Systems Biology Across Scales: A Personal View
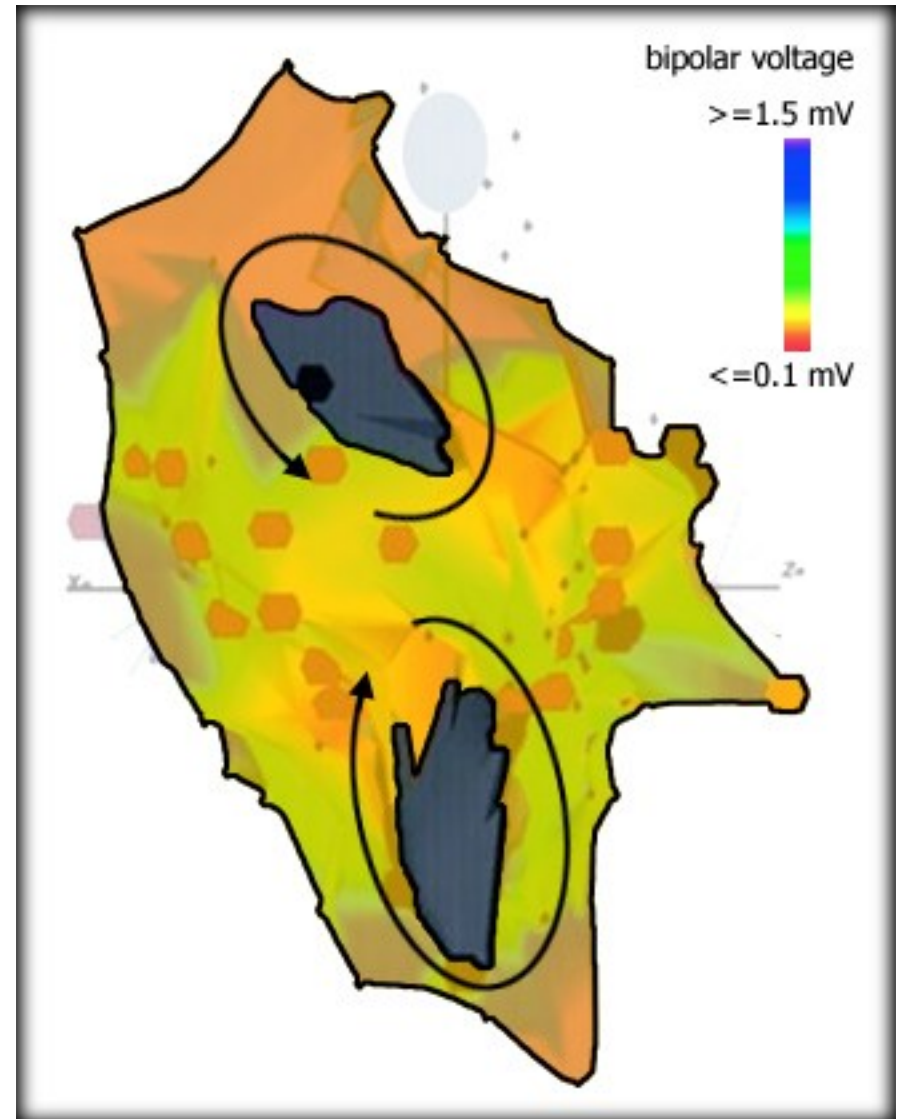# XXVIII. Waves in disordered excitable media

Sitabhra Sinha

IMSc Chennai

Disorder induces creation of spiral waves

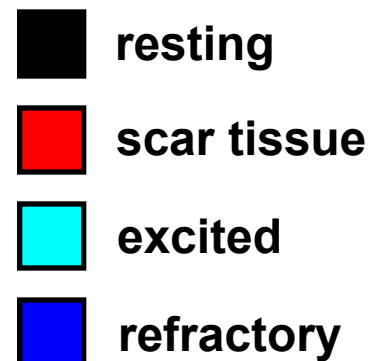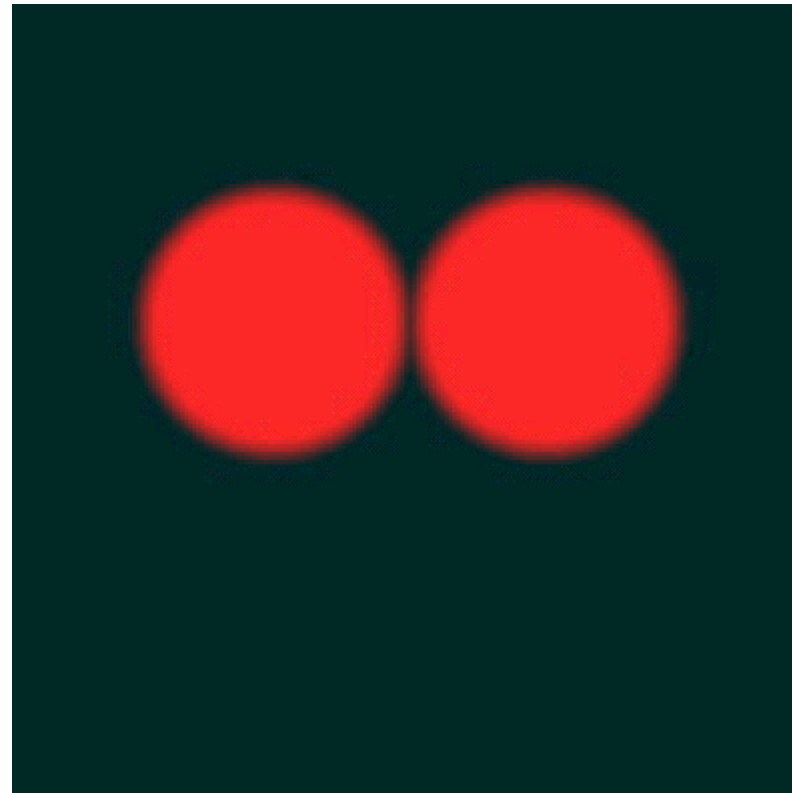- Sustained tachycardia because of *reentry* around pre-existing scar tissue

Reentry: self-sustaining feedback loop of excitation

- Clinically manifested as tachycardia

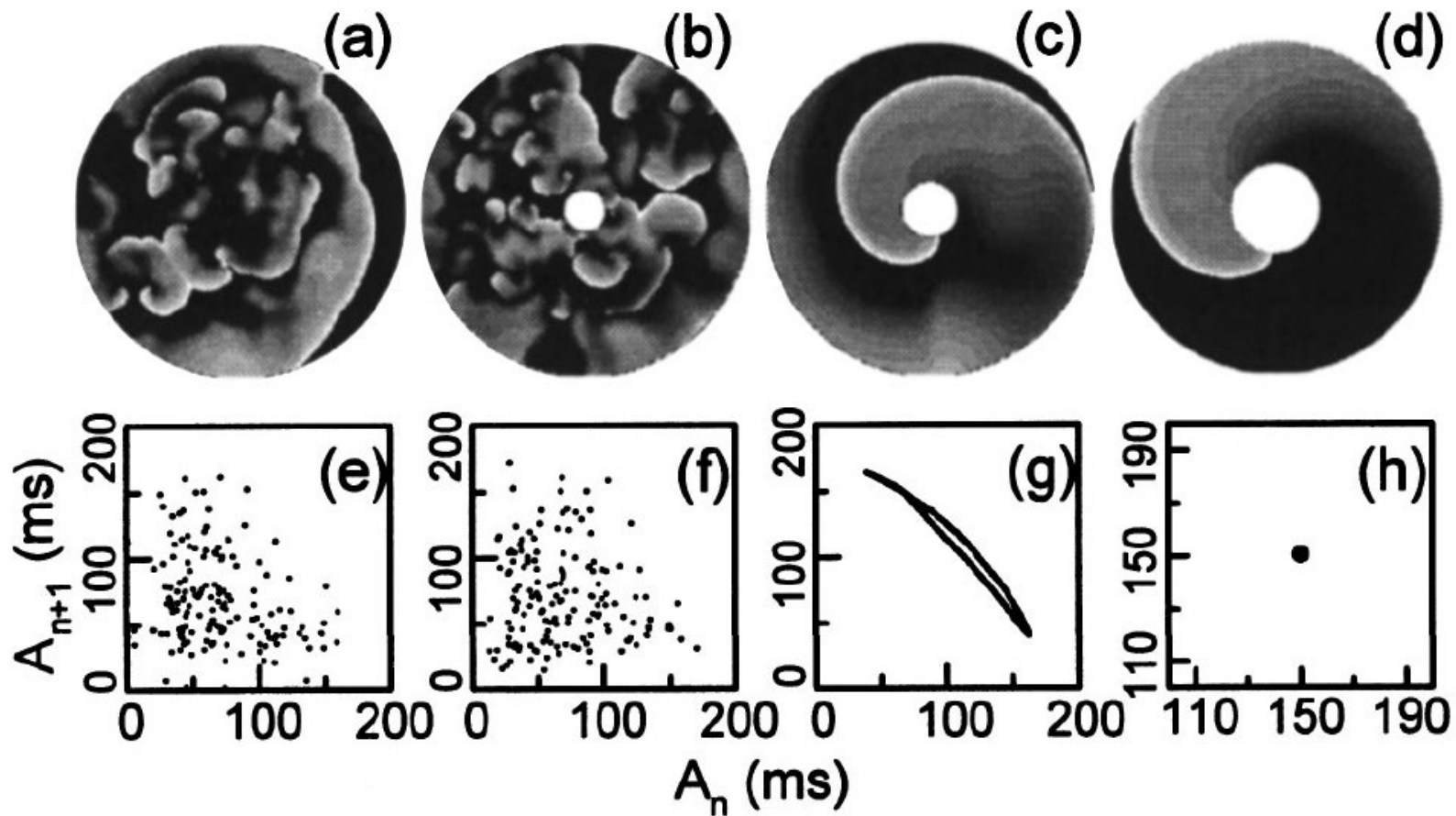- First exptly shown by G R Mines (1913)

bipolar voltage
>=1.5 mV

<=0.1 mV

biosense measurement

Creation of pinned reentrant waves around disorder (scar tissue)

