Chapter 17
Vortices Termination in the Cardiac Muscle

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17.1 Background

Control of chaos in the cardiac muscle for a long time was in hands of cardiologists only. They found a rotating wave in the heart, and called it “re-entry” since it enters to the same place again and again.

A seminal publication in 1946 by Wiener and Rosenblueth [1] induced interest of mathematicians and physicists to this problem. It became known to Soviet physicists due to M.I. Gelfand’s seminars in Moscow and schools on Nonlinear Dynamics in Nizhny Novgorod organized by A. Gaponov-Grekhov and M. Rabinovich. The interest much increased when the rotating spiral waves were found in an active chemical medium based on the Belousov oscillating chemical reaction. The Belousov chemical reaction became known to scientists due to Simon Shnol (Moscow University and Biological Research Center Puschino of the USSR Academy of Science). Shnol found general Belousov whose attempts to publish
his discovery of the oscillatory chemical reaction were rejected by referees as contradicting to thermodynamics. Shnol convinced Belousov to publish his results in the Collection of Abstracts on Radiation Medicine. Shnol requested one of his students, A. Zhabotinsky, to reproduce Belousov’s result. I (V.K.) met A. Zhabotinsky in Puschino, he was analysing the chemical mechanism of the Belousov reaction. I told him about results of the Gelfand’s seminar how to induce a rotating spiral wave in any excitable medium, and proposed to induce a rotating wave in the Belousov reaction together. A rotating wave did not arrive during weeks of experiments. The main difficulty was that the measured wave length was larger than the size of the Petri dish. This difficulty was overcome by chance, and the spiral rotating waves were obtained.

Experiments with rotating waves in this reaction became a fashionable field of research, and stimulated the theory. During long time of successful development, no decent applications arrived from this field. We discussed it with Misha Rabinovich during his visits to me in Nice, and with H. Abarbanel during my visits to Misha.

Then, after a meeting on excitable media and heart in the Kavli Institute of theoretical physics, together with Robert Gilmour, E. Bodenschatz and S. Luther we started cardiac experiments to implement the developed understanding for creating low energy methods for termination chaos in the heart. Results of these experiments were published in [6, 7]. Physical mechanisms underlying termination of free and pinned vortices are described in this short review.

Rotating electrical waves (vortices) and their instabilities underlie cardiac chaos (fibrillation) [8–10]. Physics of the vortices is well understood, e.g. [11–15]. But contemporary method of terminating the life-threatening cardiac fibrillation is still aimed at termination of not vortices, but all waves in the heart.

Over a century ago, it was found that a single vortex (rotating wave or anatomical reentry) in a heart can be terminated with an electric pulse [16]. An electrode was placed close to the anatomical obstacle around which the wave rotates and a small energy electric pulse was delivered within a certain time interval, called critical window, or vulnerable window, VW (note that for a rotating wave, such intervals repeat within each lap).

This approach alone cannot terminate fibrillation since there are multiple rotating waves with unknown geometric locations and phases [10]. That is, we have two main problems: (1) the geometric positions of their cores and (2) the positions of their critical time windows are not known during fibrillation.

An approach to overcome the problem (1) was developed [4, 17]. Due to the bi-domain electric nature of cardiac muscle [18], every defect in it that can serve as a pinning centre for a vortex is at the same time an electric inhomogeneity. This allows an electric field pulse (E-pulse) to excite the cores of all pinned vortices simultaneously, regardless of the geometric positions of their cores.

Approaches to resolve the problem (2) are being developed. They are aimed to deliver a pulse into VWs of all vortices without knowing their relative phases (“positions in time”). One of them is the phase scanning by E-pulses, with a phase step that is shorter than the VW, for all vortices in parallel. It was tested in experiment to terminate a vortex in a rabbit heart preparation [19]. Scanning with periodic E-pulses was used to terminate fibrillation [6, 7]. Termination of one vortex with periodic E-pulses was numerically investigated in [20–22].
17.2 Termination of Multiple 2 Dim Vortices

With multiple vortices, difficulties arise due to their interaction. We investigate the excitation dynamics in the vicinity of the cores of pinned vortices. This allows to draw conclusions about the overall dynamics. When the VW of a vortex is hit by the E-pulse, this vortex is displaced to a new position. If the vortex was situated close to the tissue boundary, it is terminated. Our aim is to hit the VW of every vortex by an E-pulse (“all vortices are terminated”).

