Complex Spiral Wave Dynamics on Cardiac Monolayer Tissues: alternans and beyond

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(http://turing.korea.ac.kr)

HEART - a complex functional system of cells: its hierarchical structure

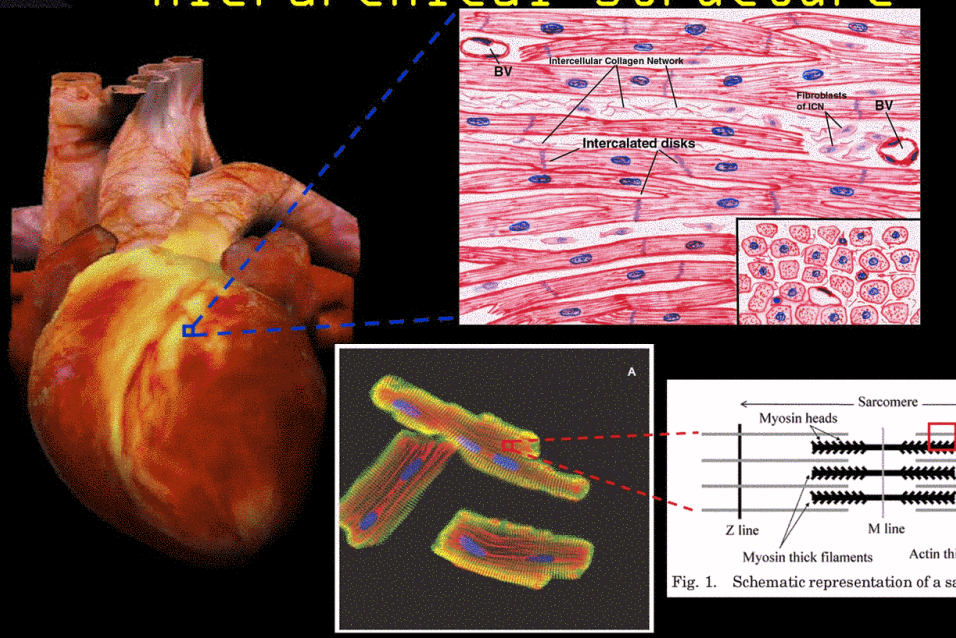
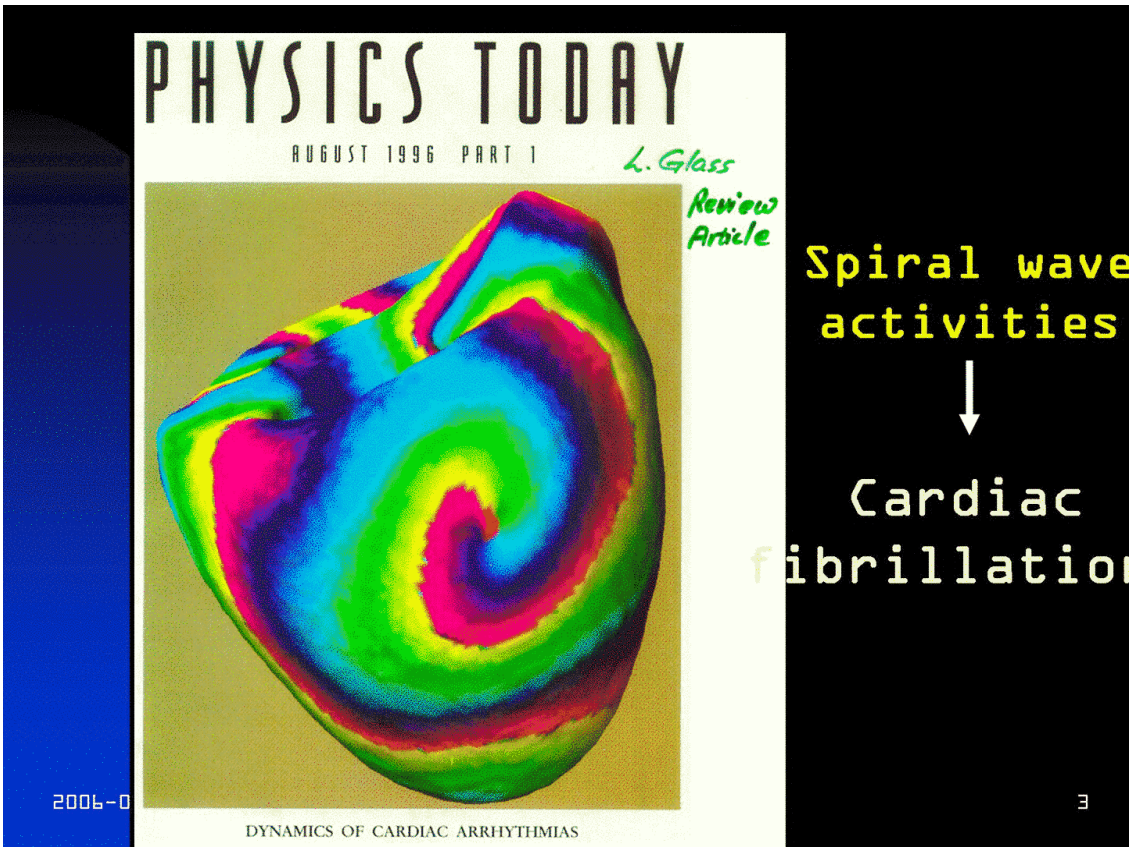


Fig. 1. Schematic representation of a sarcomere (see text).


