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(54) **IMAGE REGISTRATION METHOD**

(56) **References Cited**

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G06T 7/00 (2006.01)
G06T 11/00 (2006.01)
G06T 3/00 (2006.01)

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CPC **G06T 7/0024** (2013.01); **G06K 9/6202** (2013.01); **G06T 3/0068** (2013.01); **G06T 11/001** (2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

U.S. PATENT DOCUMENTS

2004/0136569	A1 *	7/2004	Daley et al.	382/110
2008/0137080	A1	6/2008	Bodzin et al.	
2009/0087051	A1 *	4/2009	Soenksen et al.	382/128
2010/0254589	A1 *	10/2010	Gallagher	382/133
2012/0076390	A1 *	3/2012	Potts et al.	382/133
2013/0243346	A1 *	9/2013	Cho et al.	382/255
2015/0004630	A1 *	1/2015	Lange et al.	435/7.21

FOREIGN PATENT DOCUMENTS

WO	WO 03/021231	A2	3/2003
WO	WO 2014140070	A2 *	9/2014

OTHER PUBLICATIONS

Mancenko et al "A method for Normalizing Histology slides for quantitative analysis" IEEE 2009.*

* cited by examiner

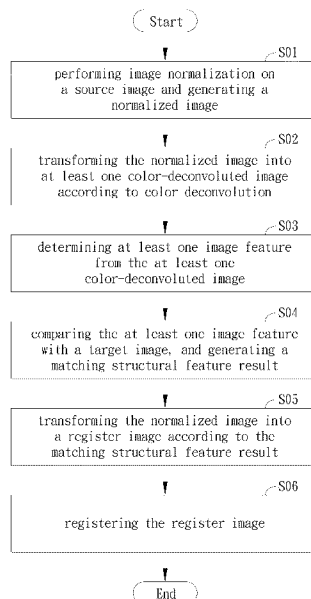
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(57) **ABSTRACT**

An image registration method for registering images into a coordinate system includes the following steps: (a) performing image normalization on a source image and generating a normalized image; (b) retrieving at least one color-deconvoluted image from color-deconvoluting the source image; (c) determining at least one image feature from the at least one color-deconvoluted image; (d) comparing the at least one image feature of the at least one color-deconvoluted image with a target image, and generating a relative matching structural feature result; and (e) transforming the normalized image into a registered image according to the matching structural feature result.

