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# An Electrical Equivalence Model for CSF Pulsatility.

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## Flow Model

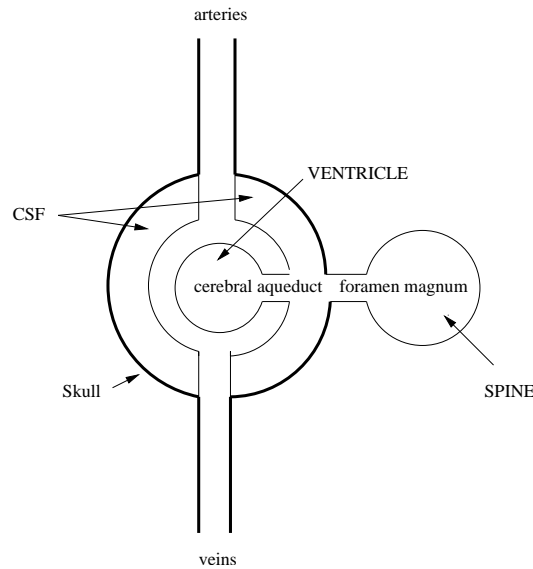


Figure 1: Simplified Biological system.

The salient biological features we wish to model are shown in Figure 1. Narrowed flow paths are expected to have associated impedances and thin boundaries are expected to have compliances which can transmit influence of pressure between fluid pools.

Assuming for now fixed values for compliances and impedances within this system we can write down an equivalent model as an electrical circuit (Figure 2 (a)). Flow paths with impedance are modelled as resistors and elastic surfaces between any two pressure reservoirs (arteries, brain, veins, CSF, VENTRICLE and SPINE) are modelled as capacitors. Unfortunately some of the components are degenerate so we can combine them to produce a simplified circuit (Figure 2(b)). As can be seen, this system has 10 free parameters and 6 possible measurements.

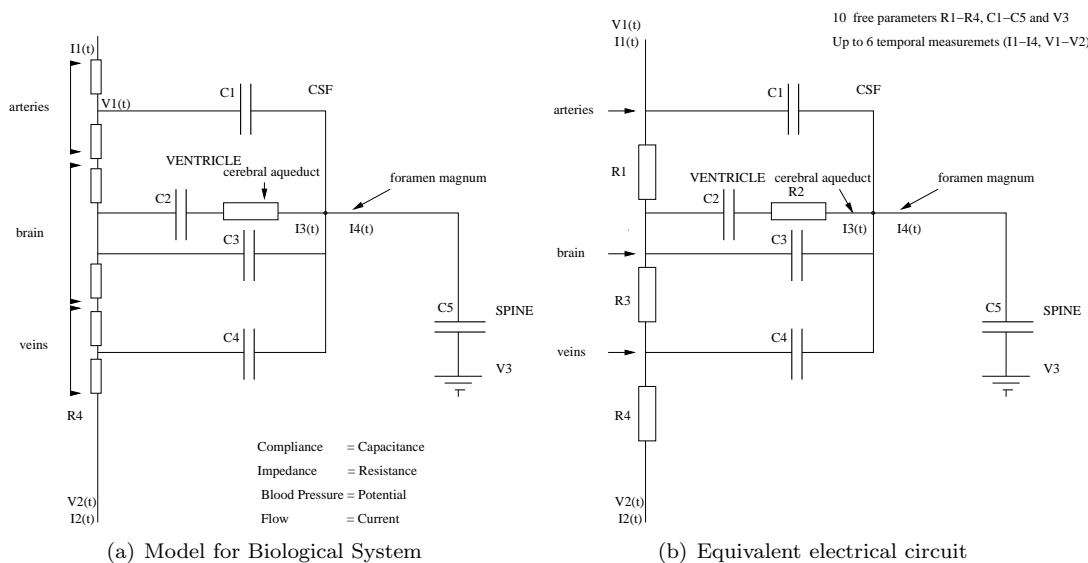


Figure 2: Electrical Circuits for the Simplified Biological Model.

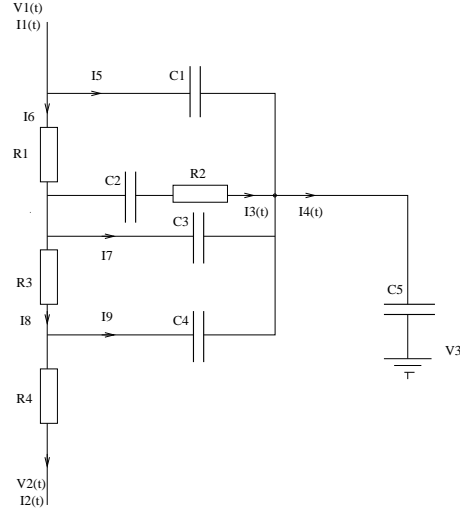


Figure 3: Current flow.

