Modelling and controlling complex dynamics in cardiac networks

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Outline

- data driven modelling in cardiac research
- transient chaos in cardiac arrhythmias
- termination of spatio temporal chaos and defibrillation

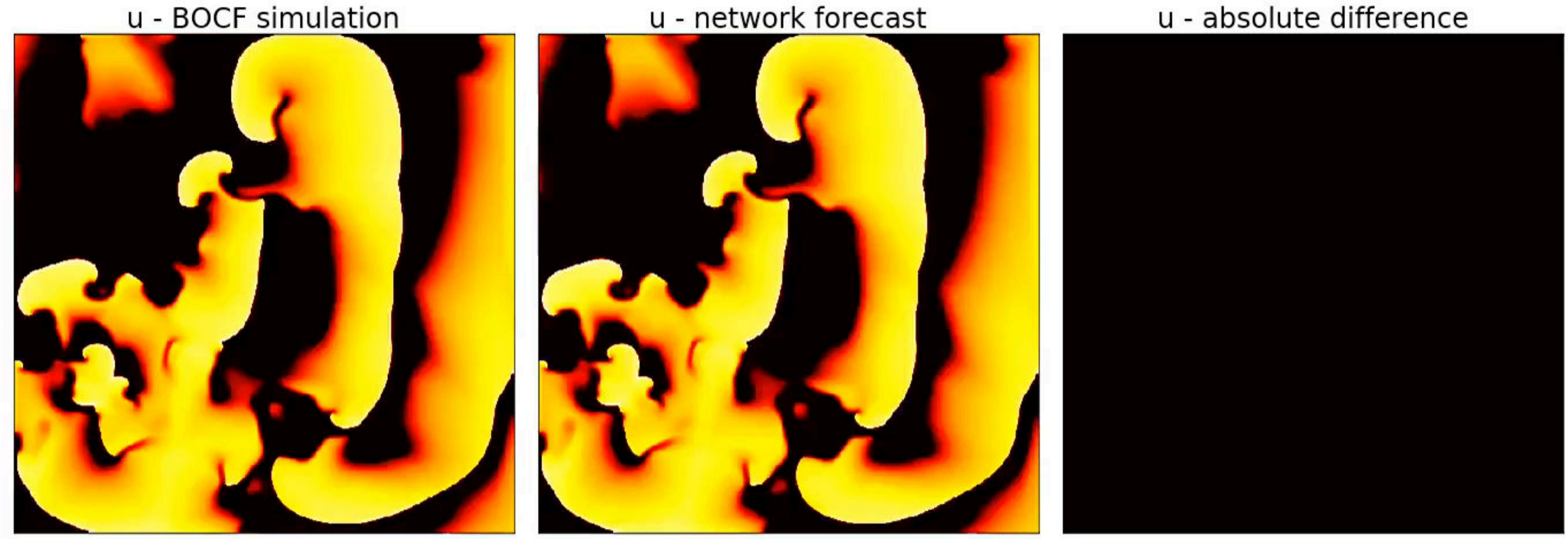
Data driven modelling in cardiac research

includes:

- data driven prediction of future evolution (e.g., membrane voltages, mechanical motion)

Iterated Forecasting of $u(t)$

true forecast difference



good for 5 spiral rotations

S. Herzog et al., Frontiers in Appl. Math. and Statistics 4, 60 (2018)

Data driven modelling in cardiac research

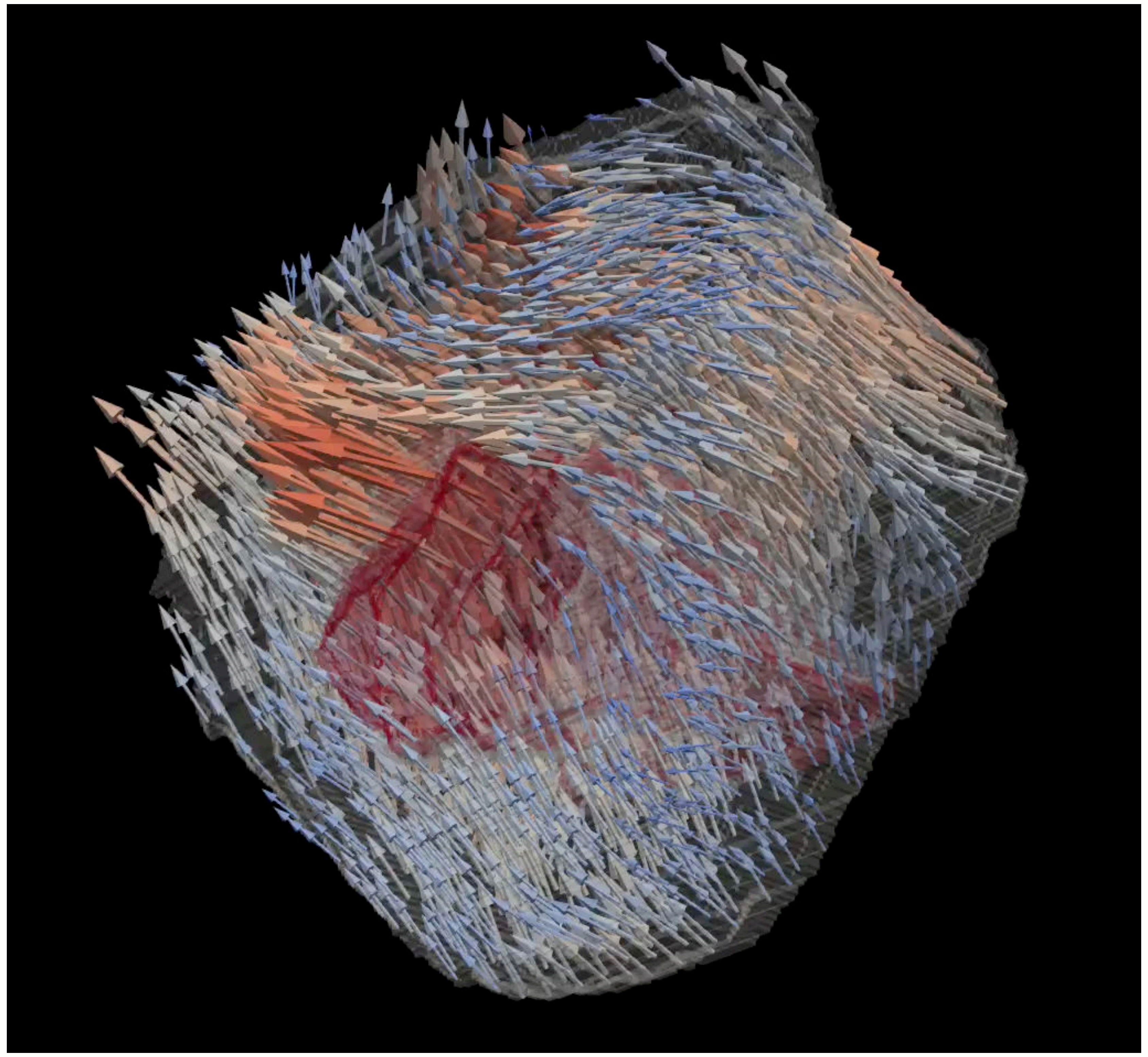
includes:

- data driven prediction of future evolution (e.g., membrane voltages, mechanical motion)
- extraction of relevant features from (noisy) raw data
  (S. Herzog et al., Frontiers Appl. Math. Stat. 6 (2021))
- classification (e.g., time series, images, evolution of patterns and shapes)
- cross estimation of observables that are difficult to measure directly from available data

Measurement Modalities

mechanical motion

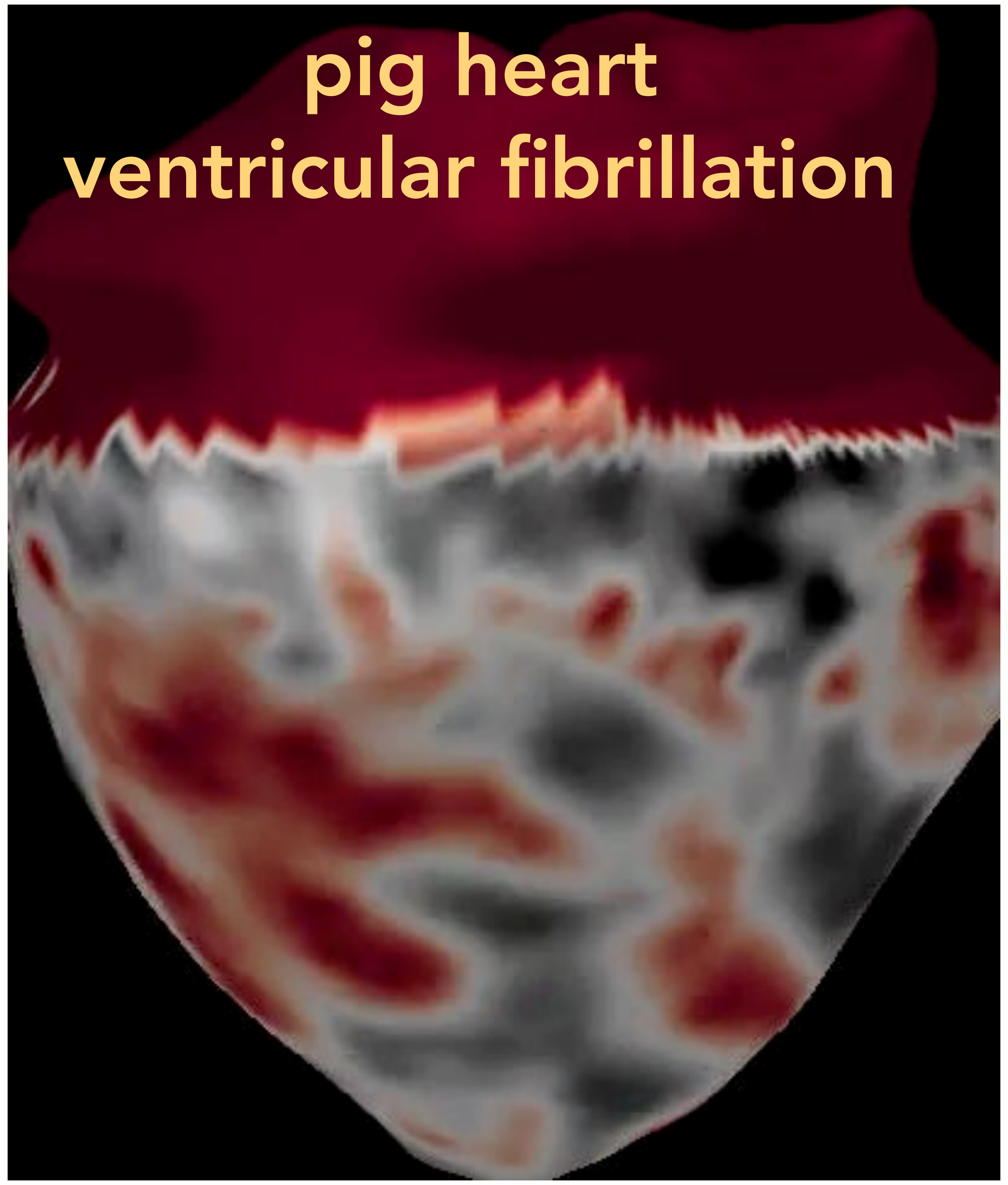
4D ultrasound



- real-time MRI
- multi-camera systems *

electrical excitation

voltage sensitive dyes*



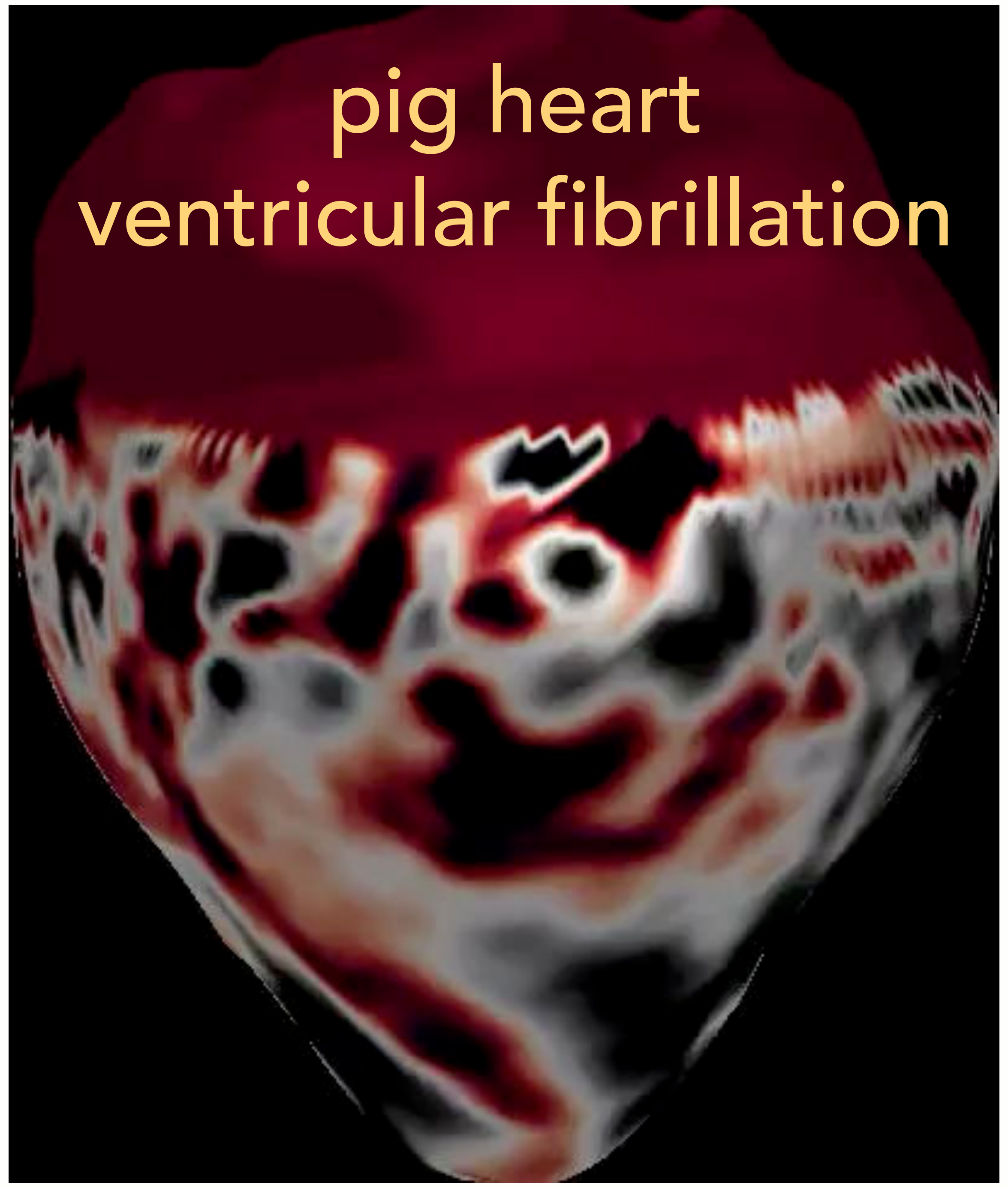
- multichannel - ECG

*surface only!

