

Spiking activity propagation in neuronal networks: reconciling different perspectives on neural coding

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Abstract | The brain is a highly modular structure. To exploit modularity, it is necessary that spiking activity can propagate from one module to another while preserving the information it carries. Therefore, reliable propagation is one of the key properties of a candidate neural code. Surprisingly, the conditions under which spiking activity can be propagated have received comparatively little attention in the experimental literature. By contrast, several computational studies in the last decade have addressed this issue. Using feedforward networks (FFNs) as a generic network model, they have identified two dynamical activity modes that support the propagation of either asynchronous (rate code) or synchronous (temporal code) spiking. Here, we review the dichotomy of asynchronous and synchronous propagation in FFNs, propose their integration into a single extended conceptual framework and suggest experimental strategies to test our hypothesis.

Convergent–divergent connection

A connectivity scheme in which neurons in a group receive inputs from many neurons in a previous group (convergent connections) and at the same time project to many neurons in subsequent groups (divergent connections).

When two elementary brain-processes have been active together or in immediate succession, one of them, on re-occurring, tends to propagate its excitement into the other. William James, 1890 (REF. 1)

One of the central problems in neuroscience is that of characterizing and understanding the neural code². The term ‘neural code’ refers to the properties of a single sequence of action potentials (spike trains) or a spike train ensemble that may be used by the brain to encode, decode and process sensory and/or cognitive information. To investigate the neural code experimental approaches are often based on presenting different inputs (stimuli) to an animal and quantifying various properties of the generated spike patterns. In this approach, encoding and decoding of sensory information is quantified from the human perspective. In some senses, however, this is a non-biological approach to elucidating the neural code, which ought to be defined and understood from the neuronal perspective. Stimulus encoding and decoding should be meaningful primarily to the subsequent processing stages (or effector organs) and not necessarily to the human observer.

In the spirit of a neuronal perspective, Perkel and Bullock proposed in their seminal report² that a candidate neural code must serve four key functions:

stimulus representation, interpretation, transformation and transmission (BOX 1). In this Review, we focus on the last of these properties — the transmission of neural activity. Because the brain is a highly modular structure, it is vitally important that spiking activity can propagate from one module to the next while preserving the information it carries. Thus, to understand the neural code and the mechanisms of processing and computation in modular neural networks, it is essential to identify the conditions under which spiking activity can propagate.

Surprisingly, the issue of spiking-activity propagation has received remarkably little attention from experimental neuroscientists (see REF. 3 for an exception). Yet, in the last decade several computational studies have specifically addressed this issue^{4–10}. The feedforward network (FFN) with convergent–divergent connections between subsequent groups of neurons (or ‘layers’) has been the model of choice in these studies. The simple FFN topology captures important features of the modular architecture of the brain (FIG. 1).

These theoretical studies have identified two separate modes that support the propagation of either asynchronous (rate code)^{6,11} or synchronous (temporal code) spiking activity^{4,8,9,12,13} (BOX 2). This dichotomy is interesting because it reflects the widespread view that rate codes and temporal codes are mutually exclusive.

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Box 1 | Properties of a neural code

In their seminal treatise, Perkel and Bullock² identified the following four functions that a candidate neural code must serve:

- Stimulus representation: certain properties of the stimulus should be able to alter the neural activity such that the stimulus can be represented using the code.
- Interpretation: the read-out mechanism should be able to correctly interpret the code and perform an action accordingly. The read-out can be muscle activation or the next stage of processing.
- Transformation: the neural code is generated and exists in a recurrent network of neurons. To perform any computation it is important that the candidate code can be transformed by the network in a controlled way.
- Transmission: the brain is highly modular. Therefore, any candidate neural code must be able to propagate from one network (module) to another with high fidelity.

Experimenters have primarily focused on understanding stimulus the first three properties mentioned above, and evidence has been collected for several candidate codes, such as the firing rate code, temporal code, correlation code and rank-order codes. Surprisingly the study of transmission has been largely ignored in the experimental literature.

In this Review, we propose an extended conceptual framework to integrate these two modes of activity propagation. We argue that rate and synchrony propagation represent, in fact, two extremes of a 'continuum' defined by the parameters of the feedforward architecture. A particular class of networks may be more suitable for rate propagation, but it can be systematically altered to a network that preferentially propagates synchrony. Specifically, we argue that the strength of synaptic couplings and the abundance of shared connections are the two key parameters of the network structure that determine the preferred mode of activity propagation. In addition, we highlight the conceptual importance of spiking-activity propagation in neural networks and provide specific suggestions to experimentally study the different modes of spiking-activity propagation *in vivo* and *in vitro*.

Models for studying spike propagation

Even though the brain is densely packed with neurons, only a very small fraction of these are activated in response to a stimulus or in a cognitive or motor task. Numerous studies that recorded single neuron activity unequivocally suggest that repeated presentation of the same stimulus or repeated execution of the same task activates roughly the same set of neurons each time. This fact is the basis for the concept of the neural assembly^{14–16}. Neural assemblies can efficiently encode sensory stimuli and information that is intrinsic to the brain, despite the fact that neural activity *in vivo* is highly variable across repeated trials^{17–19} and that individual neurons are exposed to inputs from large numbers of other neurons^{20,21}, typically through weak and unreliable synapses^{22,23}. Such neural hardware precludes the input from reliably reaching a target neuron via a single pre-synaptic neuron alone. Thus, a 'transmission line' with only a single neuron at each stage is highly unreliable. Only the seemingly redundant layout with multiple neurons at each stage, interconnected by convergent-divergent projections, may allow for reliable representation and propagation of the input²⁴.

Unreliable synapses

Synapses may fail to induce a postsynaptic potential in the target neuron despite stimulation owing to the probabilistic nature of synaptic vesicle release.

Anatomically segregated regions of the brain are highly specialized in their function (FIG. 1a). Even the performance of simple tasks requires both serial and parallel interactions among multiple brain regions^{25–27}. In fact, serial interactions among multiple brain regions may explain why the reaction time in animals performing a task often increases with task complexity^{25,26}. Together, the concepts of a modular brain and of neural assemblies provide a powerful framework for neural information processing in terms of cascades of neural assemblies interconnected by convergent–divergent links²⁵.

Donald Hebb envisaged the organization of behaviour based on networks of neural assemblies interconnected by convergent–divergent links¹⁶ as a foundation for a neuropsychological theory of brain function rooted in biological principles ('neuralizing')^{15,16}. Hebb postulated that repeated co-activation of a group of neurons strengthens synapses to, and among, the neurons in the group. As a consequence, an established assembly can be 'ignited' by partial stimulation and may thereby function as a pattern completion or pattern recognition unit (FIG. 2Aa). Hebb referred to such activation of a network of neural assemblies as a 'phase-sequence'¹⁶ (FIG. 2Ab). This notion was important because it allowed for information processing that depends on both the external input and on the internal state of the network comprising the assemblies.

As a matter of fact, the idea of a network of neural assemblies pre-dated Hebb^{1,28}. Even before the notion of neurons as the computational units in the brain was established, William James postulated a mechanism subsequently termed 're-integration' or 'recall': the joint discharge of a group of 'elementary nerve-tracts' 'awakens' a consecutive group that is identified and reinforced by 'vibrating in unison'¹ (FIG. 2B).

For neurophysiologists, the idea of neural assemblies has always been closely associated with the occurrence of activity patterns in the neural network. In a poetic and later famous metaphor, Sherrington²⁹ described the activity in the cortex upon awakening:

*Swiftly the head-mass becomes an enchanted loom
where millions of flashing shuttles weave a dissolving
pattern, always a meaningful pattern though never
an abiding one; a shifting harmony of sub-patterns.*

Decades later, Moshe Abeles invoked the idea of a 'synfire chain' of successively activated neural assemblies, arranged as convergently–divergently connected groups of neurons²⁵ (FIG. 2C), to explain the observation of spike patterns recurring with millisecond precision in awake behaving animals^{30–34}. This hypothesis was tested in a number of follow-up theoretical studies^{3,4,6–10,13} (FIG. 2D). However, the functional and statistical significance of precisely recurring spike patterns is still a highly debated issue, and the choice of the model of ongoing cortical activity may change the results and interpretations^{35–38}.

