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Abstract

In this paper, we complete the stability analysis of various human respiratory nonlinear time delay models introduced in (Vielle & Chavet 1998), (Kollár & Turi 2004), (Batzel & Tran 2000*a*), and (Batzel & Tran 2000*b*). More precisely, we present a detailed mathematical analysis of the stability of the nonlinear model trivial equilibrium, an estimate of its region of attraction and exponential estimates of the solutions starting in this region. The proposed approach is constructive and it is based on the use of Lyapunov-Krasovskii functionals of complete type for time-delay systems with a cross term in the time derivative.

1 Introduction

Roughly speaking, the respiratory system includes two compartments, lungs and lumped body tissue connected by the circulating blood (Timischl 1998), (Hoppensteadt & Peskin 1992) and it is characterized by the presence of two types of processes: the distribution of O_2 to the cells and the elimination of the CO_2 in the tissues of the body (Murray 1993). The classical way to represent the dynamics of such compartments defining the respiratory system is based on the mass balance equations. For example, the change of CO_2 volume in the lung compartment is determined by the balance between the expired/diffusion rate of CO_2 expired from/into the lungs. A similar mass balance equation holds also for the change of O_2 (see, e.g., (Timischl 1998)). In the absence of voluntary control of breathing or neurological induced changes in breathing, the physiological human respiratory control system varies the ventilation rate in response to the levels of CO_2 and O_2. In this context, without any attempt for a deeper discussion on the modelling part, the breathing process in the biological circuit controlling the carbon-dioxide level in the blood is a *transport* process that is typically represented by a set of delay differential equations.

The aim of this paper is to propose a deeper analysis of the stability properties of the trivial solution of different proposals of nonlinear models of the human respiratory system with transport delays in their representation that are encountered in the literature. More precisely, we will consider four models: (Vielle & Chavet 1998), (Kollár & Turi 2004), (Batzel & Tran 2000*b*), and (Batzel & Tran 2000*a*). In our analysis, we will exploit *explicitly* the particular structure of the system and the properties of the system's nonlinearities. Furthermore, the analysis is completed by providing an estimate of the region of attraction of the trivial solution and an exponential estimate of the solutions whose initial conditions are in this region. To the best of the authors' knowledge, there does not exist similar results and comparisons for the analysis of the respiration system. The approach considered here is based on the use Lyapunov-Krasovskii functionals of complete type (Kharitonov & Zhabko 2003) with crossing term in the time derivative (Mondié, Kharitonov & Santos 2005). Such an approach is inspired by the ideas introduced in (Melchor-Aguilar & Niculescu 2007). It should be mentioned that the estimate of the domain of attraction has also been successfully studied in the framework of Lyapunov Krasovwkii functionals with polynomial dependence on the the system state (Coutinho & de Souza 2008).

The paper is organized as follows: In Section 2, we briefly introduce the respiratory system models mentioned above (Vielle & Chavet 1998), (Kollár & Turi 2004), (Batzel & Tran 2000*b*), (Batzel & Tran 2000*a*). In Section 3, we give the main theoretical results on the asymptotic stability of the trivial solution, an estimate of the region of attraction, and exponential estimates for a class of nonlinear system. Finally, in Section 4, we perform the detailed analysis of the stability properties of the corresponding respiratory system models. Section 5 is devoted to the dirrect computation of estimates based on polar coordinates. The paper ends with some concluding remarks.

2 Mathematical model of the respiratory system

The human respiratory system can be viewed as an interconnection between a **plant** which describes the distribution of O_2 to the cells and the elimination of the CO_2 in the tissues of the body, and a physiological **controller** which regulates the CO_2 and/or O_2 partial pressure P in the body by acting on the air flow in Lungs with a time lag h. Next, we remind four models available in the literature were different structures of the plant and controller are proposed.

2.1 Mathematical Model I

In the model introduced in Vielle and Chauvet (Vielle & Chavet 1998) the *plant* describes the CO_2 exchanges in lungs and tissues and the *controller* regulates the CO_2 partial pressure in lungs with a time lag h:

$$\begin{aligned}\dot{P}_T(t) &= \kappa_1 P_L(t) - \kappa_1 P_T(t) + \kappa_2,\\ \dot{P}_L(t) &= \kappa_3 P_T(t) - \kappa_3 P_L(t) - \kappa_4(P_L(t) - \kappa_5)F(P_L(t-h)),\end{aligned} \tag{1}$$

where $\kappa_1,\ \kappa_2\ \kappa_3,\ \kappa_4$ *and* κ_5 are strictly positive constants, P_L and P_T denote the CO_2 partial pressures in lungs and tissues. Here, $F(\cdot)$ is the controller function. The following assumptions hold:

(V1) The CO_2 partial pressure in lungs is greater than the atmospheric pressure κ_5: $P_L > \kappa_5$.

(V2) The controller function $F(\nu)$ is a continuous positive function defined on $\mathbb{R}^+$ which has zero value for $\nu \leq \nu_0$ and a strictly positive derivative for $\nu > \nu_0$.

As shown in (Vielle & Chavet 1998), the equilibrium point $(\overline{P}_T, \overline{P}_L)$ of system (1) satisfies:

$$\overline{P}_T = \overline{P}_L + \frac{\kappa_2}{\kappa_1}, \tag{2}$$

$$F(\overline{P}_L) = \frac{\kappa_2\kappa_3}{\kappa_1\kappa_4[\overline{P}_L - \kappa_5]}. \tag{3}$$

By introducing the new variables $y_1(t) = P_T(t) - \overline{P}_T$, $y_2(t) = P_L(t) - \overline{P}_L$ and considering that $F(P_L(t-h)) \approx F(\overline{P}_L) + F'(\overline{P}_L)y_2(t-h)$, system (1) can be rewritten as:

$$\begin{pmatrix}\dot{y}_1(t)\\ \dot{y}_2(t)\end{pmatrix} = A_0 \begin{pmatrix}y_1(t)\\ y_2(t)\end{pmatrix} + A_1 \begin{pmatrix}y_1(t-h)\\ y_2(t-h)\end{pmatrix} + f(y_1(t), y_2(t), y_1(t-h), y_2(t-h)) \tag{4}$$

where

$$A_0 = \begin{pmatrix}-\kappa_1 & \kappa_1\\ \kappa_3 & -[\kappa_3 + \kappa_4\overline{F}]\end{pmatrix},\ A_1 = \begin{pmatrix}0 & 0\\ 0 & -\kappa_4\overline{F}_p[\overline{P}_L - \kappa_5]\end{pmatrix}, \tag{5}$$

and

$$f(y_1(t), y_2(t), y_1(t-h), y_2(t-h)) = \begin{pmatrix} 0 \\ -\kappa_4 \overline{F}_p y_2(t) y_2(t-h) \end{pmatrix}, \tag{6}$$

with $\overline{F} = F(\overline{P}_L)$, $\overline{F}_p = F'(\overline{P}_L)$.

