Neuronal Decision-Making Circuits   Minireview

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Studying the neural basis of decision-making has largely taken one of two paths: one has involved cell-by-cell characterization of neuronal circuits in invertebrates; and the other, single-unit studies of monkeys performing cognitive tasks. Here I shall attempt to bring these two disparate approaches together.

We tend to think about choices and decisions as momentous, life-changing events: whether to take a job, to get married, to buy a house. We also consider choices and decisions to be cognitive processes: we rationally enumerate the options, weigh them against our likes and dislikes, hold up the choices against our moral values, and imagine the consequences of the choices based on our previous experience and knowledge. Undoubtedly, some of our choices are accomplished this way, but we make many more choices without much rational thought: we decide to walk, but do not think about whether to take the first step with our right or left foot; we walk over to the cafeteria for lunch with little thought about the intricacies of the path we take; we may even make moral choices unconsciously and have difficulty reasoning why we make them [1]. Likewise, some animals with very little cognition (for example, slugs, crabs, even leeches) constantly make choices about how to handle external stimuli and internal drives (such as hunger, reproduction, circadian rhythms): they decide which stimuli to ignore, how to respond to another animal (for example, chase it off, escape from it, feed on it, mate with it), whether to act directly or indirectly, whether to respond immediately or to wait awhile. Many of the choices that animals make are species-specific (a dog and a cat respond very differently to a verbal command), whereas others are idiosyncratic (we would be surprised if Dick Cheney chose to emulate Mahatma Ghandi, for instance, or if Snoop Dogg decided to make a CD of Gregorian chant).

Research on how brains make decisions has been driven by two major traditions: psychological/cognitive and neuroethological/behavioral. Those working in the psychological/cognitive tradition typically study humans or animals doing behaviors that are human-like. Cortical recordings from single units in awake, behaving monkeys is the favored approach, while the monkeys perform such tasks as making sensory discriminations [2,3], judging the value of a stimulus [4] or the probability of its success [5], or playing interactive strategy games that depend on the behavior of another agent, either protoplasmic or siliconic [6]. In these studies, neurons become candidate decision-makers on the basis of three kinds of properties: first, their firing patterns are more correlated with the decision made than with either the stimulus or the motor output; second, the timing of their changes in activity closely match the timing of the behavior

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being chosen [7]; and third, stimulating localized areas of the cortex centered on that neuron can bias the decisions that the monkey makes [8]. These studies have the distinct advantage of being close to what springs to mind when we 'make a decision' [9], but they have the disadvantage of being embedded in complex brains, precluding a detailed study of the neuronal circuitry and cellular properties underlying the behavior.

