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Modeling of Cerebral Blood Flow Autoregulation Using Intracranial Pressure Estimation by means of a State Observer

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Abstract

A mathematical model of cerebral blood flow in the form of a dynamical system is considered. The cerebral blood flow autoregulation modeling problem is treated as an output regulation control problem. The cerebral autoregulation mechanism is described in terms of an output feedback control law based on measurements of the arterial-arteriolar blood flow rate values and intracranial pressure estimates made by an asymptotic state observer. Simulation results confirm good performance of the suggested cerebral blood flow autoregulation model in the form of a dynamic output feedback.

1 Introduction and problem statement

During the last decades a wide literature appeared addressing the cerebral blood circulation and autoregulation mathematical modeling (see, e.g [11, 9, 8, 7, 10, 3, 2, 5]). Understanding mathematics behind cerebral autoregulation could help us prevent various brain disorders, e.g. intracranial hemorrhages in preterm infants [7]. Using a proper mathematical model of cerebral blood flow circulation and autoregulation one could try to reproduce the autoregulation performance of a healthy human, for instance, by means of medicaments which dilate or constrict blood vessels according to a mathematically conceived time profile.

One of possible ways to model cerebral blood flow processes is based on using lumped parameter models which result in ordinary differential equations as a cerebral hemodynamics description [11, 8, 3, 5]. Such kind of cerebral blood flow models are relatively simple, but still can reproduce basic clinical results [11, 8] at least at a qualitative level. In this paper we continue to develop the approach to cerebral autoregulation modeling proposed in [5] and based on using tools of the nonlinear mathematical control theory. Consider a cerebral hemodynamics model originally suggested in [11] and written as the following dynamical system [5]:

$$\begin{aligned}
\dot{V}_a &= \frac{1}{1+k_E P_{ic} C_a}\left(-k_E P_{ic} C_a\left(\frac{P_c-P_{ic}}{R_f}-\frac{P_{ic}-P_{vs}}{R_o}+I_i\right)+(P_a-P_{ic})\dot{C}_a\right),\\
\dot{P}_{ic} &= \frac{k_E P_{ic}}{1+k_E P_{ic} C_a}\left(\frac{P_c-P_{ic}}{R_f}-\frac{P_{ic}-P_{vs}}{R_o}+I_i+(P_a-P_{ic})\dot{C}_a\right),
\end{aligned} \tag{1}$$

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where V_a is the arterial-arteriolar blood volume; P_{ic} stands for the intracranial pressure; C_a is the arterial-arteriolar compliance; P_a denotes the systemic arterial pressure; P_c is the capillary pressure; the constant values P_{vs}, R_f, R_o, I_i, k_E stand for the venous sinus pressure, the cerebrospinal fluid production and reabsorption hydraulic resistances, the rate of possible mock cerebrospinal fluid injection in surgery and the craniospinal compartment elastance coefficient, respectively; $P_a > P_c > P_{ic} > P_{vs}$. The capillary pressure P_c and the arterial-arteriolar compliance C_a quantities in the right-hand side of the system (1) can be represented as functions of the system state variables V_a and P_{ic} as follows [5]:

$$P_c = P_c(V_a, P_{ic}) = \frac{R_f R_{pv} P_a V_a^2 + k'_R(R_{pv} + R_f)P_{ic}}{k'_R(R_{pv} + R_f) + R_f R_{pv} V_a^2},$$

$$C_a = C_a(V_a, P_{ic}) = \frac{V_a}{P_a - P_{ic}},$$

where k'_R is a coefficient of the arterial-arteriolar hydraulic resistance R_a inverse proportionality to the square of the V_a variable. The arterial blood pressure dynamics are supposed to be in a steady state, i.e. $\dot{P}_a \equiv 0$. Thus, in (1) the arterial pressure P_a has a constant value which is possibly different from the basal one of a healthy human and, for instance, resulted from an acute pressure increase or drop. Additionally, for a proper range of the systemic arterial pressure values $P_a \in [P_{amin}, P_{amax}]$, the system state variables $V_a(t)$ and $P_{ic}(t)$ are required to remain positive for all $t \geq 0$ and stay within reasonable bounds

$$V_a(t) \in [V_{amin}, V_{amax}],\ P_{ic}(t) \in [P_{icmin}, P_{icmax}],\ t \geq 0.$$

The cerebral blood flow autoregulation mechanism is described in terms of the arterial-arteriolar compliance C_a time behavior. Vasodilation or vasoconstriction of the arterioles are modeled through positive or negative values of the compliance rate $\dot{C}_a$, respectively. In the current work, we take the arterial-arteriolar compliance rate $\dot{C}_a$ as a control input u, i.e. $\dot{C}_a = u$.

