Neuronal assembly dynamics in the beta1 frequency range permits short-term memory

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Contributed by N. Kopell, January 18, 2011 (sent for review November 4, 2010)

Cell assemblies have long been thought to be associated with brain rhythms, notably the gamma rhythm. Here, we use a computational model to show that the beta1 frequency band, as found in rat association cortex, has properties complementary to the gamma band for the creation and manipulation of cell assemblies. We focus on the ability of the beta1 rhythm to respond differently to familiar and novel stimuli, and to provide a framework for combining the two. Simulations predict that assemblies of superficial layer pyramidal cells can be maintained in the absence of continuing input or synaptic plasticity. Instead, the formation of these assemblies relies on the nesting of activity within a beta1 rhythm. In addition, cells receiving further input after assembly formation produce coexistent spiking activity, unlike the competitive spiking activity characteristic of assembly formation with gamma rhythms.

postinhibitory rebound | synchrony

It has been highly documented that rhythms of the central nervous system are associated with cognition (1). However, the ways in which brain rhythms are important to cognitive function are not well understood. One suggested function for rhythms has been the creation of cell assemblies (collections of neurons that are transiently synchronous). The rhythm most associated with the formation of such cell assemblies is the gamma frequency band (30–90 Hz) (2–4). Other rhythms, however, may play an important role in the formation or transformation of cell assemblies. Here, we build on experimental and modeling work concerning the beta1 frequency band (≈15 Hz), as found in rat association cortex (5, 6), to show that this version of the beta1 rhythm has special physiological properties appropriate to manipulation of cell assemblies. We are especially interested here in how networks producing this rhythm respond to familiar and novel stimuli and how the underlying physiology provides a context for combining the two. A key feature of the model given below is that the spiking during beta1 depends on rebound from inhibition, allowing activity to be maintained in the absence of continuing input. The "memory"—provided by the ability to have ongoing activity—is independent of synaptic plasticity. The model also shows that the nesting of gamma activity inside the beta1 oscillation produces different interactions of cell assemblies than in the absence of the beta1 rhythm: There is much less of the competition characteristic of cell assemblies produced within the gamma rhythm (7).

To appreciate the novel features of cell assemblies formed within the beta1 rhythm, it is necessary to understand some central features of the gamma rhythm and its assembly-forming properties. The type of gamma rhythm associated with cell assemblies is known as the pyramidal interneuron network gamma (or PING) rhythm (4). This kind of gamma is produced mainly by pyramidal cells and fast-spiking interneurons (7–11). In this rhythm, activated pyramidal cells excite fast-spiking perisomatic-targeting interneurons (FS cells) that, in turn, inhibit the pyramidal cells; the period of the oscillation corresponds to the time necessary for the inhibition to decay and allow the pyramidal cells to spike once again. Thus, the period of the gamma rhythm depends most on the decay time of the inhibition, coupled with the excitability of—and input to—the pyramidal cells.

Two main properties of the PING rhythm facilitate formation of transient, stimulus-specific cell assemblies. First, during PING, the longest important time scale is the decay time of the inhibitory synaptic input to the pyramidal cells, which essentially governs the cycle length. Thus, there are no ongoing currents lasting longer than one cycle to provide memory from cycle to cycle. Hence, as long as the input to a population of neurons remains the same, the same subset of pyramidal cells participates in the firing (4). Depending on the pattern of activation of a neuronal population, cell assemblies can be formed, abolished, or reconstituted repeatedly at subsequent gamma rhythm cycles (3). Second, there is enormous overlap in the axonal fields of FS interneurons and a great deal of convergence and divergence of inhibition in the PING circuit (12, 13). It follows that, if two subsets of cells are given enough excitation to form cell assemblies and one is given more than the other, the cells receiving the lower amount of excitation can be suppressed (7, 14). The cells with the highest excitation determine the frequency of the inhibitory cells and cause them to fire faster than if they were interacting with the less excited group of cells. This higher frequency of the FS cells suppresses the less excitable pyramidal cells. Thus, a cell assembly formed within a gamma rhythm is protected from distracting (weaker) co-presented inputs as a consequence of the circuit organization that generates the rhythm in the first place.

However, these same two properties also have their disadvantages: Resulting cell assemblies are ephemeral, changing or disappearing rapidly at the slightest alteration in input, and competitive, ensuring only the strongest driven neurons in a population can participate. These properties make the assemblies less than computationally ideal for coding sequences of sensory input when there are meaningful relationships between temporally segregated inputs. For cell assemblies to be useful in such a situation, mechanisms must exist that allow both persistence of multiple inputs and cooperation between inputs arriving at different times.