## Analysis of Current Flows

We will assume that we can represent all time varying signals in the Fourier domain so that we can analyse the equivalent circuit at a fixed set of frequencies  $w$ . We can then analyse this circuit using conventional means by specifying current flows and writing down the equations describing current and voltage.

The circuit of Figure 2 has been redrawn to include all unknown current path variables (Figure 3). We can then write down the following equations.

### Vertex Currents

$$I_1 = I_5 + I_6 \quad (1)$$

$$I_8 = I_9 + I_2 \quad (2)$$

$$I_6 = I_3 + I_7 + I_8 \quad (3)$$

$$I_4 = I_5 + I_3 + I_7 + I_9 \quad (4)$$

### Voltage loops

$$I_5 \frac{1}{jwC_1} - I_3 R_2 - I_3 \frac{1}{jwC_2} - I_6 R_1 = 0 \quad (5)$$

$$I_7 \frac{1}{jwC_3} - I_9 \frac{1}{jwC_4} - I_8 R_3 = 0 \quad (6)$$

$$I_3 \frac{1}{jwC_2} + I_3 R_2 - I_7 \frac{1}{jwC_3} = 0 \quad (7)$$

### Point to point voltages

$$V_2 - V_1 = I_6 R_1 + I_3 R_3 + I_2 R_4 \quad (8)$$

$$V_3 - V_1 = I_6 R_1 + I_3 \frac{1}{jwC_2} + I_3 R_2 + I_4 \frac{1}{jwC_5} \quad (9)$$

This is as many equations as we can usefully write down for this system and we have introduced 5 new current variables ( $I_5$  to  $I_9$ ), and we have nine equations leaving 6 degrees of freedom.

The point to point voltages require the equivalent of a pressure measurements in the biological system, we will deal with these later. To begin with we must remove the unmeasured current variables from the 7 remaining constraint equations. This should leave us with two equations composed of variables which are either measured or compliance and impedance parameters of the biological system.

## Elimination of Unwanted Variables

Eliminate  $I_8$  using equation 2 from equations 3 and 6;

$$I_6 = I_3 + I_7 + I_9 + I_2 \quad (10)$$

$$I_7 \frac{1}{j\omega C_3} - I_9 \frac{1}{j\omega C_4} - (I_9 + I_2)R_3 = 0 \quad (11)$$

Eliminate  $I_6$  using equation 10 from equations 1 and 5

$$I_1 = I_5 + I_3 + I_7 + I_9 + I_2 \quad (12)$$

$$I_5 \frac{1}{j\omega C_1} - I_3(R_2 - \frac{1}{j\omega C_2}) - (I_3 + I_7 + I_9 + I_2)R_1 = 0 \quad (13)$$

Eliminate  $I_9$  using equation 12 from equations 10, 11 and 13;

$$I_1 = I_2 + I_4 \quad (14)$$

Box 1: What goes in must come out.

This equation is entirely in terms of measured data and is therefore iriducible.

$$I_7 \frac{1}{j\omega C_3} - (I_4 - I_5 - I_3 - I_7) \frac{1}{j\omega C_4} - (I_4 - I_5 - I_3 - I_7 + I_2)R_3 = 0 \quad (15)$$

$$I_5 \frac{1}{j\omega C_1} - I_3(R_2 - \frac{1}{j\omega C_2}) - (I_2 + I_4 - I_5)R_1 = 0 \quad (16)$$

Eliminate  $I_7$  using equation 7 from equations 15 and 16;

$$I_7 = j\omega C_3 I_3 (\frac{1}{j\omega C_2} + R_2) \quad (17)$$

giving

$$I_7 (\frac{1}{j\omega C_3} + \frac{1}{j\omega C_4} + R_3) - (I_4 - I_5 - I_3) \frac{1}{j\omega C_4} - (I_4 - I_5 - I_3 + I_2)R_3 = 0 \quad (18)$$

$$j\omega C_3 I_3 (\frac{1}{j\omega C_2} + R_2) (\frac{1}{j\omega C_3} + \frac{1}{j\omega C_4} + R_3) - (I_4 - I_5 - I_3) \frac{1}{j\omega C_4} - (I_4 - I_5 - I_3 + I_2)R_3 = 0 \quad (19)$$

Finally rewrite 16 in terms of  $I_5$  and use this in 19 to produce the final irreducible equation.

