A mathematical model of the unidirectional block caused by the pulmonary veins for anatomically induced atrial reentry

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Abstract It is widely believed that the pulmonary veins (PVs) of the left atrium play the central role in the generation of anatomically induced atrial reentry but its mechanism has not been analytically explained. To understand this mechanism, a new analytic approach is proposed by adapting the geometric relative acceleration analysis from spacetime physics based on the hypothesis that a large relative acceleration can translate to a dramatic increase in the curvature of a wavefront and subsequently to conduction failure. By verifying the strong dependency of the propagational direction and the magnitude of anisotropy for conduction failure, this analytic method reveals that a unidirectional block can be generated by asymmetric propagation toward the PVs. This model is validated by computational tests in a T-shaped domain, computational simulations for three-dimensional atrial reentry and previous in-silico reports for anatomically induced atrial reentry.

Keywords Atrial reentry · Unidirectional block · Conduction failure · Relative acceleration

1 Introduction

Many observations and scientific studies indicate that the pulmonary veins (PVs) play the most significant role in atrial reentry. Numerous experimental and clinical studies have been reported to support this phenomenon [1–4] and have been used to develop a series of successful surgical procedures by isolating the PVs with ablation lesions in the left atrium (LA) [5–7]. Many hypotheses have been proposed as the microscopic or macroscopic cause of

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the PV reentry but can be classified into four major types [8]: the first hypothesis is on the properties of the PV cells for a pacemaker such as voltage-dependent Ca_i release [9], different cell morphology [10] and intracellular calcium transients [10]. The second is on the macroscopic muscular discontinuities or differential muscle thickness as observed at the PV-LA junctions of the canine atrium [11], at the sheep posterior left atrium (PLA) [12] and at the human pulmonary vein-atrial junction [13]. The third is on abrupt changes of microscopic fiber orientations as observed at the interfaces of the anterior and posterior PV-LA junction of the canine heart [11], at the sheep PLA [12] and at the PV-LA junction of the human heart [13]. This hypothesis is also thought to be the cause of conduction delay [14] at the PV-LA junction as observed in patients with paroxysmal atrial fibrillation (AF) [15, 16]. The fourth is on the presence of effective refractory period (ERP) heterogeneity within the PVs of patients with AF [15, 16] and heterogeneous repolarization of PV cells as observed in the left atrium of young male rats [17].

With the microscopic causes of reentry being recapitulated at a macroscopic level, most causes of PV re-entry can be translated as the macroscopic components of the reentry mechanism, known as the *leading-circle model*, as empirically first observed in the early 1900s by MacWilliam [18], Mayer [19] and Mines [20] and developed furthermore since then [3, 21–23]. As illustrated in Fig. 1, the leading circle model explains the mechanism of atrial reentry sustained by a circulating cardiac electric wave, whose path is larger than the wavelength of the depolarization multiplied by the repolarization period. A unidirectional block that allows only one directional propagation of the wave is a necessary condition; thus this model is classified again into two different models regarding the characterization of the unidirectional block. The first model of the unidirectional block is a geometric block caused by an anatomical obstacle for the impulse to circulate around such as a structural barrier [24]. Let us call the reentry caused by the geometric block *anatomical reentry* [25]. The second model is a refractory block caused by rapid repetitive activations without any anatomical obstacle [21]. Let us call the reentry caused by the refractory block *functional reentry* [25]. These two reentries are not always distinctive but it can be roughly identified whether the reentry is activated by one single sinus rhythm (anatomical reentry) or repetitive stimulations with a short coupling interval (functional reentry).

Anatomical reentry and functional reentry share the same propagational mechanisms such as *disproportionate sink-source mismatch* or *asymmetric safety factor* but the question of which type of reentry is likely to be generated and sustained by the aforementioned four hypotheses remains unanswered. Maybe the two reentries constitute AF together, or one instigates the prerequisite conditions for the other. From previous computational simulations of the two reentries with biologically detailed data [26–30], we observe that the two reentries can be initiated by the same cause such as conduction delay due to abrupt changes of fiber orientation. However, answers can be sought in mathematical analysis. Anatomical reentry is distinctively different from functional reentry in mathematical

Fig. 1 Illustration of the leading-circle model by unidirectional block. Adapted and modified from [3]

modeling because its governing equation is independent of time, contrary to functional reentry depending on time or at least some hypotheses on the time interval in conduction delay.

As a consequence, we aim to provide mathematical models for the PV reentries but in this paper we only focus on anatomical reentry. To achieve this goal, we introduce a new analytic tool for geometrical analysis called the *relative acceleration approach* in the perspective of *trajectory*, as well as proven computational schemes for computational simulations of atrial reentry to solve the FitzHugh–Nagumo equations on curved surfaces [31].

1.1 Trajectory instead of wavefront

A mathematical analysis of the action potential, or in general the wave propagation in excitable media, was first introduced by means of the kinematics of the wavefront, known as the *kinematics approach*, to analyze the effects of the geometrical shape or anisotropy on the behavior of excitation propagation. The kinematic equation defines the relationship between the curvature of the wavefront and its arc length on curved surfaces to derive the conditions of the *critical curvature*, or the critical amount of line curvature of the wavefront, which results in breaking up the propagation. The kinematics approach has been successfully used to describe the geometrical effects on surfaces such as non-uniformly curved surfaces [32], periodically modulated curved surfaces [33] and toruses [34] as well as ring-shaped propagation on curved surfaces [35] and propagation on moving excitable media [36]. In addition, this approach was also used to analyze the role of anisotropy in the plane: the breakup of the propagation [37] and the propagation of curved fronts in anisotropic excitable media [38]. Recently, a kinematic study using the curvature of the wavefront was adapted in various ways for cusp waves [39], scroll wave filaments [40] and accurate eikonal-curvature relation [41]. However, when considering both anisotropy and curved surfaces as the actual cardiac structure, the kinematics analysis becomes very complicated, even on the simplest curved surface. Consequently, the *higher-dimensional* anisotropic space, which is a more realistic approximation of the atrium and ventricle, seems to remain beyond the scope of the kinematic analysis.

To overcome this problem in cardiac action potential propagation, the new approach uses the concept of the *trajectory* as the path of a particle of the wave in classical mechanics, instead of the *wavefront* in the kinematic approach. This implies that the propagation delivering the electric signal to cardiac cells will be regarded as a *wave*. If we put a particle on the wavefront of the cardiac action potential at time t_0 , the continuous observation of the particle in time $t > t_0$ generates a trajectory. Consequently, in homogeneous media, the direction of the trajectory is orthogonal to the direction of the wavefront. Note that the kinematic approach focuses on the shape of the wavefront while the relative acceleration approach focuses on the distance between the trajectories. From this perspective, the relative acceleration approach can be regarded as a complementary method to the kinematics approach and vice versa, since the distribution of the trajectories reflects the shape of the wavefront. Nevertheless, we will show that the relative acceleration approach can be expressed much more concisely for anisotropic curved surfaces and a higher-dimensional anisotropic space.

The mathematical definition of the trajectory will be given more rigorously in Section 2, but the physical meaning of the trajectory can be ambiguous in the cardiac action potential. The concept of the trajectory requires the presence of traveling particles but the existence of any particle propagating through myocardial tissues on a macroscopic scale is unknown. There are complex microscopic movements of ions, such as Na^+ , K^+ , Cl^- , Ca^{2+} , through

ion channels and gap junctions but it has been unknown that certain kinds of ions can be identified as traveling particles. However, in the neighborhood of every point on a sufficiently smooth surface, a trajectory can be uniquely constructed by a smooth wavefront, which is well-defined clinically and mathematically. This is another reason we stick to sufficiently smooth surfaces so that the physical concept of the trajectory should remain the same as any other physical wave involving particle motion.

1.2 Justification on the use of curved surfaces and its properties

In the rest of this paper, the relative acceleration analysis will be given only for curved surfaces. The justification of the use of the surface for the domain is clear from the anatomical property of the PV and the thin layer of the atrium, which we are mostly interested in. Contrary to the ventricles that have an average thickness from 12.0 to 15.0 mm for an adult heart [42], the left atrium is a thin-wall structure with an average thickness of 1.89 ± 0.48 mm ranging from 0.5 to 3.5 mm [43, 44]. The question, therefore, remains whether the atrium can be uniformly approximated as a curved surface. On the other hand, the PV is well modeled as a curved surface. Hocini et al. [45] established that the cardiac tissues of the PV are thickest close to the atrium and thinner toward the lung, ranging approximately from 0.5 to 0.8 mm, which is relatively constant and less than half the average thickness of the left atrium. The aim of the following computational model is to simulate and observe the behavior of the propagation in the area of the PV; thus it is justifiable to model the atrium with the PV by a smooth curved surface. However, this does not mean that the relative acceleration analysis and the method of moving frames are only valid for two-dimensional space. The extension to higher dimensional anisotropic space can easily be derived and will be reported in later publications.

For the sake of simplicity of analysis, we suppose that the curved surface that will be used in the remaining of this paper is *two-dimensional manifold* and *locally Euclidean*. Roughly stated, a curved surface is a two-dimensional manifold in the sense that, for the neighborhood of each point on the curved surface, there exists a one-to-one representation of each curved element onto a simply connected region of the Euclidean plane [46]. Moreover, the curved surface is locally Euclidean in the sense that the curved element can be represented as a small domain of the Euclidean space in a small neighborhood of any point [47]. Rigorous mathematical definitions will not be repeated here but can be found in the cited references. For example, the surface of revolution, or any surface that is isometric to the surface of revolution, is always manifold and locally-Euclidean. This supposition yields the direct consequences of the following properties of the surface that we frequently use in this paper. (i) The first is *the existence of a pair of orthogonal curved axes at every point*, which are referred to as a *surface of an orthogonal net* and (ii) the second is that *scalars, vectors and tensors are locally continuous and differentiable*.

Since all the derivations and definitions are achieved in a curved element of arbitrary size from a tessellation of the curved surface, the above properties should be well defined *locally* but not necessarily *globally*. For example, the existence of the orthogonal curved axis, the existence of the orthogonal diffusivity tensor and the existence of the trajectory for a smooth wavefront can be easily justified *point-wisely* because the surface is assumed to be locally Euclidean. Accordingly, the quantities and equations in the following sections are given locally within a small Δx from each point. Since the use of the surface of an orthogonal net has been standard in studying waves on curved surfaces [48, 49], we do not need further mathematical justification for this supposition. Biologically, this is also *acceptable* because the shape of the cardiac tissue of the atrium and the PV is normally regarded as smooth,

and because the action potential propagates when the tissue is expanded, and thus the tissue is likely to be smooth everywhere. Moreover, we will make the problem more generally applicable by using a *locally* orthogonal curved surface rather than a curved surface with globally continuous orthogonal curved axes. Moreover, in the rest of the paper, we suppose that there exists a unique trajectory in the neighborhood of a point p on the sufficiently smooth wavefront on the curved manifold. A rigorous definition of trajectory in the context of classical mechanics and the proposition of the existence and uniqueness of trajectory for each point are shown in Appendix A.

1.3 Goal, notations and order of the paper

The goal of this paper can be summarized as follows: (i) The eikonal equation for action potential propagation is derived on anisotropic curved surfaces. (ii) The curvature flow of the action potential propagation is expressed and its component is identified for possible conduction failure. (iii) The relative acceleration analysis is proposed and validated from computational simulations or known results from kinematic analysis. (iv) The proposition that the PV can be a unidirectional block is analytically proved from the proposed analysis and its computational validations are provided. (v) The reentry mechanism predicted by the proposition is simulated in a simplified PV and atrium structure.

The *wavefront* refers to the isochrone of the depolarization phase in cardiac action potential while the *propagational direction* refers to the direction of the excitation propagation in line with the velocity vector and is orthogonal to the direction of the wavefront in isotropic media. The propagational direction at a point p at the wavefront represents the infinitesimal change of p during an infinitesimal time interval. Anisotropy has one direction reflecting the continuous alignment of the myocardial fiber and will be denoted as x^m -anisotropy to represent the anisotropy that is aligned along the x^m -axis and only one component of the diffusivity is different from 1.0. But, anisotropy can also be represented as *both directions* if both components of the diffusivity tensor are different from 1.0, to represent the discontinuous alignment of the fiber that can be approximated as an isotropic material with a different conductivity. The domain and the propagation behavior are on a macroscopic scale if not mentioned otherwise. The following notations are used in this paper. The (double) subscript and (double) superscript indexes mean that the corresponding quantity is a covariant and contravariant tensor, respectively. In principle, scalars are represented with a regular font

Table 1 Definitions and notations I

$P_i, P_i(j)$	i th trajectory, j th point in the i th trajectory
$S_j, S_j(i)$	j th wavefront, i th point in the j th wavefront
λ	Affine parameter to parameterize the trajectory
n	Selector parameter to parameterize the wavefront
y^1	Trajectory with sufficiently small curvature
y^2	Wavefront with sufficiently small curvature
x^k	Orthogonal curved axis
z^i	Cartesian coordinate axis
Π	curved surface
π^e	curved element indexed e such that $\Pi = \cup_e \pi^e$

Table 2 Definitions and notations II

d^{kk}	diffusivity coefficient in the curved axis
ς^{kk}	Diffusivity coefficient in the Cartesian coordinate
c_r	Speed function of the action potential propagation
J	Jacobian from the y^j -axis to the x^k -axis
Λ^k	$\partial y^1 / \partial x^k$
U^k	Tensor defined as $\Lambda^k \sqrt{g} d^{kk}$
E^k	Tensor defined as $\Lambda^k U^k / \sqrt{g}$
S_{kk}	Non-symmetric Ricci-type tensor in Eq. (16)
G_{kk}	Gravitational tensor due to anisotropy in Eq. (19)

without any index and vectors are represented with a bold font but a scalar variable with an upper index, as the component of a vector, is also used to indicate that the corresponding quantity is a vector. The lists of frequently used notations and definitions are displayed in Tables 1 and 2.

