The Sea Slug, *Pleurobranchaea californica*: A Signpost Species in the Evolution of Complex Nervous Systems and Behavior

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Synopsis

How and why did complex brain and behavior evolve? Clues emerge from comparative studies of animals with simpler morphology, nervous system, and behavioral economics. The brains of vertebrates, arthropods, and some annelids have highly derived executive structures and function that control downstream, central pattern generators (CPGs) for locomotion, behavioral choice, and reproduction. For the vertebrates, these structures—cortex, basal ganglia, and hypothalamus—integrate topographically mapped sensory inputs with motivation and memory to transmit complex motor commands to relay stations controlling CPG outputs. Similar computations occur in the central complex and mushroom bodies of the arthropods, and in mammals these interactions structure subjective thought and socially based valuations. The simplest model systems available for comparison are opisthobranch molluscs, which have avoided selective pressure for complex bodies, brain, and behavior through potent chemical defenses. In particular, in the sea-slug *Pleurobranchaea californica* the functions of vertebrates’ olfactory bulb and pallium are performed in the peripheral nervous system (PNS) of the chemotactile oral veil. Functions of hypothalamus and basal ganglia are combined in *Pleurobranchaea*’s feeding motor network. The actions of basal ganglia on downstream locomotor regions and spinal CPGs are analogous to *Pleurobranchaea*’s feeding network actions on CPGs for agonist and antagonist behaviors. The nervous systems of opisthobranch and pulmonate gastropods may conserve or reflect relations of the ancestral urbilaterian. Parallels and contrasts in neuronal circuits for action selection in *Pleurobranchaea* and vertebrates suggest how a basic set of decision circuitry was built upon in evolving segmentation, articulated skeletons, sociality, and highly invested reproductive strategies. They suggest (1) an origin of olfactory bulb and pallium from head-region PNS; (2) modularization of an ancestral feeding network into discrete but interacting executive modules for incentive comparison and decision (basal ganglia), and homeostatic functions (hypothalamus); (3) modification of a multifunctional premotor network for turns and locomotion, and its downstream targets for mid-brain and hind-brain motor areas and spinal CPGs; (4) condensation of a distributed serotonergic network for arousal into the raphe nuclei, with superimposed control by a peptidergic hypothalamic network mediating appetite and arousal; (5) centralization and condensation of the dopaminergic sensory afferents of the PNS, and/or the disperse dopaminergic elements of central CPGs, into the brain nuclei mediating valuation, reward, and motor arousal; and (6) the urbilaterian possessed the basic circuit relations integrating sensation, internal state, and learning for cost-benefit approach-avoidance decisions.

Introduction

A natural starting point in reconstructing the evolutionary pathways of neural and behavioral complexity is from the nature of the common ancestor of the major bilaterian radiations. While the animal is doubtless extinct, its nature can be inferred. It is expected to have been rather simple in behavior, body form, and nervous system. It lacked the behavioral and neural complexity that comes with segmentation, articulated skeletons, and more invested
reproductive strategies. Thus, approaching the evolution of complexity should include study of simpler animals likely to have retained, or reverted to, simpler, common ancestral characters.

The simplest model systems presently available for comparison are opisthobranch molluscs, which have been studied in depth for the neuronal mechanisms underlying basic decision processes. They have avoided selective pressure for complex bodies, brain, and behavior through potent chemical defenses (Wägele and Klussman-Kolb 2005; Cimino and Ghiselin 2009). In particular, the sea-slug Pleurobranchaea californica (Fig. 1) provides a model organism in which the neuronal circuitry for approach-avoidance decision has been well described. Approach-avoidance, in one form or another, is a most basic decision in foraging and most economic behavior. The neuronal circuitry can be compared directly with that of vertebrates and insects.

As a reference species to mark the evolutionary course of the complexity of the brain, Pleurobranchaea has desirable simplicities of body form, nervous system, and behavior. The neuronal circuitry has been mapped that underlies multiple types of decision fundamental to animal functions (Gillette 2014). The animals’ simple characters recapitulate those likely in the ancestral bilaterian. They are: (1) minimalist neuronal circuitry for foraging behavior; (2) a soft, unsegmented body with a hydrostatic skeleton; (3) ciliolocomotion; (4) an extensive peripheral nervous system (PNS); (5) incomplete centralization of the central nervous system (CNS); (6) a simple reproductive strategy of cooperative hermaphroditism and pelagic larvae; (7) characteristic asociality and nonaggression (except for copulation and cannibalism); and (8) an uncomplicated regulation of hunger mediated by simple gut-stretch and serotonin, without apparent regulation of feeding through hormonal messaging from nutritional stores (Gillette 2006). These characteristics are considered below.