Another variant of the neural assembly concept is based on the synchronization of oscillatory cell assemblies^{39–41}. In this context, Wolf Singer proposed the idea of a parallel 'read-out of assemblies by assemblies' as a

potential solution to the read-out problem^{40,41}. This type of read-out mechanism requires convergent–divergent connections (similar to the FFN) between the respective cortical areas within which ‘sending’ and ‘receiving’ assemblies are configured (FIG. 2E).

The idea of a cascade of neural assemblies in which single neurons can participate at multiple levels has subsequently been formalized as a feedforward network (FFN). This term refers to a network topology in which groups of neurons project their activity, by convergent–divergent links of synaptic connections, to successive groups of neurons in a repetitive manner. A repetitive sequence of such group activations can be considered a ‘transmission line’²⁴² for spike propagation (FIG. 2F). Here, the term ‘feedforward’ should not be taken as an anatomical descriptor: the repeated participation of neurons in multiple groups of an FFN creates feedback loops. This is obviously incompatible with an anatomical feedforward architecture. Refractoriness, however, prevents neurons from effectively participating in the propagation of activity among nearby groups, thereby enforcing a minimal distance between their repeated participation. Thus, even in a recurrent network, the flow of spiking activity on a local scale (‘locality’ being defined by connection delays, firing rates and refractoriness), can be treated as an FFN^{43,44,47}, independent of the anatomical network architecture.

Feedforward networks in their natural habitat

An FFN is a simple yet powerful model that may provide important insights into mechanisms of cortical computation. However, it is not straightforward to reconcile the idealized architecture of an FFN with the complex recurrent connectivity of different brain regions. Recent studies, however, show that a random network can be constructed by using the FFN as an elementary motif while maintaining overall network connectivity that is similar to conventional random networks^{45,46}. Moreover, recent analyses of network connectivity models suggest that the activity dynamics of certain types of recurrent networks are compatible with those of an FFN. Thus, from a functional perspective, recurrent random networks may behave in ways akin to an FFN^{43,44,47}.

In a biologically plausible scenario in which the FFN is part of a recurrent network, it is important to consider the interaction between the dynamics of the FFN and that of the embedding recurrent network. One approach to studying FFN dynamics under realistic conditions is to search for an FFN-type network in the recurrent connectivity of the embedding network^{10,48}. This method involves randomly choosing a group of neurons and identifying another group that is directly connected to the first group with a certain probability. This process is repeated *N* times to identify an *N* layer FFN. However, in a sparsely connected recurrent network, such as the neocortex, only sparsely connected (or ‘diluted’) FFNs can be identified^{10,48,49}. As a consequence, the connection strength between one group and the next in such FFNs needs to be increased to high values to ensure the typical FFN dynamics¹⁰. Clearly this has strong implications for the type of activity that is supported by such networks, as we will review in more detail in the following sections.

Often, modellers adopt a slightly different approach to the study of FFN dynamics in realistic scenarios by altering the connectivity, not the synaptic strengths, among neurons that form parts of the FFN. In such

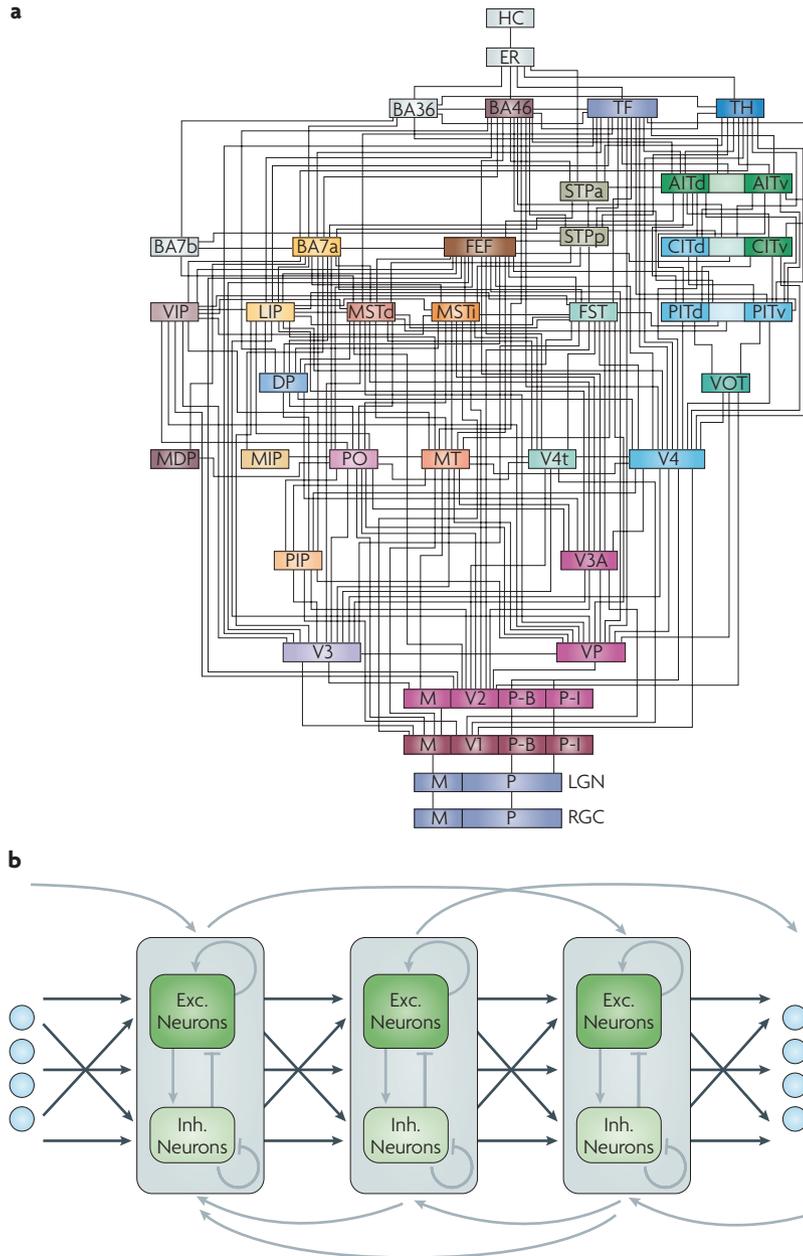


Figure 1 | The feedforward network as a model of information processing in the brain. **a** | A schematic of hierarchical processing in the visual systems of primates. Similar schematic models have also been described for other sensory and motor areas. **b** | Each module in part **a** can be considered as a recurrent network of excitatory and inhibitory neurons. Each of the rectangular boxes represents a recurrent random network. The hierarchical structure of the brain is conceived here as a network of recurrent networks with forward and backward excitatory connections. So far, only the feedforward part (shown in black) of such a network of networks has been investigated in a systematic manner. Recurrent excitation and inhibition within one group and excitatory synapses that do not contribute to the feedforward hierarchy of subsequent groups (shown in grey) have not been considered yet. Part **a** is reproduced, with permission, from REF. 27 © (1991) Oxford Journals. Exc.; excitatory, Inh.; inhibitory.

Box 2 | Experimental measurement of firing rate and synchrony

Measurement of the firing rate

The concept of 'firing rate' has long been used to quantify the response strength of a spiking neuron. Neuronal responses are often quite variable, therefore, most methods measure the firing rate effectively by averaging the spike count within a certain time window.

