*PRIMITIVE NERVOUS SYSTEMS**

By L. M. Passano

DEPARTMENT OF BIOLOGY, YALE UNIVERSITY

Communicated by G. E. Hutchinson, June 17, 1963

For nearly fifty years the dominant and accepted theory of the evolution of the nervous system has been that of G. H. Parker, developed over the course of the decade from 1909 to 1919 and summarized in his now classic book *The Elementary Nervous System.*[1] Like many successful theories, it was an oversimplification of contemporary knowledge presented in a forceful and stimulating manner. In essence, Parker viewed the initial evolution of the nervous system as involving three successive phylogenetic stages. At first there were only "independent effectors," represented today (in Parker's view) by sponge myocytes or coelenterate nematocysts. Secondly, receptor cells evolved from undifferentiated epithelium adjacent to the muscle cells. "The most primitive nerve cell from the standpoint of animal phylogeny is the sense-cell, or receptive cell, such as occurs in the sensory epithelium of the coelenterates."[1] Finally, "protoneurons" evolved between receptor and effector to give rise eventually to the reflex triad of receptor, adjustor, and effector.

Parker's was not the first theory to be expounded. A generation before him Kleinenberg[2] had used his discovery of the "neuromuscular cell" of *Hydra* to support the theory that the reflex triad originated from the division, in evolution, of what had once been a single cell. But the Hertwigs[2] identified the "neuromuscular cell" as an epitheliomuscular cell, and, invoking the biogenetic law, suggested instead a simultaneous evolution of nerve and muscle cells from separate epithelial cells, as they are formed in coelenterate development. Until Parker's theory was advanced, the Hertwigs' theory was the one generally accepted; it was rapidly replaced, however, by the strength of Parker's concept of the independent effector stage, exemplified by the sponges.

Since a great deal of what is known about nervous systems has been learned since the publication of Parker's book, in addition to a modest revival of interest in the nervous system of coelenterates, led by Pantin, it is noteworthy that the independent effector theory continues to be generally accepted. Neurophysiologists such as Bishop[3] and Grundfest[4] have emphasized that graded responses unknown in Parker's day certainly antedate the all-or-none action potential of the nerve cell axon, while the terminal secretory activity of the synaptic transmitter would also be expected to have evolved as a separate step. But neither question the fundamental sequence in Parker's theory that the independent effector evolved first and that then, in the next "brief and logical step,"[3] a special sensory cell evolved to depolarize the adjacent contractile unit at the "first synapse."[3]

Pantin, whose approach has been that of the coelenterate biologist rather than that of the neurophysiologist, has been more critical[5] of Parker's theory. Rather than being concerned with the evolution of certain physiological processes, he has considered the entire biology of the postulated ancestral forms, for "the metazoan behaviour machine from its origin. . .must have involved the structure of the whole animal, and it must have been complex enough and organized enough to meet all the varied requirements of behaviour."[5] Just as in coelenterates today, the effector of the prenervous animal was not a single cell acting individually, but an entire muscle sheet. Innervation of a single muscle cell by a receptor cell could not initiate any meaningful response without conduction to all units of a response field.

As Sherrington long ago pointed out,[6] a single protoneuron "conductor" cannot function as the "common path" necessary for nervous system integration. Inputs of many receptors must merge on common "coordinators" before integration is achieved.[7] *Integration is as fundamental as conduction to any nervous system.* An organism at the phylogenetic stage showing isolated Parkerian triads, neither integrating nor conducting to more than a single effector, would have no advantage over a previous stage without such triads, and thus is evolutionally implausible.

There are, moreover, further objections to Parker's theory than solely the inadequacy of isolated triads of receptor cells, protoneurons, and effector cells. The importance of inherent rhythmic behavior is becoming ever more apparent,[8] in part because of the investigations of actinian behavior carried out by Batham and Pantin.[9] As a result of these findings, as well as the realization that metazoan behavior is not organized cellularly, but with tissues such as muscle sheets as its units, Pantin has suggested such important modifications of Parker's theory that his views should be considered a new hypothesis. He suggests[5] that the nerve-net has originated as a supplement to a conducting and integrating muscle sheet. The nerve-net's initial function was to permit the development of specialized through-conduction tracts, allowing the evolution of such reflexes as the *Calliactis* sphincter closure. Spontaneous activity, either in the effectors (the muscle sheet) or in the "conducting nervous system itself,"[5] can supplement direct reflexes. Thus, Pantin sees the nervous system evolving (without specifying in detail from whence it came) in an integrated organism with a well-developed muscle sheet effector system. Sensory stimuli would affect this "system of independent effectors."[5] Pantin's hypothesis is a distinct improvement on Parker's, as it provides for endogenous activity within the primitive nervous system as well as meeting the other objections discussed above.

