International Society for Neuroethology

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*The following commentary by **David King** was submitted in response to **Paul Katz' President's Column** published in the March 2012 ISN Newsletter, in which he invited discussion on unifying concepts. In this column, Katz invited the ISN membership to start thinking BIG. He asked: What are the organizing principles of brains and behaviors? Can we create a modern synthesis of neuroethology?" Responses to* dgking@siu.edu.

WHAT CAN GIANT AXONS TELL US ABOUT GENETICS AND EVOLUTION?

Naturalists have long noted that behavior evolves with remarkable ease, such that adaptive alteration of instinctive behavior commonly precedes concomitant adaptive adjustment of morphology. Yet all behavior depends on the exquisitely intricate organization of an entire nervous system. Between these two commonplace observations lies a mystery that has not yet been extensively explored and is seldom even acknowledged.

How can it be that complex, integrated neural organization is so evolutionarily malleable? In particular, to what extent are the characteristic properties of individually identifiable neurons (or "equivalent sets" of cells; Bullock 1984) free to vary and evolve independently from one another?

Giant axons, which in some animals can attain diameters greater than a millimeter, epitomize how clearly some individual nerve cells can be distinguished from all others (Figure 1). These outstanding nerve fibers warrant attention not only because they are, by definition, "far larger than the other fibers in the same animal" (Bullock & Horridge 1965, II, p. 1467). Giant axons also hint at the degrees of freedom that must be available for genetic adjustment of specific cellular parameters.

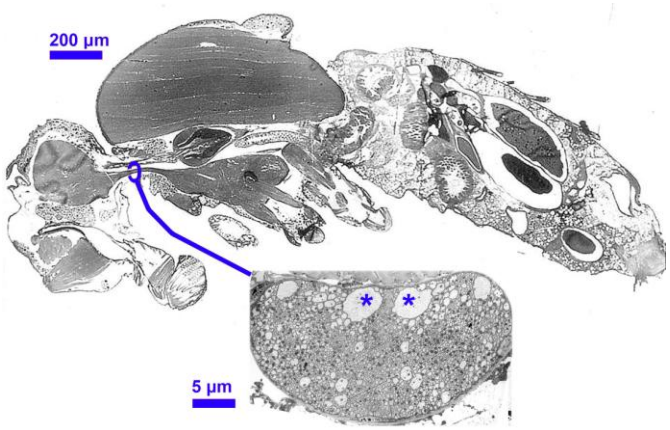

Figure. 1. The cervical connective of *Drosophila melanogaster* Meigen (family Drosophilidae). Asterisks indicate a pair of dorsomedial giant fibers.

"Repeatedly in each group, we find that related species differ in respect to possession of giant fibers, which must therefore evolve rather readily" (Bullock & Horridge 1965, I, p. 18). Thus giant axons exemplify not only the importance of axon diameter along certain neural pathways but also the facility with which evolutionary processes can adjust the properties of individual cells. And of course nerve fibers come in many sizes besides "exceedingly large" and "standard," so giant axons represent only a conspicuous extreme along a continuum of

axonal size variation. This means, to paraphrase the above observation, we repeatedly find that related species differ in their pattern of axon diameters, so that size distinctions among individual axons must evolve rather readily.

Several patterns of axon diameter are illustrated in Figures 2 through 5, from the cervical connectives of various dipteran flies. (The cervical connective is the insectan equivalent of a "spinal cord," connecting a fly's brain with the rest of its body.) Each connective contains several thousand axons, although most of the smaller ones cannot be resolved in these images.

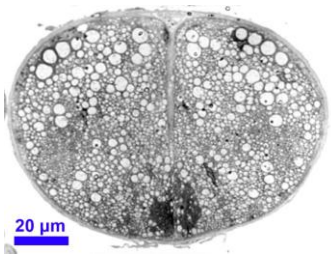

Figure 2. Tipulidae, *Tipula bicornis* Forbes.

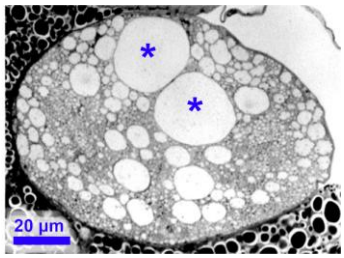

Figure 3. Lauxaniidae, *Minettia magna* (Coquillett).

