Some Bifurcations and Wave Patterns Arising in Excitable and Oscillatory Models of Neuroscience Context

B. Ambrosio

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Systems.







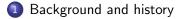
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The FitzHugh-Nagumo (FHN) Reaction-Diffusion (RD) system

$$\begin{cases} \epsilon u_t = f(u) - v + du_{xx}, (x, t) \in \Omega \times [0, +\infty[\\ v_t = u - c(x) \end{cases}$$
(1)

whith $f(u) = -u^3 + 3u$, ϵ small, and Neumann Boundary conditions (NBC). In the Neuroscience context, u represents a potential, v a recovery variable and Ω is a bounded domain in \mathbb{R}^2 or \mathbb{R} .

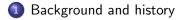


2 Patterns, Wave Propagations, Synchronization



3 Qualitative analysis-Bifurcations

Outline



2 Patterns, Wave Propagations, Synchronization

3 Qualitative analysis-Bifurcations

Hodgkin and Huxley



J. Physiol. (1952) 117, 500-544

A QUANTITATIVE DESCRIPTION OF MEMBRANE CURRENT AND ITS APPLICATION TO CONDUCTION AND EXCITATION IN NERVE

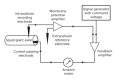
By A. L. HODGKIN AND A. F. HUXLEY

From the Physiological Laboratory, University of Cambridge

(Received 10 March 1952)









Hodgkin and Huxley

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From eqn. (6) this may be transformed into a form suitable for comparison with the experimental results, i.e.

$$g_{\mathbf{K}} = \{(g_{\mathbf{K}w})^{\frac{1}{2}} - [(g_{\mathbf{K}w})^{\frac{1}{2}} - (g_{\mathbf{K}y})^{\frac{1}{2}}] \exp((-t/\tau_n))^{\frac{1}{2}},$$
 (11)

where $g_{K\infty}$ is the value which the conductance finally attains and g_{K0} is the conductance at t=0. The smooth curves in Fig. 3 were calculated from

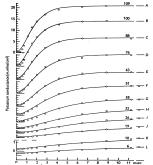


Fig. 5. Rise of pointamium consistences associated with different depolarizations. The civits are experimental points obtained on a con 17, stemp-struct or 27, 0, uing observations in an water and obtains one water (see Hodgkin & Huxkyr, 1052c). The smooth curves were drawn from equ. (11) with g₁₀=0.94 m. Mu/00⁻¹¹ and other parameters as shown in Table 1. The time and applies to all records: The ordinate scale is the same in the upper for an urres (4 to J) the opplication in m. We have two curves (K and J). The number on each curve gives the depolarization in m. We have two curves (K and J). The number on each curve gives in the same first order of a single scale scal

(日)

Hodgkin-Huxley Reaction-Diffusion system

$$C \frac{dV}{dt} = V_{xx} + I - \overline{g}_{Na}m^{3}h(V - E_{Na}) - \overline{g}_{K}n^{4}(V - E_{K}),$$

$$-\overline{g}_{L}(V - E_{L})$$

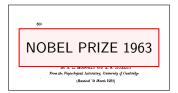
$$\frac{dn}{dt} = \alpha_{n}(V)(1 - n) - \beta_{n}(V)n$$

$$\frac{dm}{dt} = \alpha_{m}(V)(1 - m) - \beta_{m}(V)m$$

$$\frac{dh}{dt} = \alpha_{h}(V)(1 - h) - \beta_{h}(V)h$$

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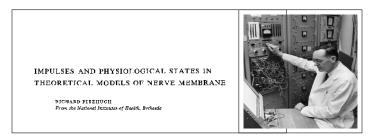
" For their discoveries concerning the ionic mechanisms involved in excitation and inhibition in the peripheral and central portions of the nerve cell membrane." See www.nobelprize.org.