Wave patterns were calculated using the Barkley model

\[ u_t = \epsilon^{-1} u(1 - u)[u - (v + b)/a] + \nabla^2 u, \quad v_t = u - v \] (17.1)

in a rectangular domain with circular holes, with no-flux boundary conditions at the outer boundaries.

Pulses of electric field \( E \) are implemented as in [23] using the boundary conditions \( n \cdot (\nabla u - E) = 0 \) at the boundaries of the holes. The numerical integration used an explicit Euler scheme with a time step of \( 1.6 \times 10^{-3} \) and central-difference approximation of Laplacian with a space step of \( \frac{1}{6} \). The Barkley model is formulated in non-dimensional units; for presentation purposes, we postulate that the time unit of the Barkley model is 20 ms and the space unit of the Barkley model is 0.5 mm; this gives physiologically reasonable time and space scales.

Figure 17.1 shows termination of two pinned vortices by E-pacing. This can be achieved generically, for any parameters of the vortices, without knowing their geometric location and time positions of the VWs.

To hit the VW with an E-pulse, the phase scanning (Fig. 17.2b) should be performed with steps \( 0 < s < \text{VW} \). Thus, the VW length (at the chosen \( E \), see Fig. 17.4h) determines suitable values of \( s \). Then, the number of pulses \( N \) to cover the whole phase of a vortex is \( N \geq T_v/s \), where \( T_v \) is the period of the vortex, \( s = T - T_v \) is the scanning step, and \( T \) is the period of E-pacing. This gives the E-pacing period \( T = s + T_v \). Thus, all parameters of E-pacing \((E, N, T)\) can be set following equations

\[ 0 < s < \text{VW}(E), \quad N \geq T_v/s, \quad T = s + T_v \] (17.2)

to guarantee that at least one E-pulse hits the VW.

What does interaction of vortices change here? In cardiac muscle, the fastest vortex entrains (or “enslaves”) slower vortices if there is normal wave propagation between them. Then, only one frequency remains; this facilitates vortices termination.

But entrainment ceases if the fastest vortex is terminated before the slower vortices, and then the frequency of the system changes (period increases). Here, two wave scenarios are possible, which we describe for the case of just two vortices with periods \( T_{v1} \) and \( T_{v2} \), such that \( T_{v1} > T_{v2} \):

1. If the periods of the two vortices are not much different, so that \( T_{v2} < T_{v1} < T \), then the pacing is still under-driving, and the slower vortex \( (T_{v1}) \) can be terminated by E-pacing with same period \( T \) (see Figs. 17.1 and 17.2b), provided that termination conditions (17.2) are met for the slower vortex.
Fig. 17.1 Parallel termination of two pinned vortices with unknown both geometrical locations and time positions of the critical (vulnerable) windows (VW). The slow vortex 1 (period $T_{v1} = 87$ ms, pinned to the 1.2 mm defect 1) is entrained by the fast vortex 2 (period $T_{v2} = 83$ ms, 1.0 mm defect 2). They are paced with electric field directed from top to bottom, $|E| = 1.3$ V/cm, pulses 2 ms duration, period 100 ms. This induces the phase scanning with the time step $s = 17$ ms. Colour code: red is a wave, green is the wave front. Time is measured from the start of pacing at $t = 0$ ms. 196 ms: a wave $W$ emitted by vortex 2 enslaves vortex 1. 204 ms: an E-pulse delivered at $t = 200$ ms induces a wave $S$. 216 ms: the right wavebreak of wave $S$ annihilates with the tip of vortex 1 (they have opposite topological charges). 232 ms: vortex 1 is unpinned and terminated. The left wavebreak of $S$ created a free vortex $F$. 336 . . . 376 ms: $F$ disappears on the boundary. 408 . . . 440 ms: Next E-pulse similarly terminates vortex 2. Barkley model, parameters $a = 0.8$, $b = 0.09$, $\epsilon = 0.02$

2. If however the periods of the two vortices are so different that

$$T_{v2} < T < T_{v1} \quad (17.3)$$

then the pacing with the same period is no longer under-driving, but over-driving. And overdrive pacing will typically entrain the remaining vortex rather than eliminate it.

