Parameter Identification in a Respiratory Control System Model

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Abstract In this paper we study parameter identification issues by computational means for a set of nonlinear delay equations which have been proposed to model the dynamics of a simplified version of the respiratory control system. We design specific inputs for our system to produce "information rich" output data needed to determine values of unknown parameters. We also consider the effects of noisy measurements in the identification process. Several case studies are included.

1 Introduction

Mathematical models describing the chemical balance mechanism of the respiratory control system are given in the form of nonlinear, parameter dependent, delay differential equations [3, 4, 5]. The analysis of the direct problem (i.e., it is assumed that the values of the parameters are known) corresponding to the model equations shows that the system has a unique equilibrium, and that the stability of this equilibrium depends on the parameter values (see [5] for details). This observation leads naturally to the question of parameter identification in the model equations based on available, but possibly noisy measurements. In this paper we present a computational procedure, applicable for large classes of functional differential equations with state-dependent delays [11, 15, 16] which can be used to perform parameter estimation in respiratory control models. We also illustrate how information rich data can enhance the effectiveness of the estimation process. Another issue we study

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is what are the most promising measurements available for identification purposes (i.e., should one measure gas concentrations or ventilation volumes)?

In Section 2 we introduce our model equations; in Section 3 we describe the numerical method we use to run simulations on the model equations. Section 4 outlines the parameter estimation process and contains several case studies. In Section 5 we provide a discussion of our findings.

2 Model equations

We consider the system of nonlinear delay equations describing a simple model of the human respiratory control system

$$\dot{x}(t) = a_{11} - a_{12}x(t) - a_{13}V(t, x(t-\tau), y(t-\tau))(x(t) - x_I) \quad (1)$$
$$\dot{y}(t) = -a_{21} - a_{22}y(t) + a_{23}V(t, x(t-\tau), y(t-\tau))(y_I - y(t)) \quad (2)$$

where $x(t)$ and $y(t)$ denote the arterial CO_2 and O_2 concentrations, respectively, $V(\cdot,\cdot,\cdot)$ is the ventilation function, τ is the transport delay, x_I and y_I are inspired CO_2 and O_2 concentrations. We assume that the ventilation function has the form

$$V(t, x, y) = G_P(t)W(x, y) \quad (3)$$

where the control gain, $G_P(t)$, is a function of time. For simplicity we assume that the time dependency of G_P is piecewise constant, and in particular,

$$G_P(t) = \begin{cases} G_{P1}, & 0 \le t < \theta_1, \\ G_{P2}, & \theta_1 \le t < \theta_2, \\ G_{P3}, & \theta_2 \le t. \end{cases} \quad (4)$$

where $\theta_1, \theta_2 > 0$, $G_{P1} \ge 0$, $G_{P2} \ge 0$ and $G_{P3} \ge 0$ are constant parameters. W is given by

$$W(x, y) = e^{-0.05y}(x - I_P). \quad (5)$$

Moreover, in (1)-(2) we have that

$$a_{11} = 863\frac{\dot{Q}K_{CO_2}P_{V_{CO_2}}}{M_{L_{CO2}}}$$
$$a_{12} = 863\frac{\dot{Q}K_{CO_2}}{M_{L_{CO2}}}$$
$$a_{13} = \frac{E_F}{M_{L_{CO_2}}}$$
$$a_{21} = 863\frac{\dot{Q}}{M_{L_{O2}}}(-m_v P_{V_{O_2}} + B_a - B_v)$$

$$a_{22} = 863\frac{\dot{Q}m_a}{M_{L_{O_2}}}$$
$$a_{23} = \frac{E_F}{M_{L_{O_2}}},$$

where the normal values of the parameters appearing on the right hand side of the above equations are listed in Table 1 (See also [3]).