"To this day their work stands as one of the best examples of how scientists can use mathematics to provide insights into complicated biological systems." Nature Education-2010

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The Bonhoeffer-Van der Pol model (FitzHugh-Nagumo equations)



$$\begin{cases} x_t = c(y + x - \frac{x^3}{3} + z) \\ y_t = -(x - a + by)/c \end{cases}$$
(2)

with 1 - 2b/3 < a, 0 < b < 1, $b < c^2$; z stimulus intensity, an arbitrary function of t which can be a Dirac (Original FitzHugh paper, p 447)

"The one to be described in the present paper considers the HH as one member of a large class of non-linear systems showing excitable and oscillatory behavior."

> This approach is, however, not so informative in explaining how trains of impulses occur in the HH equations, where interactions between all four variables are essential. Two other approaches to this problem, also based on phase space in thods, are more useful. The one to be described in the present paper considers the HH nocid to go member of a large class of non-linear systems show ng excitable and oscillator, behavior. The phase plane model used by Bonhoeffer (1941, 1948, 953) and Bonhoeffer and Langhammer (1948) to explain the behavior of passi-

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(*) (*) (*) (*) (*)

(After Liénard's Transformation)

$$\begin{cases} x_t = c(y + x - \frac{x^3}{3} + z) \\ y_t = -x/c \end{cases}$$
(3)

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Bonhoeffer (1948)

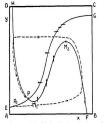


FIG. 8. xy diagram for current densities barely above rheobase. Single activation. Fig. 8 is obtained from Fig. 6 by raising the curves HF_1 and LM_2F_2 . The notations and the meaning of the lines are the same as in Fig. 6.

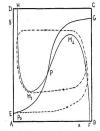


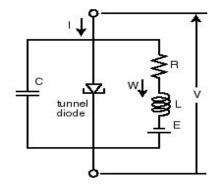
FIG. 9. xy diagram for higher current densities. Rhythmic activation. The notation and the meaning of the lines are the same as in Fig. 6.

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FitzHugh-Nagumo equations

In 1962, Nagumo et al. provided the analog equivalent circuit.



See:

Nagumo J., Arimoto S., and Yoshizawa S. (1962) An active pulse transmission line simulating nerve axon. Proc. IRE. 50:2061–2070. Now, the BVP model is called the FHN system.

The FHN ODE system

$$\begin{cases} \epsilon u_t = f(u) - v \\ v_t = u - c \end{cases}$$
(4)

whith $f(u) = -u^3 + 3u$, ϵ small.

The FHN ODE system : excitable and oscillatory behavior

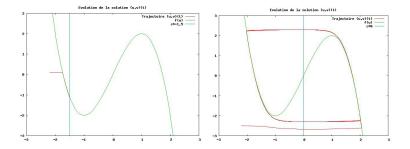


Figure: Solutions of system (4), for typical values of c.

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Theorem 1

There exists a unique stationary point. If $|c| \ge 1$ the stationary point is globally asymptotically stable, whereas if |c| < 1, it is unstable and there exists a unique limit-cycle which attracts all the non constant trajectories. Furthermore, at |c| = 1, there is a supercritical Hopf bifurcation.

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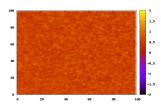
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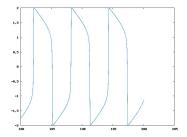
2 Patterns, Wave Propagations, Synchronization



c=0;IC:Uniform law on [0,1]



Asymptotic homogeneous space behavior for (1) ($u(x_1, x_2, 0)$). Initial conditions: uniform law on [0, 1].

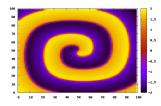


Asymptotic evolution of a solution of (1) at some space points. Red line: $u(x_1, x_2, t)$ for $(x_1, x_2) = (50, 50, t)$, for time $t \in [180, 200]$. Red line: $(x_1, x_2) = (50, 100, t)$. Blue line: $\int_{\Omega} u(x, t) dx$.