Movie: Onset of reentry in Panfilov Model

- ■ resting
- ■ scar tissue
- ■ excited
- ■ refractory

Role of structural disorder:
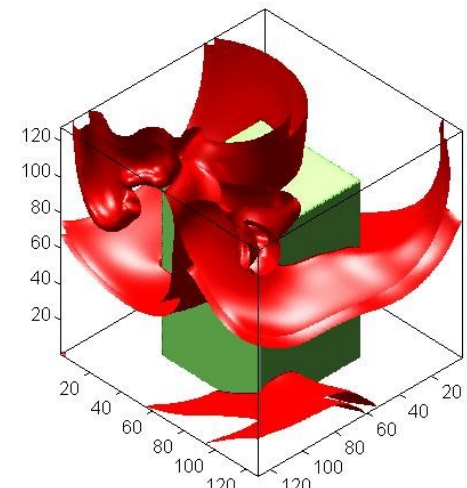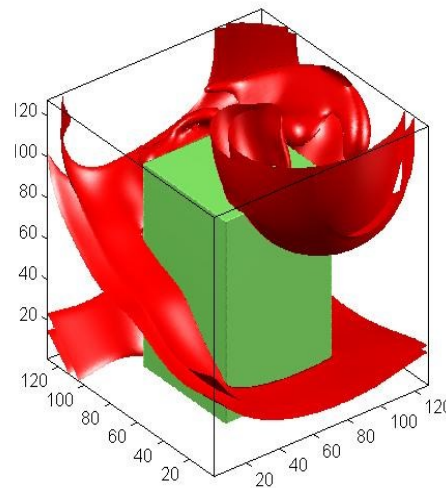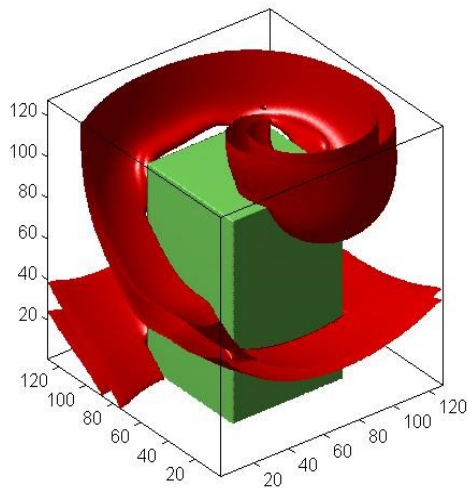# Transition from spatiotemporal chaos to pinned rotating wave

Investigating the role of defects on the propagation of electrical activity

Obstacles may prevent *breakup* of spiral waves…
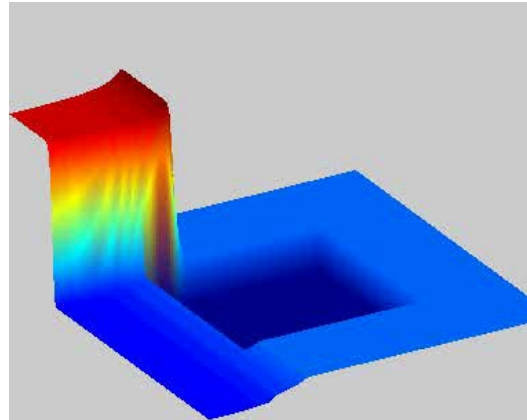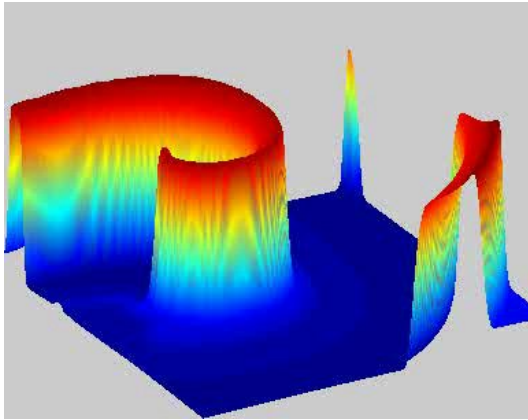
… on the other hand, we have seen *purely* disorder induced breakup of spiral waves in 3-D models of cardiac tissue
[S Sridhar, A Ghosh & SS, *EPL*, 2013]

In fact…
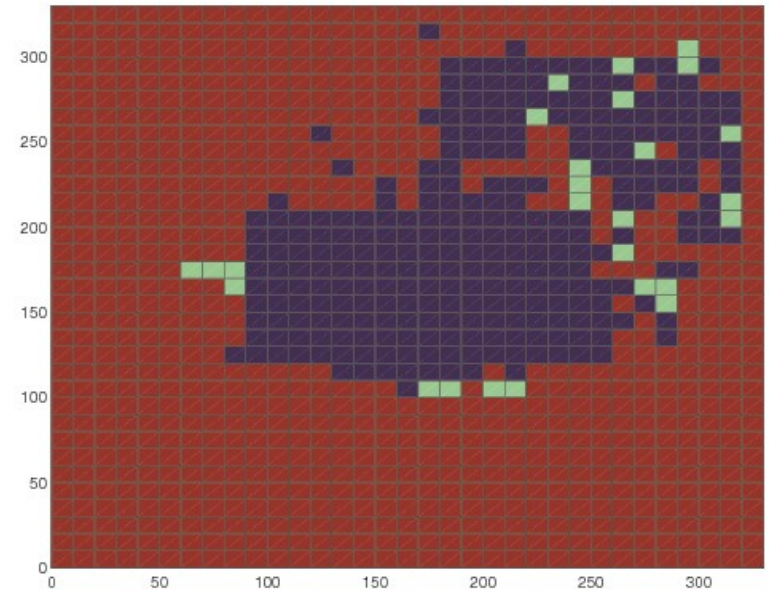## Sensitive dependence on position & size of disorder
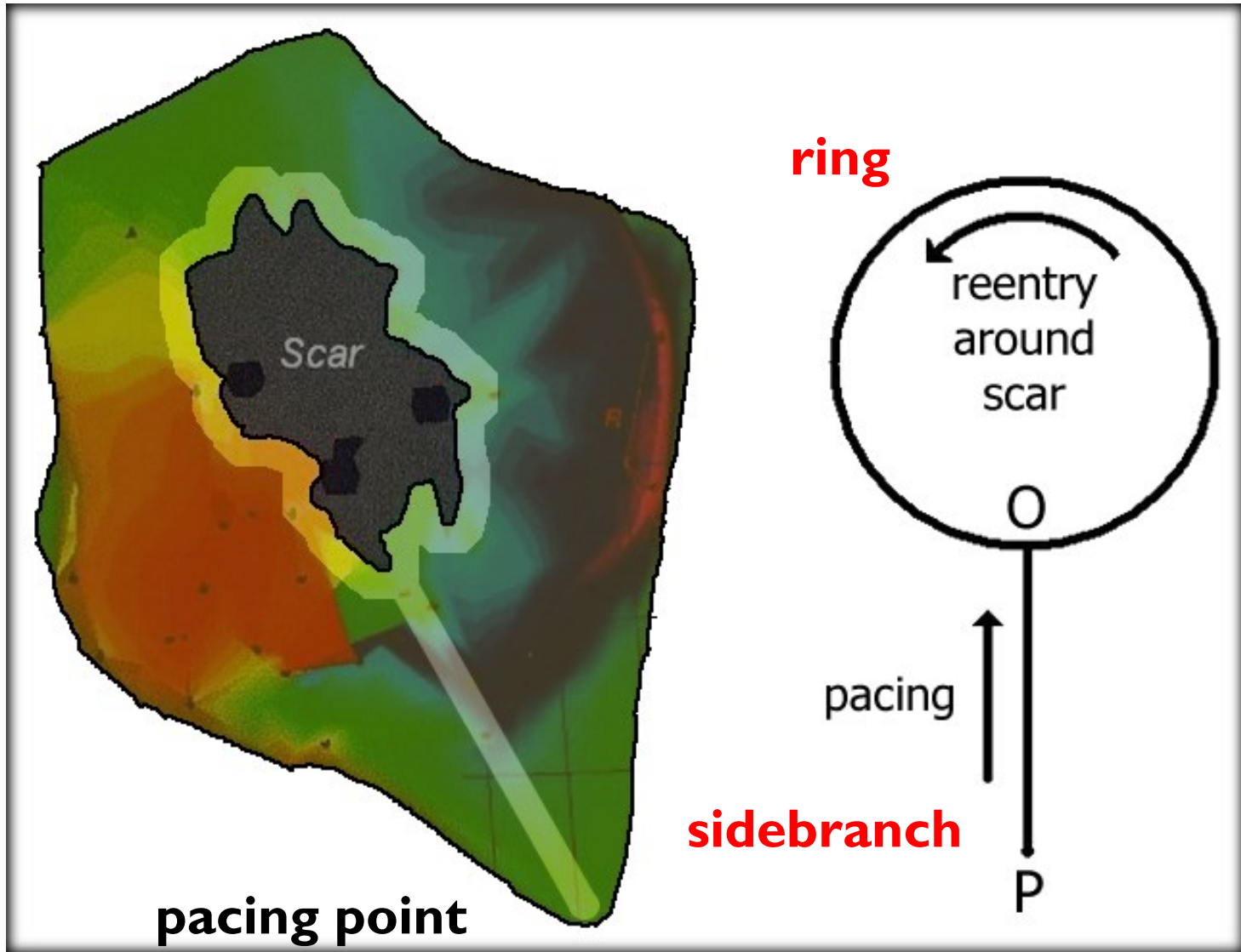

Pinned spiral

Termination of activity

Spatiotemporal chaos

Shajahan, Sinha & Pandit, *Phys Rev E*, 75, 011929 (2007)

