21

Where Are the Switches on This Thing?

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Introduction

Controlled responses differ from reflexes because they can be turned off and on. This is a critical part of what distinguishes animals from automatons. How does the nervous system gate the flow of information so that a sensory stimulus that elicits a strong response on some occasions, evokes no response on others? A related question concerns how the flow of sensory information is altered when we pay close attention to something as opposed to when we ignore it. Most research in neuroscience focuses on circuits that directly respond to stimuli or generate motor output. But what of the circuits and mechanisms that control these direct responses, that modulate them and turn them off and on?

Self-regulated switching is vital to the operation of complex machines such as computers. The essential building block of a computer is a voltage-gated switch, the transistor, that is turned off and on by the same sorts of currents that it controls. By analogy, the question of my title refers to neural pathways that not only carry the action potentials that arise from neural activity, but are switched off and on by neural activity as well. By what biophysical mechanisms could this occur?

In the spirit of this volume, the point of this contribution is to raise a question, not to answer it. I will discuss three possible mechanisms—neuromodulation, inhibition, and gain modulation—and assess the merits and short-comings of each of them. I have my prejudices, which will become obvious, but I do not want to rule out any of these as candidates, nor do I want to leave the impression that the list is complete or that the problem is in any sense solved.

Neuromodulators versus Neurotransmitters

Neuromodulators can dramatically alter the responsiveness of neurons and the transmission properties of synapses (Marder and Calabrese 1996). They also have profound impacts on behavioral responsiveness—wakefulness and sleep being a prime example. However, neuromodulators are thought to work on a rather coarse scale, both temporally and spatially. Thus, while they might be able to activate large numbers of neurons on a seconds time scale, they may not be able to target small enough groups of specific neurons rapidly enough to fulfill the switching role we seek. As a result, neuromodulation is not generally considered to be a candidate mechanism for rapid and precise switching of complex neural circuits and responses. Nevertheless, it is good to keep in mind that this standard wisdom may be wrong (see Sherman and Guillery 1998), and neuromodulation may play a bigger role in neuronal switching than we currently suspect.

Neurons or Synapses

The state of a neural circuit and the information that it represents is generally associated with the level and pattern of activity of its neurons. Following this conventional view, as I do here, switching in neural circuits corresponds to modifying that neural activity. However, it is worth mentioning an alternative way of thinking. Synapses are remarkably plastic over a large range of time scales (see Abbott and Nelson, 2000, for example). This raises the possibility that a neural circuit might more appropriately be characterized by the state of its synapses rather than by the state of its neurons. Neural activity might then play a switching role by putting synapses into an appropriate functional state, and switching might be accomplished primarily by modifying the synapses within a neural circuit. In the examples I discuss later in this chapter this is not the case; switching is accomplished by modifying neurons not synapses.

Hard versus Soft Switches

Attention can have both modulatory and gating effects on neuronal responses. For some neurons, attention modulates response amplitude while leaving selectivity unaltered (Connor et al. 1996; McAdams and Maunsell 1999; Treue and Martínez-Trujillo 1999). For other neurons, attention has a more dramatic gating effect, making it difficult to evoke any response at all in the absence of attention (Gottlieb, Kusunoki, and Goldberg 1998; Seidemann,

Zohary, and Newsome, 1998). These two types of modification correspond to what we might call soft and hard switching.

Due the existence of a threshold for action potential generation, hard switching can be accomplished by strong inhibition. In other words, a neuron can be switched from a responsive to a nonresponsive state by hyperpolarizing it below threshold so it cannot fire any action potentials. Such a mechanism has been proposed in the context of shifter circuits, an interesting discussion of and proposal for switching in neural circuits by Anderson and Van Essen (1987) and expanded upon by Olshausen, Anderson, and Van Essen (1993). An observed correlate of this form of switching may be the up- and down-state behavior seen in intracellular in vivo recordings (see Stern, Jaeger, and Wilson 1998, for example).

Using hard, on-off switching through strong inhibition requires us to postulate that inhibitory neurons play a much more active and precise role in cognitive processing than they are generally given credit for. The general picture that emerges has circuits of excitatory neurons responding to stimuli and generating motor responses, with a network of inhibitory neurons controlling these excitatory networks and the responses they generate. A puzzle here might be the relatively small fraction of inhibitory neurons in cortex given that these are supposed to be responsible for controlling and switching sensory pathways and motor responses in a precise manner.

