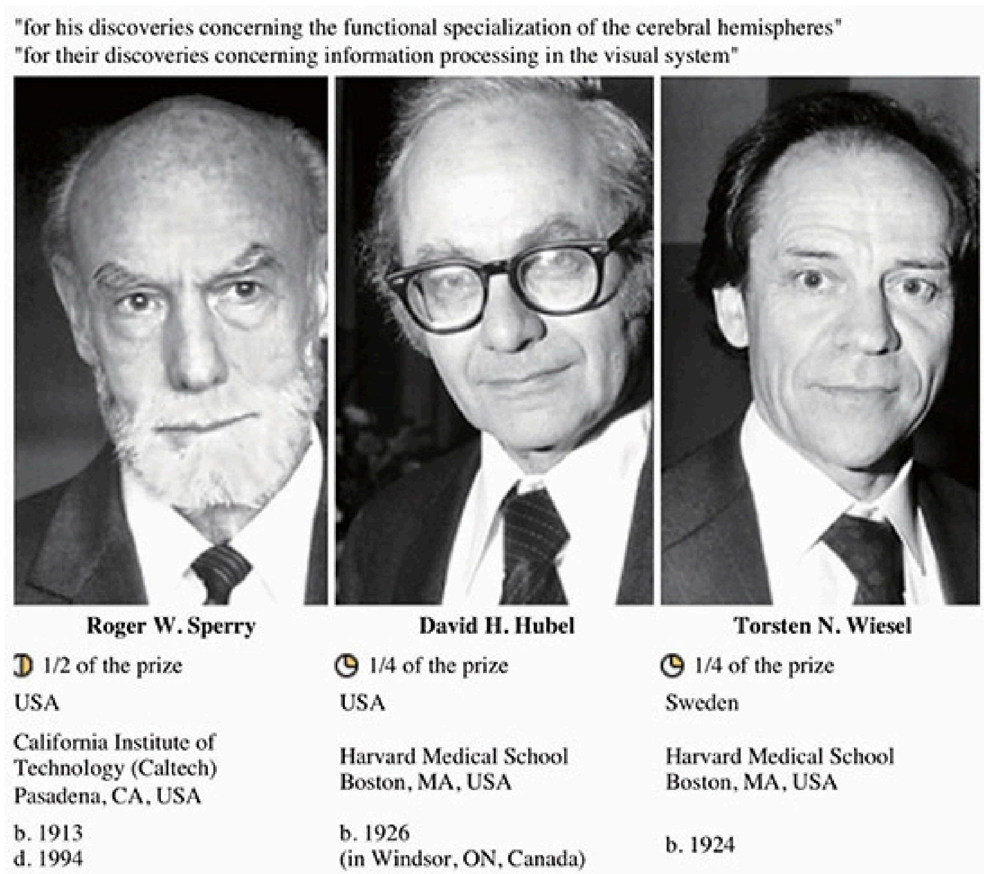
Mechanisms of stimulus feature selectivity in sensory systems

1. Orientation and direction selectivity in the visual cortex
2. Selectivity to sound frequency in the auditory cortex
3. Feature selectivity in the somatosensory system.

Orientation selectivity in the primary visual cortex

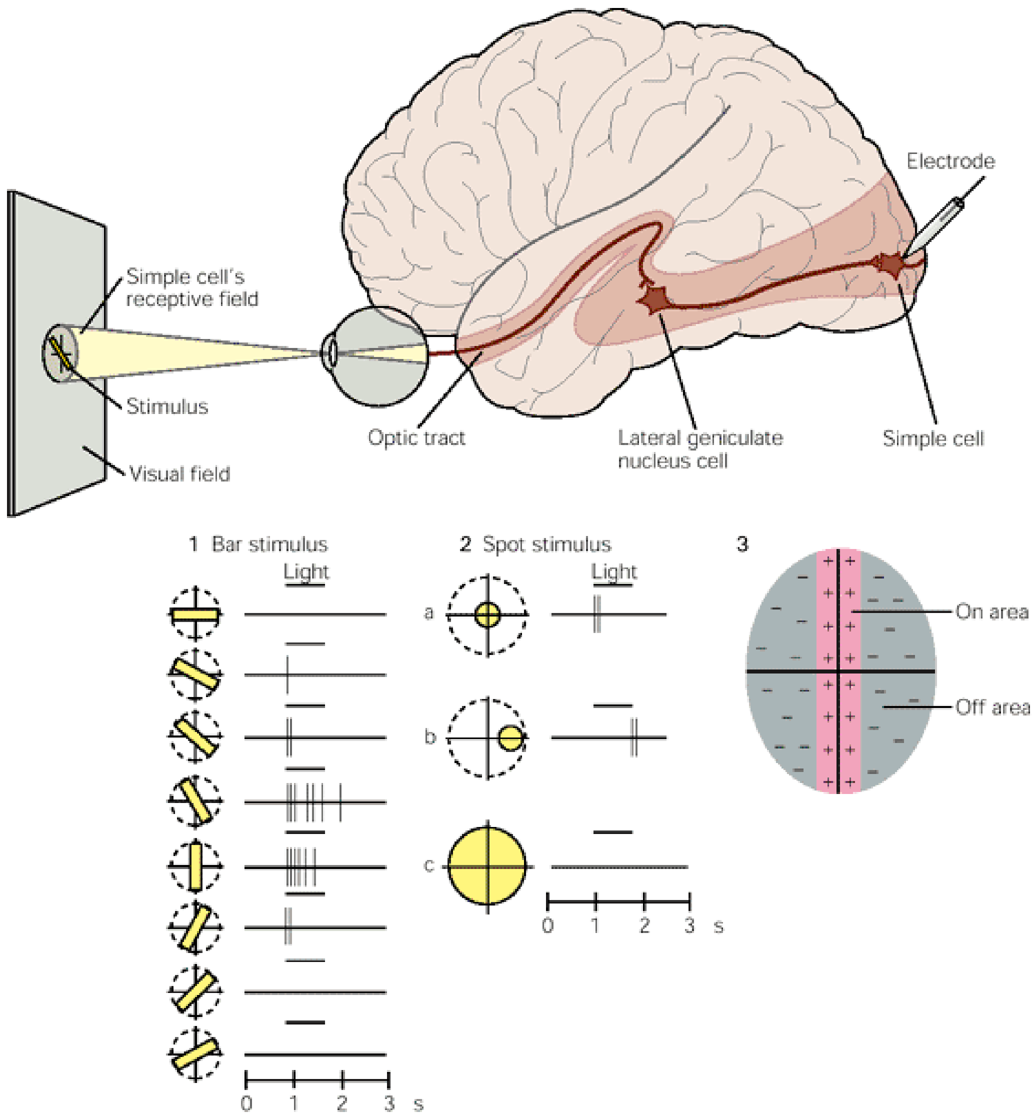
The Nobel Prize in Physiology or Medicine 1981



Orientation selectivity in the primary visual cortex

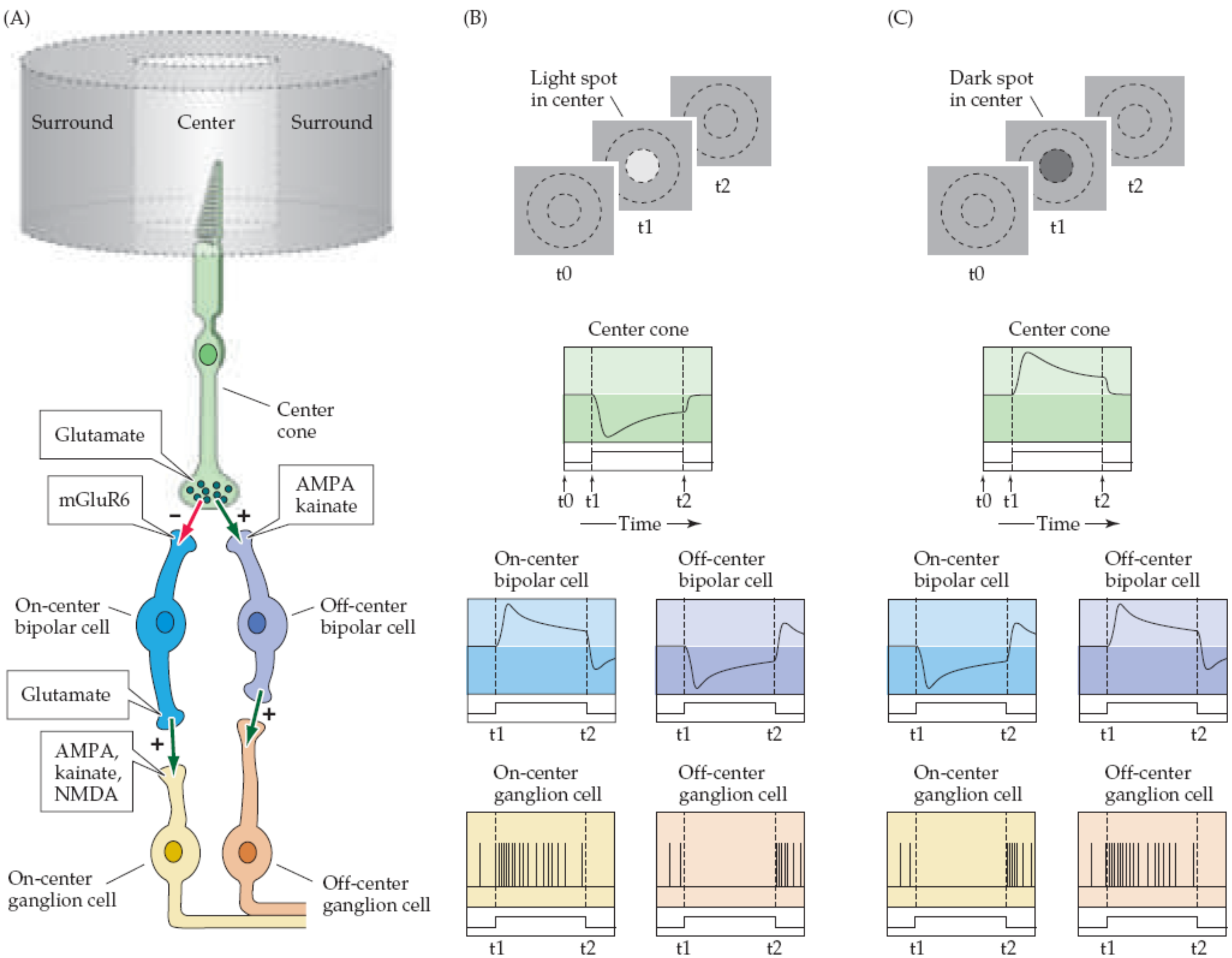
1. Hubel and Wiesel experiments
2. The H&W model – a simple feedforward model
3. Predictions of the H&W model
4. Mismatches between H&W model and experimental data
5. Recurrent models for orientation selectivity
6. Experiments that support the H&W – intracellular recording data
7. Advanced imaging experiments and the H&W model
8. Optogenetic manipulations of specific types of neurons

Orientation selectivity



Receptive fields in the retina

On and Off centers are important to generate reliable output signal (firing) in ganglion cells
The transmission between cones and bipolar cells depends on the type (on vs off) target type



Note:

- mGluR6 is metabotropic and leads to hyperpolarization of the bipolar cell
- AMPA and Kinate are ionotropic and have excitatory effect on bipolar cells

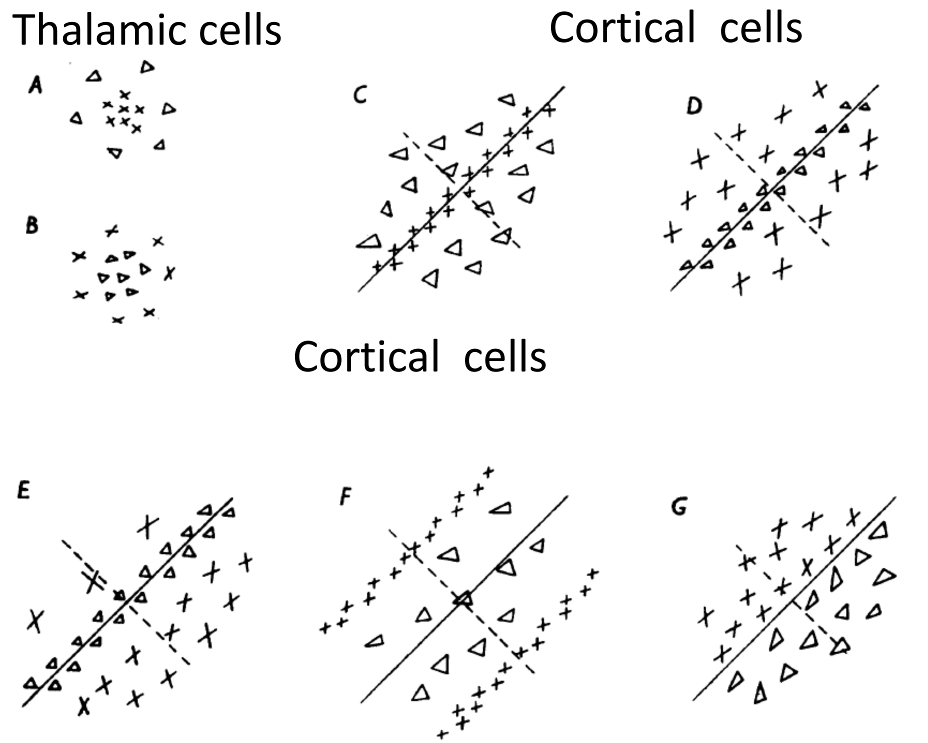
Receptive fields in V1, H&W experiments

J. Physiol. (1962), **160**, *pp.* 106–154
With 2 plates and 20 text-figures
Printed in Great Britain

RECEPTIVE FIELDS, BINOCULAR INTERACTION AND FUNCTIONAL ARCHITECTURE IN THE CAT'S VISUAL CORTEX

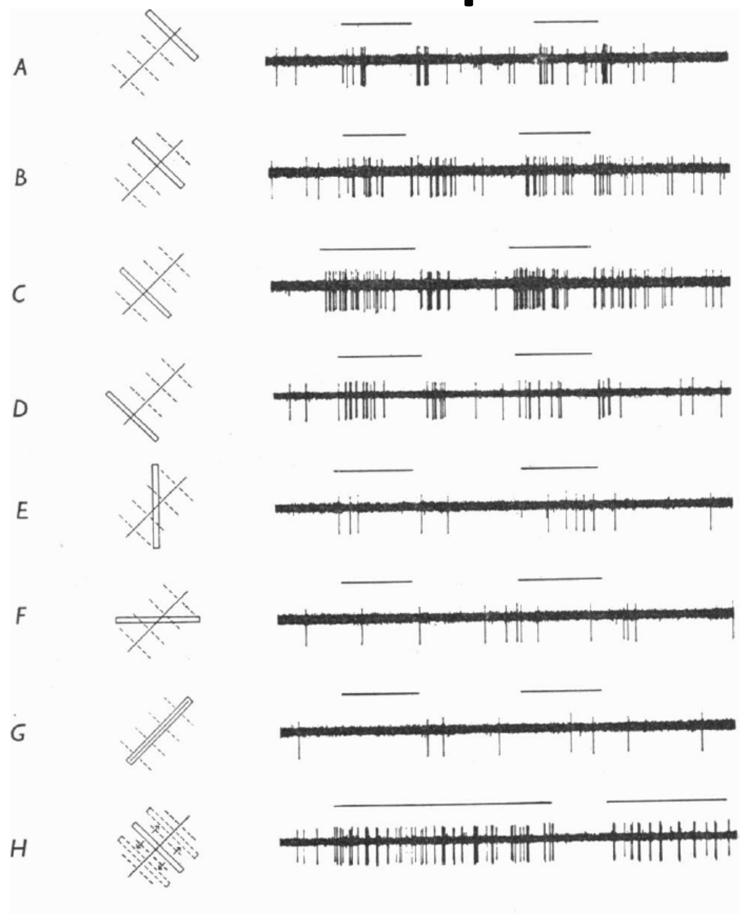
BY D. H. HUBEL AND T. N. WIESEL
From the Neurophysiology Laboratory, Department of Pharmacology Harvard Medical School, Boston, Massachusetts, U.S.A.

(*Received* 31 *July* 1961)



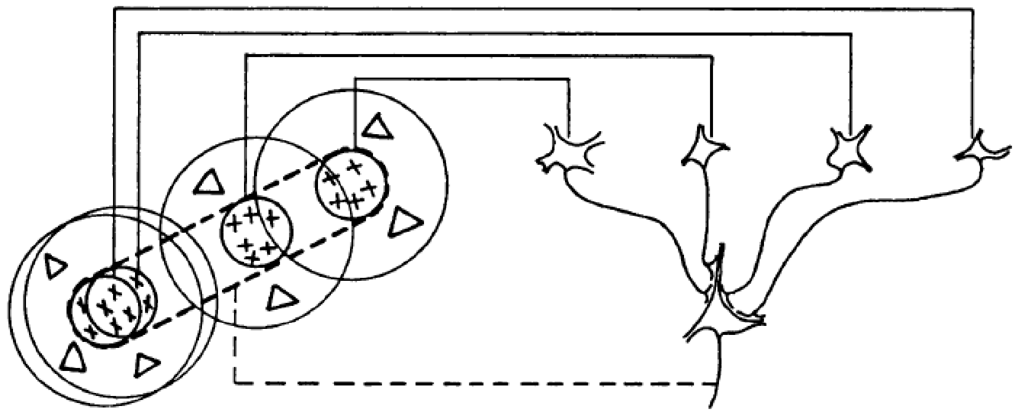
Text-fig. 2. Common arrangements of lateral geniculate and cortical receptive ields. *A*. 'On'-centre geniculate receptive field. *B*. 'Off'-centre geniculate recepive field. *C–G*. Various arrangements of simple cortical receptive fields. ×, reas giving excitatory responses ('on' responses); △, areas giving inhibitory reponses ('off' responses). Receptive-field axes are shown by continuous lines hrough field centres; in the figure these are all oblique, but each arrangement ccurs in all orientations.

Data from H&W experiments: flashing bars : “complex cell”



Text-fig. 4. Responses of a cell with a complex field to stimulation of the left (contralateral) eye with a slit $\frac{1}{8} \times 2\frac{1}{2}°$. Receptive field was in the area centralis and was about $2 \times 3°$ in size. *A–D*, $\frac{1}{8}°$ wide slit oriented parallel to receptive field axis. *E–G*, slit oriented at 45 and 90° to receptive-field axis. *H*, slit oriented as in *A–D*, is on throughout the record and is moved rapidly from side to side where indicated by upper beam. Responses from left eye slightly more marked than those from right (Group 3, see Part II). Time 1 sec.

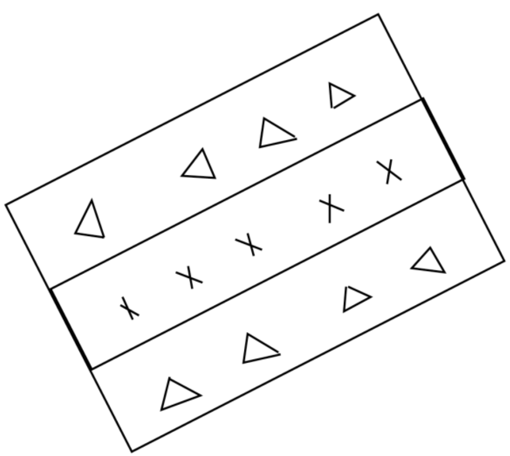
H&W model for simple cells

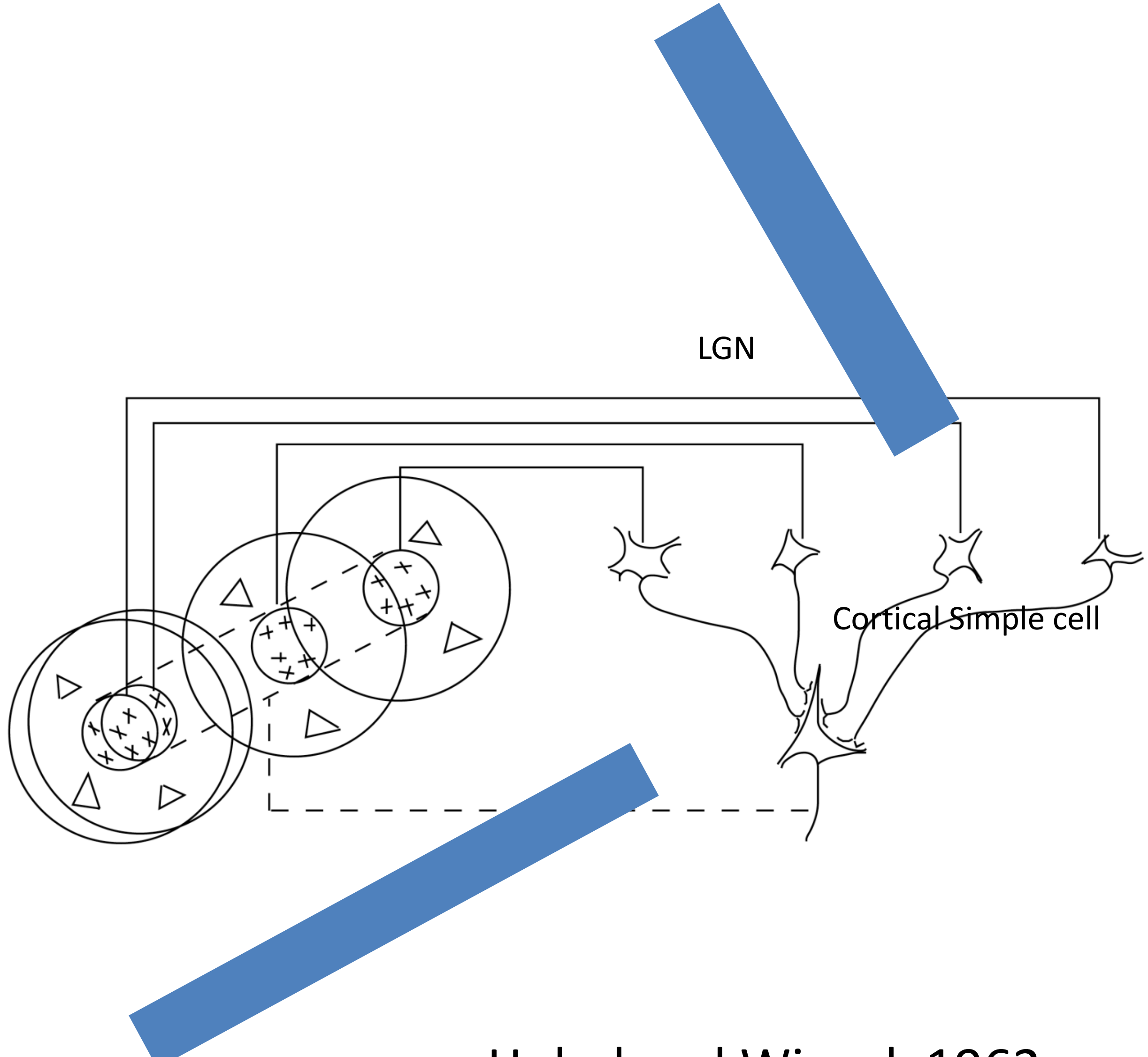


Text-fig. 19. Possible scheme for explaining the organization of simple receptive fields. A large number of lateral geniculate cells, of which four are illustrated in the upper right in the figure, have receptive fields with 'on' centres arranged along a straight line on the retina. All of these project upon a single cortical cell, and the synapses are supposed to be excitatory. The receptive field of the cortical cell will then have an elongated 'on' centre indicated by the interrupted lines in the receptive-field diagram to the left of the figure.

