MEMORY EFFECTS IN THE BIOMECHANICAL BEHAVIOR OF EX VIVO SKIN UNDER ACOUSTOMECHANICAL TESTINGS: A MULTISCALE PREISACH MODELING OF AGING

Serge Dos Santos
INSA Centre Val de Loire, Blois Campus; COMUE "Léonard de Vinci", U930 "Imagerie et Cerveau" Inserm, 3 rue de la Chocolaterie, CS23410, 41034 Blois, France
email: serge.dossantos@insa-cvl.fr

Colette Kozena and Vaclav Kus
Czech Technical University in Prague, FNSPE, Brehova 7, CZ-11519, Prague, Czech Republic

Djamel Remache
ISM Etienne Jules Marey, 163 Av. de Luminy, case 901, 13009 Marseille, France

Jean-Christophe Pittet
Orion Concept, 113 rue des Bordiers, 37100 Tours, France

Michel Gratton and Mickael Caliez
INSA Centre Val de Loire, Blois Campus; LMR, 3 rue de la Chocolaterie, CS23410, 41034 Blois, France

A novel modeling approach for describing the multiscale properties of ex vivo skin is proposed. An acousto-mechanical experiment using the mixing of a mechanical loading (conducted at 10 Hz frequency) and an ultrasonic 100 MHz TR-NEWS probing system has been implemented in order to extract the nonclassical nonlinearity of porcine skin. A 100 kN load cell, was used to measure displacement and tensile load. Various displacement rates were imposed (1 ; 0.5 and 0.1 mm/s) and the maximum elongation was set to 25 mm. To overcome the difficulty of skin aging characterization, the use of Preisach modeling (PM space) is suggested and confirmed. Since collagen fibrils exhibit a highly nonlinear mechanical response, the three main stress-strain regimes should be described pragmatically with a statistical approach provided by the Preisach model, which can be expressed as a weighted combination of relay operators (or hysterons). Hysteresis behavior coming from the complex loading of the skin is identified with the new PM space statistical approach. Statistical distributions of the PM space are obtained with various statistics. It is found that optimization techniques with $L_2$ distance and $\phi$-divergence measures induces a PM space with 1000 hysterons distributed along a mixture of two Guyer distributions. Analysis of data coming from hysteresis behavior shows that PM-space approach is suggested as a new tool for extracting multi-scale parameters containing information about aging of the skin.

1. Introduction

Human skin tissue represents a complicated bio-polymeric material with very complex mechanical behavior, highly dependent on a large number of living and environmental factors. Skin tissue is anisotropic and exhibits highly nonlinear, viscoelastic responses with memory, hysteresis and hardening/softening effects during loading. The measurement of skin’s mechanical properties (nonlinearity,
anisotropy, and viscoelasticity) is important in several fields, including medicine and cosmetics, and present a huge dispersion depending on age, gender, physical size of individual and location on the body (forearms, face, etc). Small changes in the mechanical properties are very sensitively reflecting many diseases. Their influence on the appearance of aging, and their role indicating disease and pathologies is also a societal goal of biomechanical research. The description of human skin deformation under complex stress protocol is an open problem, not only from a theoretical point of view, but also from an experimental aspect \[1\]. Although the viscoelastic properties of skin are well established from torsional, uni- or bi-axial measurements, there is a wide range of elastic moduli reported and the tests do not approximate the chronic physiologically relevant shear conditions that exist with an implant. Several approaches have been used to measure the biomechanics of human skin including tensile (uni- or bi-axial), torsion and suction tests. The objective of this approach is also to confirm and include preconditioned aspects in the Preisach modeling (PM space) representation. In a previous study\[2\], it has been found that optimization of the strain-stress curve induces a PM space with 600 hysterons distributed along a Guyer distribution. The objective of this study is to confirm the results by considering the optimization of parameter extraction.

2. Complex mechanical multiscale behavior, memory and aging

The objective to study memory properties of complex systems is motivated by the need to understand biological systems which could naturally exhibit long time behavior and memory effects and aging. These highly reverberating biological media are strongly needed for experimental methods in classical medical ultrasonic imaging or Non Destructive Testing (NDT) for exploring complex medium such as biological tissues (skin, bones or neural cells of the brain) known to exhibit memory effects. It is known that (nonlinear) memory effects are responsible for the aging of materials. Multi-modal based imaging approaches have the potential to image such nonclassical nonlinear information as already completed in NDT. Nonclassical nonlinearity has been measured recently in several experiments and configurations related to the study of material aging or degradation. The main disadvantage of quasi-static methods consists in relatively large deformations induced, which can change skin properties in a complex way. However, there are only a few studies on elastic wave propagation changes caused by mechanical loading of biological tissues, and among them, few studies including nonlinear analysis of hysteretic behavior.

