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Termination of scroll waves by surface impacts

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Three-dimensional scroll waves direct cell movement and gene expression, and induce chaos in the brain and heart. We found an approach to terminate multiple 3 dimensional scrolls. A pulse of a properly configured electric field detaches scroll filaments from the surface. They shrink due to filament tension and disappear. Since wave emission from small heterogeneities is not used, this approach requires a much lower electric field. It is not sensitive to the details of the excitable medium. It may affect future studies of low-energy chaos termination in the heart.

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Rotating spiral waves have been observed during catalytic CO oxidation on a Pt(110) surface [1, 2], in morphogenesis where they direct cell movement and gene expression [3], and in the heart where they induce cardiac chaos (fibrillation) that kills more people that any other malady. Much effort has been invested in controlling them.

A big achievement was the development of standard defibrillation techniques, which reliably terminate fibrillation. However, the method delivers a high-energy electric shock (360 J, 1 kV, 30 A, 12 ms, when applied externally, creating a large electric field ~ 5 V/cm), which is often associated with severe side effects. A field that is this large and damaging is required by this method, because its aim is to terminate all waves in the heart. However, fibrillation is induced by rotating waves [4]. Thus, new approaches to classical defibrillation are needed to terminate just rotating waves (vortices), instead of terminating all waves.

One approach is based on the classical result of Mines, 1913. He induced a rotating wave in a ring cut from a tortoise heart. He observed that the "application of an external stimulus to either of the chambers, if out of phase with the cycle," stopped circulation of the wave, Fig. 23, p. 372 in [5].

Much later, it was found that, to terminate a rotating wave, a stimulus (an electric pulse) should be delivered inside a narrow, "critical" time interval (called the "vulnerable window", or VW). A detailed theory was created, e.g. [6, 7], and the VW was measured in experiments, e.g. [8]. The physics of the VW is based on the emission of a wave with a topological charge [9] opposite to that of the rotating wave. These two waves annihilate and disappear, see e.g., Fig. 4d in [10]. This type of wave behavior is not possible in classical mechanics with the energy conservation law.

This is very interesting physics. However, it does not open a way to terminate cardiac fibrillation. Fibrillation is induced by many vortices, whose positions and phases cannot be measured by existing methods. So far, the only solution to the problem of delivering an electric field pulse (E-pulse) inside every VW, is to scan all phases. If the scanning with E-pulses is produced with a step smaller than the VW, the VW of every vortex will be hit by at least with one pulse.

Phase scanning was tested in experiments [11]. Atrial fibrillation was terminated with only 13 % of the energy required for cardioversion (standard defibrillation of AF). This was the first successful test of phase scanning. Phase scanning has also been tested successfully *in vivo* [12]. Canine atrial fibrillation was terminated by the phase scanning with a pulse energy of 0.07 J in constrast to 0.76 J required by cardioversion. The mechanism of arrhythmia termination was confirmed by optical mapping [13]. A deep understanding of how pinned 2-dimensional vortices can be terminated currently exists [10].

In this paper, we investigate what interesting solutions can be found for 3D free vortices. Rotating spiral waves in a 3D volume form scroll waves. A stable scroll wave with a straight filament has been observed in the heart volume using ultrasound imaging [14].

We found that a *surface impact* which, here, takes the form of a modification of the surface potentials by an E-field pulse, can terminate multiple three-dimensional vortices, Fig 1. We verified numerically that this type of surface impact can normally terminate up to 5 filaments.

We found also that the termination is robust to substantial deviations of the electric field direction relative to the surface normals. Successful termination of the vortices is also not sensitive to the details of the excitable medium because the mechanism involved only requires that the filament tension be positive. Our surface-impact method is also robust in the sense that its application does not require knowledge of the number of rotating waves, their locations or phases.

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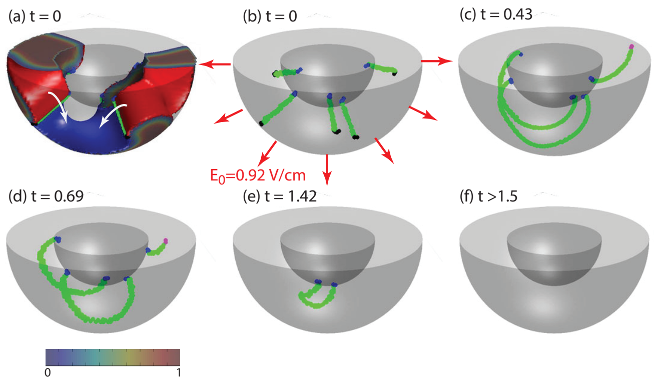

