
Annotated Bibliography For HTM Researchers

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Abstract

This document contains an annotated bibliography targeted towards those doing active research on Hierarchical Temporal Memory (HTM). The focus is on neuroscience, though there are occasional other references. The document consists of (possibly very brief) descriptions of specific papers. These descriptions emphasize the relationship to HTM Theory and don't necessarily summarize the paper itself. There is typically exactly one paper, or a couple of tightly related papers, for each subsection. We hope the content is useful for finding appropriate citations when writing HTM related papers. The material could also be useful in understanding the neuroscience behind HTM theory in more depth. One very useful feature is that the references section includes the full abstract of each paper. The bibtex file for these references are exported from the public Mendeley HTM Neuroscience group.

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*Send all flames and blame to him.

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1 Neuroanatomy

As HTM is a theory of the neocortex, we include review papers on architecture of the mammalian cortex, including the laminar and columnar structures of the cortex and thalamocortical circuits.

1.1 Thomson: Cortical anatomy

These papers by Thomson [44, 45, 43] are dense but contain a lot of detailed information about the connections into, out of, and within the various cortical layers and between different types of neurons in the cortex.

1.2 Buxhoeveden: minicolumn review

[6] Note from Jeff: *this is the best review article I know about mini-columns. Start here.*

The article also contains a bunch of data on typical measurements. From this you can gather that minicolumn widths vary quite significantly between species. The width can range from 20-60 microns, with about 40-80 microns distance in between (center to center). So there are 12 to 25 minicolumns per mm of cortex.

1.3 Constantinople and Bruno: parallel systems in the cortex

This recent paper by Constantinople and Bruno [8] challenged the classical belief of sensory processing pathway along $L4 \rightarrow L2/3 \rightarrow L5/6$ among cortical layers. Instead, it provided new evidence supporting the idea that superficial layers ($L4 \rightarrow L2/3$) and deeper layers ($L5/6$) act as parallel systems.

1.4 Horton: minicolumn naysayer

This paper [15] is a good summary of the arguments against the importance of columns. We should point out that the term "column" is very ambiguous - this article reviews all the variations but is also a bit muddled about them. In HTM the term refers strictly to mini-columns. Phenomena like macro columns, hyper columns, ocular dominance columns, etc. are emergent phenomena that group together lots of mini columns. They probably arise as a function of learning, and not really required in a strict sense. You can get lots of variations in these macro-column structures and that would be fine. So most of the article does not contradict HTM theory.

Horton completely disagrees with the notion that minicolumns have any functional significant whatsoever. He states, "dubious is the concept that minicolumns are basic modular units of the adult cortex, rather than simply remnants of foetal development".

Again we need to be precise about language. Most people debate whether the mini-column is THE basic unit of cortical function, as if the connections between cells in a mini-column compute something. In HTM theory we don't make this claim, it's false, and it leads to a lot of confusion. The cellular layer, not the mini-column, is a unit of processing. All we claim is that cells in a mini-column share similar feedforward response properties and that they mutually inhibit each other. We don't require this inhibition be local to just the mini-column, in fact it may very well extend to surrounding columns. Horton admits that mini-columns exist physically (pretty much everyone does), but he argues that they aren't functionally important.

One of his arguments is that there is a profuse connectivity across columns. This argues against the idea that the mini-column is the unit of computation but it is what we need in HTM layers.

The only claim really under contention, vis--vis the Horton paper, is whether cells in a mini-column share feedforward receptive fields. As the paper points out it is extremely difficult to detect this, as mini-columns are very narrow (35-50um wide and 2500um tall). It is also likely that the cells in a mini-column are not exactly linear. They can move about as much as they want as long as the connections are maintained. Neocortical tissue is more like tapioca and less like wood.

We propose that cells in a mini-column will exhibit very different responses during learned sequences. This exact behavior has been documented. However, some people argue this proves that

the cells in the mini-column do not share common receptive fields! So you have to be careful when reading claims. Was the animal awake, was it a brain slice, what exact stimulus is being used?

HTM theory provides an elegant explanation for the conflicting data and confusion about mini-columns.

2 Sparse Distributed Representations

A core aspect of HTM theory is that sparse distributed representations (SDRs) are used everywhere in the brain. In this section we summarize neuroscience research papers supporting various aspects of this idea.

2.1 Olshausen: Sparse coding

The 1996, 1997 papers [31, 32] by Olshausen and Field represent the first computational papers on sparse representations in the cortex. Their work has been very influential in the machine learning and neuroscience. The 2004 paper [33] is shorter and easier to read, more of a review.

2.2 SDR object representations in IT

[17] is an extensive study of SDR-like properties in IT. They measured responses of 600 neurons in monkey IT to 1000 images. They analyzed the similarity between all pairs of responses. By doing agglomerative clustering they show that objects tend to cluster according to natural categories. i.e. similar objects have similar representations. They use many different distance methods, though only one is really shown in detail.

The selectivity of single cells was imperfect compared to cell population as a whole. Many cells discriminated between combinations of categories. In other words it is a distributed representation.

They showed that lower level simple and complex features (roughly equivalent to V1, V2) cannot account for these similarity metrics.

Note that each image was only presented for 105ms, so it's essentially a flash inference case.

2.3 SDR episodic memory in hippocampus

This paper [48] provides supporting evidence that a sparse distributed neural code is used for episodic memory in human hippocampus. Specifically, they showed that (i) a small percentage of recorded neurons responded to any one target and (ii) a small percentage of targets elicited a strong response in any one neuron

2.4 Babadi: Sparseness and Expansion

The paper [2] is tangentially related to our SDR work. I am including it here only because we might want to cite it in our theory papers. I think there are several key differences:

- They are focused on sparseness combined with expansion. This is a bit strange, since expansion is not required and not found everywhere in the cortex.
- They require full connectivity matrix between the input layer and the encoding layer
- They are using analog weights and a very different distance function (Euclidean distance instead of overlap)

3 Pyramidal Neurons

Pyramidal neurons are the most numerous excitatory cells in the cortex and play important roles in advanced cognitive functions. Understanding the structure and function of these neurons is important to HTM research. This section contains research and review papers on properties of pyramidal neurons.

3.1 Spruston: Pyramidal neuron review

This paper [42] contains a very nice review of pyramidal neurons, including their various regions, active dendritic properties, number of synapses, etc. They focus on the commonalities across different cortical areas and hippocampus.

3.2 Polsky: computational subunits in dendrites of pyramidal cells

Polsky et al [36] showed that the thin basal dendrites of pyramidal cells provide a layer of independent computational 'subunits' that sigmoidally modulate their inputs prior to global summation. This challenges the often reported global linear or sublinear summation of synaptic inputs in pyramidal cells.

Similar ideas have been proposed in an earlier paper [35], which shows that pyramidal cells is best modeled as a "two-layer" neural network.

3.3 Rah: Thalamocortical inputs targeted proximal basal dendrites

Rah et al [37] used array tomography, a high resolution optical microscopy method to examine the spatial distributions of thalamocortical (TC) inputs onto L4 and L5 pyramidal neurons.

Main results:

1. TC synapses primarily target basal dendrites in L5 and proximal apical dendrites in L4 (Fig. 8).
2. TC inputs are biased toward certain branches and, within branches, synapses show significant clustering with an excess of TC synapse nearest neighbors within 5-15 μm compared to a random distribution

3.4 Yoshimura: vertical and horizontal inputs to L2/3 neurons

Yoshimura et al. [52] examined properties of horizontal inputs (lateral connections) and vertical inputs (feedforward inputs from L4) to L2/3 pyramidal cells. They found that vertical inputs (L4 \rightarrow L2/3) evoke large amplitude EPSPs of L2/3 pyramidal neurons, whereas horizontal inputs (lateral inputs from other L2/3 neurons) caused small amplitude EPSPs with large variation.

4 Active Dendrites

An important function of the neocortex is to generate predictions of what will happen in the future. In HTM theory proximal and distal dendrites recognize patterns and depolarize cells into a "predictive state". Over the last 20 years, the properties of active dendrites have become a topic of great interest to the neuroscience community. Active dendrites seem to be coincidence detectors, detecting a temporal coincidence of activity within a portion of the dendrite through "NMDA spikes". These spikes usually don't cause a neuron to spike but they seem to prime the cell and make it more likely to generate an axon potential, and generate it faster than it would have otherwise.

HTM theory says that these properties form the underlying neural mechanisms for prediction and inference. This section contains numerous papers describing current neuroscience knowledge on active dendrites. Some of the papers also show that apical dendrites also have very interesting special properties. Much of our current HTM research is focused on understanding dendritic properties in detail.

4.1 Antic: Decade of NMDA Spikes

From Jeff: *This is a short and relatively easy to read paper that covers the basics of NMDA dendritic spikes including some of the history. It might be a good introduction to the topic.*

The paper [1] describes evidence for the HTM "predictive state". A non-apical NMDA spike can depolarize a cell body (page 2998, middle of right column). The time course of this depolarization is

interesting - the paper shows evidence for a more sustained depolarization than we typically model in HTMs. This could be used to help combat temporal noise or it could support the "learn on one cell" mode.

They also provide evidence that NMDA spikes are highly localized events incorporating a small dendritic segment. They are localized in space (10-40 microns) and localized in time. See page 2998, middle of left column.

4.2 Larkum: Synaptic integration in tuft dendrites

Although this paper [19] is primarily about apical tuft dendrites it is also a good introduction to dendritic spikes in general, including basal dendrites. Figure 4H is a good summary diagram of how to think about a typical pyramidal neuron where the apical tuft dendrites act as a set of coincidence detectors similar to how the basal dendrites act as a set of coincidence detectors. The apical tuft dendrites generate a Ca spike and the basal dendrites generate a somatic Na action potential.

4.3 Branco: How dendritic segments integrate their inputs

This paper [5] contains some useful data on dendritic segments and how they integrate their inputs. Summary of findings:

1. Proximal dendrites sum over their synapses linearly. Synapses sum linearly and inputs must converge at the exact same time. They also show that more distal dendritic branches show threshold like (sigmoidal) response properties. This is nice confirmation for our model.
2. Distal dendrites have broader temporal integration windows. Quote: "We show that single cortical pyramidal cell dendrites exhibit a gradient of temporal summation and input gain that increases from proximal to distal locations. This suggests a progressive shift of computational strategies for synaptic inputs along single dendrites.
Near the base if inputs are more than a few msec apart, the evoked potential drops significantly. Confirmation that proximal dendrites act as coincidence detectors. Segments farther away from the base can sum over longer temporal intervals. At the most distal locations, evoked potential stays constant for much longer than 10 msec.
Another way to phrase this is that proximal segments require precise synchrony (coincidence detection), distal segments do not require such precise timing.
3. More distal segments have higher gain (sigmoid gain) and require fewer synapses to fire. As a consequence, they also state that really distal segments can be as effective or even more effective than proximal dendrites in driving axonal output. Not sure what to make of this.
4. They show all this in Layer 2/3 as well as Layer 5 pyramidal cells.

Some reactions to temporal property: We don't model the timing property of distal segments today, but this property could be very useful. For example longer temporal scales can be helpful in dealing with temporal noise. A longer scale will make us more resistant to temporal insertions. It could also be used to create connections from a single segment to time steps $t-1$ and $t-2$. This will make us more robust to temporal deletions. (This is similar to our old pooling idea.)

Distal inputs into L4 can be coming in at different time scales (motor commands could be slower than sensory input). A longer temporal integration period may be necessary for proper sensorimotor inference.

If apical dendrites have much larger temporal integration windows, this could be very useful for feedback which necessarily has a slower time scale.

4.4 Losonczy: Integrative Properties of Active dendrites

This paper [22] contains a detailed study of exactly how many synapses are required to initiate a dendritic spike in hippocampal pyramidal neurons.

Their study suggests that 17-20 active synapses are required for dendritic spiking. They show that the synapses need to be within 6 msec, confirming the hypothesis that these dendrites are acting like a coincidence detector. If you spread out the activity to 50 msec you do not see spiking.

