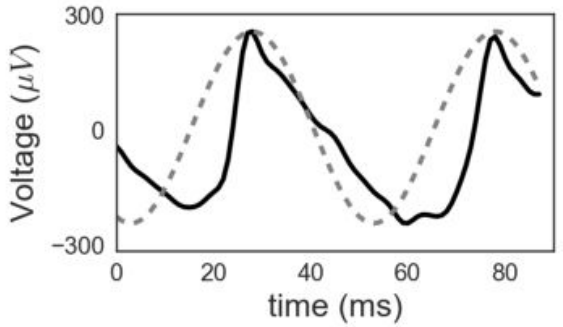
The waveform shape of brain oscillations

Scott Cole

Voytek Lab

18 May 2017

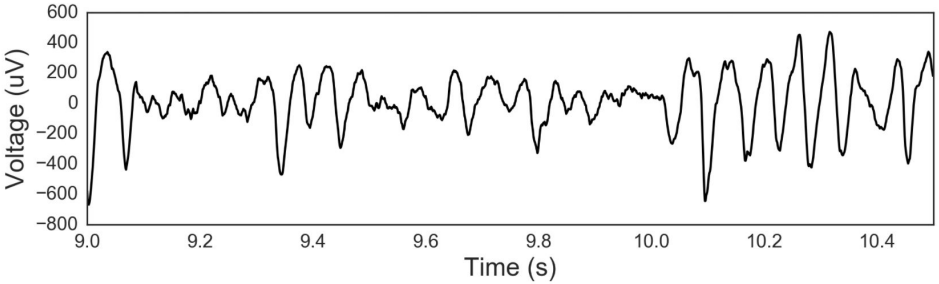
NGP Research rounds

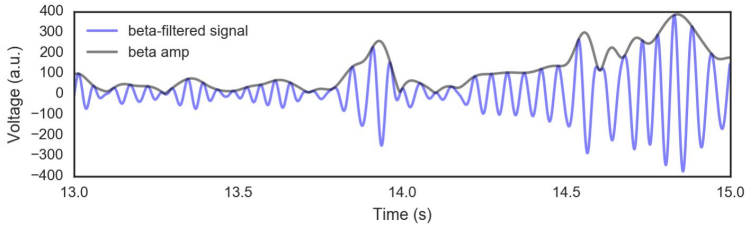


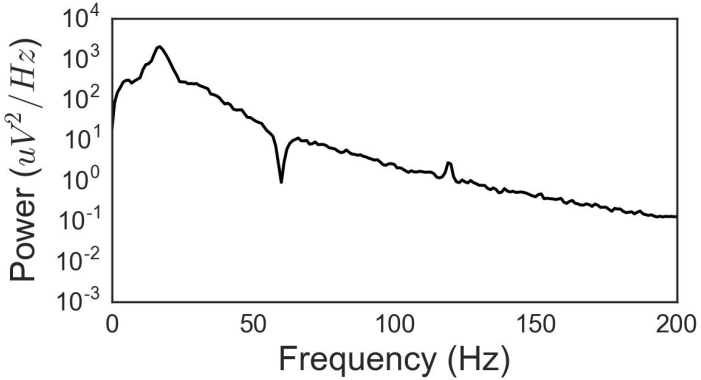
Outline

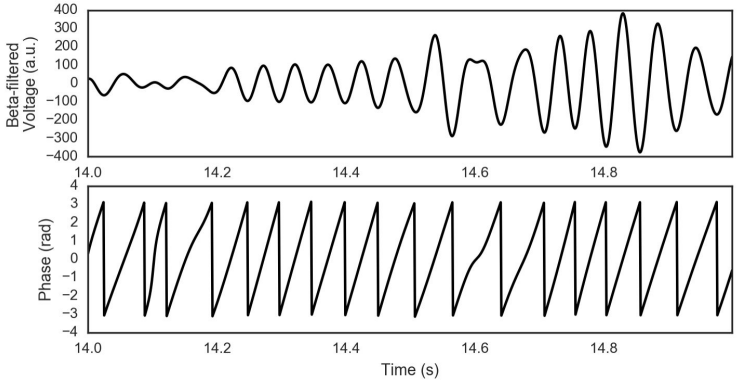
- Why waveform shape?
- **Past results**: What information might be contained in an oscillation's waveform shape?
- **Current results**: How do local hippocampal spiking patterns relate to the theta waveform shape?

Oscillations: Amplitude, frequency, phase

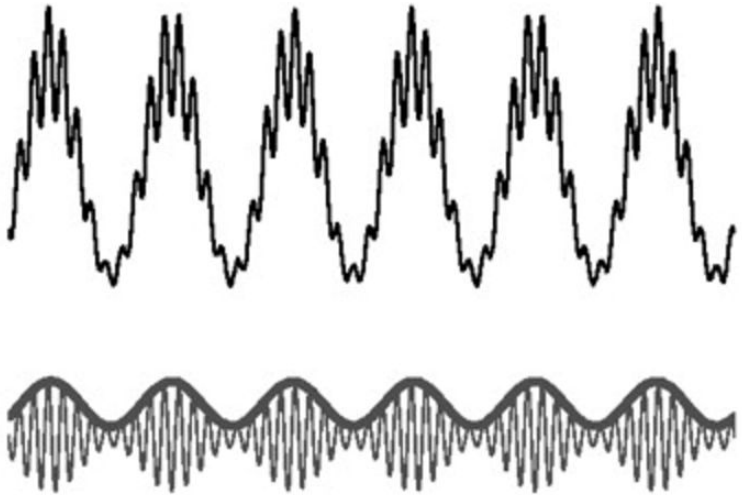




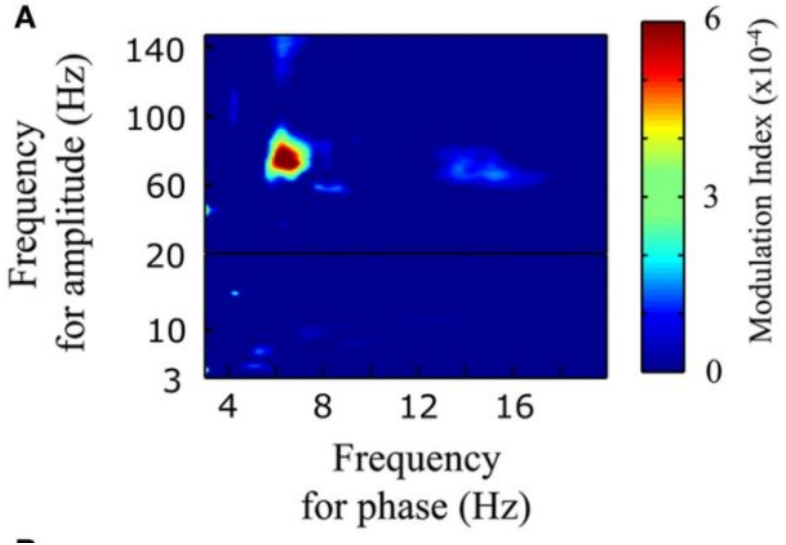




Phase-amplitude coupling



Tort et al., 2010, *J Neurophys*

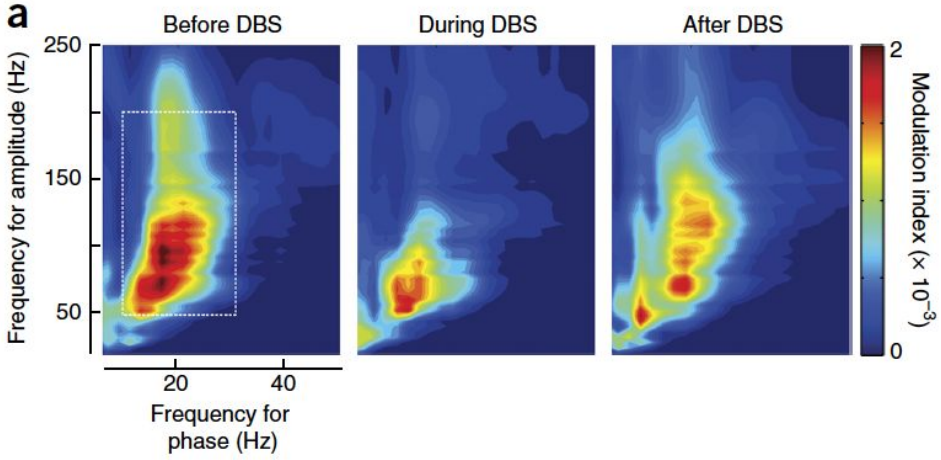


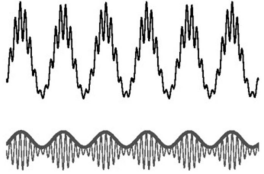
Morillon et al., 2012, *Front. Psych.*

nature neuroscience

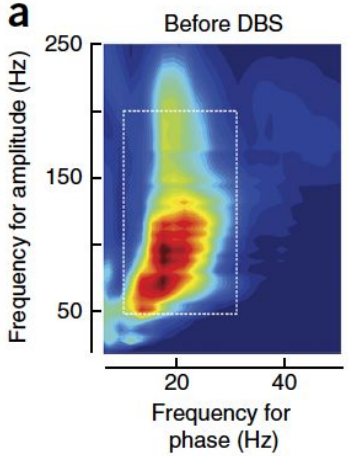
Therapeutic deep brain stimulation reduces cortical phase-amplitude coupling in Parkinson's disease

