A simple mathematical model of spontaneous swallow effects on breathing based on new experimental data

Julie Fontecave-Jallon, Pierre Baconnier

***Abstract*— The coordination of respiration and swallowing involves an interaction between two central pattern generators, and this can be disturbed in some pathological situations. To better understand this interaction, we aim in this study to characterize the effect of a spontaneous swallow on the breathing pattern. This is first realized using Respiratory Inductive Plethysmography on 11 healthy subjects. Real signals highlight several mechanisms for swallowing: ending of inspiration, prolongation of expiration or active expiration. These behaviours have been integrated in an existing model of the respiratory system simulating the activity of the respiratory centers, the respiratory muscles, and rib cage internal mechanics. The resulting model of interaction between breathing and swallowing is compatible with the observed effects and is driven for swallowing by a limited number of parameters.**

I. Introduction

The coordination of respiration and swallowing during drinking and feeding consists in the arrest of respiration during the pharyngeal phase of swallowing, and resumption of the respiratory cycle at the expiratory phase after swallowing. This coordination involves interaction between the two central pattern generators (CPGs) for respiration and swallowing. A disturbed swallow/breathing coordination resulting in aspiration (the bolus to be swallowed goes into the respiratory tract) is observed in some pathological situations like stroke or some neural diseases (see [1]). In order to detect such dysfunctions, it may be convenient to have available a model of the swallow/breathing interaction in healthy humans. The aim of the present study is to characterise the effect of a single swallow on the breathing pattern and to propose a simple model of this interaction.

It is generally admitted that even if spontaneous swallows may occur during all phases of the respiratory cycle, approximately 80% occur during the expiratory phase in humans. A swallow coinciding with the expiratory phase prolongs the duration of the expiration that had been interrupted, whereas a swallow coinciding with the inspiratory phase interrupts the inspiration immediately and is followed by a short expiratory duration [2]. Precise data on the phase relationship between respiration and swallowing [3,4] showed that swallows induce a respiratory phase resetting. Similar data obtained on cats with carotid sinus nerve stimulation instead of spontaneous swallows, have been qualitatively simulated by centrifugal perturbations of a mathematical oscillator [5]. However, this model could not simulate the abrupt shift from inspiration to expiration due to a swallow occurring during inspiration. Moreover, this study did not mention the active expiration sometimes observed after a swallow in late expiration in human subjects [3,6] and in rats [7]. We then decided to describe the effect of spontaneous swallows in normal humans on the respiratory pattern. This was carried out in 11 healthy volunteers using Respiratory Inductive Plethysmography for characterizing the respiratory pattern changes due to swallows as described in [8]. Our team has proposed a model [9,10] of the respiratory system including an oscillator simulating the respiratory CPG, a simulation of the pressure generated by the respiratory muscles driven by the CPG and a mechanical analogue of the passive thoraco-pulmonary system. The modified model proposed in the present study includes a perturbation of the oscillator compatible with the observed effects, particularly the abrupt interruptions of inspiration and active expirations.

II. Characterization of the Effects of Spontaneous Swallows on Real Respiratory Signals

A. Experimental recordings

Signal acquisitions were conducted in the TIMC-IMAG Laboratory. This study was approved by the relevant ethics committee (CHU Grenoble). Eleven healthy volunteers (6 men and 5 women, from 22 to 64 years old) participated in the study after providing informed consent.

Each subject wearing a connected Respiratory Inductive Plethysmography (RIP) jacket above its clothes, in a meal-time seated position, was asked to repeat 6 times a spontaneous swallow of saliva. Intervals of 30 seconds were kept between each deglutition and the times of all events beginnings were manually annotated by the investigator.

Thorax (THO) and abdomen (ABD) cross sectional area changes were recorded with the computer-assisted RIP vest (Visuresp®, RBI, Meylan, France). During 3-4 minutes at the beginning of each recording, breathing was also simultaneously recorded with a flowmeter (Fleish head no.1, emka Technologies, Paris, France) and a differential transducer (163PC01D36, Micro Switch, Honeywell, United States) placed on a face mask.

The RIP volume signal V_{RIP} was obtained from THO and ABD, using the method proposed by [11]. All signals were digitized at a rate of 100 Hz.