One possible candidate for such a mechanism is the beta1 rhythm (5). The beta1 rhythm has been noted in multiple studies of higher order processing (15–20). The beta1 rhythm has also been seen in vivo (21, 22) and in vitro (5) as emerging after the removal of transient excitatory (sensory) input. Another version of a broader band beta rhythm, found in motor planning, is believed to be associated with maintenance of the status quo (23). However, here we are concerned with association-area processing; it is not known if the mechanisms of the beta activity are similar. In this paper, we examine a computational model of rodent association cortex capable of producing interacting gamma and beta rhythms. We show how a distributed beta1 rhythm can

Author contributions: N.K., M.A.W., and M.A.K. designed research; N.K. and M.A.K. performed research; M.A.K. analyzed data; and N.K., M.A.W., and M.A.K. wrote the paper.

The authors declare no conflict of interest.

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This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1019676108/-/DCSupplemental.

persistently coordinate local cell assemblies without the need for synaptic plasticity. We model the impacts of sequences of familiar and novel inputs on cell assemblies and show that the beta1 rhythm provides a context within which these sequences can be encoded cooperatively in a single cell assembly.

Results

Background: Physiology of Beta1. The computational model we implement depends on the emergence of beta1 activity through the process of period concatenation as observed in vitro. Thus, we start by briefly reviewing the most salient experimental results. In a bath containing 400 nM kainate, slices of rat association cortex (S2) initially display a 40-Hz rhythm (gamma) in the superficial layers and a 25-Hz (beta2) rhythm in the deep layers (24). If excitation is then reduced by addition of a kainate antagonist, all layers change their spectral peak to 15 Hz (beta1) (5, 6). In this rhythm, the gamma and the beta2 are concatenated: One period of the beta1 oscillation consists of spiking in the deep layer, followed one gamma period later by spiking in the superficial layer, and followed one beta2 period later by spiking again in the deep layer. As revealed in in vitro experiments and simulated in computational models, the order of events in this sequence propagates between cells in deep and superficial cortical layers. Beginning in the deep layer, a burst of spikes produced by intrinsically bursting (IB) cells excites the superficial layer basket cells, which inhibit the superficial layer pyramidal cells. These superficial layer pyramidal cells rebound from the inhibition and generate spikes one gamma cycle later, activating both superficial basket cells and low-threshold spiking (LTS) interneurons. The latter then inhibit the deep layer IB cell dendrites, which rebound and burst one beta2 cycle later (Fig. 1). This scenario depends on the existence of hyperpolarization-activated currents (h-currents) in the cells that promote rebound spiking, allowing the rhythm to persist even as excitation to cortex becomes very low.

Model of Gamma Oscillation. To represent the persistent gamma activity observed in vitro, we implement a computational model adapted from ref. 6. Briefly, this model consists of two cell populations—regular spiking (RS) pyramidal cells and fast spiking basket cells—with strong synaptic interactions (Fig. 1*A*, shaded, and *Materials and Methods*). We divide the RS cell population into two groups of equal size, which we label "RS1" and "RS2" and which receive different levels of tonic excitatory drive. We will show that including strong, assembly-specific RS-to-RS synapses (perhaps resulting from spiking-timing dependent synaptic plasticity) minimally affects the simulated dynamics. In this model of the superficial layer gamma activity, the individual RS cells do not spike on every cycle of the gamma rhythm, whereas the basket cells fire at close to the population frequency (Fig. 1*B*).

We note that this rhythm is mechanistically not the same as the PING in which the RS cells fire on almost every gamma cycle (25). Also, the RS cells of this model possess additional currents not in the previous models, but critical to sustaining the beta1 rhythm (5, 6). However, this model still exhibits competition between the two subsets of RS cells. To show this competition, we consider two cases. First, we drive the subsets of RS cells with different levels of tonic excitatory input, so that RS1 receives more excitatory drive than RS2. Because RS1 receives more depolarizing input, this subset of cells spikes at a higher rate than RS2 (Fig. 1*C*). In the second case, we activate each subset of RS cells independently with the same tonic excitatory drives used in the first case. We find that the RS1 cells spike at approximately the same rate—whereas the spike rate of RS2 cells increases—compared with when both subsets receive simultaneous activation (Fig. 1*C*). These results illustrate the impact of competition between the subsets of RS cells; the simultaneous activation of both subsets decreases the spike rate of RS2—the subset receiving weaker tonic excitatory drive. We note that this competition between the RS cells is weaker than observed in previous models (14, 26). We show in the *SI Appendix* that removing one additional current (the h-current)

