

Review

Dynamics of neural activity in early nervous system evolution

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New techniques for large-scale neural recordings from diverse animals are reshaping comparative systems neuroscience. This growth necessitates fresh conceptual paradigms for comparing neural circuits and activity patterns. Here, we take a systems neuroscience approach to early neural evolution, emphasizing the importance of considering nervous systems as multiply modulated, continuous dynamical systems. We argue that endogenous neural activity likely arose early in evolution to organize behaviors and internal states at the organismal level. This connects to a rich literature on the physiology of endogenous activity in small neural circuits: a field that has built links between data and dynamical systems models. Such models offer mechanistic insight and have robust predictive power. Using these tools, we suggest that the emergence of intrinsically active neurons and periodic dynamics played a critical role in the ascendancy of nervous systems and that dynamical systems present an appealing framework for comparing across species.

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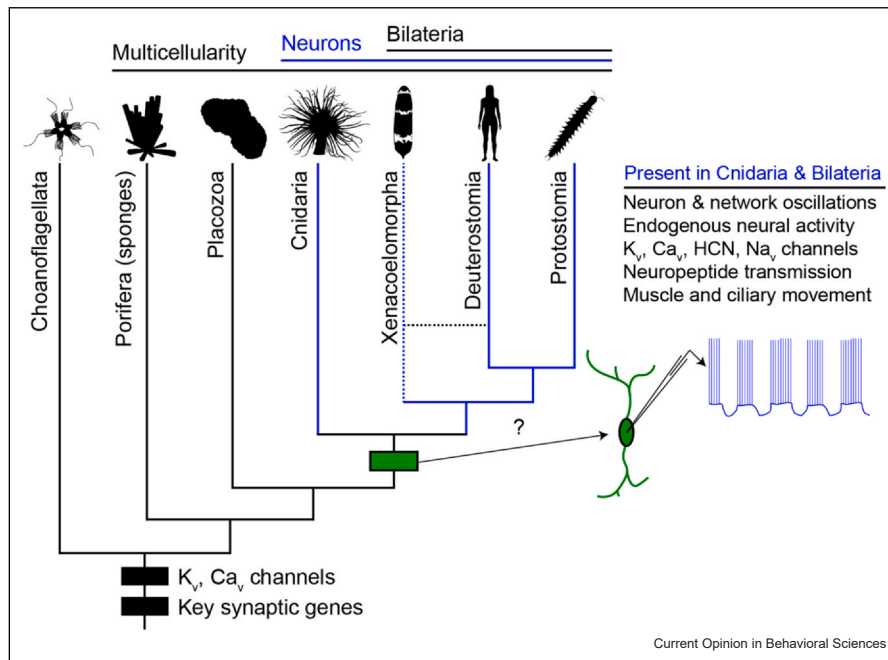
Introduction

Much of what we think about as neural arose before the nervous system. Foraging, predator avoidance, prey capture, mating, and other internal state-dependent changes in behavior all appear in single-celled organisms, powered by receptors, effectors, and ion channels that share common ancestry with those same elements in neurons [1,2] (Figure 1, Box 1). From this elaborate, pre-existing cell biological machinery, nervous systems are thought to have arisen ~600 million years ago in the form of a diffuse ‘nerve net’, with the possibility for multiple independent origins of neurons [3–7]. A fundamental goal of comparative neuroscience is to understand the origins and nature of these first nervous systems and to build on this understanding to examine principles of neural function and evolution following the massive diversification of animal life. What did the first nervous systems look like and what can we infer about their activity and potential function?

While extant organisms have undergone extensive, continuous evolutionary change, comparisons between basally branching groups, such as cnidarians, sponges, ctenophores, placozoans, choanoflagellates, and others, present the best chance of revealing information about the origins and early evolution of nervous systems (Figure 1). As perhaps the most distantly related animals with nervous systems built from homologous neurons, cnidarians — a phylum comprised of sea anemones, jellyfish, and corals — also provide opportunities to broadly explore nervous system diversity [8]. The molecular components of neurons across species are deeply conserved [9–11], yet they exhibit a wealth of complex and species-typical behaviors. In examining how this diversity of behavior arises, it is therefore important to study how neural components in each species are organized into larger systems [12].

