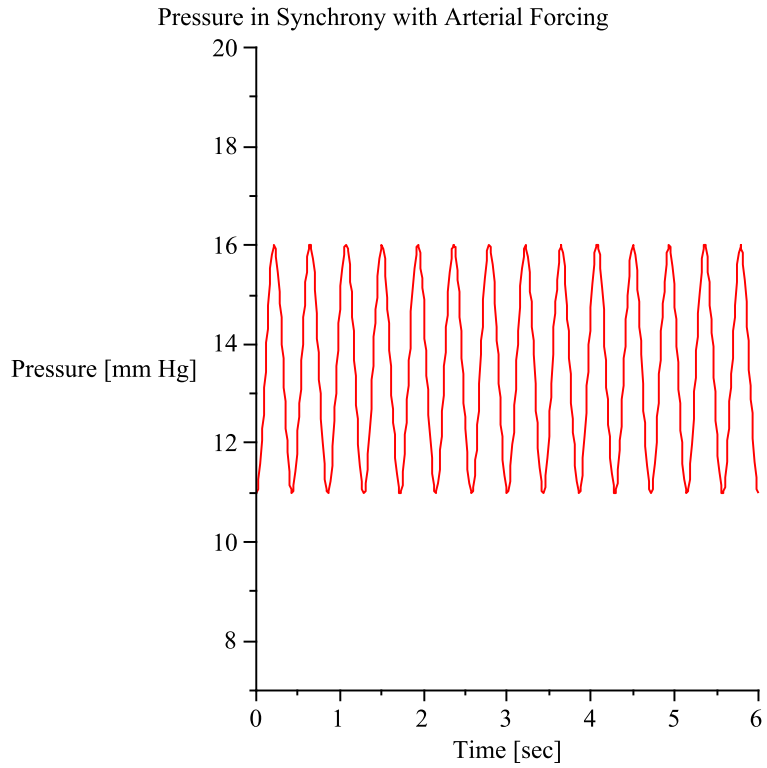
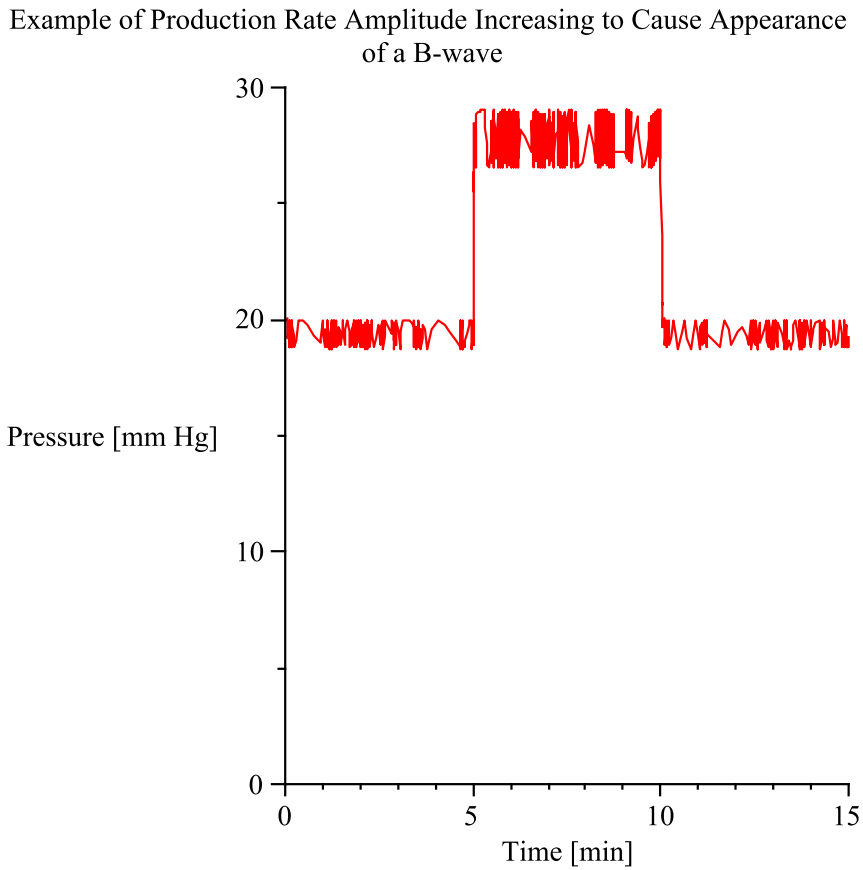


results in a waveform consistent with experiments and values of:

