Longitudinal Brain MRI Analysis with Uncertain Registration

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1. Introduction

- This work introduces a novel approach for incorporating measures of registration derived spatial uncertainty into spatially normalised statistics.
- Current approaches to spatially normalised statistics use a point-estimate of the transformation parameters, which assumes a perfect mapping.
- There is limited previous work on the use of registration uncertainty [1].
- A probabilistic registration model is used to infer a posterior distribution on the transformation parameters, rather than just a point estimate.
- Local Gaussian smoothing kernels can be derived from the registration model which compensate for the uncertainty of the mapping.
- This method is demonstrated on spatially normalised longitudinal features, created from subjects with Alzheimer's Disease, and healthy controls.

2. Methods

2.1. Registration Model

Registration can be described using a generative model: $\mathbf{Y} = \mathbf{T}(\mathbf{X}, \mathbf{w}) + \mathbf{E}$, $\mathbf{X}$,$\mathbf{Y}$ are the source and target images. $\mathbf{T}(\mathbf{X},\mathbf{w})$ is a transformation function parameterised by $\mathbf{w}$. $\mathbf{E}$ is additive i.i.d Gaussian noise, $\mathbf{E} \sim N(0,\phi^{-1})$, where ϕ is the noise precision, with an uninformative Gamma prior $P(\phi) = Ga(\phi;a_0,b_0)$.

2.2. Regularisation Prior

Regularisation is incorporated as a prior distribution on $\mathbf{w}$: $P(\mathbf{w}) = N(\mathbf{w};0,(\lambda\boldsymbol{\Lambda})^{-1})$, where $\boldsymbol{\Lambda}$ encodes the bending prior, λ determines the level of regularisation, and is inferred from the data in this framework as in [2]. λ has an uninformative Gamma prior $P(\lambda) = Ga(\lambda;s_0,c_0)$.

2.3. Model Inference

Variational Bayes (VB) [3] was used to infer the model parameters. VB provides approximate posterior distributions on the model parameters, using the mean field approximation: $P(\mathbf{w},\lambda,\phi| Y) = q(\mathbf{w})q(\lambda)q(\phi)$, where $q(\mathbf{w})=N(\mathbf{w};\mu,\boldsymbol{\Upsilon}^{-1})$, $q(\lambda)=Ga(\lambda;s,c)$, $q(\phi)=Ga(\phi;a,b)$. Analytic updates for the approximate posterior distribution hyper-parameters are derived as:

$$\begin{aligned} \boldsymbol{\Upsilon}\boldsymbol{\mu}_{new} &= \left[\alpha\bar{\phi}\mathbf{J}^T(\mathbf{J}\boldsymbol{\mu}_{old} + \mathbf{k})\right] & \boldsymbol{\Upsilon} &= (\alpha\bar{\phi}\mathbf{J}^T\mathbf{J} + \bar{\lambda}\boldsymbol{\Lambda}) \\ \frac{1}{a} &= \frac{1}{a_0} + \frac{1}{2}\alpha(\mathbf{k}^T\mathbf{k} + Tr(\boldsymbol{\Upsilon}^{-1}\mathbf{J}^T\mathbf{J})) & b &= b_0 + \frac{N_v\alpha}{2} \\ \frac{1}{s} &= \frac{1}{s_0} + \frac{1}{2}\left(Tr(\boldsymbol{\Upsilon}^{-1}\boldsymbol{\Lambda}) + \boldsymbol{\mu}^T\boldsymbol{\Lambda}\boldsymbol{\mu}\right) & c &= c_0 + \frac{N_c}{2} \end{aligned}$$

where $\mathbf{J}$ is the matrix of first order partial derivatives of the transformation parameters with respect to the transformed image $\mathbf{T}(\mathbf{X},\mu_{old})$. $\mathbf{k}$ is a vector of the residual image. μ_{new} is the current mean transformation which depends on μ_{old}. $\bar{\lambda}$ and $\bar{\phi}$ are the expectation of $q(\lambda)$ and $q(\phi)$. N_c is the number of transformation parameters, N_v is the number of active voxels, and α is the virtual decimation factor which models residual image correlation [4].

