# Mathematical modeling from ion channel to ECG

## an Introduction

Mark Potse

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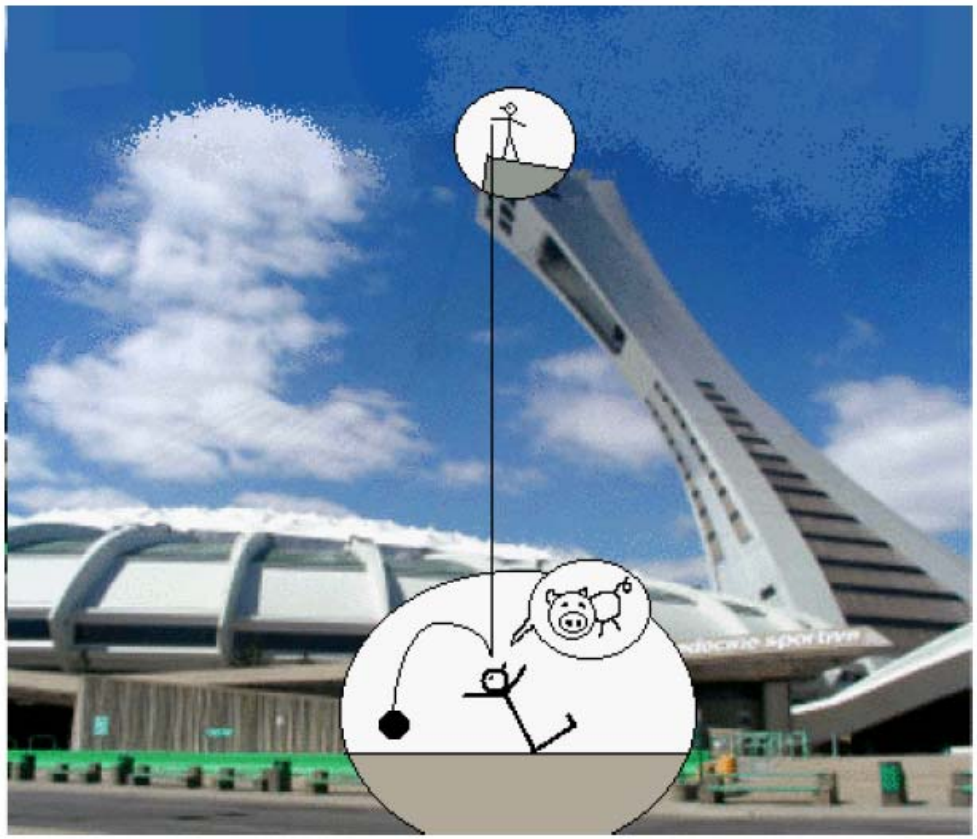
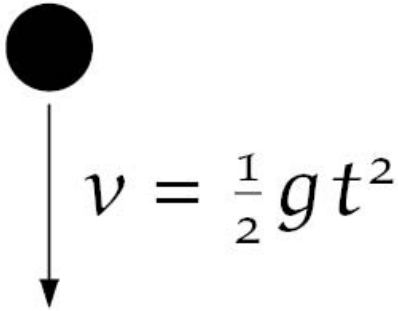
# Why a model?



reality




model

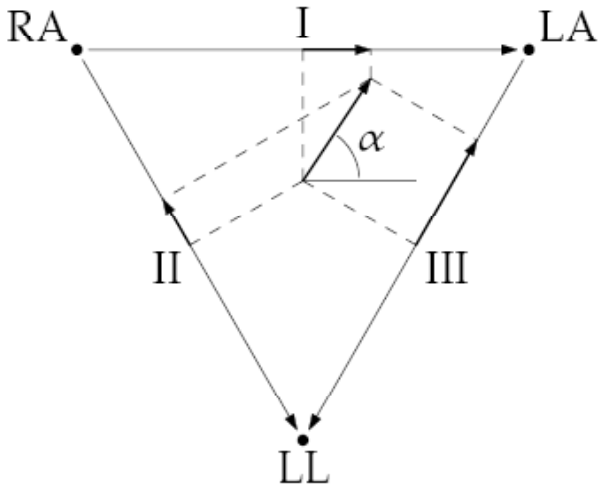
- A model is a theoretical construct that allows to translate theory into predictions

- Daily life: weather forecast
- Engineering: design of constructions
- Science: verifying theories!

# The first mathematical heart model

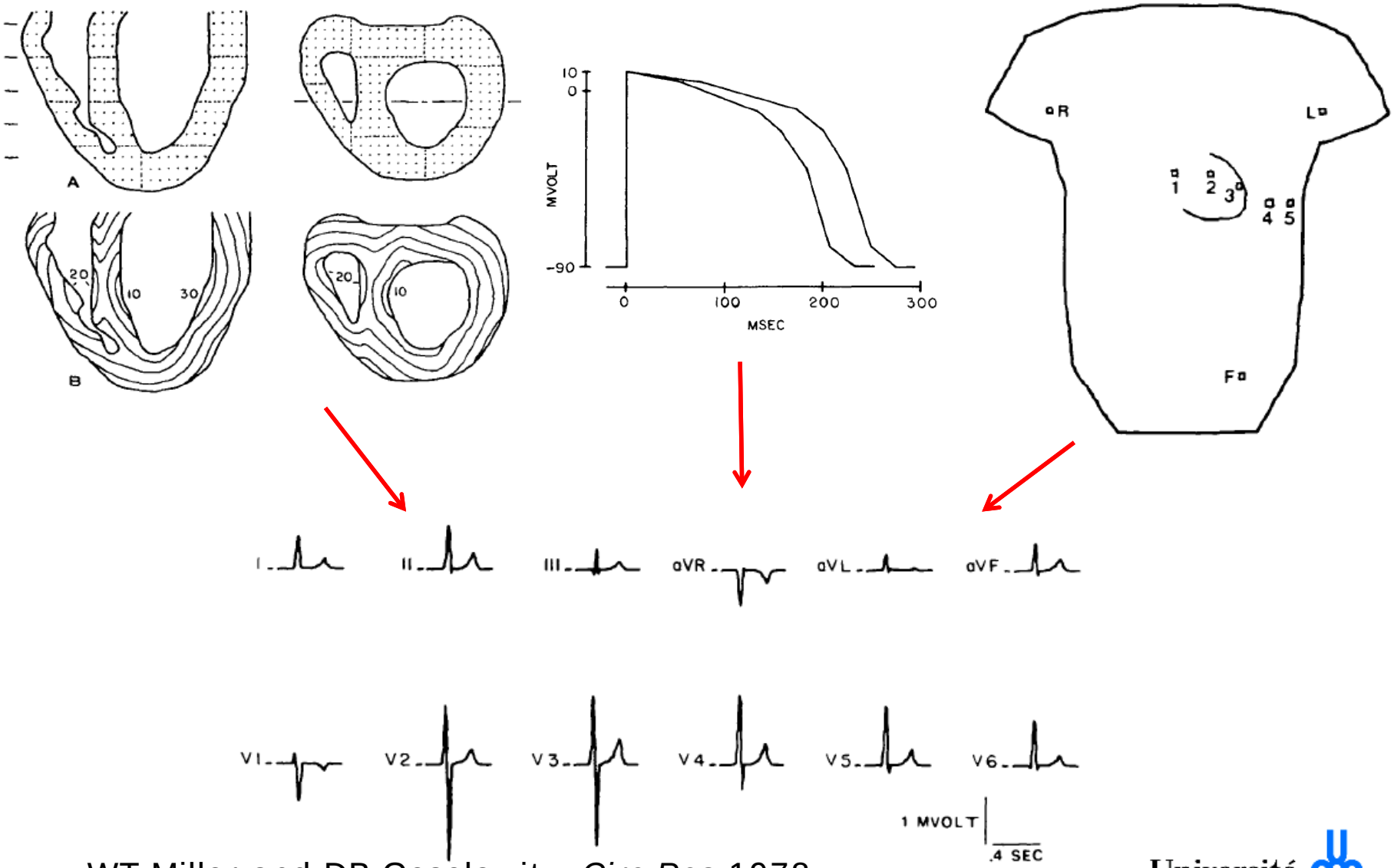


reality




model

# Multiple dipoles




WT Miller and DB Geselowitz, *Circ Res* 1978

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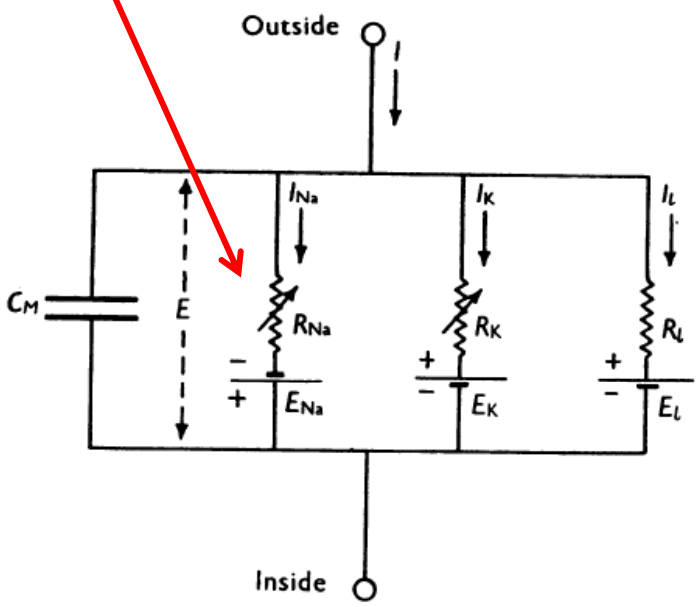
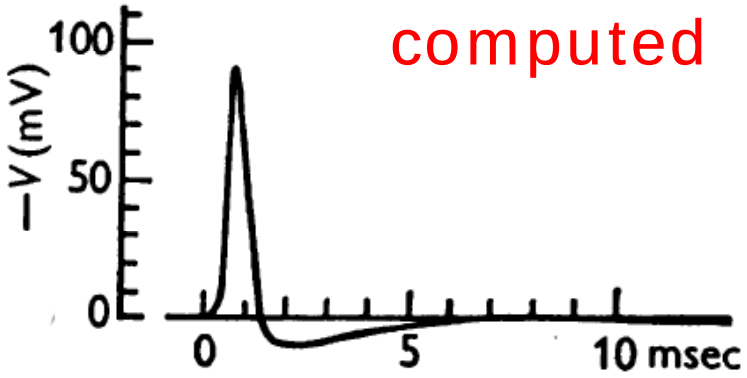
# Hodgkin-Huxley membrane model

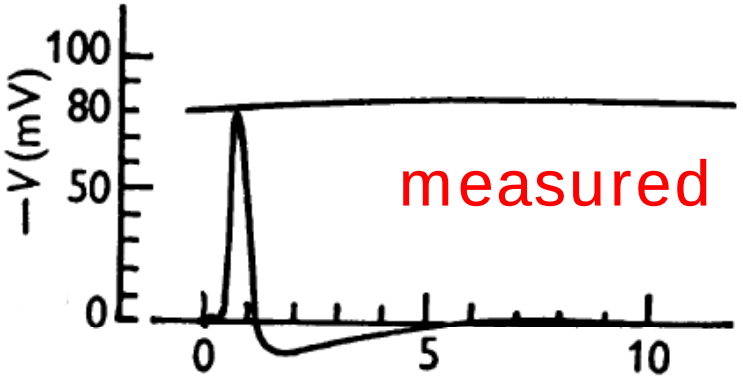
$$g_{\mathrm{Na}} = m^3 h \bar{g}_{\mathrm{Na}},$$

$$\frac{\mathrm{d}m}{\mathrm{d}t} = \alpha_m (1-m) - \beta_m m,$$

$$\frac{\mathrm{d}h}{\mathrm{d}t} = \alpha_h (1-h) - \beta_h h,$$




AL Hodgkin and AF Huxley, J. Physiol 117:500-544, 1952

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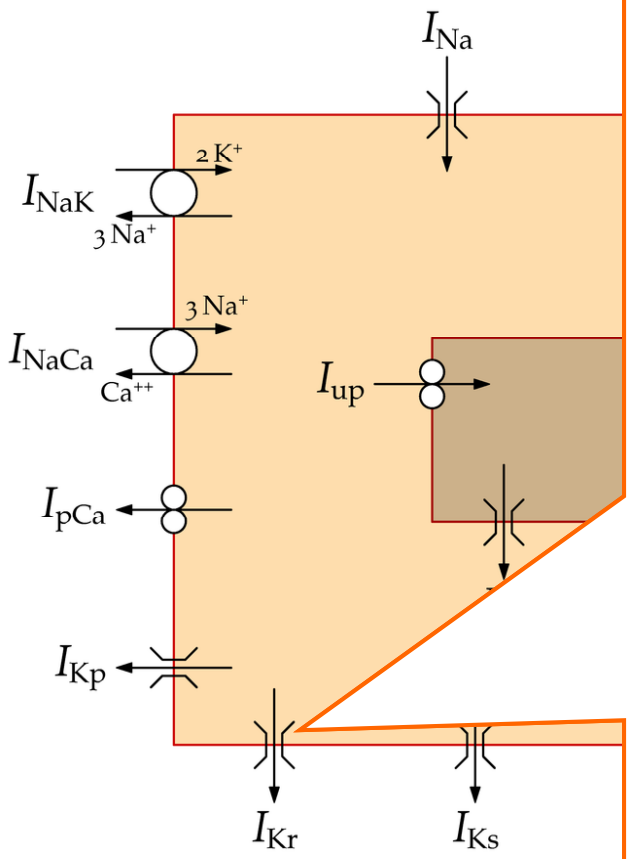
# Contemporary membrane model




$$I_{Kr} = G_{Kr}\sqrt{\frac{K_o}{5.4}}vw(V_m - E_K)$$

$$\frac{dv(t)}{dt} = \frac{v_\infty - v(t)}{\tau_v}$$

$$\frac{dw(t)}{dt} = \frac{w_\infty - w(t)}{\tau_w}$$

$$v_\infty = \frac{1}{1 + e^{(-26-V_m)/7}}$$

$$w_\infty = \frac{1}{1 + e^{(V_m+88)/24}}$$

$$\tau_v = \frac{450}{1 + e^{(-45-V_m)/10}} \cdot \frac{6}{1 + e^{(V_m+30)/11.5}}$$

$$\tau_w = \frac{3}{1 + e^{(-60-V_m)/20}} \cdot \frac{1.12}{1 + e^{(V_m-60)/20}}$$

