Towards Model-Based Estimation of the Cardiac Electro-Mechanical Activity from ECG Signals and 3D images

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* « Images of Cardiac Electro-Mechanical Activity », Cooperative research initiative involving the Inria projects Epidaure, Macs, Sinus, Sosso.

See http://www-rocq.inria.fr/who/Frederique.Clement/icema.html

Outline

- ICEMA Project
- Images of the Cardiac Electro-Mechanical Activity
- Models of the Cardiac Electro-Mechanical Activity
- Simulation of the controlled Cardiac-Muscle Contraction (D. Chapelle)
- Conclusions and perspectives

1. ICEMA: Images of Cardiac Electro-Mechanical Activity

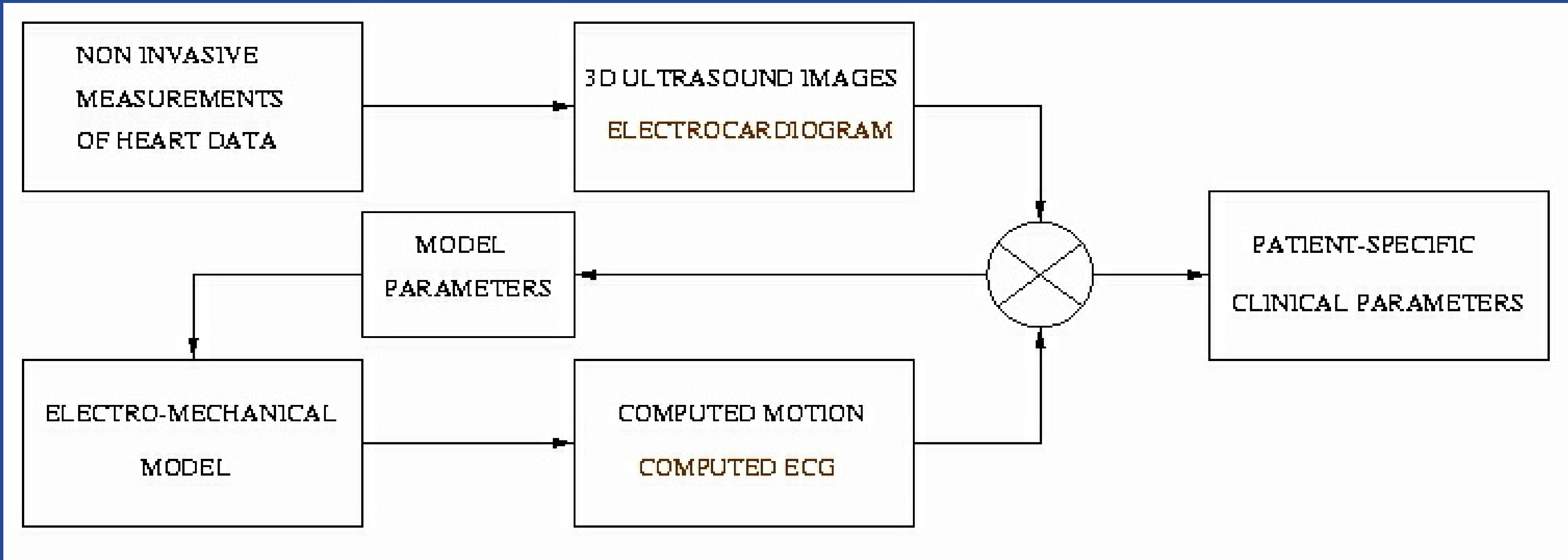
Scientific and clinical challenges:

- Combining 3D ultrasound images with N-channel ECG in order to:
  - obtain a dynamical representation of excitation-contraction coupling on the whole heart scale
  - obtain patient-specific local parameters assessing heart function

- Modeling: find a good balance between "model realism" and "well-posedness" of identification or observation problems.
- Simulation, Parameter Identification, State Observation

