Published in final edited form as:
Acta Neurochir Suppl. 2008 ; 102: 63–69.

MATHEMATICAL MODELS OF CEREBRAL HEMODYNAMICS FOR DETECTION OF VASOSPASM IN MAJOR CEREBRAL ARTERIES

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SUMMARY

Cerebral vasospasm is a typical complication occurring after Subarachnoid Hemorrhage, which may lead to delayed cerebral ischemia and death. The standard method to detect vasospasm is angiography, which is an invasive procedure. Monitoring of vasospasm is typically performed by measuring Cerebral Blood Flow Velocity (CBFV) in the major cerebral arteries and calculating the Lindegaard Index. State estimation techniques rely on mathematical models to estimate arterial radii based on available measurements.

Mathematical models of cerebral hemodynamics have been proposed by Ursino and Di Giammarco in 1991, and vasospasm was modeled by Lodi and Ursino in 1999. We propose two new models. Model 1 is a more general version of Ursino's 1991 model that includes the effects of vasospasm, and Model 2 is a simplified version of Model 1. We use Model 1 to generate Intracranial Pressure (ICP) and CBFV signals for different vasospasm conditions, where CBFV is measured at the middle cerebral artery (MCA). Then we use Model 2 to estimate the states of Model 1, from which we readily obtain estimates of the arterial radii. Simulations show that Model 2 is capable of providing good estimates for the radius of the MCA, allowing the detection of the vasospasm.

Keywords

Vasospasm; Mathematical Models; State Estimation; System Identification

1. INTRODUCTION

Vasospasm is a typical complication occurring after Subarachnoid Hemorrhage (SAH) that may lead to cerebral ischemia and death. It is known that between 5 and 10% of hospitalized SAH patients die from vasospasm. What makes vasospasm interesting is that to some extent it is predictable, preventable and treatable [1].

The typical method of detecting Vasospasm is through Angiography, which is an imaging technique that allows visualization of cerebral arteries. It is a highly invasive procedure, since it requires the insertion of a catheter into a peripheral artery and the addition of a dye for correct visualization. Continuous monitoring of arterial radius is not possible through this technique. A physiological quantity that is closely related to Vasospasm is Cerebral Blood Flow Velocity (CBFV). CBFV through a vessel of (inner) radius r is equal to the ratio of Cerebral Blood Flow (CBF) through the vessel, and its area, as follows

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$$CBFV = \frac{CBF}{\pi r^2} \tag{1}$$

CBFV may be measured non-invasively and continuously monitored using the Trans-Cranial Doppler (TCD) technique. CBFV is typically measured at the Middle Cerebral Artery (MCA) and Internal Carotid Artery (ICA), though measurements at the Anterior Cerebral Artery (ACA), and Posterior Cerebral Artery (PCA) also possible.

It is clear that knowledge of CBFV is not sufficient for the correct prediction of arterial radius *r*. An alternative method that is used often in practice is the evaluation of the Lindegaard ratio [2], which is the ratio of the CBFV at the MCA to the CBFV at the ICA. Depending on the value of *L*, a decision is made as follows: if $L < 3$, there is no spasm; if $3 \leq L < 6$, there is moderate spasm; if $L \geq 6$, the spasm is considered severe [2]. The Lindegaard ratio has been shown to correlate well with angiographic measurements of Vasospasm, but still it is an empirical approach which does not give exact information about the actual radii of the vessels as Angiography does, and also the thresholds defined for prediction of outcome are rather ad-hoc and may change for different patients.

In this work we resort to a completely different approach to estimate the radii of the arteries without directly measuring them. It constitutes a Model-based approach where state-estimation is applied to estimate physiological variables of interest such as arterial radii. The objective is to obtain a better estimation than that offered by the Lindegaard ratio, avoid the invasiveness of Angiography, and at the same time allow for continuous monitoring and possibly prediction of future spastic states.

2. METHODOLOGY

The methodology used for arterial radii estimation is a Model-based State-Estimation approach, based on the recent work [3]. We use two-step approach, consisting of Model Training and State Estimation. All the variables mentioned in this work correspond to time domain signals, sampled at 1Hz. The mathematical models used in this work have inputs, outputs, state variables and parameters. The input in this case is Arterial Blood Pressure (ABP), and the outputs are Intracranial Pressure (ICP) and Cerebral Blood Flow Velocity (CBFV). We assume measurements of all inputs and outputs are available.

The models have several parameters which are in general unknown. An example of a parameter is the nominal value of a vessel resistance (see Section 3). Since these parameters are unknown, it is necessary to estimate them using available measurements. This is the first step of the Methodology, and is called Model Training.

