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What is This?

What nervous systems do: early evolution, input–output, and the skin brain thesis

Fred Keijzer[1], Marc van Duijn[1] and Pamela Lyon[2]

Abstract
Nervous systems are standardly interpreted as information processing input–output devices. They receive environmental information from their sensors as input, subsequently process or adjust this information, and use the result to control effectors, providing output. Through-conducting activity is here the key organizational feature of nervous systems. In this paper, we argue that this input–output interpretation is not the most fundamental feature of nervous system organization. Building on biological work on the early evolution of nervous systems, we provide an alternative proposal: the skin brain thesis (SBT). The SBT postulates that early nervous systems evolved to organize a new multicellular effector: muscle tissue, the primary source of animal motility. Early nervous systems provided a new way of inducing and coordinating self-organized contractile activity across an extensive muscle surface underneath the skin. The main connectivity in such nervous systems runs across a spread out effector and is transverse to sensor-effector signaling. The SBT therefore constitutes a fundamental conceptual shift in understanding both nervous system operation and what nervous systems are. Nervous systems are foremost spatial organizers that turn large multi-cellular animal bodies into dynamic self-moving units. At the end, we briefly discuss some theoretical connections to central issues within the behavioral, cognitive and neurosciences.

1 Introduction

Asking what nervous systems do may seem superfluous: nervous systems conduct information from sensors to effectors and process it in between. This interpretation seems beyond dispute, requiring no further clarification or reflection. Witness various opening statements in recent texts on the evolution of nervous systems:

> Brains are informed by the senses about the presence of resources and hazards; they evaluate and store this input and generate adaptive responses executed by the muscles. (Allman, 1999, p. 2–3)

> Nervous systems enable organisms to receive sensory information from their external environment, process this information and regulate neurosecretory and motor systems. (Jékely, 2011, p. 914)

> The function of the nervous system is to sense and relay fast information about surroundings. The network structure of neurons serves rapid signal transmission between sensory cells and a distant unit of specific cells, such as muscle. (Watanabe, Fujisawa, & Holstein, 2009, p. 167)

These are claims about what nervous systems do at their most basic level. The view that nervous systems transmit information from sensors, process it in some way and use the result to regulate effectors not only is generally accepted in the literature on the evolution of nervous systems, but also provides the consensus textbook interpretation of what nervous systems do for basically all of the neurosciences and the cognitive sciences. The notion of information processing itself goes back to Shannon, and has been used in close connection with concepts like computation and representation, implying that brains and nervous systems are

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computational devices at a basic level (e.g., Boden, 2006). However, very often the term is used in a very loose and unspecified way and here we will focus on the input–output aspects of the information processing interpretation.

Under this input–output interpretation, nervous systems are fundamentally through-conducting devices that process information. In the limiting case, this can be as simple as a set of direct connections such as exemplified in the well-known *Braitenberg vehicles* (Figure 1): artificial creatures that react to their environment in complex ways because of the specific wiring of connections between suitably placed sensors and effectors (Braitenberg, 1984). The classic three-component reflex arc—consisting of receptors, conductors, and effectors—is another case where the connection is thought of as being direct. In the case of the human brain, the conductor part expands into high-level cognition and consciousness. Still, despite the intricacies of the central organizational architecture of nervous systems, through-conducting remains the conceptual foundation on which these elaborations are built.

In this paper, we will examine and challenge this textbook interpretation of nervous system operation by turning to the earliest evolution of nervous systems. We will argue that the input–output interpretation is

Figure 1. A Braitenberg vehicle is a little cart with two light sensitive sensors directly connected ipsilaterally to two motors driving the vehicle. This configuration makes the vehicle drive towards the light.

primarily fitted to describe relatively complex centralized nervous systems. It does less well as a characterization of the most primitive nervous systems—diffusely connected nerve nets—or as an account of the evolutionary origins of these nerve nets. We will review evidence and theoretical work from biology, which suggests that a through-conducting set-up is not a primitive feature of these early nervous systems. We claim that through-conduction, where and to the extent it is an accurate description of some nervous system activity, is a later evolutionary development built upon earlier features.

In contrast to the input–output view, we develop an alternative proposal that stresses the fundamental coordination problems faced by multicellular animals that first developed movement by muscle contraction. This form of motility required the patterned activation of extended muscle sheets dispersed over the body. We hold that the fundamental problem here was not so much to act intelligently—a problem that had already been solved in various ways without a nervous system (Section 3.3)—but to act as a *single multicellular unit*. In this story, nervous systems did not evolve initially to provide a more efficient information processing device. Nervous systems arose as a source and coordinator of patterned activity across extensive areas of contractile tissue in a way that was only loosely constrained by sensor activity.

In this view, the *central direction* of nervous system connections runs transverse—at right angles—to the through-conducting stream that runs between sensors and effectors: early nervous systems evolved as connections across a contractile tissue and in close connection to the animal epithelium or skin. In this paper, we will focus on the simplest case where the two are combined in a *myoepithelium*, an epithelium that also has contractile (myoid) properties, and which is regularly named as a potential nervous system precursor (Arendt, 2008; Lichtneckert & Reichert, 2007; Mackie, 1970; Miller, 2009). Adopting the phrase "skin brain" introduced by Holland (2003), we will refer to this idea as the *skin brain thesis*, or SBT.

Before we develop our argument for the SBT, we want to stress three general points. First, the SBT does not deny the necessity of a link between sensory cells and the activity across a myoepithelium. We also do not deny the *conceptual* possibility of interpreting nerve nets in input–output terms. The point made is that this sensory connection is comparatively weak compared with the reciprocal connections across a myoepithelium, and that these latter, transverse connections are essential to understand both why nerve nets first evolved and how they operate. Most especially, we claim that a skin brain interpretation helps to explain what basic forms of nervous systems do in a way that input–output interpretations do not.
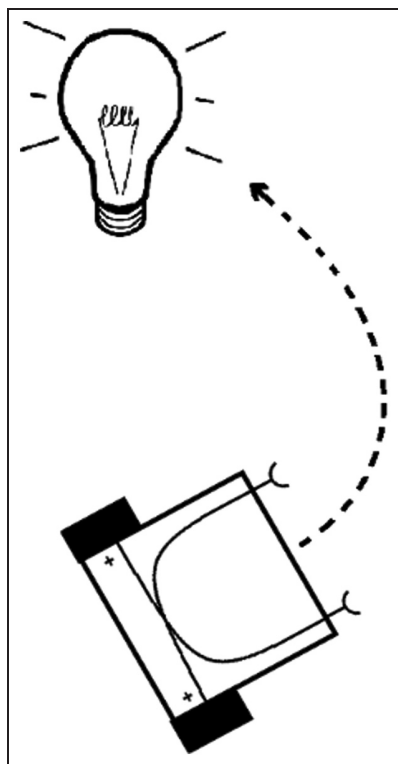
Second, we want to stress that the aim of the present paper is conceptual. The SBT is a proposal for an alternative empirical interpretation of how basic nervous systems work. Our main goal is to make it a matter of further empirical investigation whether basic nervous systems are best understood in terms of input–output devices or as skin brains. Given the general consensus that the input–output interpretation provides the foundation of what nervous systems do, challenging this interpretation for these basic cases sets up a major research challenge that needs to be, and can be tackled by further modeling studies and neurobehavioral research on these systems. This is work that still needs to be done. Here, we merely aim to make this option thinkable, and to provide it with sufficient initial plausibility.

The third point concerns the domain of the SBT. The focus of the present paper is strictly on the evolution of the first nervous systems. The argument does not directly implicate more complex centralized nervous systems, and leaves open the possibility that after an initial skin brain starting point, later nervous systems evolved further into definite input–output devices. However, justification of the SBT as a serious account of the operation of the most basic kinds of nervous systems, should provide a potent incentive for scrutinizing the input–output interpretation for more complex nervous systems. The idea that centralized nervous systems are remodeled skin brains becomes a coherent theoretical and empirical option. Thus, while the present discussion remains limited to a very basic domain, there are important potential connections with more complex cases, some of which we will sketch in the final section. Nevertheless, we want to stress that the immediate and important challenge is to develop the SBT for the basic case. Challenging the input–output consensus here is challenging enough.

The text has the following structure. In the next section, we will advance a working definition of nervous systems, and provide the most basic extant example nerve nets, such as those found in modern cnidarians like jellyfish. In Section 3, we discuss some general reasons for being critical about the input–output interpretation of nervous systems. Rather than disqualifying this interpretation, we aim to highlight some problematical sides and provide initial credibility for seeking alternative options. Section 4 introduces the key proposal of Carl Pantin, who argued that muscle coordination was the basic reason for the evolution of early nervous systems. Together, Sections 2–4 also provide a list of 11 clues that act as constraints on the SBT as developed in Section 5. In a concluding section, we return to the differences with the input–output interpretation, and give a short indication of potential wider implications.

2 What are nervous systems?

While the brain is a prominent anatomical part of the human body that cannot easily be overlooked, the situation is less clear when one turns to basic forms of nervous systems. Interestingly, the notion of a nervous system itself is less clear-cut than one might expect. Conductive tissues—tissues that conduct signals—are widespread inside and outside the animal kingdom (Mackie, 1970), and it is often difficult to differentiate "genuine" nervous systems from these other forms of conductive tissues. For example, certain sponges have a conducting system consisting of a syncytium, a collection of cells which are connected by their cytoplasm (Leys & Meech, 2006), while plants also use action potentials for signaling (Baluška, Mancuso, & Volkmann, 2006).

What differentiates nervous systems from other conducting tissues? In their classic work *Structure and Function in the Nervous Systems of Invertebrates*, Bullock and Horridge defined nervous systems in terms of their constituents: neurons.

> A *nervous system* may be defined as an organized constellation of cells (neurons) specialized for the repeated conduction of an excited state from receptor sites or from other neurons to effectors or to other neurons. (Bullock & Horridge, 1965, p. 6)

Bullock and Horridge's definition provided anatomical and physiological criteria to decide whether a nervous system is present in a specific group or phylum. In keeping with the neuron doctrine, they assumed that neurons are cells specialized for conducting electrical activity across their cell bodies and processes, which are connected to other cells through dynamically polarized (chemical) synapses and that conducting activity flowed in one direction, from dendrites to axon (e.g., Guillery, 2007). Note, however, that this pragmatic definition does not specify in what way nervous systems are functionally different from other conducting systems, apart from the specifics of their constituents. There is no system-based differentiation from other conductive tissues.

