Introduction to ‘Origin and evolution of the nervous system’

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In 1665, Robert Hooke demonstrated in Micrographia the power of the microscope and comparative observations, one of which revealed similarities between the arthropod and vertebrate eyes. Utilizing comparative observations, Saint-Hilaire in 1822 was the first to propose that the ventral nervous system of arthropods corresponds to the dorsal nervous system of vertebrates. Since then, studies on the origin and evolution of the nervous system have become inseparable from studies about Metazoan origins and the origins of organ systems. The advent of genome sequence data and, in turn, phylogenomics and phylogenetics have refined cladistics and expanded our understanding of Metazoan phylogeny. However, the origin and evolution of the nervous system is still obscure and many questions and problems remain. A recurrent problem is whether and to what extent sequence data provide reliable guidance for comparisons across phyla. Are genetic data congruent with the geological fossil records? How can we reconcile evolved character loss with phylogenomic records? And how informative are genetic data in relation to the specification of nervous system morphologies? These provide some of the background and context for a Royal Society meeting to discuss new data and concepts that might achieve insights into the origin and evolution of brains and nervous systems.

1. Robert Hooke: the first empirical evolutionist

In 1665, John Martyn and James Allestry, printers to the Royal Society, published a work of observation, description and intelligent speculation of the highest order. That work was titled Micrographia (figure 1). Its author was Robert Hooke, one of the earliest Fellows of the Royal Society [1].

Hooke was endowed with polymathic talents, including that of a surveyor and cartographer, engineer, horologist, theoretician and inventor, most notably of telescopes and a microscope [2]. In his 1976 commentary, B. R. Singer [3] remarks that Hooke’s inventions are too numerous to describe, but singles out three lectures Hooke presented to the Society regarding the perception of time, the formation of memory and the phenomenon of forgetting. These lectures elicited considerable discomfort among some of his listeners. For if, as Hooke suggested, there is a mechanistic basis for memory then Hooke had to be negating the existence of the soul [3]. We must take Hooke’s denial at his word; except that in his wonderful book Hooke’s descriptions and thoughts on several occasions reveal a side to his persona that suggests he was being wisely cautious. In thinking deeply about the immense passage of time, and observing all manner of animal structures through his microscope, Hooke noted profound similarities across species that we today recognize as very distantly related, some by at least 541 Myr—the currently accepted time of the beginning of the Cambrian and the subsequent ‘explosion’ of animal diversity [4].

An example of Hooke’s conclusions about similarities is found in his description of the splendid drawing of the compound eyes of a tabanid fly (figure 2): ‘That this curious contrivance is the organ of sight to all those various Crustaceous Animals, which are furnished with it, I think we need not doubt, if we consider but the several congruitities it has with the eyes of greater creatures’.
And there it is: ‘congruity’, a word any evolutionary biologist today recognizes as synonymous with correspondence. To ensure that his readership did not miss the implication, Hooke continues, referring to the arrangement of lenses over the surface of the insect’s eye: ‘Now, though there may be by each of these eye-pearls, a representation to the Animal of a whole Hemisphere in the same manner as in a man’s eye there is a picture or sensation in the Retina of all the objects lying almost in an Hemisphere’. Again, such crucial words: ‘in the same manner as in a man’s eye’. Micrographia contains other observations in the same vein, which should justify us giving to Robert Hooke the accolade of being the first empirical evolutionist. In view that this and its companion issue of Philosophical Transactions consider the evolution of the nervous system and the brain it would have been doubly gratifying had Hooke drawn a microscopic example of that organ. However, it was Hooke’s contemporary, the brilliantly gifted Dutch microscopist Jan Swammerdam, passionately devoted to the study of social insects, who was the first to depict a microscopic brain, one belonging to a honeybee (figure 3) [5,6].

