DYNAMICS OF REENTRANT TACHYCARDIA

Leon Glass

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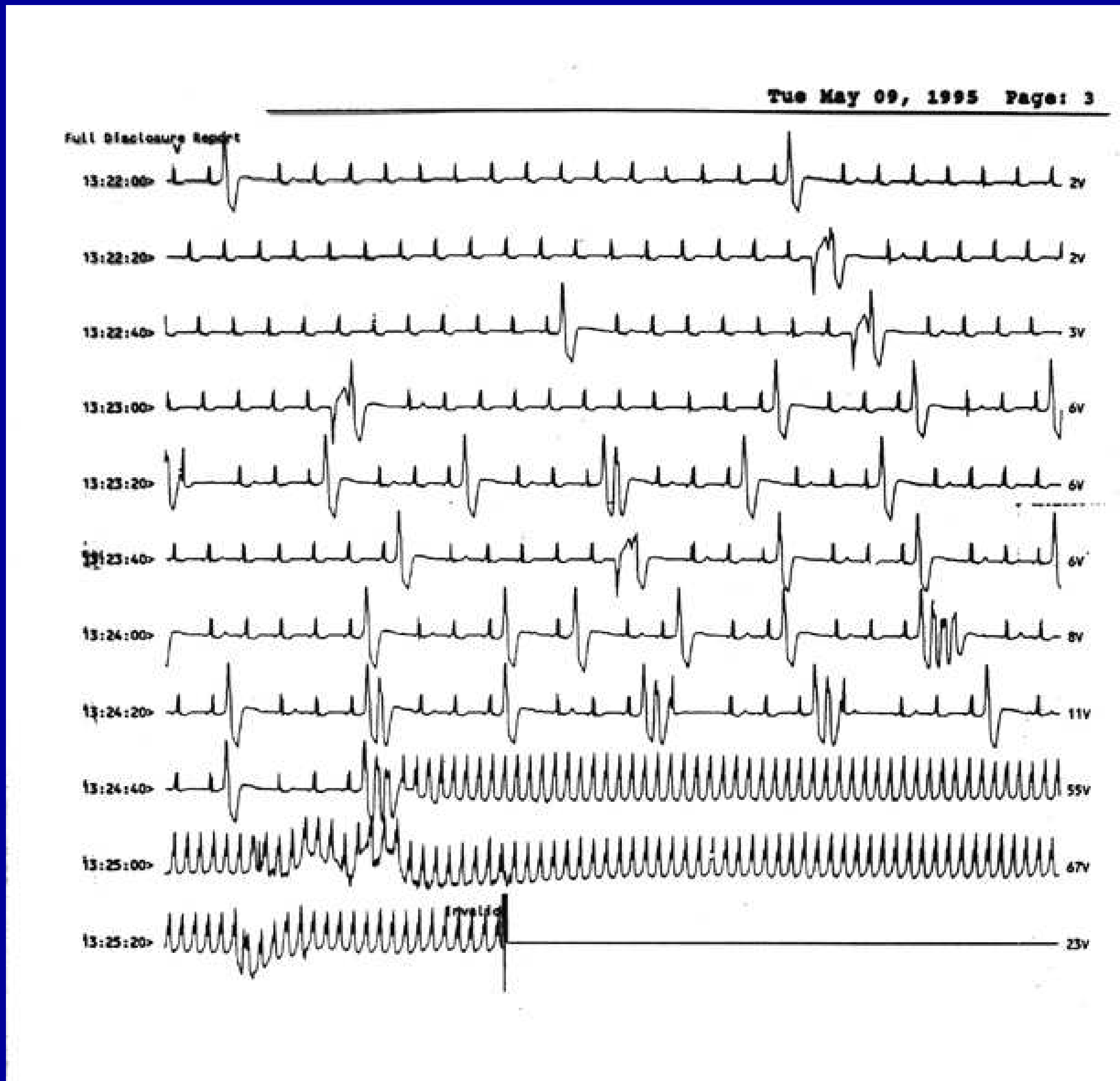
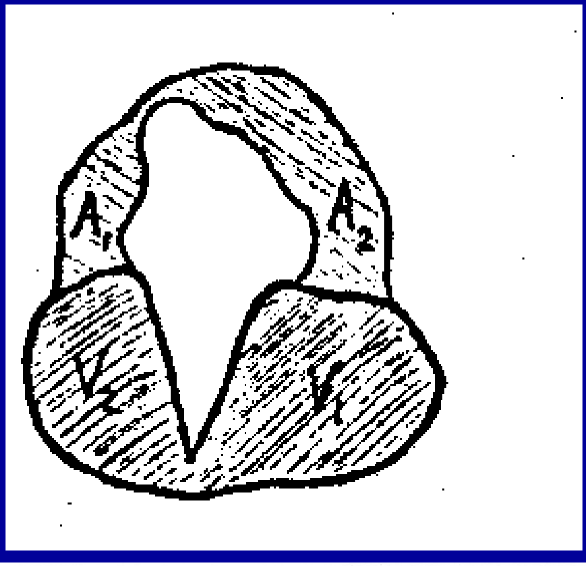
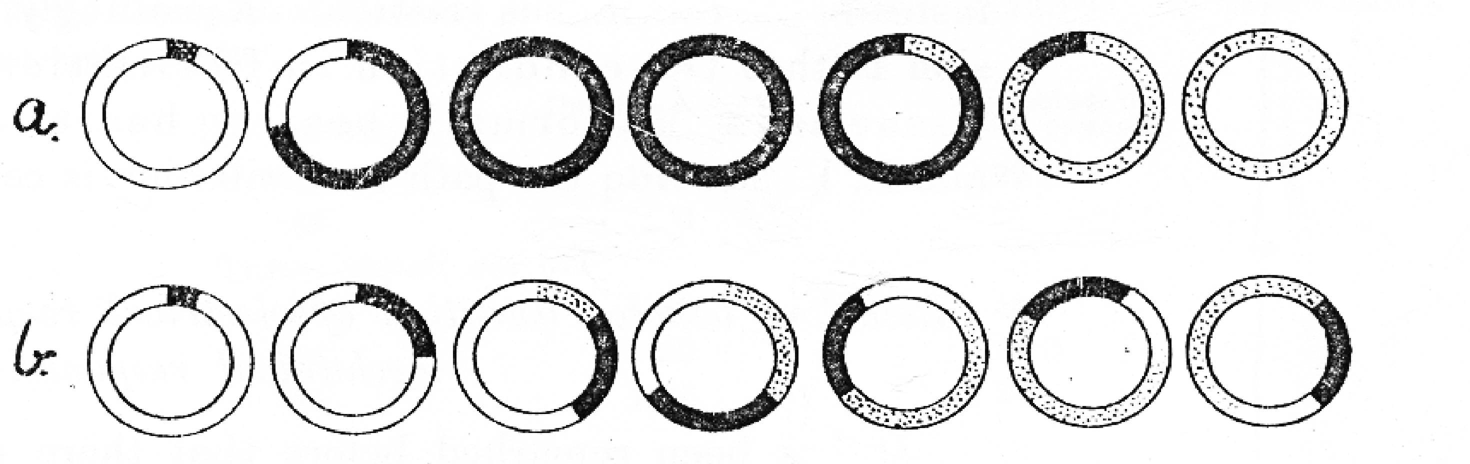
Cardiac arrhythmias suddenly start and stop



