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# The Brain as a Dream State Generator: An Activation-Synthesis Hypothesis of the Dream Process

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*Recent research in the neurobiology of dreaming sleep provides new evidence for possible structural and functional substrates of formal aspects of the dream process. The data suggest that dreaming sleep is physiologically determined and shaped by a brain stem neuronal mechanism that can be modeled physiologically and mathematically. Formal features of the generator processes with strong implications for dream theory include periodicity and automaticity of forebrain activation, suggesting a preprogrammed neural basis for dream mentation in sleep; intense and sporadic activation of brain stem sensorimotor circuits including reticular, oculomotor, and vestibular neurons, possibly determining spatiotemporal aspects of dream imagery; and shifts in transmitter ratios, possibly accounting for dream amnesia. The authors suggest that the automatically activated forebrain synthesizes the dream by comparing information generated in specific brain stem circuits with information stored in memory.*

SINCE THE TURN of the century, dream theory has been dominated by the psychoanalytic hypothesis that dreaming is a reactive process designed to protect consciousness and sleep from the disruptive effect of unconscious wishes that are released in sleep (1). Thus dreaming has been viewed as a psychodynamically determined state, and the distinctive formal features of dream content have been interpreted as manifestations of a defensive transformation of the unconscious wishes found unacceptable to consciousness by a hypothetical censor. A critical tenet of this wish fulfillment-disguise theory is that the transformation of the unconscious wish by the censor disguises or degrades the ideational information in forming the dream imagery. We were surprised to discover the origins of the major tenets of psychoanalytic dream theory in the neurophysiology of 1890 and have specified the transformations made by Freud in an earlier, related article (2). In detailing the neurophysiological origins of psychoanalytic dream theory, the concept of mind-body isomorphism, denoting similarity of form between psychological and physiological events, was seen as an explicit premise of Freud's thought.

Sharing Freud's conviction that mind-body isomorphism is a valid approach, we will now review modern neurophysiological evidence that we believe permits and necessitates important revisions in psychoanalytic dream theory. The activation-synthesis hypothesis that we will begin to develop in this paper asserts that many formal aspects of the dream experience may be the obligatory and relatively undistorted psychological concomitant of the regularly recurring and physiologically determined brain state called "dreaming sleep." It ascribes particular formal features of the dream experience to the particular organizational features of the brain during that state of sleep. More specifically, the theory details the mechanisms by which the brain becomes periodically activated during sleep and specifies the means by which both sensory input and motor output are simultaneously blocked, so as to account for the maintenance of sleep in the face of strong central activation of the brain. The occurrence and character of dreaming are seen as both determined and shaped by these physiological processes.

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The most important tenet of the activation-synthesis hypothesis is that during dreaming the activated brain generates its own information by a pontine brain stem neuronal mechanism, which will be described in detail. We hypothesize that this internally generated sensorimotor information, which is partially random and partially specific, is then compared with stored sensorimotor data in the synthesis of dream content. The functional significance of the brain activation and the synthesis of endogenous information in dreaming sleep is not known, but we suggest that state-dependent learning is at least as likely a result of dreaming as is tension reduction or sleep maintenance.

While we believe that the two processes emphasized in this paper—activation and synthesis—are major and important advances in dream theory, we wish to state explicitly and comment on some of the things that our theory does not attempt to do. The activation-synthesis hypothesis does not exclude possible defensive distortions of the value-free sensorimotor dream stimuli, but it does deny the primacy of any such process in attempting to explain *formal* aspects of dream content or the fundamental impetus to dreaming itself. The idea that dreams reveal wishes is also beyond the direct reach of our new theory, but some specific alternatives to this interpretation of several classic dream situations can be advanced.

The new theory cannot yet account for the emotional aspects of the dream experience, but we assume that they are produced by the activation of brain regions subserving affect in parallel with the activation of the better known sensorimotor pathways. Finally, the new theory does not deny meaning to dreams, but it does suggest 1) a more direct route to their acquisition than anamnesis via free association, since dream origins are in basic physiological processes and not in disguised wishes, 2) a less complex approach to their interpretation than conversion from manifest to latent content, since unusual aspects of dreams are not seen as disguises but as results of the way the brain and mind function during sleep, and 3) a broader view of their use in therapy than that provided by the transference frame of reference, since dreams are not to be interpreted as the product of disguised unconscious (transference) wishes. Dreams offer a royal road to the mind and brain in a behavioral state, with different operating rules and principles than during waking and with the possibility of clinically useful insights from the product of these differences. These points are discussed in the last section of this paper and elsewhere (3).

## WHAT IS A DREAM?

A dream may be defined as a mental experience, occurring in sleep, which is characterized by hallucinoid imagery, predominantly visual and often vivid; by bizarre elements due to such spatiotemporal distortions as condensation, discontinuity, and acceleration; and by a delusional acceptance of these phenomena as "real" at the time that they occur. Strong emotion may or may not be associated with these distinctive formal properties of the dream, and subsequent recall of these mental events is almost invariably poor unless an immediate arousal from sleep occurs.

That this technical jargon describes a universal human experience seems certain, since the five key points in this definition are easily elicited from both naïve and sophisticated individuals when they are asked to characterize their dreams. We leave aside the question of whether other less vivid and nonperceptual forms of mental activity during sleep should also be called "dreams" and confine ourselves here to the psychophysiology of the hallucinoid type of dream. In doing so, we not only simplify the immediate task at hand but may also gain insight into the mechanisms underlying the most florid symptoms of psychopathology. We mean, of course, the hallucinations and delusions of the psychotic experience, which have so often invited comparison with the dream as we have defined it here.

**TABLE 1**
**Electrographic Criteria for Behavioral State Determination**

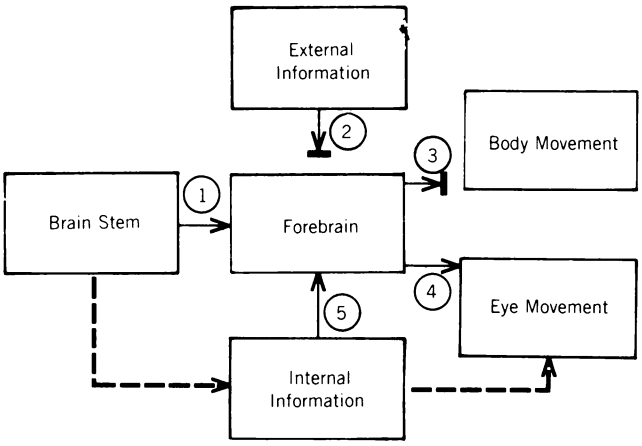
| State | Electromyogram | EEG | Electrooculogram |
|---|---|---|---|
| Waking | + | Low voltage, fast | + |
| Sleep | | | |
| Synchronized | + | High voltage, slow | — |
| Desynchronized | — | Low voltage, fast | + |

## WHAT IS THE STATE OF THE BRAIN DURING DREAMING SLEEP?

The physiological substrate of the dream experience is the CNS in one of its three principal operating states: waking (W), synchronized sleep (S), and desynchronized sleep (D). These states can be reliably and objectively differentiated by recording the EEG, the electromyogram (EMG), and the electrooculogram (see table 1). Hallucinoid dreaming in man occurs predominantly during the periodically recurrent phase of sleep characterized by EEG desynchronization, EMG suppression, and REMs (4). We call this kind of sleep "D" (meaning desynchronized, but also conveniently denoting dreaming).