2. Saint-Hilaire’s unité de composition

The explicit claim for correspondence of organization of ‘man’ and ‘arthropod’ was proposed in print in 1822, gaining the attention of a much broader public than had Hooke’s volume some 157 years earlier. The author of the newer claim was the biologist and explorer Étienne Geoffroy Saint-Hilaire—returned not so long before from Napoleon’s ill-fated Egyptian campaign—who claimed that the central nervous system of a vertebrate is the same as that of an arthropod but upside down [7]. His arthropod was a lobster, an animal appropriate to Saint-Hilaire’s reputation as a gourmand. He was likely familiar with the fashion of serving up this crustacean: split lengthwise, the halves arranged on the platter side down, the longitudinally bisected nerve cord plain to see just under the ventral cuticle which, depending on how he viewed it, would appear uppermost (figure 4a).

Geoffroy’s outrageous proposal argued for an underlying uniformity of organization in all animal groups, their differences a result of an enormous span of time (an idea resting on more features than just the nervous system). His view was perhaps fitting for a time—37 years before Charles Darwin’s stunning thesis—when questions regarding relationships among vertebrate and invertebrate animals were intense and often bitterly disputed, even though many agreed that a distinguishing feature of an animal’s primitive or advanced status was reflected by the size and arrangement of its nervous system [9,10].

As has been many times related [11,12], Geoffroy’s proposal did not sit well with his one-time friend and colleague Georges Cuvier who considered himself Europe’s
pre-eminent morphologist and who had concluded that four utterly distinctive categorizations of animals could not possibly be related to each other. Yet, despite their famous debate, which riveted the attention of the Parisian intelligentsia, despite coming off it the worse, Geoffroy’s ideas were imported to Britain by Robert Grant, the first Chair of Zoology at London’s ‘Godless College.’ They eventually became so accepted that one of Grant’s friends, the renown surgeon William Carpenter at London’s Royal Institution, wrote in his 1864 *Principles of Human Physiology* [13] that the spinal cord was obviously homologous to the ganglionated ventral column of the Articulata (Euarthropoda, today). Even the curmudgeonly Richard Owen, not to be outdone, in 1883 claimed homology of the nervous system of an amphibian and that of an inverted blowfly larva (figure 4b) [8].

Darwin’s explanation of evolution was firmly established in Europe by the time that Anton Dohrn structured his detailed theory as to how an annelid with a ventral nerve cord might evolve into a vertebrate equipped with one that is dorsal, suggesting that the common ancestor of both might have had a ring-like brain around the front of its gut [14]. He sent this long and complicated proposal to Ernst von Baer, the most eminent embryologist of his time, who politely received the missive and as politely disagreed with...
just about everything Dohrn suggested [15]. He was not the only one to do so, but probably the most civilized compared with dictatorial Middle European academics such as Ernst Haeckel and Carl Gegenbauer, likely green with envy of Dohrn’s creation of the Naples Zoological Station [16].

There the matter rested for 120 years, or at least became quiescent apart from occasional papers suggesting annelid-like or arthropod-like ancestry of vertebrates. Or sometimes there were more bizarre proposals, such as Patton’s explanation of how a chordate might derive from a horseshoe crab [17], a contortion reminiscent of Laurencet and Meyran’s contribution to the Geoffroy–Cuvier debate that the internal organization of a duck corresponded to that of a cephalopod [12].

3. Renaissance and controversies: a molecular footing

The hiatus ended in 1994 with the publication of a paper that reviewed specific works, before and after the publication of Origin of Species, which mustered the then available evidence from embryology suggesting inversion of the dorsoventral axis in a hypothetical common ancestor of vertebrates and segmented invertebrates. This review [18], written by Katharina Nübler-Jung and her then student Detlev Arendt, focused particularly on the works of Martin Rathke, Albert Kölliker, Adolf Naef, Gottfried Semper and Franz Leydig, all students of development at a time when, in parallel, pioneering neuroanatomists such as Félix Dujardin, Giuseppe Bellonci and Gustav Retzius [19] were suggesting explicit correspondence between vertebrate and arthropod brains and central nervous systems. That review was followed shortly after by a short recap in Nature [20], that assessed the available molecular genetic data underlying the specification of body axes and nervous systems in insects and vertebrates, which seemed to provide experimental evidence for Geoffroy’s dorsoventral inversion hypothesis. Subsequently, De Robertis & Sasai showed in 1996 [21], that molecular interactions of homologous genes, decapentaplegic/short gastrulation in insects and Bone morpho-