Both Parker[1] and Pantin[5] agree that it is inconceivable that any nervous system could evolve prior to the evolution of muscles or other effectors (cilia, gland cells, etc.). Admitting this, it does not necessarily follow that these primitive metazoans had to have receptors before they could evolve conductors, or, as the protoneurons of Parker were called by the Hertwigs, "ganglion cells." As soon as the possibility is admitted that neuronal activity can arise endogenously without the involvement of external energy stimulation, it becomes an open question as to whether Parker's (and Pantin's) phylogenetic sequence of independent effector, receptor-effector, and finally receptor-adjustor-effector is correct or whether receptors evolved subsequent to ganglion cells.

We propose that individual protomyocytes first evolved into assemblages of independent contractile cells, permitting more extensive movements than those resulting from contractions of individual myocytes. Certain of these cells became endogenous activity centers, or *pacemakers*, by developing unstable specialized membrane areas capable of active depolarization. Such local pacemakers synchronized contractions of adjacent cells by passive depolarization spread affecting the contractile mechanism, perhaps utilizing intercellular bridges. Groups of muscle cells responding to pacemakers would permit the evolution of recurrent feeding movements. Differentiation of these two cell types would have thus proceeded together, with what was to become muscle gradually becoming specialized for contraction and what was to become nerve becoming specialized for activity initiation. Initially both would become specialized for passive conduction of depolarization. The specialization of the nerve cell for the conduction rather than the repetitive initiation of activity is seen as a secondary development in the evolution of neurons.

The new hypothesis of the origin of the nervous system presented here is like that of the previous theories in that it, too, is the result of investigation of the coelenterate nervous system, although mainly of scyphomedusae and *Hydra* rather than the actinians which have been Pantin's prime concern. The striking regional autonomy found in many coelenterates—e.g., separate spontaneously active stalk, proximal tentacles (individually and collectively), distal tentacles, and manubrium in the *Corymorpha* polyp[10]—suggests that pacemaker loci at first did not integrate the entire organism as a unit. Rather, physiological unification by interconnected nerve-nets could have come later, after nondecremental all-or-none impulses had been achieved. It is worthwhile suggesting that such nervous unification coincided with the completion of individuation of the protocoelenterate from a colonial ancestor. Certainly analogous examples of incomplete individuation occur today within such colonial forms as *Physalia* and *Renilla.*

When such local action systems as tentacles or manubrium, each with their local pacemaker loci, were linked together, some of these pacemakers would become specialized for over-all control of the organism, whereas others would become subordinate centers controlling specific activities. Such a development would mark the achievement of the polarized synapse, as occurs in the scyphomedusan marginal ganglion. A hierarchy of pacemakers would emerge. The activity of centers controlling effectors indirectly through subordinate regional pacemakers would then become concealed, or cryptic, and such nervous activity could proceed to evolve without being directly tied to effector responses.

At the same time the nervous system could develop increased and differential sensitivities to various external stimuli, and thus integrate recurring internal activities with rhythmic external events; but even prior to this time pacemaker cells would have been influenced by impinging stimuli from external sources. Such external modulation of an existing output pattern would make them more sensitive to weak external stimuli; the same principle occurs in nearly all afferent pathways in higher animals. There is evidence that coelenterate neurons are still directly sensitive to rather short wavelength visible light,[11] a property shown by many of the lower invertebrates.

