

4 Encoding Information in Neuronal Activity

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4.1 Introduction

Neurons communicate by producing sequences of fixed size electrical impulses called action potentials or spikes. Perceptions, decisions, and ideas are all encoded into trains of action potentials, but the basis of this coding scheme is still not well understood. Deciphering this code is one of the primary goals in experimental neuroscience. This chapter presents some of the data on the firing properties of neurons, along with clues on the coding schemes that have emerged from this data.

As described in Chapter 1, it is widely believed that neurons use firing rate to signal the strength or significance of a response. This hypothesis was first proposed by [Adrian, 1926] from the study of the relationship between the activity pattern of a stretch receptor in frog muscle and the amount of weight applied to the muscle. Figure 4.1 shows some of the data that Adrian used to develop the firing rate code hypothesis. This nerve fiber has what is now considered a classic response function. The firing rate monotonically increases with an increase in the strength of the stimulus. The initial part of the response function is approximately linear and it saturates at the maximum firing rate of the neuron, which generally ranges from 100 to 500 spikes per second.

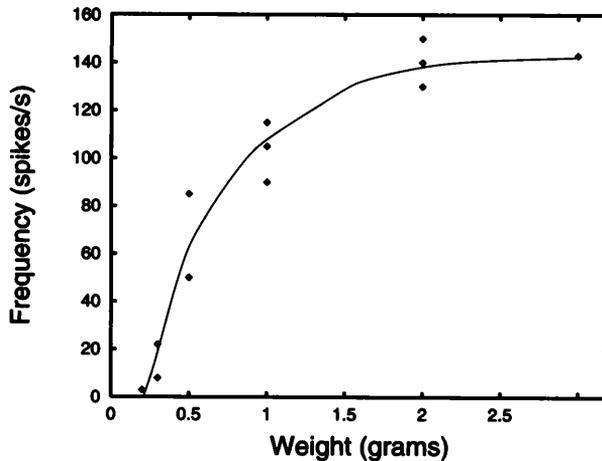


Figure 4.1. Relationship between the weight on a frog muscle and the firing rate of the muscle stretch receptor. Redrawn from Adrian, 1928.

Adrian also discovered that neurons only transiently sustain a high firing rate. In the presence of a persistent stimulus the firing rate gradually decreases [Adrian, 1926, Adrian, 1928].

This transient elevated firing is found in the majority of cells in the visual cortices [Hubel and Wiesel, 1962, Maunsell and Gibson, 1992], somatosensory cortex [Mountcastle, 1957], auditory cortex [Brugge and Merzenich, 1973] and many other brain regions. Adrian interpreted this decrease as an adaptation to the stimulus and his hypothesis was that the animal's perceived level of sensation was directly reflected by the instantaneous firing rate, as shown in Figure 4.2.

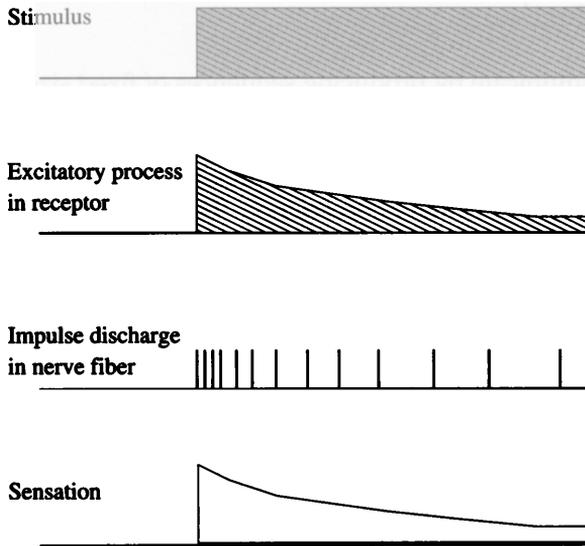


Figure 4.2. Relationship between firing rate and sensation proposed by Adrian (1928). If both the receptor and the organism habituate to a persistent stimulus with the same time scale then the post transient decrease in firing rate might exactly reflect the degree of sensation of the stimulus. Redrawn from Adrian, 1928.

The instantaneous firing rate of a neuron is considered to be a direct measure of the extent to which a recent stimulus matches the neuron's ideal stimulus.

Numerous studies in sensory and motor systems of a wide range of species have supported the validity of the firing rate code hypothesis. For example, pressure receptor cells in the skin appear to use a frequency code to signal the intensity of the stimulus. The contraction of a muscle is roughly proportional to the firing rate of the motor neuron that enervates the muscle. A subset of the output cells from the retina fire at a maximum rate when there is a bright circle of light surround by a dark angular ring illuminating a specific spot on the retina. The ideal stimulus pattern is also called the receptive field of the cell.

The success of the firing rate code hypothesis has led to a method in neuroscience in which the role of neurons is established by searching for the

stimulus that elicits the largest firing rate from a cell [Lettvin et al., 1959].

In fact the firing rate code hypothesis has led to the discovery of the role of neurons that are further from sensory receptors or muscles. Hubel and Wiesel used the firing rate hypothesis to discover that some of the neurons in the primary visual cortex are edge detectors [Hubel and Wiesel, 1959, Hubel and Wiesel, 1962].

Place cells in a brain region called the hippocampus, which is anatomically far from the sensory and motor systems, were given this name because they fire maximally when an animal is in a particular place in a particular environment [O'Keefe and Dostrovsky, 1971]. Neurons in the temporal lobes of primates have also been found fire maximally in response to particular objects or for faces.

The properties of these and many other types of neurons in the central nervous system were discovered by applying the firing rate hypothesis.

Strong physiological support for the firing rate hypothesis is also found in the model of a neuron as a temporal integrator. As a temporal integrator, a neuron will lose the precise time of arrival of individual spikes. The amount of postsynaptic depolarization will depend only on the number of spikes arriving at the neuron and the process of synaptic transmission of these spikes. Further, if the firing rate is a direct function of the level of depolarization of the cell then the firing rate is a direct indication of the internal state (or the degree to which the cell is excited).

Neurons act as temporal integrators if the time constant of integration is long in comparison with the average time between spikes. In contrast if the integration time constant is short, the neuron could also act as a coincidence detector [Abeles, 1982, Konig et al., 1996], and therefore be sensitive to the precise arrival time of the spikes for presynaptic neurons.

The hypothesis that the firing rate is proportional to the level of depolarization in cortical cells has been tested explicitly by injecting fixed amplitude current pulses into the soma (e.g. [Mainen and Sejnowski, 1995]). While the firing rate is shown to be a function of the level of depolarization in these experiments, this fixed amplitude current results in a spike train in which the intervals between spikes varies between stimulus presentations. This type of variation in neuronal response to repeated identical stimuli is sometimes interpreted as noise [Shadlen and Newsome, 1994]. The nature of this apparent noise or jitter in neuronal activity is discussed in detail in Section 4.6.

