

Chapter 5. Inverse problems in the characterization of soft connective tissue – perspective for reproduction system

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Abstract. In this chapter, we first review different situations in computational biomechanics where an inverse problem or an identification problem has to be solved. After this presentation, we present in details the finite-element model updating technique, which is traditionally used to solve inverse problems. We then present sequential methods based on the principle of Kalman filters, which can be very useful to solve inverse problems in dynamics. Finally, we present in details the virtual fields method which can be very useful and efficient in situations when full-field deformation measurements are available across the whole domain of interest of the tissue. The main objective of the chapter is to introduce the principles required to understand the theory of each family of inverse approach and to present these different methods under a unified framework. Eventually, research directions are proposed for the emerging field of pelvic biomechanics in combination with advanced imaging techniques.

Key words. Soft tissues, inverse problems, identification of constitutive parameters, elastography, non agreed standard testing, finite-element model updating, variational approach, sequential approach, Kalman filter, virtual fields method, full-field deformation measurements, pelvic system, reproduction system.

5.1 Introduction

Computational biomechanics aims at predicting the mechanical response of living systems: given for instance a complete description of the aorta and of the surrounding tissues, we can predict the deformations that are going to be induced by the deployment of a stent graft during surgical repair of an aneurysm [1–3]. More generally, we could predict the deformations of a hollow organ under the action of radial forces that could be applied for a measurement purpose using an appropriate intraluminal device. This problem of predicting the result of measurements is called the simulation problem, or the forward problem.

The inverse problem consists of using the actual result of some measurements to infer the values of the parameters that characterize the system such as unknown parameters of the

material model, unknown elements of the boundary conditions or even sometimes the unknown initial geometry of the solid before the application of any mechanical action (loadfree configuration in finite deformations).

While the forward problem has a unique solution, the inverse problem does not. As an example, consider measurements of deformations in the wall of a hollow sphere, representing an idealized hollow organ, after the application of internal pressure. Given the precise description of the wall and its mechanical behavior, and given the value of support stiffness surrounding the hollow organ (boundary conditions), we can uniquely predict the values of the radial deformation (forward problem), but there are different combinations of wall mechanical properties and surrounding support stiffness that give exactly the same radial deformation. Therefore, the inverse problem — of inferring the mechanical properties of the organ and its surrounding tissues from observations of the radial deformation provoked by a change of internal pressure — has multiple solutions (in fact, an infinite number). Because of this, in the inverse problem, one needs to make explicit any available *a priori* information on the model parameters.

Formally an inverse problem implies the reconstruction of complete unknown fields (for instance the field of unknown material properties) and is usually illposed, which means that existence and uniqueness of the solution are not always guaranteed. The illposedness may be due to a lack of reliable data and/or to an overcomplexity of the model. When access to more reliable data and complexity reduction of the model are not possible in practice, illposedness may be overcome mathematically by resorting to regularization approaches. Solving such inverse problems implies the definition of a cost function, estimating the distance between the model predictions and the measurements. The cost function is minimized in the least-squares sense. In general situations the model is solved numerically using a finite-element model updating technique (FEMU).

A subcategory of inverse problem is made by identification problems. An identification problem has a finite number of unknowns and may become well-posed. This may happen in very specific situations, for instance when full-field measurements are available [4]. In that specific case, an alternative to FEMU is possible: the Virtual Fields Method (VFM), which has been shown to be more robust and efficient in these situations [5].

In this chapter, we first review different situations in computational biomechanics where an inverse problem or an identification problem has to be solved, with a particular focus on the reproduction system. After this presentation, we present in details the FEMU technique that is traditionally used to solve inverse problems. We then present sequential method based on the principle of Kalman filters for dynamic problems. Finally, we present in details the VFM and show different cases of its possible application. Eventually, research directions are proposed

for the emerging field of pelvic biomechanics and the identification of biomechanical properties using advanced imaging techniques of soft tissue strains.

5.2 Common sources of inverse problem in soft tissue biomechanics

For the sake of illustration and in order to focus on problems on which a significant research effort has been focused, the current chapter is voluntarily restricted to two main situations:

1. Reconstruction of the field of material properties in soft tissues using medical imaging techniques that are applied *in vivo*. This situation is named “elastography of soft tissue biomechanics”;
2. Identification of material constants driving the constitutive equations of soft tissues using dedicated testing where a stress strain curve fitting cannot be simply performed by reading load and displacements measurements. This situation is named “non-agreed standard testing of soft tissue biomechanics” and mostly concerns soft tissues in *ex situ* conditions.

5.2.1 Elastography of soft tissue biomechanics

This situation occurs when one wants to derive mechanical properties of soft tissues *in vivo* and *in situ*. The basic steps are: (1) subject the tissues (organs or region of the body) to a deformation, (2) measure the displacement field in the entire domain and (3) compute the mechanical properties by solving an inverse problem.

5.2.1.1 Subject the tissues to a deformation

The most common elastography technique, strain elastography (or compression elastography), relies on manually deforming a tissue with an ultrasound transducer, and inferring the stiffness of the tissue from the deformation observed in the ultrasound images. An extension of ultrasound strain elastography is acoustic radiation force impulse (ARFI) elastography. Instead of manually compressing the tissue, ARFI creates a focused ultrasound pulse that travels through the tissue. Using rapid imaging ultrasound pulse echoes, the tissue deformation can be tracked, and analyzed to provide a qualitative stiffness map. Its main advantage over strain elastography is that it is not limited to superficial tissues that can be manually deformed, although it is still limited by ultrasound penetration depths.

The most common alternative to ultrasound elastography is Magnetic Resonance Elastography (MRE), which is a magnetic resonance imaging technique that works by measuring the shear wave propagation through soft tissues [6, 7]. The shear wave is generated by an MR-compatible mechanical transducer that is synchronized to the MR image acquisition.

In vivo, non-invasive stimuli can also be employed; the most used one being the natural blood action on the arterial wall [8].

5.2.1.2 Measure the displacement fields

The displacement field may be determined using either ultrasound (see [9] for an example), computed tomography (CT) [10] or nuclear magnetic resonance (NMR) (see [11] for an example). When using NMR, displacements are calculated from the phase of the measured magnetic field and are required to be time harmonic.

In the case of ultrasound, a speckle image of the specimen in the undeformed state is recorded. Thereafter, the specimen is deformed and another speckle image is recorded. These images are registered to yield the displacement field. More recently, efforts to provide quantitative mechanical property data from ultrasound elastography led to the development of shear wave elastography, which relies on similar physical principles to MRE, where propagation of an externally imposed acoustic wave is tracked, and used to estimate the tissue shear modulus. This stimulus can be generated by ARFI, and its propagation imaged with high frame rate ultrasound, as in the supersonic elastography technique [12].

