FROM CONSERVATIVE TO DISSIPATIVE NON-LINEAR DIFFERENTIAL SYSTEMS. AN APPLICATION TO THE CARDIO-RESPIRATORY REGULATION

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ABSTRACT. We start by coupling negative 2-circuits, which are characteristic of the presence of a regulation loop in a dynamical system. This loop can be modelled with coupled differential equations represented in a first approach by a conservative differential system. Then, an example of regulation loop with a dissipative component will be given in human physiology by the vegetative system regulating the cardio-respiratory rhythms.

1. Introduction. We revisit first the R. Thomas arabesque model [1], replacing the polynomial nonlinear differential system of negative cascades of order 2, represented by the following differential equations:

\[ \begin{align*}
    dx/dt &= y^a - z - z^a + y, \\
    dy/dt &= w^a - x - x^a + w, \\
    dw/dt &= z^a - y - y^a + z, \\
    dz/dt &= x^a - w - w^a + x,
\end{align*} \]

(1)

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by a system of two coupled Liénard equations [8, 26]. In the case where these
equations are of van der Pol or FitzHugh-Nagumo type, they can represent the
bulbar vegetative coupling between the respiratory control system and the cardio-
moderator system [2–4]. We show, as in [1], the existence of arabesques and, as in
[25], the existence of “canard” singularities, using the Gevrey series approach. The
possibility of recording, using an adapted BCI device [23], the bulbar activity, makes
it possible to envisage future applications to the optimal awakening of anesthetized
patients, by using such a modeling approach. The outline of the paper is as follows:
the first section is divided into two parts. The first part presents two systems of
arabesques and provides a proof for the conservation of the kinetic energy function.
In the second part, we consider a real planar vector field, inspired by arabesque
approach and we give a qualitative analysis of its complex solutions. In the second
section, we present a model for the coupling between the cardiac and the respiratory
activity. We propose a transform of respiratory equation representing a pathological
breath and we provide a formal solution. The last section presents the miscellaneous
for a rigorous mathematical analysis of the formal solutions.

2. Non-linear arabesques. We call “arabesques” a family of dynamical sys-
tems defined as closed chains of 2-element negative circuits [1]. An n-dimensional
arabesque system has \( n \) 2-element circuits, but in addition, it displays by construc-
tion, two \( n \)-element circuits which are both positive versus one positive and one
negative, depending on the parity (even or odd) of the dimension \( n \). In view of the
absence of diagonal terms in their Jacobian matrices, all these dynamical systems
are conservative and consequently, they cannot possess any attractor, then, analyze
their solutions can be challenging. In the case of true arabesque, we explore the
phase space via some conserved energy functions.

2.1. Real non-linear arabesques with energy functions. Let us consider the
differential system (1). Then, the following Proposition holds:

**Proposition 1.** The system (1) conserves the function \( H \) defined by:

\[
H(x, y, w, z) = x + y + w + z.
\]

**Proof.** We have: \( \partial H/\partial x = \partial H/\partial y = \partial H/\partial w = \partial H/\partial z = 1 \), hence:

\[
dH/dt = \partial H/\partial x dx/dt + \partial H/\partial y dy/dt + \partial H/\partial w dw/dt + \partial H/\partial z dz/dt
\]

\[
= (y^a - z - z^a + y) + (w^a - x - x^a + w) + (z^a - y - y^a + z)
\]

\[
+ (x^a - w - w^a + x)
\]

\[
= 0
\]

**Remark 1.** The case of an odd number of differential equations is treated in [1],
where it is shown that \( H \) is also conserved.

**Remark 2.** The signed Jacobian matrix of the system (1) is the same as the
discrete Jacobian matrix of the corresponding Boolean cascade negative 2-circuits.
In the case of Boolean circuits of any length, the occurrence of closed trajectories
of long period, analogue to those observed in the continuous case has been studied
in [12,13], and these closed trajectories are conserving also both the discrete kinetic
energy and the global frustration function of the network, in the case of a Hopfield
automata dynamics.
2.2. Complex non-linear arabesques without conserved energy functions.
If we consider non-linear arabesques and add a dissipative term, we are still in
the context of regulation loop, but we need other tools than conservative energy
functions to understand the trajectories. The present part gives an example of
how the complex solutions of real differential equations can lead to “arabesques”
trajectories which exhibit successively several patterns from their initial conditions
until their asymptotic behaviours.

