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Some Normal and Abnormal Behavioral Syndromes Due to Transmitter Gating of Opponent Processes

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Opponent processes have long been known to be a basic building block of neural circuits. This article describes properties of opponent processes in which phasic cues and tonic arousal are gated by slowly accumulating chemical transmitters. These opponent processes are called gated dipoles. *Gated dipole circuits exhibit syndromes of formal properties that can be used to support or disconfirm their generative role in a complex body of behavioral data. A wide variety of normal and abnormal behavioral and physiological data exhibit properties analogous to those of gated dipole circuits. These include data about intracellular adaptation, habituation, and rebound; dishabituation and attentional reset by an unexpected event; inverted U properties due to underarousal or overarousal; juvenile hyperactivity; parkinsonism; hyperphagic eating; simple schizophrenia; actions of analgesic agents such as endorphins, electrical brain stimulation, and loud noise; tolerance-withdrawal symptoms, and a new approach to their prevention; normal and abnormal circadian rhythms, as in narcolepsy and manic-depressive psychosis; processing of reinforcing, drive, and motivating signals. Some data predictions derived from gated dipole circuits are also summarized.*

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1. INTRODUCTION

Many mental disorders may be traced to chemical or electrical imbalances of one sort or another. By their very nature, imbalances are properties of systems. To mechanistically understand such disorders, one needs to define the interactions that characterize these systems, since the system interactions give rise to the behavioral properties that one wishes to explain. This property of many mental disorders makes it very difficult to characterize all the factors that lead to behavioral symptoms. Even in cases where a malfunction may be localized within a particular neural subsystem, this subsystem's interactions with several other subsystems may be disrupted. The other subsystems may then also contribute to abnormal symptoms. For example, if two subsystems are mutually inhibitory and one subsystem becomes abnormally hyporeactive, then the other subsystem may become abnormally hyperreactive. In such a situation, it may be difficult to decide whether the syndrome is due to hyporeactivity or to hyperreactivity. Due to the complementary reactions of the two subsystems, many measures of total system performance, such as blood samples, may show no effect or conflicting effects across subjects in whom the degree of imbalance differs.

My colleagues and I have been working over the past two decades on modeling the dynamics underlying normal types of behavior. These models instantiate principles of self-organization whereby individual behavior adapts to fluctuating environmental contingencies on a moment-by-moment basis (Grossberg, 1982a). We have repeatedly found that, as a growing mechanistic understanding of a system's normal behavior was achieved, prescribed changes in system parameters led to formal analogs of familiar abnormal behavioral syndromes. This approach has suggested explanations and predictions about how these parametric changes may generate the abnormal behaviors in question.

We have developed several theoretical approaches for characterizing the mechanisms that subserve multidimensional behaviors. In one approach we study how several properties of a model subsystem simultaneously covary when a parameter of the subsystem, such as its arousal level or transmitter production rate, is varied. Such a constellation, or formal syndrome, of subsystem properties changes in a characteristic way when a parameter of the subsystem is varied. Although no one behavioral property can characterize its generative neural mechanism, a constellation of six behavioral properties that change in a coordinated and paradoxical way when a drug is administered provides a much more constraining type of evidence. If the coordinated and paradoxical change in behavioral properties is the one that is predicted by a subsystem's parametric behavior, then the possibility that the drug influences a subsystem parameter in a manner that will cause the coordinated change becomes an attractive hypothesis. This hypothesis can then be tested in several ways

due to the manner in which the model subsystem is embedded in a more complete model of system interactions.

The present article illustrates this approach by describing the simplest examples taken from a physiological theory of opponent processes. These opponent process subsystems instantiate one principle of neural organization that arises in a larger theory of brain and behavior. In these opponent process subsystems, slowly varying chemical transmitters gate the signals within competing neural pathways in response to fluctuations of phasic cues and of tonic arousal level. Such a network subsystem is called a *gated dipole*. Many variations of the gated dipole design exist in which excitatory transmitters are replaced by a disinhibitory or inhibitory action, feedforward pathways are replaced by feedback pathways, tonically active cells are replaced by phasically reactive cells, or an intercellular network of connections is replaced by an intracellular network of reactions. The basic properties of gated dipole examples are invariant under many of these parametric changes or are altered in predictable ways that can be classified and compared.

Such a classification permits a wide variety of data to be structured as manifestations of the gated dipole design. The possibility of such a classification derives from the fact that the principle of neural organization that is instantiated by gated dipole circuitry is sufficiently general to hold in many behavioral paradigms (Section 2). One of the most striking consequences of this fact is that behavioral and physiological properties which superficially seem unrelated can be generated as formal properties of closely related gated dipole circuits. The gated dipole theory thus provides mechanistic bridges which join together apparently unrelated data domains. Using these mechanistic bridges, incomplete data from one experimental paradigm can be significantly clarified in the light of mechanistically related data from several other experimental paradigms.

For example, theoretical work on the neural mechanisms underlying reinforcement, drive, and incentive motivation originally led to gated dipole opponent processes in which transmitters such as norepinephrine were interpreted to be the slowly varying gating chemical (Grossberg, 1972a; 1972b). These opponent processes were interpreted as simple models of hypothalamic circuits. These circuits have been used as subsystems of a larger brain-behavior theory that has suggested explanations and predictions of a wide range of complex motivated behaviors (Grossberg, 1975; 1982a; 1982b; 1982c; 1984a).

With the appetitive hypothalamically interpreted circuits of gated dipole theory as a starting point, Professor G. A. Carpenter and I realized that a specialized gated dipole circuit has circadian clocklike properties. This realization led to a physiologically and anatomically predictive model of the circadian pacemaker in the suprachiasmatic nuclei of the mammalian hypothalamus. Using this model, we have now quantitatively simulated many of the important data

that are ascribed to this hypothalamic pacemaker (Carpenter and Grossberg, 1983a; 1983b; 1984a; 1984b). These results about motivated behavior and circadian rhythms suggest that the gated dipole design may be used in many specialized circuits throughout the hypothalamus.

Professor Carpenter and I also realized (Carpenter and Grossberg, 1981; 1983a) that an intracellular gated dipole process, in which the gating chemical models an intracellular Ca^{++} process, can quantitatively fit parametric intracellular data that were collected from turtle cones (Baylor and Hodgkin, 1973, 1974; Baylor *et al.*, 1974a, 1974b). Putting together these results about photoreceptors and circadian rhythms shows how one can, at least formally, transform an intracellular gated dipole circuit of photoreceptor type into a circadian pacemaker circuit. A circadian pacemaker has, for example, been reported in the eye of *Aplysia* (Jacklett, 1969). This theoretical bridge from photoreceptor circuits to circadian circuits suggests a useful way to think about the light-sensitivity of circadian pacemakers. Of more general interest is that a theory now exists in which a general design principle and sharply articulated circuit instantiations of the principle has provided a unified framework within which to analyze complex data about photoreceptor transduction, circadian rhythms, and motivated behavior. The work on motivated behavior led to the gated dipole design, but a formal parametric analysis of the implications of this design – of its possible evolutionary specializations – showed that the design *already had latent within it* formal properties akin to photoreceptor data and circadian data. Once this formal bridge was crossed, the plausibility of its physical existence could begin to be appreciated.

Similar parametric explorations of gated dipole circuits showed that their constellations of properties change in pathological ways when certain parameters are varied (Grossberg, 1972b). The striking similarities between data about certain abnormal behavioral syndromes and gated dipole property constellations suggest that pathologies in gated dipole circuits may contribute to mental disorders, such as juvenile hyperactivity, parkinsonism, hyperphagic eating, schizophrenic overarousal, certain analgesic actions, and certain abnormal circadian rhythms, as in narcolepsy and manic-depressive psychosis. These results do not purport to provide a complete theory of any of these phenomena. However the similarity of these behavioral syndromes to constellations of gated dipole properties, and the absence of alternative explanations of these syndromes, warrant that more attention be given to the possible role of gated dipole involvement. At the very least, parametric data capable of decisively supporting or contradicting a gated dipole involvement are needed to validate whatever theory may ultimately prove to be correct.

A precise processing theory does not merely unify the data base. It also shows that a single holistic concept may be used to describe several mechanistically distinct processes. For example, there exist more than one type of adapta-

tion, habituation, and arousal in my theory. In fact, at least three mechanistically distinct, and even mutually antagonistic, types of arousal are needed to explain complex motivated behavior (Grossberg, 1980; 1982a; 1982b; 1984a). The reader should therefore not assume that I use concepts like arousal in all possible ways. I use them below to heighten intuition, but I also use them in only one of several possible mechanistic senses.

A precise processing theory also unifies at the same time that it differentiates. For example, gated dipole circuits have been useful in the analysis of perceptual, cognitive, and motor processes, as well as motivational processes (Grossberg, 1980; 1982a). The circuits that control these different types of behavior may differ in detail as well as in anatomical localization, much as a photoreceptor circuit differs from a circadian circuit. I suggest below, for example, that a similar parametric breakdown may occur in gated dipole circuits of certain juvenile hyperactives and of Parkinson patients. Although the parametric breakdown is suggested to be formally similar in both cases, the circuits that are breaking down are assumed to occur in different brain regions and to control different behaviors.

This article presents only the elements of gated dipole theory. Some readers might prefer an immediate exposure to the most complex uses of these circuits to analyze normal and abnormal behaviors. I recommend that these readers study the articles cited in the References. This article addresses the many readers who believe that phasic cue inputs, tonic arousal level, opponent processes, and chemical gating actions are important components of neural networks, and who wish to know what properties are generated by networks of interacting components of this type. For these scientists it is logically easier to accept the neural existence of gated dipole circuits and to enter freely into their consideration than to deny that their properties play any role in behavior. The ensuing discussion proceeds from the simple toward the more complex, and refers the reader to supplementary reading where appropriate.

2. CHEMICAL GATES: UNBIASED TRANSMITTER-MODULATED SIGNALING

The first concepts that I consider concern the process whereby electrical signals are chemically relayed between nerve cells without a loss of sensitivity. These concepts can be derived as an answer to the following two questions.

What is the simplest law whereby one nerve cell site can send unbiased signals to another nerve site? How can an unbiased signal be maintained when it is mediated by the release of a depletable chemical?

If S(t) is the input signal to one cell site and T(t) is the output signal to the next nerve site, then the linear relationship

$$T = SB \tag{1}$$

where B is a positive constant, is clearly the simplest law of unbiased transmission. By equation 1, the outgoing signal is proportional to the incoming signal, so the signal is relayed perfectly.

When the output signal T(t) is due to the release of a chemical transmitter z(t) in response to the input signal S(t), further consideration is necessary. How is a large and sustained input S(t) prevented from depleting z(t) and thereby causing a progressively smaller signal T(t)? In other words, when T(t) is due to release of a transmitter, the term B in equation 1 may not be constant. It may decrease through time as z(t) is depleted, thereby reducing the sensitivity of T(t) to S(t). In this situation, equation 1 is replaced by the equation

$$T = Sz \tag{2}$$

and our task is to understand how z(t) approximates a constant B, viz.,

$$z \cong B \tag{3}$$

despite its depletion due to inputs S.

Equation 2 says that transmitter z is released at a rate (proportional to) T in response to input S. In other words, z *gates* S to generate T, or T is caused by a *mass action* interaction between S and z. By equation 2, either an increase in S or in z can increase T, and no output signal T can be released if either no input signal occurs (S = 0) or if no transmitter is available (z = 0).

Equation 3 requires that the *sensitivity* of T to S be maintained through time. If both equations 2 and 3 can simultaneously be implemented, then unbiased transmission by a depletable chemical will be achieved. Clearly, both equations 2 and 3 can be implemented by the algebraic equation 1. Equation 1 means that z(t) is replenished instantaneously, or at least at a rate that is rapid relative to the rate of gated release. The interesting properties of a gated dipole occur when the rate of accumulation is slow relative to the rate of gated release. In other words, more than one time scale needs to be invoked to capture the interesting properties of a gated dipole. In order to represent this type of process, an algebraic equation is insufficient. A differential equation is needed. I first consider the simplest differential equation capable of reconciling equations

2 and 3 when both the accumulation and gated release processes take place at a finite rate relative to the rate with which the signal S can fluctuate. In this situation, equations 2 and 3 are not both exactly satisfied at any one time. The process attempts to achieve unbiased transmission, but can do so only approximately due to its finite reaction rates.

