A Biomechanical Model of Muscle Contraction

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Motivations

Biochemanical basis of a global research project

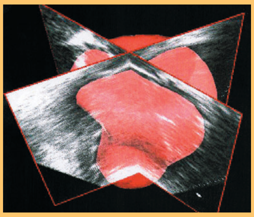
ICEMA (*I*mages of *C*ardiac *E*lectro-*M*echanical *A*ctivity)

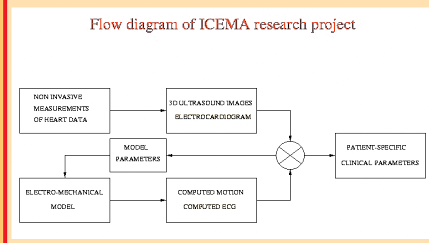
Scientific and clinical challenges

Combining 3D ultrasonographic images with electrocardiographic records in order to:

- obtain a dynamical representation of excitation-contraction coupling on the whole heart scale
- derive patient-specific local parameters assessing heart function

local contractility index $\frac{\partial \sigma}{\partial u} \quad (\varepsilon = 0)$ local relaxation index $\frac{\partial \sigma}{\partial \varepsilon} \quad (u = 0)$

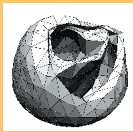


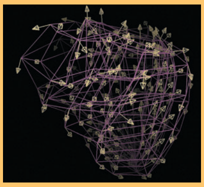


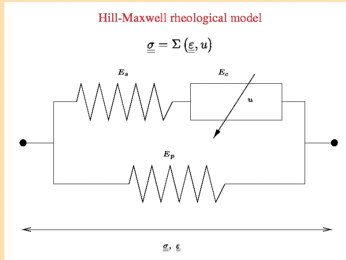
Whole heart scale

Equations of the dynamics and 3D-embedded constitutive law

$$\begin{cases} \rho \ddot{y} - \operatorname{div}(\underline{\underline{F}}(y) \cdot \underline{\underline{\sigma}}) = 0 & \text{motion equation} \\ \underline{\underline{\sigma}} = \Sigma\left(\underline{\underline{\varepsilon}}(y), u\right) & \text{constitutive law} \end{cases}$$







Cardiac fibre scale

Controlled constitutive law for the contractile elements

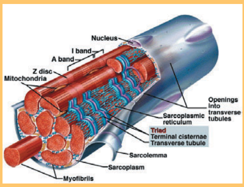
$$\begin{aligned} \dot{k}_c &= -(|u| + |\dot{\varepsilon}|)\; k_c \;+\; k_0\,|u|_+ \\ \dot{\sigma}_c &= -(|u| + |\dot{\varepsilon}|)\; \sigma_c \;+\; k_c\,\dot{\varepsilon} \;+\; \sigma_0\,|u|_+ \\ \sigma &= k_c \xi_0 + \sigma_c + \eta \dot{\varepsilon} \quad \textit{visco-elasto-plastic type} \end{aligned}$$

u electro-chemical input: action potential

$u > 0$ contraction

$u < 0$ active relaxation

$u = 0$ passive relaxation



From sarcomere to myofibre scale

Summing parallel behaviour of crossbridges

$$\begin{aligned} k_c(t) &= k_0 \int_{-\infty}^{+\infty} n(\xi, t)\, d\xi \\ \sigma_c(t) &= \sigma_0 \int_{-\infty}^{+\infty} \xi n(\xi, t)\, d\xi \end{aligned}$$

$n d\xi$ proportion of actin-myosin crossbridges whose deformation belongs to $[\xi, \xi + d\xi]$
here $-\partial_\xi W_{AM}(\xi) = \sigma_0 \xi$

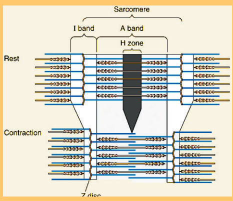
Sarcomere scale

Huxley-like sliding filament model

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

$$\begin{aligned} f(\xi, t) &= |u(t)|_+ \text{ for } \xi \in [0,1] \; (=0 \text{ elsewhere}) \\ g(\xi, t) &= |u(t)| + |\dot{\varepsilon}(t)| - f(\xi, t) \end{aligned}$$

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



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

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

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

Molecular motor scale

Motion of a myosin head

Langevin equation

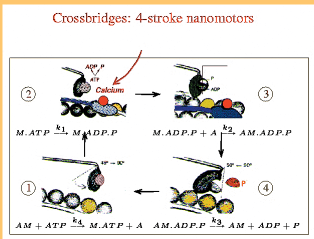
$$\eta \dot{x} = -\partial_x W_i(x) + \sqrt{2 \eta k_B T}\, b(t, \omega) + F_{ext}$$

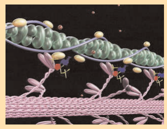
Fokker Planck equation

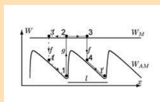
$$\partial_t p_i - \frac{1}{\eta} \left\{ k_B T \partial_x p_i + \left[\partial_x W_i(x) - F_{ext} \right] p_i \right\} = \Pi_i$$

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

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







Conclusions

We propose a chemically-controlled constitutive law of cardiac myofibre mechanics, acting on the mesoscopic scale and devoted to be embedded into a macroscopic model.

The multiscale-modelling approach allows for consistency with both the "sliding filament hypothesis" and current nanomotor theory. Further work will account for the detailed Ca^{2+} action on the different scales.

References

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ICEMA research project:
http://www-rocq.inria.fr/who/Frederique.Clement/icema.html

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y	displacement vector
ρ	mass density
$\underline{\underline{\sigma}}$	Piola-Kirchhoff stress tensor
$\underline{\underline{\varepsilon}}$	Green-Lagrange strain tensor
	$\varepsilon_{pq}(y) = \frac{1}{2}\left(\frac{\partial y_p}{\partial X_q} + \frac{\partial y_q}{\partial X_p}\right) + \frac{1}{2} \frac{\partial y_i}{\partial X_p} \frac{\partial y_i}{\partial X_q}$
$\underline{\underline{F}}$	deformation gradient
	$F_{ij}(y) = \delta_{ij} + \frac{\partial y_i}{\partial X_j} \quad j = 1, 2, 3$
E_s	serie element
E_c	contractile element
E_p	parallel element
ε	strain in myofibre direction
σ	stress in myofibre direction
σ_c	total controlled stress
k_c	total controlled stiffness

ξ	strain on the nanomotor scale
$n(\xi, t)$	density of actin/myosin crossbridges with strain ξ at time t
W_i	chemomechanical free energy of actin/myosin interaction (i = M, AM)
$f(\xi, t)$	actin/myosin crossbridge fastening rate
$g(\xi, t)$	actin/myosin crossbridge unfastening rate
$p_i(x, t)$	probability density function for a single motor to be in state i = M, AM at time t and position x
$P(x, t; I_1, \ldots, I_N)$	joint probability density function of motors located at $x + j \cdot s$ to be in state I_j = M, AM $(j = 1, \ldots, N)$
$\rho_{AM}(\xi, x, t)$	density of motors located at $x + j \cdot s$ in state AM with strain ξ (given j)
$l\, P_{AM}(\xi, t)$	probability for the equivalent motor to be in state AM with strain ξ
η	friction coefficient
$\sqrt{2 \eta k_B T} b$	thermal gaussian white noise
F_{ext}	external force

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