A Lumped-parameter Model of the Cerebrospinal System for Simulating Syringomyelia

Novak S. J. ELLIOTT [1,*], Duncan A. LOCKERBY [2], Andrew R. BRODBELT [3]

* Corresponding author: Tel.: +61 (0)8 9266 3926; Fax: +61 (0)8 9266 2681; Email: n.s.j.elliott@curtin.edu.au
1: Fluid Dynamics Research Group, Department of Mechanical Engineering, Curtin University of Technology, Australia
2: Fluid Dynamics Research Centre, School of Engineering, University of Warwick, UK
3: The Walton Centre for Neuroradiology and Neurosurgery NHS Trust, Liverpool L9 7LJ, UK

Abstract Syringomyelia is a disease in which high-pressure fluid-filled cavities, called syrinxes, form in the spinal cord (SC) which can cause progressive loss of sensory and motor functions. Poor treatment outcomes have led to myriad hypotheses for its pathogenesis, which unfortunately are often based on small numbers of patients due to the relative rarity of the disease. However, accumulating evidence in the last decade from animal studies implicates arterial pulsations in syrinx formation. In particular, it has been suggested that a phase difference between the pressure pulse in the spinal subarachnoid space and the perivascular spaces, due to a pathologically disturbed blood supply, could result in a net influx of cerebrospinal fluid (CSF) into the SC. A lumped-parameter model is developed of the cerebrospinal system to investigate this conjecture. It is found that although this phase-lag mechanism may operate, it requires the SC to have an intrinsic storage capacity due to the collapsibility of the contained venous reservoir. If this storage requirement is met then the results presented here suggest that, on mechanical grounds, a syringo-subarachnoid shunt may be a better surgical treatment option than a subarachnoid bypass for post-traumatic syringomyelia.

Keywords: Cerebrospinal Fluid, Perivascular Flow, Spinal Disease

1. Introduction

Pressure pulsations of the CSF result from changes in blood volume in the closed craniospinal cavity. Although percussive events such as coughing entrain relatively large pressure fluctuations in the spinal subarachnoid space (SSS) through venous distension [50 mmHg; 1], a recent analysis suggests that the peak pressure differentials are not consistent with syrinx locations [2]. Moreover, these events are isolated and do not offer a mechanism for the maintenance of a raised intramedullary pressure. Alternatively, the cardiac cycle provides the CSF with a source of continuous, albeit smaller, pressure pulsations. If the dynamic equilibrium of this system were adversely perturbed then the progression of any ill effects may be slow but unrelenting.

The cardiac cycle sets up a spinal CSF pulse wave, about 40% of which is generated by spinal arterial pulsations, an equal contribution comes from spinal venous pulsations and the intracranial CSF pulse wave passing through the spinal canal from the brain contributes the remaining 20% [3]. The CSF in the SSS communicates with the fluid in the SC via the perivascular spaces (PVS) that fenestrate the pial membrane. Of these, the microscopic passages around central arteries have been suggested as the main route [4]. Syringomyelia is a situation involving localized build up of fluid in the SC—which might be due to a disruption in the mechanism that normally regulates flow between the regions on either side of the pial membrane. It was demonstrated by Stoodley et al. [5] in animal studies that perivascular flow from the SSS into the central canal is abolished when the SC arterial pulsation is reduced while maintaining mean arterial pressure. The same

CSF pathway was observed into extracanalicular syrinxes [6], which was the preferential destination when accompanied with a subarachnoid block [7].

The resistance to flow through a PVS is set by the level of inflation of the vessel passing through it. This, in turn, is set by the cardiac pulse—the same pressure source that provides the CSF with its pulsation. Bilston et al. [4] proposed that phase differences between the SSS and arterial pulse waves enhance perivascular flow. In a CFD model consisting of a small section of the SSS with one PVS they found that perivascular inflow was maximal when peak SSS pressure coincided with minimum cardiac pressure. Perturbations to a normal phase difference might occur as a result of scar tissue, associated with syrinxes, interrupting the local blood supply. Although Bilston et al.'s [4] model was only intended to demonstrate the possibility of phase-dependent perivascular flow, its usefulness is limited by the fact that the greater part of the cerebrospinal system was omitted, all of which would normally be in direct hydraulic communication with the small section modelled.

