Comportement biomécanique de tissus vivants. Prise en compte de la matrice de collagéne

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   - Connective tissue organization
   - Coupling effect
   - Constitutive law
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The goal

Compute the deformation of a living tissue such as: muscle, arteries or heart submitted to internal or boundary stresses.
The cardiac muscle tissue has a highly specialized architecture, composed primarily of cardiac muscle cells (myocytes) that are 80 to 100 $\mu m$ in length and are roughly cylindrical with cross-sectional dimensions of 10 to 20 $\mu m$.
These cells are arranged in a more or less parallel weave that we idealize as “muscle fibers”

They are embedded in a complex extracellular matrix which consists mainly of collagen and elastin.

Figure 1. Cardiac myocyte composed of myofibrils, each of which contains myofilaments. The sarcomere lies between two Z-lines.
In most studies, the mechanical behavior of the connective tissue is assumed isotropic.

Experimental observations ...

Lin and Yin shown that during active equibiaxial stretch test there are significant stresses developed in the cross-fiber direction (in the tangential plane of the ventricular wall) that cannot be attributed to nonparallel muscle fibers.
In most studies, the mechanical behavior of the connective tissue is assumed isotropic.

Experimental observations...

Lin and Yin shown that during active equibiaxial stretch test there are significant stresses developed in the cross-fiber direction (in the tangential plane of the ventricular wall) that cannot be attributed to nonparallel muscle fibers.
The objectives of this study are to:

1. Suggest a realistic kinematic law coupling the passive connective tissue to the muscle fiber which may explain:
   - the developed tension in the cross fiber direction
   - the normal systolic wall thickening
2. Formulate an active three-dimensional material law for the cardiac muscle
3. Derive the related finite element formulation
4. Perform numerical tests.
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Connective tissue organization: “classical models”

- Isotropic collagen matrix
- Transversely isotropic material
- Classical models...
Connective tissue organization: anisotropy!

The scanning electron microscope reveals the basic organization of the connective tissue network.

- **Myocytes**
- **Inextensible collagen network**
Connective tissue organization: anisotropy!

Groups of myocytes can be seen to be encompassed by a rather prominent meshwork of fibrillar collagen.

Short collagen struts attach the myocytes subjacent to this meshwork to it.

- Inextensible collagen networks
- Anisotropy

⇒ New kinematic constraint
We assume that the muscular fibers are roughly cylindrical, and that two adjacent muscular fibers running on the tangential plane of the ventricular wall are surrounded by inextensible collagen bundles. So, during the contraction, the muscular fibers diameter increases and because the collagen bundles are inextensible, the adjacent fibers become closer.
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So, during the contraction, the muscular fibers diameter increases and because the collagen bundles are inextensible, the adjacent fibers become closer.
Model for coupling effect

A) passive state

B) active state

fiber
The pseudo-active kinematic constraint is written as a relationship between the extension ratios in the fiber and cross-fiber directions noted $\lambda_f$ and $\lambda_{cf} = D'/D$

$$h(\lambda_f, \lambda_{cf}) = 1 - \lambda_{cf} + (\pi - 2) \left(1 - \lambda_f^{-1/2}\right) \frac{a}{D} = 0$$
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Pseudo-active kinematic constraint

$$h(\lambda_f, \lambda_{cf}) = 1 - \lambda_{cf} + (\pi - 2) \left(1 - \lambda_f^{-1/2}\right) \frac{a}{D} = 0$$
The activation of the muscle is modeled by two transformations:
The first one, from passive state $P$ to virtual state $A_0$ changes the material properties without changing the geometry.

\[ \beta = 0 \quad \tau_P = 0 \]

\[ \Phi_{PA_0} = I \]

\[ \beta = \beta_0 \quad \tau_{A_0} = 0 \]

\[ P, A_0 \text{ (virtual)} \]

$\beta$ : Degree of change of rheology
The second one, from state $A_0$ to $A$ contracts the muscle without changing the material properties.

\[ \beta : \text{Degree of change of rheology} \]
Finally, loads are applied. The resulting transformation is not elastic.

$\beta$ : Degree of change of rheology
First step

The first step $P \rightarrow A_0$ is a non-elastic deformation described by the gradient tensor:

$$\Phi_{PA_0} = I$$

The change of the muscle properties during this first step is described by a time-dependent strain energy function per unit volume of the passive state $P$.