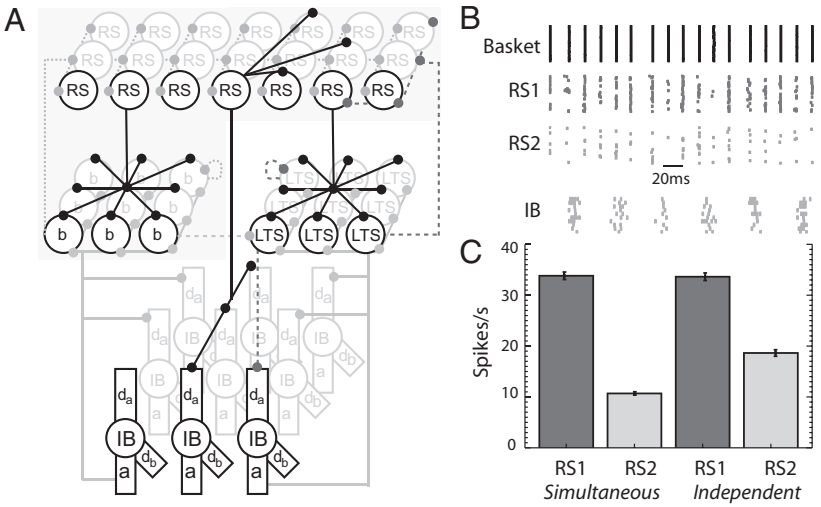

Fig. 1. Cartoon representation of the components in the computational model. (*A*) The computational model consists of two layers. The superficial layer gamma model consists of two interconnected cells types: regular spiking (RS) pyramidal cells and basket (b) cells, all modeled as single compartments. The deep layer beta2 model consists of intrinsically bursting (IB) cells modeled with four compartments (an apical dendrite, a basal dendrite, a soma, and an axon labeled d_a, d_b, IB, and a, respectively). The superficial layer also contains single compartment models of low-threshold spiking (LTS) interneurons. Excitatory synaptic connections are represented as solid lines. Each RS cell connects to all basket cells, all LTS cells, and three IB cells. Each IB cell connects to all basket and LTS cells. Inhibitory connections are represented as dashed lines. Each basket cell connects to itself, one LTS interneuron, and all RS cells. Each LTS interneuron connects to itself, four RS cells, and one IB cell. (*B*) Example of superficial layer gamma activity and deep layer beta2 activity. Each basket cell spikes on nearly every cycle of the gamma rhythm, whereas the RS cells (divided into two populations) spike more sparsely. The deep layer IB cells burst at beta2 frequency. (*C*) Histogram showing the number of spikes per second generated by RS cells when both populations are activated simultaneously (resulting in competition), and when activated independently. During competition, the RS2 assembly generates less spikes per second than when activated independently (i.e., when RS1 is not activated). During competition, the more active RS1 assembly suppresses the RS2 assembly, decreasing its firing rate by 8 Hz. In this histogram, and all histograms that follow, we summarize the results of 10 simulation realizations, each with different initial conditions and realizations of stochastic input.

from the model used here produces competition results consistent with previous, simpler models.

Model of Beta2 and Beta1. The beta2 model consists of a population of deep layer, IB pyramidal cell (Fig. 1 *A* and *B*). The IB cells support a beta2 rhythm paced by a muscarinic receptor-suppressed (M-current) in the axons (5, 6). The computational model of beta1 we use is a generalization of the model proposed in ref. 6; a cartoon representation of this model is shown in Fig. 1*A*. The model consists of two cortical layers: (*i*) A superficial layer containing single-compartment fast-spiking basket (b) cells, RS pyramidal cells and inhibitory LTS interneurons and (*ii*) a deep layer containing four-compartment IB cells, connected by gap junctions. Chemical and electrical connections link the cell populations, as described in *Materials and Methods*. The *SI Appendix* includes detailed descriptions of the model cells and their dynamic equations.

Responses to Novel Stimuli, but Not Familiar Ones, Are Sustained After the Switch to Beta1. We first consider the situation of strong inputs to two subsets of superficial RS cells, corresponding to a novel input (to RS1) and a familiar input (to RS2) (Fig. 2*A*). It has been shown (21) that novel inputs create an excitation that is both stronger and longer-lasting, as in the caricature. The strong input corresponds to higher levels of kainate in the in vitro preparation. Fig. 2*B* shows a representative rastergram of the superficial and deep layer cell activity in this high excitation situation representative of strong input. The superficial layer RS cells fire, on average, at all phases of the deep layer IB cells, which exhibit a population beta2 rhythm (Fig. 2*C*).

