GEOMETRIC SIGNAL PROCESSING AND APPLICATIONS TO BRAIN MAPPING

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ABSTRACT

We discuss spatial transformation techniques for multidimensional image registration. Examples from Brain Mapping are given. We illustrate the problem by reviewing point matching, which is the 'gold standard' in this area. The point matching formulation is not adequate for all applications, and we describe various extensions and generalizations. One important issue is multi-set registration, others are more general nonlinear models, as well as the problems of registration on the basis of intensity data and when the geometrical objects to be registered are curves, surfaces, or volumes. This leads to many interesting problems that deserve further study. Finally, we discuss the accuracy in registration. The formulation and measurement of accuracy in geometric matching are challenging and require further research.

1. INTRODUCTION

Much of conventional signal processing concentrates on the interpolation, extrapolation and smoothing of signals. The primary question being asked is 'what?'. In multidimensional signal processing the question 'where?' is often of greater importance. This question is intimately related to the geometry of the support space, rather than of the function space. Geometrical Signal Processing (GSP) is the art and science that addresses these questions. We give some sample applications.

In diagnostic and research applications, the interpretation of brain images is greatly enhanced when different data sets are compared in the same coordinate system. The ability to integrate information collected by different imaging modalities has great potential in answering basic and clinical problems in the neurosciences. Equally important is the task of stacking sectional images collected by some medical image device and displaying this stack as a 3-D entity. Image registration is at the heart of these activities.

In many biomedical studies of the brain and/or other organs, the organ is sectioned with a mechanical cutting device and the images are acquired on a per slice basis. However, information so acquired often obscures functional interrelationships involving multiple structures on sections. Thus, whenever clear and descriptive information about an entire area is needed, one has first to place these sections in a way consistent with their source volume (registration), and then perform some kind of 3-D display operation (rendering).

An early utilization of image registration techniques for brain mapping is found in the work of Hibbard and Hawkins [1]. In this work, a series of sectional images of brain metabolic activity are registered to each other in order to form a stack. The stacking provides the third dimension. This arrangement enabled Hibbard and Hawkins to study the 3-D functional effects of pharmacological substances on a rat's brain. Functional imaging techniques are able to provide information on hemodynamics, metabolism, or pharmacokinetics on a regional basis.

Different imaging techniques can provide complementary information about the body. This process is referred as multi-modality imaging. For example, in human brain imaging magnetic resonance imaging (MRI) can give excellent spatial resolution in three dimensions, while positron emission tomography (PET) can provide functional information such as location of epileptic activity. Whenever images are acquired with different devices, spatial registration is necessary. For example, Pelizzari *et al.* [2] combined anatomical images provided by MRI with functional images obtained from PET. This arrangement allows correct anatomical localization of functional structures in the brain and has been used in radiation therapy and surgical planning. In experimental biology, a 3-D anatomical-functional study by Goldszal *et al.* [3] has produced relevant information regarding the wiring of the central nervous system (CNS) and the mechanisms underlying information processing in the rodent brain.

The above applications require 2- and 3-dimensional registration of data from the same object. An even more challenging problem arises when images from different individuals must be matched. To compare PET data from different individuals Fox *et al.* [4] developed a standard coordinate system and procedures for aligning brain scans to these coordinates. This allows investigators to study variations across populations, to average brain scans so that very subtle effects can be detected, and permits the comparison and sharing of data obtained at different laboratories.

In this paper we review the conceptual formulations for 2- and 3-dimensional image registration. We focus on the registration problem of finding a transformation $y = T(x)$ for transforming geometrical spaces. Once the transformation is known, the modification of images is straightforward and we do not discuss that aspect of the problem. We first talk about several well-studied point matching techniques that provide a logical formulation of the registration problem. We also introduce the problem of multi-set matching which is an example of the problem of finding a 'standard' from imperfect data. Subsequently, we review various more complex image matching problems. Finally, we discuss the core issue of assessing the accuracy of image matching.

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2. POINT MATCHING

In this section we review a number of registration methods based on point matching. These solutions have a common formulation: we are given two sets of corresponding fiducial points (x_i, y_i) $i = 1 \ldots n$ that lie in d-dimensional space. We are asked to find a transformation $y = T(x)$ that will match the first, x point set with the second, y point set. The solutions that we review in this section find the transformation by minimizing the *residual error*

$$e = \sum_i \|y_i - T(x_i)\|^2. \qquad (1)$$

They differ by considering different classes of transformations. We will first describe the matching of two point sets, and subsequently will discuss the *multi-set* matching problem.