The following conditions for the stability of the linear part of system (4) known as the nominal system is asymptotically stable are available:

Lemma 1 *(Vielle & Chavet 1998) If κ_1, κ_3, $\kappa_4\overline{F}$, $\kappa_4\overline{F}_p[\overline{P}_L - \kappa_5]$ are strictly positive coefficients, and $\overline{F} < \overline{F}_p[\bar{P}_L - \kappa_5]$, then there exists $h_0 > 0$ such that the nominal system of* (4) *is asymptotically stable for $h \in [0, h_o)$ and unstable for $h \geq h_0$.*

Let us consider the following Hill controller function

$$F(\nu) = V_m \frac{\nu^n}{\theta^n + \nu^n}, \quad \nu \geq 0, \tag{7}$$

where $V_m > 0$ is the maximum air flow, $n > 0$ is the Hill coefficient, and $\theta > 0$ is the Hill parameter. Observe that function (7) satisfies **(V2)** if $\nu \geq \nu_0 = 0$.

Consider the parameters of system (4) and of the controller function (7) given in (Vielle & Chavet 1998): $\kappa_1 = 0.0067$, $\kappa_3 = 0.1448$, $\kappa_4 = 3200^{-1}$, $\kappa_5 =0.3$, $\theta = 48.6$, $Vm = 1330$, and $n =13.7$.

Using (2) and (3) we obtain that the equilibrium is $(\overline{P}_T, \overline{P}_L) =(47.27{,}39.97)$. Substituting into (7) implies that $F(\overline{P}_L) =85.38 mls^{-1}$ and $F'(\overline{P}_L) =27.39$.

By Lemma 1 we have that $\omega_o =0.2897$ and $h_o =7.249$, hence the nominal system of (4) is asymptotically stable for all $h \in [0, 7.249)$ and unstable for all $h \geq 7.249$.

2.2 Mathematical Model II

In Kollar and Turi (Kollár & Turi 2004) the *plant* describes CO_2 and O_2 arterial partial pressures in lungs while the *controller* regulates the CO_2 partial pressure and the O_2 partial pressure in lungs with a time lag h:

$$\begin{aligned} \dot{P}_c(t) &= 1 - \alpha P_c(t) F(P_c(t-h), P_o(t-h)), \\ \dot{P}_o(t) &= 1 - \beta P_o(t) F(P_c(t-h), P_o(t-h)), \end{aligned} \tag{8}$$

where P_c is the CO_2 partial pressures in lungs, P_o is the O_2 partial pressures in lungs, α and β are positive constants and $F(\cdot, \cdot)$ is the controller function with a transport delay. It is biologically realistic to assume that the controller function satisfies the following properties:

(K1) $F(\nu_1, \nu_2) \geq 0$ and $F(0,0) = 0$,

(K2) $F(\nu_1, \nu_2)$ is differentiable, and

(K3) $F_{\nu_1} = \partial F(\nu_1, \nu_2)/\partial \nu_1 > 0$, $F_{\nu_2} = \partial F(\nu_1, \nu_2)/\partial \nu_2 > 0$.

The unique positive equilibrium $(\overline{P}_c, \overline{P}_o)$ of system (8) is such that

$$\begin{aligned} 0 &= 1 - \alpha F(\overline{P}_c, \overline{P}_o)\overline{P}_c, \\ 0 &= 1 - \beta F(\overline{P}_c, \overline{P}_o)\overline{P}_o. \end{aligned} \tag{9}$$

By introducing the new state variables $y_1(t) = P_c(t) - \overline{P}_c$, $y_2(t) = P_o(t) - \overline{P}_o$, and considering a first order Taylor series approximation of $F(P_c(t), P_o(t))$, the system (8) can be rewritten as

$$\begin{pmatrix} \dot{y}_1(t) \\ \dot{y}_2(t) \end{pmatrix} = A_0 \begin{pmatrix} y_1(t) \\ y_2(t) \end{pmatrix} + A_1 \begin{pmatrix} y_1(t-h) \\ y_2(t-h) \end{pmatrix} + f(y_1(t), y_2(t), y_1(t-h), y_2(t-h)) \tag{10}$$

where

$$A_0 = \begin{pmatrix} -\alpha\overline{F} & 0 \\ 0 & -\beta\overline{F} \end{pmatrix}, A_1 = \begin{pmatrix} -\alpha\overline{P}_c\overline{F}_{P_c} & -\alpha\overline{P}_c\overline{F}_{P_o} \\ -\beta\overline{P}_o\overline{F}_{P_c} & -\beta\overline{P}_o\overline{F}_{P_o} \end{pmatrix}, \tag{11}$$

and

$$f(y_1(t), y_2(t), y_1(t-h), y_2(t-h)) = \begin{pmatrix} -\alpha\overline{F}_{P_c}y_1(t)y_1(t-h) - \alpha\overline{F}_{P_o}y_1(t)y_2(t-h) \\ -\beta\overline{F}_{P_c}y_2(t)y_1(t-h) - \beta\overline{F}_{P_o}y_2(t)y_2(t-h) \end{pmatrix}, \tag{12}$$

with $\overline{F} = F(\overline{P}_c, \overline{P}_o)$, $\overline{F}_{P_c} = F_{P_c}(\overline{P}_c, \overline{P}_o)$, and $\overline{F}_{P_o} = F_{P_o}(\overline{P}_c, \overline{P}_o)$.

The following stability result for the nominal system is given:

Lemma 2 *(Cooke & Turi 1994) If $\overline{F} < \overline{P}_c\overline{F}_{P_c} + \overline{P}_o\overline{F}_{P_o}$, then there exists $h_0 > 0$ such that the nominal system of* (10) *is asymptotically stable for $h \in [0, h_0)$ and unstable for $h \geq h_0$.*

In the following we analyze system (10) using the parameters $\alpha = 0.5$, $\beta = 0.8$ and the controller function

$$F(\nu_1, \nu_2) = G_P e^{-0.05(100-\nu_2)}(\nu_1 - I_P) \tag{13}$$

proposed in (Kollár & Turi 2004). Here $G_p = 0.14$ and $I_P = 0$ are the control gains and cutoff thresholds, respectively.

It follows from (9) that the the equilibrium is $(\overline{P}_c, \overline{P}_o) = (29.1842, 18.2401)$. Consequently, we obtain from (13) that $\overline{F}_{P_c} = 0.0023$, $\overline{F}_{P_o} = 0.0034$, and $\overline{F} = 0.0685$.

It follows from Lemma 2 that h_o =30.8, hence the nominal system (10) is asymptotically stable for all $h \in [0, 30.8)$ and unstable for all $h \geq 30.8$.