In the systems analysis terms used in figure 1, this D brain state is characterized by the following "sensorimotor" properties: activation of the brain; relative exclusion of external input; generation of some internal input, which the activated forebrain then processes as information; and blocking of motor output, except for the oculomotor pathway. In this model the substrate of emotion is considered to be a part of the fore-

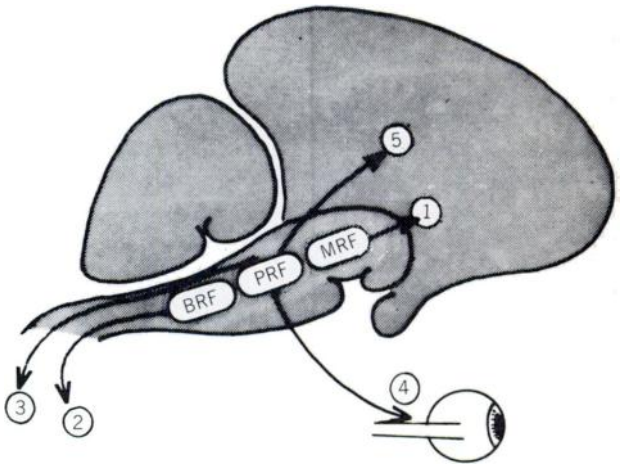
**FIGURE 1**
**Systems Model of Dream State Generation**




Processes Accounted for:

1. Activation of forebrain
2. Blockade of exteroceptive input
3. Blockade of motor output
4. Oculomotor activation
5. Provision of forebrain with internally generated information

**FIGURE 2**
**Physiological Model of Dream State Generation Using the Sagittal Section of the Cat Brain and Showing the Bulbar (BRF), Pontine (PRF), and Midbrain (MRF) Divisions of the Reticular Formation**




Processes Accounted for:

1. Activation of forebrain
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3. Blockade of motor output
4. Oculomotor activation
5. Provision of forebrain with internally generated information

brain; it will not be further distinguished here because we have no specific physiological evidence as to how this part of the system might work in any brain state. Memory is not shown but is considered to be a differentiated function of the brain that operates during the D state, such that output from long-term storage is facilitated but input to long-term storage is blocked. A highly specific hypothesis about dream amnesia has previously been derived (5) from the same evidence that we will now review in our attempt to account for the general sensorimotor aspects of the dream process.

## ELECTROPHYSIOLOGY OF THE BRAIN DURING THE DREAM STATE

The three major electrographic features of the D state are of obvious relevance to our attempt to answer the following three questions about the organization of the brain in the dream state.

*How is the forebrain activated in the D state?* Since EEG desynchronization also characterizes waking, similar mechanisms of "activation" may be involved in both instances. Physiological evidence suggests that this is so: the reticular formation of the anterior brain stem is at least as active in D sleep as it is in the waking state (see figure 2).

*How is motor output blocked in the D state?* Physiological evidence clearly shows that the profound EMG suppression of D sleep is a consequence of the direct inhibition of spinal cord motoneurons (6). As a consequence, any organized motor patterns that might be generated during the intense brain activation of D sleep cannot be expressed.

That organized movement patterns are in fact generated, but not expressed, in normal D sleep is dramatically demonstrated by cats with lesions of the anterodorsal pontine brain stem (7). The animals show all of the major manifestations of D sleep except the atonia; instead of the fine twitches of the digits and the limb jerks that are normally present in D, these cats display complex motor behaviors including repetitive paw movements and well-coordinated attack and defense sequences that have no apparent relationship to the environment.

*How is sensory imagery generated in the D state?* In waking, a corollary discharge of the oculomotor system has been shown to suppress visual transmission during saccadic eye movements, possibly contributing to the stability of the visual field during that state (8). The same mechanisms might underlie the hallucinoid dream imagery by inhibiting and exciting neurons of the lateral geniculate body (9) and the visual cortex (10) during D sleep, when retinal input is reduced and unformed.

The possibility that oculomotor impulses trigger visual imagery is particularly intriguing in view of the demonstrated quantitative correlation between eye

movement intensity and dream intensity (11). More specific correlations have also been reported to relate eye movement direction to orientation of the hallucinated gaze in dreams (12). This finding has been interpreted as indicative of "scanning" the visual field—implying cortical control of the eye movements in dreaming sleep. An alternative, although not exclusive, hypothesis is that the oculomotor activity is generated at the brain stem level and that the cortex is then provided with feed-forward information about the eye movements. According to this view, we are not so much scanning dream imagery with our D sleep eye movements as we are synthesizing the visual imagery appropriate to them. We will return to the implications of this intriguing possibility in discussing the generation of eye movements in dreaming sleep, but we wish to stress here the general significance of this clue to the identity of an "internal information generator" operating at the brain stem level in the dreaming sleep state.

The eye-movement-related inhibition of sensory relays (13), as well as the possible occlusion of exogenous inputs by internally generated excitation, may also contribute to the maintenance of sleep in the face of strong central activation of the brain. In this sense the dream process is seen as having a sleep maintenance mechanism built into its physiological substrate rather than a sleep guardian function operating at the psychological level.

A firm general conclusion can be reached at this point: the desynchronized phase of sleep is the physiological substrate of hallucinoid dreaming, as defined. This conclusion is of profound significance to psychophysiology, since we can now reliably and objectively characterize and measure many aspects of the brain when it is in the dream state. For example, one feature that emerges from the psychophysiological study of dreaming and one that was not at all evident from introspective, psychoanalytically oriented research, is that the brain enters the dream state at regular intervals during sleep and stays in that state for appreciable and predictable lengths of time. One clear implication of this finding is that dreaming is an automatically preprogrammed brain event and not a response to exogenous (day residue) or endogenous (visceral) stimuli. A second implication is that the dream state generator mechanism is periodic, that is, the dream state generator is a neurobiological clock (14). Since the length of the sleep cycle and, by inference, the frequency of dreaming, is a function of body size within and across mammalian species (15), the system controlling the length of the period must have a structural substrate. Thus we must account for size-related periodicity with our model of the dream state generator.

## AN ANIMAL MODEL OF THE BRAIN DURING THE DREAM STATE

We said that the length of the sleep cycle varies "across species." Does that mean that nonhuman animals dream? Unfortunately we cannot know, but we are willing to assert that if they do so, it is when their brains are in the D sleep state. Because we have no direct evidence of any significant difference between the brain state of man and the brain state of other mammals in D sleep, we therefore feel justified in asserting that the brain state of our experimental animal, the cat, constitutes a reasonable subject for our study of the brain as a dream process generator, whether or not cats dream. This assertion seems justified since we are restricting our attention here to formal aspects of the dream experience; our experimental model need not dream or even possess "consciousness" to be useful as a source of physiological information. If we accept this argument and use the definition of dreaming offered above, then the presence of D sleep in cats (16) offers nothing less than an animal model in which to study the neurophysiological basis of a hallucinoid mental process in man. Such a model is as important in experimental psychiatry as it is rare. Let us now turn to the biological data upon which our sketches of the brain as a dream state generator are based.

## LOCALIZATION OF THE POWER SUPPLY OR TRIGGER ZONE OF THE DREAM STATE GENERATOR

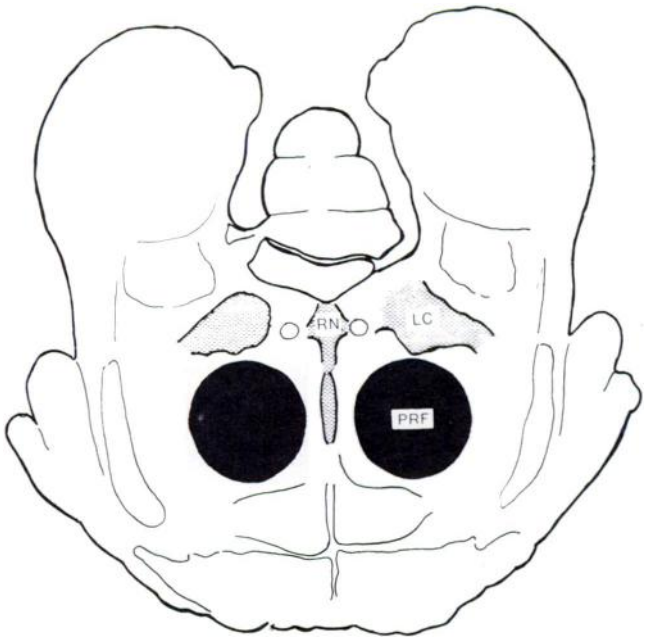
Lesion, stimulation, and recording studies pioneered by Jouvet (17) have strongly implicated the pontine brain stem as critical to the generation of the desynchronized sleep phase (see figure 3 for a summary of the neuroanatomy of this region). Important findings supporting this hypothesis include the following.

Large lesions of the pontine reticular formation prevent the occurrence of desynchronized sleep for several weeks in cats (17). This suggests that the pontine reticular formation may be the site of an executive or triggering mechanism for desynchronized sleep. Prepontine transections and forebrain ablation have no effect upon periodicity or duration of the skeletal, muscular, and oculomotor manifestations of D sleep (17). The data indicate that the trigger, the power supply, and the clock are pontine.