PHYSICS TODAY
AUGUST 1996 PART 1
L. Glass
Review Article
DYNAMICS OF CARDIAC ARRHYTHMIAS
Spiral wave activities
Cardiac fibrillation
2006-0
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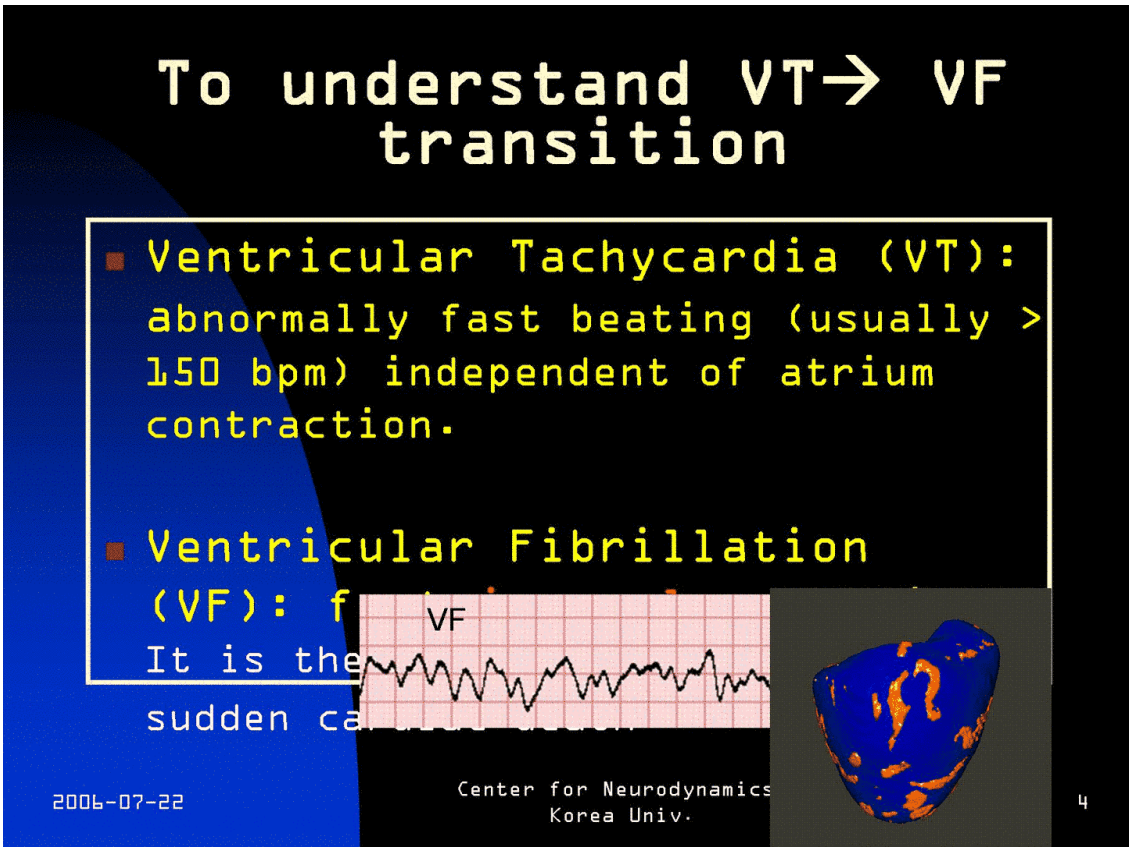
To understand VT→ VF transition
Ventricular Tachycardia (VT): abnormally fast beating (usually > 150 bpm) independent of atrium contraction.
Ventricular Fibrillation (VF): f
It is the
sudden ca
VF
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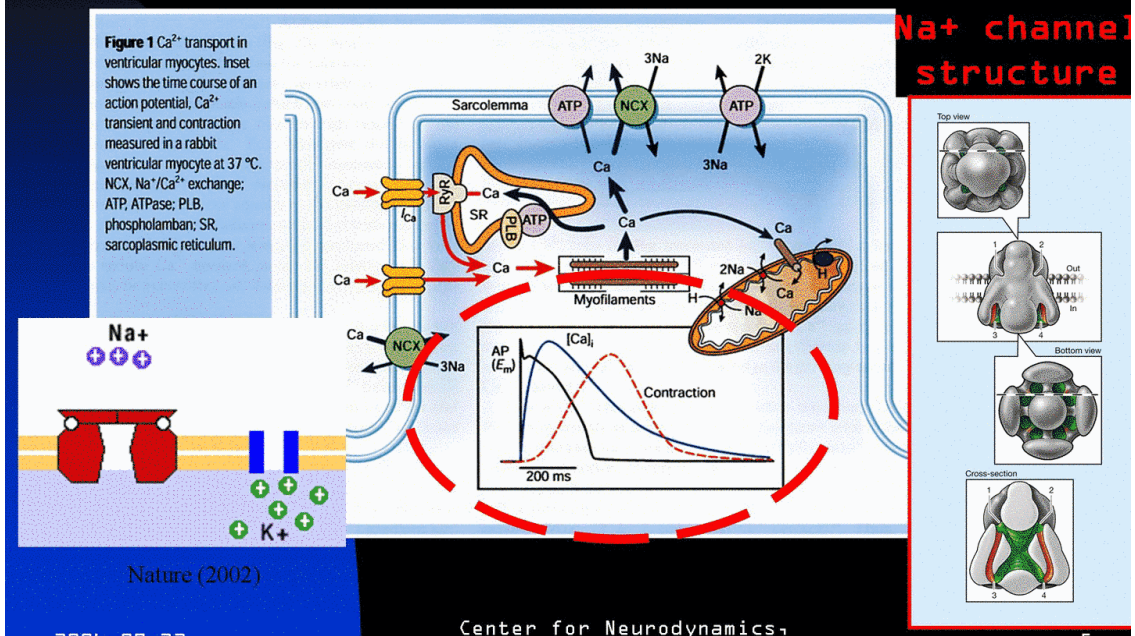
Three important observables (ΔV, Ca++, motion)

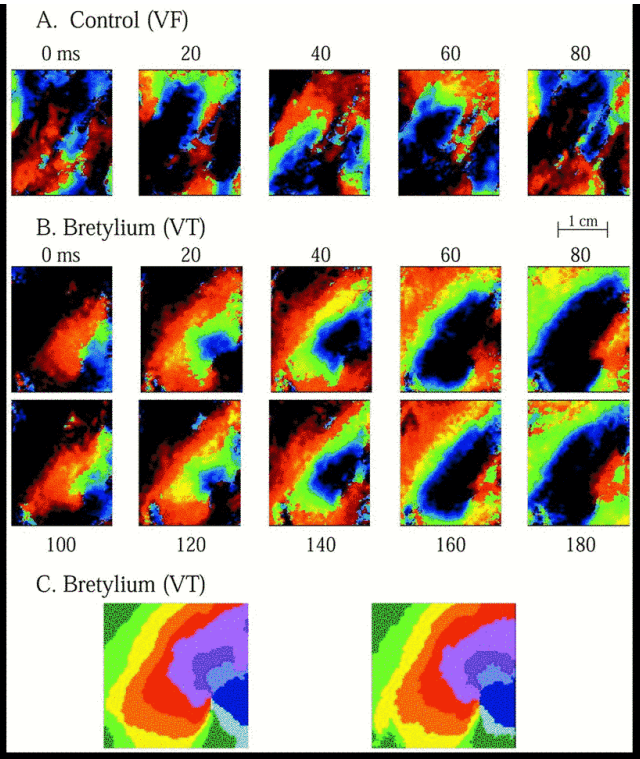
Na+ channel structure



Nature (2002)

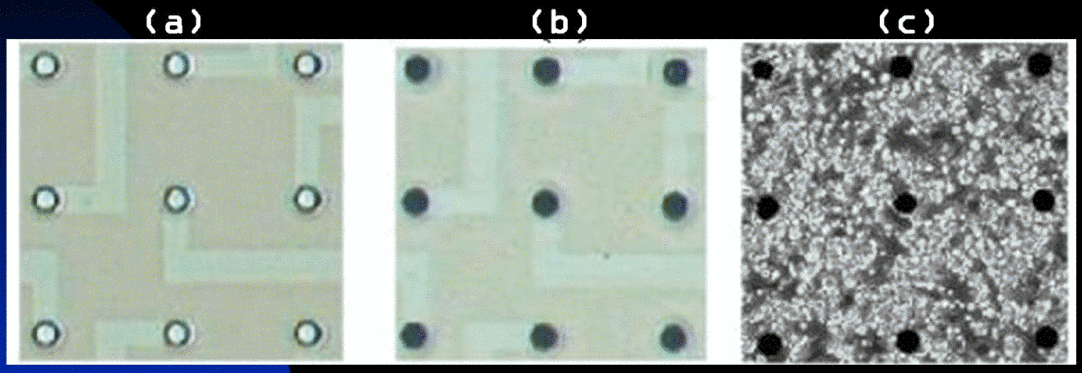
Images of VF & VT states in a slice preparation

Alan Garfinkel et al. *PNAS, USA*, 97, 6061 (2000)



Membrane potential dye: di-4-ANEPPS

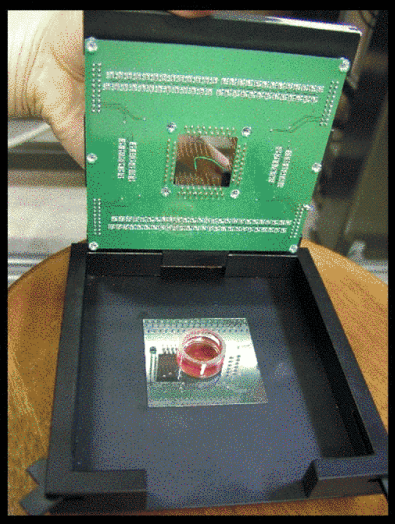
Cardiac cells on a multi-electrodes plate



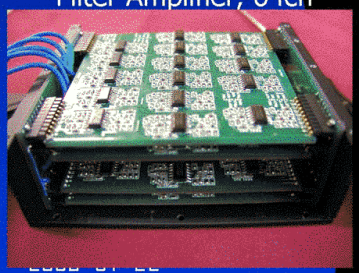
(a)ITO MEA : (electrode diameter 30μm, lattice constant 150μm), only 3 x 3 grids are shown.
(b)Platinized ITO MEA
(c)cultured cardiac cells on a platinized MEA.

