The nonlinear dynamics of the heart: collective excitation in networks of cardiac cell

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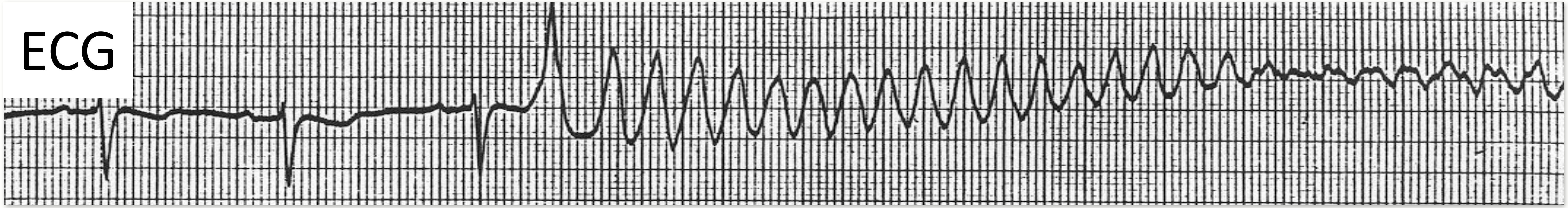
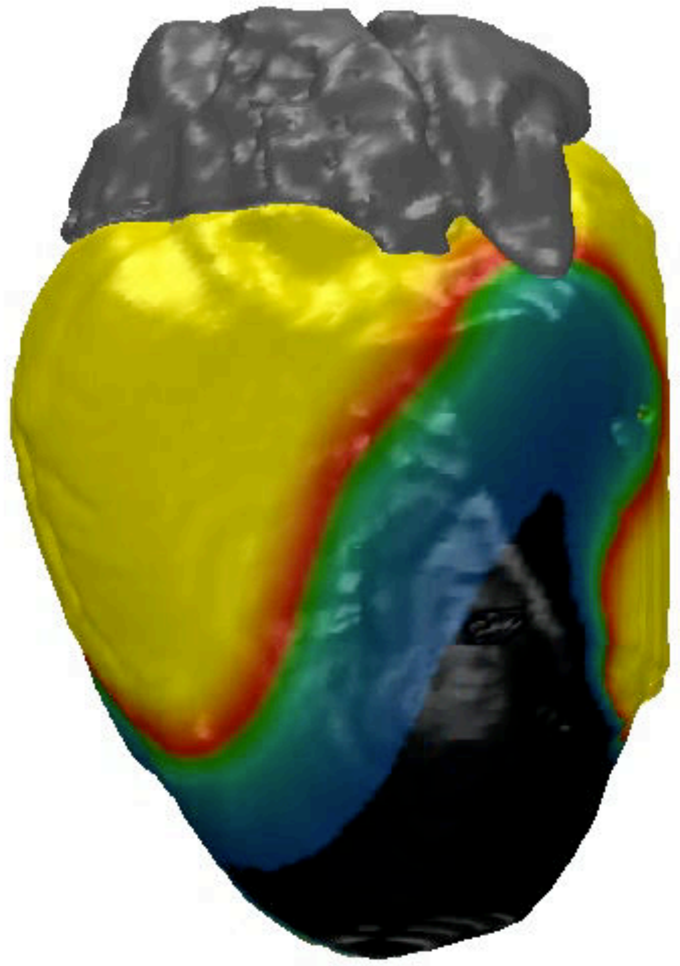
Transitions to Cardiac Arrhythmias

Normal Rhythm ⟶ Tachycardia ⟶ Fibrillation

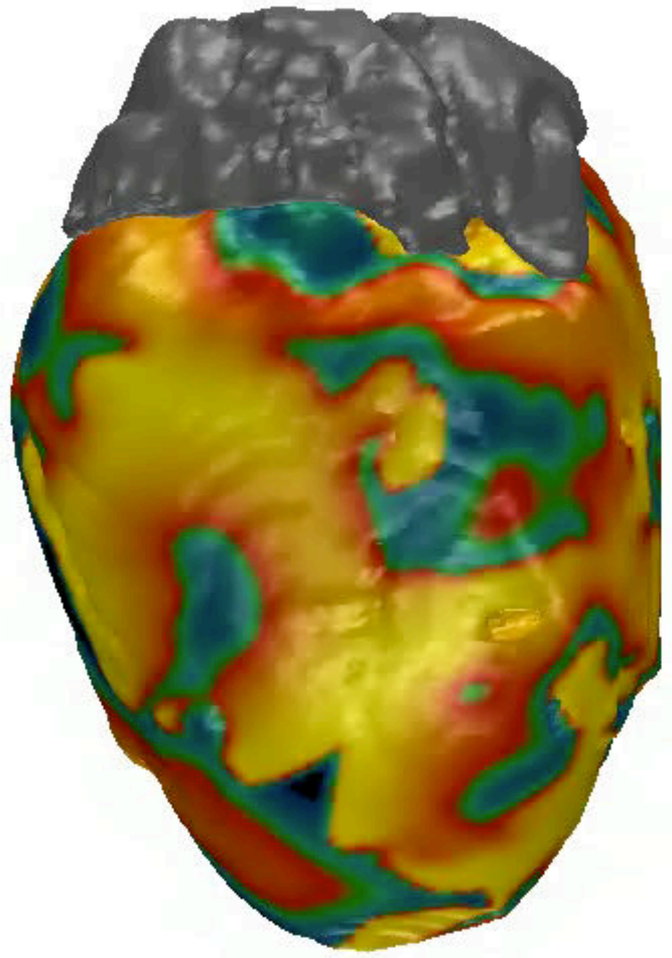


electrical excitation waves

plane waves



spiral waves



chaos

simulations: P. Bittihn

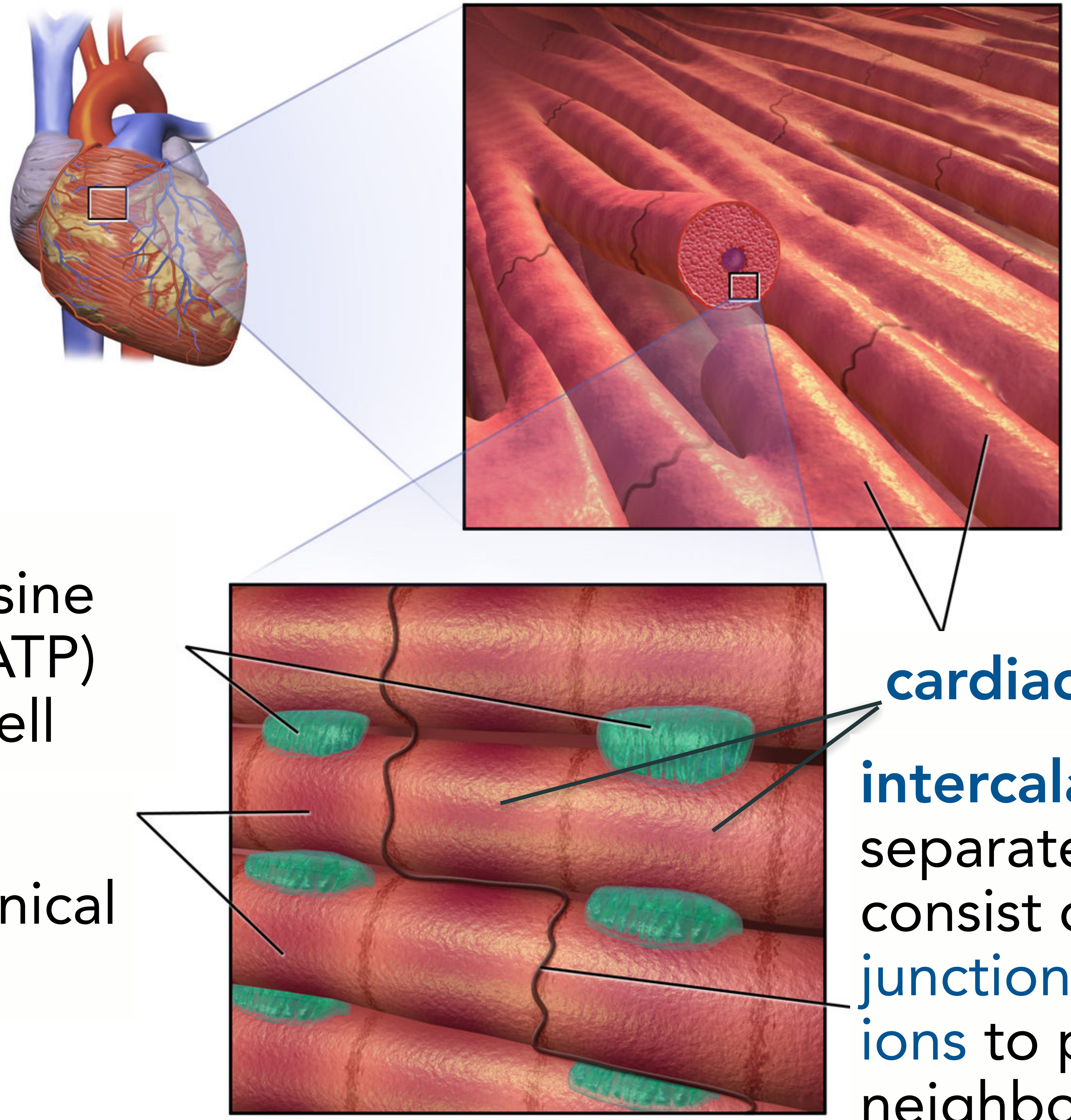
Outline

- the heart - a network of electrically and mechanically coupled contracting cardiac cells
- excitable media, (chaotic) spiral waves, and phase singularities
- measuring cardiac dynamics (optical mapping & ultrasound)

The heart - a network of electrically and mechanically coupled contracting cardiac cells

The heart: A Network of Cardiomyocytes

cardiac muscle



cardiac muscle fibers

BruceBlaus - Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=44969447

mitochondria provide adenosine triphosphate (ATP) supply of the cell

myofibrils provide mechanical contraction

cardiac muscle cells

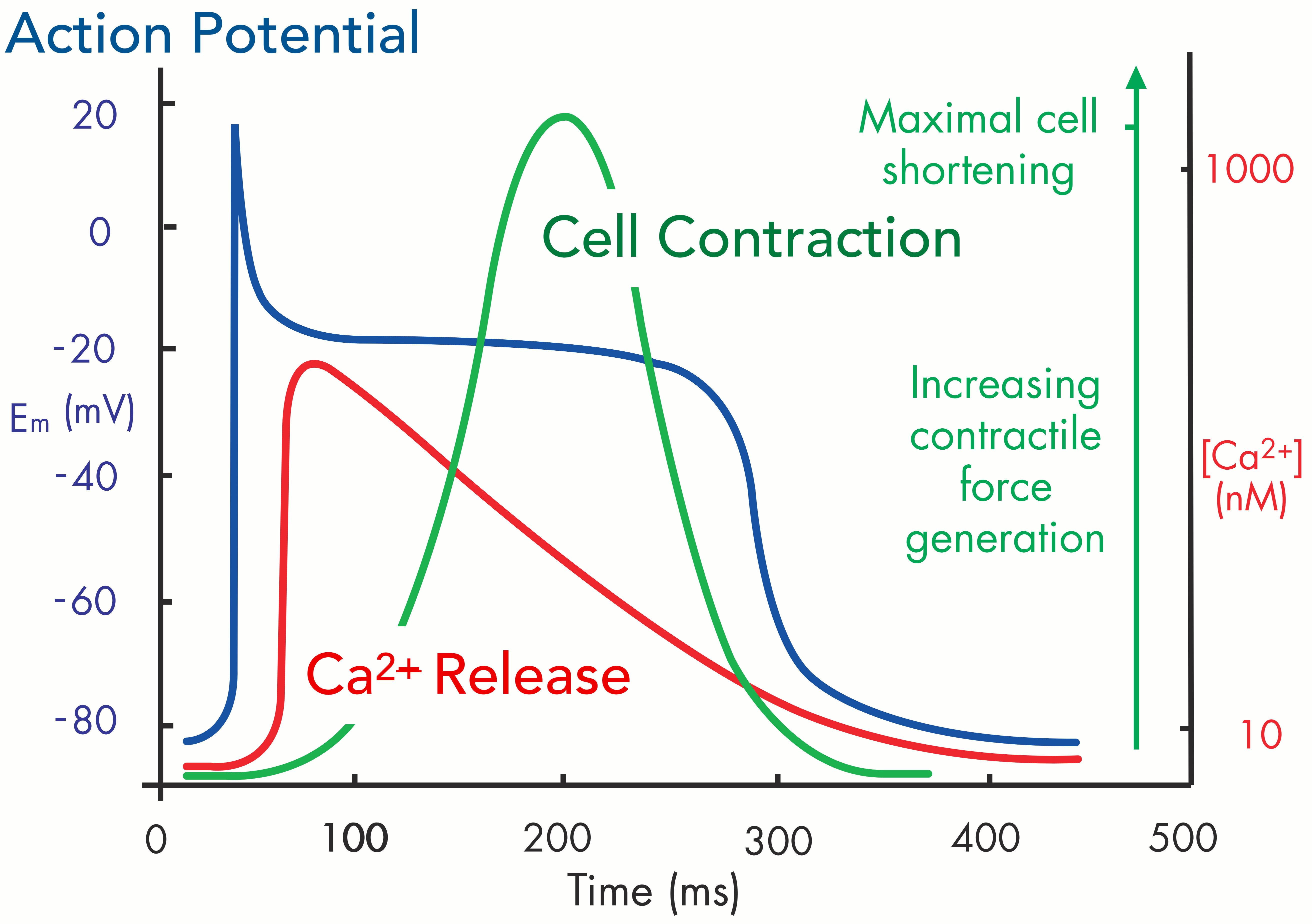
intercalated discs separate cells and consist of gap junctions that allow ions to propagate to neighbouring cell

Ventricular Cell

© Kornreich & Fenton

The heart: A Network of Cardiomyocytes

Excitation-Contraction Coupling



from: M. Scoote et al., *Heart* 89, 371–376 (2003)

electrical excitation

mechanical contraction

Mechanical perturbation induces electrical stimulation via stretch activated ion channels.

