Auditory something something surprise something

Eli Nelken and the really important people

Edmond and Lily Safra Center for Brain Sciences,

Hebrew University, Jerusalem, Israel

ISRAEL SCIENCE FOUNDATION

erc

BSF
United States – Israel
Binational Science Foundation

SFB 870
Neuronal Circuits

HFSP

Recording, analyzing, manipulating, and modeling whole brain activity

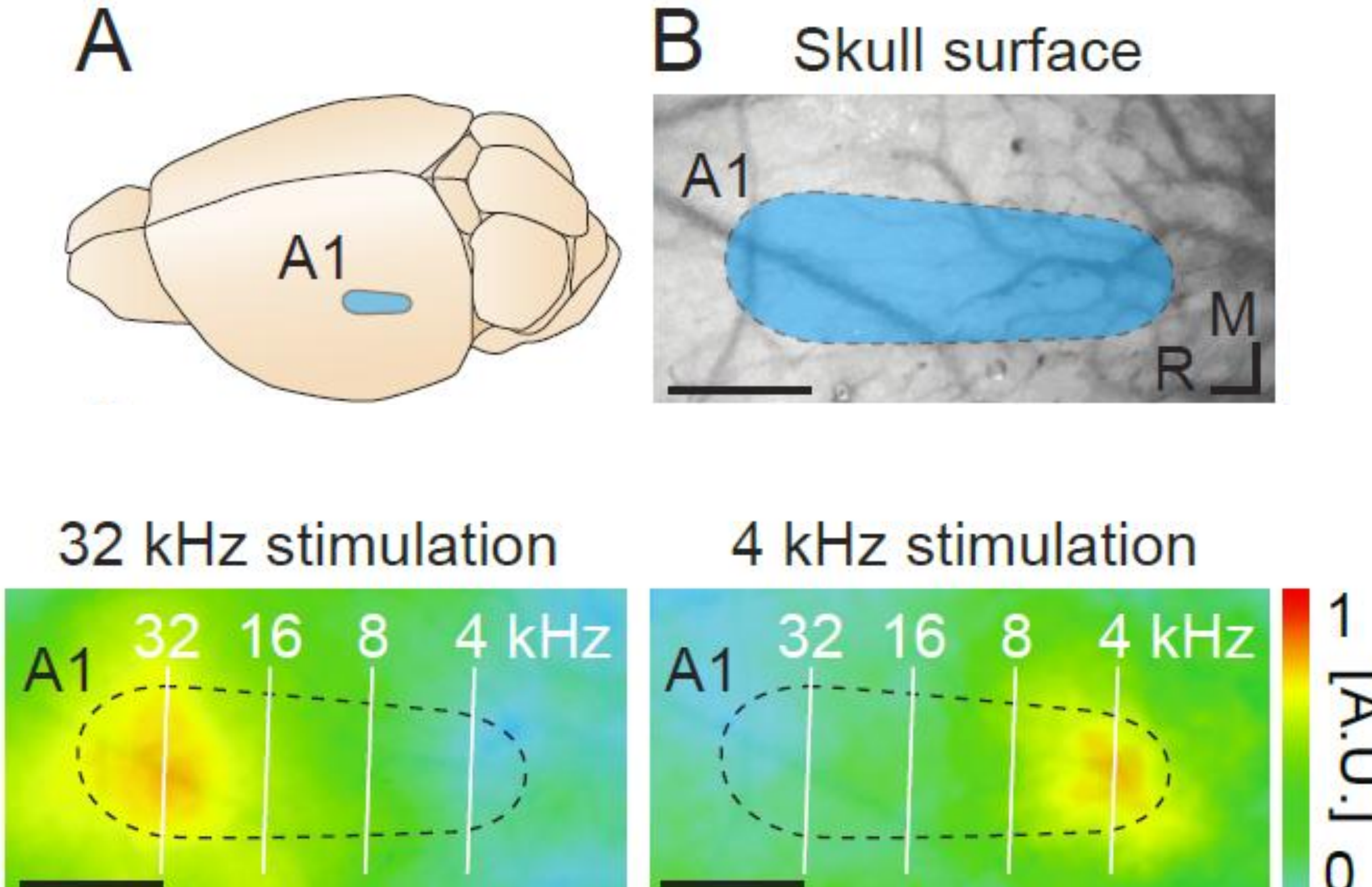
- Surprise responses in auditory cortex
- Some observations on single neurons, small populations, and mesoscopic activity

- Surprise responses in auditory cortex

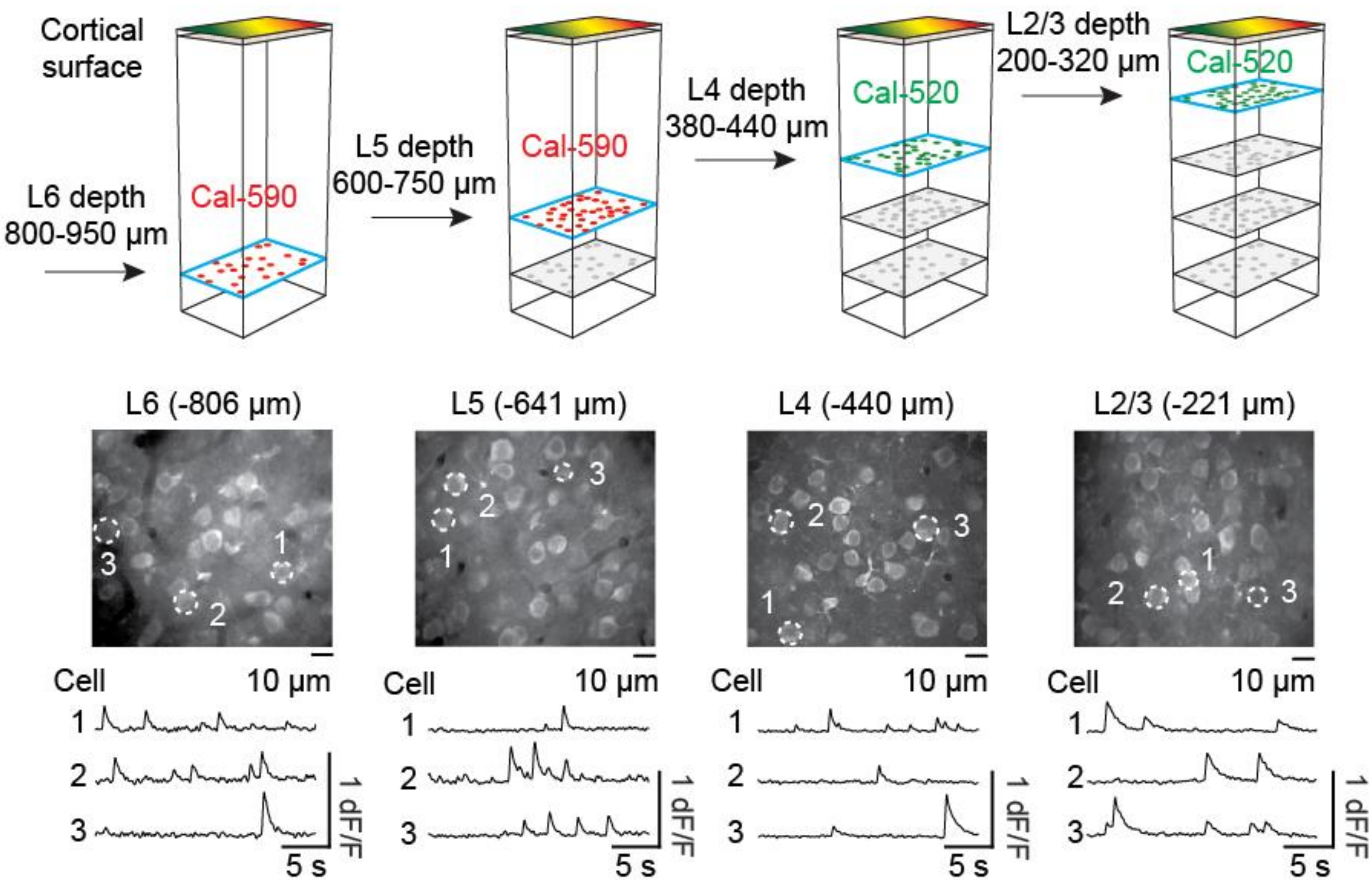
- Surprise responses in auditory cortex
    - Organization of auditory cortex

- In collaboration with Arthur Konnerth (Technical University, Munich)
  - With Carsten Tischbirek and Takahiro Noda

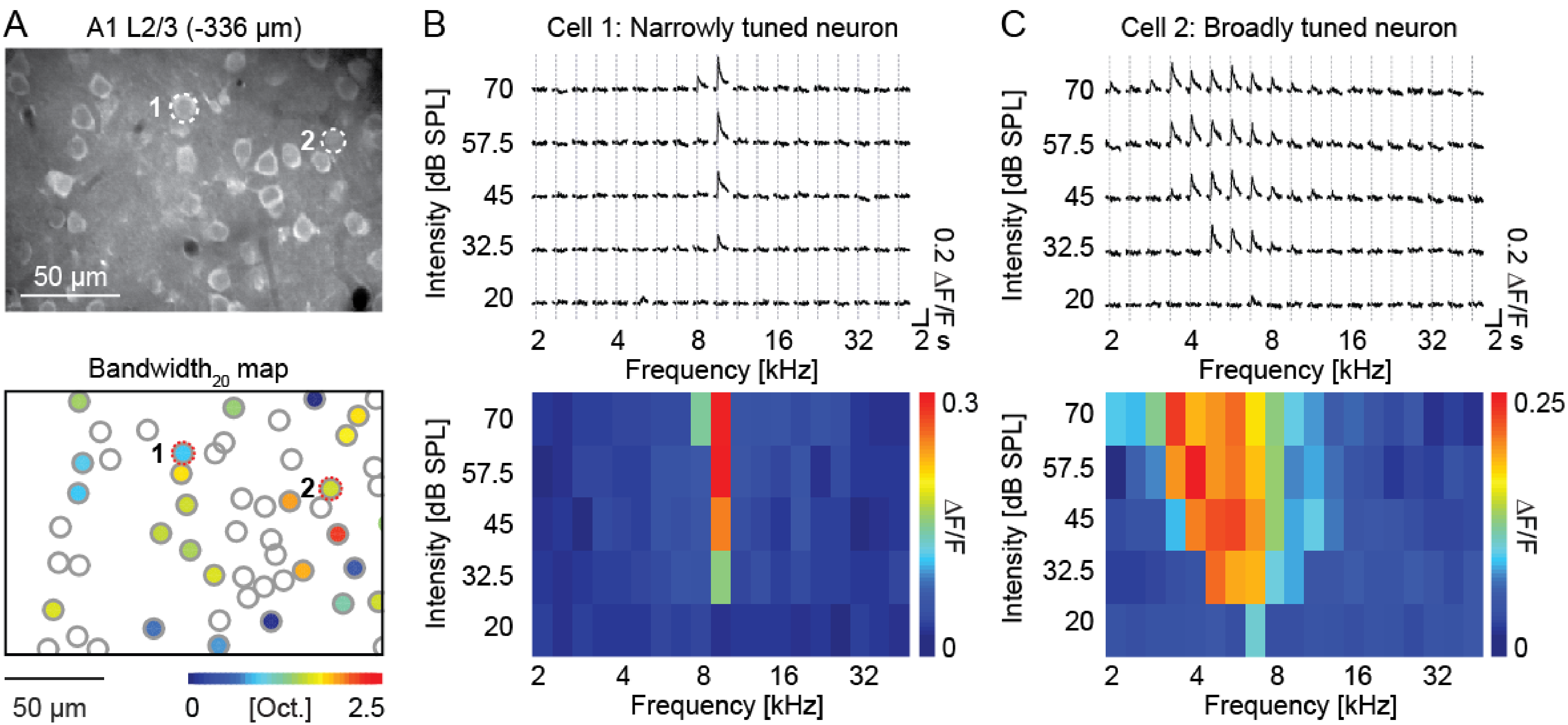
Identify the tonotopic axis (flavoprotein imaging)



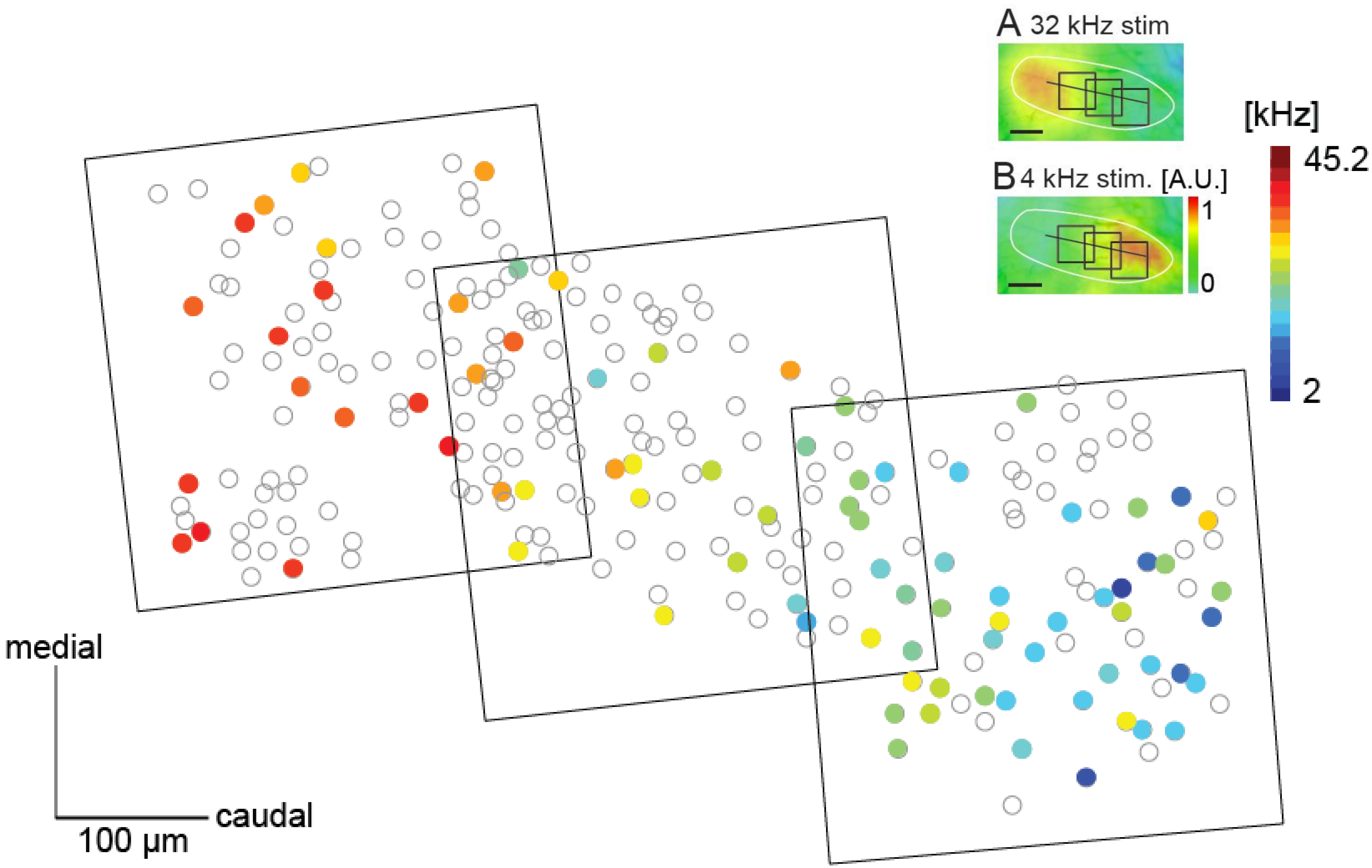
2-photon calcium imaging in multiple layers



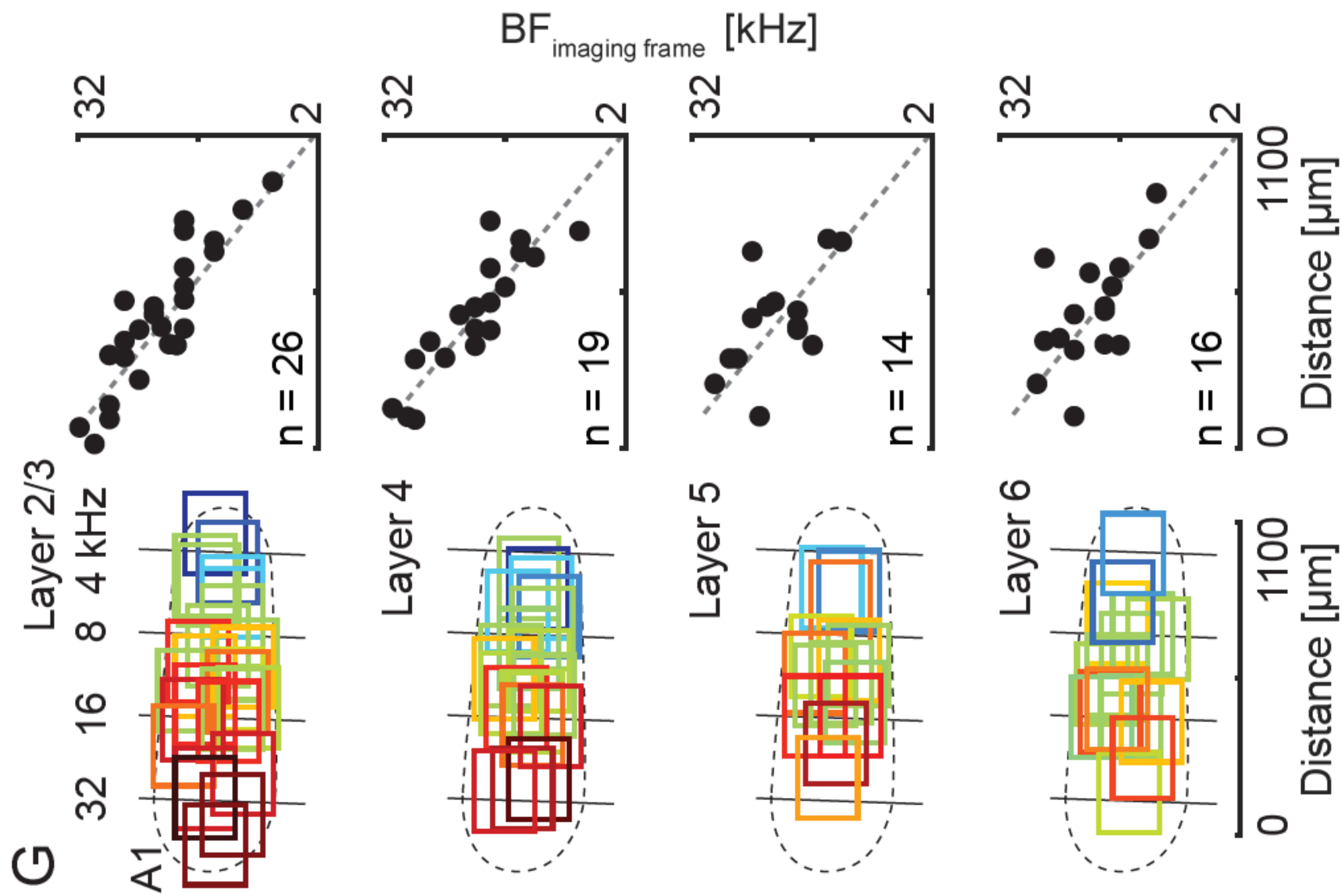
Variablity in response properties



Tonotopic organization
Many layer 2/3 planes, same animal



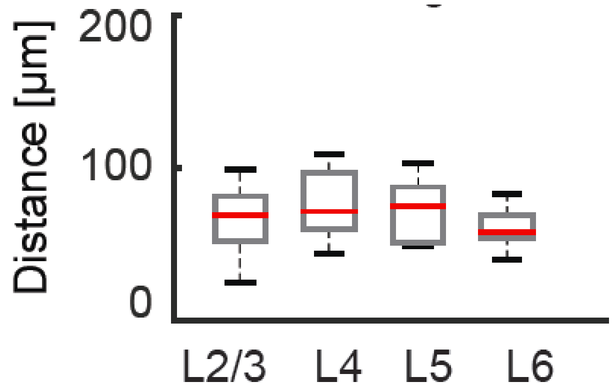
Compatibility of neuron-level and intrinsic signal tonotopic organization

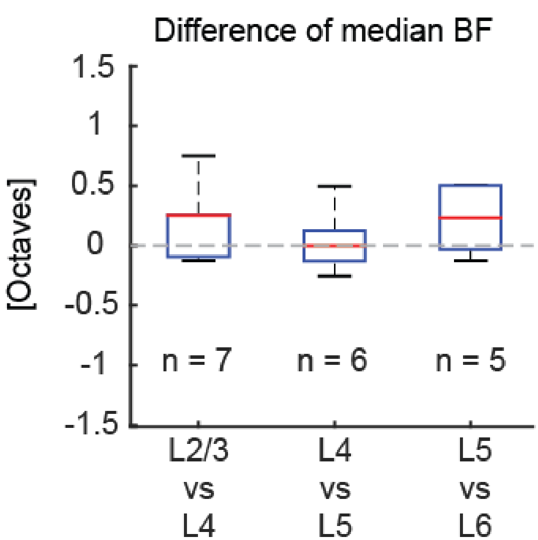


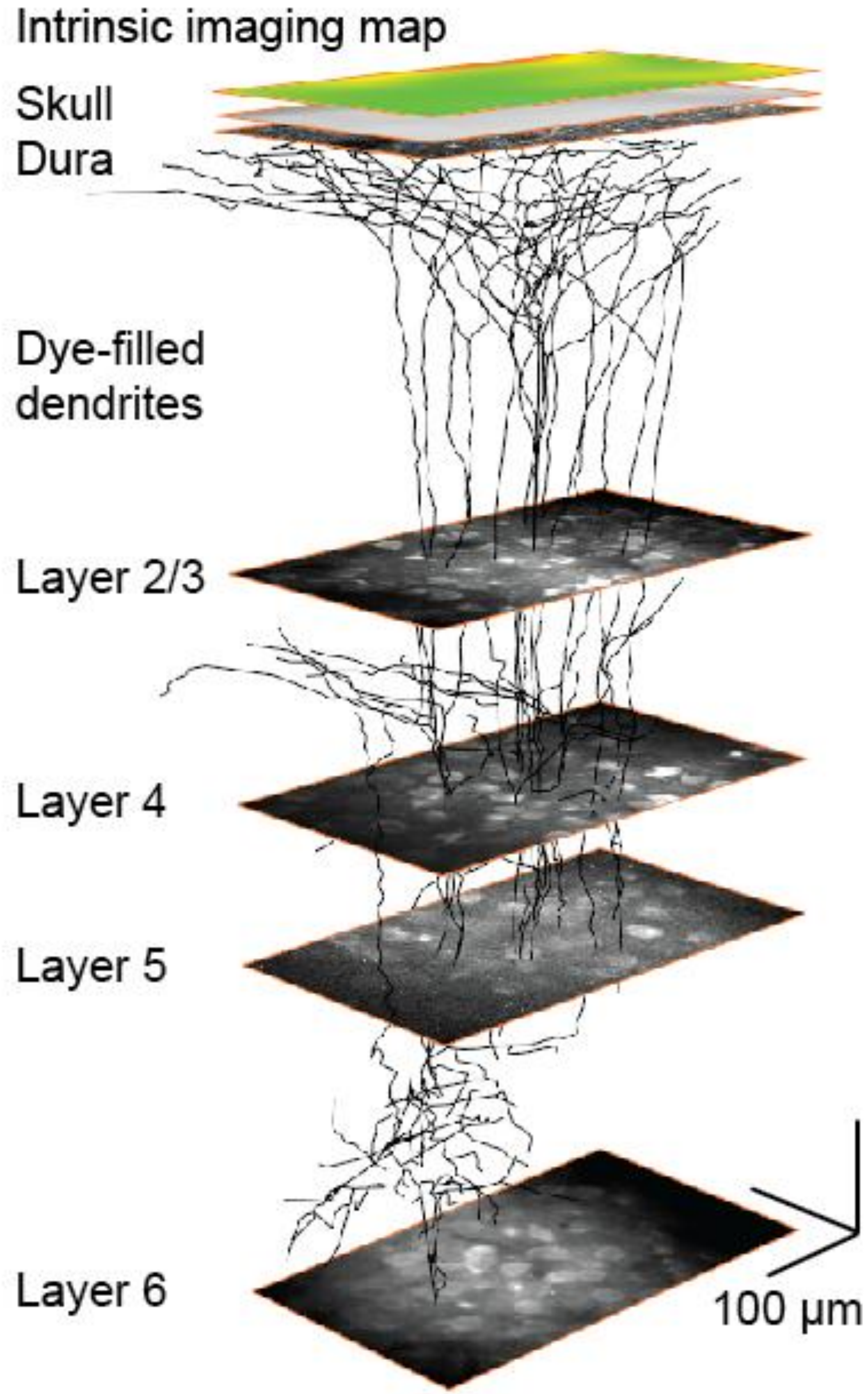
Columnar organization

E

Tangential distance to significant BF change







So what?

- Noisy tonotopic organization
- ‘microcolumns’ of about 50-100 microns, with BF range of about 1 Oct within each
  - Frequency JND in mice is at least an order of magnitude smaller
- No sharp borders
- Very similar organization across all layers

- Surprise responses in auditory cortex
  - Organization of auditory cortex
  - Why surprise?

Why surprise?