Anatomical Reentry

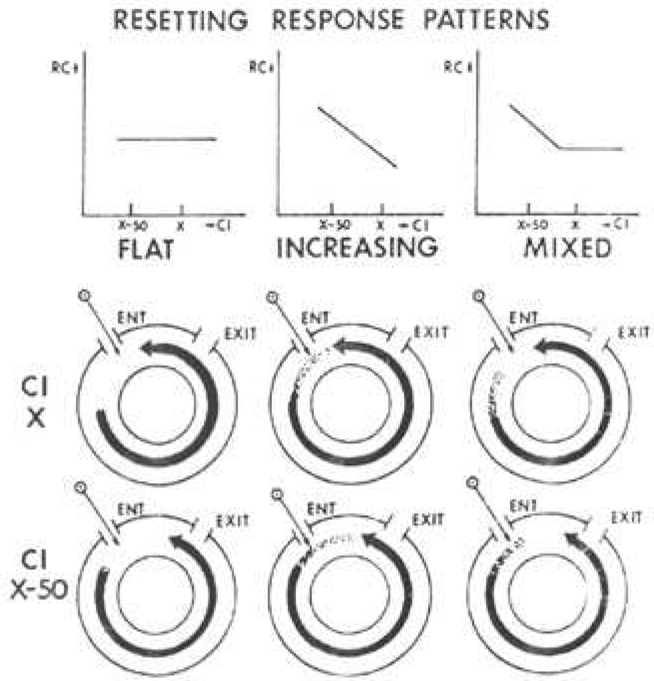




G. R. Mines (1913)

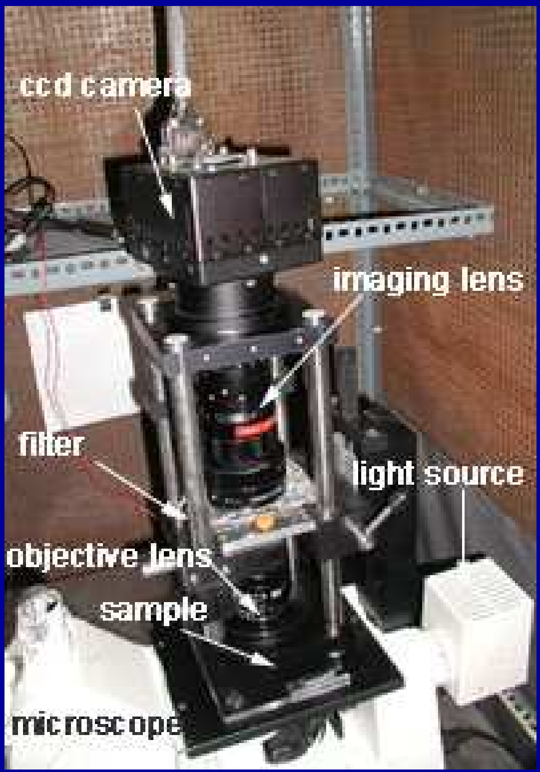
Resetting and Entrainment of Ventricular Tachycardia Associated with Infarction: *Clinical and Experimental Studies*

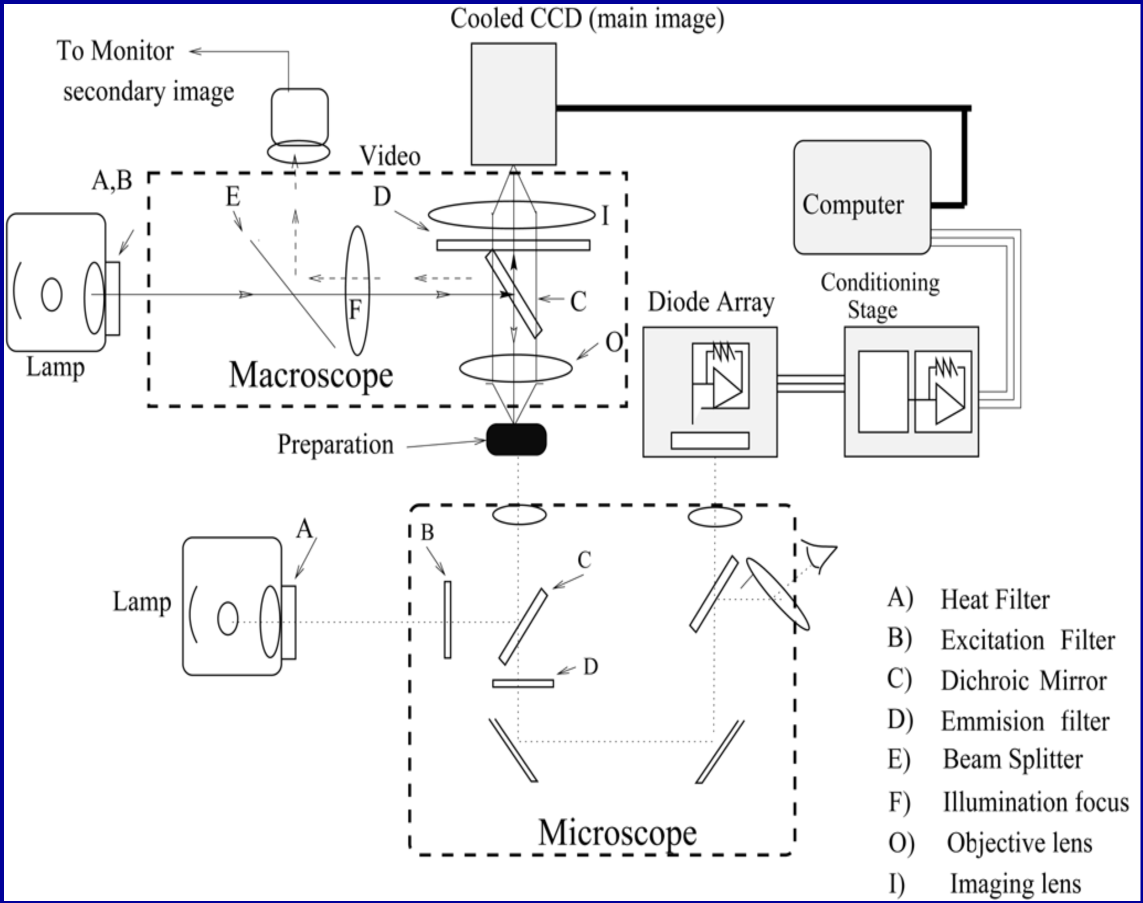
M. E. Josephson, D. Callans, J. M. Almendral, B. G. Hook, R. B. Kleiman



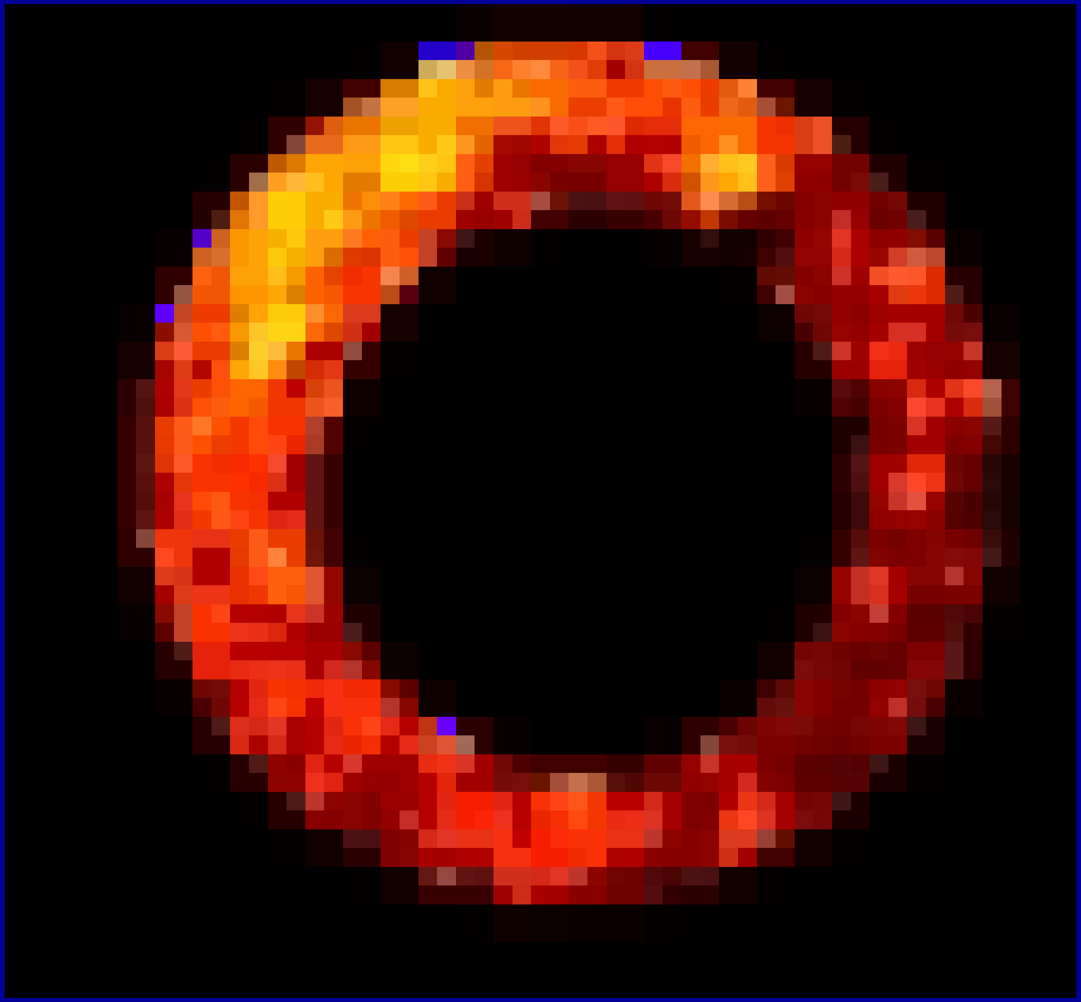
Macroscope for studying dynamics in tissue culture

(Gil Bub, Alvin Shrier, Yoshihiko Nagai, Katsumi Tateno)