To address the above concerns, a lumped-parameter model of the complete cerebrospinal system was constructed. Pial conductance was allowed to vary periodically with a phase lag with respect to the SSS vascular pressure. The governing equations were solved numerically allowing long-timescale simulations to reach a periodic steady state. The sensitivity of SSS-cardiac phase differences to changes in local and system parameters was investigated, leading to the simulation of disease conditions and treatment options.

2. Method

2.1 Theoretical model

The human cerebrospinal system was divided into a set of compartments as shown in Fig. 1. Standard circuit elements are used to denote intercompartmental compliance (capacitor) and conductance (resistor, the reciprocal quantity). The SC and SSS compartments are adjacent, being separated only by the compliant pial membrane, through which passes the PVS. The vascular pressure source is overlaid onto the SC and SSS to show diagrammatically (in two dimensions) how these three functional spaces communicate. CSF may be exchanged between the SC and SSS via the PVS, which is quantified by a conductance (z_{PVS}), and associated changes in volume may be accommodated by the compliance of the pial membrane (c_{PVS}).

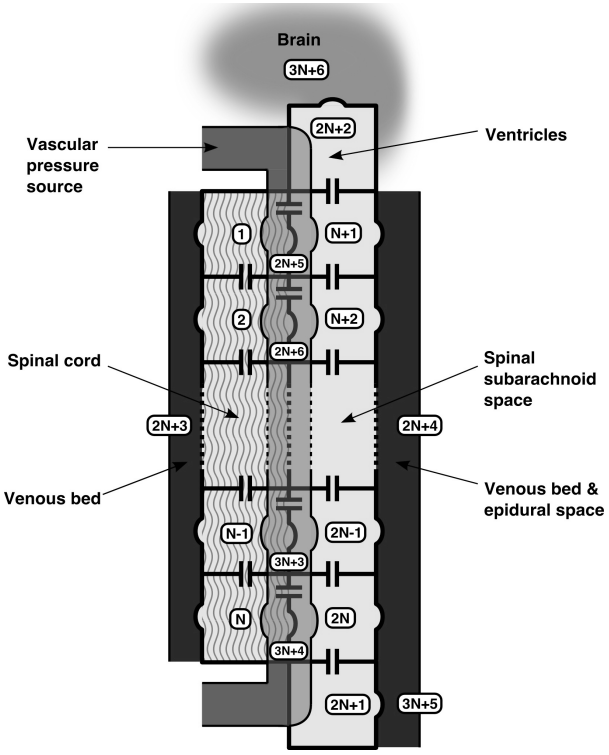

Fig. 1: Schematic diagram of the lumped-parameter model.

There are also conductances associated with CSF flow downward from the SSS proper to the extent of the filum terminale (z_{FT}), or upward into the cerebral ventricles (z_V). The vascular network in the spinal canal was functionally divided into excitation source and volume storage. The vascular source compartments provide the driving pressure to the SC and SSS via compliant interfaces ($c_{Vasc,SC}$ and $c_{Vasc,SSS,}$ respectively), representing combined arterial and venous contributions. The SC contains a venous bed compartment which, upon collapse, will eject

blood towards the heart and in doing so make room for more fluid in the SC (c_{SC}). A similar effect will occur in the SSS except that the compliance also accounts for the displacement of epidural fluid (c_{SSS}). Likewise the ventricular compartment can accommodate extra CSF by reduction in cerebral blood volume, represented as a compliance with the brain compartment (c_{Brain}). The spinal axis was discretized into N segments, each containing a SC, SSS and vascular source compartment; there were n (= $3N$+6) compartments in total, the first m (= $2N$+2) of which contained CSF.

