

and ion channels must be functionally described in order to obtain a full understanding of a CPG, we will not have a detailed, mechanistic explanation for some considerable length of time. A complete compilation of the detailed molecular biophysics of neurons will long remain the "quark" of cellular and integrative neurobiology.

The most disturbing feature of the Selverston paper is its pessimistic tone and its final leap into nihilism. Science has been marked by the episodic appearance of nihilists. Often these negative spirits have had a positive influence upon empiricism by raising doubts regarding the state of knowledge at the time, and the empiricists would respond with better experiments, more rigorous controls, and more conclusive results. Neurobiology has probably had more nihilism than most other sciences simply because of its subject – the nervous system – and its long-term goal, an understanding of brain function. As early as 1933, Niels Bohr raised the fundamental philosophical question of whether any brain was capable of understanding those connections which were responsible for its functioning, including its ability to understand. Gunther Stent (1969) examined a series of historic trends in both the arts and the sciences and predicted an end to progress as we know it (implying, of course, an end to the systematic investigation of neurobiological problems). Jerome Lettvin has repeatedly argued in public forum that the nervous system is so complicatedly and redundantly wired that no amount of experimentation will produce an understanding of its functions, and we should, therefore, simply not try.

I will refrain from the temptation of waving the banner of neurobiology by listing some of the (ever-increasing) examples of progress. Putting philosophical and theoretical considerations aside, it is patently clear that we can, and have, learned a great deal about the nervous system in general and about CPGs in particular. While there may well be some limit as to what we can understand about the functions of the nervous system set by "uncertainty principles" or by "social evolution," it is nevertheless especially distressing when an experimentalist such as Selverston embraces nihilism. One can but wonder what motivated Selverston to write the target article: either he is playing devil's advocate and attempting to evoke some patriotic response from the neurobiological community, or he believes what he has written. If the former is true, the article is unnecessary; if the latter is true, one wonders why he persists in his chosen (futile) research activities trying to understand the workings of a central pattern generator in the lobster stomach.

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Epistemology and heuristics in neural network research

Dr. Selverston has arrived at a discouraging conclusion from which he invites the reader to derive an even more discouraging implication – namely, that we lack the methods to "completely understand" central pattern generators (CPGs). He is understandably disappointed and disillusioned by the failings of the neuromime approach to modeling which, coupled with the seemingly transparent and invariant simplicity of the invertebrate nervous system, once promised to cut through the tedious experimental approach to understanding. Those of us who have addressed the mammalian nervous system, where the neurons are not individually numbered, would certainly have anticipated the conclusion, yet we have resisted the implication and persisted along rather different approaches to understanding. This is because both the understanding (epistemics) and the approaches (heuristics) assumed by Selverston are not the only ones possible, or even the most useful. We shall examine briefly the epistemology by extending the analogy of the radio receiver (as employed by Selverston) and the heuristics by considering the emerging methodology of top-down design.

Selverston makes the tacit assumption that "understanding" a CPG is equivalent to having a model whose components are in one-to-one correspondence with the components found in the real CPG. In understanding the operation of the class of devices known as radio

receivers, one would obviously have accomplished little by having a list of the components and their individual specifications. One would actually be little further ahead by having a complete circuit diagram unless one were already familiar with the principles of resonant circuits, superheterodyning, amplification, etc. that constitute *how the thing works* [cf. Puccetti & Dykes: "Sensory Cortex and the Mind-Brain Problem" *BBS* 1(3) 1978]. The principles of operation really constitute the knowledge required for understanding, and they are disembodied from the actual device (or its model). Once they are known, the construction of a truly analogous model and its confirmation are relatively trivial. It seems likely that a model which correctly embodies a principle of operation would be insensitive to small variations in the parameters or even in the numbers or connectivities of the components. Furthermore, it seems possible that the network is developmentally assembled in relation to the underlying principles – i.e., that genetics will be found to be organized in relation to rules of operation.