2.1 Biomechanical properties of the human skin : importance of hysteresis

The mechanical properties of collagen are therefore very important to biomechanics\[3\]. Due to hysteresis, loading and unloading process applied to skin samples induce two different curves, showing the existence of an energy dissipation mechanism in the biomaterial. The influence of the loading speed is also under investigation. Some studies measured the mechanical behavior of human skin subjected to low-magnitude shear loads over a range of physiologically relevant frequencies. Strain sweep, frequency response, as well as creep and recovery measurements were made on whole dermis and human skin from which the epidermis was removed. Collagen is the basic structural element for soft and hard tissues (skin, tendons, bone, etc.), giving their strength and mechanical integrity. The nonlinear stress-strain relationship in the human skin is mainly due to the uncrimping of collagen fibres in the dermis upon stretching\[4\]. In skin dermis, collagen constitutes around 75% of skin dry weight, elastin about 4%. Like mesoscopic materials, we must study not only collagen molecules, but also how the molecules wind themselves together into fibrils, how the fibrils are organized into fibers, and fibers into skin tissues. Here, the preferred orientation is defined as the mean of the orientations of two families of interweaving fibres. It was assumed that the collagen fibres are distributed according to a transversely isotropic and $\pi$-periodic von Mises distribution\[2\]. In order to choose the PM space distribution properties and parameters, some specific distributions have been tested in order to extract some real physical parameters which are linked to multi-scales properties of the skin.
2.2 Hysteresis and memory effects

Hysteresis is a phenomenon that occurs in ferromagnetic and ferroelectric materials, as well as in the deformation of some mesoscopic materials, which are flexible or compressible. For example, sand rock [5], which is one of the example of nonclassical nonlinear materials [6], for which hysteresis behavior is one of the key properties. In electronics, hysteresis is produced by positive feedback to avoid an oscillation. It seems to be a promising way to understand mesoscopic properties of biomechanical materials. When microdamage is present in biological tissues like bone, high levels of nonlinearity is found, with specific nonlinear signatures such as hysteresis and tension/compression asymmetry. The PM space model has a prominent future in the modeling of viscoelastic behavior of complex materials. Since the strain-stress characteristic of porcine skin under increasing loading is characterized by hysteretic behavior, the preconditonning signature will be investigated with the objective of extracting the memory of the skin.

3. Multimodality of nonlinear imaging of complex damaged media

Recently, an active research has been performed for the modeling of nonclassical nonlinear effects in biological tissues using memory based phenomenological approaches. The memristive effects could play a significant role in the complex nonlinear properties of biomaterials, such as damaged teeth [7], skin or brain. Nonclassical nonlinearity is now recognized to be a keystone of aging and degradation processes of mesoscopic materials. Thanks to the use of new multimodal ultrasonic imaging methods, this new class of multiscale materials can be studied with so-called phenomenological approaches like the Preisach-approach (PM space). This became more important during the last years in the field of Nonlinear Elastic Wave Spectroscopy (NEWS), which is in progress with the growing number of Non Destructive Testing (NDT) technologies. Among them, Time Reversal (TR) based NEWS systemic methods have the potential to become a powerful and promising tool for the Non Destructive Testing (NDT) industry [8] and recently in the domain of microwave localization of nonlinear scatterers [9]. Nonlinear time reversal methods provide the means to detect and localize and image structural damage in complex medium, thanks to the use of advanced signal processing techniques based on multiscale analysis, and multimodal imaging (Figure 1). The systemic approach of the TR-NEWS ultrasonic complexity generated innovation for medical applications with extended experimental results developed for echodentography on human teeth [7]. The importance and the necessity to have a reverberant medium (Figure 1) is a keystone of the success of the approach. Consequently, it induces a real potentiality for human skin characterization, since skin mechanical properties are complex and multiscale.
3.1 The physical meaning of the cross correlation function

The systemic approach of TR-NEWS has also an important feature related to the physical meaning of TR-NEWS signals. All these signal processing steps (chirp broadcasting, reception, correlation, time reversal and rebroadcasting, reception) help us to understand the physical meaning of the cross correlation function of a complex (or simple) medium. Consequently, the symmetry breaking of TR-NEWS signal coming from nonlinear effect would be measured (in the time domain thanks to the temporal representation of the cross-correlation function) by the "lost of symmetries" that should, of course, be calibrated also, and connected to excitations that break the linear behavior of the complex system such as the skin. As described previously, TR-NEWS experimental set-up which provide a physical meaning of the cross correlation function of a complex medium can be considered as an experimental evaluation of skin properties.