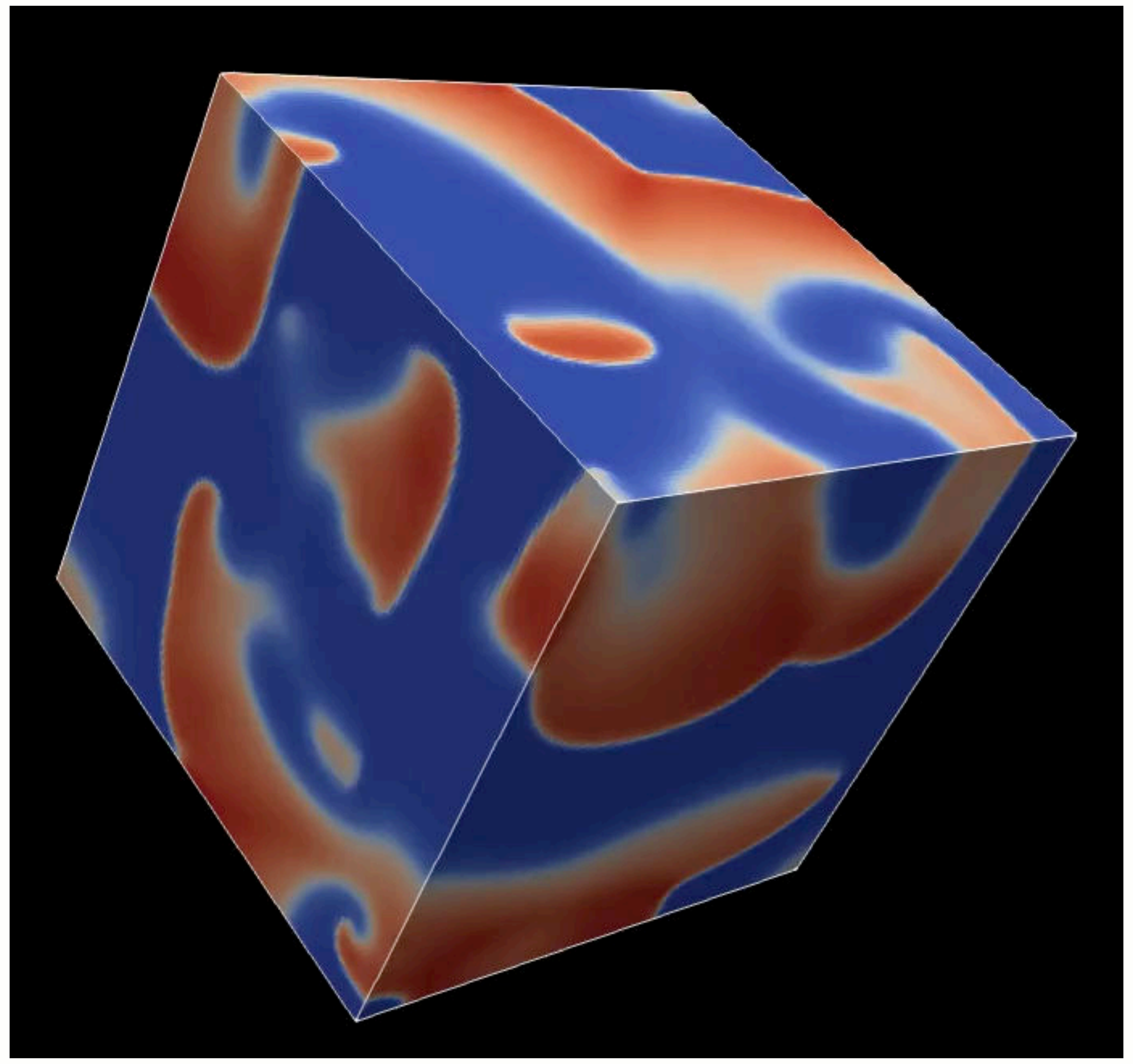
From the surface into the depth

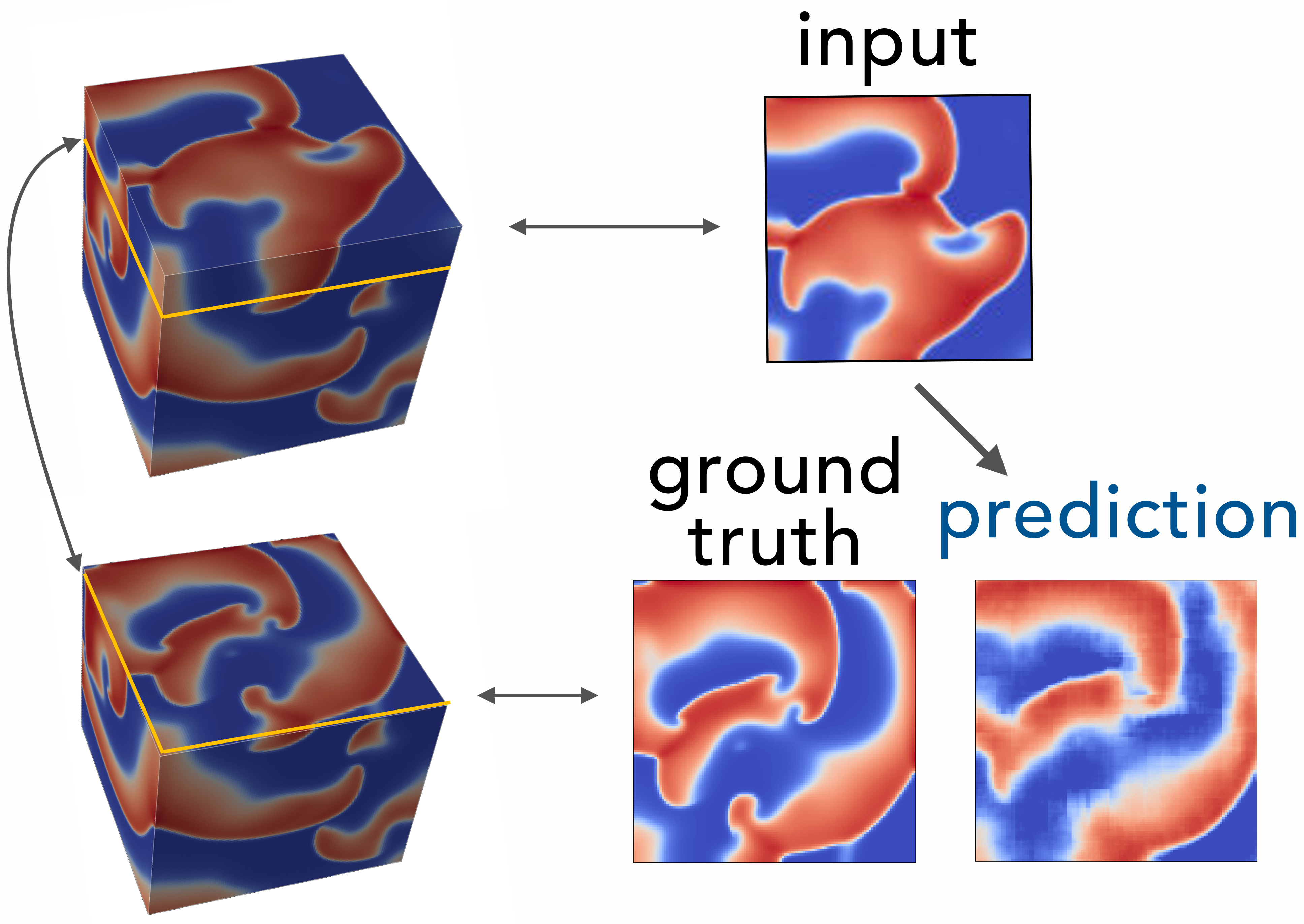
optical mapping using voltage sensitive dyes provides electrical excitation waves only on the surface of the heart

predict activity in deeper layers using Convolutional Neural Network



simulation of a 3D excitable medium





Inga Kottlarz

From Surface To Depth

3D Barkley model

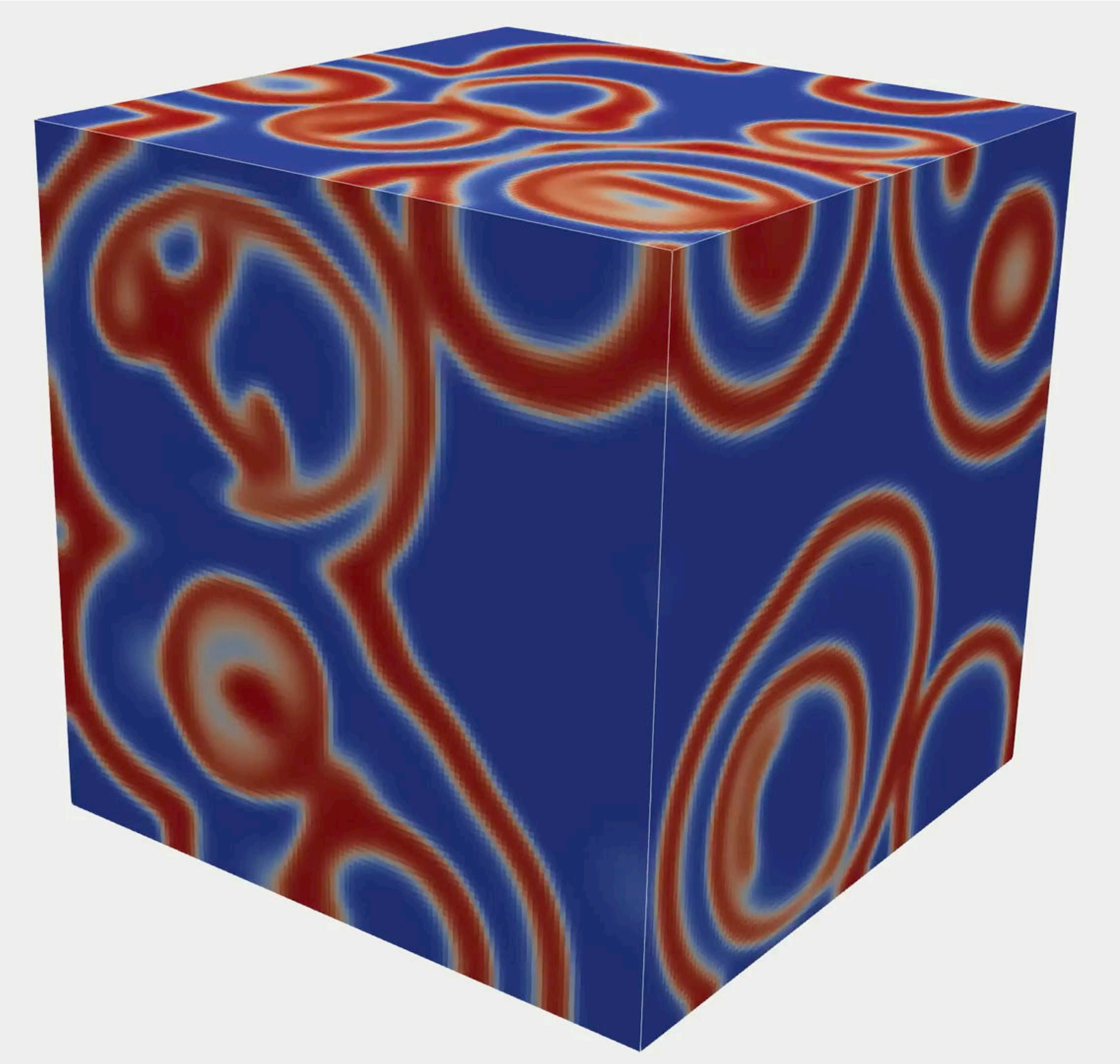
$$\frac{du}{dt} = D\nabla^2 u + \frac{1}{\varepsilon} u(1-u)\left(u - \frac{v+b}{a}\right)$$
$$\frac{dv}{dt} = u^3 - v$$

