

15µm average mouse models in Waxholm space from 16.4T 30µm images

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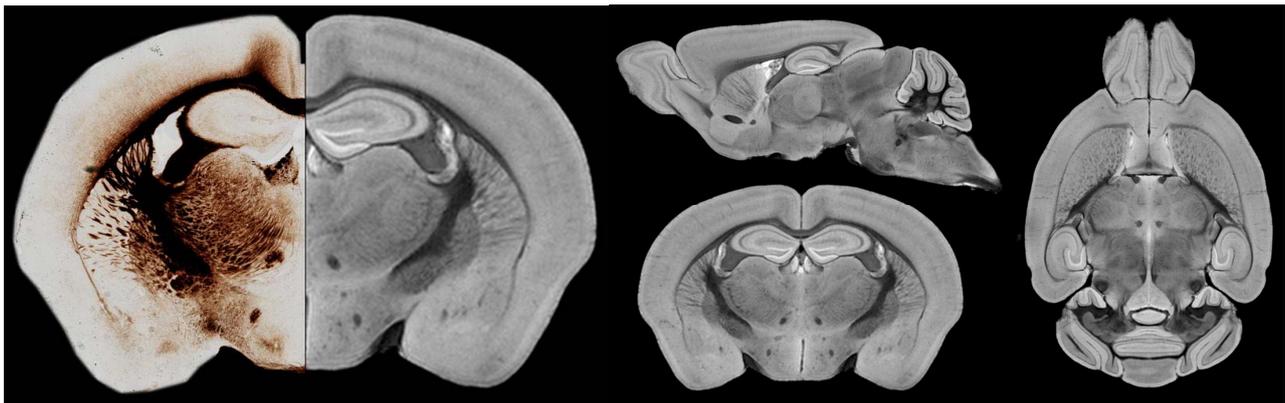
Introduction: Digital MRI atlases serve to integrate data from differing modalities, stereotaxic localisation, automatic region identification, automated segmentation and direct comparisons between individuals. While paper atlases^{1,2} can provide exquisite detail of delineated structures, they are typically based upon an individual subject's histology and as such make it difficult to identify structures in novel subjects in an automated fashion. Improvements in field and gradient strength has led to enhanced resolution and the number of segmented regions in MRI atlases. Arguably, the best current atlas is that of Dorr *et al* in 2008³, acquired at 7T with a final resolution of 32µm and 62 segmented structures.

The data in this MRI atlas was acquired at 16.4T and created using a specific adaptation of a nonlinear averaging technique that resulted in a final resolution of 15µm and is thus approaching histological clarity. The model and segmented structures⁴ is available from <http://www.imaging.org.au/>. Further detail of the segmentation process for the structures is given in another poster at ISMRM (see #1286).

Method: Eighteen animals were perfused and fixed with 4% paraformaldehyde and 0.1% Magnevist®. Brains were extracted and incubated in 0.1% Magnevist/PB for 4 days, placed in Fomblin and imaged on a 16.4T (89mm) Bruker micro-imaging system using a 15 mm SAW coil (M2M Imaging, USA). MRI was acquired using a 3D gradient echo sequence with TR/TE/FA= 50ms/12ms/30°, 82 KHz spectral bandwidth and 8 excitations with an acquisition time of 5h 15mins to produce T₁/T₂*-weighted images at 30µm³ isotropic resolution.

The images were first B₀ non-uniformity corrected using the N3 technique and intensity normalised using a histogram clamping technique. A probabilistic model was then created using a method very similar to that of Fonov *et al*⁵ and Grabner *et al*⁶. In the present case the fitting strategy consisted of 3 linear fits to the evolving internal model followed by a hierarchical series of non-linear grid transforms. These transforms started with a step size of 1.067mm followed by 0.533mm, 0.267mm, 0.2mm, 0.133mm and finished with 0.06mm. These fitting steps use progressively de-blurred data with a 3D kernel FWHM of half the current step size. Twenty iterations at each fitting stage were performed using the ANIMAL algorithm. Our technique differs from Fonov *et al*'s during the intermediate model generation in that a robust averaging process is used to reduce the effect of artefacts and small handling tears in the brain. The averaging technique places a lower weight on data at each voxel that is greater than 2 standard deviations from the current model. The fitting process took 3 weeks on a 50core commodity Debian GNU/Linux cluster.

Results: A representative tri-planar view is shown below. This model exhibits fine detail in structures not seen before, especially with regards to the thalamic nuclei. A split image of MRI and a histology slice using a Gallyas silver stain shows the level of detail available in high field MRI and how this corresponds to histology.



Conclusion: The increase in resolution and signal from the modelling process means that we can now readily identify multiple thalamic and neocortical nuclei that are not visible in individual subjects. In the future the overlaid histology will be released along with matching segmented MRI data. Code is available as part of MINC in the volgenmodel package.

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3. Dorr, A. E., *et al.* High resolution 3D brain atlas using an average MRI of 40 adult C57Bl/6J mice. *Neuroimage* **42**, 60-69 (2008)
4. Richards K, *et al.* Segmentation of the mouse hippocampal formation in MRI, *Neuroimage* **58**, 732-740 (2011).
5. Fonov, V. *et al.* Unbiased average age-appropriate atlases for pediatric studies. *Neuroimage* **54**, 313-327 (2011).
6. Grabner G *et al.* Symmetric Atlasing and Model Based Segmentation. *LNCIS* **4191**, 58-66 (2006).