ICEMA Project is a first step (May 2000-May 2002) towards these objectives

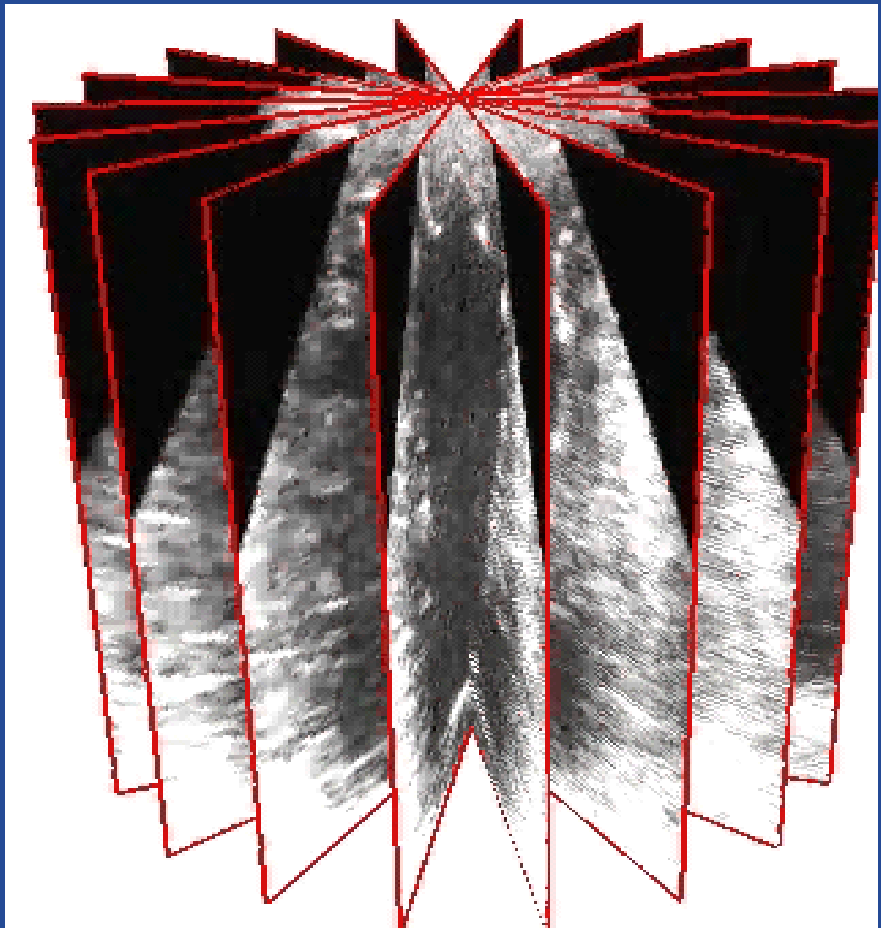
Flow diagram of the ICEMA project

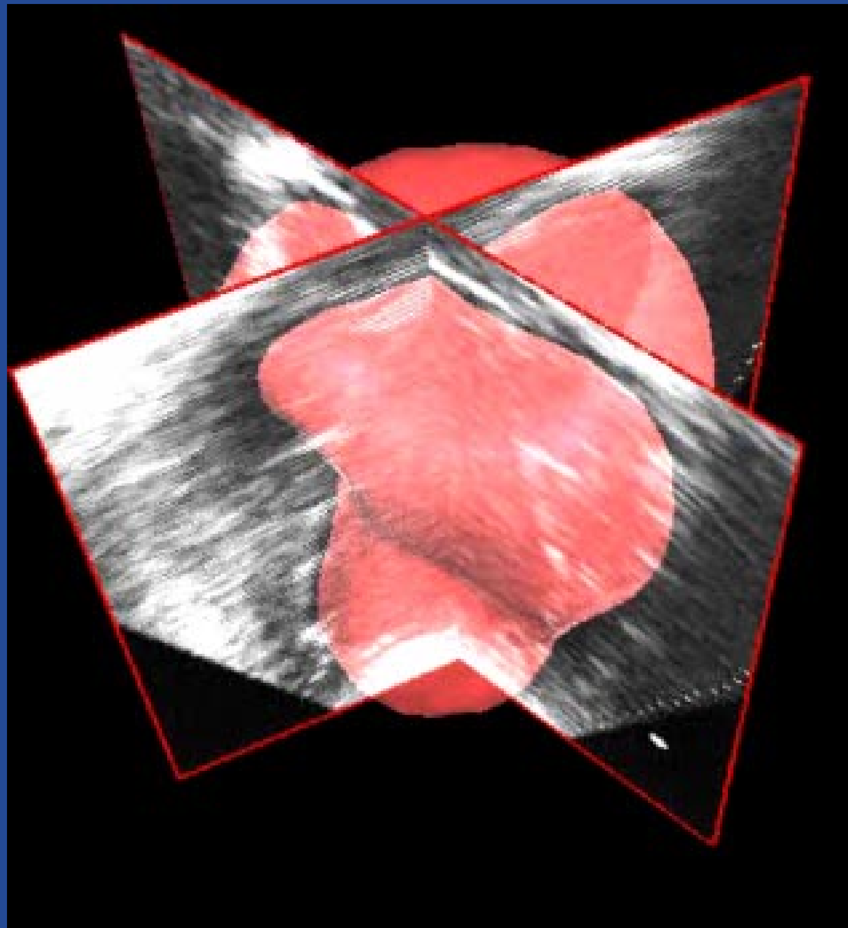


The identification problem

2. Images of the Cardiac Electro-Mechanical Activity

Deformation Imaging

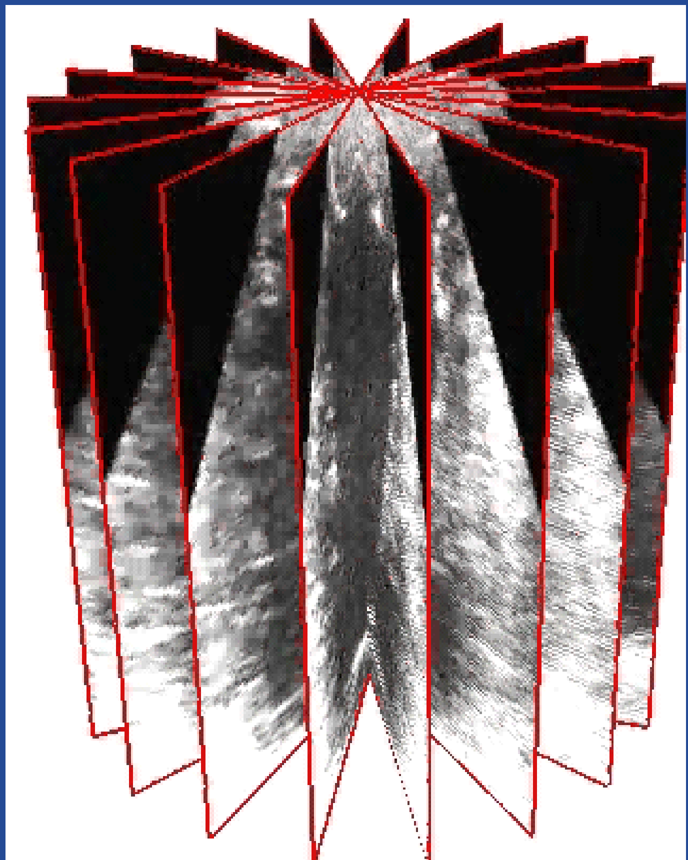


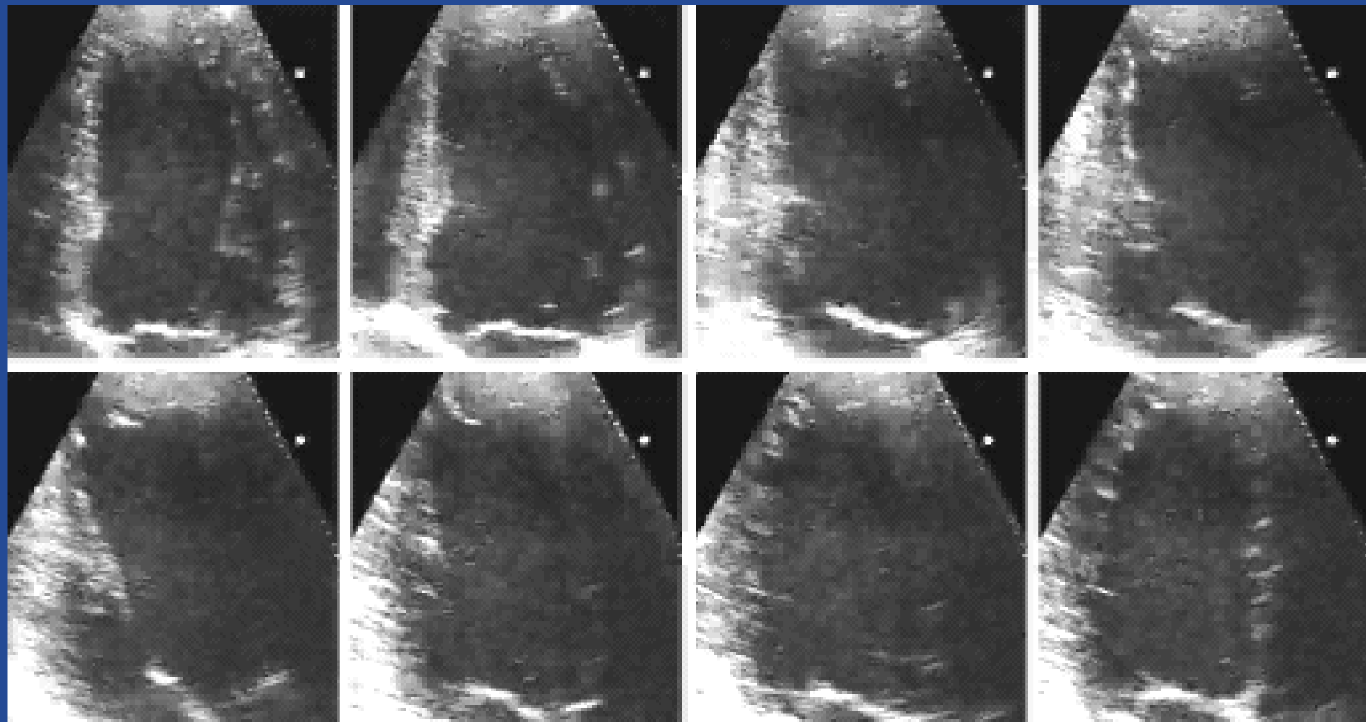


Example of ultrasound Images (before/after processing)

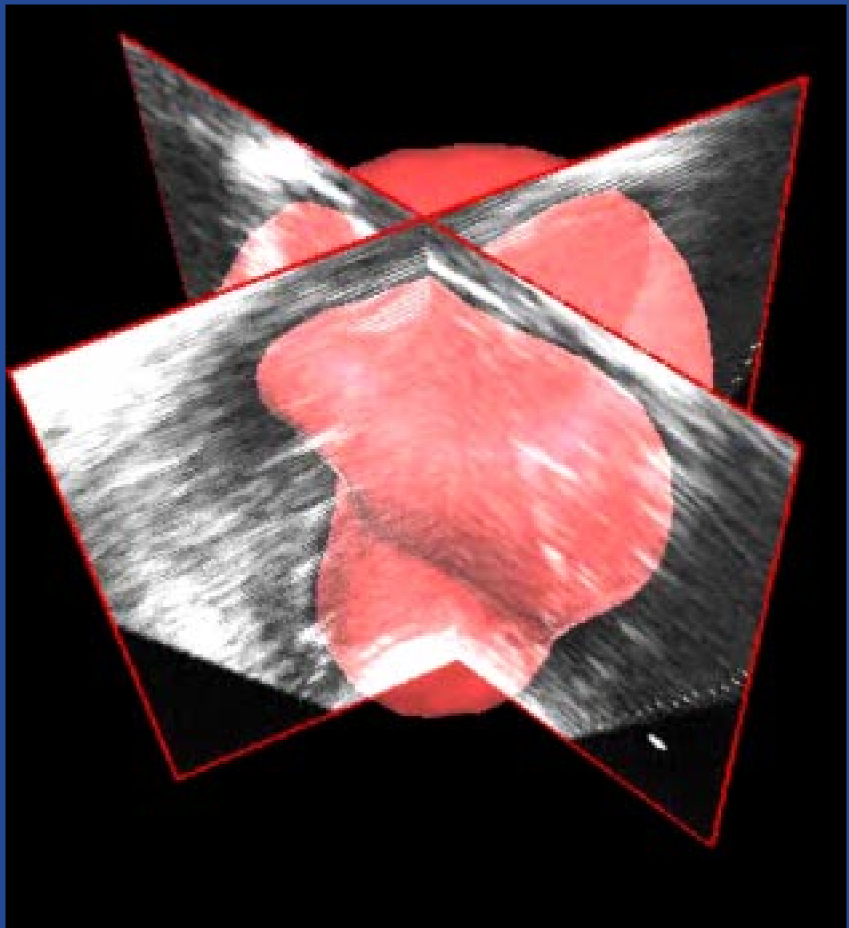
4D Echocardiography

Echocard3D Images : 9 frames, 8 instants





Model-Based Image Segmentation



Montagnat-Delingette-MICCAI'00

Method:

A simple "shape to ultrasound" model is inverted:

