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ON THE ROLE OF RANDOM TRANSVERSAL UNCOUPLING ON RE-ENTRY FORMATION

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The effect of randomly distributed connections among cells on spiral initiation by vulnerability is studied into the framework of active electronic circuits. We have observed the increase of the vulnerable region due to the transversal uncoupling among adjacent cells.

1. Introduction

Autowaves are type of waves characteristic of strongly nonlinear active media. Autowaves differ from classical waves in conservative media because they propagate at the expense of energy stored in the medium (for a complete description of autowave behavior and properties see Krinsky's seminal work [Krinsky, 1984]). In particular, spiral waves, also called re-entries or vortices, have constituted a common subject of research during the last decades. Spiral constitute a self-sustained activity with the highest frequency allowed by the medium which are believed to be the origin of life-threatening arrhythmias in cardiac tissue [Mines, 1914; Jalife, 1990]. A spiral wave overwhelms the rest of the structures in the medium and, in a certain way, it synchronizes the whole medium to the same rotation frequency.

Different methods for spiral generation have been studied in the literature, both in biological media [Allesie *et al.*, 1973] and in reaction–diffusion systems [Gomez-Gesteira *et al.*, 1994a, 1994b; Taboada *et al.*, 1994]. Maybe, among these methods, the vulnerability of the medium is the most widely studied [Allesie *et al.*, 1973; Keener & Phelps, 1989; Gomez-Gesteira *et al.*, 1994a; Starobin *et al.*, 1994]. It is a well-known fact that the behavior of an active medium changes after the passage of a wave due to the dispersion relation [Mikhailov, 1990; Tyson & Keener, 1988]. After the passage of a wave through a point, that point cannot be re-excited for a certain refractory period. Long after the passage of that wave, the medium recovers its properties and can be re-excited. Between both limits, there is a narrow region where a stimulus can propagate in the direction opposite to the movement of the previous wave, but it is stopped in the direction of the previous wave. That narrow region is called *vulnerable window* (VW). This process gives rise to a discontinuous wave front, which is the origin of a pair of rotating spiral waves. This mechanism was first studied in a homogeneous medium [Balakhovsky 1965; van Capelle *et al.*, 1980].

On the other hand, there is a natural process, called *microfibrosis*, which has been profusely studied in cardiology [Spach & Dolber, 1986]. This process, which is mainly due to aging, is characterized by the loss of transversal coupling, giving rise to the uncoupling among adjacent fibers.

The aim of this paper is to combine the phenomena previously related to show the effect of a randomly distributed transversal uncoupling on the size of the vulnerable region. The experimental setup and its related numerical model are described in Sec. 2. The effect of transversal uncoupling on re-entry initiation by vulnerability is studied in Sec. 3.

2. Experimental Setup

A sketch of a 2D electronic array (10×8 circuits) is shown in Fig. 1. Every cell in the array (a dark spot in Fig. 1), is a Chua's circuit [Madan, 1993; Chua, 1992], whose parameters are summarized in Table 1. With the set of parameters given in Table 1, each circuit behaves as an excitable cell [Muñuzuri *et al.*, 1995; Perez-Muñuzuri *et al.*, 1995; deCastro *et al.*, 1998], which can be adjusted following the method described in [Perez-Muñuzuri *et al.*, 1994]. From now on, we will identify every circuit in the array by two indexes (i, j) (i in the X direction and j in the Y direction). The origin, (1, 1), will be considered at the lower left corner. Most of the circuits are coupled through resistances at node V_1. Two different resistances were considered, a longitudinal resistance, $R_l = 4.7\ k\Omega$, which couples Chua's circuits in the X direction and a transversal resistance, $R_t = 5.6\ k\Omega$, which couples Chua's circuits in the Y direction (we have considered $R_t > R_l$ to mimic the anisotropy observed in some biological media as cardiac tissue). The experimental protocol to generate a spiral can be described using the particular choice shown in Fig. 1.

Table 1. Experimental Chua's circuit parameters.