The further evolution of the nervous system would involve the development of through-conducting tracts for specialized reflexes, as Pantin has outlined,[5] the appearance of concentrations of nerve cells as ganglia or nerve rings, and the evolution of concentrations of receptors into sense organs in association with these ganglia. Such a phylogenetic series can be seen within the coelenterates, culminating in the elaborate rhopalia of the cubomedusae. There is a tendency toward reduction in the number of ganglia, shown also by the ctenophores, that may indicate how the cephalic dominance of the bilateria was achieved. Patterned activity from interacting pacemakers would continue to dominate such central nervous systems, evolving eventually into the brain waves of the higher invertebrates.[12]

It can be seen then that this hypothesis of the primitive nervous system departs markedly from that of Parker and significantly from that of Pantin. It marks somewhat of a return toward the views of the Hertwigs of eighty-odd years ago. Nerves and muscles have evolved in parallel from the first differentiation of either, the former first developing endogenous rhythmic activity and subsequently synapses and through-conduction tracts. Sensory reception was primarily a subsidiary function of the "ganglion cells" and only with the development of hierarchies of pacemakers did specialized sensory receptors appear.

How well does this new hypothesis summarize our current understanding of the existing primitive nervous systems of the lower invertebrates?

Prosser *et al.*[13] have recently shown that depolarization across cell membranes, passively or actively, probably does not occur in a variety of sponges. This not only casts further doubts on the view that a nervous system occurs in this phylum, but also differentiates their contractile mechanism from the conducting mechanism of coelenterates, since potassium-enriched sea water solutions which block both nerve-nets in scyphomedusae do not affect sponge myocytes.

Information from the coelenterates can be divided into three categories: histological, behavioral, and that obtained from direct neurophysiological recording. There are no coelenterates as yet where anything approaching a complete picture of nerve function has been achieved; only bits of information are available.

There is clear histological evidence for the presence of two overlying nerve-nets occupying the same epithelium, in several classes of coelenterates. In *Velella* one of these nets appears to be a syncytium,[14] but in several species of scyphomedusae each nerve-net (the diffuse and the giant fiber) consists of two-dimensional feltings.[15] So-called "sense-cells," i.e., neurons with short flagella, occur only in the diffuse nerve-net, but there is no evidence that this nerve-net is more sensitive to external stimuli in the subumbrellar region where both occur. Elsewhere in the phylum, there is little to suggest such superimposed nets, although "sense cells" seem to form local assemblages in the margins between column and mesenteries in sea anemones.[16]

Concentrations of neurons occur in medusae but are unknown in polyps. As they contain the pacemakers responsible for the swimming beat and are associated with nearly all of the sense organs found in the phylum, their absence from polypoid stages might suggest that the latter have less nervous activity, but direct physiological evidence refutes this conclusion. The isolated column of the hydroid polyp *Corymorpha palma* shows a negative rheotropism[10] just as does a statocyst-equipped hydromedusan, and many coelenterates show light responses without demonstrable pigment spots or ocelli. The absence of such "ganglia" does not preclude endogenous activity any more than does the absence of recognizable receptors preclude sensitivity to external stimuli.

Recurring behavior patterns in a wide variety of coelenterates are important evidence for rhythmic nervous activity. Such activity may be regular or irregular, continuous or occasional, almost too fast to be perceived or far too slow to be perceived. For example, the rhythmic activity of *Hydra* was pointed out by Jennings,[17] but its irregularity has caused most observers to ignore it. This variability of response is actually an accurate measure of internal activity, for as Mast pointed out fifty years ago: "Everyone who has ever attempted observations on the behavior of organisms with precise methods, knows that variability even in the lower forms under constant external conditions is one of the striking characteristics in reactions. There are internal as well as external factors involved in determining what the organism is to do."[18] So it is with *Hydra*.

The range in rates of activity is remarkable. Some coelenterate rhythmic activities are shown in Table 1. It seems scarcely credible that the same mechanism can cause repetition rates of 200, 2, 0.02, and 0.0002 per minute, and perhaps for this reason, as much as for the negative histological evidence, Pantin has suggested that the slower rhythms are myogenic rather than nervous. However, in *Hydra* at least even the slow contraction rhythm (0.05–0.2 per minute) is indirectly controlled by the "rhythmic potential" pacemakers.[11] Slow actinian rhythmic activity could be nervously controlled by such an indirect mechanism. Occasionally there is evidence for a slow rhythmic activity, as the extremely regular contractions (0.03 per minute) of the basal disk ring preparation, and a rapid rhythmic activity (parietobasilar contractions up to 20 per min) in the same organism, in this case the "swimming" sea anemone *Stomphia.*[19]

