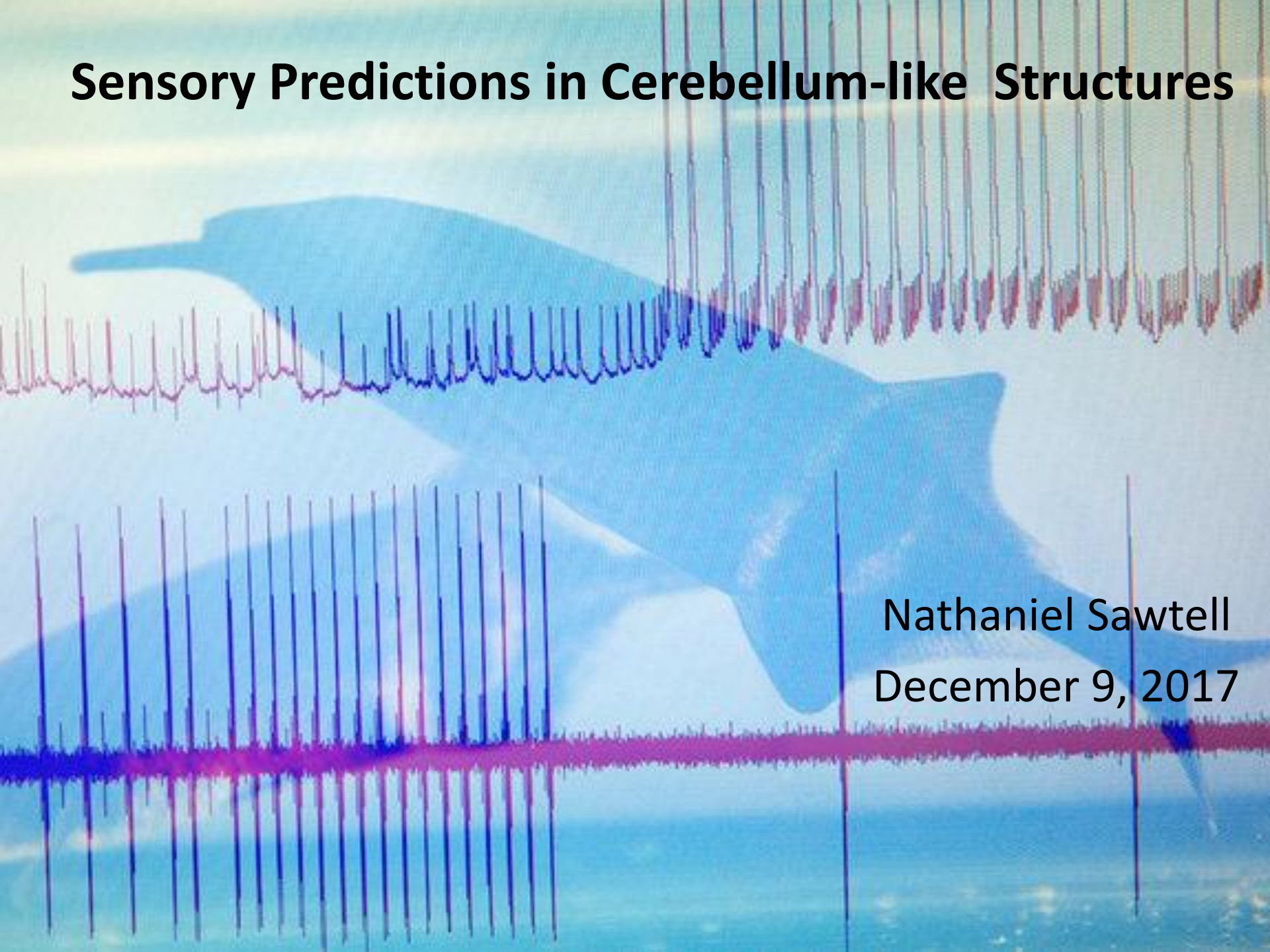
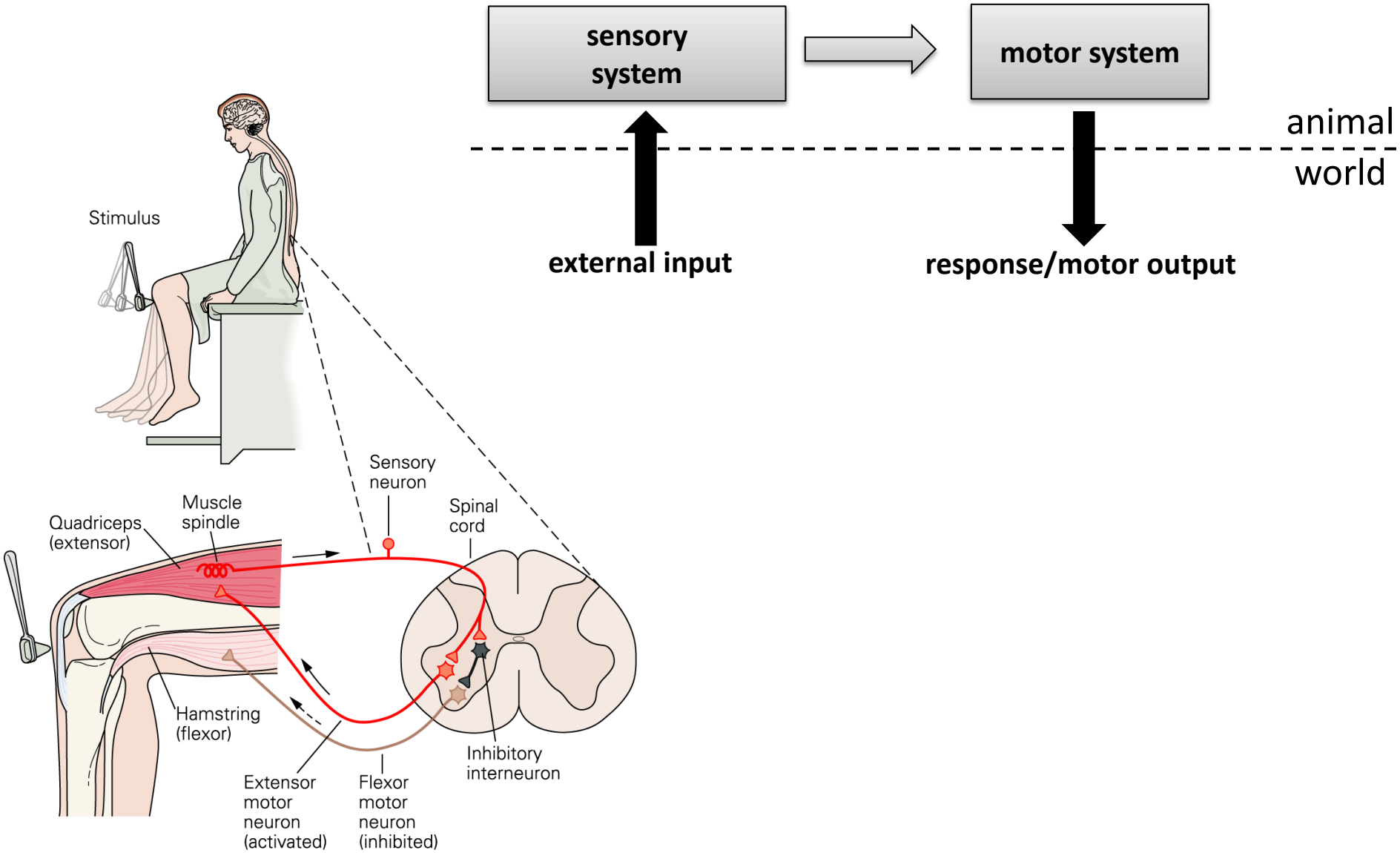
Sensory Predictions in Cerebellum-like Structures



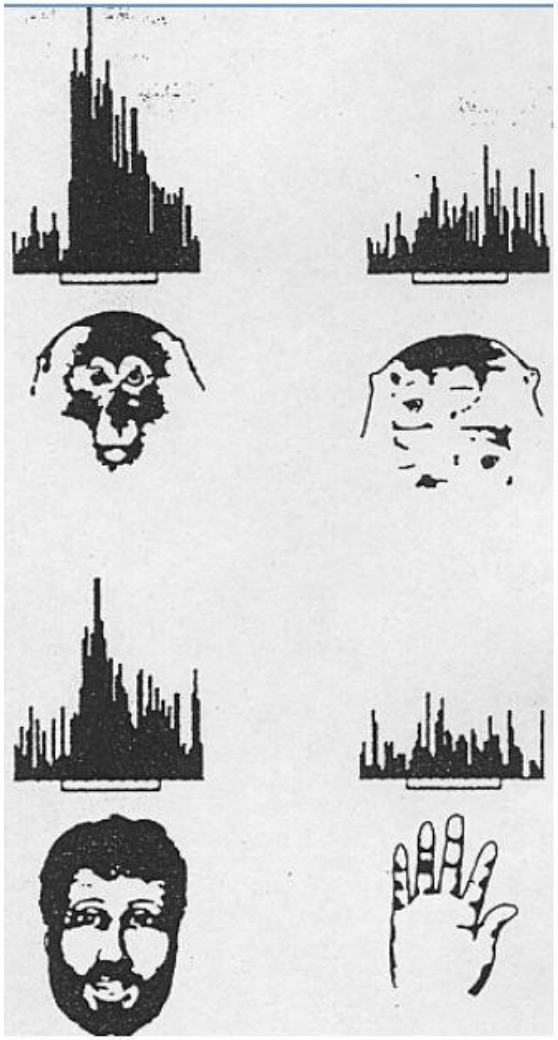
Nathaniel Sawtell

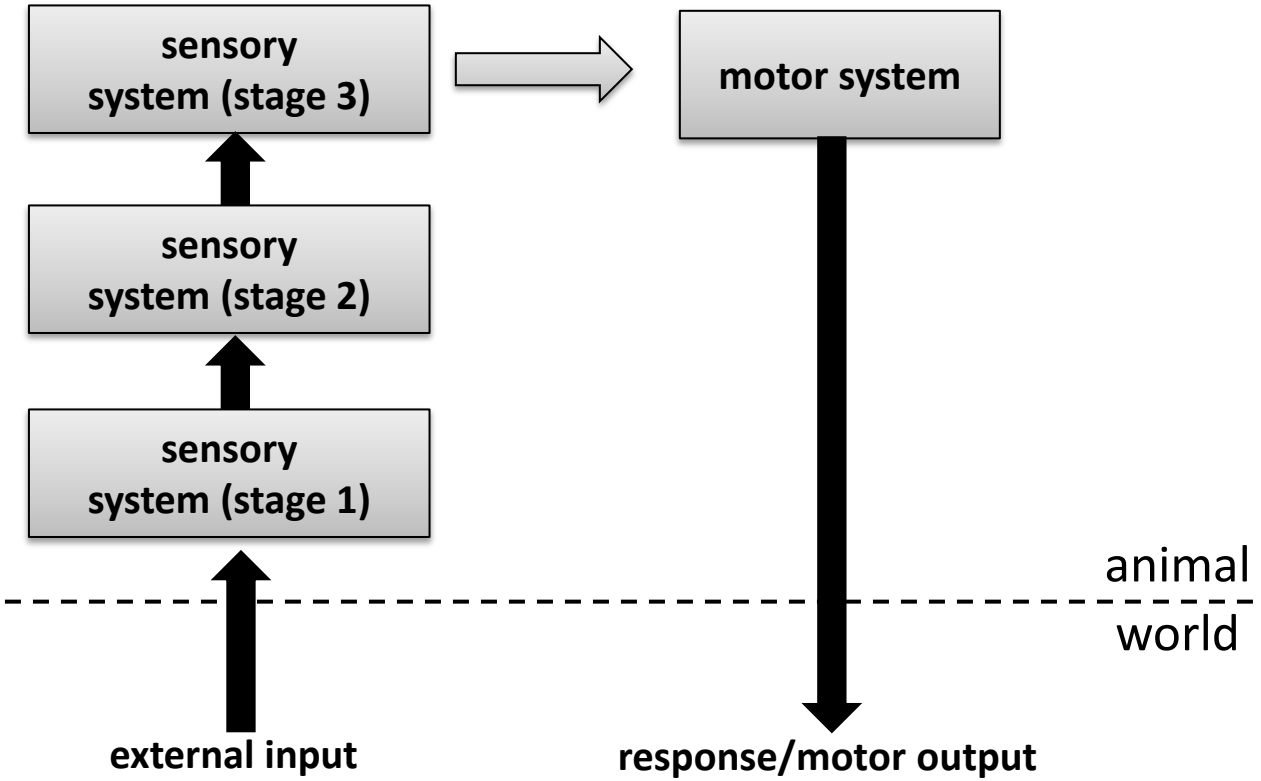
December 9, 2017

Reflex view of Brain Function



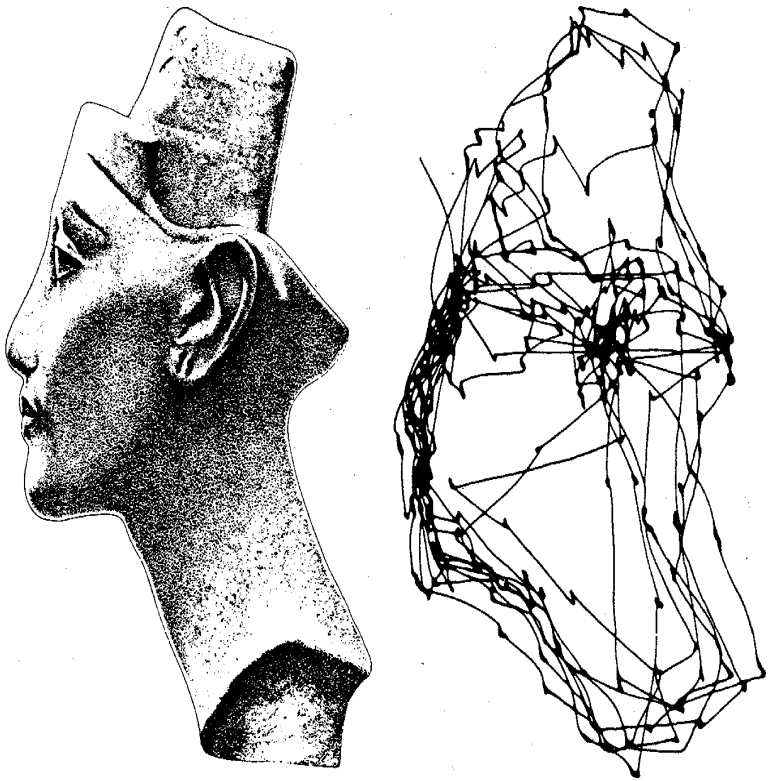
Reflex view of Brain Function, Extended



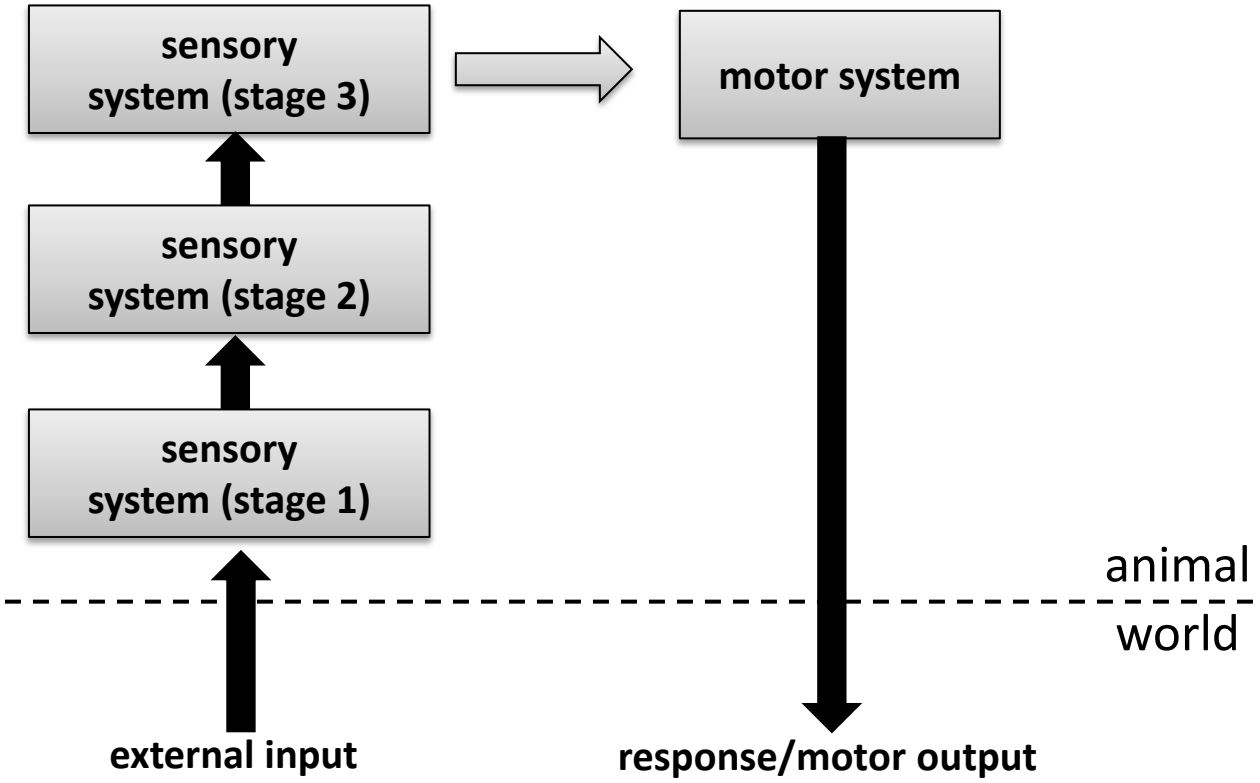


Perception is active and creative

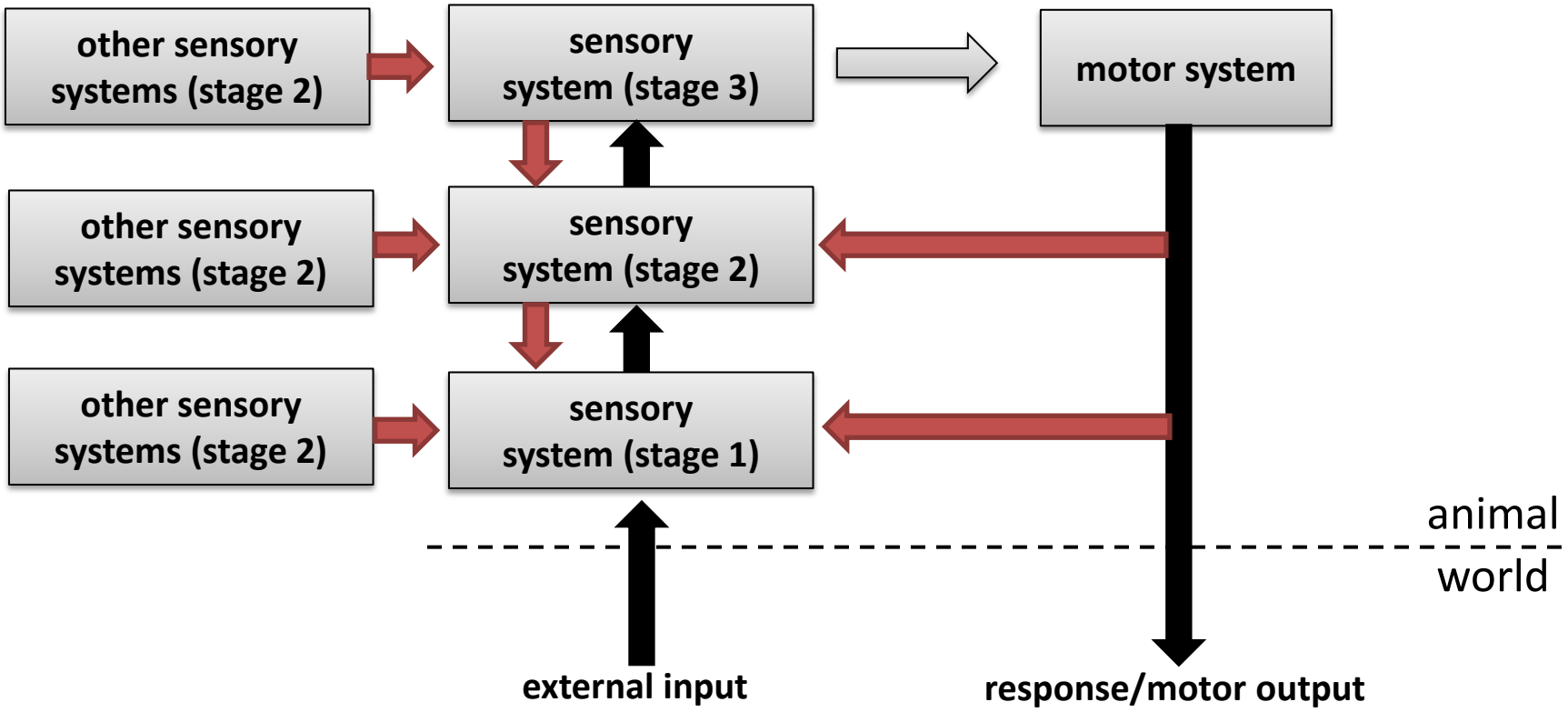
Perception is active and creative

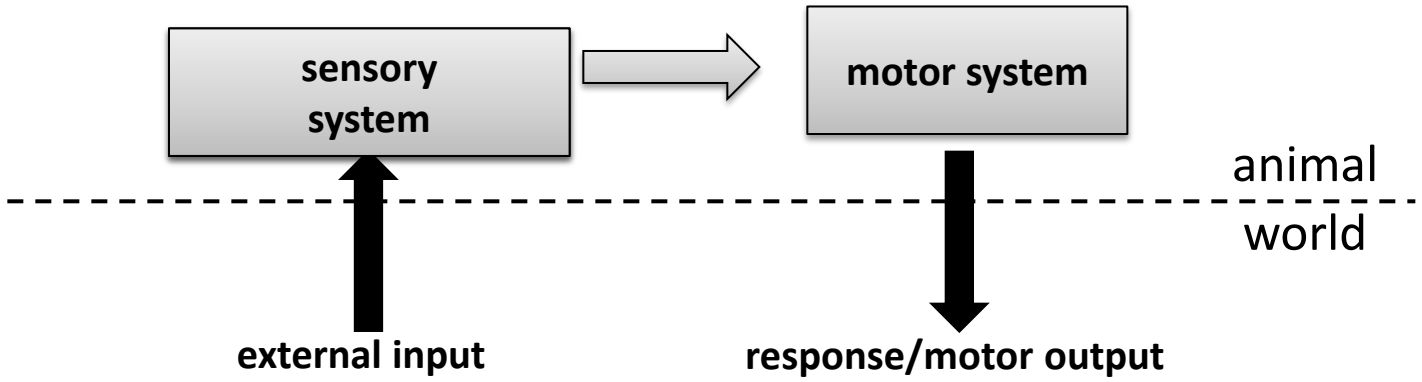


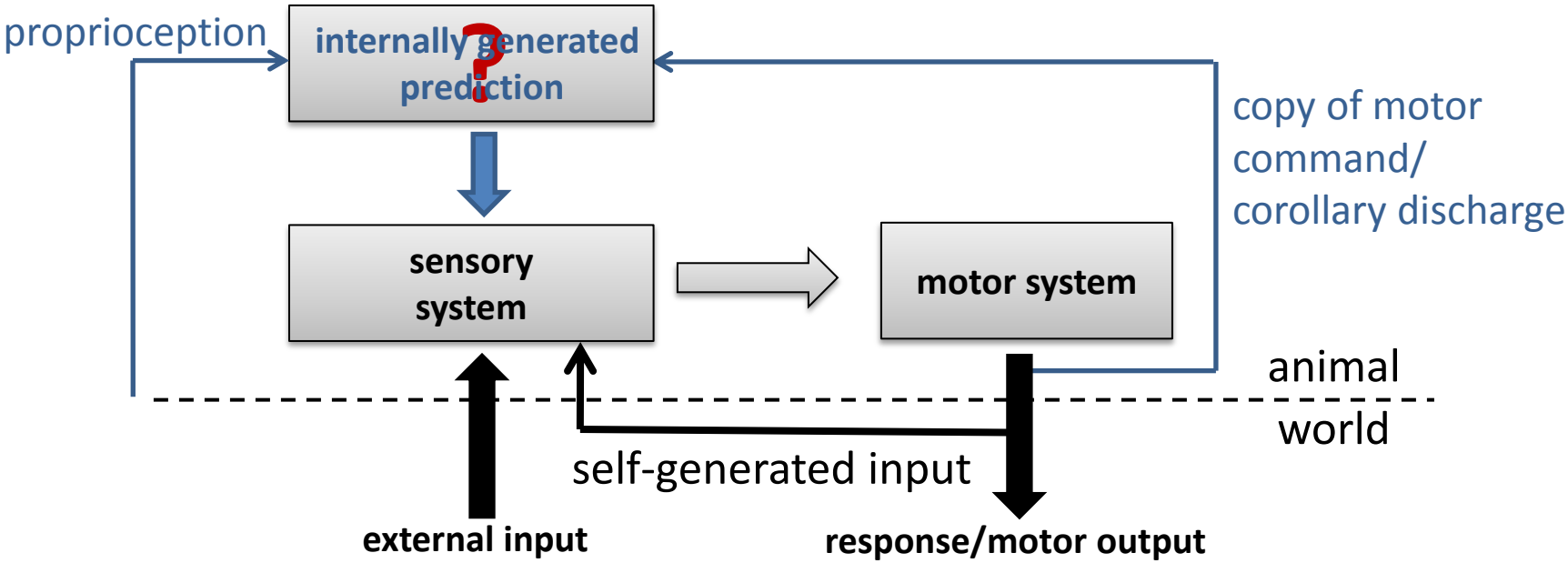
Yarbus, 1967


sensory system (stage 3)
motor system
sensory system (stage 2)
sensory system (stage 1)
animal
world
external input
response/motor output

Neural substrates for active perception

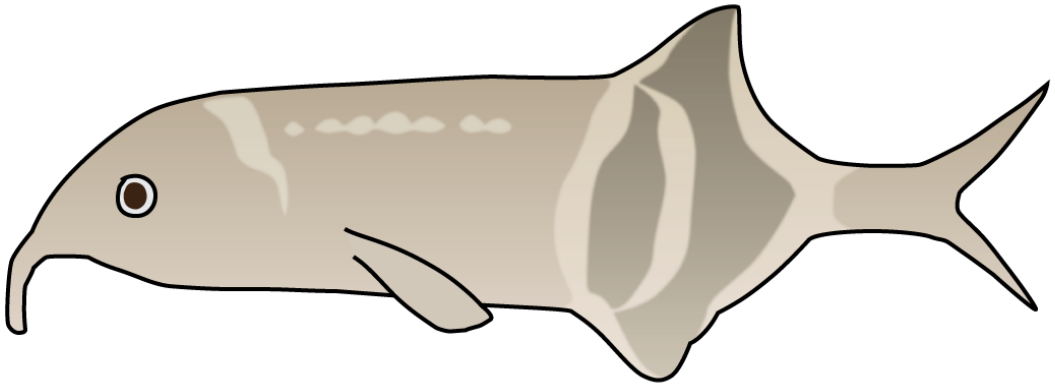


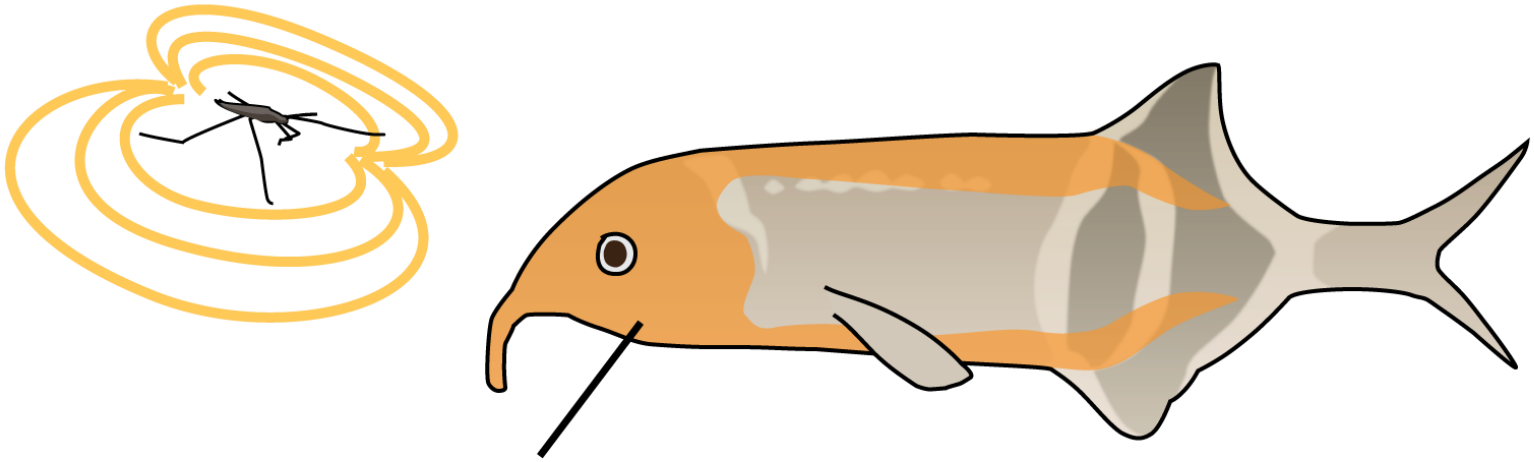

sensory system
motor system
animal world
external input
response/motor output



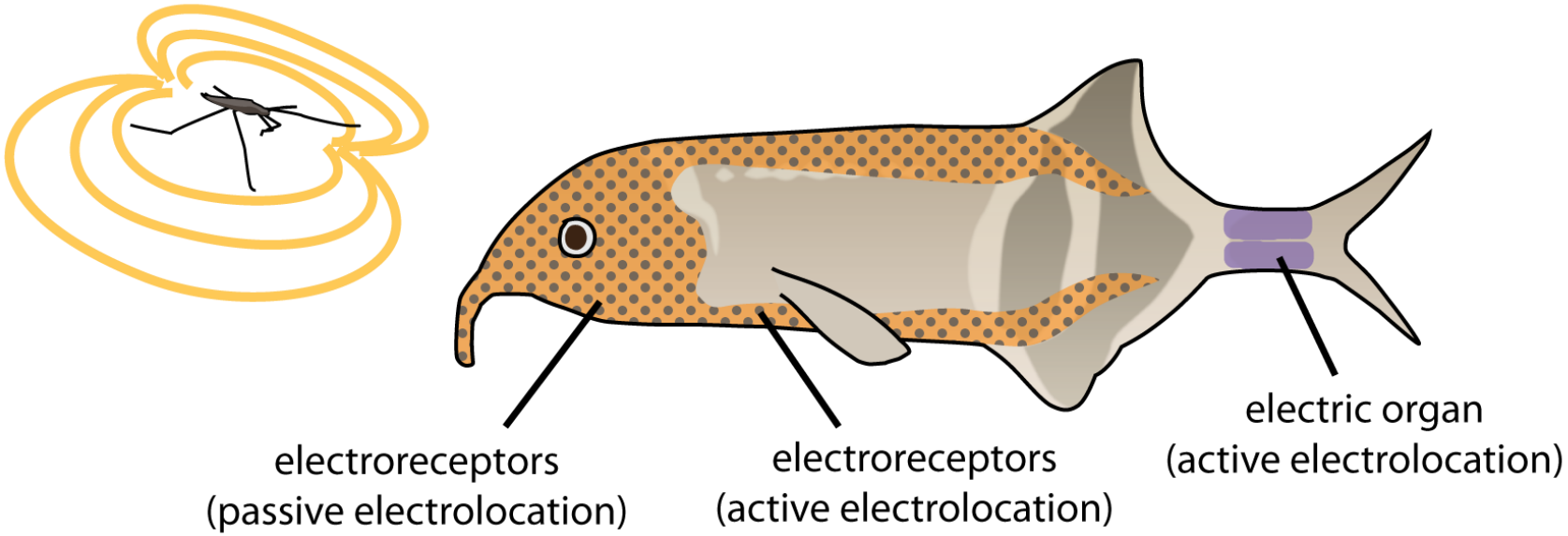
"We shall propose that the efference leaves an "image" of itself somewhere in the CNS, to which the re-afference of this movement compares as the negative of a photograph compares to its print; so that when superimposed the image disappears."

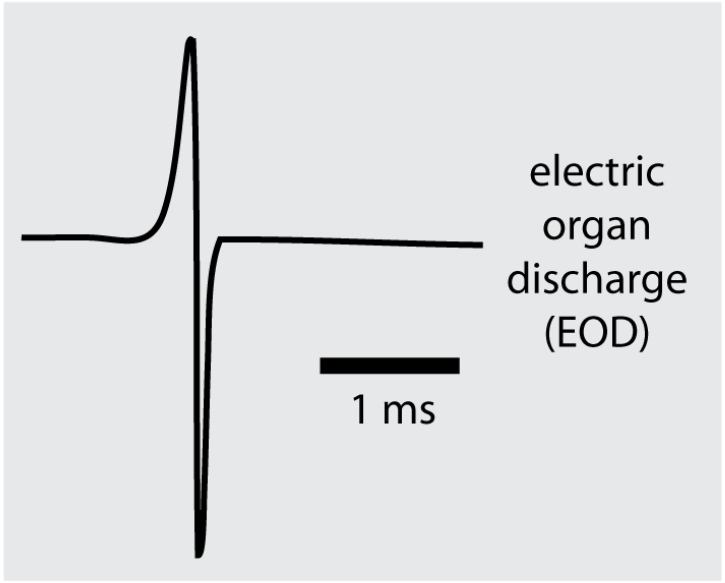
-Von Holst, *Relations between the central nervous system and the peripheral organs*, 1954

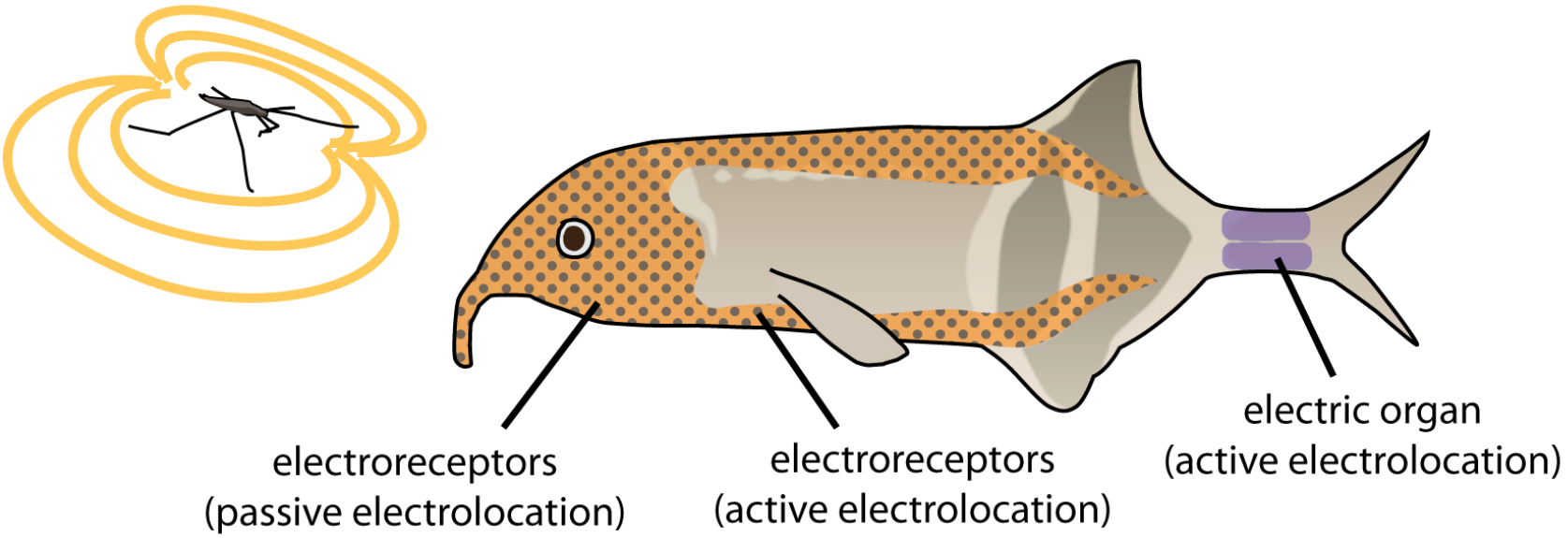


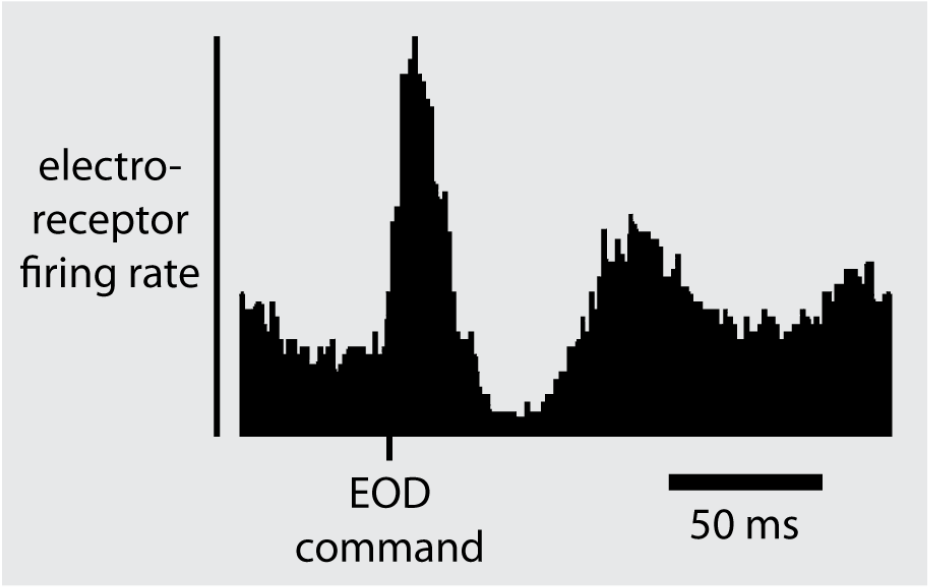


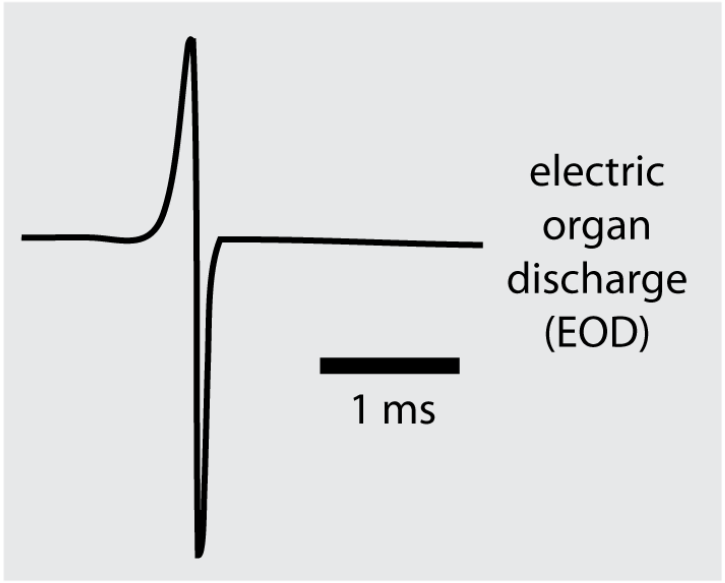
electroreceptors
(passive electrolocation)


electroreceptors
(passive electrolocation)
electroreceptors
(active electrolocation)
electric organ
(active electrolocation)

