

Comments on “Storage of 7 ± 2 short-term memories in oscillatory sub-cycles (1)”

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This paper (1) presents a hypothetical model for short-term working memory employing afterdepolarisation (ADP) to perpetuate high-frequency oscillation between low-frequency oscillations. Additionally, the model introduces inhibitory feedback to avoid synchronised firing and to separate individual spikes. While the model gives compelling performance, further tests are required to validate its effectiveness. Importantly, the paper focuses on the mechanism of perpetuating short-term memory through time, and does not elaborate the practical significance between neuronal activity and memory, such as the retrieval of short-term memory or the scanning. This is, however, an inevitable given the highly hypothetical nature of the model.

This model employs several elements to reconstruct some properties of the working memory. To understand how this model works, we examine some tractable features. The first is the emergence of oscillations at a particular high frequency, as a result of global negative feedback. The waveform of the inhibitory hyper-polarisation directly determines this global refractory period after each spike, inducing a corresponding frequency. To be consistent with experiment-derived 60-80Hz high-freq oscillation, the timescale of inhibition needs to be on the order of 10ms, which can be validated by measuring the electrical activity of interneuron. This high-freq oscillation also directly induces its second feature, which is the sequential nature of the learned spike sequence. The third is the memory capacity, that can be approximated with the ratio between the excitable period and the high-freq inhibition time-scale ($100\text{ms}/10\text{ms} \sim 10$). The mechanistic insight it provides however goes beyond the experimental evidence, which we will remark later in numerical simulations.

From a mechanistic perspective, the model employs a background sinusoidal wave (6Hz) to partition time domain into excitable and refractory periods. Information contained in spikes from last excitable period is perpetuated in the form of a slowly rising ramp via ADP. Furthermore, partitioning into sub-cycles is maintained by inhibitory feedback, which forces a globally refractory phase after each firing. With these features established, one can adjust parameters to fit experimental data.

Bearing those explanatory powers, the model does fall short in some other aspects. Firstly, the rising of ADP ramp is so slow that once a neuron fires in the cycle, it does not have a chance to fire again, i.e. each neuron can only be activated exactly once in the same alpha cycle. This feature is incompatible with real application. For example, if one wants to store a telephone no. 0767486... , the number “6” will occur 2 times. Such memory can not be explicitly mapped to a non-repeating temporal spiking sequence. Thus, one needs to carefully interpret the learned temporal spike sequence.

We can review experiments quoted in (1) to seek a resolution. Using list-match test, Sternberg measured reaction time for testee to decide whether the given object is part of the list or not to reflect the retrieval of working-memory (2). Every additional object on the list incurs a 38ms increase in reaction time, for confirming both the presence of the test object and the absence of the test object, implying that both tasks employ an exhaustive scanning search. Thus, in Sternberg’s test, we would only be required to decide whether number “6” is present in the learned number, which is within capability of such model. While such tests do not concern any order present in the

memorised object, the model stores memory explicitly as a temporal sequence, making this feature a candidate hypothesis to test for validity of the model.

The paper also briefly talks about how memory can be formed and removed. Memory can be formed by presenting activity spike through informational input to a neuron, which then fits itself to the firing sequence, depending the ADP status of all other neurons. Two removal approaches are provided. First is by overflow, where new inserted spike re-phase the firing pattern and take the place of old perpetuated spike. The second is by relieving interneuron inhibition, where all phase information is lost and all spikes simultaneously begin to fire where the first spike was firing.

In the first approach, the insertion of new spike depends on where it is presented first in the cycle. One natural choice is to spike just before any existing spike, shifting all later spikes to later. Consequently if the new spike is presented during the descending phase, it is effective before the earliest spike, thus will become the new first spike and shifting all existing spikes to later (figure 1a), which cause the last spike to drop out of the excitable window. The authors have also suggested alternative parameter to shift phases to earlier (figure 1b). Overall, the insertion works by inhibiting other spikes, at one point or another. In the scene that sequential nature do not play a specific function, the orientation of insertion seems irrelevant.