The arterial-arteriolar blood flow rate q is considered as a system output and is written as the following function of the system state variables V_a and P_{ic} [5]:

$$q = q(V_a, P_{ic}) = \frac{(R_{pv} + R_f)(P_a - P_{ic})V_a^2}{k'_R(R_{pv} + R_f) + R_f R_{pv} V_a^2}. \tag{2}$$

It is supposed that only the arterial-arteriolar blood flow rate q is available for direct measurements.

Then, the cerebral blood flow autoregulation modeling problem can be formulated as an asymptotic output regulation control problem for the nonlinear dynamical system (1) using information on the output measurements only, i.e. one has to find an output feedback control law $u = u(t, q)$ such that

$$|q(t) - q_n| \to 0 \text{ as } t \to +\infty \tag{3}$$

for all medically reasonable initial values $V_a(0) = V_{a0} \in [V_{amin}, V_{amax}]$, $P_{ic}(0) = P_{ic0} \in [P_{icmin}, P_{icmax}]$ of the system state variables. Here, q_n denotes a basal value of the cerebral blood flow required for tissue metabolism.

2 State observer design

Let us first solve the problem of the system (1) state variables V_a and P_{ic} estimation based on the arterial-arteriolar blood flow rate q measurements, to be utilized later in a state feedback

design suggested in [5]. To that end, rewrite the dynamical system (1) in terms of the q and P_{ic} variables as below

$$\begin{aligned}\dot{q} &= f_1(q, P_{ic}) + g_1(q, P_{ic})u,\\ \dot{P}_{ic} &= f_2(q, P_{ic}) + g_2(q, P_{ic})u,\\ y &= q,\end{aligned} \tag{4}$$

where q is the measured output,

$$\begin{aligned}f_1(q, P_{ic}) = {} & P_{ic}k_E q(3P_{ic}R_f - 3P_aR_f - 3P_aR_{pv} + 3P_{ic}R_{pv}\\ & + 2R_fR_{pv}q)(P_{vs}R_f - P_{ic}R_{pv} - P_{ic}R_f + P_{vs}R_{pv} + I_iR_oR_f + I_iR_oR_{pv}\\ & + R_oR_{pv}q))/(R_o(R_f + Rpv)^2(P_a - P_{ic})(P_a - Pic\\ & + P_{ic}k_E((k'_Rq(R_f + R_{pv}))/((R_f + R_{pv})(P_a - P_{ic}) - R_fR_{pv}q))^{1/2}),\end{aligned}$$

$$\begin{aligned}f_2(q, P_{ic}) = {} & P_{ic}k_E(P_{vs}R_f - P_{ic}R_{pv} - P_{ic}R_f + P_{vs}R_{pv} + I_iR_oR_f + I_iR_oR_{pv}\\ & + R_oR_{pv}q))/(R_o(R_f + R_{pv})((P_{ic}k_E((k'_Rq(R_f + R_{pv}))/((R_f + R_{pv})(P_a - P_{ic})\\ & - R_fR_{pv}q))^{1/2})/(P_a - P_{ic}) + 1),\end{aligned}$$