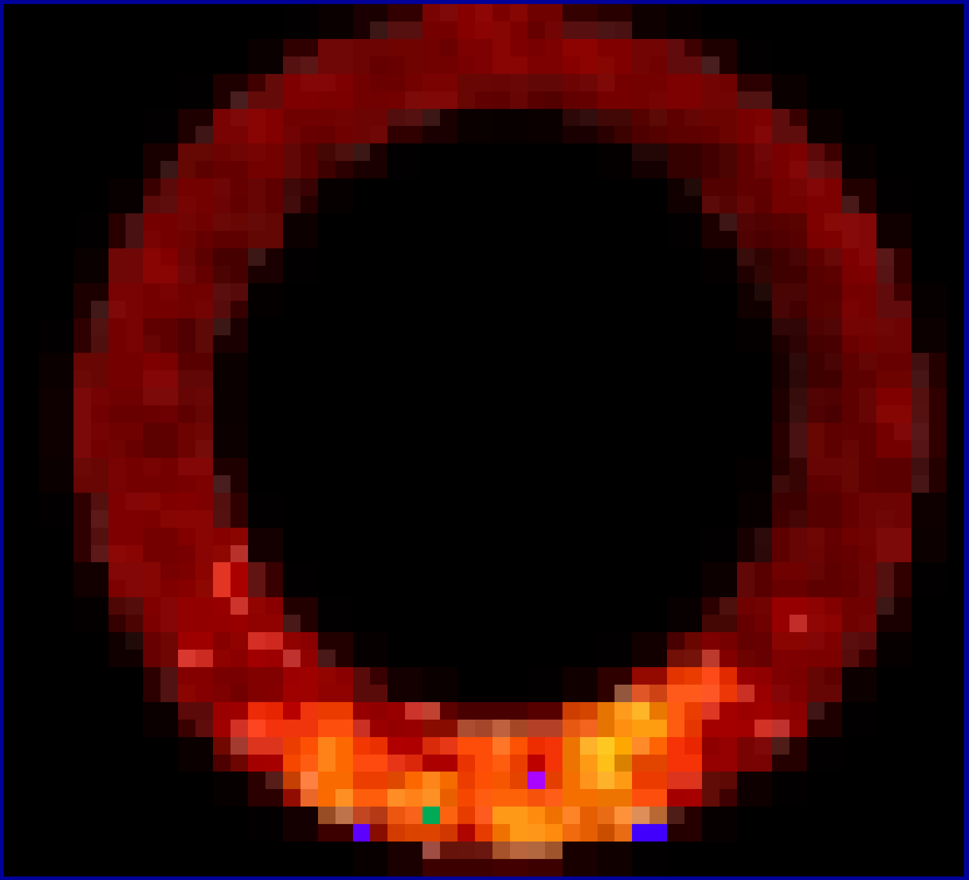


Dynamics in a Ring of Cardiac Cells

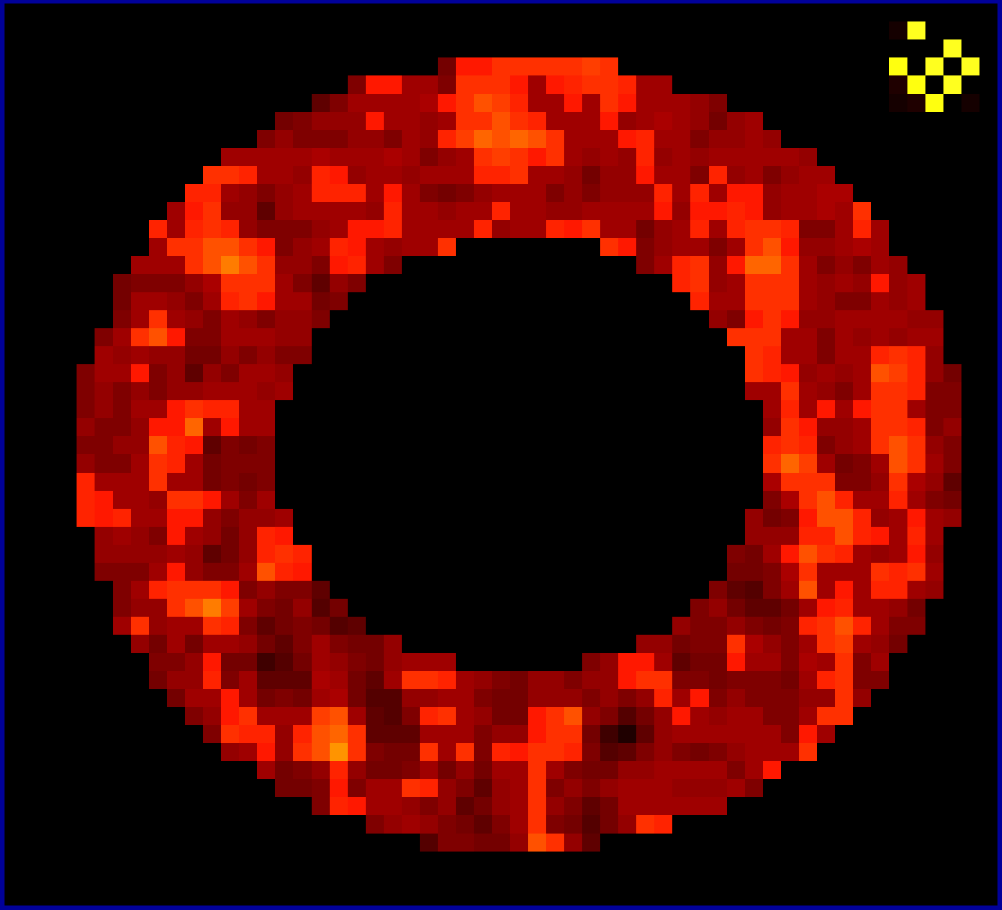


Pacemaker

Nagai, Gonzalez, Shrier, Glass, PRL (2000)



Reentry



Cardiac Ballet

Physiological properties of real heart cells

- Excitable
- Oscillatory (can be reset and entrained)
- Fatigue (less excitable following rapid stimulation – overdrive suppression)
- Heterogeneous

FitzHugh-Nagumo Model of Propagation

$$\frac{\partial v}{\partial t} = -(v+.1)(v-.9)(v-.039) - w + D\frac{\partial^2 v}{\partial r^2} + I,$$

$$\frac{\partial w}{\partial t} = (.005v - .01w + .0005)R(\zeta, v),$$

$$\frac{dz}{dt} = -\gamma_\alpha z + (\Delta z)\delta(t - t_{AP}),$$

$$\zeta(z) = \frac{.015}{z+1.},$$

$$R(\zeta, v) = \begin{cases} \frac{(1-\zeta)}{1+10e^{-10(v-.1)}} + \zeta, & \textbf{Pacemaker cells} \\ 1 & \textbf{Otherwise} \end{cases}$$

Properties of Excitation Circulating on Rings

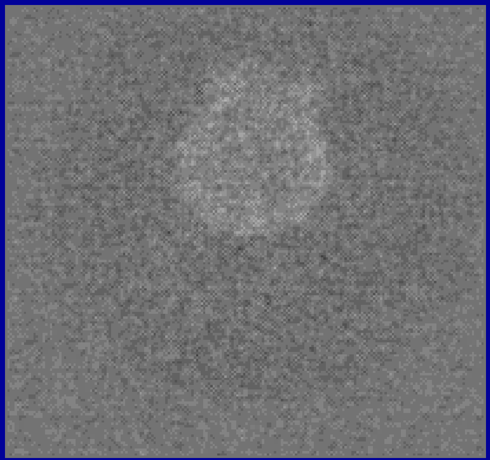
- As the ring becomes smaller, an instability develops so that the cycle time fluctuates quasiperiodically (Frame and Simson, 1988; Courtemanche, Keener, Glass, 1993)
- A single stimulus can either reset or annihilate the excitation (Glass and Josephson, 1995; Gedeon and Glass, 1999). Relevant to antitachycardia pacemakers.
- Resetting of an excitation circulating on a ring can be used to predict the entrainment by periodic stimuli (Nomura and Glass, 1996; Glass, Nagai, Hall, Talajic, Nattel, 2002)

Strategy of "Proof" of Annihilation of Pulses Circulating on Rings (Gedeon and Glass, 1999)

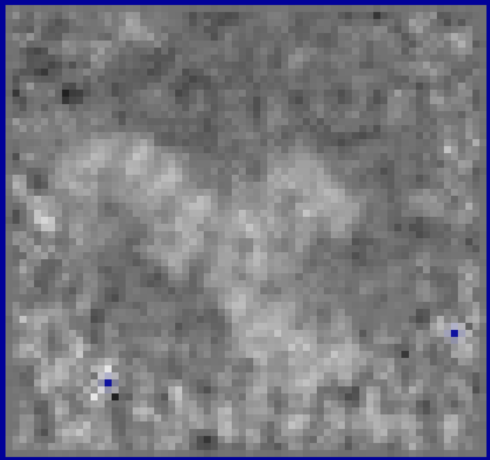
- A ring of excitable medium supports a circulating pulse
- *Continuity theorem: If a perturbation delivered at any phase of a limit cycle oscillation leaves the state point in the basin of attraction of the limit cycle, then the resetting curves are continuous.
- Resetting curves for stably circulating pulses on a one dimensional ring are discontinuous.

