Chapter 7  Steady state of circuits with dynamic synapses

7.1  Introduction

Multiplication and division are essential components of many models of cortical function (e.g., Heeger, 1993), and there is physiological evidence for divisive interactions between stimuli (Rose, 1977; Dean et al., 1980; Reid et al., 1987). However, the underlying biophysical mechanism responsible for this nonlinearity is not clear, and a number of different mechanisms are possible (Mel, 1994; Somers et al., 1996; Salinas and Abbott, 1996). Shunting inhibition is a commonly proposed mechanism for division, but the conductance changes required have not been observed so far (Berman et al., 1989; Ferster and Jagadeesh, 1992) and in fact shunting inhibition acts subtractively rather than divisively in spiking neurons (Holt and Koch, 1997; chapter 4). We suggest another possible mechanism based on the phenomena of paired pulse depression and facilitation.

In vitro in cortex, synaptic depression and facilitation have been observed at a variety of different synapses in olfactory cortex (e.g., Bower and Haberly, 1986), somatomotor areas (Thomson and West, 1993; Thomson et al., 1993a, 1993b, 1995; Thomson and Deuchars, 1994) and in visual cortex (Stratford et al., 1996; Markram and Tsodyks, 1996; Tsodyks and Markram, 1997; Abbott et al., 1997). It is not yet clear how widespread the phenomena of depression and facilitation are in vivo. Recently Abbott et al. (1997) and Tsodyks and Markram (1997) have suggested a number of ways in which synaptic depression could be computationally useful. The steady-state synaptic current delivered by synapses from layer 4 to layers 2–3 and synapses between layer 5 cells is approximately independent of presynaptic firing rate when the presynaptic firing rate is above 20 Hz, making the postsynaptic cell sensitive to fractional changes in its input rather than the absolute level. However, the layer 4 to layer 4 synapses observed by Stratford et al. (1996) show considerably less synaptic depression; synaptic current is a slowly saturating function of the presynaptic firing rate rather than a constant. We suggest that the cortex uses this slowly saturating function as an approximation to a logarithm.

Thalamic afferents to visual cortex terminate primarily on layer 4 spiny stellate cells. Anatomically, however, the majority of the input to these cells comes from other cortical sources (Peters and Payne, 1993; Peters et al., 1994). Most of this comes from cells with similar receptive fields. 40% of the excitatory synapses onto spiny stellate cells come from other spiny stellate cells, and about 45% come from layer 6 pyramidal cells (Ahmed et al., 1994; Anderson et al., 1994a, 1994b). Since layer 4 cells have a strong projection to layer 6, and layer 4 is the primary cortical target of layer 6 cells, there is an important feedback loop between these two layers. Inactivation of layer 6 cells can affect the firing rate of layer 4 cells by a factor of two or more (Grieve and Sillito, 1991, 1995). The presence of strong layer 4 to layer 4 and layer 4 to layer 6 to layer 4 feedback loops suggests that a small thalamic current is amplified by recurrent cortical excitation (Douglas and Martin, 1991).

Models based on the idea of an amplifier (Suarez et al., 1995; Somers et al., 1995; Maex and Orban, 1996) can explain a variety of puzzling physiological results but so far have assumed that synapses are non-depressing or only very slowly depressing. However, layer 6 to layer 4 synapses in vivo show pronounced facilitation. Synapse strength can increase by a factor of two or more (Ferster and Lindström, 1985a, 1985b; Stratford et al., 1996). This study suggests that the facilitation at synapses of layer 6 cell axons compensates for depression at synapses on layer 4 axons. By using a loop consisting of depressing and facilitating synapses instead of ordinary linear synapses, the cortex might be able to perform additional computations. The firing rate of layer 6 cells may be approximately the logarithm of the firing rate of layer 4 cells; additive and subtractive effects on the
layer 6 cells will have approximately multiplicative and divisive effects on the layer 4 cells.