Trial-averaged firing rate. The simplest variant is to use long observation windows but this compromises the temporal resolution of the measurement. Averaging across a sufficient number of trials using the peri-stimulus time histogram (PSTH¹²²) can improve time resolution to the millisecond range.

Single-trial firing rate. Firing rates can also be estimated from single trials and some degree of temporal averaging or kernel-based methods¹²³ must be employed to reduce statistical fluctuations. The temporal resolution of the resulting rate signal, however, will not be more accurate than a few inter-spike intervals. Hence, sparse spiking, which is typical for the neocortex (< 1 spike per second)^{25,115} does not allow for a reliable estimate of a single-trial firing rate at behaviourally relevant timescales.

Measurement of synchrony

The notions of 'synchrony' or 'correlation' refer to the joint firing of two (or more) spiking neurons. Most methods use joint spike counts (C_1 and C_2) derived from two simultaneously recorded neurons^{58,124}.

Pairwise correlations. The product $C_1 \times C_2$ (the 'raw count correlation') represents a new signal, which is non-zero if (and only if) both neurons generate at least one spike within the same time window. Subtraction of the mean spike count before correlating the two signals yields the 'count covariance', which is zero for independently spiking neurons. Additional normalization of the count variables to unit variance leads to the 'count correlation coefficient'¹²⁵, which is always a number between -1 and +1. Note that correlation-based measures are well behaved only in the case of Poissonian spike statistics. Certain properties of real spike trains, most notably their degree of regularity, may impose a considerable bias on the measurement of correlations, depending on the bin size that is chosen for analysis¹²⁶. Total pairwise correlation of a population of neurons can also be quantified by the 'fano factor'. To quantify higher-order correlations a number of methods have recently been devised^{62,127,128}.

Comparing timescales

When measuring pairwise correlations, it is crucial to subtract the individual mean spike counts (related to the firing rates) before correlating the product signal. After correcting for the mean, two neurons that spike independently have zero correlation. This procedure opens the possibility of choosing a different time resolution for measuring the spike count (usually ≥ 100 ms) and the raw correlation (≤ 10 ms). In this case the analysis goes beyond measuring just correlations — it also involves comparison of different time scales.

It is conceivable that neurons can coordinate their spikes (in pairs or in larger groups) to encode one signal, and use their individual firing rates, on a slower timescale, to encode another^{65,76,129}.

Read-out problem

The problem of how the neural activity of a single neuron or group of neurons received and transformed ('decoded') by a postsynaptic group of neurons, to result in, for example, a decision, perception or motor act.

Embedding recurrent network

A large recurrent network typically composed of excitatory and inhibitory neurons that contain feedforward networks as subnetworks.

models, neurons are arbitrarily assigned to different groups, and neurons that are assigned to one group are then made to preferentially form connections to neurons that are assigned to the next group, with a certain probability that is usually higher than for the remainder of the network^{9,50,51}. Neurons that are assigned to the FFN have a reduced connection probability to the rest of the network in order to maintain their in- and out-degree within the recurrent network. This approach has the advantage that an FFN with arbitrary parameters can be embedded within the recurrent network without altering the overall network statistics dramatically.

Both approaches to studying the FFNs in their natural habitat result in some degree of non-randomness in the network connectivity by making some number of preferential connections or by preferentially strengthening

certain synapses. This is not a trivial issue because deviations from a random or locally random connectivity in small networks may destabilize the ongoing activity in the network⁵¹. Deviations from random connectivity arise because neurons participating in the embedded FFN receive more shared inputs than the rest of the neurons. Correlations due to the shared connectivity may be amplified and can introduce dynamical instabilities in the embedding network^{51,52}. Thus, complex connectivity rules and/or specific synapse properties are required to ensure stable network activity. For example, neurons in the FFN receive stronger correlated excitation than the rest of the network and, thus, tend to destabilize the activity in the embedding network. Therefore, it was suggested that inhibitory neurons should be included in each group to balance the effects of this extra excitation⁵⁰. Recently, we have shown that by modelling synapses as conductances rather than as currents, it becomes possible to embed an FFN without destabilizing the network⁹. Furthermore, the number of neurons in a group and the inter-group synaptic strengths have a crucial effect on the FFN activity dynamics, and a neuron group size that is too large can make even an isolated FFN unstable⁵¹⁻⁵³.

Spiking-activity propagation

Evidence from neuroanatomy (there are up to 10,000 synapses per neuron^{20,21}) and neurophysiology (individual synapses are weak and unreliable) suggests that collective activation of multiple presynaptic neurons is necessary to reliably elicit a spike response in a postsynaptic neuron. Two types of descriptors are commonly used to quantify the spiking activity of a neural assembly; the firing rates of individual neurons, or of the whole ensemble, and the pair-wise or higher-order correlations among neurons in the ensemble. Each descriptor corresponds to a different neural code. Stimulus or task-related activity is said to be 'rate coded' when it can be decoded using only the firing rates of neurons in an ensemble. On the other hand, when stimulus or task-related activity can be decoded using synchrony (BOX 2), it is referred to as a time (or 'synchrony') code. Both types of neural codes impose certain constraints on the population activity. For example, an ideal firing rate code requires that the spiking activities of neurons in a population are uncorrelated^{54,55}. By contrast, synchrony is a necessary feature of spiking activity for a synchrony code, but it will render a rate code inefficient. Therefore, these two codes are commonly considered to be dichotomous.

Although firing rates and synchrony are commonly used variables for describing the activity of a neural ensemble, their quantitative estimates from the spiking activities of only few neurons is unreliable. As neural activity is not stationary, this makes it even more difficult to ascertain whether observed synchrony or correlation in spiking activities is an artefact^{56,57}. Thus, sophisticated methods are required to quantify the synchrony among neurons with non-stationary firing rates⁵⁸⁻⁶².

Despite these technical difficulties, there is ample evidence for synchrony^{37,63-70} and firing rate codes⁷¹⁻⁷⁵