The remaining sections are organized as follows: In Section 2, the hypothesis is proposed on the stopping condition of the propagation and consequently the relative acceleration equation is derived. Section 3 derives the relative acceleration equation from the FitzHugh–Nagumo equations on anisotropic curved surfaces. In Section 4, the geometric characteristics of the PV are described and the relative acceleration equation is applied to a model of the PV. Section 5 displays validations of the proposed model computational simulations of reentry and previous *in silico* studies. Discussions including restrictions and future works follow in Section 6.

2 Stopping conditions by relative acceleration

Before proceeding further to the relative acceleration equation, we will briefly describe the meaning of relative acceleration in the bundle of trajectories and explain how this can be translated into the conduction failure of the cardiac action potential propagation. Consequently, this section aims to provide the background and justification of the proposed hypothesis, which plays a critical role for the rest of the analysis, from discrete models similar to cellular automata [50]. The validity of the hypothesis, based on the crucial characteristics of the action potential propagation, is obviously independent of the scale of the system but the proof remains challenging and beyond the scope of this paper. Thus, we just leave it as a hypothesis for later rigorous validation. First, let us mathematically define trajectory as follows:

Definition Let $v = (v^1, v^2, v^3)$ be the velocity of the propagation at the point $p \in \Pi$, which is embedded in $\mathbb{R}^3 = \mathbb{R}^3(z^1, z^2, z^3)$. Then, define the trajectory P of the vector field by the following differential equations:

$$\frac{dz^1}{v^1} = \frac{dz^2}{v^2} = \frac{dz^3}{v^3}.$$

Consequently, the trajectory of the cardiac action potential propagation is naturally defined by deriving the tangent vector.

Fig. 2 Three different cases of relative acceleration in the normal direction. n^i is the separation vector connecting the same λ for the trajectories

Let P_0 be a trajectory that is assigned to be fiducial. In the neighborhood of P_0 , consider the other trajectories P_k for $k = \pm 1, \pm 2, \pm 3, \dots$ (Fig. 2). All the trajectories are given the same affine parameter λ so that $P_0(\lambda)$ and $P_k(\lambda)$ lie on the same wavefront S_λ . In other words, the *relative acceleration* of P_0 measures how $P_0(\lambda)$ advances with respect to other $P_k(\lambda)$. Two kinds of relative acceleration can be considered: the first relative acceleration is in the *propagational direction* and the second relative acceleration is in the direction of the wavefront, or in the *normal direction*. Relative acceleration in the propagational direction is obvious. Suppose that the trajectories are all parallel. If the rate of changes of $\|P_0(\lambda) - P_0(\lambda - 1)\|$ is more than the first order compared to the other trajectories, then P_0 is said to be *relatively accelerated in the propagational direction*.

On the other hand, the relative acceleration in the normal direction should be considered for three different cases: let us suppose that the rate of change $\|P_k(\lambda) - P_k(\lambda - 1)\|$ is the same for all the trajectories. First, when all trajectories are parallel as shown in Fig. 2a, the change of the separation vectors (as defined below) along each trajectory is zero; thus there is no relative acceleration in the normal direction. Secondly, if the trajectory P_0 linearly diverges from the other trajectories as shown in Fig. 2b, then the first derivative with respect to λ is non-zero but the second derivative is still zero. Consequently, there is no relative acceleration in the normal direction, either. However, if the trajectory P_0 diverges quadratically from the other trajectories as shown in Fig. 2c, neither the first nor the second derivative is nontrivial; thus the trajectory P_0 is said to be *relatively accelerated in the normal direction*.

More rigorously in mathematics, we use the following definition of relative acceleration [51], which is equivalent to what has been explained:

Definition For a smooth curved surface Π , let $\mathbf{n}_i \in \Pi$ be the separation vector to indicate how one fiducial trajectory is separated from another for the same affine parameter λ . If the separation vector $\mathbf{n} = \{\mathbf{n}^i\} \in \Pi$ is defined such that:

$$\mathbf{n}(i, k) \equiv \lim_{\Delta n \rightarrow 0} S_k(i + \Delta n) - S_k(i), \quad (1)$$

then the relative acceleration can be expressed as:

$$\text{Relative acceleration} \equiv \frac{\partial^2 \mathbf{n}}{\partial \lambda^2} = \left\{ \frac{\partial^2 n^i}{\partial \lambda^2} \right\}. \quad (2)$$

Note that the term *relative* is only relevant to the trajectory, not to the propagational velocity. The relative acceleration of trajectory indicates the changes of the propagational velocity along the wavefront, thus the relative acceleration is a point-wise value at the wavefront

Fig. 3 The smooth curve P_i is the trajectory with an affine parameter λ and the smooth curve S_j is the wavefront with the selector parameter n (left). y^1 : direction of the propagation, y^2 : direction of the wavefront (right)

and does not indicate the relative velocity compared to the propagational velocity of the neighboring points.

A brief intuitive justification of the use of relative acceleration is provided in Appendix B. We use the fact that the stopping conditions of the cardiac action potential propagation in the discrete models, known as impedance mismatch or sink-source mismatch [52, 53], can be translated as a large relative acceleration in continuous waves. In Fig. 14e, a high ratio between excited cells and excitable cells is interpreted as the abrupt expansion of the distances between the trajectories, which can be described as a large relative acceleration in the normal direction, that is, a non-uniform rate of change of speed along the wavefront. In homogeneous media, this means that the distance between particles continues to diverge along the wavefront as the wave propagates. On the other hand, Fig. 14g represents the wavefronts and trajectories of the second stopping condition where we observe a relative acceleration in the propagational direction instead of the spreading-out of the trajectories. If the acceleration occurs in the direction of the wavefront, then a large relative acceleration of trajectory seems to result in the deceleration of the propagational velocity. If the acceleration occurs in the propagational direction, then a large relative acceleration of trajectory seems to result in the acceleration of the propagational velocity but if the magnitude is sufficiently large, it leads to conduction failure. Without regarding the directions of relative acceleration, conduction failure (stopping condition) for the cardiac action potential propagation can be expressed as the following hypothesis:

Hypothesis A sufficiently large relative acceleration of the cardiac action potential propagation causes conduction failure in homogeneous and anisotropic myocardial tissues.

This hypothesis may not hold in inhomogeneous media such as damaged or malfunctioning myocardial tissue but has no restriction on the dimension of space or the changes of the conducting velocity. In spite of the clear mechanism relating to relative acceleration, the complexity of the rigorous mathematical proof of this hypothesis forces us to choose whether this hypothesis is valid or even preferred only by the results that it can produce, coincident with previously known conditions or computational simulations.

3 Deriving the relative acceleration equation

For a smooth curved surface Π with anisotropy, suppose that Π is a two-dimensional manifold that can be divided into a finite number of regions for a one-to-one map from a simply

connected region of the Euclidean plane. Moreover, we suppose Π is a surface of an orthogonal net with two orthogonal axes (x^1, x^2) and the corresponding metric tensor g_{ij} . Consider piecewise orthogonal surfaces π^e from the tessellation of the surface Π such that:

$$\Pi = \left\{ \cup_e \pi^e \mid \pi^i \cap \pi^j = \delta_j^i \right\}, \quad (3)$$

where i, j is the index for π^e and δ_j^i is the Kronecker delta. Note that each π^e being equipped with the orthogonal axis x^k constitutes the surface Π with two orthogonal axes everywhere but x^k can be discontinuous across the interfaces of π^e . The cardiac excitation propagation on anisotropic curved surfaces can be modeled by the following Fitzhugh–Nagumo (FHN) equations [35, 54, 55]: in $\mathbf{x} \in \pi^e$:

$$\frac{\partial u(x)}{\partial t} = \frac{1}{\sqrt{g}} \sum_{\alpha, \beta=1}^2 \frac{\partial}{\partial x^\beta} \left(\sqrt{g} d^{\beta\alpha} \frac{\partial u(x)}{\partial x^\alpha} \right) + F(u, v), \quad (4)$$

$$\frac{\partial v(x)}{\partial t} = G(u, v), \quad (5)$$

where g is the determinant of the metric tensor g_{ij} . The variable u is an activator and represents the membrane potential, while the variable v is an inhibitor and represents the ion channel openness or the refractoriness. The following analysis is independent of choice of the functions $F(u, v)$ and $G(u, v)$ for the shape of the cardiac action potential. For example, we may use the following functions [56]:

$$F(u(x), v(x)) = c_1 u(u - \alpha)(1 - u) - c_2 v, \quad (6)$$

$$G(u(x), v(x)) = b_1(u - b_2 v). \quad (7)$$

The constants a, b_1, b_2, c_1, c_2 determine the excitability of myocardial tissues but in the rest of this paper, we assume that these variables remain constant in every π^e and consequently in the global domain Π . Thus, inhomogeneity is not considered in this paper. As for anisotropy, we only consider the simple anisotropy that is aligned along one of two axes so that the diffusivity tensor $d^{\beta\alpha}$, written in the orthogonal curved axis x^α , is expressed as:

$$d^{\beta\alpha} = d^{\beta\alpha} \delta_\alpha^\beta = \begin{cases} d^{\alpha\alpha}, & \text{if } \alpha = \beta \\ 0, & \text{otherwise} \end{cases} \quad (8)$$

The justification of this diffusivity tensor is obvious because domain Π is a locally Euclidean manifold and the cardiac fiber always has a certain orientation in the neighborhood of every point of π^e . Moreover, the existence of this diffusivity tensor is only enforced in π^e , not globally in Π , thus mathematically this is not a strong restriction if two curved axes are chosen arbitrarily in π^e . The above equality is made possible in the orthogonal curved axis since the diffusivity tensor $d^{\beta\alpha}$ is regarded as a covariant tensor of rank 2, the same as the conjugate metric tensor $g^{\beta\alpha}$. This is justifiable in tensor calculus [57, 58] and in the context of Riemannian geometry of the cardiac tissue [59]. With this diffusivity tensor, Eq. (4) is simplified as:

$$\frac{\partial u}{\partial t} = \frac{1}{\sqrt{g}} \sum_{\alpha=1}^2 \frac{\partial}{\partial x^\alpha} \left(\sqrt{g} d^{\alpha\alpha} \frac{\partial u}{\partial x^\alpha} \right) + F(u, v). \quad (9)$$

The FHN equations derived in Eqs. (9) and (5) model the cardiac excitation propagation on anisotropic curved surfaces. In order to align the trajectory and the wavefront along each axis in π^e , the following supposition will be required:

Supposition For an orthogonal curved axis x^β at a point $p \in \pi^e$, the curvature of the trajectory y^1 and the wavefront y^2 with respect to x^β is sufficiently small to satisfy, for $\alpha, \beta = 1, 2$:

$$\left\| \frac{\partial}{\partial y^\alpha} \left(\frac{\partial y^\alpha}{\partial x^\beta} \right) \right\| < \varepsilon \ll 1. \quad (10)$$

This supposition implies that the following analysis is only valid when the wavefront is slightly curved. If we consider the procedure of the break-ups of the wavefront as the increase of the curvature up to a critical value (see Appendix B for more details), the use of this supposition means that we are only concerned with the initial deformation of the wavefront, which will eventually lead to the break-ups. This causality is supported by the acceleration term in the relative acceleration approach as shown in the latter part of this paper. In fact, this supposition has been frequently used in the kinematics approach, as shown in refs. [32, 35, 60], to omit the high-order correction terms. The normal propagation velocity V of a curved wavefront is represented by a linear function $V = V_0 - Dk$, where D is the diffusivity constant and k is the curvature of the wavefront. Then, we obtain the following proposition.

Proposition 1 *Suppose that the curved surface Π is a locally-Euclidean manifold. Then the relative acceleration equation of the FHN equation for Π is given by:*

$$-E^k \frac{\partial^2 n^i}{\partial \lambda^2} = \frac{\partial}{\partial n} \left(\frac{1}{\sqrt{g}} \frac{\partial \cup^k}{\partial x^k} v^i \right) + \frac{\partial E^k}{\partial n} \left(\frac{\partial v^i}{\partial \lambda} + \frac{\partial^2 \psi}{\partial z^i \partial z^j} v^j v^i \right) + \frac{\partial (c_r v^i)}{\partial n}. \quad (11)$$

where each component on the right-hand side is only dependent on the coordinate axis, not on the initiation of the propagation or the time variable. Thus, the above equation is suitable for the study of anatomical reentry. If the magnitude of Eq. (11) is sufficiently large at the point $p \in \Pi$, then the action potential propagation stops and conduction failure occurs in the neighborhood of the point p .

Proof see Appendix C. □

The large magnitude of the right-hand side in Eq. (11) can also mean a large relative deceleration of trajectory, but the use of an anisotropy larger than 1.0, meaning a faster conducting velocity than normal tissue, rules out the case of a large deceleration of trajectory in the propagational direction. Bear in mind that a large deceleration of trajectory corresponds to a large acceleration of the propagation velocity if the acceleration occurs in the direction of the wavefront. Thus, independent of the direction of deceleration, the propagation does not stop. Note that the relative acceleration does not have to occur in a large area simultaneously for conduction failure but it suffices for it to occur only at one point since the propagational failure can subsequently diffuse from one point to other points along the wavefront. This can be easily pictured by the game explained in Appendix B.

