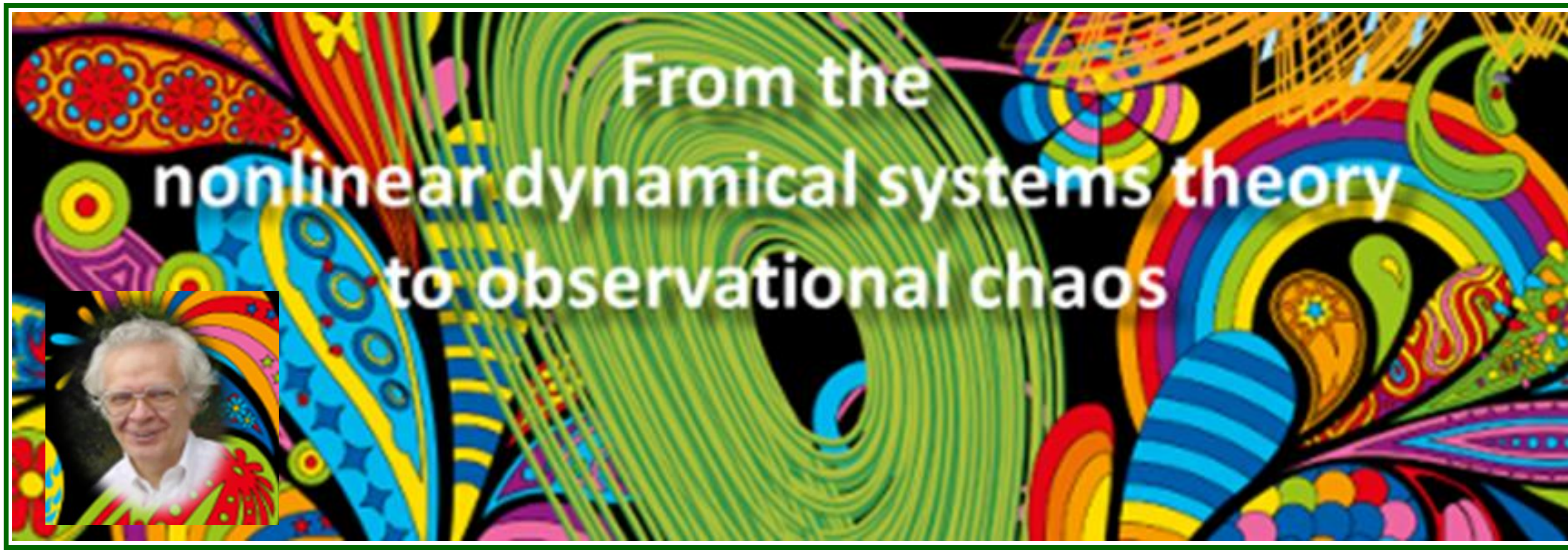

Hopf-like bifurcations in Mixed Mode Oscillations in a Fractional-Order FitzHugh-Nagumo Model

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The Hodgkin-Huxley model

The Hodgkin-Huxley model is a 4-dimensional nonlinear model which reproduces fairly the action potential of many types of neurons. It can generates chaotic solutions.

$$C\frac{dV_m}{dt} = -G_{Na}\left(V_m - E_{Na}\right) - G_K\left(V_m - E_K\right) - G_{lk}\left(V_m - V_{lk}\right)$$

$$\frac{dn}{dt} = -\left(\alpha_n + \beta_n\right)n + \alpha_n$$

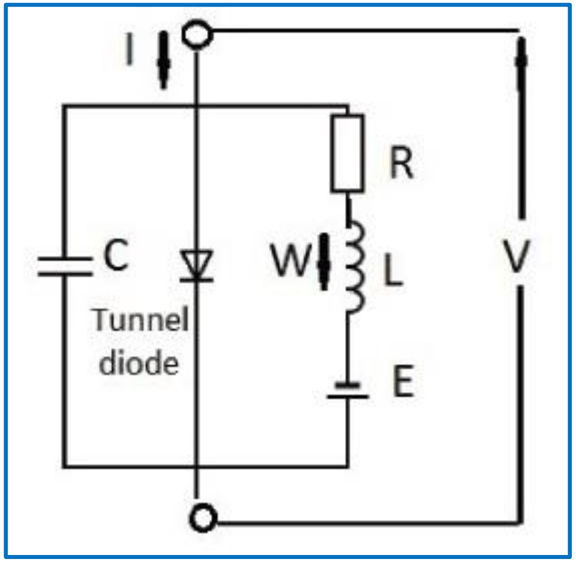
$$\frac{dm}{dt} = -\left(\alpha_m + \beta_m\right)m + \alpha_m$$

$$\frac{dh}{dt} = -\left(\alpha_h + \beta_h\right)h + \alpha_h$$

Alan Lloyd Hodgkin and Andrew Fielding Huxley described the model in 1952 to explain the ionic mechanisms underlying the initiation and propagation of action potentials in the squid giant axon. They received the 1963 Nobel Prize in Physiologie or Medicine for this work.

The FitzHugh-Nagumo model

It is a 2-dimensional approximation of the 4-dimensional nonlinear Hodgkin-Huxley model
However due to the Poincaré-Bendixon theorem, it cannot have chaotic solutions.