The governing equations take the form of a system of first-order ordinary differential equations,

$$\mathbf{C}\dot{\mathbf{p}}(t) + \mathbf{Z}(t)\mathbf{p}(t) = \mathbf{s}(t), \qquad (1)$$

where $\mathbf{p} = \{p_1, p_2, \ldots, p_m\}$ are the CSF compartment pressures, $\mathbf{C}$ and $\mathbf{Z}$ are coefficient matrices given by

$$C_{ij} = \begin{cases} \sum_{k=1}^{n} c_{i,k}, & i = j \\ -c_{i,j}, & i \neq j \end{cases}, \qquad (2a)$$

$$Z_{ij} = \begin{cases} \sum_{k=1}^{n} z_{i,k}, & i = j \\ -z_{i,j}, & i \neq j \end{cases}, \qquad (2b)$$

the elements of the source vector $\mathbf{s}$ are

$$s_i = q_i + \sum_{k=m+1}^{n} \left(c_{i,k} \frac{\mathrm{d}\, p_k}{\mathrm{d}\, t} + z_{i,k} p_k \right); \qquad (3)$$

and $c_{i,j}$ and $z_{i,j}$ denote the compliance and conductance between a pair of compartments i and j, respectively. Neither the production nor absorption of CSF are included ($q_i \equiv 0$). The brain, the venous bed of the SC, and the venous bed of the SSS combined with the epidural space are all considered to be connected to sufficient compliance for a change in volume to produce a negligible change in pressure, and none of these compartments have a flow connection with the CSF compartments so they will not contribute to $\mathbf{s}$; i.e., $\mathrm{d}p_k/\mathrm{d}t \approx 0$ and $z_{i,k} \equiv 0$ for $k = 2N$+3, $2N$+4, $3N$+5, $3N$+6.

The vascular pressure varies sinusoidally and appears as a source term; for segment k,

$$p_k(t) = \bar{p}_{\mathrm{Vasc}} + \hat{p}_{\mathrm{Vasc}} \sin\{\omega_{\mathrm{HR}}[t - (k-1)\tau_{\mathrm{seg}}]\}, \qquad (4)$$

where $\bar{p}_{\mathrm{Vasc}}$ is the mean and $\hat{p}_{\mathrm{Vasc}}$ the amplitude of the pulse, ω_{HR} is the oscillation frequency (HR denotes heart rate), and τ_{seg} is the time required for the pulse wave to travel the length of one segment. The cardiac cycle will also cause the central arteries in the PVS to pulsate and thus the conductance of the pial membrane to vary periodically. For a given compartment pair in segment i of N, the transpial conductance is defined as

$$z_{i,N+i}(t) = \bar{z}_{i,N+i} + \hat{z}_{i,N+i} \sin\{\omega_{HR}[t - (i-1)\tau_{seg}] + \pi - \theta_i\} \qquad (5)$$

2.2 Physiological parameters

The values of the various compliances and conductances were estimated from the literature (c_{SSS} [8]; c_V [9]; z_{Pia} [10]; z_{SSS} [11]; z_{SC} [12,13]; z_V [14]; marked '*' in Table 1) as well as simple calculations from anatomical measurements; these are summarized in Table 1. In all cases it was assumed that $c_{i,j} = c_{j,i}$ and $z_{i,j} = z_{j,i}$ for adjacent compartments i and j. To evaluate the source pressure and pial conductance several further quantities were required. The vascular pulse was prescribed by a mean pressure of 1.33 kPa (10 mmHg), an amplitude of 133 Pa (1 mmHg), a frequency of 1 Hz, and a pulse wave velocity of 5 m/s. The amplitude of the pial conductance pulsations was set at half the mean value.

Table 1 Values of physiological parameters.