Lowering the excitation to all cells (corresponding to the decay of excitation in the cortical column) produces a transition to the beta1 rhythm (Fig. 2*D*). During this transition, the excitation of the familiar input decays more rapidly (*Discussion*), whereas the excitation of the novel input remains, so that only RS1 cells participate in the beta1 activity. The longer duration of excitation resulting from a novel stimulus aids the formation of a beta1 rhythm. These RS cells now generate spikes at a single phase interval of the beta1 rhythm (Fig. 2*E*). Thus, the model suggests that the beta1 system is preferentially biased to the sustained activity and, therefore, detection of "novelty."

Reactivation of the Familiar Stimulus Allows Its Representation to Join with That of the Novel Stimulus. Re-presentation of the familiar stimulus results in activation of the superficial pyramidal cells not recruited in the original assembly (Fig. 3 *A* and *B*). The RS1 and RS2 cells now form a single cell assembly that fires at two phases of the beta1 rhythm (Fig. 3*C*); once nearly out of phase (i.e., near 130 degrees) with the IB cells and once just before the IB cells burst (near 0 degrees). We note that activation of the RS2 cells increases the overall number of spikes

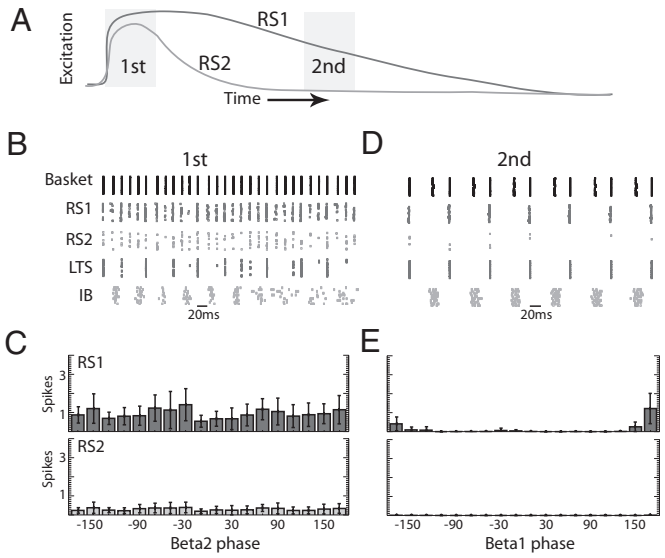

Fig. 2. Model population dynamics during intervals of high and low excitation reveal different neural rhythms. (*A*) Cartoon representation of stimulus presentation to the model. In the first interval (label 1st), both superficial layer RS assemblies receive increased excitatory drive. RS1 (upper curve) receives more drive than RS2 (lower curve), representing in the model responses to an unfamiliar stimulus by RS1 and familiar stimulus by RS2. In the second interval (label 2nd), the excitatory drive from the unfamiliar stimulus to RS1 has decayed slowly, whereas the drive from the familiar stimulus to RS2 has decayed rapidly. (*B*) Example rastergram resulting during the first stimulus presentation. The superficial layer basket and RS cells generate a gamma oscillation, whereas the deep layer IB cells generate a beta2 rhythm. (*C*) Histogram of the RS1 (*Upper*) and RS2 (*Lower*) activity as a function of beta2 phase. No phase relationship exists between the superficial layer and deep layer cells. (*D*) Example rastergram during the second stimulus presentation. Now the superficial and deep layer cells coordinate to generate a beta1 rhythm. The excitatory drive to the RS2 cells decays sufficiently so that these cells rarely participate in the beta1 rhythm. (*E*) Histograms of the RS1 and RS2 activity reveal that the RS1 cells generate spikes at a particular phase of beta1.

