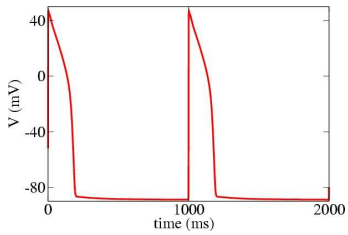
Arrhytmogenic mechanism involving intrinsic heterogeneities of cardiac tissue

Hervé Henry and Wouter-Jan Rappel

Center for Theoretical Biological Physics
UC San Diego

Introduction

Cardiac cells are excitable systems

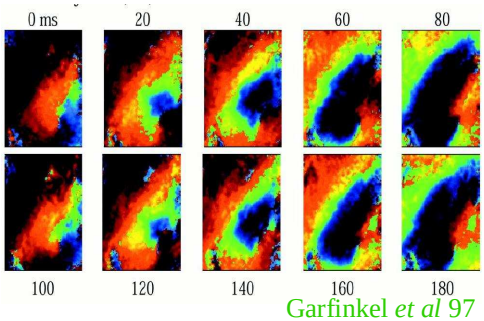


Intercellular coupling: wave propagation.

Normal rythm: plane wave
→ Contraction of muscle

Half plane wave
↓
Spiral wave: Ventricular Tacchycardia

Spiral wave instabilities
→ Ventricular fibrillation
(Sudden Cardiac Death)

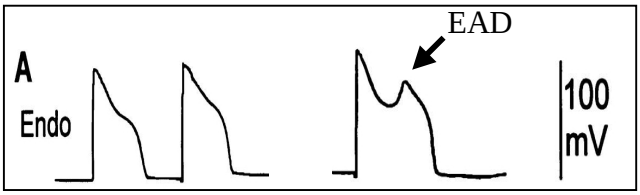


Garfinkel *et al* 97

Question: How does Ventricular Tacchycardia appear?

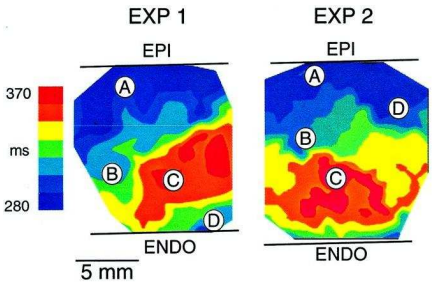
Hypothesis:

1: Early after depolarisations



G.X. Yan *et al* 2001

2: Conduction Block due to Dispersion of Repolarization



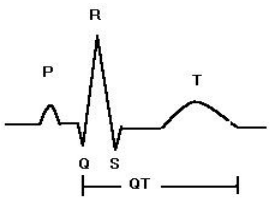
Akar *et al* 2002

→ Study in the case of Long QT Syndrome

Long QT syndrome

Known to favor a Torsade de Pointes (Ventricular Tacchycardia)

ECG:

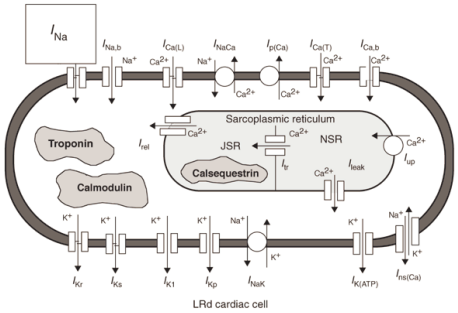


1) Longer QT interval: prolonged action potential duration. → Favors EADs

2) Wider T wave: increased dispersion of repolarizations. → Favors Conduction Blocks

Model

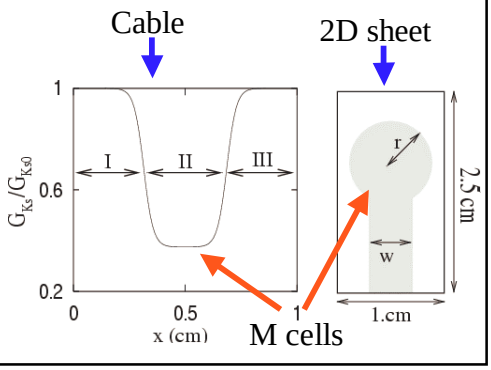
Ionic model: Luo Rudy Dynamic (2000):



$$\partial_t V = -\Sigma I_{ions} + D_c \Delta V$$

Long QT: leak of Na current during Action Potentials.

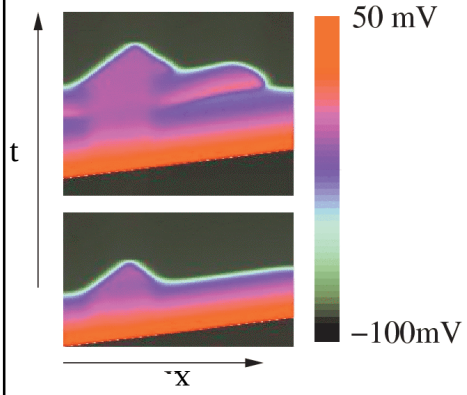
Inhomogeneities: Mcells, population of cells in the midle of ventricle with longer action potentials. → Reduction of G_{ks}

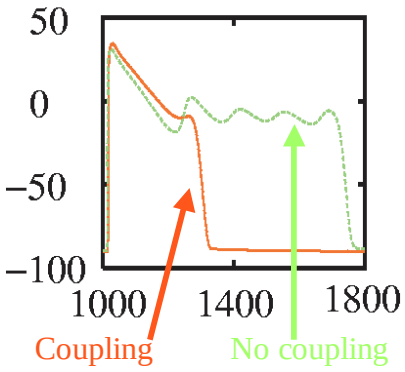


EADs

1) Regular pacing followed by late stimulus.

