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Identification of skin elasticity through a two-layer numerical model

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Abstract
The human skin exhibits a complex structure which is made up of three main layers: the epidermis, the dermis and the hypodermis. Most of studies only account for the mechanical properties of the dermis which is assumed to be the most influential layer. This leads to less complex computing and to an easier study of the solution uniqueness. Nevertheless, the effects of the epidermis and the hypodermis should be analyzed to improve the skin mechanics knowledge.
This study aimed at proposing an identification method to assess the elastic properties of a two-layer numerical model of the skin. To state for the experiments, finite element models of the skin suction test are performed on a medium which accounts for the dermis and the hypodermis. As the suction experiment usually involves large displacements and large strains, an hyperelastic neo-Hookean model is considered for the numerical calculations. This leads to a simple two-parameter optimization problem. The proposed identification method consists on the comparison of the experimental curves with a simulated space which is built for different combinations of the mechanical parameters. The optimization procedure is based on a specific stochastic optimization algorithm that requires a simulated space sampling.
As suggested by literature, to identify the skin mechanical properties, two suction probe diameters (2mm and 6mm) are considered. The obtained results clearly state that the 2mm probe is unable to distinguish the dermis from the hypodermis and thus to identify their respective mechanical parameters. Moreover, to study more complex behaviour laws, the degrees of freedom of the problem should be restrained. Hence, two specific multiobjective cost functions are compared to take advantage of both the 6mm and the 2mm experiments and thus both stresses levels. An extension of this method to more complex problems is finally proposed to introduce our future prospects.

1 Introduction

Owing to its multi-layered structure and its complex behaviour law, the analysis of the skin mechanical properties is notoriously a rather difficult problem. However, such approaches are of great interest for areas of expertise as dermatology, surgery or cosmetology. The problem complexity can be split into different aspects. The first one is related to the complex behaviour law of the skin, which is known to be nonlinear hyper-viscoelastic anisotropic and quasi-incompressible [1] and which stands for one of the current major inquiry fields

[1, 3]. The second aspect concerns the skin geometry which can be divided into three main layers, namely the epidermis, the dermis and the hypodermis. Finally, as the skin is inherently a living medium it has to be studied *in vivo*. Hence, classical mechanical approaches cannot be used to analyse such a complex composite-like material. Inverse methods are thus generally developed to compare well-defined experimental measurements [4] and numerical models of the skin tissue. Nevertheless, due to an important number of parameters to be identified in the case of a full-model, the analyses usually remain simple. Its elastic aspects are generally accounted for [1] [2]. Moreover, owing to its structure of collagen and elastin fibres which are melted into the matrix of proteoglycans [5], the dermis is generally assumed to be the most influential layer in the skin mechanical response [1, 4]. Hence, most studies focus on the dermis and model the skin as a single-layer. A previous study has proved the relevance of such approaches [6], while discussing a bi-layer model which stood for the dermis and the hypodermis. Nevertheless, the analysis of the multi-layered aspect of the skin may be an interesting point to understand better treatments insights. Such a work was initiated by Hendricks *et al.* [7] who have encountered numerical difficulties while modelling the epidermis layer.
This paper thus aimed at continuing the multi-layer survey of the skin. It proposes a multiobjective inverse method to identify the mechanical parameters of a bi-layer model. The latter stands for the dermis and for the hypodermis. These layers are stressed by using 2mm and 6mm suction probes. The experiments and their related finite element models are first briefly presented to discuss the boundary conditions and the influence of the hypodermis elastic modulus [6]. The inverse principle is then presented. It is based on the calculation of a pre-simulated space that can be compared to a numerical design of experiments. An iterative stochastic optimisation technique whose interest was proved in a previous paper [8] is then used to minimise the problem cost function. The relevance of the proposed algorithm is finally tested on numerical cases-study for both the 2mm and 6mm approaches. According to the obtained results and as a full analysis of the skin requires a large number of parameters to be identified, two multi-objective optimisation procedures are proposed. They present the advantage to decrease the problem degrees of freedom. The obtained results are finally discussed to present the work we are currently focusing on.