Coralie de Hemptinne[1], Nicole C Swann[1], Jill L Ostrem[2], Elena S Ryapolova-Webb[1], Marta San Luciano[2], Nicholas B Galifianakis[2] & Philip A Starr[1,3]



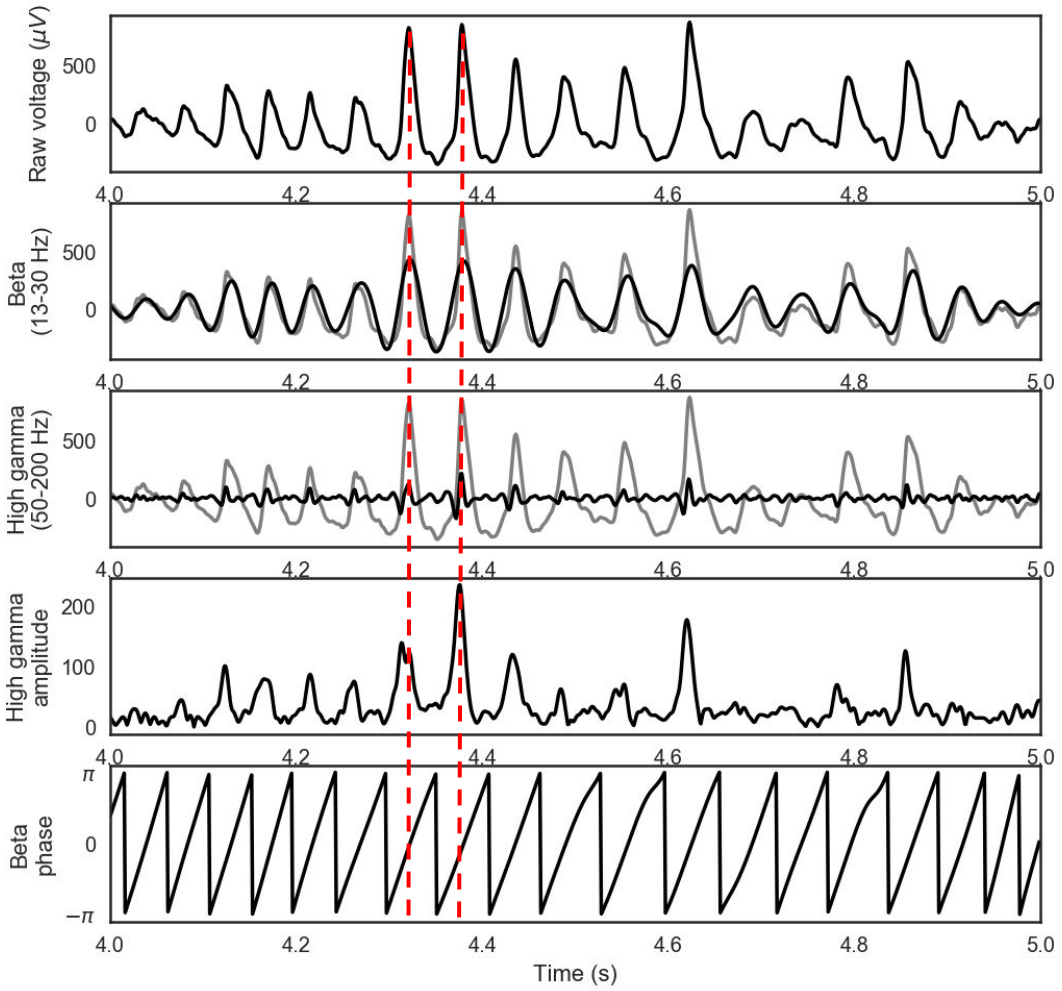


de Hemptinne et al., 2015, *Nat Neuro*

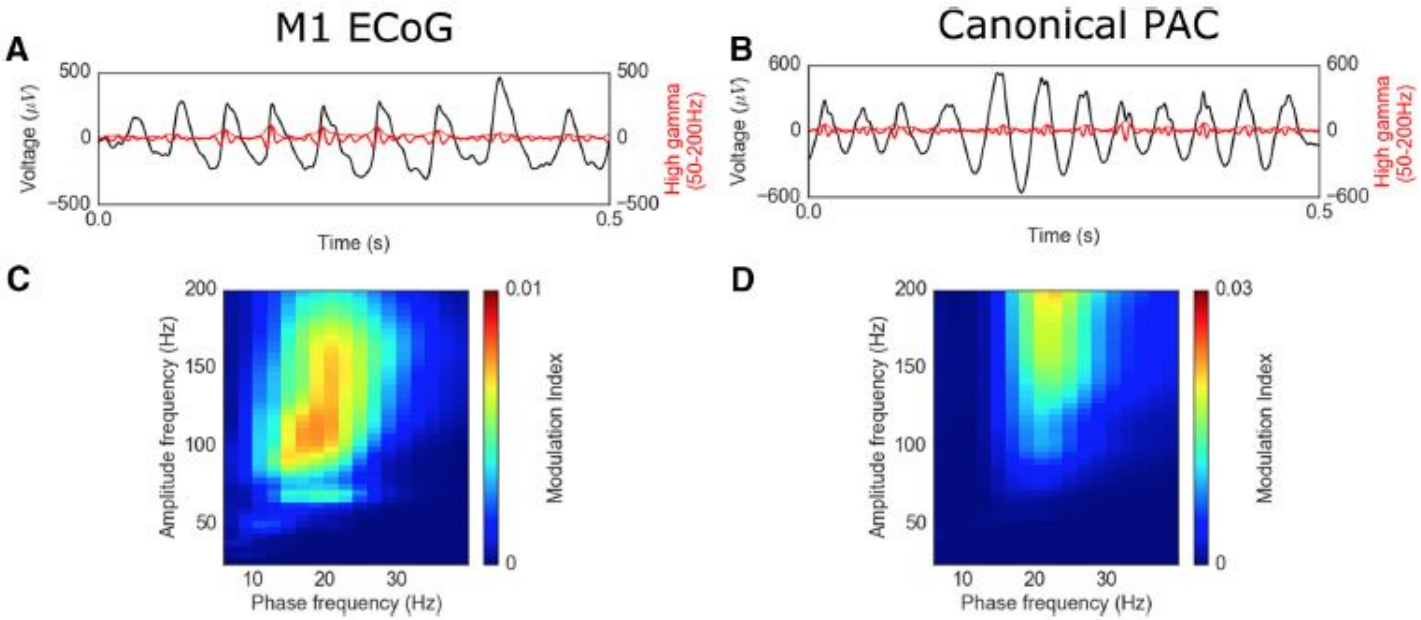


~~2 processes (beta, high gamma)~~

1 (nonsinusoidal) beta



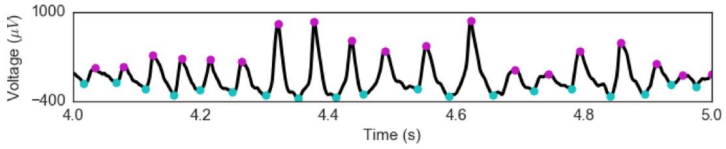
Sharp oscillations and “true PAC” yield similar PAC statistics

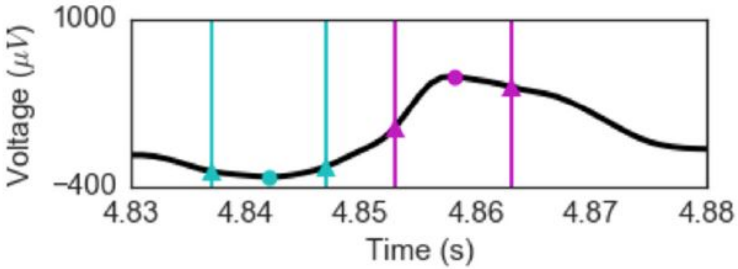


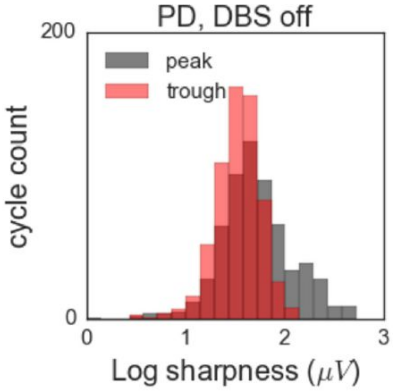
Cole et al., 2017, *J Neuro*

Does beta waveform shape change with DBS?