- $R_a = 2.86$ mm Hg/ml/min
- $C_0 = 3.98 \cdot 10^{-6}$ ml/mm Hg, and
- $a = 1.75$ ml/min.

Case 1. Simulations

Time changes in the amplitude of the pulsatile CSF formation rate (a), the base CSF formation rate ($I_f^{(e)}$), and the resistance to CSF absorption (R_a) may help explain the appearance of plateau or B waves observed in patients with hydrocephalus.

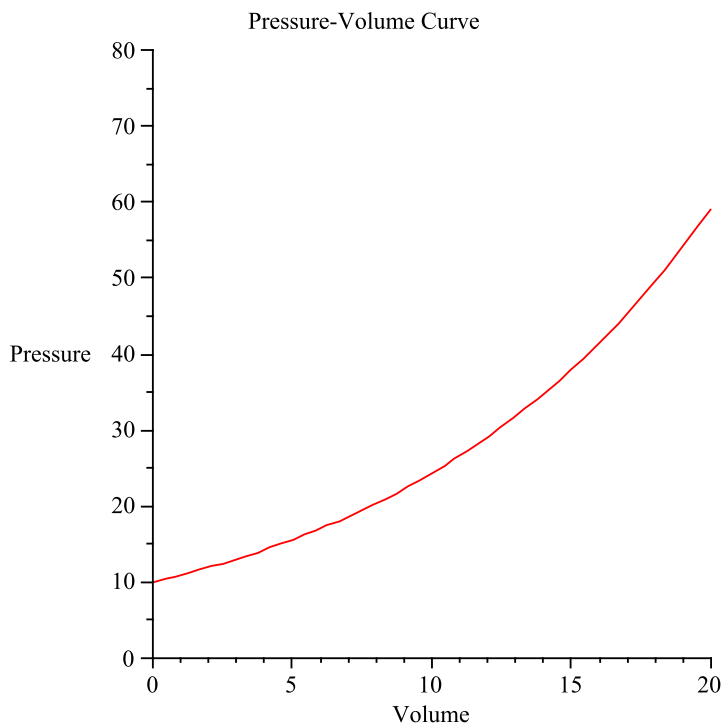


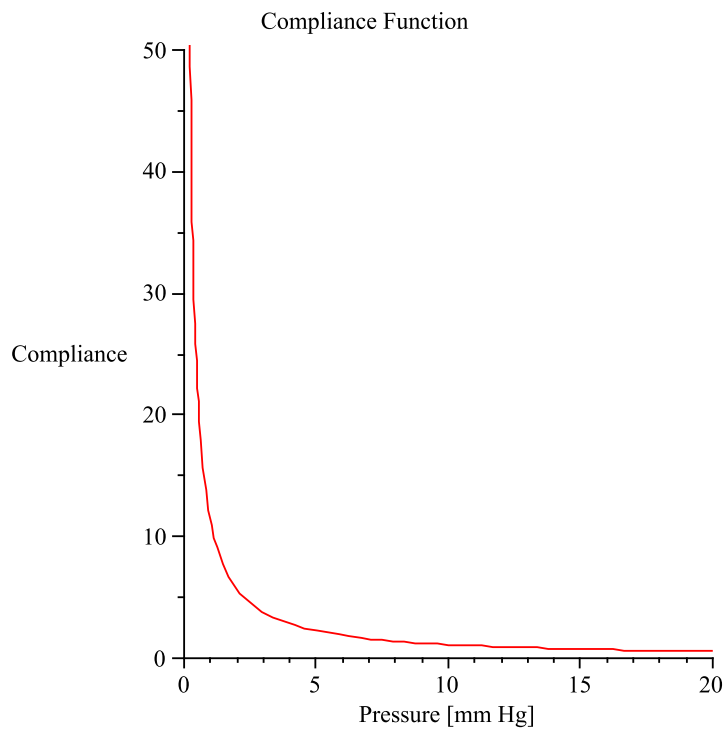
Case 2. CSF Model with Experimental Compliance

