allometrically plus secondary cycles that reflect external factors (*25*). For humans, life-span is unusually long relative to body size and is correlated with large brain size (*14*). Calculations based on the "encephalization quotient" for *Homo sapiens* (*26*) indicate that a human-sized brain is appropriate for an animal weighing 804 kg, from which we predict a period for population oscillations of 46 ± 15 years (*19*); this is approximately the period length of stable limit cycles predicted by models of human demography in 20th-century America (*27*).

Slobodkin (*7*) speculated 20 years ago that "population stability has some relatively simple relation to the physiological properties of the particular species." Allometric analysis of life history parameters and population processes should prove to be a unifying influence.

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22 December 1983; 16 April 1984

Competition Controls the Growth of an Identified Axonal Arborization

Abstract. *The shape of the axonal arborization was studied in an identified insect sensory neuron. The distribution of presynaptic varicosities within an axonal arbor was shown to be modulated by the density of neighboring terminals. Removal of neighbors near one portion of the axon terminal increased the growth rate in the denervated region and caused a compensatory retraction in other regions. The results support the hypothesis that the size of an axonal arbor is determined intrinsically, whereas the distribution of varicosities within the terminal is determined extrinsically by neighboring terminals. These findings provide a direct demonstration of the effects of competition on an identified nerve cell, as well as one of the first examples of competitive interactions in an invertebrate central nervous system.*

Flexibility is a common feature of developing neuronal connections. In many parts of the nervous system, much of this flexibility is determined by the presynaptic terminal arborizations of the afferents (*1*). One commonly reported observation (*2*) is that neighboring terminal arborizations interact with one another in a manner that restrains their growth. Removal of neighboring terminals can release a cell from this restraint, allowing the arbor to expand or invade the neighbors' vacated territory. This restraint is usually called competition (*2, 3*). Most of the evidence for this phenomenon is indirect in the sense that the behavior of single terminals is inferred from the behavior of large populations (*1, 4*). We now demonstrate the effects of such competition directly by showing its role in determining the shape of the axonal arborization of an identified insect sensory neuron. The results show how competition differentially controls the growth rates along various regions of a single arbor, and they provide direct support for theories of the control of terminal growth (*2, 4*).

In insect sensory systems, the axonal arborizations of some identified sensory neurons can be stained by a simple method (*5*). Many insect sensory neurons are associated with external hairlike struc-

Table 1. Number of varicosities (*9*) (mean ± standard deviation) in region R (ipsilateral to the soma) and in region L (contralateral to the soma). Juveniles were in the third instar.

Group	Number	Number of varicosities		
		In region R	In region L	Total
Control	10	222 ± 57	150 ± 53	373 ± 73
Experimental	10	52 ± 20*	269 ± 36*	321 ± 51†
Juvenile	11	131 ± 35‡	91 ± 23‡	225 ± 35‡

*Difference from control values, $P \leq 0.01$, determined by *t*-test. †Not significant (*10*). ‡Difference from experimental values $P \leq 0.01$ determined by *t*-test.

tures. These hairs are often individually identifiable, and thus the neuron whose soma is located at the base of each hair and whose dendrite inserts into the hair is also identifiable by the usual definition (*6–8*). The entire sensory neuron, cell body, axon, and axonal arborization can be labeled by cutting the associated hair, which is hollow, and placing a pipette filled with cobalt chloride (100 m*M*) over the cut hair. This bathes the dendrite in stain, and the sensory neuron takes up the stain. The hair and neuron we are concerned with are located on the medial aspect of the abdominal sensory appendage (cercus) of the cricket *Acheta domesticus*. The hair is identifiable by its location (letter X in Fig. 1) within an array of previously identified club-shaped hairs (indicated by numbers in Fig. 1) [see also (*6*)]. This hair and its associated neuron can be found on each cercus of every specimen. The neuron associated with the hair projects an axon from its soma, located just below the hair, through the large ipsilateral cercal nerve to the last abdominal ganglion. After entering the ganglion, this neuron's axon crosses the midline—hence the name neuron X—and arborizes in bilaterally homologous regions of the ganglion (Fig. 2, A and E). Three such neurons have been identified; all are associated with hairs on the medial aspect of the cercus (X, X′, and X″ in Fig. 2E), and we estimate that there are between 20 and 50 such receptors located in a narrow strip on the medial aspect of the cercus. The neurons associated with the remaining wind-sensitive receptors, approximately 1000 of them, do not cross the midline and have arbors restricted to one side of the midline (*7*).

