

Derivation and analysis of basic computational operations of thalamocortical circuits

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Abstract

■ Shared anatomical and physiological features of primary, secondary, tertiary, polysensory, and associational neocortical areas are used to formulate a novel extended hypothesis of thalamocortical circuit operation. A simplified anatomically-based model of topographically and nontopographically-projecting ('core' and 'matrix') thalamic nuclei and their differential connections with superficial, middle, and deep neocortical laminae is described. Synapses in the model are activated and potentiated according to physiologically-based rules. Features incorporated into the models include differential time courses of excitatory vs. inhibitory postsynaptic potentials, differential axonal arborization of pyramidal cells vs. interneurons, and different laminar afferent and projection patterns. Observation of the model's responses to static and time-varying inputs indicates that topographic 'core' circuits operate to organize

stored memories into natural similarity-based hierarchies, whereas diffuse 'matrix' circuits give rise to efficient storage of time-varying input into retrievable sequence chains. Examination of these operations shows their relationships with well-studied algorithms for related functions, including categorization via hierarchical clustering, and sequential storage via hash- or scatter-storage. Analysis demonstrates that the derived thalamocortical algorithms exhibit desirable efficiency, scaling, and space and time cost characteristics. Implications of the hypotheses for central issues of perceptual reaction times and memory capacity are discussed. It is conjectured that the derived functions are fundamental building blocks recurrent throughout neocortex, which, through combination, give rise to powerful perceptual, motor, and cognitive mechanisms. ■

INTRODUCTION

Neocortex, the largest brain structure in mammals and allometrically far larger still in humans, consists of multiple modules that share substantial architectural properties yet underlie apparently distinct functions, including the processing of disparate sensory modalities, motor behavior, planning, and abstract cognition. Most cortical regions have strongly reciprocal connections with thalamic nuclei, suggesting that thalamocortical circuits may be viewed as an integral unit of telencephalon. Neurons throughout neocortex are organized into relatively stereotypical architectures, with widely shared rules of operation and plasticity. Although many cortical studies describe differences among various cortical regions, it is posited that there are sufficient shared characteristics to justify attempts to identify common basic functionality, which

may be augmented by special purpose capabilities in some regions. The present studies focus on posterior neocortex and its reciprocal circuits with nuclei of dorsal thalamus, as distinguished from anterior neocortex / ventral thalamic circuits, which involve the striatal complex (basal ganglia) integrally in the circuit. The regularity of thalamocortical circuitry has supported decades of suggestions that it may be composed of functionally similar or even identical circuits, differing only, or predominantly, in their afferent sources and efferent targets (Szentagothai, 1975; Hubel and Wiesel, 1977; Creutzfeldt and Nothdurft, 1978; Mountcastle, 1978; Keller and White, 1989; Galuske et al., 2000; Gazzaniga, 2000, Castro-Alamancos and Connors, 1997; Jones, 1998; Heynen and Bear, 2001; Silberberg et al., 2002; Valverde, 2002).

Computational models related to these structures have variously focused on specialized aspects of cortex, selected circuitry

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within cortex, abstractions of cortical or thalamocortical circuits that contain a small number of the many key shared features of these circuits, or mathematical abstractions of hypothesized cortical function (often inferred "top-down" from observable behavior). The present paper explicitly excludes features specific to any particular region (e.g., primary sensory areas), focusing rather on the widespread characteristics shared among primary and non-primary (secondary, tertiary, polysensory, and association) cortical areas. The aim is to develop "bottom-up" hypotheses of widespread thalamocortical operation addressing the ubiquity and biological uniformity of these circuits. The work described here builds on and extends prior work in our laboratory (Ambros-Ingerson et al., 1990; Anton et al., 1991; Granger and Lynch, 1991; Coultrip et al., 1992; Coultrip and Granger, 1994; Granger et al., 1994; Aleksandrovsky et al., 1996; Kilborn et al., 1996; Whitson, 1998; Shimono et al., 2000; Granger 2002; Benvenuto et al., 2002; www.BrainEngineering.com). After introductory sections identifying predominant shared characteristics that are the foci of these studies, the models are described in two sections: one focusing on the predominantly topographic 'core' pathway connecting thalamus and cortex, and one on their equally large diffuse pathways. The discussion integrates the prior sections into the beginnings of a coordinated hypothesis of thalamocortical operation.

ANATOMICAL ARCHITECTURE OF THALAMOCORTICAL CIRCUITS

Introduction. Table 1 lists primary shared anatomical and physiological regularities of neocortex and thalamocortical circuits. The intentional omission of features such as sublamination of L.IV, and the many subtypes of neocortical inhibitory cell, is not meant to imply that additional functionality might not be conferred by such variants. Further iteration is in progress to incorporate additional features, but it is hoped that simulations incorporating the panoply of listed features may nonetheless provide initial insight into possible functionality of thalamocortical circuits.

Number of cells. There are (with a few notable exceptions, such as the primary sensory areas) approximately 80,000 neurons beneath each square millimeter of cortical surface, distributed in a stereotypic manner across the cortical layers. Despite dendritic elongation in larger brains, and corresponding increases in numbers of synaptic contacts among pyramidal cells, the number of cells stays constant per region in animals weighing from grams to kilograms (Rockel et al., 1980).

Cortical cell types. Excitatory (pyramidal) cells outnumber inhibitory cells by roughly four or five to one throughout most of cortex, again excepting the primary sensory areas (Fitzpatrick et al., 1987; Hendry et al., 1987). Excitatory neurons have axons that can extend millimeters whereas inhibitory cells project only locally (rarely more than 100 μm). Inhibitory axons synapse densely on or near pyramidal cell bodies (Keller and White, 1989). In contrast, excitatory cells receive only sparse afferents from other excitatory cells; it has been estimated that the probability of contact between two neocortical excitatory cells that are 0.2-0.3mm apart is less than 0.1, and between two such cells that are more than 1mm from each other, $p < 0.01$ (Braitenberg and Schüz, 1998).

Cortical modules. Within architectonic regions of cortex, neurons are vertically organized into anatomically defined "pyramidal cell modules" (Figure 1) consisting of distinct groups of layer V and layer II-III pyramidal cells whose apical dendrites are commingled (White and Peters, 1993; Peters et al., 1994). Architectonically distinguishable areas differ in size and population of cell layers, and there is correspondence between these region boundaries and the site of origin of their thalamic afferents. (In contrast, functional "columns" are physiologically defined, in terms of receptive field properties, rather than anatomical boundaries (Mountcastle, 1957), and are typically described as 400-500 μm in extent, comprising perhaps 200 pyramidal cell modules apiece.)

Table 1. Selected anatomical and physiological traits shared by multiple thalamocortical regions.

Cortical anatomy

- Number of neurons per layer remains relatively constant across different cortical regions
- Excitatory (pyramidal) and inhibitory cells occur at roughly a 5:1 ratio.
- Pyramidal cells emit long axons with distant targets, as well as local collaterals.
- Inhibitory cells have a radius of axonal arborization restricted to only local targets.
- Inhibitory cell axons target cell bodies, proximal dendrites, and initial axon segments of local pyramidal cells, thus powerfully influencing the responsiveness of excitatory cells.
- Neurons are arranged in layers of superficial (II-III), middle (IV) and deep (V-VI) cells.
- Neurons are vertically organized into pyramidal cell modules containing ~200 neurons.
- Columns of ~200 pyramidal cell modules are spatially localized within topographically defined thalamo-cortico-thalamic projections.

Thalamocortical anatomy

- Thalamic matrix cells project broadly and diffusely to L.I, contacting apical dendrites of neurons in II, III and V.
- Core thalamic cells project with preserved topographic organization to layers III and IV.
- Middle layer cells (layer IV) project apically to suprajacent layers II-III.
- Superficial layer cells (II-III) project basally to subjacent deep layers (V-VI).
- Layer V cells project to motor targets and, via collaterals, to thalamic matrix.
- Layer VI projects topographically to core, to overlying nucleus reticularis, and to layer IV.

Physiology & plasticity

- Synapses from thalamic core to L.IV are plastic during development, and exhibit little or no plasticity in adults.
- Synapses of superficial (II-III) and deep layer (V-VI) pyramidal cells potentiate in adults.
- Reciprocal excitatory-inhibitory connections within layers yield lateral inhibition.
- Excitatory post-synaptic potentials (PSPs) are brief (~15-20 msec).
- Inhibitory PSPs are roughly an order of magnitude longer (~100-150 msec).

Thalamic projection neurons. Neurons in thalamus exhibit immunoreactivity to one of two Ca^{++} -binding proteins, calbindin or parvalbumin. Many recent studies offer convergent evidence that calbindin cells, widespread throughout thalamus, project broadly and diffusely to multiple neighboring cortical regions, synapsing in layer I, whereas parvalbumin cells, occurring only in certain thalamic nuclei, give rise to restricted, topographically organized projections, each to an individual cortical region, synapsing in middle cortical layers (Molinari et al., 1995; Jones, 2001). Adopting the terminology of these studies, we refer to parvalbumin-immunoreactive projection cells as thalamic "core" and calbindin cells as "matrix." This terminology is intended to extend and elaborate on the long-studied distinctions in the literature between "specific" (e.g., MGv, VPL, VPM, LGd), and "nonspecific" (e.g., MGm, Pul, Pom, AD) nuclei (Killackey & Ebner, 1972; 1973; Herkenham, 1986; Berendse & Groenewegen, 1991; DeFelipe and Jones, 1991; Wyss and VanGroen, 1995; Castro-Alamancos and Connors, 1997; Jones, 1998, 2001).