$$I_5 = \frac{I_3(R_2 + \frac{1}{j\omega C_2}) + (I_2 + I_4)R_1}{\frac{1}{j\omega C_1} + R_1} \quad (20)$$

Use  $\frac{1}{j\omega C_n} = D_{nw}$  as shorthand so that all  $R$ 's are real and all  $D$ 's imaginary (all  $I$ 's are complex);

$$(D_{1w} + R_1)[I_3(D_{2w} + R_2)(D_{3w} + D_{4w} + R_3) - D_{3w}(I_4 - I_3)D_{4w} - D_{3w}(I_4 - I_3 + I_2)R_3] + D_{3w}[I_3(R_2 + D_{2w}) + (I_2 + I_4)R_1](R_3 + D_{4w}) = 0 \quad (21)$$

Box 2: Constraint equation relating currents (flows).

Notice that this equation does not contain  $I_1$ ,  $C_5$  or  $R_4$  (though  $I_1$  can be re-introduced using equation 15). Thus this equation cannot be used to determine these parameters. In addition there is an overall unknown scale factor leaving a total of 6 degrees of freedom. Remember, this constraint equation is complex and therefore provides two constraints for non-zero frequencies. The zeroth order term yields just one equation for the case of  $\langle I_3 \rangle = \langle I_4 \rangle = 0$  (ie: no net flow out of the ventricles and into the spine) with  $\langle I_2 \rangle \neq 0$  and  $D_{3w} \neq 0$ . This gives the following real valued constraint;

$$R_1 D_{4w} = R_3 D_{1w} \quad (22)$$

Box 3: Condition for zero  $\langle I_3 \rangle$  (no flow between ventricular and cranial CSF spaces).

## Using the equations relating point to point voltages

Scaling of parameters will require the use of a point to point voltage equations (such as 8 or 9). In fact an alternative point to point voltage route gives a simple measurable form immediately.

$$V_3 - V_1 = I_5 \frac{1}{j\omega C_1} + I_4 \frac{1}{j\omega C_5}$$

substituting in 20 and 14 while introducing our shorthand gives

$$V_3 - V_1 = \frac{I_3(R_2 + D_{2w}) + I_1 R_1}{D_{1w} + R_1} D_{1w} + I_4 D_{5w} \quad (23)$$

Which, again for the mean flow case and  $\langle I_3 \rangle = \langle I_4 \rangle = 0$  reduces to

$$\langle V_3 \rangle - \langle V_1 \rangle = \langle I_1 \rangle R_1 \quad (24)$$

Box 4: Using mean potentials (pressures) to scale variables.

which suggests that the scaling factor for  $R_1$  (and therefore all of the parameters) can be determined from the zeroth order term. Higher order terms (requiring Fourier terms of  $V_1(t)$ ) provide a constraint on parameter  $C_5$ , but do not require additional temporal measurement of  $V_3$ , which has been assumed to be static.

## Parameter Estimation

The above analysis (though useful as a way of exploring the role of measurements on the parameters) is not sufficient to attempt an optimal estimate of the parameters if we find that we have enough constraints to form an over-determined system. An approach based upon likelihood estimation of parameters is necessary to do that. We can build a suitable likelihood function from equation 21. By substituting 14 and re-organising terms we can get an equation of the form

$$\gamma I_3 - \alpha I_1 + \beta I_4 = 0 \quad (25)$$

where  $\alpha$ ,  $\beta$  and  $\gamma$  are complex variables given by;

$$\beta = C_2(wC_1R_1 - j)$$

$$\alpha = wC_2[C_1R_1 - C_4R_3]$$

and

$$\begin{aligned} \gamma = & j(C_1 + C_2 + C_3 + C_4) \\ & -w[C_2R_2(C_3 + C_4) + C_4R_3(C_2 + C_3) + C_1(R_1(C_3 + C_4) + C_2(R_1 + R_2) + C_4R_3)] \\ & - jw^2[C_1C_2R_1R_2(C_3 + C_4) + C_4R_3(C_1R_1(C_2 + C_3) + C_2R_2(C_1 + C_3))] \\ & + w^3C_1C_2C_3C_4R_1R_2R_3 \end{aligned}$$

Applying the variational method to the constraint equation 25 we can say that the complex residual on the constraint for each Fourier amplitude  $w$  in the measured currents is;

$$F_w = \gamma I_{3w} - \alpha I_{1w} + \beta I_{4w}$$

assuming equal random independent Gaussian errors (a scalar value) on each of the measured Fourier amplitudes on each current ( $\sigma_i$ ) we get the likelihood that we should be minimising in the form of a sum over the appropriate Mahalanobis distance terms from each measured frequency  $w$ ;

$$-Log(P) = \sum_w F_w^* F_w / var(F_w) \quad (26)$$

where the variance on the complex residual is given by

$$var(F_w) = \alpha^* \alpha \sigma_1^2 + \beta^* \beta \sigma_4^2 + \gamma^* \gamma \sigma_3^2$$

Box 5: Optimisation Function.