7 Claims, 9 Drawing Sheets



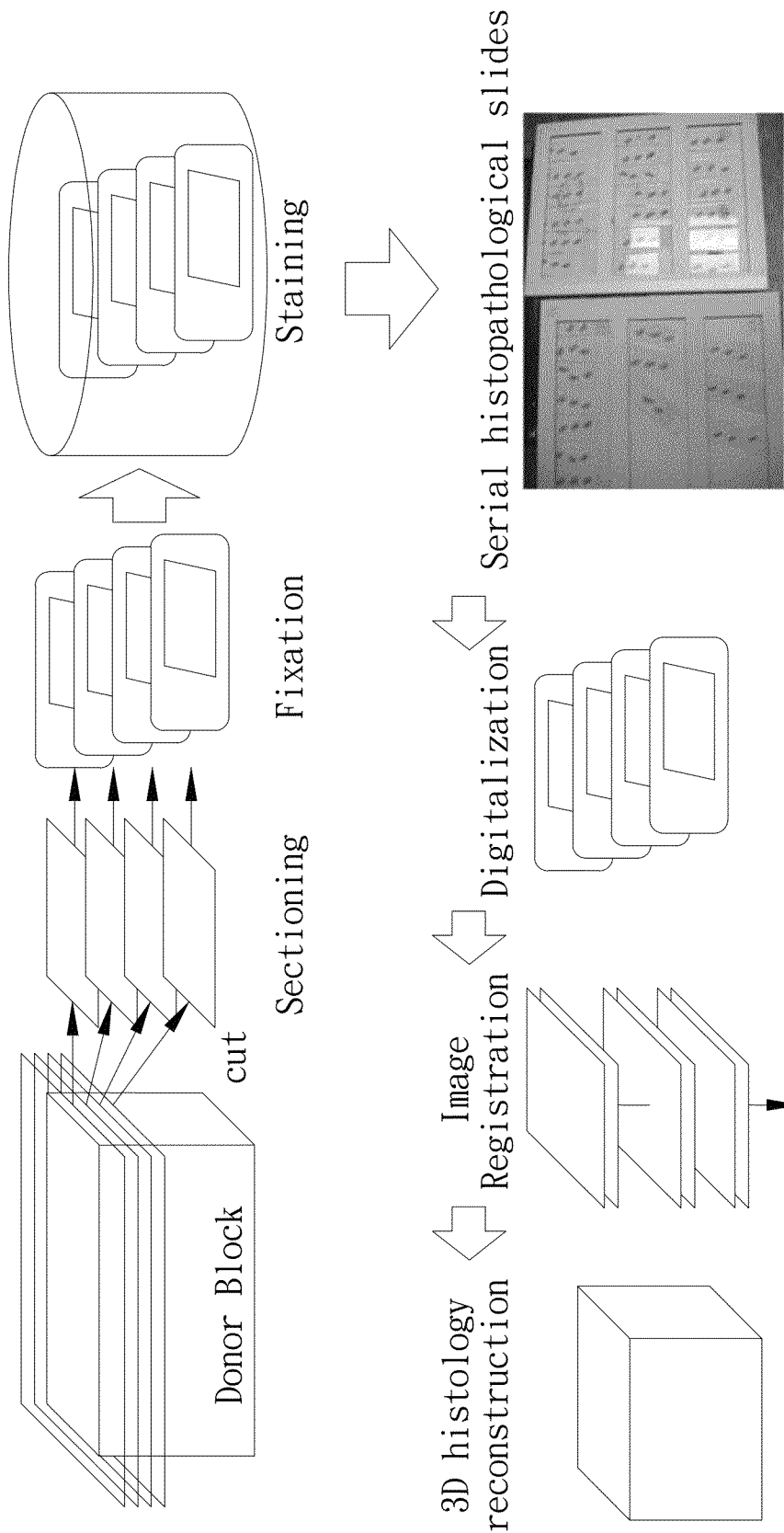


FIG. 1A

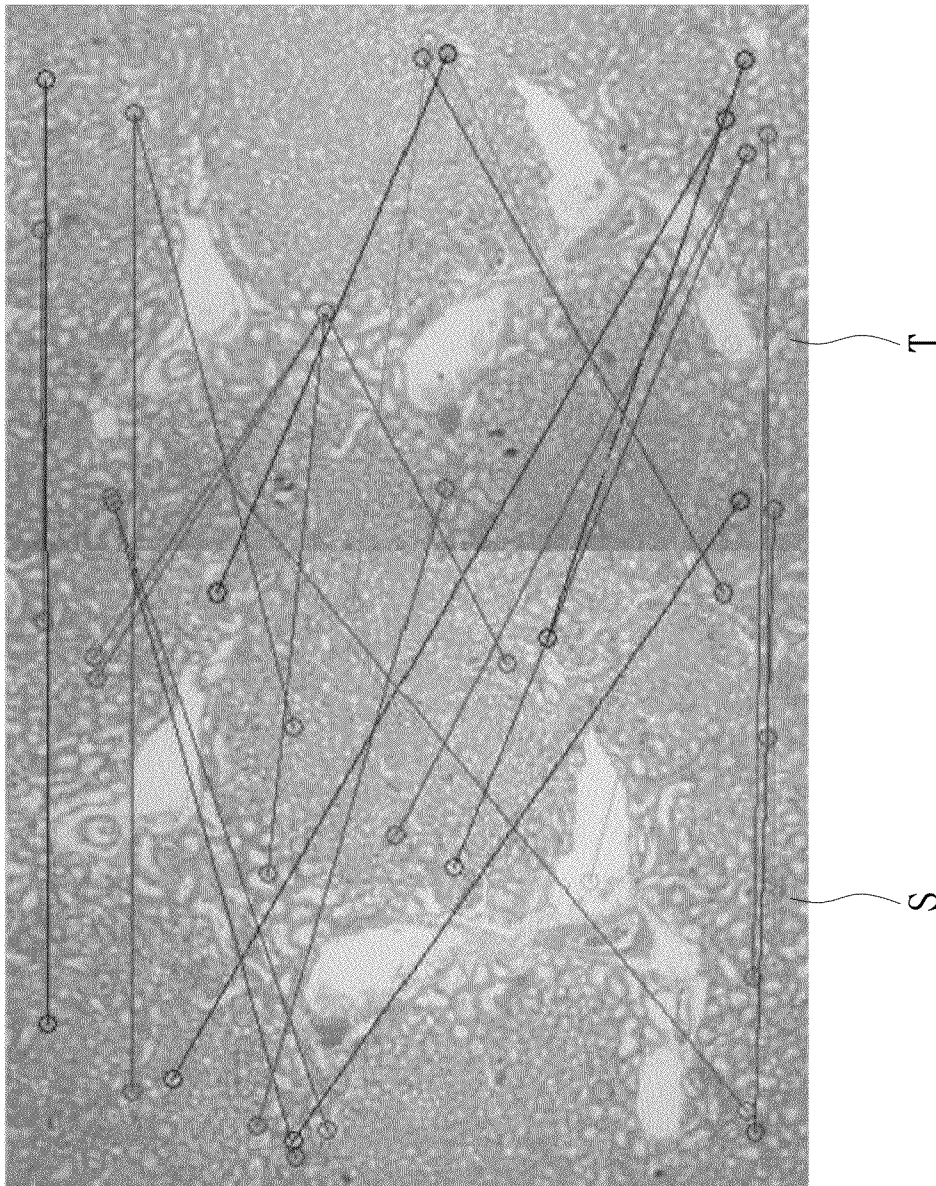


FIG. 1B

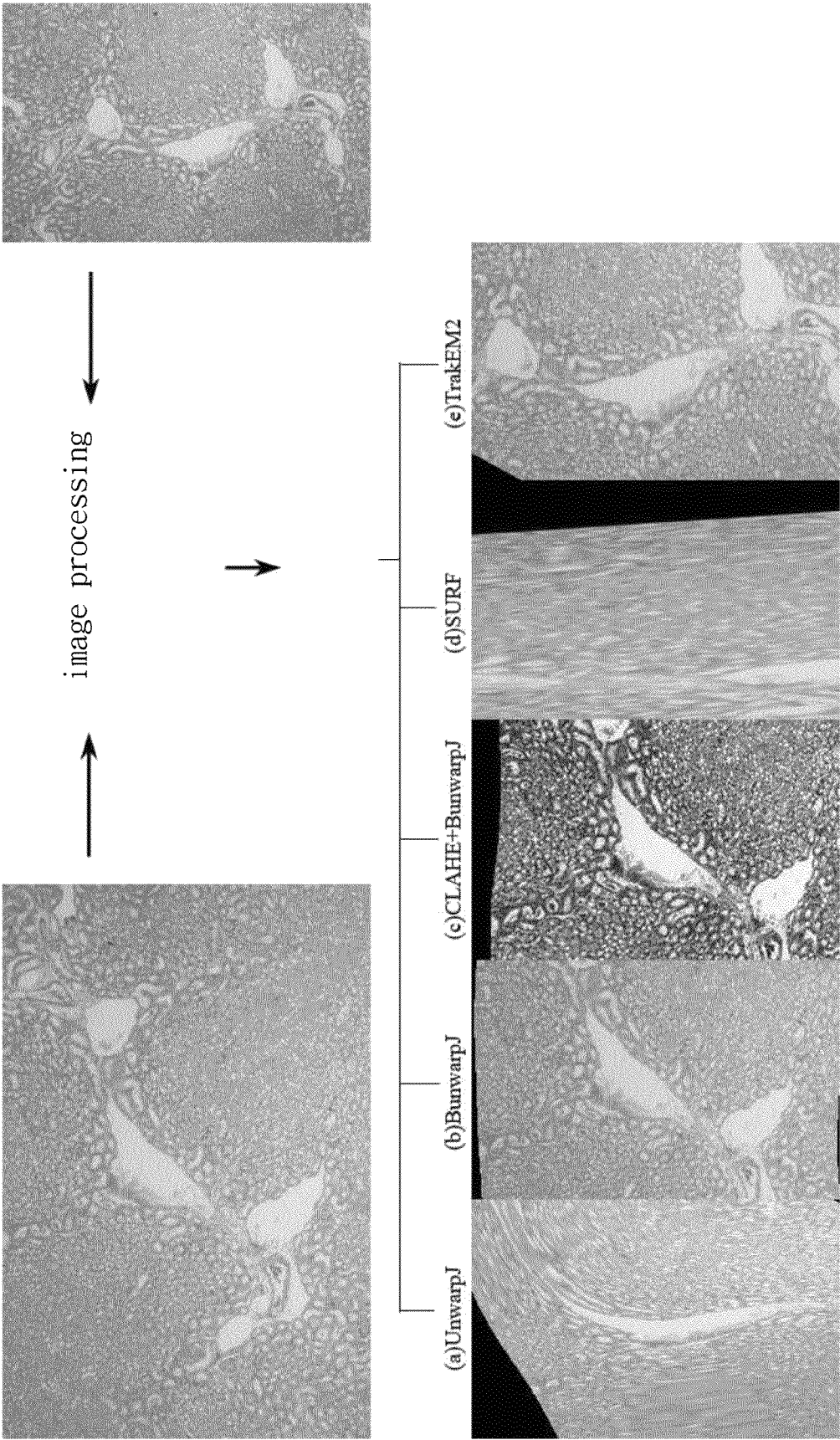


FIG. 1C

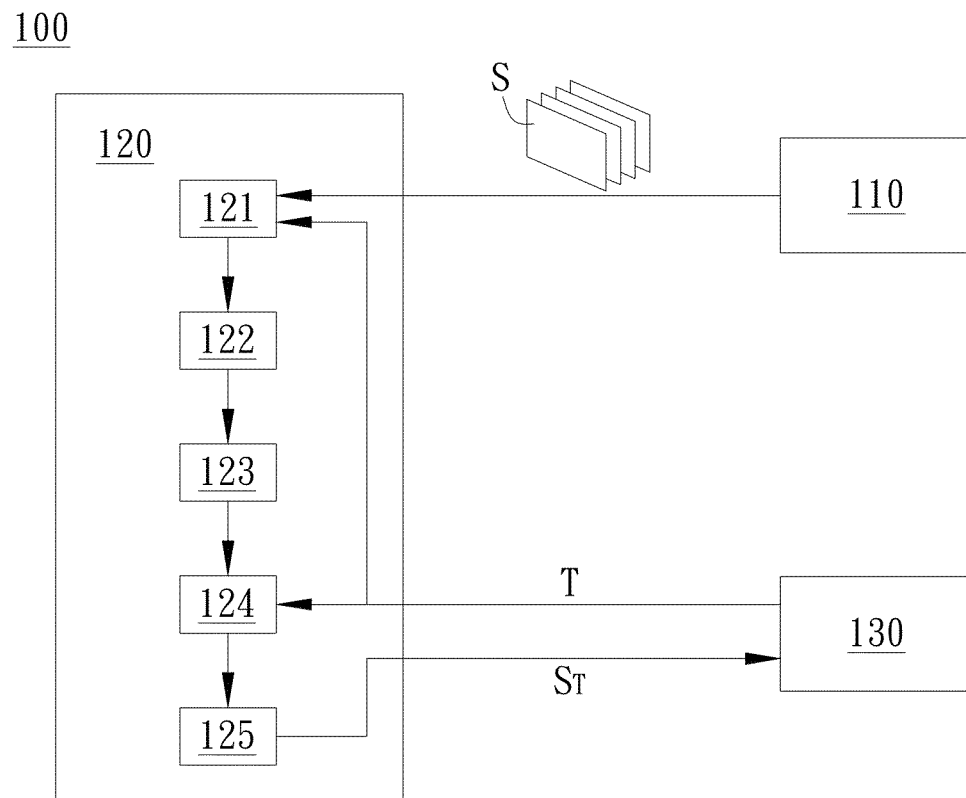


FIG. 2

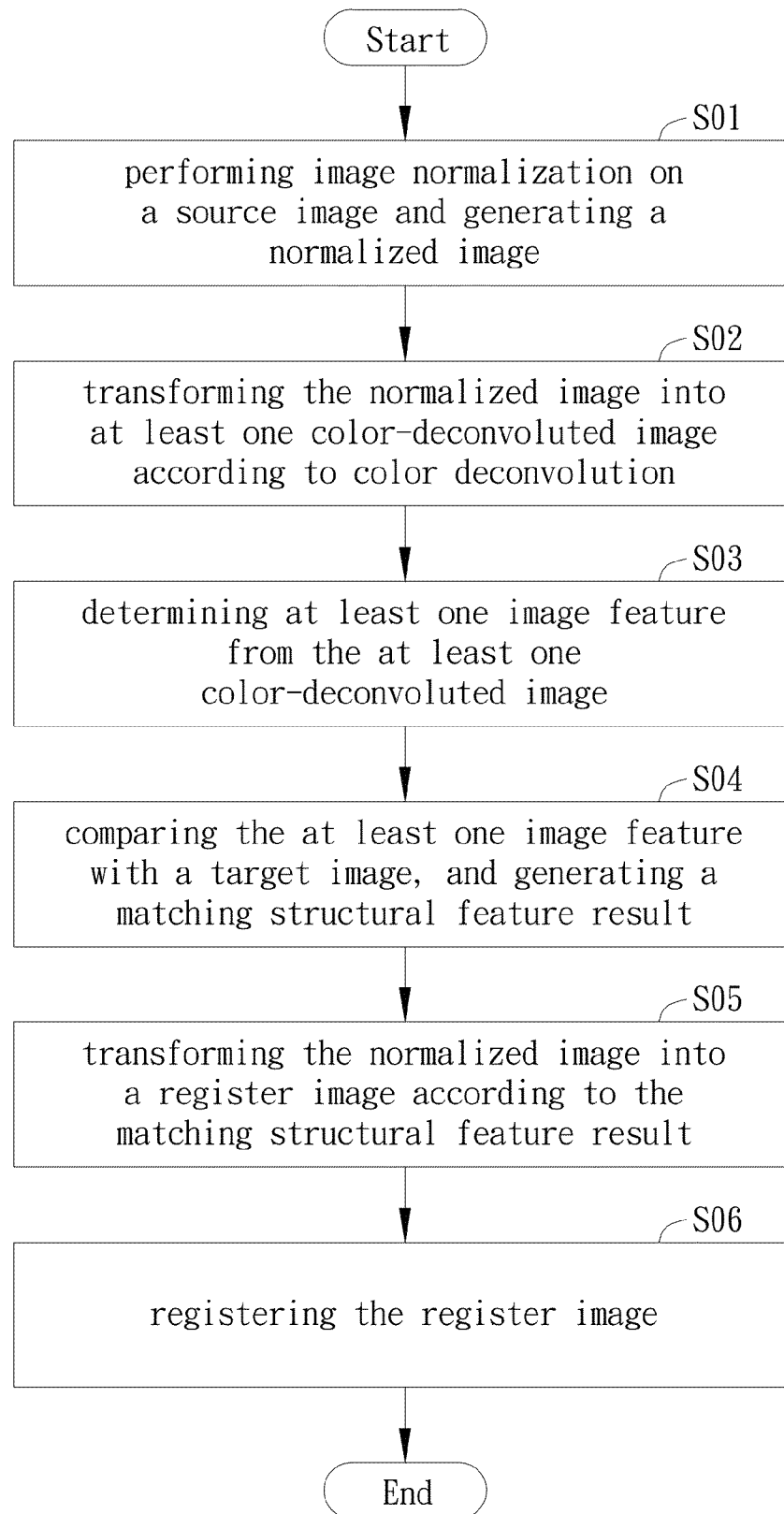


FIG. 3

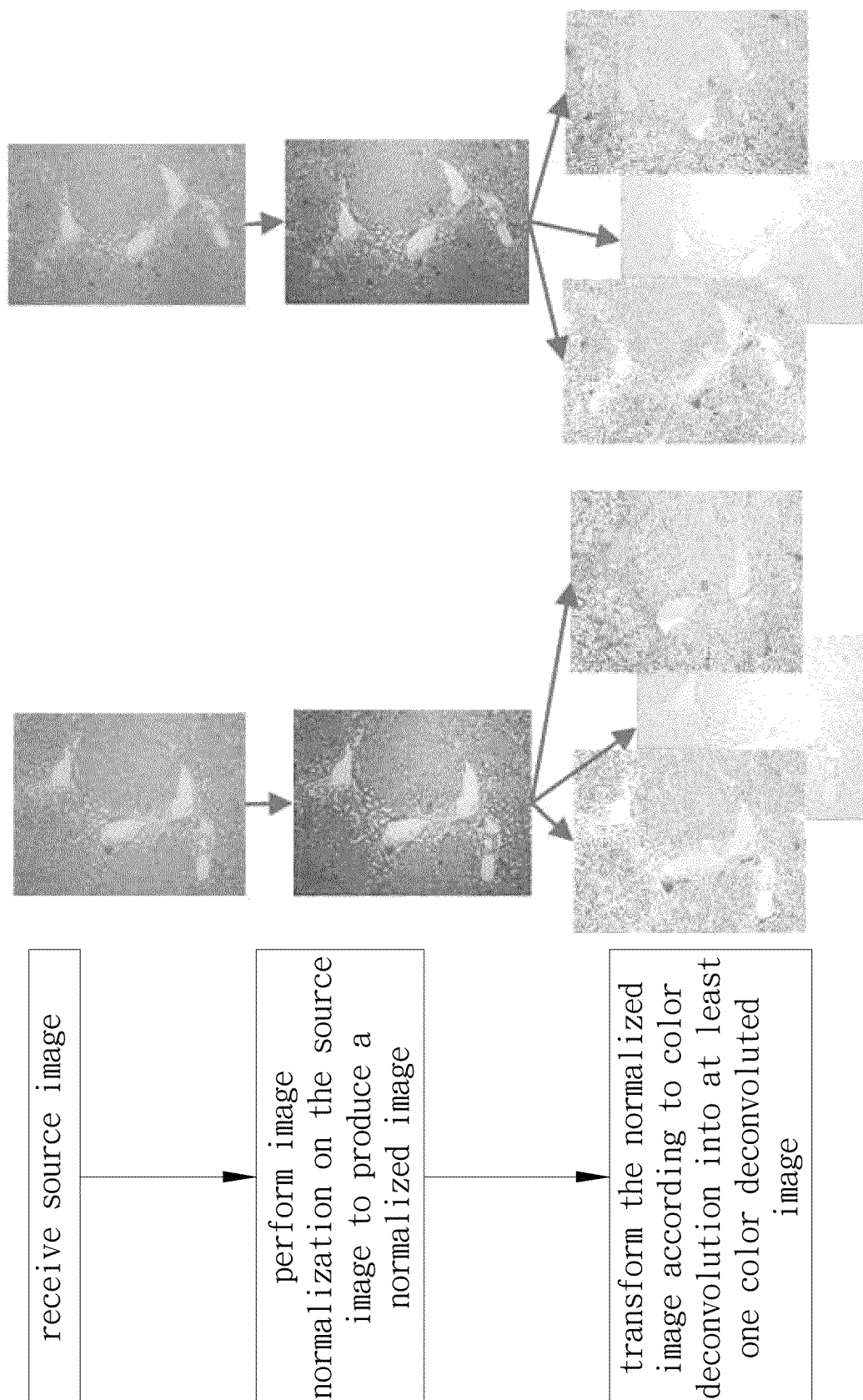


FIG. 4A

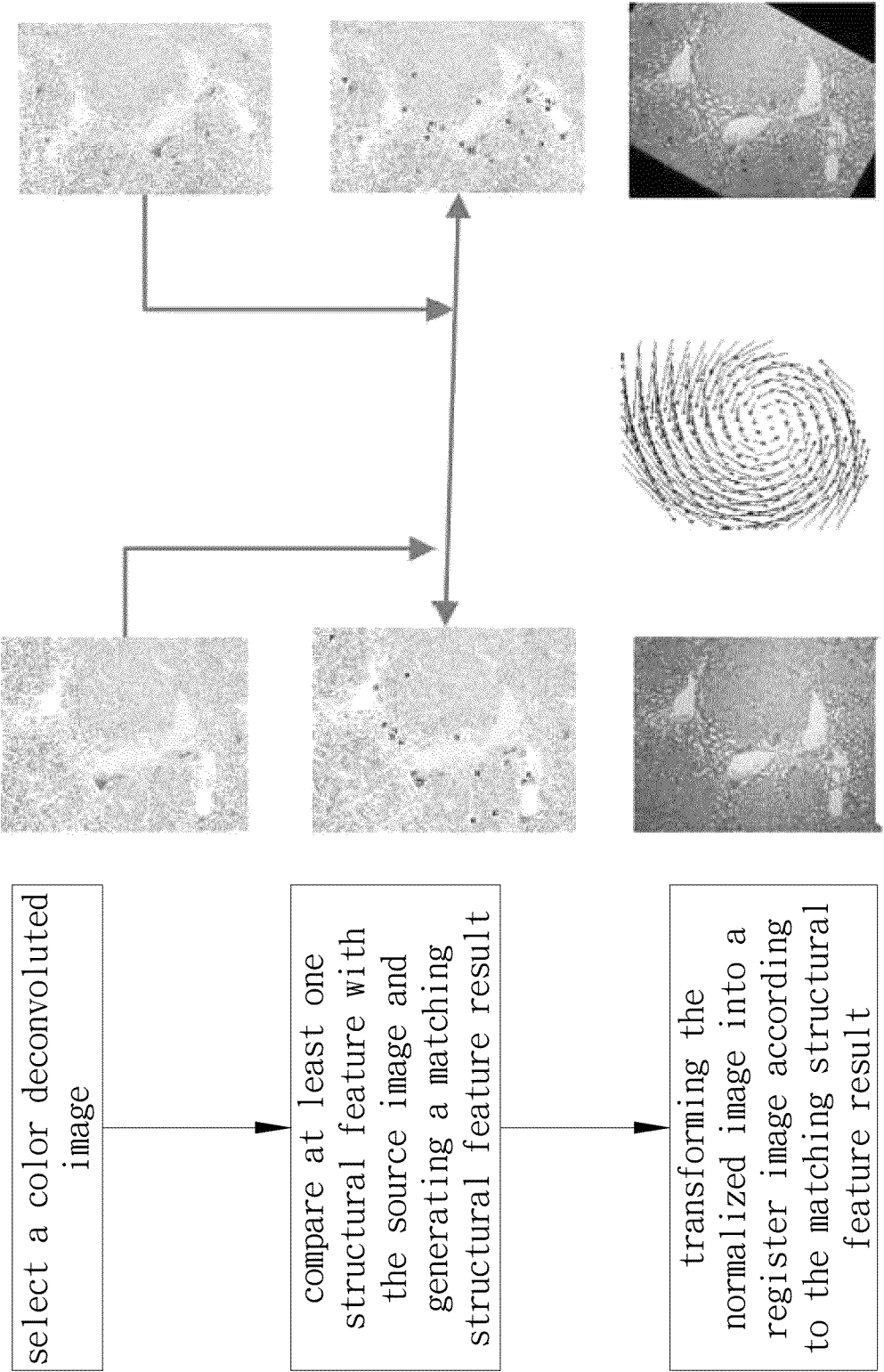


FIG. 4B

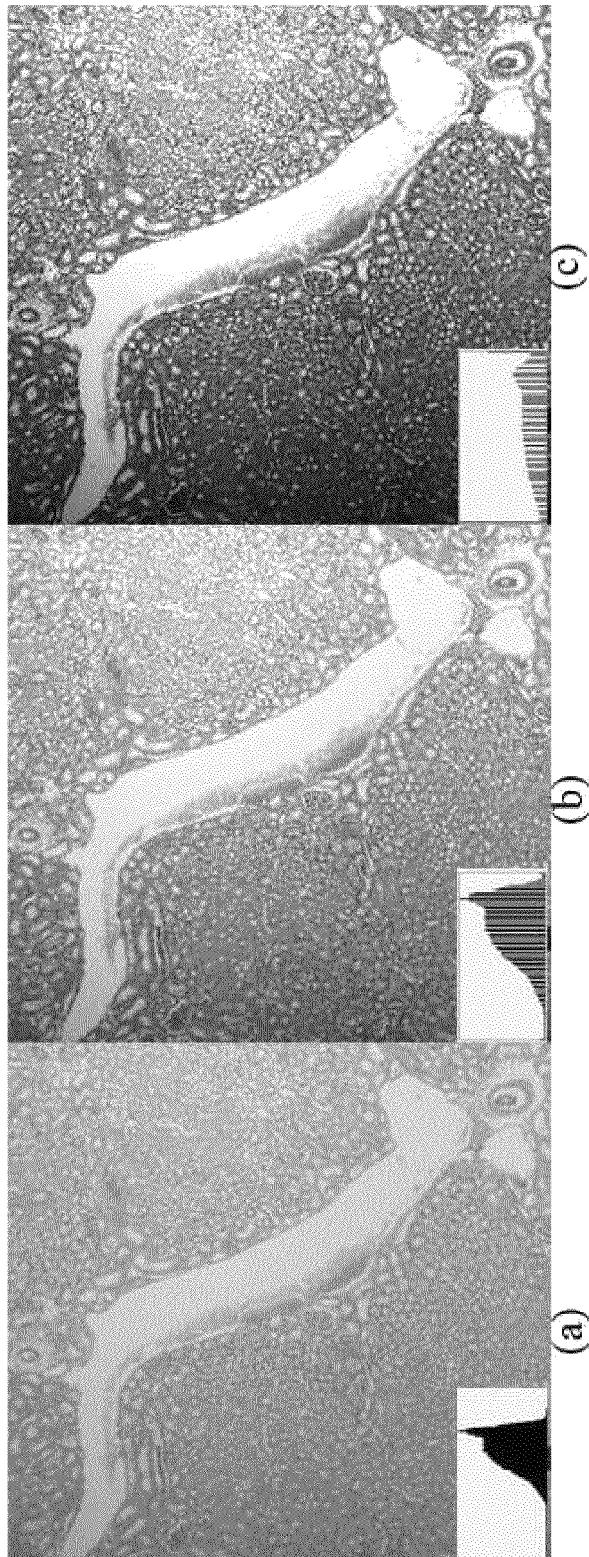


FIG. 5

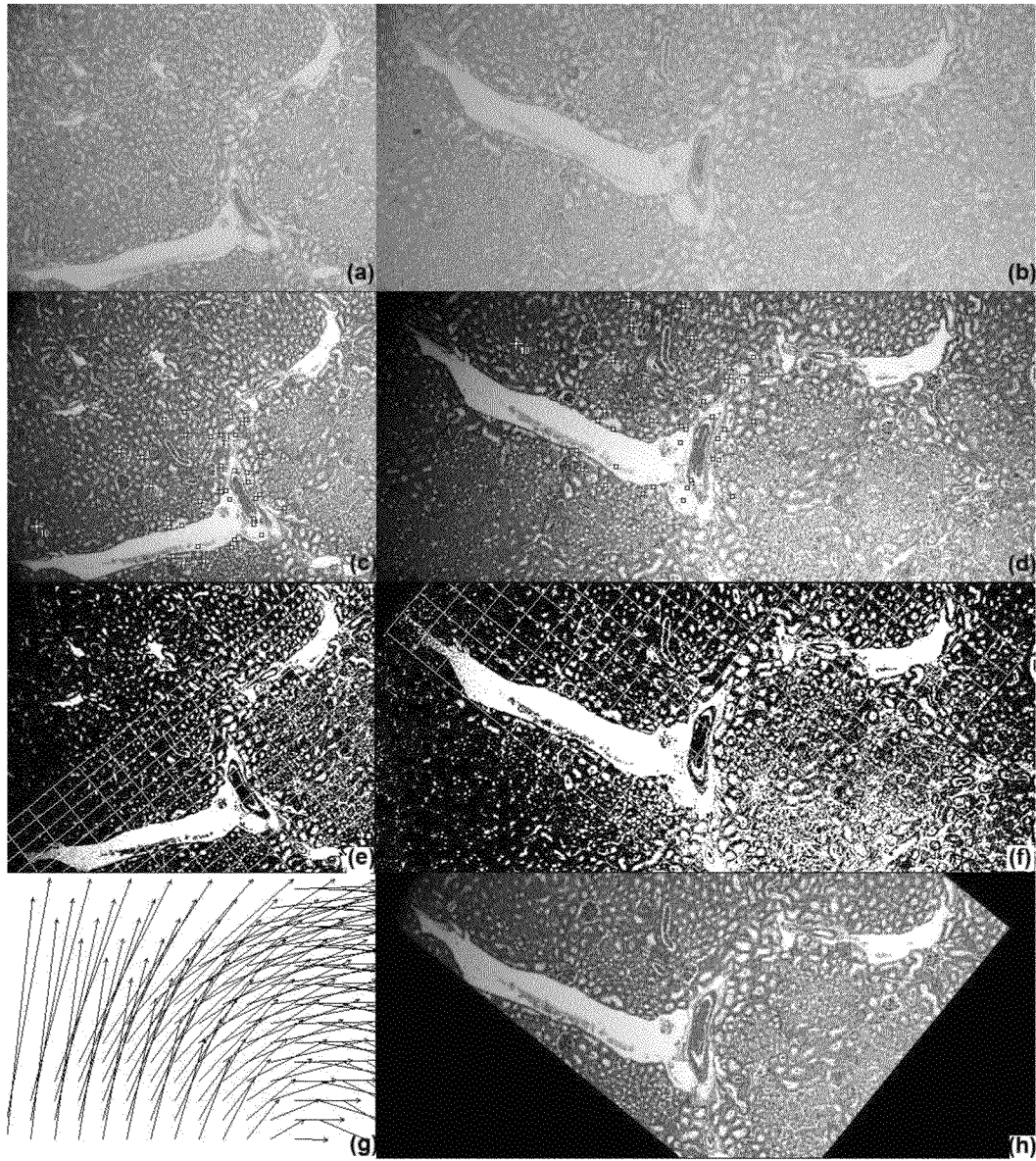


FIG. 6

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IMAGE REGISTRATION METHOD

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention generally relates to an image registration method; particularly, the present invention relates to an image registration method that can increase the accuracy of image registrations.

2. Description of the Related Art

In the field of medical science, image registration is a very important process that is widely and heavily used in a majority of the planning, improvement, and assessment of surgical and radiotherapy processes. However, variations in appearance of data, image noise, and data distortions make the image registration process that much harder to complete, resulting in unstable and poor performance of conventional image registration methods.