2.3 Mathematical Model III

In Batzel and Tran (Batzel & Tran 2000*b*) the *plant* describes CO_2 and O_2 arterial partial pressures in lungs and the *controller* regulates the CO_2 partial pressure and the O_2 partial pressure in lungs with a time lag h:

$$\begin{aligned}\dot{P}_c(t) &= a_1 - a_2 P_c(t) - a_3 P_c(t) F(P_c(t-h), P_o(t-h)),\\ \dot{P}_o(t) &= b_1 - b_2 P_o(t) - b_3 P_o(t) F(P_c(t-h), P_o(t-h)).\end{aligned} \tag{14}$$

The state variables and the assumptions are the name as those in the previous section. The system (14) has a unique positive equilibrium $(\overline{P}_c, \overline{P}_o)$ such that

$$\begin{aligned}0 &= a_1 - a_2\overline{P}_c - a_3 F(\overline{P}_c, \overline{P}_o)\overline{P}_c,\\ 0 &= b_1 - b_2\overline{P}_o - b_3 F(\overline{P}_c, \overline{P}_o)\overline{P}_o.\end{aligned} \tag{15}$$

By introducing the new state variables $y_1(t) = P_c(t) - \overline{P}_c$, $y_2(t) = P_o(t) - \overline{P}_o$ and considering a first order Taylor series approximation of $F(P_c(t), P_o(t))$, the system (14) can be rewritten as

$$\begin{pmatrix}\dot{y}_1(t)\\ \dot{y}_2(t)\end{pmatrix} = A_0\begin{pmatrix}y_1(t)\\ y_2(t)\end{pmatrix} + A_1\begin{pmatrix}y_1(t-h)\\ y_2(t-h)\end{pmatrix} + f(y_1(t), y_2(t), y_1(t-h), y_2(t-h)) \tag{16}$$

where

$$A_0 = \begin{pmatrix}-a_2 - a_3\overline{F} & 0\\ 0 & -b_2 - b_3\overline{F}\end{pmatrix}, A_1 = \begin{pmatrix}-a_3\overline{P}_c\overline{F}_{P_c} & -a_3\overline{P}_c\overline{F}_{P_o}\\ -b_3\overline{P}_o\overline{F}_{P_c} & -b_3\overline{P}_o\overline{F}_{P_o}\end{pmatrix}, \tag{17}$$

and

$$f(y_1(t), y_2(t), y_1(t-h), y_2(t-h)) = \begin{pmatrix}-a_3\overline{F}_{P_c}y_1(t)y_1(t-h) - a_3\overline{F}_{P_o}y_1(t)y_2(t-h)\\ -b_3\overline{F}_{P_c}y_2(t)y_1(t-h) - b_3\overline{F}_{P_o}y_2(t)y_2(t-h)\end{pmatrix}, \tag{18}$$

with $\overline{F} = F(\overline{P}_c, \overline{P}_o)$, $\overline{F}_{P_c} = F_{P_c}(\overline{P}_c, \overline{P}_o)$, and $\overline{F}_{P_o} = F_{P_o}(\overline{P}_c, \overline{P}_o)$.

The stability of the nominal system has the following characterization:

Lemma 3 *(Batzel & Tran 2000*b*) If $K_1K_3 - (K_1K_4 + K_2K_3) < 0$, then there exists $h_0 > 0$ such that the nominal system of* (16) *is asymptotically stable for $h \in [0, h_0)$ and unstable for $h \geq h_0$. Here, $K_1 = a_2 + a_3\overline{F}$, $K_2 = a_3\overline{P}_c\overline{F}_{P_c}$, $K_3 = b_2 + b_3\overline{F}$ and $K_4 = b_3\overline{P}_o\overline{F}_{P_o}$.*

In the following, we examine system (16) by setting $a_2 = 9.223$, $a_3 = 0.2187$, $b_2 = 0.5178$, $b_3 = 0.28$, and the controller function

$$F(\nu_1, \nu_2) = F_p(\nu_1, \nu_2) + F_c(\nu_1, \nu_2) \tag{19}$$

proposed in (Batzel & Tran 2000b). Here

$$F_p(\nu_1, \nu_2) = G_p e^{-0.05(146-\nu_2)}(\nu_1 - I_p),$$
$$F_c(\nu_1, \nu_2) = K_{Vc1} + K_{Vc2}(\nu_1 - I_c), \tag{20}$$

where $G_p = 45$ is the control gain, $I_p = 35$ is the cutoff thresholds and $K_{Vc1} = 3$, $K_{Vc2} = 0.5$ are positive constants.

It follows from (15) that the equilibrium is $(\overline{P}_c, \overline{P}_o) = (39.57, 48.46)$. One obtains from (19) that $\overline{F}_{P_c}$ =0.8429, $\overline{F}_{P_o} = 0.0783$, $\overline{F}$ =6.852.

By Lemma 3 we have that $\omega_0 = 1.765$ and $h_0 = 95$, hence the nominal of system (16) is asymptotically stable for all $h \in [0, 95)$ and unstable for all $h \geq 95$.

2.4 Mathematical Model IV

In (Batzel & Tran 2000b) a third state equation describing the CO_2 partial pressure in brain denoted by $\sigma(t)$ is introduced in the model of the previous section:

$$\begin{aligned}
\dot{P}_c(t) &= a_1 - a_2 P_c(t) - a_3 P_c(t) F(P_c(t-h), P_o(t-h), \sigma(t)),\\
\dot{P}_o(t) &= b_1 - b_2 P_o(t) - b_3 P_o(t) F(P_c(t-h), P_o(t-h), \sigma(t)),\\
\dot{\sigma}(t) &= c_1 + c_2 P_c(t-h) - c_2 \sigma(t),
\end{aligned} \tag{21}$$

The assumptions on the controller function are now:

(T1) $F(\nu_1, \nu_2, \nu_3) \geq 0$ and $F(0, 0, 0) = 0$,

(T2) $F(\nu_1, \nu_2, \nu_3)$ is differentiable, and

(T3) $F_{\nu_1} = \frac{\partial F(\nu_1,\nu_2,\nu_3)}{\partial \nu_1} > 0$, $F_{\nu_2} = \frac{\partial F(\nu_1,\nu_2,\nu_3)}{\partial \nu_2} > 0$ $F_{\nu_3} = \frac{\partial F(\nu_1,\nu_2,\nu_3)}{\partial \nu_3} > 0$.

As shown in (Batzel & Tran 2000a), system (21) has a unique positive equilibrium $(\overline{P}_c, \overline{P}_o, \overline{\sigma})$ such that

$$\begin{aligned}
0 &= a_1 - a_2 \overline{P}_c - a_3 F(\overline{P}_c, \overline{P}_o) \overline{P}_c,\\
0 &= b_1 - b_2 \overline{P}_o - b_3 F(\overline{P}_c, \overline{P}_o) \overline{P}_o,\\
0 &= c_1 + c_2 \overline{P}_c - c_2 \overline{\sigma}.
\end{aligned} \tag{22}$$

By introducing the new state variables $y_1(t) = P_c(t) - \overline{P}_c$, $y_2(t) = P_o(t) - \overline{P}_o$, $y_3(t) = \sigma(t) - \overline{\sigma}$ and considering a fist order Taylor series approximation of $F(\nu_1, \nu_2, \nu_3)$, the system (21) can be rewritten as

$$\begin{pmatrix} \dot{y}_1(t) \\ \dot{y}_2(t) \end{pmatrix} = A_0 \begin{pmatrix} y_1(t) \\ y_2(t) \end{pmatrix} + A_1 \begin{pmatrix} y_1(t-h) \\ y_2(t-h) \end{pmatrix} + f(y_1(t), y_2(t), y_1(t-h), y_2(t-h)) \tag{23}$$

where

$$A_0 = \begin{pmatrix} -a_2 - a_3\overline{F} & 0 & -a_3\overline{P}_c\overline{F}_{P_c} \\ 0 & -b_2 - b_3\overline{F} & -b_3\overline{P}_o\overline{F}_{P_o} \\ 0 & 0 & -c_2 \end{pmatrix}, A_1 = \begin{pmatrix} -a_3\overline{P}_c\overline{F}_{P_c} & -a_3\overline{P}_c\overline{F}_{P_o} & 0 \\ -b_3\overline{P}_o\overline{F}_{P_c} & -b_3\overline{P}_o\overline{F}_{P_o} & 0 \\ c_2 & 0 & 0 \end{pmatrix}, \tag{24}$$