Figure 1a shows the Model Training scenario. A Model is used to generate artificial outputs (ICP and CBFV), and the measurements of these outputs are subtracted to generate an error signal. An optimization block is used to select the set of parameters that minimizes some cost function that depends on the error. For instance, in our case we use the cost function

$$J(\theta) = \sum_{l=1}^{L} \sum_{i=1}^{N} w_l(i) [\, y_l(i) - \widehat{y}_l(i,\theta)]^2 \tag{2}$$

where *N* is the total number of measurements, *L* is the total number of outputs, θ is the unknown parameter vector, $y_l(i)$ is the i^{th} measurement of output *l*, $\hat{y}_l(i, \theta)$ is the i^{th} output *l* generated by

the model using parameter θ, and $w_l(i)$ is some weighting function. In our case, we use the weighting function that weights every variable y_l inversely proportional to the energy of the signal $y_l(i)$.

The models considered in this work are highly nonlinear, and hence Equation (2) will in general be a non-convex function of θ. As such, algorithms based on gradient descent are not guaranteed to converge to a global optimum. Hence, the optimization is done in two steps as proposed in [3]. First, a global search is performed using a genetic algorithm known as Differential Evolution (DE) [4], which has low complexity and good convergence. After the global search, a local search is performed using a standard gradient descent algorithm through the MATLAB Optimization Toolbox.

The second step of the Methodology is called State Estimation. The states typically represent some physiological variables which may not be measured directly, such as arterial radii of the vessels, compartment compliances, etc, and therefore need to be estimated. After the model has been trained, and a good value of θ is known, the estimation is performed, as shown in Figure 1b. This stage relies on models of the form shown in Equation (3) where $x(t)$ and $\dot{x}(t)$ are vectors corresponding to the state of the system at time t and its derivative with respect to time, respectively, $y(t)$ is its output vector, $u(t)$ is the input, $v(t)$ and $w(t)$ are process noise and measurement noise, respectively, and f and g are some nonlinear functions that may change with time.

$$\begin{aligned} \dot{x}(t) &= f(x(t), u(t), v(t), t) \\ y(t) &= g(x(t), w(t), t) \end{aligned} \tag{3}$$

Let $\hat{x}(t|t)$ denote the minimum Mean-Square Error (MMSE) estimate of $x(t)$ given all observations $y(t)$ up to time t. It is well known that for linear systems in Gaussian noise, the minimum MSE estimate can be obtained recursively using the Kalman Filter [5]. For non-linear systems, however, this is not the case, and a typical approach to solve the problem is to use the Extended Kalman Filter (EKF), which has the disadvantage of requiring the Jacobian matrix of the system, its calculation being error prone. Derivative-free State Estimation approaches for State Estimation in non-linear systems have also been proposed, for example, the Unscented Kalman Filter [6] and the DD1 and DD2 filters [7], which have been shown to provide better performance than the EKF. In this work we use DD1 and DD2 filters.

3. MATHEMATICAL MODELS

In Section 2 we introduced a methodology for the estimation of arterial radii based on continuous time measurements of CBFV, ABP and ICP. This methodology relies heavily on mathematical models that relate these quantities, together with the desired arterial radii. For our purpose, a good mathematical model should provide good correlation with observed quantities, and at the same time have low complexity to allow fast training and state estimation, and avoid possible instability. In general, these two characteristics will contradict each other, i.e., a less complex model will be less able to capture the interrelations between all the variables.

Another limitation of the approach is that even if we have a good model that closely matches the observed variables, it is virtually impossible to obtain continuous measurements of the actual arterial radii to compare it with its estimates. Hence, in this work we propose a simulation-based approach as follows: we develop a mathematical model of cerebral hemodynamics that is more general than previous models, and takes into account mechanisms such as Autoregulation and Vasospasm. We will denote this model as Model 1. Then, we will use Model 1 to generate artificial data for different values of spasm severity. Next, we will

develop a second model, denoted as Model 2, to estimate the arterial radii from Model 1 based on its outputs. As mentioned before, we want Model 2 to be simple, in order to reduce the complexity of the parameter and state estimation. This simulation-based approach will give us good insight into how capable are simple models to predict states from more complex ones, and is the first step towards the application of the state estimation on actual patient data.

