On Neural Codes and Perception

William T. Newsome

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JOCN: You were trained by a number of scientists whose expertise ranged from anatomy and cellular physiology up to psychophysics. Was there a plan here? Did you feel this broad training was a necessary process in order for you to study the kinds of questions you now examine?

WTN: I wish I could say that my current research program resulted from precocious insight, but that would be disingenuous. You are correct that my entree to the business was through bottom-up anatomical and physiological experiments. I received excellent training in these approaches in the laboratories of John Allman and David Van Essen, and this background in the blunt realities of brain organization has served me well in ensuing years. Fortunately, though, I was influenced at a fairly early stage by several mentors who helped me realize that the bare facts of neurophysiology and anatomy come to life most incisively in the context of behavioral and psychophysical functions that the system performs. John Allman nudged me toward this line of thinking in graduate school, but I became fully committed to it only during postdoctoral work with Bob Wurtz and collaborative experiments with Tony Movshon. I now appreciate that psychophysics and behavior define the playing field for the physiologist. The inner workings of a complex system are most sensibly probed if we have in hand (1) a reasonably clear idea of the overall function of the system, and (2) reasonably quantitative measurements of the system's capabilities. A cardinal feature of my current work, then, is that psychophysical and physiological events are monitored and manipulated simultaneously—in the same animal, on the same sets of trials, under precisely identical conditions. Applied together, the two approaches yield keener insights than either approach alone.

JOCN: That is, of course, the tremendous power of the animal (primate) model. And you say that with such conviction that I cannot resist examining the other side of the coin. At what point do animals models break down? One wouldn't want to study the brain mechanisms of ennui in rats. Are there limits in visual science as to what the monkey can teach the student of human perception?

WTN: I would think there must be limits, but I doubt that we have even begun to approach them. Behavioral, anatomical, and physiological similarities suggest that we share a great deal of visually based cognition with non-human primates, including object recognition, visually directed navigation, spatial attention, visual memory, and simple forms of decision making. Investigation of these phenomena in alert, behaving animals has been seriously engaged relatively recently. One possible limit that does concern me is in the area of abstract representation, which humans seem to accomplish mostly through linguistic mechanisms. In our laboratory, for example, we are beginning to investigate neural mechanisms underlying a simple decision process in our motion discrimination paradigm. It is unclear, however, whether the result of a monkey's decision is registered and held only in premotor circuitry that prepares the animal's operant
response, or whether the decision is implemented in a more abstract, "supramodel" circuit that then informs appropriate premotor centers. In humans, I think, the outcome of decisions can be readily held in the abstract form of a linguistic representation. In monkeys, however, the outcome of any decision may be linked much more tightly to specific actions, and thus to premotor circuitry.

JOCN: Yes, that relates to the old truth that when a nonmusician hears a tone to be remembered, it is assumed to be stored with perceptual parameters at work. When a musician hears the same tone (say B flat) she/he simply notes the referent. And surely wholly different brain mechanisms are at work with these two groups.

WTN: I would think so.

JOCN: But before we drop the interspecies tension, it should be noted there are growing lists of differences. For example, a rhesus monkey with the callosum sectioned, but the anterior commissure intact, transfers virtually all visual information. Yet humans with the same surgical manipulation transfer virtually no visual information. Humans with lesions of primary visual cortex most likely can not see. Yet monkeys with the same lesion are able to see. The volume of area striata in the human is three times what it is in monkeys. And alas, can't the slowly bird with its hugely different visual system do most of what a human and or primate can do with visual stimuli?

WTN: Certainly there must be differences. Some, like the interhemispheric transfer example you cite, probably reflect anatomical convenience more than basic functional differences. I suspect that interhemispheric coordination of visual information is probably similar in humans and nonhuman primates despite differences in the precise routes taken by interhemispheric axons. Other species differences, like those between birds and primates, probably entail more profound variation in information processing strategies. I suspect we would learn a great deal about how biological vision works by understanding both the shared and the unique processing mechanisms of visual systems as strikingly different as those of primates and birds. I work on primates because the animals are so amenable to studies in which psychophysics and physiology are combined in the same experiments; we can actually probe around inside the system while it is functioning in a reasonably normal fashion. Perhaps a clever student reading this interview will eventually show us that the same thing can be done in birds.