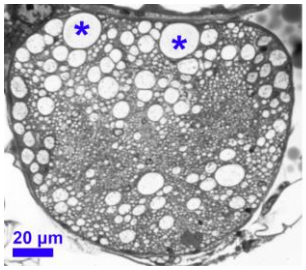

Figure 4. Muscidae, *Muscina pascuorum* (Meigen).

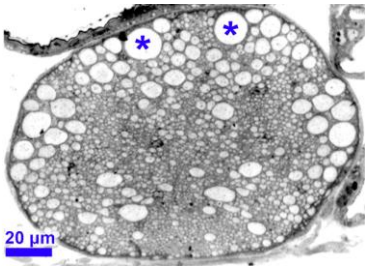

Figure 5. Sarcophagidae, *Sarcophaga bullata* Parker.

Some flies, such as the crane fly in Figure 2, have no exceptionally large axons. Other fly species, including several but not all muscoid flies, have a conspicuous pair of large dorsomedial axons (asterisks in Figures 3, 4, 5). These are putative homologs, by the criteria of similar position and course as well as relative size, for those which participate in a startle response in *Drosophila melanogaster* (King 1983; King & Valentino 1983; Wyman *et al*. 1984). The fly in Figure 3, with its especially prominent giant axons, lies midway in body size between the one shown in Figure 1 and those in Figures 4 and 5, so difference in proportional size is not a simple matter of allometry.

Additional diversity in axon size distributions is illustrated in Figures 6 through 9. Certain commonalities are evident in all of these specimens, such as the concentration of most large axons dorsally with a few bilaterally symmetrical pairs also present ventrally. But various differences are also readily apparent. Note that the two species shown in Figures 8 and 9, in spite of belonging to same family of bee flies, display distinctly different patterns of axon size.

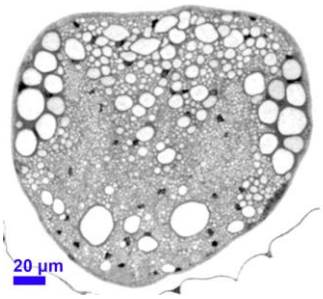

Figure 6. Tabanidae, *Tabanus calens* Linnaeus.

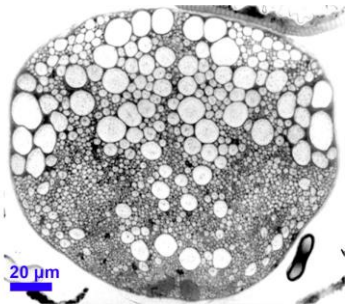

Figure 7. Syrphidae, *Helophilus fasciatus* Walker.

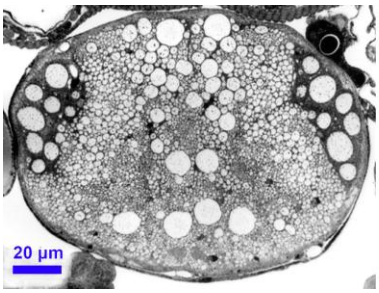

Figure 8. Bombyliidae, *Sparnopolius* sp.

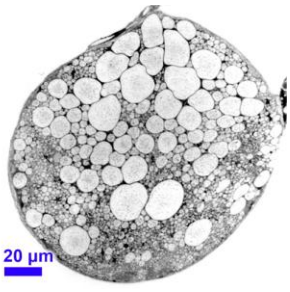

Figure 9. Bombyliidae, *Poecilanthrax* sp.

Among the many nerve cell properties with putative behavioral significance (*e.g.*, cell shape, connectivity, chemical action, membrane function, *etc*.; Bullock 2000), axonal diameter stands out both for ease of assessment and for relatively straightforward interpretation of functional impact. Larger axons increase the speed of impulse conduction as well as reliability of synaptic transmission, while smaller axons take up less volume and require less energy to build and to maintain. One can readily imagine scenarios in which selective advantage for specific axon size distributions reflects the relative importance, in different ecological niches, for signal speed and reliability along each of many diverse pathways. The typical association of giant axons with rapid escape reflexes supports this adaptationist perspective.

