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Combining landmark and intensity driven registrations

One of the challenging tasks in today image processing is image registration. Image registration is inevitable whenever images taken for example at different times or from different perspectives need to be compared or integrated. Typically, the location of corresponding points in the different views of one object or even different objects is distorted, for example, due to motion or different properties of the underlying optical systems of imaging devices. Thus, a basic problem is to find a meaningful spatial transformation of one image, such that the transformed image becomes similar to a second one. For many application, it is also desirable to guide the registration by additional information, for example, the locations of outstanding points. In this note, be present a general variational based approach for image registration which allows the choice of a user supplied similarity measure and a user supplied regularizer as well as the integration of external knowledge, like, for example, the location of outstanding points.

1. The image registration problem

In particular in medical imaging, registration schemes are known to be valuable tools in various settings, like, e.g., the comparison of pre- and post biopsy images. For an overview we refer to Brown [4], Maurer & Fitzpatrick [13], van den Elsen et al. [18], or Maintz & Viergever [12]. The currently available schemes can roughly be divided in two classes: landmark based and intensity based registration schemes. In this paper, we present a rigorous mathematical framework for combining these two techniques, in order to benefit from the advantages of both strategies.

Intensity based approaches aim to match images by minimizing an appropriate distance measure, like, e.g., the L_2-norm of the difference image or the mutual information of the two images; see, e.g., Brown [4], Collignon et al. [6], Roche [15], or Viola [19]. Based on these distance measure, a variety of registration techniques has been developed; see, e.g., D'Agostino et al. [7], Hermosillo [10], or Modersitzki [14]. These techniques are generally full automatic and yield a good registration on the average. However, they may perform poorly for specific, important locations like anatomical landmarks. On the opposite, landmark based registration techniques are designed to accurately match user specified landmarks; see, e.g., Rohr [16]. A drawback of landmark based registration is the fact that the intensities of the images are completely neglected. Consequently, the registration result away from the landmarks may be very poor.

Here, we propose a framework for combining any distance measure based registration with landmark information. We also present a general numerical procedure for computing the wanted transformation as well as a particular implementation for a specific distance measure based registration technique. The general procedure computes a displacement field which is guaranteed to produce a one-to-one match between given landmarks and at the same time aims to minimize an intensity based measure for the remaining parts of the images.

It is important to observe, that the presented novel technique for combining intensity driven and landmark based approaches is independent on the two main building blocks. Moreover, it is also easily possible to add other constraints, like, for example, the restriction to volume preserving maps.

2. The general framework

In this section we set the mathematical framework and briefly introduce the landmark based and intensity driven approaches. Finally, we describe our new approach and discuss its basic ideas.

Let $d \in \mathbb{N}$ denote the dimension of a spatial domain $\Omega \subset \mathbb{R}^d$, where without loss of generality, we assume $\Omega =]0,1[^d$. Furthermore, let $R, T : \Omega \to \mathbb{R}$ denote the two images. Hence, $T(x)$ denotes the intensity of the template at the spatial position x, where for ease of discussion we set $R(x) = b_R$ and $T(x) = b_T$ for all $x \notin \Omega$ and b_R and b_T are appropriate chosen background values. The overall goal is to find a *displacement* $u : \mathbb{R}^d \to \mathbb{R}^d$, such that ideally T_u is similar to R, where $T_u(x) = T(x - u(x))$. Note that u denotes a vector field.

There are various ways of computing a suitable displacement u. We present a variational approach which has three building blocks. The first one of them computes *internal forces*, which are defined for the wanted displacement field itself, the second one is responsible for *external forces*, which are computed from the image data, and the third one is related to external constraints. The internal forces are designed to keep the displacement field smooth during deformation while the external forces are defined to obtain the desired registration result. Constraints can be used to supply additional information about the transformation. It turns out that most of these schemes may be formulated in the following fashion; for details see, e.g., MODERSITZKI [14].

(IR) Find a displacement $u : \mathbb{R}^d \to \mathbb{R}^d$, such that

$$\mathcal{J}[u] := \mathcal{D}[R, T; u] + \alpha\mathcal{S}[u] = \min, \text{ subject to } \mathcal{C}_j[u] = 0, \ j = 1, \dots, m,$$

where $\mathcal{D}$ represents a *distance measure* (external force) and $\mathcal{S}$ determines the *smoothness* of u (internal force), and the $\mathcal{C}_j$'s specify additional constraints.

