Supporting Online Material for

Synaptic Theory of Working Memory

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Bifurcation analysis of a single population rate model To better elucidate the dynamical mechanism of the spiking network behavior, we considered a simplified rate model consisting of a single excitatory population. The state of the population is described by the average rate E (*1*), the average utilization factor u, and the average amount of available resources x. They evolve according to (*2*):

$$\begin{aligned} \tau \frac{dE}{dt} &= -E + g(JuxE + E_0) \\ \frac{du}{dt} &= \frac{U-u}{\tau_F} + U(1-u)E \\ \frac{dx}{dt} &= \frac{1-x}{\tau_D} - uxE \end{aligned} \tag{1}$$

where $g(...)$ is the neuronal gain function, J is the strength of recurrent connections, E_0 is an external input and τ is the time constant of the rate dynamics, usually assumed to be on the order of several milliseconds. In this study, we chose the smooth gain function that has an exponentially decaying subthreshold component and a suprathreshold linear part: $g(z) = \alpha log(1 + e^{z/\alpha})$.

Because we are interested in the case of strongly facilitating connections with $\tau_F >> \tau_D$, it is instructive to consider first the fast two dimensional $E - x$ subsystem that is obtained by the first and the third of the equations 1 with a constant value of u (see (*3*) for a more detailed analysis of this system). This case corresponds to purely depressing synaptic connections. For constant inputs, the system can exhibit two possible stable behaviors: a steady state with $E = const$, and a limit cycle solution corresponding to a periodic train of population spikes that emerges when the steady state solution is unstable (see Fig. S1**A**). For given values of J and E_0, there is a certain critical value of $u = u_{cr}$ that separates these two activity regimes. In the full three-dimensional system of equations 1, there is a certain range of parameters where

these two behaviors can coexist. Intuitively, this can be understood as follows. Imagine that the network, initially in the stable steady state, is perturbed by a transient external input that evokes a single population spike. Due to facilitation, the synaptic state after the termination of the population spike is characterized by increased u (facilitation) and decreased x (depression). If, after the recovery from depression, the value of u remains above the critical value u_{cr}, the network will emit another population spike, and so on. This illustrates the bistable character of network activity (see Fig. S1**B**).

Mathematical analysis of equations 1 shows that there is a certain range of parameters where three steady-state solutions coexist (see Fig. S1**C** where these solutions are plotted *vs* the input E_0). The stability of these solutions can be analyzed by linearizing the equations 1 around the corresponding fixed points. The lower solution is stable and corresponds to the asynchronous spontaneous state of the network. When the two upper solutions first appear, they are both unstable. The uppermost solution subsequently becomes stable via a sub-critical Hopf bifurcation (see e.g. (*4*)) for higher values of the input. Before this bifurcation, a stable limit cycle appears, corresponding to the periodic train of population spikes shown on Fig. S1**B**. The range of external inputs where the limit cycle coexists with the spontaneous state corresponds to the persistent population spike regime described in the main text. The bifurcation analysis was done using XPPAUT by Bard Ermentrout.

These analysis seem quite hard, so I just quickly go through it.

Spiking network The network is composed of N_E excitatory and N_I inhibitory current-based integrate-and-fire neurons, whose sub-threshold depolarization dynamics is described by

$$\tau_m \dot{V}_i = -V_i + I_i^{(rec)}(t) + I_i^{(ext)}(t) \tag{2}$$

where the subscript $i = (1, \ldots, N_E + N_I)$ refers to the neuron number, τ_m is the membrane time constant, $I_i^{(rec)}(t)$ is the current mediated by recurrent synaptic connections, and $I_i^{(ext)}(t)$ is the

external current provided by distant brain areas. Membrane resistance has been absorbed into the definition of the currents in Eq. 2. Whenever the depolarization hits a fixed threshold θ (i.e. $V_i(t) \geq \theta$), the neuron emits a spike and becomes refractory for a period τ_{arp}, after which Eq. 2 resumes from a sub-threshold reset potential V_r. External currents are modeled as Gaussian white noise