For successful termination of fibrillation, the E-pacing period should be increased to a higher value $T_2$, such that $T_{v1} < T_2$. Thus, vortices can be terminated in any case. Experiments [7] underestimated the potential of the method since this mechanism was not known yet.

A similar mechanism can also terminate a free (not pinned) vortex when its moving core passes not very far (at distance $L < \lambda$, where $\lambda$ is the wave length) from a defect in the medium, serving as a virtual electrode, Fig. 17.3. The success rate is the higher, the smaller is the distance $L$.

A mechanism reliably terminating a free rotating wave was found in 1983 [25]: waves with a frequency higher than the frequency of a rotating wave, induce its drift and termination on the boundary. Cardiologists used a high frequency pacing (anti-tachycardia pacing, ATP) well before the mechanism was understood. But ATP cannot terminate high frequency rotating waves. The mechanism found here uses electric field induced wave emission; electric field penetrates everywhere, there is no frequency limitations that exist for waves propagating in the excitable cardiac tissue.
Fig. 17.2 Phase scanning. (a): $u_1(t)$, $v_1(t)$ are recordings from the point just above defect 1, Fig. 17.1, and $u_2(t)$, $v_2(t)$ are same for defect 2. The bold black lines indicate timing of the delivered E-pulses. Shaded areas are vulnerable windows, defined as time intervals where $v \in (0.0871, 0.18)$, $u < b/a$. Seen that in spite of small phase disturbances produced by E-pulses, the topological features of the scanning are not disturbed, scanning successfully terminates the vortices. E-pulse 3 ($t = 200$ ms) reaches VW of vortex 1 and terminates it. E-pulse 5 ($t = 400$ ms) reaches VW of vortex 2 and terminates it, compare with Fig. 17.1. (b, c): schematic. Superimposed action potentials (AP) are shown. Red arrows indicate timing of the delivered E-pulses; “e” is an excitable gap, $s$ is the scanning step, $s = T - T_v$. (b) $s > 0$ for $T > T_v$, (“under-driving”), scanning reaches the VW. (c) $s < 0$, (“over-driving”), for faster pacing $T < T_v$, the scanning moves in the opposite direction. E-pulse reaches the excitable gap “e”, excites an AP thus resetting the rotation phase, and all subsequent pulses get into the same phase [22, 24]. It does not reach the VW.

Fig. 17.3 Termination of a free vortex by an E-pulse. 147 ms: A free vortex and a defect (white). 307 ms: A semi-circular wave (with wavebreaks A and B) emitted from the defect by an E-pulse, electric field directed from right to left. 323 ms: Wavebreak A fused with the vortex tip. 368 ms: After annihilation of wavebreak B with the border, only a wave without wavebreaks is left in the medium. Barkley model, parameters $a = 0.6$, $b = 0.075$, $\epsilon = 0.02$
An increased amplitude of electric field $|E|$ results in defibrillation. The only known mechanism was: the wave emission is induced from a larger number of defects [17]. We describe here another mechanism: the duration of the VW increases with the electric field, Fig. 17.4g.

**Fig. 17.4** Change of topological charge, creation of phase singularities, and vulnerable window VW. (a–d) 1 dim mechanism. (a) Nullclines of FHN equations. $M$ is the Maxwell point. The topological charge of a wave pattern is changed by an E-pulse only when an image of a nucleated
The mechanism of the VW is related to change of topological charge in 1D and creation of new topological singularities in 2D. We illustrate it using time-separation analysis for the FitzHugh–Nagumo (FHN) equations:

\[ u_t = f(u) - v + Du_{xx}, \tag{17.4} \]
\[ v_t = \varepsilon(u - kv). \tag{17.5} \]

Here \( f(u) = Au(1-u)(u-\alpha) \), and \( \varepsilon \ll 1 \) is a small parameter permitting the time scales separation (for details of relevant formalisms see review [27]). The wavefront propagation velocity \( \theta \) can be estimated by assuming that the slow variable \( v \) is approximately constant across the wavefront. The propagation of the front is then described by Eq. (17.4) alone, where \( v \) is a constant parameter. Transforming the independent variables such that \( \xi = x - \theta t \) makes Eq. (17.4) an ordinary differential equation

\[ -\theta u_\xi = f(u) - v + Du_{\xi\xi} \]

which together with boundary conditions \( u(\infty) = u_1, u(-\infty) = u_3 \), where \( u_1 = u_1(v) \) and \( u_3 = u_3(v) \) are, respectively, the lowest and highest roots of \( f(u) = v \), define \( \theta \) as a function of \( v \), see Fig. 17.4b. Here, velocity \( \theta(v) \) is negative for \( v > v_M \), where \( v_M \) is the Maxwell point, \( \int_{u_1(v_M)}^{u_3(v_M)} (f(u) - v_M) \, du = 0, \theta(v_M) = 0 \)[4].

