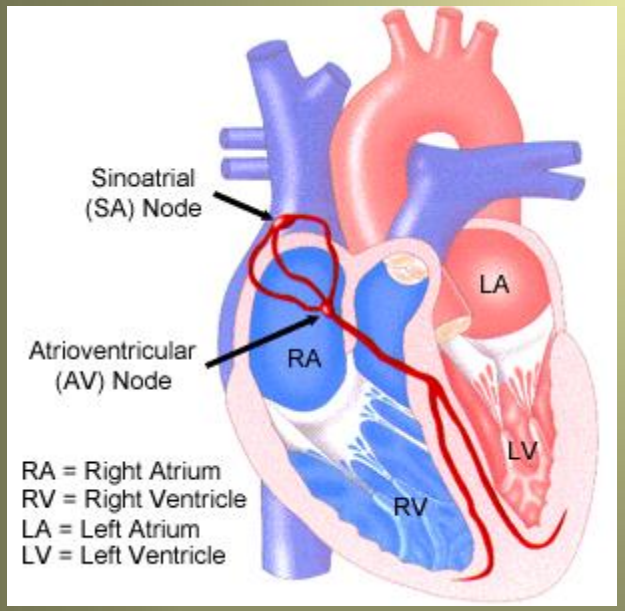
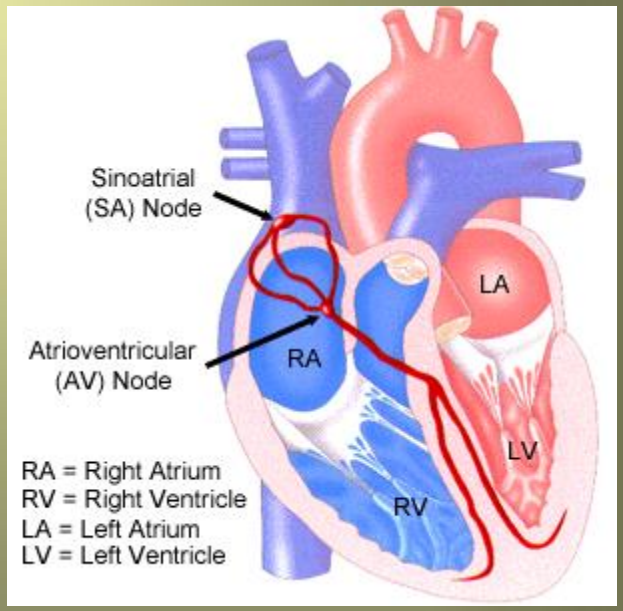
# HPC in Cardiac Electrical Activity: A DD Based Study

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# OUTLINE OF THE TALK

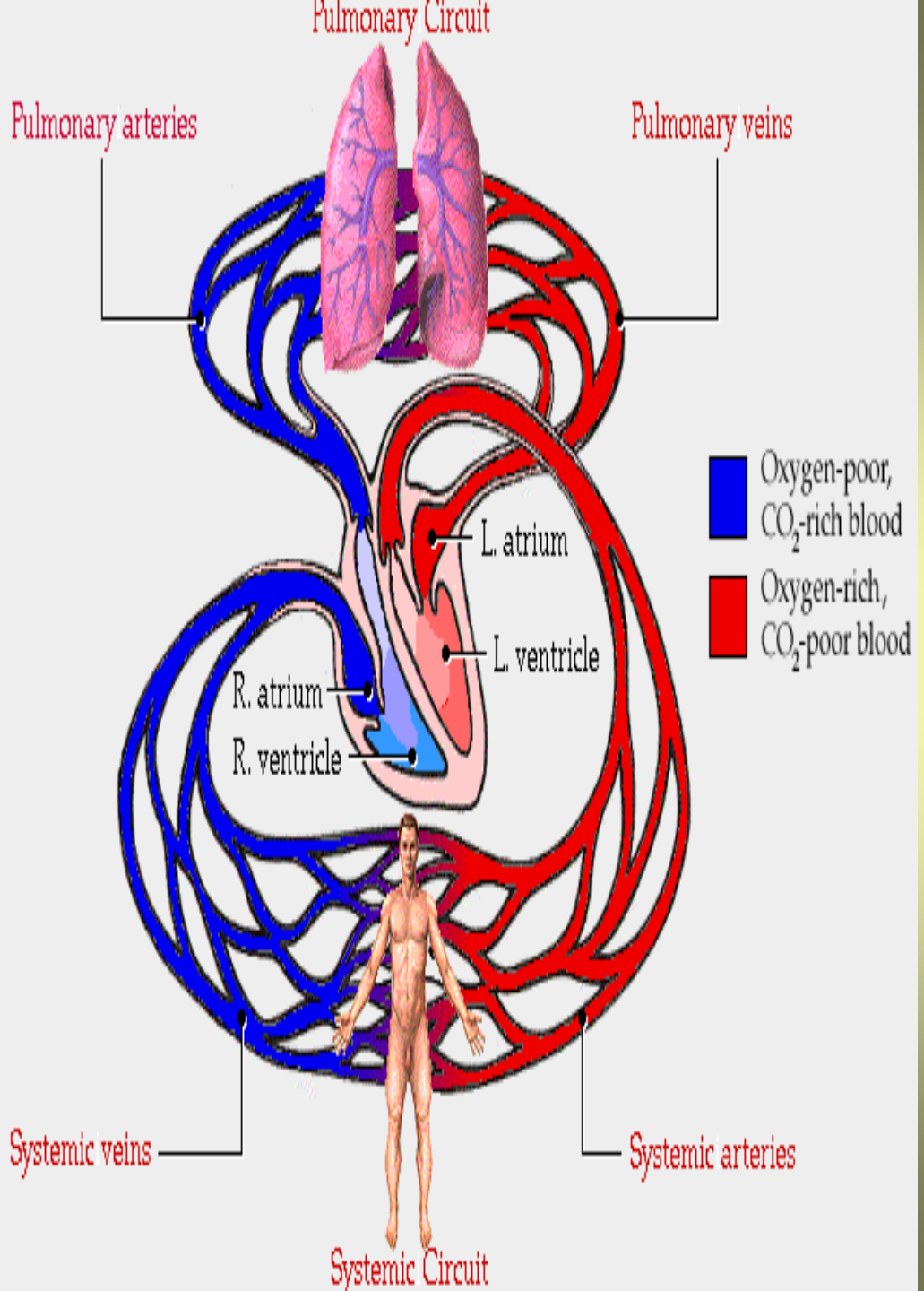
- Introduction
- Mathematical Modeling
- 0D: Basic Cell Model
- 1D Model
- 2D Models
- A look at DDM & HPC
- 3D Model
- Numerical Methodology (DD)
- Few details on Parallel Computing
- Results & Discussion

# Introduction

- What is CEA?
- Why Study about CEA?
- Earlier Works
- Some Rudimentary Details

- **Heart is an adaptive and reliable pump that maintains the circulation of blood flow throughout our life time.**
- **The Mechanical activity of heart is driven by the electrical activity of heart.**
- **During each cycle of normal activity an electrical wave propagates throughout the heart and triggers the cardiac muscle contraction.**
- **During life time of a healthy person the heart may beat over 2000 million times.**
- **Any abnormal behavior of heart can be fatal.**

- **It is important to understand the genesis and spread of cardiac excitation and its abnormalities.**
- **A first step towards this goal is to construct a mathematical model for electrical activity of heart.**
- **In mammalian heart, the ventricle is relatively thick walled, and shows spatial heterogeneity i.e. myocytes isolated from different regions of the ventricle may have different electrical activity.**
- **The modeling actually starts with basic cell modeling which in turn are incorporated into 3D models of ventricular tissue.**




- **The rhythmic pumping of heart is produced by four chambers. The two ventricles act as primary pump which eject blood into two main arteries.**
- **The right ventricle pumps blood into pulmonary artery (i.e. to lungs) and the left ventricle pumps the blood into aorta ( for systemic circulation).**
- **The two atria are auxiliary pumps that receive the blood from pulmonary and systemic circulation and pass it to fill the ventricles.**

- **It is important that the ventricles must be excited after atria so that ventricles can be filled with blood before ventricular contraction occurs, as a consequence the ventricles can efficiently pump blood to the pulmonary and systemic circulation.**

- **BUT! during the cardiac arrhythmias and FIBRILLATION this normal rhythm of events is disturbed. Cardiac arrhythmias can occur in the atria or the ventricles but those occurring in the atria are more serious and dangerous. Ventricular fibrillation is the commonest cause of sudden death if not treated immediately.**

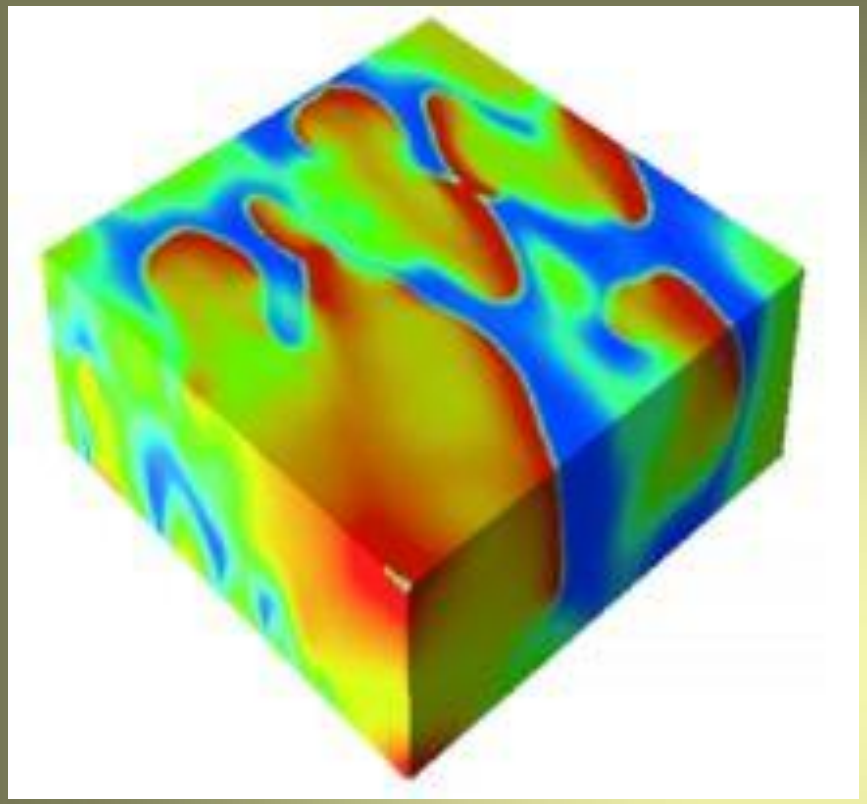
- During the ventricular fibrillation the blood circulation collapses and subsequently brain damage or death is brought about in only few minutes due to lack of oxygen supply.

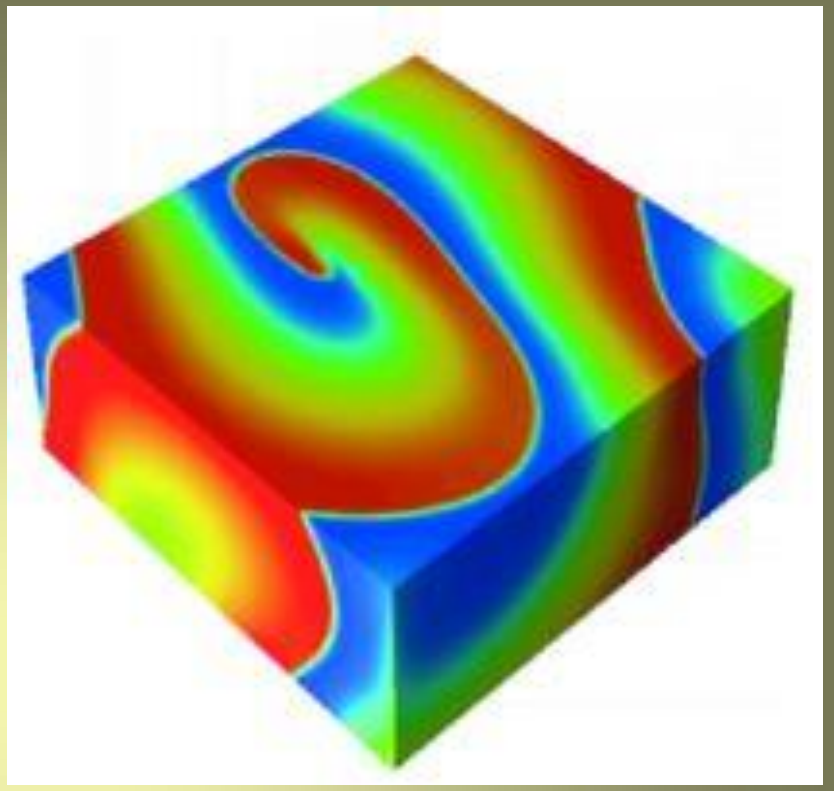
- Many ventricular arrhythmias and fibrillation are believed to be associated with abnormal spatio-temporal patterns of a rotating excitation wave i.e. re-entrant excitation wave, in which a wave of excitation repeatedly re-invades the same piece of cardiac tissue.

# Motivation for the problem

**The Number of Deaths due to the ventricle fibrillation motivates us to study the electrical activity involved during excitation process in ventricle myocardium . In India, more than 1.4 million people die every year because of cardiac arrhythmia.**

Anyone who‘s watched a hospital drama is familiar with the scene: “Heart monitor flat lines, accompanied by an eerie alarm signal”. A doctor or nurse calls out, “He’s in V-fib!” and electric paddles are charged and applied to the patient’s chest. The hope is that the shock will correct the rhythm of the heart, saving the patient’s life--at least for the moment. Cardiac researchers study about ventricular fibrillation (V-FIB). Using Computers researchers are modeling the electrical signals that pulse through the specialized cells of the heart muscle. The simulations help them understand how electrical waves become chaotic in ventricular fibrillation (VF), the major cause of sudden cardiac death.



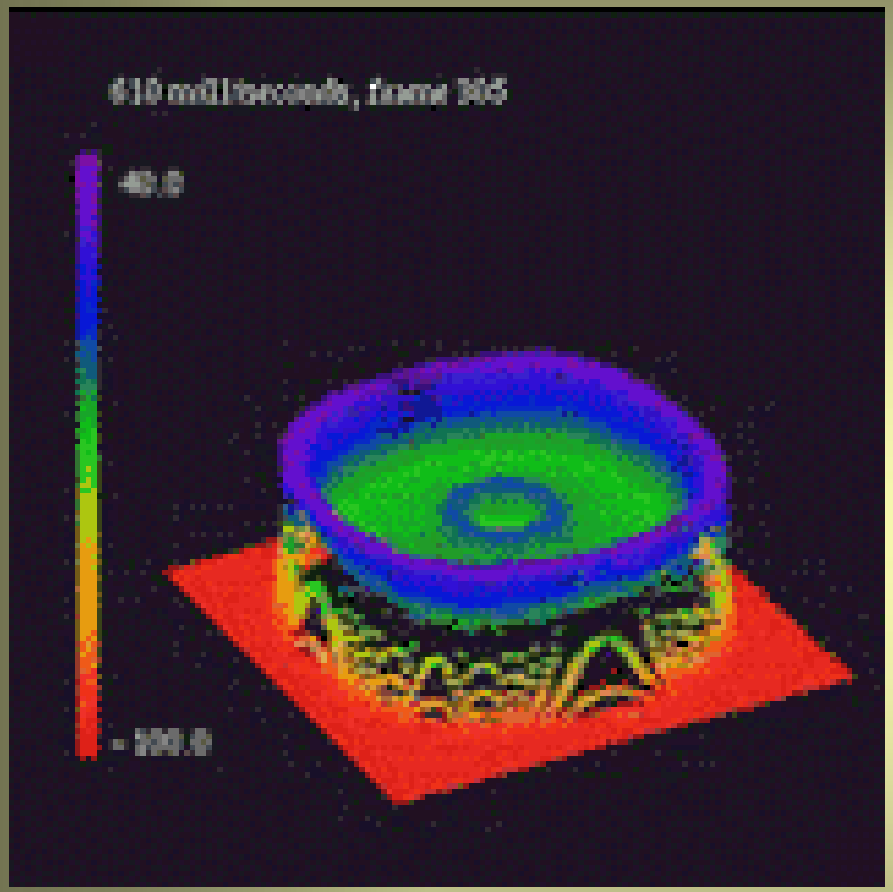


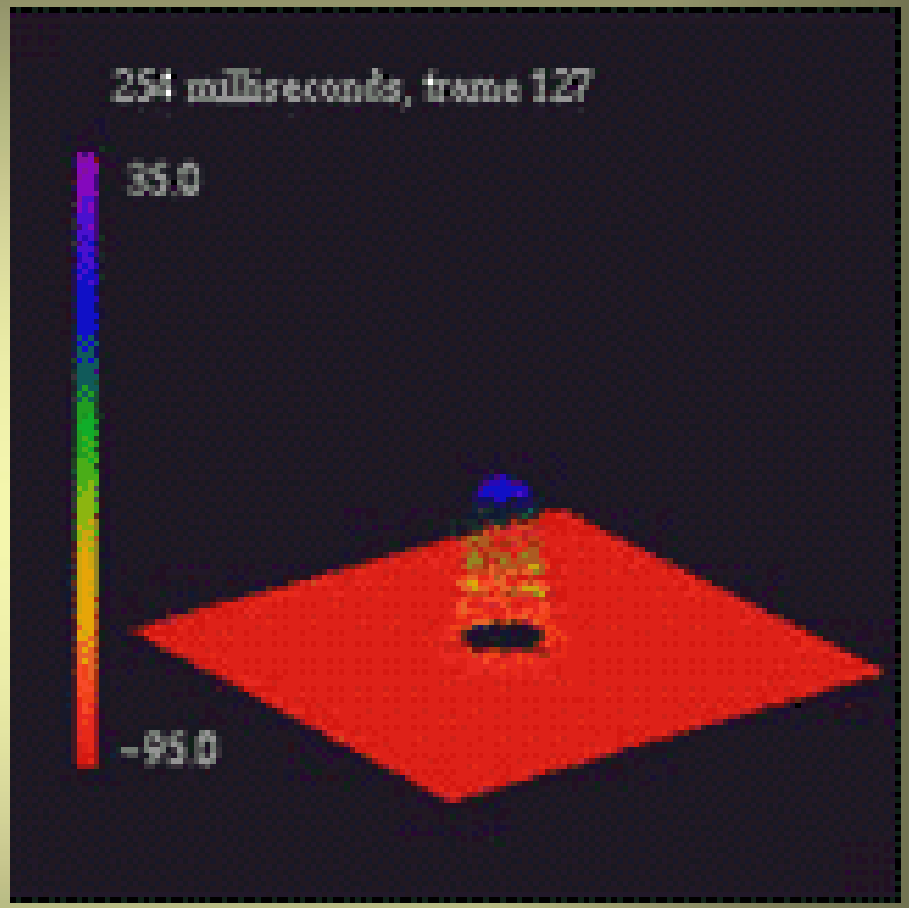
**Chaotic electrical activity during ventricular fibrillation (VF).**

**A "drug" has prevented breakdown of the scroll wave and averted VF**

**In both images voltage is color-coded from red (highest voltage, corresponding to cells that are firing) to blue (lowest voltage, corresponding to cells that are fully recovered and resting)**