2) Regular BCL and strong LQT (Period doubling and EADs)

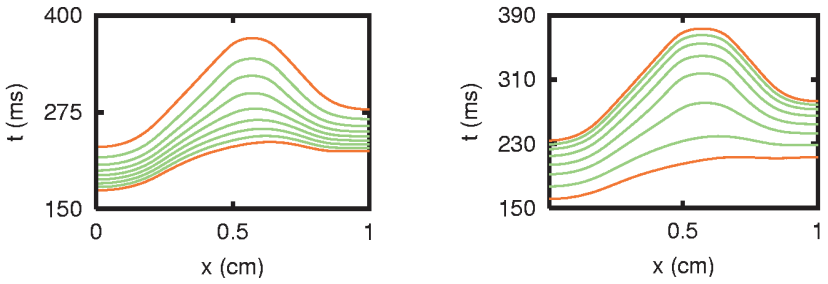




1) Coupling reduces EAD amplitude.

2) Secondary beat impossible without strongly inhomogeneous coupling (Montserrat et al 2000, Biktashev 2002)

Dispersion of Repolarization: Effects of Long QT and Pacing Period



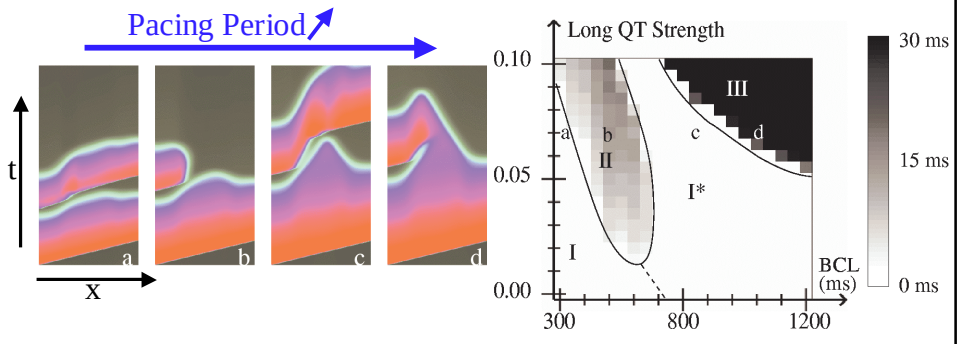
Long QT strength ↗ Pacing Period ↗

Stronger DoR

Conduction Blocks (1D)

Regular pacing and premature stimulus.

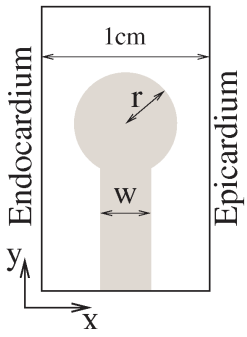
Unexpected behaviors:



Long QT Favors Conduction Blocks at long Basic Cycle length.

Two dimensions

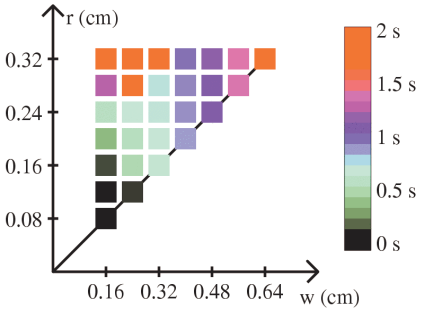
Regular line pacing on the epicardium and premature stimulus at the epicardium.



Partial conduction block

→ Sustained reentry

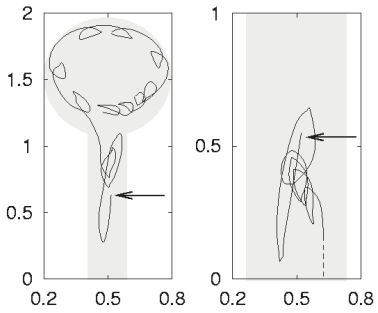
Effects of geometry on reentry length



Long lived reentries favored by:

1) wide strip .

2) big bubble at the top of the M cells region. (Pinning)



Conclusion

- EADs Can not lead to a premature stimulus without inhomogeneous coupling .
- CB is a possible arrhythmogenic mechanism.
- Importance of the geometric repartition of M cells.

Perspectives

- 3D. Possible effects of line tension. Subsequent evolution of the spiral wave.
- CB is a possible arrhythmogenic mechanism.
- Importance of the geometric repartition of M cells.