5.2.1.3 Compute the mechanical properties

Strain or compression static elastography usually assumes that regions of smaller strains indicate higher elastic modulus [13]. It is rather a technique for detecting variations in relative stiffness. The use of inversion techniques has been shown to be more robust [14, 15] but the uncertainty in the boundary conditions and in the viscoelastic effects led static elastography be preferred by transient elastography.

Transient US or MR elastography attempts to estimate the elastic properties (Young's modulus or shear modulus) of a tissue based on the relationship between mechanical properties and the propagation characteristics of mechanical vibration waves [9, 16]. The inverse problem consists in deriving the local tissue modulus from the measured displacement fields using the wave equation written in the context of linear elasticity such as

$$\rho \frac{\partial^2 \mathbf{U}}{\partial t^2} = \mu \nabla^2 \mathbf{U} + (\lambda + \mu) \nabla(\nabla \cdot \mathbf{U}) + \eta \frac{\partial \nabla^2 \mathbf{U}}{\partial t} + (\xi + \eta) \frac{\partial \nabla(\nabla \cdot \mathbf{U})}{\partial t}, \quad (1)$$

where \mathbf{U} is the displacement vector, ρ is the density of the tissue, μ is the shear modulus, λ the second Lamé coefficient, η the shear viscosity and ξ is the viscosity of the compressional wave. The variable t refers to the time. Despite some concerns over the validity of this approach, a much simplified version is often used, that estimates local wave speed from the imaging data, and calculates the shear modulus from

$$\mu = \rho v^2 \lambda^2, \quad (2)$$

where v is the frequency of the vibration and λ is the local wavelength.

While most applied studies use some form of direct numerical inversion like the one of Eq. 2, recent work is exploring the use of inversion techniques that have the potential to be more robust [14, 17–22]. They will be presented in details in the next sections of this chapter.

5.2.1.4 Applications in the pelvic system

Strain elastography of the pelvic floor carries diagnostically important information about the dynamic response of the pelvic floor muscle, which cannot be readily captured and assimilated by the observer during the scanning process. Peng et al [23] presented an ultrasound imaging presented an approach based on motion tracking quantitatively to analyze the dynamic parameters of pelvic floor muscles on the ano-rectal angle. Ami et al [24] showed that real-time ultrasonic strain elastography could provide detailed mapping and characterization of fibroids. Thyer et al [25] introduced a static-state translabial ultrasound method of measuring pubovisceral muscle strain during Valsalva and contraction.

Transient ultrasound [26, 27] and MR [28] elastography is also emerging for the pelvic system. It has been used to identify biological and technical confounders in the nonpregnant cervix when applying shear wave elastography with an endovaginal transducer [26, 27]. The frequency-dependent elastic moduli of human uterine tissue have also been characterized by Kiss et al [29] and some promising results have been obtained with *ex vivo* uteri by Hobson et al [30].

5.2.2 Non destructive invasive techniques

Whereas elastography seeks at imaging strains or material properties in soft tissues, less sophisticated techniques can simply apply some load on a tissue and measure the induced deformation at a given point. This can also be a source of inverse problems, which will not be presented in this chapter, as we eventually focus on problems involving imaging techniques and full-field measurements. We simply mention the well-known palpation technique and the technique of tissue aspiration, both involved in an interesting study related to the reproduction system conducted by Egorov et al [31]. Their approach, called vaginal tactile imaging, allowed biomechanical mapping of the female pelvic floor to quantify tissue elasticity, pelvic support, and pelvic muscle functions. An explicit axisymmetric finite element simulation of the aspiration experiment was used together with a Levenberg–Marquardt algorithm to estimate the material model parameters in an inverse parameter determination process (as described in section 3.3.1).

5.2.3 Non agreed standard testing of soft tissue biomechanics

Thousands of scientific publications provide material properties of soft tissues that were obtained by characterizing test samples excised from a dead body (cadaver). This is a source of many inverse problems [32–34]. Indeed, for many technical materials it is relatively easy to make test samples according to the agreed standards, but for most biological materials this is much more difficult due to a number of reasons listed below:

1. To create a sample it has to be taken out of a body. If it concerns human tissue it is either left over material of surgery or post mortem material. Another option is to use tissue from

animals. In all situations the material is taken out of the body, so it loses part of its integrity, the pretension found in the living system is (partly) gone or difficult to maintain, the tissue is no longer supplied with blood and will start to deteriorate quickly. However, when isolated and preserved in a proper way the negative effects of making samples of biological materials can be reduced considerably and the parameters may change, but the physical behavior will be similar to the behavior *in vivo*. Also during testing the physical and chemical environment of the material has to be controlled (humidity, temperature).

2. It is extremely difficult to make samples according to the standards (for example a dogbone shape of a soft biological material). The amount of material available is usually small or very small. Clamping is a big issue.

3. Often the material has inhomogeneous properties, so the assumption in standard tests that the stress strain field is homogeneous is not a valid assumption.

4. Especially for soft biological materials the samples can be stretched to very high deformations, they behave highly nonlinear and visco-elastic so the strain and strain rate history play an important role and localization effects appear even if they have to be neglected in standard tests.

Despite the difficulties given above, standard tests are done quite often because they are well defined and they constitute the only way to gain a good understanding of the physical behavior of the material and to define constitutive equations [32]. Some of the above problems can be circumvented or partly solved by using inverse methods. The biggest advantage of inverse methods is the enormous freedom that is created to design experiments alleviating some of the difficulties encountered in standard tests. The main inverse methods will be presented in details in the following sections.

Concerning the reproduction system, as for other tissues, knowledge of biomechanical properties is critical to further developing accurate surgical techniques and physiological prosthetic materials. The elastic properties of the pubovisceral muscle are likely to be important for pelvic organ support. However, published data are scarce. We mention here the recent biomechanical uniaxial tension tests performed on pelvic floor tissues (ligaments and organs) by Chanterreau et al [35] who characterized the mechanical properties of young pelvic soft tissues.

5.3 The finite element model updating method

5.3.1 Useful definitions and concepts

5.3.1.1 Deformation tensors

Deformations are mathematically described as functions, which map the material description X (spatial description in the reference configuration) onto the spatial description x in the current configuration such as

$$\mathbf{x} = \boldsymbol{\phi}(\mathbf{X}, t), \quad (3)$$

$$\mathbf{X} = \boldsymbol{\phi}^{-1}(\mathbf{x}, t). \quad (4)$$

The displacement vector is defined as: $\mathbf{U}(\mathbf{X}, t) = \mathbf{x} - \mathbf{X} = \boldsymbol{\phi}(\mathbf{X}, t) - \mathbf{X}$.