3.1 Analysis of each component in Eq. (11)

In this section, we study each component to verify which component is the major contributor to the magnitude of the relative acceleration.

- (1) **Velocity along the wavefront:** Taking into account the fact that the propagation is slowly varying (as frequently used in biological propagation as well as in cardiac electrophysiology [61]), the supposition (10) on the small changes of deformation with respect to the curved axis also implies the relatively small variations of the traveling velocity c_r along the wavefront. Moreover, this supposition is another expression of the constant magnitude of the tangent vector, so we notice that the last term of Eq. (11) is also sufficiently small, i.e.,

$$\frac{\partial (c_r v^i)}{\partial n} < \varepsilon \ll 1. \quad (12)$$

- (2) **Static electric force and acceleration by media:** The component $(\partial^2 \psi / \partial z^i \partial z^j)$, the twice differentiation of ψ with respect to the spatial coordinates, indicates the magnitude of the static electric force produced by the shape of the cardiac action potential. In consideration of the smooth and uniform shape of the cardiac action potential and the relatively weak amount of electric voltage, the static force is relatively small and uniform along the wavefront compared to other dynamic forces. However, the acceleration term is not trivial because of the presence of anisotropy. For the same reason, $\frac{\partial E^k}{\partial n}$ is not trivial either. Thus, again resorting to the small deformation of the wavefront, the second term can be approximated as:

$$\frac{1}{E^k} \frac{\partial E^k}{\partial n} \left(\frac{\partial v^i}{\partial \lambda} + \frac{\partial^2 \psi}{\partial z^i \partial z^j} v^j v^i \right) \approx \Lambda^k \frac{\partial (\log d^{kk})}{\partial n} \frac{\partial v^i}{\partial \lambda}. \quad (13)$$

- (3) **Curvature flow:** For simplicity, first consider the case $d^{kk} = g^{kk}$. Let the index m indicate another index different from k such that $k \neq m$. With the same property of the propagation as used in Eq. (12), the first term in Eq. (11), after being divided by E^k , is derived as:

$$\frac{1}{E^k} \frac{\partial}{\partial n} \left(\frac{1}{\sqrt{g}} + \frac{\partial \cup^k}{\partial x^k} v^i \right) = \frac{g_{kk}}{\Lambda^k} \frac{\partial}{\partial x^m} \left[\frac{1}{\sqrt{g}} \frac{\partial}{\partial x^k} \left(\frac{g_{mm}}{\sqrt{g}} \right) \right] v^i. \quad (14)$$

Note that the above tensor is very similar to the Ricci curvature tensor, which is obtained from the Riemannian curvature tensor $\mathcal{R}_{\gamma\alpha\beta\delta}$ on curved surfaces [62]:

$$\mathcal{R}_{\alpha\beta} = - \left(\frac{g_{\alpha\beta}}{g} \right) R_{1212} = \frac{g_{\alpha\beta}}{2\sqrt{g}} \sum_{k=1}^2 \frac{\partial}{\partial x^k} \left[\frac{1}{\sqrt{g}} \frac{\partial g_{mm}}{\partial x^k} \right].$$

Since the only significant difference is the differentiation of x^m for the bracket, not x^k , this means that if we differentiate Eq. (27) with respect to the affine parameter λ , we obtain the Ricci curvature tensor. Due to this similarity, we may define non-symmetric Ricci-type tensor S_{kk} , by considering the original Ricci tensor as symmetric, such that:

$$S_{kk} \equiv g_{kk} \frac{\partial}{\partial x^m} \left[\frac{1}{\sqrt{g}} \frac{\partial}{\partial x^k} \left(\frac{g_{mm}}{\sqrt{g}} \right) \right]. \quad (15)$$

In this case, Eq. (14) becomes:

$$\frac{1}{E^k} \frac{\partial}{\partial n} \left(\frac{1}{\sqrt{g}} \frac{\partial \cup^k}{\partial x^k} v^i \right) = (\Lambda^k)^{-1} S_{kk} v^i. \quad (16)$$

For general diffusivity tensors, we consider $d^{kk} = \varsigma^{kk} g^{kk}$ where ς^{kk} is the diffusivity coefficient in the plane of which Cartesian coordinate axis is mapped from each x^k . This construction of the diffusivity tensor can be easily verified for a surface of an orthogonal net. The reason we separate the diffusivity coefficient from the conjugate metric tensor is to construct the same strength of anisotropy independent of curvature. As a consequence, ς^{kk} is constant for all the anisotropy, while d^{kk} is not constant, coincident with the clinical observations. Now, Eq. (14) is expressed as:

$$\frac{1}{E^k} \frac{\partial}{\partial n} \left(\frac{1}{\sqrt{g}} \frac{\partial \cup^k}{\partial x^k} v^i \right) = (\Lambda^k)^{-1} [S_{kk} + \mathcal{G}_{kk}] v^i, \quad (17)$$

where we introduce the new tensor $\mathcal{G}_{kk}$ that is defined as:

$$\mathcal{G}_{kk} \equiv \frac{1}{\varsigma^{kk}} \frac{\partial^2 \varsigma^{kk}}{\partial x^k \partial x^m} + \left(\frac{\partial \log g^{kk}}{\partial x^m} + \frac{\partial \log g^{mm}}{\partial x^k} + \frac{1}{2} \frac{\partial g}{\partial x^k} \right) \frac{\partial \log \varsigma^{kk}}{\partial x^k}. \quad (18)$$

The first component is the second-order differentiation of the diffusivity coefficient with respect to the axis and consequently means the gravitational force induced by anisotropy. The second component is the first-order differentiation of $\log \varsigma^{kk}$ with respect to the axis multiplied by the change of the metric tensor in the neighborhood. Thus, we may refer to $\mathcal{G}_{kk}$ as a gravitational tensor, similarly used in the context of spacetime physics [51].

By combining Eqs. (12), (13) and (17), we obtain the new approximation of the relative acceleration Eq. (11):

$$-\Lambda^k \frac{\partial^2 n^i}{\partial \lambda^2} = [S_{kk} + \mathcal{G}_{kk}] v^i + \frac{\partial (\log d^{kk})}{\partial n} \frac{\partial v^i}{\partial \lambda}. \quad (19)$$

The first component represents the relative acceleration induced by the velocity v^i , while the second component represents the relative acceleration induced by the acceleration $\frac{\partial v^i}{\partial \lambda}$. Therefore, we have the following proposition:

Proposition 2 *In an isotropic locally-Euclidean manifold, the conduction failure of the action potential propagation only happens when the Ricci-type tensor S_{kk} for the curvature flow on the surface is sufficiently large. In an anisotropic locally-Euclidean manifold, the conduction failure can happen, regardless of S_{kk} , when the acceleration caused by anisotropy is sufficiently large or when the gravitational tensor $\mathcal{G}_{kk}$ induced by anisotropy is sufficiently large.*

Nevertheless, for simple curved surfaces that are frequently observed in cardiac structure, conduction failure by S_{kk} seems to be very rare or even impossible according to numerous observations and analyses leading to the following conjecture.

Conjecture If cardiac tissue lies on a locally-Euclidean manifold, then conduction failure can be only caused by anisotropy, not by the curvature flow S_{kk} .

This means that conduction failure cannot be solely caused by the curvature of the surface. A rigorous mathematical proof of this conjecture is not necessary for the remaining

analysis and is beyond the scope of this paper. Instead, this conjecture can be exemplified by several models in the following sections. Appendix D also displays that the relative acceleration Eq. (19) provides quantitatively effective predictions on the behavior of the action potential propagation. On various anisotropic curved surfaces such as plane, sphere, and torus, the analyses by Eq. (19) coincide with the results by the kinematic approaches. Even for more complex anisotropic surfaces for which the kinematic approach becomes too complicated to analyze, the relative acceleration analysis also explains the conditions of conduction failures of the computational simulations. We may not determine the exact magnitude of anisotropy or the exact radius of the curved lines to cause conduction failure but we can understand the effect of anisotropy, i.e., whether it increases the curvature of the surface leading to possible conduction failure or whether it compromises the critical curvature to guarantee propagation.

4 Geometric analysis on the PV with anisotropy

In the following analysis, we suppose that the PV and some part of the atrium in the neighborhood of the PV are a locally-Euclidean manifold. Also, we suppose for some cases that anisotropy in these areas is continuously aligned. This supposition may be viewed as a convenient simplification from the real cardiac anatomy but this geometry seems to provide sufficient analytical explanations of the reported behavior of the action potential propagation on the PV. Thus, in the remainder of this paper, we do not consider other factors such as the variable depth of the tissue, the complex alignment of anisotropy, irregular curvature or the location of the PV, which may or may not contribute to the critical behavior of the propagation.

4.1 Geometric characteristics of the PV

As explained in the introduction, the PV can be well approximated as a surface but the three-dimensional shape of the PV is very peculiar in the following ways:

[G-i] The PV has a different exterior curvature compared to that of the atrium.

Even when the shape of the atrium is approximated as a smooth surface, the PV should be constructed as a separate surface and should be planted on the atrium as a smooth column on a sphere without stretching it. This means that the intrinsic curvature of the PV can be similar to that of the atrium, while the exterior curvature of it is very different. This is possible because the shape of the PV can be constructed by cutting, pasting, and/or turning inside out some part of the atrium without stretching. Mathematically speaking [63], the Gaussian curvature of the PV can be approximately the same as that of the atrium, but the mean curvature can be strikingly different from that of the atrium.

[G-ii] The anisotropy of the PV contains at least one discontinuity.

The real atrium has multiple pulmonary veins (four for the human atrium and five or six for the canine atrium), not even mentioning the PV-like geometries such as the inferior vena cava, the superior vena cava, the coronary sinus and possibly the valve annuli. Consequently, analogous to the Hairy-Ball theorem [64], it is geometrically impossible to construct a continuous distribution of anisotropy at all interfaces between the PVs and the atrium. This problem is similar to the mathematical construction of a continuous and differentiable vector field on a connected curved surface with n holes, for example, eight holes for the human

atrium. As a consequence, the discontinuities of anisotropy inevitably happen at any point of the atrium, but according to anatomical observations they normally appear close to the root of each PV. Hocini et al. [45] reported that the anisotropy of canine PVs abruptly changes its direction or is aligned in mixed orientations at the root of the PVs but it is aligned along the longitudinal direction as the vein gets closer to the lung. Also, Verheule et al. [65] reported the circumferential orientation of anisotropy in a vein of the canine atrium being sectioned transversely at various tips of the PV sleeves. Note that the circumferential orientation of anisotropy in the PV also presupposes the discontinuity of anisotropy at some roots of the multiple PVs. It still remains a question of how to construct or approximate the mixed orientation of anisotropy but for the sake of simplicity we only consider the longitudinal anisotropy and/or the circumferential anisotropy that has discontinuities at the root of the PV.

[G-iii] Almost all the circumferential lines of the PV are not geodesic and consequently the propagation is not always parallel to the circumferential direction.

Let the circumferential line be aligned along the θ -axis in Fig. 4. If the propagation only follows the circumferential line, the behavior of the propagation is only affected by the θ -anisotropy. However, the propagation is not likely to follow the circumferential line all the time because the line is not geodesic in isotropic media and not likely to be geodesic even in anisotropic media. The circumferential path at $\theta = \pi/2$ is actually the only geodesic path in the PV because the tangent vector of the other generating curves is not parallel to the axis of revolution [66]. Consider the root of the PV when $\theta = 0$. When the propagation first reaches the root of the PV without any further acceleration due to anisotropy or curvature, the propagation does not follow the root of the PV because the propagation induced by diffusion naturally follows the geodesic path. As a consequence, the propagation climbs up to the middle or upper part of the PV through various θ and reaches the other end of the PV. In view of propagational angle, this means that the propagation should be at an oblique angle with the orthogonal axis at least at some points of the PV.

4.2 Surface of revolution for a modeling of the PV

For the modeling of the PV without compromising its above-mentioned geometric properties, a simple surface of revolution will be used as the geometric model of the PV in the plane as shown in Fig. 4. Consider a circular arc with radius R , located at r from the center of the column. The θ -axis is aligned along the circular arc and the ϕ -axis is aligned along the revolving direction. Note that the θ -axis lies in the longitudinal direction and the ϕ -axis lies in the circumferential direction. Revolve the circular arc around the

Fig. 4 Modeling of the PV by a surface of revolution. The ϕ -axis is in the circumferential direction of the column and the θ -axis is orthogonal to the ϕ -axis

x -axis, i.e., perpendicular to the plane to generate a smooth column on the plane that has the following parameterization of the surface x : For a $R, r \in \mathbb{R}^+$ and $0 \leq \theta \leq \frac{\pi}{2}, -\pi \leq \phi \leq \pi$:

$$x = (R(1 - \cos \theta), (R(1 - \sin \theta) + r) \sin \phi, (R(1 - \sin \theta) + r) \cos \phi).$$

As for anisotropy, a specific orientation of anisotropy can be chosen for some analyses, but we may also consider anisotropy aligned in both directions such that the diffusivity tensor $\mathbf{d}$ is expressed as $\mathbf{d} = \varsigma^{\theta\theta}\theta + \varsigma^{\phi\phi}\phi$. Biologically, anisotropy aligned in both directions may be regarded as media with complex conducting properties. For example, if $\varsigma^{\theta\theta} = \varsigma^{\phi\phi}$, then it is just isotropic media with a conductivity coefficient of $\varsigma^{\theta\theta}$. Moreover, the discontinuously aligned anisotropy can also be expressed as anisotropy of both directions, which can generally be approximated as an isotropic media of different conductivity velocity. From now on, the PV means this surface of revolution unless it is indicated specifically as the real PV.

