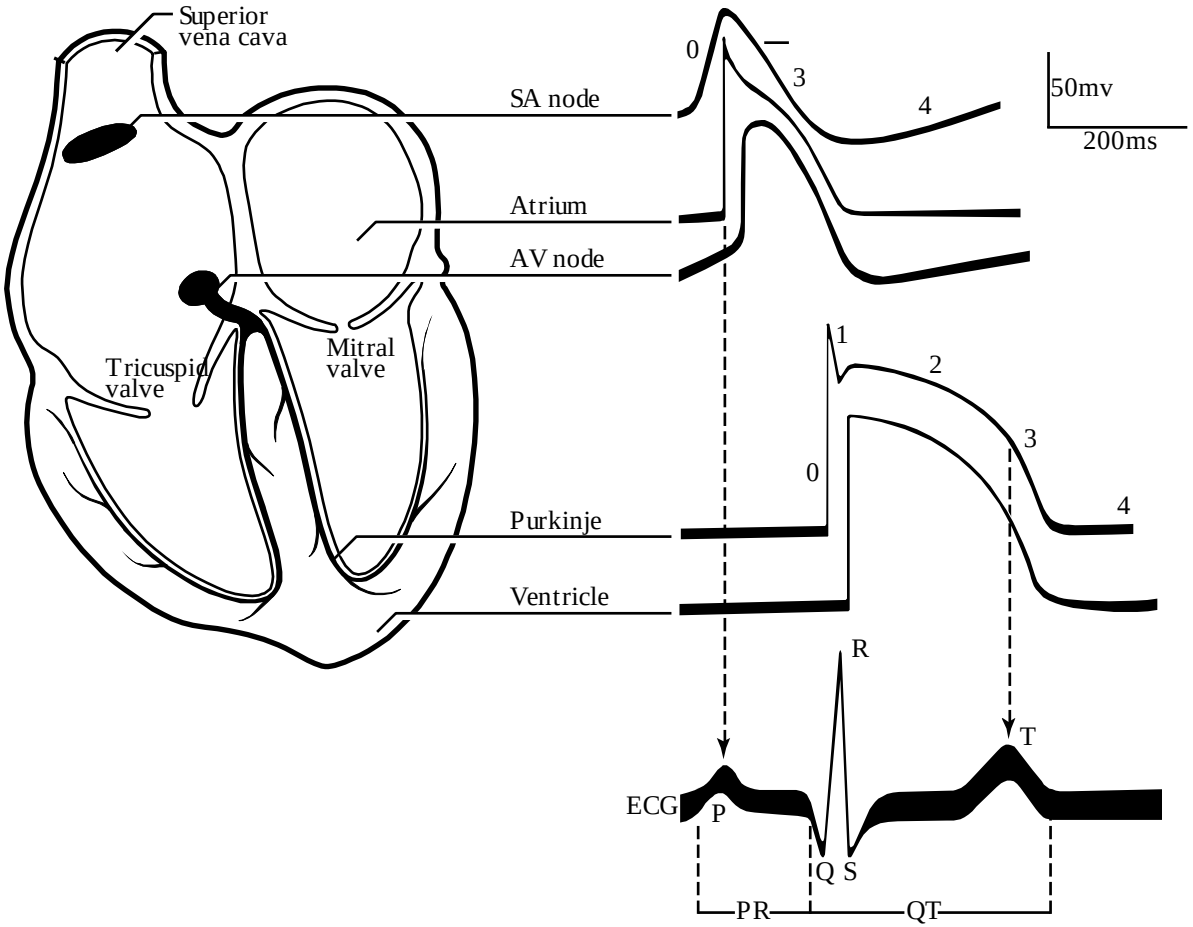
Atrial Fibrillation: An Overview

Robert F. Gilmour, Jr.

Department of Biomedical Sciences
Cornell University, Ithaca, NY

Electrical activation of the heart



ECG during atrial fibrillation (AF)

Normal sinus rythm

Atrial fibrillation

AF characteristics

- affects 2.3 million adults in the United States
- most people who develop AF are > 65 years of age
- two forms:

  intermittent (paroxysmal) AF

  episodes occur with varying frequency;

  last for a variable period of time before stopping

  chronic or persistent AF

  sustained; usually does not stop spontaneously
- most frequently associated with heart failure or valve disease

AF symptoms

- unpleasant palpitations
- chest discomfort (sensation of tightness) or pain
- sense of the heart racing
- lightheadedness, fainting
- shortness of breath and fatigue

AF: why worry?