Bullock and Horridge's definition is now widely accepted. Lichtneckert and Reichert in their review of work on nervous system evolution also subscribe to the same definition, only adding that the ability to *generate activity endogenously* must also be part of the definition (2007, p. 291), as this is now known as a common feature of nervous systems.

The most primitive forms of nervous systems still in existence can be found in cnidarians (e.g., jellyfish). Large parts of these nervous systems consist of dispersed and diffusely connected nerve nets while centralization in "brain-like" structures or ganglia remains limited (Figure 2). Activation can be passed on in any
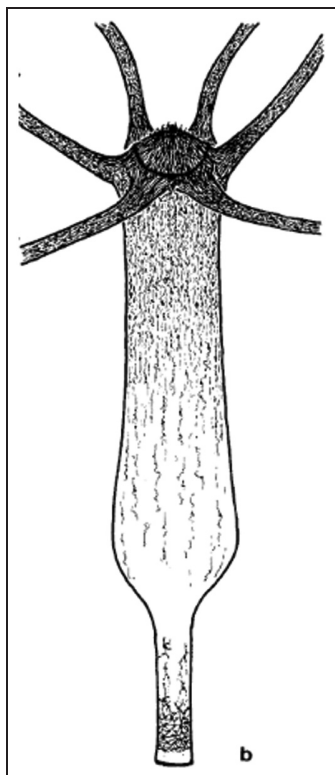
Figure 2. A nerve net drawing based on a RFamide-positive staining of the nerve net of a *Hydra oligactis*, showing denser areas around the mouth opening and its stalk (peduncle). Reproduced with kind permission from Springer (Grimmelikhuijzen, 1985).

direction across the net. For a definition of these nerve nets, we return to Bullock and Horridge:

> A *nerve net* is a system of functionally connected nerve cells and fibers anatomically dispersed through some considerable portion of an animal and so arranged as to permit diffuse conduction of nervous excitation, that is, in relatively direct paths between many points. The paths, as opposed to indirect routing through a distant ganglion or central structure, are multiple (Bullock & Horridge, 1965, p. 460)

In nerve nets, there are no—or at least few—clear tracts of neurons to conduct activity from one specific point to another. Instead, nervous activity can travel from any arbitrary spot to any other point in the net.

Two caveats are necessary. First, note that the diffuse character of how activity spreads across nerve nets derives from connections at the system level, and is fully compatible with the neuron doctrine (Mackie, 1987). Second, while nerve nets are generally considered the most primitive form that nervous systems can take (e.g., Brusca & Brusca, 2003), whether the nerve nets of modern cnidarians should be described as complete nervous systems is now disputed (Grimmelikhuijzen, 1985; Mackie, 2004b; Satterlie, 2011). Cnidarians exhibit various forms of neural centralization, and can be said to

have centralized nervous systems. Satterlie (2011) specifically argues that the nerve net part may well be a secondary adaptation to the cnidarian body plan.

Nevertheless, nerve nets remain arguably the most suitable candidate as the most primitive condition of nervous systems. First, while modern nerve nets could be a secondary adaptation, at present this is a mere possibility. It remains a good working assumption that simple, undifferentiated nerve nets are a basic form that later became more differentiated rather than the other way round. In addition, the events leading to the origins of the first neurons and nervous systems can plausibly be presumed to have taken place fairly deep in the Precambrian (e.g., Peterson, Cotton, Gehling, & Pisani, 2008; Valentine, 2004, 2007), and to have involved organisms that need not have had a close morphological similarity to any animal living today, including modern cnidarians. At present, we do not know what creatures were involved, nor how they functioned and what nervous systems did for them. Nerve nets, being a highly primitive condition, provide an empirically plausible starting point here. Finally, from a methodological perspective, taking nerve nets as the primitive condition is a specific, unambiguous proposal that can be developed and investigated in more detail. In the following, we aim to show that working with this assumption pays off, as it allows a systematic reinterpretation of what basic nervous systems do. Thus we have our first tentative clue as to what the first nervous systems did:

> Clue 1: The basic nervous system configuration consists of a diffuse nerve net.

3 Reasons for a critical attitude towards the input–output interpretation

Although the input–output view is deeply entrenched, there are issues involving nervous system functioning that are highly puzzling or awkward when the input–output view is taken as a *fundamental* account of nervous systems. The following discussion will clarify different problematic aspects of the input–output view, and provide material for three more clues.

3.1 Computational interpretations and neurodynamical complexities

The current input–output interpretation of nervous systems is closely linked to a computational information-processing interpretation. This linkage is intrinsic to the classic neuron doctrine, according to which neurons are individual entities that receive and send electrical signals to one another through synapses in an all-or-none fashion that is basically similar to electrical switches. Consistent with the neuron doctrine's one-way flow of information,

nervous systems could be interpreted as electronic circuitry, which may be far more complex than artificial circuitry, but not intrinsically different. McCulloch and Pitts (1943) provided the connection between nervous systems and logical systems, and from that time the brain could be seen as a powerful biological computer in which neurons acted as logic gates (Gardner, 1985).

The problem with this input-output interpretation is that the neuron doctrine on which it is based has been seriously undermined (e.g., Bullock et al., 2005; Guillery, 2007; Kruger & Otis, 2007) since it was first advanced by Ramon y Cajal in the late 19th century. Famously, Cajal formulated what came to be called the neuron doctrine explicitly in opposition to the then-current idea that nervous systems are reticular organizations of nerve cells directly connected to one another, through which electrical activity flows diffusely in all directions (Guillery, 2007; Kruger & Otis, 2007). Famously, Cajal won the debate on the basis of landmark empirical studies that indicated directed, one-way flows of nervous electrical activity. A lot has happened in neuroscience since then, however.

Evidence from biology and neurophysiology that undermines the sufficiency of the neuron doctrine has been accumulating for years. While the electron microscope first vindicated Cajal's view of the membranous separation at the synaptic junction in 1956, only a year later the same instrument led to the discovery of gap junctions—sometimes called electrical synapses—that directly couple nerve cells electrically, as proposed by the reticularists (Guillery, 2007). While initially the electrical transmission through gap junctions was considered a primitive form of signaling, it later became clear that these channels could be modulated and were plastic in a way that resembled chemical synapses and signaling flows (Bullock et al., 2005). Furthermore, gap junctions have been described between neurons and non-neural cells such as astrocytes (Bullock et al., 2005). The neuron doctrine can not plausibly explain the diversity of neuromodulatory substances, such as amines and neuropeptides, that remodel neuron behavior and circuitry within minutes and hours instead of the standard millisecond time scale (Bullock et al., 2005). Many of these neuromodulatory molecules are not recent evolutionary developments but have a deep genomic history. More recently, immune system elements, such as cytokines, have been shown to play critical roles in modulating neural plasticity under normal as well as challenged conditions (McAfoose and Baune, 2009; Yirmiya and Goshen, 2011), and these associations are also very old (Maier and Watkins, 1998). The neuron doctrine cannot explain these associations either. Moreover, in many neurons, action potentials can travel *backward* from the axon and cell body to the dendrites.

Then there is the astonishing dynamism of the neuron, and thus of the nervous system more generally. This dynamism begins with the plasticity of the synapses, "which are not fixed structures, but are subject to a process of continual pruning, and replacement by new synapses—the real driver of neural learning, rather than mere changes in synaptic weights" (Smythies, 2002, p. 2). Receptors for neurotransmitters, neuropeptides and other signaling molecules in the neural membrane have proved not to be roving iceberg-like structures awaiting ligands, as long supposed, but are subject to "a continual dynamic process of rapid internalization into the postsynaptic neuron," where they may be broken down or recycled to the surface and reused (Smythies, 2002, p. 2). Some neuroscientists even argue that the classic picture of the neuron as a linear computational unit is not merely highly idealized but "wildly inaccurate" (Smythies, 2002).

While most of these empirical discoveries have been around for some, or even many years, they have had so far only a limited impact on views concerning the global operation of nervous systems. A good explanation for this is the powerful influence of the input–output view itself, which fits the neuron doctrine nicely but under which the findings just described have no ready explanation. From the input–output perspective, these findings may be cast as mere details or even quirks that need not readily impact on the general information-processing operation of the brain as exemplified by the neuron doctrine. But that would be a mistake. In contrast, we hold that these developments break the tight analytic connection between the neuron doctrine and the standard input–output view by questioning the generality of the neuron doctrine itself. When these complex findings are taken as a starting point, there is ample reason for questioning and scrutinizing the input–output view of nervous systems.

Clue 2: The detailed operation of neurons and nervous systems is much more complex and diverse than can be readily accounted for by the input–output view.

3.2 Reflexes are not necessarily primitive

While the input–output view is currently most developed in its computational form as described above, an earlier and more basic form derives from the notion of reflex action. The notion of a reflex as an involuntary reaction to a stimulus has long been interpreted as a fundamental unit of behavior. In his groundbreaking work, Sherrington (1906) combined the behavioral notion of a reflex with a view on the general layout of the nervous system that incorporated the then-new neuron doctrine. Whereas previously work on reflex action had been conducted almost independently of anatomical and physiological studies (Swazey, 1968), Sherrington put reflex research on a firm physiological foundation, which led to adoption of the reflex arc as a standard unit for nervous system activity (Gallistel, 1980; Swazey, 1968). As Sherrington put it: "the whole function of the nervous system can be summed up in one word, conduction" (1906, p. 8). The neural organization representative of

the reflex arc became seen as the basic organizational principle of nervous systems and the basic representative of the input–output view (Figure 3). The reflex arc organization is still held as a good idealization and basic depiction of nervous system organization.