### 7.2 Synaptic depression model

Abbott *et al.* (1997)\(^1\) use a simple mathematical model of depressing synapses:

\[
\frac{dA}{dt} = \frac{A_\infty - A(t)}{\tau} - \gamma \sum_i \delta(t - t_i) A(t)
\]

where \(A(t)\) is the amplitude of the synapse if a presynaptic impulse occurs at time \(t\). An incoming spike decreases the amplitude of the next impulse to \((1 - \gamma)A\), and then the amplitude decays exponentially back to \(A_\infty\). Replacing the sum of \(\delta\) functions by a continuous firing rate\(^2\) \(f(t)\) gives

\[
\frac{dA}{dt} = \frac{A_\infty - A(t)}{\tau} - \gamma f(t) A(t).
\]

At steady state, then,

\[
A = \frac{A_\infty}{1 + f \gamma \tau},
\]

so the synaptic current delivered will be

\[
I_{\text{syn}} = f A = \frac{f A_\infty}{1 + f \gamma \tau}.
\]

This approximates the average synaptic current from a synapse driven by a Poisson process with rate \(f\) quite well (figure 7.1).

Abbott *et al.* (1997) measure \(\gamma \tau\) values in the range of 28 to 210 ms for synapses from layer 4 to layers 2–3. However, Stratford *et al.* (1996) report that layer 4 to layer 4 synapses in their preparation do not show visible synaptic depression when the interspike firing rate is 20 Hz. When presynaptic firing rates are increased to 80 Hz the amplitude is a factor of two smaller (Stratford, personal communication), suggesting that for these synapses \(\gamma \tau \approx 1/80\) Hz or 12.5 ms. We examine the effect of both values.

### 7.3 Effect on simple recurrent networks

Douglas and Martin (1991) suggest that the recurrent cortical input to the layer 4 cells acts as an amplifier, so the firing rate of the layer 4 cells is approximately proportional to the LGN input current but is perhaps a factor of five or so larger than it would be if only the synapses from the LGN were present. In symbols,

\[
f = \alpha (I_{\text{ff}} + I_{\text{rec}}),
\]

where \(f\) is the firing rate of the layer 4 cells, \(I_{\text{ff}}\) is the feedforward thalamic input, \(I_{\text{rec}}\) is the recurrent cortical input, and \(\alpha\) is the slope of the current–discharge curve for the cortical cells. For the moment we consider input only from other layer 4 cells, so

\[
I_{\text{rec}} = Af,
\]

---

\(^1\)Abbott *et al.* (1997) use a slightly different notation: their \(f\) is \(1 - \gamma\) and their \(r(t)\) is our \(f(t)\).

\(^2\)Abbott *et al.* (1997) work with continuous rates by assuming the interspike intervals are perfectly regular and then solving equation 7.1 for the steady state. The approach here gives a much more tractable expression which turns out to be slightly more accurate for spike trains from a Poisson process than their formulation (not shown).
where $A$ is the synaptic weight from layer 4 cells to other layer 4 cells. Solving this system,

$$f = \frac{\alpha I_f}{1 - \alpha A} = G\alpha I_f,$$

(7.7)

where $G$ is the gain (i.e., the ratio of the firing rate to what the firing rate would be in the absence of any cortical feedback). Douglas and Martin (1991) estimate that $G$ is somewhere close to 5.

If synapses are non-depressing, then $A$ is a constant, and therefore $G = 1/(1 - \alpha A)$ is a constant independent of the amount of input current. The system is a proportional amplifier. However, if $A$ is not a constant, then the response of the system is no longer proportional to its input. If we use the parameters from Abbott et al. (1997), it would not at all be surprising to find that the system does not act as a proportional amplifier at firing rates above 20 Hz, since $I_{rec}$ is approximately constant and therefore cannot be proportional to $I_f$. However, it may be more surprising that the system ceases to be a proportional amplifier long before $I_{rec}$ comes close to saturating.

With depressing synapses, equation 7.7 becomes

$$f = \frac{\alpha I_f}{1 - \frac{\alpha A_{\infty}}{1 + \gamma_f}}.$$

(7.8)

Figure 7.2 shows the solution to this equation. Note that for $\gamma_f = 12.5$ ms, $I_{syn}$ does not saturate until about 150 Hz (figure 7.1), whereas there is very little amplification above even 20 Hz.