The mathematical models derived in this work are based on the models proposed by Ursino *et al*. These models were first introduced in [8], [9] and [10]. Our work is based on the model of [8]. One inconvenience of the model in [8] is that it does not model Vasospasm, and therefore makes it inappropriate for the generation of data at different levels of spasm. Vasospasm was modeled in the work by Lodi and Ursino [11], but unfortunately several simplifications were introduced to the original Ursino model, such as a much simpler Autoregulation mechanism, and collapsing of the small and large arterial cavities into one single cavity. Hence, we combined the two aforementioned models into one more general model that takes into account Vasospasm, has a detailed Autoregulation mechanism, and has four cavities: namely those corresponding to the large arteries (MCA, ACA, PCA), followed by the large pial arteries, small pial arteries and capillaries, and finally the venous compartment. We refer to this model as Model 1, and present it in the form of an electrical circuit in Figure 2 (left circuit).

Next we introduced several simplifications to Model 1, namely collapsing small and large pial arterial cavities into one, a simpler Autoregulation mechanism, and assuming $P_v=P_{ic}$. We also added one capacitance at the large arteries to obtain a state variable that allowed us to obtain the desired MCA radius. We refer to this model as Model 2, and present it in the form of an electrical circuit in Figure 2 (right circuit).

3.1. Details of Model 1

Model 1 has one input (ABP), two outputs (CBFV at the MCA and ICP) and 10 state variables. The state r_{jk} represents the radii of the arteries at compartment i, and branch k. The index i=1 represents the proximal (medium arteries) and i=2 represents the distal (small arteries and capillaries). The index k=v represents the top branch of the compartment, which is in spastic state, and k=n is the bottom branch, which is in normal state (see Figure 2).

According to the Hagen-Poiseuille law, the hydraulic resistance of several parallel tubes of equal caliber is inversely proportional to the fourth power of the inner radius. The four states r_{jk} are related to the corresponding resistances via

$$R_{jk}=R_{jk,0}\frac{r_{jnom}^{4}}{r_{jk}^{4}},\quad j\in\{1,2\},\quad k\in\{v,n\}$$

where the sub-index “zero” indicates nominal values. The resistances between the nominal and spastic branches have an equivalent resistance of $R_{j,tot}$ in the absence of spasm. This is modeled through the following equations

$$R_{jv,0}=\frac{R_{j,tot}}{k_{pv}},\quad R_{jn,0}=\frac{R_{j,tot}}{1-k_{pv}},\quad j\in\{1,2\}$$

where k_{pv} is a parameter that depends on the artery where the spasm is present (MCA, PCA or ACA).

In the absence of spasm, the resistances at the large arteries are given by

$$R_{la,n}=\frac{R_{la,tot}}{1-k_{pv}} \quad R_{la,v}=\frac{R_{la,tot}}{k_{p,v}}=\frac{8\eta}{\pi r_v^4}l_v$$

where l_v and r_v are the length and radius of the vessel, respectively. These values are shown in Table 1 for different arteries, and will depend on the artery that has the spasm, which also corresponds to the one where CBFV is being measured. When spasm is present, the spastic radius is $\tilde{r}_v$ over a length $k_d l_v$, where k_d is the coefficient of diffusion of the spasm (a number between 0 and 1, 0 being no spasm). In this case, the resistance at the large arteries is given by

$$R_{la,v}=\frac{8\eta}{\pi r_v^4}(1-k_d)l_v+\frac{8\eta}{\pi \tilde{r}_v^4}k_d l_v+\frac{k_t}{2}\frac{\rho q_v}{\pi^2 r_v^4}\left(\frac{r_v^2}{\tilde{r}_v^2}-1\right)^2$$

where q_v is the flow through the spastic arteries (through $R_{la,v}$). CBFV at the affected arteries is $CBFV_v=q_v/(\pi\tilde{r}_v^2)$.

The spastic radius $\tilde{r}_v$ is assumed to fluctuate over its nominal value according to the following equation

$$\tilde{r}_v=\tilde{r}_{v0}\left[\frac{1}{k_f}\ln\left(\frac{P_a-P_{ic}}{P_{an}-P_{icn}}\right)+1\right]$$

In order to calculate state equations for the inner radius r_{jk} and calculating P_{jk}, from Laplace's law we obtain

$$P_{jk}r_{jk}-P_{ic}(r_{jk}+h_{jk})=T_{ejk}+T_{mkj}+T_{vjk} \quad j\in\{1,2\},\ k\in\{v,n\}$$

where h_{jk} is the thickness of the vessel and is given by

$$h_{jk}=-r_{jk}+\sqrt{r_{jk}^2+2r_{j0}h_{j0}+h_{j0}^2} \quad j\in\{1,2\},\ k\in\{v,n\}$$

and r_{j0}, h_{j0} are the corresponding values in unstressed conditions. The elastic, muscle and viscous tensions, respectively, are

$$T_{ejk}=\sigma_{ejk}h_{jk} \quad \text{, with} \quad \sigma_{ejk}=\sigma_{0j}\left[\exp\left(k_{ej}\frac{r_{jk}-r_{j0}}{r_{j0}}\right)-1\right]-\sigma_{collj}$$