Nevertheless, there are sound reasons for being uneasy with taking the reflex arc organization as the basic organizational principle of nervous systems. First, Sherrington derived this interpretation from detailed work on the spinal organization of mammals. It is thus based on complex, well-differentiated central nervous systems rather than diffuse nerve nets. We should ask whether the reflex arc organization can also be considered basic when the empirical starting point had consisted of less differentiated nervous systems. The following quote from Dean Wooldridge is illustrative here:

> The machinelike nature of the reflexes and tropisms that so extensively regulate the behavior of the lower animals was not appreciated as soon as it might have been by workers in the field. This was probably because these animal responses do not have the precision and detailed reproducibility that is usually observed in the commoner reflexes of higher animals. The spines of the sea urchin are likely to display a certain restless motion, even when no stimulus is present, and the orientation toward a potential enemy may involve a certain hesitation or lack of precision, together with a persistence of some of the original restless motion, even after the enemy has been sensed. (Wooldridge, 1963, p. 76)

Wooldridge, one of the pioneers who linked the literature on animal behavior and neuroscience to computational theory, argues that the "machinelike nature of the reflexes" of "lower animals" is *obscured* by a lack of precision and reproducibility. An alternative interpretation is also possible, however: Machinelike reflexes need not be basic at all.

Indeed, several biologists and physiologists writing on the evolution of nervous systems argue precisely this point. At an early time, Parker (1919) already discussed
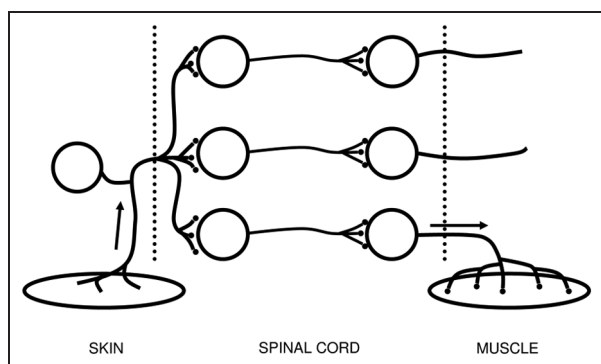
the "reflex deficiency" of lower animals. Later, Pantin observes:

> Early physiological workers were greatly impressed by the basic simplicity of the vertebrate reflex arc, in which stimulation results in a reflex motor discharge to a passive skeletal muscle. But even in the simple nervous systems of Actinians and Medusae it is clear that this is only one possible mode of nervous action. (1956, p. 177)

According to Pantin, the reflex arc is not a primitive unit but a *secondary simplification* of parts of an initially complex system (Pantin, 1956, p. 176). Similar claims were made by others who worked on the evolution and operation of basic nervous systems and were aware that this message remained unheeded outside their field (e.g., Horridge, 1968; Passano, 1963; Pavans de Ceccaty 1974). Since then, however, this message has vanished from sight, as can be witnessed in the citations that began this article (e.g., Jékely, 2011; Watanabe, Fujisawa, & Holstein, 2009).

We will return to the background and current status of these claims later on. For now, the main point is that at least some experts in the field have argued that fast, repeatable, and precise reflexes—in contrast to more general diffuse reactions to stimuli—were very likely a secondary development that did not reflect the basic organization of nervous systems. The reflex arc organization as we know it has been derived from a centralized nervous system, and it is not obvious to what extent it applies to evolutionarily early forms of nervous systems, such as nerve nets. We can now formulate our third clue:

> Clue 3: The reflex arc organization may very well be a secondary optimization of nervous systems.

3.3 Biological information processing does not require a nervous system

The input–output interpretation stresses that nervous systems function as information processing devices. However, in recent years serious claims concerning the complexity, and even cognitive, nature of the behavior of single-celled organisms have come to the fore. For example, John Allman (1999) discusses how "the most fundamental features of brains such as sensory integration, memory, decision-making, and the control of behavior, can already be found" in simple organisms such as bacteria (pp. 5–6). Recent microbiological studies agree that bacteria share many characteristics traditionally considered "cognitive" (e.g., Ben-Jacob, Becker, Shapira, & Levine, 2004; Hellingwerf, 2005; Lengeler, Müller, and di Primio, 2000; Shapiro, 2007; Taylor, 2004; Van Duijn, Keijzer, and Franken, 2006). Indeed, Jeffrey Stock and colleagues have suggested that the information processing capacities of the

Figure 3. A schematic representation of the classic reflex arc notion.

SKIN   SPINAL CORD   MUSCLE

receptor cluster at the leading pole of *E. coli* appear to constitute a "nanobrain" (Webre, Wolanin, & Stock, 2003). Moreover, it is now becoming increasingly clear that plants, in their reactions to a wide variety of external stimuli, are also capable of highly complex forms of information processing (Trewavas, 2005). Some researchers now even speak about plant neurobiology and "root brains" to refer to the signaling within and between the root tips of plants (e.g., Baluška et al., 2006).

These developments suggest that the information processing interpretation of nervous systems does not suffice to explain why nervous systems first evolved. At microscopic scales, information processing tasks required for adaptive behavior can be accomplished without any nervous system. Thus, information processing by itself does not meaningfully explain what a basic nervous system adds to an organism's behavioral repertoire.

A plausible reprisal here is that nervous systems are simply much *better* at information processing compared with the means available to bacteria, protists, and plants. While this is presumably true of complex nervous systems, the point does not seem to apply to basic forms. When one systematically compares organisms with basic nervous systems, they do not show more complex behavior than creatures without a nervous system. In his classic *Behavior of the Lower Organisms* (1906), H. S. Jennings provides a wide survey of experiments relating to the behavioral capacities of bacteria, paramecia, amoebae, and animals like hydra, sea anemones, and flatworms. On the basis of his own experiments as well as a review of the literature, Jennings identifies 12 similarities between the behaviors of unicellular organisms and metazoans with nervous systems (1906, pp. 261–263) based on the

1) variety of stimuli to which the organism can respond;
2) degree to which their behavior is determined by the organism's structure;
3) presence of regions specialized for sensation;
4) summation (computation) of stimuli;
5) degree to which the organism's behavior is determined by its history;
6) presence of both attractive and aversive reactions to stimuli;
7) whether reaction to stimulation is direct or indirect, that is, involving the release of forces already present in the organism;
8) occurrence of spontaneous action;
9) conduction of excitation in the organism;
10) changing reactions to different intensities of the same stimulus (amplification, habituation);
11) variability of reactions to stimuli, depending on the organism's physiological state; and
12) the organism's ability to sample different conditions in an attempt to avoid irritation.

According to Jennings, "the possession of a nervous system brings with it no observable essential changes in the nature of behavior. We have found no important additional features in the behavior when the nervous system is added" (p. 263).

While Jennings' observations are more than a century old, contemporary research concerning the intelligence of bacteria and plants demonstrates that they still apply, perhaps even more so than they did in Jennings' day, thanks to advances in microscopy of which Jennings himself could have only dreamed. So the issue remains: in terms of information processing abilities, basic nervous systems do not seem to add much value.

Clue 4: Basic nervous systems do not lead to more complex behavior than is often present in organisms without a nervous system.

3.4 Summary

There are good reasons to subject the standard information–processing, input–output view of nervous systems to further scrutiny. We should not assume that input–output is the whole story of nervous systems operation without looking at the relevant biological literature and research on basic nervous systems. However, even this literature is strongly influenced by input–output and information–processing interpretations, as we have already seen. Nevertheless, within the literature on the origins of the earliest nervous systems important alternative ideas can be found, and these will provide the basis for the SBT proposal.

4 The animal behavior machine

For many years, work on the evolution of the earliest and most basic nervous systems progressed slowly, yet several hypotheses emerged to explain why and how neurons and nervous systems could have evolved (e.g., Lentz, 1968; Lichtneckert & Reichert, 2007; Mackie, 1990; Moroz, 2009). Only with the rise of molecular and genomic studies in the late 1980s did the field gain serious momentum. Since then a relatively clear picture has emerged as to the evolutionary origins of many molecular constituents of nervous systems, based on comparative data from many basic animal groups and phyla. Foremost, it has become clear that there is a deep continuity at the molecular, genetic and physiological level between organisms with and without nervous systems. Key molecular components–such as ion channels, neurotransmitters and synaptic protein families–appear to have been present in precursor organisms without nervous systems, and even in single-celled ones (Greenspan, 2007; Ryan & Grant, 2009). For example, the voltage-dependent sodium channels that provide the mechanism for action potentials in nervous systems (in contrast to potassium channels that enable action

potentials in single-celled *Paramecium* (Greenspan, 2007)) have now been shown to exist in organisms without nervous systems (Liebeskind, Hilles, & Zakon, 2011). The postsynaptic density (PSD) of chemical synapses also has clear precursors in organisms without any nervous system (Ryan & Grant, 2009; Sakarya et al., 2007). In short, the electrical properties of neurons, as well as chemical signaling, predate the evolution multicellularity.

While molecular studies have been essential to unraveling the deep past of nervous systems, they must still be supplemented by studies of the macroscopic phenotype and functioning of the first organisms with nervous systems (Seipel & Schmid, 2005). At this bodily level, progress is slower and the results are less clear-cut. A wide variety of proposals have been advanced, without obvious ways to choose between them. For example, Moroz (2009) recently argued that central nervous systems, and even neurons, may have evolved several times and in various forms across the phylogenetic tree, while Jékely (2011) suggests that neural circuits arose for the control of ciliary locomotion. The ongoing discussion of such diverse hypotheses shows that molecular and genomic data alone do not solve this puzzle. There is a continuing need to develop an account of the origins of nervous systems at the bodily, morphological scale.

In such circumstances, it becomes clear why it is important to develop better, more specific ideas concerning what basic nervous systems did that increased whole-organism fitness and thereby led to the evolution of increasing complexity. Rather than particular evolutionary scenarios of how nervous systems evolved in historical time, the issue is how very basic nervous systems may have functioned, what fitness benefits they may have provided, and how those benefits may have influenced historical evolution. While this approach is closely linked to evolutionary accounts, a fundamental difference is that it addresses proximate questions about the possible dynamical operation of primitive organizations. Also, while proposals for primitive organizations remain hypothetical, they can be further developed and virtually tested, such as in simulation studies and robotics (Chiel & Beer, 1997; Webb, 2009). Here, we introduce a more abstract and generalizing conceptual approach, which targets the proximate question of how the first nervous systems could have operated to increase the fitness of a behaving organism. We aim to articulate general principles that can explain how and why neurons and the most basic nerve nets have evolved rather than any particular evolutionary scenario.