JOCN: O.K., a final question dealing with the philosophy of your approach. What are the limitations of single neuron analysis? One might think that assessing the behavior of one neuron at a time would severely limit the kind of analysis you can do.

WTN: The most obvious limitation of the single unit approach is the difficulty in analyzing neural representations involving simultaneous activity at multiple locations in the brain. This limitation can, of course, be rather severe since even simple sensory stimuli or motor acts evoke complex patterns of neural activity in the brain. A second limitation, that receives somewhat less attention, is that the single unit approach provides little information about the relative timing of neural events at different locations in the brain. The timing of neural activity in different brain structures can provide critical temporal information bearing on the possibility of cause-and-effect relationships between those structures. A final limitation is that single unit recording in the central nervous system virtually precludes precise analysis of input-output transfer functions. For any given neuron, we have only the most general notion of what its inputs might be, such notions being based largely on population studies of anatomical connections and physiological properties. The strongest statements concerning transfer functions are usually of the form: "This type of response selectivity has not been observed at prior levels of the pathway, and is probably synthesized from simpler inputs for [some specific computational or behavioral purposes]."

Having criticized the single unit approach, let me hasten to add that we have not yet begun to exhaust its usefulness. Single unit analyses are still employed profitably in conjunction with anatomical techniques to identify basic processing modules in different brain structures—what Hubel and Wiesel termed "functional architecture." I suspect that this enterprise will continue to be productive, especially if molecular techniques can provide more precise anatomical markers for neural circuits. Even more exciting to me, obviously, is the recent trend toward applying the single unit approach in behaving animals trained to perform simple cognitive tasks. More laboratories are now employing clever behavioral paradigms (frequently adapted from the experimental traditions of psychophysics and behavioral psychology) to investigate neural substrates of perception, attention, learning, memory, and motor planning, to name but a few. A wealth of new insight is emerging from these efforts, and I believe we have only scratched the surface of what can be learned.

JOCN: O.K., tell us briefly about the specific approach you take and how you use it to instruct us on how the brain enables a visual percept.

WTN: For several years we have worked in an extrastriate visual pathway that emphasizes the analysis of motion information. Our central goal has been to determine whether and how neural responses to moving visual stimuli underlie perceptual responses to the same stimuli. We chose the motion pathway not because it is intrinsically more interesting than other systems in the

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brain, but because we had evidence from prior single unit studies concerning the likely function of this pathway, Semir Zeki and Ron Dubnner first discovered that most neurons in a region of the superior temporal sulcus are directionally selective, prompting them to suggest that this area was specialized for processing motion information. This system therefore offered a good opportunity to inquire closely concerning the relationship between neural activity and a specific perceptual capability—motion vision. Our basic approach has been to train rhesus monkeys to discriminate the direction of motion in a family of random dot displays in which the difficulty of the task can be varied continuously by modulating the strength of the motion signal in the display. We have used all the tools at our disposal—pharmacological inactivation, single unit recording, microstimulation, and behavioral manipulation—to explore the relationship between neural and perceptual events.

**JOCN:** For the general reader, how would you characterize your basic set of findings?

**WTN:** There are three salient findings of interest to the general reader. First, several laboratories have now shown that inactivation or ablation of MT can selectively impair motion vision, including performance on the direction discrimination task used in our work. While these inactivation experiments confirm a prominent role for MT in motion vision, they yield little insight into the character of the signals carried by MT neurons and how those signals are processed to yield psychophysical performance. To gain insight into these issues, we next recorded from single MT neurons while monkeys performed the direction discrimination task. One of the most surprising results of this study was that single MT neurons, on average, are as sensitive to directional signals in the stochastic visual display as is the monkey psychophysically. In other words, the responses of an average MT neuron convey enough information about the direction of stimulus motion to account for the monkey's psychophysical performance. This observation flies in the face of conventional thinking about the effects of signal averaging within pools of sensory neurons: averaging should eliminate much of the noise carried by single neurons, producing psychophysical performance superior to the sensitivity of any single neuron in the pool. We are currently engaged in a modeling study to identify conditions under which various pooling models can be reconciled with our experimental measurements of neuronal and psychophysical sensitivity. This effort is producing new insights into signal pooling within the cortex and the factors that limit fidelity of the pooled signal.