Parameter	Value (m^3/Pa)	Parameter	Value (m^3/Pa·s)
c_{Pia}	2×10^{-10}	z_{Pia}*	1.0×10^{-11}
c_{SSS}*	2.9×10^{-9}	z_{SSS}*	4.3×10^{-9}
c_{SC}	1.0×10^{-10}	z_{SC}*	4.9×10^{-16}
c_{FT}	2.9×10^{-9}	z_{FT}	1.3×10^{-8}
c_V*	1.6×10^{-9}	z_V*	3.8×10^{-8}
$c_{Vasc,SSS}$	1×10^{-10}		
$c_{Vasc,SC}$	0		

3 Results

3.1 Phase-lag mechanism

Figure 2 shows the converged steady state solution for a 10-segment model having $\mathbf{p}(0) = \mathbf{0}$. A non-zero $\overline{\Delta p}$ $(= \overline{p}_{SC} - \overline{p}_{SSS})$ profile exists for each value of θ; the trend in x (rostrocaudal position, a normalised coordinate from the top to the bottom of the spine) is due to the finite pulse wave velocity. However, this mean transpial pressure difference was abolished when either the pial conductance was held constant or the intrinsic compliance of the SC (due to the collapse of the contained venous bed) was set to zero.

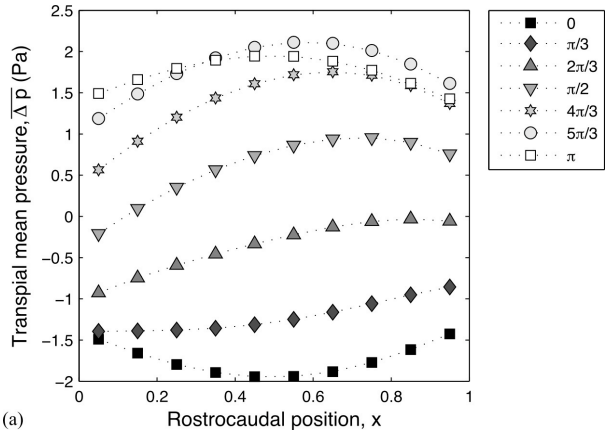

Fig. 2: Demonstration of the phase-lag mechanism.

Fluid will tend to flow into the SC when Δp is negative and back out again when Δp is positive, but if the PVS conductance varies periodically and is out of phase with Δp, inflow to the SC will be encouraged by large z but outflow will be met with reduced conductance. In other words the pial membrane acts as a dynamic valve, driven by but lagging behind the cardiac pressure. For fluid to accumulate in the SC due to this mechanism, thereby raising $\overline{\Delta p}$, additional storage volume must be made. Since the pial membrane is distensible, a pressure gradient favouring flow of CSF into the SC will also tend to constrict the SC, driving fluid out, thus the two effects will cancel. However, if the SC venous volume is at a lower pressure then these vessels may collapse and provide the space to accommodate extra CSF. This may be a viable mechanism for syrinx formation. The amplitude of transpial pulsations is invariant to θ but is damped towards the ends of the spinal canal by the ventricles and dural sac.

3.2 Disease and treatment simulations

The $\theta = \pi/2$ solution from Fig. 1 was designated as a nominal 'healthy' state for having a small and mostly positive Δp as representative of the intraspinal system. The site of post-traumatic syringomyelia (PTS) was chosen to be the mid-thoracic region of the SSS and SC corresponding to segments 5 and 6. The pathological condition was assumed to have disturbed the SC blood supply and effected a local cardiac-PVS phase difference, thus $\theta = \pi$ in segments 5 and 6 and $\theta = \pi/2$ in the remaining eight segments.

PTS is characterised by the formation of scar tissue caused by arachnoiditis, and an associated syrinx. The scar tissue tends to obstruct CSF flow through the SSS, which was simulated by lowering the SSS conductance between segments 5 and 6 ($z_{SSS} \times 10^{-6}$). Scar tissue attachment to the SC surface will stiffen the pial membrane; this was simulated by lowering the pial compliance at the same location ($c_{Pia} \times 10^{-4}$). Syrinxes will locally increase the porosity of the SC and typically elongate beyond the original injury site. This was implemented as an increase in the conductance of the SC between segments 5 to 7. These three mechanical disturbances define the disease state marked as 'PTS' in Fig. 3. As compared to the healthy state the PTS shows Δp pulsations with (a) an elevated mean, indicating fluid accumulation, and (b) a greater amplitude, suggesting a more vigorous fluid exchange. Both of these effects were more pronounced when further alterations were made to the compliance and conductance.