The pontine brain stem is thus implicated as the site of both the trigger and the clock. The periodicity of the D sleep clock in poikilothermic pontine cats lengthens as temperature declines, indicating orthodox metabolic mediation of the cycle, in contrast to the temperature independence of circadian rhythms. If we assume that the physiological substrate of consciousness is in the forebrain, these facts completely eliminate any possible contribution of ideas (or their neural substrate) to the primary driving force of the dream process.

Small lesions of the dorsal pontine brain stem, in the region of the locus coeruleus (LC), may eliminate the atonia but no other aspects of desynchronized sleep (7). This suggests that inhibition of muscle tone

**FIGURE 3**
**The Anatomy of the Pontine Brain Stem***




*On this frontal section of the cat brain stem, the cells that are selectively activated are in the paramedian reticular formation (PRF) (giganto cellular tegmental field), while the cells that are selectively inactivated lie more dorsally (in the region of the locus coeruleus [LC]) and medially (in the region of the raphe nuclei [RN]). Compare this with figure 5, which summarizes the neurophysiology and shows the anatomy in a sagittal section.

is somehow dependent upon the integrity of the LC. The elaborate motor behavior that characterizes the D sleep of cats with LC lesions has been described as "pseudo-hallucinatory" (7). Whether or not one accepts the sensory implications of that designation, the importance of motor inhibition in quelling the effects of central excitation during the dream state is clear.

This finding has an important bearing on mechanisms of dream paralysis and suggests that in the classic chase dream, the dreamer who has trouble fleeing from a pursuer is as much accurately reading the activated state of his motor pattern generator and the paralyzed state of his spinal neurons as he is "wishing" to be caught. This dream experience is so universal and the feeling of constrained motor action so impressive as to make its physiological basis in the descending inhibition of motoneurons seem to us inescapable. Conversely, this reasonable and adequate explanation of the paradox of the chase dream makes its interpretation as wish fulfillment less compelling. Other implications of the D sleep activation of various motor system pattern generators for movements and dream plots have been discussed elsewhere (3).

The vestibular system, as classically established, integrates head position and movement with eye position and posture. Pompeiano and Morrison (18) showed that lesions of the vestibular nuclei interfered with the bursts of REM but not with the isolated eye movements of D. This finding suggested that the vestibular system contributed to the elaboration and rhythmicity of the eye movements but that the eye movement generator was extravestibular. Magherini and associates (19) found that systemic injections of the anticholinesterase agent physostigmine produced rhythmic eye movements in decerebrate cats, suggesting that the eye movement generator may be cholinergic. Thus the central, automatic activation during sleep of the vestibular system may provide a substrate for endogenously generated, specific information about body position and movement. Flying dreams may thus be a logical, direct, and unsymbolic way of synthesizing information generated endogenously by the vestibular system in D sleep. In view of this reasonable and direct explanation, it seems gratuitous to "interpret" the sensual flying dream as sexual.

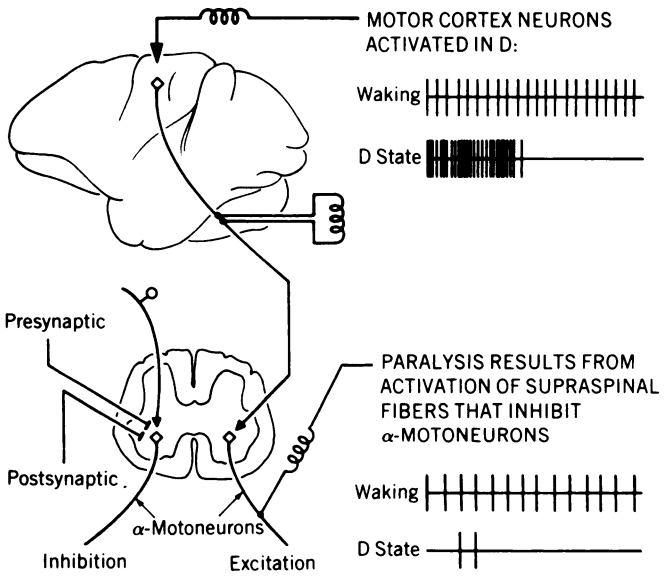
In accord with the isomorphism principle, the degree of neuronal activation in brain systems should parallel the frequency and intensity of dreams to these systems (3), and the predominance of visual sensorimotor activity in both brain and mind supports this notion. Symbol formation and the often bizarre juxtaposition of sensations in the dream may be a reflection of the heightened degree of simultaneous activation of multiple sensory channels in dreaming as compared with waking (3).

Long-term electrical stimulation of the pontine brain stem results in the earlier appearance of sleep episodes and in increases in the absolute amounts of desynchronized sleep, but it does not affect the periodicity of its occurrence (20). By implication, the delivery of electrical energy accomplishes what most psychological and behavioral treatments fail to achieve: an increase in the duration of dreaming sleep. Testing the assumption that the generator neurons are cholinoceptive, our laboratory team has recently established that injection of the cholinergic agent carbachol into the pontine reticular formation produces prolonged enhancement of D-like sleep behavior (21). In man the parenteral injection of the anticholinesterase agent physostigmine potentiates D sleep, and the pharmacologically induced episodes are associated with hallucinoid dreaming (22). The time of occurrence and duration of dreams may thus be chemically determined.

In summary, these results support the hypothesis that the pontine brain stem is the generator zone for the D sleep state. The trigger mechanism for the whole system, including the eye movement generator, may be cholinoceptive and the executive zones are probably in the reticular formation. The LC is involved, possibly in a permissive or reciprocal way, and is especially important in mediating spinal reflex inhibition. Together, these two regions may constitute the clock. We will have more to say about the hypothesis of reciprocal interaction between them later in this paper.

Although the brain stem mechanisms mediating atonia remain obscure, it is clear from the work of Pompeiano (6) that both monosynaptic and polysynaptic spinal reflexes are tonically inhibited during D sleep (see figure 4). In addition, during the bursts of REM,

**FIGURE 4**
**Mechanisms of Sleep Paralysis***




*The upper part of the figure illustrates the intense activation in D sleep of antidromically identified pyramidal tract neurons of the motor cortex. Note the relatively regular discharge in waking (W) and the clustering of discharges in D sleep in these models of 3-second epochs of microelectrode recordings (vertical lines indicate discharges). The lower portion of the figure shows the inhibitory events of D at the spinal cord level that largely prevent alpha motoneuron discharge and consequent muscle excitation, despite the activation of excitatory (arrow) pyramidal tract fibers. Both presynaptic and postsynaptic inhibition (bars) are present in D (sketched on the left side of the cord section). Absence of this inhibition in W allows alpha motoneuron discharge in response to excitation from pyramidal tract fibers (17).

there is a descending presynaptic inhibition of the most rapidly conducting (group 1*a*) spinal afferent endings. Both presynaptic and postsynaptic inhibition appear to be of brain stem origin. Phasic presynaptic inhibition has also been shown to occur in sensory relays elsewhere in the brain during D sleep (6). Thus motor output is tonically damped throughout D and sensory input is phasically damped in concert with the REM bursts. In other words, we are not only paralyzed during our dreams, but the degree to which we are paralyzed fluctuates in concert with the intensity of the internally generated information and the degree to which we suppress exogenous input.

On the basis of this evidence, the systems terminology used earlier (see figure 1) can be tentatively translated into the anatomical and physiological terms of figure 2; and the activation-synthesis hypothesis of dreaming can be stated as follows: during D sleep, a cholinergic mechanism in the reticular formation of the pontine brain stem is periodically activated. The consequences of this activation are as follows:

1. The forebrain is tonically activated, probably via the midbrain reticular formation that is also responsible for its activation during waking. Thus the forebrain is made ready to process information.

2. The spinal reflexes are tonically inhibited, possibly via the bulbar reticular formation and LC; thus motor outflow is blocked despite high levels of activity in the brain, including the motor cortex.

3. The oculomotor and vestibular systems are phasically activated by the pontine reticular formation so as to produce eye movements. This circuitry, in its entirety, is an internal information source or generator that provides the forebrain with spatially specific but temporally disorganized information about eye velocity, relative position, and direction of movement. Information may similarly be derived from the brain stem generators of patterned motor activity.

