

TRANSITION FROM VENTRICULAR TACHYCARDIA TO VENTRICULAR FIBRILLATION AS FUNCTION OF TISSUE CHARACTERISTICS IN A COMPUTER MODEL

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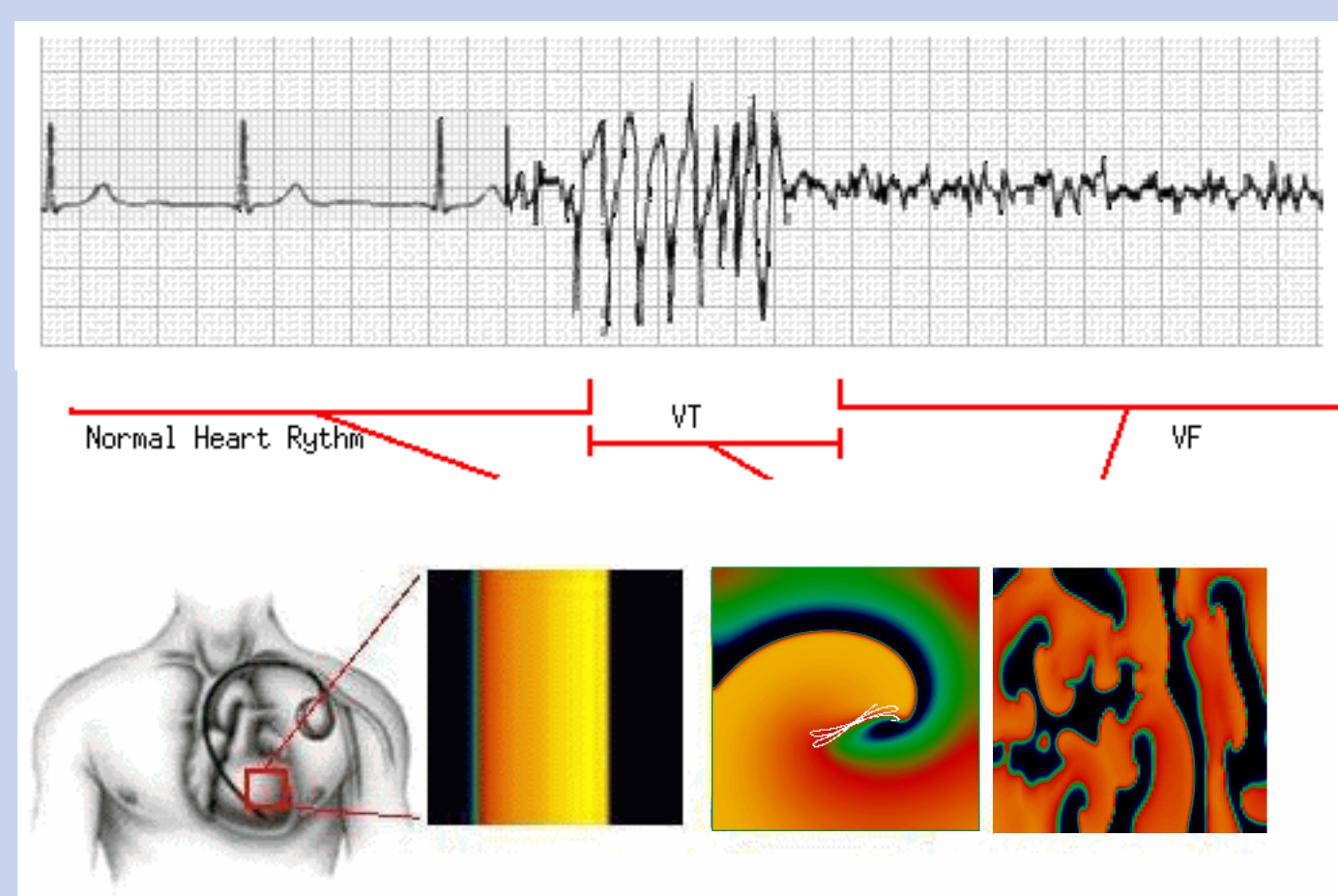
Abstract

A simplified quantitative ionic model of cardiac action potential, which reproduces accurate restitution curves, is used in conjunction with global tissue characteristics such as rotational cell anisotropy and periodic boundaries to study the transition from ventricular tachycardia (VT) to ventricular fibrillation (VF). We give an explanation for the experimental observation that there is a minimum tissue mass required for this transition to occur

Introduction

Many experiments in cardiac tissue using simultaneous multi-site electrode mappings as well as voltage sensitive dyes, have shown that in many cases VF is a consequence of several wandering spiral waves [1,2]. Therefore it has been suggested that the rapid transition from VT to VF can be associated with the breakup of a spiral wave

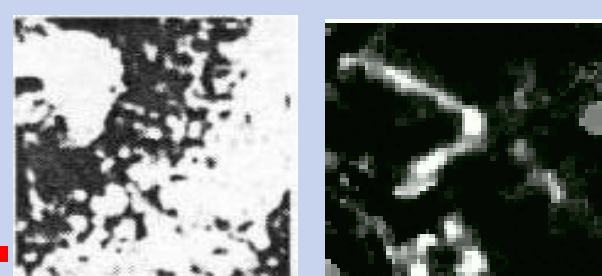
Schematic representation of the transition from normal heart beat to VT and then to VF on an ECG recording.