This electrical model consists of a voltage variable *v* (membrane potential) with a cubic non-linearity that allows regenerative self-excitation via a positive feedback, and a recovery variable *w*, which describes the combined effect of ion channels, with a linear term that affords a slower negative feedback.

C is a capacitor, R a resistor and L an inductor

$$\begin{cases} \dfrac{dv}{dt} = v - \dfrac{1}{3}v^3 - w + I \\ \dfrac{dw}{dt} = \dfrac{1}{T}(v + a - bw) \end{cases}$$

with parameters *I*, *a*, *b* and *T*.

With the change of variable x = v, y = w, $\varepsilon = \dfrac{1}{T}$

the system becomes a slow-fast system

$$\begin{cases} \dot{x} = x - \dfrac{1}{3}x^3 - y + I \\ \dot{y} = \varepsilon(x + a - by) \end{cases}$$

The fractional FitzHugh-Nagumo model

In 1983, Jonscher demonstrated that an ideal capacitor having integral constitutive equation $\boxed{v(t) = \frac{1}{C} q(t) \quad \Leftrightarrow \quad I(t) = C \frac{dv(t)}{dt}}$ cannot exist in nature.

A more realistic capacitor was proposed in 1994 by Westerlund & Ekstam with a fractional constitutive equation: $\boxed{I(t) = CD^{\alpha} v(t), \quad \alpha \neq 1}$

In 1991, Westerlund had already proposed a better constitutive relation for the inductor : $\boxed{V(t) = LD^{\beta} I(t), \quad \beta \neq 1}$

Based on these observations Liu & Xie introduced in 2010, the fractional FitzHugh-Nagumo model, where α_1 and α_2 are constants related to the loss of the capacitor and the proximity effect of the inductor.

$$\begin{cases} D^{\alpha_1} x = x - \frac{1}{3} x^3 - y + I \\ D^{\alpha_2} y = \varepsilon (x + a - by) \end{cases} \qquad \text{vs} \qquad \begin{cases} \dot{x} = x - \frac{1}{3} x^3 - y + I \\ \dot{y} = \varepsilon (x + a - by) \end{cases}$$

fractional vs integer

Fractional derivatives

The idea of fractional calculus has been known since the development of the regular calculus and it means a generalization of integration and differentiation to arbitrary order. There exist several definitions of the fractional derivatives known since centuries:

(the first example is a letter from Liebniz to the french mathematician L'Hospital in date of September 30, 1695, about the existence of the half-order derivative).

They are used for modelling numerous physical systems: dielectric polarization, visco-elastic systems, electrode-electrolyte polarization, …

In this presentation we consider both the Riemann-Liouville and the Caputo's definition (1967).

We will use also the Grünwald-Letnikov's definition for numerical simulations.

The Riemann-Liouville definition

$$\boxed{{}_a^R D_t^{\alpha} f(t) = \frac{1}{\Gamma(n-\alpha)} \frac{d^n}{dt^n} \int_a^t (t-\tau)^{n-\alpha-1} f(\tau) d\tau}$$

Using the classical Gamma function $\Gamma(z) = \int_0^{\infty} e^{-t} t^{z-1} dt$

which verifies $\Gamma(z+1) = z\Gamma(z)$

It is possible to write also this definition:

$${}_a^R D_t^{\alpha} f(t) = \frac{d^n}{dt^n} \left({}_a j_t^{n-\alpha} f(t) \right), \quad t > a, \quad n-1 \le \alpha < n$$

where ${}_a j_t^{\beta} f(t)$ is the integral Riemann-Liouvile operator

$${}_a j_t^{\beta} f(t) = \frac{1}{\Gamma(\beta)} \int_a^t (t-\tau)^{\beta-1} f(\tau) d\tau$$

Caputo's definition

Remark: Caputo's definition as well as Riemann-Liouville's one are depending upon a parameter *a* because fractional derivatives are non-local and show a memory effect

$$\boxed{{}_a^C D_t^{\alpha} f(t) = \frac{1}{\Gamma(n-\alpha)} \int_a^t (t-\tau)^{n-\alpha-1} f^{(n)}(\tau) d\tau}$$

which can be also written $\quad {}_a^C D_t^{\alpha} f(t) = j^{n-\alpha}\left(\frac{d^n}{dt^n} f(t) \right), \quad t > a$

In both definitions , $\quad n-1 \leq \alpha < n$

Those definitions are equivalent under some conditions.