Rate coding also makes it easier to model the function of the neurons, since the rate can be modeled by a single continuous variable. Essentially this removes the need to describe explicitly the behavior of the individual neurons in the system in the time domain. This simplification has been used in the majority of current models of networks of neurons.

However, in recent years evidence has been accumulating that suggests that firing rate alone cannot account for all of the encoding of information in spike trains. Some of this data supports encoding schemes that are in addition to firing rate, while other data describes changes in firing patterns that code for stimuli in the absence of changes in firing rate. Also,

experimental evidence exists that places limits on what can be achieved by a firing rate coding alone.

All of these factors also involve the notion that populations of neurons or cell assemblies [Hebb, 1949] may be involved in alternative coding schemes or in overcoming the limitations of firing rate coding.

In this chapter, examples are presented in which the firing rate code does not appear to be sufficient to understand the data. Alternatives to firing rate coding are discussed, along with some of the possible coding problems that might limit the usefulness of a firing rate code. These coding problems include limitations on the dynamic range that can be achieved using a firing rate code, and measured properties of the apparent temporal noise or jitter. Another key issue is the effect of changes in the firing rate on the transmission of a signal to a postsynaptic cell. The impact of new data on the nature of some types of synapses is also important in considering firing rate coding. However all schemes that extend the ways in which neurons are thought to code information must build on, rather than replace firing rate coding, as this scheme has been demonstrated to be highly effective in explaining a wide range of experimental data.

4.2 Synchronization and Oscillations

One of the more strongly supported alternatives or additions to firing rate coding is synchronization and oscillations in populations of neurons. Neurons in numerous cortical and subcortical areas fire in a synchronized or highly correlated manner during specific periods that have been shown to correlate with particular mental or behavioral states. In this section several examples of this phenomenon are described. In some cases the synchronization coincides with an oscillation, but the synchronization does not depend on the presence of oscillations. Also in some cases the synchrony is present in addition to a firing rate change, while in other cases the synchrony is present without any change in the firing rate of the neurons.

Vaadia and coworkers described striking evidence for correlated firing in simultaneously recorded neurons in the frontal cortex of a rhesus monkey [Vaadia et al., 1995]. The neurons were recorded while the animal performed a task in which it had to delay its response to a visually presented spatial stimulus, and the interaction between the neurons were evaluated using a joint peri-stimulus time histogram (JPSTH) [Aertsen et al., 1989]. At the start of each trial one of two possible lights (or cues) was presented for 200 ms, followed by a 3-6 second delay and a trigger signal. The cues indicated if the trial was a GO or a NO-GO trial. In a GO trial the monkey received a reward if it released a center key and selected a correct key, and in a NO-GO trial it was rewarded if it held its hand in position on the center key. The JPSTH showed changes of the normalized correlation in the firing of pairs of neurons as a function of time from a fixed temporal event, such as the onset of a stimulus or a movement. Evidence was presented to show that even though the firing rate of the neurons appeared to be the same in the interspersed GO and NO-GO versions of the task, there was a significant difference in the correlated temporal structure of the activity of pairs of neurons.

In one example the correlated firing between two neurons during the GO tasks was highest during the first second after the onset of the stimulus and lower during the next second. During the NO-GO tasks the pattern of correlated firing was reversed. The correlation was low in the first second and high in the following second. There was no difference in the firing rates between the two paradigms and no difference in the cross-correlation. These rapid changes in the correlation of activity were found in 32% of 947 pairs of recorded neurons.

Most neurons in the auditory cortex have a transient response to the onset of a stimulus [Brugge and Merzenich, 1973]. In a recent experiment multiple isolated single neurons from several sites in the auditory cortex of anesthetized marmoset monkeys were recorded from simultaneously, while the animal was presented with a pure tone stimulus (4 kHz) that is known to drive these neurons [deCharms and Merzenich, 1996].

The firing pattern, and the correlations between simultaneously recorded neurons in two separated recording sites, were examined in a number of different conditions, two of which are illustrated in Figure 4.3. In one of these conditions there is a persistent tone, and in the other there is a short (50 ms) tone. Cross correlations calculated during a 3 s period, 500 ms after stimulus onset, in each of these two conditions were compared. In both cases there was a transient change in the firing rate, but only during the persistent tone signal there was a zero phase shift synchronization between the firing of the neurons. The significance of this effect was higher when action potentials from several neurons recorded from the same site were combined and correlated with several neurons in a second recording site, suggesting that the correlated activity is a population phenomenon. This data suggests that the temporal structure of the population activity, rather than the firing rate of individual neurons, is used to encode the presence of the tone.

In a recent study sets of neurons in the primary motor cortex (M1) of the macaque monkey were found to synchronize when the animal was preparing to respond to a stimulus [Riehle et al., 1997]. In each trial the animal waited for one of four different delay periods (600, 900, 1200 and 1500 milliseconds), prior to making a motor response. The ordering of the trials was random so that the animal could not predict the length of a particular delay period. In the data from the longest delay trials there was a significant increase in the synchronized activity of pairs and triplets of neurons at points in time corresponding to the shorter delays. This synchronized activity was present without a change in the firing rate of the neurons. In contrast, the motor and sensory components of the task were correlated with changes in the firing rate of the neurons.

The synchronized firing of sets of neurons, which is suggested to be more correlated with internal, rather than external events can not be subsumed within a model or description of neuronal function that only includes firing rate. In all three examples discussed in this section firing rate did not indicate a state change that was only apparent by examining the synchronized activity of simultaneously recorded cells. The first example the synchronization supported the idea that there was a perceptual grouping of stimu-

