Durations of Unitary Synaptic Potentials Help Time a Behavioral Sequence

Abstract. *Recordings in identified neurons and muscles that mediate crayfish tailflips reveal inhibitory postsynaptic potentials of two distinct durations. Those of long duration are recorded in five classes of cells in the flexion circuit, while those of short duration are recorded in three classes of cells in the extension circuit. The durations of the inhibitory postsynaptic potentials are matched to the durations of inhibition required by the different phases of the behavior.*

Attempts to account for behavior in terms of cellular properties of the nervous system invariably rely on properties that emerge when neurons interact in large networks. However, it is sometimes possible, especially in simpler nervous systems, to relate basic cellular processes to behavior in a surprisingly direct way. Recent examples are explanations of habituation in terms of homosynaptic depression of central synapses (*1, 2*) and triggered behaviors or fixed action patterns in terms of thresholds of central "command" neurons (*2–4*). We now show that the sequential timing of events in a rapid behavioral sequence can be partly explained by the durations of unitary, inhibitory postsynaptic potentials (IPSP's).

Recent advances in our understanding of neural circuits mediating crayfish escape behavior facilitated our experiments. Crayfish escape by rapid abdominal flexions and extensions (tailflips) (Fig. 1A). A tailflip initiated by tapping the abdomen is mediated by a neural circuit consisting of a pair of large command interneurons called the lateral giants and associated afferent and efferent pathways (Fig. 1B) (*5*). Elements at every stage of the flexion circuit have been described and the connections among them characterized (*2, 3, 6–9*). The extension circuit is less well understood, but the extensor motoneurons have been mapped (*10*) and several sources of excitation to them have been identified (*11*). In the escape circuit, sensory input converges onto both the command cells and the extensor motoneurons. If the threshold of the command cell is exceeded, it fires and a tailflip follows. Flexion is produced directly via monosynaptic connections between the command cells and flexor motoneurons, but reextension requires sensory feedback (*11*).

Execution of this rapid behavioral sequence poses problems of coordination. First, the violent movement stimulates the same receptors that trigger escape, so that a positive feedback loop may exist. Second, accurate timing of reextension is required, so that extension will begin just after flexion and not interfere with it. Coordination is achieved in part by an elaborate inhibitory circuit, which is triggered by a command cell impulse and acts on elements at every stage of the escape circuit (Fig. 1B, bold lines) (*11–19*). Although command-derived inhibition is global, it is temporally patterned. It can help coordinate the response because it begins and ends at the right time. A previous report dealt with the problem of how the onset of inhibition is appropriately timed (*16*). We now consider how the proper duration of inhibition is achieved.

We first quantified the timing of the escape sequence by measuring the durations of flexion and extension phases with high-speed cinematography (*20*) (Fig. 1A). For 14 responses in three animals (Fig. 1C), the durations were 47 ± 10 msec for flexion and 60 ± 18 msec for extension (means and standard deviations). In all cases but one, extension immediately followed flexion. The time taken for complete flexion belies the rapidity of the response, since the major portion of flexion is complete within 30 msec (Fig. 1A).

How does the nervous system use inhibition to help coordinate the flexion-extension cycle? Inhibition begins in many flexor and extensor neurons within a few milliseconds of the command cell impulse (*11–15*). After an initial burst of activity the flexion circuit must be silenced for the remainder of the response (about 110 msec), while the extensors must be ready to fire at the end of the flexion phase (as brief as 30 msec). Therefore, one might expect inhibition to be brief in extensor neurons and muscles and long in flexor neurons and muscles (*21*).

The duration of inhibition in flexor and extensor motoneurons was compared by recording (*22*) IPSP's in the largest of the flexor motoneurons (the motor giants) (*6, 7, 15*) and in the extensor motoneurons (*11*). A command cell impulse indirectly produces an IPSP in both cell groups after a brief (2 to 3 msec) delay. A unitary component of the IPSP in the giant flexor motoneuron can be produced directly by selective stimulation of an identified interneuron (motor giant inhibitor, MoGI-1) which monosynaptically inhibits the giant flexor motoneuron (Fig. 1B; synapse d) (*15*). Such unitary IPSP's were measured in 19 motor giants in 17 animals. The mean duration, measured from onset until the potential declined to one half of its peak amplitude, was 48.1 ± 14.5 msec; the mean full duration (which is less accurate and was measured in only eight experiments) was 131.8 ± 40.8 msec (Fig. 2A and Table 1). It is important to stress that the long duration of the IPSP in the motor giant is a consequence of a prolonged conductance increase, as was first shown by

Table 1. Durations of IPSP's in neurons and muscle fibers that participate in crayfish escape behavior.

