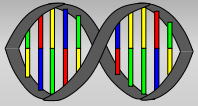


Arrhythmias By Dimension or Heart Attacks can give you Mathematics

J. P. Keener

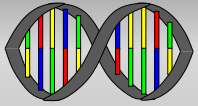
Mathematics Department

University of Utah



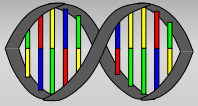
The Medical Problem

- Sudden Cardiac Arrest kills 1/2 million people in the US each year.



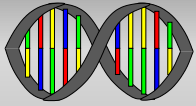
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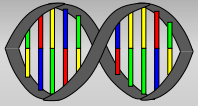
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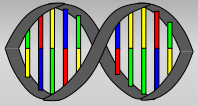
The Medical Problem

- Sudden Cardiac Arrest kills 1/2 million people in the US each year.
- Antiarrhythmic drugs are not reliable.
- Implantable defibrillators are expensive.
- Defibrillators are not always available when needed.



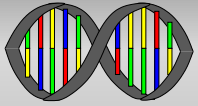
The Challenge

- Identify the different arrhythmias and their underlying mechanisms.



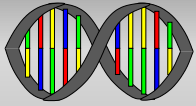
The Challenge

- Identify the different arrhythmias and their underlying mechanisms.
- Understand the cause or origin of each arrhythmia

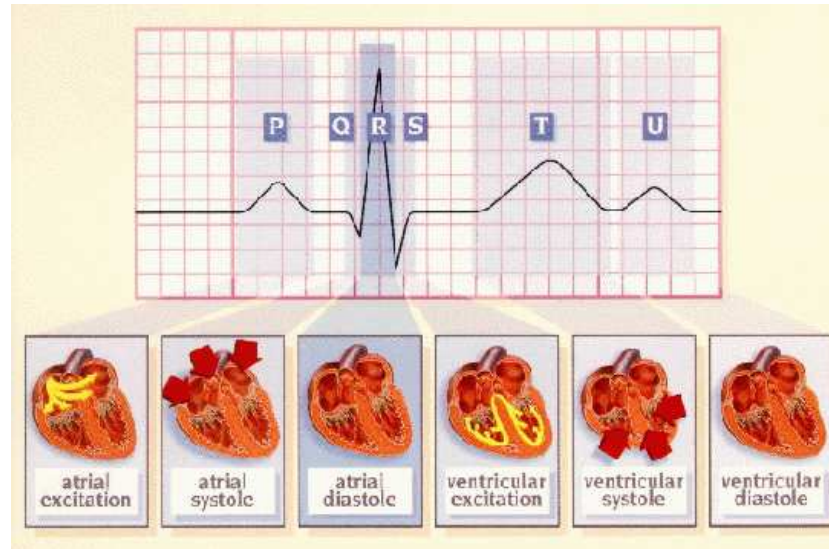


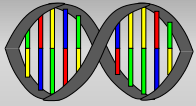
The Challenge

- Identify the different arrhythmias and their underlying mechanisms.
- Understand the cause or origin of each arrhythmia
- Determine how to control the arrhythmia.

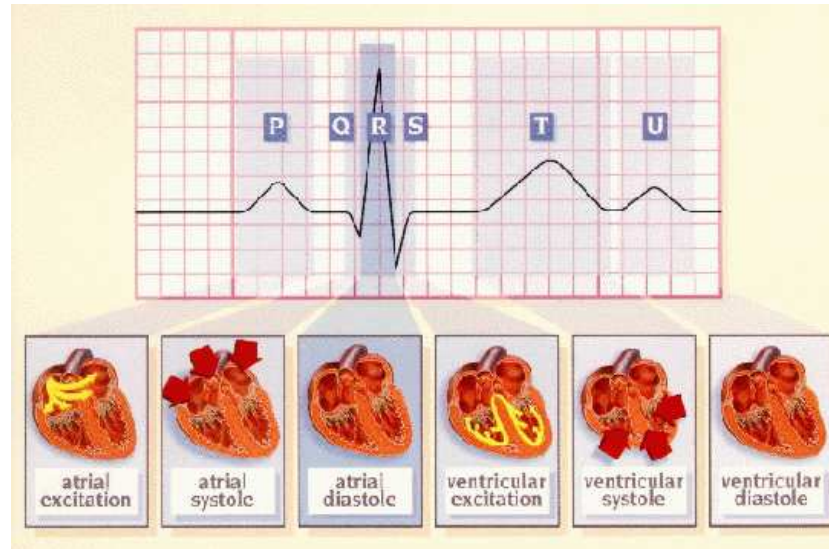


Conduction system of the heart

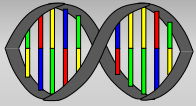




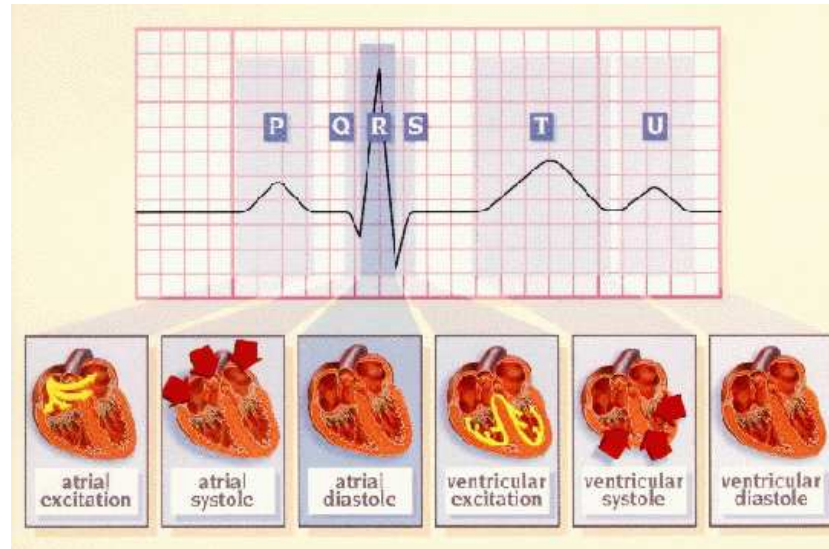
Conduction system of the heart



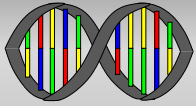
- Electrical signal originates in the SA node.