Home-built multi-channel amplifying system

Pre Amplifier, 64ch

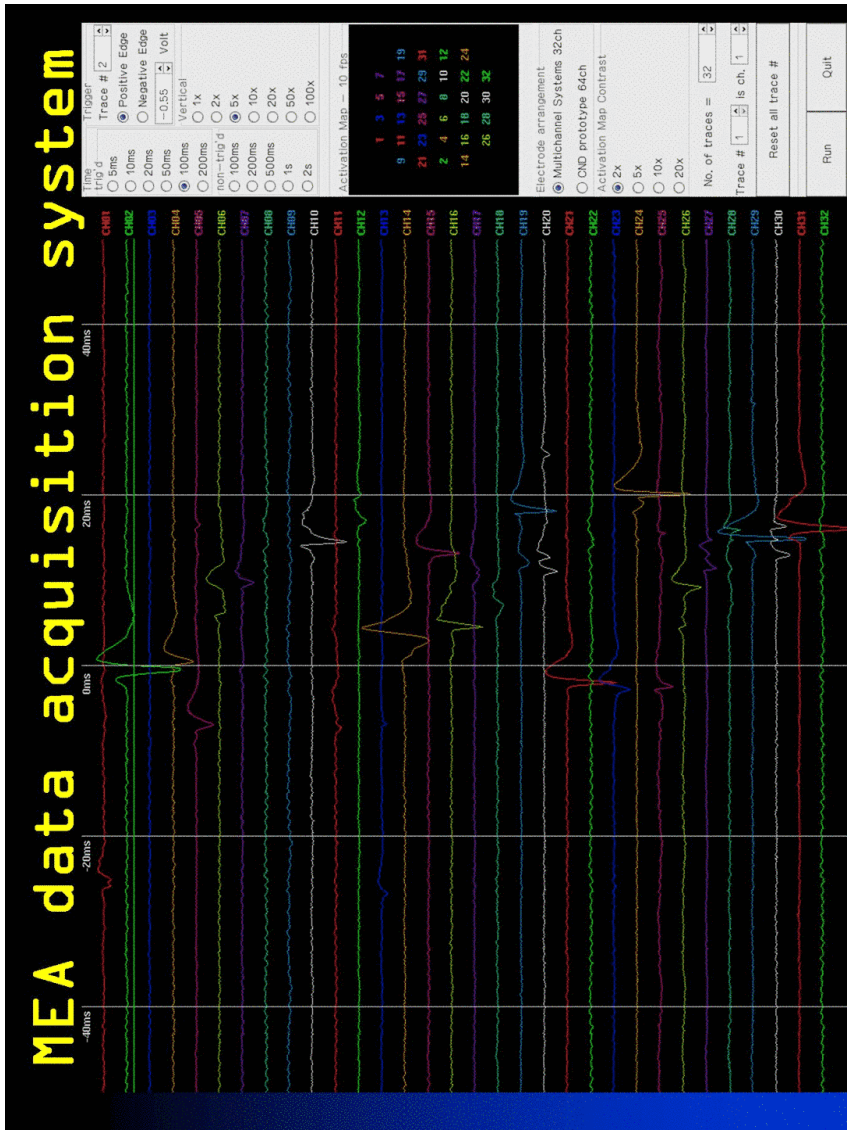


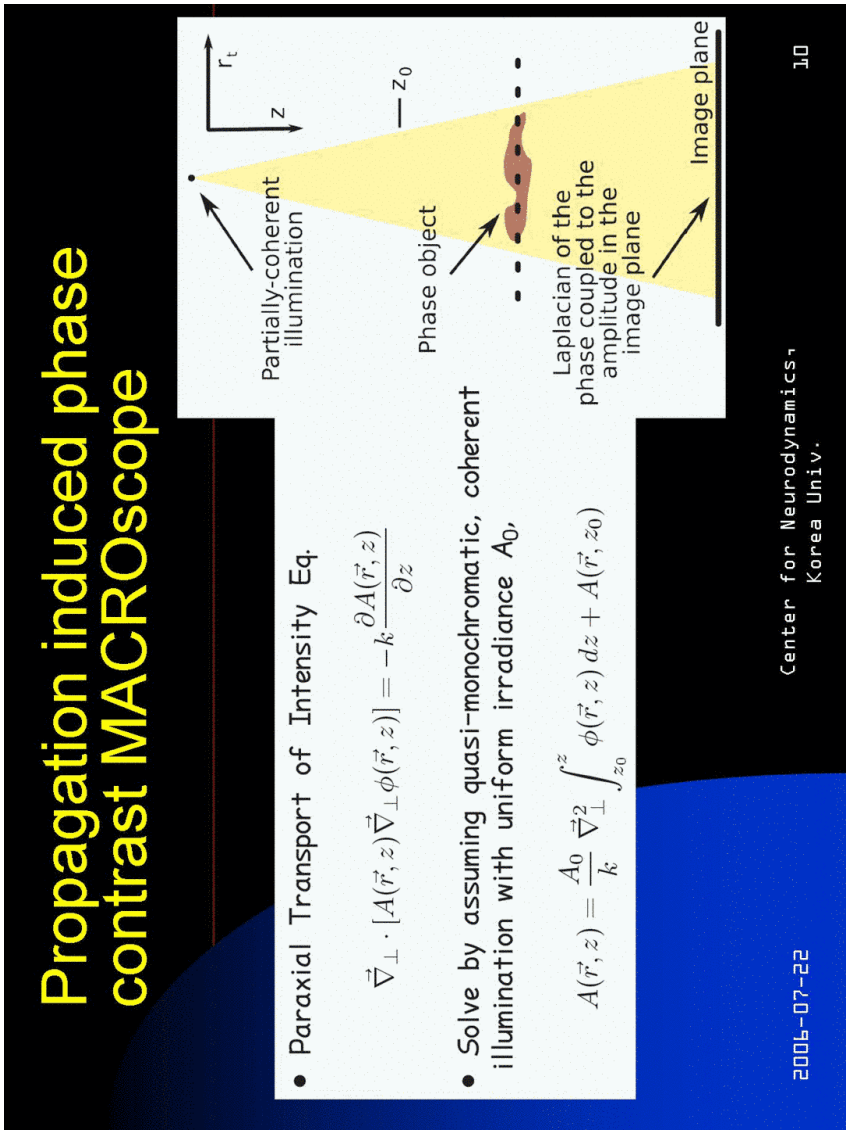
Filter Amplifier, 64ch



Pre Amplifier
- Differential Input, CMRR > 60dB
- Gain : 10 (at 900Hz)
- Filter : High pass @ 100Hz, 1 pole

Filter Amplifier
- Single-ended Input.
- Gain : 1000 (3 stages, each 10x (at 900Hz)
- Filter : Low pass @ 5kHz, 6 poles
  High pass @ 100Hz, 3 poles


MEA data acquisition system
-40ms
-20ms
0ms
20ms
40ms
Time
trig'd
Trace # 2
Positive Edge
Negative Edge
-0.55
Volt
Vertical
Activation Map – 10 fps
Electrode arrangement
Multichannel Systems 32ch
CMD prototype 64ch
Activation Map Contrast
No. of traces = 32
Trace # 1
is ch. 1
Reset all trace #
Run
Quit