2.4. Spatial Uncertainty

- This registration model provides an intrinsic measure of the uncertainty on the posterior transformation parameters in the covariance matrix $\boldsymbol{\Upsilon}^{-1}$.
- The approximate uncertainty of each voxel is a 3D Gaussian distribution.
- To compensate for the mapping uncertainty, we smooth the transformed data according to the local uncertainty distribution.

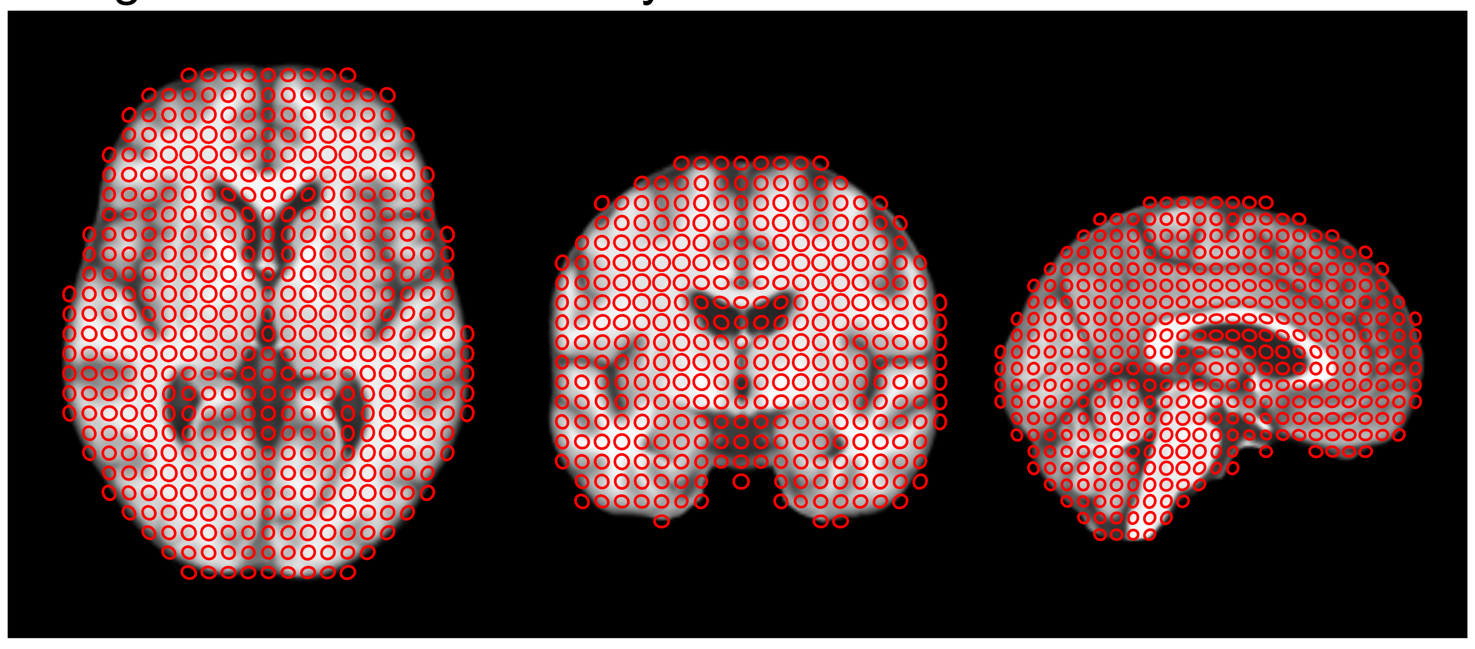


Figure 1: Illustration of the average level of registration derived uncertainty when registering healthy controls to the altas. Each ellipse indicates the FWHM of the uncertainty distribution of a voxel.

