CHAPTER 2

DEFORMABLE IMAGE REGISTRATION WITH TRADITIONAL METHOD

Highlights of the Chapter

- *Components of Deformable Image Registration*
- *Classical image registration approaches*
- *Exploration of related literatures*

This chapter encompasses the traditional approaches developed and utilized for the purpose of deformable image registration and most importantly their role in the field of medical image analysis. As in general, there exist no unique solution to a registration problem, hence deformable registration can be termed as an ill-posed problem. Typically, deformable image registration is articulated as an optimisation problem. According to [1], if I_1 is taken as the 2D moving image, I_2 is taken as the 2D fixed image and the images I_1 and I_2 can be thought of as $R^2 \rightarrow R$ mappings from 2D coordinates to image intensities, then image registration can be defined as finding the functions h and g in the mapping: $I_2(x, y) = g(I_1 (h (x, y)))$. The function g is used to describe so-called photometric differences while the function h is used to describe geometric differences. The function g can be termed as an intensity mapping function that accounts for a difference in image intensities of the same object in both of the images [2,3]. The function h is a spatial transformation that describes the mapping between the spatial coordinates of the images. These transformations take different forms depending on the registration method used.

Information derived from landmark information (such as contours or points) or from image intensities is the basis of deformable registration methods. Also hybrid models are possible using a combination of intensities and landmarks. In general, image registration can be thought of as a combination of three ingredients [4]: a similarity measure, a transformation model, and an optimization process.

2.1. Similarity Measures

Usually it is not the case that the images are perfectly matched to each other after registration. So, before evaluating the registration result qualitatively, the definition of "identical images" needs to be defined correctly. The estimation of the feature 'identical' is defined by similarity measure. The optimal registration is the one that features a transformation which maximizes this measure (or minimizes the cost function developed using the measure). Here, a number of most popular similarity metrics are introduced.

Sum of Squared Differences (SSD) is one of the most widely used similarity metrics. It is fast, simple and intuitive as it is defined by the difference of the squared pixel/voxel values between fixed and moving images on the desired region. The only requirement of using this metric is that both the images should have to be acquired by the same modality.

Normalized Cross Correlation is another well known similarity metric. Its rapid computation becomes critical in time sensitive applications. This metric has the advantage of reduced dependence on linear scaling of image intensities. This means that two images can be registered even though one is brighter. Also, it can be used as global as well as local metric too.

Mutual Information (MI) is the most commonly used metric for multimodal registration. It is a statistical measure of the correspondence between images based on information theory. It was proposed by Viola & Wells [5] and Maes et al. [6] independently. It is defined as $MI[I_1, I_2] = H(I_2) - H(I_2 \mid I_1)$, where H is the Shannon Entropy involving the conditional probability of having a pixel intensity of i_2 in an image I_2, given the information that the corresponding pixel in I_1 has intensity i_1. Also, in [7], a similarity measure suited for multimodal registration was proposed by Haber and Modersitzki based on normalised gradient fields. The idea is to consider two images as similar if intensity changes occur at the same position in both images. The image gradients are normalised and regularised.

2.2. Transformations

Medical image registration methods can be divided into two categories: parametric and non-parametric transformation functions. The former one is characterised by featuring a function that is described by a limited number of parameters. Non-parametric methods typically feature a transformation function based on a vector per voxel describing the displacement of the point represented by this voxel. This is converted to a continuous function by interpolation. A desirable quality of a function is to be homeomorphic, that is continuous, one-to-one and onto. This property ensures a unique and continuous inverse transformation. It confirms that adjacent structures are still adjacent after the transformation. A few examples are given below.

2.2.1. Parametric Transformation Functions

A registration method based on a parametric transformation function is usually formulated as a minimisation problem in which an optimal set of parameters must explicitly be found that minimises the chosen cost function. Often landmark information is used to construct a smooth mapping using a collection of landmarks in one image, which are to be matched by the transformation to another collection of corresponding reference landmark points.