$$\begin{aligned}g_1(q, P_{ic}) = {} & ((2(R_f + R_{pv})(P_a - P_{ic})((k'_Rq(R_f + R_{pv}))/((R_f + R_{pv})(P_a - P_{ic})\\ & - R_fR_{pv}q))^{1/2})/(k'_R(R_f + R_{pv}) + (R'_fR_{pv}k_Rq(R_f + R_{pv}))/((R_f + R_{pv})(P_a - P_{ic})\\ & - R_fR_{pv}q)) - (2R_fR_{pv}(R_f + Rpv)(P_a - P_{ic})((k'_Rq(R_f + R_{pv}))/((R_f + R_{pv})(P_a\\ & - P_{ic}) - R_fR_{pv}q))^{3/2})/(k'_R(R_f + R_{pv}) + (R_fR_{pv}k'_Rq(R_f + R_{pv}))/((R_f + R_{pv})(P_a\\ & - P_{ic}) - R_fR_{pv}q))^2)(P_a - P_{ic}))/((P_{ic}k_E((k'_Rq(R_f + R_{pv}))/((R_f + R_{pv})(P_a - P_{ic})\\ & - R_fR_{pv}q))^{1/2})/(P_a - P_{ic}) + 1) - (P_{ic}k_Ek'_Rq(R_f + R_{pv})^2(P_a - P_{ic}))/((k'_R(R_f\\ & + R_{pv}) + (R_fR_{pv}k'_Rq(R_f + R_{pv}))/((R_f + R_{pv})(P_a - P_{ic})\\ & - R_fR_{pv}q))((P_{ic}k_E((k'_Rq(R_f + R_{pv}))/((R_f + R_{pv})(P_a - P_{ic})\\ & - R_fR_{pv}q))^{1/2})/(P_a - P_{ic}) + 1)((R_f + R_{pv})(P_a - P_{ic}) - R_fR_{pv}q),\end{aligned}$$

$$\begin{aligned}g_2(q, P_{ic}) = {} & P_{ic}k_E(P_a - P_{ic}))/((P_{ic}k_E((k'_Rq(R_f + R_{pv}))/((R_f + R_{pv})(P_a - P_{ic})\\ & - R_fR_{pv}q))^{1/2})/(P_a - P_{ic}) + 1.\end{aligned}$$

Notice that the change of variables $q = q(V_a, P_{ic})$, $P_{ic} = P_{ic}$ defined by the relationship (2) can be seen as a diffeomorphism from

$$\Omega = \{(V_a, P_{ic})^{\mathrm{T}} \in \mathbb{R}^2 : V_{amin} \le V_a \le V_{amax},\ P_{icmin} \le P_{ic} \le P_{icmax}\} \tag{5}$$

to a proper subset of $\{(q, P_{ic})^{\mathrm{T}} \in \mathbb{R}^2 : q_{min} \le q \le q_{max},\ P_{icmin} \le P_{ic} \le P_{icmax}\}$ since its reverse is given by

$$V_a = \sqrt{\frac{k'_R(R_{pv} + R_f)q}{(R_{pv} + R_f)(P_a - P_{ic}) - R_{pv}R_fq}},\ P_{ic} = P_{ic}. \tag{6}$$

In view of (2) the denominator in (6) is always nonzero.

To construct a state observer for the dynamical system (4) let us linearize it around a nominal point $q = q_n$, $P_{ic} = P_{icr}$ in the state space. Here $P_{icr} \in [P_{icmin}, P_{icmax}]$ is a reference

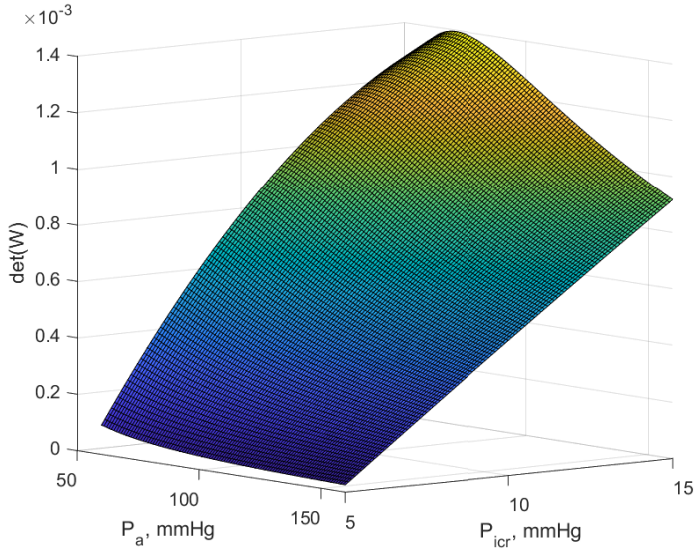

Figure 1: Determinant of the observability matrix W as a function of P_a and P_{icr}.