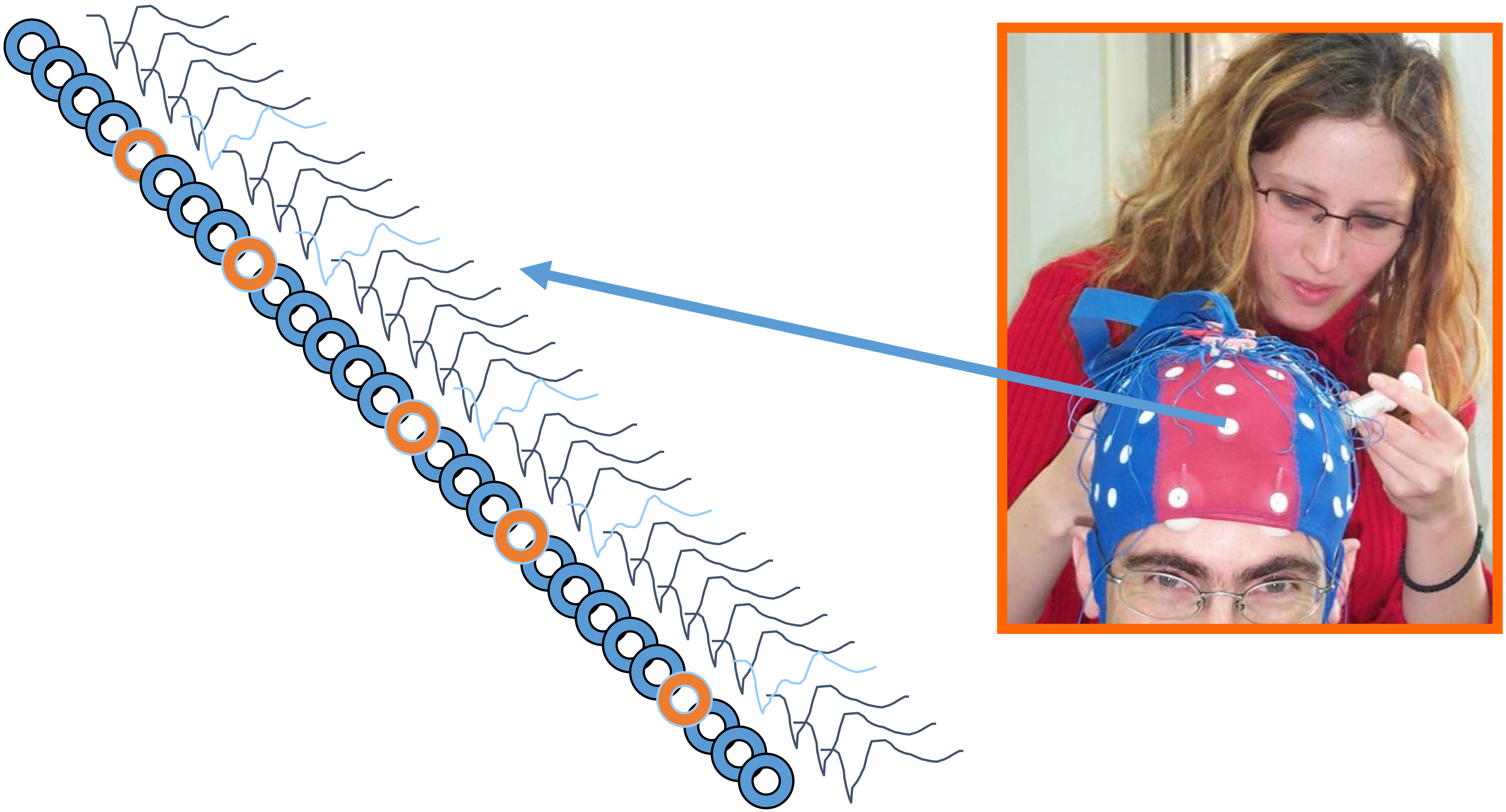
- (half-baked philosophical discussion)
- It’s Bill Bialek’s fault
- The effects are pretty large

- Surprise responses in auditory cortex
    - Organization of auditory cortex
    - Why surprise?
    - How to study surprise?

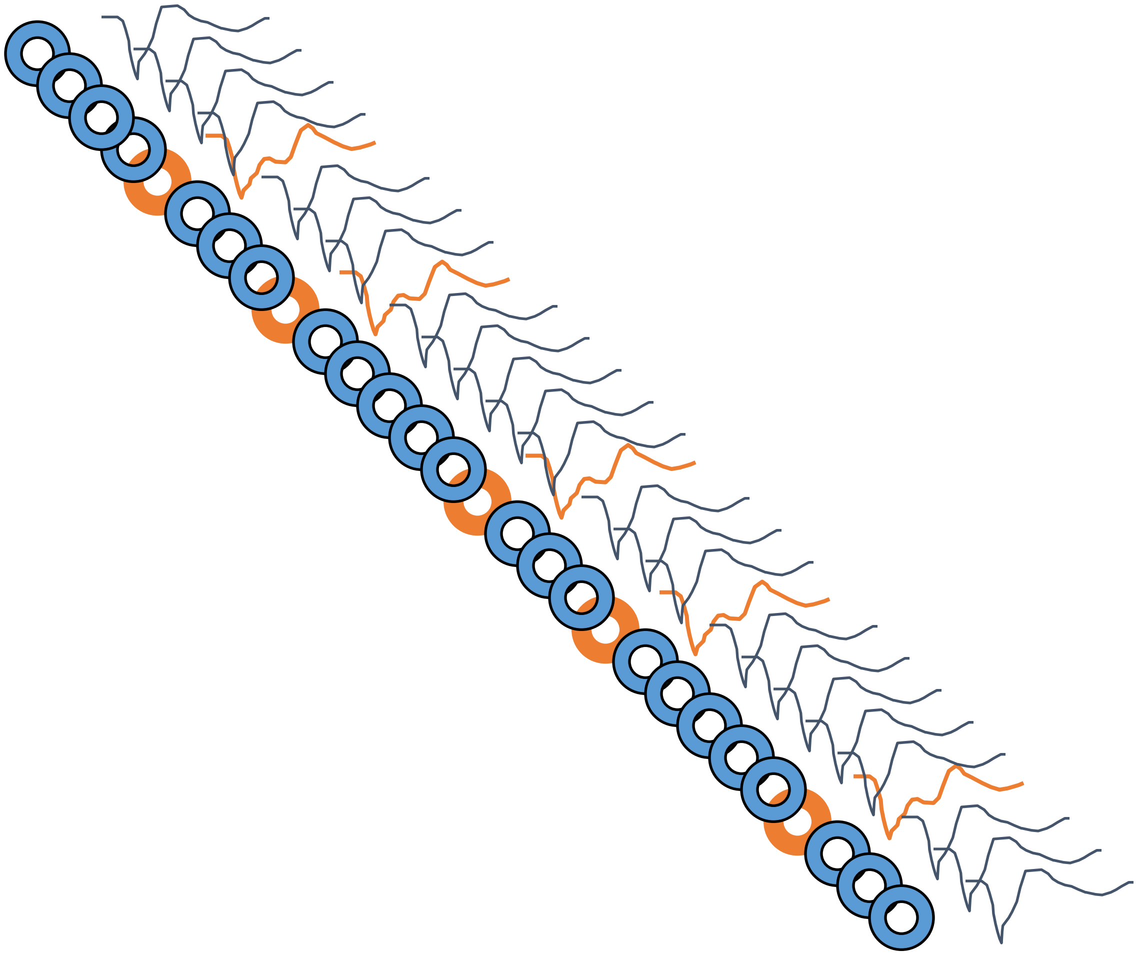
How do we study surprise in brains?

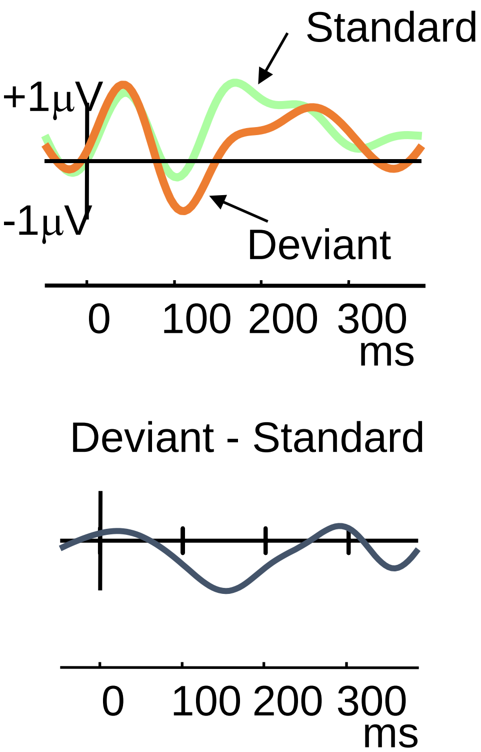
- The basic approach:
  - Generate expectations
  - Violate them
  - See whether brains react
  - If they do, conclude that an expectation was formed
- This requires additional controls
  - Some of which we performed, but I’m not going to talk about them
- In the human brain there’s a whole zoo of surprise responses

Measuring the responses to a deviant tone…



… resulting in Mismatch Negativity





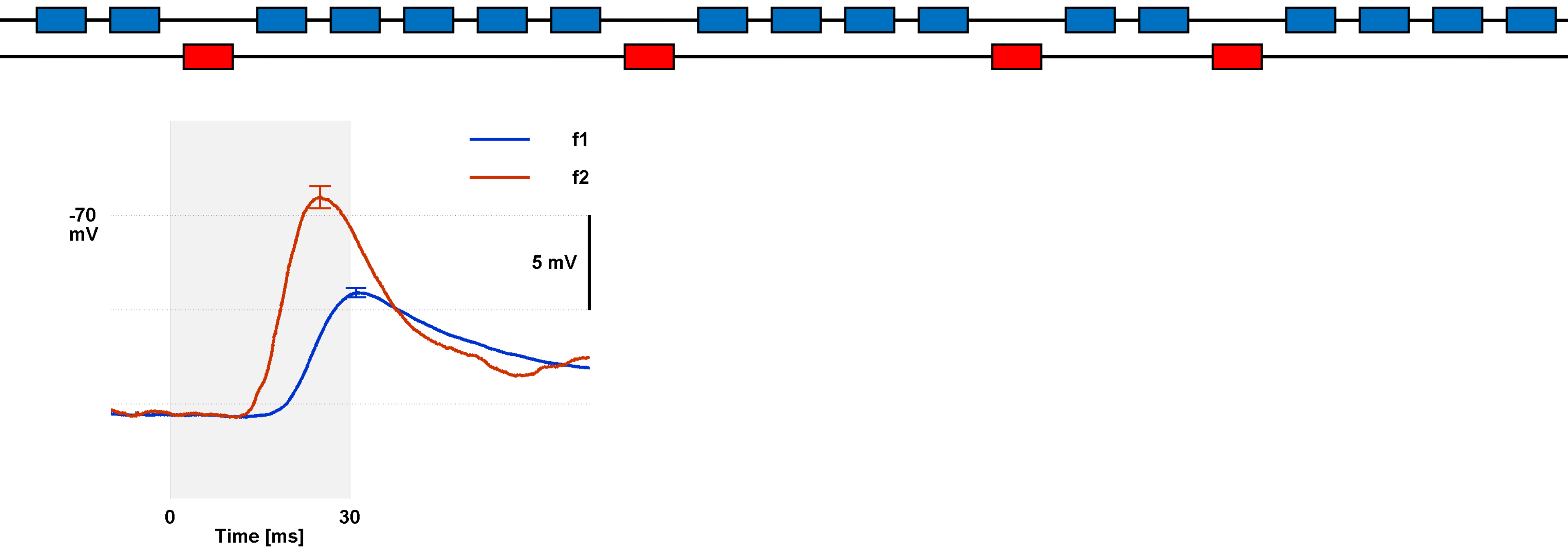
Taxonomy of ‘surprise’ responses in the human brain

- Mismatch Negativity (MMN)
  - To a large extent automatic, encodes physical features of sounds
- P300
  - Requires attention, encodes the engagement of ‘executive functions’
- N400
  - Semantics, word probability, context, …
- P600
  - Reevaluation of previous information

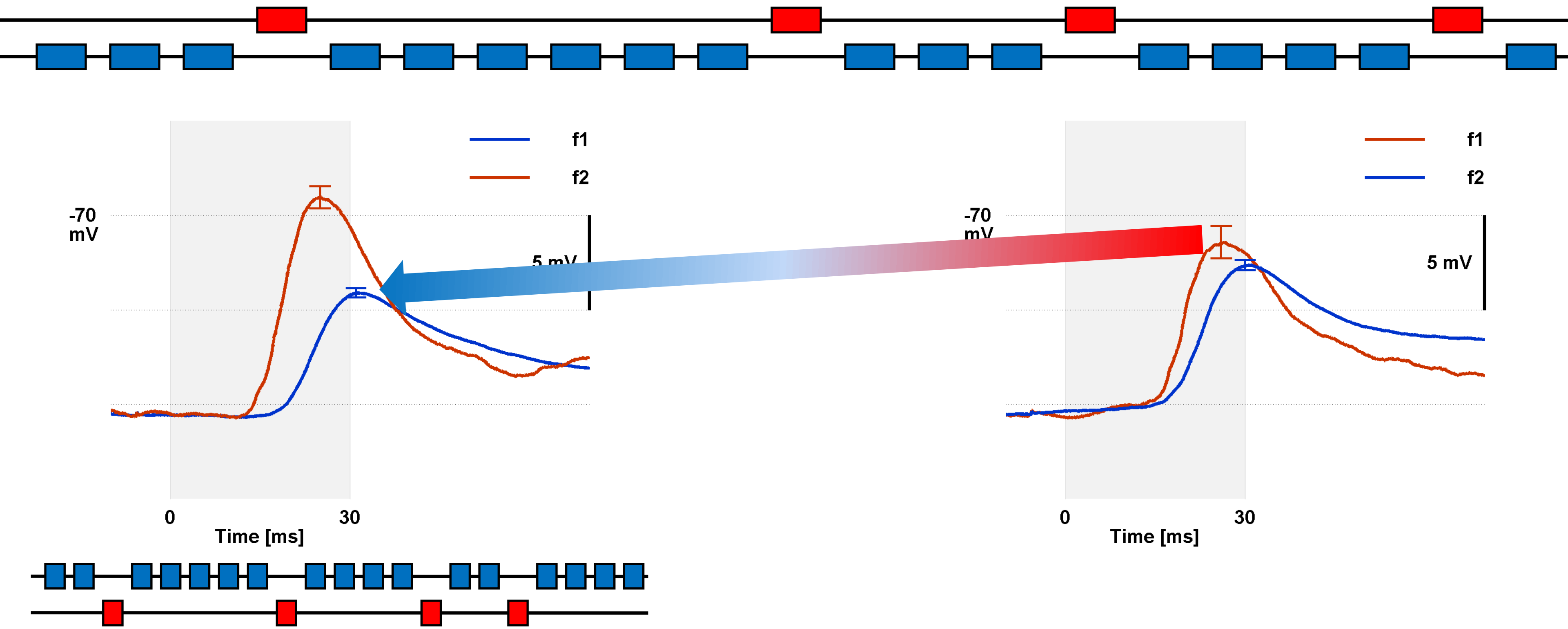
‘Surprise’ responses at the single neuron level

Nachum Ulanovsky, Nevo Ta’aseh, Itai Hershenhoren, Amit Yaron, Bshara Awwad, Leila Khouri, Maciej Jankowski, Ana Polterovich, Ruan Badrieh

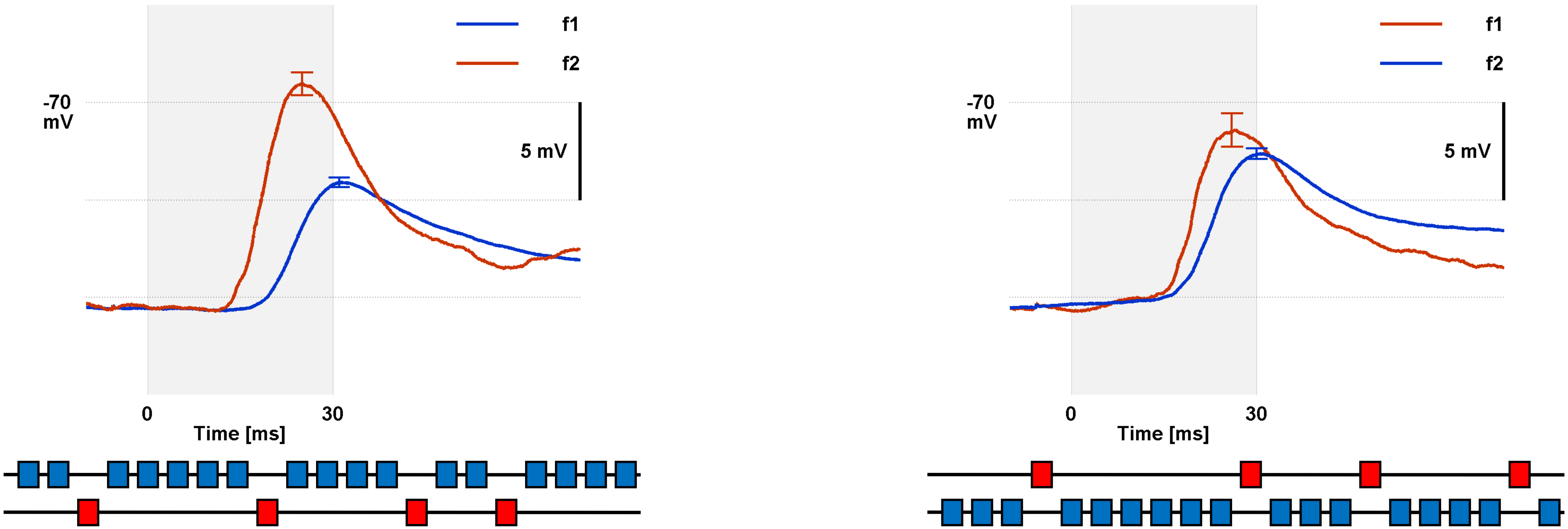
(Related work by Manolo Malmierca, Jennifer Linden, Maria Geffen, Fritjof Helmchen, Bernhard Gaese, Jan Schnupp, Bo Hong, …)



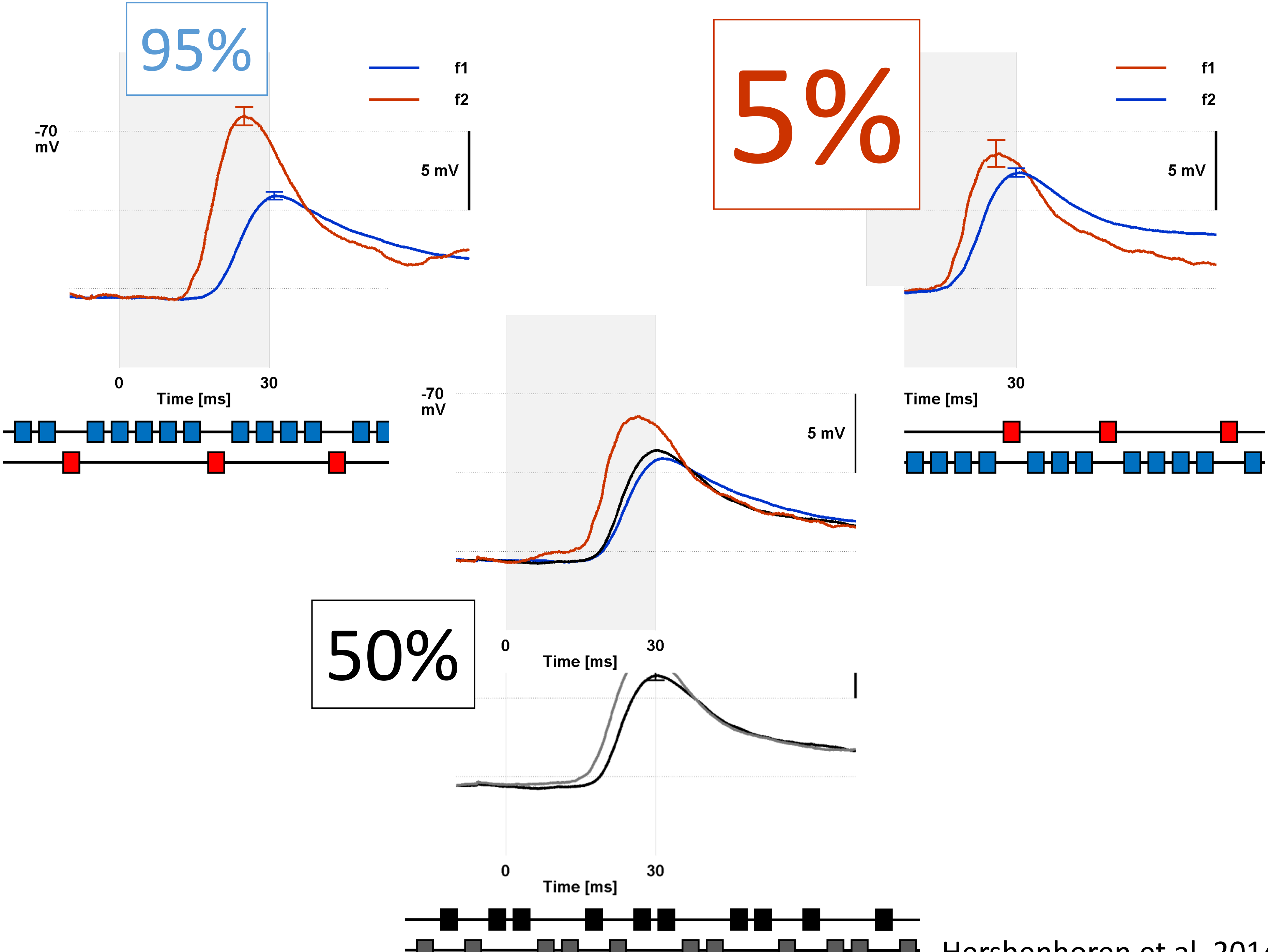
Hershenhoren et al. 2014



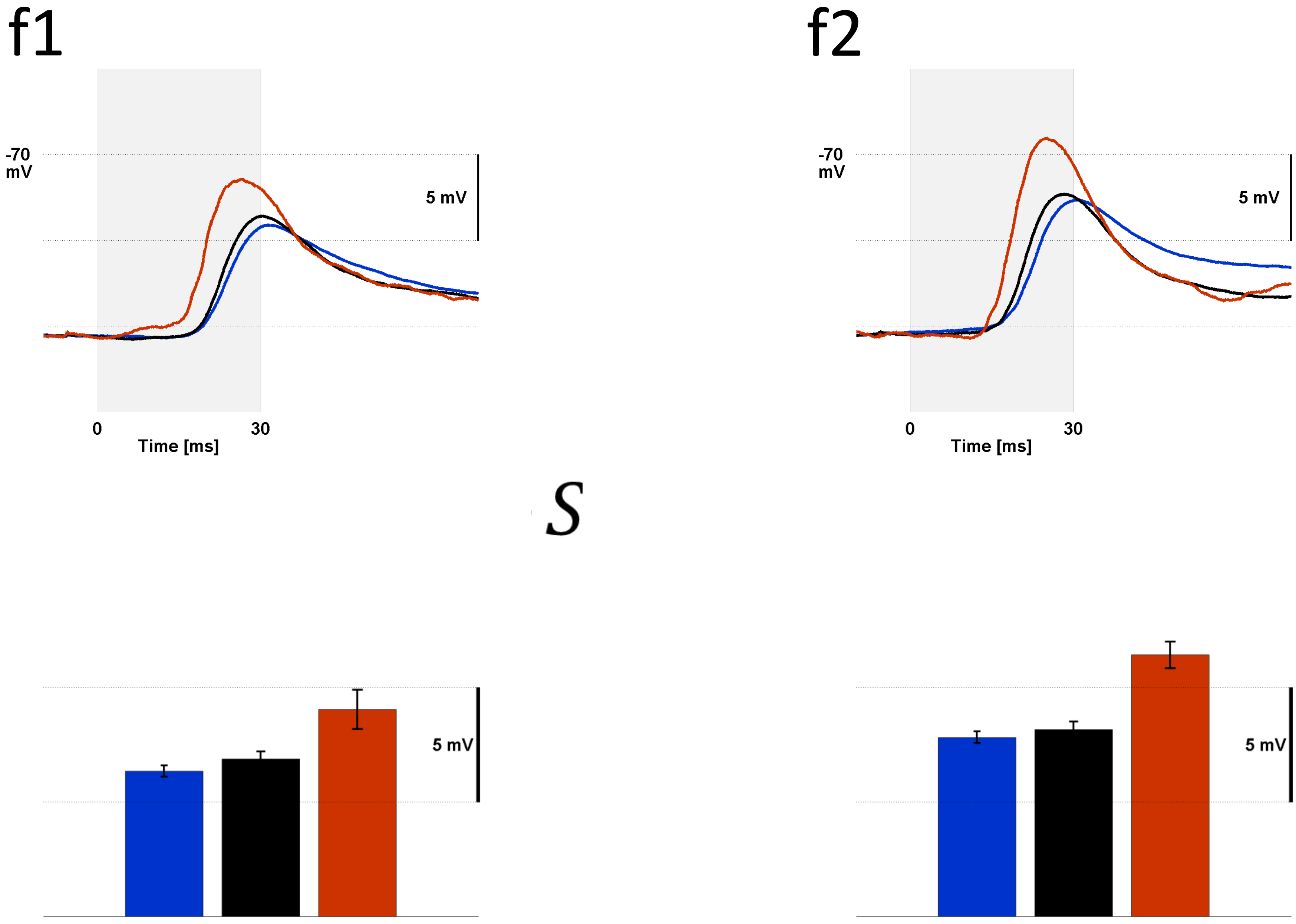
Hershenhoren et al. 2014



Hershenhoren et al. 2014



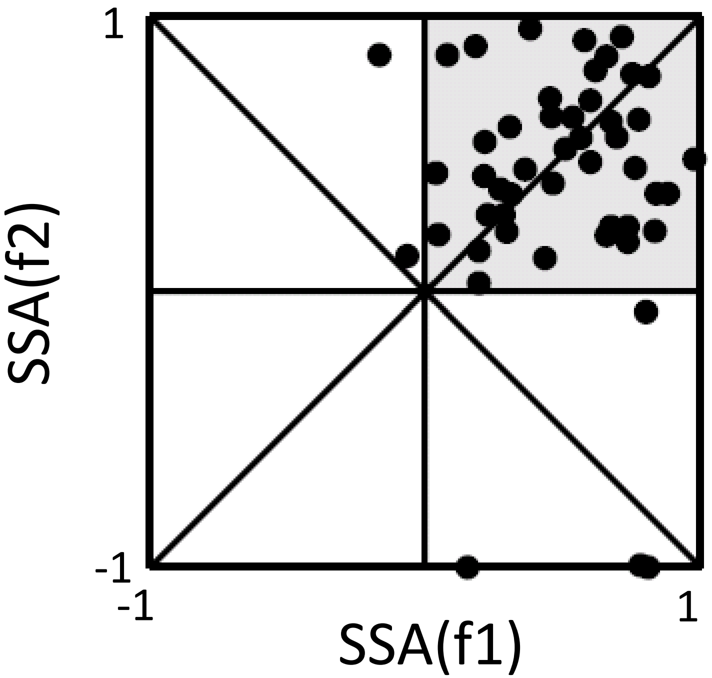
Hershenhoren et al. 2014



Hershenhoren et al. 2014

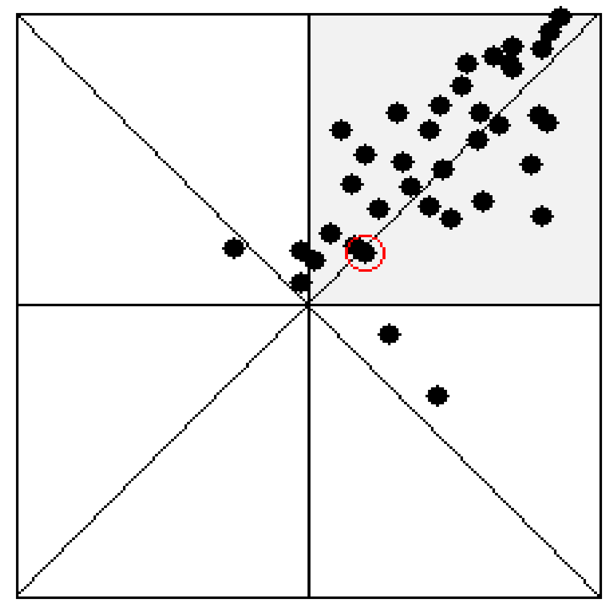
SSA in auditory cortex of anesthetized rats

