

# Processing Timescales as an Organizing Principle for Primate Cortex

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An emerging view posits a timescale-based cortical topography, with integration windows increasing from sensory to association areas. In this issue, [Chaudhuri et al. \(2015\)](#) present a cortical model wherein a hierarchy of timescales arises from local and inter-regional circuit dynamics.

In real life, the brain needs to concurrently accumulate and integrate information over multiple timescales. For example, when two monkeys from different families start to fight, other monkeys from each family track the fight: they observe the facial expressions and body positioning of the fighters as they circle (milliseconds scale), they track the movements of the fighters as they battle (seconds scale), and they avoid interactions with the opposing family until the fight (which can last for many minutes) resolves ([Cheney and Seyfarth, 1999](#)). Only a system with the ability to allow past information to exert an influence on current processing over multiple timescales, in parallel, could accomplish such a feat.

An analog for this problem of multi scale temporal processing exists in the spatial domain, and its solution in the brain is better understood. In visual cortex, neurons in early areas that code for basic features such as edges and contrast have small spatial receptive fields, i.e., a small region of visual space over which the appropriate stimulus will elicit a response. As one moves downstream to the areas that receive and compile input from earlier visual areas, neurons have increasingly large spatial receptive fields ([Hubel and Wiesel, 1962](#)), enabling them to exhibit properties such as size and location invariance. Thus, the problem of concurrent processing of information at multiple spatial scales is addressed by a hierarchical organization of increasing receptive field sizes that mirrors the flow of information from early regions to later regions.

Studies of neural dynamics in humans and non-human primates have begun to reveal a distributed, hierarchical organi-

zation of “temporal receptive windows” in the cortex, a temporal counterpart of the spatial hierarchy. Converging results from human imaging ([Hasson et al., 2008](#)), human electrocorticography ([Honey et al., 2012](#)), and monkey single-unit recordings ([Murray et al., 2014](#)) show that processing timescales range from the milliseconds range in early visual and auditory cortex, up to the seconds range in intermediate areas, and up to minutes or longer in high-level association areas such as posterior medial, lateral tempoparietal, and prefrontal cortex. Processing timescales have been measured by (1) observing activity decay rates following briefly presented stimuli, (2) computing autocorrelation properties of both stimulus-driven and spontaneous (during rest) activity, and (3) examining the durations at which changes to past input can affect responses to dynamic stimuli in the present moment. This distributed organization has been proposed to enable concurrent integration over multiple timescales, as critically needed for processing real-life continuous stimuli ([Hasson et al., 2015](#)).

To explore what neurobiological circuit mechanisms might support such a hierarchy of timescales, [Chaudhuri et al. \(2015\)](#) constructed a large-scale dynamical model based on findings from an anatomical analysis of connectivity in the macaque neocortex ([Markov et al., 2014](#)). In the model, each cortical area is described by a threshold-linear, excitatory-inhibitory recurrent network. A key feature of the model is the implementation of anatomical heterogeneity across the cortex: inspired by studies showing that the number of basal dendritic spines

on layer 3 pyramidal neurons increases from early to late cortical areas ([Elston, 2000](#)), the authors varied the density of excitatory connection strengths in each cortical area according to the position of that area in the cortical hierarchy. Their hypothesis was that this inter-regional variation in the level of recurrent excitation could give rise to a hierarchy of different timescales across the cortex.

To examine the model’s response to stimulus input, the authors simulated pulsed input to primary visual cortex. They observed propagation of responses across areas, and notably they found that decay times increased progressively along the cortical hierarchy. Similarly, when the authors simulated white-noise input, they saw in early sensory areas that temporal autocorrelation decayed rapidly (at the scale of a few hundred milliseconds), while in later areas autocorrelation persisted for much longer (at the scale of a few seconds). Time constants that were fit to the decay of each area’s autocorrelation function generally increased along the cortical hierarchy. Interestingly, there were exceptions; e.g., area 8 m, part of the frontal eye fields, expressed a long timescale despite being relatively low in the cortical hierarchy (matching empirical observations from human brain imaging), seemingly due to its connections with long-timescale prefrontal areas. When primary somatosensory cortex was stimulated, responses propagated along a separate network of areas from the visual group, again with hierarchically increasing timescales.