The computational simulations in the following section were generated by an object-oriented spectral/hp library, namely Nektar++ [67], after being modified for the diffusion-reaction solver on curved surfaces by the method of moving frames [31].

4.3 Case I: Propagation towards the θ -axis

- (1) **PV with ϕ -anisotropy**: Consider a simple case where the propagation follows only the θ -axis of the PV. This type of propagation happens only if the propagation with the planar or convex wavefront reaches the facet of the PV. Let all the anisotropy of the PV be aligned in the circumferential direction such that $\mathbf{d} = \varsigma^{\phi\phi}\phi$, $\varsigma^{\phi\phi} > 1.0$ in the block of anisotropy and $\varsigma^{\theta\theta} = 1.0$ everywhere.

RA analysis The above conditions imply that $\Lambda^\theta = 1.0$, $\Lambda^\phi = 0.0$ and $\varsigma^{\theta\theta} = 1.0$ near the root of the PV, i.e., at $\theta \approx 0$. We then obtain the relative acceleration equation as:

$$-\frac{\partial^2 n^i}{\partial \lambda^2} = -\frac{1 - \sin \theta \left(1 + \frac{r}{R}\right)}{\left(1 - \sin \theta + \frac{r}{R}\right)^2} \left(\frac{\partial \theta}{\partial n}\right) v^i - \frac{\cos \theta}{1 - \sin \theta + \frac{r}{R}} \frac{\partial v^i}{\partial n}. \quad (20)$$

Being derived from the Ricci-type tensor S_{kk} , the magnitude of the first component is relatively small and bounded; thus we also consider the second component, which we normally neglect. Since $\partial v^i / \partial n$ is approximately aligned along the direction of the wavefront, we can say that the first component is in the propagational direction, and the second component is in the direction of the wavefront. Consider the above equation near the root of the PV at $\theta \approx 0$ implying $\frac{\partial \theta}{\partial n} \approx 0$ from $n \approx \phi$. Then, the first component becomes zero and the second component reduces to $\partial^2 n^i / \partial \lambda^2 = R / (R + r) \partial v^i / \partial n$. This indicates that there is no relative acceleration in the propagational direction when it is aligned along the θ -axis. However, a certain magnitude of the relative acceleration can be generated in the direction of the wavefront caused by the geometry of the PV. Because the sign of the second component is positive, this actually means a decrease in the propagational velocity.

Lemma 1 *The PV with ϕ -anisotropy decreases the speed of the action potential propagating along the θ -axis.*

Computational modeling Figure 5 validates this analysis. For the planar propagation approaching the PV from the right wall, the propagational speed decreases in the PV due to the relative acceleration in the direction of the wavefront caused by the geometry of the PV. But, conduction failure does not occur, possibly due to the absence of anisotropy. Since

Fig. 5 PV with the ϕ -anisotropy $\varsigma^{\phi\phi} = 8.0$ in the region of $0 \leq \theta \leq \pi/2$ (a). Initiated from the right wall, the action potential (u) at $T = 750.0$ (b), $T = 850.0$ (c) represents the slow-down of the propagation in the PV

the propagation follows the direction of anisotropy in the atrium with increased conduction velocity, the decrease of the conduction speed can be more dramatic in the actual atrium as in vivo observed by Arora et al. [1]. This phenomenon seems to confirm the dominance of the circumferential anisotropy in the actual PV as reported in ref. [65].

- (2) **PV with θ -anisotropy, RA analysis, and computational modeling:** We also consider the anisotropy that is aligned along the θ -axis such that $\mathbf{d} = \varsigma^{\theta\theta}\theta$, $\varsigma^{\theta\theta} > 1.0$ in the block of anisotropy and $\varsigma^{\phi\phi} = 1.0$ everywhere. However, for the sake of simplicity, we let $\varsigma^{\theta\theta}$ be constant along the ϕ -axis. Since these conditions can be expressed as:

$$\frac{\partial \varsigma^{\theta\theta}}{\partial \theta} \gg 0 \quad \text{and} \quad \frac{\partial \varsigma^{\theta\theta}}{\partial \phi} = 0$$

$$\frac{\partial \varsigma^{\theta\theta}}{\partial n} = \frac{\partial \varsigma^{\theta\theta}}{\partial \phi} \frac{\partial \phi}{\partial n} + \frac{\partial \varsigma^{\theta\theta}}{\partial \theta} \frac{\partial \theta}{\partial n} = \frac{\partial \varsigma^{\theta\theta}}{\partial \theta} \frac{\partial \theta}{\partial n},$$

with $\partial \theta / \partial n \approx 0$, we obtain the relative acceleration equation at the PV junction where $\theta = 0$ such that:

$$-\frac{\partial^2 n^i}{\partial \lambda^2} = \frac{\partial (\log \varsigma^{\theta\theta})}{\partial n} \frac{\partial v^i}{\partial \lambda} + \frac{1}{\varsigma^{\theta\theta}} \frac{\partial^2 \varsigma^{\theta\theta}}{\partial \theta^2} v^i + \left[\frac{\partial (\log \varsigma^{\theta\theta})}{\partial \theta} - \frac{R}{R+r} \right] \frac{\partial v^i}{\partial n}.$$

Fig. 6 PV with the θ -anisotropy $\varsigma^{\theta\theta} = 8.0$ in the region of $0 \leq \theta \leq \pi/2$ (a). Initiated from the right wall, the action potential (u) at $T = 650.0$ (b), $T = 750.0$ (c) displays the acceleration due to the anisotropy, but the general behavior is not much different from the propagation in the anisotropic plane

Observe that the first two components are the same as those in relative acceleration Eq. (29) for anisotropy in the plane as shown in Appendix D. The only additional factor is the last component, which represents the relative acceleration caused by the unique shape and the anisotropy of the PV. In the last component, $\partial (\log \zeta^{\theta\theta}) / \partial \theta$ has a nontrivial magnitude as shown in Fig. 15a of Appendix D, but is a negative value that is not summed up with the positive $R/(R+r)$. Intuitively, this component indicates that the relative acceleration in the direction of the wavefront is compromised by the θ -anisotropy. As a consequence, the relative acceleration does not significantly increase. Figure 6 displays that the geometry or the θ -anisotropy of the PV does not add a significant amount of additional relative acceleration to yield conduction failure.

Lemma 2 *The PV with θ -anisotropy does not significantly change the behavior of the action potential propagating along the θ -axis, compared to the propagation of the anisotropic plane.*

4.4 Case II: Propagation with an oblique angle

- (3) **PV with ϕ -anisotropy and θ -anisotropy:** Because of the geometric characteristics of the PV (G-iii) that the excitation always propagates at an oblique angle with the θ -axis, we must take into account both the ϕ -direction and the θ -direction to better understand the mechanism of the propagation in the PV. But the consideration of both directions without any simplification may bring incomprehensible complexity into the analysis, thus, for the sake of simplicity, we suppose that the propagational direction and the direction of the wavefront are locally uniform along the wavefront. In addition, although we consider both directions of anisotropy due to the second geometric characteristics of the PV (G-ii), we also suppose that the diffusivity tensor $\zeta^{\theta\theta}$ and $\zeta^{\phi\phi}$ remain constant along the wavefront in the PV. These simplifications can be regarded as reasonable considering the relatively small width of the myocardial tissue along the θ -axis of the PV and the periodicity of $\zeta^{\theta\theta}$ and $\zeta^{\phi\phi}$ along the ϕ -axis.

RA analysis The above conditions lead to the following mathematical expressions for Λ^θ , Λ^ϕ and $\mathbf{d}$ such that $\frac{\partial \Lambda^\theta}{\partial n} = \frac{\partial \Lambda^\phi}{\partial n} = 0$, $\frac{\partial \zeta^{\theta\theta}}{\partial n} = \frac{\partial \zeta^{\phi\phi}}{\partial n} = 0$ at the wavefront in the PV. Moreover, we consider that the propagational direction is at an angle $\mathcal{A}$ with the θ -axis such that $\Lambda^\theta = \cos \mathcal{A}$ and $\Lambda^\phi = \sin \mathcal{A}$ for $0 \leq \mathcal{A} \leq \pi$ and consequently $\partial \theta / \partial n = -\sin \mathcal{A}$. Then, the above equations can be expressed as the function of $\mathcal{A}$:

$$\frac{\partial^2 n^i}{\partial \lambda^2} = \frac{R^2 \sin \mathcal{A}}{\zeta^{\theta\theta} Q^2 \cos \mathcal{A}^2 + \zeta^{\phi\phi} R^2 \sin \mathcal{A}^2} \left[\zeta^{\theta\theta} \cos \mathcal{A} [R(1 - \sin \theta) - r \sin \theta] \right. \\ \left. \times v^i - 2\zeta^{\phi\phi} \sin \mathcal{A}^2 \frac{R \cos \theta}{Q} \frac{\partial v^i}{\partial \lambda} \right],$$

where we use the new variable $Q \equiv R(1 - \sin \theta) + r$ ignoring the $\partial v^i / \partial n$ component.

Consider the changes of the relative acceleration with respect to the longitudinal axis θ for a constant angle $\mathcal{A}$. For a simple comparison, we let $v^i = \partial v^i / \partial n = 1.0$ and use both anisotropies such that $\zeta^{\theta\theta} = \zeta^{\phi\phi} = 4.0$. With these conditions, we observe in Fig. 7 that the magnitude of the relative acceleration strongly depends on $\mathcal{A}$ and θ uniformly for

Fig. 7 Relative acceleration for $\mathcal{A} = \pi/6$ (a), $\mathcal{A} = \pi/3$ (b), $\mathcal{A} = \pi/2$ (c) versus the longitudinal axis θ with $v^i = \partial v^i / \partial \lambda = 1.0$ and $\zeta^{\theta\theta} = \zeta^{\phi\phi} = 4.0$

almost all r/R ratios. The distribution of the relative acceleration along $\mathcal{A}$ remains similar for $0 \leq \theta \leq \pi/4$ but it drastically changes for $\theta = \pi/2$. The structure of the PV is not symmetric at $\theta = 0$ and we observe different relative acceleration at $\theta = 0$ and $\theta = \pi$.

Also, each plot in Fig. 7 indicates the conditions for possible conduction failure according to the previously mentioned hypothesis and propositions. Contrary to the test cases for simple surfaces in Appendix D where the relative acceleration has been compared to zero acceleration, the relative acceleration at every point inside the PV is not zero but has non-trivial magnitude possibly with different signs. Thus, the magnitude of relative acceleration for conduction failure can be measured more conveniently if it is compared to that of the normal propagation in the neighboring region. For example, let us pay our attention to the region of $0 \leq \theta \leq \pi/4$, which represents the region of the PV from the root to the middle. We only consider this region for conduction failure because the propagation comes from the root of the PV around $\theta = 0$. For $\mathcal{A} = \pi/6$, the relative acceleration ranges from 0.095 to -0.207 for $r/R = 1.0$ with a 0.302 difference. For $\mathcal{A} = \pi/3$, it ranges more widely from -0.124 to -0.759 with a 0.635 difference. But this difference rapidly drops when $\mathcal{A} = \pi/2$, i.e., when the action potential propagates along the ϕ -axis. When $\mathcal{A} = \pi/2$, it ranges from -1.0 to -1.096 with a difference of 0.096 at most. Therefore, we may conclude that even if the action potential, which propagates with an angle close to $\pi/3$ or possibly up to $\pi/6$ depending on the magnitude of anisotropy, leads to conduction failure due to the PV, the action potential with $\mathcal{A} = \pi/2$ can propagate through the same PV of the same anisotropy without conduction failure.