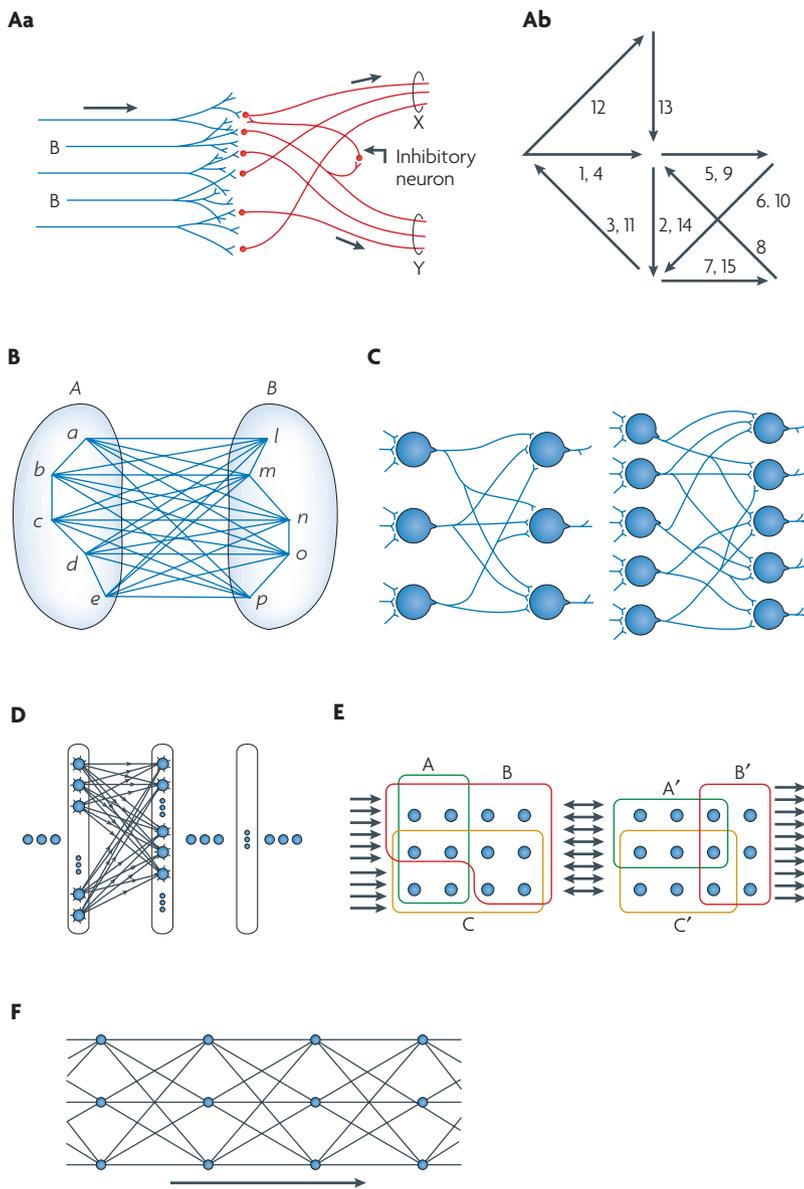


Figure 2 | Cascaded neural assemblies. A | Hebb's notion of a neural assembly (Aa). Hebb used this idea to introduce the concept of 'phase sequence' (Ab). The arrows represent a simple 'assembly' of neural pathways that fire in order according to the numbers on each arrow^{16,121}. **B** | James' concept of interactions between different brain processes (A and B are composed of sub-processes a–e and l–p, respectively)¹. **C** | Abeles used the general structure of a feedforward network (FFN) to explain the experimental observation of spike patterns with millisecond precision²⁵. The blue circles represent neurons. **D** | A more systematic version of the FFN that is shown in c. This FFN has been studied extensively by theoreticians for its dynamics and its propagation properties⁴. **E** | Singer's scheme of a 'parallel read-out' of a neural assembly by another neural assembly⁴¹. The blue circles represent neurons that are grouped together to form neural assemblies A, B and C (shown by different coloured outlines) whose activity is read by another set of assemblies A', B' and C' (REF. 41). **F** | The concept of a neural transmission line, introduced by Griffith. The blue circles represent neurons that make convergent–divergent connections to transmit neural activity⁴². Part Aa is reproduced, with permission, from REF. 16 © (1949) John Wiley & Sons. Part Ab is reproduced, with permission, from REF. 121 © (1958) W. B. Saunders Company. Part B is reproduced, with permission, from REF. 1 © (1890) Henry Holt and Company. Part C is reproduced, with permission, from REF. 25 © (1991) Cambridge Univ. Press. Part D is reproduced, with permission, from REF. 4 © (1999) Macmillan Publishers Ltd. All rights reserved. Panel E is reproduced, with permission, from REF. 41 © (2002) Academic Press. Part F is reproduced, with permission, from REF. 42 © (1963) Cell Press.

in different brain regions under various experimental conditions. In fact, as any text book on neuroscience shows, most *in vivo* recordings identify some neurons that show a task-related modulation in their firing rate. Moreover, neurons often exhibit modulations in firing rate and synchrony simultaneously, both of which may encode different aspects of neural information^{65,76,77}. Moreover, firing rate and correlation (or synchrony) are attractive candidate neural codes because both can affect network function by influencing synaptic plasticity^{78–80} and the input–output relations^{81–85} of a neuron. Thus, to study spike propagation in FFNs, most researchers have focused on propagation of either asynchronous firing rates or synchronous spike volleys in FFNs, as reviewed below.

Propagation of asynchronous firing rates

The rate code has a serious problem: even weak pairwise correlations in the spike timing can severely limit the fidelity of the rate code⁵⁴. Thus, it is important that in the propagation or processing of a rate code, spike correlations do not increase (FIG. 3a–c). However, any two neurons in an FFN group share their presynaptic inputs (depending on the connection probability between the groups) and thus, are more likely to spike together. Consequently, shared input in an FFN is likely to cause correlations in its activity^{52,86}, possibly rendering the FFN unsuitable for firing-rate propagation. FIGURE 3d and e show an example of the development of synchrony during the propagation of an asynchronous firing rate in an FFN.

Integrative properties of individual neurons also play a key role in introducing synchrony in the propagating activity of the FFN^{83,86}. Because individual synapses are weak compared to the distance-to-spiking threshold of the membrane potential, a neuron needs to integrate multiple, near-synchronous post-synaptic potentials to elicit a spike. Consequently, when a neuron is stimulated with a volley of spikes, with spike times drawn from a Gaussian distribution of width (σ_{input}), the width of the output spike time distribution (σ_{output}) may be smaller than σ_{input} . When the number of spikes in the volley can be disregarded (see REF. 4 for a more complete description), it is possible to define a linear relationship between σ_{output} and σ_{input} , such that $\sigma_{output} = \gamma \cdot \sigma_{input}$ ⁸³. Under realistic conditions, the proportionality factor γ depends on the degree of convergence, the membrane properties and the synaptic time constants, and is typically smaller than one. Thus, connectivity of FFNs and single neuron properties argue against the propagation of asynchronous firing rates.

It is conceivable that uncorrelated background activity in neurons of different FFN groups may balance the synchronizing effect of shared connectivity and neural integration properties, thereby enabling the propagation of asynchronous firing rates through the FFN⁶ (FIG. 3a–c). However, the occurrence of strong and uncorrelated noise conditions *in vivo* or in an FFN that is embedded in a recurrent network is unlikely⁹. Therefore, reducing the connection probability and increasing the synaptic strengths between subsequent

In- and out-degree

In-degree refers to the number of input synapses that a neuron receives. Out-degree refers to the number of synapses a neuron makes.

FFN groups might be a better strategy for propagating firing rates. In fact, FFNs with only 10% connectivity but strong synapses between subsequent groups can support the propagation of asynchronous firing rates with high fidelity¹⁰.

When the connection probability is increased to reduce synaptic strengths to biologically realistic values, firing-rate propagation is strongly affected in multiple ways. First, after propagation through a few initial groups, the activity becomes increasingly correlated because the synchronizing effects of shared connectivity accumulate over consecutive groups^{8,54} and hence, the activity can no longer be considered a strict-sense rate signal⁵² (FIG. 3a,b,d). In fact, it was observed that after the signal had propagated through the first five groups, the estimated firing rate had become the rate of correlated events in the group^{8,9}. Second, rate propagation without accumulating correlations was observed when the background activity was asynchronous-irregular⁸⁷⁻⁸⁹ (BOX 2). Recent work indicates that ongoing cortical activity may indeed be asynchronous-irregular⁹⁰ and thus, may support the propagation of asynchronous firing rates. Finally, it is not easy to maintain a unique representation of firing rates during propagation, as differences between rates are rapidly quenched^{8,88} (FIG. 3f,g).

In summary, the modelling studies that are reviewed above show that, in principle, firing rates can propagate through an FFN. However, in FFNs with weak synapses and high inter-group connectivity, emerging synchrony degenerates the fidelity of the propagating firing rate signal.

Experimental evidence for firing-rate propagation

It is technically challenging to address firing-rate propagation in physiological experiments because this requires simultaneous recording of spiking activities from a large number of neurons. However, using a clever iteration procedure, it is possible to ‘simulate’ an FFN *in vitro*³. Here, an FFN group of W neurons is mimicked by stimulating a neuron *in vitro* W times with Poisson-type spike trains. The output of the neuron during each stimulation is recorded and later used to stimulate the same neuron again. N repetitions of this procedure then mimics an FFN with N groups of W neurons each. In this *in vitro* ‘simulation’ of an FFN, firing rates were propagated for at least 10 groups, but with every subsequent group the activity became more synchronous³, consistent with theoretical predictions^{8,9}. Comparable findings have been reported recently in the auditory system of locusts *in vivo*, which can be functionally considered an FFN. As stimulus-driven activity travelled through the locust auditory system, correlations among neurons increased with every processing stage⁹¹. Thus, experimental and theoretical studies indicate that when firing rate signals propagate across successive groups of neurons in an FFN, synchrony emerges and an eventual loss of fidelity of the rate coded neural signal is inevitable.