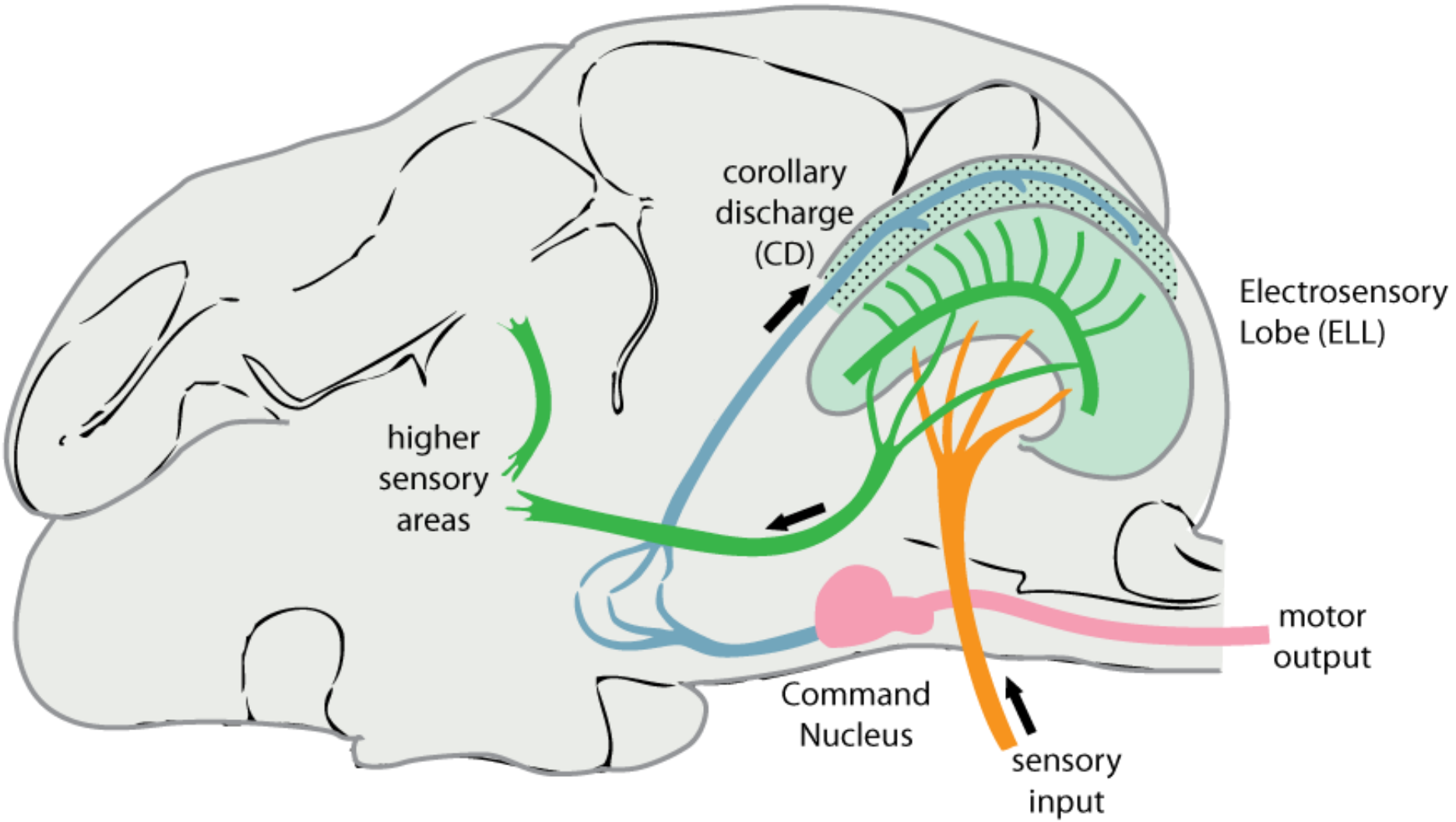

electric
organ
discharge
(EOD)
1 ms



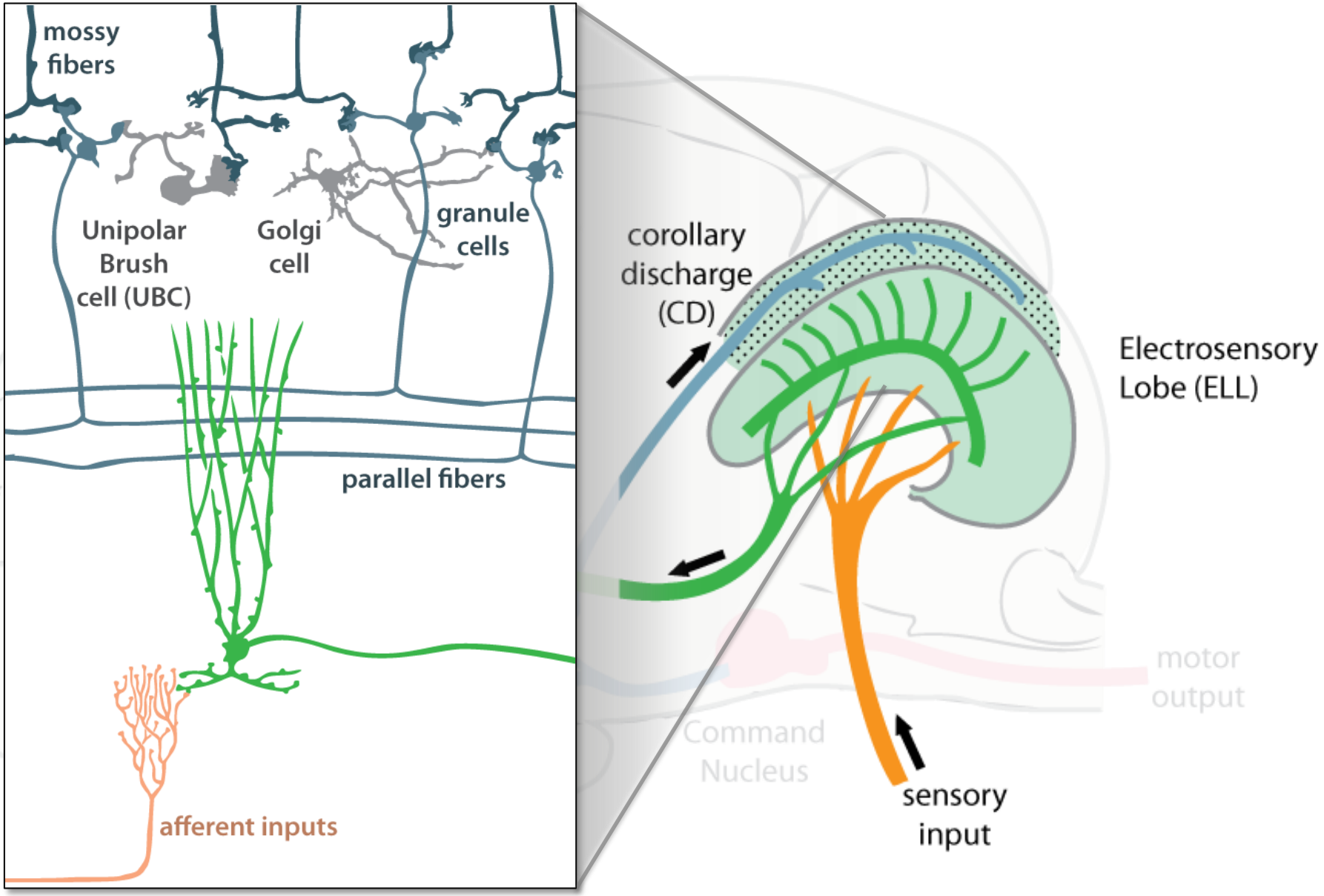




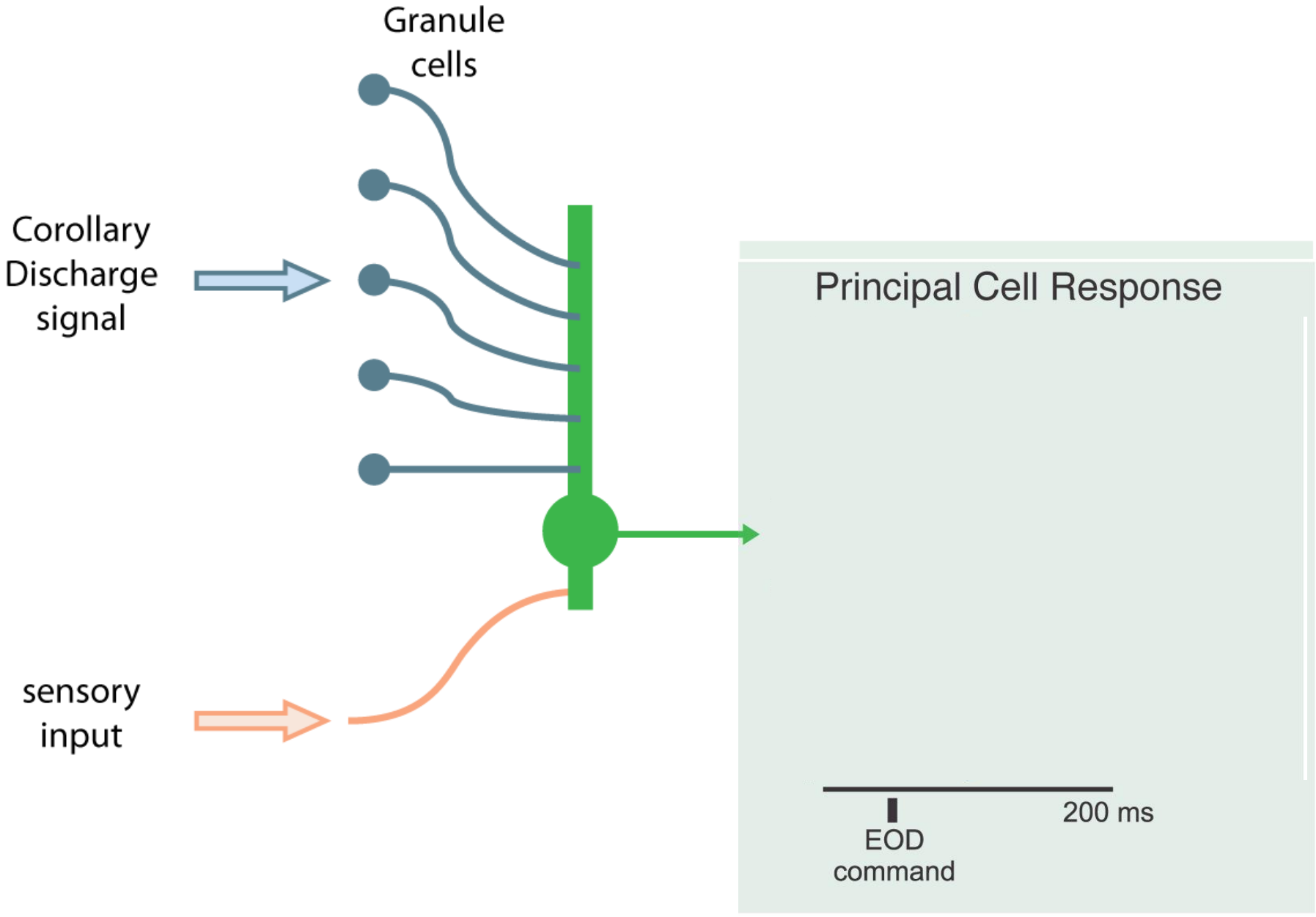
Roberts and Bell (2000)

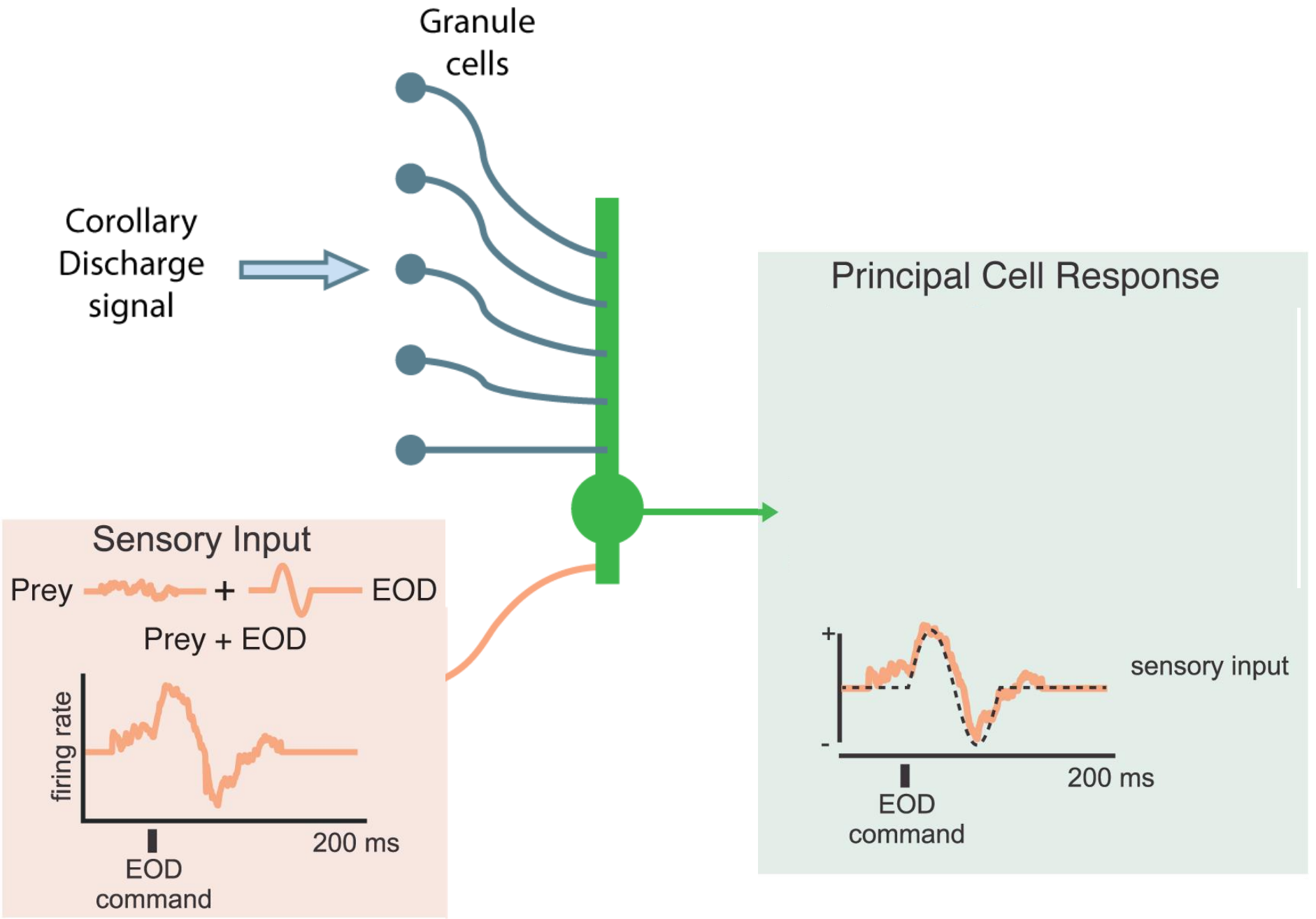


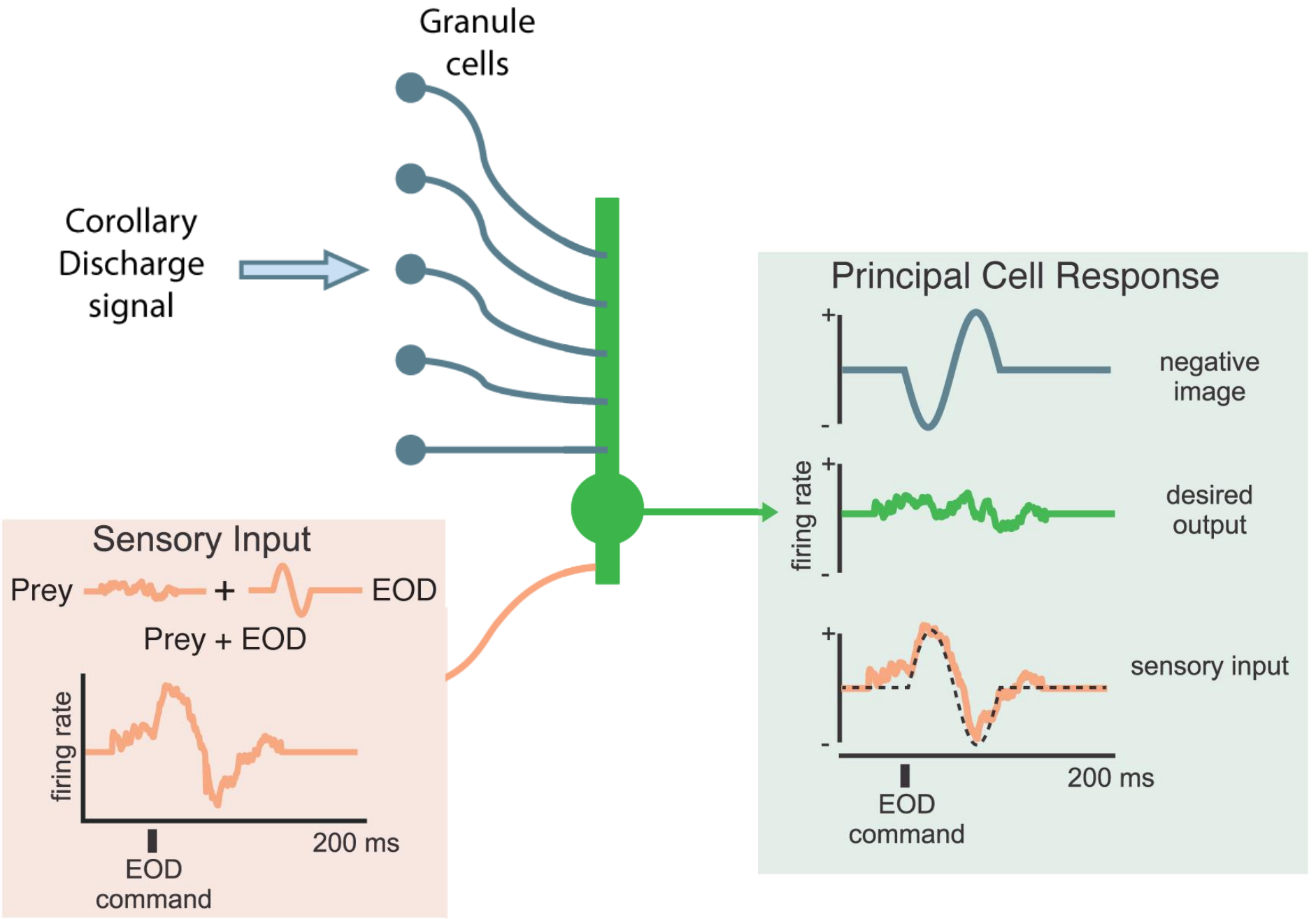
after *Meek, Grant and Bell* (1999)

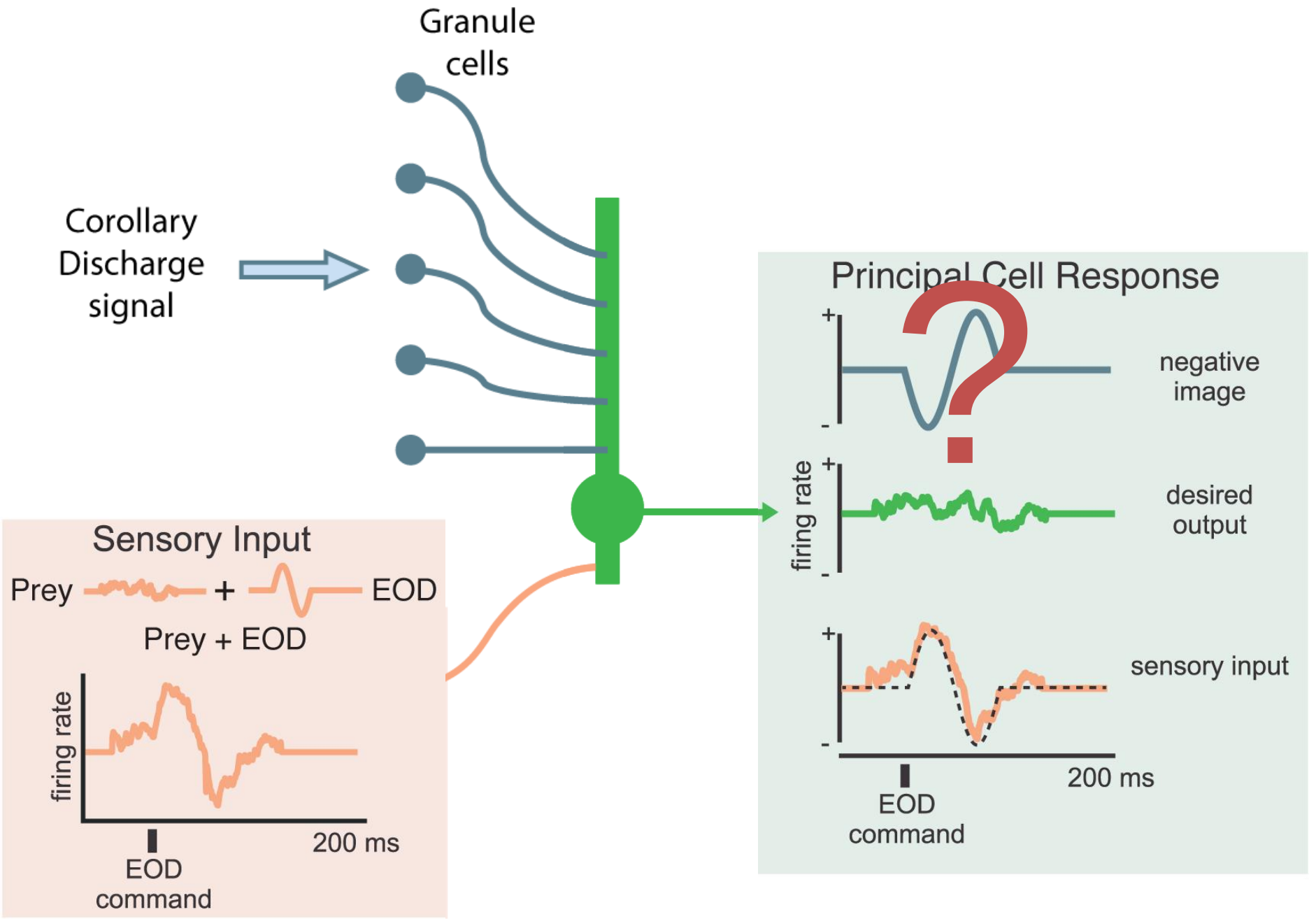


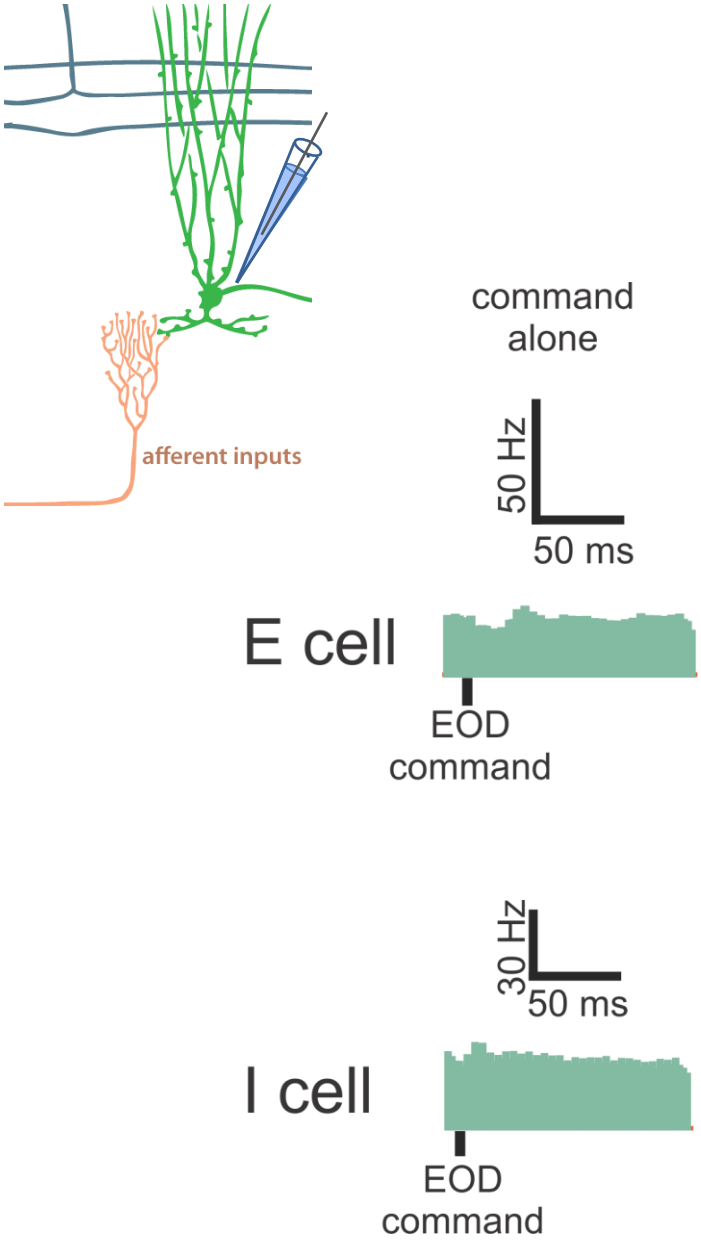
after *Meek, Grant and Bell* (1999)

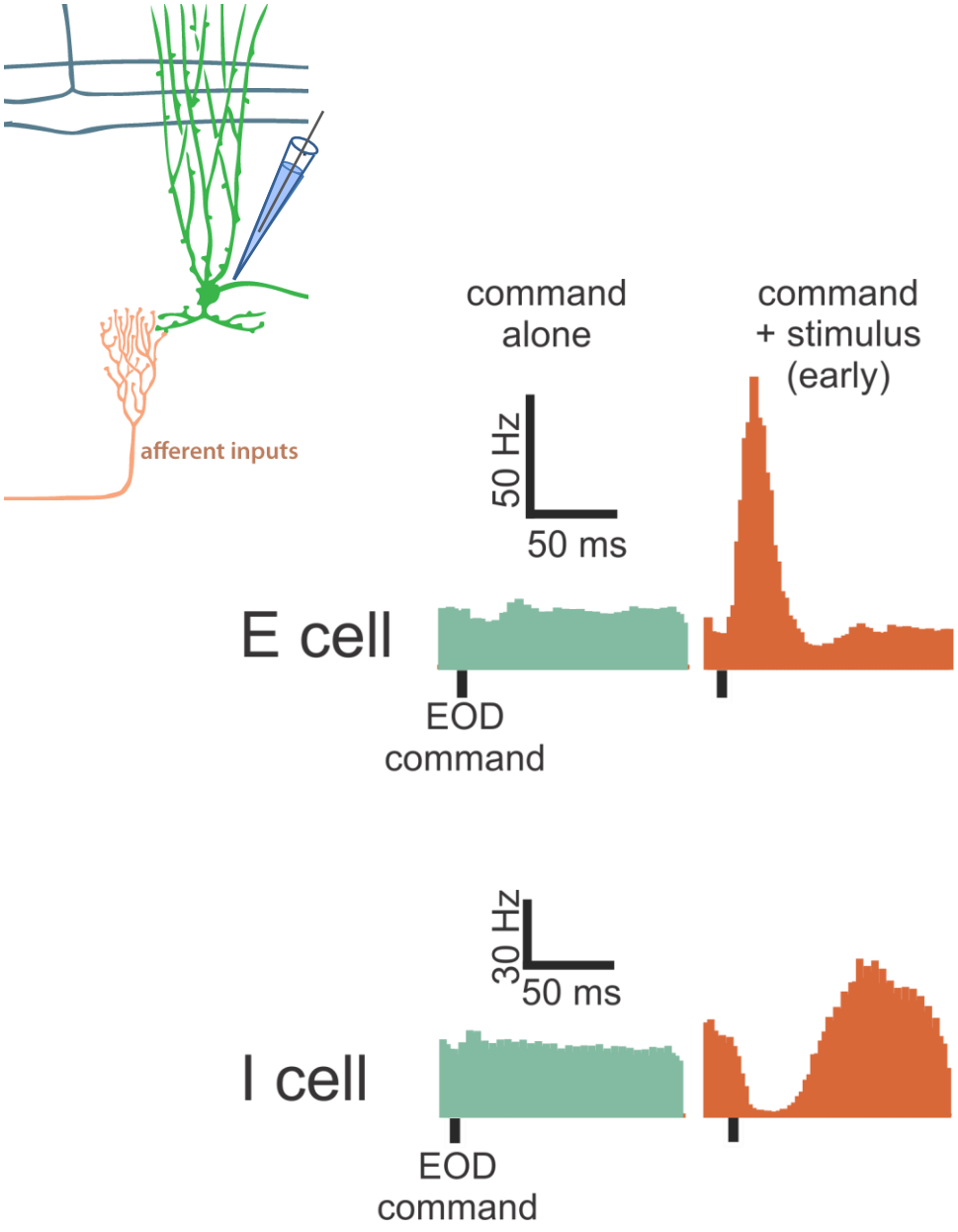

Granule
cells
Corollary
Discharge
signal
sensory
input
Principal Cell Response
200 ms
EOD
command

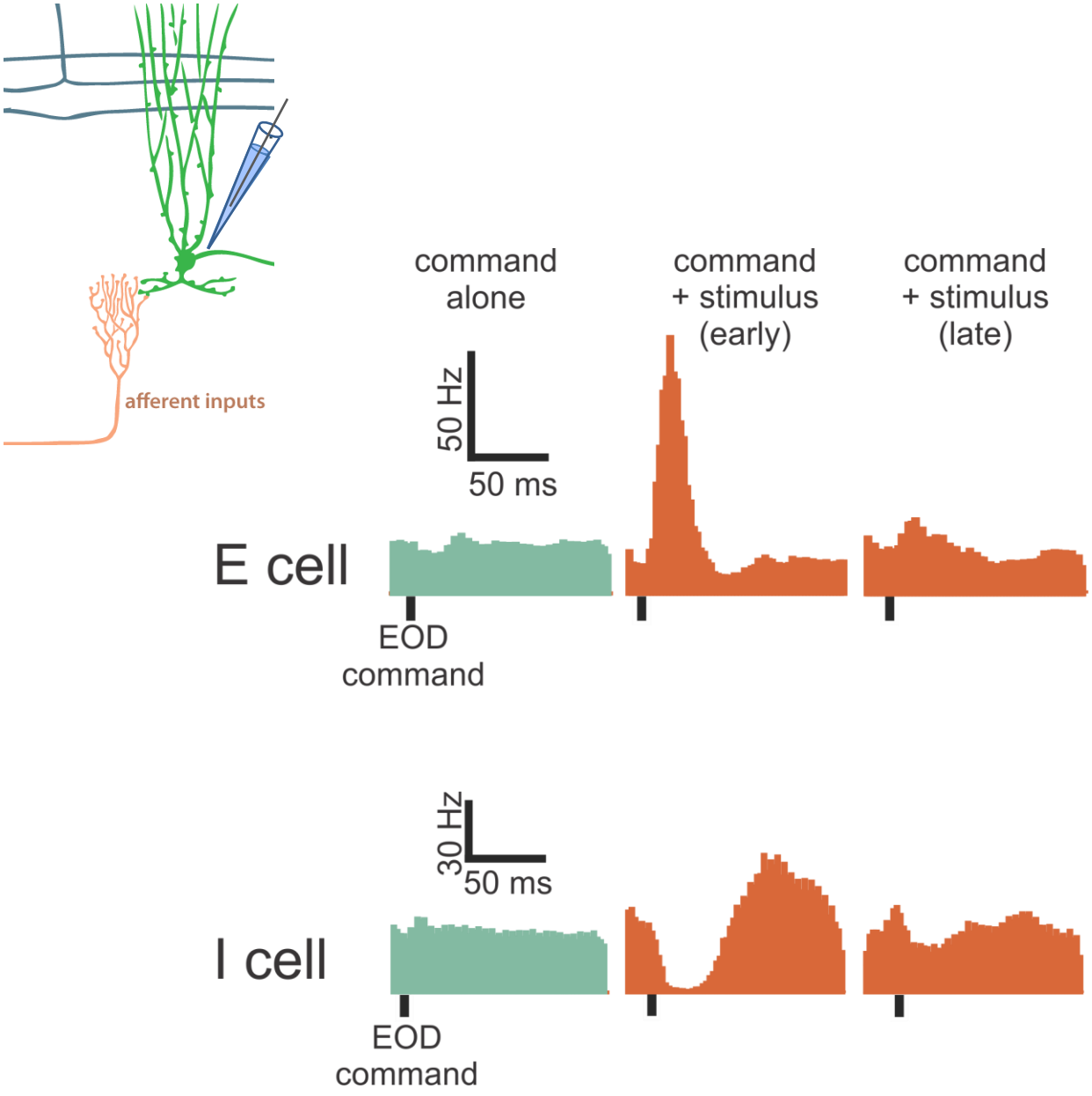

Granule cells
Corollary Discharge signal
Principal Cell Response
Sensory Input
Prey
+
EOD
Prey + EOD
firing rate
200 ms
EOD command
+
-
sensory input
200 ms
EOD command

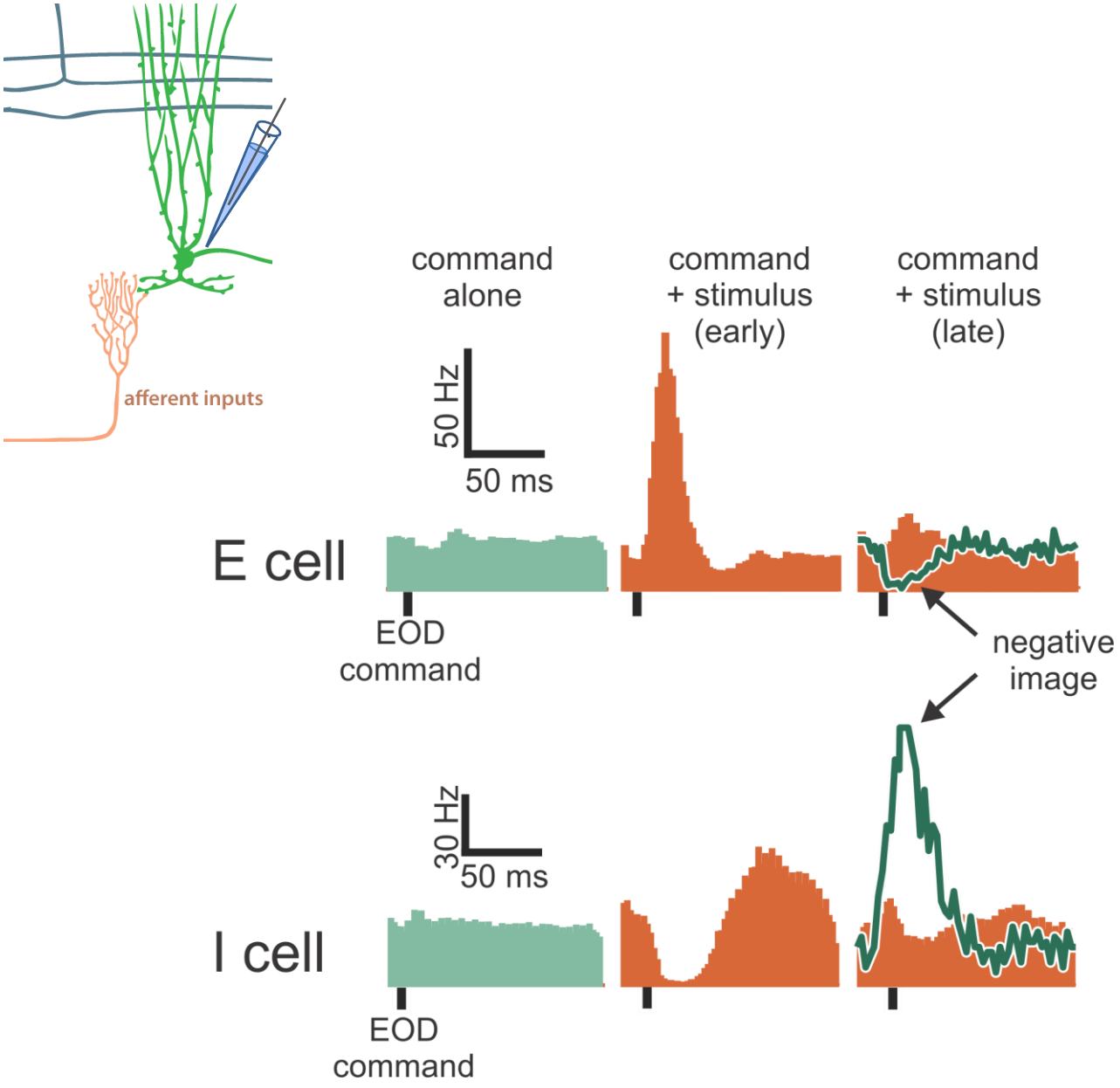

Granule cells
Corollary Discharge signal
Principal Cell Response
negative image
firing rate
desired output
sensory input
200 ms
EOD command
Sensory Input
Prey
+
EOD
Prey + EOD
firing rate
200 ms
EOD command

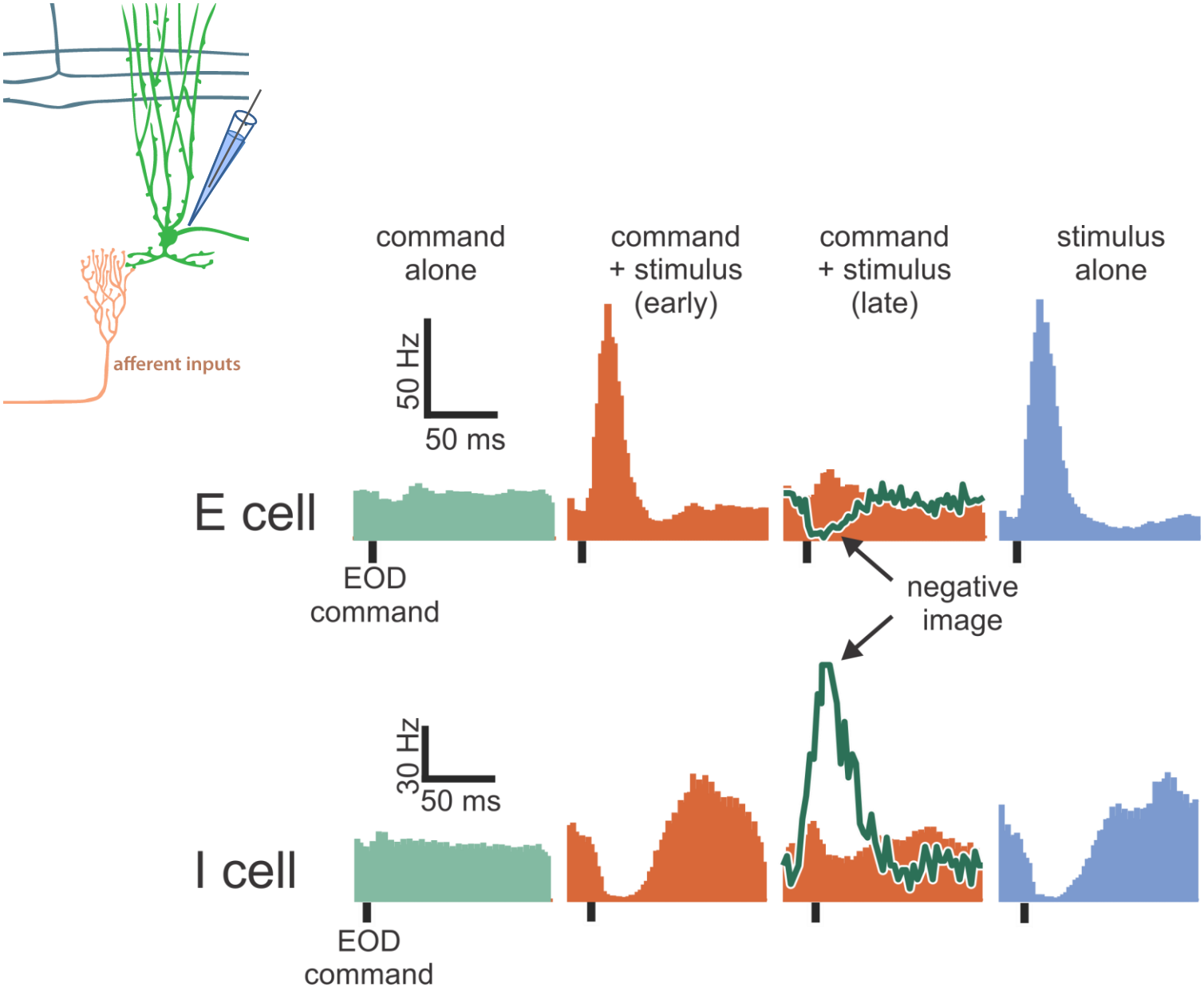

Granule cells
Corollary Discharge signal
Principal Cell Response
negative image
desired output
sensory input
firing rate
200 ms
EOD command
Sensory Input
Prey
+
EOD
Prey + EOD
firing rate
200 ms
EOD command