Parameter	Value	Tolerance
C_1	1 nF	5%
C_2	100 nF	5%
L	10 mH	10%
R_{int}	270 Ω	1%
r_0	10 Ω	
R_l	4.7 kΩ	1%
R_t	5.6 kΩ	1%

(1) Two adjacent fibers were uncoupled in a certain region (fibers 2 and 3 from cell 3 to cell 8 in Fig. 1).
(2) A single pulse was delivered at first column by a pulse generator, G_1 (Hewlett-Packard 33120A). This gives rise to a planar wave front propagating in OX^+ direction.
(3) At the same time, the initial pulse activates a monostable oscillator 555, which triggers a second pulse generator, G_2, after a certain time, T_1, which can be externally controlled.
(4) The generator G_2 delivers a single pulse at certain cells in the array (cells (8, 1) and (8, 2) in Fig. 1). The cell (8, 2) will be considered the control point from now on.
(5) The excitation is measured at three different points by means of an oscilloscope (Hewlett-Packard 54601, at a rate of 20 MSa/s). The considered measuring points are: $P_1 = (1, 2)$, $P_2 = (8, 2)$ and $P_3 = (10, 2)$.

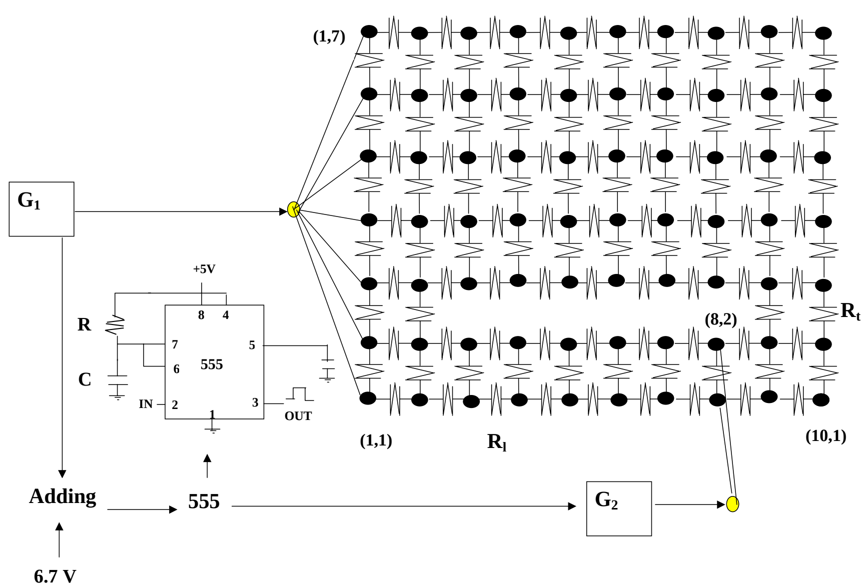

Fig. 1. Experimental setup. Black spots represent the unit cells. Circuits were resistively coupled through node V1 both longitudinally, $R_l = 4.7$ k, and transversally, $R_t = 5.6$ k. Fibers extend in X direction.

To visualize the vulnerability process see Fig. 1 in [Starmer, 1997].

The time, T_0 necessary for a pulse to propagate from the first column to control point can be easily calculated. In the particular case depicted in Fig. 1, $T_0 = 100.0 \pm 0.5$. From now on, we will only consider the time delay defined as $T_d = T_1 - T_0$. The previous setup can be described by the following set of equations [Muñuzuri *et al.*, 1995; Perez-Muñuzuri *et al.*, 1995]:

$$\begin{aligned} \dot{x}_{i,j} &= \alpha(y_{i,j} - x_{i,j} - h(x_{i,j})) \\ &\quad + D_l(x_{i+1,j} - 2x_{i,j} + x_{i-1,j}) \\ &\quad + D_t^r(x_{i,j+1} - x_{i,j}) + D_t^l(x_{i,j-1} - x_{i,j}) \\ \dot{y}_{i,j} &= x_{i,j} - y_{i,j} + z_{i,j} \\ \dot{z}_{i,j} &= -\beta y_{i,j} - \gamma z_{i,j} \quad i = 1, \ldots, 200y \\ &\qquad\qquad\qquad\quad j = 1, \ldots, 200 \end{aligned} \tag{1}$$