Pacemakers and Reentry in Tissue Culture

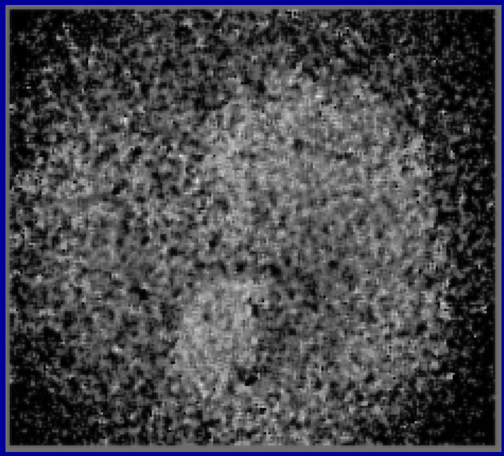
Calcium Target
(Calcium Green)



Calcium Spiral
(Calcium Green)



Voltage Spiral
(di-4-ANEPPS)



Spiral waves have been hypothesized as a mechanism for VT and VF (Wiener and Rosenblueth, Krinsky, Winfree, Allessie, Jalife, and many others)

Dynamics as a Function of Age of Tissue Culture

<u>Time in Culture</u>:

30h

39h

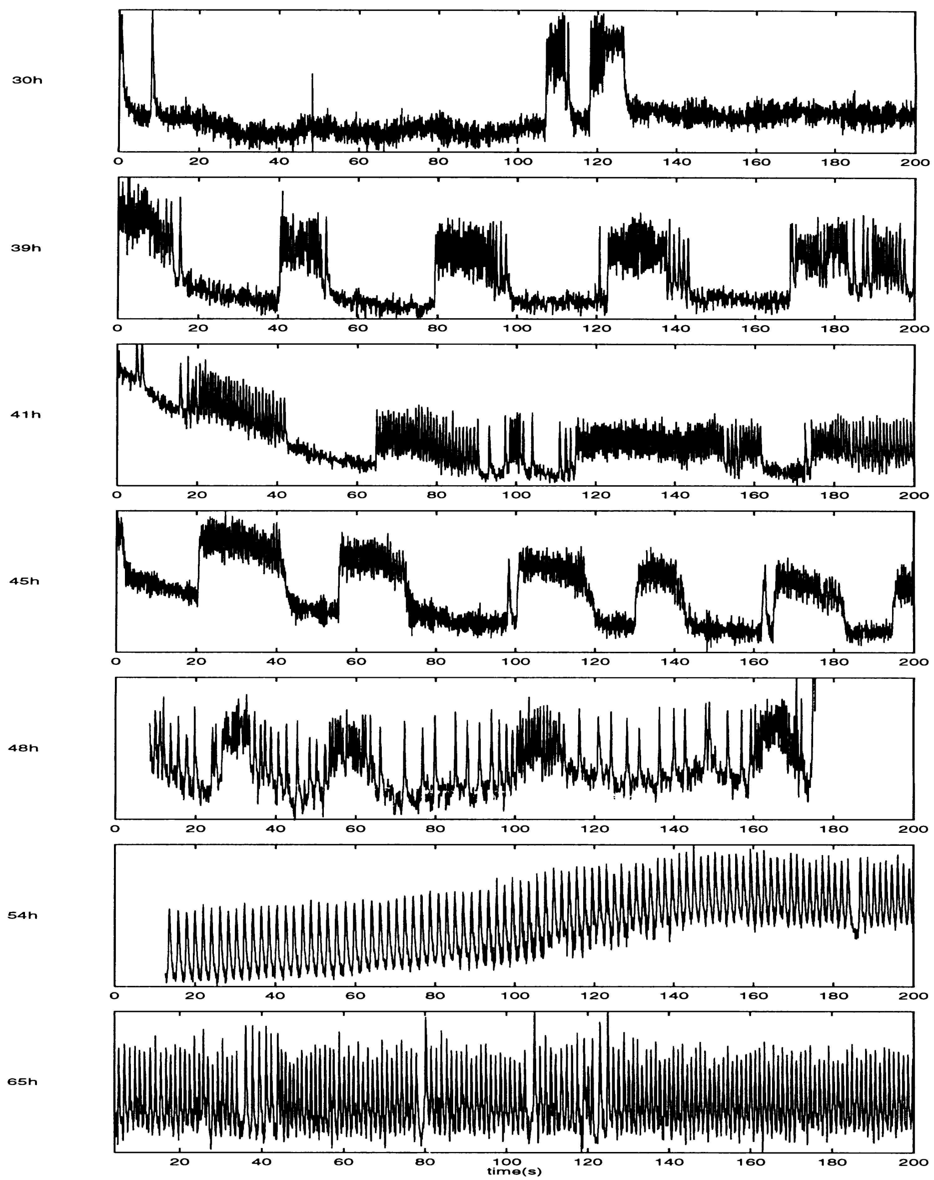
41h

45h

48h

54h

65h



Bub et al. Journal of Cardiovascular Electrophysiology 2003