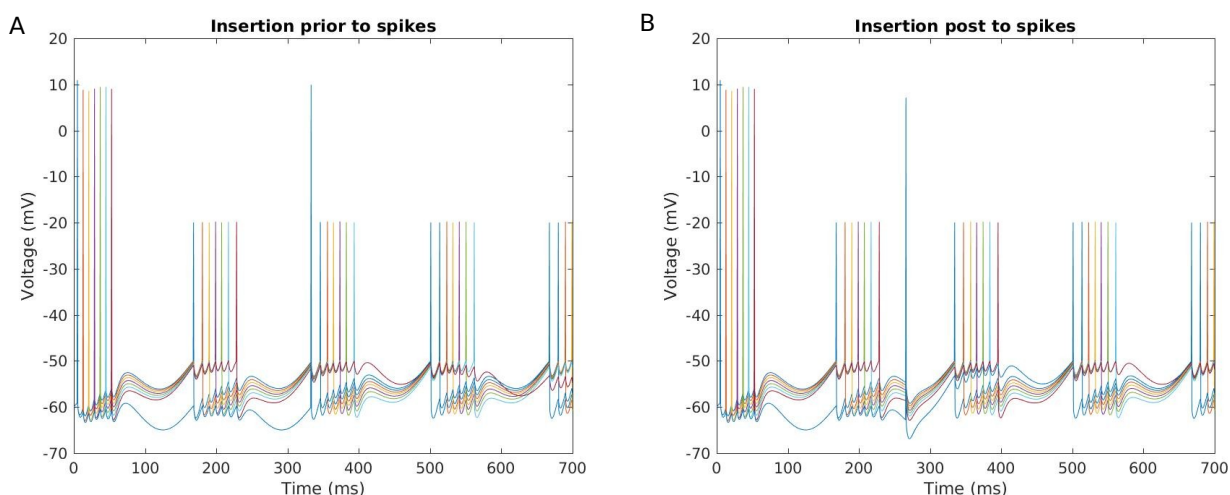


Figure 1: Insertion of new spikes according to first approach. A: new spike is presented just before the previously first spike, and shift all spikes to later. B: new spike is presented during negative phase, thus incorporated into the start of the next spike stack.

In the second approach, one can still access the presence/absence of any specific object by looking at the activity of its corresponding neuron. This echoes the unnecessary ordered feature in the original model – if one only wants to know whether a particular object is present, the non-phasic memory is still adequate for the job.

While these hypothetical ways of modifying working memory serve an adequate proof of concept, their practical relevance cannot be tested without a functional framework linking the model to real working memory. It's also not clear how such network should be trained to perform a specific function. Rather, it is constructed only to explain the experimental observables. In this sense this model is explanatory rather than mechanistic.

We also note some further disadvantages of the model:

1. The nesting process can not be iterated to construct longer nested oscillations, highlighting the explanatory nature of the nesting process. Additionally, the fact that only the excitable part of the waveform is nested also contradicts evidence from magnetoencephalographic (MEG) study (figure 2) of human cortical responses, where nesting spreads out evenly throughout the waveform without apparent affinity (3). This shape of brainwave is also confirmed in recent MEG analysis (4). Moreover, the size of the gamma spikes is observed to follow a sinusoidal trajectory, implying a further modulation of the signal by perhaps alpha wave, which is not seen in the current model.