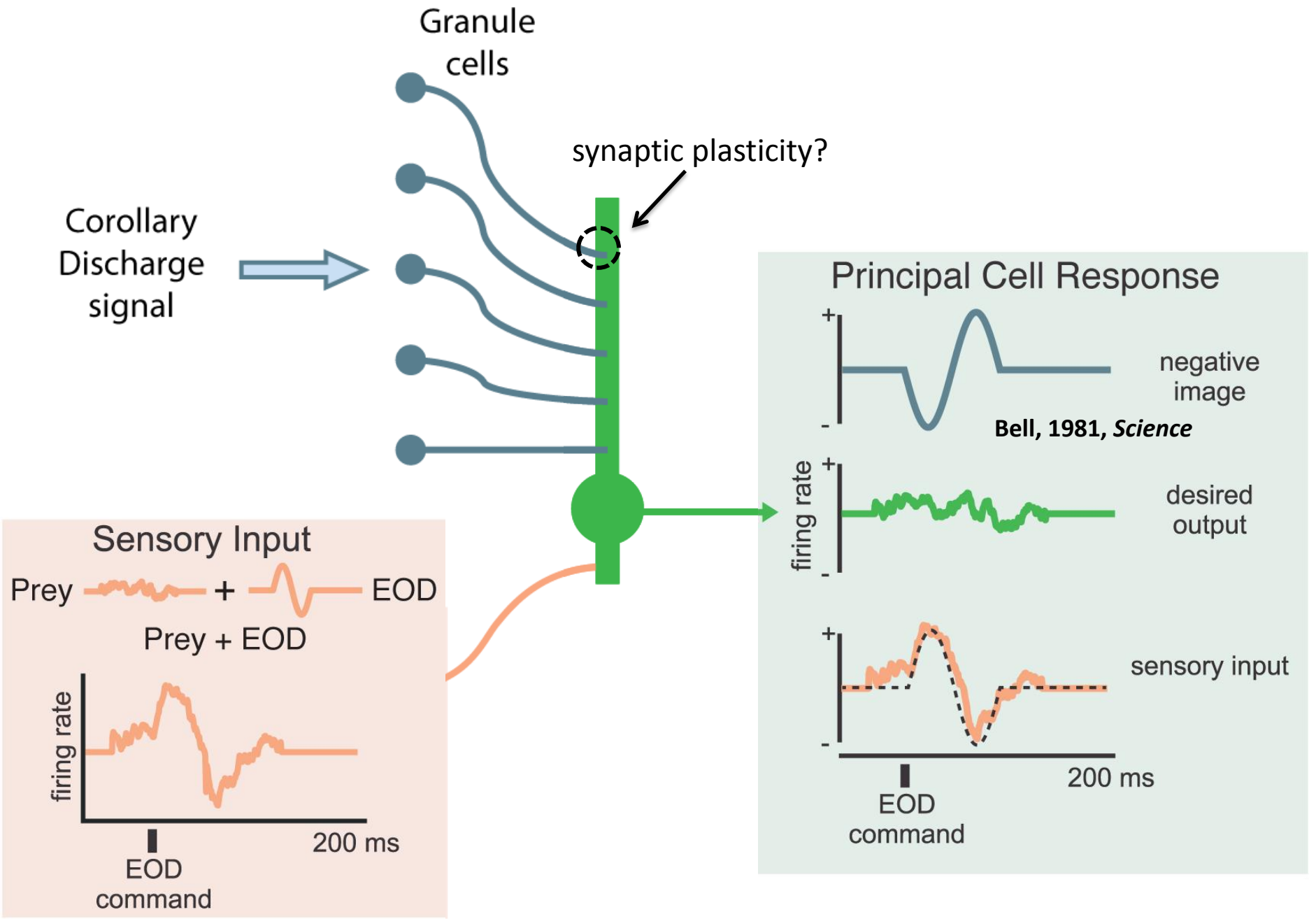

afferent inputs
command
alone
50 Hz
50 ms
E cell
EOD
command
30 Hz
50 ms
I cell
EOD
command

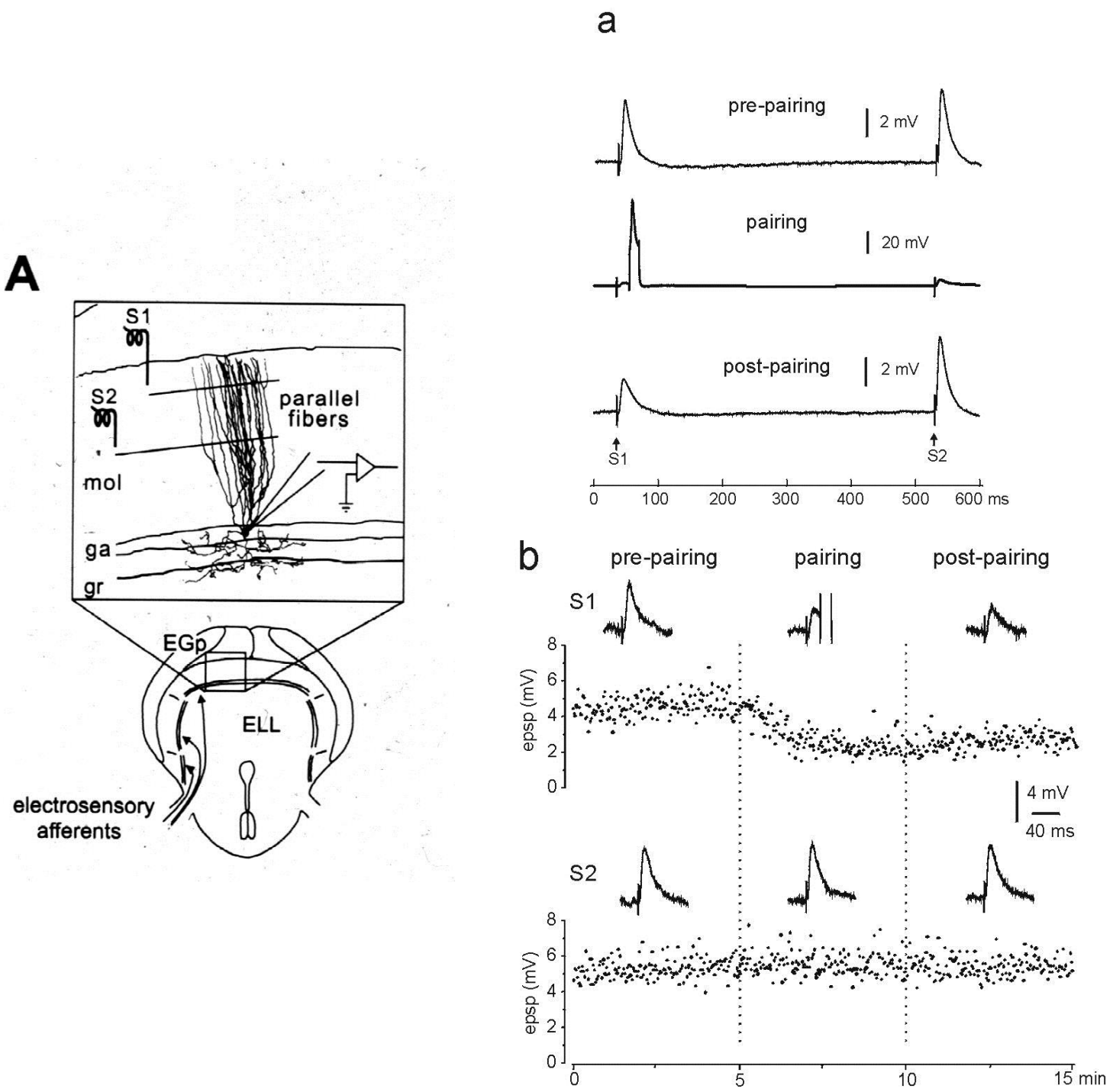

afferent inputs
command
alone
command
+ stimulus
(early)
50 Hz
50 ms
E cell
EOD
command
30 Hz
50 ms
I cell
EOD
command


afferent inputs
command alone
command + stimulus (early)
command + stimulus (late)
50 Hz
50 ms
E cell
EOD command
30 Hz
50 ms
I cell
EOD command

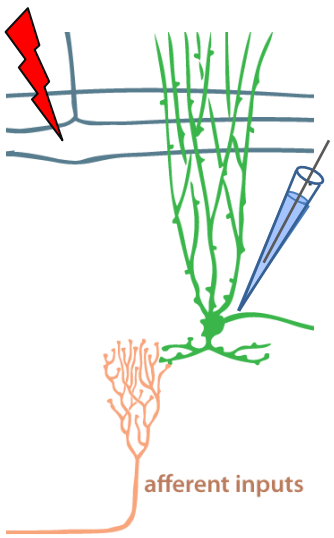

afferent inputs
command alone
command + stimulus (early)
command + stimulus (late)
50 Hz
50 ms
E cell
EOD command
negative image
30 Hz
50 ms
I cell
EOD command

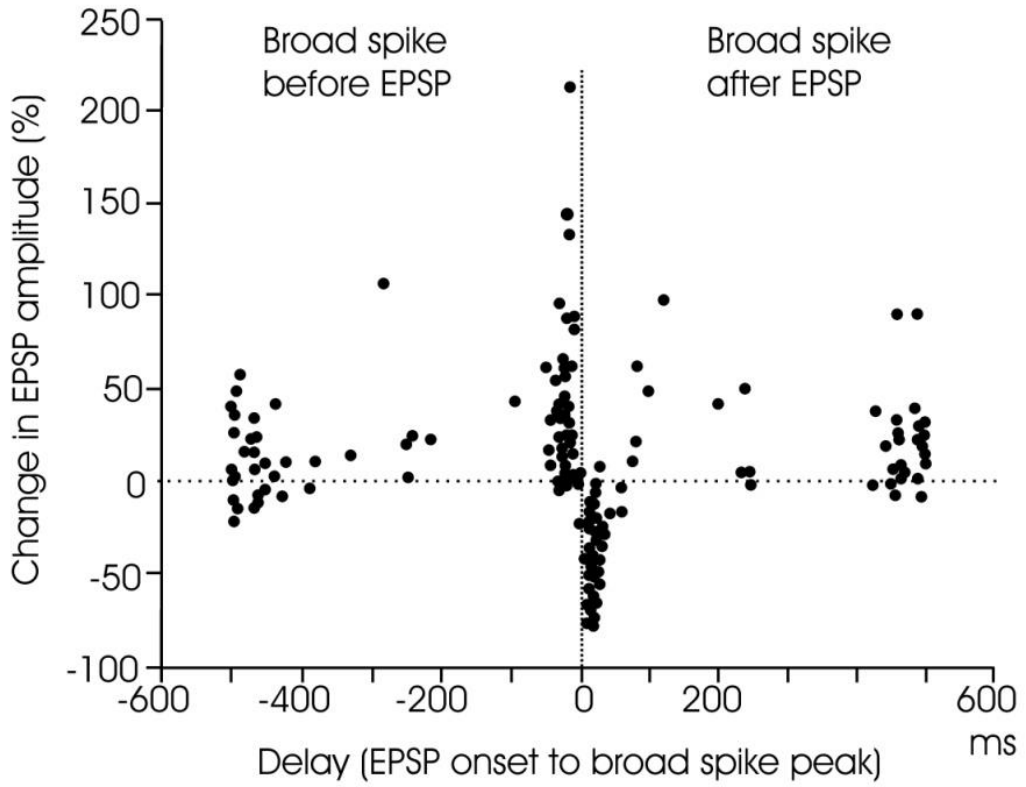

afferent inputs
command alone
command + stimulus (early)
command + stimulus (late)
stimulus alone
50 Hz
50 ms
E cell
EOD command
negative image
30 Hz
50 ms
I cell
EOD command


Granule cells
synaptic plasticity?
Corollary Discharge signal
Principal Cell Response
negative image
Bell, 1981, Science
firing rate
desired output
sensory input
200 ms
EOD command
Sensory Input
Prey
+
EOD
Prey + EOD
firing rate
200 ms
EOD command

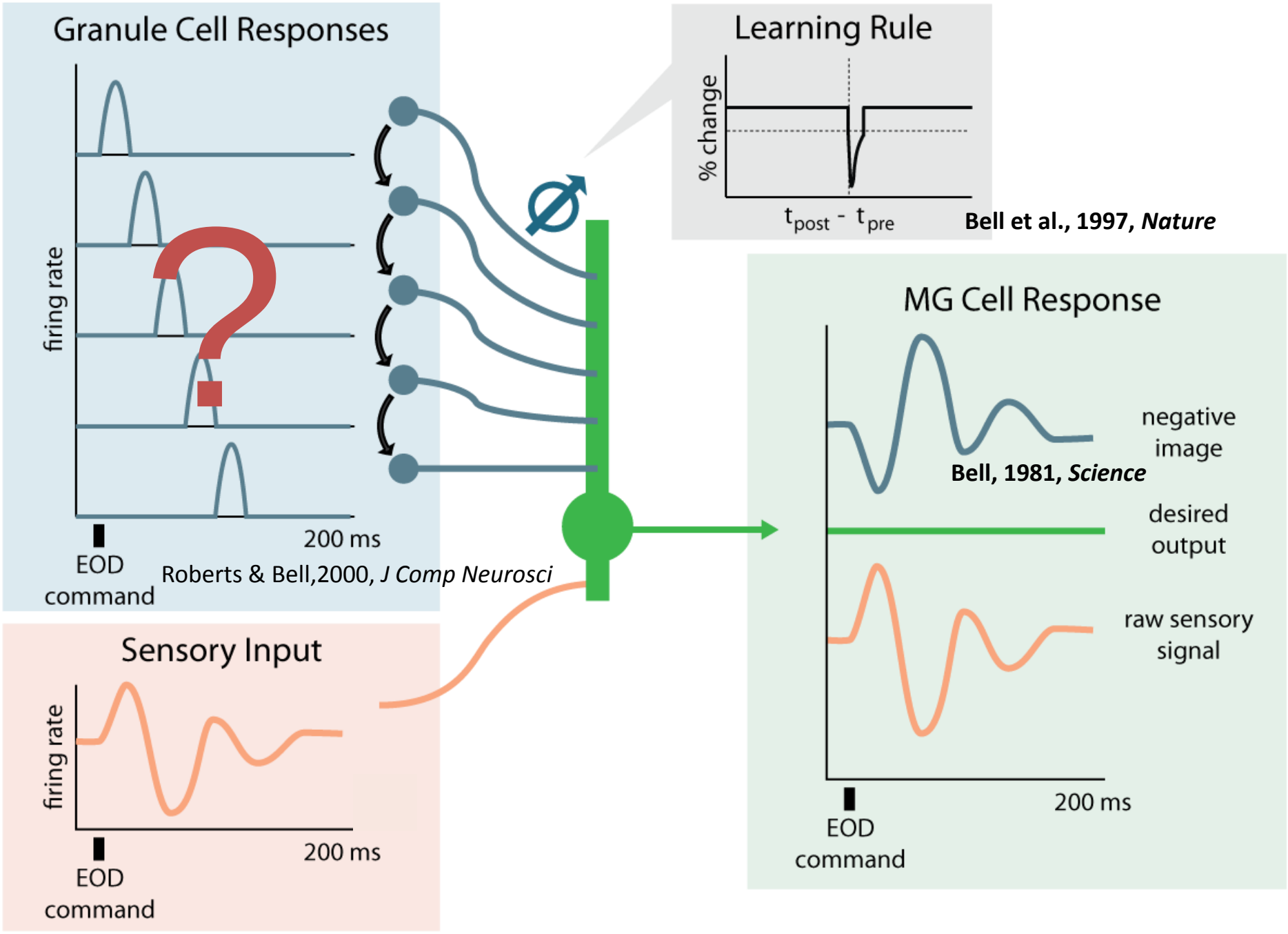

A
S1
S2
parallel fibers
mol
ga
gr
EGp
ELL
electrosensory afferents
a
pre-pairing
2 mV
pairing
20 mV
post-pairing
2 mV
S1
S2
0
100
200
300
400
500
600 ms
b
pre-pairing
pairing
post-pairing
S1
epsp (mV)
4 mV
40 ms
S2
epsp (mV)
0
5
10
15 min

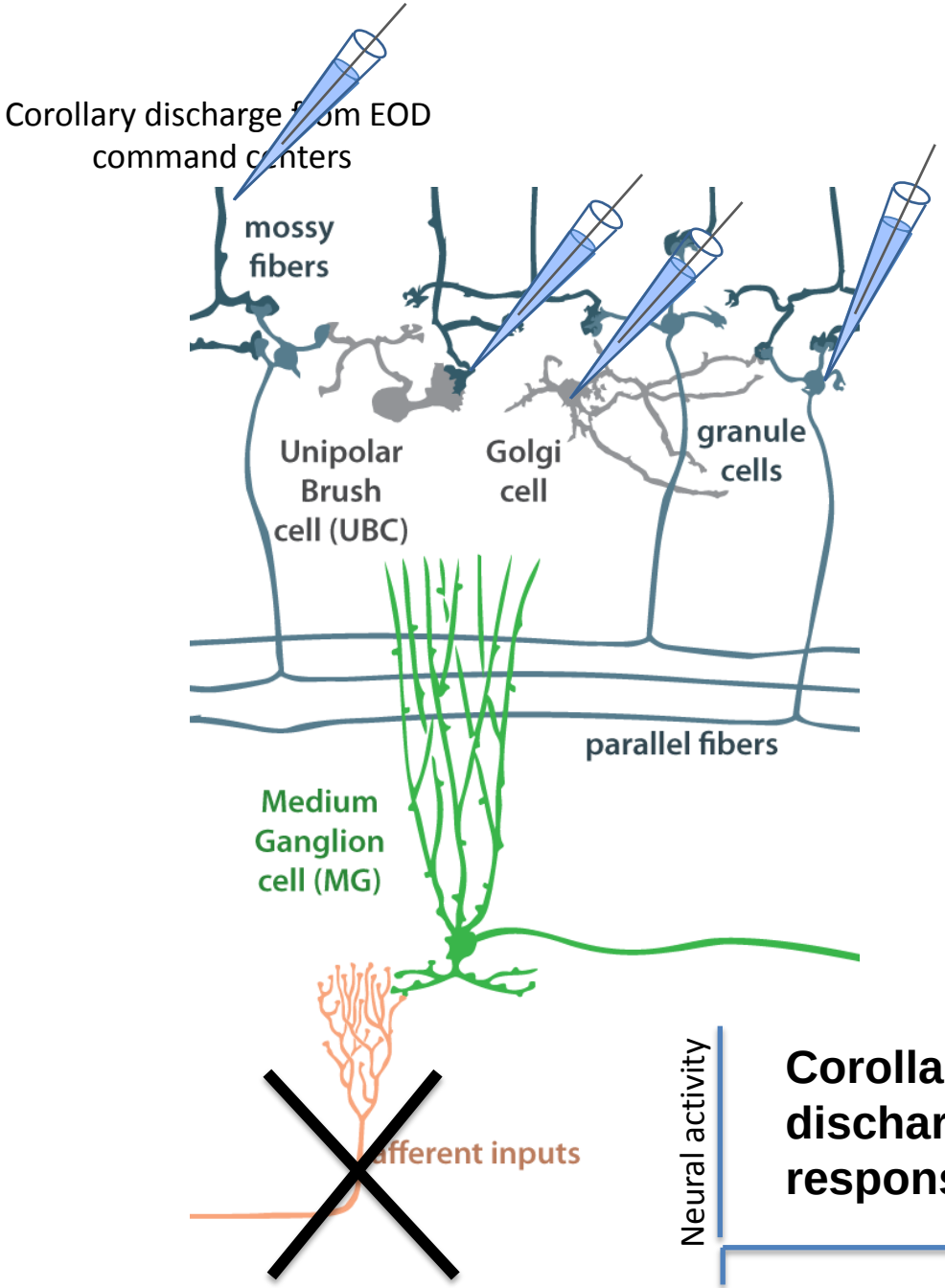
Anti-Hebbian spike timing-dependent plasticity at parallel fiber synapses *in vitro*

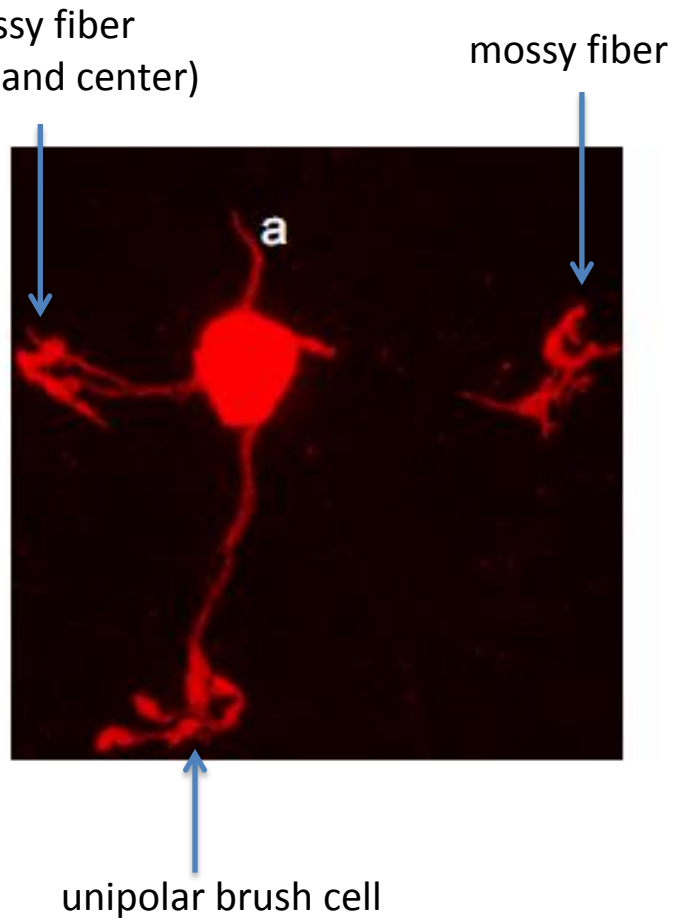


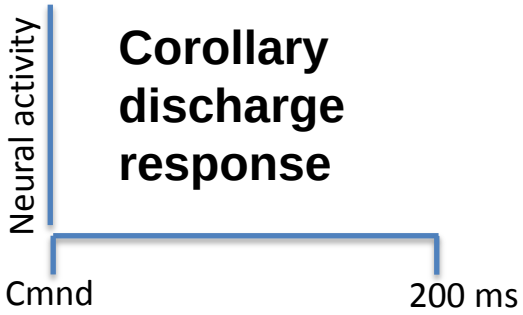


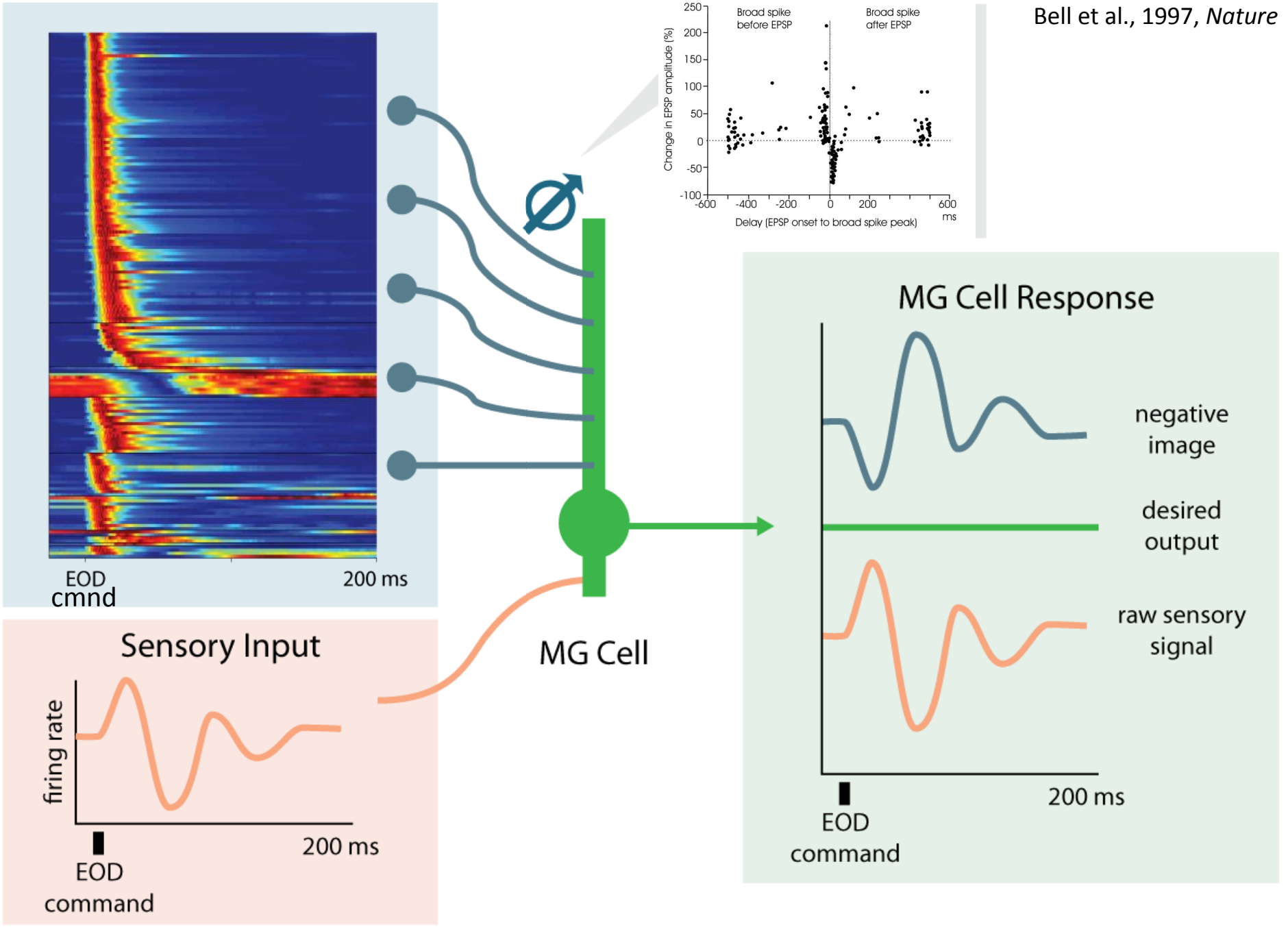
Bell et al., 1997, *Nature*


Granule Cell Responses
firing rate
200 ms
EOD
command
Roberts & Bell,2000, J Comp Neurosci
Learning Rule
% change
t_{post} - t_{pre}
Bell et al., 1997, Nature
MG Cell Response
negative
image
Bell, 1981, Science
desired
output
raw sensory
signal
200 ms
EOD
command
Sensory Input
firing rate
200 ms
EOD
command

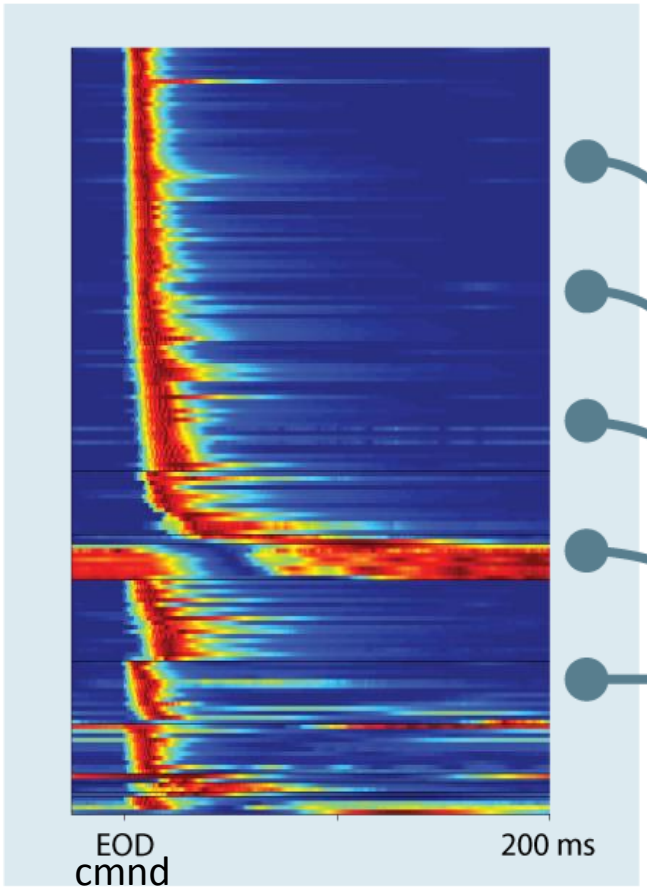

Corollary discharge from EOD command centers
mossy fibers
Unipolar Brush cell (UBC)
Golgi cell
granule cells
parallel fibers
Medium Ganglion cell (MG)
different inputs

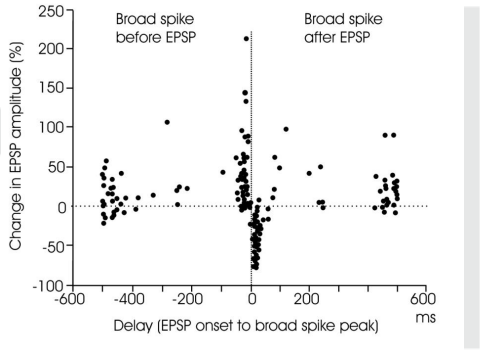

mossy fiber (command center)
mossy fiber
a
unipolar brush cell


Neural activity
Corollary discharge response
Cmnd
200 ms

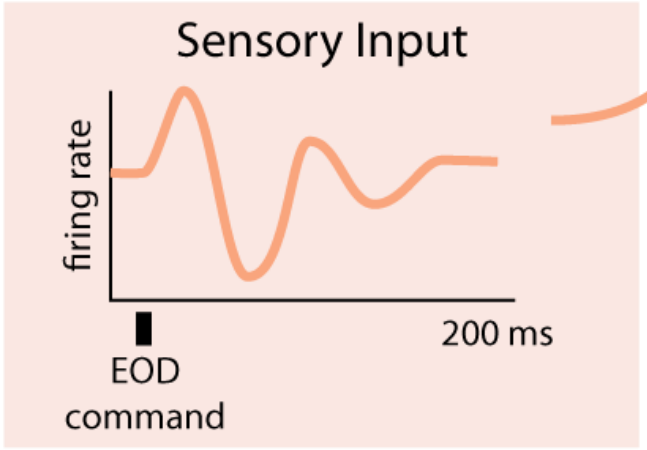


Bell et al., 1997, *Nature*

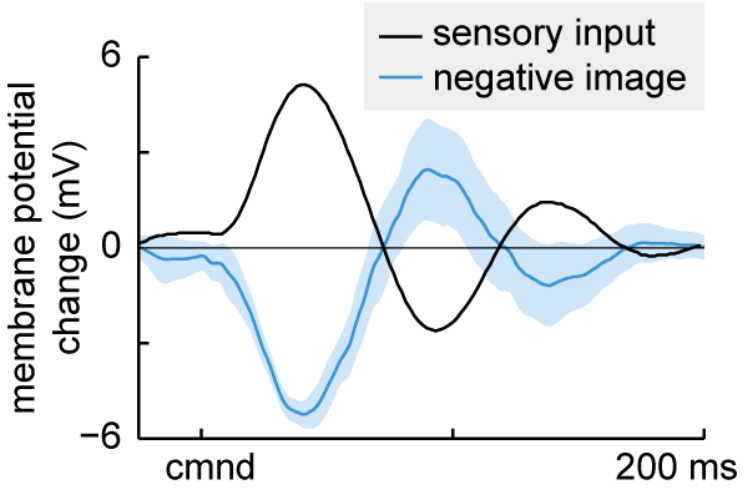




Bell et al., 1997, *Nature*

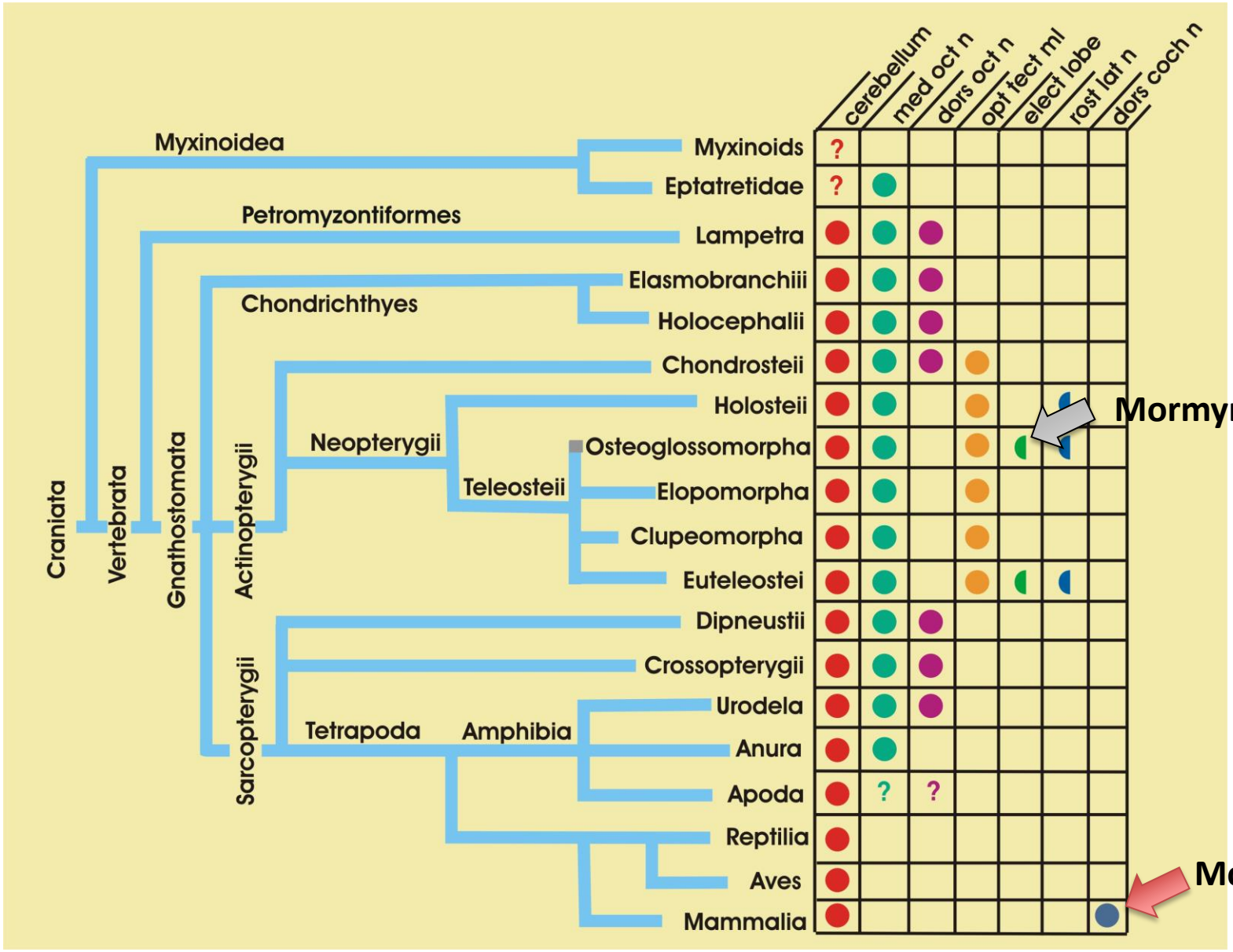


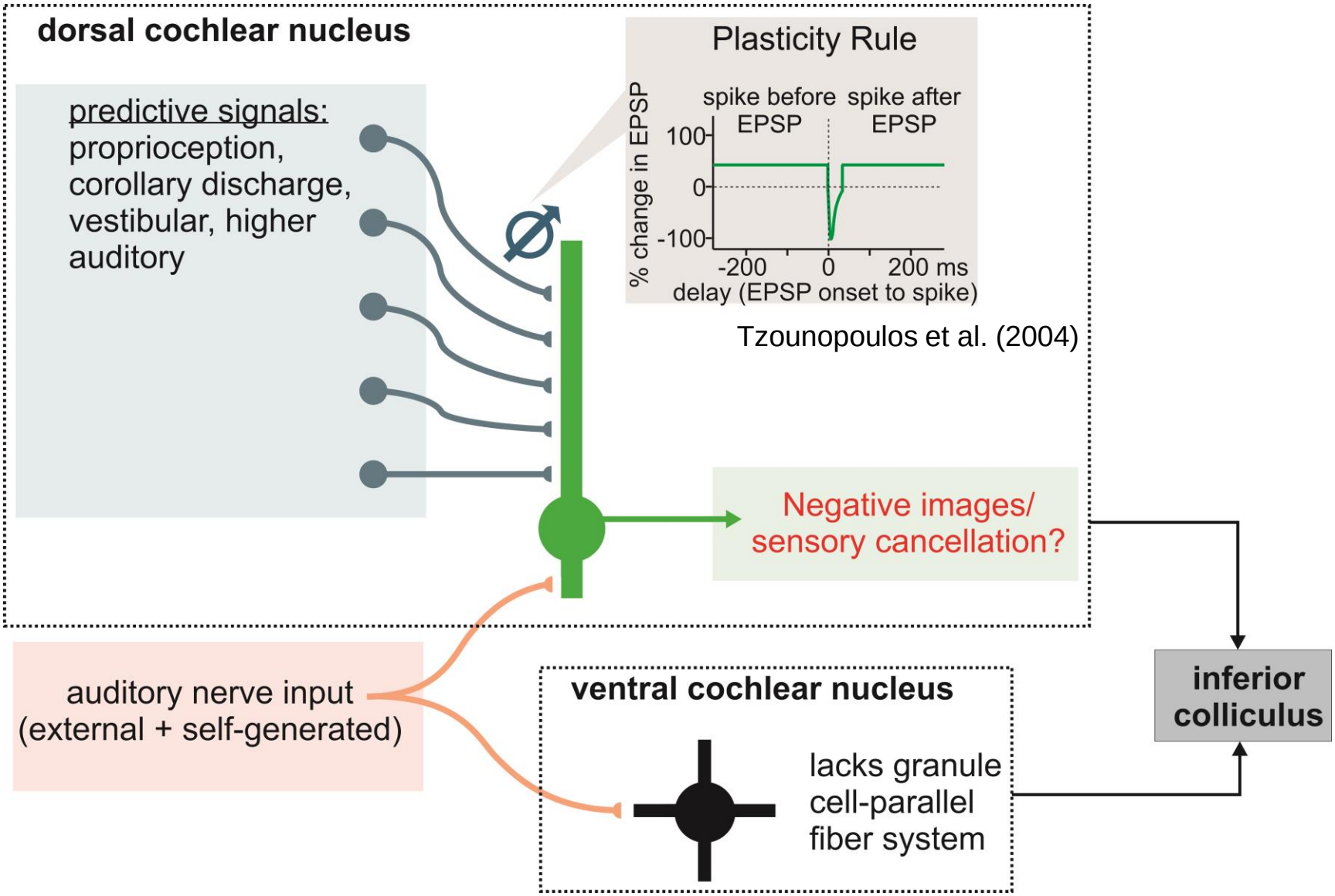
MG Cell



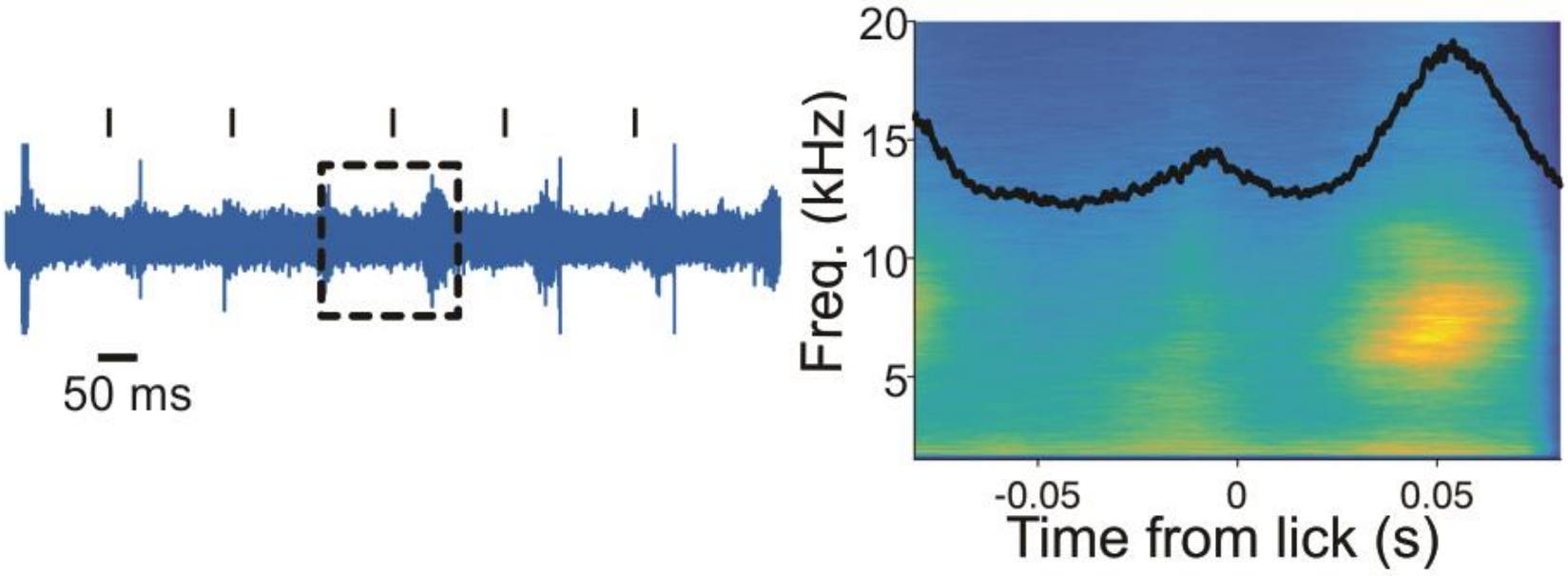
Kennedy et al., 2014

Can insights from ELL be extended to other systems?



