ULTRASONIC BIOPOLYMER CHARACTERISATION BY HYSTERESIS QUANTIFICATION

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Abstract
Nonlinear characteristics are advanced indicators of the structure of viscoelastic materials. In this contribution, we focus on biopolymers (such as articular cartilage and skin tissue), and their typical amount of energy lost by mechanical loading/unloading represented by a hysteresis curve. For hysteresis modeling we use the Preisach-Mayergoyz space model, and restricted power distribution (Guyer extended distribution). Besides the power distribution parameters, the stress protocol is required as an input to obtain the modeled hysteresis curve, and to compare with experimental results. Knowing the experimental curve, an iterative numerical procedure for identification of true density function of opening and closing pressures was applied, and an optimization algorithm sought for the best (characteristic) distribution parameters for the specific soft tissue. For articular cartilage, experiments were performed on porcine patella sample in-situ using the device for ultrasound palpation. In the case of skin tissue, hysteresis curve was obtained from evaluation of the tensile force applied by the loading machine INSTRON 8800, and corresponding displacement measurement. The porcine skin tissue was loaded ex-vivo according to the basic loading-unloading protocol. The experimental results were compared to model hysteresis curves, and the typical model parameters were obtained by minimization of the L2-distance. For articular cartilage, the mean parameter values optimized by the simulated annealing algorithm were found (mean ± standard deviation) $\alpha = 0.25 \pm 0.01$, and $\beta = 0.04 \pm 0.03$, with L2-norm $= 0.3 \pm 0.02$ for 10 repetitions. In the case of skin tissue, the model parameters were estimated as $\alpha = 2.59 \pm 0.18$, and $\beta = 0.59 \pm 0.32$, with L2-norm $= 0.03 \pm 0.03$ for 10 simulation runs. Material properties can be evaluated based on the described quantification, and potentially used for medical purposes and healing or cosmetics treatment evaluation.

Keywords: hysteresis, ultrasound, biopolymers

1. Introduction
Quantification of hysteretic behavior of biological soft tissues offers a possibility to assess the material properties related to its nonlinearity. Moreover, such information can be used for time-dependent evaluation of healing and cosmetic treatments of the tissue.

In the previous works of hysteresis evaluation, the Preisach-Mayergoyz (PM) space model was successfully used for assessment of different materials with hysteretic behaviour, such as rock [1 - 4], electromagnetic relay [5], or skin [6].

In this paper, we use ultrasound propagation, and mechanical loading of various biological materials (articular cartilage and skin tissue) to assess their hysteretic behavior non-invasively. Then, we use the PM space model to quantify the viscoelastic material properties. The true density function of the PM space was reconstructed by an inverse iterative numerical
procedure [7], [2], [8], and the simulated annealing optimization method was applied to find the best parameters of the distribution.

For articular cartilage, experiments were performed on porcine patella sample using the device for ultrasound palpation [9]. The sample was stored frozen at -20°C until the test when it was let thaw at room temperature approximately for two hours. The cartilage was manually compressed and decompressed within 3 seconds with a constant rate of loading. Simultaneously, ultrasonic signals were transmitted perpendicularly to the cartilage surface, passed through the elastomer, and were reflected from the elastomer/cartilage, and cartilage/bone interface, respectively. The signals were recorded and stored for post processing, which yields cartilage thickness and stiffness.

In the case of skin tissue, hysteresis curve was obtained by applying the tensile force on the sample ex-vivo according to the basic loading-unloading protocol. The displacement of the tissue was evaluated showing the time-evolution of the tissue strain.

In [1], the authors argue that the generalized statistical distribution from their Example 1 is a suitable distribution for a wide class of physical systems. Therefore, we use this distribution for modeling of our set of biological tissues. Finally, we compare the model hysteresis curves to experimental results to obtain the typical model parameters by minimization of the L2-distance.

2. Materials and Methods

2.1 Preisach-Mayergoyz space model

Preisach-Mayergoyz (PM) model was introduced in 1935 by F. Preisach and mathematically formulated by Krasnosel'skii and Pokrowskii in 1983. The model is described in detail in [10], and in the Section 2.1 its brief description is introduced.

Mathematical formulation of Preisach-Mayergoyz model of hysteresis is based on the idea of discretisation, i.e., that the material is composed of a large number of small units each of which shows hysteresis behavior.