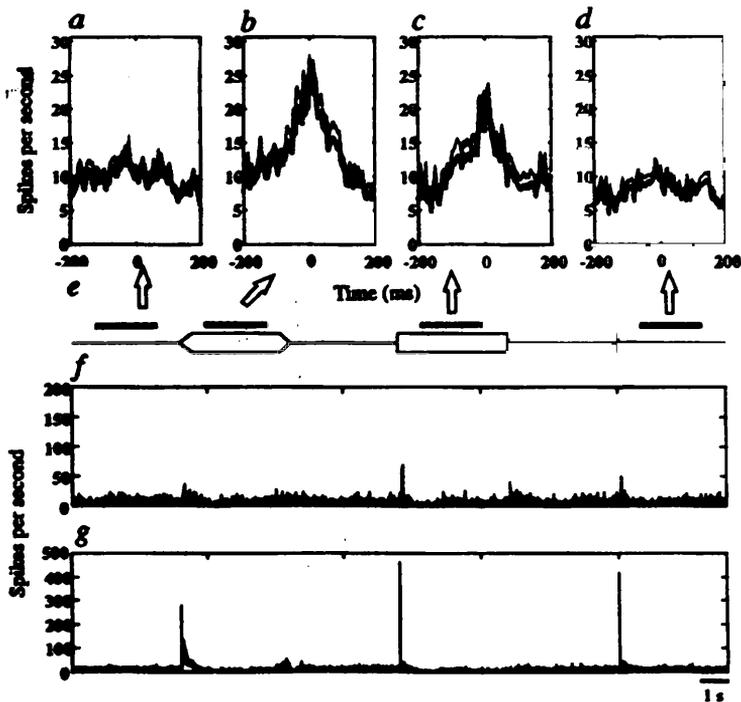


Figure 4.3. Mean firing rate and temporal correlation of neurons recorded by [deCharms and Merzenich, 1996] from the primary auditory cortex of a marmoset monkey. Part e of the figure shows the envelope of a 4kHz pure tone stimulus, f and g contain the mean firing rates of neurons simultaneously recorded from two cortical locations, and parts a-d contain average cross-correlations computed from 100 stimulus presentations. In parts a-d the mean is shown with a thick line and the mean plus standard error is shown with a thin line. Part a contains the cross correlation during a silent period before the stimulus; b is the correlation during a 3 second constant phase of a ramped onset pure tone; c is the 3 second period after a sharp onset pure tone; and d is the correlation during a silent period after a short 50 ms pure tone. Reprinted with permission from [deCharms and Merzenich, 1996.]

lus features [Milner, 1974, von der Malsburg, 1981]. In the second example the synchronization coded for the presence of a basic auditory feature, and in the third example the synchronization signaled the presence of an internal state that would otherwise not be observed (see also section 1.1.3.3).

4.3 Temporal Binding

Synchronized activity in populations of neurons in cortical and subcortical regions, and in species as diverse as turtles [Prechtl et al., 1997], pigeons [Neuenschwander et al., 1996], rats [Bragin et al., 1995], cats [Gray and Singer, 1989] and monkeys [Livingstone, 1996, Kreiter and Singer, 1996] is often found to coincide with oscillations in the gamma frequency range (20-70 Hertz). This synchronization can occur with zero phase delay across multiple visual association areas, between visual and motor areas, and between cortical

and subcortical regions. The presence of the zero phase shift synchronized firing has been shown to exist between particular subsets of neurons within an area and to occur in relation to specific behavioral events. In the cat visual system synchronized activity was found in cells in separate cerebral hemispheres [Engel et al., 1991]. The evidence for synchronized activity and the significance of this phenomenon has been recently thoroughly reviewed [Singer and Gray, 1995, Engel et al., 1997].

It has been suggested that this synchrony provides a means to bind together in time the features that represent a particular stimulus [Milner, 1974, von der Malsburg, 1981, von der Malsburg, 1995]. There is substantial evidence to suggest that the individual features of a perceived object are encoded in distributed brain regions and fire collectively as a cell assembly [Hebb, 1949].

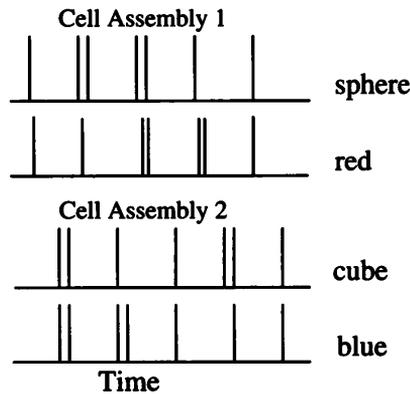


Figure 4.4. Temporal binding of features in cell assemblies. In this example both a red sphere and a blue cube are present in a scene. If sets of neurons code for the colors red and blue, and the for the shapes sphere and cube, then the correct association of color and shape might be represented in the brain by synchronizing the activity of the the neurons within each of the two cell assemblies. In this way neurons coding for red and sphere are active at a different time from those coding for blue and cube, and the two objects can be processed simultaneously.

The central idea is that there is some temporal process during which information about an object or group of objects is processed. In order to keep the attributes of these objects from interfering, they are separated in time, as illustrated in Figure 4.4. In this figure there are two cell assemblies, one that codes for the features of a red sphere and one that codes for the features of a blue cube. Within a cell assembly the neurons fire in a synchronized pattern with zero phase shift. There is a time shift between the two assemblies so that each remains coherent, and the scene is not confused with one containing a blue sphere and a red cube. With firing rate coding it is not possible to construct this type of neuronal system in which multiple, simultaneous use is made of a set of feature encoding neurons.

4.4 Phase Coding

During locomotion, the firing patterns of neurons in the rat hippocampus are modulated by a large 7-12 Hz sinusoidal oscillation called the theta rhythm. The theta rhythm is generated in the hippocampus [Green et al., 1960] from a pacemaker input located in the medial septum [Petsche et al., 1962]. It is highly coherent, with no phase shift over a large region of the hippocampus called CA1 [Bullock et al., 1990]. Many neurons in the CA1 and neighboring CA3 region of the hippocampus have a characteristic burst firing pattern [Ranck, 1973, Fox and Ranck, 1975], and the activity pattern of the majority of these neurons, called place cells, is highly correlated with the animal's location in an environment [O'Keefe and Dostrovsky, 1971].

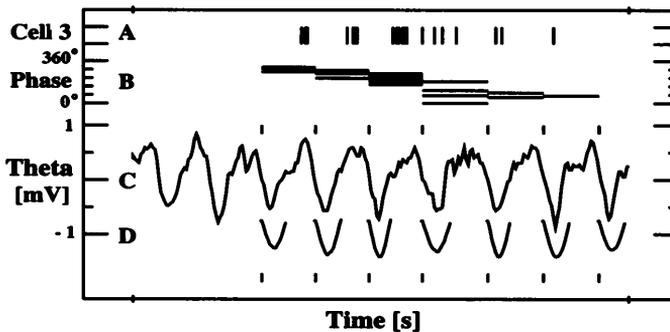


Figure 4.5. Extraction of the firing phase for each spike during a single run through the place field of a place cell on the linear runway. (A) Each action potential from cell 3 during the one second of data shown in the figure is marked with a vertical line. (B) The phase of each spike relative to the hippocampal theta rhythm. (C) Hippocampal theta activity recorded at the same time as the hippocampal unit. (D) Half sine wave fit to the theta rhythm which was used to find the beginning of each theta cycle (shown with vertical ticks above and below the theta rhythm). Reprinted from [O'Keefe and Recce, 1993].