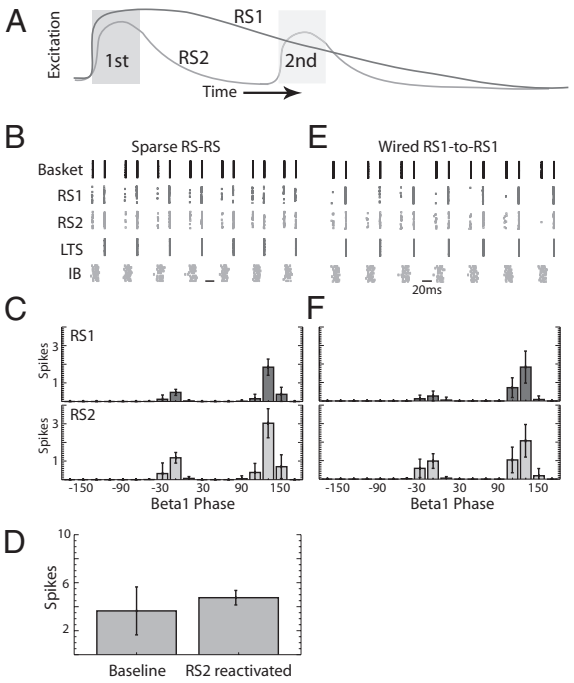

Fig. 3. Reactivation of cells by a familiar input nests superficial layer gamma activity within the beta1 rhythm. (*A*) In the second interval, the familiar input reactivates cell assembly RS2; this reactivation provides 80% of the excitatory drive delivered in the first interval. (*B*) Example rastergram during reactivation shows RS2 and RS1 become more active, now spiking twice during each beta1 cycle. (*C*) Histograms for RS1 (*Upper*) and RS2 (*Lower*) during reactivation indicate the two beta1 phases at which the superficial layer RS cells spike—once near 130 degrees, and once just before the deep layer IB cells burst. (*D*) Histogram of the number of RS1 spikes that appear out of phase with the beta1 rhythm (i.e., in phase bins ≥120 degrees and ≤−150 degrees) during the baseline beta1 condition (as in Fig. 2*D*) and during reactivation of RS2 (as in this figure). The RS1 assembly generates approximately the same number of spikes in the out-of-phase interval whether or not the RS2 cells receive the additional, familiar stimulus. (*E* and *F*) Example rastergram and histogram for model dynamics identical to *B* and *C* but including all-to-all synaptic connections between the pyramidal cells in RS1. Inclusion of these synapses has little impact on the observed dynamics.

generated by the RS1 cells because of the (sparse) excitatory synaptic connections between all RS cells. However, if we consider only intervals out of phase (≥120 degrees and ≤−150 degrees) with the beta1 rhythm, we find that the RS1 assembly generates approximately the same number of spikes whether or not the RS2 cells receive the additional, familiar stimulus (Fig. 3*D*). In this sense, there is no competition between the original cells receiving stimulation (RS1) and the new ones (RS2); unlike the situation of PING gamma (7, 14), the introduction of another and larger input to a subset of pyramidal cells (RS2) does not suppress the RS1 activity.

The history of inputs to the RS cells might also impact the excitatory connections between these cells through the process of spike-time–dependent synaptic plasticity (27). To simulate this effect, we include all-to-all (excitatory) synapses between the pyramidal cells in RS1 and find that the spiking output is essentially unchanged in the model (Fig. 3 *E* and *F*). Thus, even if the history of previous inputs is encoded in mutually excitatory connections among RS1 cells, the output is essentially unchanged; it remains encoded in the set of cells participating in the beta1 rhythm. Re-presentation of the novel input to the RS1 cells results in similar behavior, namely increased RS1 activity clustered (in this case) near three different phase intervals of the beta1 rhythm (*SI Appendix*).

Within a Beta1 Rhythm, There Is No Competition Between Multiple Streams of Inputs. In the previous section, we considered the re-presentation of inputs to RS1 and RS2 individually and found increased activity in these reactivated cells. If both the inputs are reintroduced together (Fig. 4*A*), the superficial layer generates a gamma oscillation nested in the beta1 rhythm. The RS1 cells (which receive more excitatory drive) tend to spike at three different phases in the beta1 rhythm, whereas the RS2 cells spike mainly at two phases (Fig. 4 *B* and *C*). Thus, some of the history of past involvement, here encoded as a larger input to RS1 cells, appears in the beta1 phase at which the RS cells spike. Again, we find that these results do not significantly change if recurrent excitation is added to the RS1 cells (Fig. 4 *D* and *E*). Finally, we consider the total number of spikes generated by RS1 and RS2 during beta1 when each assembly receives the re-presentation of input individually (e.g., Fig. 3 for RS2) and together (Fig. 4). We find that the spike rate of the RS1 and RS2 cells, with simultaneous inputs, are nearly the same as the spike rates when each is activated alone (Fig. 4*F*), although the beta1 phase at which the RS2 cells spike changes. This observation suggests no competition between RS1 and RS2 when the gamma activity of these assemblies is nested in beta1. To illustrate this assertion, we compute the competition ratio—the ratio of spikes generated by RS2 when activated simultaneously with RS1 versus the number of spikes generated by RS2 when activated independently. We find a ratio closer to one (i.e., less competition) during the reactivation (beta1) condition (Fig. 4*G*). Thus, the competition (i.e., partial suppression) between the subsets of superficial RS cells decreases dramatically when the gamma rhythm appears nested in beta1.