- exacerbation of pre-existing heart failure (tachycardiomyopathy)
- blood clots (emboli); stroke
- AF begets AF: structural and electrical remodeling

AF treatment

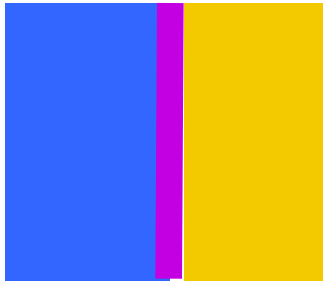
- electrical cardioversion (single large shock)
- rhythm control - maintain sinus rhythm
  - sodium and/or potassium channel blockers
  - ablation (RF, cryo, laser)
  - anti-tachycardia pacing
  - surgery (maze, corridor)
- rate control - slow ventricular rate
  - calcium channel blockers
  - beta blockers
  - digoxin
- prevention of clot formation and stroke

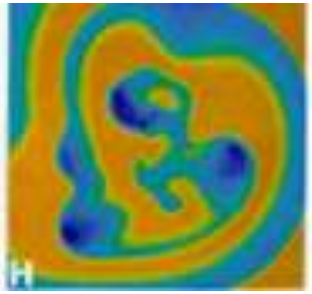
Mechanism for AF

Normal Sinus Rhythm

Tachycardia

Fibrillation



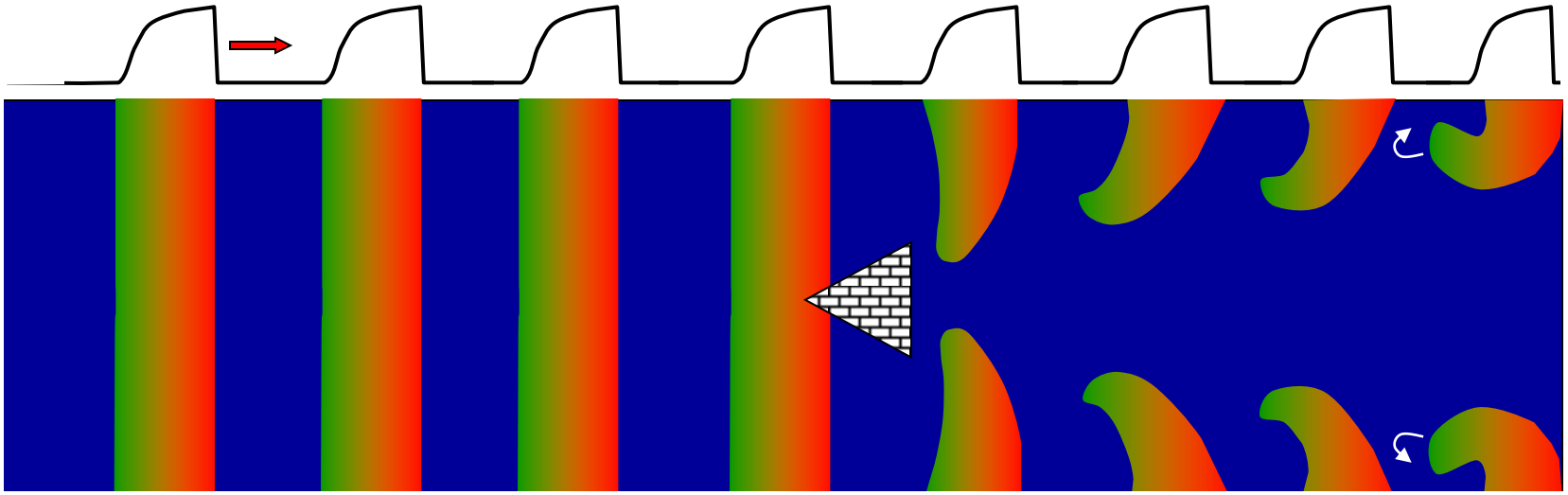


Planar wave

Spiral wave

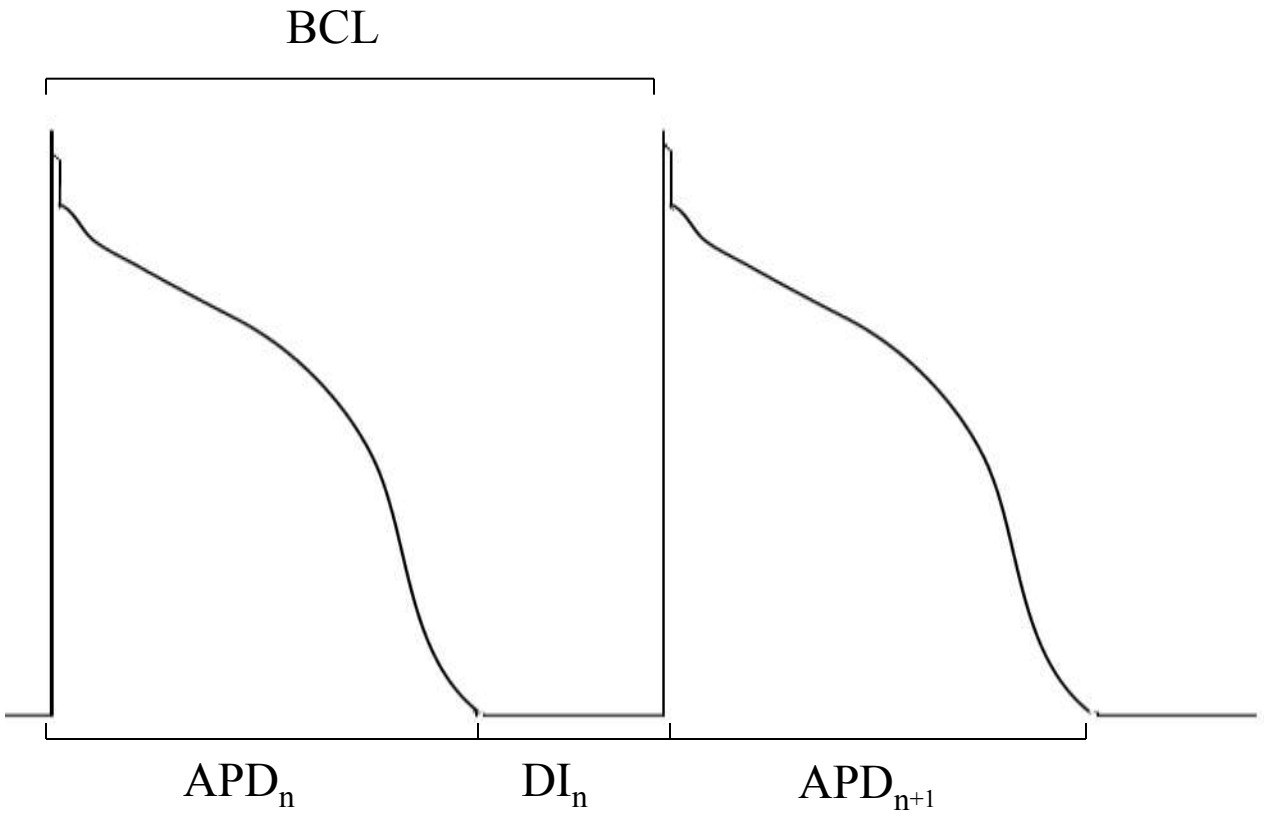
Multiple wavelets

Mechanism for AF



Courtesy of J. Weiss

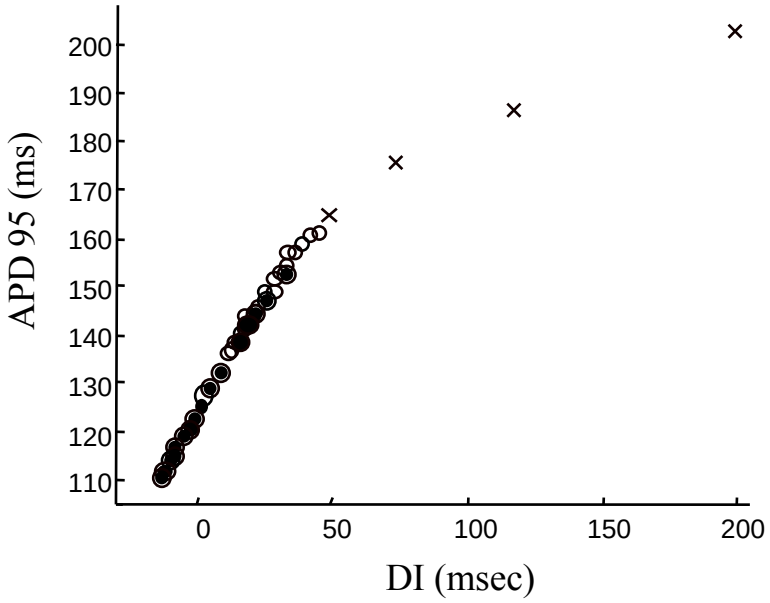
Restitution of action potential duration

