Computational Neuroanatomy from Genome Scale Gene Expression Data in the C57Bl/6J Mouse Brain

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Abstract

Modern computational methods in bio-imaging are enabling a new look at our understanding of neuroanatomy in the mammalian brain. Classical methods that have been used in this mature field include cyto/myelo architectonics, biochemical neuroanatomy, morphological studies and neural tract tracing; these approaches may now be complemented by 3D image-based gene expression studies enabling an enhanced view of the molecular component of neuroanatomy and cellular function. Here we introduce a new 3D dataset organized by spatially mapping and pooling gene expression data from the mouse brain. We present a novel anatomic gene expression based atlas (AGEA) which reflects the principal modes of mRNA expression patterns in the C57Bl/6J mouse brain and their relationship to conventional neuroanatomy. This atlas is based on large scale genome-wide *in situ* hybridization data from nearly 4,380 genes from the Allen Brain Atlas (www.brain-map.org), selected as the most pronounced gene markers in the mouse brain. After registering and quantifying signal in each 3D brain volume, we computed Pearson's correlation coefficient of each voxel to every other voxel, resulting in 53,380 3D correlation maps. A web-based browsing application was subsequently developed for the study of these maps. AGEA is a computational tool enabling the analysis and potential discovery of neuroanatomic boundaries and putative functional connectivity in the brain, and can be used to elucidate new modes of transcriptional connectivity. This new bio-image atlas should provide important data mining opportunities in computational neuroanatomy for the neuroinformatics community.
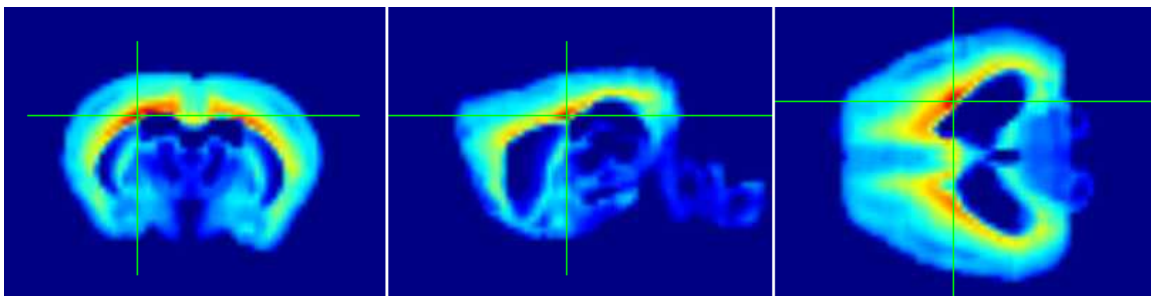
Figure 1. Gene expression correlation maps for a seed point in chosen in layer 6b of the barrel field cortex of the mouse brain shown in coronal, sagittal, and horizontal planes, respectively. In addition to the dominant laminar expression mode, some region specific correlation is evident (as viewed along the Y axis).
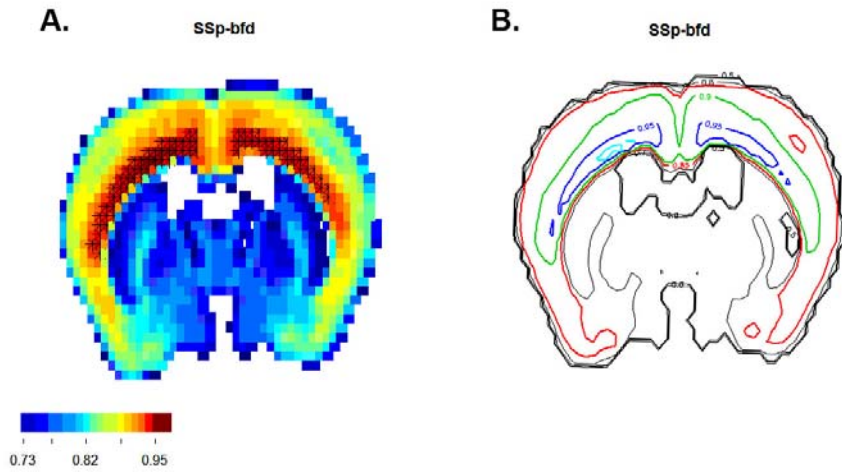
Figure 2. Correlation significance map for Figure 1 is shown in panel A, with 1.5% active voxels starred at 10% false discovery rate illustrating a layer specific pattern. Figure 2B shows a contour map depicting a multiple resolution view of correlation at various significance levels. Notable multi-scale correlation can be seen cortex-wide at level 0.85, layer-specific at 0.9, and regional-specific at 0.95.