This strain energy function is modified using an activation function $\beta(t)$.
Second step

The second transformation is an elastic deformation caused only by the active tension delivered by the fibers, and takes care of the internal kinematic constraint. This last transformation is described by the gradient tensor

$$F_{A_0A}$$
Strain energy function at an arbitrary state $H$

\[
W(E_{PH}) = -\frac{1}{2} \rho_H(I_3(E_{PH}) - 1) + W^*(E_{PH}) + \delta_{AH} W_{pseudo active}(E_{PH})
\]

with

\[
W^*(E_{PH}) = W_{pas}(E_{PH}) + \beta(t) W_{act}^f(E_{PH})
\]

\[
W_{pseudo active}(E_{PH}) = -\frac{1}{2} q_H h(E_{PH})
\]
Constitutive law - Active strain energy function

Strain energy function at an arbitrary state $H$

$$W(E_{PH}) = -\frac{1}{2} \rho_H (I_3(E_{PH}) - 1) + W^*(E_{PH}) + \delta_{AH} W_{pseudo active}(E_{PH})$$

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$$W_{pseudo active}(E_{PH}) = -\frac{1}{2} q_H h(E_{PH})$$

$E_{PH}$ : Green’s strain tensor calculated from zero-stress state $P$
Constitutive law - Active strain energy function

Strain energy function at an arbitrary state $H$

$$W(E_{PH}) = -\frac{1}{2} \rho_H (I_3(E_{PH}) - 1) + W^*(E_{PH}) + \delta_{AH} W_{pseudo}^{active}(E_{PH})$$

with

$$W^*(E_{PH}) = W_{pas}(E_{PH}) + \beta(t) W^f_{act}(E_{PH})$$

$$W_{pseudo}^{active}(E_{PH}) = -\frac{1}{2} q_H h(E_{PH})$$

$\rho_H$ : Lagrangian multiplier resulting of the incompressibility condition

$$I_3(E_{PH}) = \text{det} C_{PH} = 1$$

$$C_{PH} = 2E_{PH} + I$$ : right Cauchy-Green strain tensor
Constitutive law - Active strain energy function

Strain energy function at an arbitrary state $H$

$$W(E_{PH}) = -\frac{1}{2} p_H (I_3(E_{PH}) - 1) + W^*(E_{PH}) + \delta_{AH} W_{pseudo active} (E_{PH})$$

with

$$W^*(E_{PH}) = W_{pas}(E_{PH}) + \beta(t) W_{act}^f (E_{PH})$$

$$W_{pseudo active} (E_{PH}) = -\frac{1}{2} q_H h(E_{PH})$$

$q_H$ : additional Lagrange multiplier resulting of the coupling constraint
Constitutive law - Active strain energy function

**Strain energy function at an arbitrary state** $H$

$$W(E_{PH}) = -\frac{1}{2} \rho_H (I_3(E_{PH}) - 1) + W^*(E_{PH}) + \delta_{AH} W_{pseudo\ active}(E_{PH})$$

with

$$W^*(E_{PH}) = W_{pas}(E_{PH}) + \beta(t) W_{act}(E_{PH})$$

$$W_{pseudo\ active}(E_{PH}) = -\frac{1}{2} q_H h(E_{PH})$$

$W_{pas}$ : contribution of the surrounding collagen matrix and of the passive fiber components

$W_{act}$ : arises from the change of rheology during muscular contraction
The function $h(\mathbf{E}_{PH})$ modelling the pseudo-active constraint may be re-written, as $W_{pas}$ and $W_{act}$, in terms of the strain invariants:

$$h(\mathbf{E}_{PH}) = 1 - I_6^{1/2} + (\pi - 2) \left(1 - I_4^{-1/4}\right) \frac{a}{D}$$

$l_4$ and $l_6$ : strain invariants given by

$$l_4(\mathbf{E}_{PH}) = \mathbf{f}_P \cdot \mathbf{C}_{PH} \cdot \mathbf{f}_P \quad \text{and} \quad l_6(\mathbf{E}_{PH}) = \mathbf{f}_P^\perp \cdot \mathbf{C}_{PH} \cdot \mathbf{f}_P^\perp$$

$\mathbf{f}_P$ : unit vector in the fiber directions $f$ in state $P$

$\mathbf{f}_P^\perp$ : unit vector in the cross fiber directions $cf$ in state $P$
Active strain energy function