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B. Characterization of swallowing from real signals

RIP volume signals allow a characterization and a classification of spontaneous swallows of saliva for various subjects. We observe several patterns of swallowing, which can be gathered so as to consider 3 main situations, depending on the swallowing position in the respiratory cycle (Fig.1).

- I: When swallowing occurs during inspiration, the inspiration is stopped and swallowing is directly followed by expiration.
- E: When swallowing occurs during expiratory phase, at the end of the swallow, the expiration ends as it would have without the deglutition.
- Ea: In some cases, swallowing in expiration is followed by an active expiration which decreases the respiratory volume under the Functional Residual Volume.

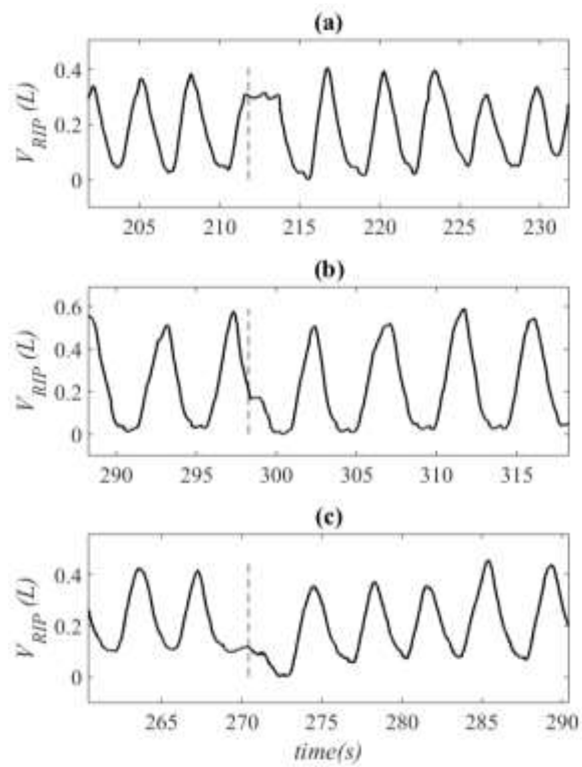


Figure 1. Typical swallowing patterns on V_{RIP} signals, depending when it occurs in the respiratory cycle: (a) swallow in inspiration I, (b) swallow in expiration E, and (c) swallow followed by an active expiration Ea. Deglutition events are illustrated by vertical dashed lines.

Table I summarizes for each subject the number of deglutition events in these 3 situations. It can be noted that most of the events occur in the expiratory part of the respiratory cycle. 86% of the spontaneous swallowing events are classified into E or Ea, respectively 55% and 31%. Only 14% of swallows occur during inspiration. This is in agreement with literature, which says that great majority of apneas which accompany a swallow are preceded and followed by expiration, but a substantial amount of swallow in healthy adults are also initiated during inspiration [12]. Moreover, for each subject, one pattern seems to be always dominating. For one subject, among 6 repetitions of swallow, at least 4 are reproducible of the same pattern (E or Ea).

TABLE I. CLASSIFICATION OF THE SWALLOWS BETWEEN INSPIRATION (I), EXPIRATION (E) AND ACTIVE EXPIRATION (EA) FOR THE 11 SUBJECTS, ACCORDING TO RESPIRATORY SIGNALS

Subject	Number of swallows		
	I	**E**	**Ea**
1	1	5	0
2	1	1	4
3	0	1	5
4	0	1	5
5	2	4	0
6	2	4	0
7[a]	1	4	0
8	1	5	0
9	0	6	0
10	1	5	0
11	0	0	6

a.one deglutition was not exploitable

III. MODEL AND SIMULATION

A. Mathematical model for ventilation

The model considered for ventilation is based on a ventilatory neuro-muscular model simulating the activity of the respiratory centers, the respiratory muscles, and rib cage internal mechanics. It is consisted of two main parts: the mechanics of the thoraco-pulmonary system, and the command and activity of the respiratory muscles. It combines a central respiratory pattern generator and a passive mechanical respiratory system [9].