The simplest differential equation capable of simultaneously implementing 2 and 3 is the following (Grossberg, 1968, 1969, 1972b) *transmitter accumulation-depletion equation*

$$(d/dt)z = A(B - z) - CSz \tag{4}$$

where A, B, and C are positive. In equation 4, the notation (d/dt)(z) denotes the net production rate of z. Term $A(B - z)$ says that z accumulates at rate A until it reaches the target level B, as required by equation 3. Term $-CSz$ says that the loss of transmitter per unit time due to gated release is proportional to Sz, as required by equation 2.

Term $A(B - z)$ may be physically instantiated in more than one way. For example, a passive accumulation of z may occur onto unoccupied sites whose total number is B. Alternatively, transmitter precursors may actively be produced at a rate AB, but feedback inhibition via term $-Az$ of transmitter z onto an intermediate stage of production may reduce the net production level to $A(B - z)$. Without such feedback inhibition, transmitter production would continue unabated until the cell ruptured.

There exist many variations on the simple equations 2 and 4. Remarkably, a variety of important data properties already follow from these equations. These properties are consequences of equation 4 only when the transmitter accumulation rate is not much faster than the transmitter release rate. None of these properties holds when transmitter accumulation is much faster than transmitter release ($A \gg CS$), since then equation 1 holds at all times. Throughout the remainder of the article, it is assumed that the accumulation rate is not much faster than the gated release rate.

3. TRANSMITTER NORMALIZATION: STEADY STATE TRANSMITTER CONCENTRATION *VERSUS* OUTPUT SIZE

Equations 2 and 4 imply an important property even in response to a constant input signal S(t). For example, let S(t) be chosen to have progressively larger constant values

$$S_0 < S_1 < S_2 < S_3 < \ldots \tag{5}$$

in a series of time intervals that are long enough for z(t) in equation 4 to equilibrate to these values. Also choose C = 1 in equation 4 for simplicity; this is equivalent to rescaling the size of S. In this situation, the outputs T(t) that occur in response to the input series satisfy the inequalities

$$T_0 < T_1 < T_2 < T_3 < \ldots \tag{6}$$

By equations 5 and 6, a larger sustained input S generates a larger sustained output T. The steady state transmitter levels, by contrast, satisfy the reverse inequalities

$$z_0 > z_1 > z_2 > z_3 > \ldots \tag{7}$$

since larger inputs S deplete transmitter z faster than smaller inputs. Thus steady state transmitter level changes in a direction *opposite* to the direction of the steady state output level. This is the first physically nontrivial property of the gating equations 2 and 4. This property shows that the steady state transmitter level z tends to compensate for increases in the input size S, without preventing larger signals S from generating larger output signals T.

The mathematical reason for this property is simple. In response to each constant input S, the net production rate of z approaches an equilibrium value. At equilibrium (d/dt)z = 0 in equation 4. Then equation 4 becomes

$$0 = A(B - z) - Sz \tag{8}$$

Solving for z in 8 yields the equilibrium value

$$z = \frac{AB}{A + S} \tag{9}$$

By equation 9, a parametric increase in the input S, as in equation 5, causes a parametric decrease in the transmitter level z, as in equation 7. Since the output T equals Sz, equation 9 implies that at equilibrium

$$T = \frac{ABS}{A + S} \tag{10}$$

By equation 10, a parametric increase in the input S, as in equation 5, causes a parametric increase in the output T, as in equation 6. Thus the fact that z multiplies S plays an important role in this explanation. This basic property of chemical gates is essential in explaining all the phenomena I review. A model of these phenomena that does not include a multiplicative gating notion will hereby be shown to be severely handicapped.

4. SHORT-TERM TRANSIENTS INTRACELLULAR ADAPTATION AND WEBER LAW

The next important property of a gating process is found by switching the input S(t) to a higher sustained level S_1 after z(t) has equilibrated to a lower level S_0. The property in question holds only if the input signal S(t) can fluctuate much faster than the transmitter z(t) can react. In fact, most of the important properties of gating actions are dynamic properties such that fast and slow reactions occur concurrently in response to input fluctuations. In the present instance at least three time-scales need to be considered in equation 4: the rate at which the input signal S fluctuates, the slower rate CS at which transmitter is released in response to S, and the slower rate A at which transmitter accumulation attempts to prevent sensitivity loss due to gated release. In the ensuing discussion I assume for simplicity that S(t) can switch between two different asymptotes S_0 and S_1 at a single time instant. This assumption is just a simplified way to discuss the fact that z(t) reacts at a much slower rate than S(t).

Suppose that S(t) switches from level S_0 to S_1 at time t_0. Before time $t = t_0$, z(t) equilibrates to the input level S_0. By equation 9, $z(t) \cong z_0$ at times $t \leq t_0$, where

$$z_0 = \frac{AB}{A + S_0} \tag{11}$$

Right after $t = t_0$, S(t) switches to S_1, but due to the slow reaction rate of z(t), z(t) still approximates z_0 for a while. Thus there is a time interval after time $t = t_0$ during which the output $T = Sz$ approximates $S_1 z_0$. By equation 11 during these times

$$T = \frac{ABS_1}{A + S_0} \tag{12}$$

Equation (12) shows that the size of T's initial reaction to S_1 is calibrated against the level S_0 to which the gate has previously equilibrated. Equation 12 takes the form of a Weber law (Grossberg, 1981, 1982a). This Weber law is due to *slow intracellular adaptation* of a chemical gate in response to a prior level of input activation. It is not the type of Weber law that is due to *fast intercellular adaptation* of a shunting on-center off-surround network in response to a spatial pattern of input activation (Grossberg, 1983). In fact equation 12 is invalid if z(t) reacts as quickly as S(t) can fluctuate, since then $T \cong ABS_1(A + S_1)^{-1}$ at all times. Both types of Weber laws are important in neural processing. The intracellular variety is, for example, needed to prevent individual photoreceptors from saturating in response to high intensities of light (Baylor and Hodgkin, 1974; Baylor *et al.*, 1974a, 1974b; Carpenter and Grossberg, 1981;

Hemila, 1977, 1978) before an on-center off-surround network of photoreceptors and horizontal cells can further transform the pattern of photoreceptor activation (Grossberg, 1982a; Ratliff, 1965; Werblin, 1971, 1974, 1975).

5. LONG-TERM TRANSIENTS: UNDERSHOOT AND OVERSHOOT DUE TO GATE HABITUATION

Suppose that the new input level S_1 is maintained long enough for the gate to equilibrate, as in Fig. 1. Then by equation 9, z(t) gradually approaches the new equilibrium level

$$z_1 = \frac{AB}{A + S_1} \tag{13}$$

and T(t) approaches the new equilibrium level $T = S_1 z_1$; that is,

$$T = \frac{ABS_1}{A + S_1} \tag{14}$$

Thus in response to a fast increase in S(t) from S_0 to S_1, T(t) quickly increases from $ABS_0 (A + S_0)^{-1}$ to $ABS_1(A + S_0)^{-1}$, and then slowly decreases to $ABS_1 \times (A + S_1)^{-1}$. The output signal T(t) hereby *overshoots* its new equilibrium level $ABS_1(A + S_1)^{-1}$ due to slow reaction rate of the gate z(t). The output level approaches the new equilibrium level as the gate slowly *habituates* to the new input level S_1.

A similar argument shows why the output *undershoots* its equilibrium level after the input switches from S_1 to a smaller value, say S_0 (Fig. 1). After the input S(t) rapidly switches from S_1 to S_0, the gate z(t) slowly increases from $AB(A + S_1)^{-1}$ to $AB(A + S_0)^{-1}$. The output is the product of these fast and slow reactions occurring in opposite directions. The output responds with a fast undershoot followed by slow equilibration.

Although these properties are mathematically elementary, they are physically subtle, and sufficiently important to emphasize them. Three properties are crucial: (i) The output is a *product* of input and gate; hence it is a *nonlinear* function of input and gate. (ii) The output depends concurrently on *fast* and *slow* reactions. (iii) The fast and slow reactions respond in *opposite* directions to input fluctuations.

Although overshoots and undershoots are familiar psychological and physiological phenomena, they have not been traced to slow gating actions by other authors. For example, Solomon and Corbit (1974) describe a theory of affective dynamics in which overshoots and undershoots occur. Solomon (1980; 1982) ascribes these overshoots and undershoots to the subtraction of two opponent processes that both evolve according to similar time scales, but

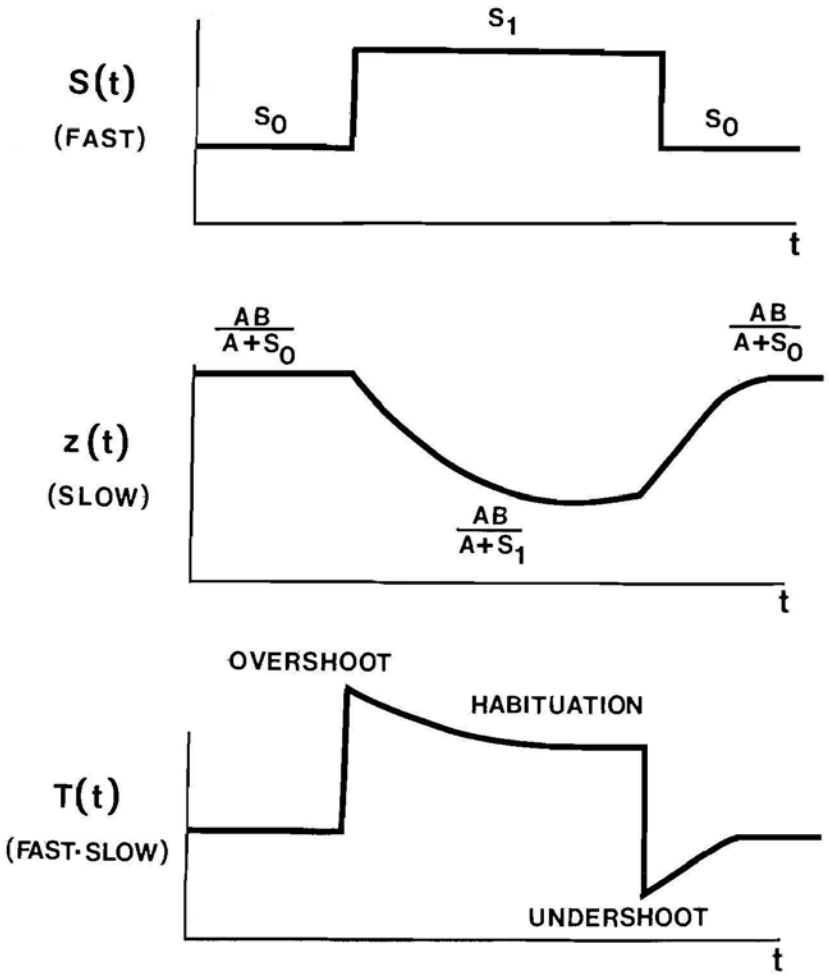

Fig. 1. Reaction of output signal T and transmitter gate z to changes in input S. The output T is the product of a fast process S and a slow process z. Overshoots and undershoots in T are caused by z's slow habituation to fast changes in S.

are staggered in time with respect to each other (Fig. 2). The two opponent processes are not defined by a dynamical model. Instead, their shapes are chosen to fit the data in different experimental paradigms. For example, the Solomon theory does not explain why the maximum size of the (a) process should sometimes, but not always, exceed the maximum size of the (b) process, or why the (b) process should be delayed in time relative to the (a) process by just the right amount to produce an overshoot and an undershoot. By contrast, the theory of affective processes introduced by Grossberg (1971; 1972a; 1972b) defines a dynamical theory of gated opponent processes in which the changing shapes of the opponent reactions to different experiments are properties of dynamical laws. Solomon's interesting results are explained by these dynamical laws at the price of replacing the opponent process of Fig. 2 by the gating process of Fig. 1. Opponent processes also play a crucial role in the gating

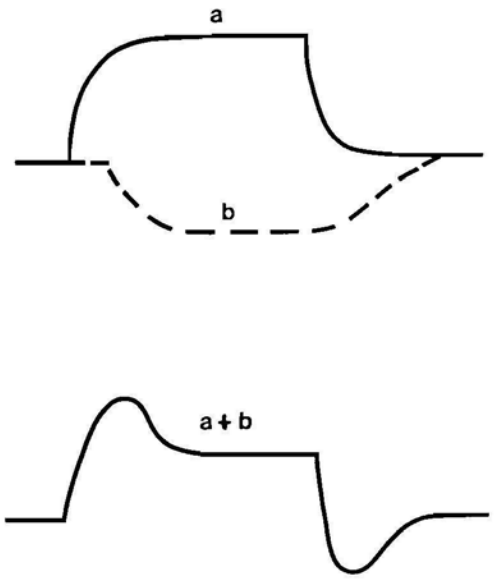

Fig. 2. In the opponent process model of Solomon (1982), overshoots and undershoots are caused by an excitatory process (a) and an inhibitory process (b) that both change at a similar rate such that (b) lags behind (a) and neither (a) nor (b) separately exhibits overshoots or undershoots.

theory, as the following sections indicate, but do not explain overshoot and undershoot *per se*.