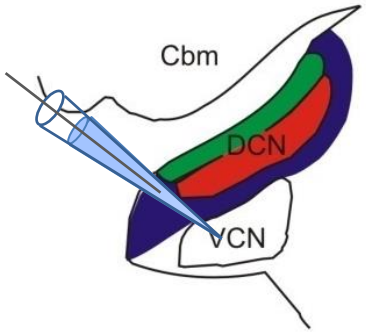

dorsal cochlear nucleus
predictive signals:
proprioception,
corollary discharge,
vestibular, higher
auditory
Plasticity Rule
spike before EPSP
spike after EPSP
% change in EPSP
100
0
-100
-200
0
200 ms
delay (EPSP onset to spike)
Tzounopoulos et al. (2004)
Negative images/
sensory cancellation?
auditory nerve input
(external + self-generated)
ventral cochlear nucleus
lacks granule
cell-parallel
fiber system
inferior
colliculus

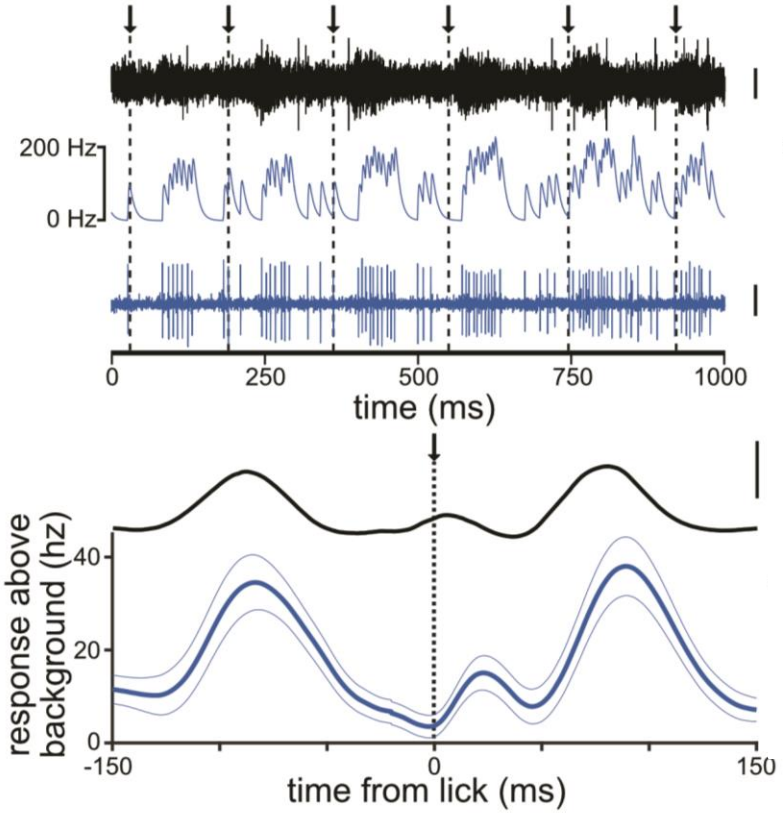
What's the sound of a mouse licking?



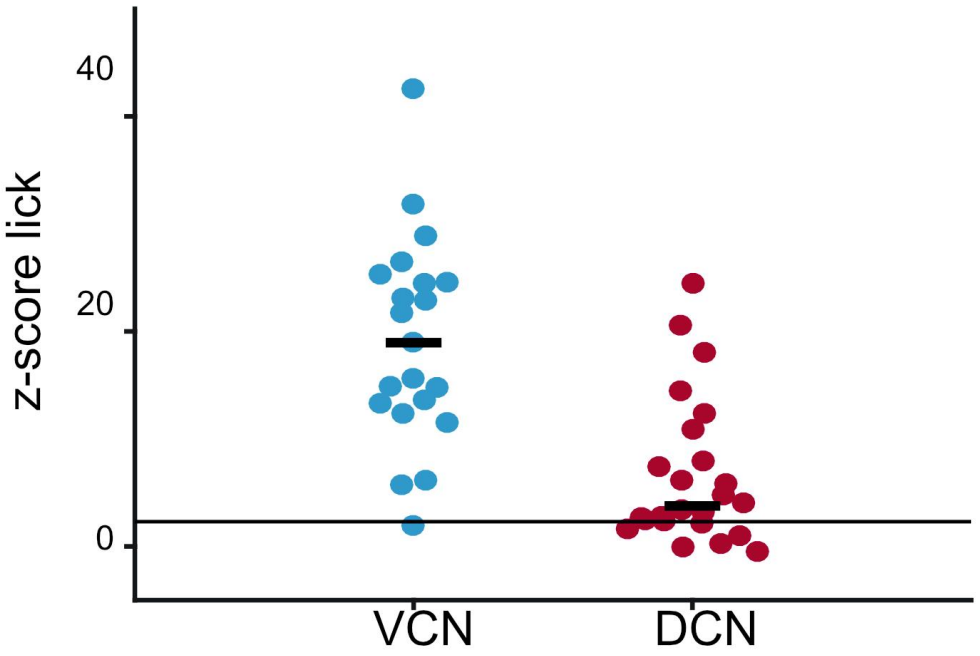
Singla et al., 2017

Responses of VCN/DCN units to self-generated sounds

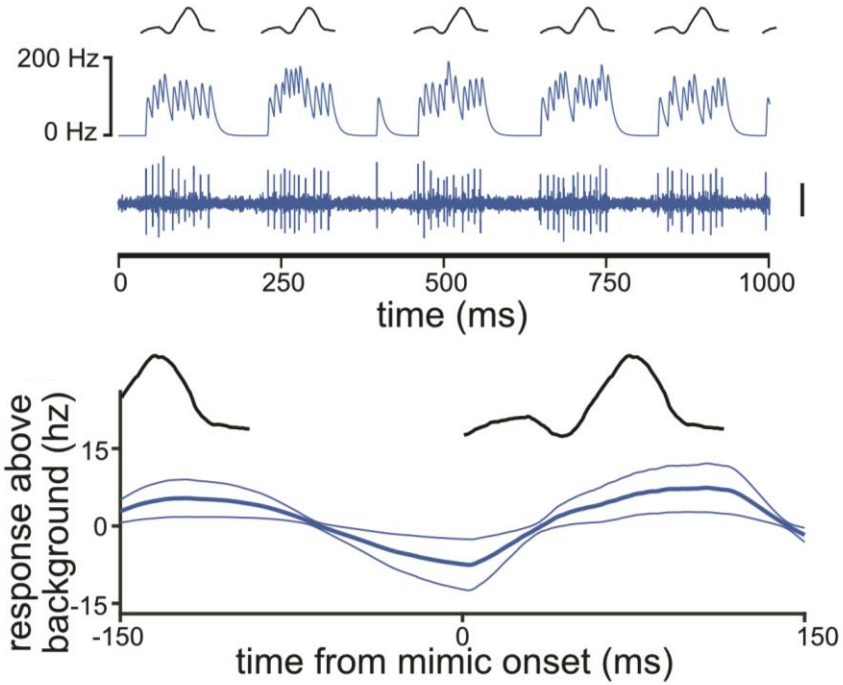


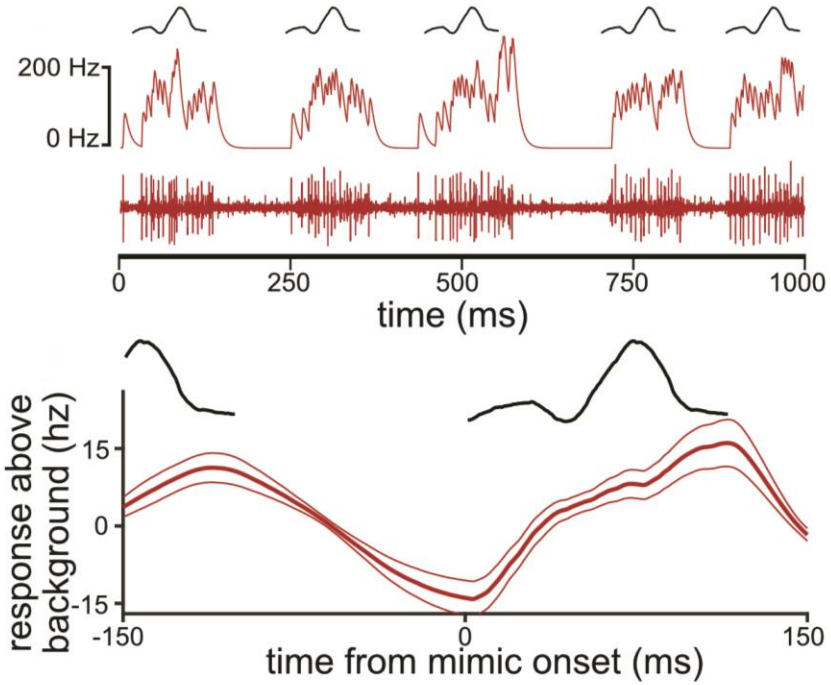


Responses of VCN/DCN units to self-generated sounds

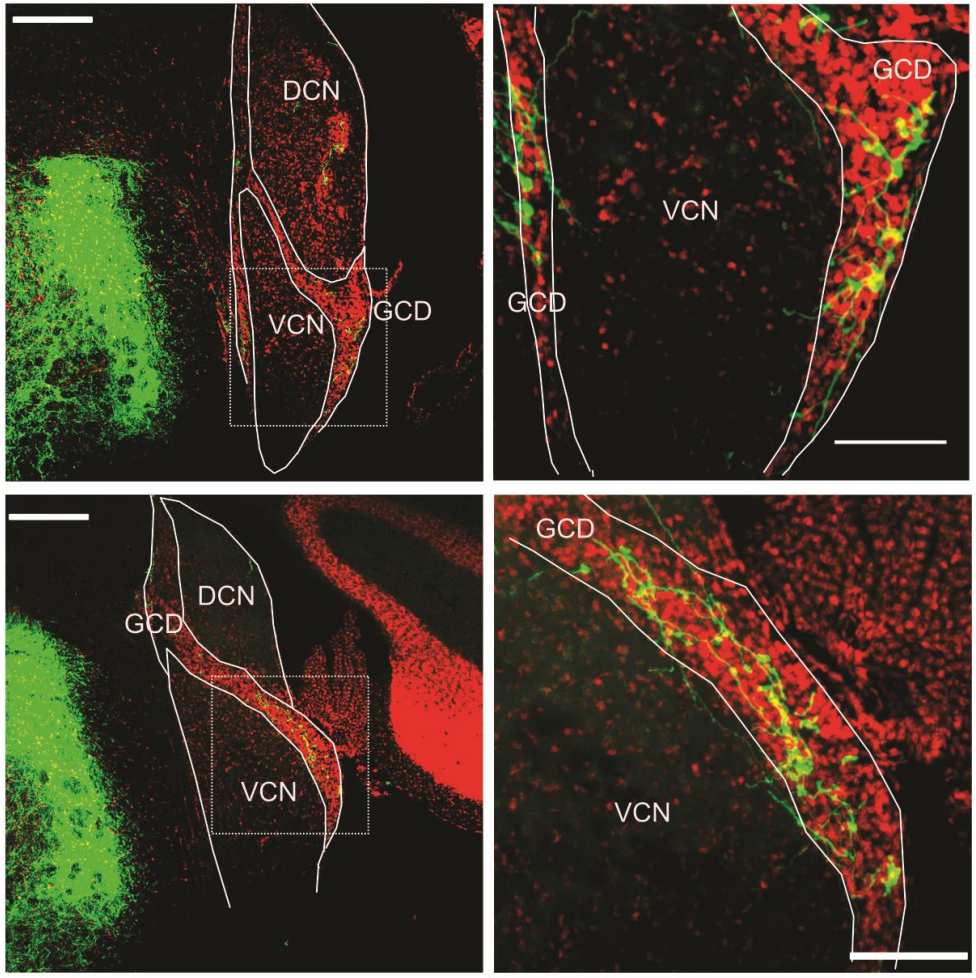


Responses of VCN/DCN units to a mimic of lick sound

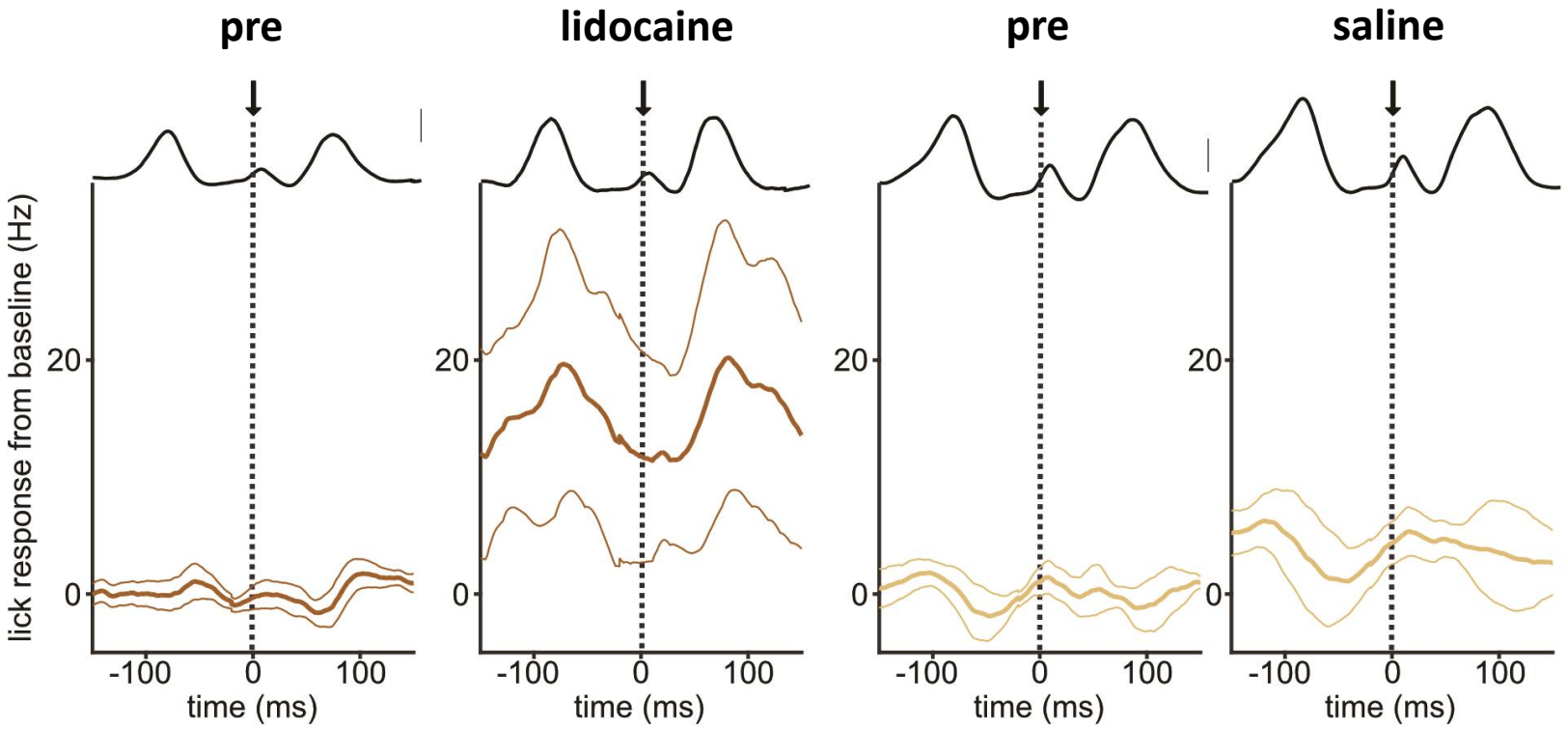


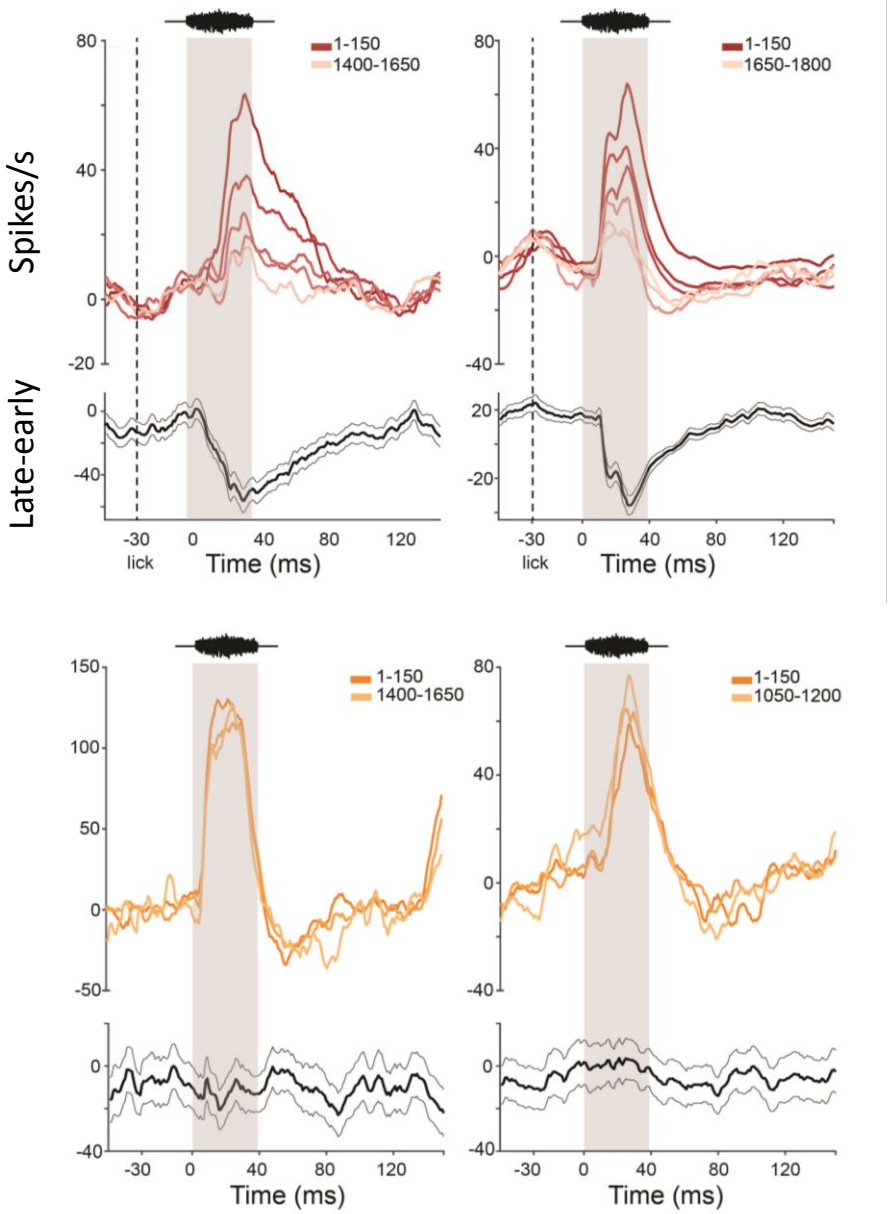


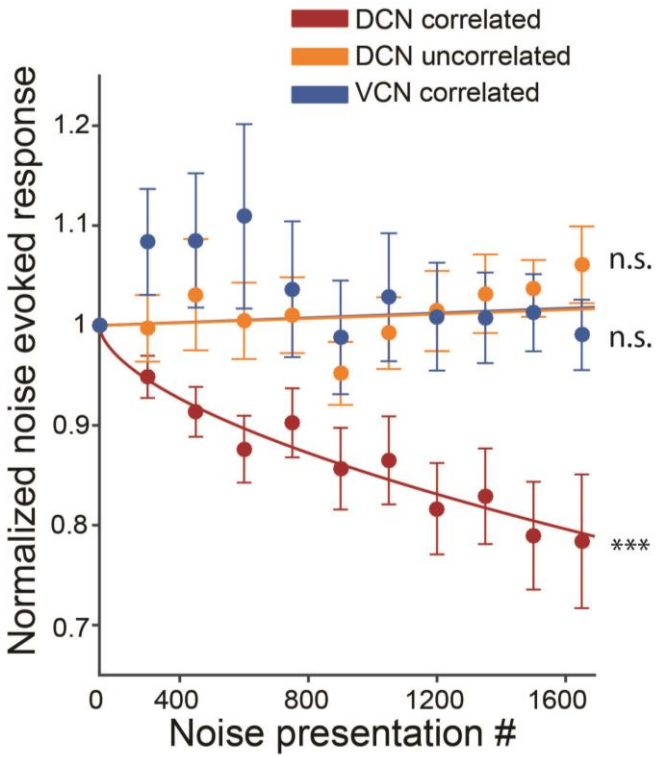
Spinal trigeminal nucleus provides mossy fiber inputs to DCN, potential source of predictive information



Inactivation of Sp5 reveals responses to licking in DCN



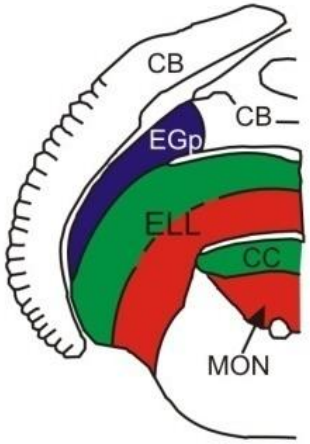

Spikes/s
Late-early
1-150
1400-1650
1650-1800
1050-1200
lick
Time (ms)


DCN correlated
DCN uncorrelated
VCN correlated
Normalized noise evoked response
Noise presentation #
n.s.
n.s.
***

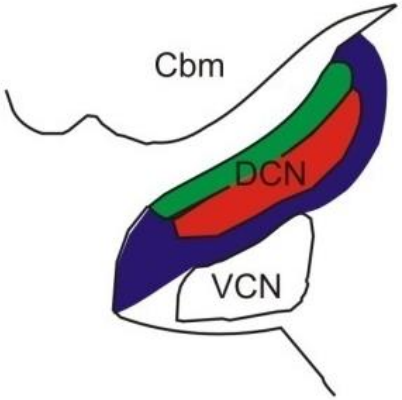
Implications for other systems?

--Cerebellum-like sensory structures in fish (ELL) and mammals (DCN) and the cerebellum itself may all perform similar functions. Both may function to adaptively filter inputs and/or predict sensory consequences of behavior.

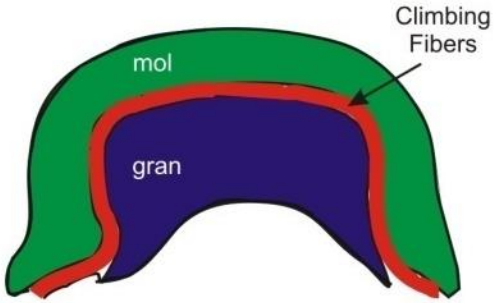
MORMYRID FISH
- ELL (electrosense)
- MON (lateral line)
- MON (audition)

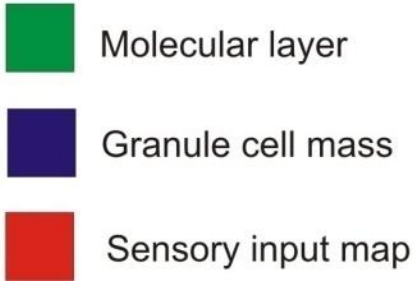


MAMMALS
- DCN (audition)



ALL VERTEBRATES
cerebellum
- many senses
- motor control





Acknowledgements

Former students

Tim Requarth
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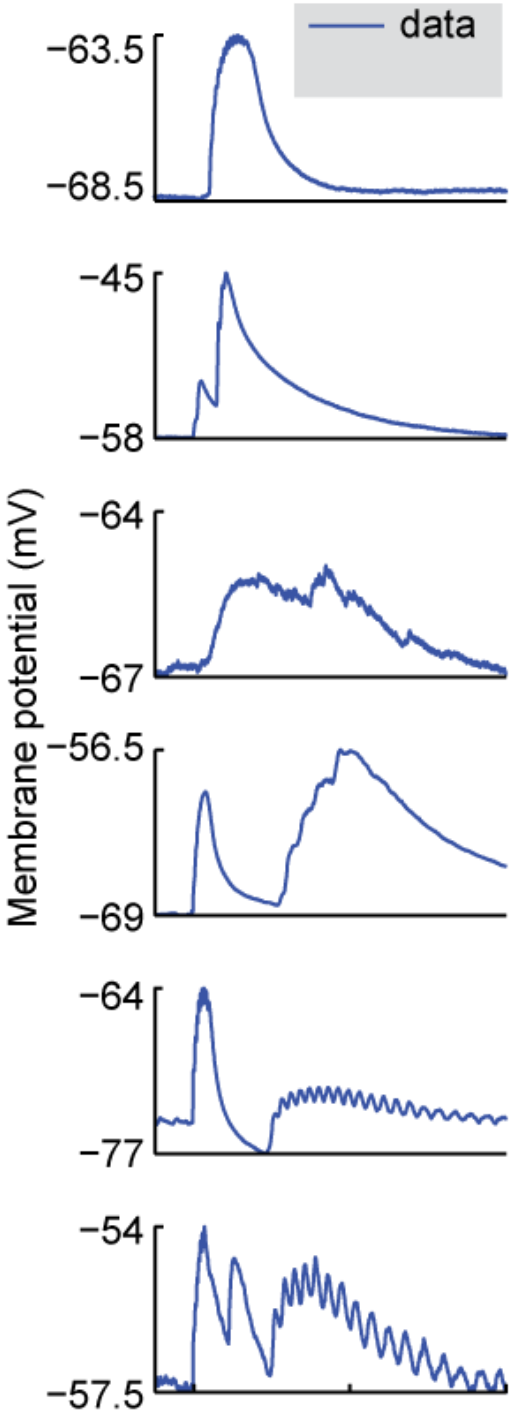
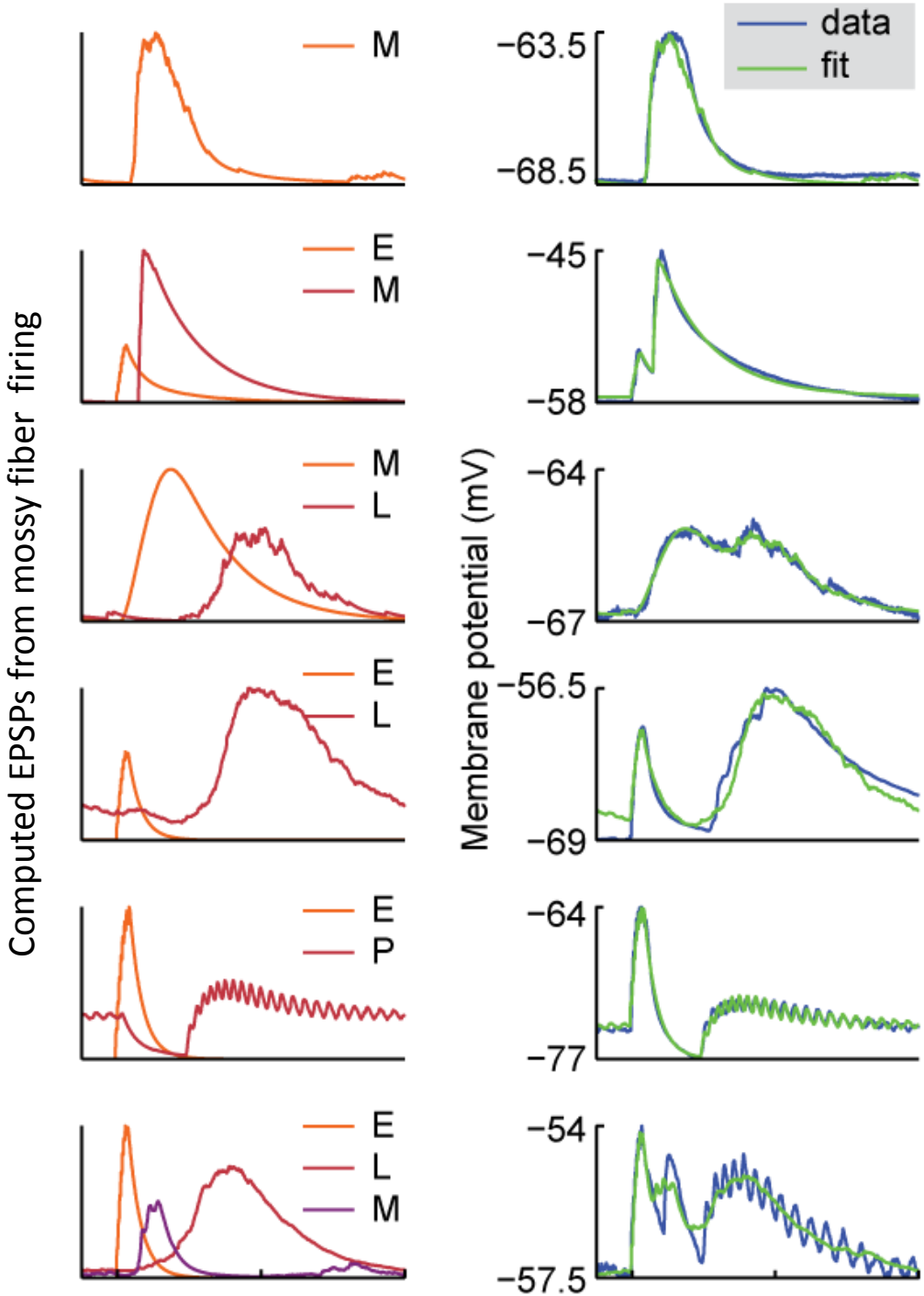
Conor Dempsey

Collaborators

Larry Abbott

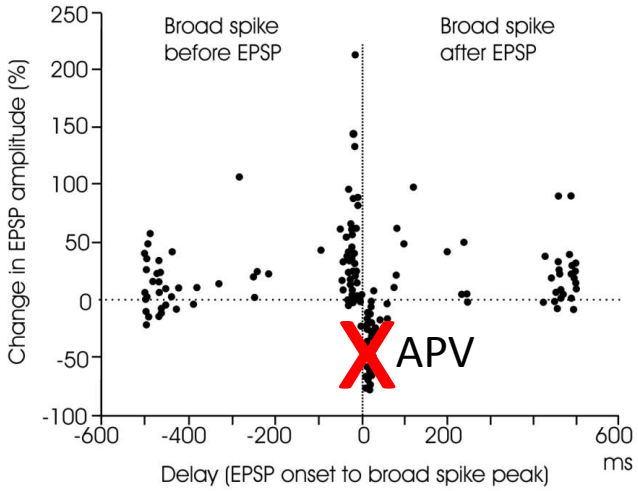
THE
IRMA T. HIRSCHL
TRUST

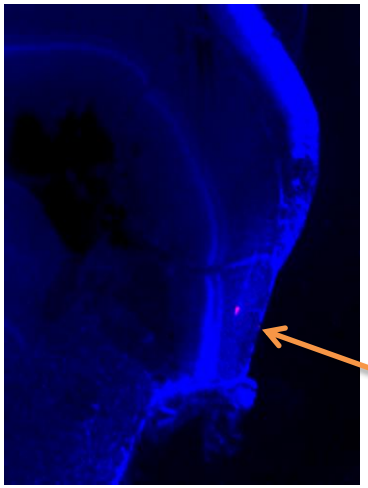

data
−63.5
−68.5
−45
−58
−64
−67
−56.5
−69
−64
−77
−54
−57.5
Membrane potential (mV)



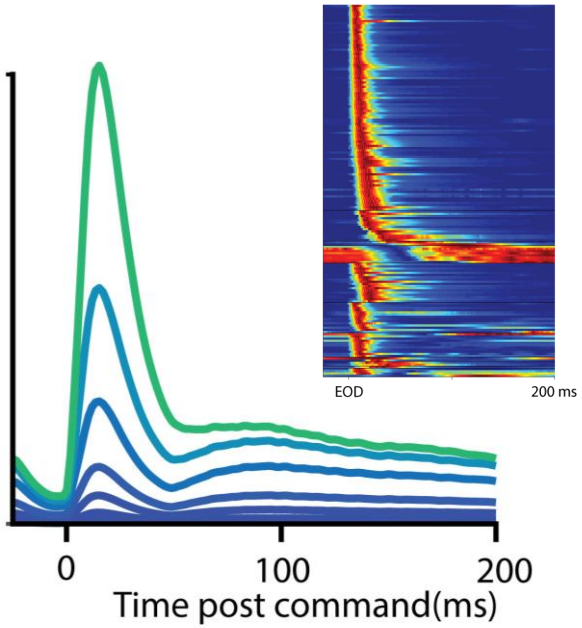
Kennedy et al., 2014

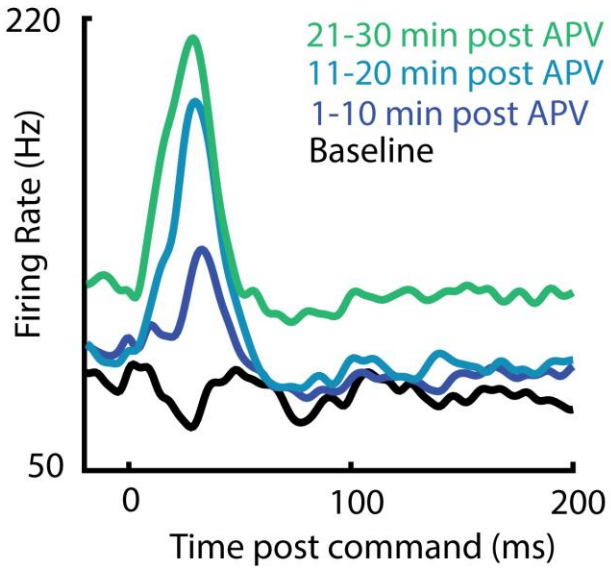
Effects of NMDA receptor blockade *in vitro* and *in vivo*



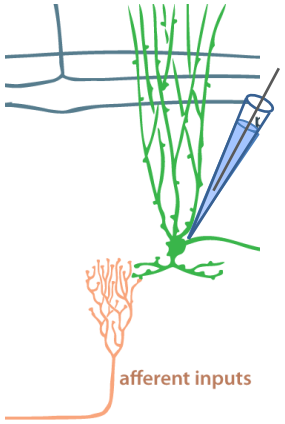


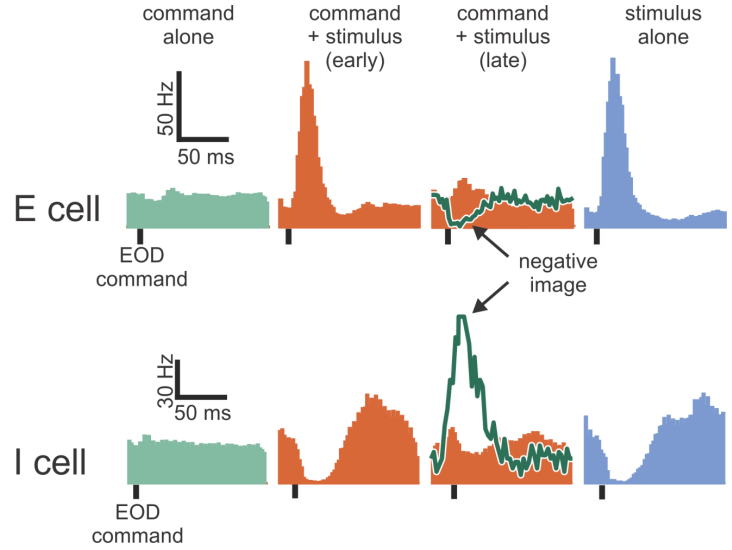
APV in molecular layer

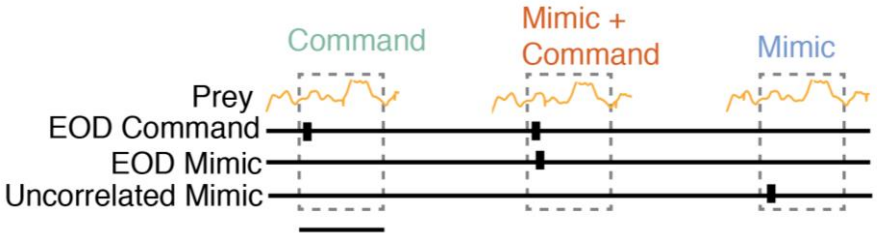


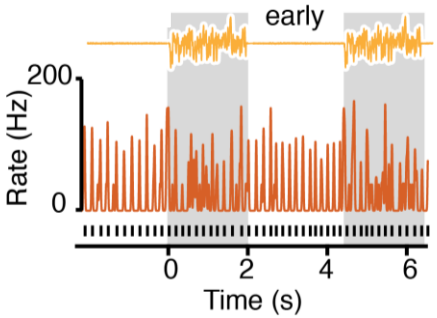


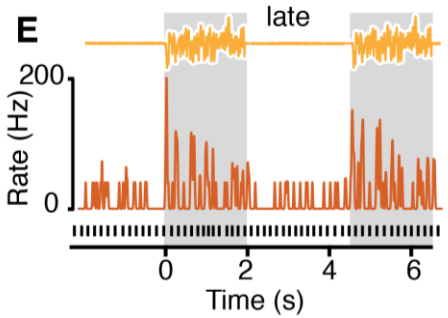
Significance of negative images for sensory processing and behavior

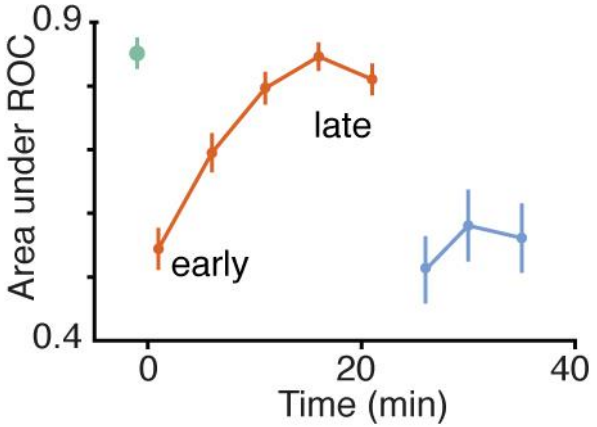


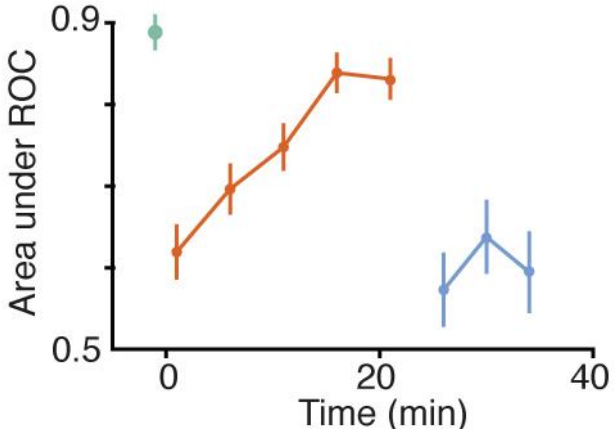




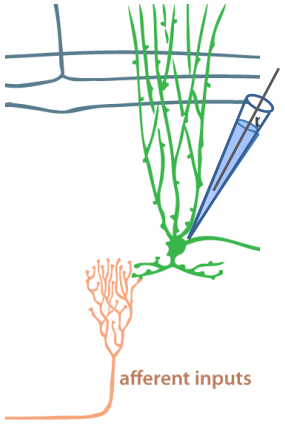


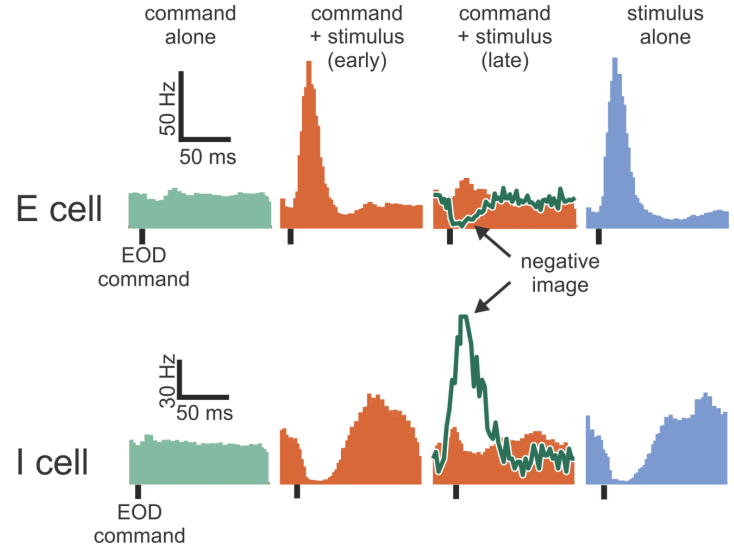


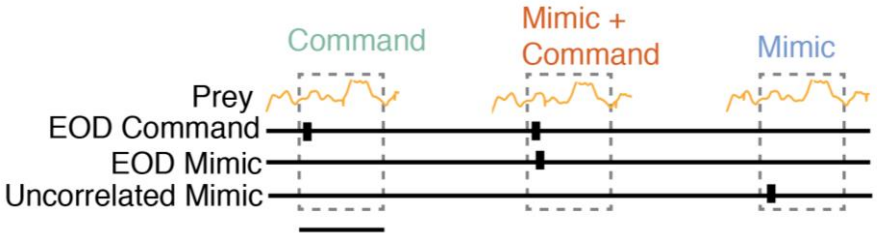


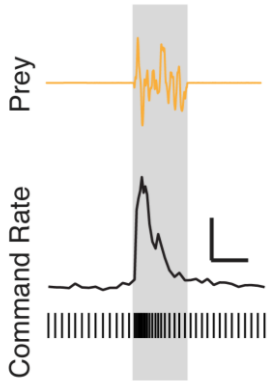


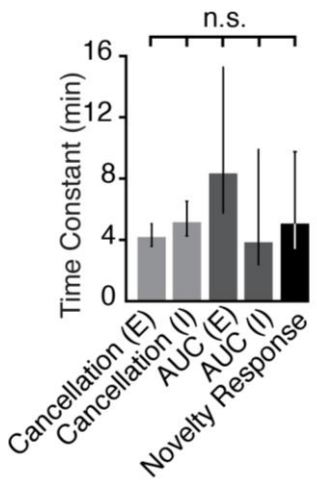
Significance of negative images for sensory processing and behavior