An alternative to the hard switching provided by strongly inhibiting neurons is a form of soft switching produced by modulating the gain of neurons. Gain modulation appears to be a primary mechanism by which cortical neurons nonlinearly combine input signals (reviewed by Salinas and Thier 2000). It shows up in a wide range of contexts including the gaze-direction dependence of visual neurons in posterior parietal cortex (Andersen and Mountcastle 1983; Andersen, Essick, and Siegel 1985), and the effects of attention on neurons in areas V4 (Connor et al. 1996; McAdams and Maunsell 1999) and MT (Treue and Martínez-Trujillo 1999). Gain modulation has been proposed as a mechanism for generating a variety of ''nonclassical'' receptive field properties of neurons in primary visual cortex (Heeger 1992), and for the neural computation of coordinate transformations relevant for tasks ranging from visually guided reaching (Zipser and Andersen 1988; Salinas and Abbott 1995; Pouget and Sejnowski 1997) to invariant object recognition (Salinas and Abbott 1997).

Although gain modulation is clearly associated with attentional effects, it is not obvious how it could be used to generate switching in neuronal circuits. Gain modulation is a more subtle effect, sometimes modify responses by only 10–20 percent, than the on-off switching we seek. Thus, for gain modulation or any other soft switching mechanism to be a viable candidate for neuronal switching, additional mechanisms must be introduced to amplify the effects of modest gain modulations to provide all-or-none, on-off switching. The remaining sections are devoted to this issue.

Amplifying Gain Modulation

How can a small amount of gain modulation lead to dramatic changes in behavior? Here, in work done in collaboration with Jian Zhang (Zhang and Abbott 2000), I discuss two possible answers to this question. These involve the circuits shown in figure 21-1. In the model of figure 21-1A, responses in a downstream neuron (the upper neuron in figure 21-1A) are normally suppressed by a rather precise balance between excitatory and inhibitory input. Gain modulation of the network neurons driving this downstream neuron (the starred neurons in figure 21-1A) disrupts this balance allowing strong excitatory input to drive the downstream neuron. Amplification arises due to the cancellation of strong excitatory drive by an equally strong balanced inhibitory input (see Shadlen and Newsome 1994; Troyer and Miller 1997, for example).

The second example uses gain modulation to alter the effective recurrent connections of a neural circuit. In the circuit of figure 21-1B, the synaptic connections among the bottom row of neurons are funneled through the upper row of neurons (such an architecture was studied in a different context by Hahnloser et al. 1999). Neurons in the upper row are subject to gain modulation (as indicated by the stars). Modifying the gain of the upper row of neurons changes the synaptic connectivity among the lower row of neurons, which can dramatically alter the selectivity and response amplitude of the network activity evoked by feedforward input.

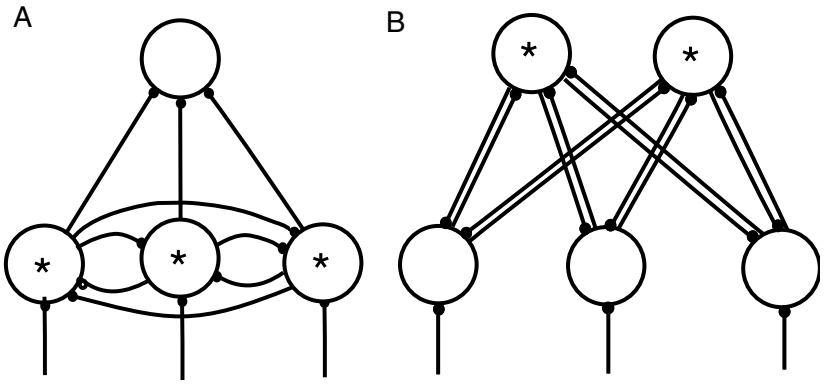

Figure 21-1. Two networks that amplify gain modulation effects. In both panels, neurons subject to gain modulation are denoted by stars. Feedforward input arising from a hypothetical stimulus enters the network through the afferents indicated at the bottom of the circuit diagrams. (A) A network of recurrently connected, gain-modulated neurons drives a downstream neuron. (B) A network of neurons (*lower row*) is interconnected by pathways that pass through a set of gain-modulated neurons (*upper row*).

Switching through Modulation of Balanced Synaptic Input

In our implementation of the circuit of figure 21-1A, hundred recurrently connected integrate-and-fire neurons with gain modulation (represented by the starred units in figure 21-1A) drive a single downstream integrate-and-fire neuron (the unstarred neuron in figure 21-1A). Feedforward inputs to the recurrently coupled network neurons were chosen so that each of them is tuned to a parameter characterizing the sensory input, which we refer to as an image orientation angle in subsequent figures. The connections between the recurrent network and the downstream neuron were developed by an anti-Hebbian learning rule, which established a balance between excitatory and inhibitory inputs to the downstream neuron (Zhang and Abbott 2000).