Therefore, we confirm that the relative acceleration strongly depends on the propagational angle $\mathcal{A}$. Figure 8a displays the difference between the relative acceleration between $\theta = 0$ and $\theta = \pi/4$. We observe that the maximum magnitude occurs around the angle of $\pi/3$ and that there is a drastic decrease as it gets closer to $\pi/2$. However, the propagational angle is not the only factor. As displayed in Fig. 8b–c, not mentioning that the ratio between r/R , which indicates the three-dimensional shape of the PV changes relative acceleration, the magnitude of each anisotropy, i.e., $\zeta^{\theta\theta}$ and $\zeta^{\phi\phi}$, is also an important factor in relative acceleration. The impact of the changes of $\zeta^{\theta\theta}$ or $\zeta^{\phi\phi}$ seems to be restricted with a maximum reduction of approximately 10%. However, as shown in the computational modeling in the next section, this small change can make a significant impact on the role of the PV as a unidirectional block. Moreover, in more general cases without our simplified

Fig. 8 Relative acceleration difference between $\theta = 0$ and $\theta = \pi/4$ versus the propagational angle $\mathcal{A}$ (a), the magnitude of θ -anisotropy (b) and the magnitude of ϕ -anisotropy (c). Default values are taken as $\mathcal{A} = \pi/4$ and $\zeta^{\theta\theta} = \zeta^{\phi\phi} = 4.0$

assumptions on the wavefront, the role of $\zeta^{\theta\theta}$ and $\zeta^{\phi\phi}$ can be more significant. Thus, we have the following lemma:

Lemma 3 *If $\zeta^{\theta\theta}$ and $\zeta^{\phi\phi}$ are not sufficiently large, then the PV with both anisotropies cannot block the action potential propagating along the ϕ -axis even when the cardiac action potential propagation at an oblique angle with the θ -axis causes conduction failure.*

Computational modeling To demonstrate the validity of the above analysis, a T-shaped domain is designed by placing a PV in the middle of it. The left rectangle is $-150 \leq y \leq 0$ and $-70 \leq z \leq 70$, while the right rectangle is $-0 \leq y \leq 150$ and $-150 \leq z \leq 150$. At the center $(0, 0, 0)$, a PV is constructed with $R = 70$ and $r = 35$. Moreover, anisotropy is aligned with $\zeta^{\phi\phi} = \zeta^{\theta\theta} = 8.0$ in the area of $-30 \leq y \leq 0$ of the PV, which is defined exclusively in the range of $0 < x < 60$. With a point-initialization in the right rectangular domain, the only pathway to propagation to the left rectangular domain is through the PV with the θ -anisotropy and the ϕ -anisotropy. When the excitation is initiated at $(0.0, 100.0, 0.0)$ as shown in Fig. 9a, the anisotropy of the PV does not generate a sufficient relative acceleration to block the propagation, since the angle $\mathcal{A}$ seems to be close to $\pi/2$. As a consequence, the action potential propagates through the PV without conduction failure as shown in Fig. 9b–c. On the other hand, when the excitation is initiated at $(0.0, 100.0, 80.0)$ as shown in Fig. 10a, the excitation propagates toward the PV with an oblique angle $\mathcal{A}$, which is

Fig. 9 PV with anisotropy of $\zeta^{\theta\theta} = \zeta^{\phi\phi} = 8.0$ and the location of point initialization at $(0.0, 100.0, 0.0)$ (a). The action potential (u) at $T = 800.0$ (b) and $T = 1000.0$ (c) to show the propagation of the PV when $\mathcal{A} \approx \pi/2$

Fig. 10 PV with anisotropy of $\varsigma^{\theta\theta} = \varsigma^{\phi\phi} = 8.0$ and the location of point initialization at $(0.0, 100.0, 80.0)$ (a). The action potential (u) at $T = 600.0$ (b), $T = 850.0$ (c) to show the conduction failure when $\mathcal{A} \approx \pi/4$

more acute than the previous case and is possibly around $\pi/4$. As displayed in Fig. 10c, this acute angle $\mathcal{A}$ induces a large relative acceleration that causes conduction failure. Since the only difference between the two simulations is the location of point-initialization and subsequently the angle $\mathcal{A}$ toward the anisotropy in the PV, these models seem to confirm the previous analysis from the relative acceleration equation for the PV with anisotropy. By generalizing the lemma 3, we propose:

Proposition 3 *The PV can be a unidirectional block by an asymmetric excitation propagation toward the PV of which media induce a low conducting velocity.*

Proof This argument is directly given from lemma 3, which means that the PV may or may not cause conduction failure depending on the propagational direction toward the axis of the PV and/or the magnitude of the anisotropy of both directions. Moreover, due to the independence of time, the consequent reentry is anatomical reentry. $\square$

5 Validations and further applications

5.1 Computational validation of the proposed anatomically induced reentry [31]

In order to validate proposition 3, computational simulations will be referred to from ref. [31] to illustrate how 3D atrial reentry can be generated by a unidirectional block of the PV. The computational simulations are performed on a simplified surface with a PV-like column but are sufficient to demonstrate the key features of the PV as a unidirectional block to generate the reentry. On the surface of revolution to model a smooth atrium with the PV, scar tissue and anisotropy are also placed as shown in Fig. 11a. In reality, large solid scars do not frequently appear adjacent to the PVs, but for simplicity of modeling, scar tissues are placed in that region to provide an oblique and asymmetric angle of the propagation towards the PV. The role of scar tissue for the construction of a unidirectional block can be substituted by various ways. For example, a similar phenomenon can be observed if the geometry of the atrium changes abruptly to adjust the propagational direction or the width of anisotropy strip is moderately reduced even with the same magnitude of the anisotropic coefficient. The FHN mono-domain equations with the reaction functions (6) and (7) are solved to simulate the cardiac action potential propagation on this surface of revolution [56]. Considering the average height of the atrium is 5 cm, we note that the domain is at least

Fig. 11 Normal propagation at $T = 50.0$ (a), $T = 100.0$ (b), $T = 225.0$ (c), $T = 250.0$ (d). $\zeta^{\theta\theta} = \zeta^{\phi\phi} = 4.0$ for the anisotropic strips. Adapted from [31]

three times larger and five times wider than the actual size. This magnification of the size of the atrium is just for the convenience of adjusting the parameters for the desired phenomena; thus the consequence of this modeling is expected to be the same for the real size of the atrium in similar circumstances. For a detailed description of the model, refer to [31].

First, let the magnitude of the anisotropy in the PV be uniformly 4.0, i.e., $\zeta^{\theta\theta} = \zeta^{\phi\phi} = 4.0$. Figure 11 displays how the action potential propagation starts from the point of initialization and terminates at another point on the other side of the point of initialization. Because of scar tissue, the action potential propagates onto the PV with an oblique angle to yield two separate waves: the short wave on the left and the long wave on the right (Fig. 11b). An oblique angle with anisotropy prevents the short wave from propagating on the PV, only leaving the propagation on the right. On the other hand, the right wave has sufficient distance to align its propagational direction in the ϕ -direction for the right anisotropy: thus the propagation still remains on the PV. The two separate waves meet again at the back, but the collision of the two waves creates an oblique angle to anisotropy again and, consequently, the action potential fails to propagate through the anisotropy on the PV (Fig. 11c). Note that the left anisotropy blocks the propagation twice because the propagational angle of both cases is not close to $\pi/2$ or the magnitude of anisotropy is not sufficiently large; thus, it is not a unidirectional block. Without the propagation on the PV, the wave converges to a point (Fig. 11d). Because the propagation started from one point and terminates at one or two points, for example, at the right and left atrial appendage, we describe this pattern of propagation as the normal propagation.

If we change the magnitude of the anisotropy to be uniformly 3.0, i.e., $\zeta^{\theta\theta} = \zeta^{\phi\phi} = 3.0$ representing a slow conducting velocity in the neighborhood of the PV as reported in refs. [11–13], then the propagation appears almost the same until $T = 200.0$ (roughly 0.126 seconds after the initiation) as shown in Fig. 12a. Similar to the previous normal propagation, the short wave is blocked by anisotropy at the first time. However, the propagation of the collided wave significantly changes because of the weakened strength of the anisotropy.

Fig. 12 Modeling of anatomically-induced atrial reentry at $T = 195.0$ (a), $T = 225.0$ (b), $T = 250.0$ (c), $T = 300.0$ (d). $\zeta^{\theta\theta} = \zeta^{\phi\phi} = 3.0$ for the anisotropic strips. Adapted from [31]

Fig. 13 Perpetual propagation of anatomically-induced atrial reentry. Transparent view from the bottom at $T = 500.0$ (a), $T = 1000.0$ (b), $T = 1500.0$ (c), $T = 2000.0$ (d). Same conditions as Fig. 12

The collided wave at the back, with a less acute angle in the φ -direction, passes through the anisotropy as shown in Fig. 12b. In other words, because the collided wave at the back approaches the anisotropy at a more acute angle than during the first propagation toward the anisotropy, the changed magnitude of anisotropy fails to stop the propagation, contrary to the normal propagation.

Consequently, the propagation successfully proceeds throughout the left anisotropy strip; firstly, a wavebreak is generated with two singularity points and at least one of them turns into the center of the spiral wave. Then, a breakthrough, or a wave appearing as a point and propagating spirally thereafter, occurs to generate an additional incoming wave overriding the wave from the SAN [12]. Thus, this wave pattern represents the anatomically induced reentry. Figure 13 also displays the perpetual propagation of the cardiac action potential propagation in one direction to illustrate atrial reentry caused by this PV with the weakened anisotropy. This propagation is actually perpetual because it never terminates and self-initiates to override the SAN more than the approximate normal termination time of $T = 250.0$ or equivalently 1.58 seconds after the initiation. Contrary to the normal propagation, the left anisotropy blocks the propagation the first time but allows the collided wave to pass through the second time. This is exactly the same role as a unidirectional block to support proposition 3.

5.2 Comparison with other in silico studies by experimental data

In this subsection, we briefly compare the proposed reentry mechanism with the previously known computational simulations of atrial reentry in the pulmonary veins with experimental data and realistic geometry.

Cherry et al. [28] successfully simulated anatomically induced reentry from a single reentrant beat as well as functional reentry with a premature beat. The significant difference is that an asymmetry is produced by the randomized heterogeneity within the PV in [28], while asymmetry in our model is caused by a deterministic propagational direction toward the PVs. However, the conclusion of ref. [28] is similar to proposition 3. For example, the two parameters of the geometric shape of the PV were considered: one is the length of the PV and the other is the circumferential diameter of the PV. As seen in Fig. 4, the former is roughly represented by R and the latter by r , though the direct comparison may be not legitimate since the geometry of ref. [28] is just a cylinder attached to the plane that has no geometrical curvature. The dependency of the parameter r/R on relative acceleration and subsequently on the reentry is displayed in Figs. 7 and 8. One conclusion of [28] is that a smaller and shorter PV is unlikely to generate the reentry from numerous simulations. By the relative acceleration method, Figs. 7 and 8 imply that a higher ratio r/R generates higher

relative acceleration; thus a unidirectional pathway is impossible because the PV prevents the propagation in most directions. Thus, only the PV with a lower ratio of r/R can be more likely to be a unidirectional block leading to the reentry. A lower r/R means a larger diameter independent of the length; thus consequently the analysis of this paper coincides with [28] and clinical studies that arrhythmogenic PVs have larger diameters [68, 69]. Nevertheless, the proposition implies that the curvature of the PV can be a more crucial factor than the size of it though the size of the PV also changes the curvature.

Reentry in PVs was also simulated on an image-based model by Zhao et al. [29, 30] but was generated by repetitive stimulation with a reduced coupling interval; thus it is a functional reentry. Asymmetry is caused by a time-dependent refractory block, not an anatomical structure. Thus, a direct comparison is difficult. But, the abrupt changes in geometry and myofiber orientation in the PV sleeves are regarded as the most significant contributors in generating reentry, which is the same as the anatomically induced reentry proposed in this paper. Similar arguments can be applied to computational simulations by Aslanidi et al. [26, 27] except the fact that conduction slowing occurs at the junction between the left superior pulmonary veins and the inter-pulmonary area.

5.3 Possible further applications

The proposed model can be easily extended to the following mathematical or computational studies on atrial reentry regarding crucial additional factors that are not considered in this paper.

- (i) *Correlation between the geometrical deformation of atrium/PVs and atrial reentry:* the metric tensor of the deformed geometry of atrium/PVs can be easily incorporated into Eq. (11).
- (ii) *Correlation between the variation of thickness of atrium/PVs and atrial reentry:* a full consideration of thickness requires three-dimensional modeling but conduction velocity and subsequently conduction failure in variable thicknesses can be approximated by modifying the diffusivity tensor on curved surfaces.
- (iii) *Critical locations of scar tissue to induce anatomically induced atrial reentry:* analysis of the trajectory can reveal which scar tissue can cause asymmetry of propagation toward the PVs to cause the reentry.

6 Discussion: limitations and future work

In spite of several successful analyses, there are two main restrictions for applying the analytic technique directly to real cardiac electrophysiological phenomena: (i) The first restriction is due to the assumption that the propagation is a traveling wave solution in homogeneous media. The shape of the cardiac action potential should be roughly maintained in the propagation for valid analysis. For example, the dramatic upstrokes or downstrokes, the rapid slow-down or speed-up caused by the heterogeneity of the cardiac tissues cannot be dealt with when using the relative acceleration approach unless other approximations are introduced. In fact, anisotropy also induces changes in the shapes of the cardiac action potential, but the changes are relatively small; thus the analysis from the relative acceleration method is not seriously flawed. (ii) The second restriction is regarding the singularities of anisotropy. The relative acceleration equation is derived in the neighborhood of a point in a curved surface; thus the discontinuity of anisotropy is not a problem but the singularity

of anisotropy is a problem. For example, when several anisotropies come across a point, it is equivalent to a singularity point in mathematics and this case cannot be considered with this study.

Nevertheless, the relative acceleration approach is an attractive option because it can be easily extended to more complex higher-dimensional anisotropic surfaces such as multiple layers of curved surfaces or three-dimensional anisotropic space, which are prevalent in the real heart. Future works are open to many possibilities. The most related work to this paper could be on a mathematical model of time-dependent functional reentry. Also, revealing the relationship between the kinematics approach and the relative acceleration approach, or in other words the relationship between the shape of the wavefront and the distribution of the trajectories, may yield more practical tools applicable to clinical and surgical planning.