Quantify waveform shape







$$\text{Sharp}_{peak} = \frac{(V_{peak} - V_{peak-5ms}) + (V_{peak} - V_{peak+5ms})}{2} = \frac{(531\mu V - 106\mu V) + (531\mu V - 444\mu V)}{2} = 256\mu V$$

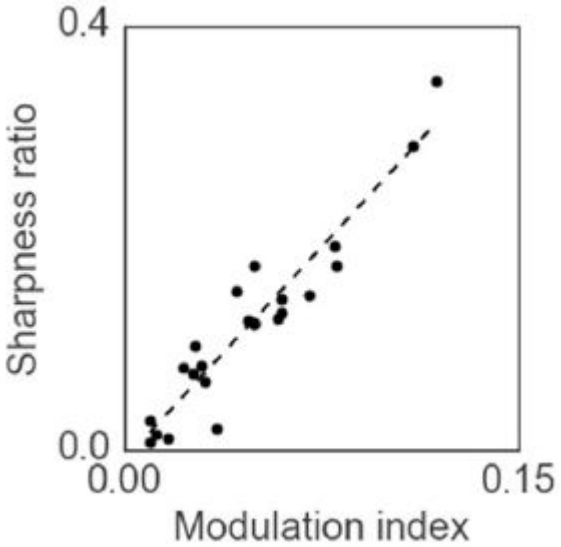
$$\text{Sharp}_{trough} = \frac{(V_{trough-5ms} - V_{trough}) + (V_{trough+5ms} - V_{trough})}{2} = \frac{(-268\mu V + 313\mu V) + (-226\mu V + 313\mu V)}{2} = 66\mu V$$

sharpness ratio

$$= \max\left(\frac{\frac{1}{N_{\text{peaks}}}\sum_{\text{peaks}}\text{Sharp}_{\text{peak}}}{\frac{1}{N_{\text{troughs}}}\sum_{\text{troughs}}\text{Sharp}_{\text{trough}}}, \frac{\frac{1}{N_{\text{troughs}}}\sum_{\text{troughs}}\text{Sharp}_{\text{trough}}}{\frac{1}{N_{\text{troughs}}}\sum_{\text{peaks}}\text{Sharp}_{\text{peak}}}\right)$$

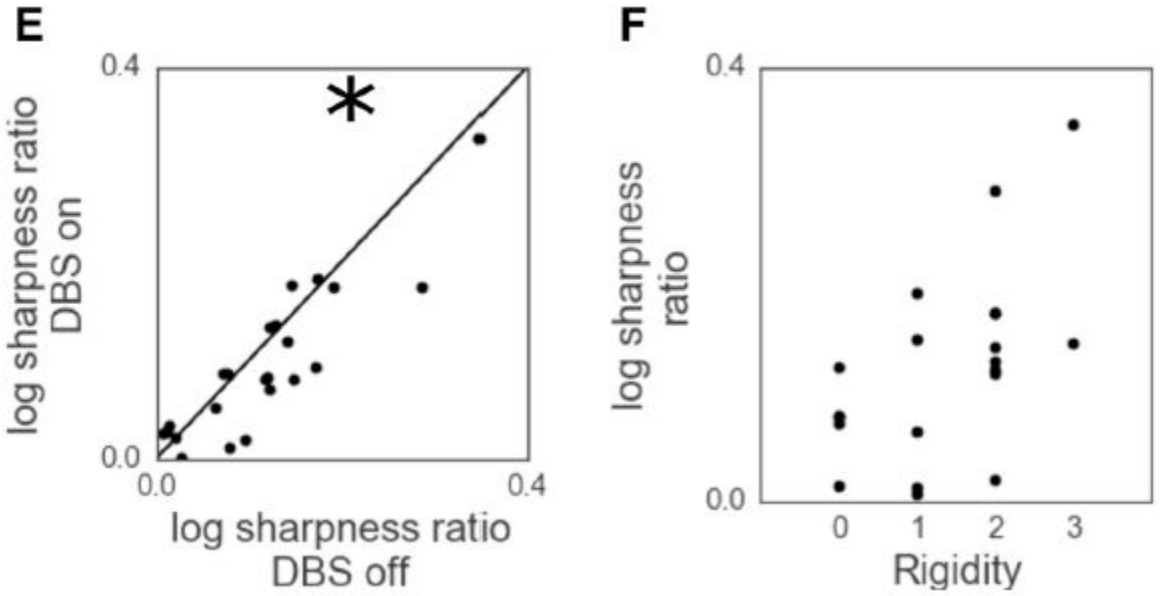
Cole et al., 2017, *J Neuro*

PAC is, essentially, sharpness



Cole et al., 2017, *J Neuro*

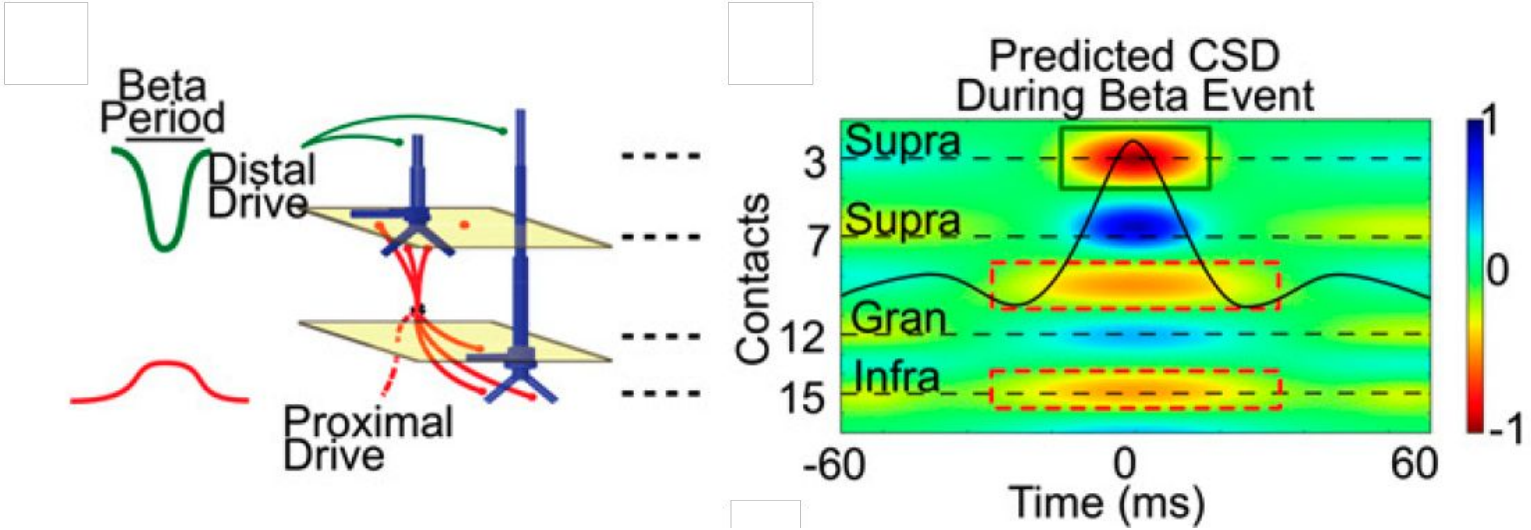
DBS makes M1 beta oscillations more symmetric



Cole et al., 2017, *J Neuro*

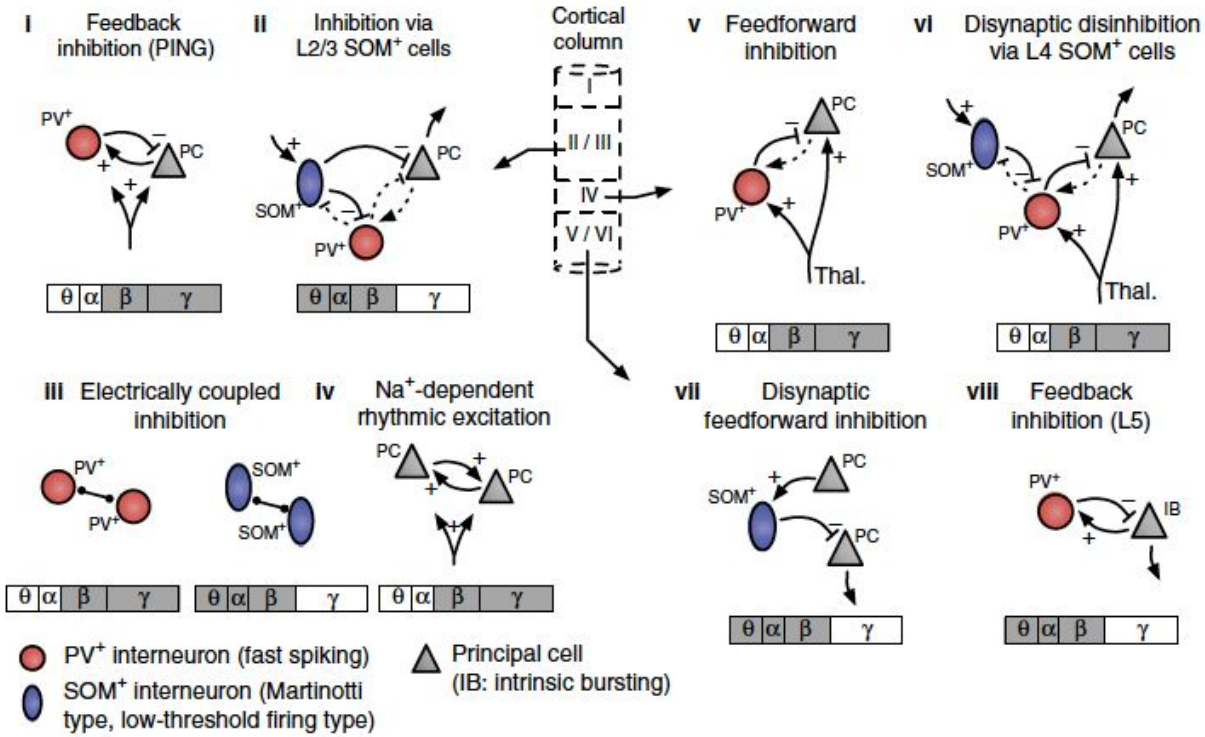
What does an increased sharpness ratio mean?

- Field potentials reflect synaptic activity
- Sharp transients may reflect synchronous synaptic activity



Sherman et al., 2016, *PNAS*

What information would waveform shape provide?