value of the intracranial pressure under basal conditions. The linearized dynamical system (4) takes the form

$$\begin{aligned} \dot{x} &= Ax + Bu + F_r, \\ y &= Cx, \end{aligned} \tag{7}$$

$$A = \left(\begin{array}{cc} \dfrac{\partial F_1}{\partial q} & \dfrac{\partial F_1}{\partial P_{ic}} \\ \dfrac{\partial F_2}{\partial q} & \dfrac{\partial F_2}{\partial P_{ic}} \end{array} \right) \Bigg|_{\substack{q=q_n,\\ P_{ic}=P_{icr},\\ u=0}}, \quad B = \left(\begin{array}{c} \dfrac{\partial F_1}{\partial u} \\ \dfrac{\partial F_2}{\partial u} \end{array} \right) \Bigg|_{\substack{q=q_n,\\ P_{ic}=P_{icr},\\ u=0}}, \quad C = (1,\ 0),$$

where $x = (q - q_n, P_{ic} - P_{icr})^{\mathrm{T}}$, $F_1(q, P_{ic}) = f_1(q, P_{ic}) + g_1(q, P_{ic})u$, $F_2(q, P_{ic}) = f_2(q, P_{ic}) + g_2(q, P_{ic})u$, $F_r = (f_1(q_n, P_{icr}), f_2(q_n, P_{icr}))^{\mathrm{T}}$.

To proceed with a linear state observer design for the system (7) one first needs to check [1] that the observability matrix

$$W = \begin{pmatrix} C \\ CA \end{pmatrix} \tag{8}$$

has the rank of two. It can be shown, see Fig. 1, that for the basal model parameter and pressure boundary values [11] $q_n = 12.5\ \mathrm{ml \cdot s^{-1}}$, $R_{pv} = 1.24\ \mathrm{mmHg \cdot s \cdot ml^{-1}}$, $R_f = 2.38 \times 10^3\ \mathrm{mmHg \cdot s \cdot ml^{-1}}$, $R_o = 526.3\ \mathrm{mmHg \cdot s \cdot ml^{-1}}$, $P_{vs} = 6.0\ \mathrm{mmHg}$, $k_E = 0.11\ \mathrm{ml^{-1}}$, $k'_R = 0.11 \times 10^4\ \mathrm{mmHg \cdot s \cdot ml}$, $I_i = 0\ \mathrm{ml \cdot s^{-1}}$, $P_{amin} = 60\ \mathrm{mmHg}$, $P_{amax} = 160\ \mathrm{mmHg}$, $P_{icmin} = 5\ \mathrm{mmHg}$, $P_{icmax} = 15\ \mathrm{mmHg}$ the observability matrix (8) is nonsingular.

Then, a state observer for the linear dynamical system (7) can be constructed as [1]

$$\dot{\hat{x}} = A\hat{x} + Bu + F_r + L(C\hat{x} - Cx), \tag{9}$$

where $L = (l_1, l_2)^{\mathrm{T}}$ is a vector of the gain coefficients chosen to provide global asymptotic stability of the zero equilibrium of the estimation error $e = \hat{x} - x$ dynamics

$$\dot{e} = (A + LC)e. \tag{10}$$

To find the observer gain vector L such that the matrix $A + LC$ is Hurwitz let us rewrite the system (7) in the variables $\zeta = Wx$ as follows

$$\begin{aligned} \dot{\zeta} &= \widetilde{A}z + \widetilde{B}u + WF_r, \\ y &= C\zeta, \end{aligned} \tag{11}$$

where

$$\tilde{A} = WAW^{-1} = \begin{pmatrix} 0 & 1 \\ \alpha_1 & \alpha_2 \end{pmatrix} \quad \tilde{B} = WB = \begin{pmatrix} CB \\ CAB \end{pmatrix}, \quad (\alpha_1, \alpha_2) = CA^2W^{-1}. \tag{12}$$

The state observer for the dynamical system (11) is readily written as below

$$\dot{\hat{\zeta}} = \widetilde{A}\hat{\zeta} + \widetilde{B}u + WF_r + \widetilde{L}(C\hat{\zeta} - C\zeta),\ \widetilde{L} = (\widetilde{l}_1, \widetilde{l}_2)^{\mathrm{T}},$$

with the state estimation error $e = \hat{\zeta} - \zeta$ dynamics having the form

$$\dot{e} = (\widetilde{A} + \widetilde{L}C)e,$$

$$\widetilde{A} + \widetilde{L}C = \begin{pmatrix} \widetilde{l}_1 & 1 \\ \widetilde{l}_2 + \alpha_1 & \alpha_2 \end{pmatrix}. \tag{13}$$

The characteristic polynomial of the matrix (13) is given by

$$\lambda^2 + (-\alpha_2 - \widetilde{l}_1)\lambda + (\widetilde{l}_1\alpha_2 - \widetilde{l}_2 - \alpha_1) = 0.$$

Hence, for any given pair of negative real polynomial roots $\lambda_1 < 0$, $\lambda_2 < 0$ the gain coefficients $\widetilde{l}_1$ and $\widetilde{l}_2$ can be found from relations

$$\alpha_2 + \widetilde{l}_1 = \lambda_1 + \lambda_2,\ \widetilde{l}_1\alpha_2 - \widetilde{l}_2 - \alpha_1 = \lambda_1\lambda_2$$

to make (13) Hurwitz.