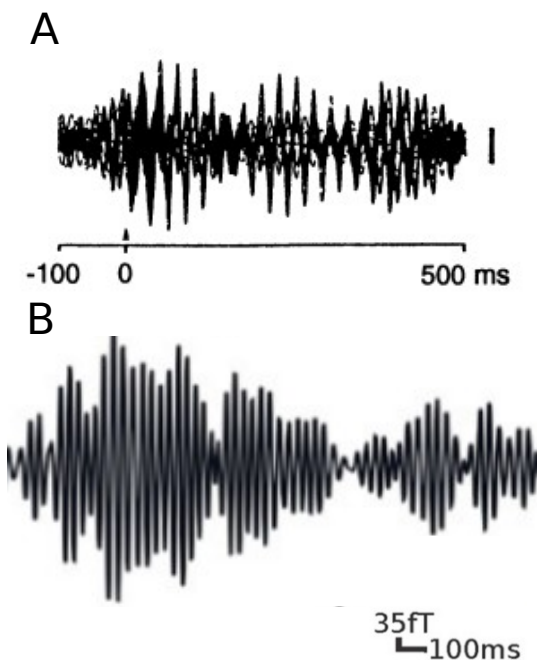


figure 2: Profiles of MEG-detected gamma claimed to reflect short-term memory. A: adapted from (3) ; B: Adapted from (4). .

2. As authors have mentioned, the removal of memory upon overflow is rapid. Once a neuron drops off, it never comes back, i.e. all-to-none decay without a transient. This notion of overflow must be supported by an explicit upper bound of short-term memory. However, we are not aware of a shared upper bound between different types (visual, verbal) of short-term memory, thus such argument cannot be easily delivered.

We go on to make some rough estimations and numerical simulations:

The model employed by the authors has the form:

$$r \cdot dV/dt = -V_i + V_{rest} + V_{osc} + V_{adp} + V_{inh};$$

Assuming small value of r (a.k.a. long timescale of leakage) gives

$$V_i = V_{rest} + V_{osc} + V_{adp} + V_{inh};$$

Set V_{rest} to -60mV . Set spike only if V_i exceeds -50mV , which implies

$$V_{osc} + V_{adp} + V_{inh} > 10\text{mV}.$$

If we assume a fast decay for V_{inh} to decay fast. Then the firing condition reduce to

$$V_{osc} + V_{adp} > 10\text{mV}.$$

If we further assume V_{osc} to be zero to focus on the effect of V_{adp} , we obtain

$$V_{adp} > 10\text{mV}.$$

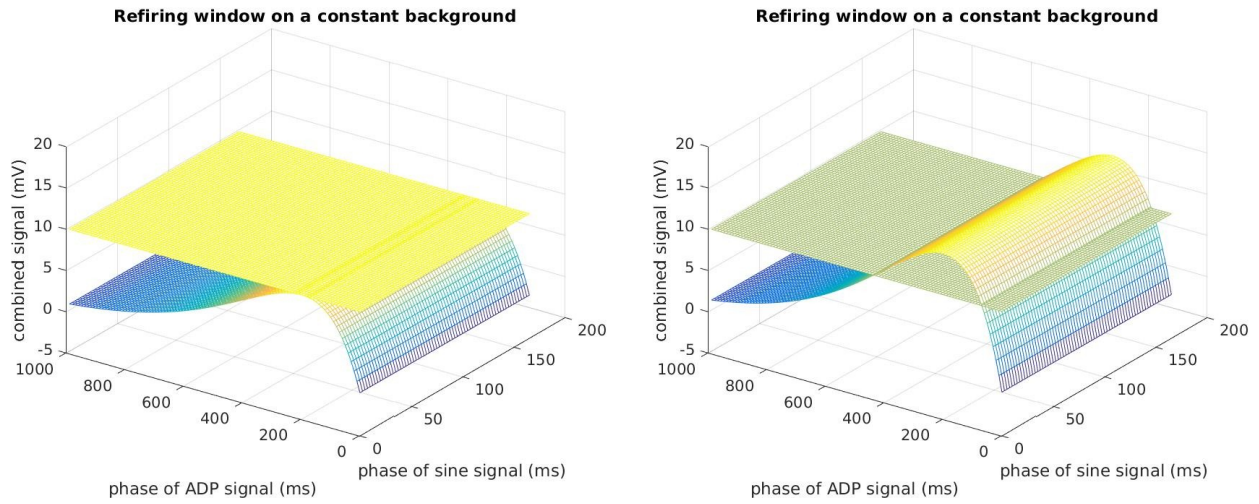


Figure 3: Visualisation of firing window on a constant background. Both model employ $V_{osc}=0$. The horizontal plane represent $V_{adp} + V_{osc}=10\text{mV}$ Left: $V_{adp}=10\text{mV} \cdot \exp(1-t/200\text{ms})$. No refiring window is present. Right: $V_{adp}=15\text{mV} \cdot \exp(1-t/200\text{ms})$, peak is raised beyond the threshold.