Reentry in a one dimensional ring

ring

reentry
around
scar

O

pacing

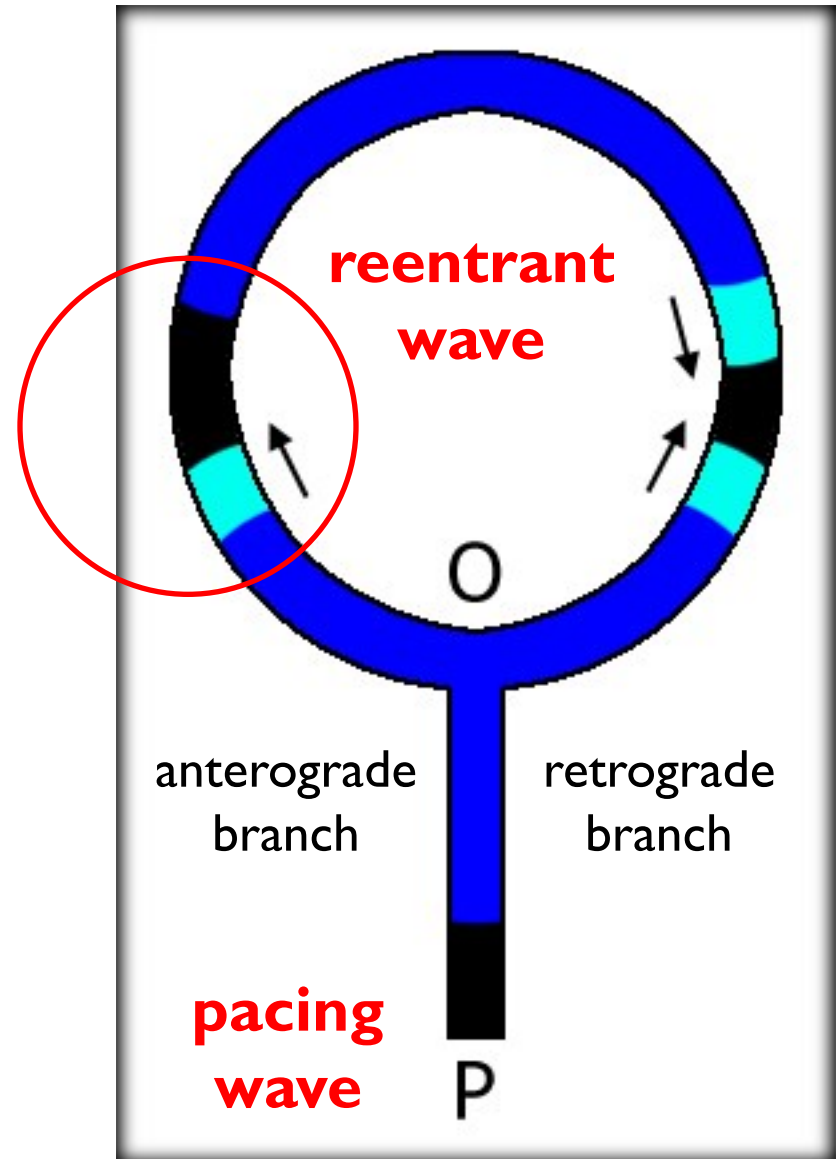sidebranch

P

Scar

pacing point

Effect of pacing on the reentry

Reentrant wave and pacing wave collide in sidebranch

Anterograde branch forms new reentrant wave

Termination of reentry not possible?

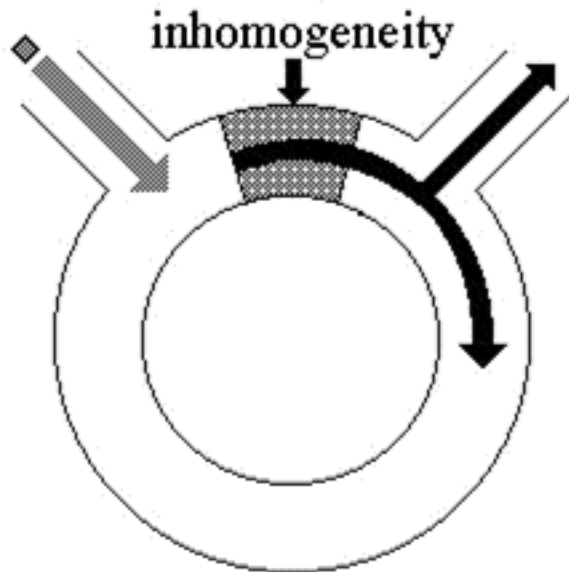**Interaction between wave front and wave back**

Termination of reentry occurs by *conduction block in the anterograde branch*

The Critical Role of Disorder

Termination of reentry occurs by
conduction block in the anterograde branch

...requires inhomogeneity in the reentry circuit !

If inhomogeneity exists in circuit waves travel faster or slower depending on location in the circuit.

So, stimulus may encounter a region that is still refractory.

Leads to block of the anterograde branch of the stimulus $\Rightarrow$ *successful termination*.

S S & D J Christini, *PRE* 66 (2002) 061903
SS, K M Stein & D J Christini, *Chaos* 12 (2002) 893

However…

… the nonlinear dynamics of wave propagation in cardiac tissue can spontaneously generate disorder even in a homogeneous medium
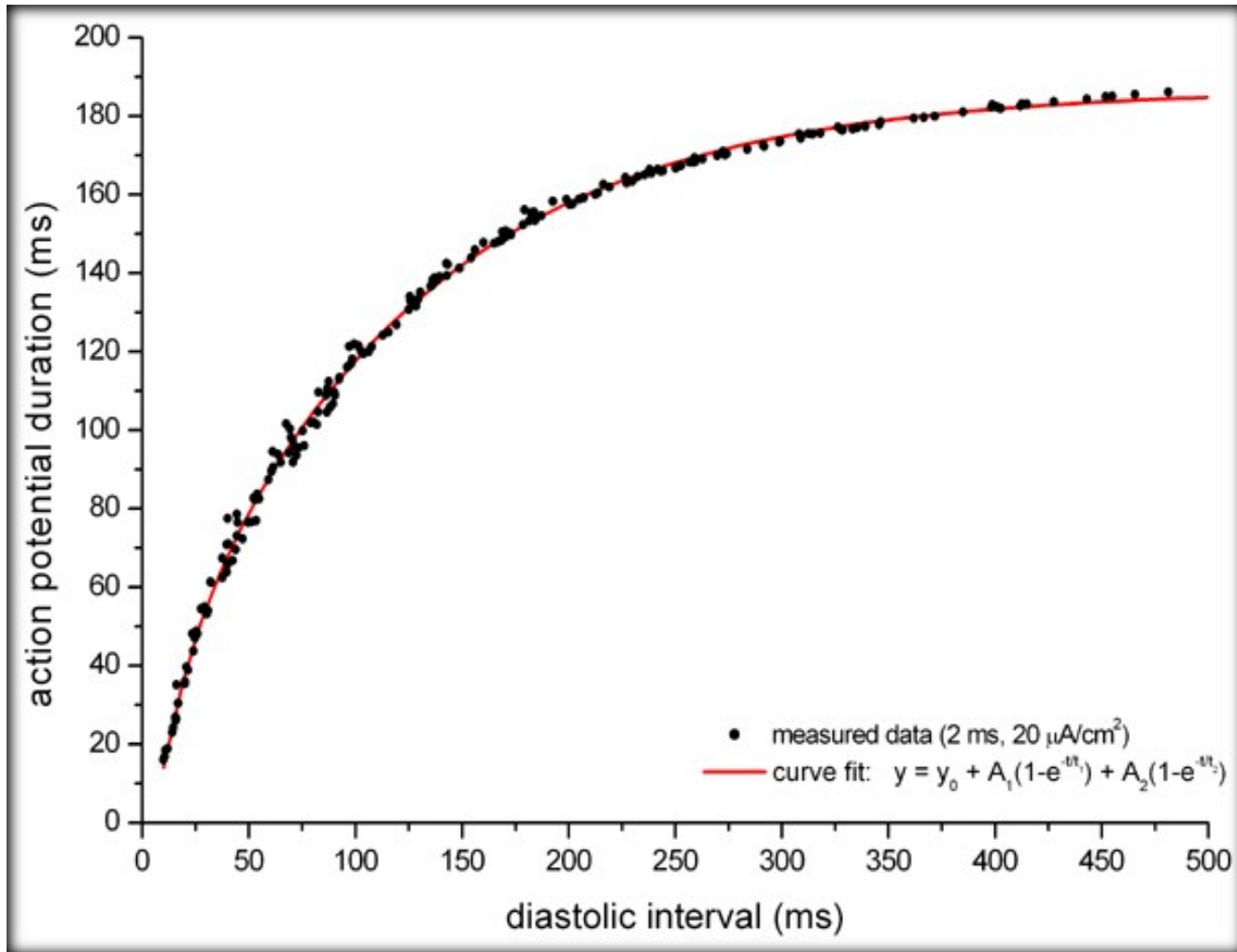
The restitution effect
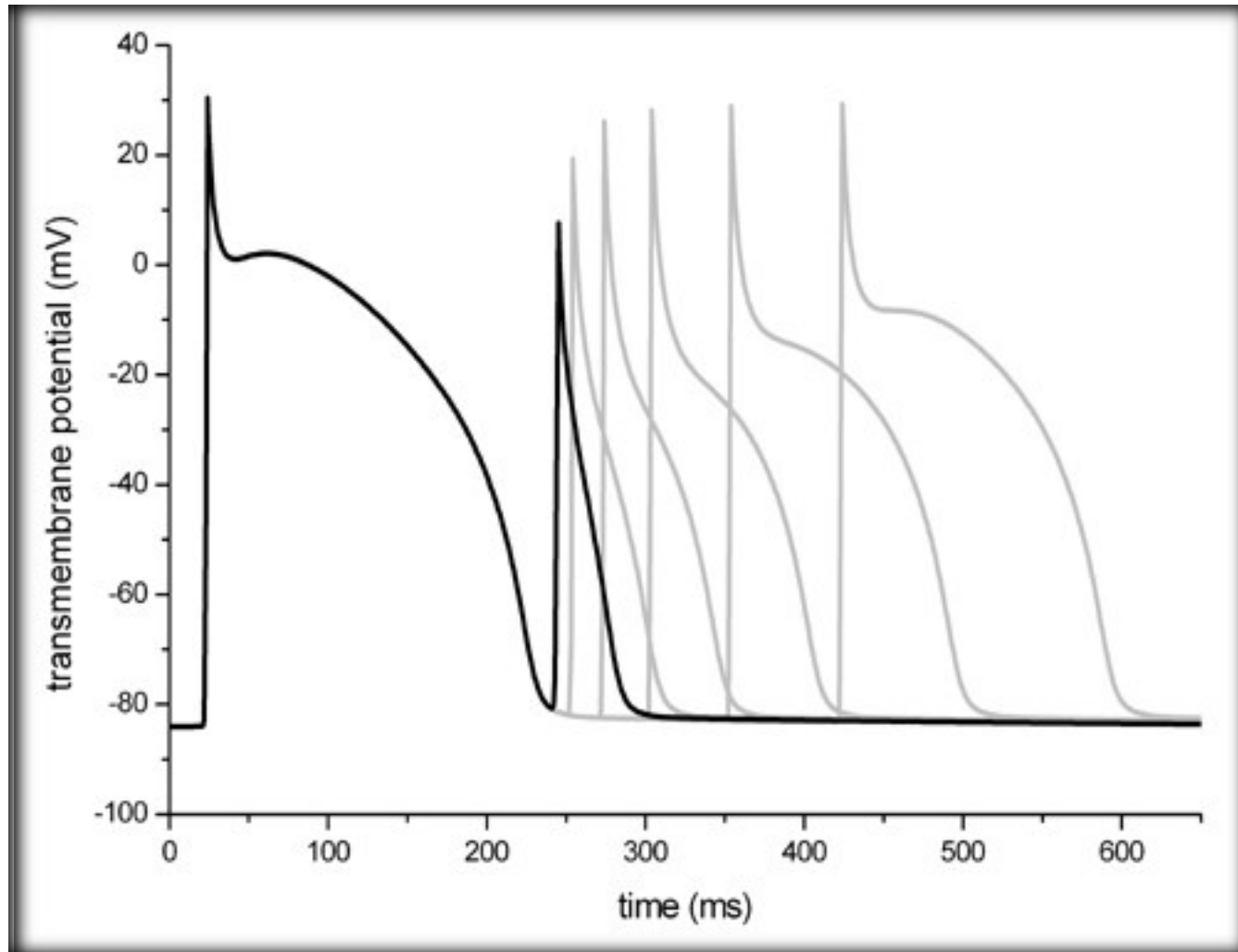
restitution in Luo-Rudy Model