Fractional derivatives have also special relationships with the Laplace transform as for example:

$$L\left\{ {}_0D_t^{\alpha} f(t) \right\} = s^{\alpha} L\left\{ f(t) \right\} - \sum_{k=0}^{n-1} s^{\alpha-1-k} f^{(k)}(0)$$

Examples of fractional derivative (Caputo's definition)

$$f : t \to f(t) = t^2, \quad f' : t \to f'(t) = 2t, \quad f'' : t \to f''(t) = 2$$

$$For \quad 1 \leq \alpha < 2 \quad {}_a^C D_t^{\alpha} f(t) = \frac{2}{\Gamma(2-\alpha)} \int_a^t (t-\tau)^{2-\alpha-1} d\tau = \frac{2(t-a)^{(2-\alpha)}}{(2-\alpha)\Gamma(2-\alpha)}$$

$${}_0^C D_t^1 f(t) = \frac{2(t-0)^{(2-1)}}{(2-1)\Gamma(2-1)} = \frac{2t}{1} = 2t = f'(t)$$

$${}_a^C D_t^{1,1} f(t) = 2.0795(t-a)^{0.9},$$

$${}_a^C D_t^{1,3} f(t) = 2.2011(t-a)^{0.7},$$

$${}_a^C D_t^{1,5} f(t) = 2.2568(t-a)^{0.5},$$

$${}_a^C D_t^{1,7} f(t) = 2.2285(t-a)^{0.3},$$

$${}_a^C D_t^{1,9} f(t) = 2.1023(t-a)^{0.1},$$

$${}_a^C D_t^{1,999} f(t) = 2.0012(t-a)^{0.001} \to 2 = f''(t) \quad for \quad a = 0,$$

Examples of fractional derivative (Caputo's definition)

$$f : t \to f(t) = t^2, \quad f' : t \to f'(t) = 2t, \quad f'' : t \to f''(t) = 2$$

$$For \quad 0 \le \alpha < 1 \quad {}_a^C D_t^\alpha f(t) = \frac{2}{\Gamma(1-\alpha)} \int_a^t (t-\tau)^{1-\alpha-1} \tau d\tau = \frac{2(t-a)^{(1-\alpha)}(2a+t-\alpha)}{(2-\alpha)(1-\alpha)\Gamma(1-\alpha)}$$

$${}_0^C D_t^0 f(t) = \frac{2(t-0)^{(2-1)}(2\times 0+t-0)}{(2-0)(1-0)\Gamma(1-0)} = \frac{2t^2}{2} = t^2 = f(t)$$

$${}_0^C D_t^{0,1} f(t) \quad = 1.0945\, t^{1.9},$$

$${}_0^C D_t^{0,3} f(t) \quad = 1.2948\, t^{1.7},$$

$${}_0^C D_t^{0,5} f(t) \quad = 1.5045\, t^{1.5},$$

$${}_0^C D_t^{0,7} f(t) \quad = 1.7024\, t^{1.3},$$

$${}_0^C D_t^{0,9} f(t) \quad = 1.9116\, t^{1.1},$$

Fractional dynamical systems

Consider the fractional-order initial value probleme in terms of Caputo derivative:

$$\begin{cases} {}_0^C D_t^{\alpha} x(t) = f\left(x(t)\right) \\ x(0) = x_0 \end{cases} \qquad (1)$$

It can be converted to the Volterra integral equation

$$x(t) = x_0 + \frac{1}{\Gamma(\alpha)} \int_0^t (t-\tau)^{(\alpha-1)} f(x(\tau)) d\tau$$

Theorem [Diethelm, 2001]: if the function $f : U \subset \mathbb{R}^n \to \mathbb{R}^n$ is continuous and satisfies the lipschitz condition on U, then for each $x_0 \in U$ the initial value problem (1) has an unique maximal continuous solution $x(t)$.

One can compute the flow

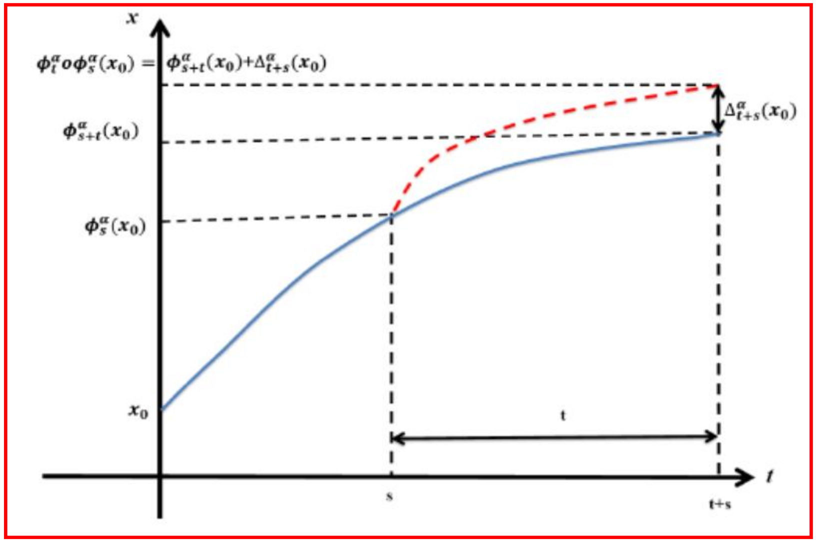
$$\Phi_t^{\alpha} \circ \Phi_s^{\alpha}(x_0(t)) = \Phi_{t+s}^{\alpha}(x_0) + \frac{1}{\Gamma(\alpha)} \int_0^s \left[(s-\tau)^{(\alpha-1)} - (t+s-\tau)^{(\alpha-1)} \right] f(\Phi_{\tau}^{\alpha}(x_0)) d\tau$$

Classical and Fractional dynamical systems

Fractional differential equations are used to describe systems with long-range interactions or systems with power-law memory.