with

$$h(x) = a_0 + a_1 x + b_1|x - x_1| + b_2|x - x_2| \tag{2}$$

with $a_1 = (m_1 + m_2)/2$, $a_0 = b_1 x_1 - b_2 x_2$, $b_1 = (m_0 - m_1)/2$, and $b_2 = (m_2 - m_0)/2$. m_1, m_2 and m_0 are the slopes of the different branches of $h(x)$. We have considered $x_1 = -1$ and $x_2 = (m_0 - m_1)/(m_2 - m_0)$. α, β, γ, m_0, m_1, m_2 were obtained from the electronic components following the expressions:

$$\alpha = \frac{C_2}{C_1}, \quad \beta = \frac{C_2}{LG^2}, \quad \gamma = \frac{C_2 r_0}{LG}.$$

in addition,

$$D_l = \frac{\alpha}{GR_l}$$

and

$$D_t^r = \begin{cases} 0, & \text{for circuits on the left side of the uncoupled region,} \\ \dfrac{\alpha}{GR_t}, & \text{for the rest of the circuits} \end{cases}$$

$$D_t^l = \begin{cases} 0, & \text{for circuits on the right side of the uncoupled region,} \\ \dfrac{\alpha}{GR_t}, & \text{for the rest of the circuits} \end{cases}$$

This system was solved by means of a FTCS explicit scheme with time step $\Delta t = 0.002$ t.u. and zero-flux boundary conditions in x variable. The following protocol was used to generate a pair of spiral waves by vulnerability. First, a planar conditioning wave was generated close to one of the boundaries of the medium. This was achieved by exciting x and y variables of the first columns of cells — both variables were reset to the maximum value on their limit cycle. The remaining cells were reset to their rest state. Following the passage of the conditioning wave over a previously chosen control position, P_c, and after a certain time delay, T_d, a new pulse was applied at P_c and its nearest neighbors, a 3×3 square centered at P_c. This new pulse resets x and y to their maximum value. As we mentioned above, spiral generation by vulnerability can even be obtained in homogeneous media [Keener & Phelps, 1989; Gomez-Gesteira *et al.*, 1994a; Winfree, 1983]. Nevertheless, to study the role of spatial inhomogeneities on spiral generation, we have considered the existence of a region without transversal coupling between adjacent cells. This region is one circuit wide and l circuits long. The region is considered to start at P_c and extend in the retrograde direction. The parameters used in numerical calculations are summarized in Table 2.

Table 2. Numerical Chua's circuit parameters.

Parameter	Value
C_1	1 nF
C_2	10 nF
L	0.04 H
R_{int}	1100 Ω
r_0	5 Ω
m_1	0.7
m_0	−1.14
m_1	50.71
ε	1
R_l	0.5 kΩ
R_t	1.0 kΩ

3. Results

The different responses to a second pulse can be observed in Figs. 2(a)–2(c). For a short time delay, $T_d = 60.0 \pm 0.5$ μs, the second pulse does not re-excite the medium, Fig. 2(a). P_1 is excited by the first pulse, then excitation is observed in P_2 and P_3 after a certain delay. The effect of the second pulse can only be observed at P_2, but does not propagate to the rest of the medium. Figure 2(c)