$$T_{vjk}=\sigma_{vjk}h_{jk} \quad \text{, with} \quad \sigma_{vjk}=\frac{\eta_j}{r_{j0}}\frac{dr_{jk}}{dt}$$

$$T_{mjk}=T_{\max,j}(1+M_{jk})\exp\left(-\left|\frac{r_{jk}-r_{mj}}{r_{tj}-r_{mj}}\right|^{n_{mj}}\right), \quad \text{with} \quad M_{jk}=\frac{M_{\min}+M_{\max}\exp(x_{jk}/k_m)}{1+\exp(x_{jk}/k_m)}$$

Volume is related to radius according to the following equation

$$V_{jk}=K_{vjk}r_{jk}^2 \quad j \in \{1,2\},\ k \in \{v,n\}$$

where $K_{vjv} = k_{pv}K_{vj}$ and $K_{vjn} = (1-k_{pv})K_{vj}$, for $j \in \{1,2\}$, from which we obtain

$$\frac{dV_{jk}}{dt}=2K_{v_{jk}}r_{jk}\frac{dr_{jk}}{dt}$$

Since dV_{jk}/dt represents the current (or flow) from node P_{jk} to node P_{ic}, we readily obtain four equations for dV_{jk}/dt through conservation of flow at the four nodes P_{jk}.

In order to compute state equations dr_{jk}/dt, we need to compute first the value of $R_{la,v}$, which at the same time depends on P_{1v}, which can be computed from dr_{1v}/dt. Solving for dr_{1v}/dt, we obtain a third order equation in $R_{la,v}$ from which we can compute its value. Then we can compute all the state equations of the system, and also the intermediate pressures P_{jk}.

The remaining states are the pressure on the venous bed P_v, the intracranial pressure P_{ic}, and the four Autoregulation variables x_{jk}, $j \in \{1,2\}$, $k \in \{v, n\}$. The state equations for these variables are

$$\tau_{1k}\frac{dx_{1k}}{dt}+x_{1k}=G_1(P_a - P_{ic} - (P_{an} - P_{icn})), \quad k \in \{v,n\}$$
$$\tau_{2k}\frac{dx_{2k}}{dt}+x_{2k}=G_2(q_{2k} - q_{2kn})/q_{2kn}, \quad k \in \{v,n\}$$

where q_{2k} is the flow through R_{2k}, $k \in \{v, n\}$, and q_{2kn} is the nominal value of q_{2k}, and is given by $q_{2vn} = k_{pv}q_n$ and $q_{2nn} = (1-k_{pv})q_n$. Finally, state equations for P_{ic} and P_v may be computed from the conservation of flow at their corresponding nodes, and noting that the diode in the circuit only allows current to flow from P_c to P_{ic} and from P_{ic} to P_{vs}.

We also need the resistance $R_{vs} = R'_{vs}\,(P_v - P_{vs})/(P_v - P_{ic})$ and the capacitances $C_{vi} = 1/k_{ven}(P_v - P_{ic} - P_{v1})$ and $C_{ic} = 1/k_E P_{ic}$.

The fixed parameters, trained parameters (nominal values) and initial values of states (nominal values) for Model 1 are shown in Table 1. For both the trained parameters, and initial values of states, the nominal values are provided, though the model training of Section 2 selects a better set of parameters which are close to the nominal ones.

3.2. Details of Model 2

Model 2 has one input (ABP), and two outputs (ICP and CBFV at the MCA). It has four states, namely, pressure at the large arteries, P_{la}, pressure at pial arteries, P_{pa}, intracranial pressure, P_{ic}, and capacitance at pial arteries, C_{pa}.

One simplification of the model is that it assumes a linear relation between volume and pressure at the large and pial arteries (recall from Model 1 that this relation is of exponential nature). Thus, we have for the volumes (V_{ka} and $V_{ka,0}$, $k \in \{l, p\}$)

$$V_{ka}=C_{ka}(P_{ka}-P_{ic}) \quad k\in\{l,p\}$$

From these volumes we can readily compute the resistances at the large and pial arteries as follows

$$R_{ka}=R_{ka,0}V_{ka,0}^2/V_{ka}^2 \quad k\in\{l,p\} \tag{4}$$

Another simplification of the model is the assumption that $P_v=P_{ic}$, which eliminates one state variable. This assumption was introduced in [9]. State equations for P_{la}, and P_{pa}, can now be obtained by differentiating (4). Care must be exercised while differentiating (4) since C_{pa} also depends on time due to autoregulation. Using $C_{ic} = 1/k_E P_{ic}$, a state equation for state P_{ic} may be obtained through the conservation of flow at node P_{ic}.