H&W model:

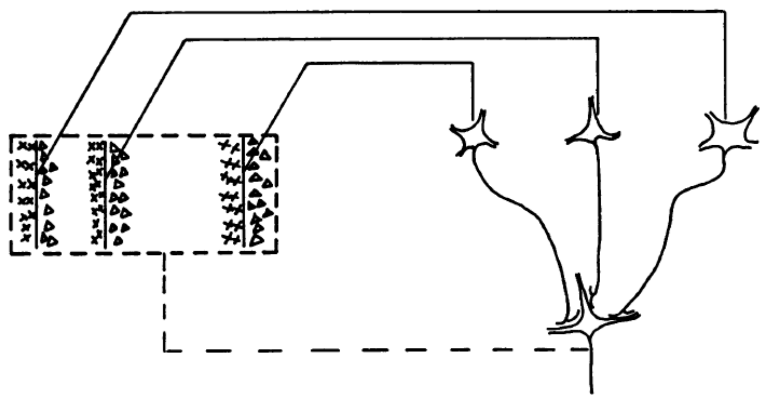
The Feedforward Model





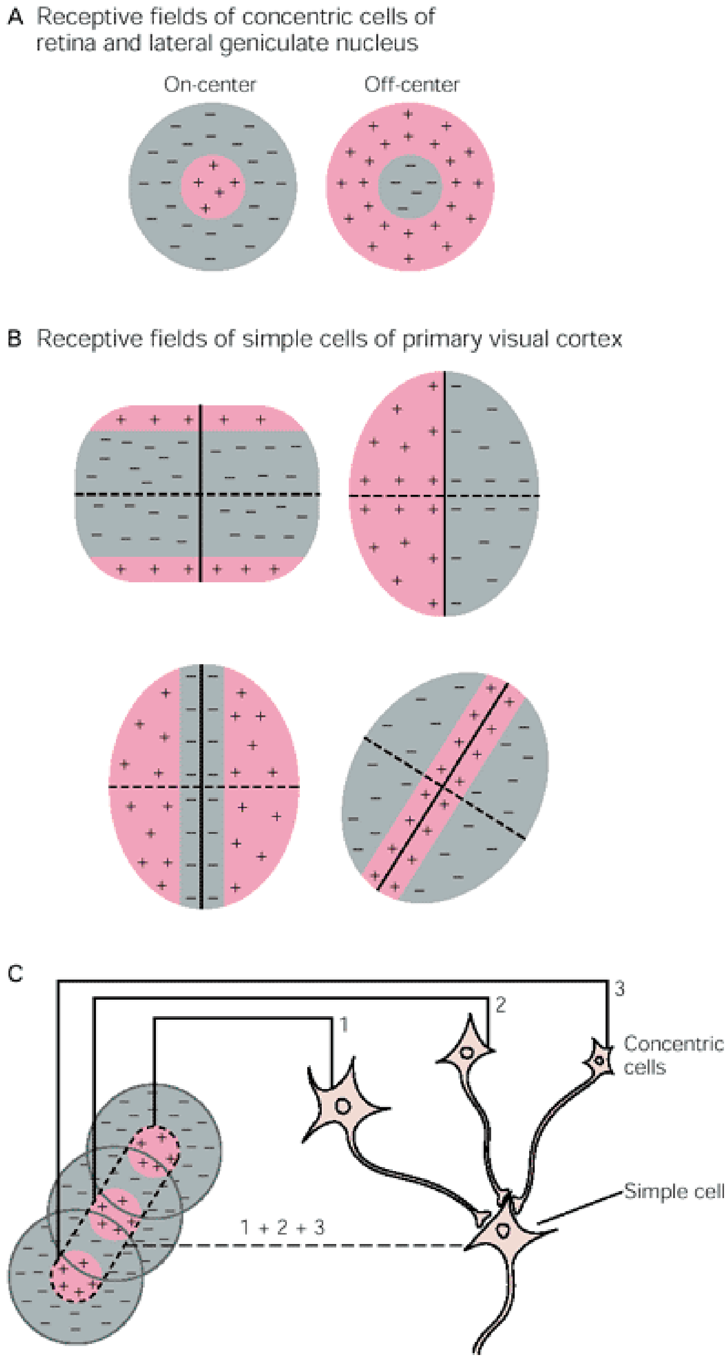
Hubel and Wiesel, 1962

H&W model for complex cells

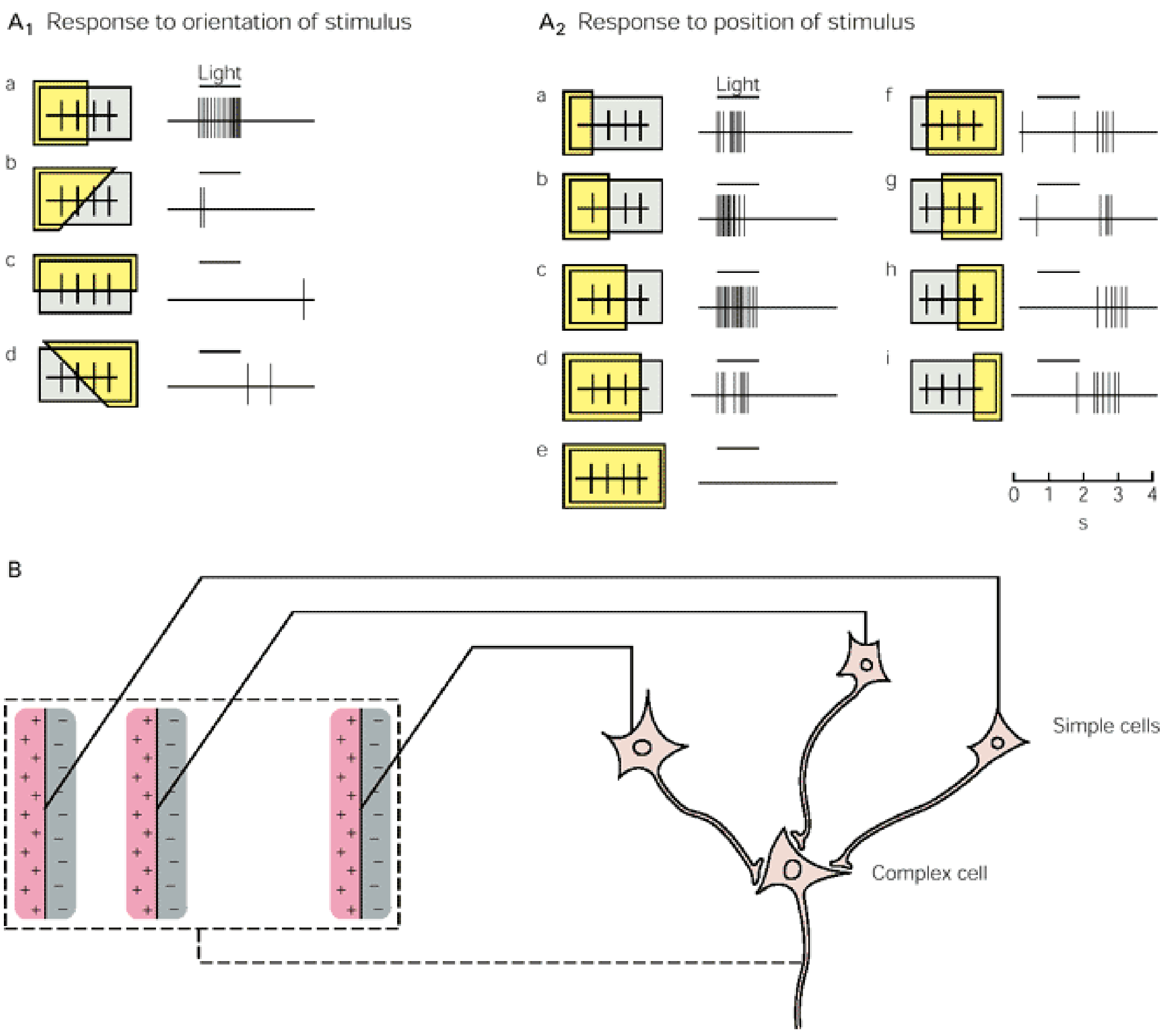


Text-fig. 20. Possible scheme for explaining the organization of complex receptive fields. A number of cells with simple fields, of which three are shown schematically, are imagined to project to a single cortical cell of higher order. Each projecting neurone has a receptive field arranged as shown to the left: an excitatory region to the left and an inhibitory region to the right of a vertical straight-line boundary. The boundaries of the fields are staggered within an area outlined by the interrupted lines. Any vertical-edge stimulus falling across this rectangle, regardless of its position, will excite some simple-field cells, leading to excitation of the higher-order cell.

H&W model for simple cells



H&W model for complex cells

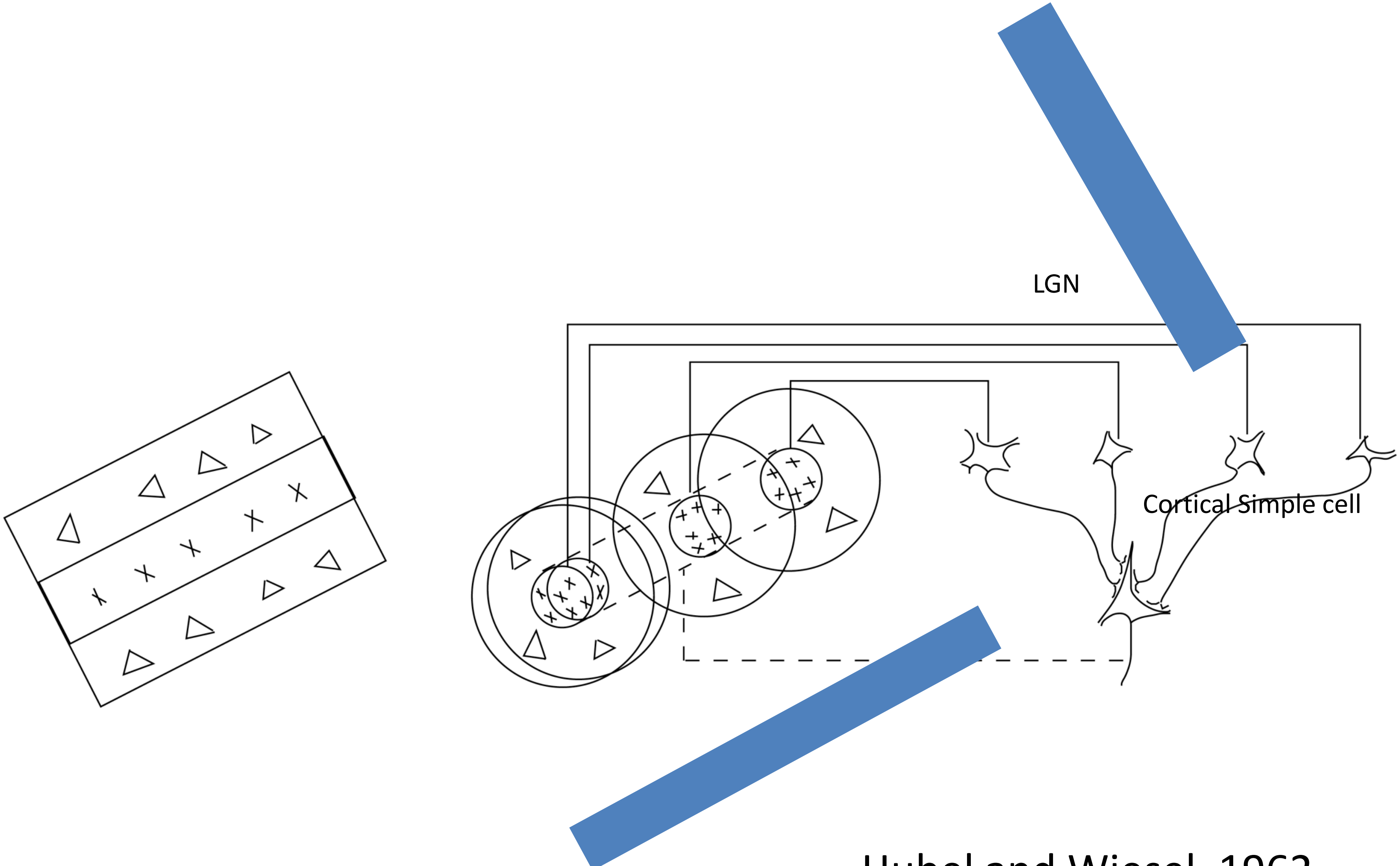


Visual cortex cell

Binacularity

The Feedforward Model

Hubel and Wiesel model



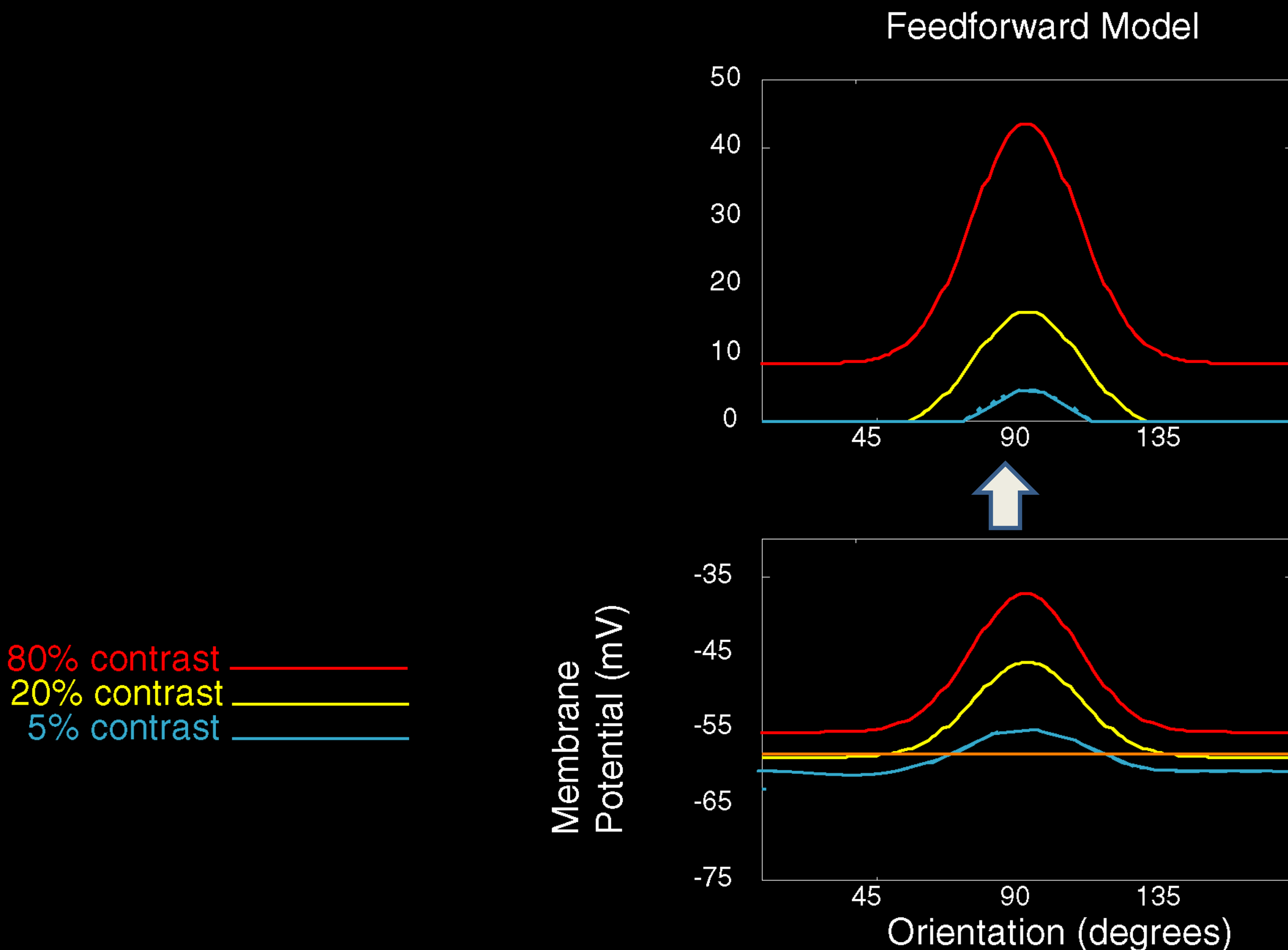
Hubel and Wiesel, 1962

Predictions of the H&W model for simple cells do not match the data

Major <u>Failures</u> of the FF model of H&W:

1. Contrast invariance
2. Cross-orientation suppression
3. Mismatch of receptive field maps and orientation tuning
4. Missing response at the null orientation
5. Pharmacology: blocking GABA(a) causes widening of TC.

Feedforward Model Fails to Predict Contrast Invariance

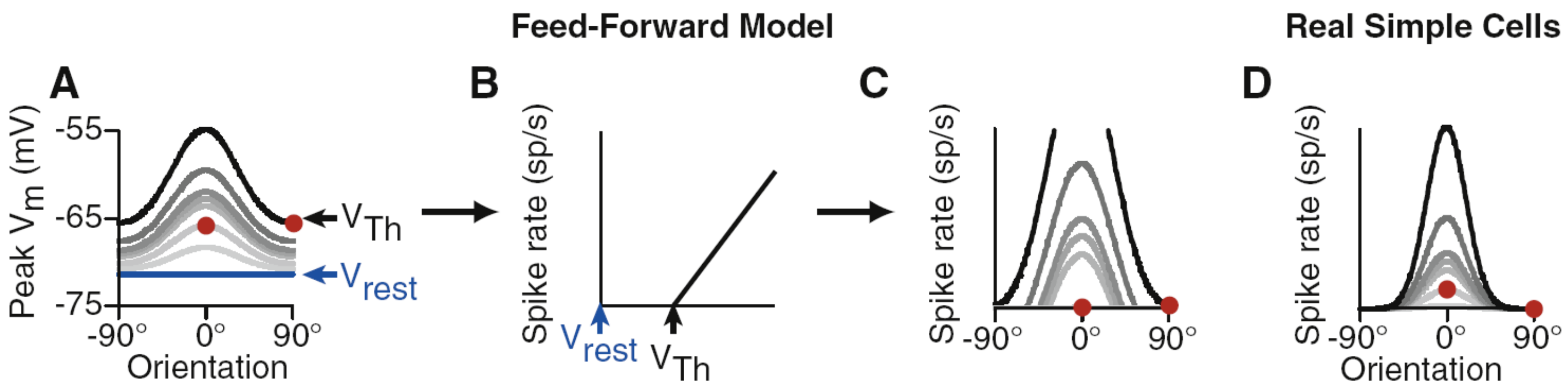


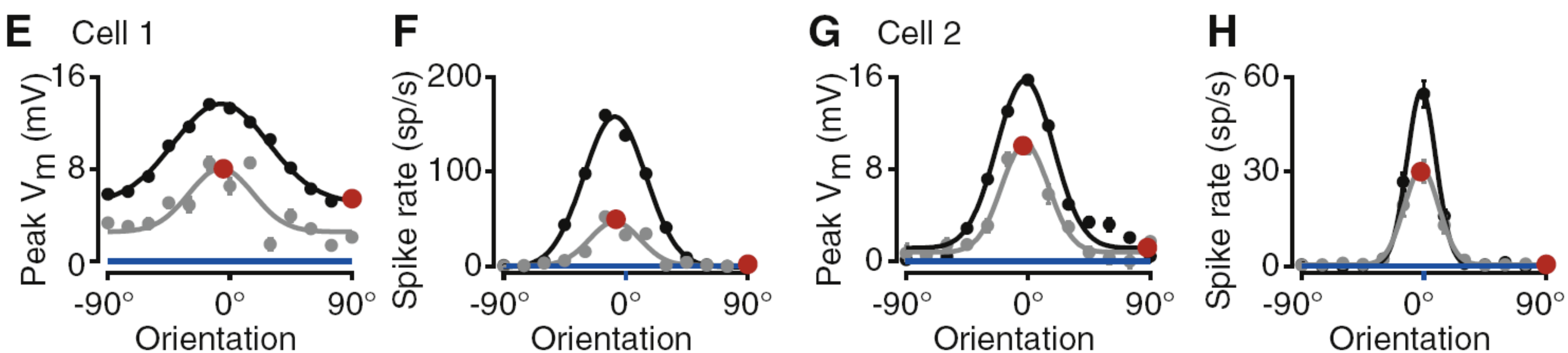
From: Ferster and Miller Annu. Rev. Neurosci. 2000. 23:441–471

Predictions of the H&W model for simple cells do not match the data

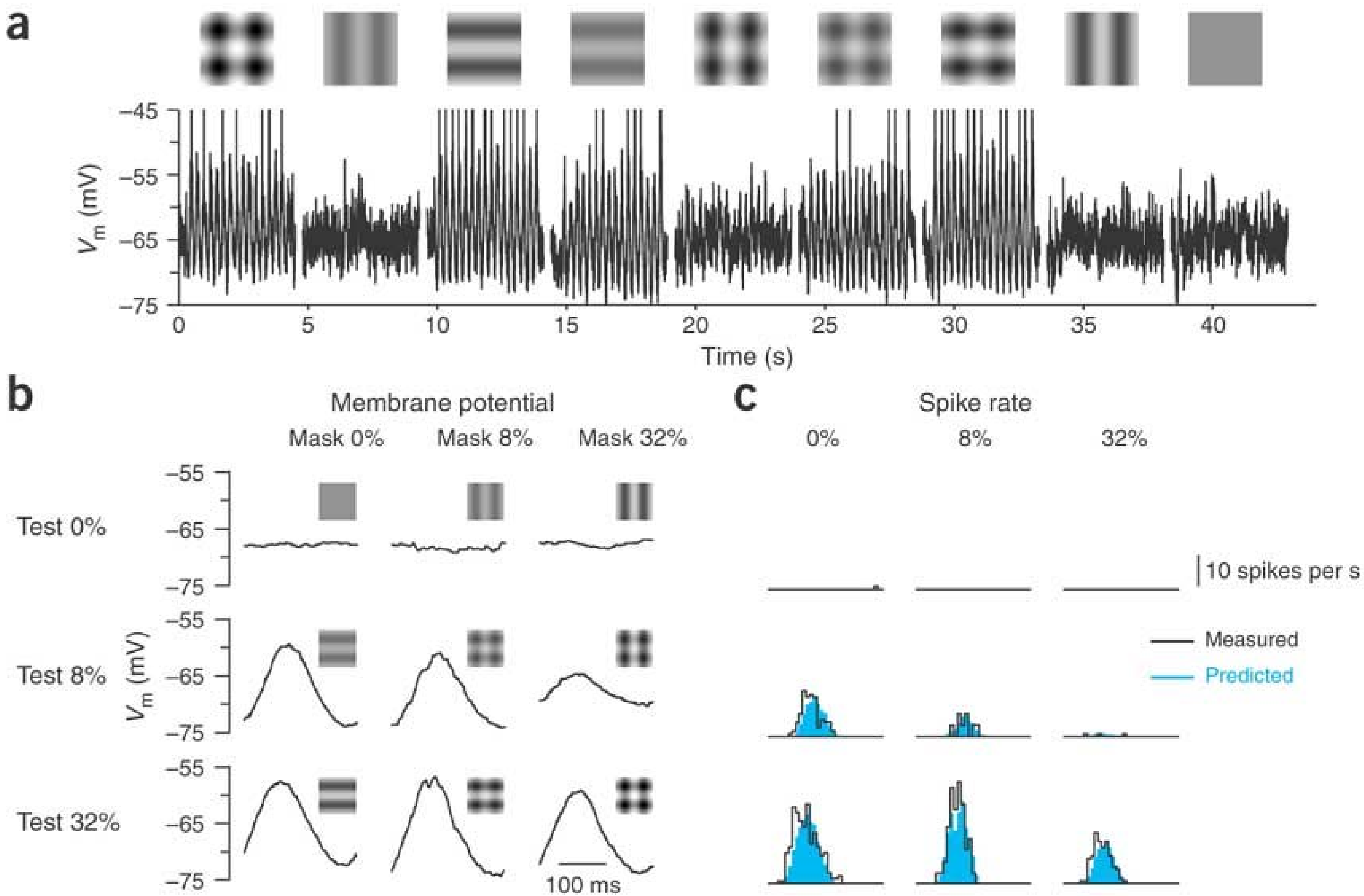
- The <u>model</u> predicts narrowing of the TC as contrast increases !
- <u>Actual data</u>: the tuning curves show contrast invariance

Predictions of the H&W model for simple cells: actual data

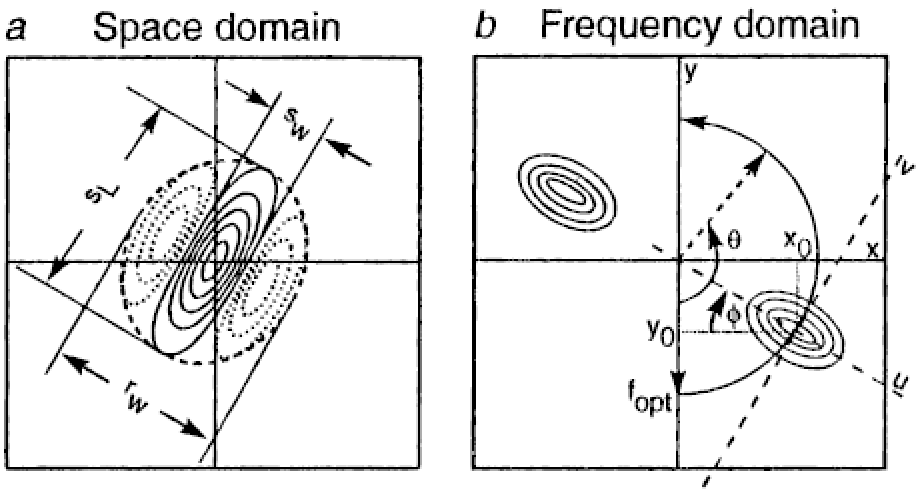




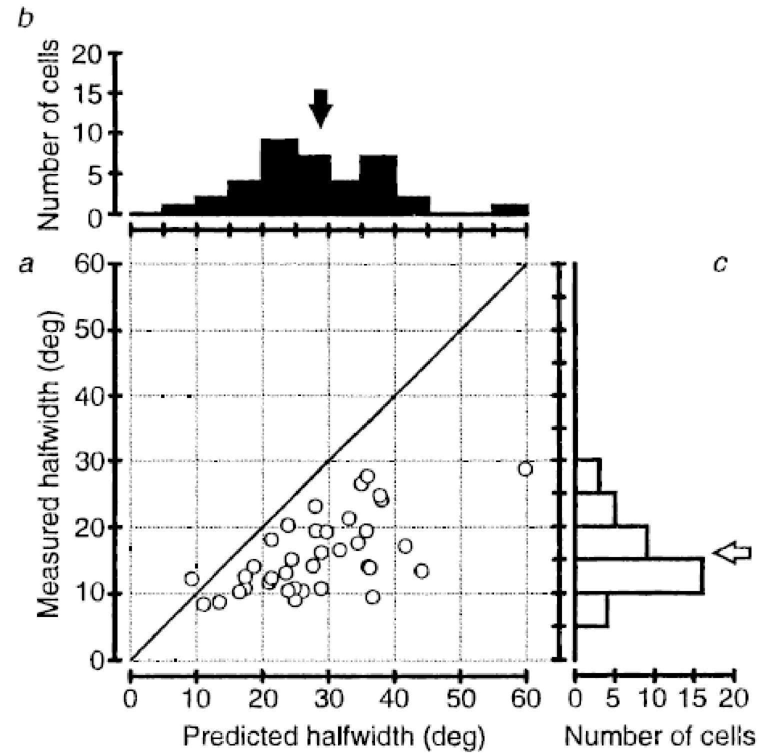
Predictions of the H&W model: Failure 2: cross-orientation suppression