APD is dependent on preceding DI

No excitation if DI below a critical value
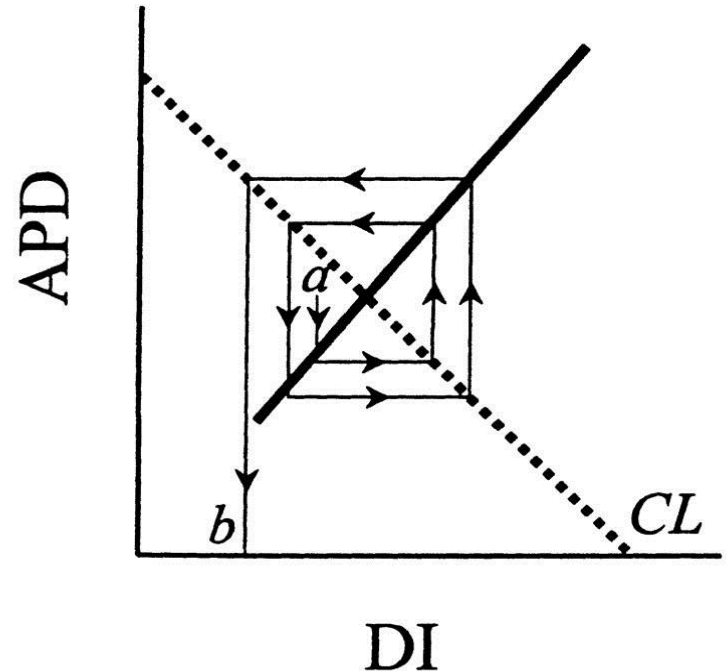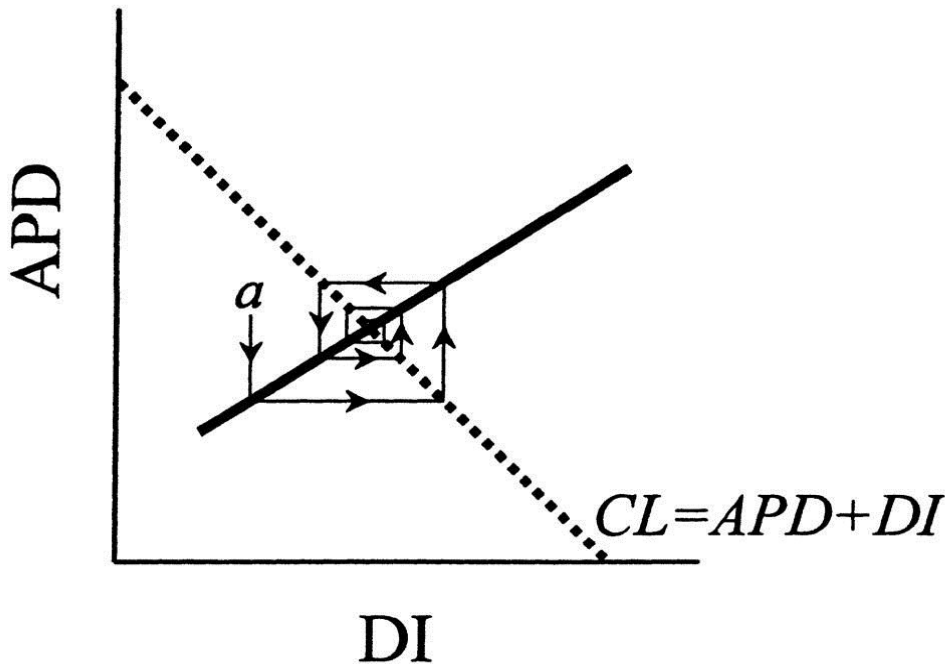
The restitution function

restitution curve in Luo-Rudy Model

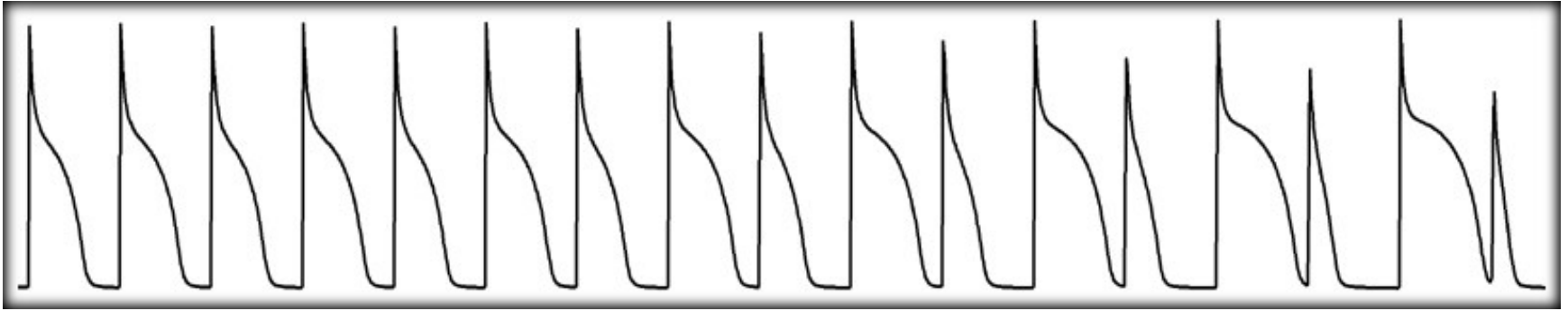$$APD_{n+1} = f(DI_n)$$

Alternans

APD restitution slope<1

APD restitution slope>1
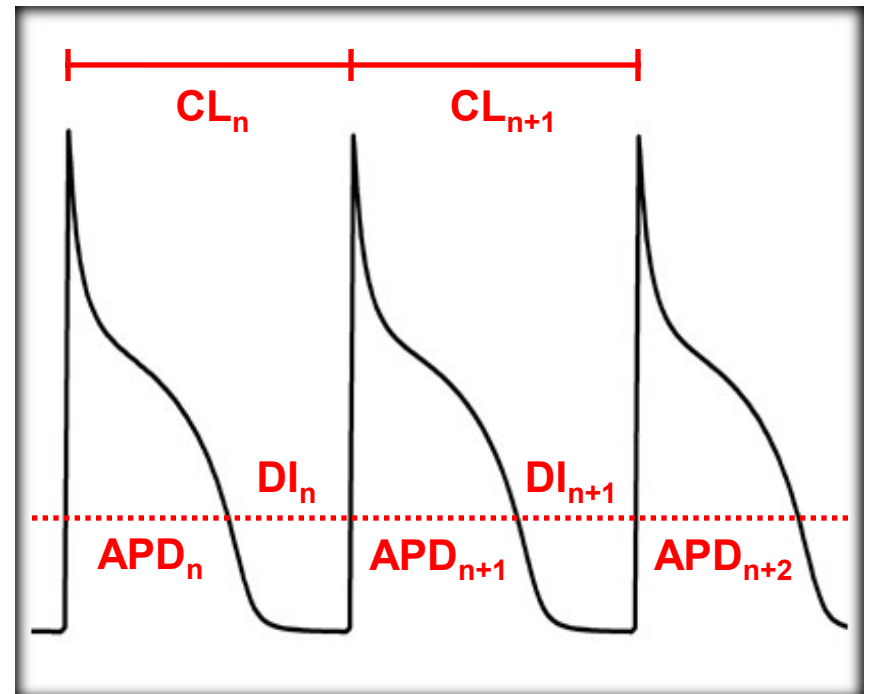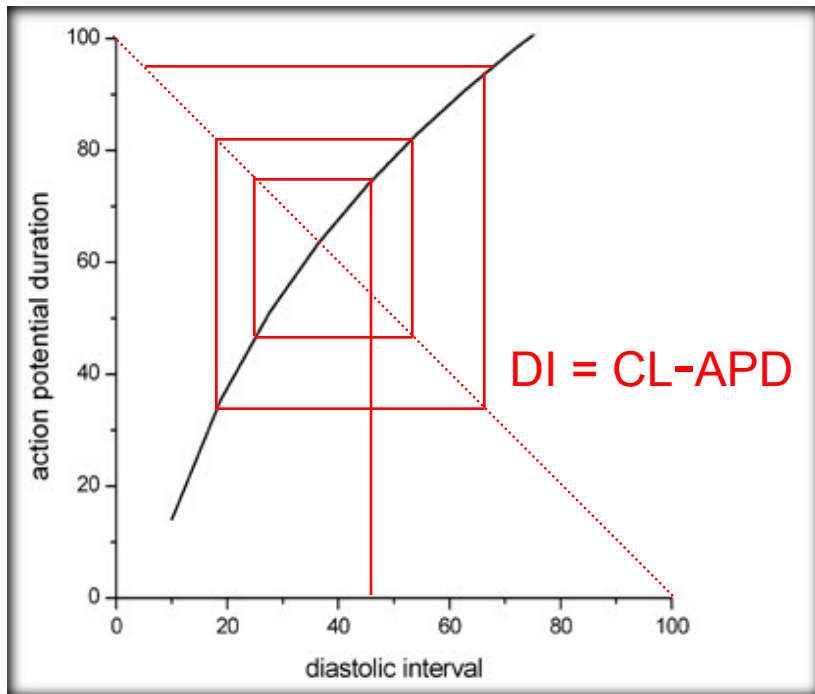
CL=APD+DI

slope depends on CL

Nolasco & Dahlen (1968):
Steepness of the restitution curve → arrhythmia

Alternans

- pacing with constant *cycle length*

fixed frequency pacing in a one dimensional fiber (Luo-Rudy Model)