6. OPPONENT PROCESSES: ANTAGONISTIC REBOUND IN GATED DIPOLES

The existence of opponent processes in the theory can be derived from several vantage points. All of these derivations lead to gated dipole opponent processes. The first derivation arose from postulates concerning reinforcement and motivation; in particular, how offset of a reinforcing cue of negative (positive) motivational sign triggers an antagonistic rebound reaction that elicits a motivational reaction of positive (negative) sign (Grossberg, 1972a; 1972b). For example, while a sustained shock remains on, it can elicit fear (Estes and Skinner, 1941). Offset of the shock can elicit a wave of relief (Denny, 1971). In this setting, antagonistic rebound ideas were used to model phenomena like extinction, secondary conditioning, learned helplessness, and conditioned avoidance responses. See Grossberg (1982b) for a recent exposition of these applications. Another derivation suggests that antagonistic rebound reactions can also occur in response to unexpected events. This property is needed to stabilize learned perceptual and cognitive representations against the erosive effects of irrelevant cues, and to help regulate the attentional switching and memory search that lead to the synthesis of new representations (Grossberg, 1980, 1982a). Herein I show

how the same network module that generates an antagonistic rebound in response to offset of a cue can also generate an antagonistic rebound in response to onset of an unexpected event (Fig. 3). This property is one of many gated dipole properties that lie outside the predictive range of the Solomon (1980; 1982) theory of opponent processes.

To indicate the generality of the offset issue, I introduce the gated dipole network using a perceptual, rather than a motivational, example. Suppose that a subject's task is to press a lever in response to the offset of a light. If light offset only turned off the cells, called *on-cells*, that code for light being on, then there would exist no cells whose activity could selectively elicit the lever-press response after the light turned off. Light offset also turns on cells, called *off-cells,* that can activate the lever-press command. Different populations of off-cells are selectively turned on by offset of different sensory cues, since using the same off-cells to respond to all event offsets would prevent the learning of different responses to different cue offsets. Also the off-cell response to light offset is transient; otherwise the off-cells would persistently generate the lever

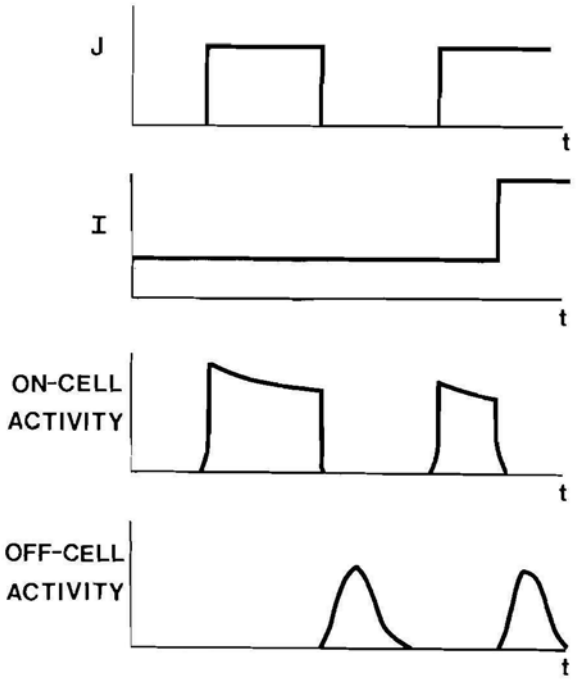

Fig. 3. A rapid decrement of a phasic input (J) and a rapid increment in arousal (I) can both trigger offset, or rebound, of a sustained on-reaction. In applications, these properties help to explain how a shock decrement (J) can be positively rewarding during classical conditioning, or how an expected event that triggers an arousal burst (I) can cause rapid reset of short-term memory and motivational rebound during instrumental conditioning.

press in the absence of light. The transient and selective activation of off-cells by a sudden offset of input to their corresponding on-cells is what I call an antagonistic rebound. In my theory, the on-cells and the off-cells are the output cells of a gated dipole opponent process

Figure 4 pictorially explains how the overshoot and undershoot reactions of the slow gate in Fig. 1 generate sustained on-responses and transient off-responses in a gated dipole network. Let me emphasize again that such a network can, in principle, be an intracellular network of reactions (Carpenter and Grossberg, 1981), rather than an intercellular interaction among whole cells. The interpretation of the network stages can change with the application. An intercellular interpretation is used herein to fix ideas.

The left-hand series of stages in Fig. 4 represents the on-channel, and the right-hand series of stages represents the off-channel. Both channels receive an equal arousal input, denoted by I, that is constant through time in Fig. 4. The

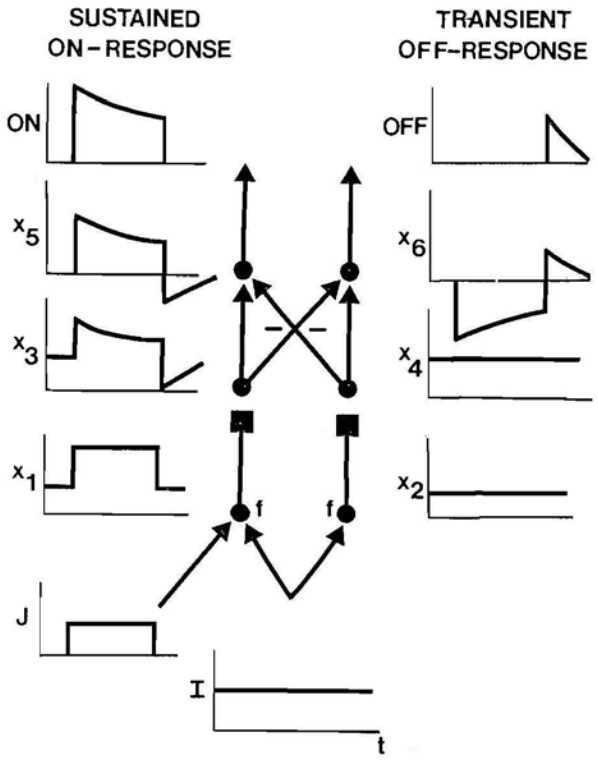

Fig. 4. Example of a feedforward gated dipole. A sustained habituating on-response (top left) and a transient off-rebound (top right) are elicited in response to onset and offset, respectively, of a phasic input J (bottom left) when tonic arousal I (bottom center) and opponent processing (diagonal pathways) supplement the slow gating actions (square synapses). See text for details.

arousal input energizes the antagonistic rebound after the on-input shuts off. The on-input, denoted by J, is delivered only to the on-channel. Input J is switched from zero to a positive level and held at that level long enough for gate equilibration to occur. Then J is shut off.

Inputs I and J are added by the activity (or potential) $x_1(t)$. Activity $x_1(t)$ responds quickly to input fluctuations, relative to the reaction rate of the network's slow gates. The graph of $x_1(t)$ has the same form as the top graph in Fig. 1: a rapid switch from a lower positive activity to a higher positive activity, followed by a rapid return to the lower level. The activity $x_1(t)$ generates an output signal $f(x_1(t))$ in its pathway that again has the form of a double switch between two positive values. The output signal $f(x_1(t))$ is gated by a slow transmitter $z_1(t)$ that accumulates and is released from the square synapse in the on-channel. Figure 1 describes the effect of this slow gate on the input to the next stage. Consequently, activity $x_3(t)$ follows an overshoot-habituation-undershoot-habituation sequence through time. Then $x_3(t)$ relays an output signal of the same form to $x_5(t)$. Activity $x_5(t)$ also receives an inhibitory signal from $x_4(t)$. To determine what happens next, we need to consider the dynamics of the off-channel.

The off-channel responses are particularly simple because the off-channel receives only the constant tonic input I. Hence $x_2(t)$ and the slow gate $z_2(t)$ in the off-channel square synapse are constant through time. The activity $x_4(t)$ is therefore also constant through time. What is the size of the constant value x_4?

For definiteness, I make the simplest assumption. Let corresponding stages in the on-channel and off-channel possess the same parameters. Since the arousal input I to both channels is also equal, the size of x_4 equals the baseline activity level of $x_3(t)$. (Any choice other than of symmetric parameters in the on-channel and the off-channel causes a shift in the relative baselines of the two channels in a predictable fashion. See Section 14.)

We can now determine the reactions of activity $x_5(t)$ through time. Since the signals from $x_3(t)$ and $x_4(t)$ subtract before perturbing $x_5(t)$, the baseline activity of $x_5(t)$ equals zero, since the baseline activities of $x_3(t)$ and $x_4(t)$ are the same. Activity $x_3(t)$ overshoots and undershoots its zero baseline when the input J is turned on and off. By contrast, activity $x_6(t)$ responds in an opposite way from $x_5(t)$; that is, $x_6(t) = -x_5(t)$, because x_3 excites x_5 and inhibits x_6, whereas x_4 inhibits x_5 and excites x_6.

The final assumption is that the output signals caused by activities $x_5(t)$ and $x_6(t)$ are rectified: Outputs are generated only if these activities exceed a nonnegative signal threshold. As a result the on-channel generates a sustained output signal while the input J is on. This output signal habituates as the gate $z_1(t)$ slowly equilibrates to the input. By contrast, the off-channel generates a transient off-response, or antagonistic rebound, after the input J shuts off.

7. INVERTED U: UNDERAROUSED DEPRESSION *VERSUS* OVERAROUSED DEPRESSION

The type of pictorial analysis described in Fig. 4, although revealing, is insufficient to explain the deepest and most surprising properties of gated dipoles. Some of these more subtle properties arise by refining the differential equations models that describe the stages of transmitter dynamics. Equations for such processes as enzymatic modulation of transmitter accumulation rate, transmitter mobilization, and transmitter reuptake have been derived from the postulate that transmitter processes do their best to accomplish unbiased signal transduction (viz., are optimal), but are subject to dynamical constraints such as finite processing rates (Carpenter and Grossberg, 1981; Grossberg, 1968, 1969, 1982a, 1984a). In these more complex models, the transmitter processes can no longer be defined by a single differential equation (4). Systems of interacting differential equations need to be studied. These refinements are not considered here.

Other important properties of gated dipoles are already latent in the simplest equations capable of instantiating Fig. 4. These properties are also related to the sensitivity with which signals can be relayed by transmitter gating processes. The properties in question show that the gated dipole circuit, as a whole, can alter network sensitivity in a way that differs markedly from the sensitivity properties of a single gated pathway. Although many refinements of these properties occur in more realistic gated dipole circuits, the main conclusions are robust consequences of the conjoint action of phasic cues, tonic arousal, chemical gates, and opponent processes. The existence of analogs of these formal properties in several abnormal behavioral syndromes is thus a fact of unusual interest.

The network properties in question are the following: One of the parameters that defines a gated dipole is its arousal level I. In a gated dipole circuit, this type of arousal energizes the antagonistic rebound when a phasic cue shuts off. Since several types of arousal exist in my theory, one must be careful not to equate this concept of arousal with holistic measures of organismic activity. For present purposes, I consider this arousal level a formal parameter that may be influenced by certain drugs.

When one parametrically varies the arousal level I, one finds that an inverted U exists in both the on-reactions and the off-reactions of a gated dipole to phasic cue onsets and offsets. In other words, dipole output becomes depressed when the arousal level I is chosen either too low (underarousal) or too high (overarousal). The underaroused and overaroused depressive syndromes at the two ends of this inverted U (Grossberg, 1972b) exhibit two remarkably different constellations of paradoxical properties. These formal properties are summarized below before being compared with similar properties of data.