A simple neuronal circuit for approach-avoidance decision

A basic set of behavioral transitions organizes foraging activity (Fig. 2). Animals transit from quiescence, characteristic of satiated states and circadian phases, to active exploratory locomotion roused by internal hunger and appetitive stimuli. Attendance to salient environmental stimuli prompts approach, in turns orienting toward the stimuli, or active avoidance. Active feeding tends to suppress avoidance, but transition to avoidance occurs upon satiation or some chance exceeding of a threshold of pain (as perhaps through noxious prey defense). In Pleurobranchaea, the neuronal basis of this organization is represented by a quite simple set of circuit relations (Fig. 3).

Appetitive state, the internal bias for appetitive and consummatory behavior, is expressed in the excitation state of the homeostatic feeding CPG (Hirayama and Gillette 2012). Thus, feeding thresholds are closely related to spontaneous activity of neurons in the feeding network. By default, the CPG for directed turns reacts to incoming stimuli by avoidance behavior. However, the excitation level of the feeding network regulates final approach-avoidance decisions by switching the turn response to positive orienting (Hirayama and Gillette 2012). Appetitive state is an integration of internal state (hunger/satiation), sensory input, and memory. Satiation is represented in the basal, spontaneous excitation state of the feeding CPG, and sums with incoming inputs from sensation and memory. Thus, in satiated animals, or those conditioned to avoid food, stimulation by food can fail to bring the feeding network to threshold excitation for changing the direction of turning, and avoidance is the result as shown in the simplified model of the neuronal network for making decisions (Fig. 4).
Unsegmented ciliolocomotors
Unsegmented bodies and ciliolocomotion both are arguably likely characters of ancestral bilaterians (Hejnol and Martindale 2008), retained in the ur-mollusc and transmitted in the opisthobranch lineage. Molluscs were left out of the rush to segmentation in the evolution of ecdysozoans, chordates, and annelids. Segmentation may have evolved independently in these lines, perhaps led by advantages lent to undulatory locomotion and burrowing by serially organized flexor/extensor muscle modules. The segmental, coupled, central pattern generators (CPGs) could be simply coordinated by descending inputs from the CNS upstream, as in leeches and lampreys (Grillner et al. 1991; Friesen and Kristan 2007). Segmentation, if acquired, might have been lost (Wanninger et al. 2009). The most basal, worm-like solenogastres molluscs are unsegmented, and the experimentation with serial calcareous plates in the skin of chitons went no further. Opisthobranchs largely retain ciliary locomotion, paddling with myriad cilia under neural control through a secreted trail of mucus. Snake-like undulatory locomotion on the substrate is uncommon in opisthobranchs and pulmonates, whose locomotion tends to be also slow compared with undulatory and legged animals of comparable size.

Extensive PNS
An extensive PNS, interfacing with the CNS, is characteristic of soft-bodied animals like the ancestral urbilaterian. The PNS, located next to the sensory interface, can perform initial filtration and contrast-enhancement of relevant stimuli (odors, images), and considerable sensory integration can occur before transmission to the CNS (Gillette 1991). In development, the CNS is formed from invaginating placodes of similar origin, and the PNS may be readily centralized in the course of evolution, which may have happened in the origin of the cortex and olfactory lobe (see below).

Simple reproductive strategies
Reproduction also follows characteristically simpler strategies. Cooperative hermaphroditism in opisthobranchs is a simpler mating strategy not generally entailing marked dimorphic specialization in body
form and behavior for particular sexual roles. In *Pleurobranchaea* there does not appear to be significant competition for male or female roles, as in some other hermaphrodites (Leonard 2006), and so there are no specific behaviors evolved that would support such competition. Animals attach a curtain-like ribbon of eggs to exposed surfaces, apparently chemically well protected from predation, from which veliger larvae emerge into the plankton. Lack of brood-care requires no further specialization either in brain or behavior.

