Effect of Inhomogeneities on the Spiral-Wave Dynamics in Models of Cardiac Tissue

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Anatomical vs. Functional Reentry

Anatomically determined (Mines, 1913)

1. Fixed length of circuit (determined by anatomical obstacle).
2. Usually excitable gap between head and tail of impulse.
3. Inverse relation between revolution time and conduction velocity.

Functionally determined (Allessie et al., 1977)

1. Circuit length dependent upon electrophysiological properties. ("Spiral waves")
2. No gap of full excitability.
3. Revolution time proportional to length of refractory period.
Nonconducting Obstacles

Spiral Wave Attachment to Millimeter-Sized Obstacles

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Background—Functional reentry in the heart takes the form of spiral waves. Drifting spiral waves can become pinned to anatomic obstacles and thus attain stability and persistence. Lidocaine is an antiarrhythmic agent commonly used to treat ventricular tachycardia clinically. We examined the ability of small obstacles to anchor spiral waves and the effect of lidocaine on their attachment.
Nonconducting Obstacles

Such inhomogeneities and obstacles, present in cardiac tissue, can yield the following:

5. **Spiral breakup, i.e., VF.**

5. **Partial suppression, i.e., VF → VT transition.**

5. **Complete suppression of VF.**
Models of Ventricular Tissue

Basically reaction-diffusion equation of the form

\[ \frac{\partial V}{\partial t} + \frac{I}{C} = D \nabla^2 V \]

Various Models; we concentrate on:

- Luo-Rudy Model (realistic);
- Reduced Priebe Beuckelmann Model;
- Panfilov Model (simplified).
In our models we have introduced nonconducting inhomogeneities (say $80 \times 80$ in a $400 \times 400$ simulation domain) and we find all the three types of behaviours mentioned above:

- Sometimes the inhomogeneity causes spiral breakup (red).
- Sometimes it suppresses VF partially and converts it into VT (blue).
- It can even suppress VF completely (green).
Obstacle in Panfilov Model - Changing the Size

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Obstacle in Panfilov Model - Shape
Obstacle in Panfilov Model - Shape
When an obstacle of side 40 mm is placed at \((x = 100 \text{ mm}, y = 160 \text{ mm})\) the spiral breaks up. A, B and C shows snapshots at time 1100 ms, 1650 ms and 2750 ms respectively. The local time series, interbeat interval IBI, and power spectrum of the transmembrane potential \(e(x,y,t)\) are shown in D, E, and F respectively.
When an obstacle of side 40 mm is placed at \((x = 100 \text{ mm}, y = 150 \text{ mm})\) the spiral gets attached to it. A, B and C shows snapshots at time 1100 ms, 1650 ms and 2750 ms respectively. The wave gets attached to the obstacle.
Spiral wave moves away from the medium in presence of the obstacle. When a square obstacle of side 40 mm is placed in the medium such that its lower-left corner is at (x =100 mm, y=140 mm) the the spiral moves away from the medium. A, B and C shows snapshots at time 1100 ms, 1650 ms and 2750 ms respectively.
An obstacle of side $l=18\text{mm}$ is placed at $(x = 58.5\text{ mm}, y = 63\text{ mm})$. The spiral turbulence persist in this case. A,B, and C shows snap shots taken at 200, 600, and 1000 ms respectively. D, E, and F show the local time series, interbeat interval, and powerspectrum calculated from a sample of 261 424 iterations.
Obstacle of side $l=18\text{mm}$ is placed at $(x = 58.5 \text{ mm}, \ y = 63 \text{ mm})$. The spiral anchores to the obstacle. A,B, and C shows snap shots taken at 200, 600, and 1000 ms respectively. D, E, and F show the local time series (taken from $(x=45 \text{ mm}, \ y=45 \text{ mm})$, interbeat interval, and powerspectrum calculated from a sample of 261 424 iterations.
Spiral moving away from simulation domain because of the obstacle at \((x = 54\text{ mm}, y = 63\text{ mm})\). A, B, and C shows snapshots taken at 200, 600, and 1000 ms respectively.
Obstacle of side $l=18\text{mm}$ is placed at $(x = 67.5\text{ mm}, y = 72\text{ mm})$. The spiral anchors to the obstacle. A,B, and C shows snap shots taken at 200, 600, and 1000 ms respectively. D, E, and F show the local time series (taken from $(x=45\text{ mm}, y=45\text{ mm})$), interbeat interval, and powerspectrum calculated from a sample of 261 424 iterations.
Animations