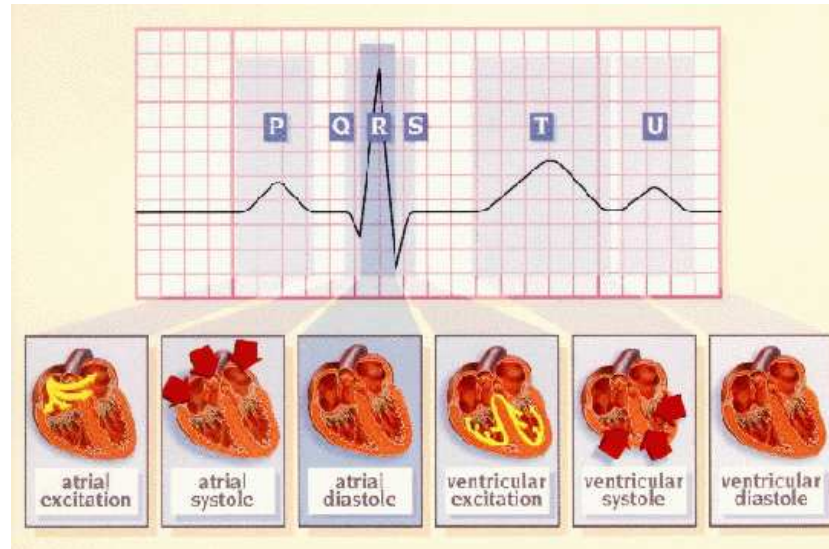
Conduction system of the heart



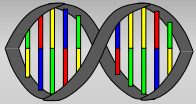
- Electrical signal originates in the SA node.
- The signal propagates across the atria, through the AV node, and throughout the ventricles.



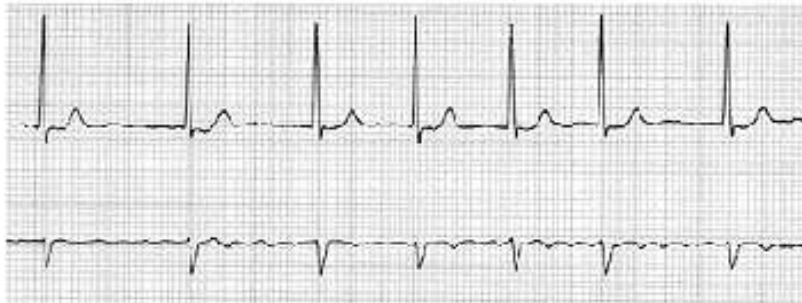
Conduction system of the heart

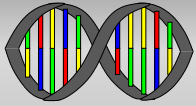


- Electrical signal originates in the SA node.
- The signal propagates across the atria, through the AV node, and throughout the ventricles.
- The muscle cells contract in unison, and then relax awaiting the next signal.



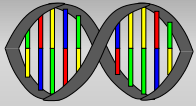
Some Examples of EKG's



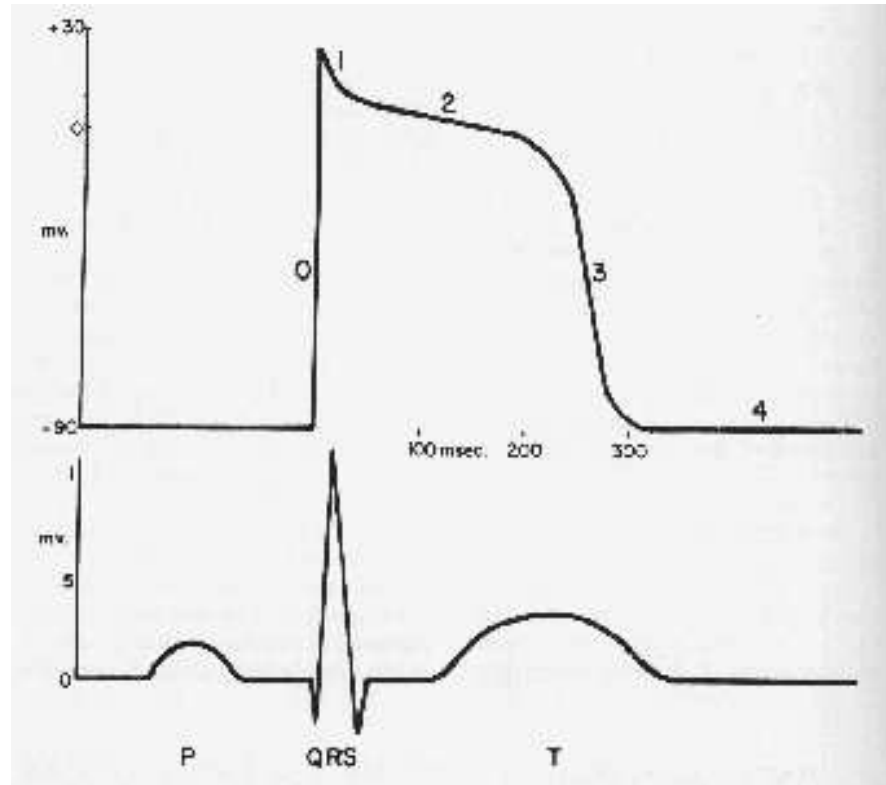


Theories of Arrhythmias

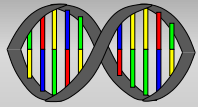
- **D=0: Individual cells run amuck.**
- D=1: There are closed (reentrant) pathways around anatomical obstacles.
- D=2: There are self-sustained spiral waves.
- D=3: There are self-sustained scroll-waves.