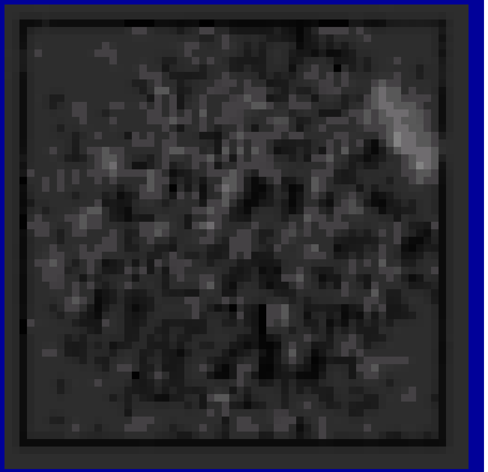
irregular activity

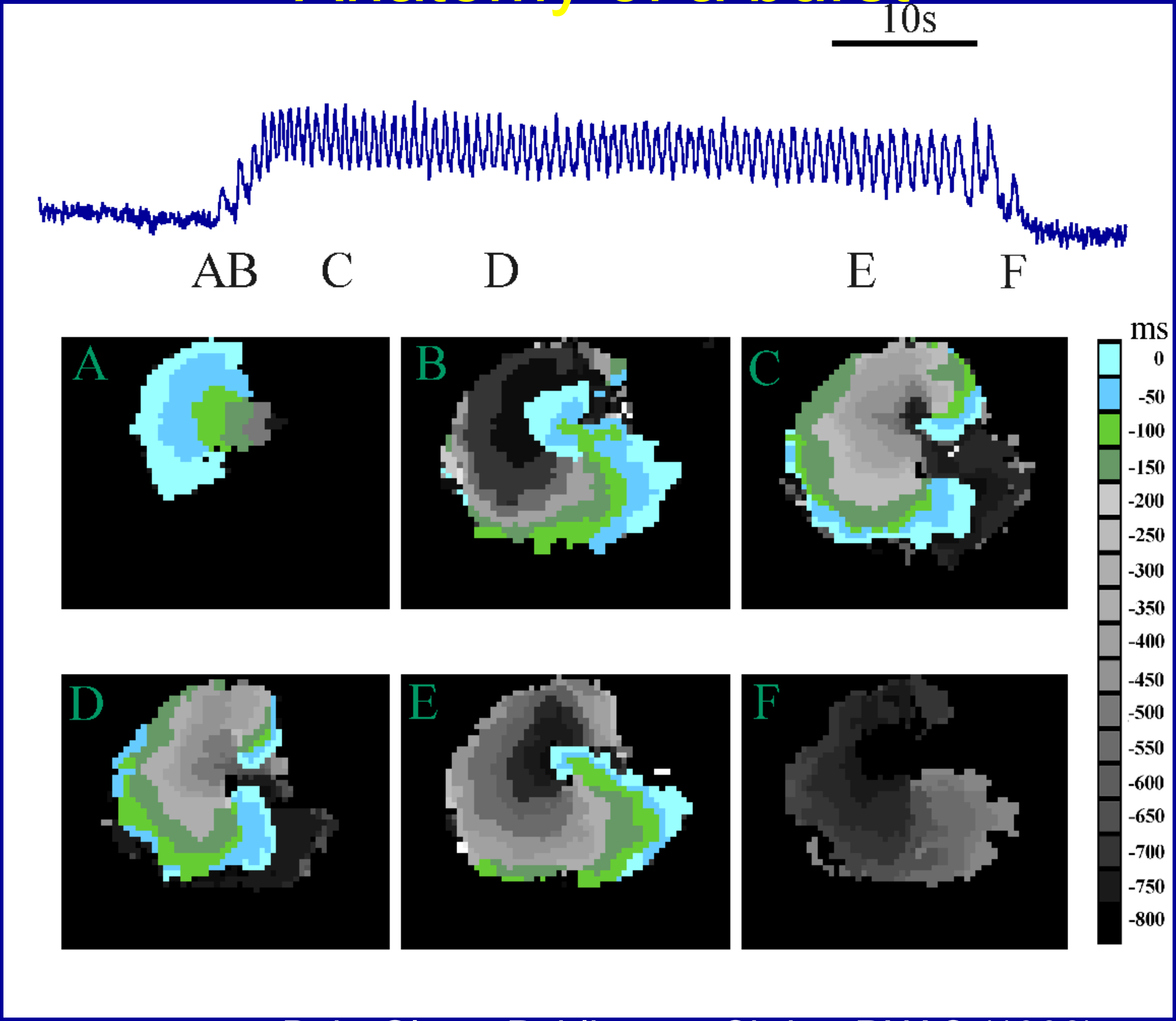
bursting spirals

stable spirals

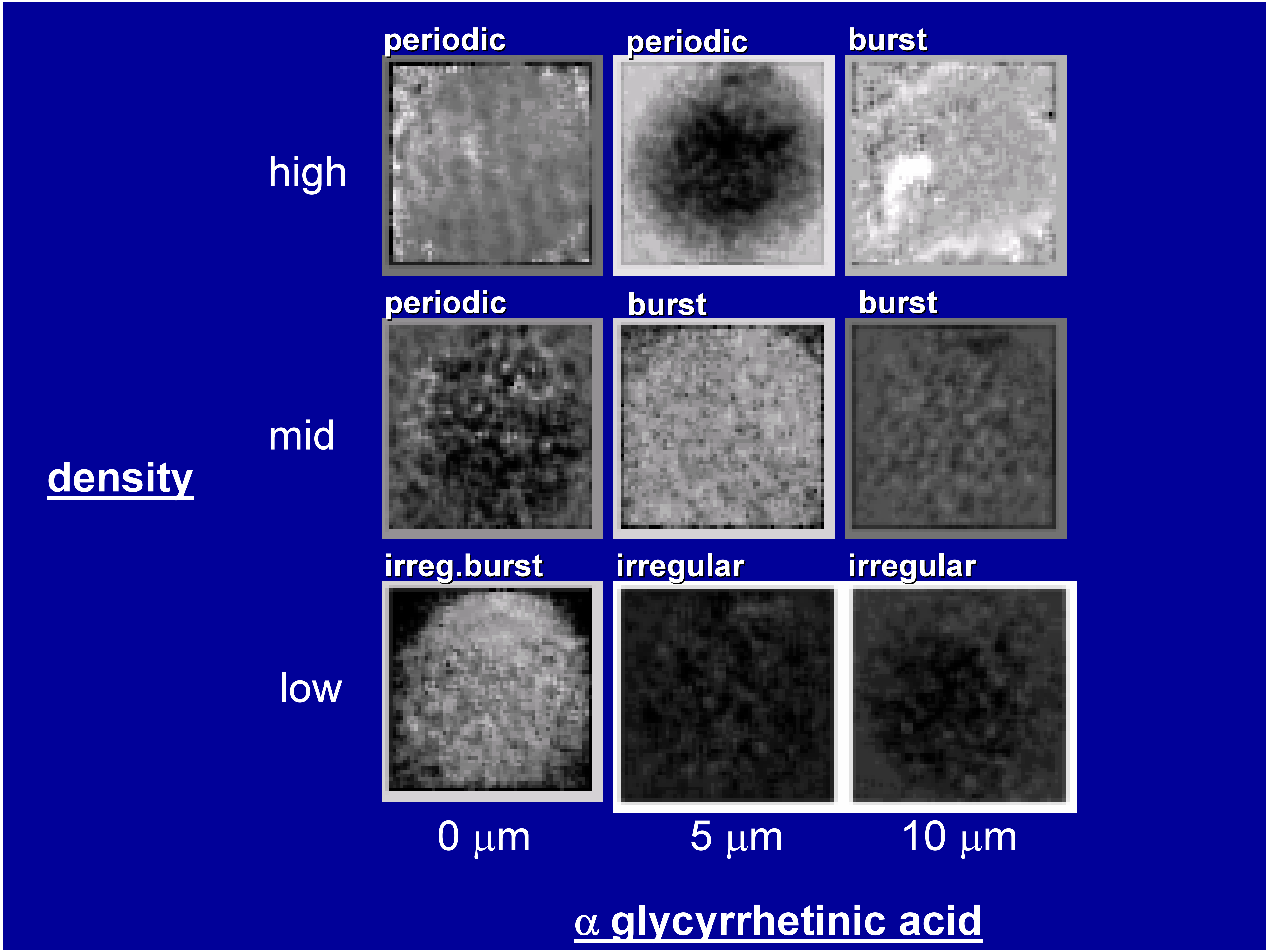
targets

Anatomy of a burst

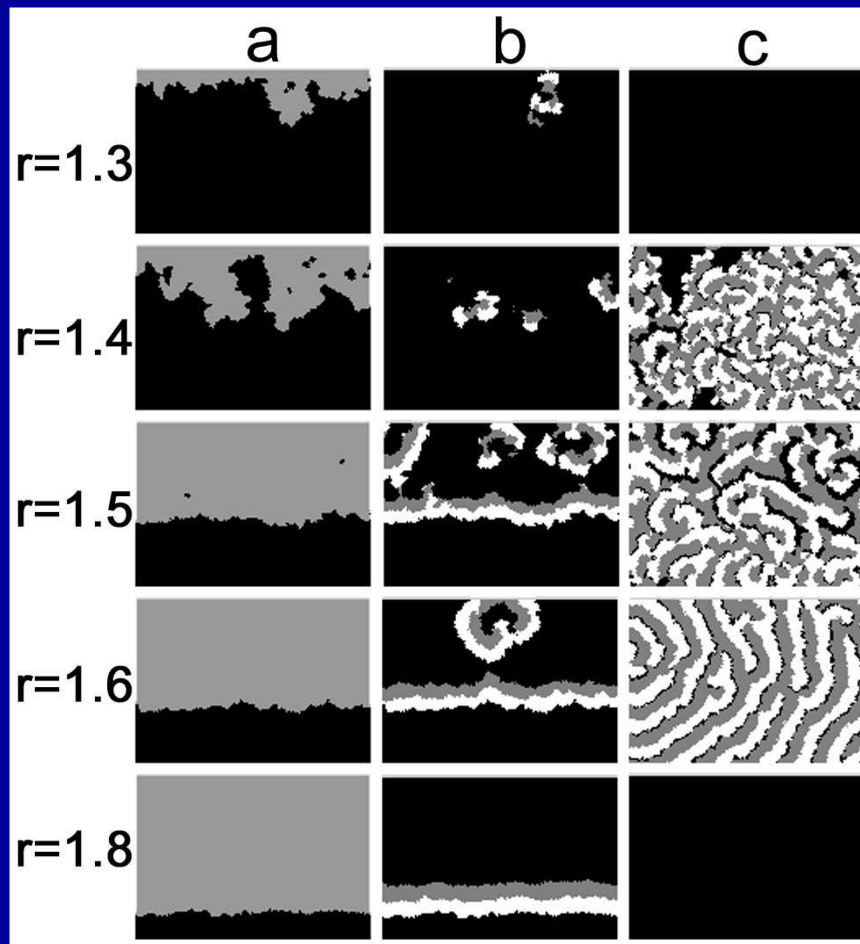




Bub, Glass, Publicover, Shrier, PNAS (1998)


density
high
mid
low
periodic
periodic
burst
periodic
burst
burst
irreg.burst
irregular
irregular
0 μm
5 μm
10 μm
α glycyrrhetinic acid

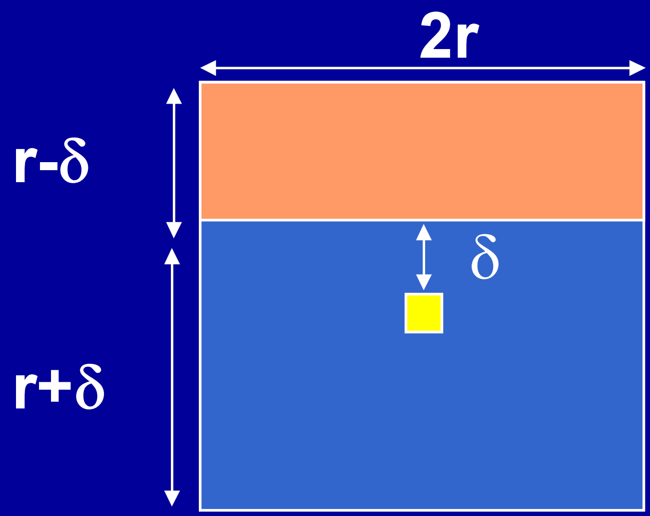
Activity starting from excitation in the top row at t=0.