The outlines of precisely such a general answer to our proximate question can be found in one of the older evolutionary proposals within the literature on this topic. Carl Pantin (1956) advanced an account of the origins of nervous systems that focused on the central importance of muscle-based animal behavior what he called the metazoan behavior machine. Before going there, we must take account of two more clues:

Clue 5: Many of the biomolecular characteristics of neurons are already present in non-neural precursor contexts.

Clue 6: Understanding what nervous systems do is a question that requires an answer at the level of the whole animal.

4.1 Pantin's muscles and functional behavior

The locus classicus in the study of the origins of the first nervous systems is G. W. Parker's *The Elementary Nervous System* from 1919. Parker took the reflex arc, as exemplified by the vertebrate spinal cord, as the basic nervous system setup that his theory had to explain. His central question was: *How could a nervous system consisting of sensors, effectors and connecting neurons have evolved?* Parker provided a clear answer in the form of a three-stage evolutionary development. In the first stage, there were only *independent effectors* without any neurons or sensors. The second stage consisted of *receptor–effector systems*. In the third and final stage, conducting nerve cells connected the sensory and motor cells across larger distances, thus enabling the full reflex arc organization so well exemplified in the spinal organization of vertebrates.

Pantin (1956) criticized this account. Parker's aim had been to provide an explanation for the reflex arc organization as the basic building block of the nervous system. Pantin asked a different question: *How do nervous systems enable organisms to move about and do things?*

Foremost, Pantin took issue with Parker's focus on single, independent effectors. In multicellular animals, functional behavior does not generally derive from single, independent effectors.

> In the Metazoa [animals] the real effector is not a single individual cell. The contraction of an individual cell is of little importance in the behaviour of animals, except in some highly specialized tissues. In the simplest animals the motor system is an entire connected field of contractile tissue, like the muscular network spread over the whole body of a Coelenterate[1] [such as jellyfish] … These contractile sheets act upon an internal fluid skeleton of water and tissue. Thus, in Coelenterates, the complex and important movements required in behaviour can only be brought about indirectly through the co-ordinated contraction of large regions of these muscle sheets …, which indirectly move and distort the body into the position or shape required. … The Metazoan behaviour machine did not evolve cell by cell and reflex by reflex. From its origin it must have involved the structure of the whole animal, and it must have been complex enough and organized enough to meet all the varied requirements of behavior. (Pantin, 1956, p. 173)

Thus Pantin and others came to doubt the primacy of the reflex arc as the fundamental substrate of nervous system organization. None denied importance of reflexes. Rather, they believed reflex arcs should be regarded as stereotyped short cuts within a muscle-based

"behavior machine" consisting of widespread contractile tissues, whose activity must be coordinated for functional behavior.

Spontaneous, endogenously generated activity was essential in this view. In work that further developed Pantin's basic idea, L.M. Passano (1963) highlighted the relevance of the nervous system's endogenous activity. Passano claimed that Pantin's muscle sheets would require internal pacemakers to enable coordinated contraction. External stimulation thus did not simply result in the reaction of a passive animal but in the modification of ongoing and self-sustaining patterns of neural activity.

Pantin and Passano are important for their stress on the specific physical and biomechanical requirements for animal behavior, and how this would have shaped the evolution and functioning of the first nervous systems. All behavior of larger animals derives from contracting muscle tissue, and nervous systems were initially mainly involved in coordinating such tissue. This idea provides the heart of the SBT, the focus of Section 5. For now, we can formulate two additional clues:

Clue 7: The main animal effector consists of muscle tissue that requires spatiotemporal coordination.

Clue 8: Coordinating extensive areas of muscle tissue requires endogenous activity.

4.2 The impact of conductive epithelia

Soon after Pantin and Passano stressed the fundamental importance of muscle coordination, the discovery of conductive epithelia altered the explanatory landscape (Mackie, 1965, 1970). George Mackie proved experimentally that the external surface of an animal can act as a conducting sheet where action potentials, once initiated, travel in all directions (reminiscent of the reticularists' ideas). These epithelial cells were electrically linked by gap junctions (Anderson, 1980; Josephson, 1985). The implications for Pantin's proposal seemed dire. The impression was that whole-body coordination of extensive muscle sheets could be accomplished by a conductive epithelium closely linked to a sheet of contractile tissue, or even by a single myoepithelium that combined both functions. There simply was no need for any nervous system at this point. Everything required to put the animal behavior machine in operation seemed to be built into conductive and contractile epithelia, which appeared to be "simultaneously sensory systems, conductive systems, and effectors" (Josephson, 1985, p. 139).

The discovery of conductive epithelia provided a new question for studies of the origins of nervous systems: *What purpose do nervous systems serve when they evolve in the presence of conductive epithelia?* The answer that became dominant focused on two characteristics of modern neurons: chemical synapses and elongated axodendritic processes. Compared with diffuse epithelial conduction, nervous systems were thought to provide more precise signaling and specific connections. In keeping with the neuron doctrine, synaptic signaling was considered important for allowing the *directionality of signaling* as well as the *modification of signals* transmitted to the next cell, including inhibition. Elongated projections evolved to provide "a more selective type of excitation" in which specific regions of effectors could be controlled independently (Mackie, 1990, p. 908), while axons and dendrites enabled neurons "to transmit beyond their immediate neighbors without exciting all the intervening cells en route" (Horridge, 1968, p. 26). Both components were combined in Mackie's hypothesis that neural connections could have evolved from conductive myoepithelia to provide specific connections between far-flung sensors and effectors (Mackie 1970).

However, there is an important difficulty with the idea that nervous systems developed on top of excitable epithelia to form precisely targeted connections. As we have seen it is a plausible assumption that the most basic and earliest form of nervous system consisted of *diffusely* connected nerve nets (Clue 1), rather than specialized tracts between definite sensors and effectors. Precisely targeted connections and wirings characteristic of reflexes only become prominent in more differentiated nervous systems (Clue 3). While diffuse nerve nets may have arisen as a secondary development from such targeted connections, this is not the most economical explanation. While long-distance connections and synaptic transmission very likely are key features of early nervous systems, *precise* connections between sensors and effectors are not.

Thus while Pantin's proposal seemed to be superseded as an account of why nervous systems first evolved, it remained insufficiently clear whether conductive epithelia could really play the role of coordinating the animal behavior machine. To this day, it remains a perfectly plausible possibility that conductive epithelia provide only a coarse form of coordination, while early nerve nets enabled more sophisticated forms. Pantin's proposal requires further attention.

4.3 Updating Pantin's proposal

Nowadays, the picture has changed again. While Mackie's scenario for the origins of nervous systems is still influential (e.g., Arendt, 2008; Jékely, 2011; Miller, 2009), it faces important difficulties. A key problem is that nervous systems are found more widely among animal phyla and classes than electrically coupled conductive epithelia. Notably, while all four major cnidarian classes have a nervous system, there is substantial evidence that only the Hydrozoa have functional gap junctions (Mackie, Anderson, & Singla, 1984; Satterlie, 2011). Given the usefulness of gap junctions (Fushiki, Hamada, Yoshimura, & Endo, 2010), it is unlikely that this major invention

has been secondarily lost in three separate cnidarian lineages. Rather, it seems that electrical coupling between cells evolved later, and separately in the Hydrozoa and in the higher animals. It is doubtful, therefore, that electrically coupled conductive (myo)-epithelia could have preceded the evolution of nervous systems.

While this argument could provide a reason to return to Pantin's original proposal, it raises problems for a modernized version in which there is a gradual evolution from conductive (myo)epithelia to diffusely connected nerve nets, both acting as coordinators of muscle-based movement. However, as discussed above, molecular studies have established that chemical signaling and electrical conduction arose very early, even before multicellularity and certainly before the first nervous systems (Clue 5). By implication, the other key feature of modern neurons—axodendritic processes—appears to be a later addition; it follows that these different neuronal features could have evolved successively and independently. Most notably:

> In this case the evolution of the first nervous systems consists of at least two separate evolutionary steps:
>
> 1. The evolution of chemical transmission, allowing cells to pass electrical signals to adjacent cells.
>
> 2. The evolution of axodendritic processes that enable electrical signals to be sent to non-neighboring cells. (Van Elburg, De Wiljes, Biehl, & Keijzer, submitted)

While nerve nets would only have arisen with the second step, a conductive system where adjacent cells pass on electrical signals through chemical transmission can be considered both as a proto-nervous system and as a primitive form of a conductive epithelium. Given the molecular evidence, this form of conductive epithelium may have been present very early in metazoan evolution and could have allowed a gradual evolutionary trajectory to full nervous systems (Van Elburg et al., submitted).

While the early evolutionary presence of chemically transmitting epithelia is hypothetical, this condition has been studied in simulations using realistic biomolecular properties (De Wiljes, Van Elburg, Biehl, & Keijzer, 2010; Van Elburg et al., submitted). These studies show that such (myo)epithelia can provide patterned activity initiated by noise alone (Figure 4) and are plausibly cast as a basic coordinative device. Given the fundamental lack of empirical data on the morphology and functioning of the Precambrian organisms involved, we will take such conductive (myo)epithelia as a sufficiently plausible basis to develop an updated version of Pantin's proposal. The ironic twist here is that while electrically conducting epithelia now are dismissed as precursors of nervous systems, a chemically transmitting equivalent may be cast both as a proto-nervous system and as the actual embodiment of Pantin's original proposal.

Pantin's proposal can now be rephrased as involving two steps. First, a basic conductive epithelial organization provided a means to coordinate basic forms of muscle-based movement. This organization can also be interpreted as a proto-nervous system as it incorporates already one key feature of full nervous systems: chemical transmission. Second, with the subsequent evolution of axodendritic processes (and full nervous systems) a new kind of organization arose that enabled a much more fine-tuned coordination of muscle-based movement. In the following, we will develop this update of Pantin's proposal further into the SBT. For now, we can summarize the above in three tentative clues:

Clue 9: Chemical transmission between adjacent cells can have provided the basis for primitive conductive epithelia that formed a half-way station to nerve nets.

