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Computational principles of microcircuits for visual object processing in the macaque temporal cortex

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Abstract

Understanding the principles of neuronal computation that underlie our cognitive abilities is a fundamental goal of neuroscience. Microcircuits are thought to be computational units embedded in a brain-wide neuronal network. Recent progress in experimental and analytical techniques has enabled the exploration of information flow in operating microcircuits of behaving monkeys. Accumulating evidence demonstrates that crucial transformations of neuronal codes for the representation and memory retrieval of visual objects occur in cortical microcircuits. Particularly, microcircuit comparisons across cortical areas provide novel principles for object processing, in which precursor codes for object features are constructed in a lower-order area before prevalence in a higher-order area. We review recent findings on microcircuit operations in macaque temporal cortex that enable object processing, and discuss future research directions.

Key words

Monkey; Simultaneous multiple single-unit recordings; Inferior temporal cortex; Functional microcircuit; Object association memory; Cell assembly

of words

3,822

Headings

- Historical overview: from Hebb's conceptualization to current understanding of microcircuit computation
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Historical overview: from Hebb's conceptualization to current understanding of microcircuit computation

Over 60 years ago, Donald Hebb introduced the concept of “cell assembly” [1], which led us to explore how an ensemble of cortical neurons is coordinated to enable crucial computations for cognitive demands. An analytical framework to substantiate the cell assembly in the brain was formulated about two decades later as the cross-correlation analysis between spike trains of simultaneously recorded neurons to quantitatively evaluate their coordination [2]. Since then, researchers have attempted to identify cell assemblies working in the brain, which encodes sensory information, cognitive processes or motor commands as cooperative activities of multiple neurons (see Box 1).

Box 1 around here

Many pioneering studies of neuronal interactions focused on the early visual system [3-7]. These lines of research established the view of well-organized wiring diagrams in which neurons make connections or receive common inputs basically according to the similarity of their receptive field properties, and revealed that the resultant synchronized spikes could then efficiently drive their common target neurons [8]. Later studies further demonstrated that neuronal interactions do not simply reflect underlying anatomical connections, but instead exhibit

dynamic modulation depending on behavioral contexts or presented stimuli [9-16].

Though numerous studies of synchronized firing provided the basic characteristics of neuronal networks in the cerebral cortex, few studies have examined information flow and neural code transformation along serially connected single neurons, which would be crucial to understand the computational principles of neuronal circuits [17, 18]. This concept of serially connected neurons corresponds to Hebb's "phase sequence", a sequential pattern of activity among multiple cell assemblies that constitutes the neuronal manifestation of a cognitive process [1, 19-22]. In a recent study, the phase sequence was substantiated as microcircuit operations in the macaque temporal cortex for object memory retrieval [23].

It is also important to understand the principles behind hierarchical processing across cortical areas [24]. Comparisons of microcircuit operations in different cortical areas can reveal how computations proceed and change across cortical regions. Recently, microcircuit operations were examined and compared in successive areas of the macaque temporal cortex. It provided novel computational principles for visual object processing: precursor codes of a given object feature are constructed in a lower-order area before becoming prevalent in a higher-order area [25].

Here, we review recent advances in the understanding of microcircuit operations and their computational principles in visual object processing. Microcircuit in this review mostly indicate a circuit whose constituent neurons are included in a sphere with a diameter of approximately 300 μ m [26]. It has been shown that neurons within this spatial range exhibit intriguing superiority in

their connection properties compared with neurons separated by longer distances, including higher connection probability [27, 28] and substantial interactions among more than a triplet of neurons [29]. In particular, we focus on neural code transformation through microcircuit operations, which was elucidated by examining information flow between single neurons in the macaque temporal cortex whose response patterns were characterized in an object association memory task (Fig. 1). Computation in this review, therefore, indicates the neural code transformation inferred by directed interactions between single neurons