The time window where this condition is met is referred to as a “refiring window.” Depending on the precise shape of the wave form, the refiring window size varies. The paper assumes an alpha function with amplitude 10mV and time constant of 200ms . Thus the refiring window is only a single point where the ADP curve touches 10mV . (see figure 3a). By increasing the amplitude of ADP signal to 15mV , an extended refiring window emerged (70ms to 430ms , figure 3b). Correspondingly, presented spikes are repeated even in absence of the sinusoidal background. (figure 4)

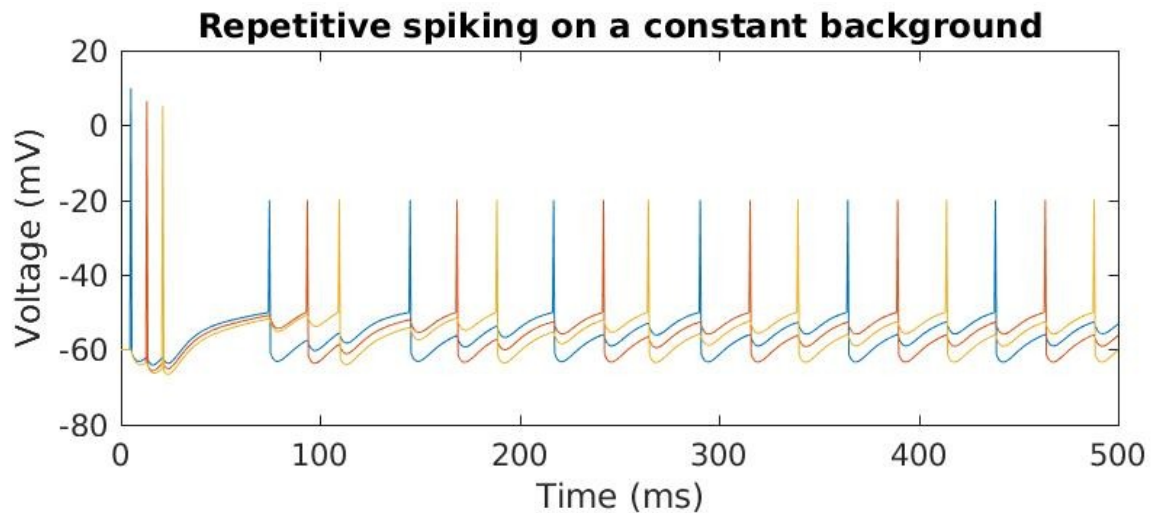


Figure 4: Spike sequence can be perpetuated even when not nested in alpha cycles.

Now let's reconsider the author's model, where they introduce an oscillating V_{osc} of amplitude 5mV and frequency 6kHz (a.k.a. period of 166ms). Where ADP signal is reinforced, a refring window emerge as a oval shape (50-510ms through ADP phase, 0-82ms through alpha signal, figure 5a,5b). Notice this means the same neuron cannot be reactivated until 50ms post-discharge, which prevent its reactivation in the same alpha cycle. Even the neuron is activated early as at 0ms, its trajectory still does not touch the refring zone of the first cycle (figure 5b). Given that the first activation is bound to take place at 0-82ms, same-cycle reactivation is strictly prohibited.