Having determined the most likely parameters for the model we can now make corrections to the flow variables  $\Delta I_n$  in order to enforce the constraint equations, in a way which minimises the change in measurement consistent with their measurement error.

$$\chi^2 = \sum_w \Delta I_1^* \Delta I_1 / \sigma_1^2 + \Delta I_3^* \Delta I_3 / \sigma_3^2 + \Delta I_4^* \Delta I_4 / \sigma_4^2$$

The minimum of this function at fixed frequency, consistent with the flow constraints <sup>1</sup> is given by;

$$\Delta I_3 = \frac{-\gamma^* F \sigma_3^2}{\alpha^* \alpha \sigma_1^2 + \beta^* \beta \sigma_4^2 + \gamma^* \gamma \sigma_3^2}$$

$$\Delta I_4 = \frac{-\beta^* F \sigma_4^2}{\alpha^* \alpha \sigma_1^2 + \beta^* \beta \sigma_4^2 + \gamma^* \gamma \sigma_3^2}$$

$$\Delta I_1 = \frac{\alpha^* F \sigma_1^2}{\alpha^* \alpha \sigma_1^2 + \beta^* \beta \sigma_4^2 + \gamma^* \gamma \sigma_3^2}$$

Notice that substitution of these equations into the expression for  $\chi^2$  above regenerates our earlier expression for  $-log(P)$ . This suggests that the other way to interpret the parameter estimation process is as direct minimisation of these residual functions.

The final thing we need to know about this result is the expected accuracy of the estimated parameters. If we concatenate the unknown variables in to a 6 dimensional vector  $z = (R_2, R_3, C_1, C_2, C_3, C_4)$ , we can write the covariance matrix on the estimated parameters as;

$$Cov(z)^{-1} = \sum_w \nabla_z F_w Cov(F_w)^{-1} \nabla_z F_w^T$$

which gives us the standard (statistical) errors and correlations on estimated parameters.

## Conclusions

In this document we have derived a model for CSF pulsatility in the head due to the passage of blood through the brain in one cardiac cycle in the form of an equivalent electrical circuit. This model does not include changes in impedance in arteries and veins. We could use cross-sectional measurement of arteries and veins to try to infer changes in impedance, but this would then prevent the analytic analysis presented here, it would be only possible to write a time stepped simulation. However, we can infer some conclusions from the above set of equations which (regardless of the simplicity of our model) must be true in general of trying to infer physical flow parameters from the biological model.

Firstly, equation 14 tells us that once we have measured any two of; arterial flow, venous flow and flow through the foramen magnum, measurement of the third one does not help to constrain directly the model parameters. Though this constraint could be used to improve accuracy of the measurements. However, it would be more sensible to pick the two measurements thought to be biologically most relevant and not measure the third.

<sup>1</sup>Substitute for  $I_1$ , differentiate w.r.t.  $I_3$  and  $I_4$ , set the resulting equations to zero and solve.

Secondly, the only things which can be measured are arterial compliance, brain compliance, ventricular compliance, venous compliance, arterial impedance, brain impedance and the impedance of the cerebral aqueduct. Even these seven parameters can only be measured up to a scale factor using equation 21 so we might as well select one and fix it to a nominal value. Thus there are 6 degrees of freedom and we would need constraints at three different frequencies  $\omega$ . This would give enough information to give estimates of the unknown variables by enforcing three (complex) constraint equations.

Finally, we cannot estimate arterial impedance, spine compliance, static pressure or scale the 7 estimated parameters without pressure measurements. As the only other information we can determine from the system would require equations 8, 9 or 23. In fact the zeroth order term, which corresponds to a relationship between mean arterial flow, mean arterial pressure and mean brain pressure, are enough to establish the scale factor (equation 24). Measurements of time dependencies for pressure and flows would however allow additional constraints on the estimation of parameters. A mean head pressure measurement is directly equivalent to  $V_3$  in our model. This means that it should be possible to infer something regarding spine compliance (spinal injury) from mean brain pressure and the time dependencies seen in the arterial flow.