4. At the same time that internal information feedback is being generated by the activation of various motor systems, exteroceptive input to sensory systems is phasically blocked. This may intensify the relative impact of the endogenous inputs to the brain, accounting for the intensity of dream imagery and preventing sleep disruption by the externally generated excitation.

This working sketch of the dream state generator, based on the classical localizing methods of experimental neurology, is intriguing but unsatisfying in that it fails to specify the mechanisms by which the pontine generator is turned on, kept active for a time, and then shut off. Further, it does not say anything about the mechanism of periodicity. To provide details about the anatomy and physiology of the periodic trigger mechanisms of the generator process, we will now turn our attention to the neuronal level of analysis. In doing so, we also come full circle in our reaffirmation of isomorphism since it was the neuron that Freud recognized as the physical unit of the nervous system on which he based his dream theory (2).

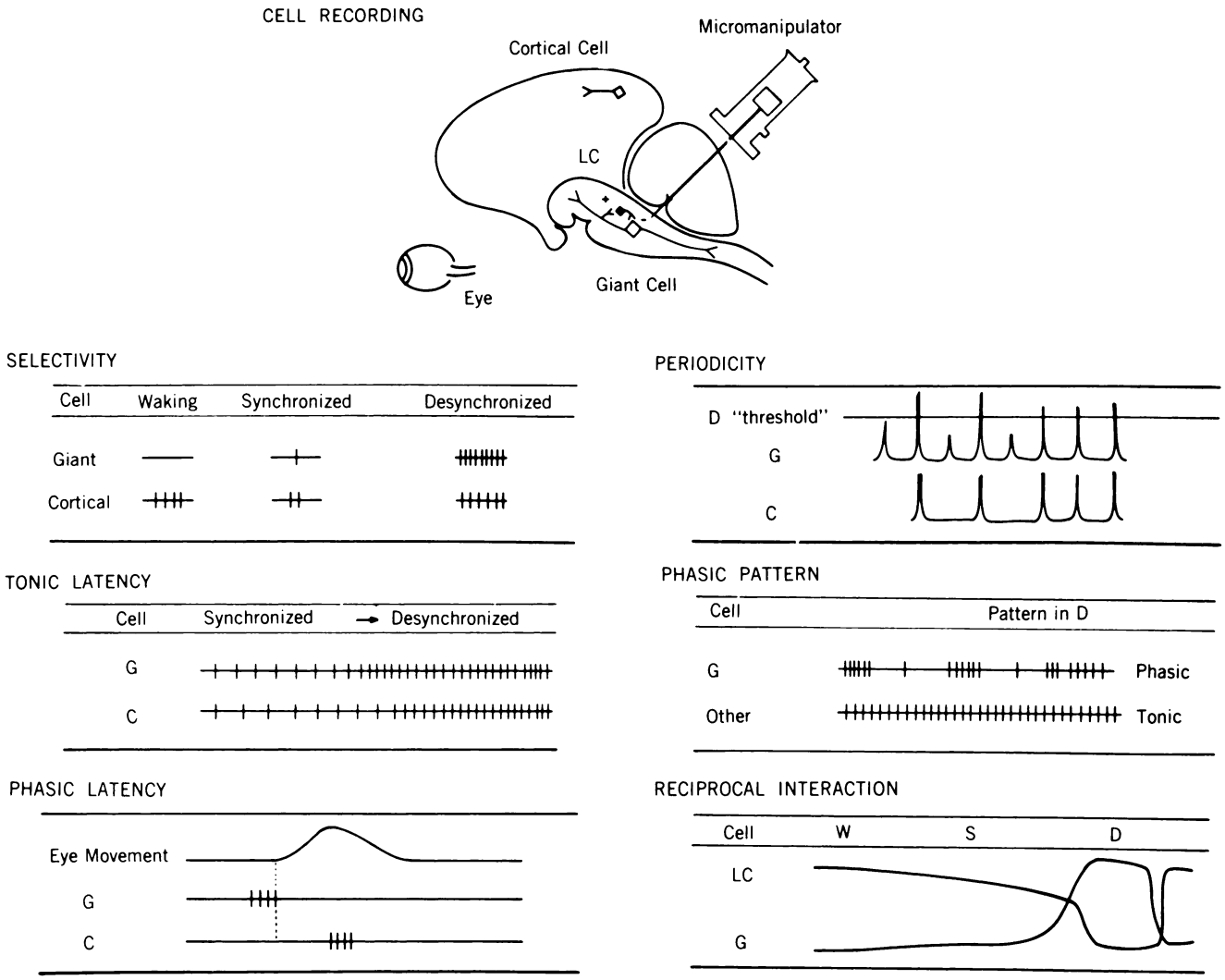
## HISTOLOGICAL FEATURES OF RELEVANCE TO THE PERIODIC TRIGGERING OF THE DREAMING SLEEP STATE GENERATOR

Several structural details of the pontine brain stem are notable as possible elements of a D sleep control device with rhythmic properties (see figure 3 for an illustration of the anatomy discussed).

In his discussion of the histology of the pontine brain stem, Cajal (23) emphasized three points:

1. The paramedian reticular giant cells, with their rostral and caudal axonal projections, are admirably suited to serve as output elements of the generator; when excited they could influence many other cells. The work of Brodal (24) and the Scheibels (25) shows that the spinal cord and thalamus receive projections from these elements. Although they are relatively few in number, conservative estimates of their postsynaptic domain indicate that each directly projects to nine million ($9\times10^6$) postsynaptic neurons. Thus the 3,000 pontine reticular giant cells in the cat might make many billions of synapses ($2.9\times10^{10}$). Since the giant cells also project to other brain stem nuclei and have recurrent axons to themselves, mutual interaction with raphe-type elements (see below) and self-reexcitation

**FIGURE 5**
**Cellular Neurophysiology of Dream State Generation***




*The cell recordings are made from hydraulically driven microelectrodes that can be stereotaxically directed at neurons in the cat brain during natural sleep. Two classes of brain stem neurons are represented by the reticular giant cell (G in the physiological models) and the LC cell; the synaptic interactions suggested are detailed in figure 8. A cortical cell is also shown.
The results of the cell recording experiments are shown in six models representing the criteria used to quantify discharge properties: selectivity—giant cells concentrate their discharge in D to a greater extent than cerebral cortical or other brain stem neurons; tonic latency—giant cells show rate increases that precede those of cortical neurons during the S to D transition; phasic latency—giant cells fire before the REMs of D, while cortical neurons fire after them; periodicity—peaks in the giant cell activation curves are periodic and the higher peaks are associated with D sleep episodes and peaks of cortical activity; phasic pattern—giant cells show a higher degree of clustered firing in D than do other neurons; and reciprocal interaction—the rate curves of giant cells and LC cells are reciprocal over the sleep cycle.

are both possible. These two features could be used to create excitability variability, with powerful consequences for the whole nervous system.

2. The raphe neurons of the midline are ideally situated and connected to regulate excitability of paramedian elements, and they also have extensive projections to other brain regions. The discovery that these cells concentrate the biogenic amine serotonin (26) gives this regulatory hypothesis an attractive corollary: these cells might regulate excitability of their postsynaptic neurons via specific transmitter substances. Another brain stem cell group, in the locus coeruleus, has been shown to concentrate the amine norepinephrine (26). There are thus at least two neuronal candidates for a level setting role, and both are probably inhibitory. Since the giant cells are excitatory (and probably cholinergic; see below), a substrate for reciprocal interaction is established.

3. Cajal (23) suggested that input to the central reticular core might be via small stellate cells in the lateral zone. This input channel, which we now know to be more diffuse than was originally suspected, could be used to abort or damp the core oscillator at critical ambient stimulus levels. This is an important feature,

since adaptation depends on the capacity to interrupt the cycle and not to incorporate all exogenous stimuli into the dream plot.