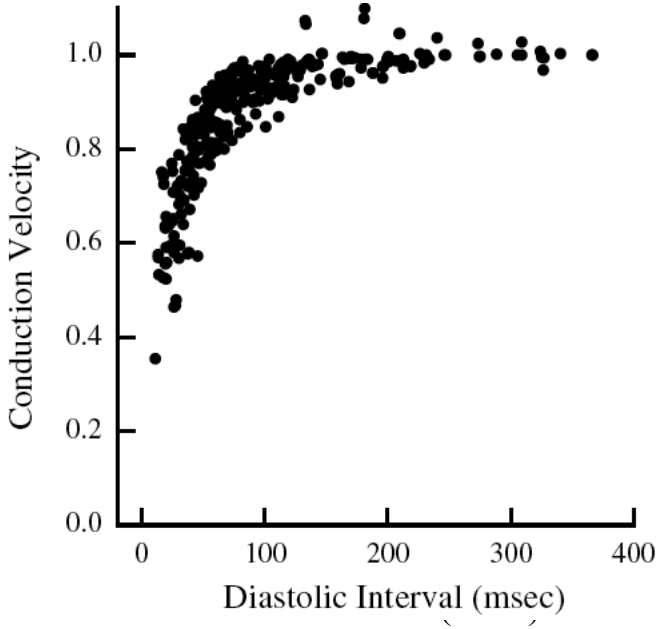


$$BCL = APD + DI$$

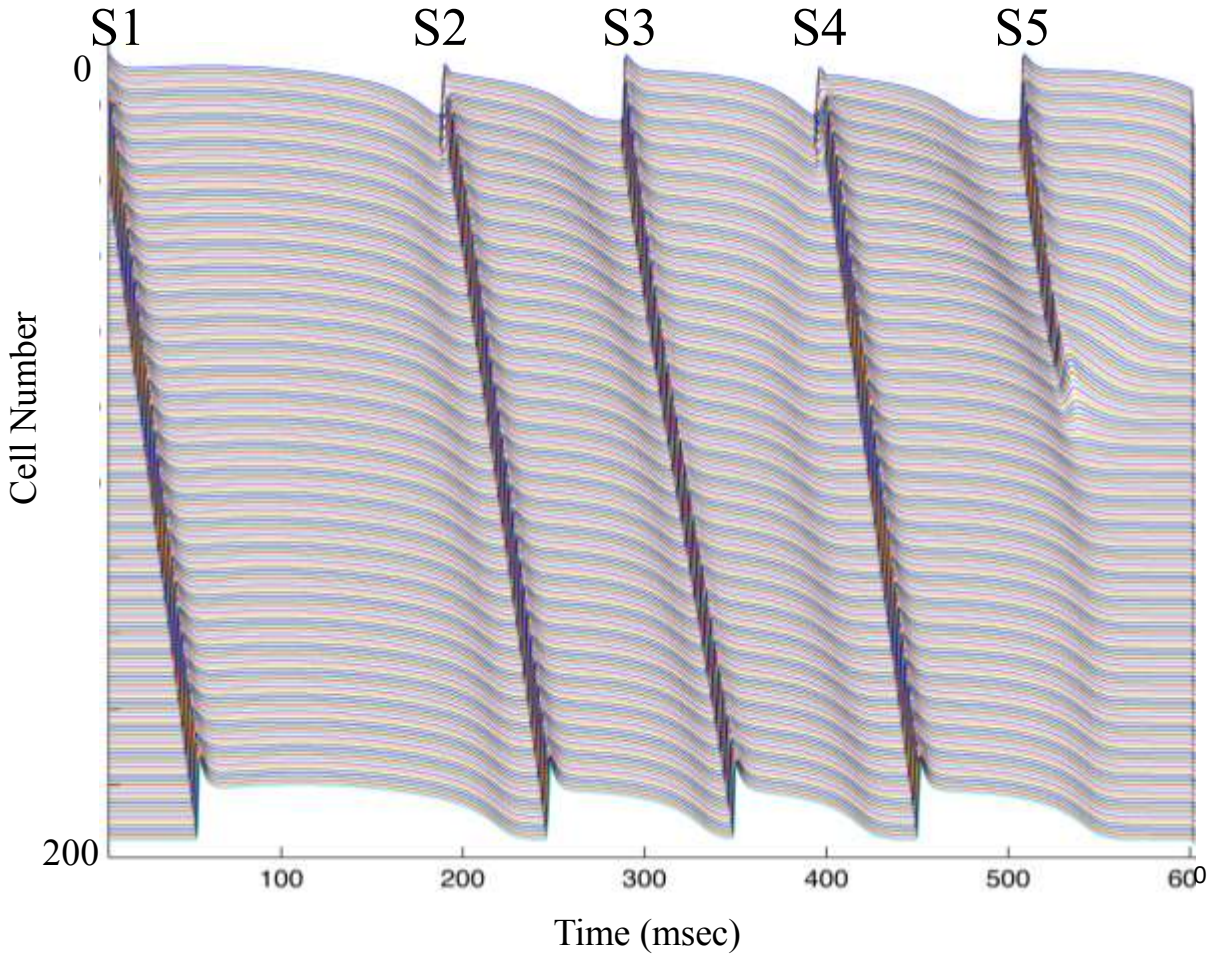
$$APD_{n+1} = f\,(DI_n)$$

APD and CV restitution during rapid pacing





APD dynamics leading to conduction block

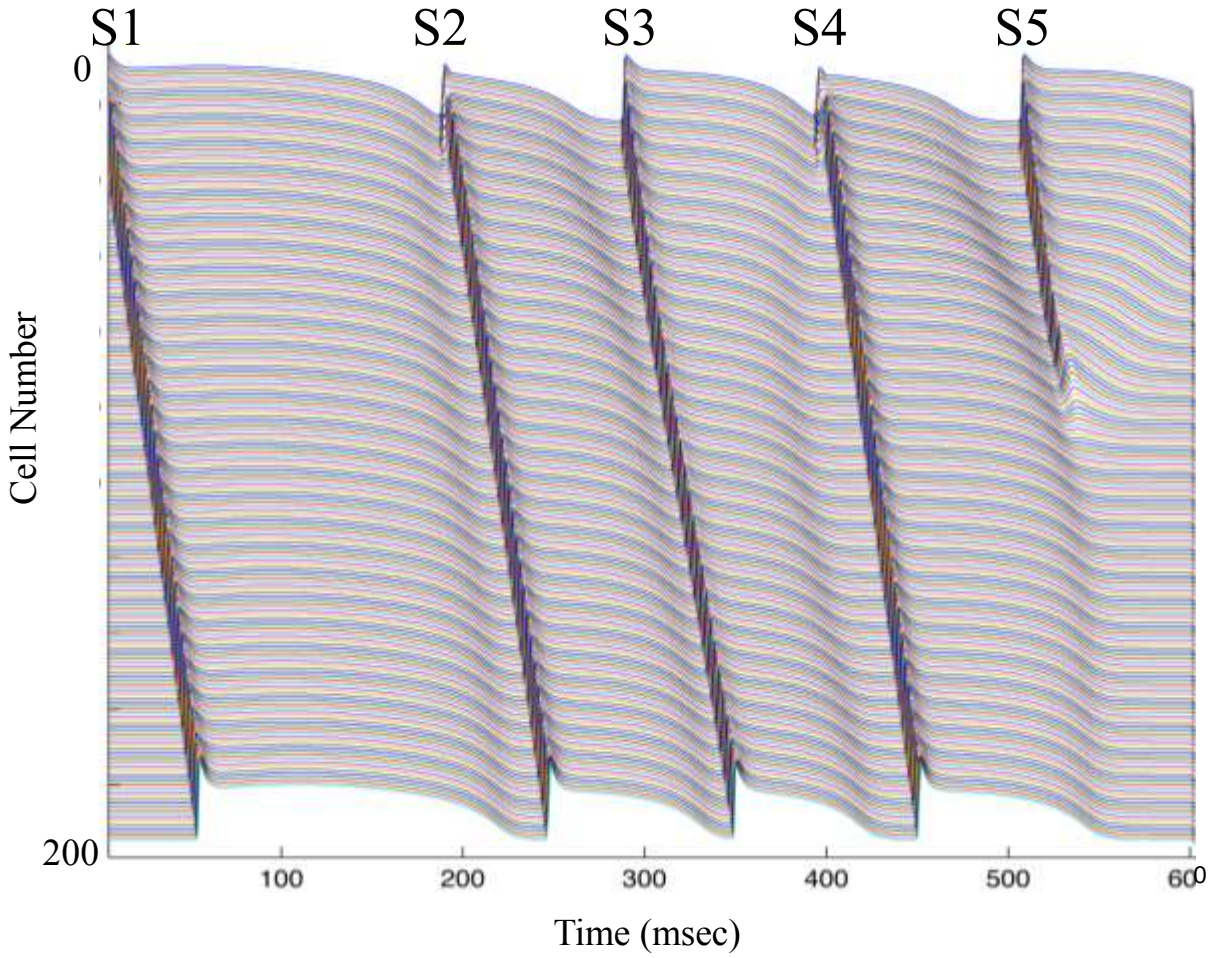


Mechanism for AF

- Triggers
  - abnormal automaticity
  - afterdepolarization-induced triggered activity

- Substrates
  - structural remodeling (fibrosis)
  - ionic remodeling
    - increased intrinsic heterogeneity of refractoriness
    - increased dynamical heterogeneity of refractoriness