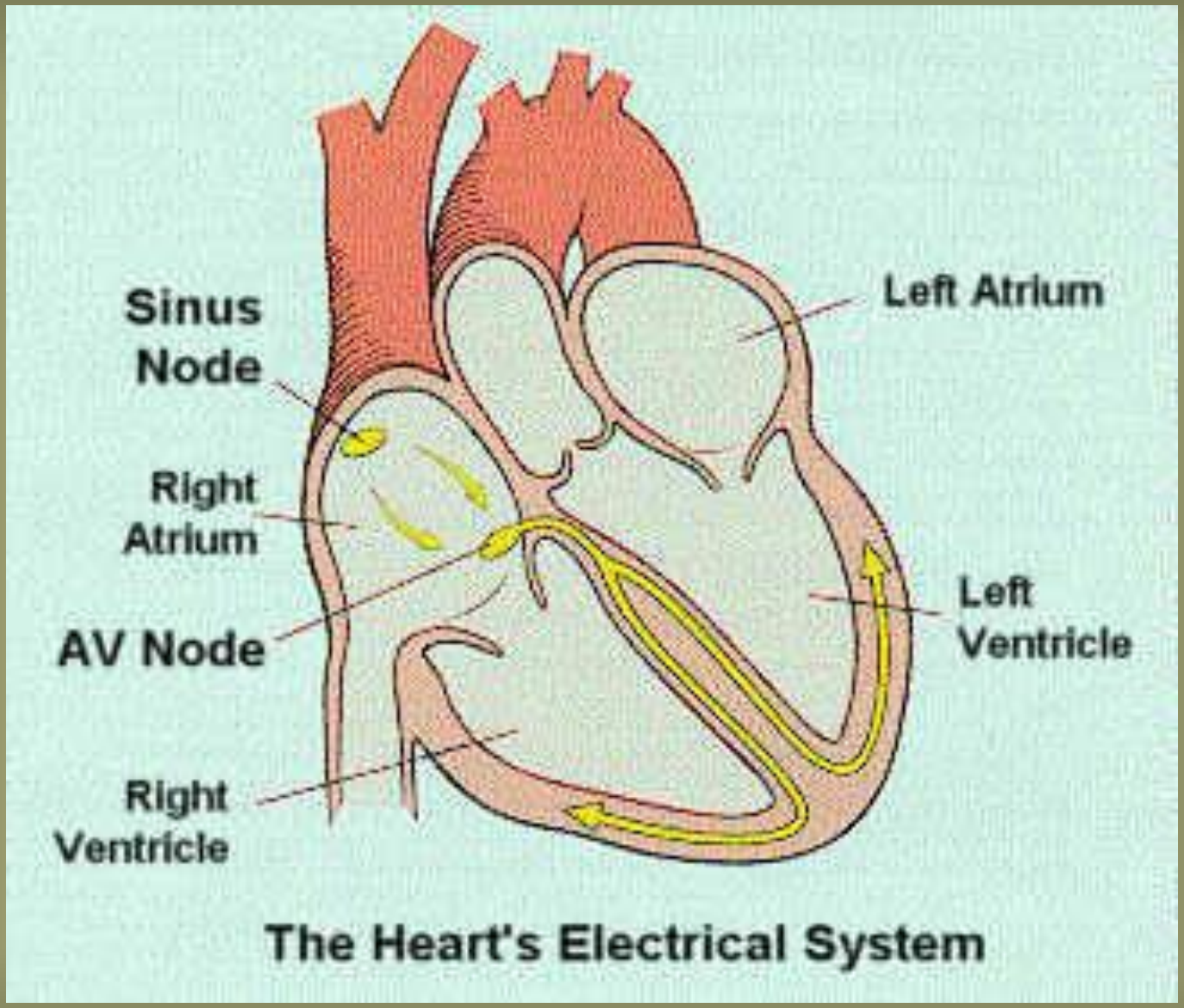
**Images courtesy of Alan Garfinkel, Zhilin Qu, Jong Kil, and James N. Weiss.**



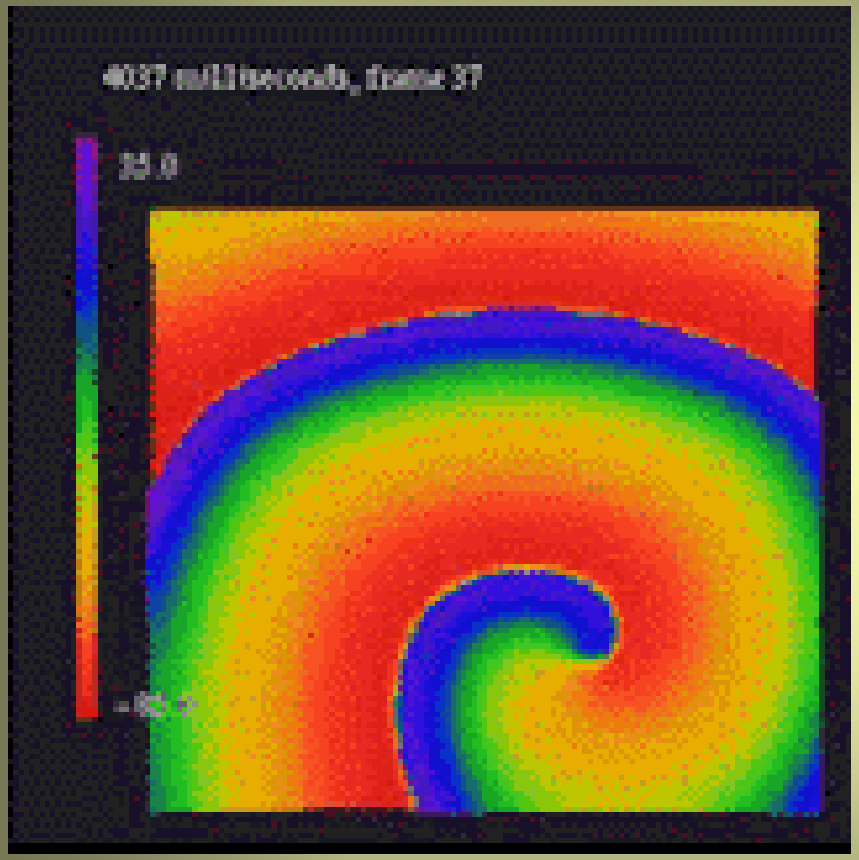




**Normal SA node burst**

**SA node burst Failure**




Shortcut to heartautoareas.lnk



Spiral excitation wave

**Spiral reentrant waves are believed to be a possible model of tachycardia. Here, a spiral reentrant wave is induced in a 256x256 lattice of atrial cells modeled as described for Oxsoft Heart V4.5 (D. Noble). The reentrant wave was initiated using the so-called S1-S2 protocol. In this protocol, a plane wave is initiated by current injection along one edge of the lattice. When this plane wave has propagated across half the lattice, a second pulse is applied to cells along the orthogonal edge. The spiral reentrant wave induced using this procedure has a rotational period of about 100 msec.**

# Earlier Works

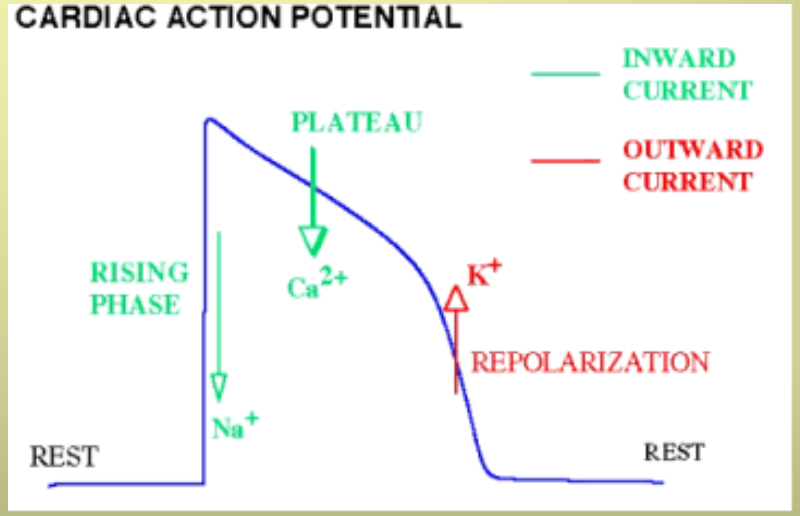
- **Noble (1962) proposed first model for electric activity in sheep purkinje cardiac cell.**
- **Mc.Allister (1975) extended Noble's model by incorporating ionic currents based on voltage clamp studies.**
- **Beeler-Reuter (1977) and Panfilov &Holden (1977) have proposed model for action potential of ventricular myocardial fibers.**
- **Difrancesco & Noble (1985) incorporated ionic pumps and concentration change effects into the CEA model of Beeler-Reuter.**

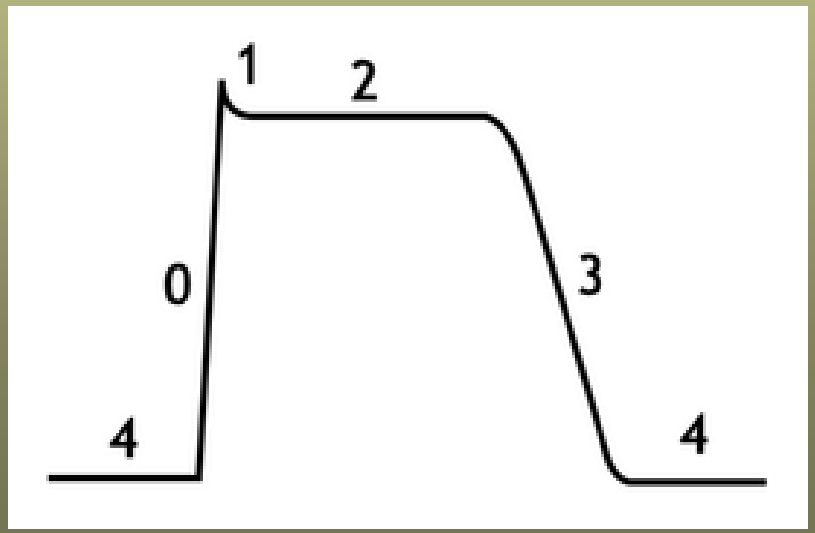
- **Luo & Rudy (1991, 1994) developed a series of models for cardiac ventricular action potential based on experimental data from ventricular cell. These models provide the basis for the study of possible arrhythmogenic mechanisms of myocytes (Viray et al 1998).**
- **Zeng (1995), Jafri et al (1998), Zipes & Jalife (1999) have proposed improved versions of Luo-Rudy model.**
- **Colli Franzone et al (2004) simulated patterns of excitation, repolarization and action potential duration cardiac Bidomain and Mono Domain Models**
- **Monica Haslien et al (2007) have proposed an unconditionally stable numerical method for Luo-Rudy 1 model used in simulations of defibrillation.**
- **Simone Scacchi (2008) has come up a hybrid multilevel Schwarz method for the bidomain mdel.**

# Some Rudimentary Elements

- There are two kinds of electrically active cells in the heart: the pacemaker cells and the excitbale cells.
- Pacemaker cells can generate electrical excitations endogenously: the pacemaker membrane slowly depolarizes and reaches the action potential threshold.
- Excitable cells do not normally show pacemaker activity, but are excited by a supra-threshold stimulus. The response to supra-threhold excitation is the ACTION POTENTIAL.

# The Cardiac Action Potential

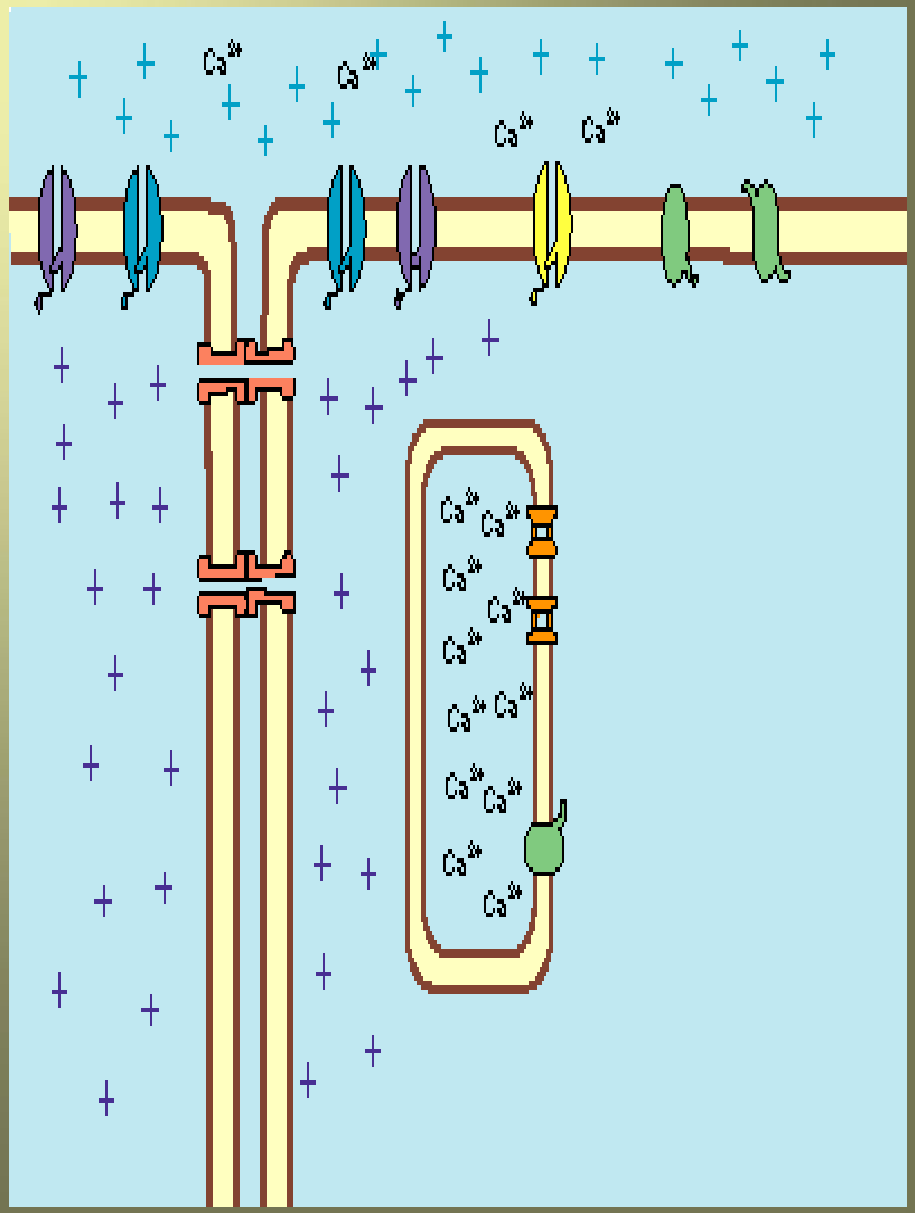



- **4: Resting Potential is stable and is influenced by Na-K ion pump current.**
- **0: Upstroke of AP is the first phase during which the potential across the membrane changes from -ve to +ve.**
- **1: Peak of AP**
- **2: Plateau of AP is a slow phase during which many membrane currents like Ca-ion current, Na-Ca current, K-ion current etc. are involved.**
- **3: Repolarization Phase of AP is rapid phase between plateau and resting states of AP due to inward K-ion current.**

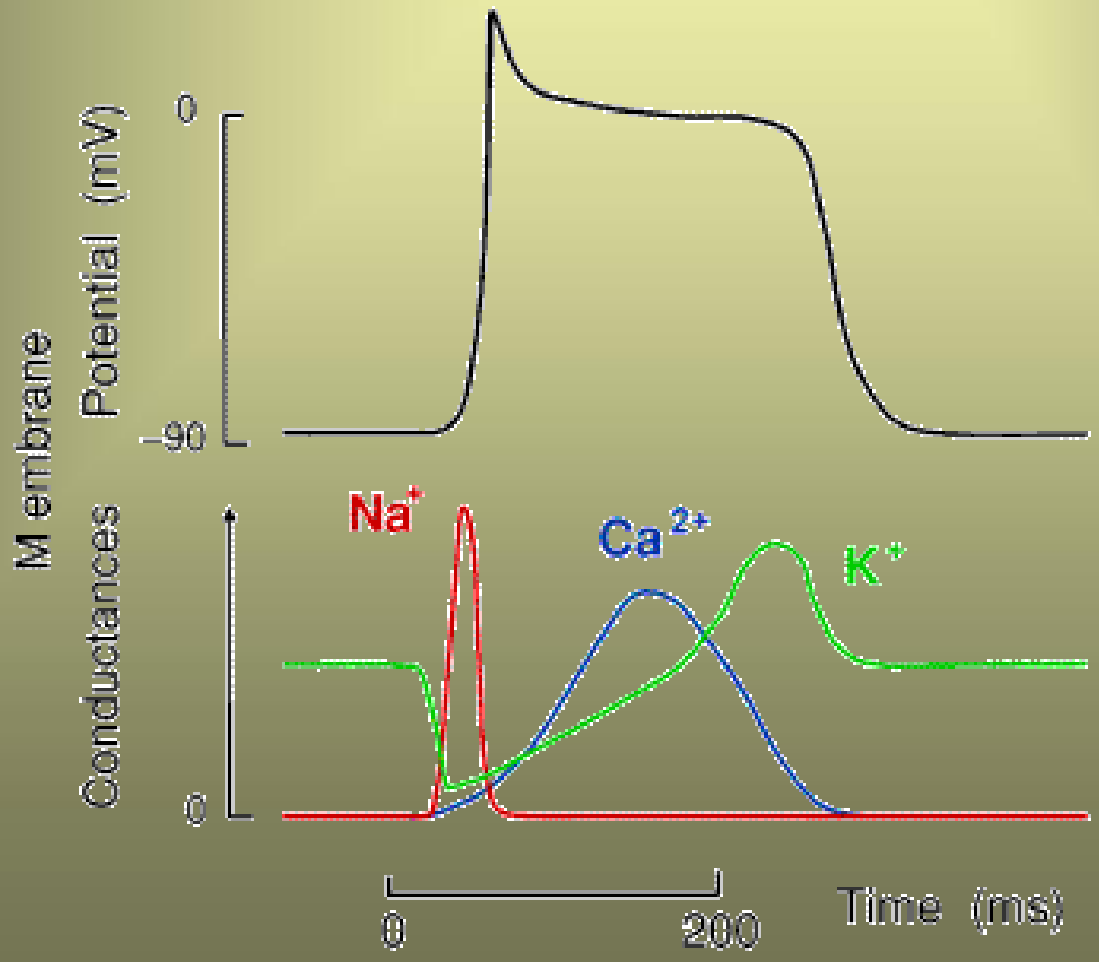
# Mechanism of excitation of Cardiac Cells

- Involves a number of ionic-currents of Na, Ca, K, Cl etc.
- The flow of ions can be passive through ion channels down an electro-chemical gradient or active by ionic-pumps which consumes energy.
- Ionic channels are GATED and their state is voltage dependent. Flow of ions across the membrane is an electric current that alters cell potential (voltage).
- Ionic current depends on membrane potential too.