Vulnerability is a cardiological term coined for initiation of fibrillation by an electric pulse. In the physical language, vulnerability in 1 dim can be related to a change of the topological charge, and in 2 and 3 dim to creation of new phase singularites. In 1 dim, the topological charge changes when the current injection nucleates a wave propagating in only one direction, Fig. 17.4d. This is in contrast to the generic case, where the topological charge is conserved, when the new wave propagates in two directions, Fig. 17.4c, or new wave is not nucleated at all (not shown). For one-directional propagation to happen, the nucleated wave should cover the points which have \( v = v_M \) corresponding to the Maxwell point \( \theta = 0 \). Then, a part of the nucleated wave has positive velocity (becoming the front of the wave)

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Fig. 17.4 (continued) wave contains the Maxwell point. (b) Wave front velocity \( \theta \) vs the slow variable \( v \). The value of \( v \) corresponding to velocity \( \theta = 0 \) is the ordinate \( v_M \) of the Maxwell point on panel (a). (c) The topological charge conservation in 1 dim. Generic case: an electric pulse 3 ms duration is delivered far from the tail of an action potential (AP). \( t = 10 \) ms after pacing: a nucleated wave, very narrow, and the electrode (black square) below it. \( t = 75 \) ms: the nucleated wave developed into two counter propagating APs. Their total topological charge is zero. (d) Violation of the topological charge conservation. \( t = 10 \) ms: an electric pulse is delivered closer to the tail of the AP, inside VW. \( t = 75 \) ms: only one AP is induced. It propagates to the left only. The topological charge is changed. Cardiac ionic model [26]. (e, f) 2 dim mechanism. (e) No phase singularities are created. An electric pulse is delivered as in (c). (f) Creation of two phase singularities, B1 and B2. An electric pulse is delivered as in (d). (g, h) VW increases with electric field in 2 dim. (g) Mechanism: the larger \( E \), the larger is the depolarized region. (h) Graph VW(\( E \))
and another part has a negative velocity (becoming the tail of the wave), as in Fig. 17.4d, f. Otherwise, all parts of the nucleated wave have velocity of the same sign. When velocity $\theta < 0$, the nucleated wave shrinks and decays. In the opposite case, it enlarges in all directions, as in Fig. 17.4c, e.

### 17.3 3 Dim Vortices

Here we show that, in 3 dimensions, a mechanism exists that can terminate a 3D vortex in the heart, using low-amplitude electric fields, which operates independently of vortex wave phase, corresponding to a VW of the full $2\pi$ radians in phase. This allows to hit the vulnerable window with every electric field pulse, making the scanning of vortex phase unnecessary.

The mechanism is based on the ability of an electric field pulse to transform the rectilinear filament of the scroll wave (i.e., the axis around which the scroll wave rotates) into a curved shape filament in an excitable layer (such as a heart wall), as illustrated in Fig. 17.5a. If a pulse of an electric field oriented parallel to the “I-shaped” filament, Fig. 17.5a(i), is applied, it depolarizes the rear surface. The filament becomes L-shaped, Fig. 17.5a(ii), since the filament is essentially the dividing line between the wavefront and waveback. In a thin layer, there is not enough room for rotation around the filament, and the scroll wave is terminated. In a thick layer, L-shaped filament relaxes within one rotation into a C-shaped filament (Fig. 17.5a(iii)). This C-shaped filament may be thought of as one-quarter of a scroll ring, assuming no-flow boundary conditions for the membrane potential on the system surfaces. Depending on system parameters, scroll rings, and therefore

![Illustration of (i) I-shaped, (ii) L-shaped and (iii) C-shaped filaments, and the scroll waves that rotate around them.](b.png)

**Fig. 17.5** (a) Illustration of (i) I-shaped, (ii) L-shaped and (iii) C-shaped filaments, and the scroll waves that rotate around them. (b) Location of our system parameters *(red star)* in Barkley parameter space. “CS” and “ES” label the contracting and expanding scroll regimes, respectively
C-shaped filaments, can shrink and disappear due to positive tension within the filament, resulting in the termination of the rotating wave.