DI = CL-APD

CL_n CL_{n+1}

DI_n DI_{n+1}

APD_n APD_{n+1} APD_{n+2}

Conduction block after alternans

no excitation
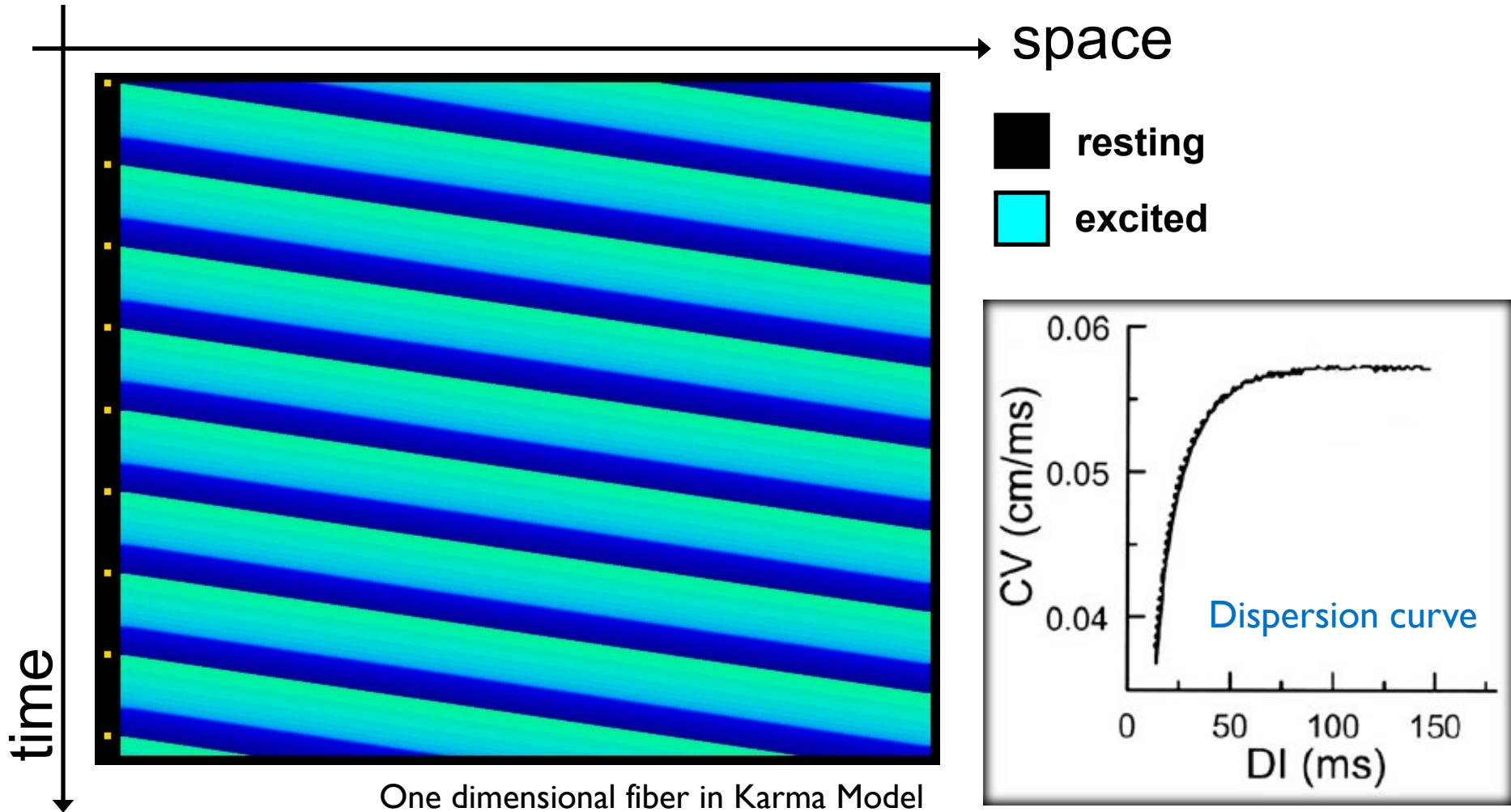
fixed frequency pacing in a one dimensional fiber (Luo-Rudy Model)
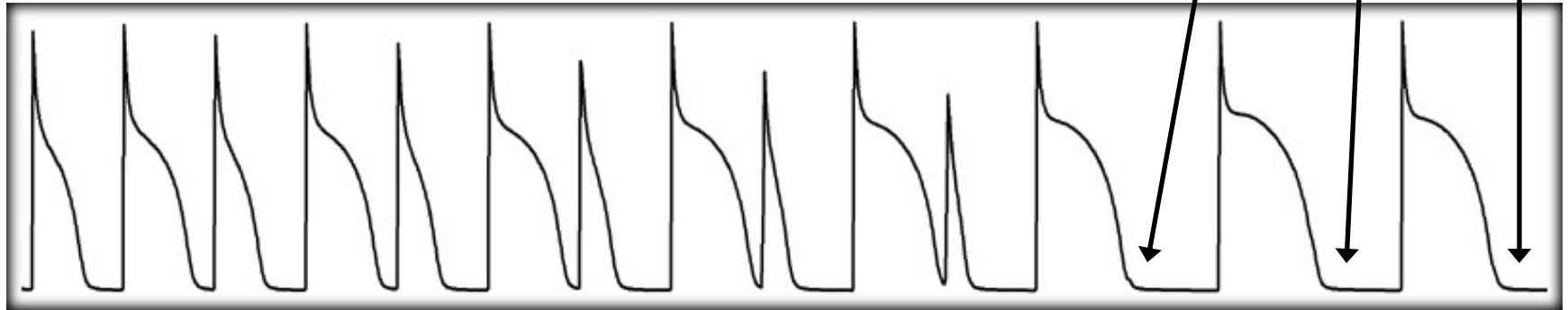
S_1 S_2 S_3 . . .

Wave propagation in 1-dimensional fiber
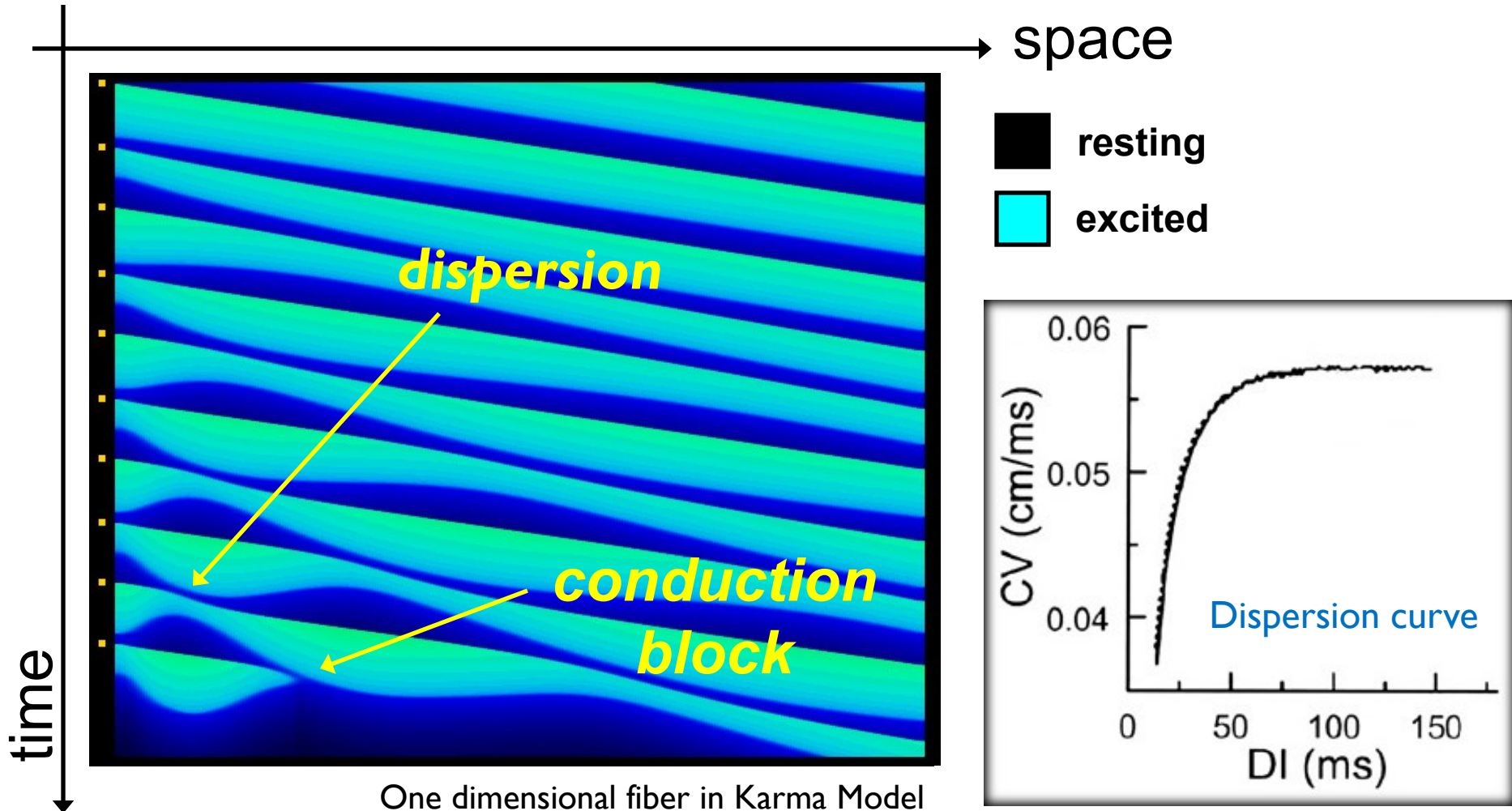
space