Finally, in view of the equalities (12) and $CW = C$ one gets

$$\widetilde{A} + \widetilde{L}C = W(A + W^{-1}\widetilde{L}C)W^{-1}.$$

Thus, the matrix $A + LC$ of the estimation error $e = \hat{x} - x$ dynamics (10) with $L = W^{-1}\widetilde{L}$ is Hurwitz and the dynamical system (9) with the gain vector $L = W^{-1}\widetilde{L}$ behaves as a global asymptotical observer for the linearized cerebral hemodynamics (7). Then, integrating the observer (9) from arbitrary initial conditions one gets an asymptotically converging estimate $\hat{x}(t)$ for the state $x(t)$ of the linear system (7), which in its turn yields the intracranial pressure $P_{ic}(t)$ estimation as $\hat{P}_{ic}(t)$ for all $t \geq 0$.

3 Cerebral autoregulation output feedback design

By using the change of the state variables $z = (z_1, z_2)^{\mathrm{T}} = \Phi(V_a, P_{ic})$ given by

$$\begin{aligned} z_1 &= \varphi_1(V_a, P_{ic}) = k_E V_a - \ln P_{ic}, \\ z_2 &= \varphi_2(V_a, P_{ic}) = \frac{-k_E R_{pv}}{R_{pv} + R_f} q + \frac{k_E}{R_o} P_{ic} - k_E \left(\frac{P_{vs}}{R_o} + I_i \right) \end{aligned} \tag{14}$$

it is shown in [5, 4] that the nonlinear cerebral hemodynamics (1) are diffeomorphic to

$$\dot{z}_1 = z_2, \ \dot{z}_2 = \tilde{f}(z_1, z_2) + \tilde{g}(z_1, z_2) u$$

on the whole set Ω given by (5) for almost all values of $P_a \in [60, 160]$. Here

$$\tilde{f}(z) = \Big[f(V_a, P_{ic}) \Big]_{(V_a, P_{ic})^{\mathrm{T}} = \Phi^{-1}(z)}, \ \tilde{g}(z) = \Big[g(V_a, P_{ic}) \Big]_{(V_a, P_{ic})^{\mathrm{T}} = \Phi^{-1}(z)},$$

$$\begin{aligned} f(V_a, P_{ic}) = {} & P_{ic} k_E^2 (P_a - P_{ic}) (R_f^2 {k'_R}^2 + 2 R_f R_{pv} {k'_R}^2 + R_{pv}^2 {k'_R}^2 + 2 R_f^2 R_{pv} V_a^2 k'_R \\ & + 2 R_f R_{pv}^2 V_a^2 k'_R + 3 R_o R_f R_{pv} V_a^2 k'_R + 3 R_o R_{pv}^2 V_a^2 k'_R + R_f^2 R_{pv}^2 V_a^4 \\ & + R_o R_f R_{pv}^2 V_a^4) (P_a R_o R_{pv} V_a^2 - P_{ic} R_o R_{pv} V_a^2 - P_{ic} R_f R_{pv} V_a^2 + P_{vs} R_f R_{pv} V_a^2 \\ & - P_{ic} R_f k'_R - P_{ic} R_{pv} k'_R + P_{vs} R_f k'_R + P_{vs} R_{pv} k'_R + I_i R_o R_f R_{pv} V_a^2 + I_i R_o R_f k'_R \\ & + I_i R_o R_{pv} k'_R)) / (R_o^2 (R_f R_{pv} V_a^2 + R_f k'_R + R_{pv} k'_R)^3 (P_a - P_{ic} + P_{ic} V_a k_E), \end{aligned}$$

$$\begin{aligned} g(V_a, P_{ic}) = {} & P_{ic} k_E^2 (P_a - P_{ic})^2) / (R_o (P_a - P_{ic} + P_{ic} V_a k_E)) \\ & + (P_{ic} R_{pv} V_a^2 k_E^2 (P_a - P_{ic})^2) / ((R_f R_{pv} V_a^2 + R_f k'_R + R_{pv} k'_R)(P_a - P_{ic} \\ & + P_{ic} V_a k_E)) - (2 R_{pv} V_a k_E k'_R (R_f + R_{pv}) (P_a - P_{ic})^3) / ((R_f R_{pv} V_a^2 + R f k'_R \\ & + R_{pv} k_R)^2 (P_a - P_{ic} + P_{ic} V_a k_E). \end{aligned}$$