The bilateral structure of neuron X is the key to analysis of its growth. When the left cercus was removed during a juvenile stage and neuron X on the remaining cercus was examined in the adult, its bilateral terminal arborization was distorted. In control neurons 40 percent of the varicosities (*9*) are located to the left of the midline (in region L of Fig. 2A), whereas in experimental neurons 84 percent of the varicosities are located to the left of the midline (in region L of Fig. 2B) (Table 1).

The shift in distribution of varicosities within the neuron X arbor is the result of two changes. First, the arbor adds varicosities at an abnormally rapid rate on the same side as the amputation (in region L of Fig. 2, A and B). This was shown by examining the juvenile arborization at the time of the amputation. Neuron X in the juvenile is very similar to the adult neuron X in shape (Fig. 2C), but it contains only about 60 percent of the number of varicosities found in the normal adult (Table 1). At the time of amputation there were 91 ± 23 (mean ± standard deviation) varicosities to the left of the midline, and under normal conditions this grows to 150 ± 53 in the adult. In experimental specimens this number increased to 269 ± 36 (region L in Table 1). This means the arbor grows faster than normal in region L (Fig. 2, A and B). We do not yet know whether this is due to a brief spurt in varicosity formation just after amputation or a gradual shift.

Second, there is a compensatory decrease in the number of varicosities on the side opposite the amputation (region R of Fig. 2, A and B). In the juvenile, the number of varicosities in region R is 131 ± 35, and normally this would increase to 222 ± 57. In the experimental group, this number decreased to 52 ± 20 (Table 1). Therefore, as a result of amputation of one cercus, sensory neuron X retracted parts of its arbor from region R.

The total number of varicosities in these experimental specimens is not significantly different from that in controls (Table 1). This suggests that total arbor size is constant and an intrinsic property of the cell (*4, 10*).

In order to understand these phenomena, it is necessary to understand the changes produced by the surgery in regions R and L. Amputation of a cercus severs the axon and removes the somata of all wind-sensitive sensory neurons on that cercus. The central stump of the axon and the axonal arborization begin to degenerate within 6 hours and are completely gone within a week (*11*). Thus removal of the left cercus would destroy most of the afferent synapses in region L (Fig. 2A). In addition, a small number of the sensory neurons on the left cercus project bilaterally (the homologs of neurons X, X′, and X″) and synapse in region R. Consequently, there would be a small amount of degeneration in this region. To calculate the relative deafferentation on the two sides of the midline, we estimated that 300 (of the 1000) wind-sensitive neurons on the left cercus project to region L. Each is assumed to have 220 varicosities in region L (*12*) (Table 1); 50 of these neurons also cross the midline and have 150 varicosities each in region R (Table 1). Simple calculation shows that amputation of the left cercus would destroy approximately 90 percent of the afferent varicosities in region L and 10 percent of those in region R. Therefore, neuron X would lose many more of its neighboring varicosities in region L than it would in region R.

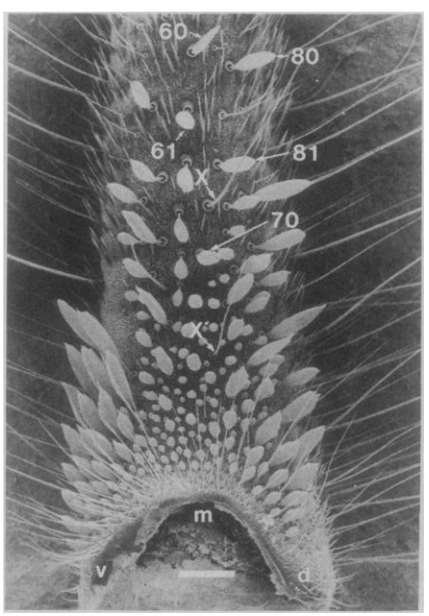

Fig. 1. Identified receptors on the cricket cercus. The scanning electron micrograph shows the medial aspect of a left cercus. Only the basal 2.25 mm of the cercus is shown. Wind-sensitive receptors X and X′ are indicated, as are numerous previously identified clavate receptors, by numbers [see (*6*)]. Abbreviations: *v*, ventral; *m*, medial; *d*, dorsal; proximal is at the bottom. Scale bar, 200 μm.

