OPINION

Portraits of communication in neuronal networks

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Abstract | The brain is organized as a network of highly specialized networks of spiking neurons. To exploit such a modular architecture for computation, the brain has to be able to regulate the flow of spiking activity between these specialized networks. In this Opinion article, we review various prominent mechanisms that may underlie communication between neuronal networks. We show that communication between neuronal networks can be understood as trajectories in a two-dimensional state space, spanned by the properties of the input. Thus, we propose a common framework to understand neuronal communication mediated by seemingly different mechanisms. We also suggest that the nesting of slow (for example, alpha-band and theta-band) oscillations and fast (gamma-band) oscillations can serve as an important control mechanism that allows or prevents spiking signals to be routed between specific networks. We argue that slow oscillations can modulate the time required to establish network resonance or entrainment and, thereby, regulate communication between neuronal networks.

The functional specialization and anatomical segregation of neuronal networks in the brain imply that it is organized as a distributed, hierarchical network of highly specialized networks of spiking neurons[1,2]. Signal processing in such a modular system manifests as patterns of spiking activity that selectively flows along a hierarchy of sub-networks. Therefore, mechanisms must exist to prevent irrelevant signals from transferring to and interfering with the processing task at hand[3,4]. In other words, brain dynamics may be understood as an ever changing pattern of pathways along which signals are effectively routed by modulation of selective connections[5–8]. Effective transmission of spiking activity from one network to another means that a pattern of spiking activity in a presynaptic network can elicit unique, discernible and reliable responses in a postsynaptic network[2,9,10]. Three key features of brain connectivity and activity challenge stable and controlled transmission of spiking activity. First, most synapses in the brain are weak[11,12] and may show short-term facilitation and depression[13,14]. Second, both ongoing and stimulus-evoked neuronal activity are highly variable[15,16]. Third, strong inhibition may impede the transmission of spiking activity[17,18]. The brain thus faces a common problem in communication: how to transmit information over noisy and inhibited channels using weak and unreliable connections.

In this Opinion article, we outline a dynamical systems-based approach to study and understand the transmission of spiking activity between groups of neurons[19]. This framework shows how synchrony-based[2,19] and oscillation-based[20] transmission schemes are two different aspects of a single underlying process. We review essential features that shape neuronal communication and combine them into a single framework that views communication from the perspective of dynamical systems. We propose the existence of two different communication systems, which can either transmit sufficiently strong messages in single transients (fast system) or use resonance and entrainment in slowly building up fast oscillations to aid in dispatching weaker signals (slow system). We also suggest that the slow system can make signals accessible to the fast system through the initiation of synaptic plasticity and that it might be switched on and off by slow inhibitory modulations coupled to the faster oscillations. We propose that such a nesting of slow and fast oscillations can have an important role in controlling the communication between neuronal networks.

Neuronal communication systems

Senders and receivers. In general, a communication system is composed of a sender, a receiver and a channel in between, along which a message is transmitted. In a neural communication system (NCS) in the neocortex, both the sender and receiver are local, recurrently connected networks of excitatory and inhibitory neurons. In subcortical regions, the sender and receiver may consist of inhibitory neurons only. What is pertinent for communication is the network dynamics that are supported by the given network architecture.

Neural transmission channel. In neuronal networks, the transmission channel is made up of axonal projections from the sender to the receiver networks. In the brain, neuronal networks are interconnected by convergent and divergent projections[21]. Such connectivity itself can alter the nature of neuronal activity[2]. For instance, sharing of presynaptic projections can introduce correlations in an otherwise uncorrelated activity, from the perspective of the postsynaptic neurons. In the neocortex, interneuronal network projections are excitatory, although they may impinge on both excitatory and inhibitory neurons. In subcortical structures, such as the basal ganglia and amygdala, the interneuronal network projections are exclusively inhibitory. Here, we restrict our discussion to the transmission of spiking activity between neocortical networks.

Parametrization of neuronal signals. Task-related information that needs to selectively propagate could be encoded in the form of firing rates[16,22,23], pairwise correlations[24,25] and/or spike pattern irregularity[26,27]. Recent data suggest that sensory information may

be encoded in 50–200-ms-long sequences of population activity (spike packets)[28]. A convenient way to characterize neuronal signals is to consider them as a volley of spikes (a pulse packet) that can be quantified by the number of spikes in the volley (α, 50–100 spikes) and their temporal dispersion (σ, ~1–10 ms), which measures the degree of synchronization of the message[19,29]. Several studies have shown that both α and σ are necessary to understand the downstream effect of a pulse packet (see REF.[2] for a review). Note that a pulse packet by itself does not carry information; rather, the code resides in the combination of neurons participating in the spike volley[11] in the sender and receiver networks. Importantly, such pulse packets can be combined with others to construct various spatiotemporal activity patterns; for example, multiple spike packets[28] can be considered as a sequence of ~5–10 pulse packets travelling through a network.

Measure of successful communication. In neocortical networks, a population of pyramidal cells dispatches a message encoded as a volley of spikes that travels along diverging and converging axons and synapses to reach a receiving network, which responds with another spike volley (FIG. 1a). We regard communication to be successful if the properties of the message (α and σ) are preserved or enhanced. A reduction in α and/or an increase in σ degrades the signal and implies that communication has failed. Importantly, the pulse packet response should be discernible from fluctuations in the baseline activity in the receiver network, implying that the receiver network was able to 'read' the incoming pulse packet[2,9,10]. This restricted definition of successful communication is preferred because it is easier to characterize communication when signal descriptors in the sender and receiver networks are the same. Thus, whether a signal is communicated successfully or fails can be studied as a function of the statistical properties of the message (α and σ), which can be estimated from experimental data[30,31].

Phase portrait of neuronal communication. When the activity in the sender and receiver networks is parametrized using α and σ, the propagation of the activity in an NCS can be visualized as a trajectory in α–σ space[2,19] (FIG. 1b). We refer to this state space representation of messages as the phase portrait of neuronal communication, representing the propagation of spiking activity as a two-dimensional discrete map. Analysis of the propagation of a pulse packet in a feedforward network composed of several serially aligned NCSs with either only excitatory neurons[19,32] or both excitatory and inhibitory neurons[33] showed that α–σ space can be divided into two contiguous regions corresponding to stable communication and no communication. These regions are separated by a separatrix[19]. If the input pulse packet is above the separatrix, it becomes stronger and more precise with every layer, and the trajectory moves towards the top-left corner of α–σ space (FIG. 1b), indicating successful propagation. Alternatively, the pulse packet progressively degrades and eventually becomes indistinguishable from background activity with a trajectory pointing towards the right-bottom corner of α–σ space (FIG. 1b). In the phase portrait, the location of the separatrix determines which pulse packets can propagate and, thus, characterizes the communication properties of an NCS.

Determinants of communication

The location of the separatrix of an NCS depends on two factors: the properties of the channel (determined by the structural connectivity and synaptic dynamics) and the receptiveness of the receiver to the incoming signal (determined by the local dynamics and noise in the receiver network). Thus, the structural connectivity and activity dynamics of the sender and receiver networks conspire to establish communication in an NCS.