3.2 Optimized excitation and signal processing

The PM space model has limitations that need to be carefully considered. Evaluation of the limits of the PM space model has been investigated elsewhere. In order to evaluate the limits of the PM space model for skin, several uniaxial loading experiments are reported in this paper. During the inversion procedure of PM space identification, some optimized signal processing methods should be taken into account in order to take into account relaxation effects, and the vanishing of internal loops which is also observed elsewhere. Some accurate experiments should be performed in order to obtain noiseless curves of the stress-strain relation for porcine skin. Furthermore, it can be seen that the hysteresis area is increasing versus amplitude. To overcome this drawback, it is necessary to develop coded signal processing that could identify PM space statistical properties, and can be suitable for real-time identification and smart system design. The objective is to account for the dynamic variables and the (quasi)-static ones through the PM space identification which is, in practice, unlikely to be done and time consuming. The PM space approach employed here provides a systemic methodology for characterizing hysteresis inherent to the skin under study. For the porcine skin analysis problem under study, the low frequency loading protocol will be coupled to a high frequency acoustic probing device involving TR-NEWS localized imaging potential. Accurate analysis of nonlinear time reversal systems needs the use of new methods of signal processing.

3.3 PM space model description

Preisach-Mayergoyz model (PM space) of hysteresis is a tool for describing materials and systems with hysteresis behavior[6]. The PM space model is based on the idea that a given material is composed of a large number of small elastic particles (units, cracks, etc.). The skin is supposed to be composed of a great number of small elementary cells (fibrines), which are called Preisach’s operators or hysterons (Figure 2) \( \hat{\gamma}_{P_c,P_o} \) [10]. Without loss of generality, these small units are called hysterons in this paper and can be found either in the closed state (valued by 1) or in the open state (valued as -1). Parameters \( P_c \) and \( P_o \) represent hysteron’s closing and opening values under the assumption that \( P_o \leq P_c \). Mathematically, the Preisach’s operator \( \hat{\gamma}_{P_c,P_o} \) of hysteron is expressed as follows

\[
\hat{\gamma}_{P_c,P_o}(u(t)) = \begin{cases} 
-1, & u(t) \leq P_o, \\
1, & u(t) \geq P_c, \\
k, & u(t) \in (P_o, P_c),
\end{cases}
\] (1)

where \( u(t) \) is an input signal and

\[
k = \begin{cases} 
1, & \exists t^* : u(t^*) > P_c \text{ and } \forall \tau \in (t^*, t), u(\tau) \in (P_o, P_c), \\
-1, & \exists t^* : u(t^*) < P_o \text{ and } \forall \tau \in (t^*, t), u(\tau) \in (P_o, P_c).
\end{cases}
\] (2)
Applying the input signal \( u(t) \), the PM space output \( y(t) \) is described and the integrated stress contribution from the skin, which is composed of a huge number of hysterons, is then expressed as a linear combination of final number of hysterons in the discrete case, \( y(t) = \sum_{i=1}^{N} \mu(P_{c_i}, P_{o_i}) \gamma_{P_{c_i}, P_{o_i}}(u(t)) \), or, in the continuous case 
\[
y(t) = \int \int_{P_c \leq P_o} \mu(P_c, P_o) \gamma_{P_c, P_o}(u(t)) \, dP_c \, dP_o,
\]
where \( \mu(P_c, P_o) \) is probability function and \( u(t) \) is the input signal, and \( N \) is a number of hysterons of the PM space and \( \mu(V_c, V_o) \) is the distribution of PM space which could be one of the following: random distribution, normal random, Guyer distribution used for PM space characterisation of rocks\(^5\), or von Mises distribution of fibers\(^2\). Main task in the field of elasticity PM space modeling is the identification of probability density function \( \mu(P_c, P_o) \). The primary goal is to determine a density of hysterons in PM space only from the knowledge of hysteresis curve and the input signal corresponding to the loading protocol. We make use both the fundamental statistical distributions (e.g. Exponential, Gaussian, Uniform, Weibull) and also two distributions originated from R. A. Guyer and K. R. McCall. Distribution Guyer 1 is defined by \( P_c = \max \cdot r_0^\alpha, P_o = P_c \cdot r_0^\beta, \alpha, \beta \in \mathbb{R} \), where ‘max’ is a maximum of input pressure, \( P_c \) and \( P_o \) are closing and opening values \( P_o \leq P_c \), \( r_c \) and \( r_o \) are random numbers uniformly distributed between 0 and 1, and \( \alpha, \beta \) represent the distribution parameters. Distribution Guyer 2 is determined as \( P_c = \max \cdot r_0^\alpha, P_o = P_c \cdot r_o^{0.25 + 0.75\mu}, \alpha, \mu \in \mathbb{R} \), where \( \alpha, \mu \) represent parameters of the distribution in this case. To identify the corresponding PM space of some material only from the knowledge of an input signal and experimentally obtained hysteresis curve, the use of the statistical theory of distribution mixtures was decided in order to better reflect the real material structure.