The units are represented by hysteresis operators $\hat{\psi}_{P_c,P_o}$, so called hysterons (Fig. 1). Outputs of such operator may assume only two values, +1 and -1, as shown in Fig. 1.

![Figure 1.: Schema of two-position hysterons $\hat{\psi}_{P_c,P_o}$ of the PM model.](image)

Numbers $P_c$ and $P_o$ correspond to switching values in response to input signal $u(t)$, called, e.g., "closing" and "opening" pressures, respectively, which has its parallel in porous media with open slots which are each closing individually under certain external pressure applied). It is assumed that $P_c \geq P_o$.

In the case of cartilage tissue which may be seen as a porous tissue, the "open slots" mean water-filled space in extracellular matrix. For skin tissue, the parallel with "closing" pressure
is realized through the extension of elastin and collagen fibres, and the “opening” state corresponds to the unstressed relaxed state of the fibres.

It is clear, that for values of input signal \( u(t) \) less than \( P_o \) the hysteron is in "open" position -1. If the values of input signal \( u(t) \) are greater than \( P_c \) than the hysteron is in "closed" position +1. The state of hysteron for values of input signal between \( P_o \) and \( P_c \) is determined by the history (memory) of the system. The hysteron can be defined as

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

(2)

where

\[
k = \begin{cases} 
1, & \exists t^*: u(t^*) > P_c \text{ and } \forall \tau \in (t^*, t), u(\tau) \in (P_o, P_c), \\
-1, & \exists t^*: u(t^*) < P_o \text{ and } \forall \tau \in (t^*, t), u(\tau) \in (P_o, P_c).
\end{cases}
\]  

(3)

Finally, an arbitrary weight function \( \mu(P_c, P_o) \), also called Preisach function together with an input \( u(t) \), and hysteron \( \hat{y}_{P_cP_o} \) represent the Preisach-Mayergoyz model as follows

\[
f(u) = \int_{P_o}^{P_c} \mu(P_c, P_o) \hat{y}_{P_cP_o}(u) dP_c dP_o.
\]  

(4)

In other words, the input \( u(t) \) (e.g., stress) is applied to the each of two-position hysterons of the system giving values \( \hat{y}_{P_cP_o}(u) = +1 \) (closing pressure) or \( \hat{y}_{P_cP_o}(u) = -1 \) (opening pressure), and the individual outputs of each hysteron are multiplied by \( \mu(P_c, P_o) \) and then integrated over all appropriate values of \( P_c \) and \( P_o \). Preisach function \( \mu(P_c, P_o) \) has a meaning of probability distribution of hysterons in Preisach-Mayergoyz (PM) space (continuous density function with compact support), which is defined by the following set of relations

\[
P_o \leq P_c, \text{and } \sigma_{\text{max}} \geq P_c, P_o \geq 0,
\]  

(5)

where \( \sigma_{\text{max}} \) is maximal value of the input signal \( u(t) \), stress. Thus, PM space forms a triangle and \( \mu(P_c, P_o) = 0 \) outside of this area. Inside the triangle, there are points (hysterons \( \hat{y}_{P_cP_o} \)) with coordinates \( (P_c, P_o) \) distributed according to the \( \mu(P_c, P_o) \) given by the properties of the material.

For example, linearly elastic material which shows only a little hysteresis will generate, as a response on the input \( u(t) \), hysterons in PM space near to the line \( P_c = P_o \), i.e. opening and closing pressures are very close. On the other hand, nonlinearly elastic materials show various distributions of hysterons over the PM space and these distributions may be related not only to the different materials but also to the healthy conditions of the respective materials, e.g., articular cartilage or skin tissue.

For our case, we have chosen the generalized statistical distribution from Example 1 of [1] which is defined as follows

\[
P_c = P_{\text{max}} \cdot r_c^\alpha, \quad \alpha \geq 0,
\]
\[
P_o = P_c \cdot r_o^\beta, \quad \beta \geq 0.
\]  

(6)
Here, the closing $P_c$ and opening $P_o$ pressures are calculated where $r_c$ and $r_o$ are random numbers uniformly distributed between 0 and 1. $P_{\text{max}}$ denotes the maximum stress $\sigma$ applied in order to reach the strain $\varepsilon$ corresponding to the minimal thickness (of cartilage), or maximal length (of skin). Note that with smaller $\beta$, the hysterons are generated closer to the diagonal line, corresponding to a linearly elastic material. On the other hand, larger the $\beta$ (and with $\alpha$ decreasing), the more viscoelastic behavior is described. In this case, the distribution of hysterons within the PM space changes towards the right side of the triangle (as shown in Fig. 2) and is more suitable for the modeling of nonlinear viscoelastic materials.

