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## Methods for the Construction of a Statistical Anatomical Atlas

The construction of a statistical atlas is generally done via the deformable registration of a set of patient anatomical data (whether that be CT or other structures) onto some common coordinate space. The most basic method is simply to choose one patient to register all other patients to, however, this creates a bias in the resulting atlas towards the "fixed" patient and is hence a source of error in the further application of such atlases. Multiple methods have been proposed to either iteratively refine a model to remove this bias or otherwise statistically construct or select a reference coordinate frame. Here we will examine two of them.

One of the early methods presented by Guimond et al<sup>1</sup> in "Average Brain Models: A Convergence Study" utilizes a iterative model approach to refine the reference image in a set of patient MRI scans of the brain. The method utilizes two characteristics of these scans: average tissue intensity and average tissue morphology. For registration, the paper theoretically assumes that each point in one image has a corresponding point in the reference image used and a matching method exists which is able to find these correspondences and provides a vector field representing those relationships.

From this assumption, the average model is constructed first by choosing one patient to be the reference, labelled  $I_R$ . Every other image in the construction set  $I_n$  is deformably registered to the reference, whereupon the resulting deformations and deformation vector fields are averaged to provide an average deformation. This resulting model is then used as the reference image for the registration of each patient once again. Thus the resulting model is iteratively used as a reference for subsequent runs of the algorithm.

To evaluate, the authors construct four models, using five iterations of the process, with the result of the previous iteration as the reference image. Four error metrics are used for these models: the average distance from the reference of the current iteration to all the elements of the set, the shape variation expressed by the residual deformation field, the shape difference between models computed at successive iterations, and the brightness disparity between successive models.

The measure of all four of these criteria decrease sharply upon the first iteration, and then shallow improvements are made each iteration thereafter. It is clear that this iterative method also approaches the centroid of the data sets. The authors also state that the root mean square distances between the atlas and the images contained in the data set used for construction stabilize around 2.88 to 3.36 millimeters, down from the total range of 4.62 to 5.51 millimeters after the first iteration of the algorithm. However, the paper fails to provide data that characterize the positive effect of this method on the validity of these models in terms of predictive power for test data excluded from the construction of the atlas. Additionally given the amount of time registration tends to take (the coherent point drift method we are currently using takes about a hundred twenty seconds for the registration of ten patient data sets), this iterative method is time consuming. For the purposes of our project, where it is likely that registration and atlas creation will have to be performed on upwards of three hundred patients multiple times, this type of refinement could be prohibitively time-consuming.

Alternatively, another route to take is the one suggested by Park et al<sup>2</sup> in "Least Biased Target Selection in Probabilistic Atlas Construction" in which the data set closest to the statistical average is chosen as the reference image. The method described is to first perform  $\frac{N(N-1)}{2}$  pairwise registrations on the data set, and to then calculate the ending energies of these registrations, which is defined as the sum of the squared second partial derivatives of the geometric transform. These bending energies can then be used to build a distance matrix D, where element  $D_{IJ}$  is the bending energy between objects I and J. Using multidimensional scaling, images can be plotted according to relative locations by Euclidean distance from each other, allowing the easy selection of the reference image or data set. Once, this reference image is chosen, all images can be mapped onto the reference, which does not require reregistration, since pairwise registration has already been done.

Known image sets were deformed and this algorithm was used as a proof of concept for the selection of the least biased image. Multidimensional scaling was done with four dimensions. Of the images present, the chosen image was 0.0106 in terms of Euclidean distance from the calculated mean of the data set, which was small compared to the overall range of distances. In terms of weaknesses, this paper only demonstrated the value of this technique on two dimensional images, with known distortions. Although the extension to three dimensions is mentioned, there is no explicit testing of the viability of this method in three dimensions. Furthermore, choosing the least biased reference does not remove bias as is the intent in methods that create a novel reference image such as those of Guimond et al.

The major benefit of the least biased selection is speed. Because registration is only performed once, this method does not increase computation time as significantly as an iterative approach would. Furthermore, because our database contains such a large number of patients, the time to perform iterative methods is orders of magnitude greater than a simply choosing the least biased target. However, there is no measured effect on the validity of constructed atlases upon application to novel patient data presented in either of these papers, and thus it is not quite clear that one of these methods is better than the other for the intended purposes of our project.

## References

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