The Topology of Defibrillation

J. P. Keener

Department of Mathematics
University of Utah

Dedication

A. T. Winfree (1941-2002)

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Background

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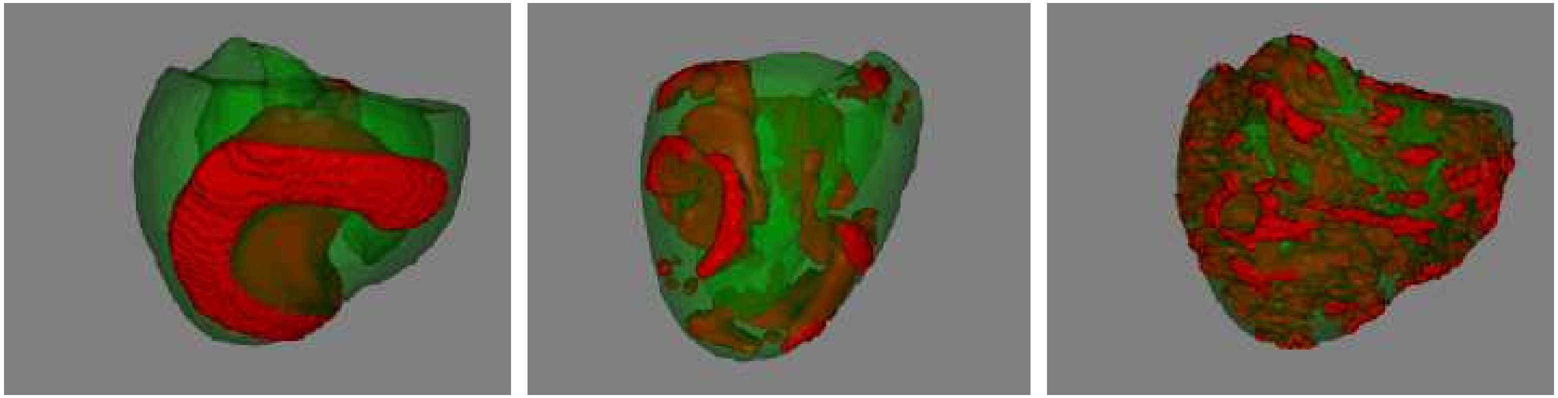
- The probability of defibrillation success is a sigmoidal function of shock amplitude, approaching 1 for large amplitude.
- The explanation of the mechanism of defibrillation remains quite controversial.
- The fundamental controversy concerns the physical origin of transmembrane currents.
- Our goal here is to understand the consequences of large scale virtual electrodes on defibrillation. (The competing hypothesis will not be discussed.)

What is Fibrillation?

Transparent View of Spiral Breakup and Fibrillation



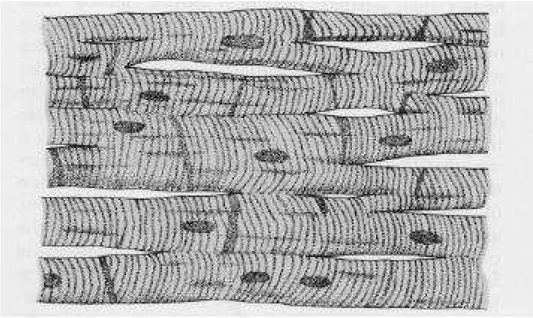
The Real Thing

Surface View Movie

3D View Movie

Modelling Cardiac Tissue

Cardiac Tissue -
The Bidomain Model:



- At each point of the cardiac domain there are two comingled regions, the extracellular and the intracellular domains with potentials ϕ_e and ϕ_i, and transmembrane potential $\phi = \phi_i - \phi_e$.

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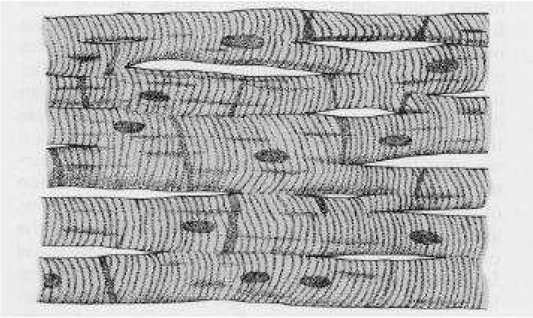

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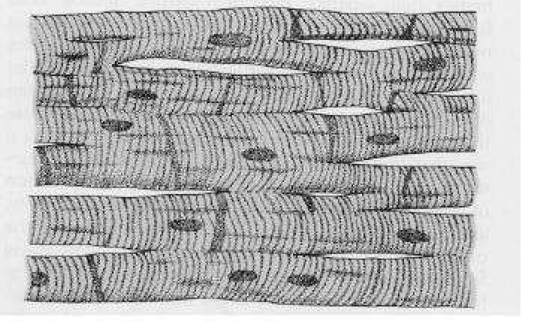

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- Total current is

$$i_T = i_e + i_i = -\sigma_e \nabla \phi_e - \sigma_i \nabla \phi_i.$$

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Kirchhoff's laws:

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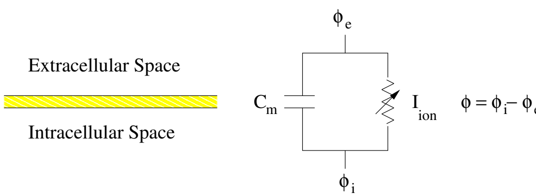

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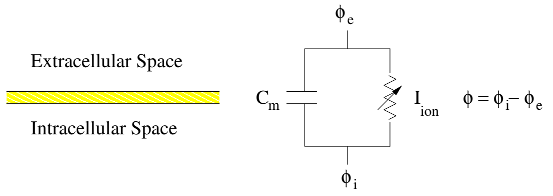

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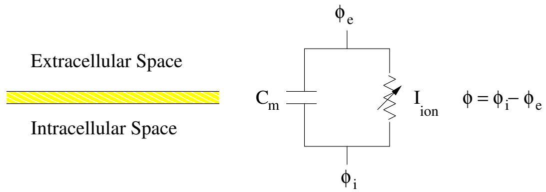

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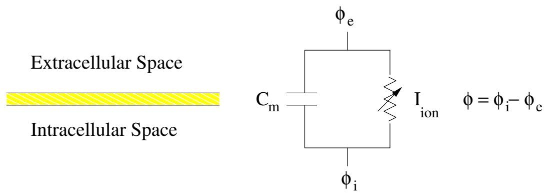

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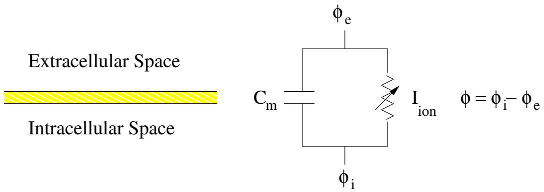

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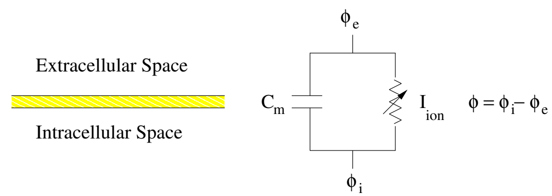
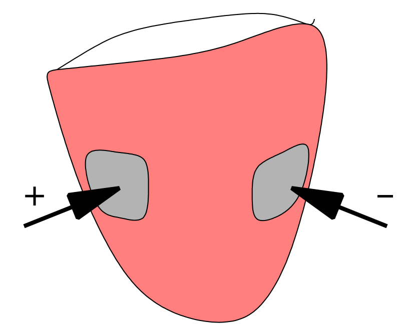


surface to volume ratio, capacitive current, ionic current, and current from intracellular space .