$a = 0.75$ $b = 0.06$ $\varepsilon = 0.08$ $D = 0.02$

grid: $120 \times 120 \times 120$

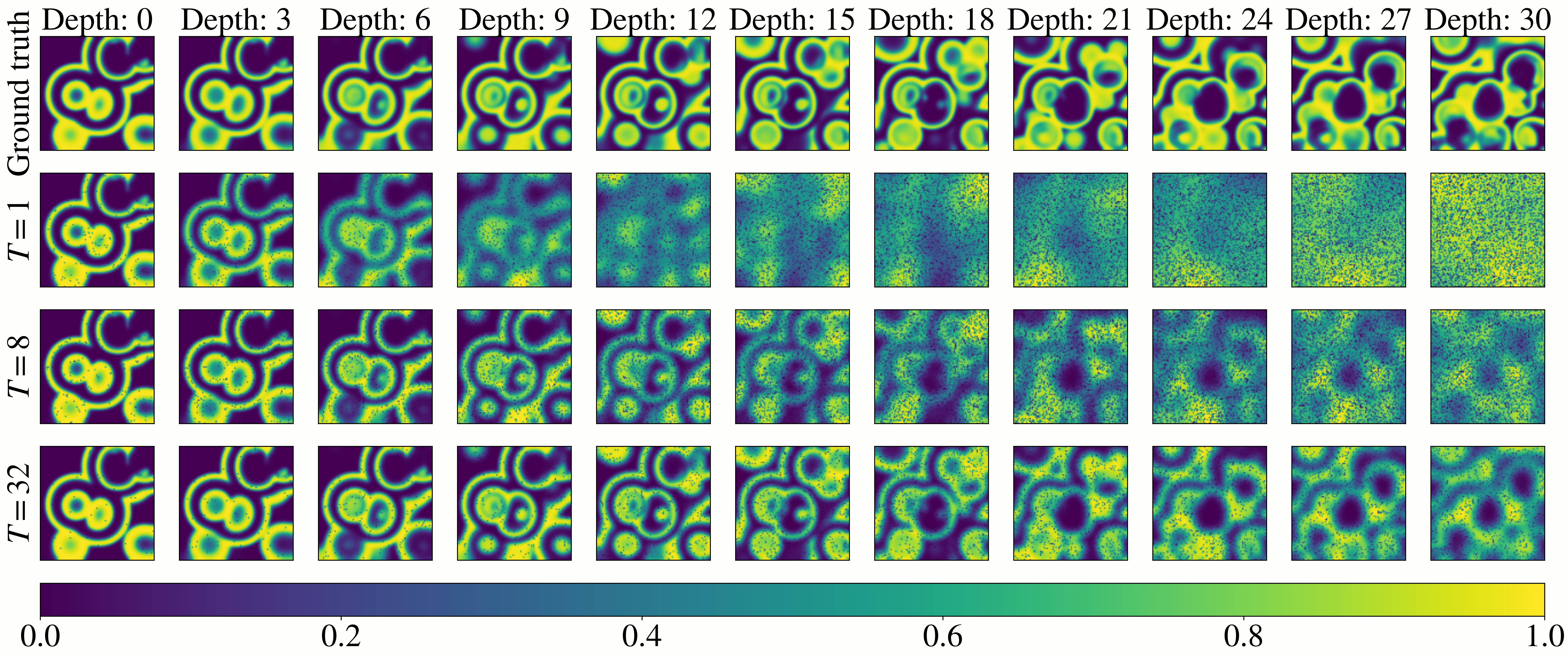
predict deeper layers from data at surface

using convolutional neural networks



Inga Kottlarz

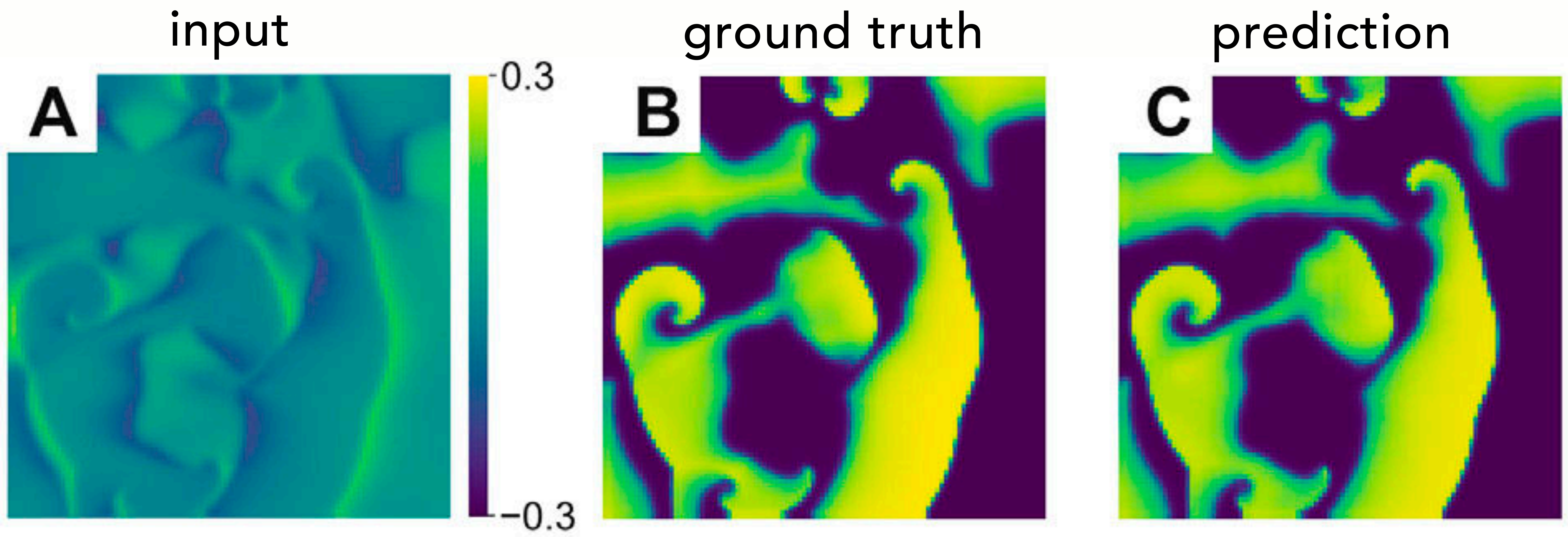
Reconstructions with different input lengths $T \in \{1, 8, 32\}$



Sebastian Herzog

Electrical excitation from mechanical deformation

mechanical deformation → **electrical excitation**



Data generated by a conceptual electro-mechanical model (BOCF model driving a mass-spring system)
Convolutional Auto-encoder provides better results than Reservoir Computing)

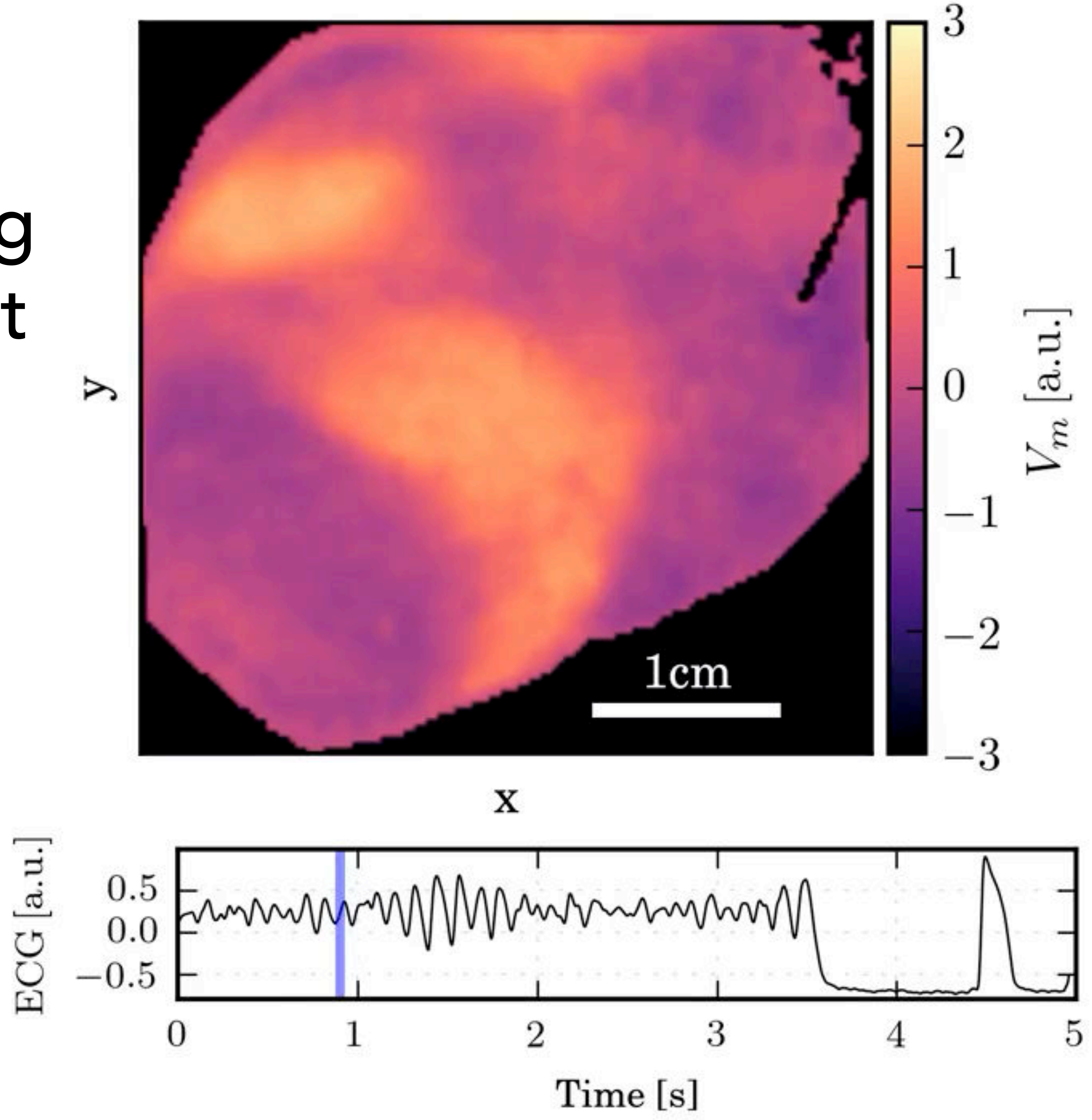
S. Herzog et al., Frontiers Appl. Math. Stat. 6 (2021)

