# New Approximating Gaussian Elastic Body Splines for Landmark-based Registration of Medical Images

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**Abstract.** We introduce a new approximation scheme for landmark-based elastic image registration using Gaussian elastic body splines (GEBS). The scheme is based on an extended energy functional related to the Navier equation under Gaussian forces and allows to individually weight the landmarks according to their localization uncertainties. We demonstrate the applicability of the registration scheme based on 3D synthetic image data as well as 2D MR images of the human brain. From the experiments it turns out that the new approximating GEBS approach achieves more accurate registration results in comparison to previously proposed interpolating GEBS as well as TPS.

## 1 Introduction

Image registration is an important task in medical image analysis. Examples for applications are the registration of images of different modalities as well as the registration of preoperative with intra- and postoperative images. While rigid registration schemes are computationally efficient, they do not allow to cope with local differences between corresponding image data. Therefore, nonrigid registration schemes are required. A special class of general nonrigid transformations are *elastic* transformations, which allow for local adaptation and which are generally based on an energy functional or the related partial differential equation. Often, spline-based approaches are used for nonrigid registration such as thin-plate splines (TPS, e.g., [1]), elastic body splines (EBS, [2]), and Gaussian EBS (GEBS, [3, 4, 5]). While TPS are based on the bending energy of a thin plate, EBS and GEBS are derived from the Navier equation (partial differential equation), which describes the deformation of elastic objects under certain forces. GEBS in comparison to EBS have the advantage that more realistic forces are used, i.e. Gaussian forces instead of polynomial or rational forces. In spline-based registration approaches, generally an *interpolation* scheme is applied that forces corresponding landmarks to exactly match each other. The underlying assumption is that the landmark positions are known exactly. In real applications, however, landmark extraction is always prone to error. Therefore, to take these localization uncertainties into account, *approximation* schemes have been proposed, for example, for TPS (see, e.g., [1]). However, approximation schemes for EBS and GEBS approaches have not yet been introduced.

## 2 Approximating Gaussian Elastic Body Splines (GEBS)

First, we briefly describe the *interpolating* GEBS approach (Kohlrausch *et al.* [3, 4]). This approach is based on the Navier equation of linear elasticity

$$\mathbf{0} = \widetilde{\mu}\Delta\mathbf{u} + (\widetilde{\lambda} + \widetilde{\mu})\,\nabla\,(\mathrm{div}\,\mathbf{u}) + \mathbf{f} \tag{1}$$

with the displacement vector field $\mathbf{u}$, body forces $\mathbf{f}$, as well as Lamé constants $\widetilde{\mu}, \widetilde{\lambda} > 0$ describing material properties. Given Gaussian forces $\mathbf{f}(\mathbf{x}) = \mathbf{c}\,f(r) = \mathbf{c}\,(\sqrt{2\pi}\sigma_f)^{-3}\exp(-r^2/(2\sigma_f^2))$ with $\mathbf{x} = (x, y, z)^T$, $r = \sqrt{x^2 + y^2 + z^2}$, and the standard deviation $\sigma_f$, an analytic solution of (1) has been derived. The resulting basis functions $\mathbf{G}$ (a $3 \times 3$ matrix) are given by (up to a constant factor)

$$\mathbf{G}(\mathbf{x}) = \left(\frac{\alpha r^2 + \sigma_f^2}{r^3}\,\mathrm{erf}(\hat{r}) - \beta\frac{e^{-\hat{r}^2}}{r^2}\right)\mathbf{I} + \left(\frac{r^2 - 3\sigma_f^2}{r^5}\,\mathrm{erf}(\hat{r}) + 3\beta\frac{e^{-\hat{r}^2}}{r^4}\right)\mathbf{x}\mathbf{x}^T \tag{2}$$

where $\hat{r} = r/(\sqrt{2}\,\sigma_f)$, $\alpha = 3 - 4\nu$, $\beta = \sigma_f\sqrt{2/\pi}$, and the Poisson ratio $\nu = \widetilde{\lambda}/(2\widetilde{\lambda} + 2\widetilde{\mu})$. Using the interpolation condition $\mathbf{q}_i = \mathbf{u}(\mathbf{p}_i)$, the scheme for spline-based elastic image registration is given by $\mathbf{u}(\mathbf{x}) = \mathbf{x} + \sum_{i=1}^{n}\mathbf{G}(\mathbf{x} - \mathbf{p}_i)\;\mathbf{c}_i$ where $\mathbf{p}_i$ and $\mathbf{q}_i$ denote the positions of corresponding $n$ landmarks of the source and target image, respectively. The coefficients $\mathbf{c}_i$ represent the strength as well as direction of the Gaussian forces and are computed from a linear system of equations (LSE) comprising the basis functions $\mathbf{G}$ and the landmarks $\mathbf{p}_i$ and $\mathbf{q}_i$.