4. Material and Methods

As described previously in\(^2\), the porcine skin used in the tests is obtained from the abdomen area of the same domestic pig. The subcutaneous fat layer was almost removed. The skin specimens were cut parallel to the pig’s spine. This direction is considered to be the direction lines of the natural tension of the porcine abdominal skin. An Instron 8800 tensile machine was used to conduct the tensile tests (figure 2). A 100 kN load cell, was used to measure displacement and tensile load. Except for the first cycle, the loading starts whenever zero force level is reached during unloading. It is important to note that all the tests performed on the various samples were accomplished within 4 hours to ensure the freshness of skin tissue. then the load was set to 0 before starting the test. Tests were performed at a constant strain rate, the same strain rate was applied for the loading and unloading steps. The loading steps are performed until a constant maximum imposed displacement value is reached. The strain rates and displacements are directly imposed through the machine crosshead. The results are obtained in terms of force-displacement. Nominal stress and strain are given by relations \( \sigma = F/S_0 \), and \( \epsilon = (D - D_0)/D_0 \) where \( F \) is applied force and \( S_0 \) is the initial area of the skin cross-section of samples, \( D \) and \( D_0 \) are the current and initial sample lengths. Figure 2 shows examples of stress-strain curve obtained from a cyclic test tension. For direct comparison with PM-space approach given by our Matlab coded simulator, we chose to represent the strain-stress curve instead of the stress-strain usual representation. It should be noted that contrary to classical results present in the literature, no averaging of experimental data was conducted. Since the PM space approach is based on statistical distribution of hysteretic elements, the natural dispersion of experimental data will be included in the distribution width of the hysteretic elements. Several displacement rates were imposed \( (V = 1; 0.5 \) and \( 0.1 \text{ mm/s}) \) and the maximum elongation was set to 25 mm. It is important to note that the hysteresis area, corresponding to an average energy loss has a range compatible with those obtained for human skin\(^1\). These data are very useful for studying the equivalence between classical nonlinearity, anisotropy, viscoelasticity parameters, and PM space parameterization of skin. The data what were analyzed with the PM space approach are coming from various experimental configurations given by Table 1. For all these measurements, the size of the sample is 100mm*30mm*2mm, cut parallel to the spinal bone. The imposed displacement is 25 mm. Acquisition sampling frequency is \( f_c = 1000\text{Hz} \).
with a re-sampling filter at \( f_r = 10 \text{Hz} \). For each testing configuration, a loading speed \( V \) is applied.

### Table 1: Properties of the porcine skin samples used for PM space identification.

<table>
<thead>
<tr>
<th>Testing configuration</th>
<th>Number of cycle</th>
<th>( V ) (mm/s)</th>
<th>Force max (kN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E2-20141007</td>
<td>144</td>
<td>1</td>
<td>0.50</td>
</tr>
<tr>
<td>E5-20141008</td>
<td>72</td>
<td>0.5</td>
<td>0.06</td>
</tr>
<tr>
<td>E1-20141010</td>
<td>15</td>
<td>0.1</td>
<td>0.30</td>
</tr>
<tr>
<td>E1-20141015</td>
<td>15</td>
<td>0.1</td>
<td>0.27</td>
</tr>
<tr>
<td>E2-20141022</td>
<td>72</td>
<td>0.5</td>
<td>0.21</td>
</tr>
<tr>
<td>E1-20141031</td>
<td>72</td>
<td>0.5</td>
<td>0.19</td>
</tr>
</tbody>
</table>

### 4.1 Measurements of the multiscale strain-stress behavior

The level of hysteresis during each deformation cycle is a measure of the viscous component of the skin response. Wang and Hayward found no significant effects of orientation in the hysteresis levels when tangentially loading and unloading skin\(^{[11]}\). As reported before, cyclic accumulation of viscoelastic and viscoplastic deformation occurs in skin during the cyclic tension-unloading and tension-tension tests. A typical uniaxial load elongation curve is divided into three parts\(^{[12]}\). In the first part, the load increases exponentially with increasing strain. The second part corresponds to a fairly linear relationship. Finally, the third part corresponds to classical nonlinearity ending with rupture. The first part is usually the physiological range in which the skin normally exists. Assuming the multi-scale coupling between these three parts, any information coming from one of the three parts could also give information about the other two parts.