Much of the discussion on early nervous system evolution has focused on the value of nervous systems for sensory-driven motor control. Interestingly, however, all known nervous systems also generate a wealth of endogenous activity, some of which is directly coupled to motor output but much of which is not [13–16]. Such activity is often periodic: in jellyfish, for example,

Figure 1



Animal phylogeny with annotated neural components. A subset of neural features that are present in both cnidarians and bilaterians are highlighted on the right: these may be due to homology or convergence. The green box highlights that intrinsically oscillating neurons may have been present in the cnidarian–bilaterian ancestor. Branch lengths are not to scale but are intended to show species relationships. Ctenophores omitted from the tree due to uncertainty in their placement but may have independently evolved nervous systems (see text). Images from PhyloPic.

Box 1 From single cells to nervous systems.

Nervous systems generate spontaneous activity that is modulated by sensory inputs and past experiences to ultimately produce behavior. This description sounds familiarly ‘neural’, but it could just as easily be used to describe the behaviors of single-celled organisms [31]. Bacteria, for example, have context-dependent navigation along sensory gradients [1]. Choanoflagellates, our closest single-celled relative, balance diverse taxis, feeding, and mating behaviors, including in a transiently multicellular context [90]. These feats are implemented in the chemistry of cellular signaling, protein interactions, and transcriptional states. This powerful biochemical processing used by single cells did not disappear following nervous system origins but was rather adopted.

As some single-celled organisms become larger, relying on diffusion becomes untenable. Paramecia achieve rapid, intracellular sensor-state-effector processes at a larger spatial scale using sensory- and voltage-gated ion channels to control membrane voltage [2]. Notably, this shift from chemistry to electricity to encode and propagate signals over longer distances appears to have evolved multiple times in multiple cell types and was a critical innovation for the evolution of neural systems [91,92]. However, even paramecia (at several hundred microns) leave open enormous potential niches that can be exploited by multicellularity.

The emergence of multicellularity and cell type specialization ultimately leads to the emergence of nervous systems. Extant multicellular animals without nervous systems include sponges and placozoans (Figure 1). These fascinating animals have a range of behaviors that arise from conserved mechanisms that are fundamental to neural function, including intercellular chemical signaling mediated by proteins that ultimately become synaptic machinery [27,28]. (Neuromodulation arguably existed before neurons, as both single- and multicellular organisms use intercellular release of peptide, small molecule, and gaseous signals to alter downstream cellular states via signaling pathways, transcription, and other ancient mechanisms that were subsequently adopted). Peptidergic signaling is of particular interest: it is present extensively in placozoa [28] and perhaps arose earlier in single-celled organisms, though appears more limited in sponges [10,11]. Neuropeptides have been shown to be markers of functional neural subtypes in all nervous systems studied [39,47,93–95], suggesting an ancient and fundamental role in neural function [46]. The use of other transmitters in early branching organisms remains unclear [39,96].

Coordinated sponge and placozoan behaviors show us that if sensation, state, and action are not sufficient causes to have a nervous system, then neither is scale alone [97]. Rather, nervous systems relieve the ceiling on what a multicellular organism is capable of. As organisms become stably multicellular with specialized cell types, the existing technologies for cell–cell communication enable coordination, perhaps via combinatorial endocrine chemical signaling [46]. With increasing size and geometric complexity, temporal precision of motor control was certainly one driving factor for the development of a nervous system [32], as was the ability to separate sensors from decision, state, and motor variables, reducing the ratio of sensors-to-actors [7,9]. However, we argue that the coordination of an organismal internal state at rapid timescales was just as pivotal, as was the ability to generate endogenous behavioral outputs.

rhythmic neural firing controls swim pulsing [17]; classical recordings have also revealed other ‘cryptic rhythmic activity’ of unknown function [18]. Because the periodic activity of single neurons can easily emerge from a small set of ion conductances [19], it is quite likely to have arisen early in nervous system evolution. When neurons are then coupled together or begin interacting with their environment through motor effectors, a wealth of controllable dynamics becomes accessible. From these observations, building on the views of classical cnidarian electrophysiologists [18], we suggest that the ability to generate endogenous neural activity that coordinates sensory, state, and motor variables was a critical driver in the origins and early evolution of nervous systems. The centrality of pacemakers in neural evolution was suggested over 50 years ago [18,20]; since this time, perspectives and tools for examining the behavior of modulated, small rhythmic circuits have greatly matured [21,22].