Let consider now dissipative differential systems without conserved energy func-
tion, but having a potential part added to a Hamiltonian part in their second mem-
ber. More specifically, let consider two variables \((x, y)\) systems whose steady
state equations display several solutions, some real (the classical steady states),
some complex, and treat them as four-dimensional systems whose variables are the
real and imaginary parts of the variables \(x\) and \(y\), namely \(\text{Re}[x], \text{Im}[x], \text{Re}[y]\)
and \(\text{Im}[y]\). Most of the work consists now of studying the complex solutions of
the steady state equations.

The cubic system chosen as example is simple, but nevertheless of a sufficient
degree of non-linearity to display multiple steady states:
\[
\begin{align*}
\frac{dx}{dt} &= y - y^3 + 0.2x + a \\
\frac{dy}{dt} &= x - x^3 + 0.3y
\end{align*}
\]

The Figure 2 shows the real fixed points in the space of variables \((xOy)\). For
\(a = 0\) (Figure 2, left panel), the steady state equations display nine real solutions,
and thus nine classical steady states. Of these nine steady states, five are saddle
points (- + symbol) and four are stable foci (- - symbol).

Adding an adequate zero-order term to one of the equations will of course not
affect the Jacobian matrix. However, by increasing the value of this zero order
term, i.e., by increasing the value of the parameter \(a\), pairs of steady states (a
saddle point and a stable focus) will converge (Figure 2, middle panel) and finally
collide on the frontier (green lines) that separates domains (Figure 2, right panel),
homogeneous as regards the signs of the eigenvalues. At this point, the two steady
states are replaced by a pair of conjugated complex solutions. The first collision
is illustrated by the Figure 2, which shows the real fixed points, i.e., the classical
real solutions of the steady state equations of the system (2) shown as red points.
Figure 2. Steady states of system 2 in phase space \((xOy)\), for \(a = 0\) (left), \(a = 0.15\) (middle) and \(a = 0.17\) (right).

In phase space \((xOy)\) of the variables \(x\) and \(y\), for three values of the increment \(a\) (\(a = 0\), the initial system, \(a = 0.15\), slightly below the value that leads to the first collision and \(a = 0.17\), slightly above this value). The signs deal with the nature of the eigenvalues of the Jacobian matrix: - + for a saddle point, - - for a stable focus, + + for an unstable focus. The lines are the frontiers that separate domains homogeneous for the nature of the eigenvalues. After four such collisions, there remain only a single stable focus and four pairs of conjugated complex solutions.

Figure 3. Left: trajectory starting from the complex solution for \(a = 0.17\) in the phase plane \((Re(x)ORe(y))\). Right: trajectory starting from the complex solution for \(a = 0.17\) in the phase plane \((Re(x)ORe(y))\) for an initial state modified by simply adding 0.000001 to the initial value \(y(0)\) of the left trajectory.

We can verify by a precise computation that for \(a = 0.17\) a pair of real fixed points has disappeared and is replaced by a pair of complex fixed points. As parameter \(a\)
increases, a second, a third and a fourth “collision” between a saddle point and a stable focus take place and generate each time one more pair of complex conjugated solutions. So that finally, there remains only one real solution, a stable focus. The four collisions take place for the values $0.1696$, $0.4214$, $0.5649$ and $0.714$, respectively.

Now, we would like to know the trajectories starting from complex fixed points. For that, we need to work in terms of a 4 dimensional system whose variables are $\text{Re}(x)$, $\text{Im}(x)$, $\text{Re}(y)$ and $\text{Im}(y)$.