1/ a classical dynamical system is a semi-group on an open set $U \subset \mathbb{R}^n$
Among the properties of semi-group its flow verifies

$$\Phi_{t+s}(x) = \Phi_t(x) \circ \Phi_s(x) \quad \forall x \in U$$



2/ a fractional dynamical systems is not a semi-group equation. It is not local: the solution of a fractional order equation on time *t* depends on its memory from the starting time t_0 to *t*.

$$\Phi_{t+s}(x) = \Phi_t(x) \circ \Phi_s(x) + \Delta_{t+s}^\alpha(x)$$

$$\Delta_{s,t}^\alpha(x_0) = \frac{1}{\Gamma(\alpha)} \int_0^s \left[(s-\tau)^{(\alpha-1)} - (t+s-\tau)^{(\alpha-1)} \right] f(\Phi_\tau^\alpha(x_0)) d\tau$$

In fact, fractional differential equations are integro-differential equations.

Stability of the fixed points of a fractional system

Theorem [Matignon, 1996]: The following fractional-order linear autonomous system

$$\begin{cases} D^{\alpha} X = AX, \\ X(0) = X_0, \end{cases} \quad X \in \mathbb{R}^n, \quad 0 < \alpha < 2, \quad A \in \mathbb{R}^n \times \mathbb{R}^n$$

Is locally asymptotically stable if and only if the eigenvalues of the Jacobian matrix

verifies $\boxed{\min_i |\arg(\lambda_i)| > \alpha \dfrac{\pi}{2}, \quad i = 1, 2, \ldots, n}$

Theorem [Abdelouahab et al., 2010]: Let E be an equilibrium point of the fractional-order nonlinear system $D^{\alpha} = f(X), \quad 0 < \alpha < 2$

If the eigenvalues of the Jacobian matrix $A = \left(\dfrac{\partial f}{\partial X} \right) \Bigg|_E$

satisfies $\boxed{\min_i |\arg(\lambda_i)| > \alpha \dfrac{\pi}{2}, \quad i = 1, 2, \ldots, n}$

then the systems is asymptotically stable at the equilibrium point E .

Stability of the fixed points of FitzHugh-Nagumo Fractional system

We consider the FFHN model

$$\begin{cases} D^{\alpha_1}x = x - \frac{1}{3}x^3 - y + I \\ D^{\alpha_2}y = \varepsilon(x + a - by) \end{cases} \qquad (2)$$

with $\alpha_1 = \alpha_2 = \alpha \in (0,2)$

In order to observe a unique fixed point in the FFHN model, we restrict the set of parameters *I*, *a*, *b* and *T*.

Proposition : $\forall\, a, b, I \in \mathbb{R}$ satisfying $-4\left(1-\frac{1}{b}\right)^3 + 9\left(I - \frac{a}{b}\right)^2 > 0$

The system has a unique equilibrium point $E = (x_e(b), y_e(b))$

where $x_e(b) = \sqrt[3]{\dfrac{-q+\sqrt{\frac{-\Delta}{27}}}{2}} + \sqrt[3]{\dfrac{-q-\sqrt{\frac{-\Delta}{27}}}{2}}$, $y_e(b) = x_e(b) - \frac{1}{3}x_e^3(b) + I$

and $\Delta = -(4p^3 + 27q^2)$, $p = -3\left(1 - \frac{1}{b}\right)$, *and*, $q = -3\left(I - \frac{a}{b}\right)$

S-asymptotically *T*-periodic solutions

The non-existence of periodic solutions of fractional-order autonomous systems with bounded lower terminal was proved in 2009 by Tavazoei & Haeri. The existence of periodic solutions with unbounded lower terminal (i.e. $a = -\infty$) was proved by Yazdani & Salarieh in 2011.

Two new definitions were introduced in 2015 by Yang et al.

Let $C_b\left(\mathbb{R}^+, \mathbb{R}^n\right)$ denote the space of continuous and bounded functions $x : \mathbb{R}^+ \to \mathbb{R}^n$ equipped with the norm $\| \cdot \|_\infty$

Definition : a function $x \in C_b\left(\mathbb{R}^+, \mathbb{R}^n\right)$ is called asymptotically *T*-periodic, if there exists a bounded continuous *T*-periodic function u and a bounded continuous function v with $\lim_{t\to+\infty} v(t) = 0$ such that $x = u + v$. The set of these functions is denoted by $AP_T\left(\mathbb{R}^+, \mathbb{R}^n\right)$