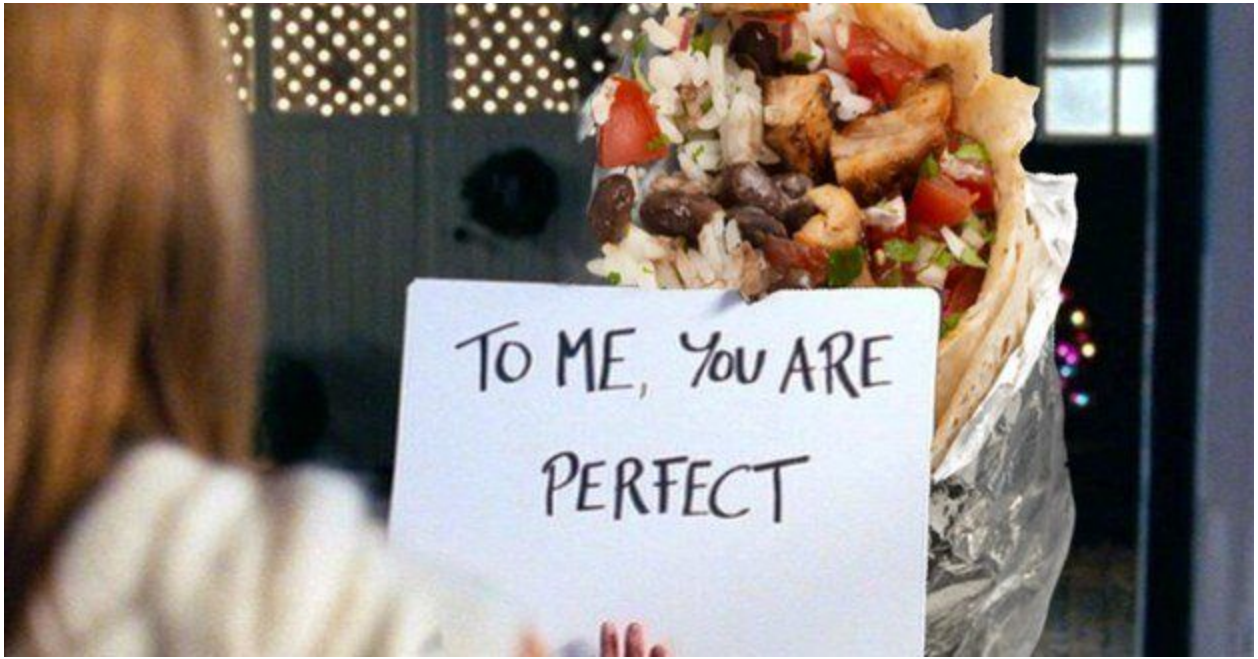
Womelsdorf et al., 2014, *Nat Neuro*

Part 1 take-away

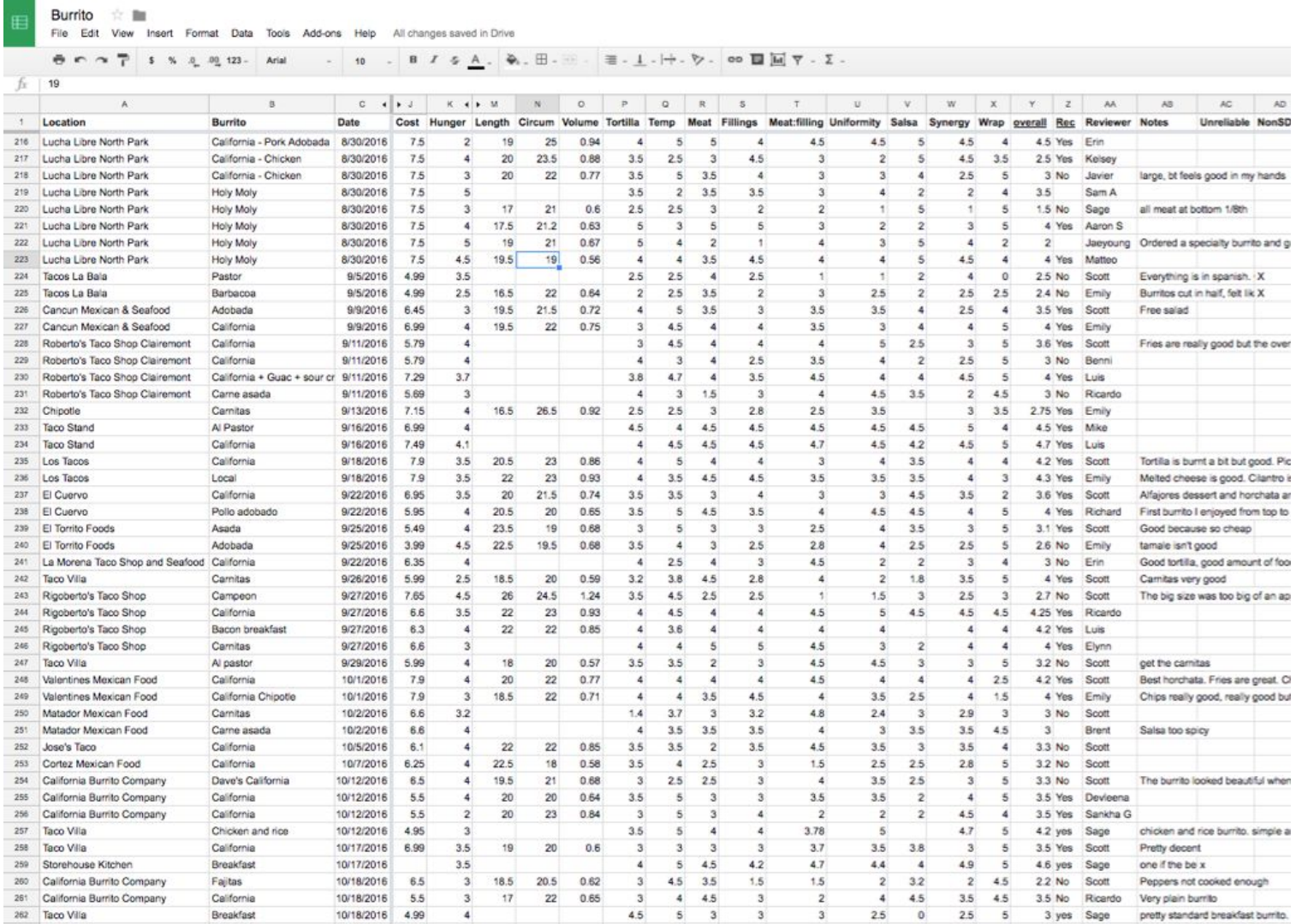
- Typical sine wave-based analyses may indirectly measure changes in waveform shape.
- The waveform shape of motor cortical beta oscillations changes with DBS treatment in PD

Part 2.