TNNP 2004 (Ten Tusscher, Noble, Noble, Panfilov; Am J Physiol H 2004)

$$\frac{dV_m}{dt} = -\frac{I_{ion}}{C_m}$$

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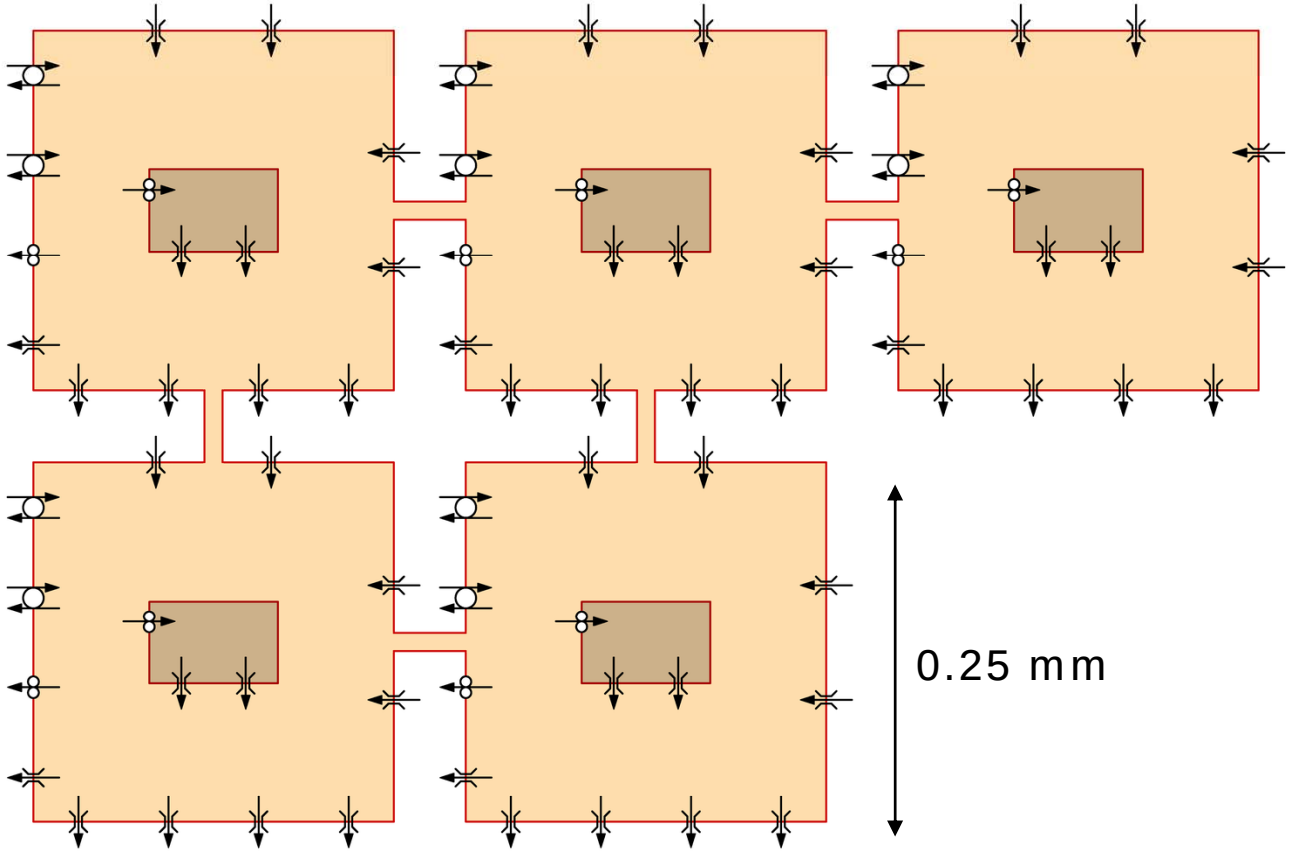
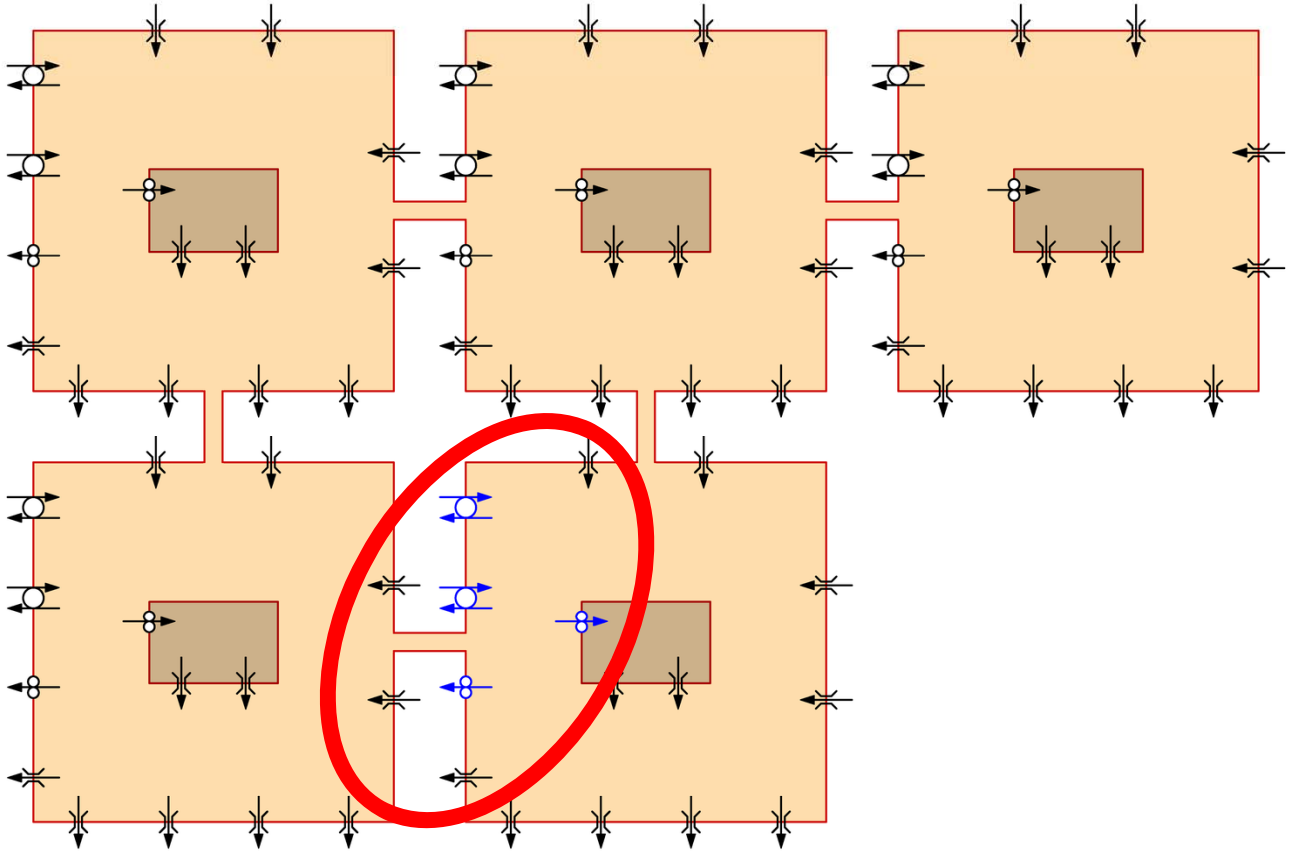
# Reaction-diffusion model

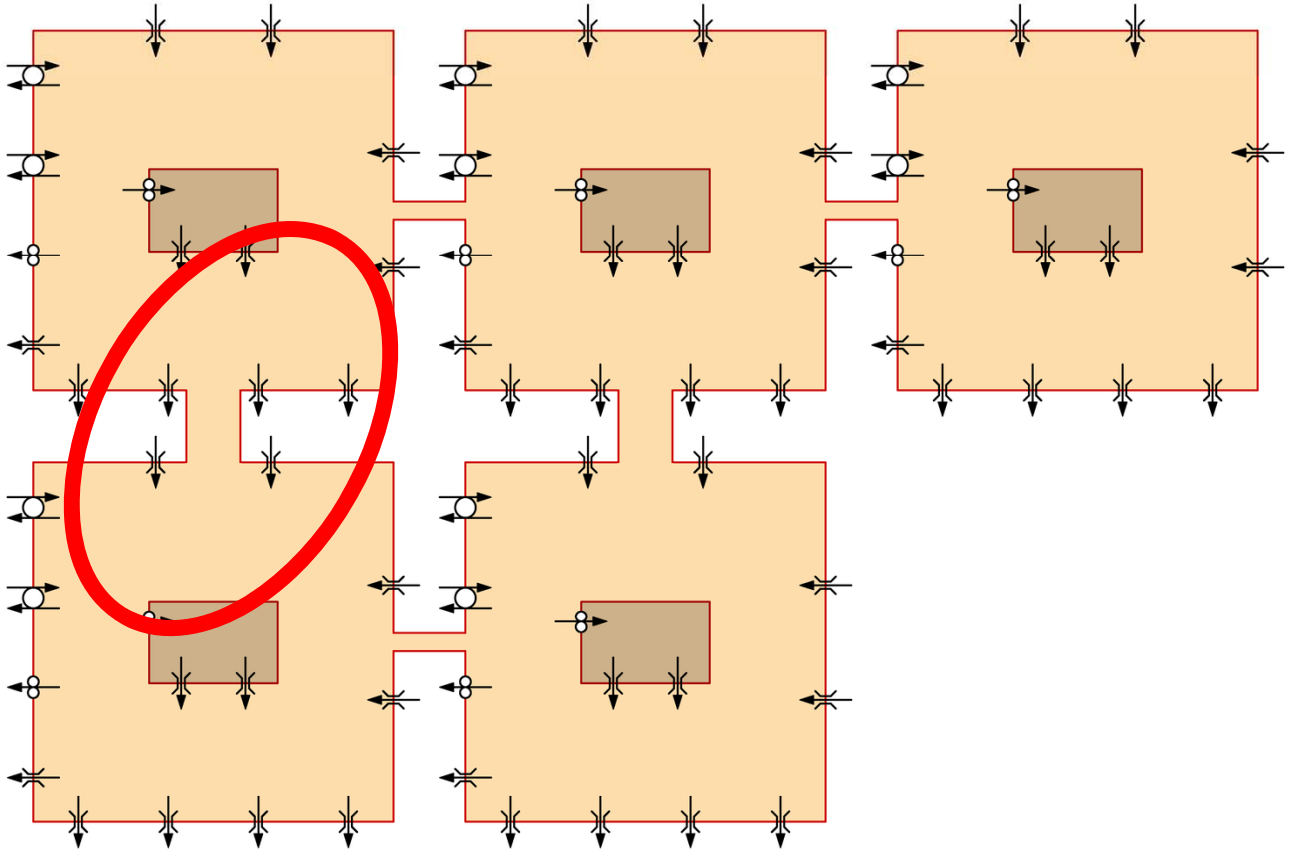



$$\frac{dV_{\mathrm{m}}}{dt} = -\frac{I_{\mathrm{ion}} + I_{\mathrm{dif}}}{C_{\mathrm{m}}}$$