The velocity is defined by taking time derivatives of the mapping as follows,

$$\dot{\mathbf{U}}(\mathbf{X}, t) = \left[\frac{\partial \boldsymbol{\phi}(\mathbf{X}, t)}{\partial t} \right]_{\mathbf{X}}. \quad (5)$$

It can also be expressed in terms of the spatial description by inserting the inverse mapping

$$\mathbf{v}(\mathbf{x}, t) = \dot{\mathbf{U}}(\boldsymbol{\phi}^{-1}(\mathbf{x}, t), t). \quad (5)$$

The deformation gradient for this motion is

$$\mathbf{F}(\mathbf{X}, t) = \frac{\partial \boldsymbol{\phi}(\mathbf{X}, t)}{\partial \mathbf{x}}. \quad (6)$$

The right Cauchy Green and left Cauchy Green stretch tensor are respectively

$$\mathbf{C} = \mathbf{F}^T \mathbf{F}, \quad (7)$$

$$\mathbf{B} = \mathbf{F} \mathbf{F}^T. \quad (8)$$

The Green-Lagrange strain tensor is:

$$\mathbf{E} = \frac{1}{2}(\mathbf{C} - \mathbf{1}), \quad (9)$$

where $\mathbf{1}$ is the identity tensor.

5.3.1.2 Stress tensors

The first stress tensor that has to be introduced is the Cauchy stress tensor $\boldsymbol{\sigma}$. It gives us the stress state in the deformed body. It is defined in the spatial configuration. The traction vector \mathbf{t} obtained from the application of the surface normal in the spatial (deformed) configuration \mathbf{n} is called the Cauchy traction vector

$$\mathbf{t} = \boldsymbol{\sigma} \cdot \mathbf{n}. \quad (10)$$

Since it gives us the actual stress of the body, the Cauchy stress is called the true stress in engineering.

It is convenient to define the second Piola-Kirchhoff stress tensor \mathbf{S} through a push-forward such as

$$\mathbf{S} = J \mathbf{F}^{-1} \boldsymbol{\sigma} \mathbf{F}. \quad (11)$$

where $J = \det(\mathbf{F})$. The \mathbf{S} tensor is defined for the reasons that it is a material tensor which is defined in the reference configuration and that it is the work conjugate of the Green-Lagrange strain tensor \mathbf{E} enabling one to define different constitutive equations. It also has the attractive property that it is symmetric.

5.3.1.3 Constitutive equations

For the sake of illustration, we restrict the presentation of inversion techniques of this chapter to the identification of a single specific hyperelastic model often used for soft biological tissues of the reproduction system. In hyperelasticity, the existence of a strain energy density

function is assumed, from which a constitutive relation between stress and strain is derived. The total energy that is needed to deform the body is only dependent on the initial and the end state, that is, the state of the body is independent of the loading path.

Let us illustrate this throughout the whole chapter with the following strain energy function defined for incompressible solids [36]

$$\psi = \frac{\mu_1}{2}(I_1 - 3) + \frac{\mu_2}{4\gamma} (e^{\gamma(I_\kappa - 1)^2} - 1), \quad (12)$$

where μ_1 , μ_2 , and γ are material parameters, I_1 is an invariant defined such as

$$I_1 = \text{tr}(\mathbf{C}), \quad (13)$$

and I_κ is a compound invariant consisting of isotropic and anisotropic contributions defined such as

$$I_\kappa = \mathbf{C} : (\kappa \mathbf{1} + (1 - 2\kappa)\mathbf{M} \otimes \mathbf{M}), \quad (14)$$

where the unit vector $\mathbf{M} = \cos\theta \mathbf{e}_1 + \sin\theta \mathbf{e}_2$ defines the orientation along which the tissue is stiffest while κ characterizes the degree of anisotropy, varying between 0 and 1.

When $\kappa = 0$, it would model a composite with all the fibers perfectly aligned in the direction \mathbf{M} and at $\kappa = 1$ the fibers would be perfectly aligned in the perpendicular direction, \mathbf{M}^\perp . Finally, $\kappa = 1/2$ models the case where fibers would have no preferential direction (isotropic). The parameters μ_1 and μ_2 are the effective stiffnesses of the matrix and fiber phases, respectively, both having dimensions of force per unit length. The γ parameter is a non-dimensional parameter that governs the tissue's strain stiffening response.

The second Piola-Kirchhoff stress tensor, \mathbf{S} , is written as

$$\mathbf{S} = 2 \frac{\partial \psi}{\partial I_1} \mathbf{1} + 2 \frac{\partial \psi}{\partial I_\kappa} (\kappa \mathbf{1} + (1 - 2\kappa)\mathbf{M} \otimes \mathbf{M}) + p \mathbf{C}^{-1}, \quad (15)$$

where p is a Lagrange multiplier accounting for the condition of incompressibility.

It gives after substitution

$$\mathbf{S} = \mu_1 \mathbf{1} + \mu_2 e^{\gamma(I_\kappa - 1)^2} (\kappa \mathbf{1} + (1 - 2\kappa)\mathbf{M} \otimes \mathbf{M}) + p \mathbf{C}^{-1}. \quad (16)$$

The Cauchy stress is given by

$$\boldsymbol{\sigma} = \mu_1 \mathbf{B} + \mu_2 e^{\gamma(I_\kappa - 1)^2} (\kappa \mathbf{B} + (1 - 2\kappa)\mathbf{m} \otimes \mathbf{m}) + p \mathbf{1}, \quad (17)$$

where

$$\mathbf{m} = \mathbf{F}\mathbf{M}. \quad (18)$$

The material parameters μ_1 , μ_2 , γ , κ and θ , including parameters describing their possible regional variations, are represented onwards with a unique vector denoted β .

5.3.2 Forward problem

The mechanical fields across the reference domain, denoted Ω_0 , are governed by the equations of dynamics. The solution of these governing equations by a numerical method is the so-called forward problem. In this section, we will simplify the problem by leaving aside the

acceleration forces (static problem). Dynamic problems will be discussed in the following section dedicated to sequential methods.

5.3.2.1 Strong form

The strong form of the quasi-static problem is: find the displacement field \mathbf{U} and the pressure p such as

$$\text{Div}[\mathbf{FS}] = \mathbf{0} \text{ on } \Omega_0, \quad (19a)$$

$$\mathbf{U} = \mathbf{g} \text{ on } \Gamma_g, \quad (19b)$$

$$\mathbf{FS} \cdot \mathbf{N} = \mathbf{t} \text{ on } \Gamma_t, \quad (19c)$$

where Ω_0 is the domain of interest, Γ_t is the boundary of the domain where tractions are applied while Γ_g is the boundary of the domain where displacements are assigned. The whole boundary of the domain is defined such as

$$\partial\Omega_0 = \Gamma_g \cup \Gamma_t, \quad (19d)$$

The equations are completed with the incompressibility constraint

$$\det(\mathbf{F}) - 1 = 0 \text{ on } \Omega_0. \quad (19e)$$

As mentioned above, this problem statement must be augmented by the stress–strain relation to specify the stress in terms of the deformation (Eq. 16 or 17).