In fact, the gain $G = 1/(1 - \alpha A_{\infty}/(1 + \gamma_f))$ drops precipitously for $f > 2$ Hz for $\gamma_f = 90$ ms and for $f > 10$ Hz for $\gamma_f = 12.5$ ms (figure 7.3). The drop is even more severe if we consider the small signal or incremental gain, i.e., the ratio of the change in output to the change in input (the
Figure 7.2: Synaptic depression dramatically reduces the output of the network, even at firing rates well before $I_{syn}$ saturates. Solid line is the output if synapses are perfectly linear. For the top dotted line ($\gamma \tau = 12.5$ ms), $I_{syn}$ saturates at firing rates of 150 Hz; for the bottom ($\gamma \tau = 90$ ms), $I_{syn}$ saturates at around 20 Hz (compare with figure 7.1). $\alpha$ was set to 1 so the gain is simply the ratio of the $y$ to $x$ coordinate and the small signal gain is the slope.

Figure 7.3: The gain $G$ (panel A) and the small signal (or incremental) gain $g$ (panel B) fall off much more steeply than one might naively expect based on the plot of $I_{syn}$ vs. $f$ (figure 7.1).
slope in figure 7.2):

\[
g = \frac{1}{\alpha} \frac{df}{dI_{ff}} = \frac{1}{\alpha} \frac{d}{dI_{ff}} \alpha (I_{ff} + I_{rec})
\]

\[
= 1 + \frac{dI_{rec}}{dI_{ff}}
\]

\[
= 1 + \alpha \frac{dI_{rec}}{df} \left( \frac{1}{\alpha} \frac{df}{dI_{ff}} \right)
\]

\[
= \frac{1}{1 - \alpha \frac{dI_{rec}}{df}}.
\]  

(7.9)

Since \( I_{rec} = f A_{\infty} / (1 + \gamma f) \),

\[
g = \frac{1}{1 - \frac{\alpha A}{(1 + \gamma f)^2}}.
\]  

(7.10)

This depends on \((1 + \gamma f)^2\) rather than on \(1 + \gamma f\). It falls off more steeply than the gain \( G \) (figure 7.3B).

### 7.3.1 Recurrence greatly amplifies deviations from linearity

Why is the effect of even a small nonlinearity in \( I_{syn} \) so dramatic? Suppose we start with a system with gain \( G_0 \), and then we perturb \( I_{rec}(f) \rightarrow I_{rec}(f)[1 + \epsilon(f)] \). From equations 7.6 and 7.7, the new gain will be

\[
G_\epsilon = \frac{1}{1 - \frac{\alpha A}{1 + \epsilon}} = \frac{1}{1 - \alpha A - \alpha \epsilon}
\]

\[
= \frac{1/(1 - \alpha A)}{1 - \alpha A/(1 - \alpha A)}
\]

\[
= \frac{G_0}{1 - G_0 \epsilon \alpha A},
\]

and since \( \alpha A = 1 - 1/G_0 \),

\[
G_\epsilon = \frac{G_0}{1 - \epsilon G_0 (1 - 1/G_0)}
\]

\[
= G_0 (1 + (G_0 - 1) \epsilon + \cdots).
\]  

(7.11)

Thus percent changes in the recurrent current have an effect proportional to the square of the gain. For example, if we change the recurrent current by 1% and the original gain is 5, there will be a change of about 20% in the output current.