Because a major motivation for the neuroethological/behavioral approach is to find underlying neuronal circuits responsible for the behaviors, neuroethologists select animals and behaviors for their simplicity, accessibility, and robustness. Such studies start with more natural behaviors and tend to consider choices between qualitatively different behaviors (such as swimming *versus* crawling, or feeding *versus* egg-laying) or between different forms of the same behavior (such as ingesting food *versus* rejecting it, or swimming *versus* scratching). The strength of this approach is that it can answer specific questions clearly and convincingly. A weakness is that the mechanisms found for decision-making in a leech might not be the same as those found in a sea slug, much less in a mammal like us. I will argue, however, that building an interface between psychology/cognition and neuroethology/behavior will help to find the neuronal circuitry and cellular mechanisms responsible for decision-making in all animals.
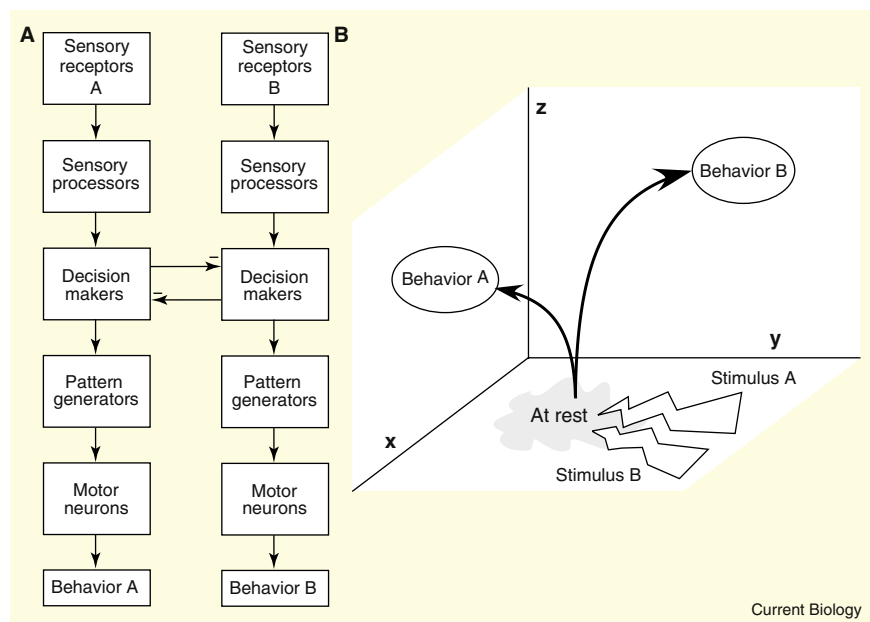
It is important to remember that many profound insights are being generated using techniques, such as functional imaging or electroencephalography, that are never likely to achieve neuronal resolution. Furthermore, deep insights have come from considering individual neurons and parts of the brain as information conveyors, with little attempt to fathom the circuitry underlying the coding and decoding of information [10,11]. The remaining discussion will assume the point of view, without further consideration, that knowing the detailed neuron-by-neuron circuitry underlying decision-making is beneficial and would make even the lower resolution or information coding studies more interpretable. To discuss the circuitry underlying decision-making requires a short consideration of two general types of neuronal mechanism that have been proposed for making decisions.

Neurons and Behavioral Choices

Historically, the first approach for understanding how brains cause behavior was to consider that all behaviors, however complex, are composed of reflexes: sensory input automatically produces a motor output [6]. The particular response produced can be influenced by many complicating factors — for example, inherent biases, internal states, age, experience, the presence of other stimuli — but the standard approach is to define the minimal stimulus-response kernel, then add on the various embellishments one at a time. In this approach, decisions are made by specific neurons at the transition between sensory and motor processing: highly processed sensory activity provides input to the decision makers, activity of which triggers a particular behavior (Figure 1A). Typically, decision makers do not themselves connect to motor neurons but instead activate a 'pattern-generator', a neuronal circuit that produces a spatiotemporal activity pattern, which in turn drives constellations of motor

Figure 1. Two different possibilities for the way that neuronal circuits decide between alternative behaviors.

(A) A reflexive possibility. Two different behaviors are triggered by different sets of sensory neurons, although the sensory neurons activated may overlap extensively in location and timing. The sensory input is then processed, often in complex ways, presenting highly abstracted input to the decision makers. Once activated, these decision makers turn on the pattern generator for behavior A and turn off the pattern generators for other behaviors; in this case, mutual inhibition between the decision makers is indicated, although the inhibition could be at any of the levels. Adapted from [12]. (B) A dynamical possibility. The graph represents the activity of three decision making neurons or groups of neurons, x, y, and z. (Such an analysis could be done for any number of neurons or neuron types, but it would require an additional axis for each one.) Stimuli A and B affect the activity of all three neurons/types, which initiates two different behaviors by triggering two different activity patterns in the three cells/clusters. The ovals represent locations in the activity space that are stable (when the activity enters either region, is sustains itself within that region). The regions between the ovals are unstable, so that activity tends to move toward one of the stable regions (they are 'attractors'), or falls back to rest.

Current Biology

neurons to produce a useful, coordinated behavior [12]. In its most extreme formulation, this approach posits that decision makers are both necessary and sufficient for selecting a behavior: stimulating them produces the behavior and ablating them eliminates at least one of the behavioral options. In this extreme view, the only time that a decision maker is ever active is during the time when its particular behavior is selected. In this scheme, understanding decision making means identifying the decision makers and determining their inputs.

In the neuroethological tradition, 'decision neurons' were originally called 'command neurons', because stimulating a single one of them reliably commanded a complex behavioral pattern [13]. Later, Kupfermann and Weiss [14] argued that real behaviors are likely to result from the activation of neuronal populations, which they termed 'command systems'. The notion that command neurons are, in fact, *the* decision makers was an assumption, a hypothesis that required testing. It also seemed reasonable that the decision to produce one behavior rather than another one would be a winner-take-all contest among command neurons, with the winner inhibiting all the losers [15]. There was some early suggestive evidence that this was accurate: intracellular recordings from 'loser' command neurons received strong inhibition when a winning behavior was elicited [16].

