Multi-dimensional mutual information image similarity metrics based on derivatives of linear scale-space

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Abstract

We propose a new voxel similarity measure which uses local image structure as well as intensity information. The derivatives of linear scale space are used to provide structural information in the form of a feature vector for each voxel. Each scale space derivative is assigned to its own information channel. We illustrate the behavior of the similarity measure for a simulated signal and 2D medical brain images to demonstrate its potential for non-rigid, inter-subject registration of 3D brain MR images as a proof of concept.

1. Introduction

Registration is a process of aligning objects within images. It is particularly useful for medical image analysis because it provides a method of placing patient anatomy in the same coordinate frame. This allows, for example, information from different imaging modalities (MR, CT), or the same imaging modality at different timepoints (serial or longditudinal), to be combined. Voxel intensity based similarity measures have been demonstrated to perform well for the automatic rigid-body registration of medical images [6] [2] [7]. However, rigid-body motion is only applicable to anatomy that is constrained by bone, whereas most organs of interest are comprised of soft tissue that undergoes non-rigid motion. Voxel intensity based similarity measures have limitations for non-rigid registration because non-corresponding anatomy can have the same intensity. This can result in false maxima of the similarity measure. One way of addressing this limitation is to use additional geometrical information of the local image structure. Here we propose using the spatial derivatives of the Gaussian scale space to provide such information. Essentially this results in a feature vector instead of a scalar (intensity) for each voxel. We require a similarity measure that is able to match images with a non-linear relationship between intensities, e.g. images of different modalities. We explore the use of multi-dimensional mutual information as a match criteria.

1.1 Related work

Shen et al. [5] designed a similarity measure that determines image similarity based on a attribute vector for each voxel at GM, WM and CSF interfaces. The attribute vector is derived from the voxel's edge type and geometric moment invariants calculated from voxel intensities in a spherical neighbourhood. This similarity measure is specifically designed for intra-modal, inter-subject MR brain image registration and requires a GM, WM and CSF segmentation.

In contrast, we aim for a general purpose registration algorithm that can be applied to intermodality data direct from the scanner without a pre-processing step. We start by establishing a set of desirable properties of the similarity measure and use these to devise a mutual information measure that utilises more structural image information than simple intensities. In this way we retain the desirable intermodality property of mutual information. We use the derivatives of the Gaussian scale space expansion of the image to provide this local information. To assess the performance of the measure we present some simulations and results of intersubject intramodality registration experiments.

2. Theory

We start with a standard intensity based similarity measure, mutual information [1] [9], that is known to perform well for rigid rigid-body registration.

2.1. Similarity measures for rigid-body registration

Mutual information measures are derived from the joint intensity distribution $P(a,b)$ which is closely related to the joint histogram. $P(a,b)$ represents the probability that corresponding voxel intensities are: a in image A and b in image B. Mutual information is defined as:

$$MI(A,B) = H(A) + H(B) - H(A,B) \quad (1)$$

Where

$$H(A) = -\int_A P(a) \log P(a) da \quad (2)$$

$$H(A,B) = -\int_{A\cap B \times A\cap B} P(a,b) \log P(a,b) dadb \quad (3)$$

Similarly, normalised mutual information, was shown by Studholme [3] to be less dependent on the amount of image overlap, is defined as:

$$NMI(A,B) = \frac{H(A)+H(B)}{H(A,B)} \quad (4)$$

2.2. Similarity measures for non-rigid registration

Basically a similarity measure should return a value that is a smooth decreasing function of misregistration. A quadratic function is thought desirable to facilitate gradient based optimisation. If we use operator L to extract the additional geometrical information from the image then L should be invariant to rigid-body transformations, that is to say that for image A and rigid transformation T: $L \circ (T \circ A) = T \circ (L \circ A)$.

2.3. Scale space derivatives

In analogy to the Taylor series expansion of a continuous function, a 3D image $I(\mathbf{x})$ can be expanded in terms of it scale space derivatives:

$$f_n = f_{i,j,k} = \frac{\partial^{i+j+k}}{\partial x^i \partial y^j \partial z^k}(G_\sigma(\mathbf{x}) * I(\mathbf{x})) \quad (5)$$

Where G_σ is the Gaussian defined as:

$$G_\sigma(\mathbf{x}) = \frac{1}{2\pi\sigma^2} \exp(-|\mathbf{x}|^2/2\sigma^2) \quad (6)$$

So the image can be expanded as this:

$$\sum_{i=0}^{\infty}\sum_{j=0}^{\infty}\sum_{k=0}^{\infty} f_{i,j,k} \quad (7)$$

The scale space derivatives are mutually independent and can be used as a set of image features that contain information about image structure.