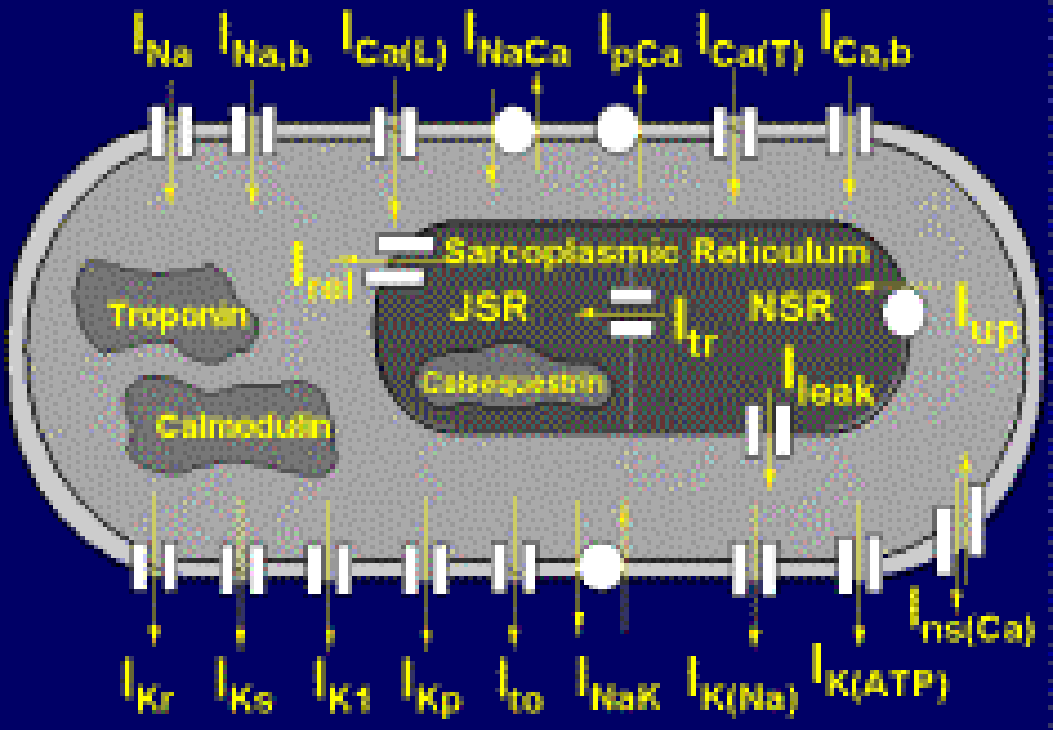


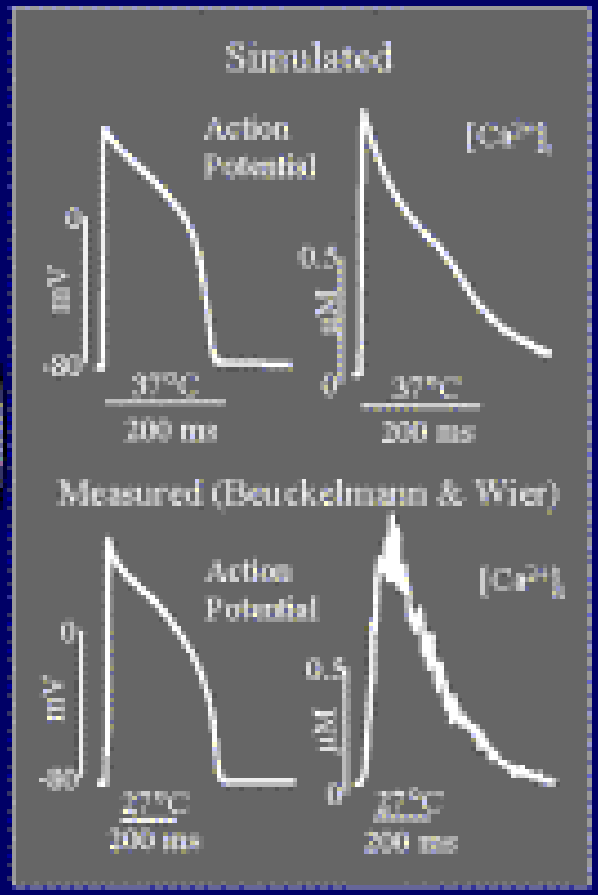
# Ionic Conductance During CEA

**Action potential and underlying conductance changes in a ventricular myocyte (from a small mammal)**

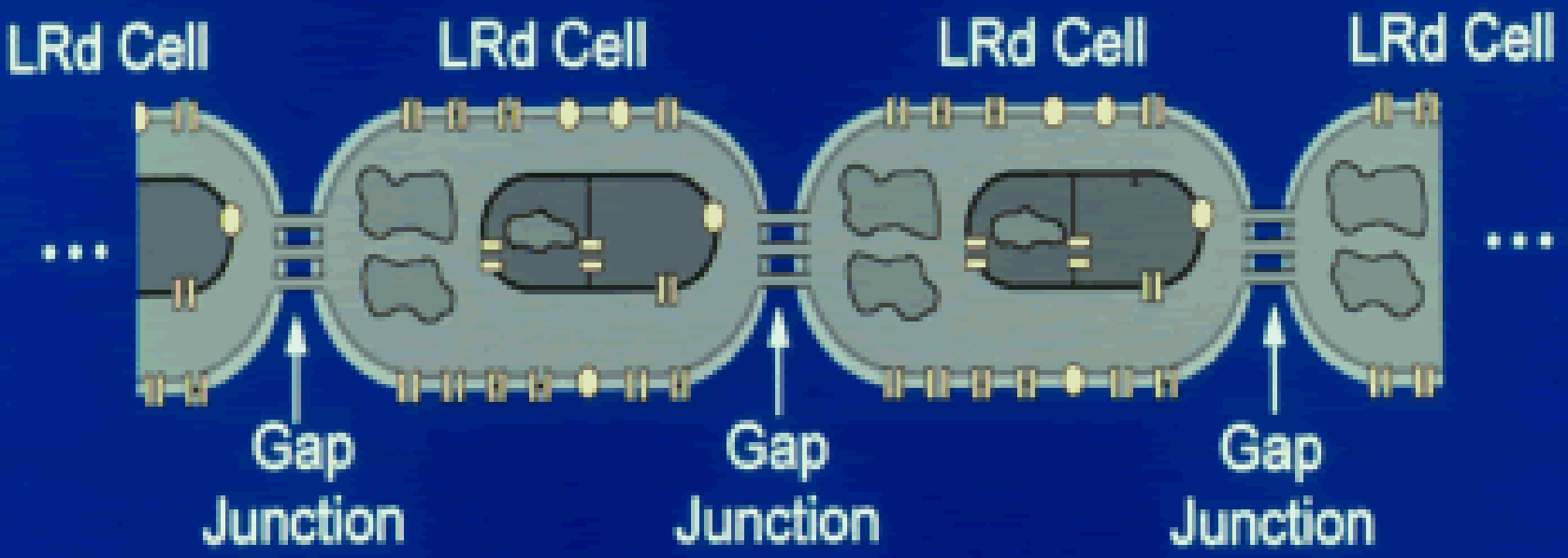


# Cardiac Cell Model



# Multicellular Cardiac Propagation



# Basic Cardiac Excitation Equations

- **Electro-Chemical Gradient：** **Flow of ions across the membrane depends on ionic concentration（Chemical Gradient） and potential across the membrane (Electrical Gradient) i.e.**

$$ECG = V_m - E_{ion},$$

$$E_{ion} = \{(RT)/(ZF)\} * \{\log(ion)_e/(ion)_i\}$$

**is called the Nerst Potential.**

# Equation for Ionic Current: (Ohm's Law)

$$i_{ion} = G_{ion}(V_m - E_{ion})$$

**$G_{ion}$:membrane ionic conductance**

**Depends on the number of conducting channels in the membrane and the properties of individual channels**

- **The sign of $(V_m - E_{ion})$ determines the direction of the movement of the ionic current. If it is -ve, the ionic current is inward i.e. the movement of +ve charge into a cell. If it is +ve, the ionic current is outward i.e. movement of +ve charge out of a cell**
- **An inward current depolarizes a cell membrane (i.e. membrane potential becomes more +ve).**
- **An outward current repolarizes a cell membrance (i.e. membrane potential becomes more negative)**

# Ion-Channel Gating Mechanism Equation

- **Ionic Channel will have many gates.**
- **Gating mechanism introduce both voltage and time dependence into the ionic-current**
- **Gates may be dependent on electrical/chemical/mechanical signals.**

$$dn/dt = a_n(1-n) - b_n n$$

**$a_n$ : gate open rate co-efficient**

**$b_n$ : gate closing rate co-efficient**

**n : fraction of gates in open state**

**1-n : fraction of gates in closed state**

# Modeling of Cardiac tissue during Cardiac Excitation process

Excitation of Cardiac tissue is due to rapid ionic currents like Sodium, Potassium, Calcium etc. through the cellular membrane, modeled by a reaction-diffusion system of PDEs

# Single Cell Luo-Rudy Model (1991) or Zero Dimensional Model

We assume that v, transmembrane potential is only function of time. Considering all the gating variable into account we have,

**General Equations:**

$$\rho C_m \frac{\partial v}{\partial t} + \rho I_{ion}(v, w) = I_{app} \quad in \quad \Omega \times (0, T)$$

$$\frac{\partial w}{\partial t} - R(v, w) = 0 \quad in \quad \Omega \times (0, T)$$

$$I_{ion} = I_{Na} + I_{Si} + I_K + I_{K_1} + I_{Kp} + I_b$$

## Reversal potentials:

$$E_{K_1} = \frac{RT}{F} \log\left[\frac{K_o}{K_i}\right]$$

$$E_{Si} = 7.7 - 13.0287 \log(Ca_i)$$

$$E_{Kp} = E_{K_1}$$

## Differential Equations:

$$\frac{\partial m}{\partial t} = \alpha_m (1.0 - m) - \beta_m m$$

$$\text{where,} \qquad \alpha_m = \frac{0.32(v + 47.13)}{1 - e^{-0.1(v+47.13)}},$$

$$\beta_m = 0.08 e^{-v/11.0}$$

$$\frac{\partial h}{\partial t} = \alpha_h (1.0 - h) - \beta_h h$$

*where,*

$$\alpha_h = \begin{cases} 0.135 e^{\left(\frac{-80.0 - v}{6.8}\right)} & ; if \quad v < -40 \\ 0 & ; if \quad otherwise \end{cases},$$

$$\beta_h = \begin{cases} 3.56 e^{0.079v} + 310000 e^{0.35v} & ; if \quad v < -40 \\ 1.0 / (0.13 (1.0 + e^{\left(\frac{-v - 10.66}{11.1}\right)})) & ; if \quad otherwise \end{cases}$$

$$\frac{\partial j}{\partial t} = \alpha_j (1.0 - j) - \beta_j j$$

*where,*

$$\alpha_j = \begin{cases} \dfrac{-127140 e^{0.2444v} - 0.00003474 e^{-0.439v} (v + 37.78)}{1.0 + e^{0.311(v + 79.23)}} & ; if \quad v < -40 \\ 0.0 & ; if \quad otherwise \end{cases},$$

$$\beta_j = \begin{cases} 3.56 e^{0.079v} + 310000 e^{0.35v} & ; if \quad v < -40 \\ 1.0 / (0.13 (1.0 + e^{\left(\frac{-v - 10.66}{11.1}\right)})) & ; if \quad otherwise \end{cases}$$

$$\frac{\partial d}{\partial t} = \alpha_d (1.0 - d) - \beta_d \, d$$

where,
$$\alpha_d = \frac{0.095 e^{-0.01(v-5.0)}}{1 + e^{-0.072(v-5.0)}},$$

$$\beta_d = \frac{0.07 e^{-0.017(v+44.0)}}{1 + e^{0.05(v+44.0)}}$$

$$\frac{\partial f}{\partial t} = \alpha_f (1.0 - f) - \beta_f \, f$$

where,
$$\alpha_f = \frac{0.012 e^{-0.008(v+28.0)}}{1 + e^{0.15(v+28.0)}},$$

$$\beta_f = \frac{0.0065 e^{-0.02(v+30.0)}}{1 + e^{-0.2(v+30.0)}}$$

$$\frac{\partial X}{\partial t} = \alpha_X (1.0 - X) - \beta_X X$$

$$\text{where,} \quad \alpha_X = \frac{0.0005 e^{-0.083(v+50.0)}}{1 + e^{0.057(v+50.0)}},$$

$$\beta_X = \frac{0.0013 e^{-0.06(v+20.0)}}{1 + e^{-0.04(v+20.0)}}$$

$$\frac{\partial K_1}{\partial t} = \alpha_{K_1} (1.0 - K_1) - \beta_{K_1} K_1$$

$$\text{where,} \quad \alpha_{K_1} = \frac{1.02}{1 + e^{0.2385(v - E_{K_1} - 59.215)}},$$

$$\beta_{K_1} = \frac{0.49124 e^{0.08032(v - E_{K_1} + 5.476)} + e^{0.06175(v - E_{K_1} + 594.31)}}{1 + e^{-0.5143(v - E_{K_1} + 4.753)}}$$

$$\text{where} \quad \mathrm{E}_{\mathrm{K}_1} = \frac{RT}{F} \log\left[\frac{K_o}{K_i}\right]$$

$$\frac{\partial Ca_i}{\partial t} = 0.07 (10^{-4} - Ca_i) - 10^{-4} I_{Si}$$

$$\text{where,} \quad \mathrm{I}_{\mathrm{Si}} = 0.09 \bullet d \bullet f \bullet (v - E_{Si}),$$

$$\mathrm{E}_{\mathrm{Si}} = 7.7 - 13.0287 \log(Ca_i)$$

# Membrane Equation:

$$I_{Na} = G_{Na} \bullet m^3 \bullet h \bullet j \bullet (v - E_{Na})$$

$$I_{Si} = 0.09 \bullet d \bullet f \bullet (v - E_{Si})$$

*where,*

$$E_{Si} = 7.7 - 13.0287 \log(Ca_i)$$

$$I_K = G_K \bullet X \bullet X_i \bullet (v - E_K)$$

*where,*

$$G_K = 0.282 \sqrt{\frac{K_o}{5.4}} \qquad X_i = \begin{cases} abc & ; \quad v < -100.0 \\ 1.0 & ; \quad otherwise \end{cases}$$

$$I_{K_1} = G_{K_1} \bullet K_1^{\infty} \bullet (v - E_{K_1})$$

*where,*

$$K_1^{\infty} = \frac{\alpha_{K_1}}{\alpha_{K_1} + \beta_{K_1}}, \qquad E_{K_1} = \frac{RT}{F} \log\left[\frac{K_o}{K_i}\right]$$

$$I_{K_p} = \frac{0.0183\,(v - E_{K_p})}{1 + e^{\frac{(7.488 - v)}{5.98}}}$$

*where,*

$$E_{K_p} = E_{K_1}$$

$$I_b = 0.03921\,(v + 59.87)$$

# Parameter Values and initial conditions [Luo-Rudy Model (1991)]

## Initial Values

| | | | |
|---|---|---|---|
| V | : -84.0000 mV | m | : 0.0000 |
| h | : 0.9811 | j | : 0.9882 |
| d | : 0.0031 | f | : 1.0000 |
| X | : 0.0060 | Ca | : 0.5113 |
| $K_1$ | : 0.7027 | $I_{Na}$ | : 0.0000 |
| $I_{Si}$ | : -0.0413 | $I_K$ | : -0.0083 |
| $I_{K1T} = I_K + I_K + I_K = 0.0618$ | | $I_{K1}$ | : 1.0079 |
| $I_m$ | : 0.0122 | | |

# Parameter values

$C_m$ : 1.00 mF/cm$^2$

R : 8324.41 mJ/(mol $^o$ K)

$K_o$ : 5.4 mM

$Ca_o$ : 1.8 mM

$Na_o$ : 140 mM

$G_K$ : 0.282 mS/cm$^2$

$G_b$ : 0.0392 mS/cm$^2$

$E_K$ : -77.0 mV

F : 96485 C/mol

T : 310 $^o$ K

$K_i$ : 145 mM

$Na_i$ : 18 mM

$G_{Na}$ : 2.3 mS/cm$^2$

$G_{Kp}$ : 0.0183 mS/cm$^2$

$E_{Na}$ : 54.4 mV

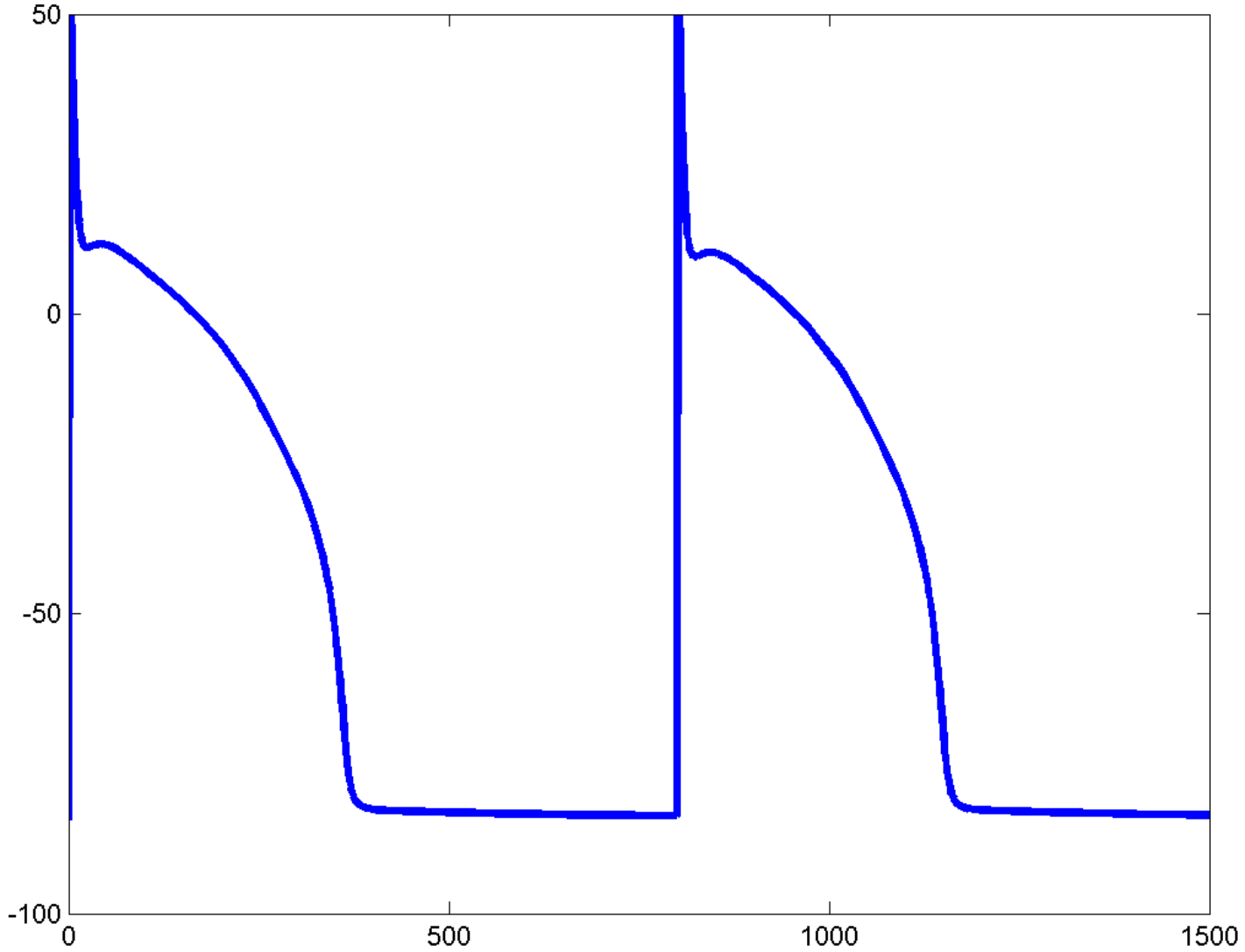
$E_b$ : -59.87 mV

# Numerical Results

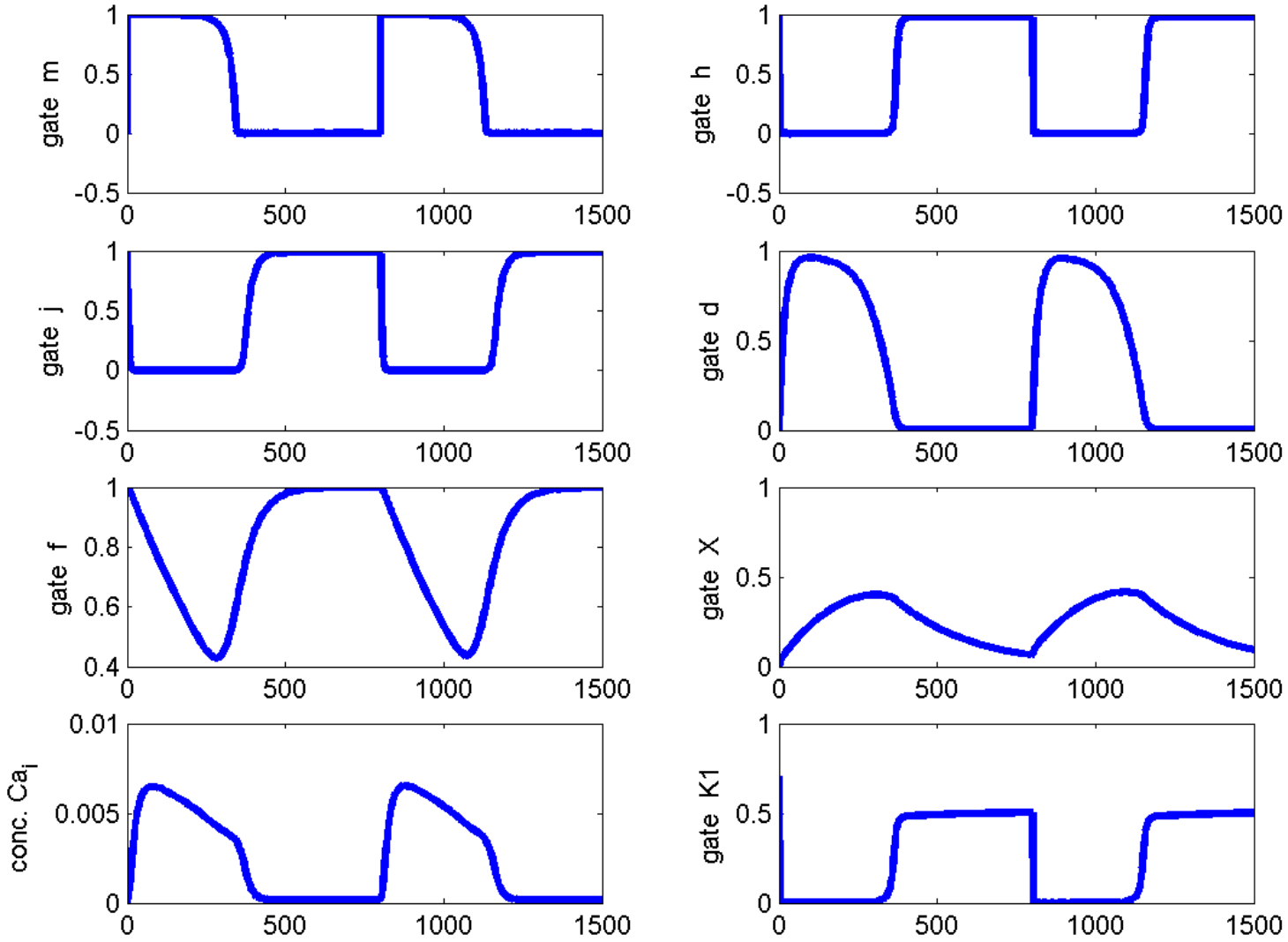
All Simulation are carried out

on

**MATLAB**




**Variation of action potential with respect to time**




**Variation of all gating variables with respect to time**

# One Dimensional Luo-Rudy Model (1991)

If we assume v, transmembrane potential as a function of time and only space variable, we get one dimensional reaction-diffusion equation for cardiac excitation process,