A uniform surface potential (interaction potential between computed shapes and measured ultrasound-images) is minimized under regularity constraints on shapes and motions).

Result:

A sequence of 3D surfaces following 3D ultrasound-images.

May be used as input data to estimate stress and strain.

Epidaure project/ATL/Philips Collaboration

ECG Imaging

Noninvasive ElectroCardioGraphic Imaging can reconstruct Cardiac Surface Potentials from Body Surface Potentials (Rudy et al, van Oosterom,...).

Method:

Realistic "Electrostatic Torso-Models" are inverted (Least-Square Pseudo-Inverse)

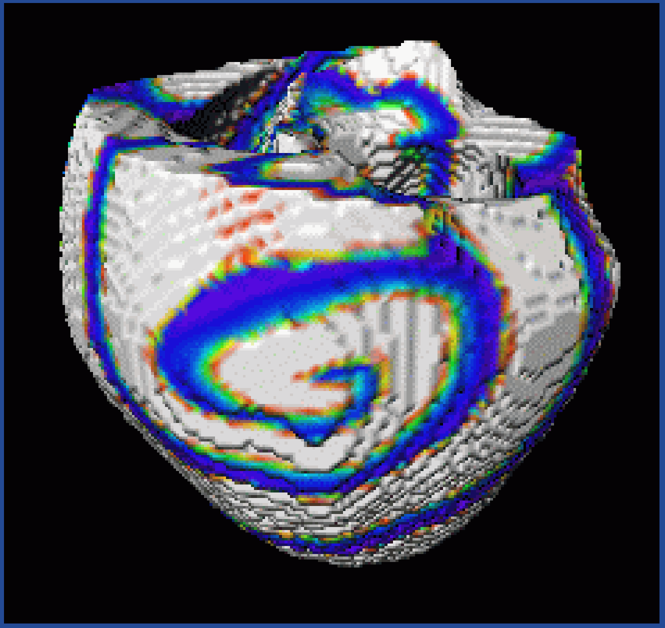
Result:

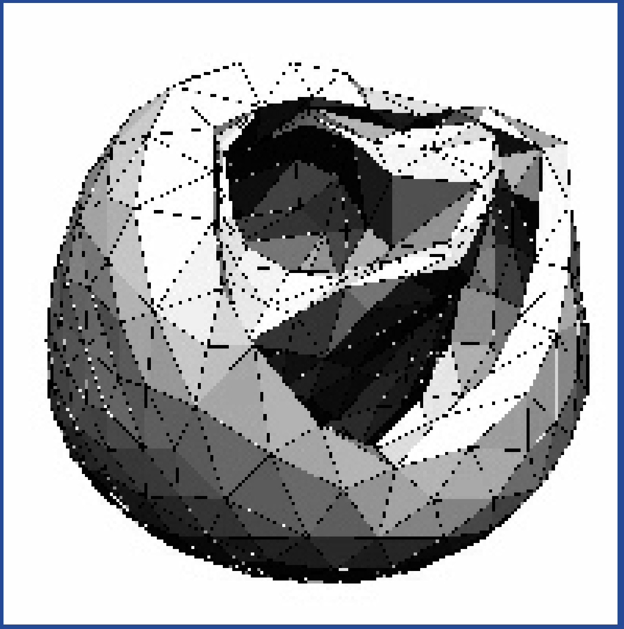
Sequences of Cardiac Surface Potentials, equivalent to the Cardiac Electric Activity.

