

# A method on calculating high-dimensional mutual information and its application to registration of multiple ultrasound images

Bo Wang <sup>\*</sup>, Yi Shen

*Department of Control Science and Engineering, Harbin Institute of Technology, PO Box 327, Harbin, PR China*

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## Abstract

Using mutual information as a criterion for medical image registration, which requires no prior segmentation or preprocessing, has been both theoretically and practically proved to be an effective method in these years. However, this technique is confined in registering two images and hard to apply to multiple ones. The reason is that unlike mutual information between two variables, high-dimensional mutual information is ill defined. In textbooks and theoretical essays, three-dimensional mutual information is proposed based on Venn diagram. Unfortunately, mutual information defined in this way is not necessarily nonnegative. In order to overcome the problem, in this paper, we introduce the mutual information matrix. By calculating its eigenvalues, high-dimensional mutual information is defined. This definition is nonnegative, bounded, and could be extended to higher dimensions, thus enables us to register more than three images. In the end, this definition is tested and proved to be effective on registration of multiple US images through simulation.

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## 1. Introduction

Different medical image modalities provide different information about anatomy and function of the imaged organs. For example, anatomical modalities depict primarily morphology, such as X-ray, Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Ultrasound (US), acquired by various imaging system. Functional modalities depict primarily information on the metabolism but have no enough information about anatomy, including  $\gamma$  camera, Single Photon Emission Computed Tomography (SPECT), Positron Emission Tomography (PET) [1]. Multimodality image registration, which combines information from several imaging modalities in a single image, may facilitate correct images and/or treatment, and could be applied on cases such as the guidance in intraoperative operation [2]. Also, monomodality registration, which concerns proper visualization of useful image information, is an

important first step in successful visualization and quantification of temporal changes in anatomy and physiology [3].

Among the methods for image registration, Mutual Information (MI) based registration excels others on that it requires no prior segmentation or preprocessing, thus enables automated registration. It has been both theoretically and practically proved to be an effective method in these years [4,5]. Ultrasound images, which are ideal for observing abdominal and thoracic organs, could be registered using mutual information after proper preprocessing [6].

Commonly, two images are involved in the registration process. However, in certain situations several images of a scene are to be registered or serial images needs to be compared. On these cases, high-dimensional MI is usually calculated by registering two images first, then registering the third image to the preregistered one [4]. However, if the first two images are misaligned, this procedure would bring error to the final image. The reason of the awkwardness is that in textbooks and theoretical essays on generalized (i.e., higher dimensional) MI [7], the definition of the measure for three images corresponds to Fig. 1. A property

<sup>\*</sup> Corresponding author. Fax: +86 451 86418378.

E-mail address: [wangb@hit.edu.cn](mailto:wangb@hit.edu.cn) (B. Wang).

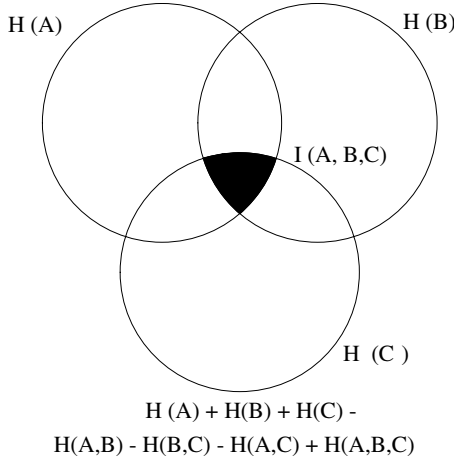


Fig. 1. Definition of three-dimensional MI (black) based on Venn diagram.

of this definition is that it is not necessarily nonnegative. Although other definitions are proposed [8,9], they have not properly solved the problem [4].

In this paper, MI matrix is introduced. By calculating its eigenvalues,  $n$ -dimensional MI is defined, and the property of MI matrix and  $n$ -dimensional MI is discussed. Then, the definition is testified in experiments and proved to be effective on registration of multiple US images.