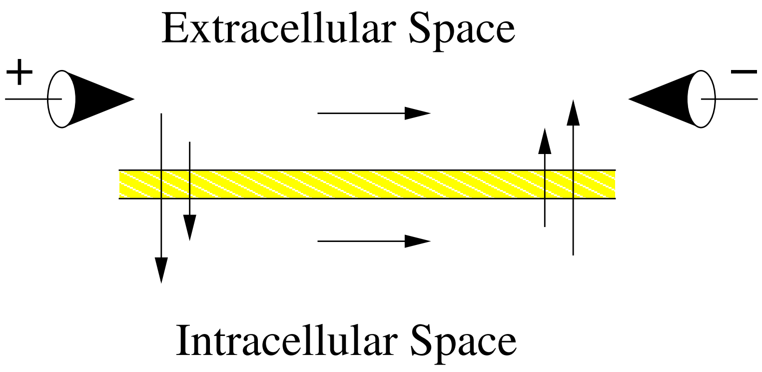
- Boundary conditions:

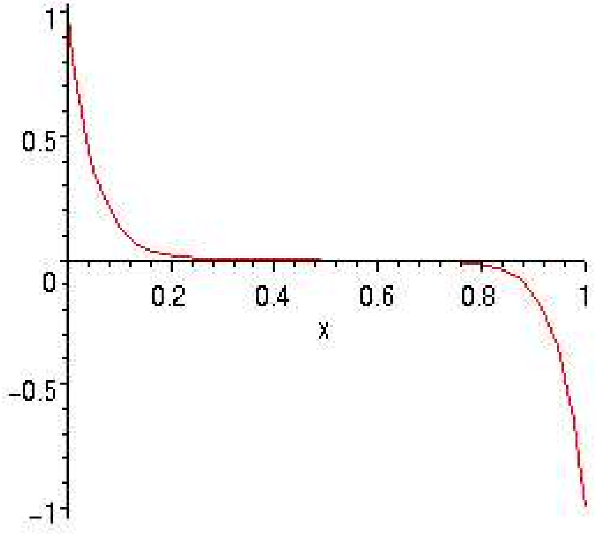
  $\mathrm{n} \cdot \sigma_i \nabla \phi_i = 0, \qquad \mathrm{n} \cdot \sigma_e \nabla \phi_e = I(t, x)$
  and $\int_{\partial\Omega} I(t, x) dx = 0$ on $\partial\Omega$.



Consequences of the Bidomain Model-I:

With current applied at the boundary of the domain, there is depolarization and hyperpolarization at the boundaries. For a homogeneous medium, in the interior (several space constants from the boundary), the transmembrane potential is unaffected.





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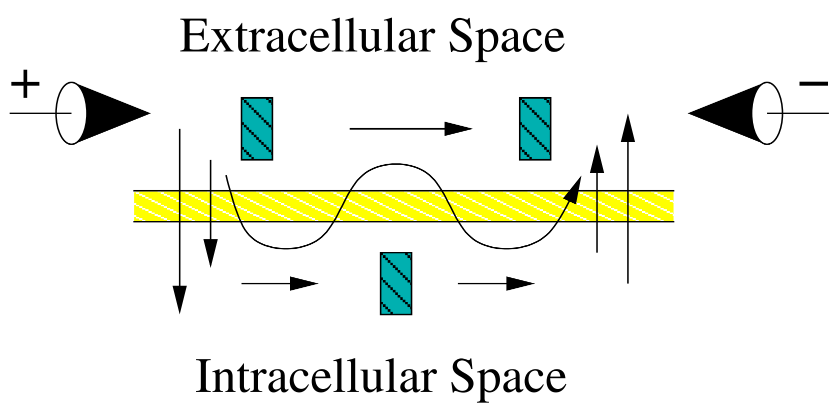

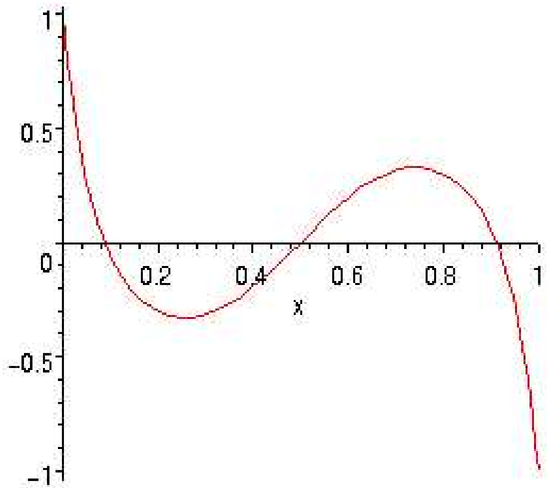

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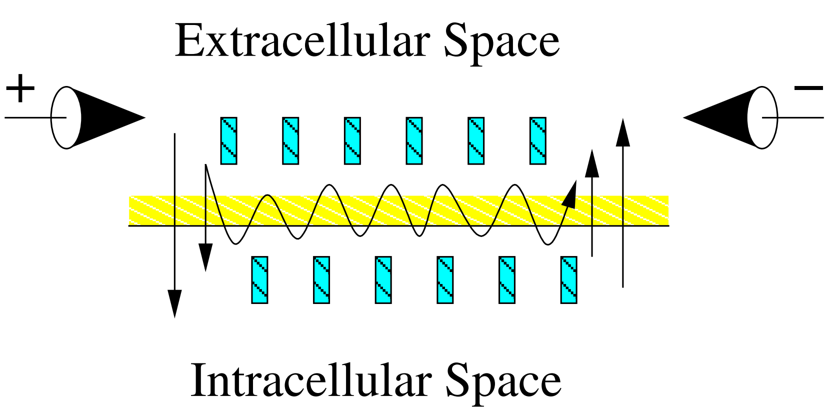

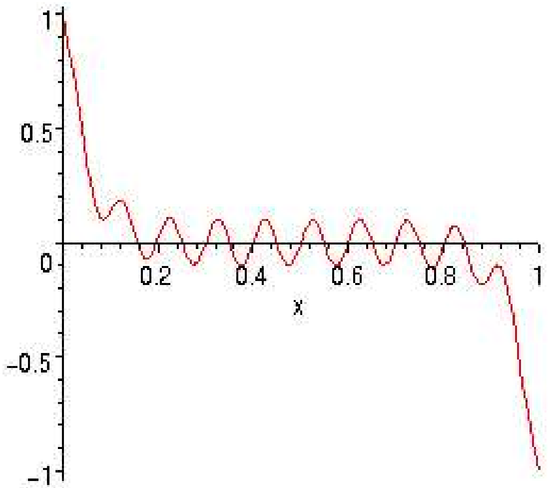

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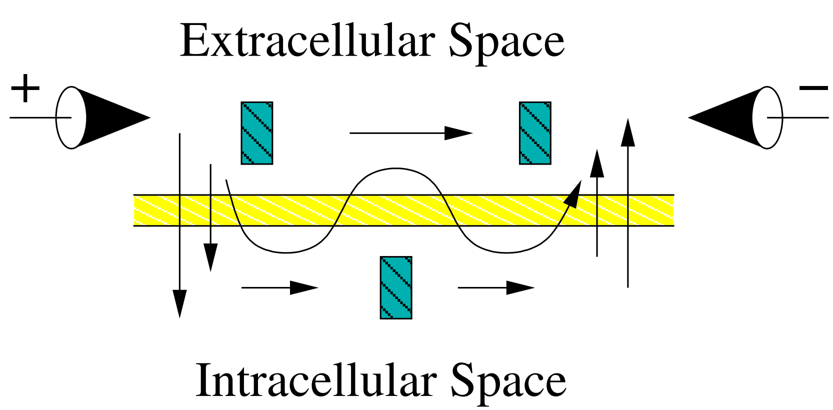
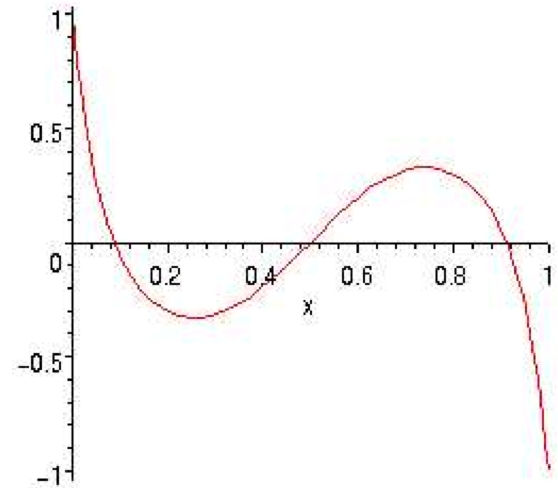
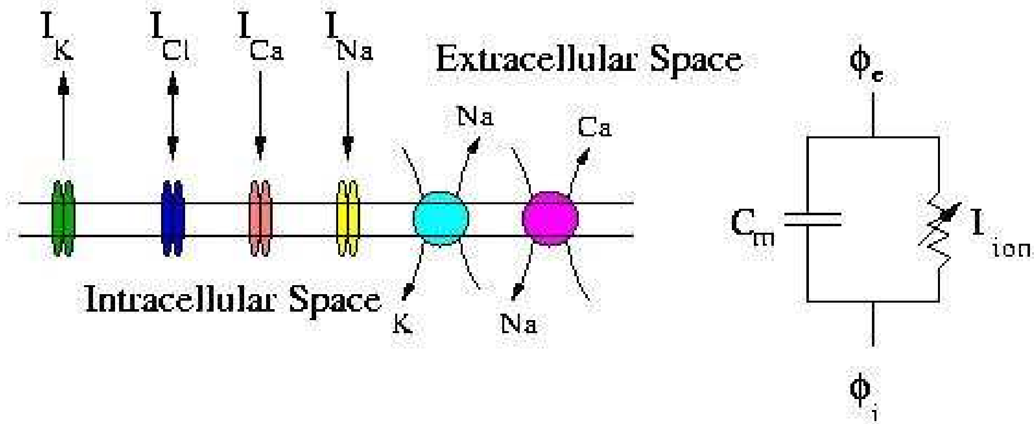




For this talk, we consider large spatial scale virtual electrodes only.