**Simple foraging strategies, asocial and unaggressive**

Foraging follows similarly simple guidelines (Gillette 2014). The animals are solitary, and are asocial and unaggressive beyond copulation and cannibalism. Without need for conspecific recognition beyond sexually mature mating partners, larger animals commonly eat smaller ones when the opportunity arises. Attributes of socially dependent cognition are absent.

**Uncomplicated regulation of appetite and decision by long-term reproductive and foraging strategies**

It is notable in opisthobranchs like *Pleurobranchaea* and *Aplysia* that they have not been shown to have the complicated regulation of appetite and behavior characteristic of many arthropods and mammals (Gillette 2006). They appear to have a less complicated regulation of hunger mediated largely by simple gut-stretch and serotonin. This differs markedly from insects and vertebrates, whose feeding behaviors are closely regulated through hormonal messaging from both the gut and nutritional stores to the brain. While peptides and their receptors related to those of mammalian brain are present in the molluscan CNS, and they have been shown to mediate various effects on the feeding CPG (e.g., Romanova et al. 2012; Bai et al. 2013), there is as yet no direct evidence for major roles in mediating satiation or appetitive state. The regulation of appetitive state in mammals by hormonal communication, such as by leptin reporting on fat stores to the hypothalamus, is associated with more complex and longer-term foraging and reproductive strategies than animals like *Pleurobranchaea* exhibit (Gillette 2006).

The bipartite sexuality of mammals and arthropods, and their reproductive strategies in mate selection and in brooding their young, or at least in placing the eggs in tightly optimal environments, demand greatly more complicated behavioral choices and sensory-motor patterning. In simple contrast, *Pleurobranchaea*’s basic economic life strategy appears to be to eat when its crop is not full, so as to grow as fast and as much as it can, to produce as many eggs as possible, get them fertilized, and find some convenient surface on which to abandon them (Gillette 2014). The regulation of the feeding CPG by nutritional stores in *Pleurobranchaea*, and as may well have been the case in urbilaterians, may be indirect. Indeed, the reproductive system may be in closer touch with the animal’s stored resources, and when conditions warrant, the reproductive system could shut down feeding in favor of reproduction through releasing egg-laying hormone (Ram et al. 1977).

**Analogies in action selection in sea-slugs and vertebrates**

Sufficient information is now available for directly comparing mechanisms for action selection in behavioral choice in the nervous systems of vertebrates and sea-slugs. They both perform the three basic
behavioral functions—acquisition of resources, defense, and reproduction. However, segmentation and an articulated skeleton endow the vertebrate with greatly more complex sensory and motor abilities than the sea-slug possesses. The skeleton anchors muscles with implanted receptors that indicate loads and stretch, as well as the relative angles of the joints. The information is mapped topographically by the brain to create a dimensional body image used to plan complex motor actions. Combined with sensory information from exteroceptors—eyes, nose, and ears—quite complicated goal-directed actions can be planned and executed rapidly with moment-to-moment corrections via changing sensory inputs. The complexity of the vertebrate body interacts with complications in sexuality (two sexes with differing agenda), in reproductive strategies (e.g., nesting, childcare), and in behavioral economics (sociality, nutritional storage); this complexity requires a quite more complicated brain.

The executive divisions of the vertebrate brain for action selection—basal ganglia, cortex, hypothalamus, and the downstream diencephalic and midbrain locomotor regions and superior colliculus—where actions are initiated and begun to be implemented, are evident in the most basal vertebrates, the lampreys (Stephenson-Jones et al. 2011). They are paralleled in the arthropod brain by analogs and possible homologs in the central complex and mushroom bodies (Strausfeld and Hirth 2013). Polychaete annelids have similar, and perhaps deeply homologous, structures (Tosches and Arendt 2013).

Correspondences in nervous function for opisthobranchs and vertebrates emerge in the flow and transformations of sensory information for approach-avoidance decision for the source of an odor localized in space (Fig. 5A). First, the odor is encoded at the periphery both for aromatic qualities and placement. This information is processed in a first stage relay where stimulus qualities may be given a degree of salience with respect to other stimuli, and still associated with a somatotopic spatial code. In the next stage a valence can be assigned on the basis of qualities of the odor, memory, and placement. This information is processed in a downstream to the CPGs that will mediate it.

