Registration of Histology and MR Images using Local Rigid Registration and Differential Evolution

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Introduction: The 3D volume reconstruction from 2D histological sections arises frequently in neuroscience research [1]. Reconstruction by simply stacking registered histological sections would not give plausible result because of volume distortions and section imperfections. Histology imperfections include nonlinear tissue distortions, such as squashing, stretching, folding and tearing, as well as artifacts like air bubbles and dust [2]. One approach to this is to perform histology reconstruction with the guidance of information extracted from anatomical images, like high-resolution Magnetic Resonance (MR) images. The main challenge in integrating MR information into histology volume reconstruction is to find MR image slices corresponding to the histological sections. Due to shrinkage and deformation caused by the sectioning procedure, a one-to-one mapping of MR image to histological section can be difficult, if not impossible. An iterative strategy is usually employed.

The 2D registration of the histological section to the corresponding MR image is a non-trivial task, because of the inherent dislocation of separated segments in histology images, which often occurs in the frontal lobes and cerebellum portions of the brain (see Fig. 1). Due to the complicated histology acquisition procedure, dislocated segments and debris are inevitable. Quality control may reduce the occurrence though. It is suggested to use average of several histological volumes to eliminate this kind of artefacts [3], or discard poor quality sections to prevent them from impairing reconstruction. However, important information may be lost. We propose using a local rigid registration method to solve this problem. The space for the registration parameters is searched using differential evolution [4, 5].

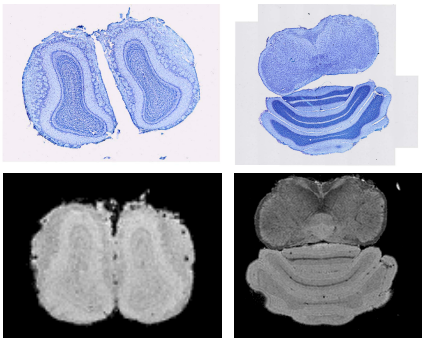

Fig. 1 Dislocated parts in histological sections (upper row) and corresponding MR images (lower row): frontal lobes (left) and cerebellum (right)

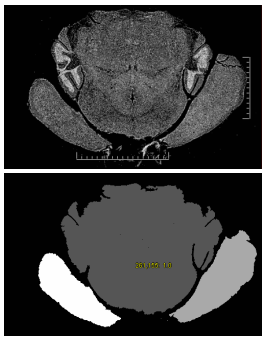

Fig. 2 A histological section before (upper) and after (lower) segmentation using morphological operations and connectivity analysis.

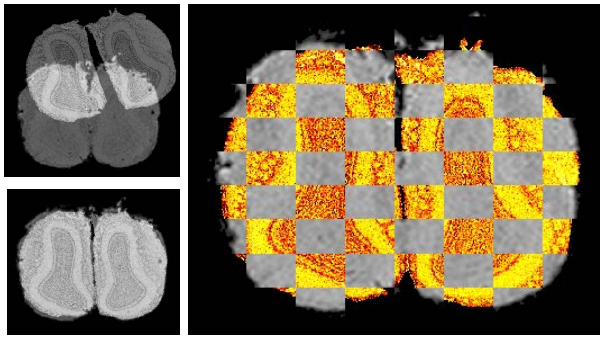

Fig. 3 The superimposition of histological section and MR image before registration (upper left) and after registration (lower left). In the checkerboard view (right), MR is in gray scale, histology section is in hot metal colour.

Methods: The histology and MR images of a mouse brain used in this study were acquired as part of the Australian Mouse Brain Mapping Consortium. Around 450 sections of histology were obtained for a C57BL/6J mouse brain with section thickness of 30 microns. MR images were acquired using a 16.4T Bruker scanner using the 3D FLASH sequence with TR=50ms, TE=12ms, and FOV=22×11.5×8.5mm. The voxel size is nearly exactly 30 microns.

To find the corresponding MR image for a given histological section is not straightforward as they are usually not in the same orientation. In this study, the matching of this correspondence is achieved as follows. First, the middle chunk of the histology volume with no noticeable splits was reconstructed by 2D rigid-body registration to form a histological sub-volume. Then, the MR volume was registered to this sub-volume and resliced into the histological volume space. By comparing the resliced MR volume and histological volume, a linear shrinkage ratio was determined, and then a matching between histology and MR images was established.

Once the corresponding MR image was found, local rigid-body registration of histology and MR images is done in two major steps. First, the split parts in any histological sections are separated by applying a series of morphological operations and connectivity analysis, as illustrated in Fig. 2. Each separated part is treated as a rigid body and any debris was removed. Second, the separated parts in the histological section are registered to the corresponding MR image using a multi-part approach in which each part in the histological image is allowed to translate and rotate independently. The original histological image is converted to a gray scale image and down-sampled from 0.65 microns to 10.4 microns to perform the registration. The background noise is removed by adaptive thresholding. The registration seeks to find a set of transformation matrices for the split parts to maximise the similarity of the combined histological section and the corresponding MR image. Normalized mutual information (NMI) is used as the similarity metric. In conventional 2D rigid-body registration, 3 parameters (2 translational and 1 rotational) are optimised. , Thus, the number of parameters in this multi-part approach is equal to 3 times the number of separated parts. Differential evolution, a global optimisation method, is used to search for the optimal parameters.

Results & Discussion: A total of 267 pairs of histological sections were registered to the corresponding MR images. By visual inspection, they all appear to be satisfactorily registered. A representative pair using this approach is shown in Fig 3. Of the 267 pairs, the normalized mutual information had an average value of 0.85, also a good indication of the convergence. Registration time for individual pairs varied from 30 to 170 seconds. This can be shortened by further optimising our implementation.

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