The firing rate of a place cell, within its preferred spatial location, called its place field, has been modeled as a two dimensional Gaussian function [O'Keefe and Burgess, 1996]. Place cells have been recorded on a linear runway, as the animal runs from end to end for a food reward. In this paradigm the time at which an animal arrives at a location varies with running speed, but the activity pattern of the cell continues to be driven by its the spatial location.

As the animal runs through the place field the phase relationship between the spikes and the theta rhythm systematically changes [O'Keefe and Recce, 1993, Skaggs et al., 1996], as shown in the example in Figure 4.5. Each time the animal runs through the place field the firing of the place cell starts at the same phase and systematically precesses through the same phase change. The total amount of phase shift that occurred as the animal ran through the place field was always less than 360 degrees.

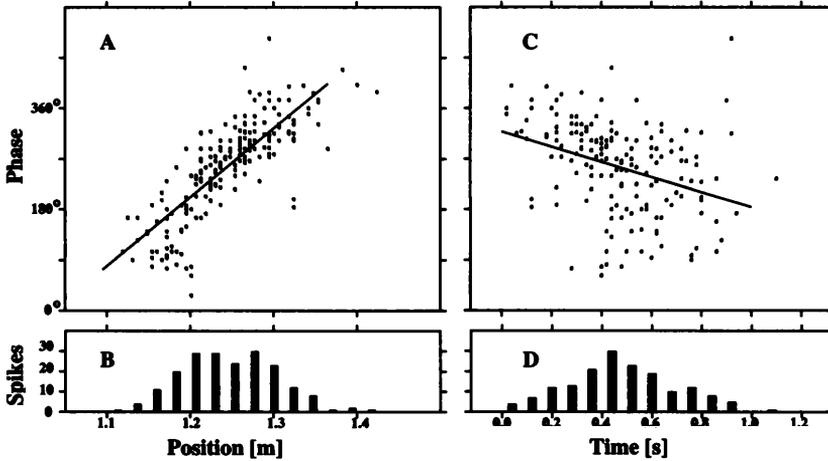


Figure 4.6. Phase of EEG at which a hippocampal place cell fired, (A) plotted against the position of the rat and (C) against the time after the rat crossed the nearest boundary of the place field. (B) and (D) show the distribution of the firing rate recorded in the 41 runs along the runway that were used to construct the figure. Reprinted from [O'Keefe and Recce, 1993].

In addition the phase relationship between the place cell activity and the theta rhythm was found to have a higher level of correlation with the animal's spatial location than with the time that the animal has spent in the place field [O'Keefe and Recce, 1993]. Figure 4.6 illustrates this phenomena. In panel A, the phase of each spike from a place cell is plotted against the position of the animal, recorded on multiple runs along the runway. Panel B shows that the firing rate of the place cell is highest in the center of the place field. In panel C and panel D the same data are plotted as a function of the time that has passed since the animal entered the place field. The phase of the firing of this cell and 14 other place cells had a higher correlation to the spatial location, and the phase of firing was a better indication of the animal's location than the firing rate of the cell.

The phase of place cell firing provides additional information on the animal's spatial location which is independent of and more informative than a firing rate code. One possibility is that these different types of information are intended for different target regions in the brain. Also phase coding, like temporal binding, provides a way for the information on neighboring spatial locations to be processed simultaneously without interference (see also Section 1.1.3.2).

4.5 Dynamic Range and Firing Rate Codes

For over forty years it has been known that a firing rate code is not the most efficient way for a neuron to transmit information with action potentials

[MacKay and McCulloch, 1952]. As a simplified illustration consider the the output signal from a neuron that has a firing rate scale that ranges from zero to 200 spikes per second. With the further assumptions that: (1) the critical time interval for integrating the signal or measuring the firing rate is 100 ms, and (2) that there is uncertainty in the generation of spikes, the hypothetical neuron has approximately 20 distinct states.

In contrast if information is coded in the length of inter-spike intervals with five millisecond precision then there are over a million possible output states (2^{20}), although not all of these states would be equally probable. There are a wide range of possible codes that have more than 20 and less than a million different states in a 100 millisecond interval. In particular the coding scheme might look largely like a firing rate, but contain additional information that is only extracted by a subset of the neurons that receive inputs from a particular neuron.

One hundred milliseconds might also be an overestimate of the length of the time interval used to transmit the coded signal. A housefly can change its flight path in reaction to a change in visual input in just 30 milliseconds [Land and Collett, 1974]. In a recent study Thorpe and coworkers showed that the total time required for human subjects to perform a pattern recognition task was 150 milliseconds [Thorpe et al., 1996]. Since this task is thought to require many synaptic steps and substantial signal propagation delays, it appears that the information sampling interval taken by each neuron must be much less than 100 milliseconds.

Some of the most convincing evidence that precise timing of spikes provides additional information, not present in firing rate alone has come from experiments carried out by van Steveninck, Bialek and coworkers. The timing sequence of action potentials in the H1 neuron of the fly have been shown to contain the information needed to reconstruct the stimulus pattern. This reconstruction implies that there is a precision on the order of a millisecond in the firing of each spike. Furthermore they have shown that the H1 neuron only produces one or two spikes in the 30 milliseconds that a fly samples before it can make a response, suggesting that the information encoded in the interspike intervals must be used by the downstream neurons. These data and analysis are presented in great detail in a recent book [Rieke et al., 1997].

4.6 Interspike Interval Variability

All of the proceeding discussion in this chapter has neglected the presence of temporal noise or jitter in the firing patterns of neurons. Temporal noise obviously reduces the number of distinguishable states of an individual neuron, independent of the coding scheme that is being used. Softky and Koch examined the variability in the interspike intervals recorded from cortical cells [Softky and Koch, 1993], that were firing at an average constant rate and found that the intervals between spikes were randomly distributed. They considered this irregularity as evidence that the neurons were acting as coincidence detectors, and that the variability was part of the signal rather than noise. However, it has been argued [Shadlen and Newsome, 1994] that this data supported the hypoth-

esis that neurons were undergoing an internal random walk that results from a roughly equal amount of inhibitory and excitatory input.

An explanation has been found for some of the measured firing irregularity in cortical neurons. Variability found in the interspike intervals of neurons in the visual cortex in anesthetized animals is in part due to the influence of intra-cortical and thalamocortical oscillations that are a direct result of the anesthesia [Arieli et al., 1996]. This noise can be reduced by using awake animals and by controlling for the noise introduced by small eye movements [Gur et al., 1997].

Some of the hypothesized noise in individual neurons might be removed by combining firing rate information accumulated from a population of neurons. Georgopoulos and coworkers have shown that in the motor cortex a population of neurons provides a better correlation to the motor activity than individual cells [Georgopoulos et al., 1986] [Wilson and McNaughton, 1993] have shown one way in which the firing rate of a population of hippocampal place cells could be combined to provide a better estimate of a rat's location.