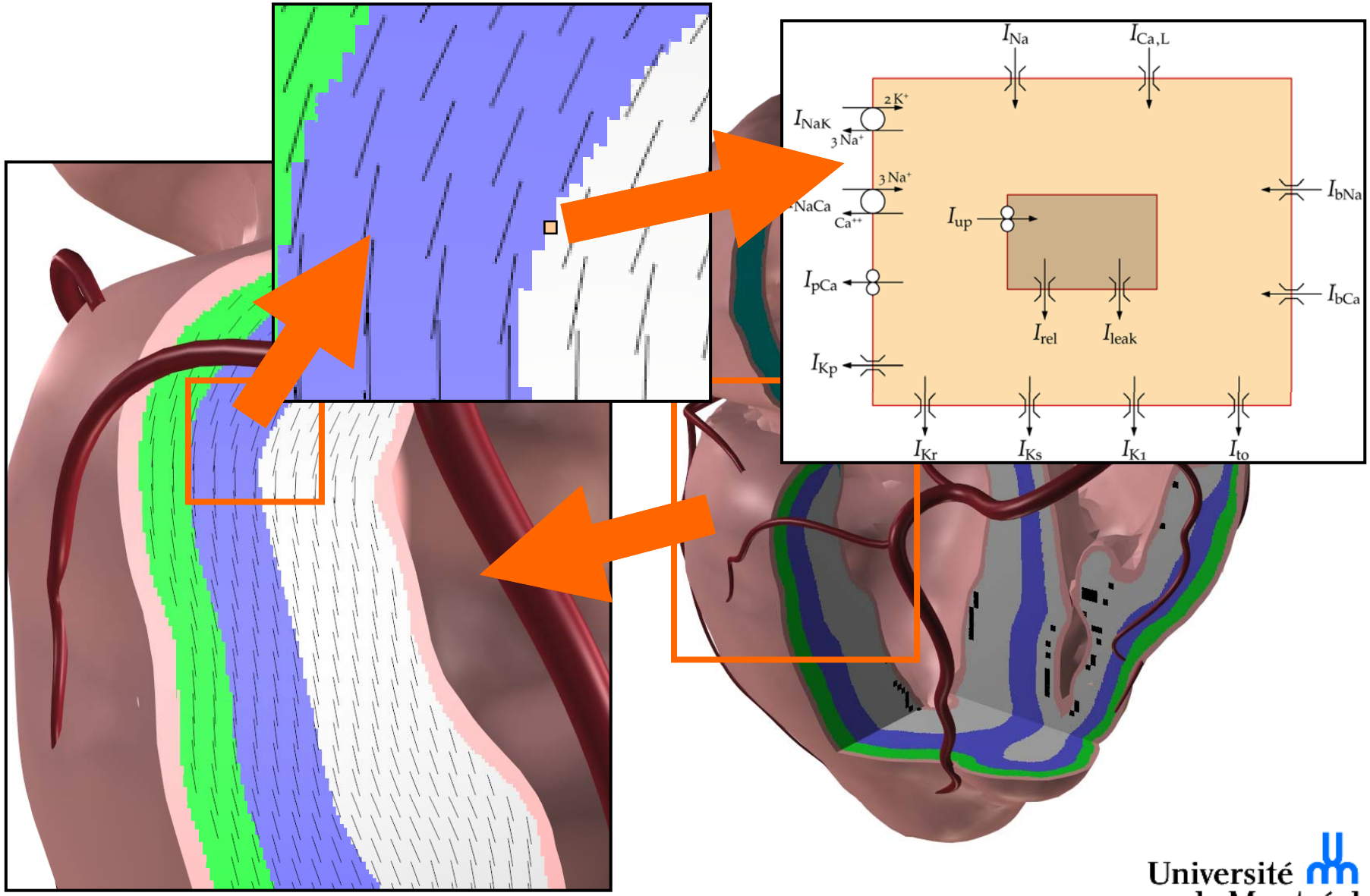
# Regional differences



# Anisotropy



# Whole ventricles: 12M elements

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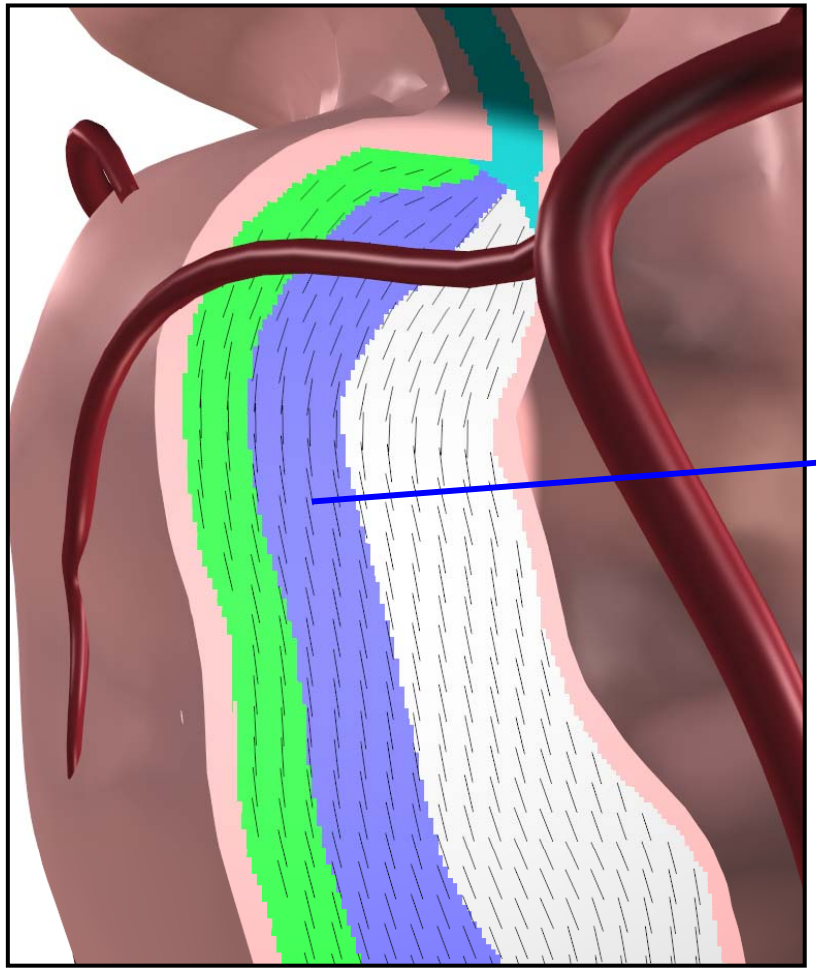
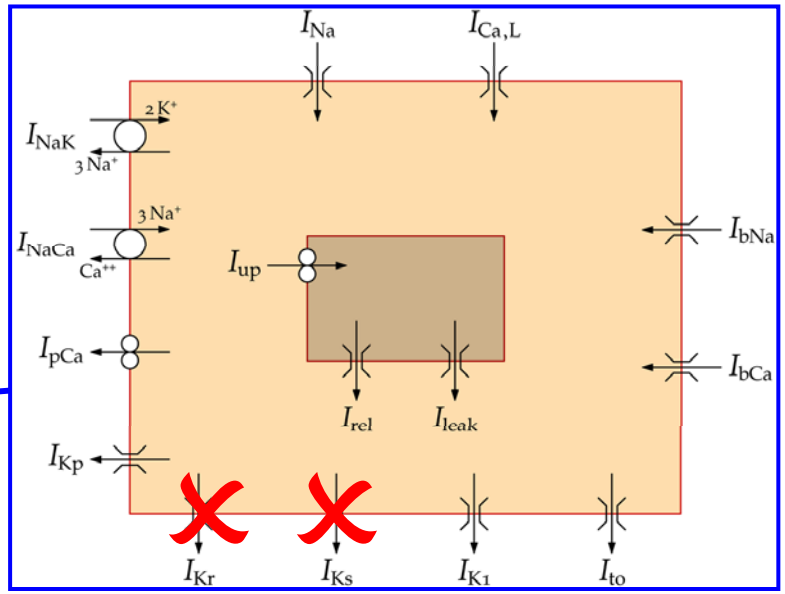
# Is reaction-diffusion necessary?



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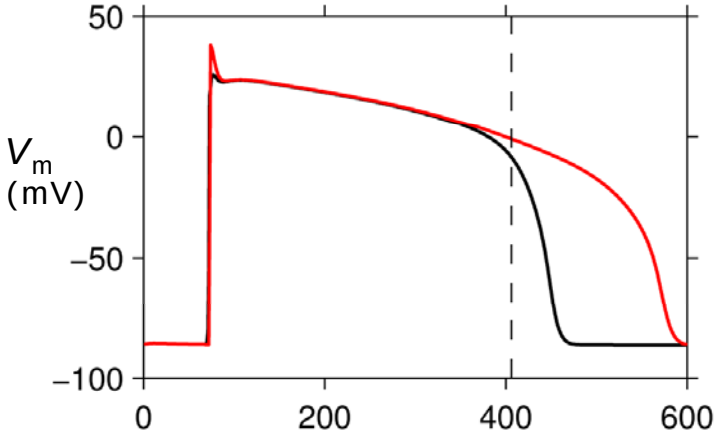
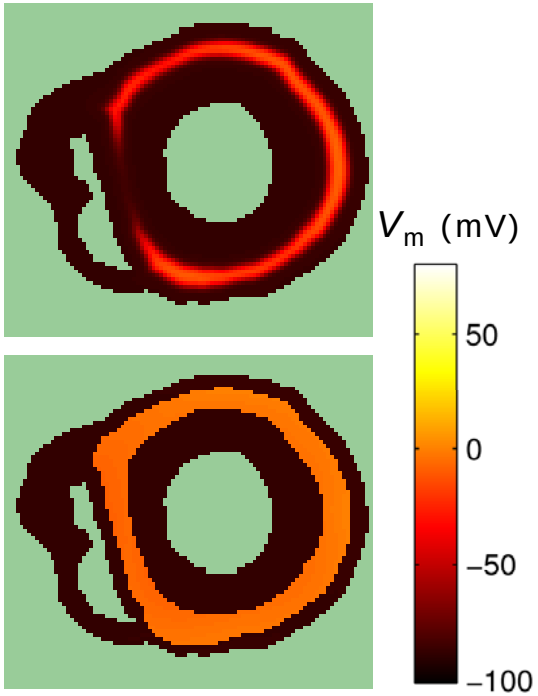
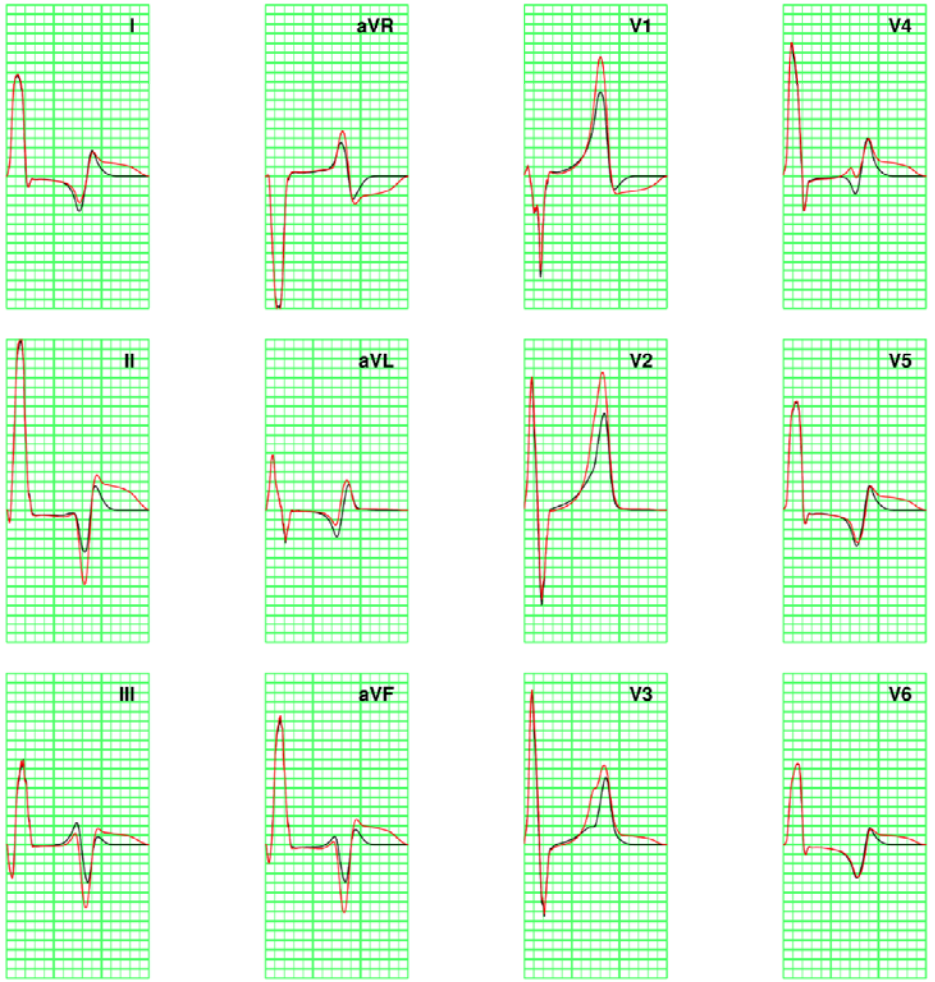