TABLE 1

RHYTHMIC ACTIVITIES IN VARIOUS COELENTERATES

Organism	Authority	Activity	Rate per minute
Many colonial hydroids: *Campanularia, Cordylophora, Obelia, Pennaria,* etc.	24	Back and forth movements in stolons; pulsations behind growing tip; hydranth twitches	0.05–0.35
Cordylophora	21	Repetitive firing after stimulation	60–300
Hydra	11, 17	Contraction bursts	0.05–0.2
	11	Rhythmic potentials	1–7
	11	Attachment bursts	10–20
Corymorpha	1,10	Feeding activity	0.25–0.33
Porpita	14	Feeding activity	2
Tubularia	21	Feeding activity	2
	21	Potentials	2–45
	21	Potentials in bursts	300
Physalia	1, 14	Raising fishing tentacles	1
Many hydromedusae	1, 15, 17	Velum contractions	6–120
Many scyphomedusae	15	Subumbrellar muscle contractions	6–80
Actinians:			
Calliactis	16, 20, 23	Circular muscle	0.07–0.1
Metridium	9	Circular muscle	0.04
	7	Phases	0.0002–0.005
Stomphia	19	Basal disk rings	0.03
	19	Parieto-basilar contractions, "swimming"	20
Renilla	25	Repetitive afterdischarges after stimulation	50

Another behavioral clue to pacemaker activity, in addition to rhythmicity, is a patterned output. This is also demonstrated by *Hydra*[11] where each over-all contraction consists of a "contraction burst" or 7–12 or more individual contractions, arranged in a characteristic time sequence. The patterns vary according to the physiological state and species of polyp. Pacemaker location can be shown by the specific blocking effect of localized hypostomal illumination. Light inhibition becomes progressively more difficult, until finally illumination is unable to halt the contraction burst. Comparable patterned behavior is also seen in the feeding reflex of *Porpita*[14] and in the intermittent swimming patterns of many hydromedusae.[17] Horridge has shown how stable and rapid rhythms can be achieved by the multiple interactions of all eight marginal ganglion pacemakers in scyphomedusae;[15] the same result—the increased rate of feeding movements in an intact polyp as compared to either isolated stalk or isolated hydranth—is evidence for multiple pacemaker control in *Corymorpha*.[10]

The most distinctive feature of coelenterate neurophysiology is *facilitation*, first shown by Pantin using the *Calliactis* sphincter muscle.[20] Facilitation means that a single nerve impulse does not cause a contraction, but that a second nerve impulse following the first causes a muscle contraction whose strength depends on the time interval between the first and second impulses. Pantin deduced that a similar mechanism, interneuronal facilitation, occurred between certain neurons, as in conduction around the sea anemone's oral disk. Facilitation also occurs at the scyphomedusan neuromuscular junction (although incompletely), within the nerve-net connecting individuals of colonial corals, and almost everywhere else within the phylum's neuromuscular system.

It was fortunate that the forms used in Pantin's classic studies do not show tendencies for spontaneous afterdischarges; with rare exceptions,[9] only when the electric stimulus is increased manyfold do two or more nerve impulses occur after a single stimulus. In other forms afterdischarges are more common. By recording its nerve impulses directly Josephson has shown how repetitive firing leads to graded conduction spread along a *Cordylophora* colony,[21] and thus, incidentally, validated the belief that direct recording of coelenterate nervous activity must be used to confirm indirect findings. It is now inferred that the same mechanism holds for other colonial forms, including the corals. The induced impulses do not necessarily arise from the site originally responding to the stimulus; thus, potential impulse initiation sites occur within the nerve-net, i.e., latent pacemakers, whose responsiveness may fluctuate in a complex manner. Subsequently, Josephson recorded the spontaneous nervous activity of the hydroid polyp *Tubularia*,[21] which shows a disconcerting variety of pacemaker sites, patterned bursts, and interactions that belie the seemingly stodgy behavior of this animal. However, this behavioral simplicity is probably erroneous, for *Tubularia* is rather closely related to both *Corymorpha* and *Porpita*, whose behavior has been mentioned above. Parker investigated *Corymorpha* because he was looking for a "simple" coelenterate to fill the gap between sponge and sea anemone, but after studying it he admitted that its behavior was far from "simple." Yet both *Tubularia* and *Corymorpha* are rather primitive hydroids.[22]

Taking *Tubularia*,[21] *Corymorpha*,[10] and *Porpita*[14] together, it can be seen that the first shows rapid, cryptic nervous activity which is both spontaneous and rhythmic, as well as intermittent pacemaker bursts. The latter genera show intermittent behavior strongly suggestive of pacemaker control, and in *Porpita* the feeding reflex consists of rapidly repeating coordinated tentacle jerks as well. It seems very likely that all three have similar nervous and behavioral mechanisms, appropriately modified to their own habits.