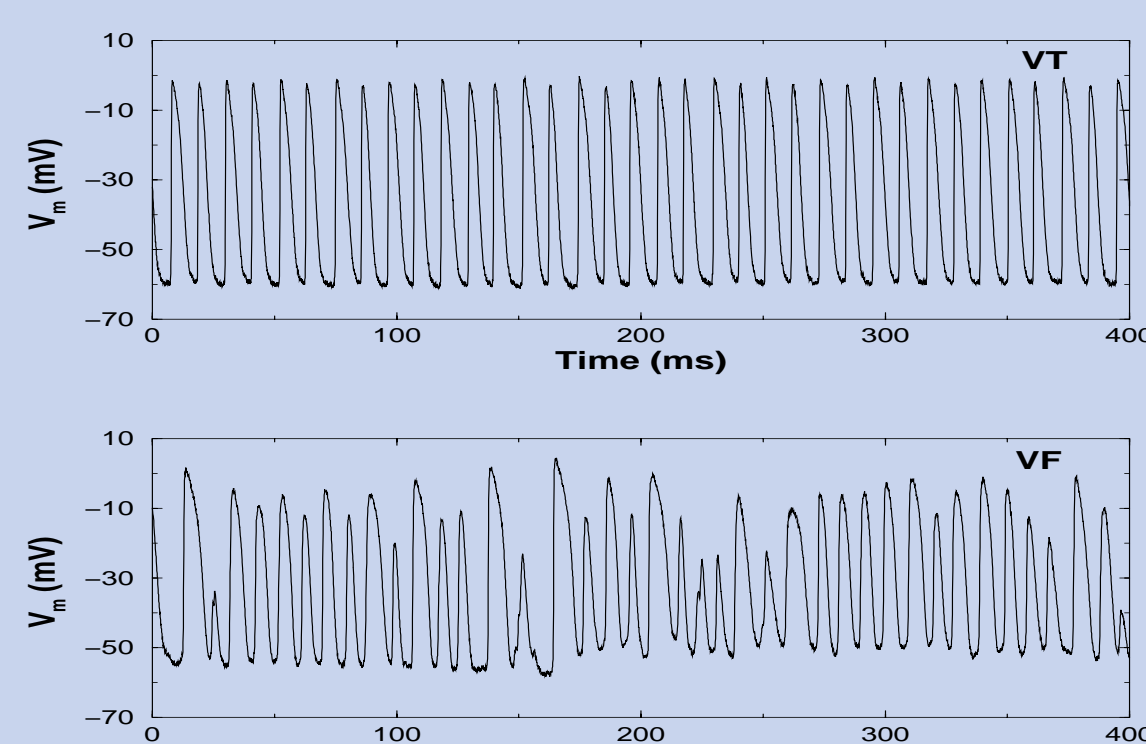
Experiments:

single spiral wave [3]

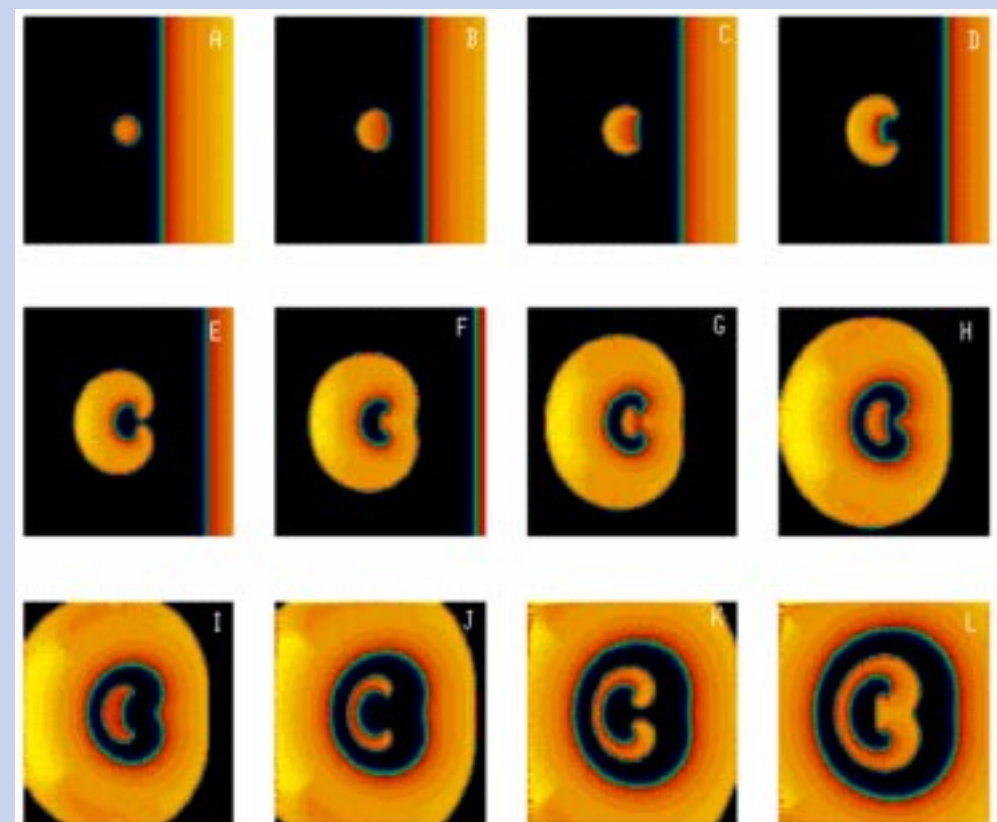
multiple waves [2]



Time course of local activity measured in a dog heart with VT (top) and VF (bottom graph)



Initiation of Spiral Waves by a Premature Stimulus



Numerical simulation. Panels A'-B' premature stimulus (S2) applied too soon, the tissue behind the plane wave is refractory and the stimulus dies out. Panels A''-B'', S2 applied too late, the tissue is readily excitable and the stimulus produces a target pattern wave. Panels A-L, S2 successfully applied during the window of vulnerability producing two mirror image spiral waves of action potential.