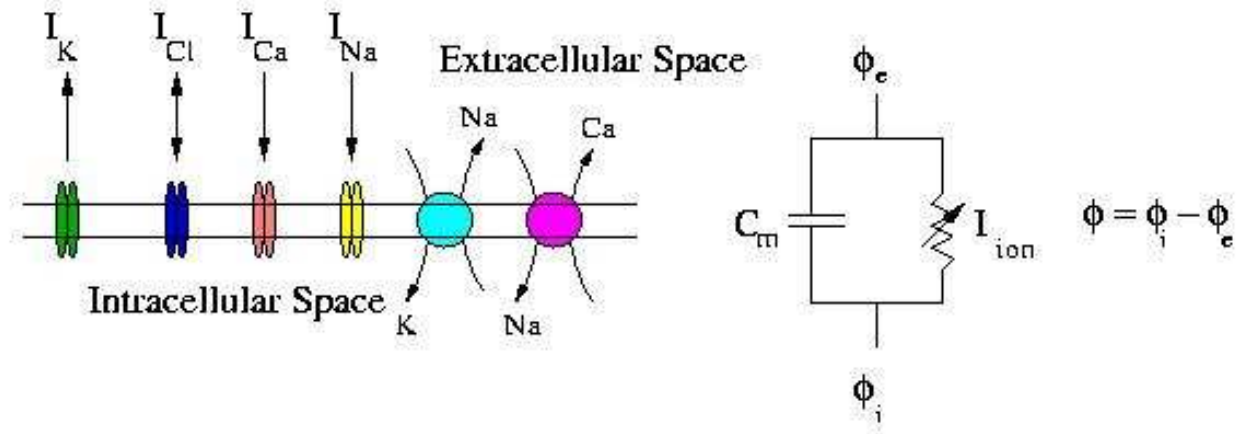
Dimension 0: Single Cells



Cellular Transmembrane potential and electrocardiogram

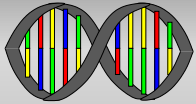


Modeling Cardiac Electrical Activity

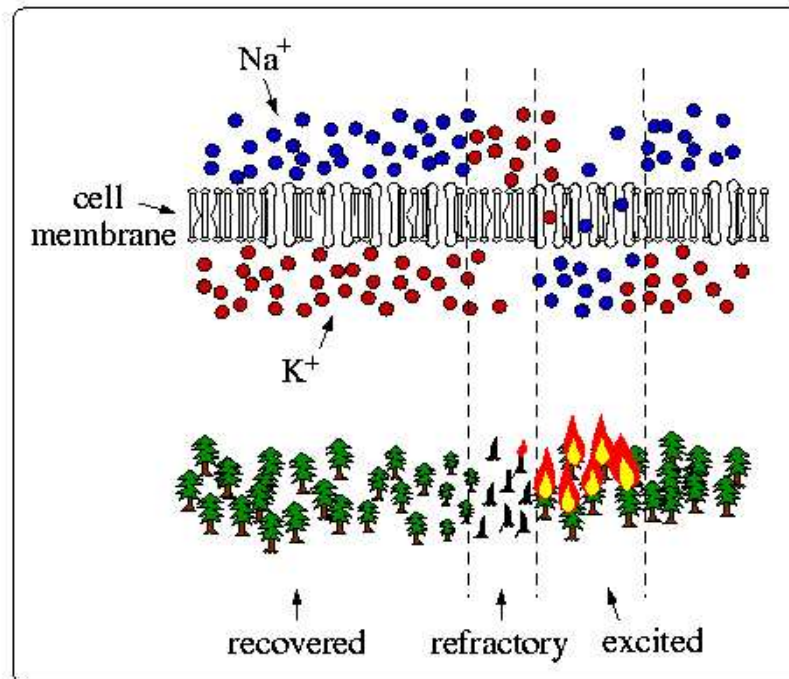


Transmembrane potential ϕ is regulated by transmembrane ionic currents and capacitive currents:

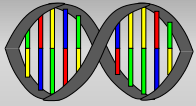
$$C_m \frac{d\phi}{dt} + I_{ion}(\phi, w) = I_{in} \quad \text{where} \quad \frac{dw}{dt} = g(\phi, w), \quad w \in R^n$$



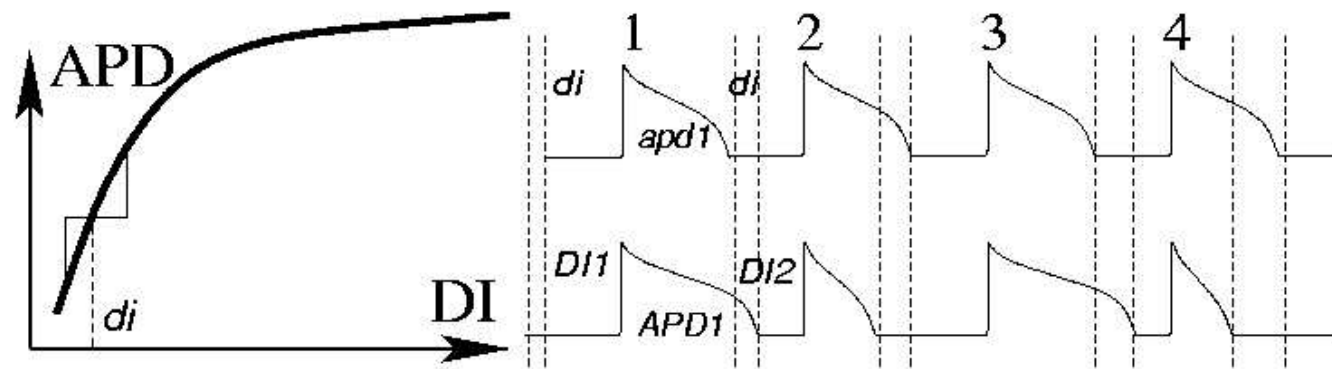
Thinking about Excitable Media



The forest fire analogy



APD Alternans



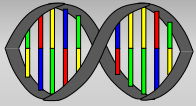
Action Potential Duration Restitution Curve