Buzzfeed



Buzzfeed



Burrito

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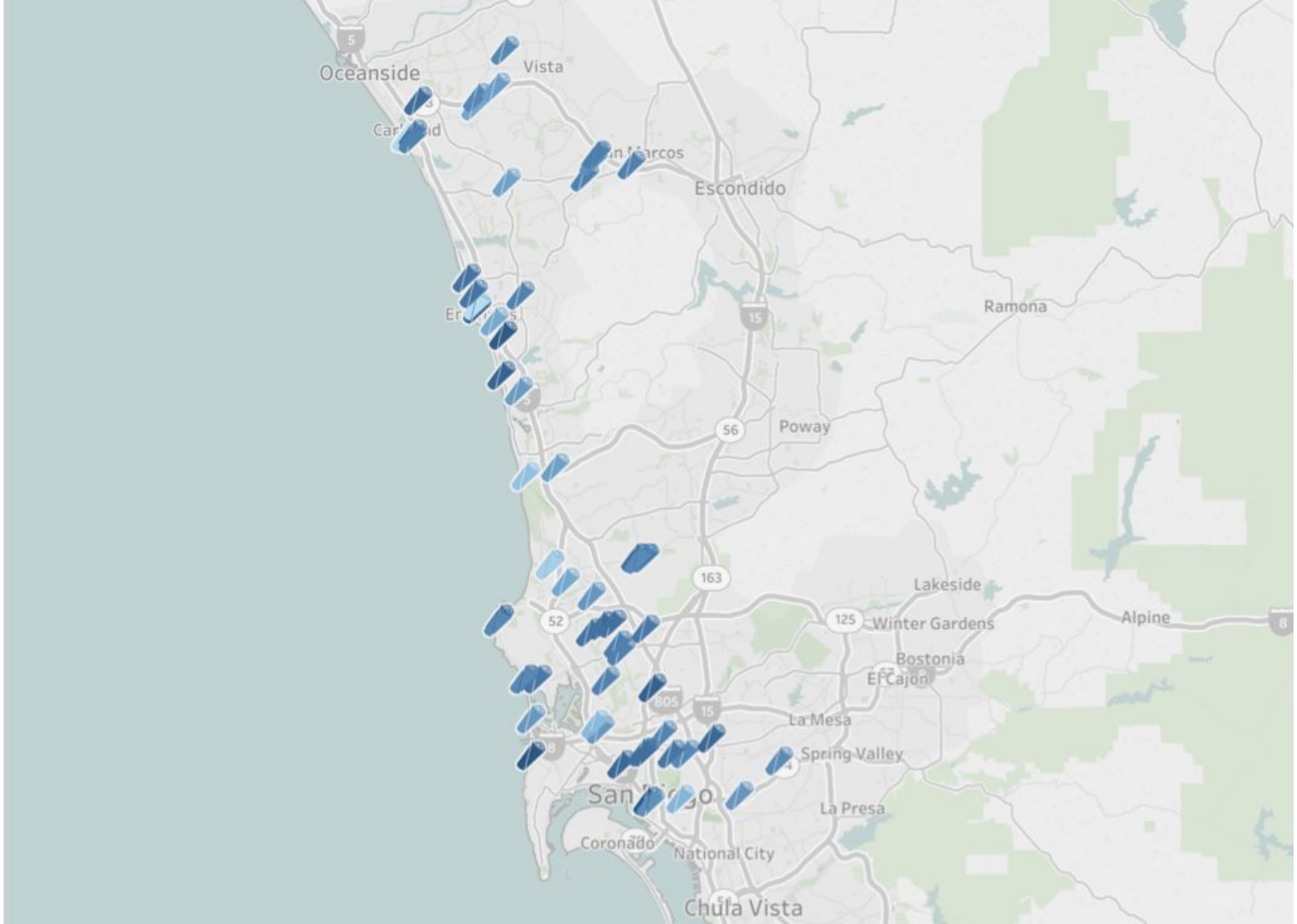
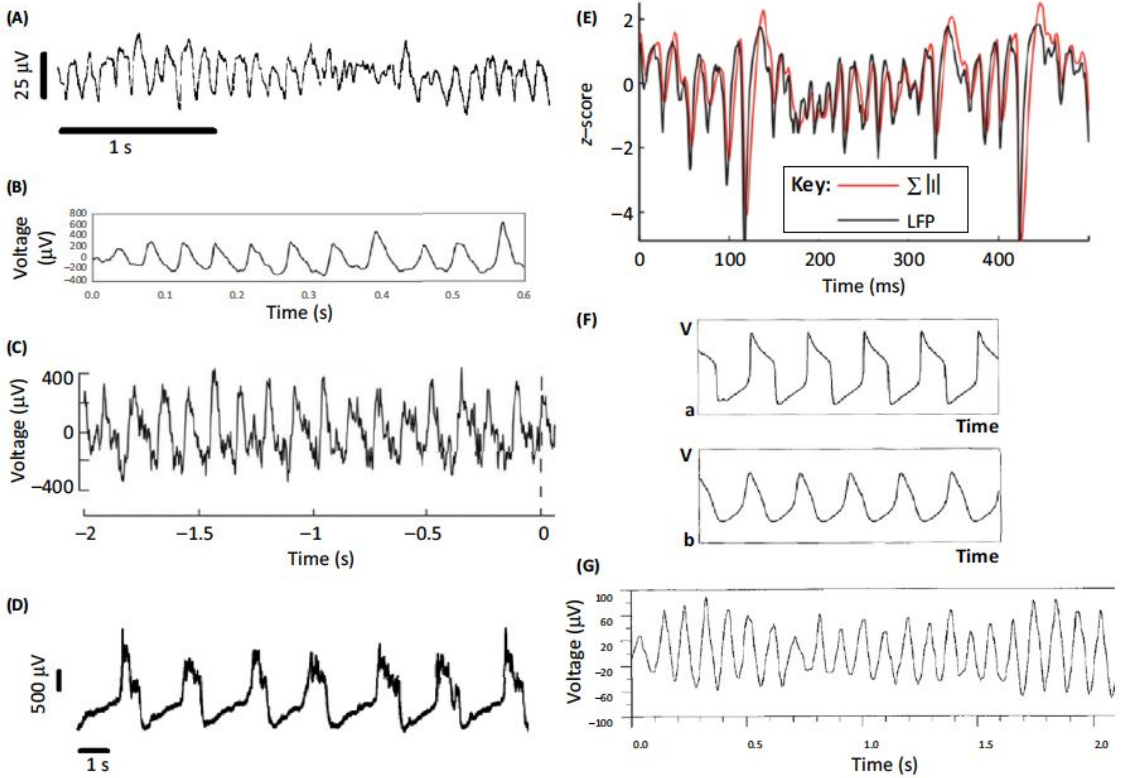
	A	B	C	J	K	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD
1	Location	Burrito	Date	Cost	Hunger	Length	Circum	Volume	Tortilla	Temp	Meat	Fillings	Meat:filling	Uniformity	Salsa	Synergy	Wrap	overall	Rec	Reviewer	Notes	Unreliable	NonSD
216	Lucha Libre North Park	California - Pork Adobada	8/30/2016	7.5	2	19	25	0.94	4	5	5	4	4.5	4.5	5	4.5	4	4.5	Yes	Erin			
217	Lucha Libre North Park	California - Chicken	8/30/2016	7.5	4	20	23.5	0.88	3.5	2.5	3	4.5	3	2	5	4.5	3.5	2.5	Yes	Kelsey			
218	Lucha Libre North Park	California - Chicken	8/30/2016	7.5	3	20	22	0.77	3.5	5	3.5	4	3	3	4	2.5	5	3	No	Javier	large, bt feels good in my hands		
219	Lucha Libre North Park	Holy Moly	8/30/2016	7.5	5				3.5	2	3.5	3.5	3	4	2	2	4	3.5		Sam A			
220	Lucha Libre North Park	Holy Moly	8/30/2016	7.5	3	17	21	0.6	2.5	2.5	3	2	2	1	5	1	5	1.5	No	Sage	all meat at bottom 1/8th		
221	Lucha Libre North Park	Holy Moly	8/30/2016	7.5	4	17.5	21.2	0.63	5	3	5	5	3	2	2	3	5	4	Yes	Aaron S			
222	Lucha Libre North Park	Holy Moly	8/30/2016	7.5	5	19	21	0.67	5	4	2	1	4	3	5	4	2	2		Jaeyoung	Ordered a specialty burrito and g		
223	Lucha Libre North Park	Holy Moly	8/30/2016	7.5	4.5	19.5	19	0.56	4	4	3.5	4.5	4	4	5	4.5	4	4	Yes	Matteo			
224	Tacos La Bala	Pastor	9/5/2016	4.99	3.5				2.5	2.5	4	2.5	1	1	2	4	0	2.5	No	Scott	Everything is in spanish. X		
225	Tacos La Bala	Barbacoa	9/5/2016	4.99	2.5	16.5	22	0.64	2	2.5	3.5	2	3	2.5	2	2.5	2.5	2.4	No	Emily	Burritos cut in half, felt lik X		
226	Cancun Mexican & Seafood	Adobada	9/9/2016	6.45	3	19.5	21.5	0.72	4	5	3.5	3	3.5	3.5	4	2.5	4	3.5	Yes	Scott	Free salad		
227	Cancun Mexican & Seafood	California	9/9/2016	6.99	4	19.5	22	0.75	3	4.5	4	4	3.5	3	4	4	5	4	Yes	Emily			
228	Roberto's Taco Shop Clairemont	California	9/11/2016	5.79	4				3	4.5	4	4	4	5	2.5	3	5	3.6	Yes	Scott	Fries are really good but the over		
229	Roberto's Taco Shop Clairemont	California	9/11/2016	5.79	4				4	3	4	2.5	3.5	4	2	2.5	5	3	No	Benni			
230	Roberto's Taco Shop Clairemont	California + Guac + sour cr	9/11/2016	7.29	3.7				3.8	4.7	4	3.5	4.5	4	4	4.5	5	4	Yes	Luis			
231	Roberto's Taco Shop Clairemont	Carne asada	9/11/2016	5.69	3				4	3	1.5	3	4	4.5	3.5	2	4.5	3	No	Ricardo			
232	Chipotle	Carnitas	9/13/2016	7.15	4	16.5	26.5	0.92	2.5	2.5	3	2.8	2.5	3.5		3	3.5	2.75	Yes	Emily			
233	Taco Stand	Al Pastor	9/16/2016	6.99	4				4.5	4	4.5	4.5	4.5	4.5	4.5	5	4	4.5	Yes	Mike			
234	Taco Stand	California	9/16/2016	7.49	4.1				4	4.5	4.5	4.5	4.7	4.5	4.2	4.5	5	4.7	Yes	Luis			
235	Los Tacos	California	9/18/2016	7.9	3.5	20.5	23	0.86	4	5	4	4	3	4	3.5	4	4	4.2	Yes	Scott	Tortilla is burnt a bit but good. Pic		
236	Los Tacos	Local	9/18/2016	7.9	3.5	22	23	0.93	4	3.5	4.5	4.5	3.5	3.5	3.5	4	3	4.3	Yes	Emily	Melted cheese is good. Cilantro i		
237	El Cuervo	California	9/22/2016	6.95	3.5	20	21.5	0.74	3.5	3.5	3	4	3	3	4.5	3.5	2	3.6	Yes	Scott	Alfajores dessert and horchata ar		
238	El Cuervo	Pollo adobado	9/22/2016	5.95	4	20.5	20	0.65	3.5	5	4.5	3.5	4	4.5	4.5	4	5	4	Yes	Richard	First burrito I enjoyed from top to		
239	El Torrito Foods	Asada	9/25/2016	5.49	4	23.5	19	0.68	3	5	3	3	2.5	4	3.5	3	5	3.1	Yes	Scott	Good because so cheap		
240	El Torrito Foods	Adobada	9/25/2016	3.99	4.5	22.5	19.5	0.68	3.5	4	3	2.5	2.8	4	2.5	2.5	5	2.6	No	Emily	tamale isn't good		
241	La Morena Taco Shop and Seafood	California	9/22/2016	6.35	4				4	2.5	4	3	4.5	2	2	3	4	3	No	Erin	Good tortilla, good amount of foo		
242	Taco Vila	Carnitas	9/26/2016	5.99	2.5	18.5	20	0.59	3.2	3.8	4.5	2.8	4	2	1.8	3.5	5	4	Yes	Scott	Carnitas very good		
243	Rigoberto's Taco Shop	Campeon	9/27/2016	7.65	4.5	26	24.5	1.24	3.5	4.5	2.5	2.5	1	1.5	3	2.5	3	2.7	No	Scott	The big size was too big of an ap		
244	Rigoberto's Taco Shop	California	9/27/2016	6.6	3.5	22	23	0.93	4	4.5	4	4	4.5	5	4.5	4.5	4.5	4.25	Yes	Ricardo			
245	Rigoberto's Taco Shop	Bacon breakfast	9/27/2016	6.3	4	22	22	0.85	4	3.6	4	4	4	4		4	4	4.2	Yes	Luis			
246	Rigoberto's Taco Shop	Carnitas	9/27/2016	6.6	3				4	4	5	5	4.5	3	2	4	4	4	Yes	Elynn			
247	Taco Vila	Al pastor	9/29/2016	5.99	4	18	20	0.57	3.5	3.5	2	3	4.5	4.5	3	3	5	3.2	No	Scott	get the carnitas		
248	Valentines Mexican Food	California	10/1/2016	7.9	4	20	22	0.77	4	4	4	4	4.5	4	4	4	2.5	4.2	Yes	Scott	Best horchata. Fries are great. Cl		
249	Valentines Mexican Food	California Chipotle	10/1/2016	7.9	3	18.5	22	0.71	4	4	3.5	4.5	4	3.5	2.5	4	1.5	4	Yes	Emily	Chips really good, really good bu		
250	Matador Mexican Food	Carnitas	10/2/2016	6.6	3.2				1.4	3.7	3	3.2	4.8	2.4	3	2.9	3	3	No	Scott			
251	Matador Mexican Food	Carne asada	10/2/2016	6.6	4				4	3.5	3.5	3.5	4	3	3.5	3.5	4.5	3		Brent	Salsa too spicy		
252	Jose's Taco	California	10/5/2016	6.1	4	22	22	0.85	3.5	3.5	2	3.5	4.5	3.5	3	3.5	4	3.3	No	Scott			
253	Cortez Mexican Food	California	10/7/2016	6.25	4	22.5	18	0.58	3.5	4	2.5	3	1.5	2.5	2.5	2.8	5	3.2	No	Scott			
254	California Burrito Company	Dave's California	10/12/2016	6.5	4	19.5	21	0.88	3	2.5	2.5	3	4	3.5	2.5	3	5	3.3	No	Scott	The burrito looked beautiful when		
255	California Burrito Company	California	10/12/2016	5.5	4	20	20	0.64	3.5	5	3	3	3.5	3.5	2	4	5	3.5	Yes	Devleena			
256	California Burrito Company	California	10/12/2016	5.5	2	20	23	0.84	3	5	3	4	2	2	2	4.5	4	3.5	Yes	Sankha G			
257	Taco Vila	Chicken and rice	10/12/2016	4.95	3				3.5	5	4	4	3.78	5		4.7	5	4.2	yes	Sage	chicken and rice burrito. simple a		
258	Taco Vila	California	10/17/2016	6.99	3.5	19	20	0.6	3	3	3	3	3.7	3.5	3.8	3	5	3.5	Yes	Scott	Pretty decent		
259	Storehouse Kitchen	Breakfast	10/17/2016		3.5				4	5	4.5	4.2	4.7	4.4	4	4.9	5	4.6	yes	Sage	one if the be x		
260	California Burrito Company	Fajitas	10/18/2016	6.5	3	18.5	20.5	0.62	3	4.5	3.5	1.5	1.5	2	3.2	2	4.5	2.2	No	Scott	Peppers not cooked enough		
261	California Burrito Company	California	10/18/2016	5.5	3	17	22	0.65	3	4	4.5	3	2	4	4.5	3.5	4.5	3.5	No	Ricardo	Very plain burrito		
262	Taco Vila	Breakfast	10/18/2016	4.99	4				4.5	5	3	3	3	2.5	0	2.5	5	3	yes	Sage	pretty standard breakfast burrito.		

