Working memory and neural oscillations: alpha–gamma versus theta–gamma codes for distinct WM information?

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Neural oscillations at different frequencies have recently been related to a wide range of basic and higher cognitive processes. One possible role of oscillatory activity is to assure the maintenance of information in working memory (WM). Here we review the possibility that rhythmic activity at theta, alpha, and gamma frequencies serve distinct functional roles during WM maintenance. Specifically, we propose that gamma-band oscillations are generically involved in the maintenance of WM information. By contrast, alpha-band activity reflects the active inhibition of task-irrelevant information, whereas theta-band oscillations underlie the organization of sequentially ordered WM items. Finally, we address the role of cross-frequency coupling (CFC) in enabling alpha–gamma and theta–gamma codes for distinct WM information.

Neuronal oscillations and working memory

Working memory (WM) involves the ability to maintain and manipulate information over short periods of time and can be subdivided into the initial encoding of information and maintenance and retrieval of WM items (Figure 1A) [1]. Because WM is centrally involved in many aspects of higher cognitive functions, a substantial amount of work has been dedicated to identifying the neuronal substrates of different WM processes [2,3].

A central question in WM research is how groups of neurons represent and sustain items in the absence of sensory inputs. One possibility is that reverberating neuronal activity in distributed cell assemblies underlies WM maintenance, as originally proposed by Hebb (Figure 1B) [4]. This proposal has recently received support through observations that rhythmic activity at low (theta, alpha) and high (beta, gamma) frequencies facilitates the formation of coherently organized groups of neurons via the establishment of transient temporal correlations [5–9].

Although rhythmic patterns of activity were first demonstrated by investigators at the beginning of the 20th century, a relationship with behavior was only established 50 years later in seminal work by Singer and colleagues [10]. Specifically, these findings revealed that action potentials generated by cortical cells in the primary visual cortex (V1) are phase-locked to the gamma rhythm in response to a visual stimulus, thereby providing evidence of a relationship between the phase of neuronal oscillations (see Glossary) and the temporal organization of neuronal activity (for a different perspective on phase-coding through gamma-band oscillations see [11]). This finding is supported by several studies that have demonstrated that neuronal oscillations enable efficient transmission and coding of information in distributed neuronal populations [7,12]. In relation to WM, several groups have demonstrated a

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Glossary

Electrocorticography (ECOG): measurement of electrical brain signals using electrodes that are implanted subdurally on the surface of the brain.
Electro/magnetoencephalography (EEG/MEG): non-invasive methods for studying brain function that reflect the electrical activity of neuronal populations with millisecond temporal resolution.
Local field potential (LFP): electric potential in the extracellular space around neurons. LFP is a widely available signal in many recording configurations, ranging from single-electrode recordings to multi-electrode arrays.
Long-range synchrony: synchronizations between widely separated brain regions (> 2 cm) as reflected, for example, in phase synchrony.
Neuronal oscillations: prominent feature of spontaneous and task-related brain activity that occur at the level of single units, local field potentials (LFPs), and EEG/MEG recordings. The traditional view is that neuronal oscillations reflect inhibition-based fluctuations of neuronal activity that emerge from the synchronous activation of large neuronal ensembles.
Phase: way of quantifying the difference between two oscillations according to some feature (peak or trough) of one of the oscillation with respect to the other.
Spectral power: reflects the amplitude of neural oscillations computed through a time–frequency transformation (TFT).