The phase independence of this mechanism arises from the symmetry of the initial conditions with respect to the combination of a translation in time and a rotation around the scroll wave. Specifically, since the electric field is initially oriented along the scroll wave axis, application of the field at a time $t = t_0$ is identical to applying the field at a different time $t = t_1$ if the coordinate system is also rotated around the scroll wave axis through an angle of $2\pi (t_1 - t_0)/T_s$, where $T_s$ is the scroll wave rotational period. Thus, the result of applying the electric field is independent of time, apart from any spatial features of the system that might break the symmetry. In particular, if the outcome of applying the electric field at any given time is termination of the scroll wave, we can also expect termination if the electric field is applied at any other time.

To study this mechanism, we conducted computer simulations in a 3D rectangular system meant to represent a portion of one of the walls of the heart. We used a simple forward Euler method on a rectangular grid to solve the monodomain Barkley model Eq. (17.1) with parameters $a = 0.8$, $b = 0.05$, $\epsilon = 0.02$, $D = 1.0$. The computational grid spacing and timestep were set to 0.167 and $1.6 \times 10^{-3}$, respectively. A scroll wave was initiated in the system with its filament oriented perpendicular to the front and rear surfaces of the system (Fig. 17.6a). These two surfaces may be thought of as portions of the endocardial and epicardial surfaces of the heart. The scroll wave was allowed to settle down over the course of at least three rotations prior to the delivery of a short-pulse, spatially uniform electric field.

Figure 17.6 shows the mechanism responsible for termination of a three-dimensional scroll wave in a thin-wall system. The scroll wave just prior to the application of the electric field pulse is displayed in Fig. 17.6a. When the pulse is applied at $t = 0$, with the electric field direction parallel to the scroll wave filament, the pulse immediately depolarizes the rear surface, as seen in Fig. 17.6b. The front surface is simultaneously hyperpolarized. The electric field pulse strength and duration used corresponded to 1.3 V/cm, 5 ms electric field pulse in a realistic heart. (This equivalence is based on an assumed threshold for wave initiation in a realistic cardiac setting of 0.2 V/cm for 5 ms, and the use in our system of a pulse field strength that is 6.5 times the threshold field.) The depolarization wavefront (red) subsequently propagates as a plane wave along the filament direction (black arrows) as shown in Fig. 17.6b, c. In this thin-layer system, the plane wave quickly depolarizes the entire space not occupied by the rotating wave or the region of hyperpolarization, leaving no place for the scroll wave wavefront to propagate. While the scroll wave moves away, in the direction indicated by black arrows in Fig. 17.6c, it loses the wavefront, and only the wave tail left, Fig. 17.6d. After, the whole medium becomes quiescent.

We also find that applying an electric field pulse 1.1 V/cm for 5 ms at any of the five time moments equally spaced in time by $0.27T_s$ resulted in termination of the scroll wave, while applying a slightly weaker pulse, 0.9 V/cm, at any of these five moments, fails to terminate the rotating wave. With termination occurring independently of the electric field application time, the vulnerable window (VW) for this thin-wall system is $2\pi$ radians.
Transmural width: 1.667

Fig. 17.6 A 3D mechanism for terminating a scroll wave in a thin-layer that results in a vulnerable window (VW) of $2\pi$. Wall thickness: 1.667; electric field strength: 1.3 V/cm for 5 ms. (a) Scroll wave after four rotations. (b) Immediate effect of an electric field pulse applied at time $t = 0$. The electric field $E_0$ (long arrow) is oriented parallel to the scroll wave filament. (c) The leading edge of the newly depolarized region (red) is a plane parallel to the $x$-$y$ plane. It propagates as a plane wave in the $z$-direction (black arrows) filling the region not occupied by the scroll wave. (d) The scroll wave loses its wavefront, and therefore terminates shortly thereafter. We have observed that the 3D scroll wave terminates irrespective of its phase (0 to $2\pi$) when the electric field is applied. For all panels: Regions occupied by action potential(s) ($u > b/a$) or its refractory period ($v > a/2 - b$) are shown as opaque. Muted colours represent the value of the membrane potential; see the colour bar.