To achieve the regulation $z_1(t) - z_{1r} \to 0$ and $z_2(t) \to 0$ as $t \to +\infty$ one can employ [5] the state feedback linearization based control

$$\begin{aligned} u = & k(V_a, P_{ic}) = \frac{1}{\tilde{g}(z_1, z_2)} \big(-\tilde{f}(z_1, z_2) - c_1 (z_1 - z_{1r}) - c_2 z_2 \big) \\ & = \frac{1}{g(V_a, P_{ic})} \big(-f(V_a, P_{ic}) - c_1 (z_1 - z_{1r}) - c_2 z_2 \big) \end{aligned} \tag{15}$$

which results in the following regulation error dynamics:

$$\begin{aligned} \overbrace{z_1 - z_{1r}}^{\cdot} &= z_2, \\ \dot{z}_2 &= -c_1 (z_1 - z_{1r}) - c_2 z_2. \end{aligned} \tag{16}$$

Hence, for any positive gain coefficients $c_1 > 0$ and $c_2 > 0$ the equilibrium point $z_1 = z_{1r}$, $z_2 = 0$ of the system (16) is globally asymptotically stable. Here, in view of (14) one takes the reference value $z_{1r} = k_E V_{ar} - \ln P_{icr}$ of the z_1 variable, with the arterial-arteriolar blood volume reference value V_{ar} being defined by the first equality in (6) with $q = q_n$, $P_{ic} = P_{icr}$.

Then, using the separation principle [6] let us replace the state variables V_a and P_{ic} in the state feedback (15) by their estimates $\hat{V}_a$ and $\hat{P}_{ic}$ obtained from the state observer (9) and

relations (6). As a result, one gets a cerebral blood flow autoregulation model in the form of the following dynamic output feedback:

$$\begin{aligned}
\dot{C}_a = k(\hat{V}_a, \hat{P}_{ic}) = \frac{1}{g(\hat{V}_a, \hat{P}_{ic})}\Big(-f(\hat{V}_a, \hat{P}_{ic}) - c_1(k_E\hat{V}_a - \ln\hat{P}_{ic} - k_E V_{ar} + \ln P_{icr}) \\
-c_2\left(\frac{-k_E R_{pv}}{R_{pv}+R_f}q + \frac{k_E}{R_o}\hat{P}_{ic} - k_E\left(\frac{P_{vs}}{R_o} + I_i\right)\right)\Big),\ c_1 > 0,\ c_2 > 0, \\
\dot{\hat{x}} = A\hat{x} + Bk(\hat{V}_a, \hat{P}_{ic}) + F_r + LC(\hat{x} - x),\ \hat{x} = (\hat{q} - q_n, \hat{P}_{ic} - P_{icr})^{\mathrm{T}}, \\
\hat{V}_a = \sqrt{\frac{k'_R(R_{pv}+R_f)q}{(R_{pv}+R_f)(P_a - \hat{P}_{ic}) - R_{pv}R_f q}}.
\end{aligned} \tag{17}$$

Notice that due to validity of the separation principle at least locally [6] the output feedback (17) guarantees the regulation $V_a(t) - V_{ar} \to 0$ and $P_{ic}(t) - P_{icr} \to 0$ as $t \to +\infty$ for initial values $V_a(0)$ and $P_{ic}(0)$ in some neighborhood of the nominal point $V_a = V_{ar}$, $P_{ic} = P_{icr}$ in the state space of the system (1). Finally, in view of the equality $q(V_{ar}, P_{icr}) = q_n$ the output regulation (3) is achieved at least locally for initial state values close to the nominal points $V_a = V_{ar}$, $P_{ic} = P_{icr}$ and $q = q_n$, $P_{ic} = P_{icr}$ in the state spaces of the systems (1) and (4), respectively.