→ Commotio Cordis

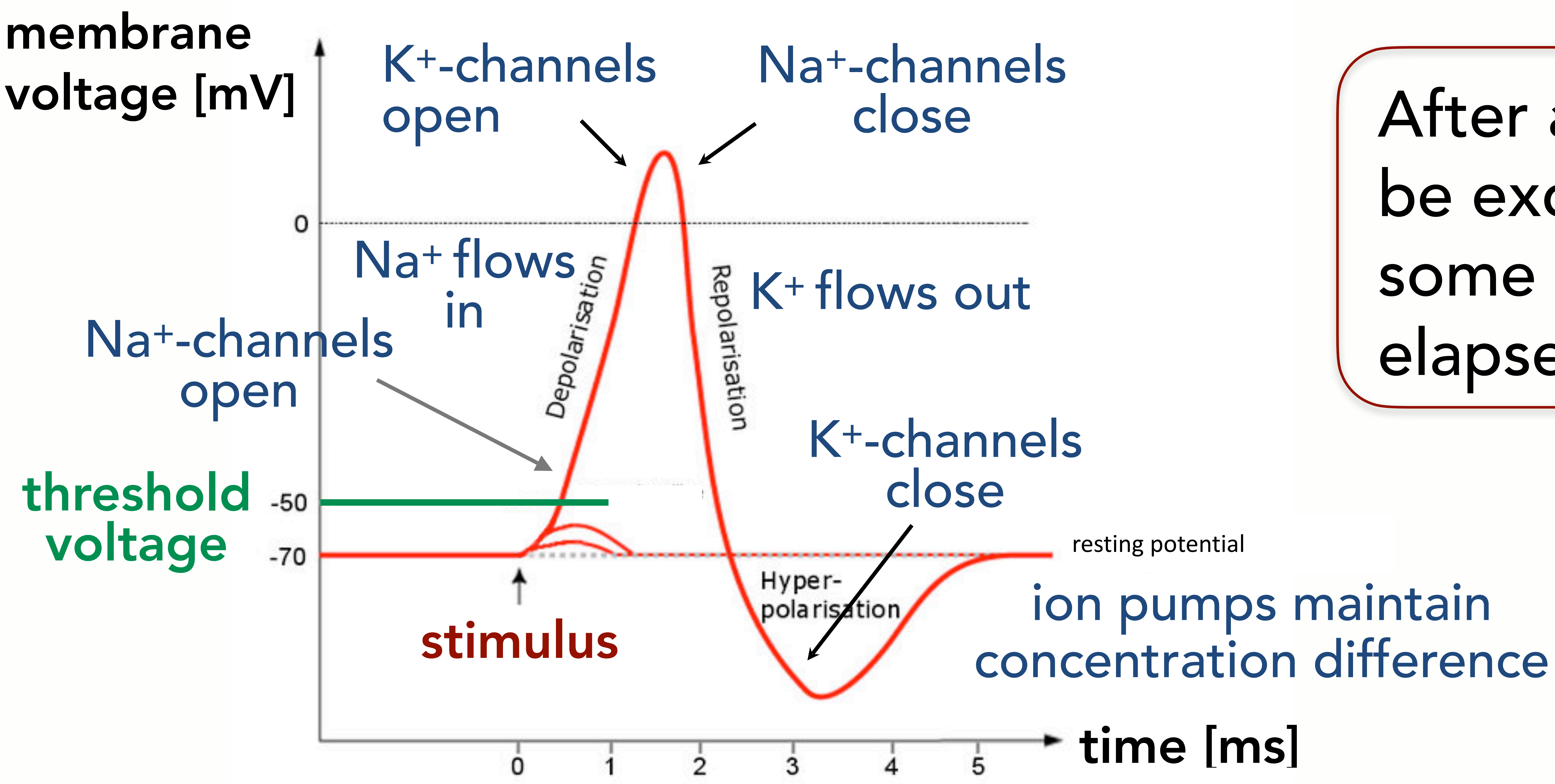
The heart muscle is an excitable medium

Cardiomyoctes (heart cells) are excitable systems

General features of an excitable system:

- dynamical system with a stable fixed point
- small perturbations (or stimuli) from the fixed point decay
- large perturbation (exceeding a certain threshold) result in a large excursion in state space finally re-approaching the stable fixed point
- form and duration of the excitation do not depend on the exact form of the perturbation
- new perturbation affects system only if it is close to fixed point, again
  $\rightarrow$ **refractory time**

Excitability: Generation of an Action Potential



adapted from Wikipedia

After an excitation the cell can be excited again not before some **refractory phase** has elapsed.

A mathematical model of an excitable system

FitzHugh-Nagumo model

$$\begin{aligned}\dot{u} &= au(u-b)(1-u) - w + I \\ \dot{w} &= \varepsilon(u-w)\end{aligned}$$

qualitative description of neuronal and cardiac dynamics

u cell membrane voltage

w recovery variable, with much slower dynamics ($\varepsilon = 0.01$)

I (external) injection current ($I = 0$)

http://scholarpedia.org/article/FitzHugh-Nagumo_model

FitzHugh-Nagumo model

$$\dot{u} = au(u-b)(1-u) - w + I$$
$$\dot{w} = \varepsilon(u-w)$$

$I = 0:$

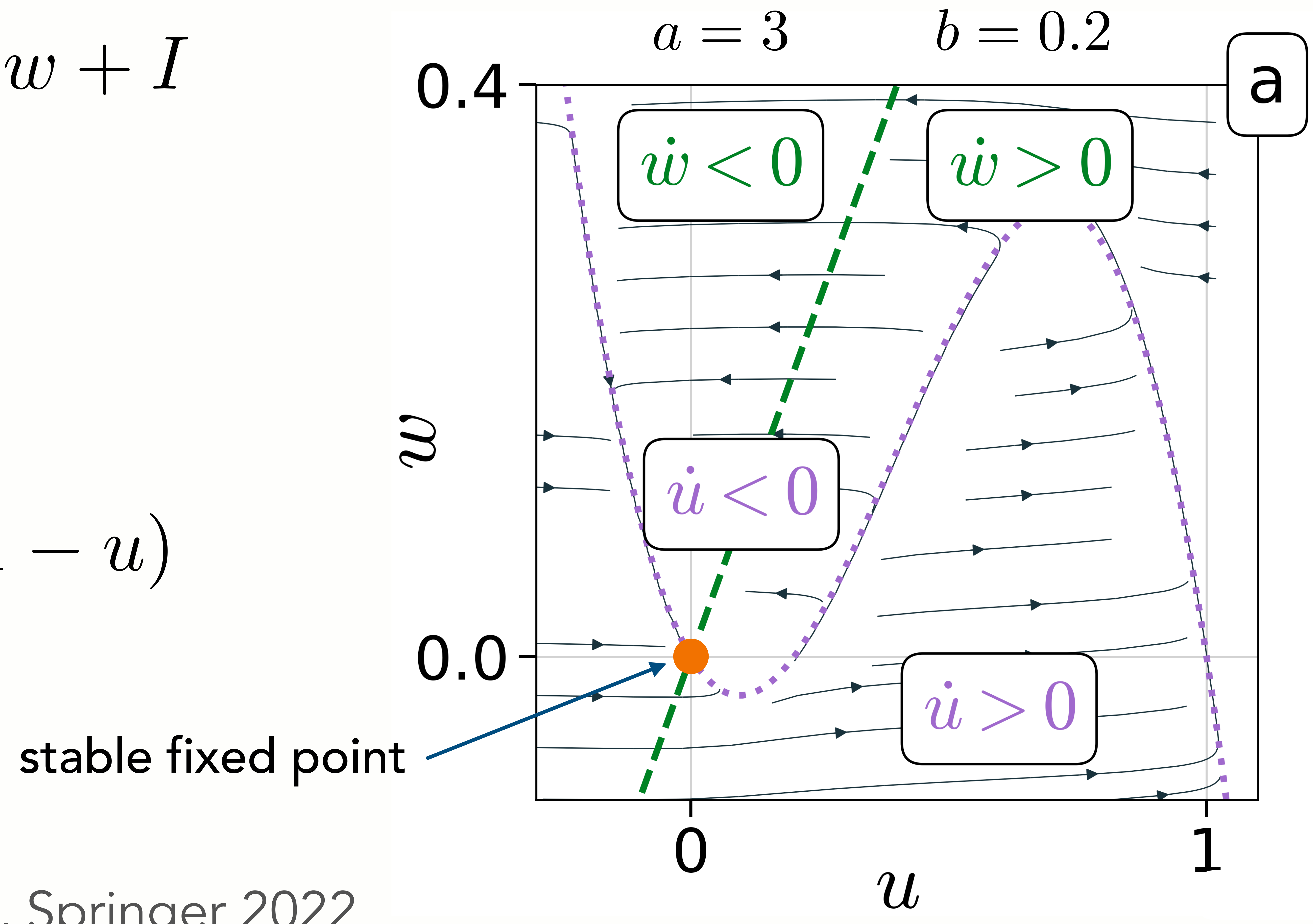
u nullcline ($\dot{u} = 0$):

$$n_u(u) = au(u-b)(1-u)$$

w nullcline ($\dot{w} = 0$):

$$n_w(u) = u$$

state space

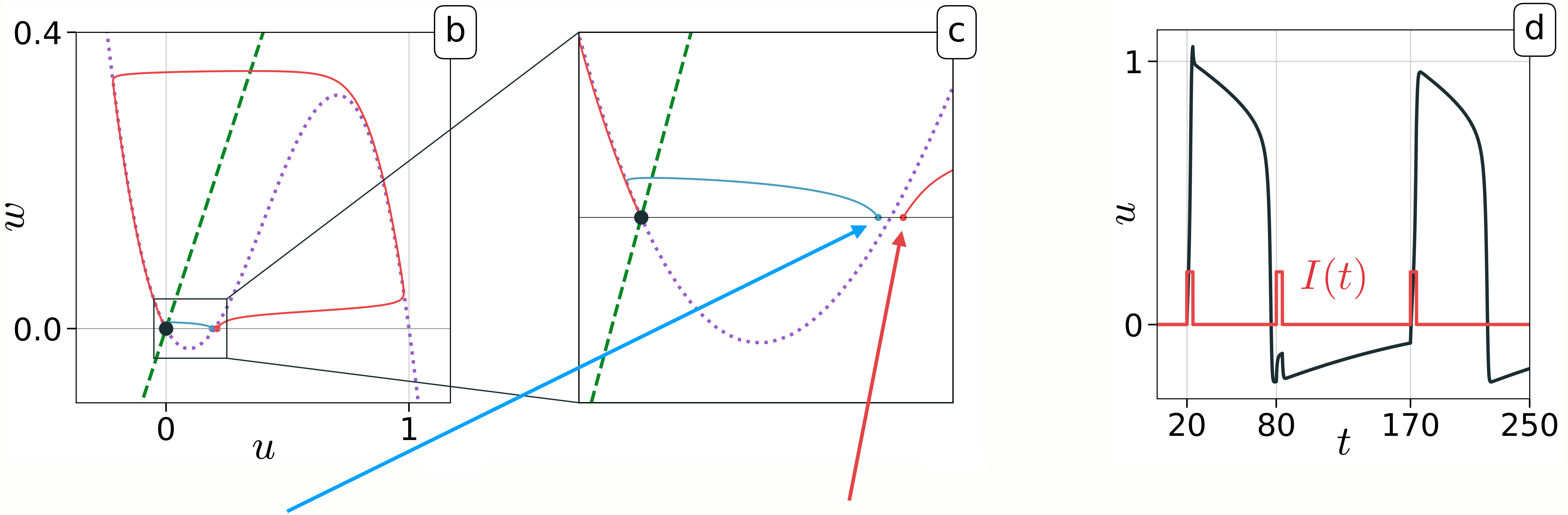


Datseris and Parlitz, Nonlinear Dynamics, Springer 2022

Excitable Systems

Impact of short rectangular current pulses $I(t)$

A second pulse during the refractory phase of the system has almost no impact.