May be used as input data to estimate Cardiac Volume Potentials.

3. Models of the Cardiac Electro-Mechanical Activity

Heart-scale Modeling





Example of Electro-Mechanical Model

E-State (FH-N) : $\frac{\partial u}{\partial t} = \operatorname{div}(D \nabla u) + f(u) - v, \quad \frac{\partial v}{\partial t} = \epsilon(ku - v)$

M-State : $\rho \frac{\partial^2 \underline{y}}{\partial t^2} = \operatorname{div}(\underline{\underline{F}}(\underline{y}) \cdot \underline{\underline{\sigma}}), \quad \text{with } \underline{\underline{\sigma}} = \Sigma(\underline{\underline{\varepsilon}}(\underline{y}), u), \quad (+B.C.)$

E-input : $u(t) = e(t) \text{ on } \partial\Omega^{\text{Purkinje}} \quad (\text{SA } B.C.)$

E-output : $\text{ecg}(d, t) = L(\nabla u(t), d)$ (ECG along direction d), u (AP)

M-output : $\Omega^{\text{Heart}}(t) = \bigcup\{\underline{y}(t)\}$ (Image), $\underline{\underline{\varepsilon}}(\underline{y})$, $\underline{\underline{\sigma}}$ (strain and stress tensors)

Measurements : $\text{ecg}^*(d_j, t), \quad \Omega^{\text{Heart}*}(t_i)$

(with $\underline{\underline{F}}(\underline{y})$ deformation gradient)

A key feature: the controlled constitutive law

A Multi-Scale Modeling Approach

Mechanical Behavior: Multi-Scale Modeling Approach

Myofibre scale:

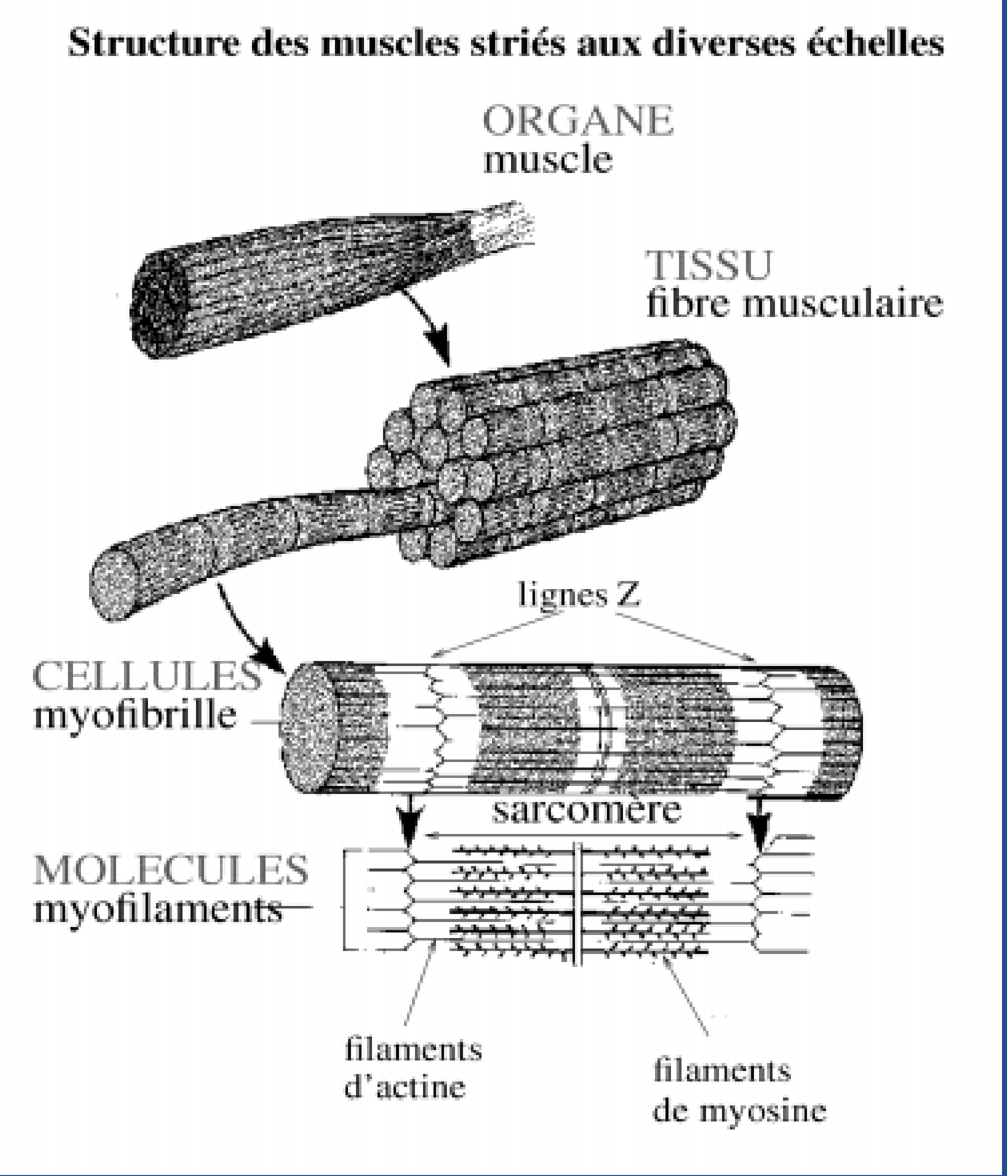
$$\begin{cases} \dot{k}_c = -(|u| + |\dot{\varepsilon}|)k_c + k_0 |u|_+ \\ \dot{\sigma}_c = -(|u| + |\dot{\varepsilon}|)\sigma_c + k_c\dot{\varepsilon} + \sigma_0 |u|_+ \\ \sigma = k_c \xi_0 + \sigma_c + \eta\dot{\varepsilon} \end{cases}$$

