# COMSOL Used for Simulating Biological Remodelling

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## Introduction

A biological tissue is, in first place, a complex aggregate of cells embedded in an extracellular matrix [1]. We attribute the complexity of these physical systems to the compresence of several biological entities, with different physical and chemical properties, which contribute to determine the mechanical properties of the tissue as a whole. For example, the presence of fibres, supposed to be statistically oriented, influences the flow of the interstitial fluid inside the tissue [1]. A fundamental characteristic of biological tissues is the property to adapt themselves to the stimuli due to the interaction with the external environment [1, 4]. We will refer to 'remodelling' as an ensemble of dissipative and irreversible processes, which occur in order to modify the internal organization of the tissue [4, 2]. The problem to model these phenomena is approached, in this work, by adapting the theory of Elastoplasticity and by interpreting remodelling as a sequence of plastic-like distortions [4, 3, 2]. For this purpose, we introduce a new kinematic descriptor of the internal structure of the body and we derive an evolution law satisfying a suitable dissipation principle [4, 3, 2]. In the following, we will proceed by presenting a mathematical model describing the mechanical behaviour of articular cartilage, in which remodelling events occur.

## Theoretical background

In this section, we shortly introduce the Reader to the fundamental aspects of the theory developed for formulating the mathematical model presented in this contribution.

### The transplant operator and the natural state

By referring to [4, 2], we address the study of remodelling by invoking the so-called *Epstein-Maugin decomposition* of the deformation gradient $\boldsymbol{F}$

$$\boldsymbol{F} = \boldsymbol{F}_{\mathrm{e}} \boldsymbol{\Pi}^{-1}, \qquad (1)$$

where $\boldsymbol{F}_{\mathrm{e}}$ is said to be the *accommodating part* of the deformation gradient [4]. The tensor $\boldsymbol{\Pi}$ is referred to as the *implant tensor* in [3]. The decomposition (1) of the deformation gradient $\boldsymbol{F}$ can be achieved by the introduction of the so-called *natural state*, a collection of undistorted and stress-free body pieces. In fact, $\boldsymbol{\Pi}$ maps vectors of the tangent space associated with the natural state into vectors of the tangent space associated with the reference configuration.
For future use, we introduce the metric tensors $\boldsymbol{G}$ and $\boldsymbol{g}$ associated with the reference configuration of the tissue and with the three-dimensional Euclidean space, respectively.

### The fibre pattern

To take into account the macroscopic effect of the fibres (see [7]), we introduce, for each point $X$ in the natural state, the set $\mathbb{S}^2_X$ of all unit vectors attached at $X$, and the function $\rho_X\colon \mathbb{S}^2_X \longrightarrow \mathbb{R}$ such that, for every $\mathfrak{m}_X \in \mathbb{S}^2_X$, $\rho_X(\mathfrak{m}_X)$ represents the probability density that a fibre is aligned along the direction identified by $\mathfrak{m}_X$. Given a function $f_X$ defined over $\mathbb{S}^2_X$, we also introduce the *directional average*

$$\ll f_X \gg \; = \int_{\mathbb{S}^2_X} f_X(\mathfrak{m}_X)\rho_X(\mathfrak{m}_X). \qquad (2)$$

With respect to the polar coordinates $\vartheta \in [0,\pi]$ and $\varphi \in [0,2\pi[$, such that $\mathfrak{m}_X$ can be written as

$$\begin{aligned}\mathfrak{m}_X &= \hat{\mathfrak{m}}_X(\vartheta,\varphi)\\ &= \sin\vartheta\cos\varphi\,\mathfrak{e}_1 + \sin\vartheta\sin\varphi\,\mathfrak{e}_2 + \cos\vartheta\,\mathfrak{e}_3,\end{aligned}$$

where $\{\mathfrak{e}_1, \mathfrak{e}_2, \mathfrak{e}_3\}$ is an orthonormal vector basis attached to $X$, equation (2) can be recast in the form

$$\ll f_X \gg = \int_0^{2\pi}\int_0^{\frac{\pi}{2}} \hat{f}_X(\vartheta,\varphi)\hat{\rho}_X(\vartheta)\sin\vartheta\,\mathrm{d}\vartheta\mathrm{d}\varphi, \qquad (3)$$

with

$$\hat{f}_X(\vartheta,\varphi) = \hat{f}_X(\vartheta,\varphi) = f_X(\hat{\mathfrak{m}}_X(\vartheta,\varphi))$$

$$\hat{\rho}_X(\vartheta) = \hat{\rho}_X(\vartheta,\varphi) = \rho_X\big(\hat{\mathfrak{m}}_X(\vartheta,\varphi)\big).$$