MUA



Taaseh et al. 2011

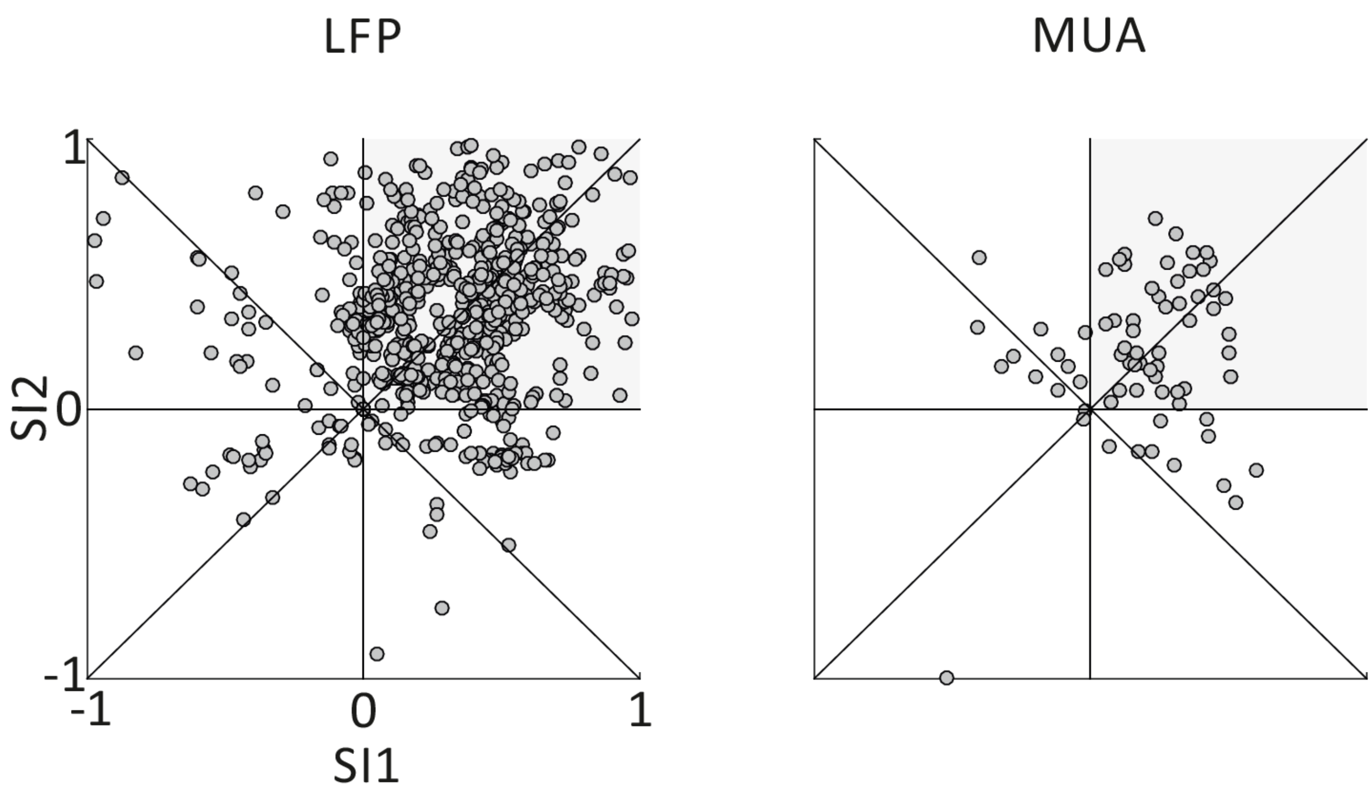
Membrane potential



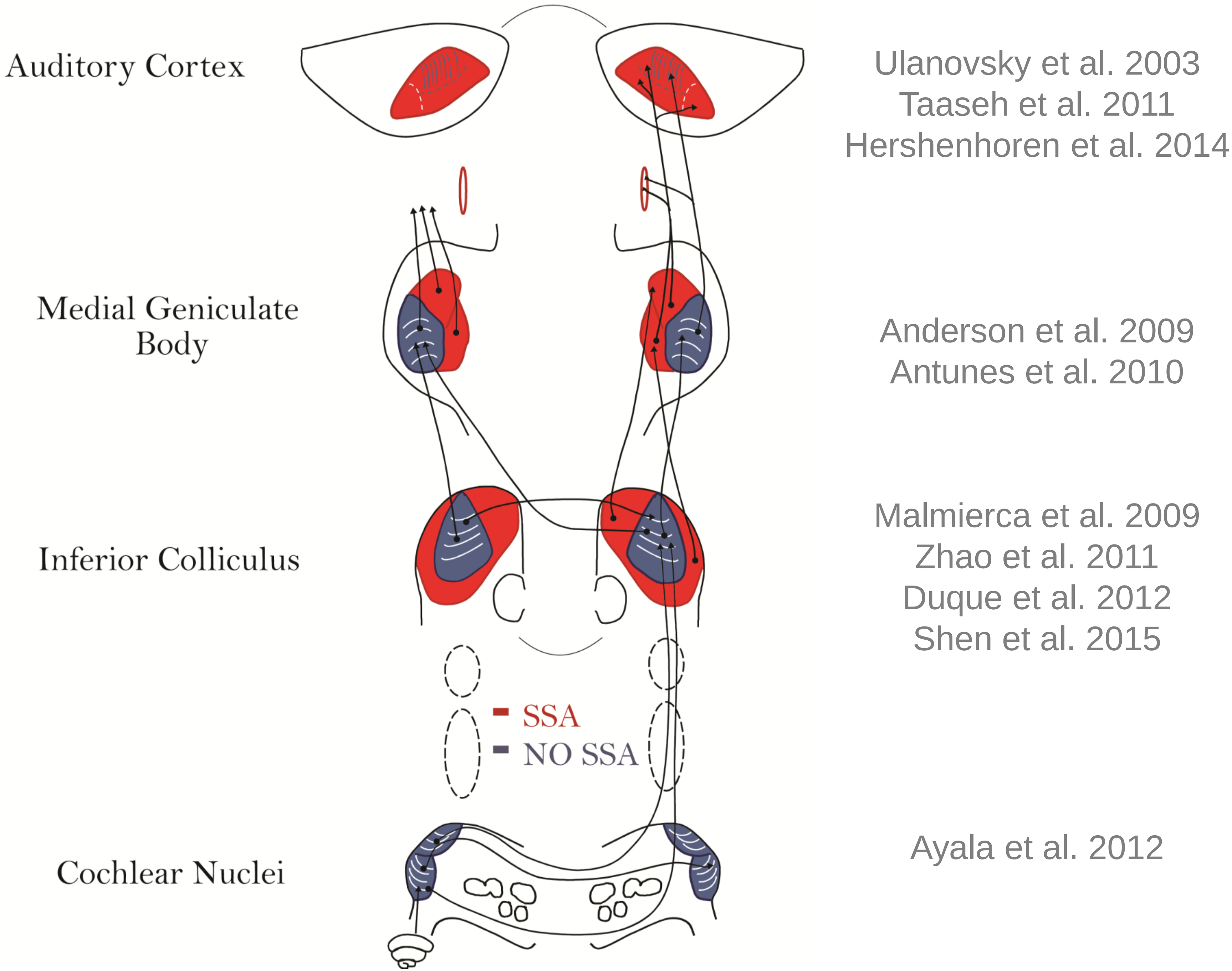
Hershenhoren et al. 2014

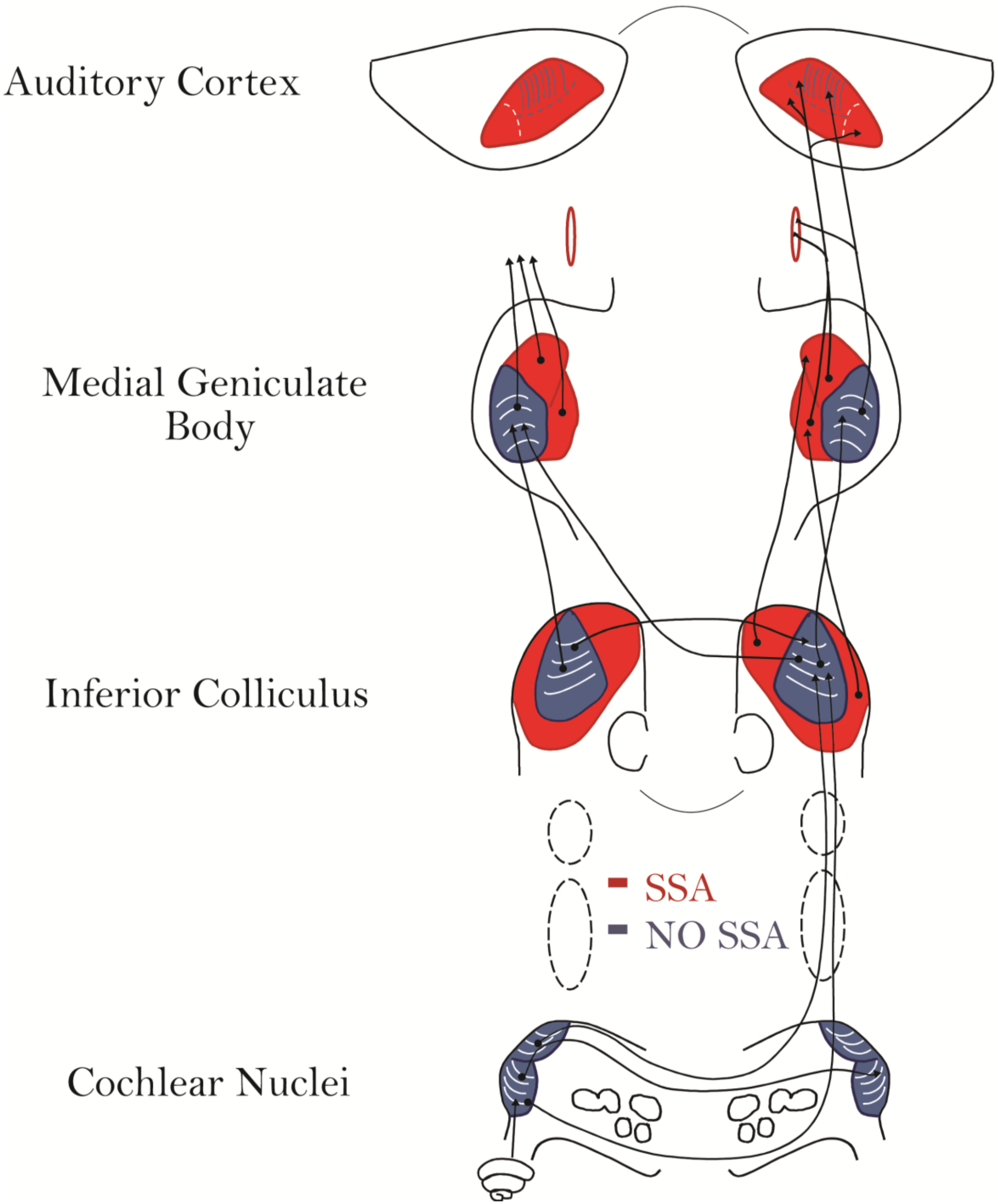
$$\mathbf{SSA} = \frac{\Delta}{\Sigma}$$

SSA in auditory cortex of awake, freely moving rats



Polterovich, Jankowski and Nelken 2018


Auditory Cortex
Medial Geniculate Body
Inferior Colliculus
Cochlear Nuclei
SSA
NO SSA
Ulanovsky et al. 2003
Taaseh et al. 2011
Hershenhoren et al. 2014
Anderson et al. 2009
Antunes et al. 2010
Malmierca et al. 2009
Zhao et al. 2011
Duque et al. 2012
Shen et al. 2015
Ayala et al. 2012

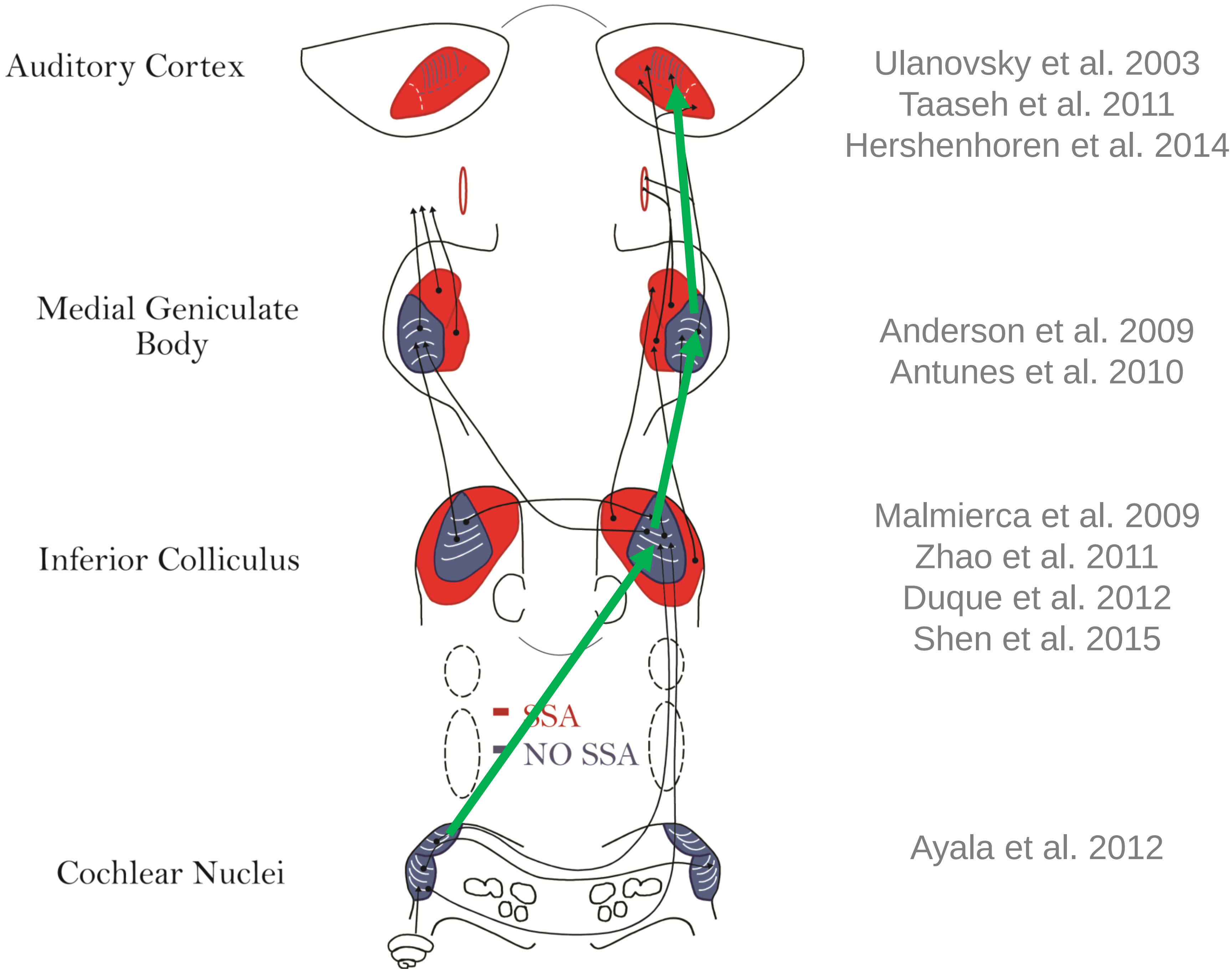


Higher processing; auditory scene analysis; object representations; …
100,000 Neurons

?????
70,000 neurons

Functional analog of V1
100,000 neurons

Feature extraction in multiple parallel pathways



Auditory Cortex
Medial Geniculate Body
Inferior Colliculus
Cochlear Nuclei
SSA
NO SSA
Ulanovsky et al. 2003
Taaseh et al. 2011
Hershenhoren et al. 2014
Anderson et al. 2009
Antunes et al. 2010
Malmierca et al. 2009
Zhao et al. 2011
Duque et al. 2012
Shen et al. 2015
Ayala et al. 2012

Party line: SSA is generated *de novo* in primary auditory cortex

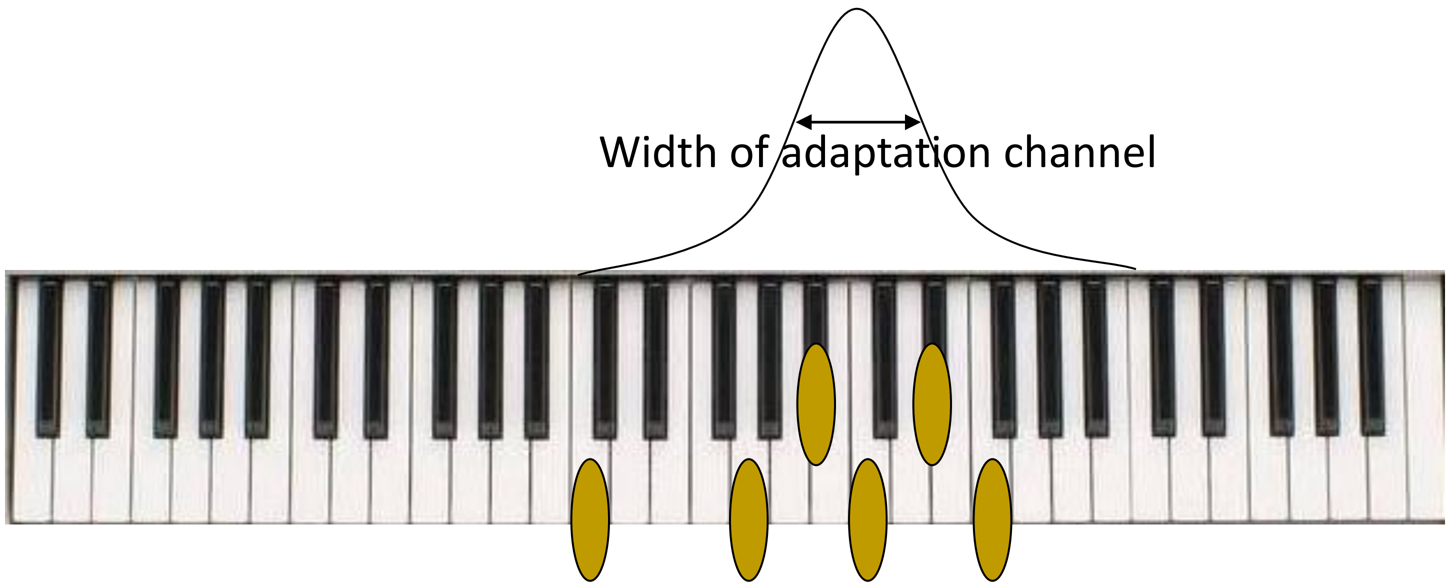
So what?

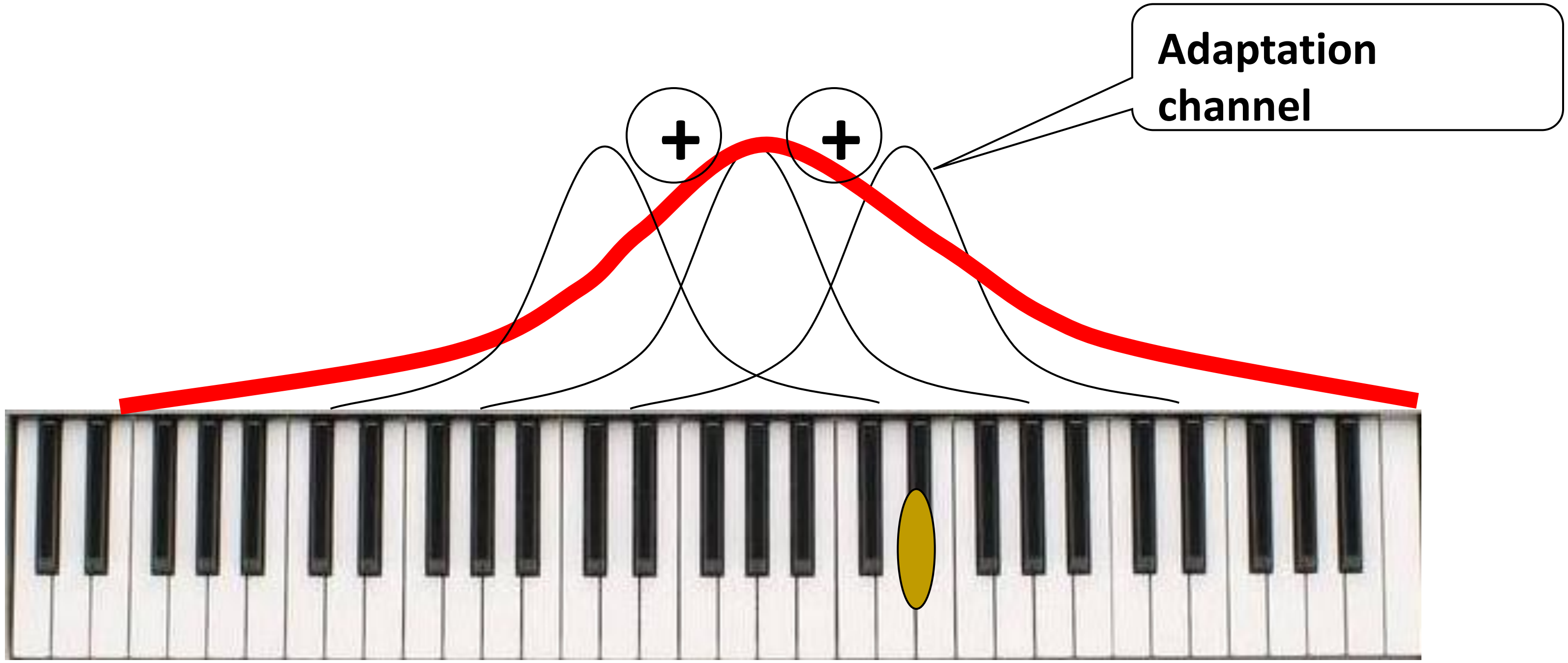
- SSA is large and robust in auditory cortex
- Is it interesting?
  - Well, it is large…
  - …it is present in awake animals…

- Surprise responses in auditory cortex
  - Organization of auditory cortex
  - Why surprise?
  - How to study surprise?
  - The simplest model of SSA doesn’t work in A1

Adaptation in narrowly tuned modules (ANTM)

- (Taaseh et al. 2011, Hershenhoren et al. 2014, reviewed in Nelken 2014)
- (Essentially the same as the model suggested by Dhruv and Carandini, Neuron 2014 for the visual cortex)
- (Will turn out to fail)


Width of adaptation channel



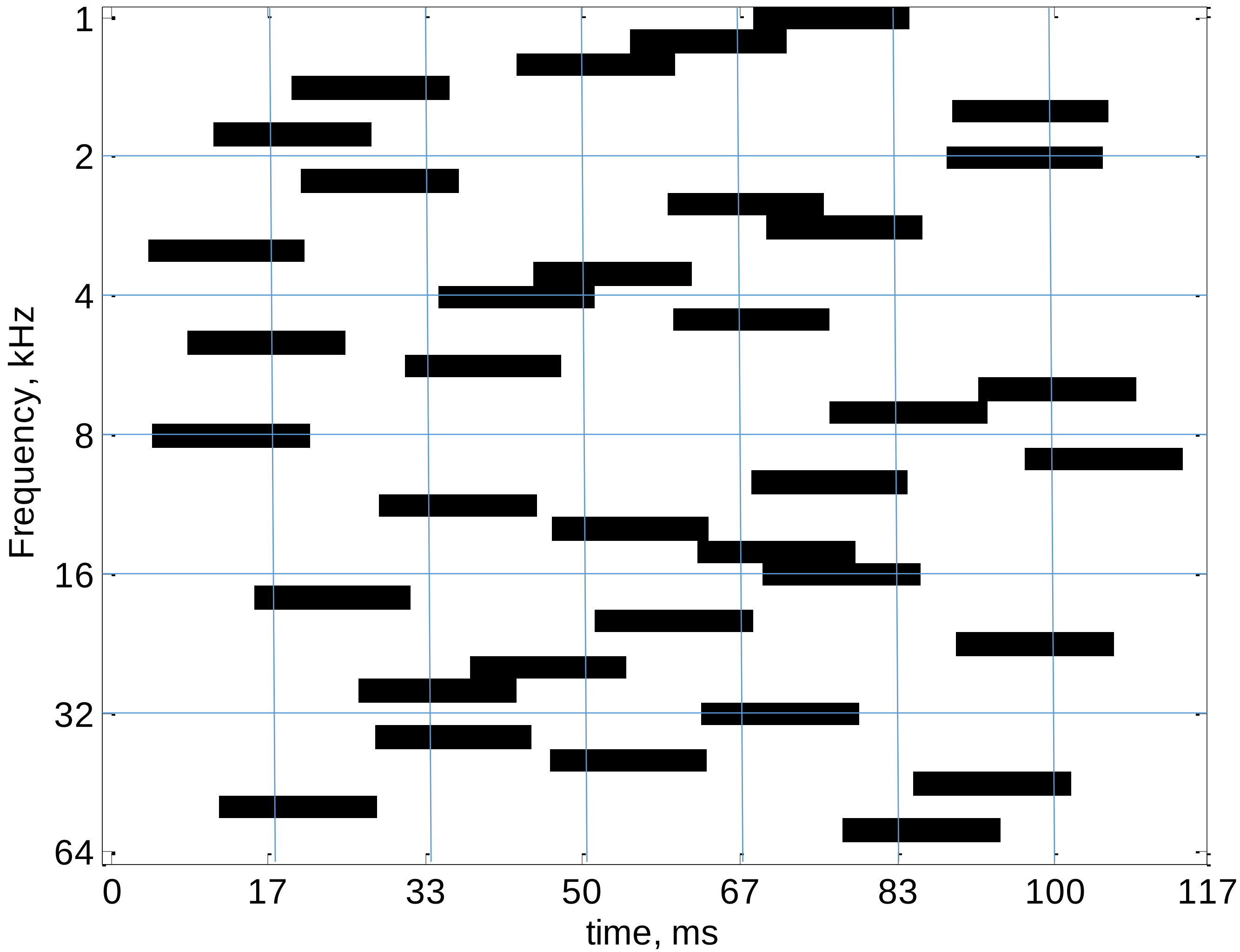
Adaptation channel
+
+

One prediction of ANTM

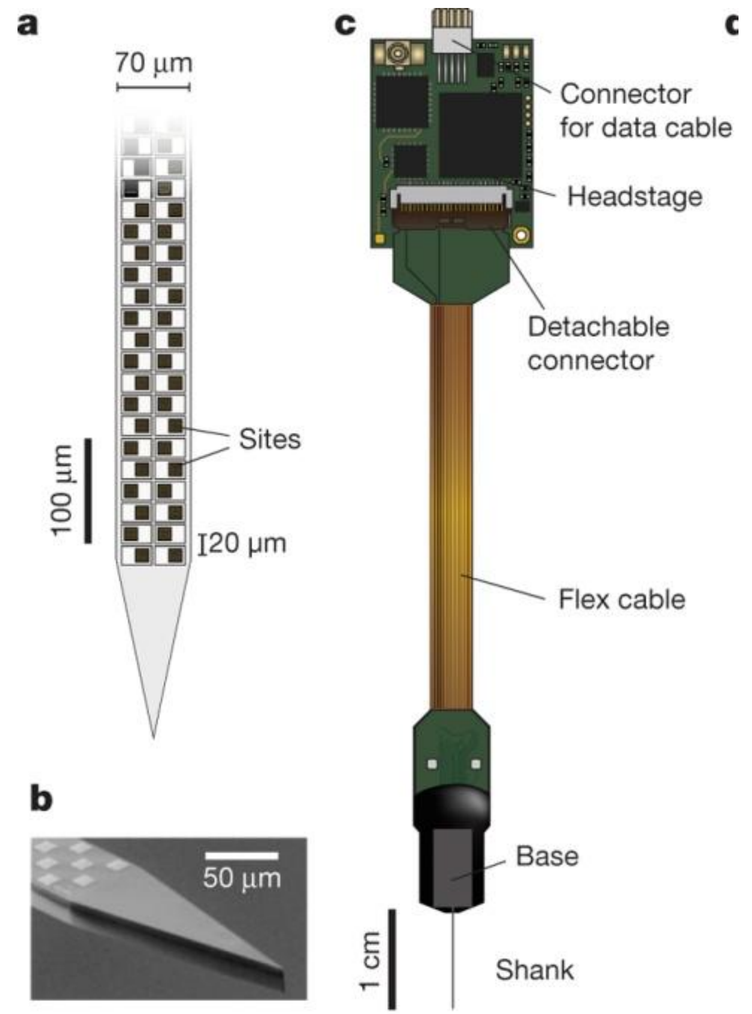
- No SSA to spectrally-balanced broadband sounds