and

$$f(y_1(t), y_2(t), y_3(t), y_1(t-h), y_2(t-h), y_3(t-h)) = \begin{pmatrix} -a_3\overline{F}_{P_c}y_1(t)y_1(t-h) - a_3\overline{F}_{P_o}y_1(t)y_2(t-h) - a_3\overline{F}_{\sigma}y_1(t)y_3(t) \\ -b_3\overline{F}_{P_c}y_2(t)y_1(t-h) - b_3\overline{F}_{P_o}y_2(t)y_2(t-h) - b_3\overline{F}_{\sigma}y_2(t)y_3(t) \\ 0 \end{pmatrix}, \tag{25}$$

with $\overline{F} = F(\overline{P}_c, \overline{P}_o, \overline{\sigma})$, $\overline{F}_{P_c} = F_{P_c}(\overline{P}_c, \overline{P}_o, \overline{\sigma})$, $\overline{F}_{P_o} = F_{P_o}(\overline{P}_c, \overline{P}_o, \overline{\sigma})$, and $\overline{F}_{\sigma} = F_{\sigma}(\overline{P}_c, \overline{P}_o, \overline{\sigma})$. Using analytical methods to obtain stability conditions for the nominal systems of the previous models is complicated. However, we can determine the stability with the help of a Mikhailov hodograph (Kolmanosvkii & Myshkis 1999).

In the following we examine system (23) by setting $a_2 = 9.2233$, $a_3 = 0.2187$, $b_2 = 0.5178$, $b_3 = 0.28$, c_1=8.1871, c_2 =0.8333 and the controller function

$$F(\nu_1, \nu_2, \nu_3) = F_P(\nu_1, \nu_2, \nu_3) + F_C(\nu_1, \nu_2, \nu_3), \tag{26}$$

given in (Batzel & Tran 2000*a*). Here $F_P(\nu_1, \nu_2, \nu_3) = G_P e^{-0.05(146-\nu_2)}(\nu_1 - I_p)$, $F_C(\nu_1, \nu_2, \nu_3) = G_C(\nu_3 - \frac{c_1}{c_2} - I_C)$,

where $G_P = 45$ and $G_C = 1.2$ are control gains and $I_P = 35$ $I_C = 35$ are cutoff thresholds. It follows from (22) that the equilibrium is $(\overline{P}_c, \overline{P}_o, \overline{\sigma}) = (39.41, 48.74, 49.23)$. We obtain from (26) that $\overline{F}_{P_c}$ =0.3477, $\overline{F}_{P_o}$ =0.0767, $\overline{F}_{\sigma}$ =1.2, $\overline{F}$ =6.82, $\overline{F}_P$ =1.5335, $\overline{F}_C$ =5.2865 and the approximate critical delay is h_0 =95.71.

3 Tools for the stability analysis of the trivial solution

In what follows we introduce results concerning the stability properties of the solutions of nonlinear systems achieved in the framework of Lyapunov-Krasovskii functionals of complete type.

We analyze nonlinear systems of the form

$$\begin{aligned} \dot{y}(t) &= A_0 y(t) + A_1 y(t-h) + f(y(t), y(t-h)), \\ y(\theta) &= \psi(\theta), \quad \theta \in [-h, 0], \end{aligned} \tag{27}$$

where $A_0, A_1 \in \mathbb{R}^{n\times n}$ are given matrices, h is the delay and $\psi \in \mathfrak{C}$ is the initial function. We denote by $y(t,\psi)$ the solution of the system with initial condition ψ, by $y_t(\psi) = \{y(t+\tau,\psi) : \tau \in [-h,0]\}$ the segment of trajectory of the system and by $\mathfrak{C} := C([-h,0],\mathbb{R}^n)$ the Banach space with norm $\|\psi\|_h := \max_{\tau\in[-h,0]} \|\psi(\tau)\|$.

We consider the following assumptions for system (27):

(A1) the nominal system

$$\dot{x}(t) = A_0 x(t) + A_1 x(t-h), \tag{28}$$

is exponentially stable.

The function $f(z_0, z_1)$ satisfies

(A2) $f(\bar{0},\bar{0}) = \bar{0}$, $\bar{0} \in \mathbb{R}^n$,

(A3) $f(z_0, z_1)$, $z_0,\ z_1 \in \mathbb{R}^n$, satisfies a Lipschitz condition in a neighborhood of the origin,

(A4) for any $\gamma > 0$ there exists $\varepsilon = \varepsilon(\gamma) > 0$ such that if $\|(z_0,z_1)\| < \varepsilon$, then $\|f(z_0,z_1)\| < \gamma\|(z_0,z_1)\|_Q$. Here

$$\|(z_0,z_1)\|_Q^2 = \begin{pmatrix} z_0 \\ z_1 \end{pmatrix}^T \underbrace{\begin{pmatrix} Q_{11} & Q_{12} \\ Q_{12} & Q_{22} \end{pmatrix}}_{Q} \begin{pmatrix} z_0 \\ z_1 \end{pmatrix},$$

where $Q \in \mathbb{R}^{2n\times 2n}$ is a positive definite matrix. Observe that if $Q = I_n$, then $\|(z_0,z_1)\|_Q = \|(z_0,z_1)\|$. I_n is the identity matrix in $\mathbb{R}^{n\times n}$.

3.1 Stability of the trivial solution of nonlinear systems

We now obtain asymptotic stability conditions for the trivial solution of the nonlinear system (27) based on the fact that a Lyapunov-Krasovskii functional of complete type $v(y_t)$ admits a quadratic bound and that its time derivative $\dot{v}(y_t)$ along the trajectories of system (27) is negative (Kharitonov & Zhabko 2003).

Lemma 4 *Consider a nonlinear system of the form* (27)*. Let positive definite matrices* $W_i \in \mathbb{R}^{n\times n}$, $i = 0,1,2$ *and a symmetric real matrix* $Z \in \mathbb{R}^{n\times n}$ *such that*

$$\begin{pmatrix} W_0 & ZA_1 \\ A_1^T Z & W_1 \end{pmatrix} > 0$$

be given. Then the trivial solution of the nonlinear system (27) *is asymptotically stable if* *there exists* $\gamma > 0$ *such that*

$$\gamma \begin{pmatrix} \frac{\Gamma}{h}Q_{11} + \frac{u_{oz}}{h}I_n & \frac{\Gamma}{h}Q_{12} & 0 \\ \frac{\Gamma}{h}Q_{12} & \frac{\Gamma}{h}Q_{22} & 0 \\ 0 & 0 & a_1u_1I_n \end{pmatrix} < \begin{pmatrix} \frac{W_0}{h} & \frac{ZA_1}{h} & 0 \\ \frac{A_1^TZ}{h} & \frac{W_1}{h} & 0 \\ 0 & 0 & W_2 \end{pmatrix}, \tag{29}$$

where $\Gamma = u_{oz}/h + a_1u_1$, $a_1 = \|A_1\|$, $u_{oz} = \|U(0, W) - Z\|$, $u_1 = \max_{\tau\in[0,h]}\{\|U(\tau, W)\|\}$, Q_{11}, Q_{22}, Q_{12}, $I_n \in \mathbb{R}^{n\times n}$. *Here,* $U(\tau, W)$ *is the Lyapunov matrix defined in Remark 12 of the appendix.*

Proof. It follows from Assumption **A1** that the nominal system (28) is exponentially stable. Then given a quadratic functional of the form

$$w(x_t) = x^T(t)W_0x(t) + x^T(t-h)W_1x(t-h) + 2x^T(t)ZA_1x(t-h) + \int_{-h}^{0} x^T(t+\tau)W_2x(t+\tau)d\tau,$$

where W_i, $i = 0, 1, 2$, are positive definite matrices, there exists a unique Lyapunov-Krasovskii functional of complete type $v(x_t)$ described by (52) in the appendix such that the time derivative of the functional along the trajectories of the nominal system (28) is $\dot{v}(x_t) = -w(x_t)$ (Mondié et al. 2005).

