Attraction and repulsion of spiral waves by inhomogeneity of conduction anisotropy—a model of spiral wave interaction with electrical remodeling of heart tissue

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Abstract Various forms of heart disease are associated with remodeling of the heart muscle, which results in a perturbation of cell-to-cell electrical coupling. These perturbations may alter the trajectory of spiral wave drift in the heart muscle. We investigate the effect of spatially extended inhomogeneity of transverse cell coupling on the spiral wave trajectory using a simple active media model. The spiral wave was either attracted or repelled from the center of inhomogeneity as a function of cell excitability and gradient of the cell coupling. High levels of excitability resulted in an attraction of the wave to the center of inhomogeneity, whereas low levels resulted in an escape and termination of the spiral wave. The spiral wave drift velocity was related to the gradient of the coupling and the initial position of the wave. In a diseased heart, a region of altered transverse coupling corresponds with local gap junction remodeling that may be responsible for stabilization-destabilization of spiral waves and hence reflect potentially important targets in the treatment of heart arrhythmias.

Keywords Inhomogeneous excitable media · Spiral wave · Spiral wave pinning · Reentry wave · Heart arrhythmias · Spiral wave attraction

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1 Introduction

The mechanical function of the heart is driven by a propagating electrochemical wave [1]. Propagation of an electrochemical wave is mediated by the generation of an action potential (an event in an electrical state of a cell membrane resulting in an inversion of the electric potential) by heart myocytes and the transport of ions through a network of tubular connections between cells (connexins) and extracellular space. If the transmembrane potential in one cell reaches a critical threshold as a result of ion transport through the cell membrane, neighboring myocytes sequentially generate action potentials, which results in a wave type propagation of electrochemical activity. In normal conditions, the activation wave spreads from the sino-atrial node through the heart in a precise, complex manner and ends propagation when there is no more excitable muscle ahead of it. One of the pathological forms of wave activity in atria is a spiral wave—a spiral-shaped activation wave re-entering the same fragment of tissue it has already propagated through. Such a perturbation interferes with the normal heart rhythm since the spiral wave circulates at a very high rate, disturbing the mechanical function of the heart. In ventricles, re-entrant activity takes the form of a scroll wave, which can be depicted as a stack of spiral waves with tips aligned along a line, which is called a scroll wave filament. The scroll wave filaments' dynamics has been implicated in the transition from ventricular tachycardia to ventricular fibrillation [2]. In this paper, we focus on the dynamics of spiral waves assuming that the atrial muscle can be, in the first degree of approximation, represented as a two-dimensional system.

Heart tissue is an inhomogeneous and anisotropic system, both structurally and functionally. Tissue inhomogeneity is a result of the regional variability of cell function (natural and pathological), while the elongated shape of the cells and the fibrous architecture of the tissue result in anisotropy. Several studies have shown that both anisotropy and inhomogeneity play a role in the initiation and sustenance of many forms of cardiac arrhythmias (especially spiral wave-based arrhythmias) [3–6], although this field is not only limited to the interest of waves in the heart, but also extends to chemical systems [7, 8]. Due to the difficulty in the simultaneous measurement of spiral wave dynamics along with the distribution of tissue inhomogeneity, mathematical modeling is used to investigate the effect of tissue inhomogeneity on spiral wave dynamics. Mathematical modeling of the role of inhomogeneity focuses on areas such as the effect of electrical cardioversion on spiral wave trajectory and stability [9–11], spiral wave formation caused by interaction of the wave with localized inhomogeneities [12–17], mutual interaction of spiral waves [18] and suppression of spiral waves by tissue inhomogeneities [19, 20]. One of the most interesting effects of system inhomogeneity is the induction of spiral wave drift [21], which is thought to play an important role in the stability of cardiac arrhythmias caused by rotating waves.