- Maciej Jankowski, Mor Harpaz, Leila Khouri

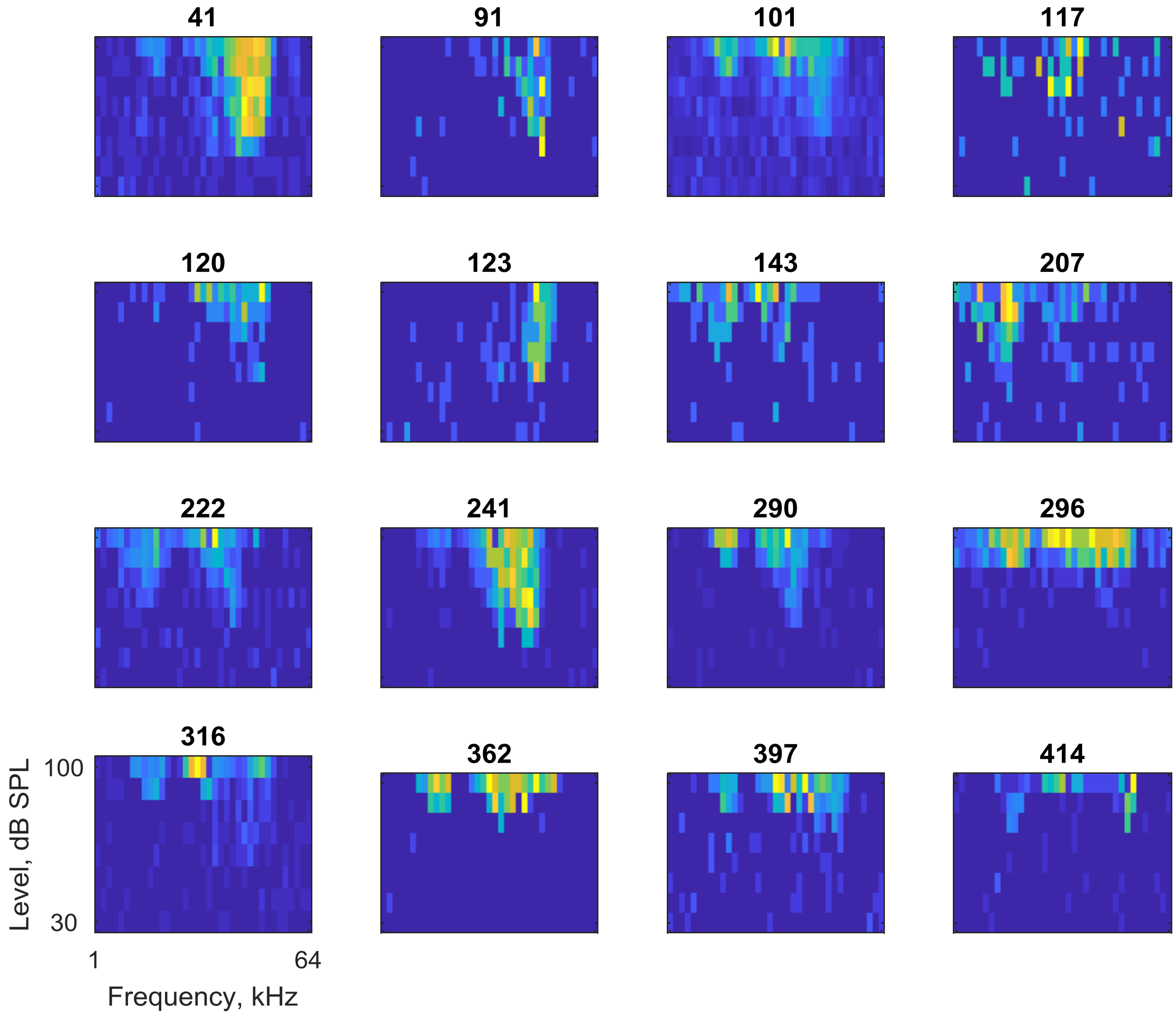
Tone clouds



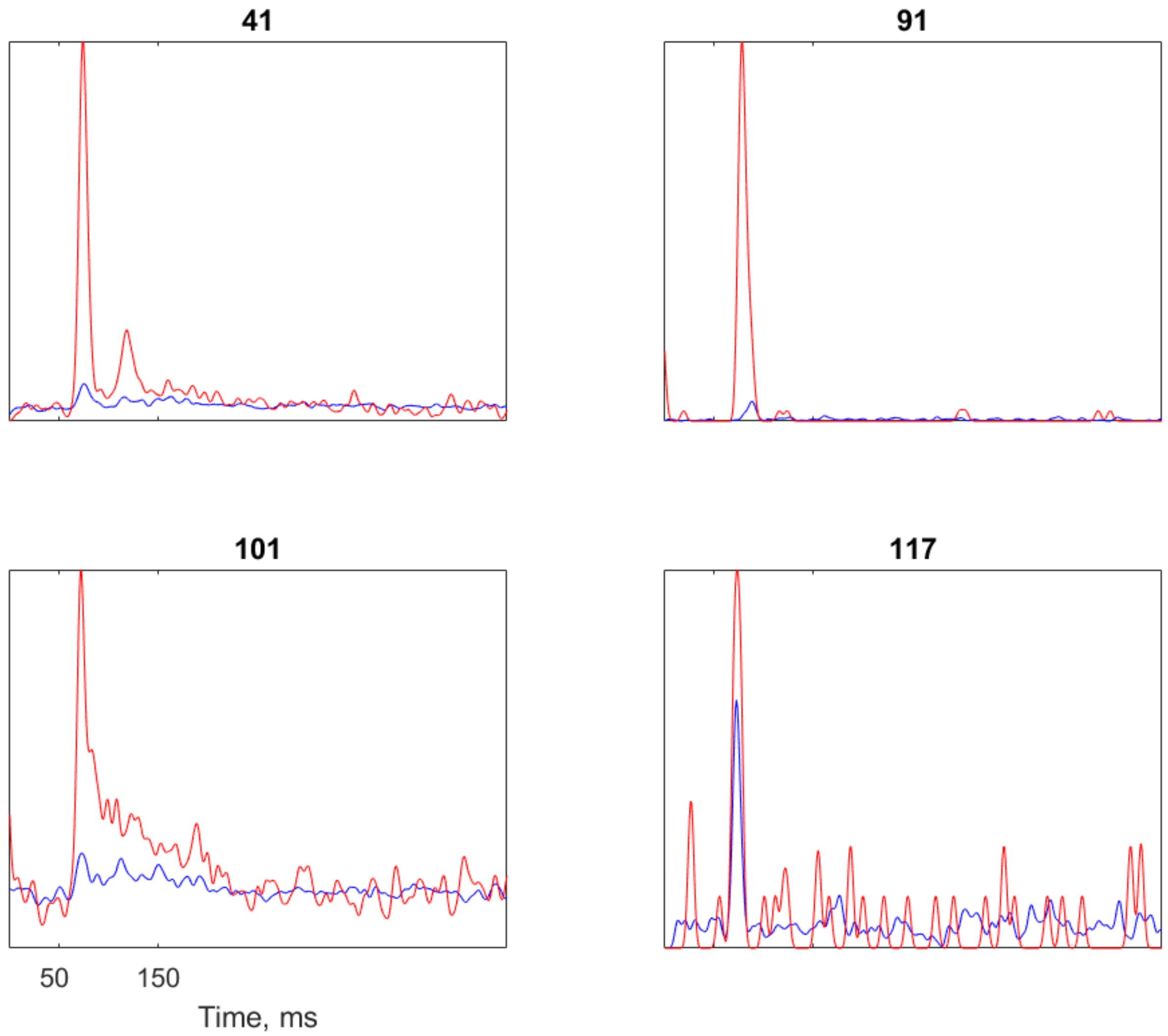
- The data were collected using Neuropixel probes
  - Recording from 384 contacts simultaneously
  - ~500 units/penetration, of which ~100 well-separated, maybe 30% with sensory responses
- 384 contacts span ~3 mm!



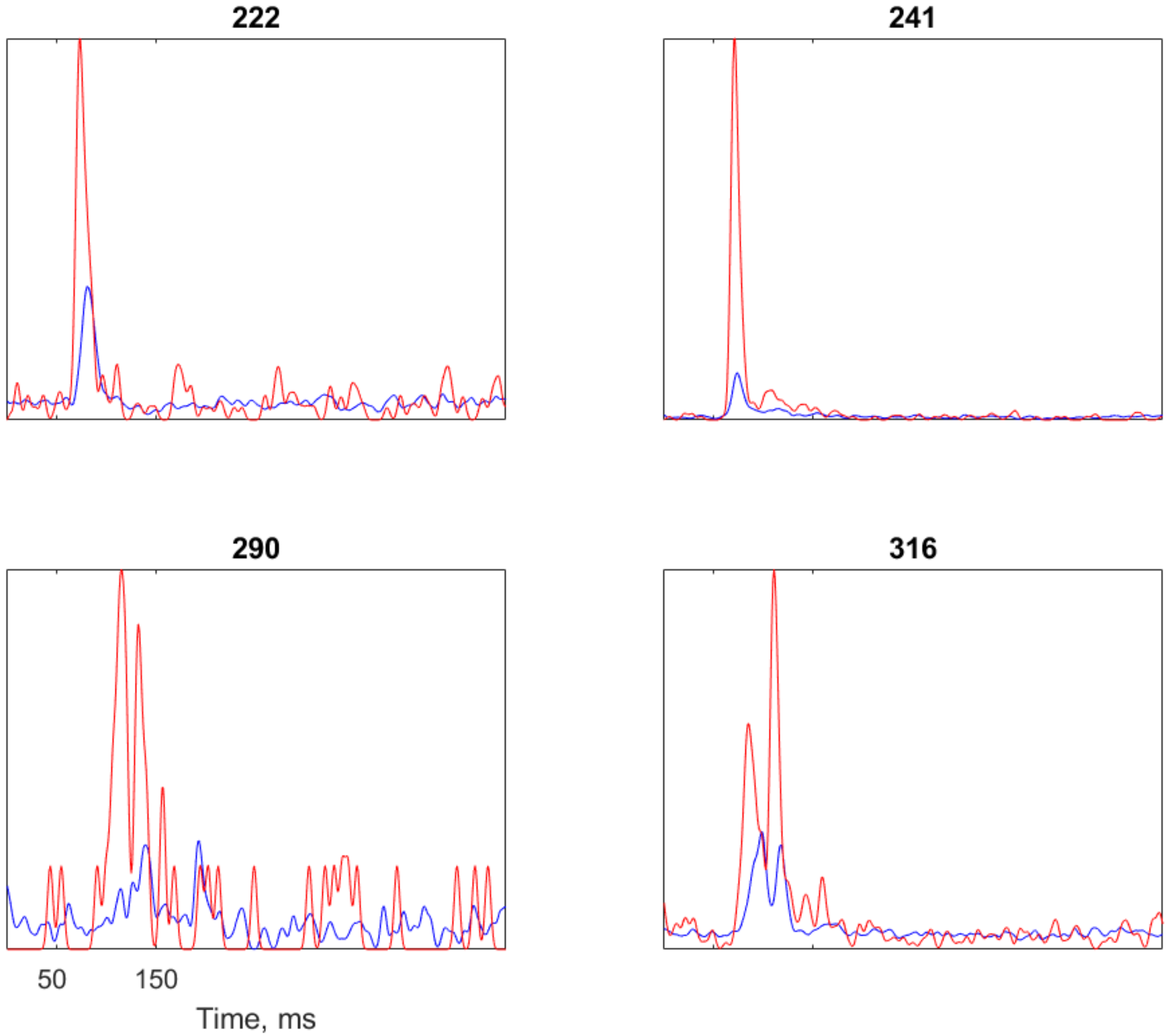
Example FRAs from auditory cortex



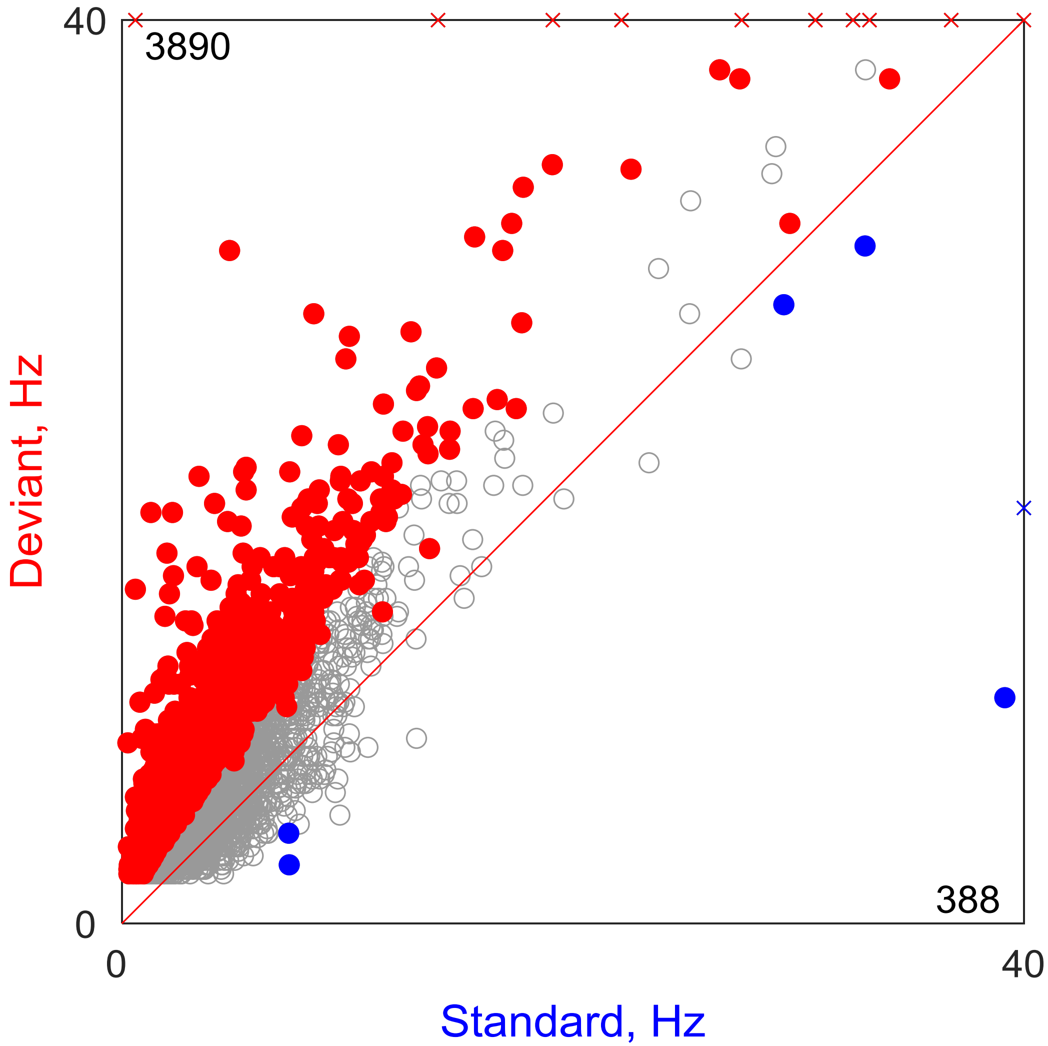
A1 reponses to tone clouds when standard and deviant



A1 reponses to tone clouds when standard and deviant

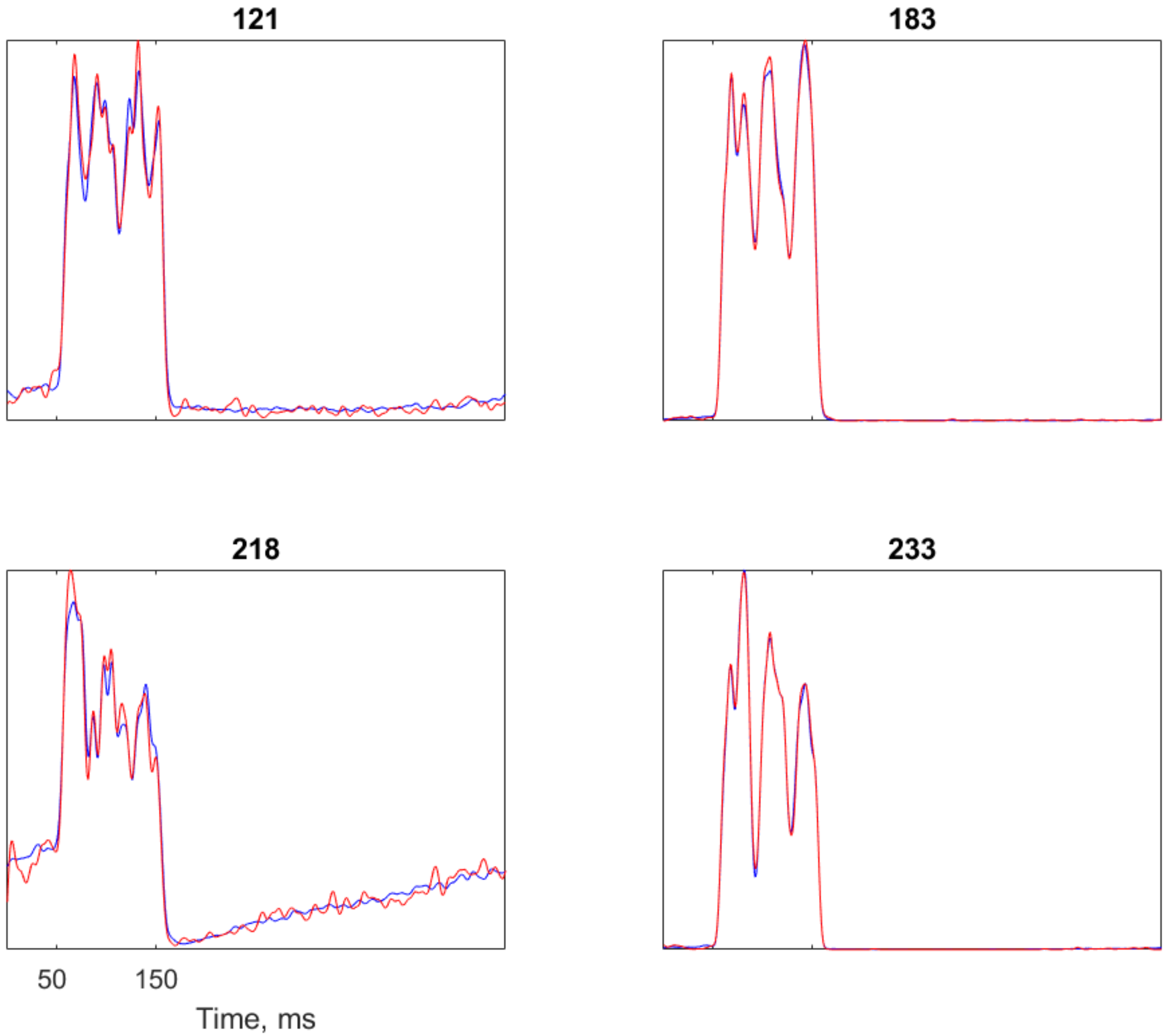


SSA to tone clouds in A1

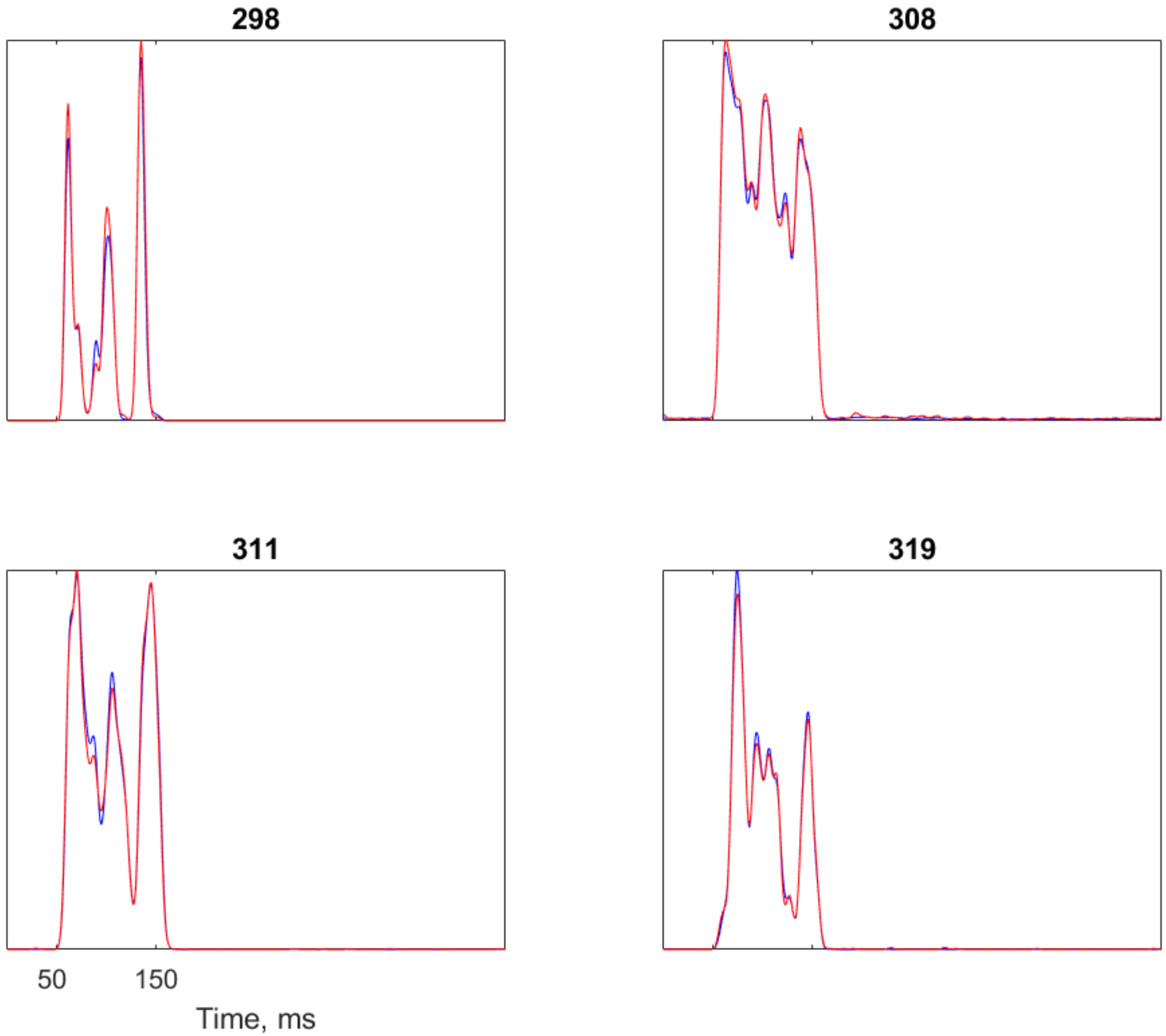


Jankowski, Harpaz, Khouri and Nelken

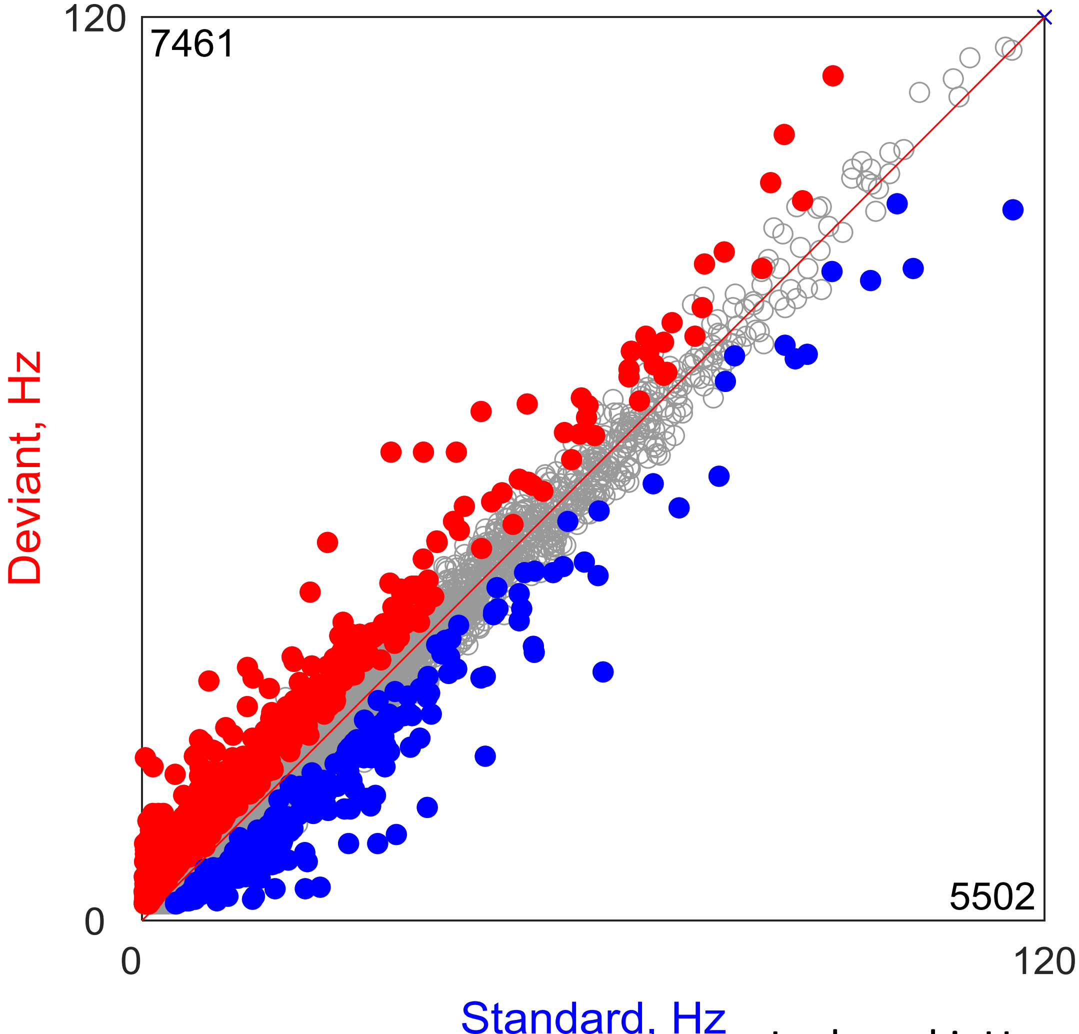
IC reponses to tone clouds when standard and deviant



