Still with Us after All These Years: Issues of Neuronal Classification Revisited

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The classic paper discussed in this essay:

Rowe MH, Stone J (1977): Naming of neurones: classification and naming of cat retinal ganglion cells. *Brain Behav Evol* 14:185–216.

This paper was written in 1976, shortly after Jonathan Stone had relocated his lab from the Australian National University (ANU) in Canberra to the University of New South Wales in Sydney. I had joined Jonathan's lab as a post-doc early in 1975, when he was still in Canberra. At that time, the Physiology Department at ANU was headed by Peter Bishop and included a number of other prominent researchers (Geoff Henry, Bill Levick, Brian Cleland, Austin Hughes), and an ever changing contingent of visiting scholars, post-docs and grad students, all working in vision. So, I had been looking forward to entering an environment filled with lively discussions of the latest ideas and results. Indeed, upon my arrival I found myself in the middle of a spirited competition between Jon's lab and another group in the department led by Bill Levick that involved competing narratives for the still emerging story of retinal ganglion cell diversity and parallel retino-geniculo-cortical pathways.

At the time, there was very widespread interest in these issues because of their implications for models of cortical organization. When Hubel and Wiesel [1962] proposed that simple and complex cells in the visual cortex represented successive stages in a signal processing hierarchy, they assumed that all receptive fields at lower

stages of the pathway, the retina and lateral geniculate nucleus, had the center-surround organization previously described by Kuffler [1953]. Soon, however, descriptions of retinal receptive fields lacking center-surround organization began to appear [Stone and Fabian, 1966; Rodieck, 1967]. Even among ganglion cells that did have center-surround receptive fields, fundamental differences in other response properties were observed [Enroth-Cugell and Robson, 1966], and it was not long before the full extent of the diversity among the ganglion cell population was well documented [Stone and Hoffmann, 1972; Cleland and Levick, 1974a, b; Stone and Fukuda, 1974; Hochstein and Shapley, 1976]. During this same period, additional evidence from Canberra [Cleland et al., 1971; Hoffmann and Stone, 1971; Wilson et al., 1976] suggested that this retinal diversity might underlie some of the diversity observed in cortical receptive fields. If that were the case, it would have required significant revision of the hierarchical scheme proposed by Hubel and Wiesel [1962], and although all of this initial work was done in cats, it quickly became apparent that primate retina and visual pathways were organized in very similar ways [Dreher et al., 1976; De Monasterio, 1978]. So any revision of the

hierarchical scheme would have wide ranging implications for vision.

There was another important dimension to the arguments between the two labs involving fundamentally different views on methodology: what is the best strategy for determining whether two different ganglion cells perform the same or different functions? Levick's group believed that the descriptive features of ganglion cells were the best clue to their function, and they categorized, labeled and assigned functional roles to ganglion cells on that basis. Our view was that the starting point for any study of ganglion cell diversity should be the study of visual perception itself: what are its limits, and what signal processing operations are involved? Armed with that information, one could then identify cell groups whose descriptive features made them suitable candidates for performing particular operations. Furthermore, our view was that the labeling of such groups should be neutral (X, Y, W instead of brisk-sustained, brisk-transient, sluggish) in order to assure that the hypothesized relationships between cell groups and visual operations could accommodate new results and new ideas. Neither lab had ever issued any formal statement or defense of their methodological approach, but it was this dimension

that became the focus of the 1977 paper [Rowe and Stone, 1977].

As it happened, by the time I arrived Jon had already been thinking about leaving Canberra for some time. So when the opportunity to move to the University of New South Wales came along, we packed everything into a van and drove to Sydney in February of 1976. Not long after the move, I came across a paper that Fred Tyner had published in *Brain, Behavior and Evolution* in 1975 [Tyner, 1975], in which he very effectively argued that the problem of classification within neuronal populations had much in common with the problem of classification within animal populations, and that neuroscientists might benefit from adopting some of the methods and ideas from the field of taxonomy. Specifically, the classification should be hierarchical rather than flat, the position of a cell group within the hierarchy should be definable in (operational) terms that are independent of the descriptive features of the group, and membership within any group should be established on the basis of multiple features, not single 'essential' features. Since a major point of contention between the Levick and Stone labs in Canberra had involved the classification (number and labels) of ganglion cell groups, we immediately recognized the relevance of Tyner's paper (and, of course, that Tyner's approach very clearly reinforced our own). But we were completely preoccupied with getting the new lab up and running and did not think about taking any action until a month or so later. We both happened to be at Bogdan Dreher's house one evening discussing life, the universe and everything as we often did, and I suggested to Jon that we take the initiative and write a paper of our own, showing explicitly how the principles and practices of taxonomy could be applied to questions of retinal ganglion cell classification. This was on a Friday evening, as I recall, and when I got to the lab the following Monday morning, Jon, who was never shy or hesitant in such matters, handed me a hand-written draft of an introduction for the new paper, and we were off and running. We each had somewhat different agendas for this paper, and it took a little while to get everything reconciled and into a coherent package, but the paper was finally submitted in October of 1976.