In general there are two ways in which a population of neurons can improve the accuracy of the encoding of a stimulus or motor output. Each neuron could have a coarse coding of the stimulus, which is made finer by the activity of a number of neurons. Alternatively each neuron could have independent noise, and this noise is removed by combining input from several neurons. In the two examples discussed here the combined population activity is more precise or informative because each neuron is providing additional information, rather than independent noise (see also Section 1.1.2.3).

If the interspike interval irregularity is noise it can only be removed if this noise is independent in the set of neurons whose activity is averaged. In a recent experiment Shoham and coworkers used voltage sensitive dyes to measure the extent to which neighboring neurons in the visual cortex have independent uncorrelated activity patterns [Shoham et al., 1997]. The activity patterns of neighboring regions of cortex were highly correlated, suggesting that a downstream neuron receives multiple projections with similar interspike intervals, and does not average out the variations. Precite and coworkers found similar results in the visual cortex of the turtle [Prechtl et al., 1997]. A wave pattern is generated as a result of the presentation of a stimulus, which changes with each presentation of the stimulus but is correlated between neighboring regions of the cortex, within the presentation of the stimulus.

In one recent study, the amount of information and noise in spike trains was quantified. The results from this experiment show that the amount of variation in the interspike interval depends on the properties of the stimulus presented to an animal [de Ruyter van Steveninck et al., 1997]. The response properties of the neurons to static stimuli were highly variable between stimulus presentations. The variance in interspike intervals between stimulus presentations was essentially proportional to the mean firing rate, suggesting that the variation was Poisson distributed. In contrast, when the stimuli were more dynamic and "natural" the response of the H1

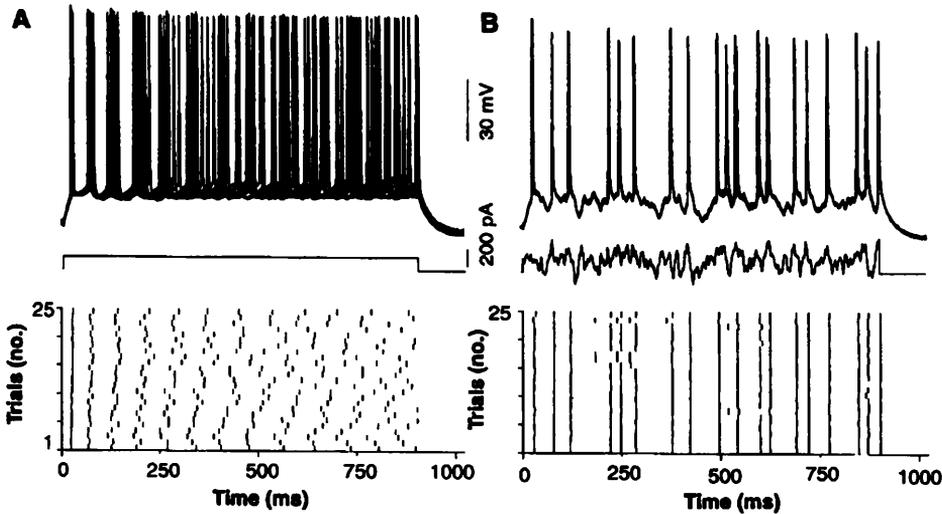


Figure 4.7. Variability of interspike intervals in a cortical neuron with constant or fluctuating current. (A) Superimposed recordings of a regular-firing layer 5 neuron, from 10 consecutive trials with a superthreshold d.c. current pulse (middle), also shown as a raster plot with 25 consecutive trials (lower). (B) The same as in (A) but the stimulus was a repeated signal fluctuating with Gaussian distributed white noise. From [Mainen and Sejnowski, 1995].

neuron to a particular signal was highly reproducible. An analysis of the information carried in the spike train showed that approximately half of the variation was signal and the other half was noise. The information rate was approximately 2.5 bits in 30 milliseconds (see also Section 1.1.3.4).

[Mainen and Sejnowski, 1995] have shown in an *in vitro* study that neurons in the visual cortex are capable of remarkably precise action potential timing. Their results suggest that the variability found *in vivo* is a result of variation in the incoming synaptic barrages from one stimulus presentation to the next. The neurons fired with a much higher temporal consistency in response to a repeated randomly fluctuating signal than to a fixed d.c. current pulse. The fluctuating signal was constructed by adding filtered white noise generated by a computer to a constant depolarizing pulse. An example of the data from this experiment is shown in Figure 4.7. The spike trains produced by the fluctuating input were reproducible to less than one millisecond.

In a recent experiment, Nowak and coworkers took this analysis a step further [Nowak et al., 1997]. They recorded from three different types of cells in the visual cortex of a ferret (*in vitro*). When presented with a fixed level current offset these cells have different characteristic firing patterns, including: regular spiking, fast spiking and bursting. In contrast when presented with activity recorded from previously described "chattering cells" [Gray and McCormick, 1996], all of the cell types had similar firing pat-

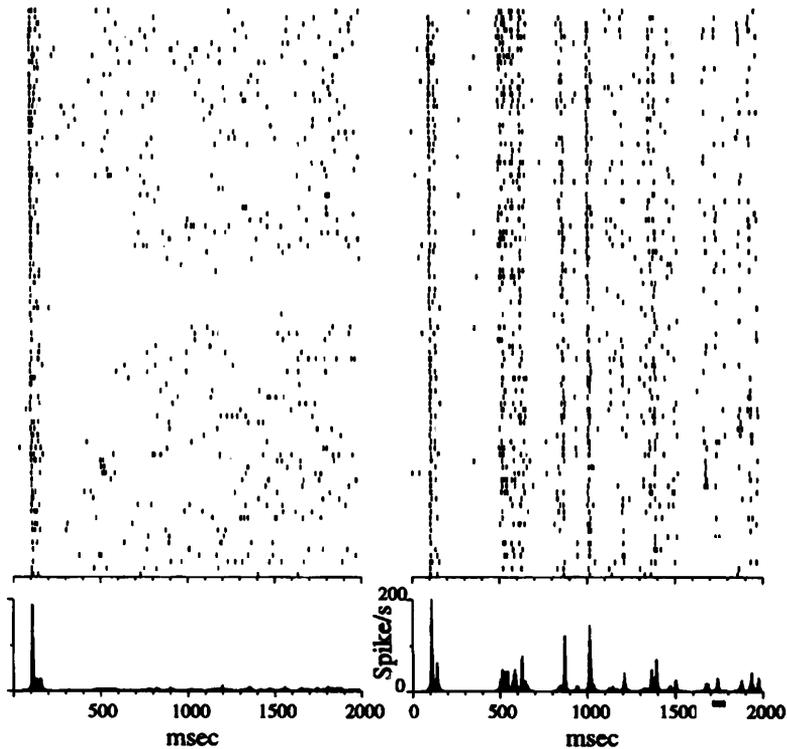


Figure 4.8. Response of one cell in area MT in a behaving macaque monkey to the two second presentation of a random dot pattern. Each raster pattern in the panel on the left shows the response of the cell to a different random dot pattern. The panel on the right shows the response to multiple presentations of the same random dot pattern, which were interleaved with other stimuli. While the response patterns in the left hand panel appear to capture only the onset of the stimulus. It is clear from the right hand pattern that other features of the stimulus pattern are reliably captured. The lower part of each panel contains a poststimulus time histogram (see Section 1.1.2.2). Reprinted from [Bair and Koch, 1996].