A thorough understanding of the principles may, however, reveal that there is more than one way to achieve a given performance. It is then incumbent on the investigator to further specify the performance to eliminate ambiguities in design. Most of the erroneous models cited by Selverston arise from failures of specification. If you think a radio is a device which makes static come out of a speaker, there will be many ways to construct one, few of which will be viewed as satisfactory for long. In applying the analogy of the radio receiver, one must remember that we are trying to *discover* the actual principles of its operation, not to invent them. The *invention* of radio proceeds rationally from a thorough and imaginative understanding of the properties of the available components. Once the device meets minimal specifications, the refinement of those specifications and improvements of design will necessarily proceed in an evolutionary manner. In *discovery*, it is not possible to overspecify; any failure to completely specify invites construction of an erroneous model.

It should be apparent from the above that there are many equally valid and "rigorous" levels of explanation. In fact, there may be no limit to the depth to which one might pursue the submolecular bases of a given behavior. Selverston would seem content to know the membrane properties of the component neurons, but surely the biophysics of the iontophores are part of "understanding," and beyond that the stereochemistry of membrane proteins beckons. Yet complete knowledge at the deeper levels is of as little help in understanding an emergent property like pattern generation as are the properties of semiconductor junctions in understanding radio reception. A thorough understanding of the higher level must inform the investigation into the next deeper layer. We submit that several levels of understanding (amenable to higher-order modeling) exist between the simple behavioral observation and a neuromime model, and that even the first has barely been scratched for most CPGs.

This orderly, gradual reductionism is becoming established as a useful and efficient information handling technique most commonly referred to as "top-down design." It is slowly becoming accepted in computer programming but is likely to be resisted by scientists because it imposes certain unusual disciplines and delayed gratification. It also requires an almost blind faith that methodological problems such as those Selverston mentions can be circumvented by more careful and informed experimental designs and strategies at whose actual methodological requirements we cannot yet guess. This carries the risk that a great deal of effort will be expended before one discovers that the methodological limitations really do prevent significant progress, a situation not unprecedented in neurophysiology. On the other hand, the leaping reductionism that tempts us to use any available technique to study a process we can't even properly describe in gross terms leads frequently to those dead ends which Selverston finds so discouraging. (In mammalian neurophysiology, the cerebellum is an example of a structure whose basic components and circuitry were made available before there was any real experimental evidence regarding its function, with the consequence that the literature is now full of things that the cerebellum *should be doing but is not*.)

What we are suggesting is that the next step should *not* be the development of ever-finer anatomical and electrophysiological tech-

niques to study those subcellular processes which, admittedly, do underlie the behavior. Rather, we must develop better descriptions and manipulations at the systems level and a lengthening list of possible principles of operation. (Selverston's catalog of mechanisms is a valuable beginning.) Ironically, this may best be done in vertebrates with more complicated and malleable behavior. Their patterns tend not to be expressed in the all-or-none fashion of invertebrate feeding or escaping but rather to demonstrate experimentally useful ranges of motivation, speed, load compensation, reflex modulation, conditioning, learning, etc., etc. Furthermore, the behaviors do not emerge suddenly and completely as invariant instincts, and thus they can be followed through normal versus deprived or altered developmental stages, starting more simply and adapting to fit their environment. Teleologically, one expects that the places in the developmental program where plasticity has been introduced should provide some useful insights into the principles of operation.

This suggests another problem which may limit our present ability to understand CPGs but which Selverston does not specifically mention. The metaphor of the radio receiver may actually be quite misleading in its assumption that neural circuits actually follow some wiring diagram. An FM radio in an area which has only AM broadcasts does not learn to extract meaningful information from the signals which it detects. CPGs, particularly in vertebrates, may be inextricably enmeshed in somatosensory perceptual systems whose wiring is specified by accumulated experience operating on self-organizing feature detectors. Our inability to completely specify many of the components and their connections may accurately reflect their nonspecification by nervous system genetics. While one does not usually think of the spinal cord as a perceptual machine with plasticity, there is accumulating evidence suggesting an anatomical substrate for adaptive changes in synaptic projections (e.g. sprouting). The nonlinear, state-dependent signals from muscle and skin stretch receptors might especially benefit from processors which could interpret them in the total context of the task in progress, a goal perhaps more suitable to an educable control system than a servomechanism. Even in simple organisms with simple behaviors, the nervous system often chooses to perform tasks with hundreds or thousands of information processing elements, even though the tasks, as we describe them experimentally, could be performed by the small number of large elements which attract our attention. We then have to consider the possibility that the understanding we really seek is not of the principles of operation of the CPG but of the rules of development and adaptation.