A qualitatively different approach to decision making, one favored by neural net theorists, is a dynamical one, illustrated in Figure 1B, in which the same decision-making neurons are active during several distinct behaviors but their activity patterns are different in each behavior [17]. These different patterns are often called 'attractor states' because they are stable — they can persist for long periods — whereas similar activity patterns are unstable and become ('fall into') one of the attractor states. The behavior produced by an attractor might be maintained (as in, standing, sitting, lying down) or cyclic (as in walking, swimming, chewing), although cyclic ones have received more attention. An important distinction between attractor and reflexive mechanisms

is that, because all the attractors are composed of the same neurons, there is no inhibitory interaction among separate populations of decision makers in the different attractor states.

Is there a single mechanism of decision-making in known neuronal circuits? The clear answer is no. Even when there is evidence for inhibition among behavioral circuits, the site and source of the inhibition are not the same in different systems. I will give some examples that are discussed more fully in a recent book chapter [12].

Reflexive *versus* Dynamical Decision-Making in Neuronal Circuits
Inhibition between Behavioral Circuits

In the European medicinal leech, *Hirudo*, feeding suppresses all responses to tactile stimuli [18]. When these leeches begin to feed, the only change in the tactile sensory pathways is presynaptic inhibition of the terminals made by the sensory neurons onto all of its central targets [19]. So, just as in mammalian pain sensation [20], the choice to not respond to mechanosensory input is made by gating out sensory input at the first synaptic site in the reflex pathway. A more complicated variation on this theme is that swimming inhibits feeding in the sea slug *Pleurobranchaea* [21]. The feeding pattern generator includes one group of neurons (I2) that excite a second group (I1 neurons), which in turn feed back to inhibit the I2 neurons along with many other neurons; this feedback helps to produce the rhythmic feeding motor pattern (Figure 2A). During swimming, particular neurons (A-ci1 and others, as yet unidentified) are excited by all the swim pattern-generating neurons, so that they are continuously active throughout the swimming bout. The A-ci1 neurons strongly excite I1 neurons, which feed strong and steady inhibition onto all the feeding-generating neurons, breaking the rhythmic feeding motor pattern and turning it off. In this case, swimming inhibits feeding by interactions at the level of pattern-generating neurons, rather than at the level of sensory input as in the leech or among
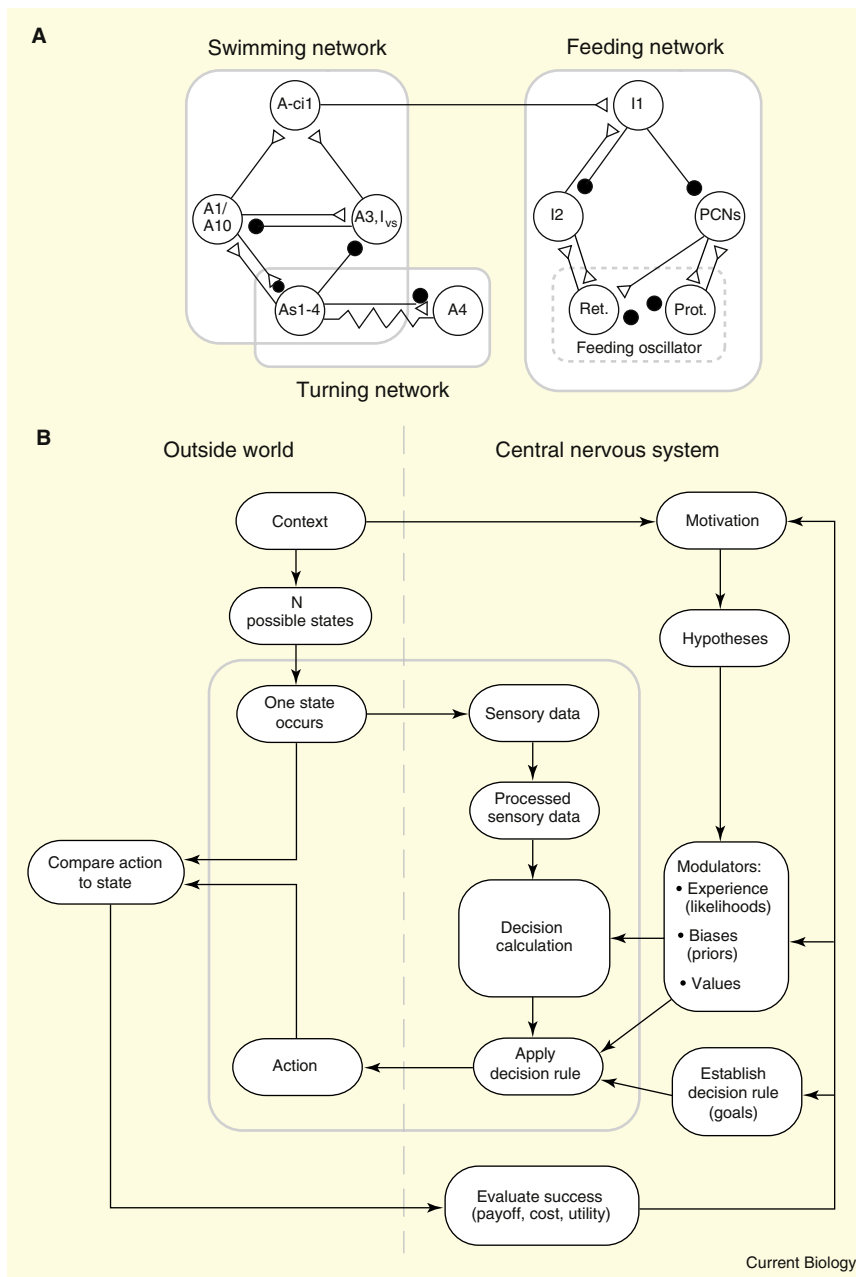
A