$$APD_n + DI_n = BCL.$$

where $APD_n = A(DI_{n-1})$ is the restitution curve. It follows that

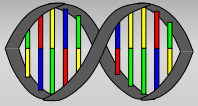
$$DI_n = BCL - A(DI_{n-1}),$$

APD Map Animated

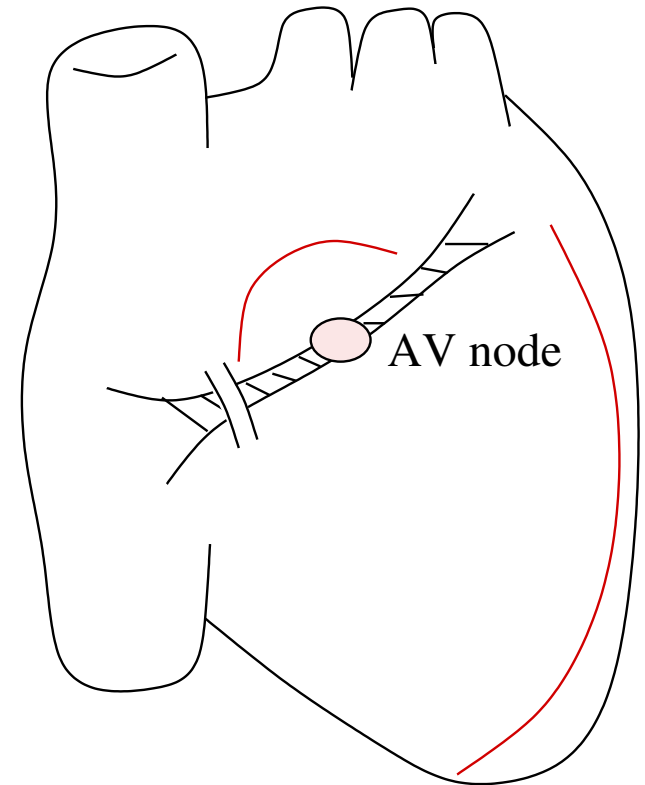
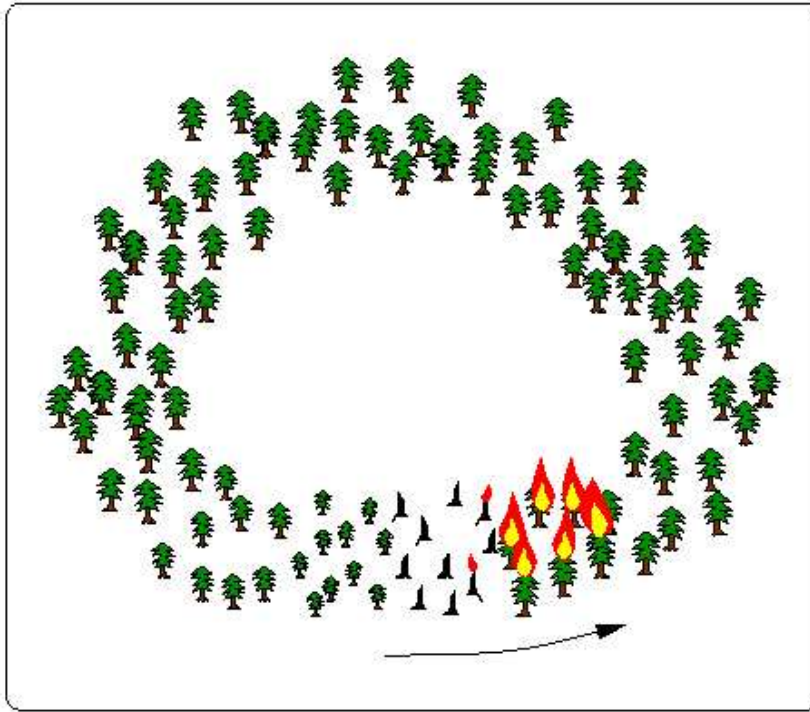


Theories of Arrhythmias

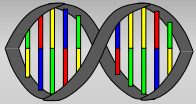
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- $D=3$: There are self-sustained scroll-waves.



1 Dimensional Reentry

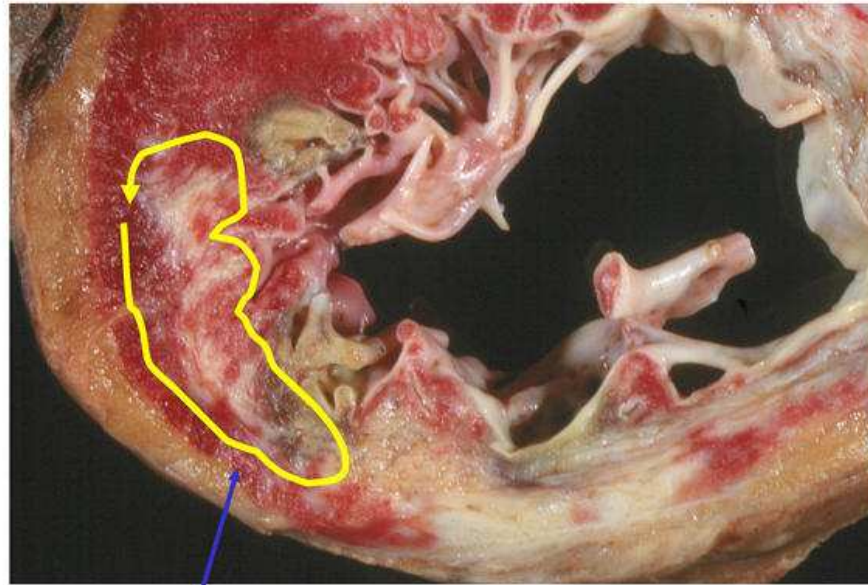


(Show movie)



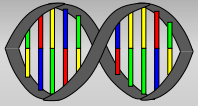
Observation

I D reentrant arrhythmias are 100% curable.