Activated T=100 | Active T=100 | Active T=1000

Cellular Automata Model of Cell Connectivity

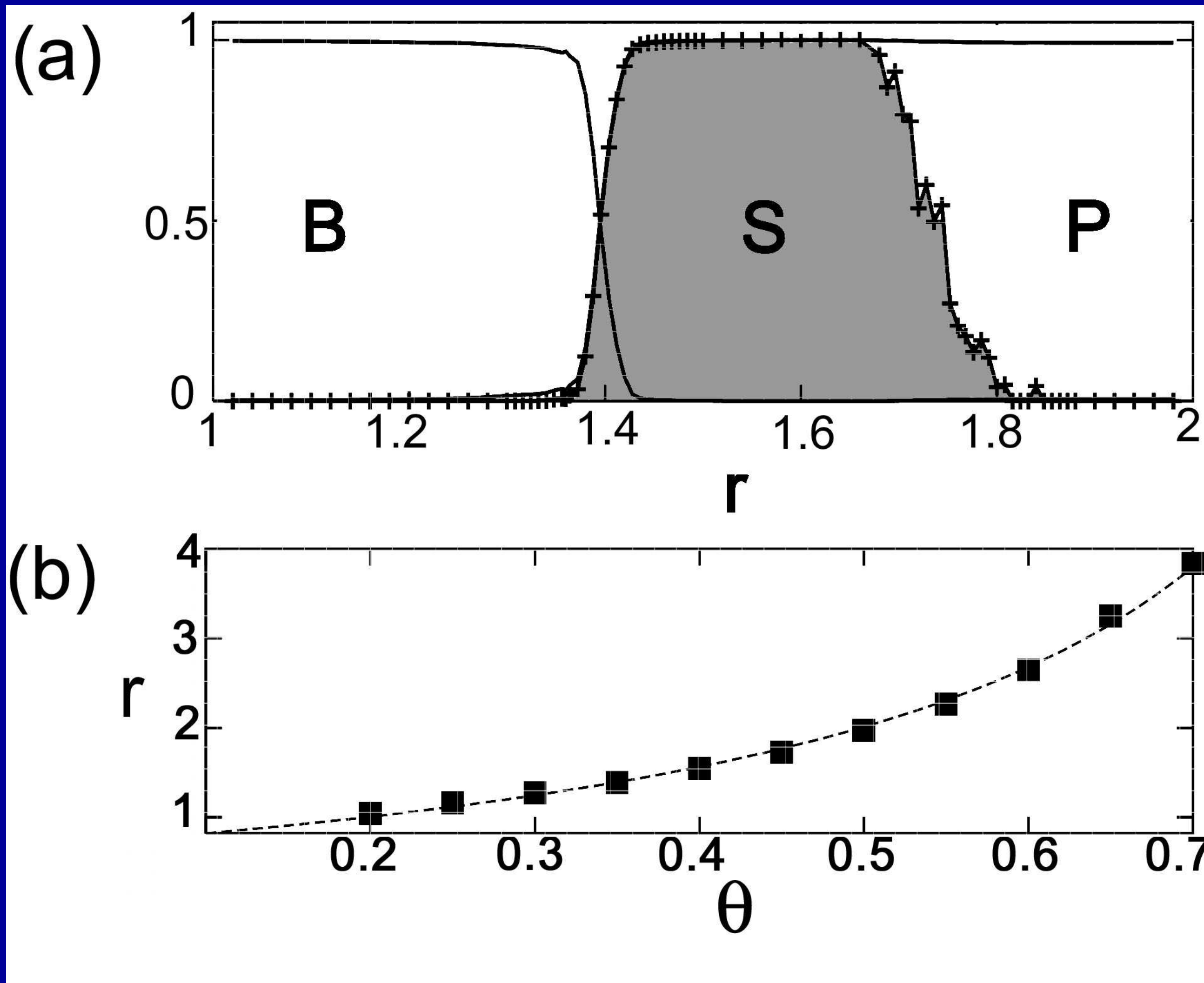
Reduction of cell connectivity is modeled by decreasing **r,** the neighborhood for interaction. Consider a cell a distance δ away from an activation front. For a cell to be active at the next iteration the ratio between the number of excited cells in its and the number of inexcited cells must be greater than the threshold.



$$\theta < 2r(r-\delta) \,/\, 2r(r+\delta)$$

$$\theta < (r-\delta) \,/\, (r+\delta)$$

Boundary of block as a function of the radius of interaction

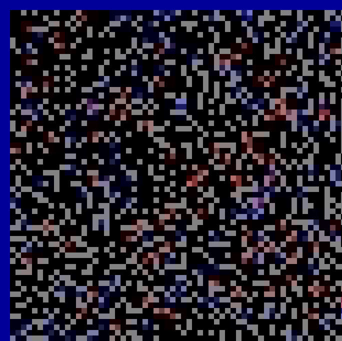


$$r_c = \delta(1+\theta)/(1-\theta)$$

Simulating bursting dynamics as a function of connectivity

1)Add spontaneous activity by giving excitable cells a probability of firing.
2) Add fatigue by giving each cell a fatigue variable η where
 a) if the cell just became excited, $\eta_{i,j}(t+1) = \eta_{i,j}(t) + F$,
 b) Otherwise, $\eta_{i,j}(t+1) = \chi\eta_{i,j}(t)$, where $0<\chi<1$ (exponential decay)
Now a cell is activated if $\eta_{i,j} + \theta <$ active/inactive

R=3, θ=0.35

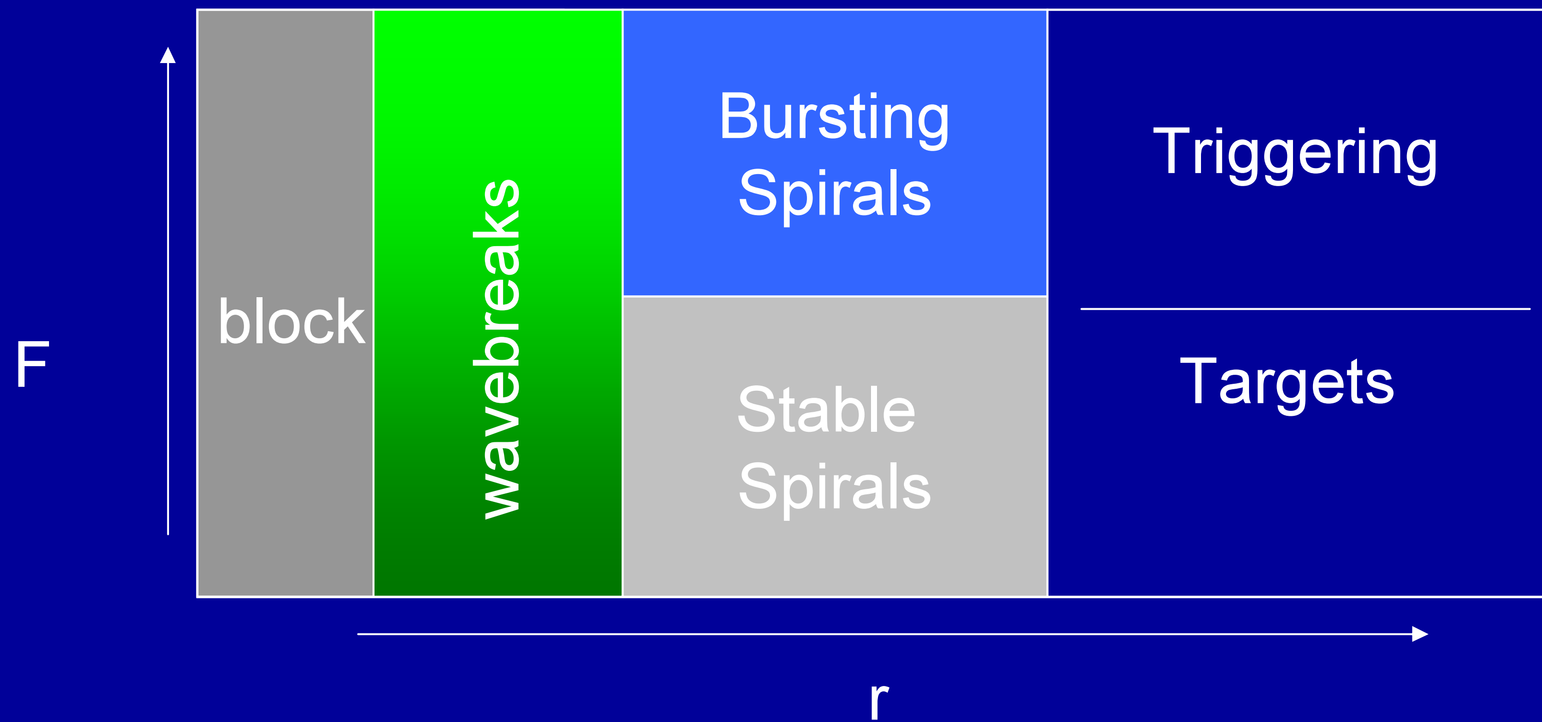


Target patterns ('periodic')

