

Time and the brain: neurorelativity

The chronoarchitecture of the brain from the neuronal rather than the observer's perspective

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Naturally, neuroscientists look at the brain from the outside when measuring how the flow of information unfolds over space and time. A neuron, on the other hand, can only 'see' through its connections, and they are spatiotemporally limited. Hence, the neural processing hierarchy from the neuroscientist's perspective and the hierarchy from the perspective of individual neurons do not agree. In order to understand the brain, only the neurons' perspective matters, thus demanding a change in the neuroscientists' perspective.

Time is relative. We all know this, but our appreciation of the importance of perspective on the experience of time is not matched by the same kind of sophistication when thinking about the brain. Here, the scientific community often maintains an overly simplistic linear view without considering the perspective of the neurons.

According to the standard model, sensory information is first processed in primary sensory areas and then processing unfolds over time along a putative brain hierarchy defined anatomically [1]. The timing of these processes is often thought to follow the same hierarchy: for example, retina, thalamus, primary visual cortex, secondary visual cortex, and so on. Electrophysiological recordings that are time-locked to the presentation of a visual stimulus show that neurons in the thalamus fire ~30 ms after stimulus onset. Neurons in the next processing stage, the primary visual cortex, fire at a latency of ~60 ms, neurons in secondary visual areas start firing at a latency of ~80 ms, and so on [2–4]. Therefore, it appears that the anatomical and functional hierarchies match with the timing of neural information processing [5,6].

This, however, is only true from the perspective of a neuroscientist who is looking at the brain from the outside. If we were to switch our perspective to that of a neuron that has a fast connection to higher visual areas, but only slower links with primary visual areas, the view of the temporal world would look different. From the perspective of such a neuron, we might 'see' visual input first through activity in higher visual areas and only later receive signals from the primary visual area (Figure 1). Hence, this neuron would disagree with the neuroscientist's view on the timing of

information processing. In fact, each neuron could in principle have a different temporal world-view, defined by the neuron's connections of different speeds. Indeed, it would be a surprise if there were a direct correspondence between the neuroscientist's view and the neuronal viewpoint of the temporal world. Think of spectators close to fireworks who will perceive the thunder and the blazing lights of the explosion at the same time, whereas those further away will perceive the thunder after the lights because sound travels slower than light. If a spectator further away did not know better, she would never agree about the timing with the spectators close to the fireworks. Neurons do not know better and therefore have to stick to the timing they 'perceive'.

This should be a familiar idea. Whereas the neuroscientist can enjoy beautiful retinotopic maps and the sensory and motor homunculus, the neurons cannot necessarily 'see' the orderly arrangement of these habitual 'somethingotopic' maps [7,8]. The reason for the different views from within a sensory map is that a neuron does not 'see' the whole brain as does (at least theoretically) the external observer. A neuron can only 'see' through its connections, and they are spatiotemporally limited. To share the neuroscientist's appreciation of a retinotopic map, a neuron would need to have connections to all the neurons that form the retinotopic map. Furthermore, these connections would need to be of the same speed, because otherwise the retinotopic map will be temporally distorted. Neither of these is the case.

It is, therefore, important to reconsider the perspective of the external observer (with an implicitly fixed temporal reference) and understand that each neuron has its own schedule of information processing. To derive each neuron's schedule is currently beyond our technical means. It would require the ability to measure the connection speed between all pairwise neuronal connections. Given that the human brain has roughly 10^{14} such connections, this may not be feasible even in the distant future. However, there are likely to be principles of organization (temporal clusters, small worlds, temporal channels) and attempts have already been made to estimate the connection speed between clusters of neurons. For example, techniques such as diffusion-weighted magnetic resonance imaging allow assessment of axon diameters and myelination of larger fiber

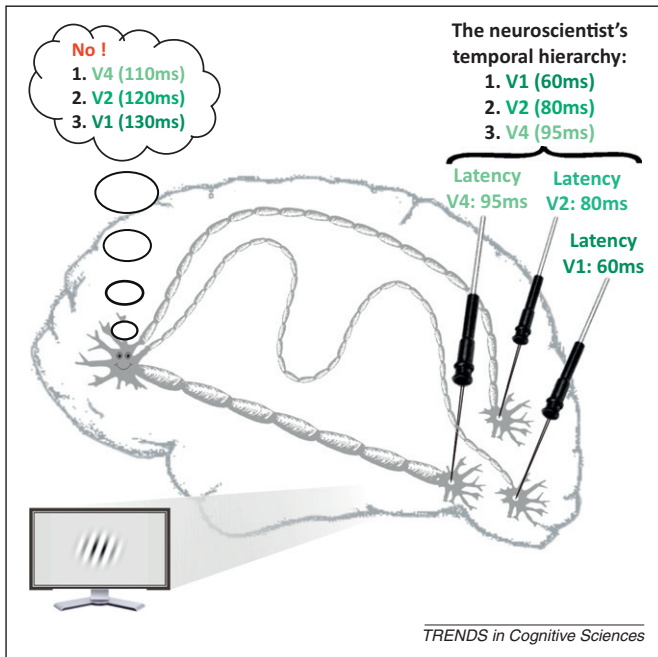


Figure 1. Conflicting temporal hierarchies. Current measures of neural response latencies that are time locked to external stimuli show that neurons in primary visual areas (V1) fire before neurons in higher ones (V2, V4, ...). However, such a temporal hierarchy is only valid from the perspective of an external observer. From the perspective of another neuron in the brain, which has a fast connection to higher visual areas, but only slower links with primary visual areas, the temporal hierarchy can be different.

bundles between brain regions [9,10]. These measures may be used to estimate the relative connection speed between regions. Including such measures in existing models of the human connectome will allow one to derive different schedules of information processing, at least for clusters of neurons.

Understanding the true temporal hierarchy of the human brain will shed new light on the neural code representing the external world. Measures such as the latency code, according to which information is carried by the timing of responses relative to stimulus onset, explicitly assume that the neuron has access to the time of stimulus onset [11]. For most neurons, this assumption does not hold. To avoid the need for an external temporal reference, it has been proposed that latency coding could rely on intrinsically generated signals, such as population responses [12,13], or on the responses of a subpopulation of neurons that tend to respond rapidly to various stimuli [14]. The activity of such neurons might represent an explicit neural signal of the stimulus timing. However, even such intrinsic signals will be ‘seen’ at different times by different neurons. This timing issue might be less problematic for local computations of cortico-cortical synapses; however, it becomes exacerbated with increasing distance and for multi-synaptic connections. It might also be less problematic if the temporal reference signal travels along with the information that has to be decoded by it [14]

or if information is carried by spatially organized oscillatory activity as in phase coding [11,15]. Nevertheless, if temporal codes matter, it is important to get the timing right and take into account each neuron’s individual temporal reference frame.

The current approach to the timing of neural information processing is technically and conceptually limited to the perspective of an external observer. The technical barriers will be overcome in the future, but the conceptual limitations can be overcome today. In order for this to happen, it is essential to realize that looking at the brain from the outside is not the same as being inside the brain. Neuroscientists need to begin working with the temporal hierarchy of the neurons and not those of the external observer. It would be a first step towards a true chrono-architecture of the brain – one based on the brain’s perspective: the only one that matters.

Acknowledgments

This work was supported by the Swiss National Science Foundation, the European Union, and the Wellcome Trust. We thank Bahador Bahrami, Narly Golestani, Michael Herzog, Frank Jäkel, Stefan Kiebel, Stefano Panzeri, Marty Sereno, Dimitri van de Ville, and Nikolaus Weiskopf for insightful discussions.

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