The small signal gain is even more sensitive to perturbations. If the original small signal gain
was \( g_0 \), then from equation 7.9 on the page before, the new small signal gain will be

\[
g_e = \frac{1}{1 - \alpha \frac{dI_{rec}}{df}(1 + \epsilon)} = \frac{1}{1 - \alpha \frac{dI_{rec}}{df} - \alpha \frac{dI_{rec}}{df}} = \frac{1}{(1 - \alpha I_{rec}/df)} \frac{1 - \alpha \frac{dI_{rec}}{df}}{1 - \alpha \frac{dI_{rec}}{df}} = \frac{g_0}{1 - g_0 \alpha \frac{dI_{rec}}{df}} = \frac{g_0}{1 - g_0 \alpha \frac{dI_{rec}}{df} - \alpha I_{rec} \frac{de}{df}}.
\]

Since \( \alpha dI_{rec}/df = 1 - 1/g_0 \) (equation 7.9) and \( \alpha I_{rec} = f - \alpha I_{ff} = (1 - 1/G)f \),

\[
g_0 = \frac{g_0}{1 - (g_0 - 1)\epsilon - g_0(1 - \frac{1}{G}) \frac{de}{df}} = g_0 \left[ 1 + (g_0 - 1)\epsilon + g_0 \left( 1 - \frac{1}{G} \right) \frac{de}{df} \right].
\]

(7.12)

For small \( \epsilon \) values, the change is proportional to \( g_0^2 \epsilon + g_0 f \frac{de}{df} \). Thus \( g \) decreases more steeply than \( G \) (figure 7.3).

### 7.4 A possible role for layer 6

The analysis so far has ignored a number of important factors, among them the layer 6 input to layer 4. Blocking layer 6 with GABA iontophoresis causes a decrease in layer 4 response amplitudes by a factor of 2 or more, so the layer 6 input is clearly important. Furthermore, the layer 6 input to layer 4 has been known for many years to show strong facilitation rather than depression \emph{in vivo} (Ferster and Lindström, 1985a, 1985b). It is possible that facilitation compensates for the synaptic depression.\(^3\)

Using the more moderate synaptic depression observed by Stratford \emph{et al.} (1996), the synaptic current \( I_{syn} \) is a slowly saturating function of the presynaptic firing rate (figure 7.1). This saturating function might be used as an approximation to a logarithm\(^4\), and the facilitation observed in the synapses from layer 4 to layer 6 might be an approximation to an exponential. The resulting loop would have a linear input–output relationship, but subtractive inhibition in layer 6 would have a divisive effect on layer 4.

#### 7.4.1 A simplified example

To illustrate the mechanism, suppose first that synaptic depression and facilitation exactly compute the logarithm and exponent:

\[
A_4 \approx A_0 \log s_4 f_4 \quad \text{for } s_4 f_4 > 1
\]

\[
A_6 \approx A_6 e^{a f_6}
\]

(7.13)

\(^3\)The layer 6 projection to the thalamus will have mathematically the same effect on layer 4 cells as the \( i \)6 projection to layer 4 if the thalamocortical synapses are non-depressing, since it merely adds an amount proportional to the layer 6 firing rate to the layer 4 input.

\(^4\)See Tal and Schwartz (1997) for a similar approximation to a logarithm using the refractory period of a neuron.
where \( s_4 \) and \( s_6 \) are constants. The firing rates of the layer 4 and layer 6 cells are given by

\[
\begin{align*}
\dot{f}_4 &= \alpha_4 (I_{ff} + A_6 f_6) \\
\dot{f}_6 &= \alpha_6 (A_4 f_4 - I_{inh})
\end{align*}
\]

(7.14)

where \( \alpha \) is the slope of the current discharge curve, \( I_{ff} \) is the synaptic current from the thalamic afferents, \( A_4 \) and \( A_6 \) are the amplitudes of the synapses on the axons of the layer 4 and layer 6 cells, and \( I_{inh} \) is an inhibitory current onto layer 6 cells. Eliminating \( f_6 \),

\[
f_4 = \alpha_4 I_{ff} + \alpha_4 A_6 e^{s_6 A_6 (A_{46} \log s_4 f_4 - I_{inh})}
\]

(7.15)

Setting \( s_6 \alpha_6 A_{46} = 1 \) makes the feedback current proportional to \( f_4 \) with a proportionality constant governed by \( I_{inh} \). The system simplifies to

\[
f_4 = \frac{\alpha_4 I_{ff}}{1 - \alpha_4 A_6 s_4 e^{-I_{inh}/A_{46}}}
\]

(7.16)

so the firing rate of layer 4 cells is proportional to their input times a function which depends on an inhibitory current. Inhibition in layer 6 therefore has a divisive effect on layer 4.