APD dynamics leading to conduction block

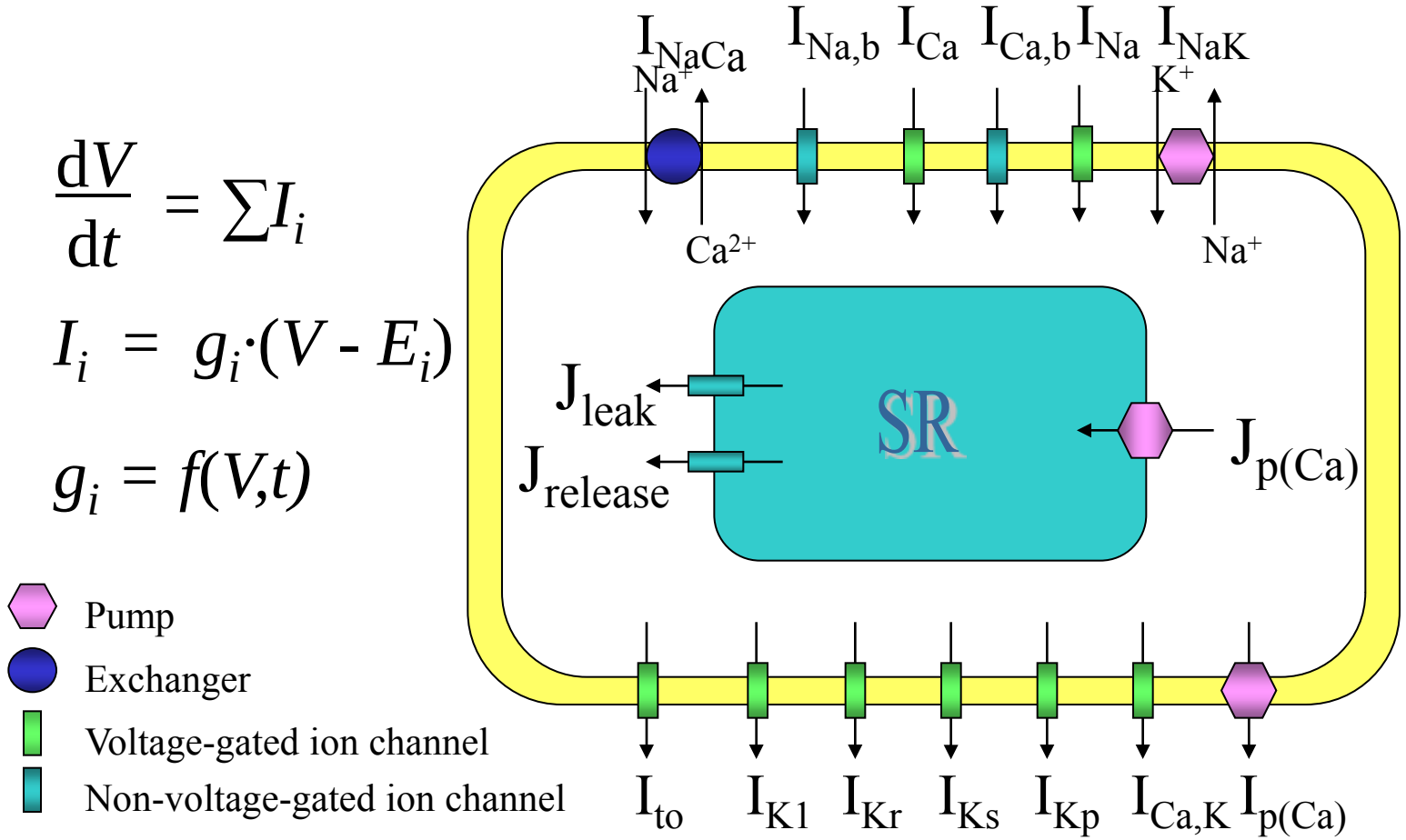


Ionic model of a canine ventricular myocyte

$$\frac{dV}{dt} = \sum I_i$$

$$I_i = g_i \cdot (V - E_i)$$

$$g_i = f(V,t)$$



~13 state variables and ~60 parameters

Fox *et al*, *Am J Physiol*, 2002

Algorithm for predicting conduction block

Equations:

$$\frac{1}{v_{back}^{S4}} - \frac{1}{v(DI_{\min})} = \left(\frac{1}{v(DI_{S4})} - \frac{1}{v(DI_{\min})}\right) - a'(DI_{S4})\left(\frac{1}{v(DI_{S3})} - \frac{1}{v(DI_{S4})}\right)$$

$$+ a'(DI_{S4})a'(DI_{S3})\left(\frac{1}{v(DI_{S2})} - \frac{1}{v(DI_{S3})}\right) - a'(DI_{S4})a'(DI_{S3})a'(DI_{S2})\left(\frac{1}{v(DI_{S1})} - \frac{1}{v(DI_{S2})}\right) > 0$$