The parameter α may be used to control the strength of the smoothness of the displacement versus the similarity of the images. The second term $\mathcal{S}$ is unavoidable. Arbitrary transformations may lead to cracks, foldings, or other unwanted deformations. From a mathematical point of view, $\mathcal{S}$ may also be seen as a regularizing term introduced in order to rule out discontinuous and/or suboptimal solutions, having in mind that image registration is an ill-posed problem.

The smoother $\mathcal{S}$

Various choices for the smoothing term $\mathcal{S}$ have been considered. This is mainly motivated by the fact that particular applications demand for particular properties of the displacement field. In view of the need for fast numerical implementations, we concentrate on differentiable regularizer $\mathcal{S}$, i.e., functionals where the GÂTEAUX-derivative $d\mathcal{S}[u; v]$, given by

$$d\mathcal{S}[u; v] := \lim_{h\to 0} \frac{1}{h}(\mathcal{S}[u + hv] - \mathcal{S}[u]) = \int_\Omega \langle \mathcal{A}[u], v\rangle_{\mathbb{R}^d} \ dx,$$

exists. Here, $\mathcal{A}$ denotes the associated linear partial differential operator. The most popular choices for intensity driven registration, the so-called *curvature* ([9]), *demon* (cf. THIRION [17]), *diffusion* ([8]), *elastic* (cf. BROIT [3] or BAJCSY & KOVAČIČ [1]), and *fluid* (cf. CHRISTENSEN [5] or BRO-NIELSEN [2]) registration are based on regularizer which belong to this class. For a general treatment and the derivation of the different partial differential operators we refer to MODERSITZKI [14].

The numerical examples shown in Section **??** are based on the so-called curvature regularizer (cf. [9])

$$\mathcal{S}[u] := \frac{1}{2}\sum_{\ell=1}^{d} \int_\Omega (\Delta u_\ell)^2 \, dx. \tag{1}$$

Here, the associated partial differential operator

$$\mathcal{A}[u] = (\Delta^2 u_1, \dots, \Delta^2 u_d)^\top \quad \text{with} \quad \Delta^2 u_\ell = \sum_{j,k=1}^{d} \partial_{x_j x_j x_k x_k} u_\ell$$

is nothing but the well-known biharmonic operator, which is rotationally invariant and decouples with respect to the spatial coordinates.

Remark 1. *Let $q \in \mathbb{N}$, $\kappa \in \mathbb{N}^d$, D^κ be a partial differential operator, $D^\kappa f := \partial_{x_1}^{\kappa_1} \cdots \partial_{x_d}^{\kappa_d} f$, and*

$$\langle f, g\rangle := \sum_{|\kappa|=q} c_\kappa \int_{\mathbb{R}^d} (D^\kappa f) \ (D^\kappa g) \ dx$$

be a semi-inner product. Note that if $2q > d$, the point evaluate functionals belongs to the dual of $H^q \cap C(\mathbb{R}^d) \cup \Pi_{q-1}(\mathbb{R}^d)$; cf. LIGHT *[11]. Since $q = 2$ in Eq. (1), the analysis presented in the following holds for spatial dimension $d < 4$.*

The distance measure

In the literature one may also find various choices for the distance measure. Again, we concentrate on those measures $\mathcal{D}$ which allow for differentiation, i.e., there exists a function $f : \mathbb{R}^d \times \mathbb{R}^d \to \mathbb{R}^d$ with

$$d\mathcal{D}[R,T;u;v] = \lim_{h\to 0} \frac{1}{h}(\mathcal{D}[R,T;u+hv] - \mathcal{D}[R,T;u]) = \int_\Omega \langle f(x,u(x)), v(x)\rangle_{\mathbb{R}^d}\ dx.$$

Here and elsewhere, f is frequently called *force field*.

Probably the most popular choice for a distance measure, having this property, is provided by the so-called *sum of squared differences* (SSD)

$$\mathcal{D}[R,T;u] \quad := \quad \tfrac{1}{2}\|R - T_u\|^2_{L_2} = \frac{1}{2}\int_\Omega (T(x-u(x)) - R(x))^2\, dx.$$

The associated force field looks like $f(x,u(x)) = (R(x)-T(x-u(x)))\cdot\nabla T(x-u(x))$. For this measure to be successful, one has to assume that the intensities of the two given images are comparable. Other distance measures, capable of dealing with multimodal images, like, e.g., mutual information (cf., e.g., Collignon et al. [6] or Viola [19]), are also under consideration; see, e.g., D'Agostino et al. [7], Hermosillo [10], or Roche [15].

