2.7 Automated segmentation of brain MR images

Many studies in basis neuroscience and neurological and psychiatric diseases benefit from fully-automated techniques that are able to reliably assign a neuroanatomical label to each voxel in magnetic resonance (MR) images of the brain. In order to cope with the complex anatomy of the human brain, the large overlap in intensity characteristics between structures of interest, and the dependency of MR intensities on the acquisition sequence used, state-of-the-art brain MR labeling techniques rely on prior information extracted from a collection of manually labeled training datasets. Typically, this prior information is represented in the form of *probabilistic atlases*, constructed by first aligning the training datasets together using linear spatial transformations, and then calculating the probability of each voxel being occupied by a particular structure as the relative frequency that structure occurred at that voxel across the training datasets.

While these "average" atlases are intuitive and straightforward to compute, they are not necessarily the best way to extract population-wise statistics from the training data. Atlases built from a limited number of training images tend to generalize poorly to subjects not included in the training database, necessitating heuristic approaches such as spatially blurring atlases used in automated segmentation algorithms. Another problem is that such atlases do not include non-linear deformations aligning corresponding structures across subjects, although this would be a natural way to model anatomical variations.

In [31], we took a critical look at the generative model implicitly underlying probabilistic brain atlases, and proposed to generalize it using tetrahedral mesh-based representations endowed with explicit deformation models. We demonstrated how Bayesian inference can be used to automatically learn the optimal properties of the resulting atlases from a set of manual example segmentations in MR images of training subjects. The learning involves maximizing the probability with which an atlas model would generate the example segmentations, or, equivalently, minimizing the number of bits needed to encode them. This procedure automatically yields sparse atlas representations that explicitly avoid overfitting to the training data, and are therefore better at predicting the neuroanatomy in new subjects than conventional probabilistic atlases [31]. An example of an optimal mesh-based atlas, built from manual annotations of 36 neuroanatomical structures in four individuals, is shown in figure 2.11.

In subsequent work aiming at automatically delineating the subregions of the hippocampus from very high resolution MR images [32, 36, 35], we supplemented the prior distribution provided by a mesh-based atlas, which models the generation of images where each voxel is assigned a unique neuroanatomical label, with a parametric likelihood distribution that predicts how such label images translate into MR images, where each voxel has an intensity. Together these distributions form a complete generative model of MR images that we then used to obtain fully automated structural measurements in a Bayesian fashion, using concepts from our earlier work [28, 29]. In particular, we estimated how the position of the nodes of the atlas mesh are optimally warped onto an image under study, while simultaneously inferring the parameters of the likelihood distribution. Figure 2.12 shows an example of a fully-automated segmentation of the subregions of the hippocampus computed using this approach.

Additional joint work in brain MR analysis we contributed to during the years 2008-2009 include group-wise segmentation of collections of images for which no manual training data is available [38, 41], non-parametric Bayesian whole-brain parcellation [39, 40] and information theoretical image alignment [37], as well as a number of clinical research papers [30, 33, 34].

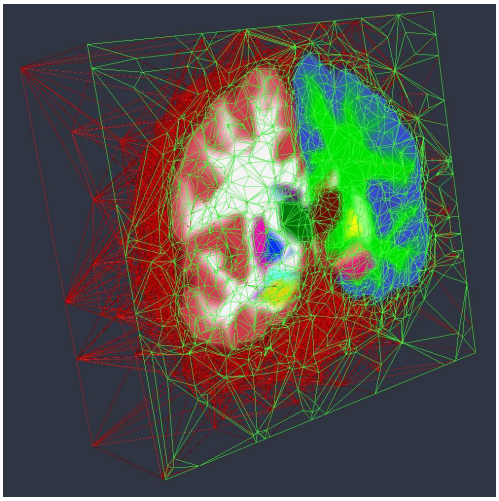

Figure 2.11: Optimal tetrahedral mesh-based atlas built from manual annotations of 36 neuroanatomical structures in 4 subjects. The prior probabilities for the different structures have been color-coded for visualization purposes.