RD

fixed-AP



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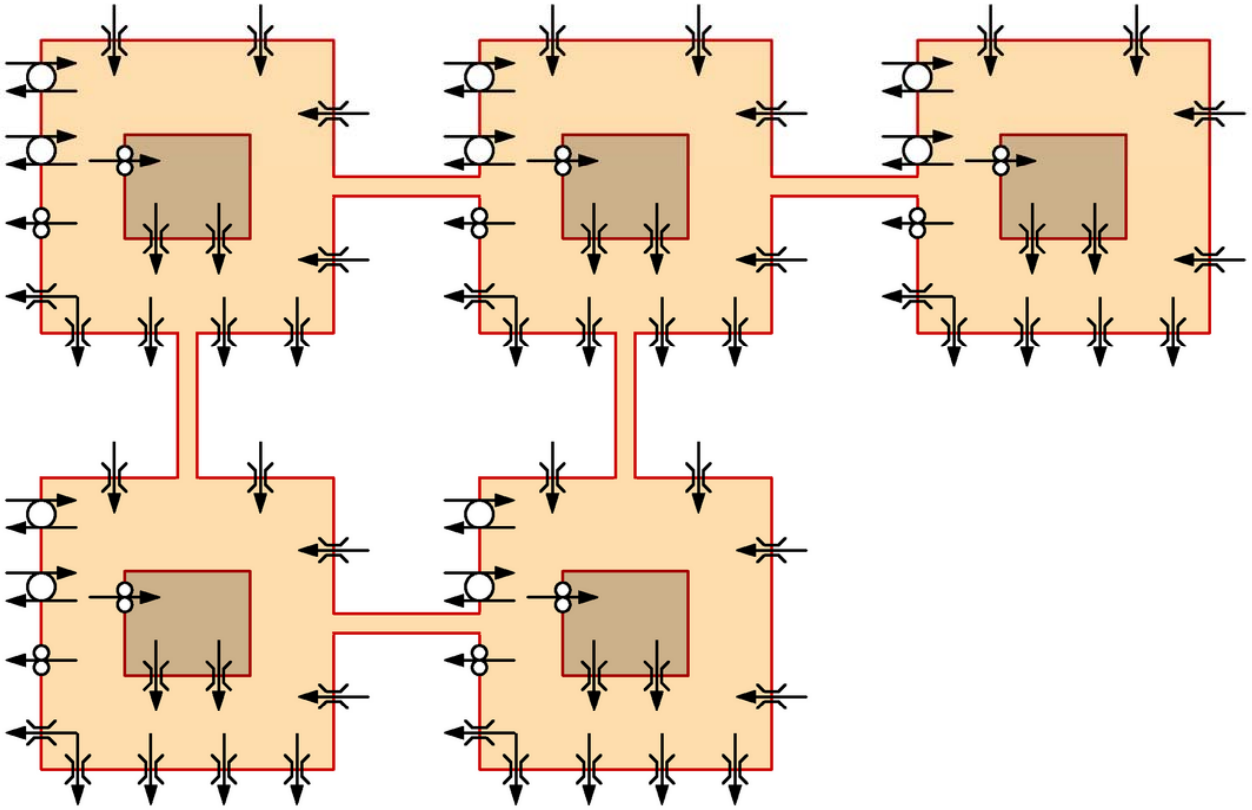
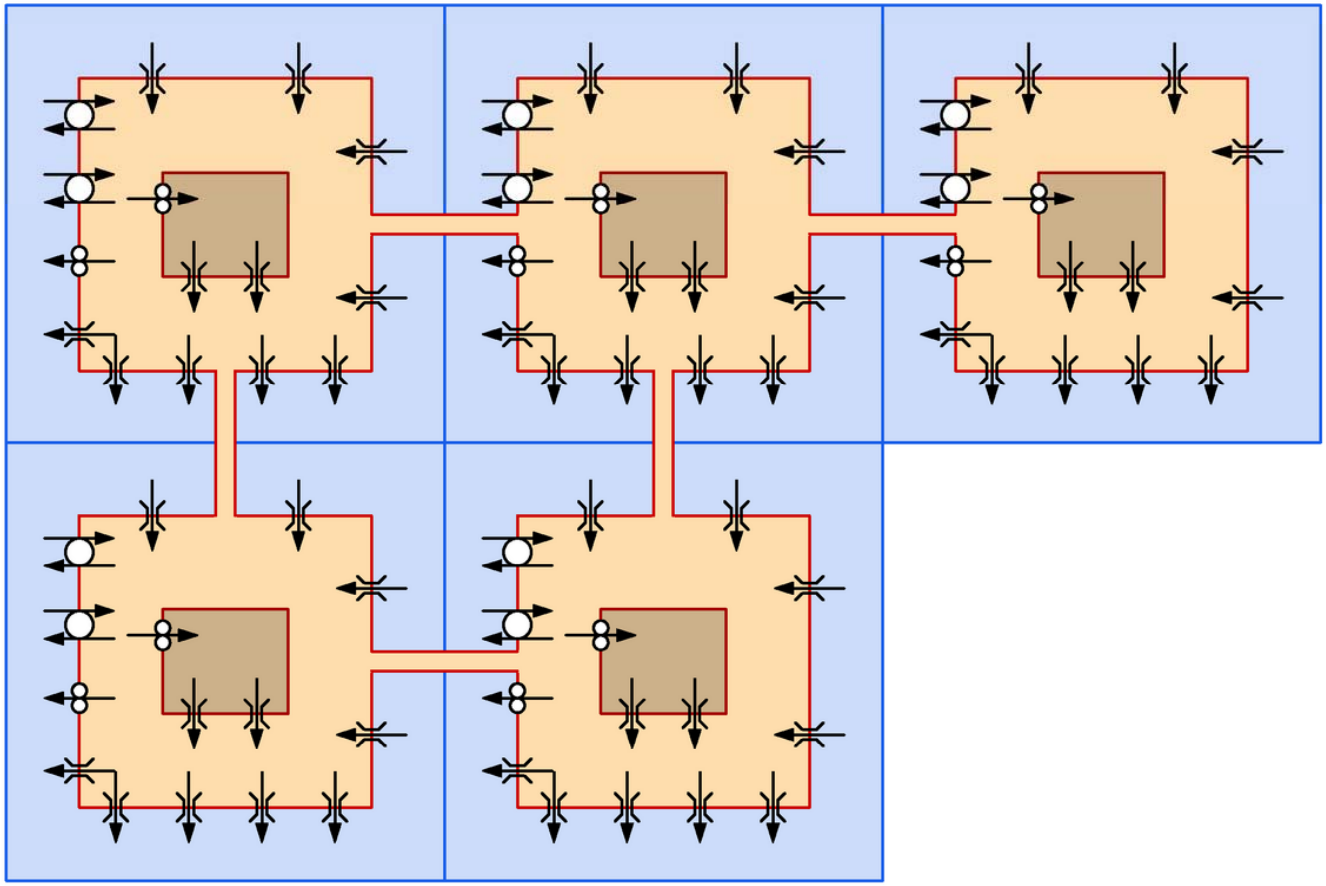
# “Bidomain” models and their application

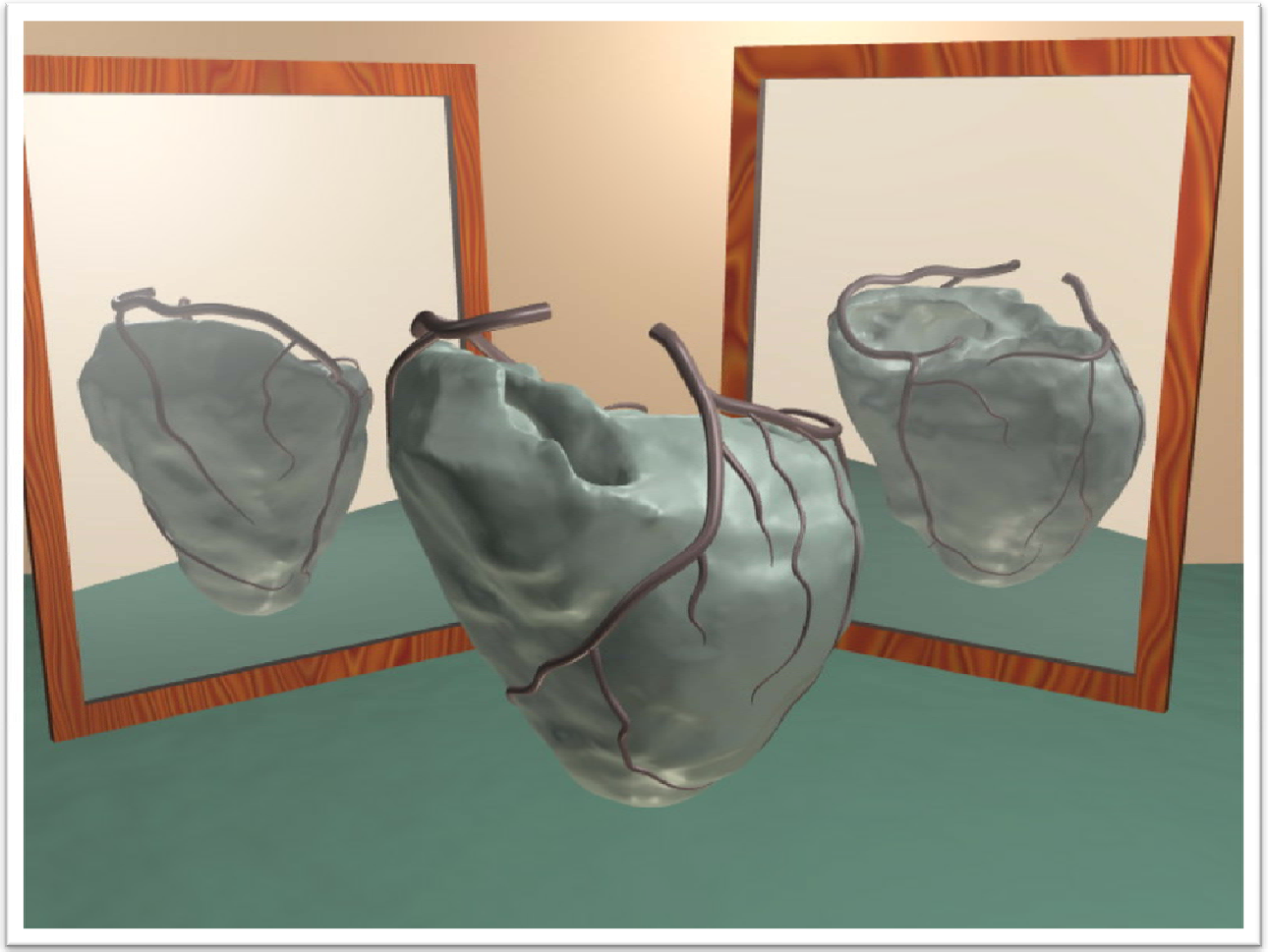


# “Bidomain” models and their application



# Computation of electrograms

$$\nabla \cdot \left( \left( G_{\mathrm{i}} + G_{\mathrm{e}} \right) \nabla \varphi_{\mathrm{e}} \right) = -\nabla \cdot \left( G_{\mathrm{i}} \nabla V_{\mathrm{m}} \right)$$



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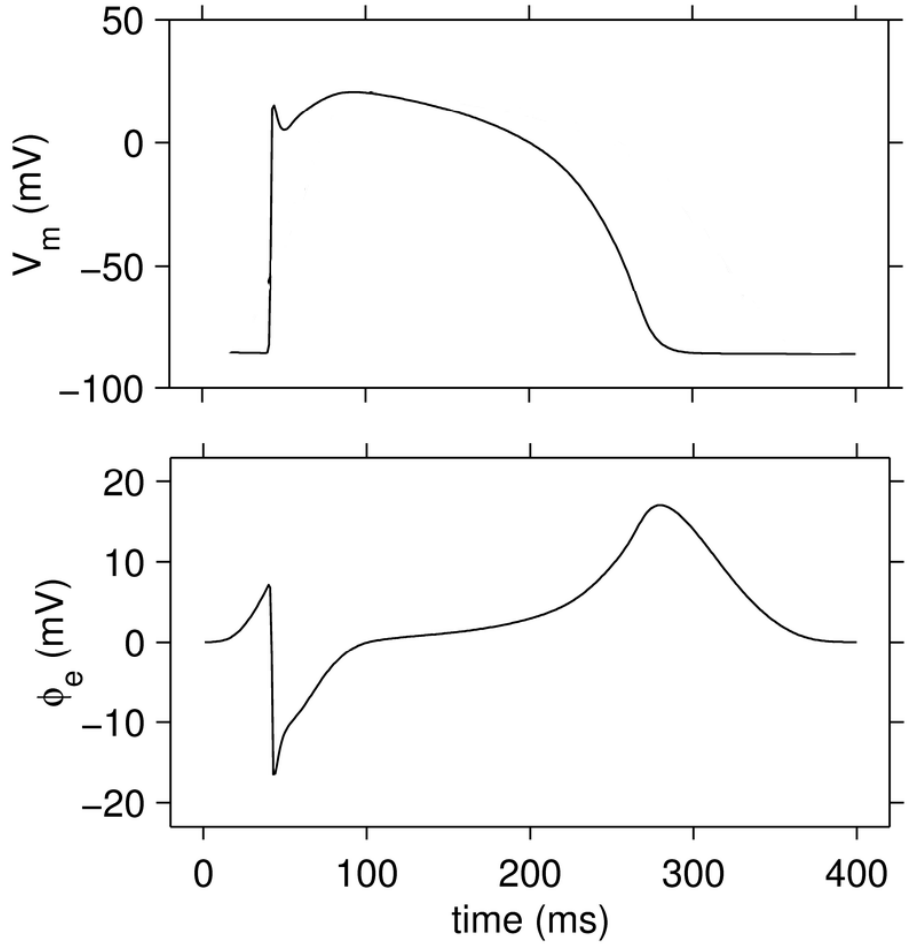
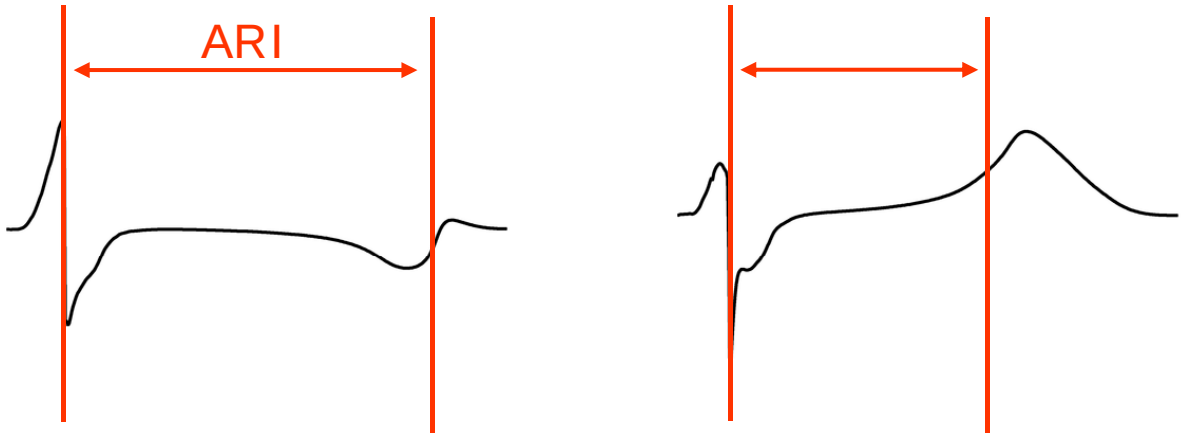
# Membrane potentials and electrograms