The third observation of general interest is that electrical microstimulation of directionally selective MT neurons can influence judgments of motion direction in a predictable manner. When a monkey discriminates between two opposed directions of motion in one of our stochastic stimuli, we can actually tilt his judgment in favor of one or the other alternative by electrically activating a column of MT neurons that responds optimally to one of the two directions. To obtain optimal effects, the train of stimulating pulses must occur during the brief display interval in which the monkey actually inspects the stimulus and arrives at his decision. This result is particularly important because it establishes a causal link between the activity of neural circuits identified at the single unit level and a specific visual capacity—direction discrimination. In other words, single unit properties measured with a microelectrode can be used to predict the behavioral consequences of perturbing activity within intricately organized circuits of the cerebral cortex. One can think of this result as being analogous to the molecular biological experiment of inserting a novel gene into a bacterium and seeing a protein of the predicted sequence emerge. We are inserting an artificial signal into the cortical circuitry and seeing a predicted behavior emerge. The opportunity for this kind of experiment is rare in systems neuroscience, but the result is most important because it confirms that the "facts" provided by single unit studies can indeed yield meaningful insight into the biological basis of behavior and cognition.

**JOCN:** The correlation of single neuron responses and psychophysical performance is fascinating but also a little bewildering. Surely lesioning a single neuron or small set of neurons would yield an animal still able to carry out the task in normal fashion. Does this argue against the sort of Barlowian view that single neurons make decisions concerning perceptual events?

**WTN:** I'm glad you asked that question, because many people seem to be confused about our position on this issue. Your question actually goes to the heart of the modeling efforts that Mike Shadlen, Ken Britten, Tony Movshon, and I have been involved in over the last couple of years. At first, the correlation of single neuron responses with performance pushes one toward Barlow's view that single neurons themselves, being optimally tuned detectors for certain classes of stimuli, are the critical signaling units that govern performance. Like you, however, I have difficulty believing that destruction of a single neuron could ever impair performance significantly. If this intuition is correct, the information carried by single neurons must be redundant to some extent. The important questions are (1) how redundant? (2) how are the partially redundant signals pooled to inform psychophysical decisions? and (3) what are the key factors that limit the quality of performance emerging from the pooling process? To explore these issues, we developed a statistical model that accepts neuronal inputs like those we actually recorded in MT and produces decisions concerning the direction of motion for
each stimulus presentation. In essence, the model allows us to mimic entire physiological/psychophysical experiments on the computer, and to identify conditions under which we can obtain the same relationships between physiological responses and performance that we observe experimentally.

Without going into onerous detail, we have great difficulty accounting for all of our experimental observations with small pools of input neurons (i.e., < 50). Thus we are tilting even farther away from optimal detector ideas in favor of models involving more extensive pooling. We can reproduce our experimental observations for large pools of simulated MT neurons under three key conditions: (1) the activity of neurons in the input pool is weakly correlated, (2) the psychophysical decision is influenced not only by optimally activated MT neurons, but also by neurons less sensitive than those we studied, and (3) noise sources exist at the pooling stage. The first condition has been confirmed experimentally by Ehud Zohary in our lab (Nature 370:140), and we based the simulations in part on his measurements of correlated activity in MT. The second condition is a matter of conjecture, but is certainly reasonable. The third condition must be true if the pooling is performed by real neurons in the brain rather than by a digital computer.