Structural connectivity between sender and receiver. The channel of an NCS is represented by the divergent and convergent synaptic connections between the sending and receiving neuronal networks, and its role in neuronal communication has been studied extensively[2,11,34]. Stronger connectivity in terms of synapse numbers and weights (FIG. 1c) shifts the separatrix down with respect to weaker connectivity and increases the range of spike volleys that can be propagated (FIG. 1d). There is a subtle difference in the way the number of synapses and their weights affect transmission. When synapses are weak, many inputs are needed to make postsynaptic neurons spike. This leads to more shared inputs and increased synchrony in the receiving neuron population. When synapses are strong, fewer input spikes suffice to elicit spikes in the postsynaptic neurons and, hence, less sharing of inputs and weaker synchrony in the receiving population. Thus, dense connectivity (more shared inputs) renders the receiver network response more synchronous[2,19,35,36], whereas sparser and stronger connections allow transmission without affecting synchrony[2,37]. By appropriately balancing the weights and the numbers of connections, it is possible to transmit both rate and synchrony signals simultaneously[2].

Neuron type and baseline excitability. The impact of structural connectivity on communication can be modulated by the neuron properties (for example, spiking dynamics[38,39] and neuronal excitability) in the receiver network. An NCS with neurons that operate in coincident detector mode requires a high α and a low σ for successful transmission. By contrast, the separatrix for an NCS with neurons operating in integrator mode is located at much lower values of α and σ. The neuronal excitability is determined by the effective spike threshold and the slope of the input–output transfer function (gain). These two properties depend on the ion channel composition of the neuron and are affected by neuromodulators[40]. Moreover, the amount of total input also influences the conductance state of the neuron[41]. Similarly, a noisy barrage from subcortical structures, notably the thalamus, can exert a modulatory effect on cortical communication properties[42]. Finally, cortico–cortical interactions by horizontal and feedback connections can also modulate excitability[43].

In the state space representation of communication, the level of excitability modifies the position of the separatrix originally defined by the number of synapses and the synaptic weights. Higher levels of baseline excitability move the separatrix downwards, facilitating the propagation of weaker signals, whereas decreasing excitability moves the separatrix upwards, having the opposite effect (FIG. 1d). Thus, in the absence of inhibition, both connection strength and baseline excitability shape the location of this excitatory separatrix.

Inhibition. Inhibitory neurons exhibit considerable genetic, chemical, morphological and electrophysiological diversity[44], with each interneuron type forming synapses on specific locations on the receiving dendrites[45,46]. In its simplest form, inhibition influences the excitability and gain of the neurons by changing the excitation–inhibition balance and the distance to threshold and shunting inputs[47,48]. Therefore, adding inhibition to the receiver network shifts the excitatory separatrix upwards and introduces a new inhibitory separatrix that reduces the