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Appendix A: Trajectory of the cardiac action potential on the surface $\mathcal{M}$

To obtain the trajectory, we use the wavefront S_j at time t_j . Let n be the parameter of S_j such that $S_j = S_j(n)$. Let us call n the selector parameter. Let $S_0 = S_0(n)$ be the wavefront at time t_0 . At $t_1 = t_0 + \Delta t$, we will have another wavefront $S_1 = S_1(n)$, which is also parameterized by the same selector parameter n . See the left plot of Fig. 3. Suppose the wavefronts S_0 and S_1 are both continuous and differentiable. For an arbitrary point $S_0(n)$ on the wavefront S_0 , let the propagational velocity be $\mathbf{v}^0(n)$. Then, the trajectory will be defined similarly to that in classical mechanics [70]:

Definition For an interval $I \in \mathbb{R}$, a trajectory $P_0(t)$ is a differentiable mapping $P_0: I \rightarrow \mathcal{M}^e$ to satisfy:

$$\left. \frac{\partial P_0}{\partial t} \right|_{S^0(n)} = \mathbf{v}^0(n) = \lim_{\Delta t \rightarrow 0} \frac{S_1(n) - S_0(n)}{\Delta t}.$$

For example, $P_0^h(t)$ let be the trajectory for the selector parameter 0 in k discrete time steps. For the final time T , let Δt be the time interval $\Delta t = T/k$. In isotropic and homogeneous media, the propagational direction is normal to the wavefront but in the presence of anisotropy, it may be aligned in the direction of anisotropy. For sufficiently small Δt , the trajectory at time $t_0 + \Delta t$ passing $S_0(n)$ is:

$$P_0^h(t_0 + \Delta t) = S_0(n) + \mathbf{v}^0(n) \Delta t = S_1(n).$$

Note that the trajectory P_n^h meets the wavefront S_j with the same parameter n , which is why n is called the *selector* of a trajectory. By repeating this procedure for $t_0 - \Delta t$, we can

construct a continuous and differentiable curve P_k in a neighborhood of $S^0(n)$ such that for a sufficiently small δ , we have:

$$\lim_{\Delta t \rightarrow 0} \|P_k^h(t_0 + n\Delta t) - P_k(t_0 + n\Delta t)\| < \delta, \quad \text{for all } n$$

With the affine parameter $\lambda = at + b$, $a, b \in \mathbb{R}^+$, or the time that is measured by the moving body's clock, the trajectory is represented as $P_k = P_k(\lambda) \in \mathcal{M}$ as well as the wavefront $S_j = S_j(n) \in \mathcal{M}$. What remains is to prove the existence and uniqueness of a trajectory for each point on the curved surface $\mathcal{M}$.

Proposition A *Consider a curved element $\mathcal{M}^e$ that is locally Euclidean and a two-dimensional manifold. For any point p on the wavefront S_j that is piece-wise continuous and differentiable in $\mathcal{M}^e$, there exists a unique and piece-wisely differentiable trajectory P_k in the neighborhood of p .*

Proof According to the above definition of the trajectory, it is sufficient to prove that, for any point p , there exists a unique vector $\mathbf{v}$ that is orthogonal in the sense of the metric g_{ij} to the tangent vector of the wavefront S_j . The consideration of general orthogonality is because of the anisotropy. Let $\mathbf{v}_{S_j}$ be the tangent vector of the wavefront S_j . The uniqueness of $\mathbf{v}_{S_j}$ is provided by the assumption that the wavefront is continuous and differentiable. Since $\mathcal{M}^e$ is a two-dimensional manifold, there is a function $\mathcal{C}$ that maps an Euclidean element $\Omega^2 \in \mathbb{R}^2$ into the curved element $\mathcal{M}^e$ such that $\mathcal{C} : \Omega^2 \rightarrow \mathcal{M}^e$. Without loss of generality, let q be the point in Ω such that $\mathcal{C}(q) = p$. Let s_k be the Euclidean axis of Ω^2 and let $\partial/\partial s_k \equiv \mathbf{v}_{s_k}$ be the tangent vector of the Euclidean axis for $k = 1, 2$. Considering the tangent vector is mapped by $\mathcal{C}$ such that [58]:

$$\mathcal{C}(\mathbf{v}_{s1}) \equiv \mathcal{C}\left(\frac{\partial}{\partial s_k}\right) = \frac{\partial \mathcal{C}}{\partial s_k} \equiv \mathbf{v}'_k, \quad \text{for each } k,$$

we see that each $\partial \mathcal{C} / \partial s_k$ becomes the tangent vector at $p \in \mathcal{M}^e$. Then, $(\mathbf{v}'_1, \mathbf{v}'_2)$ constitute a linear basis of the tangent plane at p where the tangent vector $\mathbf{v}_{S_j}$ lies, by definition. Thus, by an orthogonal procedure, for example by the Gram–Schmidt process in the tangent plane [71], there exists a unique $\mathbf{v}$ such that $\mathbf{v}$ is independent of $\mathbf{v}_{S_j}$ such that:

$$(\mathbf{v}, \mathbf{v}_{S_j}) = g_{ij}.$$

□

It is clear to see that the uniqueness of the trajectory in the neighborhood of a point p is the direct consequence of the uniqueness of the propagational vector and the smoothness of the wavefront. For example, for an isotropic sphere with a point initialization from the pole, the wavefront is aligned along the azimuthal angle and the trajectory along the polar angle for every point. It should be pointed out that the trajectory does not have to be orthogonal to the wavefront everywhere because of the feasible presence of anisotropy on the surface.

Appendix B: Relative acceleration from a discrete model

To explain qualitatively how a large relative acceleration can be interpreted as conduction failure for the justification of the following hypothesis, we first consider stopping conditions in a discrete model consisting in individual myocardial units that represent cells or tissues

by a similar procedure as cellular automata [50]. Motivated by the widely known facts on myocardial cells or tissues, we give the following properties to myocardial units:

- (i) One unit faces multiple units such as hexagonal packing.
- (ii) One unit can excite a limited number (N_{max}) of neighboring units, and when they try to excite more than N_{max} , none of the neighboring units reach their threshold potential (TP) for excitation.
- (iii) After a unit is excited, it undergoes a recovery process, called the refractory period (RP), and cannot be excited during RP.

For the structural property (i) of myocardial tissues as reported in ref. [72, 73], the property (ii) provides the unique characteristics of excitation propagation to restrict the maximum number of excited cells that one cell can excite, known as impedance mismatch or sink-source mismatch. Property (iii) is also well known. Depending on the ionic currents of Ca^{2+} and K^+ , the minimum time for the recovery of excitability is expressed as a function of RP that is also correlated with action potential duration (APD) [3].

Figure 14a shows myocardial tissues modeled as hexagonal packing. A geometric-free discrete representation is shown in Fig. 14b, where a dark color indicates the cell is excited and the white color indicates the cell is in the excitable state. Figure 14c shows the wavefront to represent the line of excited tissues at each time.

For the hexagonal packing of myocardial units as shown in Fig. 14a, we can also represent it with a geometric-free discrete model as shown in Fig. 14b in which the number of units in each layer reflects the shape of the hexagonal packing. Starting from (A1,A2) units, the excitation propagates to (B1,B2,B3) units, (C1,C2,C3,C4) units and so forth. Note that the first letter of the unit indicates that the same layer must be excited in all of the units and the excitation occurs only in alphabetical order, i.e., a C-unit cell cannot excite a B unit or a C unit. The goal of this discrete model is to expand the concept of the unit from cell to tissue, because when a cell satisfies the aforementioned properties, a tissue being a group of cells also satisfies the same properties if we neglect the time difference of excitation within a tissue.

No matter what this one unit in the discrete model represents, if we connect excited units at every time interval, we obtain the wavefront of cardiac excitation propagation. This wavefront represents a series of myocardial units that are in the process of depolarization. Consequently, the trajectory can be defined as if the cardiac wave is a physical wave, that is, a collection of moving particles. Upon these representations and notions, we describe the stopping conditions of the excitation propagation as the following: Without a loss of generality,

Let three be the maximum number of units one can excite in the model of hexagonal packing, i.e., $N_{max} = 3$.

The first stopping condition is obtained directly from property (ii). In Fig. 14d, if the A1 and A2 units attempt to excite the B-units, then each unit needs to excite an average of 3.5 units. Consequently, the electric potential of all B-units reaches below the TP and, consequently, fails to be excited. In brief, the excitation propagation stops or conduction failure occurs if:

[SG-i] The average number of units to be excited exceeds the maximum number of excitable units.

This stopping condition has often been cited when excitation propagation faces abrupt tissue expansion, such as a narrow cell strand connected to a large rectangular cell [52]. In the

same context, we can explain why a small gap between ablation lesions, burned and dead myocardial tissues by catheter, does not allow excitation leakage. It is important to note that the excessive number of B-units represents the geometric distribution of myocardial units, which can be interpreted as geometry in physics.

On the contrary, less attention has been given to the second condition. In Fig. 14f, the geometry of the hexagonal packing is the same as that of normal propagation in Fig. 14b, although the A1 unit propagates rapidly only along the B1 unit and finally to the C1 unit. This type of propagation is common in myocardial fibers or myocardial sheets, which we generally call anisotropy [59]. Because the C1 unit is the only excited cell in C-units, the C1 unit attempts to excite all the five D-units. Let T_1 be the time when the C1 unit uses all of the electric potential for the D-units. At the same time, the A2 unit proceeds to excite the (B2, B3) units and subsequently the (C2, C3, C4) units. Let T_2 be the time when the (C2, C3, C4) units are all excited. There is a critical difference concerning the times T_1 and T_2 : if T_2 is earlier than T_1 , that is, if the (C2, C3, C4) units can also contribute to exciting D-units along with the C1 unit, then all the D-units can be excited, and the propagation continues.

Fig. 14 Representation of stopping conditions for conduction failure in individual myocardial cells and continuous waves

However, if T_1 is earlier than T_2 , that is, if the (C2, C3, C4) units are excited, the D-units are already in RP so that the (C2, C3, C4) units have no units to excite and propagation stops at the D-units. In other words, excitation propagation also stops, or conduction failure occurs if

- [SG-ii] The excitation time of other C-units exceeds the propagation time from the C1 unit to the D-units consisting in more than the maximum number of units one unit can excite.

To simplify the above condition, we introduce another property of myocardial units:

- (iv) The excitation time by a myocardial unit is roughly proportional to the number of cells that one cell has to excite.

With the property (iv), the time T_1 only depends on the propagational time from the A1 unit to the C1 unit, because the time required to propagate from the C1 unit to the D-units is fixed. Moreover, the ratio of the velocity is at maximum four times higher on fibers than the standard excitable media [59]. Thus, it is reasonable to say that the time T_1 is relatively fixed. On the other hand, the excitation time of other C-units depends on the geometry of the B-units and the C-units other than the B1 unit and the C1 unit. Thus, the time T_2 varies widely and is dependent upon the geometry of the C-units and the D-units.

These discrete models can be naturally interpreted in continuous wave forms. This procedure can be performed by drawing a line for excited units at each time, which represents the front of the excitation propagation, called a wavefront in light of the waves. For example, Fig. 14c displays the wavefront (solid line) and trajectories (dotted line) of the excitation propagation for the discrete model of Fig. 14b. In waveforms, the shape of the wavefront and trajectories now reflect the geometry of myocardial tissues.

Appendix C: proof of proposition 1

To derive the eikonal equation of Eq. (9), we use the unique property of cardiac excitation propagation as a traveling wave solution. The traveling wave property of the membrane potential can be *in vitro* observable from the almost constant shape of the traveling membrane potential in homogeneous media; it has, therefore, been widely accepted and used for various analyses for cardiac action potential propagation [74, 75]. With this traveling wave of function ψ and a wave-speed $c = c(y^1, y^2)$, the membrane potential u can be expressed as:

$$u(y^1, y^2, \mathcal{T}) = \psi(y^1 - c(y^1, y^2)\mathcal{T}, y^2), \quad (21)$$

where y^1 is the path of the propagation and y^2 is the isochrone where the membrane potential u is constant with respect to y^2 such that $\partial u / \partial y^2 = 0$ as shown in the right plot of Fig. 3. Also, τ indicates the elapsed time from the wavefront with respect to the axis y^1 and y^2 . Consequently, $\tau = 0$ indicates the transition layer or just the wavefront for each λ . The definition of the trajectory for y^1 and the wavefront for y^2 are also confirmed by differentiating Eq. (21) with respect to y^2 to yield $-(\partial \psi / \partial y^1)(\partial c / \partial y^2)\tau + \partial \psi / \partial y^2 = 0$, which shows that $\partial \psi / \partial y^2 = 0$ at the moving frame where $\tau = 0$. In Eq. (9), the use of the traveling wave assumption (21) yields the following equality at the transition layer where $\tau = 0$:

$$d_y^{11} \frac{\partial^2 \psi}{\partial y^{12}} + \left[\frac{1}{\sqrt{g}} \sum_{\alpha=1}^2 \frac{\partial}{\partial y^\alpha} \left(\sqrt{g} d_y^{\alpha 1} \frac{\partial \psi}{\partial y^1} \right) + c \right] \frac{\partial \psi}{\partial y^1} + F = 0, \quad (22)$$

where the subscript is used to indicate that the corresponding quantity is expressed with respect to the generally non-orthogonal y^j axis. This implies that d_y^{21} may not be zero in spite of our assumption of the orthogonal diffusivity tensor (8). Since the axis y^j depends on the shape of the wavefront, the above eikonal equation is written in a time-dependent moving axis $y^j = y^j(\tau)$ for $\tau = 0$ on the curved surface. Remember that this eikonal equation is similar to the three-dimensional eikonal curvature equation by Keener [61] with one main difference. Due to the difference between the orthogonal curved axis and the Euclidean axis, the component $(1/\sqrt{gy}) (\partial\sqrt{gy}/\partial y^\alpha) d_y^{\alpha 1}$ in the above equation replaces the following term in the three-dimensional eikonal curvature equation, $(\partial x^k/\partial y^1) (\partial/\partial y^\alpha) (\partial y^1/\partial x^k) d_y^{\alpha 1}$. Equation (22) is well defined in Π but is not convenient for further analysis because the axis y^j depends on the behavior of the propagation such as the initialization of the propagation and subsequently the shape of the wavefront and the time variable, thus it is neither orthogonal nor time-independent. Because of this, it is inconvenient to express all the tensors with the axis y^α . Instead, we express every tensor on a fixed and orthogonal curved coordinate axis x^α , which is independent of the direction of propagation or the direction of the wavefront.