Functional correspondences appear immediately (Fig. 5B). Vertebrates’ olfactory epithelium is analogous to the sensors of primary odors in Pleurobranchaea’s chemotactile oral veil. The direction to the source of an odor for a vertebrate will be associated with the orienting movements of the head and neck that locate the direction (Wallace et al. 1998), while in Pleurobranchaea the direction is encoded topographically from multiple stimulus sites on the oral veil via a putative mechanism for lateral inhibition (Yafremava et al. 2007; Yafremava and Gillette 2011). The oral veil acts in tracking both substrate-bound odor trails and water-borne odor plumes, consonant with a recent perspective on aquatic olfaction as evolutionary precursor to the terrestrial sense (Mollo et al. 2014). Thus, the first stages of vertebrates’ olfactory processing in the olfactory bulb (salience) and pallium (place mapping) are functionally analogous to the PNS in the oral veil of Pleurobranchaea. Assignment of valence (net attractiveness or aversiveness) in the vertebrate is made through the integrated actions of pallium, basal ganglia, and hypothalamus, so that decision is made on the basis of qualities of the odor, memory, and homeostatic need. For Pleurobranchaea, the feeding CPG embodies the motivational drive of the hypothalamus and sums it with incentivized inputs from the oral veil like the basal ganglia—the final state of excitation determines whether thresholds for appetitive behaviors are reached. Premotor mapping for goal-directed motor activity in vertebrates emerges in pallium-basal ganglia interactions; in Pleurobranchaea such a site is inferred to be in the cerebral ganglia lobes, but the neurons have not yet been located.

From the basal ganglia, the patterned motor decision for approach-avoidance is transmitted to premotor regions of diencephalic and midbrain locomotor regions, then downstream to reticulospinal centers and thence to spinal CPGs. In Pleurobranchaea this corresponds to the control of turning, locomotion, and the escape swim by the multifunctional premotor network that mediates turns, locomotion, and swimming (TLS). The TLS, located in the cerebral ganglion, sends output to motorneurons and downstream CPGs by axons descending to the pedal ganglia (Jing and Gillette 1999, 2003). The TLS receives sensory information encoding the amplitude of the turn, presumably from the central site for mapping topographic stimuli. The direction of the turn, toward or away from the stimulus, is set simply by corollary outputs of the feeding CPG that may direct the flow of sensory place information from one side of the TLS network to the other by a putative, simple neuronal switch mechanism (Fig. 6).

Opisthobranchs’ pedal ganglia hold the final motor effectors for turns and locomotion (Fredman and Jahan-Parwar 1980; Popescu and Frost 2002; Jing and Gillette 2003), and CPGs for swimming in
some species (Satterlie 1985; McPherson and Blankenship 1991; Thompson and Watson 2005). They are functionally analogous to vertebrates’ hind-brains and spinal cords and to insects’ nerve cords, and may share homology as well. Thus, in olfactory tracking by Pleurobranchaea and vertebrates the close functional analogies suggest that the components are to some degree homologous in origin.

Relative to gastropod molluscs, vertebrates and arthropods depend to a greater extent on speed and coordination. The segmented bodies and skeletons of arthropods and vertebrates, their sophisticated
exteroceptors and vestibular interoceptors endow abilities for rapid and coordinated three-dimensional locomotion during foraging and escape. Opisthobranchs, with their potent chemical defenses, rarely need rush so. Thus, it seems likely that the discrete executive modules for action selection in the vertebrate brain were selected to provide efficient processing of the greatly more involved topographic mapping of sensory inputs and similar mapping for greatly more complex motor plans. The same decisions for simple approach or avoidance of salient stimuli in opisthobranchs like Pleurobranchaea entail a relatively small number of neurons that achieve similar results by the slow, deliberate control of a soft body (Jing and Gillette 2003).