### 7.4.2 More realistic synapses

Although synaptic depression is only an approximation to a logarithm, it may be a sufficiently accurate approximation to support divisive interactions. Synaptic facilitation in layer 6 cells has not yet been quantitatively characterized; we first derive a form that makes the layer 4 to layer 6 to layer 4 loop into a linear amplifier, and then we analyze the effect of inhibition in layer 4.

Equations 7.5 and 7.6 on page 84 can be modified to include layer 6:

\[
\begin{align*}
\dot{f}_4 &= \alpha_4 [I_{ff} + A_6 f_6 + A_{44} f_4] \\
\dot{f}_6 &= \alpha_6 [A_4 f_4 - I_{inh}]
\end{align*}
\]

(7.17) (7.18)

where \(|x| = 0\) if \( x < 0 \) and \( x \) otherwise. \( A_{44} \) is the amplitude of the synapses from layer 4 to layer 4, which will depend on frequency \( f \) as described by equation 7.3 on page 84; \( A_{46} \), the weight from layer 4 to layer 6, has the same frequency dependence but a possibly different amplitude. \( I_{inh} \) is inhibitory current supplied to layer 6.

We want to calculate what the form of \( A_6 \) is so that the system acts as a proportional amplifier when \( I_{inh} = 0 \). In a proportional amplifier, the total input current to layer 4 cells is proportional to the thalamic input:

\[
I_{ff} + A_6 f_6 + A_{44} f_4 = G I_{ff}
\]

where \( G \) is the gain of the network. Eliminating \( I_{ff} \) using equation 7.17,

\[
I_{ff} = \frac{f_4 - \alpha_4 A_6 f_6 - \alpha_4 A_{44} f_4}{\alpha_4} = \frac{A_6 f_6 + A_{44} f_4}{G - 1}.
\]

Following equation 7.3,

\[
A_{44} = \frac{A_{44\infty}}{1 + \gamma_{44} f_4} \quad A_{46} = \frac{A_{46\infty}}{1 + \gamma_{46} f_4},
\]

(7.19)

---

\(^5\)Note that other values of \( s_6 A_{46} \) will make the firing rate \( f_4 \) be a nonlinear function of \( I_{ff} \). This could be used, for example, to compute an approximate square (Heeger, 1992b).
Figure 7.4: Inhibitory input to layer 6 has a divisive effect on layer 4 firing rates. **A:** Firing rate of layer 4 cells as a function of the input current $I_g$ for different values of $I_{inh}$. At higher firing rates, changing $I_{inh}$ changes only the slope of the curve. **B:** Firing rate of layer 6 cells under the same conditions. The kinks in the curves in A are present because layer 6 firing rates cannot be negative; the bend occurs when the layer 6 firing rate becomes positive. Parameters: $\alpha_4 = \alpha_6 = 1$, $A_{44}\infty = 0.5$, $A_{46}\infty = 1$, $G = 5$, $\gamma_4/\gamma_4 = 12.5$ ms, $I_{inh}$ ranged from 0 to 0.02 in steps of 0.004. Note that with these parameters, $I_g$ has the same units as $f_4$ so the gain can be read directly off the graph as the ratio of $f$ to $I_g$.

Using these expressions and equation 7.18, we can eliminate $f_4$. After some algebra,

$$A_0(f) = \left( \frac{G - 1}{G \alpha_4 \alpha_6 A_{46}\infty} \right) \left( \frac{1}{1 - \frac{\gamma_4}{\alpha_6 A_{46}\infty} f_6} - \frac{A_{44}\infty}{\alpha_6 A_{46}\infty} \right)$$  \hspace{1cm} (7.20)

Note that the description of facilitating synapses in equation 7.20 is similar in form to equation 7.3 on page 84 for depressing synapses; the sign of $\gamma_T$ has been reversed, and a constant value subtracted.