The spiking is specific to a branch. The synapses do not need to be tightly spatially clustered but can be anywhere on a branch. They quote that a branch typically has 300 to 400 synapses. This suggests that a branch can detect noisy patterns (the threshold is lower than the total number of cells) or that they are detecting a union of patterns, or both.

4.5 Major: Active properties of dendrites

This paper [24] cites evidence that distal dendritic spikes often have a weaker modulatory effect. (Proximal connections are thought to have a stronger effect.)

They review different types of cell models.

They provide numbers regarding the minimum number of synapses required to trigger dendritic spikes that match up very well with our formal analysis of SDRs. NMDA spike in distal dendrites can be evoked by as few as 10 active synapses that are clustered together (page 17, top left) or 20 spread along the branch. Note that the effect of spatial clustering is slightly different than reported in [22]. However as they point out, these numbers are rough and can vary dynamically (e.g. as a result of dendritic inhibitory input).

4.6 Major: NMDA spikes in basal dendrites of pyramidal neurons

This paper [25] shows that glutamatergic inputs clustered over approximately 20-40 microm can elicit local NMDA spike/plateau potentials in terminal basal dendrites of cortical pyramidal neurons.

4.7 Golding: calcium spike in apical dendrites of pyramidal neurons

This paper [12] shows calcium spikes are initiated in the apical dendrites of CA1 pyramidal neurons and drive bursts of sodium-dependent action potentials at the soma. A predicted cell could fire bursts of action potentials through this mechanism.

4.8 Larkum: BAC firing hypothesis

Apical dendrites seem to have a special integration zone which can cause that region of the cell to be depolarized for sustained periods of time.

In addition, feedback input to apical dendrites by themselves can cause strong action potentials. If this is coincident with matching feed forward input, the cell bursting can be sustained for a period of time. Mechanisms for that are reviewed. Figure 3a is an example of this.

...this article [18] has dealt with the biophysical evidence for the existence of an associative firing mechanism in pyramidal neurons and its influence on the input/output function. This degree of integration between the micro- and macroarchitecture, as well as inbuilt complexity at the cellular level, invites speculation about whether and how the whole system utilizes this feature. The importance of this mechanism conceptually is that the pyramidal neuron is able to detect coincident input to proximal and distal dendritic regions, investing the cortex with an inbuilt associative mechanism at the cellular level for combining feed-forward and feedback information.

The BAC firing hypothesis presented here offers a cellular mechanism that addresses a number of questions about the cortex. It suggests that the pyramidal neuron cell type is an associative element which carries out the same essential task at all cortical stages: that of coupling feed-forward and feedback information at the cellular level.

Martinotti neurons blocking dendritic activity - what is this for? Need to review. Could this turn off pooling when columns burst?

4.9 Palmer: NMDA Spikes in L2/3 neurons

Few papers talk about dendritic NMDA spikes in Layer 2/3 pyramidal neurons. That is the topic of this paper [34] showing that Layer 2/3 cells act similarly to the more studied L5 and Hippocampal Ca1 pyramidal neurons.

Another study [20] studies dendritic spike in the apical dendrites of L2/3 pyramidal neurons. They conclude that L2/3 neurons can generate dendritic spikes similar to L5 neurons.

4.10 Yuste et al: Apical Dendrite as a segregated functional compartment

Yuste et al [53] proposed that the apical dendrite and basal dendrite could act as two segregated functional compartments. The authors showed that the apical zone can be activated (generated Ca²⁺ spikes) even when Na and K conductances are blocked.

In a more recent paper, Larkum et al [19] made a similar proposal (Fig. 4) with more advanced experimental techniques. They further showed that a few NMDA spikes were needed to trigger Ca²⁺ spikes in the apical zone.

5 Synapses and Plasticity

Learning requires changes of synaptic connections between neurons. In this section we review papers on synaptic plasticity, with a focus on experience-dependent formation and elimination of synapses.

5.1 Hebb and his learning rule

Although this is often stated as Hebbian learning, Hebb did not in fact write "Neurons that fire together wire together". Here is what he actually wrote in [13]:

Let us assume that the persistence or repetition of a reverberatory activity (or "trace") tends to induce lasting cellular changes that add to its stability. When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased.

The wording of his actual statement is really interesting. First, he talks about growth processes and metabolic changes. This is consistent with the notion of synapses actually growing. Second he talks about axon of cell A being near cell B - this is consistent with notion of potential synapses. Third he talks about cell A persistently taking part in cell Bs activity. This implies a temporal and causal relationship, not just instantaneous correlation. In fact he discusses sequences quite a bit in his book. If you really want to read into it, his exact wording can be seen to be consistent with active dendrites and the HTM learning rules.

5.2 Chklovskii: Potential synapses

This paper [7] includes evidence and arguments for dynamic synapse formation, potential synapses, etc. Jeff says on the NuPIC Theory mailing list:

Classic Hebbian learning is about strengthening synapses, but we are suggesting that new synapses are formed. I think you are asking how this is possible biologically. The idea for potential synapses comes from a researcher Chklovskii. An axon and dendrite that are near each other but that are not connected can still sense pre- and post-synaptic activity and this is sufficient for them to start to grow a new synapse when they are active at the same time. What is actually grown is a spine that connects the axon and dendrite. The synapse is on the end of the spine. In addition, glial cells have been shown to act as intermediaries. They can encourage a dendrite and axon to move/grow closer together when they fire at the same time. Glial cells effectively increase the number of potential synapses. Finally, the ends of the dendritic and axonal trees are constantly growing in different directions trying to find new useful connections. It is now well known that synapses and spines form

during learning and they also disappear. This can happen rapidly, in a matter of minutes in some cases.

I believe the concept of potential synapses and the growth of new synapses applies to both proximal and distal synapses. In our temporal memory implementation we decided to implement it differently purely to make the software more efficient and to use less memory. Instead of maintaining a large pool of potential synapses, most of which would have 0 permanence, we choose from the set of active cells.

5.3 Experience-dependent synaptogenesis

The review paper by Bailey and Kandel [3] presents numerous early researches supporting synapse formation during formation of long-term memory.

Zito and Svoboda 2002 [54] is a short review of activity-dependent synaptogenesis in the adult cortex. This review first presented the common view of synaptic plasticity, which argues initial establishment of synaptic connections occurs independent of learning, and experience refines existing synaptic connections, rather than create new ones (para 2, page 1). Zito and Svoboda then presented a different view, which argues "short-term plasticity depends on existing synapses, but long term changes in synaptic strength are accompanied by structural rearrangements, through formation or elimination of synapses. This second view is consistent with the current HTM algorithms.

A more recent review paper by Holtmaat and Svoboda [14] presents more recent findings with imaging techniques. I find the numbers in supplementary table S1 very useful, it shows what fraction of synapses are stable from many different studies.

5.4 Losonczy: Branch specific plasticity

HTM theory requires that if a dendritic segment becomes active and then that cell later fires, that we learn on that specific segment. This requires a coupling between segment activity and later activity at the soma. This is a fairly strong and specific prediction of HTM learning rules.

This paper[23] seems to be the first demonstrated evidence for this type of plasticity rule. First they show that there is branch (segment) specific potentiation (learning), isolated from other branches. Second, they show that the branch specific potentiation requires a back action potential (top left of page 439).

They also show that there are weak branches and strong branches. The strong branches tend to be near the soma (proximal) and the weaker branches tended to be terminal (distal). They also show that eventually the weaker branches can cause the cell to fire this is not currently modeled in HTM.

Figure 1 in their supplementary materials is very closely related to HTM theory. They hypothesize that dendritic segments are used for storing individual elements of sequence and that the efficiency of processing sequences will be increased. To quote: *The repeated occurrence of the sequence item [snip] will be stored in the increased branch coupling strength, such that subsequent arrival of the item will have an enhanced efficacy and improved capability to evoke a precise output.* Although they don't explicitly discuss prediction and high order sequences, the experiments and results in this paper are very consistent with HTMs.

5.5 Yang: Branch specific dendritic learning

This amazing paper [50] studies learning on specific dendritic branches in awake rats while they go through normal behavior. It shows learning induced dendritic branch specific formation of synapses, which is consistent with the temporal memory algorithm and high order sequences. This paper deals with high order motor sequences. Ignore the sleep part.

5.6 Imaging the growth of synapses

Most recent studies are use fancy image techniques to study synapse formation. Trachtenberg et al [46] first shows experience-dependent synapse formation and elimination with long-term imaging.

Niell et al. [29] contains a movie showing how fast synapses and dendritic segments can change dramatically within 24 hours.

6 Sequence Learning

In this section we review evidence of sequence learning in the cortex. One prediction of HTM theory is that unexpected input will cause column-level bursting activity in the cortex whereas predicted inputs are represented by SDRs. Expected input will lead to extremely sparse activity (one or two cells per active column). Another prediction is that formation and elimination of lateral connections between neurons is a key mechanism for sequence learning. These predictions are supported by the following studies.

6.1 Vinje and Gallant: Temporal sequences are sparser

Part of a classic set of studies for HTM sequence learning. This paper [47] demonstrates increasingly sparse neural activity when a neuron gets larger spatio-temporal context compared to flash input. Moreover the same set of neurons tend to fire given the same temporal context. (They show temporal context by creating that simulate eye saccades.)

There are some problems with the study. For one, the eye movements are not initiated by the monkey. Instead the movie simulates what the monkey might see during saccades. This is a huge issue. Their analysis also assumes there are no temporal correlations in neural activity. Another big problem since temporal pooling creates temporal correlations. They don't really think in terms of the monkey learning sequences. Etc.

6.2 Milner: Visual stimuli recruit intrinsically generated cortical ensembles

This paper [28] provides some supporting evidence of the Temporal Memory algorithm.

Neuroscientists traditionally think that neurons in the cortex encode sensory stimulus individually: each neuron has some preferred stimulus, which can be measured through receptive field (RF) mapping. When a stimulus comes in, a neuron will fire if it matches its RF well, and will stay silent otherwise.

What's interesting in this paper is that the authors suggest groups (ensembles) of neurons, rather than individual neurons, are the functional units of cortical activity. When a stimulus is presented, cortical activity is dominated by coactive groups of neurons. Presumably these ensembles are supported via learned recurrent excitatory connections, since they also appear during spontaneous activity.

I find this consistent with the temporal memory algorithm (previously known as the CLA algorithm), which suggest external stimulus triggers a unique sequence of cells, which are connected via lateral connections. However, the technology used in this paper (two-photon imaging) has a relatively poor temporal resolution, so it is not possible to tell whether the "coactive group of neurons" fires sequentially or simultaneously. Chetan: What else is interesting is that they found single neurons to participate in multiple ensembles, regardless of how specialized they were for a stimulus at an individual level. (See section titled "Single Neurons Participate Promiscuously in Multiple Ensembles").

Also, this is interesting: "Taken together, our findings demonstrate that when individual neurons are activated, they are more likely to be activated together with a specific set of other neurons as an ensemble. At the same time, individual neurons can participate in multiple ensembles, dynamically reorganizing their allegiance with different sets of neurons."

6.3 Meyer: surprise responses in IT

Subutai: I've been trying to locate strong experimental evidence that surprise inputs result in cells in mini column firing (aka bursting). The attached paper doesn't quite show that, but it has some other relevant information [27]. Unpredicted stimuli elicits a stronger response in IT than predicted stimuli. The mean firing rate of neurons is higher with unpredicted stimuli (Figure 2). In figure 2A you do see a slightly increased mean response rate to predicted stimuli (above baseline) but the

average response is higher for unpredicted stimuli. All this is consistent with column bursting in temporal memory. In this paper you can't tell whether the surprise is along a minicolumn or not. Additional experiments showed that unpredicted firing had slightly longer latency than predicted firing. This is consistent with predicted cells firing earlier due to depolarization. Predicted firing was about 5 msec faster than unpredicted firing, which is also about what you would expect.