Note that the dependence of $\hat{\rho}$ on $\vartheta$ only is due to the fact that the probability density is assumed to be transversely isotropic with respect to a global symmetry axis of the body, parallel to $\mathfrak{e}_3$. Hereafter, we will use the pseudo-Gaussian distribution

$$\hat{\rho}_X(\vartheta) = \frac{\hat{\gamma}_X(\vartheta)}{2\pi \int_0^{\pi/2} \hat{\gamma}_X(\vartheta')\sin(\vartheta')\mathrm{d}\vartheta'}, \qquad (4)$$

$$\hat{\gamma}_X(\vartheta) = \exp\left(-\frac{(\vartheta - Q)^2}{2\omega^2}\right), \qquad (5)$$

with $Q$ being the mean angle and $\omega$ the standard deviation of the statistical distribution.

## Model Equations

In this section, we provide a summary of the governing equations of the mathematical model presented in this paper.

### Balance of mass and momentum

By introducing a Darcian description of the fluid flow, the material form of the balance of mass for the solid phase reads

$$\dot{J} - \mathrm{Div}(\boldsymbol{K}\mathrm{Grad}\, p) = 0, \qquad (6)$$

where $J = \det \boldsymbol{F} > 0$ is the determinant of the deformation gradient tensor $\boldsymbol{F}$, $p$ is the *pore pressure* and $\boldsymbol{K}$ is the material *permeability tensor*. Under the hypothesis of negligible dissipative stress for the fluid phase, and if no body force is considered, the balance of momentum can be cast in the form [7, 4]

$$\mathrm{Div}(-Jp\boldsymbol{g}^{-1}\boldsymbol{F}^{-\mathrm{T}} + \boldsymbol{P}_{\mathrm{sc}}) = \boldsymbol{0}, \qquad (7)$$

where $\boldsymbol{P}_{\mathrm{sc}}$ is the constitutive part of the first Piola-Kirchhoff stress tensor.

### Dissipation inequality and remodelling law

It is possible to prove (see [4, 2]), that the dissipation inequality can be formulated as

$$D = D_{\mathrm{flow}} + D_{\mathrm{rem}} \geq 0, \qquad (8)$$

where $D_{\mathrm{flow}} = \boldsymbol{K}\colon[\mathrm{Grad}\, p \otimes \mathrm{Grad}\, p]$ is the dissipation associated to fluid and $D_{\mathrm{rem}}$ is the contribution to the dissipation due to the remodeling. Since $D_{\mathrm{flow}} \geq 0$, because of the semi-positive definiteness of $\boldsymbol{K}$, the inequality (8) is equivalent to require that $D_{\mathrm{rem}} \geq 0$. It has been proved [2] that

$$D_{\mathrm{rem}} = \boldsymbol{Y}\colon \mathrm{sym}(\boldsymbol{\Lambda}\boldsymbol{C}^{-1}), \qquad (9)$$

where $\boldsymbol{Y} = \boldsymbol{C}\boldsymbol{S}_{\mathrm{sc}}\boldsymbol{C}$ is an auxiliary measure of stress that is made covariant by left and right multiplication $\boldsymbol{S}_{\mathrm{sc}}$ by $\boldsymbol{C}$, $\boldsymbol{S}_{\mathrm{sc}}$ is the constitutive part of the Second Piola-Kirchhoff stress tensor, and $\boldsymbol{\Lambda} = \dot{\boldsymbol{\Pi}}\boldsymbol{\Pi}^{-1}$ is the so-called *tensor of rate of remodelling* [3, 2]. As consequence of the dissipation principle (8), we propose the following equation for describing the evolution of $\boldsymbol{\Pi}$

$$\mathrm{sym}(\boldsymbol{\Lambda}\boldsymbol{C}^{-1}) = -\zeta\left(\boldsymbol{S}_{\mathrm{sc}} - \tfrac{1}{3}\mathrm{tr}(\boldsymbol{C}\boldsymbol{S}_{\mathrm{sc}})\boldsymbol{C}^{-1}\right), \qquad (10)$$

where $\zeta$ is a positive model parameter.