Table 1 Normal parameter values

Quantity	Unit	Value
τ	min	0.1417
$\dot{Q}$	l/min	6.0
K_{CO_2}		0.0057
$P_{V_{CO_2}}$	mmHg	46.0
$P_{V_{O_2}}$	mmHg	41.0
$M_{L_{CO_2}}$	l	3.2
$M_{L_{O_2}}$	l	2.5
m_v		0.0021
m_a		0.00025
B_v		0.0662
B_a		0.1728
G_{P1}	l/min/mmHg	45.0
I_P	mmHg	35.0
x_I		0
y_I		146.0

Substitution of the normal values into equations (1)–(2) yields

$$\begin{aligned}\dot{x}(t) &= 422.4277 - 9.2233x(t) \\ &\quad -0.21875V(t, x(t-0.1417), y(t-0.1417))x(t) \qquad (6)\\ \dot{y}(t) &= -42.8946 - 0.5178y(t) \\ &\quad +0.28V(t, x(t-0.1417), y(t-0.1417))(146 - y(t)) \qquad (7)\end{aligned}$$

with ventilation function

$$V(t,x,y) = G_P(t)e^{-0.05y}(x-35), \qquad (8)$$

where G_P is defined by (3).

3 Numerical Approximation

In this section we define a simple numerical scheme to approximate solutions of (1)–(2). This method is introduced in [10] for linear scalar delay and neutral differential equations, and later this scheme was extended for a large class of nonlinear delay systems in [11, 12]. Let h be a fixed positive constant, and define the notation

$$[t]_h = \left[\frac{t}{h}\right] h,$$

where $[\cdot]$ is the greatest integer function. Then $[t]_h$ as a function of t is piecewise constant, since $[t]_h = nh$ for $t \in [nh, (n+1)h)$. For a fixed $h > 0$ we associate the system

$$\begin{aligned} \dot{x}_h(t) &= a_{11} - a_{12}x_h([t]_h) \\ &\qquad -a_{13}V([t]_h, x_h([t]_h - [\tau]_h), y_h([t]_h - [\tau]_h))(x_h([t]_h) - x_I) \end{aligned} \tag{9}$$

$$\begin{aligned} \dot{y}_h(t) &= -a_{21} - a_{22}y_h([t]_h) \\ &\qquad +a_{23}V([t]_h, x_h([t]_h - [\tau]_h), y_h([t]_h - [\tau]_h))(y_I - y_h([t]_h)) \end{aligned} \tag{10}$$

for $t \geq 0$. For negative t we associate the initial functions of (1) and (2) to (9) and (10), respectively. System (9)–(10) is a system of equations with piecewise constant argument (EPCA). Such equations were introduced and first studied by Cooke and Wiener ([6, 7, 8, 20]). The solutions, x_h and y_h, of (9)–(10) are defined as continuous functions, which are differentiable and satisfy system (9)–(10) on each interval $(nh, (n+1)h)$ $(n = 0, 1, 2, \ldots)$. Since the right-hand-side of both (9) and (10) are constant on each interval $[nh, (n+1)h)$, we get that both x_h and y_h are piecewise linear continuous functions (linear spline functions). Therefore, they are determined by their values at the mesh points nh. Introduce the sequences

$$u_n = x_h(nh) \quad \text{and} \quad v_n = y_h(nh),$$

and let

$$k = \left[\frac{\tau}{h}\right].$$

Then integrating (9) and (10) from nh to t and taking the limit $t \to (n+1)h-$, we get by simple calculation that u_n and v_n satisfy

$$u_{n+1} = u_n + h\Big(a_{11} - a_{12}u_n - a_{13}V(nh, u_{n-k}, v_{n-k})(u_n - x_I)\Big), \tag{11}$$

$$v_{n+1} = v_n + h\Big(-a_{21} - a_{22}v_n + a_{23}V(nh, u_{n-k}, v_{n-k})(y_I - v_n)\Big), \tag{12}$$

for $n = 0, 1, 2, \ldots$, where for negative integer n the sequences u_n and v_n are defined by $u_n = x(nh)$ and $v_n = y(nh)$, i.e.,the initial functions corresponding to the original system (1)–(2). Therefore the sequences u_n and v_n are well-defined and can be easily generated by the explicit delayed recurrence relations (11)–(12), so the solutions of (9)–(10) are uniquely determined. It is shown in [11] that

$$\lim_{h\to 0+} x_h(t) = x(t) \quad \text{and} \quad \lim_{h\to 0+} y_h(t) = y(t)$$

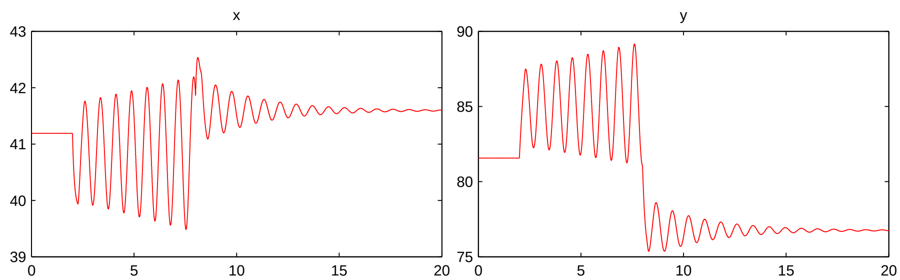
uniformly on each interval $[0,T]$ for any $T > 0$.

