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Supplemental material

A quantitative model of the cerebral windkessel and its relevance to disorders of intracranial dynamics

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https://thejns.org/doi/abs/10.3171/2023.1.PEDS22372

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APPENDIX 1

The impedance of the cranium to cerebral blood flow is the ratio of pressure to flow, which by linear lumped-parameter approximations of intracranial dynamics is expressed according to

$$\boldsymbol{Z_{cranium}} = \boldsymbol{R_{cap}} + \frac{\boldsymbol{R_{CSF}}}{\boldsymbol{\omega^2 {R_{CSF}}^2 C^2 + (\omega^2 LC - 1)^2}} + \boldsymbol{j}\left[\frac{\boldsymbol{\omega C\left(-\omega^2 L^2 + \frac{L}{C} - {R_{CSF}}^2\right)}}{\boldsymbol{\omega^2 {R_{CSF}}^2 C^2 + (\omega^2 LC - 1)^2}}\right] \tag{1}$$

where $Z_{cranium}$ is the combined impedance of the capillary and CSF path, R_{cap} is the resistance to longitudinal flow in the capillary lumina, R_{CSF} is resistance to radial oscillations in the brain, CSF path, and vasculature, ω is the radial frequency expressed in radians, C is capacitance, L is inductance , and $j = \sqrt{-1}$.

We designate the real and imaginary components of the ICP pulse suppression impedance as $R_{cranium}$ and X_{CSF}:

$$\boldsymbol{R}_{cranium} = \frac{\boldsymbol{R_{CSF}}}{\boldsymbol{\omega^2 {R_{CSF}}^2 C^2 + (\omega^2 LC - 1)^2}} \tag{2}$$

$$\boldsymbol{X_{CSF}} = \frac{\boldsymbol{\omega C\left(-\omega^2 L^2 + \frac{L}{C} - {R_{CSF}}^2\right)}}{\boldsymbol{\omega^2 {R_{CSF}}^2 C^2 + (\omega^2 LC - 1)^2}} \tag{3}$$

so that

$$\boldsymbol{Z_{cranium}} = \boldsymbol{R_{cap}} + \boldsymbol{R}_{cranium} + \boldsymbol{jX}_{CSF} \tag{4}$$

And we define

$$\boldsymbol{Z}_{CSF} = \boldsymbol{R}_{cranium} + \boldsymbol{jX}_{CSF} \tag{5}$$

where Z_{CSF} is the impedance of the ICP pulse suppression (tank part of the circuit). The ICP pulse suppression impedance phase θ_{wk} is

$$\boldsymbol{\theta_{wk}} = \mathbf{arctan}\left(\frac{\boldsymbol{X_{CSF}}}{\boldsymbol{R_{cranium}}}\right) \tag{6}$$

and thus

$$\boldsymbol{\theta_{cranium}} = \mathbf{arctan}\left[\frac{\boldsymbol{\omega C}\left(-\boldsymbol{\omega^2 L^2} + \frac{\boldsymbol{L}}{\boldsymbol{C}} - \boldsymbol{R_{CSF}}^2\right)}{\boldsymbol{R_{CSF}}}\right] \tag{7}$$

The maximal (optimal) ICP pulse suppression impedance Z_{wk} is the real part R_{wk} when the imaginary part X_{CSF} is zero. The resistance R_{wk} is then a local maximum and represents 'pure' resistance without reactance. We choose pure resistance without reactance as the normal ICP pulse suppression impedance because, in normal dynamics, there is minimal reflectance of the arterial pulse from the periphery back to the heart[9] , and this corresponds mathematically to resistance without reactance. With pure ICP pulse suppression resistance, the optimal heart rate ω_{wk} (in radians) is

$$\boldsymbol{\omega_{cranium}} = \sqrt{\frac{\mathbf{1}}{\boldsymbol{LC}} - \frac{\boldsymbol{R_{CSF}}^2}{\boldsymbol{L^2}}} \tag{8}$$

Replacing ω in the ICP pulse suppression resistance R_{wk} (equation 2) with the optimal ICP pulse suppression heart rate ω_{wk} (equation 8) we obtain
the windkessel effectiveness $\boldsymbol{W}$ (i.e., the impedance offered by the tuned ICP pulse suppression):

$$\boldsymbol{W} = \frac{\boldsymbol{L}}{\boldsymbol{R_{CSF}C}} \tag{2}$$

APPENDIX 2

Analysis method: Overview

The data processing and modeling has three steps. First, we pre-process the raw ABP and ICP recordings from dogs. Second, we create transfer function of circuit model in z domain, which corresponds to discrete-time signal. Third, we fit an ARX model to the ABP and ICP data, and obtain a corresponding z-domain transfer function. Finally, we build the relationship between the transfer function of circuit model and the transfer function of ARX model, and aim to estimate the circuit elements by minimizing the difference between the two transfer functions.