Figure 2: Generalized statistical distribution from Example 1 of [1] generated for various settings of parameters.

2.2 Experiments on soft tissues

We focus on biomaterials such as articular cartilage and skin tissue which are both soft tissues and their aging related degenerative changes are of a huge interest of medical research. Especially, early detection of deviation from normal (healthy) state, and tracking of the treatment impacts are of considerable interest.

We use ultrasound to record instantaneous changes in cartilage tissue deformation caused by mechanical compression, and obtain the hysteresis curve from these ultrasonic signals by their post-processing. In the case of skin tissue, the displacement evolution as an answer to the applied loading force is recorded directly by the loading machine, and yields the hysteresis curve of the skin sample under investigation.

2.2.1 Articular cartilage

Articular cartilage is a load-bearing soft tissue on top of the bones which protects against impacts and friction. The complex biomechanical behaviour results from interactions between cartilage constituents: water with mobile ions, collagen fibres, and proteoglycans with fixed negatively loaded charges. Cartilage exhibits nonlinear viscoelastic behavior, which may be weaker or stronger depending on healthy state of the sample.

The palpation probe is equipped with an elastomer tip of known properties which allows to determine the applied force. Ultrasonic signals are transmitted perpendicularly to the cartilage surface, pass through the elastomer, and are reflected from the elastomer/cartilage, and cartilage/bone interface, respectively. Times of flight (TOF) $t_1$, $t_2$ from both interfaces give an information about the stress $\sigma = F/A$ (due to know properties of elastomer, the area of the elastomer/cartilage interface $A$, and the $t_i$-measurement), and strain $\varepsilon = (\Delta t_0 - \Delta t)/\Delta t_0$ of the cartilage layer (defined as relative change of the cartilage thickness $d = 1/2c\Delta t$, where $\Delta t = t_2 - t_1$, and assuming the compressional wave velocity $c$ constant during the loading).
Experiments on hysteresis measurement were performed on porcine patella sample using pen-like device for ultrasound palpation [9]. The sample was stored at -20° and was let thaw at room temperature approx. for two hours before palpation test. The cartilage was manually compressed and decompressed within approx. 3 seconds with the constant rate of loading. The speed of loading during the palpation experiment had no influence in the investigated range.

Figure 3: Subfigures (a) and (b) (taken from [9]) illustrate the palpator probe with times of flight t1 and t2 of ultrasound reflections from elastomer/cartilage IEC, and cartilage/bone ICB interfaces, respectively. Part (c) shows A-mode signal with reflections from interfaces elastomer/cartilage in time t1, and cartilage/bone in time t2, respectively.

As a result of the stress applied, the hysteresis curve is obtained, as shown in Fig. 4.

Figure 4: (a) shows the input stress function of the palpation experiment, (b) depict the hysteresis curve from palpation measurement of the porcine patella cartilage.

2.2.2 Skin tissue
Skin tissue is a complex stratified biomaterial with specific mechanical behavior which derives from the two main components: elastin and collagen fibres. Its viscoelastic properties are of a great interest in the fields like dermatology, plastic surgery and cosmetics.

We use loading machine INSTRON 8800 (see Fig. 5 (a)) for applying tensile force on the sample, and to record instantaneous changes of tissue deformation and relaxation. The displacement in time is measured, and simultaneously, the force is recorded.
For skin tissue, the basic loading-unloading protocol was applied on the tissue sample of the initial length 209 mm, width 56 mm, and thickness 2.5 mm. The loading and unloading-phase was lasting for 10 seconds each, as shown in Fig. 5 (b). The maximum displacement during the test was 25 mm.

Note that in both, the compression cartilage experiment and the loading skin experiment, the applied force was oriented in the direction of movement departing from the initial state of the material. Thus, for the cartilage tissue, positive stress is achieved by compressing the sample. In the case of skin tissue, positive stress results from the sample loading. Analogously for the strain.