An explanation of the time evolution of the system (2) resides in the fact that it is no more conservative as the system (1), but mixed, potential-Hamiltonian [21]. Indeed, by defining a potential $P$ by:

$$P(x,y) = -0.1x^2 - ax - 0.15y^2$$

and a Hamiltonian energy $H$ by:

$$H(x,y) = (2y^2 - y^4)/4 - (2x^2 - x^4)/4 = (y^2 - x^2)(2 - (y^2 + x^2))/4,$$

we have:

$$\frac{dx}{dt} = -\frac{\partial P}{\partial x} + \frac{\partial H}{\partial y}, \frac{dy}{dt} = -\frac{\partial P}{\partial y} - \frac{\partial H}{\partial x}$$

When $x$ and $y$ become large, the system is quasi-conservative, because the vector tangent to the Hamiltonian level curve $T = (\frac{\partial H}{\partial y}, -\frac{\partial H}{\partial x}) = (y - y^3, x - x^3)$ dominates in norm the gradient vector $G = (-\frac{\partial P}{\partial x}, -\frac{\partial P}{\partial y}) = (0.2x + a, 0.3y)$. On a circle centered on the origin $O$ with a radius $R$, the Hamiltonian part is equal to the value $H = (y^2 - x^2)(2 - R^2)/4$, and the vector $N = (x, y)$ normal exterior to the circle has a scalar product with the velocity vector field $G + T$ of the system (2) equal to $<N, G + T> = 0.1y^2 + 0.2R^2 + x[a + y(2 - R^2)]$. Hence, the velocity vector field is going out the circle when $R$ is sufficiently large, $y \leq 0$ and $x \geq 0$, and that prevents the use of the Poincaré-Bendixson theorem leading to study numerically the solutions of (2).

The Figure 3 left shows the trajectory that starts from the complex solution for $a = 0.17$ in the phase plane $(\text{Re}(x))O(\text{Re}(y))$, namely in the real subspace. For the combinations of the other pairs of variables, the cyclic trajectories are similar, but even the trajectories are periodic, they are not limit cycles. Indeed, they are unstable and extremely sensitive to initial conditions. By taking $a = 0.30$ and showing time evolution of the variable $\text{Re}(x(t))$ starting from the complex solution, there are three successive episodes. The first episode looks steady at the scale used but, in fact, it slowly departs from the initial solution. Then, follows a long transient, apparently an erratic episode. Finally, the trajectory seems periodical as shown on the Figure 4.

3. Physiological applications.

3.1. The mechanism of the cardio-respiratory regulation. The trajectory of the Figure 4, including a transient regime followed by a periodical episode, recalls the time series that appears in the case of Cheyne-Stokes respiration. In this case, the breath presents an active phase followed by a quiescent phase (Figure 5) and can be considered as a repetition of episodes like those observed on Figure 4.

To make the model more realistic, let consider a system of two coupled van der Pol equations, representing respectively the electrical activity of the respiratory centre, cardio-regulator (or cardiovascular) centre, peripheral sinus node and peripheral baroreceptors sensing the arterial blood pressure. The central vegetative
system rules the cardiorespiratory activity located in the rachidian bulb (medulla oblongata). Its functioning is summarized on Figure 6.

The central vegetative system has two components: (i) the bulbar respiratory centre with its inspiratory (early eI and post pI) and expiratory (E) neurons, the first activating the second ones through a double inhibition and inversely the second inhibiting the first ones, and the cardio-regulator where starts and finishes vagus (pneumogastric) parasympathetic nerve with efferent and afferent vagal activity, and starts the ortho-sympathetic nerve.