One of the most interesting insights to emerge from the simulations is that very weak correlation among the input neurons places fundamental limits on the benefits of signal averaging within the nervous system. In our simulations, psychophysical sensitivity asymptotes as the size of the input pool reaches 50–100 neurons. The key intuition here is that noise which is common to all neurons in the pool (by virtue, perhaps, of common input from other neural structures) can never be averaged out. Thus pools consisting of thousands of input neurons would not improve performance appreciably beyond the level supported by 100 neurons. In a sense, then, the issue of numbers of neurons becomes somewhat defused. One might still search for models that could reconcile our data with very small numbers of neurons (i.e., < 50), but in terms of the benefits endowed by signal averaging, size appears irrelevant after the pool exceeds 100 or so neurons. In the end, this point of view need not be incompatible with Barlow's original neuron doctrine. If signals can be carried with asymptotic fidelity by small groups of 100 or so neurons, then single neurons remain a force to be reckoned with.

I should mention for interested readers that a preliminary description of our modeling results appears in The Cognitive Neurosciences, published this fall by MIT Press.

WTN: Of course it is possible. This sort of redundancy would give the organism no advantage in the short run, however, and would presumably entail a sacrifice of potential computational power. What is the optimal trade-off between present computational power and protection against future degeneration? I have no idea, but a substantial amount of protection would be provided simply by doubling the size of a sensory pool from, say, 100 to 200 neurons. Our simulations suggest that performance would be essentially unchanged by the random loss of half of these neurons.

JOCN: The stimulation experiments raise many questions. Do you think the site of the effect is in MT or is it elsewhere?

WTN: This is a strange question if you think about it carefully, but it comes up over and over again. To answer the question, we must be precise about the meaning of the phrase, "site of the effect." Do we mean the site where microstimulation directly affects neuronal activity? The site where it appears to become differentially active? The site(s) where the decision is made? The site(s) where the operant response is planned? The site(s) where perception occurs (if indeed any percept accompanies microstimulation in MT)? The meaning you choose will influence the answer I give, but I am not sure that this was a useful way for us to proceed. For me, it is more helpful to think of the monkey's performance on this task as a complex sensorimotor loop. The direction of stimulus motion is encoded implicitly in sequences of activity among retinal ganglion cells. This information is made explicit in the form of directional selectivity in neurons of the cortical motion pathway, including MT. Directional information is "read out" of this pathway by means that are not yet known, and the intention to make a specific operant response is formed and held in register in premotor circuitry. When the "go" signal occurs, motor circuits flash into action, generating the response. In principle, we could cause identical changes in the monkey's behavior by stimulating at any of these stages if we had the right number of electrodes in the right spots, active at the right times. My point is that the behavioral changes elicited by microstimulation in MT involve a cascade of activity from MT through the central nervous system to the extracocular muscles. So I'm not sure that it makes sense to speak of one "site of the effect." I prefer to think of a sensorimotor, or "cognitive" loop through the brain, and of microstimulation as a tool for intervening at discrete points in the loop.

I can relate an amusing anecdote concerning this point. I once participated in a small meeting of reputable neuroscientists, and I was being circumspect as usual about the "site" of the microstimulation effect (loops, opportunities for intervention, etc.). At one point, a particularly auspicous participant brought me to a complete
halt by interrupting: “I don’t understand, Bill, why don’t you just say that MT is where it happens?,” with pregnant emphasis on the “it.” The problem of course is that I still don’t know what it was. Perception? Cognition? Consciousness? I believe that mental phenomena result from interactions among networks of neurons. The attempt to restrict any one phenomenon to a particular brain structure (even MT?) is probably misguided in the long run. On the other hand, performance of a specific cognitive task certainly consists of computations executed in parallel and in sequence within real neural pathways. It seems to me entirely possible, with current techniques, to explore the inner workings of cognition by discovering the sites in well-defined neural pathways where the results of these computations become evident, and developing testable models of how these computations are implemented. This, at any rate, is what we hope to accomplish with our motion discrimination task.

