Probabilistic Analysis of Retinal Neuron Morphology

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1 Background Motivation

Cell morphology is often studied to quantify how cells physically respond to some stimulus, such as retinal detachment [2]. This type of analysis is very tedious, requiring scientists to measure a variety cell characteristics(e.g. soma size, dendritic field size, number of dendrites, etc.). Due to noise from the imaging process and imperfect cell labeling techniques, bioimages provide inherent uncertainty in their data, making it difficult to give precise answers to many quantifications. Due to these constraints, we introduce probabilistic methods to analyze the morphology of ganglion cells with minimal human interaction.

2 Analysis Methods

The probabilistic method employed to find the soma size is representative of the type of analyses we are performing on retinal cells, due to the limited space we just explain the soma computation here.

Somas of many cell types are not usually well defined shapes, making them difficult to measure. We can, however, approximate the soma area by splitting the soma into several 'pie slices', measuring the area of each slice, and summing over all the slices to get total area. Since we would like to convey the uncertainty in the image, the analysis should provide probabilistic results. For each slice of the soma, we take a sample at some radius from the cell center and use a function of the pixel intensities to represent the probability that the pixels at this radius are inside the soma. We continue this process over increasing radii to create a profile of probabilities, from which we would like to extract the most extreme radius that lies within the cell.

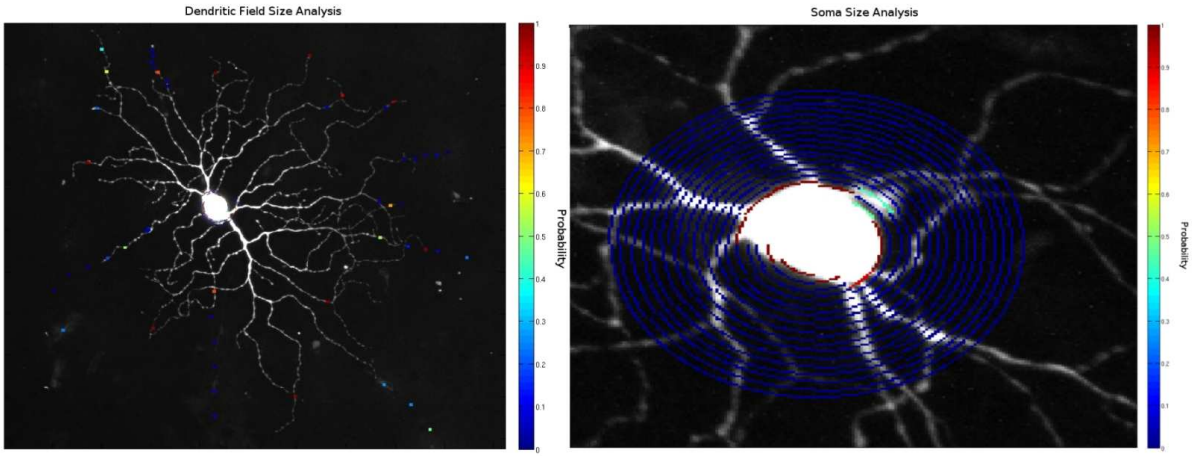

Figure 1: Visualization of the soma area and dendritic field analyses in action. The pixels on the image which are sampled are marked along with the calculated probability with which they are extreme points of the soma/dendritic field.

We are interested in calculating a single probability distribution function for the soma area. Instead of creating pdfs for each segment and calculating their joint probabilities, we can combine the samples from each segment and calculate the joint distribution directly. Since the space of possible areas for the soma is exponential in the number of slices and the number of sample radii, we perform Gibbs sampling over this space to get an approximation of the actual pdf. After finding the most probable radii for each segment, we can calculate the total area of the soma and its associated probability. Aggregating the probabilities for each area provides a pdf of the possible soma areas.

3 Validation

Validating probabilistic analysis is in itself a very difficult task and this is work still in progress. Ideally, we would like to compare our results with manual analyses performed by multiple biologists to enable us to take into account the variance between individual experts. We could build a distribution out of these manual analyses and compare that distribution to the output of our method to give a measure of accuracy. However, this is not feasible as this analysis is very tedious and time consuming work.

Currently, validation of our analysis has mainly been by visual inspection. We can create images, similar to those in Figure 1 which show the most probable extreme points. Biologists can then view a sample of these images to ensure we are picking good reasonable points to calculate the feature size.

4 Applications

These feature extraction methods allow for more interesting data analysis. After each image is analyzed, it can be represented as an N dimensional uncertain feature vector. This representation allows to maintain the feature uncertainty through the process of mining for patterns. Currently, we are investigating uncertain clustering methods, such as [1], with the goal of identifying the distinguishing morphological changes that ganglion cells undergo during a retinal detachment.

References

[1] M. Chau, R. Cheng, B. Kao, and J. Ng. Uncertain Data Mining: An Example in Clustering Location Data. *Proceedings of the 10th Pacific-Asia Conference on Knowledge Discovery and Data Mining (PAKDD 2006*, 3918:199–204.

[2] J. Coombs, D. van der List, G. Wang, and L. Chalupa. Morphological properties of mouse retinal ganglion cells. *Neuroscience*, 140(1):123–136, 2006.