2.1 Procrustes Problems

In the Procrustes problem the transformation being sought is given by

$$y = T_o(x) = Ox + t, \qquad (2)$$

where O is an orthogonal matrix and t is a translation. This transformation is called an *isometry* because it preserves distances between points. This problem has an illustrious history: it was first posed in the statistics literature [5] where the name *Procrustes Problem* was introduced. The optimal translation is equal to the difference between the centroids of the two point sets. For centered point sets (centroids at the origin) a closed-form solution for the orthogonal matrix [6] can be obtained in terms of the singular value decomposition (SVD) of the matrix

$$R_{xy} = \sum_i x_i y_i' \qquad (3)$$

The SVD solution can be used for any number of dimensions. One interesting feature of the Procrustes problem is that the transformation for matching the first point set with the second is the inverse of the transformation for matching the second set with the first. A matching problem that has this property is *symmetric*.

An interesting generalization of the Procrustes problem is to find the best *similarity* transformation, namely a transformation that maps straight lines into straight lines and preserves angles. This transformation can be expressed as

$$y = T_s(x) = aOx + t, \qquad (4)$$

where a is a scalar. This is a simple extension of the solution of the Procrustes problem [6]. Another interesting variation of the problem, solved only recently [7], is to find the best *rigid body motion*, which is given by equation (2) with the restriction $\det(O) = +1$.

2.2 Affine Matching

Affine transformations are specified by

$$y = T_a(x) = Ax + t, \qquad (5)$$

where A is a $d \times d$ nonsingular matrix. Again, we seek to minimize the residual (1). This problem can also be solved in closed form. As in the Procrustes problem, the best translation is equal to the difference between the centroids. For centered point sets the optimal A is given by

$$A = R_{yx} R_{xx}^{-1} \qquad (6)$$

where matrix R is defined in equation (3). From (6) it is clear that the affine matching problem is not symmetric. This problem is easier than Procrustes, and is intimately involved with the theory of regression.

2.3 Multi-set Matching

In many cases, (e. g., alignment of serial sections) we have several point sets that must be aligned. The multi-set matching problem is a formal model that addresses this question. We are given a collection of sets of points x_{ij}, $i = 1 \ldots n$, $j = 1 \ldots m$, all in d-dimensional space. Points with a given value of j belong to one image, and each value of i specifies corresponding points in different images . We are asked to find a collection of transformations T_j, $j = 1 \ldots m$, as well as a set of *fiducial locations* y_i, $i = 1 \ldots n$ that minimize the residual

$$e = \sum_{ji} \|y_i - T_j(x_{ij})\|^2 \qquad (7)$$

The essence of the multi-set matching problem is that the fiducial locations must be found from the data.

The solution of the multi-set matching problem depends on the class of transformations being considered. We have analyzed the multi-set Procrustes problem, $T_j(x) = O_j x + t_j$, where O_j is an orthogonal matrix and t_j is a translation. In the general case, the optimal translations align the centroids of the sets. For $m = 2$ sets the problem is mathematically equivalent to the classical Procrustes problem. For $m > 2$ and $d = 2$ we have developed iterative algorithms and have applied them to the alignment of serial sections [3, 8]. In the multi-set Affine matching problem, $T_j(x) = A_j x + t_j$, where A_j are general $d \times d$ matrices. The translation vectors again align centroids of point sets. The fiducial points y_i lie in vector spaces that are found by solving an SVD problem in m dimensions, where m is the number of sections.

3. GENERALIZATIONS

Point matching provides a setting for discussing more general problems. Unfortunately, the point matching formulation is not adequate for many application. We consider three aspects of generalization: classes of transformations, data types, and matching criteria.

3.1 Classes of Transformations

In our discussion of point matching, we have described several classes of mapping transformations: isometries, similarities, and affine. In some problems, a more general class is necessary. It may be necessary to account for curvilinear distortion.

One general approach is to write the transformation as

$$y = T(x) = \sum_k a_k f_k(x) \qquad (8)$$

where $f_k(x)$ are specific vector-valued functions of x, and a_k are scalar parameters that are adjusted for best matching. This class includes the affine transformations discussed in section 2. Bookstein proposed using functions that are derived from generalized theory of splines [9], and many other choices are possible [10].

A more general class is provided by so-called rubber sheet transformations [11, 12, 13, 14]. These transformations do not have a specific parametrization, but are constructed implicitly by attempting to minimize a distortion measure while simultaneously optimizing the 'smoothness' of the transformation.

Even more radical nonlinear transformations are used in brain flattening [15, 16, 17]. In typical volumetric matching problems one attempts to find transformations of 3-D space to account for differences between instruments or individuals. However, the cerebral cortex is a surface topologicaly equivalent to a plane that is folded to fit into the head. In brain flattening one computes a transformation that maps the convoluted structure of the cerebral cortex onto a plane.