Modeling Cardiac Electrical Activity



$$\phi = \phi_i - \phi_e$$

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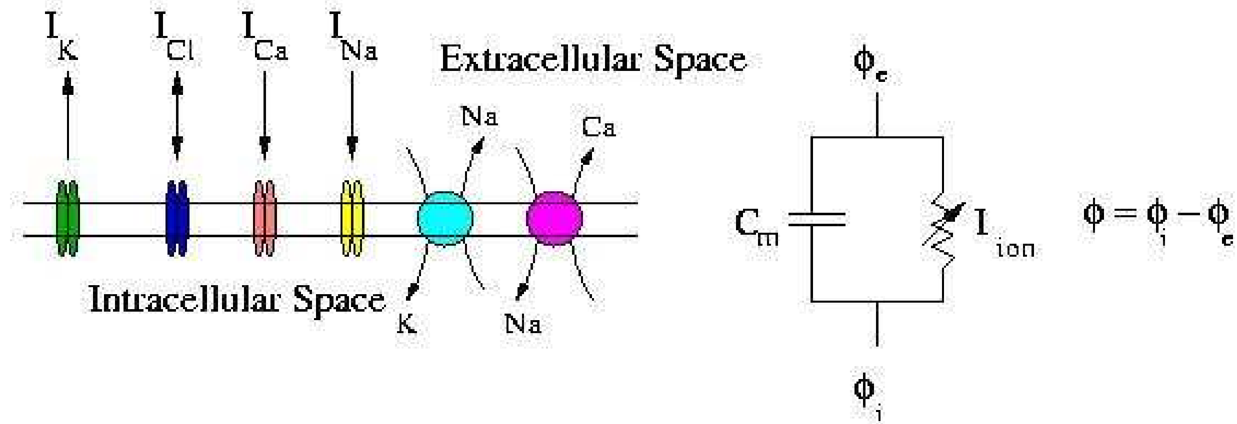

Transmembrane potential ϕ is regulated by transmembrane ionic currents and capacitive currents:

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

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Examples

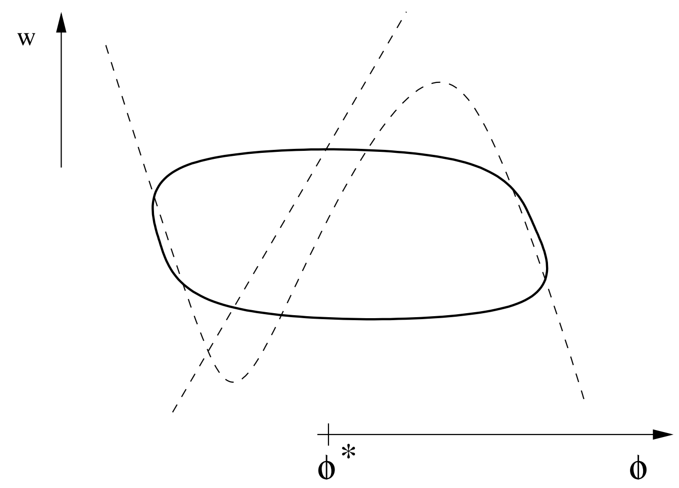
Examples include:

- Beeler-Reuter model
- Luo-Rudy model(s)
- Two Variable Models(Fitzhugh-Nagumo, Morris-Lecar, Puschino, Aliev, etc.)

"Defibrillation" in 1D

- The Initial State: Reentry on a 1-D Ring
- Case 1: Successful "defibrillation"
- Case 2: Unsuccessful "defibrillation" - Phase resetting
- Case 3: Unsuccessful "defibrillation" - Propagation reversal

The Winding Number



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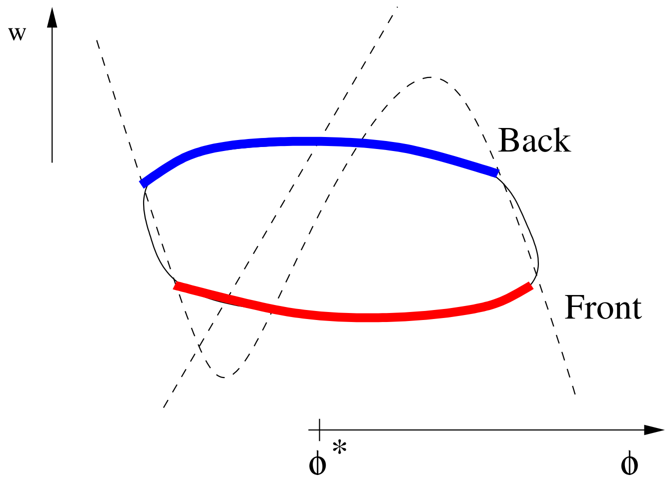

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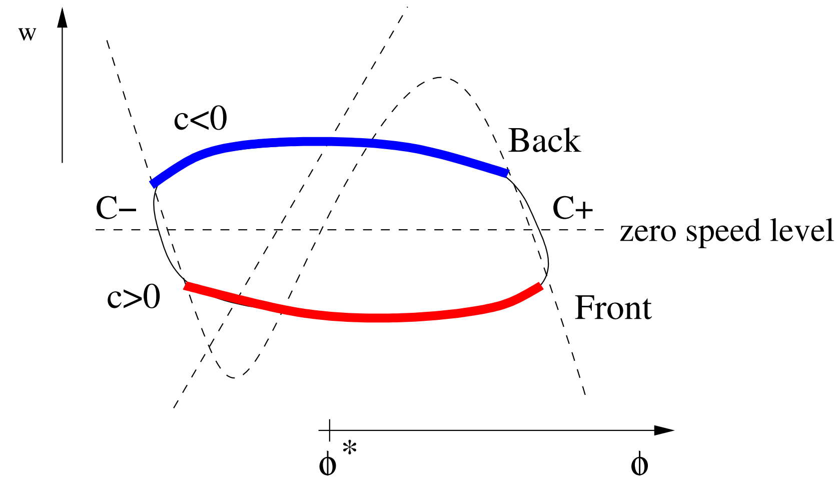

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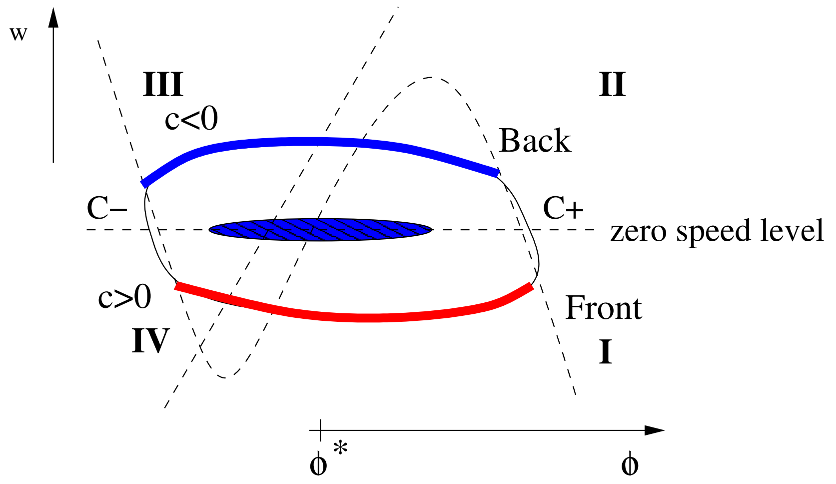