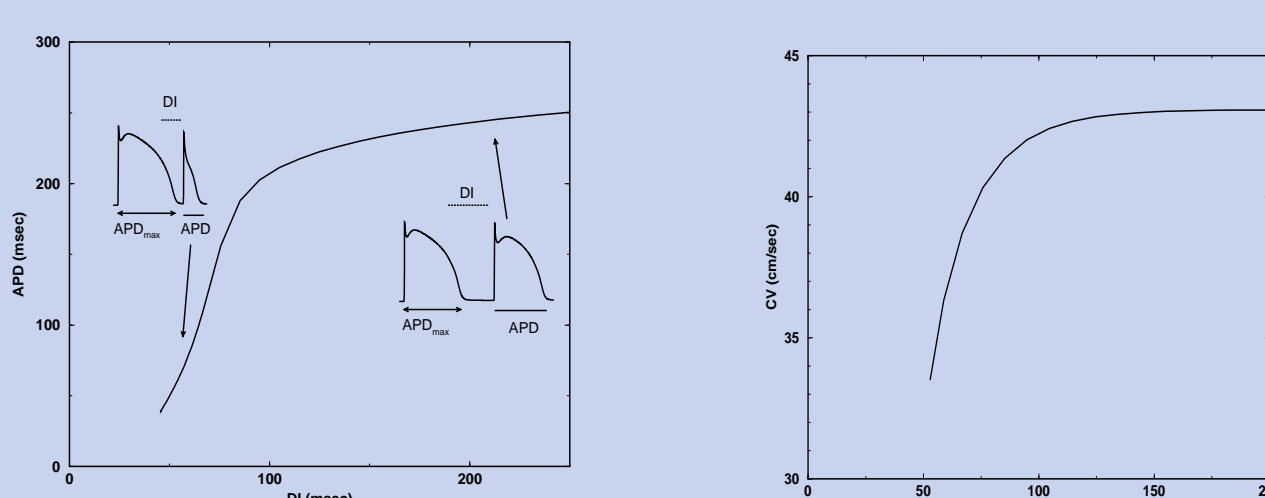
Restitution Curves

In cardiac tissue it is possible to define two characteristic curves that describe how the duration and conduction velocity of a wave depend on the time interval since the previous activation, during which the medium recovers its resting properties. This restitution functions thus reflect the electrophysiological state as well as tissue characteristics.

APD-Restitution relates the duration of an AP at a given point in the tissue with the previous diastolic interval (DI) at the same point. DI or recovery time, measures the time between a repolarization and the next depolarization of the cell membrane.

CV-Restitution relates the conduction velocity of an excitation wavefront to the previous DI at the same point where the velocity is measured.

APD-Restitution CV-Restitution



The Ionic Model

The Model Equations

3V-SIM model

The model consist of 3 variables: V the membrane voltage, v a fast ionic gate and w a slow ionic gate. I_{ion} is a sum of 3 independent currents:

$$I_{fv}(V; v) = -v p (V - V_c)(V - V_m)/\tau_d$$

$$I_{so}(V) = (V - V_c)(1 - p)/\tau_o + p/\tau_r$$

$$I_{sl}(V; w) = -w (1 + \tanh[k(V - V_c^*)]) / (2\tau_{sl})$$

The equations for the 3 variables are:

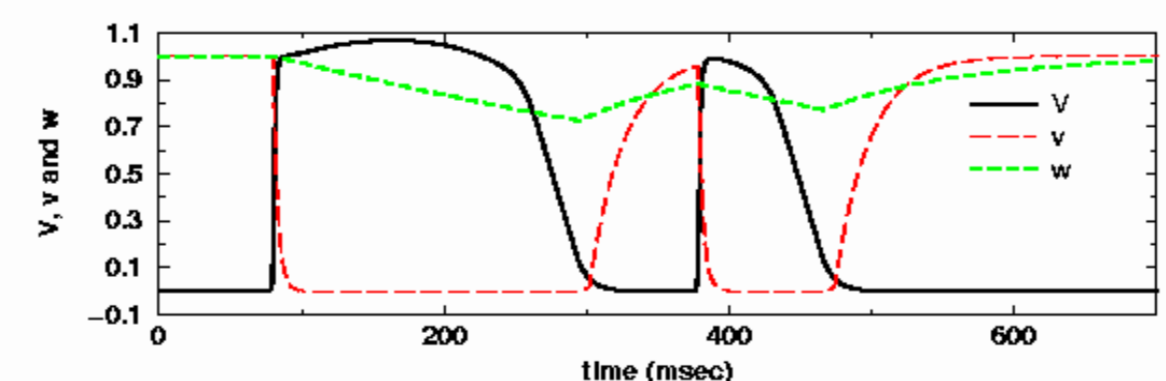
$$\partial_t V(\vec{x}, t) = \nabla \cdot (\tilde{D} \nabla V) - I_{ion}$$

$$\partial_t v(t) = (1 - p)(1 - v)/\tau_v(V) - p v / \tau_v^*$$

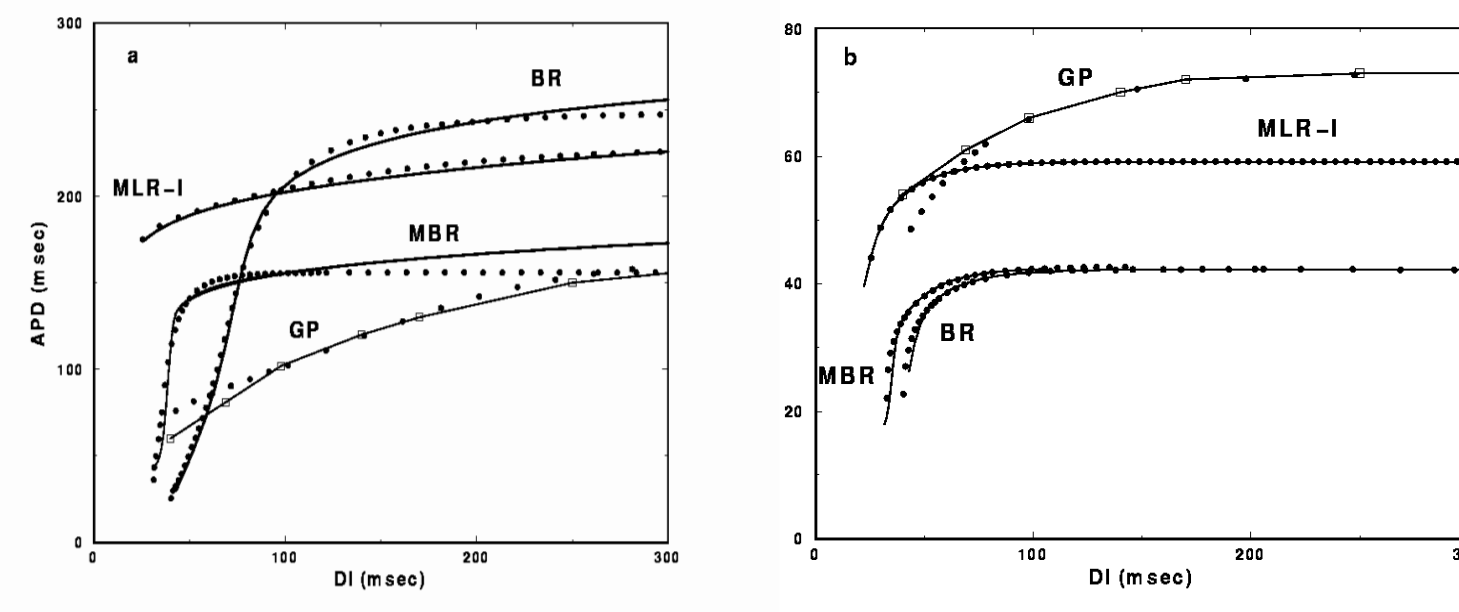
$$\partial_t w(t) = (1 - p)(1 - w)/\tau_w - p w / \tau_w^*$$

where $\tau_v(V) = (1 - q)\tau_{v1} + q\tau_{v2}$ (2)

$$p = \begin{cases} 1 & \text{if } V \geq V_c \\ 0 & \text{if } V < V_c \end{cases} \quad \text{and} \quad q = \begin{cases} 1 & \text{if } V \geq V_v \\ 0 & \text{if } V < V_v \end{cases} \quad (3)$$