**General Equations:**

$$\rho C_m \frac{\partial v}{\partial t} + div(\mathbf{M_e} \nabla v) + \rho I_{ion}(v, w) = I_{app} \quad in \quad \mathbf{\Omega} \times (0, T)$$

$$\frac{\partial w}{\partial t} - R(v, w) = 0 \quad in \quad \mathbf{\Omega} \times (0, T)$$

$$I_{ion} = I_{Na} + I_{Si} + I_K + I_{K_1} + I_{Kp} + I_b$$

# Numerical Results

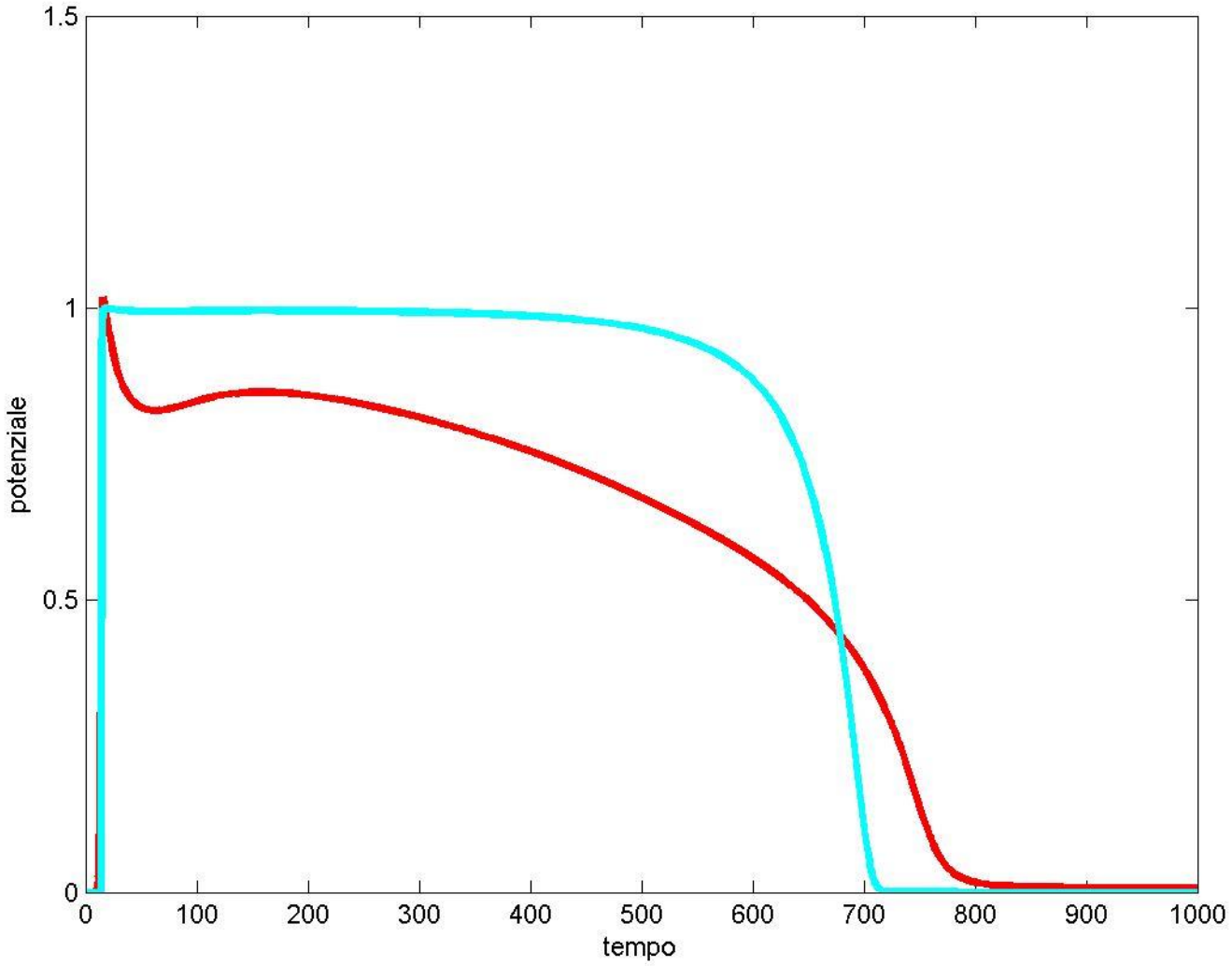
**All Simulation are carried out using**

**One Dimensional**

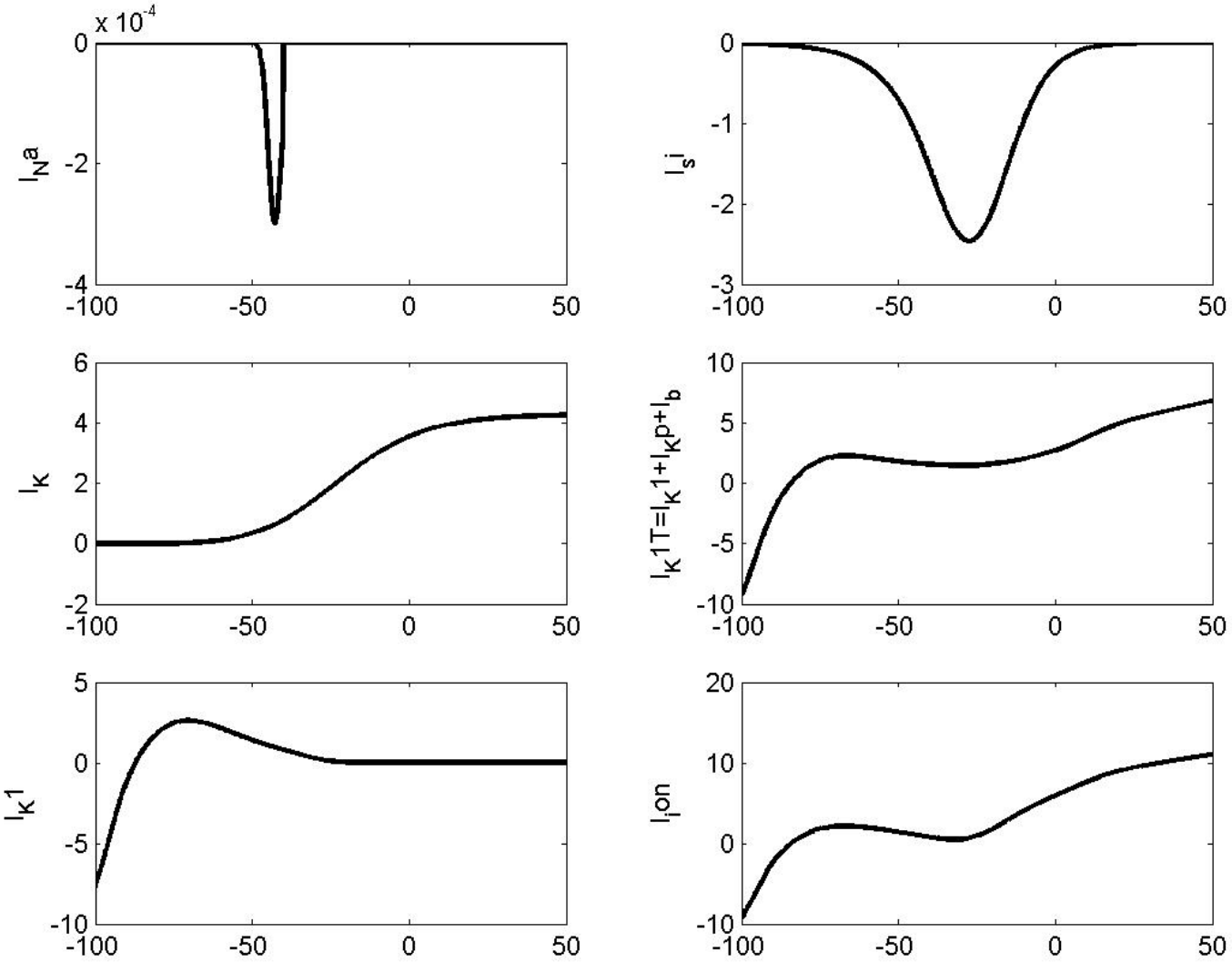
**Finite Element Method**

**Using**

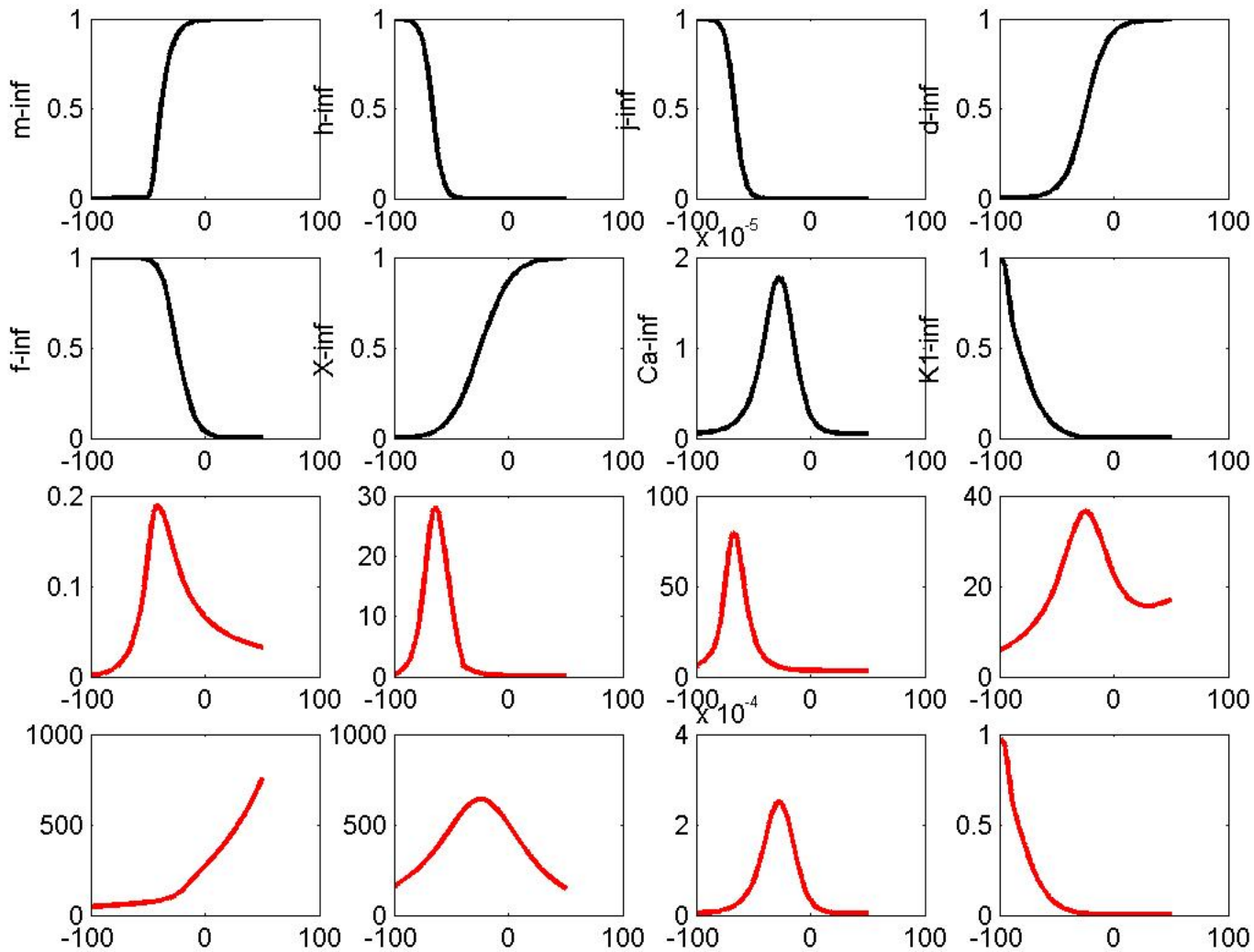
**MATLAB**




**Variation of action potential and gating variable during excitation process in a strip of cardiac tissue**




**Variation of the current during cardiac excitation process with respect to action potential**

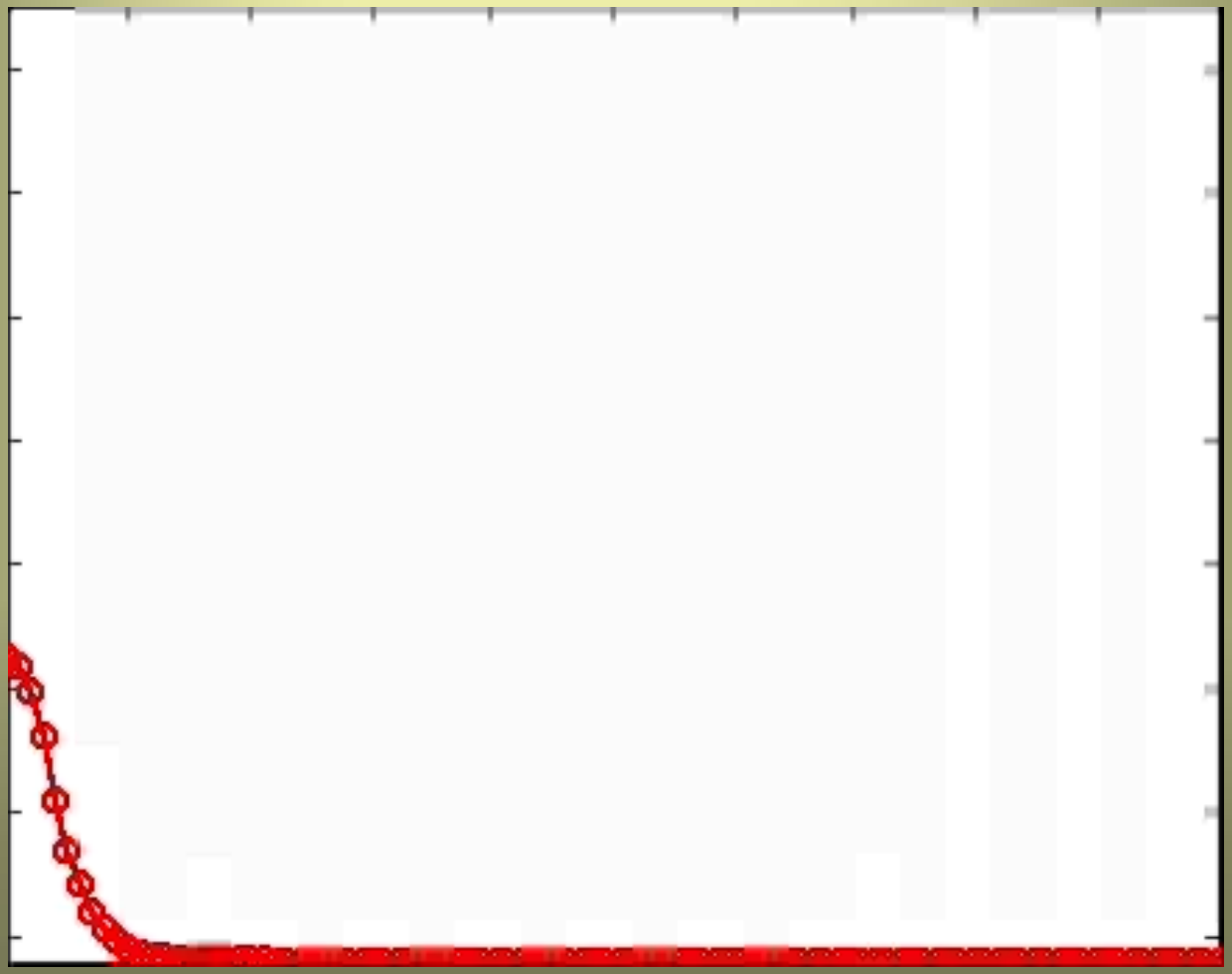



**Variation of Parameter with respect to the action potential**

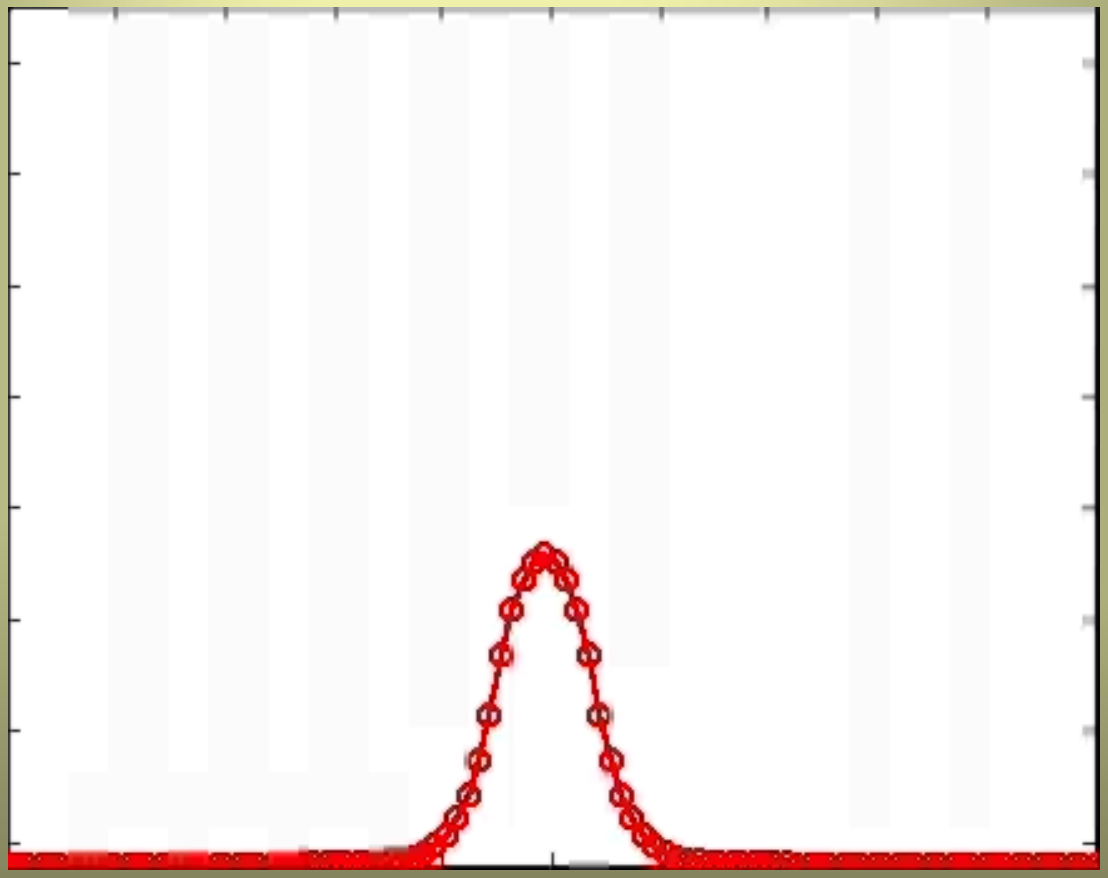
# Animation of a strip of cardiac tissue during cardiac excitation process

