Mining for Patterns on Theme Maps of Phenotyped Cells

Sayan Ranu
sayan@cs.ucsb.edu

Ambuj K. Singh
ambuj@cs.ucsb.edu

Department of Computer Science, University of California, Santa Barbara

Retinal cells contain micro-molecular mixture of 100-200 metabolic reactant monomers. Their molecular signatures give us a picture of their functional states. Excitation markers can be used to chemically discriminate cells and classify them. Each class can be remapped onto a single morphological channel called a *theme map* (Figure 1). Tracking cell classes is indispensable to analysis of cellular systems [1-4]. We present a tool that mines tissue samples to cluster cells of a particular class based on their connectivity to other classes and tracks their spatial distribution. The technique can be used to track information flow in cellular systems by studying biological circuits based on the spatial distribution of cells. For example, co-localized cells are likely to form part of a common pathway.

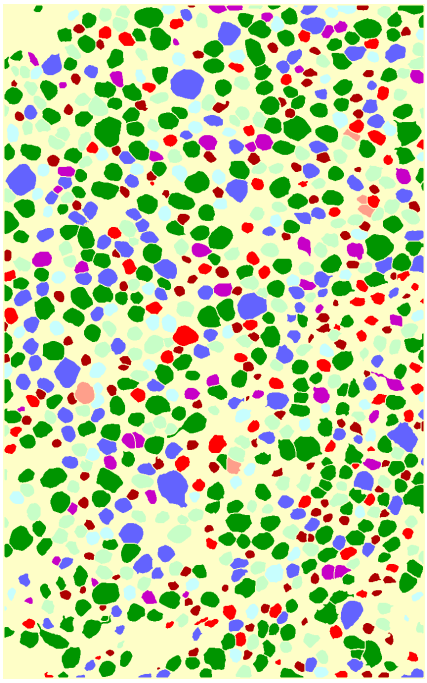

Figure 1: Theme Map

We create a graph from a given theme map. The idea behind the graph is to model the interactiveness between the cells. We perform Voronoi tiling on the image with the center of objects as the set of discrete points. An edge is created between two adjacent, visible (a line can be drawn between the cells without hitting another cell) Voronoi tiles. We performed random walks with restart on the graph to quantitatively track the connectivity of a cell to all other cells in its neighborhood.

K-means clustering was performed based on the feature vector generated. OPTICS plots [5] and Principal Component Analysis (PCA) were employed to analyze the clustering structure and chose an appropriate value for K. Each cluster was remapped as an image to examine their spatial distribution. We found that cells in some clusters form circular or elliptical regions. The region is visible only in this cluster and not the whole class (Figure 2). It seems that the cells forming the regions are interacting with a cell which lies in the center of the circular or elliptical regions. The results were re-verified with NJ clustering. Two clusters also displayed co-localization (Figure 3).

Nearest-Neighbor analysis was carried out on each cell, which demonstrated that amacrine cells with high GABA content have a likelihood of 83% to be the nearest of another cell but only 11% of the amacrine cells are NNs of each other.

In conclusion, we have developed a graph-based model to define the interactive pattern between cells in a theme map. Our experiments reveal interesting structures formed by these clusters. We are working on understanding the biological significance of these patterns.