This important result, that the VW assumes the full range of available phases when the electric field pulse is oriented along the filament direction, is not just a property of thin layers. We illustrate this in Fig. 17.7 for a scroll wave in a system with a wall thickness four times that of Fig. 17.6. The electric field pulse again depolarizes the rear surface, which interferes with the portion of the rotating wave close to that surface. However, in this case, the remainder of the scroll wave is not immediately disturbed. Instead, the trailing (blue) surface of the rotating wave recedes, as the new, induced wave attempts to fill the excitable gap. The result of these two processes is the merging of the two waves into a single wave, which then rotates around a filament that is now L-shaped, shown as a white dashed line in panel (b) of Fig. 17.7, an effect previously demonstrated by Biktashev [28]. The filament quickly relaxes to curved, “C” shape (Fig. 17.7d, e) which, based on the theory of scroll ring dynamics [29, 30], is governed by the equation,

$$\frac{dR}{dt} = -\alpha/R$$  \hspace{1cm} (17.6)

where $R$ is the local radius of a curved filament, and the constant $\alpha$, sometimes called filament tension, depends on the system parameters. In our case, with Barkley parameters $a = 0.8$ and $b = 0.05$, the system resides in the Contracting Scroll (CS) region in the parameter space, as shown in Fig. 17.5b [31]. In this regime, $\alpha$ is positive, and the filament shrinks due to positive filament tension. Shrinking
Transmural width: 6.667

Fig. 17.7  Scroll wave termination in a thick layer also has VW = 2\pi. Wall thickness: 6.667; electric field strength: 1.1 V/cm for 5 ms. (a) Scroll wave prior to application of the electric field pulse. The white dashed line denotes the scroll wave filament. (b) The filament acquires an L-shape after the electric field pulse. (c) The filament becomes C-shaped (hidden, but visible in (d) and (e)) as the waveback (in blue) recedes. (d)–(f): The curved filament shrinks, then disappears, due to the filament tension. Again, this mechanism operates, as illustrated, irrespective of when the electric field pulse is administered (i.e., a VW of 2\pi) for a pulse of sufficient strength.

and self-annihilation of the filament is seen in Fig. 17.7b–f during the course of continued rotation. The disappearance of the filament then results in termination of the scroll wave.

We again find that the mechanism produces termination irrespective of the phase of the vortex when the electric field pulse is administered. In this case, we find that the termination of the scroll wave occurs when a field 2.2 V/cm is applied at any of five moments equally spaced in time by 0.2Ts. The vulnerable window for scroll wave termination thus consists of all 100% of possible locations of the rotating wave in its rotation; thus, VW = 2\pi.

Finally, to contrast this method with conventional methods in 2D, we tried applying electric fields ranging in strength from 2.2 to 8.8 V/cm in the \pm x and \pm y directions. We also tried applying a field 2.2 V/cm in the –y direction at ten different times, equally spaced within a spiral wave period. None of these trials produced scroll wave termination.
17.4 Experiment

Results of about 500 experiments with vortices termination in the isolated pig hearts are presented in Fig. 17.8. Fibrillation was induced and terminated as in [6, 7].

Figure 17.8a shows that the optimal pacing frequency $\hat{f} = 0.77$ is below the arrhythmia frequency ($\hat{f} < 1$) as it should be for terminating pinned vortices.

Figure 17.8b shows the success rate vs normalized frequency $\hat{f} = f/f_d$ where $f_d$ is the dominant frequency of fibrillation. Error bars: the standard deviation. Dashed lines: theoretical prediction for termination of one pinned vortex (blue), two pinned vortices (red), when the slower vortex is enslaved by the faster one (red). In accordance with the mechanism explained near Eq. (17.3), the theoretical termination rate for two vortices is threefold lower than that for a single vortex. The experimental curve is between the theoretical curves for one and two pinned vortices. The black dashed line is the theoretical prediction for a mixture (50:50) of two identical vortices and two vortices with significantly different frequencies, as per Eq. (17.3).