Now, we observe that the time derivative of the functional along the trajectories of system (27) is

$$\dot{v}(y_t) = -w(y_t) + 2f^T(y(t), y(t-h))\Big[\ [\ U(0, W) - Z\ ]y(t) + \int_{-h}^{0} U(-h-\theta, W)A_1y(t+\tau)d\tau\Big]. \tag{30}$$

It follows from Assumption **A4** that for every $\gamma > 0$ the function $f(z_0, z_1)$ satisfies $\|f(z_0, z_1)\| < \gamma\|(z_0, z_1)\|_Q$. Substituting this inequality into (30) leads to

$$\begin{aligned} \dot{v}(y_t) &\le -w(y_t) + 2\gamma u_{oz}\ \|y(t)\|\ \|(y(t), y(t-h))\|_Q + 2\gamma a_1u_1 \int_{-h}^{0} \|y(t+\tau)\|\ \|(y(t), y(t-h))\|_Q d\tau \\ &\le -\int_{-h}^{0} \begin{pmatrix} y(t) \\ y(t-h) \\ y(t+\theta) \end{pmatrix}^T M \begin{pmatrix} y(t) \\ y(t-h) \\ y(t+\theta) \end{pmatrix} d\theta, \quad t \ge 0, \end{aligned} \tag{31}$$

where

$$M = \begin{pmatrix} \frac{W_0}{h} & \frac{ZA_1}{h} & 0 \\ \frac{A_1^TZ}{h} & \frac{W_1}{h} & 0 \\ 0 & 0 & W_2 \end{pmatrix} - \gamma \begin{pmatrix} \frac{\Gamma}{h}Q_{11} + \frac{u_{zo}}{h}I_n & \frac{\Gamma}{h}Q_{12} & 0 \\ \frac{\Gamma}{h}Q_{12} & \frac{\Gamma}{h}Q_{22} & 0 \\ 0 & 0 & a_1u_1I_n \end{pmatrix},$$

with $\Gamma = a_1u_1h + u_{oz}$, $a_1 = \|A_1\|$, $u_{oz} = \|U(0, W) - Z\|$, $u_1 = \max_{\tau\in[0,h]}\{\|U(\tau, W)\|\}$.

Now, if there exists $\gamma > 0$ such that $M > 0$, we have that

$$\dot{v}(y_t) \leq -\int_{-h}^{0} \lambda_{min}(M)\|(y(t),\ y(t-h),\ y(t+\tau))\|^2 d\tau \leq -\zeta\|y(t)\|^2, \quad t \geq 0, \tag{32}$$

where $\zeta = \lambda_{min}(M)/h$.

In addition, the functional $v(y_t)$ satisfies

$$\alpha_1\|y(t)\|^2 \leq v(y_t) \leq \alpha_2\|y_t\|_h^2, \quad \forall\ t \geq 0, \tag{33}$$

with α_1 and α_2 given by (56) and (57) of Theorem 11 of the Appendix, respectively.

Thus, it follows from (32) and (33) that the functional $v(y_t)$ satisfies the conditions of the Krasovskii asymptotic stability theorem (Krasovskii 1956) and we conclude that the trivial solution of system (27) is asymptotically stable. ■

3.2 Estimate of the region of attraction

The asymptotic stability of the equilibrium of the system is indeed a crucial property. But it is important from a practical point of view to know the set of initial conditions of system (27) that generates trajectories that converge to the equilibrium as t approaches infinity. This set is called the region of attraction of the equilibrium.

Definition 5 *Let the trivial solution of system* (27) *be asymptotically stable. The set*

$$R_A = \left\{\psi \in \mathfrak{C}\ :\ y(t,\psi)\ \textit{is defined}\ \forall\ t \geq 0\ \text{and}\ y(t,\psi) \underset{t\to\infty}{\longrightarrow} 0\right\},$$

is the region of attraction of the trivial solution of system (27)*.*

Definition 6 *Let the trivial solution of system* (27) *be asymptotically stable. A set* $\Omega \subset \mathfrak{C}$ *is said to be an estimate of the region of attraction of the trivial solution of system* (27) *if*

i. $0_h \in \Omega$,

ii. $\Omega \subset R_A$.

The result stated below provides an estimate of the region of attraction of the trivial solution of system (27):

Theorem 7 *Consider a system of the form* (27) *and let* γ *be a positive constant such that* (29) *holds. Then, the set*

$$\Omega = \{\psi \in \mathfrak{C} \ : \ \|\psi\|_h < \nu\} \tag{34}$$

with $\nu = \sqrt{\frac{\alpha_1}{\alpha_2}}\varepsilon/2$ *is an estimate of the region of attraction of the trivial solution of the system. Here, the constant* $\varepsilon = \varepsilon(\gamma)$ *is obtained from Assumption* ***A4*** *and the constants* α_1 *and* α_2 *are given in* (56) *and* (57) *of Theorem 11 of the appendix.*

Proof. We prove that the set (34) satisfies the Conditions of Definition 6.
First, we observe that the set (34) contains the trivial solution, i.e., $\psi = 0_h \in \Omega$.
Now, we shows that for any initial condition in the set (34) the solution of system (27) converge to zero as t approaches infinity.
It follows from Lemma 4 and Assumption **A4** that for $\gamma > 0$ such that (29) holds, there exists $\varepsilon = \varepsilon(\gamma) > 0$ such that

$$\|(y(t), y(t-h))\| < \varepsilon \ \Rightarrow \ \dot{v}(y_t) < 0, \quad \forall\, t \geq 0.$$

This implies that the functional $v(y_t)$ is decreasing for all $t \geq 0$, hence

$$v(y_t) \leq v(\psi), \quad \forall\, t \geq 0.$$

It follows from equation (54) of Theorem 11 of the Appendix that

$$\alpha_1 \|y(t)\|^2 \leq v(y_t) \leq v(\psi) \leq \alpha_2 \|\psi\|_h^2, \quad \forall\, t \geq 0,$$

therefore, for any $\psi \in \Omega$ we have that

$$\|y(t)\| \leq \frac{\varepsilon}{2}, \quad \forall\, t \geq 0.$$

Moreover,

$$\|y(t)\| \leq \frac{\varepsilon}{2}, \quad \Rightarrow \quad \dot{v}(y_t) < 0, \quad \forall\, t \geq 0.$$

Thus,

$$\lim_{t\to\infty} y(t,\psi) = 0, \quad \forall\, \psi \in \Omega. \tag{35}$$

We conclude that the set described by (34) is an estimate of the region of attraction of the trivial solution of system (27). ■

3.3 Exponential estimate of the system response

In this section, we obtain an exponential estimate for the solution of system (27) whose initial condition ψ belongs to the estimate of the region of attraction.