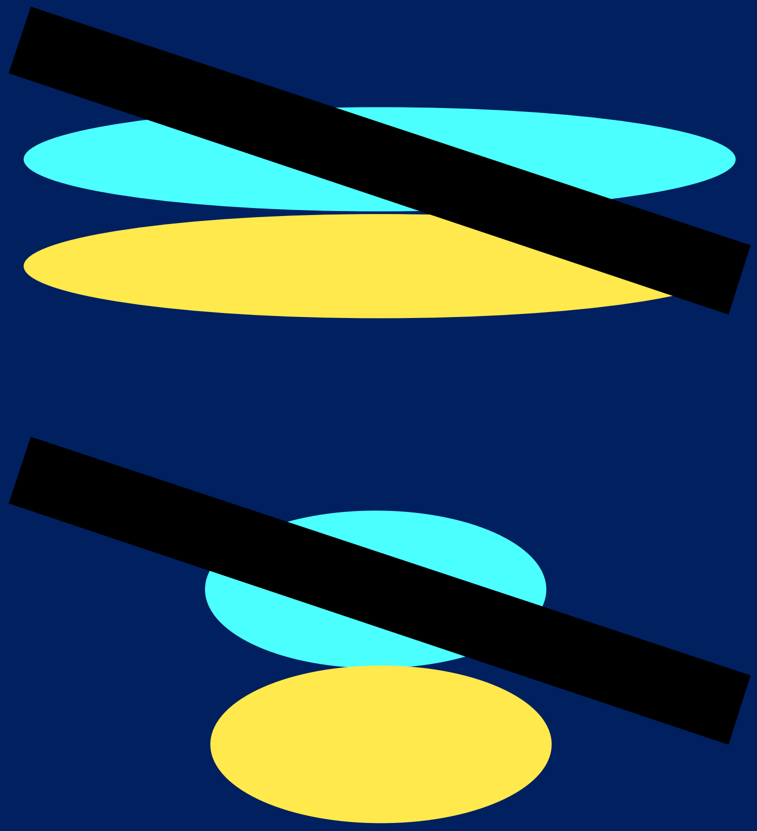
Predictions of the H&W model:
Failure 3:
Mismatch of receptive field maps and orientation tuning

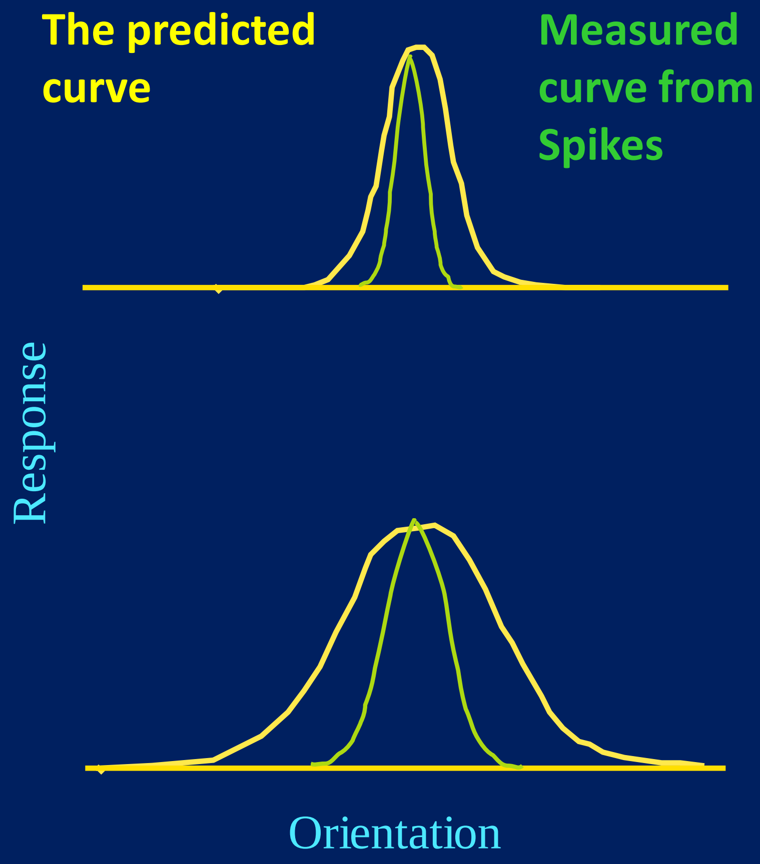


Gardner et al. 1999
Extracellular data



The relation between the structure of the receptive field and orientation selectivity

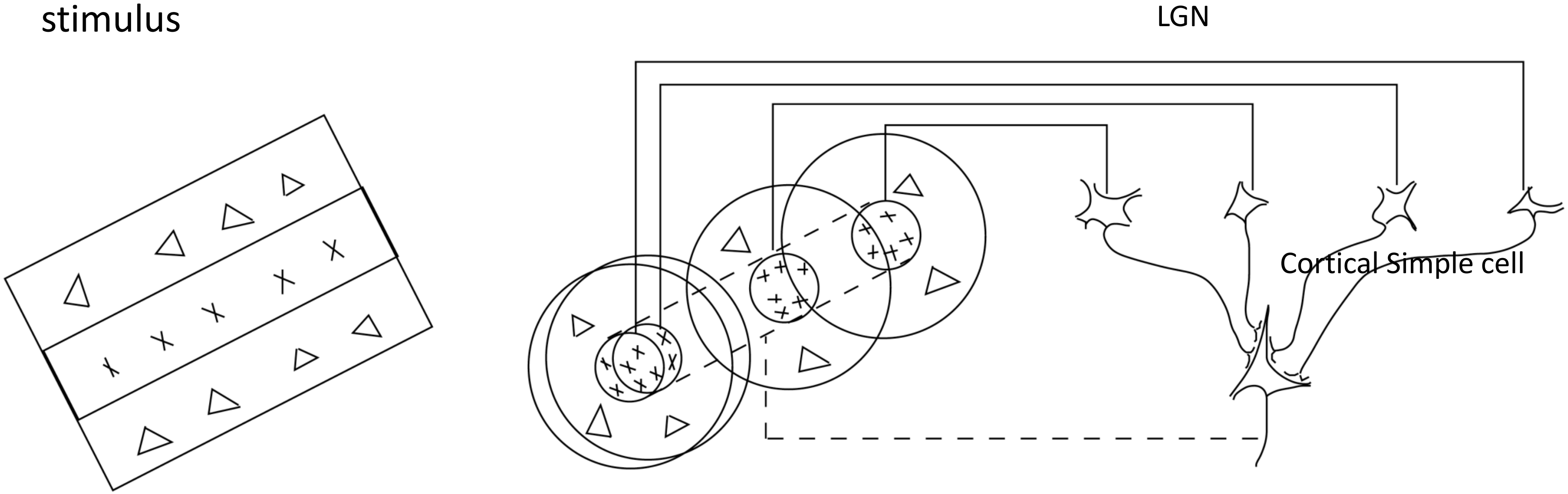




Predictions of the H&W model:
Failure 4: Missing response at the null orientation

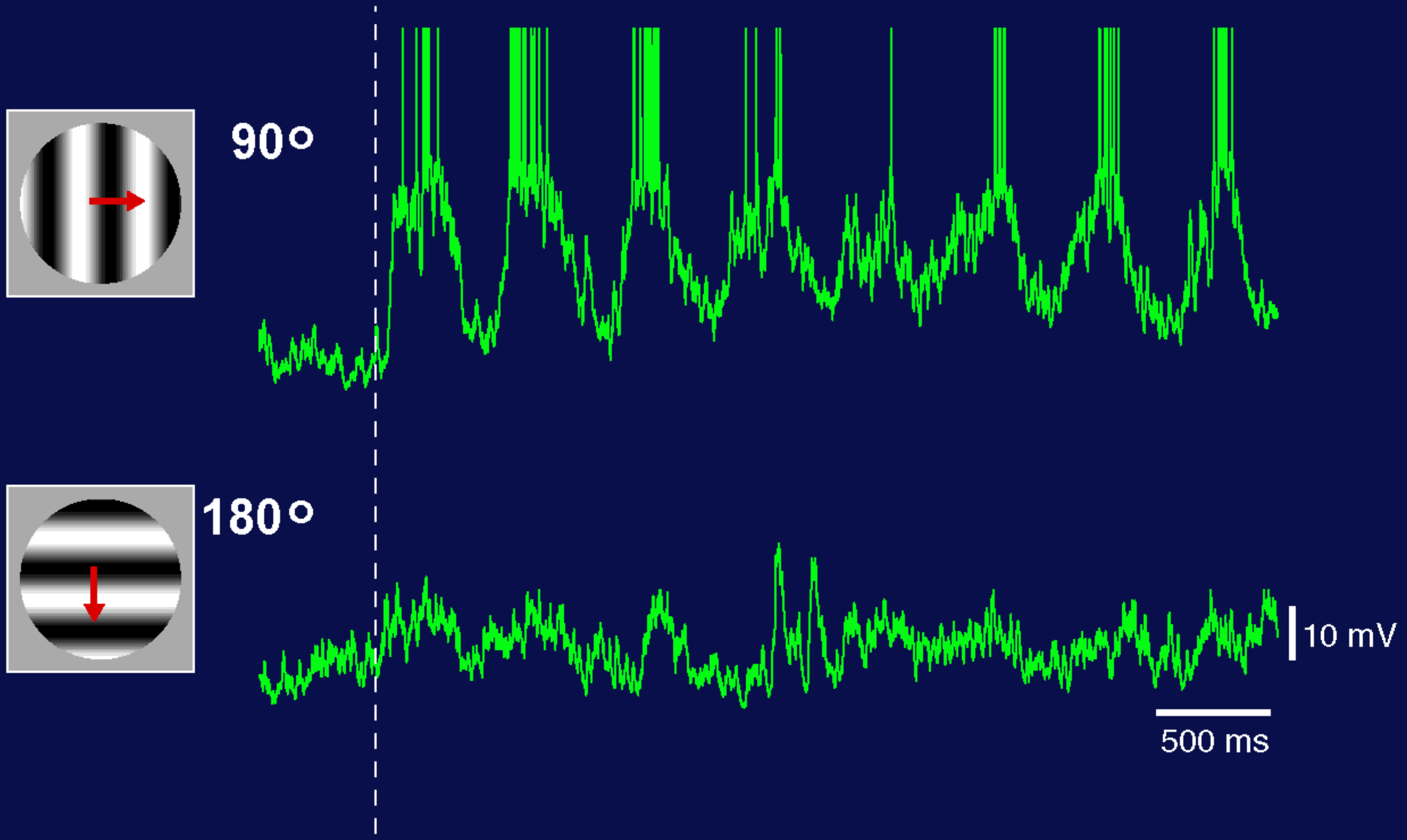
The Feedforward Model

That the V1 cells barely respond to null orientation is puzzling given the fact that the AVERAGE activation of thalamic cells is the same, regardless the orientation of the stimulus



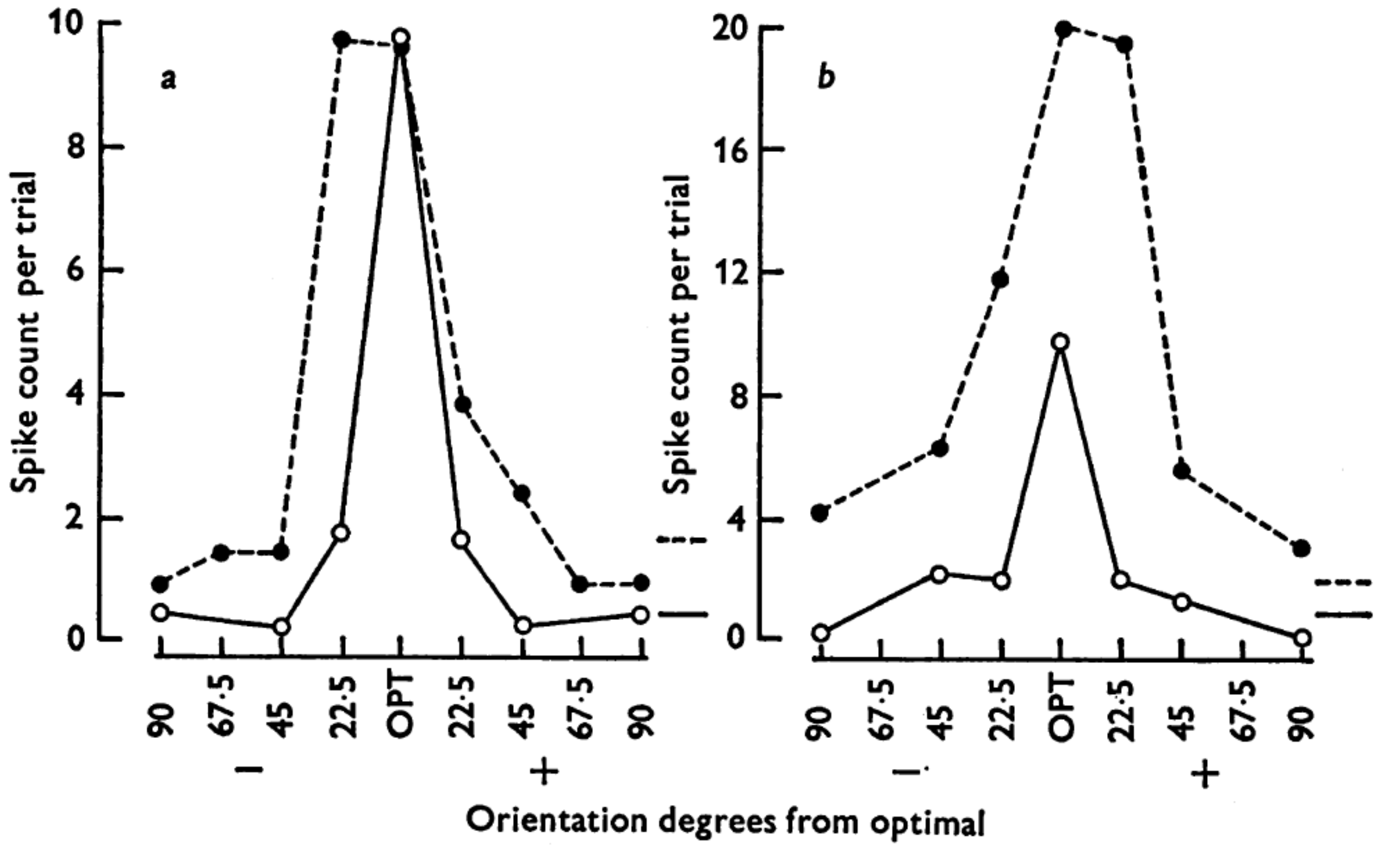
Hubel and Wiesel, 1962

The response at the null direction is low (i.e., lack of DC response even when looking at membrane potential level.



Predictions of the H&W model:
Failure 5: Pharmacolgy

The effect of bicuculline , antagonist of GABA(A), on the TC of V1 cells



Sillito 1975

Predictions of the H&W model:
Failure 5: Pharmacolgy

Bicucullin caused widening of the tuning curves, suggesting that inhibition shapes the TC of the cells

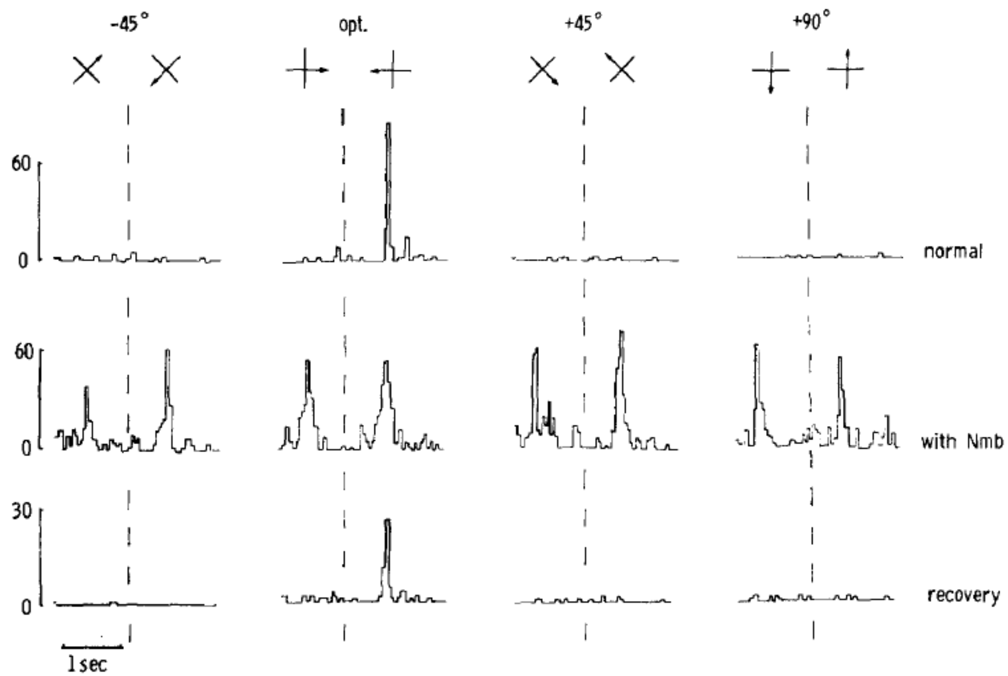


Fig. 1. Action of N-methyl bicuculline (Nmb) on simple cell orientation selectivity. Testing orientation and direction of stimulus motion is indicated above each set of PSTHs. Dotted line subdivides records into zones corresponding to the two directions of motion. Optimal orientation is arbitrarily referred to as zero, —, indicates anti-clockwise rotation from optima, +, clockwise rotation. Each PSTH constructed from 25 trials. Bin size 50 msecs. Vertical calibration indicates number of counts per bin.

Sillito et al. 1980

Excitatory and inhibitory recurrent models for orientation selectivity

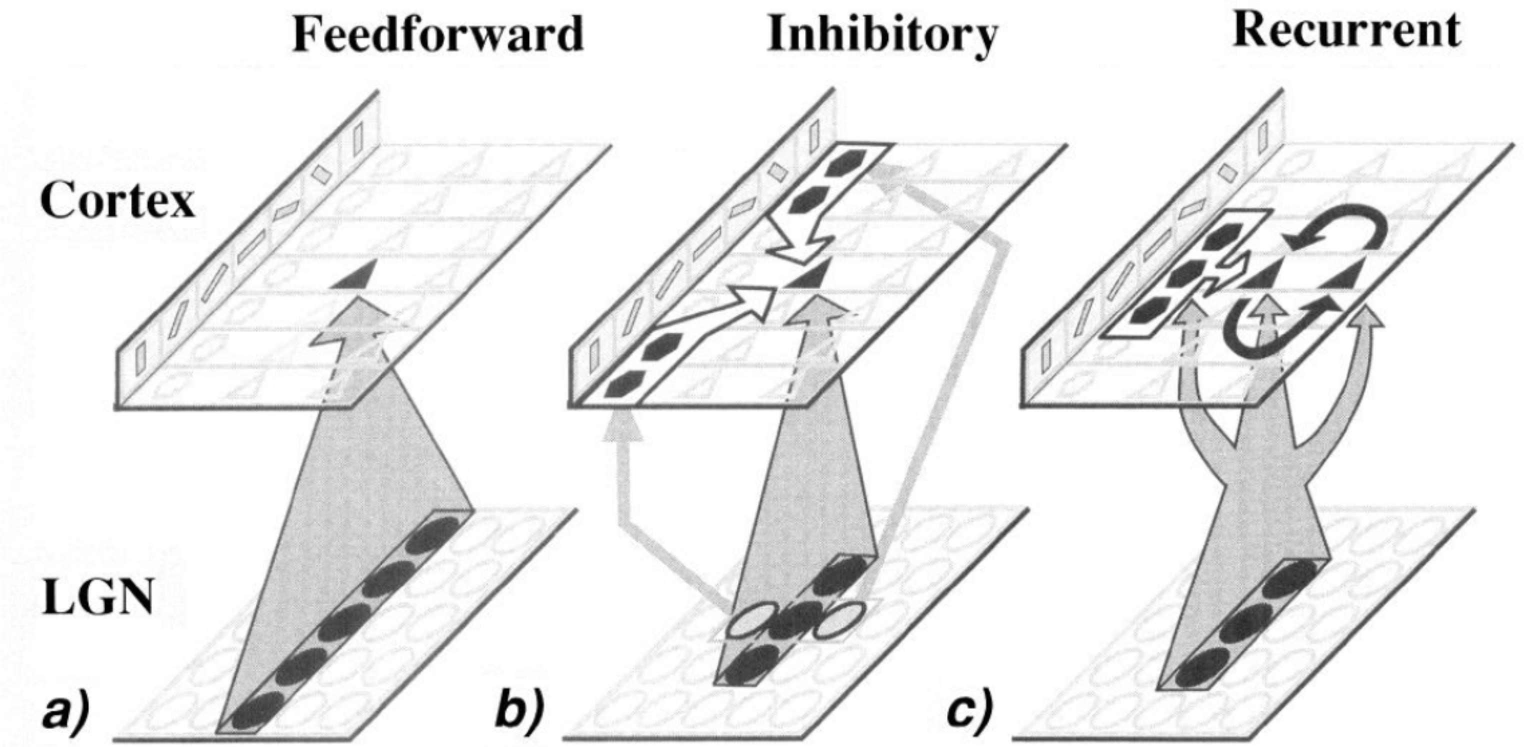
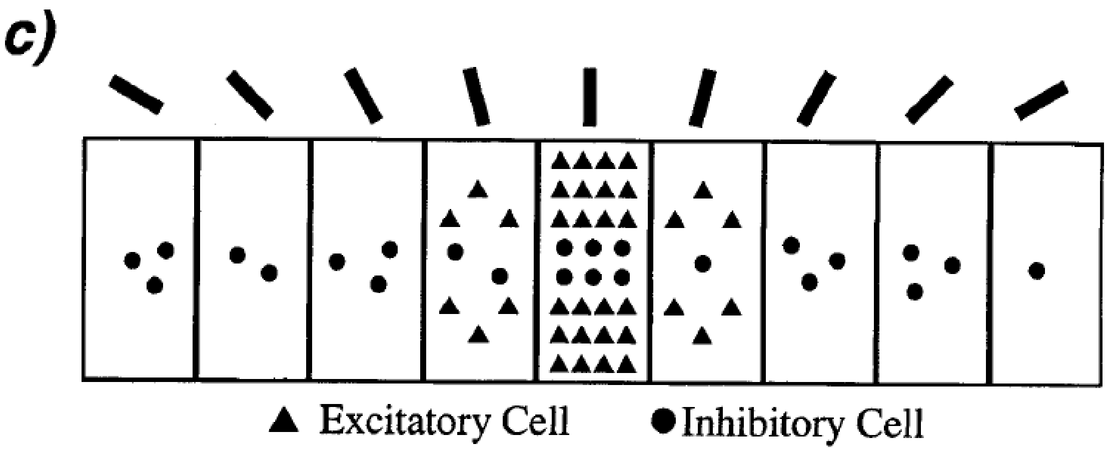


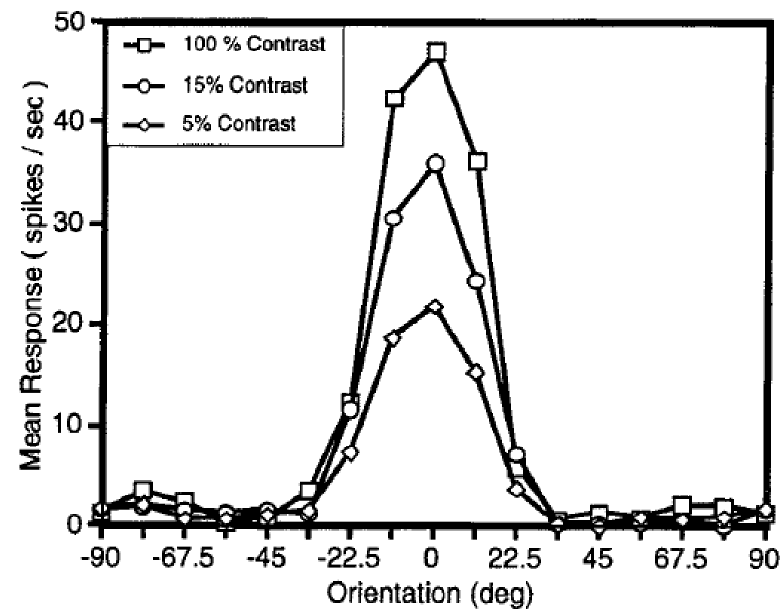
Figure 1. Models of visual cortical orientation selectivity. *a*, In feedforward models all "first-order" cortical neurons (*triangle*, excitatory; *hexagon*, inhibitory) receive converging input (*gray arrow*) from a population of LGN neurons that cover a strongly oriented region of visual space. The bandwidth or sharpness of a cortical cell's orientation tuning is determined by the aspect ratio of its LGN projection. *b*, Many inhibitory models employ a mild feedforward bias to establish the initial orientation preference of cortical neurons and utilize inhibitory inputs (*white arrows*), from cortical neurons preferring different orientations, to suppress nonpreferred responses. Here, we present a model, *c*, in which recurrent cortical excitation (*black arrows*) among cells preferring similar orientations, combined with iso-orientation inhibition from a broader range of orientations, integrates and amplifies a weak thalamic orientation bias, which is distributed across the cortical columnar population.