Propagation of synchrony

As mentioned earlier, the shared connectivity between subsequent groups of an FFN, the spike threshold and nonlinear integration properties of neurons may conspire to facilitate synchronous activity^{83,86}, causing uncorrelated firing rates to become synchronous as they propagate through an FFN^{3,8,9,91}. Does this mean that

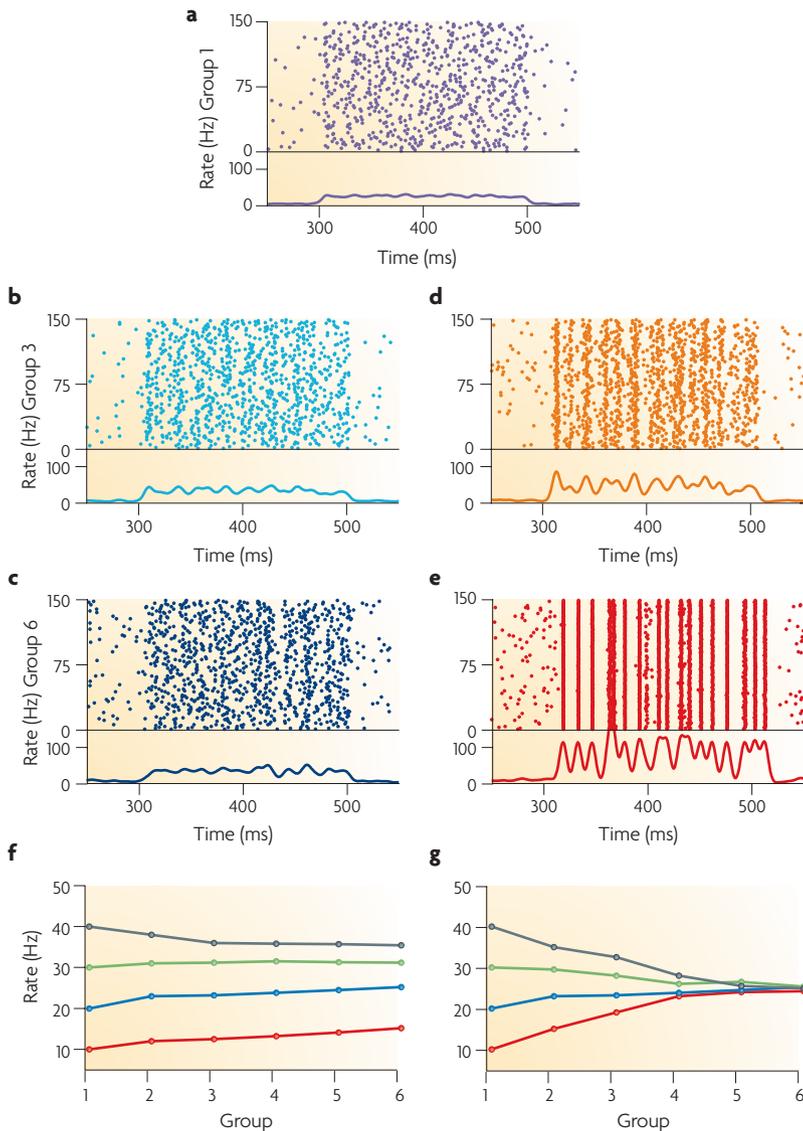


Figure 3 | Transmission of asynchronous firing rate in an FFN. **a** | Asynchronous firing rate input (20 spikes per seconds) to the first group of the feedforward network (FFN). The top part shows a spike raster diagram. Each line of dots represents the spiking of one neuron in the group. The bottom trace shows the population activity in the first group. **b,c** | Examples of stable propagation of asynchronous firing rates. The activity in the third (**b**) and sixth (**c**) groups of the FFN is shown. The absence of vertical stripes in the spike rasters and the small fluctuations in the population activity indicate that the propagating activity remains asynchronous. **d,e** | Examples of development of synchrony in the FFN. The activity in the third (**d**) and sixth groups (**e**) of the FFN is shown. As the asynchronous activity propagates through the FFN, residual transient synchrony is amplified, as indicated by the vertical stripes in the spike rasters and by the large fluctuations in the population activity. With such large synchronous events in the activity of the last group, the firing rate in the FFN degrades to become the rate of synchronous events. **f** | Illustration showing how firing rates in the FFN are unique representations, with each input firing rate resulting in a different output rate. **g** | Illustration showing a non-unique representation in terms of firing rates in the FFN. Independent of the input firing rates, all of the output firing rates rapidly converge to the same value.

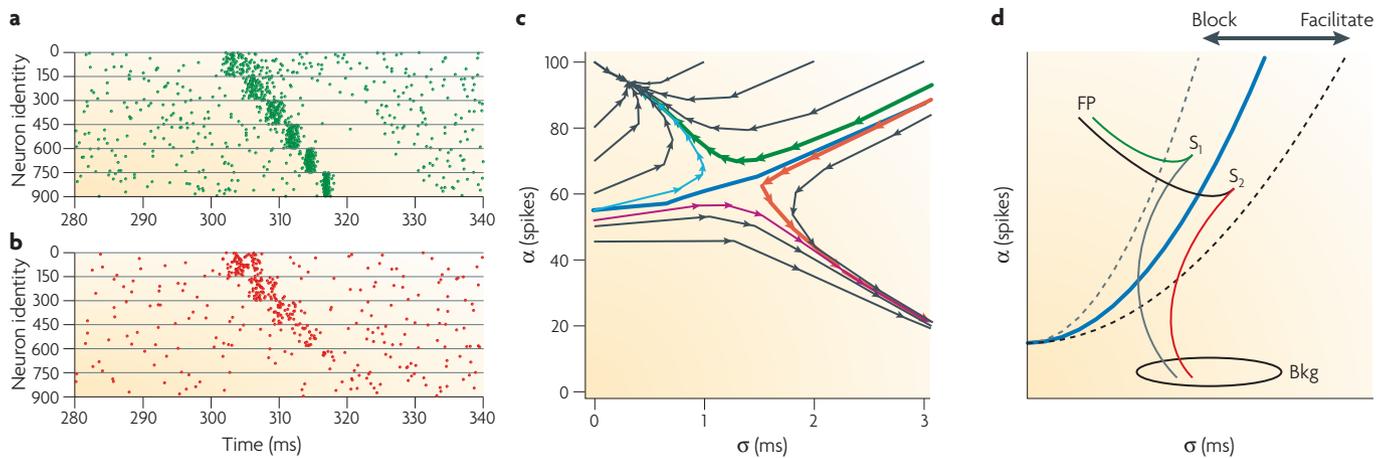


Figure 4 | Propagation of a pulse packet in an FFN. **a** | An example of stable propagation of a pulse packet. The horizontal lines in the raster plots separate successive groups of neurons within the feedforward network (FFN). Note that the pulse packet becomes progressively more synchronous as it travels through the FFN. **b** | An example of an unsuccessful propagation of a pulse packet. Here, the pulse packet becomes progressively weaker and is eventually indistinguishable from the background activity. **c** | State-space representation of pulse packet propagation. Activity in each group of the FFN is quantified by the number of spikes (α) and the standard deviation of spike times (σ). Each trajectory represents the evolution of pulse packets with specific initial parameters. The point where the trajectories converge marks the attractor of the FFN, corresponding to a stable propagation of the pulse packet. The trajectories leading to the bottom right corner (low α , high σ) indicate failed propagation. The blue line (without arrows) marks the separatrix of the FFN. **d** | The location of the separatrix in (α - σ) space can be changed by modulation of the noise level in the FFN or of integration of time constants of the neurons. The latter can be achieved by altering the latency of the feedforward inhibition. This change in the location of the separatrix can be used to facilitate or block the propagation of the activity in the FFN. For example, in the default state of the FFN, the separatrix (shown by the blue trace) allows for successful propagation of the activity of stimulus 1 (S_1 ; shown by the green trace), while the activity S_2 would fade into the background (shown by the red trace). If the separatrix is moved up (shown by the grey dotted line), propagation of activity can be blocked (shown by the grey trace). In contrast, if the separatrix is moved down (shown by the black dotted line), propagation of activity S_2 can be facilitated (shown by the black trace). Part **c** is modified, with permission, from REF. 4 © (1999) Macmillan Publishers Ltd. All rights reserved. Part **d** is modified, with permission, from REF. 92 © (2010) Springer. FP, fixed point; Bkg, background.