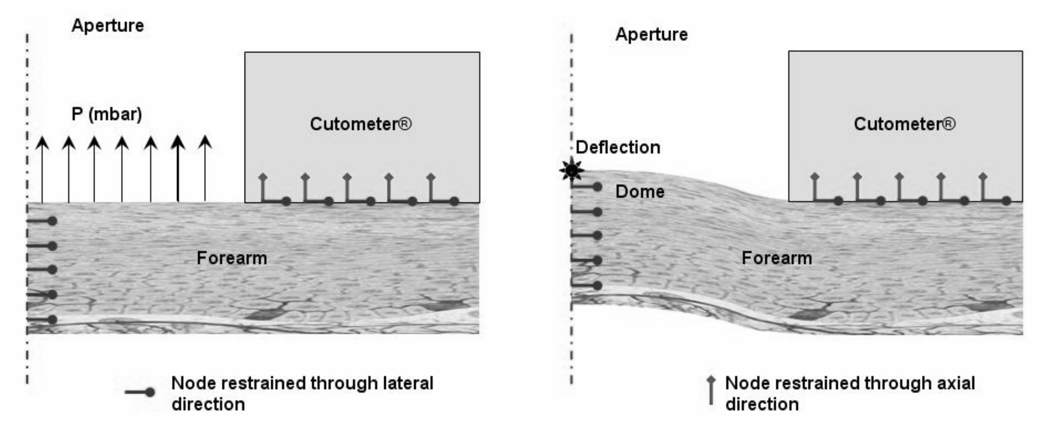

Figure 1: The suction experiment priciple

2 Method

2.1 The suction experiment principle

The suction experiment is the key-element of the analysis. It defines the measurements as well as the problem boundary and experimental conditions. The *in vivo* suction test [9] consists in applying a negative pressure to the skin using a Cutometer CM570 (Courage & Khasaka, Cologne, Germany). The skin is sucked into a cylindrical aperture and forms a dome whose deflection M is measured for each step of pressure p_t (see Figure 1). The experimental curves generally contain 50 to 100 points which is assumed to be sufficient to perform the inverse computation.

The forward problem thus consists in identifying the vector of the mechanical parameters $\mathbf{x}^*$ which is related to the experimental measurements $M(\mathbf{x},\mathbf{p},\mathbf{v})$, where $\mathbf{p}=(p_0 \ \cdots \ p_u)$ with u the number of measured point and $\mathbf{v}$ an additional vector of input parameters which can be for example related to the skin thickness [1].

2.2 The finite element general assumptions

The finite element models are performed with the Systus™ software. The problem geometry is considered as axisymmetrical. Hence, the nodes situated on the axis of symmetry are restrained through the lateral direction (see Figure 1). As the cutometer is pasted to the skin by using double-sided adhesive tapes, the skin / cutometer interface is modelled through an identical restriction of the nodes in both lateral and axial directions. A nonlinear quasi-static option is used for the calculations. Our approach consists in identifying the skin isotropic elastic mechanical properties. The suction test usually involves large displacements and deformations of the dermis and the hypodermis [6]. Hence, behaviour laws accounting for material geometrical nonlinearities have to be considered. For this theoretical approach, a quasi-incompressible neo-Hookean [10] law is considered. This point is discussed further. Its corresponding potential W is defined by:

$$W = X_1\left(I_1 - 3\right) \tag{1}$$

where X_1 is the elastic modulus and $I_1 = \boldsymbol{tr}(\mathbf{C})$ is the first right Cauchy-Green dilatation tensor. One can note that this potential concerns quasi-incompressible materials. A penalty method is used to account for the incompressibility ($\upsilon = 0.49$). Hence, to avoid the volumetric locking, the mesh is composed of quadratic 8-nodes elements with a fully reduced integration scheme.

2.3 The inverse technique principle

The inverse technique principle, previously presented in [8], proposes the calculation of a pre-optimization database which can be compared to a numerical design of experiments. This simulated space $\mathbf{\Omega}_S$ presents the advantage to run the numerical calculations only once in comparison to standard inverse approaches [2]. Indeed, as the clinical studies require large number of measurements to statistically test a product efficacy, this database improves the rapidity and thus the efficiency of the method. Furthermore, it can be easily used by medical practitioners who are generally not involved in finite element nor in optimisation techniques. The simulated space is built for expected variations of the mechanical parameters during the optimisation calculation:

$$\mathbf{\Omega}_S : (\mathbf{x},\mathbf{p},\mathbf{v}) \mapsto \mathbf{\Omega}_S(\mathbf{x},\mathbf{p},\mathbf{v}) \tag{2}$$

In our case study the vector of input parameters $\mathbf{v}$ is considered as null and $\mathbf{x} = \left[X_1^d \quad X_1^h\right]^T$, where X_1^d and X_1^h are respectively the dermis and the hypodermis elastic moduli (see Equation 1). The size and the bounds of the data base were chosen with care to provide the most accurate identification as possible. The variation field of the simulated space is:

$$\begin{cases} X_1^d(\mathrm{MPa}) \in \left(10^{-3} \quad 10^{-2} \quad \ldots \quad 9.1\times10^{-2}\right) \\ X_1^h(\mathrm{MPa}) \in \left(10^{-5} \quad 2.1\times10^{-4} \quad \ldots \quad 2.01\times10^{3}\right) \\ p(\mathrm{mbar}) \in \left(0 \quad 2 \quad \ldots \quad 10^{2}\right) \end{cases} \tag{3}$$