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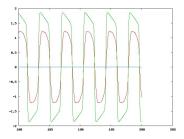
Is there other solutions?

c=0; IC:Specific



Asymptotic non-homogeneous space behavior of spiral type for (1) ($u(x_1, x_2, 190)$). Initial conditions: ($u_0(x), v_0(x) = (1, 0)$ on Left

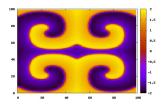
Top (LT) square, (0,1) on RT, (0,-1) on LB , (-1,0) on RB.



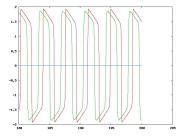
Asymptotic evolution of a solution of (1) at some space points. Red line: $u(x_1, x_2, t)$ for $(x_1, x_2) = (50, 50, t)$, for time $t \in [180, 200]$. Green line: $(x_1, x_2) = (50, 100, t)$. Blue line: $\int_{\Omega} u(x, t) dx$.

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Numerical simulations



Asymptotic non-homogeneous space behavior of four spiral type for (1) ($u(x_1, x_2, 190)$). Initial conditions: we reproduce four times the previous one with symmetry.



Asymptotic evolution of a solution of (1) at some space points. Green line: $u(x_1, x_2, t)$ for $(x_1, x_2) = (50, 50, t)$, for time $t \in [180, 200]$. Red line: $(x_1, x_2) = (50, 100, t)$. Blue line: $\int_{\Omega} u(x, t) dx$.

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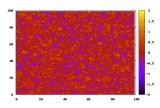
c=0;Invariant subspace

Theorem 2

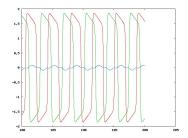
Suppose that we can divide the domain into a partition $\Omega = (\bigcup_{i \in \{1,...,l\}} U_i) \cup (\bigcup_{i \in \{1,...,l\}} V_i) \text{ such that there exists a}$ diffeomorphism ϕ that maps each U_i to V_i , $i \in \{1,...,l\}$, with $|\det J_{\phi}| = 1$, where J_{ϕ} is the jacobian of ϕ and initial conditions such that for all $x \in \bigcup_{i \in \{1,...,l\}} U_i$ and for all $t \in \mathbb{R}^+$, $(u(\phi(x), t), v(\phi(x), t)) = -(u(x, t), v(x, t))$ then the solution of (1) cannot evolve asymptotically around (\bar{u}, \bar{v}) .

See: B. A., M.A. Aziz-Alaoui, Basin of Attraction of Solutions with Pattern Formation in Slow–Fast Reaction–Diffusion Systems Acta Biotheoretica 64 (4), (2016), 311-325.

c=0; IC:Uniform law on [-1,1]



Asymptotic non-homogeneous space behavior of multiple spiral type for (1) ($u(x_1, x_2, 0)$). Initial conditions: uniform law on [-1, 1].



Asymptotic evolution of a solution of (1) at some space points. Red line: $u(x_1, x_2, t)$ for $(x_1, x_2) = (50, 50, t)$, for time $t \in [180, 200]$. Green line: $(x_1, x_2) = (50, 100, t)$. Blue line: $\int_{\Omega} u(x, t) dx$.

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Is the system (1) able to generate oscillatory signals and to propagate it?

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Is the system (1) able to generate oscillatory signals and to propagate it?

Yes, the idea being:

" Oscillatory signal initiates at some point and propagates along excitatory tissue thanks to diffusion."

We will consider functions such that:

- c(x) < -1 for x close to the border, (Excitatory dynamics for the ODE system)
- c(x) = 0 for x close to the center, (Oscillatory dynamics for the ODE system)

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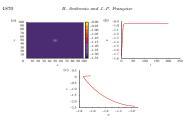


Figure 1. Solutions for $\delta = 0.01$, $c_0 = -1.3$ and (a) u(x, y, 50), (b) u(50, 50, t) (solid line) and (c) (u, v)(50, 50, t) (solid line), (a) Evolution to stationary solution for $c_0 = -1.3$ and t = 50; (b) evolution of the variable u for a central cell and $c_0 = -1.3$; and (c) evolution of (u, v) for a central cell and $c_0 = -1.3$.