Clue 10: Chemically transmitting conductive (myo)epithelia can have provided a basic form of muscle coordination.

Clue 11: Specialized axodendritic connections can have subsequently evolved to broaden the existing possibilities for muscle coordination.

5 The skin brain thesis

Pantin's proposal that the coordination of a muscle surface is the key to understanding early nerve net evolution leads to two fundamental questions:

(a) How can early nervous systems have operated?

(b) What benefits can nervous systems have provided even in the basic form of nerve nets?

Our proposal focuses on the problem of initiating and maintaining efficient and fast sensorimotor coordination for multicellular organisms of increasing size. This involved a switch from movement by cilia to movement by means of muscle contraction. Building on Clue 7, we argue that early nerve nets were primarily involved in enabling muscle-based movement. The result was behavior of similar outward intelligence as already present in many bacteria and protists (Clue 4), but now on the scale of increasingly large multicellular organisms. Nerve nets initially did not make for smarter behavior, but for muscular behavior.

Under this interpretation, the core business of such nerve nets consisted of organizing and integrating activity across contractile effector surfaces (e.g., muscle) spread out beneath an external epithelium. Such a task would involve parallel organization and coordination requiring signaling across a surface rather than a through-conducting, sequential organization based on a set of pre-existing sensors and effectors. No stimulus can specify by itself the behaviorally relevant contraction patterns across such a surface. Patterns that work—that is, patterns that lead to movements that
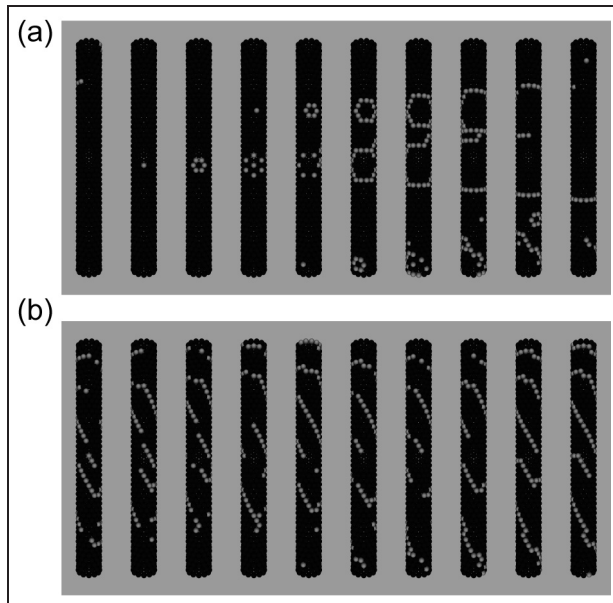
Figure 4. A simulation of a conductive myoepithelium using realistic biomolecular properties and chemical transmission between cells. (a): Ten time frames of a case where individual cells are connected to all six neighbors and spontaneous firing of single cells leads to expanding patterns that travel along a tube-like body. (b): Cells are connected to only three neighbors, forcing the spontaneous patterns to travel from bottom to top. Figure kindly provided by Ot de Wiljes.

are appropriate under the circumstances—are a function of the particular effector surface that is present in the animals rather than of any triggering stimulus. Also, based on what we know about organisms today, movement is likely to have been self-induced, while external stimuli acted rather as modulating factors on continuous effector activity.

Self-evidently, effector surface activity must continuously adapt to environmental conditions. Importantly, while we build on the idea that at evolutionary early stages the main functional problem was to initiate and maintain coherent effector surface activity in a way that was not strongly constrained by specific sensors, we also argue that the skin brain organization provides a pre-adaptation, or exaptation, for spatially extended sensors.

5.1 Motility, size, and muscle

Motility must be the key starting point for a discussion of what nervous systems do. While modern nervous systems have various other functions, it is evident that enabling an organism to move and manipulate its environment in specific ways is the prime reason for the huge investment in these metabolically expensive organs (Allman, 1999). Motility allows an organism to avoid harmful situations, seek out beneficial circumstances and change the environment outside the organism in ways that make it more amenable for the organism to

survive, thrive and reproduce. However, being motile in itself does not require a nervous system, as many organisms are quite capable of doing all of the above without one.

The complex motile behavior of many bacteria and single-celled eukaryotes is often achieved by the use of flagella and cilia. Both flagella and cilia are extensions of the cell and structurally very similar. However, cilia are shorter and tend to occur in relatively larger numbers (in patches or tracts), while flagella are long and generally occur singly or in pairs (Brusca & Brusca, 2003). Beating cilia or rotating flagella provide both a propulsive force that can move an organism through a liquid. Such behavior can be controlled by electrical signaling and action potentials, all in a single cell. *Paramecium* provides a well-studied case. The beating of a paramedicum's cilia is speeded up by hyperpolarization induced by deformation of its membrane when it collides with something on its back end (Greenspan, 2007). In contrast, a collision at the front can generate an action potential that induces a rapid uniform change in the membrane potential of the whole organism. This reverses the direction in which the cilia beat globally, moves the animal away from the obstacle, and allows the protist to reorient and propel itself in a new direction (Greenspan, 2007).

However, motility by means of cellular extensions imposes strong limitations on the size organisms can achieve. It works well for single-celled bacteria as small as 1 μm and for protists, like *Paramecium*, that are relatively huge at 180 μm (Greenspan, 2007). Multicellular metazoa such as flatworms, the size of which can be measured in millimeters, also employ this form of locomotion (Trueman, 1975). The largest creatures driven by cilia are the comb jellies, which can grow to many centimeters (Brusca & Brusca, 2003).[2] However, these latter cases are at the very limits of what cilia can do, and they require specific adaptations to fairly limited niche conditions. In all, cilia and flagella are only generally effective as a motility mechanism for creatures at or below the millimeter scale, which sets a strong constraint on the size of motile animals.

Assuming that evolutionary benefits were to be had for larger multicellular organisms to become or remain motile, the only way to achieve this was by developing a new mechanism for motility (Bonner, 2000; Dusenbury, 1996). In this context, tapping into new means for generating motility could be beneficial even when the overall functionality resulting from this motility did not change very much initially, as indicated by the findings of Jennings. To show, by way of analogy, how size matters, take the task of building Stonehenge. With toy blocks, the task is easily achieved by hand. If the structure is to be much larger, however, new ways of moving the blocks are required. The "same" task is vastly more difficult, even though the end result remains structurally similar.

As organisms grow larger, then, the evolution of muscle-based movement becomes central. As Seipel and Schmid formulate it: "The replacement of ciliary motility by muscle-driven locomotion must have represented an important selective advantage in preying and escape" (2005, p. 20). While cilia—literally—only allow your skin to crawl, internal sheets of contractile cells make it possible to use the body itself to accomplish motility. Such an arrangement only became possible with the advent of developmental processes and genomic signaling that enabled the growth of integrated multicellular bodies with specialized structures (Arendt, 2008). Muscle cells appear to have evolved by assembling new variants of motor proteins for fast and slow contraction and by forming adhesive substrates that can withstand and counteract the contraction forces generated (Seipel & Schmid, 2005). Such cellular contractions must be coordinated with respect to one another, however. Uncoordinated contractions by individual cells would not result in whole-body motility.

This, we believe, is where nervous systems come in. Nerve nets are intrinsically tied up with muscle surfaces. The origin of early nerve nets thus must be linked to the organization of coordinated activity across muscle surfaces as first stressed by Pantin. The question before us now concerns the possible contribution of early nerve nets. To provide our answer it will be necessary to turn first to a more general way of describing the source of this form of motility.

5.2 Patterning Pantin surfaces

Pantin stressed the importance of systematic large-scale contractions and extensions of muscle sheets as being the heart of the animal behavior machine: "In the simplest animals the motor system is an entire connected field of contractile tissue, like the muscular network spread over the whole body of a Coelenterate" (Pantin, 1956). In the following, we will refer to the contractile surface of any animal as the animal's *Pantin surface*. We define a Pantin surface as *the total muscle surface that an animal has available for motility*. A Pantin surface can consist of a single continuous muscle sheet—as in the basic case under discussion here—but it can also take discontinuous and three-dimensional forms when it is constituted by dispersed and various muscle groups in more differentiated animals. In all cases, the Pantin surface is a comparatively large surface or volume compared with the individual muscle cells that constitute it. At the same time it has a specific form—depending on the anatomy of the animal—and a specific and limited range of sizes—depending on individual and developmental differences. Using the Pantin surface as a general description of the muscle-based animal behavior machine, we can stipulate that motility in animals derives from patterns of contraction and extension across the Pantin surface. This description in terms of Pantin surfaces allows an abstract characterization of the specific form of the problem of using contractile tissues for whole-body motility in a way that can generalize over different body forms and inner anatomies.

At times, it will be useful to differentiate between coordination and patterning. Coordination is a standard term for synchronized movement involving activity of an organism. Limbs must move in a coordinated way to produce forward movement, for example. Patterning refers to the regular spatial relations of cells in the contraction–extension —activity induced across a Pantin surface. Suitable patterning results in coordinated activity. For the sake of convenience we often will refer to Pantin patterning as "coordination".

No detailed assumptions are made concerning the kind of organisms that first evolved a Pantin surface, but we take them to be organisms possessing a conductive epithelium and underlying contractile cells or with a myoepithelium that both conducts and contracts. In the basic case, the body itself acts as the muscle's antagonist, extending the contracted muscle surface again when activation ceases, like the jellyfish's "jelly".

To enable global animal motility, the dynamic patterning of a Pantin surface would very likely involve a number of general features. On general theoretical grounds one can predict that such patterning should at least be: (a) tailored to the animal body on which it occurs; (b) specific in the sense that it suffices for functionally adequate patterns of contraction; (c) repeatable and reliable in the sense that it can be turned on and off under appropriate circumstances; (d) resistant to minor disturbances; and (e) adapt to changes in size and constitution of the muscle sheet due to growth and other life events. What these features of dynamic patterning share is a sensitivity, via some form of feedback, to changes in global patterns.