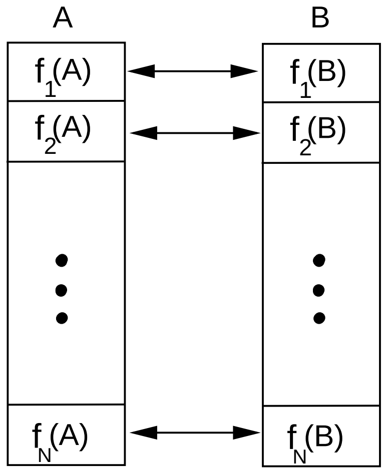

Figure 1. *Corresponding features ($f_i(A), f_i(B)$) are assigned to the same information channel.*

2.4. Multi-channel information theoretic similarity measures

We have a set of derivative features $\{f_n\}$ for each image which we propose to use to construct a feature space. We apply a multi-dimensional similarity measure to this space by assigning each derivative from the image pair $f_n(A), f_n(B)$ to an information channel, this is illustrated in Figure 1.

Equations 1 and 4 are simply 2D forms of an ND information measures. For two pairs of features the joint event is 4D, i.e. 4D joint histogram and we need two information channels. The mutual information measures are as follows:

$$MI(A_1,A_2;B_1,B_2) = H(A_1,A_2) + H(B_1,B_2) - H(A_1,A_2;B_1,B_2) \quad (8)$$

$$NMI(A_1,A_2;B_1,B_2) = \frac{H(A_1,A_2)+H(B_1,B_2)}{H(A_1,A_2;B_1,B_2)} \quad (9)$$

A_1, A_2 and B_1, B_2 refer to derivatives determined from the target and source images respectively.

3. Methods

3.1 Implementation of Gaussian scale-space

In our experiments we consider only the luminance, first and second order derivative terms of the scale space expansion. The luminance image $I_0(\mathbf{x})$ is generated by convolving the image $I(\mathbf{x})$ with a Gaussian kernel $G(\mathbf{x})$: $I_0(\mathbf{x}) = G(\mathbf{x}) \star I(\mathbf{x})$ where $G(\mathbf{x}) = \frac{1}{2\pi\sigma^2}\exp(-|\mathbf{x}|^2/2\sigma^2)$. The gradient magnitude image $I_1(\mathbf{x}) = |\nabla(I_0)|$ and the Laplacian image $I_2(\mathbf{x}) = \nabla^2(I_0)$. In the experimental work we refer to these as luminance, gradient magnitude of luminance and Laplacian of luminance. The intensity of the Laplacian of luminance image was normalised by subtracting the minimum so that its minimum is zero. To avoid truncation during convolution, the image was reflected about each boundary by half the kernel width. Gaussian convolution and differentiation (central derivative and forward and backward derivatives at the boundary voxels) were implemented in matlab (Mathworks Inc, MA, USA) for 1D signals and 2D images and in C++ using vtk (Kitware, NY, USA) classes for 3D images. In all instances, the kernel radius was chosen to be three times larger than the standard deviation to avoid truncation effects.

3.2 Implementation of multi-dimensional mutual information

A major difficulty obstacle of this approach is that the dimensionality of the joint histogram array depends on the number of derivative terms n. The array size grows as a power of n. This can lead to a sparsely populated array, also the memory required and access time grow as a power of n. Reducing the number of bins can help, but this only results in a linear reduction of size.

Image interpolation is generally the most computationally intensive part of voxel-based algorithms and grows linearly with n. A possible way of reducing the overhead could be to down-sample images. For 3D images, down-sampling by a factor of 2 reduces the number of voxels that need to be interpolated by a factor $2^3 = 8$. In summary, this approach seems viable for small n with down-sampling.

All similarity measures were also implemented in both matlab (1D signals and 2D images) and also in C++ for 3D images. For the non-rigid registration of 3D images a segmentation propagation algorithm based on the method described in [8] and the 4D similarity measures were implemented in C++ and vtk by adding to and redesigning a number of classes of the CISG registration toolbox [10].

4. Validation experiments and results

Our validation strategy is based on assessing the registration function, i.e. similarity as a function of misregistration. We desire a smooth function that increases with decreasing misregistration. We compare the new measures with standard ones on progressively more complex data. We start with a simple 1-D test signal and we consider 2-D slices extracted from clinical MR data that the measures

Our validation strategy based on a set of three progressively more difficult registration experiments. In the first a pair of 1D signal simulations with no noise are used. The second uses a pair of 2D MR brain images of the same person, in this case there is a noise difference. The third uses non-rigid registration for the inter-subject registration of a pair of 3D brain MR images of different people.