With an interpolation approach as described above the landmarks are matched exactly. This implicitly assumes that the landmark positions are known exactly, which is not realistic. To take into account landmark localization errors we extend this approach by weakening the interpolation condition, i.e. we use the approximation condition $\mathbf{q}_i \approx \mathbf{u}(\mathbf{p}_i)$. More precisely, the approximation condition is specified based on $3 \times 3$ covariance matrices $\boldsymbol{\Sigma}_i$ defining the anisotropic localization uncertainties of the $n$ landmarks. For the special case of *isotropic* localization uncertainties $\sigma_i$, the covariance matrix simplifies to $\boldsymbol{\Sigma}_i = \sigma_i^2\,\mathbf{I}$. To include localization uncertainties of landmarks in the GEBS approach, i.e. to derive *approximating* GEBS, we introduce a new energy-minimizing functional consisting of two terms. The first term $J_{Elastic}$ represents the elastic energy according to the Navier equation (1) without the force $\mathbf{f}$ and acts as a smoothness term. The second term $J_{Force}$ represents Gaussian forces specified by corresponding landmarks $\mathbf{p}_i$ and $\mathbf{q}_i$, and, in addition, incorporates the localization uncertainties $\boldsymbol{\Sigma}_i$ of the landmarks. Here, we propose a quadratic approximation

$$J_{Force} = \int\!\!\int\!\!\int_{-\infty}^{\infty} \frac{1}{\lambda n}\sum_{i=1}^{n} f(\mathbf{x} - \mathbf{p}_i)\,(\mathbf{q}_i - \mathbf{u}(\mathbf{x}))^T\,\boldsymbol{\Sigma}_i^{-1}\,(\mathbf{q}_i - \mathbf{u}(\mathbf{x}))\,d\mathbf{x} \tag{3}$$

where $\lambda > 0$ denotes the regularization parameter. The new functional then reads $J_\lambda = J_{Elastic} + J_{Force}$. For $J_\lambda$ we derive the related partial differential equation, which represents an extension of the Navier equation (1), and then determine an analytic solution. Finally, we determine the resulting LSE. Since the solution can be stated in analytic form, we end up with a computationally efficient scheme. It turns out that the analytic solution to the approximation problem consists of the same basis functions $\mathbf{G}$ as in the case of interpolation. However, the resulting LSE to compute the coefficients $\mathbf{c}_i$ is more complex. More precisely, the structure of the LSE is the same for interpolating and approximating GEBS, except that *approximating* GEBS include additional sums of weighted forces $\sum_{i=1}^{n} f(\mathbf{p}_j - \mathbf{p}_i)\boldsymbol{\Sigma}_i^{-1}$. It also turns out that the previously proposed interpolating GEBS are a special case of the new approximating GEBS.

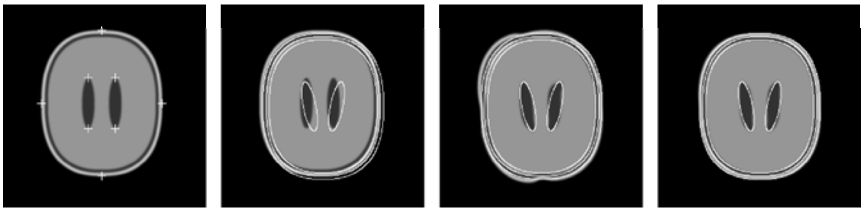
In comparison to existing spline-based approaches, the new approach based on approximating GEBS combines a number of advantages. A main advantage is that GEBS include a material parameter (Poisson ratio $\nu$), which defines the ratio between transverse contraction and longitudinal dilation of an elastic material. Therefore, the registration scheme integrates an improved physical deformation model, i.e. cross-effects can be taken into account (which is not the case for TPS). Another advantage is that Gaussian forces are used in the GEBS approach instead of polynomial or rational forces as in the previous EBS approach [2]. Gaussian forces are physically more plausible since they decrease with distance and they do not diverge. In addition, with Gaussian forces we have a free parameter (standard deviation $\sigma_f$) to control the locality of the transformation. Finally, the new approximation approach allows to individually weight the landmarks according to their localization uncertainty, which can be characterized either by scalar weights $\sigma_i$ or by weight matrices $\boldsymbol{\Sigma}_i$ representing isotropic and anisotropic uncertainties, respectively.