Let us describe now the cardio-respiratory regulation following [2–4, 11, 15, 19, 27–29]: there is an increase in heart rate (HR) during inspiration and decrease during expiration are referred to as respiratory sinus arrhythmia (RSA), and an increase in blood pressure (BP) during inspiration referred to as Traube–Hering reflex. RSA results from increase in sympathetic efferences during inspiration, which activate the sinus node, this last having its own constant basal pacemaker activity and from decrease in vagal efferences. During expiration, the vagal efferences, on the contrary, increase, inhibiting the sinus node activity. During the inspiration, the phrenic nerve activity contracts the diaphragm and the intercostal nerve activity contracts the external intercostal muscles. During the expiration, the activation of internal intercostal muscles and abdominal muscles contributes to the expiratory freination. Multiple factors other than the parasympathetic and sympathetic modulations contribute to the cardiovascular regulation, like the mechanical coupling due to the location of lungs and heart in the same thoracic cavity. For example, at the end of inspiration, pleural stretch receptors contribute to cut the inspiratory neurons
activity (Hering-Breuer reflex) and inspiration provokes also a decrease in pleural
due to a postinspiratory reflex that is mediated by the postinspiratory neurons pI. The
regulation at the inspiratory-expiratory transition is ensured by these pI neurons
in the pontine Kölliker-Fuse nucleus, providing an eupnestic inspiratory-expiratory
transition; pI neurons start the post-inspiratory vagal nerve activity, when they are
no more inhibited by the early inspiratory neurons eI: that occurs when eI neurons
(which have a constant basal activity) are inhibited by the expiratory E neurons,
these last being triggered by eI neurons and by the decrease of the pI neurons
inhibition. The role of swallowing is partly unknown but the loss of the swallowing
reflex after a brain stroke provokes a dyspneic breathing [3, 24].
3.2. Modelling the cardio-respiratory regulation. In order to analyse and interpret the data coming from the Visuresp, a smart vest recording respiratory and cardiac rhythms, it is necessary to use the mathematical modelling, namely to define non-linear differential equations to account for the relaxation behaviour mainly of the cardiac and respiratory components, but also of the baroreceptors. We will use for that van der Pol systems [5], proposed for the heart activity by van der Pol in [29] and by authors of [28] (using a differential system slightly adapted from the van der Pol equation) for the respiratory activity.

The van der Pol system representing the rhythmic respiratory activity reads:

\[
\begin{align*}
\frac{dx}{dt} &= y, \\
\frac{dy}{dt} &= -x + \varepsilon(1 - x^2)y,
\end{align*}
\]

where \(\varepsilon\) represents the an-harmonic parameter of the oscillator, with a free run (proper period) \(\tau\), equal (near the bifurcation of the van der Pol limit cycle obtained for \(\varepsilon = 0\)), to the ratio \(2\pi/Im\), where \(Im = (1 - \varepsilon^2/4)^{1/2}\) is the imaginary part of the eigenvalues of the Jacobian matrix of the system.

The van der Pol system representing the rhythmic cardiac activity reads:

\[
\begin{align*}
\frac{dz}{dt} &= w, \\
\frac{dw}{dt} &= -z + \nu(1 - z^2)w + k(y)y,
\end{align*}
\]

where \(\nu\) is the an-harmonic parameter and \(k(y)\) is the intensity of the coupling between the respiratory oscillator and the cardiac oscillator (taking into account globally the baroreceptor sensing and the sympathetic/vagal regulation).

The values of \(\varepsilon\) and \(\nu\) are fixed by the proper periods of the respiratory (about 4s) and cardiac (about 1s) oscillators, then \(k(y)\) can be obtained by measuring the instantaneous cardiac period \(T\) (which is just the interbeats duration RR) and by calculating the slope of the regression line between \(T\) and the respiratory activity (represented by the actual inspiratory duration \(t\) where occurs the cardiac beat). This slope is directly related to the correlation coefficient between \(T\) and \(t\) (Figure 7 shows the time evolution of \(T\), proving the coupling between the two oscillators).