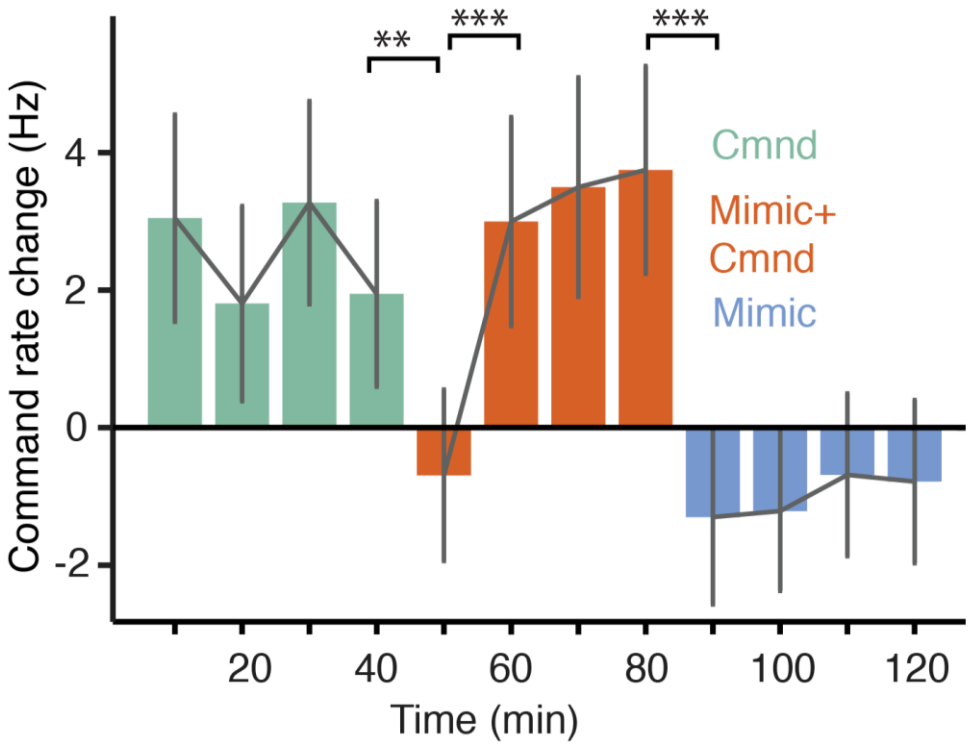




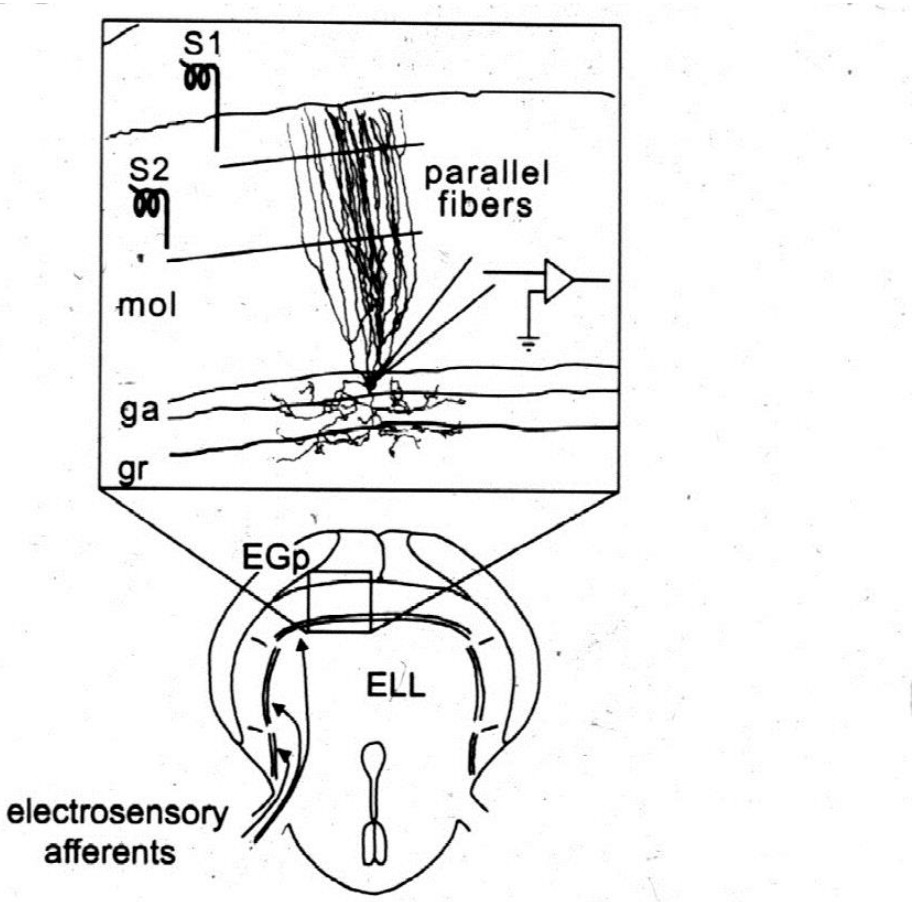






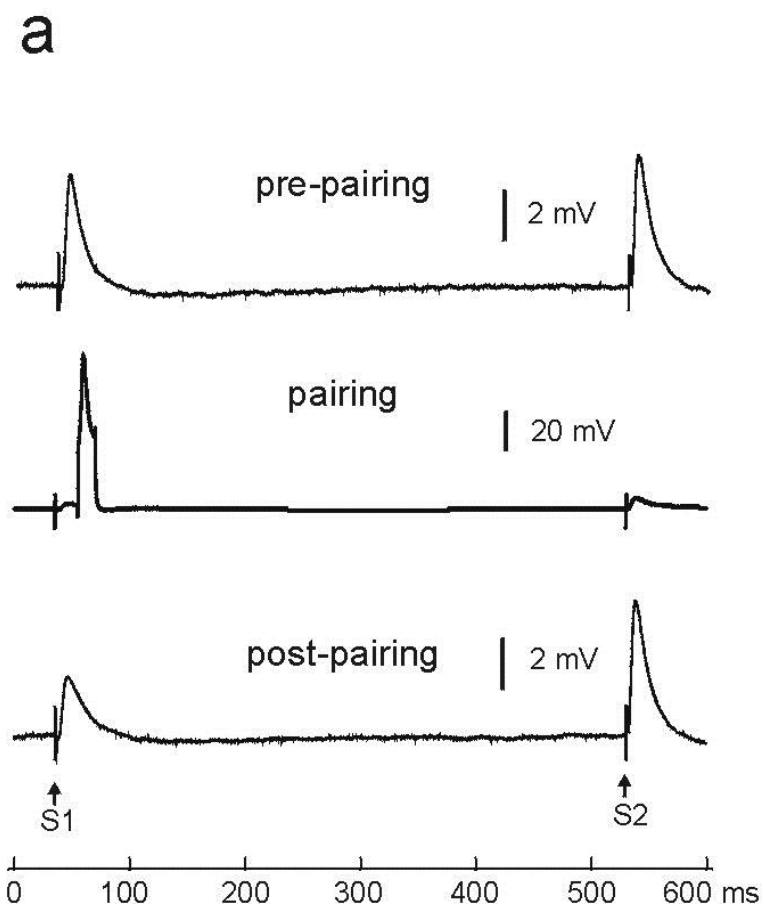


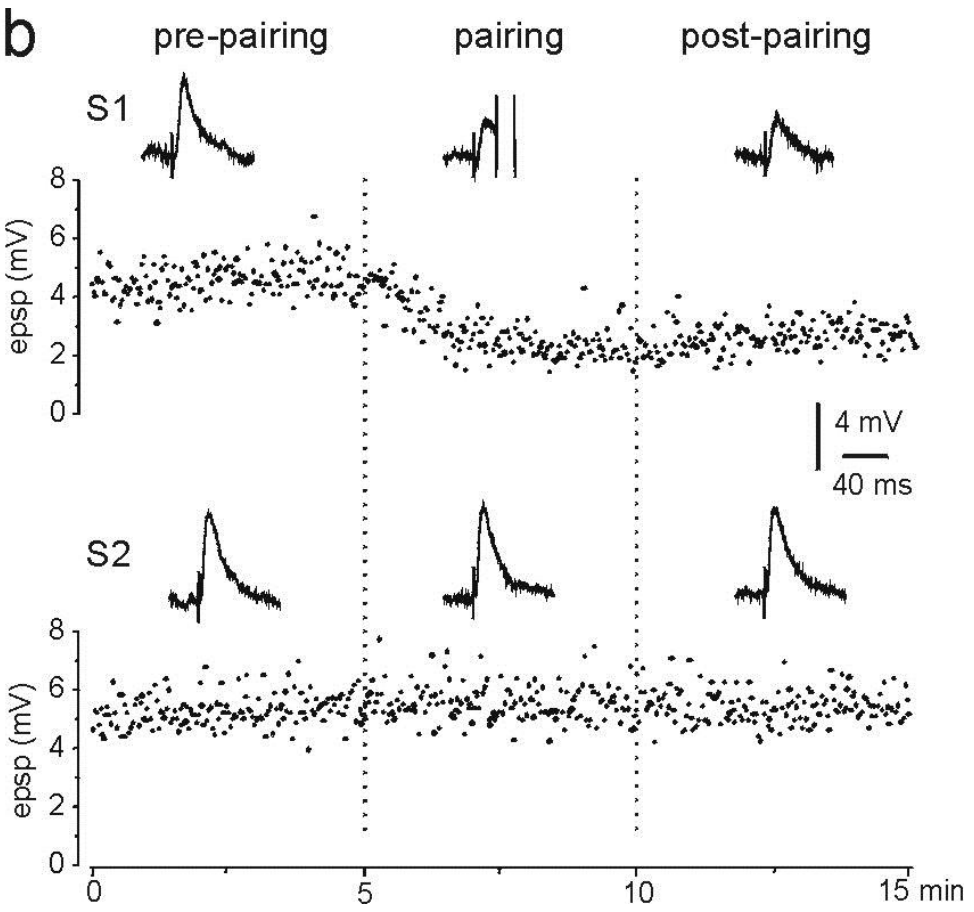
Experimental Methods for Testing Synaptic Plasticity in a Slice Preparation.



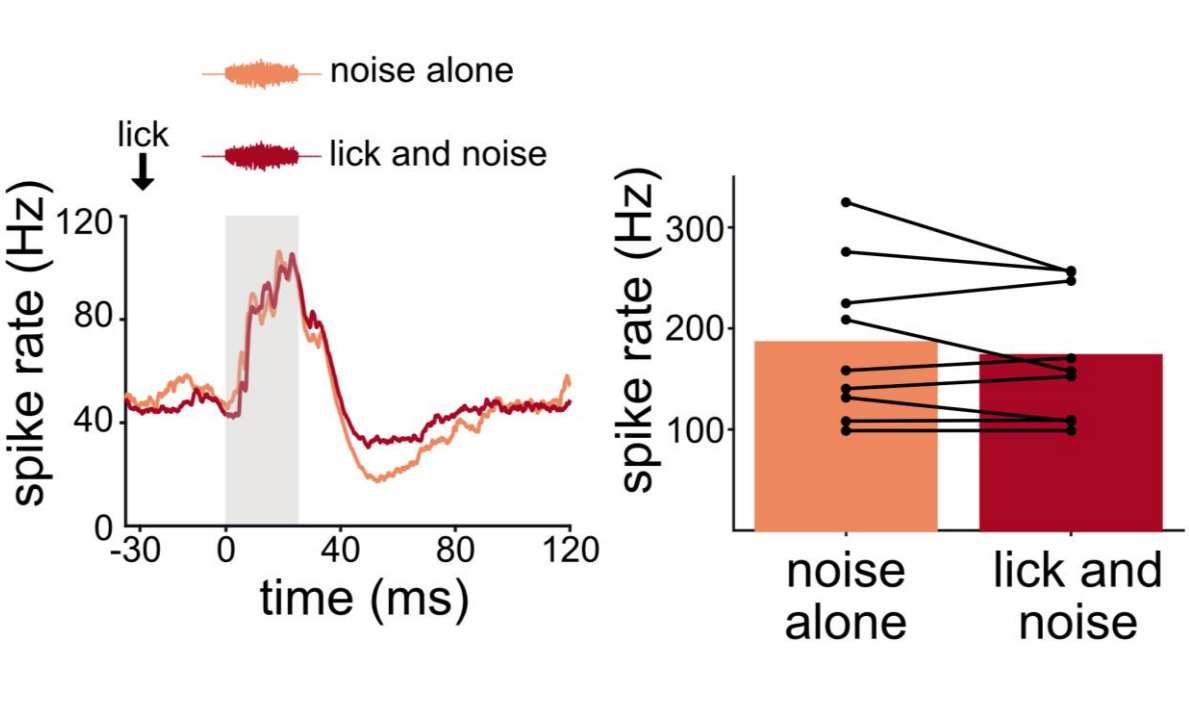
Curtis Bell

Pairing with Postsynaptic Dendritic Spike Induces Synaptic Depression

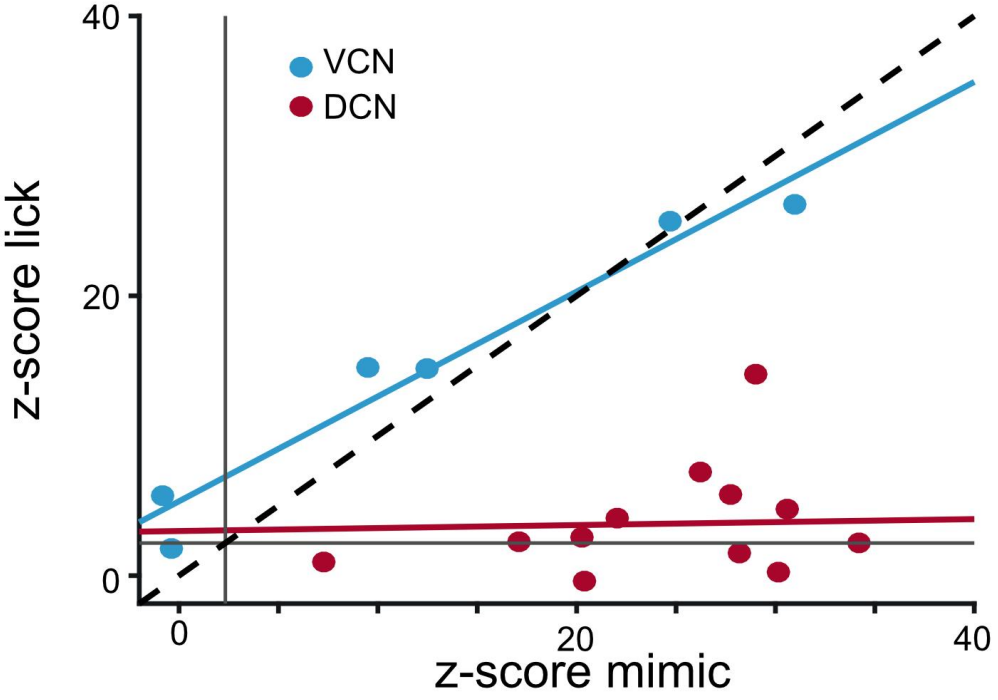




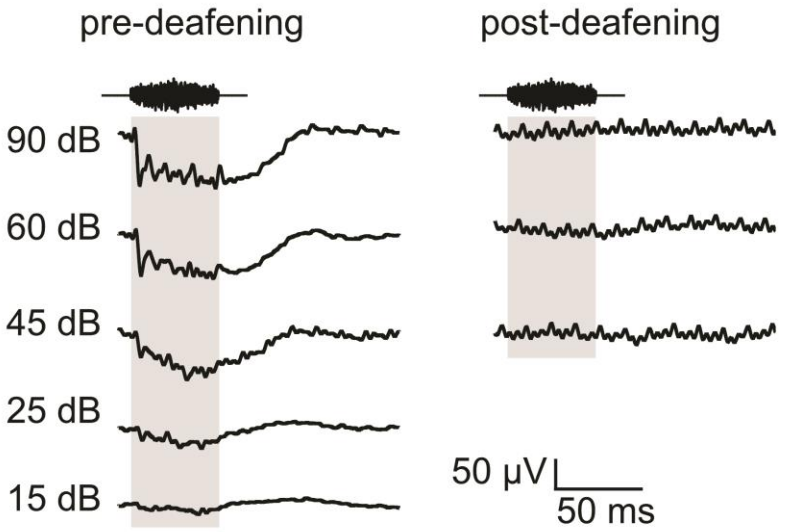
External sounds are not suppressed in DCN during licking

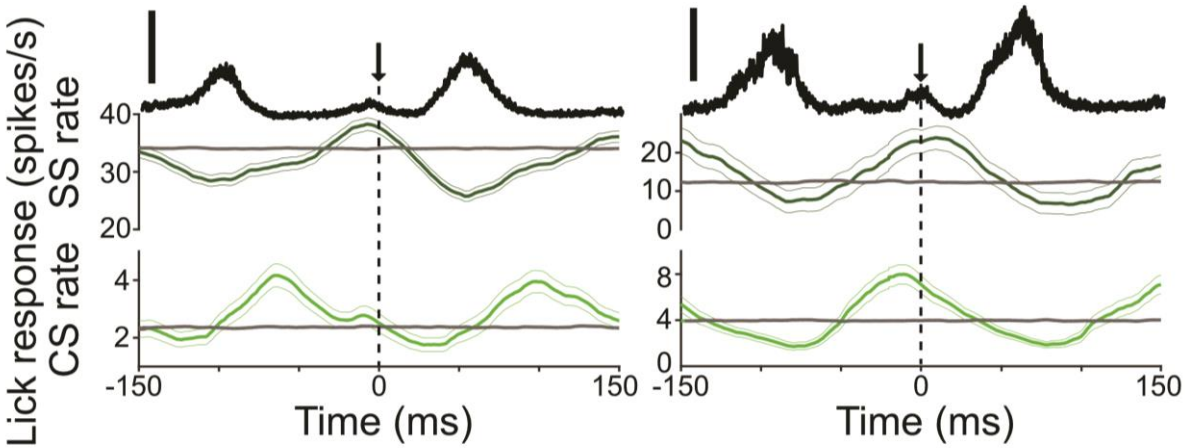


VCN/DCN units: licking versus mimic

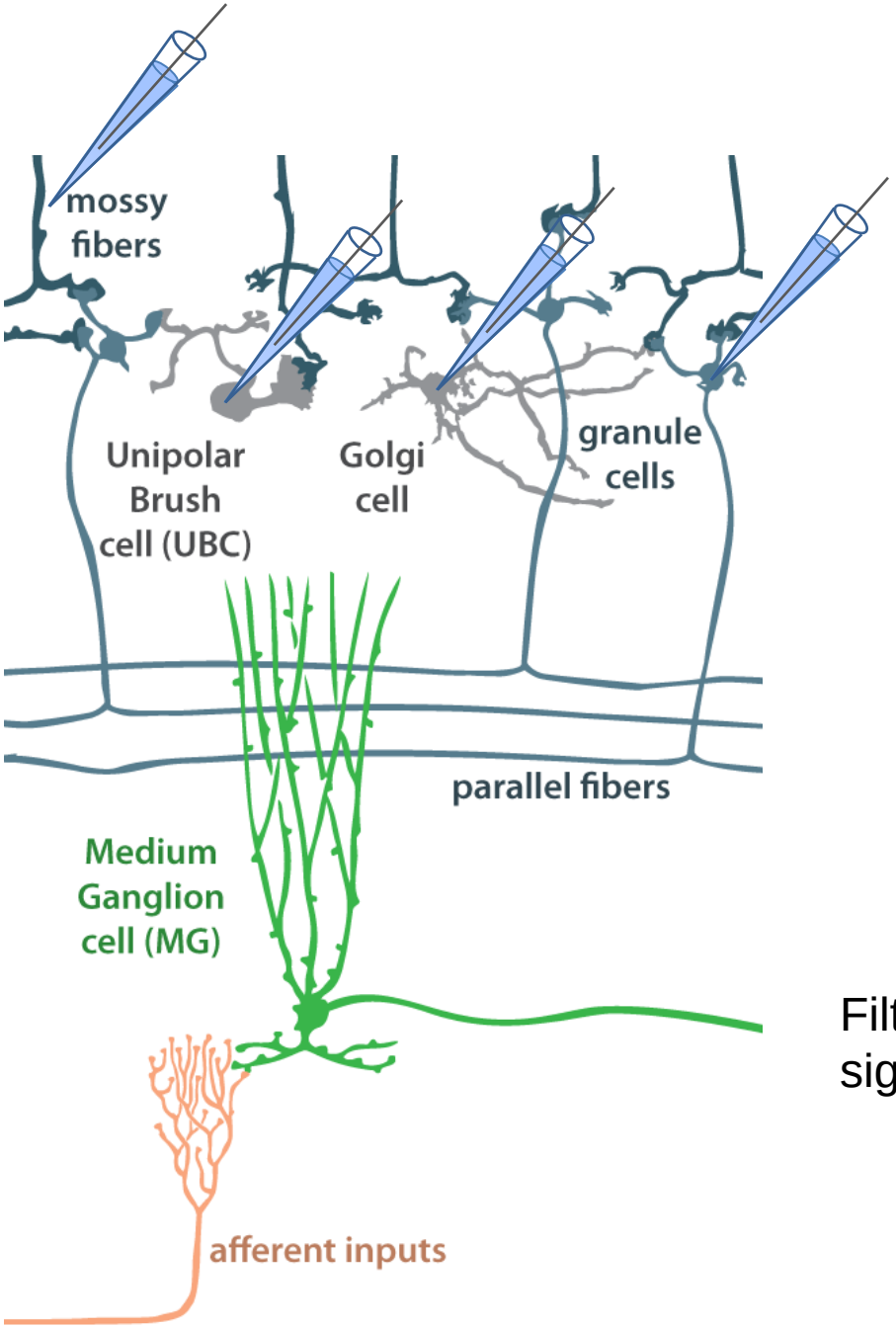


Responses of DCN interneurons to licking in deafened mice





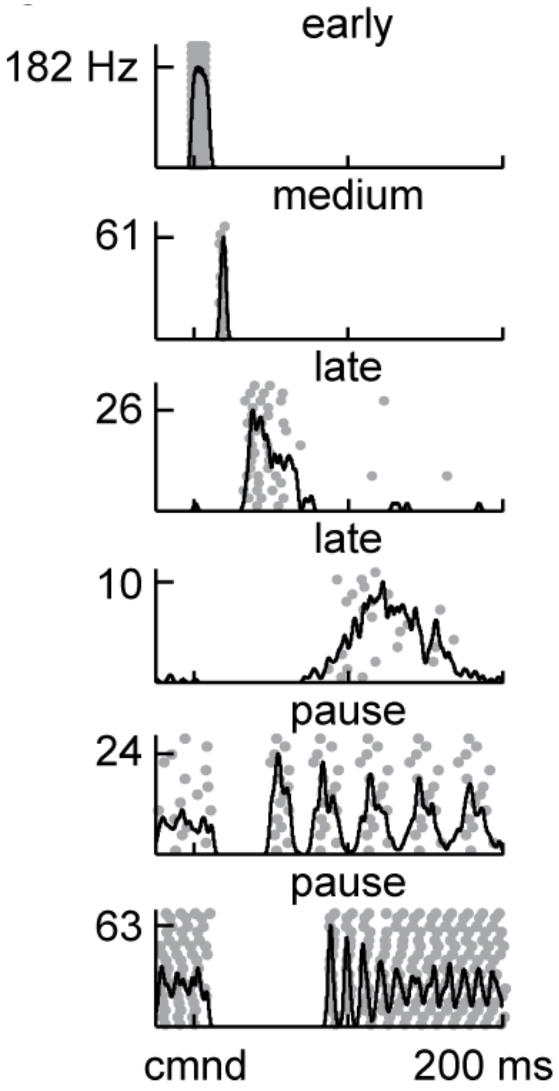
Corollary discharge signal

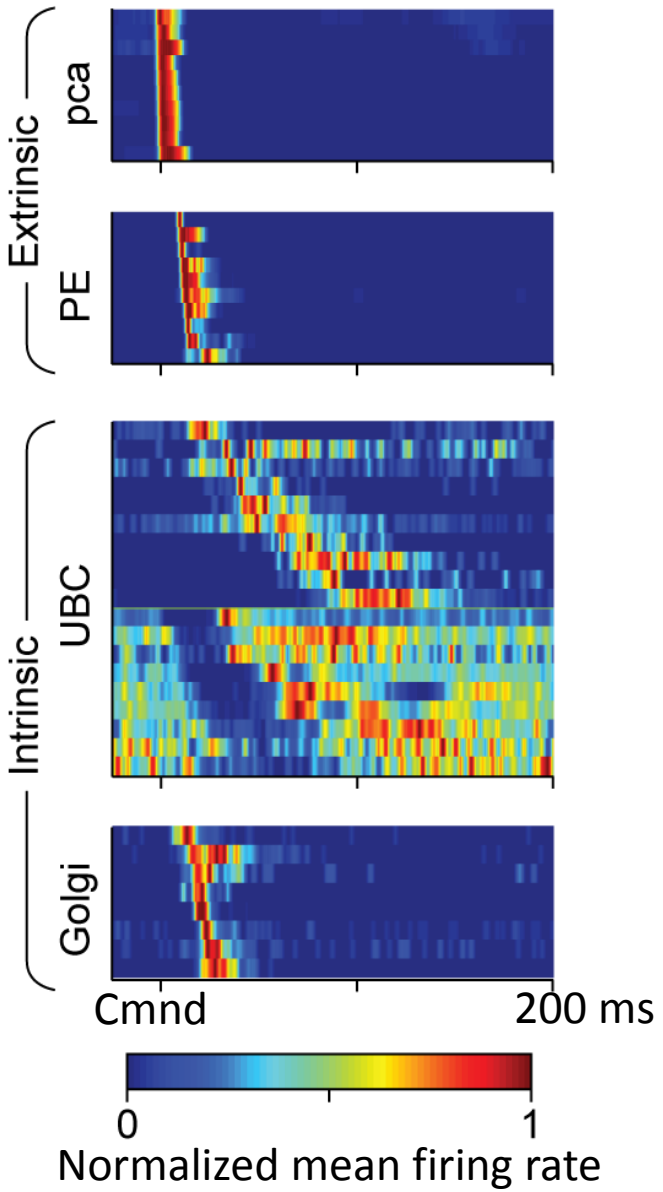


Filtered sensory signal

Raw sensory input

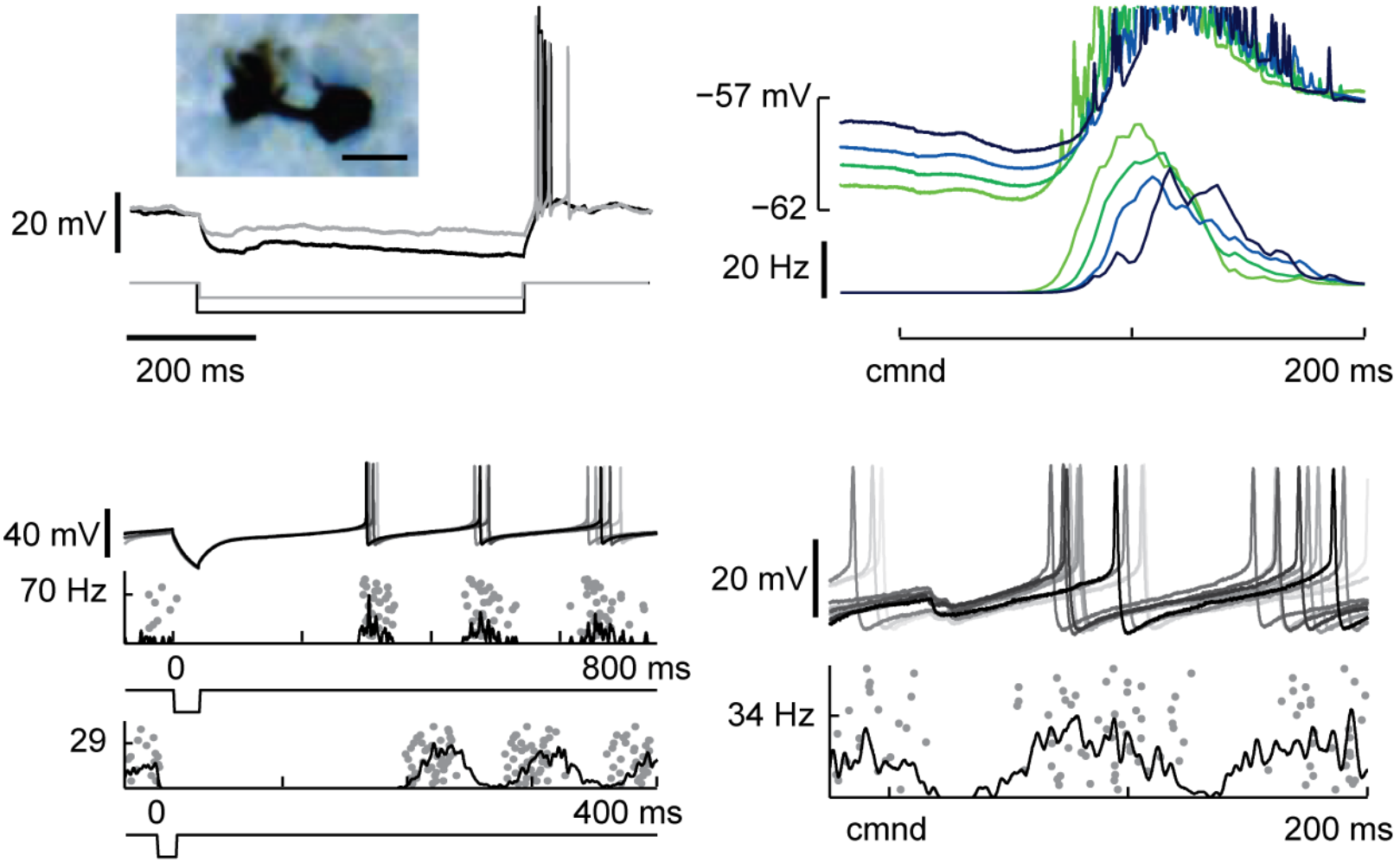
Unipolar brush cells exhibit delayed and diverse corollary discharge responses





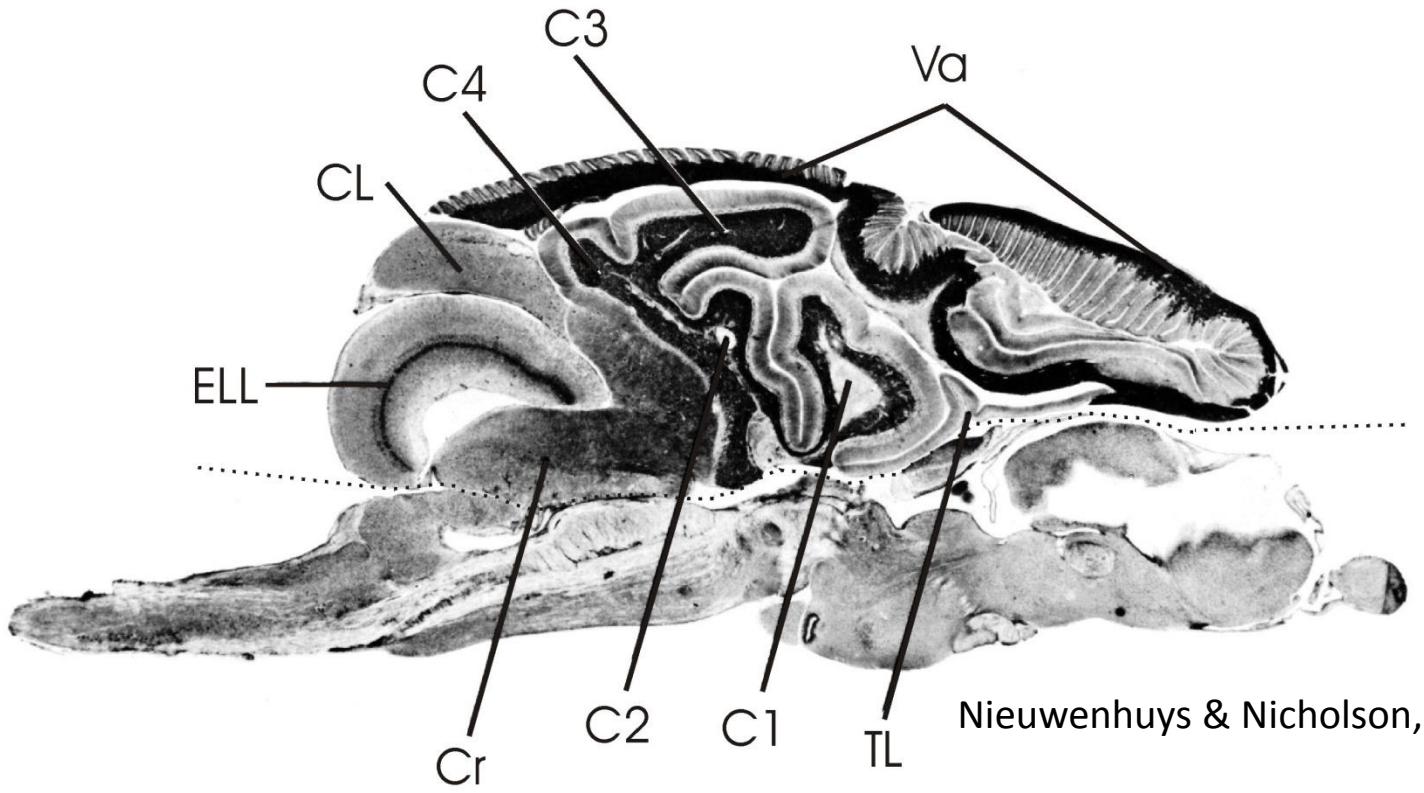
Kennedy et al., 2014

Intrinsic and synaptic properties of unipolar brush cells are likely important for generating temporally diversity



Kennedy et al., 2014

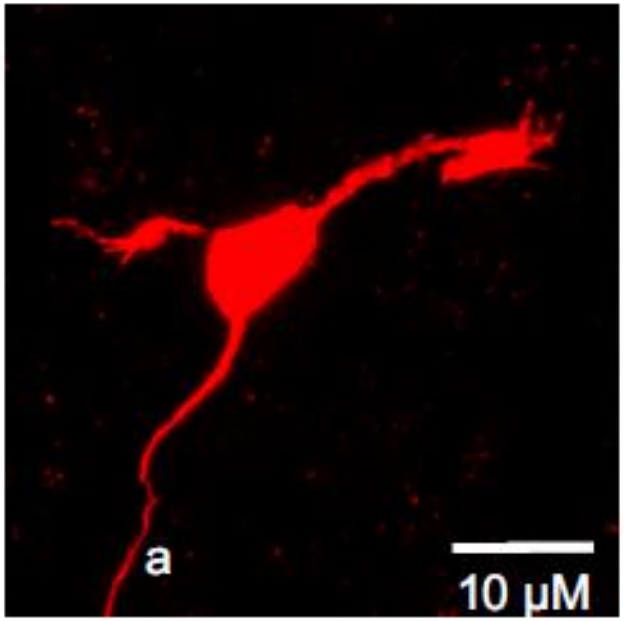
Amazing brains

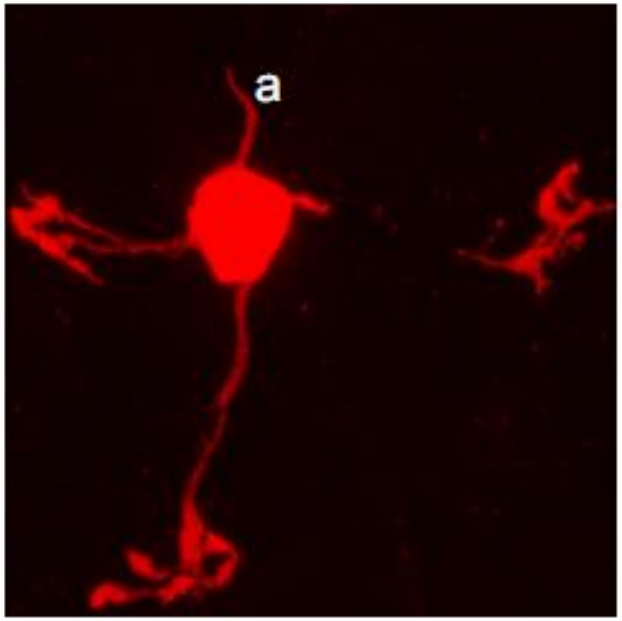


Nieuwenhuys & Nicholson, 1969

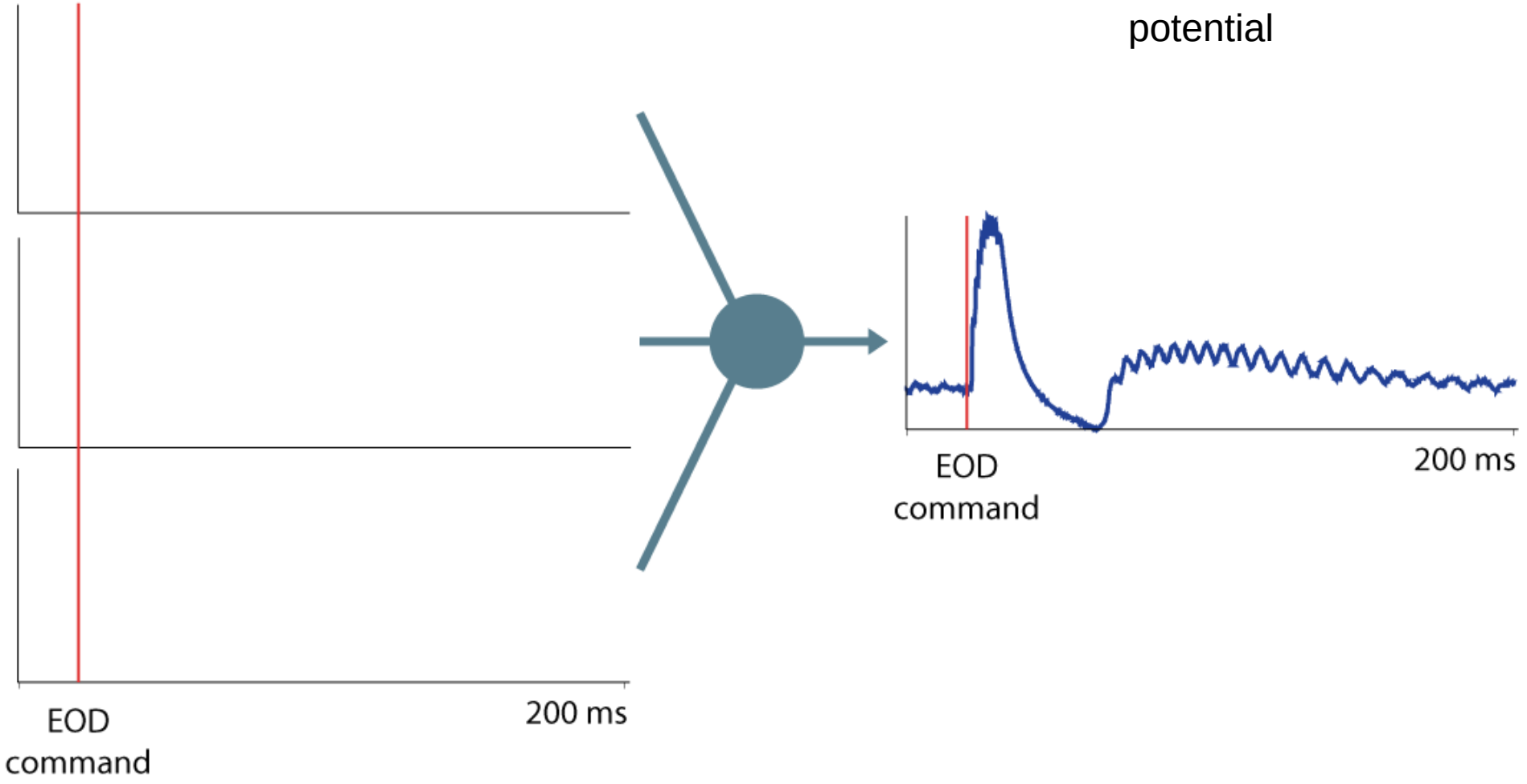
Mormyrid fish and owl monkeys have the largest brain to body mass ratios of any animals