$$I_i^{(ext)}(t) = \mu_{ext} + \sigma_{ext} \cdot \eta_i(t) \tag{3}$$

with $\langle \eta_i(t) \rangle = 0$, $\langle \eta_i(t)\eta_j(t') \rangle = \delta_{ij}\delta(t-t')$, so that μ_{ext} and σ_{ext}^2 are respectively the mean and the variance of the external currents. The recurrent current $I_i^{(rec)}(t)$ is the sum of the postsynaptic currents from all other neurons in the network targeting the neuron i

$$I_i^{(rec)}(t) = \sum_j \hat{J}_{ij}(t) \sum_k \delta(t - t_k^{(j)} - D_{ij}) \tag{4}$$

where $\hat{J}_{ij}(t)$ is the instantaneous efficacy (time dependence is due to short-term synaptic dynamics) of the synapse connecting neuron j to neuron i; the sum on k is over all the emission times, $t_k^{(j)}$, of presynaptic neuron j; D_{ij} is the transmission delay uniformly distributed between 1 and 5 ms. For simplicity, we neglect rise and decay times of the postsynaptic currents (see e.g. (*5*))

Excitatory-to-excitatory synapses display short-term plasticity according to (*6, 7*)

$$\dot{u}_j(t) = \frac{U - u_j(t)}{\tau_F} + U\,[1 - u_j(t)] \sum_k \delta(t - t_k^{(j)}) \tag{5}$$

$$\dot{x}_j(t) = \frac{1 - x_j(t)}{\tau_D} - u_j(t)x_j(t) \sum_k \delta(t - t_k^{(j)}) \tag{6}$$

where the functions multiplying the spike train are evaluated immediately before the delta functions, i.e. at $t_k^{(j)^-}$. The $\hat{J}_{ij}(t)$ to be used in Eq. 4 is given by

$$\hat{J}_{ij}(t) = J_{ij} \cdot u_j(t - D_{ij}) \cdot x_j(t - D_{ij}) \tag{7}$$

where J_{ij} is the absolute synaptic efficacy. The remaining synaptic populations, inhibitory and excitatory-to-inhibitory, exhibit linear synaptic transmission, i.e., $\hat{J}_{ij}(t) \equiv J_{ij}$. The dynamics of the network is completely described by the coupled system of non-linear equations Eqs 2-6 combined with the conditions for spike emission and refractoriness described above. These equations are integrated using an Euler scheme. Parameters used in the numerical simulations are reported in Table 1.

Long-term synaptic structuring There are p items to be memorized, each of them encoded by a subset of excitatory cells (selective population). Every selective population is formed by randomly selected fN_E neurons, where f is the coding level, enforcing the constraint that a given neuron belongs to at most one selective population (non-overlapping memories). Network connectivity is generated in the following way. Each cell receives $c(N_E + N_I)$ presynaptic connections, where c is the connectivity level, partitioned as follows: cfN_E randomly selected connections from each of the selective populations, $c(1 - fp)N_E$ randomly selected connections from the non-selective excitatory population, and cN_I randomly selected connections from the inhibitory population. The values of the efficacy for the various synaptic populations are reported in Table 1. Excitatory-to-excitatory synapses can take on two possible absolute efficacies: baseline, J_b, and potentiated, $J_p(> J_b)$. Synapses connecting two neurons within the same selective population have potentiated efficacy; Synapses connecting a selective neuron to a neuron from another selective population or to a non-selective neuron, have baseline efficacy; The remaining synapses (i.e. non-selective to selective and non-selective to non-selective) have potentiated efficacy with probability 0.1.

Overlapping populations All the figures in the main text were simulated with networks of non overlapping memories with fixed number of connections per neuron, in order to minimize the finite size effects and speed up the parameters search. We also performed more realistic simulations with overlapping memories chosen randomly with the same average size and random connectivity (*5, 8*). The qualitative behavior of the network is similar, but the population spikes are less synchronized and do not involve all the neurons in the corresponding population (Fig. S2**A**). The range of J_p for which working memory state coexists with the spontaneous activity state depends on background input and, in the case of Fig. S2, it is approximately between 0.42mV and 0.45mV. This range is about 3 times narrower than the corresponding range for the network with non-overlapping populations.