## Constitutive Framework

We suppose that the tissue we are studying exhibits a hyperelastic behaviour with respect to the *natural state*, which is a collection of undistorted and stress-free body pieces. In addition, we assume that the anelastic distortions are volume preserving, in the sense that $J_\Pi = \det(\boldsymbol{\Pi}) = 1$. If $\boldsymbol{C}_{\mathrm{e}} = \boldsymbol{F}_{\mathrm{e}}^{\mathrm{T}}\boldsymbol{g}\boldsymbol{F}_{\mathrm{e}} = \boldsymbol{\Pi}^{\mathrm{T}}\boldsymbol{C}\boldsymbol{\Pi}$ denotes the elastic part of the right Cauchy-Green deformation tensor, the strain energy function can be expressed as the sum of two contributions (see [7] and references therein)

$$\widehat{W}_\nu(\boldsymbol{C}_{\mathrm{e}}) = \widehat{W}_{\mathrm{matrix}}(\boldsymbol{C}_{\mathrm{e}}) + \widehat{W}_{\mathrm{fibres}}(\boldsymbol{C}_{\mathrm{e}}). \qquad (11)$$

The first term of the right-hand-side of (11) accounts for the hyperelastic properties of the non-fibrous matrix, while the second term represents the macroscopic effect of the fibres. In particular, we have

$$\widehat{W}_{\mathrm{matrix}}(\boldsymbol{C}_{\mathrm{e}}) = \Phi_{\mathrm{sv}}\widehat{U}(J_{\mathrm{e}}) + \Phi_{0\mathrm{sv}}\widehat{W}_0(\boldsymbol{C}_{\mathrm{e}}), \qquad (12)$$

and

$$\widehat{W}_{\mathrm{fibers}}(\boldsymbol{C}_{\mathrm{e}}) = \Phi_{1\mathrm{sv}}\widehat{W}_{\mathrm{ens}}(\boldsymbol{C}_{\mathrm{e}}). \qquad (13)$$

In (12) and (13), $J_{\mathrm{e}} = \det \boldsymbol{F}_{\mathrm{e}}$ is the elastic volumetric ratio,$\Phi_{\mathrm{sv}}$ $\Phi_{0\mathrm{sv}}$ and $\Phi_{1\mathrm{sv}}$ are the volumetric fractions of the solid phase, matrix and fibres respectively, evaluated in the natural state. In the case of a sample of tissue of cylindrical shape, it is rather customary to assume that the sample is homogeneous on each plane orthogonal to the axis of the cylinder, which is thus regarded as a symmetry axis for the sample. Furthermore, to allow for material inhomogeneities, the sample's material properties are assumed to vary along the cylinder's axis. To this end, it is convenient to introduce the normalised axial coordinate $\xi \in [0,1]$, with $\xi = 0$ and $\xi = 1$ individuating the lower and the upper surface of the sample, respectively. In this study, the considered sample of tissue is regarded as axially inhomogeneous through the spatial variability of the volumetric fractions of matrix and fibres, which, consistently with experimental data [7], are defined as

$$\Phi_{\mathrm{sv}} = -0.100\xi + 0.250, \tag{14}$$

$$\Phi_{0\mathrm{sv}} = -0.062\xi^2 - 0.038\xi + 0.046, \tag{15}$$

$$\Phi_{1\mathrm{sv}} = +0.062\xi^2 - 0.138\xi + 0.204, \tag{16}$$

The penalty term

$$\widehat{U}(J_{\mathrm{e}}) = \alpha_0 \mathcal{H}(J_{\mathrm{cr}} - J_{\mathrm{e}}) \frac{(J_{\mathrm{e}} - J_{\mathrm{cr}})^{2q}}{(J_{\mathrm{e}} - \Phi_{\mathrm{sv}})^{r}}, \tag{17}$$