In more definite terms in referring to the pathological image of FIG. 1A as an example, a specimen will first be cut into a plurality of slices, wherein each slice is fixed on a transparent slide. Then, tissue slides will be stained according to the user's requirements. Referring to the present figure as an example, routine H&E staining is used to perform histopathological analysis. After staining, the slices are arranged in serial order and then are digitalized through image scanning. After the digitalized pathological images are image registered, three-dimensional images of the specimen may be recreated by the users from the image registered pathological images. However, as shown in FIG. 1B, with respect to relatively more image noise occurring in pathological images, the results generated by conventional image registration methods are often subpar and/or unstable. In reference to FIG. 1B as an example of performing image registration according to the conventional SURF (Speeded-up Robust Features) method, the features P_S detected in the source image S have been erroneously matched to completely different features P_T in the target image. When the conventional image registration method proceeds to perform image transformations on the source image S according to the detected match points (P_S & P_T) in order to be more lined up with the structure in the target image, image source S will be transformed into an unrecognizable image due to the erroneous matching. However, even when other conventional image registration methods are employed—such as the Unwarj, Bunwarj, CLAHE+Bunwarj, TrakEM2 methods of FIG. 1C—the other conventional image registration methods still cannot accurately transform the source image S to the coordinate system of the target image T. As such, a more accurate image registration method is inevitably required.

SUMMARY OF THE INVENTION

It is an objective of the present invention to provide an image registration method that can increase the detection accuracy of structural features in images.

It is another objective of the present invention to provide an image registration method that can increase the stability and speed of image registration

It is yet another objective of the present invention to provide an image registration method that can accurately and autonomously execute image registration.

The present invention provides an image registration method for image registering at least one source image such that the contents thereof is under the same coordinate system. The image registration method includes the following steps: (a) performing image normalization on input images and

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generating normalized images; (b) retrieving at least one color-deconvoluted image from color-deconvoluting the source image; (c) determining at least one image feature from the at least one color-deconvoluted image; (d) comparing the at least one image feature of the at least one color-deconvoluted image with a target image, and generating a relative matching structural feature result; and (e) transforming the normalized image into a registered image according to the matching structural feature result.