Propagation induced phase contrast MACROscope
Paraxial Transport of Intensity Eq.
$\vec{\nabla}_\perp \cdot [A(\vec{r},z)\vec{\nabla}_\perp \phi(\vec{r},z)] = -k\frac{\partial A(\vec{r},z)}{\partial z}$
Solve by assuming quasi-monochromatic, coherent illumination with uniform irradiance A_0,
$A(\vec{r},z) = \frac{A_0}{k}\vec{\nabla}_\perp^2 \int_{z_0}^{z} \phi(\vec{r},z)\,dz + A(\vec{r},z_0)$
Partially-coherent illumination
Phase object
Laplacian of the phase coupled to the amplitude in the image plane
Image plane
r_t
z
z_0
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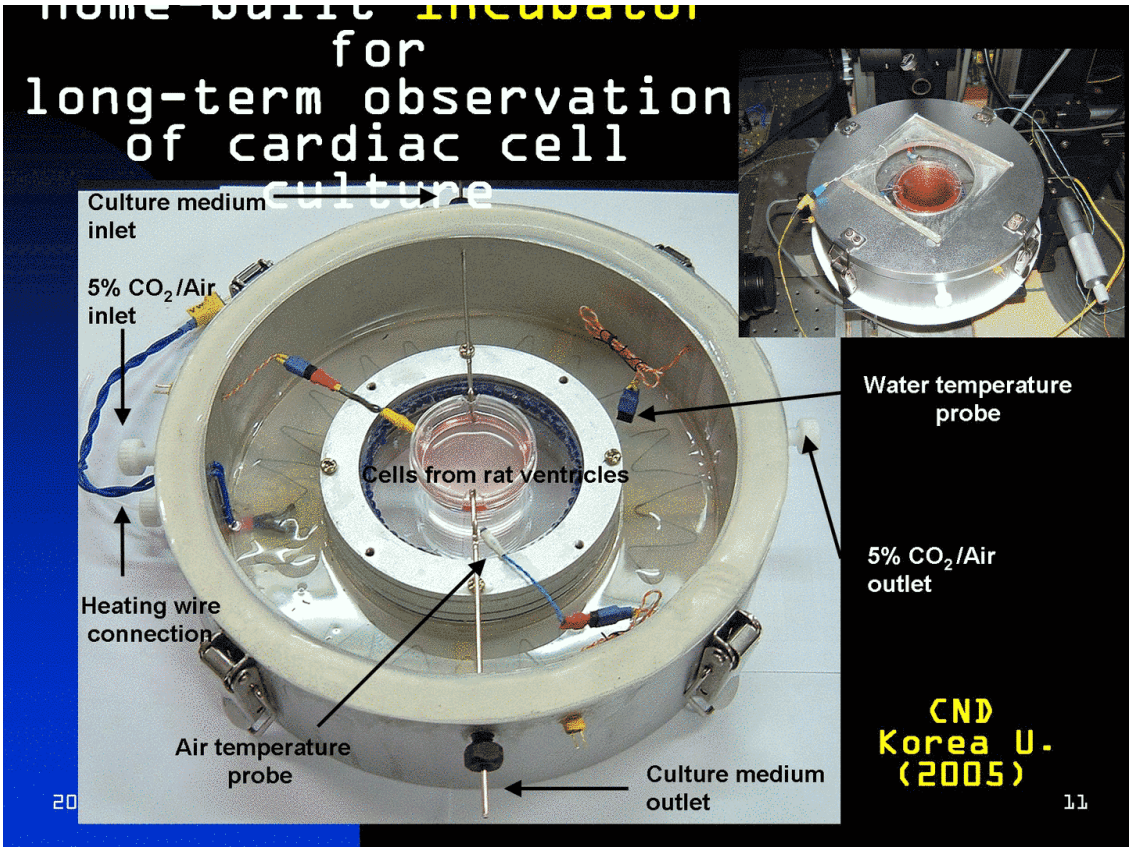
for
long-term observation
of cardiac cell
culture
Culture medium inlet
5% CO_2/Air inlet
Heating wire connection
Air temperature probe
Cells from rat ventricles
Water temperature probe
5% CO_2/Air outlet
Culture medium outlet
CND
Korea U.
(2005)
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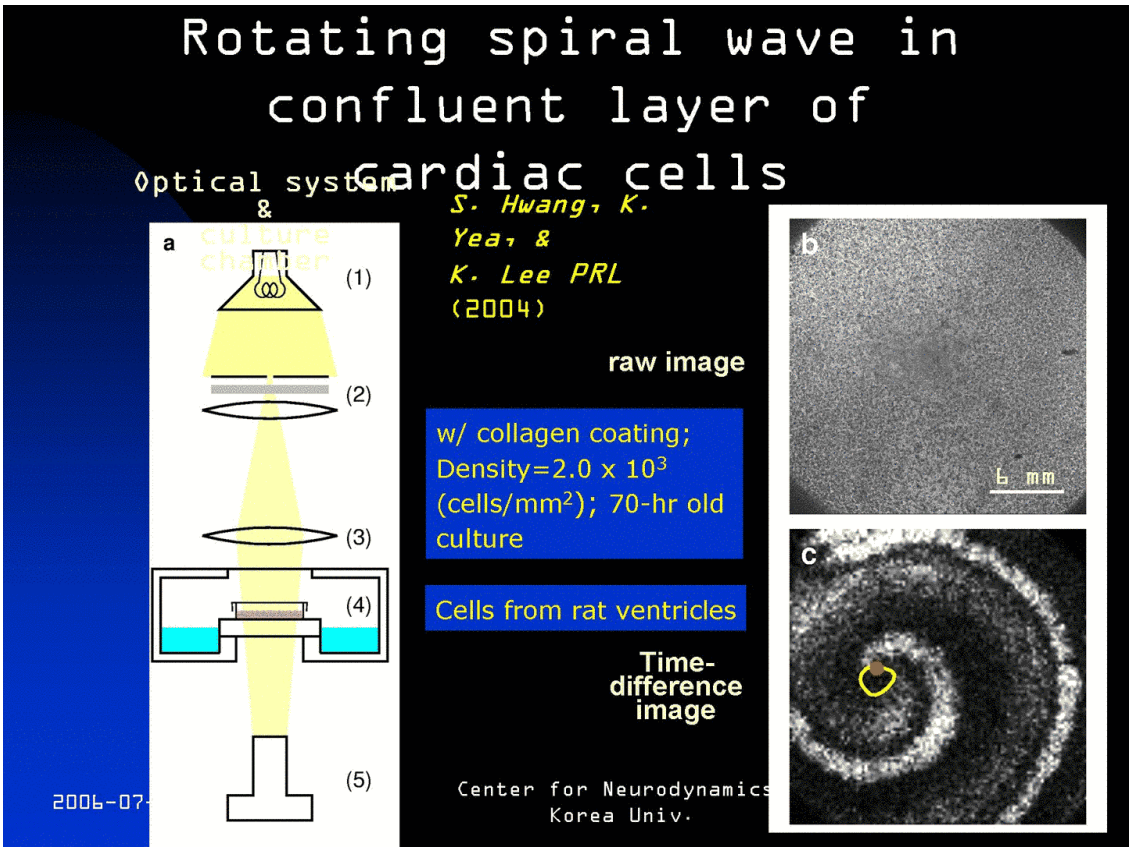
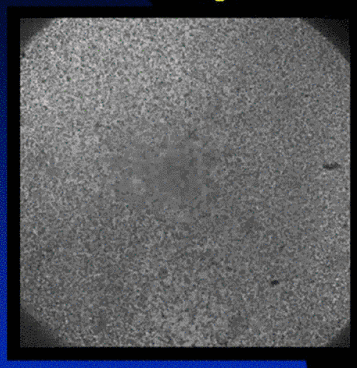
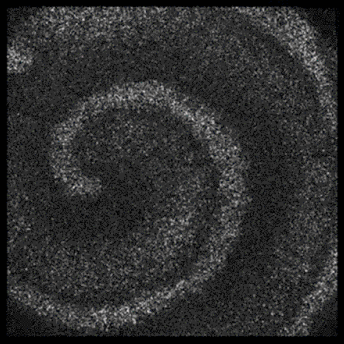

Rotating spiral wave in confluent layer of cardiac cells
Optical system & culture chamber
a
(1)
(2)
(3)
(4)
(5)
S. Hwang, K. Yea, & K. Lee PRL (2004)
raw image
w/ collagen coating; Density=2.0 x 10^3 (cells/mm^2); 70-hr old culture
Cells from rat ventricles
Time-difference image
b
6 mm
c
Center for Neurodynamics
Korea Univ.