Equation 22 would seem to require a constraint between free parameters. This can physically be reconciled by not requiring  $\langle I_3 \rangle = 0$  ie: a net flow from the ventricles into the other CSF spaces (ventricular volume change). Presumably the physical constraints on the system (including rigidity of the skull) would then come into play, altering the brain impedance ( $R_3$ ) until equation 22 were satisfied. This model thus predicts the circumstances for ventricular enlargement as an imbalance between arterial impedance and compliance, brain impedance and venous compliance.

The approach we would avocate for parameter estimation is as follows. Firstly, the arterial compliance should be computed using equation 24. Then equation 26 should be minimised as a function of the remaining parameters normalised to  $R_1$ . The estimated flows  $I_3$  and  $I_4$  can be corrected back to zero mean and constraint 22 may also be enforced if there is no expectation of hydrocephalus (pressure imbalance between the ventricular and extra cortical CSF).

The results presented here can also be used for modelling. Given the compliances and impedances of the system and the arterial and cerebral aqueduct flow, all other flows and pressures can be computed starting from equation 25 and working back through the other results. The model could thus be used in a forward manner in order to determine the effects of parameter changes on flow and pressure curves.

## Outstanding Issues

The primary concern must be the accuracy of the measured flow data. It is crucially important that we determine the ability to estimate statistically significant amplitudes at three different frequencies from the data available.

The model identified is the simplest we can manage at this stage and in places, particularly the resistances, it is very difficult to identify specific parts of the anatomy as separable parameters (Figure 4). Further refinement might include splitting the arteries to model the effects on the ventricular and extra-cortical compliances separately by including an extra capacitance fed from some point along the artery (Figure 4 capacitance b). The model by Ursino also splits the arteries into proximal and distal components (Figure 4 capacitance a). We may also wish to model compliance between the ventricular and extra-cortical CSF spaces (Figure 4 capacitance c), or compliance of the head (Figure 4 capacitance d).

We would expect all mechanisms relating to net production of CSF to be negligible within a single heart cycle and model-able as a linear function which would have no effect on any non-zero frequency Fourier terms. These processes are however included in the model by Ursino (Figure 4 resistor/diode couplings II and III). Though some production mechanisms (such as from arteries (Figure 4 diode/resistor coupling I) have been neglected. The other major difference between this model and the one presented here is that the equivalent of ventricular and extra-cerebral compliances do not exist in the Ursino model. Instead there is only the equivalent of our spine compliance which Ursino has used for inter-cranial compliance and (being earthed on one side) has the physical analogy of being set in a vacuum, thus preventing the presence of a non-zero mean pressure in the brain. This has been compensated by the use of a “mock CSF injection rate” (Figure 4 current generator at e ), which is not needed in our model.

I have made no attempt to put the relevant dimensions or units on this model for a flow system. We will need to have all of our measurements in a sensible unit scale. Also, we will inevitably find that the equivalence between compliance and capacitance is not straight forward. Compliance is the equivalence of permittivity not capacitance, and to get compliance (the measure of tissue elasticity) we will need scaling variables such as cross-sectional areas and volumes. This means that it will be very difficult to establish expected fixed values which will be valid across different individuals, meaning that all parameters may needed to be determined for everyone for each case. This places a fundamental limit on the complexity of the model that our data will support. More attention needs to be paid to these issues when we have data.

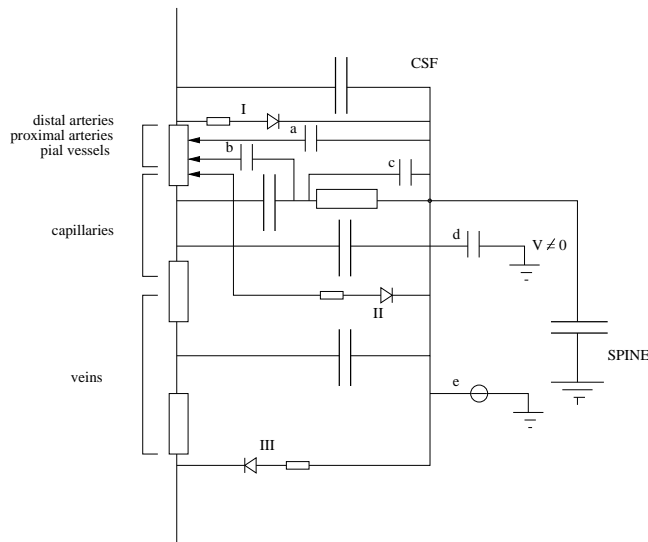


Figure 4: Modified electrical circuit.

## References

M.Ursino and M.Giulioni, Quantitative Assessment of Cerebral Autoregulation from Transcranial Doppler Pulsatility : a computer simulation study. Medical Engineering and Physics, 25 (2003), 655-666.