To derive inverted U properties, I consider the simplest formulas capable of instantiating Fig. 4. The first task is to estimate the steady state size of the

on-activity x_5 while J is on, and the maximum size of the off-rebound x_6 after J is shut off. Let the output signal generated by x_1 while J is on equal $S_1 = f(I + J)$, and the output signal by x_2 at all times equal $S_2 = f(I)$. By equation 9 the equilibrated size of gate z_1 to S_1 is

$$z_1 = \frac{AB}{A + S_1} \tag{15}$$

and of gate z_2 to S_2 is

$$z_2 = \frac{AB}{A + S_2} \tag{16}$$

The output signal T_1 to x_3 is thus

$$T_1 = S_1 z_1 = \frac{ABf(I + J)}{A + f(I + J)} \tag{17}$$

and the output signal T_2 to x_4 is

$$T_2 = S_2 z_2 = \frac{ABf(I)}{A + f(I)} \tag{18}$$

Eliminating all possible extra parameters for simplicity, suppose that the output signal of x_3 equals T_1 and of x_4 equals T_2. Also suppose that the steady state on-activity x_5 satisfies

$$x_5 = T_1 - T_2 \tag{19}$$

due to opponent processing. By equations 17 and 18

$$x_5 = \frac{A^2 B[f(I + J) - f(I)]}{[A + f(I)][A + f(I + J)]} \tag{20}$$

To estimate the off-rebound x_6, let J switch back to zero after z_1 (approximately) attains the asymptote in equation 15. Then x_1 quickly switches to the value f(I), whereas z_1 approximately satisfies equation 15 for a while, so that

$$T_1 \quad \frac{ABf(I)}{A + f(I + J)} \tag{21}$$

By contrast, T_2 does not change because it is influenced only by I. An off-rebound occurs only if $x_6 > 0$. As in equation 19, we define x_6 by

$$x_6 = T_2 - T_1 \tag{22}$$

due to opponent processing. By equations 18, 21, and 22,

$$x_6 = \frac{ABf(I)[f(I + J) - f(I)]}{[A + f(I)]\ [A + f(I + J)]} \tag{23}$$

approximates the size of the off-rebound shortly after J shuts off.

When equations 20 and 23 are compared, a surprising conclusion becomes evident:

$$\frac{x_6}{x_5} = \frac{f(I)}{A} \tag{24}$$

Thus the *relative* sizes of the steady on-response and the off-rebound depend only on the arousal level, and increases with the arousal level. This type of property leads to predictions concerning the ability of underaroused animals to learn escape responses in response to aversive cues (Grossberg, 1972b), and permits estimates of the transducing signal f to be made from observable data (Grossberg, 1981).

Equations 20 and 23 possess the inverted U property that we seek. To discuss this property more precisely, we must impose some constraints on the signal. function f(w). A natural choice is a nonnegative function f(w) that becomes constant at both low and high values of the activity level w, and increases with the activity level w at intermediate values of w. Any such signal function f(w) generates an inverted U in response to parametric changes in I. This is because $f(I + J) = f(I)$ whenever I is chosen too small or too large. Consequently, both $x_5 = 0$ and $x_6 = 0$ at extreme choices of the arousal level. By contrast, at intermediate choices of I, $f(I + J) > f(I) > 0$ because f(w) is an increasing positive function of intermediate values of w. Then $x_5 > 0$ and $x_6 > 0$. Thus both x_5 and x_6 increase from zero to positive values and then return to zero values as I increases.

Two remarks should promptly be made to sharpen one's understanding of a gated dipole's inverted U. Even the function $f(I + J) - f(I)$ exhibits an inverted U. By contrast with this function, equations 20 and 23 also contain terms in their denominators. These terms can be traced to properties of the slow reaction rate of the transmitter gates. They are due to gate habituation and Weber law modulation. These gate-derived terms are the sources of all nontrivial properties of a gated dipole's inverted U.

For example, an inverted U can obtain in equations 20 and 23 even if f(w) does not saturate at large values of w. For simplicity, consider the signal function $f(w) = \max(w, 0)$. This threshold-linear signal function grows linearly after w exceeds the threshold value zero. By equations 20 and 23, both x_5 and

x_6 approach zero as I increases, despite the absence of signal function saturation. This is because I appears in a quadratic term I^2 in the denominator of 20 and 23, but I either is absent or appears linearly in the numerator. Thus in a gated dipole, both gate habituation and signal function saturation can depress dipole output if arousal level gets too large.

In all physical applications of gated dipoles, the signal function f(w) does become constant at both small and large activity values w. Henceforth, I use the simplest type of signal function that continuously interpolates two constant activity levels. This type of function is a sigmoid, or S-shaped, function (Fig. 5). In many applications, f(w) becomes zero at small values of w. Such a sigmoid function acts like a signal threshold at low values of w, is approximately linear at intermediate values of w, and saturates at large values of w.

Deeper reasons than simplicity *per se* also dictate the choice of a sigmoid signal function. In many applications of gated dipoles, the on-channel excites itself via positive feedback and the off-channel excites itself via positive feedback (Section 14). In such a feedback gated dipole, a sigmoid signal function is the simplest signal function that prevents the dipole from amplifying noise via its positive feedback loops (Grossberg, 1982a).

8. THE UNDERAROUSED DEPRESSIVE SYNDROME

When the arousal level I is chosen too small, both the on-output and off-output of a gated dipole exhibit an "abnormal" behavioral syndrome with remarkable properties:

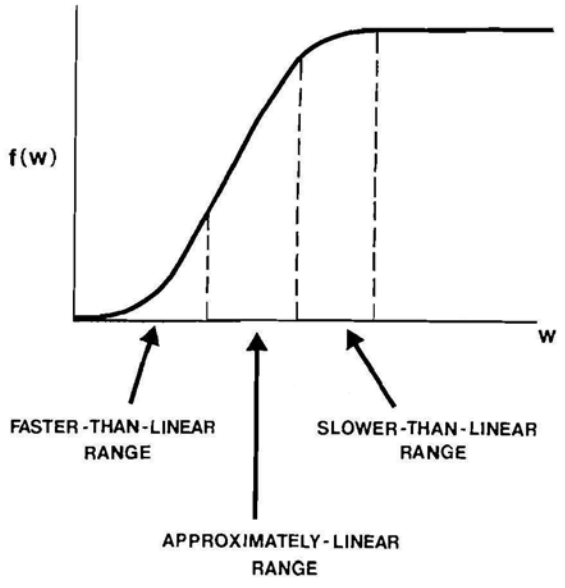

Fig. 5. An S-shaped, or sigmoid, transformation of activity w into an output signal f(w). The output may represent either the number of action potentials (spikes) per unit time or an electrotonic signal, depending upon the application.

A. The output threshold is elevated in response to phasic inputs J. In other words, a larger J is needed to elicit a positive on-output from an underaroused dipole.

B. The on-reactions are hypersensitive to unit increments in J values that exceed the elevated threshold. In other words, larger than normal on-outputs are produced by equal suprathreshold increments in J in an underaroused dipole than in a normally aroused dipole.

C. These hypersensitive reactions are reduced by a drug that acts like an arousal "up." In other words, a drug that causes a parametric increase in arousal level I decreases dipole sensitivity to increments in J.

D. Too much of the "up" drug depressed output size by carrying the dipole over its inverted U into the overaroused (large I) range.

E. Hyposensitive off-reactions occur in response to phasic input decrements, even though hypersensitive on-reactions occur in response to phasic input increments. In particular, no off-rebound whatsoever may occur in response to cutting J in half to J/2, and cutting J/2 to 0 may cause an abnormally small off-rebound.

F. Sudden increments ΔI in arousal level that cause an off-rebound in a normally aroused dipole can cause a paradoxical enhancement of the on-response (dishabituation) in an underaroused dipole.

See Grossberg (1984a) for recent proofs of these properties. The properties A–F are intuitively paradoxical because of the following considerations.

Naive intuition suggests that an increase in threshold is accompanied by a decrease in sensitivity, or at least by no change in sensitivity. Properties A and B show that this expectation is not upheld in a gated dipole. Properties A and B can be intuitively understood by considering equation 20. Property A is easy to understand. If I is abnormally small, then a larger value of J is needed to make $f(I + J)$ exceed the threshold of f. Only when $f(I + J)$ exceeds threshold can the difference $f(I + J) - f(I)$ become positive to elicit a positive on-response. Note that this explanation does not postulate a change in the threshold of f. The system as a whole behaves as if a threshold has changed.

Property B has a more subtle explanation that depends upon two effects acting together. If I is abnormally small, then given a fixed input value J, both $f(I)$ and $f(I + J)$ in the denominator of equation 20 are also abnormally small. Every increase in $f(I + J) - f(I)$ due to a unit increase ΔJ in J is amplified by this small denominator. The sigmoid function f also contributes to hypersensitivity. To see this, choose a value of J that just brings $f(I + J)$ to threshold. A unit increment ΔJ in J then brings $f(I + J + \Delta J)$ into a range of f's graph where f is in-

creasing at a faster-than-linear rate (Fig. 5). Consequently, linear increments in ΔJ cause faster-than-linear increments in $f(I + J + \Delta J) - f(I)$. When I is chosen normally, such values of $J + \Delta J$ are cancelled by a larger denominator. Also $f(I + J + \Delta J)$ is then in its approximately linear, rather than its faster-than-linear, range (Fig. 5).

The last two sentences explain Property C. Although a drug that increases I is an "up," it desensitizes the gated dipole both by increasing the denominator of equation 20 and by moving the numerator terms out of the faster-than-linear range of f's growth. Such an arousal "up" also decreases the threshold of the dipole. No biochemical description of the drug's site of action can explain these properties. They are literally created by the network interaction.

Property D is also due to two properties acting together. If arousal I is chosen too large, then $f(I + J) - f(I)$ in the numerator becomes small, while $f(I)$ and $f(I + J)$ in the denominator become large, no matter how input J is chosen.

Property E is especially paradoxical because it seems to be the opposite of property B. This property requires some mathematical manipulation to be understood. Property E is a special case of the property that

$$R(J/2 \rightarrow 0) > R(J \rightarrow J/2) \tag{25}$$

In other words, the off-rebound $R(J \rightarrow J/2)$ caused by cutting J in half is smaller than the off-rebound $R(J/2 \rightarrow 0)$ caused by shutting J/2 off. An analogous property has been observed in instrumental conditioning experiments wherein the phasic input is a shock intensity and the off-rebound calibrates the rewarding effect, or relief, caused by quickly reducing the shock level (Campbell, 1968; Myers, 1969). Since the phasic input is reduced by J/2 units in both $R(J/2 \rightarrow 0)$ and $R(J \rightarrow J/2)$, the fact that $R(J/2 \rightarrow 0) \neq R(J \rightarrow J/2)$ shows that this reward mechanism is nonadditive.

Equation (25) was proved in Grossberg (1972b) as a special case of a formula that predicts an infinite number of relationships between the relative effects of different shock decrements at different arousal levels. See Grossberg (1984a) for a related analysis. The prediction that no rebound whatever may occur when J/2 is switched off is a special case of a prediction that three leading indices should covary as arousal level, in the gated dipole sense, is parametrically changed: (i) the ability of an animal to learn an escape act in the presence of fearful cues; (ii) the relative advantage of partial reward over continuous reward; and (iii) the ability of reducing a shock level J by half to positively reward operant behavior.

Property F is one of the most surprising consequences of gated dipole circuitry. This property is of sufficient importance that it merits a separate discussion.

9. REBOUND IN RESPONSE TO AN UNEXPECTED EVENT: INFORMATION PROCESSING REGULATED BY A NONASSOCIATIVE MEMORY

Offset of a phasic input is not the only way to cause an antagonistic rebound in a gated dipole. A sudden increment in nonspecific arousal that occurs while a phasic input is on can also cause a rebound, as in Fig. 3. Such a rebound occurs despite the fact that the arousal increment equally activates both the on-channel and the off-channel of the dipole. The asymmetric levels of gate habituation in the on-channel and the off-channel calibrate the rebound. Gate habituation hereby acts like a form of memory, distinct from associative memory, that enables a nonspecific event to cause a highly differentiated response across a field of gated dipoles.

In applications to motivated behavior and cognitive processing, such an arousal burst is assumed to be triggered by an unexpected event. Thus the same gated dipole machinery which produces a rebound in response to offset of a specific cue in classical conditioning can also produce a rebound in response to nonoccurrence of an expected event in instrumental conditioning (Grossberg (1981; 1982b). The dipoles that are reset by an unexpected event are usually interpreted to occur in a field of cortical dipoles wherein different sensory cues activate dipole on-cells. In this type of sensory setting, gated dipole properties have proved useful in studies of cognitive development (Grossberg, 1980), attentional processing (Grossberg, 1978; 1982b), and speech and language (Grossberg, 1984b).

For present purposes I consider how these properties contribute to an understanding of a gated dipole's underaroused depressive syndrome.