Regular cardiac spiral wave

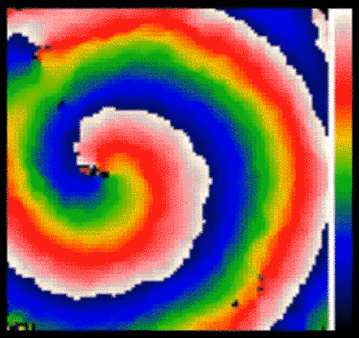
Raw image

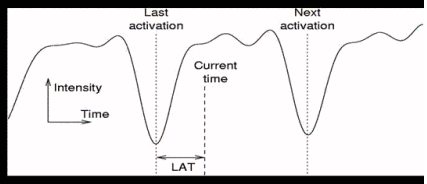


Time-diff. image



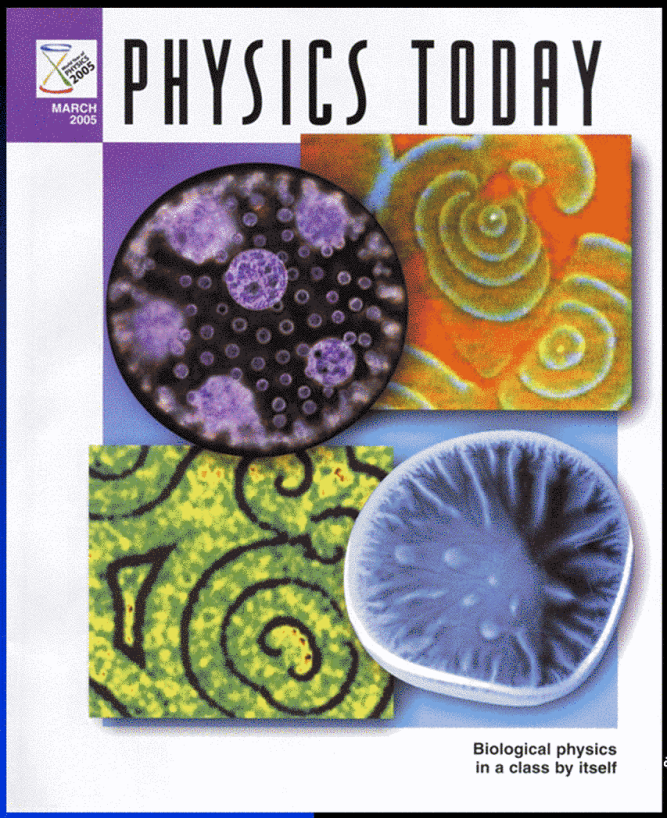
LAT image





Local Activation Time:

$LAT(t) = t - t_n$



Spiral waves are ubiquitous & (some of) their properties are very common!

A pair of period-2 oscillatory spiral waves in BZ EXPERIMENT

J. Park and K. Lee, *PRL 83*, 5393 (1999)

Disk diameter:

20 mm

One-side fed gel reactor:

0.89 M H_2SO_4,

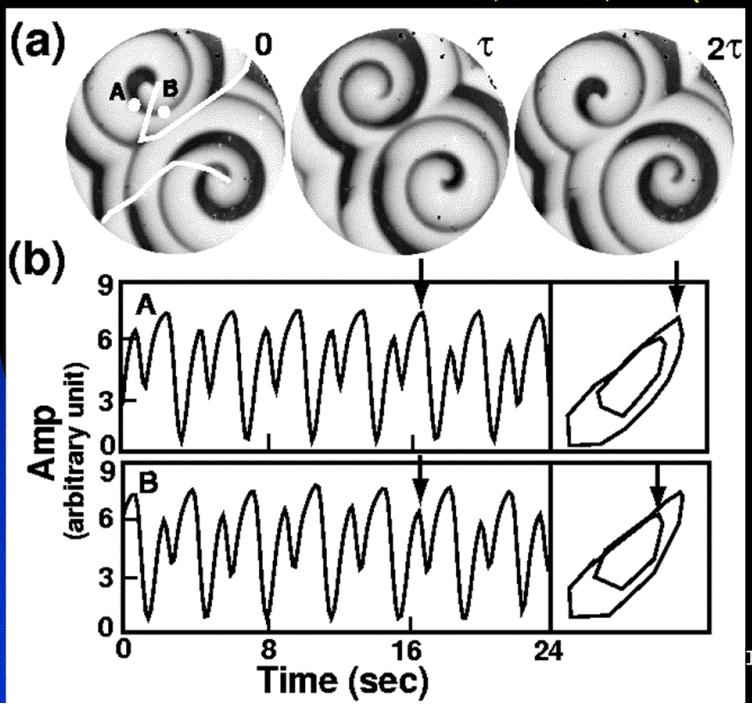
0.06 M $KBrO_3$,

0.27 M melonic acid,

2.5 M ferroin,

0.1 mM NaBr,

0.1 mM SDS



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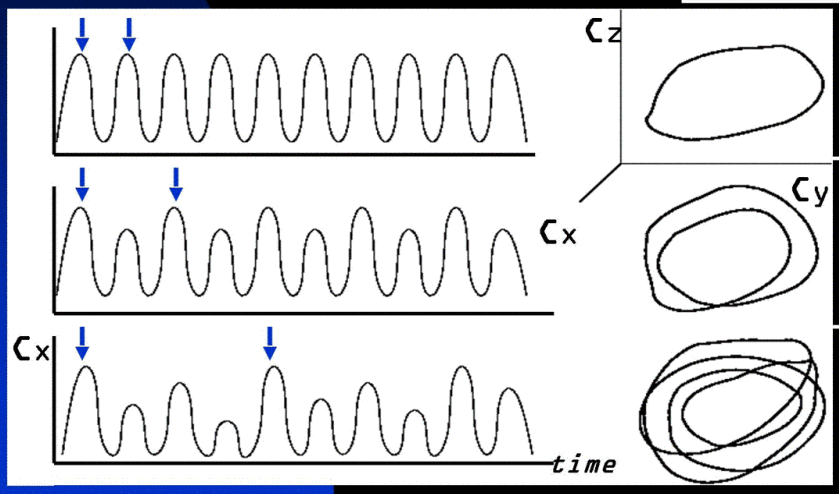
Complex-periodic oscillations in a Roessler system

$$\dot{C}_x = -C_y - C_z$$
$$\dot{C}_y = C_x + A C_y$$
$$\dot{C}_z = C_z C_x - C C_z + B$$



period-1 cycle ($C=C_1$)

period-2 cycle ($C=C_2$)

period-4 cycle ($C=C_3$)

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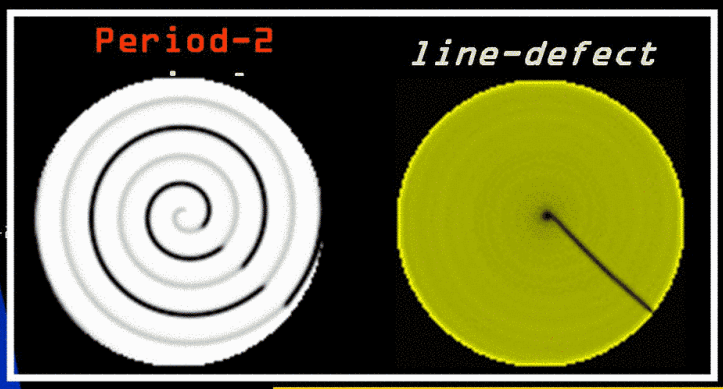
Period-2 spiral wave with one *line-defect* in a Rössler system

Parameters:
A=0.2,
B=0.2,
C=3.84,
$D\Delta t/(\Delta r)^2=1.6\times10^{-1}$



$$V(x,t)=\frac{1}{\tau}\int_0^{\tau}[G(x,t+t')-G(x,t+t'-\tau)]dt'$$

[References]
Goryachev et al., *Chaos* 10 (2000); PRL(1999), PRL(1998), PRL(1996)

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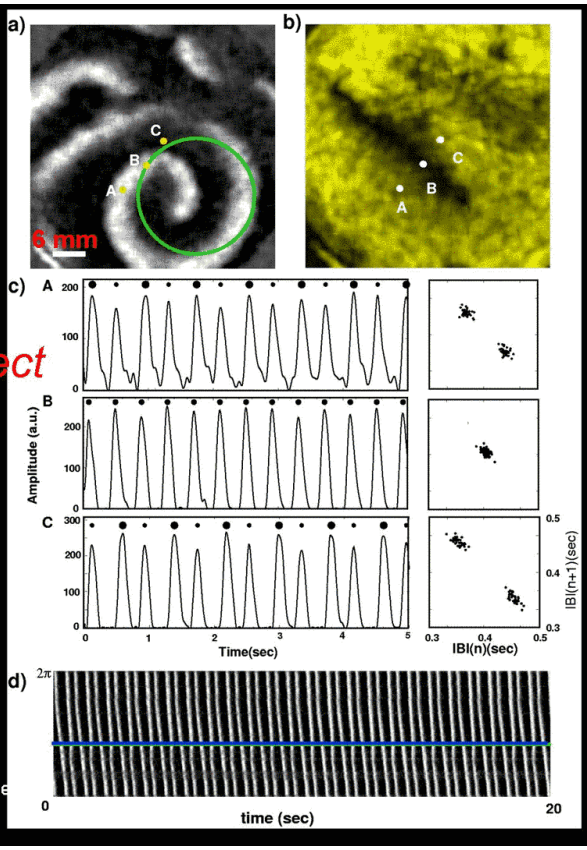
Would these complex spiral wave phenomena mean anything to a real cardiac system?