Information flow in microcircuits for cognitive computations

Although most previous studies on the functional connectivity have focused on synchronized neuronal firings [9-13, 27, 28], the directionality of information flow also has been investigated in some studies using anaesthetized cats. Toyama *et al.* [3] demonstrated that simultaneously recorded pairs of neurons in the primary visual cortex exhibit various patterns of correlated firings. Alonso and Martinez [30] conducted paired recordings from two different classes of V1 neurons: simple cells in layer 4 and complex cells in layers 2/3. They conducted cross-correlation analyses for these cell pairs, and found that complex cells in layer 2/3 predominantly receive monosynaptic inputs from simple cells in layer 4 with overlapping receptive fields and similar orientation selectivity. Directed connectivity in the opposite direction was found to be much rarer. This study demonstrated that circuit computations can be examined by identifying the direction of

information flow between connected neuron pairs, in which different response properties have been characterized for the constituent neurons [3, 31, 32]. A similar approach can be applied to studies of microcircuits in higher-order visual areas of behaving monkeys, thereby elucidating the computational principles underlying cognitive processes, such as memory retrieval or representation of visual objects.

In macaques, the final stage of object shape processing lies in the inferior temporal (IT) cortex, which is located at the end of the ventral visual pathway [33-36]. Neurons in this region not only represent complex objects, but also exhibit learning-dependent plasticity in their response selectivity [37-40], which could lead to the storage of object memories. Indeed, Messinger *et al.* [41] demonstrated that, during pair-association learning between visual objects, neurons in the perirhinal cortex gradually changed their activities to encode the object pairs being learned, and this occurred within several hundred trial repetitions. However, no studies had demonstrated so far the operations of microcircuits in the IT cortex that were developed as a result of learning. A recent study in macaque IT cortex demonstrated directed signal flow in a microcircuit for the generation of retrieval signals for learned object memory [23]. The authors conducted simultaneous recordings from multiple single-units in area 36 of the perirhinal cortex, while monkeys performed an object association memory task (Fig. 1, top). The Granger causality analysis (see Box 1) was then applied to identify the signal flow among the regular-spiking, presumable pyramidal neurons [40] coding for the object memories. Using this task, two

functionally different classes of memory neurons had been characterized in the IT cortex (Fig. 1, top): “cue-holding neuron” [42], which encodes the presented cue stimulus during the subsequent delay period, and “pair-recall neuron” [42-44], whose delay activity codes for the to-be-recalled paired-associate of the cue stimulus. The authors found that during the memory retrieval period, neuronal signal flow emerged predominantly from cue-holding neurons to pair-recall neurons (Fig. 2a). The signal flow was most prominent in the gamma frequency range (30 to 120 Hz), consistent with previous reports on its predominance in local interactions between neurons [45-47]. To evaluate the functional impact of this signal flow on the activities of downstream neurons, simultaneous recordings were obtained from triplets of memory neurons: one cue-holding neuron and two pair-recall neurons. The Granger causality analysis for these triplets revealed that the signal flow from a cue-holding neuron to a pair-recall neuron (PR1) was accompanied by further signal flow predominantly from PR1 to the other recall neuron (PR2) (Fig. 2b). This result suggests that the signal flow from cue-holding neurons to pair-recall neurons triggers the signal propagation among the assembly of recall neurons, leading to robust representation of the object to be recalled. From these results, the authors proposed a model of microcircuit operations for object memory retrieval (Fig. 2c). This study demonstrated information flow between functionally different classes of memory neurons, and implicated how the retrieval signal of visual object memory is generated and propagated within a microcircuit in the primate temporal cortex. These data, combined with previous studies showing sequential

firing patterns of simultaneously recorded neurons in behaving rats [48, 49], demonstrate that Hebb's concept of "phase sequence" [1, 19-22], sequential activations of cell assemblies that implements cognitive demands, was substantiated in behaving animals. Note that the entity of Hebb's concept of cell assembly as reverberating activities still remains controversial [50]. Calcium imaging techniques enabling simultaneous recordings from over thousands of neurons (e.g., [51] for *in vitro* study) might provide a line of *in vivo* evidence of these concepts in future studies. These microcircuit operations would reflect learning-induced synaptic modifications [39, 52-54], and spike timing-dependent synaptic plasticity might be involved in the signal direction [49, 55, 56] given the temporal relationship between the activities of cue-holding and pair-recall neurons (Fig. 1, top). As shown in the above study, functional microcircuit analysis, especially that focuses on the signal flow between neurons whose response properties have been characterized in a cognitive task, can provide a profound insight into the principles of neuronal computation that underlie various cognitive processes. Hebb's concepts would be useful to constitute a hypothesis regarding interactions between functionally different classes of neurons that are mediated by the delay activities. Whether these concepts again play a crucial role for generating appropriate hypotheses is a subject for future studies.