A Lienard oscillatory system is used as basis for modelling the respiratory rhythm generator, since the use of these 2-dimensional ordinary differential equations systems is universal in biological modelling. As in [10], the model of central respiratory pattern generator is then defined by the following equations, where x and y are the variables of the Lienard system (x a hidden variable, and y the activity of the respiratory rhythm generator), and V the alveolar volume. The constant A is referring to the Hering-Breuer reflex, triggered to prevent over-inflation of the lungs, and α allows to cover a wide range of respiratory frequencies. When y<0 (resp. y>0) the oscillator is considered in inspiratory (resp. expiratory) phase.

$$\frac{dx}{dt} = \alpha.\left((\mathrm{a}.y^2 + \mathrm{b}.y).(x + y) - \mathrm{A}.\frac{dV}{dt} \right) \quad (1)$$

$$\frac{dy}{dt} = \alpha.x \quad (2)$$

The pressure generated by the respiratory muscles (P_{mus}) is the result of the conversion by the muscles of the respiratory pattern generator output into a pressure. As in [9], P_{mus} is a function of y taken as simple as possible, with B a constant.

$$P_{mus} = \begin{cases} B.y & \text{if} \quad y < 0 \\ 0 & \text{if} \quad y > 0 \end{cases} \tag{3}$$

The human mechanical respiratory system links the airflow and the alveolar volume via the pleural pressure (P_{pl}.), with $\mathrm{E_{alv}}$ the elastance of the alveola and $\mathrm{R_a}$ the airways resistance.

$$\frac{dV}{dt} = -\frac{P_{pl} + \mathrm{E_{alv}}V}{\mathrm{R_a}} \tag{4}$$

Finally, in presence of muscular activity, the alveolar volume is driven by P_{pl} and P_{mus}, following equation (5), $\mathrm{E_{cw}}$ being the elastance of the chest wall.

$$P_{pl} = P_{mus} + \mathrm{E_{cw}}V \tag{5}$$

The standard values for the respiratory parameters of the model are listed in Table II.

TABLE II. RESPIRATORY MODEL PARAMETERS VALUES

Parameters	***Values***
$\mathrm{E_{alv}}$	5 $cmH_2O.l^{-1}$
$\mathrm{E_{cw}}$	4 $cmH_2O.l^{-1}$
$\mathrm{R_a}$	6 $cmH_2O.l^{-1}.s$
A	1 $cmH_2O.l^{-1}$
B	1 cmH_2O
a	-0.5
b	-3

B. *Mathematical model for swallowing*

When studying the relationship between breathing and deglutition, it was observed that a physiological apnea occurs as a brief closure of the larynx to protect the airway from the aspiration of the bolus ingested [13]. Therefore, in the model just described, the variable V corresponding to the alveolar volume will be considered constant during the duration of the swallow, since no air exchange occurs during this event. This is also in agreement with the experimental recordings of V_{RIP} signals. In other words, equation (4) is replaced during swallowing by:

$$\frac{dV}{dt} = 0 \tag{4'}$$

Deglutition stops the respiratory oscillator and keeps the ventilatory motor neurons at their level of activity [4,5]. Moreover, deglutition modifies the state of the respiratory oscillator so that it reaches a level, corresponding to an “expiratory state”. These behaviors are simulated by equations (1’) and (2’), replacing (1) and (2) of the respiratory oscillator.

$$\frac{dx}{dt} = 0 \tag{1'}$$

$$\frac{dy}{dt} = \frac{D}{t_s} \tag{2'}$$

D is a positive constant, corresponding to the vertical distance of displacement in the phase space (x,y). The parameter t_s is the swallowing duration. The displacement speed is then considered constant during deglutition.

The end of swallowing releases the respiratory oscillator, which takes back the control of the ventilatory motor neurons. Thus, as soon as deglutition is completed, equations (1’), (2’) and (4’) turn back into equations (1), (2) and (4).

Finally, it was also observed [1,3,6,7] that abdominal muscles activity increases during swallowing apnea and continues during the following expiration, which could in some cases increase expiratory force in an active expiration. This active expiration, also observed in our experimental results, is considered in our proposed model. The pressure generated by the respiratory muscles is either null during passive expiration or proportional to the activity of the respiratory rhythm generator during inspiration and active expiration. We introduce a threshold of active expiration, noted τ_{ea}, which allows the partition of the phase space in 3 central respiratory states: inspiration, passive expiration and active expiration. Equation (3) for P_{mus} is replaced by (3’).

$$P_{mus} = \begin{cases} B.y & \text{if} \quad y < 0 \\ 0 & \text{if} \quad 0 < y < \tau_{ea} \\ B.y & \text{if} \quad y > \tau_{ea} \end{cases} \tag{3'}$$

The active expiratory state can be reached during the simulation of a deglutition, if the increase in y (or D) is big enough to make y exceed τ_{ea}.