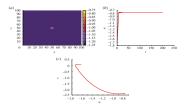


Figure 2. Solutions for $\delta = 0.01$, $c_0 = -1.195$. (a) u(x, y, 50), (b) u(00, 50, 1) (solid line) and $(c \circ (u, v_i)(05, 00, 1)$ (solid line). (a) Evolution to stationary solution for $c_0 = -1.195$ and t = 50; (b) evolution of the variable u for a central cell and $c_0 = -1.195$; and (c) evolution of (u, v) for a central cell and $c_0 = -1.195$;

Phil. Trans. R. Soc. A (2009)

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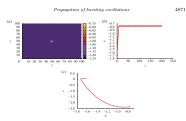


Figure 3. Solutions for $\delta = 0.01$, $c_0 = -1.13932$ (T = 2000). (a) u(x, y, 500, (b) u(50, 50, r) (solid line) and (c) (u, v)(50, 50, r) (solid line). (a) Solution for $c_0 = -1.19302$ and t = 50. (b) evolution of the variable u for a central cell and $c_0 = -1.19302$; and (c) evolution of (u, v) for a central cell and $a_0 = -1.19302$.

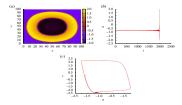
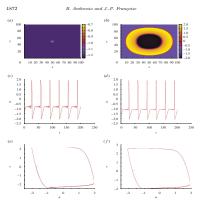


Figure 4. Solutions for $\delta = 0.01$, $\alpha_0 = -1.19302$ (T = 2000). (a) u(x, y, 1.950), (b) u(0, 0, 0, 1). (solid line) and (c) u, u, 0(5, 0, 0) (solid line). (a) Solution for $\alpha_0 = -1.19302$ and t = 50; (b) evolution of the variable u for a central cell and $\alpha_0 = -1.19302$; and (c) evolution of (u, v) for a central cell and $\alpha_0 = -1.19302$.

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(b) Numerical simulations of system (4.1) and propagation of the bursting oscillations

The same result is observed numerically: there is a threshold such that, if the excitability c₀ is below the threshold, the solution evolves to a stationary solution. If it is above, there is a propagation of the bursting oscillations. The number of

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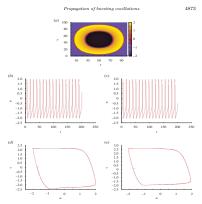


Figure 6. Solutions for $\delta = 0.01$, $\alpha = -1.15$, $(a) u(x_2, y, 55)$, (b) u(00, 50, t) (solid line), (c) u(01, 50, t) (solid line), (d) u(01, t) (solid line), (d) u(0

spikes increases as $\gamma \rightarrow 0$ and/or as $c_0 \rightarrow -1$. Initial conditions are around the values $u(0, x) = -1, v(0, x) = 0.1, \delta = 0.01$; propagation of bursting oscillations is seen in figure 7.

Phil. Trans. R. Soc. A (2009)

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$c \times and t$ -dependant. Propagation of bursting signals (2D)

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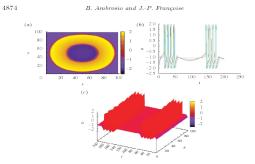


Figure 7. Solutions of the system (4.1), for γ =0.05 and c = -1,05. (a) u(x, y, 28), (b) u(50, 50, t) (red line), u(51, 50, t) (green line) and u(99, 50, t) (blue line) and (c) u(x, 49, t) (red line).

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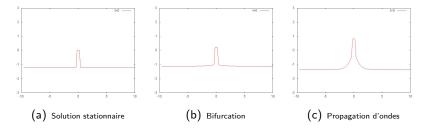


Figure: Bifurcation from stationnary solution to wave propagation.