Example 1. In this example we study numerically the effect of changing the control gain for the stability of the solutions of the respiratory system (1)–(2). We assume normal table values except that we use $\tau = 0.25$, i.e., we consider (6)-(7) with ventilation (3)–(5). Furthermore, in (4) we select $\theta_1 = 2$, $\theta_2 = 8$ for the switching times, and $G_{P1} = 45$, $G_{P2} = 60$ and $G_{P3} = 30$ for the control gains. We start the system from its equilibrium corresponding to the $G_P(t) = G_{P1}$ constant gain, i.e., use constant initial functions

$$x(t) = 41.1906, \qquad t \le 0, \quad \text{and} \quad y(t) = 81.5645, \qquad t \le 0,$$

The numerical solution corresponding to the discretization constant $h = 0.001$ is shown in Figure 1.

Fig. 1



We can see from the figure that the equilibrium of the system with gain $G_P(t) = G_{P2}$ is unstable, (in fact, it is asymptotically periodic if we compute the solution for a long enough time interval), but after switching back to gain constant $G_P(t) = G_{P3}$, it is again asymptotically stable.

4 Parameter Estimation

We consider again system (1)–(2) with ventilation (3)-(4). We assume that some of the parameters in this system are not known, and we denote the unknown parameters by $\gamma_1, \dots, \gamma_m$. We can consider, for example, the control gain constants G_{P1}, G_{P2} and G_{P3} as the unknown parameters (in that case $m = 3$ and $\gamma_i = G_{Pi}$ for $i = 1,2,3$), or the transport delay τ can be the only unknown parameter ($m = 1$, $\gamma_1 = \tau$), but we can consider any other parameters in equations (1) and (2), or in the ventilation function (3)–(4) to be unknown. The goal is to determine the values of these unknown parameters, assuming we know the measurements of the solutions at finitely many times, $t_1, t_2, \dots, t_M$. One standard approach to this problem is to define a least-square cost function, and then find the parameter values with the least possible cost.

First we need to introduce the following notation. Assume all parameters (including the initial functions) except $\gamma_1, \dots, \gamma_m$ in (1)–(2), (3)-(4) are fixed. Then the solutions corresponding to particular selections of the parameter values $\gamma_1, \dots, \gamma_m$ of this problem are denoted by

$$x(t;\gamma_1,\dots,\gamma_m) \quad \text{and} \quad y(t;\gamma_1,\dots,\gamma_m).$$

Suppose the measurements of x and y at the time t_i are denoted by X_i and Y_i, respectively, for $i = 0,\dots,M$. We will use equally spaced measurements over a time interval $[T_0, T]$, i.e.,

$$t_i = T_0 + \frac{T - T_0}{M} i, \qquad i = 0, 1, \dots, M. \tag{13}$$

Of course, any time values could be used. Then we define the cost function by

$$J(\gamma_1,\dots,\gamma_m) = \sum_{i=1}^{M} (x(t_i;\gamma_1,\dots,\gamma_m) - X_i)^2 + \sum_{i=1}^{M} (y(t_i;\gamma_1,\dots,\gamma_m) - Y_i)^2. \tag{14}$$

Then the mathematical problem is to find the parameter values $\gamma_1, \dots, \gamma_m$ which minimize the cost function J.