Note that the unconstraint image registration problem (IR) gives a pure distance measure registration scheme.

The incorporation of landmarks

Let us now briefly introduce the landmark constraints. To this end, let the landmarks $r^j, t^j \in \mathbb{R}^d$, $j = 1,\dots,m$, be given. The idea is to find a smooth displacement u such that

$$\mathcal{C}_j[u] := u(t^j) - t^j + r^j = 0 \text{ for } j = 1,\dots,m. \tag{2}$$

Note that the transformation is given by $\phi(x) = x - u(x)$ and hence Eq. (2) reads $\phi(t^j) = t^j - u(t^j) = r^j$, i.e., t^j is mapped onto r^j, $j = 1,\dots,m$. As it is apparent, the distance between R and T is no longer part of the functionals $\mathcal{C}_j$. The images enter into the constraints only through the landmarks.

To compute the Gâteaux-derivative of $\mathcal{C}_j$, it is helpful to consider the point-evaluation functional δ; see also Remark 1. With $\delta_z[u] = u(z)$, the interpolation constraints read $\mathcal{C}_j[u] = \delta_{t^j}[u] - t^j + r^j = 0$, $j = 1,\dots,m$, and the derivative is given by $g_j[u] = \delta_{t^j}$.

Note that the image registration problem (IR) without distance measure (or with $\mathcal{D}[R,T;u] := 0$) gives a plain landmark registration scheme:

(IR-L) Find a displacement $u : \mathbb{R}^d \to \mathbb{R}^d$, such that $\mathcal{S}[u] = \min$, subject to $\mathcal{C}_j[u] = 0,\ j = 1,\dots,m$.

The Euler-Lagrange equations (ELE) of (IR-L) are

$$0 = \mathcal{A}[u] + \sum_{j=1}^m \lambda_j g_j[u] \quad \text{and} \quad \mathcal{C}_j[u] = 0, \quad j = 1,\dots,m; \tag{3}$$

cf., e.g., Rohr [16].

For the particular choices of $\mathcal{S}$ (cf. eq. (1)) and $\mathcal{C}_j$ (cf. eq. (2)), the ELE (3) simplifies to

$$\Delta u_\ell + \sum_{j=1}^m \lambda_{j,\ell}\ \delta_{t^j_\ell} = 0, \quad \ell = 1,\dots,d, \quad \text{and} \quad \mathcal{C}_j[u] = 0, \quad j = 1,\dots,m,$$

where $\delta_{t^j_\ell}$ denotes the uni-variate point evaluation functional. Let ρ^j denote a fundamental solution (or Greens function) of $A[\rho^j] = -\delta_{t^j}$, the wanted solution can be phrased as

$$u = \sum_{j=1}^m \lambda_j \rho^j = \left(\textstyle\sum_{j=1}^m \lambda_{j,1}\rho^j_1,\ \dots,\ \sum_{j=1}^m \lambda_{j,d}\rho^j_d\right),$$

where the free coefficients $\lambda_{j,\ell}$ are determined by the interpolation constraints, i.e., $B^\ell \lambda^\ell = b^\ell$, where

$$\lambda^\ell = (\lambda_{\ell,1}, \ldots, \lambda_{\ell,m})^\top \in \mathbb{R}^m, \quad B^\ell_{j,\nu} := \rho^\nu_\ell(t^j), \quad B^\ell = [B^\ell_{j,\nu}]^m_{j,\nu=1} \in \mathbb{R}^{m\times m}, \quad b^\ell = (r^j_\ell - t^j_\ell)^m_{j=1} \in \mathbb{R}^m.$$

The EULER-LAGRANGE equations for the registration problem (IR)

Summarizing, the ELE for the image registration problem (IR) read

$$f(x, u(x)) + \alpha \mathcal{A}[u](x) + \sum_{j=1}^m \lambda_j g_j[u] = 0, \quad x \in \Omega. \tag{4}$$

Here, f is related to the GÂTEAUX-derivative of the distance measure $\mathcal{D}$ and the partial differential operator $\mathcal{A}$ is related to the GÂTEAUX-derivative of the smoother $\mathcal{S}$, and g_j is related to the GÂTEAUX-derivative of the constraint $\mathcal{C}_j$. If in particular the landmark interpolation constraints are under consideration, $g_j[u] = \delta_{t^j}$