Does the variation in processing timescales across regions arise from region-specific local circuit properties, or from

the position of a region within the network macroarchitecture, or from a combination of the two properties? To test this, Chaudhuri et al. examined the effects of abolishing the inter-area structure of local microcircuitry, or inter-areal projections, and of both together. When differences in local microcircuitry (i.e., the gradient of excitatory input strength across areas) were removed, time constants decreased and the relationship between regional timescale versus hierarchical level was eliminated. When the empirical architecture of long-range projections was removed, regional timescales were moderately reduced overall, and each area's timescale strictly reflected its position in the hierarchy.

Finally, the authors explored the consequences of local microcircuit heterogeneity for functional connectivity in the model. When local heterogeneity was removed, the correlation between functional connectivity and anatomical connectivity was drastically reduced. Empirical studies of the primate brain show that functional connectivity and anatomical connectivity are related, but not strongly so. The current finding offers a possible explanation: resting state functional connectivity is typically calculated under the assumption of homogeneity across areas. Thus, the correspondence of gross functional and anatomical connectivity might be better understood by accounting for local circuit properties that vary in a regular manner along the macro-scale anatomical hierarchy. Additionally, the authors found that areas with long timescales were especially important for functional connectivity in the model: the longer an area's timescale, the greater the impact on global activity patterns when the area was lesioned.

Chaudhuri et al. have insightfully demonstrated how anatomical connectivity—both within and between regions—can produce a hierarchy of timescales in neuronal population activity. There are a number of other mechanisms that will be important to consider in future work. First, it will be important to consider variations in processing timescales that may arise from changes in the local biophysical properties of neurons across the cortical hierarchy: for example, the density of “fast” and “slow” glutamate receptors (Wong and Wang, 2006) as well as the

density of presynaptic calcium channels and other regulators of synaptic depression and facilitation (Zucker and Regehr, 2002). Second, ascending neuromodulatory systems will directly regulate the persistence of neuronal population activity, and this effect may apply to varying extents as a function of the diffuse projections targeting higher and lower levels of the cortical hierarchy. Finally, cortical processes can achieve very long timescales via interactions with the medial temporal lobe, which supports direct reinstatement of prior neuronal states. The recurrent mechanisms in the model of Chaudhuri et al. produce timescales up to the order of seconds, but it will be important for future work to determine how some circuits appear to integrate information over minutes of time, and whether hippocampal interactions are a necessary component of this process.

When we refer to the “integration” of information over time, we mean, broadly, the modification of an input signal in light of past states of a circuit. The model of Chaudhuri et al. instantiates the influence of past stimuli on current responses by slowing the decay of activity in higher levels of the hierarchy and is thus closer to a more specific mathematical sense of integration. The persistent activity state observed in higher-level areas reflects accumulation of inputs over time and has been theorized to support cognitive processes such as working memory and decision-making. While this simple mathematical notion of input accumulation fits well with a buildup of evidence prior to a decision, it is important to question whether the ability to accumulate information over time is generally sufficient for supporting functions that require the combination of prior and present information. Past and present input may have a more complex relationship, above and beyond simple summation: for example, the meaning of—and neural responses to—the words “she carefully closed all of the windows” will change if they are preceded by the words “When Frieda left her apartment for vacation” versus “When Frieda logged onto her friend's laptop.” It seems that a circuit would need abilities beyond signal summation to differentiate these cases; some manner of experience-based expectation is at play, enabling

past input (“apartment” versus “laptop”) to rapidly influence the meaning of, and neural responses to, stimuli a few seconds later (“windows”). Observations like these—which indicate that active traces of past information within each local circuit modify online processing—encourage the development of a new family of biophysical circuit models that will allow for complex mixing of recent memory with continuous input (Hasson et al., 2015).

Despite the empirical observations of slower processing in higher-order systems as noted above, we should not forget that slow processes unfold in sensory circuits (Yaron et al., 2012), and higher-order systems may respond very quickly (Kirchner et al., 2009). More generally, for a system as complex as a neuronal circuit, it can be overly reductionist to assign a single timescale of activity (Marom, 2010). It is important, therefore, to conceive of processing timescales as a bias of activity within a system that can operate on multiple scales, rather than a prescription of activity at a single scale. The flexibility of processing timescales has an analog in the spatial domain: neurons will often exhibit some level of response outside the immediate range of their spatial receptive fields, which is dependent on task, context, and attention demands (Op De Beeck and Vogels, 2000). Just as spatial receptive fields have been a powerful construct for visual research, temporal receptive windows may serve as a useful organizing principle for old and new discoveries in the dynamics of cortical processing.

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