6.4 Fishman: Oddball responses in auditory cortex

From EEG recordings, people know that unexpected stimulus ("deviant" sounds in this study), will elicit stronger response. This paper [10] studies the neural mechanisms and brain regions underlying this effect in the primary auditory cortex. They confirmed that spiking response were larger when elicited by the unexpected stimulus, and the difference between expected and unexpected stimulus were more prominent in later activity. The unexpected stimulus can be introduced either in an oddball paradigm in which rare deviant tones are randomly interspersed among frequent standard tones (Fig. 1B), or in a random sequence where tone is unexpected (Fig. 1C).

One downside of this study is they used a very simple sequence for the oddball paradigm. It will be more interesting to see whether the same phenomenon holds when they play a more complex tone sequence (an oddball within a melody). They conclude that the difference between unexpected stimulus and repeated expected stimulus is due to stimulus specific adaptation (rather than prediction).

6.5 Gavornik: sequence learning in V1

Main result: Gavornik and Bear [11] shows that neurons in V1 adapt to sequences. Apparently sequence learning has not been demonstrated in V1 before. Mice were trained on a particular sequence of sinusoidal gratings, ABCD. After training ABCD evoked a much larger response than DCBA. Also much larger than ABCD in a control group. They found that timing makes a difference. A change in the timing of ABCD causes lower responses as well.

Other results: The mice learn very quickly, within one day (2 mins of total visual stimulation). During this time they saw the sequence 200 times. The sequences were robust to dropout. ABCD had similar responses to A_CD, both of which were larger than E_CD. Their results don't seem to be layer specific. They find larger responses to trained sequences in all layers. Sequence learning was stimulus specific and localized; it did not transfer to the other eye.

Oddity 1: Why would responses be larger for a trained sequence? We would expect sparser activity after training. They are measuring evoked field potential in layer 4. After discussing with Paxon it seems there is some controversy as to what LFP or VEP actually measures. It measures activity in all cells: both inhibitory and excitatory but there is evidence that it might be more sensitive to inhibitory cells. In either case a larger response could be consistent with HTM theory, since there would be a fair amount of inhibitory suppression within mini columns for predicted sequences.

Oddity 2: they claim that sequence learning occurs without NMDA receptor activation (page 3). I didn't understand that portion. Does that mean NMDA spikes are not required?

6.6 Martin: Functional heterogeneity in neighboring neurons of V1

Main result: Although neurons in V1 are clustered according to their stimulus preferences, responses to complex visual stimuli are highly heterogeneous between adjacent neurons [26]. In response to gratings and visual noise, signal and noise correlations were well correlated with each other, but less so for responses to movies.

Similar results are reported in [51], which shows that when stimulated with complex, time-varying natural scenes (i.e., movies), nearby striate neurons exhibit highly sparse and heterogeneous responses.

Other result: "trial-to-trial fluctuations (termed noise) were poorly correlated between neighboring neurons, suggesting low degrees of common input." This is consistent with our assumption that cells in the same mini-column has different lateral connections.

7 Temporal Pooling and Invariances

The idea of temporal pooling is that after learning, predicted inputs will lead to stable (invariant) representations in higher levels of the cortical hierarchy despite changes of inputs at lower levels of the hierarchy. We summarize supporting neuroscience evidences for this idea below.

7.1 Li and DiCarlo: Learning invariances

This paper [21] very closely supports HTM temporal pooling ideas, including the role of sensori-motor inference in forming invariant representations. A detailed summary follows:

They found neurons in monkey IT that responded strongly to a particular object P (preferred) and moderately to another N (non-preferred). Tested position tolerance of these objects to get a baseline. The difference between the responses to P and N is the selectivity for this neuron. They did this for about 100 neurons in two monkeys, and many different objects.

They then altered temporal contiguity of stimuli and tested the effects on these invariant representations.

In the experiment, monkeys viewed altered stimuli for several hours. Basically there were three positions for each object: centered, 3 above and below. For a given P object, the position above or below was designated the swap position. As eyes moved around, a P object would be shown in the swap position but was replaced by the N object during saccade. (Each saccade lasts 23 msecs.) This would happen every time P object was shown in the swap position. A P object in the non-swap position didn't change when the monkey saccaded. (The swap position was randomly changed for different objects.) The monkey is effectively blind during a saccade, so they don't see the change - they just see the new object after fixation.

Their prediction: invariance selectivity at swap position would change. Selectivity in the non-swap position won't change. This is what happened. At swap position cells did not discriminate as well between P and N. Neuron became more responsive to N and less responsive to P, but only at that location. Change was location specific and shape specific, so very specific to this particular invariance. These changes cannot be explained by attention affects or retinotopic adaptation (everything was counter balanced).

However another paper of theirs seemed to indicate that temporal contiguity alone was not enough. Looks like eye movements may also be required (this is their reference 10 - Cox and DiCarlo, 2005. Attached paper 2).

They call this effect Unsupervised temporal tolerance learning or UTL. This is just temporal pooling for us. The behavior they describe is exactly the pooling behavior we would expect in layer 3.

In [9] they have the same experiment as [21], but here they used human subjects and a same-difference psychological test. Swapped objects were much more likely to be confused than non-swapped objects. They did the same experiment without eye saccades, and did not see the effect.

"Moreover, the confusions are predictable in that they are what is expected if the visual system assumes that object identity is stable across the short time interval of a saccade."

7.2 Isik et al: Learning invariance using temporal associations

Yuwei: Here [16] is a modeling study from Tomaso Poggio's lab that is very relevant to the idea of temporal pooling. This paper aims to explain the "invariance disruption" experiments, which is the study Subutai found that supports temporal pooling. In that experiment, Li and DiCarlo [21] showed that individual IT neurons change their selectivity in a position-dependent manner after exposure to the altered visual experiment. The modeling study here used a temporal association learning rule to learn transformation invariance through natural visual experience. The basic underlying idea is very similar to temporal pooling: since the external visual scene usually changes at a slow time scale, "temporal adjacency" is a good cue that two images are of the same object.

I think the major difference between this study and what we have is they don't distinguish between predicted and unpredicted inputs. In our algorithm, we only start temporal pooling when the input is predicted. They also don't have a motor component in their model. Nevertheless, I feel this line of

study (developing invariance with temporal association rules) is very relevant for us to think about temporal pooling. i am planning to take a look at some papers along these lines.

Jeff: In addition to Yuwei's observations I would add: - They make a distinction between generic transformations (such as image translations) and class-specific translations (such as rotation through plane). They argue that generic transformations apply to all objects but class-specific transformations do not. I am struggling to see if this distinction really exists. I would prefer that temporal pooling works the same in all cases and that this distinction doesn't exist.

Another thing they talk about which I found odd is they ask, why should training continue throughout life? They say generic transformations can be set early in life. This seems ridiculous to me. Perhaps they are trying to show that HMAX (which doesn't learn at all) is a good model. They show a chart (figure 2) showing that for translation fixed HMAX is as good as learning temporal pooling.

8 Thalamocortical Pathways

8.1 Sherman and Guillery: The Book

For those interested in going deeper into the role of the thalamus, this is an excellent book [40]. Suggested by Jeff, it is a well written summary of a modern view of cortico-thalamic connections. It describes, for example, the connections between every cortical region and the thalamus including the role of sub-cortical motor centers. It does require some neuroscience background but is much easier to read than many of the really dense neuroscience papers. The diagrams are also very clear.

9 Sensorimotor Inference

The idea of sensorimotor inference is that cortex makes predictions of future inputs based on both the current inputs and a copy of motor command that is about to be executed. Some supporting evidences is summarized below.

9.1 Bartoli: SDR representations of tools

This paper [4] is concerned with merging of information from visual properties of tools to the motor coordinates for using and interacting with those tools. Looking at premotor and motor populations of neurons coding for specific hand configurations.

An "affordance" is the set of stuff that can be done to an object. It is the possibility of some actions that can be performed on an object.

Neurons in premotor cortex code for object specific and grip specific actions. (Rochat, 2010). A subset of these neurons fire for executing a specific hand-object and a specific visual representation of that object. (Murata 97) This activity is independent of whether that action actually occurs later.

This paper shows that the same specific patterns observed in monkeys also occurs in humans. They visually show specific tools to people, and observe very specific "motor plans" arising as a result of the stimuli. The main contribution is to "close the gap" between monkey and human data. In addition, they show that very specific visuomotor representations can form in humans as soon as 150 msec after visual presentation of the object. They did a TMS study, so the stimulated premotor cortex (they did not perform direct neural recordings). They did record activity from hand muscles.

9.2 Saleem: Integration of visual and locomotion in V1

The Saleem study [39] clearly showed that V1 (at least in mouse) integrates visual motion and locomotion signals during active navigation. Specifically,

1. Many V1 neurons are tuned for running speed (Fig. 1-2). There is a specific preferred running speed, more than a nonspecific increase of activity level [30].
2. Nearly half of the V1 neurons were reliably driven by the combination of visual speed and run speed (i.e., neurons are tuned to a weighted sum of visual speed and run speed Fig. 3)

3. As a population, V1 neurons predicted a linear combination of visual and run speeds better than either visual or run speeds alone (Fig. 4).

9.3 Rauschecker: where and what pathway in auditory cortex

The "where" and "what" pathway, which was originally proposed to describe the dorsal and ventral pathway of the visual system, may be generalized to other sensory modalities. Specifically, this paper [38] showed that one region of the auditory cortex is selective to spatial locations and another region is selective to auditory pattern or objects.

9.4 Wolpert: Forward models

This paper [49] discussed sensorimotor inference from a computational perspective. They proposed a forward model that uses the current state of the motor system and motor command to predict the next state. This is similar to our sensorimotor inference algorithms. The forward model concept in this paper is widely used in motor control and sensorimotor inference.

9.5 Sommer: Efference Copy

This review paper [41] summarizes a series of studies that established a pathway for corollary discharge signal (the motor command copy to sensory cortex), explains how predictive shifting of receptive field is constructed with CD signal, and how visual stability is achieved despite eye-movements.

References

- [1] Srdjan D. Antic, Wen Liang Zhou, Anna R. Moore, Shaina M. Short, and Katerina D. Ikonomu. The decade of the dendritic NMDA spike, 2010.

Abstract: *In the field of cortical cellular physiology, much effort has been invested in understanding thick apical dendrites of pyramidal neurons and the regenerative sodium and calcium spikes that take place in the apical trunk. Here we focus on thin dendrites of pyramidal cells (basal, oblique, and tuft dendrites), and we discuss one relatively novel form of an electrical signal ("NMDA spike") that is specific for these branches. Basal, oblique, and apical tuft dendrites receive a high density of glutamatergic synaptic contacts. Synchronous activation of 10-50 neighboring glutamatergic synapses triggers a local dendritic regenerative potential, NMDA spike/plateau, which is characterized by significant local amplitude (40-50 mV) and an extraordinary duration (up to several hundred milliseconds). The NMDA plateau potential, when it is initiated in an apical tuft dendrite, is able to maintain a good portion of that tuft in a sustained depolarized state. However, if NMDA-dominated plateau potentials originate in proximal segments of basal dendrites, they regularly bring the neuronal cell body into a sustained depolarized state, which resembles a cortical Up state. At each dendritic initiation site (basal, oblique, and tuft) an NMDA spike creates favorable conditions for causal interactions of active synaptic inputs, including the spatial or temporal binding of information, as well as processes of short-term and long-term synaptic modifications (e.g., long-term potentiation or long-term depression). Because of their strong amplitudes and durations, local dendritic NMDA spikes make up the cellular substrate for multisite independent subunit computations that enrich the computational power and repertoire of cortical pyramidal cells. We propose that NMDA spikes are likely to play significant roles in cortical information processing in awake animals (spatiotemporal binding, working memory) and during slow-wave sleep (neuronal Up states, consolidation of memories).*

- [2] Baktash Babadi and Haim Sompolinsky. Sparseness and Expansion in Sensory Representations. *Neuron*, 83(5):1213–1226, August 2014.

