Excitable Media as Model of Cardiac Arrhythmia

Werner Lehner
23.03.11

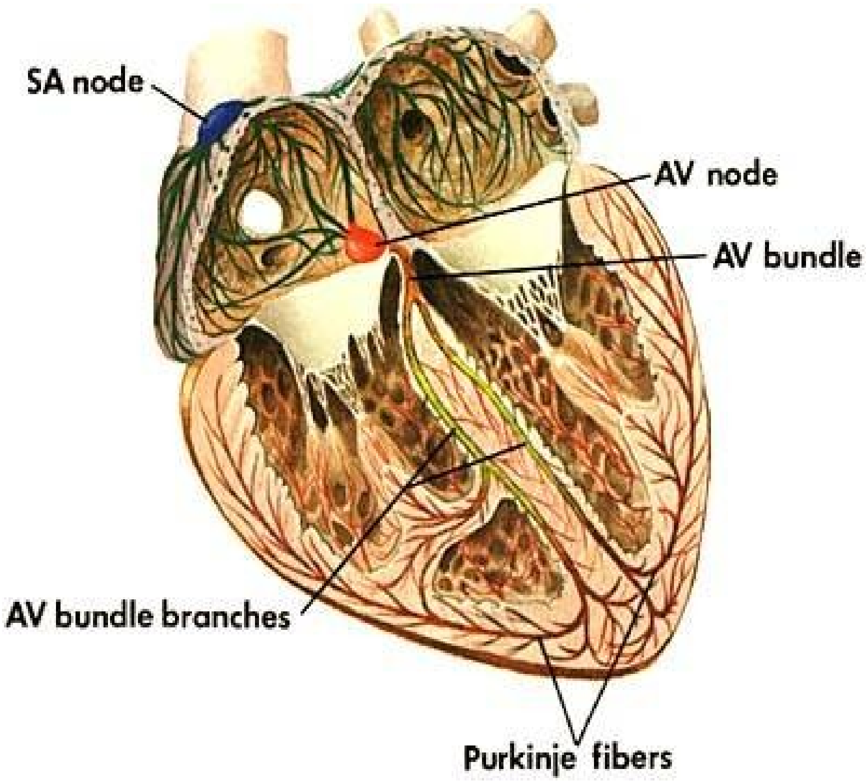
Outline

- Cardiac Arrhythmias
  - Cardiac Conduction System
  - Action Potential
  - Fibrillation
  - Reentry

- Modeling
  - Model
  - BZ-Reaction
  - Finite Element Method
  - Software

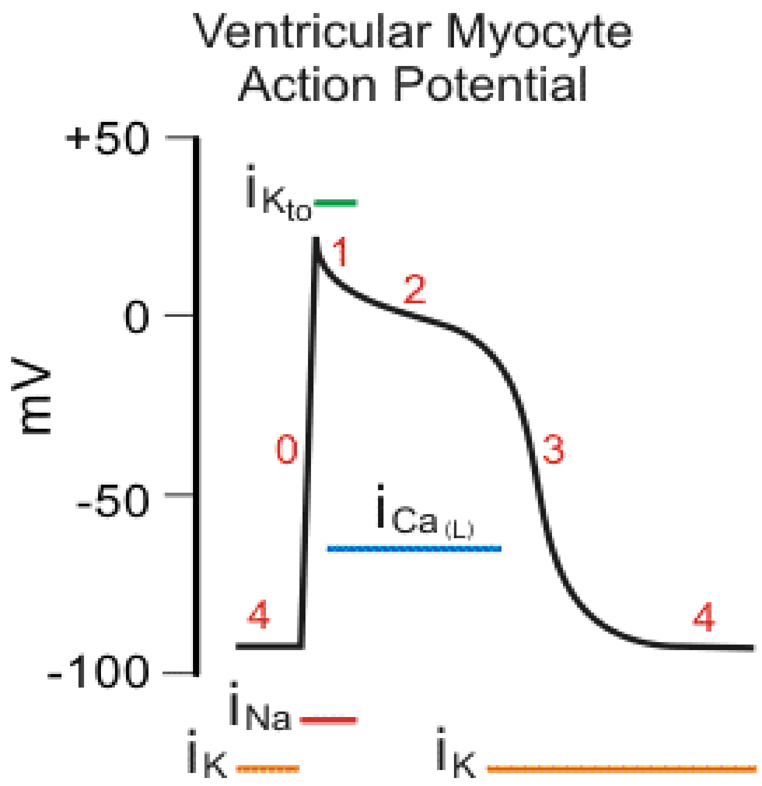
- Simulations
  - Plain
  - Sphere
  - Real Geometry

Cardiac Conduction System



- SA-node: primary pacemaker
- AV-node: electrical connection between atria and ventricles
- Av-bundle (His-bundle): transmission to apex
- Purkinje fibers: distribution to ventricular myocardium
- Contraction starts at apex
- AP spreads across ventricles (gap-junctions

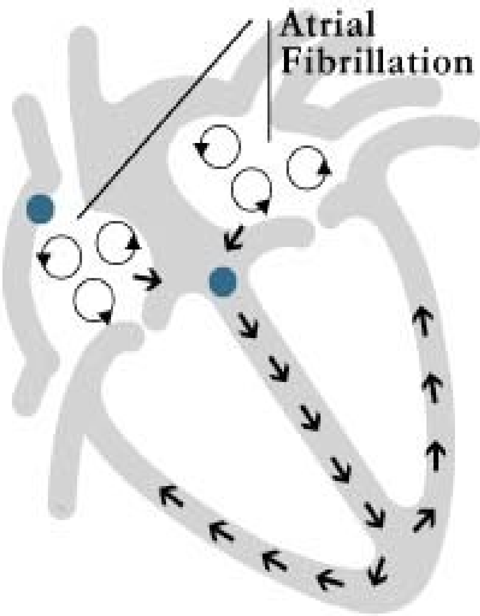
Action Potential



- Rapid change of transmembrane Potential
- Complex system of ion channels
- Resting Potential (4)
- Threshold Potential: ~ -70mV
- Fast depolarization (0)
- Slow repolarization (2,3)
- Effective refractory period (ERP): new AP can not be triggered
- No back-propagation of APs
- All-or-none-characteristic