FIG. 1: **Simultaneous termination of multiple scroll waves.** In **(b-f)** only filaments are shown (green). **(b)** A radial electric field pulse (0.92 V/cm) is delivered at time $t = 0$. **(c)** All filaments are disconnected from the outer hemisphere. **(d-f)** They shrink and disappear. **(a)** Same as (b) with the leading (red) and trailing (blue) edges of waves shown. *Notations.* White arrows show the sense of rotation of the waves.The membrane potential u on the boundaries is displayed in muted colors (see colorbar). In **(b-f)**, the ends of the filaments are color-coded blue, pink or black, depending on whether they terminate on the inner, top or outer surface, respectively. Dimensionless time $t = \hat{t}/T_s$ is used, where T_s is the approximate scroll wave rotation period

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Our simulations employed the Barkley equations [15]:

$$\frac{\partial u}{\partial t} = D\nabla^2 u + \epsilon^{-1} u(1-u)(u-(v+b)/a) \quad (1)$$

$$\frac{\partial v}{\partial t} = u - v \quad (2)$$

where u is the membrane potential and the slow variable v describes inactivation and reactivation. The equations were solved using a forward Euler method on a 3D, rectangular grid in a 3D cylindrical system or in a hemispherical-shell-shaped system as in Fig. 1.

The boundary of the tissue was modeled using the standard assumption of zero intracellular current. In the presence of an external electric field, $\mathbf{E}_0$, this condition becomes [16]

$$\hat{n} \cdot \nabla(u - \mathbf{E}_0 \cdot \mathbf{x}) = 0 \quad (3)$$

(effectively a Neumann boundary condition). It follows directly from the bidomain equations.

For the E-field pulse, we used either a uniform, z-directed electric field or a radial electric field of the form $\mathbf{E}_0(r) = E_0 \hat{\mathbf{r}}(r_0/r)^2$, where r_0 is the outer radius of the hemispherical shell. The radial field is perpendicular to the surfaces of hemispheres, and is parallel to the top surface, Fig. 1b.

Parameters values ($a = 0.8$, $b = 0.05$, $\epsilon = 0.02$, and $D = 1.0$) were chosen inside the regime of positive filament tension [17]. In this regime, the radius R of the filament is governed by the equation [6, 18]

$$dR/dt = -\alpha/R \quad (4)$$

To make the result robust, the parameters were situated far from the boundary of this regime. Thus, reasonable variations of the parameters will not destroy the result.

We used a dimensionless grid spacing Δx=0.167 and a time step of $\Delta t = 1.6 \times 10^{-3}$. In the Barkley model we found the electric space constant to be $\lambda = 3.38\ \Delta x$, i.e. 3.38 grid cells. So, we took Δx to represent a length of 0.3 mm, to fit with the cardiac tissue $\lambda \sim$1mm. We took $\Delta t = 0.064$ ms. This yields a scroll wave rotation period of $T_s = 2120\ \Delta t = 135$ ms and a duration of the electric field pulse τ of 5 ms, a typical value used in defibrillation.

We chose the box sizes $\sim 10\lambda$. This allowed us to resolve the voltage distribution near the boundaries with reasonable runtimes. Cylindrical system: diameter: 11.8λ, height: 8.6λ. Elliptical cylinder: major axis: 11.8λ, minor axis: 8.9λ, height: 11.8λ. The hemispherical shell: inner radius: 5.9λ , outer radius: 11.8λ.

Scroll waves were initiated in the system with their filaments oriented perpendicular to the surfaces of the system, Figs. 1b and 3b. The waves were allowed to settle down during at least three rotations prior to the delivery of the electric field pulse.

Figure 1 shows termination of 5 scrolls by a pulse of a properly configured electric field (a radial field for a spherical surface). Fig. 1b shows the initial positions of the 5 filaments before delivering the E-pulse. The E-pulse detaches all filaments from the outer surface, Fig. 1c. The detached end of every filament connects to either the detached end of another filament or the upper flat surface (the pink dot in Figs. 1c,d). The curved filaments shrank due to the filament tension, Fig 1e, and disappeared, Fig 1f.

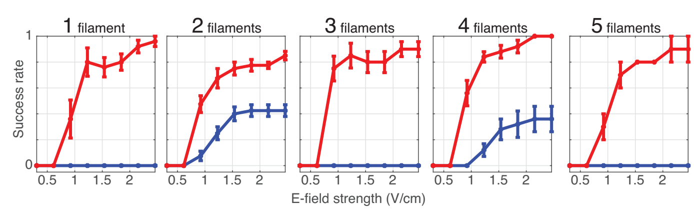

FIG. 2: **Success rate of termination of all scroll waves** in the hemispherical shell. The red trace shows the results for a radially-directed E-field pulse, the blue trace, for a z-directed pulse. Error brackets indicate standard error of the mean. We see that, for a radial E-pulse, the E-field amplitude, E_{50}, that produces a success rate of 0.5, is approximately the same (1 V/cm) irrespective of the number of vortices.