A third approximation of the model is a much simpler Autoregulation mechanism at the pial arteries as in [11]. This is accomplished using a state variable for the compliance at the pial arteries

$$\tau_{aut}\frac{dC_{pa}}{dt}+C_{pa}=C_{pa0}\sigma(x), \quad x=G_{aut}(q_{pa}-q_0)/q_0$$
$$\sigma(x)=\frac{(1+\Delta\sigma/2)+(1-\Delta\sigma/2)\cdot\exp(4x/\Delta\sigma)}{1+\exp(4x/\Delta\sigma)}$$

where q_{pa} is the flow through R_{pa}, and $\Delta\sigma = \Delta\sigma_{\max}$ if $x<0$ and $\Delta\sigma_{\max}$ if $x>0$. Finally, the radius at the large arteries is given by $r_{la} = (k_{rla}/R_{la})^4$. The total CBFV at the large arteries is given by $v_{la} = q_{la}/\pi r_{la}^2$, where q_{la} is the flow through R_{la}. Cerebral Blood Flow Velocity at the MCA is approximated by a sixth of the total, i.e., $CBFV_{MCA} = v_{la}/6$.

The fixed parameters, trained parameters (nominal values) and initial values of states (nominal values) for Model 2 are shown in Table 2.

4. SIMULATION RESULTS AND DISCUSSION

The two models (Model 1 and Model 2) were implemented in C code and the Differential Equation solver CVODE was used for the simulations. The parameter and state-estimation algorithms were implemented in MATLAB.

Figure 3 shows the radius at the MCA versus time in seconds. The dashed curve corresponds to the actual MCA radius of Model 1. This radius was gradually decreased during simulation from about 0.14 cm to 0.11 cm. The solid curve shows the Estimate obtained using Model 2. It can be noted that even though the estimated radius is slightly off by about 0.01 cm, it correctly tracks the dashed curve and allows estimation of the variation in radius.

It is interesting to note that the changes in arterial radius are being tracked based on measurements of CBFV only. From Equation (1), we recall that these two variables are related also to Cerebral Blood Flow (CBF), but CBF is never being measured directly. Although this may seem counterintuitive, this is the main advantage of the model-based approach. This approach takes into account several inter-relations between CBF, CBFV, ABP and ICP, which are captured by the differential equations of the model.

We also note that the simpler Model 2 is able to estimate the MCA radius from Model 1, even though these two models have several differences. This is a first step towards the application of the estimation framework using Model 2, to the much more relevant problem of estimating vasospasm from real patient data.

BIBLIOGRAPHY

1. Macdonald, RL.; Weir, B. Cerebral Vasospasm. Academic Press; San Diego: 2001.
2. Lindegaard KF, et al. Cerebral vasospasm after subarachnoid hemorrhage investigated by means of transcranial Doppler ultrasound. Acta Neurochirurgica (Vienna) 1988;24:81–84.
3. Hu X, Nenov V, Bergsneider M, Glenn TC, Vespa P, Martin N. Estimation of Hidden State Variables of the Intracranial System Using Constrained Nonlinear Kalman Filters. IEEE Transactions on Biomedical Engineering 2006;54(4):597–610. [PubMed: 17405367]
4. Storn R, Price K. Differential Evolution: A Simple and Efficient Adaptive Scheme for Global Optimization over Continuous Spaces. J Global Optimization 1997;11:341–359.
5. Kailath, T.; Sayed, AH.; Hassibi, B. Linear Estimation. Prentice Hall; NJ: 2000.
6. Wan EA, Van Der Merwe R. The unscented Kalman filter for nonlinear estimation. The IEEE 2000 Adaptive Systems for Signal Processing, Communications, and Control Symposium 2000:153–158.
7. Norgaard M, Poulsen N, Ravn O. New Developments in State Estimation for Nonlinear Systems. Automatica 2000;36
8. Ursino M, Di Giammarco P. A Mathematical Model of the Relationship Between Cerebral Blood Volume and Intracranial Pressure Changes: The Generation of Plateau Waves. Annals of Biomedical Engineering 1991;19:15–42. [PubMed: 2035909]
9. Ursino M, Lodi CA. A simple mathematical model of the interaction between intracranial pressure and cerebral hemodynamics. Journal of Applied Physiology 1997;82:1256–1269. [PubMed: 9104864]
10. Ursino M, Lodi CA. Interaction among autoregulation, CO2 reactivity, and intracranial pressure: a mathematical model. Am J Physiol Heart Circ Physiol 1998;274:H1715–H1728.
11. Lodi CA, Usino M. Hemodynamic Effect of Cerebral Vasospasm in Humans: A Modeling Study. Annals of Biomedical Engineering 1999;27:257–273. [PubMed: 10199702]