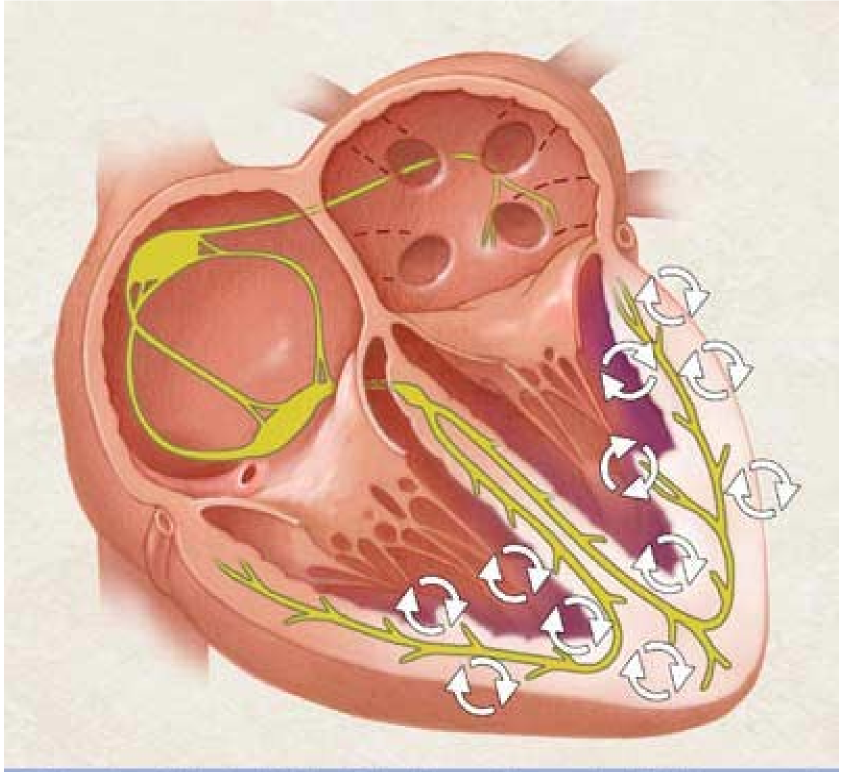
Fibrillation

- Uncoordinated, very rapid activity
- Complex, chaotic electrical patterns
- Atrial (AF), ventricular fibrillation (VF)
- APs propagate on irregular pathways
- Deterioration of atrial/ventricular function
- ECG: P-wave replaced by fibrillatory waves (AF)



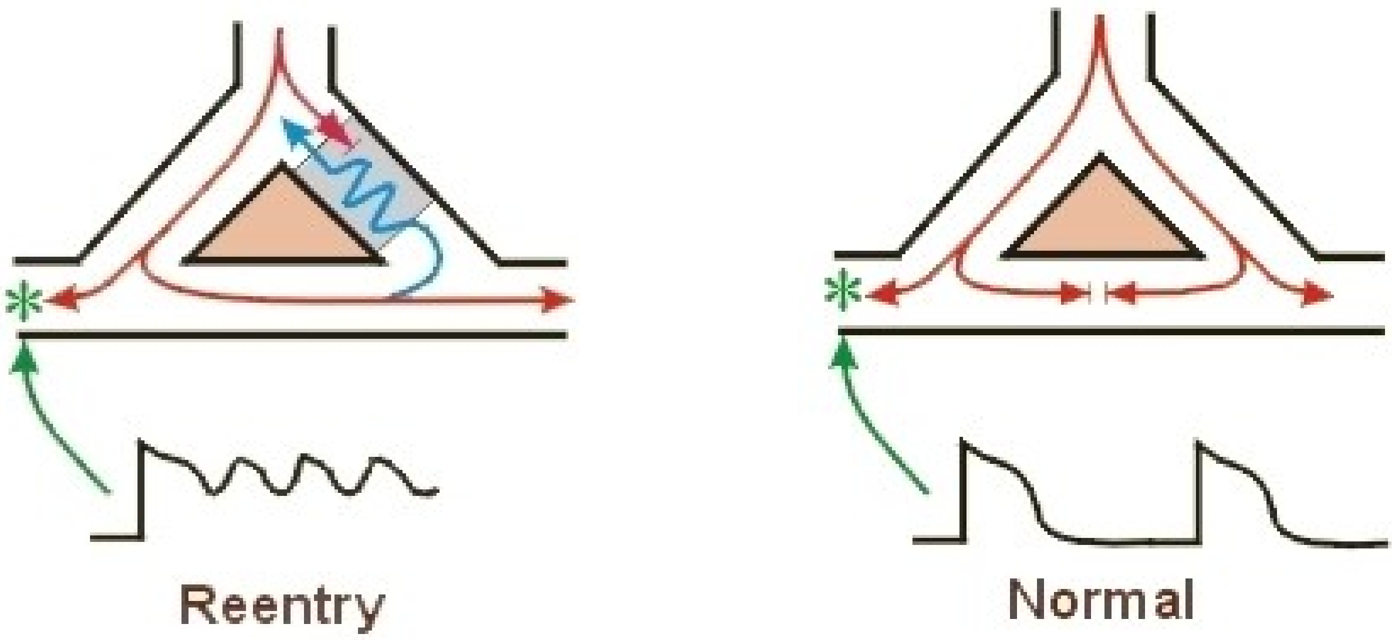
Fibrillation

- Substrate: inhomogeneities in electrophysiol. properties of myocardium (refractory period, conduction velocity, excitability)
- Fractionation of wavefronts in such areas (multiple wavelet mechanism)
- Formation of self-perpetuating impulses (reentry mechanism)

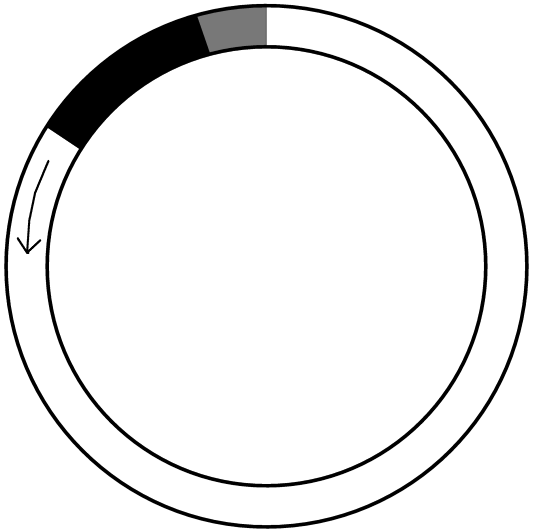


Reentry

- Obstacle: anatomic (myocardial infarction), functional (refractory area)
- Unidirectional conduction block
- Wavelength = conduction velocity x refractory period
- Reentry possible if pathway >= wavelength



Reentry



“Leading circle”: source of spiral waves

Therapy

- Drugs (change electrophysiol. parameters, AF)
- Ablation (AF): destruction of reentry pathways
- Defibrillation (VF): depolarization of the whole myocardium by internal or external high-energy shock
- No mild therapy available (VF)

Termination of (multiple) Reentry by local low-energy Stimulation?