10. REBOUND *VERSUS* DISHABITUATION

The properties of dipole reset in response to an unexpected event depend upon the choice of the signal function f(w). The reset that occurs using a linear signal function f(w) differs in an important way from the reset that occurs using a sigmoid signal function. In particular, rebound and dishabituation can simultaneously occur in different dipoles of a dipole field using a sigmoid signal function (Fig. 6), but not using a linear signal function. Dishabituation refers to the property that an enhanced on-reaction, rather than antagonistic off-rebound, occurs in response to an unexpected event (Grossberg, 1982b; 1984a). Arousal increments ΔI that cause off-rebounds in a normally aroused dipole can cause dishabituation reactions in an underaroused dipole.

The formula that determines whether a rebound occurs in response to an arousal increment is derived just like the formula for rebound in response to

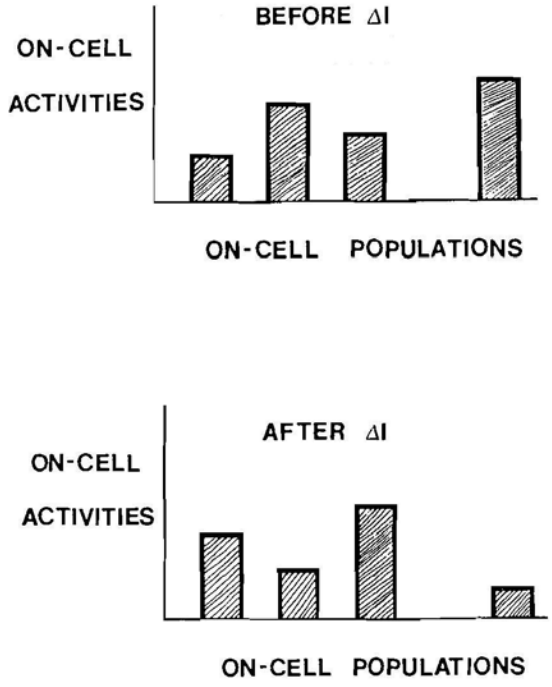

Fig. 6. Short-term memory reaction to an arousal-mediated (ΔI) unexpected event. The arousal burst ΔI tends to rebound populations that were very active before the expected event and to dishabituate populations that were weakly active before the unexpected event. Inactive populations remain inactive, but they are sensitized by a gain change. This type of global reset event gives more short term memory activity to those populations that did not control the actions leading to the unexpected outcome.

phasic cue offset (Section 7). In the present case, after the dipole equilibrates to arousal I and phasic input J, arousal is suddenly increased to a higher level I*. A rebound then occurs if and only if the following function is positive:

$$\frac{A^2B[f(I^*) - f(I^* + J)] + AB[f(I^*)f(I + J) - f(I)f(I^* + J)]}{[A + f(I)]\ [A + f(I + J)]} \tag{26}$$

If f(w) is chosen to be a linear function, say f(w) = w, then equation 26 simplifies to the formula

$$\frac{ABJ(\Delta I - A)}{(A + I)(A + I + J)} \tag{27}$$

where $\Delta I = I^* - I$. By equation 27, a dipole with a linear signal function rebounds only if $\Delta I > A$. This criterion is independent of J. Thus in a field of

such gated dipoles, if one dipole rebounds, then all active dipoles rebound. In other words, if a novel event is sufficiently unexpected to reset one dipole, then it resets the whole field of active dipoles. Equation 27 also implies that this global reset event is *selective* in the following sense. The amount of rebound increases with the level of phasic input J, and equals zero if the dipole was previously inactive (J = 0).

When a sigmoid signal is used, a qualitatively different type of reset can occur in response to an unexpected event. A sigmoid signal f(w) is faster-than-linear at small activity values w, before becoming approximately linear at intermediate w values (see Fig. 5). In the approximately linear range, a rebound property analogous to equation 27 is found. The faster-than-linear range controls the new reset property.

A sigmoid function such as $f(w) = w^2(1 + w^2)^{-1}$ is, for example, approximated in its faster-than-linear range by $f(w) = w^2$. The exact form of the faster-than-linear term is not crucial to drawing the following conclusion: There exists a rebound threshold g(I, J) such that a rebound occurs if and only if

$$\Delta I > g(I, J) \tag{28}$$

Unlike the linear case, where the rebound threshold equals the constant A, as in equation 27, the rebound threshold g(I, J) is a decreasing function of arousal I and phasic input J. For example, if $f(w) \cong w^2$ at small w values, then

$$g(I, J) = \frac{A - I(I + J) + (A - I^2)^{\frac{1}{2}}[A + (I + J)^2]^{\frac{1}{2}}}{2I + J} \tag{29}$$

Because g(I, J) decreases as J increases, equation 28 shows that it is easier to rebound a dipole which has previously been very active ($J \gg 0$) than a dipole which has previously been inactive ($J \cong 0$). Thus those cells which contributed most to the network's erroneous expectations and actions by giving rise to the largest output signals are maximally suppressed due to the unexpected outcome of these signals.

If by contrast

$$\Delta I < g(I, J) \tag{30}$$

then a rebound does not occur. In fact, when equation 29 holds, an enhanced on-reaction occurs if $\Delta I < AJ^{-1}$. This enhanced on-reaction is a dishabituation reaction to the unexpected event.

The preceding discussion suggests that dishabituation to an unexpected event is a more subtle property than habituation. Habituation occurs whenever a slow gate responds to a sustained input. Dishabituation occurs only if the prop-

er relationship holds between I, J, ΔI, and the signal function. Since g(I, J) is a decreasing function of J, it is easier to dishabituate the on-channel of a dipole that was weakly active than the on-channel of a dipole that was very active before the unexpected event occurs. In applications to attentional processing, this property helps to explain how overshadowed cues, which previously were treated as irrelevant, can become attentionally more salient after an unexpected event occurs (Grossberg, 1982b).

Since g(I, J) is a decreasing function of I, the threshold g(I, J) is increased during an underaroused syndrome. Consequently, inequality 30 is much more likely to occur in an underaroused dipole than in a normally aroused dipole. Underarousal hereby tends to enhance, or dishabituate, activities that would otherwise be suppressed by an unexpected event. In other words, activities that would in the normal course of things be reset can be paradoxically enhanced in an underaroused gated dipole.

The formal properties of an overaroused gated dipole are entirely different.

11. THE OVERAROUSED DEPRESSIVE SYNDROME

Overaroused depression of a gated dipole has two major properties:

A. The output threshold is reduced in response to phasic inputs J.
B. The on-reactions are hyposensitive to unit increments in J values that exceed the elevated threshold.

Thus although essentially all positive choices of J "exceed threshold" in the overaroused syndrome, no net output arises from the dipole because $f(I + J) - f(I)$ is approximately zero and the denominator terms $f(I)$ and $f(I + J)$ are maximally large, no matter how J is chosen.

12. HYPERACTIVE ORIENTING REACTIONS AND INVERTED U IN VERBAL BEHAVIOR

Before considering empirical applications of the gated dipole syndromes, it is important to note that a dysfunction in the type of nonspecific arousal that influences gated dipole circuits may affect more than gated dipole circuitry in the total network, as well as in the brain. Overarousal of a gated dipole subsystem can cause paradoxical effects both directly and indirectly. The direct effect of overarousal is to suppress gated dipole responsiveness. Indirect effects can be caused by upsetting the balance that normally exists between a gated di-

pole subsystem and a different subsystem of the network. For example, in models of attention and discrimination learning (Grossberg, 1975; 1982b), a gated dipole subsystem transforms the reinforcing properties of expected cues into motivating signals that support consummatory behavior. This gated dipole subsystem competes with an orienting subsystem that controls orienting reactions to unexpected cues. Overarousal of the gated dipole subsystem can directly suppress emotional reactions to familiar cues and indirectly disinhibit the orienting subsystem. Hyperreactive orienting reactions may hereby be generated by hyporeactive emotional reactions (Ellinwood and Kilbey, 1980). Thus even if we agree that some gated dipole circuits are overaroused in the sense that their arousal level I is large, this does not imply that the total network reactivity is depressed. In particular, any metabolite that is produced both within the consummatory subsystem and the orienting subsystem may show no effect of gated dipole underarousal in one part of the consummatory subsystem. This type of argument can be stripped free of gated dipole considerations to caution against using nonspecific measures of behavioral activity to characterize any disorder that is due to a subsystem sensitivity change.

Section 9 suggests that inappropriate reactions to unexpected events can also occur in an underaroused gated dipole subsystem. By contrast with the hyperreactive orienting reactions that may be indirectly released by an overaroused gated dipole subsystem, the hyperreactive reactions that can occur in an underaroused gated dipole subsystem are direct properties of this subsystem. Although these two types of reactions may look similar to casual behavioral inspection, they are differentiable in terms of their triggering events and parametric properties. Moreover, this type of hyperreactivity creates another argument against using nonspecific measures of behavioral activity to calibrate arousal level. Whereas the arousal level of an underaroused gated dipole is reduced, its suprathreshold outputs are enhanced. Thus compensatory reactions that can neutralize nonspecific measures can occur within a single subsystem.

In addition to causing paradoxical disinhibitory reactions, dysfunctions in nonspecific arousal may cause inverted U reactions in neural circuits that are not gated dipoles. For example, in studies of serial verbal learning, Grossberg and Pepe (1970; 1971) discovered an inverted U that occurs when arousal is parametrically changed in a network capable of serially learning and performing a list of verbal items. The underaroused end of this inverted U is easy to understand: an insufficient amount of arousal is available to energize the encoding of short-term memory patterns into long-term memory. The overaroused end of the inverted U is more difficult to understand because an ample amount of arousal is available to energize learning and performance. However, the *patterning* of long-term memory encoding and read-out through time is dramatically impaired by overarousal. As a consequence, one finds a collapse of contextual constraints on learning and performance, fuzzy response categories, and a ten-

dency to elicit rhymes and other low order associations. In order to gain a better parametric understanding of this overaroused syndrome, Grossberg and Pepe (1971) predict how the normal pattern of errors during serial verbal learning should change as arousal is parametrically increased, say by amphetamine.

Underarousal or overarousal may afflict a number of different subsystems in the brain. If a gated dipole circuit is impaired, then one type of parametric breakdown is expected. If a network that processes verbal lists is affected, then an entirely different parametric breakdown is expected. If both sorts of networks are affected, then a composite syndrome is anticipated to occur. In all cases, a breakdown in one subsystem can trigger abnormal reactions across several subsystems. All these factors must be kept in mind when considering the following comparisons between the formal properties of underaroused depression in a gated dipole and the behavioral properties of certain juvenile hyperactives and Parkinson patients.

13. COMPARISON OF THE UNDERAROUSED DEPRESSIVE SYNDROME WITH JUVENILE HYPERACTIVITY AND PARKINSONISM

Underarousal in Tables I and II has the operational definition that drugs which are arousing to normal subjects can improve the behavioral symptoms of certain hyperactives and Parkinson patients. This behavioral fact is compatible with the linking hypothesis that these drugs cause an increase in the arousal level I of the afflicted gated dipoles. Underarousal has *no other meaning* in this discussion.

Tables I and II compare formal dipole properties with experimental properties of each syndrome. The tables also indicate certain experiments that still need to be done to confirm or refute gated dipole involvement. Table I translates formal dipole properties into behavioral properties of hyperactive children. Table II translates formal dipole properties into behavioral properties of Parkinson patients. Tables I and II suggest that different dipole subsystems may be underaroused in the two disorders and that behaviors which seem to be totally different may share similarly designed mechanistic substrates. Items 5 and 6 in Tables I and II may be particularly useful sources of experimental tests. In the case of juvenile hyperactivity, for example, paradoxical dishabituation reactions to unexpected events may contribute to distractability by differentially enhancing the salience of irrelevant cues. In the case of parkinsonism, the bracing reactions due to unexpected pushes may be caused partly by enhanced on-reactions of the motor commands that were active before the push. If these interpretations are correct, then the enhanced on-reactions should be triggered by the evoked potentials that calibrate novelty in the afflicted subsystems.

Table I. Symptoms of Juvenile Hyperactivity

1. *High threshold to phasic cues*

   Thresholds during an electroencephalic audiometry test are reduced by medication (Weber and Sulzbacher, 1975)

2. *Suprathreshold hyperactivity*

   Defines behavioral syndrome

3. *Brought "down" by a drug "up"*

   Certain of these children seem to suffer from catecholamine deficiencies (Shaywitz *et al.*, 1977; Shekim *et al.*, 1977). Amphetamine is used as a treatment (Swanson and Kinsbourne, 1976; Weiss and Hechtmann, 1979)

4. *Too much "up" causes an overaroused syndrome*

   Amphetamine psychosis can occur in response to large drug doses (Ellinwood and Kilbey, 1980; MacLennan and Maier, 1983)

5. *Hyposensitive to $J \rightarrow J/2$*

   Unknown. Does cutting a reward or punishment in half cause an abnormally small affective reaction of opposite sign? Does halving the intensity of a previously sustained visual cue cause an abnormally small negative aftereffect?