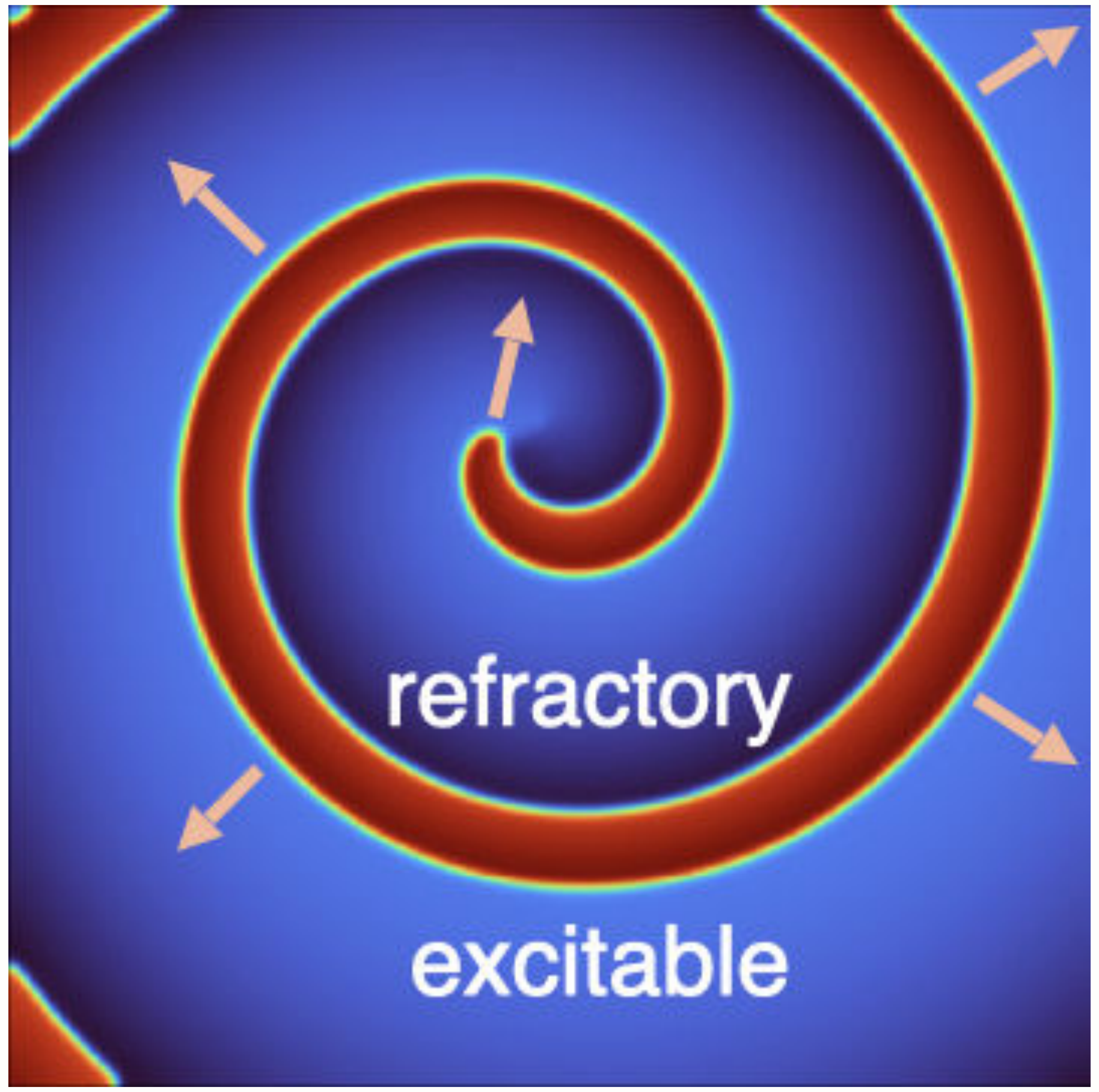
A small perturbation below threshold returns immediately to the fixed point.

A perturbation above threshold results in an excursion in state space and an action potential.

Excitable Media

- An excitable medium
- is a spatially extended nonlinear dynamical system
- which has the capacity to propagate excitation waves,
- and which cannot support the passing of another wave until some time has passed (refractory period/phase)

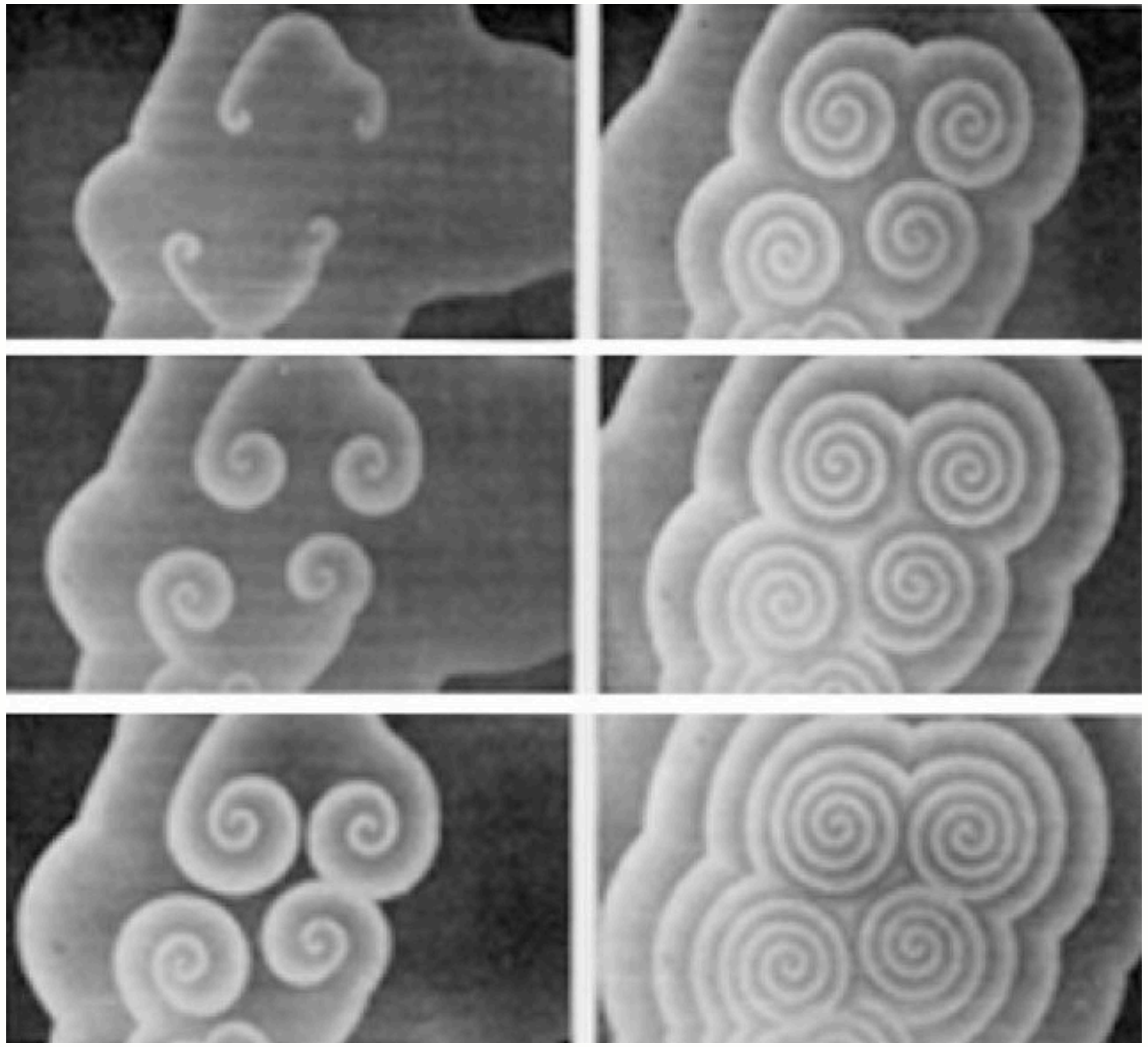
  → refractory region/zone



The existence of a refractory region means that an excitation wave cannot propagate in any direction but only to the excitable region of the medium.

As a result, rotating waves, also called spiral waves may occur.

The Belousov-Zhabotinsky (BZ) reaction



Development of spiral waves after hydrodynamic breaking of a concentric wave

www.scholarpedia.org

Geographic Tongue

inflammatory condition of the mucous membrane of the tongue

The spatiotemporal Fitzhugh-Nagumo model

$$
\begin{aligned}
\dot{u} &= au(u-b)(1-u) - w + d\Delta u \\
\dot{w} &= \varepsilon(u-w)
\end{aligned}
$$

fundamental model describing an excitable medium

spatial coupling via diffusion term

spatial domain with no-flux boundary conditions

Depending on initial conditions and specific perturbations plane waves, concentric waves or spiral waves can be generated.

