Published in final edited form as:

Nat Neurosci. 2009 April ; 12(4): 365–366. doi:10.1038/nn0409-365.

First report of action potentials in a *C. elegans* neuron is premature

SR Lockery^a, MB Goodman^b, and S Faumont^a

^aInstitute of Neuroscience, University of Oregon, Eugene, Oregon 97403-1210, USA

^bDepartment of Molecular and Cellular Physiology, Stanford University, Stanford, CA 94305-5345, USA

Since the publication of an essentially complete wiring diagram of the *C. elegans* nervous system more than 20 years ago¹, there has been intense interest in the question of whether *C. elegans* neurons fire action potentials. Thus, the recent report by Mellem *et al.*² of action potentials in a *C. elegans* neuron is likely to receive considerable attention. Having carefully reviewed the data, however, we find that the regenerative events described by Mellem *et al.*² were incorrectly labeled as action potentials and are more accurately described as graded regenerative potentials.

Action potentials are one instance of a broad class of regenerative events. Such events are caused by intrinsic positive feedback as a result of a voltage activated depolarizing current; this current is usually carried by voltage-gated Na⁺ channels, voltage-gated Ca²⁺ channels or both. The other types of regenerative events are graded regenerative potentials, intrinsic oscillations, and plateau potentials. An action potential *per se* has three distinguishing features (Fig. 1A–C). First, its amplitude is invariant with respect to the amplitude, duration, and waveform of the stimulus that evoked it; once triggered it goes to completion. Second, it is intrinsically self-terminating as a result of events set in motion by the action potential upstroke such as activation of hyperpolarizing current and inactivation of depolarizing current. Third, it has a stereotyped waveform which, like amplitude, is invariant with respect to the amplitude, duration, and waveform of the stimulus. Thus, every action potential is a regenerative event, but not every regenerative event is an action potential.

Recording in situ from the motor neuron class RMD, Mellem *et al.*² observed voltage transients in response to current injection in the form of a rising and falling ramp (Fig. 1a, ref. 2), or a 50 ms depolarizing step (Fig. 2a,b and 3a,b,d–f, ref. 2). They report that approximately half of these events were followed by a stable plateau potential (as in Fig. 2, top row). This is the first demonstration of plateau potentials in a *C. elegans* neuron, and it is likely to have important implications for our understanding of information processing in this system. Mellem *et al.*² use the term “action potential” to refer to the initial voltage transient. The authors report that plateau potentials occur spontaneously (Fig. 1e and 3c, ref. 2), but they do not report the observation of spontaneous “action potentials.”

The voltage transients described by Mellem *et al.*² fail to meet the criteria for action potentials in three key respects. First, the amplitude of the transients is strongly dependent on the amplitude and duration of the stimulus (Fig. 2, top row, and 3a, ref. 2). Second, there is no evidence that they are terminated intrinsically, as defined above. On the contrary, the onset of repolarization always coincides with the offset of the step (Fig. 2 and 3a,b,d,e–f, ref. 2) or the falling phase of the ramp (Fig. 1c, ref. 2). Third, the waveform of the transients is not invariant with respect to changes in the stimulus (compare Fig. 1a, 1c, and 2, ref. 2). Thus, the data in Mellem *et al.*² do not constitute the demonstration of action potentials in RMD neurons.

The voltage transients in question appear instead to be graded regenerative potentials. Such potentials, which have been documented previously in nematodes^{3,4}, superficially resemble action potentials but, unlike the latter, their amplitude and waveform are highly sensitive to the size, duration, and waveform of the stimulus. Graded potentials occur in cells in which the regenerative current is too small to drive an initial depolarization to completion each time the current is activated (Fig. 1D–F). The regenerative currents underlying RMD's graded regenerative potentials and plateau potentials are likely to be the same. This relationship can be inferred from the fact that membrane potential relaxes to a plateau potential following large current pulses (>6 pA).

The question of when to use the term “action potential” transcends semantics. Action potentials support coding schemes that utilize firing rate or spike timing whereas graded regenerative potentials do not. Thus, it would be wrong to conclude from the data of Mellem *et al.*² that neuronal signaling in *C. elegans* necessarily involves coding schemes familiar to us from spiking nervous systems. Action potentials may yet be found under different conditions in RMD, or in other classes of *C. elegans* neurons. But until then, the distinction between graded regenerative potentials and action potentials should be kept in mind by theorists and experimentalists interested in both information processing and the molecular basis of neuronal signaling in *C. elegans*.

References

1. White JG, Southgate E, Thomson JN, Brenner S. The structure of the nervous system of the nematode *Caenorhabditis elegans*. *Philos Trans R Soc Lond B Biol Sci.* 1986; 314:1–340. [PubMed: 22462104]
2. Mellem JE, Brockie PJ, Madsen DM, Maricq AV. Action potentials contribute to neuronal signaling in *C. elegans*. *Nat Neurosci.* 2008; 11:865–867. [PubMed: 18587393]
3. Davis RE, Stretton AOW. Signaling properties of *Ascaris* motoneurons: graded active response, graded synaptic transmission, and tonic transmitter release. *Journal of Neuroscience.* 1989; 9:415–425. [PubMed: 2563763]
4. Goodman MB, Hall DH, Avery L, Lockery SR. Active Currents Regulate Sensitivity and Dynamic Range in *C. elegans*. *Neurons Neuron.* 1998; 20:763–772.

Fig. 1.

Simulated action potentials and graded regenerative potentials. A–C. Canonical Hodgkin-Huxley model of the action potential. Upper traces are voltage and lower traces are injected current. The amplitude and waveform of the action potentials are essentially invariant with respect to the amplitude (A), duration (B), and waveform (C) of the stimulus. In A–C, the onset of repolarization is independent of stimulus offset, indicating that the action potential is self-terminating. D–E. Modified Hodgkin-Huxley model illustrating the main features of graded regenerative responses. The modified model uses the same equations as the canonical model, but with the maximum Na^+ and K^+ conductances reduced to produce graded responses instead of action potentials. In the modified model amplitude and waveform are now stimulus dependent, and the onset of repolarization always coincides with stimulus offset, indicating that the events are no longer self-terminating, as in Mellem *et al.*².