Cross-correlograms In order to examine the sharpness of population spikes, we computed cross-correlograms (CCs) for high- and low- firing neuron pairs (Fig. S2**B,C**). Spike trains are binned with a 2ms bin, corresponding to the absolute refractory period, so that in each bin there is either a spike or none. Positive and negative part of the CC are computed according to

$$CC_{+}^{(ij)}(\tau) = \frac{1}{\langle S_i \rangle \langle S_j \rangle (T-\tau)} \sum_{t=0}^{T-\tau} S_i(t) S_j(t+\tau) \quad (8)$$

$$CC_{-}^{(ij)}(\tau) = \frac{1}{\langle S_i \rangle \langle S_j \rangle (T-\tau)} \sum_{t=0}^{T-\tau} S_i(t+\tau) S_j(t) \quad (9)$$

where $S_{i(j)}(t)$ is the binned spike train of neuron $i(j)$, and $\langle S_{i(j)} \rangle$ is the corresponding average; T is the total trial duration; τ is the time-lag. Note that time is measured in units of the time bin, and CCs are normalized to 1, that would result from uncorrelated spike trains. Population-averaged CCs are then obtained by averaging the normalized single-pair CCs over all possible pairs (i, j) with $i > j$.

References and Notes

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Single-cell parameters	**E**	**I**
Θ - Spike emission threshold	20mV	20mV
$V^{(r)}$ - Reset potential	16mV	13mV
τ - Membrane time constant	15ms	10ms
$\tau^{(arp)}$ - Absolute refractory period	2ms	2ms
Network parameters	**Values**	
f - Coding level	0.10	
p - Number of memories	5	
c - Probability of synaptic contact	0.20	
N - Number of excitatory/inhibitory cells	8000	2000
$\mu^{(ext)}$ - Mean external current	23.10mV	21.0mV
$\sigma^{(ext)}$ - Standard deviation of external current	1.0mV	1.0mV
Synaptic parameters	**Values**	
J_{IE} - Synaptic efficacy $E \to I$	0.135mV	
J_{EI} - Synaptic efficacy $I \to E$	0.25mV	
J_{II} - Synaptic efficacy $I \to I$	0.20mV	
J_b - Baseline level of $E \to E$ synapses	0.10mV	
J_p - Potentiated level of $E \to E$ synapses	0.45mV	
γ_0 - Fraction of potentiated synapses before learning	0.10	
δ - Synaptic delays	$0.1 - 1$ms	
Short-term synaptic dynamics parameters	**Values**	
U - Baseline utilization factor	0.20	
τ_F - Recovery time of utilization factor	1500ms	
τ_D - Recovery time of synaptic resources	200ms	
Selective stimulation	**Values**	
T_{cue} - Duration	350ms	
A_{cue} - Contrast factor	1.15	
Reactivating signal	**Values**	
Duration	250ms	
Contrast factor	1.05	
Periodic reactivating signal	**Values**	
Duration	100ms	
Period	250	
Contrast factor	1.075	

Table S 1: Parameters used to produce Fig. 2**A** and 3**A**. For Fig. 2**B** and 3**B**, $\mu_{ext} = 23.80$mV to E neurons; For Fig. 2**C**, $\mu_{ext} = 24.30$mV to E neurons. For Fig. S2 $\mu_{ext} = 24.20$mV to E neurons, and $J_p = 0.44$mV.

If u is above u_cr, network activity keeps emitting new spikes.

