Classification of retinal ganglion cell types according to dendritic branching and somal characteristics.

2015-01-19

# Introduction

How many types of mammalian retinal ganglion cell (RGC) are there? The answer to this question depends partly on how you define a neuronal type [Cook1998-bh], but it is commonly assumed that RGC types have distinct morphologies and physiologies. The pioneering work of Boycott and Wässle (1974) suggested that there were at least three morphological classes (alpha, beta and gamma) of RGC in cat, and these three types mapped onto previously-defined physiological classes (X, Y and W) [Cleland 1971, 1973]. For example, alpha cells were defined as having larger dendritic fields and somata compared to neighbouring beta cells. Since these early studies, subsequent work has primarily focused on finer divisions of the gamma class which was thought to be a mixed grouping (REF). Furthermore, it is unclear whether individual morphological features alone are unique predictors of cell type, as demonstrated by the large overlap in RGC somata area (their Figure 6) among the alpha/beta/gamme cat RGCs, but that multiple features should be considered simultaneously when classifying neurons. [Rodieck and Brening 1983] formalised this notion, proposing to use multiple features to define a multidimensional “feature space” in which to define RGC types. If cells form distinct types, then the expectation is that cells of the same type should cluster together in one part of this feature space, and that different cell types occupy different parts of feature space.

Recent advances in imaging and genetics have led to a dramatic increase in data available, especially from mice but also other species, to explore whether cells of distinct types form clusters in multidimensional space. Estimates for mouse retina vary from 12 (Kong et al., 2005) to 22 (Völgyi et al., 2009) based either on manual classification of cell types to unsupervised approaches. These unsupervised approaches use statistical methods to determine the optimal number of clusters in the data (e.g. using silhoutte widths technique; REF). However, these approachees have no ground-truth data to compare with the predicted number of cell types.

In this study, we analyse the morphology of RGCs from several mutant mice lines where typically one or a few types of RGC is labelled with GFP. We use supervised machine learning techniques to predict whether the anatomical features can predict the “genetic type” of the mouse, i.e. the mouse line from where the cell was labelled. This provides us with ground-truth data which we can use to evaluate our methods againts. From each RGC we measured fifteen features, from which we found five that were highly predictive of cell type. We compare our findings with a recent study (Sumbul2014) where near-perfect classification was achieved when information about stratification depth is included. We suggest that our anatomical measures can provide a reliable basis for classification in the absence of stratification depth information, and thus that the Brenning and Rodieck (1983) method of classification is robust when applied to mouse RGCs.

# References

**Boycott BB**, **Wässle H**. The morphological types of ganglion cells of the domestic cat’s retina. *J Physiol* 240: 397–419, 1974.

**Kong J-H**, **Fish DR**, **Rockhill RL**, **Masland RH**. Diversity of ganglion cells in the mouse retina: unsupervised morphological classification and its limits. *J Comp Neurol* 489: 293–310, 2005.

**Völgyi B**, **Chheda S**, **Bloomfield SA**. Tracer coupling patterns of the ganglion cell subtypes in the mouse retina. *J Comp Neurol* 512: 664–687, 2009.