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# Neural codes: Firing rates and beyond

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**ABSTRACT** **Computational neuroscience has contributed significantly to our understanding of higher brain function by combining experimental neurobiology, psychophysics, modeling, and mathematical analysis. This article reviews recent advances in a key area: neural coding and information processing. It is shown that synapses are capable of supporting computations based on highly structured temporal codes. Such codes could provide a substrate for unambiguous representations of complex stimuli and be used to solve difficult cognitive tasks, such as the binding problem. Unsupervised learning rules could generate the circuitry required for precise temporal codes. Together, these results indicate that neural systems perform a rich repertoire of computations based on action potential timing.**

Most neurons use action potentials (APs), brief and uniform pulses of electrical activity, to transmit information. APs are generated when the membrane potential of a neuron reaches a threshold value. They travel down the axon toward synapses terminating at postsynaptic neurons, where they initiate postsynaptic currents (PSCs) that summate to trigger (or inhibit) new APs.

A sequence, or "train," of APs may contain information based on rather diverse coding schemes. In motor neurons, for example, the strength at which an innervated muscle is flexed depends solely on the "firing rate," the average number of APs per unit time (a "rate code"). At the other end of the spectrum lie complex temporal codes based on the precise timing of single APs. They may be locked to an external stimulus such as in the auditory system or be generated intrinsically by the neural circuitry.

The wide range of coding schemes raises a number of questions. What is the temporal precision of signals sent out by a given neuron? Do all of its numerous postsynaptic target cells receive the same information? If not, what determines the individual signal? How can postsynaptic neurons read out the information? What is the functional relevance of correlations in the APs of several neurons? Which processes could generate the neural circuitry required for precise temporal codes?

In sensory neurons that are strongly driven by external inputs, data analyses based on reverse-correlation methods and information theory have allowed to answer some of these questions and to successfully "read the neural code" (1). In areas with nonlinear feedback and strong convergence from different modalities these methods are of limited applicability. However, rapid advances in neurophysiological techniques have recently opened a new round of studies that combine experimental neurobiology, computer simulations, and theoretical analysis.

Electrophysiological recordings from synaptically coupled neurons in the neocortex have revealed that synapses do not respond to each AP in the same manner; synaptic transmission is not linear (2, 3). The nonlinearity arises because the PSC caused by one AP depends on the timing of the previous APs. Thus, although the APs on one axon are identical events, their effects on a postsynaptic cell vary from AP to AP.

The history dependence can be quantified in terms of the sensitivity of transmission to a particular frequency of activation. There are two broad classes of frequency dependencies—synapses in which transmission depresses during a high-frequency AP train and synapses in which transmission facilitates. Measurements of the PSC in target neurons show that connections that depress can only transmit very low presynaptic discharge rates.

As the rate rises, synaptic depression has the surprising effect that the amplitude of a single PSC becomes inversely proportional to the firing rate (2, 3), resulting in a saturation of the time-averaged PSC. This effect occurs at a specific frequency, which has been termed the limiting frequency, because beyond this frequency synaptic connections can no longer convey information about the presynaptic discharge rate. However, since a certain time is required for the synapse to depress when the presynaptic frequency changes, these connections are very effective in detecting time derivatives of discharge rates.

The second class of connections, facilitating synapses, has an entirely different frequency dependence (4). Below the frequency at which the time-averaged PSC is maximal—the so-called peak frequency—facilitation enables such synapses to compute the average discharge rate multiplied by the integral of the rates within the synapse-specific time constant of facilitation; i.e., the synapses can "count" the number of presynaptic APs in immediately preceding bursts. Above the peak frequency, facilitating synapses are similar to depressing synapses, in that they are again characterized by a limiting frequency below which they transmit discharge rates and above which they transmit the time derivatives of these rates.

Therefore, each synapse selects a unique melange of features of the presynaptic AP train and transmits only a specific subset of the information contained in the entire train. Different aspects of the same train are read out by different target cells. This rich repertoire of elementary synaptic computations could easily support the formation of "synfire chains" (5) and indicates that precise temporal activity patterns are important for signal processing on the system level.

While early models of cortical processing suggested that individual neurons are sufficient to represent detailed descriptions of relevant features of the environment, it is now generally accepted that unambiguous representations are based on population codes. One of the reasons for this conclusion is the observation that the firing rate of individual neurons in general cannot provide an unambiguous description, even for simple stimuli.



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Abbreviations: AP, action potential; PSC, postsynaptic current.

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Neural responses to particular features are broadly tuned and can be modulated by changes in more than one feature dimension. Firing rates of individual cells are therefore ambiguous descriptions of features and can only be interpreted by comparison across responses of different neurons. This implies the existence of distributed representations. In the presence of multiple independent stimuli, these representations have to be distinguished. Processing of distinct features then requires a separation of the functional interactions within different populations to avoid false conjunctions.