enforces the condition $J_{\mathrm{e}} \geq \Phi_{\mathrm{sv}}$. In (20) $\alpha_0 = 0.125$ [MPa], $J_{\mathrm{cr}} = \Phi_{\mathrm{sv}} + 0.1$ is a threshold value for $J_{\mathrm{e}}$, $r = 0.5$, $q = 2$ are material parameters which give us information about the rate at which the term $\widehat{U}(J_{\mathrm{e}})$ diverges when $J_{\mathrm{e}}$ tends to $\Phi_{\mathrm{sv}}$, and $\mathcal{H}$ is the Heaviside function, which is active whenever its argument is strictly greater than zero. The isotropic contribution $\widehat{W}_0(\boldsymbol{C}_{\mathrm{e}})$ is the Holmes-Mow like term [5]

$$\widehat{W}_0(\boldsymbol{C}_{\mathrm{e}}) = \alpha_0 \frac{\exp(\alpha_1[I_1 - 3] + \alpha_2[I_2 - 3])}{[I_3]^{\alpha_3}} \tag{18}$$

where $\alpha_1 = 0.778$, $\alpha_2 = 0.111$ [MPa], $\alpha_3 = 1$ are material parameters and $I_1 = \mathrm{tr}(\boldsymbol{C}_{\mathrm{e}})$, $I_2 = \frac{1}{2}\left[\mathrm{tr}(\boldsymbol{C}_{\mathrm{e}})^2 - \mathrm{tr}\left(\boldsymbol{C}_{\mathrm{e}}{}^2\right)\right]$ and $I_3 = \det(\boldsymbol{C}_{\mathrm{e}})$ are the first three principal (isotropic) invariants of $\boldsymbol{C}_{\mathrm{e}}$. In (13), the term $\widehat{W}_{\mathrm{ens}}(\boldsymbol{C}_{\mathrm{e}})$ is the sum of two contributions

$$\widehat{W}_{\mathrm{ens}}(\boldsymbol{C}_{\mathrm{e}}) = \widehat{W}_{1\mathrm{i}}(\boldsymbol{C}_{\mathrm{e}}) + \langle\langle \widehat{W}_{1\mathrm{a}}(\boldsymbol{C}_{\mathrm{e}}, \mathbb{a}) \rangle\rangle, \tag{19}$$

where $\widehat{W}_{1\mathrm{i}}(\boldsymbol{C}_{\mathrm{e}})$ describes the isotropic contribution of the fibres and has the same functional form of (18) and

$$\widehat{W}_{1\mathrm{a}}(\boldsymbol{C}_{\mathrm{e}}, \mathbb{a}) = \mathcal{H}(I_4 - 1)\frac{c}{2}[I_4 - 1]^2, \tag{20}$$

represents the anisotropic effect of the fibre pattern, with $\mathbb{a} = \mathbb{m} \otimes \mathbb{m}$ being the structure tensor field defined in the natural state, $\mathbb{m}$ the unit vector field defining the direction of the fibre, $I_4 = \boldsymbol{C}_{\mathrm{e}} : \mathbb{a}$ is the fourth invariant of $\boldsymbol{C}_{\mathrm{e}}$ and $c = 7.46$ [MPa] is an elastic coefficient. To introduce the constitutive expression of the permeability tensor $\boldsymbol{K}$, we follow [5] where $\boldsymbol{K}$ is split additively as:

$$\boldsymbol{K} = J k_0 \boldsymbol{C}^{-1} + J^{-1} k_0 \boldsymbol{\Pi} \langle\langle \boldsymbol{Z} \rangle\rangle \boldsymbol{\Pi}^{-1} \tag{21}$$

The first term on the right-hand side of (21) is an isotropic term, whereas the second one models the effects of the fibres. In particular, $\boldsymbol{Z}$ is given by

$$\boldsymbol{Z} = \frac{\mathbb{a}}{I_4}, \tag{22}$$

and $k_0$ is the Holmes-Mow scalar permeability [5], which is constitutively assigned as

$$k_0 = k_{0\mathrm{v}} \left[\frac{J_{\mathrm{e}} - \Phi_{\mathrm{sv}}}{1 - \Phi_{\mathrm{sv}}}\right]^{\kappa} \exp\left[\frac{m_0}{2}\left(J_{\mathrm{e}}{}^2 - 1\right)\right]. \tag{23}$$