IC reponses to tone clouds when standard and deviant



Weak SSA (if any) to tone clouds in IC



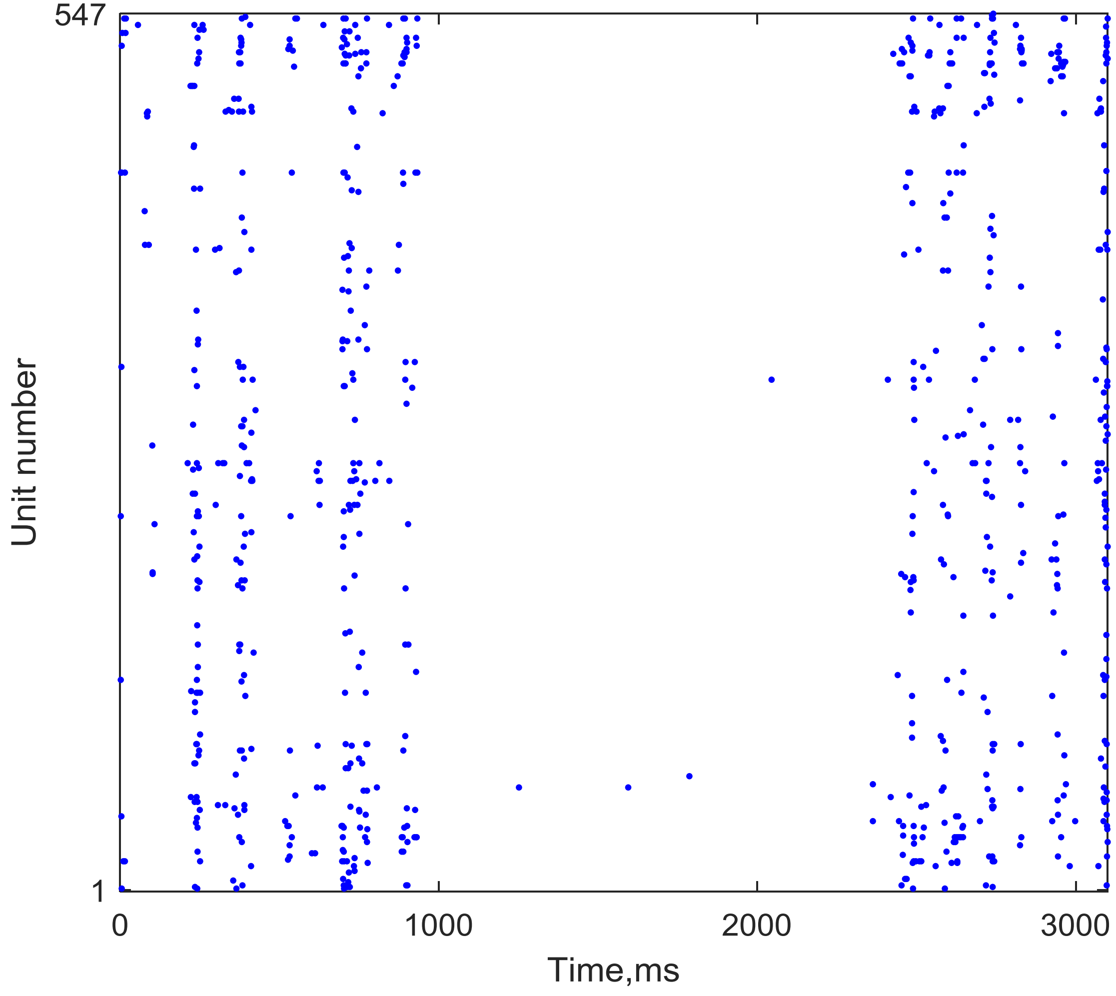
Jankowski, Harpaz, Khouri and Nelken

So what?

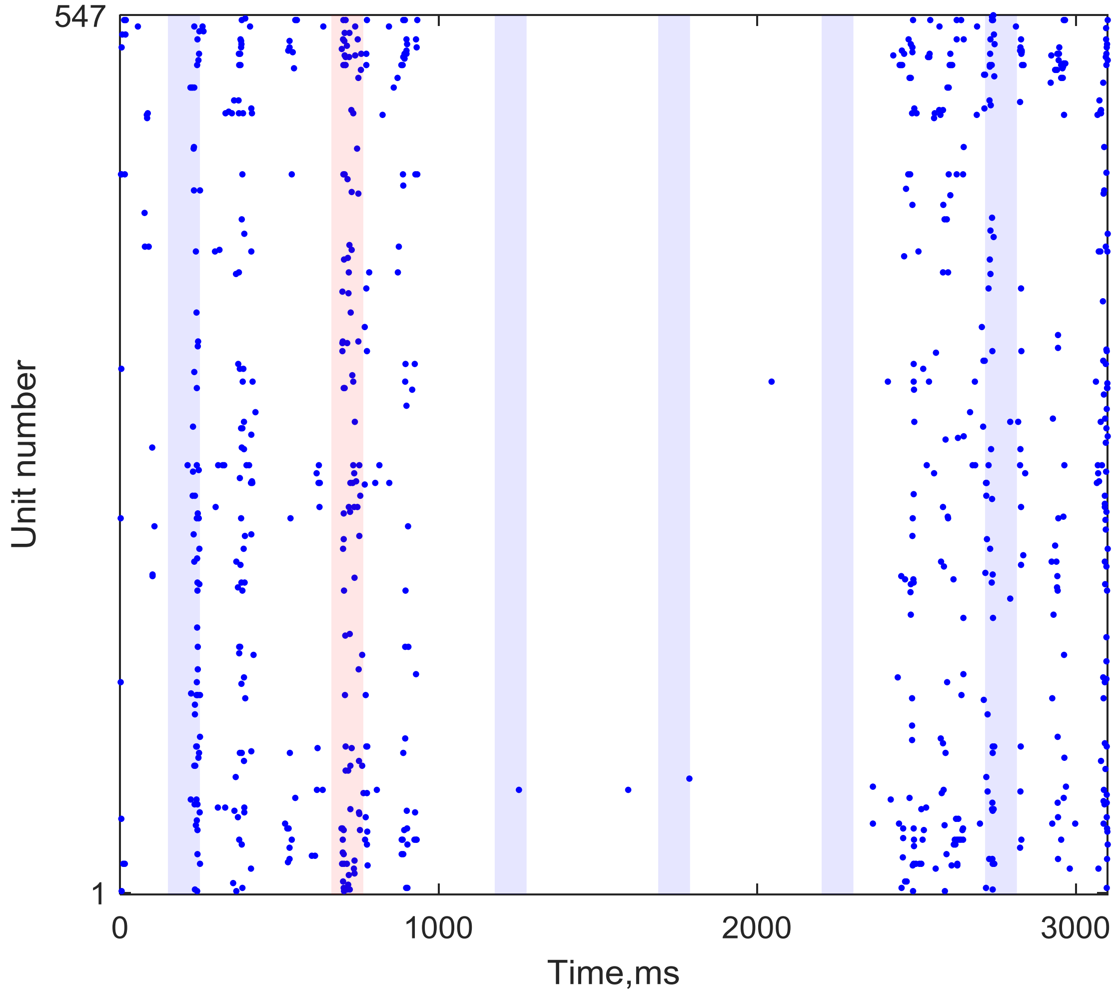
- (Large) SSA to tone clouds in auditory cortex
- ANTM can't explain SSA in auditory cortex
- Neurons discriminate between essentially any two clouds, even when their responses to the clouds in unbiased contexts are similar
- Subcortically, SSA to tone clouds is weak
  - We have some excuses, need to check them

(an aside on the largest difference between IC and A1)

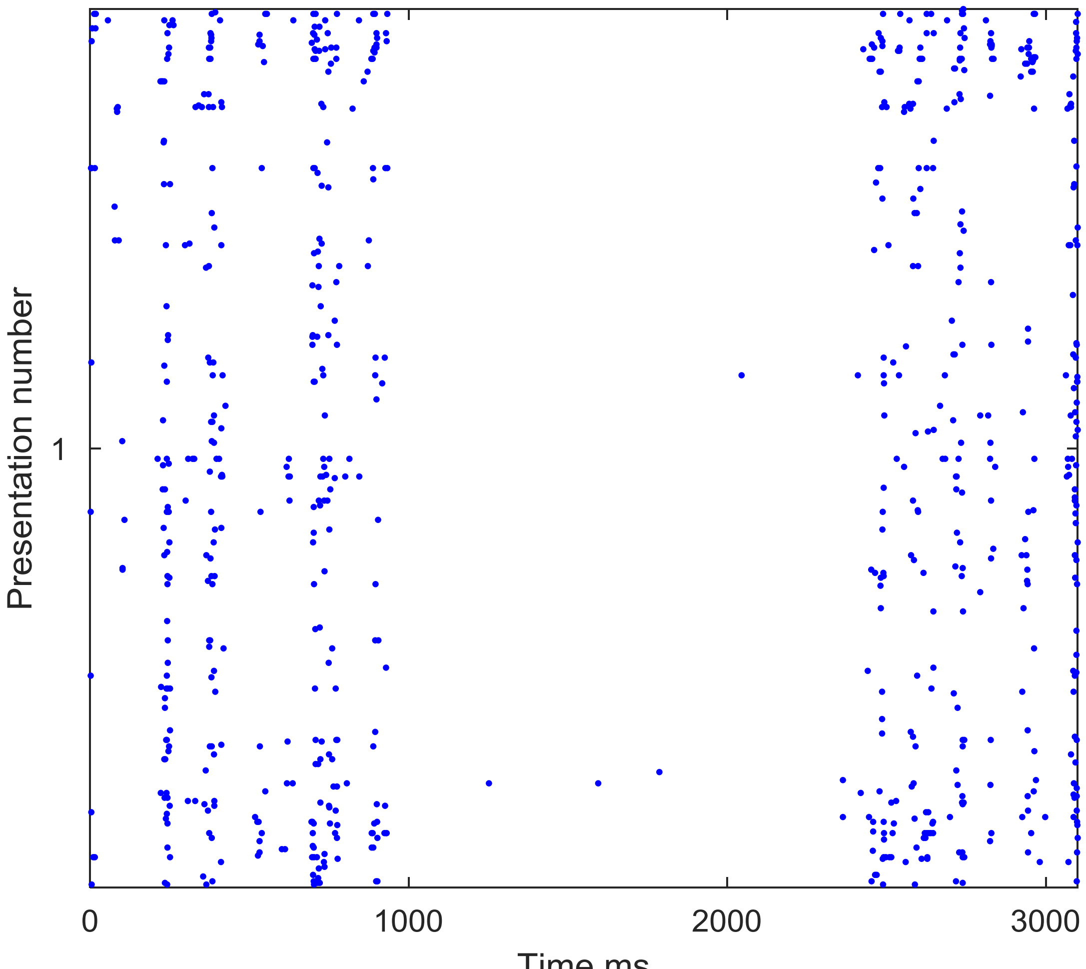
Cortical activity under anesthesia is highly correlated



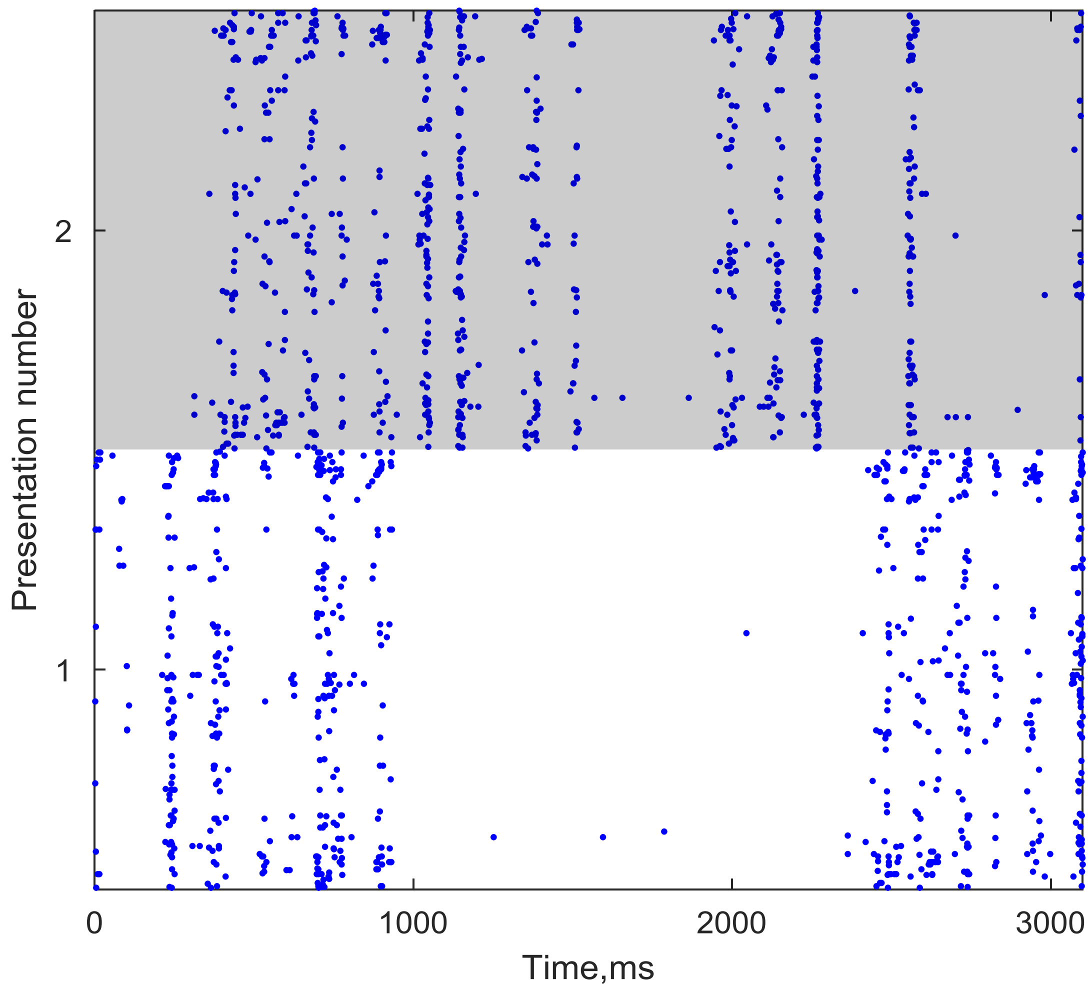
Cortical activity under anesthesia is highly correlated



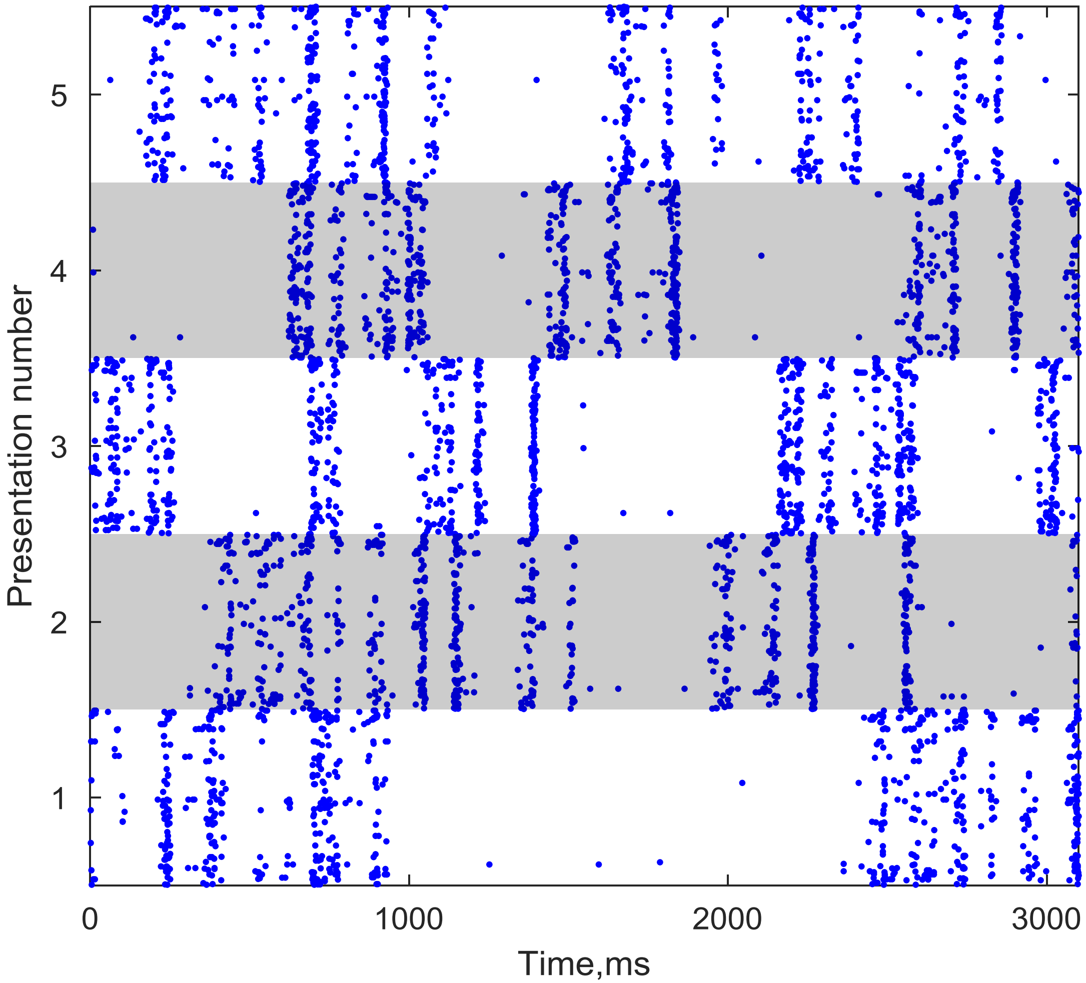
Cortical activity under anesthesia is highly correlated



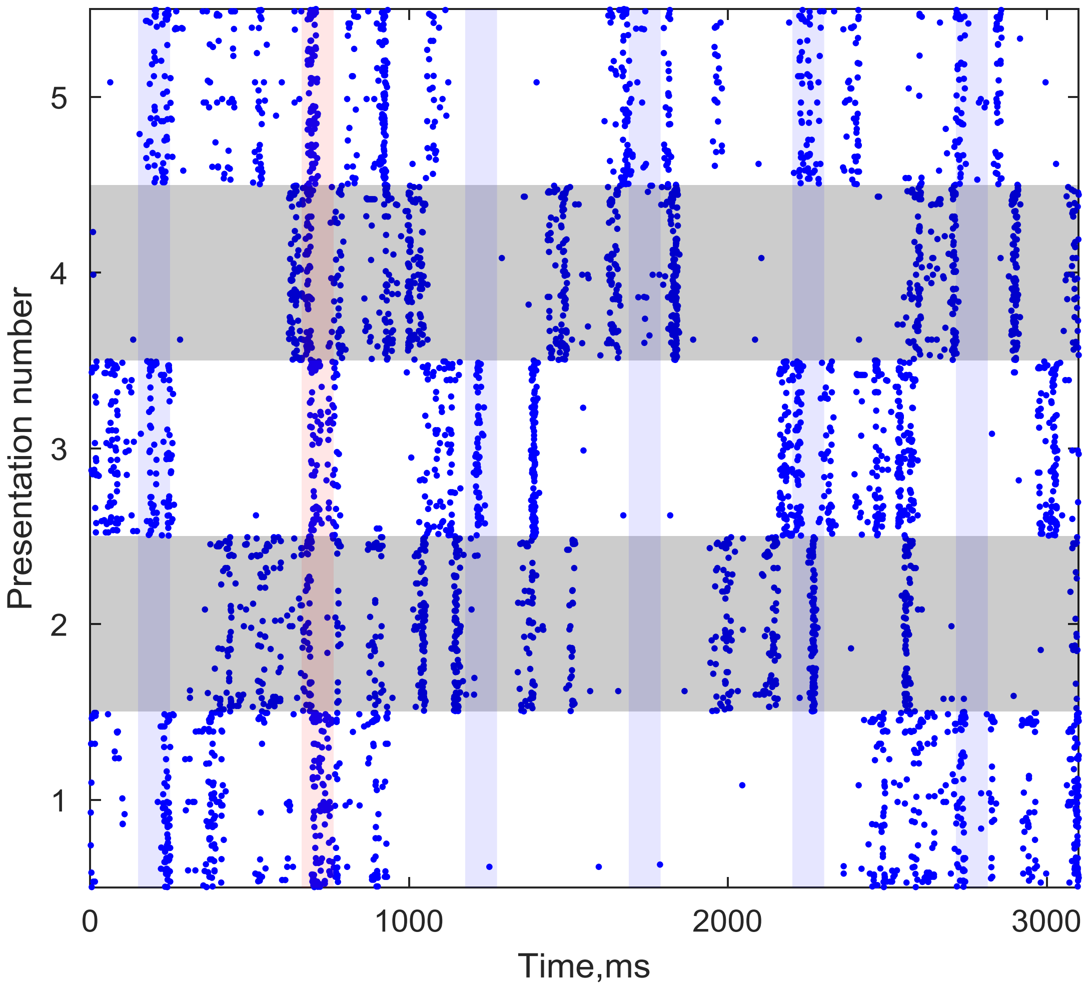
Population events occur at different times in different trials



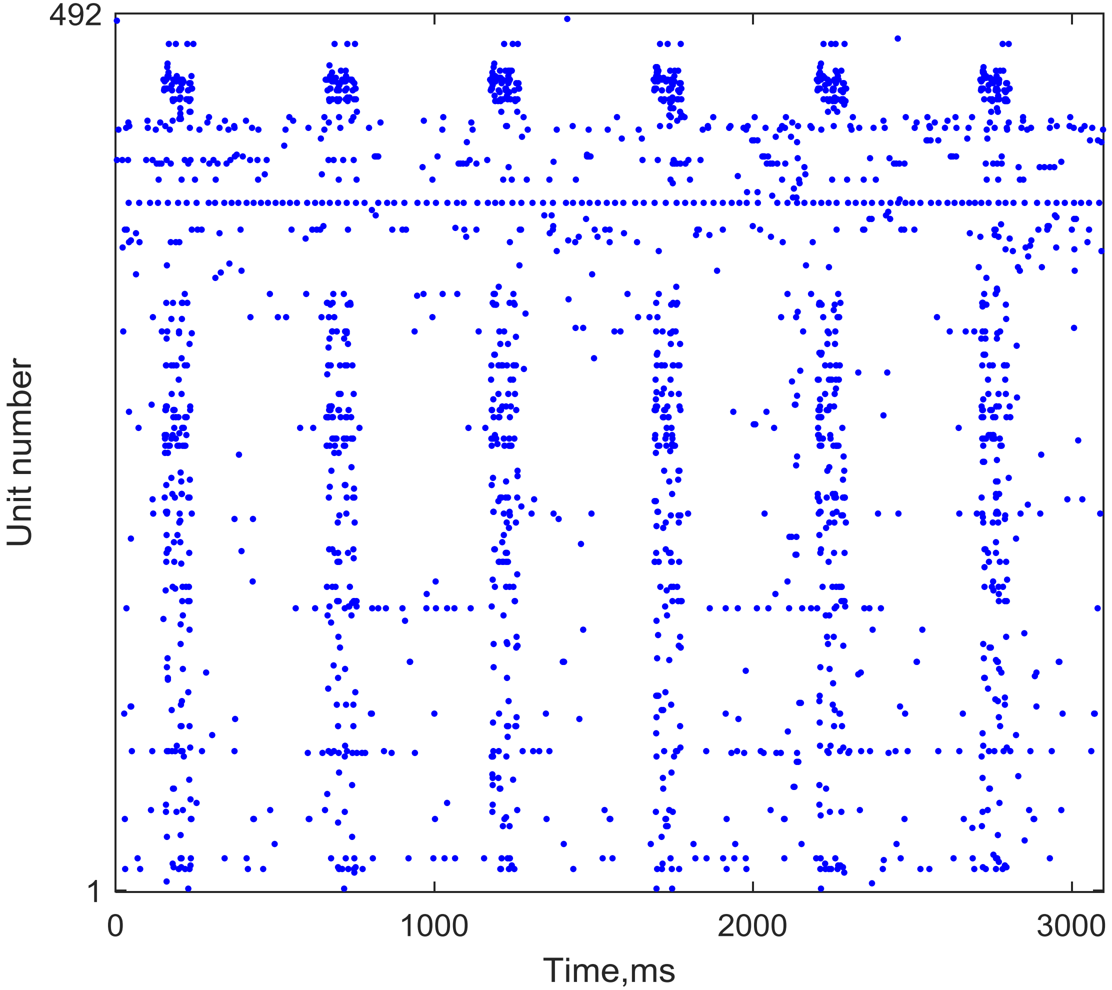
Where was the stimulus?



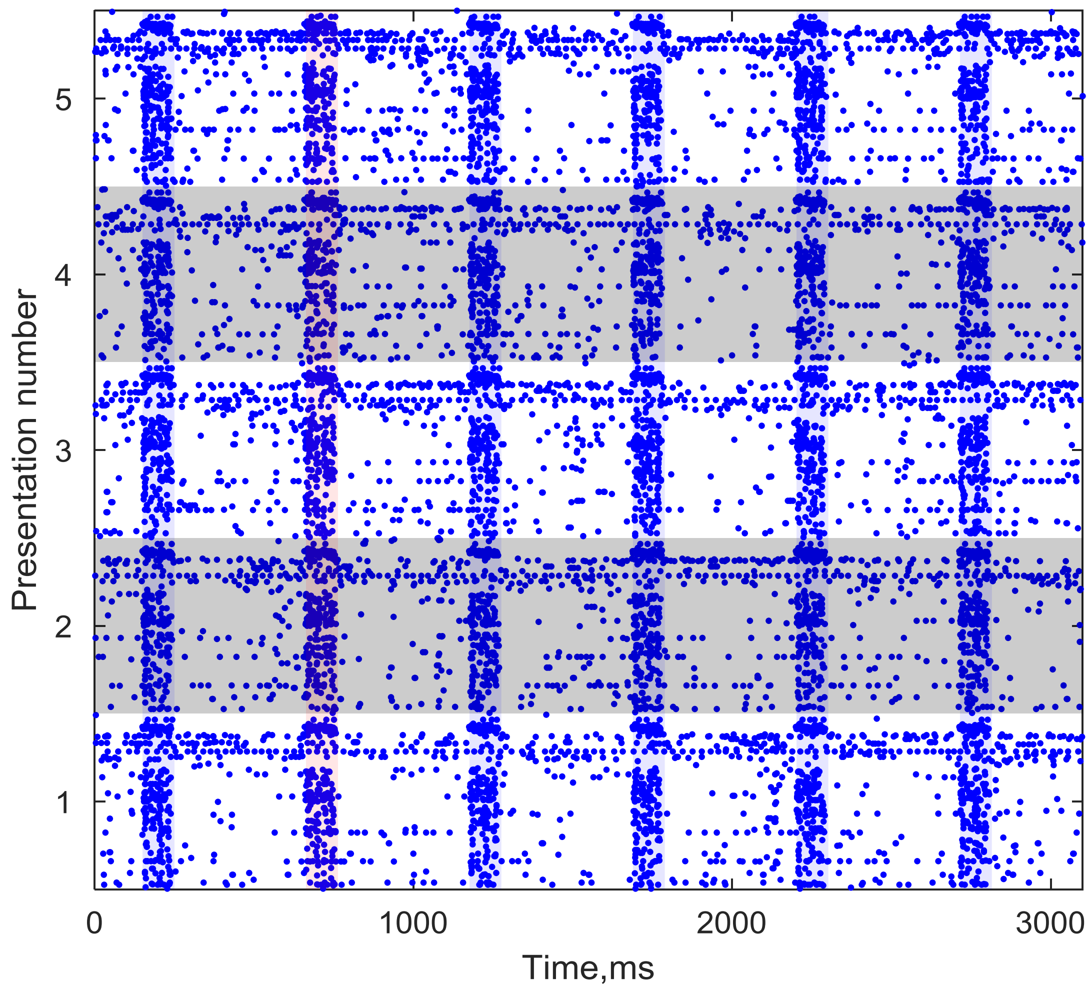
Where was the stimulus?