5.3.2.2 Weak form

The weak form can be derived easily from the strong form by multiplying Eq. 19 with a vector test function, integrating-by-parts over the reference domain, and utilizing the traction boundary condition. The incompressibility constraint is multiplied by another scalar test function and integrated over the reference domain. The weak form is given by: find $\underline{U} \equiv [\mathbf{U}, p]$ such as

$$\mathcal{A}(\underline{W}, \underline{U}; \beta) - (\mathbf{w}, \mathbf{t})_{\Gamma_t} = 0 \quad \forall \underline{W} \equiv (\mathbf{w}, q) \in V \times P, \quad (20)$$

where \mathcal{A} is an operator defined such as

$$\mathcal{A}(\underline{W}, \underline{U}, \beta) = \int_{\Omega_0} \nabla \mathbf{w} : [\mathbf{FS}] d\Omega_0 + \int_{\Omega_0} (J - 1) q d\Omega_0, \quad (21a)$$

and $(\cdot, \cdot)_{\Gamma_t}$ is the $L^2(\Gamma_t)$ inner product evaluated over the Γ_t reference boundary domain such as

$$(\mathbf{w}, \mathbf{t})_{\Gamma_t} = \int_{\Gamma_t} \mathbf{w} \cdot \mathbf{t} dS_0, \quad (21b)$$

whereas V , S and P are vectorial spaces of second order tensors defined such as

$$V = \{\mathbf{w} | \mathbf{w}_i \in H^1(\Omega_0), \mathbf{w}_i = 0 \text{ on } \Gamma_g\}, \quad (22)$$

$$S = \{\mathbf{u} | \mathbf{u}_i \in H^1(\Omega_0), \mathbf{u}_i = \mathbf{g}_i \text{ on } \Gamma_g\}, \quad (23)$$

$$P \subseteq L^2(\Omega_0). \quad (24)$$

The weak form may be discretized by selecting finite dimensional spaces $S^h \subset S$, $V^h \subset V$ and $P^h \subset P$ and using Galerkin's approach. This leads to a nonlinear algebraic problem for the displacement and pressure degrees of freedom that may be solved using the Newton Raphson method. It can be solved uniquely for every feasible set of material parameters and arbitrary geometries and leads to a nonlinear system of equations of the type

$$\mathcal{A}(\underline{W}^h, \underline{U}^h; \beta) - (\mathbf{w}^h, \mathbf{t}^h)_{\Gamma_t} = 0. \quad (25)$$

Starting with an initial vector $\underline{U}^h(0)$, the resolution consists in recursively linearizing the nonlinear system of equations around $\underline{U}^h(n)$ assuming

$$\underline{U}^h(n+1) = \underline{U}^h(n) + \epsilon \delta \underline{U}^h(n), \quad (26)$$

$$\mathcal{A}(\underline{W}^h, \underline{U}^h(n+1); \beta) = \mathcal{A}(\underline{W}^h, \underline{U}^h(n); \beta) + \epsilon \mathcal{B}(\underline{W}^h, \delta \underline{U}^h(n); \beta, \underline{U}^h(n)), \quad (27)$$

where \mathcal{B} is an operator defined such as

$$\mathcal{B}(\underline{W}, \delta \underline{U}; \beta, \underline{U}) = \lim_{\epsilon \rightarrow 0} \frac{d}{d\epsilon} \mathcal{A}(\underline{W}, \underline{U} + \delta \underline{U}; \beta), \quad (28)$$

$$\mathcal{B}(\underline{W}, \delta \underline{U}; \beta, \underline{U}) = (\underline{W}, \underline{K}(\beta, \underline{U}) \cdot \delta \underline{U})_{\Omega_0} = (\underline{K}^T(\beta, \underline{U}) \cdot \delta \underline{U}, \underline{W})_{\Omega_0}, \quad (29)$$

where $(\cdot, \cdot)_{\Omega_0}$ is the $L^2(\Omega_0)$ inner product evaluated in the Ω_0 reference domain, $\underline{K}(\beta, \underline{U})$ is a linear operator defined in the $S \times P$ space transforming any field \underline{W} in $\underline{K}(\beta, \underline{U}) \cdot \underline{W}$, whereas $\underline{K}^T(\beta, \underline{U})$ is the adjoint of $\underline{K}(\beta, \underline{U})$.

5.3.3 Inverse problem

5.3.3.1 Definition of the cost function

The inverse problem consists in the reconstruction of the material and geometric parameters, β , given the relevant (measured) displacements fields \mathbf{U}_{meas} .

The inverse problem is stated as follows: given n_{meas} measured displacement fields $\mathbf{U}_{\text{meas}}^1, \mathbf{U}_{\text{meas}}^2, \dots, \mathbf{U}_{\text{meas}}^n$, find the N_β material properties $\beta = [\beta_1, \beta_2, \dots, \beta_{N_\beta}]$ such that the objective function

$$\pi(\beta) = \frac{1}{2} \sum_{i=1}^{n_{\text{meas}}} w_i \|\mathbf{T}\mathbf{U}^i - \mathbf{T}\mathbf{U}_{\text{meas}}^i\|^2 + \frac{1}{2} \sum_{j=1}^{N_\beta} \alpha_j R(\beta_j) \quad (30)$$

is minimized under the constraint that the displacement fields satisfy the equilibrium equations written in their weak form in Eq. 20 or after discretization in Eq. 25 (for the sake of simplification, no difference is made anymore in the notation between discretized and continuous variables onwards). In Eq. 30, each field \mathbf{U}^i correspond to a different set of boundary conditions \mathbf{t}^i , for instance corresponding to different time steps t_i of overall loading. Since we expect their magnitudes to be quite different at each step i , each displacement field is multiplied by a weighting factor w_i , which is selected to ensure that the contributions to the objective function

from all measurements are of the same order. The tensor \mathbf{T} is selected to possibly weight different components of displacement differently.

The second term is the regularization term where α_j is the regularization parameter. This has to be chosen appropriately depending on the noise level in the measured displacements and on the illposedness of the problem. The regularization term can be thought of as a penalty term in the objective function that ensures a certain smoothness to the reconstructed material properties. A possible function proposed by the group of Oberai and Barbone [19–21] is

$$R(\beta_j) = \int_{\Omega_0} \sqrt{|\nabla\beta_j|^2 + c^2} d\Omega_0. \quad (31)$$

where $\nabla\beta_j$ is the gradient of material properties and c is a coefficient controlling the regularization [19–21].