The forward problem thus consists in identifying $\mathbf{x}^*$ so as to minimize the following cost function $\mathcal{J}$:

$$\mathcal{J} : (\mathbf{x}) \mapsto \frac{1}{2}\mathbf{D}(\mathbf{x})^T\mathbf{D}(\mathbf{x}) \tag{4}$$

where for iteration j, $\mathbf{D}(\mathbf{x}^j)^T = [d_1(\mathbf{x}^j) \; \dots \; d_u(\mathbf{x}^j)]$, with $d_t(\mathbf{x}^j) = M(\mathbf{x}^*, p_t) - \mathbf{\Omega}_S(\mathbf{x}^j, p_t)$, and $t = 1, \cdots, u$. During the calculation, non-simulated values (i.e. values that are not described by the mesh defined in Equation 3) are computed with Lagrange's cubic interpolation (Matlab^{TM}) of the existing data.
According to literature various approaches can be used to solve such a problem, as the Gauss-Newton [11] and the Recursive Least Squares [12] algorithms. However, these methods are known to be sensitive to the initial values of the calculation, and, without a specific line-search technique, they may oscillate around local extrema or diverge [8]. Finally, Levenberg-Marquardt [13] approaches are more stable but may lead to time and memory consuming calculations. Hence, a specific stochastic procedure, which is theoretically able to reach the problem global minimum, was developed [8].

2.4 The stochastic algorithm principle

The proposed approach is based on a window focusing stochastic calculation [8]. From one iteration to the next, the bounds of the simulated space are modified to border the problem global minimum. Hence, it corresponds to a difference between the bounds close to zero. The algorithm works within four steps (see Figure 2):

1. The maximal $\overline{\mathbf{x}} = \boldsymbol{max}(\mathbf{x})$ and minimal $\underline{\mathbf{x}} = \boldsymbol{min}(\mathbf{x})$ bounds of the problem are identified.
2. N random vectors that are uniformly distributed between $\underline{\mathbf{x}}$ and $\overline{\mathbf{x}}$ are then computed at iteration j so as to set a matrix of random parameters:

$$\mathbf{X}^j = \{ {}_1\mathbf{x}^j, \; {}_2\mathbf{x}^j, \dots, \; {}_N\mathbf{x}^j \} \tag{5}$$

   where ${}_k\mathbf{x}^j$ is the k^{th} vector generated at iteration j.
3. The cost function $\mathcal{J}$ is evaluated and the obtained results are sorted according to their increasing values.
4. The N_b best candidates are then chosen (i.e. the N_b lowest cost functions) and the new bounds (at iteration $j+1$) are identified through the calculation of:

$$\begin{cases} \overline{\mathbf{x}}^{j+1} = \boldsymbol{max}({}_l\mathbf{x}^j), & 1 \le l \le N_b \\ \underline{\mathbf{x}}^{j+1} = \boldsymbol{min}({}_l\mathbf{x}^j), & 1 \le l \le N_b \end{cases} \tag{6}$$

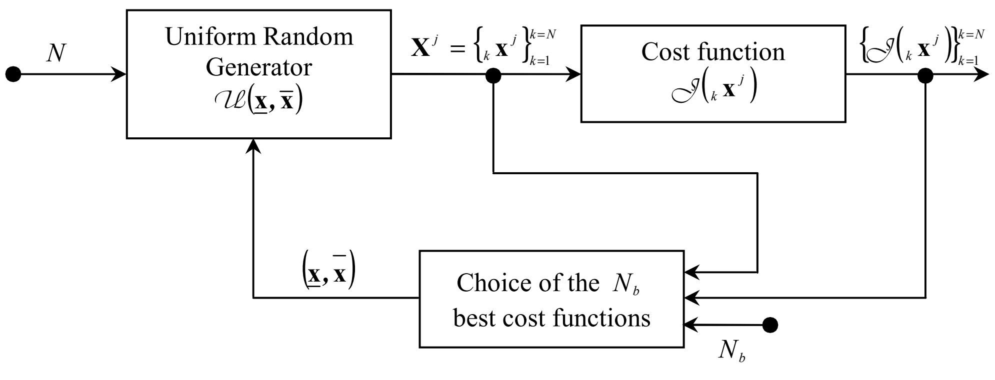

Figure 2: The stochastic algorithm principle

This procedure is iterated till the residual between two consecutive iterations satisfies a stop criterion $C^j = \left|E^{j-1} - E^j\right|$, where E^j is the correlation error which is defined as:

$$E^j = \frac{1}{u}\left(\sum_{t=1}^{t=u}\left(M\left(\mathbf{x}^*, p_t\right) - \mathbf{\Omega}_S\left(\mathbf{x}^j, p_t\right)\right)^2\right)^{1/2} \tag{7}$$

For an infinite number of samples N the algorithm was proved to converge to the problem global minimum [14, 15]. Nevertheless, according to a probability ρ of reaching this minimum with an accuracy e, N can be estimated as [14, 15]:

$$N = \boldsymbol{ln}(1-\rho) / \boldsymbol{ln}(1-e) \tag{8}$$

The sensitivity of the algorithm to N and N_b, has been previously studied [8] in order to determine standard values of these parameters ($N = 1000$ and $N_b = 20$). For our case study $C = 10^{-6}\,\mu\text{m}$.