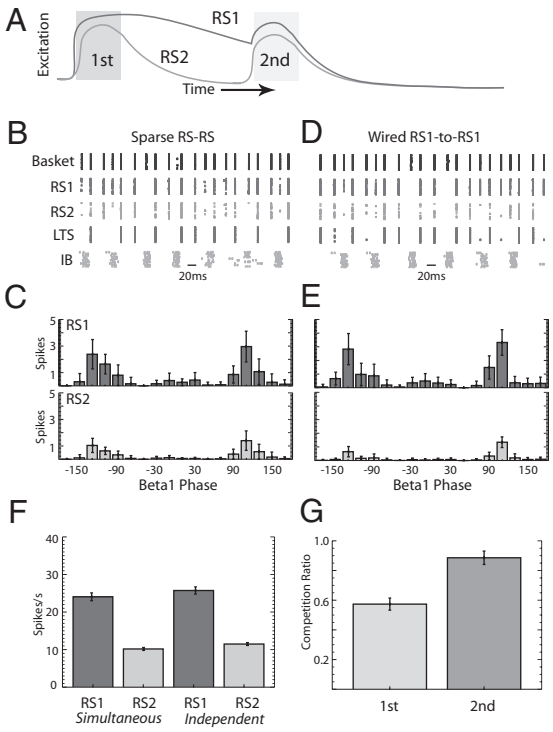

Fig. 4. Reactivation of cells by inputs nests superficial layer gamma activity within the beta1 rhythm. (*A*) In the second interval, inputs reactivate cell assemblies RS1 and RS2. (*B*) Example rastergram during reactivation shows RS2 and RS1 become more active, now spiking two or three times during each beta1 cycle. (*C*) Histograms for RS1 (*Upper*) and RS2 (*Lower*) during reactivation indicate the beta1 phases at which the superficial layer RS cells spike. Both assemblies generate spikes near ±120 degrees, and RS1 also spikes near 0 degrees. (*D* and *E*) Example rastergram and histogram for model dynamics identical to *B* and *C* but including all-to-all synaptic connections between the pyramidal cells in RS1. Inclusion of these synapses has little impact on the observed dynamics. (*F*) Histogram showing the number of spikes per second generated by RS cells when both populations are reactivated simultaneously (*Left*) and when reactivated independently (*Right*). Both assemblies generate approximately the same number of spikes per second when activated simultaneously (as in this figure) or independently (as in Fig. 3 for RS2). (*G*) The competition ratio is the number of spikes generated by RS2 when activated simultaneously with RS1 versus when activated independently. In the first presentation of the stimulus, the RS2 assembly generates fewer spikes when activated simultaneously with RS1. In the second presentation, RS2 generates nearly the same number of spikes whether or not RS1 is simultaneously activated.

Discussion

It has been frequently suggested that the formation of cell assemblies (i.e., populations of synchronously active neurons) is an important aspect of how the brain performs computations (1, 2). However, the mechanisms and neural rhythms by which cell assemblies form and evolve with different inputs have not been thoroughly explored. Here, we show in a computational model that the physiology associated with different rhythms can produce different mechanisms for cell assembly formation and manipulation. We focused on the beta1 rhythm observed in the rodent association system and showed how cell assemblies constrained by this physiology differ from cell assemblies associated with gamma rhythms alone. Three important contrasts distinguish the beta1 and gamma rhythm generating systems. First, cell assemblies formed in the typical gamma oscillation require ongoing input, whereas cell assemblies formed in beta1 are self-sustaining via rebound from inhibition. Second, cell assemblies concurrently generated in the superficial layer (PING) gamma oscillation compete with one another. In contrast, these layers can create a coordinated cell assembly if there is a beta1 rhythmic background. Third, the self-sustaining cell assemblies during beta1 allow later input to create a unified cell assembly linking past and present inputs.

In a recent review, A. Engel and P. Fries (23) suggested that beta frequency oscillations are useful for the maintenance of the status quo, such as holding a fixed position or maintaining short-term memory. We agree with that suggestion, but go further in two ways. First, we suggest a mechanistic reason why at least this version of the beta1 rhythm is well adapted to maintaining cell assemblies in the absence of further input. Second, we suggest why

the beta1 rhythm in multimodal areas is well adapted to allowing manipulation of cell assemblies to perform new computations.