P-2 oscillatory cardiac spiral wave having a *static line defect*

125 hr *in vitro*



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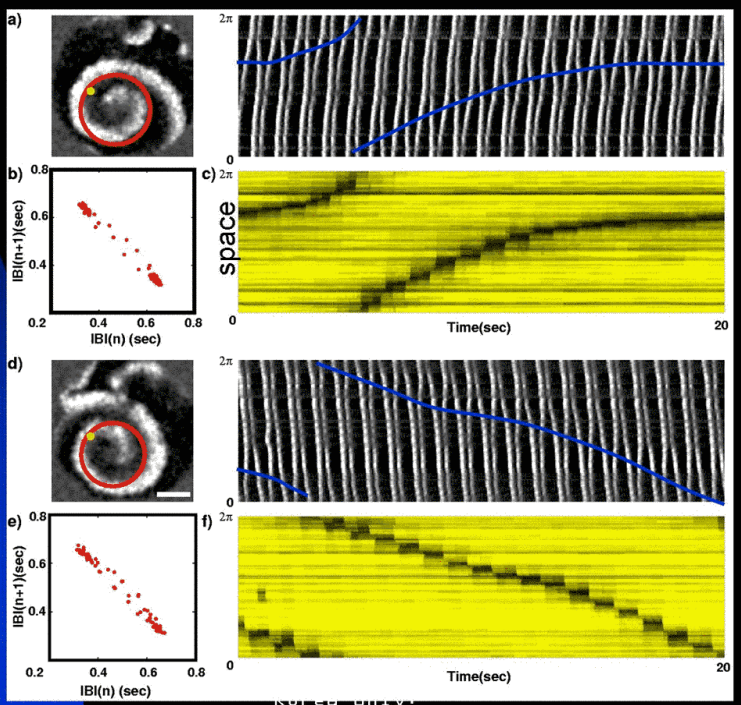
Slowly rotating line-defect

114 hr *in vitro*

30 min later



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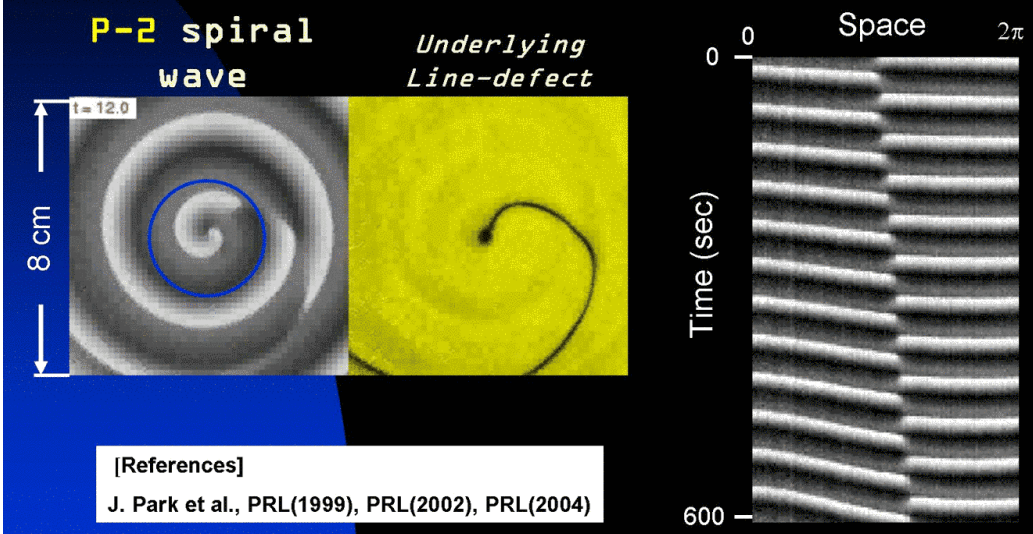
Period-2 oscillatory spiral wave in a BZ reaction-diffusion system



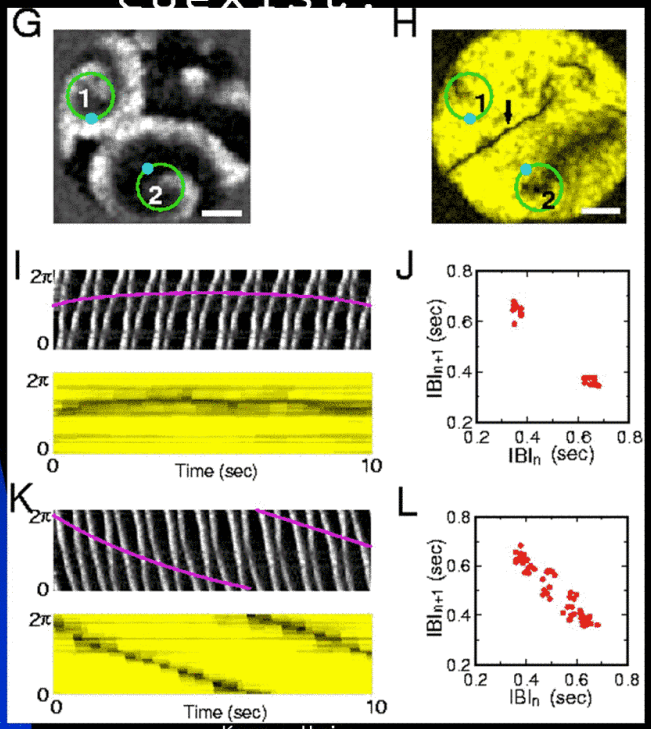
[References]

J. Park et al., PRL(1999), PRL(2002), PRL(2004)

Two different types can coexist!

having *a static line defect*

having *a rotating line defect*



Can the individual cardiac myocytes be a P-2 oscillator

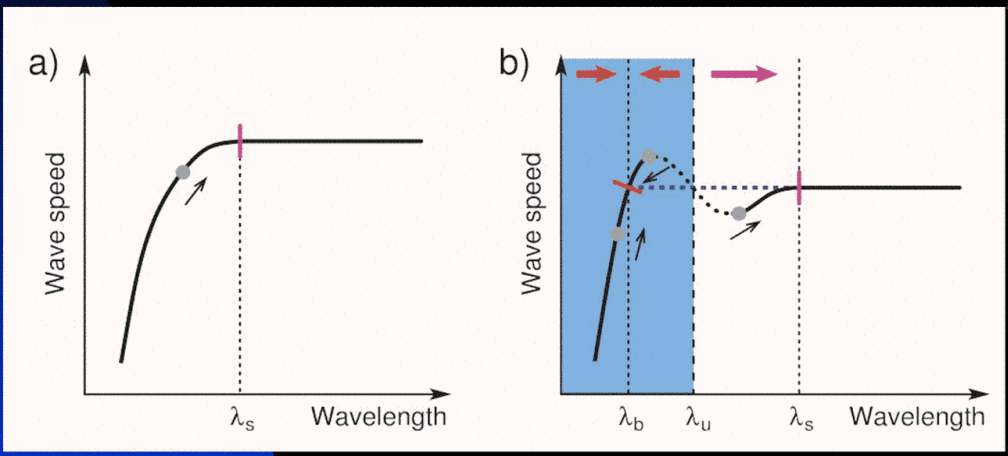
1) with pacing ?