**Animation shows excitation process of a strip of cardiac tissue during cardiac excitation process. Artificial current is given at different location.**

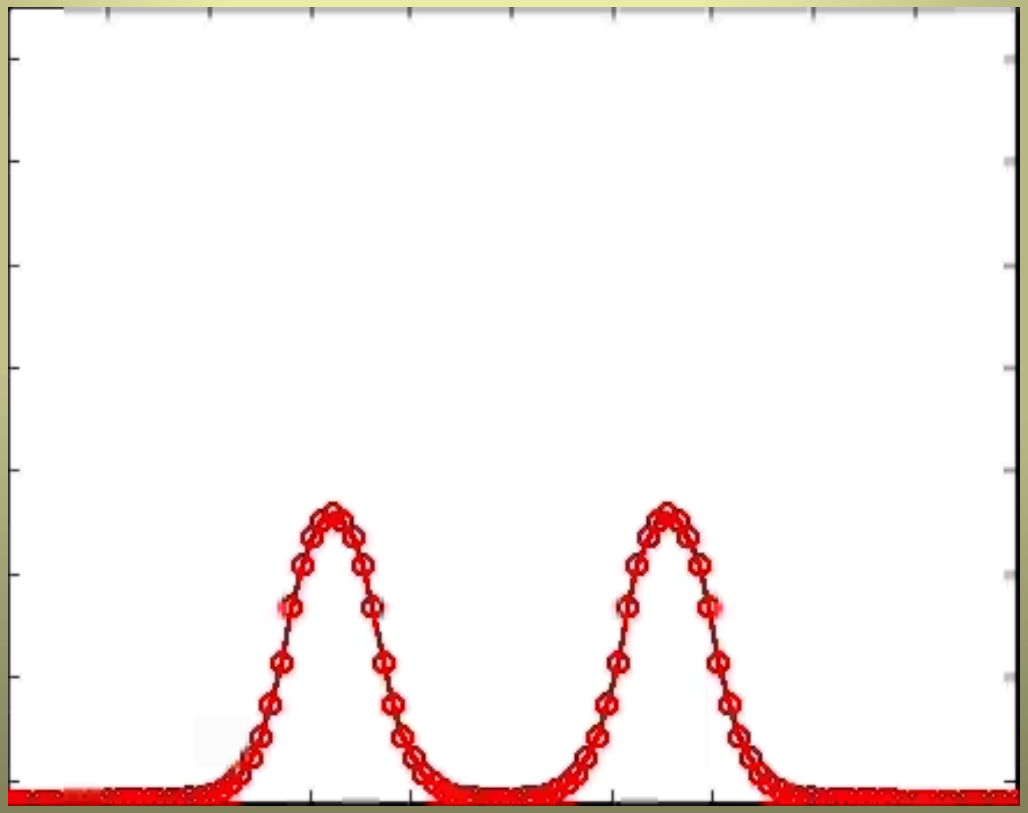
# Current given at starting nodal points of Cardiac Tissue



# Current given at middle of Cardiac Tissue



# Current given at one third and two third of Cardiac Tissue



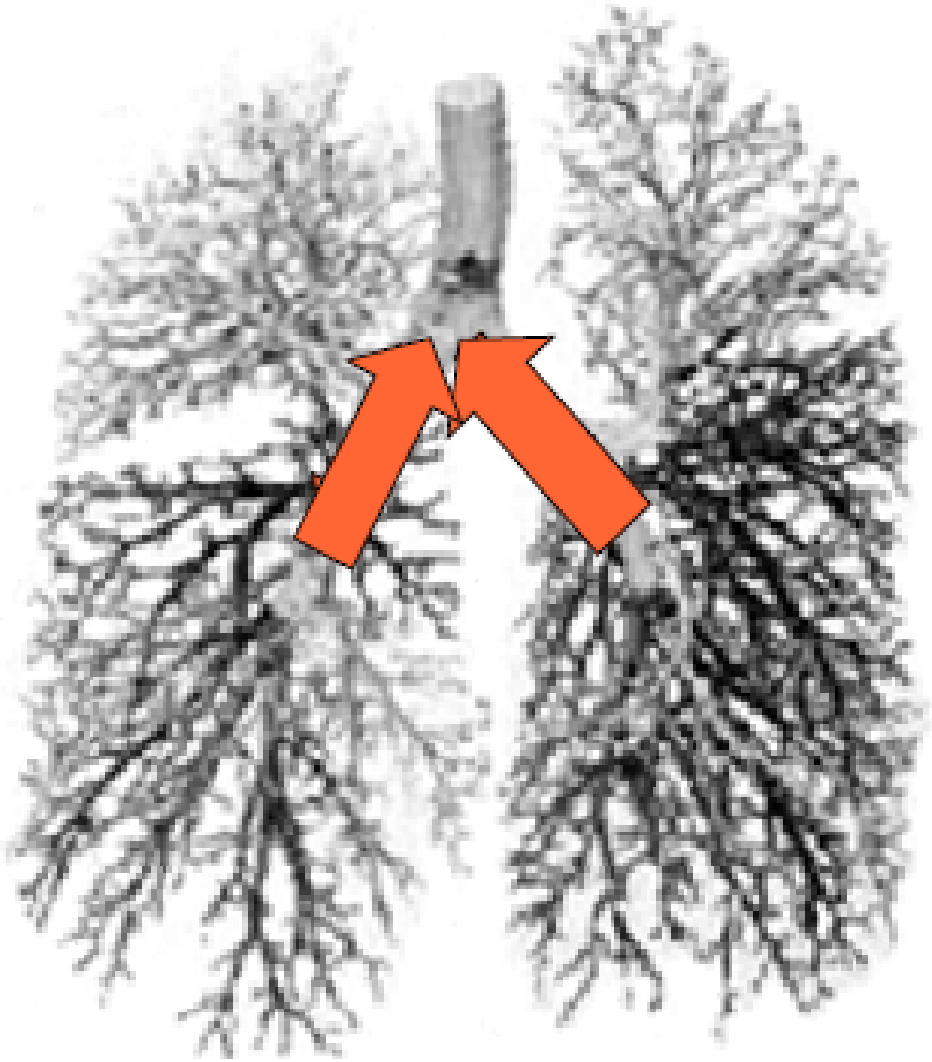
A quick look at:

# Domain Decomposition Method

# Definition and motivation

- **Domain decomposition (DD) is a "divide and conquer" technique for arriving at the solution of problem defined over a domain from the solution of related problems posed on subdomains**
- ***Motivating assumption #1:*** **the solution of the subproblems is qualitatively or quantitatively "easier" than the original**
- ***Motivating assumption #2:*** **the original problem does not fit into the available memory space**
- ***Motivating assumption #3 (parallel context):*** **the subproblems can be solved with some concurrency**

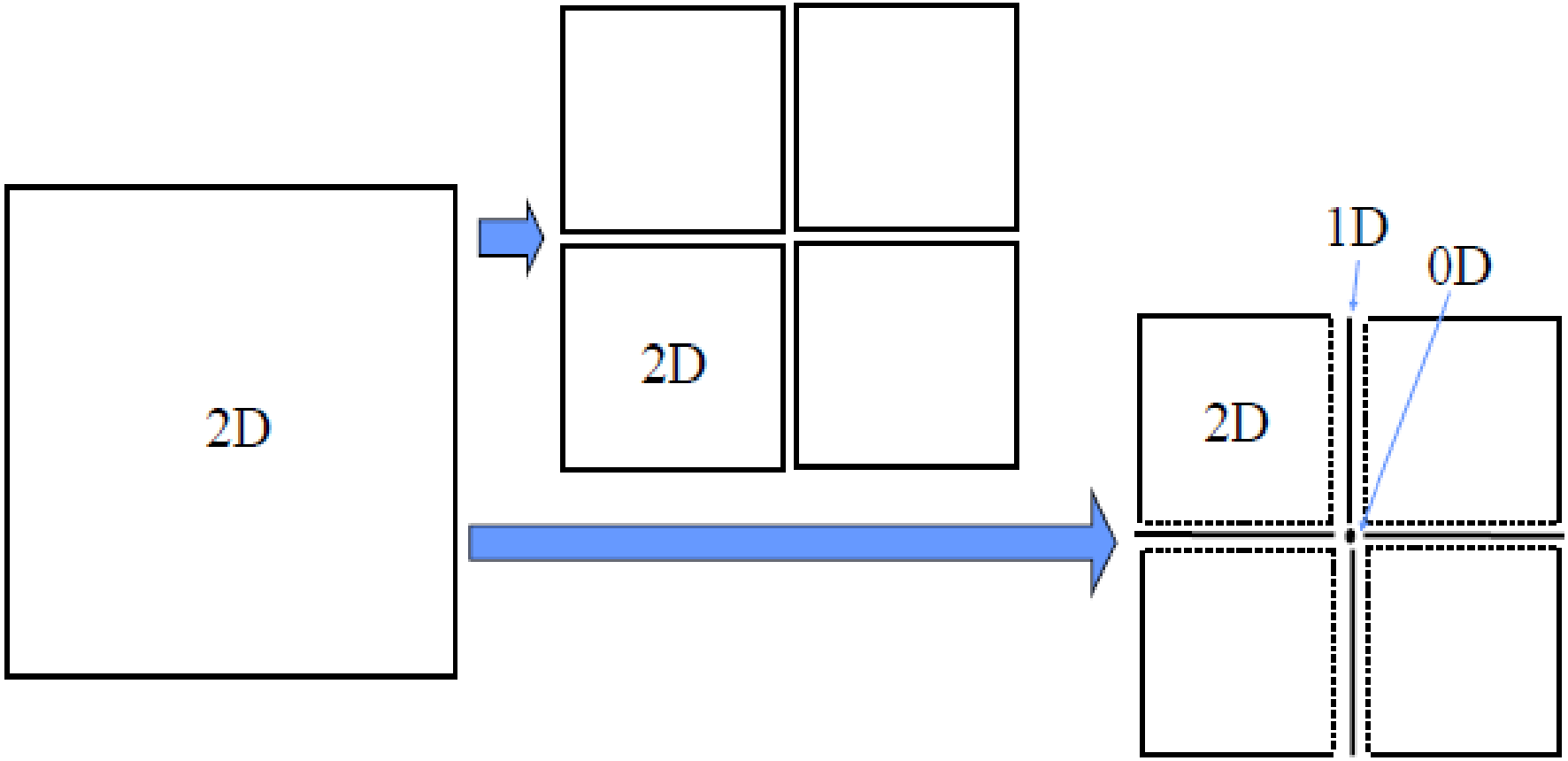
# Divide, conquer, and combine – as natural as breathing



- Most of the *volume* of the lung just transports air and blood down ("divide" phase) to microstructures, where they mix
- Most of the *area* of the lung is at these smallest scales, where gaseous exchange ("conquer") occurs efficiently
- The oxygenated blood and deoxygenated air then "recombine" for output

# Subproblem structure

- The subdomains may be of the same or different dimensionality as the original



# The earliest DD paper?

Gesammelte

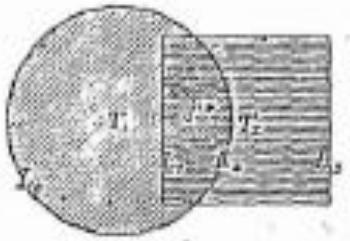
Mathematische Abhandlungen

von

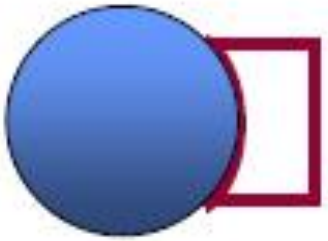
H. A. Schwarz.

Ueber einen Grenzübergang durch alternirendes Verfahren.

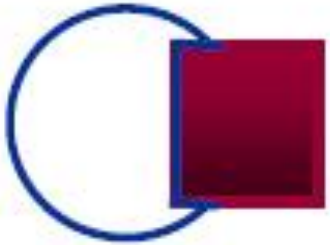
Zürich, im August 1870.



What Schwarz proposed…



Solve PDE in circle with BC taken from interior of square



Solve PDE in square with BC taken from interior of circle

And iterate!

# Decomposition strategies for $\mathcal{L}u=f$ in $\Omega$

- **Operator decomposition**

$$\mathcal{L}=\sum_k \mathcal{L}_k$$

- **Function space decomposition**

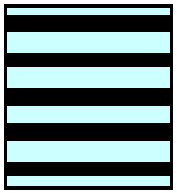
$$f=\sum_k f_k \Phi_k, u=\sum_k u_k \Phi_k$$

- **Domain decomposition**

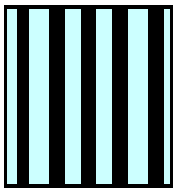
$$\Omega=\bigcup_k \Omega_k$$

# Operator decomposition

- **Consider ADI**



$$[\frac{I}{\tau/2}+\mathcal{L}_x]u^{(k+1/2)}=[\frac{I}{\tau/2}-\mathcal{L}_y]u^{(k)}+f$$



$$[\frac{I}{\tau/2}+\mathcal{L}_y]u^{(k+1)}=[\frac{I}{\tau/2}-\mathcal{L}_x]u^{(k+1/2)}+f$$

- **Iteration matrix consists of four multiplicative substeps per timestep**
  - **two sparse matrix-vector multiplies**
  - **two sets of unidirectional bandsolves**
- **Parallelism *within* each substep**
- **But global data exchanges *between* bandsolve substeps**

# Function space decomposition

- **Consider a spectral Galerkin method**

$$u(x,y,t) = \sum_{j=1}^{N} a_j(t)\Phi_j(x,y)$$

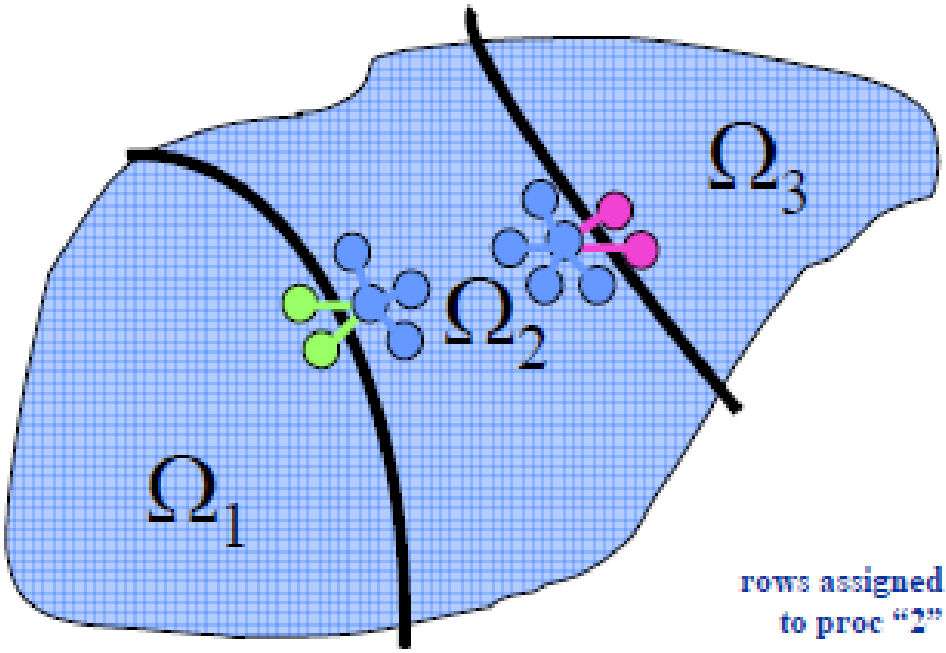
$$\frac{d}{dt}(\Phi_i, u) = (\Phi_i, \mathcal{L}u) + (\Phi_i, f), i = 1,\ldots,N$$

$$\Sigma_j(\Phi_i, \Phi_j)\frac{da_j}{dt} = \Sigma_j(\Phi_i, \mathcal{L}\Phi_j)a_j + (\Phi_i, f), i = 1,\ldots,N$$

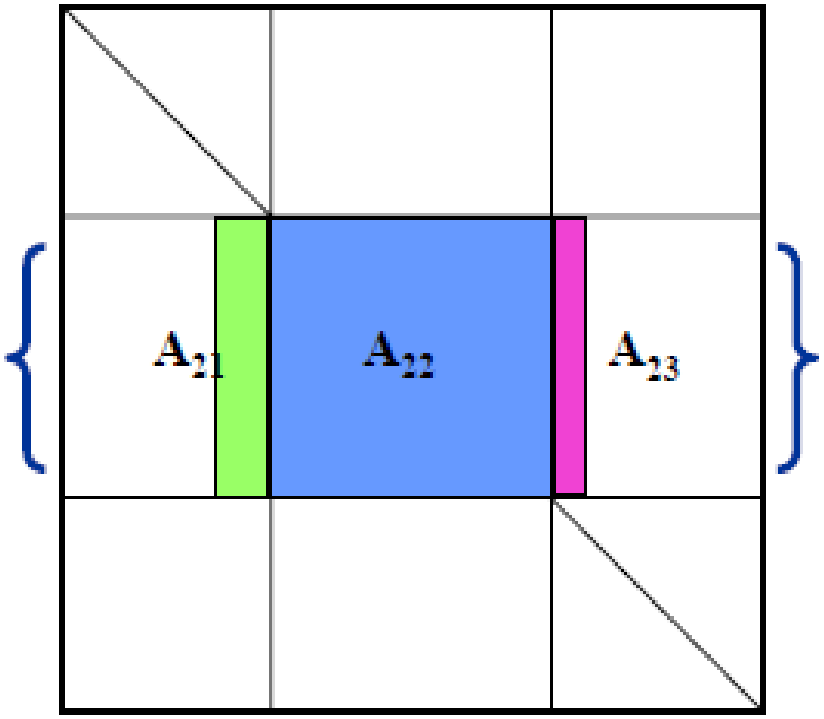
$$\frac{da}{dt} = M^{-1}Ka + M^{-1}f$$

- **Method-of-lines system of ODEs**
- **Perhaps** $M \equiv [(\Phi_j, \Phi_i)], K \equiv [(\Phi_j, \mathcal{L}\Phi_i)]$ **are diagonal matrices**
- **Parallelism across spectral index**
- **But global data exchanges to *transform back* to physical variables at each step**

# SPMD parallelism w/domain decomposition




rows assigned
to proc "2"




Partitioning of the grid induces block structure on the system matrix (Jacobian)

# Now, let's compare!

- **Operator decomposition (ADI)**
  - natural row-based assignment requires *global all-to-all, bulk* data exchanges in each step (for transpose)
- **Function space decomposition (Fourier)**
  - Natural mode-based assignment requires *global all-to-all, bulk* data exchanges in each step (for transform)
- **Domain decomposition (Schwarz)**
  - Natural domain-based assignment requires *local surface* data exchanges, *global reductions*, and *optional small global* problem

(Of course, domain decomposition can be interpreted as a *special* operator or function space decomposition)