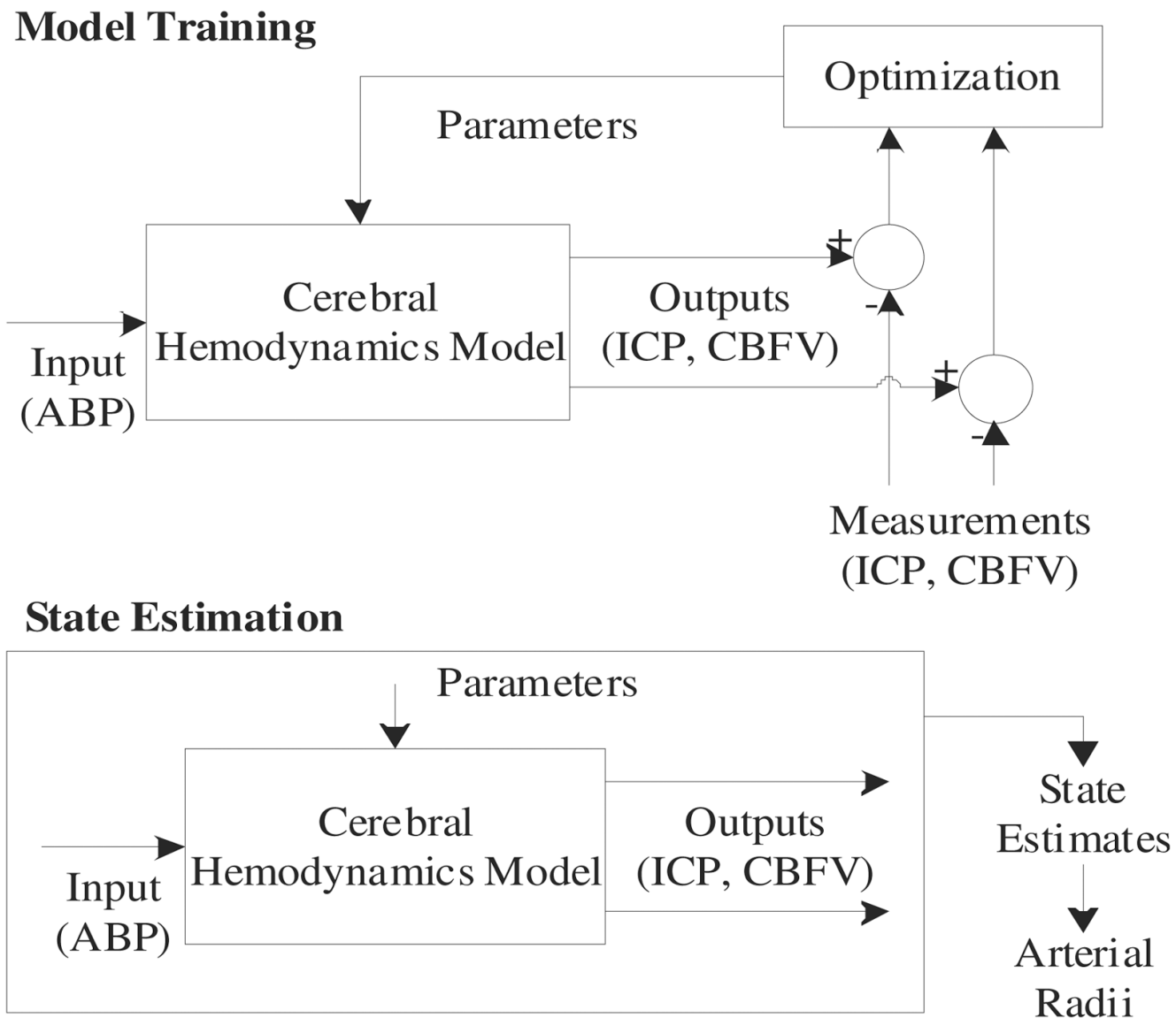

Figure 1.
Model Training and State Estimation

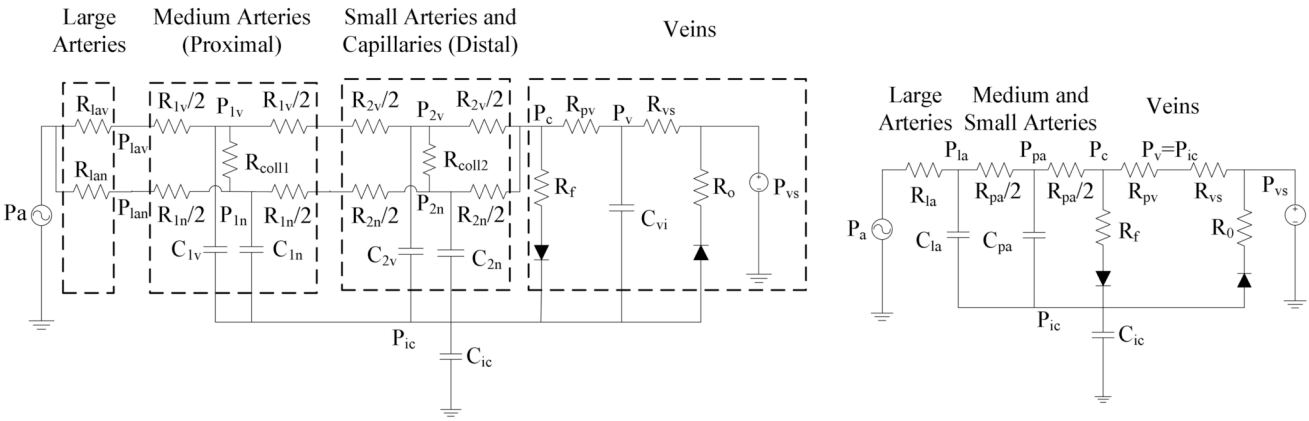

Figure 2.