The objective function defined in Eq. 30 is usually minimized using a gradient based optimization method [19–21]. For this, we need an efficient way to compute the gradient of this function with respect to the material properties. If we represent the regional variations of material properties using N piece-wise linear finite-element shape functions whose nodal values are the parameters of the inverse problem and if we consider the use of gradient-based algorithms, we can show that a straightforward calculation of the gradient requires N solves of the forward elasticity problem. This cost is computationally prohibitive for typical values of N . To circumvent this difficulty, the adjoint method, which requires only two solves (independent of N) to compute the gradient, is the most appropriate.

5.3.3.2 The adjoint method

In order to evaluate the gradient vector, the adjoint equations can be derived at the continuous or the discrete level. Changing β by a small (infinitesimal) amount $\delta\beta$ will cause the displacement fields \mathbf{U}^i to change of a small amount $\delta\mathbf{U}^i$ and the pressure p will change accordingly of a small amount δp . The relationship between $\delta\mathbf{U}^i$ and $\delta\beta$ can be obtained by differentiating Eq. 20 with respect to \mathbf{U} and β . One obtains

$$\mathcal{B}(\underline{W}, \delta\mathbf{U}^i; \beta, \mathbf{U}^i) + \mathcal{C}(\underline{W}, \delta\beta; \mathbf{U}^i, \beta) = 0, \quad (32)$$

where \mathcal{C} is an operator defined such as

$$\mathcal{C}(\underline{W}, \delta\beta; \mathbf{U}^i, \beta) = \lim_{\epsilon \rightarrow 0} \frac{d}{d\epsilon} \mathcal{A}(\underline{W}, \mathbf{U}^i; \beta + \epsilon\delta\beta). \quad (33)$$

Similarly, differentiating the objective function gives

$$D_\beta \pi(\beta, \delta\beta) = \sum_{i=1}^{n_{\text{meas}}} (w_i \mathbf{T} \delta\mathbf{U}^i, \mathbf{T} \mathbf{U}^i - \mathbf{T} \mathbf{U}_{\text{meas}}^i)_{\Omega_0} + \frac{1}{2} \sum_{j=1}^{N_\beta} \alpha_j D_\beta R(\beta_j, \delta\beta_j). \quad (34)$$

where D_β denotes the differentiation with respect to the components of β .

To compute the gradient of our objective function, one could select a basis on which to represent $\delta\beta$. Then for each basis vector, one solves Eq. 32 for $\delta\mathbf{U}^i$. Finally Eq. 34 can be used to compute the gradient for that single component of β . One would then select the next basis vector for $\delta\beta$, and repeat the process.

A particularly efficient alternative to the brute force method just described is to use the adjoint equations. The following (linear) boundary value problems is introduced for the n_{meas} functions $\underline{W}^i \in V \times P$ such as

$$\mathcal{B}(\underline{W}^i, \underline{V}; \beta, \underline{U}^i) + (w_i \mathbf{TV}, \mathbf{TU}^i - \mathbf{TU}_{\text{meas}}^i)_{\Omega_0} = 0 \quad \forall \underline{V} \equiv [\mathbf{V}, q] \in V \times P. \quad (35)$$

Introducing the linear operator $\underline{\underline{K}}^T(\beta, \underline{U}^i)$, one obtains

$$\left(\underline{\underline{K}}^T(\beta, \underline{U}^i) \cdot \underline{W}^i, \underline{V} \right)_{\Omega_0} + (w_i \mathbf{TV}, \mathbf{TU}^i - \mathbf{TU}_{\text{meas}}^i)_{\Omega_0} = 0 \quad \forall \underline{V} \equiv [\mathbf{V}, q] \in V \times P, \quad (36)$$

which finally can be written such as

$$\underline{\underline{K}}^T(\beta, \underline{U}^i) \cdot \underline{W}^i = \mathbf{TU}^i - \mathbf{TU}_{\text{meas}}^i. \quad (37)$$

In terms of \underline{W}^i , we now may compute the gradient as follows. First, we note that since $\delta\mathbf{U}^i \in V \times P$, we may replace \underline{V} in Eq. 36 with $\delta\mathbf{U}^i$. This gives

$$\mathcal{B}(\underline{W}^i, \delta\mathbf{U}^i; \beta, \underline{U}^i) + (w_i \mathbf{TV}, \mathbf{TU}^i - \mathbf{TU}_{\text{meas}}^i)_{\Omega_0} = 0. \quad (37)$$

Similarly, since $\underline{W}^i \in V \times P$ we may replace \underline{W} in Eq. 32 with \underline{W}^i . This gives

$$\mathcal{B}(\underline{W}^i, \delta\mathbf{U}^i; \beta, \underline{U}^i) + \mathcal{C}(\underline{W}^i, \delta\beta; \underline{U}^i, \beta) = 0. \quad (38)$$

We now subtract Eq. 38 from Eq. 37 to find

$$(w_i \mathbf{TV}, \mathbf{TU}^i - \mathbf{TU}_{\text{meas}}^i)_{\Omega_0} = \mathcal{C}(\underline{W}^i, \delta\beta; \underline{U}^i, \beta). \quad (39)$$

Eq. 39 shows that once we have computed \underline{W}^i , we can directly evaluate the gradient of our data matching term for any number of $\delta\beta$ directions without solving another boundary value problem. The final expression for the gradient results by substituting Eq. 39 into Eq. 34 to obtain

$$D_{\beta}\pi(\beta, \delta\beta) = \sum_{i=1}^{n_{\text{meas}}} \mathcal{C}(\underline{W}^i, \delta\beta; \underline{U}^i, \beta) + \frac{1}{2} \sum_{j=1}^{N_{\beta}} \alpha_j D_{\beta} R(\beta_j, \delta\beta_j). \quad (40)$$

5.3.3.3 Minimization of the cost function and resolution of the inverse problem

In a finite-element implementation all variables including displacement, pressure and material properties, can be represented by linear finite element basis functions. The optimization variables are the nodal values of the material parameters, and the gradient with respect to these variables is given by Eq. 40 such as

$$\mathbf{g} = D_{\beta}\pi(\beta, \delta\beta). \quad (41)$$

More precisely, we can represent with the same shape functions as for the displacement and the pressure fields. Then the discrete gradient vector $\nabla\pi(\beta)$ may be given by each of its j_A component which are defined such as

$$\begin{aligned} g_{j_A}(\beta) &= D_\beta \pi(\beta, N_A(X)e_j) \\ &= \sum_{i=1}^{n_{\text{meas}}} c(\underline{W}^i, N_A(X)e_j; \underline{U}^i, \beta) + \frac{1}{2} \sum_{j=1}^{N_\beta} \alpha_j D_\beta R(\beta_j, N_A(X)e_j), \end{aligned} \quad (41)$$

where e_j is a N_β dimensional vector with 1 in the j th component and zeros everywhere else.

