Lesion preserving image registration with applications to human brains

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Abstract. The goal of image registration is to find a transformation that aligns one image to another. In this paper we present a novel automatically image registration approach for images with structural distortions (e.g. a lesion within a human brain). The main idea is to define a suitable matching energy, which effectively measures the similarity between the images. The minimization of the matching energy is an ill-posed problem. Hence, we add a regularity energy borrowed from linear elasticity theory, which incorporates smoothness constraints into the displacement. The resulting energy functional is minimized by a Levenberg-Marquardt iteration scheme. Finally, we give a two-dimensional example of these applications.

1 Introduction.

An important problem in two- and three-dimensional medical image analysis is to match two similar images, resulting from the same or from different imaging modalities. Especially in brain research the development of fast deformable image registration algorithms has been an active topic of research in recent years. Here, a typical approach is the minimization of a suitable distance functional. Minimization strategies currently used deal with Navier-Stokes equilibrium equations for linear elasticity given by a partial differential equation (PDE). Here, the external forces, given by the derivatives of the distance functional, are applied to the template-image. The template-image is deformed until an equilibrium state (described by the PDE) between the external forces and internal forces resisting the deformation is achieved. The resulting displacement field \( u \) satisfies the PDE with external forces \( f \), see, e.g. [1, 2, 6, 10, 16].

Driven by ever more powerful computers, these algorithms have become important tools, e.g. in guidance of surgery, diagnostics, quantitative analysis of brain structures (interhemispheric, interareal and interindividual), ontogenetic differences between cortical areas, and interindividual brain studies. Although these techniques have been applied very successfully for both the uni- and the
multimodal case (e.g., see [1, 2, 6–10, 12, 16, 17, 20]) these techniques may be less appropriate for studies using brain-damaged subjects, since there is no compensation for the structural distortion introduced by a lesion (e.g., a tumor, ventricular enlargement, large regions of a typical pixel intensity values, etc.). Generally the computed solution cannot be trusted in the area of a lesion. The magnitude of the effect on the solution depends on the character of the registration scheme employed. It is not only that these effects are undesirable, but also that in some cases one is especially interested in where the lesion would be in the other image. If, for instance, we want to know which function of the brain is usually performed by the damaged area, we could register the lesioned brain to an atlas and map the lesion to functional data within the reference space.

In more general terms the problem can be phrased as follows. Given a deformable template image $T$ and a reference image $R$ as well as a domain $G$ including a segmentation of the lesions. The aim of the proposed image registration algorithm is to find a “smooth” displacement-field $u$, which:

Minimizes a given similarity functional between $T$ and $R$ under the condition that:

The lesion $G$ is conserved in the transformed template image $T$.

The main idea is to define a suitable distance functional, which effectively measures the similarity between the images. The presented approach can be seen as the well known “image inpainting approach” (e.g., see [3–5]) for the unknown displacement-field $u$, see [13]. The minimization of the presented matching energy is an ill-posed problem (see [16]). Hence, we investigate a Levenberg-Marquardt scheme for minimization of the novel distance functional. Here, we first linearize the least squares functional. The linearized functional is minimized within a so-called trust region around the actual solution. The trust region is quantified by a metric, which measures the elastic energy of the displacement.

2 A lesion preserving image registration algorithm

2.1 A lesion preserving similarity functional

In the situation that the intensities of the given images are comparable, a proper choice of for a distance functional is the so-called sum of squared differences between the images

$$D(u) = \frac{1}{2} \int_{\Omega} \left( T(x_1 - u_1(x), \ldots, x_d - u_d(x)) - R(x_1, \ldots, x_d) \right)^2 dx. $$

This is a common criterion. It is used, for example, in the case that the images are recorded with the same imaging machinery, the so-called mono-modal image registration. Due to the absence of information in the domain $G$, we define a lesion-mask by

$$\lambda_G(x) = \begin{cases} 1 & \text{if } x \in \Omega \setminus G, \\ 0 & \text{if } x \in G \end{cases}$$
and consider the following similarity functional

\[
D_\epsilon(u) = \frac{1}{2} \int_{\Omega} \left( T(x_1 - u_1(x), \ldots, x_d - u_d(x)) - R(x_1, \ldots, x_d) \right)^2 \, dx
\]

\[
= \frac{1}{2} \int_{\Omega} \lambda_G(x) \left( T(x_1 - u_1(x), \ldots, x_d - u_d(x)) - R(x_1, \ldots, x_d) \right)^2 \, dx.
\]