Consider that the diffusivity tensor $d_y^{\alpha\beta}$ is expanded with respect to the curved axis x^k such that [57, 58]:

$$d_y^{\alpha 1} \left(\equiv \sum_{k,l=1}^2 d^{kl} \frac{\partial y^\alpha}{\partial x^k} \frac{\partial y^1}{\partial x^l} \right) = \sum_{k=1}^2 d^{kk} \frac{\partial y^\alpha}{\partial x^k} \frac{\partial y^1}{\partial x^k}, \quad (23)$$

where the diffusivity coefficient d^{kk} is expressed with respect to x^j and the second equality is obtained from our choice of anisotropy that is only aligned along one of the orthogonal curved axes (equation (9)). As for $\sqrt{gy}$, the transformation rule by multiplying the determinant of the Jacobian $J \equiv [\partial x^j/\partial y^i]$ applies as $\sqrt{gy} = J\sqrt{g}$ [76]. As a result, by substituting Eq. (23) into Eq. (22), we obtain:

$$\left(\sum_{k=1}^2 E^k \right) \frac{\partial^2 \psi}{\partial y^{12}} + \left\{ \sum_{k=1}^2 \frac{1}{\sqrt{g}} \frac{\partial U^k}{\partial x^k} + c_r \right\} \frac{\partial \psi}{\partial y^1} + F = 0, \quad (24)$$

where we introduced the new variables $\Lambda^k \equiv \partial y^1/\partial x^k$, $U^k \equiv \Lambda^k \sqrt{g} d^{kk}$ and $E^k = \Lambda^k U^k / \sqrt{g}$ with the speed variable c_r that is defined as:

$$c_r \equiv c + \sum_{k=1}^2 \frac{U^k}{\sqrt{g}} \left\{ \frac{1}{J} \frac{\partial J}{\partial x^k} + \sum_{\alpha=1}^2 \frac{\partial}{\partial y^\alpha} \left(\frac{\partial y^\alpha}{\partial x^k} \right) \right\}.$$

Moreover, according to the supposition (10), for sufficiently small positive constants ε_1 and ε_2 and for $k, \alpha = 1, 2$, the following quantities are sufficiently small;

$$\left\| \frac{1}{J} \frac{\partial J}{\partial x^k} \right\| < \varepsilon_1 \ll 1, \quad \text{and} \quad \left\| \frac{\partial}{\partial y^\alpha} \left(\frac{\partial y^\alpha}{\partial x^k} \right) \right\| < \varepsilon_2 \ll 1.$$

Consequently, the speed function c_r is approximately the same as c , i.e., $c_r \approx c$, independent of the time variable and the geometrical factors such as d^{kk} , Λ^k and g_{kk} .

With the proposed hypothesis, what remains is to obtain the critical factors for the relative acceleration in the action potential propagation. In the ambient space of π^e , i.e., in $\mathbb{R}^3$, we regard the y^1 -axis as the trajectory and project it into the ambient space of a higher dimension [47, 51]. In eikonal Eq. (22), being originally derived in π^e , we extend the curved surface π^e in the neighborhood of each point in the following way: consider a curved surface

as a two-dimensional submanifold embedded in three-dimensional Euclidean space z^i . The function $\psi(y^1, y^2)$ can be extended to a function $\psi(z^1, z^2, z^3)$ in a tubular neighborhood of the surface where the directional derivative of ψ along the surface normal is zero. Define ψ on an open subset around π^e . Let $\mathbf{Y}_1 : \mathbb{R}^2 \rightarrow \mathbb{R}^3$ be the coordinate map for the y^1 -axis in the ambient space $\mathbb{R}^3$. With the affine parameter λ and the selector parameter n , we introduce the following notation,

$$P_n(\lambda) = \mathbf{Y}_1(\lambda, n) \equiv (\gamma_n^1, \gamma_n^2, \gamma_n^3) \in \mathbb{R}^3,$$

where γ_n^i is the component of $\mathbf{Y}_1$ for the Cartesian coordinate axis z^i . Moreover, since $\psi(x^1, x^2)$ was extended to $\psi(z^1, z^2, z^3)$, we can express the differentiation with respect to y^1 by the chain rule:

$$\frac{\partial \psi}{\partial y^1} = \sum_{i=1}^3 \frac{\partial \psi}{\partial z^i} \frac{\partial z^i}{\partial y^1} = \sum_{i=1}^3 \frac{\partial \psi}{\partial z^i} \frac{\partial \gamma_n^i}{\partial \lambda}, \quad (25)$$

where the second equality is obtained by using the fact that $\partial z^i / \partial y^1$ is the i th component of the tangential vector of the path $\mathbf{Y}_1$, which is the same as $\partial \gamma_n^i / \partial \lambda$. Note that the above equality is nothing but the expression of the derivative in terms of moving frames as $\nabla \psi \cdot \mathbf{v}^1$ where $\mathbf{v}^1$ is the tangent vector of the y^1 -axis [46]. Moreover, differentiating again with respect to y^1 yields:

$$\frac{\partial^2 \psi}{\partial y^{1^2}} = \sum_{i=1}^3 \left(\frac{\partial \psi}{\partial z^i} \frac{\partial^2 \gamma_n^i}{\partial \lambda^2} + \sum_{j=1}^3 \frac{\partial^2 \psi}{\partial z^i \partial z^j} \frac{\partial \gamma_n^i}{\partial \lambda} \frac{\partial \gamma_n^j}{\partial \lambda} \right). \quad (26)$$

By substituting the Eqs. (25) and (26) into Eq. (24), we obtain:

$$\frac{\partial \psi}{\partial z^i} \left\{ E^k \frac{\partial^2 \gamma_n^i}{\partial \lambda^2} + \left(\frac{1}{\sqrt{g}} \frac{\partial U^k}{\partial x^k} + c_r \right) \frac{\partial^2 \gamma_n^i}{\partial \lambda} \right\} + E^k \frac{\partial \psi}{\partial z^i \partial z^j} \frac{\partial \gamma_n^i}{\partial \lambda} \frac{\partial \gamma_n^j}{\partial \lambda} + F = 0, \quad (27)$$

where the summation notation is used for easier reading and the indexes i and j are summed up to three and the index k is summed up to two. To obtain the relative acceleration equation, we differentiate the above equation with respect to the selector parameter n along the wavefront. Considering that the reaction function F is constant along the wavefront, leading to $\partial F / \partial n = 0$, we obtain:

$$\frac{\partial \psi}{\partial z^i} \left\{ E^k \frac{\partial^2 n^i}{\partial \lambda^2} + \frac{\partial E^k}{\partial n} \left(\frac{\partial v^i}{\partial \lambda} + \frac{\partial^2 \psi}{\partial z^i \partial z^j} v^j v^i \right) + \frac{\partial}{\partial n} \right\} \left[\left(\frac{1}{\sqrt{g}} \frac{\partial U^k}{\partial x^k} + c_r \right) v^i \right] = 0, \quad (28)$$

where we used the variable n^i for the separation vector as defined in Eq. (1) and v^i for the tangent vector of the trajectory $\mathbf{Y}_1$, which are defined as $n^i \equiv \partial \gamma_n^i / \partial n$ and $v^i \equiv \partial \gamma_n^i / \partial \lambda$ for $1 \leq i \leq 3$. Each upper index indicates the component of a vector in the Cartesian coordinate z^i , for example, $n = (n^1, n^2, n^3)$. In addition, we used the interchangeability of the differentiation [51] in the direction of n and λ for the above equation such that:

$$\frac{\partial}{\partial n} \left(\frac{\partial^2 \gamma_n^i}{\partial \lambda^2} \right) = \frac{\partial}{\partial n} \left(\frac{\partial}{\partial \lambda} \right) \left(\frac{\partial}{\partial \lambda} \right) \gamma_n^i = \left(\frac{\partial}{\partial \lambda} \right) \left(\frac{\partial}{\partial \lambda} \right) \frac{\partial \gamma_n^i}{\partial n} = \frac{\partial^2 n^i}{\partial \lambda^2}.$$

Without loss of generality, we may consider the case only when the quantity inside the bracket of Eq. (28) is zero, independent of $\partial \psi / \partial z^i$. Then we obtain Eq. (11).

Appendix D: Examples and validations of the relative acceleration analysis

In the following examples on various curved surfaces, we will display how mathematical analysis from the relative acceleration Eq. (19) coincides with computational results and how the curvature of the geometry changes the impact of anisotropy for conduction failure. For easier reading, each example is organized such that **Problem** means the setting of cardiac excitation propagation on a curved surface, **RA analysis** means the analysis and predictions from Eq. (19), **Computational modeling** and **validation** means the validation by computation simulations in the above computational scheme and some references, respectively.

D.1 Anisotropic plane

Problem 1 Consider a block of anisotropy in the middle of a plane. For a plane with $-100 \leq x \leq 100$ and $-100 \leq y \leq 100$, let the block be located in $-50 \leq x \leq 50$ and $-50 \leq y \leq 50$. Let the anisotropy be aligned with the direction of the x -axis, denoted as x -anisotropy, which expresses the diffusivity tensor $\mathbf{d}$ as $\mathbf{d} = \zeta^{xx} \mathbf{x}$ in the block of anisotropy and $\zeta^{yy} = 1.0$ everywhere. See Fig. 15a. Also, allow the excitation to propagate in the form of a plane wave in the $-x$ direction front of the right wall and, consequently, the wavefront is in the direction of the y -axis.

RA analysis Since these conditions mean that $g^{xx} = g^{yy} = 1$ and $\Lambda^x = 1$, $\Lambda^y = 0$, the relative acceleration Eq. (19) boils down to:

$$-\frac{\partial^2 n^i}{\partial \lambda^2} = \frac{\partial (\log \zeta^{xx})}{\partial y} \frac{\partial v^i}{\partial \lambda} + \frac{1}{\zeta^{xx}} \frac{\partial^2 \zeta^{xx}}{\partial x \partial y} v^i, \quad (29)$$

where we used $n = y$ and $\partial v^i / \partial n = 0$. From the above equation, it is obvious that a large relative acceleration can be achieved *only* by increasing the magnitude of anisotropy in the plane, especially at the interfaces of anisotropy where $\partial^2 \zeta^{xx} / (\partial x \partial y)$ is large. This result is compatible with the break-up conditions drawn from the kinematics approach as shown by Morozov et al. [38].

Computational modeling In computational simulation, we similarly observe that a large relative acceleration can only occur at the interfaces of the anisotropy block, i.e., in the line of $y = \pm 50$ for the first component and two points $(50, 50)$ and $(50, -50)$ for the second

Fig. 15 For $\zeta^{xx} = 4.0$. Anisotropy block is located in the middle (a). After initiating from the right wall, the membrane potential (u) at $T = 300.0$ (b), $T = 500.0$ (c) from the right wall

Fig. 16 For $\zeta^{xx} = 10.0$. The distribution of ζ^{xx} (solid line) and $\partial(\log \zeta^{xx})/\partial y$ (dashed line) along the y-axis (a). After initiating from the right wall, the membrane potential (u) at $T = 200.0$ (b), $T = 300.0$ (c)

component. See Fig. 16a for the distribution of ζ^{xx} and $\partial(\log \zeta^{xx})/\partial y$ along the y-axis. With $\zeta^{xx} = 4.0$, conduction failure does not happen as shown in Fig. 15b and c. However, increasing the magnitude of anisotropy up to $\zeta^{xx} = 10.0$, though this large magnitude seems to be unrealistic in a biological system, leads to conduction failure in the block of anisotropy because the relative acceleration has increased significantly at the interface. Note that if the anisotropy changes slowly such that $\partial^2 \zeta^{xx}/(\partial x \partial y)$ remains bounded, then no conduction failure would be induced by the anisotropy.

Problem 2 (RA analysis and validation) Conduction failure can also occur even inside an anisotropic block. If the direction of anisotropy is oblique to the propagational direction, then conduction failure can happen inside anisotropy. Let ζ be the magnitude of anisotropy and θ be the angle with respect to the direction of the excitation propagation. For the sake of simplicity, let the magnitude of anisotropy (ζ) be constant in Π . For the same planar propagation as before, the relative acceleration equation is expressed as:

$$-\frac{\partial^2 n^i}{\partial \lambda^2} = -\zeta \tan \theta \frac{\partial \theta}{\partial y} \frac{\partial v^i}{\partial \lambda} + \left[-\frac{\partial \theta}{\partial x} \frac{\partial \theta}{\partial y} - \tan \theta \frac{\partial^2 \theta}{\partial x \partial y} \right] v^i. \quad (30)$$

Note that this equation implies that the action potential propagation can also be blocked by the significant variable angle θ of the direction of anisotropy as well as the magnitude. This result coincides with Davydov et al. [77], who displayed that the chiral anisotropy, which is aligned along the circumferential direction of circles, can break up the excitation propagation, but Eq. (30) suggests a host of possibilities for conduction failure by variations of the direction of anisotropy.