time

resting
excited

Dispersion curve

One dimensional fiber in Karma Model

Wave propagation in 1-dimensional fiber

space

One dimensional fiber in Karma Model

- resting
- excited

dispersion

conduction block

time
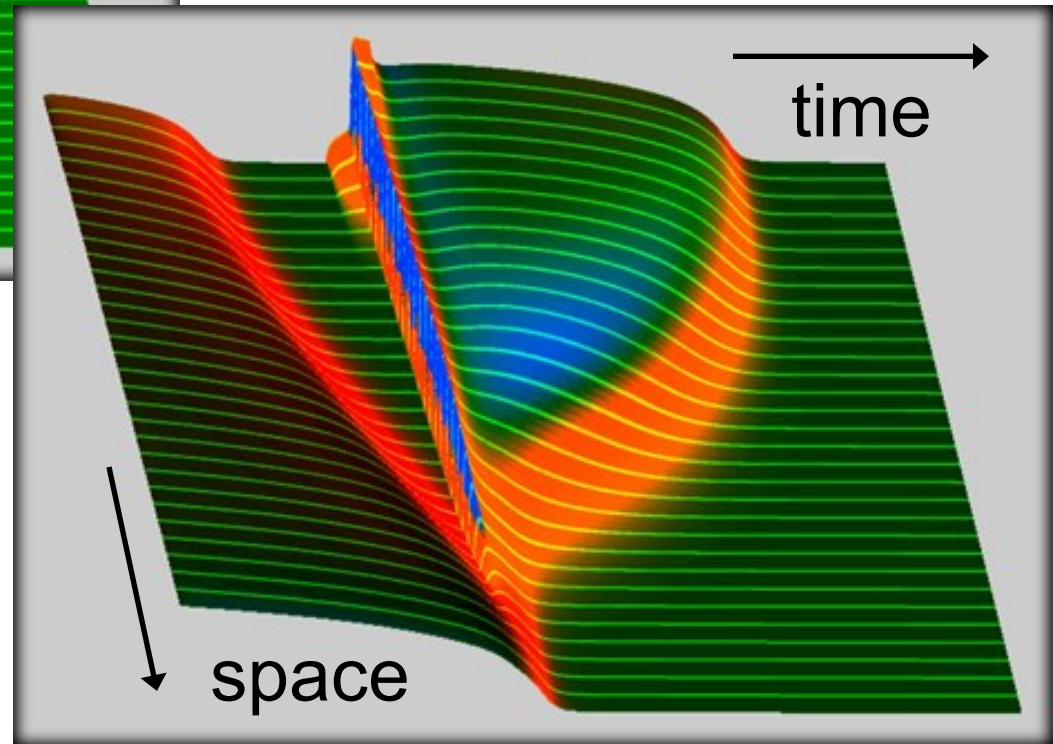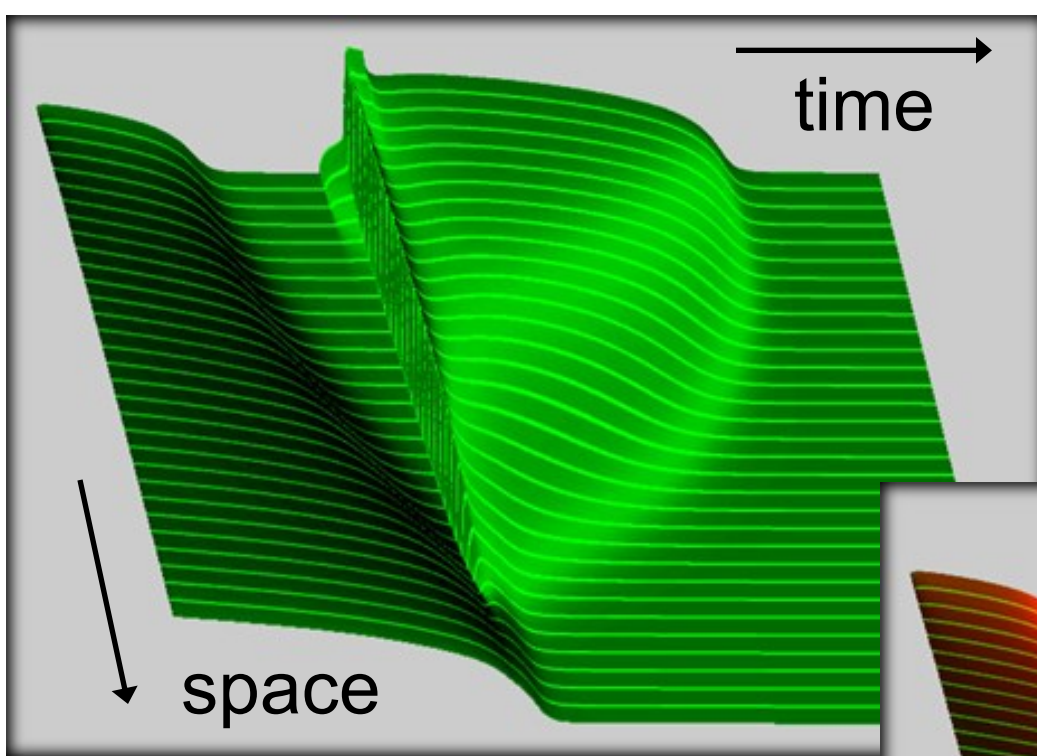
Dispersion curve

- Decreasing the cycle length leads to modulation of the APD and can lead to *conduction block*
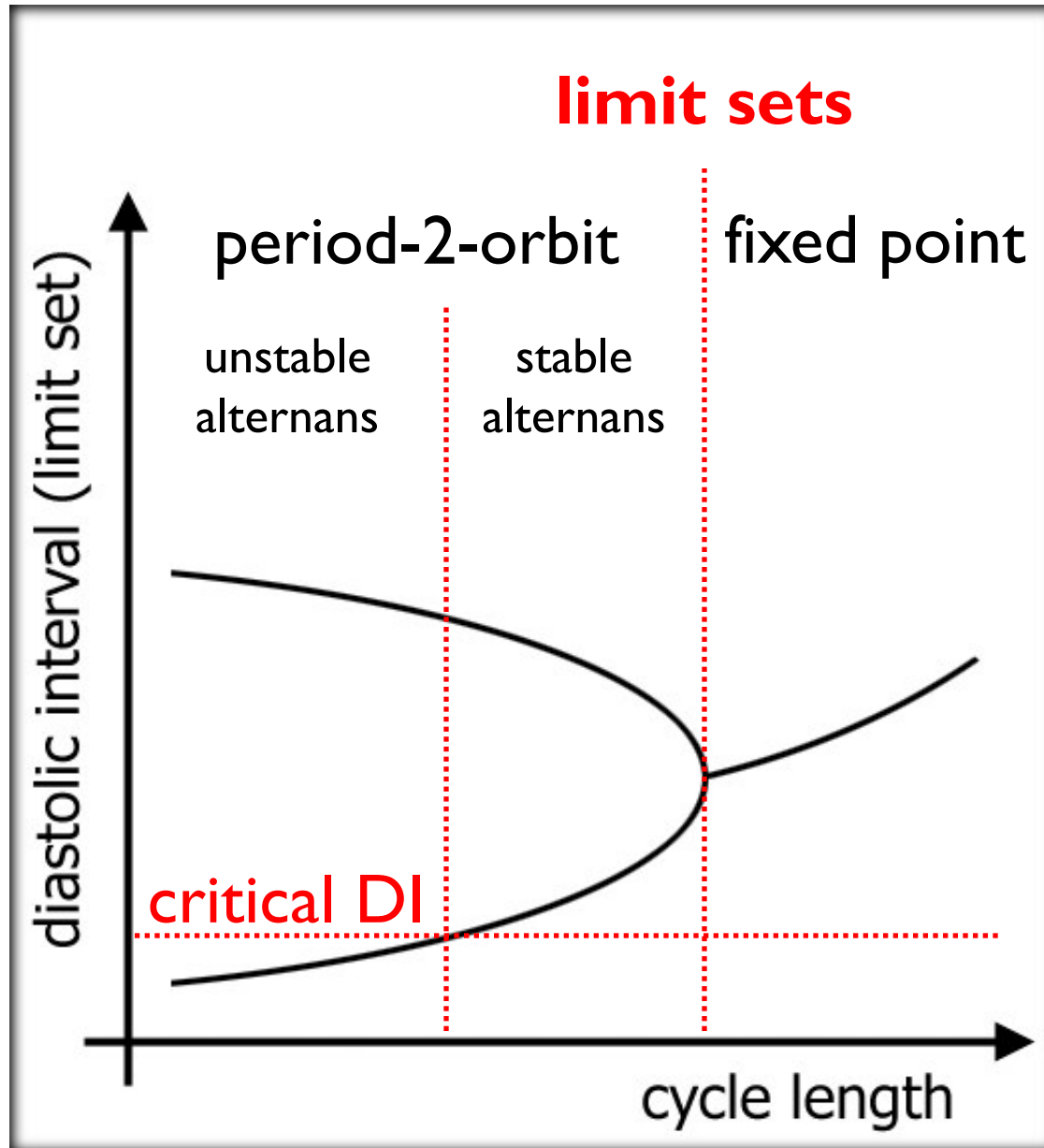
Conduction block in 1-dimensional fiber

ionic currents
- negative
- positive

- Decreasing the cycle length leads to modulation of the APD and can lead to *conduction block*

Bifurcation

What does that mean for termination of VT?