Core thalamic projections. Projections from thalamic core cells synapse on neurons in all

cortical layers to some extent (Keller and White, 1989) but predominantly in deep layer III and in layer IV in granular cortex, as well as on the apical dendrites of layer VI neurons. These afferents, which preserve topographic organization, are often described as the primary input to sensory neocortical regions, though quantitative anatomical studies report that these afferents comprise $\leq 6\%$ of the synapses onto layer IV target cells, with the majority of the remaining afferents coming from lateral cortico-cortical connections (Freund et al., 1985; Freund et al., 1989; Peters and Payne, 1993; Peters et al., 1994; Ahmed et al., 1997). Projections from a given thalamic core region extend to a cortical area roughly 0.5-1.0 mm wide, somewhat larger than the size of physiologically-delineated functional columns (Jones, 1981). Layer VI axons project back topographically to the thalamic core cells from which they receive inputs, as well as to the portion of the nucleus reticularis (NRt) topographically overlying the target core cells (Liu and Jones, 1999). NRt in turn generates GABAergic projections to these thalamic core cells (DeFelipe and Jones, 1991; Jones, 2001).

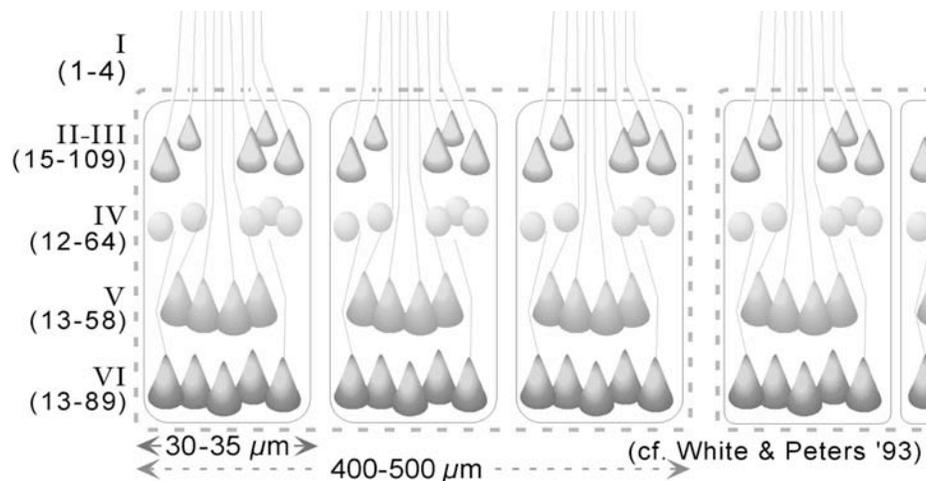


Figure 1. Organization of neocortical modules. Anatomical grouping of apical dendrites of neurons in layers II, III, and V, define “pyramidal cell modules” (solid lines) whose layers typically contain the listed numbers of neurons [White & Peters, 1993]. Functional columns (dotted lines), described physiologically rather than anatomically, are approximately 400-500 μm in diameter, encompassing perhaps 200 pyramidal cell modules.

Matrix thalamic projections. The afferents from thalamic matrix neurons predominantly synapse in layer I, chiefly on the apical dendrites of neurons from layers II, III, and V. The first detailed reports on these projections, in which it is emphasized that they occur as a prevalent feature of cortical anatomy, describe them as “nonspecific,” i.e., the projections from a small thalamic region project to a broad cortical area, and projections to a small cortical area originate in a broad expanse of nonspecific thalamus (Lorente de No, 1938). These early findings have been confirmed and extended repeatedly (Killackey and Ebner, 1972; Killackey and Ebner, 1973; Herkenham, 1986; Jones, 1998), and it has been consistently confirmed that matrix cells projecting to a given cortical area receive projections back from layer V of that cortical area, without intervening NRt contacts (Conley and Diamond, 1990; Rouiller et al., 1991; Bourassa and Deschenes, 1995; Deschenes et al., 1998).

Two thalamocortical circuits. Within cortex, the major vertical projections are from layer IV apically to layers II and III (Mitani et al., 1985; Burkhalter, 1989; Schwark and Jones, 1989), and from these superficial layers basally to layers V and VI (Schwark and Jones, 1989; Henry, 1991; Wallace et al., 1991). The projection patterns described are thus arranged into two large thalamocortical circuits: 1) topographic projection of thalamic core cells > middle cortical

layers > superficial layers > deep layers, with reciprocal topographic feedback from layer VI back to both the core cells and to the overlying portion of nucleus reticularis; 2) matrix cells projecting nontopographically to layer I and receiving projections back from layer V, without interposed nucleus reticularis projections. Evidence suggests that the repeating thalamocortical, cortico-cortical, and corticothalamic projection patterns hold not only for primary sensory areas including VPM/VPL, LGd, and MGv to layer IV, and Pom, LP/Pul, and MGM to layer I of somatosensory, visual and auditory cortices, respectively (Killackey and Ebner, 1972; Ryugo and Killackey, 1974; Ribak and Peters, 1975; Herkenham, 1980; Kelly and Wong, 1981; Swadlow, 1983; Rieck and Carey, 1985; Herkenham, 1986; Jensen and Killackey, 1987; Winer and Larue, 1987; Scheel, 1988; Conley and Diamond, 1990; Rouiller and Welker, 1991; Bourassa and Deschenes, 1995; Huang and Winer, 2000), but also for a wide array of thalamic nuclei, intralaminar and nonintralaminar alike (Jones and Hendry, 1989; Rausell et al., 1992; Molinari et al., 1994; Molinari et al., 1995; Kuroda et al., 1998; Mitchell and Cauller, 2001; Rauschecker et al., 1997; Jones, 1998; Reep and Corwin, 1999; Linke and Schwegler, 2000; Jones, 2001)). For those cortical areas not receiving topographic projections from thalamus, the

extensive topography-preserving cortico-cortical projections from superficial layers to recipient middle layers with reciprocal projections from the target's deep layers back to the source's superficial layers, may subserve a related function (Harth et al., 1987; Mumford, 1992; Olson and Musil, 1992; Miller 1996; Barbas and Rempel-Clower, 1997; Catania and Kaas, 2001; Batardiere et al., 2002; Ichinohe and Rockland, 2002; Rockland, 2002; Swadlow et al., 2002).

PHYSIOLOGICAL OPERATION OF THALAMOCORTICAL CIRCUITS

Sequential circuit activation. Peripheral inputs activate thalamic core cells which in turn participate in topographic activation of middle cortical layers; e.g., ear > cochlea > auditory brainstem nuclei > ventral subdivision of medial geniculate nucleus (MGv) > A1; in contrast, matrix nuclei are most strongly driven by corticothalamic feedback (Bender, 1983; Diamond et al., 1992b; Diamond et al., 1992a), supporting a system in which peripheral afferents first activate core nuclei, which in turn activate cortex (via a stereotypical vertical pattern already described: middle layers > superficial layers > deep layers), which then activate both core and matrix nuclei via corticothalamic projections (Mountcastle, 1957; Hubel and Wiesel, 1977; Di et al., 1990; Kenan-Vaknin and Teyler, 1994).

Excitatory and inhibitory interaction. Axons of inhibitory interneurons densely terminate preferentially on the bodies, initial axon segments, and proximal apical dendrites of excitatory pyramidal cells in cortex, and thus are well situated to exert powerful control over the activity of target excitatory neurons. When a field of excitatory neurons receives afferent stimulation, those that are most responsive will activate the local inhibitory cells in their neighborhood, which will in turn inhibit local excitatory cells. The typical time course of an excitatory (depolarizing) postsynaptic potential (PSP) at normal resting potential, in vivo, is brief (15-20 msec), whereas corresponding GABAergic inhibitory PSPs last roughly an order of magnitude longer (100-150 msec) (Castro-Alamancos and Connors, 1997). Thus excitation tends to be brief, sparse, and

curtailed by longer and stronger feedback inhibition.

Activity rates. The rate of repetitive activation in thalamocortical circuits ranges from the "delta" (1-4 Hz) and "theta" frequency bands (4-12 Hz or ~80-250 msec per time step) through the "gamma" range (30-40 Hz or 25-33 msec per step) (Steriade, 1997; Chrobak and Buzsaki, 1998; Shimono et al., 2000; Sarter and Bruno, 2000; Fries et al., 2001; Rozov et al., 2001; Canales et al., 2002; Knoblauch and Palm, 2002; Pesaran et al., 2002). There is strong evidence for ascending influences (e.g., basal forebrain) on inhibitory neurons (Freund and Meskenaite, 1992; Gulyas et al., 1996; Blasco-Ibanez et al., 1998; Gulyas et al., 1999) modulating their response properties, in turn affecting the probability of response of excitatory cells during the peaks and troughs of such "clocked" inhibitory cycles. Evidence of intrinsic rhythmic currents in thalamic and cortical cells (Kim et al., 1995; Bush and Sejnowski, 1996; Destexhe et al., 1999; Zhu and Connors, 1999) is compatible with extrinsic ascending influences, acting either independently or in concert with them. Three modes of activity have typically been reported for thalamic neurons: tonic, rhythmic, and arrhythmic bursting. The latter appears predominantly during non-REM sleep whereas the first two appear during waking behavior (McCarley et al., 1983; Steriade and Llinas, 1988; McCormick and Feese, 1990; Steriade et al., 1990; McCormick and Bal, 1994; Steriade and Contreras, 1995). It has been variously argued that rhythmic burst mode may provide better signal to noise and thus facilitate detection of a stimulus, and that tonic mode contains more detailed information about a stimulus (Guido et al., 1992; Guido et al., 1995; Mukherjee and Kaplan, 1995; Sherman, 2001). Others have suggested that distinctions between modes based on differential information are not warranted (e.g., Reinagel et al., 1999).