In the case of a linear behavior, one can define the linear operator $\underline{\underline{K}}_j(\beta, \underline{U}^i)$, which operates over the $S \times P$ space according to

$$\lim_{\epsilon \rightarrow 0} \frac{d}{d\epsilon} \mathcal{A}(\underline{W}^i, \underline{U}^i; \beta + \epsilon N_A(X)e_j) = \left(\underline{W}^i, \underline{\underline{K}}_j(\beta, \underline{U}^i) \cdot \underline{U}^i \right)_{\Omega_0}. \quad (42)$$

Having an efficient method to derive the gradient of the cost function, an iterative algorithm can be implemented to find the optimum value. Starting with an initialization β_0 , the algorithm of the steepest descent tries for to find a scalar α such as the cost function $\pi(\alpha) = \pi(\beta_n + \alpha g_{j_A}(\beta))$ reaches its minimum at $\beta_{n+1} = \beta_n + \alpha g_{j_A}(\beta)$ (line search).

The initial guess β_0 for the material parameters is usually homogeneous and then the gradient is calculated using the procedure described above, the whole process being repeated until convergence.

A more efficient algorithm than the steepest descent is the BFGS method. In numerical optimization, the Broyden–Fletcher–Goldfarb–Shanno (BFGS) algorithm is an iterative method for solving unconstrained nonlinear optimization problems. The search direction p_n at stage n is given by the solution of the analogue of the Newton equation

$$B_n p_n = -\nabla\pi(\beta_n), \quad (43)$$

where B_n is an approximation to the Hessian matrix which is updated iteratively at each stage, and $\nabla\pi(\beta_n)$ is the gradient of the cost function evaluated at β_n . A line search in the direction p_n is then used to find the next point β_{n+1} . Instead of requiring the full Hessian matrix at the point β_{n+1} to be computed as B_{n+1} , the approximate Hessian at stage n is updated by the addition of two matrices according to

$$B_{n+1} = B_n + U_n + V_n. \quad (44)$$

Both U_n and V_n are symmetric rank-one matrices, but their sum is a rank-two update matrix. From an initial guess β_0 and an approximate Hessian matrix B_0 the following steps are repeated as β_n converges to the solution.

1. Obtain a direction p_n by solving:

$$B_n p_n = -\nabla\pi(\beta_n). \quad (45)$$

2. Set $s_n = \alpha_n p_n$.

3. Perform a line search to find an acceptable stepsize α_n in the direction found in the first step, then update $\beta_{n+1} = \beta_n + s_n$.

$$4. y_k = \nabla\pi(\beta_{n+1}) - \nabla\pi(\beta_n). \quad (46)$$

$$5. B_{n+1} = B_n + \frac{y_n y_n^T}{y_n^T s_n} - \frac{B_n s_n s_n^T B_n}{s_n^T B_n s_n}. \quad (47)$$

Practically, B_0 can be initialized with $B_0 = I$, so that the first step will be equivalent to a gradient descent, but further steps are more and more refined by B_n , the approximation to the Hessian.

5.3.4 Applications to the pelvic system

FEMU was previously applied to the pelvic system by Silva et al [37, 38]. They used an inverse finite element analysis to calculate the Mooney–Rivlin constitutive model parameters for the passive mechanical behavior of the pelvic floor muscles. The numerical model of the pelvic floor muscles and bones was built from magnetic resonance axial images acquired at rest. Note also that Kauer et al. [17] applied FEMU with the tissue aspiration technique to estimate in vivo soft tissue material model parameters in the pelvic system.

5.4 Sequential methods

The FEMU approach presented in the previous section, which consists in minimizing a least-squares criterion which includes a regularization term and the difference between the observations and the model prediction, is often called a variational approach. When one has to model a **dynamic** system, as in the case of fluid-structure interactions (FSI) for hemodynamics, one of the main difficulties of a variational approach like the FEMU method lies in the iterative evaluation of the criterion, involving many solutions of the forward problem, and its gradient – typically adjoint-based – which usually requires a laborious implementation.

Alternatively, a sequential approach, based on a generalization of the Kalman filter, can be implemented. With sequential algorithms, the model prediction is improved at every time instant by analyzing the discrepancy between the actual measurements and the model observation outputs [39]. In the fully linear case, it was proved that the Kalman filter gives the same result as a variational approach based on a least squares criterion.

Let $\mathbf{U}^i = \mathbf{U}(t_i)$ be the state variable at every time step t_i (typically \mathbf{U}^i denotes in this section the finite element approximation of the displacements and the velocities in the soft tissue and possibly in a surrounding fluid). We assume that the state variable satisfies nonlinear dynamics equations, without any model uncertainties, and that this may bring the following equation

$$\mathbf{U}^{i+1} = \mathbf{A}(\mathbf{U}^i, \mathbf{t}^{i+1}; \beta), \quad (47)$$

where \mathbf{t}^{i+1} represent the loading and β represent the vector of model parameters to be identified.

We suppose that measurement observations are available at t_i

$$\mathbf{U}_{\text{meas}}(t_i) = \mathbf{U}_{\text{meas}}^i = \mathbf{H}\mathbf{U}^i + \boldsymbol{\zeta}(t_i), \quad (48)$$

where \mathbf{H} represents an observation operator applied to the real state variable $\mathbf{U}^i = \mathbf{U}(t_i)$ and $\boldsymbol{\zeta}(t_i)$ includes the measurement noise and the discretization error. Measurements are assumed to be available at every time step t_i , $1 \leq i \leq n_{\text{meas}}$.

In a sequential approach, the inverse problem can be viewed as minimizing a cost function at every time step t_i like

$$\begin{aligned} \pi(\mathbf{U}^{i+1}, \beta^{i+1}) = & \frac{1}{2} \|\mathbf{U}_{\text{meas}}^{i+1} - \mathbf{H}\mathbf{U}^{i+1}\|_{W^{-1}}^2 + \frac{1}{2} \|\beta^{i+1} - \beta^i\|_{(P_i^\beta)^{-1}}^2 \\ & + \frac{1}{2} \|\mathbf{U}^{i+1} - \mathbf{A}(\mathbf{U}^i, \mathbf{t}^{i+1}; \beta^i)\|_{(P_i^U)^{-1}}^2. \end{aligned} \quad (49)$$