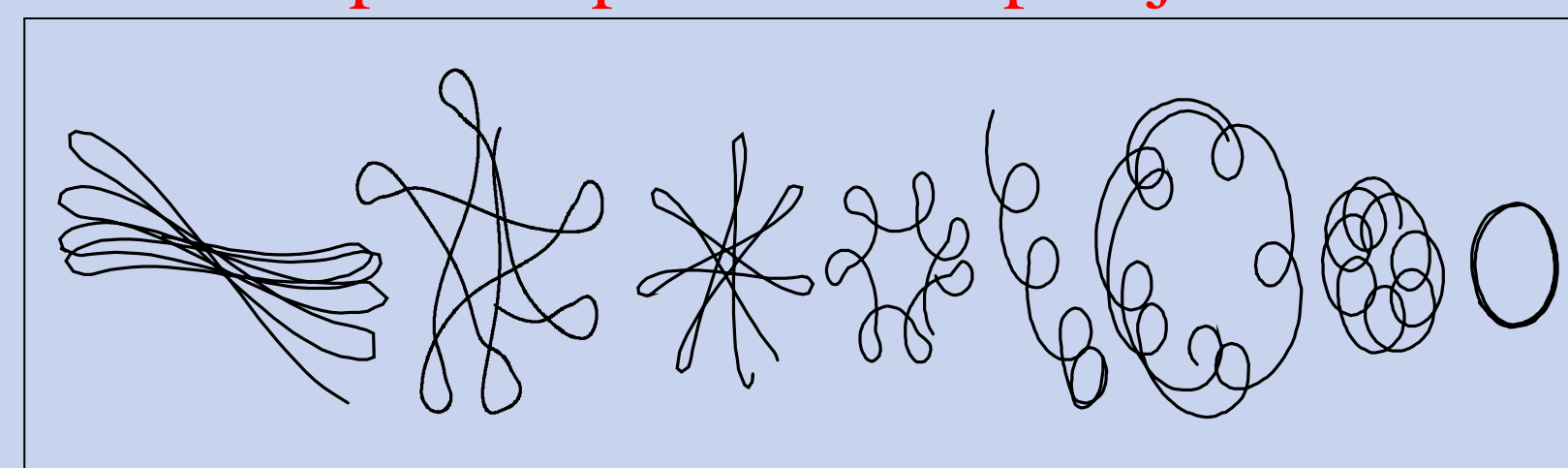


APD-Restitution (fitted to other models) CV-Restitution (fitted to other models)



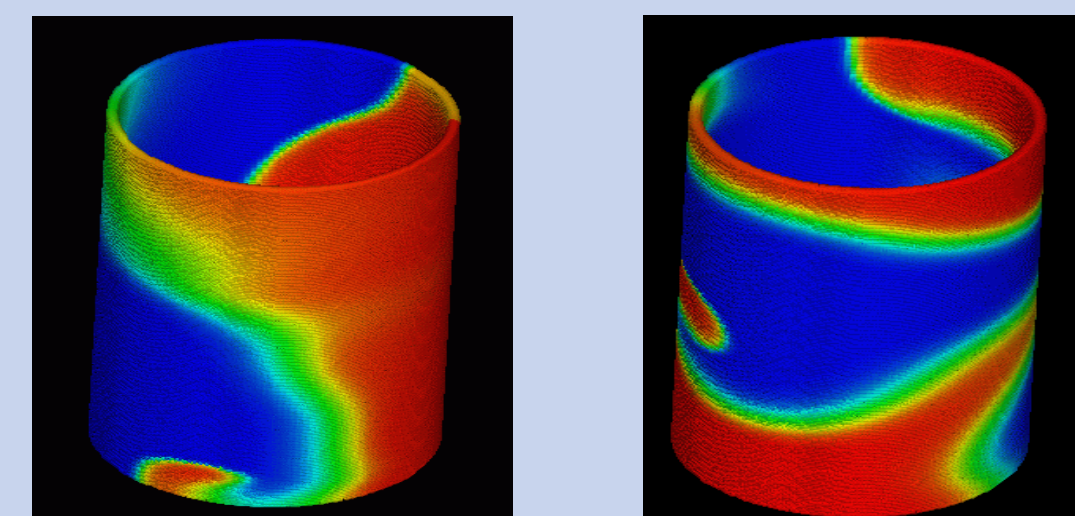
The parameters of the model can be varied to reproduce arbitrary (experimental and numerical) APD and CV restitutions. Different restitutions produce different dynamics on spiral waves. For example the transition from linear core to circular core trajectories can be produced by changes in sodium and/or calcium currents. For example, the following graph shows this transition using the 3V-SIM fitted to the modified Beeler-Reuter ionic model where the sodium current increases from right to left.