### 2.2 A Levenberg-Marquardt iteration for minimizing the similarity functional

In order to minimize the functional \( D_\epsilon(u) \) we use the Levenberg-Marquardt iteration scheme. The Levenberg-Marquardt method is a variant of the Gauß-Newton iteration for the minimization of \( D_\epsilon \). Here, for a current approximation \( u^{(k)}(x) \) the nonlinear image difference \( h(u) = T(x - u(x)) - R(x) \) is replaced by its linearization around \( u^{(k)}(x) \) within a ball of radius \( \|u\|^2 \leq \eta \) where the energy norm \( \|\cdot\|_E \) is defined by

\[
\|v\|_E = \sqrt{\langle v, v \rangle_E} \quad \text{with inner product} \quad \langle v, w \rangle_E = \int_{\Omega} w^t(x) L v(x) \, dx
\]

and a symmetric positive definite operator \( L \). For our specific application we use the following operator

\[
L u(x) := -\mu \Delta u(x) - (\mu + \lambda) \nabla (\nabla u(x))
\]

with the so-called Lamé constants \( \lambda \) and \( \mu \). Using the method of Lagrange multipliers, this is easy seen to be equivalent to minimize the quadratic functional

\[
Q(u) = \int_{\Omega} \frac{\lambda_k(x)}{2} \left( h_k + J_k u(x) \right)^2 \, dx + \alpha \langle L u, u \rangle,
\]

where \( h_k := h(u^{(k)}(x)) = T(x - u^{(k)}(x)) - R(x) \),

\[
J_k := J_k(u^{(k)}(x)) = \frac{\partial h}{\partial u}(u^{(k)}(x)) = \left( \frac{\partial h}{\partial u_1}(u^{(k)}(x)), \ldots, \frac{\partial h}{\partial u_d}(u^{(k)}(x)) \right)
\]

and the mask

\[
\lambda_k(x) = \begin{cases} 1 & \text{if } x \in \Omega \setminus G_k, \\ 0 & \text{if } x \in G_k \end{cases}
\]

for the transformed subdomain \( G_k = \{y \mid y = x - u^{(k)}(x) \quad \forall x \in G \} \).

### 2.3 The model of a clamped elastic membrane

The second term in equation (1) can be regarded as a penalty for "elastic stresses" resulting from the displacements of the images. This is a suitable model in many medical applications, for example, when pressure or movement is applied to a patient. By using Dirichlet boundary conditions the resulting displacements may be interpreted physically as the displacement of a clamped elastic membrane. For each iteration step we have the following result.
Theorem 1. Using Dirichlet boundary conditions for the operator \( L \) at \( \partial \Omega \), the unique minimizer \( u^*(x) \in (H^1_0(\Omega))^d \) of (1) is characterized by the following variational equation

\[
\int_{\Omega} \varphi(x) (\frac{\lambda_k(x)}{2} J_k J_k + \alpha L) u(x) dx = -\int_{\Omega} \lambda_k(x) J_k h_k \varphi(x) dx \quad \forall \varphi \in (H^1_0(\Omega))^d.
\]

(2)

Proof. Noting that

\[
\int_{\Omega} \frac{\lambda_k(x)}{2} (h_k + J_k u(x))^2 dx + \alpha \int_{\Omega} u^4(x) L u(x) dx = \int_{\Omega} \lambda_k(x) (2 J_k^t h_k u(x) + h_k^2) dx \\
+ \int_{\Omega} u^4(x) (\lambda_k(x) J_k J_k + \alpha L) u(x) dx.
\]

Since the operator \( L \) is symmetric positive definite by using Dirichlet boundary conditions and \( J_k J_k \) is symmetric positive semidefinite, it follows that the bilinear form

\[
B[u,v] := \int_{\Omega} u^4(x) (\lambda_k(x) J_k J_k + \alpha L) v(x) dx
\]

is symmetric and positive definite. Consequently, the weak solution of (1) is unique and given by the solution of (2). \( \square \)

Note that by the definition of \( \lambda_k(x) \) the classical solution of (2) is given by the boundary value problem

\[
(\alpha L + J_k^t J_k) u(x) = -J_k^t h_k \quad \text{for} \quad x \in \Omega \setminus G_k, \\
\alpha L u(x) = 0 \quad \text{for} \quad x \in G_k, \\
u(x) = 0 \quad \text{for} \quad x \in \partial \Omega.
\]

(3) \hspace{1cm} (4) \hspace{1cm} (5)

2.4 A parameter choice rule

An important problem is the proper choice of the parameter \( \alpha \) in practical applications. A small \( \alpha \) leads to strong artifacts due to the influence of high-frequency structures in the image data (e.g., the noise). Increasing \( \alpha \) removes the artifacts and allows only smoother transformations. The result becomes worse if the parameter increases further.