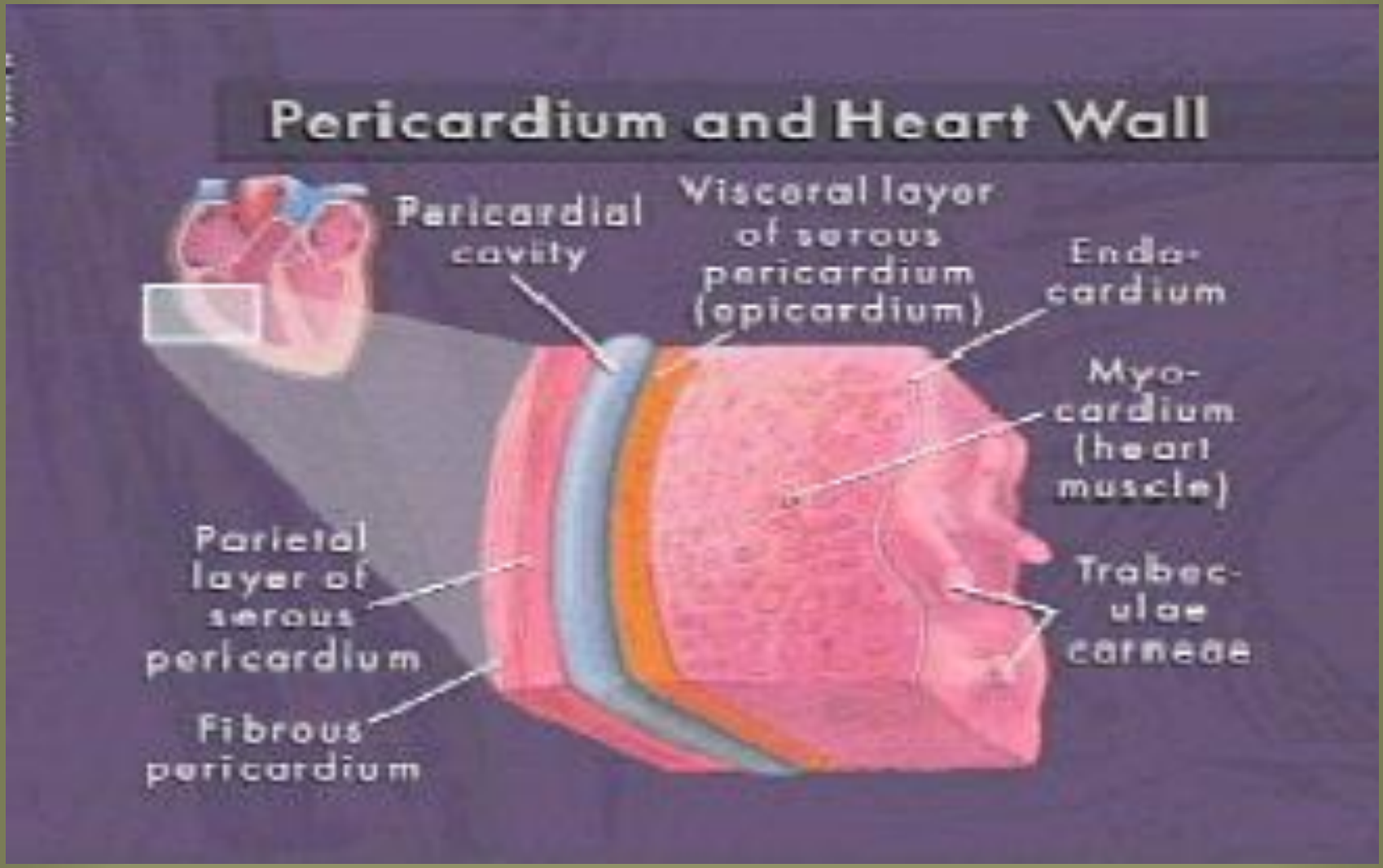
# State of the art

- Domain decomposition is the dominant paradigm in contemporary terascale PDE simulation
- Several freely available software toolkits exist, and successfully scale to thousands of tightly coupled processors for problems on quasi-static meshes
- Concerted efforts underway to make elements of these toolkits interoperate, and to allow expression of the best methods, which tend to be modular, hierarchical, recursive, and above all — *adaptive*!
- Many challenges loom at the "next scale" of computation
- Implementation of domain decomposition methods on parallel computers has inspired many useful variants of domain decomposition methods
- The past few years have produced an incredible variety of interesting results (in both the continuous and the discrete senses) in domain decomposition methods, with no slackening in sight

# Krylov-Schwarz parallelization summary

- Decomposition into concurrent tasks
  - by domain
- Assignment of tasks to processes
  - typically one subdomain per process
- Orchestration of communication between processes
  - to perform sparse matvec – near neighbor communication
  - to perform subdomain solve – nothing
  - to build Krylov basis – global inner products
  - to construct best fit solution – global sparse solve (redundantly)
- Mapping of processes to processors
  - typically one process per processor

*back to Cardiac Tissue Modeling*



# The Macroscopic Bidomain Model

Cardiac tissue is modeled as superimposed intra and extracellular media connected by a distributed cellular membrane.

Cardiac tissue is anisotropic due to the fiber structure. Macroscopic model of the conductivity tensors $\mathbf{M_i}$ (intracellular), $\mathbf{M_e}$ (extracellular)

$$\mathbf{M_{i,e}} = \sigma_t^{i,e}(\mathbf{x})\mathbf{I} + (\sigma_l^{i,e}(\mathbf{x}) - \sigma_t^{i,e}(\mathbf{x}))\, a(\mathbf{x})a^T(\mathbf{x})$$

Where $\sigma_l^{i,e}, \sigma_t^{i,e}$ = conductivity coefficients along and cross fiber at x (axially symmetric)

**a(x)** = unit vector tangent to the fiber at x

Given $I_{app}^{i,e} : \Omega \times (0,T) \to R$ (applied current per unit volume)

$v_0 : \Omega \to R, \quad w_0 : \Omega \to R^M$ (initial condition)

find $u_i, u_e : \mathbf{\Omega} \times (0,T) \to \mathbf{R}$ (intra and extra cellular potentials)

and $v = u_i - u_e =$ (transmembrane potential)

w : $\mathbf{\Omega} \times (0,T) \to \mathbf{R^M}$ (gating variables)

such that

$$\begin{cases} \rho C_m \dfrac{\partial v}{\partial t} - div(\mathbf{M_i} \nabla u_i) + \rho I_{ion}(v,w) = I_{app}^i & in \quad \mathbf{\Omega} \times (0,T) \\ \rho C_m \dfrac{\partial v}{\partial t} + div(\mathbf{M_e} \nabla u_e) + \rho I_{ion}(v,w) = I_{app}^e & in \quad \mathbf{\Omega} \times (0,T) \\ \dfrac{\partial w}{\partial t} - R(v,w) = 0 & in \quad \mathbf{\Omega} \times (0,T) \end{cases}$$

# The Hodgkin-Huxley model for the ionic currents

$$I_{ion}(v,w) = \sum_{k=1}^{N} G_K \prod_{j=1}^{M} w_j^{p_{jk}} (v - v_k)$$

*where,* $v_k$ = resting potential for the k-ionic current

and $p_{j_k}$ are integers

$w = (w_1, w_2, \ldots\ldots, w_M)$ are gating variables related to the flow of different ions through channels of the membrane modeled by the system of ordinary differential equations

$$\frac{\partial w_j}{\partial t} = R_j(v, w_j) = \alpha_j(v)\,(1.0 - w_j) - \beta_j(v)\,(w_j)$$

$$w_j(\mathbf{x}, 0) = w_{j,0}(\mathbf{x}) \qquad 0 \le w_j \le 1$$

$$\alpha_j, \beta_j > 0$$

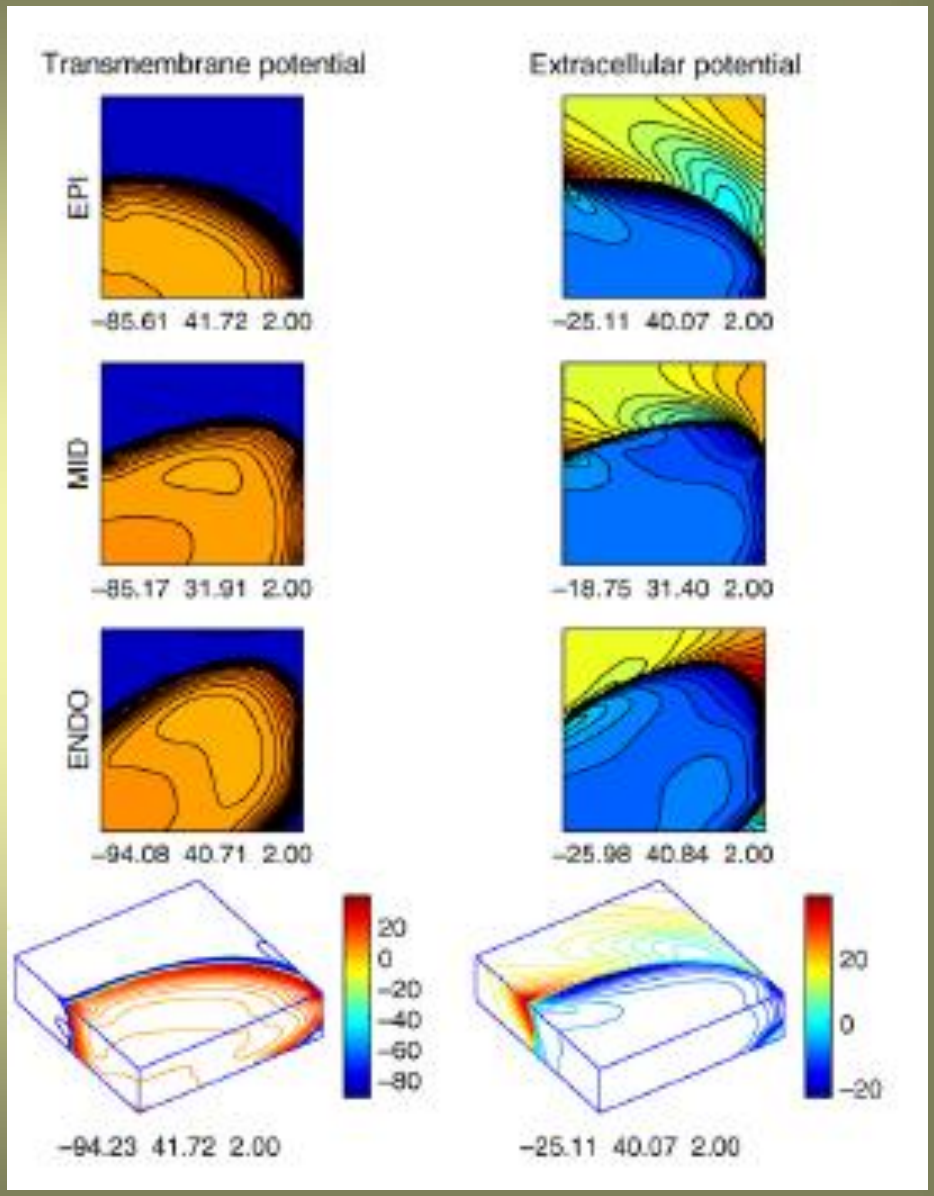
**3D-Slab Domain**

2.76 × 2.76 × 0.08 cm^3

257× 257× 49 nodes

Model is run for complete heartbeat of say 400 ms with 3000 time steps

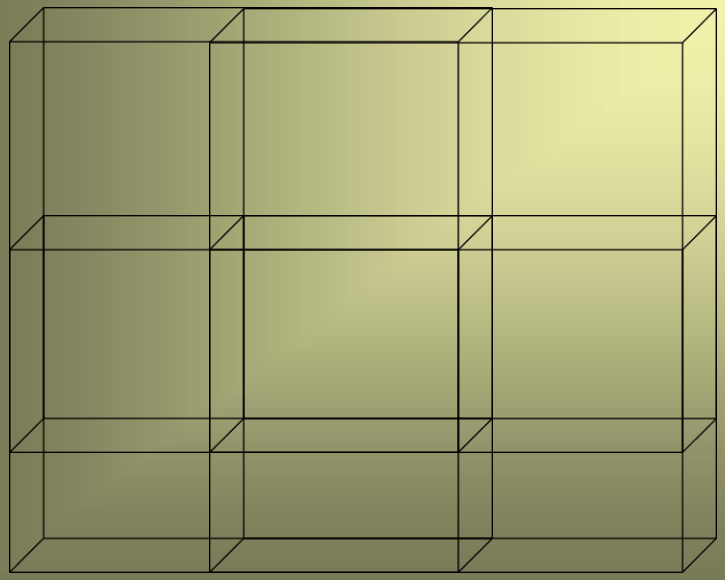
**Spatial maps of trans-membrane and extra-cellular potentials computed 40 ms after the stimulus is given at a vertex of the domain**

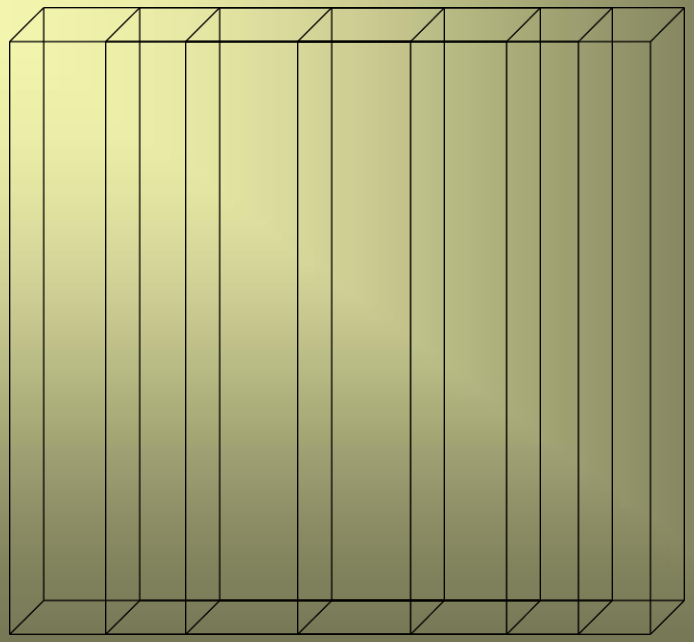


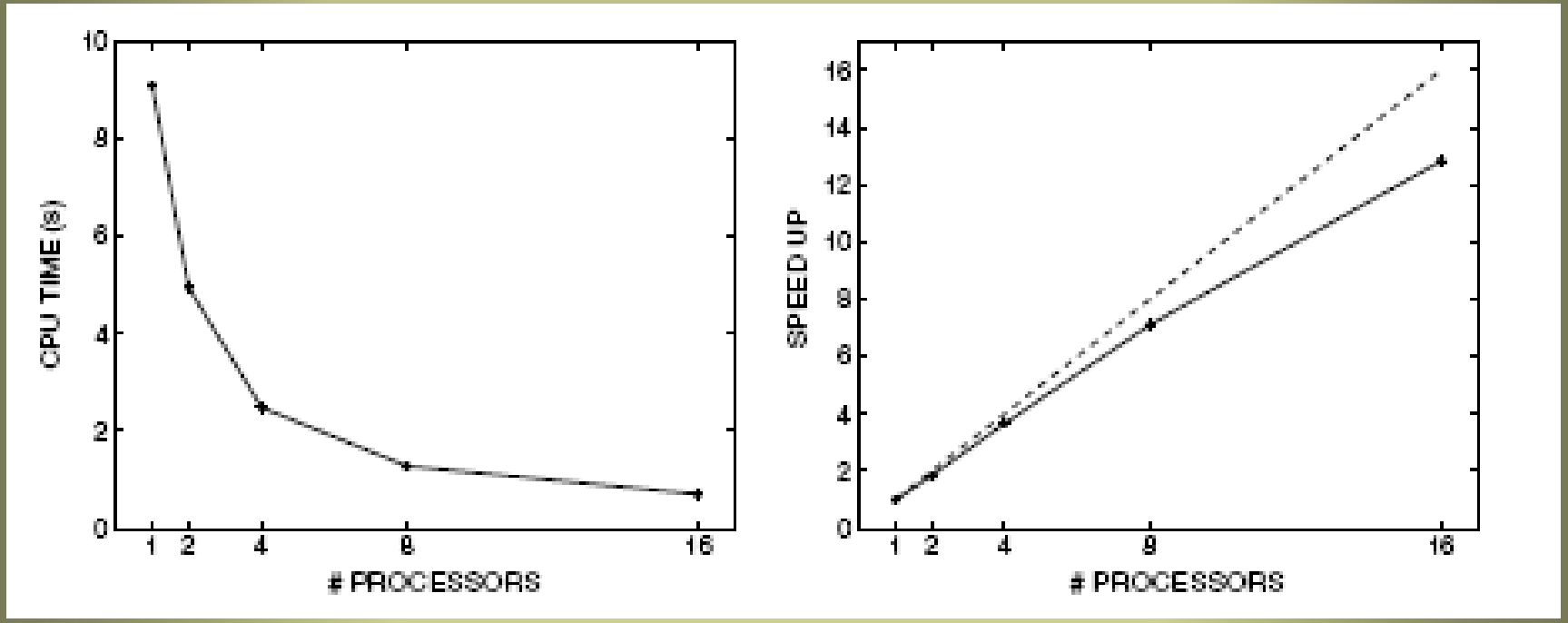
**3D-Slab Domain**

2.76 × 2.76 × 0.08 cm^3

257× 257× 33 nodes








Speedup on Linux Cluster of 16 nodes

(based on first 40 time steps)

Many refinement of the original Hodgkin Huxley model have been proposed by fitting experimental data with more complex model like

- Beeler-Reuter (1977) with N=4, M=7
- Luo-Rudy 1 (1991) with N=6, M=8
- Luo-Rudy 2 (1994) with N=10, M=8
- Fitzhugh Nagumo Model
- Roger McCulloch Model
- Alieve Panfilov Model etc.

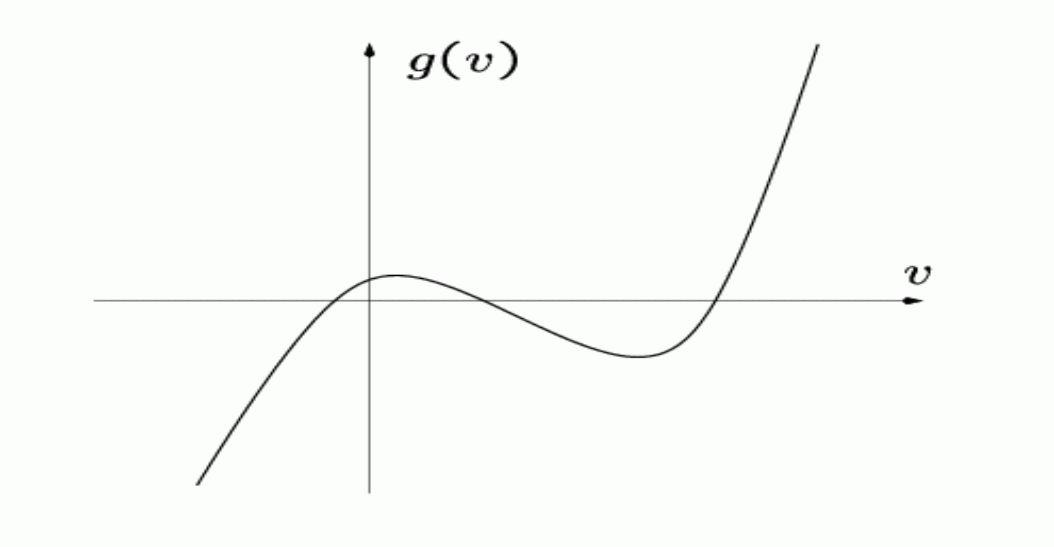
# Three Dimensional Modeling of Ventricle Myocardium tissue using Roger Model

# The simplified FitzHugh-Nagumo system

Instantaneous current voltage law with only one gating variable w

$$\begin{cases} I_{ion}(v,w) = g(v) + \beta w \\ R(v,w) = \beta v - \gamma w \end{cases}$$

$g$ cubic-like function, $\beta, \gamma > 0$



Simplified Model: assume and get only one equation for the transmembrane potential v and one for the gating variable w (and use Fitzhugh-Nagumo variant by Roger & Mc Culloch, 1994):

$$\rho C_m \frac{\partial v}{\partial t} + div(\mathbf{M}\nabla v) + \rho I_{ion}(v,w) = I_{app} \quad in \quad \Omega \times (0,T)$$

$$\frac{\partial w}{\partial t} = c_2\left(\frac{v}{v_p} - c_3 w\right) \quad in \quad \Omega \times (0,T)$$

+ Neumann boundary conditions for v and initial conditions for v and w

$$\mathrm{I}_{\mathrm{ion}}(v,w) = Gv\left(1-\frac{v}{v_{th}}\right)\left(1-\frac{v}{v_p}\right) + c_1 vw, \begin{cases} v_{th} & threshold\ \ potential \\ v_p & peak \quad potential \end{cases}$$

$$\mathbf{M(x)} = \sigma_t(x)\,\mathbf{I} + (\sigma_t(\mathbf{x}) - \sigma_t(\mathbf{x}))\,\mathbf{a(x)}\,\mathbf{a}^{\mathbf{T}}\mathbf{(x)}.$$