One standard approach to solve this problem used e.g., in [1, 2, 13, 14, 17] is the following: find finite dimensional approximate solutions x^N, y^N of (1)-(2), and define the corresponding cost J^N as

$$J^N(\gamma_1,\dots,\gamma_m) = \sum_{i=1}^{M} (x^N(t_i;\gamma_1,\dots,\gamma_m) - X_i)^2 + \sum_{i=1}^{M} (y^N(t_i;\gamma_1,\dots,\gamma_m) - Y_i)^2,$$

and find the minimizer $(\gamma_1^N, \dots, \gamma_m^N)$ of J^N. One can show (see, e.g., [14]) that, under minor assumptions, a subsequence of $(\gamma_1^N, \dots, \gamma_m^N)$ approaches to the minimizer of J.

In this paper we consider a sequence of discretization constants, h_N, tending to 0, and use the approximation scheme defined in the previous section corresponding to h_N as the numerical scheme in the above process. Then if N is large enough, i.e., equivalently, h_N is small enough, we find the minimizer of the corresponding cost function J^N by a a nonlinear least square minimization code, based on a secant method with Dennis-Gay-Welsch update, combined with a trust region technique. See Section 10.3 in [9] for detailed description of this method. Then we consider the result as the approximation of the minimizer of J. Here we know that for the “true parameters” the value of the cost function is 0, so if the numerical method stops at a parameter value where the cost function is not close to 0, then we can conclude that the method is terminated at a local minimum instead of a global minimum. Then we restart the method from a different initial parameter value. Of course, we know that the numerical method converges only locally, so we have to find initial guesses close enough to the true parameter values in order to observe convergence. Another important issue in the parameter estimation process is that whether two different parameter sets can generate the same measurements, i.e., the question of identifiability of the parameters. This is a difficult theoretical problem (see, e.g., [18, 19] or Example 5.4 in [14]). The lack of identifiability can be another reason for getting non converging approximations.

In the remaining part of this section we give several numerical examples to demonstrate the applicability of the above parameter estimating process for the respiratory system (1)–(4). In all these examples we achieved good recovery of the original parameters, which also indicated that we numerically observed identifiability of the considered parameters.

Example 2. In this example we generated measurements of (1)–(4) corresponding to the normal parameter values listed in Table 1 and using a constant gain coefficient function $G_P(t)$, i.e.,

$$G_{P1} = G_{P2} = G_{P3} = 45.$$

We assume that the system is at the equilibrium, so we use initial conditions $x(t) = 41.1906$ and $y(t) = 81.5645$ which correspond to the equilibrium values. The measurements are taken over the interval $[T_0, T] = [0, 2]$ using formula (13) with $M = 11$. We consider the coefficients a_{12}, a_{13}, a_{22} and a_{23} to be unknown, and the goal in this example is to estimate these parameter values using the measurements. In this example we used discretization stepsize $h = 0.01$ and the initial parameters

$$a_{12} = 8.5, \qquad a_{13} = 0.3, \quad a_{22} = 0.6, \quad \text{and} \quad a_{23} = 0.4.$$

The first three steps of the numerical method can be seen in Figure 2. The solid line is the solution x, y and the ventilation function W along the solutions corresponding to the true parameters, and the circles are the measurements of the respective functions at sample time points. The dotted curves are the solutions x, y and the ventilation V along the solutions corresponding to parameter values generated by the numerical scheme in the first two steps. We can see that the graphs approach to the graph corresponding to the true parameter values even in the first few steps. Table 2 contains the value of the cost function, the actual parameter value, and the error of the particular parameter when compared to the true parameter value at each step. (We denote the error in the parameter γ by $\Delta(\gamma)$.) The method converges in five steps, but in each parameter value a small error can be observed. Our explanation for this error (which can be seen running the code from different initial values, as well) is that the constant solution is not "rich enough" for better estimation.

Example 3. In this example we change the gain constants in the ventilation to move the solutions away from the equilibrium. We use switching times $\theta_1 = 0.2$ and $\theta_2 = 0.4$ and gain constants