Cycle length in ring is determined by its size

Pacing decreases the cycle length and creates or enlarges modulations around the ring

If conduction block occurs in the ring (not in the sidebranch) *VT* is stopped

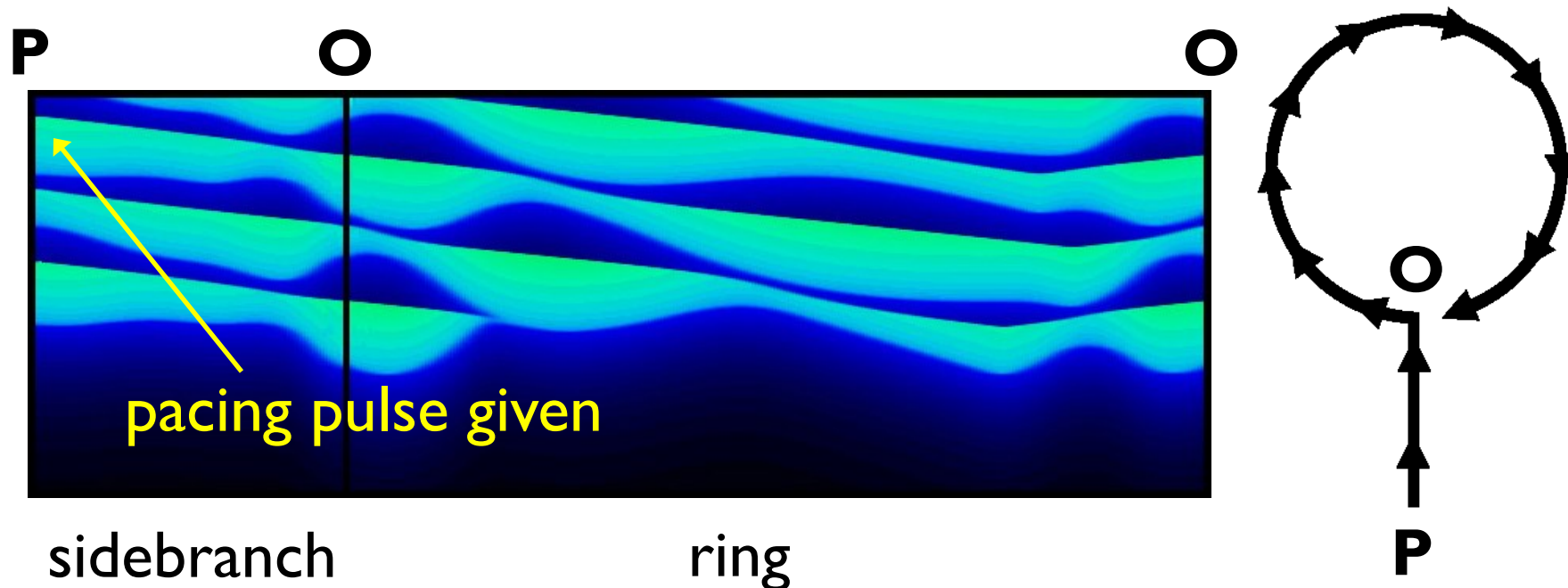pacing pulse given

sidebranch   ring

What does that mean for termination of VT?

Cycle length in ring is determined by its size

Pacing decreases the cycle length and creates or enlarges modulations around the ring

If conduction block occurs in the ring (not in the sidebranch) *VT* is stopped

pacing wave enters the ring
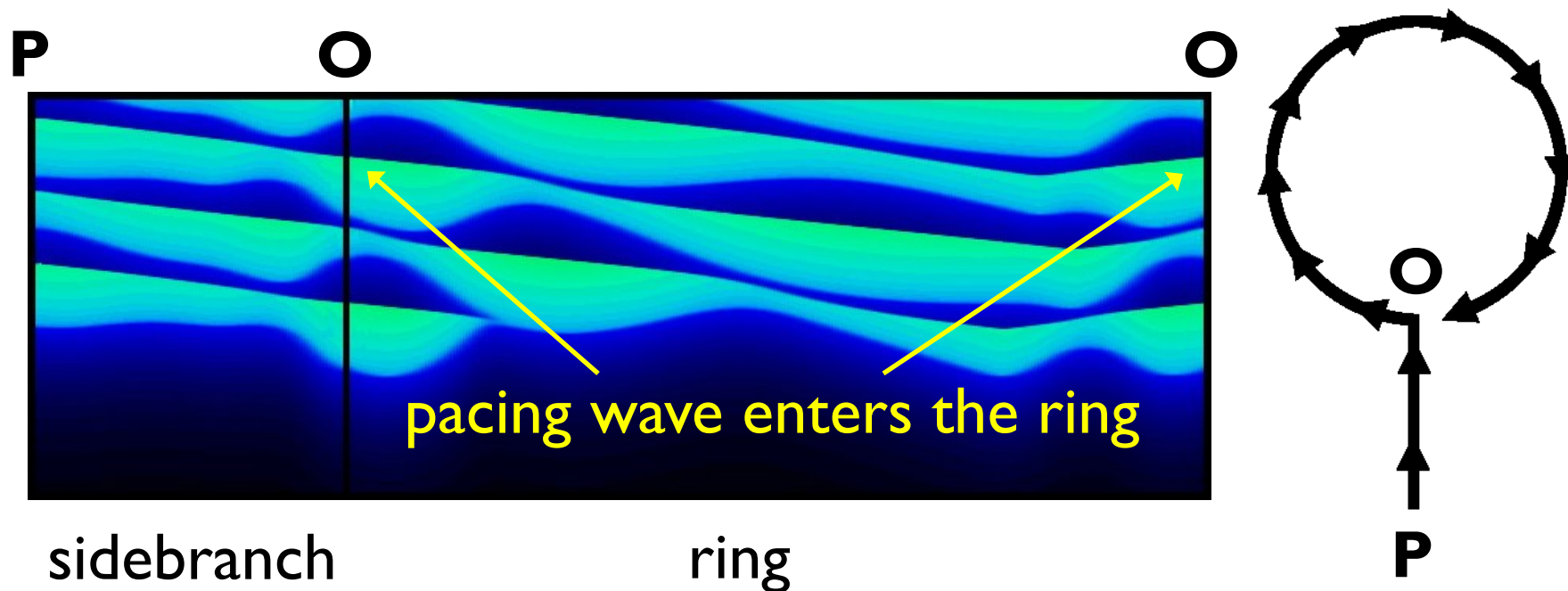
sidebranch   ring

What does that mean for termination of VT?

Cycle length in ring is determined by its size

Pacing decreases the cycle length and creates or enlarges modulations around the ring

If conduction block occurs in the ring (not in the sidebranch) *VT* is stopped

P   O   O

waves collide
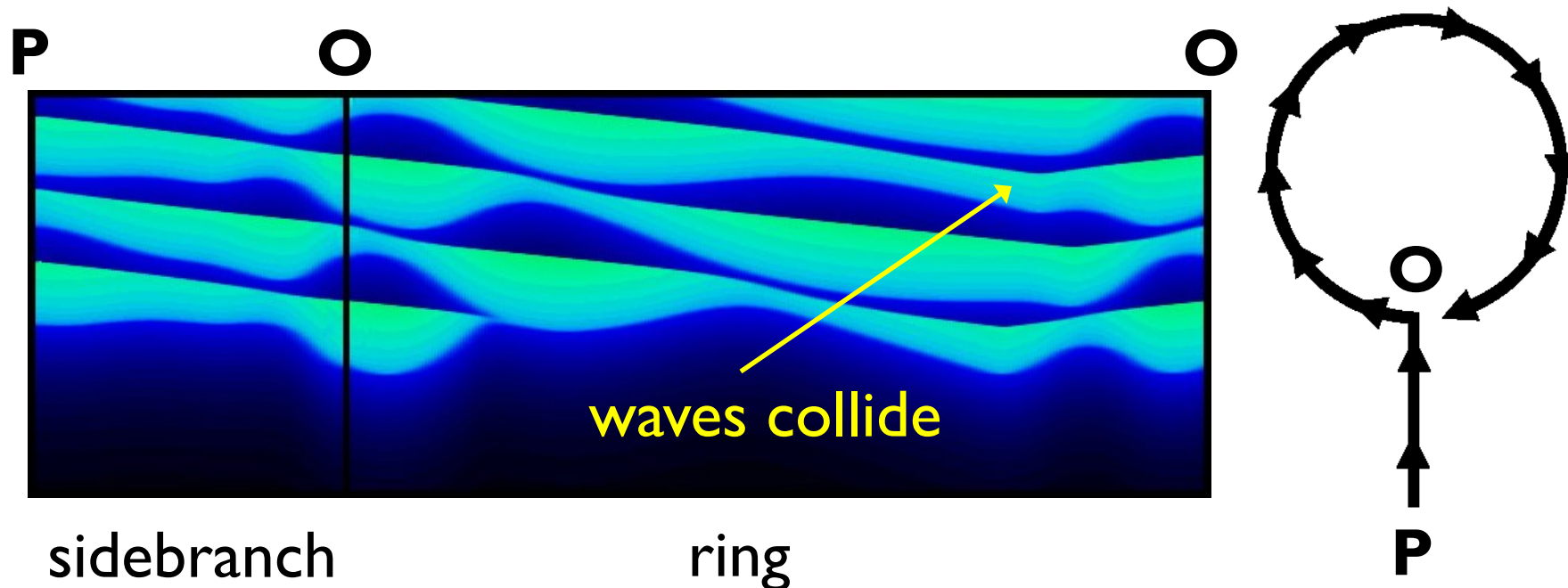
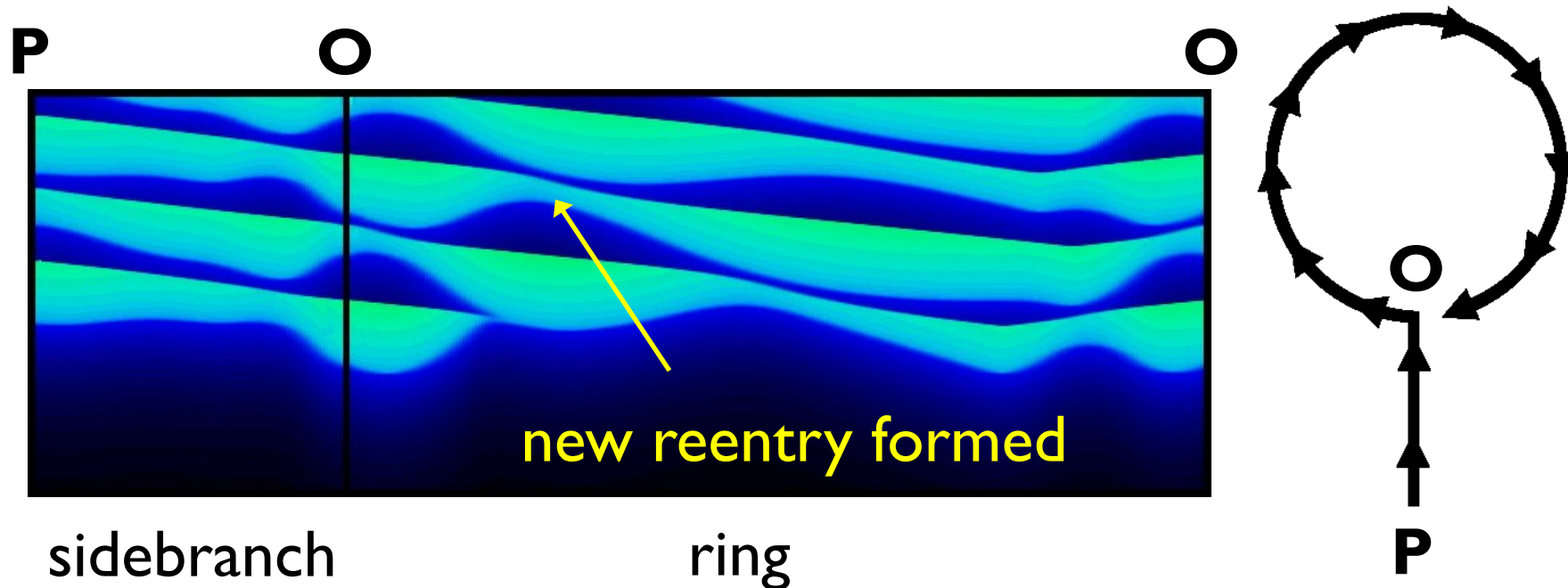sidebranch   ring