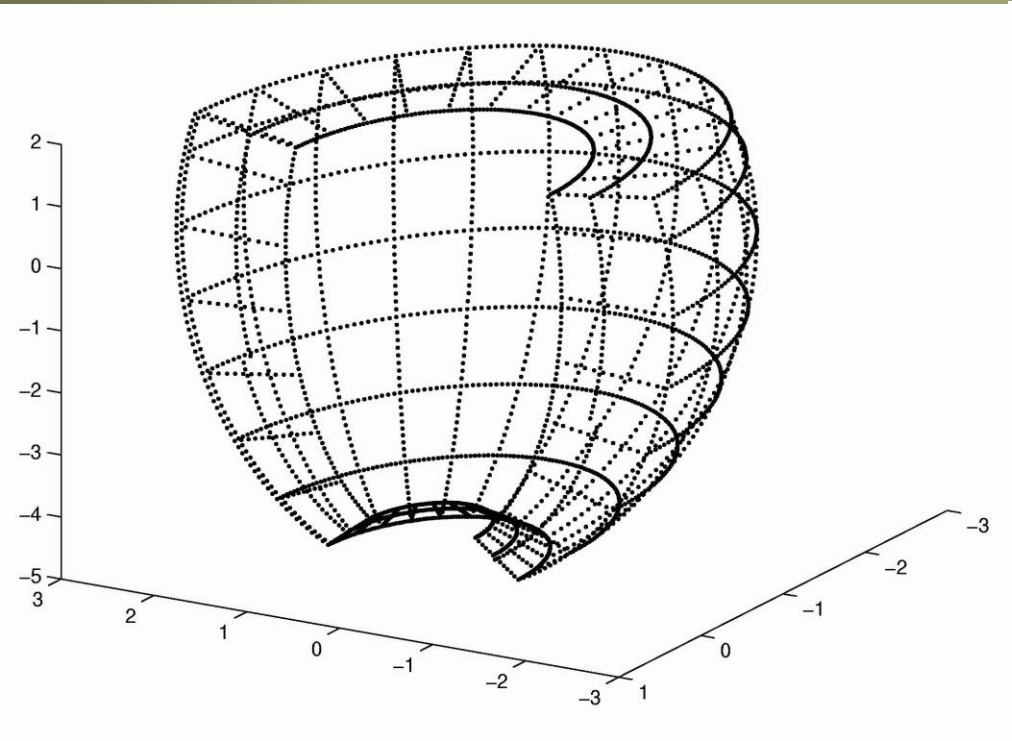
# Domain Discretization

$$\begin{cases} x = a(r)\cos\theta\cos\phi & \theta_{\min} \le \theta \le \theta_{\max} \\ y = b(r)\cos\theta\sin\phi & \phi_{\min} \le \phi \le \phi_{\max} \\ z = c(r)\sin\theta & 0 \le r \le 1 \end{cases}$$

$$a(r) = a_1 + r(a_2 - a_1)$$

$$b(r) = b_1 + r(b_2 - b_1)$$

$$c(r) = c_1 + r(c_2 - c_1)$$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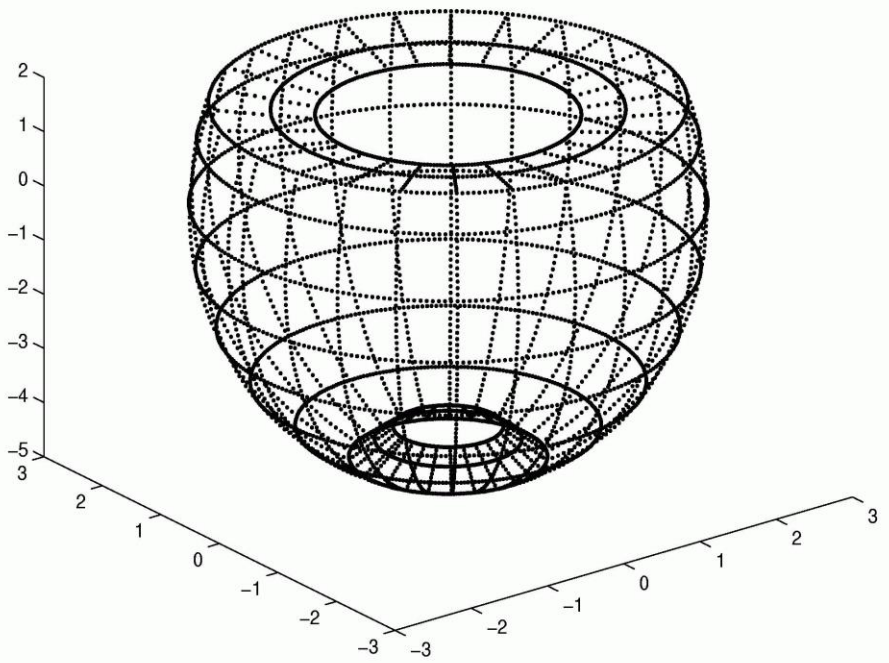
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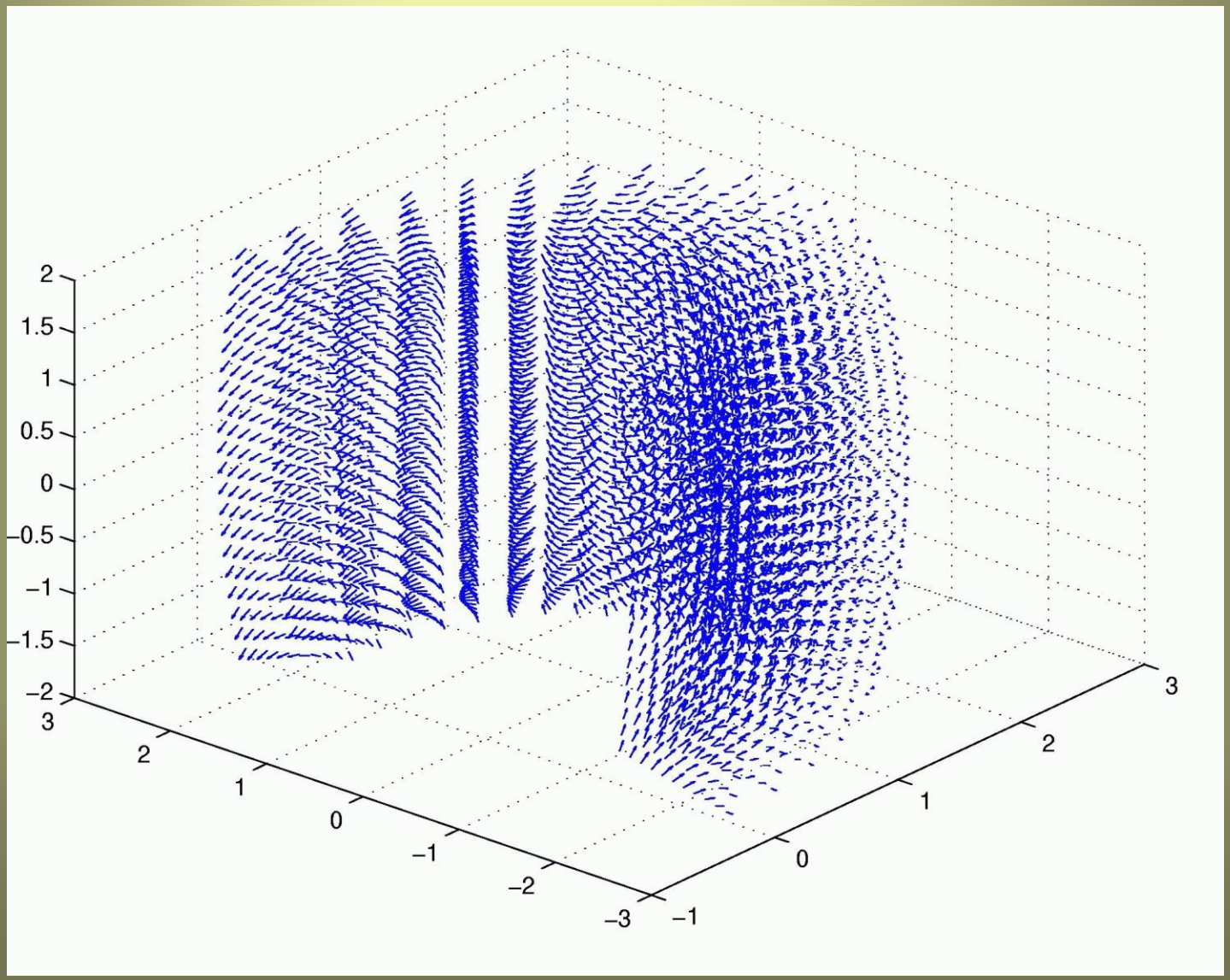
# Fiber direction (a(x) vector field)



# Variation Formulation

Find $v, w \in L^2(0,T;V)$ such that $\forall \gamma \in V, t \in (0,T)$

$$\rho C_m \frac{\partial}{\partial t}(v(t),\varphi) + a(v(t),\varphi) + \rho(I_{ion}(v,w),\varphi) = (I_{app},\varphi)$$

$$\frac{\partial}{\partial t}(w(t),\varphi) = c_2(v(t),\varphi) - c_3(w(t),\varphi),$$

\+ initial conditions and

$$V = H^1(\Omega) = \left\{ \varphi : \varphi, \frac{\partial \varphi}{\partial x_i} \in L^2(\Omega)\ i = 1,2,3 \right\},$$

$$(\varphi,\psi) = \int_\Omega \phi\psi \mathrm{dx},$$

$$a(\varphi,\psi) = \int_\Omega (\nabla\varphi)^T \mathbf{M} \nabla\psi \, dx.$$

# Finite Element discretization in space

Structured grid of $(n_i, n_j, n_k)$ hexahedral isoparametric elements

$$\rho C_m \mathbf{M} \frac{\partial v_h}{\partial t} + \mathbf{A} v_h + \rho \mathbf{M} I_{ion}^h (v_h, w_h) = \mathbf{M} I_{app}^h$$

$$\frac{\partial w_h}{\partial t} = c_2 v_h - c_3 w_h$$

*where,* $V_h = \left\{ \varphi_h : \varphi_h \text{ is continuous in } \Omega \text{ and } \varphi_h\big|_K \text{ is trilinear} \right\}$

mass matrix $\mathbf{M} = \mathbf{M}^{\mathbf{T}} = (m_{ij}) = \sum_K \int_K \varphi_i \varphi_j dx$

stiffness matrix $\mathbf{A} = \mathbf{A}^{\mathbf{T}} = (a_{ij}) = \sum_K \int_K (\nabla \varphi_i)^T \mathbf{M} \varphi_j dx$

$I_{ion}^h, I_{app}^h =$ finite element interpolents $I_{ion}, I_{app}$

# Time discretization: semi-implicit method

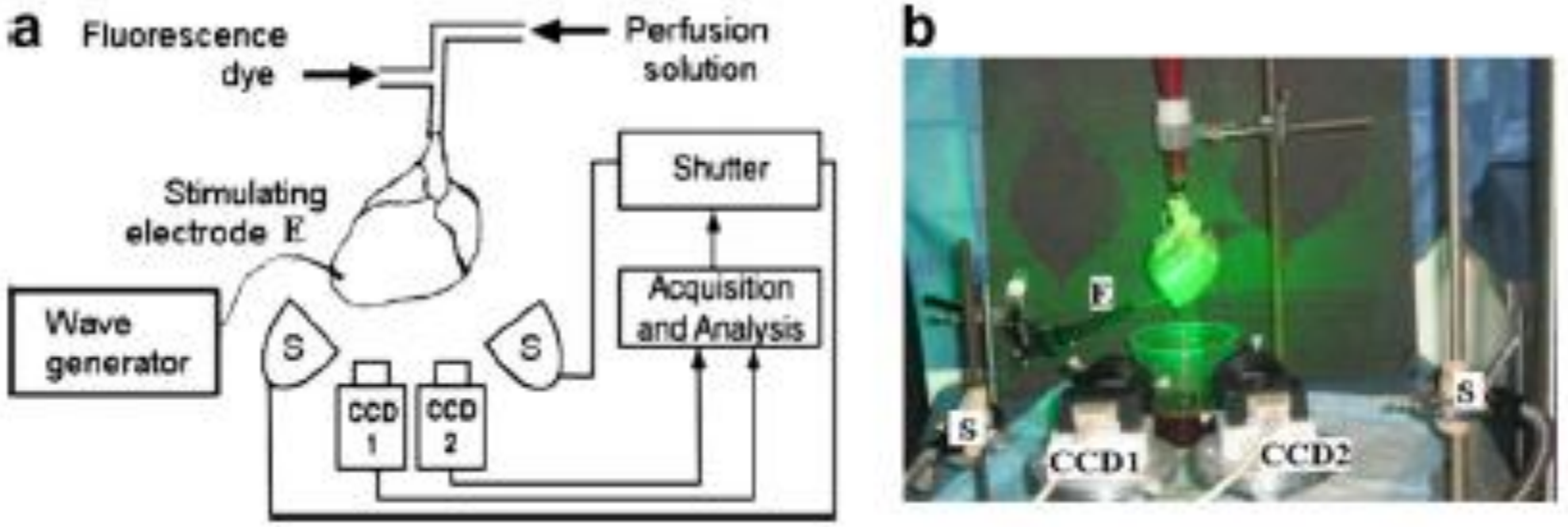
implicit Euler for diffusion term + explicit for nonlinear reaction term implicit Euler for the gating equation.
(Other choices are also possible: Crack-Nicolson, adaptive methods etc.)

$$\rho C_m \mathbf{M} \frac{v^{n+1} - v^n}{\Delta t} + \mathbf{A} v^{n+1} + \rho \mathbf{M} I_{ion}^h (v^n, w^n) = \mathbf{M} I_{app}^h$$

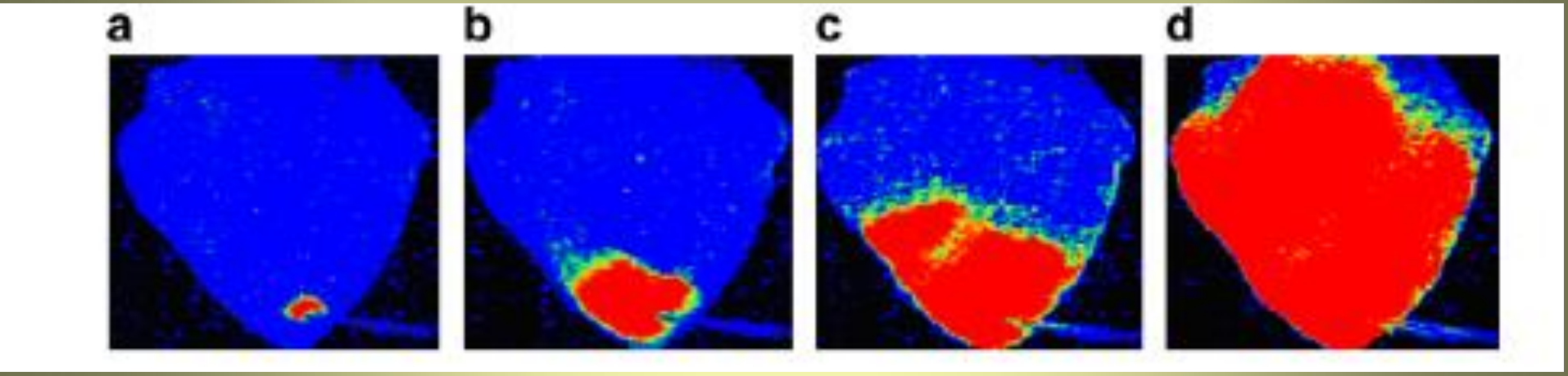
$$\frac{w^{n+1} - w^n}{\Delta t} = c_2 v^{n+1} - c_3 w^{n+1}$$

Mass matrix **M** is approximated by lumping.

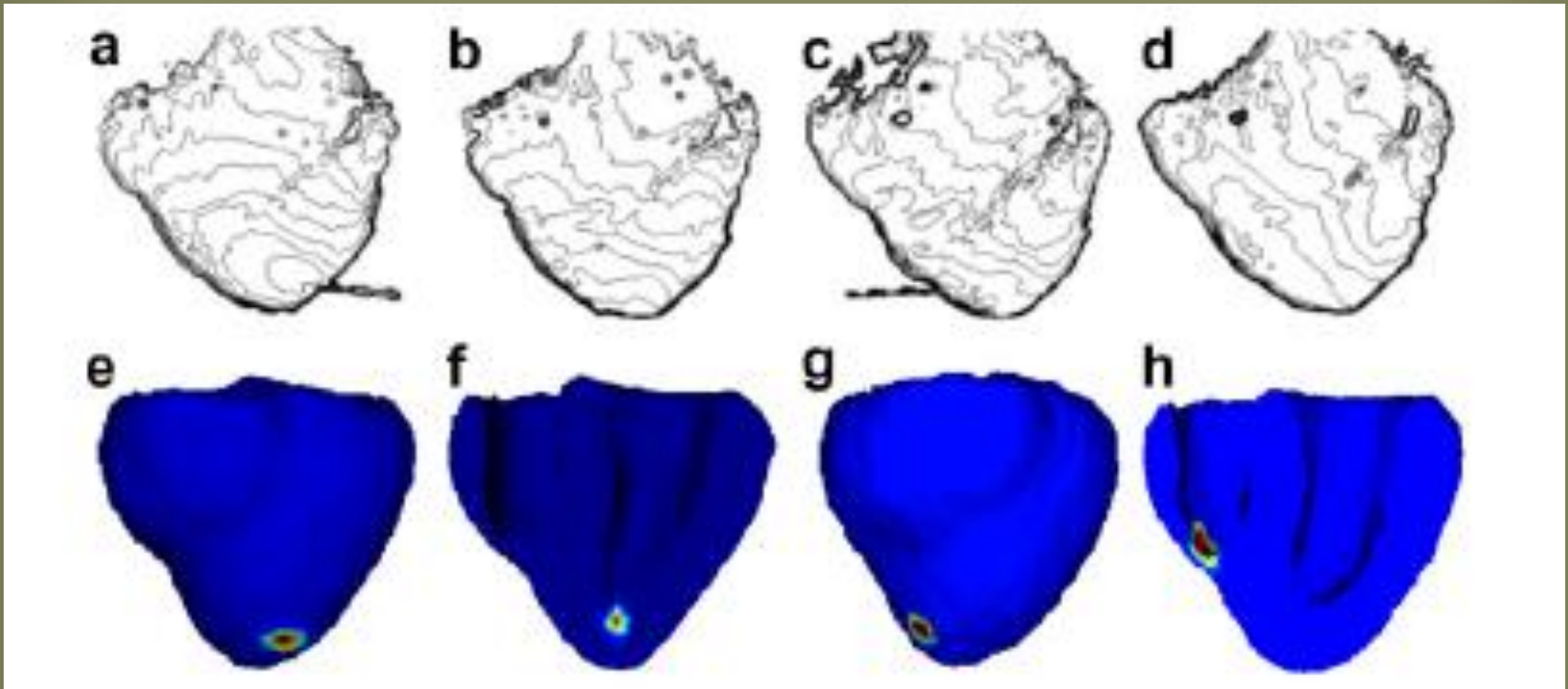
# Extract from M. Pop et al (2008), MIA




Schematic of the optical experiment using a dual-camera system to record the action potential from heart perfused ex vivo via a Lagendorff system and a snapshot of the actual experiment **(From M.Pop et al (2008), Medical Image Analysis)**