- **Transformations based on Radial Basis Functions**

Radial Basis Functions (RBF) depends only on the distance between two points. Creating a global function based on a set of RBFs is a powerful way to describe the geometric transformation. Thin plate splines(TPS) are such radial basis functions that are derived from minimisation of a smoothness measure based on the partial derivatives of the transformation [8]. Multiquadratics, inverse multiquadratics, elastic body splines (EBS), Gaussian functions are also used as the basis functions for RBF-based transformations [9]. A Gaussian based variant of EBS is developed by Kohlrausch et al. named as Gaussian elastic body splines (GEBS) [10].

Osorio et al. [11] described the use of feature matching and RBF interpolation in registration for radiotherapy. It allows simultaneous registration of multiple organs while extra user specified point or line features can also be added. Feature matching and TPS approximation is solved parallely using an iterative method called thin plate spline robust point matching.

- **Transformations based a Grid of Control Points**

A number of control points arranged in a regular grid with uniform spacing is the base approach to parameterising a transformation using basis functions. An often used technique is cubic B-splines, which are defined using four basis functions. As the transformation function is locally controlled, it is termed as free form deformation (FFD). The advantage of using this is that, when evaluating the effect of moving a control point, only the vicinity of this point needs to be considered. In [12] a cubic B-spline FFD transformation approach is applied using MI as a similarity measure for registration of MR images and used in mammography. Multiple authors in radiotherapy used the FFD approach combined with a MI as similarity metric [13, 14,15].

- **Mesh based Models**

Dividing the entire image into polygons (2D) or polyhedra (3D) of some models for registration. The subdivision follows boundaries in the images. This idea is utilized for finite element analysis [16, 17, 19] or spring-mass based registration [18, 20]. Mostly the registration approach is to use organ segmentations for creating a mesh of points connected by triangles (organ surface), tetrahedra or hexahedra (organ volume). This is called model based registration.

2.2.2. Non-parametric Transformation Functions

As mentioned, this field (section 2.3.3) consists of a displacement vector per voxel of the reference image. Interpolation between these vectors defines continuous transformation. The grid based displacement vector field representation constitutes a vast number of degrees of freedom.

2.3. Optimization Methods

It is being observed that in a non-parametric registration, there can be many fields of displacement vectors resulting in the same deformed image and therefore the same cost value as calculated by the chosen similarity measure. Hence, the similarity metric is usually combined with a regularisation term. For parametric transformations, a combination of a regularisation energy term on the parameters and the properties of the parameterisation function is utilized. While RBFs work by providing a smooth interpolation of prescribed displacements. For some non-parametric methods the regularisation imposed is an implicit result of a search strategy instead of a term included in the cost function to optimise.

2.3.1. Hierarchical Approaches

Hierarchical coarse-to-fine approach is utilized in most practical implementations of image registration methods.of. A lot of examples of such possible approaches are given in [21]:

- **Multiresolution approaches** are those where the approximation of deformation is done on low resolution versions of the images first and then the result of this coarse registration is used as a starting point for a registration at a higher resolution and continues until the highest resolution. A multiresolution strategy has a better chance of avoiding local minima.
- **Gaussian scale space** convolves the input images with a Gaussian filter of successively increasing standard deviation (while preserving image resolution), in a coarse to fine manner.
- **Increasing complexity of the transformation** is used for functions consisting of a number of basis functions like a Fourier series. Initial registration estimates coefficients of the first terms (large scale info), fixes it, and further estimates next coefficients (increasing details).
- **Increasing complexity of registration method** consecutively uses different registration methods. Deformable registration methods require an initial global registration to be done.

2.3.2. Methods for Parametric Registration

A number of numerical methods are available for optimising the cost function for parametric registration methods [22]. The most popular are the gradient descent (GD), conjugate gradients (CG), the Levenberg - Marquardt algorithm (LMA), the Broyden - Fletcher - Goldfarb - Shanno (BFGS) and its limited-memory counterpart (L-BFGS). The efficiency of computing the derivative of the cost function with respect to each of its parameters is considered as the key ingredient for having an efficient optimisation.. If these derivatives cannot be found analytically they can be estimated using finite difference approximations.