Spatial codes across multiple time windows. The question of what "codes" are used to store and convey information among thalamocortical circuits is one of the central issues of

neuroscience. Strong constraints are imparted by three primary characteristics of thalamocortical circuits.

- Synchronous activity of wide regions of cortex (modulated in part by ascending systems affecting the periodic responsivity of inhibitory cells) makes the probability of excitatory cell spiking lower during peak inhibition and higher during inhibitory troughs.
- The average time course of excitatory postsynaptic potentials in cortical pyramidal cells (~ 10-15 msec) limits the temporal precision of spike trains that such a neuron may emit.
- Summation characteristics and integration (e.g., capacitance) time constants of dendrites, map many distinct spike train input patterns into nearly indistinguishable postsynaptic voltage transients, severely limiting the temporal precision with which a target neuron can "read" differences among slightly-different spike trains (Magee, 2000; Magee and Cook, 2000).

It is thus hypothesized here that information is passed largely by spatial patterns of activity occurring during recurring windows of relatively low inhibition, during activity that is approximately synchronous. Moreover, different spatial patterns at successive activity peaks (over the course of tens to hundreds of milliseconds)

may convey distinct information about a single input.

Glutamatergic synapses. As shown in Figure 2, the vast majority of excitatory synapses are glutamatergic. An excitatory axon targeting the apical dendrite of an excitatory cell typically terminates at a spine, which contains ~500-1000 AMPA- and NMDA-type glutamate receptors (Bekkers and Stevens, 1989). An average neocortical pyramidal cell in humans reportedly receives 25-80 thousand such afferents (Cragg, 1967; Rockel et al., 1980; Braitenberg and Schüz, 1998 pp. 190-191), (with a few notable exceptions such as area 17, which has an unusually high density of neurons per square mm and a correspondingly low number of synapses per neuron (Cragg, 1967; O'Kusky and Colonnier, 1982)), and typical methods may lead to systematic undercounting of synapses (Guillery and Herrup, 1997; von Bartheld, 1999, 2001). In certain regions, notably thalamus and layer IV cortex, as well as glutamatergic synapses onto inhibitory neurons, the NMDA receptors contain the (rare in the adult) NR3A subunit (Wong et al., 2002), which has been shown to inhibit the expression of NMDA receptor ion channels (Das et al., 1998).

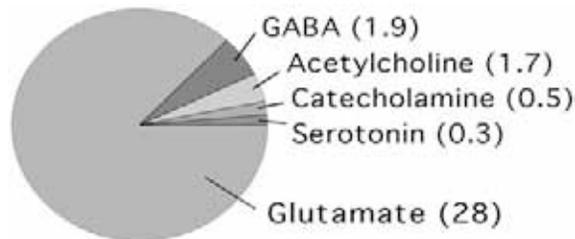


Figure 2. Measured quantities (in picomoles per mg) and relative percentages of the most common types of receptors in mammalian brain (quantities shown are for mouse).

Neocortical synaptic potentiation. NMDA-dependent long-term potentiation of synaptic connections in neocortex has been shown in superficial and deep layers of multiple regions (Komatsu et al., 1988; Hirsch and Crepel, 1990; Iriki et al., 1991; Bear and Kirkwood, 1993; Kirkwood et al., 1993; Kimura et al., 1994; Castro-Alamancos et al., 1995; Hess et al., 1996;

Kudoh and Shibuki, 1996; Buonomano and Merzenich, 1998; Rioult-Pedotti et al., 2000; Heynen and Bear, 2001; Seki et al., 2001). Memories that are rapidly induced (i.e., with little or no practice), long lasting (potentially for decades) and high-capacity (enough to hold the memories of a lifetime) presumably require a biological mechanism with corresponding

characteristics. Biological phenomena that last only for limited duration (decrementing over time), or are slow to induce (e.g., minutes of constant stimulation), or are not synapse-specific (and thus not high capacity) may underlie some form of short-term memory (or other operation) but not rapidly-induced, high-capacity long-term

memory, an important type of memory and the one under study in the present work. "LTP" here refers specifically to the endogenously occurring synaptic phenomenon that has the properties just listed, enabling it to serve as the substrate of lifelong memories.

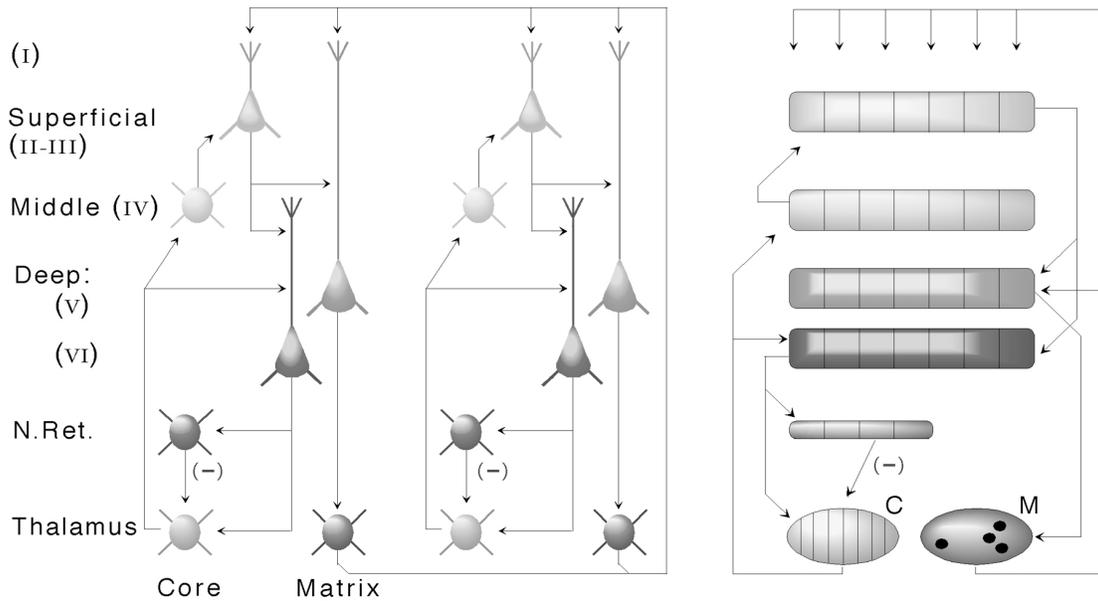


Figure 3. Key features of anatomical organization of thalamocortical circuits to be modeled (See text.) Core thalamic cells project topographically to layer IV and III of particular cortical areas; from these arise projections to superficial layer cells (II-III), which in turn project to deep layers (V-VI). Matrix cells project broadly and non-topographically to multiple cortical areas, synapsing in layer I on the apical dendrites of layer II, III and V cells. Layer V cells generate nontopographic projections back to matrix; layer VI cells project to core and to overlying (GABAergic) nucleus reticularis, which in turn project to core thalamic cells. (Left) Organization of layers and projections. (Right) Simplification of the circuit projection patterns.

SIMPLIFICATION AND MODELING

Simplified operation. Based on the biological regularities specified, a greatly simplified set of operations is posited (Table 2) with the intent of illustrating a hypothesis of fundamental processing steps carried out by thalamocortical circuits in response to sequential inputs.

Features and thalamocortical modules. The topography of the connections from the periphery to Ct and from Ct to cortical L.IV are assumed to have correspondences with feature sets occurring in the periphery, or

generalizations of these arising from combinations of features. For initial regions of visual cortex, for instance, these might consist of center-surround features, line segments with different orientations, with increasingly complex features arising from combinations of these. Downstream regions (secondary and onward) are hypothesized to consist of more complex features abstracted from combinations of earlier features. For purposes of illustration, divisions of thalamus and cortex according to features will be designated via arbitrary feature sets denoted by letters.

Table 2. Simplified steps in thalamocortical operation.

i)	First input from periphery topographically activates core nucleus (Ct).
ii)	Ct topographically activates corresponding middle layers.
iii)	Activated middle layer modules vertically activate corresponding suprajacent layers.
iv)	Output from superficial layers topographically activates deep layers.
v)	Diffuse feedback from L.V output to matrix nucleus (Mt).
vi)	Topographic feedback from L.VI output to NRt and to Ct, selectively inhibiting the portion of the input corresponding to the cluster response.
vii)	Next input (or portion of input) arrives; Ct topographically activates middle, superficial, deep layers.
viii)	Layer V receives combination of nontopographic input from Mt, produced by prior input, and topographic activation from superficial layers produced by current input.
ix)	Intersection of these inputs selects sparse L.V response and synaptic potentiation.
x)	Repeat steps v) to ix) until input completed.

Activation sequence. For instance, in response to an input stream consisting of arbitrary primitive features A-B-C, the system first activates the region or regions of Ct corresponding to the feature ‘A,’ which activates first layer IV, then II-III, and then V-VI of the corresponding cortical regions. Then L.VI sends feedback topographically to Ct and to the overlying inhibitory NRt, selectively inhibiting that portion of the input but allowing through whatever feature came next (in this case, ‘B’); while L.V sends diffuse feedback to Mt, generating a deterministic but nontopographic activation pattern in Mt. That pattern is then sent from Mt broadly and diffusely to superficial and deep layers of cortex, while the next input (‘B’) is sent topographically from Ct to cortex.