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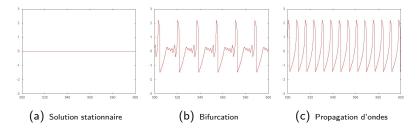


Figure: Bifurcation from stationnary solution to wave propagation.

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Networks: Synchronization of Patterns

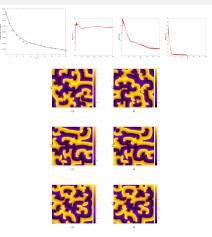


Figure: Fully connected network. Case c(x) = 0.

See B. A., M A Aziz-Alaoui. V L E Phan, "Large time behaviour and synchronization of complex networks of reaction-diffusion systems of FitzHugh-Nagumo type" IMA JAM,84(2), (2019), 416-443

Outline

Patterns, Wave Propagations, Synchronization



3 Qualitative analysis-Bifurcations

We set

$$\mathcal{H} = L^2(0,1) \times L^2(0,1)$$

 $\mathcal{V} = H^1(0,1) \times H^1(0,1)$ where $H^1(0,1)$ is the classical Sobolev space. $||\cdot||$ will denote the norm on \mathcal{H} .

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We consider $\begin{cases}
 u_t = \alpha u - u^3 - v + u_{xx} \\
 v_t = u
\end{cases}$ (5)

on the domain (0,1) with Neumann Boundary conditions.

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Note first that (0,0) is a constant solution of (5). The linearized system around this point is given by:

$$\begin{cases} u_t = \alpha u - v + u_{xx} \\ v_t = u \end{cases}$$
(6)

on the domain (0,1) with Neumann Boundary conditions.

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Using the spectral decomposition, we can give a detailed and comprehensive analysis of the qualitative behavior of (6). Classically, we set:

$$\varphi_0(x) = 1$$
, and $\forall k \in \mathbb{N}^* \, \varphi_k(x) = \sqrt{2} \cos(k\pi x)$.

We recall that the family $(\varphi_k)_{k \in \mathbb{N}}$ is an other normal basis of L^2 , and that the functions φ_k satisfy:

$$-(\varphi_k)_{xx} = \lambda_k \varphi_k$$

and

$$(\varphi_k)_x(0)=(\varphi_k)_x(1)=0,$$

with

$$\lambda_k = k^2 \pi^2.$$

Looking for solutions of the form,

$$u(t) = \sum_{k=0}^{\infty} u_k(t) \varphi_k, v(t) = \sum_{k=0}^{\infty} v_k(t) \varphi_k$$

leads by projection on the eigenspace generated by (φ_k, φ_k) to the resolution of the two dimensional ODE systems indexed by k, and denoted by E_k :

$$(E_k) \begin{cases} u_{kt} = (\alpha_k - \lambda_k)u_k - v_k \\ v_{kt} = u_k \end{cases}$$
(7)

The eigenvalues of matrix

$$A_k = egin{pmatrix} lpha - \lambda_k & -1 \ 1 & 0 \end{pmatrix}$$

are given by

$$\sigma_k^1 = \frac{1}{2} \left(\alpha - \lambda_k - \sqrt{(\alpha - \lambda_k)^2 - 4} \right), \ \sigma_k^2 = \frac{1}{2} \left(\alpha - \lambda_k + \sqrt{(\alpha - \lambda_k)^2 - 4} \right)$$

We summarize the remarkable properties of σ_k^1 and σ_k^2 in the following proposition.