In *Hydra* it has been possible to study both behavior and the coordinating system directly, at the same time and for extended periods.[11] But our knowledge of its nervous structure is still so inadequate that it is impossible to be sure that what has been recorded has been nervous activity alone; the endodermal muscle sheet might be a conducting net as well as an effector. Nevertheless, tentatively and primarily for convenience, we will use the term *nervous* here. It is obvious that this question must be resolved in deciding whether the nervous system is a primary or secondary development.

The basic nervous activity in *Hydra* consists of spontaneous "rhythmic potentials"[11] originating from any one of a number of potential pacemakers in the lower column and stalk. These pulses are conducted without decrement throughout the column (distances in excess of 2 cm in the large *H. piradi*) without causing any discernible muscle responses. Their rhythm may be quite irregular or it may be very constant, while their rate also varies. Rhythmic potential pacemakers are directly sensitive to light, so that at dawn there is a nearly twofold increase in the rhythmic potential frequency which only slowly declines during the day.[11] The behavior patterns of the polyps show parallel changes.

The main action system of *Hydra*, the ectodermal longitudinal muscles, effects the periodically recurring contraction burst. With a patterned sequence of coordinated powerful contractions, the polyp is pulled down into a tight ball. Each contraction is preceded by an impulse originating from the hypostome region and conducted down the column by a nerve-net separate from that of the rhythmic potentials. Re-extension appears to be passive. Localized light stimulation can halt such contraction bursts by acting directly on the burst pacemaker.

The dark-adapted *Hydra* shows a characteristic response to light involving the tentacles, column, and contraction burst frequency. This response is mediated through the rhythmic potential system, since it will occur in an identical manner when only the rhythmic potential pacemakers are illuminated.[11] This is taken as proof of the dominant role of the rhythmic potential system. It is evident that this system is a cryptic coordinating network, primarily endogenously active but susceptible to external (light; strong mechanical), proprioceptive, and enteroceptive stimuli. It controls the animal's activity by its control of subordinate but semiautonomous pacemakers which, in turn, control effector systems. The rhythmic potential system is the machinery for spontaneous activity.

In scyphomedusae there is no hidden rhythmic pacemaker activity in the diffuse nerve-net, probably because of the rhythmic activity of the giant fiber nerve-net innervating the subumbrellar muscles. Diffuse nerve-net impulses act on the marginal ganglion pacemakers which, in turn, initiate impulses in the giant fiber nerve-net. What is noteworthy in this advanced nervous system is the dearth of afferent stimuli. Spontaneity occurs in its absence. The specialized sense organs associated with the marginal ganglia—the rhopalia—do not appear to originate nerve impulses in either of the two through-conducting nerve-nets. There is nothing to suggest a primary role for sensory receptors in the evolution of these nervous systems.

In the forty-odd years since Parker's book appeared there has been a renewed appreciation of the complexity and organismic unity of the lower animals. We now recognize the existence of spontaneous activity, of rhythmic behavior patterns of considerable complexity, of the interactions of multiple pacemaker loci existing within several superimposed conducting systems, of cryptic nervous activity; all these changes of view allow the biologist to account for the behavior of entire organisms, with its phases and diversity, without invoking purposefulness. For example, a cryptic pacemaker system could provide the physiological machinery, the chronometry, for the "... variety of more or less periodic active systems ..."[9]

which occur in coelenterates. Parker's theory is no longer adequate and must be replaced, but whatever hypothesis is followed, the totality of the organism's behavior must be explained in developing a comprehensible view of the nervous system of primitive animals and its evolution.

The author wishes to thank Drs. E. D. Hanson and C. P. Mangum and Mr. F. M. Williams for their help with this manuscript.