Potential Reentry Circuit paths

Why could this reentrant arrhythmia not be cured?

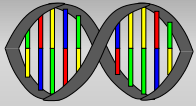


The APD Instability in 1D

Stable Pulse on a Ring

Unstable Pulse on a Ring

Collapse of Unstable Pulse

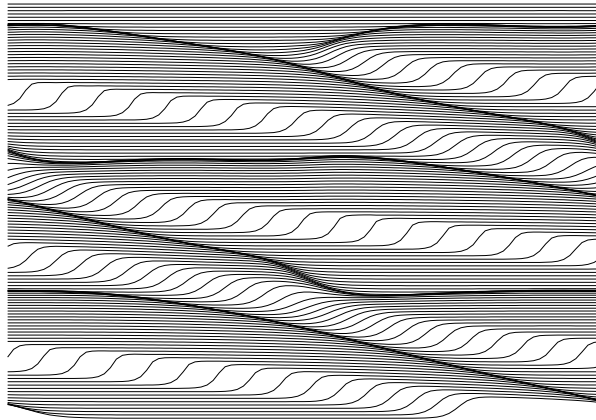


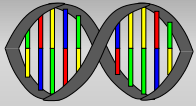
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Unstable Pulse on a Ring

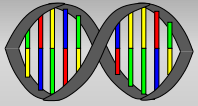
Collapse of Unstable Pulse



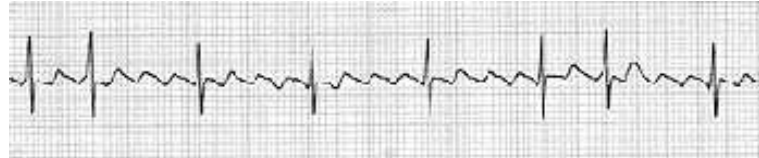


Theories of Arrhythmias

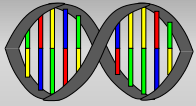
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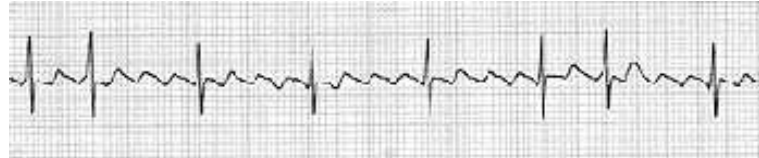
Dimension 2: Spirals



Atrial Flutter

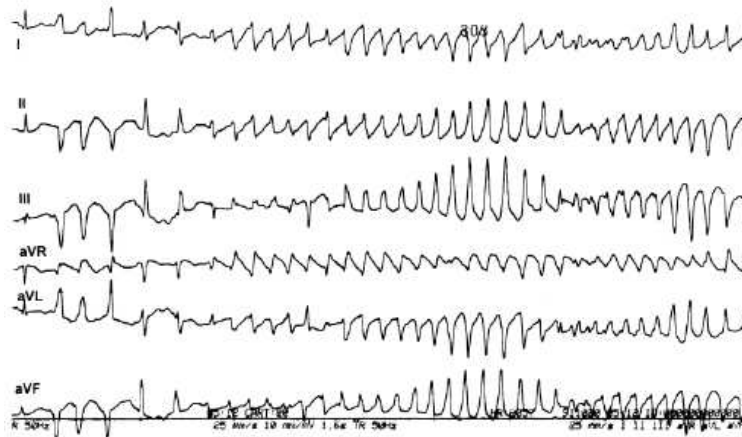


Dimension 2: Spirals

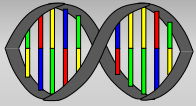


Atrial Flutter

Spiral instability - Meander:



Torsade de Pointe

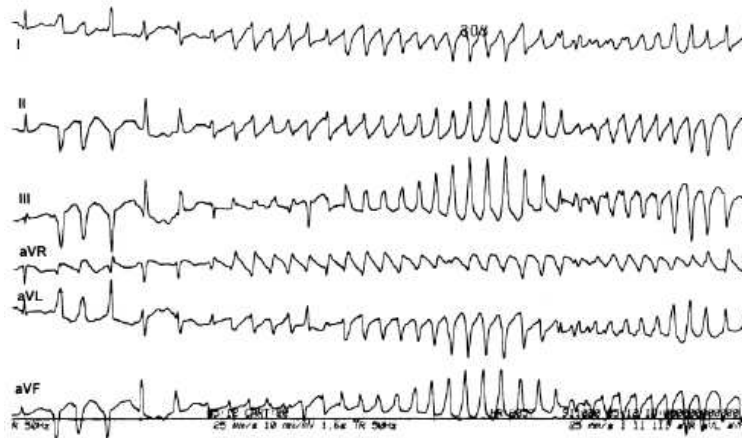


Dimension 2: Spirals

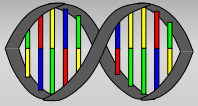


Atrial Flutter

Spiral instability - Meander:

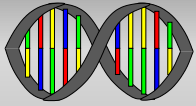


Torsahd duh Pwahn



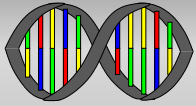
The APD Instability in 2D

Spiral Breakup

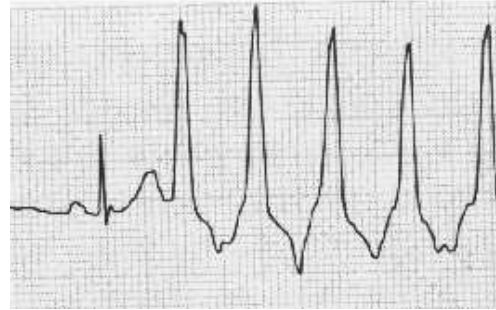


Theories of Arrhythmias

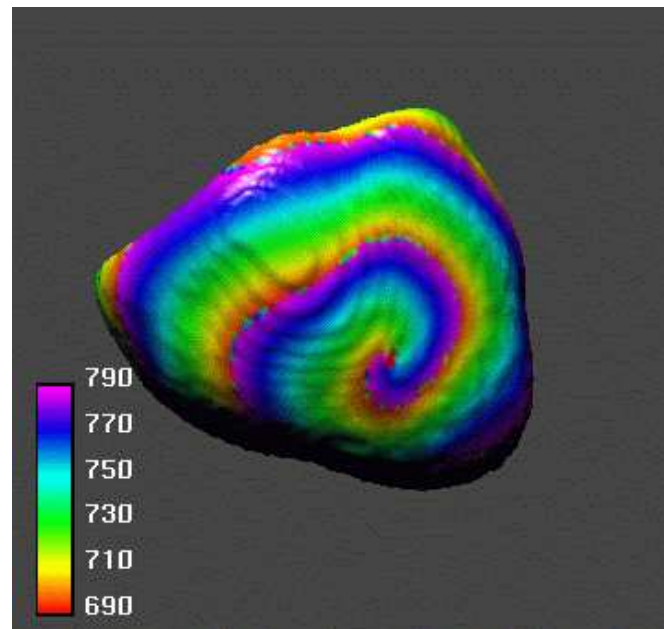
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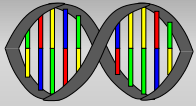


Dimension 3: Ventricular Reentrant Activity



Ventricular Monomorphic Tachycardia

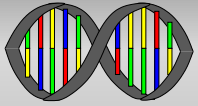




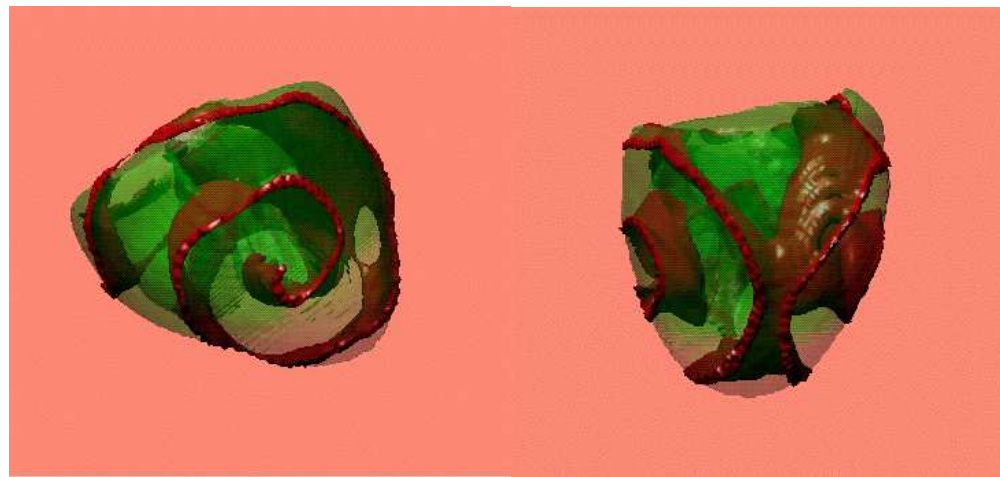
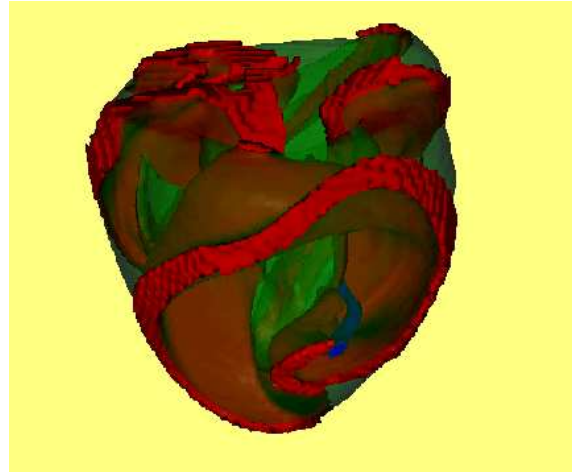
Dimension 3: Scroll Waves



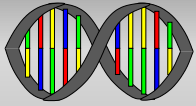
Scroll Waves: Columns in the Ionic style, 400 B.C.