Resting oxygen consumption by the brains of mormyrid fish is three times larger than for any other creature, including humans


a
10 µM

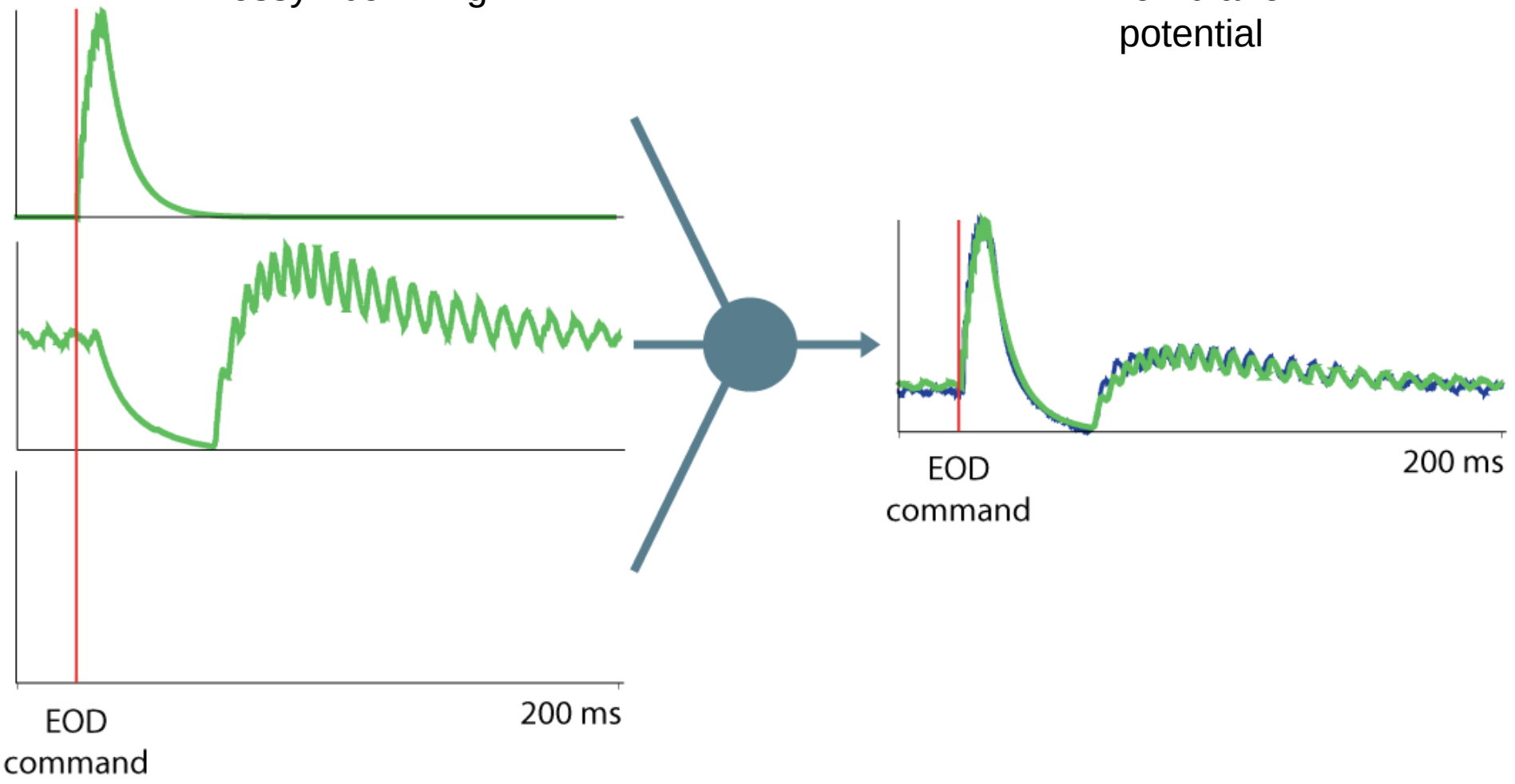

a

Granule cell membrane potential



Computed EPSPs from mossy fiber firing

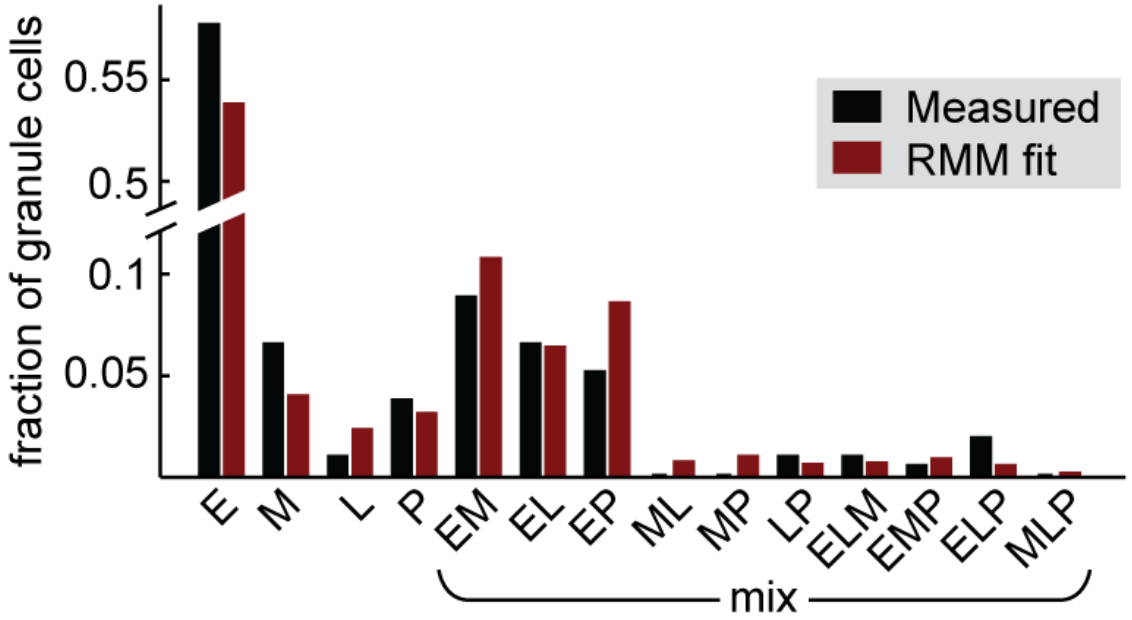
Granule cell membrane potential

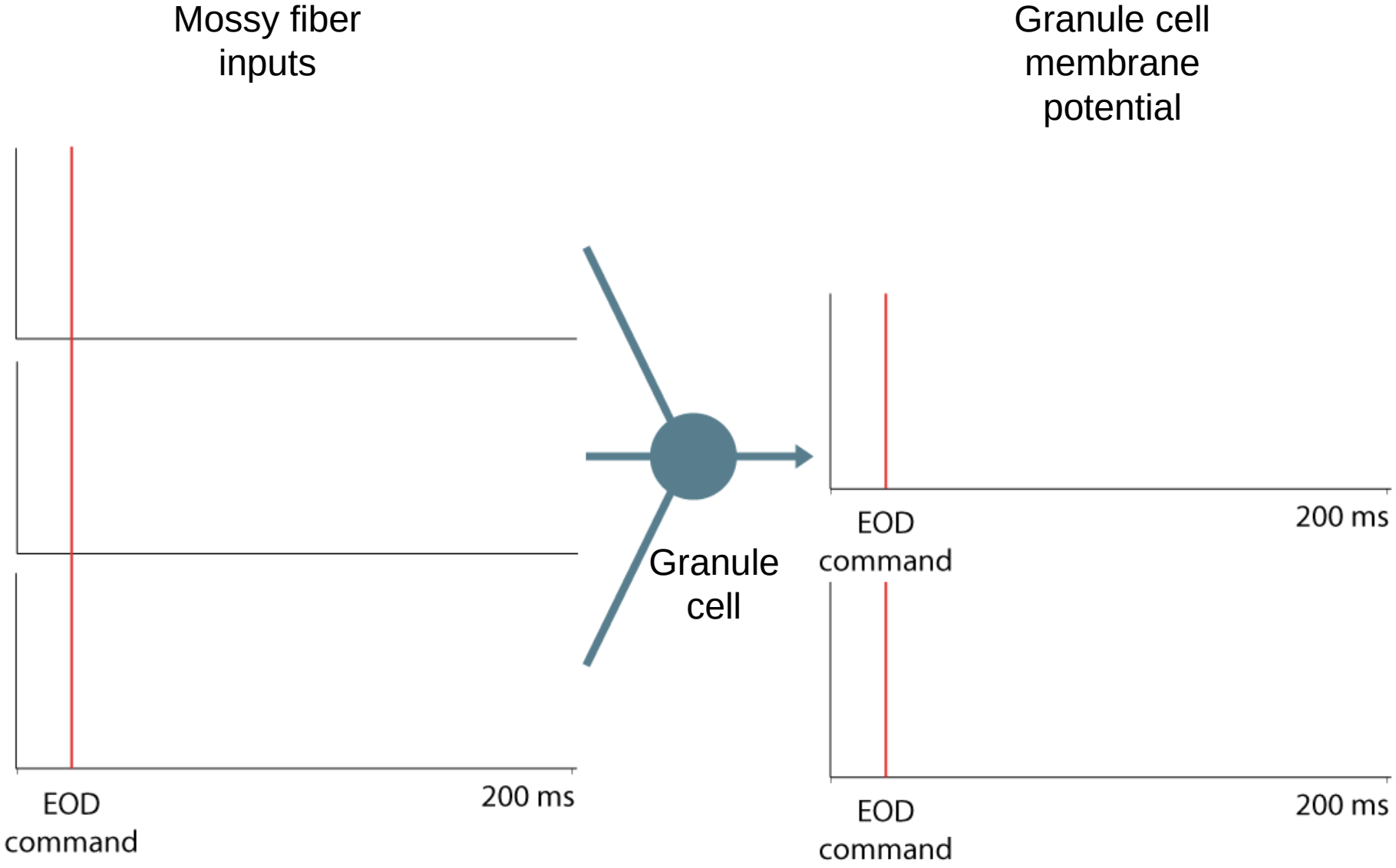


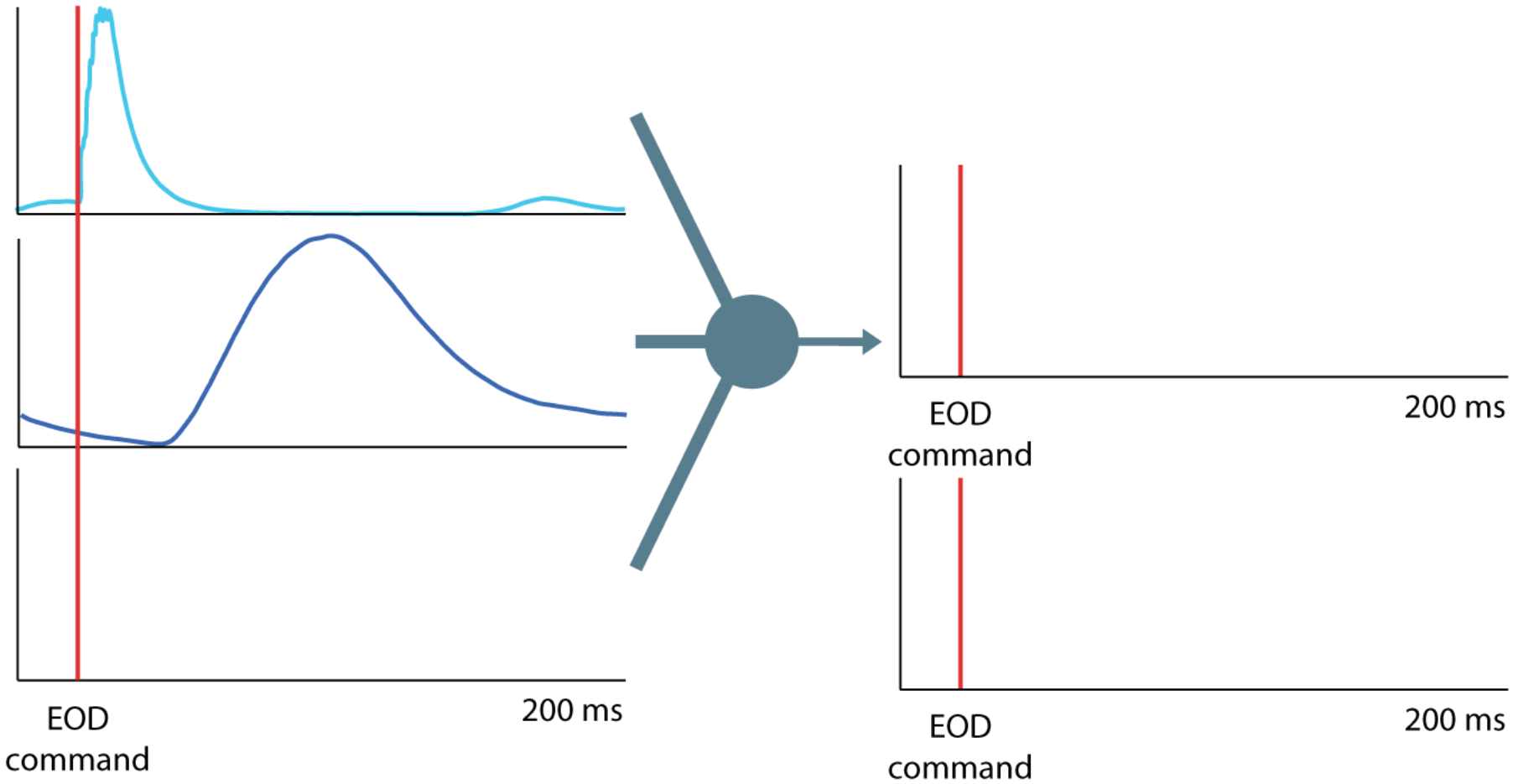
-GC corollary discharge response can be explained by simple summation of a small number of excitatory inputs.

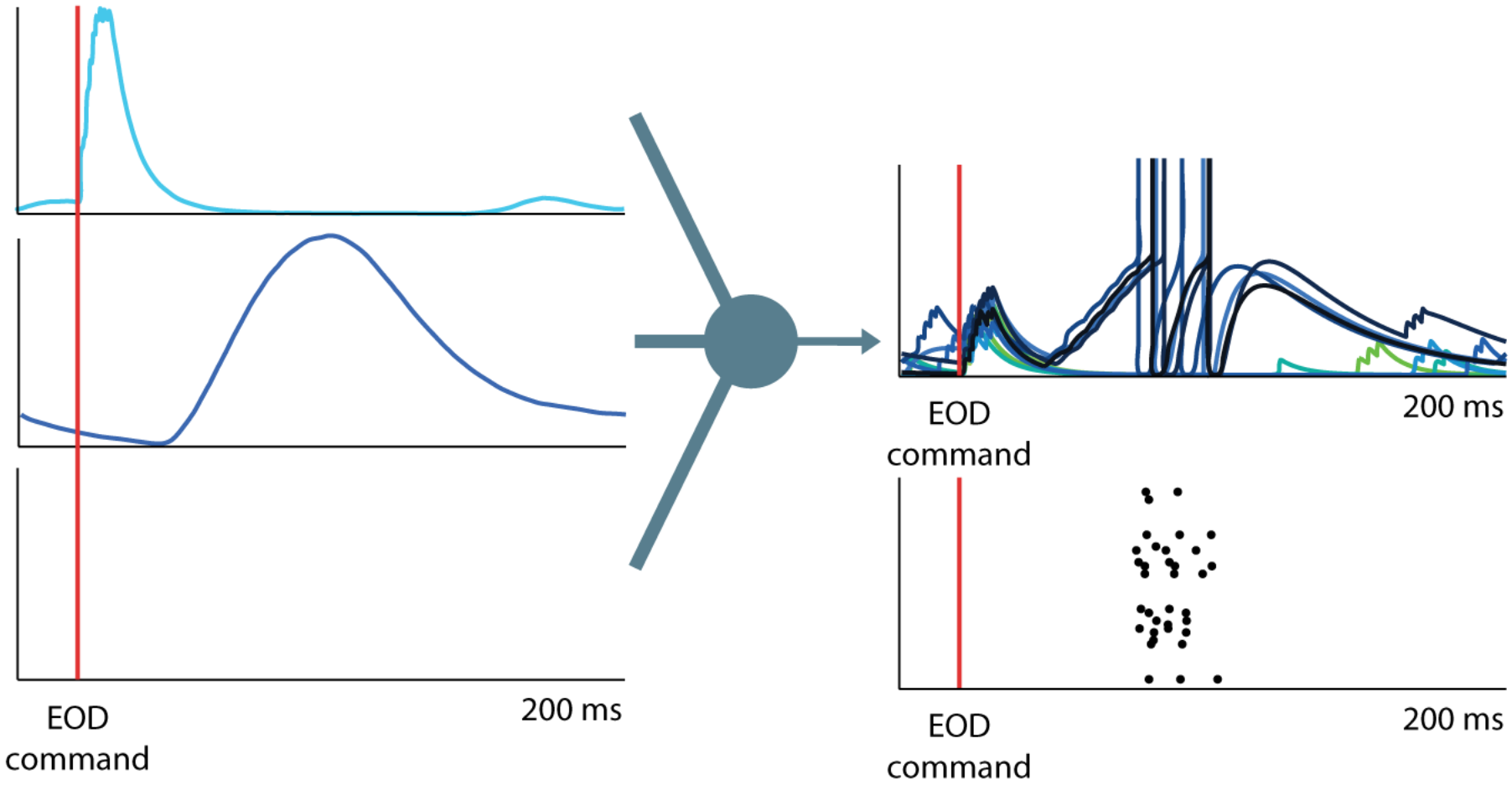
-Proportions of different functional classes of mossy fiber and UBC inputs.

-Different functional classes appear to be mixed randomly.

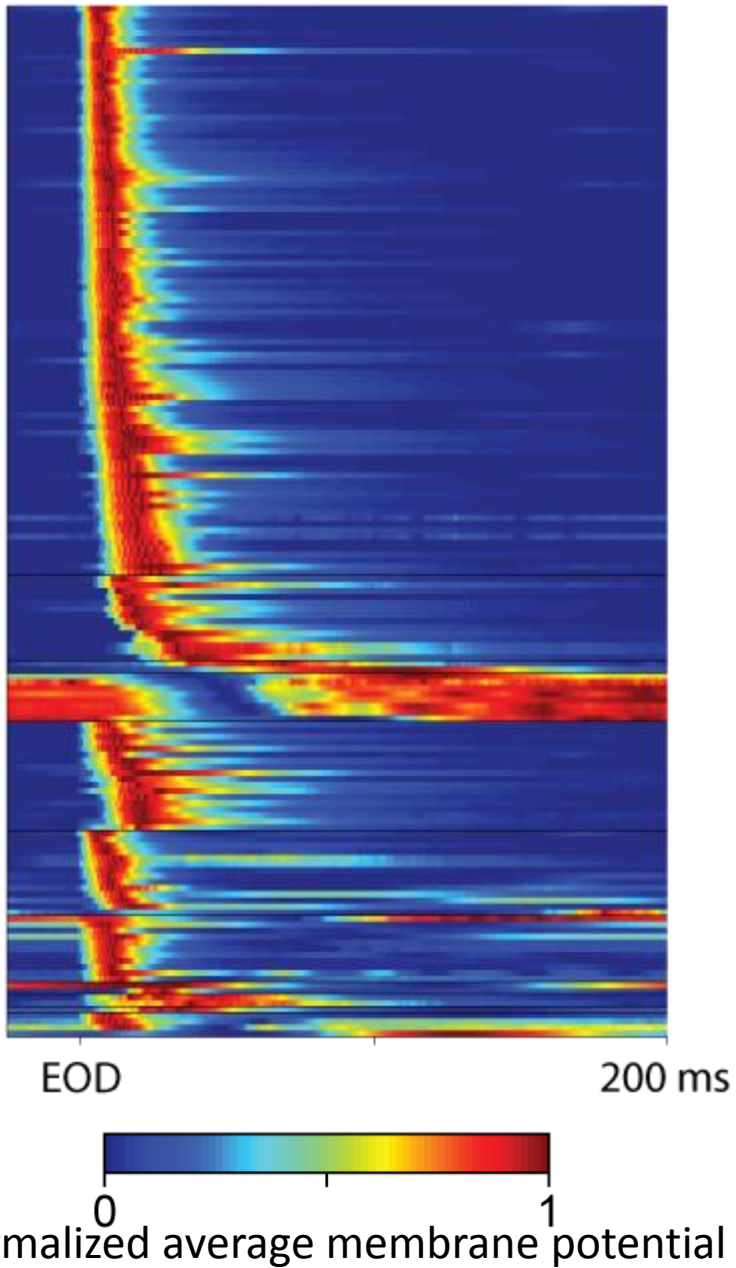



Mossy fiber inputs
Granule cell membrane potential
EOD command
200 ms
Granule cell
EOD command
200 ms
EOD command
200 ms


EOD
command
200 ms
EOD
command
200 ms
EOD
command
200 ms

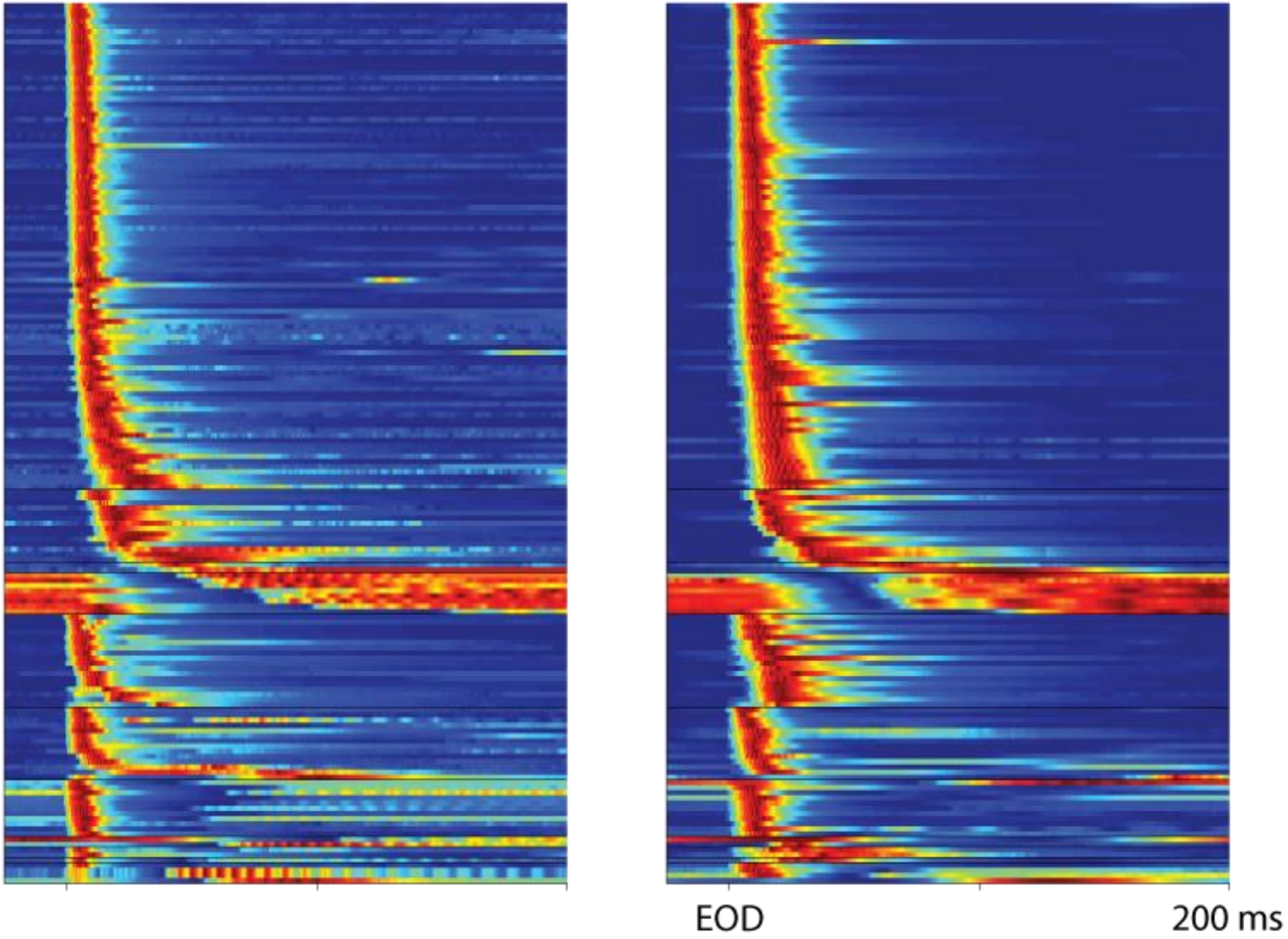

EOD
command
200 ms
EOD
command
200 ms
EOD
command
200 ms

Sample synthetic granule cells

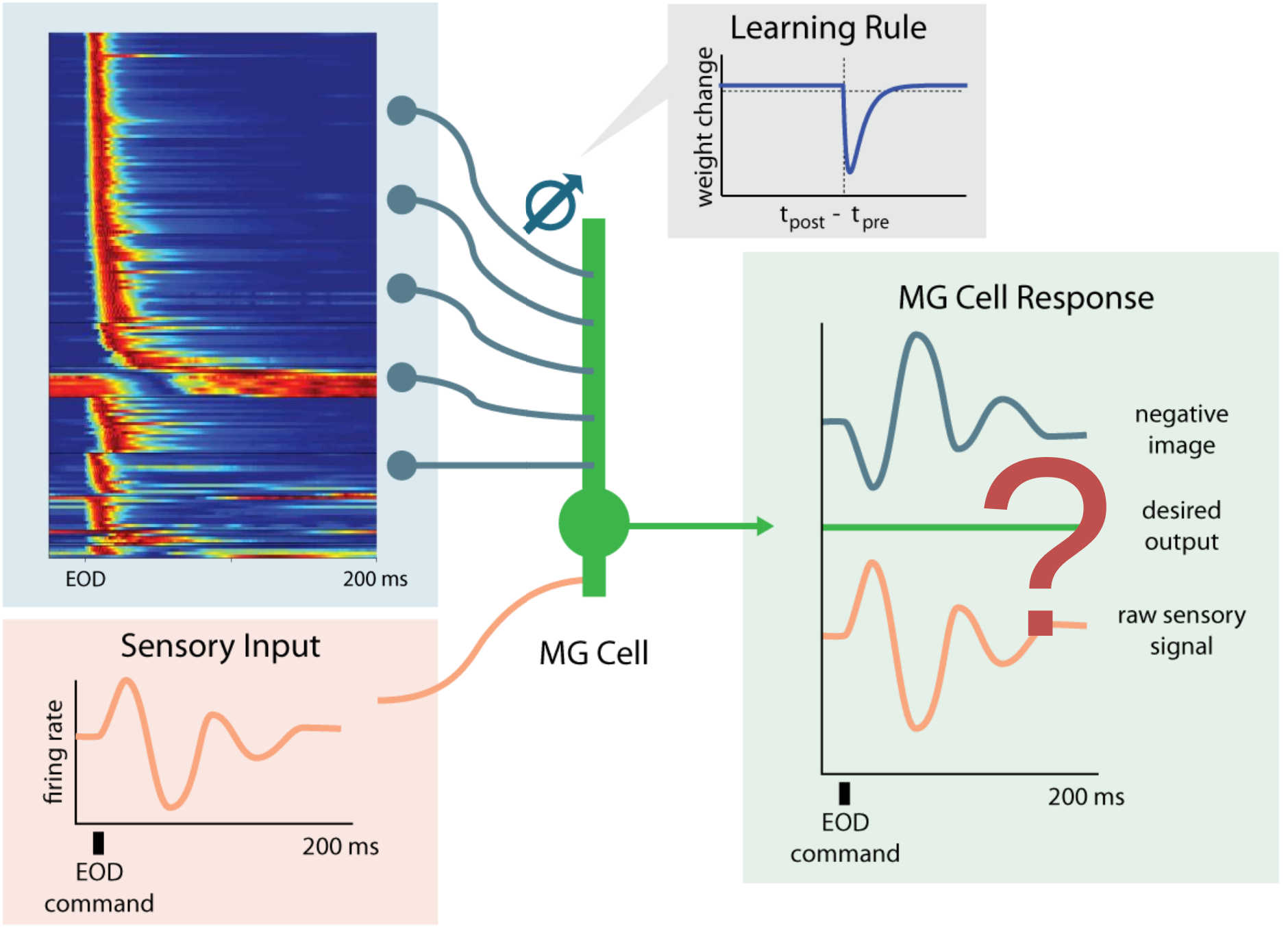


Recorded granule cells

Sample synthetic granule cells

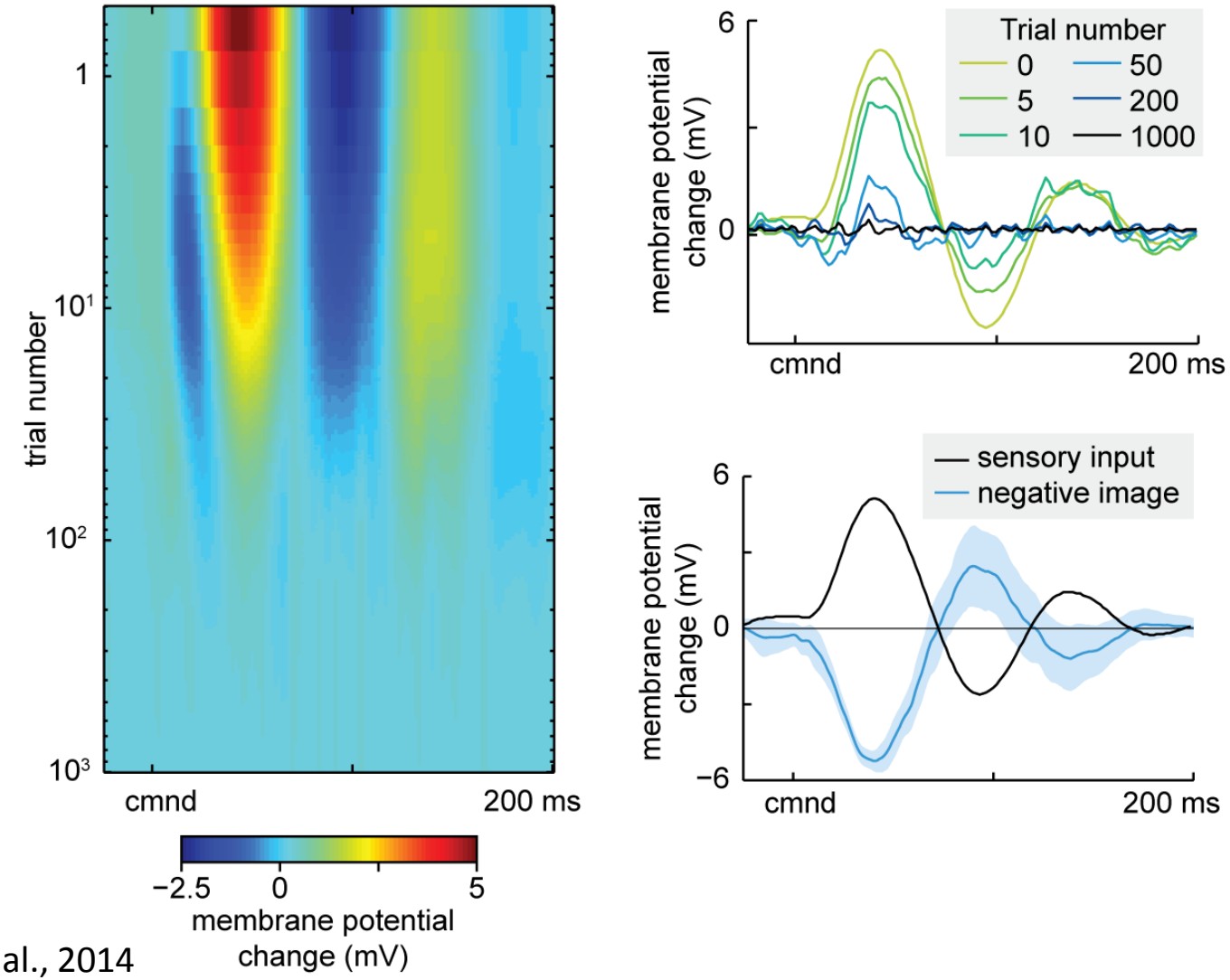


Kennedy et al., 2014



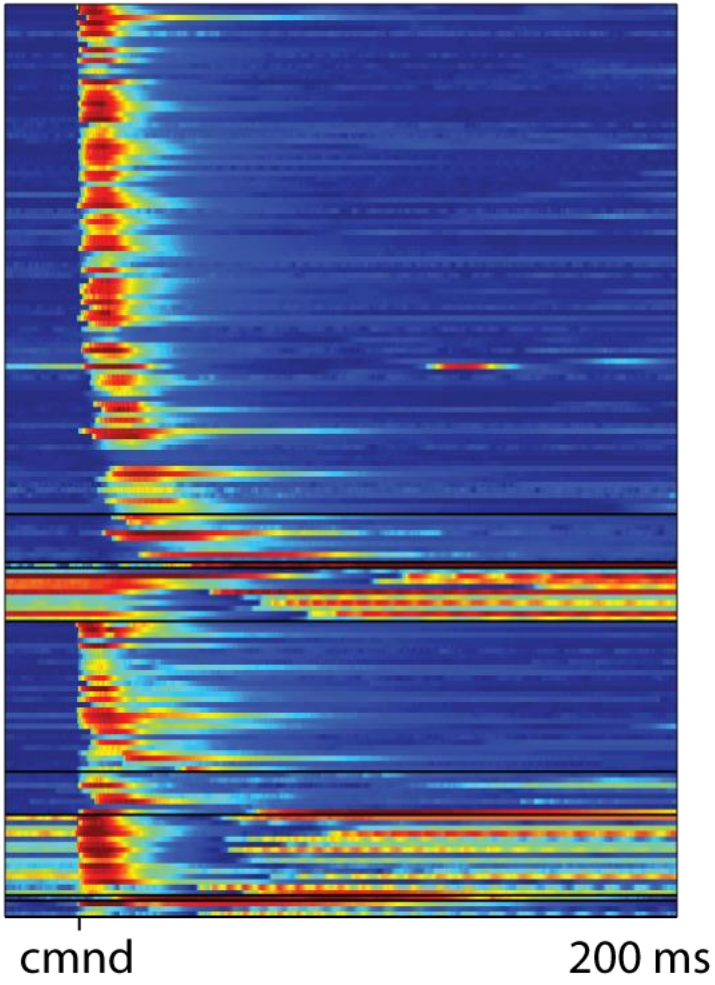
after *Roberts and Bell* (2000)

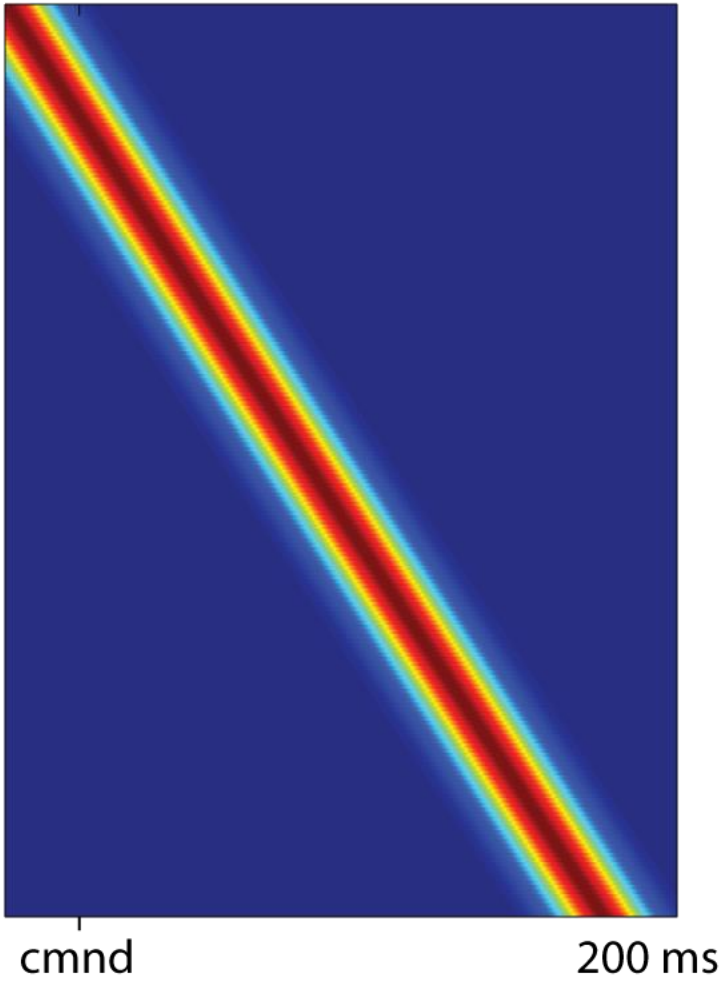
Granule cells provide a sufficient temporal basis for negative image formation and sensory cancellation



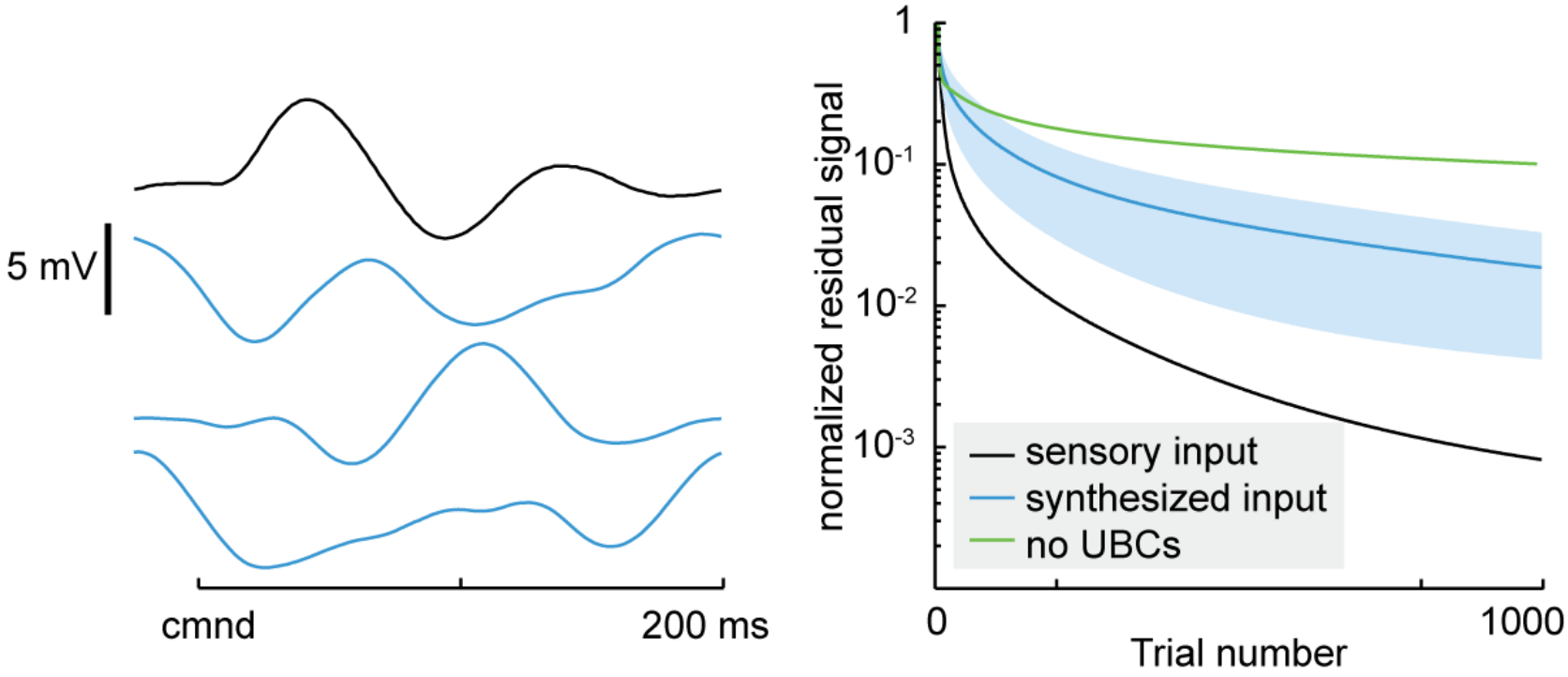
Kennedy et al., 2014

Why this basis?