To test the effectiveness of this process, we randomly generated 24 sets of initial conditions (ICs) in the hemispherical shell system, containing one (5 ICs), two (8 ICs), three (4 ICs), four (5 ICs) or five scroll waves (2 ICs). Either a radial or z-directed electric field pulse was applied to each of these 24 cases with one of 8 field strengths ranging between 0.31 to 2.46 V/cm at one of 5 times, equally spaced within a scroll wave period T_s.

The results are summarized in Fig. 2. We found that the scroll waves were terminated with a very low radial

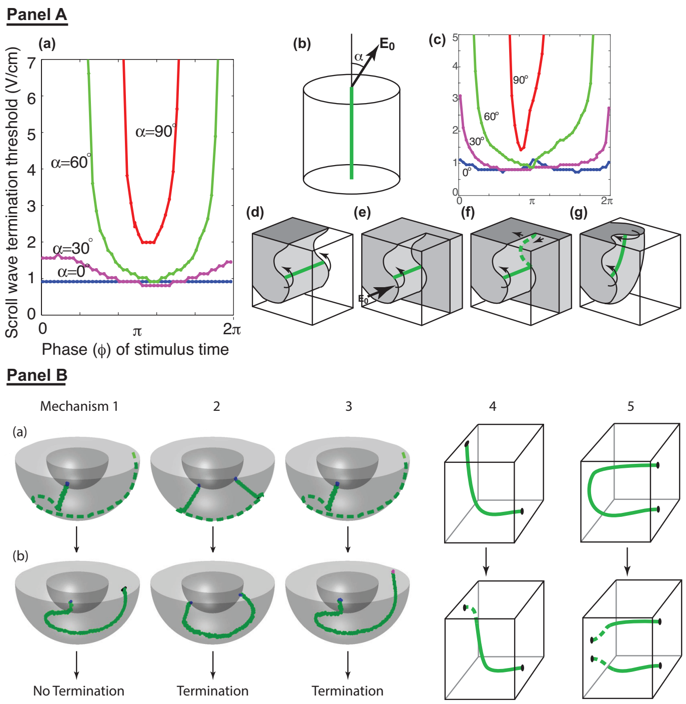

FIG. 3: **Panel A: Mechanisms of scroll termination by a surface impact. (a,b)** A circular cylinder: **(a)**. Numbers near each curve indicate the angle α the E-field makes with the filament of the scroll. **(b)**. The rotational symmetry forces the terminating threshold to be independent of phase for $\alpha = 0$. **(c)** A graph similar to (a) measured in an elliptical cylinder. There is no rotational symmetry here. **(d-g)** The dynamics of filament detachment: **(d)** A scroll wave. The filament is shown in green. **(e)** An E-pulse depolarizes the rear surface. The filament disconnects from it. **(f)** A new segment of the filament is created (green dashed), which attaches to the upper surface. **(g)** The C-shaped filament shrinks due to the filament tension, and eventually disappears. **Panel B: Mechanisms affecting termination of a scroll**. **(a)** Immediately after the E-pulse. Green dashed lines denote newly-created filament segments. **(b)** After 1/4th of a scroll wave period. **Mechanism 1.** A uniform, z-directed field fails to terminate a single filament. **Mechanism 2.** Two filaments with the opposite topological charge are terminated by the z-directed field. **Mechanism 3.** Termination of a single filament by the radial field. **Mechanism 4.** Reattachment of a filament end. **Mechanism 5.** Reattachment of the center of a filament.

E-field, below 1 V/cm. Since energy scales as E^2, this represents a 25-fold decrease in energy compared to standard defibrillation, where $E \sim 5$ V/cm.

The results were also interesting in another respect. If only depolarization of the surface and detaching the filaments were required for termination of the scrolls, surface excitation, induced at ~ 0.2 V/cm [12], would be sufficient. This indicates that more complex mechanisms, explained in Fig. 3, are essential here.

The success rate of the z-directed E-field (Fig. 2, blue lines) is zero for termination of 1, 3 or 5 filaments. The filaments are only terminated in pairs, as filaments with opposite topological charges merge; see Fig. 3, Mechanisms 1 and 2. In contrast, the radially-directed field can terminate unpaired filaments by forcing them to reattach to the top surface, creating a C-shaped filament, Fig. 3, Mechanism 3.

What happens when the radial electric field inducing filament detachment is not parallel to the filament? Figure 3a shows that, for $\alpha = 0$, the threshold is small, 1 V/cm, and does not depend on the the phase ϕ of the scroll. The threshold increases with increasing angle α. At $\alpha = 90°$, we recover the classical narrow critical window, the VW.