Resulting from an Huxley model on the sarcomere scale (Bestel, MS,2000):

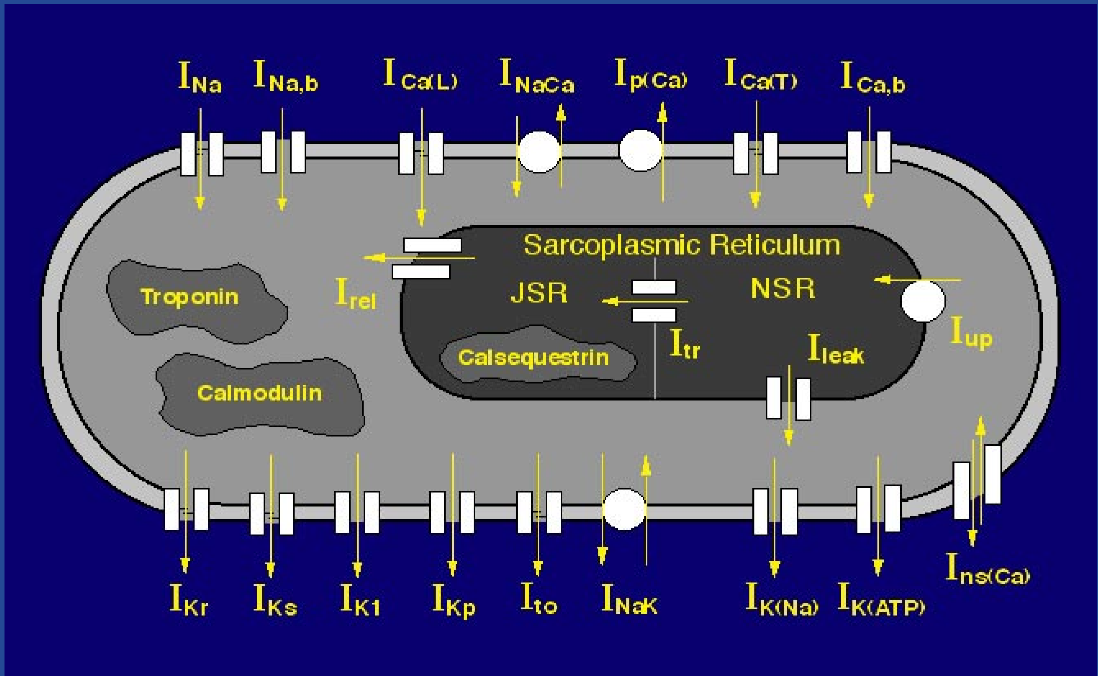
$$\begin{cases} \partial_t n + \dot{\varepsilon}\partial_\xi n = f(1-n) - gn \\ \sigma(t) = \int_{-\infty}^{+\infty} \partial_\xi W_1(\xi) n(\xi,t) d\xi + \eta\dot{\varepsilon} \end{cases}$$

which represents the collective behavior, on the molecular scale, of 2-state myosin nanomotors (Jülicher, Adjari et Prost, 97)

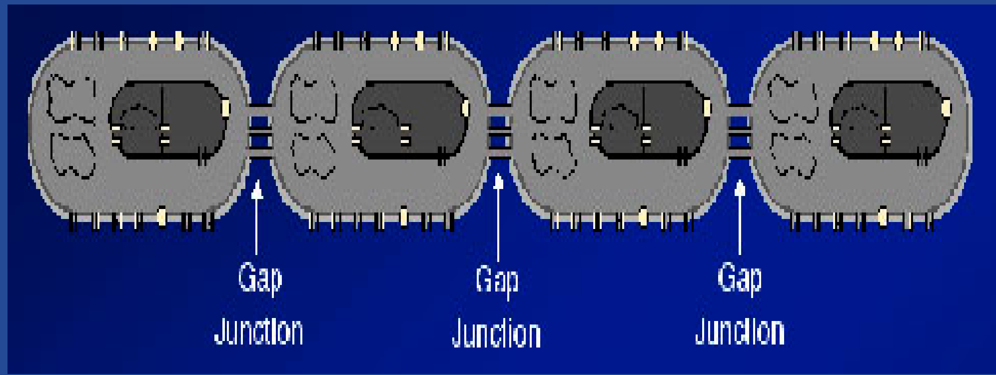
$$\eta\dot{x} = -\partial_x W(x,t) + \sqrt{2\eta k_B T} b + F$$



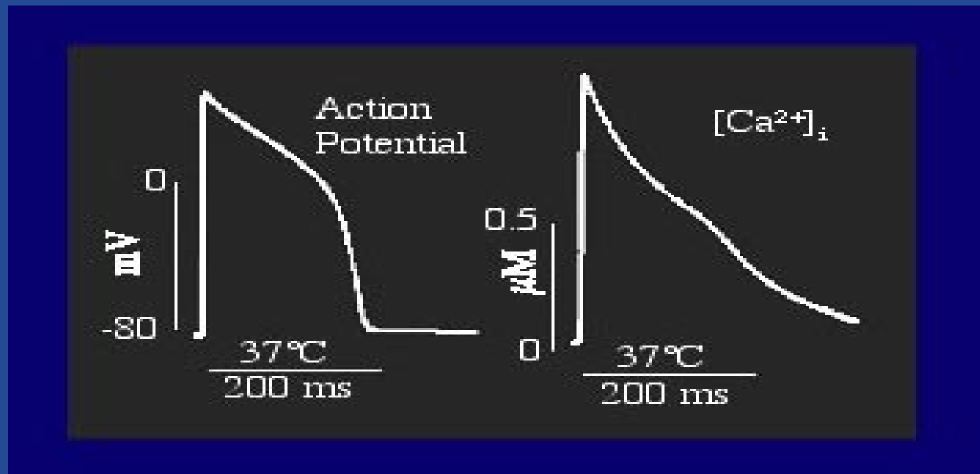
Electrical Behavior: Multi-Scale Modeling Approach



☞ Cardiac Cell



Cardiac fibre ☟ Action Potential ☟



Models of various complexities:

Luo-Rudy (with ionic currents) , …

Or,

FitzHugh-Nagumo

(simple model of the Action Potential).

4. Application: Simulation of controlled Cardiac Muscle Contraction

D. Chapelle

5. Conclusions and perspectives

Results:

- Image-segmentation techniques

- An electrically-controlled constitutive law for cardiac myofibres.
  It is currently being embedded into a 3D macroscopic model.