Corollary 8 *Consider a system of the form* (27)*. Then, for any $\psi \in \Omega$ the solution $y(t,\psi)$ of system* (27) *satisfies the following exponential estimate*

$$\|y(t,\psi)\| \leq \delta \|\psi\|_h e^{-\varsigma t}, \quad t \geq 0, \tag{36}$$

where $\delta = \sqrt{\frac{\alpha_2}{\alpha_1}}$ and $2\varsigma = \min\{\lambda_{\min}(R_1)/\eta_1, \lambda_{\min}(R_2)/\eta_2\}$, $\eta_1 = u_{zo} + hu_1 a_1$, $\eta_2 = u_1 a_1 + w_1 + hw_2 + hu_1 a_1^2$, $R_2 = W_2 - \gamma\ a_1 u_1 I_n$ and $R_1 = \begin{pmatrix} W_0 - \gamma[\Gamma Q_{11} + u_{oz} I_n] & ZA_1 - \gamma \Gamma Q_{12} \\ A_1^T Z - \gamma \Gamma Q_{12} & W_1 - \gamma \Gamma Q_{22} \end{pmatrix}$.

Proof. We know that

$$\begin{aligned} \dot{v}(y_t) \leq & - \Big(y^T(t)\ y^T(t-h)\Big) R_1 \begin{pmatrix} y(t) \\ y(t-h) \end{pmatrix} \\ & - \int_{-h}^{0} y^T(t+\tau) R_2 y(t+\tau) d\tau \\ \leq & - \lambda_{\min}(R_1)\|y(t)\|^2 - \lambda_{\min}(R_2) \int_{-h}^{0} \|y(t+\tau)\|^2 d\tau, \quad t \geq 0. \end{aligned} \tag{37}$$

It follows from (52) that

$$v(y_t) \leq \eta_1 \|y(t)\|^2 + \eta_2 \int_{-h}^{0} \|y(t+\tau)\|^2 d\tau, \quad t \geq 0. \tag{38}$$

Now, using (37) and (38) we have that

$$\frac{dv(y_t)}{dt} + 2\varsigma v(y_t) \leq 0, \quad t \geq 0, \tag{39}$$

where $2\varsigma = \min\{\lambda_{\min}(R_1)/\eta_1, \lambda_{\min}(R_2)/\eta_2\}$. Multiplying by $e^{-2\varsigma t}$ both sides of (39) we get

$$\frac{d}{dt}(e^{2\varsigma t} v(y_t)) < 0, \quad t \geq 0.$$

Integrating this inequality from 0 to t and using the fact that the solution goes to zero as t tends to infinity we get

$$v(y_t) \leq e^{-2\varsigma t} v(\psi), \quad t \geq 0,$$

thus (56) and (57) imply that

$$\alpha_1 \|y(t)\|^2 \leq v(y_t) \leq e^{-2\varsigma t} v(\psi) \leq \alpha_2 e^{-2\varsigma t} \|\psi\|, \quad t \geq 0.$$

Finally, recalling that $y(t)$ depends on ψ, i.e. $y(t) = y(t,\psi)$, we conclude that $\|y(t,\psi)\| \leq \sqrt{\frac{\alpha_2}{\alpha_1}} \|\psi\|_h e^{-\varsigma t}, \quad t \geq 0.$ ■

4 Analysis of the human respiratory system

We now analyze the stability properties of the respiratory systems described in Section 2. Due to space limitations we provide the detailed analysis for model I and we give final results for the remaining ones.

The asymptotic stability and exponential stability are equivalent for time delay linear systems because theirs solutions are of exponential type (Gu, Kharitonov & Chen 2003). Therefore, the Assumption **A1** holds in all cases. It is trivial to prove that the Assumptions **A2** and **A3** hold in all the models under study.

In the following subsections we proceed as follows for each respiratory model:

First, we prove that Assumption **A4** is satisfied,

Second, we propose positive definite matrices $W_i \in \mathbb{R}^{n\times n}$, $i = 0, 1, 2$ and a symmetric real matrix $Z \in \mathbb{R}^{n\times n}$ such that

$$\begin{pmatrix} W_0 & ZA_1 \\ A_1^T Z & W_1 \end{pmatrix} > 0$$

holds. Following the methodology proposed in (Garcia-Lozano & Kharitonov 2006) we compute the Lyapunov matriz $U(\tau, W)$ associated to $W = W_0 + W_1 + hW_2 - A_0^T Z - ZA_0$.

Third, we obtain a positive constant γ such that the LMI (29) is feasible. Substituting γ into Assumption **(A4)** yields $\varepsilon = \varepsilon(\gamma)$.

Fourth, we get the quadratic bounds α_1 and α_2 using Theorem 11 of the appendix. The estimate of the region of attraction Ω of the trivial solution of the respiratory system follows from substituting these quadratic bounds and γ into (34).

Finally, an exponential estimate of the solution is obtained from Corollary 8.

Detailed computations for Model I

First, for the nonlinear part (6) we have that

$$\|f(z_0, z_1, z_2, z_3)\|^2 < \frac{(\kappa_4 \overline{F}_p)^2 \varepsilon^2}{4} \|(z_0, z_1, z_2, z_3)\|_Q^2,$$

where $Q = I_4$ is the identity matriz in $\mathbb{R}^{4\times 4}$. Therefore, for any $\gamma > 0$ there exits $\varepsilon = \varepsilon(\gamma)$ solution of the equation

$$\varepsilon = \frac{2\gamma}{\kappa_4 \overline{F}_p} \tag{40}$$

such that $\|f(z_0, z_1, z_2, z_3)\| < \gamma \|(z_0, z_1, z_2, z_3)\|_Q$ if $\|(z_0, z_1, z_2, z_3)\| < \varepsilon$.

Second, choosing $h = 0.5$ and the matrices

$$W_0 = \begin{pmatrix} 1.0766 & -1.9225 \\ -1.9225 & 6.3512 \end{pmatrix}, W_1 = \begin{pmatrix} 0.5379 & -0.8637 \\ -0.8637 & 2.7929 \end{pmatrix},$$
$$W_2 = \begin{pmatrix} 0.6935 & -1.8198 \\ -1.8198 & 5.3915 \end{pmatrix}, \ Z = \begin{pmatrix} 0.8711 & -0.3431 \\ -0.3431 & 1.0586 \end{pmatrix},$$

and following the methodology proposed in (Ochoa & Kharitonov 2005, Garcia-Lozano & Kharitonov 2006) we compute the function $U(\tau, W)$ associated to $W = W_0 + W_1 + hW_2 - ZA - A^T Z$. In this case, u_{oz} =87.174 and u_1 =88.0726.

Third, using (29) we have $\gamma \in$(0,0.002378). Substituting γ =0.002377 into (40) yields ε =0.5554. We also have from (56) and (57) that $\alpha_1 \in$(0,6.2347] and $\alpha_2 \geq$153.1868.

Fourth, we conclude from Theorem 7 that for α_1 =6.2346 and α_2 =153.1868 the set

$$\Omega = \{\psi \in \mathfrak{C} \ : \ \|\psi\|_{0.5} \leq 0.05603\}.$$

is an estimate of the region of attraction of the trivial solution of system (4).