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1A is a flow chart diagram of a conventional image registration;

FIG. 1B is the conventional matching of relative structural features;

FIG. 1C is the image registration result of the conventional image registration method;

FIG. 2 is an embodiment of the image registration system of the present invention;

FIG. 3 is an embodiment of the flow chart diagram of the image registration method of the present invention;

FIG. 4A is an embodiment of the flow chart of image normalization;

FIG. 4B is an embodiment of the flow chart of the image registration;

FIG. 5 is another embodiment of image normalization; and

FIG. 6 is another embodiment of image registration of the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The present invention includes an image registration method, preferably for use in an image registration system. In an embodiment, the image registration method and image registration system has application in the medical field. However, they are not restricted to being used only in the medical field. In other embodiments, the image registration method and image registration system of the present invention may be utilized in any other technical fields. Please refer to FIG. 2 of an embodiment of the image registration system **100** of the present invention. In the present embodiment, the image registration system **100** at least includes a source-image provider unit **110**, an image registration unit **120**, and a storage unit **130**. In more concrete terms, the image registration system **100** follows a particular image registration process to transform pathological images into registerable images. The following will explain the method and system of the present invention in more detail.

As shown in FIG. 2, the image registration unit **120** will receive from the source-image provider unit **110** at least one source image S. In the present embodiment, source-image provider unit **110** is an image database for storing a plurality of digitalized image files of serially arranged slides. In more definite terms, after a specimen has been sliced into a plurality of slices and then stained, the stained slices may then be scanned into digital pathology image files. These pathology image files are then stored in the source-image provider unit **110**. However, in other different embodiments, the source-image provider unit **110** may be any other device, such as magnetic resonance imaging devices (MRI device), X-ray imaging devices, or any other related devices. For example, in the instance that the source-image provider unit **110** is a MRI device, the source-image provider unit **110** can directly generate the plurality of digitalized pathology images of a patient.