Example of spiral wave tip trajectories

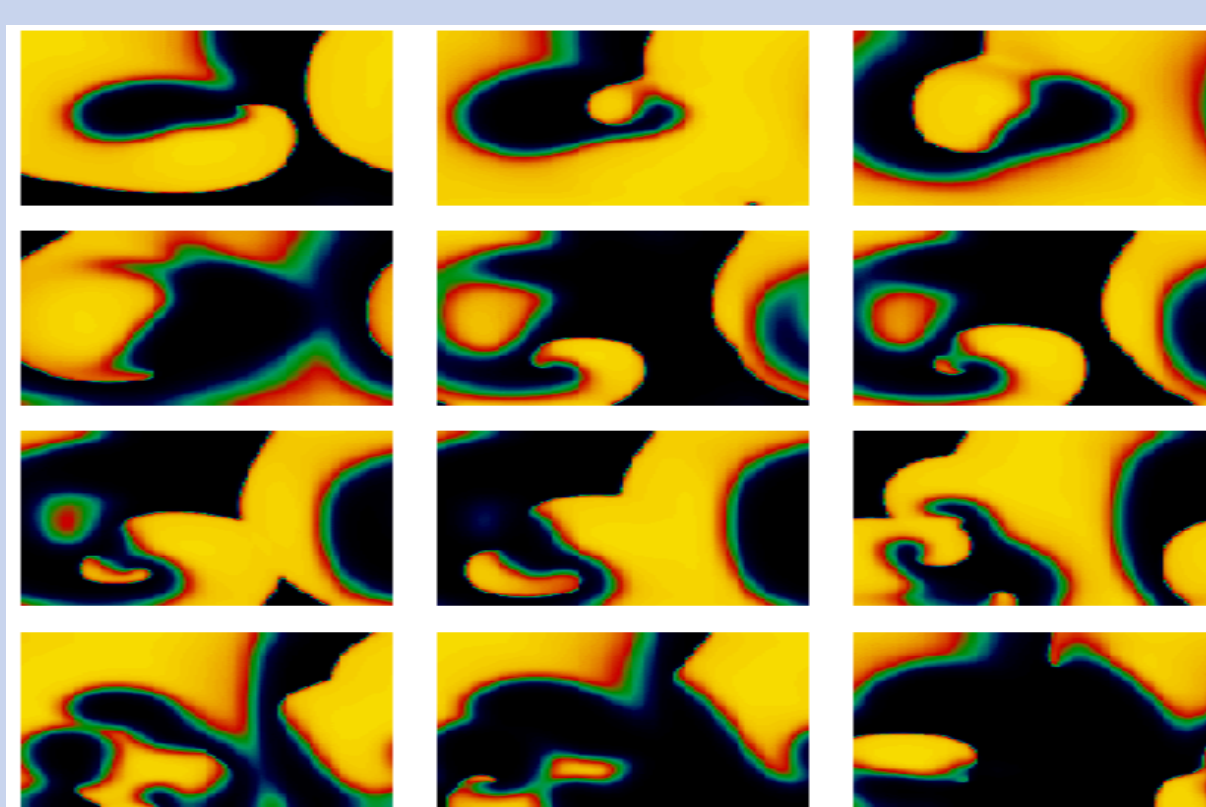


Spiral Wave Breakup by Periodic Boundary Conditions

We used the 3V-SIM (fitted to the MBR) to study the stability of spiral waves as function of tissue size and periodic boundary conditions by first simulating a cylindrical ventricle. For cylinders with a perimeter larger than the spiral's wave length, we found no difference in dynamics when compared to a spiral rotating on a square sheet of tissue with zero flux boundary conditions. Nevertheless, when the perimeter is compared to the wave length, then the spiral wave tip becomes perturbed by the incoming waves generated by itself.

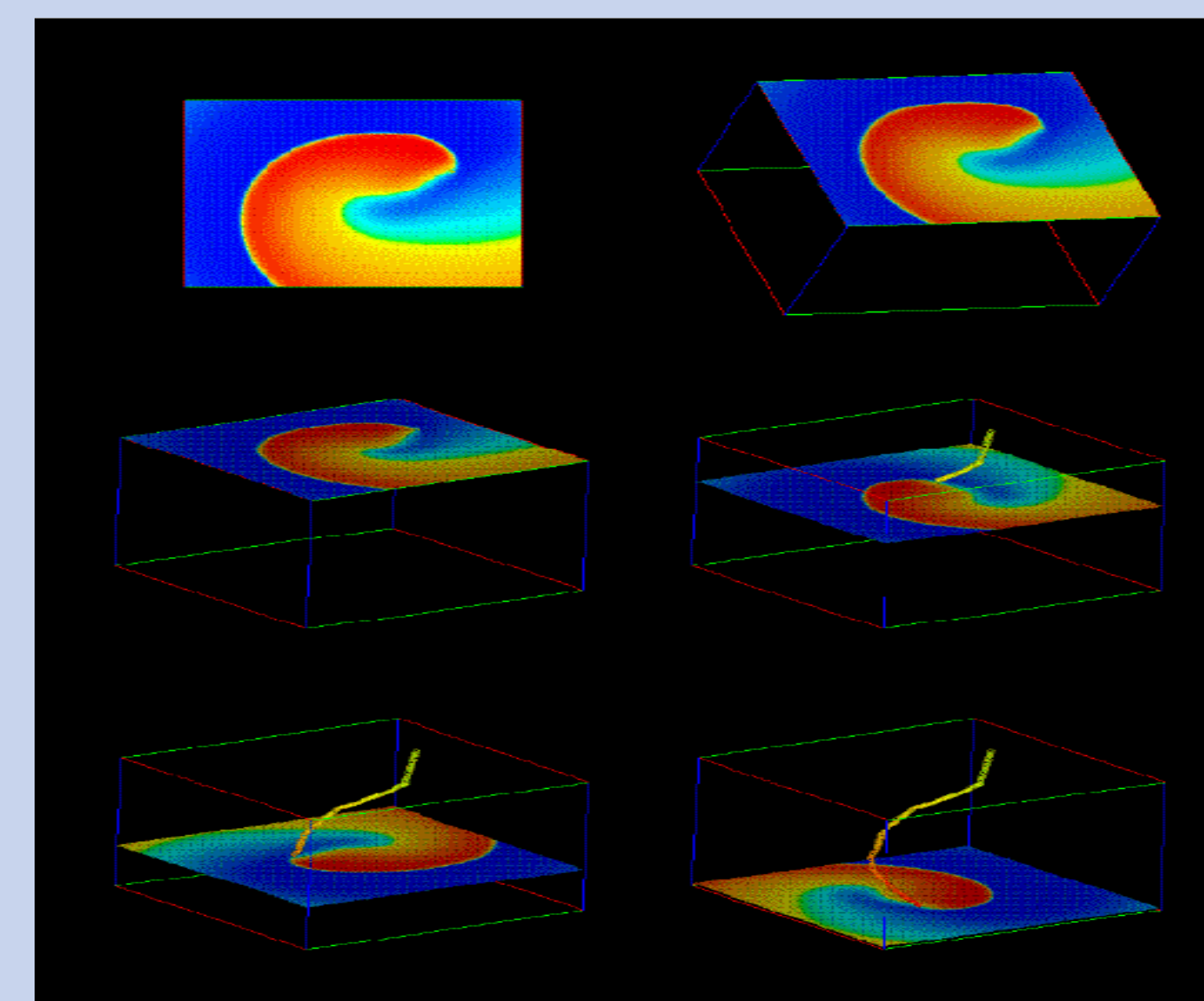


The collision of incoming waves, with a higher frequency than the one of rotation, produces a drift on the spiral. This drift is proportional only to the ratio between the cylinder's perimeter and the length of the wave-tip-trajectory (core). For spiral waves in the hyper-meander regime, there is a window of perimeter sizes between the drift and minimum size before termination, for which otherwise stable spirals will break. The breakup is produced by conduction blocks between the spiral wave tip and self incoming waves generated by uneven regions of repolarization due to the hyper-meander tip.