It is computationally advantageous for the cortex to have a means to hold patterns of neuronal activity coding for features of a sensory object in short-term (working) memory. For example, within a single sensory modality, a memory of previously presented stimuli can be used to compare and contrast subsequent stimuli to reach basic similarity/novelty distinctions in sequences of input time-distributed over hundreds of milliseconds to several seconds. The dynamic signature associated with retention of past stimuli in such sequences appears to involve predominantly the beta1 rhythm. Visual short-term memory tasks reveal strong beta1 activity during retention (28, 29), which also correlates with accompanying BOLD responses (30). In addition, working memory impairment is associated with a decrease in phase and coherence measures within the beta1 frequency band (31). For multimodal sensory processing, short-term memory is equally important. It is highly unlikely that each modality of stimulus associated with a target object will arrive concurrently in cortex. Thus, any neuronal assembly coding for the object must be built up over time. Such multimodal processing is also strongly associated with beta1 rhythm generation (16). The idea of memory being held in ongoing neuronal rhythms is far from new (e.g., ref. 32), but here we present a mechanism by which this phenomenon may occur.

From a mechanistic perspective, the beta1 rhythm provides an ideal substrate for preserving neuronal assemblies over time. It is formed after periods of strong cortical excitation, because this excitation decays (5). The persistence of the rhythm, in the absence of strong, transient drive critically depends on the presence of the hyperpolarization-activated conductance—the h-current. Due to rebound spiking, coordinated activity in infra- and supragranular cortical layers persists, in the absence of strong depolarization, in key neuronal subtypes—superficial layer RS and deep layer IB neurons (6). Using such a mechanism, the neuronal population code for a transiently presented sensory stimulus can be remembered through the iterative pattern of spike coincidences in the slower beta1 rhythm. It should be noted that neuronal assemblies can be remembered in cortex for periods of time much longer than that associated with short-term memory (e.g., ref. 33). In these cases, it is highly likely that specific patterns of use-dependent synaptic plasticity are critical. However, in the current work, such plasticity did not play a significant role in the creation and manipulation of cell assemblies.

In the absence of any excitatory drive, the beta1 rhythm cannot manifest. Therefore, stimuli that generate long, slowly decaying periods of activation are far more likely to generate a beta1 rhythm than rapid transient periods of activation. Transient stimulation of excitatory afferents can generate such long, slowly decaying responses in cortex only if the pathway being activated has remained quiescent previously (e.g., refs. 21 and 34), suggesting that the beta1 rhythm may be selectively generated by unfamiliar or infrequent sensory stimuli. In ref. 21, this suggestion was shown to be the case for simple auditory tone sequences, and reports showing strong beta1 generation in short-term memory tasks used novel stimuli for each trial (28).

We use these long, slowly decaying profiles of excitation, and the accompanying beta1 rhythm, in this study to distinguish between frequently presented (familiar) stimuli and rarely presented (unfamiliar) stimuli. Frequency of presentation affects the duration and power of induced gamma band responses (21), a phenomenon related to repetition suppression (35); although the work in ref. 35 is about rates rather than spectral power, there is an increasing corpus of literature showing that gamma (alone but particularly with delta) is the single most powerful predictor of spike density (36, 37). In contrast, we propose that unfamiliar stimuli appear to involve different network processes, which involve beta1 rhythm generation.

When an unfamiliar stimulus is co-presented with a familiar one, the most obvious computation to be performed is to decide whether the two are related. However, owing to the repetition suppression of the familiar stimulus, the initial drive resulting from the familiar stimulus (here to RS2) is not as strong as that resulting from the unfamiliar stimulus (here to RS1). Co-presentation of stimulus pairs, with biased drives, leads to strong competition, with the weaker drive effectively being ignored (38), a process associated with lateral inhibition (14). In the present simulations, the stronger driven (unfamiliar) assembly dominates during the initial gamma rhythm, a time before the beta1 rhythm is established (Fig. 1*C*). This competitive process may not always serve as the appropriate computational outcome. For example, if an unfamiliar stimulus is presented during a sequence of familiar stimuli, then it could be argued that the familiar stimulus must have some contextual validity. What computation provides the context? The model presented here provides a possible solution: If the familiar stimulus is presented again during the retention period for the unfamiliar stimulus (the protracted beta1 rhythm), then no competition is seen. Instead, the subset of neurons responding to the unfamiliar stimulus spike at the same rate whether or not another subset of neurons responds to the familiar stimulus (Fig. 4*F*). The two assemblies become modified, yet both remain, thus encoding for both stimuli. This encoding as a single assembly is consistent with the "binding-by-synchrony" hypothesis (39). We note that, although the RS cells responding to the two stimuli tend to fire at the same phases (and hence are bound) in this model of rat association cortex, the different firing rates of the two RS assemblies may permit independent representation in other cortical regions.