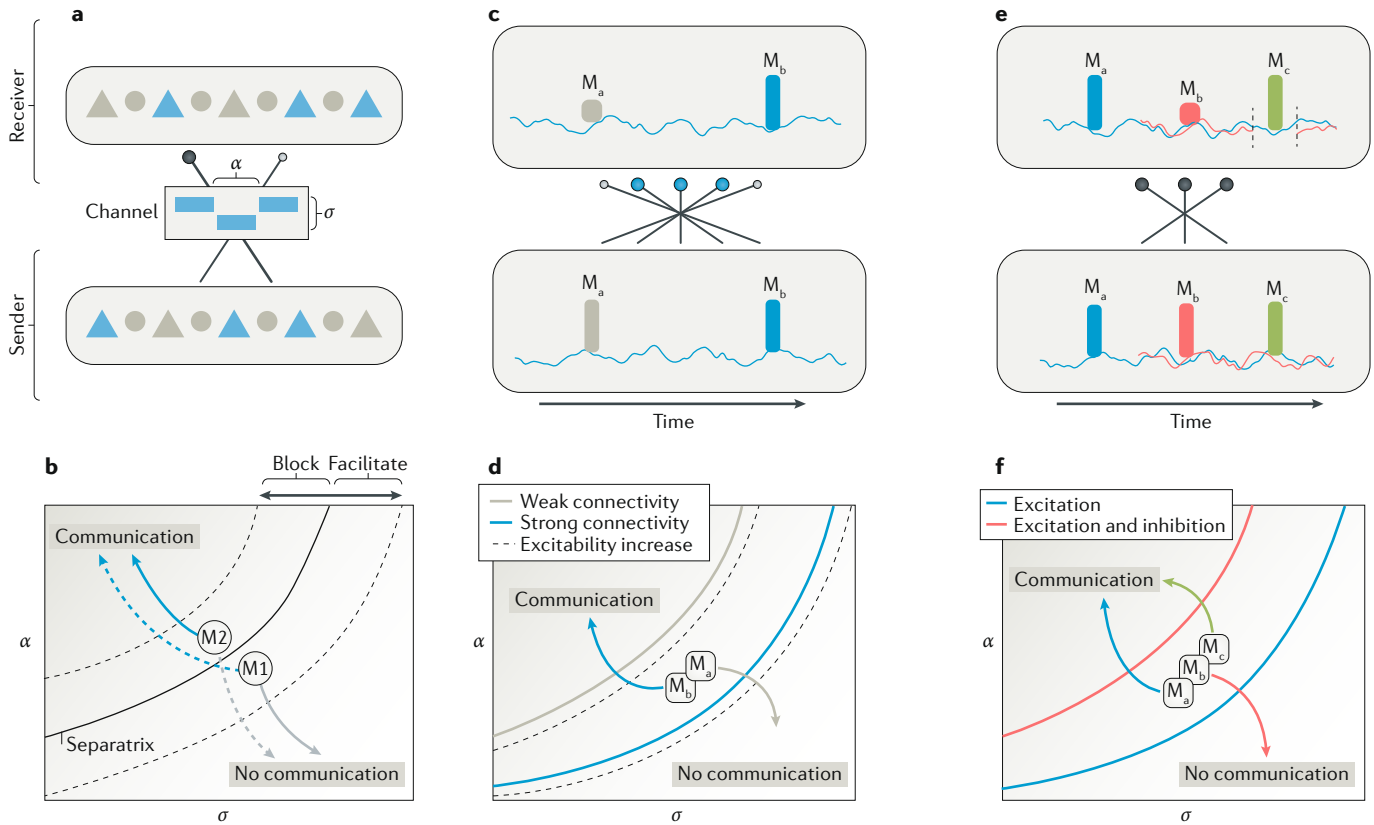

Fig. 1 | **Elements of communication in neuronal networks. a** | A neuronal communication system consisting of a sender, receiver and channel (connectivity) in which a spike volley flows from selected pyramidal cells (blue triangles) in a sender group to selected pyramidal cells in a receiver group. The large black-filled and small grey-filled circles indicate strong and weak synapses, respectively. Inhibitory neurons (grey circles) determine the dynamics in the sender and receiver and modulate spike flow. Each spike volley is quantified by the number of spikes (α) and their synchronization (σ). **b** | Neuronal communication can be described in a two-dimensional state space spanned by α and σ of a message (for example, M1 or M2). Each trajectory describes the temporal evolution of a message as it is propagated from the sender to the receiver, given its α and σ, leading either to successful propagation (solid blue trajectory) or to communication failure (solid grey trajectory). A separatrix in this message space (black curve) delineates a communication from a non-communication region. The location of the separatrix is determined by structural and dynamical parameters and can be shifted (dashed black lines) to facilitate previously blocked messages (for example, M1 (dashed blue trajectory)) or to block messages that could otherwise propagate (for example, M2 (dashed grey trajectory)). **c** | M_a and M_b show two instances of the same message. The grey vertical bars indicate α (height) and σ (width) when the sender and receiver are connected via weak connections (small grey circles). The blue vertical bars indicate α and σ of a message when sender and receiver are connected via strong connections (large blue circles). The light blue trace shows the local excitation in the sender and receiver neurons. **d** | This scheme shows part **c** rendered in α–σ space, with separatrices for weak and strong connectivity (grey and blue solid lines, respectively). Increasing the synaptic weights shifts the separatrix for weak connectivity downwards to the separatrix for strong connectivity, thereby facilitating the communication of messages that otherwise fail to propagate (compare the grey and blue message trajectories). An increase in neuronal excitability also shifts the separatrix downwards (dashed lines). **e** | The scheme depicts a scenario that is similar to that shown in part **c**. Now, however, it shows fixed connectivity (black circles) and includes inhibitory neurons in the sender and receiver. The blue and red traces show the excitation and inhibition, respectively, in sender and receiver neurons. The blue vertical bars represent successful propagation in the absence of inhibition (M_a), whereas the red vertical bars represent failure of propagation in the presence of inhibition (M_b). When inhibition is transiently removed in the receiver (vertical dashed lines), the message (M_c) can be communicated (green bars)[33]. **f** | This scheme shows part **e** rendered in α–σ space. The red and blue traces show separatrices in the absence and presence of inhibition, respectively. Inhibition blocks a message. A message that can be propagated in the excitation-only case (M_a, blue trajectory) is blocked by the introduction of inhibition (M_b, red trajectory). However, temporary disinhibition of the receiver at the moment of message arrival moves the separatrix back to the blue line and permits communication (M_c, green trajectory).

region of communication (FIG. 1e,f).

At the network level, irrespective of the interneuron types, the relative timing and amplitude of excitation and inhibition are the main determinants of network activity dynamics[49–51]. In the following section, we discuss how inhibition affects communication in an NCS by determining the activity regime of the sender and/or receiver.

Role of local network dynamics

A change in the balance and relative timing of excitation and inhibition can give rise to qualitatively different dynamical states in sender and receiver networks (BOX 1; Supplementary information). When excitation and inhibition are approximately balanced, the network exhibits an asynchronous-irregular (AI) state, in which neurons spike irregularly and independently of each other. A sufficient increase in excitation (or decrease in inhibition) renders the neuronal activity more synchronous and irregular (synchronous-irregular state). Despite the irregular firing of neurons, the network can exhibit oscillations. Because individual neurons do not spike in every oscillation cycle, this activity is termed the stochastic oscillation (SO) regime[50,52] (BOX 1; Supplementary information).

Box 1 | **Oscillations and synchrony in neuronal network activity dynamics**

Population synchrony

Synchrony arises when neurons receive common inputs. Even in sparsely connected random networks (connection probability = 0.1), there are enough shared inputs to cause a population-wide synchronization[57]. When average excitation and inhibition are balanced, the means of the excitatory and inhibitory inputs cancel each other and individual neurons spike owing to membrane potential fluctuations, resulting in irregular spiking. If two neurons receive a shared excitatory input, they elicit correlated spikes. However, if the same shared input also arrives at the two neurons via shared inhibitory projections, the shared inputs are cancelled[58,59]. That is, when neurons share both excitatory and inhibitory inputs, the shared inputs are suppressed, resulting in asynchronous spiking. Thus, balanced excitation and inhibition lead to an asynchronous-irregular regime[49]. When the average excitation and inhibition are balanced but shared inputs are not completely cancelled (for example, owing to a mismatch in their relative timings), individual neuron spiking becomes correlated while remaining irregular, resulting in the synchronous-irregular regime[49].

Population oscillations

Differences in the inputs to excitatory and inhibitory populations lead to population oscillations. This can occur because of increased excitation of the excitatory population and/or increased inhibition of the inhibitory population (Supplementary information). As the inhibition to excitation (I/E) ratio is increased, the network makes a transition from a non-oscillatory state to an oscillatory state (Andronov–Hopf bifurcation)[50,52]. Oscillations emerge for lower I/E ratios and for stronger effective excitatory inputs (Supplementary Figure 1).

Because neuronal networks are driven by noisy external inputs, neurons do not act as oscillators, despite the phenomenon of population oscillations. Given the inhibition-dominated regime, the firing rates of individual neurons are smaller than the oscillation frequency, and a different set of neurons participates in each cycle. Therefore, these oscillations are stochastic oscillations (SOs)[52].

In the SO state, excitation of the excitatory neuronal population or inhibition of the inhibitory neuronal population creates an imbalance, leading to a cycle of increased activity of excitatory population, followed by increased activity of inhibitory population, decreased activity of excitatory populations, decreased activity of inhibitory population, increased activity of excitatory population and so on. Thus, there is a phase shift between the excitatory and inhibitory activity (Supplementary Figure 1). In addition, all four types of connections in the network (E→I, E→I, E→I and I→I) contribute to oscillations[50,64].

Close to the bifurcation, the steady state appears non-oscillatory. However, in this state, a small perturbation (for example, a pulse packet) results in a damped oscillation (Supplementary Fig. 1). The time required by the perturbation to die out depends on the effective distance between the network operating point and the bifurcation line. As the operating point of the network moves closer to the bifurcation, the network response may also display more complex dynamics alongside oscillations[109].

Both synchrony and oscillations can coexist in a neuronal network because they arise owing to the imbalance of excitation and inhibition, but synchrony does not automatically imply oscillations and vice versa.

Entrainment and resonance in neuronal oscillators

When we drive one of the populations of a neuronal network oscillating at an intrinsic frequency of $\omega_0 = 2\pi f_0$, with an oscillatory external input $I_E = A_F \sin(\omega_F t + \Phi_F) = A_F \sin(\Phi_F(t))$, the network shows entrainment and/or resonance. Here, A_F is the amplitude, ω_F is the angular frequency and Φ_F is the phase. We denote the response oscillation amplitude as R_{net} and the phase as $\Phi_{net}(t)$.

A network is entrained when the network response and the input frequency are the same ($\omega_{net} = \omega_F$) and, hence, the phase difference between input and output remains constant over time ($\Delta\Phi(t) = \Phi_{net}(t) - \Phi_F(t) = \text{const.}$). Entrainment is observed for a limited range of $\Delta\omega = \omega_F - \omega_0$. This range of $\Delta\omega_F$ for entrainment increases with an increase in A_F. In the space spanned by $\Delta\omega$ and A_F, the region in which entrainment occurs is called the Arnold tongue[110] (Supplementary Fig. 2). In the Arnold tongue, the phase difference ($\Delta\Phi(t)$) converges to a fixed value after a few oscillation cycles. Outside the Arnold tongue region, $\Delta\Phi(t)$ continues to change with time, independent of R_{net}. At the border of the Arnold tongue, the relative phase grows in a step-like manner, making jumps of 2π (phase slips)[111].

For a fixed A_F, R_{net} changes in a non-monotonic fashion as a function of $\Delta\omega$ (REF.[110]) (Supplementary Fig. 2). The network response is maximal for $\Delta\omega = 0$. Unlike the entrainment phenomenon, the network resonance may or may not maintain a constant phase difference with the input oscillation.

Note that both entrainment and resonance require several cycles before the response magnitude, frequency and phase reach fixed values (FIG. 2a,b and Supplementary Fig. 2). Finally, although entrainment and resonance often appear concomitantly, they are different phenomena. Entrainment is observed when the network is exhibiting persistent oscillations, whereas resonance can occur even when the network is not exhibiting any persistent oscillations.