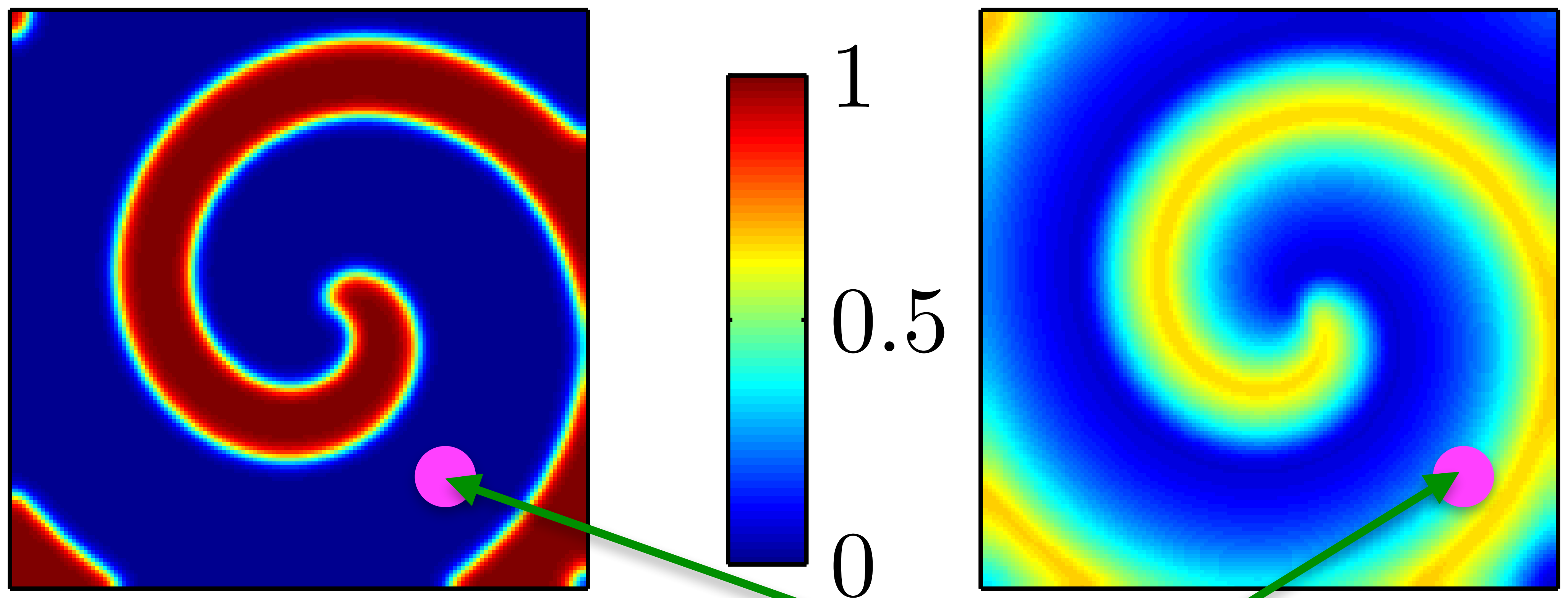
Excitable Media

Fitzhugh-Nagumo model

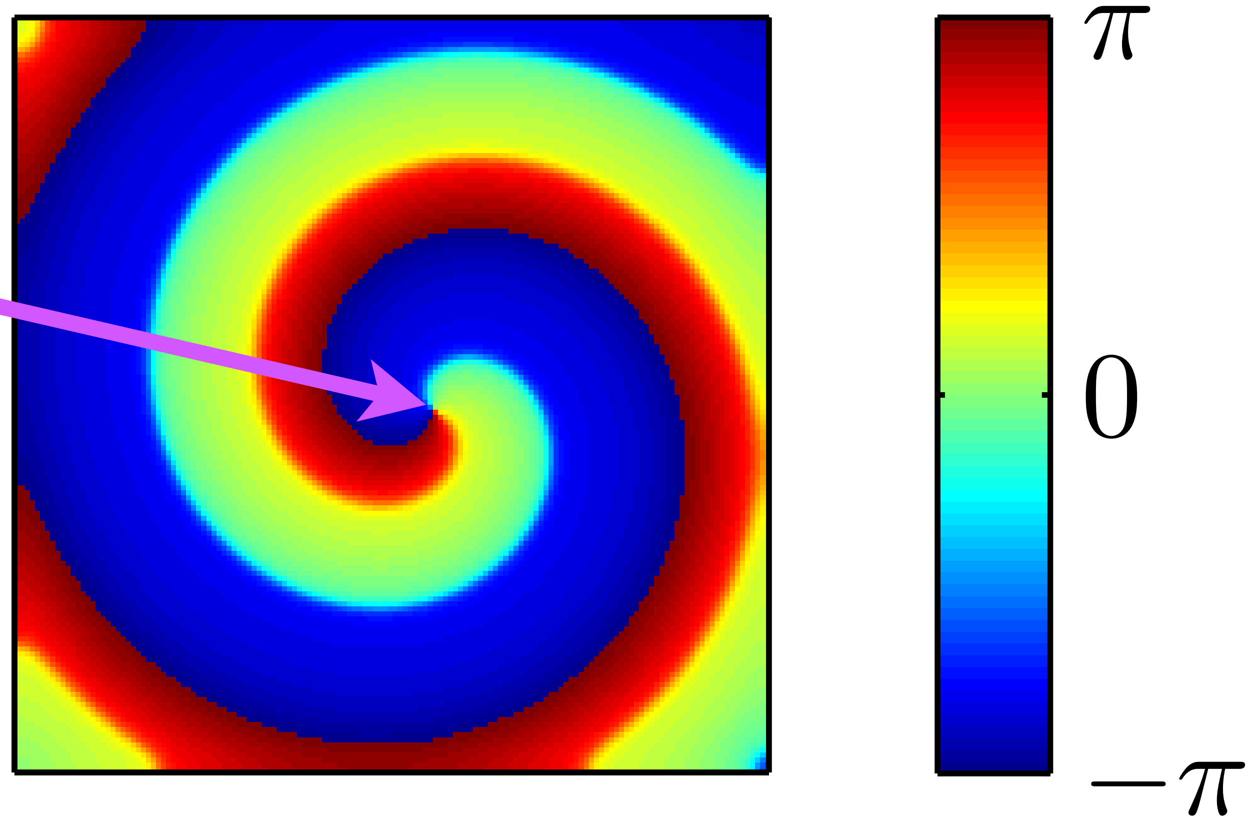
$$a = 3, \; b = 0.2, \; \varepsilon = 0.01, \; d = 1$$

Spiral Tips and Phase Singularities

u v

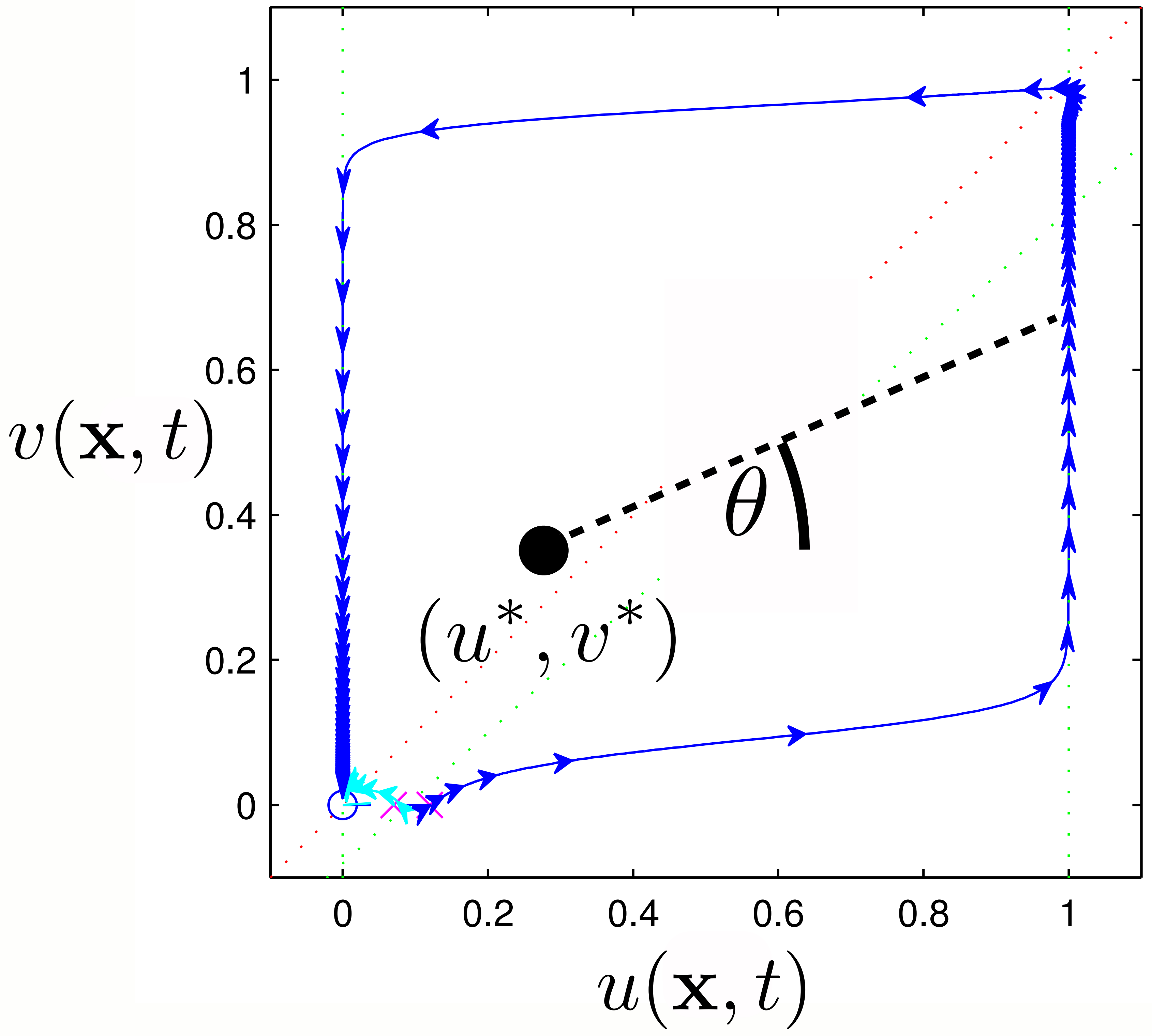


θ location $\mathbf{x}$



phase singularity

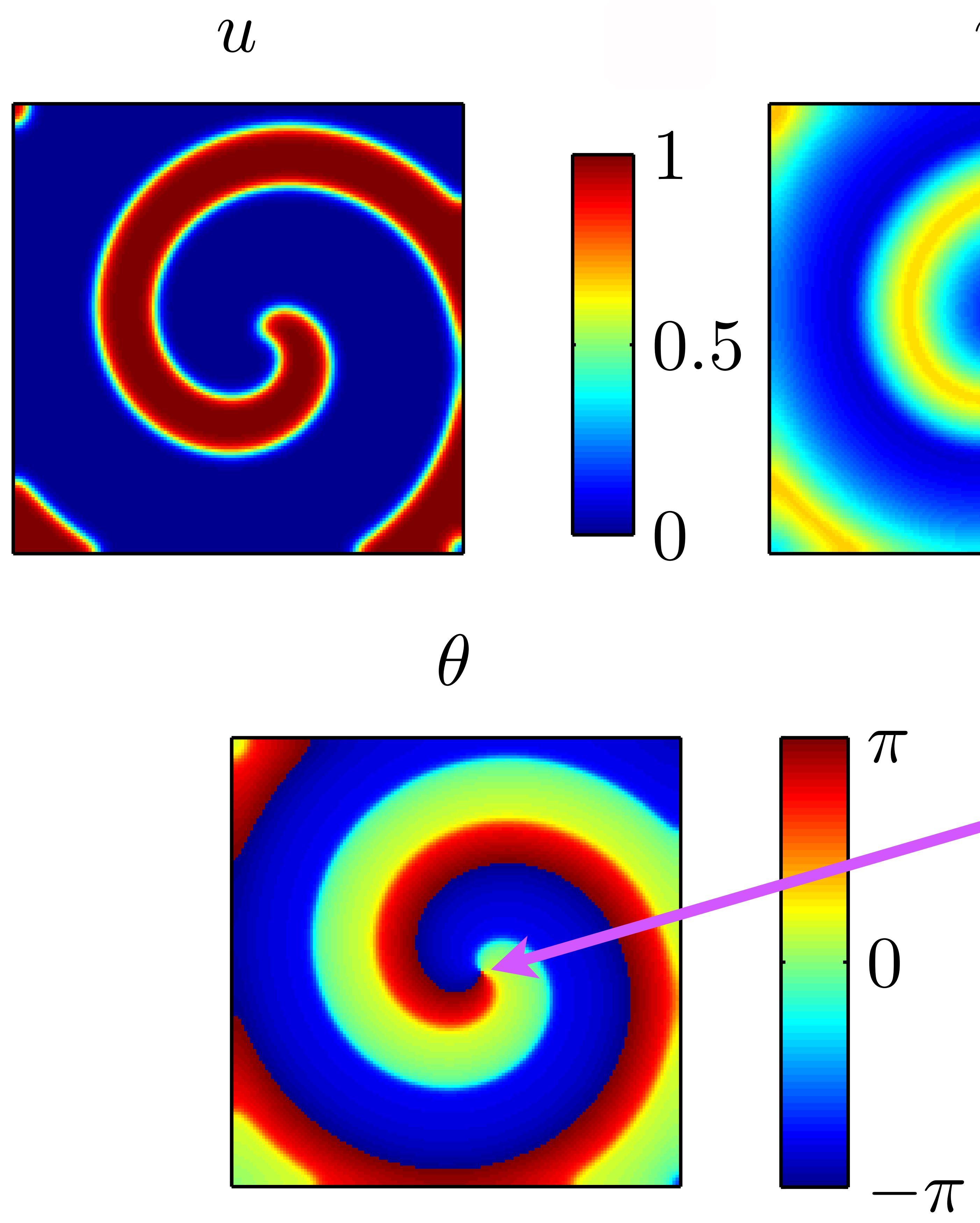
estimate phase at each location $\mathbf{x}$



phase

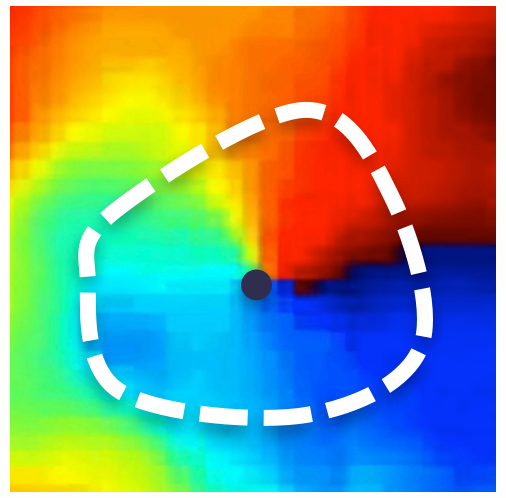
$$\theta(\mathbf{x}, t) = \arctan 2(u(\mathbf{x}, t) - u^*, v(\mathbf{x}, t) - v^*)$$