For $\alpha = 0$, independence from the phase ϕ of the scroll follows from the rotational symmetry of the cylinder, Fig. 3b. A similar graph, Fig. 3c, was measured in the elliptical cylinder, where no rotational symmetry is present. The termination threshold is again small $\sim$1V/cm (blue curve), for any phase.

The termination mechanism is shown in Figs. 3d-g. The transition from Fig. 3e to Fig. 3f induced by an E-pulse is not trivial. When the E-pulse started, the depolarized region is created on the rear wall, Fig. 3e. When the E-pulse is finished, the depolarized region starts shrinking, and the excitable medium expands back. The rotating wave enters into the restoring region of the excitable medium. The expansion velocity vector is directed towards the left-rear wall, i.e., perpendicular to the previous velocity vector. Thus the new movement is rotation, and the spiral front becomes a filament, the green dashed line in Fig. 3f.

The new filament segment terminates on the upper boundary of the tissue, Fig. 3f. This C-shaped filament shrinks due to the filament tension, and disappears. This mechanism was found in [19]. It was used in [20] to explain the delayed success in termination of a three-dimensional reentry, a very useful result.

The new filament segment shown in Fig. 3f must be formed far enough from the rear surface, (i.e., at a distance greater than some critical distance, l_{crit}) for it to survive. Otherwise, the new segment will reattach to the rear wall through Mechanism 4, leaving it I-shaped and therefore non-terminating. We have observed that creating the depolarized layer with thickness $l > l_{crit}$ requires a minimum E-field strength of $\sim$1 V/cm, which is larger than that required for mere depolarization of the surface ($\sim$0.2 V/cm). The E-field strength $\sim$1 V/cm is still much smaller than that required for the immediate termination of all wave activity ($\sim$5 V/cm).

Termination occurs through the same mechanism whether the system is a cube (Fig. 3d–g), a cylinder (Fig. 3b) or a hemispherical shell (Fig. 1 or Fig. 3, Mechanisms 2 and 3); that is, C-shaped or U-shaped filaments shrink and disappear. In a hemisphere, note that the inner and outer walls correspond to the front and rear surfaces of the cube, respectively, (or the upper and lower surfaces of the cylinder). The upper surface of the hemispherical shell plays the role of the top surface of the cube (or the side wall of the cylinder).

Fig. 3, panel B, Mechanism 1 shows why a z-directed field cannot terminate a single filament (or any odd number of filaments). For these cases, the filament is observed to reattach to the same outer wall following the end of the E-pulse (note the black dot in Mechanism 1(b) indicating reattachment to the outer wall). In contrast, for a radial E-field, the filament reattaches to the top surface (Mechanism 3, note the pink dot).

The difference in outcomes between Mechanisms 1 and 3 arises from the fact that, with the z-field, a strip just below the equator on the outer surface is always left unexcited, leading to reattachment of the unpaired filament to this strip, in the case of an odd number of vortices. This strip does not exist for the case of a radial field, when the field is everywhere parallel to the outer surface normal. Mechanism 2 in Fig. 3, panel B shows that, when the number of vortices is even, it is possible for the filaments to pair up, leading to a U-shaped filament, which then disappears due to its curvature. These observations explain Fig. 2, which shows the inability of a z-directed field to terminate any odd number of vortices, while a radial field can terminate any number of vortices with a high degree of success.

What is the degree of applicability of this method to a real cardiac setting? No fundamental scientific objections are seen. There are technical means to create an electric field that is perpendicular to the cardiac surface. A high accuracy is not required here. To detach the filament, we need only create a depolarized layer on the surface thicker than a critical thickness, l_{crit}. This only requires that the perpendicular component E_p of E field be large enough. Small deviations α of the electric field direction from the perpendicular direction do not create a problem since $E_p = E\cos\alpha$ and $\cos\alpha \approx 1 - \alpha^2/2 + \ldots$. Still, the computational model considered here is highly idealized, and further research is required to see how the proposed method will work when more realistic features are considered.

In experiments, excitation of the cardiac surface requires only ~ 0.2 V/cm [12]. Surprisingly, our numerics required a much larger electric field, ~ 1 V/cm, to terminate the scrolls. This indicates that other mechanisms are involved here, e.g. Mechanisms 4 or 5 in Fig. 3. Their future investigation may find it is possible to decrease the electric field below 1 V/cm.

In summary, we have found that a surface impact can terminate multiple scrolls. A pulse of a properly configured electric field detaches filaments of all scrolls from the surface. They shrink due to the filament tension and disappear. This approach is robust and not sensitive to the details of the excitable medium. It may help to direct future studies of low-energy defibrillation methods in the heart.

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