Transient Chaos in Cardiac Arrhythmias

Transient Scroll Wave Dynamics during Ventricular Fibrillation

Experiment

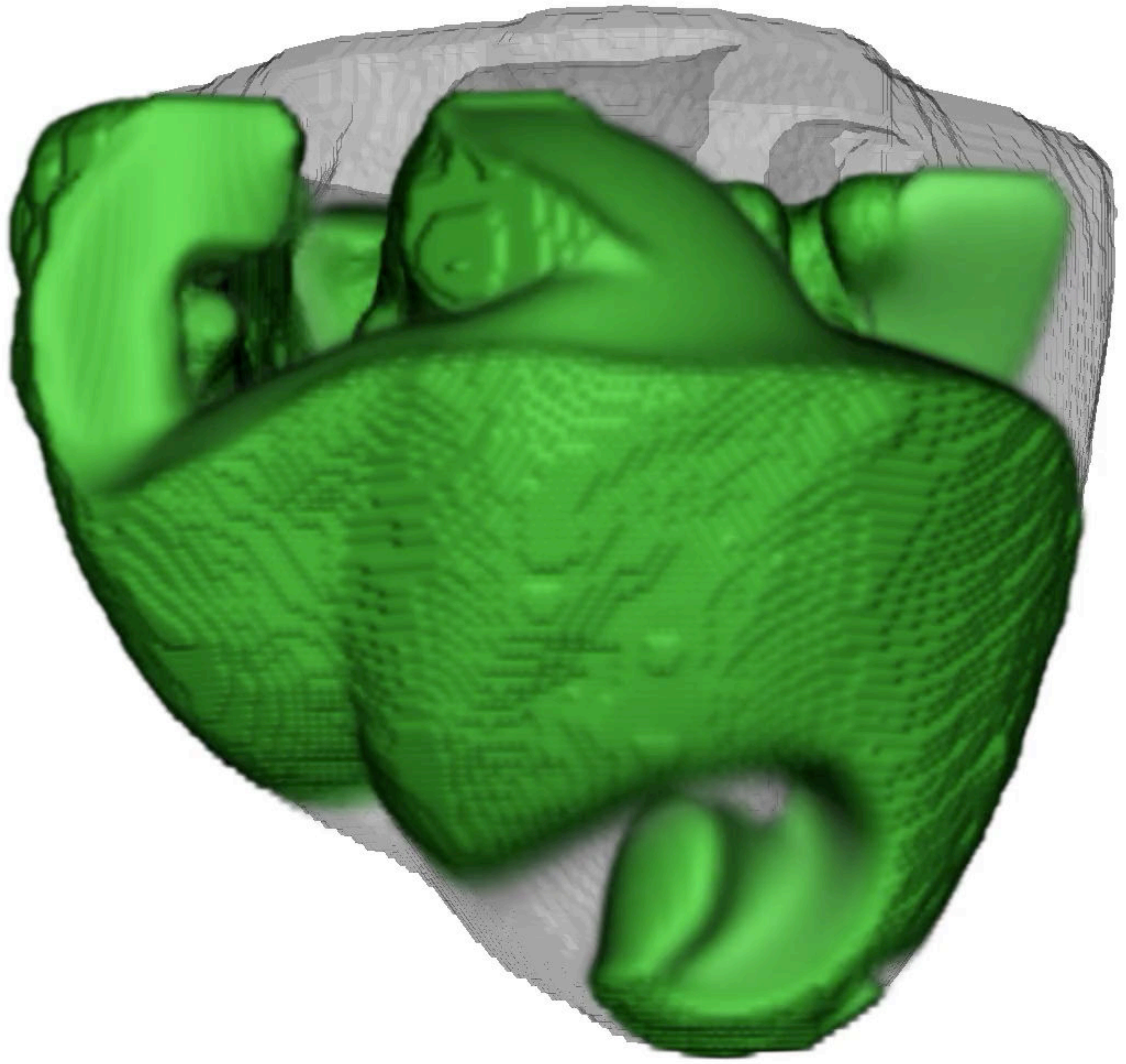
Optical mapping of a rabbit heart



Sebastian Berg
Daniel Hornung
Marion Kunze

Simulation

in a rabbit heart geometry



Thomas Lilienkamp

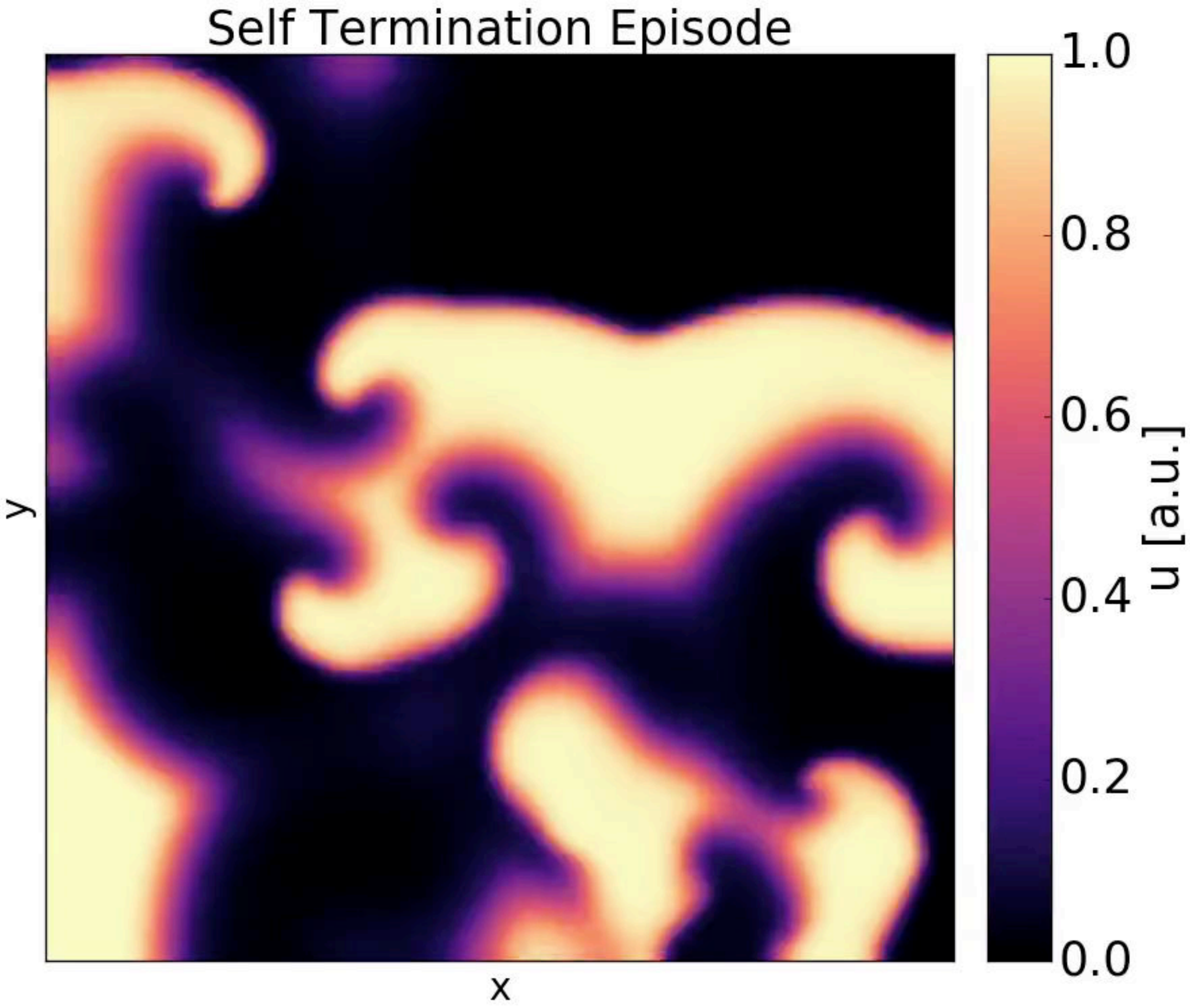
Transient Chaos

Simulation using the Fenton-Karma model

$$\frac{\partial u}{\partial t} = \nabla \cdot \underline{\mathbf{D}} \nabla u - I_{Ion}(u, \mathbf{h})/C_m$$
$$\frac{\partial \mathbf{h}}{\partial t} = \mathbf{g}(u, \mathbf{h})$$

gating variables $\mathbf{h} = (v, w)$

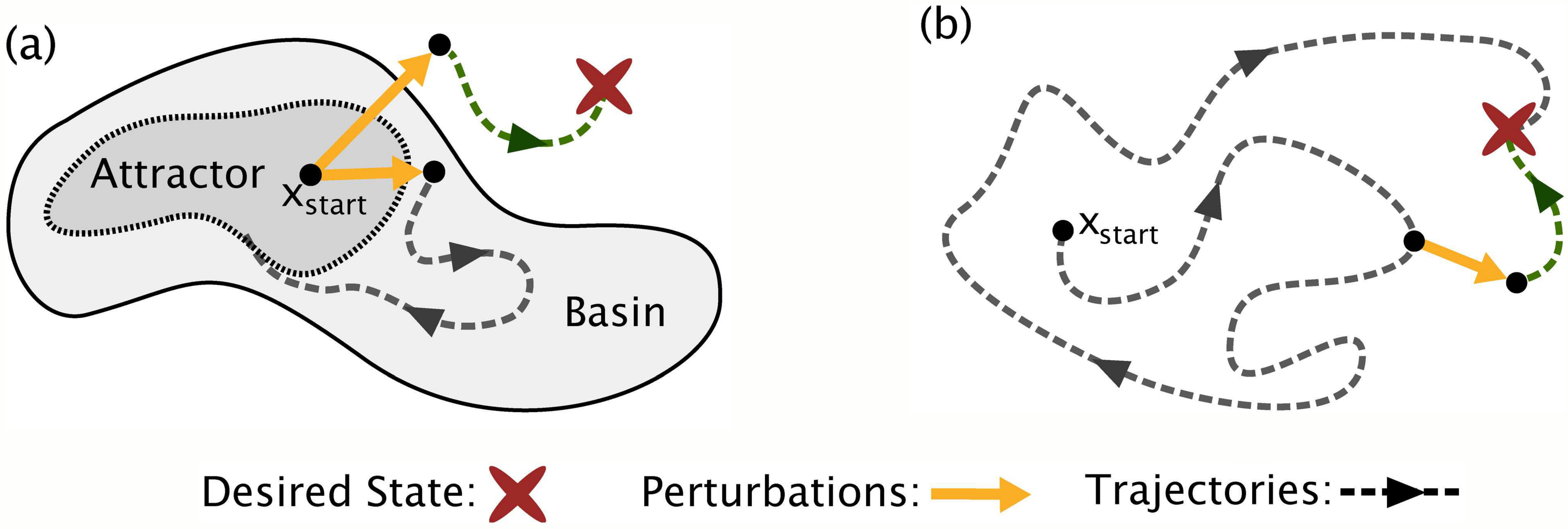
average transient lifetime increases exponentially with system size



T. Lilienkamp et al., Phys. Rev. Lett. 119 (2017)
T. Lilienkamp and U. Parlitz, Phys. Rev. Lett. 120 (2018)

Potential Implications of Transient Chaos for Defibrillation

Persistent chaos vs. Transient chaos



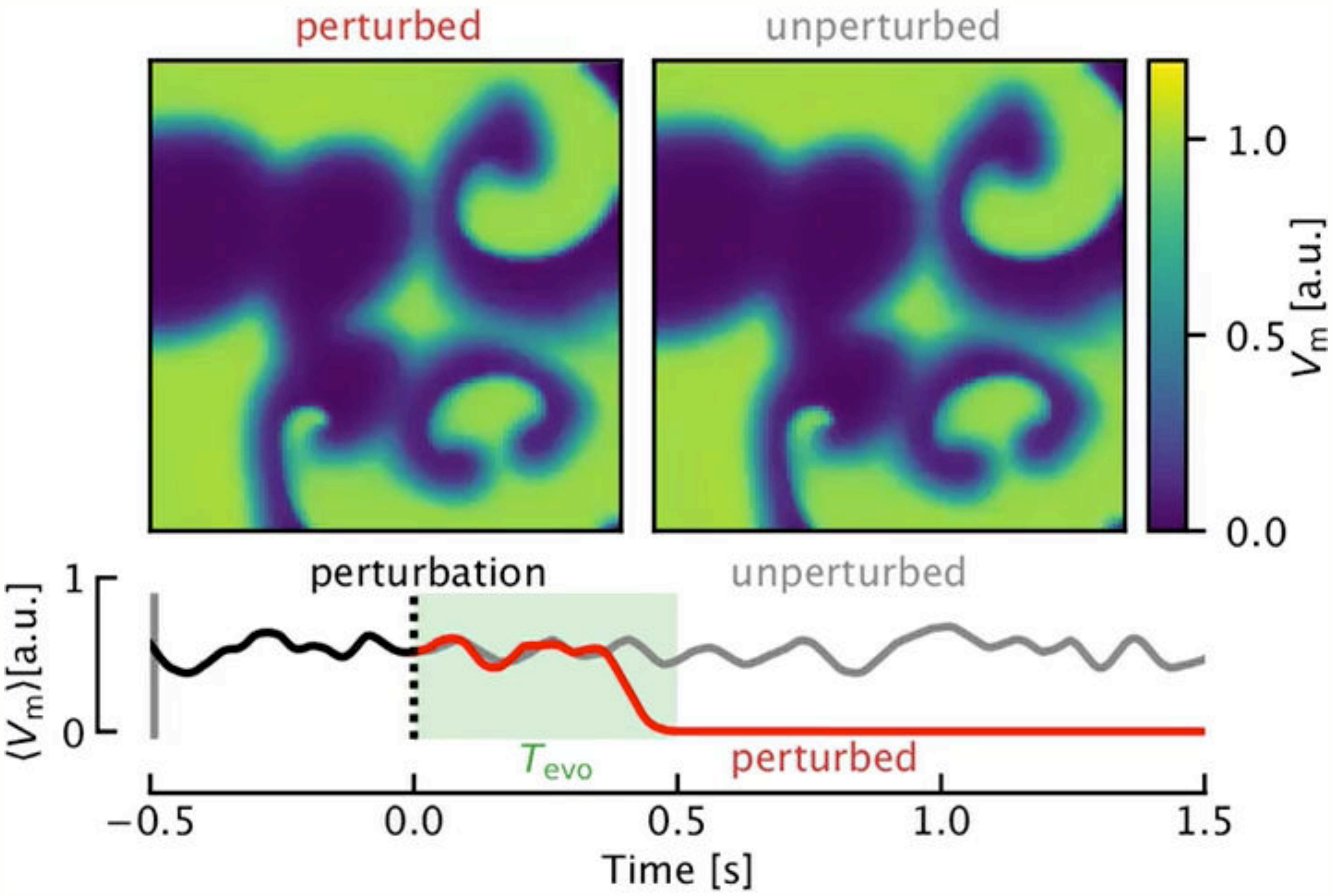
control: kick state into basin of another attractor | kick state to neighbouring orbit with (much) shorter transient time

minimal perturbation strength required | can be achieved with (very) small perturbations