Since the experimental neuron X adds varicosities in region L and retracts them from region R, apparently it is able to detect the relative number of neighbors locally and shift its resources to the location containing the fewest neighbors. These changes in growth of the axonal arbor of neuron X fit the concept of competition as it is presently defined (*2, 3*). This result is one of the first pieces of evidence for competitive interactions in an invertebrate nervous system. Earlier investigations of the insect central nervous system did not reveal competitive interactions (*8, 12*). However, a phenomenon similar to the one we observed was detected in the central nervous system of the leech. Individual sensory cells in the leech expand their receptive fields when neighboring cells are destroyed (*13*). Although no synaptic interactions are involved in the leech, the phenomenon parallels our results very closely. This combination of experiments on leeches and crickets suggests that competitive interactions are more widespread in invertebrates than had previously been supposed.

The cue for the shift in distribution of varicosities in the neuron X terminal might be available synaptic space on the target neurons (*14*). Data on the anatomy of the postsynaptic cells under these

experimental conditions (*15, 16*) can be used to assess the effect of synaptic space. For example, the growth of the dendrites of the medial giant interneuron (MGI) is stunted in these experiments; the large medial dendrite, which is embraced by the neuron X arbor (Fig. 2E), is 70 percent as long as normal and has roughly 49 percent of its normal surface area (*15, 16*). Thus, although the growth of neuron X is faster than normal in region L, the growth of its targets is slower than normal. In spite of this apparent inconsistency, it is possible that synaptic space is a cue for the growth of neuron X. Since surgery destroys approximately 90 percent of the terminals in the region, but the target neurons shrink by only 49 percent, there is still considerable room for expansion.

However, the cue for rapid growth cannot simply be available synaptic space because some regions of the target area that were deafferented were never invaded by neuron X. For example, the large lateral dendrite of MGI was massively deafferented, but neuron X did not shift varicosities into that region of the neuropil. This restriction of the experimental terminal to its normal target area suggests that competition can shape arbors only within a predetermined target region. As has been discussed in detail elsewhere (*6, 12, 17*) these cricket sensory neurons are thought to obtain information that is correlated with their peripheral position, and it is this information which determines their initial pattern of growth and guides them to their target region. This positional information (*6, 12*) or chemoaffinity (*18*) apparently constrains the growth of the terminal to a local region, and competitive interactions work within this constraint.