In (26), the coefficient $k_{0\mathrm{v}}$ is a given function of the material point through the volume ratio in the natural state, i.e.,

$$k_{0\mathrm{v}} = k_{0\nu}^{(0)} \left[\frac{e_{\mathrm{v}}}{e_{\nu}^{(0)}}\right]^{\kappa} \exp\left[\frac{m_0}{2}\left(\left(\frac{1+e_{\mathrm{v}}}{1+e_{\nu}^{(0)}}\right)^2 - 1\right)\right] \tag{24}$$

where $k_{0\nu}^{(0)} = 3.7729 \cdot 10^{-3}\,\mathrm{mm}^4(\mathrm{Ns})^{-1}$ is the referential permeability, $e_\nu = (1 - \Phi_{\mathrm{sv}})/\Phi_{\mathrm{sv}}$ is the void ratio in the natural state, $e_\nu^{(0)} = 4$ is a reference value for the void ratio, while $\kappa = 0.0848$ and $m_0 = 4.638$ are model parameters [5, 6, 4]. The expressions for the mean angle $Q$ and the standard deviation $\omega$ in (6) are respectively given by

$$Q(\xi) = \frac{\pi}{2}\left\{1 - \cos\left(\frac{\pi}{2}\left[-\frac{2}{3}\xi^2 + \frac{5}{3}\xi\right]\right)\right\} \tag{25}$$

$$\omega(\xi) = 10^3[(1 - \xi)\xi]^4 + 3 \cdot 10^{-2} \tag{26}$$

Finally, for the remodelling law (13) we have that

$$\zeta = \lambda \left[\frac{\|\mathrm{dev}(\boldsymbol{\sigma}_{\mathrm{sc}})\| - \sigma_Y}{\|\mathrm{dev}(\boldsymbol{\sigma}_{\mathrm{sc}})\|}\right]_+, \tag{27}$$

where $\lambda$ is a material parameter defined by the relation $\lambda = \lambda_0 \left(\frac{\phi_{sv}}{J}\right)^2$, with $\lambda_0 = 0.5\ (\mathrm{MPa} \cdot \mathrm{s})^{-1}$, $\sigma_{\mathrm{sc}}$ is the constitutive Cauchy stress tensor, $\sigma_Y = 0.002$ MPa is a constant yield stress and $[\cdot]_+$ extracts the positive part of the function to which it is applied [4, 2].

## Simulations

To solve Equations (6), (7), and (11), we implemented a benchmark problem in COMSOL. After performing the polar decomposition $\boldsymbol{\Pi} = \boldsymbol{V}.\boldsymbol{R}$ [6], we assume that $\boldsymbol{R}$ reduces to a shifter from the natural state to the reference configuration of the tissue [6] and we thus consider $\boldsymbol{V}$ as the only unknown factor of $\boldsymbol{\Pi}$. This allows us to close the mathematical problem, which consists of ten scalar equations (i.e., (6), (7) and (11)) in the ten unknowns $p$, $(\chi^a)_{a=1}^3$ $(V^{AB} = V^{BA})_{A,B=1}^3$ [2].

**Benchmark test**

The mechanical properties of articular cartilage can be investigated by means of an *unconfined compression test* on a cylindrical specimen of articular cartilage [7, 4, 3]. To simulate this test and solve for $\chi, p$ and $\boldsymbol{V}$, we impose the boundary conditions

$$\begin{cases} \chi^3 = f \\ (-\boldsymbol{K}\text{Grad}\, p).\boldsymbol{N} = 0 \end{cases} \quad \text{on } \partial B_R^{(u)}, \qquad (28)$$

$$\begin{cases} (-Jp\boldsymbol{g}^{-1}\boldsymbol{F}^{-\mathrm{T}} + \boldsymbol{P}_{sc}).\boldsymbol{N} = \boldsymbol{0} \\ p = 0 \end{cases} \quad \text{on } \partial B_R^{(l)}, \qquad (29)$$

$$\begin{cases} \chi(X,t) - \chi(X,0) = \boldsymbol{0} \\ (-\boldsymbol{K}\text{Grad}\, p).\boldsymbol{N} = 0 \end{cases} \quad \text{on } \partial B_R^{(L)}. \qquad (30)$$