Gain modulation is applied to the neurons in the recurrent network by adjusting the effective membrane time constant of the integrate-and-fire model. Figure 21-2A shows the effect of the gain modulation on the response of one network neuron to different stimulus angles. This is a typical gain-modulated response tuning curve similar to those seen experimentally (see McAdams and Maunsell 1999, for example). The modulation is multiplicative, and the modulated neurons retain their selectivity when their response amplitudes are modified. When the network is gain modulated, different neurons are modulated differently. Figure 21-2B shows the effect of modulation on the entire population response of the network to a single stimulus orientation. The amount of modulation is small for all network neurons.

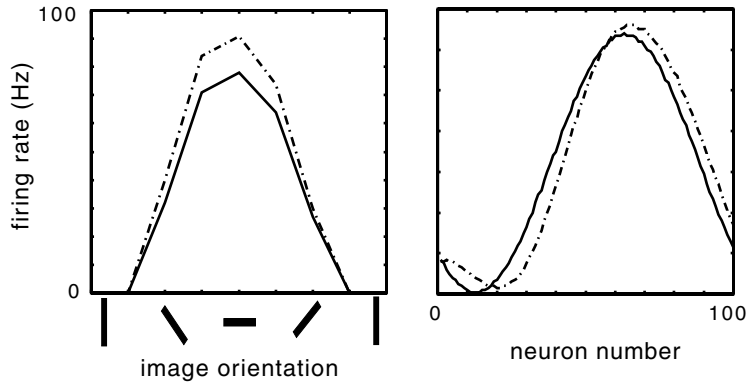

Figure 21-2. Gain modulation of the network neurons of figure 21-1A. *Left,* each network neuron is tuned to the orientation of the stimulus as indicated by its firing rate in response to different image orientations. Solid curve is without gain modulation and dashed curve is with gain modulation. *Right,* the entire population response to a given stimulus orientation is plotted by graphing the firing rate of each neuron as a function of its identifying index. Gain modulation shifts the responses indicated by the solid curve to responses indicated by the dashed curve.

Figure 21-3 shows that modest gain modulation of the network neurons has a large impact on the response of the downstream neuron. Without modulation, the downstream neuron responds weakly, if at all, to the stimulus (upper panel of figure 21-3). When the population activity of the network neurons is slightly modified by gain modulation, the cancelation of balanced excitatory and inhibitory inputs responsible for this weak response is disrupted, and the downstream neuron responds to the stimulus vigorously and in a selective manner (lower panel of figure 21-3).