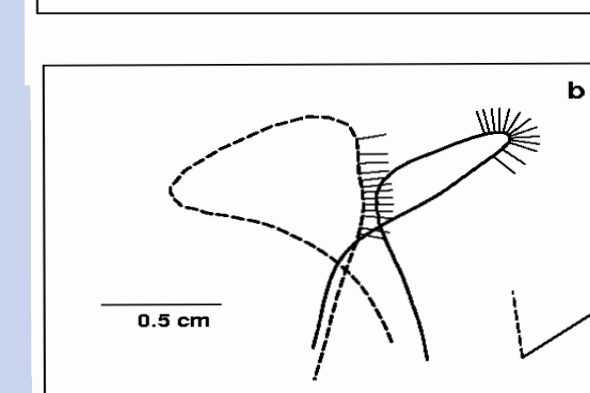
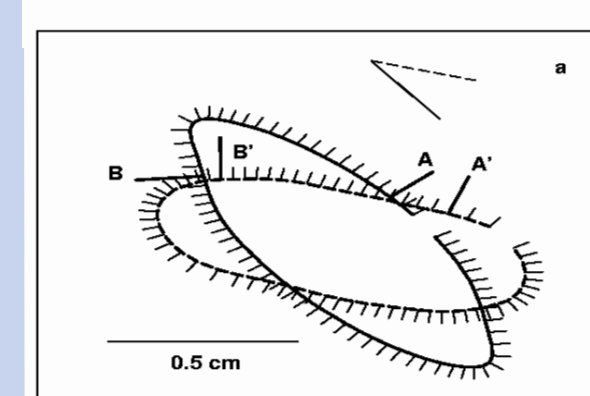
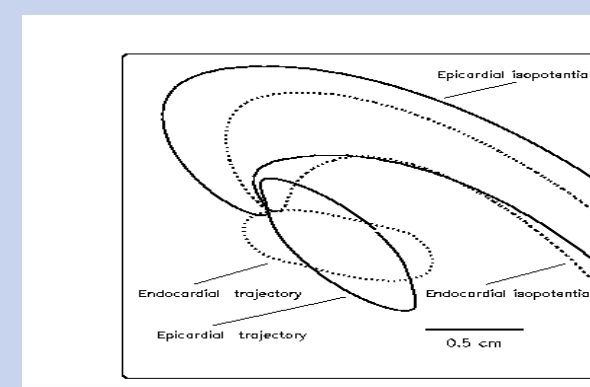
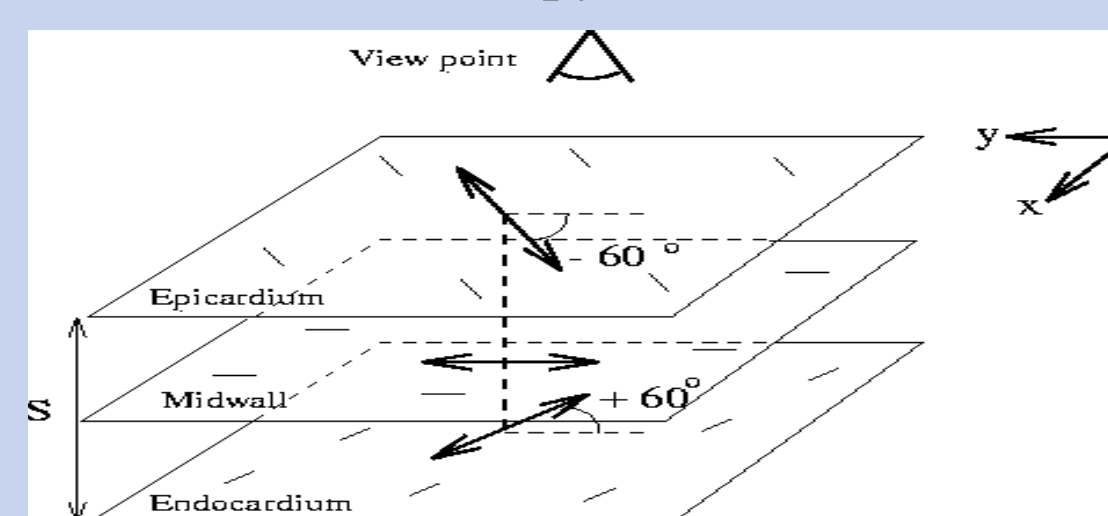


The top figure shows breakup of a spiral wave (fitted to the MBR) on a cylinder (unfolded where the vertical boundaries are periodic) with a 4 cm diameter. Note that the spiral would be stable on a larger tissue or on the same size tissue but with zero flux boundary conditions.

3D and Rotational Anisotropy



In 3D spiral waves become scroll waves, and the tip a vortex line with curvature twist and torsion (top graph). We studied the stability of spiral waves in 3D considering the natural rotational anisotropy of the fibers (bottom graph).