Many kinds of heart disease are associated with the remodeling of the heart muscle resulting in a perturbation of connectivity between muscle fibers [4, 22]. Since the trajectory of a spiral or scroll wave propagating through a heart muscle is affected by both of these factors [23, 24], their nature and mechanism of interaction is important for understanding the mechanisms of arrhythmias. In particular, reports on the anchoring properties of areas with decreased cell coupling indicate their important role in arrhythmogenesis [25, 26].

Several important questions have been raised and explored, focusing on the interaction of spiral and scroll waves with the architecture of muscle fibers with specific attention to how fiber orientation affects the trajectory of the wave [24, 27–29] and its stability [2, 30]. The majority of work has focused on the dynamics of scroll waves in 3D systems. Interaction

of a spiral wave with fiber orientation in 2D systems has been less extensively studied, focusing on the effect of a non-uniform fiber orientation on the trajectory of the spiral wave [24], its stability [26], conduction velocity [31] and its role in the emergence of spiral waves during electrical cardioversion [32]. Greater interest in the interaction between fiber architecture and wave conduction in 3D compared with 2D systems is most likely a result of a more uniform fiber orientation in ventricles, which can be measured using diffuse tensor magnetic resonance imaging [33]. In contrast, the atrial muscle is often assumed to be a 2D structure for the analysis of wave conduction and dynamics due to the fact that it is only a few millimeters thick. Also, little is known about the detailed architecture of atrial fibers with studies reporting mainly qualitative observations [34].

Interesting results were obtained by C. Cabo and P. Boyden [26]. These investigators found that the spiral wave tended to drift toward and stabilize at regions of low-transverse coupling. Low-transverse coupling may correspond to local tissue fibrosis and result in the alteration of the conduction properties [4]. Since localized regions of fibrosis were observed in the infarcted heart muscle, their results could explain the stability of post-infarct arrhythmia.

In this paper, we continue the investigation of the relationship between structural inhomogeneity and spiral wave drift. We aim to assess how spatially extended inhomogeneity of transverse uncoupling of cells affects the trajectory of the spiral wave in a 2D system. The novel aspect of this study lies in the spatially extended and gradual variation of the cell uncoupling. This model may provide greater insight into spiral wave dynamics in the vicinity of patchy areas of tissue fibrosis.

2 Methods

Due to the large number of parameters involved in the modeling of spatial inhomogeneities and their interaction with voltage membrane kinetics, in the first phase of our exploration of the problem we used a simple model of wave propagation (FitzHugh-Nagumo model) and introduced inhomogeneity as a spatially extended area of lateral decoupling as a linear function of the distance from the center of inhomogeneity. The modified FitzHugh-Nagumo model was chosen to simulate the dynamics of wave propagation because of its simplicity and well-known properties [35]:

$$\frac{\partial v}{\partial t} = \frac{1}{\mu} \left(v - \frac{1}{3}v^3 - w \right) + \nabla \hat{D} \nabla v \quad (1)$$

$$\frac{\partial w}{\partial t} = \mu (v + \beta - \gamma w) \quad (2)$$

$$\hat{D} = \begin{bmatrix} D_{xx} & D_{xy} \\ D_{yx} & D_{yy} \end{bmatrix} \quad (3)$$

where v is the transmembrane voltage and w is the total slow current. The default values of the model parameters were set to $\gamma = 0.5$, $\mu = 0.3$, $\beta = 0.7$. Parameter β controls excitability—greater values represent a less excitable system. Since we focus on the dynamics of waves in the myocardium, we excluded small values of β at which the system becomes self-oscillatory. Parameter γ controls the onset and the dynamics of repolarization

and μ controls the relative timescales of the voltage and inhibition current. The spiral wave in such a system exhibits stable and rigid rotation. Computations were carried out on a two-dimensional, 200×200 rectangular grid. D is a diffusion tensor determining the connectivity between the system elements. In our case, only D_{xx} and D_{yy} are not equal to zero and have initial values of 4 and 1, respectively. These values were set in order to model anisotropic conduction in heart tissue. Due to a lack of consensus in the literature (published ratios of coupling coefficients range from 1:1 to 11:1 [36–38]), we set the ratio of the diffusion coefficients in the perpendicular and horizontal directions to 1:4. The second-order Runge-Kutta integration scheme was used with a space step $\Delta x = 0.4$ (thus the length of the system edge was 80) and a time step $\Delta t = 1.4(\Delta x^2)/D_{\max}$ where $D_{\max}$ is the largest value among the diffusion tensor elements. Since we do not aim to quantitatively reconstruct physiological phenomena, we used dimensionless units in our study. We used zero-flux boundary conditions to minimize the effect of the sample borders.