Pantin's proposal can now be rephrased: early nervous systems evolved to pattern a Pantin surface (Clue 7), largely dependent on self-generated activity (Clue 8). Expanding Pantin's proposal we incorporate two additional clues: Chemical transmission between adjacent cells could have provided primitive (and proto-neural) conductive (myo)epithelia (Clue 9), which may have constituted a basic form of muscle coordination (Clue 10). An important question remains, however: Can Conductive epithelia act as successful Pantin patterners?

5.3 Excitable myoepithelia

The simplest example that combines a non-neural conductive epithelium with a Pantin surface is a conductive myoepithelium where conducting cells double as contractile units. A modern example consists of the striated swimming muscle in many hydromedusae and siphonophores (Mackie, 2004a). However, as we are not addressing the details of any modern model organism

or myoepithelium, we propose a conceptualization that allows the articulation of general principles involved in coordination by such means. A good place to start such a general approach comes from the consideration that conductive epithelia constitute *excitable media* that can be modeled and understood in terms of self-organizing pattern formation (Meron, 1992; Zykov, 1987, 2008).

The term excitable media came into use when it was realized that the mechanisms behind the traveling wave patterns in autocatalytic chemical reactions like the Belousov–Zhabotinsky reaction had properties that were very similar to action potential propagation as described by Hodgkin and Huxley (Meron, 1992). Other examples of excitable media are Turing patterns on animal skins or even human crowds producing the "Mexican wave" traveling round a football stadium (Farkas, Helbing, & Vicsek, 2002). More complex cases—also in three dimensions—are provided by the heart, where electrical signals travel through both neural and muscle tissue to produce coordinated contraction (Nash & Panfilov, 2004; Panfilov, Keldermann, & Nash, 2007).

Excitable media are well known for the ways in which local diffusion or conduction characteristics allow the production of global patterns across the medium. When excitatory and inhibitory activity spread at different speeds, a broad variety of global patterning can arise. Such patterns can also be controlled and forced, for example, by feedback mechanisms or other kinds of modulation (Sakurai, Mihaliuk, Chirila, & Showalter, 2002; Vanag & Epstein, 2008). Excitable media can be described in an intuitively tractable way in terms of cellular automata:

1. Each cell can be in either an excited, a receptive, or a refractory state.

2. Excited cells become refractory after a certain length of time, and must stay that way for a fixed period until returning to the receptive state.

3. Receptive cells are transformed to the excited state if a certain proportion of their neighbours are excited. (Ball, 2009, p.123)

Conductive myoepithelia—both modern and our hypothetical chemically conducting ones—are clear instances of excitable media. Local electrical activity is passed onward, triggering neighboring cells and so on leading to the buildup of large (bodily) scale patterns across the epithelial surface. Whether and if so which patterns arise will depend on, and change with, variables like the conductive properties of the cells, the kind and number of cellular connections and the size and form of the Pantin surface (De Wiljes et al., 2010). We want to stress that the biomolecular makeup of the cells involved is very rich, providing different ion channels, chemical transmitters, feedback loops and so on

that offer sufficient instruments for a rich potential array of large-scale patterning (Clue 5). A good example would be the presence of mechanosensitive ion channels that respond to tension in cell membranes such as might be produced by contraction (Hamill & Martinac, 2001; Sachs, 2010).

Important ingredients of patterning by excitable media are mixtures of excitation and inhibition traveling at different speeds across the medium. A chemically transmitting myoepithelium could manage the excitation and inhibition, for example, if cell-to-cell signaling goes through different chemical synapses. In modern cnidarians, different speeds of signaling may be accomplished by different ion channels. *Aglantha digitale* provides an existence proof for this possibility: A large Na^+-dependent excitatory post-synaptic potential and a much slower, low-amplitude Ca^{2+}-based excitatory action potential allows two different speeds of conduction in the same nerves (Mackie, 2004b).

Generally speaking, it seems plausible that the toolbox provided by an excitable myoepithelium is, by and large, sufficient to fulfill the basic theoretical requirements for suitable Pantin patterning to a significant degree (De Wiljes et al., 2010). The rich biomolecular make up of living tissue allows for many different possibilities of patterning as well as the incorporation of various forms of feedback from the macroscopic patterns to the biomolecular and cellular level (Sakurai et al., 2002; Vanag & Epstein, 2008).

At the same time, there are also obvious limitations to the patterning possibilities of excitable myoepithelia because of their anatomical structure as uniform sheets of conductive tissue. Providing patterns tailored to the requirements of a particular Pantin surface seems difficult for a uniform structure. Local modifications at a biomolecular level, such as the dispersal of specialized ion channels and other features, can help to adapt the sheet's patterning to local requirements. But it also seems evident that beneficial changes could be made at a larger anatomical level that would add to and modify the sheet-like organization. The inability of signals carried by epithelial conduction to jump across intermediate tissue without activating it is a major limitation, for example. This limits the setup to a single connected epithelium that must encompass all, or at least large parts, of the animal.

Both the mentioned possibilities as well as the limitations demand further investigation to assess their importance and empirical status. Further studies will also be required to assess the biomolecular, physiological and anatomical mechanisms that may realize them. We cannot address these empirical issues here, but generally speaking it is clear that excitable myoepithelia have a number of characteristics that are highly appropriate for organizing motility through muscle contraction, while at the same time such a structure has an obvious limitation as a Pantin patterner.

5.4 Nerve nets as modifiable and discontinuous excitable media

When excitable myoepithelia are interpreted as a basic Pantin patterner, how does the evolution of the first nerve nets fit in? While it has been common to stress the need for specific neural connections at this stage, as does Mackie, in line with the input–output interpretation, we want to highlight the *diffuse* character of primitive nerve nets.

In contrast to the input–output interpretation, the SBT casts early nervous systems in a role that *combines the development of extended processes and synaptic connections with a diffuse network structure*. While an excitable myoepithelium can plausibly act as a basic Pantin patterner, there are limitations. At the same time, Pantin patterning remains a prime directive for all forms of muscle-based motility and we propose that the functioning of early nervous systems is related to overcoming some of these limitations.

The SBT can now be formulated as the proposition that *early nerve nets evolved when some conducting cells—either within or connected to the myoepithelium—evolved elongated processes and synaptic connections in a way that modified and enhanced the patterning capabilities of a pre-existing myoepithelium.* Rather than providing specific connections from sensors to effectors, the proper function of such nerve nets was to control, modify and extend the available self-organized patterning across a Pantin surface. The key adaptation provided by early nerve nets was the way in which they added to the generic self-organizing properties of pre-existing epithelial and muscular tissues.

Evolving a loose network of conducting cells with far-flung processes and synapses has two important general advantages above a myoepithelium. First, there are new options for generating self-organizing patterned activity across a Pantin surface. One interesting possibility that deserves further attention derives from a modeling study by Jeltsch, Müller, Grimm, Wissel, and Brandl (1997). They showed that adding a limited number of long-distance connections within an excitable medium could lead to larger-scaled patterning across the medium. When translated to the present case, this could imply that adding long distance connections in the form of neural processes could enable wave-like patterning across *larger* Pantin surfaces. In this way, patterning could be adapted to larger-sized animals and changes in body size during growth. Having chemical synaptic connections would also add to the excitable properties of the myoepithelium and nerve net system, for example, by enabling inhibition. Whether these particular features of nerve nets actually acted in the roles mentioned remains speculative at present, but these options are open to investigation and would provide clear ways in which even very limited nerve nets could change the self-organizing properties of pre-existing excitable myoepithelia.

A second general advantage of nerve nets, compared with conductive myoepithelia, is their enormous flexibility. While excitable myoepithelia consist of a continuous unbroken sheet, nerve nets can take many forms. They can be repositioned inside the organism, isolating their functioning from external disturbances. They can send activation across intervening tissues without activating the latter. Nerve nets can also, because of their anatomical makeup, be more easily tailored to its Pantin surface at an anatomical level. With nerve nets, it becomes possible for the Pantin surface to be split up and become dispersed across separate muscle groups rather than remaining a single connected muscle sheet. Specialized antagonist muscle groups become a subsequent possibility. Even if nerve nets may initially have been generally uniform, breaking this symmetry predictably also could provide benefits. Examples might include developing inhibitory tracts between antagonist muscles, or circuitry to support standardized global (reflex) reactions to predictable stimuli (Clue 3).

With this latter claim, we come finally to the sensory aspects of a skin brain organization. First, note that sensory inputs in the form of local molecular or cellular sensitivity to chemical and physical environmental features are metabolically cheap, and present in all life forms (Smith, 2008). Such sensitivity is often used independent of any nervous system. Given the general usefulness of such sensitivity, existing nervous systems would almost self-evidently incorporate such sensors. Such sensors can take up a role as modulators of ongoing Pantin patterning, inducing switching between different main patterns or a change of direction. For particular ecologically relevant stimuli, we may plausibly assume that specific setups which lead to fast, highly stereotypical reactions recognizable as reflexes.

However, sensory inputs of this kind do not by themselves provide sensitivity to extended surface structures. This requires spatially extended physical arrays of sensory elements acting together like the retina or skin, not individual pinpricks. Again, within extended sensors—in particular the retina—transverse interactions between elements within the sensory array are crucial, for example, reciprocal inhibition to enhance contrast. An interesting connection can now be drawn between such a sensory setup and a skin brain organization. Obviously, this connection needs to be fleshed out, but still a transverse neural organization provides a plausible precondition for such extended sensors as well as their connection to self-induced movement.

To summarize, the SBT claims that nerve nets originated as a new mechanism by which Pantin surfaces could be more intricately and flexibly patterned to accommodate efficient motility at larger bodily scales. At a fundamental level nerve nets are fitted to spatial patterning and to accommodating spatially patterned feedback. Early nerve nets dynamically bonded the multicellular organism into an integrated behavioral

system that could act as a single unit. They first supplemented, but eventually dominated precursor (myo)epithelia in most animals. Importantly, on the SBT account early nerve nets did not evolve as a clumsy way to connect sensors to effectors, but, rather, as a dedicated structure for organizing a new kind of effector. Nerve nets later evolved special-purpose optimizations or adaptations and eventually developed centralization.