B

Figure 2. Neural networks that produce decisions in monkeys and sea slugs.

(A) The circuitry underlying the interactions among swimming, feeding, and turning in the sea slug, *Pleurobranchaea*. Circles represent individually identified neurons or small clusters of neurons. Open triangles are excitatory synaptic connections and blackened circles are inhibitory connections. Lines ending in both symbols indicate a connection that is mixed inhibitory and excitatory. Adapted from [12]. (B) A network that summarizes the kinds of decisions made by monkeys in selecting among two or more sensory stimuli. The smaller boxes represent the kinds of features and information processing that take place in the outside world (to the left of the dashed line) and in the monkey's brain (to the right of the line). In the original diagram, there were equations in many of the boxes representing the kinds of processing that are performed in the brain. The large grey box encloses the core decision-making elements. The other boxes modify the function of the decision making core (inside the large grey box). Adapted from [3].

decision-makers are *not* dedicated to a single behavior, but instead are active during several behaviors — they are *multifunctional*. Similarly, the pattern generators for turning while crawling and for swimming in the sea slug are composed of the same neurons, operating in different modes [23]. At low levels of tactile stimulation, the slug crawls in a direction dictated by the relative levels of activity in four serotonergic command neurons (As1-4); as the tactile sensory input is increased, the system becomes oscillatory and produces a swim-like escape response (Figure 2A).

Evidence for Dynamics: Covariation Is the Key

Appropriately placed tactile stimulation of a leech produces either swimming or crawling with nearly equal probability [24]. Using voltage-sensitive dyes to monitor the activity of many individual neurons at once, only a few neurons were found to have membrane potential trajectories that were different before swimming from their trajectories before crawling. Because these neurons had different activity patterns before either behavioral motor pattern was expressed, they were good candidates for being decision-makers. Stimulating these neurons individually, however, did not influence whether swimming or crawling occurred. Looking more deeply into the activity patterns, the co-varying activity of a small set of neurons discriminated between swimming and crawling at an even earlier time (an average of 290 milliseconds earlier) than did any of the individually discriminating neurons. Depolarizing or hyperpolarizing one of these 'group-discriminating' neurons (cell 208) significantly biased the behavior toward crawling or swimming. Surprisingly, the

decision-makers, a suggested mechanism by which feeding in a sea slug diminishes its withdrawal response to touch [16].