2.3 Results

2.3.1 Simulation experiment

For quantification of hysteresis curves obtained from the experiments, we used PM model where a set of 3000 points \((P_c, P_o)\) was generated according to the rule of the Equation (6). Thus, the input parameters are the stress protocol (see Fig. 4 (b)), and parameters \(\alpha\), \(\beta\) of the random distribution of the closing and opening pressures \((P_c, P_o)\). In order to obtain the best estimate of the parameters, and thus also the model of the tissue hysteresis, we applied the simulated annealing algorithm. The preliminary tests have shown a considerable sensitivity to the choice of the initial values \(\alpha\) and \(\beta\).

Therefore, we made beforehand an initial test of initial parameter values. In particular, we sought for a minimal mean of \(L_2\)-norm calculated from three repetitions where the hysteresis curves simulated using the specific initial values were compared with the experimental hysteresis curve. We found the minimum of \(L_2\)-norm for \(\alpha = 0.2\), and \(\beta = 0.0\) which resulted in the initial PM model, and initial hysteresis curve as shown in Fig. 6.

![Figure 6](image-url)
For skin tissue, the initial guesses of the model parameters were made based on the Reference [6].

2.3.2 Experiment and model results comparison

Next, we let run the simulated annealing algorithm to find the optimal values of $\alpha$ and $\beta$, and to minimize the $L_2$-norm of the distance between the simulated and the experimental hysteresis curve. This seeking was repeated 10 times and then averaged. We found mean characteristic parameter values for articular cartilage of porcine patella $\alpha = 0.25 \pm 0.01$, and $\beta = 0.04 \pm 0.03$ with mean $L_2$-norm $0.3 \pm 0.02$, as illustrated in Fig. 7.

Figure 7: (a) PM model and (b) the simulated hysteresis curve (blue-dashed) compared to the experiment (black solid). The mean parameters optimized by the simulated annealing algorithm are $\alpha = 0.25 \pm 0.01$, and $\beta = 0.04 \pm 0.03$.

For skin tissue, the loading-unloading protocol resulted in the following estimates of the model parameters (mean $\pm$ standard deviation): $\alpha = 2.59 \pm 0.18$, and $\beta = 0.59 \pm 0.32$, with $L_2$-norm $0.03 \pm 0.03$ for 10 repetitions. The corresponding PM space with generated hysteresis curve and parameter estimate evolution is shown in Fig. 8.

Figure 8: (a) PM model and (b) the simulated hysteresis curve (blue-dashed) compared to the experiment (black solid) of the basic loading/unloading stress protocol applied on the skin tissue. The mean parameters optimized by the simulated annealing algorithm are $\alpha = 2.59 \pm 0.18$, and $\beta = 0.59 \pm 0.32$.

In contrast to the cartilage measurements where the tissue was compressed by the palpator, and unloaded afterwards, in the case of skin tissue the sample was loaded in order to extend its initial length, and unloaded afterwards. This resulted in the essential difference in $(P_c, P_o)$ distribution within the PM space, and in different shape of the hysteresis curves.
2.5 Discussion

In principle, one can choose a different distribution of the closing and opening pressures \((P_c, P_o)\) than in Equation (6). However, a single distribution should be kept for all samples in order to enable comparison of parameters among the samples. The distribution we have chosen is comfortably simple, and reasonably well captures various properties of the materials.

Recall that relatively small values of \(\beta\) is a property of a linearly elastic material, contrary to relatively large values of \(\beta\) and small values of \(\alpha\), which suggest a viscoelastic behavior.

Our investigation of articular cartilage has shown that, for the chosen PM model distribution, the parameter \(\beta\) is significantly smaller than \(\alpha\), thus it exhibits relatively low amount of nonlinearity. For skin tissue, the model parameters are one order higher but maintain the same ratio as for the cartilage. This suggests that the ratio \(\beta/\alpha\) may be an interesting characteristic of biological tissues, whose values for larger class of biological materials should be further investigated to probe its universality. On the other hand, its variations could reflect tissue degeneration.

3. Conclusion

Various distribution types and their combinations may be used for hysteresis curve modeling. (See, for example, Ref. [6] where a mixture of distributions with several parameters is considered.) In our opinion, using the distribution of Equation (6) with only few parameters \((\alpha, \beta)\) has a merit of facilitating physical interpretation of the model parameters, and their relation to the material properties.

Under assumption that the same distribution is used, the comparison of various materials may provide reasonable results pointing the characteristic material parameters under normal conditions which are related to their mechanical properties. We anticipate that these methods could be sensitive not only regarding various biomaterials but also to assess degenerative changes of the tissue, or valuate the effects of medical and cosmetic treatment.

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