

should be kept in mind by theorists and experimentalists that are interested in both information processing and the molecular basis of neuronal signaling in *C. elegans*.

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Mellem *et al.* reply: Recently, we reported the first evidence of action potentials in the nervous system of *C. elegans*¹. Approximately 50% of the regenerative events that we observed in response to current stimulation were isolated action potentials. The remaining 50% were followed by progression into a plateau potential and were altered by genetic or pharmacological manipulations. We also observed spontaneous all-or-none changes between hyperpolarized and depolarized states. Lockery *et al.* argue that the term ‘action potential’ should be reserved for a specific type of regenerative event that is associated with rate or spike timing coding schemes. In their view, a regenerative event

should be called an action potential only if it meets three criteria: its amplitude is invariant, its waveform is invariant and it is intrinsically self-terminating. However, the broader scientific community does not use this narrow definition. In fact, action potentials are used to describe a wide variety of regenerative events found in neurons, adrenal and pituitary cells^{2,3}, and even in algae and plant cells⁴. Probably the best-known examples of long and variable duration action potentials are found in cardiac cells. Another example is the action potential described in retinal horizontal cells, which is variable in magnitude, waveform and response to depolarizing stimuli⁵. A final example is the variable duration action potential identified in *C. elegans* pharyngeal muscle⁶. Indeed, the diversity of action potentials is enormous and recent studies have begun to elucidate the molecular mechanisms that lead to this diversity^{6,7}.

The regenerative events that we have described in *C. elegans* are diverse: at times they have reproducible, stereotyped waveforms (data not shown), at others they are associated with long-lived plateau states (Fig. 3g of ref. 1), and at yet other times they show spontaneous fluctuations of invariant amplitude (Fig. 1e of ref. 1). These findings should be of considerable importance to current efforts to model network activity in *C. elegans*. Because an earlier study suggested that all neurons in *C. elegans* shared “...a common mechanism of sensitivity and dynamic range”⁸, modeling studies might make

the assumption that all responses are simply graded in *C. elegans*; however, our studies clearly indicate the presence of regenerative, highly nonlinear voltage changes in at least some neurons¹.

These are exciting times for *C. elegans* neurobiology. Our initial observations raise a multitude of fascinating questions about the cellular and synaptic signaling mechanisms that contribute to action potential generation and plateau potentials, as well as the importance of this digital-like signaling for circuit function. Undoubtedly, future studies that address these questions and others will help to reveal fundamental strategies for information processing by nervous systems.

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