To solve the semi-linear EULER-LAGRANGE equations either a fixed-point type iteration scheme

$$\alpha \mathcal{A}[u^{(k+1)}](x) = -f(x, u^{(k)}(x)) - \sum_{j=1}^m \lambda_j g_j[u^{(k)}] = 0, \quad k \geq 0,$$

or a time-marching iteration

$$\partial_t u^{(k+1)}(x,t) = -f(x, u^{(k)}(x,t)) - \alpha \mathcal{A}[u^{(k+1)}](x,t) - \sum_{j=1}^m \lambda_j g_j[u^{(k)}], \quad k \geq 0,$$

with $u^{(0)}(x, 0) = 0$, may be employed. The main work in each iteration is the solve for $u^{(k+1)}$, i.e., the solution of a linear partial differential equation. Here, we are using a finite-difference approximation of the equation followed by the application of an efficient solver for the resulting linear system of equations. For many regularizers $\mathcal{S}$, the related sparse linear systems do have a rich structure, which may be used to advantage. Here, specific implementations lead to overall schemes with complexity $\mathcal{O}(N \log N)$ or even $\mathcal{O}(N)$, where N denotes the number of voxel. The actual complexity depends on the chosen smoother $\mathcal{S}$; for details see MODERSITZKI [14].

Obviously, multiresolution type techniques can be used in order to reduce computation time and for an additional regularization of the registration problem (IR). However, for ease of presentation the following derivation is on one scale only.

The precise formulation of Eq. (4) for the ℓth component of the multivariate functions reads

$$f_\ell(x, u(x)) + \sum_{\nu=1}^d \left(\mathcal{A}_{\ell,\nu}[u_\nu] + \textstyle\sum_{j=1}^m \lambda^\ell_j g^\ell_j \right) = 0 \quad \text{and} \quad \mathcal{C}_j[u_\ell] = 0, \quad j = 1, \ldots, m.$$

Here, $u = (u_1, \ldots, u_d)^\top$, the point evaluation function δ is univariate, i.e., $\delta_{t^j}[u_\ell] = u_\ell(t^j) \in \mathbb{R}$, and $\mathcal{A}_{\ell,\nu}$ denotes the ℓth component of the operator $\mathcal{A}$ acting on the νth component of u. For example, if $\mathcal{S} = \mathcal{S}^{\text{curv}}$ (cf. eq. (1)), we have $\mathcal{A}_{\ell,\nu} = \sum_{j,k=1}^d \partial_{x_j x_j x_k x_k}$ if $\ell = \nu$ and $\mathcal{A}_{\ell,\nu} = 0$ if $\ell \neq \nu$.

Let ρ^j denote the multivariate fundamental solution or Greens-functions of $\mathcal{A}[\rho^j] = -\delta_{t^j}$. Then the wanted solution can be written as

$$u = \sum_{\nu=1}^m \lambda_\nu \rho^\nu = \left(\textstyle\sum_{\nu=1}^m \lambda^1_\nu \rho^\nu_1, \ldots, \sum_{\nu=1}^m \lambda^d_\nu \rho^\nu_d \right)^\top.$$

The free coefficients λ^ℓ_ν are determined by the interpolation constraints

$$\sum_{\nu=1}^m \lambda^\ell_\nu \rho^\nu_\ell(t^j) = d^j_\ell, \quad j = 1, \ldots, m, \quad \ell = 1, \ldots, d,$$

which may be written in compact notation as $B^\ell \lambda^\ell = b^\ell$, where

$$\begin{aligned} \lambda^\ell &:= (\lambda^\ell_1, \ldots, \lambda^\ell_m)^\top \in \mathbb{R}^m, \\ B^\ell_{j,\nu} &:= [\rho^\nu_\ell(t^j)]^m_{j,\nu=1} \in \mathbb{R}^{m\times m}, \end{aligned}$$

$$\text{and} \quad b_j^\ell \quad := \quad (d_\ell^1, \ldots, d_\ell^m)^\top \in \mathbb{R}^m.$$

For various choices of $\mathcal{S}$, the Greens-functions are explicitly known. Often they are given in terms of a (univariate) radial basis function $\hat\rho$ via $\rho_\ell^\nu(x) = \hat\rho(\|x - x^{T,\nu}\|_{\mathbb{R}^d})$. This is in particular the case, for the choice $\mathcal{S} = \mathcal{S}^{\text{curv}}$. Equipped with appropriate boundary conditions, this choice leads to the well-known thin-plate-splines.

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