2.3.3. Methods for Non-parametric Registration

Regularisation is very important for non-parametric transformations. A few examples of non-parametric registration methods are given below.

- **Elastic Matching**

A linear elastic continuum model based registration method was presented in [24], works by finding an equilibrium between external forces applied to the elastic continuum (derived using local similarity of pixels/voxels) and internal forces that arise from elastic properties being modeled (assuming small local elastic deformations with a linear relationship between them and restoring forces). Navier equation, a partial differential equation is utilized for regularisation. In [23], a linear elastic model is used in combination with a Fourier series parameterisation of the transformation by Christensen and Johnson for an inversely consistent registration.

- **Demons Algorithm**

In [25, 26], Thirion introduced Demons method where registration is done by finding a driving force at each point using optical flow based on the intensity gradient of the image. Each pixel/voxel has an associated deformation vector with the information of mapping in the reference image. Gaussian filter is used for flow regularization. A speedup 40 % is achieved by reformulating the driving forces in [27], using gradient information from both source and reference images, and validated on CT images from multiple cancer sites.

- **Viscous-fluid Registration**

This registration method is designed by Christensen et al. in [28] for handling large geometric displacements between two images along with homeomorphic mappings. A continuum physics based motion model like viscous fluid is used for regularising the registration.

Here, a body force vector field is taken as driving force, derived using image intensities by finding the local direction of steepest decrease of an SSD similarity measure. This method requires an iterative solution of a partial differential equation (PDE) while another PDE must be solved in each iteration to find a vector field of velocities. An eigenfunction basis of a linear operator representing relationship between velocities and body forces, speeds up the calculation of the velocity vector field using a convolution filter, presented by Bro-Nielsen et al. in [29]. A full multi-grid solver is utilized in [31] for solving the viscous-fluid PDE for faster implementation and use this method to also achieve a multiresolution implementation. In [30] the viscous-fluid registration method is extended to include the use of landmark information.

- **HAMMER**

Shen et al. [32] introduced the ”hierarchical attribute matching mechanism for elastic registration” (HAMMER). This advanced hierarchical registration is based on intensities, edge information, as well as segmentation of images into different types of tissue (mainly used for characterisation of voxels based on geometric moment invariants). Driving vectors with the most distinct attributes are used first and then gradually other points are added to avoid local minima.

- **Optical Flow based Registration Methods**

The estimation of optical flow signifies the detection of a quantitative measure related to the change of image intensity information between two images. It is a field of ’optical velocity’ vectors consisting of the changes in space coordinates, showing the direction of image intensity flow. In the Horn and Schunck algorithm [33], an intensity and a penalising (of non-smooth flow fields) term based cost function is minimised to find the optical flow field. An invertibility cost term is added to this method in [34] to obtain inverse consistent registration.

2.4. Notable Works

Penney et al. [35] presented a method to register a pre-operative 3D CT or MR volume to a set of intra-operative tracked ultrasound images using modified version of the iterative closest point algorithm based on the combination of the liver vessels and liver surface features. Further in [36], the new preoperative MR -US registration algorithm converts the intensity values of the MR and ultrasound images into vessel probability values and then registration is carried out between the vessel probability images. A fast intraoperative non-rigid registration of the preoperative models to the ultrasound volume is proposed by Lange et al. in [37], which is based on the vessel center lines and consists of a combination of the Iterative Closest Point algorithm and multilevel B-Splines. In [38], they again developed a method of combining anatomical landmark information with a fast non-parametric intensity registration approach to incorporate prior knowledge into the registration process. Wein et al. [39] developed a new method that allows simulations of medical ultrasound from CT in real-time. They are combined with a robust similarity measure and serves as the foundation of a fully automatic registration. Again in [40], they presented a method for dense-field deformable registration of CT and 3D ultrasound using a robust multi-channel local similarity metric. A semi-automatic non-rigid registration method for matching pre-operative CT/MR images and intraoperative ultrasound images is proposed in [41]. The global motion is modeled by an affine transformation, while the local deformation is described by Free-Form Deformation (FFD) based on B-splines. Weon et al. [42] developed a robust position estimation system of a moving liver lesion which estimates the lesion position by registering a US image to 4D MR images, even if the US image does not include the lesion. More details on the useful articles about rigid and non-rigid registration is noted in Table 2.1.