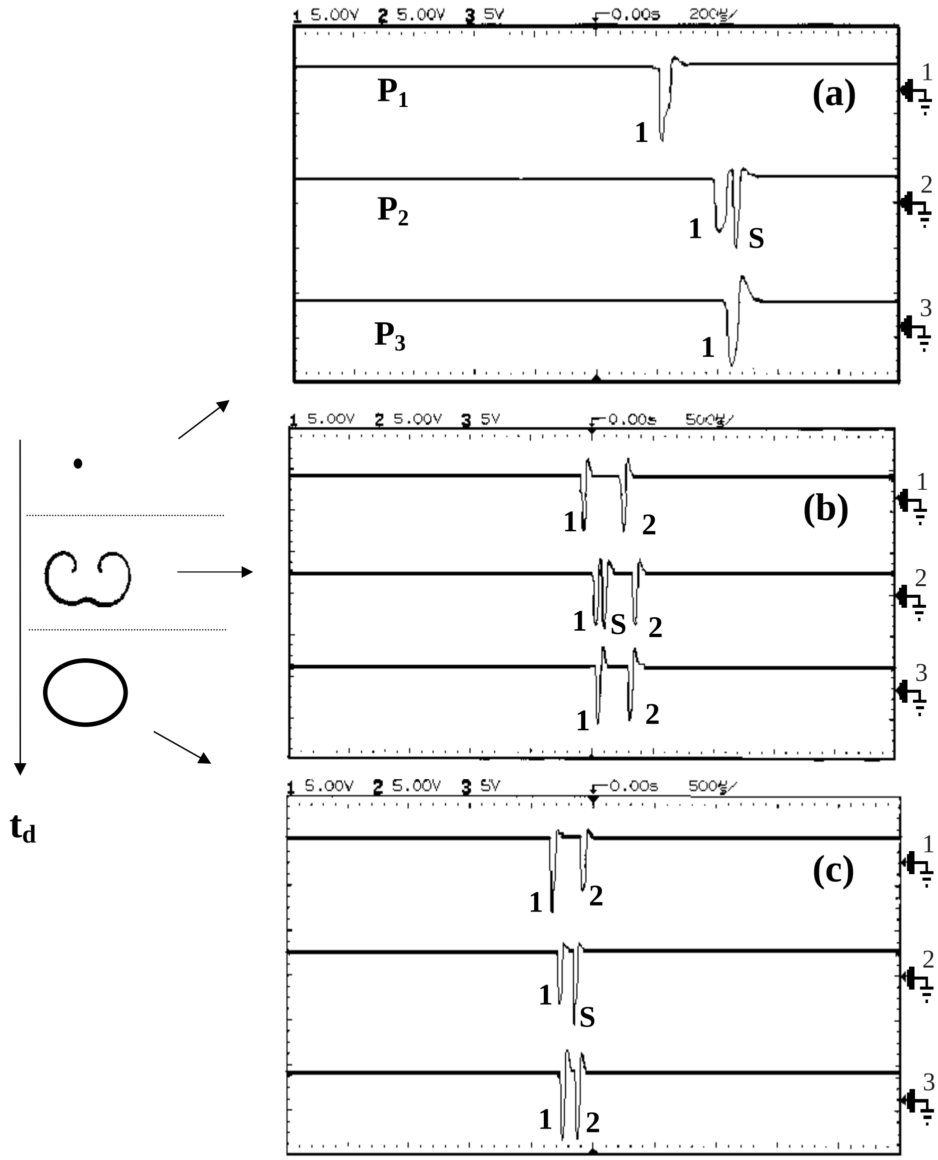

Fig. 2. System response to a second stimulus. (a) For $T_d = 60.0 \pm 0.5$ μs the second pulse, S, does not produce any response. (b) For $T_d = 90.0 \pm 0.5$ μs the second pulse can only propagate in the retrograde direction. This gives rise to a full rotation around the abnormal region. (c) For $T_d = 110.0 \pm 0.5$ μs the second pulse can propagate in both directions.

shows the opposite behavior. For a long time delay, $T_d = 110.0 \pm 0.5$ μs, both the effect of the first and the second pulse can be observed at the three measuring points. For an intermediate time delay, $T_d = 90.0 \pm 0.5$ μs, spiral generation by vulnerability can be observed in Fig. 2(b). The first pulse, 1 is observed at the measuring points. The effect of the external stimulus, S, is shown at the second measuring point. That stimulus is initially stopped in the direction of the first pulse. It can only propagate in the retrograde direction and it is first observed at P_1. Then, the excitation surrounds the uncoupled region and reaches first P_3 and then P_2, points 2 in Fig. 2(b). This gives rise to a full rotation around the uncoupled region and subsequently to the formation of a self-sustained excitation. The obtained structure, no propagation, discontinuous propagation or full propagation, is depicted on the left side of Fig. 2.