Distributing specialized responsibilities for action selection among the different brain modules of vertebrates also came with evolution of interesting neuronal mechanisms for rapid patterning in action selection and motor control. In particular, the frequent involvement of serial inhibitory lines within the basal ganglia, and from them to downstream motor centers, is not apparent in the CNSs of opisthobranchs. Such serial inhibitory lines involve neurons with a high level of spontaneous spike activities, and they are involved in comparisons of excitation in parallel circuits, such as in the direct (net inhibitory) and indirect (net disinhibitory) pathways of the basal ganglia that may compare the costs and benefits of given actions (Houk 2007). The outputs of the basal ganglia to downstream motor centers are also disinhibitory to motor circuits with a high underlying state of excitation, and permit rapid expression of quite complex motor programs. Disinhibitory processes in action selection and motor control in molluscs are not so prominent as to have been notable in the history of molluscan neuroethology. Indeed, GABAergic neurons are sparse in the molluscan CNS relative to the vertebrate CNS (Diaz-Rios et al. 1999; Gunaratne et al. 2014).

Comparative aspects of serotonergic networks

Serotonergic neurons of Pleurobranchaea and other molluscs (Sudlow et al. 1998) are mostly embedded in diverse motor networks in the CNS, including the CPGs of feeding and multifunctional TLS, and the pedal ganglion’s locomotor effectors. The serotonergic neurons are also coupled electrically and chemically to form a distributed network active in mechanisms of general arousal. In contrast, the central serotonergic neurons of vertebrates are concentrated into the raphe nuclei, from where they innervate the rest of the nervous system, including the motor CPGs (reviewed by Gillette 2006). The connectivity and functions of serotonergic neurons of molluscs and vertebrates show marked analogies. Thus, vertebrates’ serotonergic neurons are also coupled among the various nuclei, have specific innervation targets in the brain and spinal cord, and receive reciprocal feedback from the CPGs and

Fig. 6 A simplified model for control of the turn by excitation state of the feeding motor network. A simple neuronal switch mechanism under control of corollary discharge from the CPG mediating feeding is postulated. (A) When the activity of the network is low, sensory inputs from the oral veil drive avoidance turns, away from the site of the stimulus. (B) Increased activity of the network changes the avoidance response to an approach-turn toward the stimulus by a postulated disinhibitory mechanism that shifts activity to the contralateral side of the turn motor network. (This figure is available in black and white in print and in color at Integrative and Comparative Biology online.)
sensory-motor integrative regions that they innervate (Gillette 2006). Like their molluscan analogs, they act in arousal mechanisms. However, in the vertebrates, their central roles in arousal mechanisms now serve the hypothalamic peptidergic networks that became ascendant with increasing behavioral and reproductive complexity. Their concentration into the raphe nuclei may therefore be another instance of efficient packaging and modularization of function. These considerations imply that the serotonergic neurons of the common ancestor were integral components of CPGs, as they are for the CPGs of feeding and TLS in opisthobranchs. With increasing CNS complexity they would have coalesced into the various raphe nuclei, retaining aspects of their connectivity and functions.

**Analogies across the molluscan PNS and the vertebrate CNS**

The PNS of gastropods performs relatively sophisticated and integrative functions that are centralized in vertebrates and arthropods. The head-region PNS in *Pleurobranchaea*’s oral veil includes bilateral tentacle ganglia, other quite small but discrete ganglia, primary receptors, neuronal processes with multiple neurotransmitters, and receptors for appetitive chemicals such as trimethylglycine (Bicker et al. 1982; Moroz et al. 1997; Gillette et al. 2000). An important function of the PNS in the oral veil is encoding the loci of target stimuli. Sensory stimuli are mapped along the oral veil such that stimuli applied more laterally induce larger turns than stimuli near the midline (Yafremava et al. 2007). Moreover, if multiple stimuli are applied simultaneously to different sites in the oral veil, both the afferent sensory discharge and the resultant turn average their responses toward a predicted target center, indicative of a peripheral averaging mechanism like recurrent inhibition (Yafremava et al. 2007; Yafremava and Gillette 2011). Such positional mapping creates an internal representation of external physical features, which is used by the TLS network to accurately turn to an estimated stimulus center or to orient away from it (Yafremava et al. 2007; Yafremava and Gillette 2011). In principle, this resembles the predatory body movements in toads and snakes directed by the optic nerve mapping to the optic tectum (Ewert 1997); in mammals such mapping directs saccades, turning of the head, and reaching (Lunenburger et al. 2001).