terns. They also presented the cells with a range of different noise signals with different spectral characteristics. When presented with real input the cells had a more variable firing pattern, but the firing was more consistent between stimulus presentations. The consistency was present in a much higher reliability and in less temporal jitter.

A similar result was also found in cells in the medial temporal area (V5 or MT) of the awake behaving macaque monkey [Bair and Koch, 1996]. Evidence suggests that this area is involved in visual motion processing [Dubner and Zeki, 1971]. Bair and Koch examined the activity patterns of neurons in response to different random stimuli. As shown in Figure 4.8, when data from different random stimuli were compared the response could be characterized by a transient followed spikes separated by a Poisson random set of interspike intervals. This data alone could be interpreted as evidence for errors or noise in neuronal activity

[Shadlen and Newsome, 1994]. However when presented multiple times with the same random stimulus (right panel of Figure 4.8) there was a high degree of consistency in the firing pattern of the neuron and very little jitter.

Most recently Buracas and coworkers [Buracas et al., 1997] used a Gabor function pattern moved in two or eight directions to study firing patterns of neurons in area MT of behaving macaque monkeys. They measured the information provided by the spike train in response to a stimulus that moved uniformly to one which randomly reversed direction every 30 to 300 ms. The primary finding in this study was that the neurons produced approximately 1 bit of information per second with a constant speed stimulus, and as many as 29 bits per second in response to dynamically changing stimulus.

The results were consistent with the findings of Bair and Koch in that the neurons fired with a reliable sequence in response pattern to a repeated random stimulus, but with highly variable spike trains in response to different random stimuli. They suggest that a neuron codes for the stimulus that results in the highest information rate, rather than the stimulus that produces the highest firing rate.

Buracas and coworkers also measured the information rate as a function of the time after the start of the constant stimulus pattern. Consistent with prior findings of in primate inferior temporal cortex [Optican and Richmond, 1987, Tovee et al., 1993] most of the information is in the first few hundred milliseconds after the onset of the stimulus pattern.

Recent experimental evidence suggests that more realistic stimuli and dynamic stimuli that place more demands on the processing of information within a system of neurons result in reliable and more variable firing patterns of the neurons.

4.7 Synapses and Rate Coding

Some of the strongest evidence against a simple rate code has come from recent studies of the nature of synaptic transmission between pyramidal cells in layer 5 of the rat visual cortex [Markram, 1997]. Paired activation in these synapses, as in other brain regions, has been shown to increase the influence of the presynaptic cell on the activity of the postsynaptic cell in a manner initially suggested by [Hebb, 1949]. However the properties of the synapses both before and after this change are not ideal for the use of rate coding.

As illustrated in Figure 4.8, [Markram and Tsodyks, 1996] demonstrated that modification of the synapse does not result in an increase in synaptic efficacy at all frequencies. With the frequency of input spikes shown in the figure, the response to the initial presynaptic action potential is potentiated, but the response to the subsequent action potentials is attenuated. The top trace contains the average excitatory post-synaptic potential (EPSP) before (solid line) and after (dashed line) pairing activity in the two pyramidal cells, measured as a result of the stimulation sequence shown in

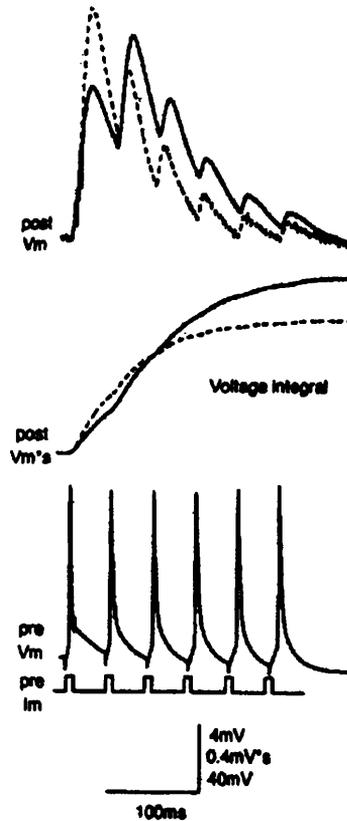


Figure 4.9. Effect of paired activation of synaptically connected layer V tufted cortical cells. The top panel shows the average EPSP before (solid line) and after (dashed line) paired activation. The center panel shows the integral of the normalized EPSPs, and the lower panel shows the presynaptic stimulation. Modified from [Markram, 1997].

the bottom trace. The center part of the figure contains the integral of the EPSP data shown in the top part of the figure. Note that one effect of the potentiation of the initial input and depression of later inputs is to increase the synchrony in the activity of the pre and post synaptic cells.

In later studies [Tsodyks and Markram, 1997, Abbott et al., 1997] it was shown that the post-transient effective synaptic strength is inversely proportional to the firing rate of the presynaptic neuron. This effectively cancels the persistent firing rate signal in the postsynaptic neuron, but leaves a strong response to a transient change in firing rate. These new insights into the synaptic modification rules suggest that some synapses do not effectively transmit persistent rate code information. This issue will be dis-

4.8 Summary and Implications

In this chapter, a small number of selected examples have been presented to illustrate the ways in which the rate coding hypothesis is being changed.

Recent data on the temporal structure of the activity of neurons and the properties of synaptic transmission have highlighted a need to use more realistic computational models to study the properties of systems of neurons. Highlighted differences in the reliability of neuronal firing that result when comparing stimulation with artificial and with more realistic inputs. In particular fixed firing rates and fixed synaptic weights will most likely be insufficient to model the properties of real neurons. The spiking neuron models described in the other chapters of this book capture some of the essential structure needed to construct useful models of systems of neurons. The importance of explicitly modeling the temporal structure of neuronal activity has been made elsewhere [Gerstner et al., 1993], and they have demonstrated that an associative memory can be constructed with spiking neurons.