There are multiple reasons for this lack of competition in beta1. One has to do with the contrast between the gamma (PING) mechanism and the beta1 mechanism: In the former, the dominant assembly activates the shared interneurons; the non-dominant assembly is not sufficiently activated to fire before the wave of inhibition and is suppressed. In the beta1 mechanism, the superficial interneurons are activated and timed partly by the deep layer IB cells, which are not tied to either assembly. In the PING rhythm, when the drive goes up, so does the frequency; indeed, that is the source of the competition among assemblies. By contrast, if two superficial layer cell assemblies receive different drives during beta1, both continue to be active, contributing additional spikes within each beta1 period. Another major reason has to do with the h-current in the RS cells: When RS cells are inhibited, the inward h-current is activated, depolarizing the cells and making them harder to suppress.

In summary, the beta1 rhythm is unique (to the best of our knowledge) in providing a mechanism for ongoing manipulation of cell assemblies. Thus, although it shares with other rhythms (40–42) the ability to create a nest for higher frequencies, the beta1 rhythm has its own special functional properties, following from the central role of the rebound from inhibition in its rhythmogenesis. Rebound (driven by the h-current as predicted in the present simulations) permits persistence in the oscillatory response to temporally discrete stimuli and also reduces assembly suppression based on lateral inhibition. Thus, our simulations predict that the ability of the beta1 rhythm to facilitate inter- and intralaminar interactions may form both a substrate for synaptic plasticity-independent short-term memory and a means to create a cortical representation for present stimuli in the context of those received in the recent past.

Materials and Methods

The computational model of the gamma rhythm includes single-compartment models of 80 RS cells and 20 basket cells, interconnected with all-to-all synapses. In addition, each basket cell possess an autapse, and each RS cell possesses sparse connections randomly assigned to other RS cells (i.e., each of the 80 RS cells connects to three randomly chosen other RS cells), regardless of

whether the cells belong to RS1 or RS2. The computational model of the beta2 rhythm consists of 20 IB cells. We model each cell with four compartments—two dendrites (proximal and distal), a soma, and an axon—and connect the IB population with gap junctions (each IB cell connects to three other IB cells) between the axons. In the transition to beta1, a population of 20 LTS interneurons (single-compartment models) become essential for propagating the rhythm between cortical layers. Detailed equations for the model cells are provided in *SI Appendix*.

In the superficial layer, the three different cell types are connected by synapses (AMPA- and $GABA_a$ -receptor mediated), whereas in the deep layer, the IB cells are connected by gap junctions. Between the cortical layers, AMPA-receptor mediated ascending connections (from the deep to superficial layer) begin at the axonal compartment of the IB cells and terminate on all basket and LTS cells. $GABA_a$-receptor mediated descending connections (from the superficial to deep layer) begin from individual LTS cells and terminate on the apical dendrite of individual IB cells (i.e., each of the 20 LTS cells connects to one of the 20 IB cells). Unlike previous models (6), here we include excitatory descending connections from RS cells to IB apical dendrites with each IB cell receiving inputs from 3 of 80 RS cells. These descending connections are known to include both NMDA- and AMPA-receptor–mediated currents (43). The slow decay of the NMDA currents acts effectively as a constant excitatory drive to the deep layer IB cells. The faster AMPA currents, however, may potentially disturb the beta1 rhythm, which relies on spiking activity propagated between the cortical layers (6). This disturbance does not occur in the model because the AMPA-mediated current are shunted at the IB dendrites by simultaneously arriving $GABA_a$ input from the LTS cells (*SI Appendix*). As in ref. 6, the transition to the beta1 regime requires two transformations: (*i*) hyperpolarization of all cells relative to the high excitation state that supports the faster gamma and beta2 rhythms, and (*ii*) inclusion of NMDA-mediated synapses connecting each IB cell axon to all IB cell basal dendrites.

In this model, the one compartment RS cell is considered to represent all of the compartments of the RS cell and, therefore, is given the h-current, which is known to exist more distally along the RS dendrites (44). The interneuron population now includes other inhibitory cells that are known to project more distally, thus evoking the h-currents. We hypothesize that the perisomatic-projecting interneurons dominate in the highly driven PING case, whereas other interneurons are active during the beta1 regime. Because we are interested here in the properties of the dynamics in the beta1 regime, we do not model the above details explicitly, which would require multiple compartments for the RS cells and more than one class of interneurons, without adequate constraining data. Instead, we focus on an essential property of the inhibition to the RS cells in the beta1 regime: that it can produce rebound excitation (5, 6).

ACKNOWLEDGMENTS. We thank P. Fries for his helpful comments on a previous version of this paper. N.K. is partially supported by National Science Foundation Grant DMS-0717670. M.A.K. holds a Career Award at the Scientific Interface from the Burroughs Wellcome Fund.

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