Abstract: *In several sensory pathways, input stimuli project to sparsely active downstream populations that have more neurons than incoming axons. Here, we address the computational benefits of expansion and sparseness for clustered inputs, where different clusters represent behaviorally distinct stimuli and intracluster variability represents sensory or neuronal noise. Through analytical calculations and numerical simulations, we show that expansion implemented by feed-forward random synaptic weights amplifies variability in the incoming stimuli, and this noise enhancement increases with sparseness of the expanded representation. In addition, the low dimensionality of the input layer generates overlaps between the induced*

representations of different stimuli, limiting the benefit of expansion. Highly sparse expansive representations obtained through synapses that encode the clustered structure of the input reduce both intrastimulus variability and the excess overlaps between stimuli, enhancing the ability of downstream neurons to perform classification and recognition tasks. Implications for olfactory, cerebellar, and visual processing are discussed.

Tags: Neuroscience,SDR

- [3] C H Bailey and E R Kandel. Structural changes accompanying memory storage. *Annual review of physiology*, 55:397–426, January 1993.

Tags: Synapses

- [4] Eleonora Bartoli, Laura Maffongelli, Marco Jacono, and Alessandro D’Ausilio. Representing tools as hand movements: early and somatotopic visuomotor transformations. *Neuropsychologia*, 61:335–44, August 2014.

Abstract: The term *affordance* defines a property of objects, which relates to the possible interactions that an agent can carry out on that object. In monkeys, canonical neurons encode both the visual and the motor properties of objects with high specificity. However, it is not clear if in humans exists a similarly fine-grained description of these visuomotor transformations. In particular, it has not yet been proven that the processing of visual features related to specific affordances induces both specific and early visuomotor transformations, given that complete specificity has been reported to emerge quite late (300-450ms). In this study, we applied an adaptation-stimulation paradigm to investigate early cortico-spinal facilitation and hand movements synergies evoked by the observation of tools. We adapted, through passive observation of finger movements, neuronal populations coding either for precision or power grip actions. We then presented the picture of one tool affording one of the two grasps types and applied single-pulse Transcranial Magnetic Stimulation (TMS) to the hand primary motor cortex, 150ms after image onset. Cortico-spinal excitability of the Abductor Digiti Minimi and Abductor Pollicis Brevis showed a detailed pattern of modulations, matching tools affordances. Similarly, TMS-induced hand movements showed a pattern of grip-specific whole hand synergies. These results offer a direct proof of the emergence of an early visuomotor transformation when tools are observed, that maintains the same amount of synergistic motor details as the actions we can perform on them.

Tags: Sensorimotor Inference

- [5] Tiago Branco and Michael Häusser. Synaptic integration gradients in single cortical pyramidal cell dendrites. *Neuron*, 69(5):885–92, March 2011.

Abstract: Cortical pyramidal neurons receive thousands of synaptic inputs arriving at different dendritic locations with varying degrees of temporal synchrony. It is not known if different locations along single cortical dendrites integrate excitatory inputs in different ways. Here we have used two-photon glutamate uncaging and compartmental modeling to reveal a gradient of nonlinear synaptic integration in basal and apical oblique dendrites of cortical pyramidal neurons. Excitatory inputs to the proximal dendrite sum linearly and require precise temporal coincidence for effective summation, whereas distal inputs are amplified with high gain and integrated over broader time windows. This allows distal inputs to overcome their electrotonic disadvantage, and become surprisingly more effective than proximal inputs at influencing action potential output. Thus, single dendritic branches can already exhibit nonuniform synaptic integration, with the computational strategy shifting from temporal coding to rate coding along the dendrite.

Tags: Neuroscience,Sequence Learning

- [6] D. P. Buxhoeveden. The minicolumn hypothesis in neuroscience. *Brain*, 125(5):935–951, May 2002.

Abstract: The minicolumn is a continuing source of research and debate more than half a century after it was identified as a component of brain organization. The minicolumn is a sophisticated local network that contains within it the elements for redundancy and plasticity. Although it is sometimes compared to subcortical nuclei, the design of the minicolumn is a distinctive form of module that has evolved specifically in the neocortex. It unites the horizontal and vertical components of cortex within the same cortical space. Minicolumns are often considered highly repetitive, even clone-like, units. However, they display considerable heterogeneity between areas and species, perhaps even within a given macrocolumn. Despite a growing recognition of the anatomical basis of the cortical minicolumn, as well as its physiological properties, the potential of the minicolumn has not been exploited in fields such as comparative neuroanatomy, abnormalities of the brain and mind, and evolution.

Tags: Anatomy,Neuroscience

- [7] D B Chklovskii, B W Mel, and K Svoboda. Cortical rewiring and information storage. *Nature*, 431(7010):782–8, October 2004.

Abstract: *Current thinking about long-term memory in the cortex is focused on changes in the strengths of connections between neurons. But ongoing structural plasticity in the adult brain, including synapse formation/elimination and remodelling of axons and dendrites, suggests that memory could also depend on learning-induced changes in the cortical 'wiring diagram'. Given that the cortex is sparsely connected, wiring plasticity could provide a substantial boost in storage capacity, although at a cost of more elaborate biological machinery and slower learning.*

Tags: Neuroscience,Synapses

- [8] Christine M Constantinople and Randy M Bruno. Deep cortical layers are activated directly by thalamus. *Science (New York, N.Y.)*, 340(6140):1591–4, June 2013.

Abstract: *The thalamocortical (TC) projection to layer 4 (L4) is thought to be the main route by which sensory organs communicate with cortex. Sensory information is believed to then propagate through the cortical column along the L4L2/3L5/6 pathway. Here, we show that sensory-evoked responses of L5/6 neurons in rats derive instead from direct TC synapses. Many L5/6 neurons exhibited sensory-evoked postsynaptic potentials with the same latencies as L4. Paired in vivo recordings from L5/6 neurons and thalamic neurons revealed substantial convergence of direct TC synapses onto diverse types of infragranular neurons, particularly in L5B. Pharmacological inactivation of L4 had no effect on sensory-evoked synaptic input to L5/6 neurons. L4 is thus not an obligatory distribution hub for cortical activity, and thalamus activates two separate, independent "strata" of cortex in parallel.*

- [9] David D Cox, Philip Meier, Nadja Oertelt, and James J DiCarlo. 'Breaking' position-invariant object recognition. *Nature neuroscience*, 8:1145–1147, 2005.

Abstract: *While it is often assumed that objects can be recognized irrespective of where they fall on the retina, little is known about the mechanisms underlying this ability. By exposing human subjects to an altered world where some objects systematically changed identity during the transient blindness that accompanies eye movements, we induced predictable object confusions across retinal positions, effectively 'breaking' position invariance. Thus, position invariance is not a rigid property of vision but is constantly adapting to the statistics of the environment.*

Tags: Neuroscience,Temporal Pooling

- [10] Yonatan I Fishman and Mitchell Steinschneider. Searching for the mismatch negativity in primary auditory cortex of the awake monkey: deviance detection or stimulus specific adaptation? *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 32:15747–58, 2012.

Abstract: *The mismatch negativity (MMN) is a preattentive component of the auditory event-related potential that is elicited by a change in a repetitive acoustic pattern. While MMN has been extensively used in human electrophysiological studies of auditory processing, the neural mechanisms and brain regions underlying its generation remain unclear. We investigate possible homologs of the MMN in macaque primary auditory cortex (A1) using a frequency oddball paradigm in which rare "deviant" tones are randomly interspersed among frequent "standard" tones. Standards and deviants had frequencies equal to the best frequency (BF) of the recorded neural population or to a frequency that evoked a response half the amplitude of the BF response. Early and later field potentials, current source density components, multiunit activity, and induced high-gamma band responses were larger when elicited by deviants than by standards of the same frequency. Laminar analysis indicated that differences between deviant and standard responses were more prominent in later activity, thus suggesting cortical amplification of initial responses driven by thalamocortical inputs. However, unlike the human MMN, larger deviant responses were characterized by the enhancement of "obligatory" responses rather than the introduction of new components. Furthermore, a control condition wherein deviants were interspersed among many tones of variable frequency replicated the larger responses to deviants under the oddball condition. Results suggest that differential responses under the oddball condition in macaque A1 reflect stimulus-specific adaptation rather than deviance detection per se. We conclude that neural mechanisms of deviance detection likely reside in cortical areas outside of A1.*

Tags: Auditory,Sequence Learning

- [11] Jeffrey P Gavornik and Mark F Bear. Learned spatiotemporal sequence recognition and prediction in primary visual cortex. *Nature Neuroscience*, 17:732–7, 2014.

Abstract: Learning to recognize and predict temporal sequences is fundamental to sensory perception and is impaired in several neuropsychiatric disorders, but little is known about where and how this occurs in the brain. We discovered that repeated presentations of a visual sequence over a course of days resulted in evoked response potentiation in mouse V1 that was highly specific for stimulus order and timing. Notably, after V1 was trained to recognize a sequence, cortical activity regenerated the full sequence even when individual stimulus elements were omitted. Our results advance the understanding of how the brain makes 'intelligent guesses' on the basis of limited information to form visual percepts and suggest that it is possible to study the mechanistic basis of this high-level cognitive ability by studying low-level sensory systems.

- [12] N L Golding, H Y Jung, T Mickus, and N Spruston. Dendritic calcium spike initiation and repolarization are controlled by distinct potassium channel subtypes in CA1 pyramidal neurons. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 19(20):8789–98, October 1999.

Abstract: In CA1 pyramidal neurons of the hippocampus, calcium-dependent spikes occur in vivo during specific behavioral states and may be enhanced during epileptiform activity. However, the mechanisms that control calcium spike initiation and repolarization are poorly understood. Using dendritic and somatic patch-pipette recordings, we show that calcium spikes are initiated in the apical dendrites of CA1 pyramidal neurons and drive bursts of sodium-dependent action potentials at the soma. Initiation of calcium spikes at the soma was suppressed in part by potassium channels activated by sodium-dependent action potentials. Low-threshold, putative D-type potassium channels [blocked by 100 μ M 4-aminopyridine (4-AP) and 0.5–1 μ M α -dendrotoxin (α -DTX)] played a prominent role in setting a high threshold for somatic calcium spikes, thus restricting initiation to the dendrites. DTX- and 4-AP-sensitive channels were activated during sodium-dependent action potentials and mediated a large component of their afterhyperpolarization. Once initiated, repetitive firing of calcium spikes was limited by activation of putative BK-type calcium-activated potassium channels (blocked by 250 μ M tetraethylammonium chloride, 70 nM charybdotoxin, or 100 nM iberiotoxin). Thus, the concerted action of calcium- and voltage-activated potassium channels serves to focus spatially and temporally the membrane depolarization and calcium influx generated by calcium spikes during strong, synchronous network excitation.

- [13] DO Hebb. The organization of behavior: a neuropsychological theory. *Science Education*, 44(1):335, 1949.

Abstract: Since its publication in 1949, D.O. Hebb's, *The Organization of Behavior* has been one of the most influential books in the fields of psychology and neuroscience. However, the original edition has been unavailable since 1966, ensuring that Hebb's comment that a classic normally means "cited but not read" is true in his case. This new edition rectifies a long-standing problem for behavioral neuroscientists—the inability to obtain one of the most cited publications in the field. *The Organization of Behavior* played a significant part in stimulating the investigation of the neural foundations of behavior and continues to be inspiring because it provides a general framework for relating behavior to synaptic organization through the dynamics of neural networks. D.O. Hebb was also the first to examine the mechanisms by which environment and experience can influence brain structure and function, and his ideas formed the basis for work on enriched environments as stimulants for behavioral development. References to Hebb, the Hebbian cell assembly, the Hebb synapse, and the Hebb rule increase each year. These forceful ideas of 1949 are now applied in engineering, robotics, and computer science, as well as neurophysiology, neuroscience, and psychology—a tribute to Hebb's foresight in developing a foundational neuropsychological theory of the organization of behavior.