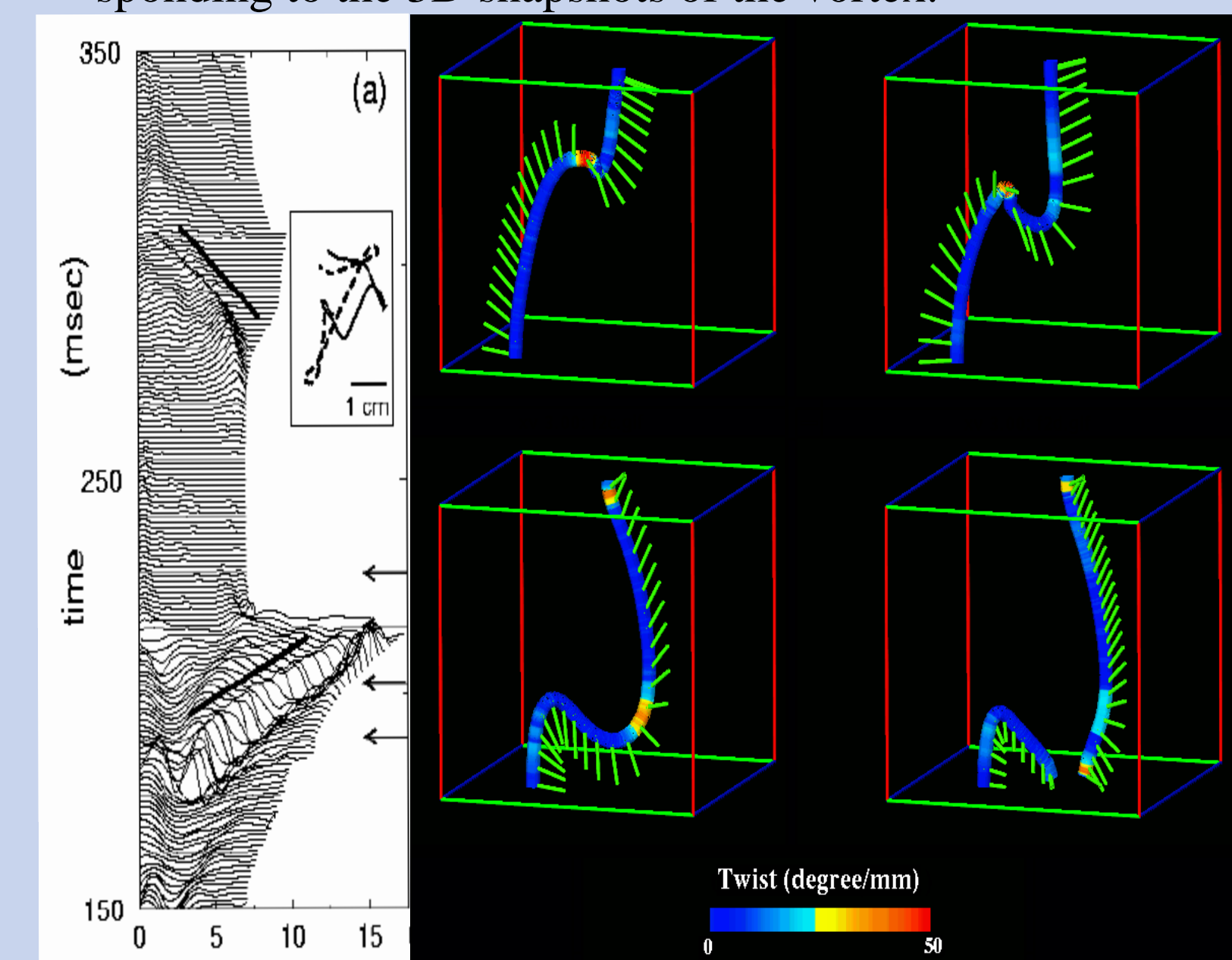


For thin slabs with small rotational anisotropy stable scroll waves behave similarly to spiral waves in 2D. However, as the rotational anisotropy and thickness are increased the vortex lines can elongate and curve due to a highly localized twist induced by the fiber rotation. These elongated vortices collide with the tissue boundaries and produce a wave breakup which leads to multiple waves characteristic of VF. First top figure shows the nature of the vortex twist, where we plotted the contour and trajectory of a spiral wave in the epi- and endocardium where the thickness is 2.2 mm and fiber rotation (FR) is 12°/mm

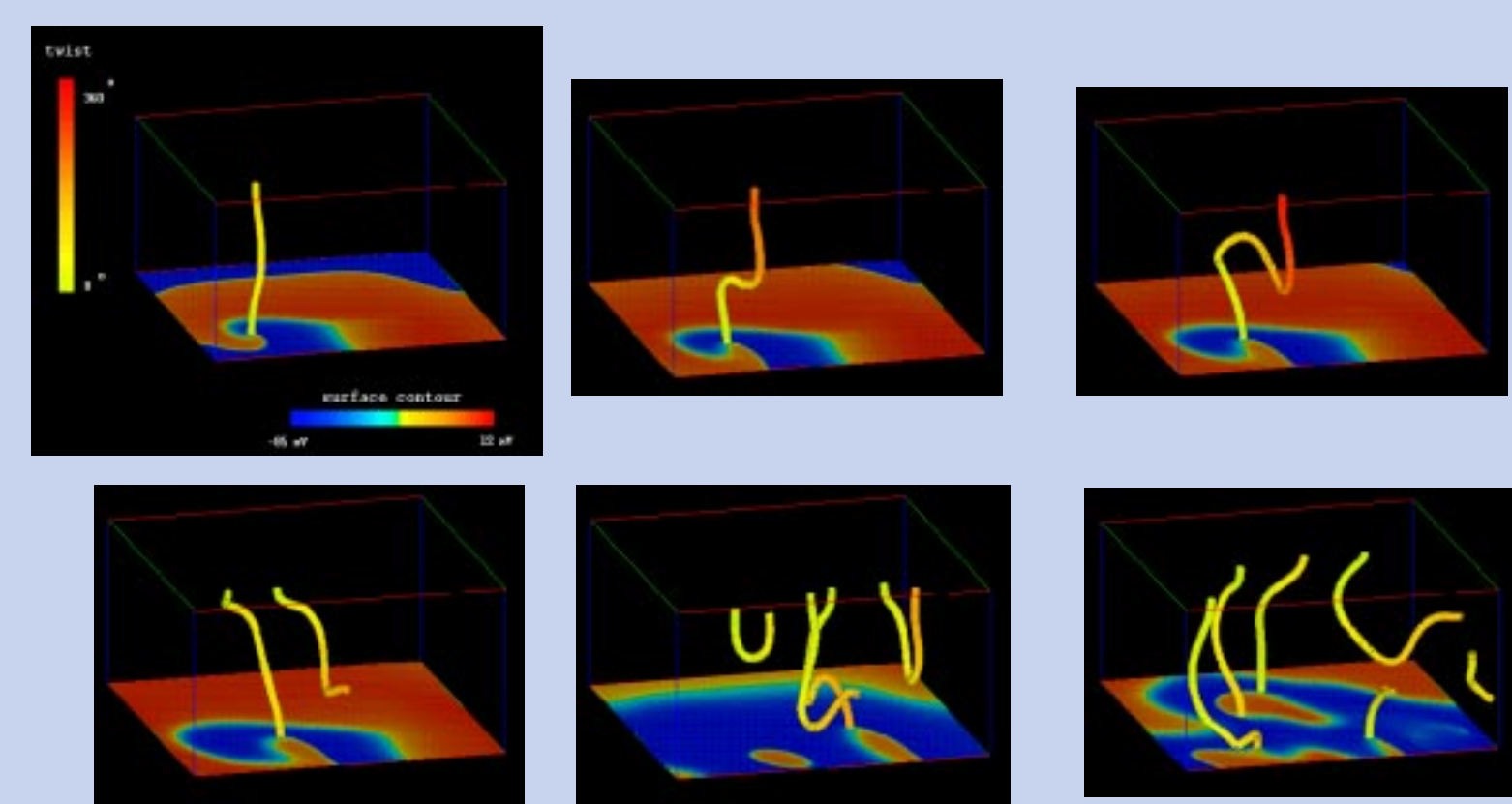
and the spiral wave follows a circular core (distorted ellipses because of tissue anisotropy 1:0.33 ratio). The major axes of the ellipses are rotated by an angle roughly equal to the total FR and the anisotropic velocity induces a phase difference in the spiral rotation between the epi- and end-cardium. A twist is produced when the spiral at one end leads in time the one at the other end during the pivot turn.