In inferior colliculus…



In inferior colliculus…

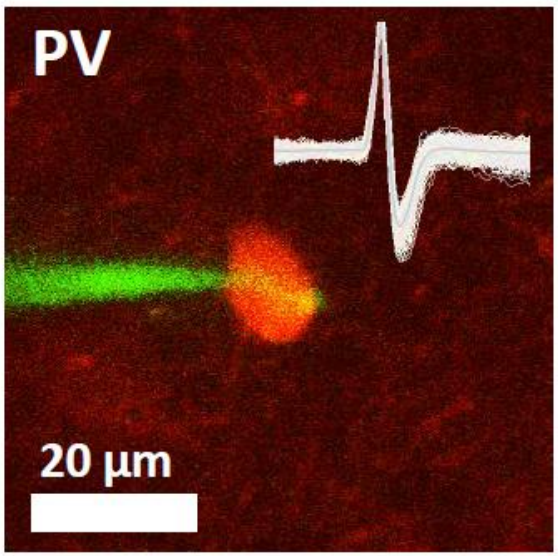


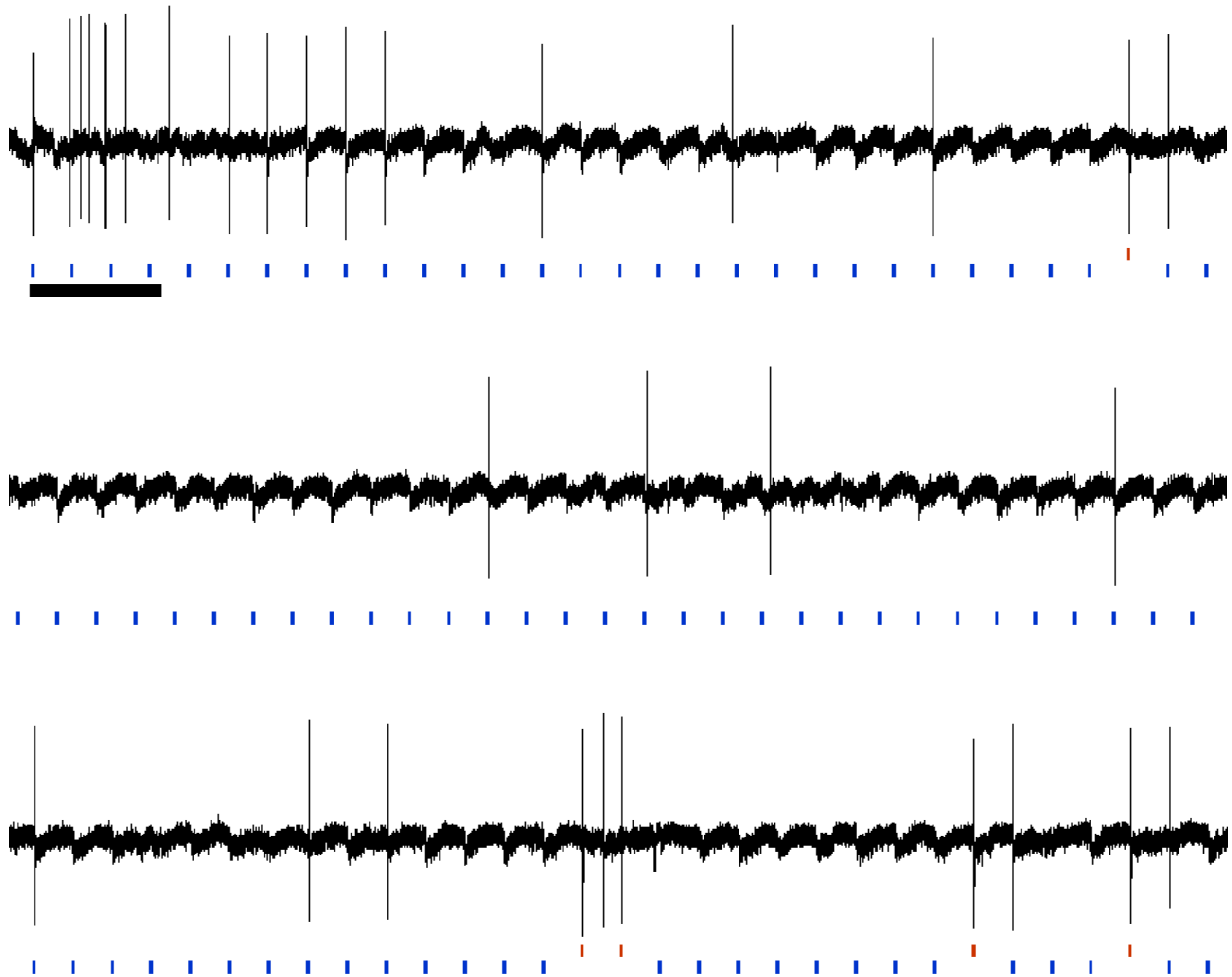
(close aside)

- Surprise responses in auditory cortex
    - Organization of auditory cortex
    - Why surprise?
    - How to study surprise?
    - The simplest model of SSA doesn’t work in A1
    - SSA and inhibitory interneurons in A1

- Tohar Yarden

Targeted patching of inhibitory interneurons

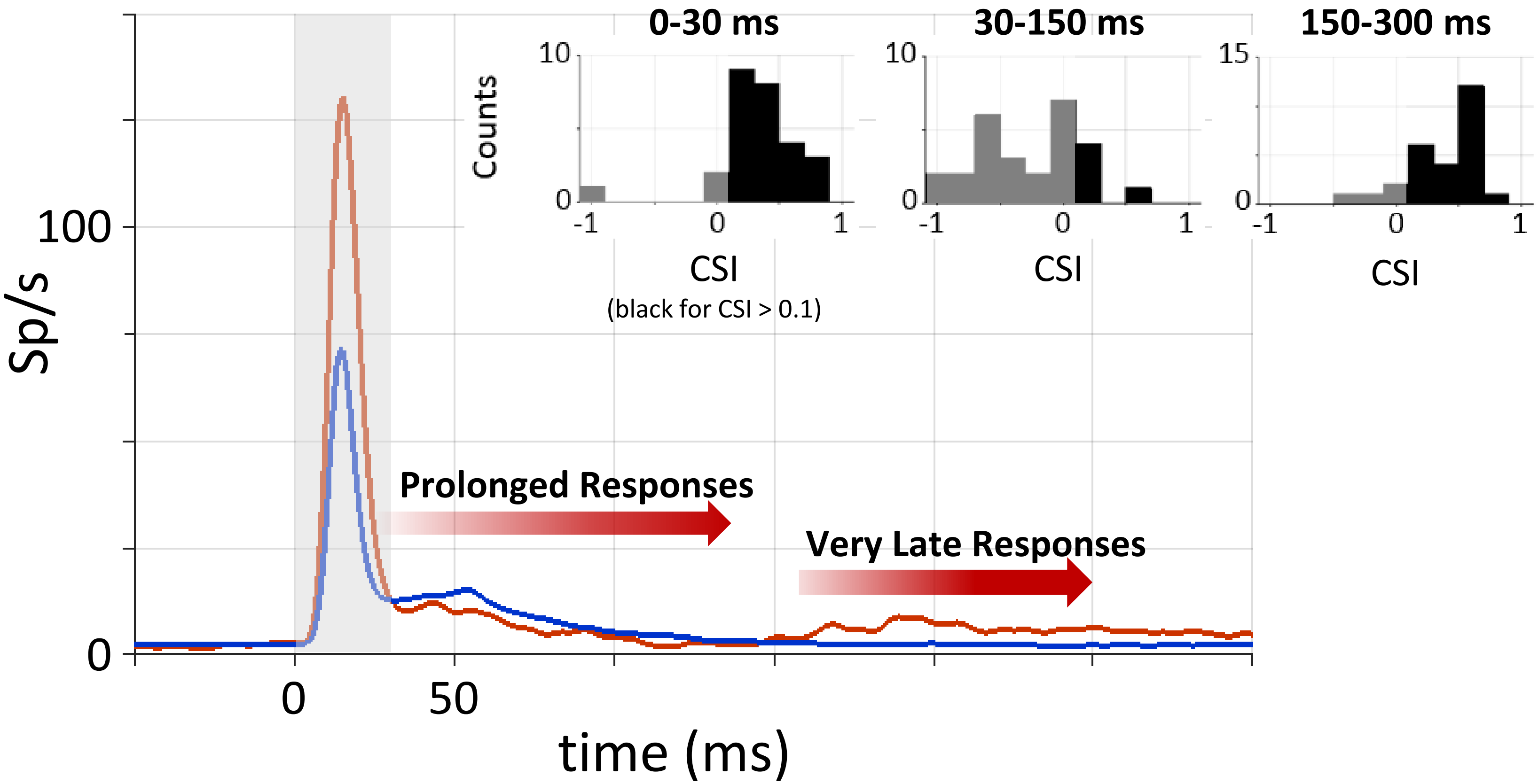




....(also in SST-cre, VIP-cre mice)

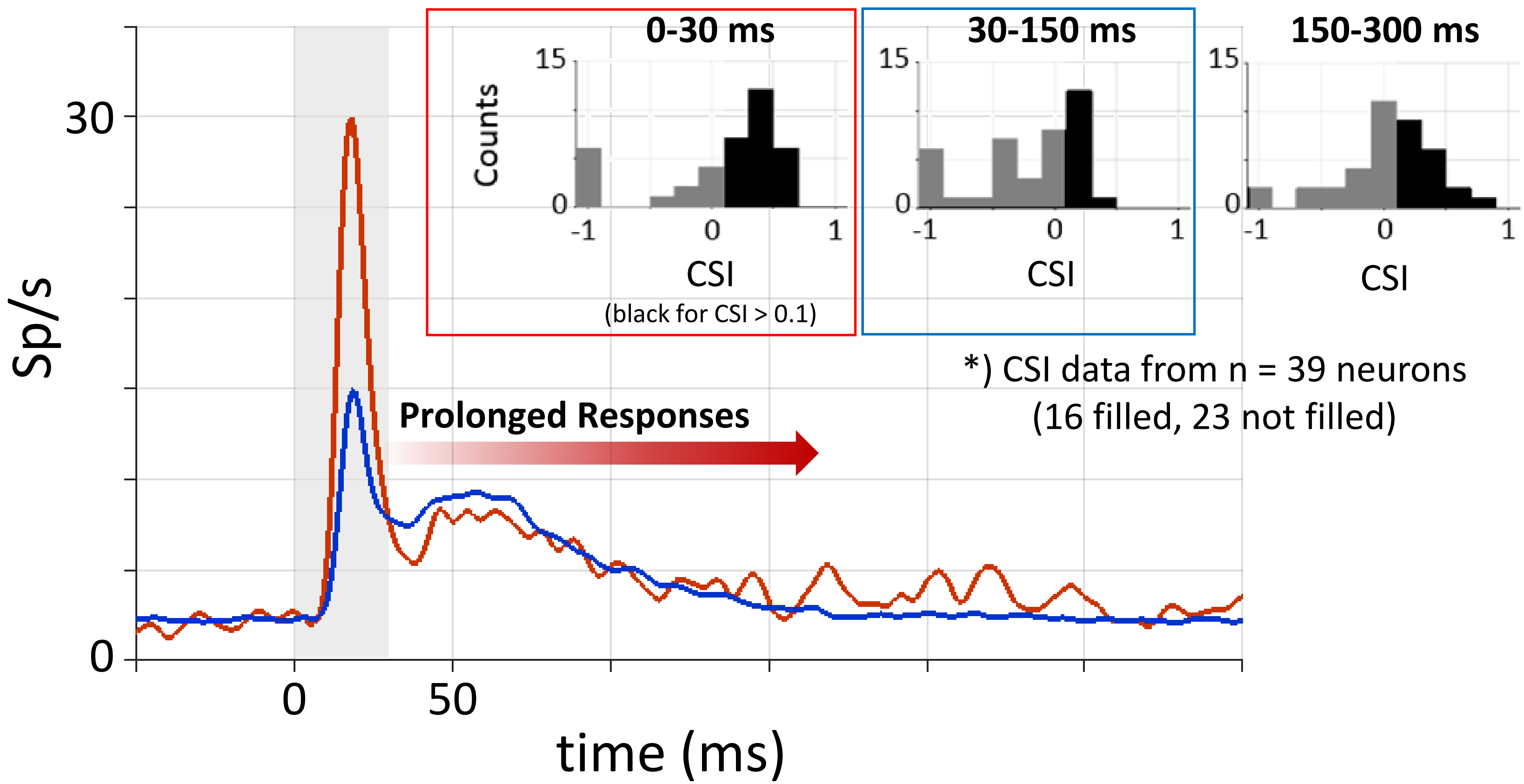
PV

(n = 27 labeled, FS neurons)



SST

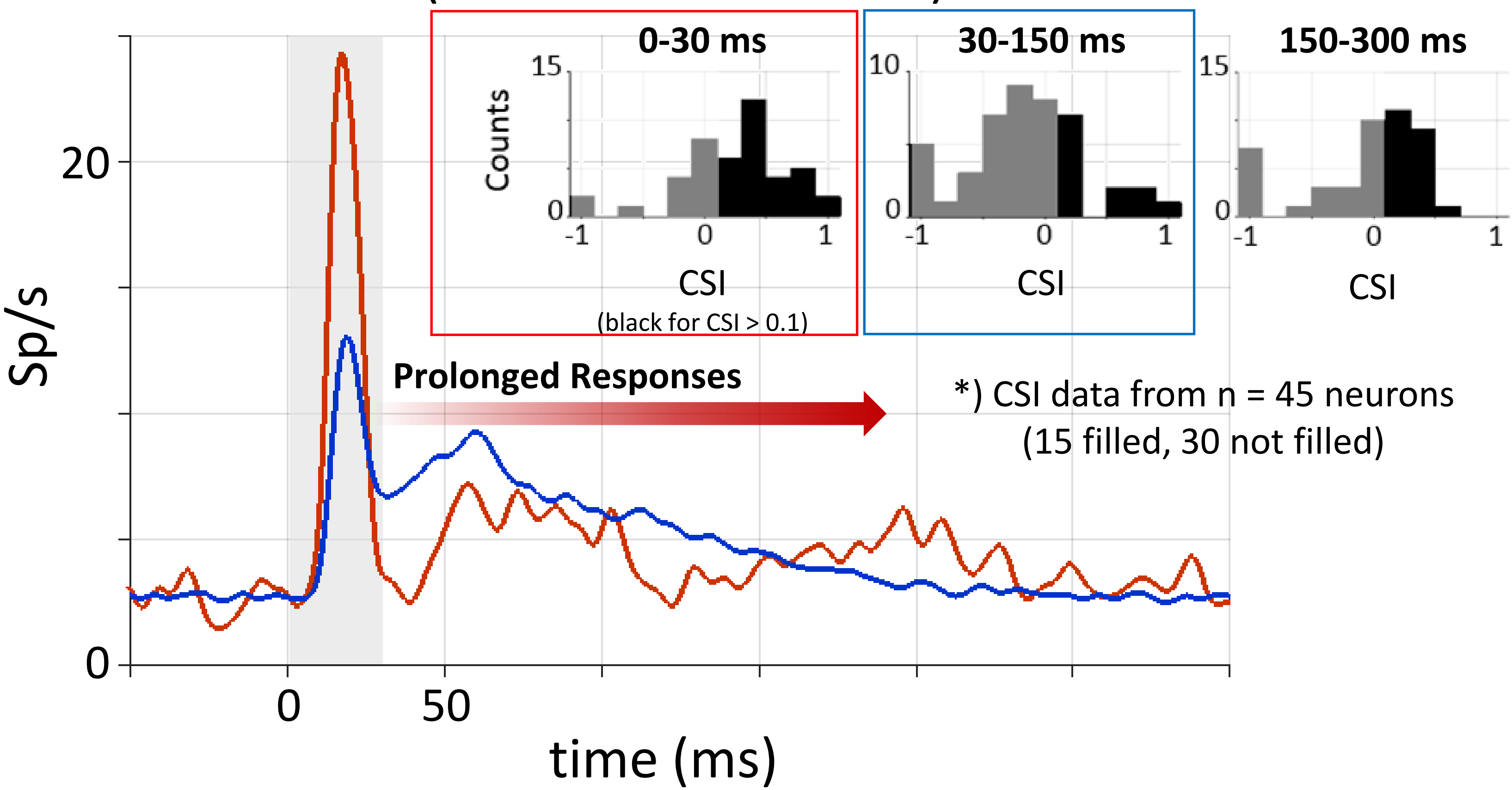
(n = 16 filled neurons)



*) CSI data from n = 39 neurons
(16 filled, 23 not filled)

VIP

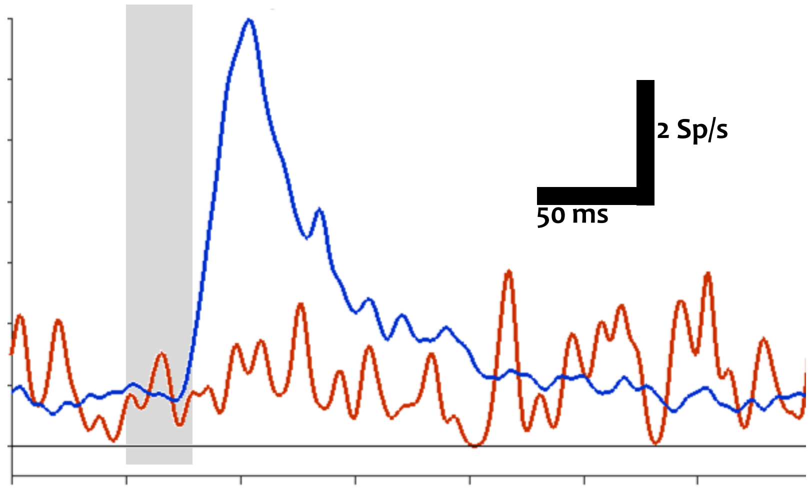
(n = 15 filled neurons)



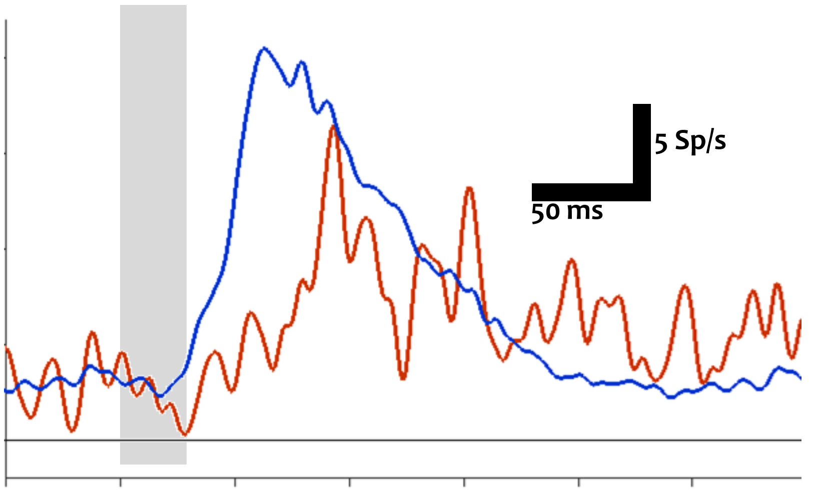
SST+ and VIP+ neurons show heterogeneous responses…

Some SST+ and VIP+ neurons are selective for standards

SST+



VIP+



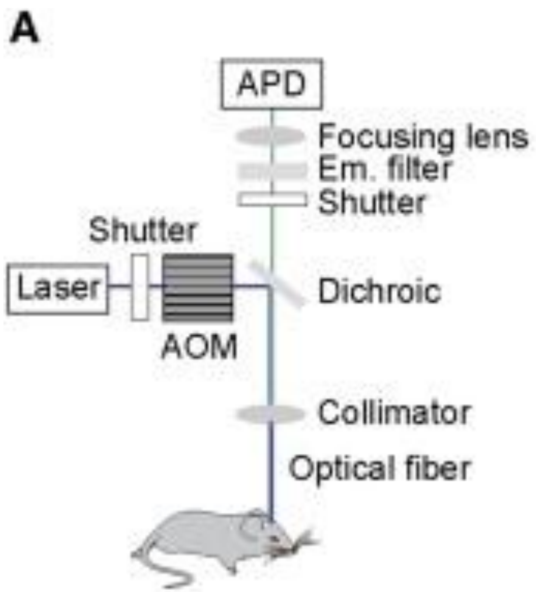
So what?

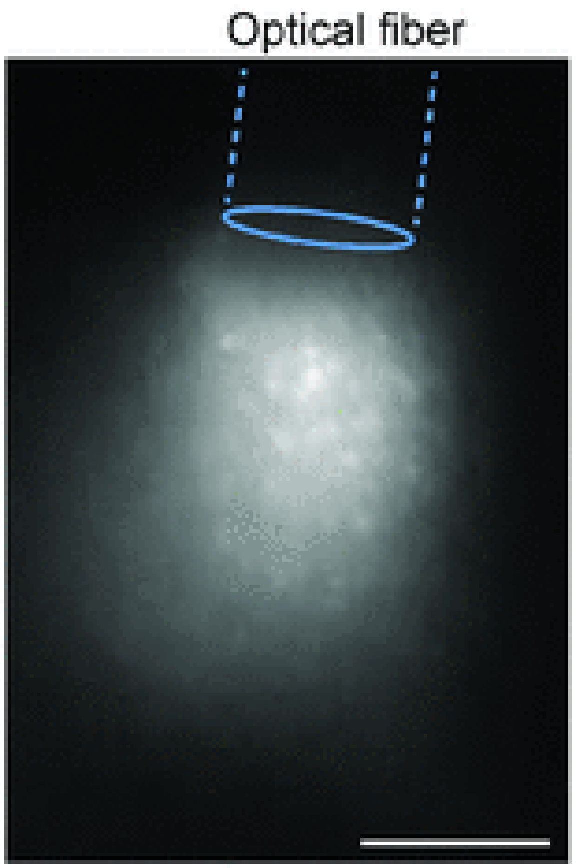
- During stimulus presentation, inhibitory interneurons show SSA with pretty much the same properties of the pyramidal network
- Interesting temporal dynamics after stimulus offset
- The excitatory neurons that were targeted didn’t show late activity…
- …But…

- Surprise responses in auditory cortex
  - Organization of auditory cortex
  - Why surprise?
  - How to study surprise?
  - The simplest model of SSA doesn’t work in A1
  - SSA and inhibitory interneurons in A1
  - Mesoscopic SSA