Evidence for Dynamics: Multifunctional Decision Neurons

Touching a leech at its front end reliably elicits a shortening response, even if the animal is in the midst of swimming [22]. In line with the 'inhibition-among-decision-neurons' hypothesis, this tactile stimulus strongly inhibits one of the most powerful swim command neurons (cell 204). When three other command neurons (cells Tr1, SE1, and 61) were tested in exactly the same way, however, they were found to be *excited* during shortening. This means that 75% of the neurons that command swimming when stimulated individually are excited by stimuli that elicit shortening, a behavior incompatible with swimming. This finding suggests that individual

two populations of neurons did not overlap: the group discriminators were a separate population from the individual discriminators. This implies that the 'individual discriminators' did not help to make the decision, but rather carried out the decision that was made nearly 300 milliseconds earlier by the co-varying group discriminators. In fact, the previously identified command neurons for swimming were among the individual discriminators, implying that their role is to activate a motor program rather than to decide which behavior to choose.

A similar conclusion about the function of command neurons came from a study of the role of two identified command neurons in initiating feeding in the pond snail *Lymnaea* [25]. Because neither command neuron was active earlier than one of the central pattern-generating interneurons, their functional role appears to be to set the frequency of the feeding rhythm and to determine the burst durations of motor neurons. This study concluded that the decision to start feeding was most likely made by distributed excitation among the CPG neurons rather than by specialized command neurons.

The Future: Possible Cross-Influences

Because the two traditions — the psychological/cognitive and the neuroethological/behavioral — are interested in different aspects of decision-making, is there any reason for them to interact? Are there lessons to be learned in bringing together the two approaches? I believe that the nervous systems of all complex animals — those with 302 or more neurons [26] — have common mechanisms for dealing with the outer and inner worlds. The facts that action potentials were first explained in squid [27,28], synaptic potentials in frogs [29], lateral inhibition in horseshoe crabs [30], and mechanisms of synaptic plasticity in the sea hare, *Aplysia* [31], bring home the power of the comparative approach: using whatever animal is best suited to answer a particular question [32]. So, how can research on behavioral choice in invertebrates inform research on vertebrate decision-making?

For all the elegance of correlating neuronal firing patterns with behavioral choices in monkeys, and the ability to influence those choices by stimulating localized regions of the brain, the models that emerge from such studies (Figure 2B) are formal, with boxes that represent firing rates and psychophysical capabilities [3,6]. A major thrust of this work is to describe the relationships among the boxes, ideally by rigorously fitting data with equations developed from psychophysics. Invertebrate studies, on the other hand, yield specific circuit diagrams and biophysical models that explain how the behavioral choices could be made [12]; in Figure 2A, the circles and lines represent individually identified neurons and the connections among them. Furthermore, such circuit diagrams suggest how circuit modules can be used to produce different behaviors and how to test whether the circuits use neuromodulation or changes in dynamics to switch from one behavior to another [17]. Hence invertebrate studies can, in principle, add biophysical reality to the formal arrows and boxes generated by monkey studies.

How about the other direction: how can the mammalian studies influence the invertebrate studies? A major contribution of the psychophysical approach used to study monkey decision-making is the hard-headed quantification of the experimental data and the parsing of the different elements of decision-making, such as sensory discrimination, built-in biases, experience (also called 'priors'), and values [3,6,9]. Despite a tradition of using behavioral data to test quantitative models in ethology [33], neuroethological studies of decision making tend to be relatively qualitative and model-light. For the invertebrate studies to inform monkey work, invertebrate systems must be tested on psychophysical tasks comparable to those used for monkeys, There have been some steps in this direction, such as studying the cost-benefit calculations made by slugs in selecting from their behavioral repertoire [34] and how food value affects foraging choices in locusts [35]. The cellular mechanisms of these behavioral capabilities are much more likely to be found in invertebrate preparations, but they will be of only marginal interest to monkey experimenters unless the level of psychophysical detail is similar and the behavioral capabilities prove to be at least qualitatively the same. This would open the mammalian experiments to the richness of circuitry and modulation known for invertebrate nervous systems [12,17,36]. This kind of synergy would add considerable strength to the study of behavioral choice.

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