Proposition 1

When α crosses λ_k from left to right, σ_k^1 and σ_k^2 cross the imaginary axis from left to right. Furthermore,

$$\lim_{k \to +\infty} \sigma_k^1 = -\infty \text{ and } \lim_{k \to +\infty} \sigma_k^2 = 0^-.$$

Theorem 3 (Linearized System)

For $\alpha < 0$, for any initial condition $(u(\cdot, 0), v(\cdot, 0))$ in \mathcal{H} , we have

 $\lim_{t\to+\infty}||(u,v)(t)||=0.$

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Theorem 4

Let $k \in \mathbb{N}^*$. For $\alpha = \lambda_k$, (0,0) is a center for system E_k , a source for E_l if l < k and a sink for E_l if l > k. Furthermore, if: $u_l(0) = v_l(0) = 0$ for $l \in \{0, ..., k - 1\}$ then

$$\lim_{t\to+\infty}||(u,v)(t)-\varphi_k(u_k(t),v_k(t))||=0.$$

Otherwise,

$$\lim_{t\to+\infty}||(u,v)(t)||=+\infty.$$

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Theorem 4 (part 2) For $\lambda_k < \alpha < \lambda_{k+1}$, (0,0) is a source for E_l si $l \le k$ and a sink for E_l if l > k. Furthermore, if $u_l(0) = v_l(0) = 0$ for $l \in \{1, ..., k\}$ then

 $\lim_{t\to+\infty}||(u,v)(t)||=0.$

Otherwise

$$\lim_{t\to+\infty}||(u,v)(t)||=+\infty.$$

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Theorem 5 (Nonlinear System)

For $\alpha < 0$, for any initial condition $(u(\cdot, 0), v(\cdot, 0))$ in \mathcal{H} ,

 $\lim_{t\to+\infty}||(u,v)(t)||=0.$

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Proof

- Lyapunov Function
- LaSalle's Principle

Theorem 6 For $0 < \alpha < \lambda_1$, if u(x) = -u(1-x) and v(x) = -v(1-x) then for all IC in \mathcal{H} $\lim_{t \to +\infty} ||(u, v)(t)|| = 0$

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Proof

- Invariant Subspace
- Lyapunov Function
- LaSalle's Principle

Theorem 7 For $0 < \alpha < \lambda_1$, there exists a sequence $(\mu_k)_{k \in \mathbb{N}}$ such that if $(u_k(0), v_k(0)) \in B(0, \mu_k) \subset \mathbb{R}^2$

then

$$\lim_{t\to+\infty} ||(u(t) - u_0(t), v(t) - v_0(t))|| = 0,$$

where $B(0, \mu_k)$ is the ball of center (0, 0) and radius μ_k .

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- Projection onto subspaces
- Nonlinear terms bounded by:

$$C\sum_{i=1}^{\infty}|u_i|\sum_{i=1}^{\infty}u_i^2$$

- Estimation on each subspace
- Lyapunov function

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Asumptions on c(x)

We assume that the function c(x), depending on a parameter p > 0, is regular and satisfies the following conditions:

$$c(x) \leq 0$$
 $\forall x \in (-a, a),$ (8)

$$c(0)=0, \tag{9}$$

$$c'(x) > 0 \quad \forall x \in (-a, 0), \ c'(x) < 0 \ \forall x \in (0, a), \ (10)$$

$$c'(-a) = c'(a) = 0,$$
 (11)

$$\begin{aligned} \forall x \in (-a, a), & x \neq 0, \quad c(x) \text{ is a decreasing function of } p, \quad (12) \\ \forall x \in (-a, a), & x \neq 0, \quad \lim_{p \to 0} c(x) = 0, \quad (13) \end{aligned}$$

$$\forall x \in (-a, a), x \neq 0, \qquad \qquad \lim_{p \to +\infty} c(x) = -\infty. \tag{14}$$

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Typical example

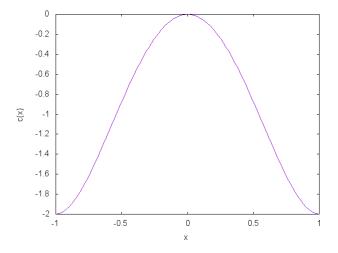


Figure: Graph of c(x) for p = 5.