Spiral Tips and Phase Singularities



phase singularity

compute number of spiral waves in a domain $\mathcal{D}$



$$\oint_{\partial\mathcal{D}} \vec{\nabla}\theta \cdot d\vec{l} = 2\pi(n-m)$$

n # clockwise

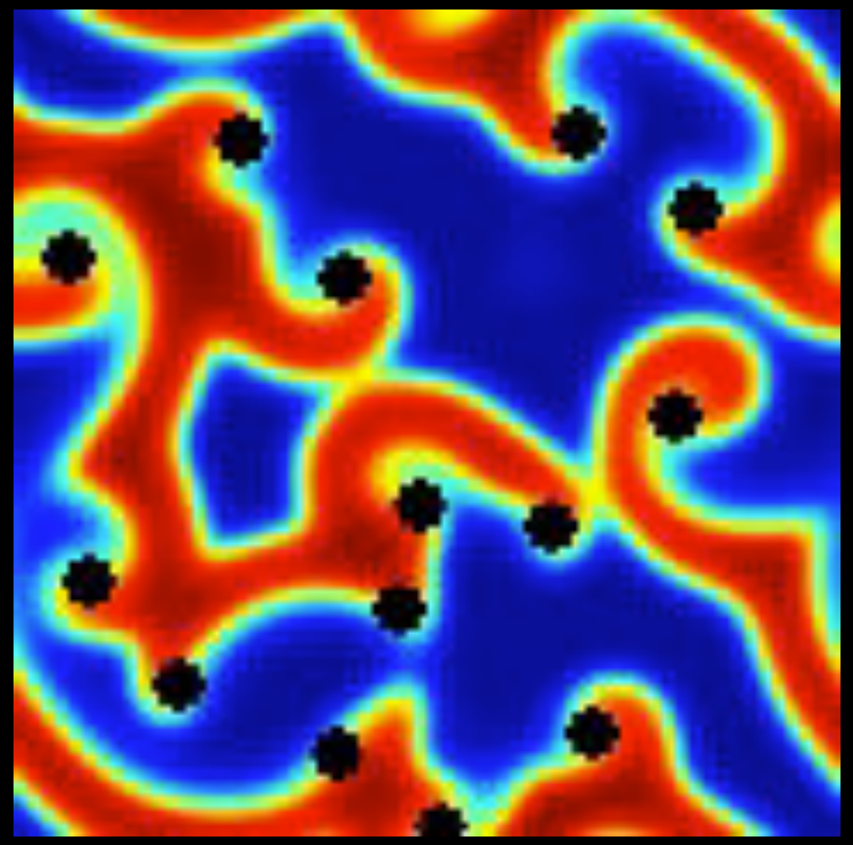
m # counter clockwise

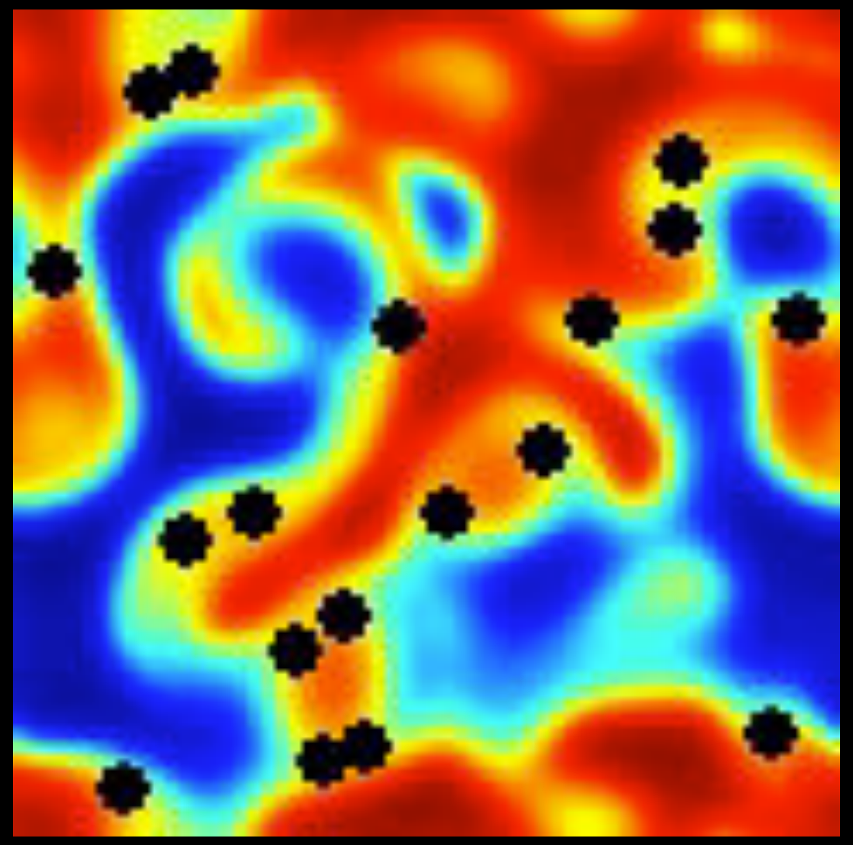
rotating spirals

alternative approach: D.R. Gurevich and R.O. Grigoriev, *Chaos* 29, 053101 (2019)