Inhibited cell	Mean duration to half-amplitude (msec)	Mean total duration (msec)	Type of measure	*N*	Inhibitor identified	Reference
		Flexion circuit				
a. Tactile afferents	33	50	Voltage	1	No	(*12*)
b. Sensory interneurons	27	50	Voltage	6	No	(*13*)
c. Lateral giant	30	70	Conductance	1	No	(*14*)
d. Motor giant	48	>100	Voltage	18	Yes	(*15*)*
Motor giant	30		Conductance	1	Yes	
e. Flexor muscle fibers	38	>70	Conductance	7	Yes	(*16*), (*26*)
		Extension circuit				
f. Muscle receptors	12	30	Voltage	3	Yes	(*17*)
g. Extensor motoneurons	13	20	Voltage	18	No	(*11*)*
h. Extensor muscle fibers	20	40	Voltage	3	Yes	(*18*), (*27*)

*Also measured in this report.

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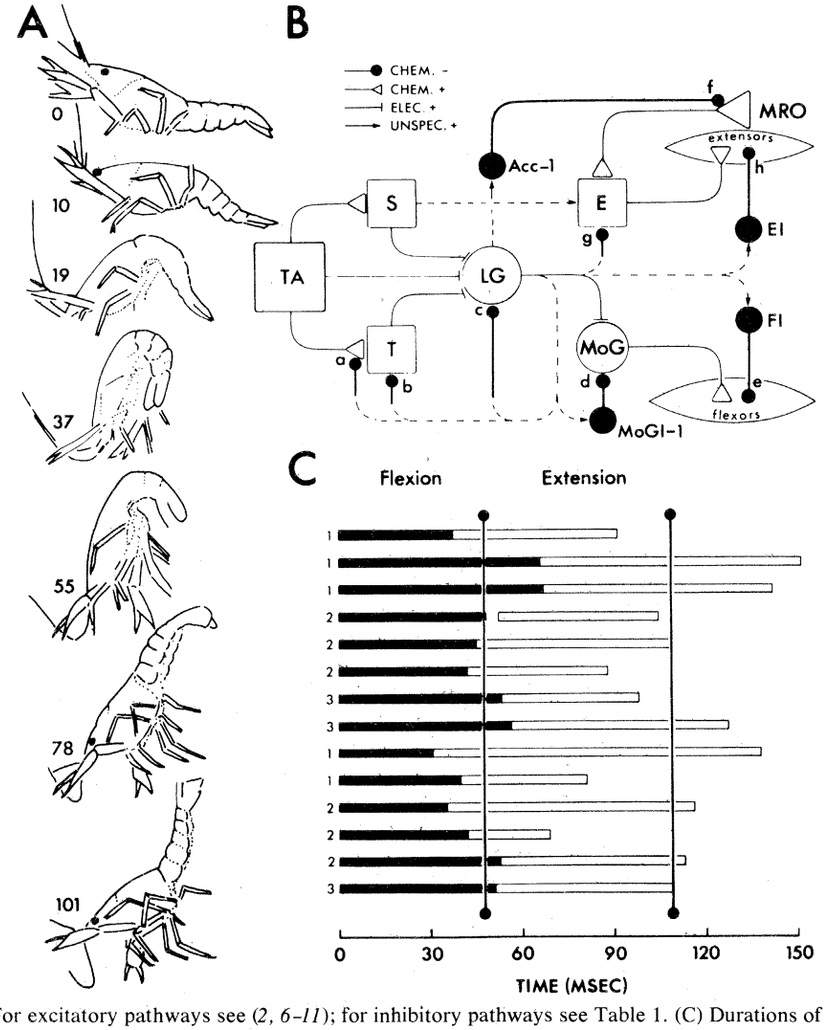
Hagiwara (*23*). The motor giant's time constant is only 3 msec (*8*) and so contributes little to the response duration.

Inhibitory interneurons responsible for IPSP's in extensor motoneurons are unidentified, so IPSP's were produced indirectly by stimulating the command cells (Fig. 1B, synapse g). Even though such IPSP's may be compound, they were less than one-third as long as the IPSP's in the flexor motoneuron. The mean duration to half-amplitude of IPSP's in extensor motoneurons was 13.5 ± 3.5 msec; the mean full duration was 25.4 ± 6.1 msec (18 cells in 15 crayfish, Fig. 2B).