Spiral waves were initiated by setting the spatial distribution of v and w to the distribution within a propagating spiral wave: for each element of the simulation grid, its phase was calculated as:

$$\theta = \frac{r - k\varphi - 2\pi kn}{2\pi k} \quad (4)$$

where r and φ are polar coordinates of a given point with respect to the center of the spiral wave, k is its winding number and n is a natural number set in a way to obtain a phase between 0 and 1. The values of the variables v and w for a given element of the grid were set depending on the phase. $\theta = 0$ corresponded to the resting state and $\theta = 1$ corresponded to cell depolarization. All intermediate values of the variables were copied from a stationary distribution of the variables within the action potential cycle. Such a predefined distribution of the variables v and w was an initial condition from which the spiral wave evolved easily. The trajectory of the spiral wave was reconstructed by tracking the position of its tip. The position of the spiral wave tip was defined as a crossing point of the iso-value contours ($v = 0$) obtained with a time delay $\Delta t = 0.25$.

Local transverse uncoupling was modeled by the introduction of a spatial dependence of the diffusion tensor coefficients D_{xx} and D_{yy} (see Eq. 3). In each case where inhomogeneity was introduced, D_{xx} was constant throughout the system while D_{yy} changed according to the formula:

$$D_{yy} = \min \left(D_{yy}^{center} + \eta r, D_{yy}^{\max} \right) \quad (5)$$

where D_{yy}^{center} is transverse coupling (D_{yy} in the diffusion tensor) at the center of the sample, $D_{yy}^{\max}$ is the maximum value of D_{yy} (set to 1 unless otherwise stated), r is the distance from the center of the sample and η is a coefficient determining the dependence of D_{yy} on the distance from the center of the system. We used a linear dependence of the transverse coupling on the distance due to a lack of experimental data characterizing such distributions in remodeled heart tissues. An example of the distribution of the diffusion coefficients is presented in Fig. 1. In such a system, the spiral wave was initiated and its wave tip trajectory was recorded.

In order to remove the effect of circular motion of the spiral wave tip on the calculation of the length of the drift trajectory, we calculated an averaged trajectory using a sliding window with length equal to one rotation of the spiral (approximately 6 time units in our model).

Fig. 1 Example trajectories of the spiral wave drift toward the center of inhomogeneity from four different initial positions (denoted by *arrows*) for $D_{xx} = 4$, $D_{yy} = 1$, $\eta = 0.03$, $D_{y0} = 0.3$ (a). Averaged trajectory using a sliding window average of 6 *time units* length (approximate cycle length of the spiral) (b). The *grid* in the background illustrates the distribution of the diffusion coefficients. The length of the horizontal bar corresponds to D_{xx} (the direction of the muscle fibers) and the length in the vertical direction corresponds to D_{yy} . In order to simplify the description of the results, the initial positions of the wave in this case are denoted by the symbols L1, L2, L3, and L4

Examples of the trajectories before and after averaging are shown in Fig. 1. The length of spiral wave drift was calculated as the length of the averaged trajectory from its initial position to the time at which the spiral wave crossed distance 3.2 from the center of inhomogeneity. We used this threshold to remove the effect of the significant slowing down of the drift in proximity of the center of inhomogeneity. The average velocity of the drift was defined as a quotient of drift length and time. To quantify the extent of the circular motion of the spiral wave tip, the area encircled by the trajectory was calculated as the product of the horizontal and vertical dimensions of the trajectory created during spiral wave circular rotation.