Fig. 2

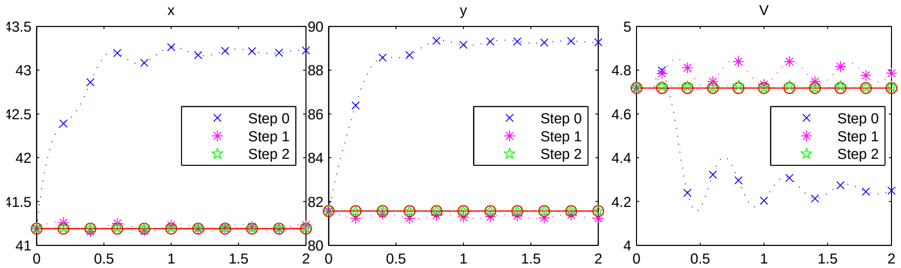


Table 2 Estimation of $a_{12}, a_{13}, a_{22}, a_{23}$, case $G_{P1} = G_{P2} = G_{P3} = 45$

step	cost	a_{12}	a_{13}	a_{22}	a_{23}	$\Delta(a_{12})$	$\Delta(a_{13})$	$\Delta(a_{22})$	$\Delta(a_{23})$
0	287.84623772	8.50000	0.30000	0.60000	0.40000	0.72330	0.08125	0.08220	0.12000
1	0.38419648	8.80052	0.30321	0.86988	0.36664	0.42278	0.08446	0.35208	0.08664
2	0.00077480	8.81127	0.30535	0.86543	0.37275	0.41203	0.08660	0.34763	0.09275
3	0.00056159	8.81142	0.30538	0.86538	0.37282	0.41188	0.08663	0.34758	0.09282
4	0.00043748	8.81160	0.30541	0.86535	0.37287	0.41170	0.08666	0.34755	0.09287
5	0.00034371	8.81177	0.30544	0.86533	0.37290	0.41153	0.08669	0.34753	0.09290
6	0.00034371	8.81177	0.30544	0.86533	0.37290	0.41153	0.08669	0.34753	0.09290

$$G_{P1} = 45, \quad G_{P2} = 0, \quad G_{P3} = 60.$$

This corresponds to the physical case when one takes normal breaths, then stops breathing for 12 seconds (between time 0.2 and 0.4 minutes), but then takes larger breaths for a while. We again try to estimate a_{12}, a_{13}, a_{22} and a_{23}. We used the same initial parameter values, measurements and $h = 0.01$ as in Example 2. The numerical results can bee seen in Figure 3 and in Table 3. In this case we achieved perfect recovery of the true parameter values up to 5 decimal digits accuracy in the fifth step.

Fig. 3

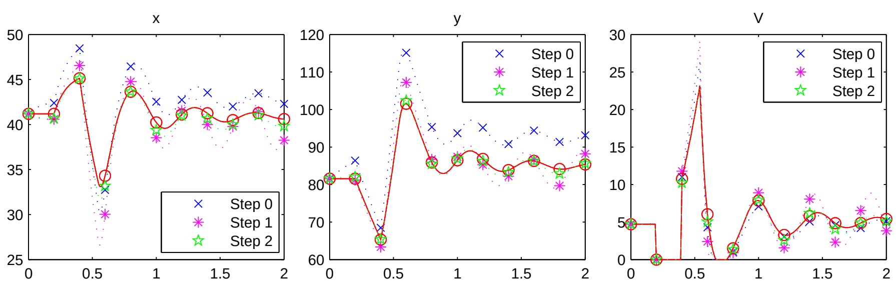


Table 3 Estimation of $a_{12}, a_{13}, a_{22}, a_{23}$, case $G_{P1} = 45$, $G_{P2} = 0$, $G_{P3} = 60$

step	cost	a_{12}	a_{13}	a_{22}	a_{23}	$\Delta(a_{12})$	$\Delta(a_{13})$	$\Delta(a_{22})$	$\Delta(a_{23})$
0	350.31169443	8.50000	0.30000	0.60000	0.40000	0.72330	0.08125	0.08220	0.12000
1	51.72675038	8.86517	0.33654	0.63847	0.30804	0.35813	0.11779	0.12067	0.02804
2	3.54921161	9.21149	0.25766	0.53943	0.29705	0.01181	0.03891	0.02163	0.01705
3	0.00525638	9.21676	0.22070	0.51609	0.27984	0.00654	0.00195	0.00171	0.00016
4	0.00000009	9.22328	0.21876	0.51779	0.28000	0.00002	0.00001	0.00001	0.00000
5	0.00000000	9.22330	0.21875	0.51780	0.28000	0.00000	0.00000	0.00000	0.00000

Example 4. Now we use the same measurements and $h = 0.01$ as in Example 3, but this time we consider G_{P1}, G_{P2} and G_{P3} as the unknown parameters in the system. (The switching times are the same as in the previous example.) Starting from the initial guess $G_{P1} = G_{P2} = G_{P3} = 40$, we again get good approximation of the true parameters, as can be seen in Figure 4 and in Table 4.