- [14] Anthony Holtmaat and Karel Svoboda. Experience-dependent structural synaptic plasticity in the mammalian brain. *Nature reviews. Neuroscience*, 10(9):647–58, September 2009.

Abstract: Synaptic plasticity in adult neural circuits may involve the strengthening or weakening of existing synapses as well as structural plasticity, including synapse formation and elimination. Indeed, long-term in vivo imaging studies are beginning to reveal the structural dynamics of neocortical neurons in the normal and injured adult brain. Although the overall cell-specific morphology of axons and dendrites, as well as of a subpopulation of small synaptic structures, are remarkably stable, there is increasing evidence that experience-dependent plasticity of specific circuits in the somatosensory and visual cortex involves cell type-specific structural plasticity: some boutons and dendritic spines appear and disappear, accompanied by synapse formation and elimination, respectively. This Review focuses on recent evidence

for such structural forms of synaptic plasticity in the mammalian cortex and outlines open questions.

Tags: Synapses

- [15] Jonathan C Horton and Daniel L Adams. The cortical column: a structure without a function. *Philosophical transactions of the Royal Society of London. Series B, Biological sciences*, 360:837–862, 2005.

Abstract: This year, the field of neuroscience celebrates the 50th anniversary of Mountcastle's discovery of the cortical column. In this review, we summarize half a century of research and come to the disappointing realization that the column may have no function. Originally, it was described as a discrete structure, spanning the layers of the somatosensory cortex, which contains cells responsive to only a single modality, such as deep joint receptors or cutaneous receptors. Subsequently, examples of columns have been uncovered in numerous cortical areas, expanding the original concept to embrace a variety of different structures and principles. A "column" now refers to cells in any vertical cluster that share the same tuning for any given receptive field attribute. In striate cortex, for example, cells with the same eye preference are grouped into ocular dominance columns. Unaccountably, ocular dominance columns are present in some species, but not others. In principle, it should be possible to determine their function by searching for species differences in visual performance that correlate with their presence or absence. Unfortunately, this approach has been to no avail; no visual faculty has emerged that appears to require ocular dominance columns. Moreover, recent evidence has shown that the expression of ocular dominance columns can be highly variable among members of the same species, or even in different portions of the visual cortex in the same individual. These observations deal a fatal blow to the idea that ocular dominance columns serve a purpose. More broadly, the term "column" also denotes the periodic termination of anatomical projections within or between cortical areas. In many instances, periodic projections have a consistent relationship with some architectural feature, such as the cytochrome oxidase patches in V1 or the stripes in V2. These tissue compartments appear to divide cells with different receptive field properties into distinct processing streams. However, it is unclear what advantage, if any, is conveyed by this form of columnar segregation. Although the column is an attractive concept, it has failed as a unifying principle for understanding cortical function. Unravelling the organization of the cerebral cortex will require a painstaking description of the circuits, projections and response properties peculiar to cells in each of its various areas.

Tags: Anatomy, Laminar structure, Neuroscience

- [16] Leyla Isik, Joel Z Leibo, and Tomaso Poggio. Learning and disrupting invariance in visual recognition with a temporal association rule. *Frontiers in computational neuroscience*, 6:37, January 2012.

Abstract: Learning by temporal association rules such as Foldiak's trace rule is an attractive hypothesis that explains the development of invariance in visual recognition. Consistent with these rules, several recent experiments have shown that invariance can be broken at both the psychophysical and single cell levels. We show (1) that temporal association learning provides appropriate invariance in models of object recognition inspired by the visual cortex, (2) that we can replicate the "invariance disruption" experiments using these models with a temporal association learning rule to develop and maintain invariance, and (3) that despite dramatic single cell effects, a population of cells is very robust to these disruptions. We argue that these models account for the stability of perceptual invariance despite the underlying plasticity of the system, the variability of the visual world and expected noise in the biological mechanisms.

Tags: Temporal Pooling

- [17] Roozbeh Kiani, Hossein Esteky, Koorosh Mirpour, and Keiji Tanaka. Object category structure in response patterns of neuronal population in monkey inferior temporal cortex. *Journal of neurophysiology*, 97:4296–4309, 2007.

Abstract: Our mental representation of object categories is hierarchically organized, and our rapid and seemingly effortless categorization ability is crucial for our daily behavior. Here, we examine responses of a large number (≥ 600) of neurons in monkey inferior temporal (IT) cortex with a large number ($\geq 1,000$) of natural and artificial object images. During the recordings, the monkeys performed a passive fixation task. We found that the categorical structure of objects is represented by the pattern of activity distributed over the cell population. Animate and inanimate objects created distinguishable clusters in the population code. The global category of animate objects was divided into bodies, hands, and faces. Faces were

divided into primate and nonprimate faces, and the primate-face group was divided into human and monkey faces. Bodies of human, birds, and four-limb animals clustered together, whereas lower animals such as fish, reptile, and insects made another cluster. Thus the cluster analysis showed that IT population responses reconstruct a large part of our intuitive category structure, including the global division into animate and inanimate objects, and further hierarchical subdivisions of animate objects. The representation of categories was distributed in several respects, e.g., the similarity of response patterns to stimuli within a category was maintained by both the cells that maximally responded to the category and the cells that responded weakly to the category. These results advance our understanding of the nature of the IT neural code, suggesting an inherently categorical representation that comprises a range of categories including the amply investigated face category.

Tags: Neuroscience,SDR

- [18] Matthew Larkum. A cellular mechanism for cortical associations: an organizing principle for the cerebral cortex. *Trends in neurosciences*, 36(3):141–51, March 2013.

Abstract: A basic feature of intelligent systems such as the cerebral cortex is the ability to freely associate aspects of perceived experience with an internal representation of the world and make predictions about the future. Here, a hypothesis is presented that the extraordinary performance of the cortex derives from an associative mechanism built in at the cellular level to the basic cortical neuronal unit: the pyramidal cell. The mechanism is robustly triggered by coincident input to opposite poles of the neuron, is exquisitely matched to the large- and fine-scale architecture of the cortex, and is tightly controlled by local microcircuits of inhibitory neurons targeting subcellular compartments. This article explores the experimental evidence and the implications for how the cortex operates.

- [19] Matthew E Larkum, Thomas Nevian, Maya Sandler, Alon Polsky, and Jackie Schiller. Synaptic integration in tuft dendrites of layer 5 pyramidal neurons: a new unifying principle. *Science* (New York, N.Y.), 325:756–760, 2009.

Abstract: Tuft dendrites are the main target for feedback inputs innervating neocortical layer 5 pyramidal neurons, but their properties remain obscure. We report the existence of N-methyl-D-aspartate (NMDA) spikes in the fine distal tuft dendrites that otherwise did not support the initiation of calcium spikes. Both direct measurements and computer simulations showed that NMDA spikes are the dominant mechanism by which distal synaptic input leads to firing of the neuron and provide the substrate for complex parallel processing of top-down input arriving at the tuft. These data lead to a new unifying view of integration in pyramidal neurons in which all fine dendrites, basal and tuft, integrate inputs locally through the recruitment of NMDA receptor channels relative to the fixed apical calcium and axosomatic sodium integration points.

- [20] Matthew Evan Larkum, Jack Waters, Bert Sakmann, and Fritjof Helmchen. Dendritic spikes in apical dendrites of neocortical layer 2/3 pyramidal neurons. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 27(34):8999–9008, August 2007.

Abstract: Layer 2/3 (L2/3) pyramidal neurons are the most abundant cells of the neocortex. Despite their key position in the cortical microcircuit, synaptic integration in dendrites of L2/3 neurons is far less understood than in L5 pyramidal cell dendrites, mainly because of the difficulties in obtaining electrical recordings from thin dendrites. Here we directly measured passive and active properties of the apical dendrites of L2/3 neurons in rat brain slices using dual dendritic-somatic patch-clamp recordings and calcium imaging. Unlike L5 cells, L2/3 dendrites displayed little sag in response to long current pulses, which suggests a low density of $I(h)$ in the dendrites and soma. This was also consistent with a slight increase in input resistance with distance from the soma. Brief current injections into the apical dendrite evoked relatively short (half-width 2–4 ms) dendritic spikes that were isolated from the soma for near-threshold currents at sites beyond the middle of the apical dendrite. Regenerative dendritic potentials and large concomitant calcium transients were also elicited by trains of somatic action potentials (APs) above a critical frequency (130 Hz), which was slightly higher than in L5 neurons. Initiation of dendritic spikes was facilitated by backpropagating somatic APs and could cause an additional AP at the soma. As in L5 neurons, we found that distal dendritic calcium transients are sensitive to a long-lasting block by GABAergic inhibition. We conclude that L2/3 pyramidal neurons can generate dendritic spikes, sharing with L5 pyramidal neurons fundamental properties of dendritic excitability and control by inhibition.

Tags: Dendrites,Pyramidal neurons

- [21] Nuo Li and James J DiCarlo. Unsupervised natural experience rapidly alters invariant object representation in visual cortex. *Science*, 321(5895):1502–1507, 2008.

Abstract: Object recognition is computationally challenging because each object produces myriad retinal images. Neurons at the highest cortical stage of the primate ventral visual stream (inferior temporal cortex; IT) likely underlie the ability of the visual system to tolerate that image variation – their responses are selective to different objects, yet tolerant (invariant) to changes in object position, scale, pose, etc. (1-6). Understanding object recognition will require solving the mystery of how the brain constructs this neuronal tolerance. Here we report a novel instance of neuronal learning that suggests the underlying solution. Specifically, we show that targeted alteration of the natural temporal contiguity of unsupervised visual experience causes specific changes in the position tolerance (invariance) of IT neuronal selectivity. This unsupervised temporal tolerance learning (UTL) is substantial, increases with experience, and is significant even in single IT neurons after just one hour. Coupled with previous theoretical work (7-9) and the finding that this same experience manipulation changes the position tolerance of human object perception (10), we speculate that UTL may reflect the mechanism by which the ventral visual stream builds and maintains tolerant object representations. The relatively fast time-scale and unsupervised nature of UTL open the door to advances in systematically characterizing the spatiotemporal image statistics that drive it, understanding if it plays a role in other types of tolerance, and perhaps connecting a central cognitive ability – tolerant object recognition – to cellular and molecular plasticity mechanisms.

Tags: Neuroscience, Temporal Pooling

- [22] Attila Losonczy and Jeffrey C Magee. Integrative properties of radial oblique dendrites in hippocampal CA1 pyramidal neurons. *Neuron*, 50(2):291–307, April 2006.

Abstract: Although radial oblique dendrites are a major synaptic input site in CA1 pyramidal neurons, little is known about their integrative properties. We have used multisite two-photon glutamate uncaging to deliver different spatiotemporal input patterns to single branches while simultaneously recording the uncaging-evoked excitatory postsynaptic potentials and local Ca²⁺ signals. Asynchronous input patterns sum linearly in spite of the spatial clustering and produce Ca²⁺ signals that are mediated by NMDA receptors (NMDARs). Appropriately timed and sized input patterns (approximately 20 inputs within approximately 6 ms) produce a supralinear summation due to the initiation of a dendritic spike. The Ca²⁺ signals associated with synchronous input were larger and mediated by influx through both NMDARs and voltage-gated Ca²⁺ channels (VGCCs). The oblique spike is a fast Na⁺ spike whose duration is shaped by the coincident activation of NMDAR, VGCCs, and transient K⁺ currents. Our results suggest that individual branches can function as single integrative compartments.

Tags: Dendrites, Neuroscience

- [23] Attila Losonczy, Judit K Makara, and Jeffrey C Magee. Compartmentalized dendritic plasticity and input feature storage in neurons. *Nature*, 452(7186):436–41, March 2008.