Data analysis: data preprocessing

As mentioned in the text, the data sets only contain the raw ABP and ICP time series, and their time stamps. For each data set, we estimate the real-time heart rate in a moving window. In each window, we detect the peaks of systolic and diastolic arterial pressures and their corresponding time stamps. The average heart rate in this window is calculated by counting the pairs of systolic and diastolic peaks and normalizing it by time length. Except for computing the heart rate, we filter the raw data because we are analyzing the fundamental frequency band and we want to avoid aliasing, so we apply a lowpass filter and a band-stop filter on each raw dataset. The lowpass filter is used for removing high-frequency noise and the band-stop filter for removing the respiratory effect which is usually located around $0.1{\sim}0.5Hz$. For implementation, we chose Butterworth filters.

Circuit Analysis: Transfer Function

The transfer function is defined as the ratio of the Laplace transform of the output (the ICP, i.e., voltage across the resistor) to the Laplace transform of input (the ABP, i.e., voltage of the sources). Given the impedances of the circuit elements R_{cap}, R_{CSF}, sL and $1/sC$, the transfer function of the ICP pulse suppression circuit is

$$\begin{aligned} \boldsymbol{H(s)} &= \frac{\boldsymbol{V_o(s)}}{\boldsymbol{V_i(s)}} = \frac{\boldsymbol{R_{cap}}}{\boldsymbol{R_{cap}} + \frac{(\boldsymbol{1/sC})\,(\boldsymbol{R_{CSF}} + \boldsymbol{sL}))}{(\boldsymbol{1/sC}) + (\boldsymbol{R_{CSF}} + \boldsymbol{sL})}} \\ &= \frac{\boldsymbol{R_{cap}LCs^2} + \boldsymbol{R_{cap}R_{CSF}Cs} + \boldsymbol{R_{cap}}}{\boldsymbol{R_{cap}LCs^2} + \left(\boldsymbol{R_{cap}R_{CSF}C} + \boldsymbol{L}\right)\boldsymbol{s} + \boldsymbol{R_{cap}} + \boldsymbol{R_{CSF}}} \end{aligned} \tag{10}$$

The dynamics of pressure and flow in the ICP pulse suppression can be described by second-order differential equations. To facilitate discrete time-data analysis, we map the transfer function from the Laplace domain to the Z domain. We use the Tustin (bilinear) approximation (Oppenheim)

$$\boldsymbol{z} = \boldsymbol{e^{sT}} \approx \frac{\boldsymbol{1} + \frac{\boldsymbol{sT}}{\boldsymbol{2}}}{\boldsymbol{1} - \frac{\boldsymbol{sT}}{\boldsymbol{2}}} \tag{11}$$

$$\boldsymbol{s} \approx \frac{\boldsymbol{2}}{\boldsymbol{T}} \times \frac{\boldsymbol{z} - \boldsymbol{1}}{\boldsymbol{z} + \boldsymbol{1}} \tag{12}$$

where T is the sampling interval. The z-domain transfer function of the ICP pulse suppression circuit is

$$\boldsymbol{H_c(z)} \approx \frac{\boldsymbol{N_0} + \boldsymbol{N_1 z^{-1}} + \boldsymbol{N_2 z^{-2}}}{\boldsymbol{D_0} + \boldsymbol{D_1 z^{-1}} + \boldsymbol{D_2 z^{-2}}} \tag{13}$$

where the coefficients are

$$\begin{gathered} \boldsymbol{N_0} = \boldsymbol{4R_{cap}LC} + \boldsymbol{2TR_{cap}R_{CSF}C} + \boldsymbol{T^2R_{cap}} \\ \boldsymbol{N_1} = \boldsymbol{2T^2R_{cap}} - \boldsymbol{8R_{\,cap}LC} \\ \boldsymbol{N_2} = \boldsymbol{4R_{cap}LC} - \boldsymbol{2TR_{cap}R_{CSF}C} + \boldsymbol{T^2R_{cap}} \\ \boldsymbol{D_0} = \boldsymbol{4R_{cap}LC} + \boldsymbol{2TR_{cap}R_{CSF}C} + \boldsymbol{T^2}\left(\boldsymbol{R_{cap}} + \boldsymbol{R_{CSF}}\right) + \boldsymbol{2TL} \end{gathered} \tag{14}$$

$$D_1 = 2T^2\left(R_{cap} + R_{CSF}\right) - 8R_{cap}LC$$

$$D_2 = 4R_{cap}LC - 2TR_{cap}R_{CSF}C + T^2\left(R_{cap} + R_{CSF}\right) - 2TL$$