4.1 Geometrical scaling of synthetic signal

A test signal was constructed by low-pass filtering a signal consisting of two rectangular pulses. We chose to model the imaging system using a unit width Gaussian low pass filter. The luminance, gradient magnitude of luminance and and Laplacian of luminance signals were generated from the test signal using a Gaussian filter of standard deviation $\sigma = 6$ samples. Figures 2 and 3 illustrate the test signal and scale space derivatives.

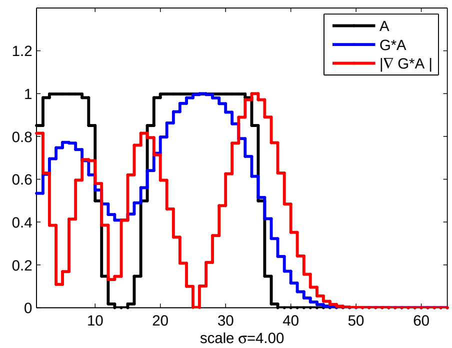

Figure 2. *Test signal (A) and derived signals used for registration simulation experiments.Gaussian filtered Luminance signal (G*A) ($\sigma = 4$) and gradient magnitude of luminance $|\nabla G * A|$ ($\sigma = 4$).*

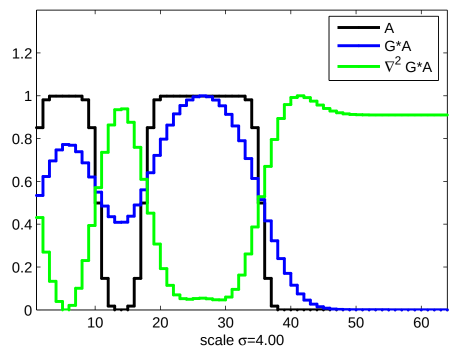

Figure 3. *Test signal (A), Gaussian filtered Luminance signal (G*A)($\sigma = 4$) and Laplacian of luminance $\nabla^2 G * A$ ($\sigma = 4$).*

To assess the behavior of similarity measures as a function of misregistration (registration function) a copy of the

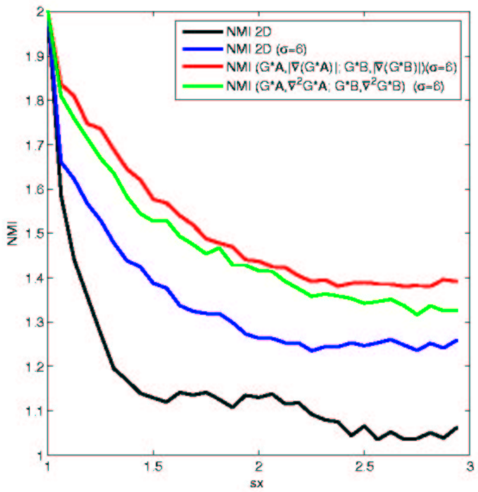

Figure 4. *Similarity plots of standard and 4D Normalised mutual information (NMI) for the 1D test signal as a function of geometric scale change (s_x,$1 \leq s_x \leq 3$). Standard form: NMI(A,B). Standard with Gaussian blurring ($\sigma = 6$): NMI(G*A,G*B). 4D NMI with Gaussian and gradient magnitude of luminance input channels ($\sigma = 6$): NMI $(G * A, |\nabla(G * A)|; G * B, |\nabla(G * B)|)$. 4D NMI with Gaussian and Laplacian of luminance input channels ($\sigma = 6$): NMI $(G * A, \nabla^2 G * A; G * B, \nabla^2 G * B)$.*

test signal was geometrically scaled relative to the original signal. The similarity of these two signals was measured as a function of the scale factor (s_x,$1 \leq s_x \leq 3$), where $s_x = 1$ represents perfect registration.

Figure 4 shows the resulting graph for four similarity measures: standard normalised mutual information, standard normalised mutual information applied to luminance signal, 4D normalised mutual information using luminance, 4D normalised mutual information using luminance.

For the standard form, there is a false maximum at $s_x \approx 1.6$ and the function is ill-conditioned for $s_x > 1.6$. Gaussian smoothing helps condition the registration function, but it flattens around $s_x = 1.9$. For the 4D measures, both are well-conditioned and relatively easy to optimise.