Outline

- Cardiac Arrhythmias
  - Cardiac Conduction System
  - Action Potential
  - Fibrillation
  - Reentry

- Modeling
  - Model
  - BZ-Reaction
  - Finite Element Method
  - Software

- Simulations
  - Plain
  - Sphere
  - Real Geometry

Modeling

- Goals:
  - Simulation of reentrant-excitation
  - Simulation of electric stimulation
  - Stimulation-algorithm for termination of reenrty

- ToDo:
  - Choice of appropriate mathematical Model
  - Method for numerical solution
  - Software-framework
  - Simulations

Models

- Cell-based models:
  - Model for membrane potential of a single cell
  - Emulation of ion-channel functionality
  - e.g. Hodgkin-Huxley-Model:

$$C_{Mem} \frac{dV_{Mem}}{dt} = I_{Na} + I_K + I_{Ext} + I_L$$

- in most cases very complex (>30 PDEs)
- Tissue = network of many single cells → numerical effort

Models

- Excitable media
  - Model for system of many cells
  - Reaction-diffusion system
  - AP described by activator-inhibitor system (“reaction”):

$$\frac{\partial u}{\partial t} = f(u,v) \quad , \quad \frac{\partial v}{\partial t} = \varepsilon g(u,v)$$

  - AP-propagation (“diffusion”)

$$\dot{u} = D \nabla^2 u$$

  - U: membrane potential („activator“)
  - V: repolarization current („inhibitor“)
  - AP-characteristics: ref. period, no damping, all-or-none

EM-Models

- Starobin-Starmer:

$$\frac{\partial u}{\partial t}=D\nabla^2 u+\lambda(u)u-m-v \quad , \quad \frac{\partial v}{\partial t}=\varepsilon(\gamma u-v)$$

- Panfilov:

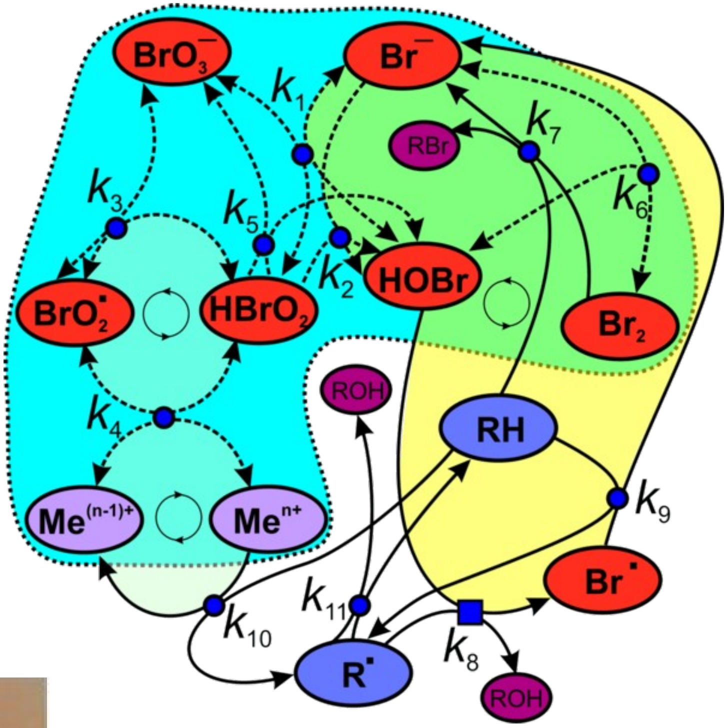
$$\frac{\partial u}{\partial t}=D\nabla^2 u+\lambda(u,v)u-m-v \quad , \quad \frac{\partial v}{\partial t}=\varepsilon(u,v)(\gamma u-v)$$

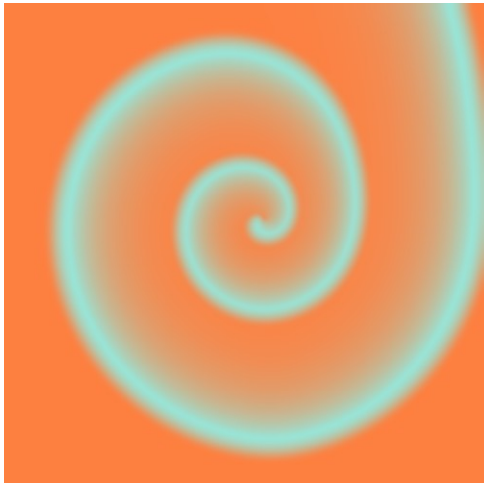
- Tyson-Fife (BZ-reaction)

$$\frac{\partial u}{\partial t}=D\nabla^2 u+u-u^2-(fv+\phi)\frac{u-q}{u+q} \quad , \quad \frac{\partial v}{\partial t}=\varepsilon(u-v)$$

BZ-Reaction

- Nonlinear chemical oscillator
- High complexity
- Well-known example of a excitable medium
- Good correspondence between simulation and experiment
- Simplification of complex systems to few variables is feasible





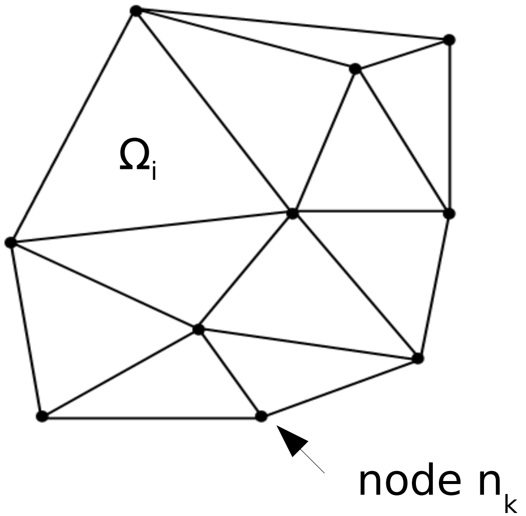
simulation

experiment

Finite Element Method

- Strong form (e.g Poisson-eq):

$$-\nabla^2 u = f$$



- Division of domain Ω in M subdomains (meshing)

$$\Omega = \sum_{j=1}^{M} \Omega_j$$

- Weak form:

$$\int_\Omega v \nabla^2 u = \int_\Omega vf \longrightarrow \int_\Omega \nabla v \nabla u = \int_\Omega vf$$

- Sobolov space H:

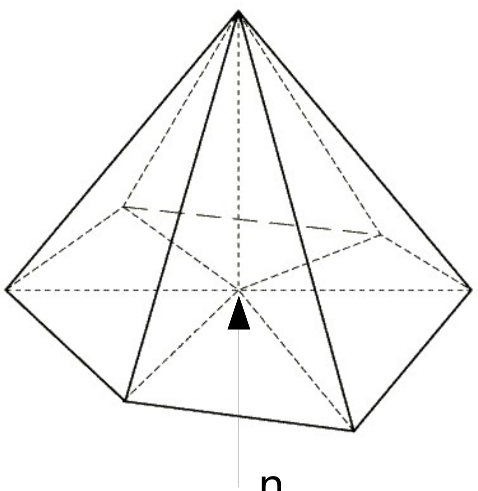
$$v \in H_0^1(\Omega) : \int_\Omega [(v')^2 + v^2] d\Omega < \infty$$

$$v, u \in H_0^1(\Omega) : \int_\Omega v \nabla^2 u = \int_\Omega vf \quad \forall v \longleftrightarrow -\nabla^2 u = f$$

Finite Element Method

- Basis of H, e.g. linear:

$$\Phi_i(x,y)=\alpha_i+\beta_i x+\gamma_i y \quad , \quad \Phi_i(n_k)=\delta_{ik}$$



- Approximation of u:

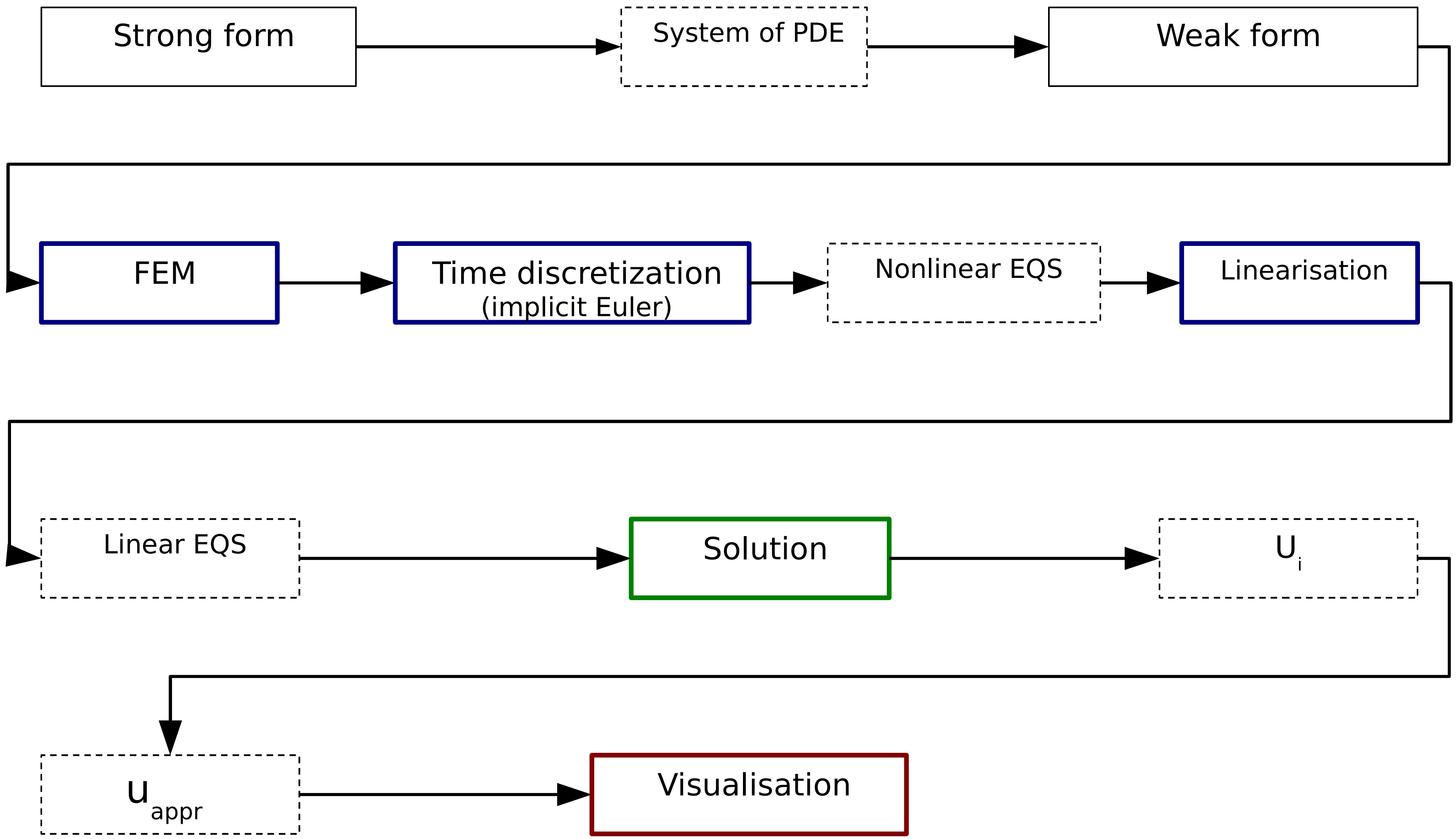
$$u_{appr}=\sum_{i=1}^{N} u_i \Phi_i$$

- Calculation of u_i:

$$\sum_{i=1}^{N} u_i \underbrace{\int_{\Omega} \nabla \Phi_i \nabla \Phi_j}_{A_{ij}} = \underbrace{\int_{\Omega} f \Phi_j}_{b_j} \longrightarrow \sum_{i=1}^{N} u_i A_{ij} = b_j \longrightarrow \underline{\underline{A}} \cdot \underline{u} = \underline{b}$$

- Solution of linear equation system $\rightarrow u_i \rightarrow u_{app}$

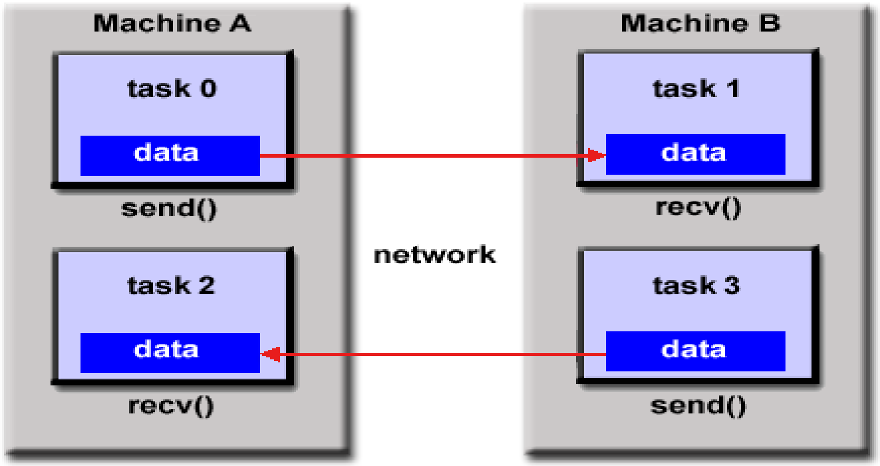
Numeric Workflow



Software

- Written in C++ under Linux
- Used libraries:
  - PETSc (Portable, Extensible Toolkit for Scientific Computation): LEQ-Solver
  - Hermes3d: FEM
  - VTK/Paraview: Visualization

- Parallelization MPI-2 (SPMD, distributed memory)