D.2 Anisotropic sphere

Problem 3 The relative acceleration analysis can be similarly applied to the propagation on an anisotropic sphere. However, there is a difference. Contrary to the propagation in the plane, the planar propagation is impossible. Instead, the propagation should be pointwisely initiated, for example, an initiation from the north pole. Geometry tells us that point-initialized excitation follows the line of the polar angle (θ) and the wavefront is aligned along the azimuthal angle (ϕ). For a sphere of radius $r = 50.0$, consider a block of anisotropy located in $-\pi/4 \leq \phi \leq \pi/4$ and $-0.6 \leq \theta \leq 0.6$. See Fig. 17a. Let the direction

of anisotropy be both along the θ - and ϕ axis in general but because of the propagational direction, only θ -anisotropy will contribute to the changes of the propagation.

RA analysis Geometrically, these conditions imply that $g^{\theta\theta} = 1/r^2$ and $\Lambda^\theta = 1$, $\Lambda^\phi = 0$, thus relative acceleration Eq. (19) is expressed as:

$$-\frac{\partial^2 n^i}{\partial \lambda^2} = \frac{\partial (\log \varsigma^{\theta\theta})}{\partial \varphi} \frac{\partial v^i}{\partial \lambda} + \left(\frac{1}{\varsigma^{\theta\theta}} \frac{\partial^2 \varsigma^{\theta\theta}}{\partial \varphi \partial \theta} + \frac{\partial (\log \varsigma^{\theta\theta})}{\partial \varphi} \cot \theta \right) v^i, \quad (31)$$

where we used $(1/\sqrt{g})(\partial(\sqrt{g}g^{kk})/\partial x_k) = g^{kk}\Gamma_{mk}^m$, $m \neq k$ as proved in Appendix E. Equation (31) is similar to Eq. (29) for the plane, but the last additional component, i.e., $\partial(\log \varsigma^{\theta\theta})/\partial \varphi \cot \theta$, appears. The above component indicates the dependency of the relative acceleration on the location of anisotropy with respect to the point of initialization. For example, for the point of initialization at the pole, let θ be the azimuthal angle of the sphere from the pole. Then, the magnitude and sign of the above component change as the location of anisotropy changes. Figure 18a displays that the above component changes signs at $\theta = \pi/2$ and the magnitude of it increases as θ gets closer to 0 or π . Consequently, since the change of signs of the above component can increase or decrease the total magnitude of the relative acceleration, Eq. (31) implies that conduction failure also depends on the location of anisotropy with respect to the location of point initialization. In the perspective of the trajectory, this analysis is no surprise. With point initialization at the north pole, the trajectories diverge in the northern hemisphere up to the equator and from the equator the trajectories converge in the southern hemisphere. Thus, the use of anisotropy to increase the divergence of trajectories will add its relative acceleration only for the trajectories in the northern hemisphere and will decrease it for the trajectories in the southern hemisphere.

Computational modeling To confirm the above analysis, a block of anisotropy is placed on the sphere such that the first interface that the propagation meets is located at $\theta = \pi/4$ distance from the point of initialization, i.e., in the northern hemisphere. As shown in Fig. 17b and c, the block of anisotropy with a sufficiently large magnitude causes conduction failure. On the other hand, move the point of initialization away from the block of anisotropy such that the first interface that the propagation meets is located at $\theta = 3\pi/4$ distance from the point of initialization, i.e., in the southern hemisphere. Then, the block of the same anisotropy, with the same magnitude of anisotropy as before, does not cause conduction failure as shown in Fig. 18b and c. This phenomenon seems to be well explained by the change

Fig. 17 For $\varsigma^{\theta\theta} = 10.0$. The block of anisotropy is located in the middle $\pi/4 < \theta < 3\pi/4$ on a sphere (a). After point-initialized from the north pole, the membrane potential (u) at $T = 300.0$ (b), $T = 400.0$ (c). 10.3 Anisotropic torus

Fig. 18 For $\varsigma^{\theta\theta} = 10.0$. Magnitude of the last component in Eq. (31) with respect to θ (a). The block of anisotropy is located in the bottom $3\pi/4 < \theta < \pi$. After point-initialized from the north pole, the membrane potential (u) at $T = 600.0$ (b), $T = 700.0$ (c)

of signs of the last component in Eq. (31) representing the convergence and divergence of the trajectories.

D.3 Anisotropic torus

Problem 4 The excitation propagation in a torus is strikingly different from the propagation in a plane or sphere in the sense that we cannot find one axis to represent the direction of propagation. For example, reminder that $\Lambda^k \equiv \partial y_1 / \partial x_k$, $\Lambda^x = 1$ and $\Lambda^y = 0$ for planar propagation in the plane and $\Lambda^\theta = 1$ and $\Lambda^\phi = 0$ for a sphere with point-initialization. However, Λ^θ and Λ^ϕ for a torus is not always constant. With the radius of the meridian r and the radius of the great circle R , let θ be the axis around the meridian and ϕ be the axis around the great circle. Then, a torus can be parameterized such that $\mathbf{x} = ((R + r \cos \theta) \sin \phi, (R + r \cos \theta) \cos \phi, r \cos \theta) \varphi$, $0 \leq \theta \leq \pi$, $-\pi \leq \varphi \leq \pi$. Then, no matter where or how the excitation starts, Λ^ϕ and Λ^θ are always neither constant nor zero. This fact makes the analysis complicated but to make the problem simpler, we first consider that there is no anisotropy.

RA analysis and validation We first consider an isotropic torus such that $\varsigma^{\phi\phi} = \varsigma^{\theta\theta} = 1.0$. To make the problem even simpler, we suppose that the wavefront is at the angle of η with respect to θ such that $\Lambda^\theta = \cos \eta$ and $\Lambda^\phi = \sin \eta$. Let Λ^θ and Λ^ϕ be constant along the wavefront. Since $g^{\theta\theta} = 1/r^2$ and $g^{\phi\phi} = 1/(R + r \cos \theta)^2$, relative acceleration Eq. (19) is expressed as:

$$-\frac{\partial^2 n^i}{\partial \lambda^2} = \frac{R + r \cos \theta}{\Lambda^{\theta^2} (R + r \cos \theta)^2 + \Lambda^{\phi^2} r^2} \left[\cos \alpha \frac{R \cos \theta + r}{R + r \cos \theta} v^i - \cos \alpha \sin \theta \frac{\partial v^i}{\partial \lambda} \right]. \quad (32)$$

Note that each component shows strong dependency on the meridian r for the fixed R . In other words, the above relative acceleration equation for an isotropic torus implies that the relative acceleration can be significantly changed by resizing the meridian r . This result coincides with the kinematic analysis by Davydov et al. [35], which demonstrated that the critical curvature for breaking-up the wave can be generated by adjusting the ratio R/r of the torus.

Problem 5 Consider anisotropy on a torus. However, for the sake of simplicity, we suppose the propagation follows locally the ϕ axis only in a small region of the torus. Let $R = 100.0$

and $r = 50.0$. Let the center of the torus be located at $(0, 0, 0)$. The block of anisotropy is placed in the area of $-50.0 \leq x \leq 50.0$ and $0.0 \leq y \leq 150$. If the propagation is point-initialized at $(-150.0, 0, 0)$, then the propagation approximately follows the ϕ -axis in the area of the anisotropy block.

RA analysis With the anisotropy of both directions and $\Lambda^\theta = 0$ and $\Lambda^\phi = 1$, we obtain:

$$-\frac{\partial^2 n^i}{\partial \lambda^2} = \frac{\partial (\log \zeta^{\phi\phi})}{\partial n} \frac{\partial v^i}{\partial \lambda} + \frac{\partial^2 \zeta^{\phi\phi}}{\partial n \partial \phi} v^i + \frac{2r \sin \theta}{R + r \cos \theta} \left(\frac{\partial \theta}{\partial n} \right) \left[\zeta^{\phi\phi} \frac{\partial v^i}{\partial \lambda} + \frac{\partial \zeta^{\phi\phi}}{\partial \phi} v^i \right], \quad (33)$$

where we used $\partial \phi / \partial n = 0$ according to the assumption that the propagation follows the ϕ -axis in the area, thus $n = \theta$. The first two components are the same as the relative acceleration generated by anisotropy in the plane but the last component is an additional component for an anisotropic torus. Because of this last component, the behavior of cardiac excitation propagation displays the following unique phenomena: the first phenomenon is that the relative acceleration depends on the θ angle. Considering $2r \sin \theta / (R + r \cos \theta)$ increases as θ approaches $\pi/2$, it can be predicted that there is a larger relative acceleration in the area where θ is closer to $\pi/2$. The second phenomenon is as follows; because the last term adds additional relative acceleration, the critical magnitude of $\zeta^{\phi\phi}$ for conduction failure is slightly less than that for anisotropy in the plane. This is possible because all the components in Eq. (33) have the same sign when $\zeta^{\phi\phi}$ is larger than 1.0, which is the choice of our anisotropy. This result seems to support the conjecture that the curvature of geometry can increase the effects of anisotropy on curved surfaces.

Computational modeling The predictions of these unique phenomena in a torus can be confirmed in computational simulations. Consider a torus of $R = 100.0$ and $r = 50.0$ centered at $(0, 0, 0)$. Let the block of anisotropy be located in $-50.0 \leq x \leq 50.0$ and $0.0 \leq y \leq 150.0$ as shown in Fig. 19a. In Fig. 19b and c, when the propagation is approximately in the direction of the ϕ axis, the anisotropy $\zeta^{\phi\phi} = 8.0$, which is less than $\zeta^{\phi\phi} = 10.0$ for the previous cases, generates the largest acceleration in the area where $\theta = \pi/2$. But, the block of anisotropy fails to generate a sufficiently large relative acceleration for the area where θ is small. This agrees with the firstly predicted phenomenon from Eq. (33). However, the $\zeta^{\phi\phi}$ anisotropy cannot block the propagation in the result. This could be just a matter of direction of the propagation. Figure 20b and c displays that additional anisotropy in another direction $\zeta^{\theta\theta}$ can add additional relative acceleration in the area where θ is small and consequently

Fig. 19 Location of the anisotropy block (darkened) with $\zeta^{\phi\phi} = 8.0$ (a). After point-initialized at the rightmost point of the above torus, the membrane potential (u) at $T = 500.0$ (b) and at $T = 1000.0$ (c)

Fig. 20 Anisotropy block with $\varsigma^{\phi\phi} = 8.0$ and $\varsigma^{\theta\theta} = 8.0$. After point-initialized at the rightmost point of the above torus, the membrane potential (u) at $T = 800.0$ (a), $T = 900.0$ (b) and $T = 1000.0$ (c)

can stop the propagation. Note that in the plane, whatever the direction of the propagation, anisotropy with a magnitude of 8.0 cannot block the propagation for conduction failures. This confirms the second predicted phenomenon by relative acceleration Eq. (33).

Appendix E: differentiation of $\sqrt{g}g^{kk}$

Lemma D Consider any index k and the index m different from k and suppose that x^m is in the Killing direction. Then, the following equation holds:

$$\frac{1}{\sqrt{g}} \frac{\partial (\sqrt{g}g^{kk})}{\partial x^k} = g^{kk} \Gamma_{mk}^m. \quad (34)$$

Proof In the following calculations, the sum is taken over all the indices repeated above and below except k . Let us differentiate $\sqrt{g}g^{kk}$ with respect to the axis x_k . Using the chain rule and using $\frac{\partial \sqrt{g}}{\partial x_k} = \sqrt{g} \Gamma_{\mu k}^\mu$, we obtain:

$$\frac{\partial (\sqrt{g}g^{kk})}{\partial x^k} = \sqrt{g} \left(g^{kk} \Gamma_{\mu k}^\mu + \frac{\partial g^{kk}}{\partial x^k} \right). \quad (35)$$

To replace the differentiation of g^{kk} with the differentiation of the metric tensor g_{kk} , we use the identity of $g^{i\infty}g_{\infty j} = \delta_j^i$ to obtain:

$$\frac{\partial (\sqrt{g}g^{kk})}{\partial x^k} = \sqrt{g}g^{kk} \Gamma_{\mu k}^\mu + \sqrt{g}g^{kv} \left(g_{v\mu} \frac{\partial g^{k\mu}}{\partial x_k} \right), \quad (36)$$

and the equation obtained by differentiating $g^{kk}g_{k\infty} = \delta_\mu^k$:

$$\frac{\partial g_{v\mu}}{\partial x^k} g^{k\mu} + g_{v\mu} \frac{\partial g^{k\mu}}{\partial x^k} = 0.$$

Note that this reduces Eq. (36) to the following:

$$\frac{\partial (\sqrt{g}g^{kk})}{\partial x^k} = \sqrt{g}g^{kk} \Gamma_{\mu k}^\mu - \sqrt{g}g^{kv} g^{k\mu} \frac{\partial g_{v\mu}}{\partial x_k}. \quad (37)$$

Replace the differentiation of g^{kk} with the equalities in Γ_{ijk} and Γ_{jk}^i , which are Christofel symbols of the first kind and the second kind respectively, such that:

$$\frac{\partial g_{v\mu}}{\partial x^k} = \Gamma_{vk\mu} + \Gamma_{\mu kv}, \quad \Gamma_{\mu k}^k = g^{kv} \Gamma_{v\mu k}.$$

With these equalities and the condition of orthogonality of the curved axis x_k , Eq. (37) becomes:

$$\frac{1}{\sqrt{g}} = \frac{\partial(\sqrt{g}g^{kk})}{\partial x^k} = g^{kk} (\Gamma_{mk}^m - \Gamma_{kk}^k), \quad m \neq k. \quad (38)$$

For surfaces of revolution such as spherical shells and toruses, the curved axis x^m representing the rotational direction is in the direction of the Killing vector, or the Killing direction, which satisfies the condition $\partial g_{\infty v} / \partial x^m = 0$ [51] and consequently Eq. (34). $\square$

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