The IPSP durations for four other neurons within the escape circuit and for flexor and extensor muscle fibers are available from prior reports (*12–14, 16–18*). The durations of all eight IPSP's are compared in Table 1, which shows that IPSP's in flexion elements are long-lasting, while IPSP's in extension elements are brief.

For those four neurons where the presynaptic inhibitory neuron is identified, the durations of the IPSP's are intrinsic to the synapses, and are not due to different durations of impulse trains in presynaptic elements (Fig. 1B, synapses d, e, f, and h) (*15–18*). For the remaining four neurons (Fig. 1B, synapses a, b, c, and g) the IPSP's may be compound, but even if they are, their unitary components are probably still of the appropriate duration. For example, the time courses of primary afferent depolarization (*12*) and of postsynaptic inhibition in sensory interneurons (*13*) resemble summed, unitary postsynaptic potentials (PSP's) that arrive nearly synchronously. Neither of these PSP's show the plateau that would be expected if trains of PSP's of short duration were determining the duration of inhibition.

We have shown (Table 1) that short IPSP's (20 to 40 msec) occur in extensor elements (muscles, motoneurons, and proprioceptors that excite the extensor motoneurons). The short duration frees the extension circuit for excitation following flexion. Long IPSP's (50 to >100 msec) occur in flexor elements just after they are excited and keep them inhibited throughout the remainder of the tailflip. The duration of inhibition can be lengthened by repetitive activity of inhibitory interneurons; in fact, repetitive activity has been noted for three of the four identified inhibitory neurons (*16, 19*). Nevertheless, the durations of unitary IPSP's, which determine the minimum inhibitory



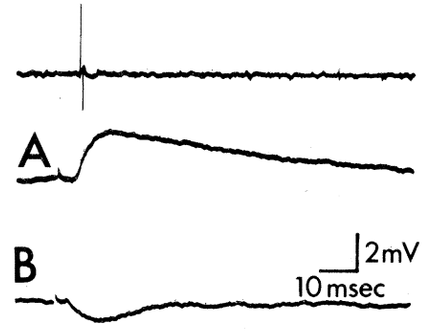


Fig. 1 (left). (A) A flexion-extension cycle initiated by a tap to the abdomen. Tracings from 16-mm film taken at 250 frames per second; numbers indicate elapsed time, in milliseconds, from first movement. (B) Simplified diagram of the lateral giant escape circuit with emphasis on command-derived inhibition. Tactile afferents (*TA*) converge onto transient (*T*) and sustained (*S*) sensory interneurons which in turn synapse on the command cell (lateral giant, *LG*). The command cell produces flexion via direct connections with flexor motoneurons, the largest of which is the motor giant (*MoG*). Extension follows within 30 to 50 msec. The triggering mechanism for extension is unknown, but sources of excitation to the extensor motoneurons (*E*) include the muscle receptor organs (*MRO*'s) and sensory interneurons. Eight separate inhibitory synapses are known (solid circles, labeled a to h); all are activated in an isolated nerve cord by a lateral giant impulse. Four identified inhibitory neurons are labeled *Acc-1* (accessory 1), *EI* (extensor inhibitor), *FI* (flexor inhibitor), and *MoGI-1* (motor giant inhibitor), while four pathways containing unidentified inhibitory interneurons are indicated by dashed lines. For excitatory pathways see (*2, 6–11*); for inhibitory pathways see Table 1. (C) Durations of flexion (solid bars) and extension phases of escape responses. The mean durations of the flexion phase and total response are indicated by the vertical lines. Numbers in front of each bar identify the animal. The first eight responses were elicited by tapping the abdomen and were mediated by the lateral giant command cells, the last six sequences were elicited by tapping the head and were mediated by the medial giant axons, which are command cells that activate many of the same inhibitory cells as the lateral giants. Fig. 2 (right). Examples of IPSP's of short and long duration. (A) An IPSP in the largest flexor motoneuron (*MoG* in Fig. 1B) produced by stimulating an interneuron (*MoGI-1* in Fig. 1B) whose impulse is shown on the top trace. This is typical of IPSP's seen at synapse d in Fig. 1B. For details see (*15*). The IPSP is depolarizing because the resting potential of the motoneuron is more negative than the equilibrium potential for the IPSP, which is mainly or exclusively because of an increase in chloride conductance (*7*). (B) An IPSP in an extensor motoneuron following an *LG* impulse (not shown). This is typical of IPSP's seen at synapse g in Fig. 1B. For details see (*11*).

intervals, are matched to the functions they perform.