Context-dependent switching in neuronal signal flow across cortical layers

Detailed wiring diagrams among neurons in different cortical layers have been disclosed *in vitro*

by conducting multiple-patch recordings with slice preparations of primary sensory cortices [57-59]. A series of these studies in combination with anatomical explorations have provided a view of reliable wiring patterns for neurons across different cortical layers, constituting a “canonical cortical circuit” [59-61]: in a sensory area, feed-forward inputs from the prior area are delivered into layer 4 before reaching layers 2/3, followed by transfer to layers 5/6. Whether this laminar signal flow is also observed *in vivo* and whether it would dynamically change according to behavioral contexts or presented stimuli has long been a fundamental question in cortical processing [62].

Examination of laminar circuits *in vivo* has been faced with a difficulty to determine from which layer the data was recorded, especially when researchers have to acquire the data repeatedly from the same animal, as is typical for experiments involving cognitive tasks with trained animals. One of the most powerful tools for acquiring cortical depth information is the current source density (CSD) analysis using local field potentials (LFPs) that are simultaneously recorded across different cortical layers. CSD is the second spatial derivative of the LFP signal, and provides an estimation of current flow across the neuronal cell membrane. In the cerebral cortex, if LFP signals were recorded with equally spaced multi-contact linear probe penetrated perpendicularly to the pial surface, calculated CSD then exhibits reliable laminar patterns [63, 64]. In particular, when a sensory stimulus is presented, the earliest signal of such current flow is the incoming current into neurons in the granular layer (a cortical layer known as layer 4, which does

not include pyramidal neurons as opposed to neighboring layers 3 and 5), and this current flow can be detected as the earliest current “sink” in the stimulus-evoked CSD profile. Indeed, the depth where the earliest sink can be observed consistently matches the location of the granular layer as determined by histology. Using this technique, cortical depth information can be obtained for each channel of a multi-contact linear probe in a given recording track without histological examination. This enables to investigate laminar processing in the cortex of animals performing a cognitive task [64-66].

Recently, Takeuchi *et al.* [67] applied this technique to investigate information flow across laminar circuits in the perirhinal cortex of macaques performing an object-association memory task. They focused on laminar signal flow during the memory retrieval period and its relationship to the signal flow during cue presentation just before the retrieval period. Simultaneous recordings from neurons and LFPs across different layers were performed using a multi-contact linear probe. For each recording track, the depth of the granular layer was identified on the basis of the CSD analysis, for which the earliest current sink corresponded to the granular layer in histology. Neuronal interactions were then examined by cross-correlation analysis of neuronal spike trains recorded in different layers [68, 69]. They found that, when a cue stimulus was presented, neuronal signals flowed from the granular layer to the supra-granular layer, and from the supra- to the infra-granular layer, as expected from the canonical circuits in primary sensory cortices [68]. During the memory retrieval period, however, the direction of the signal reversed,

and it flowed from the infra-granular to the supra-granular layer. These results suggest that information flow across laminar circuits in macaque temporal cortex reverses for different cognitive demands, i.e., encoding or retrieval of long-term object memory. The results elucidate the role of laminar signal flow, and also provide an intriguing insight into the relationship between encoding and retrieval of cortical long-term memory for visual objects.

□

Principles of hierarchical computations across cortical areas for visual object representation

Microcircuit operations within a single cortical area are discussed above. However, microcircuit analyses in two adjacent areas and comparisons of their computations can provide insights into how neuronal computations proceed across the cortical hierarchy.