Somers et al. 1995

Role of inhibition in orientation selectivity:

Lateral inhibition: inhibition suppresses the response more in non-preferred orientations and thus narrowing the TC at high contrasts



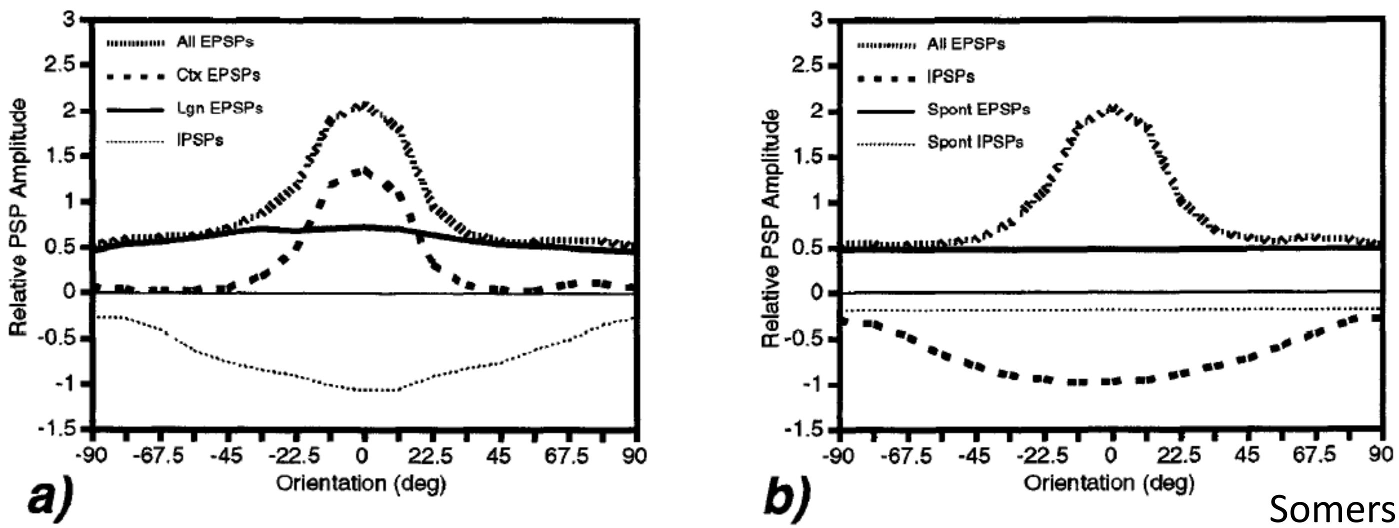


Somers et al. 1995

Recurrent models for orientation selectivity

There are two processes that sharpen thalamic inputs and allow contrast invariance:

1. Lateral inhibition at non-preferred orientations
2. Amplification of thalamic inputs by recurrent excitatory connections

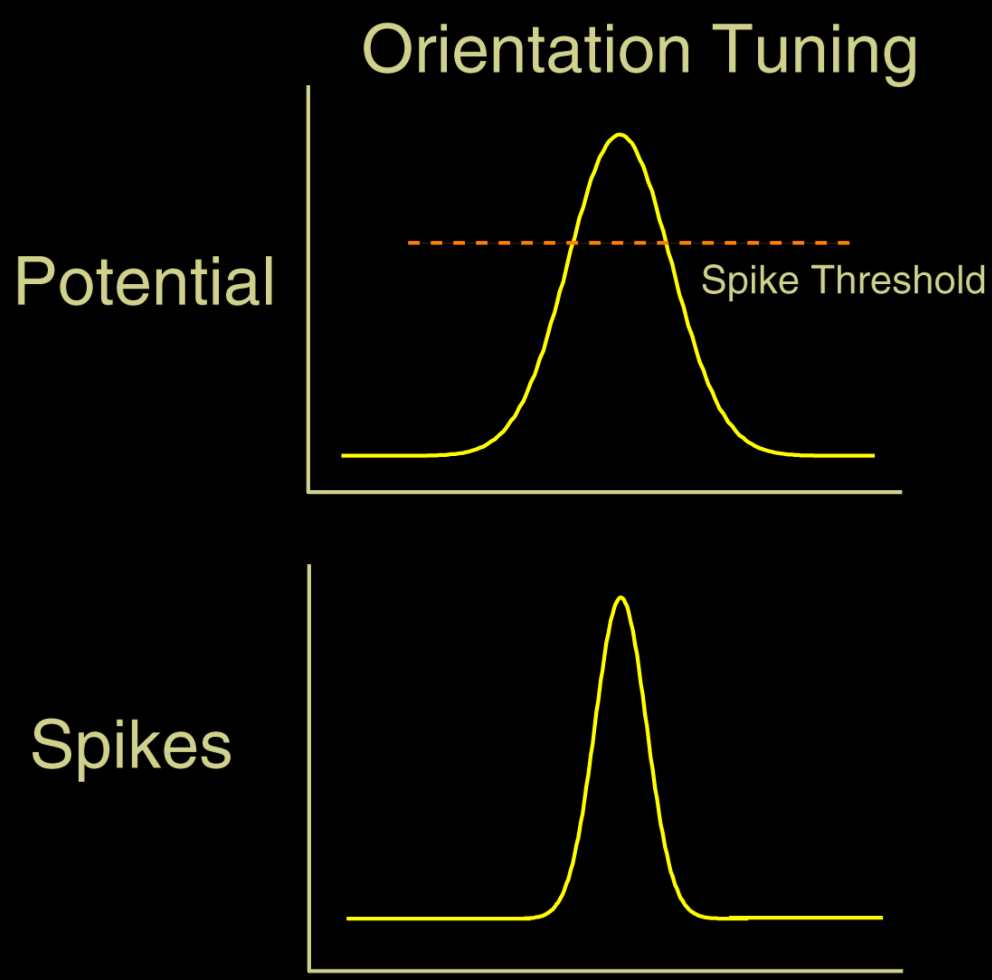


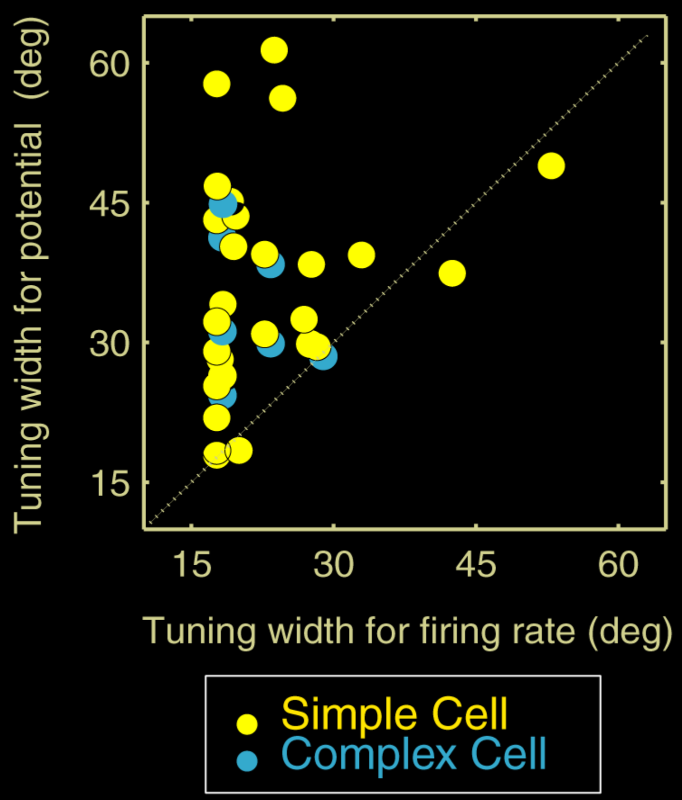
Somers et al. 1995

Figure 4. Orientation tuning of postsynaptic potentials. *a*, Postsynaptic potentials evoked in the example cell by thalamic excitatory, cortical excitatory, and cortical inhibitory synaptic inputs. LGN EPSPs were very broadly tuned. IPSPs were strongest at the preferred orientation (0°) and weakest at the cross-orientation (90°). Cortical EPSPs provided the strongest orientation-selective input. Net EPSPs were, therefore, well-tuned for 0° stimuli. *b*, Averaged EPSP and IPSP inputs for all excitatory (n = 84) cells in the 0° column. Both EPSPs and IPSPs were largest in response to stimuli of the preferred orientation. Cross-orientation stimuli evoked IPSPs that were only mildly stronger than spontaneously evoked (no stimulus) IPSPs. All PSPs were scaled by $g_{leak}/(1000\ C_m)$.

Prediction: the width of TC inhibition should be wider than for excitation TC
We will see if this is true later…

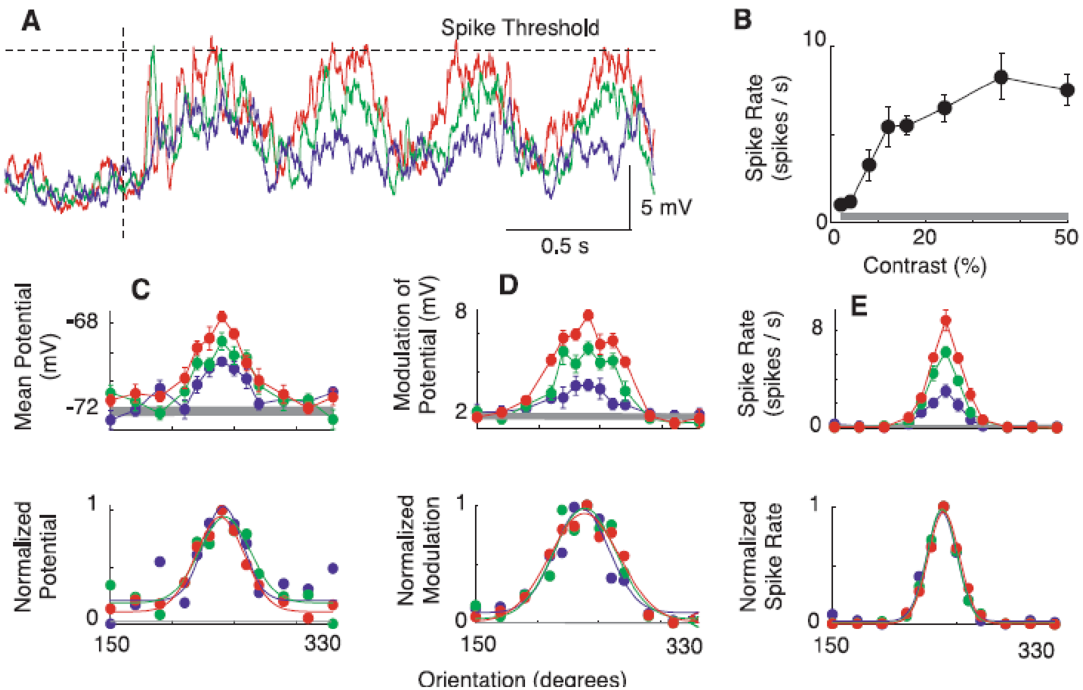
The Iceberg Effect

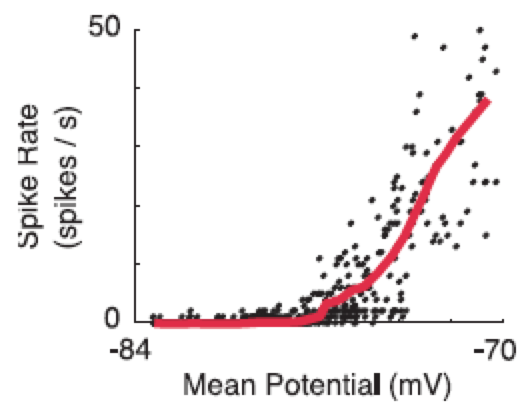




Experiments that support the H&W – intracellular recording data. The role of noise in contrast invariance

1. Contrast invariance

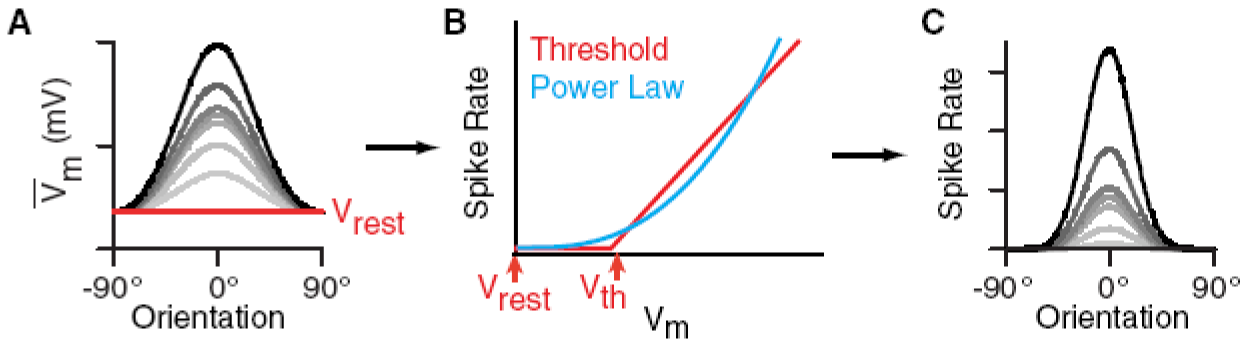




Anderson et al. 2000

Experiments that support the H&W – intracellular recording data. The role of noise in contrast invariance

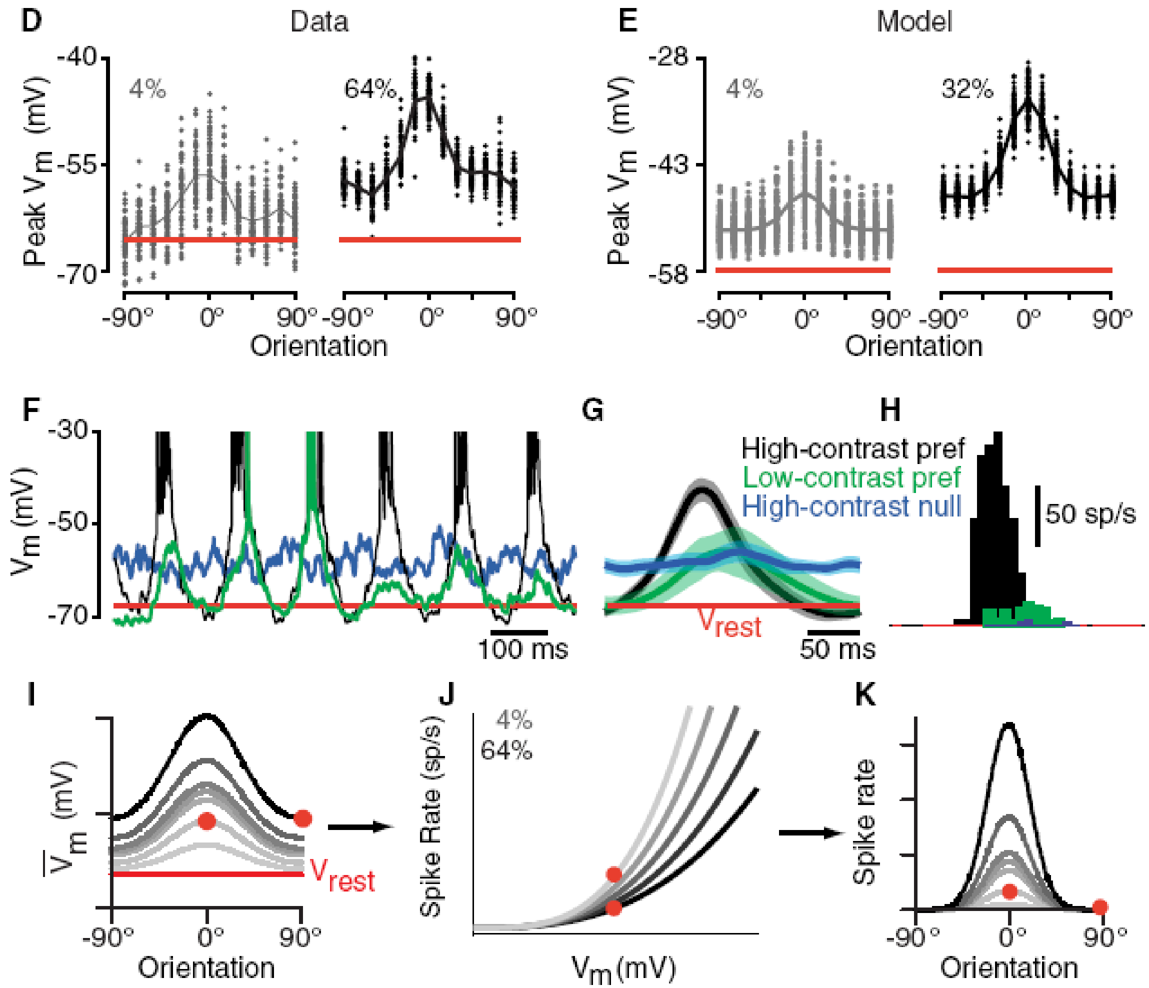
1. Contrast invariance



Priebe and Ferster 2012

Experiments that support the H&W :
The role of noise in contrast invariance

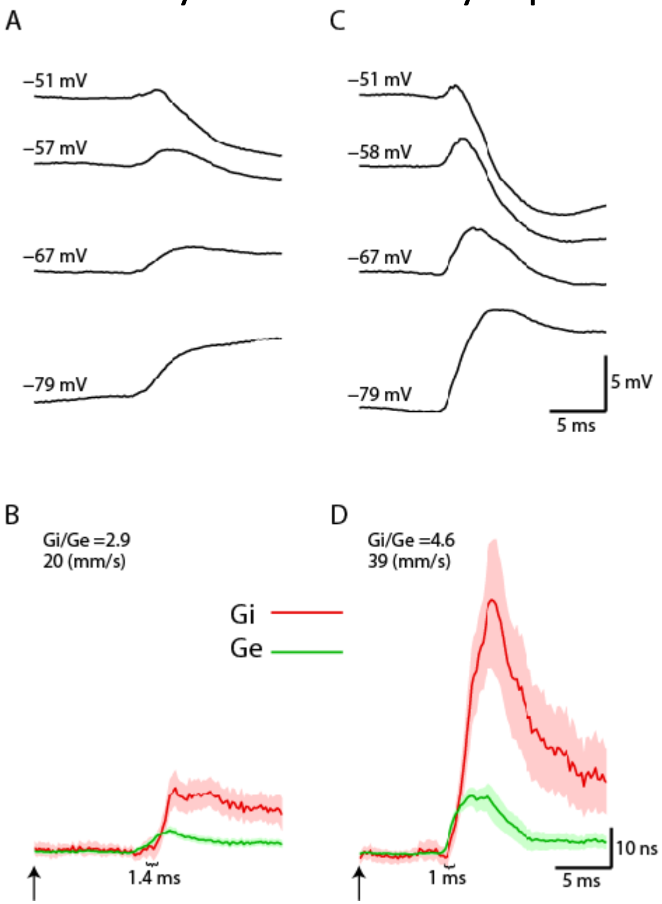
1. Contrast invariance



Priebe and Ferster 2012

Experiments that support the H&W – measurements of sensory evoked conductance in-vivo

2. TC of excitatory and inhibitory inputs



$$c\frac{dV}{dt} = -G_l(V - E_{rest}) - G_i(V - E_i) - G_e(V - E_e) + I$$

Synaptic current

Ei ~= -80 mV
Ee~ = 0 mV

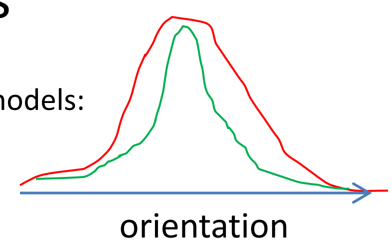
Heiss et al. 2008

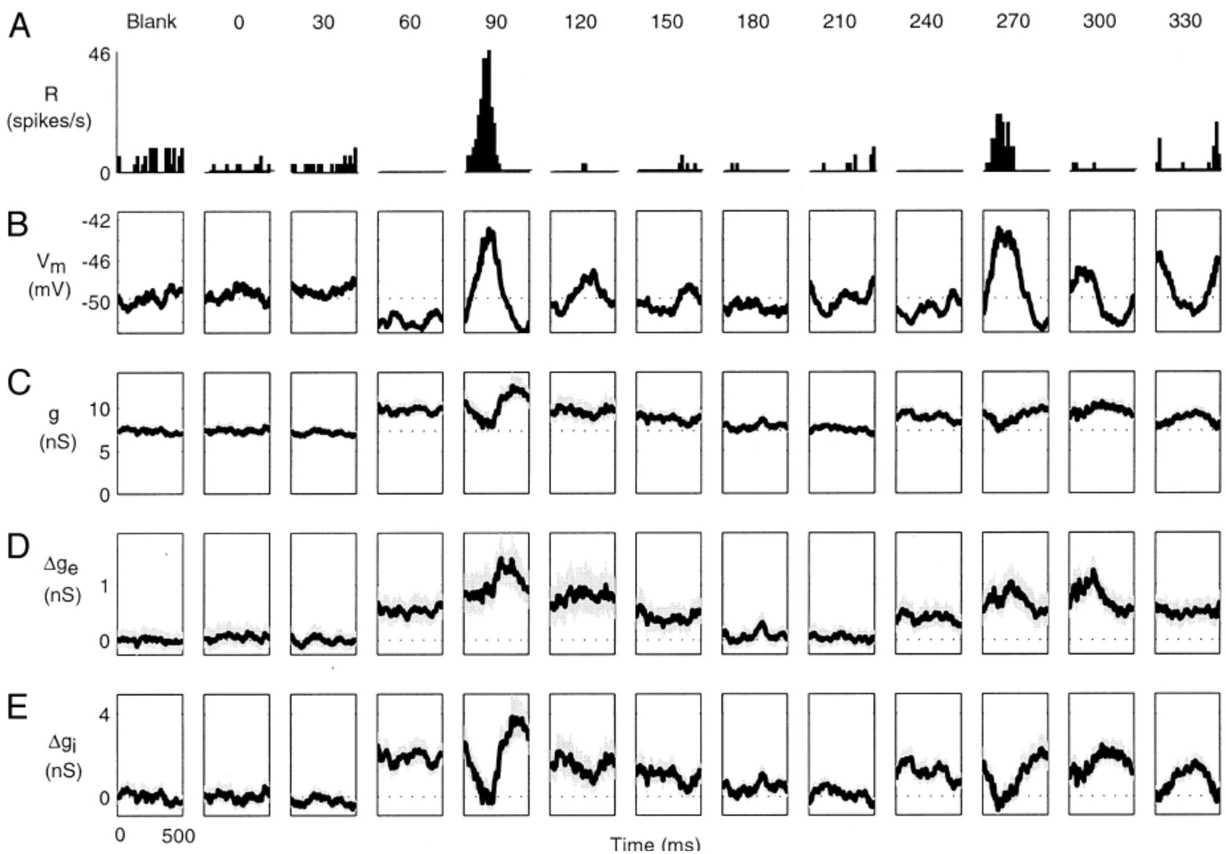
Experiments that support the H&W – Excitatory and inhibitory inputs have similar TC

