INVERSE BIOMECHANICAL MODELS OF THE BRAIN

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INTRODUCTION

Finite Element (FE) techniques are now commonly employed for simulating bio-mechanical properties of the head, e.g. in surgery simulation [1-3] or impact simulation [4-5]. To compute such forward simulations, the magnitude and directions of forces acting on the head need to be specified. If this prior information is not available, time series examinations may be employed and registered by a non-linear transformation. The resulting deformation field is used to derive a force field, based on incorporated realistic material parameters. Force fields need to be analyzed for their singularities (force "sources" and "sinks") in order to provide a comprehensive 3D visualization. In analogy to the inverse problem of localizing sources of electromagnetic brain activity from potential measurements on the scalp, we denote this approach as "inverse" bio-mechanical models. We focus here on the problem of setting up a suitable modeling context.

This work is performed within the international collaboration project SimBio [6], funded by the European Commission, which aims at implementing a generic environment for bio-numerical simulation of human body parts.

THE REGISTRATION ALGORITHM

A source volume image is mapped to a target by applying vector-field transformations to the underlying coordinate system. In order to produce bio-mechanically plausible results, transformations are constrained to be consistent with the physical properties of deformable elastic solids. Furthermore, transformations need to preserve topology in order to yield an anatomically valid result.

An approach which implements these constraints in a rather flexible algorithm was recently proposed by Christensen [7] and is embedded in the mathematical framework of the *Grenander model* of anatomy [8-9]. A fundamental problem with a large class of image registrations techniques is that the estimated transformation g from a template image T to a target S does not equal the inverse of the estimated transformation h from S to T. Thus, a third constraint needs to be enforced that these transformations are consistent, i.e., inverse to one another. Now, the registration problem can be stated as:

Jointly estimate the transformations h and g such that h maps T to S and g maps S to T subject to the constraint that $h = g^{-1}$.

We assume that the 3D image volumes T and S are MRI images collected from similar anatomical populations. Each image is defined to be a function of $x \in \Omega = [0, 1]^3$. The transformations are vector-valued functions that map the image domain Ω to itself, i.e., $h: \Omega \rightarrow \Omega$ and $g: \Omega \rightarrow \Omega$. Throughout it is assumed that $h(x) = x + u(x)$, $h^{-1}(x) = x + \hat{u}(x)$, $g(x) = x + w(x)$ and $g^{-1}(x) = x + \hat{w}(x)$, where $h(h^{-1}(x)) = x$ and $g(g^{-1}(x)) = x$. All fields $h, g, u, \hat{u}, w$ and $\hat{w}$ are (3 x 3) vector-valued functions of $x \in \Omega \Rightarrow \Omega$. Transformations are optimized by minimizing a symmetric cost function $C(h, g)$, which consists of three terms discussed in more detail below. To ensure consistency constraints, the transformations h and g are jointly estimated.

The first term uses the image intensity as a similarity measure of the native and transformed images:

$$C_1(T(h),S)+C_1(S(g),T) = \int_\Omega \left(T(h(x)-S(x)\right)^2 dx + \int_\Omega \left(S(g(x)-T(x)\right)^2 dx .$$

This cost function does guarantee that h and g are inverse to each other, because the respective contributions of h and g to the cost function are independent. In order to obtain a consistent transformation, an additional inverse transformation constraint is enforced:

$$C_2(u,\hat{w})+C_2(w,\hat{u}) = \int_\Omega \left\| u(x)-\hat{w}(x) \right\|^2 dx + \int_\Omega \left\| w(x)-\hat{u}(x) \right\|^2 dx$$

$$= \int_\Omega \left\| h(x)-g^{-1}(x) \right\|^2 dx + \int_\Omega \left\| g(x)-h^{-1}(x) \right\|^2 dx,$$

The inverse transformation h^{-1} is computed from h by solving the minimization problem:

$$h^{-1}(y) = \arg\min \left\| y - h(x) \right\|^2 \; \forall \; y \in \Omega.$$

Similarly, g^{-1} is computed from w. A sufficient condition to ensure that the inverse transformation h^{-1} exists and is unique is that h is a diffeomorphism. However, minimizing C_2 does not ensure that the transformations h and g are diffeomorphic transformations except when $C_2(h, g) = 0$. To enforce the transformations to be diffeomorphic, a continuum mechanical model is applicable such as linear elasticity. Thus, the third term of the cost function is defined as:

$$C_3(u) + C_3(w) = \int_{\Omega} \left\| \Lambda u(x) \right\|^2 dx + \int_{\Omega} \left\| \Lambda w(x) \right\|^2 dx$$