In the present embodiment, the image registration unit **120** transforms received source images **S** into images registerable in the storage unit **130** according to a specific image processing method. In the present embodiment, the storage unit **130** may be another image database different from the source-image provider unit **110**. In this circumstance, the storage unit **130** primarily stores pathology images processed by the image registration unit **120**. However, in other different embodiments, the storage unit **130** may be a server, computing device, or any other systems that have use for images that have undergone image registration. As shown in FIG. 2, the image registration unit **120** can further include a color deconvolution module **122**, a structure-determining module **123**, a feature-matching module **124**, and an image transformation module **125**. These modules will be explained in greater detail below with the image registration method of the present invention.

Please refer to FIG. 3 of an embodiment of a flow chart diagram of the image registration method of the present invention. The image registration method includes steps **S01** to **S06**. The following will explain the image registration method in greater detail.

Step **S01** includes performing image normalization on the source image to generate a normalized image. In for definite terms in reference to FIGS. 2 and 4A, the image normalization module **121** in the image registration unit **120** will first receive one or a plurality of source images **S** from the source-image provider unit **110**. In the present embodiment, image normalization module **121** will receive the plurality of source images **S** at once. Particularly, source-image provider unit **110** is able to aggregate and organize all the source image files before transmitting them together all at once to the image normalization module **121**. However, in other different embodiments, source-image provider unit **110** may transmit the source images **S** in batches or installments over time to the image normalization module **121** according to the connection bandwidth between the source-image provider unit **110** and the image normalization module **121**. In addition, before the image normalization module **121** reaches the limits of its image processing capabilities, the image registration unit **120** may also notify the source-image provider unit **110** to transmit the source images **S** in the above described installments to lessen the load on the image normalization module **121**. In this manner, the image registration unit **120** may better control and manage the image registration process. In the present embodiment, after the image normalization module **121** receives the source image **S**, the image normalization module **110** will start to perform normalization on the source image **S**. Particularly, the image normalization module **110** can detect the brightness and/or contrast levels of the source image **S**, and then transform the source image **S** into a normalized image according to an image standard along with the detected brightness/contrast levels.

In the present embodiment, as shown in FIGS. 4A and 5, the image normalization process may be executed according to the distribution of the image histogram of the source image **S**. In more definite terms, and in reference to exhibit (a) and (b) of FIG. 5 as an example, the image histogram distribution of the source image **S** in exhibit (a) and (b) are both concentrated in the middle. In the present embodiment, the image normalization module **121** may stretch out the two tail ends of the image histogram distribution in exhibit (a) and (b) according to a default standard. In this manner, the image histogram distribution of exhibit (a) and (b) may be more uniform in line with the image histogram distribution of exhibit (c). However, in other different embodiments, users may set how the image normalization module **121** adjusts the source image **S** into the

normalized image according to their liking. In addition, in another embodiment, the image normalization module **121** may retrieve a target image **T** from the storage unit **130**. In the present embodiment, the target image **T** is a type of reference image for the image registration unit **120** to use as reference for adjusting the processing of the source image **S**. After receiving the target image **T**, the image normalization module **121** can detect the histogram image from the target image **T** and will accordingly set the image standard (default standard) as the detected histogram image. In this manner, all source images **S** can be normalized under the same standard. However, even if the image normalization module **121** does not use the histogram image distribution of target image **T** as a reference, the image normalization module **121** may still receive the target image **T** from the storage module **130**. In the present embodiment, as shown in FIG. 4A, the image normalization module **121** may also perform image adjustments or image processing on both the source image **S** and the target image **T** according to the default standard.

Step **S02** includes retrieving at least one color-deconvoluted image from color-deconvoluting the source image. As shown in FIGS. 2 and 4A, color deconvolution module **122** will separate the normalized image into at least one color deconvoluted image according to color deconvolution methods. In the present embodiment, the color deconvolution module **122** preferably splits the normalized image into three color deconvoluted images: red, blue, and green (RGB) color deconvoluted images. The purpose of this is to resolve the problem of identifying structures from the specimen slices after it has been stained. In the present embodiment, for instance, if the staining process utilizes red dye to stain the specimen, the red dye will be absorbed by specific cells in the specimen slice and be stained. When the color deconvolution module **122** splits the normalized image into red, blue and green color deconvoluted images, the red color deconvoluted image will represent the structures that have been stained red in the slice by the red dye (ex. cell nucleus). Meanwhile, in the present example, the green color deconvoluted image may represent the background of the image slice. Through the method of color deconvolution, the image registration system **100** may effectively decrease in large amounts the image data that needs to be processed or analyzed. At the same time, the method of color deconvolution can also make prominent the structures in the image. Therefore, by decreasing the amount of images needing to be processed or analyzed, the image registration unit **120** can more quickly complete the image processing and analyzing procedures. However, in other different embodiments, color deconvolution module **122** can separate the normalized image into color deconvoluted images of other different colors. For instance, if the specimen slice was stained with other different colors, or the source image **S** is retrieved from MRI devices or such related devices, the color deconvolution module **122** can adjust how the normalized image is separated into one or more different colors of color deconvoluted images according to the different situations.

Step **S03** includes determining at least one image feature from the at least one color-deconvoluted image. As shown in FIGS. 2, 4A and 4B, in the present embodiment, the color deconvolution module **122** select and transmit one of the one or more color-deconvoluted images from the normalized image of the source image **S** to the structure determining module **123**. In terms of the mentioned red dye example, in the present embodiment, the structure determining module **123** will receive the red color-deconvoluted image corresponding to the normalized image of the source image **S** from the color deconvolution module **122**. At the same time, the structure

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determining module **123** will receive the red color-deconvoluted image corresponding to the normalized image of the target image T from the color deconvolution module **122**. In other words, the structure determining module **123** will respectively receive color deconvoluted images of the same color but corresponding to the different normalized images (source image S and target image T). In simpler terms, if the selected color deconvoluted image of the normalized image of the source image S is viewed as a first image, and the color deconvoluted image of the normalized image of the target image T is viewed as a second image, the second image preferably has the same color as the first image.

When the structure determining module **123** receives the first image and the second image, the structure determining module **123** will respectively determine at least one image feature from the first image and the second image. In the present embodiment, the image feature may be a feature of the structure. However, in other different embodiments, the image feature may be other characteristics or features. In reference to FIGS. **4B** and **6** and as shown in FIG. **6**, exhibit (c) and (d) are respectively the first image and the second image. In the present embodiment, the structure determining module **123** will respectively determine the image (structural) features in the first image and the second image. In reference to FIG. **6** as an example, exhibit (c) and (d) are marked with a plurality of square or round shaped labels to indicate the positions of structural features. It should be noted that since the color deconvolution process was done, the amount of image data needing to be process or analyzed by the structure determining module **123** will be far less than conventional image registration methods. Therefore, when trying to determine structural features, the image registration system **100** of the present invention will be faster than the conventional image registration method. In addition, since the amount of image data that is required to be analyzed is smaller and since any data pertaining to the background or any other info not relating to the identified structure of the image had already been disregarded in the color deconvolution process, the structure determining module **123** can more accurately identify or determine each structural feature in the image, such as cell nuclei, cell walls, and other related structural features.