3 Results

3.1 Problem boundary conditions

The proposed approach consists first in discussing the attachment of the skin layers to the underlying tissues, to highlight the interest in using different probe diameters for such analyses. An hypodermis/bone interface is modelled through different boundary conditions: restrained nodes in lateral and axial directions, restrained nodes in axial direction, and non restrained nodes (i.e. the interface is suppressed). A 1mm-thick layer stands for both the epidermis and the dermis whereas the second one (1mm-thick as well) represents the hypodermis. Two probe diameters (2mm and 6mm) are considered. As it was previously described a neo-Hookean law is used to model the skin. The elastic modulus of the dermis X_1^d was set to 80kPa whereas the hypodermis one X_1^h varies (see Equation 1).

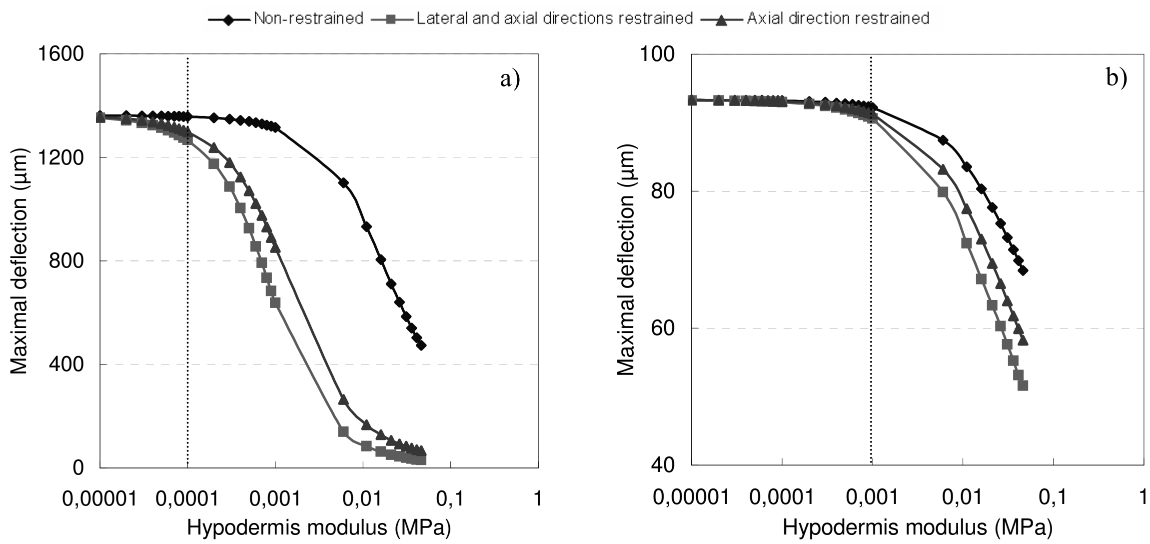

Figure 3: Maximal deflection (i.e. deflection obtained at maximal pressure p=100mbar) according to different boundary conditions and different values of the hypodermis elasticity modulus, for 6mm- (a) and 2mm- (b) diameter probes.

Figure 3 plots the maximal deflection according to different boundary conditions and different values of the hypodermis elastic modulus. As one would expect, the non-restrained model presents the highest deflections. For low values of X_1^h, which constitutes a reliable assumption [2, 6], similar deflections are calculated in every cases. Discussing the boundary conditions is a complex problem. However, given the particular structure of the hypodermis which is made of groups of adipocytes enclosed by conjunctive septa linking the dermis with subjacent structures, the non-restrained hypothesis seems inappropriate. This analytical aspect has been confirmed by observations made by Hendricks [2] and Diridollou [16] who demonstrated significant hypodermal axial deformation in suction test, which could not otherwise appear if the interface was entirely free. For both 6mm and 2mm models, the lateral displacements restriction hardly affects the results. Hence the fully restrained model will now on be considered for the identification.
One more interesting point can be highlighted while studying the influence of the hypodermis elastic modulus. Indeed, the 2mm model shows similar deflections as long as $X_1^h \leq 10^{-3}\,\text{MPa}$, whereas they differ according to the 6mm calculation. This result clearly correlates the work of Agache [4] that have presented the maximal deflection versus the pressure and the probe diameters. Larger apertures minimize the influence of the top-layers and, thus, should be used to assess the sub-dermal properties. Hendricks *et al.* [7] have presented similar conclusions while studying the influence of the probe diameter on a single-layer identification. According to the recorded variations they have refined their model to a two-layer structure. The degrees of freedom of the inverse problem can consequently be reduced according different measurements. Hence, more complex problems may be analyzed.