There is a conceptually well-established approach to studying evolution at the molecular and cellular levels, where one can examine the evolutionary history of genes and cell types [23–25]. In comparison, evolutionary comparisons at the systems level remain more ambiguous. Here, we offer a perspective on a subset of this problem, asking which challenges the first nervous systems were able to solve, which tools they had at their disposal, and which frameworks we can use to compare across distant species, and perhaps to infer ancestry. We approach these questions through the lens of cnidarian neurobiology and dynamical systems, with the hope of moving toward common frameworks for evolutionary systems neuroscience.

Functional perspectives on the origins of nervous systems

It is notoriously difficult to infer what ancestral organisms looked like using only existing animals. However, as the sister group to nearly all organisms with nervous systems, cnidarians offer opportunities to make inferences about the origins, evolution, and architecture of early nervous systems [8] (Figure 1). Cnidarians and bilaterians diverged roughly 600 million years ago, shortly after the origin of nervous systems: the conservation of key developmental pathways, aspects of neuronal cell biology, and some network structural features suggest that a nervous system appeared in their last common ancestor [8,26]; earlier divergent phyla such as porifera [27] (sponges) and placozoans [28] lack true nervous systems, while ctenophores (comb jellies) have a molecularly and structurally dissimilar nervous system that may have arisen independently [29,30] (Figure 1).

The nervous system of the cnidarian–bilaterian ancestor is thought to have been a nerve net, that is, diffuse,

tissue-spanning populations of cells that interact with each other via chemical or electrical coupling, specialized for controlling 2D sheets of effectors [20,31,32]. In support of this idea, both cnidarians and early divergent groups of bilaterians — like a subset of the worm-like invertebrates within Xenacoelomorpha — have nervous systems that include portions that could be described as nerve nets [33–37] (Figure 1).

What constitutes a nerve net? Anatomically they are diffuse, meaning the distance between pairs of neurons is both consistent and large relative to cell body diameter. Conversely, a collection of cells ceases to be called a nerve net if they become organized into a more tightly packed or structured group [38]. In many cnidarian and xenacoelomorph species, nerve nets exist alongside considerably more complex neural architectures that likely evolved secondarily — for example, the nerve rings of hydrozoan medusae likely represent condensations of an ancestral nerve net into a structure that now has a clearly different organization [38].

It is difficult, however, to delineate when a neural population has enough physical structure to no longer be called a nerve net. A functional definition of nerve nets would therefore be useful, including for thinking about drivers of nervous system evolution. Functionally, nerve nets are sometimes defined as an ensemble of cells in which the spiking of any neuron triggers a reproducible spatiotemporal pattern in the rest of the ensemble, as in *Hydra* nerve nets [35]. Alternatively, the probability of recruitment of downstream partners might vary from spike to spike and fall off with distance from the initiating neuron. Interestingly, the RFamide⁺ subnetwork in the jellyfish *Clytia* does not fit smoothly into either definition despite its clear status as an anatomical nerve net: it consists of columns of commonly corecruited neurons, separated by apparent boundaries across which probability of activity propagation is reduced [39].

Spatially extended coactivation of neurons is thus a prominent functional feature of nerve nets. One hypothesis is that these evolved as a way to rapidly convey information across the body of an organism once growth exceeded the scale that could be efficiently spanned by single cells or endocrine signaling. Many neural events like jellyfish pulsing [40], *Hydra* contractions [41], and anemone peristalsis [42] require patterned whole-body muscle contractions that could not be co-ordinated by epithelial conduction or endocrine mechanisms alone. This is consistent with the evolutionary hypotheses that nerve nets developed to co-ordinate sheets of contractile tissue [32,43]. These hypotheses emphasize co-ordination of movement over stimulus-response processing (which can be accomplished without neurons) and pose neurons themselves as evolving by way of a single predecessor cell type with both contractile and excitable

properties specializing into distinct muscle and neural components [5,18,32,44]. Extending this hypothesis, parallel nerve nets or hierarchical structure between nets might then have emerged from duplication and divergence in structure and/or signaling molecule usage. Apparent boundaries between subpopulations within a net, like those seen in the RFamide⁺ subnetwork, could have emerged as a site for context-specific gating of activity propagation through the organism. Such divergence into subpopulations with weak interpopulation coupling could allow repurposing of an original neuromuscular system for other functions.