## CELLULAR ACTIVITY IN THE PONTINE BRAIN STEM DURING THE SLEEP CYCLE

A direct experimental approach to the question of D state control has been made with cats by recording from individual neurons in many parts of the brain as the sleep cycle normally evolved. In this experimental paradigm, the frequency and pattern of extracellular action potentials, which are the signal units of nerve cells, are taken as indices of a cell's excitability; the influence of a recorded neuron upon other cells and that neuron's own control mechanism may also be inferred from the data. This method has the advantage of being relatively physiological since it does little to alter or damage the properties of the system under study. When cats are kept active at night, they will sleep under the necessary conditions of restraint during the daytime. The microelectrodes can then be stereotaxically directed at the brain stem and individual cell activity recorded for as long as 20 hours, allowing many successive sleep cycles to be studied (see figure 5).

The pontine brain stem control hypothesis has been tested in three ways at the level of single cells.

*Selectivity criterion: which cells change rate most in D?* We assumed that cells which showed pronounced alterations in discharge rate over the sleep cycle were more likely to be playing a controlling role than those showing minimal change. We further assumed that those cells having peaks of activity in phase with the D phase of the cycle were more likely to be specifically and actively involved in dreaming sleep state control than those with multiple peaks. We found that the giant cells of the pontine tegmentum concentrated their discharge in the D phase of sleep to a greater extent than any other group of neurons (27). They became our prime candidate for a generator function.

*Tonic latency criterion: which cells change rate first in D onset?* If the cells with positive discharge selectivity were driving the dreaming sleep phase of the sleep cycle, then their rates would be expected to increase in advance of the behavioral state change. Such phase leads might well be longer than those of the follower neurons under the control of the giant cells. The giant cells, when recorded over entire sleep cycles and through repeated sleep cycles, were found to change rate continuously (28). Significant rate increases occurred *as long as 5 minutes* before a desynchronized sleep phase. When the 2 minutes just prior to desynchronized sleep onset were studied, a rate increase in a pool of giant cells was observed 10 seconds before a similar increase in a pool of cerebral cortical neurons.

The rapidly accelerating limb of the giant cell activity curves at D sleep phase onset indicated that this was a time of maximal excitability change in this pool of neurons. The goodness of fit of the data by an exponential curve indicated that reexcitation within the pool might be superimposed upon disinhibition from without. The positive tonic latency indicated that the activation of the forebrain might be a consequence of activation of the brain stem but that the converse could not be the case.

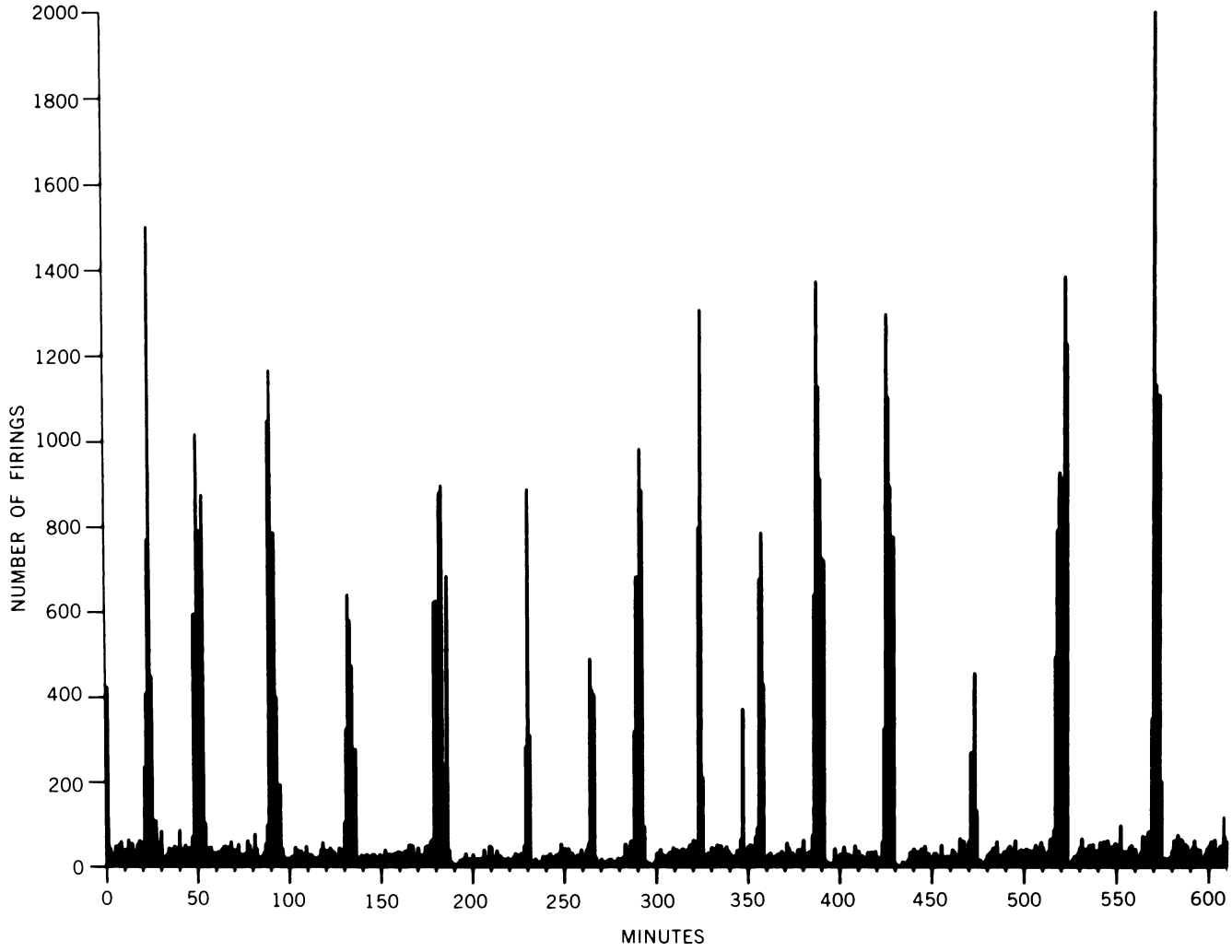
*Phasic latency criterion: which cells fire before eye movements of D?* Because of the proximity and direct projections to oculomotor neurons from giant cells, we tested the possibility that they might be generating the REMs so characteristic of the desynchronized phase of sleep by determining the time of occurrence of short-term rate increases by the giant cells in relation to eye movement onset. On the average, such rate increases were more prominent and anticipated eye movement by longer intervals than other brain stem neurons (29). Rate increases by presumed follower elements (in the posterolateral cerebral cortex) *followed* the eye movements by many milliseconds. It could therefore be concluded that the eye movements might be initiated by giant cells but could not be generated by cortical neurons. This finding practically wrecks the scanning hypothesis and strongly favors the idea that visual cortical events are determined by events in the oculomotor brain stem.

At this point we felt justified in concluding that the giant cells of the pontine tegmentum were critical output elements in a sleep cycle control mechanism. More particularly, we proposed that they might be generator elements for some of the tonic and phasic excitatory events in the desynchronized sleep phase of the cycles: most important to the activation-synthesis hypothesis of dreaming are the determination of EEG desynchronization (activation of the forebrain) and REMs (provision of forebrain with internally generated information). At the very least, we felt that we had found an important avenue to understanding sleep cycle control, since we could now examine the properties and possible mechanisms of giant cell excitability regulation. In this regard there are three additional points worthy of emphasis.

*Periodicity criterion.* Long-term recordings of giant cells revealed peaks of activity in phase with each full-blown desynchronized sleep episode (30) (see figure 6). Less prominent peaks were associated with abortive episodes and were rarely seen with no electrographic evidence of desynchronized sleep. Spectral analysis of these long-term data confirmed the impression of powerful periodicity in the discharge peaks, indicting that 1) sleep cycles are periodic, 2) underlying cell activity is probably even more so, and by definition, 3) cell excitability is under the control of a neurobiological clock. The possible mechanisms of excitability control are thus of great interest.