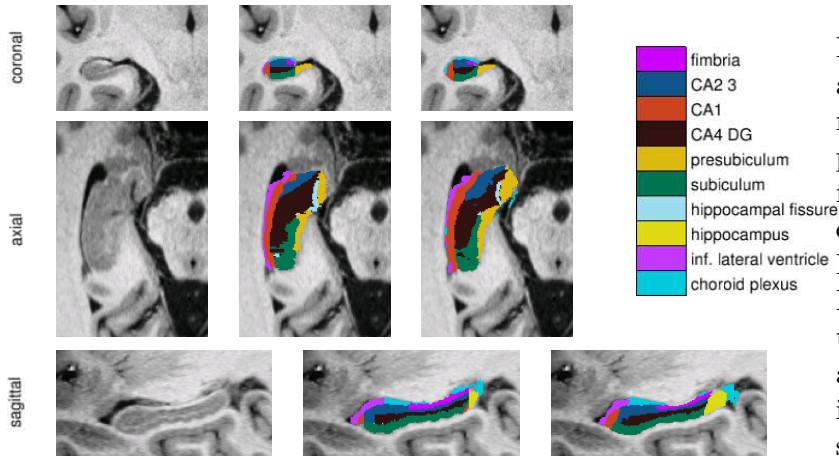

Figure 2.12: Fully automated segmentation of hippocampal subfields from ultra-high resolution MR scans. From left to right: MR data, manual delineations, and corresponding automated segmentations.

[17] A. Ilin and T. Raiko. Practical approaches to principal component analysis in the presence of missing values. Tech. report TKK-ICS-R6, Helsinki University of Technology, TKK reports in information and computer science, Espoo, Finland, 2008.

[18] L. Kozma, A. Ilin, and Tapani Raiko. Binary principal component analysis in the Netflix collaborative filtering task. In *Proceedings of the IEEE International Workshop on Machine Learning for Signal Processing*, Grenoble, France, September 2009.

[19] J. Luttinen, A. Ilin, and Juha Karhunen. Bayesian robust PCA for incomplete data. In *Proc. of the 8th International Conference on Independent Component Analysis and Blind Signal Separation (ICA 2009)*, pp. 66–73, Paraty, Brazil, March 2009.

[20] J. Zhao, Q. Jiang. Probabilistic PCA for t distributions. *Neurocomputing*, 69:2217–2226, 2006.

[21] C. Archambeau, N. Delannay, M. Verleysen. Robust probabilistic projections. In *Proc. of the 23rd International Conference on Machine Learning (ICML 2006)*, pp. 33-40, New York, NY, USA, 2006.

[22] P. Gao, A. Honkela, M. Rattray, and N. D. Lawrence. Gaussian process modelling of latent chemical species: applications to inferring transcription factor activities. *Bioinformatics* 24(16):i70–i75, 2008.

[23] A. Honkela et al. A model-based method for transcription factor target identification with limited data. *Proc Natl Acad Sci U S A*, 2010. doi:10.1073/pnas.0914285107

[24] M. Harva. Algorithms for approximate Bayesian inference with applications to astronomical data analysis. *TKK Dissertations in Information and Computer Science*, TKK-ICS-D3, Espoo, Finland, 2008. Available at `http://lib.tkk.fi/Diss/2008/isbn9789512293483/`.

[25] S. Refsdal. On the possibility of determining Hubble's parameter and the masses of galaxies from the gravitational lens effect. *Monthly Notices of the Royal Astronomical Society*, 128:307–310, 1964.

[26] J. C. Cuevas-Tello, P. Tino, and S. Raychaudhury. How accurate are the time delay estimates in gravitational lensing? *Astronomy & Astrophysics*, 454:695–706, 2006.

[27] M. Harva and S. Raychaudhury. Bayesian estimation of time delays between unevenly sampled signals. *Neurocomputing*, 72(1-3):32–38, 2008.