At the intersection of the two activation patterns, potentiation is presumed to occur. In this instance, the nontopographic Mt pattern arising from L.V feedback due to feature ‘A’ will be ‘stored’ in the topographic region corresponding to the pattern for input feature ‘B.’

Repetition of this series of operations constructs a chain of stored features, whereby the Mt activation pattern for the first feature (A) is stored in the topographic location for B, the Mt pattern arising from B is stored in the topographic location for C, etc.

Core thalamocortical circuit: Iterative hierarchical clustering

Lateral inhibition and synaptic potentiation in superficial layers. Simulated superficial cells that initially respond to a particular input pattern become increasingly responsive not only to that input but also to a range of similar inputs (inputs that share many active lines, e.g., small Hamming distances from each other), such that similar but distinguishable inputs will come to elicit identical patterns of output from layer II-III cells, even though these inputs would have given rise to slightly different output patterns before potentiation.

Clustering. These effects can be described in terms of the mathematical operation of “clustering,” in which sufficiently similar inputs are placed into a single category or cluster. This can yield useful generalization properties, but somewhat counterintuitively, it prevents the system from making fine distinctions among members of a cluster. For instance, four images (Figure 4, top row) initially elicit four slightly different patterns of cell firing activity in layer II-III cells (middle row) but after repeated potentiation episodes, all four images elicit identical activation patterns (bottom row). Results of this kind have been obtained in a number of different models with related characteristics (von der Malsburg, 1973; Grossberg, 1976; Rumelhart, 1985; Coultrip et al., 1992).

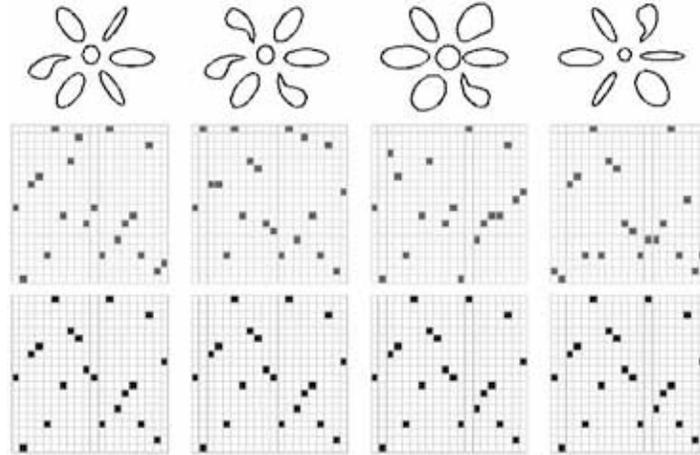


Figure 4. Examples of patterns of initial superficial layer cell response to similar but slightly different inputs (top), both before (middle row) and after (bottom row) potentiation episodes. Before potentiation, slightly different inputs elicit slightly different patterns of cell responses. After potentiation, these inputs all elicit identical or nearly identical response patterns.

Iterative hierarchical clustering. Superficial layer responses activate deep layers, and output from layer VI initiates feedback activation of nucleus reticularis (NRt), which in turn inhibits the core thalamic nucleus (Ct). Since, as described, topography is preserved throughout this sequence of projections, the portions of Ct that become inhibited will correspond topographically to those portions of L.II-III that were active. On the next cycle of thalamocortical activity, the input (e.g., image) will arrive at Ct against the background of the inhibitory feedback from NRt, which has been shown to last for hundreds of milliseconds (Huguenard and Prince, 1994; Cox et al., 1997; Zhang et al., 1997). Thus we hypothesize that the predominant component of the next input to cortex is just the uninhibited remainder of the input; whereupon the same operations as before are performed. The result is that the second cortical response will consist of a quite distinct set of neurons from the initial response, since most of the input components giving rise to that first response are now inhibited. Analysis of the second (and ensuing) responses in computational models has shown successive sub-clustering of an input: the first cycle of response identifies the input's membership in a general category of similar objects (e.g., flowers), the next response (a fraction of a second later) identifies its

membership in a particular subcluster (thin flowers; flowers missing a petal), then sub-sub-cluster, etc. Thus the system repetitively samples across time, differentially activating specific target neurons at a series of successive time points, to discriminate among inputs.

Operation of the algorithm. An initial version of the method arose from studies of feedforward excitation and feedback inhibition in the olfactory cortex and bulb (Ambros-Ingerson et al., 1990; Anton et al., 1991), and was readily generalized to non-olfactory modalities (e.g., vision, audition) whose superficial layers are closely related to those of olfactory cortex, evolutionarily and structurally (Granger and Lynch, 1991). Figure 5 illustrates an instance of the organization of figures into hierarchies by successive superficial layer cortical responses. If the figure indicated by the double underline were shown to the model, its first cortical response would be identical for any of the figures shown; its second response (tens to hundreds of milliseconds later) would be specific to the figures on the far left, and its third response would be specific to just the individual image itself. Thus the sequence of cortical responses reads out information corresponding to stepwise traversal through hierarchically organized perceptual memories.

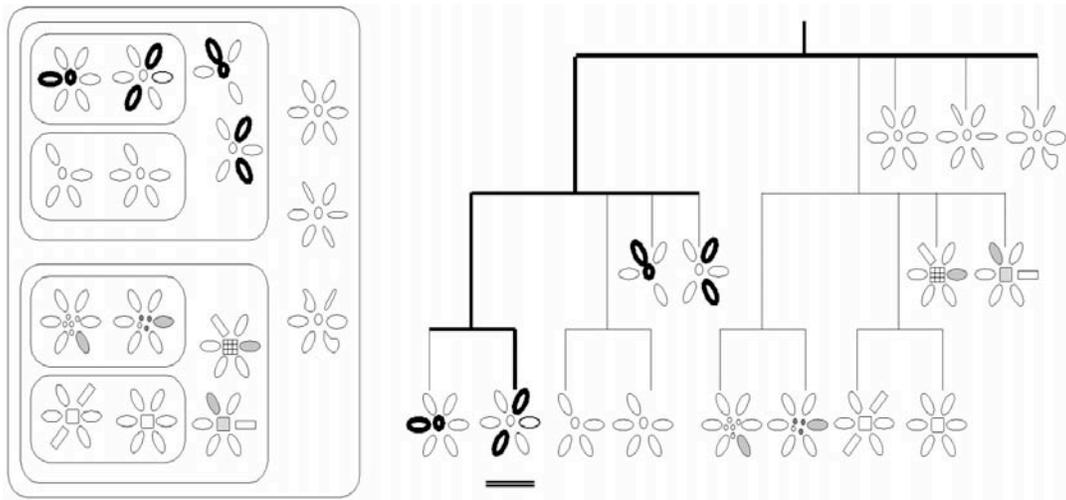


Figure 5. Sample hierarchy of images, shown via embedding (left) and via a hierarchical tree (right.) All images share certain features, e.g., six petals plus center (outermost or top-level cluster), yet each differ in ways that group them into natural sets, e.g., presence of darkened petals, different fill patterns (middle level clusters), as well as containing specific combinations of features differentiating them from others (most embedded or bottom-level individuals).

Complexity and application. The method can be cast as an algorithm (see Methods section). The costs of the algorithm for the performance of hierarchical clustering on arbitrary inputs compare favorably with those in the (extensive) literature on such methods (Ambros-Ingerson et al., 1990; Gluck and Granger, 1993; Kilborn et al., 1996). Elaboration of the algorithm has given rise to families of computational signal processing methods whose performance on complex signal classification tasks has consistently equaled or outperformed those of competing methods, e.g., (Coultrip and Granger, 1994; Kowtha et al., 1994; Granger et al., 1997; Benvenuto et al., 2002).

Matrix thalamocortical circuit: High-capacity sequence storage and retrieval

Nontopographic organization. In contrast to the topography-preserving projections between Ct and cortex, the diffuse projections from L.V to Mt and from Mt back to cortex are modeled as sparsifying and orthogonalizing their inputs, i.e., any structural relationships that may obtain among inputs are not retained in the resulting projections. Thus input patterns in Mt or in L.V that are very similar may result in very different

output patterns (and similar output patterns can arise from quite different inputs). As has been shown in previously published studies, due to the nontopographic nature of layer V and Mt activity, synapses are very sparsely selected in layer V to potentiate; i.e., relatively few storage locations (synapses) are used per storage/learning event (Granger et al., 1994; Aleksandrovsky et al., 1996; Whitson 1998).

Storage of category sequence. When the system is presented with a static input, such as the flowers above, superficial layer cells produce an iterative series of hierarchically related responses to the input as described, and these responses will activate deep layer cells, some of whose synapses will potentiate (Figure 6). The sequence of responses ‘learned’ in layer V corresponds to sparsified codes assigned to the sequence of hierarchical outputs produced by layers II-III. If a learned sequence is presented again, the system will produce the sequence of responses that occurred during learning of the input, retrieving first information about the cluster, then subcluster, etc.