genetic protein/chordin in vertebrates, determine apposing dorsoventral polarity, thus leading to the formation of the ventral nervous system in insects and the formation of the dorsal nervous system in vertebrates. It is this publication, more than any other, that seemed to vindicate Geoffroy’s proposal 174 years previously.

These papers, as must have been expected, elicited in their readers overarching questions. Might central nervous systems have originated just once? Did an originally ventrally disposed brain and cord in an ancestral invertebrate give rise to a dorsal central nervous system in a lineage that gave rise to the vertebrates? Did nervous systems originating from a common ancestor subsequently elaborate divergently across phyla, becoming lost in some? Alternatively, did central nervous systems evolve several times independently such that observed similarities across phyla are the consequences of convergent evolution?

From these questions originated the rationale for two successive meetings sponsored by the Royal Society to discuss the origin and evolution of the nervous system. This and its companion issue are the published results of those two events, the first held in London and the second following at the Society’s venue at Chicheley Hall in Buckinghamshire.

The meetings and their proceedings reflect opinions, certainly controversies and even some tensions: all very healthy phenomena. Discussions ranged from claims for genealogical correspondences of neural systems across phyla to the disputation of such claims largely because of crucial gaps in our knowledge and the still unsatisfied requirement for congruence of gene networks and neural organization to be mapped onto molecular phylogenies. Differences of a calmer nature pervaded discussions about the time of origin of nervous systems and the conditions required for their emergence. A source of controversy is estimating when animals with nervous systems first appear and how the first centralized nervous systems might have arisen. Such questions are posed against a frustrating lack of fossil evidence for animals earlier than the Lower Cambrian.

4. Organization and contributions to this issue

Papers for this first issue are grouped into two distinct themes. The first focuses on origins and early evolution of the central nervous system. The second centres on origins of chordate and vertebrate central nervous system, then progresses to the evolution of brain elaborations. The interface between the two themes is demarcated by an appeal by Hejnol & Lowe [22] for caution regarding conclusions about homology that derive from developmental and neuroanatomical studies without mapping these and gene networks [23,24], as well as those neural anatomies proposed as relating to them [25], onto a molecular phylogenetic framework. Controversy and tension thus arises from studies claiming a single origin of brains equipped with circuits that mediate behavioural choice and memory, and thus the evolved loss of such circuits in numerous lineages, against the proposition that central nervous system elaboration likely evolved many times independently, with convergent evolution rather than homology able to explain observed correspondences.

The first group of contributions is led by Erwin’s [26] discussion regarding when and under what conditions the Metazoa originated. It is argued that molecular clock data suggest metazoan origins occurred 750–800 Ma, yet the first unequivocal evidence for bilaterians is far more recent implying a cryptic period of up to 200 Myr during which central nervous systems probably evolved during ecological conditions that would have favoured the evolution of complex nervous systems. Budd’s [27] contribution follows this paper by cautioning us about what is known, or the lack thereof, about evolutionary events and ecologies that may or may not have promoted brain evolution. In his article, Budd provides arguments for a likely origin in the late Ediacaran of animals equipped with nervous systems, an origin that is concomitant, and linked to, major environmental and nutrient alterations. Budd also cautions against simplistic conclusions regarding trace fossils, reminding his readers that organisms without nervous systems can have behaviours (it is certainly thought-provoking that tracks made today across an uneven seabed some 700 m down by an abyssal protist, the grape-size Goniasphaerica, are remarkably like those claimed as fossilized tracks of ancient bilaterians [28]).