Abstract: Although information storage in the central nervous system is thought to be primarily mediated by various forms of synaptic plasticity, other mechanisms, such as modifications in membrane excitability, are available. Local dendritic spikes are nonlinear voltage events that are initiated within dendritic branches by spatially clustered and temporally synchronous synaptic input. That local spikes selectively respond only to appropriately correlated input allows them to function as input feature detectors and potentially as powerful information storage mechanisms. However, it is currently unknown whether any effective form of local dendritic spike plasticity exists. Here we show that the coupling between local dendritic spikes and the soma of rat hippocampal CA1 pyramidal neurons can be modified in a branch-specific manner through an N-methyl-D-aspartate receptor (NMDAR)-dependent regulation of dendritic Kv4.2 potassium channels. These data suggest that compartmentalized changes in branch excitability could store multiple complex features of synaptic input, such as their spatio-temporal correlation. We propose that this 'branch strength potentiation' represents a previously unknown form of information storage that is distinct from that produced by changes in synaptic efficacy both at the mechanistic level and in the type of information stored.

Tags: Dendrites, Neuroscience, Plasticity

- [24] Guy Major, Matthew E Larkum, and Jackie Schiller. Active properties of neocortical pyramidal neuron dendrites. *Annual review of neuroscience*, 36:1–24, 2013.

Abstract: Dendrites are the main recipients of synaptic inputs and are important sites that determine neurons' input-output functions. This review focuses on thin neocortical dendrites, which receive the vast majority of synaptic inputs in cortex but also have specialized electrogenic properties. We present a simplified working-model biophysical scheme of pyramidal neurons that attempts to capture the essence of their dendritic function, including the ability to

behave under plausible conditions as dynamic computational subunits. We emphasize the electrogenic capabilities of NMDA receptors (NMDARs) because these transmitter-gated channels seem to provide the major nonlinear depolarizing drive in thin dendrites, even allowing full-blown NMDA spikes. We show how apparent discrepancies in experimental findings can be reconciled and discuss the current status of dendritic spikes in vivo; a dominant NMDAR contribution would indicate that the input-output relations of thin dendrites are dynamically set by network activity and cannot be fully predicted by purely reductionist approaches.

- [25] Guy Major, Alon Polsky, Winfried Denk, Jackie Schiller, and David W Tank. Spatiotemporally graded NMDA spike/plateau potentials in basal dendrites of neocortical pyramidal neurons. *Journal of neurophysiology*, 99(5):2584–601, May 2008.

Abstract: Glutamatergic inputs clustered over approximately 20–40 microm can elicit local N-methyl-D-aspartate (NMDA) spike/plateau potentials in terminal dendrites of cortical pyramidal neurons, inspiring the notion that a single terminal dendrite can function as a decision-making computational subunit. A typical terminal basal dendrite is approximately 100–200 microm long: could it function as multiple decision-making subunits? We test this by sequential focal stimulation of multiple sites along terminal basal dendrites of layer 5 pyramidal neurons in rat somatosensory cortical brain slices, using iontophoresis or uncaging of brief glutamate pulses. There was an approximately sevenfold spatial gradient in average spike/plateau amplitude measured at the soma, from approximately 3 mV for distal inputs to approximately 23 mV for proximal inputs. Spike/plateaus were NMDA receptor (NMDAR) conductance-dominated at all locations. Large Ca^{2+} transients accompanied spike/plateaus over a approximately 10- to 40-microm zone around the input site; smaller Ca^{2+} transients extended approximately uniformly to the dendritic tip. Spike/plateau duration grew with increasing glutamate and depolarization; high Ca^{2+} zone size grew with spike/plateau duration. The minimum high Ca^{2+} zone half-width (just above NMDA spike threshold) increased from distal (approximately 10 microm) to proximal locations (approximately 25 microm), as did the NMDA spike glutamate threshold. Depolarization reduced glutamate thresholds. Simulations exploring multi-site interactions based on this demonstrate that if appropriately timed and localized inputs occur in vivo, a single basal dendrite could correspond to a cascade of multiple co-operating dynamic decision-making subunits able to retain information for hundreds of milliseconds, with increasing influence on neural output from distal to proximal. Dendritic NMDA spike/plateaus are thus well-suited to support graded persistent firing.

Tags: Dendrites

- [26] Kevan A C Martin and Sylvia Schröder. Functional heterogeneity in neighboring neurons of cat primary visual cortex in response to both artificial and natural stimuli. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 33(17):7325–44, April 2013.

Abstract: Neurons in primary visual cortex of many mammals are clustered according to their preference to stimulus parameters such as orientation and spatial frequency. Nevertheless, responses to complex visual stimuli are highly heterogeneous between adjacent neurons. To investigate the relation between these observations, we recorded from pairs of neighboring neurons in area 17 of anesthetized cats in response to stimuli of differing complexity: sinusoidal drifting gratings, binary dense noise, and natural movies. Comparisons of the tuning curves revealed similar orientation and direction preferences for neighboring neurons, but large differences in preferred phase, direction selectivity, and tuning width of spatial frequency. No pair was similar across all tuning properties. The neurons' firing rates averaged across multiple stimulus repetitions (the "signal") were also compared. Binned between 10 and 200 ms, the correlation between these signals was close to zero in the median across all pairs for all stimulus classes. Signal correlations agreed poorly with differences in tuning properties, except for receptive field offset and relative modulation (i.e., the strength of phase modulation). Nonetheless, signal correlations for different stimulus classes were well correlated with each other, even for gratings and movies. Conversely, trial-to-trial fluctuations (termed "noise") were poorly correlated between neighboring neurons, suggesting low degrees of common input. In response to gratings and visual noise, signal and noise correlations were well correlated with each other, but less so for responses to movies. These findings have relevance for our understanding of the processing of natural stimuli in a functionally heterogeneous cortical network.

Tags: Sequence Learning

- [27] T. Meyer and C. R. Olson. Statistical learning of visual transitions in monkey inferotemporal cortex, 2011.

Abstract: One of the most fundamental functions of the brain is to predict upcoming events on the basis of the recent past. A closely related function is to signal when a prediction has been violated. The identity of the brain regions that mediate these functions is not known. We set out to determine whether they are implemented at the level of single neurons in the visual system. We gave monkeys prolonged exposure to pairs of images presented in fixed sequence so that each leading image became a strong predictor for the corresponding trailing image. We then monitored the responses of neurons in the inferotemporal cortex to image sequences that obeyed or violated the transitional rules imposed during training. Inferotemporal neurons exhibited a transitional surprise effect, responding much more strongly to unpredicted transitions than to predicted transitions. Thus, neurons even in the visual system make experience-based predictions and react when they fail.

Tags: Neuroscience, Sequence Learning

- [28] J.-e. K. Miller, I. Ayzenshtat, L. Carrillo-Reid, and R. Yuste. Visual stimuli recruit intrinsically generated cortical ensembles. *Proceedings of the National Academy of Sciences*, 111(38):E4053–61, September 2014.

Abstract: The cortical microcircuit is built with recurrent excitatory connections, and it has long been suggested that the purpose of this design is to enable intrinsically driven reverberating activity. To understand the dynamics of neocortical intrinsic activity better, we performed two-photon calcium imaging of populations of neurons from the primary visual cortex of awake mice during visual stimulation and spontaneous activity. In both conditions, cortical activity is dominated by coactive groups of neurons, forming ensembles whose activation cannot be explained by the independent firing properties of their contributing neurons, considered in isolation. Moreover, individual neurons flexibly join multiple ensembles, vastly expanding the encoding potential of the circuit. Intriguingly, the same coactive ensembles can repeat spontaneously and in response to visual stimuli, indicating that stimulus-evoked responses arise from activating these intrinsic building blocks. Although the spatial properties of stimulus-driven and spontaneous ensembles are similar, spontaneous ensembles are active at random intervals, whereas visually evoked ensembles are time-locked to stimuli. We conclude that neuronal ensembles, built by the coactivation of flexible groups of neurons, are emergent functional units of cortical activity and propose that visual stimuli recruit intrinsically generated ensembles to represent visual attributes.

Tags: Neuroscience, SDR, Sequence Learning

- [29] Christopher M Niell, Martin P Meyer, and Stephen J Smith. In vivo imaging of synapse formation on a growing dendritic arbor. *Nature neuroscience*, 7(3):254–60, March 2004.

Abstract: The form of a neuron’s dendritic arbor determines the set of axons with which it may form synaptic contacts, thus establishing connectivity within neural circuits. However, the dynamic relationship between dendrite growth and synaptogenesis is not well understood. To observe both processes simultaneously, we performed long-term imaging of non-spiny dendritic arbors expressing a fluorescent postsynaptic marker protein as they arborized within the optic tectum of live zebrafish larvae. Our results indicate that almost all synapses form initially on newly extended dendritic filopodia. A fraction of these nascent synapses are maintained, which in turn stabilizes the subset of filopodia on which they form. Stabilized filopodia mature into dendritic branches, and successive iterations of this process result in growth and branching of the arbor. These findings support a ‘synaptotropic model’ in which synapse formation can direct dendrite arborization.

Tags: Synapses

- [30] Christopher M Niell and Michael P Stryker. Modulation of visual responses by behavioral state in mouse visual cortex. *Neuron*, 65(4):472–9, February 2010.

Abstract: Studies of visual processing in rodents have conventionally been performed on anesthetized animals, precluding examination of the effects of behavior on visually evoked responses. We have now studied the response properties of neurons in primary visual cortex of awake mice that were allowed to run on a freely rotating spherical treadmill with their heads fixed. Most neurons showed more than a doubling of visually evoked firing rate as the animal transitioned from standing still to running, without changes in spontaneous firing or stimulus selectivity. Tuning properties in the awake animal were similar to those measured previously in anesthetized animals. Response magnitude in the lateral geniculate nucleus did not increase with locomotion, demonstrating that the striking change in responsiveness did not result from peripheral effects at the eye. Interestingly, some narrow-spiking cells were spontaneously active during running but suppressed by visual stimuli. These results demonstrate powerful cell-type-specific modulation of visual processing by behavioral state in awake mice.

- [31] B A Olshausen and D J Field. Emergence of simple-cell receptive field properties by learning a sparse code for natural images. *Nature*, 381(6583):607–9, June 1996.

Abstract: *The receptive fields of simple cells in mammalian primary visual cortex can be characterized as being spatially localized, oriented and bandpass (selective to structure at different spatial scales), comparable to the basis functions of wavelet transforms. One approach to understanding such response properties of visual neurons has been to consider their relationship to the statistical structure of natural images in terms of efficient coding. Along these lines, a number of studies have attempted to train unsupervised learning algorithms on natural images in the hope of developing receptive fields with similar properties, but none has succeeded in producing a full set that spans the image space and contains all three of the above properties. Here we investigate the proposal that a coding strategy that maximizes sparseness is sufficient to account for these properties. We show that a learning algorithm that attempts to find sparse linear codes for natural scenes will develop a complete family of localized, oriented, bandpass receptive fields, similar to those found in the primary visual cortex. The resulting sparse image code provides a more efficient representation for later stages of processing because it possesses a higher degree of statistical independence among its outputs.*

Tags: SDR

- [32] Bruno A. Olshausen and David J. Field. Sparse coding with an overcomplete basis set: A strategy employed by V1? *Vision Research*, 37:3311–3325, 1997.

Abstract: *The spatial receptive fields of simple cells in mammalian striate cortex have been reasonably well described physiologically and can be characterized as being localized, oriented, and bandpass, comparable with the basis functions of wavelet transforms. Previously, we have shown that these receptive field properties may be accounted for in terms of a strategy for producing a sparse distribution of output activity in response to natural images. Here, in addition to describing this work in a more expansive fashion, we examine the neurobiological implications of sparse coding. Of particular interest is the case when the code is overcomplete - i.e., when the number of code elements is greater than the effective dimensionality of the input space. Because the basis functions are non-orthogonal and not linearly independent of each other, sparsifying the code will recruit only those basis functions necessary for representing a given input, and so the input-output function will deviate from being purely linear. These deviations from linearity provide a potential explanation for the weak forms of non-linearity observed in the response properties of cortical simple cells, and they further make predictions about the expected interactions among units in response to naturalistic stimuli.*

Tags: SDR

- [33] Bruno A. Olshausen and David J. Field. Sparse coding of sensory inputs, 2004.