The numerical simulation results of the cerebral blood flow autoregulation design (17) performance under the model parameter values of a healthy adult [11] indicated in Section 2 are shown in Figs. 2 – 5 for the arterial pressure steady state value $P_a(t) \equiv 120$ mmHg, control and observer gain coefficients $c_1 = 0.0076$, $c_2 = 2.0038$ and $l_1 = -3.001$, $l_2 = -7.196$ respectively. The initial values of the system and observer state variables were taken as follows: $V_a(0) = 11.6899$ ml, $P_{ic}(0) = 7.5406$ mmHg, $\hat{q}(0) = q(0) = 12.0616$ ml/s, $\hat{P}_{ic}(0) = 7.3898$.

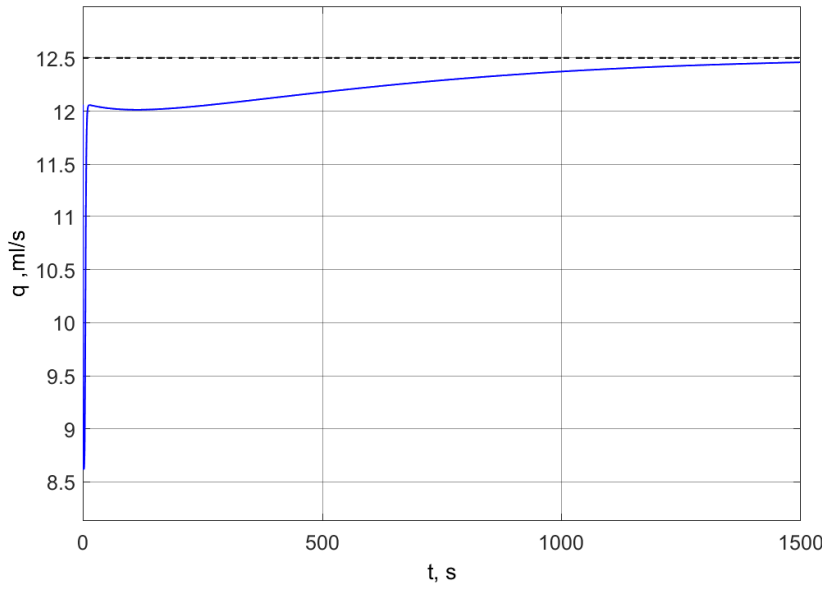

Figure 2: Arterial-arteriolar blood flow rate q (solid blue line) and its reference value q_n (dashed line) as time functions.

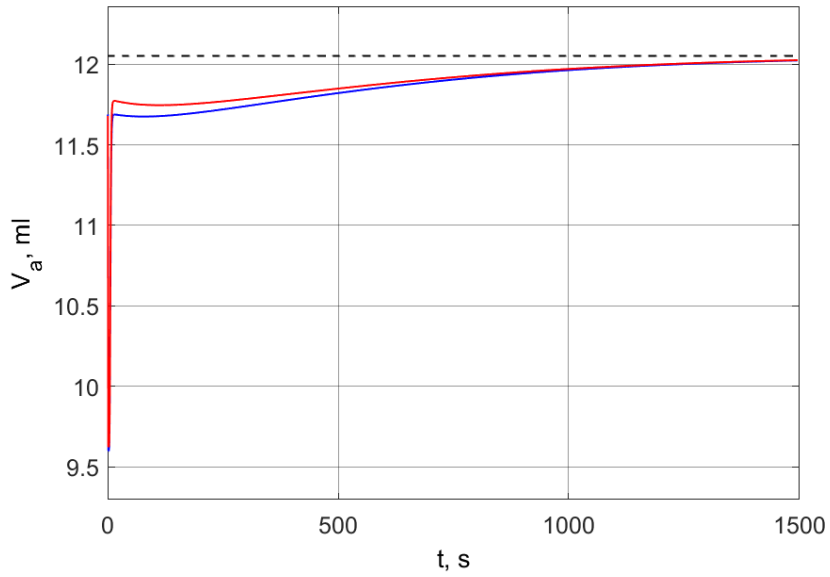

Figure 3: Arterial-arteriolar blood volume V_a (solid blue line), its estimation $\hat{V}_a$ (solid red line) and its reference value V_{ar} (dashed line) as time functions.