Wray’s paper [29] adds to the controversy about the timing of metazoan evolution and divergence, explaining that sequence data suggest metazoan origins far earlier than
indicated by the fossil record. His suggestion is that these early animals likely comprised planktonic and meiofaunal taxa, which are undetectable in the fossil record and remained cryptic until the first predators in the Cambrian drove the evolution of complexity of receptors and nervous systems that integrated sensory information. Such acquisitions would also be linked with larger body size and appendicular attributes. What might have driven the evolution of those predators, however, is unknown.

The prospect that even early brains that may have existed at the base of the Cambrian might eventually be resolvable comes from observations by Edgecombe et al. [30] described in the fourth contribution, demonstrating that neural tissue is not as fragile as reputed and that there is solid evidence for fossilized brains in Lower Cambrian specimens, mainly of arthropods. Carbon film traces, sometimes enhanced by pyrite deposition, resolve ground pattern arrangements of brains and ladder-like ganglia that correspond to the two major euarthropod groups, chelicerates and pancrustaceans, the dating of which in Cambrian Stage 3 (521 Ma) accords with molecular clock estimates for their divergence.

The next four contributions concern the possible evolutionary drivers of neurons and nervous systems, and considerations regarding evolved loss. Jekely et al. [31] discuss the evolutionary choices that might determine nervous system origins, and explore how considerations of option space allow an assessment of factors that were likely crucial for the evolution of the first nervous system. However, as argued by Ryan & Chiodin [32], evidence suggesting that ctenophores are the sister group to all other animals extends the possibility that two groups, sponges and placozoans, have lost their nervous systems and are thus prime examples of nervous system evolved reduction and loss, a possibility all too seldom approached by the evolutionist community. Simple nervous systems, such as the ‘diffuse’ nerve nets of cnidarians have traditionally been considered basal or primitive. However, as described by Kelava et al. [33], recent work that is elucidating the molecular networks responsible for the development of an anthozoan nervous system reveals a conserved underpinning of nervous system development across Cnidaria and Bilateria, in particular with respect to genes that contribute to the determination of neuronal differentiation. When nervous systems first appeared is further discussed by Arendt et al. [34] who provides a panorama of ideas regarding cell type diversification relating to the effectiveness of feeding, which he suggests resulted in the evolution of large motile animals, the internalization of ciliated digestive surfaces, and the consequent evolution of neurons that initially contributed to the control of the first gut. The proposition follows that further elaboration, in particular the evolution of gastric pouches, enabled natural selection to promote larger body mass and body organization that demanded greater coordination provided by a nervous system with greater differentiation of cell types and network organization. Arendt concludes by proposing that such a scenario may have led to the first bilaterians in the Ediacaran, possibly represented by Dickinsonia.

The second group of contributions is led by Linda Holland’s [35] synthesis, which starts out by observing that attempts to employ ‘evo-devo’ strategies—gene expression relating to development—to envisage extinct bilaterian ancestors are deficient in resolving whether, for example, the vertebrate brain is an apomorphy having no antecedent, or whether it arose ancestrally from the rostral part of the dorsal cord, such as found in Amphioxus (Cephalochordata). The predominant view is that an ancestral bilaterian possessed a brain and centralized nerve cord and that this was the antecedent of the chordate CNS, with the derived hemichordates suffering evolved reduction and loss. Holland reminds the reader that there is a minority view that the ancestor of the chordate nervous system lacked a brain and that chordate and hemichordate nervous systems evolved independently. While these views conflict, new research strategies are described, such as phylostratigraphic analysis, that may possibly resolve them [36].