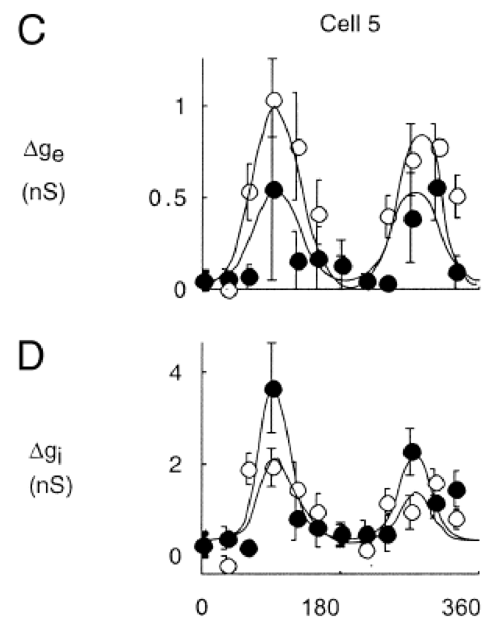
Hence: inhibition is unlikely to sharpen thalamic inputs

2. TC of excitatory and inhibitory inputs

Prediction from recurrent models:







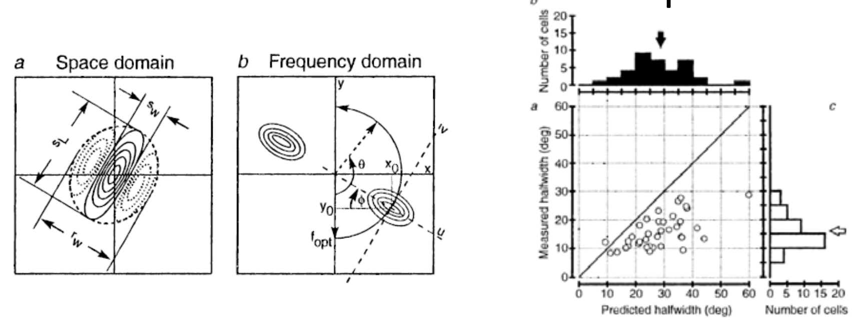
*The width of inhibition TC is not wider than for excitation

Anderson et al. 2000

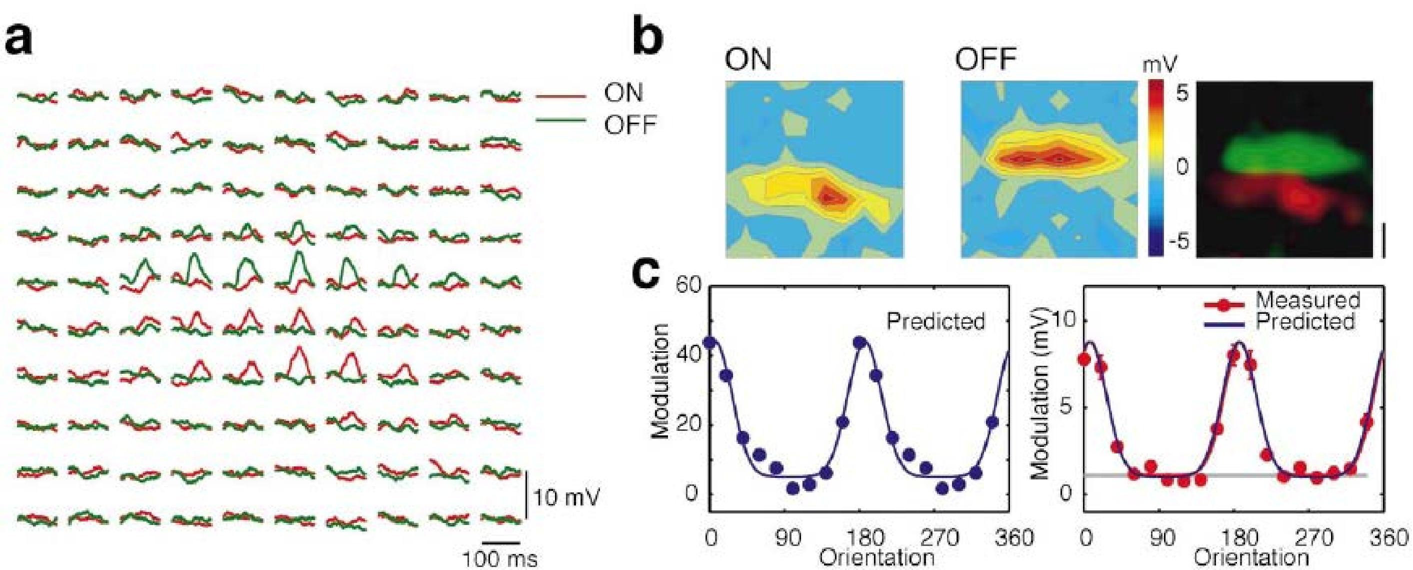
Experiments that support the H&W – Mismatch of receptive field maps and orientation tuning.

Intracellular data show why TC and RF do not match at spikes level - this is because of the iceberg effect. At Vm level they nicely match

Spikes data



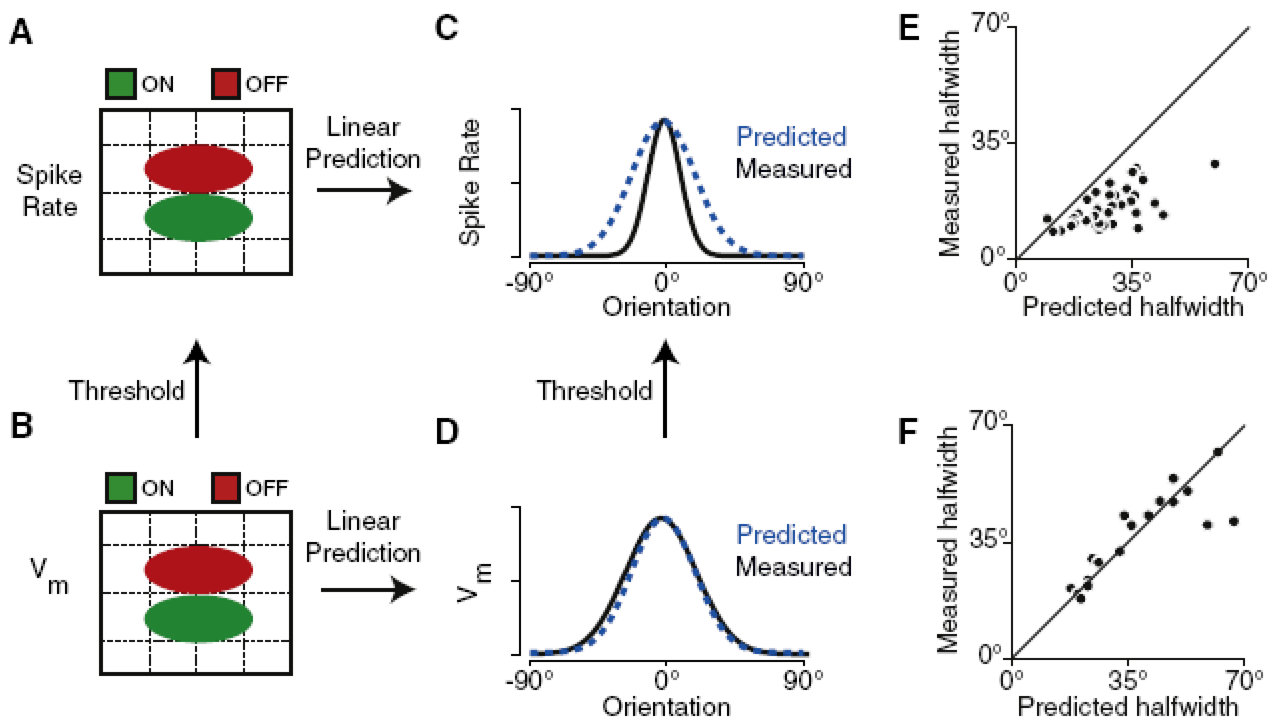
Vm data



Lampl et al. 2001

Experiments that support the H&W – Mismatch of receptive field maps and orientation tuning.

Intracellular data show why TC and RF do not match at spikes level - this is because of the iceberg effect. At Vm level they nicely match



Priebe and Ferster 2012

Experiments that support the H&W – Cross-orientation suppression

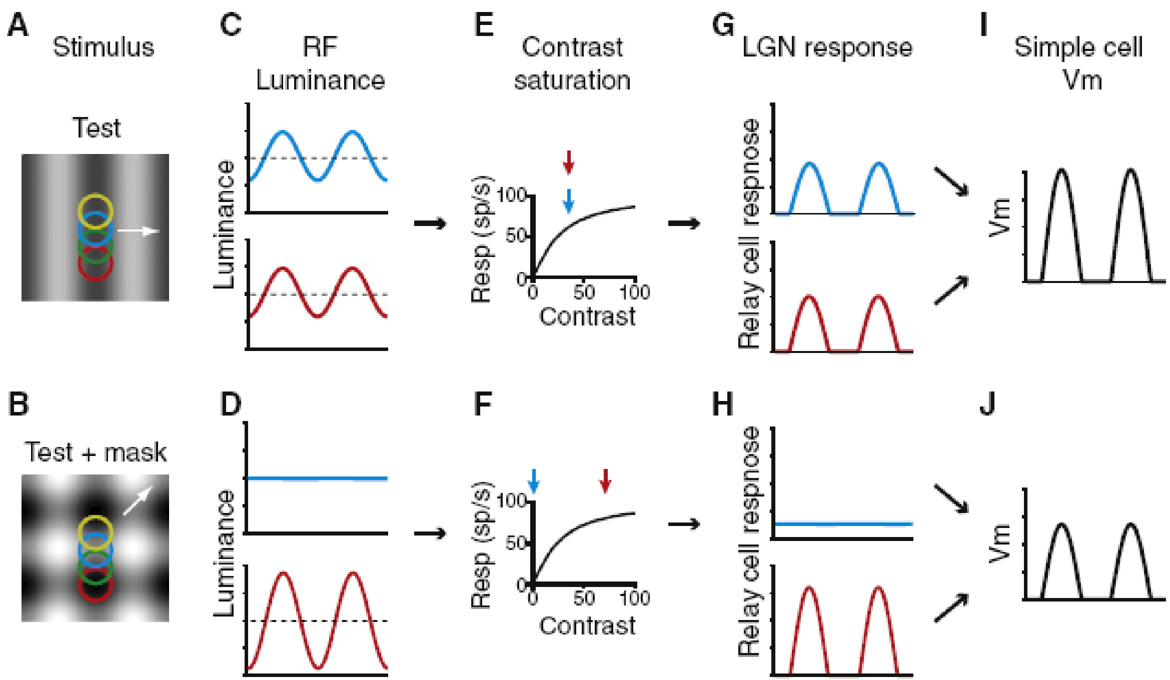
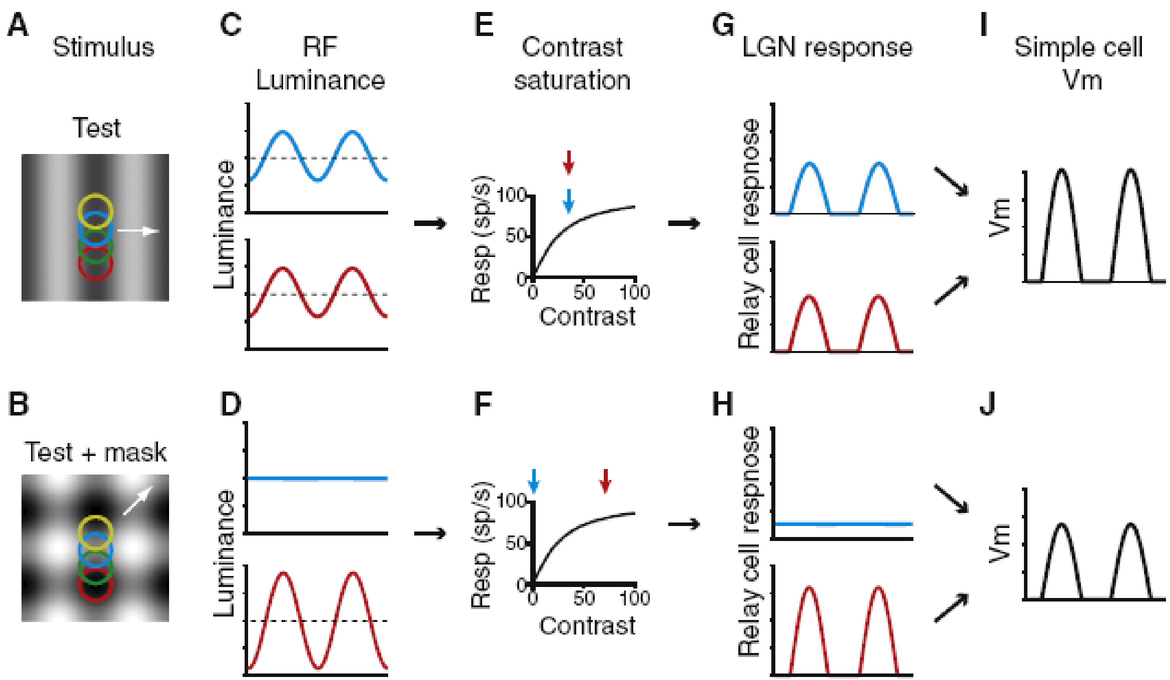


Figure 2. Cross-orientation Suppression in a Feedforward Model of Visual Cortex
(A and B) The spatial receptive fields of LGN relay cells (colored circles) are superimposed on top of a 32% contrast vertical grating (A) or a plaid composed of 32% horizontal and vertical gratings (B).
(C and D) Stimulus luminance is plotted as a function of time for two LGN relay cells, indicated by color (C, grating; D, plaid).
(E and F) The contrast response curve of LGN relay cells. The arrows indicate the contrast passing over each relay cell's receptive field (E, grating; F, plaid).
(G and H) The modeled responses of the relay cells based on the contrast passing over their receptive fields include both saturation and rectification (G, grating; H, plaid).
(I and J) The average input to a target V1 simple cell. The average relay cell input is about 10% less for the plaid stimulus (I) than for the grating stimulus (J).

Priebe and Ferster 2012

1. Experiments that support the H&W – Cross-orientation suppression



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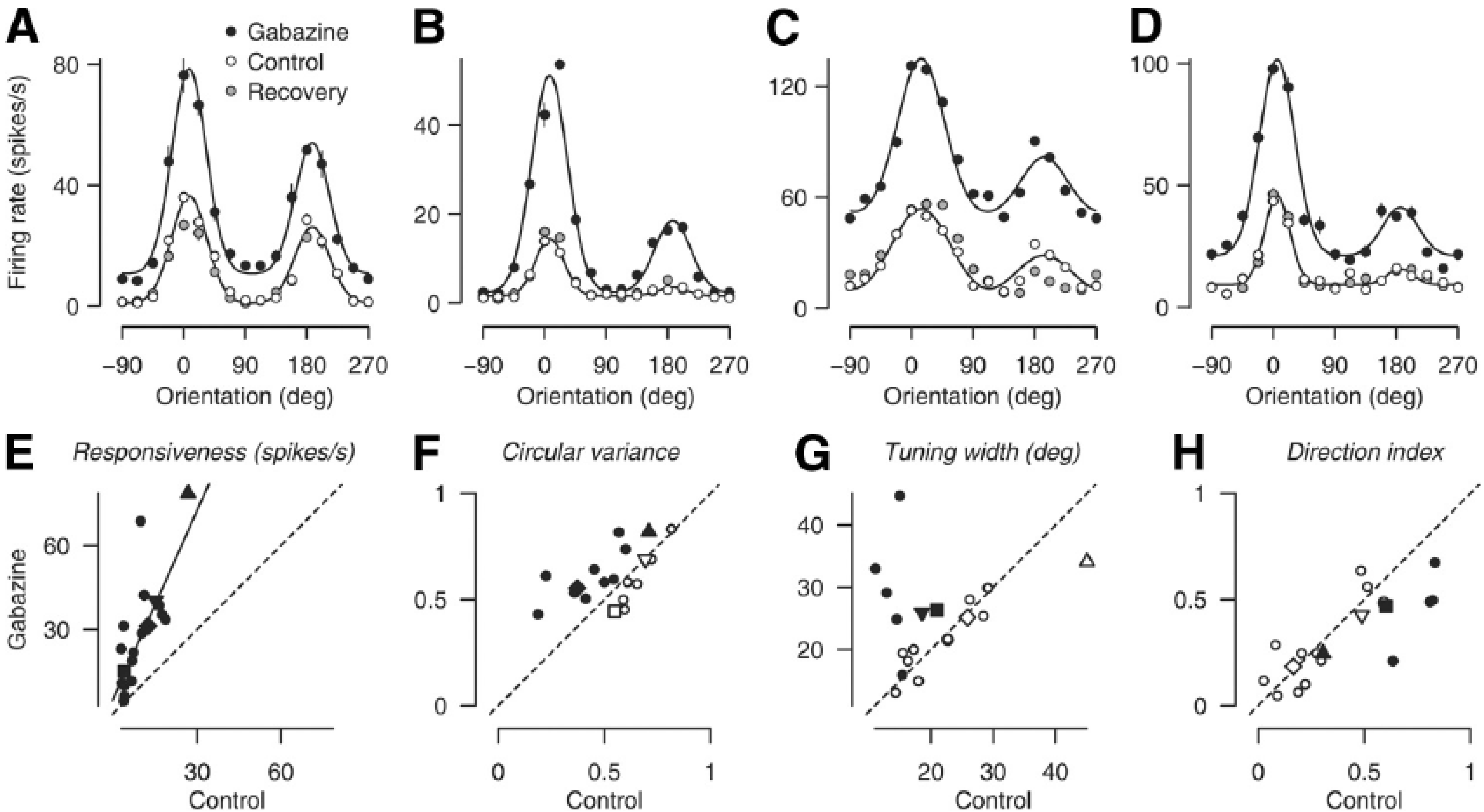
Priebe and Ferster 2012

Experiments that support the H&W:
New insights on the pharmacological effects on TC



Katzner et al. 2011

Experiments that support the H&W:
New insights on the pharmacological effects on TC – the iceberg effect

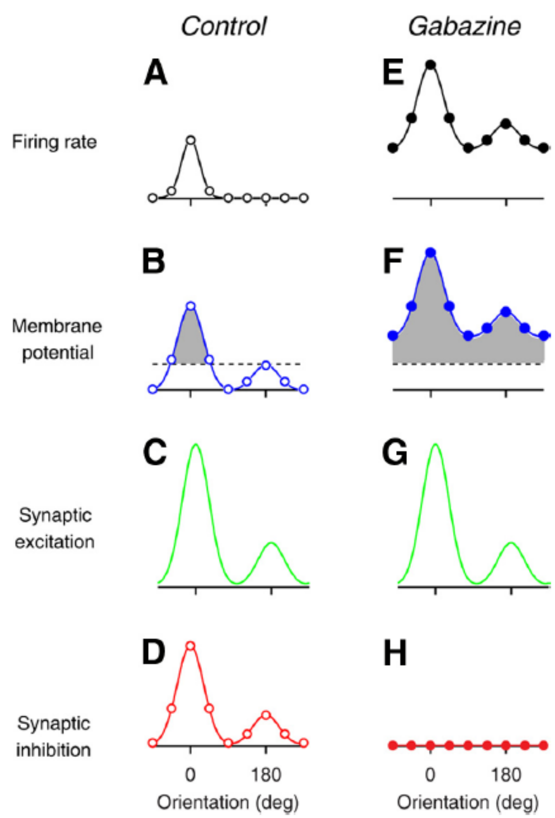
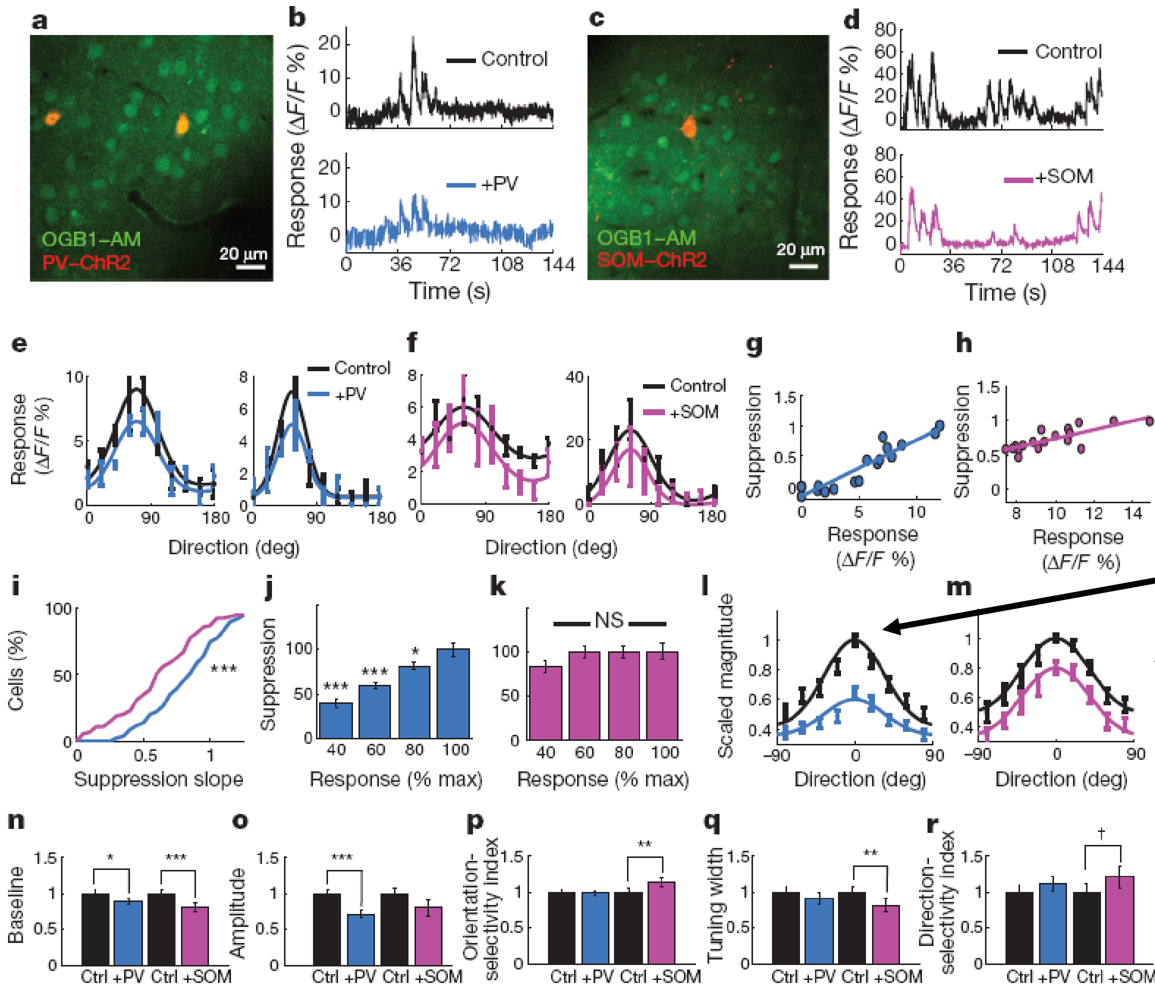


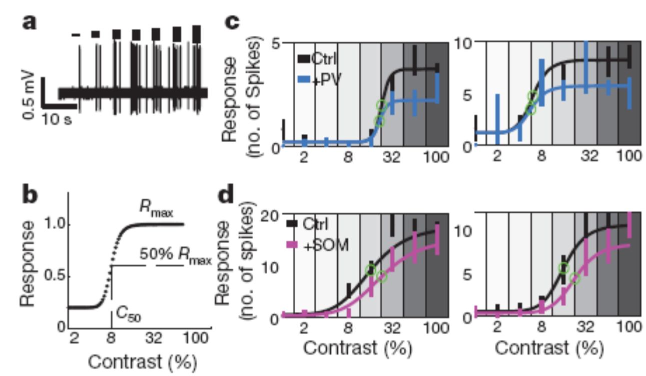
Figure 7. A simple cellular model. ***A***, Tuning of firing rate in control condition. ***B***, Corresponding tuning of membrane potential responses. Dashed line indicates threshold. Shaded area indicates responses that elicit nonzero firing rates. ***C***, Tuning of excitation. ***D***, Tuning of inhibition, under the simplified assumption that inhibition has the same tuning as excitation (matching inhibition). In the untuned inhibition version of the model, this curve would be flat. ***E–H***, Same, under gabazine.