→ Yes! (Dr. Shiferaw & Zhao's talks)

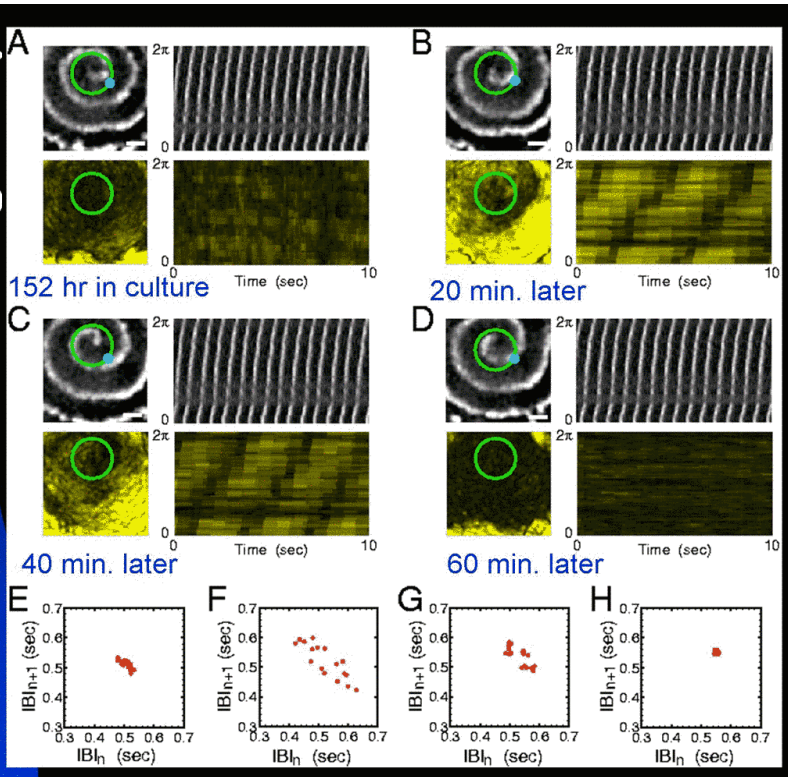
2) without pacing (i.e., spontaneously)?

→ Yes!

Non-monotonic Dispersion Curve



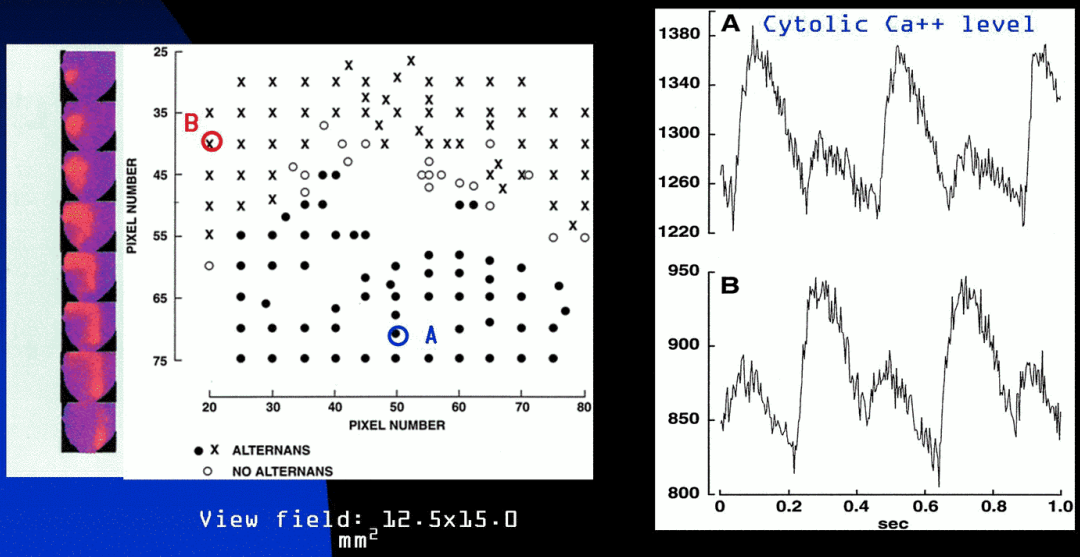
Near a P-1 to P-2 transition



Would these phenomena mean anything to cardiologists?

Discordant alternans in a rabbit heart in ischemia

Clusin et al., Circulation 104, 2082 (2001)



View field: 12.5x15.0 mm^2

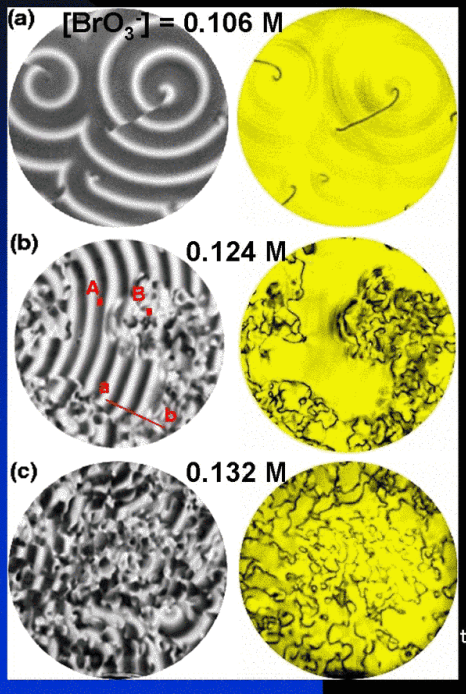
Significance of P-2 oscillatory spiral waves

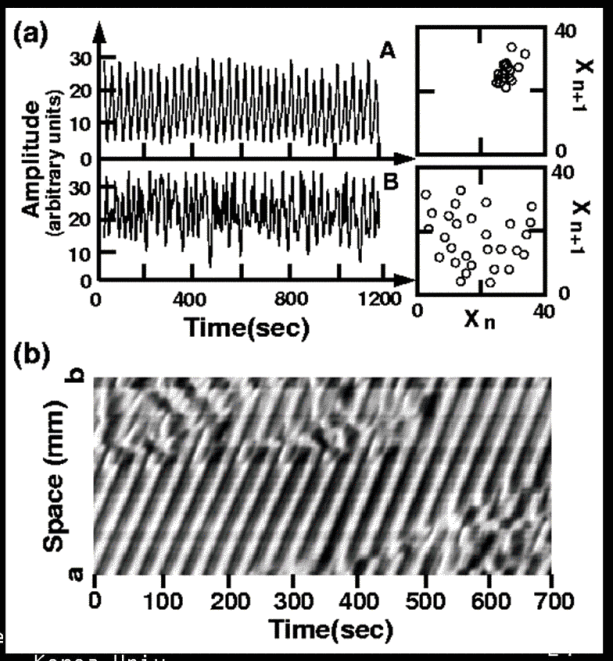
Clusin's review paper, Crit. Rev. Clin. Lab. Sci. 2003, 40(3):337-375, Calcium and Cardiac Arrhythmias: DADs, EADs, and Alternans

V. ACTION POTENTIAL DURATION ALTERNANS DURING ISCHEMIA*

Particularly important advances in cardiac cellular electrophysiology in the last few years involve the elucidation of the mechanisms of ventricular fibrillation (VF) during acute myocardial ischemia. The onset of VF during coronary occlusion is known to be preceded by beat-to-beat variation in the amplitude of the electrocardiographic T-wave. This observation was first made in 1950,[39] and in 1977 high-quality recordings were obtained of the transmembrane action potential in pig hearts with floating microelectrodes, which showed that after about 3 min of ischemia there is beat-to-beat fluctuation in the duration of the cardiac action potential,[40] which can occur with very little variation in action potential amplitude (Figure 2). This fluctuation in action potential duration produces dispersion of refractoriness that would cause degeneration of a rapid ectopic or reentrant arrhythmia (e.g., a rotor) into VF.[41]

Transition to a line-defect mediated "turbulent" state (BZ experiment)





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Complex-periodic oscillations driven by a meandering spiral core