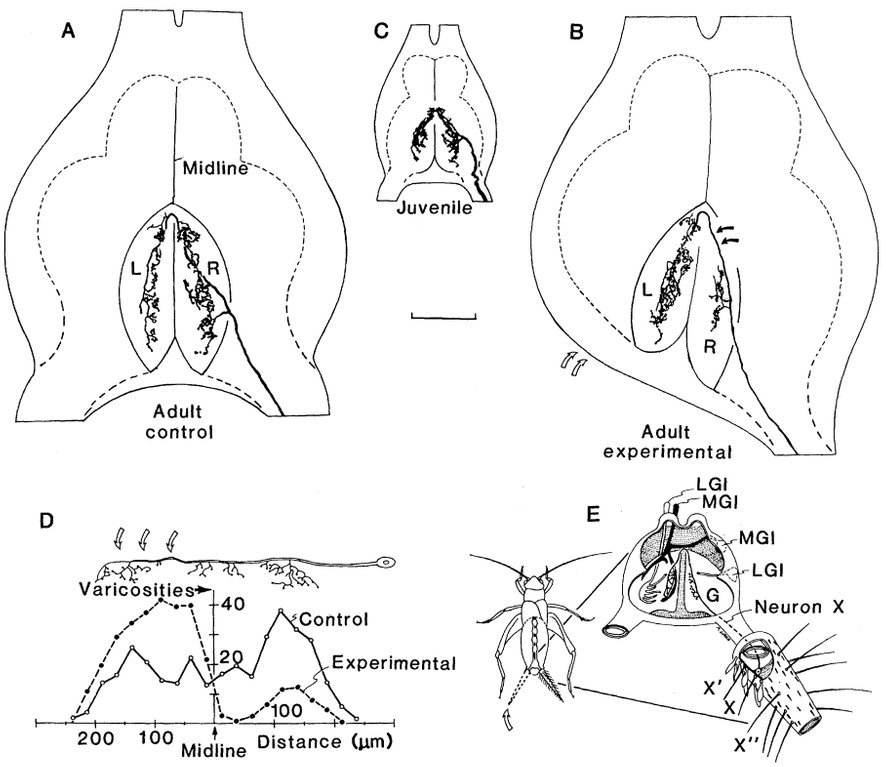

Fig. 2. Growth of the terminal arborization of neuron X. (A) The terminal arborization of neuron X in an untreated adult. Dashed lines indicate the boundary between the neuropil and the cell bodies. Regions labeled L and R indicate the neuropil occupied by neuron X and its immediate neighbors. These regions are outlined for purposes of exposition and do not represent physically obvious boundaries. (B) The terminal arborization of neuron X in a specimen that had the left cercus removed in the third instar. The ganglion is asymmetric, and there is no cercal nerve (open arrows). Solid arrows indicate a region where all varicosities have been retracted. The area indicated by the solid arrows makes the difference between this specimen and the one in (A) qualitatively obvious, but this complete loss does not happen in every specimen as the quantitative data of part D indicate. (C) The terminal arbor of neuron X obtained from a juvenile that had reached the third instar of postembryonic development. This is the stage of development at which the left cercus would be removed to begin the experiment. Calibration bar for (A), (B), and (C), 100 μm. (D) Quantitative analysis of the differences between the experimental and control arborizations. The bend in the neuron X axon has been straightened and the midline is taken as a reference point. Distance from the midline is plotted on the abscissa. The average number of varicosities located in 25-μm-wide strips, arranged perpendicular to the axon, was plotted on the ordinate. Each point is the average number of varicosities in that bin for ten specimens. The experimental terminal is quite asymmetric; it has more varicosities than normal at every point along the arbor ipsilateral to the amputated cercus (open arrows) and fewer than normal at every point contralateral to the amputated cercus. (E) An artist's summary of those aspects of the cercal sensory system discussed in the text. The right neuron X is shown with the left cercus removed (open arrow). The white area on each side of the midline, the cercal glomerulus (G), is the region of termination of all the wind-sensitive sensory neurons. In the experimental specimen, the left glomerulus is deafferented. The two largest interneurons in the abdominal nervous system, the MGI and LGI, are shown in their respective locations relative to the neuron X terminal. The effects of the removal of the left cercus on these interneurons were studied anatomically and physiologically in previous publications (*15, 16*) and are discussed in the context of the present results.

These anatomical results have clear functional implications. Repeated removal of one cercus, starting early in life, enhances the responses of some interneurons to the remaining cercal sensory input (*16, 19*). For example, the MGI was more effectively driven by a standard stimulus in a treated animal than in a control animal (*16*). This increased excitation is consistent with the present anatomical results. In the region where sensory neuron X expands, we would expect it to make more contacts with the MGI and thus increase the responsiveness of the MGI to cercal stimulation (*16*). In the region where neuron X retracts, the bilaterally homologous MGI (not shown) would be likely to lose synaptic input and thus exhibit reduced responsiveness to the remaining cercus; this has not been tested. In contrast to the MGI, the lateral giant interneuron (LGI), shown in Fig. 2E, exhibited no change in excitatory synaptic input from the remaining cercus (*16*). This finding is consistent with the fact that neuron X does not normally contact the dendrites of LGI, nor does it do so in experimental specimens. This provides physiological support for the idea that neuron X does not sprout into foreign territory. Rigorous demonstration that our anatomical observations are causally related to altered monosynaptic connections will require a study of unitary synaptic events at this synapse (*7*).

These results allow us to begin to formulate the rules governing the growth of axonal arborizations. First, neuron X seems to have an intrinsic tendency to arborize in a restricted part of the central nervous system. This tendency is determined by positional cues the neuron obtains in the periphery at the time of its birth, as discussed in detail elsewhere (*12, 17*). This aspect of a neuron's phenotype is stable and is not influenced by

extrinsic cues. Second, the size of the axonal arbor (the total number of varicosities) appears to be an intrinsic property of the differentiated neuron. This feature of the neuron is also relatively immune to external cues. Finally, the distribution of varicosities within an axonal arbor is subject to modulation by neighboring terminals (*2, 4*). Thus, competition works within constraints set by intrinsic properties of the neuron.