### 4.2 PM space optimization and optimization techniques

We employ numerical optimization stochastic methods called simulated annealing (SA) and fast simulated annealing (FSA) optionally in combination with the blind random search for the PM space density identification\(^{[13]}\). For the assessment of that deviation we use either classical \( L_2 \)-distance or \( \phi \)-divergences which are more robust against either outliers or other unpredictable measurement errors\(^{[14]}\).

### 4.3 A comparative result on porcine skin

The experimentally measured hysteresis curves of porcine skin tissue and the input signals have been processed. First, a simple PM space (without using the distribution mixtures) was obtained by means of the simulated annealing. Then, with respect to the standard use, various distributions were tested, especially Guyer 1 and Guyer 2. In this case, the corresponding hysteresis curve is only roughly (comparatively) similar to original hysteresis curve and thus the result is not satisfactory. The value of \( L_2 \)-distance (standard Euclidean distance calculated along both the hysteresis curves and defined in \(^{[15]}\)) is equal to 2.688 which is too large with respect to classical results obtained in AE domain.

To solve this inaccuracy the layout of hysterons in PM space by means of distribution mixtures\(^{[16]}\) was used using the same algorithm in order to reach significantly lower deviation from experimentally obtained hysteresis curve. We achieved the lowest deviation of \( L_2 \)-distance for the distribution mixture combined through the Guyer 1 distribution and the Guyer 2 distribution. An example of this identification is shown in Figure 2. The first component Guyer 1 fanned out along the diagonal, i.e. representing almost elastic hysterons without hysteretic behavior. The second component is placed
mainly at the bottom of the PM space, where the hysterons have small opening values. Thereby, a very surprising result was achieved and the assumption that the mixture of distributions could better reflect the real material, was confirmed. The number of hysterons used was 1000 and the exact values of parameters found the the porcine skin are given in Table 1. All the PM space distributions were identified for the other measurements on porcine skin tissues versus experimental configurations. In all cases the optimal layout of hysterons was identified in the form of distribution mixture of Guyer 1 and Guyer 2 distribution with parameters indicated in the Table 2.

Table 2: Weight of distribution Guyer 1, value of deviation $L_2$ and statistics of parameters $\alpha_1, \beta_1$ of Guyer 1 and $\alpha_2, \mu_2$ of Guyer 2, 100 repetitions

<table>
<thead>
<tr>
<th>Weight</th>
<th>$\lambda_1$</th>
<th>$\alpha_1$</th>
<th>$\beta_1$</th>
<th>$\alpha_2$</th>
<th>$\mu_2$</th>
<th>$L_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample mean</td>
<td>0.78</td>
<td>2.984</td>
<td>0.086</td>
<td>0.710</td>
<td>25.61</td>
<td>0.914</td>
</tr>
<tr>
<td>Sample variance</td>
<td>0.00079</td>
<td>0.02929</td>
<td>0.00280</td>
<td>0.04430</td>
<td>99.2335</td>
<td>0.00414</td>
</tr>
</tbody>
</table>

5. Conclusion

Various materials have been tested for the validation of the concept (such as polymers, multiscale elastic layer in contact with complex reverberant bio-materials) before the real application on ex vivo skin. It is shown that a 1000-dimentional PM space could approximate the mechanical viscoelasticity of the skin under uni-axial loading. The complex behavior of the skin and its mechanical substitutes are studied using an experimental and pragmatic approach (phenomenological parameters) that couple macroscopic mechanical loading of the skin and microscopic ultrasonic imaging based on local parameter evaluations. Analysis of data coming from hysteresis behavior shows that the PM-space approach could be adapted as a new tool for extracting multi-scale parameters containing information about the aging of the skin. As a perspective, this approach will be compared to the numerous experimental protocols using various devices developed in order to measure the skin’s mechanical properties, like applying suction, biaxial tension, in-plane shear, normal indentation, or torsion to the surface area of skin of interest. The objective to extend this modern approach to the skin and the human brain, whose memory effects are currently accepted, gives this approach a promising future for modern engineering, and medical biomechanical imaging.
6. Acknowledgments

This work is supported by the Région Centre Val de Loire (France) under the PLET project, and by the Czech Ministry of Education grant SGS15/214/OHK4/3T/14 and RLM2015068.

References