In 1978, Marmarou et al. determined that the pressure-volume relationship is exponential, implying that compliance is of the form

$$C = \frac{1}{kP},$$

where $\frac{\ln 10}{k}$ is known as the pressure-volume index (PVI).





Case 2. CSF Model with Experimental Compliance

The governing differential equation now becomes

$$\frac{1}{kP(t)}\frac{\mathrm{d}P}{\mathrm{d}t} + \frac{1}{R_a}(P(t) - P_{ss}) = I_f^{(e)} + a\sin^2(\omega t), \tag{8}$$

which is a Riccati equation with solution

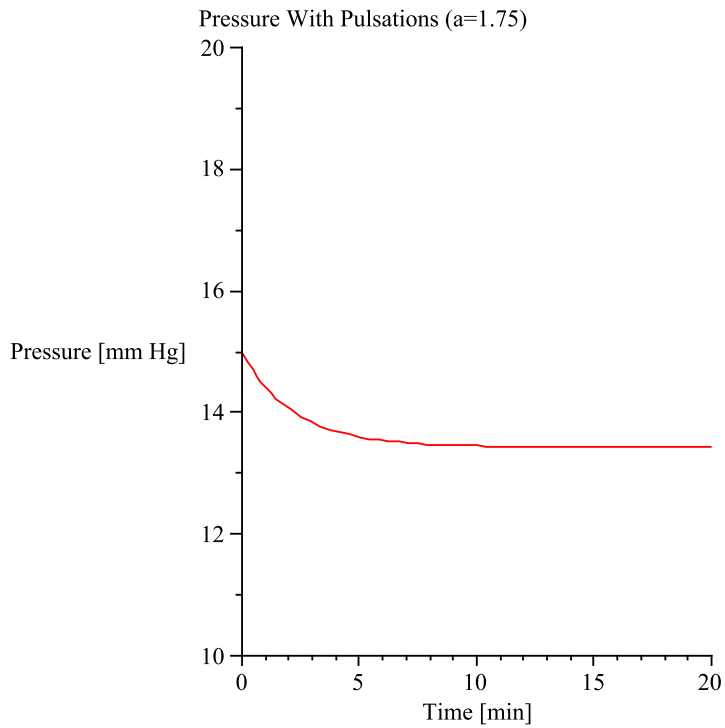
$$P(t) = \frac{P_0 e^{k(I_f^{(e)} + \frac{P_{ss}}{R_a} + \frac{a}{2})t - \frac{k}{4\omega}a\sin(2\omega t)}}{1 + k\frac{P_0}{R_a}\int_0^t e^{k(I_f^{(e)} + \frac{P_{ss}}{R_a} + \frac{a}{2})s - \frac{k}{4\omega}a\sin(2\omega s)}\mathrm{d}s}. \tag{9}$$

Case 2. Simulations

Using parameter values of

- $R_a = 2.8$ mm Hg/ml/min [Shapiro 1979]
- $I_f^{(e)} = 0.35$ ml/min
- $k = \frac{2.3026}{25.9}$ ml^{-1} [Shapiro 1979]
- $a = 1.75$ ml/min