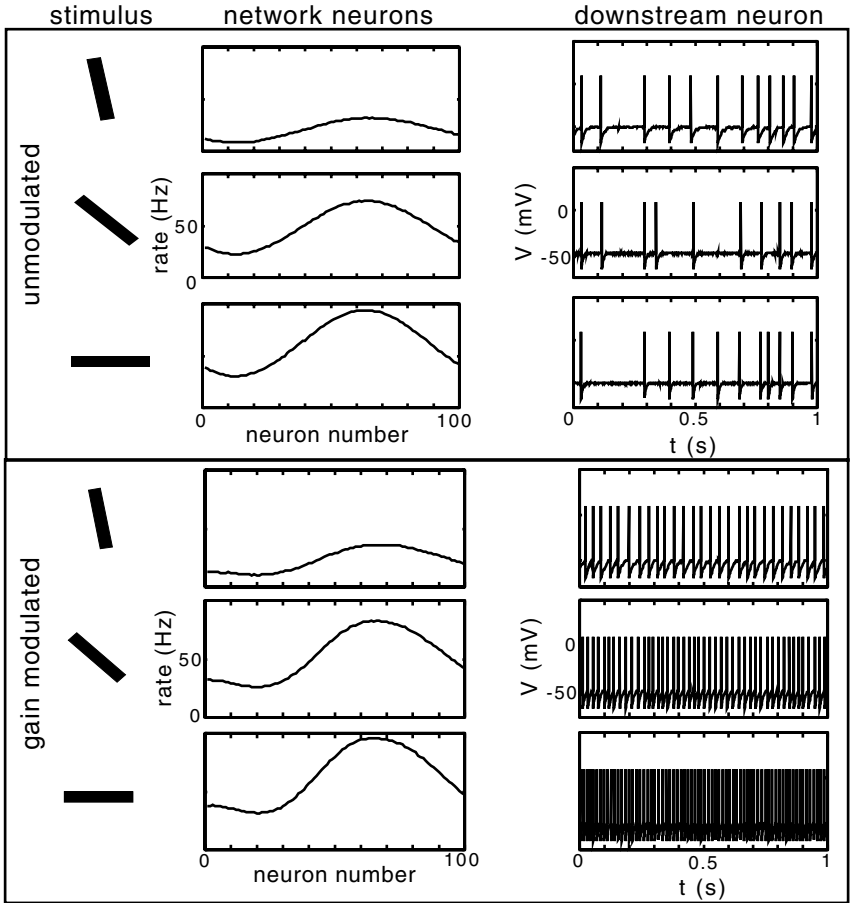

Figure 21-3. Responses of the network and downstream neurons to different stimulus orientations without and with gain modulation. Stimulus orientations are indicated at left. Population responses of the network neurons are plotted in the left column of graphs in the same format as in the right panel of figure 21-2. The membrane potential of the downstream neuron is shown in the right column of plots. *Top,* without gain modulation, the downstream neuron responds weakly to the stimulus. *Bottom,* with gain modulation, the downstream neuron shows a strong, tuned response to the stimulus.

Any system for attention-based switching must distinguish attended stimuli from large-amplitude (i.e., high-contrast) stimuli. In another words, we want to pay attention to stimuli because they are significant, not simply because they are intense. This is a potential problem with switching achieved by hyperpolarizing a neuron below its action potential threshold. For a given level of hyperpolarization, an intense enough stimulus might evoke a response. In the model with balanced input, increasing image intensity (contrast) raises the level of both excitatory and inhibitory input to the downstream neuron, so the net effect is small (left column of figure 21-4). A strong, contrast-dependent response is only generated when gain modulation throws off this balance (right column of figure 21-4).

Switching through Gain Modulation of Recurrent Pathways

A recurrent network can selectively amplify specific aspects of the input it receives, with selectivity determined by the synaptic connections within the network (Abbott, 1994; Douglas et al., 1995). When recurrent excitation is strong (near the limit of instability), the network amplifies by a large factor, and it becomes highly selective. The amplitude of the network response in this case is very sensitive to the overall level of excitation within the network.

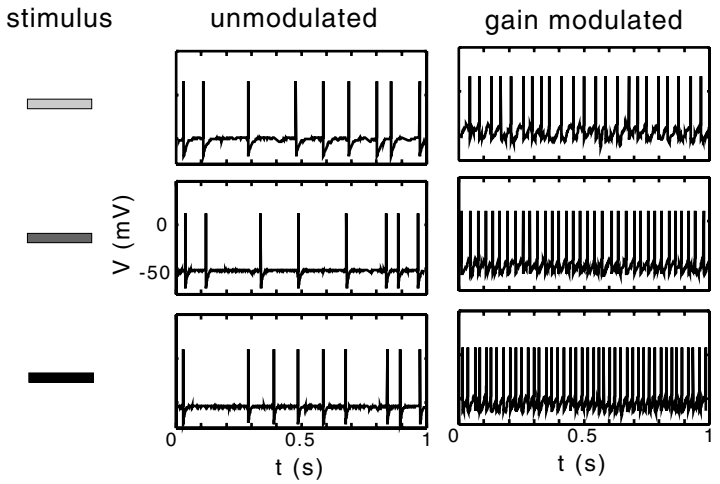

Figure 21-4. Effect of contrast on the responses of the downstream neuron. The level of contrast of the stimulus is indicated at left. The left column of plots shows the membrane potential of the downstream neuron in the absence of gain modulation of the network neurons. The response is weak and independent of contrast. The right column of plots shows that the responses of the downstream neuron are strong and sensitive to contrast when the network neurons are gain modulated.

In the architecture of figure 21-1B, the recurrent connections among the network neurons are affected by the gain of the gain-modulated neurons. Suppose that we label the neurons in the lower row of figure 21-1B with indices i or j and those in the upper row with an index a. Let M_i^a denote the strength of a synapse from gain-modulated neuron a to network neuron i and N_j^a denote the strength of a synapse from network neuron j to gain-modulated neuron a. In a linear approximation, the matrix of synaptic weights for the network neurons is proportional to $\sum_a M_i^a N_j^a$. If neuron a is gain modulated by a factor g_a, this connectivity matrix is modified to $\sum_a g_a M_i^a N_j^a$. Thus, gain modulation modifies the connectivity of the network. This can have a large effect on the response of the network, especially if it is operating with a high degree of amplification.

Discussion

To extend our understanding of neural circuits from the representation of information to cognitive processing, we must face complex issues of neural control and switching of neural circuits. At the present time, we are more in a gathering than a ruling-out situation, and any reasonable candidate switching mechanism for controling sensory and motor circuits is worth studying and analyzing.