In *Pleurobranchaea* the CNS neurons encoding the sensory map have not been found yet, but the locus should be functionally analogous to the superior colliculus/optic tectum and may also embody rudiments of the medial entorhinal cortex and hippocampus in its positional-mapping functions. It is within reason to suppose that the urbilaterian employed similar peripheral and central neural networks for chemosensory spatial representations and for planning motor responses.

**Dopaminergic neurons in the PNS**

The dopaminergic networks of opisthobranchs’ nervous systems potentially reflect the organization of the common ancestor, largely originating in the sensory network of the PNS, and mediating roles in the valuation and reward of sensory stimuli. The dopaminergic systems of *Pleurobranchaea* and the other gastropods so far examined are quite distinct from those of other major animal divisions—chordates, arthropods, and annelids—in that the largest portion of dopaminergic neurons originates in the peripheral nerve network of peripheral nerves (Salimova et al. 1987; Kabotyanski and Sakharov 1990; Croll et al. 1999; Croll 2001; Vallejo et al. 2014). The dopaminergic afferents have capacities for motor arousal similar to those of DAergic neurons of mammalian substantia nigra; they can drive the feeding CPG in *Aplysia* (Kabotyanski et al. 1998) and *Pleurobranchaea* (J. W. Brown and R. Gillette, unpublished data). They also mediate food-related reward in an operant conditioning paradigm, and cause learning-related changes in the buccal feeding CPG of *Aplysia* (Nargeot et al. 1999; Brembs et al. 2002; Bedecarrats et al. 2013), similar to functions of substantia nigra pars compacta ventral tegmental area in mammals (Stephenson-Jones et al. 2011; Ryczko et al. 2013). Analogies and potential homologies for vertebrates’ and insects’ CNSs have been reviewed (Strausfeld and Hirth 1999; Brembs et al. 2002; Bedecarrats et al. 2013), and for chemotactile spatial representations and for planning motor responses.
for central integration of postural information, the peripheral plexus mediates both local reflexes and peripheral sensory integration for central decisions (Gillette 1991). For instance, in *Pleurobranchaea*'s oral veil there is a lateral inhibition-like mechanism used in localizing prey that averages topographically mapped stimuli (Yafremava and Gillette 2011), perhaps involving the dopaminergic system because D2 receptor blockers abolish it (J. W. Brown and R. Gillette, in preparation); (2) dopaminergic sensory cells are transiently found in molluscan early trocho-ophore larvae (Croll et al. 1997, 2003), possibly reflecting the ancestral condition; and (3) dopaminergic sensory cells appear in a stem phylum (Cnidaria) (Carlberg 1992; Antcil et al. 2002) preceding bilaterians. Primary dopaminergic sensory neurons are also found in nematodes where they are critical for foraging (Sulston et al. 1975; Sawin et al. 2000).

Interactions of dopamine, serotonin, GABA, and perhaps other neurotransmitters in the PNS potentially mediate rather complex computations, perhaps including incentivizing of stimuli. In addition to numerous dopaminergic primary sensory cells and afferents, the oral veil of *Pleurobranchaea* contains numerous GABAergic processes (Noboa and Gillette, unpublished data). Moreover, serotoninergic endings from central cell bodies broadly innervate putative sensory cells in the oral veil (Moroz et al. 1997). Serotonergic innervation is entirely central in origin from neurons driven by the feeding CPG (Sudlow et al. 1998). Exogenous 5-HT amplifies sensory discharge in the oral veil nerves (Achler 2006). Thus, as the content and release of 5-HT by serotonergic neurons involved in feeding are regulated by satiation (Hatcher et al. 2008; Dyakonova et al. 2015), the amplifying function of 5-HT may well be regulated by satiation. Preliminary observations indicate that peripheral dopamine and GABA mediate profound effects on sensory input to the CNS. The interactions of peripheral dopamine, GABA, and 5-HT could potentially perform quite sophisticated computations to represent the values of appetitive stimuli. Actions of dopamine in potentiating learning mechanisms in the feeding CPG of the buccal ganglion of *Aplysia* suggest that similar actions in the oral veil of *Pleurobranchaea* might lay down the learning traces for prey odors associated with noxious defenses (Noboa and Gillette 2013). In this regard, the innervation of the oral veil by serotoninergic endings of neurons active in the feeding network would be consistent with the feedback from rewards that would potentiate mechanisms of learning.