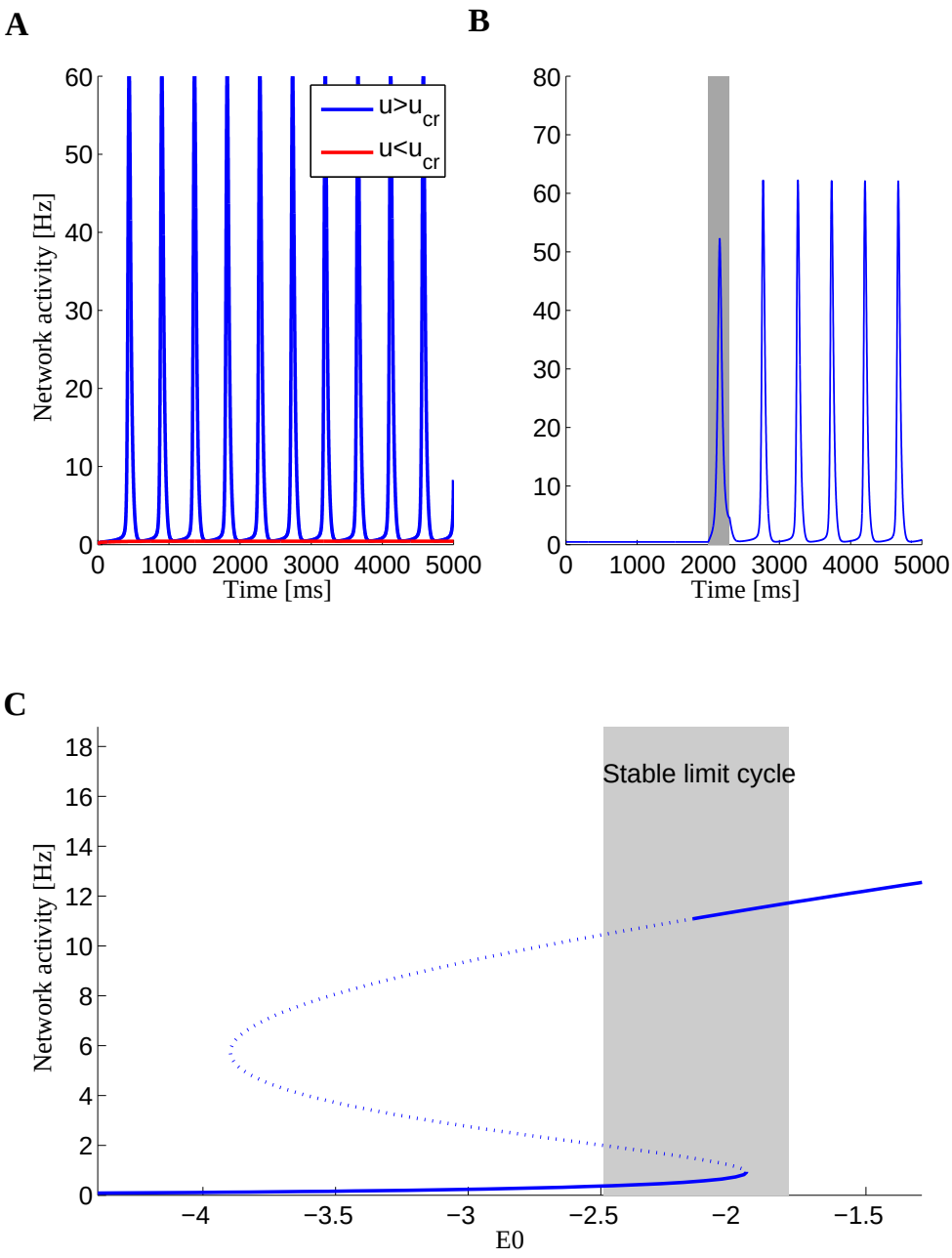

Fig. S 1: Analysis of rate model. **A** Behavior of a network with depressing synapses. Stable steady state for $u < u_{cr}$ and population spikes for $u > u_{cr}$. **B** Example of bistability with facilitating synapses. The input is fixed at $E_0 = -2.3$ except for 300 msec marked in dark shading where $E_0 = -1$. **C** Bifurcation diagram showing E as a function of E_0. Solid and dashed lines mark stable and unstable steady states respectively. The shaded area denotes the range of external input with a stable limit cycle solution. The parameters are: $J = 4$, $E_0 = -2.3$, $\alpha = 1.5$, $\tau = 13msec$, $\tau_D = 200msec$, $\tau_F = 1500msec$, $U = 0.3$. For panel A $\tau_F = 0$ resulting in $u_{cr} = 0.62$, and $u = 0.4, 0.8$ for the red and blue curves respectively.