**JOCN:** Granted that the proper pattern of stimulation at any stage of the pathway can, in principle, create identical behavioral effects, would you agree that these different stimulation regimes might create entirely different internal experiences for the animal?

**WTN:** Absolutely. Imagine for a moment that someone did microstimulation experiments on my brain as I performed this direction discrimination task. Presumably, the experimenters would have several ways of causing me to choose upward motion even when the visual stimulus contained downward motion. One way would be to stimulate early regions of my visual system in a way that mimicked precisely the pattern of neural activity evoked by an upward stimulus. At the other extreme, they could simply intervene at the last moment in my oculomotor pathways to change my operant response. Now I certainly believe that my internal experience would be vastly different under these two regimes. In the former, I would actually have seen upward motion. In the latter, I would be grossly alarmed, wondering why my brain did not produce the eye movement I intended to make. Furthermore, I believe the nature of this internal experience matters for our understanding of nervous system function. In some circles, it seems fashionable to suppose that internal experience is irrelevant from a scientific point of view. If we can completely explain a sensorimotor behavior in terms of causes and their effects in central neural pathways, we have accomplished everything important and can move on to the next problem. I disagree strongly with this point of view. Even if I could explain a monkey’s behavior on our task in its entirety (in neural terms), I would not be satisfied unless I knew whether microstimulation in MT actually causes the monkey to see motion. If we close up shop and go home before answering this question and understanding its implications, we have mined silver and left the gold lying in the tailings.

Here I must admit to a major problem, though, since the monkey’s internal experience is not transparent to me. We have indirect evidence concerning the nature of the animal’s experience during microstimulation of MT, but I must finally admit that I do not know whether the monkey actually sees motion when we stimulate MT. To correlate perceptual experience with neural activity at this level, I believe we will ultimately have to find ways to perform conceptually similar experiments in humans.

**JOCN:** Cognitive neuroscience loves that sentiment. But back to the monkey. In an ideal world, where you could collect any data you wanted on this task, what would the final answer look like? When would you feel that you truly have an answer to how motion is perceived?

**WTN:** Sorry, Mike, but I don’t have a good answer to that question this year. In saying this, I do not intend to be coy or obtuse. If I could answer your question straightforwardly, the implication would be that the conceptual terrain is reasonably clear, leaving hard work and a technical breakthrough or two as the only impediments to a complete understanding of motion perception. I am not that sanguine. In most branches of cognitive neuroscience, we are confronted ultimately with the curious spectacle of our own brains trying to understand themselves at their most sophisticated levels of functioning. I have substantive doubts whether we can ever accomplish this task in a completely satisfactory manner, though I would certainly enjoy coming back briefly a couple of hundred years from now to see what progress has been made!

For the time being, then, I suspect we must feel our way toward these ambitious goals from the bottom up, letting the new light obtained at each level of inquiry hint at the questions to be asked at the next level. We do not grope blindly, however, because careful psychological study of cognition can provide a reasonably clear view of many phenomena we wish to understand.

From this perspective, the best answer I can offer to your question is a list of the issues that seem most pressing at our present level of inquiry. I have offered several already, mostly fitting under the rubric of understanding information flow through the various pathways tapped by our direction discrimination task. The more difficult issue, ultimately, is to understand how internal mental experience is related to this flow of information within neural pathways. I have already alluded to the type of experiment that seems desirable to begin addressing this issue—stimulating functionally defined circuits within the cortex of other humans, the only subjects, perhaps, with whom we share enough mental experience to make this issue truly approachable. This endeavor would require a substantive technical breakthrough, of course, so that neural circuits could be activated with fine spatial...
and temporal resolution in a minimally invasive manner. Even this level of inquiry would be no panacea, however, since as many questions would likely be raised as answered. But I feel certain that the “next” generation of important questions would at least become clear at that point.

Though I am sensitive to the issue of “hard” limits to our understanding, the overall endeavor of cognitive neuroscience is grand. It is worth the dedication of a scientific career, and it certainly beats cloning another gene!

JOCN: Thank you.

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