Nevertheless, identifying an adaptive advantage for a particular assortment of axon sizes comprises only part of a complete evolutionary explanation. Before natural selection can favor increased conduction rates for some individual axons and decreased rates for others, there must first exist considerable flexibility for genetically "tuning" the sizes of individual nerve fibers. Just how many such details of neuronal organization can be individually informed by a finite genome? How many "genes," or

genetic loci for adjustment, must exist to enable such facile evolutionary adaptation of the neural substrates for behavior? In other words, how are genomes organized to supply variation of appropriate quality and quantity to sustain behavioral evolution?

The simplicity of the protein code, with its direct correspondence between DNA sequence and amino acid sequence (subject of course to certain complexities of translation from RNA to protein, including excision of introns), should not be expected for the encoding of cellular morphology or organismal behavior. These emerge only through complex developmental and epigenetic interactions involving multiple genes as well as the external environment. Nevertheless, for any feature to be subject to natural selection, there must be a heritable correspondence between selectable differences in phenotype (including behavior) and DNA sequence differences at specific genetic loci.

Yet genetic sources for variability sufficient to specify the distinguishing functional parameters of uniquely identifiable cells, such as the diameters of giant axons, are certainly not obvious in current genome maps. If evolutionary adjustment of such cell parameters depended on variation in protein coding genes, the task would seem to require a far greater number of genes than are found in any animal's genome, even if genes had nothing else to do. This apparent paradox suggests a question. What manner of mutations, and of genetic information, must be necessary as the material basis for behavioral evolution?

Conventional evolutionary theory characterizes mutations as the accidental result of imperfect DNA replication and then simply presumes that "random" mutations must be adequate to sustain all adaptive evolution. Challenging this traditional view is a growing appreciation of implicit genetic "protocols" for mutation. These are mechanisms which constrain mutations within patterns that increase their potential or probability for adaptive utility (Doyle *et al*. 2006; Doyle & Csete 2011) and which could be shaped by indirect selection precisely for that function (King 2012).

By focusing attention on the necessity for versatile, high-resolution genetic control over neural organization, comparative study of neuronal and behavioral evolution in closely related taxa (as suggested here by axon diameter in flies) may help elucidate molecular sources of adaptive variation. For example, might neuronal properties be "tuned" not by conventional genes (i.e., protein coding sequences) but by combinations of regulatory sequences, perhaps comprised of simple tandem repeats which are far more numerous than genes (*cf*. Fondon *et al*. 2008)? On the other hand, might there also be features of neural organization which emerge from deeper principles of self-organizing development rather than from individual cell-by-cell adjustment, such as nested sets of fundamentally similar *ur*-circuitry?

Such questions invert the typical paradigm of evo-devo investigation. Instead of using developmental genetics to explain evolutionary transformation, this neuroethological approach would apply knowledge of comparative neuronal anatomy to address fundamental questions of genomic organization.

References

Bullock, T.H. (1984) Comparative neuroscience holds promise for quiet revolutions. *Science* 225: 473-478.

Bullock, T.H. (2000) Revisiting the concept of identifiable neurons. *Brain, Behavior and Evolution* 55: 241-247.

Bullock, T.H., & Horridge, G.A. (1965) *Structure and Function in the Nervous Systems of Invertebrates*. W.H. Freeman & Co., San Francisco.

Doyle, J.C., *et al*. (2006) An engineering perspective: The implicit protocols. In *The Implicit Genome*. Lynn H. Caporale, Ed.: pp. 294–298. Oxford University Press, New York.

Doyle, J.C. & Csete, M. (2011) Architecture, constraints, and behavior. *PNAS* 108: 15624-15630.

Fondon III, J.W., *et al*. (2008) Simple sequence repeats: Genetic modulators of brain function and behavior. *Trends in Neurosciences* 31: 328-334.

King, D.G. (1983) Evolutionary loss of a neural pathway from the nervous system of a fly (*Glossina morsitans*, Diptera). *Journal of Morphology* 175: 27-32.

King, D.G. (2012) Indirect Selection of Implicit Mutation Protocols. *Annals of the New York Academy of Science* 1267: 45-52.

King, D.G. & Valentino, K.L. (1983) On neuronal homology: A comparison of similar axons in Musca, Sarcophaga and Drosophila (Diptera: Schizophora). *Journal of Comparative Neurology* 219: 1-9.

Wyman, R.J., *et al*. (1984) The *Drosophila* giant fiber system. In: *Neural Mechanisms of Startle Behavior*, R. Eaton, ed. Plenum Press, New York.

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