Pulse packets can arise either intrinsically in the sender network or through external stimuli (spike packets[28]) relayed, for example, by the thalamus[53,54]. The sender may also generate rhythmic pulse packets with different α and σ when operating in the SO regime or close to the transition between the AI and SO regimes[55]. In the AI state, pulse packets may arise owing to brief, irregular and noise-induced instabilities in the sender network dynamics.

Sender and receiver in an AI state. When both the sender and receiver networks operate in an AI state[49,56–59] and are connected via either dense, weak synapses or sparse, strong synapses, communication is dominated by the so-called synfire mode, in which pulse packets with sufficient synchrony (σ) and strength (α) propagate at a speed determined by the axonal and synaptic delays (fast communication mode)[32]. Recent measurements of activity propagation from the primary visual cortex (V1) to V2 provide experimental support for this mode of transmission[60]. Increasing inhibition in the network while maintaining the AI regime reduces the excitability of the neurons, and the excitatory separatrix is replaced by the higher located inhibitory separatrix (FIG. 1f). In that case, only stronger and more synchronous pulse packets propagate[32] (FIG. 1e). Careful manipulation of the timing of inhibition relative to excitation can be used to transiently move this inhibitory separatrix above or below the original separatrix[33]. Although recurrent inhibition in the ongoing AI activity might be prohibitive for propagating particular signals, temporary disinhibition of the receiver could lower the separatrix and open the communication gate to communicate otherwise blocked messages (FIG. 1e,f). Thus, when both the sender and receiver networks are in an AI state, a change in magnitude and timing of inhibition in the receiver can build a flexible gating mechanism for a variety of transient and tonic signals[33,61].

A crucial problem with the synfire mode of communication is that the requirement of dense and weak or sparse and strong connectivity, together with the presence of inhibition, constrains physiological communication among networks to strong messages, because the inhibitory separatrix may be located quite high in α–σ space. Furthermore, the measurement of signatures of synchronous pulse packets in cortical activity heavily depends on the choice of null hypothesis[62,63]. When sender and/or receiver networks operate in oscillatory states, new modes of communication based on network resonance (FIG. 2a) and entrainment (FIG. 2b) may arise

