Circuits and the single neuron

Paul S. Katz
Department of Biology, Neuroscience and Behavior Graduate Program
University of Massachusetts Amherst

Although it is common to discuss neural circuits as if they were like electronic circuits in which the components serve a single function, in fact neurons can serve different functions simultaneously, at different times, or under different circumstances. Nowhere is this clearer than in invertebrates, where individual neurons can be recognized and studied over long periods of time and under different conditions (1). The concept of multifunctional circuits was well enunciated in 1989 by Peter Getting, who was working on the marine mollusc, *Tritonia diomedea* (now *T. exsulans*) (2). This slow-crawling sea slug has been a premier species for studying the neural basis of rhythmic behavior for decades (3, 4). The central pattern generator (CPG) underlying its rhythmic escape swim is composed of a small number of individually identifiable neurons that each play a particular role the production of this behavior. However, the animal rarely swims and the CPG neurons have different functions under other circumstances. For example, a set of serotonergic neurons called the Dorsal Swim Interneurons (DSIs) are members of the swim CPG and fire rhythmic bursts of action potentials during the swim, but maintain an elevated firing rate for up to an hour following the swim episode. During this time, they help accelerate the crawling speed by activating efferent neurons that project to the foot (5).

In a new paper, “Surprising multifunctionality of a *Tritonia* swim CPG neuron: C2 drives the early phase of post swim crawling despite being silent during the behavior” (6), Hill and co-workers demonstrate that another *Tritonia* swim CPG neuron called C2 also accelerates crawling. The surprising aspect of this multifunctionality is that C2 is not normally active during crawling. The researchers address this conundrum by suggesting that there are different phases of the crawling behavior that are influenced by different neurons at different times. Thus, not only do individual neurons take on different roles at different times, but also seemingly consistent behaviors can be driven by different neural mechanisms at different times.

The researchers combined intracellular microelectrode recording and stimulation with large-scale voltage-sensitive dye (VSD) optical recording using a photodiode array. The power of this technique is that it allows hundreds of neurons to be monitored simultaneously. The team was able to record the activity of individual neurons during a swim episode and during crawling. They then determined the effect that intracellular stimulation of C2 had on those same neurons.

Although the activity of large numbers of neurons can be recorded with VSDs, few of those neurons can be unambiguously identified the way that C2 and DSI can. However, this is not to say that those neurons are not identifiable by other criteria. The VSD recordings of the ventral pedal ganglia showed a very distinct spatial pattern of neuronal activation (Fig. 1 A,B), which corresponded remarkably well to the locations of serotonergic neurons as determined by immunohistochemistry in another study (7) (Fig. 1C). Thus, combining large-scale recordings with immunohistochemistry or *in situ* hybridization (8) offers the possibility of identifying and mapping a larger number of neurons in sea slugs, similar to efforts in *Drosophila* for correlating activity and neural identity mapping (9).

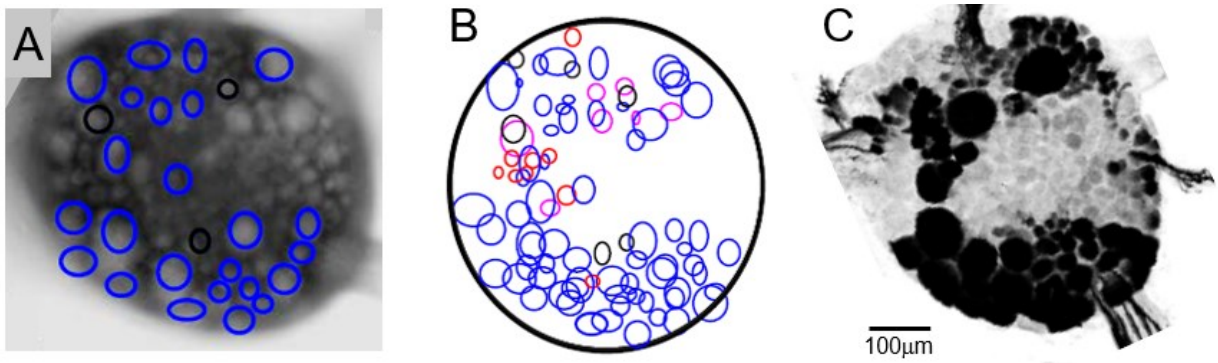

Figure 1. Comparison of optical recording and serotonin immunohistochemistry. A. The ventral side of a *Tritonia* pedal ganglion showing the locations of neurons that fired more action potentials during the crawling period than during a quiescent period. **B.** A composite map from six preparations shows distinct regions of neurons that increased their firing rate during the crawling period. The blue circles are neurons that were active during the dorsal phase of the swim motor pattern. **C.** Serotonin immunoreactive neurons in the pedal ganglion have the same basic organization as the neurons active during the crawling phase. A and B are from Ref (6). C was modified from ref (7).

Not only can neurons be reliably identified across individuals within a species, but they can also be recognized across species. In fact, the C2 neuron has been identified in four other sea slug species (10). In one of these species, *Pleurobranchaea californica*, the C2 homolog (known as A1) is also a member of the swim CPG (11) and is multifunctional, inhibiting feeding behaviors in response to noxious stimuli (12). The other species do not swim like *Tritonia* or *Pleurobranchaea* and the C2 neuron does not function as part of a CPG. Thus, not only can the role played by a neuron differ over time within an individual, but it can also differ over evolutionary time across species (13).

In conclusion, it is important to recognize the biases inherent in words borrowed from other; *circuits* of neurons do not have the properties of electrical circuits. We talk about hard-wired circuits meaning anatomically-defined connections. Yet neurons and synapses both exhibit extensive plasticity in their properties. This allows neurons to be multifunctional in a variety of ways: they can serve multiple functions at the same time, they serve multiple functions at different times, and they can change function over evolutionary time. The paper by Hill *et al*. (6) shows that even a neuron that has been studied for decades can still contain surprises.

Figure legend

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