Terminating spiral wave chaos a with few single perturbations

Fenton-Karma model

T_{evo}= 500 ms



T. Lilienkamp and U. Parlitz, Chaos 30, 051108 (2020)

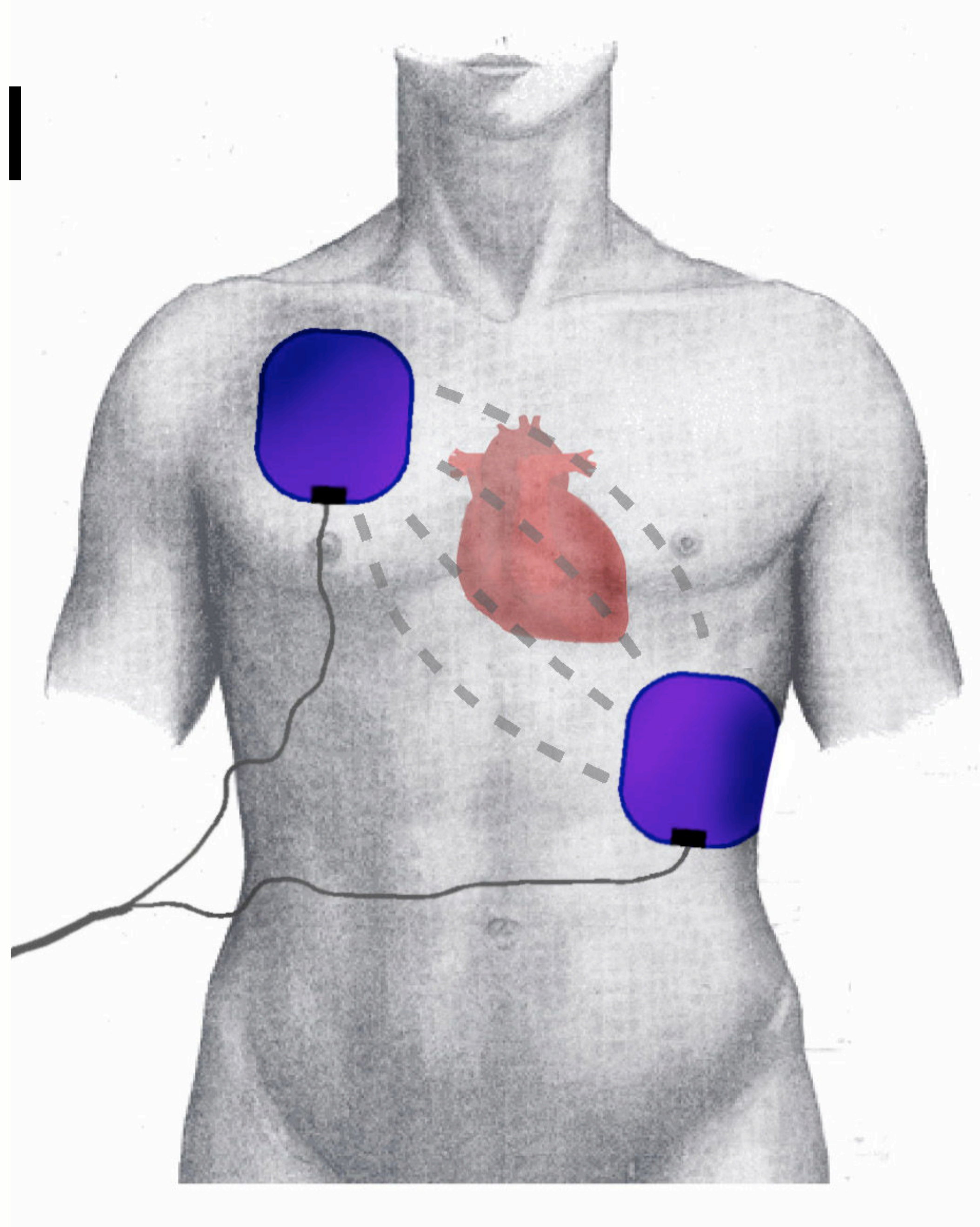
Terminating Cardiac Arrhythmias (Defibrillation)

Terminating Cardiac Arrhythmias

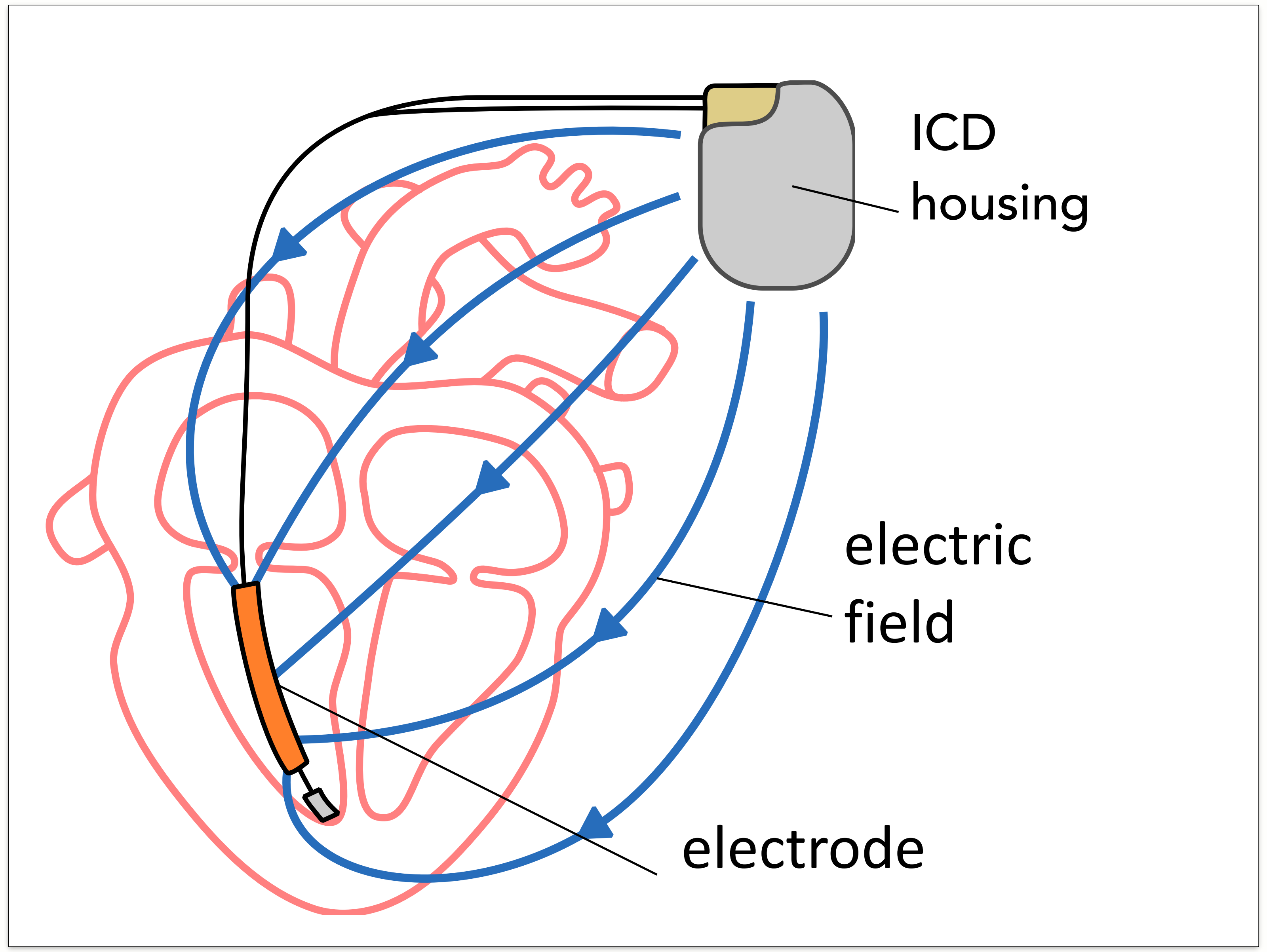
Defibrillation

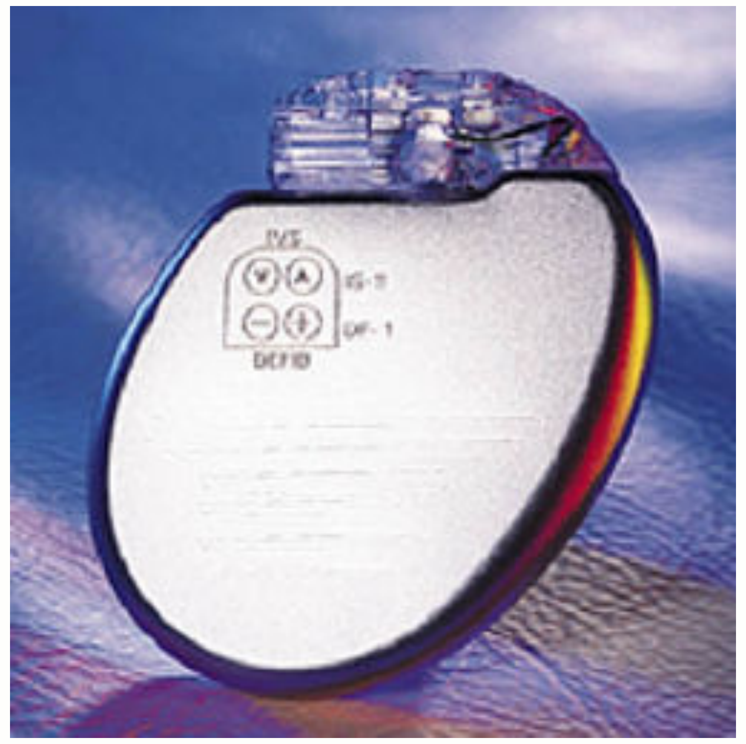
Principle: Reset electrical activity of all cells by synchronous excitation

external



internal



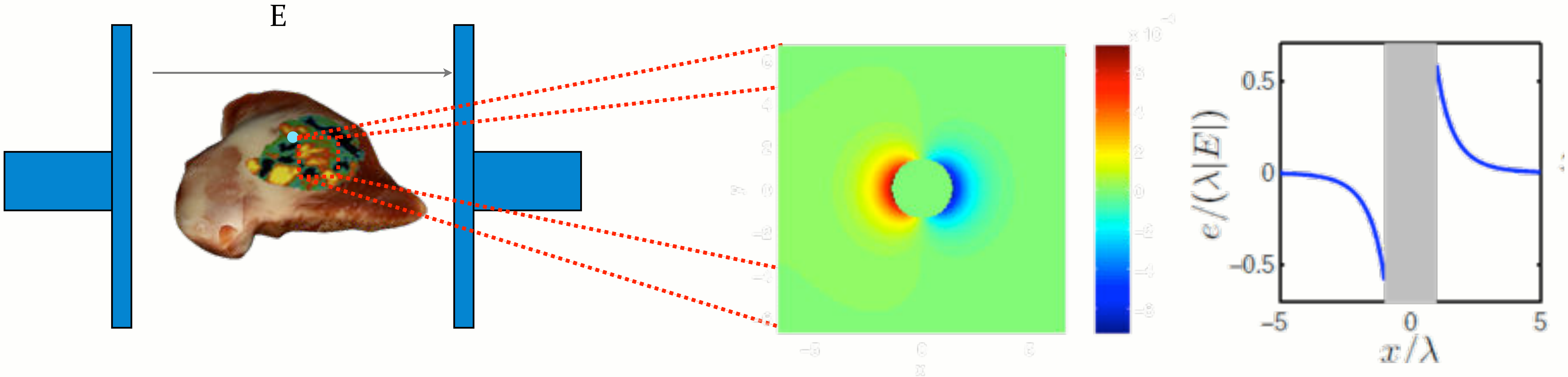


Electric shocks: energy 360J (external) 40 J (internal) 1000 V 30 A 12 ms

Severe side effects: tissue damage - traumatic pain

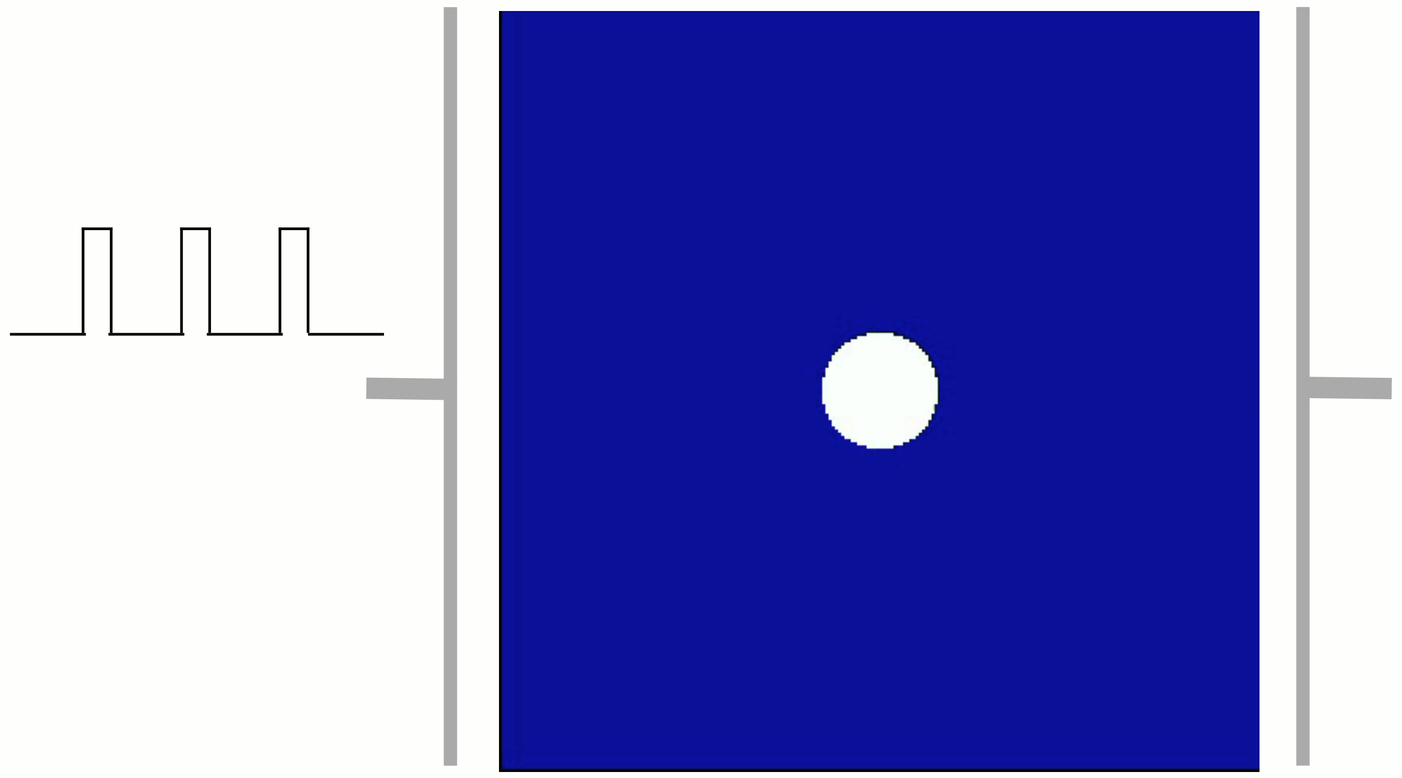
G.P. Walcott et al., Resuscitation 59, 59-70 (2003)

Virtual Electrodes



Blood vessels, scars, fatty tissue

- are obstacles to electrical conduction
- may act as virtual electrodes



Super-threshold depolarization leads to wave emission if a short rectangular electric field pulse is applied.