3. Experiments and Materials

- The probabilistic registration model was implemented into FNIRT [5], a multi-level free-form deformation algorithm using a B-spline basis set.
- Longitudinal features were generated and spatially normalised from ADNI [6].
- 162 subjects for training (81 AD, 81 NC), 149 for testing (68 AD, 81 NC).
- Spatially normalised Jacobian maps were either: not smoothed, smoothed using a Gaussian kernel (σ=2mm), or smoothed according to the registration uncertainty.

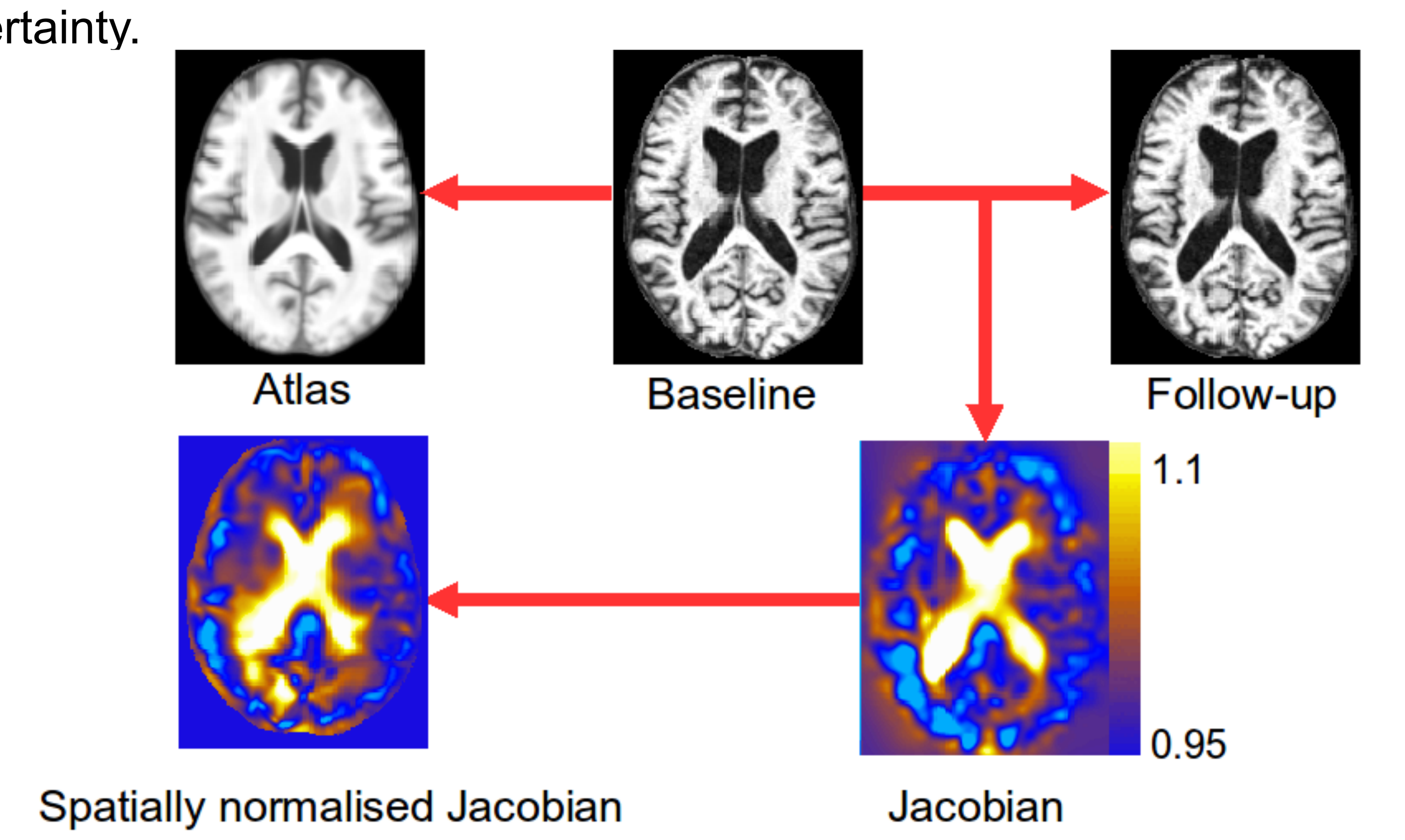
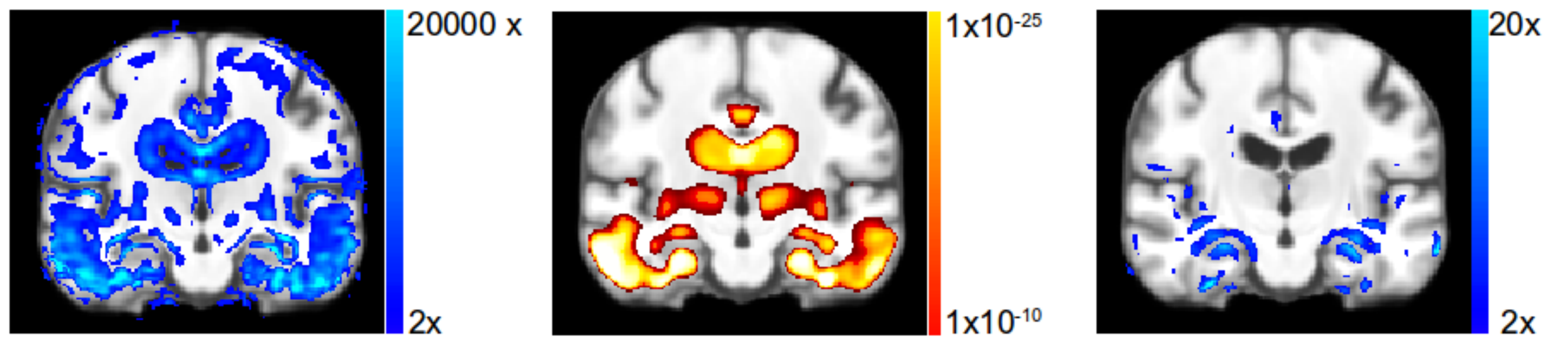