4.2 Translational misregistration of a brain sub-image

This experiment was designed to simulate non-rigid registration of clinical brain image data. We can evaluate the behavior of our proposed similarity measure by taking two 2D images of the same anatomy and misregistering a small sub-image of one relative to the other. The data was acquired by scanning a volunteer's brain with a special T1W 3D gradient echo MR sequence with two interleaved readout lines. This data was reconstructed into two 3D spatial images separated by an interval of TR (a few milli-seconds). Essentially the difference between the two images is noise, but there is also a small difference in motion artefacts due to fast flowing blood. These images can be considered as a registration gold-standard, and the graphs of the registration function tell us how the similarity measure behaves as a function of misregistration for images with a noise difference. We took an axial slice through the lateral ventricles and extracted a 32×32 pixel sub-image as illustrated in Figure 5. Then we misregistered the sub-image relative to the other image by applying a x-translation t_x, t_x increases from left to right direction in Figure 5. $t_x = 0$ voxels represents perfect registration. Figure 6 shows the results of the experiment. The standard NMI flattens out for $|t_x| > 4$ voxels making it difficult to optimise. Gaussian smoothing widens the capture range to $|t_x| = 6$ voxels while the 4D measures have the widest capture range of $|t_x| = 7$ voxels. This behavior could be important for multi-resolution optimisation, thought useful for recovering large deformation.

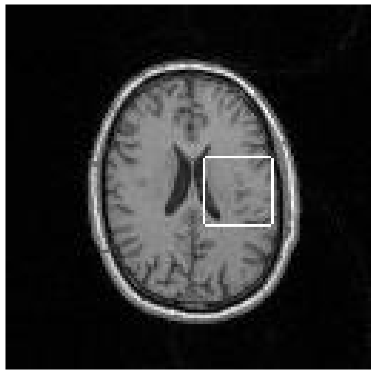

Figure 5. *Illustration of the 32×32 pixel sub-image of the brain used for registration experiments.*

4.3 Segmentation propagation from atlas to clinical image

It is possible to use non-rigid registration to propagate segmentations from one subject image space into another. We apply the method described in [8], based on registering the MNI atlas [4] to the subject image, and then use the non-rigid transformation to propagate the segmentation of the lateral ventricles into the subject space. Figure 7 shows the results of the segmentation propagation with the new 4D similarity measure and the standard one. There are relatively small differences, however, the blue contour appears

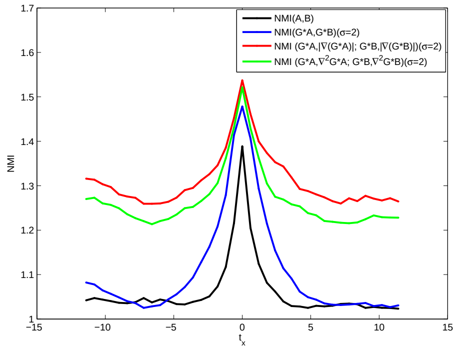

Figure 6. *Plots of the similarity as a function of translational misregistration for a pair of 2D MR Brain images. Standard NMI (no blurring); standard $NMI(G_\sigma * A, G_\sigma * B)$; $NMI(G_\sigma * A, |\nabla G_\sigma * A|; G_\sigma * B, |\nabla G_\sigma * B|)$ and $NMI(G_\sigma * A, \nabla^2 G_\sigma * A; G_\sigma * B, \nabla^2 G_\sigma * B)$ Images are misregistered in the range $-15 < t_x < 15$ voxels. The Gaussian width is $\sigma = 2$ voxels.*

smoother and closer to the ventricular boundary.

5. Discussion and Conclusions

We have established a set of desirable properties of similarity measures for non-rigid image registration of intermodality data. We have used these to design a novel similarity measure based on the derivative of Gaussian scale space. We demonstrated that this has a wider capture range than standard forms for large deformations using a synthetically misregistered signal. We have also shown that this is present when translating a sub-image for 2D brain slices. For non-rigid inter-subject 3D brain image registration of there is similar performance to the standard measure.

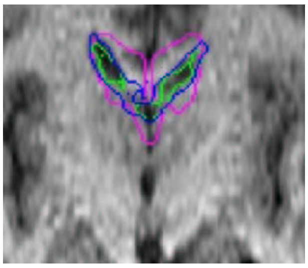

Figure 7. *Comparison of the non-rigid inter-subject registration of 3D MR brain images with the new 4D and the standard 2D similarity measures. The boundary of the lateral ventricle have been propagated into the space of the subject image using non-rigid registration. The unregistered ventricular boundary is shown in purple, the propagation with the standard 2D NMI is shown in green and 4D propagation with $NMI(G * A, |\nabla G * A|; G * B, |\nabla G * B|)$ is in blue.*

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