Time Series Modeling and Transfer Function

An ARX model is a model of observed time series where a given observation (e.g., ICP) is a linear function of previous observations and of current and past values of another time series (e.g., ABP), also known as input. The name ARX stands for Autoregressive with extra input. In the literature, ARX is also referred to as the Autoregressive with Exogenous Variables model, the exogenous variable being the input variable.

Both input ABP and output ICP are time series data. We model the cerebral ICP pulse suppression in the time domain by a linear autoregression of the ICP with an exogenous input (ABP), thus creating an ARX model. When $\boldsymbol{x}[\boldsymbol{n}]$ and $\boldsymbol{y}[\boldsymbol{n}]$ are discrete input and output signals representing ABP and ICP time series, respectively, the formulation of ARX model is

$$\boldsymbol{y}[\boldsymbol{n}] = \sum_{i=1}^{p} \boldsymbol{a}_i \boldsymbol{y}[\boldsymbol{n}-\boldsymbol{i}] + \sum_{j=0}^{q} \boldsymbol{b}_j \boldsymbol{x}[\boldsymbol{n}-\boldsymbol{j}] + \boldsymbol{\varepsilon}[\boldsymbol{n}] \quad (15)$$

where the first summation is a linear combination of previous p outputs with $a_i, i = 1,2,3 \dots, p$ as weights, and the second summation is a linear combination of current input and q previous inputs with $b_j, j = 0,1,2 \dots, q$ as weights. The $\varepsilon[n]$ is a disturbance or observation noise. The p and q are called as orders of the model. And the symbols $a_i, i = 1,2,3 \dots, p$ and $b_j, j = 0,1,2 \dots, q$ are the coefficients of the model. Thus, the current ICP sample is expressed as a linear regression of previous ICP samples and ABP samples. Given the ARX model, the corresponding z-domain transfer function of the dynamic system is

$$\boldsymbol{H}(\boldsymbol{z}) = \frac{\boldsymbol{b}_0 + \boldsymbol{b}_1 \boldsymbol{z}^{-1} + \cdots + \boldsymbol{b}_q \boldsymbol{z}^{-q}}{\mathbf{1} - \boldsymbol{a}_1 \boldsymbol{z}^{-1} - \cdots - \boldsymbol{a}_p \boldsymbol{z}^{-p}} \quad (16)$$

When the order $p = 2$ and $q = 2$, the transfer function is simplified to

$$\boldsymbol{H_{ARX}}(\boldsymbol{z}) = \frac{\boldsymbol{b_0} + \boldsymbol{b_1 z^{-1}} + \boldsymbol{b_2 z^{-2}}}{\boldsymbol{1} - \boldsymbol{a_1 z^{-1}} - \boldsymbol{a_2 z^{-2}}} \tag{17}$$

Relationship between Electrical Circuit Model and Time Series Model

Comparing equation (13) and equation (17), the transfer function of the ARX model has the same form as the transfer function of the proposed circuit model. We connect them and estimate the circuit elements by time series analysis. Ideally, the coefficients should satisfy

$$\begin{aligned} -\boldsymbol{a_1} &= \boldsymbol{D_1}/\boldsymbol{D_0} \\ -\boldsymbol{a_2} &= \boldsymbol{D_2}/\boldsymbol{D_0} \\ \boldsymbol{b_0} &= \boldsymbol{N_0}/\boldsymbol{D_0} \\ \boldsymbol{b_1} &= \boldsymbol{N_1}/\boldsymbol{D_0} \\ \boldsymbol{b_2} &= \boldsymbol{N_2}/\boldsymbol{D_0} \end{aligned} \tag{18}$$

Note that the coefficients $a_i, i = 1,2$ and $b_j, j = 0,1,2$ in equation (17) can take any values. However, the coefficients $N_i, i = 0,1,2$ and $D_j, j = 0,1,2$ in equation (13) have to satisfy the relationships in equation (14). Obviously, the transfer function of the circuit is a subset of the transfer functions of the ARX model. In equation (18), the mapping from the right side (circuit elements) to the left side (coefficients of the ARX model) is one-to-one. But given a set of ARX coefficients, it is not always possible to find the corresponding set of circuit elements which satisfy these equations. We discuss how to obtain a solution in the following section.