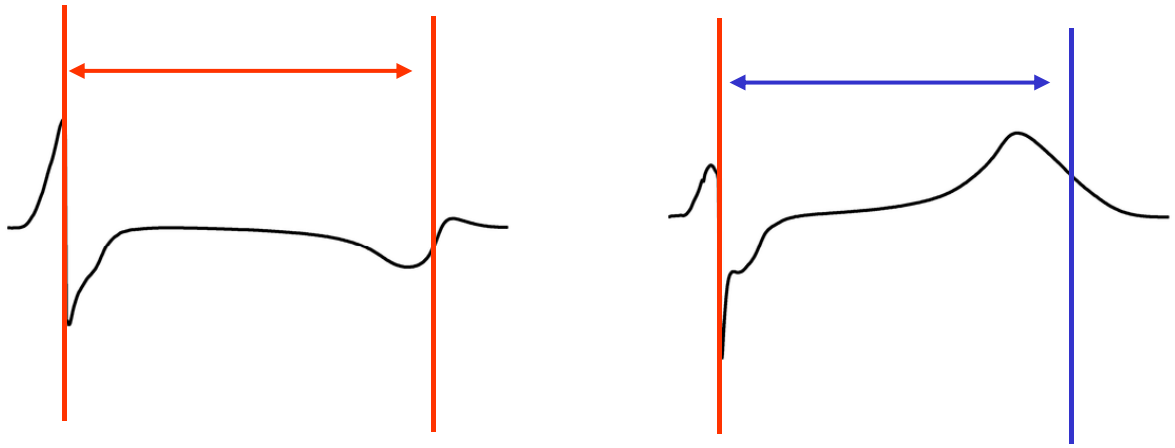


# Activation-Recovery Intervals

Wyatt




alternative



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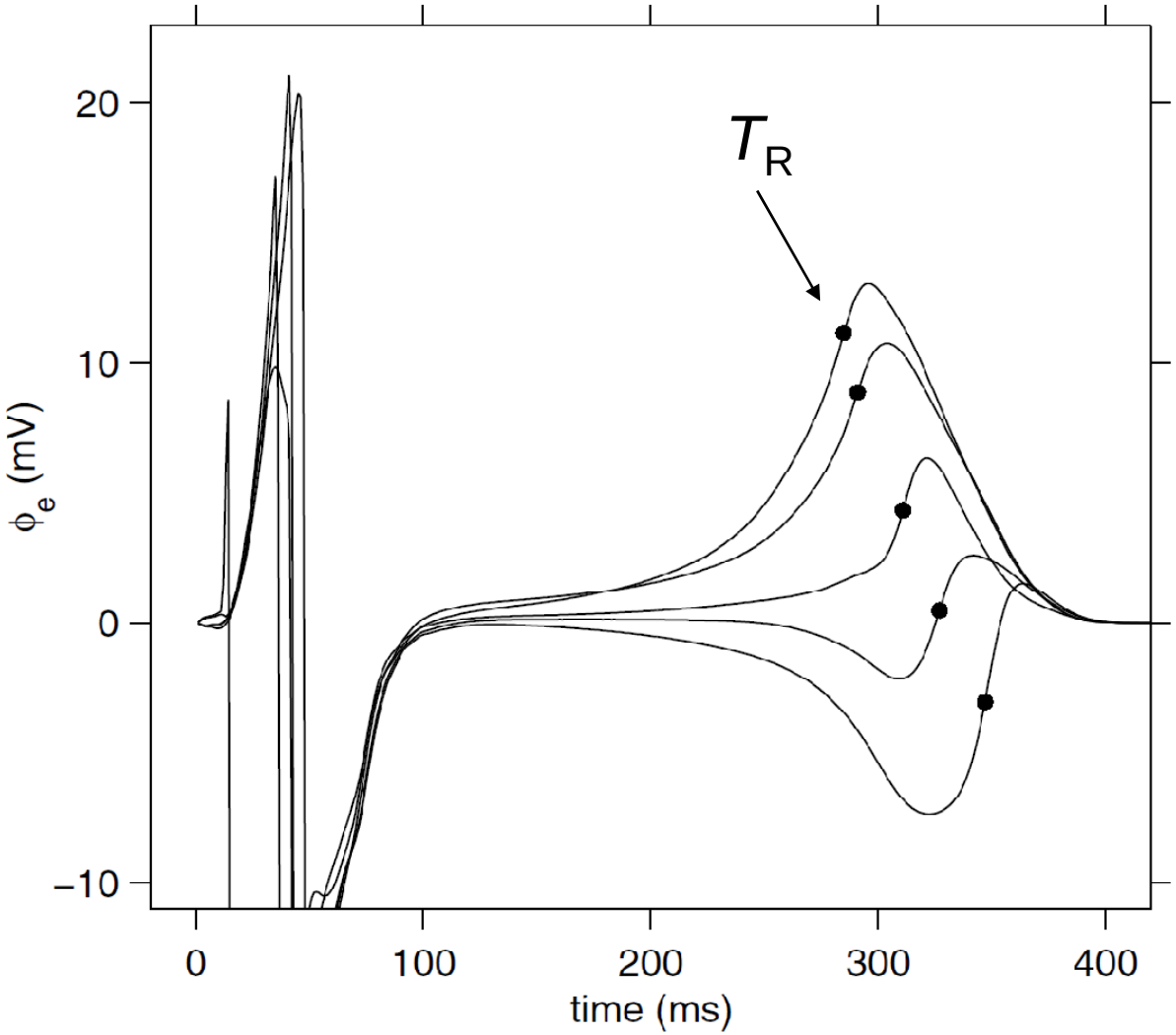
# Electrograms

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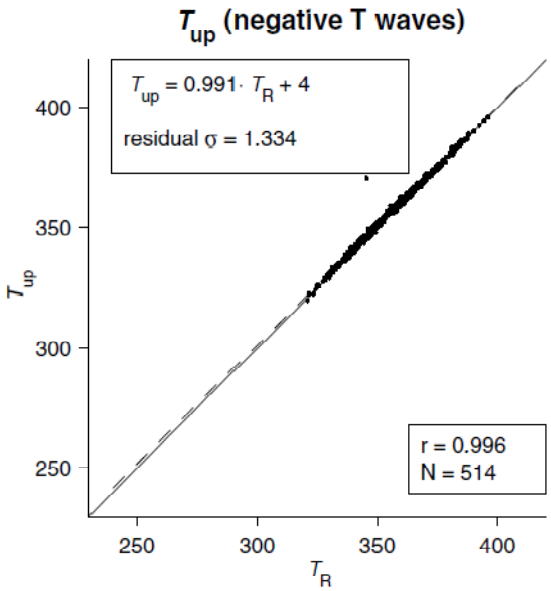
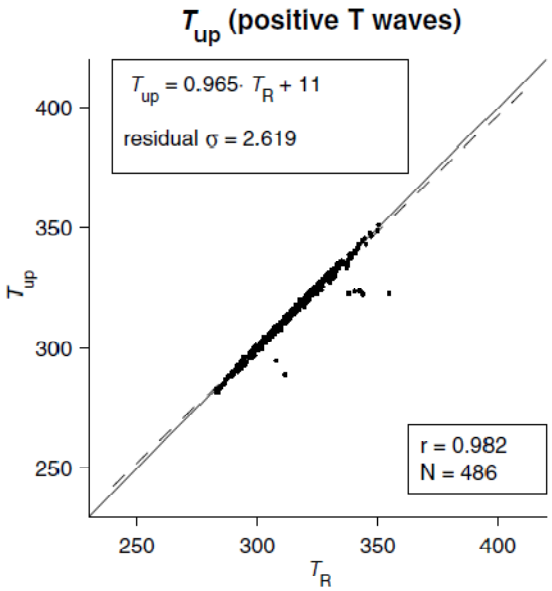
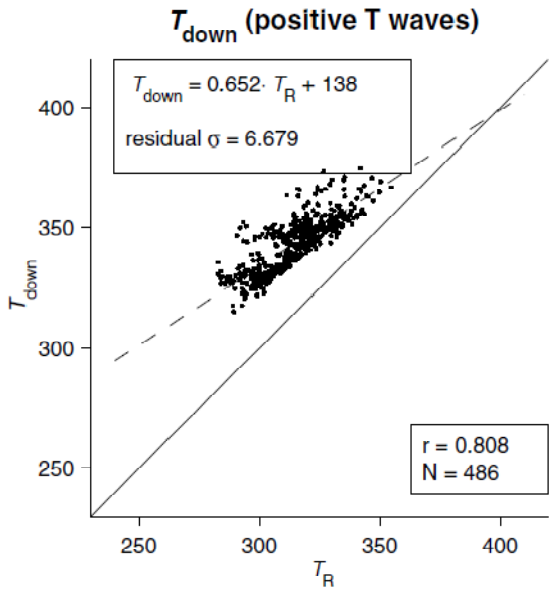
# Repolarisation

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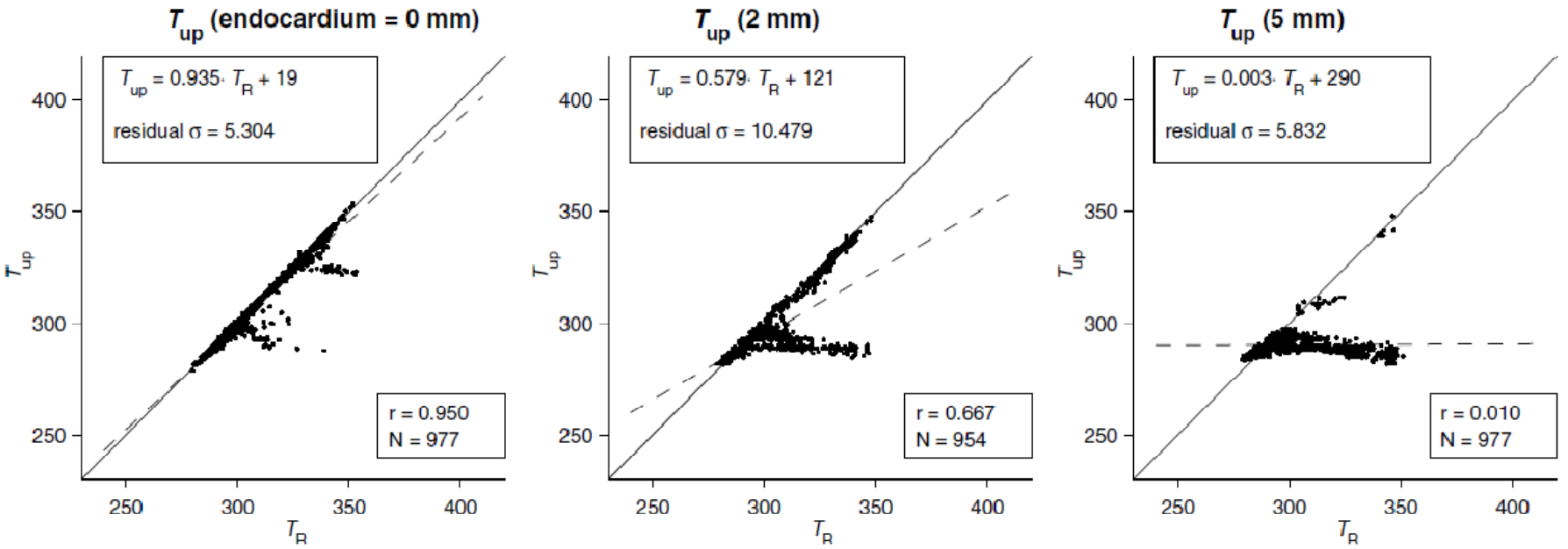
# Electrode in the cavity

