MODEL-BASED IDENTIFICATION OF THE NONLINEAR ANISOTROPIC MECHANICAL PROPERTIES OF *IN-VIVO* HUMAN SKIN

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Abstract: The *in-vivo* mechanical properties of human skin are identified by using a nonlinear optimisation procedure. An optimal fit between the results of multiple biaxial loading experiments and a finite element model of the experiments is obtained. This method provides a consistent framework to integrate the results of multiple experiments in order to characterise the mechanical properties of soft membranes with complex internal structure. This approach has been used to identify the quasi-static stress-strain relationship of human skin as a nonlinear anisotropic material using an exponential strain-energy function.

Introduction

Langer was the first to investigate the relation between structure and mechanical behaviour in human skin [1]. From the observation that stab wounds caused by a circular object had an oval shape, he derived a set of lines indicating the directions in skin with the least amount of cross-sectional residual tension. Microscopic investigations showed that these lines coincided with the predominant collagen directions within the skin. Langer's lines are a map of the anisotropy in human skin, and define the coordinate system for a constitutive law based on the structural directions within the tissue (Figure 1).

Human skin is in general anisotropic, nonlinear and exhibits strong viscoelastic behaviour [2]. The requirement for preconditioning of the sample, in order to achieve a repeatable stress-strain relationship between loading cycles, and loss of strain energy between loading and unloading cycles, has been reported [3]. To complicate matters, differences in mechanical behaviour have been shown to be dependent on age and body location [4, 5].

More generally, identification of the mechanical properties of soft biological tissue is difficult because these materials are usually anisotropic, inhomogeneous, and exhibit highly nonlinear stress-strain relationships. Furthermore, the mechanical properties can alter markedly when the tissue is removed from its *in-vivo* environment.

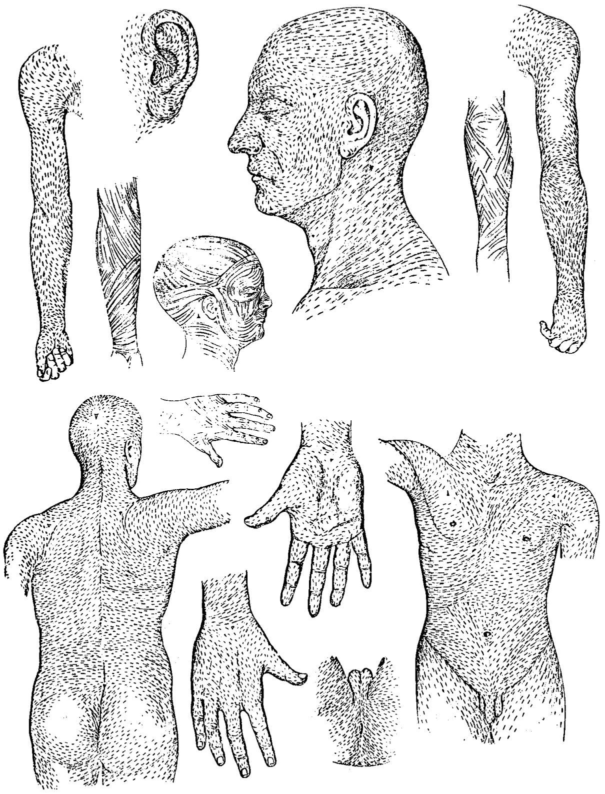

Figure 1: Langer's lines indicating the predominant collagen directions in skin (reproduced from [1]).

In order to identify the nonlinear anisotropic mechanical properties of *in-vivo* human skin we have constructed a versatile biaxial rig that can induce a rich set of strains on a ~40mm diameter sample. The set of constitutive parameters that best match the experimental results are determined by comparing the deformations measured from experiments with those predicted by a large-deformation model

Methods

A biaxial testing rig (Figure 2) was used in this study to investigate the stress-strain properties of *in-vivo* human skin. The biaxial rig consists of 16 independent displacement actuators (*Physik Instrumente* M227.27), each with a travel range of 50 mm and resolution of 0.2 µm. Attached to the end of each displacement actuator were custom-built 2D force transducers, with a range of 2 N and a resolution of 1 mN. These force transducers were used to measure the force vectors

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applied to the skin of the subject at each of the 16 attachment points.