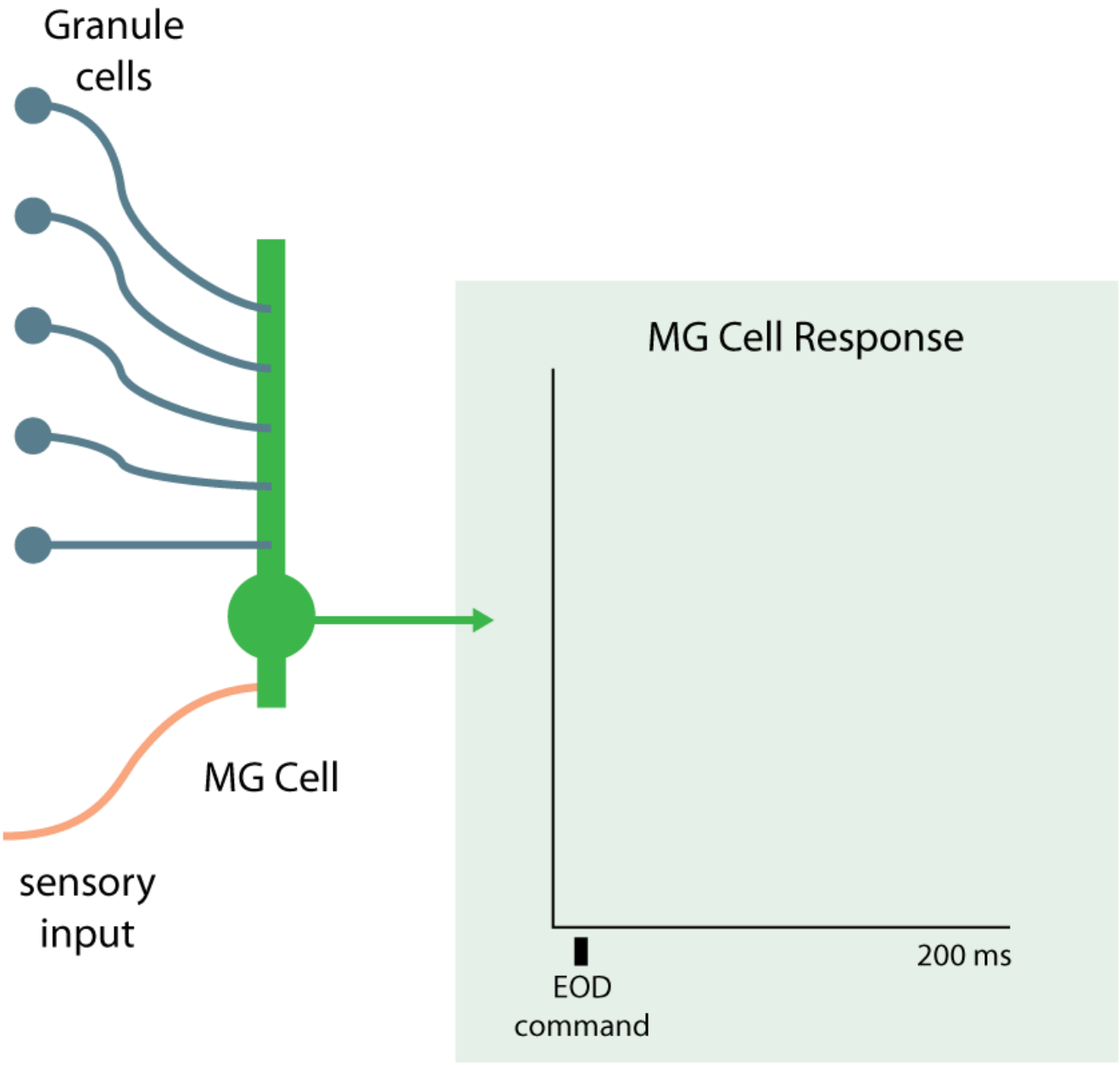


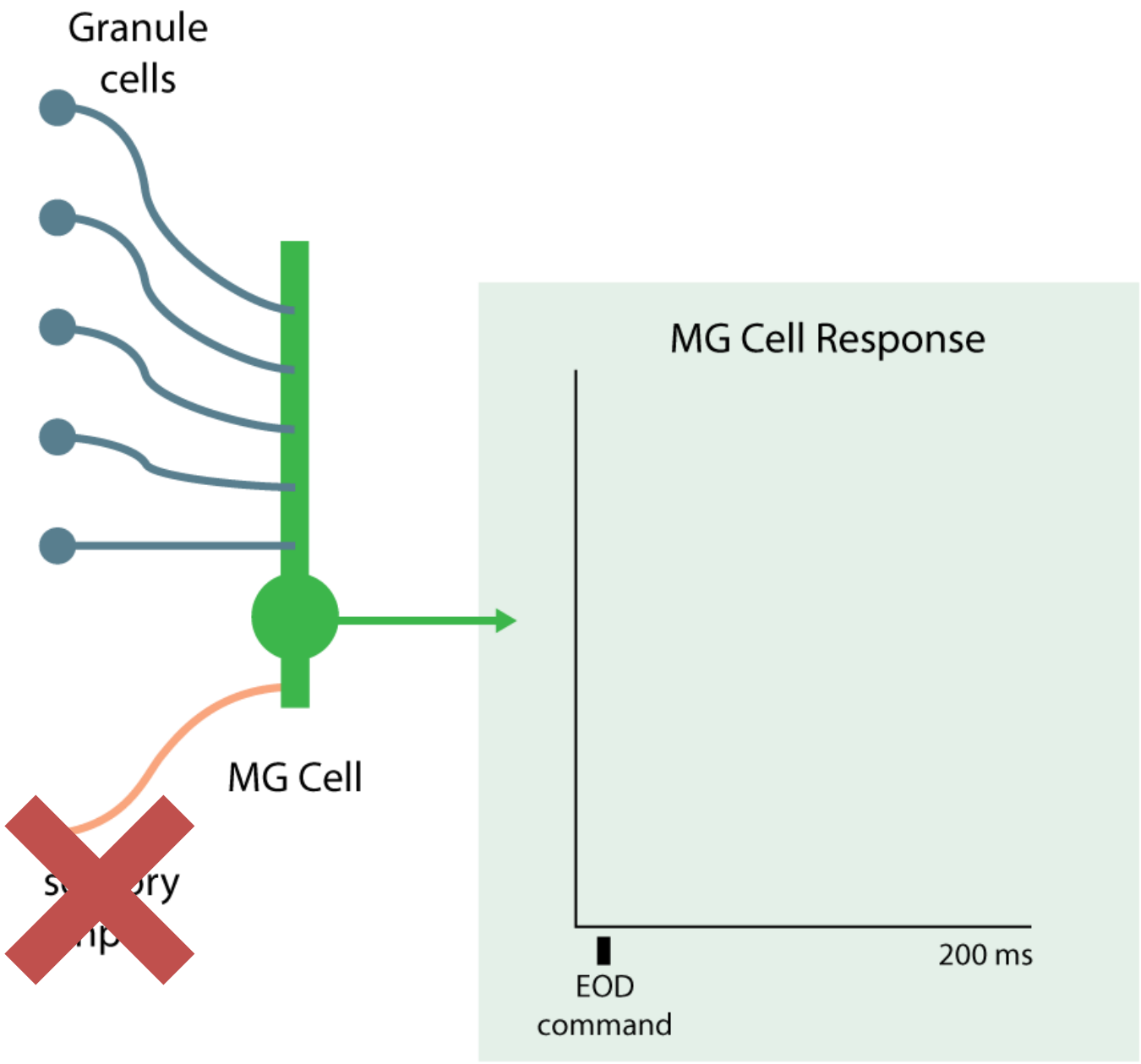


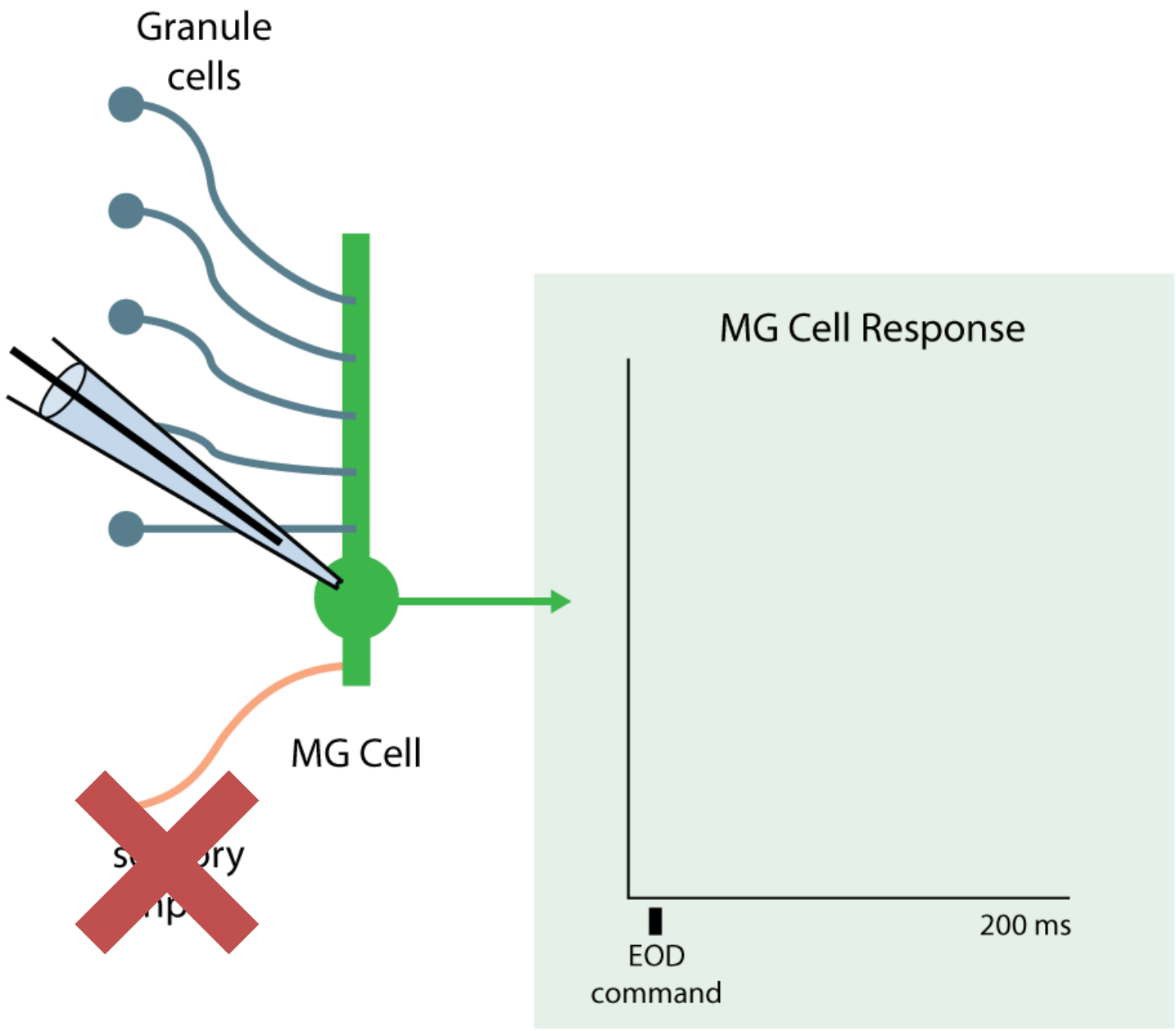
Temporal structure of GC corollary discharge responses is matched to self-generated sensory signals

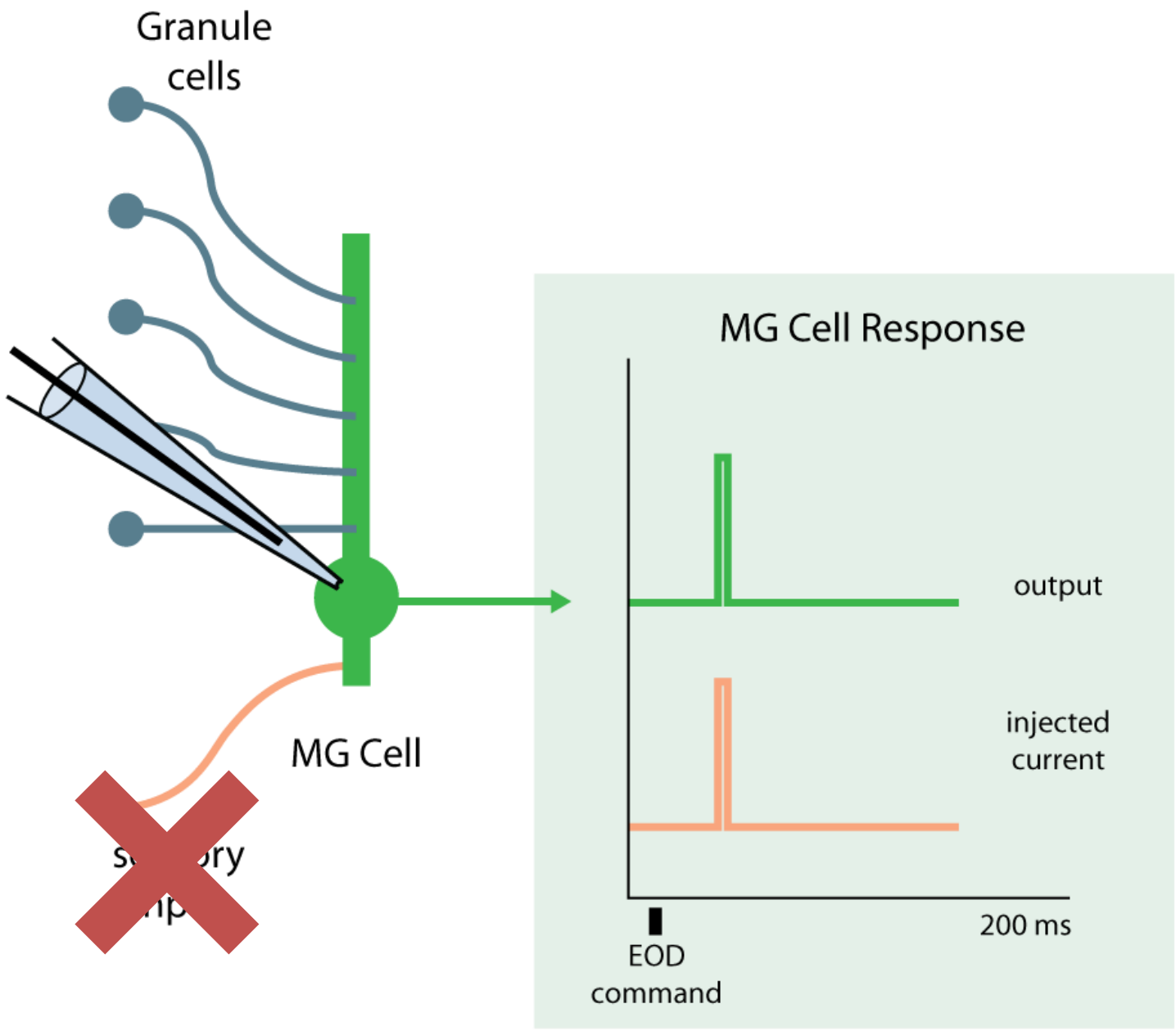


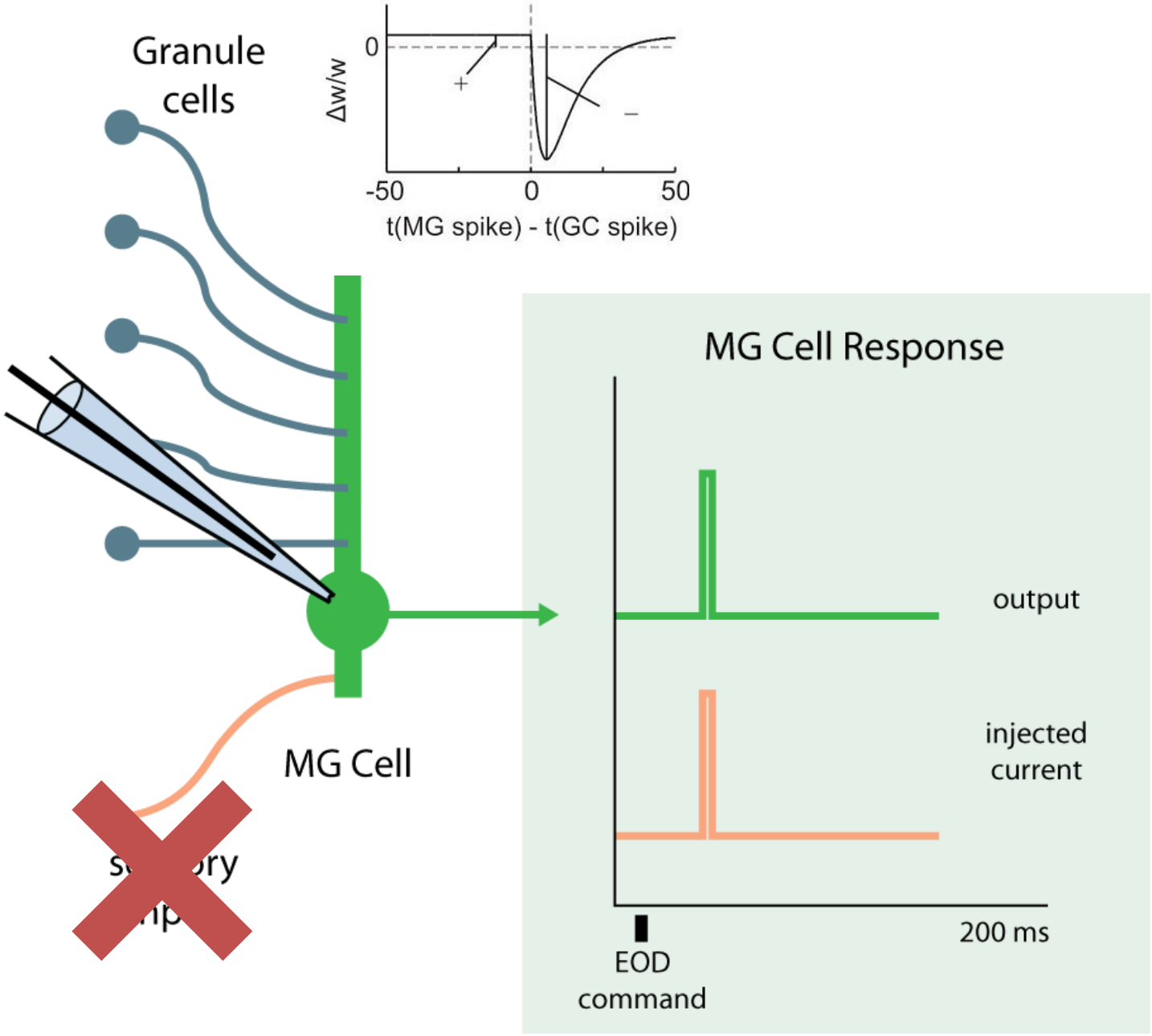
Kennedy et al., 2014

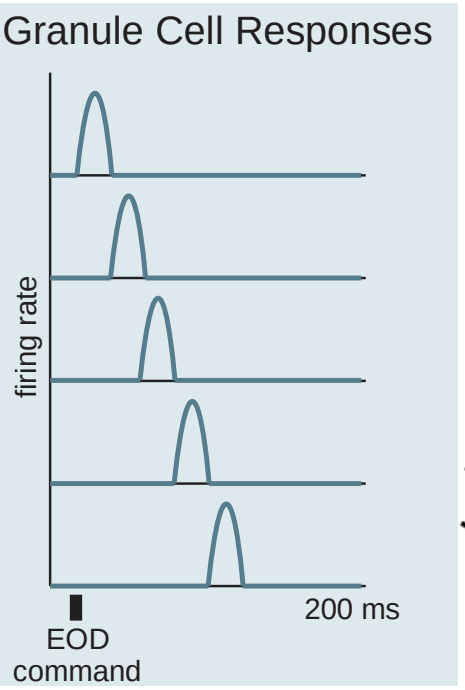

Granule
cells
MG Cell
sensory
input
MG Cell Response
200 ms
EOD
command

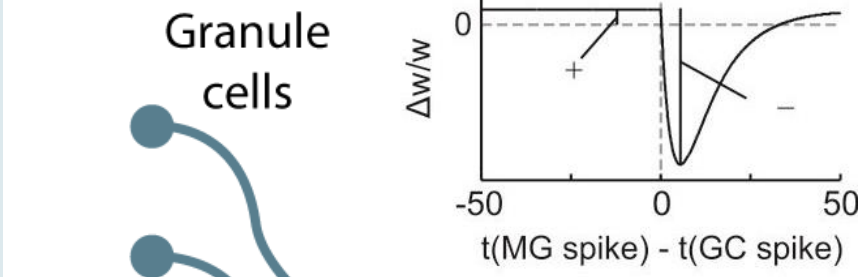

Granule
cells
MG Cell
MG Cell Response
200 ms
EOD
command

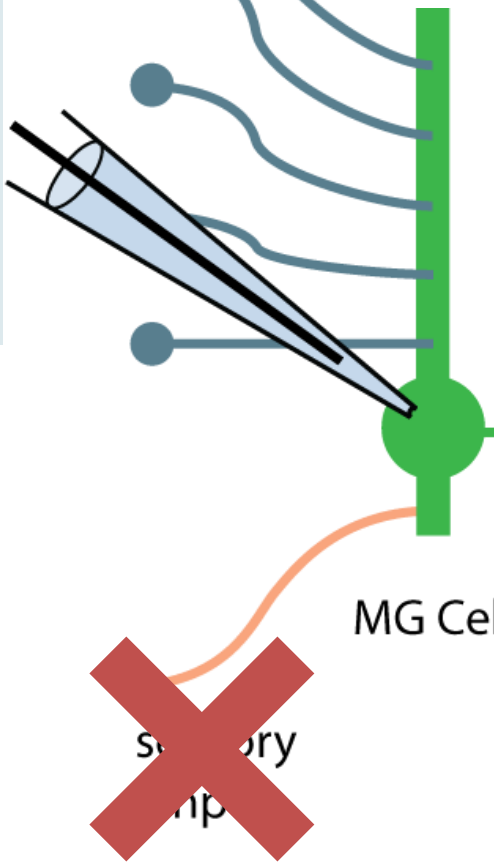

Granule
cells
MG Cell
MG Cell Response
200 ms
EOD
command

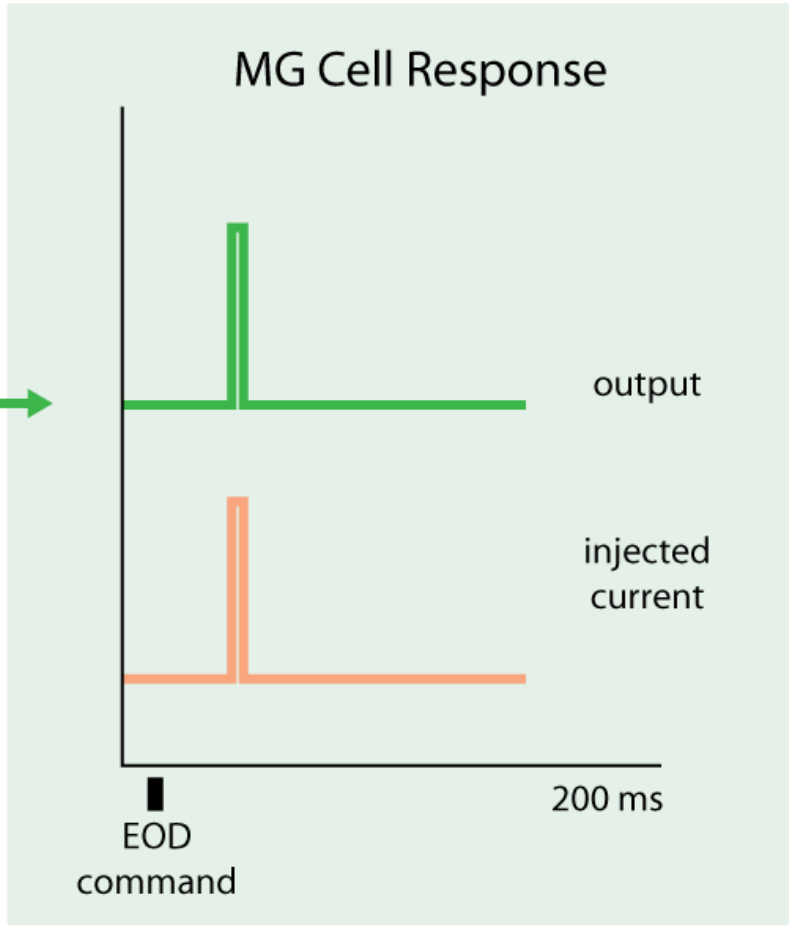

Granule
cells
MG Cell
MG Cell Response
output
injected
current
200 ms
EOD
command

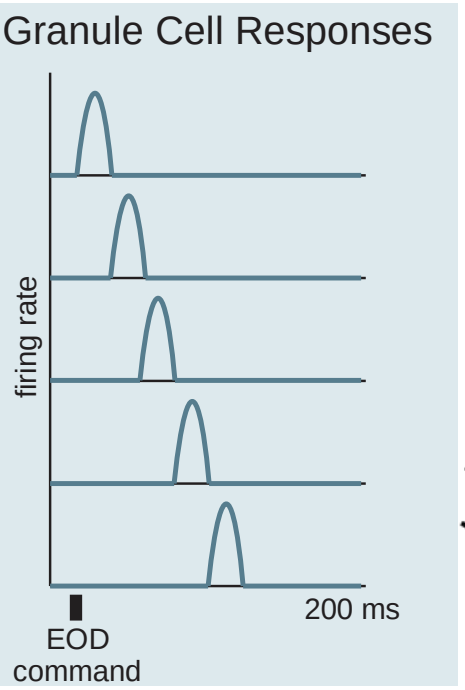

Granule cells
0
Δw/w
+
–
-50
0
50
t(MG spike) - t(GC spike)
MG Cell
MG Cell Response
output
injected current
200 ms
EOD command

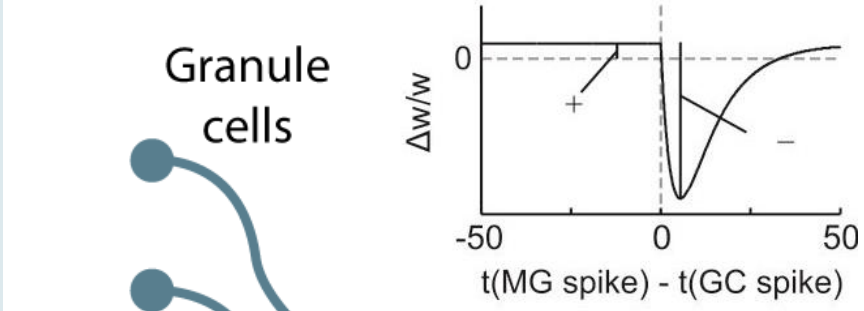

Granule Cell Responses
firing rate
200 ms
EOD
command

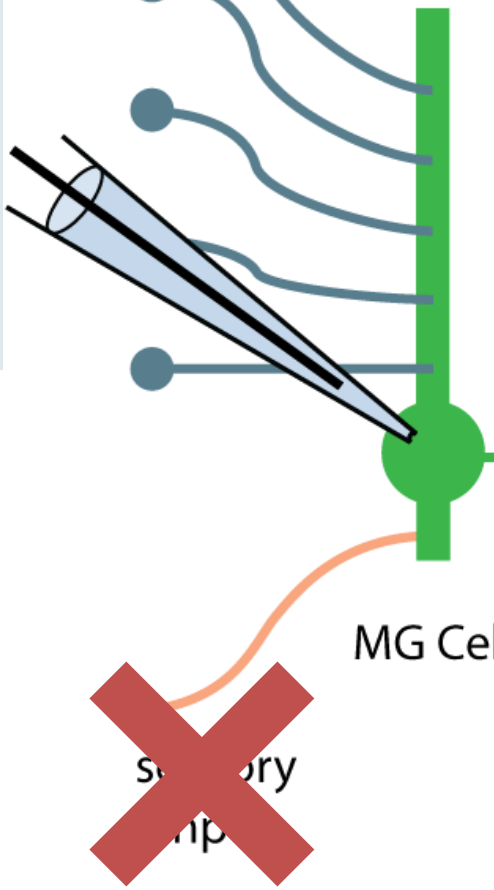

Granule
cells
Δw/w
0
+
–
-50
0
50
t(MG spike) - t(GC spike)

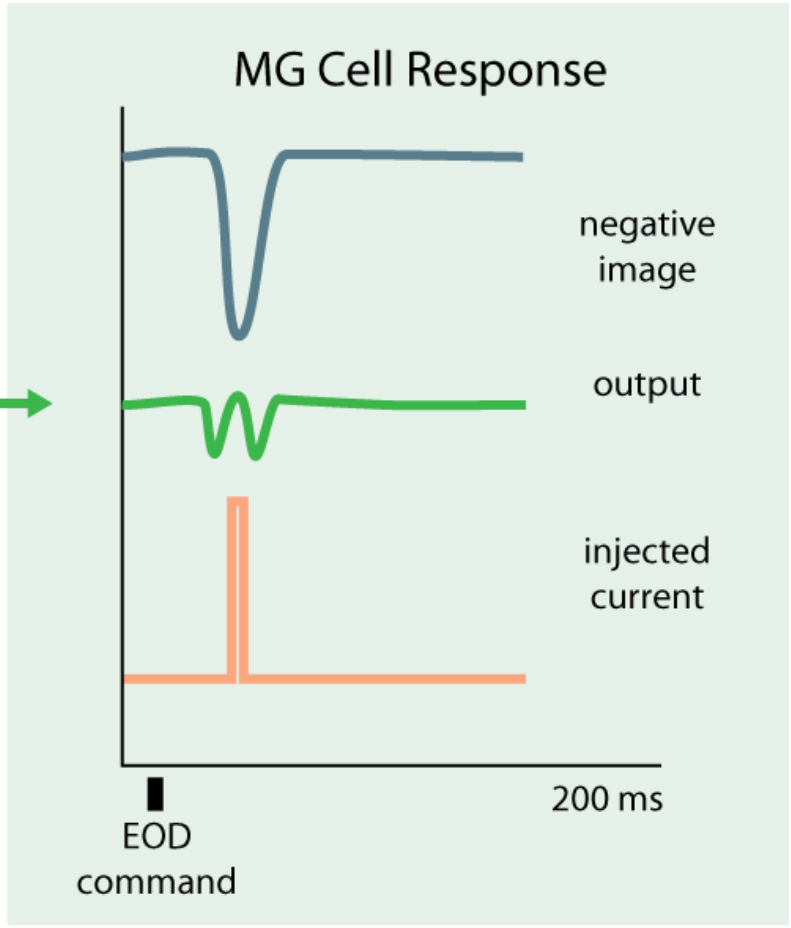

MG Cell

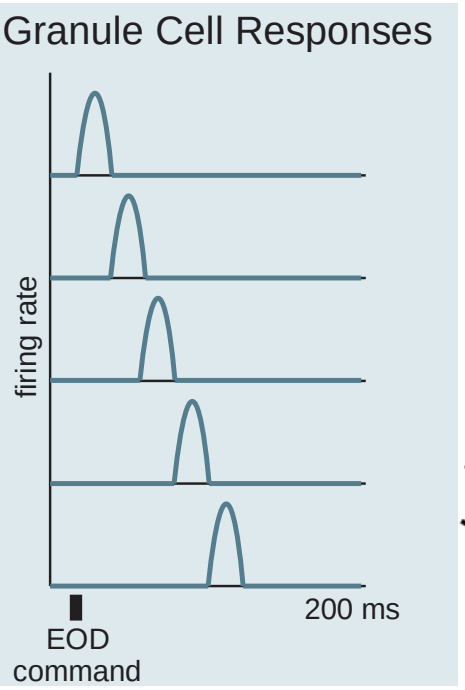

MG Cell Response
output
injected
current
200 ms
EOD
command

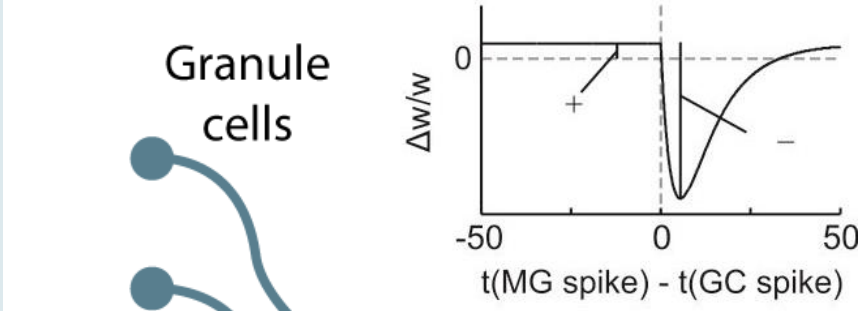

Granule Cell Responses
firing rate
200 ms
EOD
command

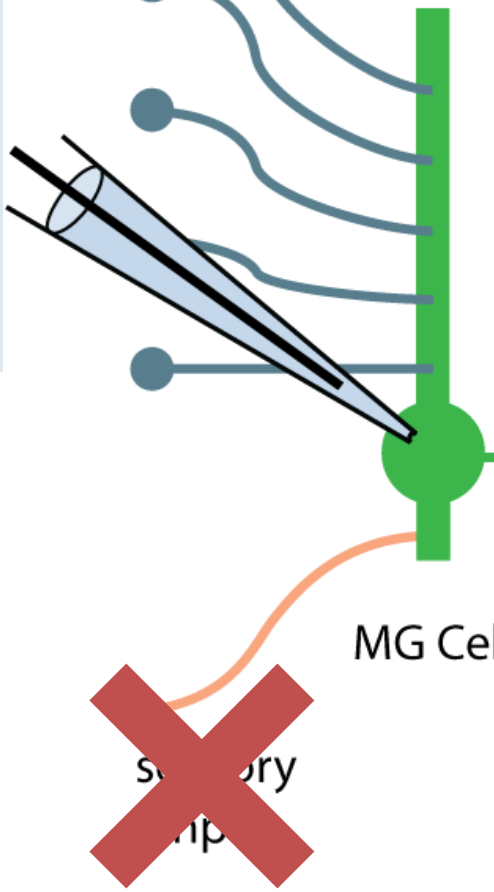

Granule
cells
Δw/w
0
+
–
-50
0
50
t(MG spike) - t(GC spike)

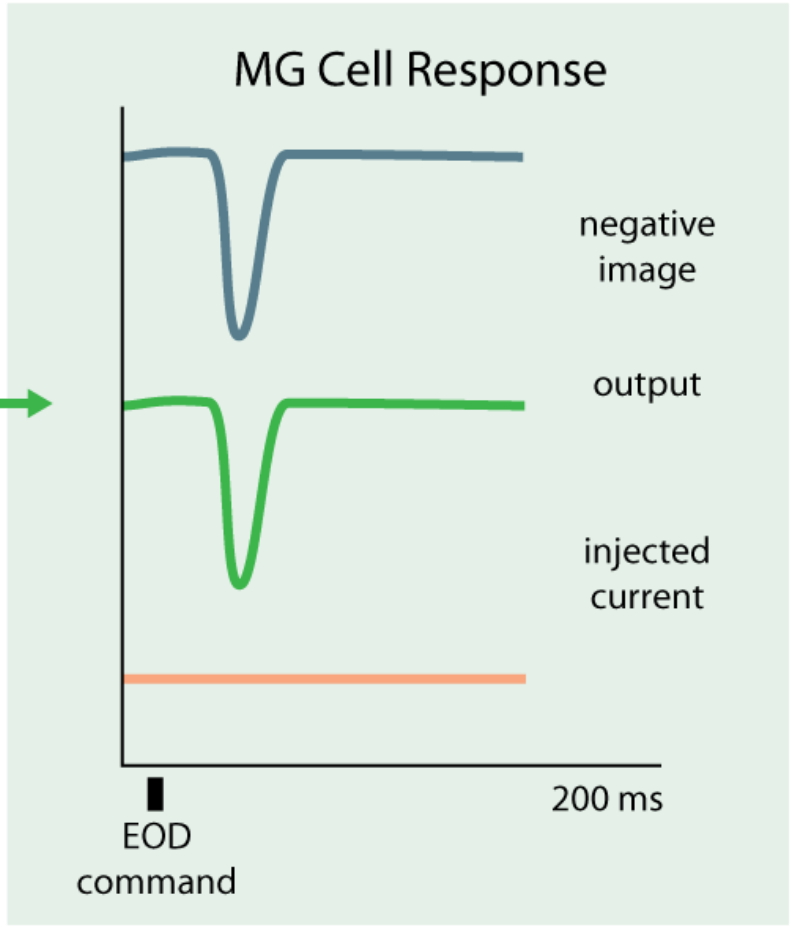

MG Cell

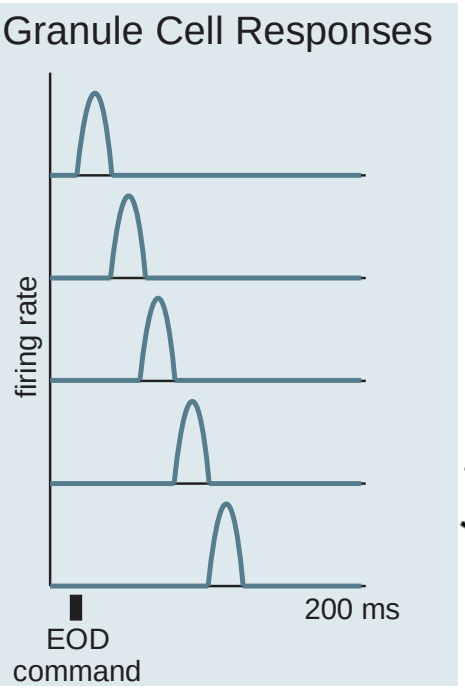

MG Cell Response
negative
image
output
injected
current
200 ms
EOD
command

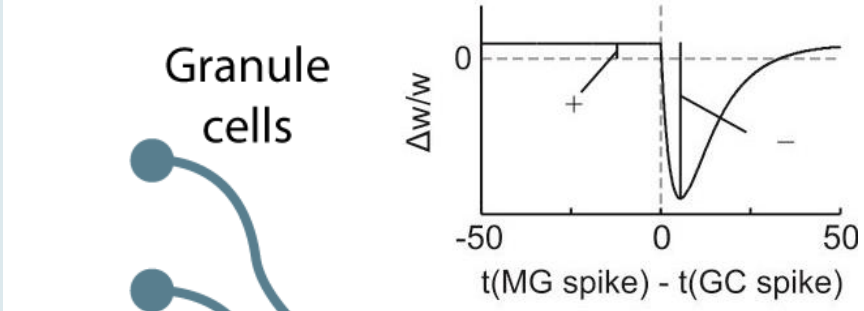

Granule Cell Responses
firing rate
200 ms
EOD
command

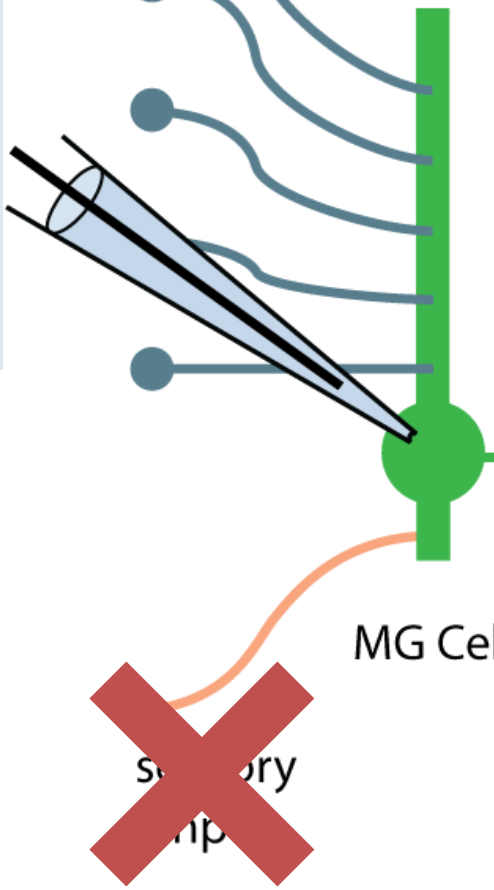

Granule
cells
Δw/w
0
+
–
-50
0
50
t(MG spike) - t(GC spike)