The synaptic mechanisms that determine the durations of the IPSP's in the crayfish are unknown. However, γ-aminobutyric acid (GABA) is the putative transmitter at two synapses with PSP's of long duration [those onto the motor giant (*6, 7*) and onto the flexor muscles (*24*)] and at two synapses with PSP's of short duration [those onto the muscle receptor organ (*25*) and onto the extensor muscles (*24*)]. Since these synapses are accessible, it should be possible to distinguish among explanations based on different durations of transmitter release, transmitter inactivation, or postsynaptic response.

The behavioral significance of PSP durations shown here calls attention to the importance of PSP durations in neural information processing and should encourage investigations of the mechanisms that determine the time courses of synaptic events.

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20. Photography at 250 frames per second was accomplished with a Hycam 16 mm camera (Redlake Laboratories) and Kodak Ektachrome EFB 449. Film was viewed with a stop-frame projector; durations were measured from the first detectable movement.
21. An interesting but, at first sight, confusing feature of the escape response is that most of the flexor elements are silent during the actual flexion movement. This is because the flexor motor discharge is abrupt, ending within about 10 msec of stimulation, while delays caused by excitation-contraction coupling and by inertia retard the onset of movement. Hence peak velocity of flexion may occur roughly 20 msec after stimulation, at a time when all of the neural elements that triggered the flexion are being inhibited.
22. For details of electrophysiological recordings see (*6, 7, 11, 15, 16*). Briefly, 3*M* KCl or potassium acetate electrodes were placed in cell bodies or muscle fibers; ganglia were desheathed and the preparations superfused with oxygenated crayfish saline at 14° to 18°C.
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Pitch Memory: An Advantage for the Left-handed

Abstract. *In an auditory or musical memory task, subjects made pitch recognition judgments when the tones to be compared were separated by a sequence of interpolated tones. The left-handed subjects performed significantly better than the right-handed and also had a significantly higher variance. Further analysis showed that the superior performance was attributable largely to the left-handed subjects with mixed hand preference.*

People who are left-handed differ as a group from those who are right-handed and display more heterogeneity, in terms of both direction and degree of cerebral dominance. (i) In the overwhelming majority of the right-handed population, speech is represented in the left cerebral hemisphere; however, in about two-thirds of the left-handed population, speech is represented in the left hemisphere and in about one-third, in the right. (ii) Although the right-handed tend to show a clear-cut dominance of the left hemisphere for speech, a considerable proportion of the left-handed have some speech representation in both cerebral hemispheres (*1*).

Interest has developed in the possibility that such neurological differences might be reflected in differences in various abilities. Thus, some investigators have argued for a relationship between left-handedness or mixed hand preferences and reading disability (*2*). Others have presented evidence that left-handed persons or those with mixed hand preference perform more poorly than right-handed persons on visuospatial tasks (*3*). In contrast, I now report what is, to my knowledge, the first evidence for an association between left-handedness and superior auditory or musical processing ability. The research was prompted by the observation that among subjects selected for high performance on a pitch memory task, an unexpectedly high proportion were left-handed. I therefore planned an experiment to determine whether the two populations differ statistically in terms of their ability to make pitch memory judgments.

Table 1. Performance levels of all four handedness populations on the pitch memory task. Each subgroup was compared with the moderately left-handed subgroup by means of a median test.

Group	*N*	Average error (%)	χ^2
Right-handed			
Strongly	52	36.9	10.02*
Moderately	24	41.0	9.65*
Total	76	38.1	
Left-handed			
Moderately	23	29.0	
Strongly	30	35.3	4.45†
Total	53	32.5	

*$P < .01$. †$P < .05$.

A test tone was presented and followed by a sequence of six interpolated tones and then by a second test tone. The test tones were either identical in pitch or differed by a semitone. The subjects indicated on paper whether the test tones were the same or different. All tones were 200 msec in duration and separated by 300-msec pauses, except that a 2-second pause intervened between the last interpolated tone and the second test tone. The tones were sine waves with frequencies taken from an equal-tempered chromatic scale (International Pitch; A = 435 hertz) ranging over an octave from middle C (259 hertz) to the B above (488 hertz). The interpolated tones were chosen at random from this range, except that no interpolated sequence contained repeated tones or tones that were identical in pitch to either of the test tones. Twenty-four sequences were presented in two groups of 12, with 10-second pauses between sequences within a group and 2-minute pauses between the groups. Before the experimental session began, the procedure was explained

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