Translation:

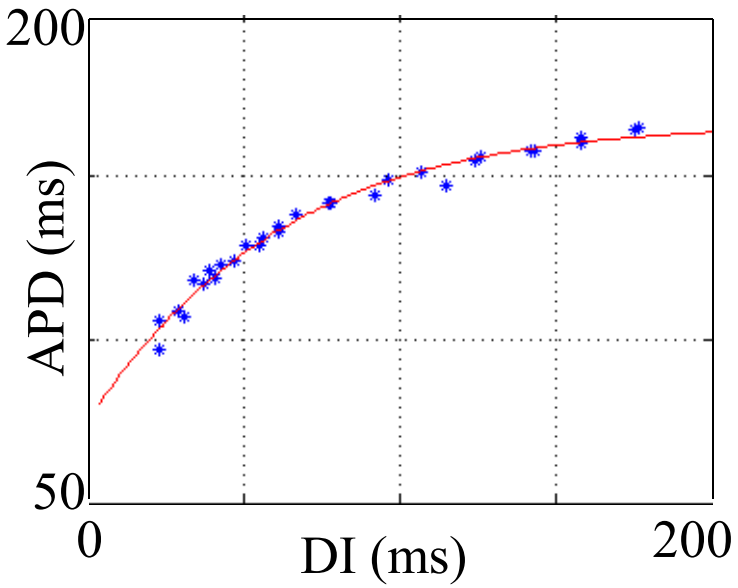
Differences in consecutive wavefront velocities and steep APD restitution tend to conduction produce block.

In vivo tests of the theory

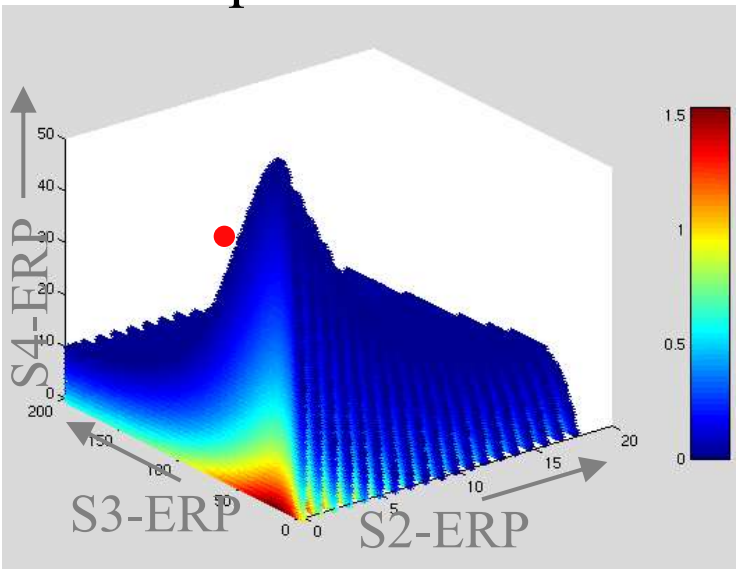
- MAP catheters were placed in the right and left ventricles of closed-chest anesthetized affected German shepherd dogs.
- A pacedown protocol was performed to determined the APD restitution function for each ventricle.
- Each restitution function was substituted into the predictive algorithm to generate series of 4 premature pacing intervals predicted to produce block.
- At least 16 pacing intervals (SSSS…SLSL….LLLL) were delivered to each ventricle to determine which sequences initiated VF.

Right ventricle

APD restitution function



Premature pacing intervals that produce block

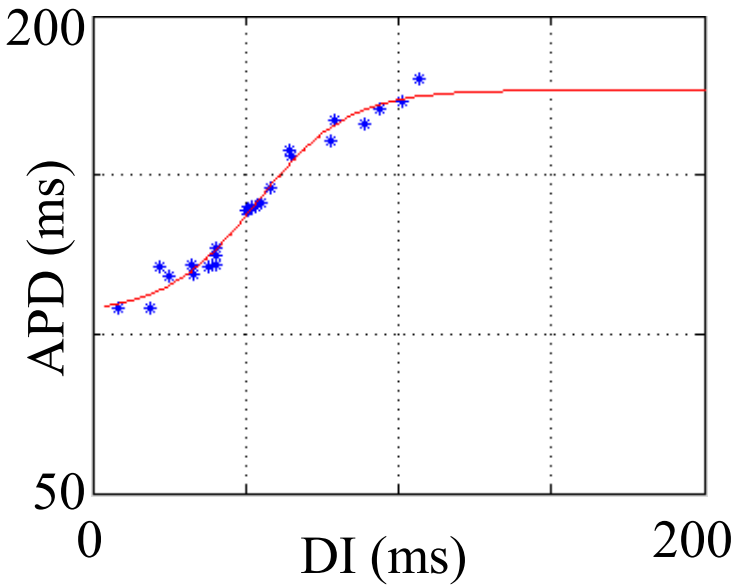


S2 - ERP = 1-5 ms “short”
S3 - ERP = 15-50 ms “long”
S4 - ERP = 1-5 ms “short”
S5 - ERP = 1-5 ms “short”