---

* Supported in part by research grant G-14574 from the National Science Foundation.

[1] Parker, G. H., *The Elementary Nervous System* (Philadelphia: J. B. Lippincott Co., 1919).

[2] Kleinenberg, N., *Hydra, eine Anatomisch-entwicklungsgeschichtliche Untersuchung*, (Leipzig: Engelmann, 1872); Hertwig, O., and R. Hertwig, *Studien zur Blättertheorie. Heft* **I**: *Die Actinien...*, (Jena: G. Fischer, 1879).

[3] Bishop, G. H., *Physiol Rev.*, **36**, 376 (1956).

[4] Grundfest, H., in *Evolution of Nervous Control from Primitive Organisms to Man*, ed. A. D. Bass., Publ. no. 52 (Washington: AAAS, 1959), p. 43.

[5] Pantin, C. F. A., *Pubbl. Staz. Zool. Napoli*, **28**, 171 (1956).

[6] Sherrington, C. S., *The Integrative Action of the Nervous System* (New Haven: Yale University Press, 1906).

[7] In an earlier exposition of his theory, in *J. Exptl. Zool.*, **8**, 1 (1910), Parker recognized that his hypothetical primitive nervous system would not fulfil the requirements of the reflex arc, but this difficulty was not stressed in his book.[1]

[8] Wells, G. P., *The Sources of Animal Behaviour* (London: H. K. Lewis and Co., 1955).

[9] Batham, E. J., and C. F. A. Pantin, *J. Exptl. Biol.*, **27**, 264 (1950); *ibid.*, **27**, 290 (1950); *ibid.*, **27**, 377 (1950); Pantin, C. F. A., *Proc. Roy. Soc.*, **B140**, 147 (1952); Batham, E. J., and C. F. A. Pantin, *J. Exptl. Biol.*, **31**, 84 (1954).

[10] Parker, G. H., *J. Exptl. Zool.*, **24**, 303 (1917).

[11] Passano, L. M., and C. B. McCullough, these PROCEEDINGS, **48**, 1376 (1962).

[12] Bullock, T. H., *Yale J. Biol. Med.*, **17**, 657 (1945).

[13] Prosser, C. L., T. Nagai, and R. A. Nystrom, *Comp. Biochem. Physiol.*, **6**, 69 (1962).

[14] Mackie, G. O., *Trans. Roy. Soc. Can.* **V53**, 7 (1959); *Discovery Repts.*, **30**, 369 (1960); *Quart. J. Microscop. Sci.*, **101**, 119 (1960).

[15] Horridge, G. A., *Quart. J. Microscop. Sci.*, **97**, 59 (1956); *J. Exptl. Biol.*, **36**, 72 (1959).

[16] Batham, E. J., C. F. A. Pantin, and E. A. Robson, *Quart. J. Microscop. Sci.*, **101**, 487 (1960); Robson, E. A., *ibid.*, **102**, 319 (1961).

[17] Jennings, H. S., *Behavior of the Lower Organisms* (New York: Columbia University Press, 1906).

[18] Mast, S. O., *Light and the Behavior of Organisms* (New York: John Wiley and Sons, 1911).

[19] Hoyle, G., *J. Exptl. Biol.*, **37**, 671 (1960); Robson, E. A., *ibid.*, **38**, 343 (1961); *ibid.*, **38**, 685 (1961).

[20] Pantin, C. F. A., *J. Exptl. Biol.*, **12**, 119 (1935); *ibid.*, **12**, 156 (1935).

[21] Josephson, R. K., *J. Exptl. Biol.*, **38**, 579 (1961); *Comp. Biochem. Physiol.*, **5**, 45 (1962).

[22] Rees, W., *Bull. Brit. Museum, Zool.*, **4**, 1 (1957).

[23] Needler, M., and D. M. Ross, *J. Marine Biol. Assoc. U.K.*, **37**, 789 (1958); Ewer, D. W., *J. Exptl. Biol.*, **37**, 812 (1960).

[24] Hale, L. J., *Quart. J. Microscop. Sci.*, **101**, 339 (1960); Fulton, C., *J. Cell. Comp. Physiol.*, **61**, 39 (1963).

[25] Nicol, J. A. C., *J. Exptl. Biol.*, **32**, 619 (1955).