If the numerous somata of peripheral dopaminergic sensory neurons reflect an ancestral urbilaterian condition, then these neurons may have become centralized in the evolution of deuterostomes and proto- stomes that lack an extensive PNS. They are most analogous to the dopaminergic neurons of the vertebrate olfactory bulb that modulate thresholds and affect discrimination learning (Escanilla et al. 2009). It is also possible that they coalesced into the major dopaminergic nuclei of *substantia nigra pars compacta*, and ventral tegmental area, and the several other smaller dopaminergic nuclei. No one of them is more than a few synapses away from the primary sensory afferents with which they would have been associated in the common ancestor.

In contrast to the estimated thousands of subepithelial sensory neurons, central dopaminergic neu- rons are represented in opisthobranch and pulmonate snails in a relatively few somata (generally less than 200) scattered around the CNS (Croll et al. 1999, 2001; Croll 2001; Vallejo et al. 2014). Where they have been investigated (in the feeding network of *Aplysia* and the breathing network of the pond snail *Lymnaea*), they are elements of pattern-generating CPGs (Syed and Winlow 1991; Kabotyanski et al. 1998). They may parallel somewhat in function the 5-HT neurons also embedded in molluscan CPGs. More information is needed beyond the few instances available. However, it is also possible that dopaminergic neurons of CPGs in the urbilaterian aggregated and proliferated in evolution into the central nuclei that regulate motor arousal. The association of DA systems in molluscs with peptidergic and neurosecretory networks, so prominent in vertebrates in the physiology of reproduction, is a likely profitable area of exploration in reconstructing the evolutionary paths of the CNS.

**Neural and behavioral organization of the ancestor**

Notable differences between the decision circuits in vertebrates and molluscs suggest novel direction in the evolution of complexity. While the feeding network in *Pleurobranchaea* does the job of the vertebrate basal ganglia in summing appetitive state and directing decisions for approach or avoidance, the mechanisms of action appear quite different. The basal ganglia compare potential costs and benefits of likely actions through summation of activities in parallel direct and indirect pathways from striatum to output neurons of *substantia nigra reticulata* and *globus pallidus*; this is not clearly reflected in the known circuitry of the mollusc’s feeding network, although disinhibitory mechanisms are postulated to underlie the neuronal switch from avoidance to
approach (Fig. 5). Indeed, the inhibitory, GABAergic, medium spiny neurons that make up the direct and indirect pathways, and the GABAergic disinhibitory outputs to downstream motor centers, have no identified neuronal analogs in gastropods’ brains. The specialization of the basal ganglia for comparison of multiple incentives and actions can be reasonably related to the enhanced complexity of vertebrates’ sensory-motor abilities, their complex sociality, and their more invested reproductive strategies. Some cocktail-napkin modeling could suggest intermediate evolutionary steps leading from the neural circuitry of a simple ciliolocomotor like Pleurobranchaea to the minimum for a swimming lamprey-like organism with segmentation, endoskeleton, and high-resolution exteroceptors like eyes and lateral lines.

The simple organization of Pleurobranchaea’s circuitry for approach-avoidance decisions is more likely to resemble that of the urbilaterian ancestor than for any other model system so far studied in detail, based on its simple life-style and morphology, as considered earlier. The basic computation in decision is the integration of sensation with internal state and memory. Decision is made on an hedonic basis in terms of satisfaction of homeostatic drives and/or negative incentives (pain), as it is for vertebrates (Gillette et al. 2000). Like vertebrates, Pleurobranchaea makes decisions not strictly on the basis of information per se, but on how such information appears in the contexts of satiation and experience. That is, the use of “affect” itself as information in humans (Clore et al. 2001) is likely to have an ancient origin in decision circuitry already present in the urbilaterians. The parallels for gastropods with vertebrates and insects of the neuronal circuitry for sensory decision and its implementation suggest that comparative molecular profiling of identified neurons could provide valuable insights into the evolutionary paths and constraints of the evolution of complexity in brains and behaviors.

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