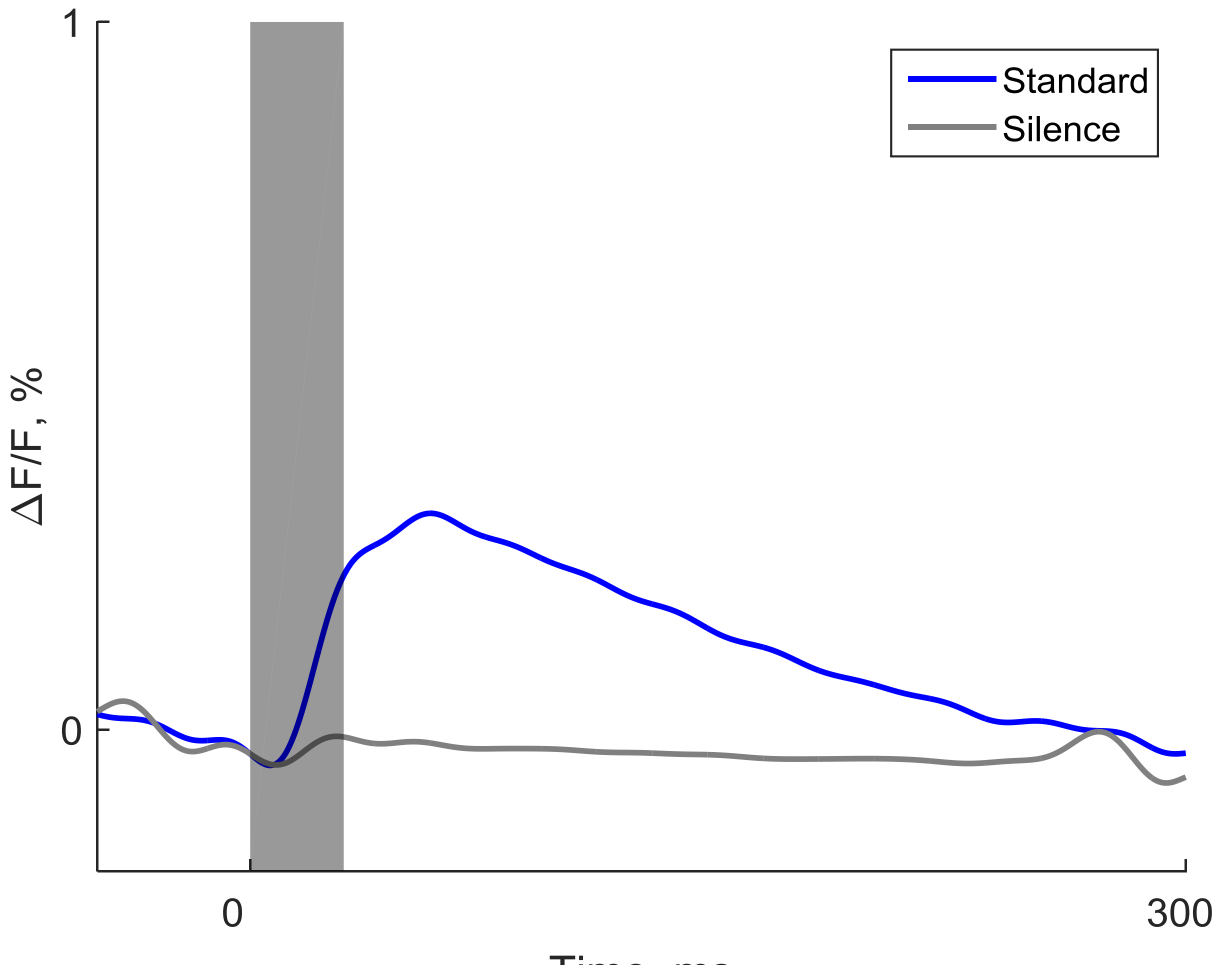
- Dina Moshitch, Kamini Sehwarat

Fiber photometry



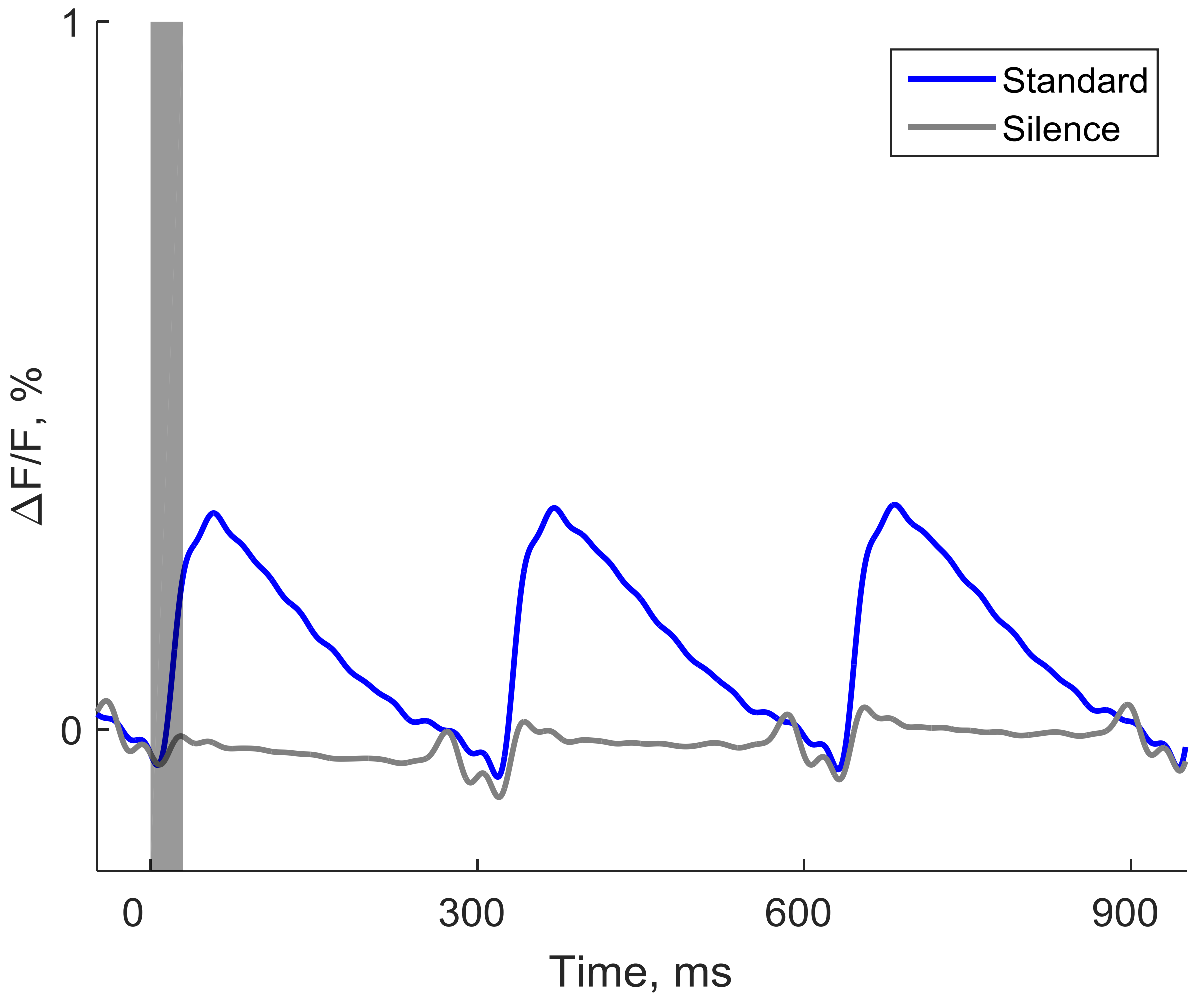


Sensory calcium responses using fiber photometry



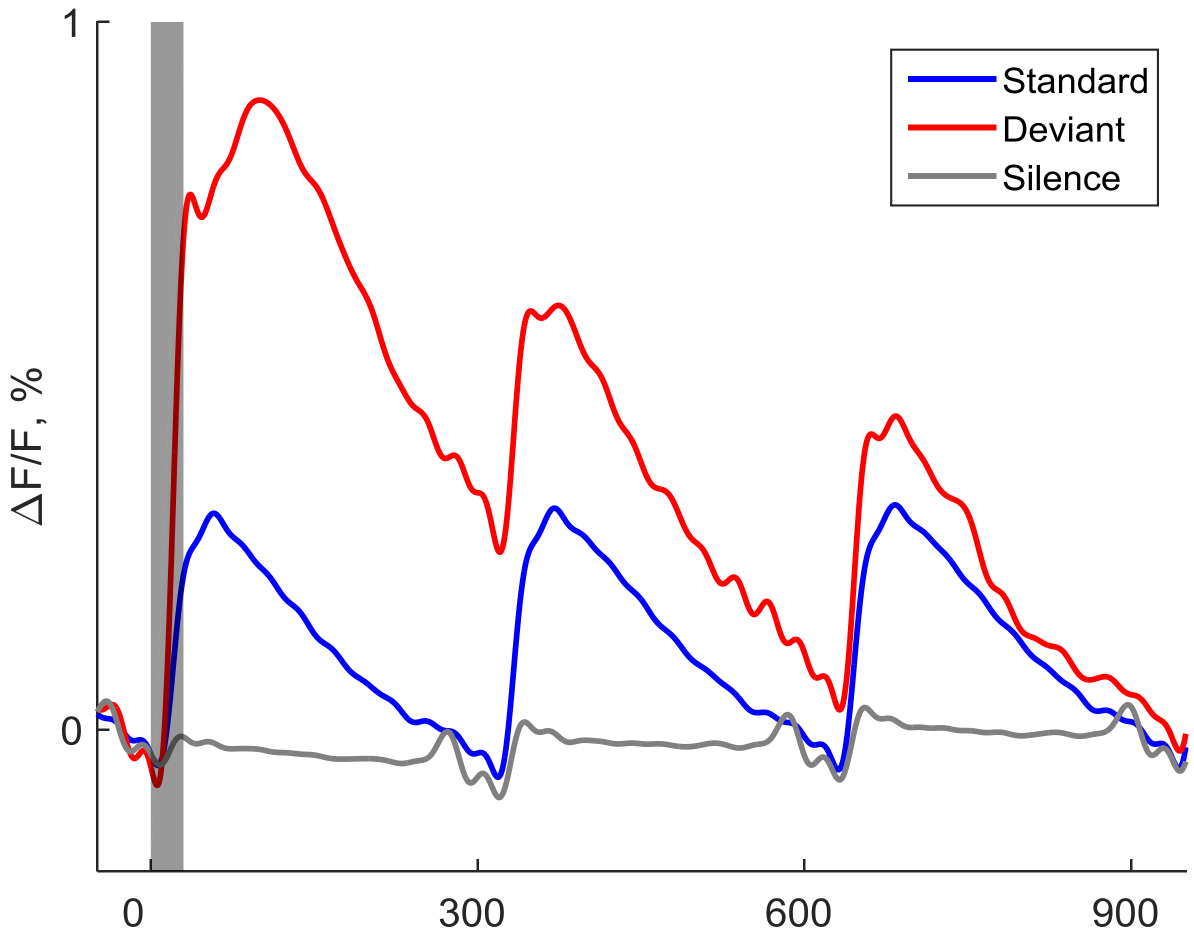
Dina Moshitch

Sensory calcium responses



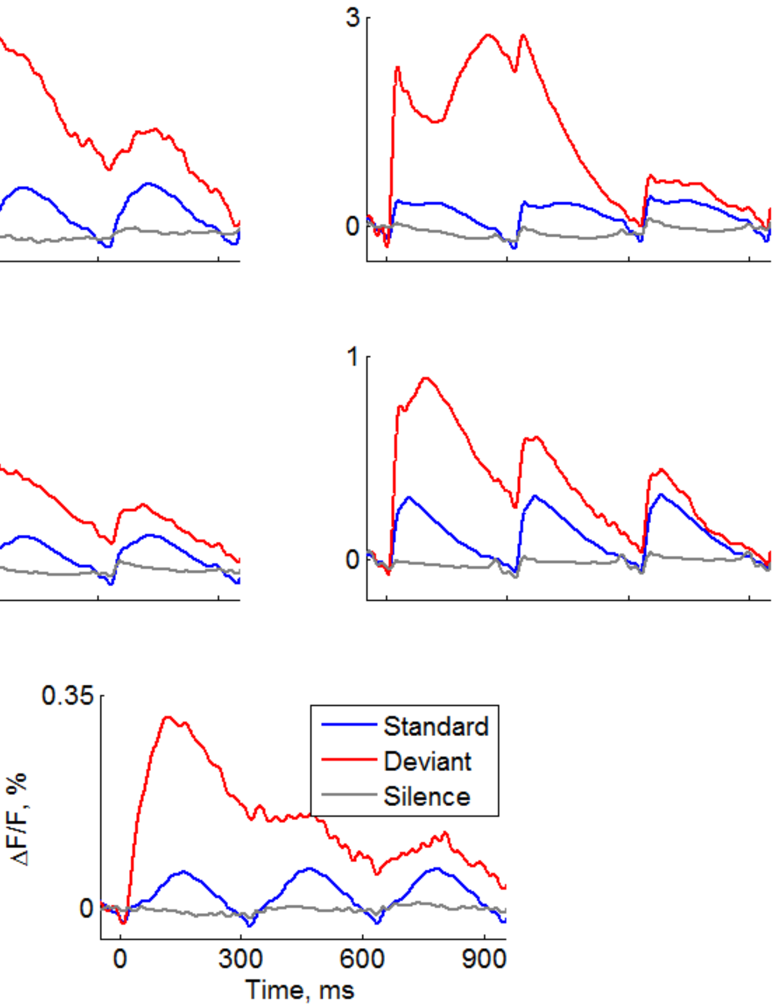
Dina Moshitch

Stimulus specific adaptation in calcium responses



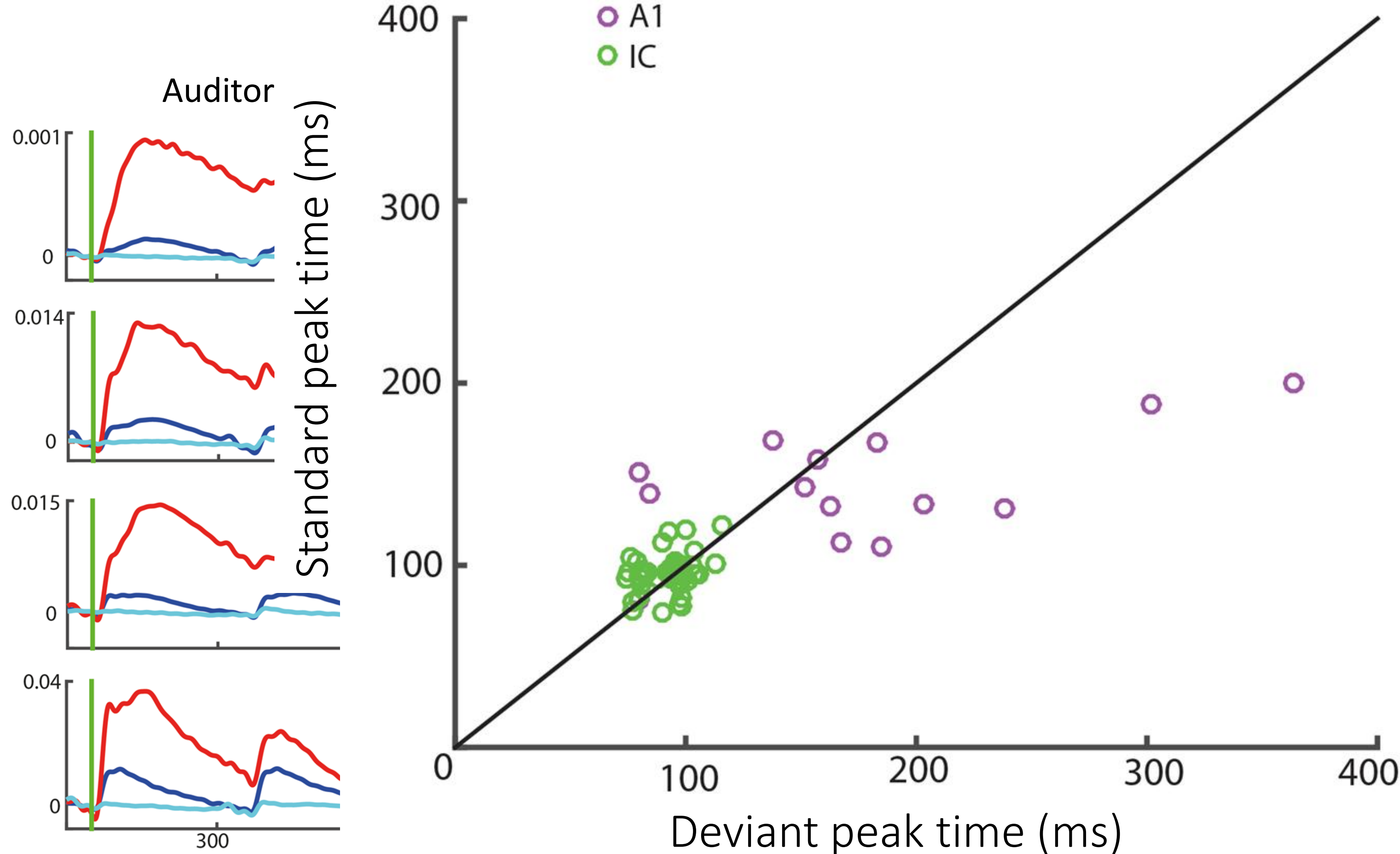
Dina Moshitch

Deviants evoke a long-lasting calcium transient

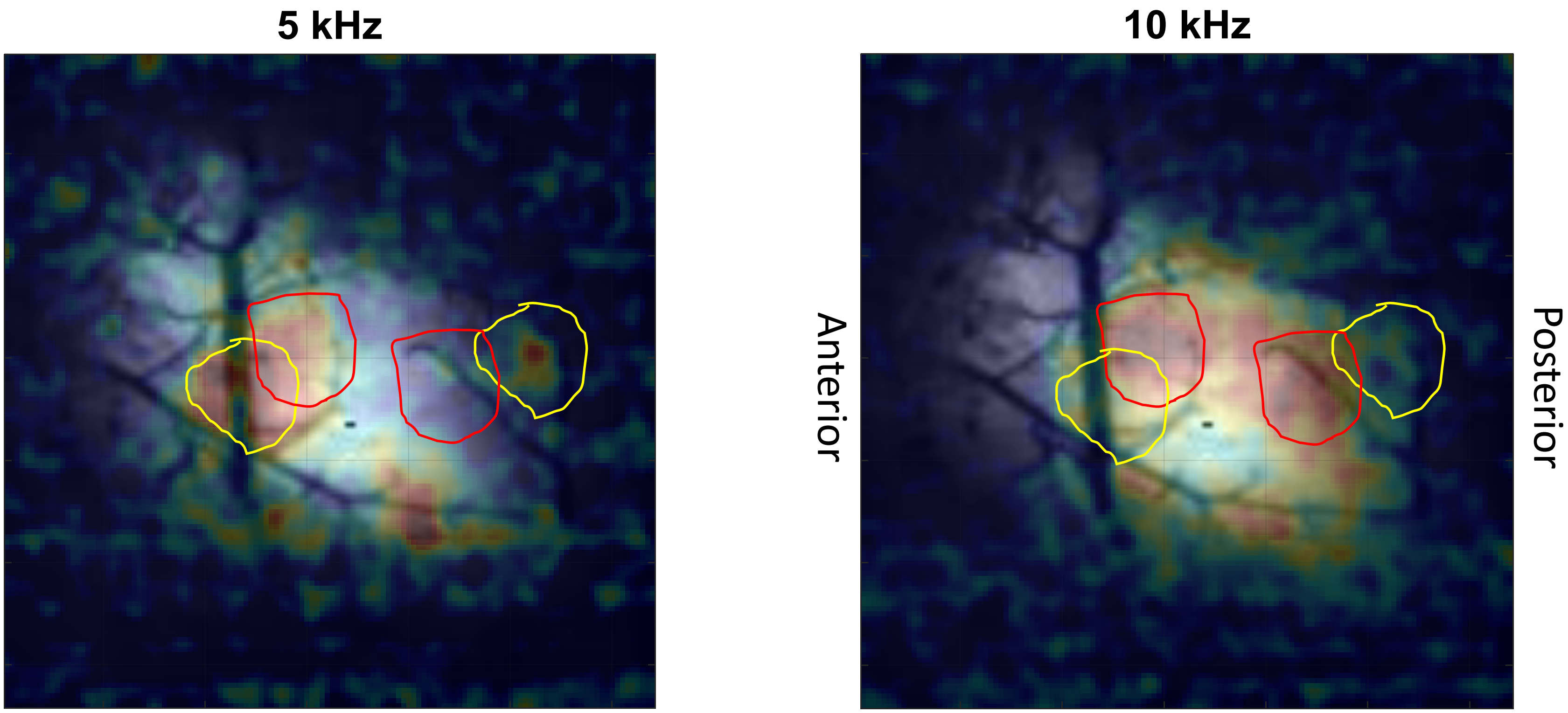


Dina Moshitch

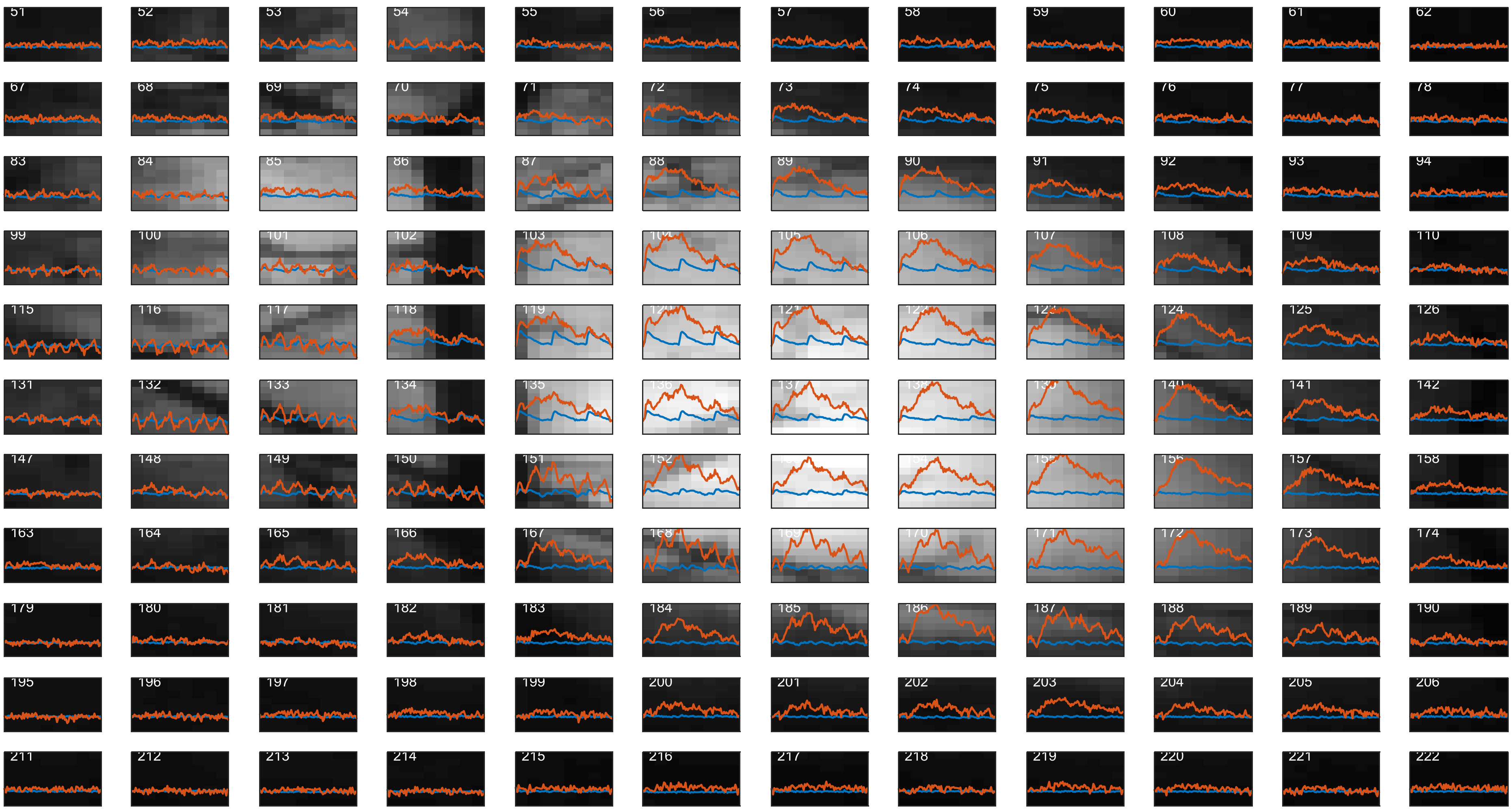
The late waves are (thalamo)-cortical



Large scale tonotopy using calcium signals



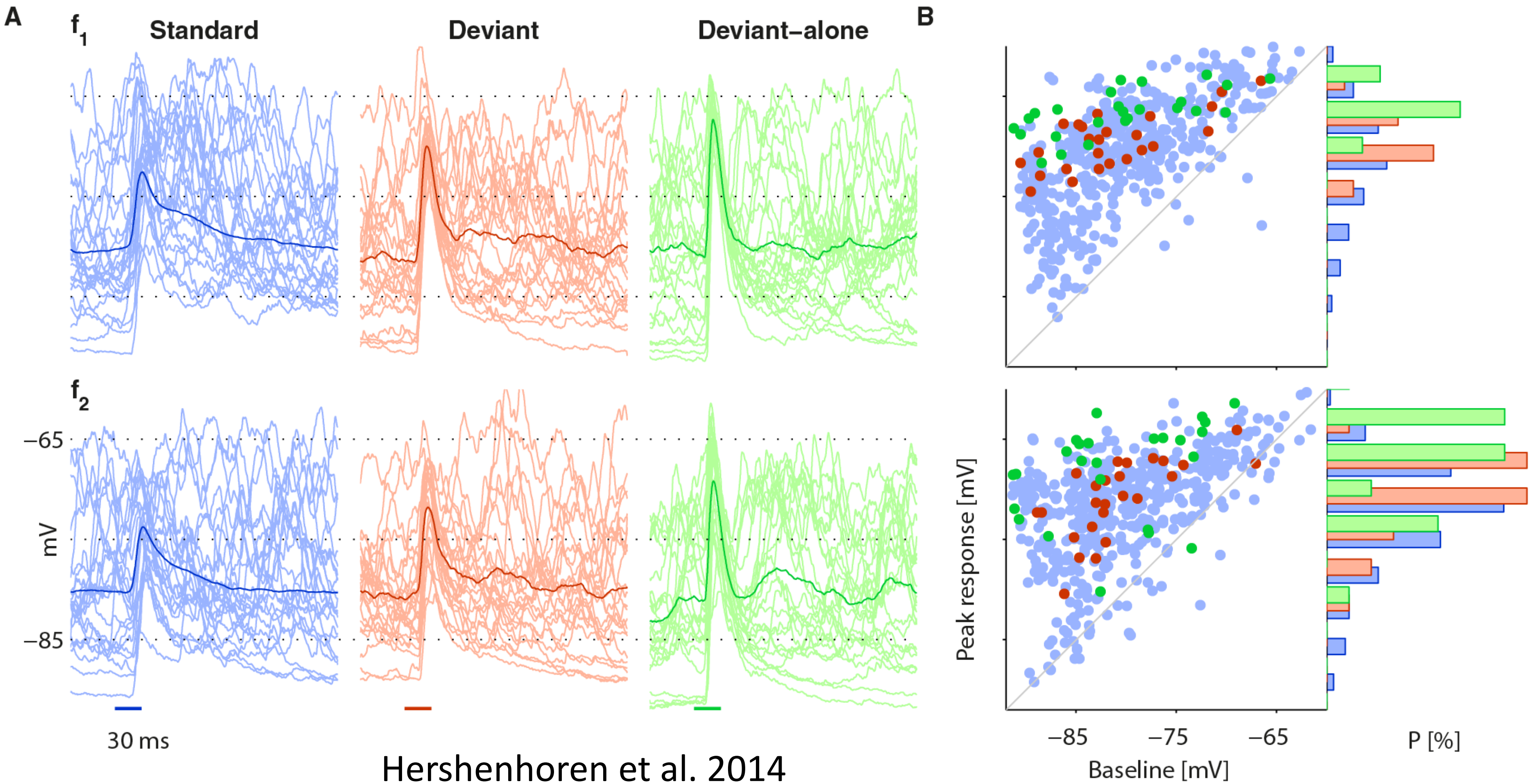
Widefield SSA



Where do the late response come from?