Figure 17.8c shows the success rate for defibrillation energies not exceeding $\hat{e}$, for frequencies $\hat{f}$ shown near each curve. Normalized energy $\hat{e} = e/e_1$, where $e_1$ is the threshold $E_{50}$ energy of defibrillation by 1 shock. Graphs (b, c) and the experimental curve in (a) are calculated from data in [32]. The optimal pacing frequency $\hat{f} = 0.77$ is below the arrhythmia frequency ($\hat{f} < 1$) as it should be for terminating pinned vortices. An interpretation of the experimental results is that about half of VF episodes was induced by pinned vortices of very close periods. These experiments evidence that pinned vortices, hidden from direct observation, are significant in fibrillation.

Fig. 17.8 Fibrillation termination in the isolated pig hearts. The success rate of defibrillation in 486 experiments by 5 biphasic E-pulses. (a) Success rate vs normalized frequency $\hat{f} = f/f_d$ where $f_d$ is the dominant frequency of fibrillation. Error bars: the standard deviation. Dashed lines: theoretical prediction for termination of one pinned vortex (blue), two pinned vortices (red), when the slower vortex is enslaved by the faster one (red). In accordance with the mechanism explained near Eq. (17.3), the theoretical termination rate for two vortices is threefold lower than that for a single vortex. The experimental curve is between the theoretical curves for one and two pinned vortices. The black dashed line is the theoretical prediction for a mixture (50:50) of two identical vortices and two vortices with significantly different frequencies, as per Eq. (17.3). (b, c) Success rate for defibrillation energies not exceeding $\hat{e}$, for frequencies $\hat{f}$ shown near each curve. Normalized energy $\hat{e} = e/e_1$, where $e_1$ is the threshold $E_{50}$ energy of defibrillation by 1 shock. Graphs (b, c) and the experimental curve in (a) are calculated from data in [32]. The optimal pacing frequency $\hat{f} = 0.77$ is below the arrhythmia frequency ($\hat{f} < 1$) as it should be for terminating pinned vortices. An interpretation of the experimental results is that about half of VF episodes was induced by pinned vortices of very close periods. These experiments evidence that pinned vortices, hidden from direct observation, are significant in fibrillation.
Notice that elimination of a free, rather than pinned, vortex by inducing its drift via the mechanism described in [25] requires the pacing frequency to be above the arrhythmia frequency, \( \hat{f} > 1 \).

The theoretical estimation shown in dashed black line fits the experiment better than curves for one or two different vortices. It indicates that in about a half of fibrillation cases, the frequencies of the vortices were not much different, see Eq. 17.3.

This estimation was obtained in an axiomatic model which assumed that the strength of electric field is sufficient to ensure the normalized vulnerable window of about 0.24 (see below for more detail of the axiomatic model). Minimum energy for termination of a pinned vortex is achieved when the electric field strength is chosen so that the normalized vulnerable window \( \sqrt{W}(E) = 1/N \), where \( N \) is the number of pacing pulses.

Maximum of the success rate is achieved when the pacing frequency \( f = f_{\text{best}} \), where \( f_{\text{best}} \) is the frequency for which the normalized scanning step \( \mathbf{s}_n = 1/N \).

When \( f < f_{\text{best}} \), i.e. \( T > T_{\text{best}} \), the scanning step \( \mathbf{s}_n > \sqrt{W} \), and the vulnerable window may be missed while scanning, thereby decreasing the success rate. When \( f > f_{\text{best}} \), so \( T < T_{\text{best}} \), the scanning step \( \mathbf{s}_n < \sqrt{W} = 1/N \), and not all phases are scanned. This also decreases the success rate.