As we mentioned above, the existence of a randomly distributed uncoupled regions can modify the vulnerable behavior depicted in the previous figure. In Fig. 3, the VW is shown to increase with L. L was considered to be the perimeter of the abnormal coupling region ($L = 2l + 4$), where l is the number of transversally uncoupled cells. Three different

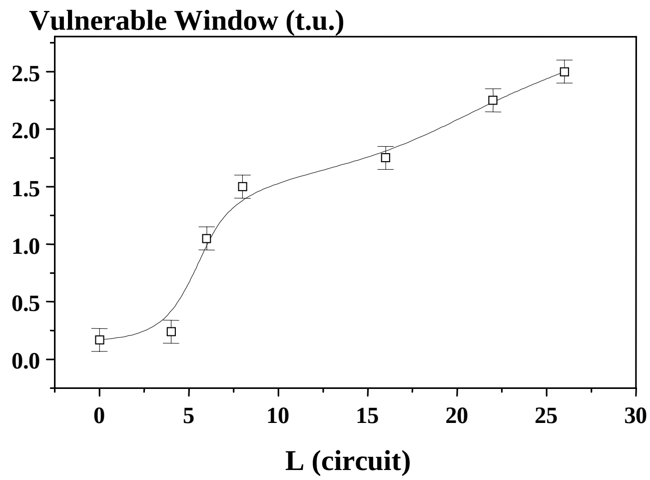

Fig. 3. Dependence of the inhomogeneous region perimeter on the VW extent. For small L, the VW only varies slightly with L. There exists a certain interval, for intermediate L values, where the VW depends strongly on L. Finally, for bigger L values VW increases almost linearly with L. In all case, L was considered to be smaller than the wavelength of both spirals, $\lambda = 40$ circuits.

regions can be observed depending on L. For small L values, even for $L = 0$, the vulnerable window is small and increases slightly with L. For intermediate L values, the window increases strongly with L. Finally, for big L values the window increases with L but with a smaller slope. Note that the wavelength of the obtained spiral wave is $\lambda = 40$ circuits.

4. Conclusion

Spiral waves can be initiated by vulnerability, even in homogeneous media as described in the literature [Keener & Phelps, 1989; Gomez-Gesteira *et al.*, 1994a; Winfree, 1983]. In addition, this effect can be enhanced by the existence of local inhomogeneities. Basically, there are two mechanisms that favor spiral initiation, viz. the vulnerabilitys process previously described and the existence of an obstacle. It is well known that when a wave collides with an obstacle, spirals are initiated if the velocity of the wave is less than a critical value [Starobin, 1996; Gomez-Gesteira *et al.*, 1994b]. So, the use of a premature stimulus will produce a slow propagating wave and it is possible to start spiral waves at the obstacle boundaries.

As we have shown in previous section, the size of the vulnerable window depends on the extent of the abnormal region. For inhomogeneities smaller than the typical spiral wavelength three different regions were observed. In particular, there is a critical zone where the size of the VW depends strongly on the abnormal region size.

The increasing of the VW with L can be explained in terms of the behavior of the proto-spirals generated by a properly timed stimulus. It is a well-known fact that the size of the VW decreases when comparing 1D and 2D media [Gomez-Gesteira *et al.*, 1994a]. In 2D, some of the initially discontinuous wave fronts become continuous in time. This is due to the collision between both proto-spirals, which annihilate each other. In the case observed in the previous section, the abnormal region behaves as an obstacle, in such a way that one of the spiral tips rotates around that area, which prevents it for colliding with the other tip. Thus, the bigger the inhomogeneity extent, the bigger the vulnerable window is.

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References

Allesie, M. A., Bonke, F. I. M. & Scopman, T. Y. G. [1973] "Circus movement in rabbit atrial muscle as a mechanism in tachycardia," *Circ. Res.* **33**, 54–62.

Balakhovsky, I. S. [1965] "Several modes of excitation movement in ideal excitable tissue," *Biofizika* **10**, 1063–1067.

Chua, L. O. [1992] "The genesis of Chua's circuit," *Int. J. Electron Commun.* **46**, 250–257.

deCastro, M., Gómez-Gesteira, M. & Pérez-Villar, V. [1998] "Influence of the distance on the interaction between an autonomous pacemaker and a re-entry," *Phys. Rev.* **E57**(1), 949–954.