It is also important to note an alternative hypothesis: that nervous systems first evolved to control ciliated cells rather than contractile tissue, with putative cnidarian–bilaterian ancestors using cilia for digestion and/or locomotion [31,45]. In this framework, the first nerve nets may have developed as secretory cells that regulated and synchronized the beating of ciliated cells, with a potential central role for combinatorial chemical signaling [46]. Hence, this theory poses neuromodulation as a core function of the earliest nervous systems. Nerve nets might also be a product of horizontal integration, meaning that nervous systems emerged from a series of vertical, local reflex arcs which then became horizontally connected [5]. Indeed, there are numerous examples of simple reflex arcs in cnidarians and bilaterians, perhaps the most extreme being a neural population that detects light and directly causes oocyte maturation by releasing a peptide onto oocyte precursors in the jellyfish *Clytia*; that is, a single neuron reflex [47,48]. Studies of cell type evolution are providing insights into these possibilities, with support existing for each hypothesis [5]. It is also important to consider the possibility that neurons and nerve nets have arisen repeatedly in evolution [4,5].

From reflexes to dynamics

While this discussion of nerve nets suggests functional advantages — for fast signal propagation and for interactions between reflex arcs — it has not addressed the dynamics of activity in those networks beyond the level of a single propagating neural event. What does activity in nerve nets look like, and why?

Decades of studying invertebrate neural networks have guided neuroscientists away from a view of bilaterian behavior as emerging from dedicated, event-driven ‘command’ pathways and toward a model of neural populations as interacting dynamical systems [22]. This is because many neurons are ‘multiplexers’ that participate in and influence the dynamics of multiple distributed subnetworks that generate multiple behavioral outputs [22,49,50].

In addition to extrinsically driven waves of neural activity that propagate from sensory receptors to effectors,

nervous systems also produce endogenous activity that arises from intrinsically active neurons. A striking feature of all nervous systems that have been studied to date, including those of cnidarians, is the presence of multiple endogenous rhythms [20] (Figure 1). This rhythmic activity can serve the developmental [51,52], state [53,54], and behavioral control [16,55,56] needs of multicellular animals across multiple timescales. Examples in the context of motor output include jellyfish swimming via rhythmic pulsing of the bell [40], *Hydra* extension-contraction cycles [57], and the peristalsis of many sea anemones [42,58]. Such endogenous activity was so prominently observed in classical cnidarian electrophysiology that some of the first theories of nervous system origins suggested that pacemaker activity drove the origins of nervous systems; in these theories, duplication and divergence of pacemakers led to a hierarchical organization, with higher-level subnetworks becoming insulated from effectors, leading to endogenous, non-motor rhythms [18].

Endogenous and extrinsically driven neural activity interact reciprocally: the pattern and magnitude of endogenous activity might determine whether a sensory input elicits a motor output and conversely whether sensory signals can change the subsequent dynamics of endogenous neural firing [22,59,60]. Further complicating this is the fact that neurons interact not just through fast synaptic transmission but also via diverse chemical signals, such as neuropeptides, that induce changes in network state by altering the physiological properties of neurons and their connections [21]. Sensory cues and endogenous activity also interact indirectly, as when endogenously generated movement changes an animal’s sensory environment [61,62]. Because of these extensive interactions, the endogenous activity of the nervous system is an open system: interactions with the animal’s environment keep its state from reaching equilibrium.

Multiplexing and endogenous activity efficiently allow the electrochemical state of the nervous system to maintain information about an animal’s history and survival needs and to use that integration to alter the way the animal holistically responds to new sensory cues. This view of neural networks as multiplexed and dynamic holds true in diverse bilaterian circuits, from worms to primates [21,22,63–65]. We believe such a dynamical perspective is also critical when thinking about the origins and evolution of nervous systems.