- This model is consistent with (Multiscale EM-Modeling):
  - (Mechanics) The ``sliding filament hypothesis'' and current nanomotor theory.
  - (Electricity) Different control levels: AP-control (tissue) and Ca^{2+} (cells).

Perspectives:

- Joint processing of 3D ultrasound images and N-channels ECG based on EM-Models could reduce ill-posedness of some "inverse problems", could give more insight...

  ⇒ We need EM-Signals, E-preprocessing techniques for ICEMA…

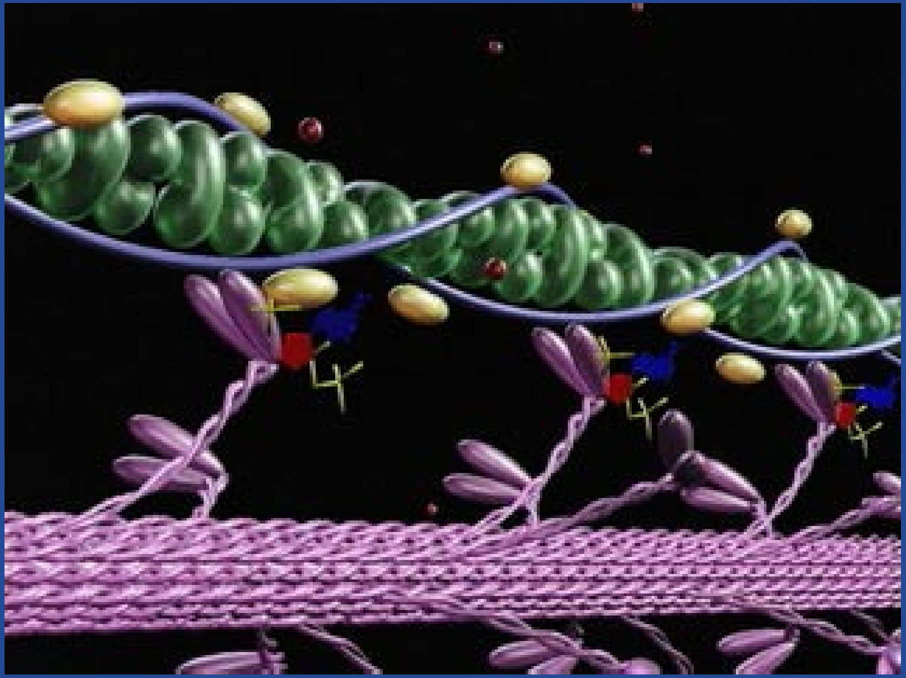
- Multiscale EM-modeling could allow zooming where needed ?
  - From the tissue scale "Simple AP-Propagation/Complex Geometry"
  - To the cell scale "Complex Ionic-currents/Simple Geometry"

  Useful for studying inhomogeneous domains (locally fatty or fibrous tissue) ?

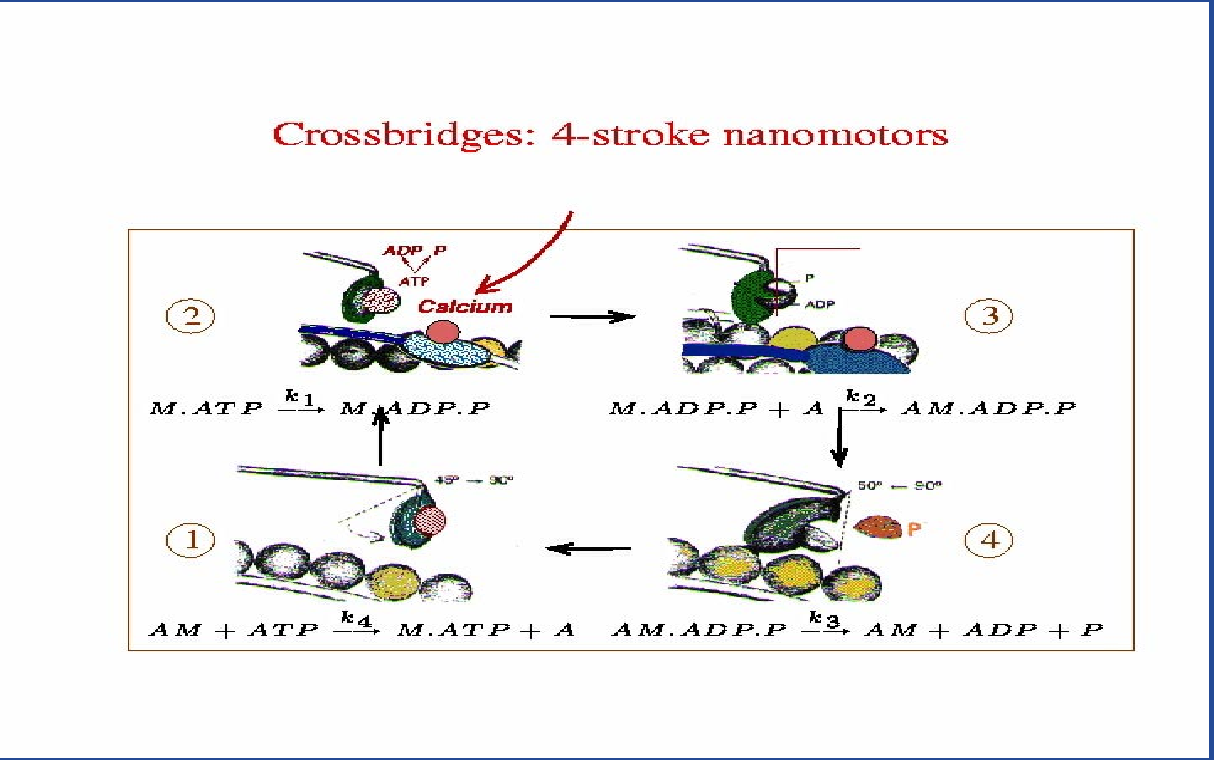
- Useful for the diagnosis of ARVD (Arrhytmogenic Right Ventricular Dysplasia) ?