Spiral waves were either attracted toward the geometrical center or drifted toward the edge of the system and terminated after collision. The former case was classified in this paper as trapping and the latter as spiral wave escape. Escape is not used here in a strict sense—in case of more a spatially extended system, spiral waves may return to the vicinity of the inhomogeneity. Rather, the term escape is used here to denote a case when the spiral wave drifted outside the area of inhomogeneity.

3 Results

The spiral waves demonstrated two types of behavior depending on the model parameters: attraction (drift toward the center of inhomogeneity) and repulsion (drift outward toward the edge of the sample). In order to assess the parameter space related to both types of behavior, we performed simulations varying the model parameters β , γ and η with the spiral wave initially located halfway between the center and the edge of the sample. The results are

shown in Figs. 2 and 3. For low values of β and γ the spiral wave drifted toward the center of the trap (see Fig. 2). The trajectory of the spiral wave was a superposition of the drift caused by inhomogeneity with the circular motion of the spiral wave tip related to the rigid rotation of the wave. Increasing β and γ resulted in the area of the circular motion of the spiral wave tip increasing, and at a critical point the spiral wave was no longer attracted to the center but drifted toward the edge of the sample. The attraction and repulsion area in the $\beta - \gamma$ plot was separated by a line described by the equation $\beta = -0.55\gamma + 0.99$; $\eta = 0.03$, $\mu = 0.2$. A similar behavior was obtained in the $\beta - \eta$ plane (equation of the separation line: $\beta > -0.2\eta + 0.73$; $\gamma = 0.5$, $\mu = 0.2$) (see Fig. 3).

In order to better characterize the anisotropic nature of the spiral wave drift towards the center of inhomogeneity, we performed calculations at the initial positions of the spiral wave distributed along a circle with a radius equal to 24 and centered at the inhomogeneity (see Fig. 4a). Calculations were performed for different values of the D_{yy} gradient controlled by the coefficient η (Fig. 4) and for four different values of the current inhibition parameter β (Fig. 5). In all cases, the spiral wave drifted toward the center of inhomogeneity. With an increase in η and β , trajectories become more curved, especially trajectories starting from locations perpendicular to the fiber orientation. However, the shift caused by an increasing curvature was not uniform and a characteristic S-shaped clustering of the trajectories was obtained—more pronounced with an increase in η (see the dark patches formed by the trajectories clustering in Fig. 4 for high values of η and Fig. 5 for high values of β). An increase of η shortened the drift time and increased the trajectory length, resulting in an

Fig. 2 Area of the circular motion of the spiral wave tip (in grayscale) for different values of parameters β and γ . The area of the circular rotation was quantified as the product of the horizontal and vertical dimensions of the trajectory of the spiral wave's circular motion. With an increase in β and γ , the trajectory of the spiral wave's circular motion was also increased up to the point at which the spiral wave started to drift toward the edge of inhomogeneity. Calculations performed for $\eta = 0.03$ and $\mu = 0.2$. Below are examples of three trajectories showing transition from attraction (corresponding to dots 1 and 2) to escape (dot number 3 on main plot). The arrow denotes the initial position of the spiral wave

Fig. 3 Area of the circular motion of the spiral wave tip (in grayscale) for different values of parameters β and η . The area of the circular rotation was quantified as the product of the horizontal and vertical dimensions of the trajectory for spiral wave circular motion. With an increase in β and η the trajectory of the spiral wave's circular motion also increased up to the point at which the spiral wave started to drift toward the edge of the inhomogeneity. Calculations performed for $\eta = 0.03$ and $\mu = 0.2$. The arrow denotes the initial position of the spiral wave

increase in the conduction velocity (Fig. 4). Changes of the trajectory length and drift time are most prominent at the starting locations perpendicular to the fiber orientation. However, the position of the maximum of the drift time depends on η (maximum at $\varphi = -1.73$ and $\varphi = 1.4$ for $\eta = 0.01$; $\varphi = -1.33$ and $\varphi = 1.8$ for $\eta = 0.02$; $\varphi = -1.43$ and $\varphi = 1.75$ for $\eta = 0.03$; $\varphi = -1.33$ and $\varphi = 1.8$ for $\eta = 0.04$). The drift length for trajectories located at $\varphi = 0$ and $\varphi = -\pi$ was not affected by increasing η . The average