C. *Model computing*

The model equations are implemented and simulated under Matlab® software. Differential equations are solved using the fourth order Runge-Kutta method. The integration step used is h=0.01s and the initial values are $x_0 = 2$ (no unit), $y_0 = -1$ (no unit) and $V_0 = 0$. Simulations are carried out during 40 seconds, with one swallowing event simulated after around 20 seconds. The precise beginning of the swallow is different for each simulation so as to observe the model behaviors depending on the swallowing position in the respiratory cycle. All simulations are carried out with respiratory parameter values in Table II and α=1. Parameters D and τ_{ea} can be changed and adjusted for the various simulations, as well as the swallowing duration t_s.

D. *Simulations*

Considering the experimental results, simulations are carried out to highlight the 3 main situations. Simulated signals are shown in Fig.2 for one swallow occurring in inspiratory phase (I), in Fig.3 for one swallow occurring in expiratory phase (E) and in Fig.4 for one swallow occurring during expiration and causing an active expiration (Ea).

The phase space (x,y) is represented on the left, showing the limit cycle of the respiratory oscillator, and the vertical displacement due to deglutition. On the right, the signals of volume (V) and airflow (dV/dt) highlight the apnea caused by the swallowing event (constant volume and no airflow).

Figure 2. Model simulation of swallowing during inspiration (t_s=2, D=12, τ_{ea} =5).

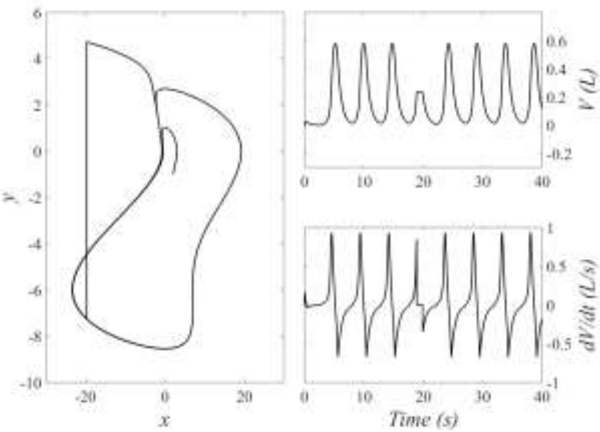
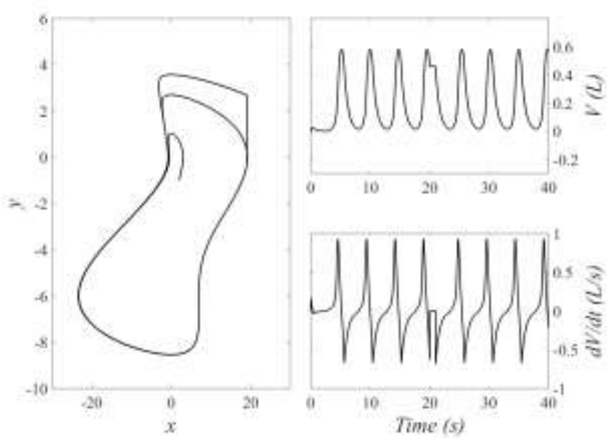


Figure 3. Model simulation of swallowing during expiration (t_s=1, D=3, τ_{ea} =5).



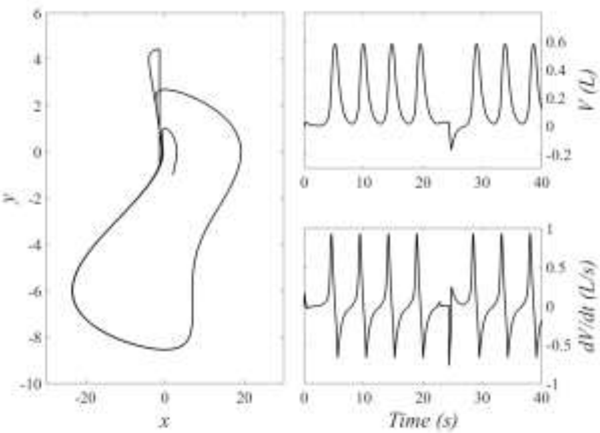
IV. CONCLUSION

Swallowing is a strong central interaction. During deglutition, there is a diversion of the respiratory center neurons function. The swallow can lead either to changes of respiratory phase (break in inspiration and path to expiration) or to expiration extension, and even to an amplification of the expiration, as an active expiration.