Figure 2: Longitudinal feature generation pipeline

4. Results



Increase in factor of statistical significance from un-smoothed data

Adaptively smoothed level of statistical significance

Increase in factor of statistical significance from 2mm Gaussian smoothed data

Figure 3: The central image shows the statistical significance (p-value) acquired from voxelwise t-tests between the spatially normalised Jacobians of the two populations. The left and right images show the factor of increase in the voxelwise statistical significance when using the proposed adaptive smoothing over either not smoothing the data, or using a 2mm Gaussian kernel. All the scales are logarithmic.

Smoothing method	Correct rate	Sensitivity	Specificity	RBF σ	Soft Margin
No smoothing	0.852	<u>**0.838**</u>	0.864	33	100
Gaussian Smoothing (σ= 2mm)	0.866	<u>**0.838**</u>	0.889	51	100
<u>**Adaptive Smoothing**</u>	<u>**0.873**</u>	<u>**0.838**</u>	<u>**0.9012**</u>	55	100

Table 1: Classification results when spatially normalised Jacobian maps were masked using a t-test ($p<0.05$) on the training set, then decomposed using PCA. An RBF SVM was applied using the set of principal components which make up 99% of the variance. The SVM parameters were optimised using leave-one-out cross validation.

Smoothing method	Correct rate	Sensitivity	Specificity	RBF σ	Soft Margin
No smoothing	0.846	0.721	0.95	110	10^4
Gaussian Smoothing (σ= 2mm)	0.846	0.721	0.95	150	10^4
<u>**Adaptive Smoothing**</u>	<u>**0.873**</u>	<u>**0.75**</u>	<u>**0.975**</u>	40	10^3

Table 2: Classification results using the 2000 most significant voxels (assessed by t-test) in the training set. An RBF SVM was used and the parameters optimised using leave-one-out cross validation.

5. Discussion

- We introduce a generic and principled approach to consider uncertainty in non-rigid registration.
- This estimated uncertainty can be used to derive an adaptive local smoothing kernel.
- This approach to image smoothing has been demonstrated to improve the ability to classify subjects with Alzheimer's Disease using longitudinal features.

References

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