$I_4$ and $I_6$: strain invariants given by

$$I_4(E_{PH}) = f_P \cdot C_{PH} \cdot f_P$$
and

$$I_6(E_{PH}) = f_P^\perp \cdot C_{PH} \cdot f_P^\perp$$

$f_P$: unit vector in the fiber directions $f$ in state $P$

$f_P^\perp$: unit vector in the cross fiber directions $cf$ in state $P$
Mathematical formulation

Conservation equations

Local equilibrium: \[ \text{div} \, \tau_H + \rho \, b = \rho \, \gamma = 0 \]
Incompressibility: \[ \det \Phi_{PH} = 1 \]
Pseudo-active kinematic constraint: \[ \delta_{AH} \, h(l_4, l_6) = 0 \]

\[ \tau_H \]: Cauchy stress tensor  
\[ \rho \]: density  
\[ b \]: body force per unit mass  
\[ \gamma \]: acceleration vector  
\[ \Phi_{PH} \]: gradient tensor
Conservation equations

Local equilibrium:
\[ \text{div} \tau_H + \rho \mathbf{b} = \rho \gamma = 0 \]

Incompressibility:
\[ \det \Phi_{PH} = 1 \]

Pseudo-active kinematic constraint:
\[ \delta_{AH} h(I_4, I_6) = 0 \]

Cauchy stress tensor

How is defined \( \tau_H \)?
We proceed in two steps

1. In a first step and at a given degree of activation $\beta(t)$, we derive and quantify the internal pseudo-active stresses by looking the free contraction configuration of the tissue (state $A$).

To incorporate the active muscle contraction, an active fiber stress was applied in the deformed fiber direction $f_H$.

2. In a second step we apply the loads on the active myocardial tissue under the internal pseudo-active stresses previously found.
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1. In a first step and at a given degree of activation $\beta(t)$, we derive and quantify the internal pseudo-active stresses by looking the free contraction configuration of the tissue (state $A$).

   To incorporate the active muscle contraction, an active fiber stress was applied in the deformed fiber direction $f_H$.

2. In a second step we apply the loads on the active myocardial tissue under the internal pseudo-active stresses previously found.
First step: free active state

\[ \tau_A = -p_A I + \Phi_{PA} \frac{\partial W^* (E_{PA})}{\partial E_{PA}} \Phi_{PA}^T + \beta(t) T^{(0)} f_A \otimes f_A + \tau_{active} \]

\[ \tau_{active}^{pseudo} = \Phi_{PA} \frac{\partial W^{pseudo} (E_{PA})}{\partial E_{PA}} \Phi_{PA}^T \]

\[ = T^f_A f_A \otimes f_A + T^{cf}_A f'_A \otimes f'_A \]

\[ f_A = \Phi_{PA} \cdot \frac{f_P}{|| \Phi_{PA} \cdot f_P ||} \]

\[ f'_A = \Phi_{PA} \cdot \frac{f_P^\perp}{|| \Phi_{PA} \cdot f_P^\perp ||} \]
These two stress tensor components $T_A^f$ and $T_A^{cf}$ are activation-dependent and behave as some internal tensions in the fiber and cross-fiber directions of unit vectors $\mathbf{f}_A$ and $\mathbf{f}'_A$. These pseudo-active tensions are defined by:

$$
T_A^f = 2 \frac{\partial W_{\text{pseudo active}}(\mathbf{E}_{PA})}{\partial l_4(\mathbf{E}_{PA})} \parallel \Phi_{PA} \cdot \mathbf{f}_P \parallel^2
$$

$$
T_A^{cf} = 2 \frac{\partial W_{\text{pseudo active}}(\mathbf{E}_{PA})}{\partial l_6(\mathbf{E}_{PA})} \parallel \Phi_{PA} \cdot \mathbf{f}'_P \parallel^2
$$
Second step

