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A 3D Selection & Query Tool for the GeneAtlas Project

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MASTERS PROJECT REPORT

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Motivation

Understanding the relationships between genes is of invaluable importance to researchers of genetic conditions and disorders. Each gene in the genome will be expressed, actively producing proteins, in only a subset of the body's cells. The particular areas in which genes do or do not synthesize proteins often share certain patterns, and these shared gene expression patterns may indicate potential relationships between genes.

A gene that is inactive in some area of the body is unlikely to be related to conditions in that region. Similarly, two genes that are highly active in the same cells are likely to be related. The ability to efficiently find genes with a particular expression pattern would enable researchers to more easily identify gene networks and to find genes – or groups of genes – related to a particular condition.

Computational Challenges

Organizing data about gene expression patterns is essentially a data-mining problem, and there is no lack of data involved: for each gene (of approximately 23,000 in the mouse genome), we can obtain a 'stack' of images – scanned cross-sections of a postnatal day 7 mouse brain – through a process called *in situ hybridization*. In situ hybridization identifies the cells in which the target gene is active; however, the process only provides information about one gene per set of images, meaning that each gene's data requires a separate stack of images taken from a new specimen.

As a result, the images taken for one gene cannot be meaningfully overlaid and compared with those of another – the size and shape of the brain varies non-trivially between mice, so that there is a clear need for a robust mapping between images for different genes.

GeneAtlas

The GeneAtlas project provides this mapping by constructing an atlas (in the form of a three-dimensional mesh of tetrahedra and octahedra) representing the various regions of the brain

and by deforming this atlas onto each set of images. Having done this, the expression data for all genes can be registered onto a single atlas for each of the unit volumes – tetrahedra and octahedra – of the atlas. The atlas then serves as a single data structure in which the expression patterns of genes, taken even from dissimilar samples, can be meaningfully compared.

My Contribution

Having created this mapping, the question of how a researcher should interact with the data remains a challenging problem. How does a user, given a keyboard and mouse, select a three-dimensional region of interest and search for a particular expression pattern? My contribution to the GeneAtlas project has been to develop a selection tool that addresses this problem. Within this tool, a user can select a region, specify an expression pattern, search the database for matching genes, and view the expression patterns of the results. I have implemented three methods of selecting polyhedra within the tool, in an attempt to find more practical and efficient ways for researchers to precisely specify a region. The first and second methods allow selection of individual polyhedra and selection of whole anatomical regions of the brain, respectively. The third method, which I will refer to as lasso selection, offers a novel contouring approach to save time and minimize the need for the user to be familiar with the complexities of the underlying polyhedral mesh.

The selection tool is implemented as a Java applet using the Java Binding for OpenGL (JOGL) library, allowing use from within a browser with the benefit of hardware-accelerated graphics. The various methods of selection are carried out in a hybrid 2D/3D interface: a 3D viewport provides the visual cues necessary to orient the user and to display the selection in its spatial context. An auxiliary 2D viewport shows a movable cross-section of the atlas, within which a researcher can use the mouse to select polyhedra – an operation that would be prohibitively unintuitive in a purely three-dimensional viewport. In addition to the core functionality, the tool contains other features related to versatile visualization of the atlas and gene expression data.

Resources

The GeneAtlas project is online at http://geneatlas.org. The 3D selection tool can be found under the '3D Queries' section in the left-hand navigation. This report and the slides from my presentation are also available online, at http://donmccurdy.com/projects/geneatlas.