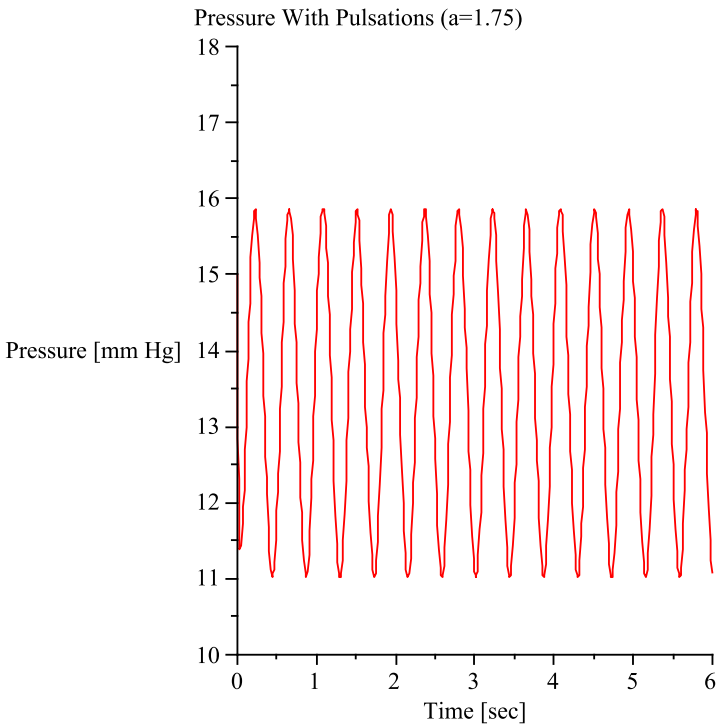
the compliance of the compartment is approximately 0.8 ml/mm Hg which is too large to allow pulsations with a peak-to-peak amplitude of 5 mm Hg.



Case 2. Simulations

To decrease compliance, the pressure-volume index must decrease.

Choosing $PVI = 0.002$ ml gives $k = 1151.3$ ml^{-1}
which corresponds to a compliance of approximately
$C = 6.4 \cdot 10^{-5}$ ml/mm Hg. Setting $a = 1.75$ ml/min results in a presure profile with peak-to-peak amplitude of about 5 mm Hg.



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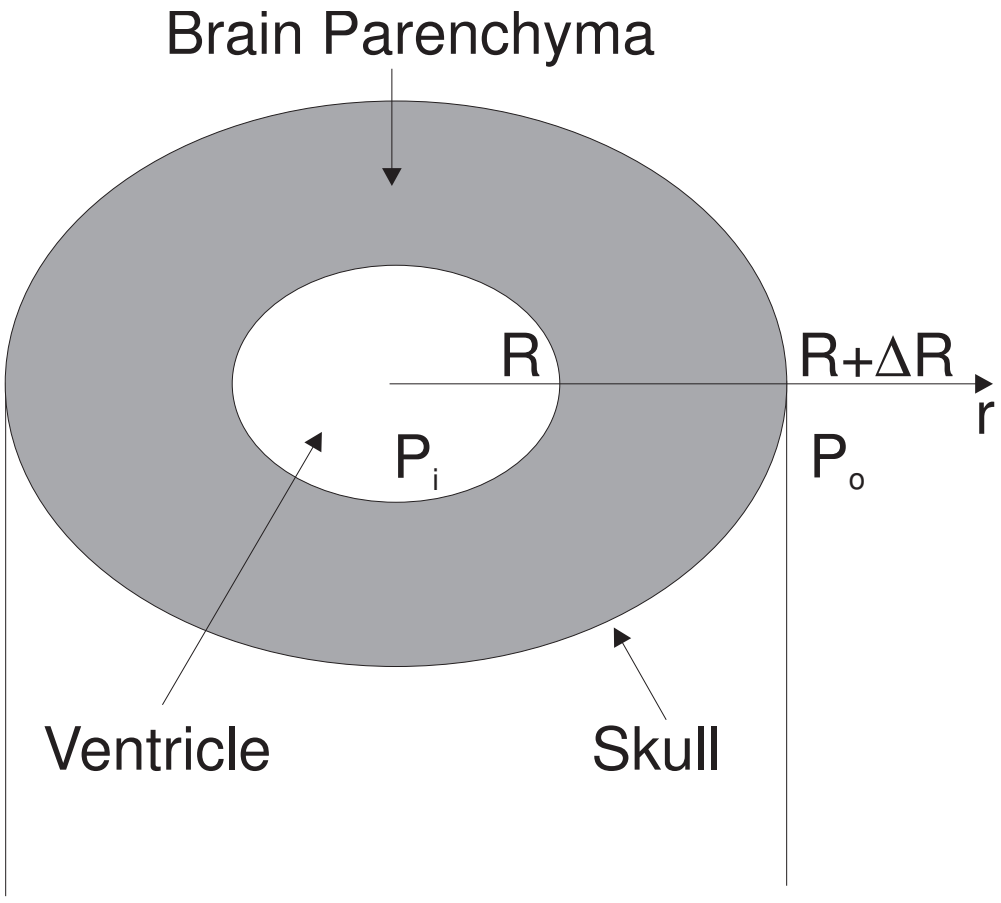
- The model assumes that pressure is equal everywhere in the compartment which is not true in the cranium,
  (i.e. compare the pressure at the foramen magnum to that of the subarachnoid space.)
- Thus, we need to develop a distributed model, like the poroelastic model, which allows pressure to vary in space as well as in time.