3.2 Single-objective identifications with 6mm and 2mm apertures

This section aimed at presenting theoretical single-objective identifications of a bi-layer media. 6mm and 2mm experiments are separately considered for the calculations. The considered simulated space is described by Equation 3 and the problem cost function is defined in Equation 4. This numerical test simply consists in extracting a simulated curve from the database and in verifying the relevance of the proposed approach. The chosen curve was plotted by using $X_1^d = 0.0055\text{MPa}$ and $X_1^h = 0.00041\text{MPa}$. All the presented results were analysed through numerous configurations. As the stochastic identification is based on a random sampling of the simulated space, results can vary from one calculation to another. Hence, 100 identifications were considered for each study case.
One can note that for the 6mm-calculation (see Figure 4.a), the required parameters are identified for every cases. This clearly shows the relevance of the proposed algorithm. Moreover, it proves that the optimization problem presents a unique solution. Indeed, the stochastic algorithm is theoretically able to reach the global minimum of the problem but is unable to distinguish between multiple minima. The 2mm results present a more unusual distribution. The identification error respectively reaches 2% and 72% of the required X_1^d and X_1^h. This effect can be discussed through Figure 3.b. Owing to the considered hypodermis elastic modulus, in a certain order of magnitude, similar solutions of the problem can be found. Obviously, the hypodermis proposes a restrained influence on the results while considering such a diameter. Once more the analyses of Hendricks *et al.* [7] and Agache [4] are verified.
One can thus suppose that the 6mm experiment can be used to identify the mechanical properties of a bi-layer model of the skin. Nevertheless, dealing with an experimental curve is a quite more complex problem. Hence, this should be discussed according to reliable experimental cases. Figure 5 presents 100 identifications performed on a single experimental curve. Owing to the measurement uncertainties and to the simulated space sampling, the identified parameters could vary from one calculation to another. Mean values of the elastic moduli can be determined ($X_1^d = 0.09\text{MPa}$ and $X_1^h = 3.7\times10^{-4}\text{MPa}$). However, the results clearly show that, according to the set of parameters $N = 1000$, $N_b = 20$ and $C = 10^{-6}\,\mu\text{m}$, different solutions can be identified. Nevertheless, the comparison of the experimental and simulated data (see Figure 6.a) show a high correlation error (see Equation 7) which may explain the observed variations. This points out the question of the skin behaviour law and its highly nonlinear characteristics. One can remark that while using a more complex hyperelastic potential [6] (see Equation 9), which is based on two elastic moduli X_1 and X_2, the correlation is clearly improved (see Figure 6.b).

$$W = X_1\left(I_1 - 3\right) + X_2\left(I_1 - 3\right)^2 \tag{9}$$

However, such calculations lead to much more complex optimization problems. Hence, discussing the uniqueness of the solution and the relevance of the calculations becomes difficult. As it was previously presented a "dual-experimental" technique can reduce the problem degrees of freedom. The 2mm probe mainly stresses the epidermis whereas the 6mm one induces strains in both the layers. A combination of these phenomena through a multi-objectives problem, can be used to distinguish between the contribution of the dermis and the hypodermis on the overall skin mechanics.