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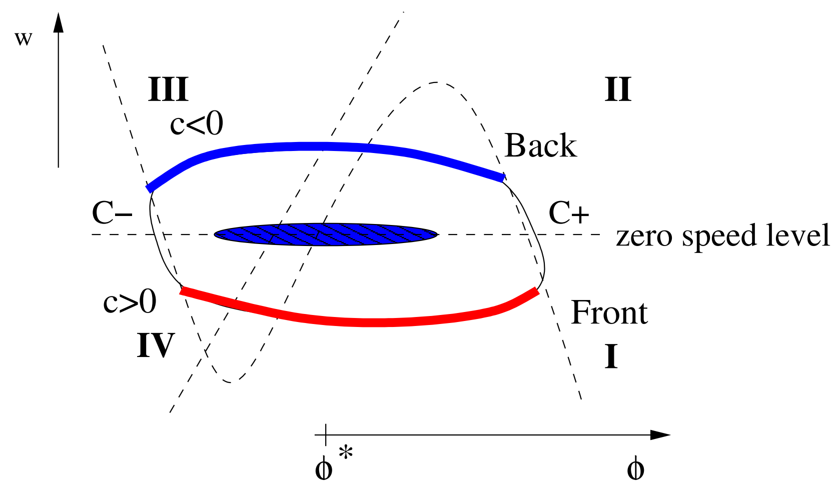

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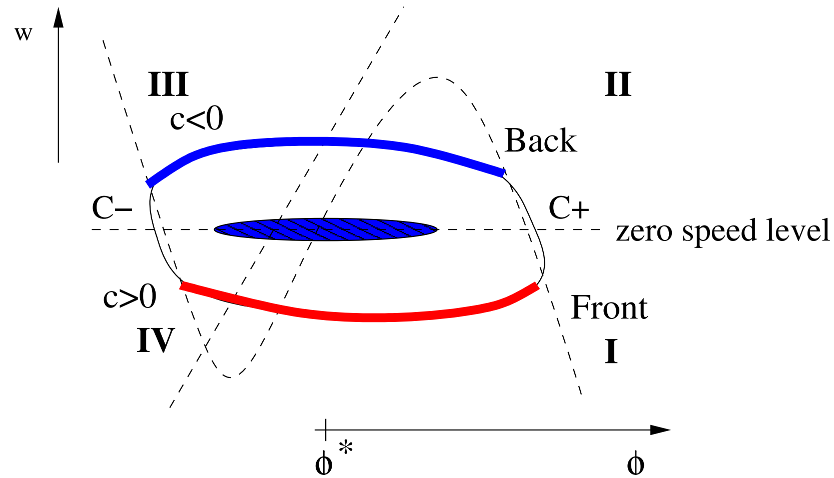

- There is a reentrant wave if and only if the winding number is nonzero.
- "Defibrillation" is successful if a nonzero winding number is converted to zero winding number.

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Changing the Winding Number

The winding number can be changed in two ways:

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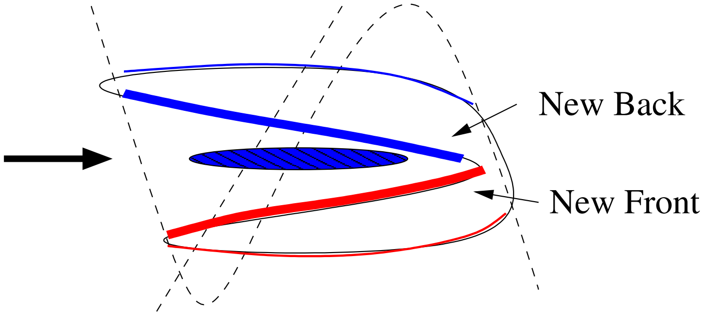
- A Depolarizing Stimulus:



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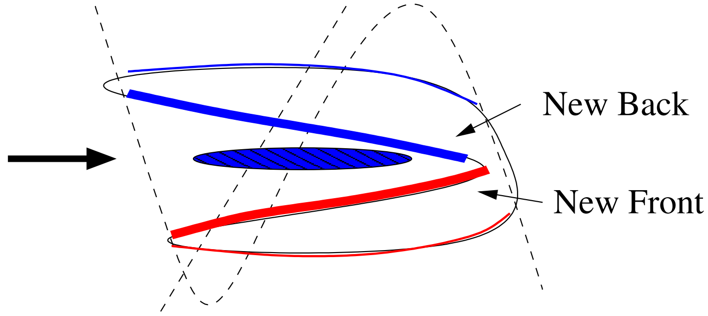
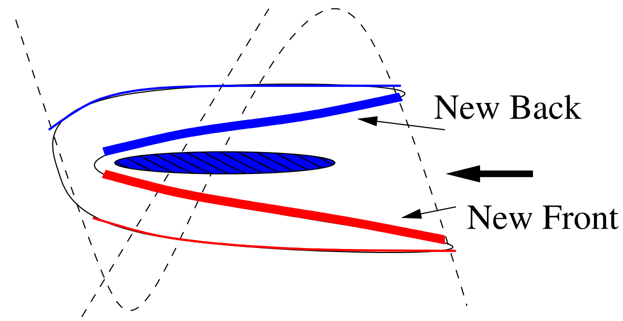
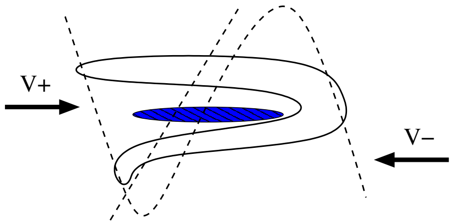


- A Hyperpolarizing Stimulus:



Probability of successful defibrillation:

Probability(success) =
Probability(C- is depolarized and
C+ is not hyperpolarized)



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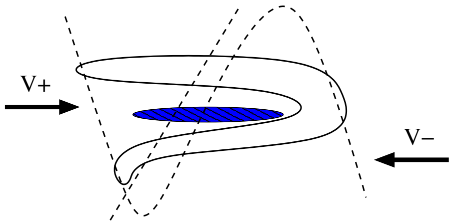

+ Probability(C+ is hyperpolarized and
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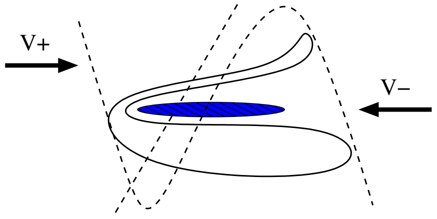

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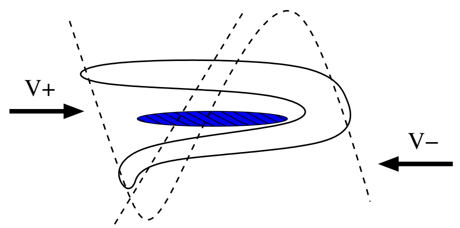

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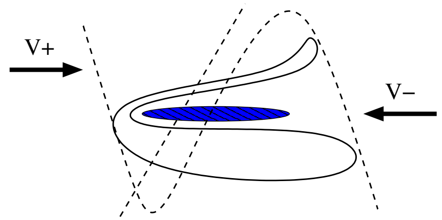
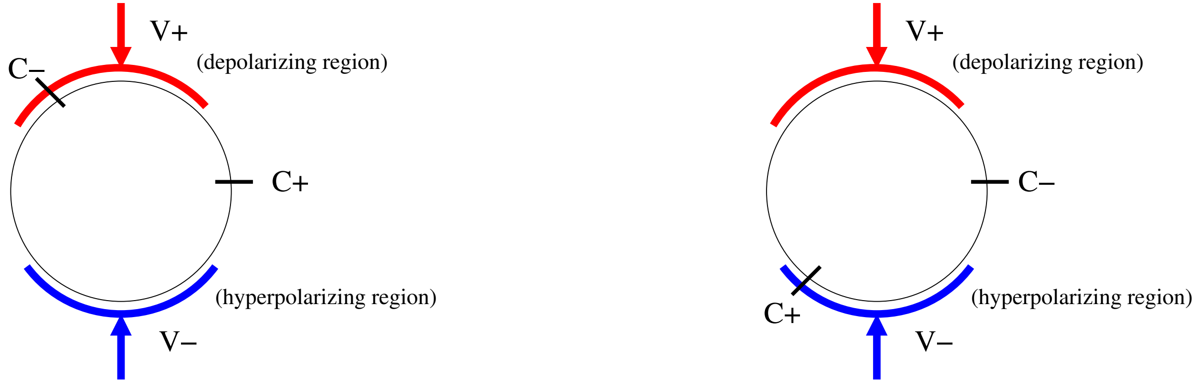
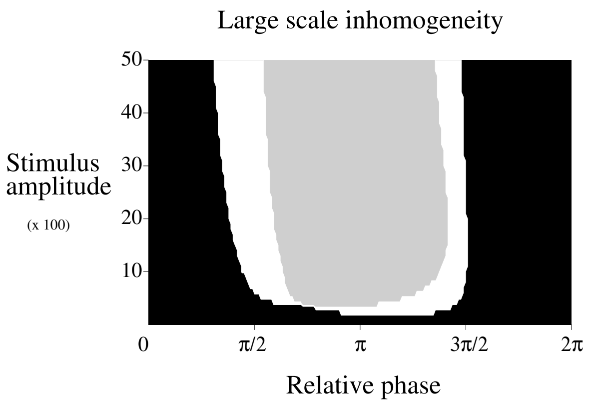