Two surgical treatments for PTS were simulated: (i) a *syringo-subarachnoid shunt* and (ii) a *subarachnoid bypass*. The first procedure involves implanting a short plastic tube that perforates the syrinx so as to provide permanent drainage into the SSS. The shunt was simulated by raising the pial conductance

and setting it to be constant in the segment below the blockage. This had the effect of reducing $\overline{\Delta p}$ across the level of the syrinx, to zero in the caudal and mid regions and to a negative value at the rostral end. Likewise the shunt acted to attenuate the amplitude of transpial pulsations in the region of the disease to values at or below that of the healthy state. These results favour the syringo-subarachnoid shunt as a treatment for syrinxes in association with arachnoiditis.

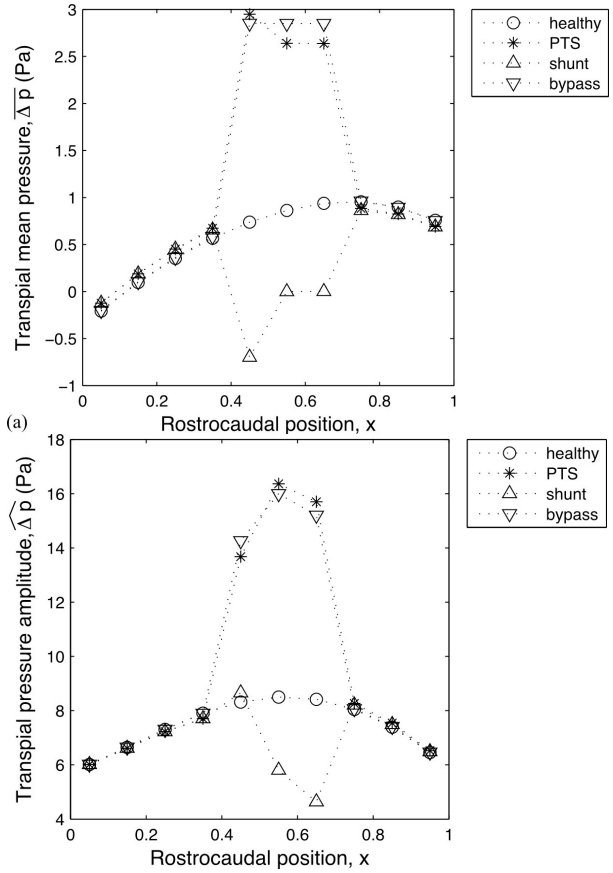

Fig. 3: Simulated disease and surgical treatments.

The subarachnoid-bypass procedure involves forming an alternative CSF pathway between opposite sides of a SSS obstruction. An 'ideal' bypass was implemented as a conductance between the SSS compartments in segments 4 and 7, with a value proportional to the normal SSS conductance; i.e., a hydraulic short-circuit. The simulated bypass tended to equalise $\overline{\Delta p}$ across the span of the syrinx but the magnitude remained approximately the same as for the diseased state. The amplitude of transpial pulsations was scarcely affected by the bypass. These results suggest that the bypass procedure does little to alleviate the pressure pulsations acting across the pial membrane. However, in practice this procedure has been used with some success [15]. A subarachnoid bypass, in addition to being a passageway, may form an outpouching of the SSS (a 'pseudomeningocele') thereby acting as a CSF storage reservoir, which was not simulated here. Therefore, the efficacy of a subarachnoid bypass may have more to do with the compliance of the passageway than its flux function.

4 Conclusions

The phase-lag mechanism for perivascular flow may lead to fluid accumulation in the SC if the contained venous reservoir provides sufficient volume compliance. If this mechanism is in operation in PTS then a shunt might provide a more effective mechanical solution than a subarachnoid bypass.

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