Hybrid Spline-based Multimodal Registration using a Local Measure for Mutual Information

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Abstract. We introduce a new hybrid approach for spline-based elastic registration of multimodal medical images. The approach uses point landmarks as well as intensity information based on local analytic measures for mutual information. The intensity similarity metrics are computationally efficient and can be optimized independently for each voxel. We have successfully applied our approach to synthetic images, brain phantom images, as well as real multimodal medical images.

1 Introduction

In modern radiology, image registration is important for diagnosis, surgical planning, and treatment control. A challenge is to cope with the broad range of applications as well as the large spectrum of imaging modalities. Previous approaches for image registration can be classified according to the transformation model and the used image information. Typical transformation models are rigid and elastic transformations. Regarding the used image information, registration schemes can be subdivided in landmark-based and intensity-based approaches. For intensity-based approaches, it is important to distinguish between monomodal and multimodal registration problems, as both classes require different types of similarity metrics. In monomodal registration, images from the same modality are aligned, which can be achieved by, e.g., using the sum of squared intensity differences (SSD). Registration of images of different modalities, however, requires multimodal similarity metrics such as mutual information (MI). In general, metrics for MI are computationally expensive because they require the estimation of probability density functions based on joint histograms (e.g., [1, 2]).

In recent years, increased attention has been paid to hybrid registration approaches that integrate landmark-based schemes with intensity-based schemes (e.g., [3, 4, 5, 6, 7]). However, only few hybrid approaches are designed for multimodal images (e.g., [3, 4, 5]) and, although MI is employed as similarity measure, often only application to monomodal images is reported. Furthermore, previous spline-based approaches typically use coarse physical deformation models such as B-splines (e.g., [3, 4]) or thin-plate splines (e.g., [5]), and incorporate intensity information using global, computationally expensive measures for MI.

In this contribution, we present a new hybrid approach for spline-based elastic registration of multimodal medical images. Our approach is formulated as an energy-minimizing functional that incorporates point landmarks and intensity information as well as a regularization based on Gaussian elastic body splines (GEBS) [8]. Moreover, the intensity information is evaluated locally based on analytic measures for MI. These measures are computationally efficient since they do not require the estimation of probability density functions.

2 Materials and methods

2.1 Hybrid spline-based registration

Our new hybrid approach for elastic registration of multimodal images is based on an energy minimizing functional J_{Hybrid} that incorporates both landmark and intensity information and a regularization term:

$$J_{\mathrm{Hybrid}}(\mathbf{u}) = J_{\mathrm{Data},I}(g_1, g_2, \mathbf{u}^I) + \lambda_I J_I(\mathbf{u}, \mathbf{u}^I) + \lambda_L J_{Data,L}(\mathbf{u}) + \lambda_E J_{El}(\mathbf{u}) \quad (1)$$

The first term $J_{\mathrm{Data},I}$ describes the intensity-based similarity measure between the source and target image, g_1 and g_2, respectively. In the second term J_I the intensity-based deformation field $\mathbf{u}^I$ is coupled with the final deformation field $\mathbf{u}$ using a weighted Euclidean distance. The term $J_{\mathrm{Data},L}$ incorporates the landmark information based on approximating GEBS. The fourth term J_{El} represents the regularization of the deformation field according to the Navier equation, which constrains the deformation field to physically realistic deformations. The overall functional J_{Hybrid} is minimized alternatingly w.r.t. $\mathbf{u}^I$ and $\mathbf{u}$. In previous work [7], $J_{\mathrm{Data},I}$ was defined based on the sum of squared intensity differences, thus the approach was only applicable to monomodal registration. Here, we present a new formulation of $J_{\mathrm{Data},I}$ for multimodal registration as well as a new scheme for minimizing J_{Hybrid} w.r.t. $\mathbf{u}^I$.