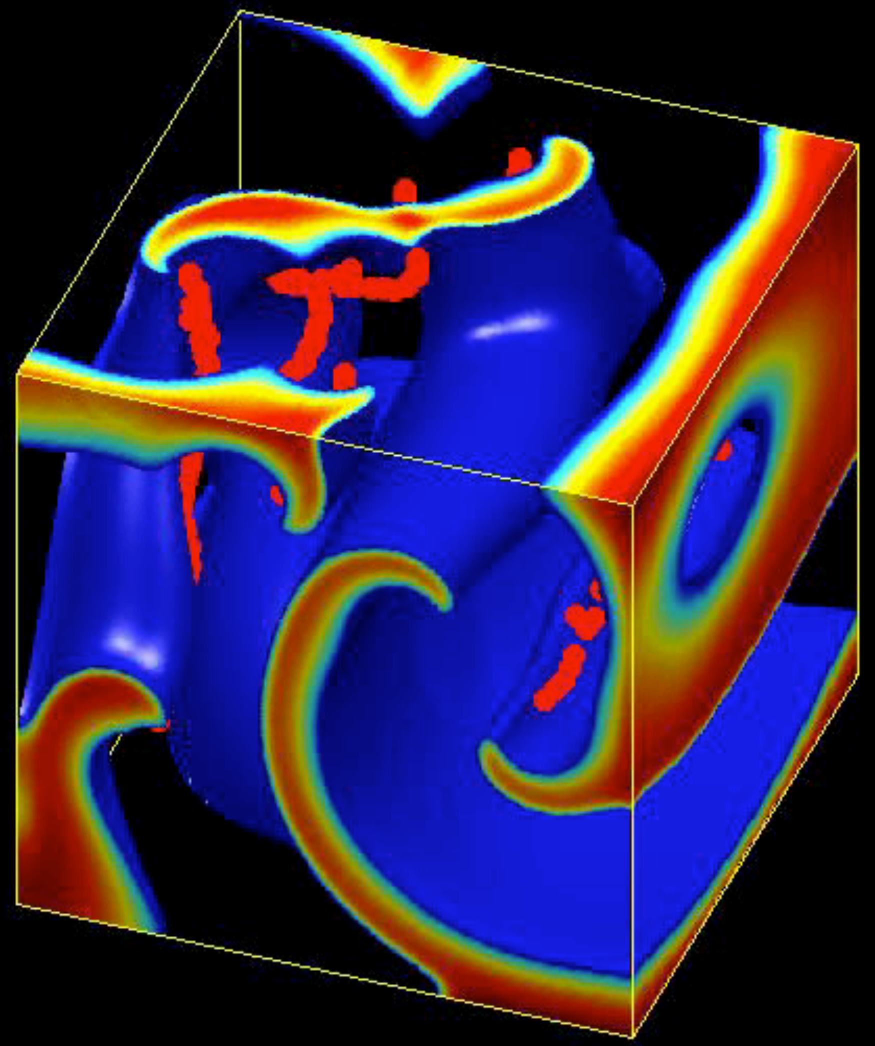
Dynamics of Phase Singularities

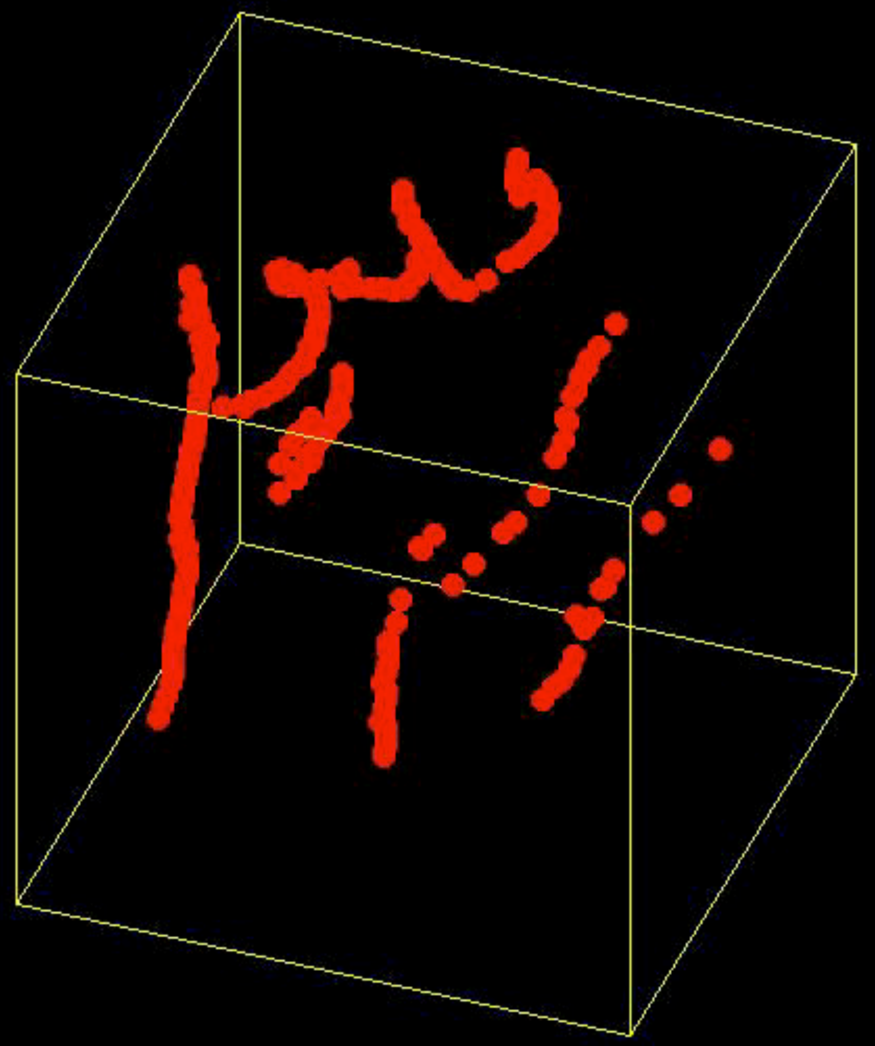
2D





3D





scroll waves

filaments

F. Fenton, E. Cherry

thevirtualheart.org

WebGL simulations

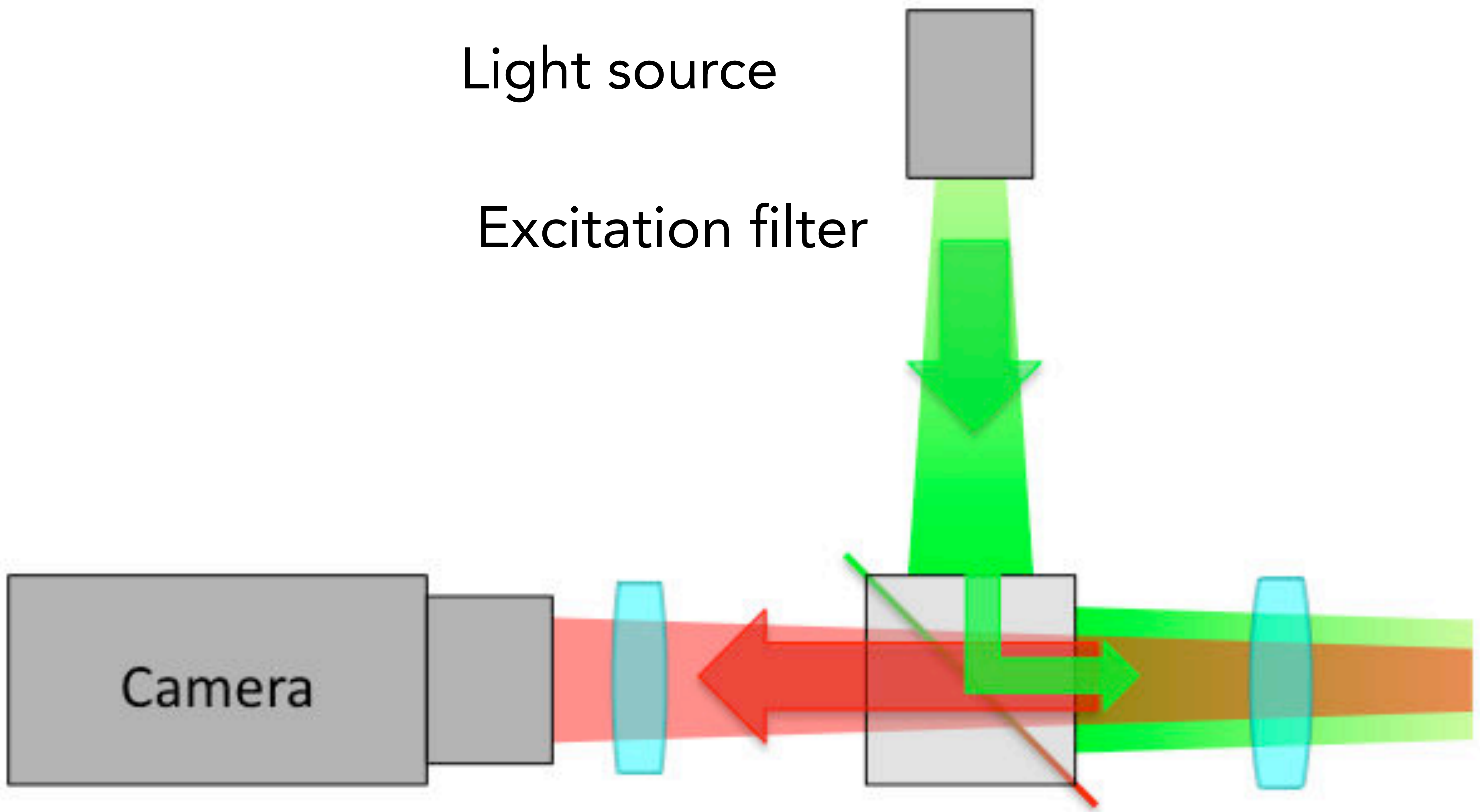
http://thevirtualheart.org/GPU/WebGL_GPU_spiral_waves_heart.html

Measuring cardiac dynamics

using optical mapping and high-speed ultrasound

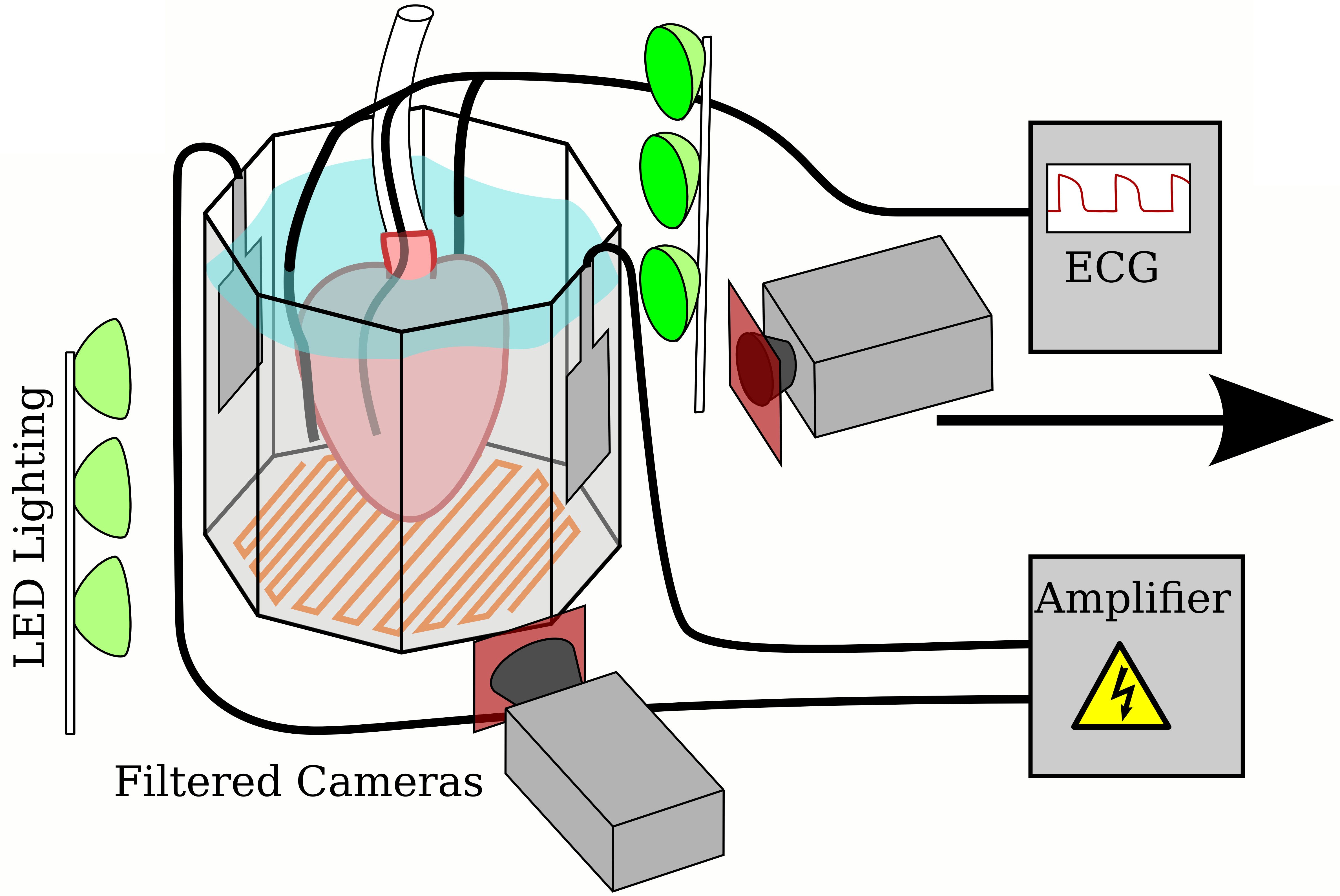
Optical Mapping

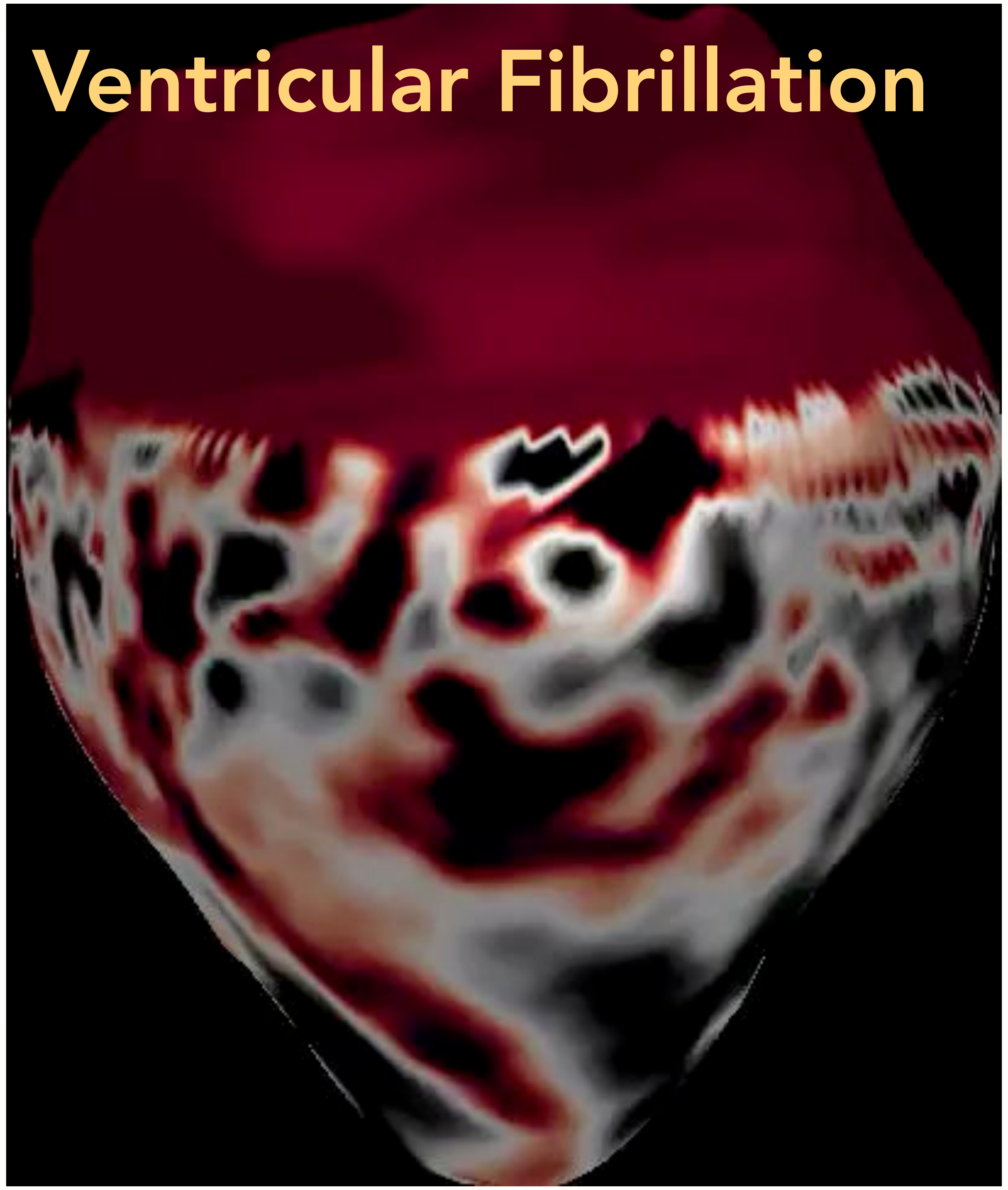
Visualisation of **membrane voltage** and **Ca^{+} concentration** on the **surface of the heart** using **fluorescent dyes**