Outline

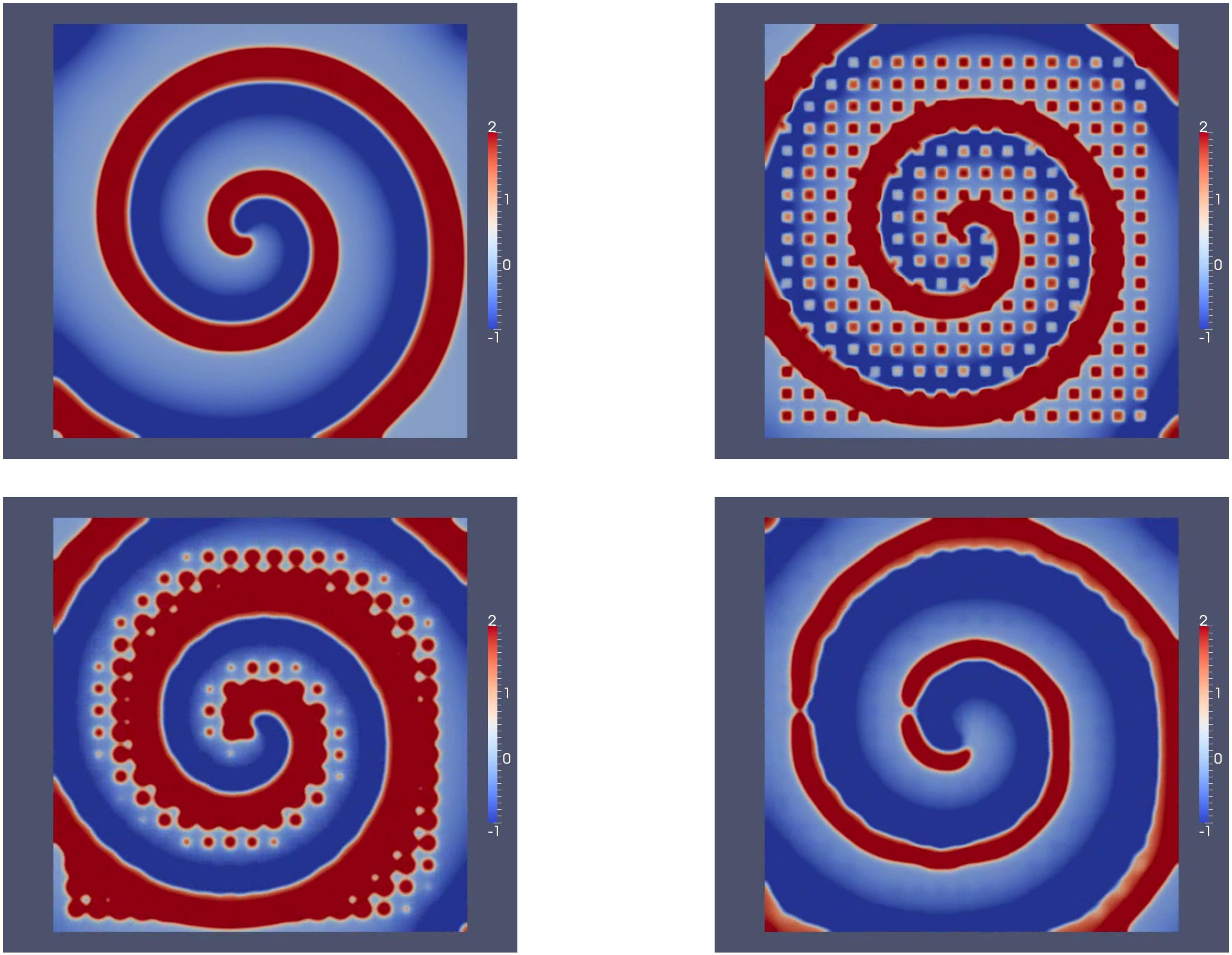
- Cardiac Arrhythmias
  - Cardiac Conduction System
  - Action Potential
  - Fibrillation
  - Reentry

- Modeling
  - Model
  - BZ-Reaction
  - Finite Element Method
  - Software

- Simulations
  - Plain
  - Sphere
  - Real Geometry

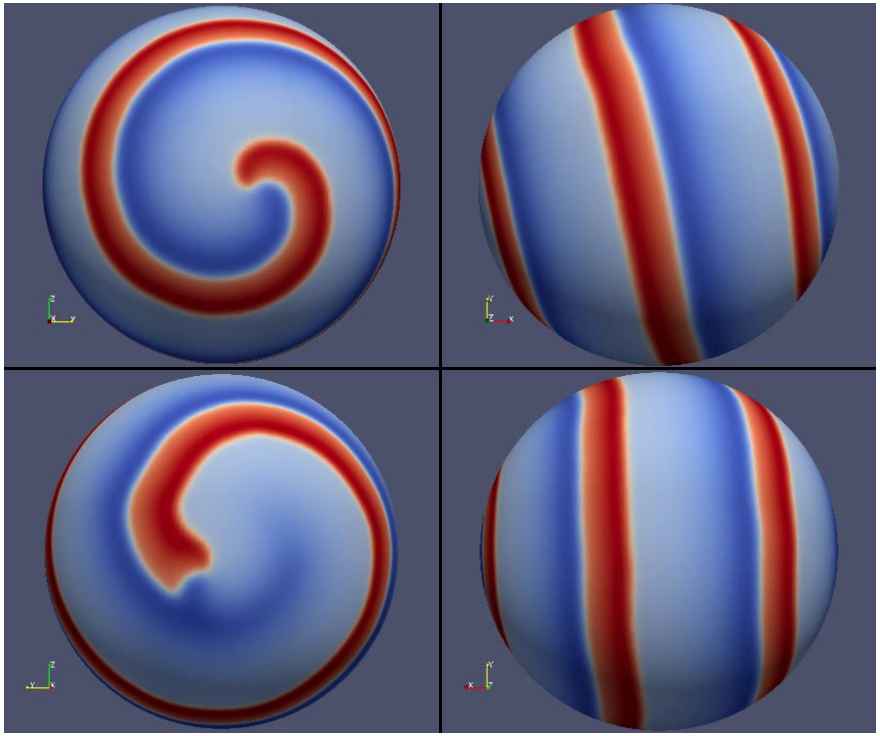
Simulation 1

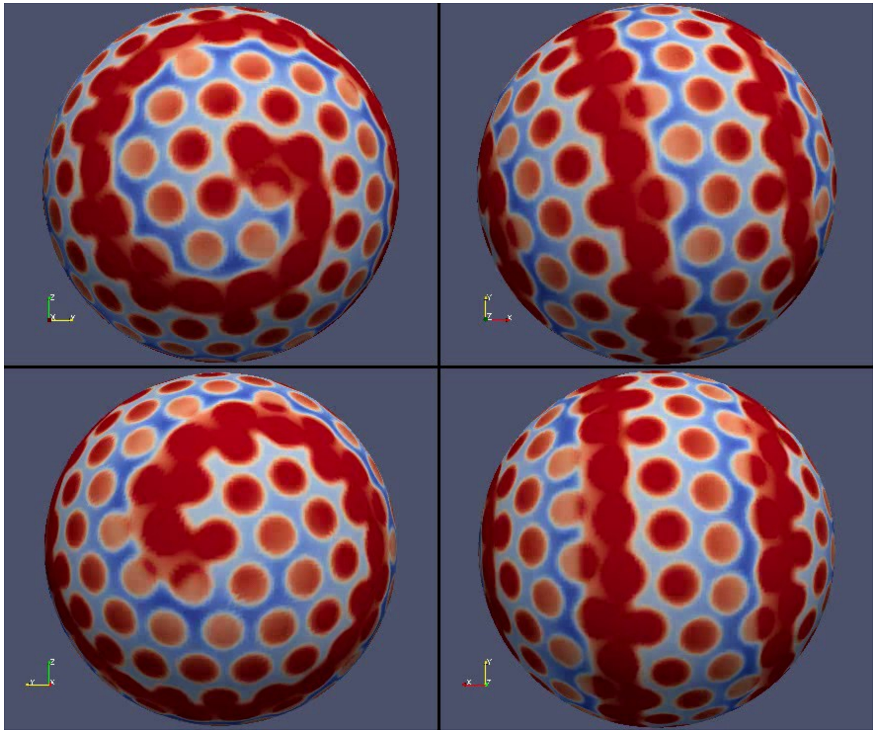
Spiral wave on plain domain (600x600x2 nodes), grid stimulation