Fig. 4 Averaged trajectories (63 trajectories in total) of the spiral wave drift toward the center of inhomogeneity from starting locations distributed along the circumference of a circle of radius 24. φ denotes the angle coordinate of the initial point in a polar coordinate system located at the center of inhomogeneity (a). Length of the trajectories, time of drift and average drift velocities (b)

Fig. 5 Averaged trajectories (63 trajectories in total) of the spiral wave drift toward the center of inhomogeneity from starting locations distributed along the circumference of a circle of radius 24 as a function of parameter β . φ denotes the angle coordinate of the initial point in a polar coordinate system located at the center of inhomogeneity (a). Length of the trajectories, time of drift and average drift velocities (b)

drift velocity increases with η for all initial locations with maxima at locations to the left and right of the inhomogeneity ($\varphi = 0$ and $\varphi = -\pi$) (Fig. 4b). In case of varying β , the trajectory length and drift time showed less prominent variability. Only for $\beta = 0.72$ (which was close to the total inhibition of conduction at the given parameters) did the drift time and length become significantly higher. The drift velocity decreased with increasing β (Fig. 5b) due to the inhibition effect of β on wave conduction.

In order to assess the effect of the parameters η and the global anisotropy level on the trajectory shape and drift characteristics, we performed a set of calculations at four initial locations (L1, L2, L3, and L4; see Fig. 1). The parameter η was varied between 0.01 and 0.04 (for lower values the properties of the drift remained unchanged except for an increase in the drift time; for larger η the radius of inhomogeneity was much smaller than the initial distance of the spiral wave from the center, which resulted in a lack of attraction (results not shown)). The global anisotropy was controlled by setting D_{xx} between 4 (1:4 anisotropy level assumed in this study) and 1 (which corresponds with an isotropic system since $D_{yy} = 1$). The resultant shapes of the trajectories are shown in Fig. 6, which presents trajectories as a function of η for four different values of D_{xx} . The longest trajectories were obtained for the maximum value of η . However, an increase in η caused an increase in the trajectory length only at positions perpendicular to the fiber orientation (L2 and L4).

Plots of the time of drift, trajectory lengths and average drift velocities for the trajectories starting at L1 and L2 are shown in Fig. 7. The results at locations L3 and L4 are similar and were not presented. The drift length beginning at location L1 was not significantly affected by η nor by D_{xx} (Fig. 7b). However, the time of drift decreased exponentially with an increase in η and D_{xx} (Fig. 7a) with a decay coefficient ranging from -0.72 to -0.75 for drift times as functions of η and from -0.97 to -1.03 for drift times as functions of D_{xx} (coefficient of determination of the exponential regression $R^2 > 0.96$). The decrease of drift time resulted in an increase of the average drift velocity (Fig. 7c). The drift originating from

As a function of η :

Fig. 6 Trajectories of spiral wave drift as a function of η for $D_{xx} = 1$, $D_{xx} = 2$, $D_{xx} = 3$ and $D_{xx} = 4$. Calculations were performed at four initial positions of the spiral wave (L1 and L3 along the horizontal axis of inhomogeneity and L2 and L4 on the vertical axis at distance 24 from the center of the trap). The η parameter has the greatest impact on the shape of those trajectories of the drift that start at locations L2 and L4

location L2 had different properties. The time of drift, trajectory length and, consequently, the average drift velocity showed a very weak dependence on D_{xx} (Fig. 7d–f). The greatest effect was for $\eta = 0.01$, which resulted in a 9 % increase of the drift time from $D_{xx} = 1$ to $D_{xx} = 4$ and a 6 % increase in trajectory length resulting in a 2 % decrease in the average drift velocity. However, the drift from L2 was much more sensitive to the changes in η . With an increase in η , the drift time decreased, the trajectory length increased and the average drift velocity increased with a strong linear dependence (coefficient of determination of linear regression $R^2 > 0.99$ in all cases).