Optical mapping in Langendorff perfusion system

using voltage sensitive fluorescent dyes



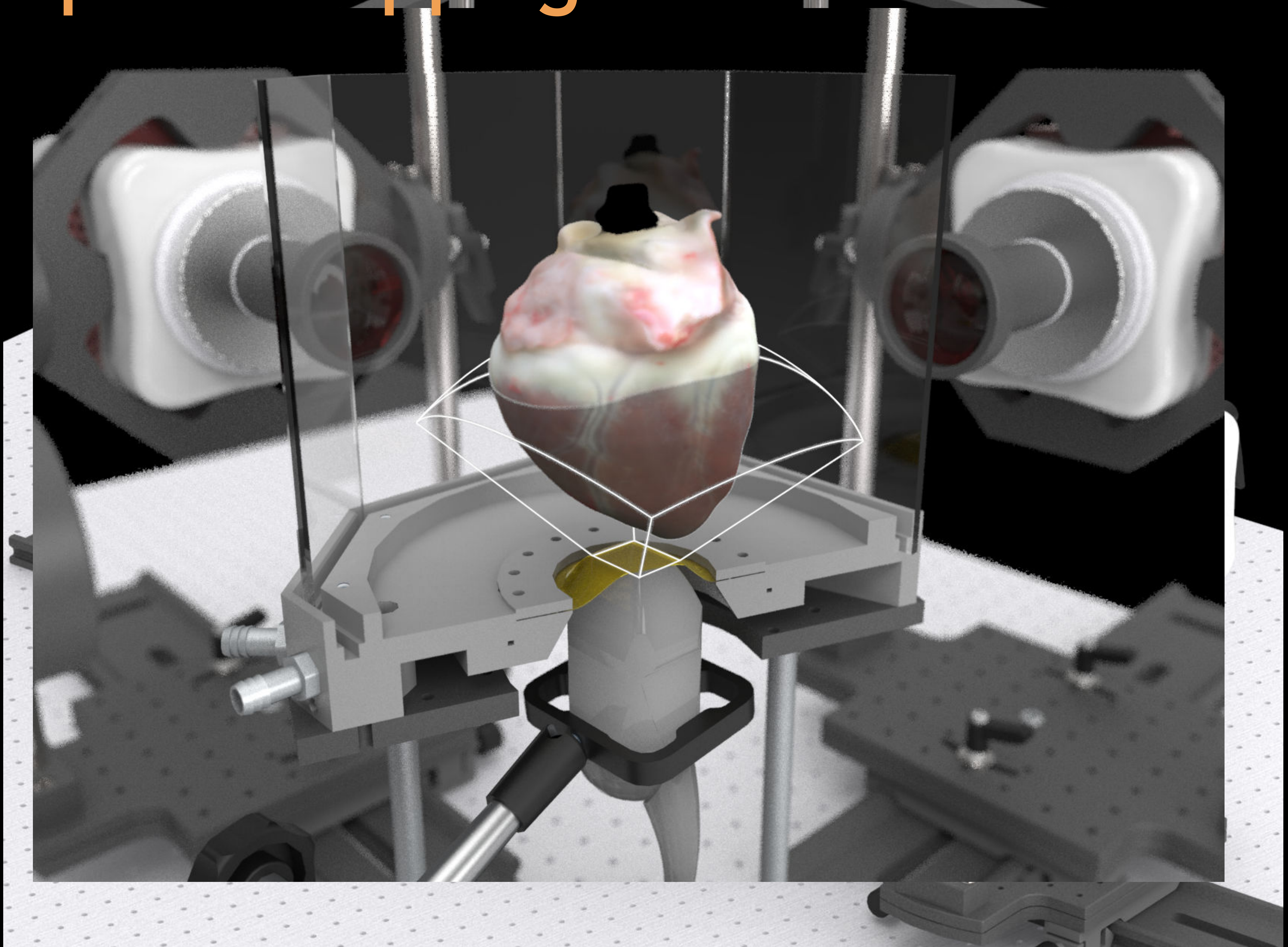


pig heart

100.000 – 200.000 cases of sudden cardiac deaths in Germany per year

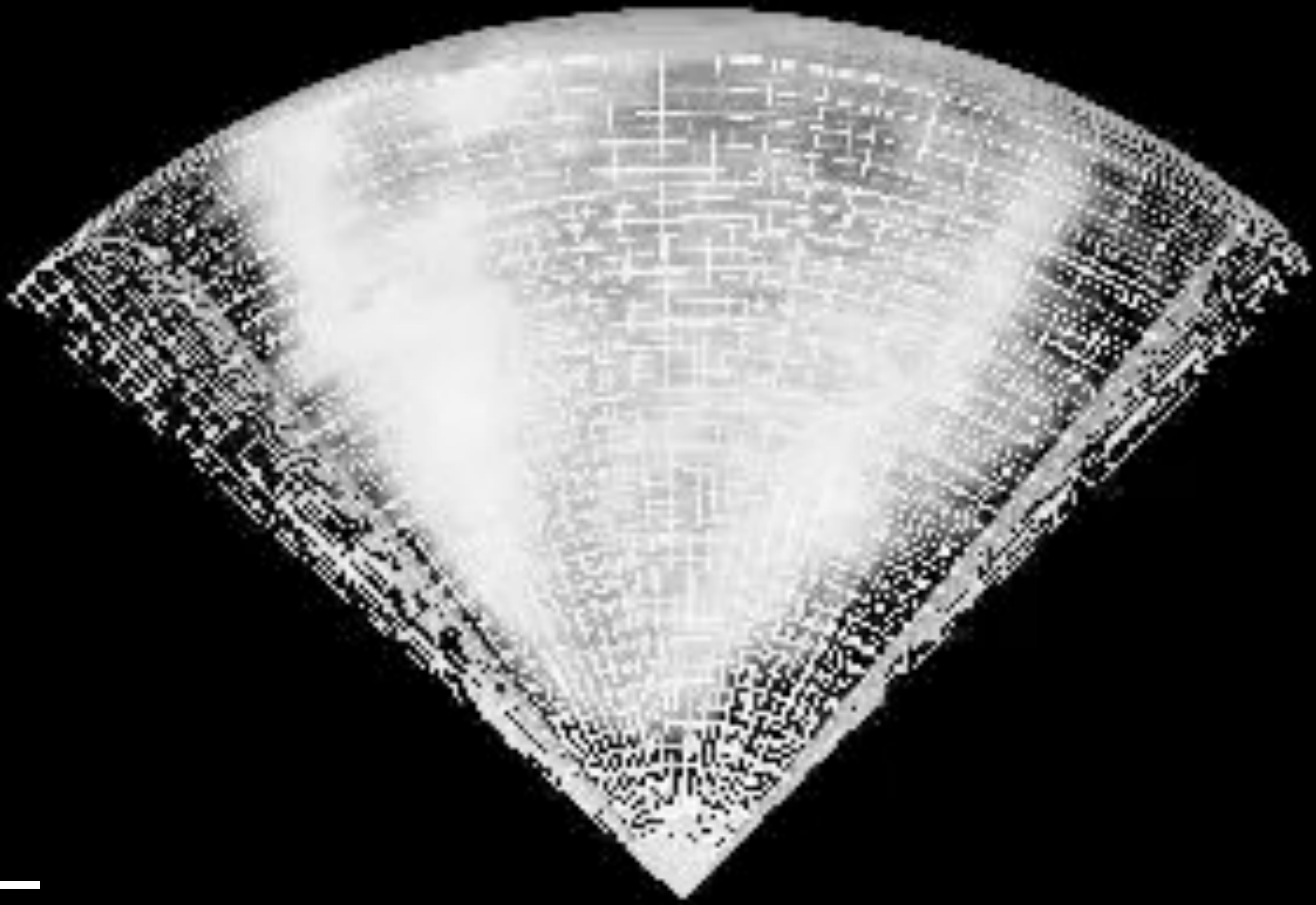
J. Schröder-Schetelig

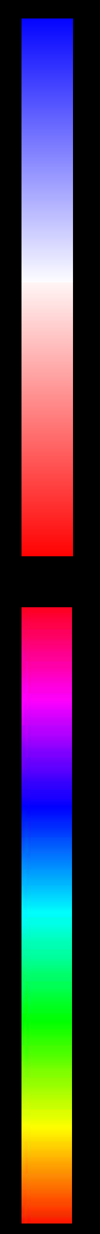
Optical Mapping and 4D Ultrasound



Visualizing mechanical scroll waves within the heart muscle using highspeed ultrasound

Mechanical Filament





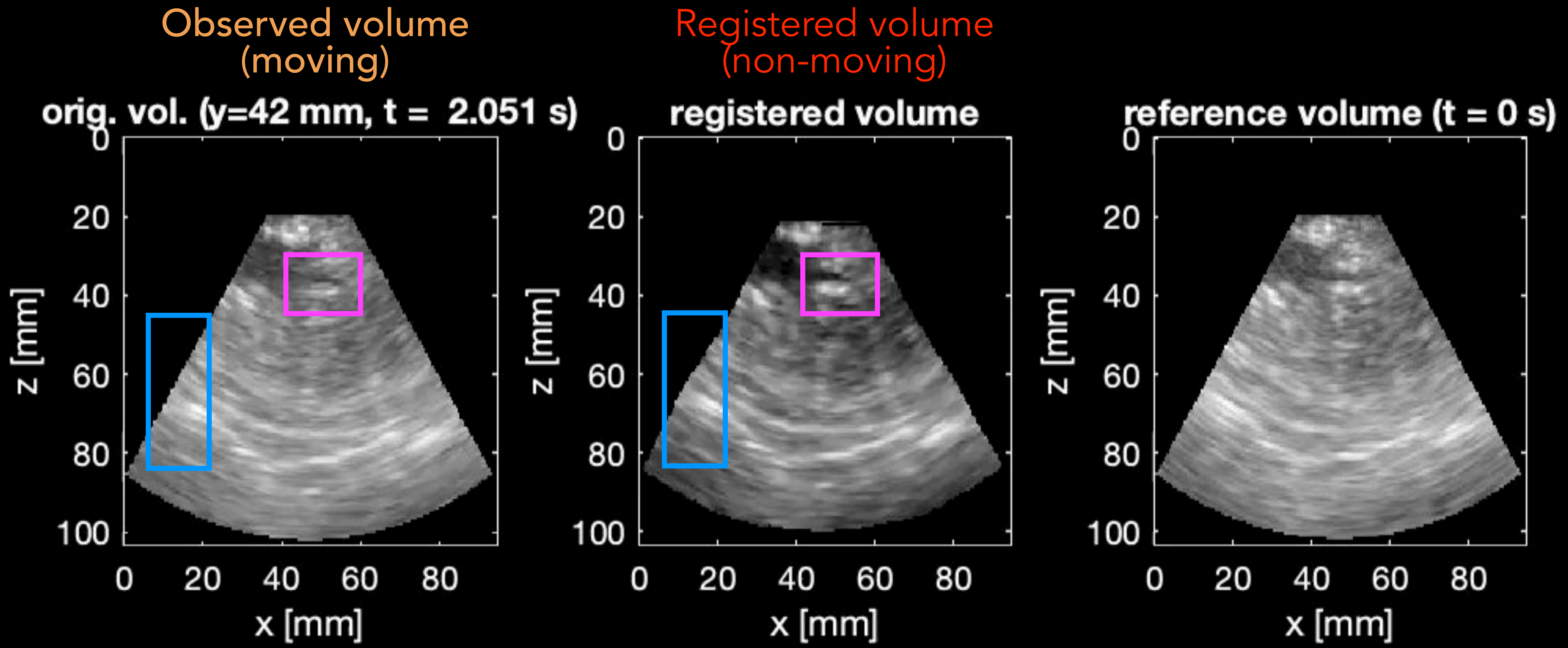
Acuson SC2000 (Siemens Inc.),
Transducer 4Z1c,
2.8 MHz,
134 vps,
0.5 mm