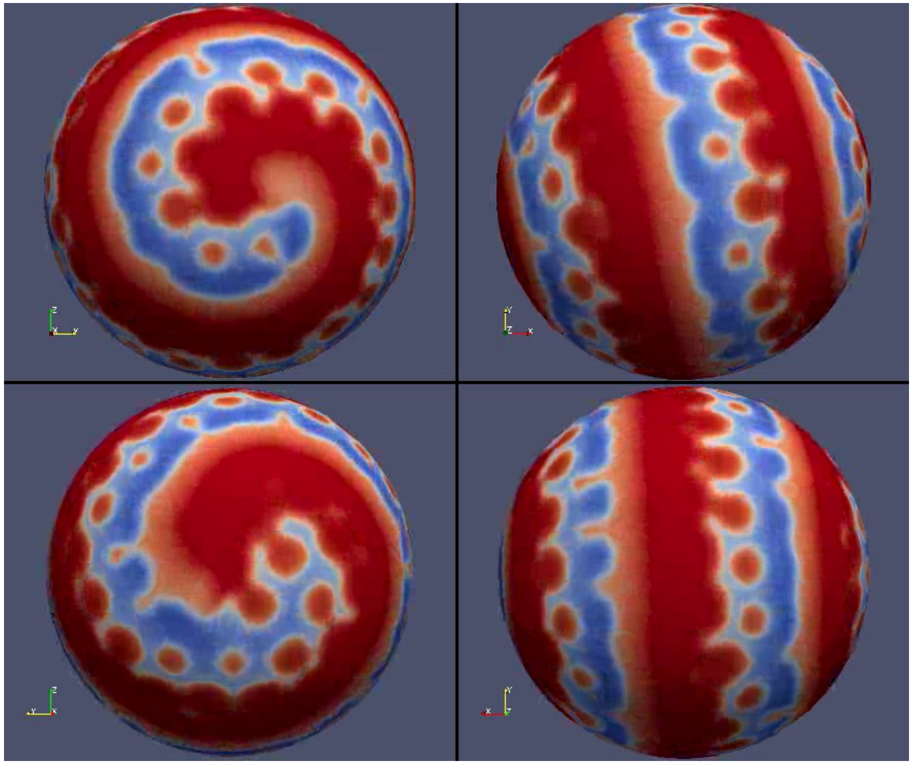
Simulation 2

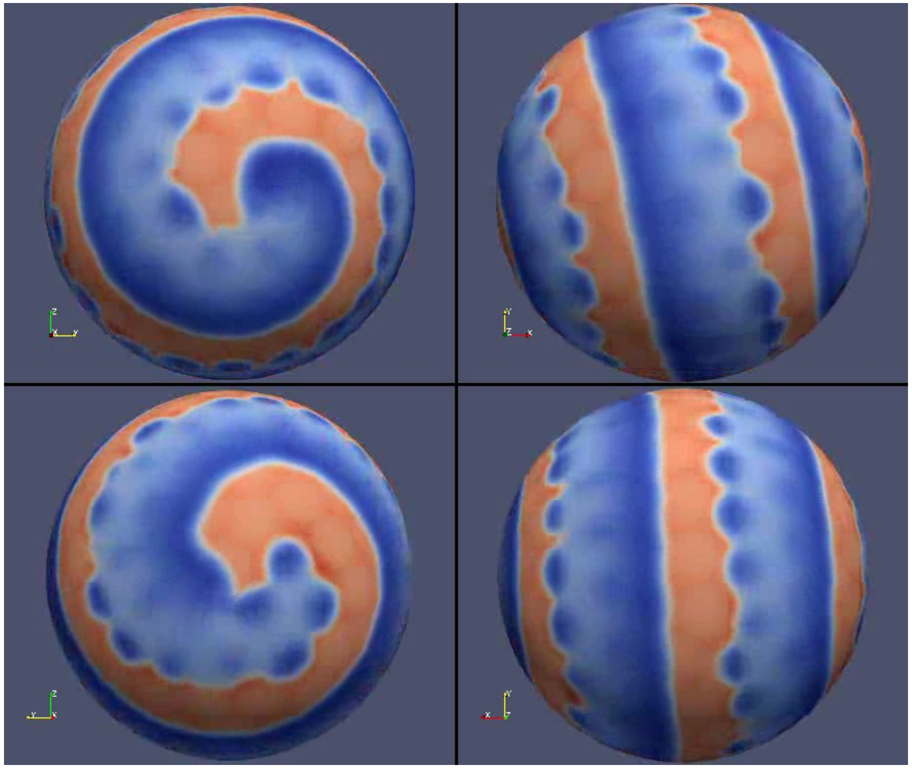
Spiral wave on spherical shell (r=50, d=2, 70000 nodes)