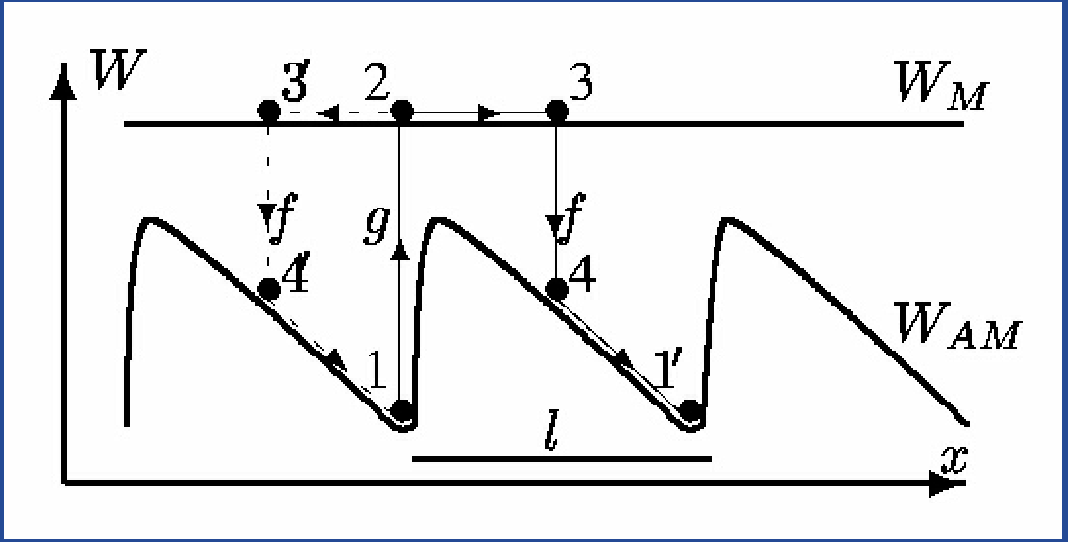
More on the Micro-Macro Approach

Molecular motor scale



(Funhouse Films)


Crossbridges: 4-stroke nanomotors
Calcium
2
3
1
4
M.ATP $\xrightarrow{k_1}$ M.ADP.P
M.ADP.P + A $\xrightarrow{k_2}$ AM.ADP.P
AM + ATP $\xrightarrow{k_4}$ M.ATP + A
AM.ADP.P $\xrightarrow{k_3}$ AM + ADP + P


W
W_M
W_{AM}
f
g
l
x

Motion of a myosin head

Langevin equation

$$\eta \dot{x} = -\partial_x W_i(x) + \sqrt{2\eta k_B T} b(t,\omega) + F_{ext}$$

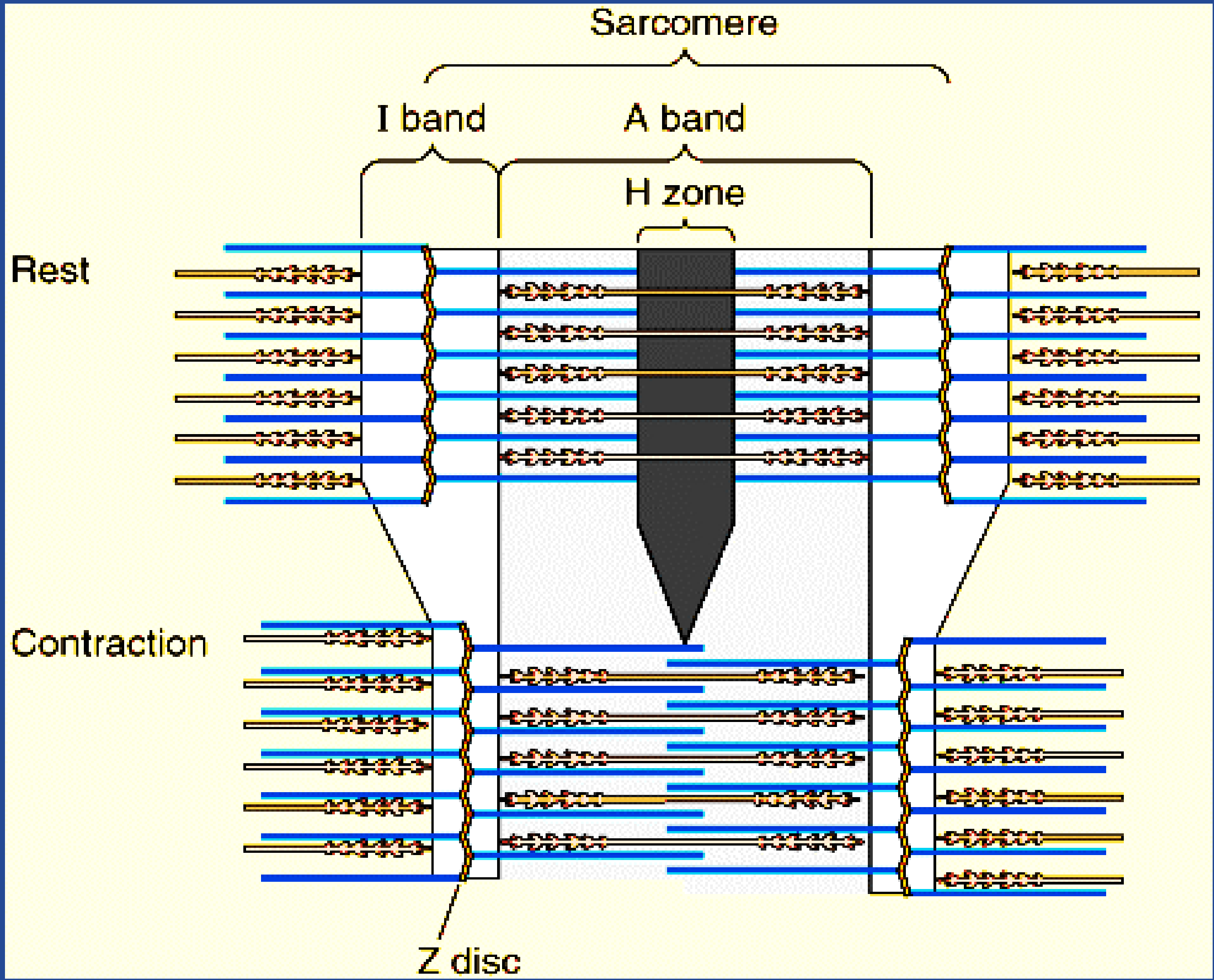
Fokker Planck equation

$$\partial_t p_i - \frac{1}{\eta}\Big\{k_B T \partial_x p_i + \big[\partial_x W_i(x) - F_{ext}\big] p_i\Big\} = \Pi_i$$

$$\Pi_{AM} = -\Pi_M = f\, p_M - g\, p_{AM} \qquad i = M,\, AM$$

u troponin-bound $[Ca^{++}]$ ion

Sarcomere-Scale Modeling



Geometrical properties:

Myosin heads rest sites lie a distance l away from one another
Actin binding sites lie a distance s away from one another

$$W_{AM}(x+l) = W_{AM}(x) \qquad (s/l \text{ not a rational number})$$

Statistical properties: from molecular to sarcomere scale

1 The collective behaviour of motors is equivalent to that of a unique motor, with $P_{AM}(\xi,t) = l < \rho_{AM}(x,\xi) >_N$, $\xi = x \bmod l$

2 $n(\xi,t) = l\, P_{AM}(\xi,t)$ and $P_M(\xi,t) = 1/l - P_{AM}(\xi,t) + O(1/N)$

$$\text{where} \quad \rho_{AM}(x,\xi) = \frac{1}{N}\sum_{j=1}^{N} \delta_{AM,I_j}\delta(x+j\cdot s-\xi), \qquad I_j = M, AM$$

$$< \rho >_N = \lim_{m\to\infty} \frac{1}{2m}\int_{-ml}^{ml} dx \sum_{I_1,\dots,I_N} \rho(\xi;x,I_1,\dots,I_N)p(x,I_1,\dots,I_N)$$

Huxley-like sliding filament model

$$\partial_t n + \dot{\varepsilon}\,\partial_\xi n = f(1-n) - gn$$

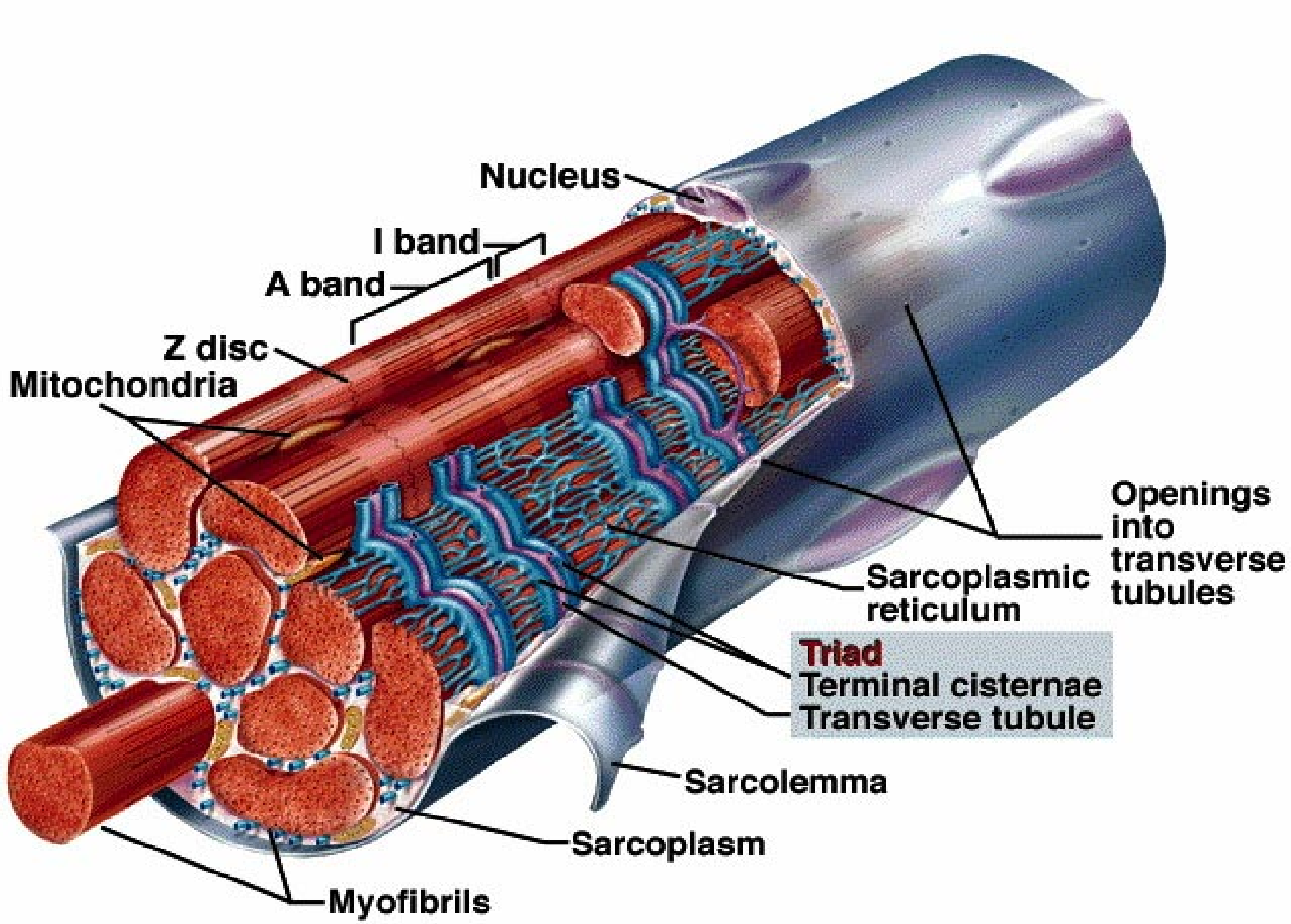
$$\sigma(t) = -\int_{-\infty}^{+\infty} \partial_\xi W_{AM}(\xi) n(\xi,t) d\xi + \eta\dot{\varepsilon}$$

$$f(\xi,t) = |u(t)|_+ \text{ for } \xi \in [0,1] \ (=0 \text{ elsewhere})$$

$$g(\xi,t) = |u(t)| + |\dot{\varepsilon}(t)| - f(\xi,t)$$

u intracellular $[Ca^{++}]$

Cardiac Fibre-Scale Modeling



From sarcomere to myofibre scale

Summing parallel behaviour of crossbridges

$$k_c(t) \;=\; k_0 \int_{-\infty}^{+\infty} n(\xi,t)d\xi$$

$$\sigma_c(t) \;=\; \sigma_0 \int_{-\infty}^{+\infty} \xi n(\xi,t)d\xi$$

$nd\xi$ proportion of actin-myosin crossbridges whose deformation belongs to $[\xi, \xi + d\xi]$

here $-\partial_\xi W_{AM}(\xi) = \sigma_0 \xi$

Controlled constitutive law for the contractile elements

$$\dot{k}_c = -\left(|u| + |\dot{\varepsilon}|\right) k_c + k_0 \, |u|_+$$

$$\dot{\sigma}_c = -\left(|u| + |\dot{\varepsilon}|\right) \sigma_c + k_c \dot{\varepsilon} + \sigma_0 \, |u|_+$$

$$\sigma = k_c \xi_0 + \sigma_c + \eta \dot{\varepsilon} \quad \textit{visco-elasto-plastic type}$$

u electro-chemical input: action potential

$u > 0$ contraction

$u < 0$ active relaxation

$u = 0$ passive relaxation