Buzzfeed


Oceanside
Vista
Escondido
Ramona
Poway
Lakeside
Winter Gardens
Alpine
Bostonia
El Cajon
La Mesa
Spring Valley
La Presa
Coronado
National City
Chula Vista
5
56
163
52
125
805
15
8

Buzzfeed

Part 2. Review of neural oscillation waveform shape



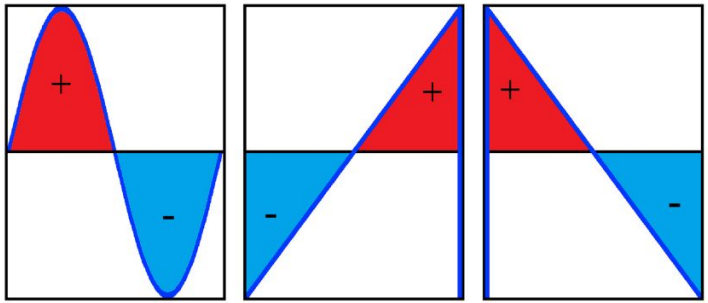
Cole & Voytek, 2017, *Trends Cog. Sci.*

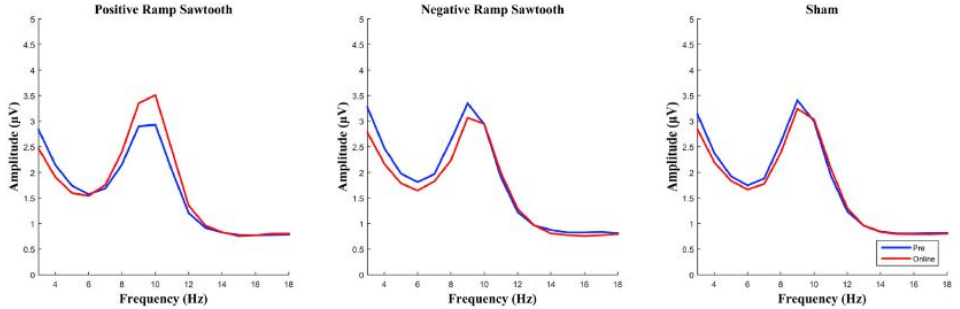
Disambiguating multiple oscillators in same frequency band

- EEG: Alpha rhythm and mu rhythm (e.g. Pfurscheller et al., 1997, *Neuroimage*)
- Slow oscillations and “sawtooth waves” (e.g. Pearl et al., 2002, *Sleep Med.*)
- 3 distinct alpha rhythms in gustatory cortex (Tort et al., 2010, *J. Neuro.*)

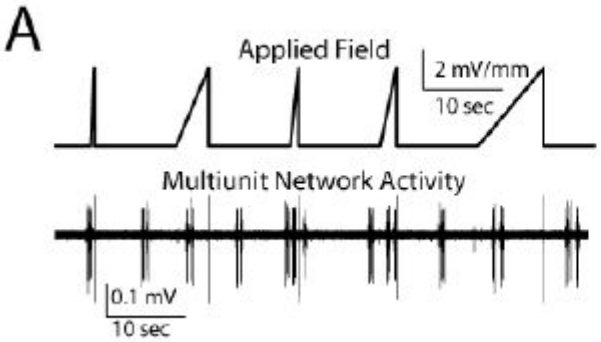
Oscillatory neurostimulation

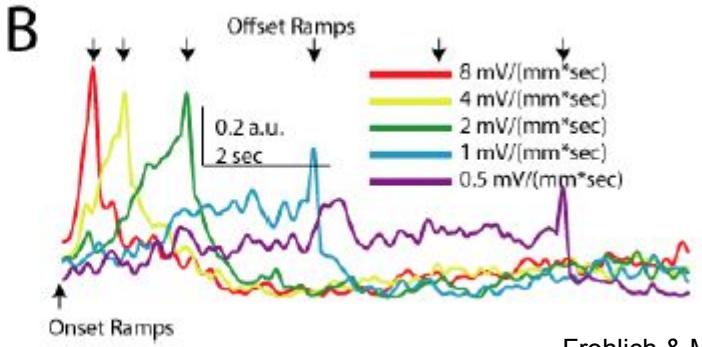
Electroconvulsive therapy
Sine waves vs. rectangular wave stim.
(Weiner et al., 1986, *Ann. N. Y. Acad. Sci.*)