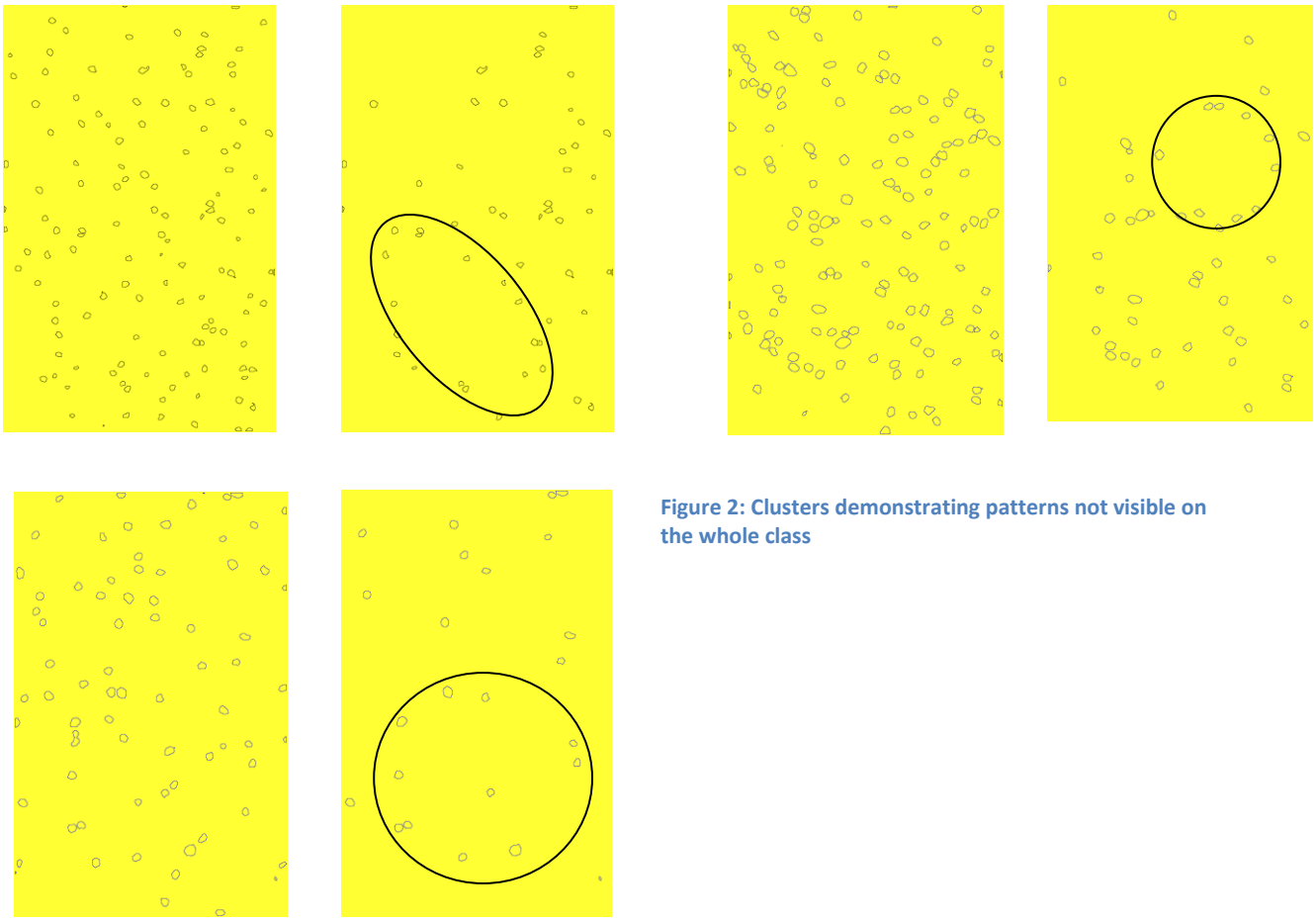

Figure 2: Clusters demonstrating patterns not visible on the whole class

References:

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5. M Amkerst, M. M. Breunig, H. Kreigel, and J Sander, *OPTICS: Ordering points to identify the clustering structure*. SIGMOD, 1999

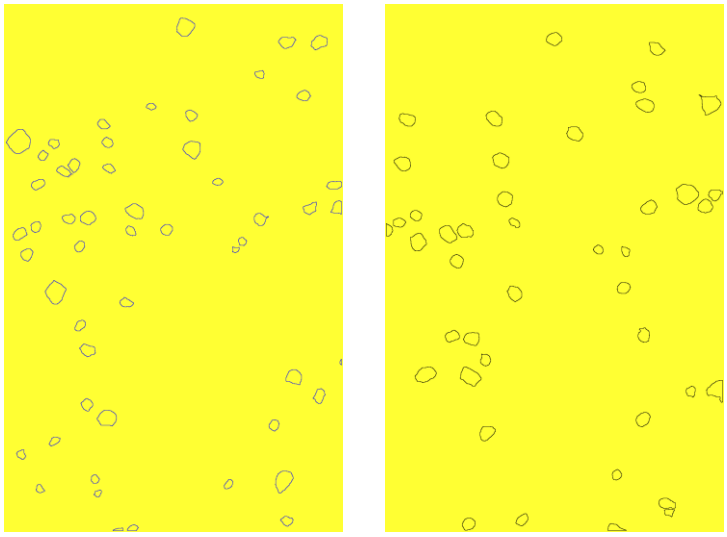

Figure 3: Co-localization displayed between clusters from two different classes