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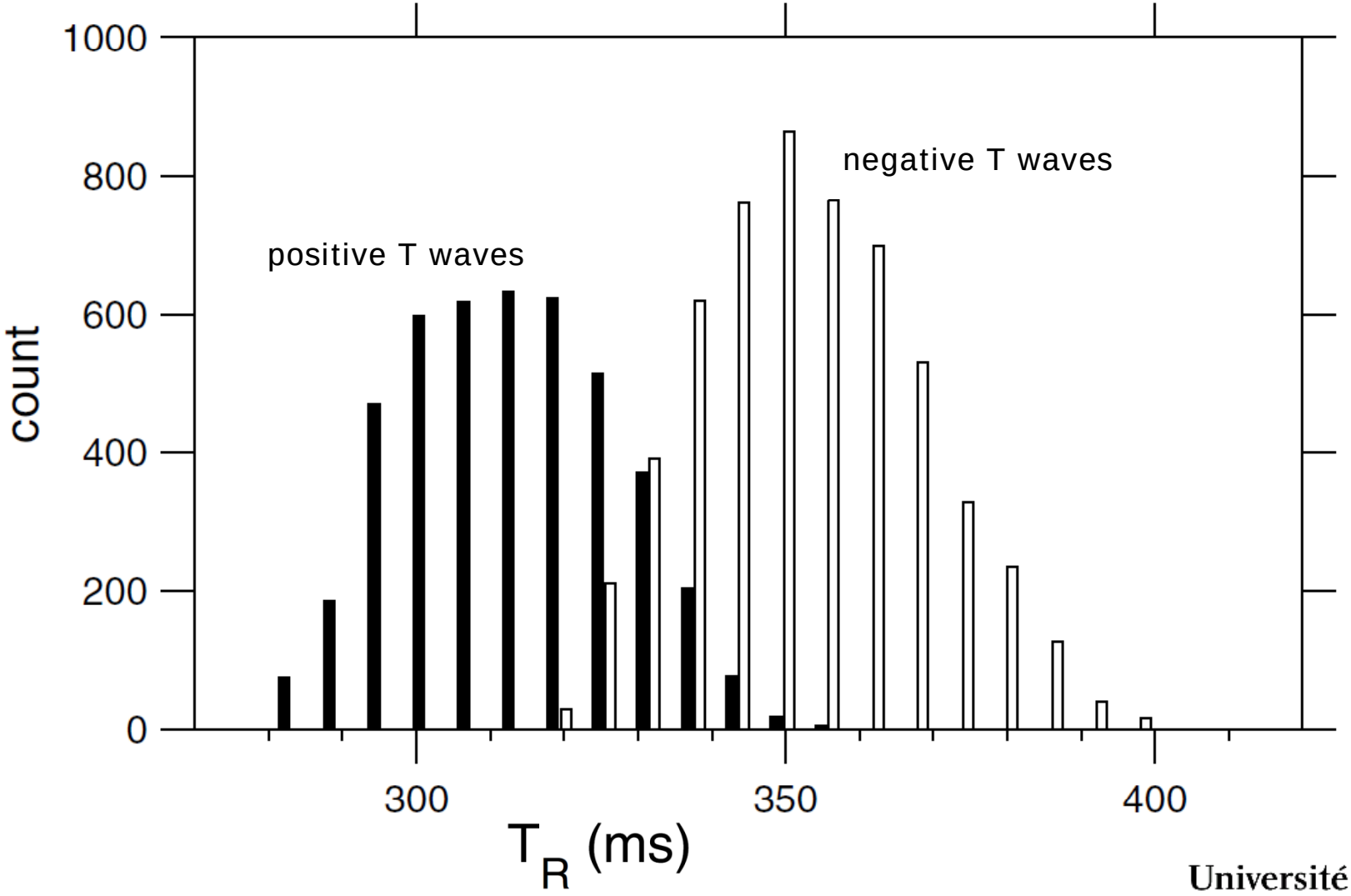


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# Understanding ST depression in the stress-test ECG

Mark Potse, Alain Vinet,
A.-Robert LeBlanc, Jean G. Diodati,
Réginald Nadeau

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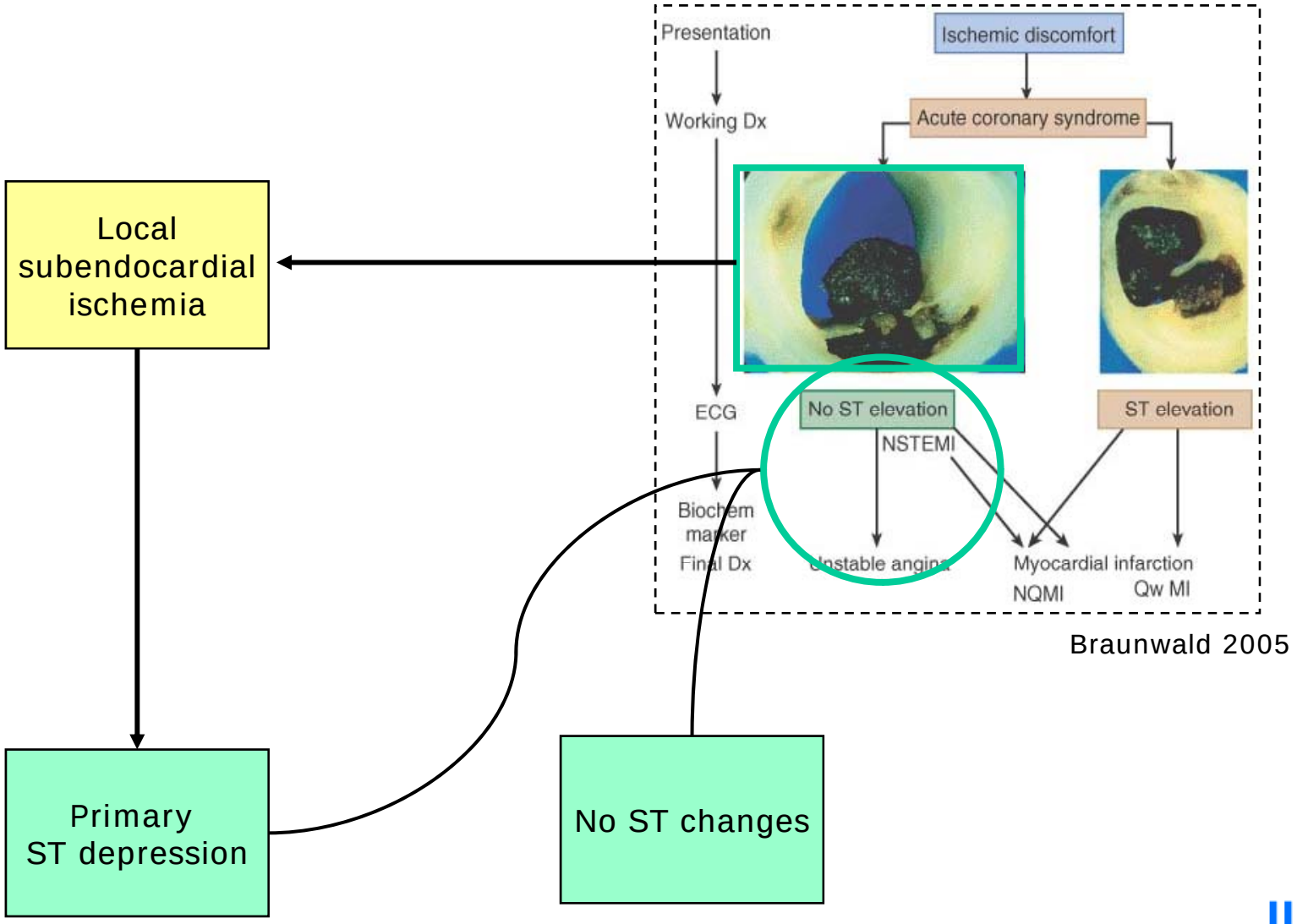
# Occlusion and ST depression



# Problem 1: animal models of ST↓ need rapid pacing

*Am J Physiol Heart Circ Physiol* 291: H2889–H2896, 2006.
First published August 11, 2006; doi:10.1152/ajpheart.00400.2006.

## Progressive epicardial coronary blood flow reduction fails to produce ST-segment depression at normal heart rates

**Marilyn de Chantal,[1,4] Jean G. Diodati,[1,2,4] James B. Nasmith,[1,2,4] Robert Amyot,[1,2,4] A. Robert LeBlanc,[1,4] Erick Schampaert,[1,2,4] and Chantal Pharand[1,3,5]**

*[1]Research Center, [2]Division of Cardiology and [3]Pharmacy Department, Hôpital du Sacré-Cœur de Montréal, Montréal, Québec, Canada; and Faculties of [4]Medicine and [5]Pharmacy, Université de Montréal, Montréal, Québec, Canada*

# Problem 2: relation between area and ST↓ is complicated

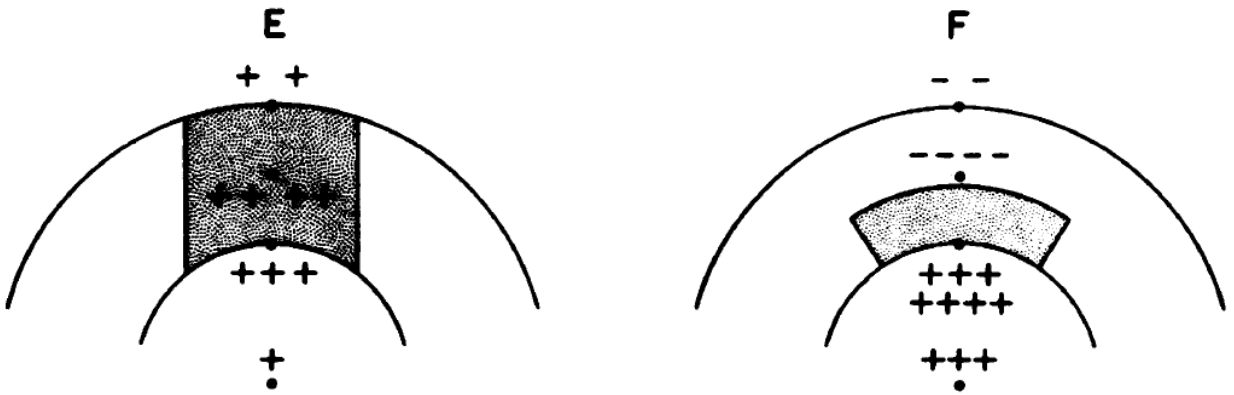



**FIGURE 10** Polarity and relative magnitude of TQ-ST segment deflections computed at epicardial intramyocardial, endocardial, and intracavitary locations and various shapes of ischemic involvement. + (−)TQ-ST segment deflection indicates negative (positive) TQ segment and positive (negative) ST segment displacement. Dark circles refer to electrode positions.

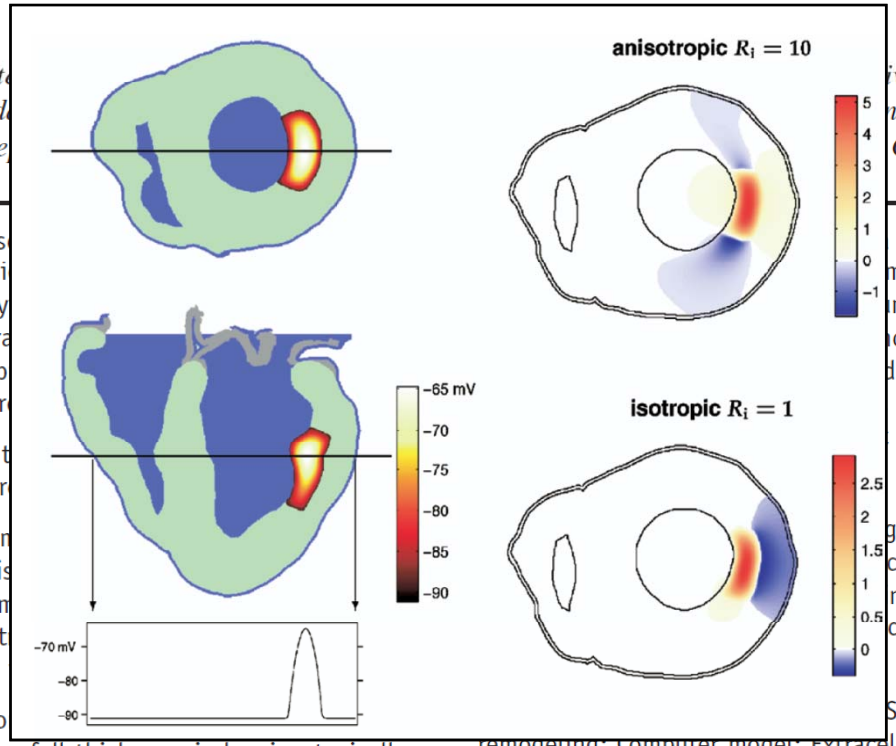
R. P. Holland et al, *J Clin Invest* 1977.