Dowsett & Herrmann, 2016, *Front. Hum. Neuro.*

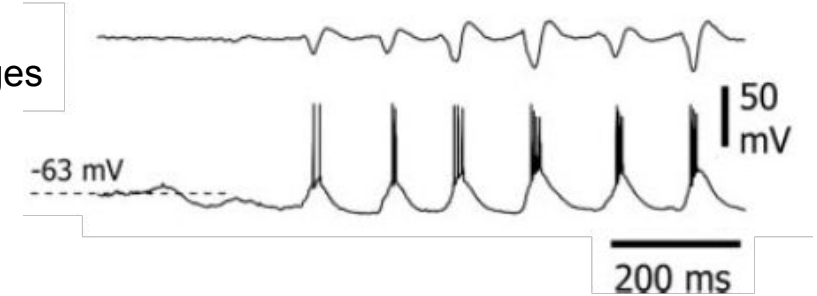




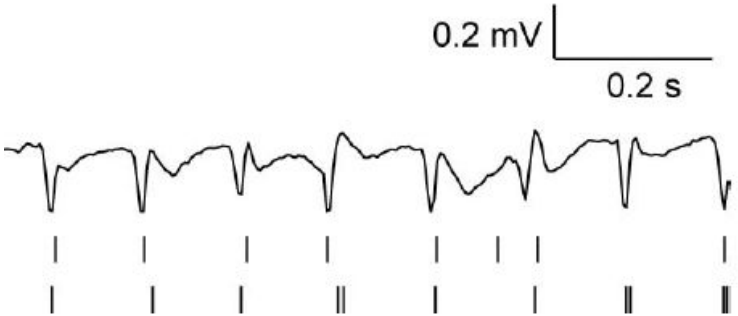
Frohlich & McCormick, 2010, *Neuron*

Waveform shape and spiking

Spike-wave discharges in corticostriatal neurons

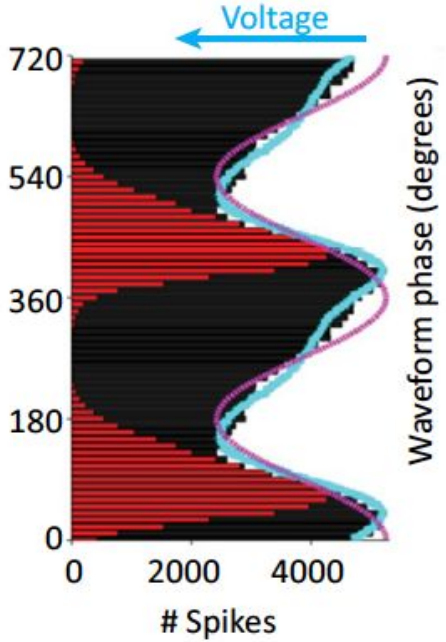


Slaght et al., 2004, *J Neuro*



Alpha rhythm in gustatory cortex

Fontanini & Katz, 2005, *J Neurophys*



Belluscio et al., 2012, *J Neuro*

Slow oscillations and glia

Electroencephalography and clinical Neurophysiology 107 (1998) 69–83

Invited review

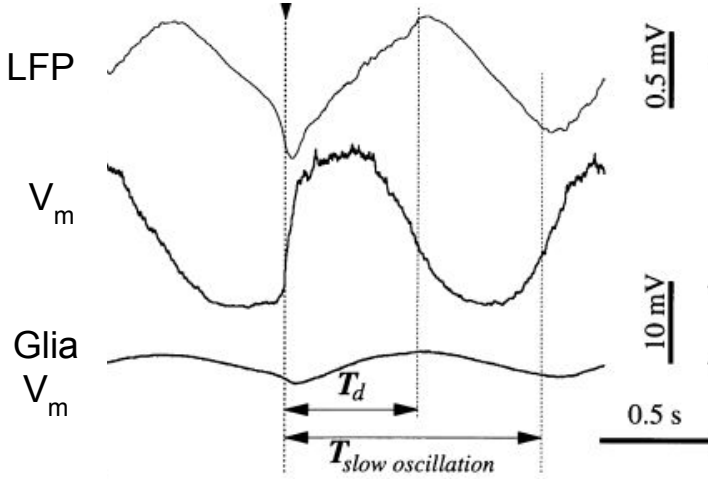
Electrophysiological correlates of sleep delta waves[1]

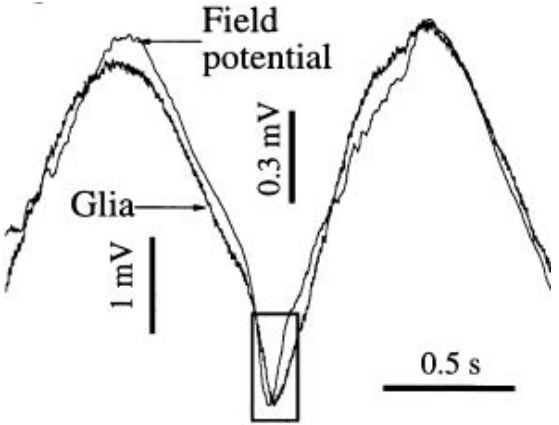
F. Amzica, M. Steriade

Laboratoire de Neurophysiologie, Faculté de Médecine, Université Laval, Québec, G1K 7P4 Canada

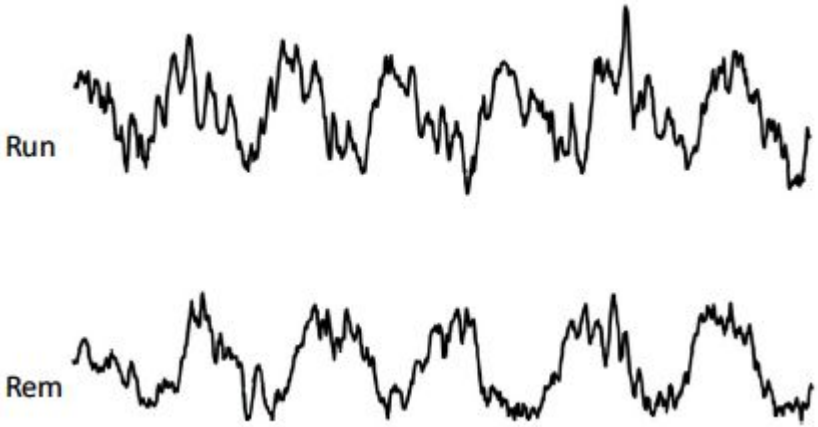
Accepted for publication: 28 February 1998

We believe that analyses of EEG data should take into consideration the actual aspect of waves and, if possible, their relationship with the state of the cellular aggregates of the corticothalamic network. Obviously this is not possible by merely a spectral approach. Fourier spectra are not able to discriminate between periodic phenomena and waves with a given shape, i.e. with a given spectral content.

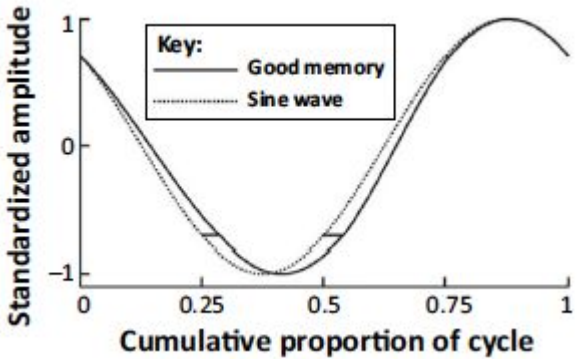


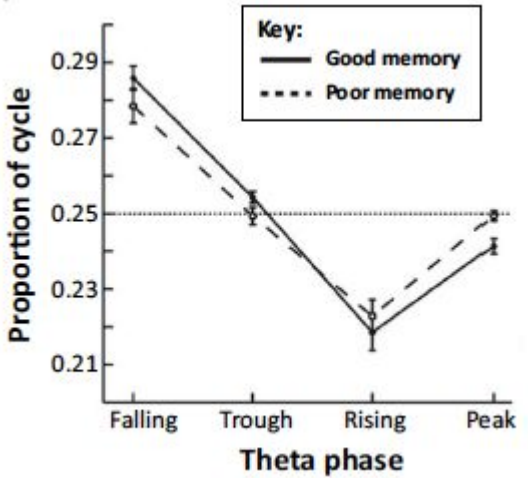


Waveform shape and behavior



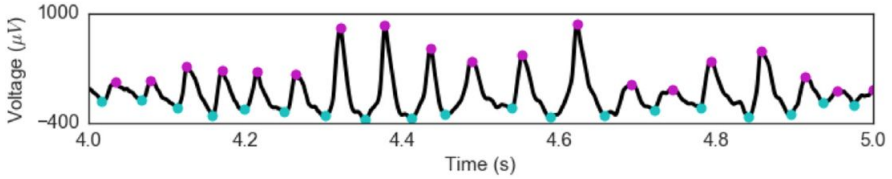
Belluscio et al., 2012, *J Neuro*





Trimper et al., 2014, *Hippocampus*

Oscillations as a series of events



612.822.3

THE INTERPRETATION OF POTENTIAL WAVES IN THE CORTEX.

By E. D. ADRIAN and B. H. C. MATTHEWS.

(*From the Physiological Laboratory, Cambridge.*)

(*Received April* 4, 1934.)

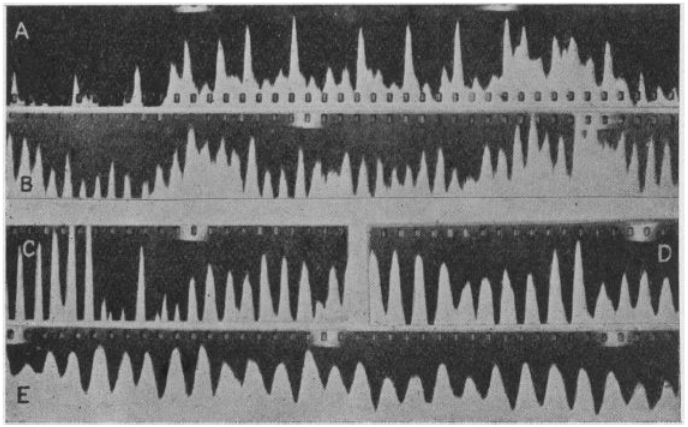


Fig. 7. Evolution of injury discharge in cat (C. and E. anæsthesia). Puncture of cortex by fine wire. A, large monophasic waves 30 per sec.; B, later, frequency 76 per sec.; C, later, frequency 72 per sec.; D, later, frequency 56 per sec.; E, later, frequency 48 per sec. Time marker gives 1/4 sec. intervals.