Because groups of active neurons dynamically change with changing stimuli, a selective binding of responses in general cannot be achieved by fixed connections. Rather, static anatomical connections constitute a super-set of connections between all neurons that may eventually need to interact. Thus, a dynamic mechanism is required to transiently strengthen interactions within changing populations and to isolate them from signals related to other representations. Synchronization of neural responses participating in the representation of the same content would be a particularly useful mechanism to dynamically bind related responses for further joint processing—the so-called Correlation Hypothesis (6).

Recent experimental investigations in cat and awake monkey visual cortex have revealed that neurons in the same or in different cortical areas can synchronize their activity with a precision of a few milliseconds if they are activated by a single stimulus (7, 8). Synchronization disappears if these neurons are activated by two different, independent stimuli. In accordance with the Correlation Hypothesis, the same two neurons thus can synchronize their activity if they engage in the representation of the same stimulus and desynchronize if they belong to two different populations that represent two independent stimuli. These results suggest that precise synchronization can serve to dynamically define neuronal populations and thereby contribute at the system level to information processing in the brain.

In the visual cortex, synchronization is achieved rapidly and is often accompanied by approximately periodic activity (7). Both phenomena can be replicated in simplified model networks where, as desired, the relative timing of APs encodes stimulus features (9). A related encoding scheme utilizes ubiquitous subthreshold oscillations (10) of the membrane potential to represent slowly varying external signals by the phases of APs relative to the underlying oscillation (11). In the olfactory system there is evidence for yet another coding scheme in which neurons fire preferentially in certain cycles of a large-scale oscillation (12). Further variants are to be expected because any state-dependent parameter of the single-neuron dynamics, such as the membrane time ''constant,'' may potentially serve a computational role within a temporal code.

The auditory pathway is a particularly attractive system to study neural codes in which the timing of APs is tightly governed by the temporal structure of the external stimulus. Behavioral experiments show that barn owls can locate sound sources in complete darkness to within about one degree of azimuthal angle. This requires information processing with a temporal precision of less than 5 ms. How is this possible, given that time constants of typical neurons are at least one order of magnitude larger?

First, the relevant time constants of neurons in the early auditory pathway are comparatively short. The typical width of a postsynaptic potential is about 0.5 ms. This is at least one order of magnitude smaller than in the visual cortex. Second, temporal precision is mediated by precisely phase-locked APs. On the cochlear level, a sound wave is separated into different frequency components. Neurons in downstream nuclei are sensitive to stimuli in a narrow frequency band only. The APs of these neurons occur preferentially around a typical phase with respect to the external sound wave. Third, strong convergence patterns suggest that the signal-to-noise ratio is improved by pooling (13).

A simple model for AP generation allows us to understand the observed phase locking (14). If the model neuron is driven by APs that arrive coherently and with a pronounced periodic structure, then the output APs are phase locked. The input, however, can be coherent only if all transmission lines from the cochlea converging on one neuron have matching delays. To achieve this coherence, delay lines have to be tuned during an early developmental period.

The selection of appropriate delays can be reproduced by an unsupervised learning procedure (14). In the model, a synapse to a downstream neuron is strengthened if the presynaptic AP precedes the postsynaptic AP slightly (by 0–1 ms). The connection is weakened if the presynaptic AP occurs a few milliseconds after the postsynaptic AP. The effect of such a correlation-based learning rule is an adaptation of the auditory pathway to the exact timing of pulses arriving from the left and the right ear, a necessary step for the localization of external sound sources.

The above experimental and theoretical findings show that neurons possess a rich repertoire of elementary algorithms to process highly structured temporal codes. Together with appropriate learning rules, this computational repertoire results in large-scale activity with pronounced temporal correlations, as seen under *in vivo* conditions.

We are thus led to a view of neural coding that is quite distinct from the classical picture of information processing based solely on firing rates. When a sensory stimulus arrives, various neural subsystems run through complex iterations of computations based on AP timing. Within each iteration, a multitude of fragments of information from different neurons reach the synapses of a single neuron. Only some fragments are ''selected'' by the synaptic dynamics and contribute to the discharge of new APs, which are injected back into the network, thus serving to amplify these ''relevant'' aspects of information for further processing. The picture is complicated by the fact that this sequence of fragmentation, selection, and amplification is performed in a massively parallel manner and without fixed cycle times. Sensitivity to synchronized activity entrains this neural orchestra on the system level in a dynamic fashion and allows it to play coherent and stimulus-dependent tunes as well as internally generated variations of previous themes.


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