Estimating the Circuit Elements according to Time-series Model

As mentioned above, we cannot obtain the estimates of the circuit elements from the time series model directly. Considering that the ICP pulse suppression notch appears around the heart rate, in order to compare and analyze the transfer functions in a specific frequency band, we derive the mathematical expressions of the transfer functions in the frequency domain. Given equation (13), the transfer function in the frequency domain is given by

$$\boldsymbol{H_c\left(e^{j\omega}\right)=\frac{N_0+N_1e^{-j\omega}+N_2e^{-j2\omega}}{D_0+D_1e^{-j\omega}+D_2e^{-j2\omega}}} \tag{19}$$

Applying Euler's formula $e^{j\omega}=\cos(\omega)+\mathrm{j}\sin(\omega)$, we can rewrite the transfer function with separate real and imaginary parts:

$$\boldsymbol{H_c\left(e^{j\omega}\right)=\frac{N_rD_r+N_iD_i}{D_r^2+D_i^2}+j\,\frac{N_iD_r-N_rD_i}{D_r^2+D_i^2}} \tag{20}$$

where

$$\begin{aligned}\boldsymbol{N_r}&=\boldsymbol{N_0\cos(2\omega)+N_1\cos(\omega)+N_2}\\ \boldsymbol{N_i}&=\boldsymbol{N_0\sin(2\omega)+N_1\sin(\omega)}\\ \boldsymbol{D_r}&=\boldsymbol{D_0\cos(2\omega)+D_1\cos(\omega)+D_2}\\ \boldsymbol{D_i}&=\boldsymbol{D_0\sin(2\omega)+D_1\sin(\omega)}\end{aligned} \tag{21}$$

Similarly, the transfer function of the ARX model can also be rewritten as

$$\boldsymbol{H_{ARX}\left(e^{j\omega}\right)=\frac{B_rA_r+B_iA_i}{A_r^2+A_i^2}+j\,\frac{B_iA_r-B_rA_i}{A_r^2+A_i^2}} \tag{22}$$

where

$$\begin{aligned}\boldsymbol{B_r}&=\boldsymbol{b_0\cos(2\omega)+b_1\cos(\omega)+b_2}\\ \boldsymbol{B_i}&=\boldsymbol{b_0\sin(2\omega)+b_1\sin(\omega)}\\ \boldsymbol{A_r}&=\boldsymbol{\cos(2\omega)-a_1\cos(\omega)-a_2}\\ \boldsymbol{A_i}&=\boldsymbol{\sin(2\omega)-a_1\sin(\omega)}\end{aligned} \tag{23}$$

Then we compare their real and imaginary parts separately, and define a cost function by:

$$\boldsymbol{\mathcal{J}}(\boldsymbol{\theta}) = \sum_{\boldsymbol{\omega}} \left\{ \left[\boldsymbol{\mathcal{Re}}\left(\boldsymbol{H}_{\boldsymbol{c}}(\boldsymbol{e}^{\boldsymbol{j\omega}})\right) - \boldsymbol{\mathcal{Re}}\left(\boldsymbol{H}_{\boldsymbol{ARX}}(\boldsymbol{e}^{\boldsymbol{j\omega}})\right) \right]^{\mathbf{2}} + \left[\boldsymbol{\mathcal{Im}}\left(\boldsymbol{H}_{\boldsymbol{c}}(\boldsymbol{e}^{\boldsymbol{j\omega}})\right) - \boldsymbol{\mathcal{Im}}\left(\boldsymbol{H}_{\boldsymbol{ARX}}(\boldsymbol{e}^{\boldsymbol{j\omega}})\right) \right]^{\mathbf{2}} \right\} \tag{24}$$

where the unknown vector $\boldsymbol{\theta}$ contains the circuit elements R_{cap}, R_{CSF}, L and C. The cost function indicates the sum of squared distances between the real parts and imaginary parts of the transfer functions from the circuit and the ARX model at each frequency. We minimize $\mathcal{J}(\boldsymbol{\theta})$ over the frequency band containing the heart rate and under the constraints$\boldsymbol{\theta} > \mathbf{0}.$