Finally, it follows from Corollary 8 that the solution $y(t, \psi)$ of system (4) such that $\psi \in \Omega$ satisfies

$$\|y(t, \psi)\| \leq 5.394\|\psi\|_{0.5} e^{-2.593\times 10^{-7} t}, \quad t \geq 0. \tag{41}$$

Summary of results for models I to IV

Parameter	Region of Attraction ν	Exponential estimate δ	ς
Model I	0.05603	5.394	2.593×10^{-7}
Model II	0.00618	5.4471	1.054×10^{-7}
Model III	0.00479	53.81	6.72×10^{-7}
Model IV	0.00846	18.5	3.67×10^{-7}

Remark 9 *The estimates of the regions of attractions presented here are conservative. Notice that the matrices W_i, $i = 0, 1, 2$ and Z can be used as free parameters for further improvements.*

5 Estimates of the region of attraction based on polar coordinates

The estimates obtained in the previous section are very conservative due to the type of inequalities used to compute γ and ε. In this section we achieve a better estimate by using a direct model analysis to find the constant ρ greater than $\varepsilon/2$ such that

$$\|y(t)\| < \rho \quad \Rightarrow \quad \dot{v}(y_t) < 0, \ t \geq 0.$$

As in the previous section, we only present the detailed analysis for Model I. The analysis of the other models is similar to the first one.

If the nominal system of (4) is exponentially stable, then there exists a unique Lyapunov-Krasovskii quadratic functional of complete type $v(\cdot)$ such that the time derivative of the functional along the trajectories of system (4) is

$$\begin{aligned}\dot{v}(y_t) &= -w(y_t)\\ &\quad + 2f^T(y(t), y(t-h))\Big[\left[\, U(0,W) - Z \, \right] y(t)\\ &\quad + \int_{-h}^{0} U(-h-\tau, W) A_1 y(t+\tau) d\tau \Big], \quad t \geq 0. \end{aligned} \tag{42}$$

where the function $f(y(t), y(t-h))$ and the matrix A_1 are given by (6) and (5), respectively.

Now, we define $U(0,W) - Z := \begin{pmatrix} u_{01} \, u_{02} \\ u_{02} \, u_{03} \end{pmatrix}$, $U(-h-\tau, W) := \begin{pmatrix} u_{11}(-h-\tau) \, u_{12}(-h-\tau) \\ u_{21}(-h-\tau) \, u_{22}(-h-\tau) \end{pmatrix}$.

Substituting into (42) we have that

$$\begin{aligned}\dot{v}(y_t) &= -w(y_t)\\ &\quad - 2\kappa_4 \overline{F}_p \left[u_{02} y_1(t) y_2(t) y_2(t-h) + u_{03} y_2^2(t) y_2(t-h) \right]\\ &\quad + 2(\kappa_4 \overline{F}_p)^2 (P_L - \kappa_5) \int_{-h}^{0} u_{22}(-h-\tau) y_2(t) y_2(t-h) y_2(t+\tau) d\tau\\ &\leq -w(y_t)\\ &\quad + 2\kappa_4 \overline{F}_p \left[\mid u_{02} \mid \mid y_1(t) y_2(t) y_2(t-h) \mid + \mid u_{03} \mid \mid y_2^2(t) y_2(t-h) \mid \right]\\ &\quad + 2(\kappa_4 \overline{F}_p)^2 (P_L - \kappa_5) u_{22} \int_{-h}^{0} \mid y_2(t) y_2(t-h) y_2(t+\tau) \mid d\tau, \end{aligned} \tag{43}$$

where $u_{22} = \max_{\tau \in [-h,0]} \{ \mid u_{22}(-h-\tau) \mid \}$.

Taking

$$y_1(t) = \rho(t) \sin \theta(t), \quad \text{and} \quad y_2(t) = \rho(t) \cos \theta(t), \tag{44}$$

leads to

$$\begin{aligned}\|(y(t), y(t-h), y(t+\tau))\|^2 &= \|y(t)\|^2 + \|y(t-h)\|^2 + \|y(t+\tau)\|^2, \ \tau \in [-h, 0]\\ &\leq 3\rho^2, \ \tau \in [-h, 0], \end{aligned} \tag{45}$$

where $\rho = \max_{\tau\in[-h,0]}\{\rho(t+\tau)\}$.

Now, substituting (45) and (44) into (43) we get

$$\begin{aligned}\dot{v}(y_t) \leq \int_{-h}^{0} \Big\{ & -3\lambda_{min}(N)\rho^2 \\ & + 2\kappa_4\overline{F}_p\rho^3\left[\frac{|u_{02}|}{h}\,|\sin\theta(t)\cos\theta(t)\cos\theta(t-h)| + \frac{|u_{03}|}{h}\,|\cos\theta(t)\cos\theta(t-h)|\right] \\ & + 2(\kappa_4\overline{F}_p)^2(P_L-\kappa_5)u_{22}\rho^3|\cos\theta(t)\cos\theta(t-h)\cos\theta(t+\tau)|\Big\}d\tau, \end{aligned} \tag{46}$$

where

$$N = \begin{pmatrix} W_0/h & ZA_1/h & 0 \\ A_1^T Z/h & W_1/h & 0 \\ 0 & 0 & W_2 \end{pmatrix}. \tag{47}$$

We see that, $|\sin\theta(t)\cos\theta(t)\cos\theta(t-h)| \leq 0.5$, $|\cos\theta(t)\cos\theta(t-h)| \leq 1$, and $|\cos\theta(t)\cos\theta(t-h)\cos\theta(t+\tau)| \leq 1$, for all $t \geq 0$, therefore

$$\dot{v}(y_t) \leq \int_{-h}^{0}\left(-3\lambda_{min}(N)\rho^2 + 2\kappa_4\overline{F}_p\left[\frac{0.5|u_{02}|}{h} + \frac{|u_{03}|}{h} + u_{22}\kappa_4(P_L-\kappa_5)\overline{F}_p\right]\rho^3\right)d\tau. \tag{48}$$

Thus,

$$\text{if} \quad \|y(t)\| < \rho, \quad \text{then} \quad \dot{v}(y_t) < 0, \quad , \quad \forall\, t \geq 0,$$

where

$$\rho = \frac{3\lambda_{min}(N)}{2\kappa_4\overline{F}_p\left[\frac{0.5|u_{02}|}{h} + \frac{|u_{03}|}{h} + u_{22}\kappa_4(P_L-\kappa_5)\overline{F}_p\right]}. \tag{49}$$

We are now ready to estimate the region of attraction of system (4) with the help of Theorem 7.

Choosing $h = 0.5$ and the matrices

$$\begin{aligned} W_0 &= \begin{pmatrix} 0.5 & 0 \\ 0 & 0.5 \end{pmatrix}, W_1 = \begin{pmatrix} 0.5 & 0 \\ 0 & 0.5 \end{pmatrix}, \\ W_2 &= \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}, \quad Z = \begin{pmatrix} 0 & 0 \\ 0 & 0 \end{pmatrix}, \end{aligned} \tag{50}$$

we compute the function $U(\tau, W)$ associated to $W = W_0 + W_1 + hW_2 - ZA - A^T Z$ (Ochoa & Kharitonov 2005). For this case we obtain that $|u_{02}|$ =2.6, $|u_{03}|$ =1.76 and u_{22} =1.76. It follows from (47) that $\lambda_{\min}(N) = 1$, using (49) we obtain $\rho = 26.06877$. We also have from (56) and (57) that $\alpha_1 \in$(0,0.898] and $\alpha_2 \geq$296.56.