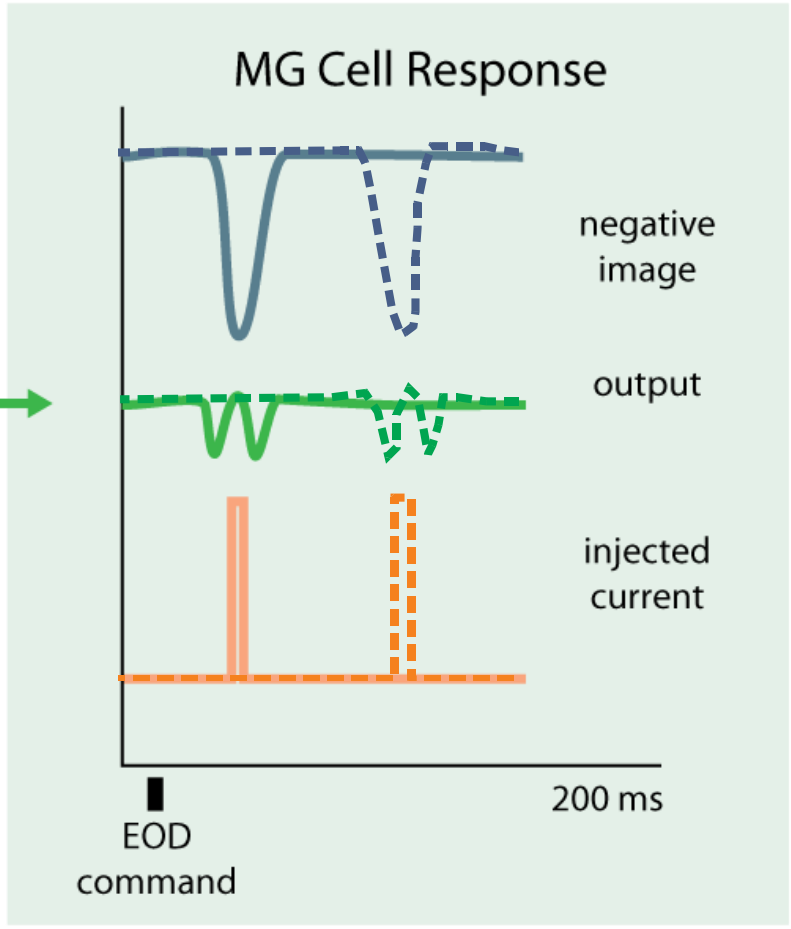

MG Cell

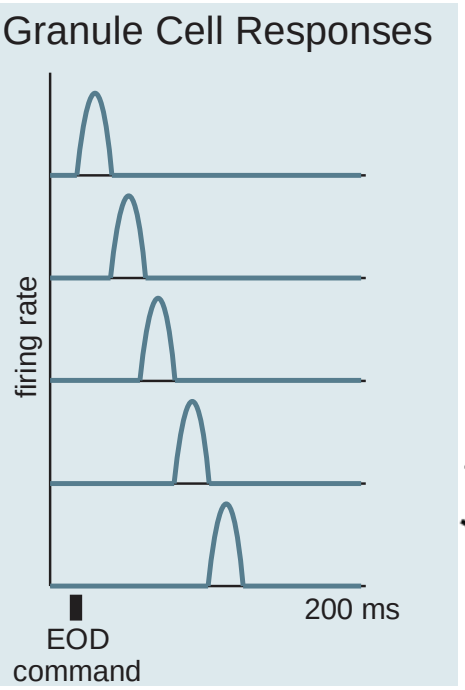

MG Cell Response
negative
image
output
injected
current
200 ms
EOD
command

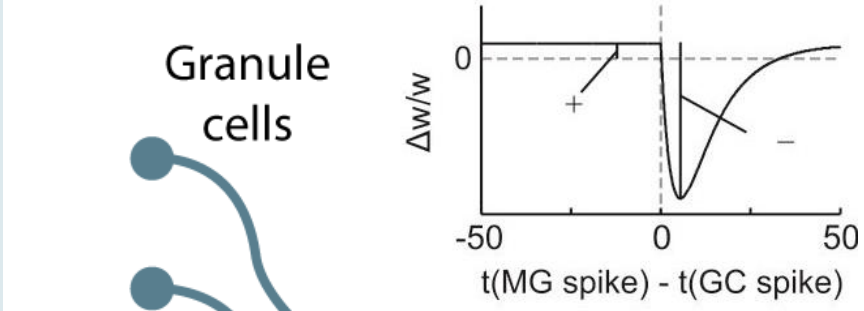

Granule Cell Responses
firing rate
200 ms
EOD
command

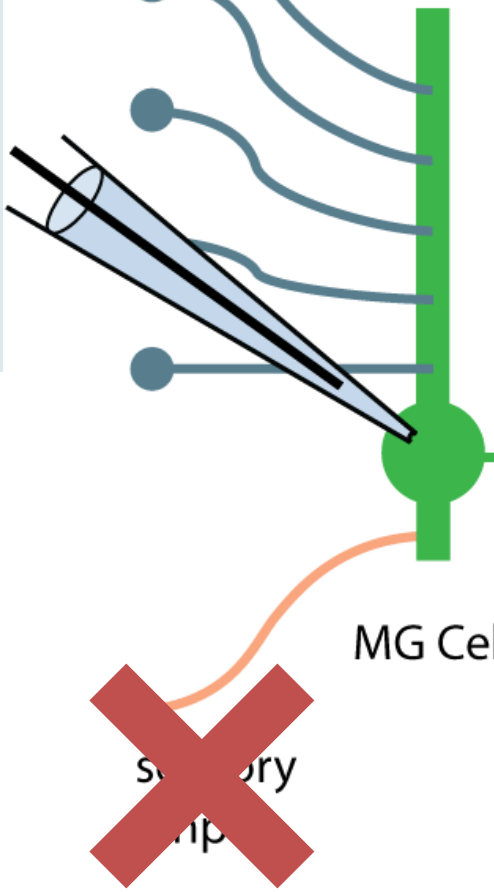

Granule
cells
Δw/w
0
+
–
-50
0
50
t(MG spike) - t(GC spike)

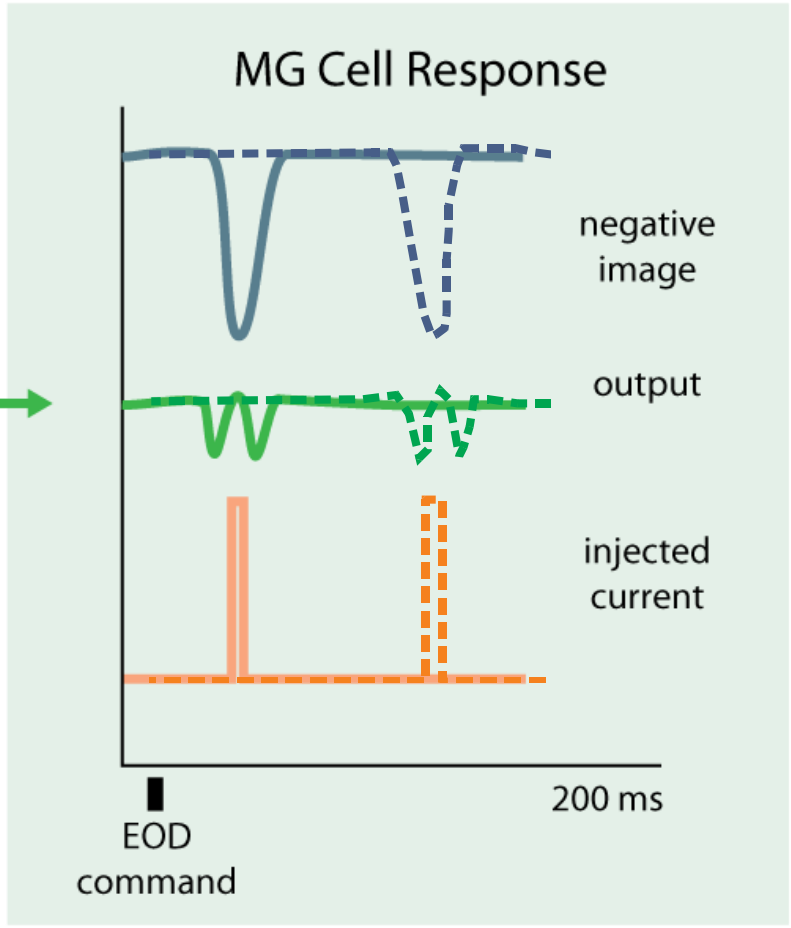

MG Cell

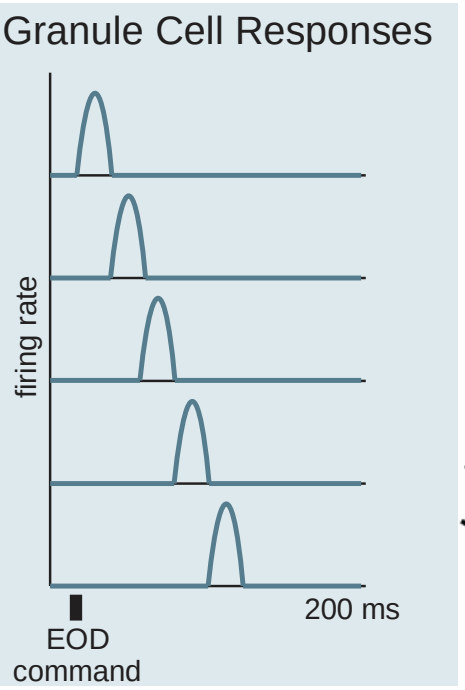

MG Cell Response
negative
image
output
injected
current
200 ms
EOD
command

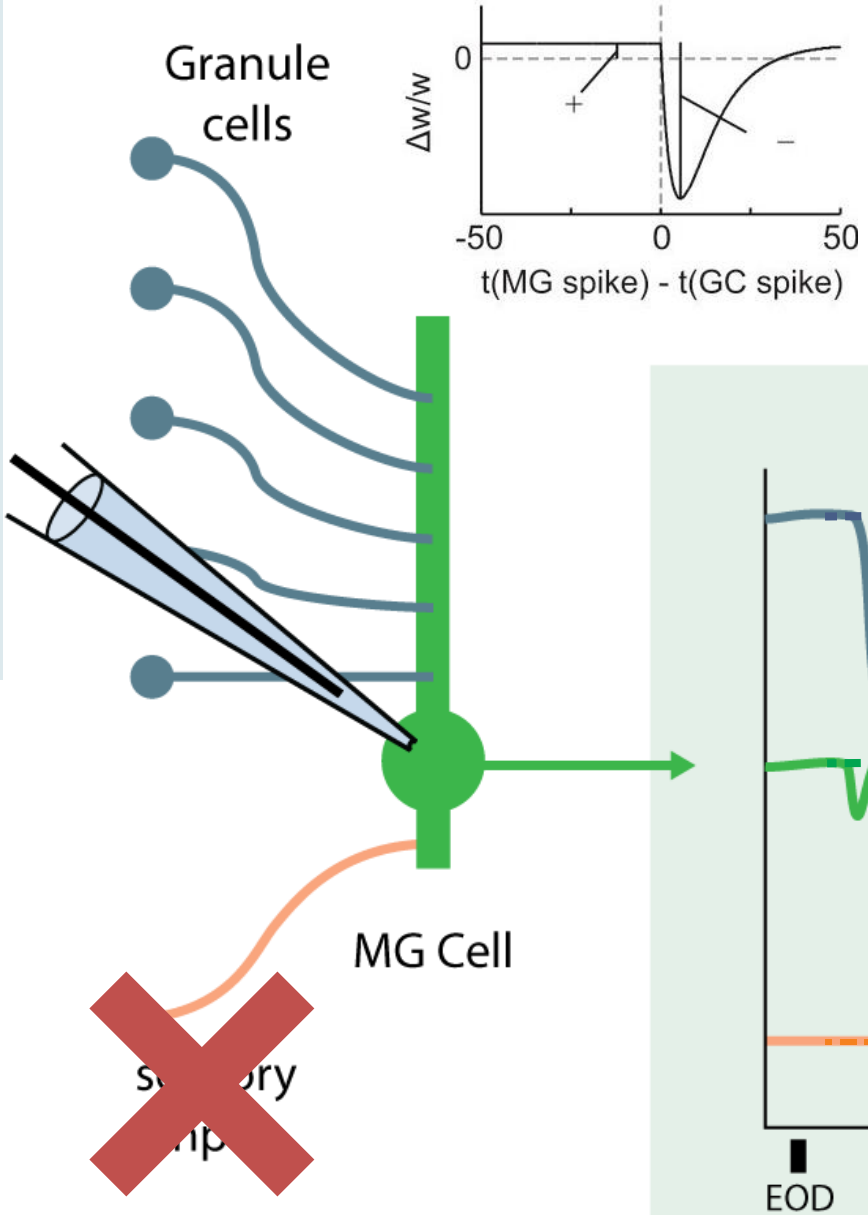

Granule Cell Responses
firing rate
200 ms
EOD
command

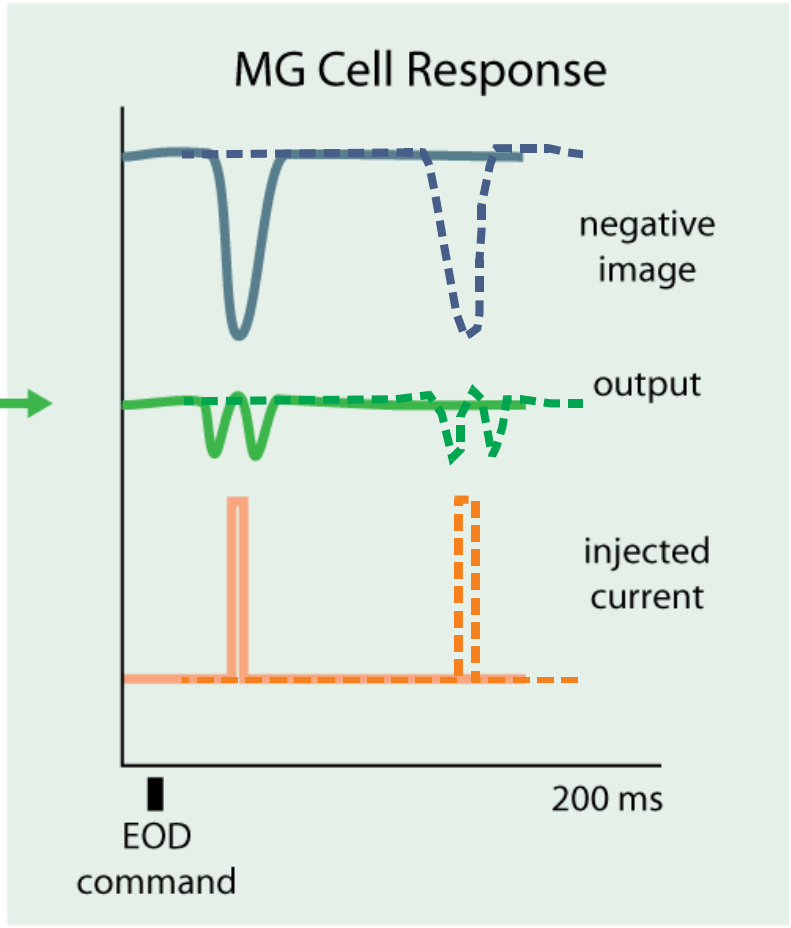

Granule
cells
Δw/w
0
-50
0
50
t(MG spike) - t(GC spike)


MG Cell

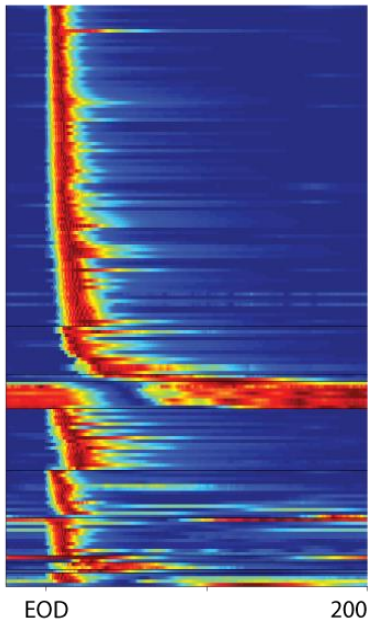

MG Cell Response
negative
image
output
injected
current
200 ms
EOD
command

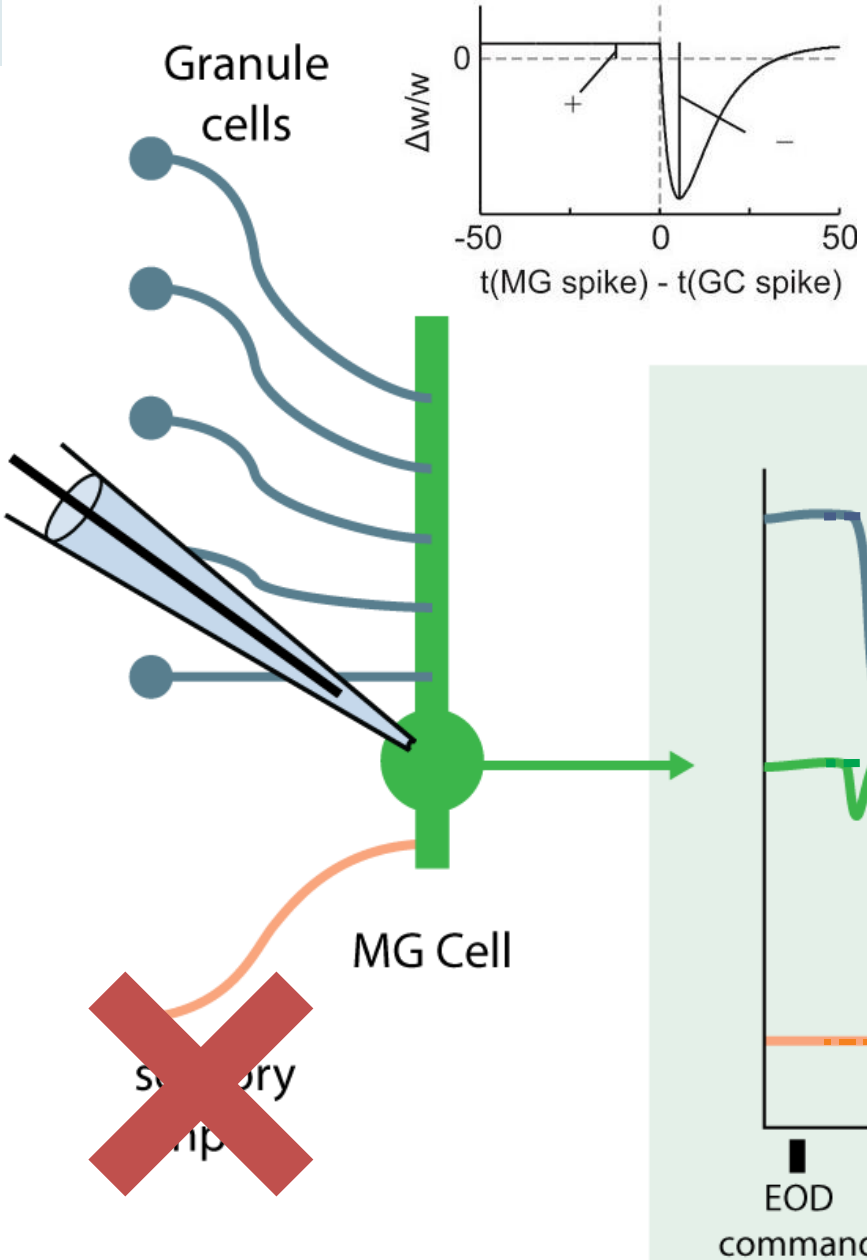

Granule Cell Responses
firing rate
200 ms
EOD
command

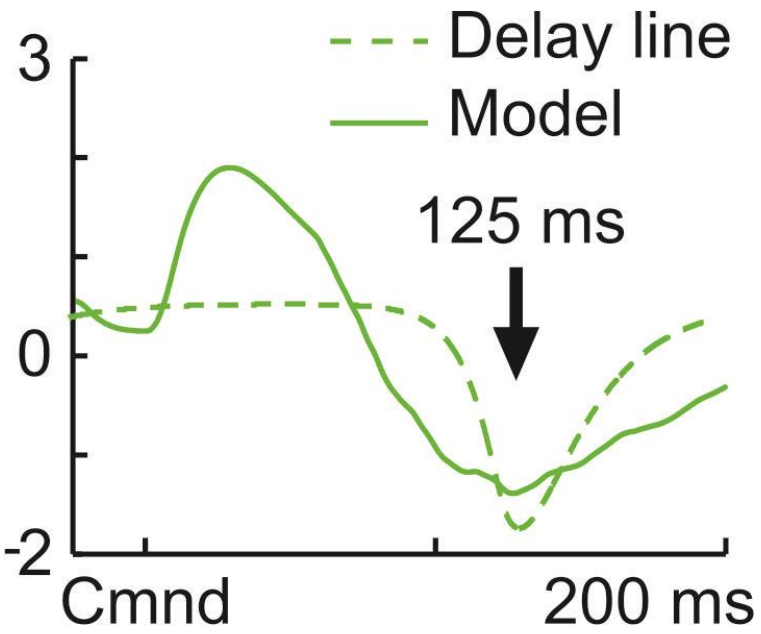

Granule
cells
0
Δw/w
+
–
-50
0
50
t(MG spike) - t(GC spike)
MG Cell


MG Cell Response
negative
image
output
injected
current
200 ms
EOD
command

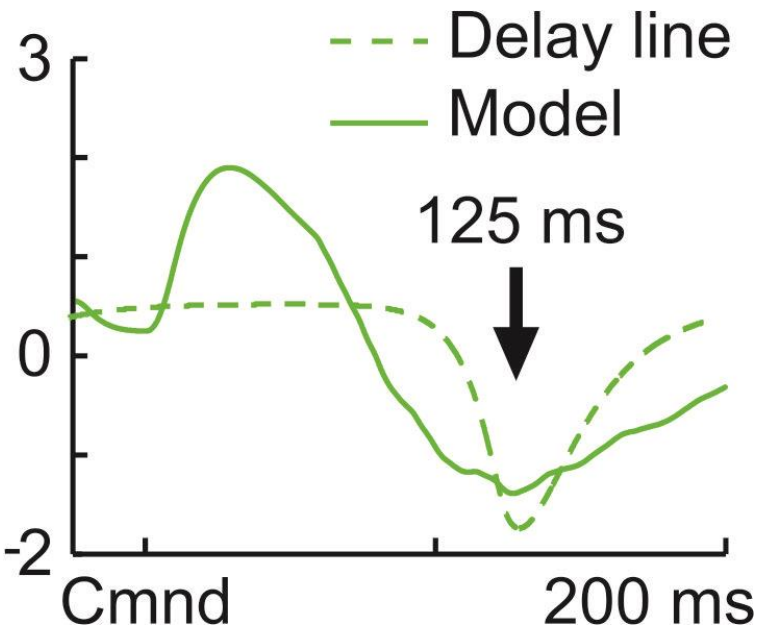
Granule Cell Responses

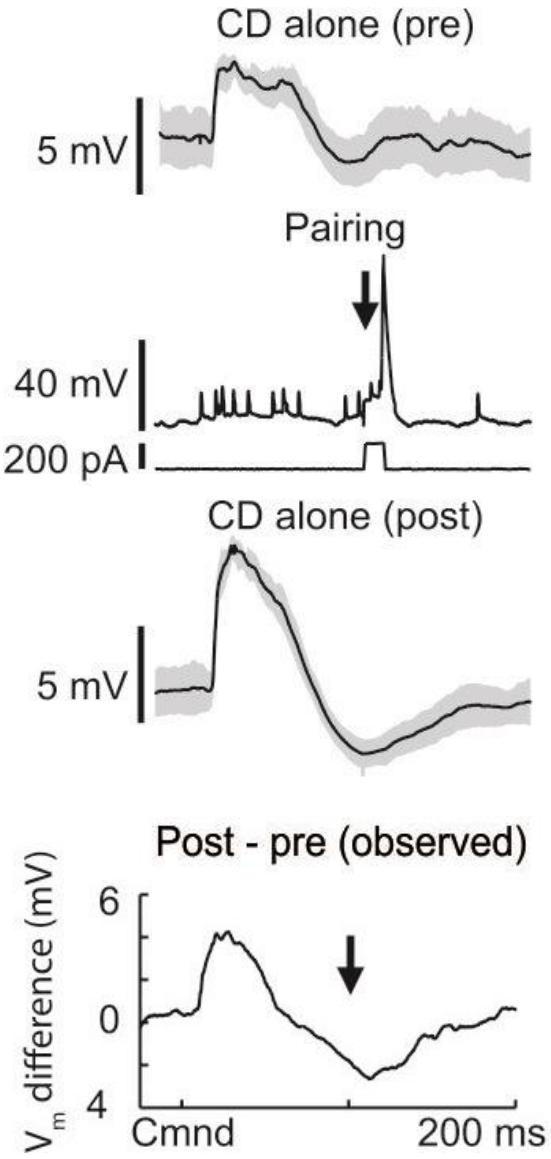






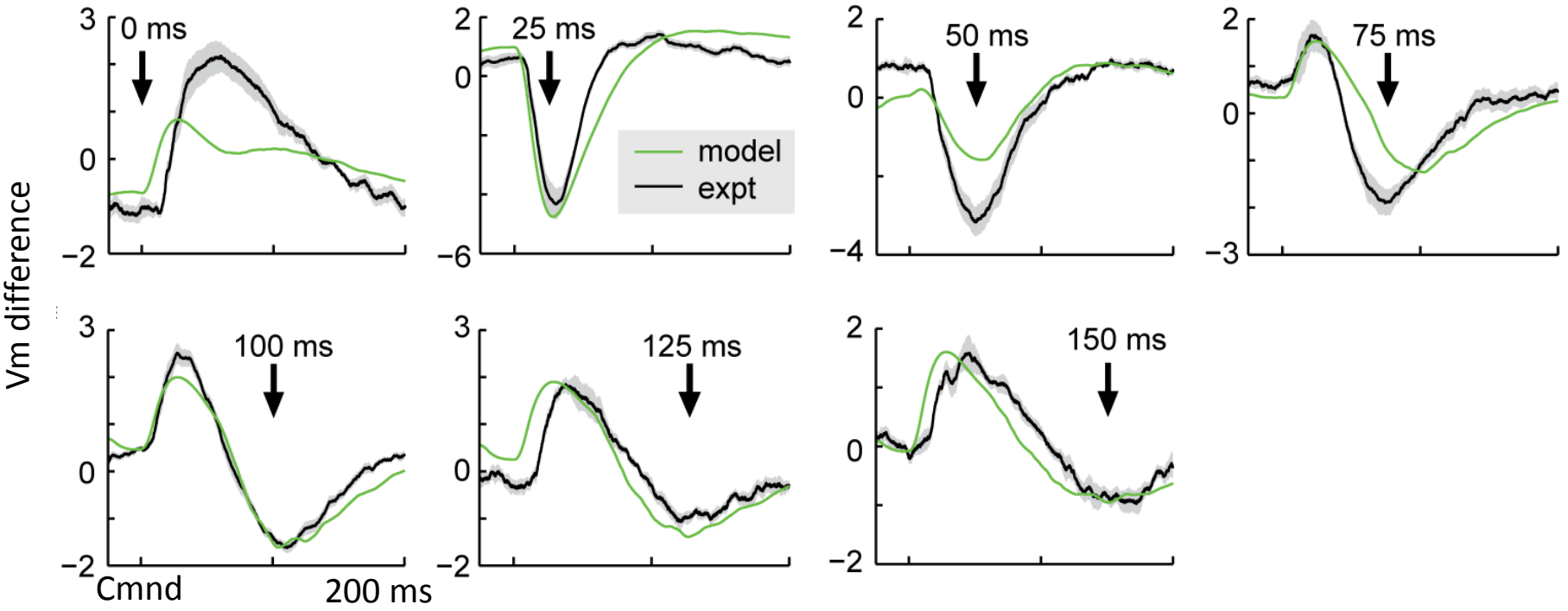
Kennedy et al., 2014



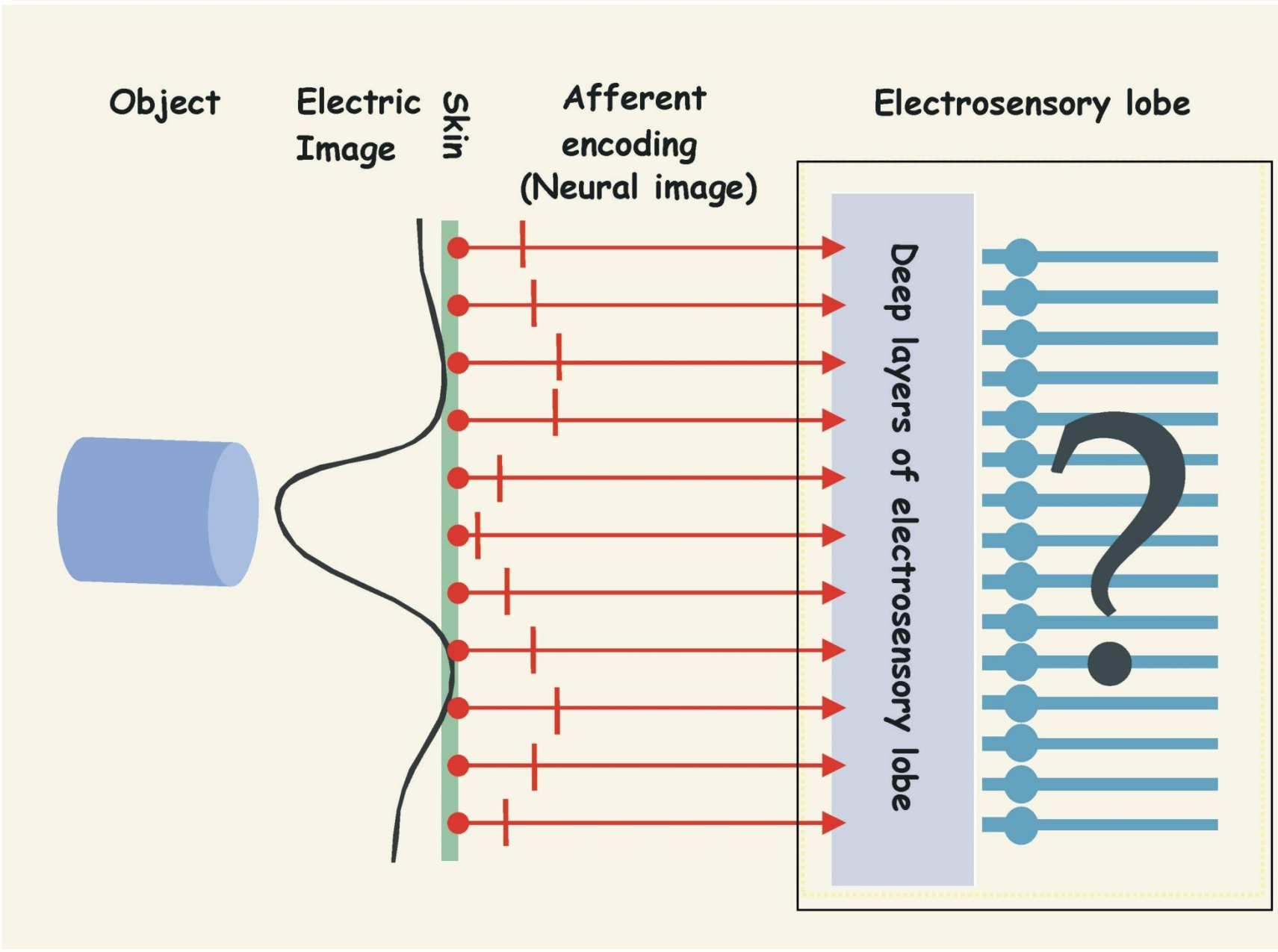


Kennedy et al., 2014

Temporal structure of GC corollary discharge responses accounts for unusual features of negative images

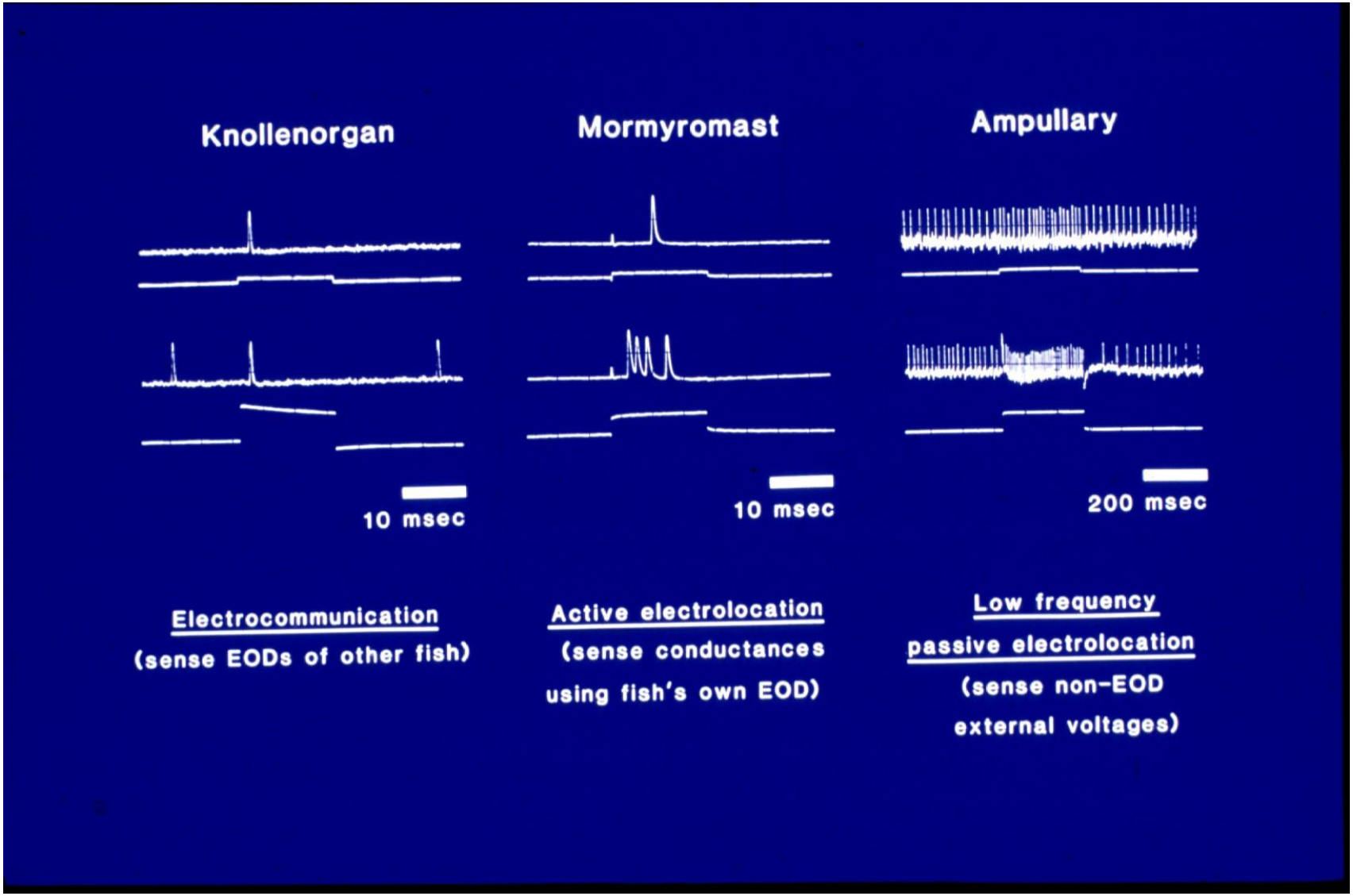


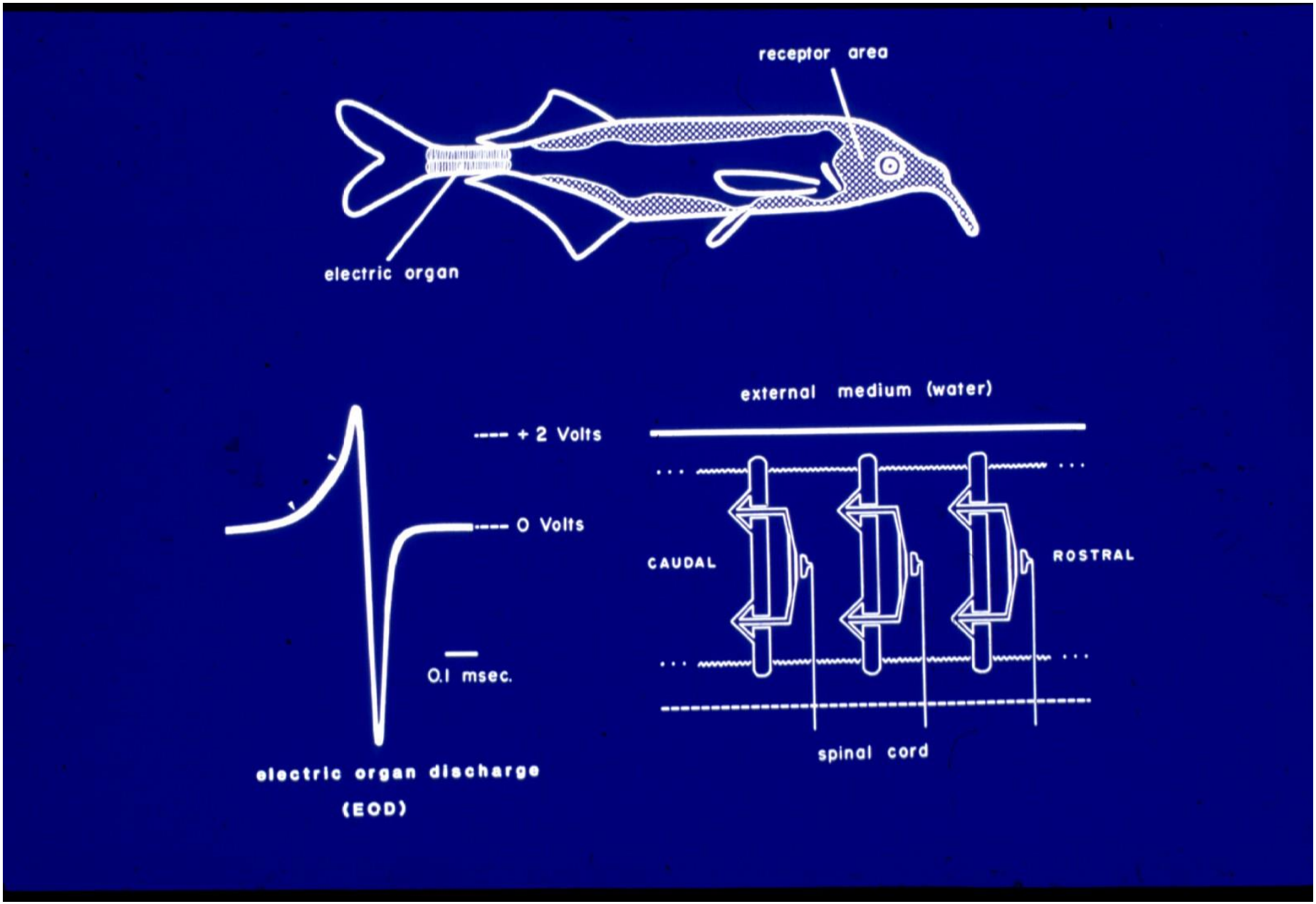
Kennedy et al., 2014



From Lionel Gomez

Three Types of Electroreceptors in Mormyrid Fish




receptor area
electric organ
+ 2 Volts
0 Volts
0.1 msec.
electric organ discharge
(EOD)
external medium (water)
CAUDAL
ROSTRAL
spinal cord

Curtis Bell

Electric fish measure distance in the dark

Gerhard von der Emde*, Stephan Schwarz*, Leonel Gomez†‡, Ruben Budelli‡ & Kirsty Grant†

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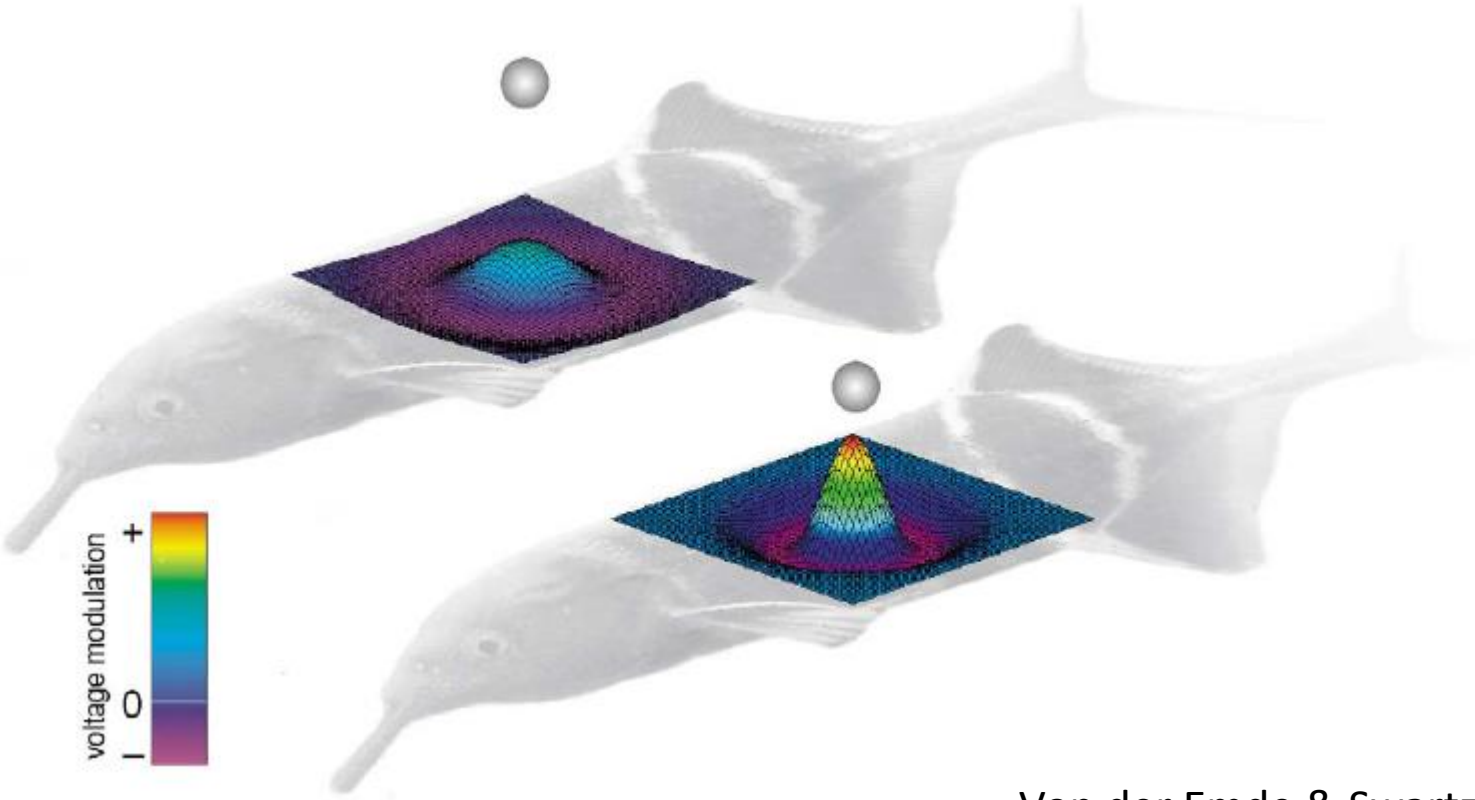
‡ Department of Biomathematics, Faculty of Science, University of the Republic of Uruguay, Montevideo, Uruguay



Von der Emde & Swartz, 2002