6 Conclusions

Our aim was to question the input–output interpretation for basic nervous systems—nerve nets—and to develop the outlines of an alternative interpretation of what nervous systems do. In this final section, we will first discuss how the SBT is different from the input–output interpretation, and subsequently position the SBT in a wider conceptual domain, provided by the cognitive, neural and behavioral sciences.

6.1 An alternative for the input–output interpretation

The SBT offers a genuinely new conceptual approach for understanding nervous systems at a whole systems level. Starting with the most primitive neural organizations—proto-neural myoepithelia and nerve nets—we argue that both are characterized by connections transverse to the standard sensor-effector direction and evolved their characteristics to bind the many cellular units of muscle sheets together into a unitary system. Nervous systems are in this view not organized around—or rather between—sensors and effectors. They are themselves a precondition for both extended contractile effectors as well as multicellular sensory arrays.

Myoepithelia and nerve nets can still be interpreted as input–output devices. However, now that an alternative is available it can be seen more clearly that the notions of input and output are of limited use to understand how they function. An input–output framework highlights a temporal sequence, while the notion of "output" refers to a generalized functional abstraction that is not intrinsically tied to any particular physical organization. This notion does not reflect the activity patterns across a Pantin surface. Myoepithelia and nerve nets send activation *across* the effector, not *to* the effector. Pantin patterning refers to the spatial and physical organization of patterns across a multicellular tissue of a specific size and constitution that is part of a particular bodily organization. In contrast to "output", this refers to a biophysical form of organization. Such patterns constitute a physical domain that can be readily investigated, both experimentally and by modeling. Thus, while an input–output interpretation casts the operation of basic nervous systems in terms of abstract, computational functions, the SBT draws it as a producer of complex but concrete dynamical patterns of activation.

We have stressed from the beginning that the SBT provides a *conceptual reinterpretation* of nervous system functioning. Nevertheless, the SBT is at heart an empirical thesis. As an empirical proposal, the SBT requires much more research and detail before it can be accepted. However, the SBT makes it thinkable that we may need to reinterpret nervous systems operation at a fundamental systems level. While the proposal is as yet succinct when it comes to sketching the trees, it does provide a totally new outlook on the forest.

6.2 Theoretical connections

So far, we limited our discussion to basic nerve nets. Still, we believe the resulting reinterpretation has potential relevance for a much wider domain, indeed, several domains.

Nervous systems: Foremost, the SBT is relevant for clarifying what nervous systems are. Above, we used physiological criteria to differentiate nervous systems from other systems or tissues. The SBT provides a systems-based interpretation that sets up a clear target for ongoing discussions on brain-like structures in non-animals such as plants (Baluška et al., 2006) and artificial "nervous systems" in robotics (Beer, 1997; Froese & Ziemke, 2009).

Biological theories on the evolution of nervous systems: While the SBT is itself not tied to detailed phylogenetic scenarios, it does provide important additional constraints on such scenarios by clarifying the way in which early nervous systems can have operated.

Neuroscience: The SBT has close links to theories of motor control that focus on neural circuits for movement (e.g., Orlovsky, Deliagina, & Grillner, 1999; Stein, Grillner, Selverston, & Stuart, 1997), to neuroethological studies of animal behavior (e.g., Greenspan, 2007; Marder, 1998), to dynamic approaches within neuroscience (e.g., Buzsáki, 2006), and to modeling approaches within neuroscience (e.g., Chiel & Beer, 1997; Ijspeert, Crespi, & Cabelguen, 2005) and embodied cognition (Pfeifer & Bongard, 2007). However, the SBT is not a thesis about motor control or behavior but a conceptualization of whole nervous systems—albeit basic ones—in which enabling motility is the foundation of nervous system operation. This involves a reappraisal of the motility-related domain itself, of the theoretical relevance of basic nervous systems, as well as new targets for modeling approaches, e.g., (myo)epithelia, nerve nets and Pantin surfaces.

Embodied cognition: The field of embodied cognition has yet to develop a generally accepted interpretation of the fundamental notion of embodiment itself (e.g. Clark, 2008; Thompson, 2007). The SBT provides a new way to understand embodiment, in the examples typically invoked in the field, by casting it in terms of a

dynamic, motile entity unified through transverse patterning by a nervous system.

Animal behavior: There remains a wide spread tendency to look at behavior in terms of reactions to stimuli, or tasks that can be described and accomplished without reference to any species in particular. The skin brain proposal casts animal behavior as a dynamical phenotype, necessarily tied to the species or class of animals under consideration. Sherrington once observed that "posture follows movement like a shadow" (Stuart, 2005). We would like to stress that dynamically changing body posture is a precondition for all task-oriented animal behavior. Animal behavior is a part of animal organization.

Central nervous systems: Applying the SBT to centralized nervous systems, and ultimately the human brain, will be an important challenge that we cannot address here. However, the very existence of an alternative for the input–output interpretation at a basic level warrants a more general scrutiny of input–output thinking as the general description of nervous systems. It is an open question to what extent centralized forms are really different from skin brains and the information processing interpretation will need to be argued for rather than assumed.

Obviously, these potential implications of the SBT remain tentative at present and establishing their validity is beyond the present paper. However, even naming these tentative theoretical connections shows that the exotic domain of basic nerve nets can itself be taken as a matter of central concern for the behavioral, cognitive and neurosciences, simply because of such potential repercussions. It will matter a great deal for all these fields how the study of basic nervous systems develops.

Notes

1. The term "Coelenterate" is no longer in use. Coelenterates have now been separated into the phyla Cnidaria and Ctenophora.
2. These organisms are modern and do have nervous systems. Neither the evolution of nervous systems, nor the evolution of muscle-based movement ever led to the disappearance of cilia or movement by cilia. Cilia remain a very effective form of animal locomotion in many circumstances and are for example also lining the trachea of our own lungs to sweep out mucus and dirt.

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References

Allman, J. (1999). *Evolving brains*. New York, NY: Scientific American Library.

Anderson, P. A. V. (1980). Epithelial conduction: Its properties and functions. *Progress in Neurobiology*, *15*(3), 161–203.

Arendt, D. (2008). The evolution of cell types in animals: Emerging principles from molecular studies. *Nature Reviews Genetics*, *9*, 868–882.

Ball, P. (2009). *Nature's patterns: Shapes*. Oxford, UK: OUP.

Baluška, F., Mancuso, S., & Volkmann, D. (Eds.) (2006). *Communication in plants: Neuronal aspects of plant life*. Berlin, Germany: Springer.

Beer, R. D. (1997). The dynamics of adaptive behavior: A research program. *Robotics and Autonomous Systems*, *20*, 257–289.

Ben-Jacob, E., Becker, I., Shapira, Y., & Levine, H. (2004). Bacterial linguistic communication and social intelligence. *Trends in Microbiology*, *12*(8), 366–372.

Boden, M. (2006). *Mind as machine: A history of cognitive science (two volumes)*. Oxford, UK: Oxford University Press.

Bonner, J. T. (2000). *First signals: The evolution of multicellular development*. Princeton, NJ: Princeton University Press.

Braitenberg, V. (1984). *Vehicles: Experiments in synthetic psychology*. Cambridge, MA: MIT Press.

Brusca, R. C., & Brusca, G. J. (2003) *Invertebrates, 2nd edition*. Sunderland, MA: Sinauer Associates.

Buzsáki, G. (2006). *Rhythms of the brain*. New York, NY: Oxford University Press.

Bullock, T. H., Bennett, M. V. L., Johnston, D., Jospehson, R., Marder, E., & Fields R. D. (2005). The neuron doctrine, redux. *Science*, *310*, 791–793.

Bullock, T. H., & Horridge, G. A. (1965). *Structure and function in the nervous systems of invertebrates*. San Francisco, CA: Freeman.

Chiel, H. J., & Beer, R. D. (1997). The brain has a body. *Trends in Neurosciences*, *20*, 553–557.

Clark, A. (2008). Pressing the flesh. *Philosophy and Phenomenological Research*, *76*, 37–59

De Wiljes, O. O., Van Elburg, R. A. J., Biehl, M., & Keijzer, F. A. (2010). Early nervous systems. In H. Fellermann, M. Dorr, & M. M. Hanczyc (Eds.), *Artificial life XII* (p. 239–240). Cambridge, MA: MIT Press.

Dusenbery, D. B. (1996). *Life at small scale: The behavior of microbes*. New York, NY: W. H. Freeman and Company.

Farkas, I., Helbing, D., & Vicsek, T. (2002). Social behaviour: Mexican waves in an excitable medium. *Nature*, *419*(6903), 131–132.

Froese, T., & Ziemke, T. (2009). Enactive artificial intelligence: Investigating the systematic organization of life and mind. *Journal of Artificial Intelligence*, *173*, 466–500.

Fushiki, D., Hamada, Y., Yoshimura, R., & Endo, Y. (2010). Phylogenetic and bioinformatic analysis of gap junction-related proteins, innexins, pannexins and connexins. *Biomedical Research*, *31*(2), 133–142.

Gallistel, C. R. (1980). *The organization of action: A new synthesis*. Hillsdale, NJ: Erlbaum.

Gardner, H. (1985). *The mind's new science*. New York, NY: Basic Books.

Greenspan, R. J. (2007). *An introduction to nervous systems*. Cold Spring Harbor, NY: CSHL Press.

Grimmelikhuijzen, C. J. P. (1985). Antisera to the sequence Arg-Phe-amide visualize neuronal centralization in hydroid polyps. *Cell and Tissue Research*, *241*, 171–182.

Guillery, R. W. (2007). Relating the neuron doctrine to the cell theory: Should contemporary knowledge change our view of the neuron doctrine? *Brain Research Review*, *55*, 411–421.

Hamill, O. P., & Martinac, B. (2001). Molecular basis of mechanotransduction in living cells. *Physiological Review*, *81*, 685–740.

Hellingwerf KJ (2005) Bacterial observations: A rudimentary form of intelligence? *Trends in Microbiology 13*(4), 152–158.

Holland, N. (2003). Early central nervous system evolution: An era of skin brains? *Nature Reviews Neuroscience*, *4*(8), 617–627.

Horridge, G. A. (1968). The origins of the nervous system. In G. H. Bourne (Ed.), *The structure and function of nervous tissue, Vol. 1* (pp. 1–31). New York, NY: Academic Press.