Asynchronous–irregular
A network state characterized by irregular firing of individual neurons (measured by the coefficient of variation of the inter-spike-interval distribution) and by asynchronous population activity (measured by pairwise correlation or fano factor) (BOX 2).

Fixed point
If the system arrives at this point in its state-space, it remains there permanently in the absence of disturbances (a steady state). Fixed points can be stable or unstable.

Attractor
A fixed point in the state-space that attracts all of the system trajectories passing through its neighbourhood.

Saddle node
A fixed point that attracts some nearby trajectories but repels others.

State-space
A multi-dimensional space defined by variables that characterize the system state. If there are N such variables, each state is represented by a point in an N -dimensional state-space.

FFNs are more suitable for propagating synchronous activity, and that even weak synchrony in the activity will be amplified during propagation?

To study the propagation of synchrony in an FFN, the notion of a pulse packet was introduced^{4,12} — that is, an ensemble of α spikes, the times of which are drawn from a Gaussian distribution with standard deviation σ . Thus, propagation of synchrony in an FFN can be quantified by estimating α and σ of the spiking activity in successive neuron groups as a pulse packet travels through the FFN. When α and σ of each group are plotted against each other, the resulting trajectory presents a discrete description of the pulse packet's evolution in the (α - σ)-state space (FIG. 4c). For an isolated FFN of appropriate group size, there are two fixed points — an attractor and a saddle node in the two-dimensional state-space. A line passing through the saddle node termed the 'separatrix' divides the state-space into two regimes. Activity starting above the separatrix (FIG. 4) eventually converges into the attractive fixed point, indicating a stable propagation of the pulse packet (FIG. 4a,c). By contrast, activity starting below the separatrix (FIG. 4d) eventually fades into the background activity (FIG. 4b,c). Over the first few initial groups, such fading of activity may be perceived as progressive (not necessarily monotonic) broadening and/or diminishing of propagating activity.

The location of the separatrix in the (α - σ) state-space is the most important feature for the propagation of a pulse packet in an FFN. Multiple properties of the FFN, such as background activity of the embedding network⁹, noise level¹³ and temporal correlations between excitation and inhibition⁹² can alter the location of the separatrix and thus, affect the propagation of the pulse packet (FIG. 4d). Moreover, heterogeneity in the FFN, particularly in the numbers of FFN synapses and their synaptic strengths, may introduce complex dynamics (for example, oscillations and chaotic attractors) in the FFN^{93,94}.

A qualitatively similar state-space was obtained when an FFN was embedded in a locally connected random network⁹. The low firing rate and asynchronous–irregular activity of the embedding network provided the most suitable substrate for propagating a pulse packet through the embedded FFN. Synchrony in the embedding network shifted the separatrix upwards, thereby reducing the probability of the successful propagation⁹ (FIG. 4c,d). The emerging picture can be likened to the propagation of waves in the sea — when the sea surface is calm, sea waves may propagate over long distances. By contrast, even strong waves may not propagate far in a rough sea.

The results obtained by extensive numerical simulations were further corroborated by analytical treatments of the problem. Analytical studies have identified synaptic

noise⁵, the input–output transfer function of the neuron⁹⁵ and the refractory properties of the neural membrane⁷ as factors that influence the properties of the FFN.

Experimental evidence for synchrony propagation

Systematic experiments have not been carried out to investigate the propagation of synchronous activity (for example, of pulse packets). Some recent studies, however, have indirectly addressed this issue in cortical networks and in the thalamocortical system. In the song-generation system of songbirds, which is functionally equivalent to an FFN⁹⁶, propagation of correlated activity was more likely than that of uncorrelated activity^{97–99}. Similar results were reported for the locust auditory system⁹¹. Finally, thalamic projections onto layer IV neurons in the somatosensory cortex of rodents were found to be weak, such that only synchrony among the thalamic afferents could reliably elicit a response in the sensory cortex¹⁰⁰. The *in vitro* simulation of FFNs, discussed above, also showed an amplification of synchrony during propagation³.

Thus, multiple computational studies, together with indirect support from experiments, argue that FFNs are more suited to propagating synchronous spikes than asynchronous firing rates.

Firing rate versus synchrony propagation

Why are there two different activity propagation modes? A detailed look at the various FFN models reveals that FFNs that have been studied so far belong to two different classes: class I FFNs^{4,5,7–9,12,13,52}, which are characterized by full (or at least, dense) connectivity with weak synapses (high shared connectivity), and class II FFNs^{6,10}, which are characterized by sparse connectivity and strong synapses (low shared connectivity). Because shared connectivity can induce correlations in activity, it is not surprising that class I FFNs support the propagation of synchrony, whereas class II FFNs support the propagation of asynchronous firing rates.

This subdivision into two classes of FFNs raises the question of whether there is an FFN that can sustain the propagation of firing rates and synchrony, without affecting the fidelity of either signal during propagation. To address this question, we simulated an FFN with 6 groups, each with 150 excitatory neurons⁹ (A. Kumar, S. Rotter and A. Aertsen, unpublished observations). Each neuron received balanced excitatory and inhibitory inputs and spiked in an asynchronous–irregular manner at a mean firing rate of 2 spikes per second (see Supplementary information S1 (box)). In the FFN, neurons in one group were connected to the neurons in the next group, with conductance-based synapses. The two main FFN parameters — synaptic strength (J_c) and the probability of a synapse being formed between neurons in successive groups (ϵ) — were varied systematically. This enabled the full FFN parameter space to be explored, covering class I and class II FFNs as well as intermediate FFNs. Neurons in the first group of the FFN were stimulated with a pulse packet or with asynchronous firing rates. The parameters of the stimulus, as it evolved through the FFN, were used to quantify the activity propagation (BOX 3; FIG. 5).

FIGURE 5a shows the propagation of asynchronous firing rates (estimated by the signal-to-noise ratio of firing rate SNR_R ; BOX 5) in the FFN as a function of ϵ and J_c . For small ϵ and J_c (FIG. 5a), no activity propagated through the FFN because the input was too weak. High values of ϵ and J_c made the network spontaneously active. This reduced the SNR_R considerably, and it was not possible to discern any signal from the ongoing background activity. For moderate values of ϵ (0.1–0.5) and J_c (0.1–0.3 mV) a large region in the (ϵ – J_c) parameter space (FIG. 5a; enclosed by solid and dashed black lines) supported a high SNR_R . However, as discussed above, a genuine rate code also requires the activity to remain asynchronous as it propagates. The region for which synchrony in the propagating rate signal remained low (correlation <0.1) is indicated in FIG. 5a. Clearly, the two regions, black-bound and grey-bound, only partially overlap. Thus, imposing both constraints — high SNR_R and low synchrony — dramatically reduces the parameter range and this supports a high fidelity rate code signal: the narrow band enclosed by solid grey and black lines in FIG. 5a marks the region in the FFN parameter space in which an asynchronous firing rate signal is faithfully propagated (high SNR_R , low synchrony).