As an estimate of the fastest vortex frequency we use the dominant frequency. Below is a formal description of the axiomatic model used. Let \( \phi_j^1 \in [0, 1) \), \( j = 1, 2, n = 1, \ldots, N \), \( N = 5 \), describe the phase of \( j \)th vortex just after the delivery of the \( n \)th E-pulse, \( T_j \) be the own periods of the vortices, \( T_2 > T_1 \), and correspondingly \( \mathbf{s}_n = (T - T_j)/T_d \) are the scanning steps normalized by the measured dominant period, \( T_d \). We postulate \( \phi_{n+1}^j = (\phi_n^j + s) \mod 1 \), subject to the following corrections: (1) if \( \phi_{n+1}^j \in [1 - \overline{E}_G, 1) \), where \( \overline{E}_G \) is the normalized duration of the excitatory gap, then \( \phi_{n+1}^j \) is replaced with 0: this describes resetting the \( j \)th phase by the E-pulse; (2) if \( \phi_{n+1}^j \in [1 - \overline{E}_G - \sqrt{W}, 1 - \overline{E}_G) \), where \( \sqrt{W} \) is the normalized duration of the vulnerable window, then the \( j \)th vortex is considered terminated; (3) if neither vortex is terminated, then the slower vortex’s phase is enslaved by the faster one’s, \( \phi_{n+1}^2 = (\phi_{n+1}^1 - D) \mod 1 \), where \( D \) is a fixed phase delay; (4) if both vortices are terminated, iterations stop and E-pacing is deemed successful. Figure 17.8 shows results of Monte-Carlo simulations with random initial phases of vortices and normal distributions of parameters \( \hat{T}_1 = 1 \pm 0.1 \) and \( \hat{T}_2 = 1.6 \pm 0.05 \) (mean\( \pm \)standard deviation), with other parameters fixed at \( \overline{E}_G = 0.4 \), \( \sqrt{W} = 0.2 = 1/N \), \( D = 0.25 \). Note that the normalized vulnerable window \( \sqrt{W} \) depends on the strength of the electric field in the pacing pulses.

The three curves correspond to simulations with two-vortex initial conditions (red line), with initial conditions where only one vortex is present from the start (blue line), and a 50:50 mixture of the two (the black dashed line).

We see that the axiomatic model predicts that for two vortices, the success rate should be lower than for one vortex, for frequencies between the frequencies of the leading vortex and the led vortex. This is due to the cases then the leading vortex is terminated first, dominant frequency changes and the conditions for termination for
the remaining, slower vortices are no longer optimal. As the figure shows, the actual experimental data best correspond to a mixture of one- and two-vortex cases.

However in the experiments the arrhythmia in all cases was VF rather than VT, so presumably involved more than one vortex. Note that in the axiomatic model, a case of one vortex is similar to that of two or more vortices of identical periods. Hence we conclude that the most likely interpretation of the available experimental data is that about half of VF episodes was induced by vortices of very close periods.

These experiments evidence that pinned vortices, hidden from direct observation, are significant in fibrillation.

17.5 Discussion

Here, we investigated two extreme cases: permanently pinned vortices and permanently free vortices. There is no sharp transition between them. In cardiac muscle, there are heterogeneities of all sizes, including those to which vortices pin weakly. A weakly pinned vortex is pinned for some time only, then leaves the pinning centre and moves as a free vortex, again for some time. When moving and meeting a pinning centre, it may pin to it, or may reach the boundary of the tissue and disappear. Such intermediate types of rotating waves can be more easily terminated while they are pinned.

Vortices termination can be induced also by other mechanisms different from vulnerability, e.g. pacing-induced drift of a free vortex [25], unpinning of weakly pinned vortices [33, 34] and by 3 dim mechanisms [35].

3 dim models are widely used in investigation of wave patterns induced by rotating waves, e.g. [14, 29]. Study of vortices termination in 2 dim models is a necessary step for developing understanding mechanisms of 3 dim vortices termination in the heart. A 3-dim mechanism of defibrillation was described in [28, 35, 36]. Termination vortices underlying fibrillation is only a small part of a problem preventing and curing the cardiac arrhythmias where combination of molecular and dynamics approaches is prominent [37].

In conclusion, we have shown mechanisms of terminating pinned and free vortices by electric field pulses when the geometric positions of their cores, and the phases of rotation are not known. We have demonstrated a new, low-energy, scroll wave termination mechanism that is an apparent solution to the problem of small vulnerable windows that are characteristic of other low-energy methods. When an electric field pulse is applied with field component oriented parallel to the scroll wave filament, we obtain wave termination with a vulnerable window of the full 2π radians using field strengths much smaller (1.1 V/cm for thin layers; 2.2 V/cm for wide layers) than those typically required by standard methods (5–6 V/cm for standard defibrillation). This reduces pulse energy requirements by an order of magnitude (since energy scales as $E_0^2$), thus minimizing pain, tissue damage and battery requirements. Since the VW is 2π, the new mechanism also eliminates the need to apply multiple electric field pulses to scan phases of all rotating waves. We
therefore expect that the new mechanism will play an important role, alongside other mechanisms, in the future design of low-energy defibrillation stimulus protocols.

These results form the physical basis for creation of new effective methods for termination vortices underlying fibrillation.

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Competing Interests We have no competing interests.

References