P

What does that mean for termination of VT?

Cycle length in ring is determined by its size

Pacing decreases the cycle length and creates or enlarges modulations around the ring

If conduction block occurs in the ring (not in the sidebranch) *VT* is stopped

new reentry formed
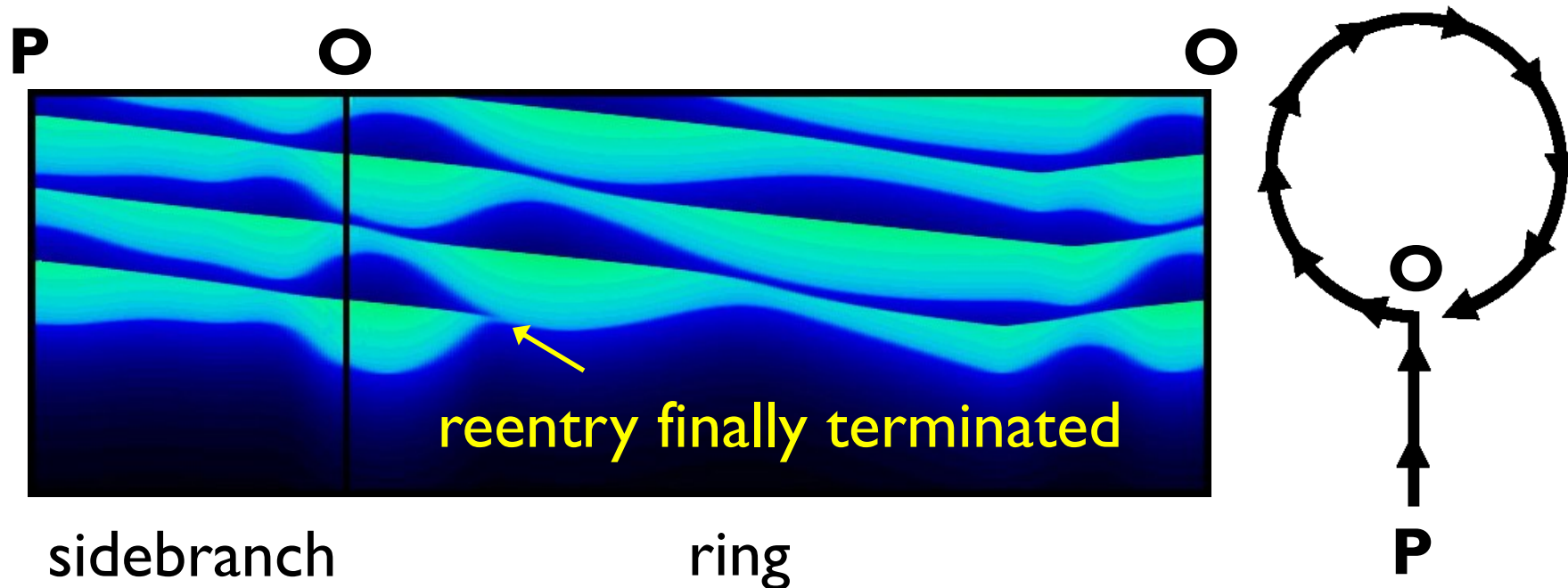
sidebranch   ring

What does that mean for termination of VT?

Cycle length in ring is determined by its size

Pacing decreases the cycle length and creates or enlarges modulations around the ring

If conduction block occurs in the ring (not in the sidebranch) *VT* is stopped

P   O   O

reentry finally terminated

sidebranch   ring

O

P

Diffusion + Restitution + Dispersion →
Dynamical disorder through <u>pattern forming instability</u>
(like Turing patterns)
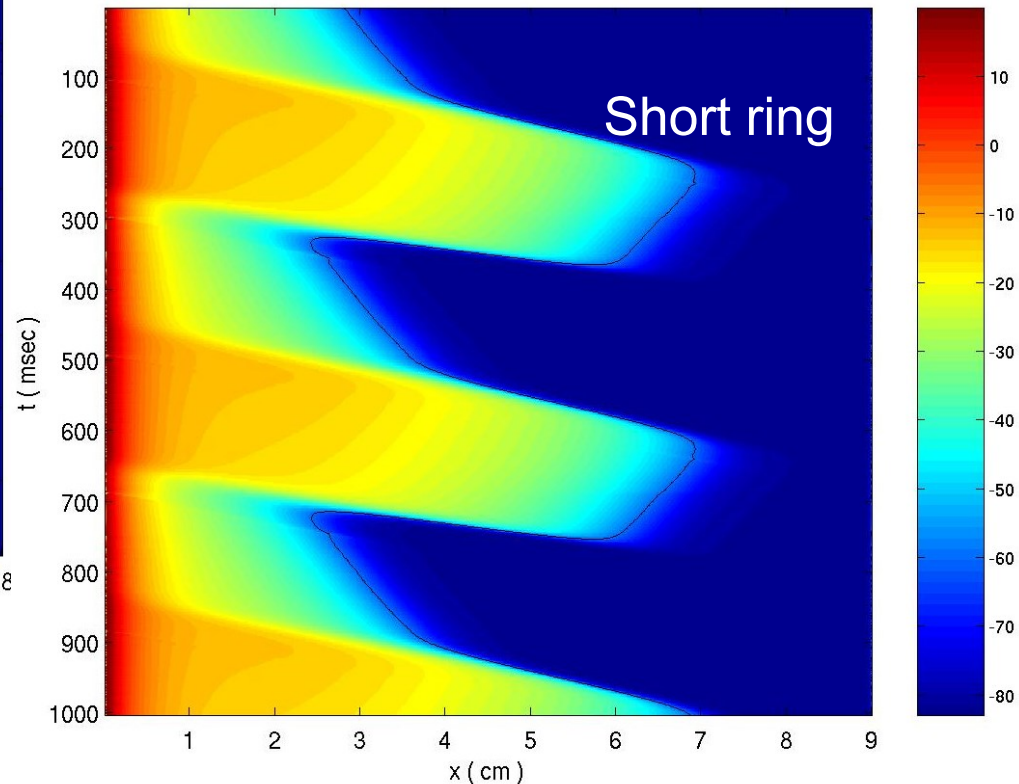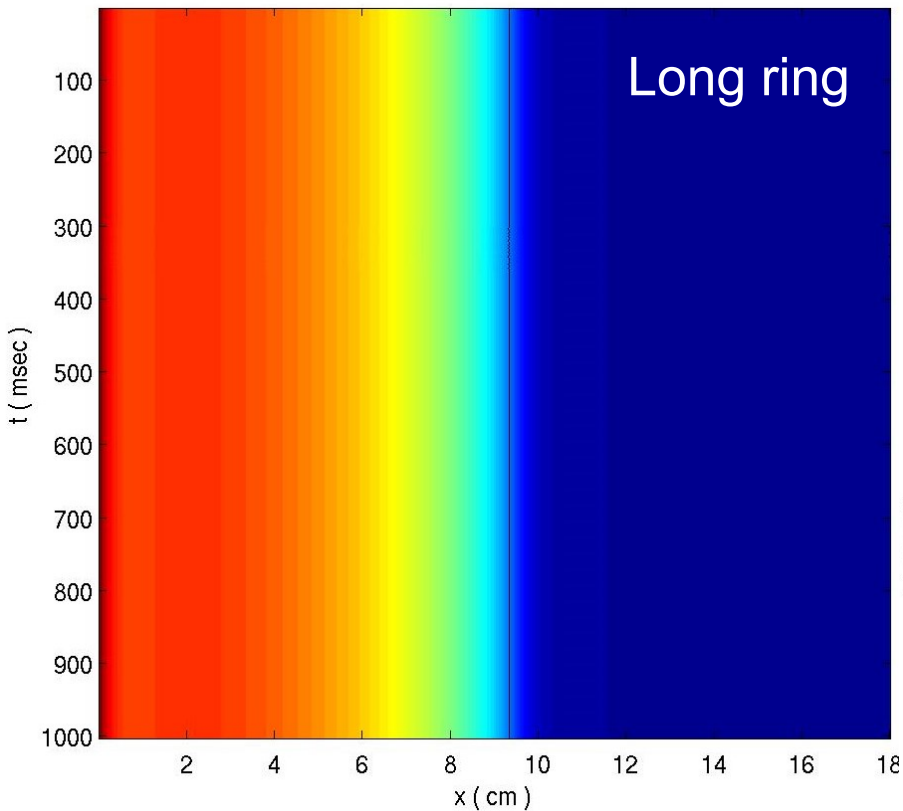
Reference frame fixed with respect to moving wavefront