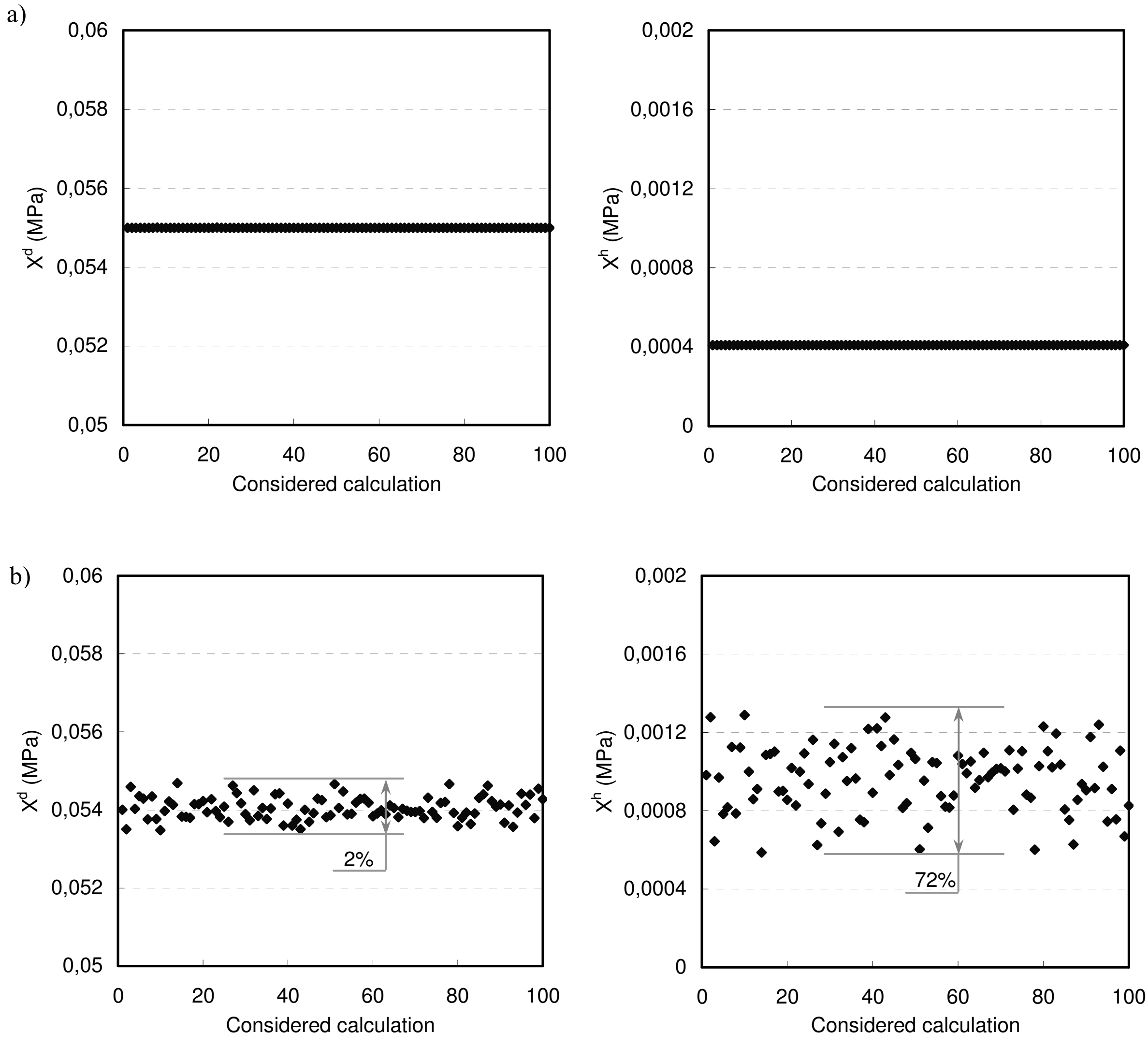

Figure 4: Identified mechanical paramaters according to the considered calculation for a 6mm- (a) and a 2mm- (b) calculation. $N = 1000$, $N_b = 20$ and $C = 10^{-6}\mu m$.

3.3 Multi-objective approach

The multi-objective approach consists in combining the 2mm and the 6mm experiments for the inverse calculations. 6mm and 2mm experiments are thus simultaneously considered for the calculations. Two main techniques are proposed: a weighting and a ratio methods.

3.3.1 The weighting approach

The weighting approach consists in a linear combination of the cost functions related to the 6mm and the 2mm calculations. The new problem is thus defined as:

$$\mathcal{J} : (\mathbf{x}) \mapsto \frac{1}{2}\left(\alpha \mathbf{D}^{2mm}(\mathbf{x})^T \mathbf{D}^{2mm}(\mathbf{x}) + (1-\alpha)\mathbf{D}^{6mm}(\mathbf{x})^T \mathbf{D}^{6mm}(\mathbf{x})\right) \tag{10}$$

where $\alpha \in [0 \ ; \ 1]$ is the weighting parameter and $\mathbf{D}^{6mm}$ and $\mathbf{D}^{2mm}$ are respectively related to the 6mm and the 2mm calculations.

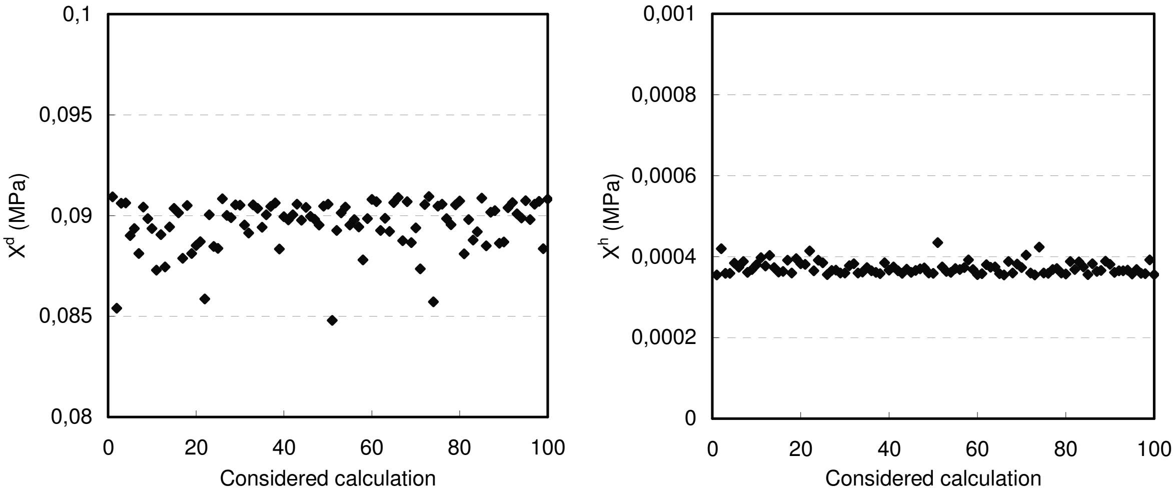

Figure 5: Identified mechanical paramaters according to an experimental case study. The 6mm probe is considered. $N = 1000$, $N_b = 20$ and $C = 10^{-6}\,\mu\text{m}$.