**Snapshots of AP propagation at different times obtained through Optical imaging (from M. Pop et al (2008)**



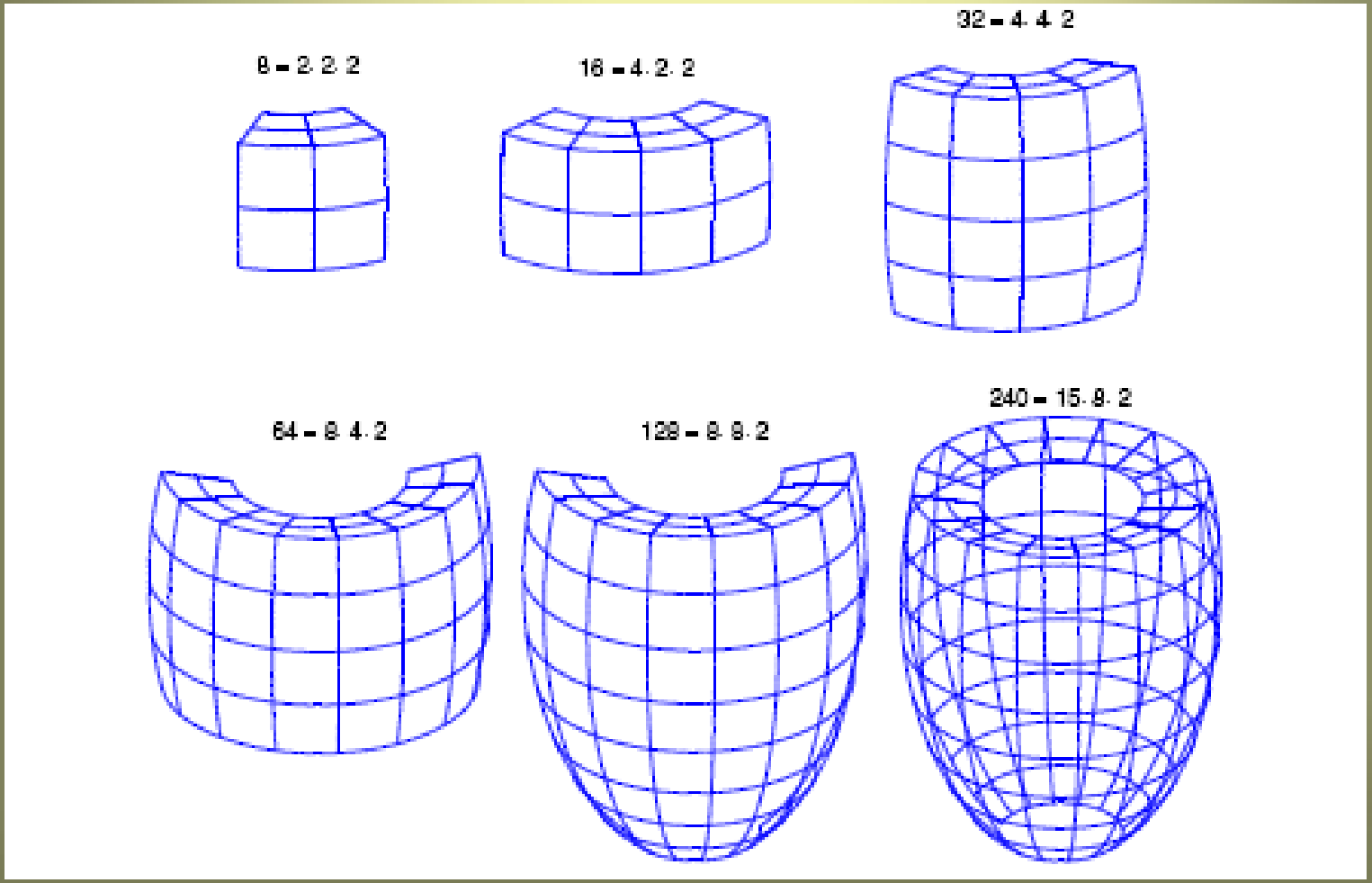

Isochronal maps from placing the electrode at different sites on the heart: (a-e) isochronal lines obtained in Optical images, (e-f) exact electrode placing locations (From M.Pop et al (2008))

# *Methodology Used*

For the Finite Element Code we need to have,

- Three dimension data structure that is equally distributed over all the processors.
- Assembling of this mass and stiffness matrix are required which is done by all the processor efficiently.
- Once all these tasks done the problem is reduced into a algebraic system describe in above equation.
- To solve this algebraic system we may use a suitable iterative solver like **Conjugate Gradient** and preconditioner like **Block Jaccobi**.

# Domain Decomposition



# Numerical Results

**All Simulation is carried out using**

**Three Dimensional unsteady**

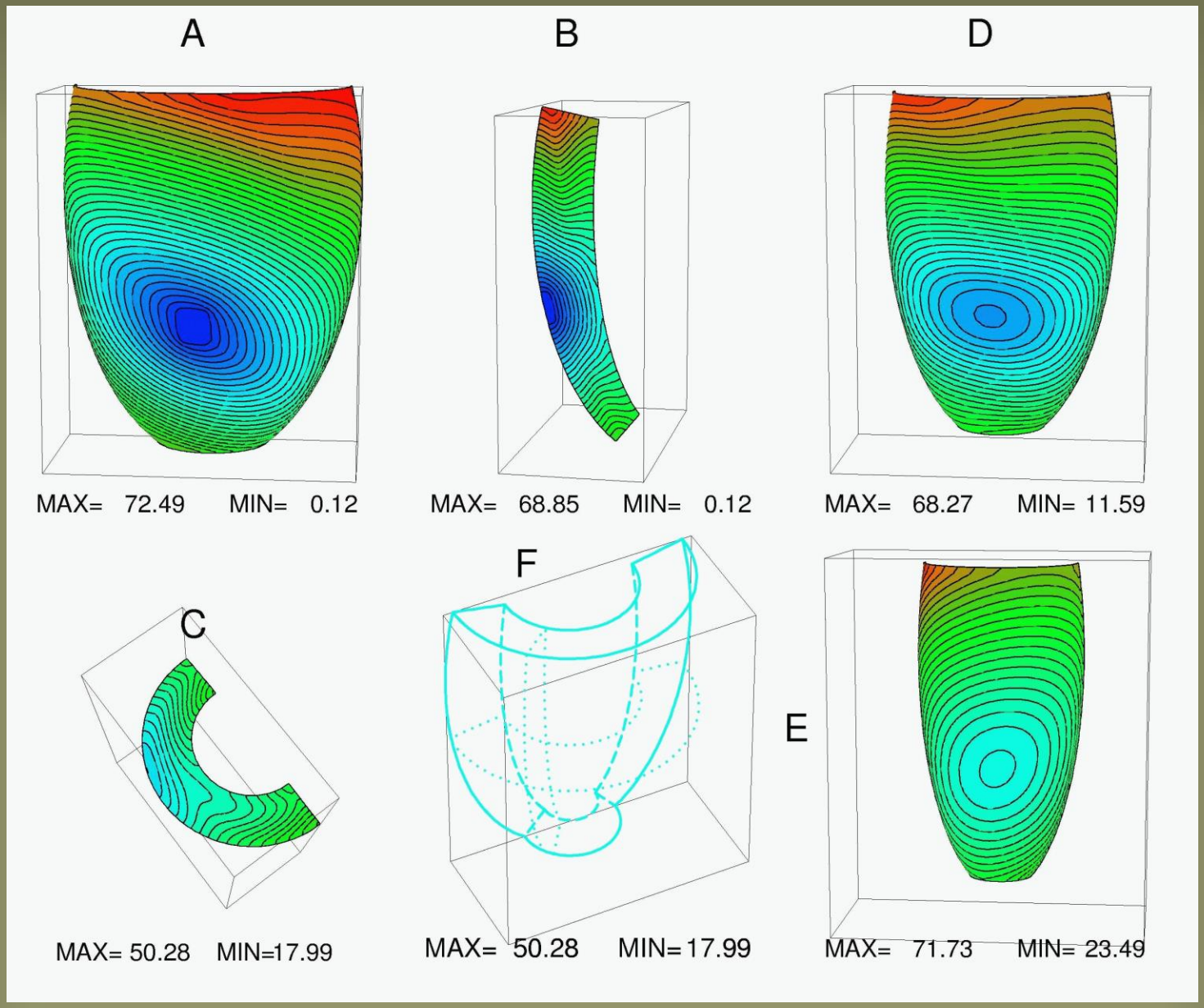
**Parallel**

**Finite Element method**

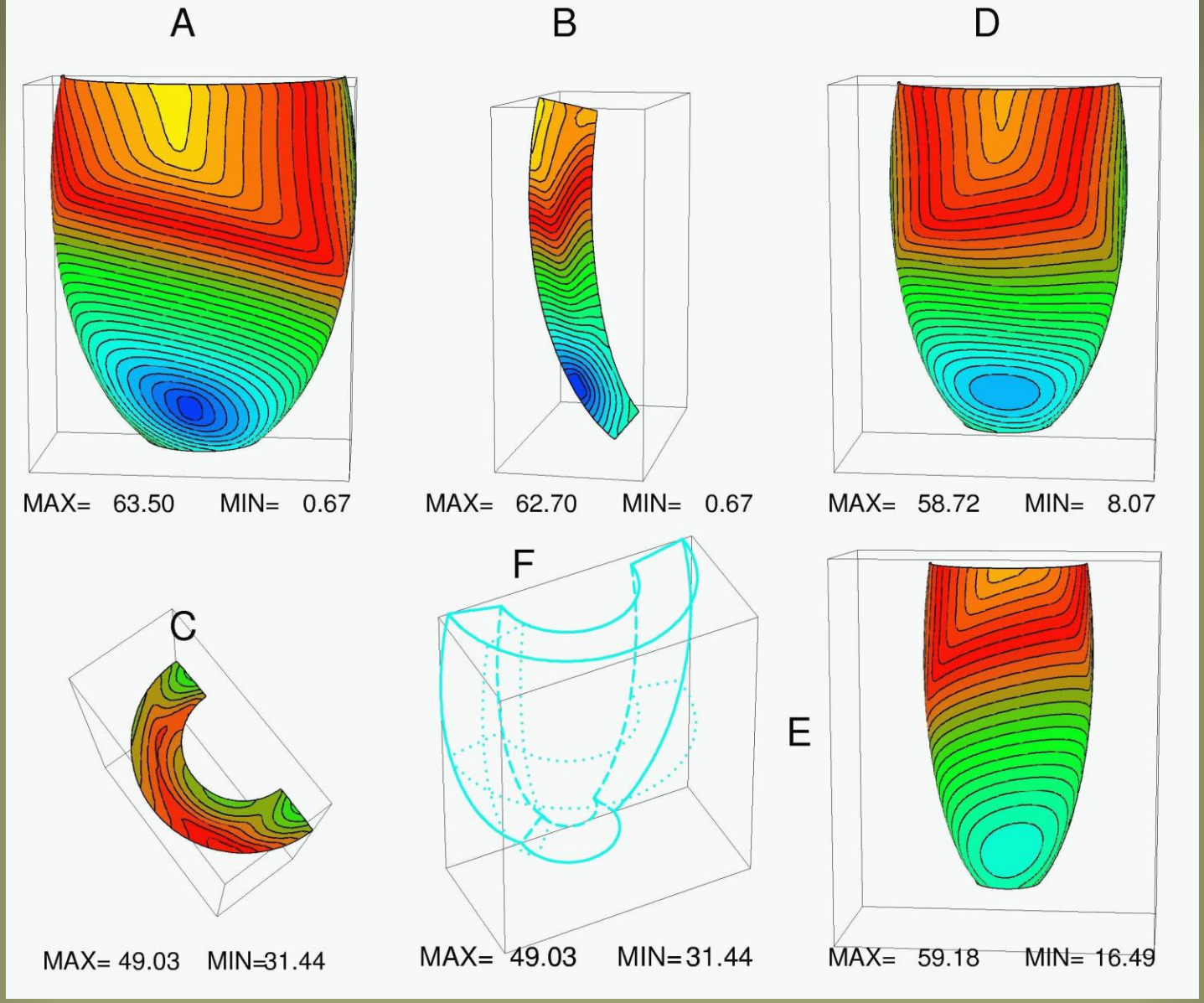
**Using**

**Massage Passing Interface**

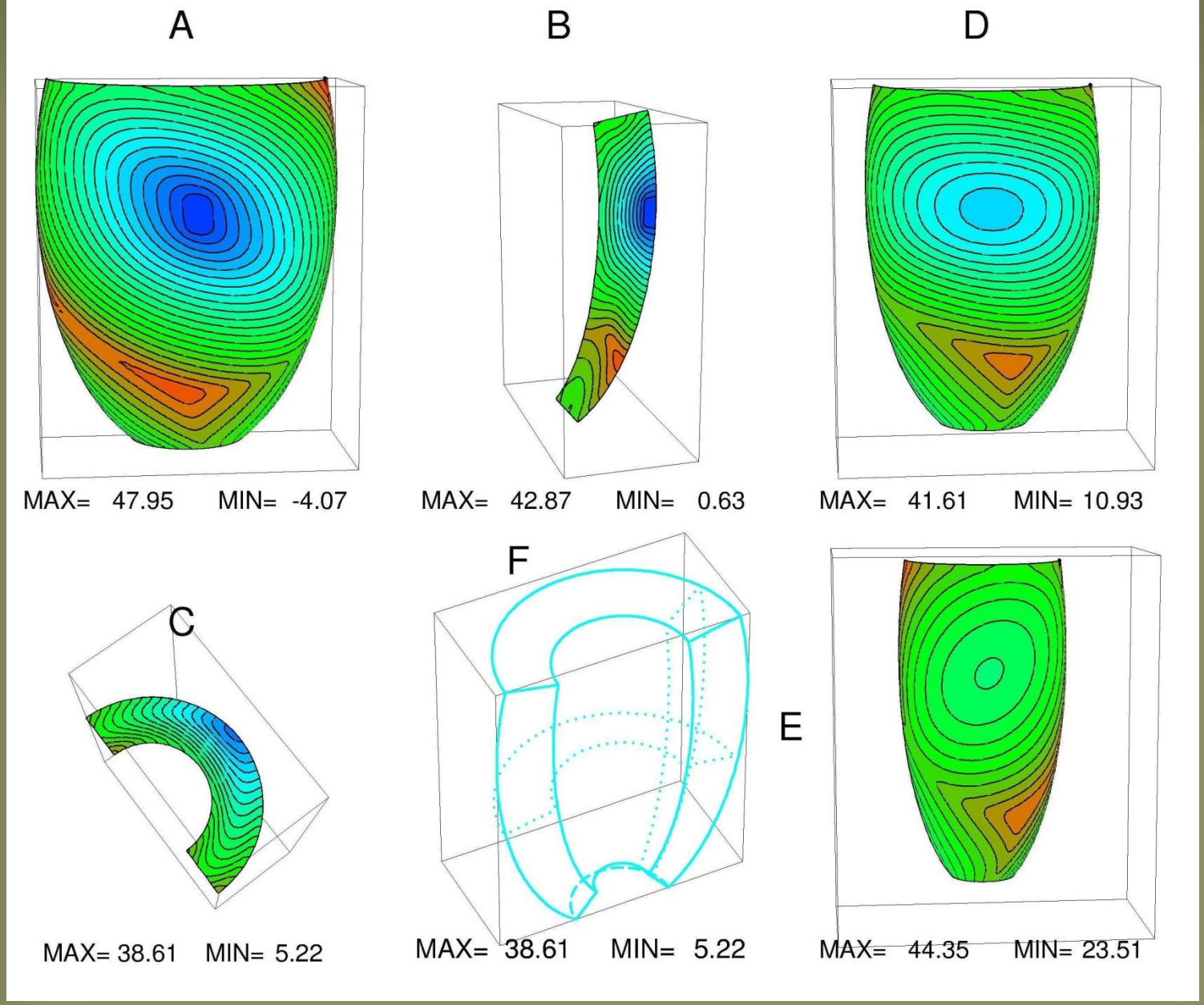
**Library(MPI)**



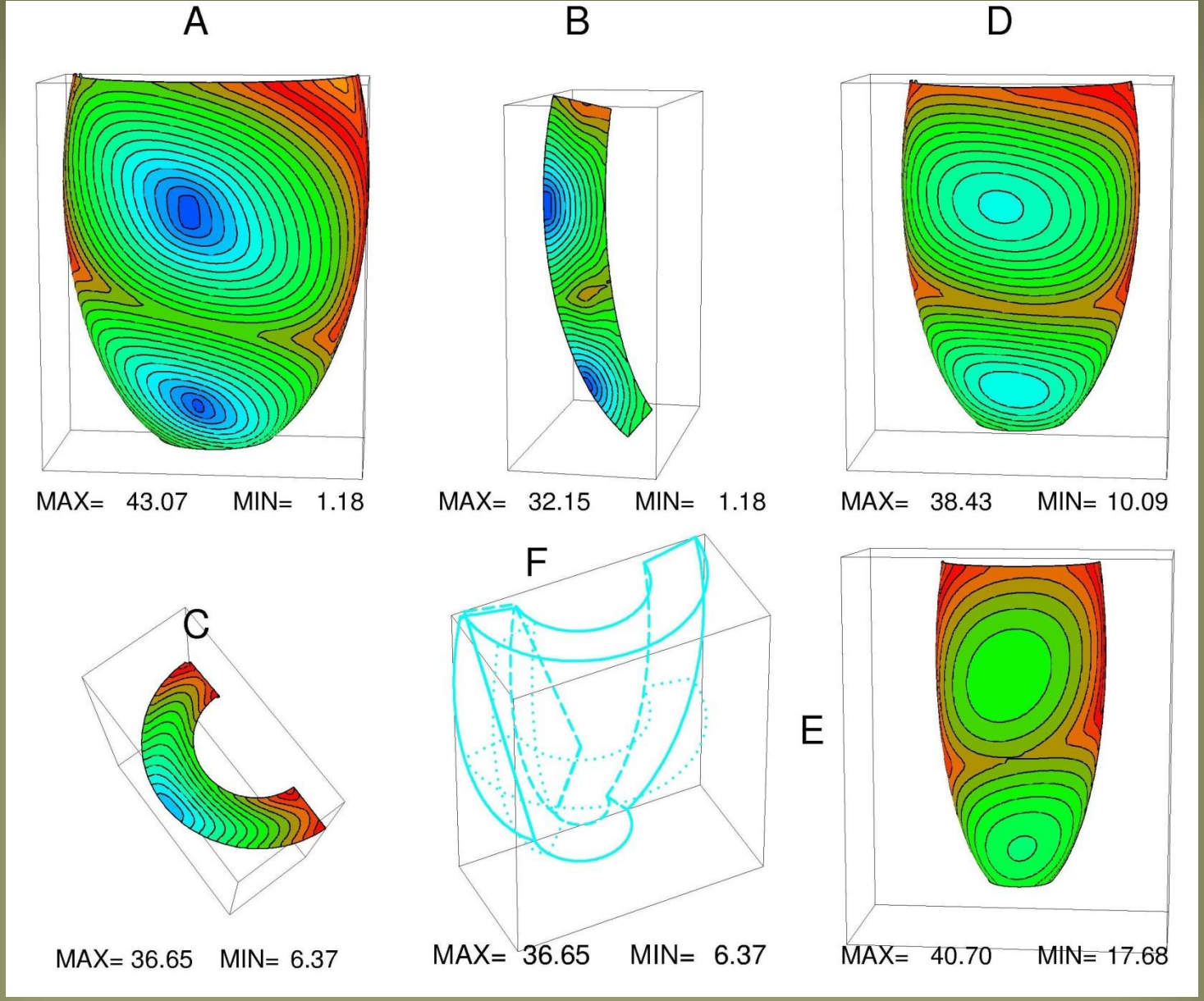

**One Stimuli (front): isochrones on epicardium(A), endocardium(E) and various sectional views**




**Two Stimuli (front): isochrones on epicardium (A), endocardium (E) and various sectional views**




**Two Stimuli (back) : isochrones on epicardium(A), endocardium (E) and various sectional views**




**Four Stimuli (front) : isochrones on epicardium(A), endocardium (E) and various sectional views**

# Conclusions

- Numerical simulation of cardiac excitation is developed
  - Implementing Luo-Rudy model (1991) with eight gating variables in one dimension.
  - Implementing Roger model with one gating variable in three dimension.
- Three dimensional Finite Element Parallel code, based on detailed 3D anisotropic model, is developed for Large scale simulation of cardiac excitation process on distributed memory parallel computer IBM sp2. It is used for simulating the cardiac excitation process on Ventricular myocardium during Complete heart beat.

# Further Development

- More detailed models like bidomain model are used to get more realistic situation. Also more detailed model like Luo-Rudy (1994) will also make the model more detailed and tried to simulate perfectly.
- For time discretization more efficient time advancement approximation make model more accurate for example: second order methods, adaptivity etc.
- More general geometry like addition of atria and more realistic approximation using MRI data techniques.