We apply the loads on the active myocardial tissue under the internal pseudo-active stresses previously found

\[
\tau_C = -p_C I + \Phi_{PC} \frac{\partial W^*}{\partial \mathbf{E}_{PC}} \Phi_T^{PC} \\
+ \left( \beta(t) T^{(0)} + T_A^f \right) \mathbf{f}_C \otimes \mathbf{f}_C + T_A^{cf} \mathbf{f}_C' \otimes \mathbf{f}'_C
\]
Lagrangian variational formulation

\[
\int_V P_{IJ} \Phi_{J}^{\alpha} \nabla_I (\delta u_\alpha) \, dV = \int_V \rho (b^\alpha - \gamma^\alpha) \, \delta u_\alpha \, dV + \int_{A_2} s \cdot \delta u \, dA
\]

Incompressibility:
\[
\int_V \left( \det g_{IJ}^{(x)} - 1 \right) \, p^* \, dV = 0
\]

Kinematic constraint:
\[
\delta_{AH} \int_V h(l_4, l_6) \, q^* \, dV = 0
\]

\[\delta u\]: admissible displacement vector
\[A_2\]: part of \(\partial V\) subject to boundary load conditions.
\[P\]: the second Piola-Kirchhoff stress tensor
\[g\]: the metric tensor
The Q1 – Q0 element

3D finite element with trilinear Lagrange interpolation for the positions (Q1)
Uniform pressure and Lagrange multiplier at the center of the element e (Q0)
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Active cylindrical structure: heart or artery

Simplified model

Internal pressure $P_i$

Fiber
Active cylindrical structure: heart or artery

3D cylindrical mesh
http://www.netlib.org/minpack/index.html

Nonlinear system is solved using:
- quasi-Newton method
- finite difference approximation of the jacobian matrix
- QR decomposition of the resulting linear system
- stepeast descent algorithm

http://www.netlib.org/toms/698

Fortran implementation in double precision
Pressure-dependent tonus: active behaviour vs passive state

![Graph showing pressure and muscular tonus](image-url)

- **Pressure**: Green line
- **Tonus: passive**: Red line
- **Tonus: active**: Blue line

**Axes**:
- **P_i or Tonus (kPa)**
- **Pressure**

**Legend**:
- Green line: Pressure
- Red line: Tonus: passive
- Blue line: Tonus: active

**Values**:
- Pressure range: 0 to 18 kPa
- Tonus range: 0 to 18 kPa

**X-axis**:
- Values range from 0 to 1.2

**Y-axis**:
- Values range from 0 to 18 kPa
Pressure-dependent tonus: active behaviour vs passive state

Variations of interior radius

- Passive
- Active
- Active + kinematic constraint

Radius (mm)

0 0.2 0.4 0.6 0.8 1 1.2

2 2.05 2.1 2.15 2.2 2.25
Pressure-dependent tonus: active behaviour vs passive state

Variations of exterior radius

- Passive
- Active
- Active + kinematic constraint

Radius (mm)

0 0.2 0.4 0.6 0.8 1 1.2
Pressure-dependent tonus: active behaviour vs passive state

Variations of height

- Passive
- Active
- Active + kinematic constraint

Radius (mm)

0.0235
0.023
0.0225
0.022
0.0215
0.021
0.0205
0
0.2
0.4
0.6
0.8
1
1.2
Pressure-dependent tonus : active behaviour

![Graph showing the relationship between pressure and muscular tonus](image)

- **Pressure and muscular tonus**
- **Y-axis**: Pressure or muscular tonus (kPa)
- **X-axis**: 
  - 0 to 1.2
  - 0 to 1.8

Legend:
- **Pressure** (red line)
- **Tonus** (yellow line)
Pressure-dependent tonus: active behaviour

Variations of interior radius

- active + kinematic constraint
  - active

Interior radius (mm)

0  0.2  0.4  0.6  0.8  1  1.2
Pressure-dependent tonus: active behaviour

Variations of exterior radius

active + kinematic constraint
active

Exterior Radius (mm)

0 0.2 0.4 0.6 0.8 1 1.2
Pressure-dependent tonus: active behaviour

Variations of height

(active + kinematic constraint)

(active)

Height (mm)
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This study shows that the connective tissue skeleton in the left ventricle may have a large influence on the cardiac performance.

The formulation is based on a new constitutive law taking into account a possible interaction between the muscular fibres and the surrounding collagen matrix.

Additional experimental works must be done in order to study thoroughly the spatial organization of the myocardial collagen fibrils.
- The fibers’ direction is more complex in the case of arteries.
- Arteries are composed of multi-layer material: adapt the constitutive law.

![Diagram of arterial structure](image)
Treat a very complex structure: the heart.