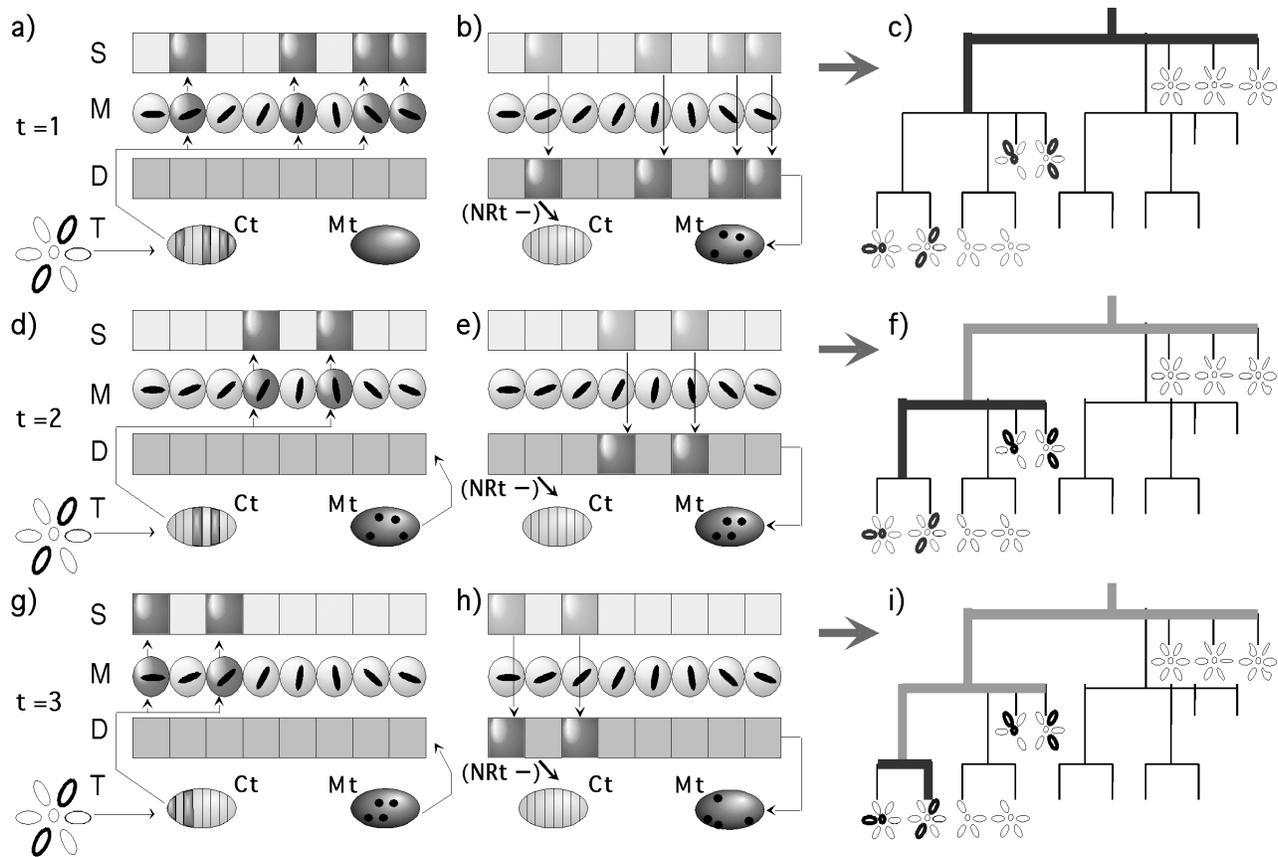


Figure 6. Sequential operations at three successive time steps ($t=1,2,3$) in middle (M), superficial (S), and deep (D) cortical layers, core and matrix thalamic projections (Ct & Mt), and inhibitory nucleus reticularis thalami (NRT-), in response to a static input (a specific flower image, shown at left). **a)** At time $t=1$, most prominent features of the input image (flower) are transmitted via topographically activated regions of core thalamic nucleus Ct to corresponding regions of middle cortical layer (M), to superficial layer (S). **b)** Superficial layers (S) activate deep layers (D) which topographically inhibit active core cells Ct (via layer VI to GABAergic NRT) and nontopographically excite matrix cells Mt (via layer V). **c)** The superficial layer cortical response will be identical for any of a number of similar images, corresponding to membership in a cluster. **d)** At time $t=2$ (next synchronized activity peak), the same image arrives at Ct in the presence of long-lasting inhibition from NRT; thus different core cells "win" the race to fire, topographically exciting different regions of middle and superficial cortical layers. These new responses thus correspond to secondary features of the input that appear now that the primary features are "masked" by inhibitory feedback. **e)** Deep layers learn the sequence of superficial layer responses. **f)** This second superficial layer response corresponds to members of a sub-cluster in the hierarchy. **g), h), i)** Analogous to d, e, f.

Response to time-varying inputs

Time-varying inputs. The above analysis described the operation of the system in response to static inputs (e.g., a fixed gaze on a fixed image). If the input is changing over time, or if the input is scanned a portion at a time (e.g., via saccades), then the same steps occurring in the circuit (Table 2) produce a related but different effect. Cortical pyramidal cells preferentially respond to onsets and offsets,

i.e., transitions among inputs (e.g., somatosensory cortex (Peterson et al., 1998), auditory cortex (Recanzone et al., 2000), visual cortex (Rols et al., 2001; Bair et al., 2002)). Figure 7 illustrates the operation of the system for a sequence of inputs a, b, c.

Convergence of deep layer inputs. The activation of layer V in rapid sequence via activation by superficial layers (in response to an

element of a sequence) and via activation by Mt (corresponding to feedback from previous element in sequence) selects responding cells sparsely from the most activated cells in the layer (Coultrip et al., 1992) and selects synapses on those cells sparsely as a function of the sequential pattern of arriving inputs. Thus synapses potentiated at a given step in layer V correspond to the input occurring at that time step together with orthogonalized feedback arising from input just prior to that time step (Aleksandrovsy et al., 1996; Whitson, 1998).

Input-specific responses; novelty detection. The overall effect is "chaining" of elements in the input sequence, via the "links" created due to layer V activity from coincident inputs corresponding to current and prior input

elements. As in the operating rule described by (Granger et al., 1994), the sparse synaptic potentiation enables the cells in layer V to act as a novelty detector, selectively responding to those strings that have previously been presented. Whereas superficial layer cells in the model respond to any of a number of sufficiently similar inputs (the "clustering" effect described earlier), the deep layer cells respond only to the input sequences that have actually occurred previously, due to the orthogonalizing input from Mt combining with superficial layer input. Thus the layer V activation patterns even for very similar input sequences will be very different from each other, or, put differently, the probability that two similar input sequences will elicit similar sequences of layer V patterns is low.

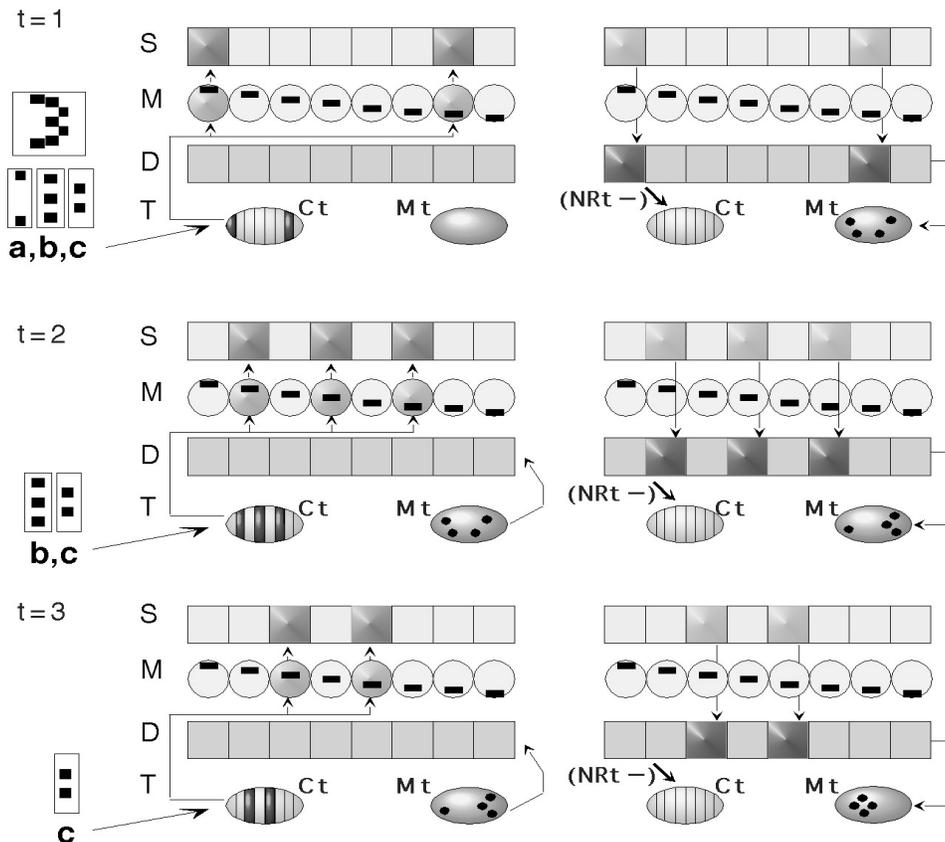


Figure 7. Sequential operations in cortical and thalamic models in response to time-varying input. In the example, a sequence of input patterns corresponds to an aperture passing left to right across an image (upper left) with sampling occurring at successive synchronous activity peaks in thalamocortical circuits. Since the input at time 2 is different from the input at time 1, a different pattern of cortical regions will respond, and as before, the ordered sequence of superficial layer responses will be learned by the deep layer.

Chained sequence memory. Figure 8 illustrates the implicit data structures created by the operation of the system: trees in which initial elements of sequences branch to their multiple possible continuations ("tries," Knuth, 1997). As a result, sufficient information exists in the stored memories to permit completion of arbitrarily long sequences from just prefixes that uniquely identify the sequence. Thus the sequence "Once upon a time" may elicit (or "prime") many possible continuations whereas

"Four score and seven" or "Now is the time for all good men" elicit specific continuations. Once activation of a unique prefix has occurred, completion of the remainder of the sequence can be achieved by a number of means. The only potentiated synapses activated at the end of the prefix are those that became potentiated during storage of the sequence. Selective response of those cells will elicit the same Mt response as had occurred in the sequence.