S. Hwang, T. Kim & K. Lee, PNAS (cover story in physiology section, 2005)

5 Days in Vitro

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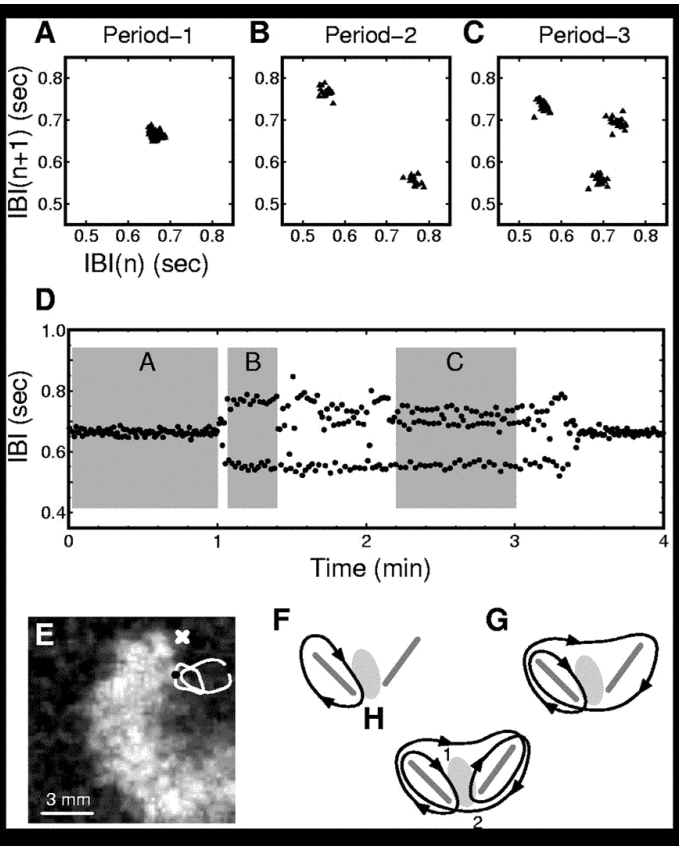
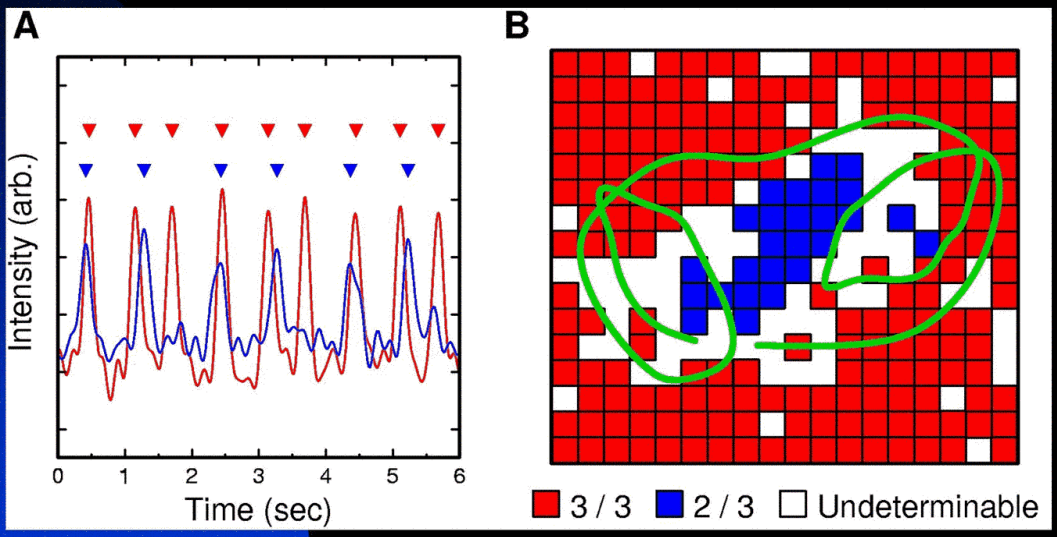


Identification of Partial Conduction Block



Samulnori

(a traditional Korean dancing performance)

Summary

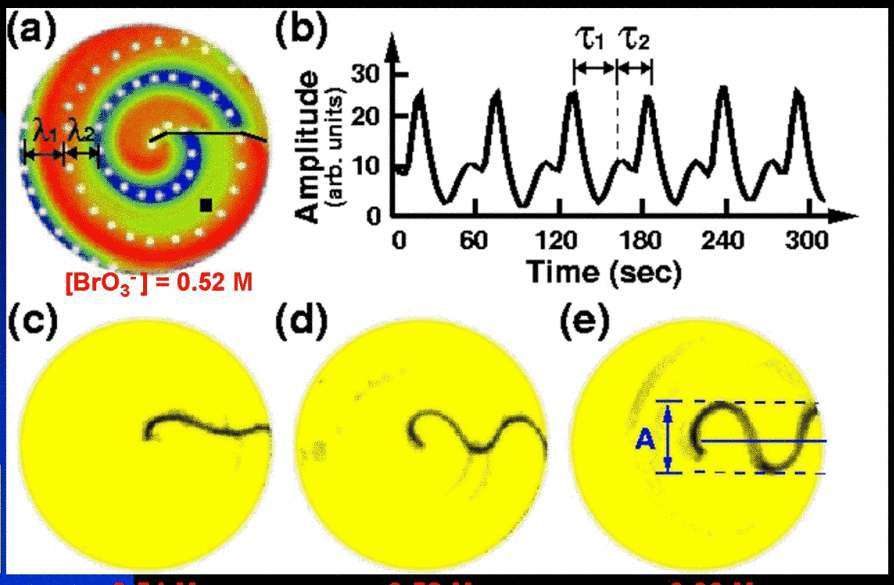
- Alternans can be viewed as a temporal (ECG) manifestation of period-2 oscillatory spiral waves.
- Line defects are a very general feature of any period-2 oscillatory media.
- Localized defects (infarcts) can generate various rhythms [cover story (physiology), PNAS 2005].
- "Line defect-mediated" spatiotemporal chaos is a plausible passway to cardiac fibrillation.
- Various pharmacological studies can

Transverse instability of *line-defect*

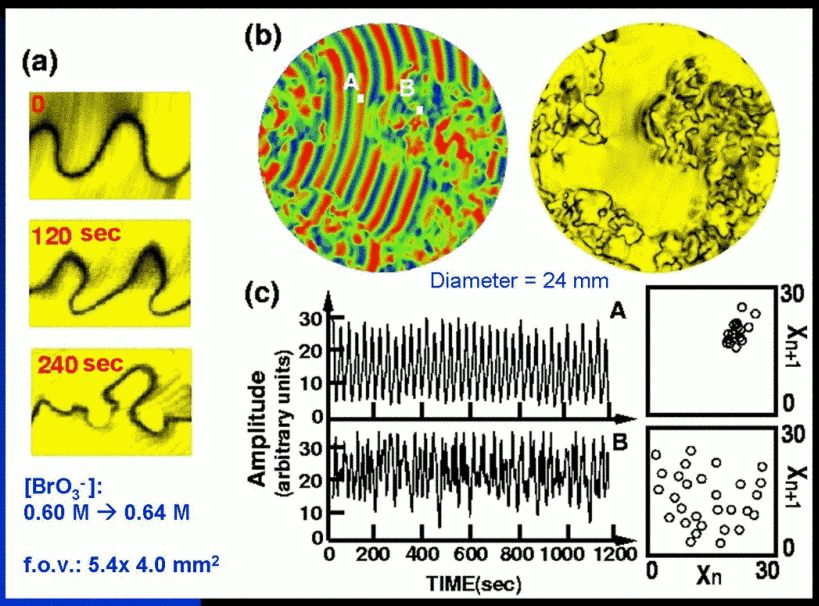
Diameter: 5.6 mm

Two-side fed reactor:
SIDE A
0.90 M H_2SO_4,
0.50 – 0.64 M $KBrO_3$,
SIDE B
0.53 M MA,
2.5 M ferroin,
0.1 mM NaBr,
0.1 mM SDS

Flow rate = 120 ml/hr,
Volume = 10 ml,
Temp 22 °C



Line-defect proliferation & turbulent patch formation



Long-term wave activity of a layer of cultured cardiac cells