The integrity of the cardio-respiratory coupling allows the vegetative system to adapt (voluntarily or automatically) to the effort: first the breathing is ruled by the will or entrained by a muscular activity and secondarily it entrains the heart. Such a capacity of adaptation disappears in degenerative diseases like the Parkinson’s or Alzheimer’s diseases, and in the complicated type II diabetes. Watching a parameter like the correlation coefficient is then particularly interesting in the elderly people surveillance by dedicated cardiorespiratory sensors like the Visuresp. By analysing the nycthemeral (day-night) curves of a patient equipped by this cardiorespiratory specific sensor, we observe that the cardiac instantaneous period \(T\) is indeed anticorrelated with the duration of the inspiration in which occurs the cardiac cycle, due to the RSA (Figure 7): the cardiac rhythm is accelerating during the inspiration and the heart decelerates during the expiration. The progressive disappearance of this coupling during neurodegenerative pathologies allows for diagnosing early the entrance in the chronic dysfunctions of the cardio-respiratory system related to these diseases.

Other pathologies of central origin cause abnormalities of the respiratory rhythm, such as the Cheyne-Stokes respiration (Figure 5). The Cheyne-Stokes respiration is a pathological breathing passing progressively from a normal rhythm to a gradually decreased rhythm until a temporary apnoea, this pattern duration being between 30 seconds and 2 minutes. The corresponding pattern is called “crescendo-diminuendo”
rhythm and it characterizes the Cheyne-Stokes respiration, provoking a decrease of the serum partial pressure of oxygen and an increase of the carbon dioxide one. This pathological breath is characterized by an increase of the an-harmonic parameter $\varepsilon$. To force the breathing and avoid asphyxia, we can add a periodical forcing in equations (4). In order to ensure a smooth transition from apnoea to breath, we multiply this forcing by an “intensity” function regulating the strength of the forcing. In the following section, we will show that it exists an intensity function, which allows a smooth transition from rest to oscillating states. It is worth to notice that this result can be applied to any forced van der Pol (cf. [26]). The same approach can be used for simulating the disappearance (pathologic in neurodegenerative diseases and physiologic during the sleep) of the respiratory sinus arrhythmia (RSA).

We consider now equations (3), where $\varepsilon$ is high and where we have added a periodical forcing $g(t)$ and an intensity function $k(t)$:

$$
\begin{align*}
\frac{dx}{dt} &= y, \\
\frac{dy}{dt} &= -x + \varepsilon(1 - x^2)y + k(t)g(t),
\end{align*}
$$

(5)

After rescaling $y = \varepsilon y$ and $t = t/\varepsilon$, the system becomes:

$$
\begin{align*}
\frac{dx}{dt} &= y, \\
\mu \frac{dy}{dt} &= -x + (1 - x^2)y + k(t)g(t),
\end{align*}
$$

(6)

where $0 < \mu = 1/\varepsilon^2 \ll 1$, which corresponds to relaxation waves very far from the harmonic case.

This situation corresponds to the classical problem of the van der Pol system with a periodical forcing, which has been intensively studied (see for example [5–9,16–18, 22,25]), but only in the case of a classical forcing (e.g., constant or cosine). In [26], we prove the existence of canard solutions for a large family of nonautonomous equations, which contains in particular the equations (5). It is well known that the

Figure 7. Evolution of the instantaneous cardiac period $T$, which is anti-correlated with the duration $t$ of the inspiration in which occurs the cardiac cycle (after [2])
forced van der Pol equation:
\[ \mu \frac{d^2 u}{dt^2} + (u^2 - 1) \frac{du}{dt} + u = \alpha, \]
where \( \alpha \) is a parameter, is a singular perturbed differential equation having canard solutions for some values \( \alpha(\mu) \). Canards are special solutions of slow-fast systems, that is, systems of ODEs where the variables evolve on different time scales, due to the presence of a small parameter \( 0 < \mu \ll 1 \). Canard trajectories follow the attracting part of the fast nullcline of the differential system, pass close to a bifurcation point of the fast subsystem and then follow the repelling part of the fast null-cline for a large amount of time. The canard phenomenon was first discovered by Benoît, Callot, Diener & Diener [5] in the van der Pol oscillator, and studied by means of non-standard analysis. Later on, similar results were established with standard techniques, in particular by matching asymptotic and geometrical approaches to singular perturbation theory (the so-called blow-up method [9]). Apart from the fact that they follow repelling objects for long intervals of time, canards (in 2D-systems) are special in that they exist for a very narrow parameter interval, which can be proved to be exponentially small in \( \exp(k/\mu) \) for some \( k > 0 \). The transition through canard solutions in parameter space is usually referred to as an explosion. In the case where \( k(t)g(t) = \alpha \) is a constant parameter, there are exactly two canard solutions and E. Matzinger proved in [25] the existence of a uniform asymptotic development of a solution in sectors centred at the value \( u = 1 \) and calculated an explicit approximation of this solution. We prove in [26] the existence of formal solutions, which are Gevrey asymptotic to over-stable solutions for a large class of equation which contains the equation (6).