Fig. 4

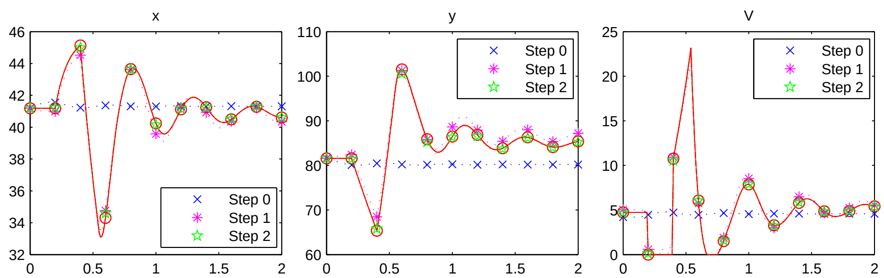


Table 4 Estimation of G_{P1}, G_{P2} and G_{P3}

step	cost	G_{P1}	G_{P2}	G_{P3}	$\Delta(G_{P1})$	$\Delta(G_{P2})$	$\Delta(G_{P3})$
0	483.75379438	40.00000	40.00000	40.00000	5.00000	40.00000	20.00000
1	14.01499742	47.97180	5.86922	68.70514	2.97180	5.86922	8.70514
2	0.90980645	44.53413	1.28130	59.25469	0.46587	1.28130	0.74531
3	0.04368879	45.07905	0.28985	59.98344	0.07905	0.28985	0.01656
4	0.03010176	44.99316	0.28580	60.00549	0.00684	0.28580	0.00549
5	0.01160245	44.80199	0.28644	60.08301	0.19801	0.28644	0.08301
6	0.01160203	44.80199	0.28644	60.08302	0.19801	0.28644	0.08302

Example 5. In this example we repeat the previous experiment with the only difference that in the measurements of x and y there is a random error of normal distribution with absolute value less than 0.3. The corresponding numerical results can be seen in Figure 5 and in Table 5. With these noisy measurements the numerical

Fig. 5

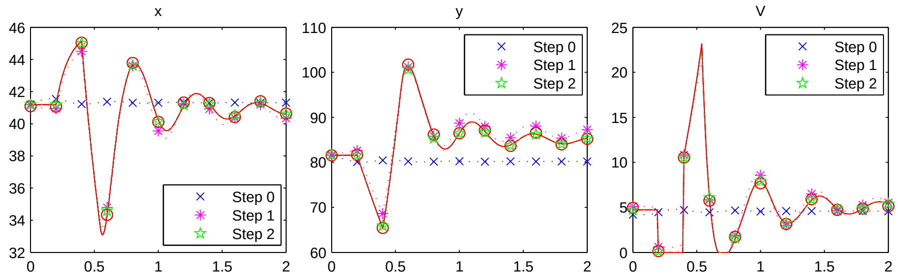


Table 5 Estimation of G_{P1}, G_{P2} and G_{P3} using noisy measurements of x and y

step	cost	G_{P1}	G_{P2}	G_{P3}	$\Delta(G_{P1})$	$\Delta(G_{P2})$	$\Delta(G_{P3})$
0	485.59595635	40.00000	40.00000	40.00000	5.00000	40.00000	20.00000
1	14.52482670	47.17405	5.54416	68.35639	2.17405	5.54416	8.35639
2	1.15085189	43.70021	1.16266	58.68728	1.29979	1.16266	1.31272
3	0.24101584	44.26992	0.20717	59.44590	0.73008	0.20717	0.55410
4	0.22474717	44.17809	0.20403	59.46826	0.82191	0.20403	0.53174
5	0.20156319	43.98286	0.20541	59.55063	1.01714	0.20541	0.44937
6	0.20156185	43.98286	0.20541	59.55066	1.01714	0.20541	0.44934

results still converge, but we can observe larger errors, in G_{P1} and G_{P3}, than in the previous example.