Step **S04** includes comparing the at least one image feature of the at least one color-deconvoluted image with a target image, and generating a relative matching structural feature result. As shown in FIGS. **4B** and **6**, in the present embodiment, a feature matching module **124** will receive from the structure determining module **123** the first image and the second image. According to the labels marking the positions of the one or many structural features in the first and second images by the structure determining module **123**, the feature matching module **124** will compare the structural features found in the first image with the structural features found in the second image. In the present embodiment, the feature matching module **124** will compare the first image and the second image to find structural features that correspond with each other between the images. Since the images have been through normalization and color-deconvolution processes, the structures in the first image and the second image will be very clear and evident once the present step in the process has been reached. That is, there would not be any excess amount of image noise data. Therefore, the feature matching module **124** can accurately match features of the first image with corresponding features in the second image. Accordingly to

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the matching relationship between each structural feature, the feature matching module **124** will generate and transmit a relative matching structural feature result to an image transformation module **125**.

However, in other different embodiments, the feature matching module **124** may receive the target image T from a storage unit **130**. In this circumstance, the target image T received by the feature matching module **124** can include default structural feature labels. In the present embodiment, users may preemptively manually register default labels on the target image T to identify recognizable structural features and then store that target image T in the storage unit **130**. Under these circumstances, the feature matching module **124** can compare the first image with the target image T received from the storage unit **130**. In other words, the image registration unit **120** does not need to use modules **121-123** to perform image processing and analysis on the target image T. By having the user manually identify the structural features of image T, the image registration unit **120** can conserve system resources while completing the image registration process faster. In addition, through this method, users may at any time adjust or raise the accuracy of determining structure features by the image registration system **100**.

Step **S05** includes transforming the normalized image into a registered image according to the relative matching structural feature result. Particularly, the image transformation module **125** in the image registration unit **120** will perform image transformations of the normalized image of the source image S onto the coordinate system of the normalized image of the target image T according to each of the image feature matching relationship included in the relative matching structural feature result. In other words, the present invention will perform fast coarse image registration with the features as the basis. As shown in the first image of exhibit (e) and the second image of exhibit (f) in FIG. **6**, the image transformation module **125** will first analyze the relationship between the structural features of the second image (ie. 1. The color deconvoluted image of the second image corresponding to the color deconvoluted image of the first image that corresponds to the target image; or 2. the target image T received from the storage unit **130**) with the coordinate system of the second image. Similarly, the image transformation module **125** will also analyze the relationship between the structural features of the first image and the coordinate system of the first image. The image transformation module **125** will then use a direct matching process where the features are used as a regional basis to improve the regional registration results. In more definite terms, according to each of the matching pairs of the structural features identified by the feature matching module **124** of the first and second images as well as the analysis on the coordinate systems of the first and second images by the image transformation module **125** (as shown in FIG. **6(e)** and **(f)**), the image transformation module **125** can generate the linear transformation relations as shown in FIG. **6(g)**. As shown in FIGS. **4B** and **6**, after the image transformation module **125** has calculated the linear transformation relations, the image transformation module **125** will transform the normalized image of the source image S corresponding to the first image onto the coordinate system of the target image T according to the linear transformation relations as shown in FIG. **6(h)**.

Step **S06** includes registering the register image. In terms of FIGS. **2**, **4B**, and **6** as an example, the image registration

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unit **120** will transmit the register image S_T to the storage unit **130** to complete image registration after the image transformation module **125** has transformed the normalized image of the source image S into the register image S_T .

Although the preferred embodiments of the present invention have been described herein, the above description is merely illustrative. Further modification of the invention herein disclosed will occur to those skilled in the respective arts and all such modifications are deemed to be within the scope of the invention as defined by the appended claims.

What is claimed is:

1. An image registration method for image registering at least one source image to enable the images to be registered in the same coordinate system, the method comprising:

(a) performing image normalization on a source image and generating a normalized image;

(b) retrieving at least one color-deconvoluted image from color-deconvoluting the source image, wherein the normalized image is transformed into three color deconvoluted images according to color deconvolution, and the three color deconvoluted images are respectively a red color deconvoluted image, a blue color deconvoluted image, and a green color deconvoluted image;

(c) selecting one of the three color deconvoluted images as a first image, and then determining at least one image feature from the first image;

(d1) transforming a target image into at least one color deconvoluted image according to color deconvolution;

(d2) selecting from the at least one color deconvoluted image corresponding to the first image as a second image;

(d3) determining at least one image feature from the second image, and then setting the at least one image feature from the second image as a default structural feature;

(d4) comparing the image feature of the first image with the default structural feature to generate the relative matching structural feature result; and

(e) transforming the normalized image into a register image according to the matching structural feature result.

2. The image registration method of claim **1**, wherein the target image includes at least a default structural feature, the step (d) further comprises:

comparing the at least one image feature with the at least one default structure feature to determine whether the at least one image feature corresponds to the at least one default structural feature.

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3. The image registration method of claim **1**, wherein the step (c) further comprises:

determining the at least one image feature from the red color deconvoluted image.

4. The image registration method of claim **3**, wherein the step (d) further comprises:

transforming the target image into at least one color deconvoluted image according to color deconvolution, wherein the at least one color deconvoluted image includes a red color deconvoluted image.

5. The image registration method of claim **4**, wherein the step (d) further comprises:

comparing the red color deconvoluted image of the normalized image with the red color deconvoluted image of the target image to generate the relative matching structural feature result.

6. The image registration method of claim **1**, wherein the step (e) further comprises registering the register image.

7. An image registration method for image registering at least one source image to enable the images to be registered in the same coordinate system, the method comprising:

(a) performing image normalization on a source image and generating a normalized image, wherein image normalization is performed by:

(a1) detecting a brightness level of the source image, and generating the normalized image from the source image according to an image standard and the brightness level; and

(a2) detecting a contrast level of the source image, and increasing or decreasing the contrast level of the normalized image according to the detected contrast level of the source image;

(b) retrieving at least one color-deconvoluted image from color-deconvoluting the source image;

(c) determining at least one image feature from the at least one color-deconvoluted image;

(d) comparing the at least one image feature of the at least one color-deconvoluted image with a target image, and generating a relative matching structural feature result; and

(e) transforming the normalized image into a register image according to the matching structural feature result.

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