= P(C- $\in$ V+ and C+ $\notin$ V-) + P(C+ $\in$ V- and C- $\notin$ V+)

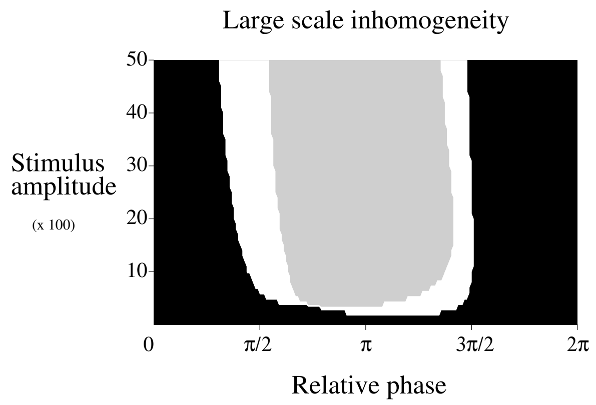


Conclusion:



- On a 1D ring, elimination of reentry requires proper timing.

Conclusion:



- On a 1D ring, elimination of reentry requires proper timing.
- Probability of success does not approach one for large stimulus amplitude.

Two Dimensional Reentry

Two Dimensional Space is subdivided into several regions:

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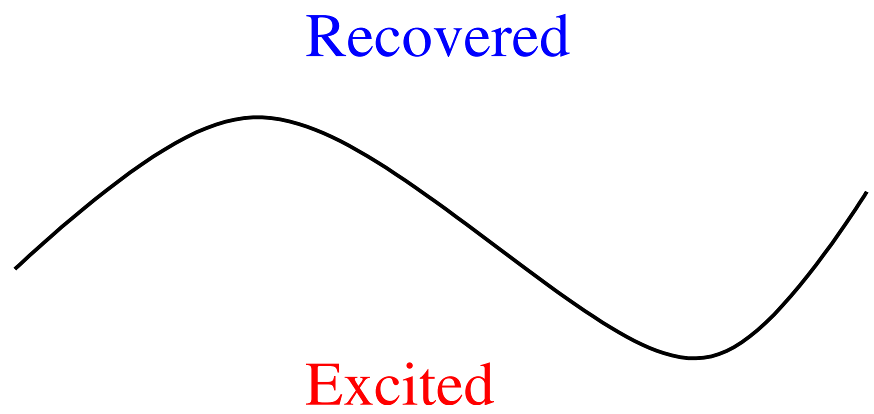

- Excited and Recovered, separated by sharp transitions.

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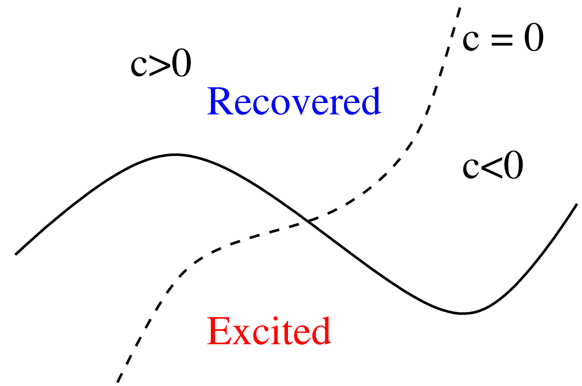

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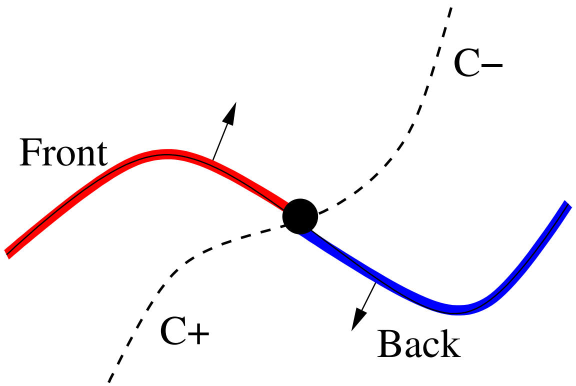

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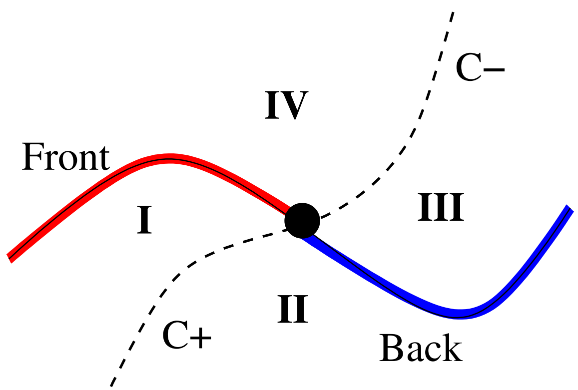

- Excited and recovered, separated by sharp transitions.
- Positive speed or negative speed, separated by the zero speed curve.
- Transitions with C>0 are fronts, with C<0 are backs.
- Intersections of two curves are phase singularities, with associated winding number.

Initiation of Reentry - The Winfree Mechanism

- In 1D: movie
- In 2D: movie

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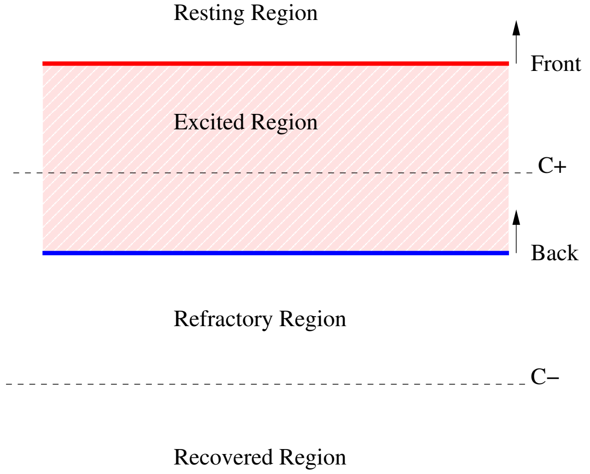
Before the stimulus is applied:



Initiation of Reentry - The Winfree Mechanism

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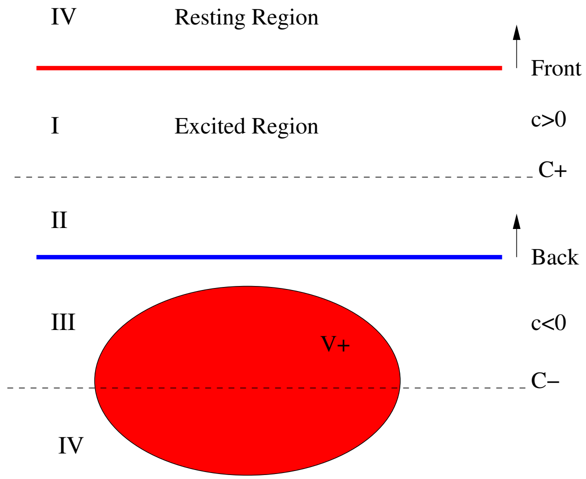
When the stimulus is applied:



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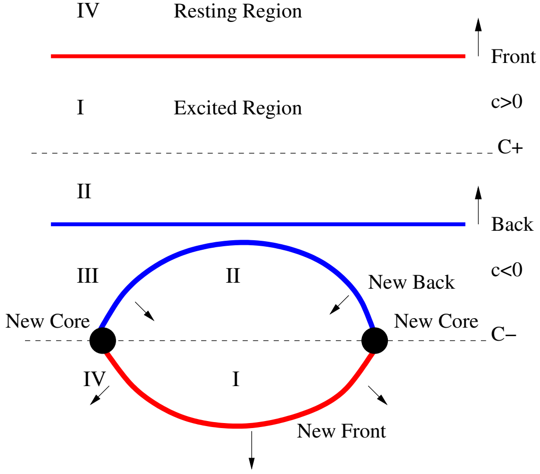

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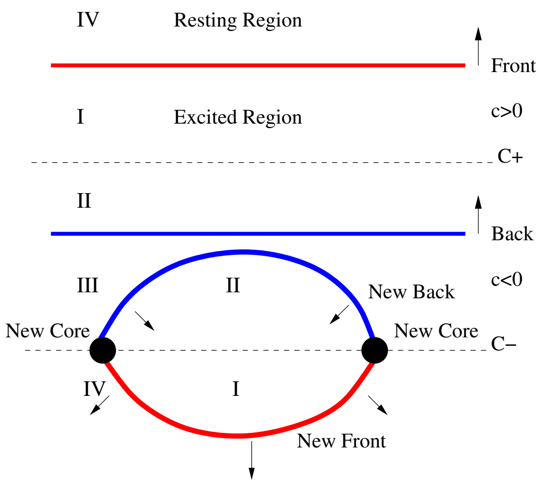

Observation: Each intersection of the boundary of the depolarizing virtual electrode V+ with curve C- creates a new spiral core.