## 2. Theory

### 2.1. MI matrix

Here we define  $n$ -dimensional MI matrix as:

$$MI = \begin{bmatrix} I_{11} & I_{12} & \dots & I_{1n} \\ I_{21} & I_{22} & & \vdots \\ \vdots & & \ddots & \vdots \\ I_{n1} & \dots & \dots & I_{nn} \end{bmatrix} \quad (1)$$

where  $I_{ij}$  ( $i, j = 1 \dots n$ ) denotes the MI between images  $i$  and  $j$ . Since  $I_{ij} \geq 0$  ( $i, j = 1, 2 \dots n$ ) and  $I_{ii} \geq I_{ij}$  ( $i \neq j$ ), MI matrix is a selfadjoint positive definite matrix. Its eigenvalues (also the singular values) provide a measurement of the length of the vectors. Suppose  $\lambda_i$  is the  $i$ th eigenvalue of MI matrix, from the theory of linear algebra, we know that:

$$(1) \quad \lambda_i \geq 0 \quad (2)$$

$$(2) \quad \sum_{i=1}^n \lambda_i = \text{tr}(MI) = \sum_{i=1}^n I_{ii} \quad (3)$$

### 2.2. $N$ -dimensional mutual information

From Shannon defined entropy, we know that when the number of a series of data increased, the entropy it carries would increase exponentially. Thus, we define  $n$ -dimensional MI as follows:

$$I(x_1, x_2 \dots x_n) = 1 + \frac{\sum_{i=1}^n \frac{\lambda_i}{\sum_{i=1}^n \lambda_i} \lg \left( \frac{\lambda_i}{\sum_{i=1}^n \lambda_i} \right)}{\lg(n)} \quad (i = 1, 2 \dots n) \quad (4)$$

where  $\lambda_i$  ( $i = 1, 2 \dots n$ ) are the eigenvalues of the MI matrix. This definition guarantees that  $n$ -dimensional MI is positive, and  $0 \leq I(x_1, x_2 \dots x_n) \leq 1$ . When  $\lambda_1 = \lambda_2 = \dots = \lambda_n$ , i.e. when  $I_{ij} = 0$  ( $i \neq j$ ) and  $I_{11} = I_{22} = \dots = I_{nn}$ , which means the images are not correlate to each other, the  $n$ -dimensional MI reaches its minimum. When the  $n$  images are identical,  $I(x_1, x_2 \dots x_n) = 1$ .

Define the distance between two images to be  $d = |i - j|$  ( $i, j = 1 \dots n$ ). When serial US images being captured at different time need to be registered, suppose that neighboring images tend to have higher MI compared with distant images. Also, noticed that if there is variation of elements in the MI matrix which is caused by the transformation of a single image, with the same magnitude of variation, larger distance between the transferred image and the reference image would result with greater variation of  $n$ -dimensional MI.

## 3. Experiments

Since the US images are captured within short time interval, we suppose there is not great deformation of the organs, and hence only discuss 2-D rigid body registration, which involves rotation and translation.

### 3.1. Preprocessing

In order to deal with the relatively poor image quality of US images compared with the CT and MRI images, and getting a smooth mutual information surface to enhance the accuracy of registration, US images call for some basic preprocessing.

#### 3.1.1. Filtering

We first filter the US images with a median filter with a  $3 \times 3$  kernel. This process could suppress speckles and in turn smoothed the resulting MI function [6,10].

#### 3.1.2. Interpolation

Most of the time, the reference image and the floating image may be misaligned with each other. In order to calculate MI, we need to apply interpolation to one of the images. The widely used interpolation algorithms are Nearest Neighbor (NN) interpolation, bilinear interpolation and bicubic interpolation. Here, we chose nearest neighbor interpolation based on its advantages that it requires little computation and will not introduce new pixel to the image after interpolation. Also, we notice that there is other method such as PV interpolation, which could acquire much more smooth mutual information function [6].

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