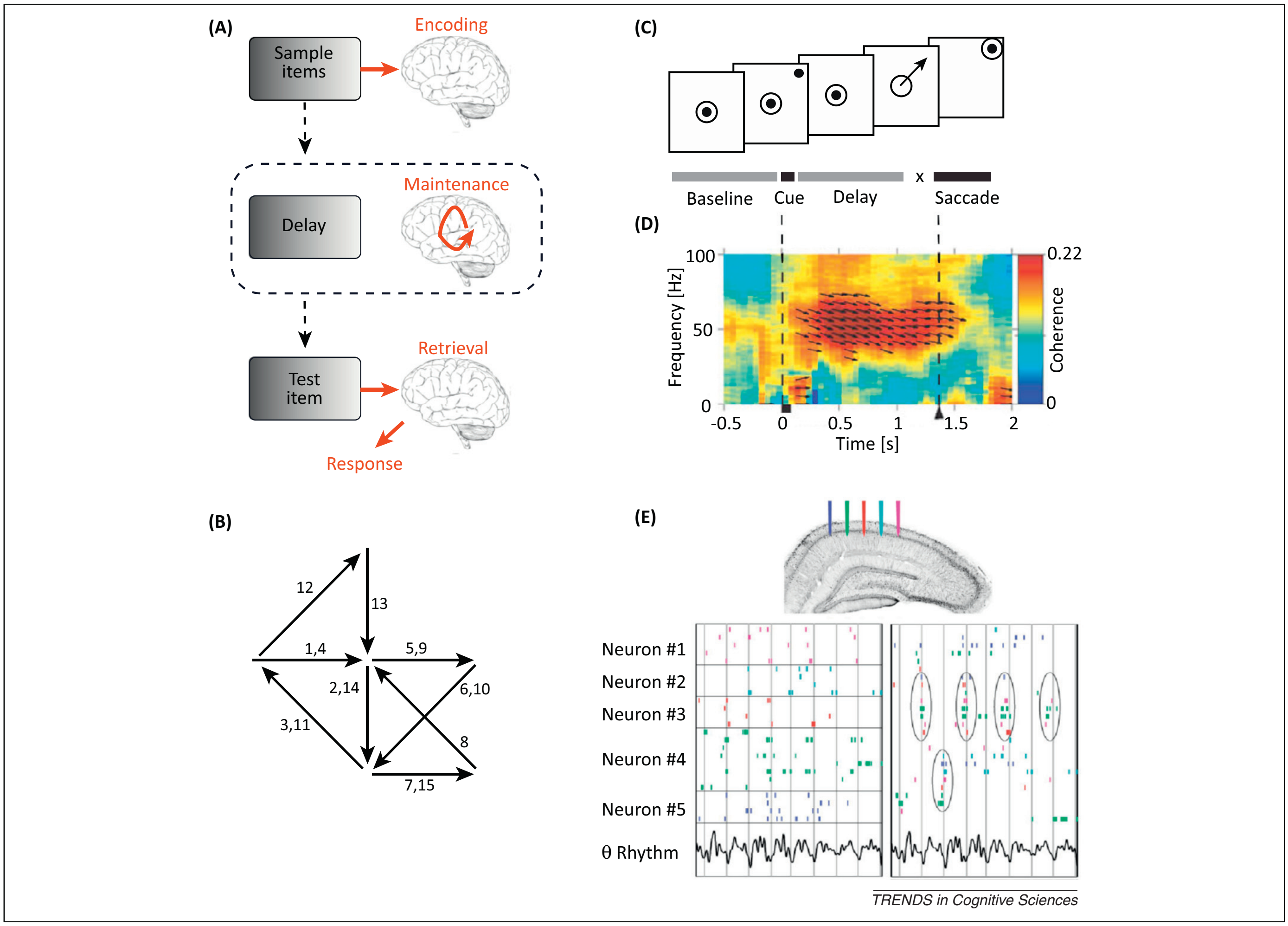

Figure 1. Working memory (WM), neuronal oscillations, and cell assemblies. **(A)** The three stages of WM comprise encoding, maintenance, and retrieval phases. **(B)** Schematic representation of a Hebbian cell assembly. Arrows represent a sequence of neural cell assemblies in which each cell assembly fires according to the numbers on top of each arrow. Once each cell assembly in the loop has fired, the sequence begins again with the first cell assembly. Thus, sequential reactivation of cell assemblies creates a loop (reverberating circuit) that could support sustained neuronal spiking activity during WM maintenance. Modified from [4]. **(C,D)** Example of a delayed occulomotor response task. The cue indicates the spatial position on the screen that has to be memorized. After the delay period, the monkey has to perform a saccade towards the memorized location. The enhancement of spike-field coherence during the delay period reflects the temporal alignment of anatomically distributed neurons with the phase of local field potential (LFP) gamma-band activity. This relationship could underlie the formation of reverberating cell assemblies in parietal cortex during WM retention. Modified from [13]. **(E)** Theta-based activation of cell assemblies in the hippocampus: electrode positions (upper panel) and raster plots (lower left and right panels) of spiking activity for five neurons in the hippocampus. Vertical lines indicate troughs of theta activity (bottom trace). After reordering of the data via a stochastic search for precise temporal relationships, individual cell assemblies become visible around the troughs of theta activity (right lower panel). Modified from [81].

correlation between the timing of neuronal spiking, the phase of oscillatory activity in local field potentials (LFPs), and WM delay activity (Figure 1C–E) [13,14].

Evidence of a relationship between neuronal oscillations and the maintenance of WM items in humans has been provided by electro-/magnetoencephalographic (EEG/MEG) and electrocorticographic (ECOG) recordings. These studies have reported enhanced amplitude and synchrony of oscillatory activity and WM load-specific modulations at different frequencies, in particular in theta (4–7 Hz), alpha (8–13 Hz), and gamma (30–200 Hz) ranges (Table 1). However, the functional role of these different frequencies, as well as their relationship to distinct WM processes, has remained unclear.

Here we propose a framework for integrating the different findings on neuronal oscillations during WM maintenance. Specifically, we suggest that gamma-band oscillations reflect a generic mechanism for active maintenance of WM information, whereas theta-band activity is specifically involved in the temporal organization of WM items. By contrast, oscillatory activity at alpha frequencies is not relevant for WM information *per se*, but has a critical role in protecting WM items from non-relevant information. As a result, distinct forms of WM information rely on different oscillatory networks that are grouped through cross-frequency coupling (CFC) into different WM codes.

WM delay activity and gamma-band oscillations

Initial research focused on the relationship between gamma-band activity and perceptual processes [15]. However, it soon became clear that high-frequency oscillations are not restricted to visual responses but also occur during a wide range of cognitive and executive processes, including WM. Indeed, gamma-band oscillations occur in all cortical areas and most subcortical structures and are particularly prominent in superficial layers [16].

Experimental and theoretical studies suggest that gamma-band oscillations in the range 30–100 Hz emerge from