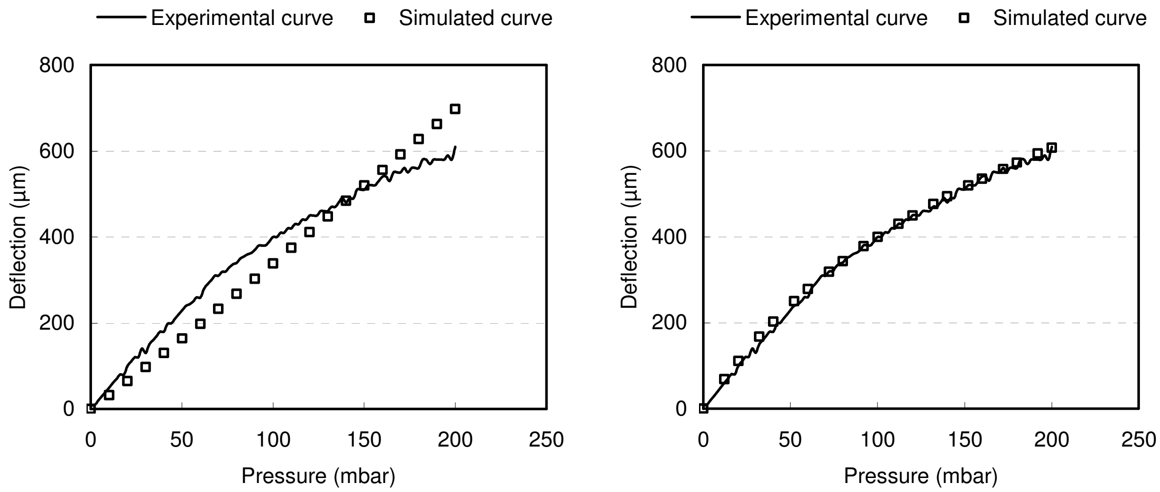

Figure 6: Comparisons between experimental measurements and simulated curves. a) for a neo-Hookean behaviour law $X_1^d = 0.091\text{MPa}$ and $X_1^h = 3.6\times10^{-4}\,\text{MPa}$. b) for an extended hyperelastic potential [8] $X_1^d = 0.06\text{MPa}$, $X_2^d = 31\text{MPa}$, $X_1^h = 3.4\times10^{-4}\,\text{MPa}$ and $X_1^h = 0.9\times10^{-4}\,\text{MPa}$.

Obviously for $\alpha = 1$ the 2mm simulated space is strictly considered whereas for $\alpha = 0$ the calculation is performed on the 6mm one. As it was previously presented (see Figure 4.b) the identifications can differ in that latter case. The sensitivity of the calculations can be plotted versus α. Figure 7 clearly demonstrates that above 0.75 the obtained results could differ from the required ones ($X_1^d = 0.0055\text{MPa}$ and $X_1^h = 0.00041\text{MPa}$). This was successfully checked for numerous calculations. Considering $\alpha = 0.5$, for example, leads to identify the required parameters in every case study.

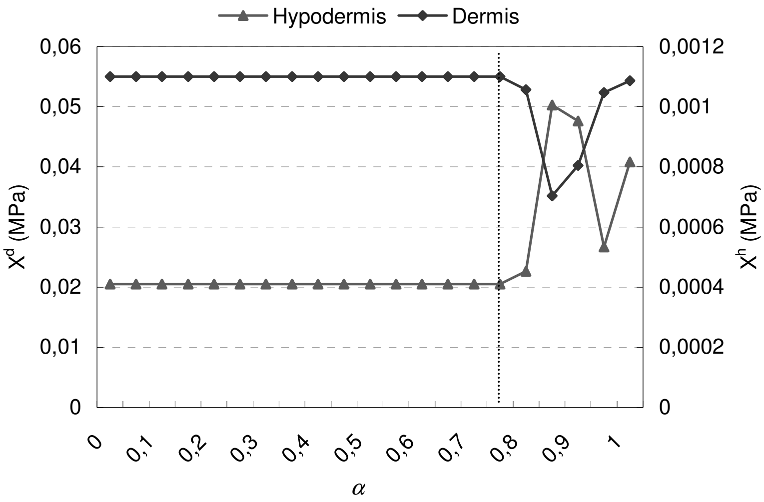

Figure 7: Identified mechanical paramaters according to α. $X_1^d = 0.0055\text{MPa}$ and $X_1^h = 0.00041\text{MPa}$, $N = 1000$, $N_b = 20$ and $C = 10^{-6}\mu\text{m}$.