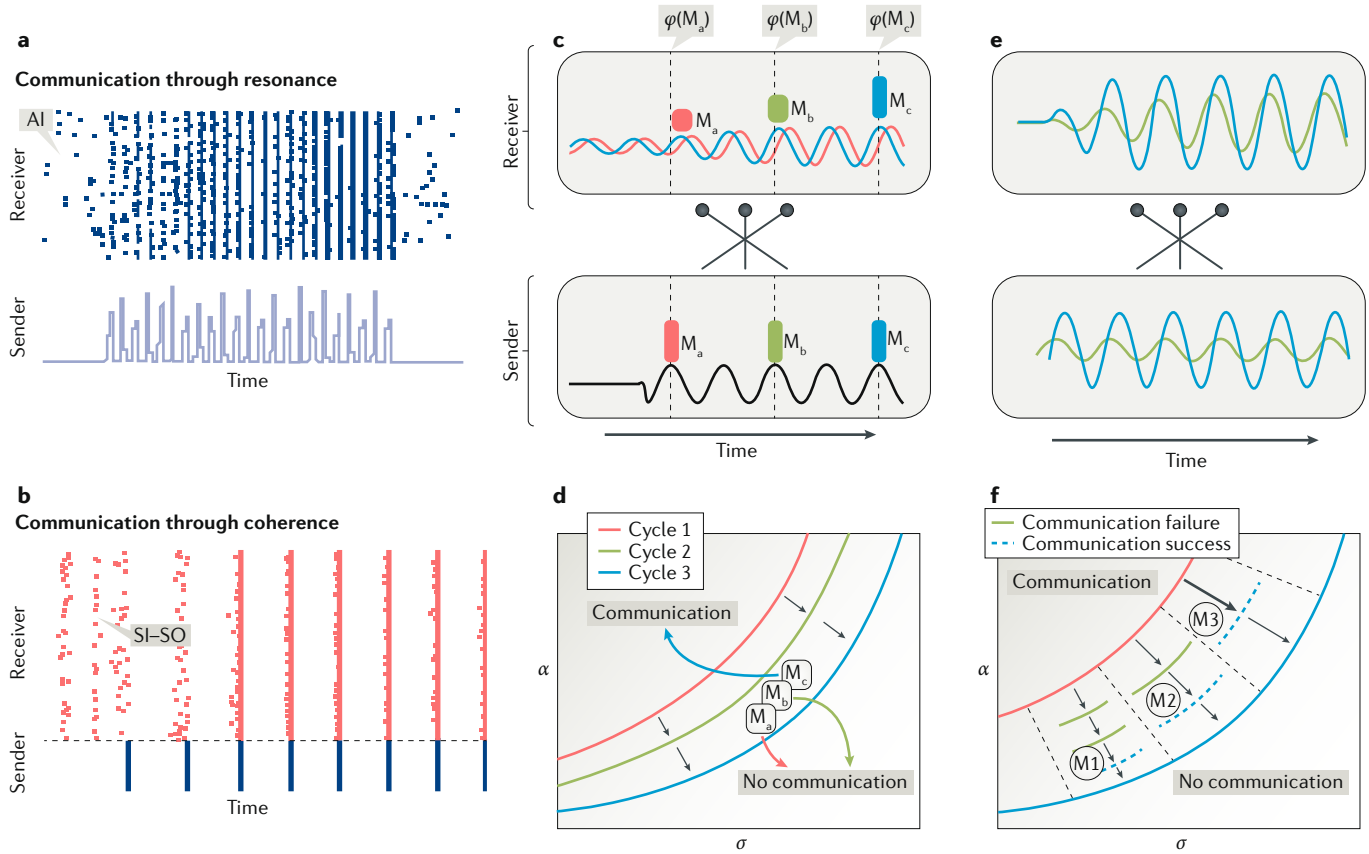

Fig. 2 | **Neuronal communication with gamma oscillations. a** | Communication through resonance. The top image shows spiking activity in the receiver network, whereas the bottom image shows a periodic train of pulse packets. Each pulse packet has different spike (α) and temporal dispersion (σ) values. In the absence of pulse packets, the receiver shows asynchronous-irregular (AI) activity. Because of network resonance, periodic pulse packets gradually induce strong oscillations in the receiver. After a few cycles, the network reliably responds to each incoming pulse packet. **b** | Communication through coherence. Spiking activity in the receiver is denoted by red dots, and the input train of periodic pulse packets is shown by the vertical blue lines. In the absence of periodic pulse packets, the receiver network shows stochastic oscillations (SOs) in the gamma range, while neurons spike in a synchronous-irregular (SI) manner. Because of network entrainment, the phase of the receiver oscillations gradually becomes aligned with the phase of the incoming pulse packets. **c** | Evolution of spike volleys in oscillation-based communication. The red and blue horizontal traces show oscillatory excitatory and inhibitory activity in the receiver. The black trace shows gamma oscillations in the sender. Periodic pulse packets enhance the amplitude of oscillations (resonance) in the receiver and change its phase (Φ) with every cycle (entrainment). Messages M_a and M_b arrive when receiver oscillations are weak and not aligned with the sender oscillations and, therefore, fail to propagate to the receiver (red and green vertical bars). After a few cycles, oscillations are strong and aligned with the sender oscillations and, therefore, message M_c is successfully propagated (blue vertical bars). **d** | This scheme shows part **c** rendered in α–σ space. The red line denotes the separatrix when receiver oscillations are weak and not aligned with the sender oscillations (inhibitory separatrix), whereas the blue line represents the separatrix when receiver oscillations are strong and aligned with the sender oscillations. The green line denotes the separatrix when receiver oscillations are moderately strong and partially aligned with the sender oscillations. The black arrows indicate how the separatrix changes with each oscillation cycle. The red and green trajectories indicate failure of propagation, whereas the blue trajectory indicates successful communication. **e** | In oscillation-based communication, the speed of propagation depends on the amplitude of the oscillations. Stronger stimuli (blue trace) elicit higher amplitude responses in the receiver, and amplification of receiver oscillations occurs in fewer cycles than for weaker stimuli (green trace). **f** | The initial α and σ values of each message (M1, M2 and M3) determine the number of gamma cycles that are required to establish communication with the receiver. The red line denotes the separatrix when receiver oscillations are weak and not aligned with the sender oscillations, whereas the blue line represents the separatrix when receiver oscillations are strong and aligned with the sender oscillations. The solid green and dashed blue lines indicate how much the separatrix is lowered with each oscillation cycle (arrows). For successful propagation, the message must lie above the dashed blue line in α–σ space. For strong messages (M3), the red separatrix is lowered sufficiently in only one oscillation cycle, whereas for weak messages (M1), the red separatrix is lowered sufficiently only after three oscillation cycles. Part **a** is adapted from REF.[64], CC-BY-4.0. Part **b** is adapted with permission from REF.[70], Wiley-VCH.

and enable the transmission of weak inputs over weakly connected networks.

Sender in an SO state and receiver in an AI state. When the sender exhibits SOs[50,52,64] or the input is oscillatory, a receiver network operating in an AI state can switch to periodic activity, which is gradually amplified through resonance (BOX 1; FIG. 2a; Supplementary information). Network resonance occurs when the input frequency coincides with the natural resonance frequency of the receiver network (FIG. 2a,c). Even though a single pulse packet may not be sufficiently strong to overcome the recurrent inhibition, it creates a damped oscillation in an otherwise AI state, in which periods of strong and weak inhibition alternate[64]. If the next pulse packet arrives within the weakly inhibited phase of the damped oscillation ($\pm T/4$; T being the period of the resonance frequency), the receiver response will be larger than the response to the previous pulse packet.

In this fashion, a message composed of an appropriately timed periodic train of pulse packets will be progressively amplified, as inhibition is gradually silenced during the weakly inhibited phase, and eventually will be strong enough to be propagated to the receiver network. This scheme of communication, referred to as communication through resonance[64], lowers the inhibitory separatrix with every oscillatory cycle until, in the best-case scenario, inhibition vanishes entirely and communication is limited only by the excitatory separatrix (FIG. 2d). However, whereas communication through resonance enables the transmission of weak signals, such communication is inherently slow, as several cycles are required to lower the separatrix enough to enable signal propagation (BOX 1; Supplementary information).

Sender in an AI state and receiver in an SO state. A somewhat different scenario arises when a message arrives at a receiver network that is already involved in ongoing oscillations, with inhibition changing rhythmically (BOX 1; Supplementary information). Such oscillations may serve several computational roles[65]. Here, we restrict our discussion to the role of oscillations in the communication of spikes between neuronal networks. These oscillations imply that the inhibitory separatrix fluctuates between two different locations with enhanced and reduced communication properties, respectively. A transient signal that is dispatched at random times will correspondingly arrive at a random phase of the oscillation and, hence, will propagate with low probability[66,67]. To establish reliable communication, the phase of the incoming message needs to be aligned to the disinhibited phase of the receiver oscillation[68]. Once the correct phase is established (for example, by an oscillation reset mechanism[51,68]), communication is as fast as it would be in the synfire mode, even though communication is feasible only at specific intervals determined by the receiving network oscillation frequency.

Sender and receiver in an SO state. A natural scenario in which the input stimulus can be aligned to the correct phase of the receiver network oscillation arises when the incoming message is composed of a periodic train of pulse packets and the receiver network is oscillating with the same frequency as the periodic input pulse packet train[64,69,70]. When the phase of the pulse packets and the receiver network oscillation match, communication is straightforward, as the pulse packets arrive in the non-inhibited phase of the receiver oscillation and the inhibitory separatrix is sufficiently lowered. However, in a more likely scenario, when the phase of the receiver oscillation does not match the input periodicity, the incoming periodic pulse packets entrain the postsynaptic network oscillation by resetting the phase of the receiver network oscillation at each cycle until, after a number of cycles, the oscillations of the sender and receiver are aligned and the two oscillations become phase-locked[70] (BOX 1; FIG. 2b,c). Thus, the entrainment of the receiver network can be thought of as an adjustment in the phase of the periodic movement of the inhibitory separatrix such that it is at the lowest level when an incoming pulse packet arrives. Such (unidirectional) entrainment is the working principle of 'communication through coherence', which posits that phase alignment of two narrow-band oscillations in the gamma range is a prerequisite of neuronal communication[20,71–77]. Notably, the response gain in the entrained receiver is at its highest and, hence, communication is optimized when the sender and receiver frequencies match, similar to the resonance described above[64,70] (BOX 1). Resonance and entrainment may work together to enhance communication of signals that would otherwise be blocked in the AI state. Because a pure AI state is quite unlikely and any ongoing activity probably contains oscillatory bursts, some degree of entrainment is probably always involved as the oscillatory input becomes aligned with the ongoing damped oscillations. Recent computational models have shown that entrainment and resonance may not be necessary for communication because weakly connected sender and receiver networks (but only if both have identical parameters) can be tuned to spontaneously generate coincident oscillation bursts and enable selective routing[55].

Although oscillation-based mechanisms (communication through coherence and communication through resonance) are intuitive, some experimental data are not consistent with this idea: first, oscillation frequencies are variable over space and time[78]; second, oscillations last only for a short duration[79]; and, third, communication depends on the power of gamma oscillations in the sender and not on the receiver networks[80]. Furthermore, oscillation-based mechanisms (communication through coherence and communication through resonance) slow communication and require several cycles to finally establish communication by lowering the inhibitory separatrix enough with each oscillation cycle to enable signal propagation[64] (FIG. 2e,f).

Gating oscillatory communication

The communication mechanisms described above are based on rhythms in the gamma range (40–70 Hz), generated by networks of excitatory and inhibitory neurons[81–83] (BOX 1; Supplementary information). Although gamma oscillations are predominantly observed in the superficial and middle layers of the neocortex, deeper layers are able to generate rhythms at lower frequencies (alpha (8–12 Hz) and beta (15–30 Hz) ranges), flowing in the feedback direction of the cortical hierarchy[84–86]. These slower oscillations may also be created by long and indirect excitatory–inhibitory feedback loops, involving different types of inhibitory neurons with larger time constants. Importantly, experimental studies have demonstrated that slower rhythms affect the phase, frequency and amplitude of (faster) gamma oscillations[87].