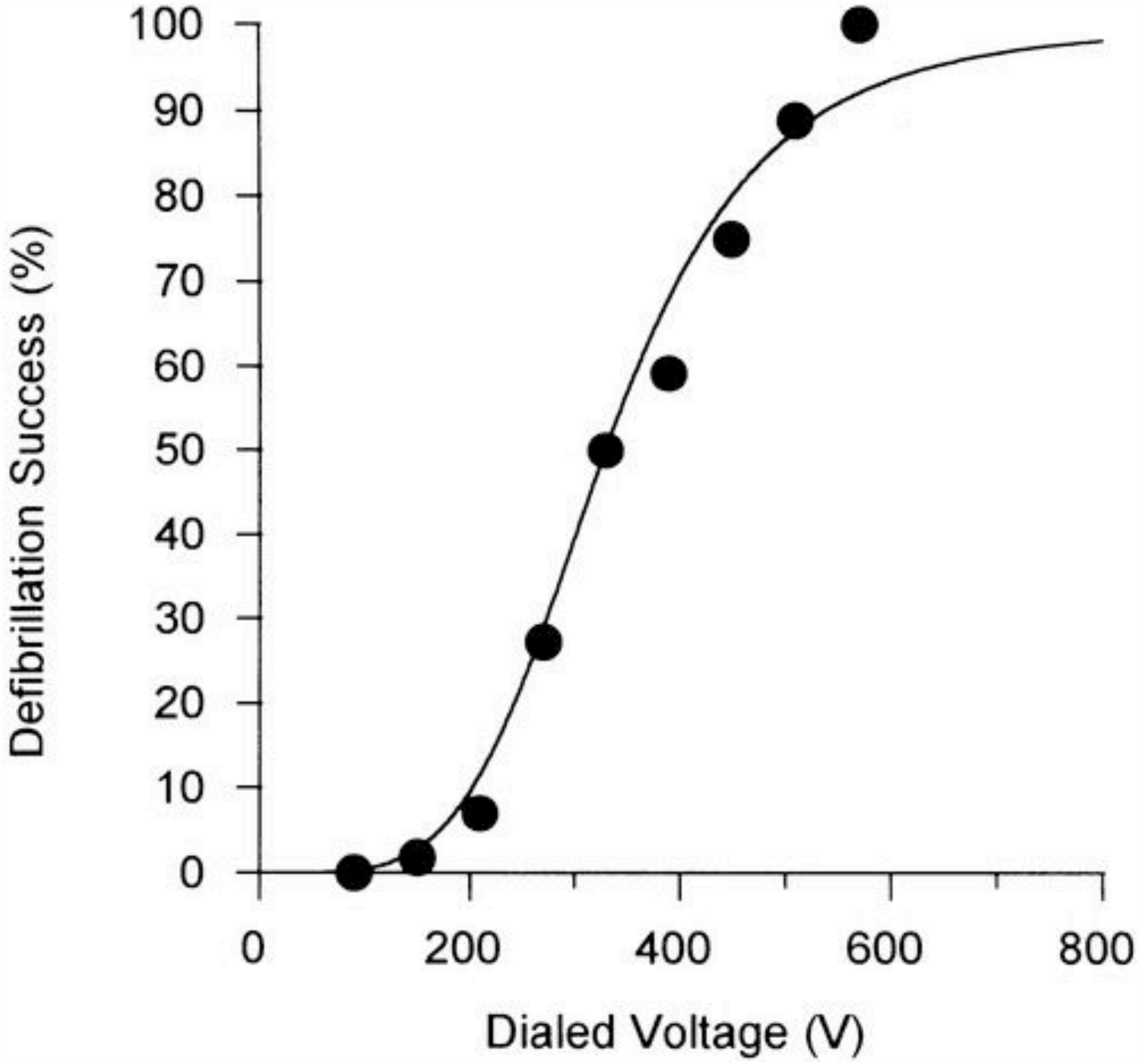
A. Pumir and V. Krinsky, J. Theor. Biol. 199, 311 (1999); P. Bittihn et al., Phys. Rev. Lett. 109, 118106 (2012)

Termination with a single electrical pulse - conventional defibrillation

Probability of defibrillation versus shock voltage for 273 shocks in 23 hearts

sigmoid dose-response curve

from: K.F. Kwaku and S.M. Dillon, Circulation Research 79, 957–973 (1996)

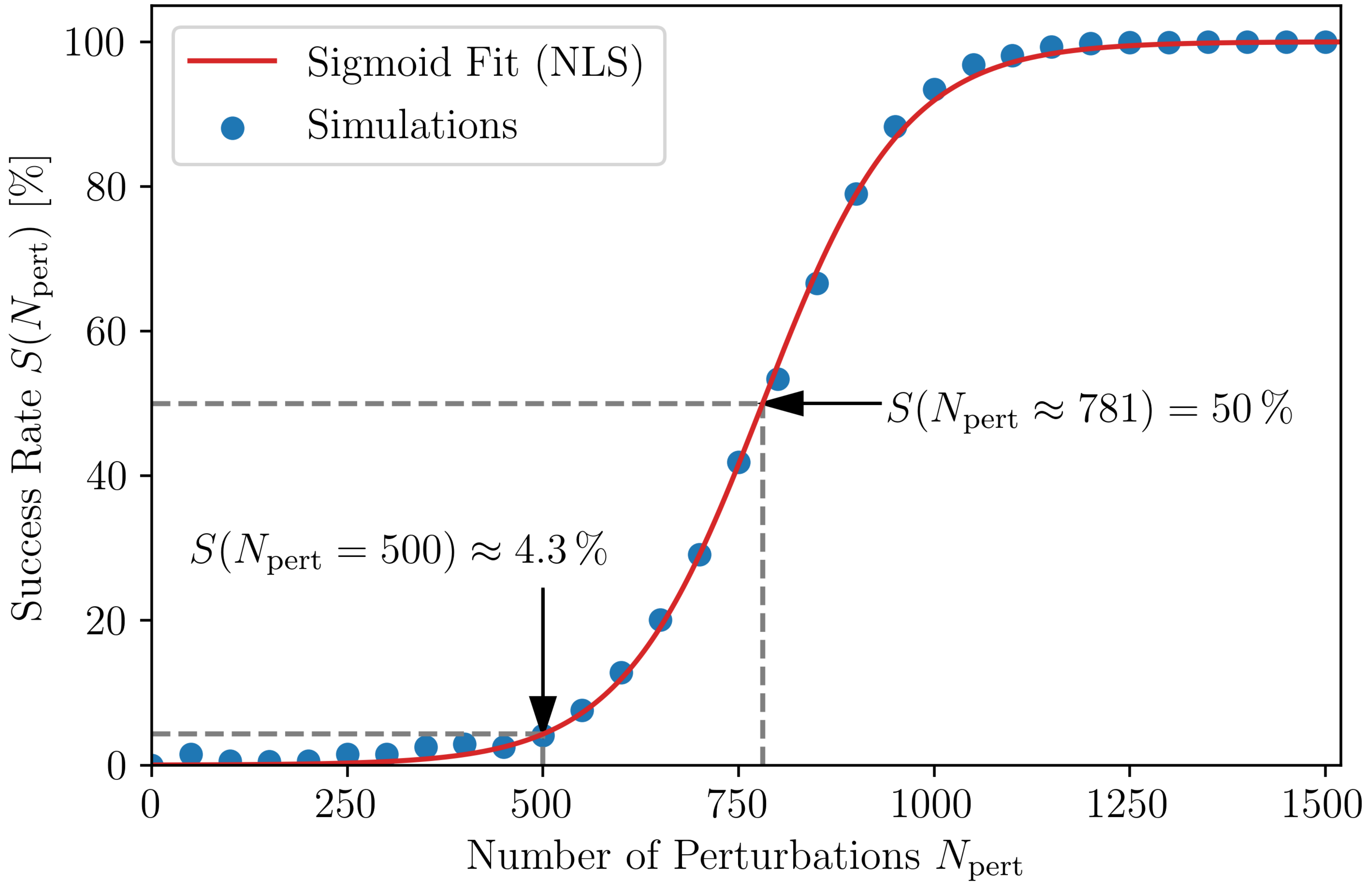


Pulse timing matters

simulation study with virtual electrodes simulated by local current injection

- 50 random configurations of N_{pert} perturbations sites acting like virtual electrodes
- 20 realisations (initial conditions)
- compute average success rate from 1000 examples for different numbers N_{pert} of activated virtual electrodes
- larger N_{pert} corresponds to higher field strengths of applied pulses

dose-response curve



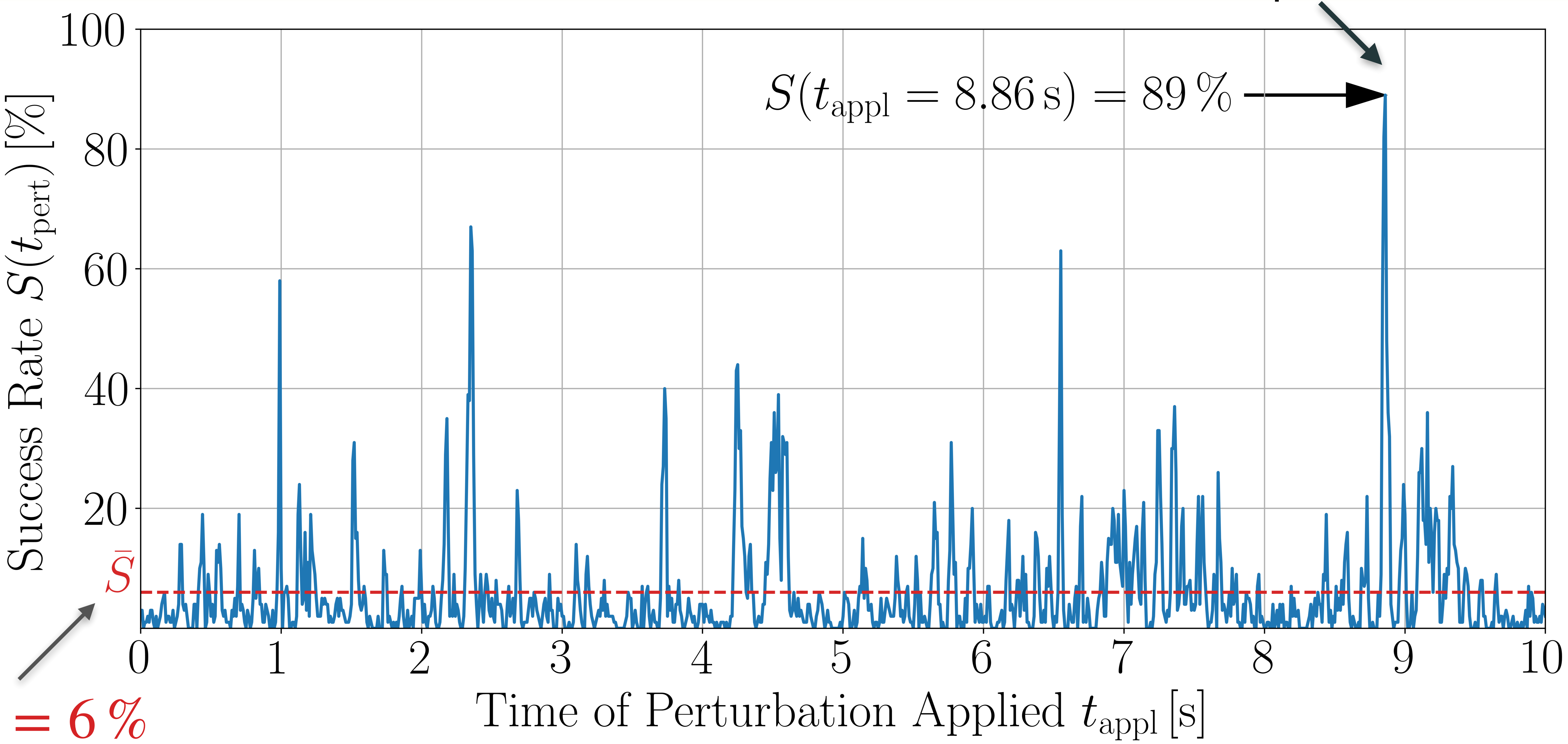
Success of termination attempts strongly depends on current state of the system