*Phasic pattern criterion.* The pattern of giant cell discharge within each D sleep episode indicated that classical pacemaker mechanisms are *not* involved in giant cell excitability regulation (31). Regular inter-

**FIGURE 6**
**Discharge Activity of a Giant Cell Neuron Recorded over Multiple Sleep-Waking Cycles***



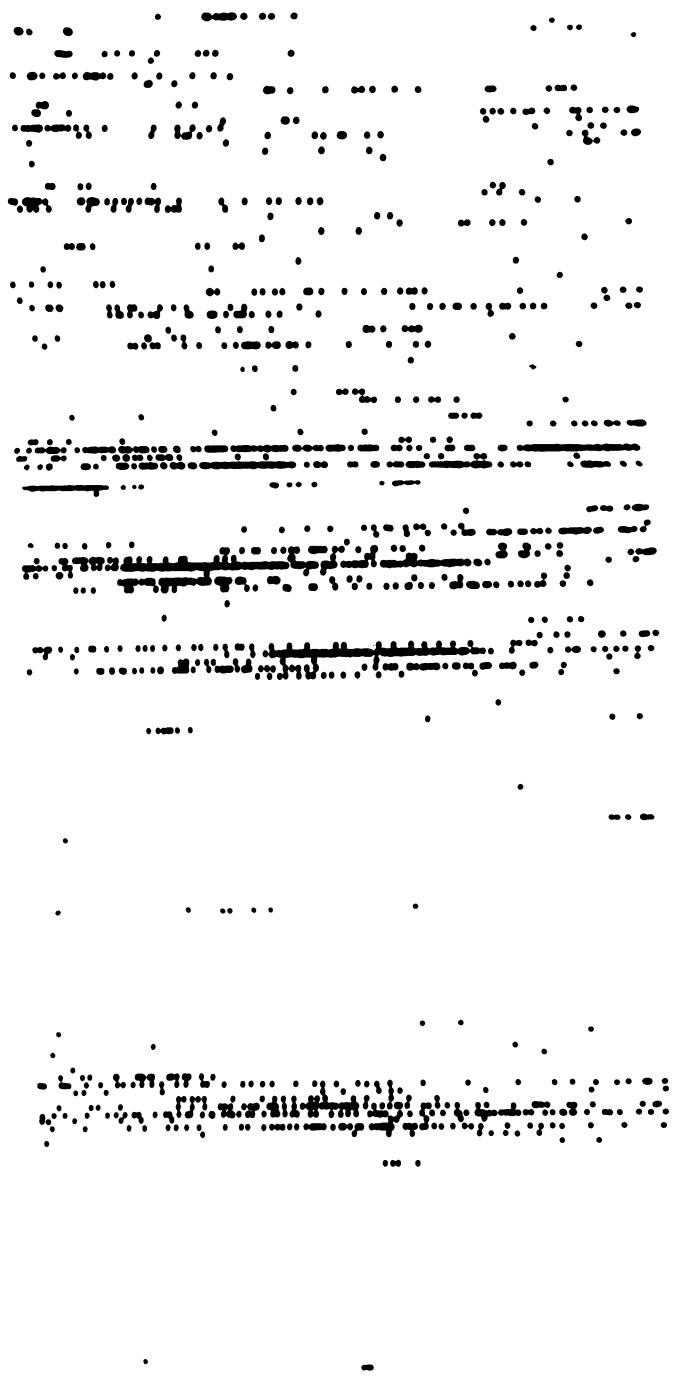

*Each peak corresponds to a desynchronized sleep episode, and a regular trend of discharge activity over a cycle is observable: a peak in desynchronized sleep; a rapid decline at the end of the desynchronized sleep episode; a trough, often associated with waking; a slow rise (in synchronized sleep and preceding all electrographic signs of desynchronized sleep); and an explosive acceleration at the onset of desynchronized sleep. Note also the extreme modulation of activity and the periodicity (30).



spike intervals were exceptional, indicating that the rate increases were not caused by endogenous membrane depolarizations. The tendency, rather, was for giant cells to discharge in intermittent, prolonged clusters of irregularly distributed spikes as if the cells were responding to excitatory postsynaptic potentials from other neurons (see figure 7). In our view, a likely source of much of this input, especially as the longer clusters developed, was other giant cells. Once other neurons were excited, feedback from them is to be expected. It also seemed likely that the clusters of giant cell discharge were causally related to the eye movement bursts of the D sleep phase.

*Reciprocal interaction criterion.* If giant cell excitability change is not an intrinsic property of the giant cells, what other cell group might regulate it and in what way might that regulation be effected? Since all indices showed giant cells to discharge first in relation to both the tonic and phasic events of desynchronized sleep, we considered the possible contribution of inhibitory neurons. Since interneurons do not appear to exist in the giant cell fields, such cells should be discrete from but proximal to the giant cell. To be effective, projections should be abundant and should have inhibitory transmitter action upon the giant cells. Reciprocal rate changes during the sleep cycle are to be expected if such cells exist. We have discovered just such changes in a small number of unidentified cells in the region of the posterior locus coeruleus and the nucleus subcoeruleus (32). Not only is discharge concentration of these elements quantitatively inverse to those of the giant cells in the phases of the cycle, but their decelerating rate curve is the approximate mirror image of that of the giant cells

**FIGURE 7**
**Temporal Clustering of Extracellularly Recorded Discharges of Cat Giant Cell Neurons During D Sleep***



*Each discharge is represented by a dot; the time sequence runs left to right and top to bottom, with each line 1 second in duration. The figure encompasses about 200 seconds of D sleep activity. Clustering is visible as closely spaced dots and, over longer durations, as "bands" of activity, some of which appear to occur rhythmically. Note the various durations of clusters and the presence of shorter duration clusters of activity within longer duration clusters. Clusters are delimited by periods of relative inactivity. Such sequences of giant cell neuronal activity are temporally associated with runs of eye movements and ponto-geniculo-occipital waves, and similar sequences of executive neuron discharges may represent the neuronal substrate of dream sequences in man (Hobson and McCarley, unpublished data).

at desynchronized sleep onset as seen in part C. We called such cells "D-off" cells to contrast their activity curves with those of the giant cells, prototypes of the "D-on" species of neurons. We do not know if the "D-off" cells are catecholaminergic but their location and discharge properties make this possible.

McGinty and associates (33) have found similar reciprocal rate changes in the dorsal raphe nucleus (DRN) neurons and we have recently confirmed this finding. The low regular rates of discharge by these cells in waking suggest a level-setting or pacemaker function. Their location and discharge properties are the same as those cells thought to be serotonergic on the basis of pharmacological experiments (34). Since both the LC and DRN are adjacent to and project to giant cells, and since giant cells receive abundant serotonergic and catecholaminergic endings, we thought that the mutual interconnections of these D-on and D-off cells could form a substrate for reciprocal interaction which regulated sleep cycle oscillation (30).

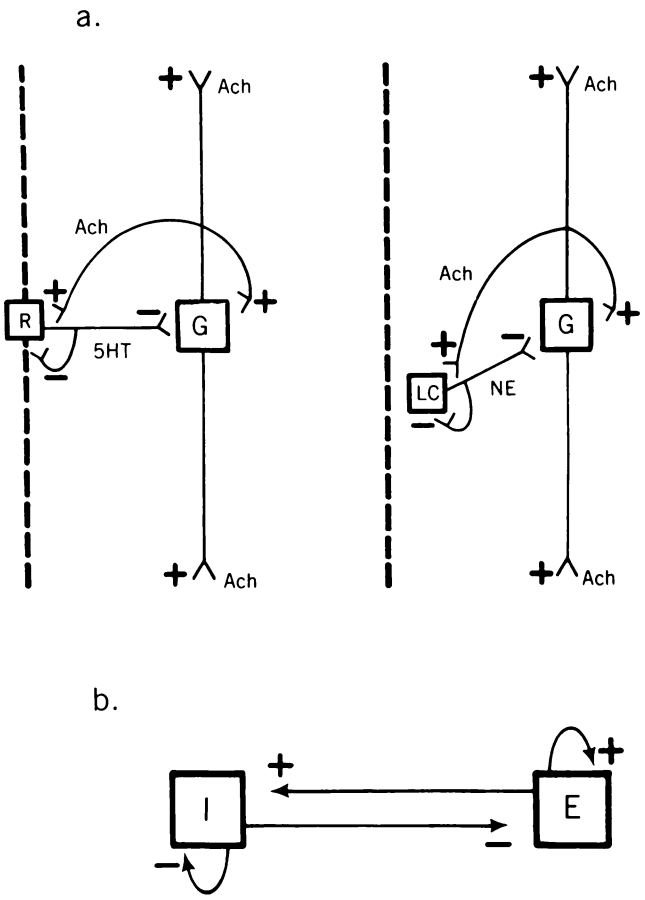
## A MODEL FOR A BRAIN STEM SLEEP CYCLE OSCILLATOR

Restricting attention to within-sleep changes, we constructed a physiological model that bears a striking resemblance to the a priori schema derived from Cajal (see figure 8, top portion). Most of the connections have been demonstrated but many of the synaptic assumptions are as yet unproven physiologically. In addition to being explanatory, the model suggests experiments, particularly those employing pharmacological methods, the results of which will lead to its future modification. Since the LC, DRN, and giant cell groups are chemically differentiated, we deduced that their action and interaction may involve specific neurotransmitters.