Ijspeert, A. J., Crespi, A., & Cabelguen, J. M. (2005). Simulation and robotics studies of salamander locomotion. *Neuroinformatics*, *3*, 171–195.

Jékely, G. (2011). Origins and early evolution of neural circuits for the control of ciliary locomotion. *Proceedings of the Royal Society B*, *278*, 914–922.

Jeltsch, F., Müller, M. S., Grimm, V., Wissel, G., & Brandl, R. (1997). Pattern formation triggered by rare events: Lessons from the spread of rabies. *Proceedings of the Royal Society of London B*, *264*, 495–503.

Jennings, H. S. (1906). *Behavior of the lower organisms*. New York, NY: Macmillan.

Josephson, R. J. (1985). Communication by conducting epithelia. In M. J. Cohen & F. Strumwasser (Eds.) *Comparative neurobiology: Modes of communication in the nervous system* (pp. 133–148). New York, NY: Wiley.

Kruger, L., & Otis, T. S. (2007). Whither withered Golgi? A retrospective evaluation of reticularist and synaptic constructs. *Brain Research Bulletin*, *72*, 201–207.

Lengeler, J. W., Müller, B. S., & di Primio F. (2000), Neubewertung kognitiver Leistungen im Lichte der Fähigkeiten enzelliger Lebewesen (A reevaluation of cognitive capacities in light of the capacities of unicellular organisms).*Kognitionswissenschaft, 8*, 160–178.

Lentz, T. L. (1968). *Primitive nervous systems*. New Haven, CT: Yale University Press.

Leys, S. P., & Meech, R. W. (2006). Physiology of coordination in sponges. *Canadian Journal of Zoology*, *84*, 288–306.

Lichtneckert, R., & Reichert, H. (2007). Origin and evolution of the first nervous system. In G. F. Striedter & J. L. R. Rubinstein (Eds.) *Evolution of nervous systems, Vol. 1: Theories, development, invertebrates* (pp. 289–315). Amsterdam, The Netherlands: Elsevier.

Liebeskind, B. J., Hillis, D. M., & Zakon, H. H. (2011). Evolution of sodium channels predates the origin of nervous systems in animals. *PNAS*, *108*(22), 9154–9159.

Mackie, G. O. (1965). Conduction in the nerve-free epithelia of siphonophores. *American Zoologist*, *5*, 439–453.

Mackie, G. O. (1970). Neuroid conduction and the evolution of conducting tissues. *Quarterly Review of Biology*, *45*, 319–332.

Mackie, G. O. (1987). Nerve nets. In G. Adelman (Ed.), *Encyclopedia of neuroscience, Volume II* (pp. 747–749). Boston, PA: Birkhäuser.

Mackie, G. O. (1990). The elementary nervous system revisited. *Integrative and Comparative Biology*, *30*(4), 907–920.

Mackie, G. O. (2004a). Epithelial conduction: Recent findings, old questions, and where do we go from here? *Developments in Hydrobiology*, *178*, 73–80.

Mackie, G. O. (2004b). Central neural circuitry in the jellyfish *Aglantha*: A model "simple nervous system". *Neurosignals*, *13*, 5–19.

Mackie, G. O., Anderson, P. A. V., & Singla, C. L. (1984). Apparent absence of gap junctions in two classes of Cnidaria. *Biological Bulletin*, *167*, 120–123.

Maier, S. F., & Watkins, L. R. (1998). Cytokines for psychologists: Implications of bidirectional immune-brain communication for understanding behavior, mood, and cognition. *Psychological Review*, *105*, 83–107.

Marder, E. (1998). From biophysics to models of network function. *Annual Review Neuroscience*, *21*, 25–45.

McAfoose, J., & Baune B. T. (2009). Evidence for a cytokine model of cognitive function. *Neuroscience & Biobehavioral Reviews*, *33*, 355–366.

McCulloch, W., & Pitts, W. (1943). A logical calculus of the ideas immanent in nervous activity. *Bulletin of Mathematical Biophysics*, *5*, 115–133.

Meron, E. (1992). Pattern formation in excitable media. *Physics Reports*, *218*(1), 1–66.

Miller, G. (2009). On the origin of the nervous system. *Science*, *325*, 24–26.

Moroz, L. (2009). On the independent origins of complex brains and neurons. *Brain, Behavior and Evolution*, *74*(3), 177–190.

Nash, M. P., & Panfilov, A. V. (2004). Electromechanical model of excitable tissue to study reentrant cardiac arrhythmias. *Progress in Biophysics and Molecular Biology*, *85*(2–3), 501–522.

Orlovsky, G., Deliagina, T., & Grillner, S. (1999). *Neuronal control of locomotion: From mollusc to man*. Oxford, UK: Oxford University Press.

Panfilov, A. V., Keldermann, R. H., & Nash, M. P. (2007). Drift and breakup of spiral waves in reaction-diffusion-mechanics systems. *PNAS*, *104*(19), 7922–7926.

Pantin, C. F. A. (1956). The origin of the nervous system. *Publicazioni della Stazione Zoologica di Napoli*, *28*, 171–181.

Parker, G. H. (1919). *The elementary nervous system*. Philadelphia, PA: Lippincott.

Passano, L. (1963). Primitive nervous systems. *Proceedings of the National Academy of Sciences of the USA*, *50*(2), 306–313.

Pavans de Ceccaty, M. (1974). The origin of the integrative systems: A change in view derived from research on coelenterates and sponges. *Perspectives in Biology and Medicine*, *17*, 379–390.

Peterson, K. J., Cotton, J. A., Gehling, J. G., & Pisani, D. (2008). The Ediacaran emergence of bilaterians: Congruence between the genetic and the geological fossil records. *Transactions of the Royal Society B*, *363*, 1435–1443.

Pfeifer, R., & Bongard, J. (2007). *How the body shapes the way we think*. Cambridge, MA: MIT Press.

Ryan, T. J., & Grant, S. G. N. (2009). The origin and evolution of synapses. *Nature Reviews Neuroscience*, *10*(10), 701–712.

Sachs, F. (2010). Stretch-activated ion channels: What are they? *Physiology*, *25*, 50–56.

Sakarya, O., Armstrong, K. A., Adamska, M., Adamski, M., Wang, I-F., Tidor, B., Degnan, B. M., et al. (2007) A post-synaptic scaffold at the origin of the animal kingdom. *PLoS ONE 2*(6), e506.

Sakurai, T., Mihaliuk, E., Chirila, F., & Showalter, K. (2002). Design and control of wave propagation patterns in excitable media. *Science*, *296*, 209–2012.

Satterlie, R. A. (2011). Do jellyfish have central nervous systems? *Journal of Experimental Biology*, *214*, 1215–1223.

Seipel, K., & Schmid, V. (2005). Evolution of striated muscle: Jellyfish and the origin of triploblasty. *Developmental Biology*, *282*, 14–26.

Shapiro, J. A. (2007) Bacteria are small but not stupid: cognition, natural genetic engineering and socio-bacteriology. *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences, 38*, 807–819.

Sherrington, C. (1906). *The integrative action of the nervous system*. New Haven, CT: Yale University Press.

Smith, C. U. M. (2008). *Biology of sensory systems* (2nd edition). Hoboken, NJ: John Wiley & Sons.

Smythies, J. (2002). *The dynamic neuron: A comprehensive survey of the neurochemical basis of synaptic plasticity*. Cambridge, MA: MIT Press.

Stein, P. S. G., Grillner, S., Selverston, A. I., & Stuart, D. G. (Eds) (1997). *Neurons, networks and motor behavior*. Cambridge, MA: MIT Press.

Stuart, D. G. (2005). Integration of posture and movement. *Human Movement Science*, *24*, 621–643.

Swazey, J. P. (1968). Sherrington's concept of integrative action. *Journal of the History of Biology*, *1*(1), 57–89.

Taylor, B. L. (2004). An alternative strategy for adaptation in bacterial behavior. *Journal of Bacteriology*, *186*, 3671–3673.

Thompson, E. (2007). *Mind in life*. Cambridge, MA: Belknap.

Trewavas, A. J. (2005). Green plants as intelligent organisms. *Trends in Plant Science*, *10*, 413–419.

Trueman, E. R. (1975). *The locomotion of soft-bodied animals*. London, UK: Arnold.

Valentine, J. W. (2004). *On the origin of phyla*. Chicago, IL: University of Chicago Press.

Valentine, J. W. (2007). Seeing ghosts: Neoproterozoic bilaterian body plans. In P. Vickers-Rich & P. Komarower (Eds), *The rise and fall of the Ediacarian biota* (Special Publications, 286, pp. 369–375). London, UK: Geological Society

Vanag, V. K., & Epstein, I. R. (2008). Design and control of patterns in reaction-diffusion systems. *Chaos*, *18*, 026107.

Van Duijn, M., Keijzer, F. A., & Franken D. (2006). Principles of minimal cognition: casting cognition as sensorimotor coordination. *Adaptive Behavior*, *14*, 157–170.

Van Elburg, R. A. J., De Wiljes, O. O., Biehl, M, & Keijzer, F. A. (submitted). A behavioural perspective on the early evolution of nervous systems: A computational model of excitable myoepithelia.

Watanabe, H., Fujisawa, T., & Holstein, T. W. (2009). Cnidarians and the evolutionary origin of the nervous system. *Development, Growth & Differentiation*, *51*, 167–183.

Webb, B. (2009).Animals versus animats: Or why not model the real iguana? *Adaptive Behavior*, *17*, 269–286.

Webre, D. J., Wolanin, P. M., & Stock J. B. (2003). Bacterial chemotaxis. *Current Biology*, *13*, 47–49.

Wooldridge, D. (1963). *The machinery of the brain*. New York, NY: McGraw Hill.

Yirmiya, R. & Goshen I. (2011). Immune modulation of learning, memory, neural plasticity and neurogenesis. *Brain, Behavior, and Immunity*, *25*, 181–213.

Zykov, V. S. (1987). *Simulation of wave processes in excitable media*. Manchester, UK: Manchester University Press.

Zykov, V. S. (2008). Excitable media. *Scholarpedia*, *3*(5), 1834.

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