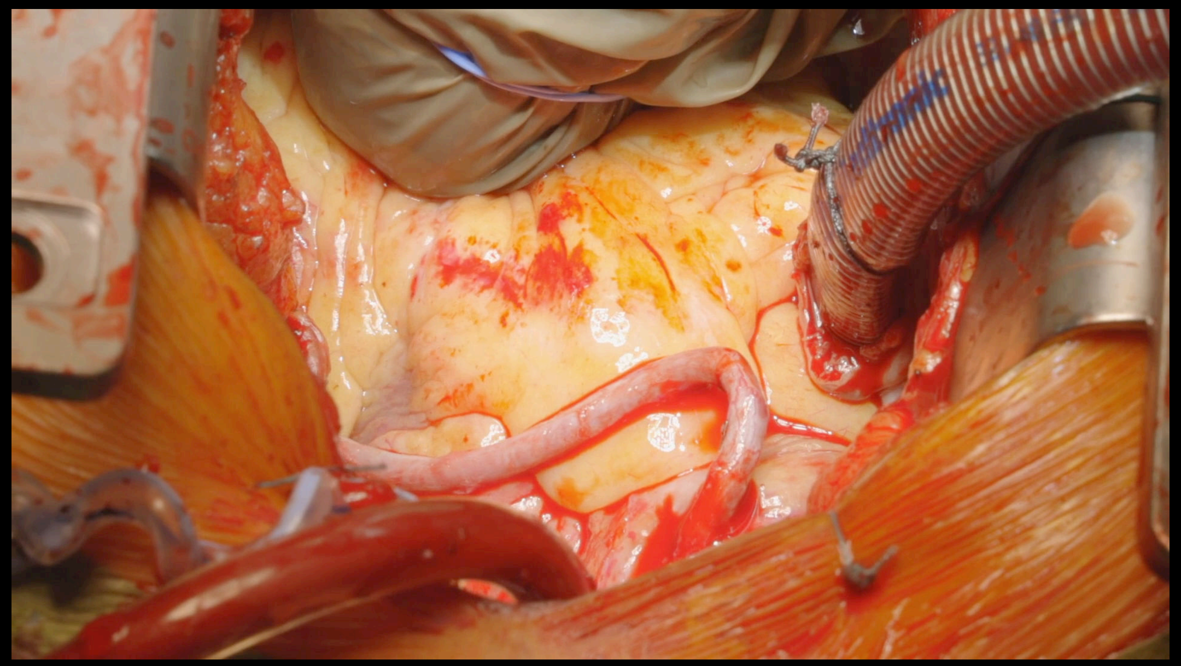
1 cm

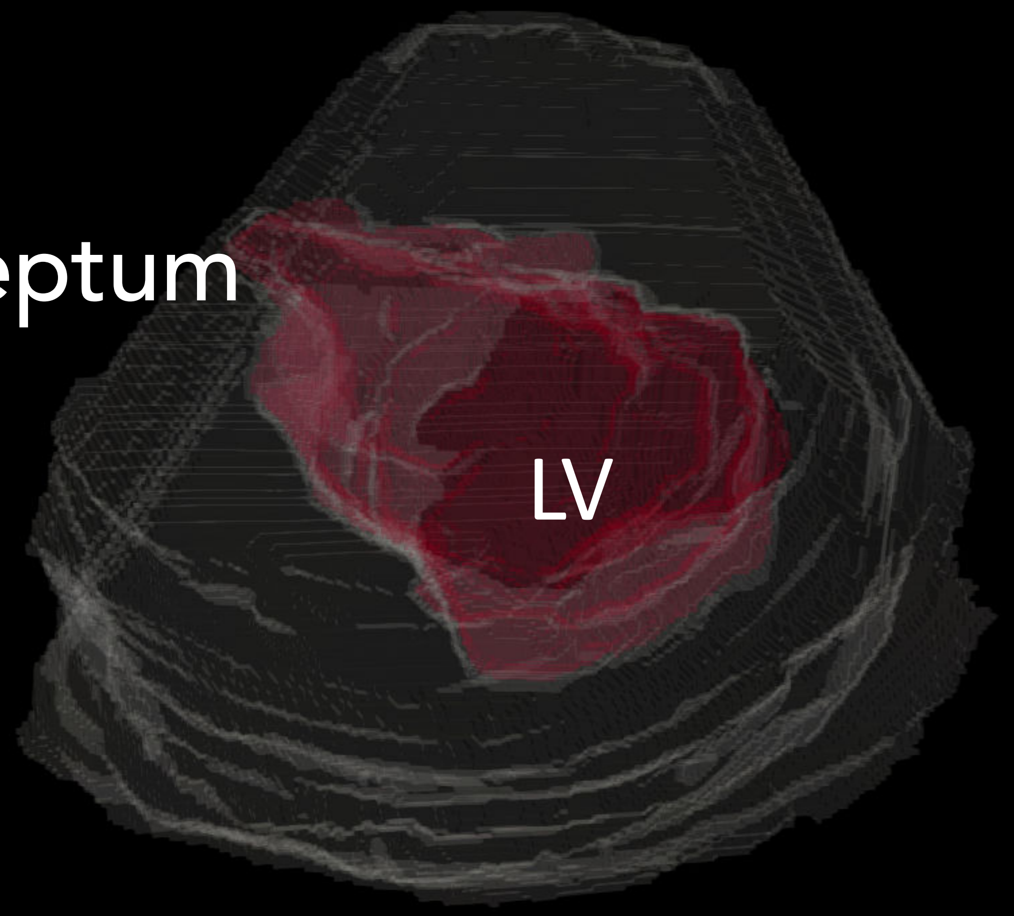
J. Christoph et al.
Nature (2018)

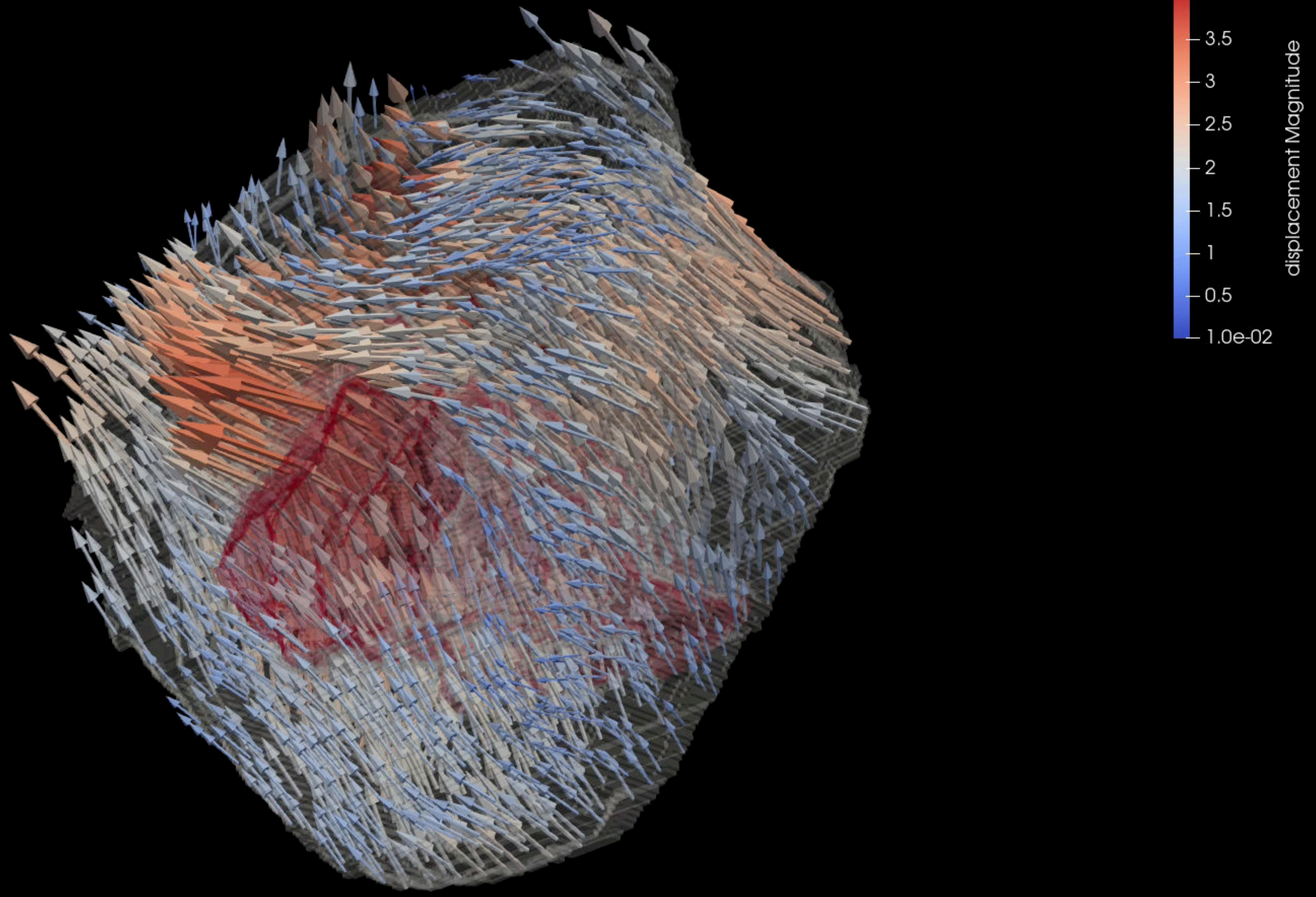
Ultrasound imaging of a human heart during by-pass surgery

Motion analysis estimates a **3D displacement vector field** that describes the motion of the tissue









- In 1874, Vulpian coined the term "mouvement fibrillaire" for chaotic muscular movements of the ventricles
- High-resolution 4D ultrasound resolves mechanical motion during ventricular fibrillation

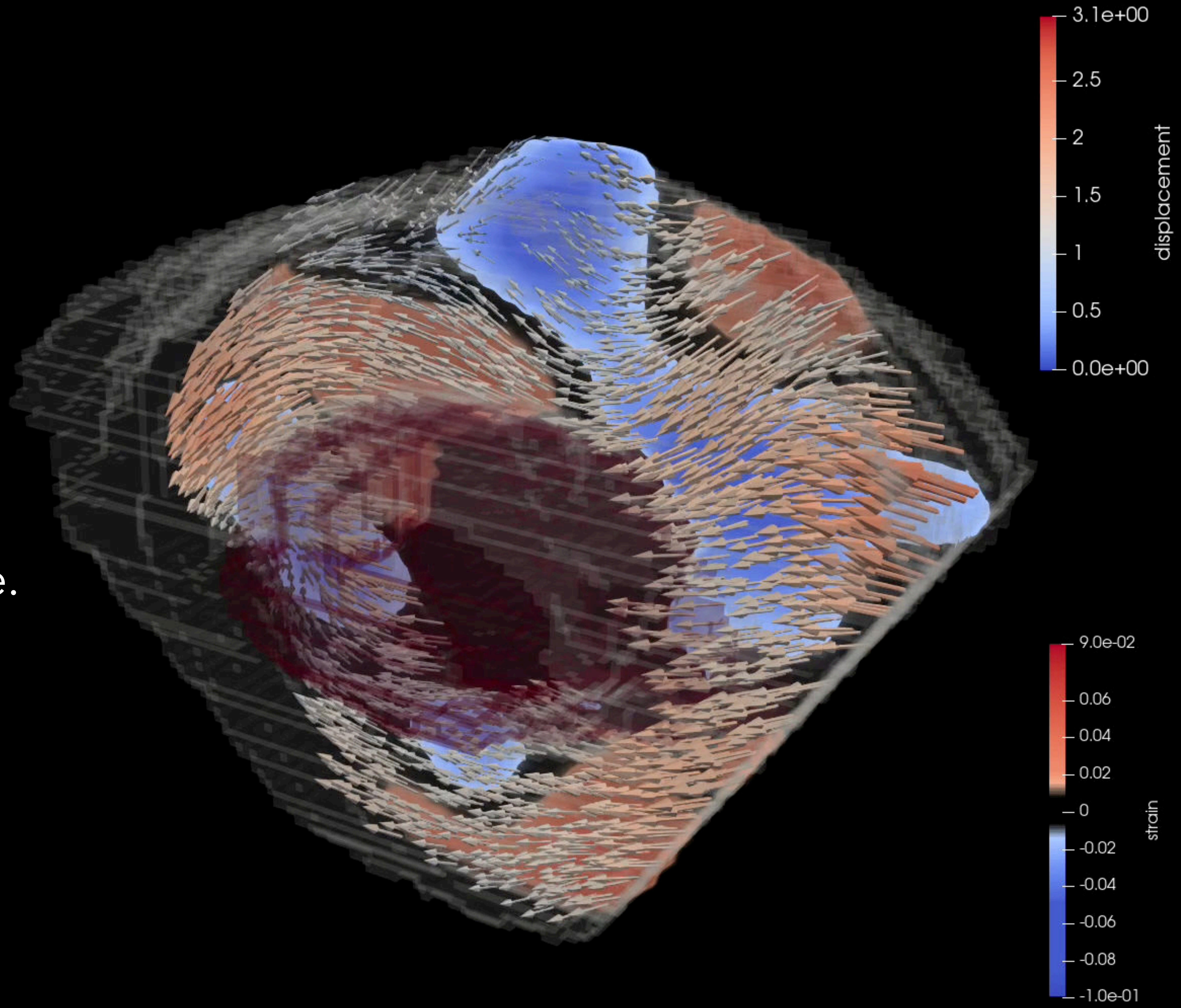
displacement vector field

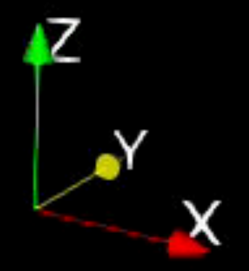
↓

strain tensor

↓

change of tissue volume, i.e.
compression or **dilatation**





Summary

The heart

- consists of a network of electrically and mechanically coupled excitable elements
- forming an excitable medium that supports plane waves, spiral waves, and
- (life-threatening) **spatio-temporal chaos** (e.g., ventricular fibrillation)
- which can be experimentally observed using optical mapping and high-speed ultrasound

Outlook:

- data driven modelling of cardiac dynamics
- transient spatiotemporal chaos
- (low-energy) defibrillation using sequences of weak pulses

Acknowledgement

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Thank you!