‘Intelligence’ is usually ascribed to two classes of vertebrates—avians and mammals—and one order of invertebrates, Octopoda. However, in the next contribution, Roth [37] argues for evidence of convergent evolution of intelligence concomitant with the elaboration of multimodal integration centres, such as the cephalopods’ vertical lobes, the insect mushroom bodies and various derivations of the vertebrate pallium. Roth’s thesis is that elaboration and enlargement of such centres relate to the evolution of spatial learning for foraging, social and self-motivated learning. Examples are found particularly in hymenopterous insects, octopus, certain avians such as corvids, cichlid fish and primates. A very different view is provided by Fiore et al. [38], who argue for correspondence of action selection centres in arthropods and vertebrates. These are, respectively, the central complex and basal ganglia, both situated in the most anterior part of the brain. Both centres mediate equivalent functions and have equivalent circuitry, developmental programmes and pathologies. The selection of actions by both is proposed to rely on circuits providing feed forward and feedback loops including winner-takes-all computations modulated by dopamine signalling. These many similarities suggest an origin from an ancestral ground pattern in the brain of the common ancestor of insects and vertebrates.

A nuanced view of the significance of corresponding neural characters in insects and vertebrates is presented by Farris [39] in her paper on the evolution of brain elaboration. She asserts that brains evolved independently in protostomes and deuterostomes and that, in both, similar selective pressures were the drivers of evolved increases in brain size and the number of integrative centres. Similar modifications during development in vertebrates and insects are proposed to have resulted in similar neuroarchitectural traits and, in agreement with Roth, Farris emphasizes that the acquisition of spatial learning relates to enlargement of certain multimodal brain centres, such as the insect mushroom bodies. However, while some correspondences might relate to deep homology of bilaterian brains in the context of genetic programmes that underlie homologous domains, Farris points to the limited repertoire of mechanisms that can provide brain elaboration and contends that increased structural and functional diversity must, therefore, be the result of homoplasy not homology.

Chakraborty & Jarvis [40] point out that little is yet known about mechanisms that underlie the evolution of neural pathways, and to acquire the relevant data requires a far more comprehensive appreciation of what are, across species, homologies, homoplases and novelities. The authors review genomic and molecular techniques that allow a window into the appearance of novel pathways and brain functions. These techniques suggest that during evolution
entire systems of centres and their connections can duplicate and then assume novel functions in a manner reminiscent of gene duplication. Pathways underlying vocal learning and vocal communication in birds and humans provide examples.

The final paper in this issue is by Harvey Karten [41], the doyen of comparative vertebrate neuroanatomy, whose discoveries over a period of 50 years have led to a deep understanding of the characterization of neuronal populations in non-mammalian forebrain and the evolutionary relationship of these to neural pathways and circuits, and their molecular profiles, which reveal fundamental commonality in the brains of birds and mammals. The conclusion, drawn from numerous studies, is that the organization of connectivities and neuronal relationships in mammalian neocortex are ancient, originating early in the evolution of vertebrates according to Darwin’s principle of natural selection.

5. Some concluding remarks

The contributions of this volume illustrate the requirement of numerous disciplines for debating the origin and evolution of the nervous system. The fossil evidence for preserved nervous systems is only starting to emerge, which will help to establish refined hypotheses when and under what conditions metazoan body plans and nervous system(s) evolved. Similarly, genome sequencing, especially of those species that represent crucial outgroups for cladistic considerations, are needed to establish safe foundations for comparative transphyletic analyses that are able to span larger phylogenetic distances. So far, this has relied on developmental genetic studies comparing homologous genes, their expression patterns and function. But it is becoming clear that these comparisons are insufficient to relate gene action to nervous system elaboration (ranging from nerve net to centralized nervous systems and brains), unless a unifying genetic theory can be established that is able to causally relate gene network activity to the morphology of characters and character states across phylogenetic distances [42,43]. Such a unifying theory, encompassing the acquisition of evolutionary novelties as well as the evolved loss of morphological characters, is required to explain these remarkable genealogical correspondences among nervous systems and their parts, spanning fossil evidence to neural circuits and behaviour, that can be observed in ‘endless forms most beautiful’ [44] and how they may have come about.

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Guest Editor profiles

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