3.3. Comparison of simulations with experimental data. The model of forcing the cardiac rhythm by the respiratory rhythm (RSA) consists of 4 differential equations of van der Pol type:

\[
\begin{align*}
\frac{dx}{dt} &= y \\
\frac{dy}{dt} &= -\omega_1 x + \varepsilon (1 - x^2/b_1^2) y \\
\frac{dz}{dt} &= w \\
\frac{dw}{dt} &= -\omega_2 z + \nu (1 - z^2/b_2^2) w + ky
\end{align*}
\]

(7)

The parameters have been chosen to ensure a qualitative similarity between simulations and cardiorespiratory signals (Figure 8). The period estimators are fixed as \( \tau = 2\pi/\omega_1 \approx 4s \) for the respiratory rhythm and as \( T = 2\pi/\omega_2 \approx 1s \) for the cardiac rhythm. The simulations of the Figure 10 have been obtained with simplified equations (8), supposing that the cardiac forcing comes from a harmonic oscillator whose period is about four times more than its free run frequency:

\[
\begin{align*}
\frac{dx}{dt} &= y \\
\frac{dy}{dt} &= -2\pi x + 2(1 - x^2) y + \cos(0.64t)
\end{align*}
\]

(8)

By comparing simulations and experimental data, we see a qualitative agreement at the transition between waking and sleep states, at which empirical instantaneous cardiac period RR diminishes in mean and amplitude (Figure 8), correlation between lengths of successive RR intervals increases and mean amplitude of ECG signal slightly increases (Figure 9). This behaviour is also observed on the simulation of the cardiac activity (Figure 10). To be more convincing, the model (8) has to be simulated with a forcing coming from the respiratory signal \( y \) and no more from a non-autonomous forcing term (here a cosine), and a noise has to be added to the second term of the equations (6).
in particular to the equation ruling the inspiratory activity $y$, in order to take into account numerous perturbations like swallowing, motion, etc.

4. Conclusion and perspectives. We have shown in this paper that, starting from a pure theoretical problem, i.e., the existence of arabesques solutions in non-linear conservative ODEs, we could by adding a dissipative term obtain stable oscillations with the possibility of appearance of singularities called “canards” in the literature, passing from a stationary regime without oscillations to a periodic regime by varying progressively a parameter like the an-harmonic coefficient of the van der Pol pendulum.

The modified equations are useful in the physiology of the cardio-respiratory regulation in human. We will give in future works:

i) details of the proofs announced in this paper about the existence of “canard” solutions in the equations (5) (cf. [26])

ii) more simulations of the coupled system showing their qualitative agreement with experimental observations acquired in empirical situations of cardio-respiratory decoupling. In the real system, the respiration can be voluntarily ruled, hence an exogenous control can replace the endogenous one, e.g., for better preparing the heart to the effort. In a control perspective [20, 32], for example in the framework of the surveillance at home [10, 30, 31] and in the context of multi-scale systems [14], an elucidation of the internal cost function the vegetative system is trying to optimize could then be important for defining the best strategies for the preparation to effort, by avoiding the struggle of the will or of an artificial respirator against the endogenous cardio-respiratory regulation. Techniques like the potential-Hamiltonian decomposition used in
Figure 9. Experimental data showing that during sleep the amplitude of the cardiac signal increases and its period (RR interval) decreases, with an augmentation of the correlation between the lengths of successive cardiac cycles.

this paper could then be useful in finding subsets of the state space where the conservative part of the coupled dynamics is dominant, elucidating what “energy” is conserved, and if this energy is diminished by adding a dissipative potential part to the dynamics.