As in [7], we choose the operator Λ to describe linear elasticity:

$$\Lambda = -\alpha \Delta - \beta \nabla \nabla + \gamma I$$

$$= \begin{pmatrix} -\alpha\Delta - \beta\dfrac{\partial^2}{\partial x_1^2} + \gamma & -\beta\dfrac{\partial^2}{\partial x_1 x_2} & -\beta\dfrac{\partial^2}{\partial x_1 x_3} \\[2ex] -\beta\dfrac{\partial^2}{\partial x_2 x_1} & -\alpha\Delta - \beta\dfrac{\partial^2}{\partial x_2^2} + \gamma & -\beta\dfrac{\partial^2}{\partial x_2 x_3} \\[2ex] -\beta\dfrac{\partial^2}{\partial x_3 x_1} & -\beta\dfrac{\partial^2}{\partial x_3 x_2} & -\alpha\Delta - \beta\dfrac{\partial^2}{\partial x_3^2} + \gamma \end{pmatrix},$$

but in general Λ can be any non-singular linear differential operator.

The displacement fields are represented by a 3D Fourier series:

$$u(x) = \sum_{i=0}^{N_1-1} \sum_{j=0}^{N_2-1} \sum_{k=0}^{N_3-1} \mu_{ijk} \, e^{\hat{j} <x, \omega_{ijk}>}$$

$$w(x) = \sum_{i=0}^{N_1-1} \sum_{j=0}^{N_2-1} \sum_{k=0}^{N_3-1} \eta_{ijk} \, e^{\hat{j} <x, \omega_{ijk}>}$$

where the basis coefficients μ_{ijk} and η_{ijk} are (3 x 1) complex-valued vectors, $\omega \equiv [2\pi i/N_1, 2\pi j/N_2, 2\pi k/N_3]$, and N_1, N_2, N_3 correspond to the voxel dimensions of the images T and S. The coefficients μ_{ijk} and η_{ijk} are constrained to have complex conjugate symmetry during the estimation process.

Initially, only the low frequency components are used, effectively resulting in a multi-resolution approach. The transformations $\hat{h}$ and $\hat{g}$ are estimated by using a gradient decent algorithm to determine coefficients μ_{ijk} and η_{ijk}. Periodically, the number of basis coefficients is increased until a pre-defined spatial resolution of the displacement field is obtained. Lagrange multipliers are used to weight between the three cost function terms. The computation time for a midrange PC is in the order of 2h for volumes of 64^3 voxels. Parallelization on HPC platforms is useful and straightforward for larger volumes, candidate functions are the 3D FFT and the determination of the inverse transformations h^{-1} and g^{-1}.

To analyze vector fields for their singularities, we use the approach described by Philipou and Strickland [10].

CLINICAL VALIDATION

The algorithms described in this papers are evaluated by studying two different classes of brain diseases. Patients with probable neuro-degenerative diseases are examined within the course of a long-term study in conjunction with the Department of Psychiatry at the University Clinic, Leipzig. The study currently comprises of 150 patients, in which the first examination time point (TP1) was completed, and follow-up examinations (TP2) started recently. 20 cases with a significant atrophy rate (from volumetric measurements) were selected as a subset, and their data sets were subjected to this analysis procedure.

As a second group, 20 cases were selected from the patient pool of the Day-Care Clinic of Neuropsychology (University Clinic, Leipzig) who are suffering from focal brain lesions (after cerebral infarction, haemorrhage or severe head trauma). Patients are scanned routinely by MRI at the time of admission and discharge (approx. 3 resp. 12 months after onset). Data sets obtained at TP1 and TP2 were evaluated by inverse bio-mechanical models in order to derive the deforming forces induced by restorative processes after focal brain damage.

Neurobiological results will be reported in a subsequent publication.

SUMMARY

We proposed an approach for setting up "inverse" bio-mechanical models of the brain. Our aim is to understand the mechanical consequences of pathological and restorative processes which go along with degenerative and focal brain diseases. This first attempt includes processes only which proceed on a long-term time scale, because we expect that the assumption of linear elasticity still holds. At a later stage, this framework may be extended to govern non-linear behaviour (e.g., during surgical interventions, intra-cerebral hemorrhages, skull fractures) as well.

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