(i.e., time when pulse is applied)

average success rate of 100 different configurations of N_pert = 500 perturbations independently applied every 10 ms

perturbation was successful if there are no phase singularities left after 500ms

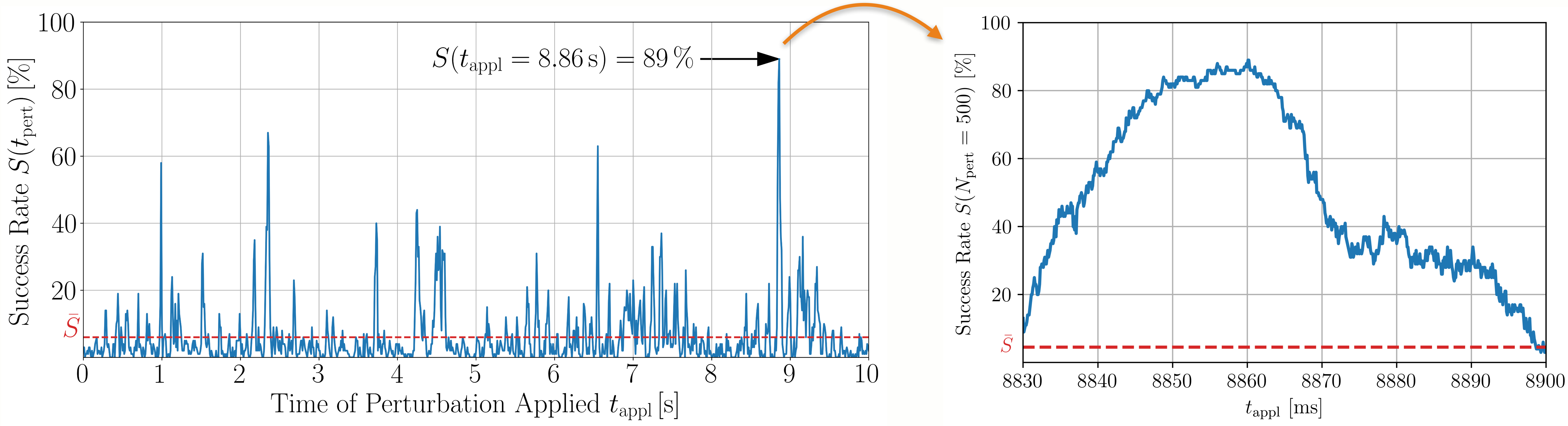
80% / 6% - 14.3 times higher probability



average success rate $\bar{S} = 6\,\%$

Width of the peaks

N_{pert} = 500 perturbation sites (∽ virtual electrodes)



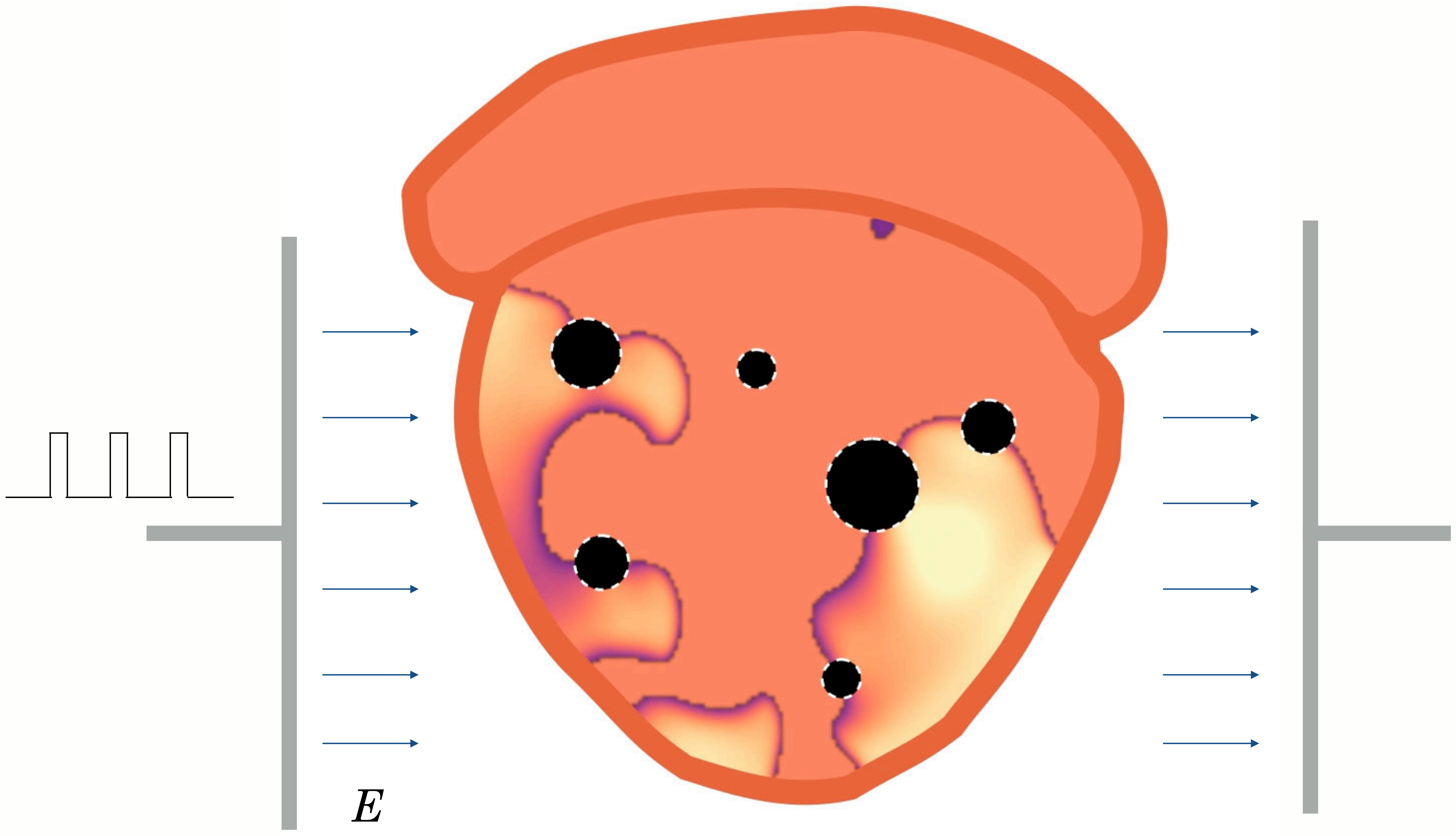
There are short windows in time where the termination of chaos (∽ fibrillation) is possible with low N_{pert} (∽ low energy).

Challenge: Detect these windows using information from observable time series, only!

Terminating Cardiac Arrhythmias

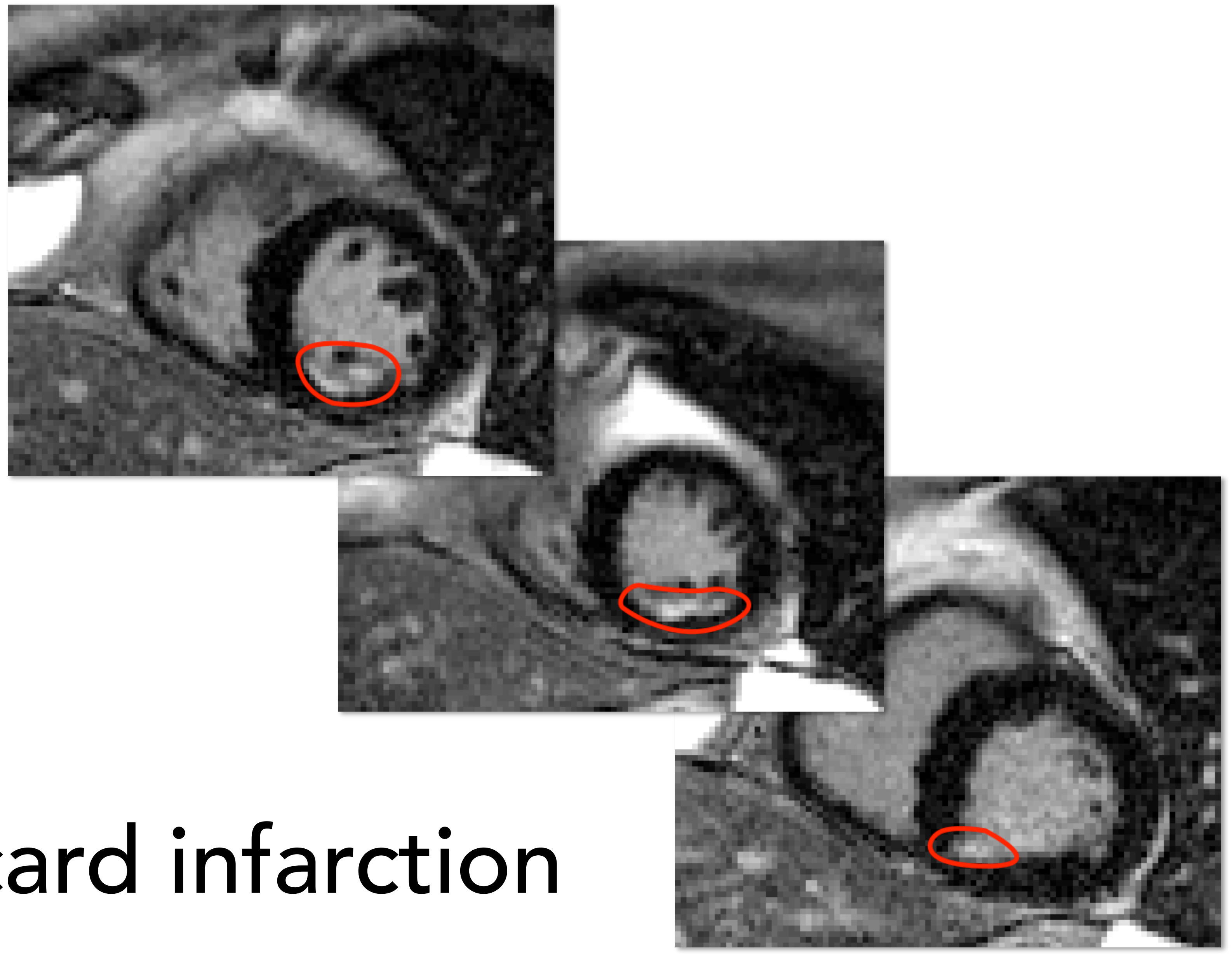
Terminate with a sequence of (weak) pulses instead of a single strong shock