Abstract: *Several theoretical, computational, and experimental studies suggest that neurons encode sensory information using a small number of active neurons at any given point in time. This strategy, referred to as 'sparse coding', could possibly confer several advantages. First, it allows for increased storage capacity in associative memories; second, it makes the structure in natural signals explicit; third, it represents complex data in a way that is easier to read out at subsequent levels of processing; and fourth, it saves energy. Recent physiological recordings from sensory neurons have indicated that sparse coding could be a ubiquitous strategy employed in several different modalities across different organisms. ?? 2004 Elsevier Ltd. All rights reserved.*

Tags: SDR

- [34] Lucy M Palmer, Adam S Shai, James E Reeve, Harry L Anderson, Ole Paulsen, and Matthew E Larkum. NMDA spikes enhance action potential generation during sensory input. *Nature neuroscience*, 17:383–90, 2014.

Abstract: *Recent evidence in vitro suggests that the tuft dendrites of pyramidal neurons are capable of evoking local NMDA receptor-dependent electrogenesis, so-called NMDA spikes. However, it has so far proved difficult to demonstrate their existence in vivo. Moreover, it is not clear whether NMDA spikes are relevant to the output of pyramidal neurons. We found that local NMDA spikes occurred in tuft dendrites of layer 2/3 pyramidal neurons both spontaneously and following sensory input, and had a large influence on the number of output action potentials. Using two-photon activation of an intracellular caged NMDA receptor antagonist (tc-MK801), we found that isolated NMDA spikes typically occurred in multiple branches simultaneously and that sensory stimulation substantially increased their probability. Our results demonstrate that NMDA receptors have a vital role in coupling the tuft region of the layer 2/3 pyramidal neuron to the cell body, enhancing the effectiveness of layer 1 input.*

Tags: Dendrites, Neuroscience

- [35] Panayioti Poirazi, Terrence Brannon, and Bartlett W Mel. Pyramidal neuron as two-layer neural network. *Neuron*, 37(6):989–99, March 2003.

Abstract: *The pyramidal neuron is the principal cell type in the mammalian forebrain, but its function remains poorly understood. Using a detailed compartmental model of a hippocampal CA1 pyramidal cell, we recorded responses to complex stimuli consisting of dozens of high-frequency activated synapses distributed throughout the apical dendrites. We found the cell's firing rate could be predicted by a simple formula that maps the physical components of the cell onto those of an abstract two-layer "neural network." In the first layer, synaptic inputs drive independent sigmoidal subunits corresponding to the cell's several dozen long, thin terminal dendrites. The subunit outputs are then summed within the main trunk and cell body prior to final thresholding. We conclude that insofar as the neural code is mediated by average firing rate, a two-layer neural network may provide a useful abstraction for the computing function of the individual pyramidal neuron.*

Tags: Pyramidal neurons

- [36] Alon Polsky, Bartlett W Mel, and Jackie Schiller. Computational subunits in thin dendrites of pyramidal cells. *Nature neuroscience*, 7(6):621–7, June 2004.

Abstract: *The thin basal and oblique dendrites of cortical pyramidal neurons receive most of the synaptic inputs from other cells, but their integrative properties remain uncertain. Previous studies have most often reported global linear or sublinear summation. An alternative view, supported by biophysical modeling studies, holds that thin dendrites provide a layer of independent computational 'subunits' that sigmoidally modulate their inputs prior to global summation. To distinguish these possibilities, we combined confocal imaging and dual-site focal synaptic stimulation of identified thin dendrites in rat neocortical pyramidal neurons. We found that nearby inputs on the same branch summed sigmoidally, whereas widely separated inputs or inputs to different branches summed linearly. This strong spatial compartmentalization effect is incompatible with a global summation rule and provides the first experimental support for a two-layer 'neural network' model of pyramidal neuron thin-branch integration. Our findings could have important implications for the computing and memory-related functions of cortical tissue.*

Tags: Dendrites

- [37] Jong-Cheol Rah, Erhan Bas, Jennifer Colonell, Yuriy Mishchenko, Bill Karsh, Richard D Fetter, Eugene W Myers, Dmitri B Chklovskii, Karel Svoboda, Timothy D Harris, and John T R Isaac. Thalamocortical input onto layer 5 pyramidal neurons measured using quantitative large-scale array tomography. *Frontiers in neural circuits*, 7:177, January 2013.

Abstract: *The subcellular locations of synapses on pyramidal neurons strongly influences dendritic integration and synaptic plasticity. Despite this, there is little quantitative data on spatial distributions of specific types of synaptic input. Here we use array tomography (AT), a high-resolution optical microscopy method, to examine thalamocortical (TC) input onto layer 5 pyramidal neurons. We first verified the ability of AT to identify synapses using parallel electron microscopic analysis of TC synapses in layer 4. We then use large-scale array tomography (LSAT) to measure TC synapse distribution on L5 pyramidal neurons in a 1.00 × 0.83 × 0.21 mm(3) volume of mouse somatosensory cortex. We found that TC synapses primarily target basal dendrites in layer 5, but also make a considerable input to proximal apical dendrites in L4, consistent with previous work. Our analysis further suggests that TC inputs are biased toward certain branches and, within branches, synapses show significant clustering with an excess of TC synapse nearest neighbors within 5–15 μm compared to a random distribution. Thus, we show that AT is a sensitive and quantitative method to map specific types of synaptic input on the dendrites of entire neurons. We anticipate that this technique will be of wide utility for mapping functionally-relevant anatomical connectivity in neural circuits.*

Tags: Pyramidal neurons

- [38] J P Rauschecker and B Tian. Mechanisms and streams for processing of "what" and "where" in auditory cortex. *Proceedings of the National Academy of Sciences of the United States of America*, 97(22):11800–6, October 2000.

Abstract: *The functional specialization and hierarchical organization of multiple areas in rhesus monkey auditory cortex were examined with various types of complex sounds. Neurons in the lateral belt areas of the superior temporal gyrus were tuned to the best center frequency and bandwidth of band-passed noise bursts. They were also selective for the rate and direction of linear frequency modulated sweeps. Many neurons showed a preference for a limited*

number of species-specific vocalizations ("monkey calls"). These response selectivities can be explained by nonlinear spectral and temporal integration mechanisms. In a separate series of experiments, monkey calls were presented at different spatial locations, and the tuning of lateral belt neurons to monkey calls and spatial location was determined. Of the three belt areas the anterolateral area shows the highest degree of specificity for monkey calls, whereas neurons in the caudolateral area display the greatest spatial selectivity. We conclude that the cortical auditory system of primates is divided into at least two processing streams, a spatial stream that originates in the caudal part of the superior temporal gyrus and projects to the parietal cortex, and a pattern or object stream originating in the more anterior portions of the lateral belt. A similar division of labor can be seen in human auditory cortex by using functional neuroimaging.

Tags: Sensorimotor Inference

- [39] Aman B Saleem, Asl Ayaz, Kathryn J Jeffery, Kenneth D Harris, and Matteo Carandini. Integration of visual motion and locomotion in mouse visual cortex. *Nature neuroscience*, 16(12):1864–9, December 2013.

Abstract: Successful navigation through the world requires accurate estimation of one's own speed. To derive this estimate, animals integrate visual speed gauged from optic flow and run speed gauged from proprioceptive and locomotor systems. The primary visual cortex (V1) carries signals related to visual speed, and its responses are also affected by run speed. To study how V1 combines these signals during navigation, we recorded from mice that traversed a virtual environment. Nearly half of the V1 neurons were reliably driven by combinations of visual speed and run speed. These neurons performed a weighted sum of the two speeds. The weights were diverse across neurons, and typically positive. As a population, V1 neurons predicted a linear combination of visual and run speeds better than either visual or run speeds alone. These data indicate that V1 in the mouse participates in a multimodal processing system that integrates visual motion and locomotion during navigation.

Tags: Sensorimotor Inference

- [40] S. Murray Sherman and Rainer W. Guillery. *Functional Connections of Cortical Areas: A New View from the Thalamus*. The MIT Press, 2013.

Abstract: In this book, two leading authorities on the thalamus and its relationship to cortex build on their earlier findings to arrive at new ways of thinking about how the brain relates to the world, to cognition, and behavior. Based on foundations established earlier in their book *Exploring the Thalamus and Its Role in Cortical Function*, the authors consider the implications of these ground rules for thalamic inputs, thalamocortical connections, and cortical outputs. The authors argue that functional and structural analyses of pathways connecting thalamus and cortex point beyond these to lower centers and through them to the body and the world. Each cortical area depends on the messages linking it to body and world. These messages relate to the way we act and think; each cortical area receives thalamic inputs and has outputs to motor centers. Sherman and Guillery go on to discuss such topics as the role of branching axons that carry motor instructions as well as copies of these motor instructions for relay to cortex under the control of the thalamic gate. This gate allows the thalamus to control the passage of information on the basis of which cortex relates to the rest of the nervous system.

Tags: Neuroscience,Thalamus

- [41] Marc A Sommer and Robert H Wurtz. Influence of the thalamus on spatial visual processing in frontal cortex. *Nature*, 444(7117):374–7, November 2006.

Abstract: Each of our movements activates our own sensory receptors, and therefore keeping track of self-movement is a necessary part of analysing sensory input. One way in which the brain keeps track of self-movement is by monitoring an internal copy, or corollary discharge, of motor commands. This concept could explain why we perceive a stable visual world despite our frequent quick, or saccadic, eye movements: corollary discharge about each saccade would permit the visual system to ignore saccade-induced visual changes. The critical missing link has been the connection between corollary discharge and visual processing. Here we show that such a link is formed by a corollary discharge from the thalamus that targets the frontal cortex. In the thalamus, neurons in the mediodorsal nucleus relay a corollary discharge of saccades from the midbrain superior colliculus to the cortical frontal eye field. In the frontal eye field, neurons use corollary discharge to shift their visual receptive fields spatially before saccades. We tested the hypothesis that these two components—a pathway for corollary discharge and neurons with shifting receptive fields—form a circuit in which the corollary discharge drives the shift. First we showed that the known spatial and temporal properties of

the corollary discharge predict the dynamic changes in spatial visual processing of cortical neurons when saccades are made. Then we moved from this correlation to causation by isolating single cortical neurons and showing that their spatial visual processing is impaired when corollary discharge from the thalamus is interrupted. Thus the visual processing of frontal neurons is spatiotemporally matched with, and functionally dependent on, corollary discharge input from the thalamus. These experiments establish the first link between corollary discharge and visual processing, delineate a brain circuit that is well suited for mediating visual stability, and provide a framework for studying corollary discharge in other sensory systems.

Tags: Sensorimotor Inference

- [42] Nelson Spruston. Pyramidal neurons: dendritic structure and synaptic integration. *Nature reviews. Neuroscience*, 9(3):206–21, March 2008.

Abstract: *Pyramidal neurons are characterized by their distinct apical and basal dendritic trees and the pyramidal shape of their soma. They are found in several regions of the CNS and, although the reasons for their abundance remain unclear, functional studies—especially of CA1 hippocampal and layer V neocortical pyramidal neurons—have offered insights into the functions of their unique cellular architecture. Pyramidal neurons are not all identical, but some shared functional principles can be identified. In particular, the existence of dendritic domains with distinct synaptic inputs, excitability, modulation and plasticity appears to be a common feature that allows synapses throughout the dendritic tree to contribute to action-potential generation. These properties support a variety of coincidence-detection mechanisms, which are likely to be crucial for synaptic integration and plasticity.*

Tags: Pyramidal neurons

- [43] Alex M Thomson. Neocortical layer 6, a review. *Frontiers in neuroanatomy*, 4:13, 2010.