Form and function of endogenous neural activity

Endogenous activity, like that of the jellyfish swimming system, offers an alternative to a sensor-effector view of nervous systems. It also raises the questions: what might

Box 2 Behaviors of dynamical systems.

A system of multiple interacting variables exists at any moment time at a point in 'state space' defined by the value of each variable [98]. If the values of variables change with time, then the set of points the system traverses in state space yields a 'trajectory' of the system. In the absence of external input, the trajectory of a system of interacting variables approaches what is called its 'asymptotic' behavior, which can take one of three forms:

- *Steady-state behavior.* In the absence of external inputs, a state system might converge to a fixed value, called a stable fixed point or *attractor*. For example, the Nernst equilibrium of a neuron's membrane potential is a stable fixed point. If the state of the system is perturbed a small distance away from a fixed point, it will evolve back toward that point; the region of state space for which the system recovers to a fixed point is called the point's *basin of attraction*. Systems can also exhibit multiple stable fixed points (called *multistability*), in which case an extrinsic input can push the system from the basin of attraction of one stable fixed point into another. Stable attractors of a system can also form more complex shapes, including lines, rings, planes, and nonlinear surfaces.
- *Oscillations.* In two or more dimensions, systems can have limit cycles: periodic trajectories traversed by the system state over time. Like fixed points, limit cycles have basins of attraction, such that systems perturbed away from a limit cycle will recover toward that cycle over time. Two classic examples of limit cycles in neuroscience are the Hodgkin-Huxley model of action potential generation [99] and the Wilson-Cowan model of interacting excitatory and inhibitory populations [100]. Oscillations are easiest to study in low-dimensional systems or systems in which separation of timescales leads to only a few dimensions of dynamics that matter. Predicting the number and form of potential periodic signals in higher-dimensional systems is an unsolved problem of mathematics [66].
- *Chaos.* In the absence of stable fixed points or periodic limit cycles, systems can have chaotic dynamics, meaning that behavior is time-evolving and aperiodic, and their exact long-term behavior cannot be predicted. Such systems may show transiently periodic dynamics, but these are unstable and eventually vanish.

Behaviors of nonlinear systems as they converge toward these asymptotic behaviors are called 'transient dynamics'. Because systems only converge to their asymptotic behavior in the absence of noise and under zero or fixed external input, the behavior of biological systems can in fact be dominated by their transient dynamics. Two components of these transient dynamics are relevant to system behavior:

- *Transient oscillations.* Depending on how state variables interact, the state of a system approaching a stable fixed point can produce transient, damped oscillations. In neural circuits, coupling of a fast excitatory population with slow inhibitory feedback is one way to attain damped oscillations. Similarly, systems with stable limit cycles typically show oscillations that grow or decay in amplitude until they settle into the limit cycle. Chaotic systems can also produce transient periodic dynamics.
- *Persistence.* The rate at which a system approaches its steady-state behavior can be much slower than the intrinsic time constants of its constitutive elements. The different dimensions of a system might also approach their steady-state values at different rates: if some dimensions approach steady-state values much faster than others, this 'separation of timescales' can create effectively low-dimensional dynamics from high-dimensional systems. The separation of timescales is a boon to theoretical models, as it means that fast dynamics can be ignored and replaced with their steady-state values, allowing complex high-dimensional systems to be simplified to the point that they may be fruitfully studied. Conversely, fast dynamics can be studied in isolation by assuming that slow-evolving components of the system are essentially constant.

A final useful feature of nonlinear systems is the prevalence of *phase transitions*, wherein small changes in a system parameter, such as the input current to a neuron, can cause sudden and dramatic changes in its behavior. For example, a Type II Hodgkin-Huxley model neuron will abruptly transition from resting at a subthreshold membrane potential to periodic spiking as the magnitude of an input current is increased [101]. Mathematically, the study of these phase transitions is called *bifurcation analysis*. Changing the extrinsic input to a dynamical system, or any other system parameter, changes the location of its fixed points and limit cycles; sufficient change can cause these to collide, changing the topology of the system's state space.