Katzner et al. 2011

Two Photon (2P) Imaging and optogenetic studies of the visual cortex

1. Contrast invariance





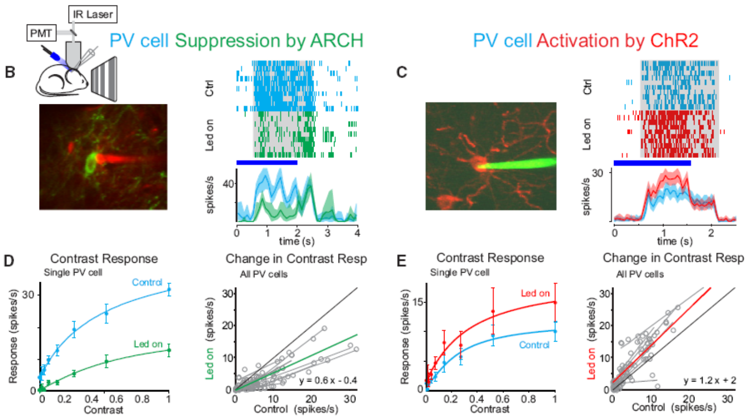
Divisive

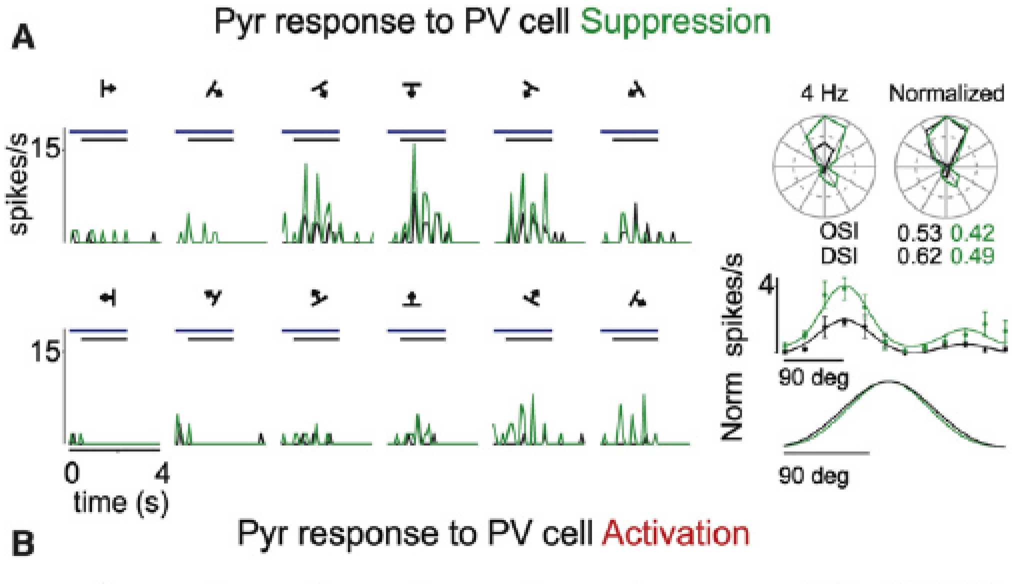
Subtraction

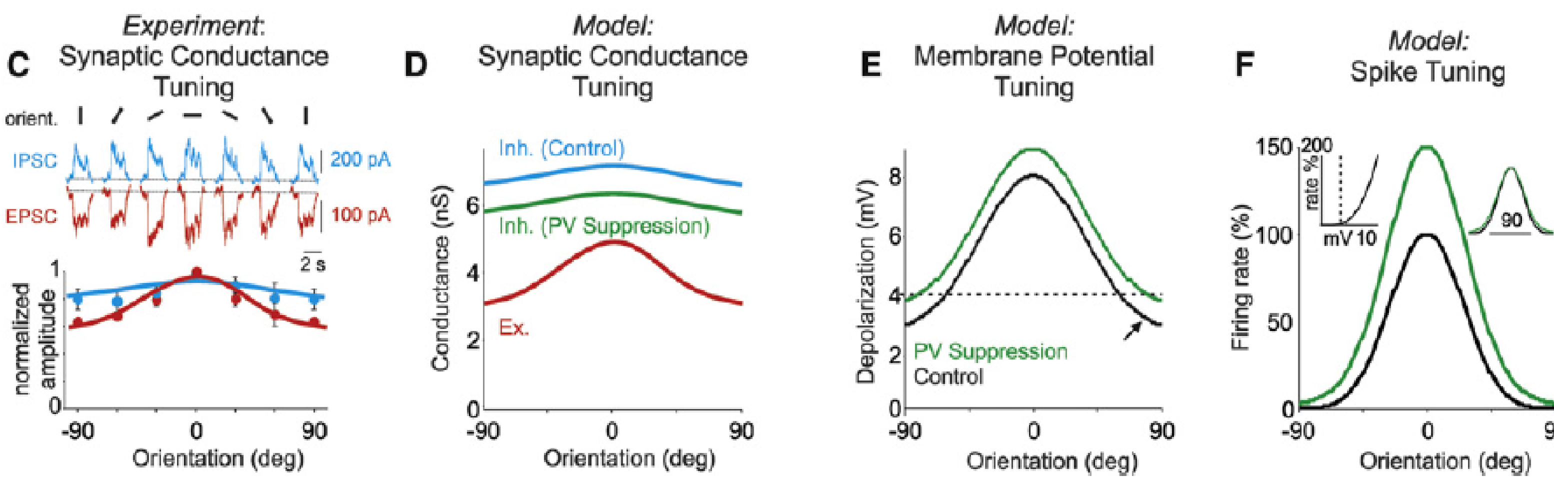
Wilson et al. 2012

Optogenetic studies of the visual cortex

1. Contrast invariance

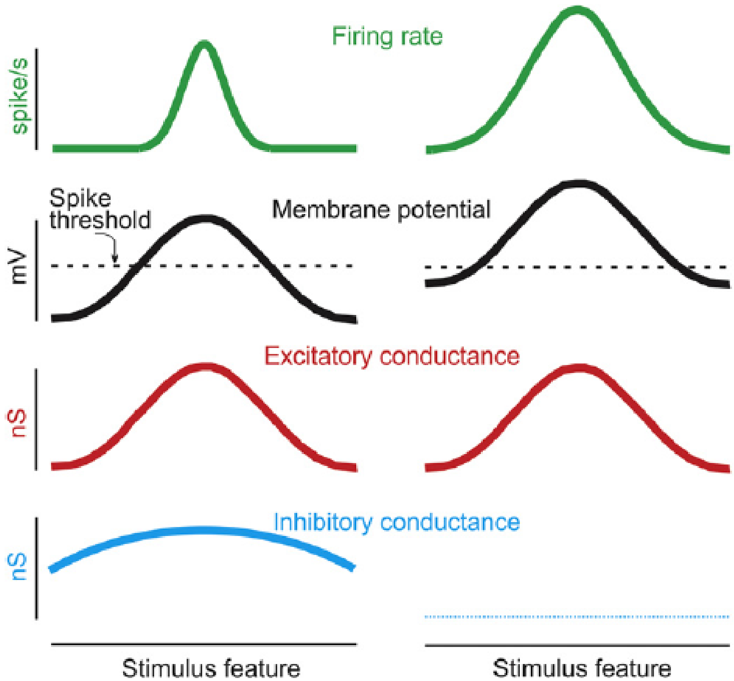






Attalah et al. 2012

Recurrent models for orientation selectivity



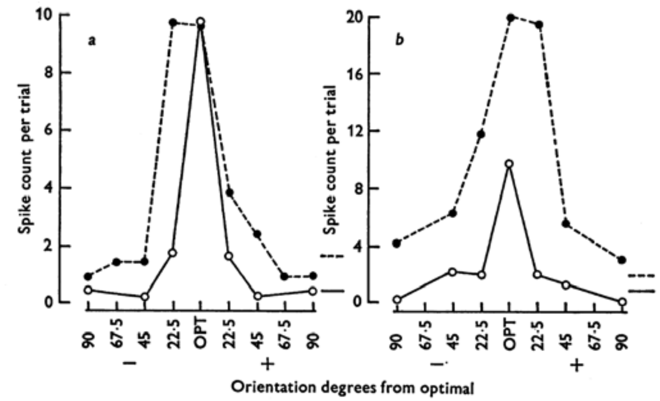


Figure 4. Inhibition Sharpens Stimulus Selective Spike Output via the "Iceberg Effect"

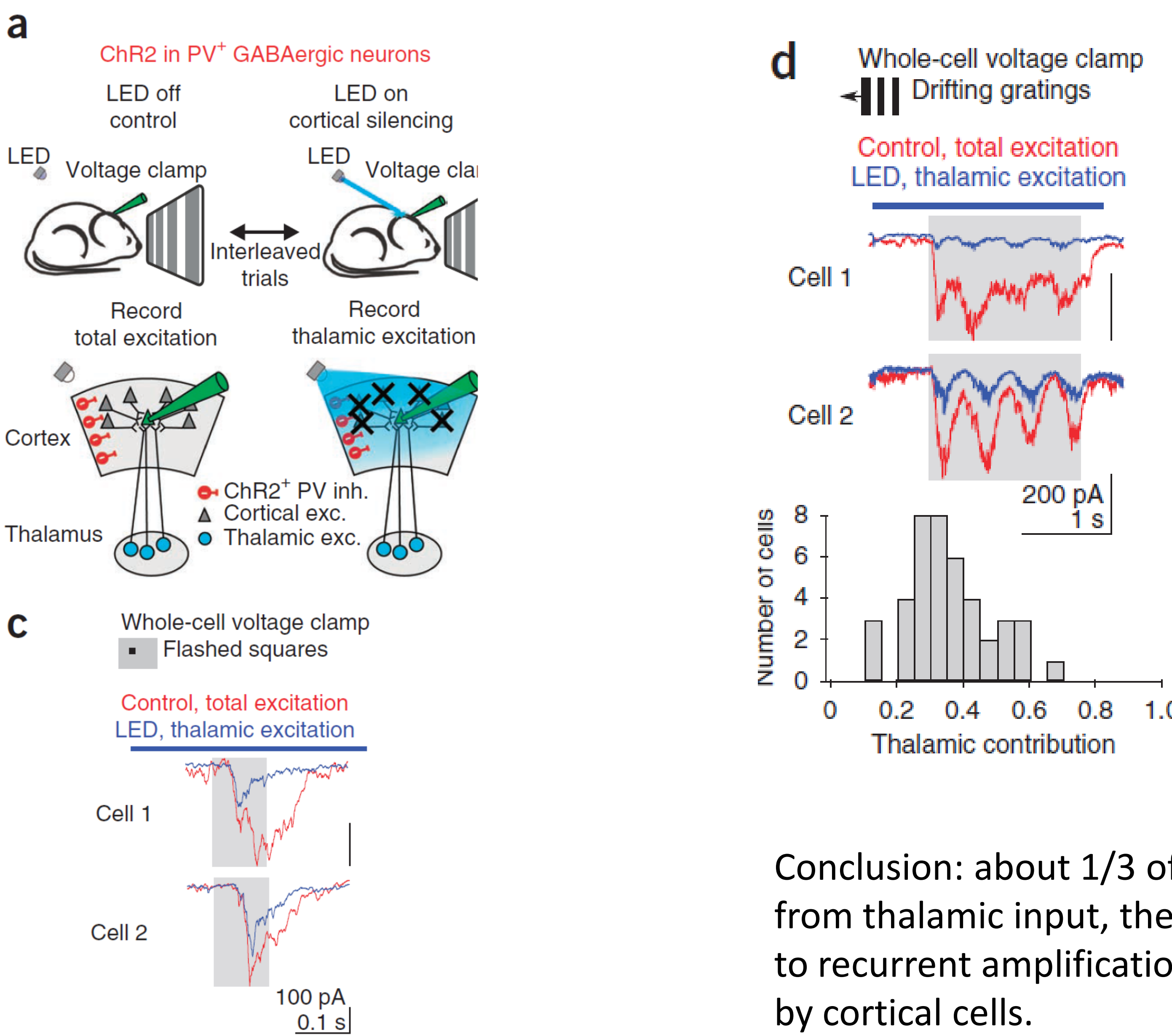
Schematic illustrates hypothetical tuning curves for firing rate (green), membrane potential (black), excitatory (red), and inhibitory (blue) conductances of a cortical neuron to stimulus features (e.g., orientation). Action potential firing occurs only when membrane potential exceeds a fixed spike threshold (dotted line). Responses are shown in the presence (left) and absence (right) of a weakly tuned inhibitory conductance. Inhibition leads to more narrowly tuned spike output by allowing only the strongest (preferred) excitatory stimuli to drive the membrane potential above spike threshold.

Issacoson and Scanziani 2011

Optogenetic studies of the visual cortex

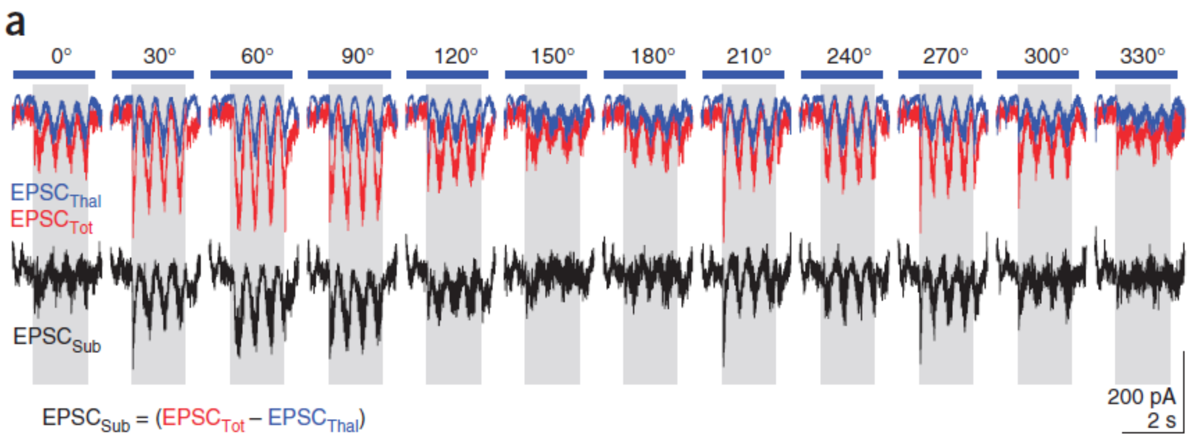
Lien and Scanziani, 2013

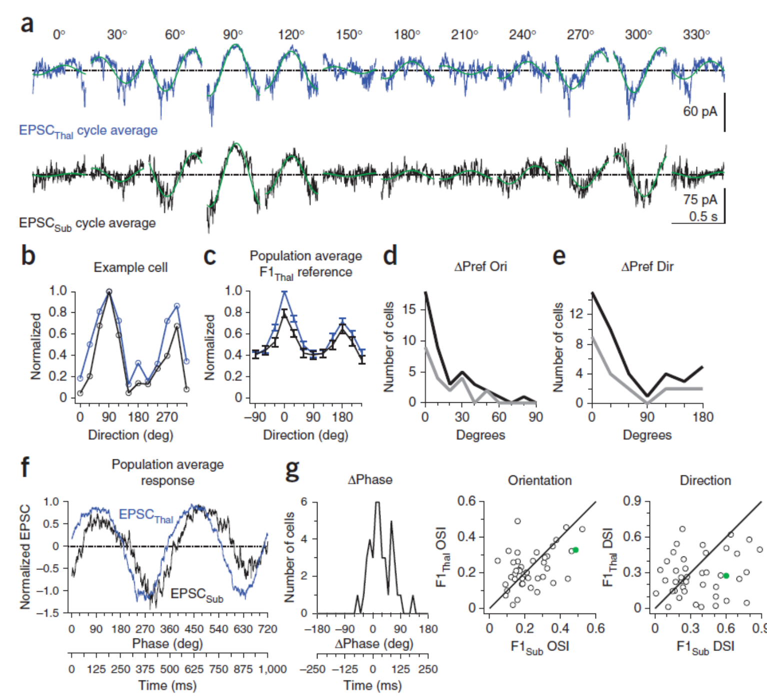
To find the tuning of thalamic inputs they silenced cortical firing while patching layer 4 cells of V1



Conclusion: about 1/3 of E in cortex comes from thalamic input, the other 2/3 is due to recurrent amplification of these input by cortical cells.

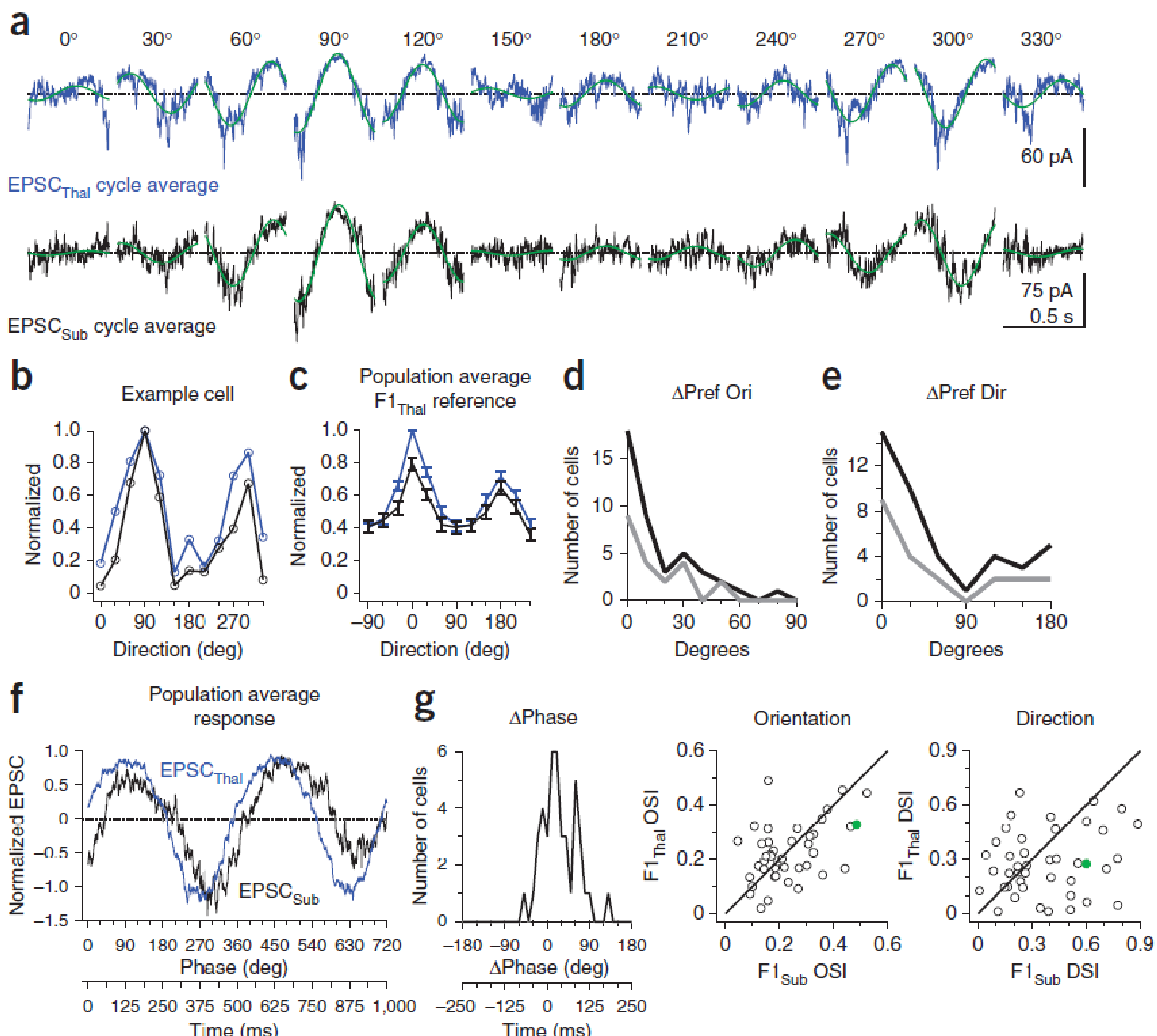
Cortical circuits amplify tuned thalamic inputs without altering orientation selectivity





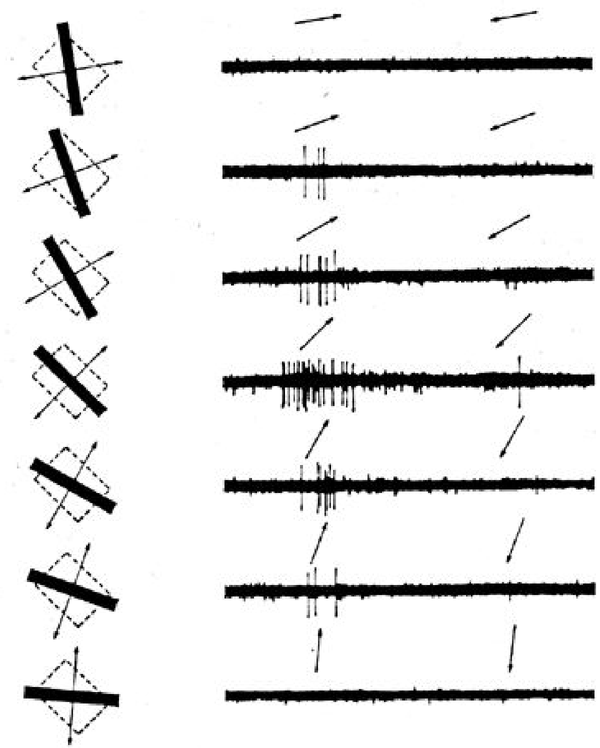
Cortical circuits amplify tuned thalamic inputs without altering orientation selectivity

