



# Response to Alpi *et al.*: Plant neurobiology – all metaphors have value

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A recent letter to *Trends in Plant Science* signed by 36 scientists criticized the newly named area of plant neurobiology [1]. This letter stated that ‘Its proponents have suggested that higher plants have nerves, synapses, the equivalent of a brain localized somewhere in the roots, and an intelligence’ and that these provocative ideas had developed over the past three years. It concluded that plant neurobiology does not add to our understanding of plant physiology, plant cell biology or signaling. I know of no plant biologist who contradicts the centuries-old anatomical evidence that shows that plants do not have nerves or a brain. Plant neurobiology is a metaphor. The claim quoted above by Amedeo Alpi *et al.* [1] is factually incorrect, which could lead an unbiased reader to question the accuracy of any statements in the letter. However, metaphors can have substantial value and these few examples given below, out of many, substantially illustrate the value of neurobiology metaphors to plant biology and signaling.

## Darwin’s ‘brain’

It was in 1880, not 3 years ago, that Charles Darwin [2] concluded that ‘...the tip of the root *acts like the brain* of one of the lower animals, the brain being seated within the anterior end of the body receiving impressions from the sense organs and directing the several movements’. Was Darwin’s brain metaphor correct? I believe so.

In discussing bacterial chemotaxis, the brain biologist, John Allmann, [3] states that ‘...strictly speaking bacteria do not have nervous systems...but some of the most fundamental features of brains, such as sensory integration, memory, decision making and the control of behaviour, can all be found in these simple organisms’. Darwin (Ref. [2], see page 573 for quote) had experimentally demonstrated that root growth was altered in response to signals (control of behavior); that signals such as gravity, light, moisture and touch signals could be sensed simultaneously (sensory integration), that growing roots could distinguish between these signals and judge which was the most crucial to respond to (decision making and memory). More recent confirmatory demonstrations of Darwin’s statements have been referenced [4].

Based on the known differentiation of function within complex brains, a few experimental questions can be posed about the root ‘brain’. Are internal signals from the shoot sensed in different cell groups from those sensing external signals? Sensory cells for gravity are well defined but are those for touch, light and moisture each

sensed in separate cell groups? Are decisions about responses to any of the four signals found in different cell groups, and are these cells separate from the control of specific growth responses?

The value of metaphors resides in the experimental questions thrown up that may not be immediately obvious in their absence. Metaphors help stimulate the investigative imagination of good scientists.

## McClintock’s genetic intelligence

In her Nobel prize acceptance speech in 1983, the plant biologist Barbara McClintock stated ‘A goal for the future would be to determine the extent of knowledge the cell has of itself and how it uses that knowledge in a thoughtful manner when challenged’ [5]. McClintock is using the metaphor of a brain (thoughtful) applied to signal transduction processes (challenge), not an uncommon application, as witness the decade-old field of phosphoneral biology [6]. David Thaler [7] described McClintock’s research as uncovering ‘the evolution of genetic intelligence’ and James Shapiro [8] as ‘genomes functioning as true intelligence systems which can be readjusted when conditions require’. Intelligence at this molecular level is unlikely to disappear when considering cell or whole plant behaviour; these authors regard the genome as an adaptively variable system [9] – such behavior is regarded by psychologists as intelligent [10].

Can we define better what McClintock’s neurobiological metaphor means for cellular signal transduction? Both brains and signal transduction processes are ‘small world’ networks: a structural arrangement that optimizes information transfer and is probably universal in all natural networks [11–13]. Networks are constructed from nodes and connectors, and in ‘small world’ arrangements some nodes (hubs) are more heavily connected than others, providing robustness in performance. Calcium/calmodulin, an almost ubiquitous transducer in plant cells, is a highly connected hub. Other transduction molecules and possible transduction pathways have been identified in plant cells but there is little information as to their linkage density in a ‘small world’ arrangement.

McClintock’s neurobiological metaphor asks for knowledge of the cellular state (i.e. the current adaptive transduction network, its constituent proteins and its self-referencing by feedback). In brains, the current state is represented by the holistic, integrated, activity of all nerve cell connection strengths, and this points to what is lacking in the present plant signal transduction studies. There is little sense yet of an integrated, plant cell

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transduction network or how the structure of this network changes with environmental experience and development. McClintock's goal will remain merely a challenge until this omission is properly addressed. Instead, there is an over-emphasis on identifying the constituents involved rather than on determining network connections and, crucially, measuring connection strengths. These determine the relative importance of information flow through any transduction pathway in any particular signaling situation.