2.2 Multimodal registration using analytic expressions for MI

For the intensity-based similarity measure $J_{\mathrm{Data},I}$, we suggest to use local analytic measures for MI. Let g be an image of dimension d over the continuous domain $\Omega \subset \mathbb{R}^d$, and $N_R(\mathbf{x})$ be the neighborhood of radius R around a point $\mathbf{x} \in \Omega$. For R being sufficiently small, the first order Taylor approximation $T_g(\mathbf{x}) \simeq \nabla g(\mathbf{x})^T \cdot \mathbf{x} + g_0(\mathbf{x})$ can be used as an approximation of $g(\mathbf{x})$ in the neighborhood of $\mathbf{x}$, where ∇g denotes the image gradient. The intensities $g(\mathbf{x})$ in the neighborhood $N_R(\mathbf{x})$ can be characterized by a random variable $\mathbf{g}$, which can be described by a probability density function. In [9] it was shown that for two images g_1 and g_2 the mutual information can then be approximated by

$$MI_{\mathrm{orig}}(\mathbf{x}) : \quad \max\{c_d - \log_2 |\sin\theta|\}, \quad (2)$$

where θ represents the angle between $\nabla g_1(\mathbf{x})$ and $\nabla g_2(\mathbf{x})$, and c_d is a constant that depends on the dimension d. However, due to properties of the logarithm,

$MI_{\text{orig}}(\mathbf{x})$ yields very high values if the argument $|\sin\theta|$ is close to zero and thus leads to unstable results. In [9], MI is evaluated globally, i.e. the similarity for each voxel is integrated over the whole image. If at a single voxel $|\sin\theta|$ is zero or close to zero, the global measure yields a high value, since adding logarithmic terms is equivalent to the logarithm of the product of the arguments ($\sum_i \log_2 s_i = \log_2 \prod_i s_i$). To circumvent this problem, in [9] a simplified metric is used which omits the logarithm and replaces the sine by a squared cosine:

$$MI_{\text{simp}}(\mathbf{x}): \quad \max\{c_d - \log_2 |\sin\theta|\} \equiv \min\{-\cos^2\theta\} \tag{3}$$

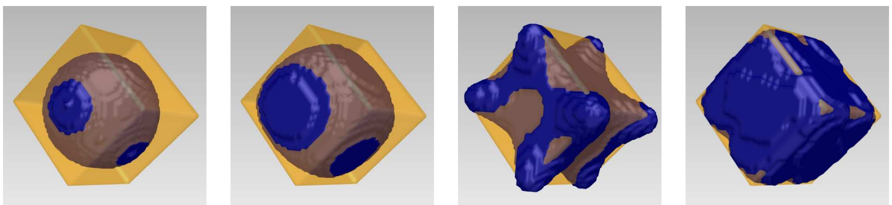
Instead, we suggest an alternative to cope with this problem, where the logarithm is still included but a constant $\epsilon > 0$ is introduced. This measure is more similar to the original measure in (2) and allows robust computation:

$$MI_{\text{new}}(\mathbf{x}): \quad \max\{c_d - \log_2 |\sin\theta|\} \equiv \min\{\log_2 |\epsilon + \sin\theta|\} \tag{4}$$

In our approach, we use $MI_{\text{simp}}(\mathbf{x})$ and $MI_{\text{new}}(\mathbf{x})$ for $J_{\text{Data},I}$ in (1). Optimization of J_{Hybrid} is computed alternatingly w.r.t. $\mathbf{u}^I$ and $\mathbf{u}$. For minimization w.r.t. $\mathbf{u}^I$, $J_{\text{Data},I} + \lambda_I J_I$ has to be minimized. To this end we have derived analytic expressions for the partial derivatives of $MI_{\text{simp}}(\mathbf{x})$ and $MI_{\text{new}}(\mathbf{x})$. In contrast to [9], in our approach MI is evaluated locally, i.e., optimization of $\mathbf{u}^I$ is computed independently for each voxel, which improves the efficiency.

3 Results

We have applied the new registration scheme to synthetic images, to brain phantom images, and to real medical images. In a first experiment, we have applied the new registration scheme to different 3D synthetic images. Fig. 1 (left), for example, shows the case of a sphere and a cube. Note that the images have inverted contrast to simulate a multimodal registration problem. Thus, a registration scheme using SSD would fail. Eight landmarks were defined at the corners of the cube, and the registration is computed based on the metric MI_{new}. The other images in Fig. 1 show the results for pure landmark-based, pure intensity-based, and hybrid registration. For landmark-based registration, only the corners of the cube are aligned. Using the pure intensity-based registration approach, the faces of the sphere are aligned, but not the corners. The



(a) Unregistered (b) Intensities (c) Landmarks (d) Hybrid

Fig. 1. 3D synthetic images: Registration of a sphere with a cube

Table 1. Registration of phantom images: Mean geometric error $\overline{e}_{\text{geom}}$ for different metrics using different types of image information.