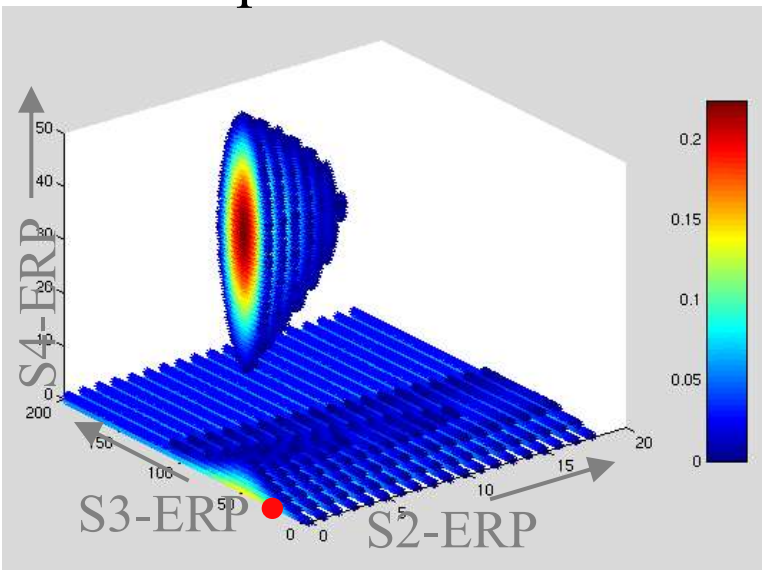
Short	Short
Long	Long
Short	Short
Short	
⇩	⇩
VF	No VF

Left ventricle

APD restitution function



Premature pacing intervals that produce block



S2 - ERP = 1-5 ms “short”
S3 - ERP = 15-50 ms “long”
S4 - ERP = 15-50 ms “long”
S5 - ERP = 1-5 ms “short”

Short	Short
Long	Long
Short	Short
Short	
⇩	⇩
No VF	VF

Averting AF: Device

- Implantable pacemaker
- Sense/stimulate lead in the right atrium
- Determine restitution relation
- Process restitution relation to create library of relative risk for sequences of premature beats (3-5)
- Monitor local activation intervals
- If intervals are “benign” (i.e., low risk), do nothing
- If more than 2 intervals are in a “malignant” sequence (i.e., high risk), preempt next “long” interval with a pacing stimulus
- Update library periodically; create libraries for specific activities (exercise, sleep, drugs, etc.)

Collaborators

QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.

Niels Otani
Cornell

QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.

Valentin Krinsky
Nice

Jeff Fox
GNS

Eberhard Bodenschatz
MPI Göttingen

Sydney Moïse
Cornell

Anna Gelzer
Cornell

QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.

Alain Karma
Northeastern

Wouter Rappel
UC San Diego

Dante Chialvo
Northwestern

Elizabeth Cherry
Flavio Fenton
Cornell

David Christini
Cornell Weill

Mark Riccio
Cornell

Cornell: Mike Enyeart, Alisa Mo, Dima Raskolnikov, Martin Ryan
MPI Göttingen: Stefan Luther, Gisa Luther, Amgad Squires

Model Checking-Abstract Interpretation

Normal atria

Full ionic model (IM) - dynamical model (DM) - accurate prediction of arrhythmogenic sequences (P)

Diseased atria
IM’ - DM’ - P’
IM” - DM” - P”

Averting AF: assumptions

- AF is caused by one or more reentrant action potential waves.
- Initiation of reentrant excitation requires unidirectional conduction block.
- Induction of unidirectional conduction block requires intrinsic and/or dynamical heterogeneity of refractoriness.

Averting AF: assumptions

- Conduction block occurs when an action potential wavefront collides with the back of the wave that precedes it ("head" engages refractory "tail").
- A collision occurs when the velocity of the wavefront is higher than the velocity of the waveback it is following.
- Collisions can be predicted from simple conduction velocity (CV) and action potential duration (APD) restitution functions (APD = a(DI), CV = v(DI), where DI = diastolic interval).