Notice how the spiral in the epi- already finished the turn while the one in the endo- has not started yet. The amount of twist is then produced every pivot turn (twice per period) and the amount of twist not only depends on the FR but also on the curvature of the tip trajectory. Being larger when the spiral is in the hyper-meander regime (see Fig. a,b).

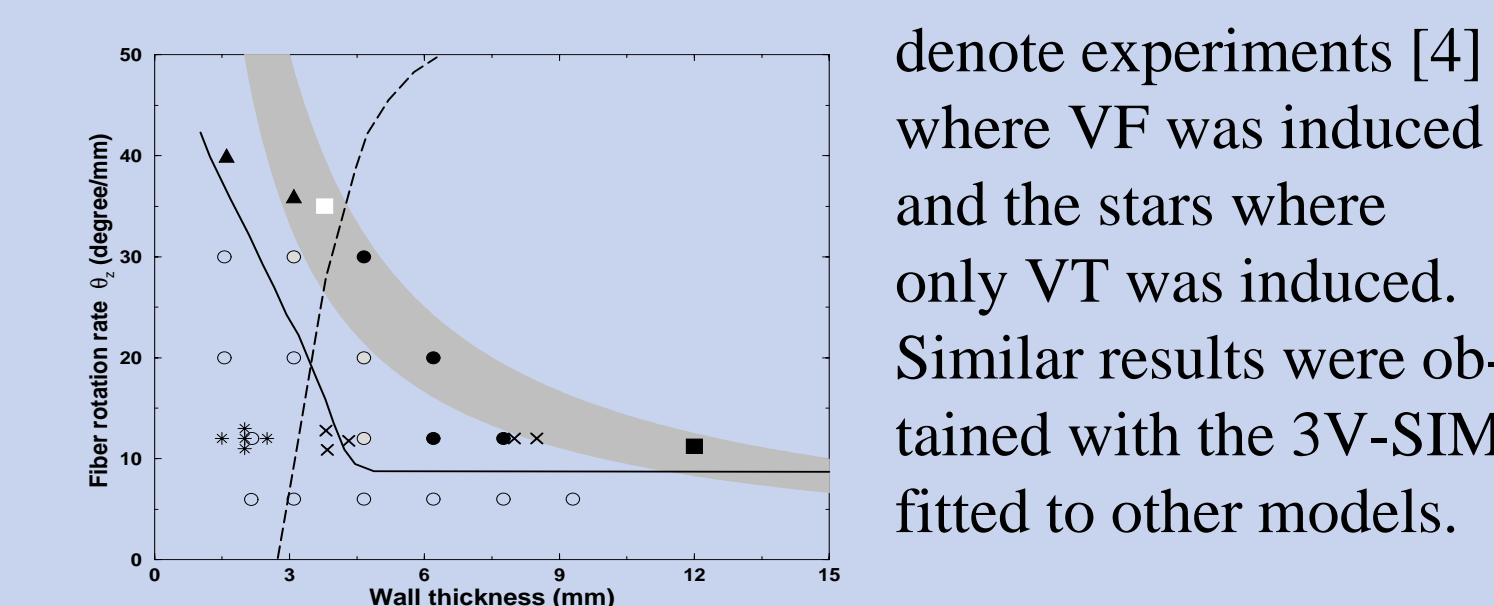
The propagation of twist along a vortex filament and its elongation is shown in the next graphs. The simulation corresponds to a spiral wave on a tissue with 7.5mm of thickness and 12°/mm. a) twist vs arclength along the filament for 200 ms. The arrows indicate the time corresponding to the 3D snapshots of the vortex.



The following are 3D snapshots showing the main creation event of vortex lines that lead to the decay of VT into VF under this framework. The bottom surface shows the voltage activation at the endo-cardium. As the vortex elongates it touches the boundaries forming extra half rings which expand and produce new vortices and a complex spatiotemporal activity.



The summary of simulation results using the 3V-SIM fitted to the MBR model is shown in the next figure. The gray area represents mammalian hearts. The solid line separates the boundaries between stable VT (below the line) and developed VF (above).



Conclusions

Spiral breakup due to periodic boundary conditions may be present in normal hearts when a hypermeandering spiral wave is generated (or drifts) close to the apex where the perimeter of the heart is small. Also, the anisotropic fiber architecture of the left ventricular wall is a major predisposing factor for the degeneration of VT to VF. Our numerical simulations have demonstrated that transmural fiber rotation causes 3D scroll waves to become unstable and to spontaneously decay into wave turbulence above a minimum wall thickness comparable to the one observed in some experiments [4].

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- [3] J.M. Davidenko et al., Nature 355, 349 (1992).
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