Metric	Unregistered	Landmarks	Intensities	Hybrid
MI_{simp}	7.85	3.41	2.74	2.02
MI_{new}	7.85	3.41	2.41	1.61

best result is obtained using the hybrid approach, since both the faces and the corners are aligned.

To quantitatively evaluate the registration accuracy, we have used multimodal phantom images (MRI-T1 and MRI-T2) from the BrainWeb database [10]. We have generated a deformation field $\mathbf{u}_{\text{orig}}$ based on eight landmarks using GEBS, which is applied to the MRI-T2 image to obtain a target image with known deformation. After registration, we compared the computed deformation $\mathbf{u}$ with the original deformation $\mathbf{u}_{\text{orig}}$ and quantified the registration accuracy by the mean geometric error $\overline{e}_{\text{geom}} = \overline{\|\mathbf{u}_{\text{orig}} - \mathbf{u}\|}$. Table 1 gives the results. Without registration, the mean error is $\overline{e}_{\text{geom}} = 7.85$ pixels. Using only landmarks, we have $\overline{e}_{\text{geom}} = 3.41$ pixels. Registration using intensities leads to a significant reduction of the registration error to $\overline{e}_{\text{geom}} = 2.74$ pixels for MI_{simp} and $\overline{e}_{\text{geom}} = 2.41$ pixels for MI_{new}. When using the hybrid scheme, we obtain the best result $\overline{e}_{\text{geom}} = 2.02$ pixels for MI_{simp} and $\overline{e}_{\text{geom}} = 1.61$ pixels for MI_{new}.

We have also applied the new registration scheme to real, clinically relevant medical images. In Fig. 2 (top), we show PET (left) and CT (right) images of the thorax. For registration, we placed three landmarks, and computed the registration using only intensities (b) and using the hybrid approach (c) based on MI_{new}. It can be seen that using the hybrid scheme, we obtain a significant improvement compared to the pure intensity-based scheme.

4 Discussion

We introduced a new hybrid spline-based approach for elastic registration of multimodal images which incorporates point landmarks, intensity information, as well as a physically-based regularization. Since the approach uses a local analytic measure for Mutual Information, the required derivatives can be calculated analytically, and optimization can be performed independently for each voxel. We have demonstrated the applicability of our approach using synthetic images, phantom images of the brain, and real medical images. It turned out that our new similarity measure is more accurate than a previously proposed measure. We also found that the hybrid approach achieves more accurate registration results compared to a pure intensity-based and a pure landmark-based scheme.

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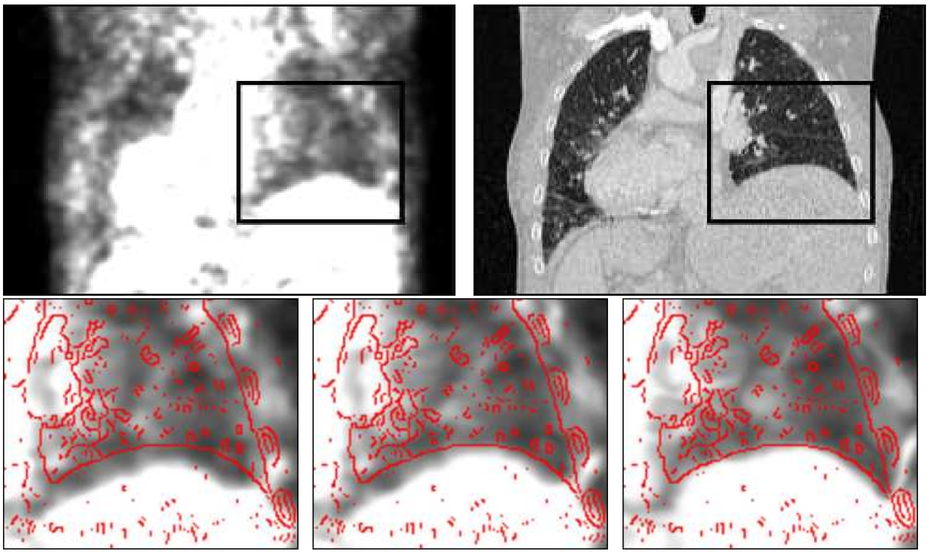
Fig. 2. Top: PET (left) and CT (right) images. Bottom: Edge overlay of a section before registration (a), after intensity-based registration (b), and hybrid registration (c).



(a) (b) (c)

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