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25 November 1983; accepted 23 March 1984

Is There an Evoked Vascular Response?

Abstract. *Event-related potentials of the brain are enhanced when stimulation is synchronized with diastolic phases of cerebral or cephalic pulse pressure waves. A cerebral vascular event has been found to be temporally consistent with the event-related potential. Averaged evoked vascular responses were measured with bioimpedance techniques from the brain and the arm. Changes in brain blood volume occurred 150 to 250 milliseconds after stimulation synchronized with diastolic but not systolic phases of the cerebral pulse pressure wave. The time course of this phenomenon defies the usually accepted characteristics of metabolic activity. The evoked vascular response may be a neurally mediated event in anticipation of altered metabolic demand, and it offers the possibility of measurement in real time.*

A major problem in assessing cerebral metabolism during mental processing is temporal resolution of measurement. The 2-deoxy-D-glucose autoradiographic techniques in animals (*1*) and the positron emission tomographic approach in human subjects (*2*) provide promising tools for localization; the temporal resolution of these procedures, however, is 30 to 40 minutes, which is unsuitable for assessing event-related mental activity. An invasive method has recently been described for measuring local cerebral blood flow in animals with a temporal resolution of 30 to 40 seconds (*3*). We now report a noninvasive method for measuring transient responses of the cerebral vasculature in the range of milliseconds in conscious human subjects. The method permits the assessment of neurogenic hemodynamics reflecting mental activity in real time.

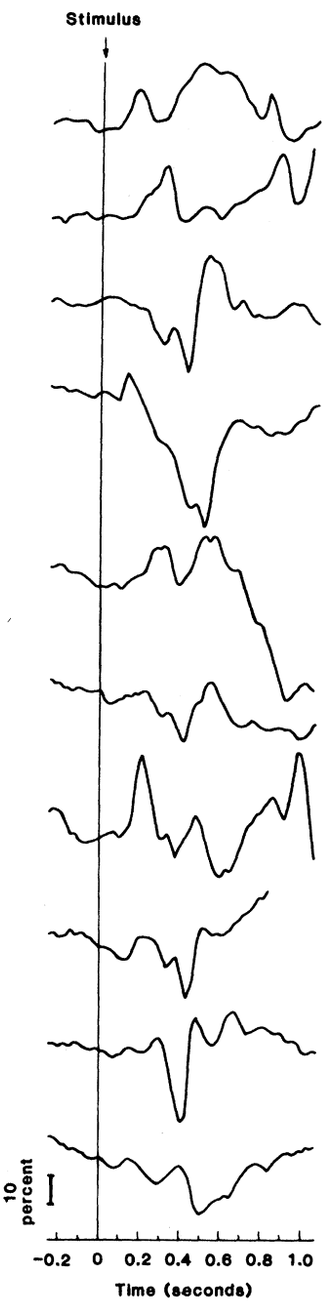

Fig. 1. Individual difference waves. Each wave is the result of subtracting 40 diastole-stimulated wave forms (250 msec prestimulus and 1250 msec poststimulus) from 40 nonstimulated wave forms. Each subject's record shows a stimulus-induced volumetric change occurring between 200 and 400 msec. Most wave forms reflect transient changes in volume without changes in flow, since impedance signals tend to return to baseline within the short sampling period. Even though the cardiac period varied considerably among the subjects, the temporal characteristics of the waves were consistent. The 10 percent change shown refers to the percentage change from the nonstimulated wave form.

Electrophysiological procedures, such as event-related potentials (ERP's) of the brain, are reliable temporal measures of neural function (*4*). Such ERP's measure obligatory "reflexes" of the brain linked to physical stimuli as well as endogenous responses, such as stimulus evaluation and decision time (*5*). Cardiovascular phase influences evoked responses of the brain (*6*). Stimulation synchronized with the diastolic phase derived from the carotid or ophthalmic artery augments the ERP; conversely, stimulation during the systolic phase attenuates the ERP.

These and other influences on sensory threshold (*7*) have been proposed to result from the influence of baroreceptors on higher centers of the brain (*8*). However, irrespective of cardiovascular phase, brief auditory stimuli also evoke