This has been illustrated by experimental RIP signals, recorded on eleven healthy subjects.

We have then proposed a simple model of deglutition in interaction with an existing model of the respiratory system. This is a model of deglutition by vertical displacement in the phase space, driven by a limited number of parameters (distance D of displacement and active expiratory threshold τ_{ea}), which have to be set for each subject in order to simulate the various swallowing mechanisms observed.

Figure 4. Model simulation of swallowing followed by active expiration (t_s=1.5, D=5, τ_{ea} =3).



REFERENCES

[1] T. Bautista, Q.-J. Sun, and P. Pilowsky, "The generation of pharyngeal phase of swallow and its coordination with breathing: Interaction between the swallow and respiratory central pattern generators," *Progress in Brain Research*, Vol. 212, ch.13, 2014.

[2] T. Nishino, T. Yonezawa, and Y. Honda, "Effects of Swallowing on the Pattern of Continuous Respiration in Human Adults," *Am Rev Respir Dis*, Vol. 132, no. 6, 1985, pp. 1219-1222.

[3] B.J. Martin, J.A. Logemann, R. Shaker, and W.J. Dodds, "Coordination between respiration and swallowing: respiratory phase relationships and temporal integration," *J Appl Physiol*, Vol. 76, no.2, 1994, pp. 714-723.

[4] D. Paydarfar, R.J. Gilbert, C.S. Poppel, and P.F. Nassab, "Respiratory phase resetting and airflow changes induced by swallowing in humans," *J Physiol*, vol. 483.1, 1995, pp. 273-288.

[5] D. Paydarfar, F.L. Eldridge, and J.A. Paydarfar, "Phase resetting of the respiratory oscillator by carotid sinus nerve stimulation in cats," *J Physiol*, Vol. 506, no 2, 1998, pp. 515–528.

[6] A.I. Hardemark Cedborg, E. Sundman, K. Boden, H. Witt Hedstrom, R. Kuylenstierna, O. Ekberg, and L.I. Eriksson1, "Co-ordination of spontaneous swallowing with respiratory airflow and diaphragmatic and abdominal muscle activity in healthy adult humans," *Exp Physiol* Vol. 94, no. 4, 2009, pp 459–468.

[7] Y. Saito, K. Ezure,I. Tanaka, and M. Osawa, "Activity of neurons in ventrolateral respiratory groups during swallowing in decerebrate rats," *Brain Dev.*, Vol. 25, no 203, 2003, pp. 338–345.

[8] A. Moreau-Gaudry, A. Sabil, G. Benchetrit, and A. Franco, "Use of Respiratory Inductance Plethysmography for the detection of swallowing in the Elderly," *Dysphagia*, vol. 20, 2005, pp. 297-302.

[9] S. Thibault, L. Heyer, G. Benchetrit, and P. Baconnier, "Ventilatory support: a dynamical systems approach," *Acta Biotheoretica*, vol. 50, 2002, pp. 269-279.

[10] J. Fontecave Jallon, E. Abdulhay, P. Calabrese, P. Baconnier, and P.-Y. Gumery, "A model of mechanical interactions between heart and lungs," *Philosophical Transactions of the Royal Society A: Mathematical,Physical and Engineering Sciences*, vol. 367, no. 1908, 2009, pp. 4741–4757.

[11] A. Eberhard, P. Calabrese, P. Baconnier and G. Benchetrit "Comparison between the respiratory inductance plethysmography signal derivative and the airflow signal", *Adv Exp Med Biol*, vol. 499, 2001, pp. 489–494.

[12] M. Kijima, S. Isono, and T. Nishino, "Coordination of Swallowing and Phases of respiration during added respiratory Loads in Awake subjects," *Am J Respir Crit Care Med*, vol. 159, 1999, pp.1898-1902.

[13] A.I. Hardemark Cedborg, K. Boden, H. Witt Hedstrom, R. Kuylenstierna, O. Ekberg, L.Eriksson, and E. Sundman, "Breathing and swallowing in normal man – effects of changes in body position, bolus types, and respiratory drive," *Neurogastroenterol Motility*, Vol. 10, no. 1111, 2010, pp. 1365-2982.