It has been widely believed that the neuronal representation of a given feature is generated at the cortical area where that representation is prevalent. One of the best known examples of this concept is the emergence of orientation selectivity in the primary visual cortex (V1) [70-72]. However, another possibility also can be raised, in cortico-cortical processing, that a small number of representations are generated at a prior stage and then transferred to the next stage where these representations become prevalent through an increase in the number of neurons showing that representation (“precursor-code creation and subsequent proliferation” hypothesis). Indeed, some projection neurons in V1 already exhibit functional characteristics resembling those

of neurons in their target area. For example, while neurons of layer 4C in macaque V1 rarely show direction selectivity (i.e., motion sensitivity), most layer 4B neurons, which receive inputs from layer 4C and send ascending projections to area MT, exhibit prominent direction selectivity as do neurons in their target area [73]. Using antidromic responses to electrical stimulation in macaques, Movshon and Newsome [74] directly examined the functional properties of V1 projection neurons targeting area MT, and found that these neurons indeed exhibit strong direction selectivity and “special complex” receptive fields, i.e., broad selectivity to both spatial and temporal frequencies.

In the macaque IT cortex, it has been shown that the neuronal representations of object-associations are predominant in area 36, but minor in area TE, which is hierarchically the prior stage to area 36 (Ref. [75]). Therefore, it has been thought that associative object representations are generated in area 36. However, the circuit mechanisms underlying this transformation of neuronal codes to object associations have not been elucidated. Hirabayashi *et al.* [25] tested the above “precursor-code creation and subsequent proliferation” hypothesis for associative object representations in the IT cortex. They conducted simultaneous recordings from multiple single-units in each of areas TE and 36 while monkeys performed an object-association memory task (Fig. 1, top). The functional microcircuits that generate the associative object representation in these areas were then investigated using the cross-correlation analysis. In both areas, they identified serial functional connectivity between the regular-spiking, presumable

pyramidal neurons [40], which implied that “target” neurons received inputs from the “source” neurons via mono- or pauci-synaptic connections (see Box 1). Response tunings of these neurons were characterized to examine the neural code transformations through these microcircuits. They found that in area TE, associative object representations were predominantly observed in the target neurons compared with the source neurons (Fig. 3a), suggesting that the representation of object association is indeed generated in these TE microcircuits. Given the anatomical evidence of dense connectivity and hierarchical relationships between these areas [76, 77], these associative representations generated in area TE would be then transferred to the next area 36. In contrast to area TE, the representational bias was not observed between the functionally connected neurons in area 36 any more, but instead, both the source and target neurons represented object-associations with similar strength. Though the temporal average of associative codes was similar to each other, target neurons exhibited a slower development of the associative codes in their cue responses (Fig. 3b). This result suggests that in area 36, associative representations propagate through recurrent neuronal interactions, by which neuronal codes gradually develop over time [78-80] (see the next section for details). Together, these results suggest that associative representations are generated as a small number of “precursor” codes through convergent microcircuits in area TE, and these precursor codes are then transferred to area 36, where those representations “proliferate” through recurrent neuronal interactions, leading to a predominance of associative codes in this area (Fig. 3c). This study was the first to directly

compare the microcircuit operations in two successive cortical areas, and this strategy revealed a striking difference between the neuronal computations executed at each cortical stage. The framework of visual feature representation through microcircuit operations across successive cortical areas provides a novel insight into the computational principles of object representations across the cortical hierarchy.

Gradual development of neuronal codes through recurrent circuits in primate temporal cortex

Gradually developing neuronal codes have been reported in the macaque IT cortex for various object processes. Brincat and Connor [81] examined the characteristics of object representations in the posterior IT cortex by systematically investigating single-unit activities in response to a set of over a thousand artificial object shapes composed of combinations of multiple contour fragments. The effective elements driving responses in each neuron were examined by fitting the response tuning profile with a model function that characterized the tuning. The model was composed of multiple terms, each corresponding to the neuronal response to a single contour fragment (linear processing) or to a combination of the fragments (non-linear processing). Using these descriptions of neuronal responses, the dynamics of linear and non-linear processing were then examined [78]. Interestingly, the non-linear processes took a substantially longer time compared with the linear processes (Fig. 4a and b). They also found, via network simulation, that