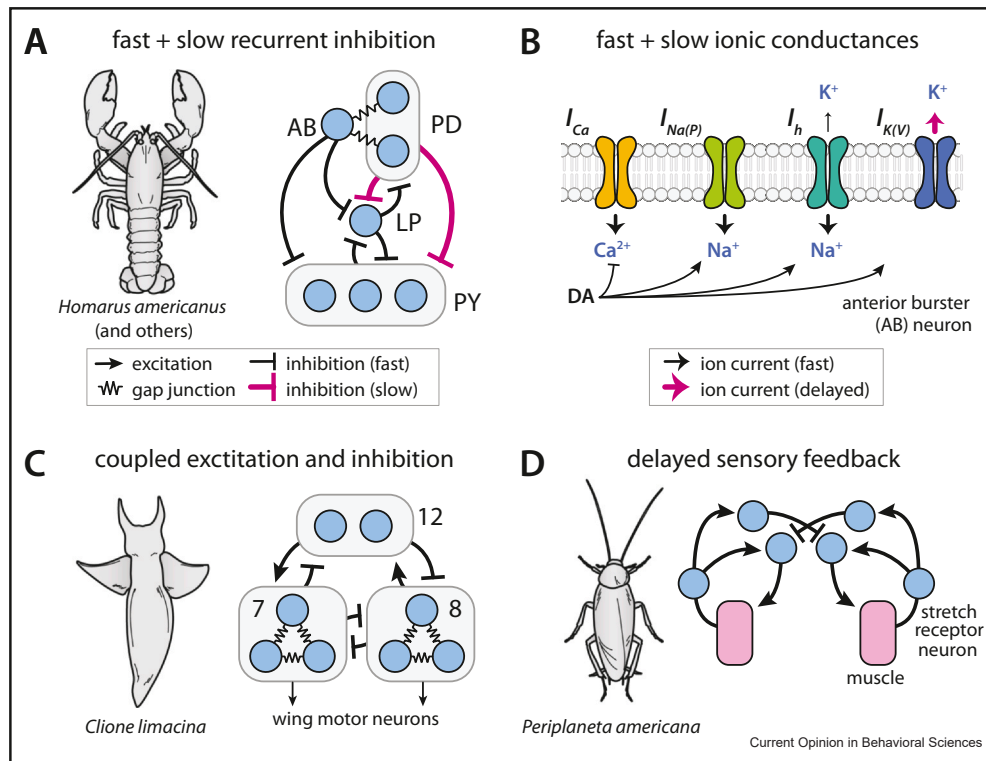
ancestral forms of endogenous neural activity have looked like, when did they arise, and how could they have been used? To examine this, we turn to dynamical systems theory. A dynamical system is a set of variables that evolve over time according to some predefined rules. Nonlinear dynamical systems can exhibit many behaviors, but these can be categorized into only a small number of types (Box 2).

The abundance of endogenous rhythms found in nervous systems makes sense from a dynamical systems perspective: periodic dynamics abound when system variables are coupled but evolve with different timescales [66]. Numerous two-dimensional neuronal spiking models produce periodic firing; for example, in the periodic-spiking Morris-Lecar model [19], the membrane potential of a neuron is maintained by a fast voltage-sensitive calcium conductance paired with a

delayed voltage-dependent potassium conductance. Voltage-gated calcium and potassium channels predate the nervous system and show that the ability to generate intrinsic oscillations requires minimal diversity of ion channel selectivity and voltage-gating kinetics [67,68] (Figure 1). This supports the idea that such neural oscillations may have emerged quickly and been important in early nervous system evolution [18].

Because of their simplicity, periodic dynamics also readily arise at levels beyond the single neuron. For example, periodic dynamics can be generated, or the periodicity of single neurons enhanced, in small networks of neurons where reciprocal interactions between cells with fast versus slow synaptic transmission introduce a difference of timescales [69]. In excitable tissue with different spatial and temporal scales of excitation and inhibition, propagating activity can produce