Thus, for α_1 =0.897 and α_2 =296.56 it follows from Theorem 7 that the set

$$\Omega = \{\psi \in \mathfrak{C} \ : \ \|\psi\|_{0.5} \leq 1.4341\}$$

is an estimate of the region of attraction of the trivial solution of system (4).

Summary results for models I to IV

parameters	σ	α_1	α_2	Region of attraction ν
Model I	26.068	0.897	296.56	1.4341
Model II	6.514	3.387	28.63	2.2407
Model III	0.489	0.02	89.23	0.00748
Model IV	1.016	0.0227	32.1	0.02702

Remark 10 *For the Model IV we use spherical coordinates:*

$$y_1(t) = \rho \sin\theta(t) cos\phi(t), \ y_2(t) = \rho \sin\theta(t) \sin\phi(t), \ \text{and } y_3(t) = \rho\cos\theta(t),$$

6 Discussion of results

In the following table we summarize relevant data from sections 4 and 5. The first column is the CO_2 arterial partial pressure in lung equilibrium, while the second and third columns are the values of the parameter ν for the estimates of the region of attraction obtained via the functional general approach and the polar coordinate direct approach, respectively.

	PC_{O_2}(mmHg)	ν (section 4)	ν (section 5)
Model I	39.97	0.05603	1.4341
Model II	29.18	0.0615	2.2407
Model III	39.57	0.004792	0.008458
Model IV	39.41	0.008458	0.02702

The main advantage of the approach based on Lyapunov-Krasovskii functionals introduced in section 3 is that it allows to estimate the region of attraction of a wide class of systems using a systematic methodology. In addition, it allows to obtain exponential estimates of the system response. A consequence of the generality of the method is the conservativeness of the results.

The approach of section 5 is based on the use of polar (or spherical) coordinates combined with a direct, case by case, analysis of the negativity of the time derivative of the functional. As one can observe on the above Table, a significant reduction of the conservatism of the result obtained with this direct approach, when compared to the approach of section 3. The improvement is the consequence of the direct analysis of each model and of the use of polar coordinates. However, this approach does not provide a general methodology. Moreover, it is restricted to two or tree variable systems.

It is acknowledged in the literature (Gaohua & Kimura 2008), (Howard, Milhorn, Benton, Ross & C. Guyton 1965) that the CO_2 arterial partial pressures in lungs is about 40 mmHg. Clearly, the equilibriums of the model of Kollar (Kollár & Turi 2004) is far from this value while those of Vielle, Batzel y Batzel II are close to it. As the model of Vielle provides the less conservative region of attraction and a realistic equilibrium we recommend this model for analyzing the behavior of the system with respect to initial conditions.

7 Concluding remarks

In this paper, we derive conditions under which the trivial solution of the nonlinear respiratory system models proposed in (Vielle & Chavet 1998), (Kollár & Turi 2004), (Batzel & Tran 2000*b*), and (Batzel & Tran 2000*a*) are asymptotically stable, and we propose two estimate of the region of attraction and an exponential estimate for the solutions of systems that starting in the estimate of the region of attraction. The approach considered in the paper is based on the use of Lyapunov-Krasovskii functionals of complete type with a cross term in the time derivative.

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8 Appendix

In this appendix we recall the main results on the functionals of complete type needed in our analysis.

8.1 Lyapunov-Krasovskii functionals of complete type

We summarize the result presented in (Kharitonov & Zhabko 2003) and (Mondié et al. 2005) on functionals with prescribed time derivative with cross terms.
We consider a time delay system of the form

$$\dot{x}(t) = A_0 x(t) + A_1 x(t-h), \tag{51}$$

where A_0 and $A_1 \in \mathbb{R}^{n\times n}$.

Theorem 11 *If the system* (51) *is exponentially stable, then for any given positive definite matrices $W_i \in \mathbb{R}^{n\times n}$, $i = 0,1,2$ and a symmetric real matrix $Z \in \mathbb{R}^{n\times n}$ such that*

$$\begin{pmatrix} W_0 & ZA_1 \\ A_1 Z & W_1 \end{pmatrix} > 0,$$

the functional

$$\begin{aligned} v(x_t) = &- x^T(t) Z x(t) + x^T(t) U(0,W) x(t) \\ &+ 2x^T(t) \int_{-h}^{0} U(-h-\tau, W) A_1 x(t+\tau) d\tau \\ &+ \int_{-h}^{0}\int_{-h}^{0} x^T(t+\tau_1) A_1^T U(\tau_1-\tau_2, W) A_1 x(t+\tau_2) d\tau_1 d\tau_2 \\ &+ \int_{-h}^{0} x^T(t+\tau)\big[W_1 + [h+\tau] W_2\big] x(t+\tau) d\tau, \end{aligned} \tag{52}$$

satisfies the following:

$$\dot{v}(x_t) = -w(x_t), \quad \forall\, t \geq 0, \tag{53}$$

and

$$\alpha_1 \|x(t)\|^2 \leq v(x_t) \leq \alpha_2 \|x_t\|_h^2, \quad \forall\ t \geq 0, \tag{54}$$

where

$$\begin{aligned} w(x_t) =& x^T(t)W_0x(t) + x^T(t-h)W_1x(t-h) \\ &+ 2x^T(t)ZA_1x(t-h) \\ &+ \int_{-h}^{0} x^T(t+\tau)W_2x(t+\tau)d\tau. \end{aligned} \tag{55}$$

$\alpha_1 \in (0, \alpha^*]$, *with* α^* *such that*

$$\begin{pmatrix} W_0 & ZA_1 \\ A_1^T Z & W_1 \end{pmatrix} + \alpha^* \begin{pmatrix} A_0 + A_0^T & A_1 \\ A_1^T & 0 \end{pmatrix} > 0, \tag{56}$$

and $\alpha_2 > 0$ *satisfies*

$$\alpha_2 \geq \kappa(1+h). \tag{57}$$

Here, $\kappa \geq \max\{u_{zo} + hu_1a_1, u_1a_1 + w_1 + hw_2 + hu_1a_1^2\}$*,* $u_{oz} = \|U(0,W) - Z\|$*,* $u_1 = \max_{\tau\in[0,h]}\{\|U(\tau,W)\|\}$*,* $a_1 = \|A_1\|$ *and* $w_i = \|W_i\|$*,* $i = 1, 2$*.*

Remark 12 *The matrix* $U(\tau, W)$ *is called the Lyapunov matrix associated to* $W = W_0 + W_1 + hW_2 - A_0^T Z - ZA_0 \in \mathbb{R}^{n\times n}$ *and the unique solution of the analogue of the Lyapunov Equation for time delay systems is (Ochoa & Kharitonov 2005)*

$$U'(\tau, W) = U(\tau, W)A_0 + U(\tau - h, W)A_1, \quad \tau \geq 0, \tag{58}$$

$$U(-\tau, W) = U^T(\tau, W), \quad \tau \geq 0, \tag{59}$$

$$-W = U'(+0, W) - U'(-0, W). \tag{60}$$