Slow oscillations, especially in the alpha band, are hypothesized to periodically add pulsed inhibition to a network generating faster oscillations[88–90]. The function of such nesting of slow and fast rhythms remains unclear. Based on experimental findings demonstrating high alpha power in cortical areas coding task-irrelevant information[91,92], the notion of the 'gating through inhibition' framework[88,91] was proposed. This framework suggests two ways by which alpha oscillations can affect gamma-oscillation-based communication. First, pulsed alpha inhibition is internally coordinated such that gamma activity coming from the sender arrives consistently at the inhibitory phase of the alpha rhythm, thereby blocking gamma-oscillation-based communication. Second, changes in alpha power alter the number of gamma cycles that can occur within the excitable phase of the alpha rhythm, with lower alpha power allowing more gamma cycles to occur and vice versa[93]. The reduced number of gamma cycles (at high alpha power) would then interfere with the transmission of a phase code implemented through alpha–gamma coupling[94].

Here, we propose a different explanation of how the coupling between fast and slow oscillations may play a role in communication. We assume that the excitability window of alpha rhythms determines the number of consecutive gamma oscillation cycles in the receiver networks[88]. The duration of this window

may be influenced by the alpha rhythm amplitude and frequency. Because the build-up of resonance and/or entrainment (necessary for communication of weak inputs) requires a certain number of gamma cycles[64,70], the excitability window duration of alpha rhythms can control the slow mode of communication between the sender and receiver. Although alpha rhythms with shorter excitability phases restrict gamma-based communication (FIG. 3a), alpha rhythms with a longer excitability window may relax this restriction on communication by allowing more consecutive gamma oscillation cycles, sufficient to build up resonance and entrainment (FIG. 3a).

It is also conceivable that the strength of alpha inhibition, encoded as the alpha amplitude, determines whether gamma resonance and entrainment between the sender and receiver are completely removed during the inhibitory phase of the slow rhythm. Thus, when the alpha amplitude is high, gamma coherence between the sender and receiver is completely abolished during the inhibitory period, forcing resonance and entrainment to start anew from the same

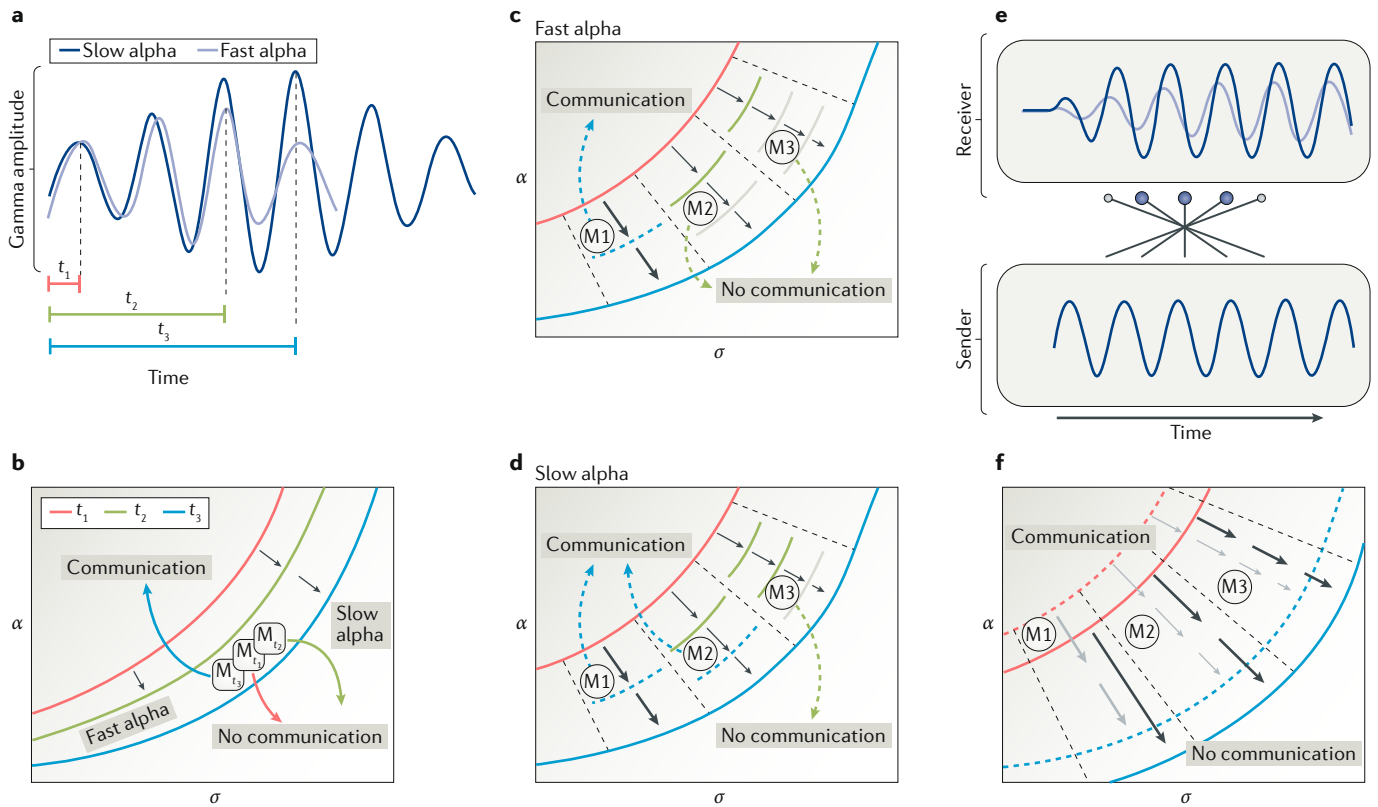

Fig. 3 | **Communication with gamma oscillations is modulated by slower oscillations in the alpha range. a** | Modulation of the gamma oscillation amplitude by alpha-band oscillations. Slow alpha-band oscillations allow for more gamma-band cycles (dark blue trace) than faster alpha-band oscillations (light blue trace). t_1 denotes the peak of the first gamma cycle, t_2 denotes the time at which the maximum gamma oscillation amplitude is reached for faster alpha-band oscillations and t_3 denotes the time at which the maximum gamma oscillation amplitude is reached for slower alpha-band oscillations. **b** | This part shows the location of the separatrix in spike number (α) and temporal dispersion (σ) space at t_1, t_2 and t_3. With slow alpha-band oscillations, the separatrix can be lowered to the location marked by the blue line, whereas for fast alpha-band oscillations, the separatrix can only be lowered to the location marked by the green line. The message (M) can be communicated only in the presence of slow alpha-band oscillations (blue trajectory). M will not propagate in the presence of faster alpha-band oscillations (green trajectory) or during the first cycle of oscillations (red trajectory). **c** | Propagation of activity in the presence of fast alpha-band oscillations rendered in α–σ space. The red line shows the location of the separatrix at the onset of the gamma oscillation in the presence of alpha oscillations (inhibitory separatrix), and the blue line shows the separatrix when receiver oscillations reach their maximum amplitude in the absence of alpha-band oscillations. The solid grey lines indicate how much the separatrix is lowered with each oscillation cycle (marked by the arrows). The solid green lines indicate how much the separatrix is lowered in the presence of alpha-band oscillations. For successful propagation, the message must lie above the dashed blue line in α–σ space. When gamma oscillations are modulated by fast alpha oscillations, only M1 can be propagated (blue dashed trajectory); M2 and M3 will fail to propagate (green dashed trajectories). **d** | Propagation of activity in the presence of slow alpha-band oscillations, which allow more gamma-band cycles in a single alpha-band cycle. In this scenario, messages M1 and M2 can propagate (blue dashed trajectories), but M3 cannot propagate (green dashed trajectory). **e** | Effect of connectivity between the sender and receiver on oscillation-based communication. The scheme shows the response of a receiver network to oscillatory input with the same amplitude in the context of weak (grey circles) or strong (black circles) connectivity. With strong connectivity between the sender and receiver, the response in the receiver reaches the maximum oscillation amplitude in fewer oscillation cycles (dark blue trace) than in a scenario with weak connectivity between the sender and receiver (light blue trace). **f** | Effect of excitability of receiver neurons and connectivity between the sender and receiver on oscillation-based communication rendered in α–σ space. An increase in excitability or connectivity shifts the excitatory (blue dashed line) and inhibitory (red dashed line) separatrices downwards (solid blue and red lines). The arrows indicate the change in the location of the separatrix with each oscillation cycle (grey arrows denote weak connectivity or lower neuronal excitability, and black arrows denote strong connectivity or higher neuronal excitability). Thus, increases in connectivity or neuronal excitability increase the speed of communication by reducing the number of cycles required to enable communication. This change in the speed of communication is shown for three different messages (M1, M2 and M3).