The optimal balance between the two extremes is a tough issue. In practice the costs of tuning the parameter are high and for most methods only "trial and error" approaches are available. In our implementation we determine \( \alpha \) using a trust-region approach as presented in [12].

2.5 Discretization and approximation of the boundary value problem

In order to discretize the operator \( J_k \) in equation (3), we have to fix an overlap between the subdomains \( G_k \) and \( \Omega \setminus G_k \). Therefore we enlarge \( G_k \) by one point
parallel to the boundary of $G_k$, see figure 1. The extended domain is named by $U$. The operator $J_k$ is approximated by using central differences for all points $x \in \Omega \setminus (G_k \cup U)$. For instance for the three-dimensional case, we have

$$J_k = \frac{1}{2} \left( T_{i+1,j,l}^k - T_{i-1,j,l}^k, T_{i,j+1,l}^k - T_{i,j-1,l}^k, T_{i,j,l+1}^k - T_{i,j,l-1}^k \right)^t,$$

where

$$T_{i,j,l}^k = T(x_i - u_1^{(k)}(x_i, x_j, x_l), x_j - u_2^{(k)}(x_i, x_j, x_l), x_l - u_3^{(k)}(x_i, x_j, x_l))$$

the template image deformed by $u^{(k)}$. In order to discretize the elliptic operator $L$, we use a finite difference approach and we approximate the partial derivatives by second order approximations, for details see [11].

2.6 Fast solution methods

In practice, the solution of the linear system (3)–(5) is the time consuming part of the Levenberg-Marquardt iteration. For the resulting discrete system a multigrid Correction Scheme (CS) was used (with optimal multigrid complexity $O(N)$ for $N$ picture elements) as a solver, for details see e.g. [11,15]. Since the resulting system is symmetric and positive definite other solvers like Krylov subspace methods [21], can be used. Note, that the underlying operator is anisotropic and consequently fast Fourier transformation (FFT) (see [22]) based solver cannot be used.

In order to speed up the minimization process, we have implemented the Levenberg-Marquardt iteration within a scale-space framework as presented in [14].
The Levenberg-Marquardt iteration is first performed on a rough scale. The result of this scale is then propagated to a finer scale and the iteration is restarted here. This process is continued down to the finest scale of the underlying scale-space, yielding the final registration result.

3 Results

We demonstrate the algorithm on a pair of deformed histological sections. The template section was lesioned in three places. Figure 2 shows the reference (a) and the undamaged template (b). The contour marks the silhouette of the reference section. Two registrations have been performed. One where no region $G$ has been defined and one where the region $G$ corresponds to the lesions. Results for the former are displayed on the left, and results for the latter are displayed on the right. In the second row the lesioned template along with the transformation field is shown, and the last row displays the results of the registrations. Here we used $\mu = \lambda = 1$.

From the transformation fields it is obvious that when no region $G$ is defined the surrounding tissue is "pulled" into the lesion. With the proposed approach the transformation is interpolated into the regions defined by $G$ and the lesion is preserved.

4 Conclusion

In this paper we have presented a pixel-based approach for nonlinear image registration for images with structural distortions (e.g., a lesion within a human brain). The problem can be traced back to a modified functional whose minimizers represent the mapping which transforms one image into another. We achieve the minimizing of this functional by a Levenberg-Marquardt iteration in a few steps. The small number of iterations and the finite dimension of the problem act as a regularization. Although we have only showed two-dimensional results, the method has already been applied in artificial 3D cases [13], and in a patient study involving patients suffering from ischaemic lesions [18, 19], using a Landweber scheme instead of the Levenberg-Marquardt scheme.

References

Fig. 2. In the first row the reference (a), template (b) are shown. Registrations without and with the definition of a region $G$ have been performed. In the second column the lesioned template and the transformation fields for the former (c) and the latter (d) are displayed. The corresponding results can be found in the last row. The contour around the sections corresponds to the silhouette of the reference.