6. *Paradoxical dishabituation by unexpected events*

   Distracted by irrelevant sensory cues. Do reduced P300 evoked potentials coincide with distracting events?

14. COMPARISON OF THE UNDERAROUSED DEPRESSIVE SYNDROME WITH HYPOTHALAMIC HYPERPHAGIA

A formal underaroused depressive syndrome can be generated by manipulations other than parametric decreases in arousal level I. In Grossberg (1984a), I show how cutting a pathway in a gated dipole model of a hypothalamic eating circuit can cause an underaroused syndrome with all the major properties of hyperphagia, including a sustained bout of voracious eating until an obese weight is attained (Kent and Peters, 1973; Singh, 1973; Wampler, 1973), followed by maintenance of this weight by frequent meals (Balagura, 1972) despite the fact that the obese system is finicky, or hypersensitive, to the tastes and other reinforcing properties of food (Teitelbaum, 1955). A lesion of pathways 2 or $5 \rightarrow 7$ in Fig. 7 can cause such a formal lesion. A closely related network lesion can cause obesity without finickiness (Graff and Stellar, 1962; Hoebel, 1976).

Table II. Symptoms of Parkinsonism

1. *High threshold to phasic cues*	Difficulty in initiating movements
2. *Suprathreshold hyperactivity*	Difficulty in terminating movements after they begin.
3. *Brought "down" by a drug "up"*	In parkinsonism, dopamine-rich cells of the substantia nigra show marked degeneration (Weiner and Klawans, 1978). L-dopa, a dopaminergic agonist, is used as a treatment
4. *Too much "up" causes an overaroused syndrome*	Too much L-dopa can elicit schizophrenic symptoms (Riklan, 1973; Wallach, 1974). In the reverse direction, antipsychotic drugs that block dopamine receptors (Kuhar *et al.*, 1978) can in sufficient quantities produce a catalepsy suggestive of Parkinson's disease (Hornykiewicz, 1975)
5. *Hyposensitive to $J \rightarrow J/2$*	Unknown
5. *Paradoxical dishabituation by unexpected events (Section 14)*	Parkinson bracing to an unexpected push (Schallert *et al.*, 1979). Do novelty-mediated motor potentials increase with the amount of bracing?

In the model, the difference between these syndromes is due to the placement of the lesion relative to the chemical gates.

To explain interdisciplinary data about motivated behaviors such as eating, the gated dipole circuit of Fig. 4 needs to be modified and embedded in a network capable of controlling the reinforcing, drive, choice, and motivational aspects of consummatory behavior. Figure 7 depicts such a network, which is described herein to illustrate how gated dipole circuits may be embedded into a more realistic processing framework. The gated dipole cells are labeled 4–9. Pathway 3 is a nonspecific arousal pathway. Pathway 1 subserves a slowly varying, metabolically mediated hunger input that increases with hunger drive. Pathway 2 subserves a slowly varying satiety input that increases with gastric distension and metabolic indices of digestion. Neither of these pathways are rapidly varying phasic inputs such as J in Fig. 3. The inputs in pathways 1 and 3 and in pathways 2 and 3 summate to cause total arousal inputs that are asymmetrically distributed across the on-channel and off-channel of the dipole. Phasic inputs are delivered through conditionable pathways, such as 11 and 12, that are ac-

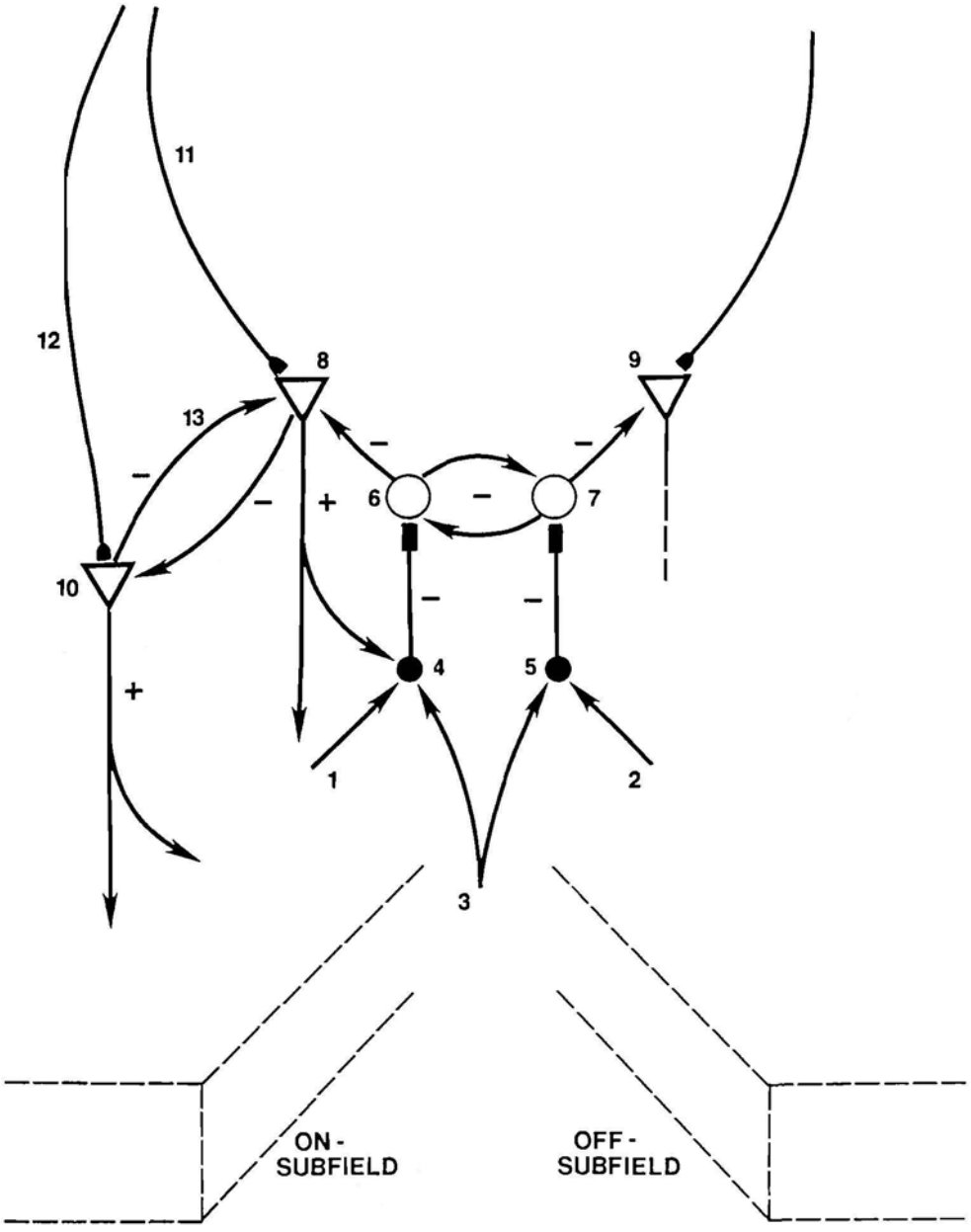

Fig. 7. A motivational dipole field. Gated dipoles are interconnected so that their on-channels (e.g., 4 → 6 → 8 → 4) interact competitively (e.g., 13) within a feedback network, and their off-channels (e.g., 5 → 7 → 9 → 5) also interact competitively within a feedback network. Each gated dipole receives a total arousal input consisting of a basal level (e.g., 3) and a slowly varying internal drive input (e.g., 1 and 2). Rapid phasic inputs are delivered via pathways activated by unconditioned reinforcers or conditioned reinforcing cues (e.g., 11). The combined effect of all reinforcing cues and drive inputs to the network helps to explain such properties as how reinforcers can override homeostatic constraints in the control of appetite behaviors.

tivated by food-related conditioned reinforcing cues. The slow gates occur within the square synapses in pathways 4 → 6 and 5 → 7. In this network, they are inhibitory transmitters that form part of disinhibitory pathways 4 → 6 → 8 and 5 → 7 → 9. When interpreted as catecholamines, these transmitters help to explain data about the action of chlorpromazine and monoamine oxidase inhibitors on motivated behavior (Grossberg, 1982c, p. 348; Olds, 1977, pp. 59–75). The pathways 4 → 6 → 8 → 4 and 5 → 7 → 9 → 5 define positive feedback loops within the on-channel and the off-channel of each dipole. These positive feedback loops maintain a steady baseline of motivated behavior, help to control sharp switching between different motivated behaviors, and hysteretically buffer each motivated behavior against reset by adventitious fluctuations in environmental cues. The positive feedback loops accomplish this by forming part of a competitive network that joins together cells such as 8 and 10. The competition between these cells (e.g., pathway 13) determines which motivated behavior will be chosen at any moment due to a favorable balance of its external reinforcing cues (e.g., 11) and internal drives (e.g., 1 and 2) relative to those of other behaviors. The articles by Grossberg (1982b; 1982c; 1984a) more extensively discuss how feedback gated dipoles regulate motivated behaviors.

15. SOME OVERAROUSED SYNDROMES: SIMPLE SCHIZOPHRENIA AND TWO TYPES OF ANALGESIA

In a motivational dipole field such as Fig. 7, overarousal can cause flat affect, or insensitivity to the emotional and motivational meaning of cues. If the source of overarousal also influences neural networks that process verbal lists, then contextual collapse, fuzzy response categories, and punning can also result (Grossberg and Pepe, 1970; 1971). These properties are all symptoms of simple schizophrenia (Maher, 1977). A likely source of overarousal in schizophrenia is the dopamine hyperactivity of cells in the ventromedial tegmental area, medial to the substantia nigra, that terminate in the limbic forebrain or cortex (Lloyd, 1978; Sternberg *et al.*, 1982).

Several possible sources of overarousal exist in a network such as Fig. 7. All of these arousal sources can cause similar formal properties. The nonspecific arousal pathway 3 might be overaroused. Abnormal enhancement of transmitter production or postsynaptic sensitivity in pathways such as 4 → 6 and 5 → 7 can also have an analogous effect. The resultant enhanced inhibition of the tonic cells 6 and 7 would disinhibit the tonic cells 8 and 9, thereby adding to the total arousal received by cells 4 and 5, and exacerbating the problem by inhibiting the cells 6 and 7 even more. Cells such as 8 and 10 are interpreted in the theory as formal analogs of hippocampal pyramidal cells (Grossberg, 1975; 1982c). This interpretation suggests the possibility that hippocampal pyramidal cells may be abnormal in certain schizophrenics.

Overarousal does not always lead to deleterious behavioral effects. The theory interprets the actions of certain analgesics as causing an overaroused gated dipole syndrome. The reduction in sensitivity that obtains in the overaroused state partially explains the ability of analgesics to reduce the perceived aversiveness of a painful stimulus.