Recruiting Networks of Virtual Electrodes for Terminating Cardiac Arrhythmias

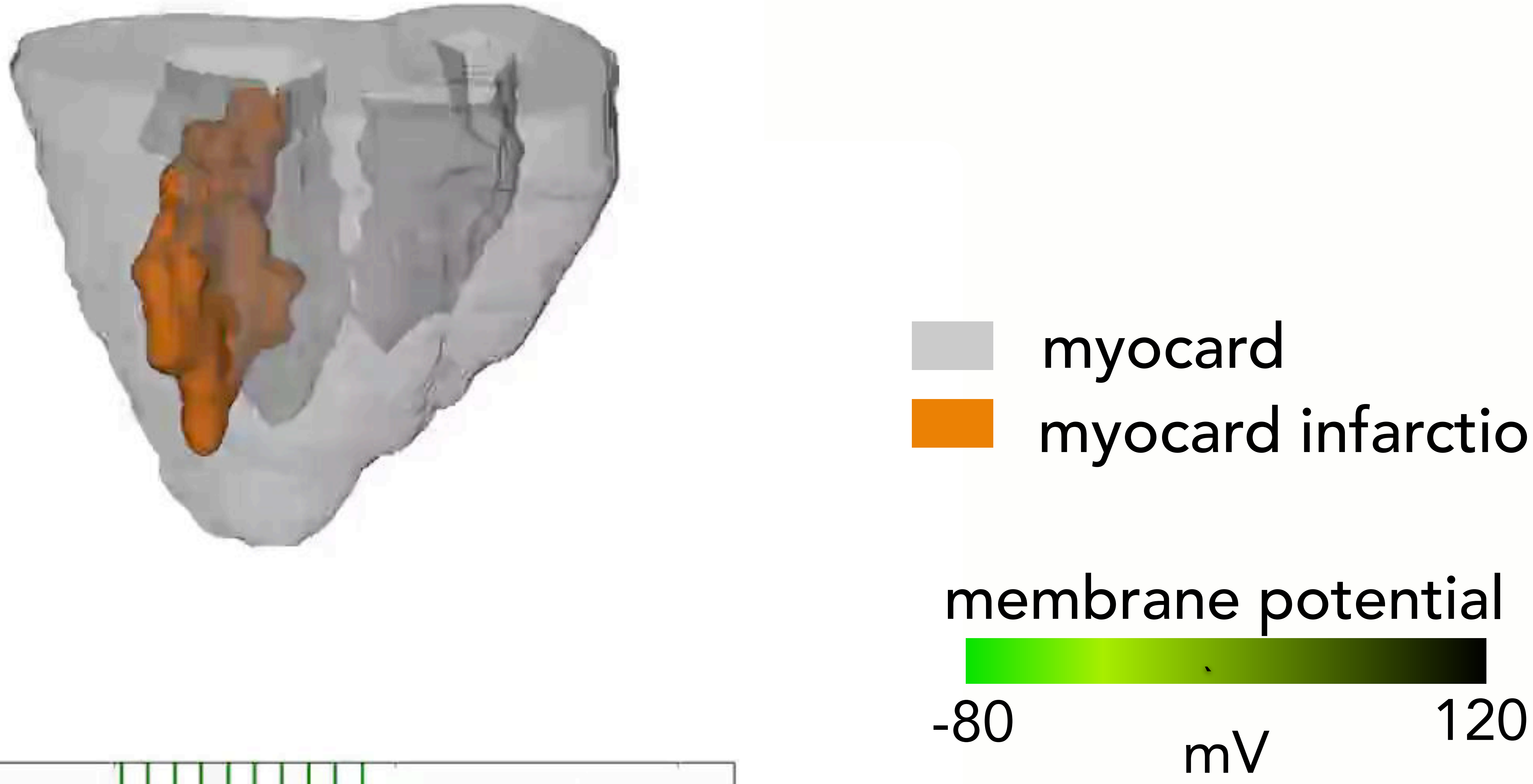


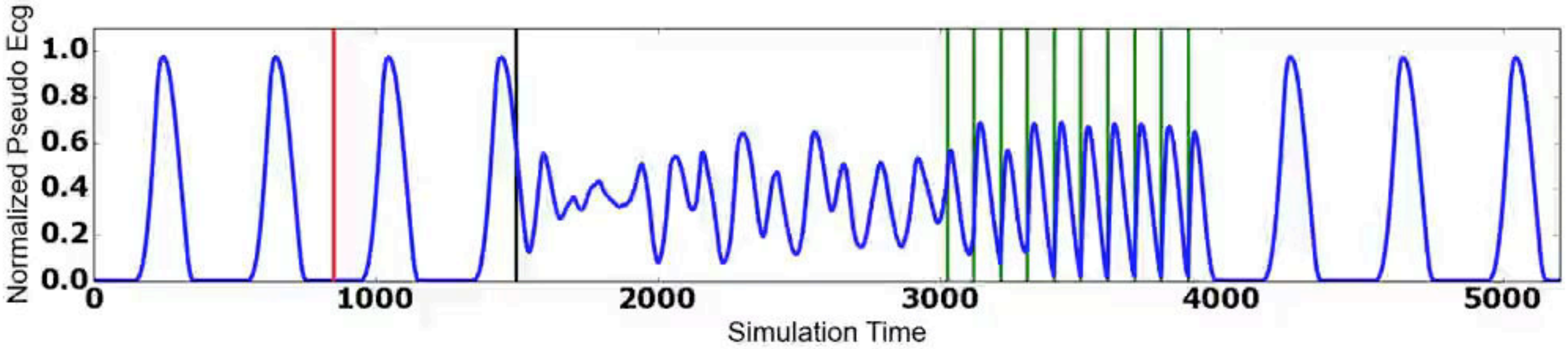
Animation: T. Lilienkamp

Simulation using a MRT-based heart model



myocard infarction





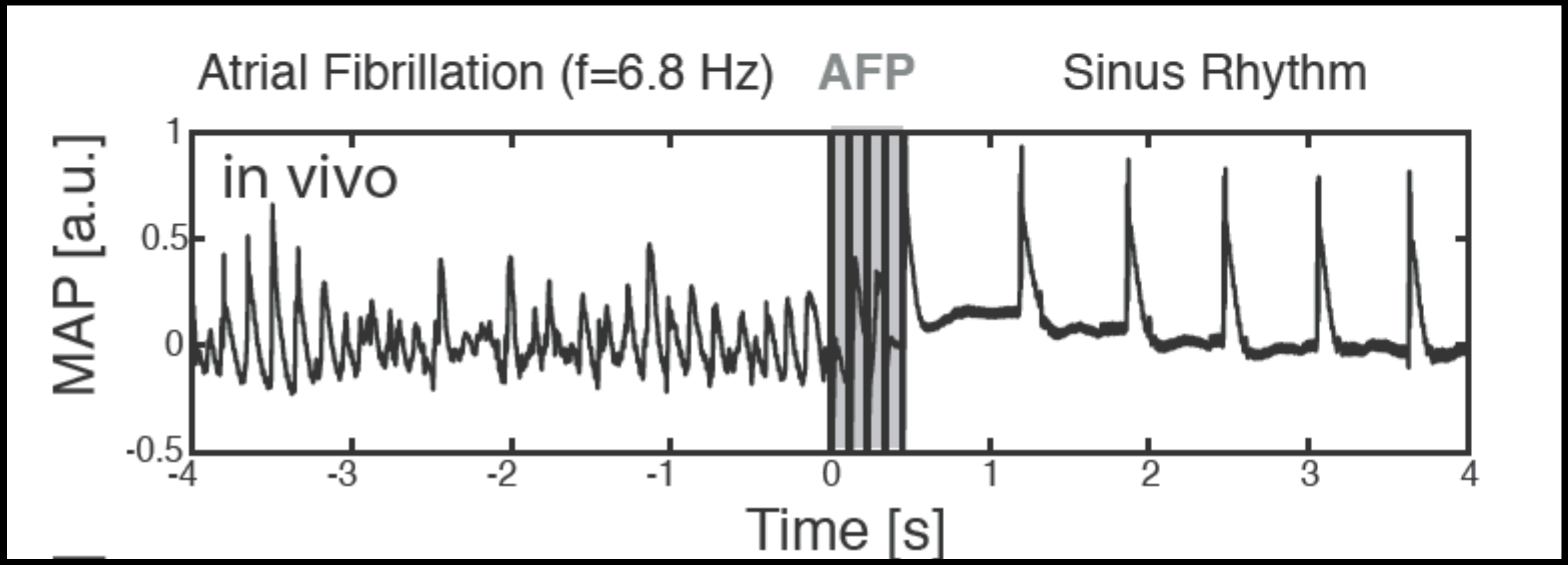
T. Lilienkamp

Low-Energy Anti-Fibrillation Pacing (LEAP)

N = 5 low energy pulses

E = 1.4 V/cm

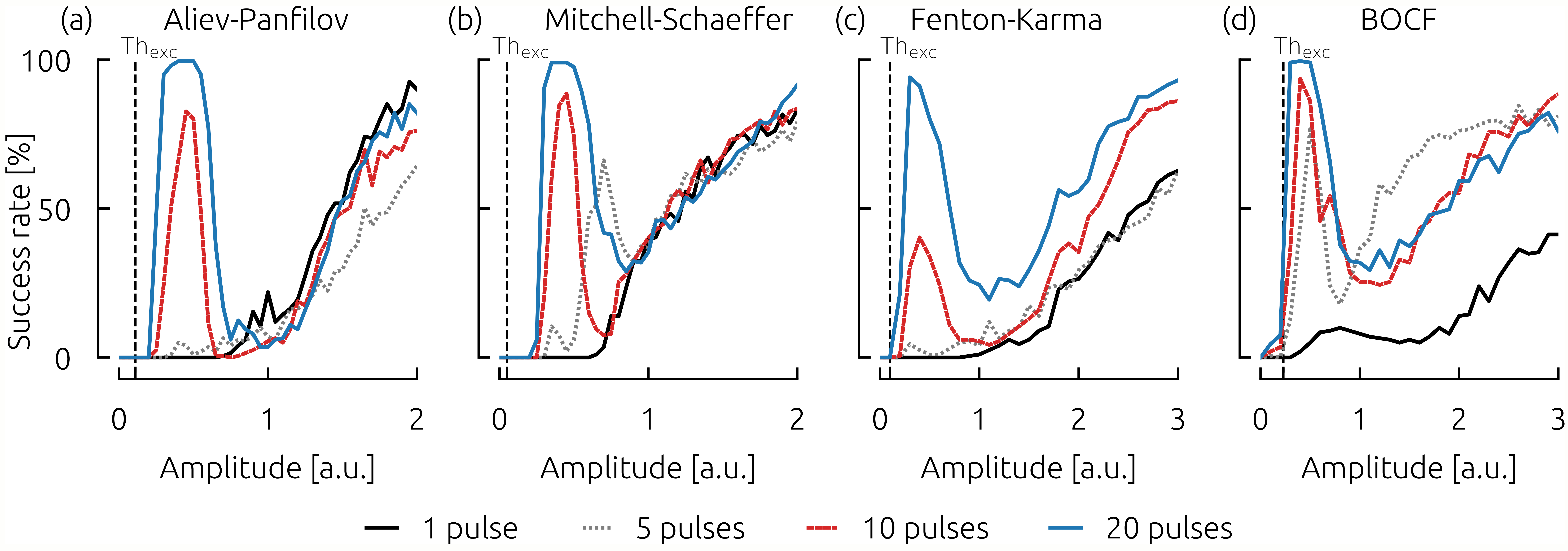
dt = 90 ms



S. Luther et al., Nature 475, 235 (2011)

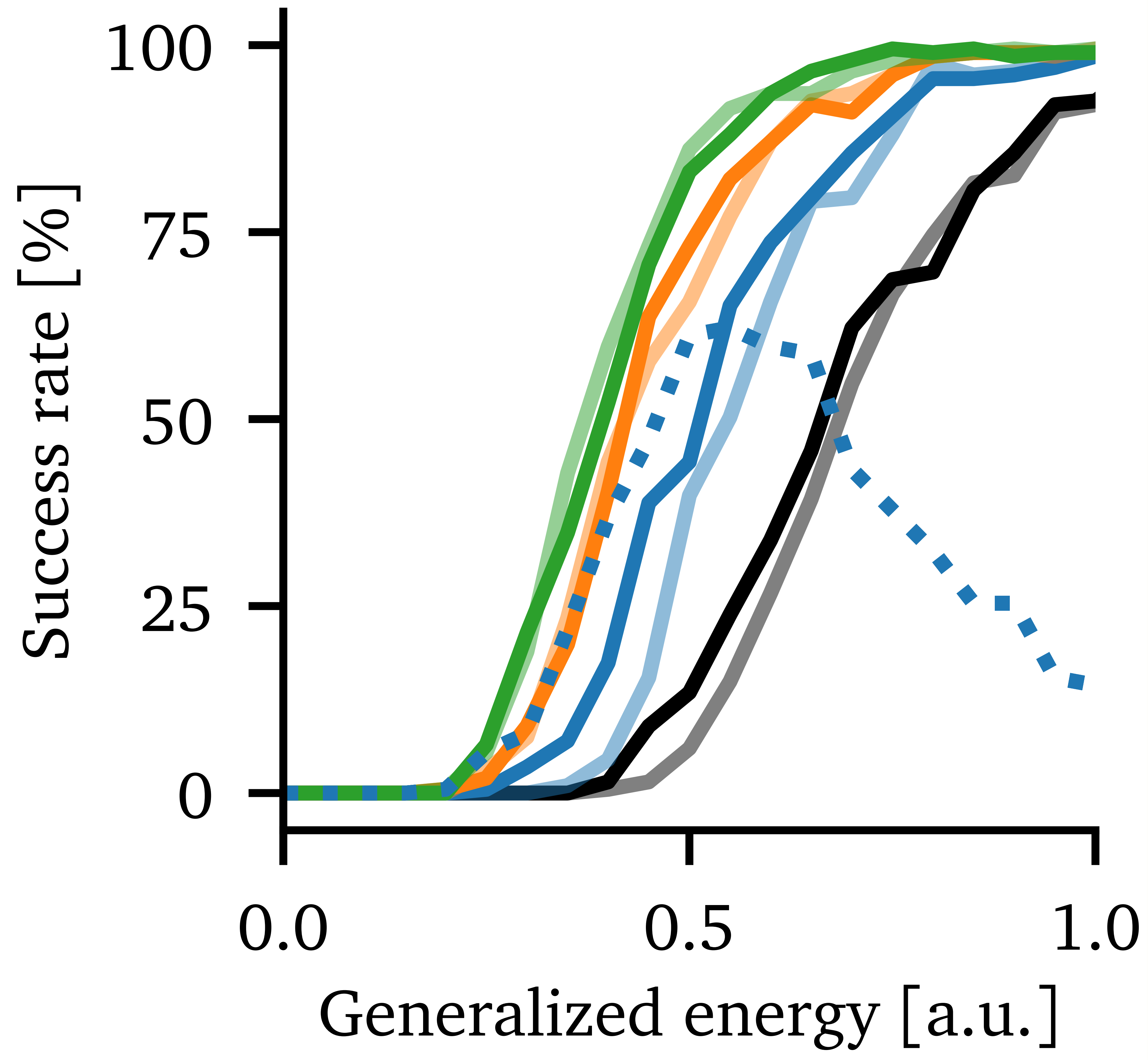
Terminating Cardiac Arrhythmias

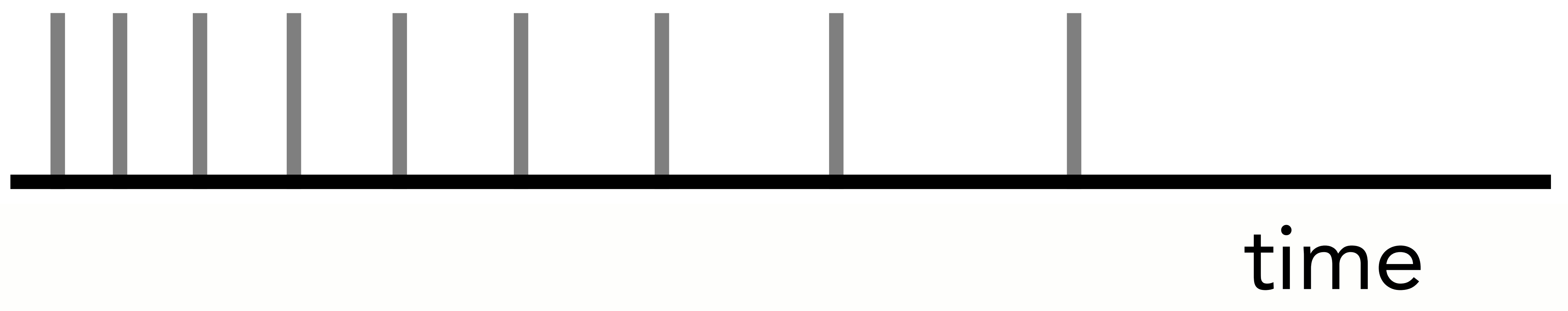
Using sequences of pulses may result in non-monotonous dose-response curves and a peak of high termination probability at low pacing energy



T. Lilienkamp et al., Scientific Reports 12, 12043 (2022)

Use non-equidistant pulse sequences: Deceleration Control





10 equidistant pulses

5 non-equidistant pulses

10 non-equidistant pulses

15 non-equidistant pulses

20 non-equidistant pulses

Summary

- data driven modelling is a promising approach to predict excitable cardiac dynamics and to reconstruct quantities that are difficult observe directly
- complex cardiac dynamics can be governed by transient chaos
- simulation results indicate that pulse timing is crucial for efficient termination of arrhythmic activity
- (decelerated) pulse sequences of low energy may provide an alternative for defibrillation avoiding strong shocks with adverse side effects

Acknowledgement

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Thank you!