The geometry of the sample and its induced deformations were recorded using a high resolution CCD camera (*Atmel Camelia 4M*). The actuator control, data acquisition from the force transducers, and the image acquisition from the camera were all performed using an integrated software system developed with LabView (National Instruments). This software supported actuator control in either position- or force-feedback modes, allowing deformation states to be specified in terms of stress or strain

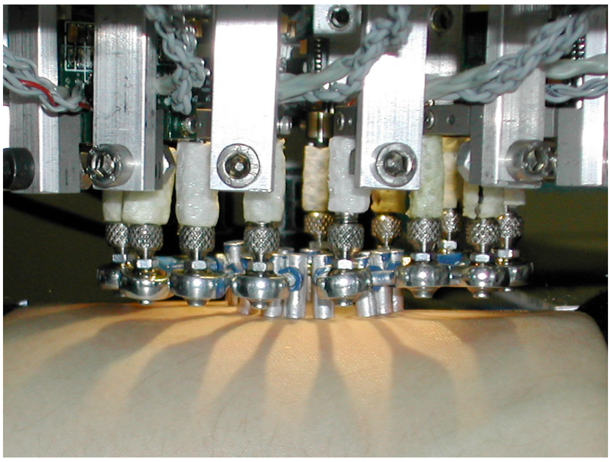

Figure 2: The biaxial testing rig attached to the skin of subject.

The actuators induce a deformation field that is measured with ~1 μm accuracy using a novel 2D cross-correlation based image analysis algorithm [6]. This technique traced the displacements of small regions, typically 64 × 64 pixels, with an accuracy of approximately one twentieth of a pixel. The accuracy of the cross-correlation relies on high-contrast high-frequency information within the images, which was provided by staining the tissue sample with fine-grain carbon powder before each experiment.

Data from experiments were combined in a finite element model to analyze the sample deformations. The geometry of the samples was represented with a circular mesh of 192 elements, using bicubic hermite basis functions, and the skin modelled in two-dimensions as an incompressible material using large-deformation plane-stress theory. The displacements of the nodal positions in a deformed state are (Figure 3) used to illustrate the deformation of the geometry upon applying loading at the sixteen attachment nodes (Figure 4). An additional 800 internal data points were traced using the cross-correlation technique. The displacements of these were used for geometric fitting when estimating the material parameters of a constitutive law.

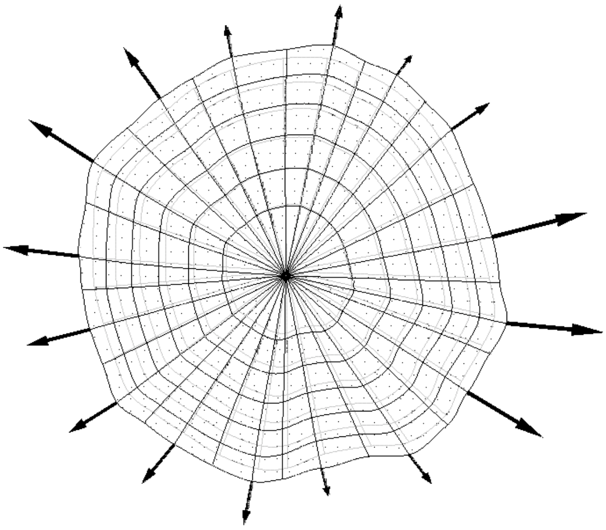

Figure 3: The finite element model of a test sample containing all data from a single deformed state of an experiment on *in-vivo* human skin. The light grey mesh represents the undeformed geometry. The deformations occurring when the sample is subject to loading, indicated by the force vector arrows, are represented by the black mesh. The dots indicate the data points used to evaluate geometrical residuals during estimations of the constitutive stress-strain relationship.

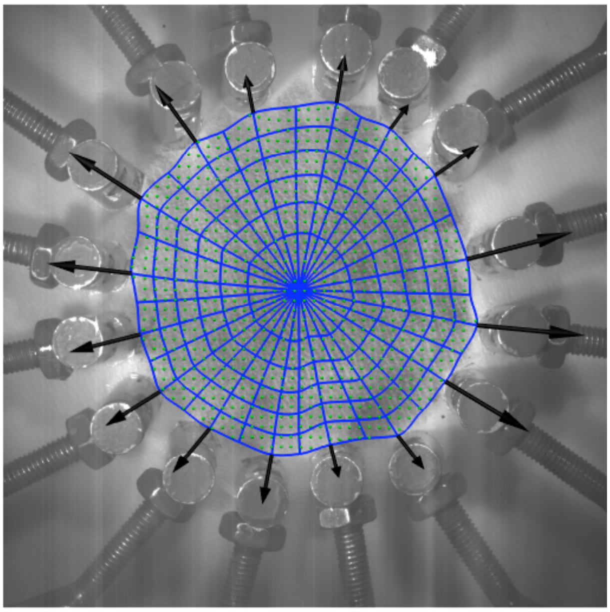

Figure 4: The finite element model superimposed upon an image of the skin showing the relative placement of the mesh and 16 attachment points.

