Atrial Fibrillation: An Overview

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Electrical activation of the heart
Normal sinus rhythm

Atrial fibrillation

ECG during atrial fibrillation (AF)
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

\[ \text{BCL} = \text{APD} + \text{DI} \]

\[ \text{APD}_{n+1} = f(\text{DI}_n) \]
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

\[
\frac{dV}{dt} = \sum I_i 
\]

\[
I_i = g_i (V - E_i)
\]

\[
g_i = f(V,t)
\]

~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 determine 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

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

Premature pacing intervals that produce block

Short
Long
Short
Long
Short

VF
No VF
Left ventricle

Premature pacing intervals that produce block

APD restitution function

S2 - ERP = 1-5 ms  “short”
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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

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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).