Obviously, we are digging in for a long siege before we can seriously contemplate modeling at the neuromime level in the mammalian CNS. Should this discourage us? No, because we are at this very moment directly attacking the real questions regarding the principles of operation of the CPGs. By the time that is completed, either the methodological problems will be solved (or we will discover indirect ways around them), or we will have realized that there are other demonstrations of understanding at least as satisfying as a neuromime model.

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Central pattern generators and sensory input

Selverston emphasizes that "it is unlikely that present techniques will ever yield a complete understanding of any but the simplest of [CPGs]." He also remarks that "modeling studies have not added much," and he claims that "this is due . . . to the poor quality and incomplete nature of the data provided. . . ." He advises using a "simple" system. Undoubtedly he is right, but a "simple system" only means that others, which include a greater number of variables, are more complex.

I interpret Selverston's paragraph on "present strategies" as indicating the necessity of fully understanding all the mechanisms involved in the processes that evoke a rhythmic behavior. However, it is not clear to me whether his purpose is to seek a model for a simple preparation or to attain total knowledge of such preparation. Either can

constitute a useful model for the study of physiological mechanisms in more complex preparations.

The author defines a central pattern generator (CPG) as a group of neurons that can produce a rhythmic motor activity with a characteristic pattern, independently of the sensory input. However, it has been reported that a CPG can be turned on by special inputs. Our own evidence supports the existence of an innate central pattern which would be responsible for a rhythmic response (Luco 1963).

The third thoracic ganglion of *Blatta germanica* was stimulated in vitro through the abdominal connectives and activity was recorded from a single motor axon. The afferent input served only to trigger the rhythmic response, and once this response had been initiated it followed its course independently at the electrical stimulus.

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Single-cell versus network properties and the use of models

Selverston's target article provides considerable insight into CPGs and our ability to understand them. I would like to point out some additional considerations regarding the involvement of single-cell and network properties in determining CPG output. The author, in a typical fashion, divides the mechanisms underlying CPG functioning into two different classes: (1) CPGs which depend on single-cell properties such as endogenous bursters and repetitively firing neurons; and (2) CPGs whose output "emerges" as a result of network interactions. The problem with this classification system is that it is becoming apparent that, in the case of the few CPG networks whose component cell membrane properties have been studied, both mechanisms can be essential and can interact to determine CPG output.

A good example of the involvement of single-cell properties in determining the output of a CPG network involves the pyloric and gastric systems in the stomatogastric ganglion of the lobster. The pyloric system contains three electrically coupled endogenous bursting neurons, and the remaining pyloric and gastric neurons have been considered to be passive follower neurons. Russell and Hartline (1978), however, have demonstrated that many of these passive follower neurons have the ability to generate plateau potentials due to intrinsic "burster" properties and may therefore be intermediate burster neurons. Plateau potentials could be elicited by a short depolarizing pulse and were found to cause a membrane potential transition to a more depolarized potential and concomitant repetitive firing. Central synaptic input is required to unmask plateau potentials, which has many implications regarding the involvement of plateau potentials. Russell and Hartline conclude that the properties of individual cells of a CPG network can be of paramount importance to the functioning of the network.

Our own studies on the cyberchρον system in the snail *Helisoma* have also pointed out the importance of specialized single-cell properties in determining the output of a CPG network. The cyberchρον system is a CPG network consisting of approximately twenty electrically coupled neurons which control the feeding behavior of the snail. The cyberchρον network was originally thought to burst as a result of regenerative excitation mediated through the electrical coupling (Kaneiko, Merickel, & Kater 1978). Further examination of the properties of individual cyberchρον neurons demonstrated that cyberchrons are a heterogeneous population of neurons, some of which have endogenous burster properties (Merickel & Gray 1980). Therefore, the cyberchρον CPG output now appears to be dependent on both single-cell properties, which provide the driving rhythm, and network interactions mediated through the electrical coupling, which provide synchronization and probably plasticity.

The above two examples suggest that it is more appropriate to consider the output of CPG networks in terms of mechanisms which span a continuum from specialized single-cell properties to emergent network properties rather than in terms of either single-cell or network properties. Therefore, it may well be the rule rather than the exception