# Modern theory

## The effect of lesion size and tissue remodeling on ST deviation in partial-thickness ischemia

Mark Potse, PhD,*† Ruben Coronel, MD, PhD,‡ Stéphanie Falcao, MSc,*§ A.-Robert LeBlanc, PhD,*† Alain Vinet, PhD*†

*From the *Research Cent… …iversité de Montréal, Montréal, Québec, Canad… …niversity of Amsterdam, The Netherlands, and §De… …Canada.*




**BACKGROUND** Myocardial is… …reduced anisotropy ratio of or depression in electrocardi… …may result from hypertrophy pression in epicardium overly… …mstances that are likely to the ischemia is nontransmura… …crease of the extracellular does not always cause ST dep… …d, ST depression was found, ST depression is hard to repr… …in very large and thin isch-

**OBJECTIVE** The purpose of t… …may occur in left-main or cumstances in which ST depr…

**METHODS** We studied ischen… …g and geometric factors can of the human heart. A realis… …cardial leads. We note at the induced changes in resting n… …n most circumstances, while was based on diffusion of ext… …ct, even in partial-thickness eter, transmural extent, and …

**RESULTS** Our simulations co… …STEMI; Gap junctions; Tissue tial-thickness ischemia, like full-thickness ischemia, typically causes ST elevation in an anisotropic model of the ventricles. However, we identified three situations in which ST depression can

remodeling; Computer model; Extracellular potassium

(Heart Rhythm 2007;4:200–206) 

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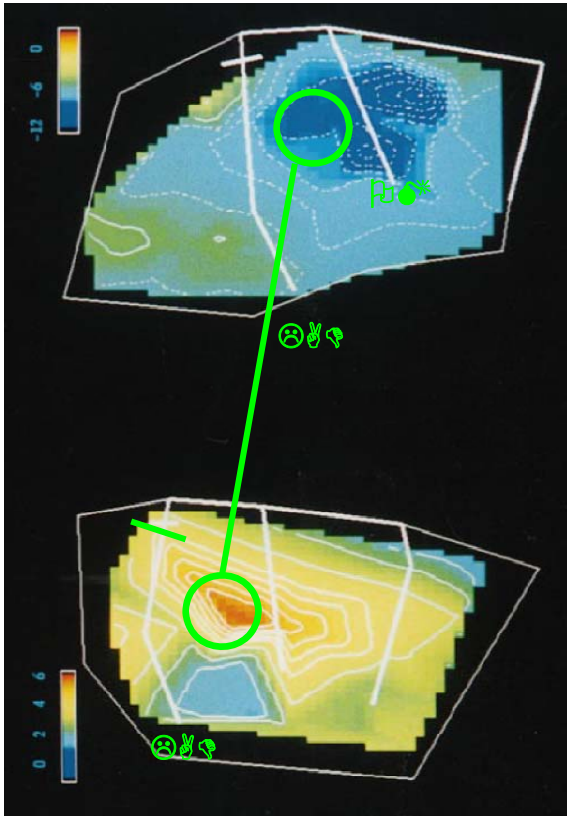
# Animal model

## Source of Electrocardiographic ST Changes in Subendocardial Ischemia

Danshi Li, Chuan Yong Li, Ah Chot Yong, David Kilpatrick



(*Circ Res.* 1998;82;957-970.)

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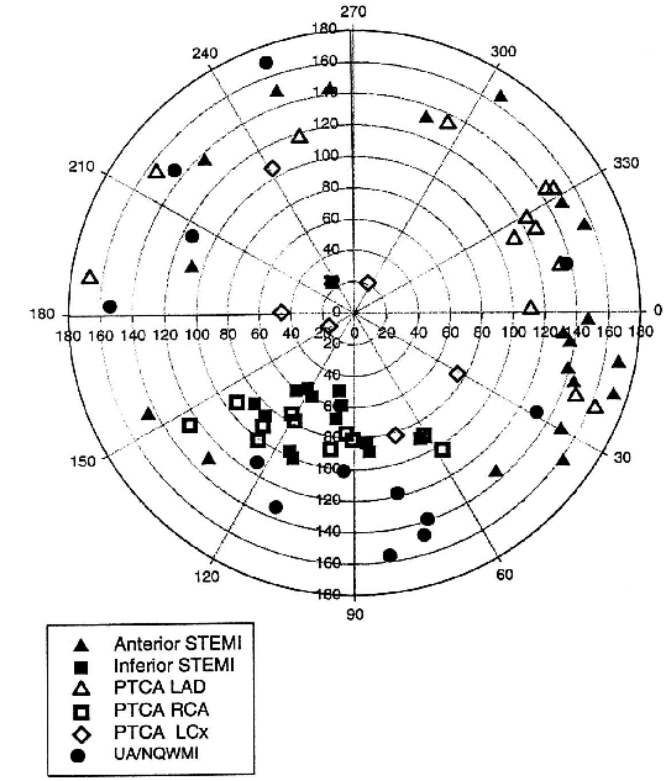
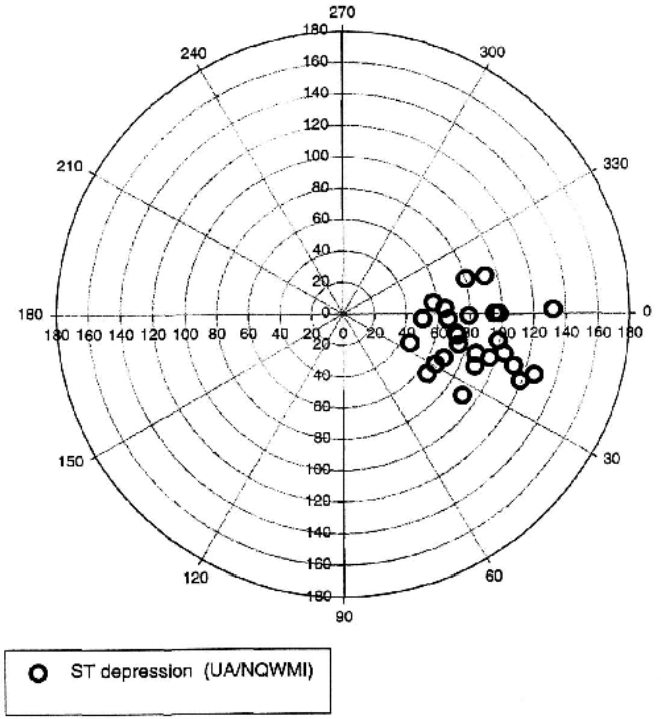
# Problem 3: *ST depression* in patients cannot be located…

ST-elevation vectors




ST-depression vectors




JB Nasmith, C Pharand, B Dubé, S Matteau, A-R LeBlanc, R Nadeau. Localization of maximal ST segment displacement in various ischemic settings by orthogonal ECG: Implications for lead selection and the mechanism of ST shift. Can J Cardiol 2001;17(1):57-62.

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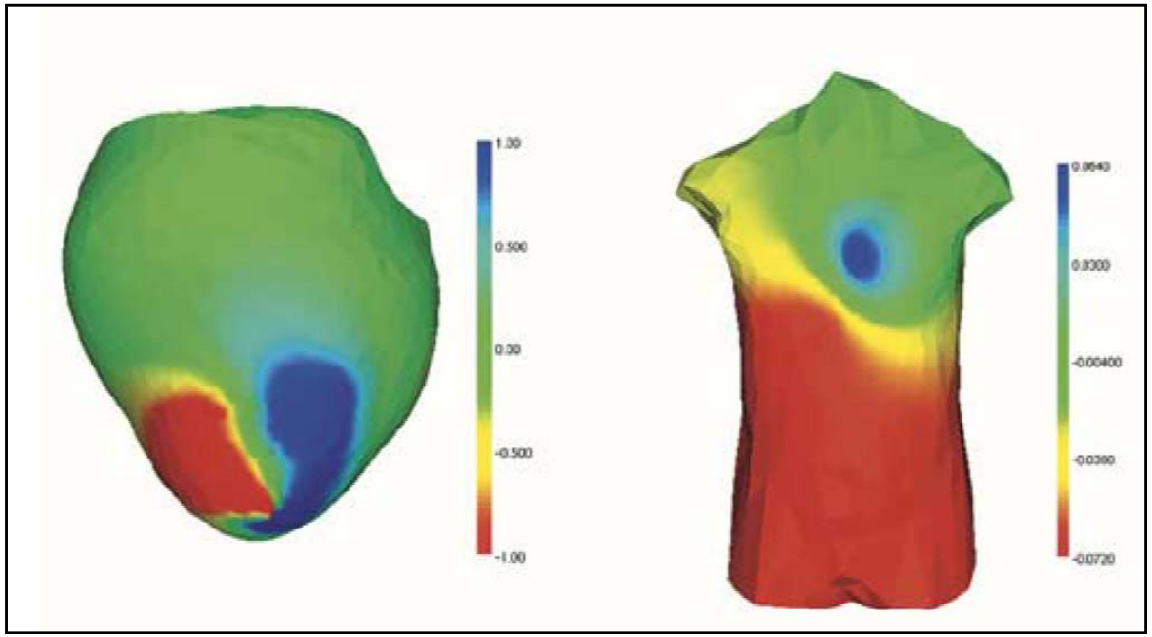
## ... *but subendocardial ischemia* can!

IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, VOL. 52, NO. 5, MAY 2005 799

# Simulation of ST Segment Changes During Subendocardial Ischemia Using a Realistic 3-D Cardiac Geometry

Mary C. MacLachlan*, Joakim Sundnes, and Glenn Terje Lines

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# Occlusion and ST depression revisited

Increased heart rate →
Reduced diastolic filling time

Elevated LV pressure

Reduced contractility

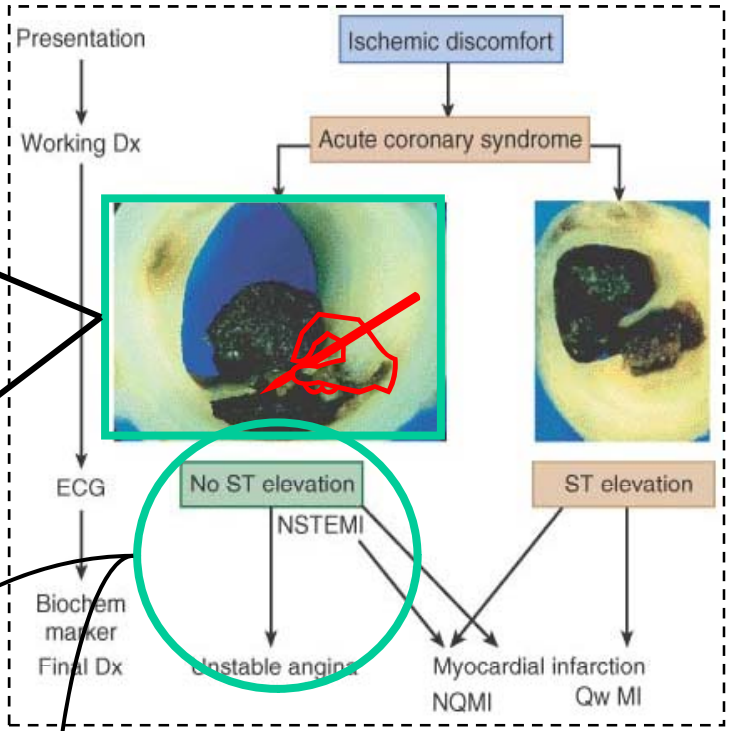
Global subendocardial ischemia

Local subendocardial ischemia

?