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The stationary solution is given by

$$\begin{cases} \bar{v} = f(\bar{u}) + d\bar{u}_{xx} \\ \bar{u} = c(x) \end{cases}$$
(15)

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The linearized system around (\bar{u}, \bar{v}) writes:

$$\begin{cases} \epsilon u_t = f'(\bar{u})u - v + du_{xx} \\ v_t = u \end{cases}$$
(16)

We would like to proceed to projection on appropriate subspaces as in previous sections. To that end, we are interested in solutions of the following equation

$$f'(c(x))u + du_{xx} = \lambda u \tag{17}$$

with NBC. Note that equation (17) is a regular Sturm-Liouville problem.

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Spectral analysis

Theorem 8

There exists an increasing sequence of real numbers (λ_n) and an orthogonal basis $(\varphi)_{n \in \mathbb{N}}$ of $L^2(-a, a)$ such that:

$$\begin{array}{rcl} (d\varphi_{nxx}+f'(\bar{u})\varphi_n &=& \lambda_n\varphi_n\\ \varphi'_n(-a) &=& \varphi'_n(a) &=& 0. \end{array}$$

Furthermore,

$$\lim_{n \to +\infty} \lambda_n = +\infty,$$

$$\lambda_0 = \inf_{u \in H^2(-a,a), |u|_{L^2(-a,a)} = 1} d \int_{(-a,a)} |u_x|^2 dx - \int_{(-a,a)} f'(c(x)) u^2 dx.$$
and
$$\lambda_n = \frac{\pi^2 n^2}{4a^2} + O(n)$$

The projection on the kth subspace writes

$$(E_k) \begin{cases} \epsilon u_{kt} = -\lambda_k u_k - v_k \\ v_{kt} = u_k \end{cases}$$
(18)

while the eigenvalues are given by

$$\begin{cases} \sigma_1^k = \frac{1}{2\epsilon} \left(-\lambda_k - \sqrt{(\lambda_k^2 - 4\epsilon)} \right) \\ \sigma_2^k = \frac{1}{2\epsilon} \left(-\lambda_k + \sqrt{\lambda_k^2 - 4\epsilon} \right) \end{cases}$$
(19)

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Spectral analysis

Theorem 9

For each p, the number of eigenvalues with positive real part is finite. For p small enough, σ_1^0 and σ_2^0 have a positive real part. For p large enough, all the eigenvalues σ_1^k and σ_2^k have negative real part. There is an Hopf Bifurcation: there exists a value p_0 for which as p crosses p_0 from right to left, σ_1^0 and σ_2^0 are complex and their real part increase from negative to positive. The other eigenvalues remaining with negative real parts. Furthermore,

$$\lim_{k \to +\infty} \sigma_k^1 = -\infty \text{ and } \lim_{k \to +\infty} \sigma_k^2 = 0^-.$$

See: B. A.," Hopf Bifurcation in an Oscillatory-Ecxitable Reaction-Diffusion system with spatial heterogeneity", International Journal of Bifurcation and Chaos, 27(5), (2017)

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Theorem 10

For $p > p_0$, there exists a sequence $(\mu_k)_{k \in \mathbb{N}}$ such that if

 $(u_k(0),v_k(0))\in B(0,\mu_k)$

then

$$\lim_{t\to+\infty}||(u(t),v(t))||=0,$$

where $B(0, \mu_k)$ is the ball of center (0, 0) and radius μ_k .

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Theorem 11

There exists $\delta > 0$ such that for $p_0 , there exists a sequence <math>(\mu_k)_{k \in \mathbb{N}}$ such that if

 $(u_k(0),v_k(0))\in B(0,\mu_k)$

then

$$\lim_{t\to+\infty} ||(u(t) - u_0(t), v(t) - v_0(t))|| = 0,$$

where $B(0, \mu_k)$ is the ball of center (0, 0) and radius μ_k .

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Thanks!

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