In (32), (33), and (34), $\partial B_R^{(u)}$, $\partial B_R^{(l)}$, and $\partial B_R^{(L)}$ denote, respectively, the upper, the lateral and the lower part of the boundary $\partial B_R$, $f$ is the loading ramp defined by

$$\begin{cases} L - \frac{t}{T_{\text{ramp}}} \mathrm{u_T}, \text{ for t} \in [0, T_{\text{ramp}}] \\ L - \mathrm{u_T}, \text{ for t} \in [T_{\text{ramp}}, \mathrm{T_{end}}] \end{cases} \qquad (31)$$

where $\mathrm{u_T} = 0.20$ mm is a target displacement, $T_{\text{ramp}} = 20$ s is the instant of time at which the ramp ends, $T_{\text{end}} = 300$ s is the instant of time at which the experiment ends and $L = 1$ [mm] is the initial length of the specimen, and $\boldsymbol{N}$ is the normal vector to $\partial B_R$. Finally, we impose the initial conditions

$$\begin{cases} \boldsymbol{\chi}(X,0) = X, & (35a) \\ p(X,0) = 0 & (35b) \\ \boldsymbol{V}(X,0) = \boldsymbol{G}^{-1}(X). & (35c) \end{cases}$$

**COMSOL implementation**

To implement equation (6), we used the Darcy's Law package (Fluid Flow module), with the components of the permeability tensor taken from (21). To solve Equation (7), we used the Solid Mechanics package (Structural Mechanics module), in which we modified the weak form to implement the constitutive part of the second Piola-Kirchhoff stress tensor. Finally, the DODE package (Mathematics module) has been used to implement the remodelling law (11).

**Results**

In this section, we would like to show influence of the tissue's anisotropy on the development of the distortions related to remodelling. We do that by comparing the production of distortions in two different cases. First, we solve Equations (6), (7) and (11) with boundary and initial conditions (28) - (30) by turning off all the anisotropic terms accounting for the presence of the fibres. We will refer to this case as to 'Model M1' [2]. This amounts to solve the fully isotropic version of the complete model, which is indicated by 'Model M2' [2]. With reference to Figure 1, we notice that, if we take into account the presence of the fibres, 'Model M2' predicts a production of anelastic that is bigger than that characterising 'Model M1'. To measure the magnitude of the plastic-like distortions associated with remodelling, we introduced the Frobenius norm $\|\boldsymbol{E}_\mathrm{p}\|$ of the Almansi-Euler like strain tensor $\boldsymbol{E}_\mathrm{p} = \frac{1}{2}[\boldsymbol{\Pi}^{-\mathrm{T}}.\boldsymbol{\Pi}^{-1} - \boldsymbol{G}]$. In particular, while in the case of 'Model M1' the trend of $\|\boldsymbol{E}_\mathrm{p}\|$ is linearly increasing, in the case of 'Model M2' the quantity $\|\boldsymbol{E}_\mathrm{p}\|$ grows quite rapidly and it seems to reach a stationary value.

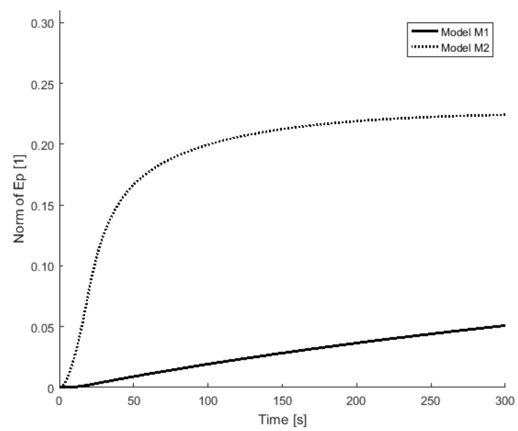


**Figure 1**. Evolution of the Frobenius norm of the deviatoric stress dev($\boldsymbol{\sigma}$) as function of time, in correspondence of the material point $X_U$ of Cartesian coordinates (1.3, 0.0, 1.0) [mm].

## Conclusions and future work

In this work, we presented a mathematical model developed to investigate the mechanical behaviour of a certain class of biological tissues. In particular, we focused on the study of articular cartilage, as a fibre-reinforced soft porous medium filled with an interstitial fluid. In addition, we enriched the model by considering the presence of dissipative remodelling phenomena, i.e., the possibility for the tissue to reorganize its internal structure. This has been done by referring, essentially, to the theory of Elastoplasticity [4].

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