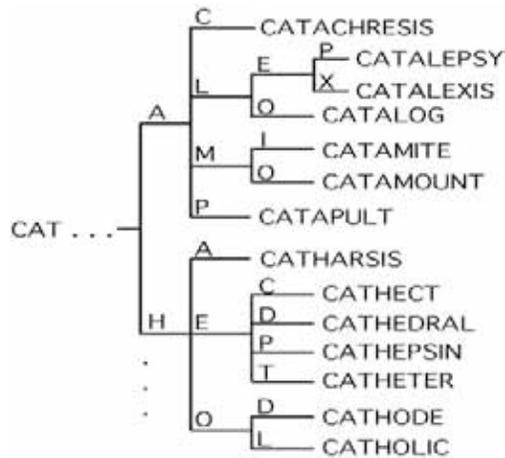


Figure 8. Data structures implicitly constructed by sequence storage in layer V. Letter sequences in the model are intended to represent sequences of arbitrary features as described in the text.

Analysis of thalamocortical circuit algorithm

Measures of required storage. The resulting algorithm (see Methods) can be characterized in terms of computational storage methods that are used when the number of actual items that occur are far fewer than those that could in principle occur. For instance, the number of possible eight-letter sequences in English is $26^8 \approx 200,000,000,000$, yet the eight-letter words that actually occur in English number less than 10,000, i.e., less than one ten-millionth of the possible words. A storage area capable of storing all possible eight-letter words would require the huge commitment of 26^8 storage locations, more than 99.999999% of which would remain forever unused. Since it is not known in advance which of the possible sequences will occur in the language and which

will not, space cannot be pre-assigned for specific sequences.

Efficient storage via hash functions. The sparseness of stored entries (the extremely low ratio of actual to possible data) leads to a very widely-used and well-studied form of data storage in which occurring items are mapped directly to a storage location via a "scatter-storage" or "hash" function (so termed for its typical method of using mixtures of an item's features to compute its location). Hash functions enable large amounts of data to be stored with extreme efficiency (typically requiring only a fixed small number of operations to store each new word) in a very compact space. The methods operate by assigning words directly to a storage location, but their efficiency depends on the absence of

"collisions," i.e., two words being mapped to the same location. For hash functions, there is a tradeoff between the speed of storing a new entry and the space required for the storage: the smaller the space allocated to hold the entire dictionary, the higher the likelihood of collisions.

Storage and collision. A hash function cannot guarantee that collisions will not occur, so either "collision-resolution" mechanisms must be in place, or the method will be unable to guarantee perfect memory of every input. The hypothesized distribution of L.V patterns to Mt and vice versa bears quantitative correspondence to the operation of a hash function that lacks a collision-resolution scheme, i.e., a hash function in which it is possible for multiple inputs erroneously to map to the same output, and thus for memory errors to occur. Estimates can be made of the rate of errors of retrieval of stored

sequences, as a function of the size of the network and the number of sequences stored.

Simplified model. In the model, each of the columnar modules in cortex that can be differentially targeted by topographic input from Ct can represent a feature which may appear in any sequence, such as sequences of oriented line segments, sequences of Braille dots, etc. (Letters of the alphabet are used in the examples herein for illustrative convenience, not because implications for linguistic applicability are intended.) Figure 9 outlines the simulation of just layer V and Mt. Layer V is divided into modules corresponding to topographic features. Each module consists of synapses that can be either naïve or potentiated. Each input element selects a columnar module or modules via the topographic mapping from the model Ct. If input feature "P" arrives at time t_1 , and input "A" at t_2 , the model layer V output arises deterministically from the sequence "P-A."

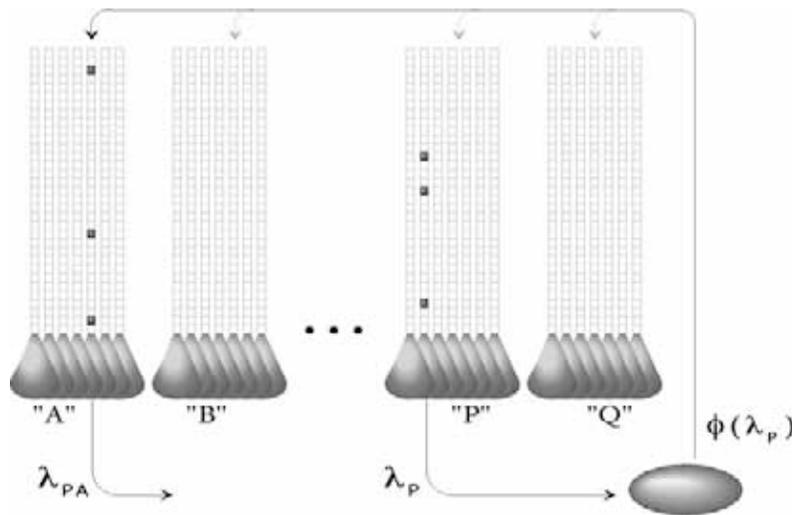


Figure 9. Simplified model of interaction across time steps between layer V and the thalamic matrix Mt. Layer V is divided into modules corresponding to topographic features. Each module consists of synapses that can be either naïve or potentiated. Each input element selects a columnar module or modules via the topographic mapping from Ct. Each vertical column in the figure represents a cell; each compartment represents a synapse on that cell's apical dendrites. If input feature "P" arrives at time t_1 , layer V of the model will produce vector λ_P , a computed hash code representing the cell activity output that would be elicited from layer V by this input. This becomes input to Mt, which returns a hash function of its input, $\phi(\lambda_P)$. That in turn becomes input from Mt to cortex on the subsequent time step, t_2 . If the extrinsic input at that time step is feature "A," then the corresponding topographic module(s) will be activated, the synapses in layer V of that module that are activated by the input from Mt are potentiated, and the model layer V output arises deterministically from the sequence "P-A." The processing continues until the end of the input sequence, creating a "chained" memory selective to the input.

Theoretical analysis of errors of retrieval. As input sequences appear and are "stored" via the methods described, the L.V networks "fill up" with potentiated synapses as a function of the number of times that the corresponding feature occurs in the sequences. Synaptic potentiation "stores" an input, and activation of a previously potentiated synapse "retrieves" that stored input. Errors of retrieval occur whenever a novel sequence is erroneously recognized as having been previously seen. This can occur whenever the components of other sequences occur in a new sequence. If synapses $X_1, X_2, X_3, Y_1, Y_2, Y_3,$ and Z_1, Z_2, Z_3 have been potentiated by sequences X-Y and X-Z, then sequence Y-Z will erroneously be recognized as though it had been seen before. If there are σ synapses in a given L.V network, then there is a $1/\sigma$ chance that any given synapse will be already potentiated, and thus the probability of that not occurring, i.e., an as-yet-unused synapse selected, is $U=(1-1/\sigma)$. For α distinct cortical modules, each containing σ layer V synapses, η of which are potentiated for each new individual input item stored, the probability of selecting an as-yet unused synapse for each new input is $U^{\eta/\alpha}$. After W sequences of length L have been learned, the probability of all constituent inputs having selected new synapses is $P_N = U^{WL\eta/\alpha}$. After these data have been stored, then when a new input occurs, there is a chance of $P_E = 1 - P_N$ that the new input will erroneously activate previously potentiated synapses and thus be falsely recognized (Granger et al., 1994, eq.1; Aleksandrovsky et al., 1996; Whitson, 1998). As before, if η synapses are, on average, activated for each element of an input sequence, and each sequence contains on average L elements, then the probability of false recognition of a new string is the probability of finding η potentiated synapses

for each of the L inputs in the sequence, approximately $P_{RE} = P_E^L$.

Empirical studies of model capacity. Figure 10 illustrates the pattern of information "stored" in a small model thalamocortical system. Panel a) illustrates the 'memory' of a system with just 50 synapses in each of 26 modules, after storage of 200 six-letter sequences. It can be seen that many of the attempted potentiation episodes collided, i.e., potentiation was attempted on synapses that were already fully potentiated, and thus much of the attempted storage did not occur successfully; retrieval errors will result. Panels b and c illustrate the same model but with 100 synapses per module. This network exhibits relatively fewer collisions after storage of the 200 sequences (b), but storage of 400 sequences into the same network causes many collisions (c). Panel (d) graphs the probability of retrieval errors occurring in these small memory circuits as a function of the number of sequences that have been stored in them. The left curve corresponds to retrieval error probabilities for a network with $\sigma = 50$ synapses per module (i.e., $50 \times 26 = 1300$); the right curve is for a network with $\sigma = 100$ synapses per module (thus $100 \times 26 = 2600$). For the left-hand curve, the error probability remains extremely low ($p \leq 0.01$) until about 125 sequences have been learned, at which point the errors begin to rise. Thus this small network can successfully learn and retrieve about 125 sequences, effectively packing sequences consisting of more than $125 \times 6 = 750$ letters into just 1300 bits of storage, or, on average, about 1.7 bits to successfully store the name and sequential position of each letter. The right-hand curve shows roughly 250 sequences learned with low error: $\sim 250 \times 6 = 1500$ letters stored in 2600 bits of storage space, again less than two bits per storage event.