3.2. Data Types

A distinction should be made between extrinsic and intrinsic matching [10]. Extrinsic matching is based on points in the image that have been inserted to serve as fiducial points for alignment. Intrinsic data are features of the image that are used for alignment. In many problems, such as matching images between different individuals, it is difficult or impossible to produce extrinsic reference points or structures.

Perhaps the most natural intrinsic reference data is the gray value distribution in the image. A more general approach to intrinsic matching is to extract geometric features from images, and to perform matches on the basis of these data. For example, one may preprocess multidimensional images to extract points, curves, surfaces and volumes, and to subsequently match these structures. We will call these data *geometrical objects.* Some of the most valuable geometrical features are derived from the support region (the set of points where the image is non-zero). Some geometrical objects may be derived from others: surfaces may be computed from volumes and centroids (points) may be computed from regions. Examples of derived geometrical features are the centroid and central moments [18]. These data lead to simple image matching algorithms [1].

In matching, correspondence between geometrical objects is of great practical importance. Point matching leads to easy solutions because we assume that we know the correspondence between the points to be matched. If correspondence is not provided, the problem of matching is much more difficult. Establishing correspondence between large collections of points is computationally unfeasible, so that point matching techniques have limited applicability.

3.3 Matching Criteria

In point matching we minimize a residual based on distances, but this criterion can only be used if the data available are in the form of points with established correspondences. In many cases neither points nor correspondences may be available.

One general criterion is the cross-correlation function. This may be applied directly to images. It has been used for matching with rigid-body transformations [19] and for elastic mappings [11]. It can be generalized to correlating geometric objects [20]. The disadvantage of cross-correlation is that it does not relate directly to distances between points in space.

If correspondence is known, the residual is a good matching criterion. The Minkowski distance function (or distance transform) may be used if correspondence is not known. Let S be a set of points in the reference object. The distance transform of the set S is defined as

$$d(x, S) = \min_{p \in S} \|x - p\|. \tag{9}$$

If R is the set of points in the object to be matched, and $T(x)$ is the transformation, the distance matching criterion is

$$e = \sum_{x \in R} d^2(T(x), S). \tag{10}$$

This can be treated like the residual (1), and best match is found by minimizing it over a given class of transformations. This criterion has several attractive properties. It is directly related to distances between points. It does not require point correspondences to be established, and furthermore is applicable to the matching of lines, surfaces, and volumes where point correspondence is not applicable. This criterion also has an important *subset property*: if $T(R) \subset S$ then $e = 0$. Thus it indicates, in a very clear way, when a perfect match has been achieved. This distance criterion has been used for multimodality image matching [2].

4. THE BEST METHOD

We see that there are many ways of formulating image matching problems, involving various data sets classes of transformations. In choosing the best method, it is important to formulate criteria for the evaluation of optimality. We will describe one approach to this problem, and examine some of its implications.

Suppose we have two spaces: we will call one of them X, the test space and the other Y, the reference or atlas space. We wish to compute a specific mapping $T: X \to Y$ that will 'align' the two spaces. We do this by finding a transformation T_1, belonging to a class $\mathcal{T}$ by minimizing some error measure. For example, in the Procrustes problem $\mathcal{T} = I$, the class of all isometries (2), while in affine alignment $\mathcal{T} = \mathcal{A}$, the class of all affine transformations (5). In both methods the error measure is the residual d defined in equation (1). We ask: which method is better?

It may be intuitively plausible to choose the method that produces the smallest residual error. It can be shown that the residual with the affine method is smaller than for the Procrustes method, so one might think that this is the technique of choice. We investigated this question in experiments on serial section alignment [8]. Sections were prepared with six extrinsic fiducial points: three points for alignment, and the remaining three points were used to measure the alignment error. We found that the affine method produced smaller residuals but much larger actual errors than the Procrustes method. Errors were further reduced by using the multi-set Procrustes method to find accurate fiducial locations.

In conclusion, image matching deals with the problems of finding the transformations for aligning images and multidimensional data sets that reside in different geometrical spaces. There is a rich collection of problems that depend on the character of data available and the type of transformation to be performed. The field includes many unsolved conceptual and computational problems.

Among the problems to be solved is that of finding the best 'reference' or 'atlas' image or dataset. We have formulated one version of this problem in section 2.3. There are, however, issues that this abstraction does not address. In the alignment of data sets from different individuals the location of fiducial points may be different, and these differences or variations may be of diagnostic value. Euclidean distance is appropriate in some problems. However, if the objects being matched are not rigid, we feel that the 'reference' data set should include not only the location of fiducial points but also information about their variability. One of the unsolved problems in matching is to develop techniques for characterizing this variability, and to extract appropriate information on variability from collections of multidimensional images.

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