In this expression, $\|\cdot\|_{W^{-1}}^2$, $\|\cdot\|_{(P_i^\beta)^{-1}}^2$ and $\|\cdot\|_{(P_i^U)^{-1}}^2$ denote some norms used to measure the observations, the parameters and the state, respectively. These norms give a different weight to the different terms and therefore accounting for the ‘‘confidence’’ in the different quantities. From a statistical viewpoint, the ‘‘confidence’’ can be viewed as the inverse of covariance matrices (W , P_i^β and P_i^U), which explains the notation. It is important to notice that P_i^β and P_i^U are updated at every time step as the confidence in the model increases. The cost function may be rewritten such as

$$\begin{aligned} \pi(\mathbf{U}^{i+1}, \beta^{i+1}) = & \frac{1}{2} (\mathbf{U}_{\text{meas}}^{i+1} - \mathbf{H}\mathbf{U}^{i+1})^T W^{-1} (\mathbf{U}_{\text{meas}}^{i+1} - \mathbf{H}\mathbf{U}^{i+1}) + \frac{1}{2} (\beta^{i+1} - \beta^i)^T (P_i^\beta)^{-1} (\beta^{i+1} - \beta^i) \\ & + \frac{1}{2} (\mathbf{U}^{i+1} - \mathbf{A}(\mathbf{U}^i, \mathbf{t}^{i+1}; \beta^i))^T (P_i^U)^{-1} (\mathbf{U}^{i+1} - \mathbf{A}(\mathbf{U}^i, \mathbf{t}^{i+1}; \beta^i)). \end{aligned} \quad (50)$$

The sequential approach, also known as filtering, addresses the minimization problem in the following way: it modifies the predictions ($\beta^{i+1} = \beta^i$ and $\mathbf{U}^{i+1} = \mathbf{A}(\mathbf{U}^i, \mathbf{t}^{i+1}; \beta^i)$) with a correction term that takes into account the discrepancy between actual measurements and observations generated by the model such as

$$\mathbf{U}^{i+1} = \mathbf{A}(\mathbf{U}^i, \mathbf{t}^{i+1}; \beta^i) + \mathbf{K}^U (\mathbf{U}_{\text{meas}}^{i+1} - \mathbf{H}\mathbf{A}(\mathbf{U}^i, \mathbf{t}^{i+1}; \beta^i)), \quad (51)$$

$$\beta^{i+1} = \beta^i + \mathbf{K}^\beta (\mathbf{U}_{\text{meas}}^{i+1} - \mathbf{H}\mathbf{A}(\mathbf{U}^i, \mathbf{t}^{i+1}; \beta^i)). \quad (52)$$

The quantity $\mathbf{U}_{\text{meas}}^{i+1} - \mathbf{H}\mathbf{A}(\mathbf{U}^i, \mathbf{t}^{i+1}; \beta^i)$ is known as the innovation, and the operators \mathbf{K}^U and \mathbf{K}^β depend on the method. For linear problems, the most famous sequential approach is the Kalman filter.

Concerning the computational complexity, whereas the variational method has to solve several forward and adjoint problems on the whole interval $[t_0, t_{n_{\text{meas}}}]$, the estimation in the sequential algorithm is computed by solving only once the filtered dynamics. However, the optimal the operators \mathbf{K}^U and \mathbf{K}^β are determined by operations (multiplications, inversions,

etc.) involving full matrices of the size of the state and the observations, which may make Kalman-based filters prohibitive for discrete problems derived from partial differential equations (PDEs).

The Kalman filter presented above is only valid when the dynamics and the observation operator are linear. In case of nonlinear operator, as it is the case for the hyperelastic identification problem considered in this chapter, the most straightforward extension consists in deriving tangent operators at every time step. This is the extended Kalman filter. However it has two drawbacks: the computation of tangent operators and the precision of the estimated values. The latter is critical as it can be shown that when $\zeta(t_i)$ is a white Gaussian noise, the nonlinear operators propagate a bias in the results. This is commonly circumvented by using the Unscented Kalman Filter [39], which instead of deriving tangent operators, approximates the operators \mathbf{K}^U and \mathbf{K}^β from the values taken by the nonlinear operators at a set of vectors chosen initially and called particles.

5.5 The virtual fields method

5.5.1 General introduction

The Virtual Fields Method (VFM) was developed to identify the parameters governing constitutive equations, the experimental data processed for this purpose being displacement or strain fields. It will be shown in this chapter that one of its main advantages is the fact that, in several cases, the sought parameters can be directly found from the measurements, without resorting to finite-element analysis.

The VFM relies on the Principle of Virtual Power (PVP), which is written with particular virtual fields. It represents in fact the weak form the local equations of equilibrium which are classically introduced in mechanics of deformable media. Assuming a quasi-static transformation (absence of acceleration forces) and assuming the absence of body forces, the PVP can be written as follows for any domain defined by its volume Ω_{t_i} in the current configuration and by its external boundary $\partial\Omega_{t_i}$

$$- \underbrace{\int_{\Omega_{t_i}} \boldsymbol{\sigma} : (\nabla \otimes \mathbf{v}^*) d\omega}_{W_{int}^*} + \underbrace{\int_{\partial\Omega_{t_i}} \mathbf{t}^i \cdot \mathbf{v}^* ds}_{W_{ext}^*} = 0 \quad , \quad (53)$$

where $\boldsymbol{\sigma}$ is the Cauchy stress tensor, \mathbf{v}^* is a virtual velocity field defined across the volume of the solid, $\nabla \otimes \mathbf{v}^*$ is the gradient of \mathbf{v}^* , \mathbf{t}^i are the tractions across the boundary (surface denoted $\partial\Omega_{t_i}$), W_{int}^* is the virtual power of internal forces and W_{ext}^* is the virtual power of external forces.

A very important property is in fact that the equation above is satisfied for any kinematically admissible (KA) virtual field \mathbf{v}^* . By definition, a KA virtual field must satisfy the boundary conditions of the actual velocity field in order to cancel the contribution of the

resulting forces on the portion of the boundary along which actual displacement are prescribed. It must be pointed out that this requirement is not really necessary in all cases, but this point is not discussed here for the sake of simplicity. KA virtual fields are also assumed to be \mathcal{C}^0 functions.

The principle of virtual power (PVP) has been used for the identification of material properties since 1990 [40] through the virtual fields method (VFM), which is an inverse method based on the use of full-field deformation data. The first step of the VFM consists in introducing the constitutive equations. In the case of hyperelasticity and still neglecting acceleration forces, Eq. 53 becomes

$$- \int_{\Omega_{t_i}} (J^i)^{-1} \mathbf{F}^i \frac{\partial \psi}{\partial \mathbf{E}^i} (\mathbf{F}^i)^T : (\nabla \otimes \mathbf{v}^*) d\Omega_{t_i} + \int_{\partial\Omega_{t_i}} \mathbf{t}^i \cdot \mathbf{v}^* ds = 0 , \quad (54)$$

where \mathbf{F}^i and \mathbf{E}^i are respectively the Cauchy Green stretch and the Green Lagrange strain tensors derived from the measured displacement field \mathbf{U}^i at time step t_i , and $J^i = \det(\mathbf{F}^i)$. This supposes implicitly that \mathbf{F}^i can be reconstructed across the whole domain using the measured displacement fields [41, 42].