Square obstacle, VF
Square obstacle, VT
Square obstacle, NS
Two obstacles, VF
Two obstacles, VT
Two obstacles, NS
3D, ST
3D, RS
3D, NS
The colour of each small square indicates the final state of the system: red indicates spiral turbulence, blue a single anchored spiral, and green a quiescent state with no spirals, when the position of the lower-left hand corner of the obstacle coincides with that of the small square.
Stability Diagram

Effect of Inhomogeneities on the Spiral-Wave Dynamics in Models of Cardiac Tissue
Ionic Inhomogeneities

- How do other kinds of heterogeneities in cardiac tissue affect spiral-wave dynamics?
- The role of ionic heterogeneities in the system.
- Ionic heterogeneities can arise from ischemia, chronic heart failure or even from genetic disorders.
- They typically affect APD, and its timescales. They can also change the system from periodic to quasiperiodic and chaotic states.
Complex-periodic spiral waves in confluent cardiac cell cultures induced by localized inhomogeneities

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Edited by Harry L. Swinney, University of Texas, Austin, TX, and approved May 23, 2005 (received for review February 24, 2005)

Spatiotemporal wave activities in excitable heart tissues have long been the subject of numerous studies because they underlie differential forms of cardiac arrhythmias. In particular, understanding states are found to be common in this system. Analysis on their tip trajectory orbits suggest that there are many localized inhomogeneities interacting with spiral tips. We find that these
Ionic Inhomogeneities

Fig. 1. Complex-period meandering spiral wave around a heart of conduction (A, B, C). Time series (D) are taken in the absence of inhomogeneity. (E) and (F) show the spiral wave propagation in the presence of inhomogeneity. (G) shows the spiral wave propagation in the presence of inhomogeneity with a defect. (H) shows the spiral wave propagation in the presence of inhomogeneity with a hole.
Changing $\epsilon_1$ in Panfilov Model

Figure shows the snapshots of $V$ values after 3300 ms and associated powerspectra for different values of $\epsilon_1$. (A) When $\epsilon_1=0.03$; Note that there is only fundamental frequency in the powerspectrum corresponding to Hz indicating periodic spiral wave dynamics. (B) When $\epsilon_1=0.02$, there are two independent fundamental frequencies indicating quasiperiodic nature of the spiral-wave dynamics. (C) When $\epsilon_1=0.01$, the spiral waves break up and power spectrum is broad, indicating spatiotemporally chaotic dynamics.
Changing $\epsilon_1$ in Panfilov Model

With $\epsilon_1^{out}=0.01$ and $\epsilon_1^{in}=0.02$, and inhomogeneity placed at (130 mm, 80 mm) spiral moves away from the medium. The above snap shots are taken at 1100 ms (A), 1650 ms (B) and 2200 ms (C).
Changing $\epsilon_1$ in Panfilov Model

The Spiral wave gets anchored to the inhomogeneity. Here $\epsilon_1^{out} = 0.01$ and $\epsilon_1^{in} = 0.02$. The inhomogeneity is placed at (100 mm, 90 mm). Though the spiral gets anchored note that the period of spiral wave is not constant, and exhibits quasiperiodic behaviour.
Conclusions

- VF: breakup of spiral/scroll waves induced by reentrant activity.
- Spiral turbulence is a spatiotemporally chaotic phenomenon in Panfilov, BR and LR models.
- The durations of chaotic transients depend on system size (small mammals are less likely to get heart attacks than large mammals).
- Spiral breakup in these models can be controlled by low-amplitude pulses.
Our simulations show that cardiac arrhythmias depend sensitively on the shape, size, and positions of conduction inhomogeneities in ventricular tissue.

This must arise because of a fractal basin that separates the domain of attraction of VF from those of VT and quiescent behaviour.

Our work provides a natural explanation for the large variety of experimental results.
Conclusions

Ionic and timescale heterogeneities also result in spiral suppression, anchoring, and complex spiral wave dynamics.

Optimal anti-tachycardia pacing and defibrillation protocols might well have to be tailor made for different patients (as is done already to some extent).
Publications