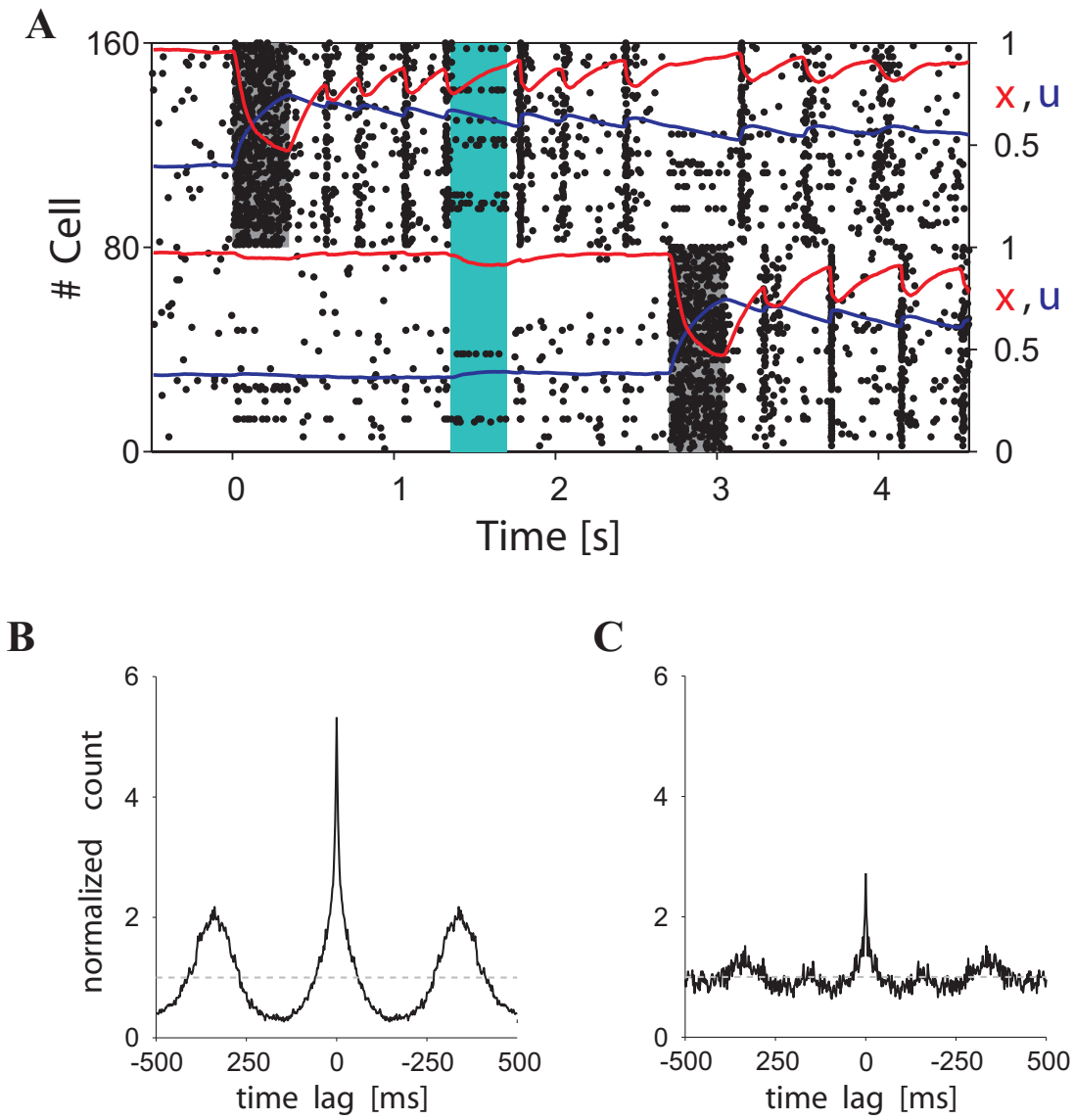

Fig. S 2: Simulation with overlapping populations. **A** The first item is loaded into memory at time zero (dark shading at the top) resulting in a train of population spikes. A non-specific noisy input is applied to randomly selected 15% of neurons in the entire excitatory network (light shading). The second item is loaded into memory at time $t = 2.7s$. Red curve - average value of available resources (x) in the synaptic connections of the target populations. Blue curve - average value of utilization factor (u) for the same synapses. **B** Averaged cross-correlogram over the population of target cells with emission rate below 5Hz during the persistent PSs regime. **C** Averaged cross-correlogram over the population of target cells with emission rate above 8Hz during the persistent PSs regime. Note that the peak at zero-lag significantly decreases, while the secondary peaks at about the period of the PSs nearly disappears. Cross-correlograms have been computed collecting data from a simulation with 50s delay period. Parameters as in Table 1 except $\mu_{ext} = 24.20$mV to E neurons and $J_p = 0.44$mV.