Box 3 | Measuring spike propagation

When a synchronous or asynchronous ensemble of spikes is injected into the first group of a feedforward network (FFN), successful propagation means that the input can be recovered in the subsequent layers of the FFN. Therefore, the first criterion for successful activity propagation is that it should be discernible from the background activity. Second, in the course of propagation the nature of the activity should not change, that is, synchronous activity should remain synchronous and likewise for asynchronous activity. In the following, we define two descriptors that address these two criteria of successful propagation⁹.

Signal-to-noise ratio

Signal-to-noise ratio (SNR) for the propagation of a firing rate is defined as the ratio between the stimulus-induced firing rate in the N^{th} group of neurons of a network and the firing rate in these neurons before the stimulus occurred.

$$SNR_R(N) = \frac{fr(N, t_{rate})}{fr(N, t_{bkg})}$$

t_{rate} refers to the time interval during which the stimulus was present and t_{bkg} refers to a time interval before the rate stimulation occurred. t_{rate} and t_{bkg} are of the same duration. $fr(N, t)$ refers to the average firing rate of the N^{th} group of neurons in the respective time interval.

Similarly, the SNR for synchrony can be defined as:

$$SNR_S(N) = \frac{A(N, t_{pp})}{A(N, t_{bkg})}$$

where t_{pp} refers to the duration of the pulse packet, and t_{bkg} refers to a time interval before the pulse packet stimulation. $A(N, t)$ refers to the total spike count in the N^{th} group of neurons in the respective time interval t .

According to this framework, a high-fidelity transmission of spiking activity would be associated with either maintenance of SNR after the first group or even an increase in the value of SNR as the activity propagates through the FFN. SNR can also be estimated by taking the ratio of concurrent activity in the last group and the neurons in the embedding network.

Pairwise correlation

For rate code transmission, correlations should be kept close to zero within every group of an FFN, whereas for synchrony transmission, correlations in every group of the FFN should be maximized (see also BOX 2).

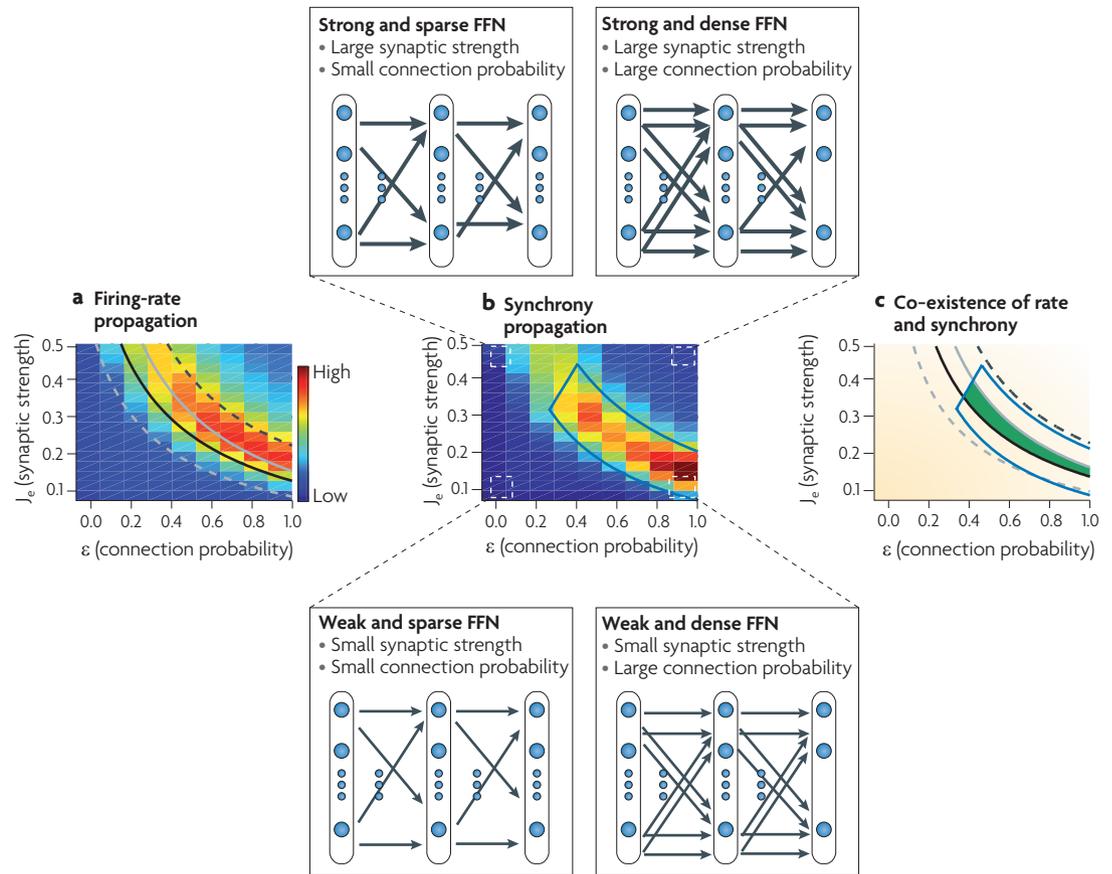


Figure 5 | Coexistence of firing rate propagation and synchrony propagation. **a** | Signal-to-noise ratio of firing rate propagation (SNR_r) in the sixth group of the feedforward network (FFN) is shown as a function of connection probability (ϵ) and synaptic strength (J_e). The solid and dashed black lines enclose the region in the (ϵ - J_e) space with high SNR, indicating stable propagation of firing rates. The solid and dashed grey lines enclose the region in the (ϵ - J_e) space where the activity in the sixth group could be considered asynchronous (pairwise correlation-coefficient < 0.1). Thus, the region enclosed by solid grey and black lines can be considered suitable for asynchronous firing rate propagation. **b** | Signal-to-noise ratio of synchrony (SNR_s) propagation. SNR_s in the sixth group of the FFN is shown as a function of ϵ and J_e . The blue lines mark the region that is suitable for stable propagation of synchronous activity. **c** | The black and grey lines from part **a** and the blue lines from part **b** are plotted together to identify the region in the (ϵ - J_e) parameter space that is suitable for propagation of both asynchronous firing rate and synchronous pulse packets (shown by green shading). The four insets show extreme cases of an FFN architecture, considering the synaptic strength (shown by the thickness of the arrows) and the connection probability between neuron groups (a greater number of arrows represents greater connection probability).

FIGURE 5b shows the signal-to-noise ratio of a propagating pulse packet (signal-to-noise ratio of synchrony (SNR_s ; BOX 5) as a function of ϵ and J_e . There is a region in (ϵ - J_e) space (enclosed by blue lines) in which the pulse packet propagated with high SNR_s . When the regions that allow for a stable propagation of firing rates (FIG. 5a) and synchrony (FIG. 5b) are superimposed, the region of the (ϵ - J_e) parameter space that supports stable propagation of firing rate and synchrony can be identified (FIG. 5c; shown in green). FIGURE 5 also reveals that the two classes of FFNs are in fact situated in diagonally opposite corners of the FFN parameter space (insets). Therefore, it is not surprising that different studies have reached partially opposing conclusions concerning the propagation of their 'favoured' activity mode in the FFN.

In summary, a general structure of FFNs allows, in principle, stable propagation of asynchronous firing rates and synchronous pulse packets, provided that

the FFN parameters ϵ and J_e are chosen appropriately. Further modifications in the general architecture of the FFN, for example increased group size, inclusion of recurrent connections within groups or heterogeneity in neuron properties, may further increase the parameter space that allows for propagation of both types of spiking activity.