Fig. 7 Time of drift, drift length, and average drift velocity as functions of η for $D_{xx} = 1$, $D_{xx} = 2$, $D_{xx} = 3$ and $D_{xx} = 4$. *Upper row:* Calculations performed for spiral waves initiated at location L1. *Bottom row:* calculations performed for spiral waves initiated at location L2 (perpendicular to the fiber orientation). Both L1 and L2 are at distance 24 from the center

4 Discussion and conclusions

In this study, we analyzed the drift of a spiral wave in anisotropic excitable media caused by a linear gradient of transverse coupling. We found that, depending on model parameters, the spiral wave drifts toward the center of inhomogeneity or toward the edge of the system and terminates. The shape of the trajectory, length and time of drift depend on the initial position of the wave, the coupling gradient and the anisotropy level (defined as the ratio of D_{yy}/D_{xx}) with attraction strength related to the gradient of the transverse coupling.

With respect to the initial position of the spiral wave, we found spiral waves located horizontally on both sides of the inhomogeneity to have a significantly faster average drift velocity (Figs. 4b and 5b). Such an increase is due to a lack of trajectory curving for spiral waves starting at those locations compared to the trajectories of spiral waves starting at locations perpendicular to the horizontal fiber orientation. A shorter trajectory results in a short drift time and therefore a larger average conduction velocity. This property demonstrates that the orientation of tissue fibers defines the orientation of the fastest attraction of spiral waves. Trajectories of the spiral waves initiated further from these locations curve toward the direction of faster attraction (horizontal in the presented model) resulting in an S-shaped clustering of the trajectories (Figs. 4a and 5a).

Spiral waves starting at locations perpendicular to fiber orientation and above the center of inhomogeneity tend to drift to the right side of the system and spiral waves starting from below the center tend to shift towards the left side of the system (see Figs. 4a and 5a). This asymmetry of the distribution of the trajectories is caused by the chirality of the spiral wave (anti-clockwise rotation in this study).

A schematic explanation of spiral wave drift in the presence of a linear gradient of the anisotropy level is shown in Fig. 8. The reasoning is based on a similar explanation of drift in presence of the gradient of excitability [39] and caused by an advective field [40]. Figure 8a shows a distribution of the diffusion tensor components D_{xx} and D_{yy} . D_{xx} remains constant and there is a linear gradient of D_{yy} in the horizontal direction. A spiral wave initiated in the middle of such a system drifts towards the left edge of the system (direction of the greater anisotropy level). We hypothesize that the mechanism of this drift is related to local differences in the vertical component of the wave propagation (v_y) during rigid

Fig. 8 Schematic explanation of spiral wave drift in presence of a gradient of diffusion tensor anisotropy. Description in the text

rotation. When a spiral wave arm propagates to the right side of the tip position (which would correspond with 12 to 6 o'clock if we would locate a clock at the spiral wave core), the vertical velocity is slightly greater than in case of propagation on the left side from the tip (between 6 and 12 o'clock). This difference in v_y (denoted as δv_y in Fig. 8b) causes a faster rotation of the arm resulting in a smaller horizontal shift of the tip compared with in-phase rotation on the left side of the tip (in simple words, the wave arm has less time to propagate to the right before turning back). The sum of the consecutive differences in the horizontal shift results in a drift toward an area of lower D_{yy} . The same mechanism causes a spiral wave drift in the case of diffusion tensor inhomogeneity presented in this study. The scenario presented in Fig. 8 is equivalent to a drift in the presence of an advective field analyzed in detail by Krinsky et al. [40]. Although the diffusion tensor inhomogeneity presented in this study is not equivalent to the linear gradient of an external field, the mechanism of the drift is the same. The drift velocity tangential and perpendicular to direction of inhomogeneity results in a linear drift trajectory with the direction dependent on several model parameters, mostly on the degree of inhomogeneity and the relation between the wavelength and excitation wavelength (width of the spiral wave arm). In our system, the degree of inhomogeneity varies across the system, resulting in varying directions of spiral wave drift. This property results effectively in curved and spiral shaped trajectories of drift, as opposed to linear trajectories in the work of Krinsky.

