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# Gaussian process prediction of the stress-free configuration of pre-deformed soft tissues: Application to the human cornea

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Image-based modeling is a popular approach to perform patient-specific biomechanical simulations. One constraint of this technique is that the shape of soft tissues acquired in-vivo is deformed by the physiological loads. Accurate simulations require determining the existing stress in the tissues or their stress-free configurations. This process is time consuming, which is a limitation to the dissemination of numerical planning solutions to clinical practice. In this study, we propose a method to determine the stress-free configuration of soft tissues using a Gaussian process (GP) regression. The prediction relies on a database of pre-calculated results to enable real time predictions. The application of this technique to the human cornea showed a level of accuracy five to ten times higher than the accuracy of the topographic device used to obtain the patients' anatomy; results showed that for almost all optical indices, the predicted curvature error did not exceed 0.025 D, while the wavefront aberration percentage error did not overcome 5%. In this context, we believe that GP models are suitable for predicting the stress free configuration of the cornea and can be used in planning tools based on patient-specific finite element simulations. Due to the high level of accuracy required in ophthalmology, this approach is likely to be appropriate for other applications requiring the definition of the relaxed shape of soft tissues.



## 1. Introduction

The recent progress in medical image analysis and numerical simulation tools enabled the development of patient-specific planning solutions based on biomechanical simulations. The anatomical information for each patient is derived from medical imaging and finite element simulations are used to evaluate the outcome of specific surgical interventions. Additionally, such simulation platforms could allow monitoring of the disease, its progression and the efficacy of available treatments and procedures.

One of the problems with this approach is that the medical images acquired in-vivo describe the tissue in its physiological situation, which is frequently under stress. This is typically the case for soft tissue such as ligaments, arteries or the human eye. However, the level of initial strain in the tissue cannot be directly measured on the patient, therefore the biomechanical models are considering an initially unloaded "stress-free" configuration. Several methods were proposed to pre-stress the measured 'initial' geometry [1–8]. Among these methods, some researchers proposed an inverse elastostatic approach centered on the reverse application of in-vivo conditions to explicitly estimate the stress-free configuration, hence one non-linear simulation step is required to update the deformation gradient tensor [3–5]. Others adopted a modified updated Lagrangian formulation [1,2,6], to estimate the stress in the tissue using a forward calculation, where the procedure continuously updates the deformation tensor during the simulation of the in-vivo state. Although these methods provided accurate results, they require complex implementations, and – especially when the tissue is considered incompressible – a thorough knowledge of continuum mechanics as well as the solution of a non-linear problem. By contrast, an easier approach has been proposed by Pandolfi et al. [9,10], where a simple analytic calculation is combined with finite element analysis to obtain the stress-free configuration of the tissue. High accuracy can be achieved with this approach, but the solution requires the iterative solution of a finite element problem, which is time consuming [2,9–11].

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Calculation time represents an important issue for the acceptability of the planning tool in clinical routine. Therefore, the stress-free configuration of the tissues should be obtained as efficiently as possible. For this reason, the aim of this study was to evaluate prediction of the relaxed shape of the tissue with a stochastic approach. The Gaussian process (GP) is one of the most widely used stochastic and non-parametric processes for modeling dependent data observed over space or time. It has been used for several biomechanical applications to predict human gait kinematics [12], abdominal aortic aneurysms [13] or for the estimation of swimming velocity [14]. Our hypothesis was that this method could also be suitable to estimate the patient-specific stress-free configuration starting from clinical images. In this work, the parameters describing the shape of the tissue were modeled as a Gaussian process, which was used to predict the stress-free configuration without any further finite-element analysis. The method has been applied in ophthalmology for the prediction of the relaxed shape of the cornea that will be used in a planning solution for refractive surgeries.

## 2. Material and methods

In order to compute the stress free configuration of the cornea using a Gaussian process approach, several steps were necessary. First, the corneal geometrical information was acquired with a topography device (Section 2.1); the geometrical information thus obtained was used to deform a spherical cornea template to create patient-specific finite element meshes (Section 2.2). Patient specific models were then pre-stressed with an iterative approach (Section 2.3) and the resulting stressed corneas were divided into training and test data (Section 2.4.1). The training data was used to build the Gaussian process model (Section 2.4.2) and the test data was used to assess the quality of the prediction obtained with the fitted Gaussian process model (Section 2.4.3).