The TCs of cortical inputs are similar to the TCs of thalamic inputs



Direction selectivity in V1

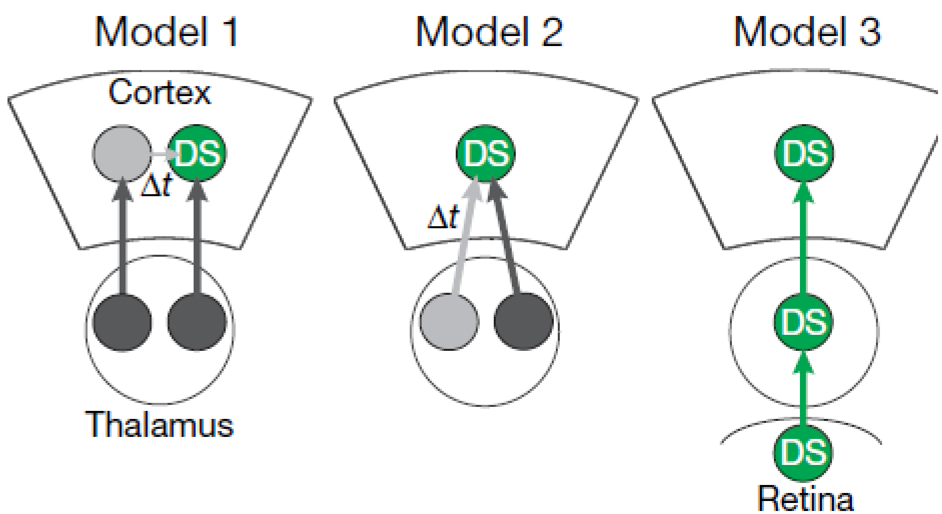
V1 physiology:
direction
selectivity



From H&H

Direction selectivity in V1

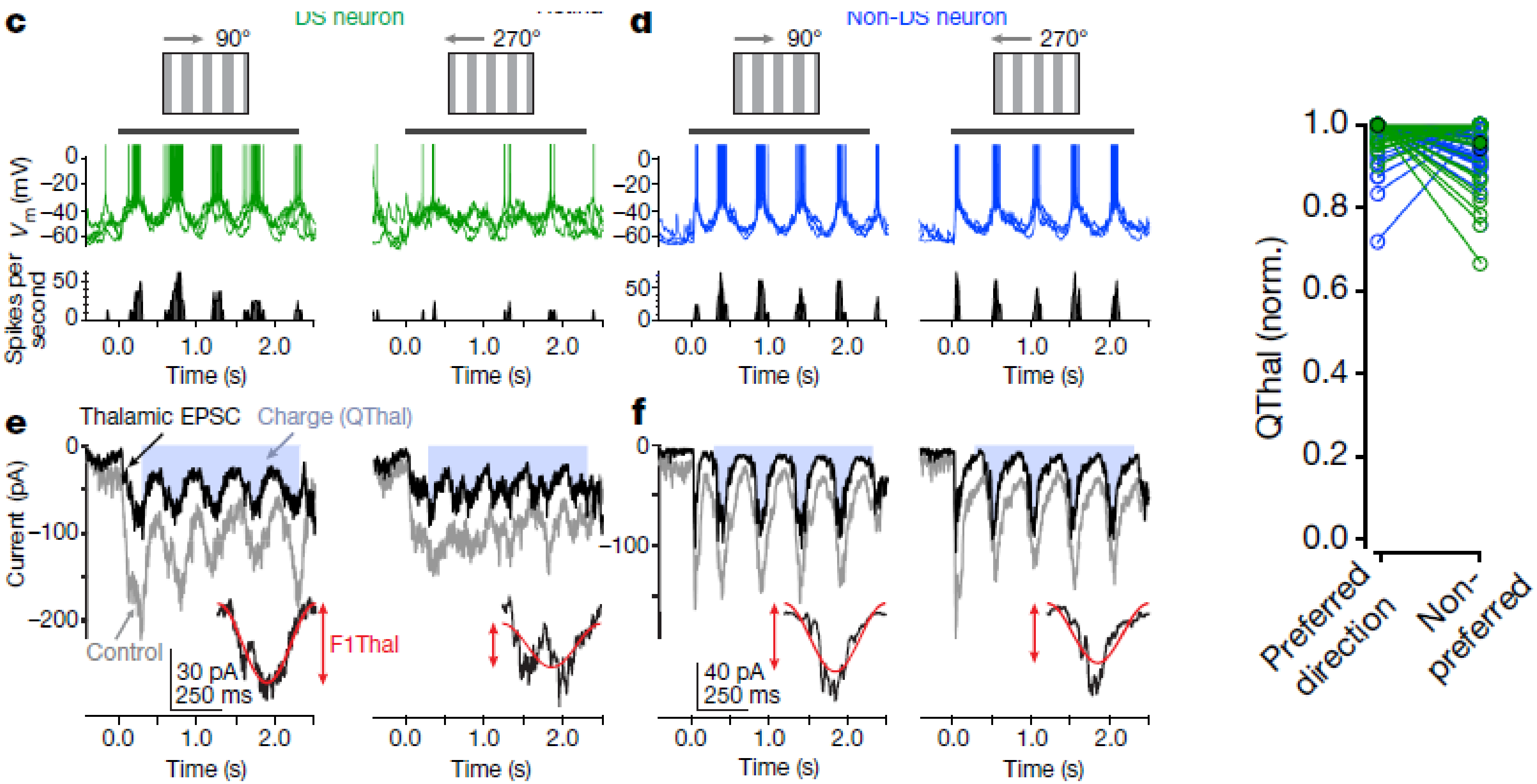
Intracortical TC Convergence Retina



Lien and Scanziani 2018

Direction selectivity in V1

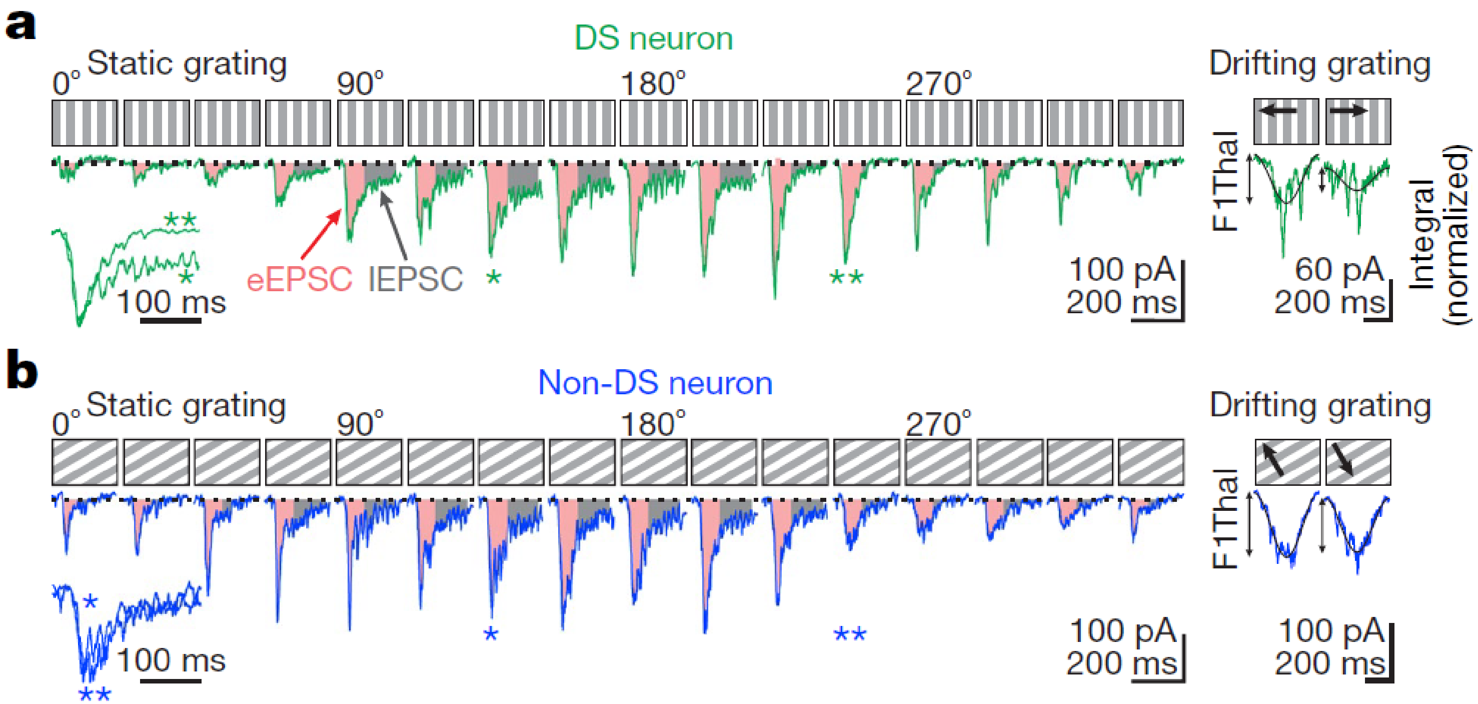
Isolation of thalamic inputs of L4 cells in PV-ChR2 cells (cortical silencing)



Thalamic input is also direction selective!   Lien and Scanziani 2018

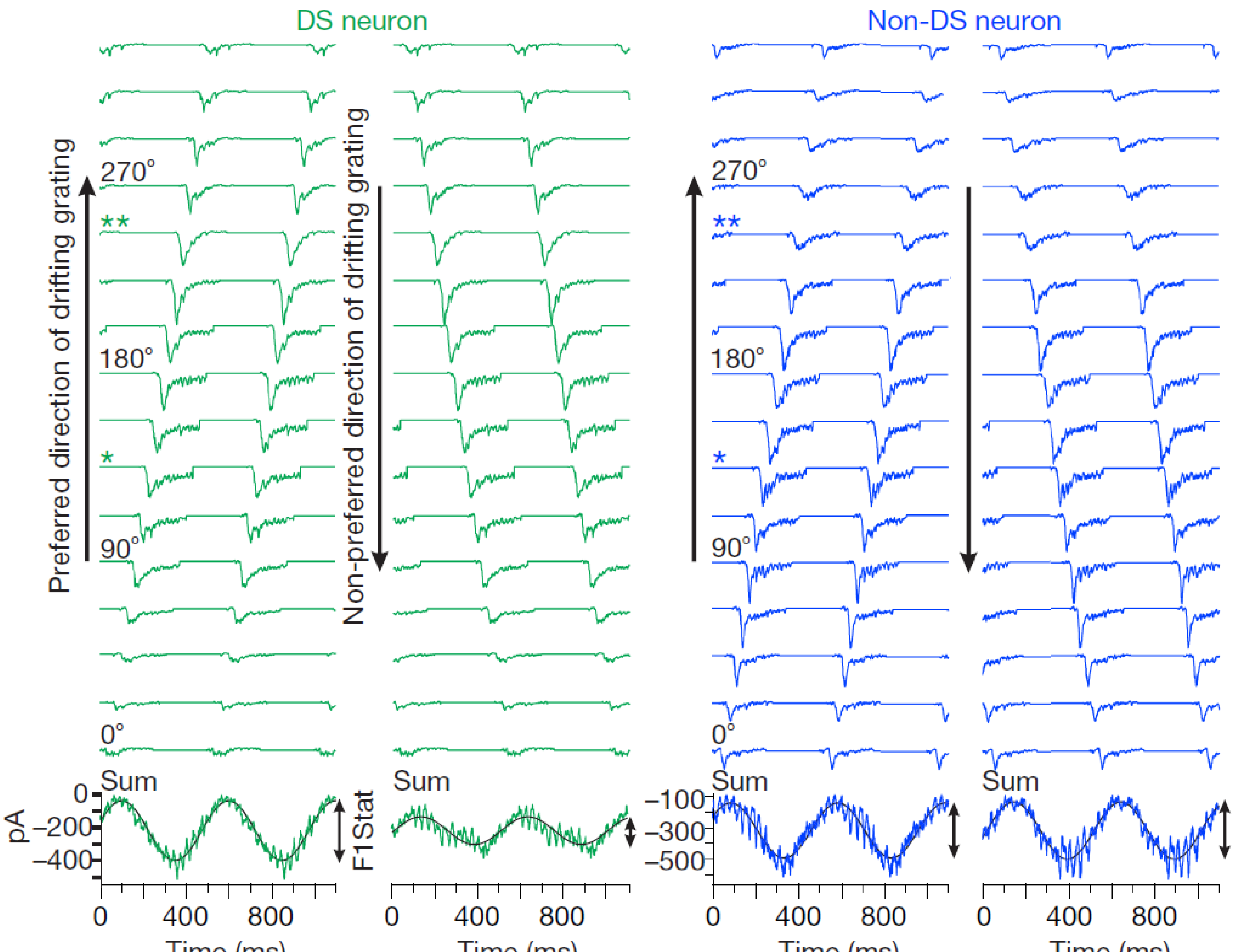
Direction selectivity in V1

Static stimulation at different spatial phases shows that TC component of DS cells exhibits two components:
fast decaying response (eEPSP) and late (slow) response (lEPSP) and in non-DS there is only one type of response.



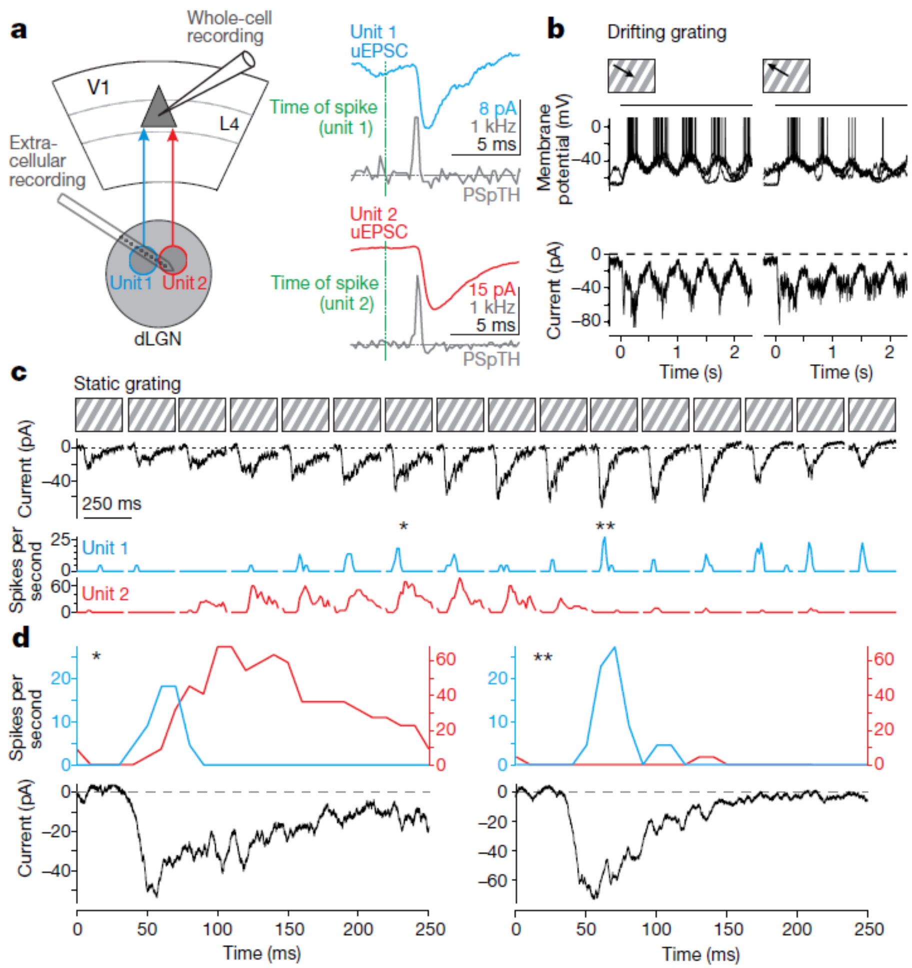
Direction selectivity in V1

Simulation of summation



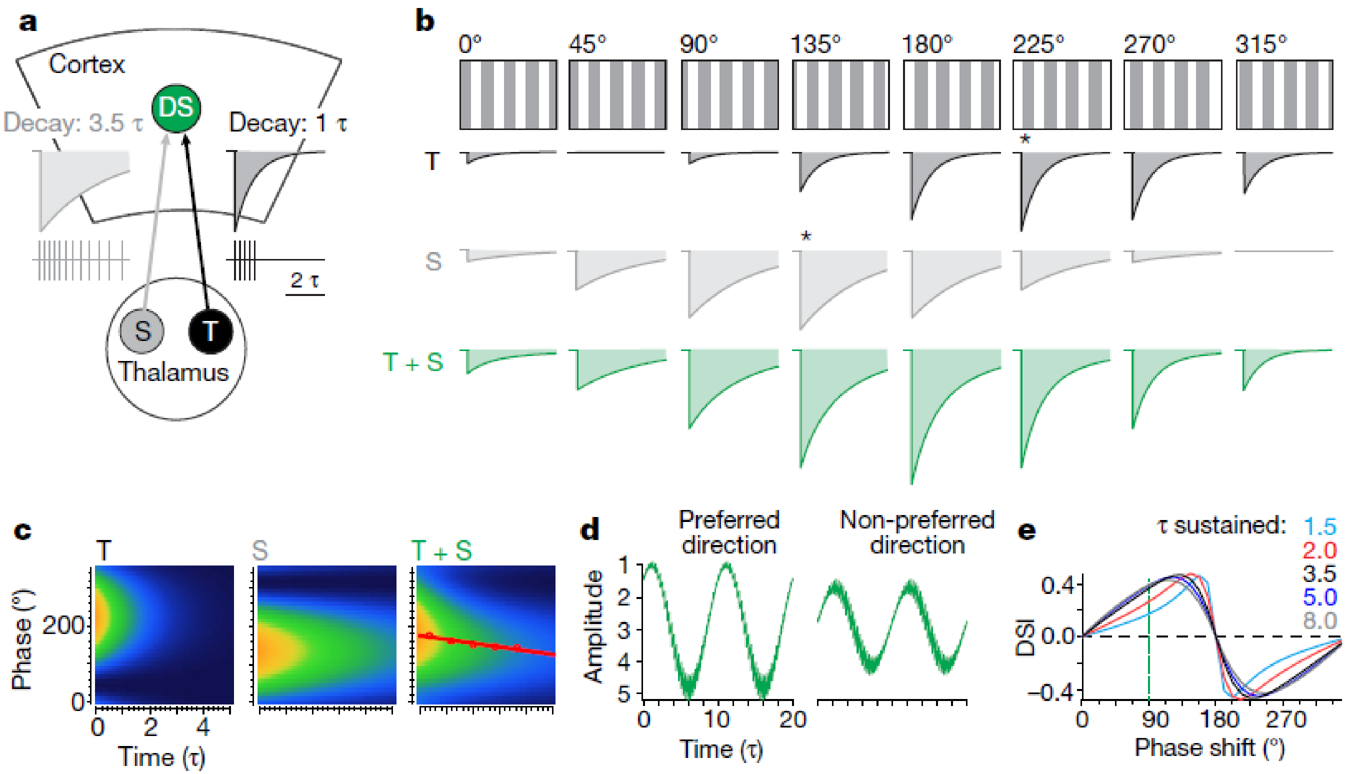
Direction selectivity in V1

Recordings in thalamus with cortical recordings.
Two types of TC cells: 1) transient firing at certain phases (blue unit). 2) sustain firing at other phases (red unit).



Direction selectivity in V1

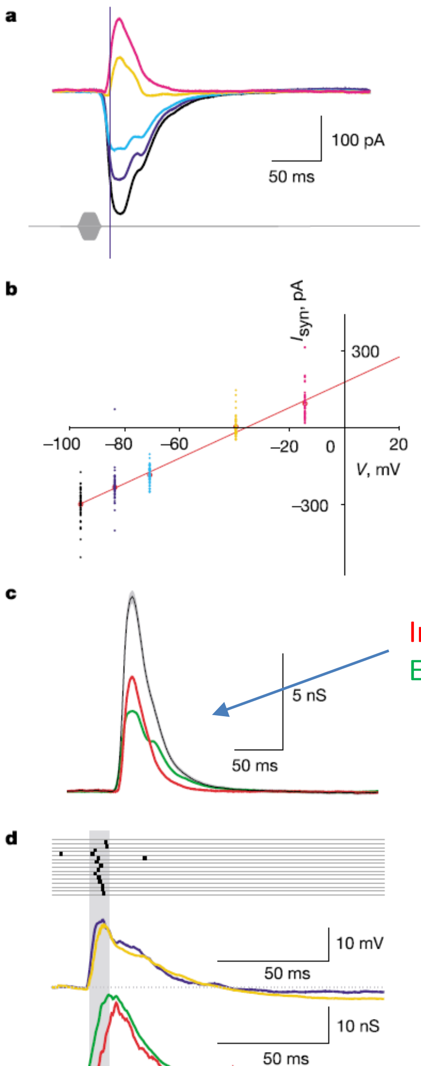
Model of thalamo-cortical convergence for DS of cortical cells.



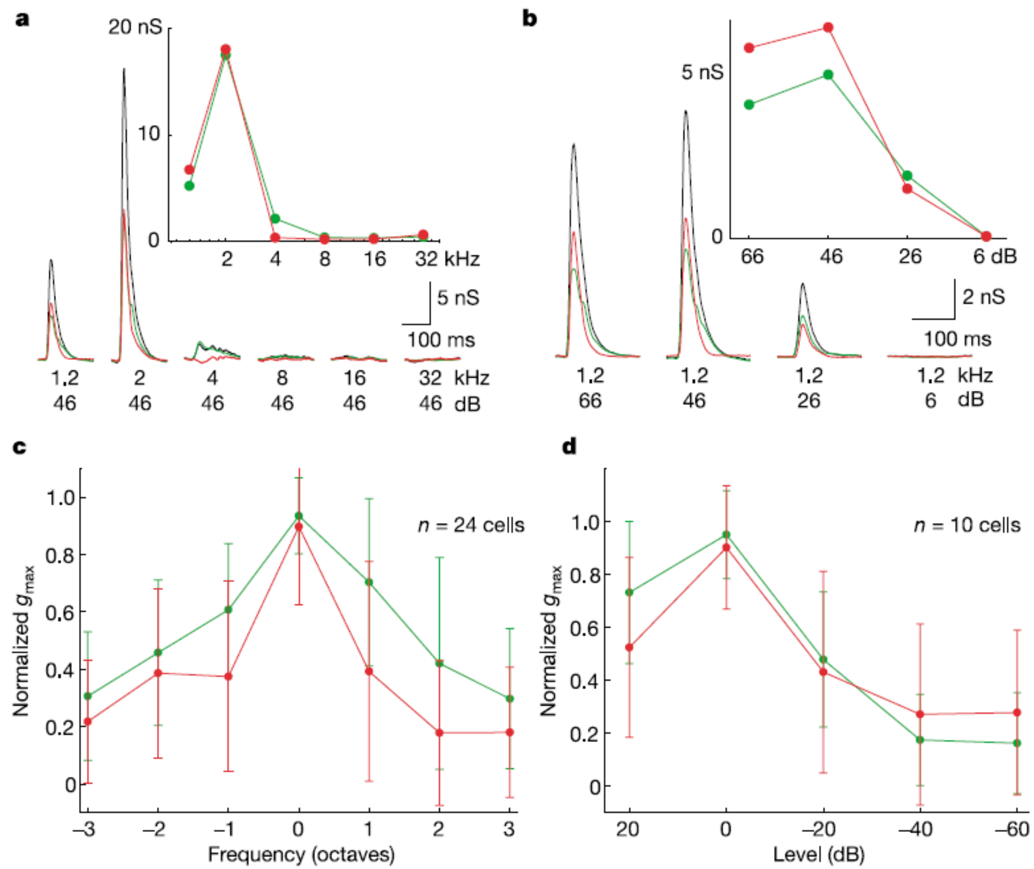
Auditory cortex – Excitation and inhibition are co-tuned to sound intensity and frequency

1. Inhibition?

Voltage clamp experiments of A1 neurons

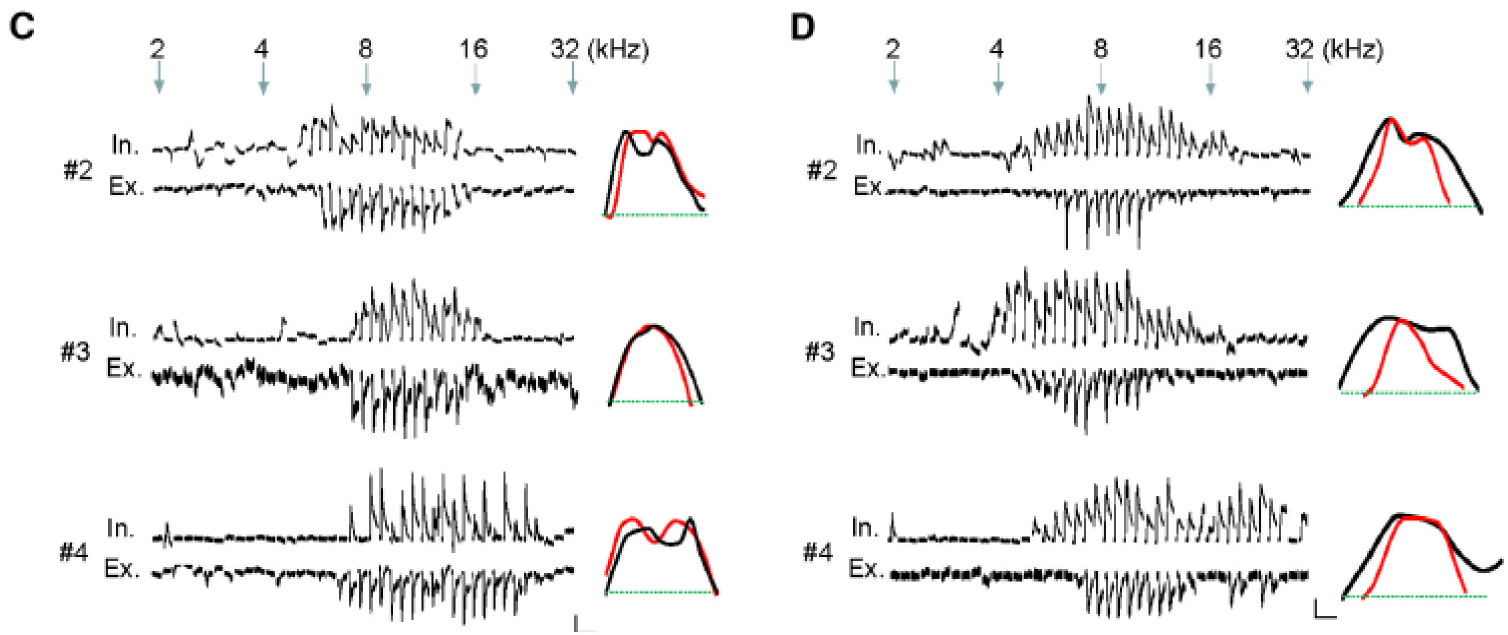


Inhibition
Excitation



Wehr and Zador 2003

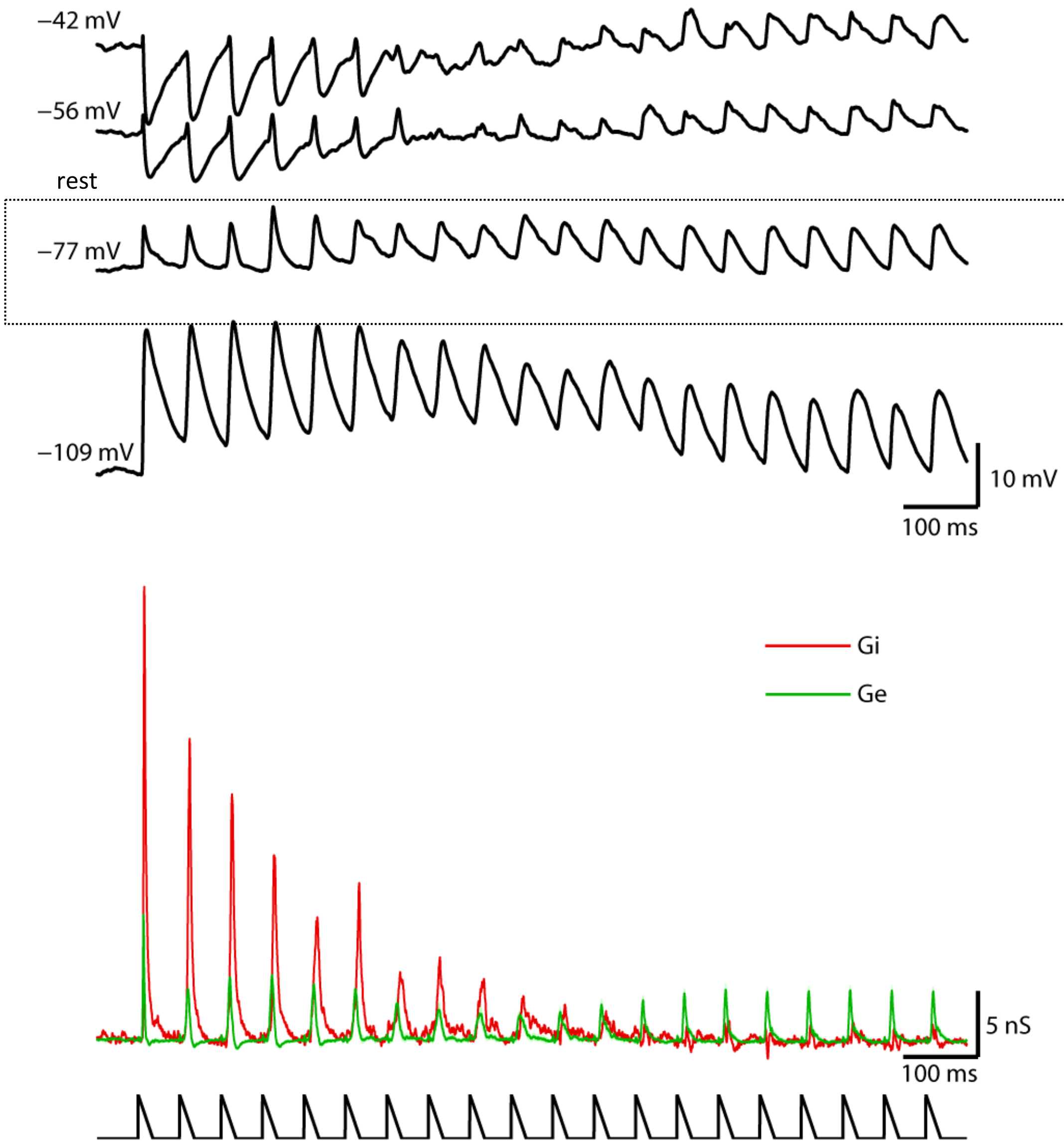
Auditory cortex – Excitation and inhibition are co-tuned to sound intensity and frequency
AWAKE MICE