the relatively slow dynamics of non-linear components could be explained by introducing recurrent interactions between neurons with similar response tunings. Further examples of slow dynamics have been reported in other studies. Freiwald and Tsao [80] showed that view-invariant face identification is attained in the most anterior face patch, and this signal build up gradually, taking over 300 ms from cue onset before reaching the maximum representation. Furthermore, Sugase *et al.* [82] found that global information, such as whether a presented stimulus was a face or non-face object, was processed before fine information such as the identity of a face. These observations of gradually built-up neuronal signals could reflect a common underlying mechanism, similar to associative coding in the target neurons of area 36 (Ref. [25]). Gradual development of neuronal codes as a consequence of complex processing on the presented visual object might be, therefore, a general mechanism in the IT cortex, and recurrent neuronal networks may be responsible for these complex processings.

Concluding remarks

Recent advances in experimental and analytical tools have led us to a profound understanding of microcircuit operations and their computational principles: substantiation of Hebb's phase sequence, findings of context-dependent switching of cortical laminar signal flow, and the computational principle of "precursor-code creation and subsequent proliferation." An important issue for future studies to address is relationships between computations at different hierarchical

levels, i.e., how are microcircuit operations regulated by laminar circuits or by the global networks in the brain (see Box 2)?

Optogenetic approaches are promising tools for investigation of neuronal circuits, especially across different brain areas, and are already widely applied for this purpose. Zhang *et al.* [18] injected recombinant adeno-associated virus coding for retrogradely transportable channelrhodopsin-2 (ChR2) into rat hippocampus, and measured the responses of hippocampus-targeting projection neurons in the entorhinal cortex that were identified by their responses to optical stimulation in the entorhinal cortex. Combining optogenetic approaches with simultaneous recordings from multiple single neurons across layers in macaque temporal cortex would provide a unified framework on the operations of the neuronal network that spans different levels of the cortical hierarchy.

Outstanding questions around here

Box 1. Analytical tools for investigating functional connectivity between single neurons

Over several decades, various analytical tools have been developed to investigate the functional connectivity between single neurons. At present, several different analytical tools are utilized to calculate the functional connectivity from spike trains of simultaneously recorded neurons (functional connectivity for cellular imaging data is treated in [83]). A brief introduction to current analytical techniques continues below (for optogenetic approaches, see [84]).

1. Cross-correlation

Since the pioneering work of Perkel *et al.* [2], cross-correlation analysis of neuronal spike trains has been one of the most prevailed methods for detecting the functional connectivity between neurons. When a pair of neurons receive common inputs, these neurons tend to fire together, which can be detected as the center peak on a cross-correlogram, in which the spike probability of one neuron (neuron 1) is calculated as the function of time from individual spikes emitted from the other neuron (neuron 2). Further, if neuron 1 connects to neuron 2 in a serial manner, then the spike firings of neuron 2 should tend to follow those of neuron 1 with a delay of several ms, which would be detected as a displaced peak on the cross-correlogram [3, 7, 14, 16, 23, 25, 30-32, 47, 68, 85-88].

2. Coherence

Coherence is the normalized cross-spectrum, i.e., the Fourier-transformed cross-correlation of two time series, normalized by the product of power spectra. Coherence measure provides the spectral structure of the functional connectivity between neurons, and thereby provides improved detectability of connectivity in general, compared with cross-correlation, because coherence includes the effects of correlation structures with a large time lag far beyond that of the primary peak on the correlogram [89]. The phase of coherence could provide information on the lag between the two signals, but care should be taken when interpreting phase information as the sign of activity lead/lag because the phase has a circular nature (e.g., a phase of 270 degree is also corresponds to -90 degree, see also [90] for the relationship between the phase and lag). Though coherence has been primarily calculated between continuous signals such as LFP or EEG [90-92], a recently developed multi-taper method [89] has promoted its application to spike trains [23, 45-47], since it provides a low bias and a high signal to noise ratio for the calculation of spectral measures.