It is difficult to judge the true impact of a paper from the number of citations alone: one does not know if the citing authors liked, disliked, agreed or disagreed with

the points in the paper. Somewhat more gratifying to me was the fact that at least up through the 1990s, people I encountered at meetings would tell me that the paper had been required reading in classes they had taken as grad students. And as recently as 2005 [Migliore and Shepherd, 2005], arguments very similar to ours have been used to advocate a multivariate approach to identifying 'functional phenotypes' of neurons; so it is clear that the fundamental issues we discussed are still relevant. On the featured issue of nomenclature, at the time we focused on the X, Y, W terminology as it was applied to neurons in the cat. Emphasis since then, at the systems level at least, has increasingly shifted to primates, where a new nomenclature has been developed; P- and M-cells in place of X- and Y-cells, respectively [Shapley and Perry, 1986], and K-cells in place of W-cells [Casagrande, 1994]. While not perfect, these terms are at least functionally neutral and avoid most of the problems we drew attention to.

However, visual science has progressed enormously over the intervening years, based on the efforts of investigators far too numerous to list here, and a whole new set of questions and issues has evolved. The traditional approach of defining receptive fields in terms of average responses to simple, artificial stimuli has been supplemented with tools based on information theory and Bayesian statistics that allow experimenters to quantify precisely the mutual information encoded in neural responses to complex natural stimuli. This approach has revealed that visual neurons dynamically adapt their responses, on multiple time scales, to the statistical structure of natural stimuli in ways that make the traditional receptive field concepts seem excessively static. The early controversy about serial versus parallel pathways with vaguely defined destinations largely ignored top-down influences on basic perceptual processes and has evolved into a recognition that serial, parallel and recurrent circuits all contribute to the creation of a distributed network representation of the external world. At the same time, it has become increasingly evident that neural responses at successive stages of this network are increasingly sparse (i.e. having high information content per spike). This reflects a design principle usually attributed to Barlow [1961], that visual circuits must use limited resources to create maximally efficient representations of the external world. Permeating all of this progress is

the dramatic increase in the use of computational methods over the last 35 years, coupled with the recognition that nervous system operations in general are probabilistic in nature rather than deterministic.

We did not fully anticipate any of these developments in 1977. We had simply seized an opportunity, provided by Tyner, to present a formal argument for one particular methodology, and our understanding and appreciation of the issues involved grew considerably while we were writing. In retrospect, I would consider the paper a success to the extent that it brought these issues to the attention of others at the time. Hopefully, recent developments such as the wide availability of computational tools and methods have allowed visual science to move on to more refined versions of these issues. Hypotheses and mechanisms can now be framed in the language of mathematics, which avoids many of the problems created by the use of words. So, for example, the notion of 'sparse' refers to a property of a probability distribution that can be specified and measured precisely, and is free of any verbal ambiguity. Choosing the right words will always be important, but to the extent that experimenters focus on finding the right quantitative model to represent the behavior of a cell or circuit, problems of relating measurable characteristics of neurons to their functional roles can be more easily addressed.

Looking back, I was very fortunate to have experienced such immersion into both the substance and style of science as a post-doc, and Jon's lab was a great place to learn. I am especially grateful that the immersion was made more complete and more pleasant by the fact that Jon and his wife, Margaret, basically treated me as a member of their family, as did Bogdan Dreher and his wife, Sophie, after the move to Sydney. I do regret not having more interaction with Bill Levick and Brian Cleland while I was in Canberra. Although we disagreed with them on many issues, I still regard much of their work as setting a gold standard for rigorous and careful experimentation. Finally, in addition to those we acknowledged in the 1977 paper [Rowe and Stone, 1977]. I would like to add a previously unacknowledged debt to Walter Riss, the founding editor of *Brain, Behavior and Evolution*. I am very grateful that he was not only interested in these issues, but also willing to use the pages of the journal to support such abstract discussions when other editors might not have been.

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