Figure 2



Diverse biological mechanisms for periodic neural activity. Neuroscientists have uncovered and modeled mechanisms for the generation of periodic intrinsic neural activity at the level of single cells, small ‘central pattern generator’ networks, and neuromuscular systems. **(a)** The pyloric rhythm of the crab and lobster stomatogastric ganglion is maintained by a recurrently inhibitory circuit with a mixture of fast and slow inhibition that contributes to periodicity [69]. **(b)** The anterior burster (AB) neuron of the pyloric circuit is also itself intrinsically active, a property that is maintained by a mixture of fast and slow ionic conductances. Core to this intrinsic activity are three fast depolarizing currents (a calcium current [I_{Ca}], a persistent sodium current [$I_{Na(P)}$], and a hyperpolarization-activated inward current [I_h]) and a slow hyperpolarizing current (a delayed-rectifier potassium current [$I_{K(V)}$]) [102]. These currents are modulated by dopamine (DA) to alter the pyloric rhythm. **(c)** Persistent activity can also be maintained by mixtures of excitation and inhibition, as in the *Clione limacina* swimming central pattern generator of the pedal ganglion. The group 7 and 8 interneurons are mutually inhibitory and alternately active, and drive dorsal and ventral flexion of the two swim wings, while two nonspiking group 12 interneurons generate plateau potentials to transition between phases of the swim cycle [103]. **(d)** Sensory feedback is thought to play a role in shaping the dynamics of some central pattern generators, for example, in the case of insect locomotion [104].

Shown here is an ‘extreme’ hypothesized circuit for generation of periodic motion in the absence of any intrinsically periodic neural activity, adapted from Ryu and Kyo [105].

periodicity in the form of either standing or traveling waves. [70,71] Finally, periodic dynamics are often maintained by sensory feedback, when activation of a motor effector triggers the response of mechanosensory receptors that feed back onto that effector [72,73]. Combinations of neural, circuit, and environmental feedback drivers of periodic neural activity therefore permit a remarkable diversity of periodic pattern-generating networks to emerge (Figure 2).

In considering whether periodic dynamics could have been drivers of the early diversification and dominance of neural systems, three next questions arise regarding the generation and co-ordination of periodically driven behaviors: (1) how is periodic activity synchronized across a pool of several hundred neurons? (2) to what extent can the degree of synchrony across this pool be

controlled? and (3) how is periodic activity initiated or terminated? The synchronization of independently periodic systems is easy to achieve. Even weak coupling between oscillators has been shown to be sufficient to entrain them to oscillate in phase [74,75]; biomechanical models in *Hydra* have leveraged this principle to show that electrical coupling of neurons can co-ordinate synchronization of muscle contractions [41]. Similarly, swim rhythms in jellyfish could be maintained by electrical or synaptic coupling between intrinsically oscillating neurons, which have been identified in multiple species [17,37,76].

More complicated is the problem of altering the degree of synchrony in a population to generate more flexible behaviors. For example, while bell contractions in swimming jellyfish often look symmetrical, the bell is

also able to produce asynchronous contraction patterns that result in turns [40]. This switching might be seen as a transition of the ring activity between standing and traveling waves. Shifts in the magnitude or spatial extent of excitation or inhibition are implicated in transitions between standing and traveling waves in other systems [77] and could similarly suffice to desynchronize jellyfish swim pulses to produce turning. Alternatively, neuromodulatory input could achieve a phase advance or delay in a subsection of neurons by increasing or decreasing excitability, or multiple nerve nets could be used to propagate signals of different speeds or target different muscles [78]. Finally, both symmetric and asymmetric phase relations can emerge from the dynamics of coupled van der Pol oscillators, suggesting that switching between stable modes of a system of coupled oscillators could allow transitioning between straight swimming versus turning [76]. Careful observation and biomechanical modeling of the jellyfish swim motor system will be required to identify mechanisms for swimming that can support both synchronous and asynchronous contraction, as well as fast transitioning between the two.