3. Granger causality

Granger causality analysis [93] was originally developed in the field of economics to evaluate causal relationships between multiple variables (e.g., the exchange rate and stock prices). Granger causality states, based on linear regression modeling of time series, that if the current value of a time series A can be estimated more precisely by using the past values of both the time series A

itself and another time series B than using only the past values of A, then signal B has a causal influence on signal A in Granger's sense. The concept of Granger causality has been extended to the frequency domain [94] and this analytical tool has been applied primarily to continuous signals in the neuroscience field [90, 95-102]. A recently developed nonparametric Granger causality analysis [103-105] has enabled the application of this method to spike data, which cannot be directly examined in the conventional Granger causality analysis due to discreteness (see also [106-109]). Using this technique, Hirabayashi *et al.* [47] examined Granger causality between simultaneously recorded pairs of single IT neurons in macaques performing a visual discrimination task, and found that the direction of neuronal signal flow within a microcircuit can dynamically change during the course of stimulus presentation. This study demonstrated that Granger causality analysis can be a powerful tool to examine the dynamics of information flow between single neurons during cognitive tasks.

Box 2. Outstanding questions

❑ How do neuronal circuits across different hierarchical levels coordinate for implementation of a specific cognitive demand?

❑ How do inhibitory interneurons contribute to neural code transformations in cortical microcircuits for object processing? Optogenetic approaches will be effective in dissecting the functional differences across different classes of inhibitory interneurons.

□ What are the dynamics and mechanisms of learning-dependent developments of neuronal circuitry for object memory, where various classes of memory neurons are embedded?

□ What roles do higher-order thalamic structures play during object processing in the IT cortex?

Saalmann *et al.* [110] demonstrated that pulvinar activation plays a crucial role in the interactions between areas V4 and TEO in macaques performing an attention task paradigm.

□ How do top-down signals contribute to memory retrieval and neuronal representations of visual objects, and to the learning-dependent development of neuronal circuitry for object memory?

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Acknowledgments

This work was supported by a Grant-in-Aid for Specially Promoted Research from MEXT to Y.M. (19002010), by a CREST grant from Japan Science and Technology Agency to Y.M., by a grant from Takeda Science Foundation to Y.M., and by a Grant-in-Aid for Young Scientists (B) from MEXT to T.H. (25870142).

Figure legends

Figure 1. Microcircuits and their organization for object association in macaque temporal cortex.

Top, Schematic diagram showing activities of functionally different classes of neurons in macaque inferior temporal (IT) cortex. In this task, monkeys were presented with a cue stimulus first, and two different objects were then presented following the delay period, one of which was the paired-associate of the cue-stimulus and the other a distracter. The monkeys were then rewarded when they correctly chose the paired-associate. Monkeys were trained to learn six pairs of objects. Using this task, several types of IT neurons showing different response patterns have been identified [42, 43, 75]. These neurons potentially interact during the cue and/or memory retrieval period in the task. Middle, potential connectivity diagram among functionally different classes of neurons that are involved in the object association memory task. Cue information might be transformed into associative object representation and/or memory retrieval signal of the target to be recalled, through microcircuit operations (the third row). Bottom, microcircuit organization across the cortical hierarchy. Transformed neuronal codes through microcircuit operations in a given cortical area would be then transferred to the next area, where a different microcircuit further processes the incoming information with a different computational principle inherent to the area. These steps, as a whole, would constitute hierarchical processing of visual objects in the temporal cortex (modified, with permission, from Ref. [23]).