We developed a technique to estimate the material parameters associated with mechanical constitutive relations using a forward solve algorithm (Figure 5). A typical experiment had multiple loading cycles, where each consisted of up to fifteen deformation states with associated boundary forces. With an initial estimate of the material parameters, the constitutive model initially solved the forward problem for each deformed state of a loading cycle by applying the recorded boundary forces to the undeformed geometry. The algorithm then proceeded by applying small changes to each of the material parameters and, for each change, solving the forward problem for all of the deformed states. For each solution, geometric residuals were evaluated between the simulated deformations and the experimentally determined displacements at each of the data point. As comparisons were made between the displacements at each deformed state of a loading cycle, a total of ~10,000 residuals were used for the optimization. Once all the geometric residuals were obtained, a non-linear, least square, optimization algorithm evaluated new estimates of the material parameters in the constitutive law. The complete forward solve procedure was repeated until the parameter estimates satisfied a specified optimizer criterion, which indicated that an optimal solution had been found.

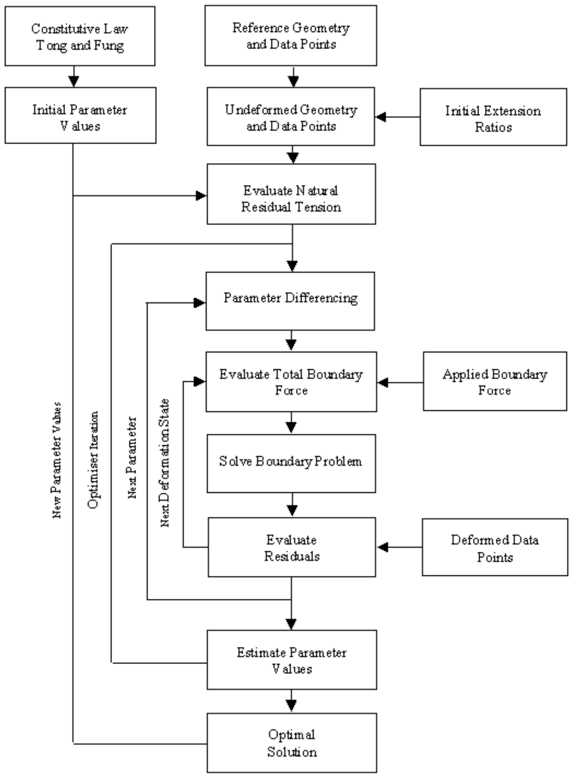

Figure 5: The flow of control associated with the nonlinear optimisation procedure used to estimate the material constitutive parameters.

The recorded forces provide the boundary conditions in a large-deformation finite element model of the membrane, using estimated constitutive parameters in a nonlinear anisotropic exponential strain-energy function

$$W = \frac{1}{2}\left(\alpha_1 e_1^2 + \alpha_2 e_2^2 + \alpha_3 e_{12}^2\right) + \frac{c}{2}\exp\left(a_1 e_1^2 + a_2 e_2^2\right),$$

to predict the resulting deformation field. e_1, e_2, and e_{12} represent the strain components. The equation has a total of six material parameters (α, c, and a) that need to be estimated from experimental data. This constitutive relation is based upon one originally derived by Tong and Fung [7] to describe the behaviour of rabbit skin subject to biaxial loading [3]. It was developed to model the quasi-static stress-strain properties of skin as an anisotropic, non-linear material.

A nonlinear optimisation procedure returned the set of constitutive parameter values that minimised the difference between the experimental and model displacement fields across multiple experiments.

Results

The stress-strain curves generated from the modified Tong and Fung's strain energy function, using material parameters obtained from five experiments, are shown in Figure 6. Note that the derived stress-strain relationships for strains along, and transverse to, the Langer lines illustrate the highly nonlinear anisotropic nature of human skin. These experiments were performed on the skin of the inner part of the forearm, on four age- and gender-matched subjects. Differences between the subjects were observed, while the two experiments performed on the same subject only showed minor differences. Dependencies on body location and age in the mechanical behaviour of human skin have previously been shown [4, 5]. The result from the current study further shows that variations must also be expected for a single location on comparable subjects. This indicates that accurate simulations of the stress-strain behaviour in human skin, in a clinical context, can only be achieved if these simulations are based on experimental data obtained from the specific sample in question.

Discussion

The combination of biaxial loading experiments investigate the mechanical properties of *in-vivo* human skin. Estimates of material parameter values for a constitutive law describing the anisotropic and non-linear stress-strain properties of human skin was obtained from multiple experiments. The variations between the estimated parameter values indicate that differences of mechanical properties exist between similar individuals.