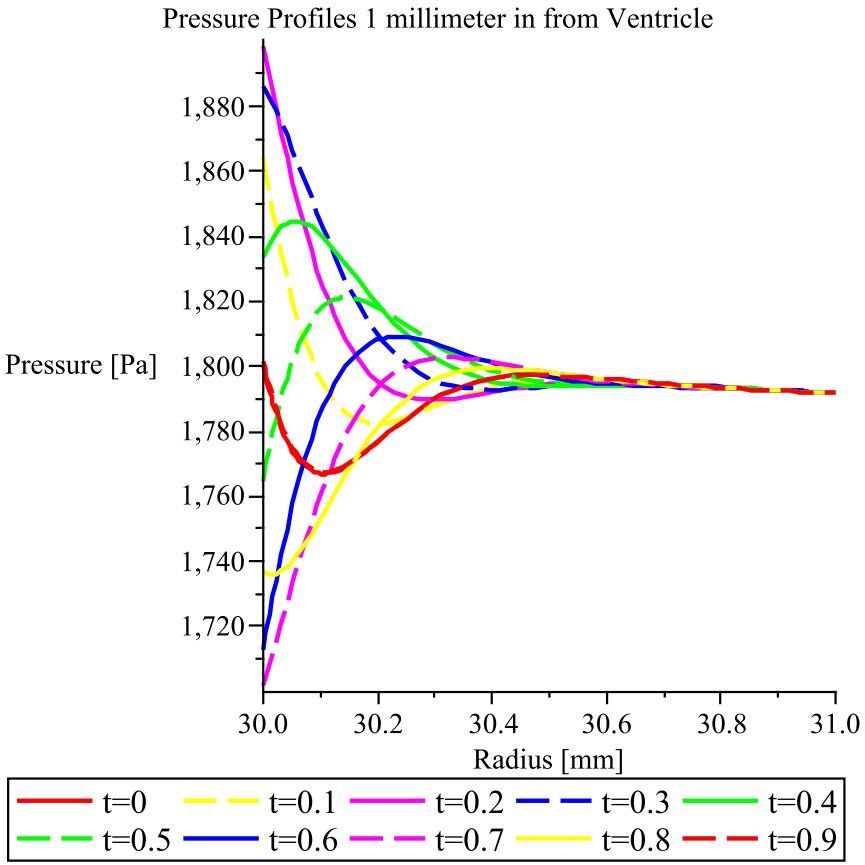
A Poroelastic Model

Following Kenyon [1976] and Tenti et al. [1999], the model geometry is a thick walled porous cylinder:



A Poroelastic Model

Applying periodic forcing to the boundaries to simulate the effect of CSF pulsations on the brain parenchyma results in CSF oscillating in and out of the parenchyma near the boundaries.



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Future Directions

Using the poroelastic model,

- determine if the mechanical effects of the CSF pulsations on the parenchyma are significant.
- determine the difference between the CSF pulsations when the cranium is closed compared to when it is open (i.e. under surgical conditions).
- extend these ideas to syringomyelia.

References

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