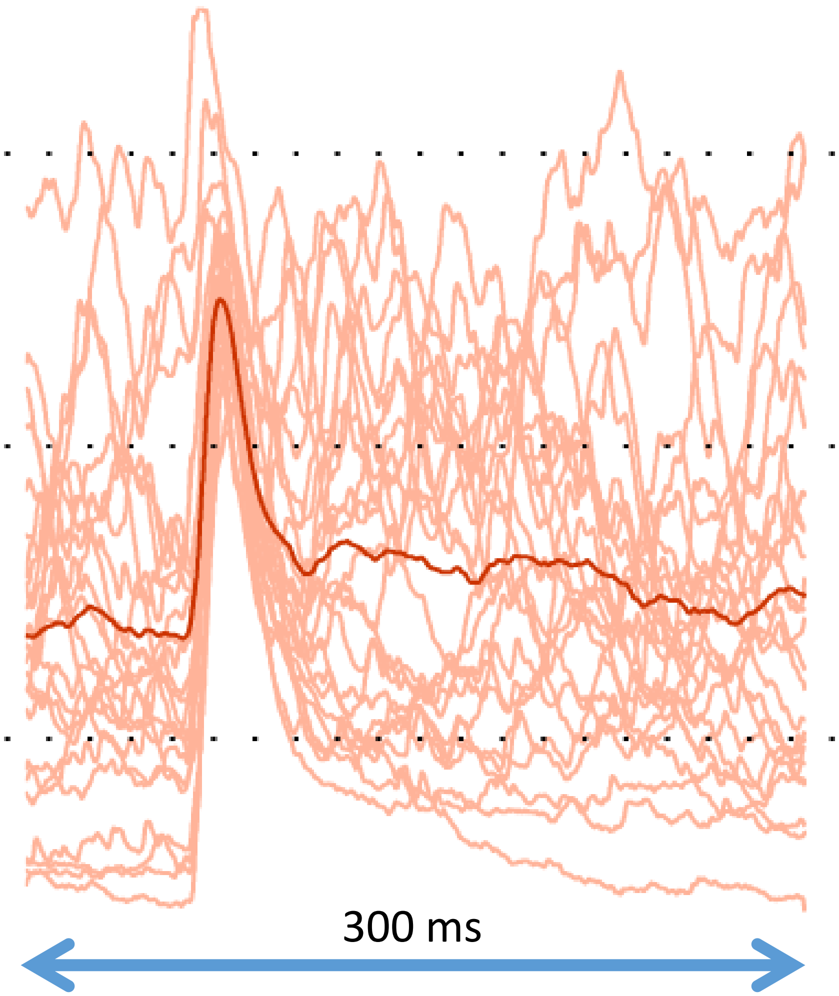
- Late responses of single neurons are highly variable

Late responses of single neurons are highly variable



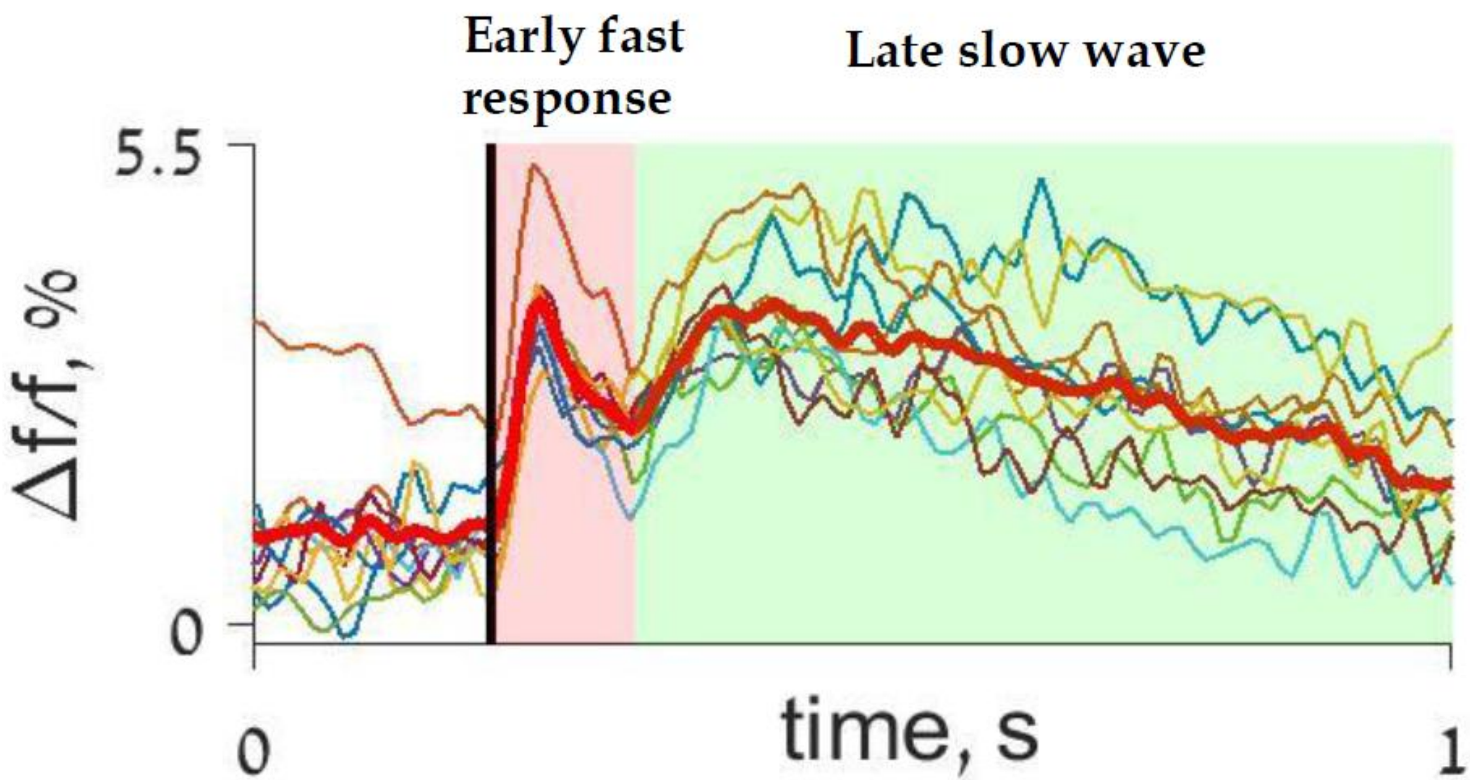
Hershenhoren et al. 2014

Small, variable late effect...

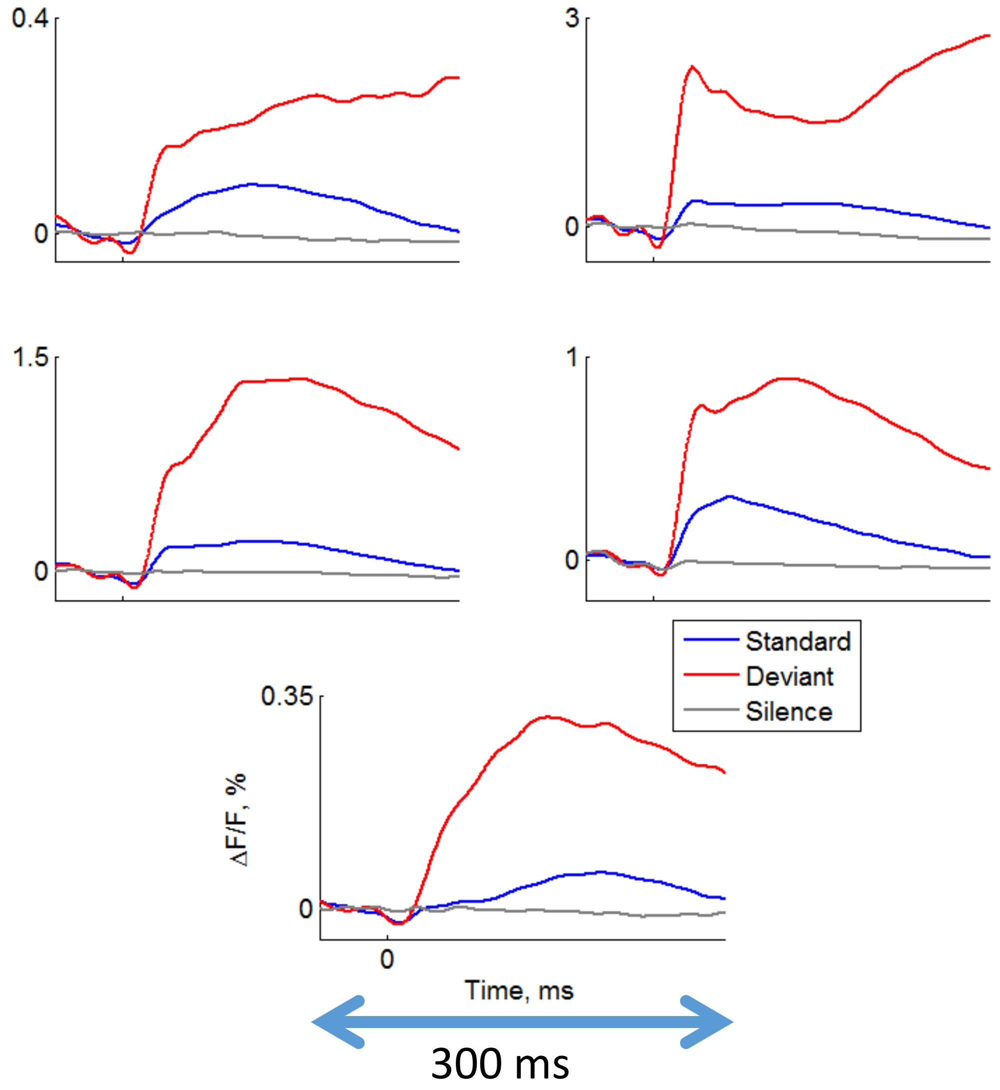


Hershenhoren et al. 2014

…large, reproducible late responses



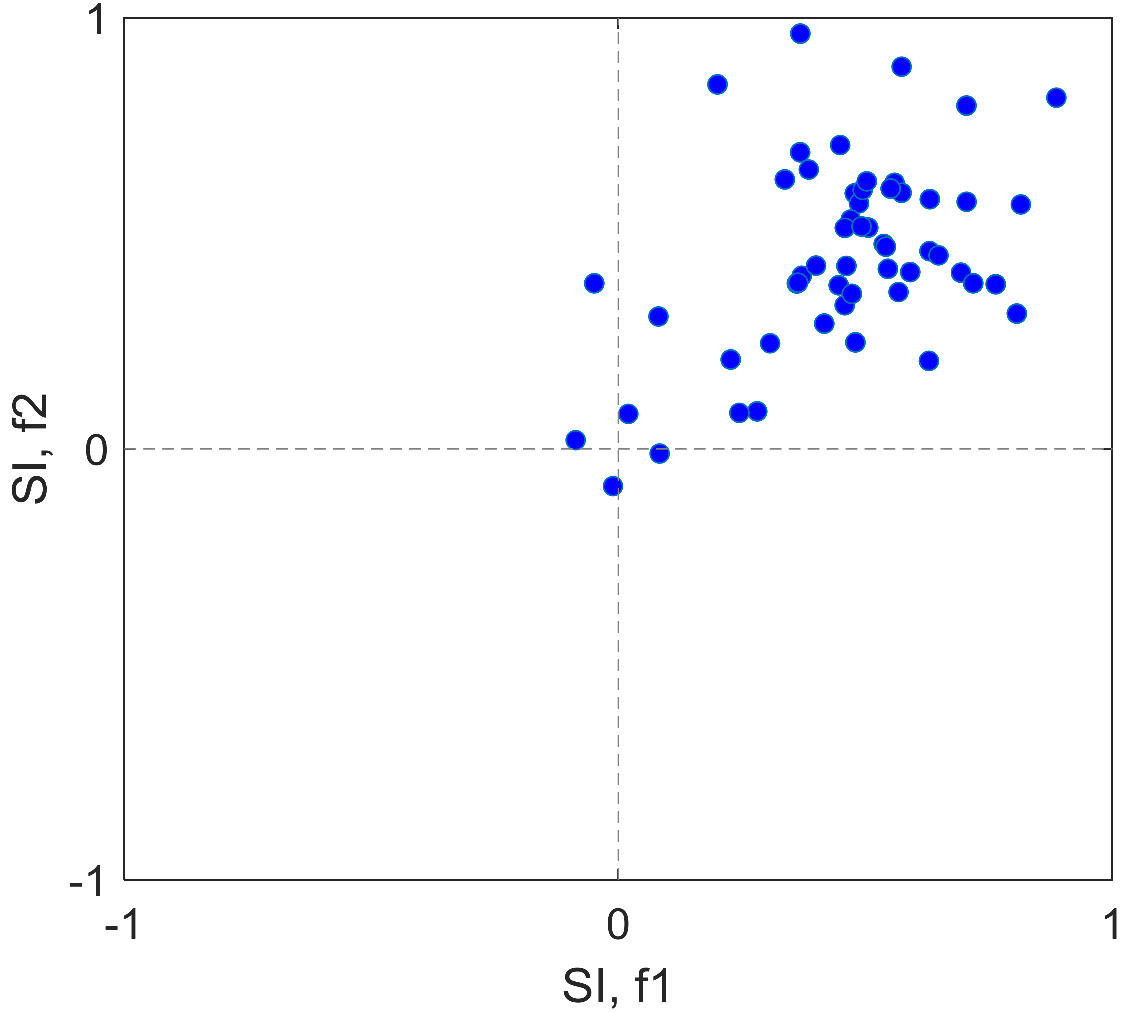
…Large, late effects



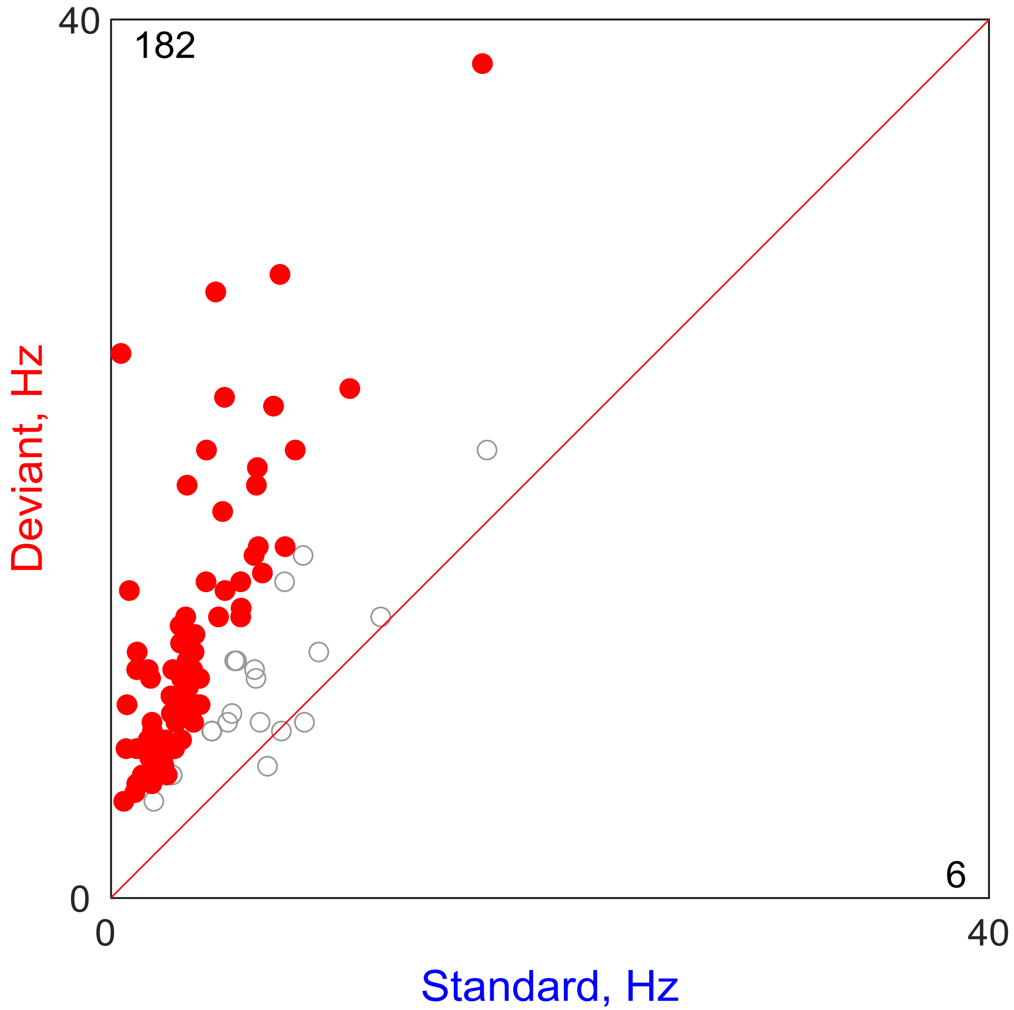
Where do the late response come from?

- Late responses of single neurons are highly variable
- Distributed neuronal populations?
  - Neuropixel recordings

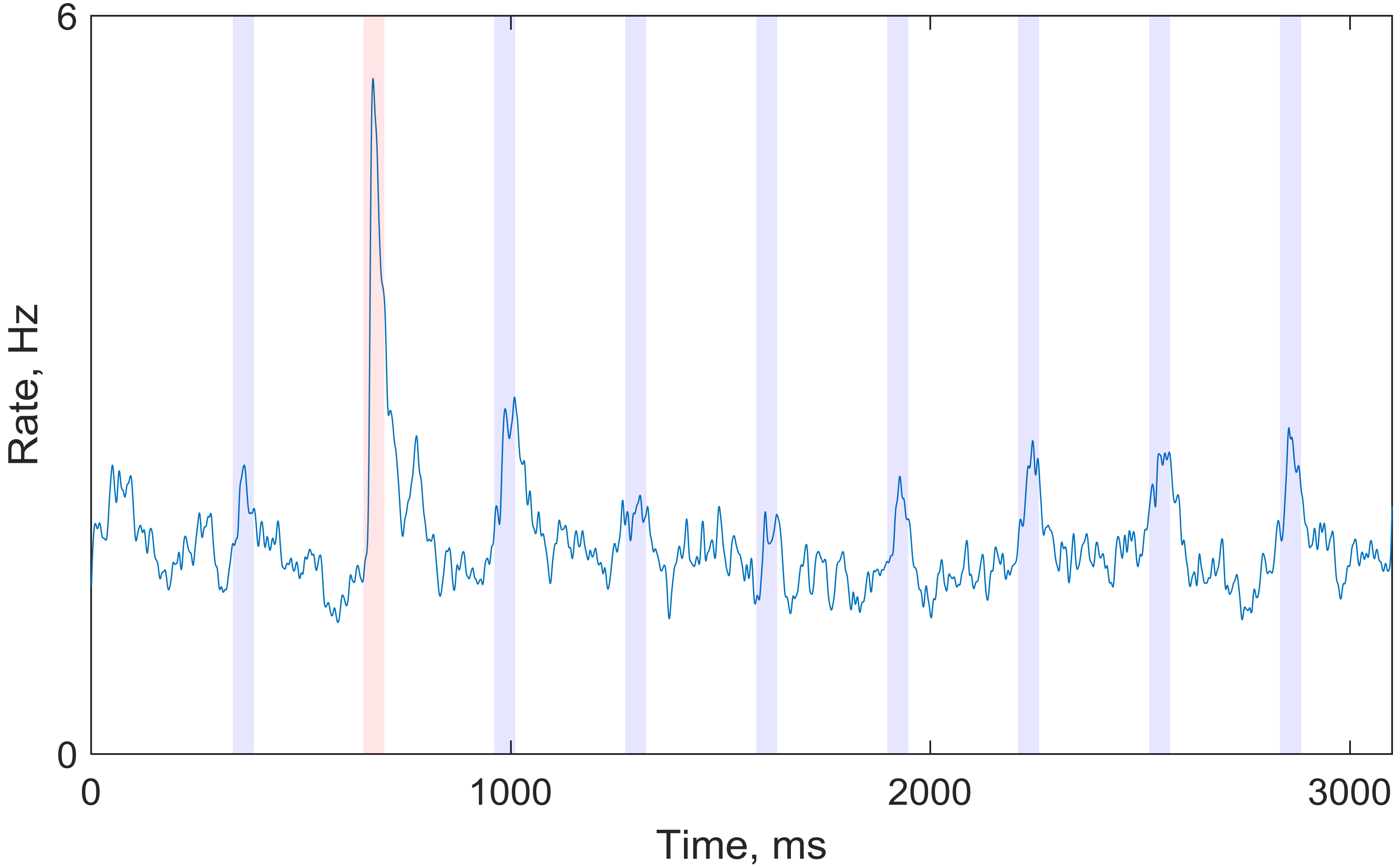
SSA in A1 using Neuropixel recordings



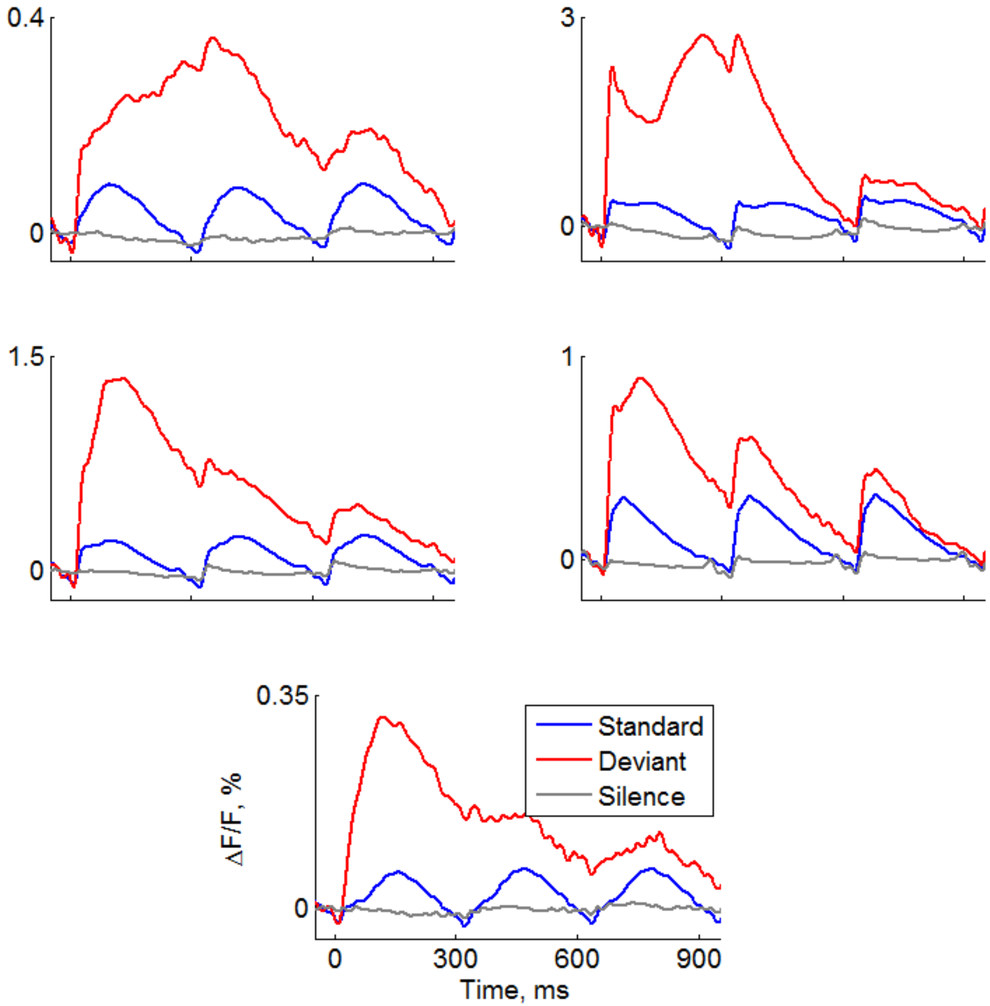
SSA in A1 using Neuropixel recordings



Average responses around a deviant

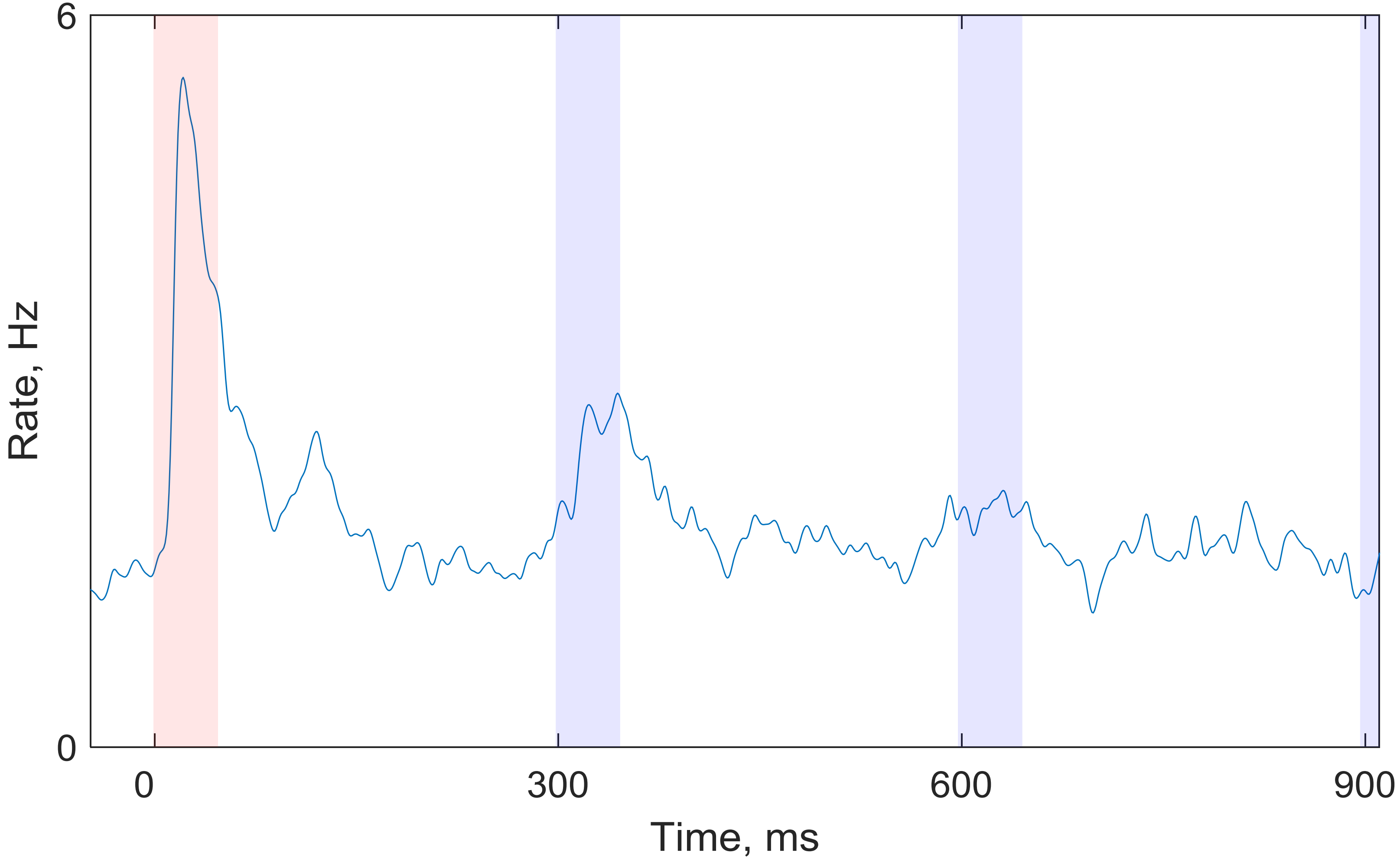


Deviants evoke a long-lasting calcium transient



Dina Moshitch

Average responses around a deviant



So what?

- Large calcium waves following deviants
- Single neurons, as well as populations of ~100 neurons, don’t show a clear correlate

What have we learned from 20 years of research about SSA?

- Science is hard and progresses slowly
  - Maybe because we are not that clever in matching questions to methods

What have we learned from 20 years of research about SSA?

- Science is hard and progresses slowly
- Multiple time scales that are relevant to the processing of the natural scene
  - Not only the 10-1000 ms time scale which is the one usually studied in sensory coding
  - Some of our results suggest dependence of the responses on 10s of past stimuli (>10 s)
  - Large effects

What have we learned from 20 years of research about SSA?

- Science is hard and progresses slowly
- Multiple time scales that are relevant to the processing of the natural scene
- Significant cortical contributions
- Dynamical mysteries
- High selectivity to random white stimuli

Thank you!

(courtesy of Jonathan Fritz)