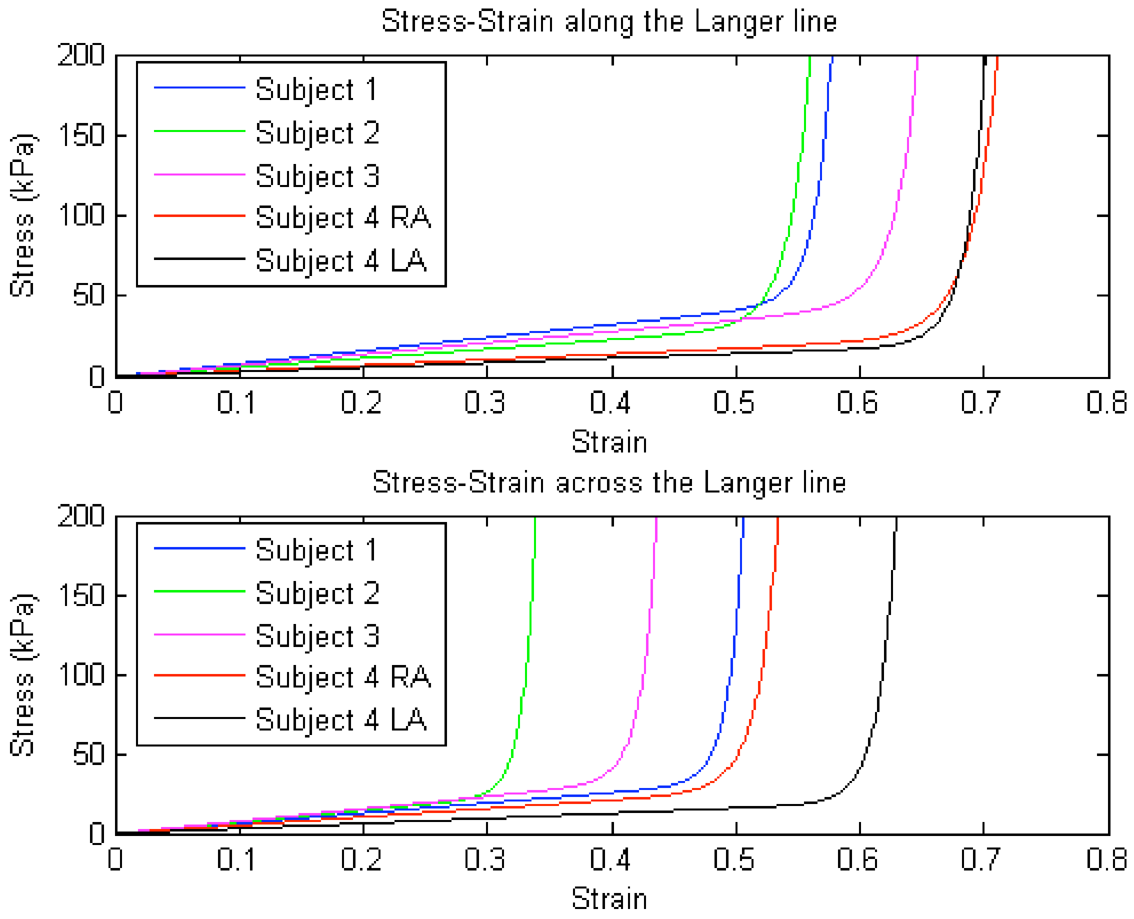

Figure 6: The stress-strain relationship generated from a constitutive model using material parameter values estimated from *in-vivo* experiments on human skin of four individuals. The two experiments on the same subject were conducted two weeks apart.

In order to describe accurately the mechanical behaviour of most types of soft tissue, a constitutive model has to account for the anisotropic and non-linear stress-strain properties. There are many constitutive laws presented in the literature that are capable of modelling these properties in different soft tissue types [7, 8, 9]. Most soft tissues does, however, also exhibit strong viscoelastic behaviour showing stress relaxation and creep, and a constitutive law will not be complete without incorporating these time dependent effects. The biaxial testing rig was successfully used to obtain viscoelastic measurements. However, in this initial study only quasi-static deformation data was modelled.

One limitation of the biaxial testing rig was that it could only obtain data in 2-D. The finite element analysis thus correspondingly modelled the tissue as a 2-D membrane using plain stress theory. In order to improve the model accuracy further, more detailed information of the tissue microstructure in the third dimension would be required. We are currently investigating combining biaxial loading with optical coherence tomography as a method for determining this information.

Conclusions

Nonlinear optimisation has been used to determine the optimal set of constitutive parameter values that best match multiple experimental measurements of *in-vivo* mechanical tests to large-deformation models of human skin under multiple loading conditions. This model-based analysis may be used to identify the mechanical behaviour of other anisotropic, inhomogeneous, nonlinear materials.

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