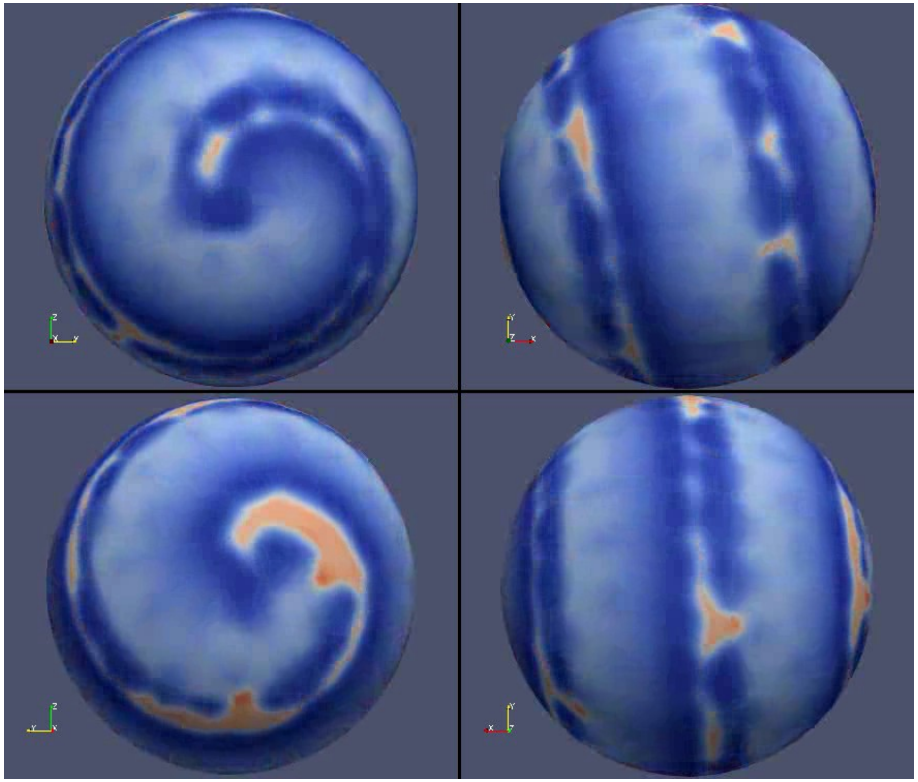


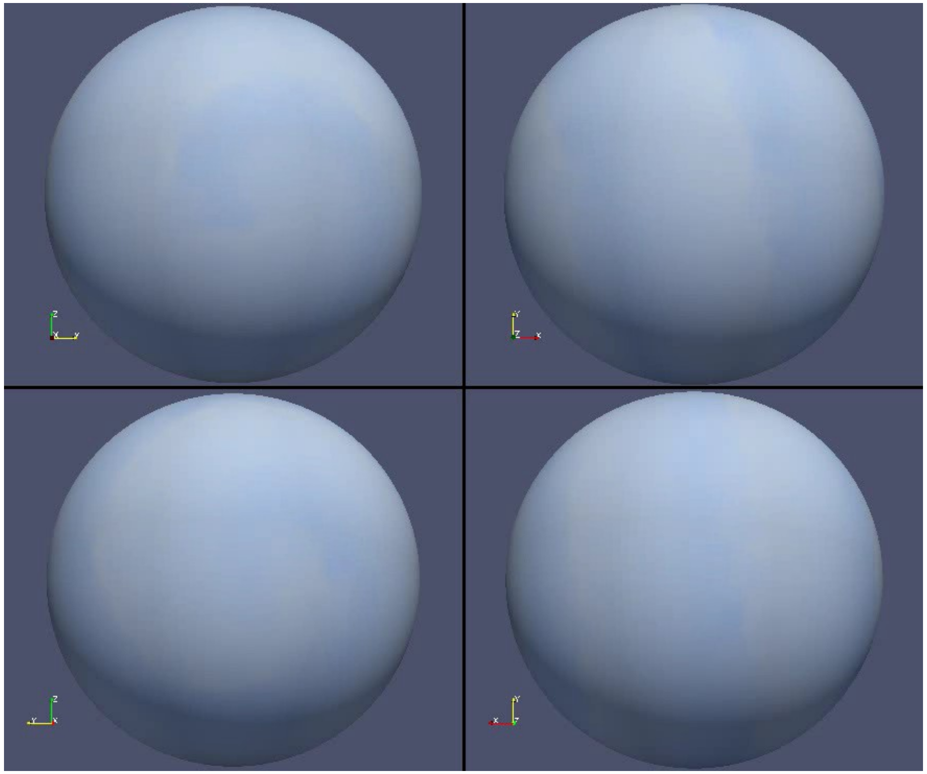
Simulation 2



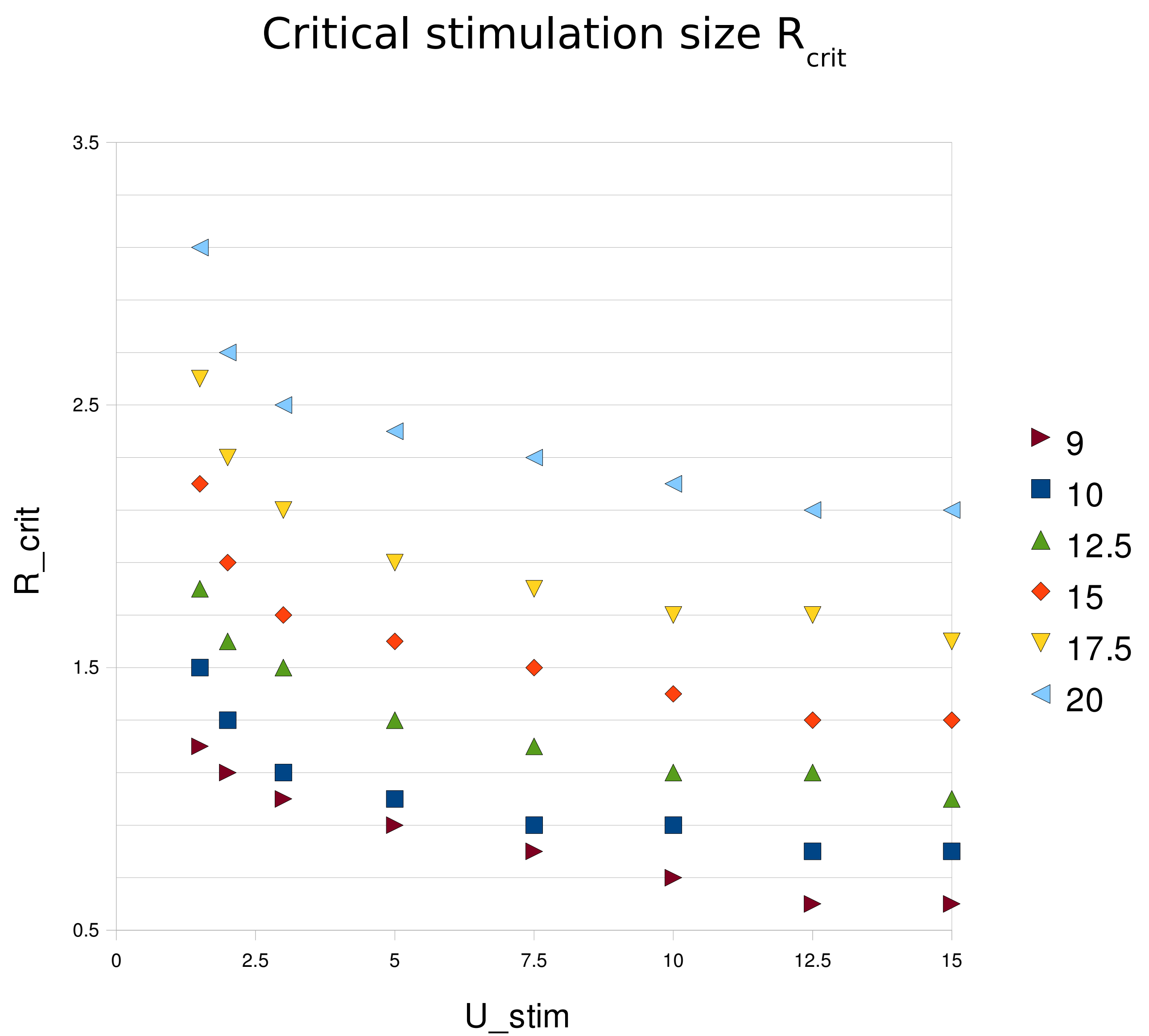


Simulation 2