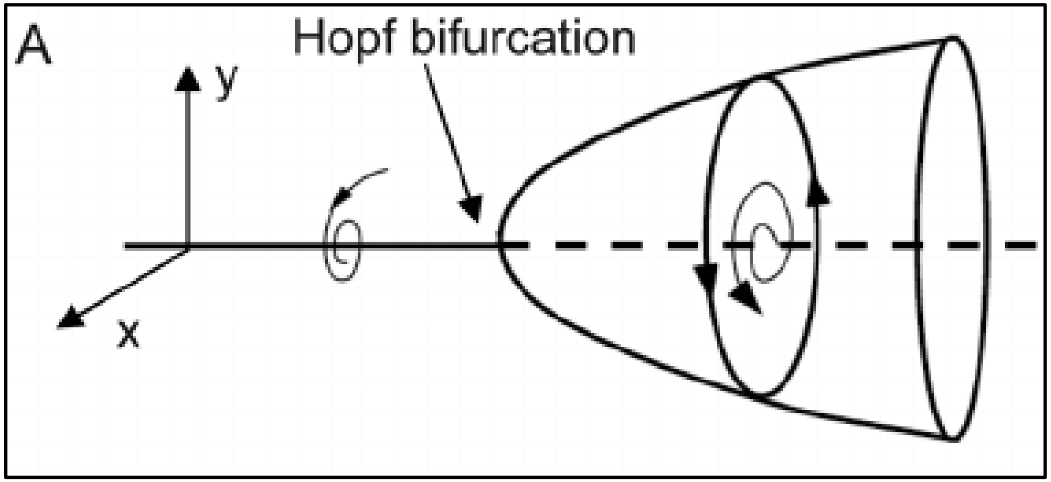
Definition: a function $x \in C_b\left(\mathbb{R}^+, \mathbb{R}^n\right)$ is called S-asymptotically*T*-periodic, if there exists $T > 0$ such that $\lim_{t\to+\infty}\left(x(t+T) - x(t)\right) = 0$. In this case T is said to be an asymptotic period of x

The set of these functions is denoted by $SAP_T\left(\mathbb{R}^+, \mathbb{R}^n\right)$

Both sets $AP_T\left(\mathbb{R}^+, \mathbb{R}^n\right)$ and $SAP_T\left(\mathbb{R}^+, \mathbb{R}^n\right)$ equipped with the norm $\| \cdot \|_\infty$ are Banach spaces. Moreover one has : $AP_T\left(\mathbb{R}^+, \mathbb{R}^n\right) \subset SAP_T\left(\mathbb{R}^+, \mathbb{R}^n\right)$

Hopf Bifurcation

The classical Hopf bifurcation happens when a stable fixed point lost its stability to a periodic solution



However a fractional order equation cannot displays periodic solution.

Hopf-Like Bifurcation (HLB)

Since periodic solutions of fractional-order autonomous systems do not exist implies that **the classical Hopf bifurcation does not exist for such systems**.

Therefore we introduce the paradigm of Hopf-Like Bifurcation when a fixed point changes its stability property as a pair of complex conjugate eigenvalues $\lambda_{\mp}$ of the Jacobian matrix at the fixed point cross a boudary of an angular sector $|\arg(\lambda_{\mp})| = \alpha\frac{\pi}{2}$ of the complex plane, giving rise to a small amplitude*S*-asymptotically *T*-periodic solution.

Hopf-Like Bifurcation for the Fractional-order FitzHugh Nagumo Model:

To analyze the HLB in system (2) at its unique fixed point $E = (x_e(b), y_e(b))$ with respect to the parameter *b*, we define the function

$$M(b,\alpha) = \alpha\frac{\pi}{2} - \left|\arctan\left(\frac{\sqrt{-(x_e^2(b) - b\varepsilon - 1)^2 + 4\varepsilon}}{x_e^2(b) + b\varepsilon - 1}\right)\right|$$

Theorem: Let the fractional order be fixed and *b** be the value of the solution *b* to $M(b,\alpha) = 0$.

If $(x_e(b) - b\varepsilon - 1)^2 < 4\varepsilon$ and

$$\left(2x_e(b)\frac{dx_e(b)}{db}\left(b^2\varepsilon - b(x_e^2(b) - 1\right) - 2 + \left(x_e(b) - 1\right)^2 - 2\varepsilon\right)\Big|_{b=b^*} \neq 0$$

Then the system (2) undergoes an HLB at the unique equilibrium *E* when *b* = *b**

Canard (Duck) and Mixed-Mode Oscillations

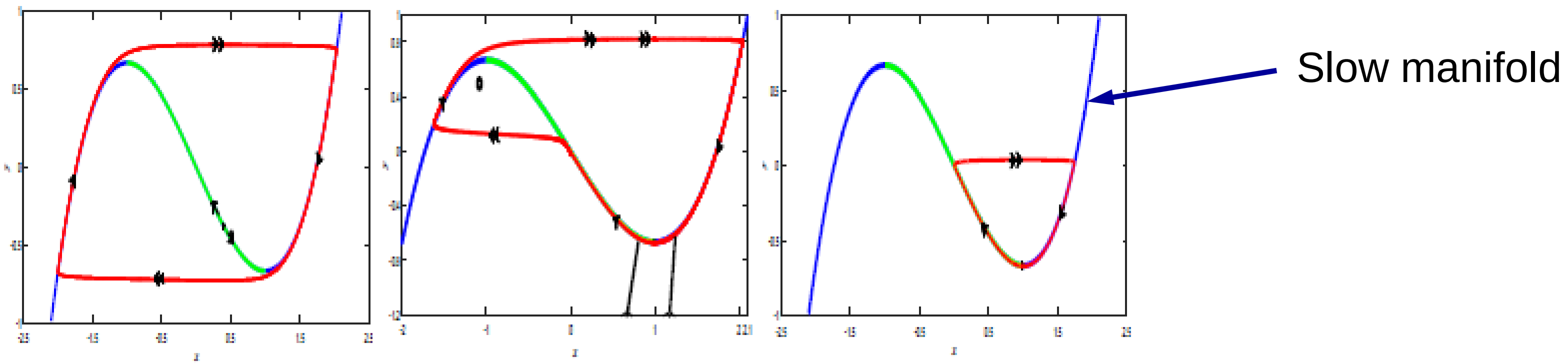
Consider the famous Van der Pol equation [Van der Pol, 1926] described in the Lienard plane:

$$\begin{cases} \dot{x} = x - \frac{1}{3}x^3 - y + I \\ \dot{y} = \varepsilon(a - x) \end{cases}$$

(3) (it is a slow-fast system when ε is small)

In 1981, Benoît, and Diener M., Diener F., discovered the « canard » trajectories :

Un « explosion » of the size of the solution :



(a) (b) (c)

(a) : *a = 0,99874045124**4*, (c): *a = 0,99874045124**6*

Mixed-Mode Oscillations (MMO)

The Mixed Mode oscillation arises in slow-fast systems when the solutions display some specific patterns called (MMO) : L large amplitude oscillations are followed by s small amplitude oscillations. Such patterns are denoted simply L^s

Such patterns are very common in the original 4-D model of Hodgkin-Huxley, modelling the spikes observed in action potential of many types of neurons.

The 4-D Hodgkin-Huxley model displays also chaotic solutions.

We can show that (MMO) arise also in the Fractional FitzHugh-Nagumo 2-D model, and more important : chaotic oscillations are observed in this 2-D model, which cannot be the case in integer 2-D ODE, due to the Poincaré-Bendixon theorem.

Canard cycles in the FFHN model

The Fractional FitzHugh-Nagumo 2-D model, is a slow fast system:

$$\begin{cases} D^{\alpha}x = x - \frac{1}{3}x^3 - y + I \\ D^{\alpha}y = \varepsilon(x + a - by) \end{cases}$$

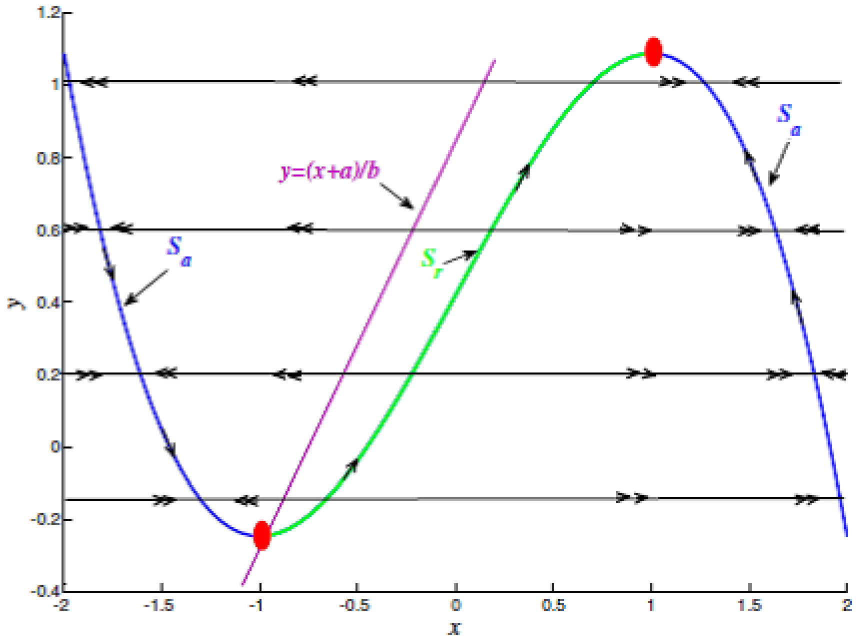
The frozen system reads:

$$\begin{cases} D^{\alpha}x = x - \frac{1}{3}x^3 - y + I \\ D^{\alpha}y = 0 \end{cases}$$

and the slow critical manifold is: $S_0 = \left\{ (x,y) \in \mathbb{R}^2 \,\middle|\, y = x - \frac{1}{3}x^3 + I \right\}$