[28] K. Van Leemput, F. Maes, D. Vandermeulen, and P. Suetens. Automated Model-based Bias Field Correction of MR Images of the Brain. *IEEE Transactions on Medical Imaging*, 18(10):885–896, 1999

[29] K. Van Leemput, F. Maes, D. Vandermeulen, and P. Suetens. Automated Model-based Tissue Classification of MR Images of the Brain. *IEEE Transactions on Medical Imaging*, 18(10):897–908, 1999

[30] T. Autti, M. Mannerkoski, J. Hämäläinen, K. Van Leemput, and L. Åberg. JNCL patients show marked brain volume alterations on longitudinal MRI in adolescence. *Journal of Neurology*, 255(8):1226–1230, 2008

[31] K. Van Leemput Encoding Probabilistic Brain Atlases Using Bayesian Inference. *IEEE Transactions on Medical Imaging*, 28(6):822–837, 2009

[32] K. Van Leemput, A. Bakkour, T. Benner, G. Wiggins, L.L. Wald, J. Augustinack, B. C. Dickerson, P. Golland, and B. Fischl. Automated Segmentation of Hippocampal Subfields from Ultra-High Resolution In Vivo MRI. *Hippocampus*, 19(6):549–557, 2009

[33] B. Fischl, A. A. Stevens, N. Rajendran, B. T. T. Yeo, D. N. Greve, K. Van Leemput, J. Polimeni, S. Kakunoori, R. L. Buckner, J. L. Pacheco, D. H. Salat, J. Melcher, M. P. Frosch, B. T. Hyman, P. E. Grant, B. R. Rosen, A. J. W. van der Kouwe, G. C. Wiggins, L. L. Wald, J. C. Augustinack. Predicting the Location of Entorhinal Cortex from MRI. *NeuroImage*, 47(1):8–17, 2009

[34] M. K. Mannerkoski, H. J. Heiskala, K. Van Leemput, L. E. Åberg, R. Raininko, J. Hämäläinen, and T. H. Autti. Children and adolescents with learning and intellectual disabilities and familial need for full-time special-education show regional brain alterations: A voxel-based morphometry study. *Pediatric Research*, 66(3):306-0311, 2009

[35] K. Van Leemput, A. Bakkour, T. Benner, G. Wiggins, L. L. Wald, J. Augustinack, B. C. Dickerson, P. Golland, and B. Fischl. Model-Based Segmentation of Hippocampal Subfields in Ultra-High Resolution In Vivo MRI. *Proceedings of the MICCAI 2008 Workshop on the Computational Anatomy and Physiology of the Hippocampus (CAPH'08)*, pp. 46–55, September 6, 2008, New York, USA

[36] K. Van Leemput, A. Bakkour, T. Benner, G. Wiggins, L. L. Wald, J. Augustinack, B. C. Dickerson, P. Golland, and B. Fischl. Model-Based Segmentation of Hippocampal Subfields in Ultra-High Resolution In Vivo MRI. *Lecture Notes in Computer Science*, 5241:235–243, 2008

[37] M. R. Sabuncu, B. T. T. Yeo, T. Vercauteren, K. Van Leemput, and P. Golland. Asymmetric image-template registration. *Lecture Notes in Computer Science*, 5761:565–573, 2009

[38] T. Riklin Raviv, K. Van Leemput, W. M. Wells, and P. Golland. Joint Segmentation of Image Ensembles via Latent Atlases. *Lecture Notes in Computer Science*, 5761:272–280, 2009

[39] M. R. Sabuncu, B. T. T. Yeo, K. Van Leemput, B. Fischl, and P. Golland. Supervised Nonparametric Image Parcellation. *Lecture Notes in Computer Science*, 5762:1075–1083, 2009

[40] M. R. Sabuncu, B. T. T. Yeo, K. Van Leemput, B. Fischl, and P. Golland. Nonparametric Mixture Models for Supervised Image Parcellation. *Proceedings of the MICCAI 2009 Workshop on Probabilistic Models for Medical Image Analysis (PMMIA 2009)*, pp. 301-313, September 20, 2009, London, UK

[41] T. Riklin Raviv, B. Menze, K. Van Leemput, B. Stieltjes, M. A. Weber, N. Ayache, W. M. Wells, and P. Golland. Joint Segmentation via Patient-Specific Latent Anatomy Model. *Proceedings of the MICCAI 2009 Workshop on Probabilistic Models for Medical Image Analysis (PMMIA 2009)*, pp. 244-255, September 20, 2009, London, UK