If synaptic facilitation in layer 6 cells follows this equation, then layer 4 cells will respond linearly to their input. This expression has a pole for $f_6 = \alpha_6 A_{46}\infty / \gamma_4$, so facilitation cannot have exactly this form, but we will consider only layer 6 firing rates far from the pole.

Since depression is not exactly logarithmic and facilitation is not exactly exponential, this will not exactly implement the log-and-exponentiation transform described above. However, it performs remarkably well. Figure 7.4 shows simulations of the circuit.

The firing rate of layer 6 cells cannot be negative, so there is no divisive effect at very low firing rates. The curve in panel A from which all the lines diverge is the input–output relationship when layer 6 cells are turned off; parameter values have been set so the system has a gain of about 1.5 under those circumstances. When layer 6 cells do begin firing, the system acts almost linearly; it is not exactly linear but so close that it is not easy to see the deviations from linearity on the graph. In this range, changing $I_{inh}$ primarily changes the slope of the curve rather than shifting it.

### 7.4.3 What is the arithmetic operation?

Using this mechanism, subtractive inhibition in layer 6 has a divisive effect on layer 4, but so far we have not specified precisely what the divisor is. It is possible to work out the exact input–output relationship from equations 7.17 through 7.20, but the result is complicated and not useful. Instead, we resort to approximate solutions. Figure 7.5 shows the gain $G$ and the small signal gain $g$ as a function of inhibitory current to layer 6 cells. The gain turns out to be well described by a function
of the form

\[ G(I_{inh}) = \frac{G(0) - 1}{1 + \beta I_{inh}} + 1 \]  

(7.21)

where \( G(0) \) is the gain without any inhibition and \( \beta \) is a constant. Since the feedback is excitatory, the gain cannot be less than 1; that is the origin of the +1 term. A number of models require that the output be divided by a factor of \( 1 + g(x) \) (Heeger, 1992a; Heeger et al., 1996) so this form may be quite useful. The precise expression for \( g(x) \) depends on what sort of depression or facilitation the inhibitory synapses onto layer 6 show.

### 7.5 Conclusions

Synaptic depression has a profound effect on recurrent circuits because any deviation from linearity is amplified greatly by the recurrence. Even if the synapses depress only weakly, as measured by Stratford et al. (1996), the resulting network can hardly be called an “amplifier” at steady state. This effect cannot be counteracted simply by increasing the weight of the recurrent synapses. The gain will still fall off precipitously at higher firing rates, because of the \( 1/(1 + \gamma \tau f) \) term in the denominator of equation 7.8.

Synaptic depression could perform a useful function in an amplifier circuit if it is coupled with synaptic facilitation. If layer 4 to layer 6 synapses display weak synaptic depression, the current into layer 6 could be approximately the logarithm of the layer 4 firing rate. Facilitation in the synapses from layer 6 to layer 4 could approximately undo the effect of the depression. Subtractive inhibition in layer 6 would have an approximately divisive effect on layer 4.

Such a mechanism makes several testable predictions about responses in layer 4 and layer 6:

1. Layer 4 synapses onto layer 6 should show weak paired pulse depression as described by equation 7.19, and layer 6 cells should show facilitation with corresponding parameters given by equation 7.20 over the relevant range of firing rates. A considerable amount of variability in parameter values is most likely present in cortex, but facilitation in the layer 6 population as a whole should approximately compensate for depression in the population of layer 4 synapses.

2. Divisive interactions should not be visible immediately, in the transient response; it should take a few spikes for the layer 4 synapses to depress and the layer 6 synapses to facilitate to reach their steady state levels. Divisive interactions might be apparent only for slowly changing stimuli.

3. Divisive interactions should be visible only in layer 4, not layer 6.
4. Divisive effects should not be visible when the layer 6 cell population is silenced by GABA iontophoresis as in the experiments by Grieve and Sillito (1991, 1995).

5. Layer 6 cells should have a contrast response curve that saturates earlier than layer 4.

To my knowledge, no one examining divisive interactions or contrast response curves has reported what layers they recorded from.