Initiation of Reentry - II

With a hyperpolarizing stimulus -
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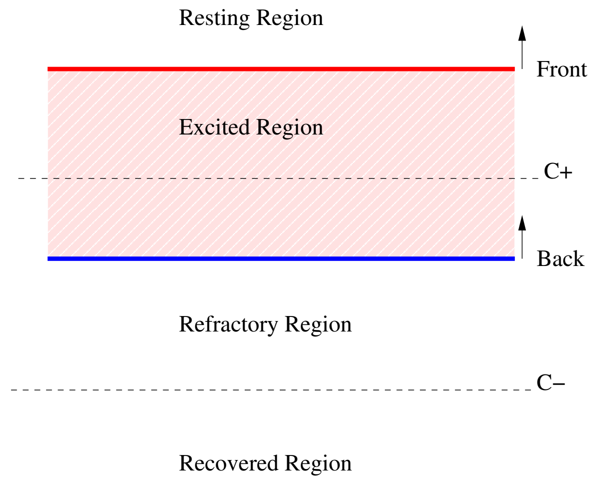
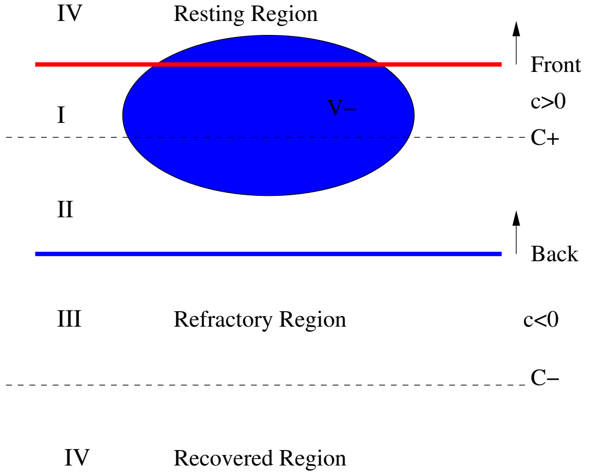


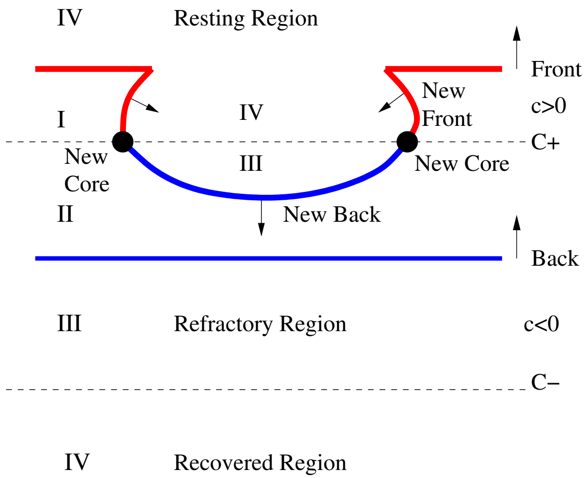
Initiation of Reentry - II

With a hyperpolarizing stimulus -
When the stimulus is applied:



Initiation of Reentry - II

With a hyperpolarizing stimulus - stimulus is applied:



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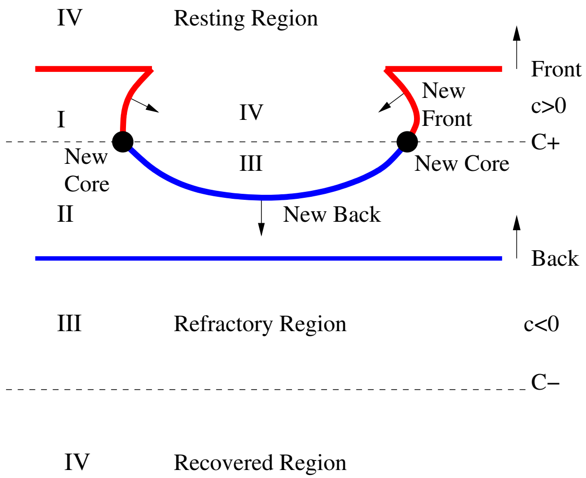
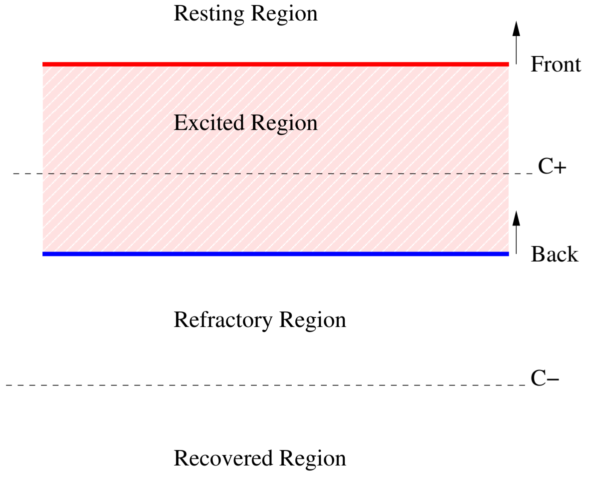


Observation: Each intersection of the boundary of the hyperpolarizing virtual electrode V- with curve C+ creates a new spiral core.

Virtual Electrodes

With both hyperpolarizing and depolarizing virtual electrodes:



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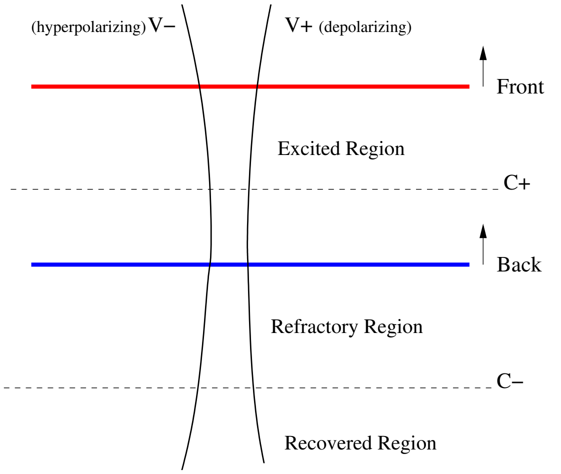

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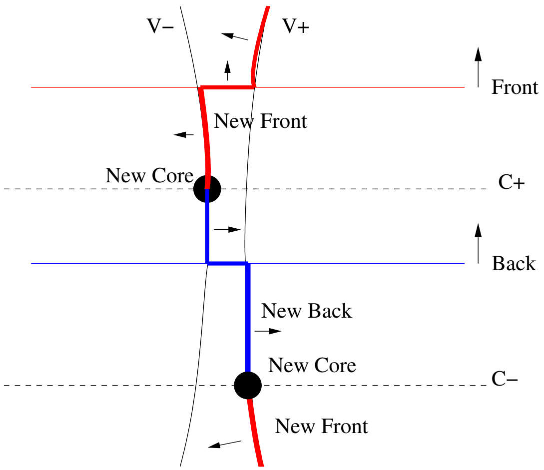

Virtual Electrodes

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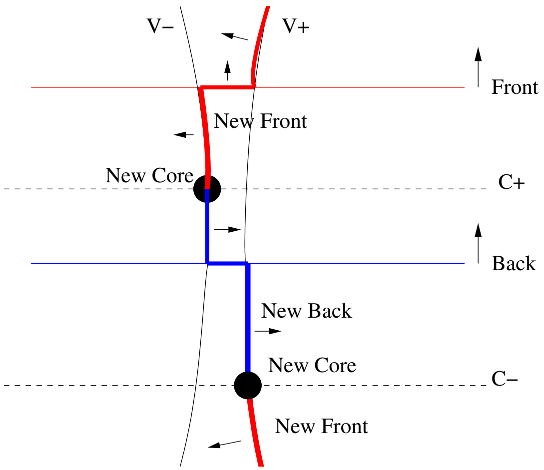
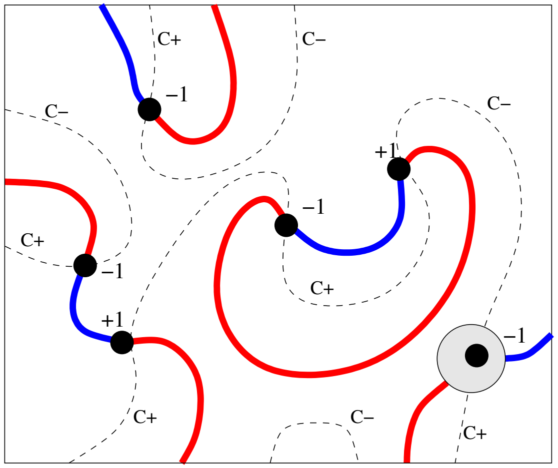


Observation: Juxtaposition of hyperpolarizing and depolarizing virtual electodes can create a new spiral pair.