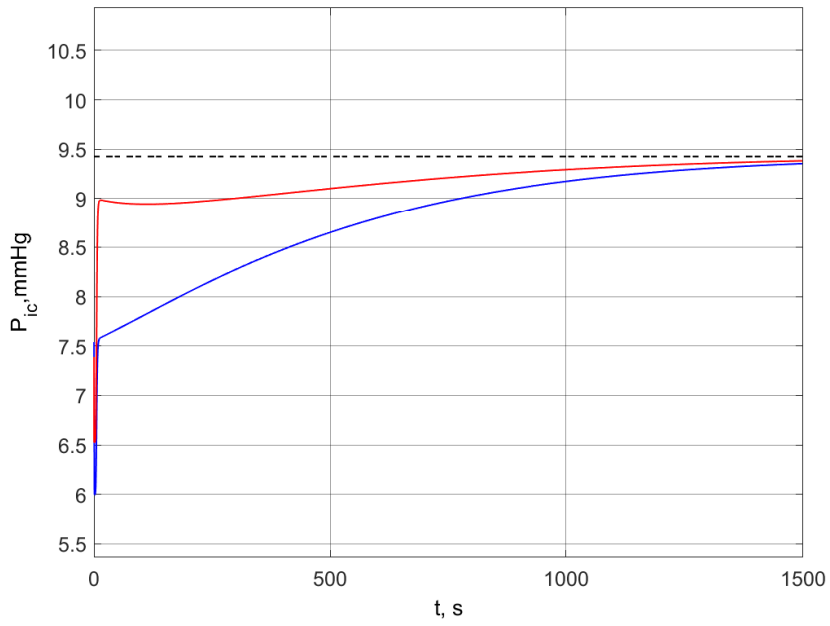

Figure 4: Intracranial pressure P_{ic} (solid blue line), its estimation $\hat{P}_{ic}$ (solid red line) and its reference value P_{icr} (dashed line) as time functions.

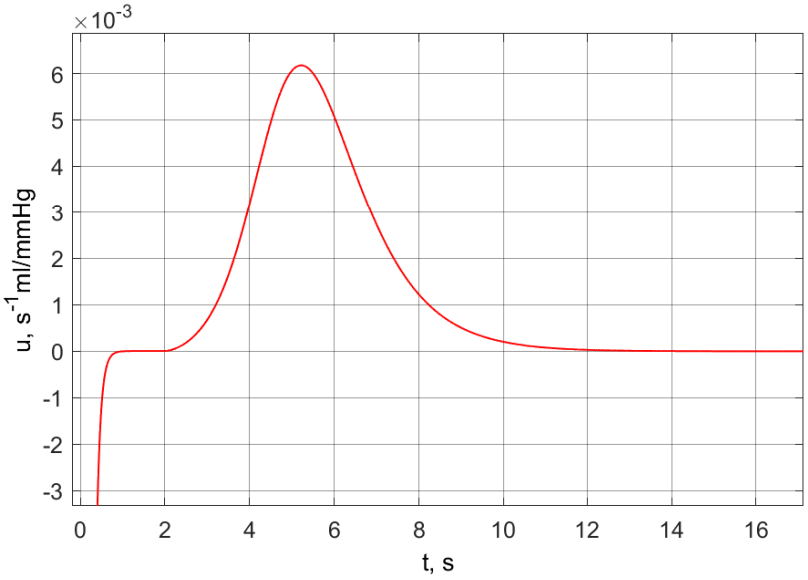

Figure 5: Arterial-arteriolar compliance rate $\dot{C} = u$ initial time behaviour.

4 Conclusion

In this note, we considered the cerebral blood flow autoregulation modeling problem as an output regulation control problem. The cerebral autoregulation process is treated a dynamic output feedback using measurements of the arterial-arteriolar blood flow rate values and intracranial pressure estimates made by an asymptotic state observer. Numerical simulation results demonstrated good performance of the suggested cerebral blood flow autoregulation model and provided medically reasonable transients within required regulation times and bounds. Still, it is worthwhile to notice that future research can be focused on strengthening of the suggested output feedback design to provide the system's state and, in particular, the intracranial pressure estimates that are valid not only locally around a nominal linearization point but e.g. globally. It also should be guaranteed that the state variables remain within required bounds during transients for the whole range of initial values and gain coefficients like it is done in [5] for the proposed cerebral autoregulation state feedback design.

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