baseline activity during each alpha cycle. By contrast, when the alpha amplitude is smaller, the effects of gamma resonance and entrainment may only partly be cancelled by alpha inhibition. In this scenario, resonance and entrainment may be reached in fewer cycles.

Overall, the role of such slow inhibitory rhythms in controlling communication between two networks can be visualized in terms of the movement of the inhibitory separatrix. As a consequence of this dependence of resonance and entrainment on the duration of the excitability window, weak stimuli requiring boosting through gamma oscillations for successful communication might be blocked by the presence of a high-amplitude or high-frequency alpha modulation (FIG. 3b) by not allowing the inhibitory separatrix to move sufficiently downward during gamma communication while being communicated with lower modulation amplitude or frequency (FIG. 3b). How far the inhibitory separatrix should be shifted depends on the pulse packet characteristics. Stronger and more synchronous pulse packets may reach full resonance and communicate even in the presence of shorter excitability windows, whereas weaker pulse packets may not be sufficiently amplified within the same excitability window and, hence, may fail to propagate (FIG. 3c,d).

A prediction of this framework is that modulation of the amplitude and/or frequency of alpha rhythms will alter the communication of only weaker messages that require several gamma cycles to be communicated (FIG. 3c,d). Transmission of sufficiently strong messages, transmitted in one transient or requiring 2–3 gamma cycles, should be independent of the power and frequency of the alpha rhythm. This remains possible when a message arrives at the excitable phase of the alpha modulation or when coherent alpha rhythms exist in the sender and receiver. Such phase alignment between alpha range oscillations has indeed been observed and was suggested to play an active role in information representation and processing beyond a purely inhibitory effect[95].

On the basis of our framework, we suggest that coherent alpha oscillations, even with high amplitude or higher frequency, may employ the synfire mode of communication to rapidly process salient information represented by strong pulse packets (larger α and/or smaller σ) or route familiar information along pathways that have already been reinforced by synaptic plasticity. Such fast routing does not depend on the alpha oscillation amplitude or frequency but can be gated by adjusting the phase of alpha between sender and receiver networks. By contrast, novel information that is encoded by weaker pulse packets (smaller α and/or larger σ) would require gamma-oscillation-based communication, which can be controlled by flexibly adjusting the alpha oscillation amplitude and/or frequency. Note that these principles may also hold for slow modulations with higher frequencies, such as the beta band[96,97], as long as the modulation is inhibitory. This framework leads to an interesting prediction: in attention experiments, coarse information about distractors may still be routed even in the presence of coherent alpha oscillations with high amplitude and may have measurable behavioural consequences.

Faster oscillatory communication

How can gamma-oscillation-based communication be accelerated? We propose four possibilities. First, changes in the local connectivity result in an increase in the frequency of gamma oscillations. In this scenario, even though it would take the same number of cycles to build up network resonance, with a shorter oscillation period, communication will be accelerated[20]. Second, local plastic changes bring the network closer to the bifurcation of an oscillatory state, such that it takes fewer oscillation cycles to build up resonance. Third, given the rhythmic pairing between the sender and receiver networks, the feedforward excitatory synapses involved are strengthened. This would imply that the sender–receiver system coupled with weak or sparse connections would be transformed into a more strongly coupled system. Indeed, periodic pairing at multiple timescales (<2 ms timescales given by the axonal time delay, ~20 ms timescales given by gamma rhythms and ~100 ms timescales given by slow rhythms) can induce different types of rate-dependent and timing-dependent plasticity[82,98–100] to strengthen feedforward connectivity and switch from a rhythm-based communication

Glossary

Asynchronous-irregular (AI) state
An activity state in which individual neurons spike in an irregular manner, independent (asynchronous) of other neurons in the network. In this state, the irregularity of the inter-spike-interval is close to unity, and correlations between a pair of neurons are close to zero.

Convergent and divergent projections
Projections in a connectivity scheme in which neurons in a group receive input from many neurons in a previous group (convergent) and, at the same time, project to many neurons in the subsequent groups (divergent).

Communication through resonance
A mode of communication in which the non-oscillatory receiver network is periodically activated by the sender and generates an amplified oscillatory response through resonance. Once the oscillations in the receiver are strong enough, only the pulse packets aligned to the peak (or trough if the oscillation is effectively inhibitory) are transmitted to the receiver network.

Communication through coherence
A mode of communication in which both the sender and receiver oscillate with the same frequency and phase (coherent). In this model of communication, only the pulse packets aligned to the peak (or trough when the oscillations are effectively inhibitory) are transmitted to the receiver network.

Effective spike threshold
The difference between the average membrane potential and the spike threshold of a neuron.

Excitatory separatrix
A separatrix of a feedforward network consisting of only excitatory neurons.

Inhibitory separatrix
A separatrix of a feedforward network consisting of both excitatory and inhibitory neurons. As inhibition is introduced in the network, the excitatory separatrix moves upwards, indicating that in the presence of inhibition, stronger and more synchronous pulse packets are allowed to transmit.

Oscillation-based communication
When communication between the sender and receiver is mediated by communication through either resonance or coherence.

Separatrix
A line that separates the two-dimensional space spanned by the two descriptors (α and σ) of a pulse packet. An input pulse packet starting above the separatrix eventually converges to a fixed point corresponding to a high α and a low σ. By contrast, an input pulse packet starting below the separatrix eventually converges to a fixed point corresponding to a small α and a high σ.

Synchronous-irregular state
An activity state in which individual neurons spike in an irregular manner but different neurons are correlated with each other. In this state, the irregularity of the inter-spike-interval is close to unity, and correlations between a pair of neurons are non-zero.

Synfire mode of communication
This mode of communication is observed when the input pulse packet is strong and synchronous enough to be above the separatrix. Alternatively, such communication occurs when the connectivity is sufficiently dense to lower the separatrix such that even weak or asynchronous pulse packets can propagate without the need for oscillations.

Stochastic oscillation
(SO). A type of oscillation in neuronal networks in which the average activity of the neuron population shows a regular oscillation but individual neurons do not spike in each cycle and instead spike in an irregular manner.

strategy to synfire mode communication. Fourth, changes in baseline excitability through neuromodulation and excitatory top-down input[101–103], which enhance the excitability of receiver neurons, can also boost[104] and accelerate gamma communication. Such attentional effects may be observed behaviourally in shorter reaction times and might be implemented by slower rhythms[20,101], especially in the theta range (4–8 Hz), which periodically enhance the excitability of receiver networks. In addition, feedback beta oscillations (12–30 Hz) have been implicated in the attentional modulation of gamma rhythms[105]. Note that, in this scenario, theta-like rhythms periodically excite receiver networks, whereas the alpha rhythms, as discussed above, rhythmically inhibit receiver networks.