Each cnidarian taxon also has spontaneous changes in endogenous neural activity that are not directly coupled to motor actions. For example, ‘cryptic rhythmic activity’ has been described in classical jellyfish electrophysiology [18], and *Hydra* have several distinct nerve nets that are continuously generating endogenous activity [35,79]. In many species of jellyfish, the rhythmic pulsing of the bell is also organized into bouts, with the animal transitioning seemingly spontaneously between periods of swimming versus quiescence [80]. These transitions between distinct behavioral states could reflect a bistable ‘swim command’ population that switches on to drive periodic firing in neurons of the jellyfish nerve ring. In neurons poised close to a bifurcation point (the spike threshold), a small increase in extrinsic input is sufficient to trigger a phase transition from quiescence to oscillating. A ring network that generates swimming contractions could also itself be bistable, with either noise or slow adaptation leading to periodic switching between states [81]. Finally, neuromodulation is often used to switch network states in bilaterians [21]: whether such a mechanism is similarly used in cnidarians, for example, using their prevalent neuropeptides [82], remains unknown. Regardless, the wealth of behaviors and states that can arise from intrinsically active neurons with simple coupling rules highlights how they could have led to the rapid emergence and diversification of sensory, state, and motor capabilities and subsequent ascendancy of nervous systems in the animal kingdom.

Concluding thoughts

Prior thinking on nervous system origins has justifiably often focused on issues of sensory-motor control as drivers of early evolution, particularly in distributing

sensory information and coordinating the control of muscle and cilia effectors. However, dating back to the 1960’s, cnidarian electrophysiologists were highlighting the possible centrality of endogenous rhythmic activity in early nervous system evolution [18]. Since this time, dramatic progress has been made in our understanding of small rhythmic neural networks as multiply modulated, multiplexed, dynamical systems (Figure 2) [21,22,50]. With new abilities to record large-scale neural activity in cnidarian species [8,35,39], this is an exciting time to revisit and extend these classical ideas.

While periodic neural activity is useful for driving rhythmic behaviors, such as the pulsing of a jellyfish, its role in coordinating an organismal internal state was likely just as pivotal and presents important, contrasting challenges and perhaps a quite different evolutionary history. While cell biological mechanisms implementing sensory processing and behavioral control may have been largely superseded by neural activity dynamics with the emergence of the nervous system, mechanisms implementing internal states appear to continue to rely heavily on deeply conserved cell biological mechanisms in the form of neuromodulation [21]. A deeper understanding of mechanisms implementing sensory, state, and motor variables across many cnidarian systems will be important for resolving these issues.

Powerful new genetic tools permit the observation of neural dynamics in nervous systems of intact, behaving animals, particularly small and transparent marine invertebrates like cnidarians. This exciting technology is creating a new frontier in comparative systems neuroscience, analogous to how breakthroughs in genomic, transcriptomic, and single-cell sequencing have led to a revolution in comparative genomics and cell type evolution. Because these methods can be applied *in vivo* in behaving animals, they also offer the opportunity to examine nervous system function in the context of changing sensory cues and resulting motor responses. This permits us to ask how endogenous neural activity bidirectionally interacts with extrinsically driven activity to shape animal behavior, and how modulation of endogenous activity can alter this interaction. These capabilities demand corresponding advances in frameworks for comparison and evolutionary reconstruction at the systems level.

Dynamical systems offer one such framework, which we have applied to consider the origins and early evolution of nervous systems. One appealing aspect of this framework is that it allows for comparisons between features that emerge from dramatically different systems. For example, despite their very different circuit architectures, the heading system in the *Drosophila* central complex shows strikingly similar computational features — formation of an activity bump on a ring attractor — to

head-direction systems in the vertebrate hippocampal formation [83,84]. Similarly, persistent neural activity arises in many neural systems to maintain information over time, for example, in the oculomotor system for eye stabilization [85], the cortex for working memory [86], and the hypothalamus for maintenance of motivational states [87]. Systems can therefore achieve similar dynamics yet be implemented in quite different ways, raising interesting challenges for thinking about homology in neural systems [88]. For example, this could enable drift at the level of implementation as long as the output is stable, or repeated convergence on dynamics, as in the examples above. Indeed, convergent evolution is a theme that has been repeatedly observed of both neural components [89] (Figure 1) and such higher-level systems features.

We have argued that the emergence and prevalence of oscillators, both single cells and at the network level, may have been pivotal in driving the birth and evolutionary ascendancy of nervous systems. Looking forward, it will be important to better understand how these systems function at the cell biological, electrophysiological, ultrastructural, circuit, and dynamical levels across diverse species.

Declaration of Competing Interest

The authors declare no competing interests.

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