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REFERENCES

[1] C. Antonopoulos, V. Basios, J. Demongeot, P. Nardone and R. Thomas, Linear and nonlinear arabesques: A study of closed chains of negative 2-element circuits, Int. J. Bifurcation and Chaos, 23 (2013).

[2] D. M. Baekey, Y. I. Molkov, J. F. R. Paton, I. A. Rybak and T. E. Dick, Effect of baroreceptor stimulation on the respiratory pattern: Insights into respiratory-sympathetic interactions, Respiratory Physiology & Neurobiology, 174 (2010), 135–145.

[3] T. G. Bautista, Q. J. Sun and P. M. Pilowsky, The generation of pharyngeal phase of swallow and its coordination with breathing: Interaction between the swallow and respiratory central pattern generators, Prog. Brain Res., 212 (2014), 253–275.

[4] T. Beauchaine, Vagal tone, development, and Gray’s motivational theory: Toward an integrated model of autonomic nervous system functioning in psychopathology, Development and Psychopathology, 13 (2001), 183–214.

[5] E. Benoît, J. L. Callot, F. Diener and M. Diener, Chasse au canard, Collect. Math., 31 (1981), 37–74.
Figure 10. Simulations of system (8) showing for the sleep state a cardiac rhythm (top) with a period slightly less and an amplitude slightly larger than the corresponding values calculated for the awake state (bottom) (obtained with the online simulation tool https://www.zweigmedia.com/RealWorld/deSystemGrapher/func.html).

[6] K. Bold, C. Edwards, J. Guckenheimer, S. Guharay, K. Hoffman, J. Hubbard, R. Oliva and W. Weckesser, The forced van der Pol equation. II: Canards in the reduced system, SIAM J. Appl. Dyn. Syst., 2 (2003), 570–608.

[7] M. Brøns, Bifurcations and instabilities in the Greitzer model for compressor system surge, Mathematical Engineering in Industry, 2 (1988), 51–63.

[8] J. Burke, M. Desroches, A. Granados, T. J. Kaper, M. Krupa and T. Vo, From canards of folded singularities to torus canards in a forced van der Pol equation, J. Nonlinear Sci., 26 (2016), 405–451.

[9] M. Canalis-Durand, J. P. Ramis, R. Schafke and Y. Sibuya, Gevrey solutions of singularly perturbed differential equations, J. Reine Angew. Math., 518 (2000), 95–129.

[10] J. Demongeot, G. Vironne, F. Duchêne, G. Benchetrit, T. Hervé, N. Noury and V. Rialle, Multi-sensors acquisition, data fusion, knowledge mining and alarm triggering in health smart homes for elderly people, Comptes Rendus Biologies, 325 (2002), 673–682.

[11] J. Demongeot and J. Waku, Application of interval iterations to the entrainment problem in respiratory physiology, Phil. Trans. R. Soc. Lond. Ser. A Math. Phys. Eng. Sci., 367 (2009), 4717–4739.
[12] J. Demongeot, M. Noual and S. Sené, Combinatorics of Boolean automata circuits dynamics, *Discrete Appl. Math.*, **160** (2012), 398–415.

[13] J. Demongeot, H. Ben Amor, H. Hazgui and A. Lontos, La simplicité, dernier avatar de la complexité, OpenEdition, Marseille, 2014. Available from: [http://books.openedition.org/cdf/3393](http://books.openedition.org/cdf/3393).

[14] J. Demongeot, J. Bezy-Wendling, J. Mattes, P. Haigron, N. Glade and J. L. Coatrieux, Multiscale modeling and imaging: The challenges of biocomplexity, *Proceedings of the IEEE Society*, **91** (2003), 1723–1737.