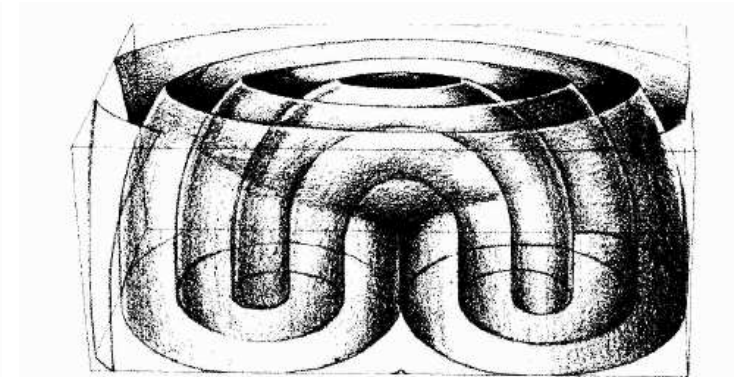
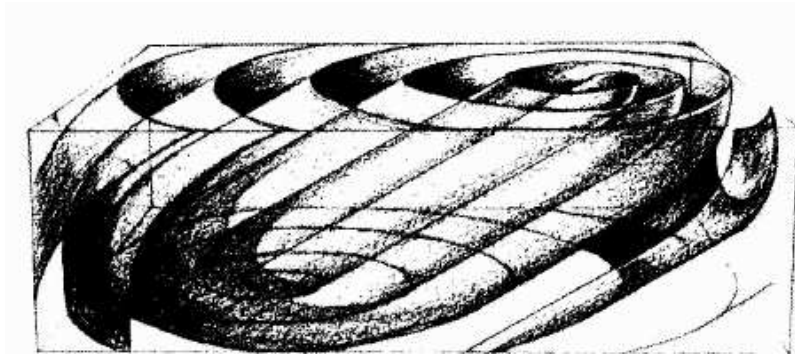
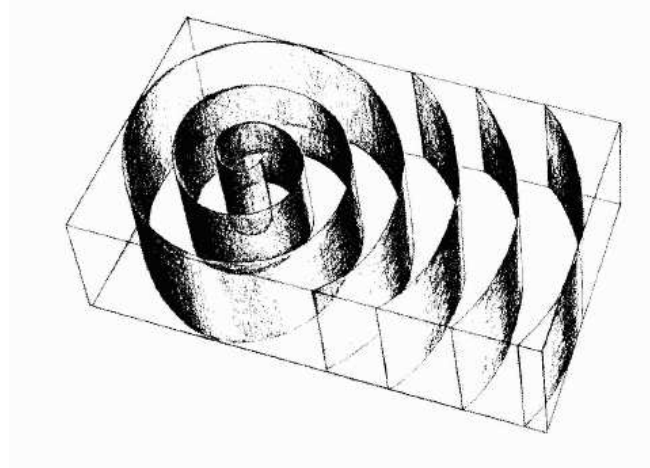
Dimension 3: Cardiac Scroll Wave



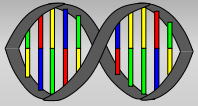
3 D structure of a single scroll wave



Scroll Wave Cross-Sections



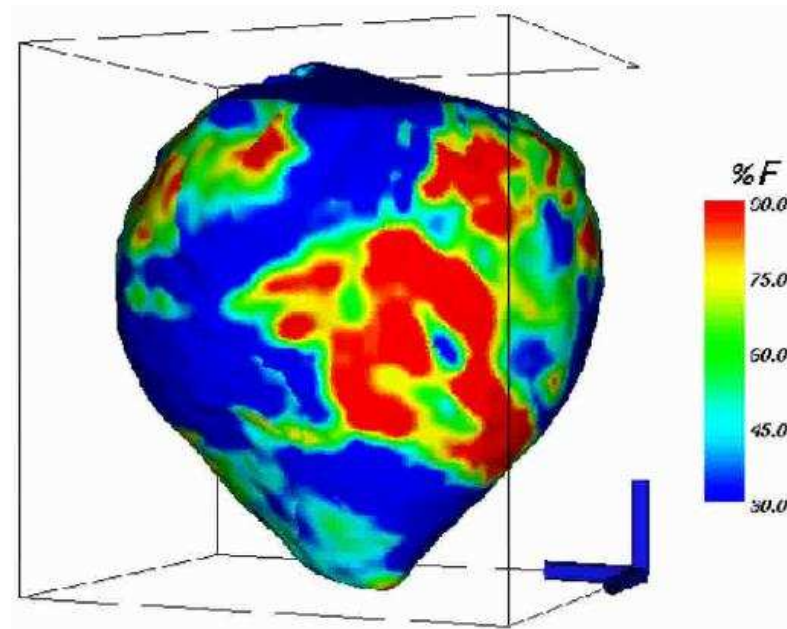
Lesson to learn: Target patterns are not necessarily created by
an autonomous oscillator.



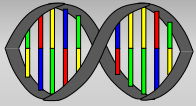
Ventricular Fibrillation



Ventricular Fibrillation



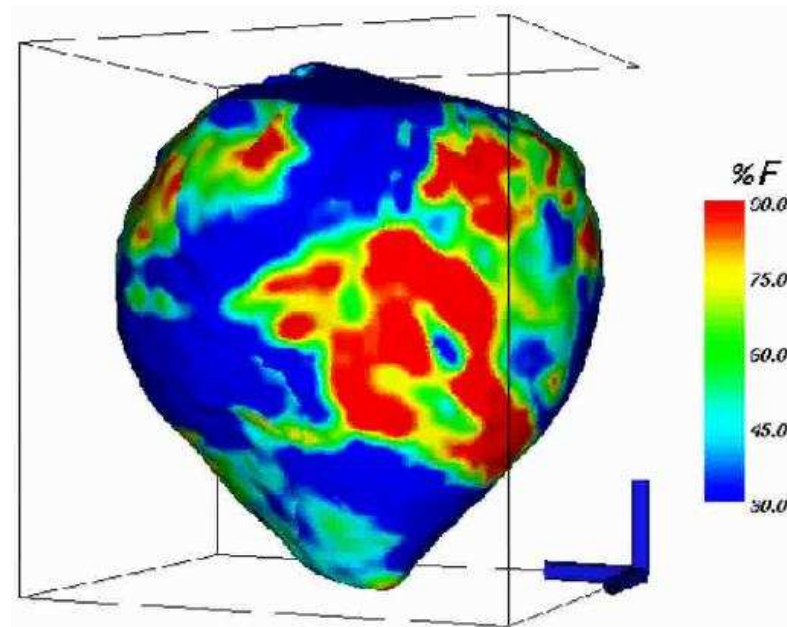
(Real Data)