The more general Model 1 (left) and the simpler Model 2 (right)

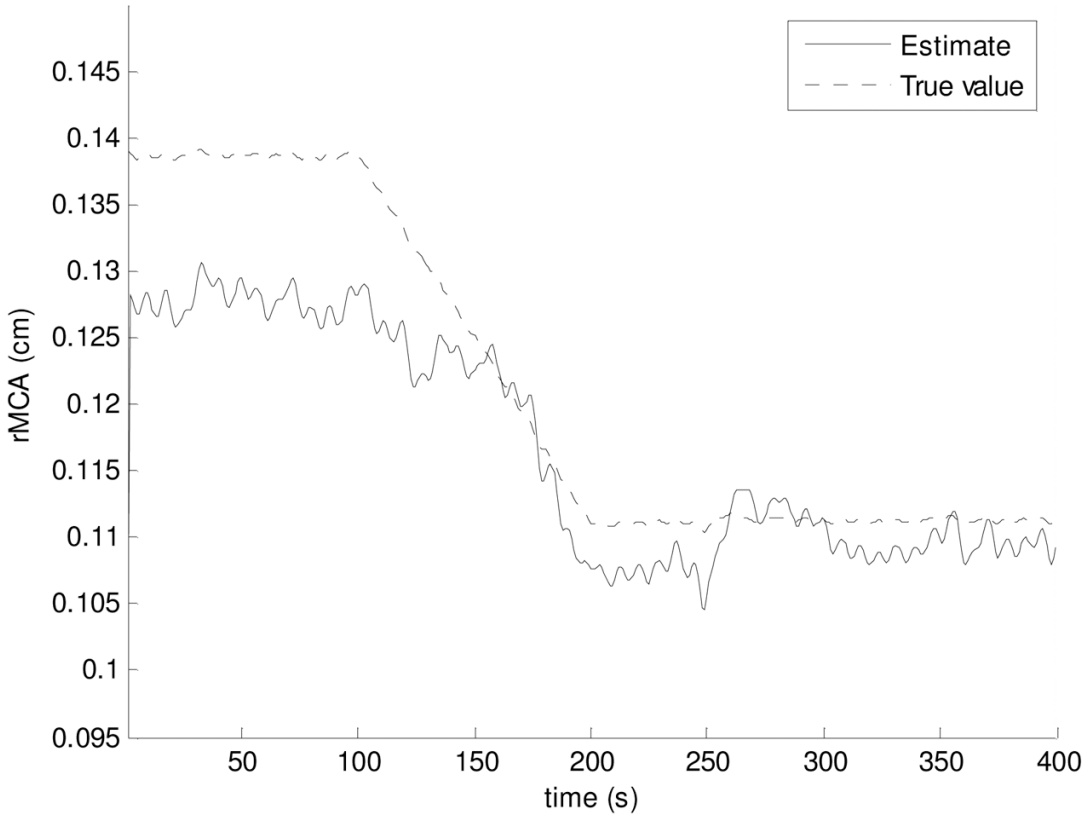

Figure 3.
Actual (dashed) and Estimated (solid) MCA arterial radius versus time.