[15] O. Dergacheva, K. J. Griffioen, R. A. Neff and D. Mendelowitz, Respiratory modulation of premotor cardiac vagal neurons in the brainstem, *Respiratory Physiology & Neurobiology*, **174** (2010), 102–110.

[16] M. Desroches, J. P. Francoise and L. Megret, Canard-induced loss of stability across a homoclinic bifurcation, *ARIMA Rev. Afr. Rech. Inform. Math. Appl.*, **20** (2015), 47–62.

[17] F. Dumortier and R. Roussarie, Canard cycles and center manifolds, *Mem. Amer. Math. Soc.*, **121** (1996).

[18] W. Eckhaus, Relaxation oscillations including a standard chase on French ducks, in *Asymptotic Analysis II*, Lecture Notes in Math., **985**, Springer, Berlin, 1983, 449–494.

[19] D. G. S. Farmer, M. Dutschmann, J. F. R. Paton, A. E. Pickering and R. M. McAllen, Brainstem sources of cardiac vagal tone and respiratory sinus arrhythmia, *J. Physiology*, **594** (2016), 7249–7265.

[20] M. Fliess and C. Join, Dynamic compensation and homeostasis: A feedback control perspective, preprint, [arXiv:math/1801.04959](https://arxiv.org/abs/math/1801.04959).

[21] L. Forest, N. Glade and J. Demongeot, Liénard systems and potential-Hamiltonian decomposition - Applications in biology, *C. R. Biologies*, **330** (2007), 97–106.

[22] J. Grasman, H. Nijmeijer and E. J. M. Veling, Singular perturbations and a mapping on an interval for the forced van der Pol relaxation oscillator, *Phys. D.*, **13** (1984), 195–210.

[23] R. Grave de Peralta, S. Gonzalez Andino and S. Perrig, Patient machine interface for the control of mechanical ventilation devices, *Brain Sci.*, **3** (2013), 1554–1568.

[24] H. Khlaifi, D. Istrate, J. Demongeot, J. Boudy and D. Malouche, Swallowing sound recognition at home using GMM, *IRBM*, **39** (2018), 407–412.

[25] É. Matzinger, Étude des solutions sur-stables de l’équation de van der Pol, *Ann. Fac. Sci. Toulouse Math.* (6), **10** (2001), 713–744.

[26] L. Megret and J. Demongeot, Gevrey solutions of singularly perturbed differential equations, an extension to the non-autonomous case, *Discrete Contin. Dyn. Syst.*, preprint.

[27] D. J. A. Moraes, B. H. Machado and D. B. Zoccal, Coupling of respiratory and sympathetic activities in rats submitted to chronic intermittent hypoxia, *Prog. Brain Res.*, **212** (2014), 25–38.

[28] T. Pham Dinh, J. Demongeot, P. Baconnier and G. Benchetrit, Simulation of a biological oscillator: The respiratory rhythm, *J. Theor. Biol.*, **103** (1983), 113–132.

[29] B. van der Pol and J. van der Mark, The heart beat considered as a relaxation oscillator and an electrical model of the heart, *Philos. Mag.*, **6** (1928), 763–775.

[30] G. Virone, N. Noury and J. Demongeot, A system for automatic measurement of circadian activity deviations in telemedicine, *IEEE Trans. Biomed. Eng.*, **49** (2002), 1463–1469.

[31] G. Virone, B. Lefebvre, N. Noury and J. Demongeot, Modeling and computer simulation of physiological rhythms and behaviors at home for data fusion programs in a telecare system, in *IEEE Healthcom*, Piscataway, 2003, 111–117.

[32] M. Winter-Arboleda, W. S. Gray and L. A. D. Espinosa, On global convergence of fractional Fliess operators with applications to bilinear systems, in 51st Annual Conference on Information Sciences and Systems (CISS 1), IEEE Press, Piscataway, 2017, 1–6.

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