In preliminary tests of the model, we have found that microinjection of the cholinomimetic substance carbachol into the giant cell zone not only gives more potent desynchronized sleep phase enhancement than injections into the adjacent tegmental fields but simultaneously activates giant cells. The results also indicate that an opposite effect is obtained at locus coeruleus sites (as if an inhibitory cell group were being activated). We have not yet tested this last hypothesis directly, but the LC cells do resume firing before the end of D sleep. We assume that as FTG excitation declines and LC inhibition grows, the cycle ends. In the decerebrate cat, physostigmine-induced D episodes are associated with activation of neurons in the giant cell and suppression of firing by cells in the LC and DRN (35).

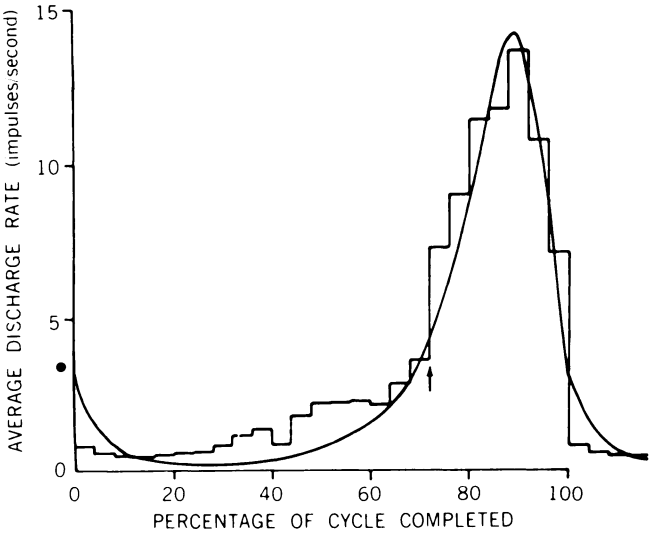
The physiological model can be reduced to a simple unit susceptible to mathematical analysis (see figure 8, bottom portion). Cell group E (giant cell) and cell group I (raphe and/or LC) are assumed to be mutually interconnected; cell group E is excitatory to itself and to group I, which inhibits itself and group E. Growth of

**FIGURE 8**
**Reciprocal Interaction Model of Generator Process***




*Physiological models used to organize and interpret results of pharmacological experiments on desynchronized sleep. The G cells are seen as executive elements; they excite with and are excited by acetylcholine (Ach). They interact reciprocally with two aminergic cell groups, the LC and raphe (R), which utilize norepinephrine (NE) and serotonin (5HT) respectively. Both amines are hypothesized to be inhibitory to the G cells. D sleep will therefore be enhanced by increasing G cell excitability, and this can occur by either adding cholinergic drive or subtracting aminergic inhibition. Conversely, D sleep will be suppressed by subtracting cholinergic drive or by adding aminergic inhibition.
Formal reduction of the elements in the top portion of the figure yields the general model of reciprocal interaction, of inhibitory (I,-) and excitatory (E, +) populations, each of which contains a self-loop as well as a projection to the other set. The resulting oscillation of activity in the two sets can be mathematically described by the Lotka-Volterra equations.

**FIGURE 9**
**Time Course of Giant Cell Activity over the Sleep Cycle***

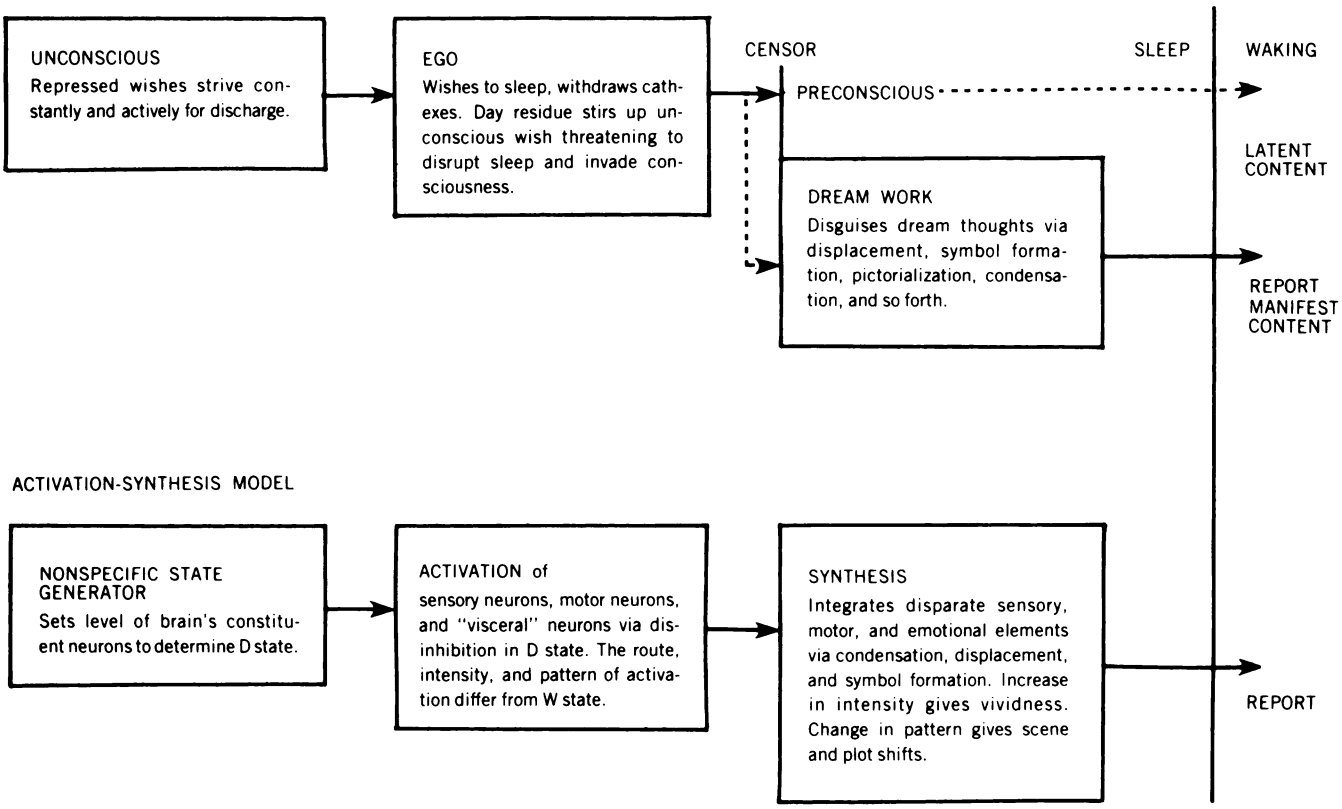



*The histogram shows the average discharge level (impulses/second) of a giant cell neuron over 12 sleep-waking cycles, each normalized to constant duration. The cycle begins and ends with the end of a desynchronized sleep period. The arrow indicates the average time of D sleep onset. The smooth curve is derived from a mathematical model of sleep cycle control and shows a good fit to the experimental data. The probability of obtaining dream-like mentation reports might be expected to show the same trajectory as these curves (30). Reprinted by permission from *Science*, volume 189, pages 58–60, July 4, 1975. Copyright 1975 by the American Association for the Advancement of Science.

activity in one group occurs at the expense of growth in the other, and vice versa. As such the cell groups are analogous to two populations, prey and predator, whose interaction can be described by a set of nonlinear differential equations, the Lotka-Volterra equations (30). As shown in figure 9, the time course of activity of cell group E closely resembles that predicted by these equations. It is now possible to plot the activity curves of cell group I and compare the actual data with the curves predicted by the model. The phase lag between the reciprocal cycles remains to be explained and the previously noted fact that cycle length is proportional to brain size suggests that a distance factor may be at work. The distance between the two cell fields could be such a factor through its determination of protein transport time. Assuming an average LC-FTG internuclear distance of 2.5 mm and a fast protein transport time of 96 mm/day, a period length of about 35 minutes is predicted for the cat. This figure is within limits normal for that species. Another possible substrate for the long, size-dependent time constant of the cycle is the recently discovered class of long-duration postsynaptic transmitter actions (36) that may be mediated by second messengers such as cyclic AMP (37). Since the cyclic nucleotides activate protein kinases, the metabolic activity of the neuron, including the synthesis of neurotransmitters, can be linked to and entrained by membrane events.

