**INVERSION: A robust method for co-registration of MPRAGE and Diffusion MRI images**

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**Introduction** – Accurate registration between MPRAGE and diffusion MRI images is essential for many multi-modal neuroimaging studies. Inter-modal registration methods typically use optimization methods based on Normalized Mutual Information (NMI) or Correlation Ratio (CR). However, these cost functions are known to be non-convex and non-smooth, which can cause registration algorithms to converge to sub-optimal solutions. We describe INVERSION (Inverse contrast Normalization for VERY Simple registrationION), a method based on the use of the simpler sum of squared differences (SSD) cost function, that robustly aligns MPRAGE and b=0 s/mm² images by leveraging known contrast relationships between these two modalities.

**Method** – It is well known that the contrast in an MPRAGE brain image is approximately the inverse of the contrast in a T2-weighted b=0s/mm² image (i.e., white matter > gray matter > CSF in an MPRAGE image, while CSF > gray matter > white matter in a T2-weighted image). In INVERSION, this relationship is exploited to transform the b=0s/mm² image to look like an MPRAGE image. This transformation means that inter-modal image registration methods can be replaced by simpler and more robust methods designed for registering images from the same-modality. In this work, we invert the intensity histogram of the b=0s/mm² image, and then register this image to the MPRAGE image using the SSD cost function. In practice, we also apply histogram matching to the inverted b=0s/mm² image and MPRAGE image to further refine the intensity match. In order to study the robustness of the proposed method we acquired an MPRAGE image, a diffusion dataset (single-shot EPI, TE=115ms, TR=10s, 65x65x65 mm³ resolution), and a B₀ inhomogeneity map for a single subject. The diffusion dataset was first corrected for susceptibility induced distortion using the acquired inhomogeneity map. Then the MPRAGE image was aligned to the b=0s/mm² image using a manually guided rigid registration procedure. This manual result was used as a gold-standard to compare the accuracy of different automatic registration methods. In order to understand the properties of different cost functions, we studied how they changed as a function of mis-registration (translation along the x-axis). Consistency of the solutions obtained by different cost functions was evaluated by applying 36 known rigid transformations to the MPRAGE image and assessing the registration quality achieved with each cost function using our implementation of CR and NMI. The registration accuracy was quantified using RMS error. All cost functions were optimized using simple gradient decent.

**Results** – Fig.1 shows a slice of the MPRAGE, inverted b=0s/mm² image and original b=0s/mm² image. Fig.2 shows qualitative result of proposed INVERSION method on an in-vivo dataset. Fig.3 shows plots of different cost functions as a function of translation along x-axis. It can be noticed that the cost in the proposed INVERSION method is the smoothest among all the cost functions and is convex over the translation range. These features mean that the INVERSION cost function can be much easier to numerically optimize and can be more sensitive to mis-registration over a broader range. Further, it can also be seen that both NMI and CR are “noisy”, and have relatively flat regions of the cost function at large translations, which make optimization difficult. Fig.4 shows plots of residual RMS errors in the solution obtained by different cost functions for the applied transformations. It should be noticed that the performance of the proposed method is consistent (RMS error of approx. 0.5mm) across all applied transformations. Both NMI and CR show good performance with small transformations but were not consistent and accurate for larger transformations.

**Conclusions** – We described a new method, INVERSION, for registering MPRAGE and diffusion MRI b=0s/mm² images. Unlike most multi-modal registration approaches, our approach uses a locally smooth, and frequently convex, cost function. We transform the contrast of the b=0s/mm² image to match the contrast of the MPRAGE image, and achieve consistently accurate performance using the simple SSD cost function. The INVERSION method was evaluated for rigid registration, but is easily extended to affine and non-rigid registration.


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