.**Table 2.1.** Exploration of related useful literatures

Ref. No.	Author	Registration Class	Similarity Measure	Remarks
[12]	Rueckert et al., 1999	Affine + Non-rigid ; Monomodal (Breast; MR)	Normalized MI	Defining the spatial relationship using FFD and B-Splines
[35]	Penney et al., 2001	Rigid, Multimodal (Liver; US, CT/MR)	Mean closest distance	Used ICP; vessel centerline and liver surface as features
[45]	Roche et al., 2001	Rigid; Multimodal (Brain; US, MR)	Bivariate Corr. Ratio	Intensity and gradient magnitude combined
[32]	Shen et al., 2002	Affine + Non-rigid ; Monomodal (Brain; MR)	Attribute Vectors	Hierarchical Attr. Matching Mechanism for Elastic Reg.
[37]	Lange et al., 2004	Non-rigid; Multimodal (Liver; US, CT)	Dist.-Vessel Centre Line	Combined the ICP algorithm and multilevel B-Splines
[36]	Penney et al., 2004	Rigid; Multimodal (Liver; US, MR)	Normalized CC	Images are converted to vessel probability images
[43]	Ashburner, J., 2007	Non-rigid ; Monomodal (Brain; MR)	Mean Squared Diff.	Diff. Anatomical Reg. using Exponentiated Lie algebra”
[44]	Avants et al., 2008	Non-rigid ; Monomodal (Brain; MR)	Cross-correlation	Symmetric image normalization method (SyN)
[39]	Wein et al., 2008	Affine; Multimodal (Liver; simulated US, CT)	Correlation Ratio	Image intensities are remapped
[38]	Lange et al., 2009	Non-rigid; Multimodal (Liver; US, CT)	Dist.- Norm. Grad. Field	Landmark-intensity combined information is utilized

Ref. No.	Author	Registration Class	Similarity Measure	Remarks
[40]	Wein et al., 2010	Non-rigid; Multimodal (Liver; sim. US, CT)	Local Cross Correlation	Automatic non-linear deformation mapping
[46]	Nam et al., 2011	Affine; Multimodal (Liver; US, CT)	Dist.- Edge Matching	Refinement using vessel and surface information
[41]	Lu et al., 2012	Affine + Non-rigid; Multimodal (Liver, Kidney; US, CT/MR)	Mutual Information	HPV interpolation (partial volume based on the Hanning windowed sinc function) used
[42]	Weon et al., 2012	Affine + Non-rigid; Multimodal (Liver; US, CT/MR)	Dist.-Vessel Centre Line	Inferior Vena cava (IVC) and the liver surface are adopted as anatomical features
[47]	Parisot et al., 2012	Rigid; Monomodal (Brain; MR)	Distance Metric	Expectation Maximization algorithm utilized
[48]	Khan et al., 2013	Affine + Non-rigid; Monomodal (Brain; MR)	Mean Square Error	Subcortical and cortical shape matching; Multi Structure Locally Optimal Large Deformation Diffeomorphisms
[49]	Reducindo et al.,2014	Rigid + Non-rigid; Monomodal & Multimodal (Brain; CT, MR)	Entropy, Variance	Parametric, Optical Flow, Local Variability Measures
[50]	Xu et al., 2014	Non-rigid; Monomodal (Liver; CT)	Mutual Information	MORFEUS, finite element model (FEM)-based multiorgan deformable image registration method using TPS

This chapter outlined the details and importance of image registration, more specifically deformable image registration in the field of medical image analysis. Critical review of existing algorithms helped to understand how previously proposed algorithms encounter the major challenges of this field. Further, the concepts have been utilized to meet the goals of the thesis.

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