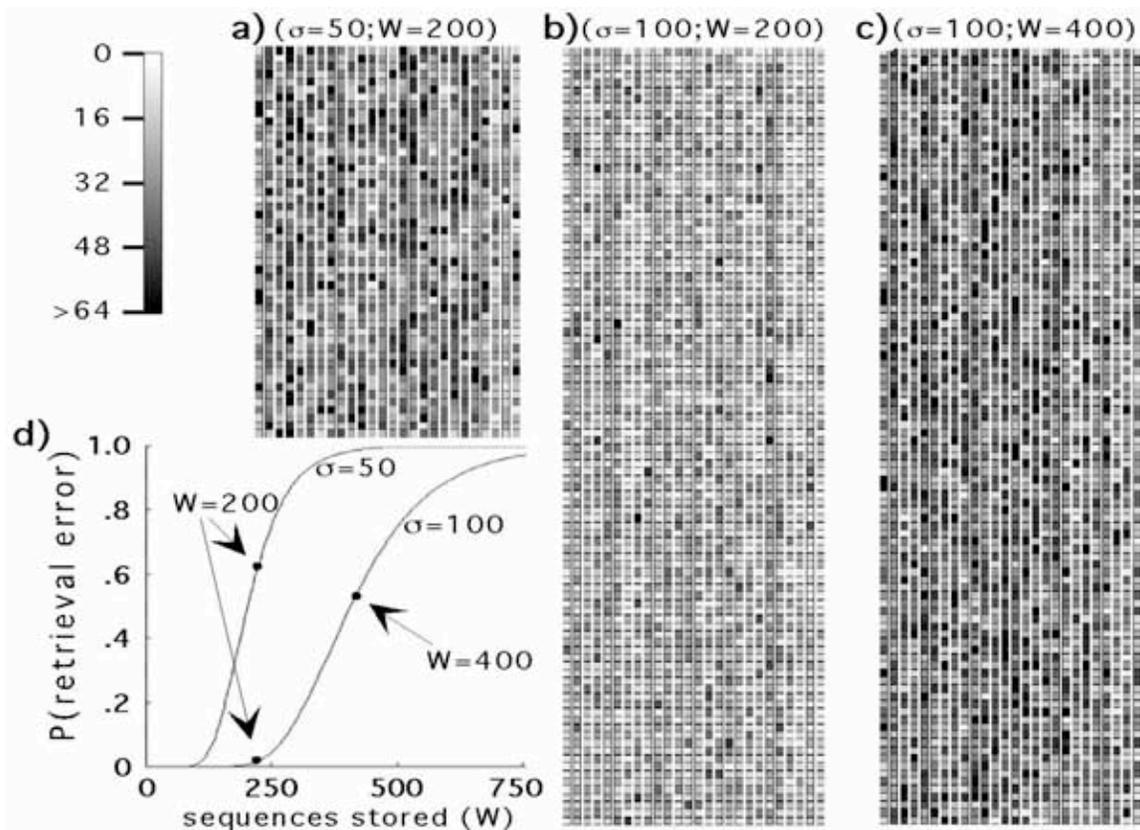


Figure 10. Rate of potentiation of synapses in thalamocortical model. Each large rectangle represents the state of the "memory" of the model after potentiation in response to a number of inputs. Each vertical column represents a "module" (see text); each element (row) in a column corresponds to the synapses in that column. The color of each synapse indicates the number of times potentiation has been attempted at that synapse (legend upper left). At white locations, no potentiation has occurred; at other locations there have been multiple attempts to potentiate a given synapse (collisions). **a)** Collision rate in a model with $\sigma = 50$ synapses in each of 26 modules, after storage of 200 six-letter sequences. **b)** Collisions in a model with $\sigma = 100$ synapses in each of 26 modules, after storage of 200 six-letter sequences. **c)** The same model as in b, after storage of 400 sequences. **d)** Theoretical values of the probability of retrieval error as a function of sequences stored in the two models ($\sigma=50$ and $\sigma=100$).

Experiments with a larger model. Figure 11 shows the empirical (points) and theoretical (curves) probabilities of retrieval errors in a larger network, consisting of 100,000 synapses per module. Approximately 75,000 sequences (of length 20) are learned before the retrieval error probability climbs beyond 0.01; i.e., $75,000 \times 20 = 1,500,000$ letters are stored in 2,600,000 bits, again requiring roughly 1.7 bits to store information about each letter and its sequence position, without exceeding $p \leq 0.01$ of retrieval error. Two theoretical curves are

shown, corresponding to five synapses versus four synapses potentiated per input element. Empirical results (points) are shown for $\eta = 5$, but as the network becomes loaded, the probability of collisions increases, lowering the effective number of previously unpotentiated synapses that become potentiated at each step, whereas in each theoretical curve, all synapses potentiated at each step were previously unpotentiated (see Whitson 1998).

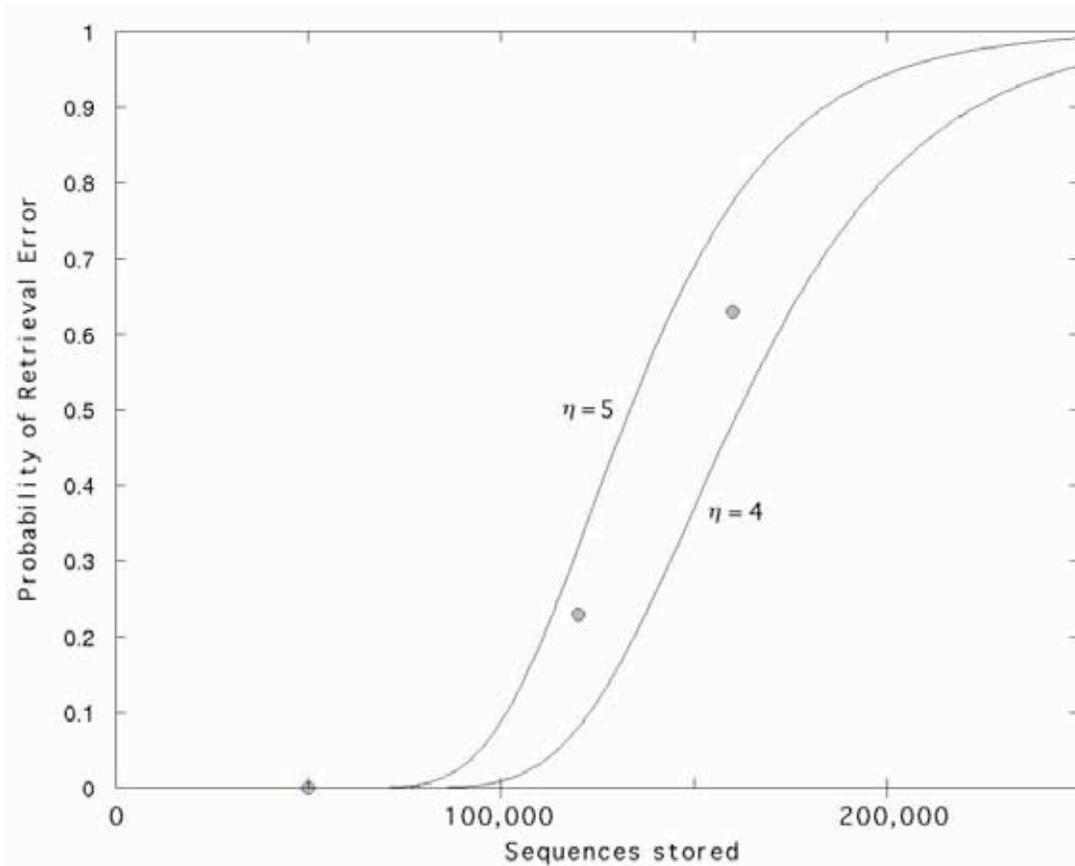


Figure 11. Probability of retrieval errors as a function of number of sequences stored in a relatively large model. The network consists of 26 columnar modules, each containing 100,000 layer V-cell synapses. Inputs are sequences of 20 letters ($L=20$). Theoretical curves are shown for values of $\eta=4$ and $\eta=5$; empirical values are shown for storage of 120,000 and 160,000 20-letter sequences, potentiating five synapses per input ($\eta=5$). See text for discussion.

DISCUSSION

Summary. A novel extended hypothesis of shared basic functions of thalamocortical circuits is derived from their shared anatomical designs, physiological operating patterns, and plasticity rules. A simplified model thalamocortical system is introduced and its responses to static and to time-varying information are described. Examination of the resulting simplified storage and retrieval operations shows their relationship with well-studied algorithms for related functions, including categorization via hierarchical clustering, and sequential storage via hash encoding. Comparison of the new algorithms against their standard computational counterparts illustrates that the derived thalamocortical algorithms exhibit desirable efficacy, scaling, and space and time cost characteristics.

Components modeled. Operation of the model is based on the known anatomical and physiological patterns of the topographic (core thalamus > middle cortical layers > superficial layers > deep layers > nucleus reticularis > core thalamus) and diffuse (matrix thalamus > layer I > layer V > matrix thalamus) circuits reciprocally connecting thalamus and cortex. Plasticity is assumed to occur in cortical glutamatergic synapses via long-term potentiation, in a low-precision manner (synapses are potentiated from initial to full strength, i.e., only a single bit of information is conveyed). Shared characteristics are the focus of the work, and thus features specific to certain cortical regions (e.g., sublamination of layer IV in primary sensory cortical areas) are explicitly omitted. As a result, no attempt is made to study differential functions that might be conferred by these special features.