### Neurons and auxin transport

Cells, tissues, whole organisms, populations and ecosystems are all networks constructed from appropriate constituents, and there are organizing and control principles shared by all networks [14]. In the brain network, the anatomical neuron is the basic unit. However, in modeling other networks, a metaphorical neuron unit, a simple non-linear input/output device, is commonly used whether the interacting constituents are enzymes, cells, lymphocytes, transistors, social insects or even people [15]. Alpi *et al.* [1] criticized the terminology of describing auxin-transporting cells as neurons [16]. But auxin-transporting cells are part of a cellular network in roots and shoots and, as metaphorical neurons, the important issue raised is what happens to an auxin signal once it enters a transporting cell. If environmental experience modifies cell molecular constituents (as above), then the output auxin signal surely becomes environment dependent and not determinate as commonly envisaged. Perhaps a relay mechanism involving auxin-induced auxin synthesis operates [14], but again the neurobiology metaphor points to the need for new experimental investigations that are not currently performed.

### Self-organizing intelligence

Brains are self-organizing structures. During brain development, organization and structure emerges as a result of purely local signals between the constituent cells via multiple feedback loops. Crucially, no individual cell or groups of cells have any overview of the emerging structure [13,17–19]. Organizational changes emerge as critical sizes are reached and longer elements of communication are constructed, leading to the 'small world' configuration of the mammalian brain previously described [12,13]. This bottom-up approach, the clear absence of an overall leadership cell or tissue, would seem tailor-made to fit higher plant organization with its multiple growing points and modular structure. A 'small world' structure is evident in higher plants, consisting of clumps of locally communicating cells within meristems, coupled via longer range simpler communication to the activities of others. Such coupling should permit enhanced signal propagation speed and computation [20].

Despite the apparent ubiquity of self-organization in many areas of biology [21–23], I have detected little or no current interest in exploring its potential for understanding plant behavior. Yet observations of, for example, the behavior of social insect colonies have indicated some of the simple rules of interaction (communication) between the constituent organisms that govern the costs and

### Box 1. Self-organization and auxin transport

In their letter, Alpi *et al.* [1] dealt particularly with auxin transport. I have therefore included this box because it might provide some useful pointers about auxin transport from self-organization theory. There is a striking similarity between the spatial organization of foraging trails in ants and the geometry of vascular branching patterns in leaves [29,30]. In both cases, the final morphology results in the minimal use of energy for either food collection or resource distribution. But the geometry of foraging trails is optimized to minimize energy expenditure using bidirectional transit. The formation of leaf vascular channels might then require not only downward auxin flow [31] but an upward and, thus, bidirectional movement of other currently unknown signals such as cytokinins or water that require investigation. Axon guidance commonly uses bidirectional signaling too, and perhaps for the same reason [32]. The mechanism proposed by Tsvi Sachs [31] to explain the origin of auxin-transporting cellular channels by progressive reinforcement of an initially weak path is uncannily similar to the mechanism used by ants to firm up initially faint food-gathering pheromone tracks. Similarities in the branching rules that govern the coverage of space by foraging ants and the occupation of space by roots or shoot branches that also minimize energy use have been noted [30,33]. Although the signals used will probably be species specific, the rules that govern the way signals are used to construct tissues or colonies from cells or organisms might, like natural network structures, be universal and easier to uncover in social insect colonies. Insect colonies can gather information, evaluate, deliberate, form a consensus, make choices and implement decisions [23], but at a speed more familiar to plant behavior than that found in most animals. I intend to expand discussion on these important subjects at a later date.

benefits of adaptive changes, minimize energy usage, control information flow and, crucially, generate collective intelligence (Box 1) [23–25] – types of behavior exhibited by both higher plants [26] and mammals but in mammals specified by the brain.

Plausible mechanisms to explain the growth of 'small world' networks using robust self-organization have been proposed [20,27] that go beyond the particulars of any individual system and could be universal. However, neurobiologists found it necessary to include spatial constraints within these mechanisms to make them biologically plausible and enable 'small world' organization during brain development [13]. This neurobiological mechanism, incorporating signal decay with distance, is of direct relevance to understanding plant meristem organization (Darwin's brain) and helps explain the origins of small world structure in higher plants.

### Conclusion

"There's is no such thing as a central dogma into which everything will fit – any mechanism you can think of you will find – even if it is the most bizarre form of thinking. Anything. So if the material tells you 'it may be this', allow that. Don't turn it aside and call it an exception, an aberration. So many good clues have been lost in that manner" Barbara McClintock [28]. Neurobiology metaphors are neither an exception nor an aberration but an essential adjunct to the imaginative scientific mind in confronting some of the most recalcitrant problems in plant biology. These few examples contradict the claims [1] that plant neurobiology has nothing to offer plant physiology, cell biology or signaling.

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