## 3 Experimental Results

We have applied the new approximating Gaussian EBS approach to register 3D synthetic image data as well as 2D MR images of the human brain. In the synthetic experiments we generated 3D image data based on the superposition of superellipsoids (using different sizes, orientations, and homogeneous intensities), which represent a simplified 3D MR image of a human head comprising different tissues such as skin, skull, brain, and the ventricular system (see Fig. 1, left). To simulate local differences in the images, we locally varied the shape of the ventricular system. In addition, we applied a translation of the overall image. In total, we used 12 corresponding landmarks. Moreover, we artificially misplaced a subset of three landmarks to simulate landmark extraction in clinical routine, which generally is prone to error (i.e. the left-, top-, and right-most landmarks in Fig. 1, left). To quantitatively analyze the registration accuracy, we computed the mean intensity error $\overline{e}_{int}$ between the source and target image as well as between the transformed source and target image.

Applying the new approach using anisotropic localization uncertainties of the landmarks *without* misplaced landmarks, the mean intensity error $\overline{e}_{int}$ improved by 85.8% w.r.t. to the unregistered images. In comparison, for interpolating

**Fig. 1.** 2D section of the 3D source image as well as 2D sections of the 3D source image overlayed with computed edges of the target image: Without registration as well as with registration using interpolating and approximating GEBS (from left to right).

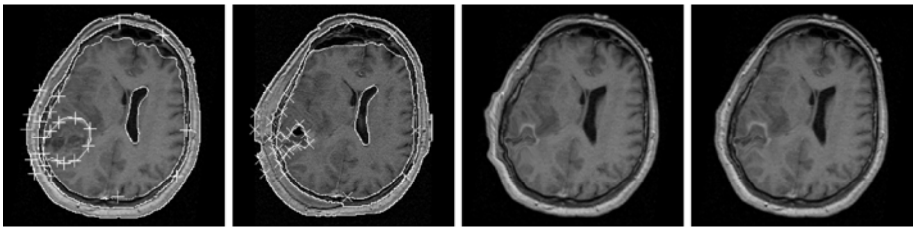


GEBS the results are similar with an improvement of 79.0%. *With* misplaced landmarks the new approximating GEBS approach still improved $\bar{e}_{int}$ by 79.5% (Fig. 1, right). In comparison, interpolating GEBS yield significantly worse results with an improvement of only 16.6% (Fig. 1, middle right). Moreover, for interpolating TPS the results are worse, i.e. achieving improvements of only 46.3% without and 14.3% with artificially misplaced landmarks.

We have also applied the new approximating Gaussian EBS approach to register pre- and postsurgical MR images of the human brain. The images shown in Fig. 2 are 2D MR images of a patient before (left) and after (middle left) resection of a tumor. 22 landmarks have been placed at the contours of the tumor and at the contours of the head in the vicinity of the tumor (white lines). Five additional landmarks have been placed at the top, right, and bottom part of the image. Prior to elastic registration the images have initially been aligned by an affine transformation. Note that after affine transformation the ventricular system is well aligned, thus the resection of the brain tumor has hardly an effect on the position and size of the ventricular system. For the Gaussian forces of the GEBS approach we chose a standard deviation of $\sigma_f = 5$ voxels, and the Poisson ratio is set to $\nu = 0.49$, which corresponds to brain tissue. Using interpolating TPS and interpolating GEBS for image registration (not shown here), it turns out that in both cases the vicinity of the tumor and resection area are well registered. However, in the case of TPS there are significant deviations at the ventricular system, and, therefore, the overall registration result is not usable. In contrast, using GEBS only deforms the source image in the vicinity of the displaced landmarks (i.e. within the tumor and resection area).

Using *approximating* GEBS in this experiment does not improve the registration accuracy significantly. The reason is that the corresponding landmarks have been chosen very well. To demonstrate the applicability of approximating GEBS, we have misplaced five landmarks on the left side of the outer skull (see Fig. 2, left), i.e. we shifted the five landmarks upwards along the outer skull. For these landmarks, we defined the localization uncertainties in accordance with their displacements, whereas for the other landmarks we chose relatively small isotropic localization uncertainties. Fig. 2 shows the registered source image using *interpolating* GEBS (middle right) and *approximating* GEBS (right) for this

**Fig. 2.** Registration of 2D MR brain images (from left to right): Pre- and postsurgical images as well as registered source image using interpolating and approximating GEBS.



second set of landmarks. It turns out that the misplaced landmarks significantly affect the registration result in the case of *interpolating* GEBS, see the unrealistic oscillations on the left side of the outer skull in Fig. 2 (middle right). In contrast, using *approximating* GEBS the influence of the misplaced landmarks is relatively low, while the tumor and resection area are still well registered.

## 4 Conclusion

We have presented a new approximation scheme for elastic image registration based on Gaussian elastic body splines (GEBS). The scheme is based on an extended energy functional related to the Navier equation using Gaussian forces and incorporates both isotropic as well as anisotropic localization uncertainties of the landmark positions. Our experimental results show that the scheme is superior to previously proposed interpolating GEBS as well as TPS.

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