Applied to a Random Pattern

The result of the stimulus is a labyrinth of fronts and backs, connecting spiral cores.
Initial pattern:



Applied to a Random Pattern

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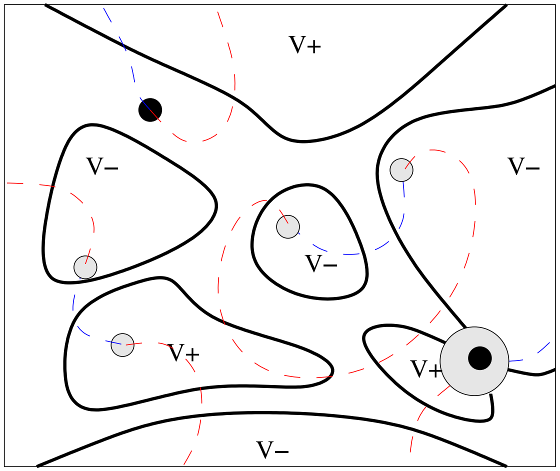
Stimulus pattern:



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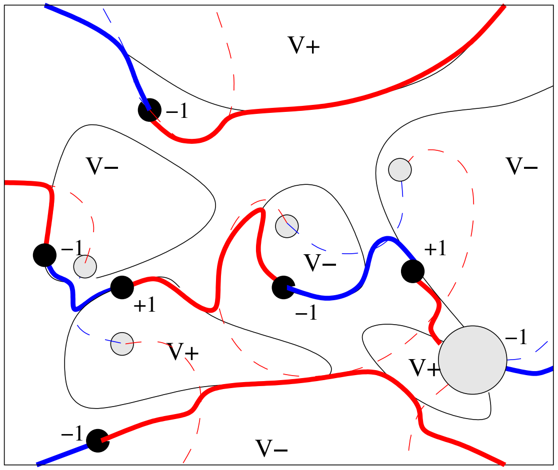
Pattern after stimulus:



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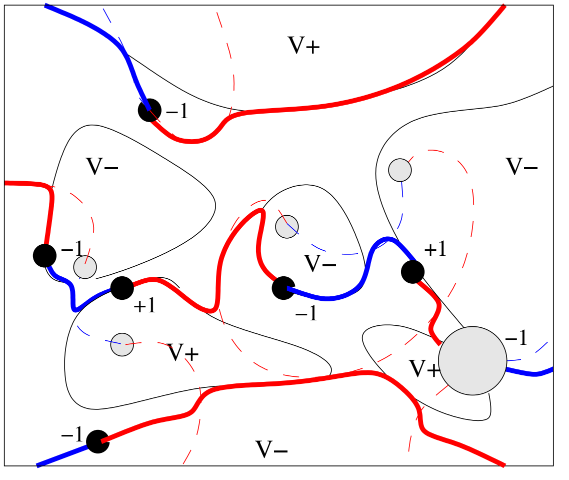

Conclusion:

- Application of a boundary current can never directly defibrillate tissue.
- Defibrillation is successful only if all of the spirals that are created collapse and disappear.

Necessary Conditions

Two necessary conditions for successful defibrillation:

Imagine the Possibilities
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University of Utah

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- Total parity of the interior (away from the boundary) must be zero after the stimulus has ended.
- All spiral pairs must be sufficiently close together to spontaneously collapse.

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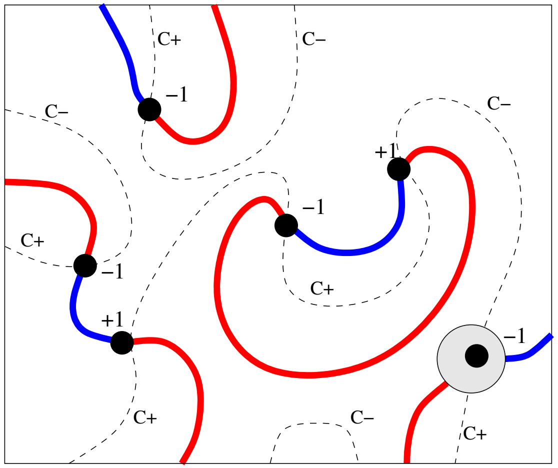

Total parity -2

Necessary Condition I

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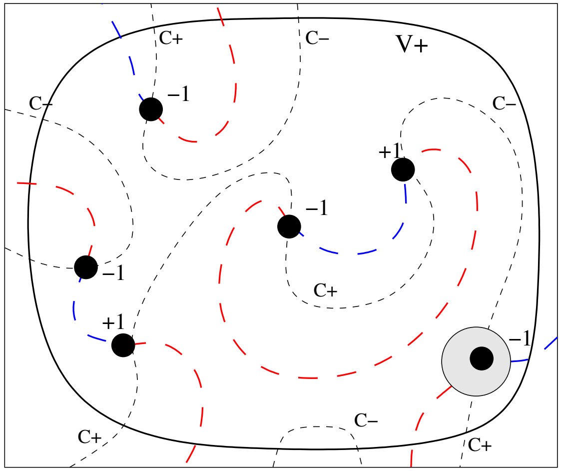

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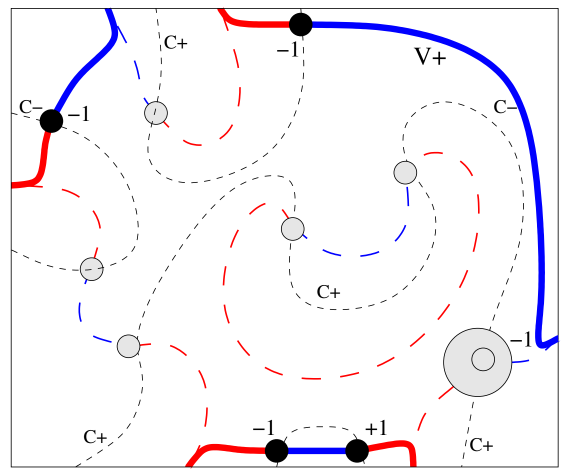
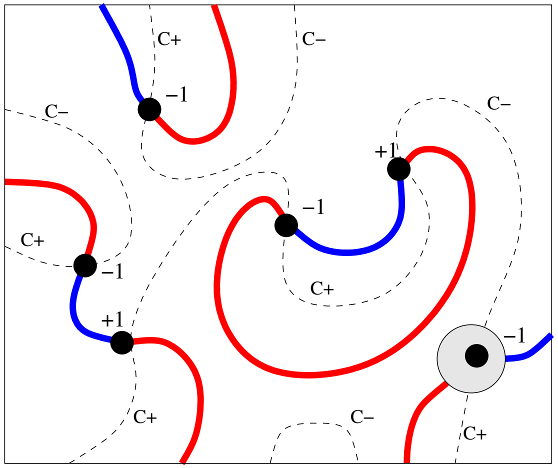


Total parity -2

Total parity is not changed by any closed depolarization or hyperpolarization region.

Necessary Condition I

Suppose the stimulus region encloses the boundary.