Example 6. In this example we assume that we do not have direct measurements of the solutions x and y, instead, we suppose we can measure the value of the ventilation function along the solution. Let $\bar{G}_{P1}, \bar{G}_{P3}, \bar{G}_{P3}$ denote the true parameters,

$$V_i = V(t_i, x(t_i; \bar{G}_{P1}, \bar{G}_{P3}, \bar{G}_{P3}), y(t_i; \bar{G}_{P1}, \bar{G}_{P3}, \bar{G}_{P3})), \qquad i = 0, 1, \ldots, M,$$

and now we use the following cost function

$$\tilde{J}(G_{P1}, G_{P3}, G_{P3}) = \sum_{i=0}^{M} (V(t_i, x(t_i; G_{P1}, G_{P3}, G_{P3}), y(t_i; G_{P1}, G_{P3}, G_{P3})) - V_i)^2$$

instead of the one defined by (14). Otherwise we used the same initial parameters and discretization constant as in the previous example. The corresponding results can be found in Figure 6 and in Table 6. We can see that the measurements of the ventilation contained enough information on the parameters to guarantee the convergence of the method. In fact, in this case the last step was even better than that in the previous example.

Example 7. We repeat the previous experiment but adding a random error of normal distribution with absolute value less than 0.3 to the measurements of V used in the

Fig. 6

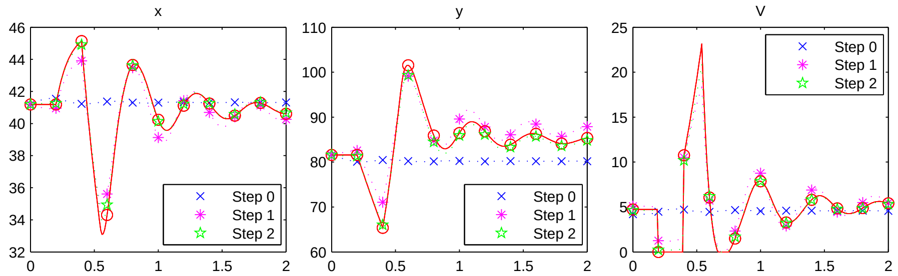
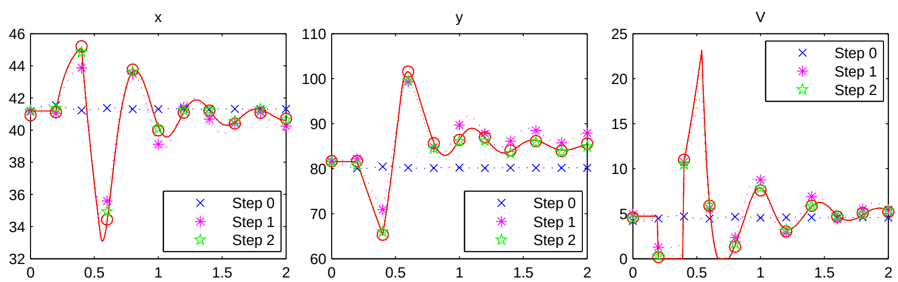


Table 6 Estimation of G_{P1}, G_{P2} and G_{P3} using measurements of V

step	cost	G_{P1}	G_{P2}	G_{P3}	$\Delta(G_{P1})$	$\Delta(G_{P2})$	$\Delta(G_{P3})$
0	42.10899178	40.00000	40.00000	40.00000	5.00000	40.00000	20.00000
1	2.63937045	48.52067	12.50361	71.69544	3.52067	12.50361	11.69544
2	0.22630530	44.09782	2.03095	57.15278	0.90218	2.03095	2.84722
3	0.00867380	45.50737	0.13858	60.12323	0.50737	0.13858	0.12323
4	0.00443630	45.31892	0.13395	60.05083	0.31892	0.13395	0.05083
5	0.00044917	45.01624	0.13081	59.99976	0.01624	0.13081	0.00024
6	0.00025245	44.95685	0.12889	60.00478	0.04315	0.12889	0.00478

previous example. With these noisy measurements the numerical approximations still converge, but the rate of convergence is very slow. We listed only the first 7 steps of the numerical method in Table 7, and the first two iterates in Figure 7. We can observe larger error than in the previous example.