Figure 2. Information flow in a microcircuit of macaque perirhinal cortex underlying retrieval of object association memory. **(a)** Population results of the Granger causality from cue-holding (CH) neurons to pair-recall (PR) neurons (top) and in the opposite direction (bottom). Vertical white lines represent cue onset and offset. Note that CH and PR for the causality analysis encoded the same object pair. During the memory retrieval period, neuronal signal flow emerged predominantly in the direction from CH to PR. **(b)** Population results of the Granger causality for CH-PR1-PR2 triplet recordings. Top, Granger causality from PR1 to PR2 triggered by that from CH to PR1. Abscissa, the time from the maximum Granger causality from CH to PR1 in each triplet. Bottom, Granger causality from PR2 to PR1 triggered by that from CH to PR1. Note that all the neurons in a given triplet encoded the same object pair. The results show that directed neuronal interactions from CH to PR trigger the subsequent signal flow to another PR, suggesting signal propagation among PR neurons for robust representation of the to-be-recalled target object. **(c)** Proposed model for microcircuit operations underlying object memory retrieval in the macaque perirhinal cortex. Blue and red neurons show cue-holding and pair-recall neurons, respectively. The brightness of neurons indicates their firing rates. Bars between neurons depict the functional connectivity. Arrows between neurons indicate directed interactions. This study demonstrated the neuronal entity of Hebb's "phase sequence" [1, 19-22, 48, 49] for object memory retrieval in the macaque temporal cortex (modified, with permission, from Ref. [23]).

Figure 3. Neuronal circuits for associative object representation across macaque temporal areas.

(a) Response profiles of pairs of TE neurons that exhibited significant connectivity in the direction from source-neurons (bottom) to target-neurons (top). Functional connectivity was predominantly observed in the direction from neurons coding for a single object to neurons encoding a learned pair of objects, suggesting that converging microcircuits generate the representations of learned object associations. These converging microcircuits were predominantly observed in area TE, but not in area 36, suggesting that the representations of object associations are generated in area TE, but not in the higher-order area 36. **(b)** Dynamics of associative coding for source- and target-neurons in area 36. Abscissa, time from the half maximum of the pair-coding index (PCI) for the source-neuron in each cell pair. PCI is calculated for each individual neuron as the response correlation for all learned pairs of stimuli, providing a degree to which the neuronal responses encode object associations [75]. While the source-neurons showed a rapid increase in the strength of associative coding following cue onset, target-neurons exhibited a gradual build-up of associative coding, suggesting the involvement of recurrent neuronal interactions. Note that response latencies of the source- and target-units by themselves did not differ significantly in area 36 either for the optimal stimulus or its paired associate. **(c)** A proposed model for establishing the representations of object associations across the hierarchy in macaque IT cortex. A small number of representations for object associations are created in the lower-order area (area TE), which are then transferred to the higher-order area (area

36), where the representations “proliferate” through recurrent neuronal interactions to become prevalent in this area. By comparing microcircuit computations between neighboring cortical areas, this study provides a novel computational principle for visual object processing across the cortical hierarchy (modified, with permission, from Ref. [25]).

Figure 4. Gradual development of neuronal representations constructed by complex processing via recurrent neuronal interactions. **(a)** Response profile of a representative neuron in the IT cortex. In this study, neuronal response profiles to a large ($> 1,000$) stimulus set were fitted by model functions in which responses were represented by the weighted sum of several different terms, each corresponding to the response to a contour fragment in a stimulus or a combination of the fragments. Left, example stimuli including contour fragments that locate near the tuning peaks. This neuron responded primarily to two different contour fragments (left, blue) and their combination (left, green). Right, observed (gray histograms) and predicted (black traces) responses to the example stimuli. Blue and green traces depict the predicted responses for single- and multiple-contour fragments, respectively. Note that the non-linear response to the combination of curvatures (green) developed more slowly than the linear response to each curvature (blue) in a given object. **(b)** Left, population dynamics of linear (blue) and non-linear (green) components of neuronal responses. Note that the non-linear component exhibited substantially slower development compared with the linear component. Right, schematic diagram

of a presumed mechanism underlying the distinct dynamics of linear and non-linear responses. Model simulation with combined feed-forward inputs and recurrent neuronal interactions largely reproduced the observed population response dynamics. The results shown in this study, together with similar observations of the gradual development of neuronal representations in macaque temporal cortex [25, 79, 80, 82], suggest that this scheme may provide a general neuronal mechanism underlying object representation in macaque temporal cortex (modified, with permission, from Ref. [78]).

Fig. 1

Fig. 2

Fig. 3

(a)

Stimuli closest to part tuning peak

Predicted & observed responses

(b)

Fig. 4