Where in the brain are the genes expressed

Trygve B. Leergaard [1,*] **and Ilya Zaslavsky** [2,*]

[1] *Centre for Molecular Biology and Neuroscience & Institute for Basic Medical Sciences, University of Oslo, Norway*
[2] *San Diego Supercomputer Center, University of California, San Diego, USA*

Correspondence*:
Trygve B. Leergaard, t.b.leergaard@medisin.uio.no
Ilya Zaslavsky, zaslavsk@sdsc.edu

A commentary on A high-resolution anatomical framework of the neonatal mouse brain for managing gene expression data
by Erh-Fang Lee, Jyl Boline and Arthur W. Toga

The need to determine the distribution of a given cellular or molecular marker within the brain is common to a wide range of neuroscience investigations. Localization is an essential parameter both for the interpretation of findings in an anatomical and functional context, as well as for comparing findings across specimens. Knowledge of temporal and spatial gene expression patterns in the brain is of particular importance for understanding correlations between genotype and phenotype, during development, in normal adults, as well as in disease. In situ hybridization and similar measurements of molecular distributions, selectively label cells expressing particular genes or gene products in tissue sections. However, lack of structural background information in the surrounding tissue makes the identification of anatomical boundaries difficult. Variations in the used section plane complicate matters further. As a result, studies of gene expression distributions tend to be restricted to limited regions, and reported findings are typically difficult to compare.

In this issue, Arthur Toga and collaborators present a high-resolution three-dimensional atlas framework for managing localization of gene expression in the newborn C57/6J mouse brain (Lee et al., 2007). Their cytoarchitectonic atlas is reconstructed from a densely sampled series of Nissl stained sections registered to a previously published MRI template atlas (Lee et al., 2005). In their paper, Lee et al. (2007) demonstrate atlas-based management, visualization, and analysis of gene expression image data normalized to a common atlas space. Images of arbitrarily oriented sections showing in situ hybridization gene expression patterns are linearly registered to the atlas on the basis of available anatomical landmarks. The localizations of expression patterns observed in the atlas-registered images are represented by (manually defined) contour lines that in turn allow three-dimensional (3-D) reconstruction, 3-D co-visualization with atlas structures, and quantitative analyses of distributions. By adopting the same anatomical nomenclature and hierarchical structure relationship as used for the adult mouse brain (MacKenzie-Graham et al., 2003), comparisons with adult neuroarchitecture are readily made. By storing image position parameters (defining the spatial position of images in atlas space) and boundary data (representing the labelling) in flexible XML documents, interoperability with other atlas or data management systems is ensured. Thus, this novel 3-D, high-resolution atlas of the newborn mouse brain equips developmental biologists with a novel and powerful tool package, potentially useful for whole-brain mapping of distribution patterns as well as other types of research involving the newborn mouse brain. Further, being part of the Biomedical Informatics Research Network (www.nbirn.net), the atlas is associated with a larger collection of brain atlases and tools, providing potential integrative analyses as well as comparison between animal models.

As the importance of digital atlases, spatial indexes, and management systems for distribution data from developing and adult rodent brains is increasingly recognized worldwide (see, e.g. Boline et al., 2007), several parallel advanced atlas systems emerge (see e.g. MacKenzie-Graham et al., 2003 ; Carson et al., 2005 ; Lein et al., 2005 ; Lee et al., 2005 , 2007) , providing both overlapping and complementary resources. Since such systems are tailored for different needs, and because their intrinsic complexity will likely pose an important threshold for the average user, the time is probably ripe for a consumers guide to different 3-D digital mouse (and rat) brain atlases.

Conflict of interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Full citation: Leergaard TB and Zaslavsky I (2008) Where in the brain are the genes expressed. Front. Neuroinform. 1:9. doi:10.3389/neuro.11.009.2007

REFERENCES

Boline J, Hawrylycz M, Williams RW (2007), Mouse and Rat Brain Digital Atlasing Systems, Nature Precedings. http://precedings.nature.com/documents/1046/version/1 Carson JP, Ju T, Lu HC, Thaller C, Xu M, Pallas SL, Crair MC, Warren J, Chiu W, Eichele G (2005). A Digital Atlas to Characterize the Mouse Brain Transcriptome. PLoS Computational Biology 1, e41 Lee EF, Jacobs RE, Dinov Ip, Leow A, Toga AW (2005). Standard atlas space for C57BL/6J neonatal mouse brain. Anatomy and Embryology 210, 245-263. Lee EF, Boline J, Toga AW (2007). A high-resolution anatomical framework of the neonatal mouse brain for managing gene expression data. Frontiers in Neuroinformatics, In press. Lein ES et al. (2007). Genome-wide atlas of gene expression in the adult mouse brain. Nature 445, 168-176. MacKenzie-Graham A, Jones ES, Shattuck DW, Dinov ID, Bota M, Toga AW (2003). The Informatics of a C57BL/6J Mouse Brain Atlas. Neuroinformatics 1, 397-410.