### *2.1. Patient data*

The shape of 1738 patients' corneas was acquired with a Pentacam HR Scheimpflug camera. The data collection was anonymously and complied with the local ethical regulations. About half of these corneas were categorized as healthy (776 corneas), which includes all the maps without manifestation of pathology or previous refractive intervention. This topography device allows an accurate measurement of the anterior and posterior surface of the cornea (accuracy of a few microns) and to export the geometric measurements as Zernike [15] polynomials. The Zernike coefficients $W(r,\theta)$ describe the elevation data of both the anterior and the posterior corneal surfaces. This decomposition is frequently used to describe the shape of the corneal surface, because the Zernike polynomials $Z_n^m$ represent an orthonormal basis where each polynomial function describes a distinct optical property of the refractive surface (i.e. defocus, astigmatism, coma, trefoil, quadrafoil). Therefore, any points on the corneal surface can be defined in a polar coordinate system $r,\ \theta$ as:

$$W(r,\theta) = \sum_{n=0}^{k} \sum_{M=-n}^{n} W_n^m Z_n^m(r,\theta)$$

where $W_n^m$ are the Zernike coefficients defining the weights, $n$ and $m$ are respectively the order and phase of the polynomial. Zernike polynomials up to order $k \leq 6$ have been considered in this study.

### *2.2. Finite element model*

Patient-specific models of the cornea were obtained by morphing a template finite element mesh to the topographic measurements. The three-dimensional template mesh included both the cornea and sclera (Fig. 1), which were meshed with about 40,000 linear hexahedral elements. The morphing process has been described previously [16]. Briefly, the mesh of the template anatomy was defined based on spherical primitives corresponding to the dimension of an average cornea. The nodes on the surface of this template mesh were projected on the anterior, and respectively posterior, surfaces of the cornea defined by the Zernike polynomials. Interpolation was used to arrange the internal nodes and avoid distorted elements. A no-displacement boundary condition has been applied to the nodes located on the cut-section through the sclera. A normal intraocular pressure of 15 mmHg has been applied on the internal surface of the mesh.

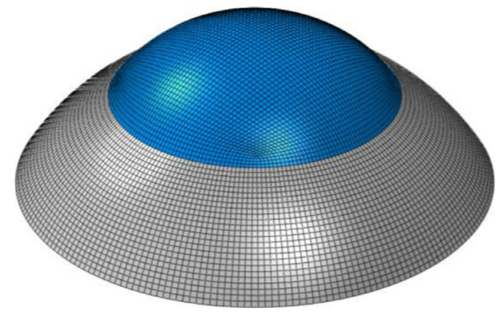

**Fig. 1.** Spherical finite element mesh of the cornea, which was used as a template to mesh the patients' anatomy obtained in-vivo. The blue and the gray parts represent the cornea and the sclera respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

A mechanical model previously published and validated has been used to describe the mechanical behavior of the tissue [16,17]. Briefly, the strain energy function of the constitutive material model is given below:

$$\Psi = U + \bar{\Psi}_m + \frac{1}{\pi}\int \Phi(\theta)\left(\bar{\Psi}_{f1} + \bar{\Psi}_{f2}\right)d\theta$$

where $U$ describes a penalty function to ensure incompressibility of the material, $\bar{\Psi}_m$ is a neo-Hookean material representing the tissue matrix, $\bar{\Psi}_{f1}$ and $\bar{\Psi}_{f2}$ are modified Ogden materials [18] modeling the main collagen fibers and the collagen cross-linking, respectively. The probability distribution function $\Phi$ defines a realistic fiber distribution [19] by assigning weights to each fiber direction. Material constants were determined using three sets of experimental data obtained on button inflation tests [20] and strip extensiometry [21].

### *2.3. Iterative pre-stressing process*

The in-vivo corneal shape measured by the Pentacam device was stressed by the physiological intraocular pressure. An iterative approach was applied to progressively move the nodes of the patient-specific finite element mesh toward their stress-free shape. In this study the iterative approach, proposed by Elsheikh et al. [11] and Pandolfi et al. [9,10], was used.

Assuming the coordinates of the patient-specific model ($X_0$) as the target of the iterative process, $x_i$ describes the corneal geometry after each iteration $i$ resulting from the nodal displacement induced by the intraocular pressure (IOP). The computed nodal displacements $u_i$ are then used to estimate the stress-free form $X_i$ and the error $e_i$:

$$e_i = x_i - X_0 = (X_i + u_i) - X_0$$
$$X_{i+1} = X_0 - u_i$$

This means that during the first iteration of the pre-stressing algorithm, the IOP is applied on a finite element mesh having the shape of the cornea in its stressed configuration, as measured on