At least two distinct actions of analgesics can be distinguished in a gated dipole circuit. The first type of analgesic action overarouses the nonspecific arousal source of a gated dipole (Fig. 8A), say pathway 3 in Fig. 7. The analgesic action of loud noise (Gardner *et al.*, 1961) and of electrical stimulation of the brain (Watkins and Mayer, 1982) may partly work in this way. In Fig. 8A, the phasic input J represents an aversive input, such as a shock or an endog-

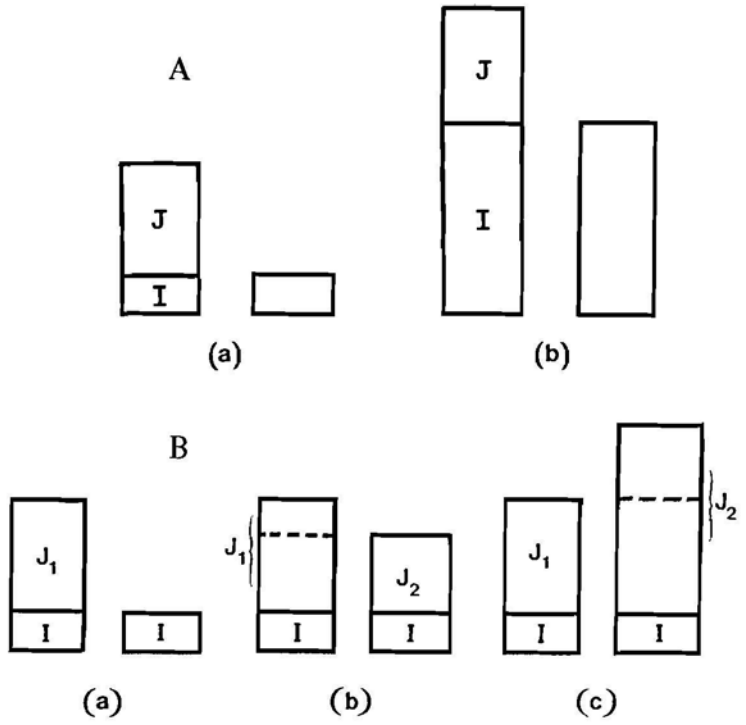

Fig. 8. Two types of analgesic action. A) In (a) and (b), the aversive input J is constant. A larger arousal level I is caused in (b) by the analgesic agent. If enough analgesic is used, the dipole becomes overaroused and its negative onreaction in response to J is depressed. B) In (a)–(c), a constant aversive input J_1 is maintained as larger antagonistic inputs J_2 are caused by parametric increases in the analgesic agent. So long as $J_2 < J_1$, as in (a) and (b), the dipole's total arousal is $I + J_2$ and the net aversive input is $J_1 - J_2$. Both overarousal and net phasic decrement can hereby occur. In (c), $J_2 > J_1$. The total arousal level is $I + J_1$ and a net positive input $J_2 - J_1$ is experienced. A similar analysis shows how a formal hyperphagic syndrome is generated by a lesion in the satiety gating pathway $2 \rightarrow 5 \rightarrow 7$ of Fig. 7 (Grossberg, 1984a). Such a lesion causes an underaroused syndrome after the model becomes "obese."

enously active source of signals. The tonic input I represents arousal level. As I increases, J does not change. However, the net reactions of the on-channel and off-channel are depressed due to overarousal.

The second type of analgesic action generates a phasic input J_2 that antagonizes the aversive phasic input J_1 (Fig. 8B). Just so long as $J_1 > J_2$, the total input $I + J_2$ acts like the dipole's arousal level. (For present purposes, I ignore the effects of other inputs, such as conditional reinforcer signals.) The *net* phasic input to the antagonistic channel is then $J_1 - J_2$, since $J_1 - J_2 = (J_1 + I) - (J_2 + I)$. Thus an increase in J_2 increases the arousal level *and* decreases the net aversive input. An analgesic agent that acts by antagonizing the channel of an aversive input can thus have a powerful analgesic effect by causing both overarousal and net aversive decrement. If $J_2 > J_1$, then the arousal level is $I + J_1$, and the net phasic input is $J_2 - J_1$. Such a cross-over from net negative effect to net positive effect can never occur just by increasing the nonspecific arousal I. The perceived positivity of $J_2 - J_1$ depends upon the size of $I + J_1$. A fixed value of $J_2 - J_1$ elicits less perceived positivity as J_1 is increased, since the dipole is then more overaroused. This property may be used on an animal model to test whether a drug has an antagonistic action.

These parametric properties may be useful in testing whether increased production or release of endorphins (Gintzler, 1980; Guillemin, 1978) may act as antagonizing agents of this type, say by modulating the release of their target transmitter gates (Barker *et al.*, 1978; MacDonald and Nelson, 1978). The fact that actions of this type can influence net arousal level as they alter net dipole output (Fig. 8B) may help explain why both excesses and deficiencies of brain opiates have been cited as causes of mental diseases such as schizophrenia and depression (Marx, 1981): A modulatory alteration of a transmitter gate's release rate can move the affected dipole through its entire inverted U.

Watkins and Mayer (1982) have reported a series of studies concerning footshock-induced analgesia whose interpretation may be clarified by properties of opiate-modulated transmitter gating actions in opponent processes. For example, Watkins and Mayer (1982) describe how the analgesic effect of a brief front-paw shock decays as a function of time elapsed since the shock. This effect may be interpreted as a positive antagonistic rebound effect. In this regard, Watkins and Mayer (1982) did a classical conditioning experiment in which a nonelectrified shock chamber was the conditioned stimulus (CS), grid shock delivered to the front paws of rats was the unconditioned stimulus (UCS), and tail-flick inhibition was the unconditioned response (UCR). After CS-UCS pairings, exposure to the CS produced potent analgesia that can be antagonized by naloxone. Watkins and Mayer (1982, p. 1188) interpret this effect by saying "animals can learn to activate their endogenous opiate systems to inhibit pain." Whereas this interpretation is compatible with their data, a related but distinct phenomenon may also be contributing to these results. If the CS precedes footshock on learning trials, then why does the CS elicit learned analgesia on recall

trials? Should not the CS elicit a net negative reaction on recall trials, as suggested by the large literature about conditioned fear reactions that has accumulated since the classic paper of Estes and Skinner (1941)? Since classical conditioning typically enables a CS to reproduce the main effects of the UCS, direct conditioning of a CS to analgesia is expected if a net analgesic reaction occurs while the CS is still on. This may be the case in the Watkins and Mayer (1982) experiment because their CS is the shock chamber itself. Hence the CS can become associated with events that occur after the shock UCS is turned off. These events can include a positive relief rebound in addition to any analgesic reaction that may have been directly elicited by the prior shock. Even if a conditioned fear reaction is evident until the UCS turns off, then an analgesic action may still be produced on recall trials, albeit indirectly. The unexpected nonoccurrence of footshock after CS presentation may trigger a positive relief rebound, much as occurs in partial reward and overshadowing paradigms (Grossberg, 1975; 1982b).

In order to distinguish these several interpretations, parametric studies need to be done in which the degrees of analgesia before and after the UCS is turned off, and while the CS is still on, are compared with the net affect during recall trials. Also the time course of both effects needs to be parametrically analyzed. For example, the time course of analgesia after a brief shock seems to be similar to the time course of analgesia after classical conditioning (see Watkins and Mayer, 1982, Figs. 1 and 8). It seems paradoxical that the conditioned effect does not endure for a longer time. If both effects are primarily mediated by antagonistic rebounds, however, then this property is easily explained.

16. THE ANALOGY BETWEEN HABITUATION-REBOUND AND TOLERANCE-WITHDRAWAL: PREVENTING WITHDRAWAL

The antagonistic rebound due to phasic input offset in Fig. 4 is due to three factors acting together: (i) Habituation of a chemical gate to presence of a phasic cue. (ii) Slow recovery of the chemical gate after the phasic cue is shut off. (iii) Competition, or opponent processing, between on-channel and off-channel outputs.

These factors may be tersely summarized by the dictum: No Habituation Implies No Rebound.

Another useful way to think about the relationship between habituation and rebound is as follows. In order to achieve an on-channel signal $T = Sz$ of *fixed* size as z progressively habituates, larger inputs S are needed. The increments in S offset the decrements in z to cause constant mass action production of T. From this perspective, a comparison between habituation and drug tolerance, and between antagonistic rebound and drug withdrawal is strongly sug-

gested. If this analogy is valid on the level of mechanism, then it clarifies the more familiar dictum: No Drug Tolerance Implies No Drug Withdrawal. From this perspective, the slow elimination of an addictive drug to minimize withdrawal is analogous to the slow decrease of a phasic input to enable its slow gate to equilibrate without causing rebound.

The comparison of habituation-rebound with tolerance-withdrawal reactions suggests a new strategy for minimizing withdrawal symptoms in response to rapid termination of a tolerance-inducing drug. Habituation occurs as in accumulation-depletion equation 4: $d/dt\ z = A(B - z) - CSz$, because the constant rate A at which z accumulates cannot keep up with the increasing rate CS at which z is depleted. This problem can be overcome formally by enzymatically modulating the accumulation rate A at a rate that increases with S. If the accumulation and depletion rates remain balanced over a wide range of doses S, then tolerance, and hence withdrawal, does not occur. Giving parallel doses of a drug that activates A along with the drug that activates S can achieve such a balance.

Although this possibility may be of purely academic interest at present, it is not biologically irrelevant. Carpenter and Grossberg (1981) suggest, for example, that just such an enzymatic modulation occurs in vertebrate cones. This light-induced enzymatic step enables model photoreceptors to remain sensitive to large fluctuations in photon density through time. In this formal sense, vertebrate cones seem to have overcome their possible "addiction" to light. An analogous question arises concerning the auxiliary mechanisms whereby a gated dipole circuit seeks an arousal level that keeps it near the peak of its inverted U. This issue leads beyond the scope of this article.

17. NORMAL AND ABNORMAL CIRCADIAN RHYTHMS

Gated dipole networks, such as those in Fig. 7, have been used to explain data about motivated behaviors, such as eating and drinking, that are controlled by hypothalamic circuits (Olds, 1977). Another part of the hypothalamus, the suprachiasmatic nuclei (SCN), contain a circadian pacemaker for the control of wake-sleep and activity-rest circadian rhythms (Moore, 1973; 1974). It is natural to inquire whether all hypothalamic circuits, including those in the SCN, are built up from suitably specialized gated dipole networks.

My colleague G. A. Carpenter and I have developed a physiological model of the SCN circadian process that is capable of quantitatively simulating many SCN-controlled circadian phenomena that have not previously been qualitatively explained (Carpenter and Grossberg, 1983b; 1984a; 1984b). These phenomena include split rhythms, several types of long-term aftereffects, phase response curves of nocturnal and diurnal mammals, SCN ablation studies, Aschoff's rule and its exceptions in nocturnal and diurnal mammals, and the suppressive effects

of intense constant light on circadian rhythms. This model is of potential interest to biological psychiatrists for several reasons.

The first reason is that each process in the circadian model is homologous to a process in the eating model. The analog of the eating model's satiety signal is a fatigue signal that is delivered to the circadian pacemaker through the model's "bloodstream." The analog of conditioned reinforcer signals in the eating model is a slowly varying gain signal that buffers the circadian pacemaker against adventitious changes in light, such as cloudy weather. Thus the circuits that control circadian rhythms and emotion-related behaviors may share many design features in common, including their depressive syndromes.

In this regard, Carpenter and I could not fail to notice that narcolepsy is associated with catecholaminergic and serotonergic deficiencies that are treated using tricyclic antidepressants (Mefford *et al.*, 1983). Is narcolepsy, at least in part, a manifestation of an underaroused depressive syndrome associated with a rhythm-generating gated dipole circuit? Of special interest is the possibility that narcolepsy and the obese state of hyperphagia are mechanistically homologous, notably the etiology of frequent short sleep and eating bouts in the two syndromes.

A related issue concerns the ability of any operation that alters the parameters of the model's chemical gating processes to phase shift or change the period of its rhythm. Relevant behavioral evidence shows that antidepressant drugs can alter the mood of manic-depressive patients as they alter the phase of the patients' wake-sleep circadian cycle (Wehr *et al.*, 1979; Kafka *et al.*, 1982; Wehr and Wirz-Justice, 1982). Pharmacological evidence shows that serotonin can induce phase shifts in the circadian pacemaker within the eye of *Aplysia* (Eskin and Takahashi, 1983).

Another clinically important issue concerns our working hypothesis that the output of the SCN pacemaker modulates the arousal input to hypothalamic motivational circuits, such as those controlling eating, drinking, sex, and fear. For example, the output of the circadian model may modulate the arousal input carried by pathway 3 in Fig. 7. From this perspective, the inverted U in sensitivity of a motivational gated dipole is a normal property of its day-to-day performance. Just as a large satiety input after a meal can cause an overaroused syndrome that desensitizes an eating circuit's response to food-related cues, a small arousal level can desensitize all motivational circuits by creating an underaroused syndrome while the network is asleep. Pathological alterations in the level of circadian pacemaker output could hereby induce pathological (e.g., depressive) syndromes in hypothalamic circuits further upstream by altering their levels of arousal. By the same token, feedback to the circadian pacemaker, say via the fatigue signal, may be abnormal due to abnormalities in one or more motivational circuits upstream.

To end the article I briefly describe the gated circadian pacemaker and some of the data that it can reproduce. If nothing else, this exercise makes plain

the fact that gated dipole circuits are capable of very subtle behaviors. One does not require complex components to generate complex behaviors. Even simple networks of simple components can generate very subtle behaviors.