In the phase portrait, both enhancing synaptic weights and excitability correspond to a gradual downward shift of the inhibitory and excitatory separatrices. This shift renders more messages amenable to rapid communication and reduces the number of gamma cycles required for the transmission of weaker messages, thereby accelerating communication (FIG. 3e,f).

Predictions

From our above analyses, we derive the following set of possible future experiments and predict their possible outcomes.

The location of the separatrix and its movements in the presence of oscillations can be measured using modern advances in optogenetics technology. By stimulating a selective group of neurons with pulse packets of specified values of (α, σ) and recording the response in downstream networks, the location of the separatrix and its possible variations in the presence of oscillations in the receiver network can be experimentally measured.

Our models show that the signatures of both oscillation-based and synchrony-based communication are also visible in the subthreshold membrane potentials. Specifically, the synchronized pulse packets should create biphasic responses in the subthreshold membrane potential[32], in which rapid depolarization is followed by a hyperpolarization phase (owing to recurrent inhibition). Moreover, we should be able to observe signatures of resonance and entrainment in the form of a progressive increase in oscillation amplitude in the receiver network.

We predict that stimuli represented by weak pulse packets (for example, unfamiliar or low-contrast stimuli) are communicated using slow oscillation-based communication modes (communication through coherence or resonance) and, therefore, are propagated slowly and are associated with long reaction times. By contrast, stimuli represented by strong and synchronous pulse packets (for example, familiar or high-contrast stimuli) can be communicated using the fast synfire mode and are associated with short reaction times. This also implies that weak or unfamiliar stimuli are more susceptible to changes in the power and frequency of alpha-band oscillations.

Even in the presence of high-amplitude and alpha oscillations in the sender and receiver, communication may still be possible through the synfire mode to transmit coarse information about distractors, as long as the alpha modulation is coherent.

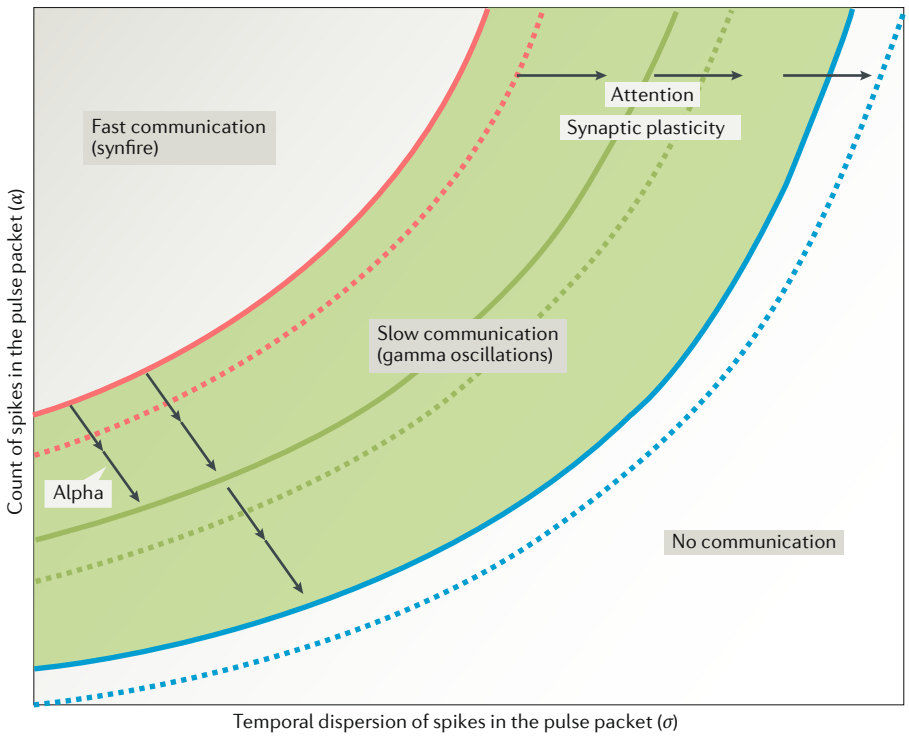

Fig. 4 | **Summary of neuronal communication in α–σ state space.** Fast communication in the synfire mode is located above the inhibitory separatrix (solid red line), whereas communication of messages between the inhibitory separatrix and the excitatory separatrix (solid blue line) benefits from gamma oscillations through disinhibition by resonance and entrainment. A slow inhibitory modulation of the receiver through alpha oscillations sets a boundary for disinhibition and, hence, the size of the gamma oscillation region (green separatrix). Changes in excitability, mediated through attention and synaptic plasticity (potentiation), shift the separatrices downwards (dashed lines) and accelerate gamma communication; that is, the number of gamma cycles (arrows) that are required to move the inhibitory separatrix down to the level of the excitatory separatrix is reduced. α, spike count; σ, temporal dispersion.

Conclusions

In this article, we present an attempt to synthesize several aspects of neuronal communication in neuronal networks into a single coherent framework (FIG. 4). Usually, the communication of spike volleys between neuronal networks is divided into two separate fields. In oscillation-based mechanisms for neuronal communication, the sender and receiver share common rhythms[20], whereas in synchrony-based communication, common inputs from the sender to the receiver create synchrony[2,19]. Therefore, these two communication modes are often taken to be inherently different[106].

Here, we argue that these two types of synchronization do not fundamentally differ. Instead, they both describe communication between networks with spike volleys represented in phase space, spanned by the number of spikes and their synchronization. In both cases, synchronous spiking events are routed from a sending population to a receiving population, and the impact of a volley in the receiver is determined by common input synchrony generated in the sender. The impact of this common input depends on several factors, as reviewed above. In our view, the main difference

between the two types of communication is in the speed of communication. The fast mode (synfire mode) of communication is possible when the message is sufficiently strong and synchronous. Such messages can be found in α–σ space above the inhibitory separatrix, which combines the impact of synaptic numbers, weights, excitability and inhibition (FIG. 4). By contrast, slow gamma communication is effective in the phase diagram subspace between the inhibitory separatrix and the excitatory separatrix and acts via rhythmic disinhibition based on resonance and entrainment, which naturally requires the message to be dispatched in several cycles to achieve communication. Note that, by this definition, synfire communication can also be found in the presence of gamma oscillations, that is, when the first cycle of a gamma burst is already strong enough to establish communication and the disinhibitory effect of subsequent gamma cycles is not required. The location of the separatrices and, hence, the relative prevalence of the synfire and gamma modes of communication can be modulated by attentional top-down modulation, affecting the amplitude, frequency and phase of slow alpha modulations, together with the baseline excitability in the gamma networks (FIG. 4). The spatiotemporal pattern of enhanced communication in target areas and blocked communication in distractor areas across the brain may then be subject to top-down control from higher-order cortical areas, possibly by using competition[101] in priority maps, such as in the frontal eye field and lateral intraparietal cortex[107,108], and working-memory-related regions, such as the prefrontal cortex. Moreover, the learning of weak stimuli through synaptic plasticity mechanisms results in a gradual shift from slow gamma routing to fast synfire communication.

In summary, we have argued that both synchrony-based and oscillation-based communication between neuronal networks in the brain can be understood using a single theoretical framework, which provides a better understanding of the possible functional role of nesting slow and fast oscillations.

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