It is clear that firing rate coding is used by neurons to signal information. However the temporal structure of this firing rate code is likely to contain additional information, which may only be used by a subset of the downstream neurons that receive the message. These examples also highlight the importance in simultaneously measuring the activity patterns in large numbers of neurons and the temporal interactions between these neurons.

References

- [Abbott et al., 1997] Abbott, L. F., Varela, J. A., Sen K., and Nelson, S. B. (1997). Synaptic depression and cortical gain control. *Science*, 275:220–224.
- [Abeles, 1982] Abeles, M. (1982). Role of cortical neuron: integrator or coincidence detector? *Isr. J. Med. Sci.*, 18:83–92.
- [Adrian, 1926] Adrian, A. D. (1926). The impulses produced by sensory nerve endings: Part i. *J. Physiol. (Lond.)*, 61:49–72.
- [Adrian, 1928] Adrian, E. D. (1928). *The Basis of Sensation: The Action of the Sense Organs*. W. W. Norton, New York.
- [Aertsen et al., 1989] Aertsen, A. M., Gerstein G. L., Habib M. K., and Palm, G. J. (1989). Dynamics of neuronal firing correlation-modulation of effective connectivity. *J. Neurophysiol.*, 61:900–917.
- [Arieli et al., 1996] Arieli, A., Sterin A., Grinvald, A., and Aertsen, A. (1996). Dynamics of ongoing activity: explanation of the large variability in evoked cortical responses. *Science*, 273:1868–1871.
- [Bair and Koch, 1996] Bair, W. and Koch, C. (1996). Temporal precision of spike trains in extrastriate cortex of the behaving macaque monkey. *Neural Computation*, 6:1184–1202.
- [Bragin et al., 1995] Bragin, A., Jandó, G., Nádasdy, Z., Hetke, J. K., Wise K., and Buzsáki, G. (1995). Gamma (40–100 Hz) oscillation in the hippocampus of the behaving rat. *J. Neurosci.*, 15:47–60.
- [Brugge and Merzenich, 1973] Brugge, J. F. and Merzenich M. M. (1973). Responses of neurons in auditory cortex of the macaque monkey to monaural and binaural stimulation. *J. Neurophysiol.*, 36:1138–1158.
- [Bullock et al., 1990] Bullock, T. H., Buzsáki, G. and McClune, M. C. (1990). Coherence of compound field potentials reveals discontinuities in the cal-subiculum of the hippocampus in freely-moving rats. *Neuroscience*, 38:609–619.
- [Buracas et al., 1997] Buracas, G.T., Zador, A., DeWeese, M., and Albright, T.D. (1997). Efficient discrimination of temporal patterns by motion-sensitive neurons in primate visual cortex *Neuron*, in press.
- [de Ruyter van Steveninck et al., 1997] de Ruyter van Steveninck, R., Lewen, G. D., Strong, S. P., Koberle, R., and Bialek, W. (1997). Reproducibility and variability in neural spike trains. *Nature*, 375:1805–1808.
- [deCharms and Merzenich, 1996] deCharms, R. C. and Merzenich, M. M. (1996). Primary cortical representation of sounds by the coordination of action-potential timing. *Nature*, 381:610–613.
- [Dubner and Zeki, 1971] Dubner, R. and Zeki, S. M. (1971). Response properties and receptive fields of cells in an anatomically defined region of the superior temporal sulcus in the monkey. *Brain Research*, 35:528–532.
- [Engel et al., 1991] Engel, A. K., Konig, P., Kreiter, A., and Singer, W. (1991). Interhemispheric synchronization of oscillatory neuronal responses in cat visual cortex. *Science*, 252:1177–1179.

- [Engel et al., 1997] Engel, A. K., Roelfsema, P. R., Fries, P., Brecht, M., and Singer, W. (1997). Role of the temporal domains for response selection and perceptual binding. *Cerebral Cortex*, 7:571–582.
- [Fox and Ranck, 1975] Fox, S. E. and Ranck, J. B. (1975). Localization and anatomical identification of theta and complex spike cells in dorsal hippocampal formation of rats. *Exp. Neurol.*, 49:299–313.
- [Georgopoulos et al., 1986] Georgopoulos, A. P., Schwartz, A., and Kettner, R. E. (1986). Neuronal populations coding of movement direction. *Science*, 233:1416–1419.
- [Gerstner et al., 1993] Gerstner, W., Ritz R., and vanHemmen J. L. (1993). Why spikes? Hebbian learning and retrieval of time-resolved excitation patterns. *Biol. Cybern.*, 69:503–515.
- [Gray and McCormick, 1996] Gray, C. M. and McCormick, D. A. (1996). Chattering cells: superficial pyramidal neurons contributing to the generation of synchronous oscillations in the visual cortex. *Science*, 274:109–113.
- [Gray and Singer, 1989] Gray, C. M. and Singer W. (1989). Stimulus-specific neuronal oscillations in orientation columns of cat visual cortex. *Proc. Nat. Acad. Sci.*, 86:1698–1702.
- [Green et al., 1960] Green, J. D., Maxwell, D. S., Schindler, W. J., and Stumpf, C. (1960). Rabbit eeg "theta" rhythm: its anatomical source and relation to activity in single neurons. *J. Neurophysiol.*, 23:403–420.
- [Gur et al., 1997] Gur, M., A. Beylin, and Snodderly, D. M. (1997). Response variability of neurons in primary visual cortex (v1) of alert monkeys. *J. Neurosci.*, 17:2914–2920.
- [Hebb, 1949] Hebb, D. O. (1949). *The Organization of Behavior*. Wiley, New York.
- [Hubel and Wiesel, 1959] Hubel, D. H. and Wiesel T. N. (1959). Receptive fields of single neurons in the cat's striate cortex. *J. Physiol.*, 148:574–591.
- [Hubel and Wiesel, 1962] Hubel, D. H. and Wiesel, T. N. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *J. Physiol.*, 160:106–154.
- [Konig et al., 1996] Konig, P., Engel, A. K., and Singer, W. (1996). Integrator or coincidence detector? the role of the cortical neuron revisited. *Trends in Neurosci.*, 19:130–137.
- [Kreiter and Singer, 1996] Kreiter, A. K. and Singer, W. (1996). Stimulus-dependent synchronization of neuronal responses in the visual cortex of awake macaque monkey. *J. Neurosci.*, 16:2381–2396.
- [Land and Collett, 1974] Land, M. F. and Collett, T. S. (1974). Chasing behavior of houseflies (*fannia canicularis*): A description and analysis. *J. Comp. Physiol.*, 89:331–357.
- [Lettvin et al., 1959] Lettvin, J. P., Maturana, H. R., McCulloch, W. S., and Pitts, W. (1959). What the frog's eye tells the frog's brain. *Proc. Inst. Rad. Eng.*, 47:1950–1961.