Response to static inputs. Recurrent feedback in the model from cortical layer VI to the thalamic reticular nucleus topographically inhibits activated thalamic core cells, iteratively "masking" features of an input to which the cortex has responded, thus eliciting subsequent responses to secondary and then tertiary portions of the input over successive rapid activation steps. Similar inputs come to elicit similar or identical responses from the first cycle of operation of the thalamocortical model, whereas subsequent cycles, respond differentially to the differences among even very similar inputs. Over trials, stored memories of static inputs become spontaneously organized into a hierarchy of similarity-based clusters, sub-clusters, and sub-subclusters. In response to a stimulus, the model produces a series of responses that traverse the hierarchy, describing the input at successively finer-grained levels. For more than one response to an input to be produced, the input must be present over more than one cycle of thalamocortical operation. For cycles occurring in the gamma frequency range, an input need be present for just 25 msec per cycle; for cycles at theta frequencies, inputs must be present for 200 msec per cycle. If inputs change more rapidly than the extant activity cycle of the synchronized circuits, then only a single response (e.g., category) to each input (e.g., each element in a sequence) can occur.

Response to time-varying inputs. The proposed mechanism is consistent with widespread observations of synchronous thalamocortical activity. In response to changing inputs, the model divides continuous input into time segments as a function of its cyclic operating rates, from gamma to theta. The diffuse forward and backward connections connecting layer V and thalamic matrix select synaptic storage sites that do not retain the topography of their inputs, thus spreading the resulting record widely over the target synaptic fields. The coöccurrence of thalamic core input from a current stimulus, with matrix input arising from layer V feedback from the immediately prior stimulus, gives rise to "chaining" of stored elements, such that the ordered sequence of inputs, rather than an unordered set, is selectively stored and retrieved.

(Since the output of superficial layers corresponds, as described, to clusters or categories of similar inputs, the sequences stored in layer V are actually sequences of categories.) Formalization of the method illustrates its relation to a well-studied family of algorithms that map inputs to storage locations nontopographically via "hash" functions, which rapidly and efficiently allocate storage without significant wasted space. Analysis showed that the capacity of a given network was linearly related to its size, indicating that very large networks achieve the same rate of synaptic use as small networks (Granger et al., 1994; Whitson 1998).

Generality of the findings. Against the background of substantive similarity of many cortical areas, intriguing differences have recently been demonstrated (Galuske et al., 2000; Elston and Rockland, 2002; Read et al., 2002), raising questions of the extent to which these differences indicate subtly different genetic designs for different cortical regions, versus divergence arising during development due to differential stimulation patterns presented to initially similar cortical structures.

Behavioral implications. An observed property of the model is that perceptual recognition, i.e., distinguishing among similar complex items, occurs not as a separable operation, but rather as a special case of the larger system for sequential categorization of inputs. Almost any damage to the model will differentially spare early responses more than later ones, impairing categorization less than recognition. The model's operation specifically predicts that hierarchically organized stimuli will give rise to a) more errors and b) increased latency in recognition of members of subcategories. Animals show this pattern (Granger et al., 1991), and experiments on human subjects are being carried out to test these predictions on stimuli of the type used by Reber et al. (1998a,b) who report that visual cortical areas show less activity when subjects are asked to categorize images than when asked to recognize them. Intriguingly, anterior cortical areas (as opposed to sensory regions) exhibit more activity during categorization than recognition. Human subjects

robustly recognize objects first at "basic" categorical levels (e.g., bird, screwdriver) and subsequently at successively subordinate levels (sparrow, Phillips screwdriver) (Mervis, 1981; Schlaghecken, 1998; Kuhl, 2001). Experts (e.g., birdwatchers) exhibit faster recognition of objects in their areas of expertise, suggesting the learning of corresponding idiosyncratic "basic" or "entry" levels of recognition. (Since successive read-outs from this system arise from masking of prior inputs, the system distinguishes among mixtures of different components, but not among mixtures of different amounts of the same components.) Significant differences in short categorization vs. longer recognition reaction times (Jolicoeur et al., 1984) are concordant with hypotheses of structured perceptual memories that are hierarchically configured and sequentially traversed during recognition. Synchronized electrical brain activity recorded during complex sensory processing (Sobotka, 1997; Caplan, 2001) is consistent with a cyclic mechanism underlying these sequential recognition steps.

Physiological implications. The sparse and highly distributed storage of time-varying inputs in the model suggests that localization of cortical activity may not be a feature of typical sensory processing, possibly rendering the task of identifying the site of storage of particular memories intractable. The model specifically predicts that there exist cortical neurons which, after familiarization with a set of members of a perceptual category (e.g., images), will exhibit nonlinear "categorical" behavior: they will respond selectively either to all the members of that category or to none of them. At each successive cycle of physiological activity, a cell will respond, or not, to all members of a category or subcategory, etc. Some experimental data on this question exist and support the prediction, in the modality of olfaction in rodents (McCollum et al., 1991) and, recently, vision in primates (Freedman et al., 2001). (Moreover, work in progress suggests anterior cortico-striatal production of categorical cortical neuronal signaling in response to perceptual stimuli for which reinforcement information has been acquired via basal ganglia.)

Cortico-cortical extension. Outputs of superficial layers of many cortical regions combine to become input to middle and superficial layers of downstream regions, whose deep layers in turn send reciprocal feedback to the originating superficial layers (Barbas and Rempel-Clower, 1997; Saleem et al., 2000; Catania and Kaas, 2001; Batardiere et al., 2002; Swadlow et al., 2002). Cortico-cortical processing may differ substantially from thalamocortical operations, though recent single-axon tracing studies indicate that the terminal arbors from cortico-cortical (superficial to middle layer) projections are about the same size as geniculocortical terminations in layer IV of primary visual cortex (Rockland, 2002), suggesting a potential relation between thalamocortical inputs to primary sensory cortex and corticocortical inputs to downstream cortex. It is anticipated that the resulting statistical recombination of sequence elements will give rise to sequences of categories, abstracting from fixed brief feature sequences to templates applicable to a range of longer and more complex inputs.

Data structures linking object components. The steps carried out by the model enable coordinated deposition of distributed information, offering a potential alternative to some computational hypotheses of the function of cyclic (e.g., gamma) activity. The "binding" problem (in which it is posited that co-oscillating brain regions may signal relationships among distributed stored parts of a coherent representation) arises in some models from the need to associate separate aspects of the representation of a single item (e.g., from stored features wheel, leg, car, and table, to the fact that it is the car that has wheels and the table that has legs). In the model envisioned here, salient parts of inputs are recognized independently; the relative relationships (e.g., relative distances and angles) among the parts are stored as elements of a sequence; and recognition proceeds via such a sequence, serially reconstructing relations among the constituent features, which may be sequentially traversed during visual saccades. Multiple different sequences of features may correspond to any given object, depending on the order of saccades that occur, and some

features might be present in some views and not others, such as different angles or occlusions. Hierarchically constructed categories of sequences would correspond to the union of the different possible traversals, defining the object. Elaboration and expansion of auditory telencephalon in mammalian brain preceded that of vision. The shared anatomical characteristics of their circuits, and the sequential nature of complex visual processing hypothesized here, suggests possible origins of visual processing from auditory precursors.

Hypothesis. Functions of neural-like networks have included simple clustering, generalization, Boolean operations, and novelty detection, with more complex operations arising, if at all, from the combination and interaction of multiple simpler systems. It is conjectured that the derived thalamocortical functions forwarded here (hierarchical clustering and sequential hash-

```

for input X
  for C ε win(X,W)
    Wj ← Wj + k(X - C)
  end for
  X ← X - mean(win(X,W))

```

end for

[where X = input vector; W = layer I weight matrix; C = winning column vector (superficial layer cell) in W; k = learning rate; win(X,W) = most responsive column vector in W that respond to X before lateral inhibition, e.g., $A_j, \max(X \cdot W_j)$.]

Formalization of matrix circuit operation. Simplification enables the algorithmic behavior of the matrix circuit in response to the presentation of arbitrary time-varying input to be estimated. For purposes of this analysis,

```

for input sequence X(L)
  for C ε TopographicSuperficialResponse(X(L))
    for V(s) ε C ∩ MtResponse(X(L-1))
      Potentiate( V(s) )
      Mt(L) ← NontopographicDeepResponse(V)
    end for
  end for
end for

```

[where L is the length of the input sequence; C = columns activated at step X(L); V(s) is the synaptic vector of a layer V cell, Mt(L) is response of matrix thalamic nucleus to feedback activation pattern from layer V.]

or scatter-storage) are fundamental building blocks whose recurrence throughout neocortex give rise to powerful systems for perceptual, motor, and cognitive processing through combination of these components. Two primary features not modeled in the present paper are the patterns of cortico-cortical connectivity linking different neocortical regions, and subcortical connections (especially the extensive cortico-striatal circuits coupled with anterior neocortex). Each is the subject of ongoing work, anticipated to yield additional classes of computation.

METHODS

Formalization of core circuit operation. The iterative subclustering activity of the connections between core thalamic nuclei and cortex has been simplified and mathematically characterized as a novel algorithm for the well-studied statistical task of hierarchical clustering:

synapses will be assumed to be binary (either naïve or potentiated), and the mechanisms described thus far will be simplified to the following algorithmic steps:

In this algorithm, a sequence of length L elicits a pattern of response according to the core algorithm given above. Each activated superficial cell C in turn activates deep layer cells. Feedforward activity from the matrix thalamic nucleus Mt (inactive at the time of the first input item in the sequence, and active from then on) also activates layer V . Synapses on cells receiving activation from both sources (the intersection of the two inputs) become potentiated, and the activity pattern in layer V is fed back to the matrix nucleus Mt . The loop repeats for each of the L items in the sequence, with the input activity from each item interacting with the activity in Mt from the previous step.

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