An important point is that the mathematical model parallels, but is not identical to, the physiological model. This means that even if the specific assumptions about physiological interaction are incorrect, the mathematical model may be viable and useful in another system—for example, the coupling of the circadian and ultradian oscillators (14) or, at another level of analysis, in a molecular system. This is particularly important to keep in mind since it is also at the molecular level that time constant elements necessary to explain the long periodicity of the sleep-dream cycle may be found.

**FIGURE 10**
**Two Models of the Dream Process***




*In the psychoanalytic model the motive force of the process is the dynamically repressed unconscious wish that is released from control in sleep. The dream thoughts that emerge threaten consciousness and sleep; they are deterred by the censor. The "dream work" transforms the unconscious wish by the processes that are listed. The product, or manifest content, that becomes conscious thus contains only disguised elements of the original (latent) dream thoughts.
The activation-synthesis model is designed to contrast activation-synthesis theory with the guardian-censorship theory illustrated in the top portion of this figure. The motive force of the process is seen to be nonspecific neural energy or excitation hypothesized to arise from a nonspecific generator. This excitation affects the component systems of the forebrain represented in the upper box: sensory systems generate scene frames, structural fragments, and qualitative features; cognitive systems generate ideas that may be conscious (day residue thoughts) or unconscious (instinctually determined); emotion is also generated at this first stage. The dream report, easily obtainable if a state change to waking occurs, is seen as an accurate reflection of the integrated product of disparate, internally generated elements.

## PSYCHOLOGICAL IMPLICATIONS OF THE CELLULAR NEUROPHYSIOLOGY OF DREAM SLEEP GENERATION

Hallucinoid dreaming is regarded as the psychological concomitant of D sleep. Brain activity in the D state has been analyzed to account for activation of the forebrain, occlusion of sensory input, blockade of motor output at the spinal cord level, and the generation of information within the system. The evidence that the pontine brain stem contains a clock-trigger mechanism that contributes to activation of the forebrain, occlusion of sensory input, and the generation of internal information has been reviewed. The periodicity of the triggering mechanism is hypothesized to be a function of reciprocal interaction of reciprocally connected, chemically coded cell groups in the pontine brain stem.

The psychological implications of this model, which we call the activation-synthesis hypothesis of the dream process (schematically represented in figure 10), contrast sharply with many tenets of the dream theory provided by psychoanalysis (also represented in figure 10) in the following ways:

1. *The primary motivating force for dreaming* is not psychological but physiological since the time of occurrence and duration of dreaming sleep are quite constant, suggesting a preprogrammed, neurally determined genesis. In fact, the neural mechanisms involved can now be precisely specified. This conclusion does not, of course, mean that dreams are not also psychological events; nor does it imply that they are without psychological meaning or function. But it does imply that the process is much more basic than the psychodynamically determined, evanescent, "guardian of sleep" process that Freud had imagined it to be; and it casts serious doubt upon the exclusively psychological significance attached to both the occurrence and quality of dreams.

2. *Specific stimuli for the dream imagery* appear to

arise intracerebrally but from the pontine brain stem and not in cognitive areas of the cerebrum. These stimuli, whose generation appears to depend upon a largely random or reflex process, may provide spatially specific information which can be used in constructing dream imagery; but the unusual intensity, intermittency, and velocity of the eye movements may also contribute to features of the dream experience which are formally bizarre and have been interpreted as defensive by psychoanalysis. Thus such features as scene shifts, time compression, personal condensations, splitting, and symbol formation may be directly isomorphic with the state of the nervous system during dreaming sleep. In other words, the forebrain may be making the best of a bad job in producing even partially coherent dream imagery from the relatively noisy signals sent up to it from the brain stem.

The dream process is thus seen as having its origin in sensorimotor systems, with little or no primary ideational, volitional, or emotional content. This concept is markedly different from that of the "dream thoughts" or wishes seen by Freud as the primary stimulus for the dream. The sensorimotor stimuli are viewed as possibly providing a frame into which ideational, volitional, or emotional content may be projected to form the integrated dream image, but this frame is itself conflict free. Thus both the major energetic drive for the dream process and the specific primary stimulus of the dream content are genotypically determined and therefore conflict free in the specifically psychodynamic sense of the term.

3. *The elaboration of the brain stem stimulus* by the perceptual, conceptual, and emotional structures of the forebrain is viewed as primarily a synthetic constructive process, rather than a distorting one as Freud presumed. Best fits to the relative inchoate and incomplete data provided by the primary stimuli are called up from memory, the access to which is facilitated during dreaming sleep. The brain, in the dreaming sleep state, is thus likened to a computer searching its addresses for key words. Rather than indicating a need for disguise, this fitting of phenotypic experiential data to genotypic stimuli is seen as the major basis of the "bizarre" formal qualities of dream mentation. There is, therefore, no need to postulate either a censor or an information degrading process working at the censor's behest. The dream content elaborated by the forebrain may include conflictually charged memories, but even this aspect of dream construction is seen as synthetic and transparent rather than degradative and opaque.

4. *With respect to the forgetting of dreams*, the normally poor recall is seen principally to reflect a state-dependent amnesia, since a carefully effected state change, to waking, may produce abundant recall even of highly charged dream material. There is thus no need to invoke repression to account for the forgetting of dreams. This hypothesis is appealingly economical, and in the light of the reciprocal interaction hypothesis dream amnesia can now be modeled in a testable way as the result of a different balance between cholinergic and aminergic neuronal activity and the resulting effects on second messengers and macromolecules (5). Among its other surprising gifts to psychophysiology, dreaming sleep may thus also provide a biological model for the study of memory, and a functional role for dreaming sleep in promoting some aspect of the learning process is suggested.

## SUMMARY AND CONCLUSIONS

Assuming that isomorphism, or identity of form, must characterize the simultaneous physiological and psychological events during dreaming, we have reviewed the general and cellular neurophysiology of dreaming sleep in search of new ways of accounting for some of the formal aspects of dream psychology. We have noted that the occurrence of dreaming depends upon the periodic activation of the forebrain during sleep. We have hypothesized that the activated forebrain synthesizes the dreams by fitting experiential data to information endogenously and automatically generated by reticular, vestibular, and oculomotor neurons in the pontine brain stem. A specific physiological and mathematical model of the pontine generator, based upon single cell recording studies in cats, is described: the model posits reciprocal interaction between inhibitory aminergic (level-setting) and excitatory cholinergic (generator) neurons.

Some of the "bizarre" formal features of the dream may directly reflect the properties of the brain stem neuronal generator mechanism. The physiological features of the generator mechanisms and their corresponding psychological implications include the following: the automaticity and periodicity of activation indicate a metabolically determined, conflict-free energetics of the dream process; the random but specific nature of the generator signals could provide abnormally sequenced and shaped, but spatiotemporally specific, frames for dream imagery; and the clustering of runs of generator signals might constitute timemarks for dream subplots and scene changes. Further, the activation by generator neurons of diffuse postsynaptic forebrain elements in multiple parallel channels might account for the disparate sensory, motor, and emotional elements that contribute to the "bizarreness" of dreams; the suppression of motor output and sensory input simultaneous with central activation of both sensory and motor patterns could assure the maintenance of sleep in the face of massive central excitation of the brain; and the change in the ratio of neurotransmitters affecting forebrain neurons might account for dream amnesia and indicate a state-dependent alteration of neural plasticity, with implications for the learning process.

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