Abstract: *This review attempts to summarise some of the major areas of neocortical research as it pertains to neocortical layer 6. After a brief summary of the development of this intriguing layer, the major pyramidal cell classes to be found in layer 6 are described and compared. The connections made and received by these different classes of neurones are then discussed and the possible functions of these connections, with particular reference to the shaping of responses in visual cortex and thalamus. Inhibition in layer 6 is discussed where appropriate, but not in great detail. Many types of interneurons are to be found in each cortical layer and layer 6 is no exception, but the functions of each type remain to be elucidated (Gonchar et al., 2007).*

Tags: Anatomy,Neuroscience

- [44] Alex M Thomson and a Peter Bannister. Interlaminar connections in the neocortex. *Cerebral cortex (New York, N.Y. : 1991)*, 13(1):5–14, January 2003.

Abstract: *This review summarizes the local circuit, interlaminar connections in adult mammalian neocortex. These were first demonstrated with anatomical techniques, which indicate some of the exquisite spatial precision present in the circuitry. Details, such as the class(es) of neurons targeted by some of these projections, have begun to be added in studies that combine paired/triple intracellular recordings with dye-filling of connected neurons. Clear patterns are emerging from these studies, with 'forward' projections from layer 4 to 3 and from 3 to 5 targeting both selected pyramidal cells and interneurons, while 'back' projections from layer 5 to 3 and from 3 to 4 target only interneurons. To place these data in a wider context, the major afferent inputs to and efferent outputs from each of the layers are discussed first.*

Tags: Anatomy,Laminar structure,Neuroscience

- [45] Alex M Thomson and Christophe Lamy. Functional maps of neocortical local circuitry. *Frontiers in neuroscience*, 1:19–42, 2007.

Abstract: *This review aims to summarize data obtained with different techniques to provide a functional map of the local circuit connections made by neocortical neurones, a reference for those interested in cortical circuitry and the numerical information required by those wishing to model the circuit. A brief description of the main techniques used to study circuitry is followed by outline descriptions of the major classes of neocortical excitatory and inhibitory neurones and the connections that each layer makes with other cortical and subcortical regions. Maps summarizing the projection patterns of each class of neurone within the local circuit and tables of the properties of these local circuit connections are provided. This review relies primarily on anatomical studies that have identified the classes of neurones and their local and long distance connections and on paired intracellular and whole-cell recordings which have documented the properties of the connections between them. A large number of*

different types of synaptic connections have been described, but for some there are only a few published examples and for others the details that can only be obtained with paired recordings and dye-filling are lacking. A further complication is provided by the range of species, technical approaches and age groups used in these studies. Wherever possible the range of available data are summarised and compared. To fill some of the more obvious gaps for the less well-documented cases, data obtained with other methods are also summarized.

Tags: Anatomy, Neuroscience

- [46] Joshua T Trachtenberg, Brian E Chen, Graham W Knott, Guoping Feng, Joshua R Sanes, Egbert Welker, and Karel Svoboda. Long-term in vivo imaging of experience-dependent synaptic plasticity in adult cortex. *Nature*, 420(6917):788–94, 2002.

Abstract: Do new synapses form in the adult cortex to support experience-dependent plasticity? To address this question, we repeatedly imaged individual pyramidal neurons in the mouse barrel cortex over periods of weeks. We found that, although dendritic structure is stable, some spines appear and disappear. Spine lifetimes vary greatly: stable spines, about 50% of the population, persist for at least a month, whereas the remainder are present for a few days or less. Serial-section electron microscopy of imaged dendritic segments revealed retrospectively that spine sprouting and retraction are associated with synapse formation and elimination. Experience-dependent plasticity of cortical receptive fields was accompanied by increased synapse turnover. Our measurements suggest that sensory experience drives the formation and elimination of synapses and that these changes might underlie adaptive remodelling of neural circuits.

Tags: Synapses

- [47] William E. Vinje and Jack L. Gallant. Natural Stimulation of the Nonclassical Receptive Field Increases Information Transmission Efficiency in V1. *J. Neurosci.*, 22(7):2904–2915, April 2002.

Abstract: We have investigated how the nonclassical receptive field (nCRF) affects information transmission by V1 neurons during simulated natural vision in awake, behaving macaques. Stimuli were centered over the classical receptive field (CRF) and stimulus size was varied from one to four times the diameter of the CRF. Stimulus movies reproduced the spatial and temporal stimulus dynamics of natural vision while maintaining constant CRF stimulation across all sizes. In individual neurons, stimulation of the nCRF significantly increases the information rate, the information per spike, and the efficiency of information transmission. Furthermore, the population averages of these quantities also increase significantly with nCRF stimulation. These data demonstrate that the nCRF increases the sparseness of the stimulus representation in V1, suggesting that the nCRF tunes V1 neurons to match the highly informative components of the natural world.

Tags: Neuroscience, Sequence Learning

- [48] John T Wixted, Larry R Squire, Yoonhee Jang, Megan H Papesh, Stephen D Goldinger, Joel R Kuhn, Kris A Smith, David M Treiman, and Peter N Steinmetz. Sparse and distributed coding of episodic memory in neurons of the human hippocampus. *Proceedings of the National Academy of Sciences of the United States of America*, 111(26):9621–6, July 2014.

Abstract: Neurocomputational models hold that sparse distributed coding is the most efficient way for hippocampal neurons to encode episodic memories rapidly. We investigated the representation of episodic memory in hippocampal neurons of nine epilepsy patients undergoing intracranial monitoring as they discriminated between recently studied words (targets) and new words (foils) on a recognition test. On average, single units and multiunits exhibited higher spike counts in response to targets relative to foils, and the size of this effect correlated with behavioral performance. Further analyses of the spike-count distributions revealed that (i) a small percentage of recorded neurons responded to any one target and (ii) a small percentage of targets elicited a strong response in any one neuron. These findings are consistent with the idea that in the human hippocampus episodic memory is supported by a sparse distributed neural code.

Tags: SDR

- [49] D M. Wolpert and R C. Miall. Forward Models for Physiological Motor Control. *Neural networks : the official journal of the International Neural Network Society*, 9(8):1265–1279, November 1996.

Abstract: Based on theoretical and computational studies it has been suggested that the central nervous system (CNS) internally simulates the behaviour of the motor system in planning, control and learning. Such an internal "forward" model is a representation of the motor system that uses the current state of the motor system and motor command to predict the next state. We will outline the uses of such internal models for solving several fundamental computational problems in motor control and then review the evidence for their existence and use by the CNS. Finally we speculate how the location of an internal model within the CNS may be identified. Copyright 1996 Elsevier Science Ltd.

- [50] Guang Yang, Cora Sau Wan Lai, Joseph Cichon, Lei Ma, Wei Li, and Wen-Biao Gan. Sleep promotes branch-specific formation of dendritic spines after learning. *Science (New York, N.Y.)*, 344(6188):1173–8, June 2014.

Abstract: How sleep helps learning and memory remains unknown. We report in mouse motor cortex that sleep after motor learning promotes the formation of postsynaptic dendritic spines on a subset of branches of individual layer V pyramidal neurons. New spines are formed on different sets of dendritic branches in response to different learning tasks and are protected from being eliminated when multiple tasks are learned. Neurons activated during learning of a motor task are reactivated during subsequent non-rapid eye movement sleep, and disrupting this neuronal reactivation prevents branch-specific spine formation. These findings indicate that sleep has a key role in promoting learning-dependent synapse formation and maintenance on selected dendritic branches, which contribute to memory storage.

Tags: Dendrites, Sequence Learning

- [51] Shih-Cheng Yen, Jonathan Baker, and Charles M Gray. Heterogeneity in the responses of adjacent neurons to natural stimuli in cat striate cortex. *Journal of neurophysiology*, 97(2):1326–1341, 2007.

Abstract: When presented with simple stimuli like bars and gratings, adjacent neurons in striate cortex exhibit shared selectivity for multiple stimulus dimensions, such as orientation, direction, and spatial frequency. This has led to the idea that local averaging of neuronal responses provides a more reliable representation of stimulus properties. However, when stimulated with complex, time-varying natural scenes (i.e., movies), striate neurons exhibit highly sparse responses. This raises the question of how much response heterogeneity the local population exhibits when stimulated with movies, and how it varies with separation distance between cells. We investigated this question by simultaneously recording the responses of groups of neurons in cat striate cortex to the repeated presentation of movies using silicon probes in a multi-tetrode configuration. We found, first, that the responses of striate neurons to movies are brief (tens of milliseconds), decorrelated, and exhibit high population sparseness. Second, we found that adjacent neurons differed significantly in their peak firing rates even when they responded to the same frames of a movie. Third, pairs of adjacent neurons recorded on the same tetrodes exhibited as much heterogeneity in their responses as pairs recorded by different tetrodes. These findings demonstrate that complex natural scenes evoke highly heterogeneous responses within local populations, suggesting that response redundancy in a cortical column is substantially lower than previously thought.

Tags: Neuroscience, Sequence Learning, Vision

- [52] Y Yoshimura, H Sato, K Imamura, and Y Watanabe. Properties of horizontal and vertical inputs to pyramidal cells in the superficial layers of the cat visual cortex. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 20(5):1931–40, March 2000.

Abstract: The purpose of this study is to elucidate the integrative input mechanisms of pyramidal cells receiving horizontally projecting axon collaterals (horizontal projection) and vertical input from layer IV. We performed whole-cell recordings from pyramidal cells in layer II/III and focally activated other single pyramidal cells monosynaptically connected via long-distance horizontal (LH) projections (the distance between presynaptic and postsynaptic cells was 350–1200 micrometer) in slice preparations of the kitten primary visual cortex. In addition, presynaptic single fibers in layer IV (vertical input) and/or short-distance horizontal (SH) inputs from neighboring single pyramidal cells (distance within 100 micrometer) in layer II/III were activated. Unitary EPSPs evoked by the activation of LH and SH connections had smaller amplitude and larger coefficient of variation than those evoked by stimulating the vertical input. Paired-pulse stimulation of the LH and SH inputs caused the depression of the second EPSP, whereas that of vertical inputs caused either facilitation or depression of the second EPSP. The EPSPs evoked by simultaneous activation of LH and vertical inputs summated linearly at the resting membrane potential. However, the EPSPs evoked by stimulation of the two inputs were nonlinearly (supralinearly) summated when the postsynaptic membrane

was depolarized to a certain level. Similar EPSP interaction was observed in response to simultaneous activation of the LH and SH inputs.

Tags: Pyramidal neurons

- [53] R Yuste, M J Gutnick, D Saar, K R Delaney, and D W Tank. Ca²⁺ accumulations in dendrites of neocortical pyramidal neurons: an apical band and evidence for two functional compartments. *Neuron*, 13(1):23–43, July 1994.

Abstract: *Apical dendrites constitute a prominent feature of the microcircuitry in the neocortex, yet their function is poorly understood. Using fura-2 imaging of layer 5 pyramidal neurons from slices of rat somatosensory cortex, we have investigated the Ca²⁺ influx into dendrites under intracellular, antidromic, synaptic, and receptor-agonist stimulation. We find three spatial patterns of Ca²⁺ accumulations: an apical band in the apical dendrite approximately 500 microns from the soma, an accumulation restricted to the basal dendrites, soma, and proximal apical dendrite, and a combination of both of these. We show that the apical band can be activated antidromically and synaptically and that, under blocked Na⁺ and K⁺ conductances, it generates Ca²⁺ spikes. Thus, the apical band may serve as a dendritic trigger zone for regenerative Ca²⁺ spikes or as a current amplifier for distal synaptic events. Our results suggest that the distal apical dendrite should be considered a separate functional compartment from the rest of the cell.*

Tags: Dendrites, Pyramidal Neurons

- [54] Karen Zito and Karel Svoboda. Activity-dependent synaptogenesis in the adult Mammalian cortex. *Neuron*, 35(6):1015–7, September 2002.

Abstract: *Recent electron microscopic studies provide evidence that the adult cortex generates new synapses in response to sensory activity and that these structural changes can occur rapidly, within 24 hr of sensory stimulation. Together with progress imaging synapses in vivo, the stage appears set for advances in understanding the dynamics and mechanisms of experience-dependent synaptogenesis.*

Tags: Synapses