R=1.8, θ=0.35

bursting

Organization of dynamics in parameter space

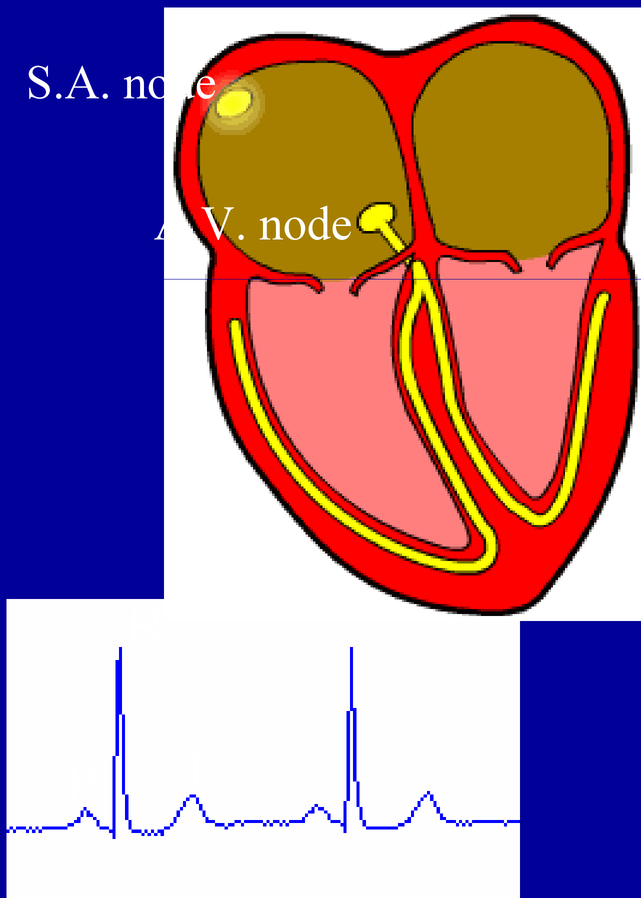


Practical Applications

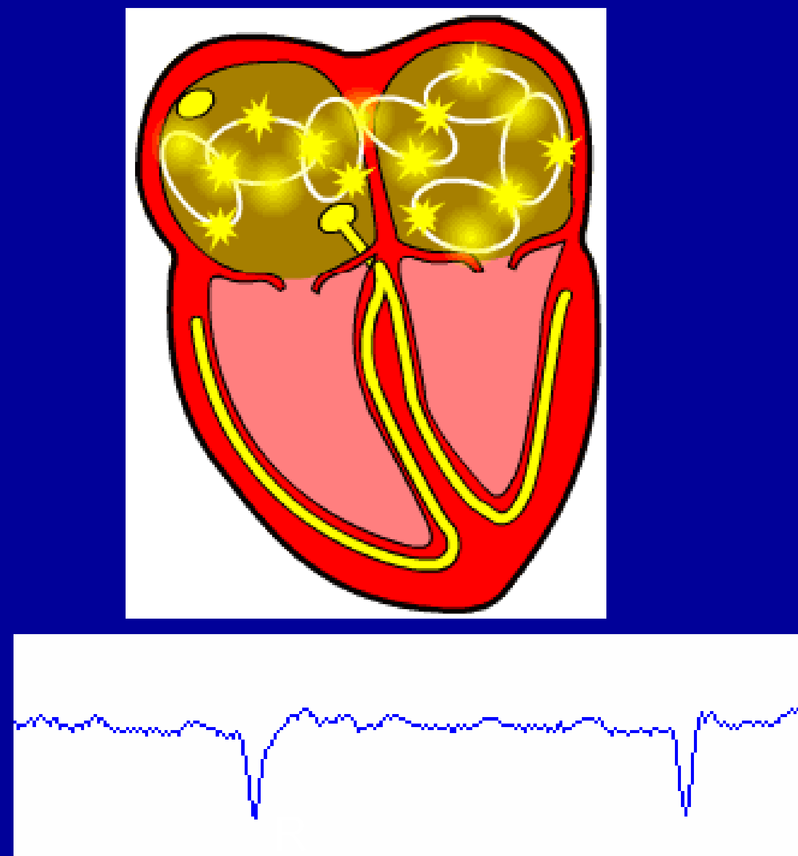
- Analyze complex rhythms for diagnosis and prognosis

Can you detect atrial fibrillation based on the RR intervals?