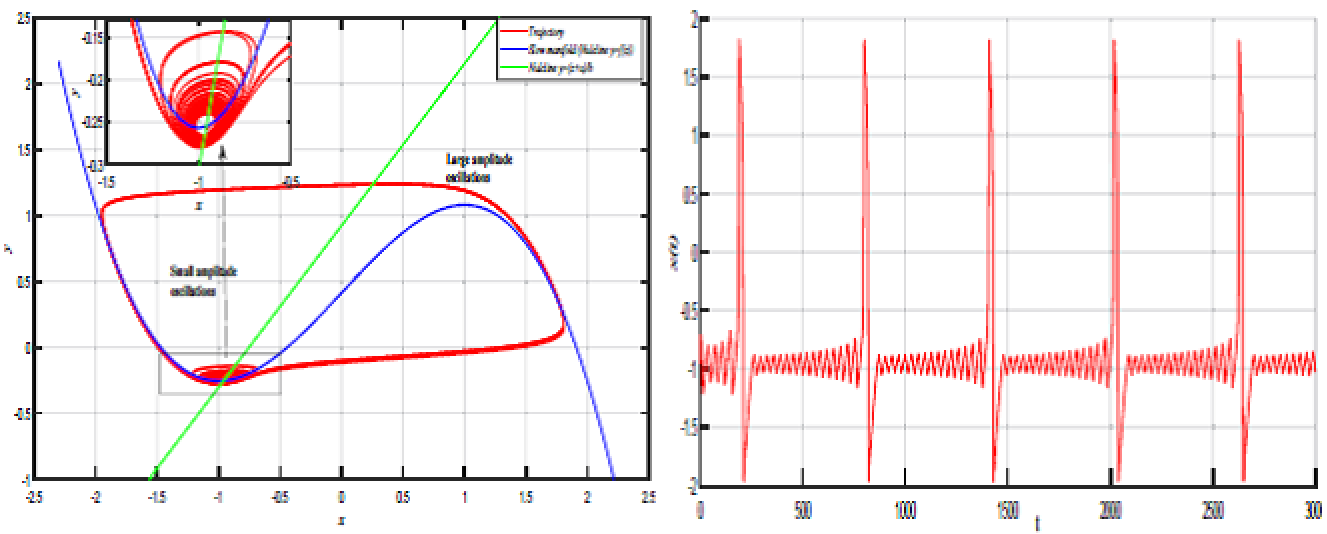
In blue stable part of the critical Manifold

In green unstable part



Canard cycles in the FFHN model

One can observe numerically such kind of MMO:

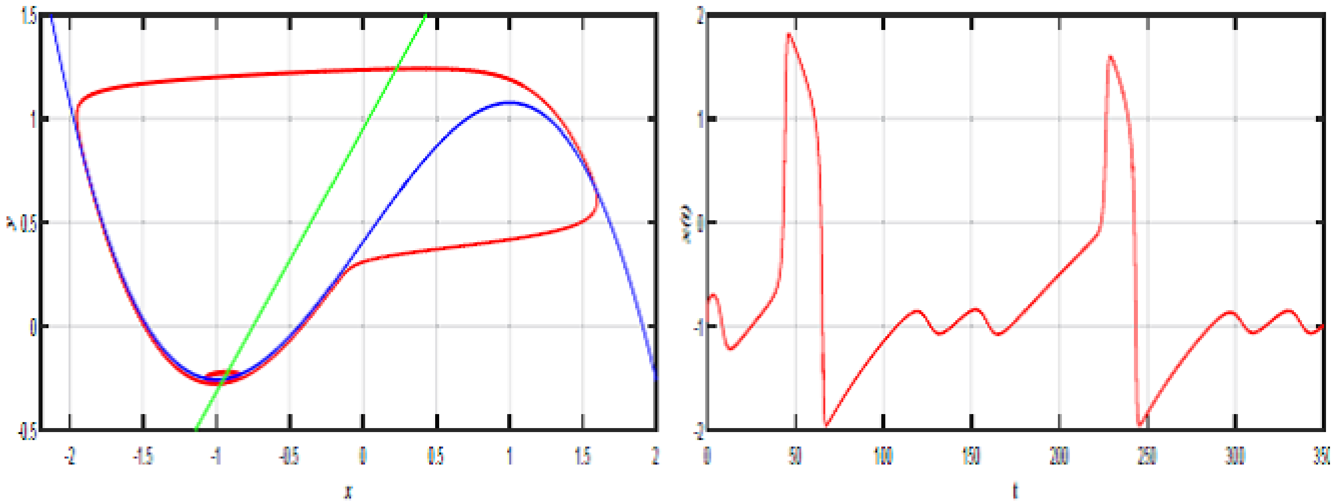


(a) (b)

For $a = 0{,}75$, $I = 0{,}41$, $\varepsilon = 0.05$ and $b = 0.815$

Canard cycles in the FFHN model

For a = 0,75, I = 0,41, ε = 0.05 One can observe numerically the increasing number of small oscillations:

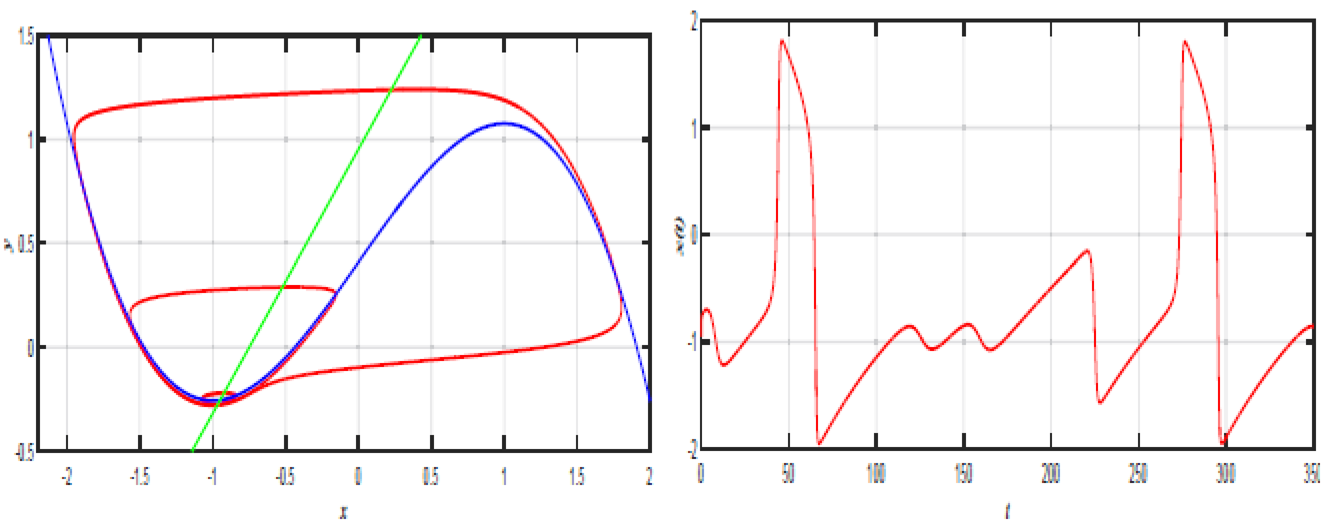


(a) (b)

1^2 solution for b = 0,7863948204251

Canard cycles in the FFHN model

For a = 0,75, I = 0,41, ε = 0.05



1^3 solution for *b* = 0,7863948204252

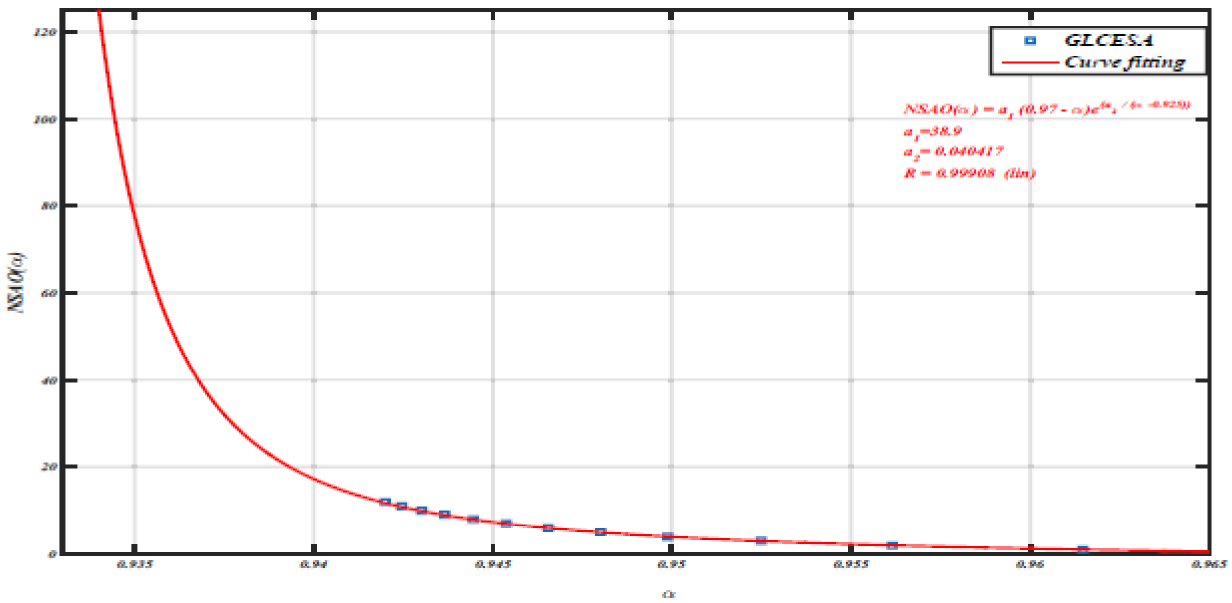
MMO versus parameter α

NSAO = number of small oscillation between two large ones:

$NSAO(\alpha)$	$tf(\alpha)$	PSD	$\bar{\alpha}_i$
12	610.69	[0.9419, 0.9422]	0.9419865649848
11	577.39	[0.9422, 0.9425]	0.9424658807848
10	539, 24	[0.9428, 0.9434]	0.9430130879415
9	504.79	[0.9434, 0.9440]	0.9436601053460
8	472.07	[0.9440, 0.9446]	0.9444332599613
7	403.39	[0.9452, 0.9462]	0.9453719917284
6	366.80	[0.9462, 0.9472]	0.9465298907124
5	333.88	[0.9472, 0.9482]	0.9479883536832
4	296.46	[0.9492, 0.9512]	0.9498957361566
3	233.18	[0.9512, 0.9532]	0.9524863819805
2	189.15	[0.9552, 0.9592]	0.9561361504262
1	155.12	[0.9592, 0.9632]	0.9614783464776
0	113.26	[0.9672, 0.9752]	0.9677434182069

MMO versus parameter α

NSAO = number of small oscillation between two large ones versus α



Moreover one can compute chaotic solutions for the FFHN model!

Thank you for your attention