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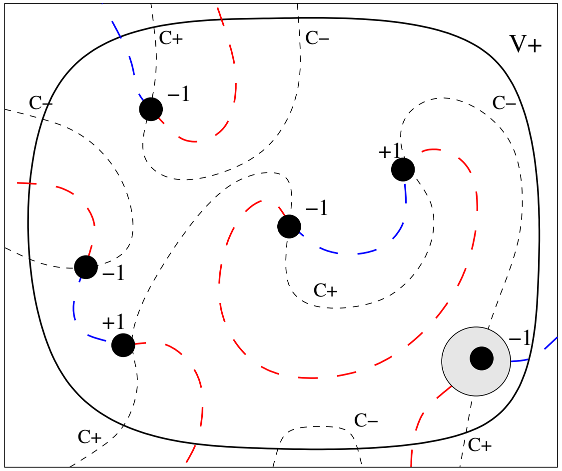

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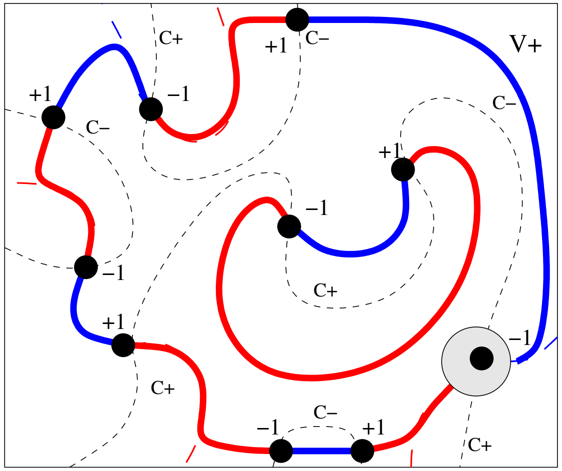

Total parity 0

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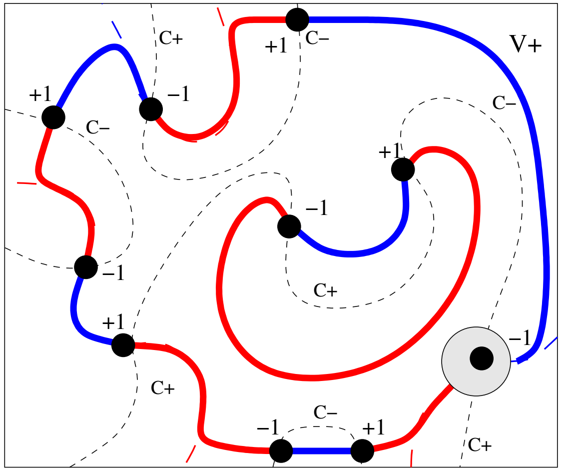
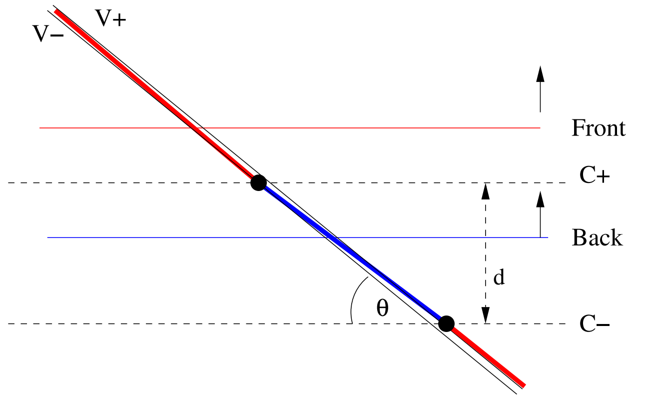


Total parity 0

Total parity becomes zero if the entire boundary is enclosed by a single depolarizing (or hyperpolarizing) region. (But this is physically impossible!)

Necessary Condition II

All spiral pairs must be sufficiently close together to spontaneously collapse.



Even with large stimuli, the separation of spiral pairs varies randomly with orientation.

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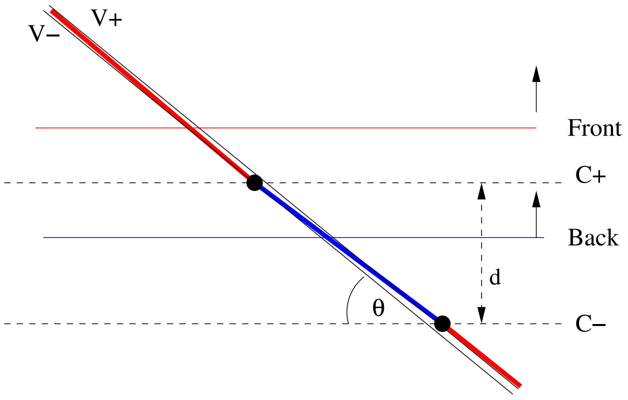
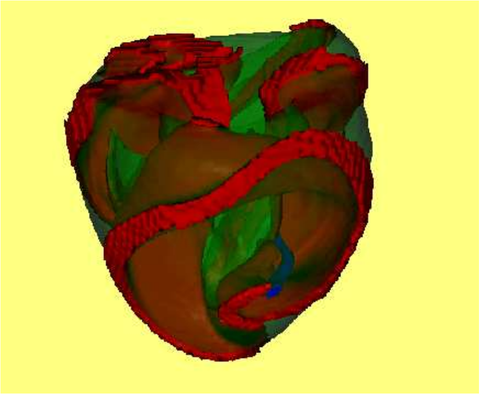


Even with large stimuli, the separation of spiral pairs varies randomly with orientation.
Conclusion: It is highly unlikely that a randomly applied stimulus will achieve both of these. Hence, it is unlikely that defibrillation by this mechanism will be successful.

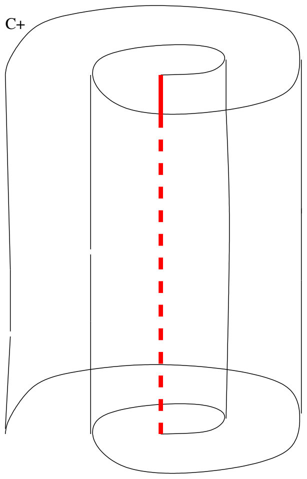
3 Dimensional Reentry - Scrolls

- In 3 dimensions, reentrant patterns are scrolls and the phase singularities are curves (filaments).



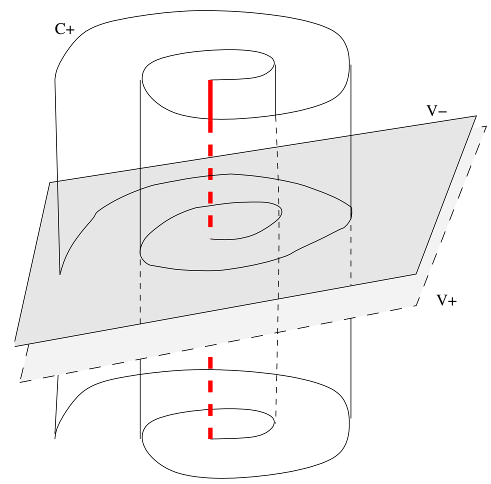
- Filaments are the intersections of the Front/Back surface with the C=0 surface.

Interaction of Scrolls with Virtual Electrodes



- The intersection of the boundary of the V+ (depolarization) surface with the C- surface will produce a new scroll wave filament.
- The intersection of the boundary of the V- (hyperpolarization) surface with the C+ surface will produce a new scroll wave filament.

Interaction of Scrolls with Virtual Electrodes



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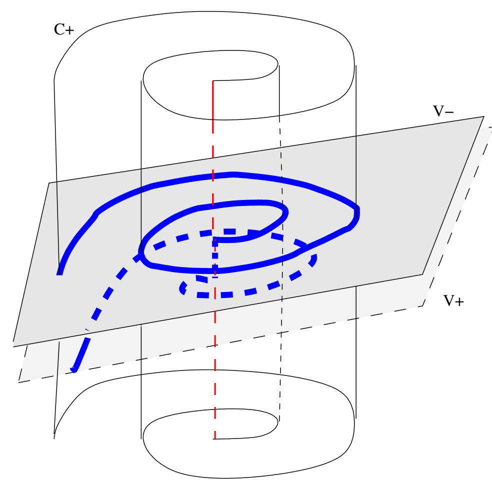

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Conclusions

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- A filament that is initially attached to an anatomical obstable or a boundary will remain attached unless a virtual electrode completely encases the obstacle or boundary.
- Because it is physically impossible for a virtual electrode to encase a boundary, initially transmural filaments will remain transmural after the shock is applied.

Final Conclusions

- Virtual electrodes can change the topology of a reentrant pattern but rarely do they successfully eliminate all reentrant activity, even with very large stimulus amplitude.

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Final Conclusions

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- Only with carefully placed electrodes and carefully timed stimuli on small domains can defibrillation success be achieved relatively often.
- The probability of defibrillation success does not approach one as the stimulus amplitude gets large for a "generic" arrangement of electrodes.
- The virtual electrode mechanism does not give an adequate explanation of clinical defibrillation success.

Acknowledgments

Collaborators

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

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This talk can be viewed at
http://www.math.utah.edu/ keener/lectures/topology

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

The End