Inhibition in the FFN

Computational studies of activity propagation in isolated FFNs have largely disregarded the role of inhibition within or across different layers in the FFN. Only a few studies implicitly included intra- and inter-layer inhibition when studying the dynamics of FFNs that are isolated⁸ or embedded in a recurrent network^{9,10,50–52}. However, these studies did not focus on isolating the role of inhibition in shaping activity propagation. Only in one study was inhibition between subsequent layers explicitly

used to stabilize the dynamics of the embedding network⁵⁰. A recent study showed that small changes in the latency of feedforward inhibition can alter the location of the separatrix⁹². One of the implications of this finding is the possibility that activity propagation can be selectively gated (FIG. 4d). A recent theoretical study has described conditions under which recurrent inhibition may decorrelate the activity in recurrent networks⁸⁹. Such decorrelated background activity (asynchronous–irregular) is better suited to propagate synchrony in the FFNs that are embedded in a recurrent network⁶. However, more systematic analysis is needed to understand how decorrelating the effects of recurrent inhibition would affect the activity propagating through the embedded FFNs. Apart from being of theoretical interest, this would also help to interpret activity propagation in *in vivo* FFN-type systems (for example, song-generation in songbirds or hearing in insects) where inhibition is ubiquitous.

Gating the propagating spiking activity

Apart from transmission itself, the regulation of spiking activity propagation is an equally important point to consider. In a modular system like the brain, cognitive functions such as action-selection require that a particular signal is able to be directed to one of multiple subsequent processing stages^{26,101}. In this scenario, the brain needs a mechanism to control the propagation of activity over multiple, interacting signal pathways. Thus, selective blocking or boosting of a neural signal could be an efficient mechanism for fast action-selection on millisecond timescales¹⁰². Recently it was shown that a detailed balance of excitation and inhibition at the receiving FFN group is a potent way to control the tonic (slowly changing) part of a neural spike signal¹¹. This mechanism, however, fails to control the propagation of neural activity transients (rapid changes) that occur frequently in a natural stimulus environment as a consequence of stimulus driven changes in firing rates or due to the emergence of correlations in the network^{64,103–105}. Selective gating of such activity transients can, however, be achieved by exploiting the sensitivity of the separatrix location to the relative latency between excitation and inhibition¹⁰⁶ (FIG. 4d). By carefully modulating the latency of excitation and inhibition, it is possible to either block or facilitate the propagation of activity transients: temporal gating (FIG. 4d). Thus, when combined with excitation–inhibition balance, temporal gating constitutes a powerful mechanism to control the propagation of mixtures of transient and tonic neural activity components (J. Kremkow, A. Aertsen and A. Kumar, unpublished observations).

Spike propagation and computing

Thus far in this review of propagation of spiking activity, we have considered the FFN as a transmission line⁴². According to this idea, a faithful propagation of spiking activity in an FFN does not interfere with the ongoing activity and the nature of the propagating activity remains unaffected during propagation. However, the idea of preserving a spike signal across different stages should not be taken too literally. Obviously, if neither rate (rate code)

nor synchrony (time code) change across layers, the network would not perform any useful computation.

It can be argued, however, that in a system composed of multiple FFNs, the selection of a particular FFN and the subsequent routing of its activity propagation are themselves elementary computations^{26,27,101,107}.

The FFN, independently of the underlying neuron model, with its convergent–divergent connections is a powerful computing device that can solve a host of complex computational problems¹⁰⁸. So far, the possibilities of computing with FFNs of spiking neurons have not been widely explored. The state-space of the FFN (such as α – σ space) already indicates that by carefully controlling the separatrix (FIG. 4d), the spike response in any given layer of the FFN can be controlled in multiple ways. Furthermore, variation of the synaptic weights and latencies in the FFN could be used to recruit different dynamic states for information processing^{93,94}. Thus, in principle, FFNs with spiking neurons can perform meaningful transformations on the propagating activity. Now that we understand how different types of neuronal activity may propagate in an FFN, future research can exploit the computational potential of such networks with convergent–divergent connections.

Future directions

The simple yet powerful architectural concept of the FFN provides a minimal framework for studying coding and for interpreting certain aspects of information processing in the brain. So far, theoretical work has focused on the propagation of firing rates and synchrony in FFNs. However, it is equally important to study how other potential neural codes, such as rank-order coding^{109–112}, correlation codes^{39,66–70,113}, sparse codes^{114–117} and spatio-temporal patterns^{15,118} propagate in FFNs. Similarly, the issue of interactions between FFNs⁹ and a related issue, the coding capacity of a recurrent network that consists of FFNs⁴⁵, need to be studied systematically. Having understood the transmission properties of FFNs it is important to further investigate the computational properties of FFNs. In fact, such lines of investigation could draw inspiration from the extensive body of literature in the field of artificial neural networks¹⁰⁸.

When activity propagates in an FFN, groups of neurons are activated in a sequential manner (potentially seen as spatiotemporal spike patterns in multi-electrode recordings). This has prompted the idea that using simple biologically plausible plasticity mechanisms, such as spike-timing-dependent plasticity (STDP)⁷⁸, might facilitate the dynamic emergence of FFNs in recurrent networks¹¹⁹. However, even an artificially embedded FFN network fails to survive in a recurrent balanced network as STDP tends to isolate it from the embedding network¹²⁰. On the other hand, spontaneous activity in large random networks with STDP may have pulse packet-like spiking patterns⁴⁹. It is possible that the failure to sustain an embedded FFN in a recurrent plastic network is an artefact of the specific STDP implementation⁴⁶. Therefore, it is important to further explore different plasticity rules that may support stable dynamics in the FFN and the embedding network.

Rank-order coding

A spatiotemporal pattern of spikes in which the temporal rank of spikes carries information about a stimulus or cognitive state.

Sparse code

A coding scheme in which strong activation of a relatively small set of available neurons is used for information representation.

Surprisingly, only a handful of experimental studies have addressed the issue of spiking-activity propagation between neuronal networks^{3,91,97–99}, notwithstanding its obvious importance for a candidate neural code². These experiments have provided partial support to the theoretical predictions that spiking activity tends to become more synchronous during propagation over multiple networks and, therefore, that a neural code based on synchronous activity may be more suitable. However, a direct experimental confirmation (or refutation) of the theoretical predictions is currently lacking.

To address the question of spiking-activity propagation, careful experimental testing of only a few layers of connected neuron groups would be highly instructive. Multiple brain regions, such as the thalamocortical system, the entorhinal-hippocampus network, the basal ganglia and the amygdoid complex, are potential candidates for studying the propagation of spiking activity and the underlying neural code *in vivo*. Controlled stimulation of appropriately selected neural networks *in vivo* using either electrical or optical methods to generate activity patterns that conform with either pulse packet or asynchronous firing rate type input, could provide an effective paradigm. Standard physiological experiments using simple (artificial) or natural sensory stimuli are unlikely to provide clear conclusions regarding these issues. No matter how simple or natural a stimulus might appear from the human perspective, sensory organs (especially

actively sensing organs) may transform the stimulus in a highly nonlinear fashion such that — already after the first processing stages — neurons may not receive a purely asynchronous firing rate or synchrony modulation — in real life, clear dichotomies tend to be rare.

Conclusions

To understand the neural code is fundamental to neuroscience. Perkel and Bullock² suggested four fundamental functions that a candidate neural code must serve. Three key functions of the neural code — stimulus representation, interpretation and transformation properties — have been extensively studied, both theoretically and experimentally. Here, we have reviewed the literature on the fourth function, namely transmission. **Theoretical studies have suggested contrasting possibilities for the propagation of firing rates and synchrony in a widely studied network model, the FFN. We show that these two seemingly conflicting results represent two extremes of a continuum.** Given the importance of this issue, experimental testing is vital. Fortunately, recent developments in experimental methods enable such testing in different brain regions. **Our conclusion, that a specific FFN architecture may simultaneously support stable propagation of activity in both regimes, opens new possibilities for neural information processing strategies that exploit both firing rate and spike correlations as candidate neural codes.**

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Competing interests statement

The authors declare no competing financial interests.

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