Primary ST depression

No ST changes




Braunwald 2005

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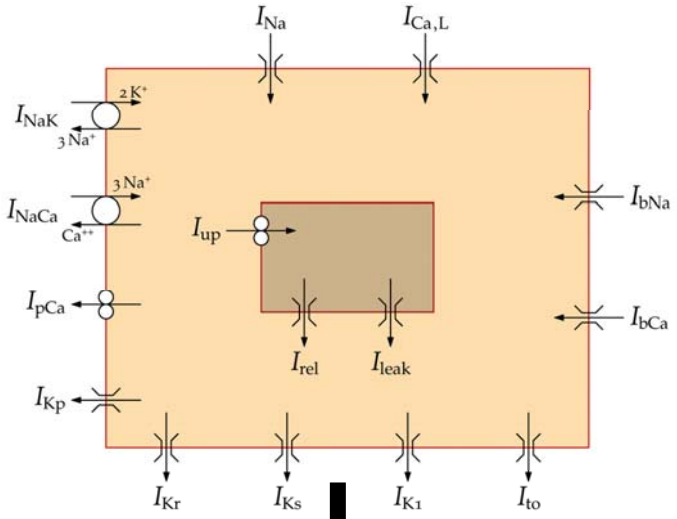
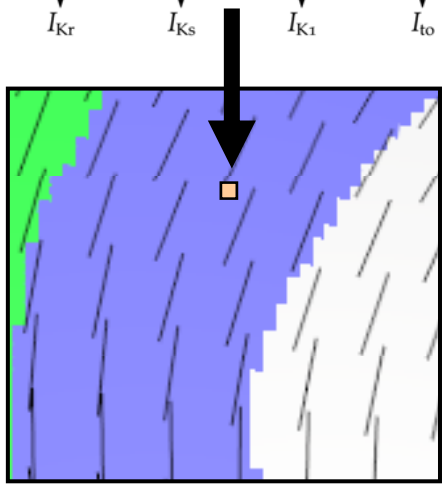
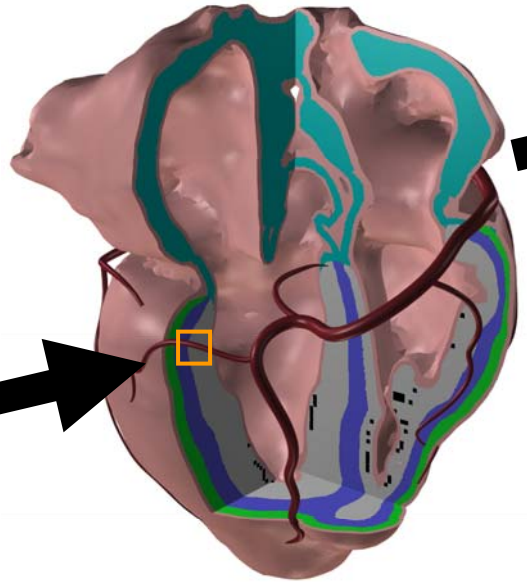
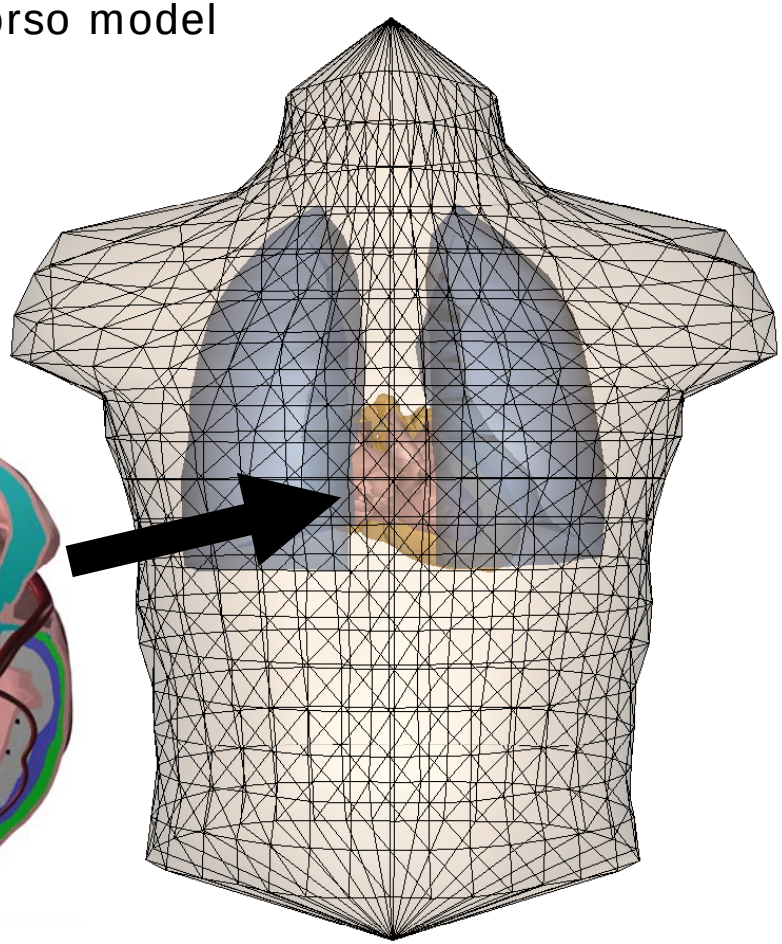
# Methods

- Reaction-diffusion model of the human heart
- Inhomogeneous boundary-element torso model







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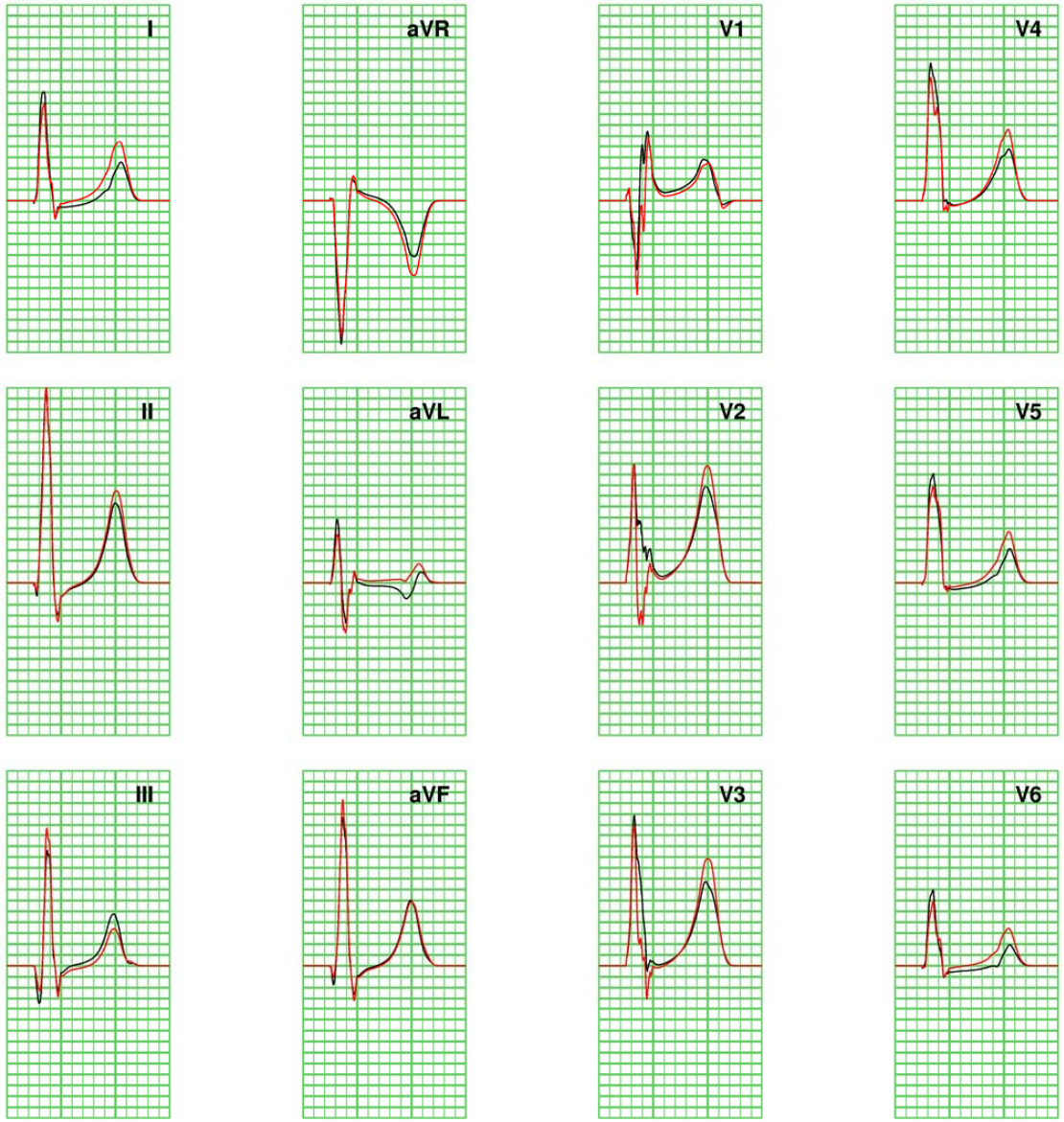
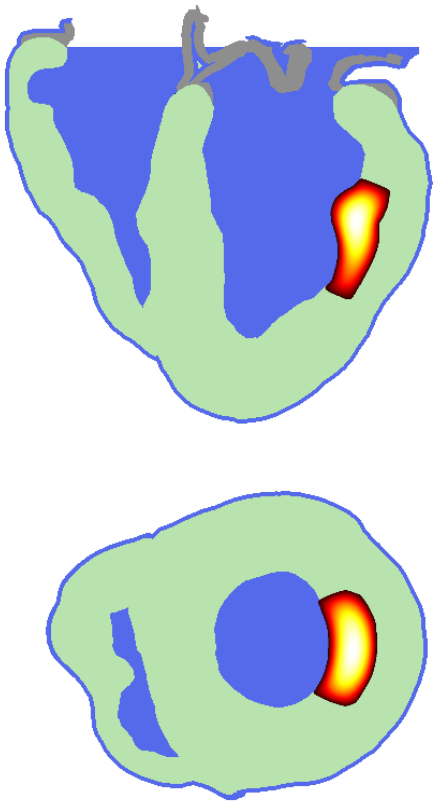
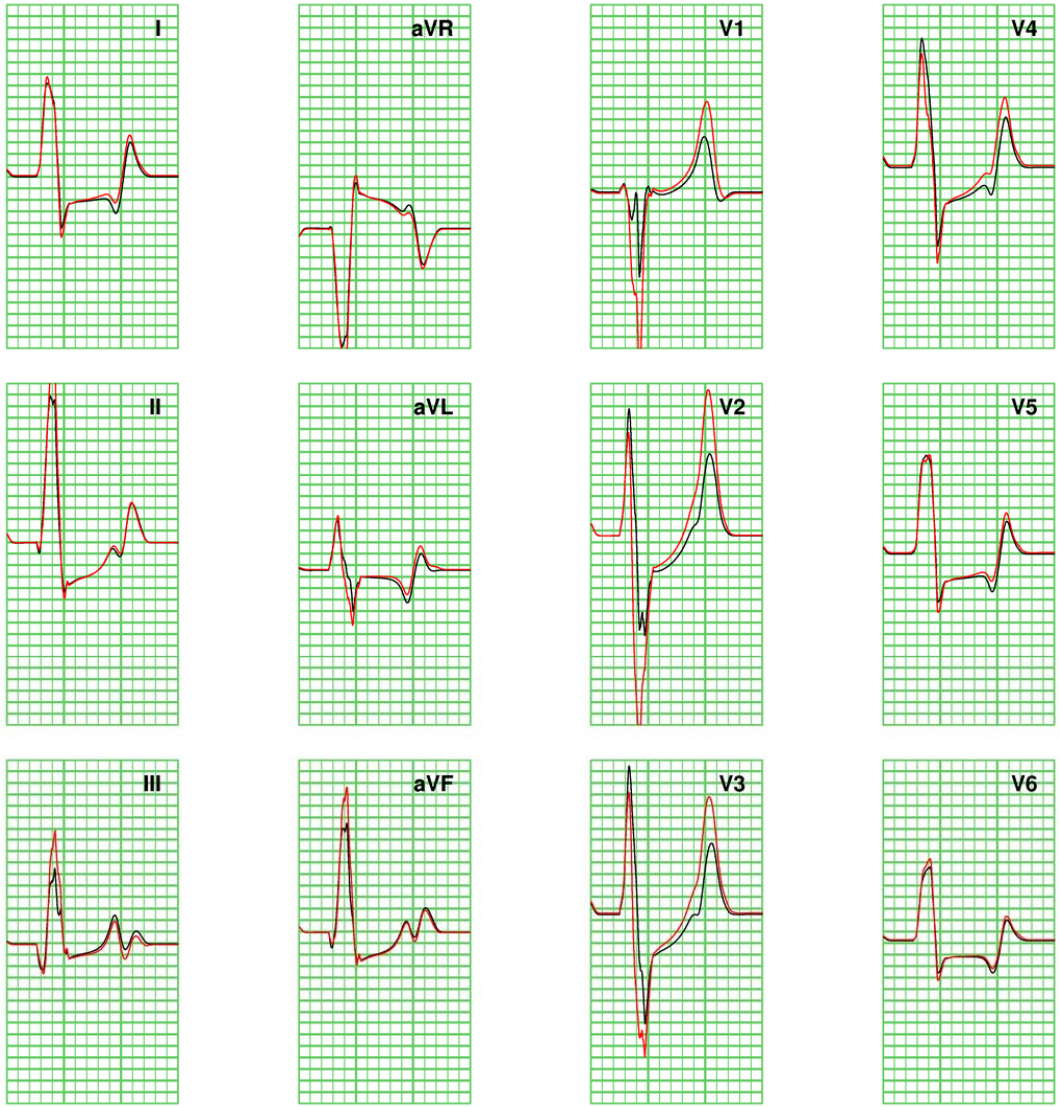
# Local subendocardial ischaemia



# Global subendocardial ischaemia




isotropic

anisotropic

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# Conclusion

- Local subendocardial ischaemia does not cause ST depression in overlying leads
- Global subendocardial ischaemia causes a “Stress-test ECG”
- Tissue anisotropy has little influence on the ECG changes due to global subendocardial ischaemia
- Primary ST depression may indicate a global perfusion problem rather than a single partial occlusion

# References


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**Holland** RP, Brooks H, Lidl B. Spatial and Nonspatial Influences on the TQ-ST Segment Deflection of Ischemia. *J Clin Invest* 1977; 60:197-214.

**Nasmith** JB, Pharand C, Dubé B, Matteau S, LeBlanc AR, Nadeau R. Localization of maximal ST segment displacement in various ischemic settings by orthogonal ECG: Implications for lead selection and the mechanism of ST shift. *Can. J. Cardiol*. 2001; 17:57-62.

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