18. RHYTHM AS A SUCCESSION OF SELF-GENERATED REBOUNDS

Why should a (suitably designed) gated dipole oscillate at all? The answer is that the rhythm is due to an unending succession of self-generated antagonistic rebounds. When a phasic input to the on-channel of a gated dipole turns off, an antagonistic rebound occurs in its off-channel. If the on-channel and off-channel excite themselves via positive feedback, then offset of the rebound in the off-channel may act like offset of a phasic input to the off-channel. A rebound in the on-channel is hereby caused. Then offset of the rebound in the on-channel triggers another rebound in the off-channel, and the process continues indefinitely. Just as a single oscillation of a slow gate is needed to generate an indi-

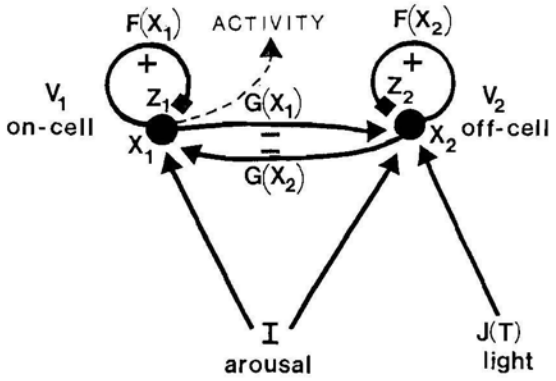

Fig. 9. A gated circadian pacemaker circuit. The potential x_1 of an on-cell (population) and the potential x_2 of an off-cell (population) obey membrane equations. Transmitter z_1 gates the positive feedback signal $F(x_1)$ from the on-cell (population) to itself, and transmitter z_2 gates the positive feedback signal $F(x_2)$ from the off-cell (population) to itself. Term I is the nonspecific arousal level, which is held constant during the stimulations. The off-cells inhibit the on-cells via signal $G(x_2)$ and the on-cells inhibit the off-cells via signal $G(x_1)$. The light input J(T) excites the off-cells in the nocturnal model (depicted here) and the on-cells in the diurnal model. The output from x_1 is assumed to modulate the activity of motivational circuits, say by influencing the arousal levels (e.g., pathway 3) in Fig. 7.

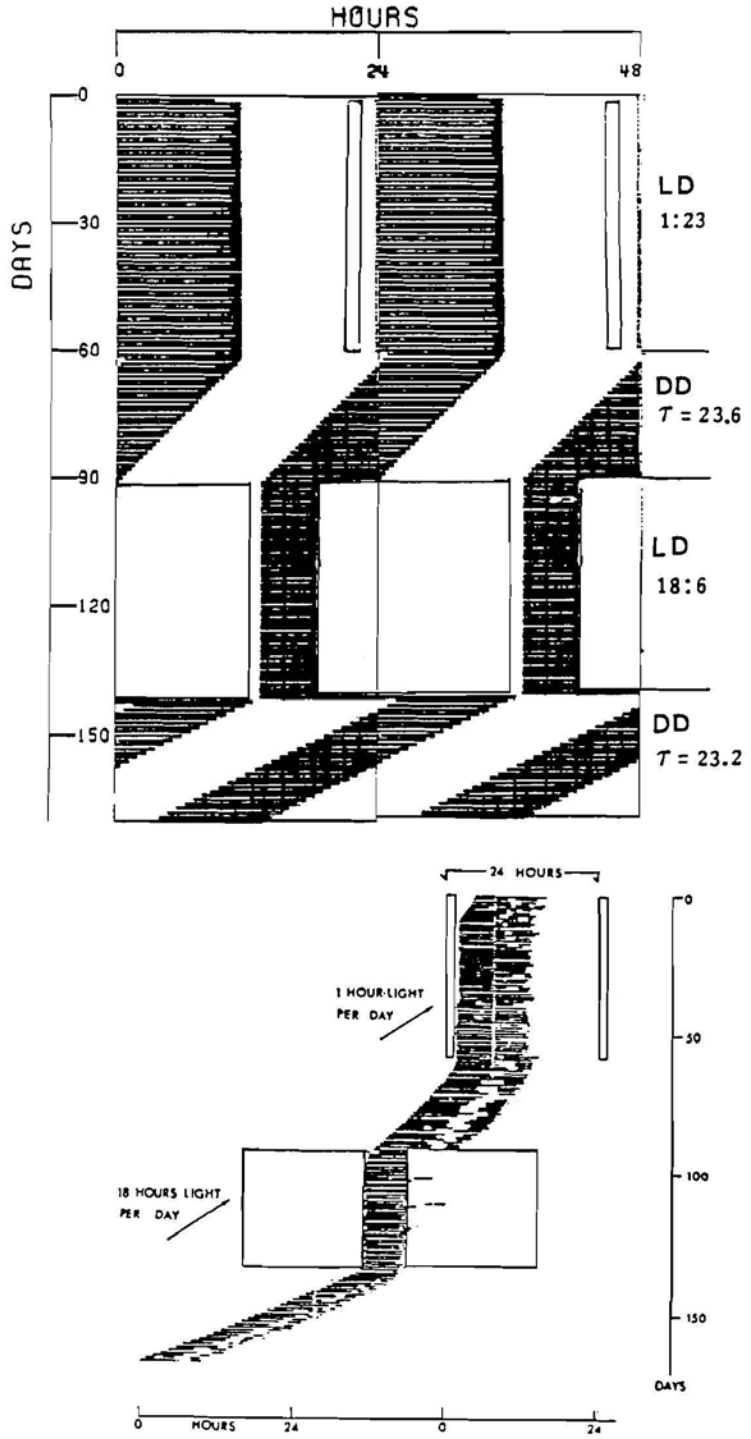

Fig. 10. Simulation of long-term aftereffects of photoperiod is a nocturnal model. The simulation is above the data reported in Pittendrigh (1974). Light was turned on for 1 hr, followed by 23 hr of darkness, for 60 days. The bracketed white regions define the time intervals during which light is on. A free-run in the dark for 30 days followed. The model's free-running period (τ) was 23.6 hr, equal to the period of 23.6 hr in the data. Then 18 hr of light were followed by 6 hr of darkness for 50 days. Thereafter the model free-ran in the dark with a period of 23.2 hr, compared to a period of 23.0 hr in the data. In both model and data, the free-running activity level after 1-hr light pulses exceeded that after 18-hr light pulses.

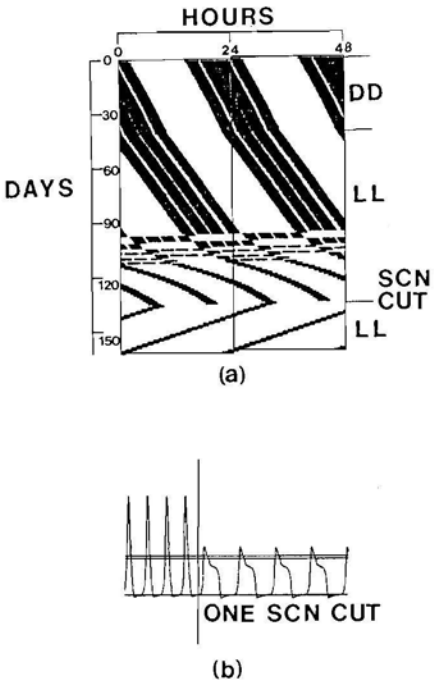

Fig. 11. Simulation of a split rhythm experiment of Pickard and Turek (1982) in a nocturnal model. The dark bars indicate the times at which the model animal is active. In (a), the model is kept in the dark (DD) for 41 days and then is placed in constant light (LL). Initially, the free-running period (τ) increases, as predicted by Aschoff's rule (Aschoff, 1979). On Day 97, the rhythm starts to split, and the split rhythm stabilizes after 15 days of transitional activity. One model SCN is ablated on day 135, after which the split rhythm is abolished. The subsequent τ is shorter than any previous τ. The split rhythm is abolished due to a decrease in the total number of pacemaker on-cells, depicted in Fig. 9, and the resulting decrease in a feedback signal that is a metabolic index of fatigue. In (b), the on-cell potential $x_1(t)$ is shown 2 days before the ablation and 4 days after the ablation. Note the qualitative difference in wave form and activity levels before and after ablation.

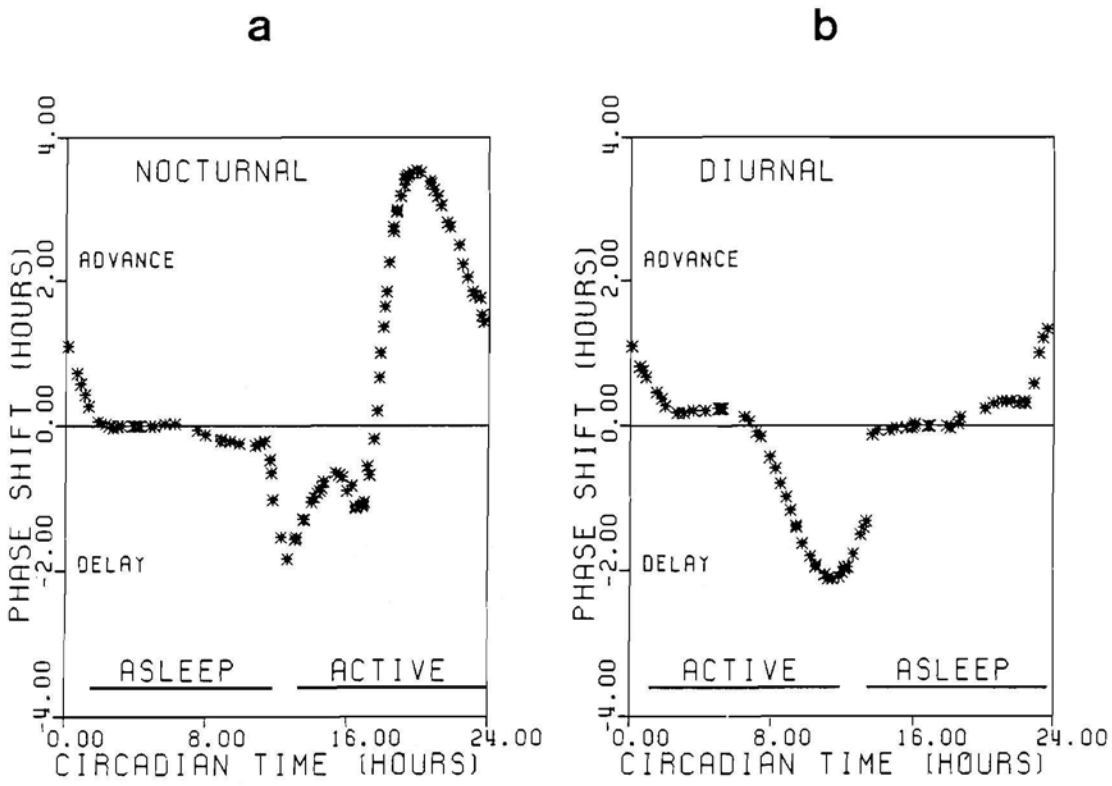

Fig. 12. Phase response curves of the nocturnal and diurnal models in response to brief pulses of light. Both phase response curves are identical when eye closure during sleep does not attenuate the effectiveness of light. When eye closure does attenuate the light input to the pacemaker, the dead zone of the phase response insensitivity is produced during the subjective day of a nocturnal model but not of a diurnal model, as in the data (Pohl, 1982).

vidual rebound in any gated dipole (see Fig. 1), a sustained oscillation of the slow gates in a gated pacemaker maintains its circadian rhythm. Many neural transmitters are known to oscillate with a circadian rhythm (Naber *et al.*, 1981; Kafka *et al.*, 1981a, 1981b). The model's transmitters oscillate because their gating action forms part of the pacemaker mechanism, not merely because they are driven by a separate pacemaker.

Figure 9 depicts one of the gated pacemaker circuits that are assumed to occur in the SCN. Figure 10 simulates long-term after-effects in the deermouse, which is a nocturnal mammal (Pittendrigh, 1974). Figure 11 simulates an example in the (nocturnal) hamster of Aschoff's (1979) rule, the slow onset of split rhythms, and the elimination of split rhythms by ablating one of the two SCN nuclei (Pickard and Turek, 1982). Figure 12 simulates the phase response curves of nocturnal and diurnal mammals to pulses of light, including the "dead zone" of phase resetting insensitivity that occurs in nocturnal, but not diurnal, mammals (Pohl, 1982).

19. CONCLUDING REMARKS

This article illustrates the remarkable diversity of properties, and the predictive and explanatory power, of neural network circuits that are built up from tonically aroused, chemically gated, opponent processes. These examples suggest that gated dipole circuits instantiate a fundamental principle of neural design, and recommend the intensive investigation of such circuits, both formally and in relation to interdisciplinary data, by a large number of investigators.

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