References

L.F. Abbott. ''Decoding neuronal firing and modeling neural networks,'' *Quarterly Review of Biophysics* **27** (1994): 291–331.

L.F. Abbott and S.B. Nelson. (2000) ''Synaptic plasticity: Taming the beast,'' Nature Neuroscience **3** (2000): 1178–1183.

R.A. Andersen, G.K. Essick, and R.M. Siegel. ''Encoding of spatial location by posterior parietal neurons,'' *Science* **230** (1985): 450–458.

R.A. Andersen and V.B. Mountcastle. ''The influence of the angle of gaze upon the excitability of light-sensitive neurons of the posterior parietal cortex,'' *Journal of Neuroscience* **3** (1983): 532–548.

C.H. Anderson and D.C. Van Essen. ''Shifter circuits: A computational strategy for dynamic aspects of visual processing,'' *Proceedings of the National Academy of Sciences of the United States of America* **84** (1987): 6297–6301.

D.E. Connor, J.L. Gallant, D.C. Preddie, and D.C. Van Essen. ''Responses in area V4 depend on the spatial relationship between stimulus and attention,'' *Journal of Neurophysiology* **75** (1996): 1306–1308.

R.J. Douglas, C. Koch, M. Mahowald, K.A.C. Martin, and H.H. Suarez. ''Recurrent excitation in neocortical circuits,'' *Science* **269** (1995): 981–985.

J.P. Gottlieb, M. Kusunoki, and M.E. Goldberg. ''The representation of visual salience in monkey parietal cortex,'' *Nature* **391** (1998): 481–484.

R. Hahnloser, R.J. Douglas, M. Mahowald, and K. Hepp. ''Feedback interaction between neuronal pointers and maps for attentional processing,'' *Nature Neuroscience* **8** (1999): 746–752.

D.J. Heeger. ''Normalization of cell responses in cat striate cortex,'' *Visual Neuroscience* **9** (1992): 181–198.
E. Marder and R.L. Calabrese. ''Principles of rhythmic motor pattern generation,'' *Physiological Reviews* **76** (1996): 687–717.
C.J. McAdams and J.H.R. Maunsell. ''Effects of attention on orientation-tuning functions of single neurons in macaque cortical area V4,'' *Journal of Neuroscience* **19** (1999): 431–441.
B.A. Olshausen, C.H. Anderson, and D.C. Van Essen. ''A neurobiological model of visual attention and invariant pattern recognition based on dynamical routing of information,'' *Journal of Neuroscience* **13** (1993): 4700–4719.
A. Pouget and T.J. Sejnowski. ''Spatial transformations in the parietal cortex using basis functions,'' *Journal of Cognitive Neuroscience* **9** (1997): 222–237.
E. Salinas and L.F. Abbott. ''Transfer of coded information from sensory to motor networks,'' *Journal of Neuroscience* **15** (1995): 6461–6474.
E. Salinas and L.F. Abbott. ''Invariant visual responses from attentional gain fields,'' *Journal of Neurophysiology* **77** (1997): 3267-3272.
E. Salinas and P. Thier. ''Gain modulation: A major computational principle of the central nervous system,'' *Neuron* **27** (2000): 15–21.
M.N. Shadlen and W.T. Newsome. ''Noise, neural codes and cortical organization,'' *Current Opionion in Neurobiology* **4** (1994): 569–579.
S.M. Sherman and R.W. Guillery. ''On the actions that one nerve cell can have on another: Distinguishing drivers from modulators,'' *Proceedings of the National Academy of Science (USA)* **95** (1998): 7121–7126.
E. Seidemann, E. Zohary, and W.T. Newsome. ''Temporal gating of neural signals during performance of a visual discrimination task,'' *Nature* **394** (1998): 72–75.
E.A. Stern, D. Jaeger, and C.J. Wilson. ''Membrane potential synchrony of simultaneously recorded striatal spiny neurons in vivo,'' *Nature* **394** (1998): 475–478.
S. Treue and J.C. Martínez-Trujillo. ''Feature-based attention influences motion processing gain in macaque visual cortex,'' *Nature* **399** (1999): 575–579.
T.W. Troyer and K.D. Miller. ''Physiological gain leads to high ISI variability in a simple model of a cortical regular spiking cell,'' *Neural Computation* **9** (1997): 971–983.
J. Zhang and L.F. Abbott. ''Gain modulation in recurrent networks,'' In Bower, J. ed. *Computational Neuroscience, Trends in Research 2000* (Amsterdam: Elsevier, 2000), 623–628.
D. Zipser and R.A. Andersen. ''A back-propagation programmed network that simulates response properties of a subset of posterior parietal neurons,'' *Nature* **331** (1988): 679–684.