Gomez-Gesteira, M., Fernandez-Garcia, G., Muñuzuri, A. P. Perez-Muñuzuri, V., Krinsky, V. I., Starmer, F. C. & Perez-Villar, V. [1994a] "Spiral formation by a premature re-excitation: Vulnerability," *Physica* **D76**, 359–368.

Gomez-Gesteira, M., del Castillo, J. L., Vazquez-Iglesias, E., Perez-Muñuzuri & Perez-Villar, V. [1994b] "Influence of the critical curvature on soiral initiation in an excitable medium," *Phys. Rev.* **E50**(6), 4646–4649.

Keener, J. P. & Phelps, F. M. [1989] "Consequence of the anisotropic structure of myocardium," in *Lectures on*

Mathematics on Life Sciences **21** (American Mathematical Society), pp. 151–181.

Krinsky, V. I. [1984] *Selforganization. Autowaves and Structures Far from Equilibrium*, ed. Krinsky, V. I. (Springer-Verlag), pp. 9–19.

Jalife, J. [1990] *Mathematical Approaches to Cardiac Arrhythmias* Ann. N. Y. Acad. Sci. **591**.

Madan, R. N. [1993] *Chua's Circuit: A Paradigm for Chaos*, World Scientific Series on Nonlinear Science, Series B, Vol. 1 (World Scientific, Singapore).

Mikhailov, A. S. [1990] *Foundations of Synergetics I* (Springer-Verlag).

Mines, G. R. [1914] "On circulating excitations in heart muscles and their possible relation to tachycardia and fibillation," *Trans. R. Soc. Can.* **4**, Sec. 5, 43-53.

Muñuzuri, A. P., Pérez-Muñuzuri, V., Gómez-Gesteira, M., Chua, L. O. & Pérez-Villar, V. [1995] "Spatiotemporal structures in discretely-coupled arrays of nonlinear circuits: a review," *Int. J. Bifurcation and Chaos* **5**, 17–50.

Pérez-Muñuzuri, V., Alonso, M. & Pérez-Villar, V. [1994] "Resonance patterns in one-dimensional arrays of coupled nonlinear excitable systems," *Int. J. Bifurcation and Chaos* **4**(6), 1631–1638.

Pérez-Muñuzuri, V., Muñuzuri, A. P., Gómez-Gesteira, M., Pérez-Villar, V., Pivka, L. & Chua, L. O. [1995] "Nonlinear waves, patterns and spatio-temporal chaos in cellular neural networks," *Phil. Trans. R. Soc. Lond.* **A353**, 101–113.

Spach, M. S. & Dolber, P. C. [1986] "Relating extracellular potentials and their redivatives to anisotropic propagation at a microscopic level in human cardiac muscle," *Circ. Res.* **58**(3), 356–371.

Starmer, C. F. [1997] "The cardiac vulnerable period and re-entrant arrhythmias: targets of anti- and proarrhythmic processes," *Patient and Clinical Electrophysiology* **20**(2), Part II, 445–454.

Starobin, J. M. & Starmer, C. F. [1996] "Boundary layer analysis of waves propagating in an excitable medium: Medium conditions for wave-front-obstacle separation," *Phys. Rev.* **E54**, 430–437.

Taboada, J. J., Muñuzuri, A. P., Perez-Muñuzuri, Gomez-Gesteira, M. & Perez-Villar, V. [1994] "Spiral breakup induced by an electric current in a Belousov–Zhabotinsky medium," *Chaos* **4**(4), 519–524.

Tyson, J. J. & Keener, J. P. [1988] "Singular perturbation theory of traveling waves in excitable media (a review)," *Physica* **D32**, 327–361.

van Capelle, F. J. L. & Durrer, D. [1980] "Computer simulation of arrhythmias in a network of coupled excitable elements," *Circ. Res.* **47**, 454–466.

Winfree, A. T. [1983] "Sudden cardiac death: A problem in topology," *Sci. Am.* **248**(5), 144–161.