A more detailed analysis of the effect of inhomogeneity parameters on spiral wave drift (simulations of drift as a function of inhomogeneity gradient η and longitudinal coupling D_{xx}) showed a sensitivity of the trajectory shape on η and a comparatively very weak dependency on D_{xx} . D_{xx} only affected the time of drift of the spiral waves starting at location L1 (corresponding with the diffusion direction defined by D_{xx}). This is to be expected since the trajectory is oriented along the x-axis and thus D_{xx} defines the conduction velocity in this direction. An increase of the parameter η caused a decrease of the drift time and an increase of the average drift velocity at all starting points of the spiral wave. However, its effect on shape was more prominent for the spiral wave starting at locations perpendicular to the fiber orientation.

Spiral waves show an interesting behavior as a function of current inhibition parameters β and γ and inhomogeneity gradient η . The high values of the parameters caused the spiral wave to drift toward the edge of the sample and terminate (trajectory (3) in Fig. 2). At low values, the spiral wave was attracted to the center (trajectory (1) and (2) in Fig. 2). In an intermediate state, the spiral wave circulated around the center of the system (trajectory (2) in Fig. 3). The trajectory of the spiral wave was a superposition of the drift caused by inhomogeneity with a circular trajectory related to the rigid rotation of the wave. Such bifurcation of spiral wave dynamics has an interesting implication, suggesting that low excitability may cause detachment of the spiral wave from this type of inhomogeneity.

In this study, we used a simple mathematical model to study the attraction of the spiral wave to localized inhomogeneity of coupling anisotropy corresponding to a local transverse uncoupling of cells in heart muscle. We showed that inhomogeneity forms a spiral wave trap, attracting the spiral wave to its geometrical center. In heart tissue, such a structure would correspond to a region of transverse uncoupling, and, as such, may be an important factor in stabilization of spiral wave pivots, increasing the propensity of the heart to sustain arrhythmias. The role of spiral wave pinning in arrhythmogenesis has already been discussed by several authors. Spiral wave pinning to millimeter-sized obstacles, to areas of decreased excitability and disrupted conductivity was postulated as a stabilizing factor of arrhythmia [25, 41, 42]. However, all structures discussed were small in size,

pinning the spiral wave only if the tip was in close vicinity of the structure. The structure presented in this paper is an example of global inhomogeneity attracting and pinning spiral waves even at a large distance from the pinning center.

Spiral wave traps may act within the heart tissue as stabilizing centers preventing the termination of the spiral waves by collision with non-conducting areas (e.g., the edge of valve orifices) and thus lowering the probability of spontaneous termination of the arrhythmia. Therefore, they may be important targets for elimination by radiofrequency ablation or other proposed modes of unpinning [43–45]. However, due to a lack of technology for mapping of muscle fiber orientation in vivo, it will be difficult to use the results presented here in current clinical practice. Before such technology is developed, mathematical modeling or tissue engineering [46] provides an opportunity to search for characteristic fiber structures, which could be clinically relevant and experimentally investigated in the future.

5 Study limitations

The model used in this study is a monodomain formulation using FHN kinetics to describe voltage dynamics. Cardiac tissue is a bi-domain system with different diffusion constants for intracellular and extracellular space. Also, FHN kinetics, although reconstructing basic properties of cell depolarization, lacks several finer aspects of voltage membrane kinetics. However, in this study, we aimed to focus on structural considerations and to explore the properties of the spiral wave drift and attraction. Further studies are required to assess the role of model kinetics.

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