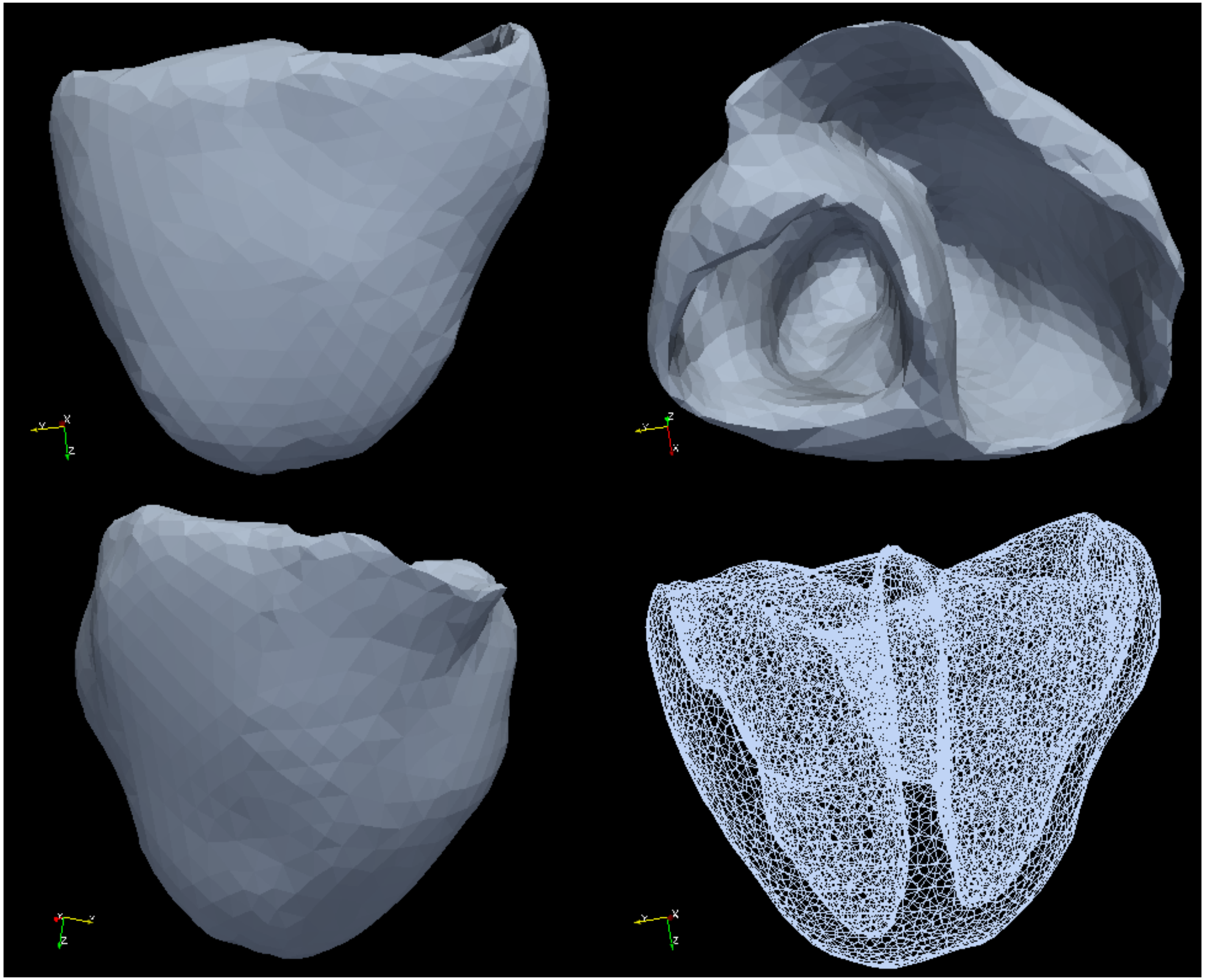


Simulation 2

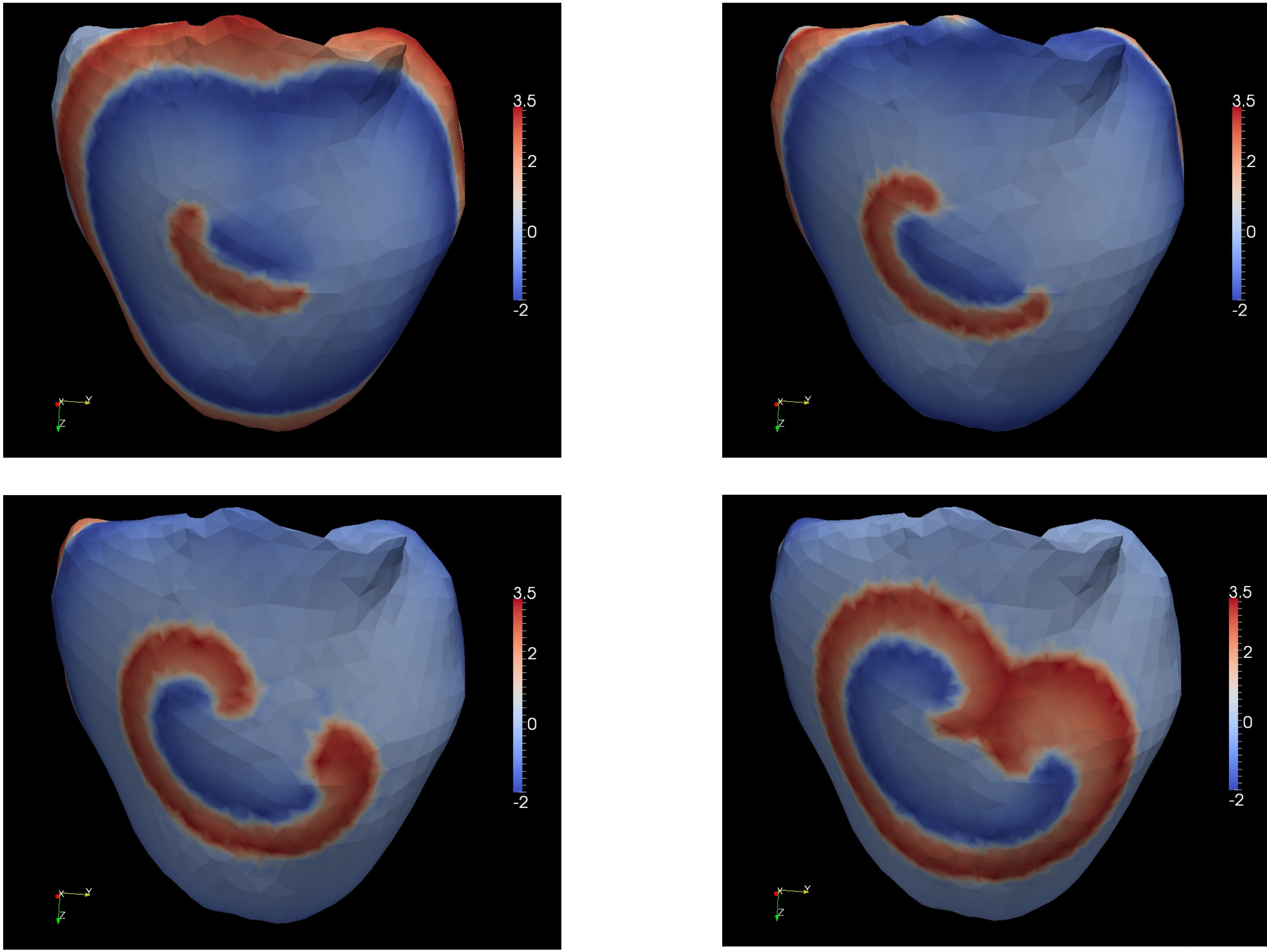


Simulation 3

Mesh of human ventricles



Simulation 3



Simulation 3