Normal

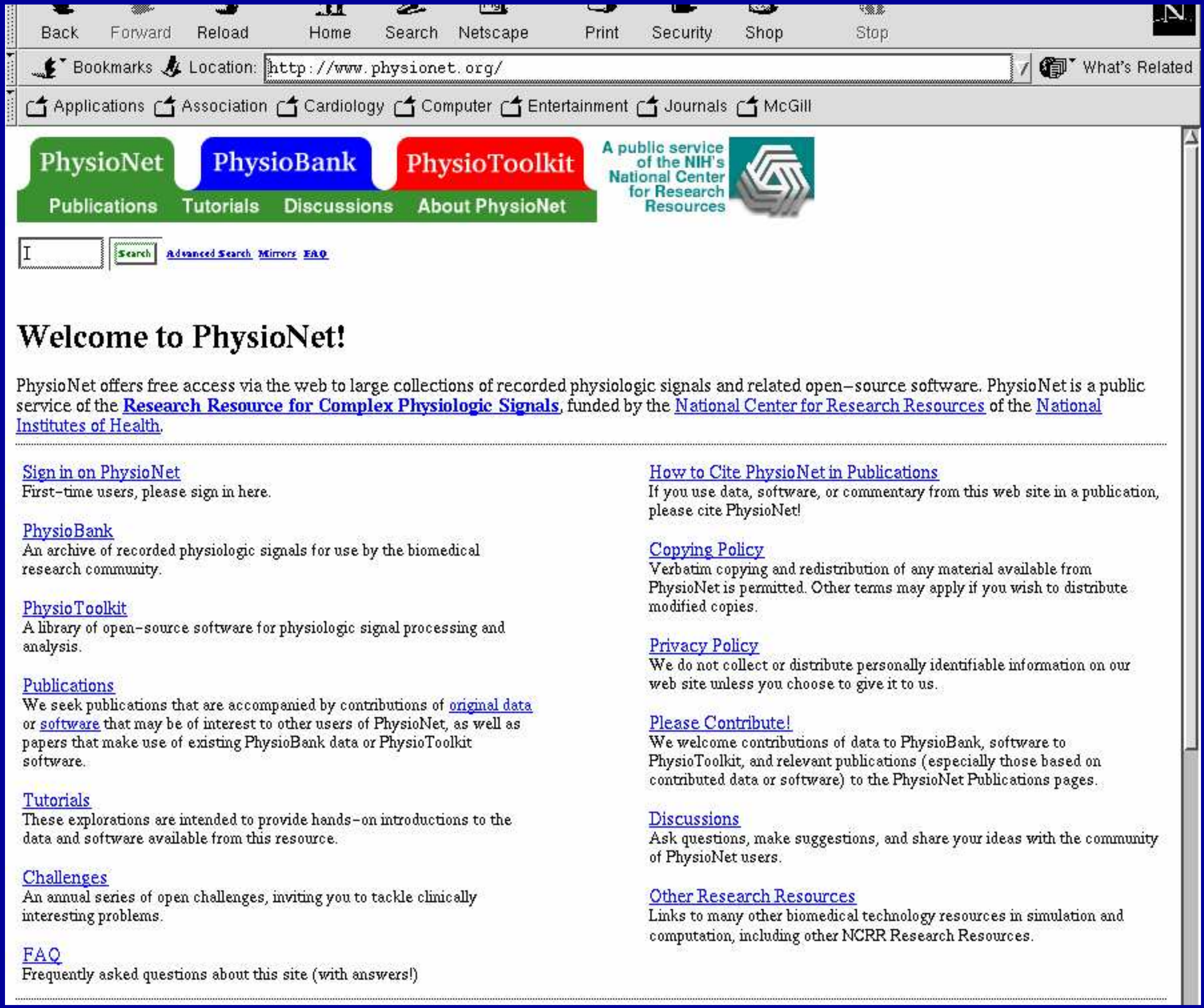


Atrial fibrillation



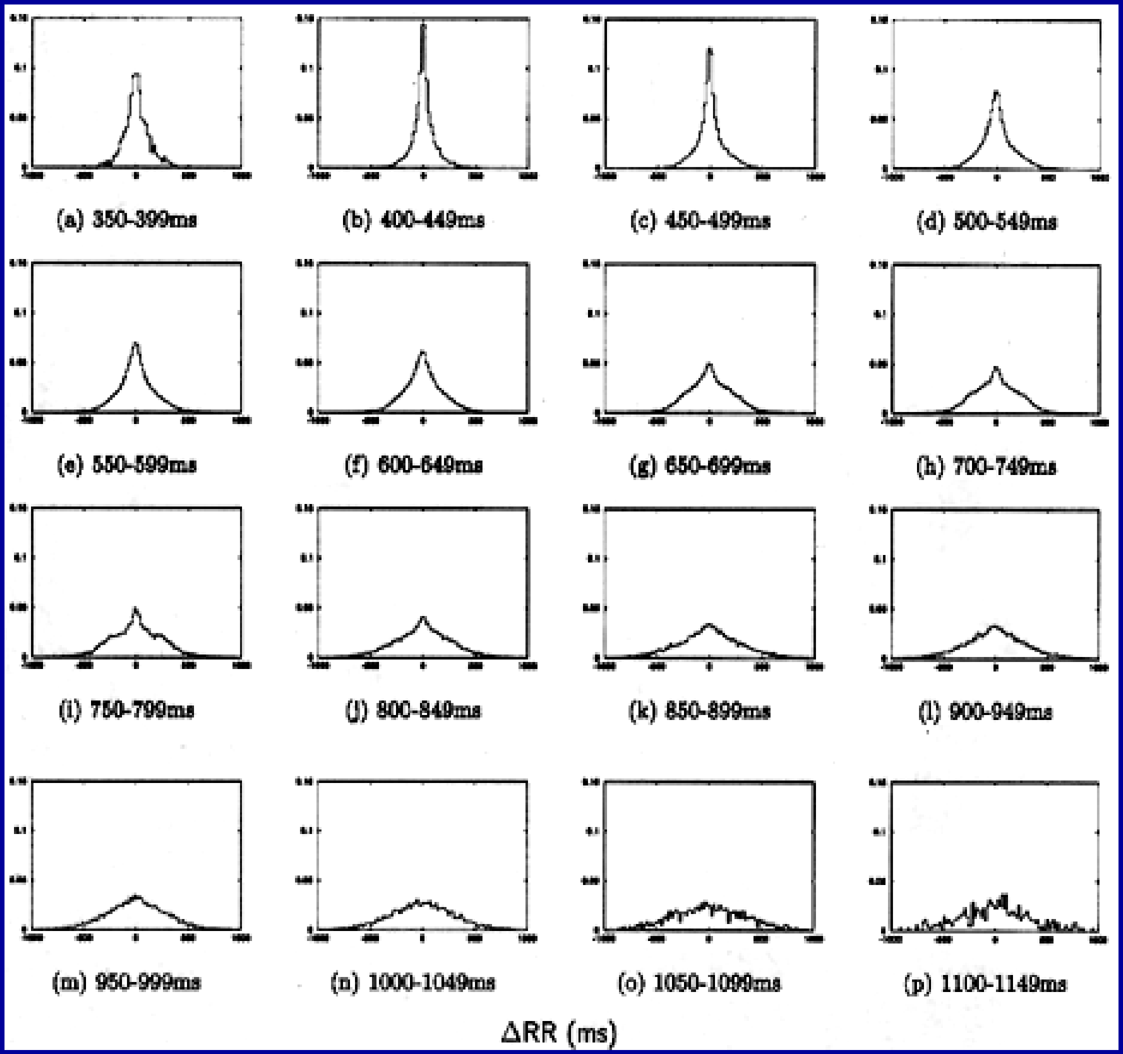
http://www.aboutatrialfibrillation.com

National Resource for Complex Physiologic Signals
A. Goldberger, Director



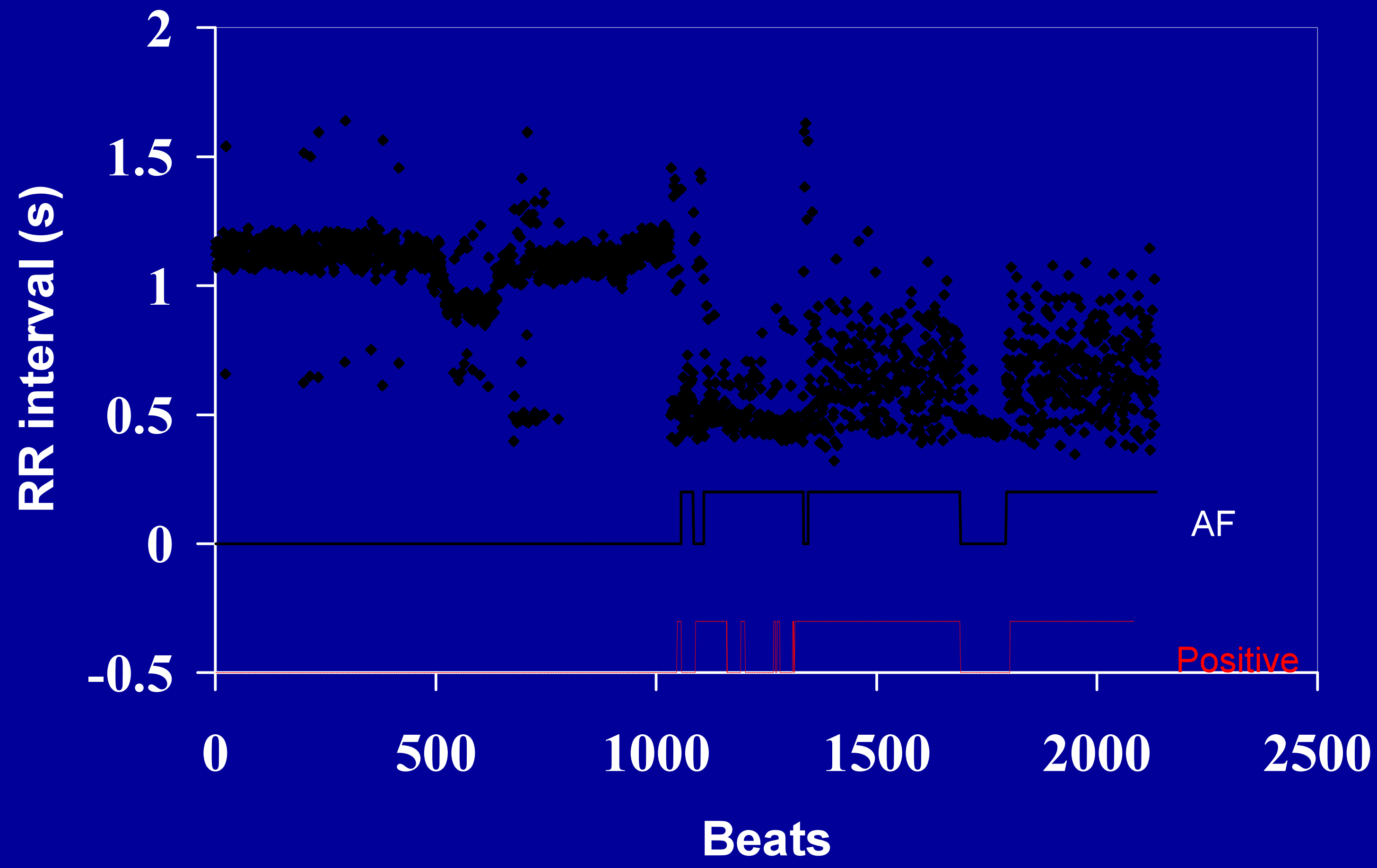
http://www.physionet.org

Use Histograms of ΔRR Intervals to detect AF



Tateno and Glass (2001)

Data Analysis: MIT-BIH arrhythmia database (From PhysioNet)



Conclusions

- Experimental systems and mathematical models of reentry show paroxysmal rhythms similar to paroxysmal reentrant rhythms. To date these have NOT been a focus for theoretical analysis.
- Applications that use nonlinear mathematics for better diagnosis, and control of cardiac arrhythmias are under development

Acknowledgments

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