Eq. 54 being satisfied for any KA virtual field, any new KA virtual field provides a new equation. The VFM relies on this property by writing this equation above with a set of KA virtual fields chosen *a priori* [5]. The number of virtual fields and their type depend on the nature of the strain energy function. Two different cases can be distinguished:

1. the strain energy density function depends linearly on the sought parameters. Writing Eq. 54 with as many virtual fields as unknowns leads to a system of linear equations which provides the sought parameters after inversion.

2. the strain energy density function involve nonlinear relations with respect to the constitutive parameters. In this case, identification must be performed by minimizing a cost-function derived from Eq. 54.

With our constitutive equation defined in Eq. 12, we obtain:

$$- \int_{\Omega_{t_i}} \mu_1 \mathbf{B}^i : (\nabla \otimes \mathbf{v}^*) d\Omega_{t_i} - \int_{\Omega_{t_i}} \mu_2 e^{\gamma(I_k^i - 1)^2} (\kappa \mathbf{B}^i + (1 - 2\kappa) \mathbf{m}^i \otimes \mathbf{m}^i) : (\nabla \otimes \mathbf{v}^*) d\Omega_{t_i} +$$

$$- \int_{\Omega_{t_i}} p^i \nabla \cdot \mathbf{v}^* d\Omega_{t_i} = \int_{\partial\Omega_{t_i}} \mathbf{t}^i \cdot \mathbf{v}^* ds . \quad (55)$$

Measurements usually provide the deformed configuration so it is convenient that this equation is written in the deformed configuration.

The equation is valid for any virtual fields. As we are not interested in p^i , it has been shown that \mathbf{v}^* should be chosen such as: $\nabla \cdot \mathbf{v}^* = 0$.

Other rules for choosing appropriate virtual fields are very specific to each problem. A systematic choice was proposed for linear elastic constitutive equations [43, 44] and further extended to elastoplasticity [45] and hyperelasticity [46]. These virtual fields were optimized for minimizing noise effects in the case of linear elasticity. In the case of hyperelastic constitutive equations, noise in the data is less an issue as tissues undergo large strains. In that case, we have recently proposed virtual fields that would be appropriate for different types of loading (tension inflation test [47], bulge inflation test [48]). They permit to obtain equations such as

$$\mu_1 A_{ij} + \mu_2 \kappa B_{ij}(\gamma) + \mu_2 (1 - 2\kappa) C_{ij}(\gamma, \theta) = L_{ij}, \quad (56)$$

where A_{ij} , B_{ij} , C_{ij} , and L_{ij} can be evaluated directly from the experimental measurements. Index i is for the different time steps for which deformations and loads are measured and index j is for different possible choices of virtual fields.

Eq. 56 is an equation of the unknown material parameters for each choice of virtual field i and at every stage j of the test. The equation is linear in μ_1 , $\kappa\mu_2$ and $\mu_2(1 - 2\kappa)$ but it is nonlinear in γ and θ . The solution is found by minimizing a cost function defined such as

$$\pi(\beta) = \sum_j \sum_i (\mu_1 A_{ij} + \mu_2 \kappa B_{ij}(\gamma) + \mu_2 (1 - 2\kappa) C_{ij}(\gamma, \theta) - L_{ij})^2. \quad (57)$$

This cost function can be minimized by the simplex method or using a genetic algorithm in case of multiple minima.

In summary, the VFM is an efficient method for the identification of material properties but it requires specific conditions for its application, especially the availability of deformation gradients across the whole domain of interest. Such requirement is not needed by variational or sequential methods presented before.

5.5.2 Applications to soft tissues

Regarding applications to soft tissues, the VFM was first applied to the identification of uniform material properties in arterial walls [47]. Recent extension in the same field were proposed for the inverse characterization of regional, nonlinear, anisotropic properties of murine aortas with different types of lesions [49–51].

The VFM was recently applied successfully in biaxial tension by Kazerooni et al [52] to identify the parameters of a Holzapfel model [53] for the skin. In ophthalmology, it was used by Girard et al [54], Zhang et al. [55] and further by [46] to identify material properties of the lamina cribosa, which is a connective tissue structure in the optical nerve head of great interest to researchers studying development and progression of glaucoma.

There are no applications so far to pelvic biomechanics. However, recent developments in the VFM for elastography applications [56, 57] are promising for future applications in that field.

5.6 Conclusions and future directions emerging field of pelvic biomechanics

Inverse problems consist of using the actual result of some measurements to infer the values of the parameters that characterize the system such as unknown parameters of the material model, unknown elements of the boundary conditions or even sometimes the unknown initial geometry of the solid before the application of any mechanical action (loadfree configuration in finite deformations). There are many other situations in soft tissue biomechanics where inverse problems have to be resolved. For the sake of illustration, the current chapter was voluntarily restricted to two main situations: elastography of soft tissue biomechanics and nonstandard testing of soft tissues. First we presented in details the FEMU technique which is traditionally used to solve inverse problems. We then presented sequential method based on the principle of Kalman filters for dynamic problems. Finally, we presented in details the VFM and showed different cases of its possible application.

For each approach, the main objective was to introduce the principles required to understand the theory of the methods. This is the first time that a book chapter presents these different methods under a unified framework. Specific applications of each method may be found in the referred journal publications.

There are many directions which are the topic of intense research at the moment in soft tissue biomechanics and where inverse problems have to be resolved. Without wanting to be exhaustive, we can point the 3 following directions which may require research efforts in the inverse problem community in the near future and which may have a significant impact in reproduction biomechanics:

1. Development of robust inversion techniques to estimate the viscoelastic properties from elastography imaging data. This is an ongoing area of research, as this is an inherently ill-conditioned numerical problem. Poor quality datasets with low signal-to-noise ratio tend to provide unreliable tissue property estimates, with different biases depending on the inversion algorithms applied. The viscoelastic properties of the pubovisceral muscle or other soft tissues of the pelvic system are likely to be important for organ support and probably affect progress in labor [58].

2. Development of robust inversion techniques to estimate the parameters of growth and remodeling models. The migration of cells through the fibrous network of the extracellular matrix is an integral part of many biological processes, including tissue morphogenesis, wound healing and cancer metastasis. For instance, the dramatic changes in the material behavior of the cervix over the normal period of gestation by considering the turnover of collagen from mature crosslinked fibers to immature loosely connected fibrils [59]. Accurate measurements

of constitutive parameters for models aimed at predicting these effects will deserve significant research efforts in the future.

3. representation of the data uncertainties. The most general (and simple) theory is obtained when using a probabilistic point of view, where the a priori information on the model parameters is represented by a probability distribution over the 'model space.' A great challenge of computational soft tissue biomechanics is to transform this a priori probability distribution into a range of uncertainty in the predictions. This may be important for treatment planning based on biomechanical deformable image registration for instance [60].

5.7 References

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