- [Livingstone, 1996] Livingstone, M. S. (1996). Oscillatory firing and interneuronal correlations in squirrel monkey striate cortex. *J. Neurophysiol.*, 75:2467–2485.
- [MacKay and McCulloch, 1952] MacKay, D. and McCulloch, W. S. (1952). The limiting information capacity of a neuronal link. *Bull. Math. Biophys.*, 14:127–135.
- [Mainen and Sejnowski, 1995] Mainen, Z. F. and Sejnowski, T. J. (1995). Reliability of spike timing in neocortical neurons. *Science*, 268:1503–1506.
- [Markram, 1997] Markram, H. (1997). A network of tufted layer 5 pyramidal neurons. *Cerebral Cortex*, 7:523–533.
- [Markram and Tsodyks, 1996] Markram, H. and Tsodyks M. (1996). Redistribution of synaptic efficacy between neocortical pyramidal neurons. *Nature*, 382:807–810.
- [Maunsell and Gibson, 1992] Maunsell, J. H. and Gibson, J. R. (1992). Visual response latencies in striate cortex of the macaque monkey. *J. Neurophysiol.*, 68:1332–1344.
- [Milner, 1974] Milner, P. M. (1974) A model for visual shape recognition. *Psychol. Rev.*, 81:521–535.
- [Mountcastle, 1957] Mountcastle, V. (1957). *J. Neurophysiol.*, 20:408–434.
- [Neuenschwander et al., 1996] Neuenschwander, S., Engel, A. K., Konig, P., Singer, W., and Varela, F. J. (1996). Synchronization of neuronal responses in the optic tectum of awake pigeons. *Vis. Neurosci.*, 13:575–584.
- [Nowak et al., 1997] Nowak, L. G., Sanchez-Vives, M. V., and McCormick, D. A. (1997). Influence of low and high frequency inputs on spike timing in visual cortical neurons. *Cerebral Cortex*, 7:487–501.
- [O'Keefe and Burgess, 1996] O'Keefe, J. and Burgess, N. (1996). Geometric determinants of the place fields of hippocampal neurons. *Nature*, 381:425–428.
- [O'Keefe and Dostrovsky, 1971] O'Keefe, J. and Dostrovsky, J. (1971). The hippocampus as a spatial map. preliminary evidence from unit activity in the freely-moving rat. *Brain Research*, 34:171–175.
- [O'Keefe and Recce, 1993] O'Keefe, J. and Recce, M. L. (1993). Phase relationship between hippocampal place units and the eeg theta rhythm. *Hippocampus*, 3:317–330.
- [Optican and Richmond, 1987] Optican, L. M. and Richmond, B. J. (1987). Temporal encoding of two-dimensional patterns by single units in primate inferior temporal cortex. iii. information theoretic analysis. *J. Neurophysiol.*, 57:162–178.
- [Petsche et al., 1962] Petsche, H., Stumpf, C., and Gogolak, G. (1962). The significance of the rabbit's septum as a relay station between the mid-brain and the hippocampus. i. the control of hippocampal arousal activity by the septum cells. *Electroencephalogr. Clin. Neurophysiol.*, 14:202–211.

- [Prechtl et al., 1997] Prechtl, J., Cohen, L. B., Pesaran, B., Mitra, P. P., and Kleinfeld, D. (1997). Visual stimuli induce waves of electrical activity in turtle cortex. *Proc. Nat. Acad. Sci.*, 94:7621–7626.
- [Ranck, 1973] Ranck, J. B. (1973). Studies on single neurons in dorsal hippocampal formation and septum in unrestrained rats. *Exper. Brain Research*, 41:461–555.
- [Riehle et al., 1997] Riehle, A., Grun, S., Diesmann, M., and Aertsen, A. (1997). Spike synchronization and rate modulation differentially involved in motor cortical function. *Science*, 278:1950–1953.
- [Rieke et al., 1997] Rieke, F., Warland, D., de Ruyter van Steveninck, R., and Bialek, W. (1997). *Spikes-Exploring the Neural Code*. MIT Press, Cambridge, MA.
- [Shadlen and Newsome, 1994] Shadlen, M. N. and Newsome, W. T. (1994). Noise, neural codes and cortical organization. *Curr. Opin. Neurobiol.*, 4:569–579.
- [Shoham et al., 1997] Shoham, D., Hebener, M., Schulze, S., Grinvald, A., and Bonhoeffer, T. (1997). Spatio-temporal frequency domains and their relation to cytochrome oxidase staining in cat visual cortex. *Nature*, 385:529–533.
- [Singer and Gray, 1995] Singer, W. and Gray, C. M. (1995). Visual feature integration and the temporal correlation hypothesis. *Ann. Rev. Neurosci.*, 18:555–586.
- [Skaggs et al., 1996] Skaggs, W. E., McNaughton, B. L., Wilson, M. A., and Barnes, C. A. (1996). Theta-phase precession in hippocampal neuronal populations and the compression of temporal sequences. *Hippocampus*, 6:149–172.
- [Softky and Koch, 1993] Softky, W. R. and Koch, C. (1993). The highly irregular firing of cortical cells is inconsistent with temporal integration of random epsps. *J. Neurosci.*, 13:334–350.
- [Thorpe et al., 1996] Thorpe, S., Fize, D., and Marlot, C. (1996). Speed of processing in the human visual system. *Nature*, 381:520–522.
- [Tovee et al., 1993] Tovee, M. J., Rolls E. T., Treves, A., and Bellis, R. P. (1993). Information encoding and responses of single neurons in the primate visual cortex. *J. Neurophysiol.*, 70:640–654.
- [Tsodyks and Markram, 1997] Tsodyks, M. and Markram, H. (1997). The neural code between neocortical pyramidal neurons depends on the transmitter release probability. *Proc. Nat. Acad. Sci.*, 94:719–723.
- [Vaadia et al., 1995] Vaadia, E., Haalman, I., Abeles, M., Bergman, H., Prut, Y., Slovin, H., and Aertsen, A. (1995). Dynamics of neuronal interactions in monkey cortex in relation to behavioural events. *Nature*, 373:515–518.
- [von der Malsburg, 1981] von der Malsburg, C. (1981). The correlation theory of brain function. *Internal Report 81-2. Göttingen: Max-Planck Institute for Biophysical Chemistry.*
- [von der Malsburg, 1995] von der Malsburg, C. (1995). Binding in models of perception and brain function. *Curr. Opin. Neurobiol.*, 5:520–526.

- [Wilson and McNaughton, 1993] Wilson, M. A. and McNaughton, B. L. (1993). Dynamics of the hippocampal ensemble code for space. *Science*, 265:1055–1058.

Part II

Implementations