3.3.1 The ratio approach

The ratio approach consists in coupling the measurements and the databases by using a ratio calculation. The problem cost function is then calculated through Equation 4, by using a new simulated space $\mathbf{\Theta}_S$ (see Equation 11, where $\mathbf{\Theta}_{S\,i,t}$ are the components of $\mathbf{\Theta}_S$ for the considered $\mathbf{x}_i$ at step t) which is defined according to the measurements ratio Γ (see Equation 12, where Γ_t are the components of the vector Γ for each step of pressure t). The multi-objective aspect of the problem is thus treated as a single one.

$$\mathbf{\Theta}_{S\,i,t} = \mathbf{\Omega}_S^{6mm}{}_{i,t} \big/ \mathbf{\Omega}_S^{2mm}{}_{i,t} \tag{11}$$

$$\Gamma_t = M_t^{6mm} \big/ M_t^{2mm} \tag{12}$$

Figure 8 illustrates a ratio calculation according to the numerical curves obtained for $X_1^d = 0.0055\text{MPa}$ and $X_1^h = 0.00041\text{MPa}$. The main advantage of the proposed method lies on its ability and on its rapidity to converge. Indeed the test calculation is performed in 1.2s for 10 iterations whereas the weighting algorithm usually requires 20 iterations which are computed in 3.8s. According to experimental analyses, that are generally based on numerous experimental curves [1], such a time-saving procedure could be useful. Finally, as less iterations are required for the convergence, the problem seems to be better-posed, and, owing to the ratio calculation, less multiple solutions may be expected. Hence, more complex problems (e.g. more complex behaviour laws and structured models) may be studied.

4 Discussion

This article was first intended to discuss a multiobjective inverse method to identify the mechanical parameters of a bi-layer model of the skin. Indeed, such an analysis can be of potential interest to study the insight of a medical treatment. A bi-layer model of the skin suction experiment, which stands for the dermis and the hypodermis under a pressure stress, was first proposed. The boundary conditions of the problem were first compared to physiological aspects of the skin and to results related to the hypodermis influence on the above layers. According to literature [2, 4] multi-layered media should be analysed through different suction probe diameters. 6mm- and 2mm- chambers were modelled to analyse the interest in using multi-objectives cost function to identify the mechanical parameters related to a neo-Hookean behaviour law. The identification procedure is based on a stochastic technique [8] which requires the sampling of the simulated database. Its main advantage lies in the convergence to the problem global minimum. Single-objective cost functions were then tested on the 2mm and the 6mm simulated space. The obtained results clearly show that the 2mm calculation facilitates the identification of the top layers whereas the 6mm one can be generalized to an entire model. However, for more complex problems (e.g. more complex behaviour laws and more complex structures) the degrees of freedom should be as much as possible restrained. Hence, multi-objectives cost functions may be used. Two approaches were finally compared: a weighting and a ratio combination of both the simulated spaces. As the first technique requires a specific choice of the weighting parameter and as it proposes more time and memory consuming calculations, the ratio algorithm seems to present better abilities for such analyses.

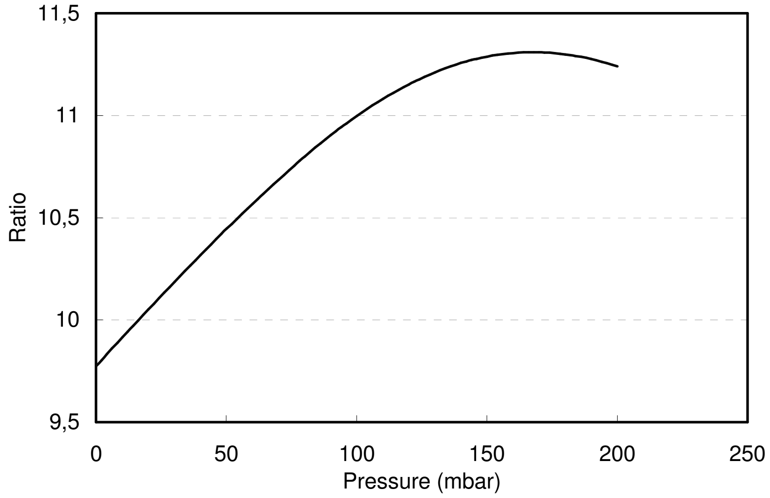

Figure 8: Illustration of the ratio calculation according to numerical curves obtained for $X_1^d = 0.0055\text{MPa}$ and $X_1^h = 0.00041\text{MPa}$.

More complex problems can thus be analysed. Nevertheless, for multi-parameters identifications, the simulated space built may require an important number of numerical calculations. Actual designs of experiments and surfaces responses, for example based on Krieging techniques, should thus be considered. One more important aspect can also be highlighted. Owing to the complex behaviour of the skin, which is known to be nonlinear viscoelastic anisotropic quasi-incompressible and pre-stressed [6], the identification of mechanical parameters according to a unique experiment may be impossible. Stressing the skin in different ways (e.g. using the suction test, the extensometry [3] and the indentation [17]) might be a successful approach. Indeed, each of these tests can point out different aspects of the skin mechanics and their combination may lead to detail the effect of a treatment. Finally the entire structure of the skin (*stratum corneum*, epidermis, dermis and hypodermis) can be identified through echographic measurements or by using optical coherence tomography to better understand the treatment insights kinetics.

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