Table 1

Parameters for Model 1

Fixed Parameters

P_{vs} = 6.07437 mmHg	r_{m1} = 0.027 cm
P_{an} = 100 mmHg	r_{m2} = 0.0128 cm
q_n = 12.5 ml s^{-1}	r_{t1} = 0.018 cm
P_{icn} = 9.5 mmHg	r_{t2} = 0.0174 cm
P_{lan} = 92.5 mmHg	n_{m1} = 1.83
$P_{1normal}$ = 85 mmHg	n_{m2} = 1.75
P_{cn} = 25 mmHg	η_1 = 232 mmHg.s
$R_{latot} = (P_{an}-P_{lan})/q_n$ mmHg.s.ml^{-1}	η_2 = 47.8 mmHg.s
$R_{1,tot} = 2(P_{lan}-P_{1normal})/q_n$ mmHg s ml^{-1}	σ_{01} = 0.1425 mmHg
$R_{2,tot} = (P_{lan}-P_{cn})/q_n - R_{1tot}$ mmHg s ml^{-1}	σ_{02} = 11.19 mmHg
ρ = 7.87563e-4 mmHg s^2/cm^2	$k_{\sigma 1}$ = 10
k_t = 1	$k_{\sigma 2}$ = 4.5
k_f = 12	σ_{coll1} = 62.79 mmHg
k_m = 0.5	σ_{coll2} = 41.32 mmHg
R_{pv} = 0.875 mmHg.s.ml^{-1}	G_1 = 0.02 $mmHg^{-1}$
R'_{vs}= 0.3656 mmHg.s.ml^{-1}	τ_1= 10 s
P_{v1} = −2.5 mmHg	G_2 = 5.2 $mmHg^{-1}$
R_f= 2.38e3 mmHg.s.ml^{-1}	τ_2 = 20 s
R_0 = 0.526e3 mmHg.s.ml^{-1}	r_{10} = 1.5e-2 cm
M_{min} = −1	r_{20} = 7.5e-3 cm
M_{max} = 1	h_{10} = 3e-3 cm
$T_{max,1}$ = 2.16 mmHg.cm	h_{20} = 2.5e-3 cm
$T_{max,2}$ = 1.50 mmHg.cm	r_{1nom} = 0.023435 cm
k_{v1} = 4640 cm	r_{2nom} = 0.007346 cm
k_{v2} = 154320 cm	

Vessel Parameters for different arteries

MCA: k_p = 0.3, r_v = 0.14 cm, l_v = 10.87 cm

ACA: k_p = 0.1, r_v = 0.09 cm, l_v = 5.57 cm

PCA: k_p = 0.1, r_v = 0.095 cm, l_v = 6.92 cm

Trained Parameters (nominal)

k_e = 0.11 ml^{-1}	k_{ven} = 0.31 ml^{-1}
C_{max} = 0.2 ml $mmHg^{-1}$	R_{coll1} =56 mmHg.s.ml^{-1}
k_d = 0.368	R_{coll2} =56 mmHg.s.ml^{-1}

Initial Values of States (nominal)

r_{1v} = 0.023435 cm	P_{ic} = 9.5 mmHg
$r_{1n} = r_{1v}$ cm	$x_{1v} = x_{1n} = x_{2v} = x_{2n} = 0$

r_{2v} = 0.007346 cm	P_v = 14.0682 mmHg
$r_{2n} = r_{2v}$ cm	

Table 2

Parameters for Model 2

Fixed Parameters	
P_{vs} = 6.07437 mmHg	$\Delta\sigma_{max}$ = 6
q_n = 12.5 ml s^{-1}	$\Delta\sigma_{min}$ = 0.6
P_{ic0} = 9.5 mmHg	R_{pv} = 0.875 mmHg.s.ml^{-1}
P_{pa0} = 58.75 mmHg	R'_{vs} = 0.3656 mmHg.s.ml^{-1}
G_{aut} = 2 $mmHg^{-1}$	R_f = 2.38e3 mmHg.s.ml^{-1}
τ_{aut} = 20 s	R_0 = 0.526e3 mmHg.s.ml^{-1}
k_{rla} = 3.04e-4 mmHg s cm	
Trained Parameters (nominal)	
k_e = 0.11 ml^{-1}	V_{la0} = 2.5 cm^3
C_{la} = 2.5/(P_{la}–P_{ic}) ml $mmHg^{-1}$	R_{la0} = 0.6 mmHg.s.ml^{-1}
C_{pa0} = 0.202 ml $mmHg^{-1}$	R_{pa0} = 5.4 mmHg.s.ml^{-1}
Initial Values of States (nominal)	
P_{la} = 92.5 mmHg	P_{ic} = 9.5 mmHg
P_{pa} = 58.75 mmHg	C_{pa} = 0.202 ml $mmHg^{-1}$