Ventricular Fibrillation

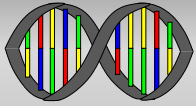


Ventricular Fibrillation



(Real Data)

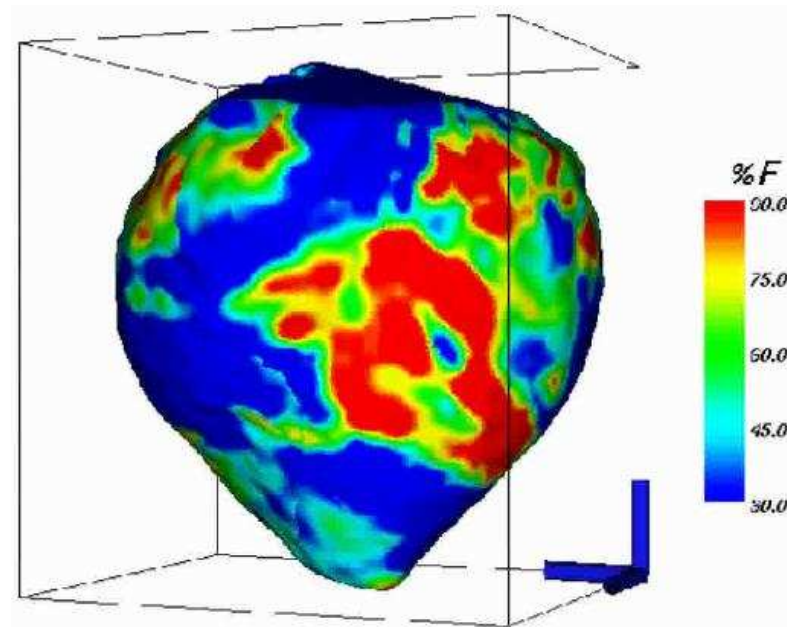
Why do we not see self-sustained spirals?



Ventricular Fibrillation

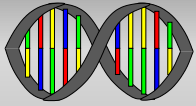


Ventricular Fibrillation

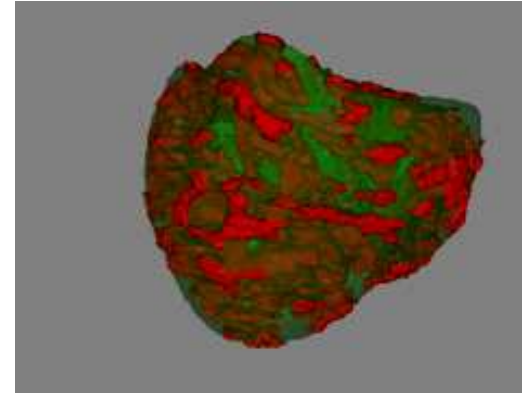
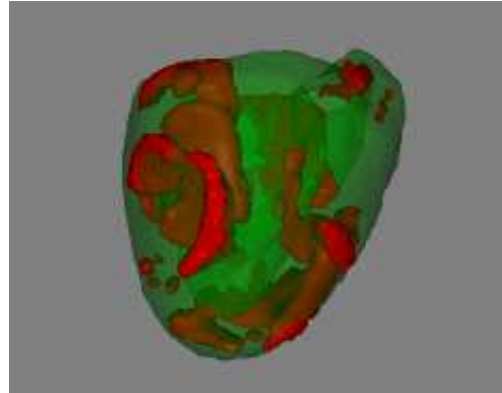
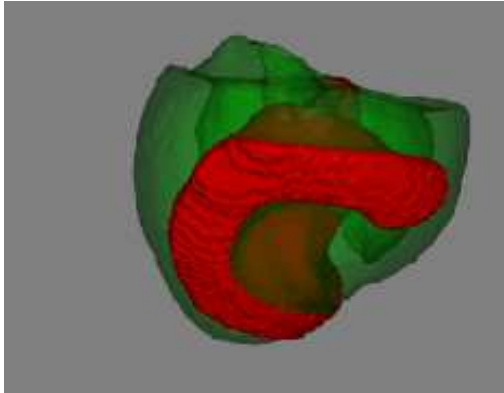


(Real Data)

Why do we not see self-sustained spirals?

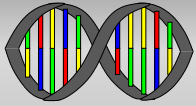


Transparent View of Fibrillation



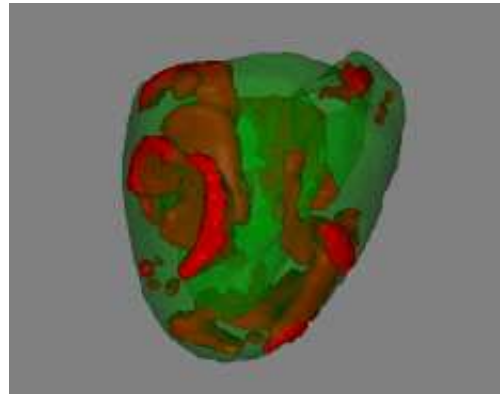
Surface View Movie

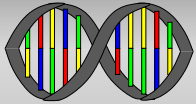
3D View Movie



Summary

Mathematics gives us tools to "see" things that cannot be seen in other ways.





Acknowledgments

Collaborators

- Sasha Panfilov, University of Utrecht
- Brad Peercy, Rice University
- Eric Cytrynbaum, UC Davis, University of British Columbia

Funding for this research kindly provided by the NSF.

This talk can be viewed at

<http://www.math.utah.edu/~keener/lectures/Arrhythmias>

No Microsoft Products were used or harmed during the production of this talk.

The End