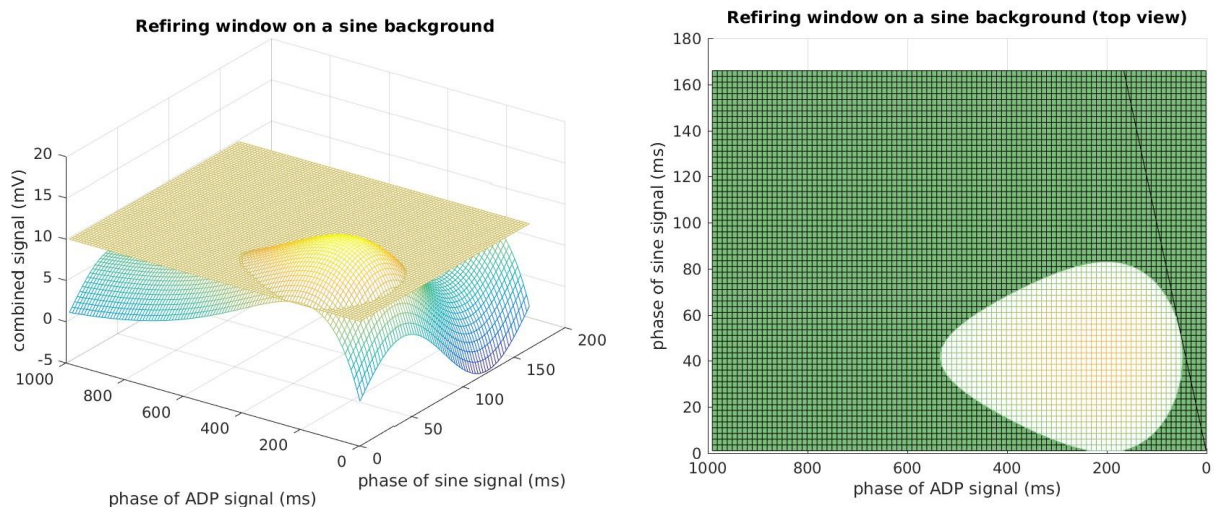


Figure 5: Refringing window on a sine background. The horizontal plane represent $V_{adp} + V_{osc} = 10\text{mV}$. Left: side-view, Right: top-view, the solid line indicates a trajectory following a discharge at 0ms phase of oscillatory signal.

Taken together, we comment that:

1. ADP is the central element that perpetuates the information and itself is adequate for this single goal. It is, however, unclear whether neurons firing at the same time could represent separate memories.
2. Applying an interneuronal global negative feedback (or lateral inhibition) separates spikes into temporal groups at gamma spacing, with the gamma spacing merely reflecting the timescale of the

feedback. This temporal spacing would establish an upper bound for the processing rate of the brain, if we assume the brain works in a serial order (which itself is an arguable assumption).

3. The memory capacity of 7 is a questionable and unnatural result. In principle, the maximum number of separable items that can be stored at gamma spacing is only limited by the timescale of ADP. That is, any stored item must be retrieved before its ADP signal drops out of the refractory window.

Consequently, the number of gamma spacings that can fit in this period of time determines the maximum number of separable items/spikes. We understand that authors have purposely chosen parameters to fit experimental observations.

4. A discrete sudden discharge upon crossing threshold is the basis of coding information. It is the root of the consequent repetitive dynamics. It would be interesting to experimentally explore the timescale of the threshold and how it can be related to epileptic neuronal activities.

Overall, without an established framework for short-term memory retrieval and deposit, the described model still makes fruitful predictions, with the most important one relating memory processing rate to interneuronal/lateral inhibition. It is interesting to see whether processing rate indeed correlates with the timescale of the lateral inhibition, by devising a reliable metric/protocol to measure the processing rate. In contrast, the short-term memory itself is an ill-defined concept with little measurable quantities. Still more work needs to be done to understand the nature of short-term memory and to devise an intervention that blocks its access or deposit. It's only with such experimental interventions that we can establish a more reliable mechanistic model.

References:

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