Li et al, 2014

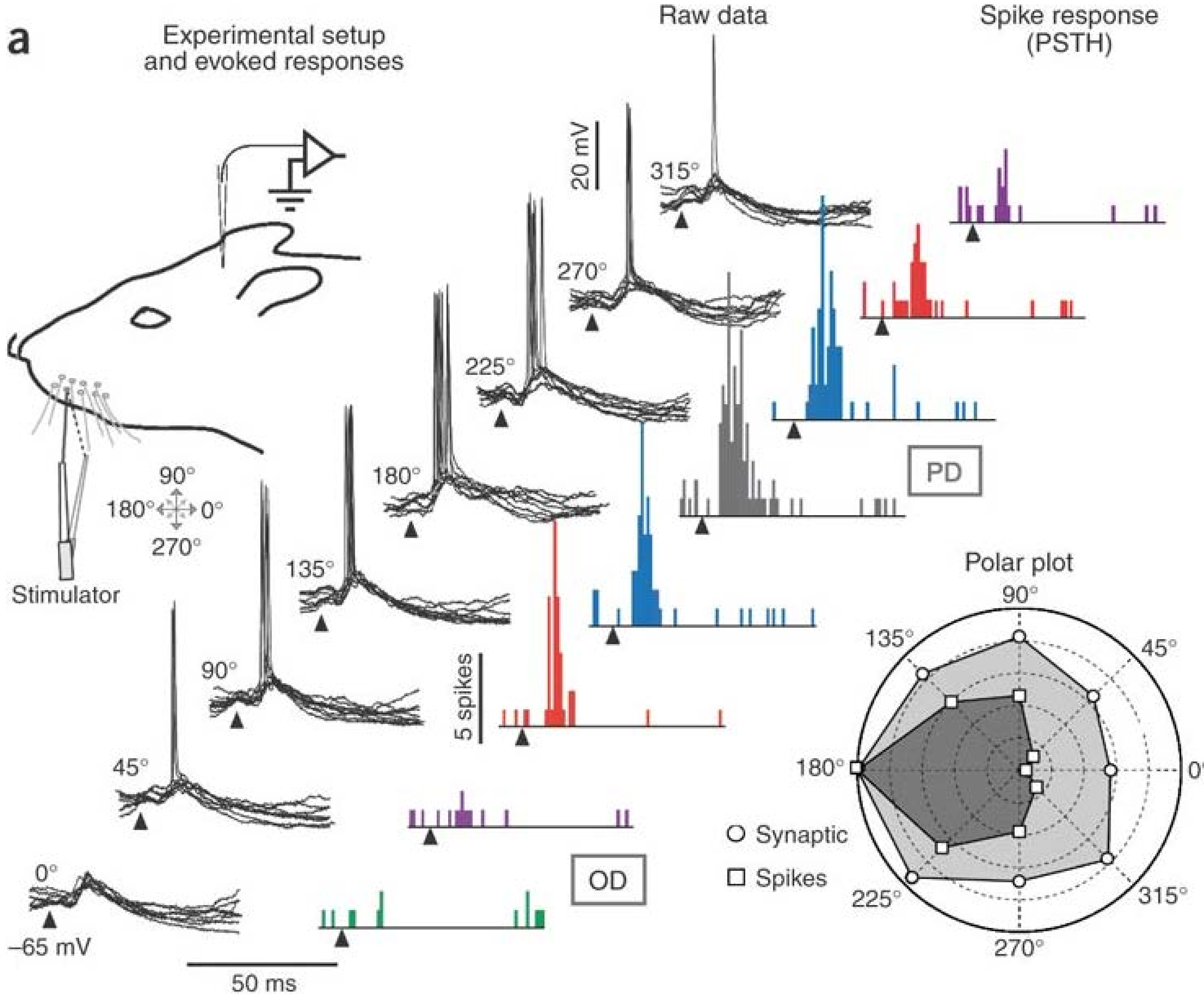
Adaptation of excitation and inhibition in barrel cortex

Inhibition adapts faster and to greater degree than excitation



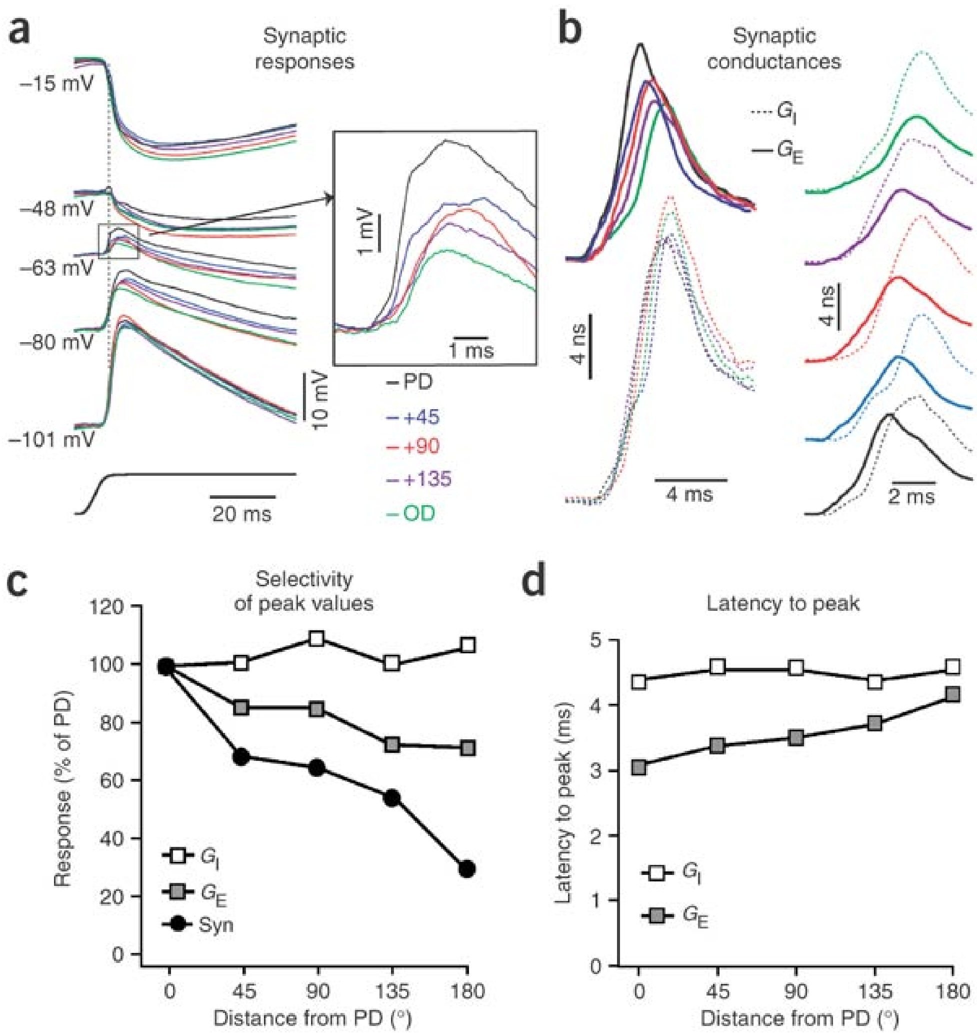
Heiss et al. 2008

Selectivity to direction of whisker deflection



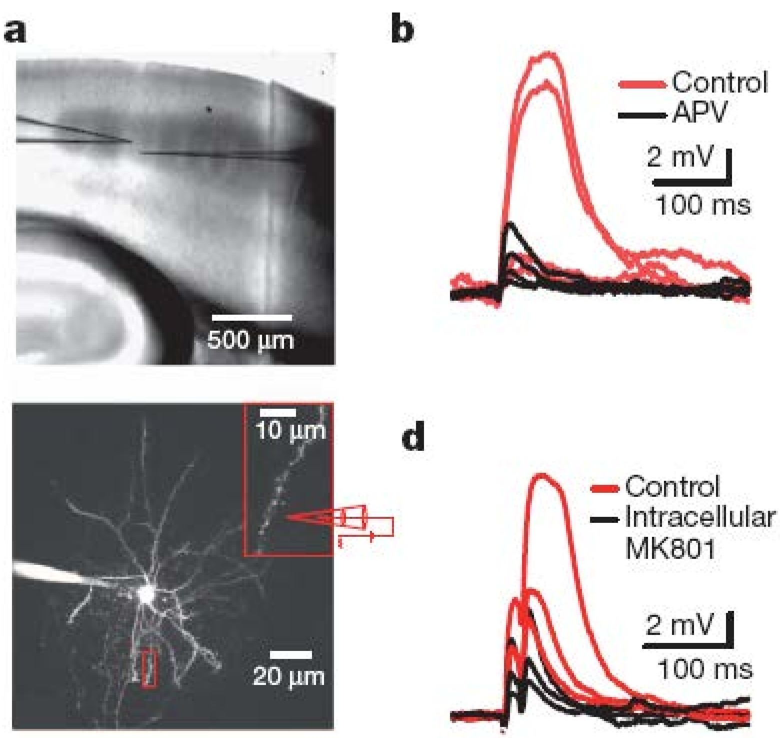
Wilent and Contreras 2005

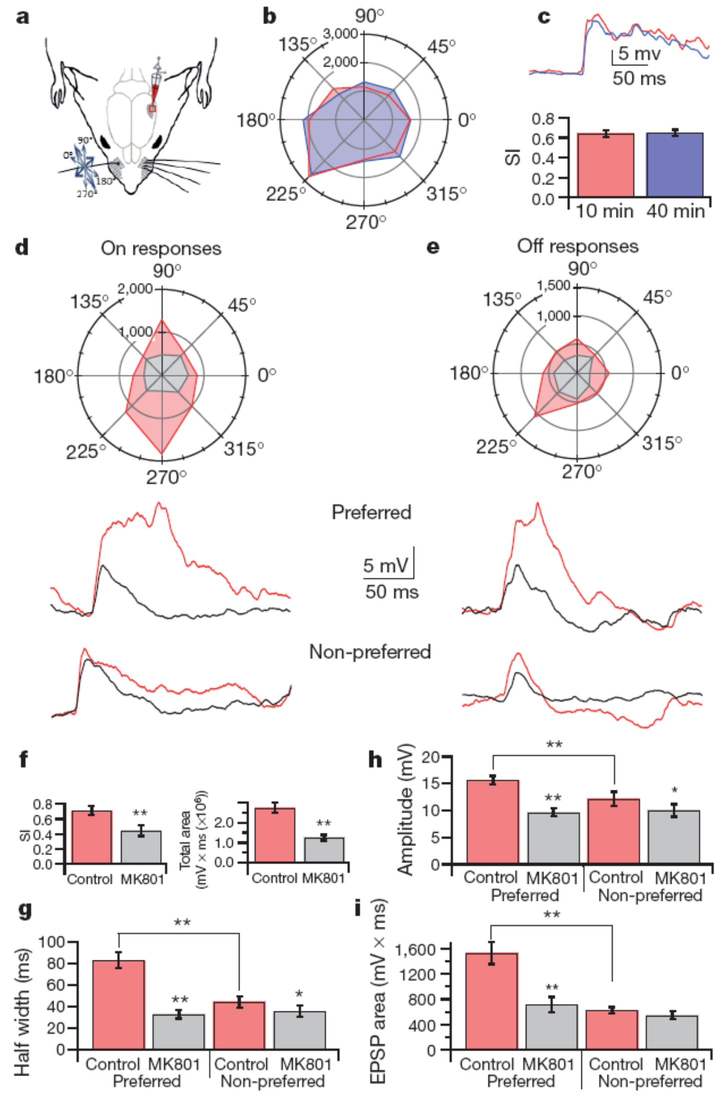
Selectivity to direction of whisker deflection: Excitation but not inhibition is selective



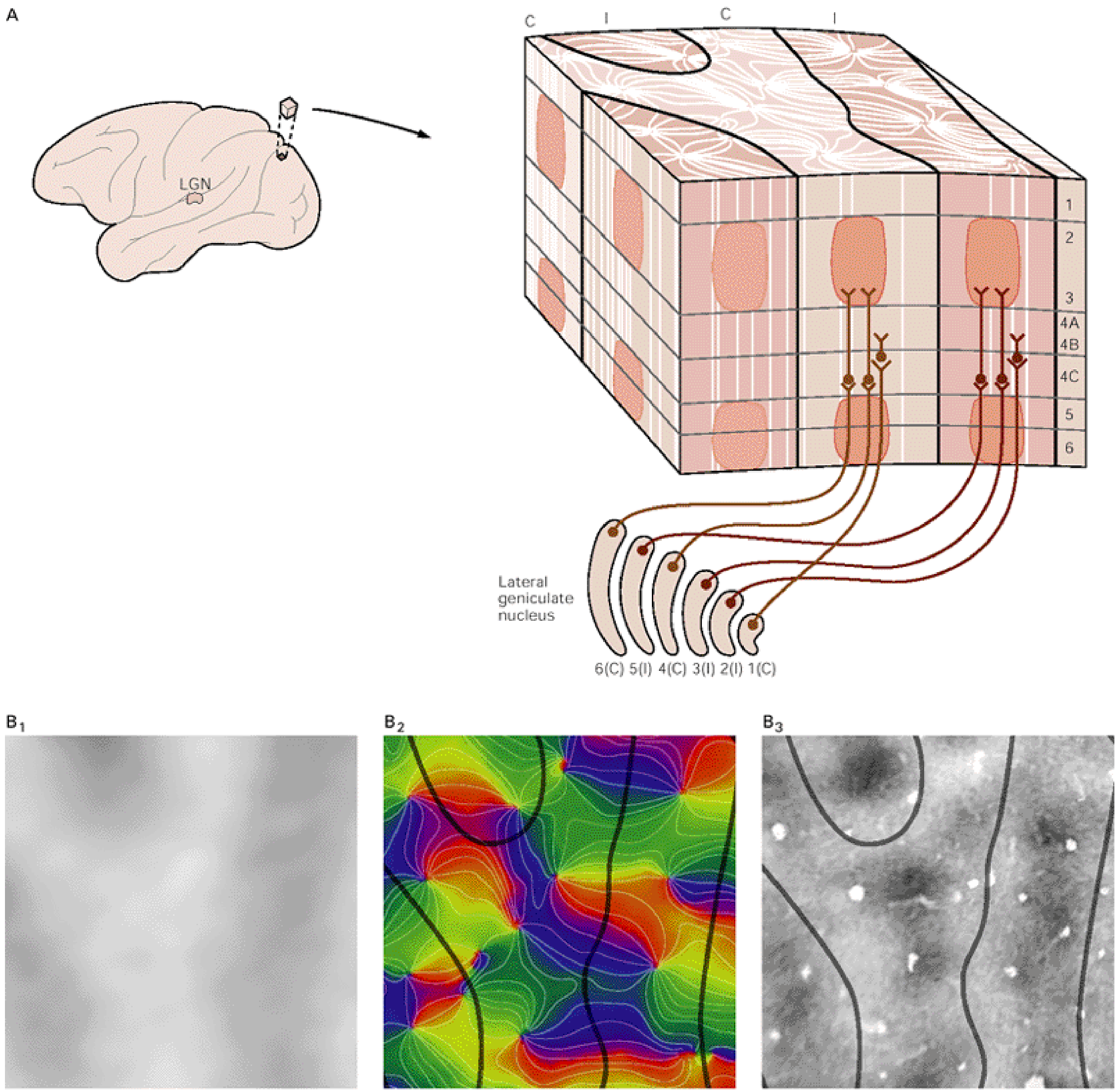
Wilent and Contreras 2005

Selectivity to direction of whisker deflection: Response to preferred direction is NMDA dependent



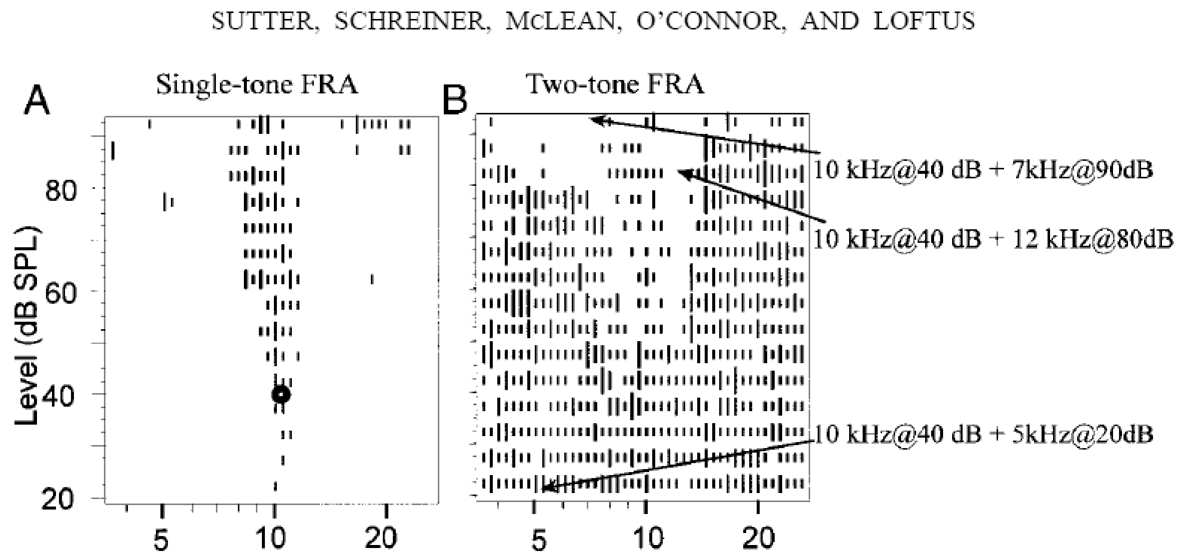


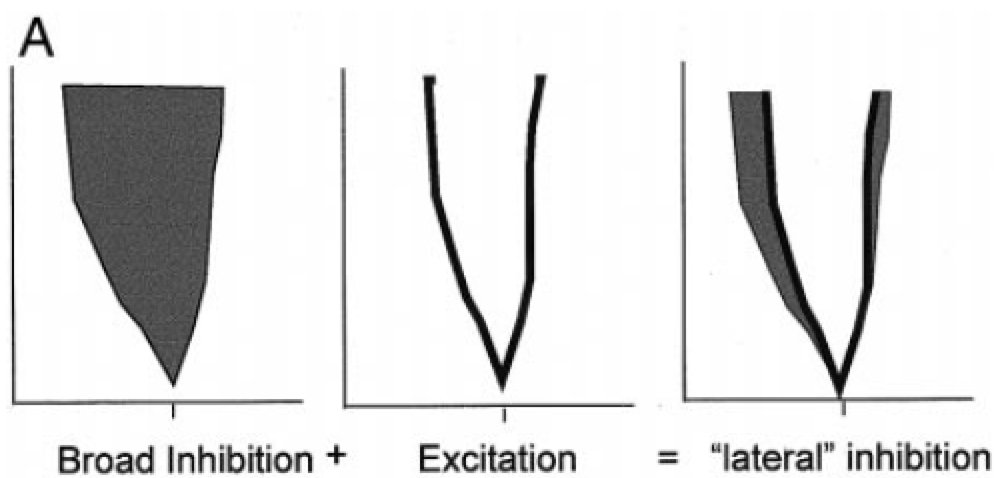
Lavzin et al. 2012


A
C
I
C
I
LGN
1
2
3
4A
4B
4C
5
6
Lateral geniculate nucleus
6(C) 5(I) 4(C) 3(I) 2(I) 1(C)
B1
B2
B3

Auditory cortex – lateral suppression

1. Inhibition?

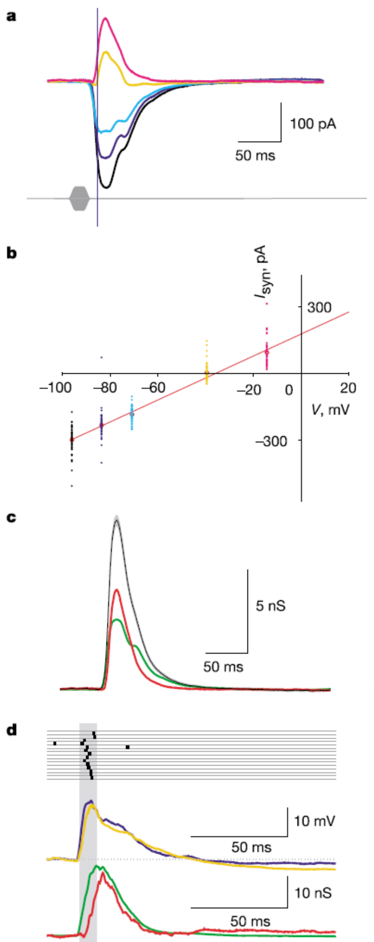


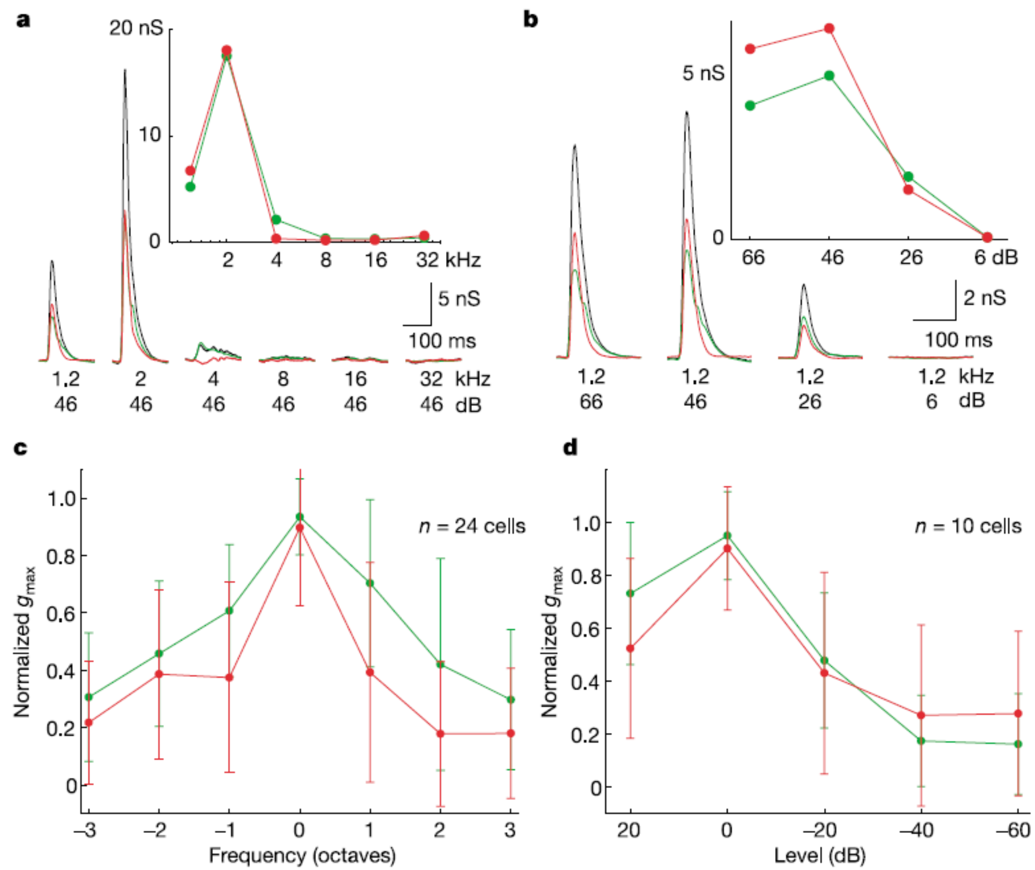


Sutter et al. 1999

Auditory cortex – Excitation and inhibition are co-tuned to sound intensity and frequency

1. Inhibition?





Wehr and Zador 2003