Fig. 7



Example 8. In this example we assume that the transport delay τ is the only unknown parameter. If we start the system from its equilibrium, then changing the time delay has no effect on the solution, therefore it is not possible to identify the delay from such measurement. Therefore it is necessary to move the system away from the equilibrium. We apply the same procedure as before, i.e., we change the gain values at the switching times as follows

Table 7 Estimation of G_{P1}, G_{P2} and G_{P3} using noisy measurements of V

step	cost	G_{P1}	G_{P2}	G_{P3}	$\Delta(G_{P1})$	$\Delta(G_{P2})$	$\Delta(G_{P3})$
0	41.06549791	40.00000	40.00000	40.00000	5.00000	40.00000	20.00000
1	2.69930168	47.91054	12.67821	71.49751	2.91054	12.67821	11.49751
2	0.26392223	43.53271	2.32477	56.08888	1.46729	2.32477	3.91112
3	0.10162997	43.60376	0.87665	57.97591	1.39624	0.87665	2.02409
4	0.10161041	43.59960	0.87671	57.97828	1.40040	0.87671	2.02172
5	0.10148228	43.54956	0.88325	57.97853	1.45044	0.88325	2.02147
6	0.10142830	43.52050	0.89136	57.96415	1.47950	0.89136	2.03585
7	0.10135694	43.47035	0.90820	57.93390	1.52965	0.90820	2.06610

$$\theta_1 = 0.2, \quad \theta_2 = 0.4, \quad G_{P1} = 45, \quad G_{P2} = 0, \quad G_{P3} = 60.$$

We also observed that if we use measurements on the interval where the solution is still constant, i.e., on $[0, 0.2]$, then at these points the solution again does not depend on the delay, and the numerical minimization method will not usually converge. Therefore now we used the interval $[T_0, T] = [0.3, 2]$ to make measurements using equidistant time points with $M = 11$. Starting from $\tau = 0.25$ and using $h = 0.0005$ we obtained a convergent sequence, what can be seen in Figure 8 and in Table 8. We get again a very good approximation of the original delay value, $\tau = 0.1417$. In this experiment the convergence of the scheme is sensitive for the selection of the initial parameter value. The reason of it is that if at any step the numerical scheme produces a "large" τ, then using that τ the corresponding solution will be constant on $[0.3, 1]$, therefore the minimization will fail. Also, in identifying the delay the discretization constant has to be very small, since otherwise small change in the delay has no effect on the approximate solution, so the minimization will fail. For the same reason, in the minimization code the parameter which determines the time steps of computing approximate derivatives has to be relatively large (compared to the previous examples) otherwise again the change in the delay will not effect the solution, so the minimization will fail.

Fig. 8

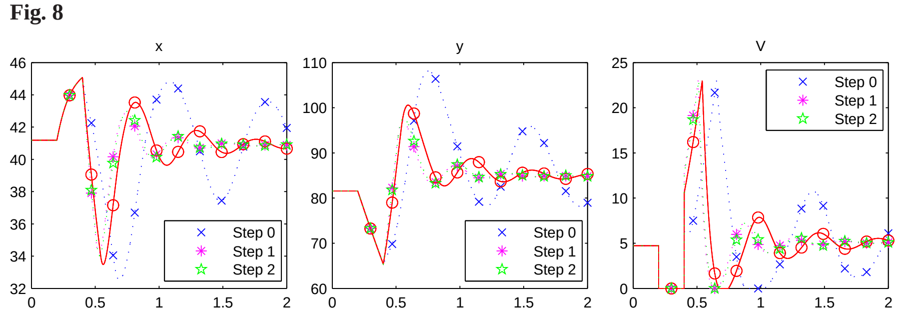


Table 8 Estimation of τ

step	cost	τ	$\Delta(\tau)$
0	458.59350832	0.25000	0.10830
1	53.96078682	0.10704	0.03466
2	42.51290806	0.11226	0.02944
3	20.15586956	0.12306	0.01864
4	0.29816598	0.14364	0.00194
5	0.00000000	0.14178	0.00008

5 Conclusions

We have investigated parameter identification issues in a simplified model of the respiratory system. Case studies indicated identifiability of various system parameters, e.g., coefficients, gains, and transport delay. We obtained strong evidence that "information rich" input data significantly improves the accuracy of the determination of unknown parameters. Our numerical simulations also showed that identification of system parameters is more or less equally possible either by measuring O_2, CO_2 concentrations or ventilation data. The method presented here is applicable to models with multiple state-dependent delays [17, 16].

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