Part 2 take-away

- Neural oscillation waveform shape is diverse
- Waveform shape can differentiate distinct oscillators
- Waveform shape can relate to spiking statistics or glial membrane voltage
- Waveform shape can relate to behavior

Part 3: Waveform shape and spiking statistics

Data (crcns.org)

Simultaneous extracellular spiking (CA1, CA3) and

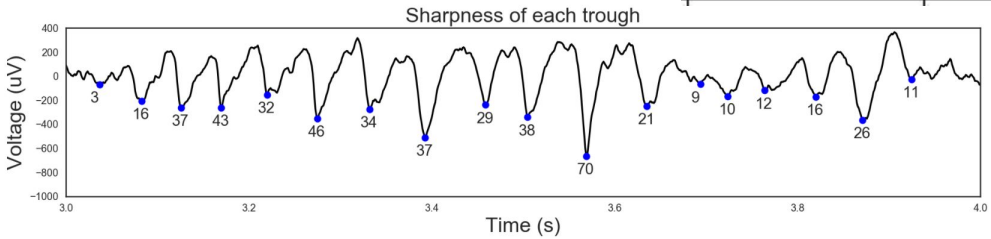
Theta oscillations in hippocampus (CA1)

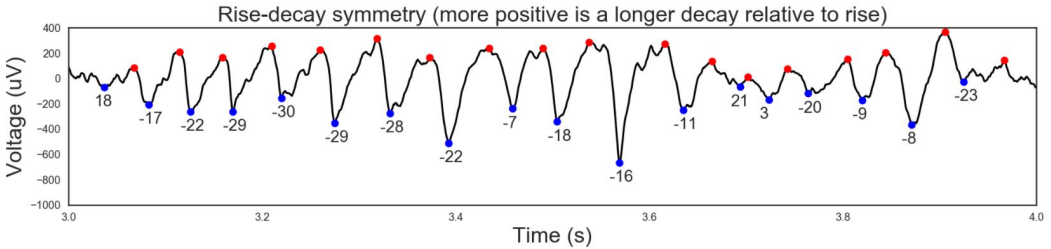
Hypothesis

Theta waveform shape relates to local spiking statistics

Cycle-by-cycle analysis approach

	amp_mean	period	ptsym_time	rdsym_time	spike_main_time	t2t_Nspikes	t2t_spikerate	sync_time	sync_strength	sync_neu_weight
65	33.885516	80	-30	18	0.090361	6.0	45.253012	0.090361	1.943417	1.943417
66	150.330740	47	-5	-17	0.328431	2.0	12.274510	0.328431	1.000000	1.000000
67	190.075717	44	10	-22	0.717742	10.0	100.967742	0.596774	2.000000	2.000000
68	166.715680	51	7	-29	0.878205	8.0	64.205128	0.653846	2.000000	2.000000
69	174.285019	50	3	-30	0.737288	4.0	42.440678	0.703390	1.923211	1.923211





1. Does trough sharpness relate to spike synchrony?

- Model-based approach:

$$y_i = \beta_0 + \beta_1 x_{i,1} + \beta_2 x_{i,2} + \ldots + \beta_n x_{i,n} + \varepsilon_i$$

  - Synchrony strength ~ amplitude + period + trough sharpness
- Hypothesis
  - Adding trough sharpness to the model will increase R^2 **Not really**
  - Trough sharpness will have a positive coefficient

Feature set	CA1 pyramidal	CA1 interneuron	CA3 pyramidal	CA3 interneuron
Amplitude, frequency	.022	.030	.004	.022
+ Trough sharpness	.030	.036	.006	.030
All shape features (symmetry, sharpness)	.044	.067	.012	.059

2. Does rise-decay symmetry relate to spike timing?

- Model-based approach:
  - Synchrony time ~ amplitude + period + rise-decay symmetry
- Hypothesis
  - Adding rise-decay symmetry to the model will increase R^2
  - Rise-decay symmetry will have a positive coefficient (trough-centered) **p = 0.002**

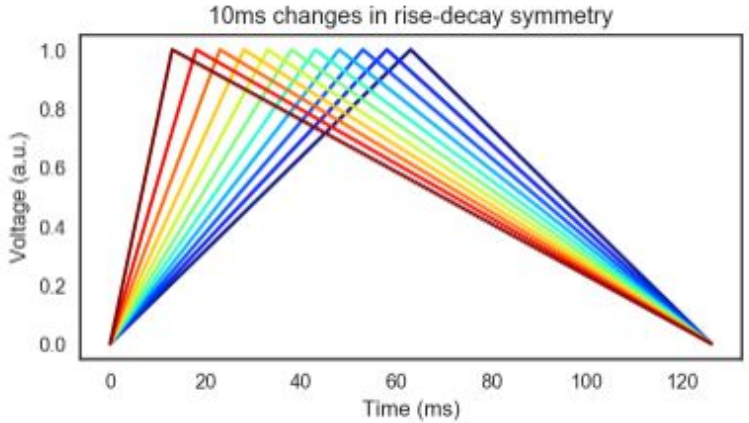
Feature set	CA1 pyramidal	CA1 interneuron	CA3 pyramidal	CA3 interneuron
Amplitude, frequency	.007	.011	.003	.003
+ Rise-decay symmetry	.010	.014	.005	.008
All shape features (symmetry, sharpness)	.017	.019	.009	.012

2. Does rise-decay symmetry relate to spike timing?

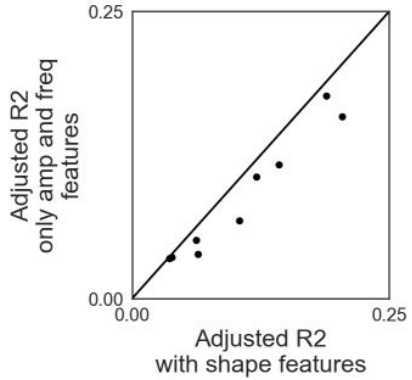
Effect size

For every 10ms difference between rise and decay time:
0.7ms difference in synchronized spike time.

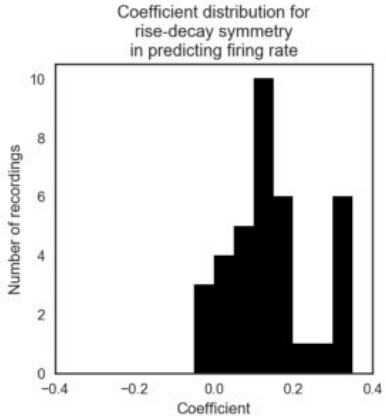
Faster rise → Sooner synchrony time

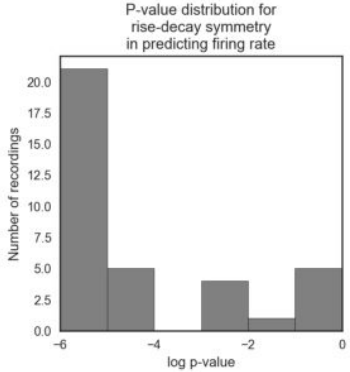


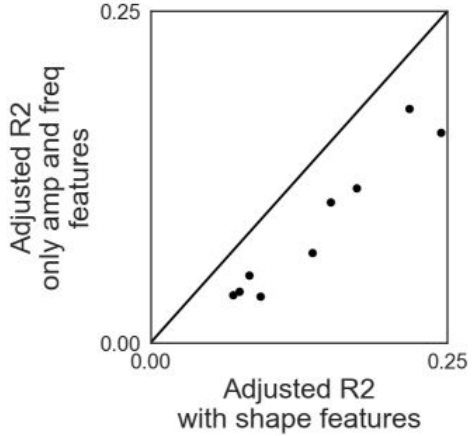
3. Waveform shape and CA1 interneuron firing rate



Feature set	R^2 (adjusted)
Amplitude, frequency	.087
+ Rise-decay symmetry	.107
All shape features (symmetry, sharpness)	.138





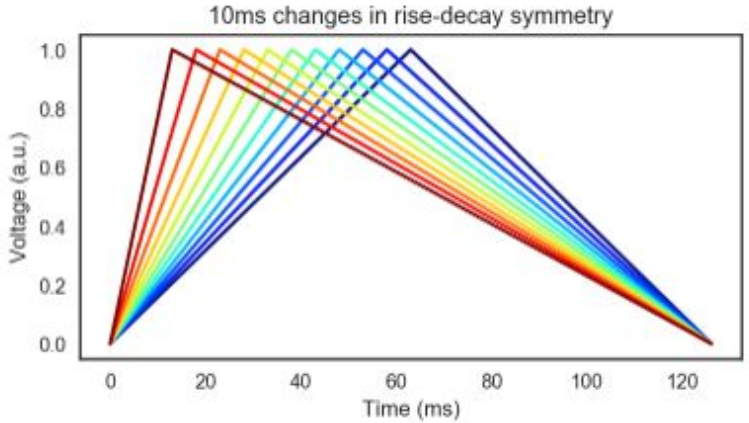


3. Waveform shape and CA1 interneuron firing rate

Effect size

For every 10ms difference between rise and decay time:
1.5% change in interneuron firing rate.

Faster rise → Faster firing



Summary

1. Traditional Fourier-based metric may indirectly reflect waveform shape
2. Waveform shape of oscillations may reflect physiology in a variety of cases
3. Hippocampal theta waveform shape provides scant information about local and upstream spiking

Future directions

- More rats
- Compare CA1 LFP to spiking in upstream projection from entorhinal cortex (layer 3)
- Integrate running speed into the model
- More rigorous inclusion criteria
  - Currently judge whether or not a cycle is really in an oscillation
  - Minimum number of spikes
- Single neuron analysis (bursting)
- Alternative statistical analysis
  - Allows for arbitrary time lags

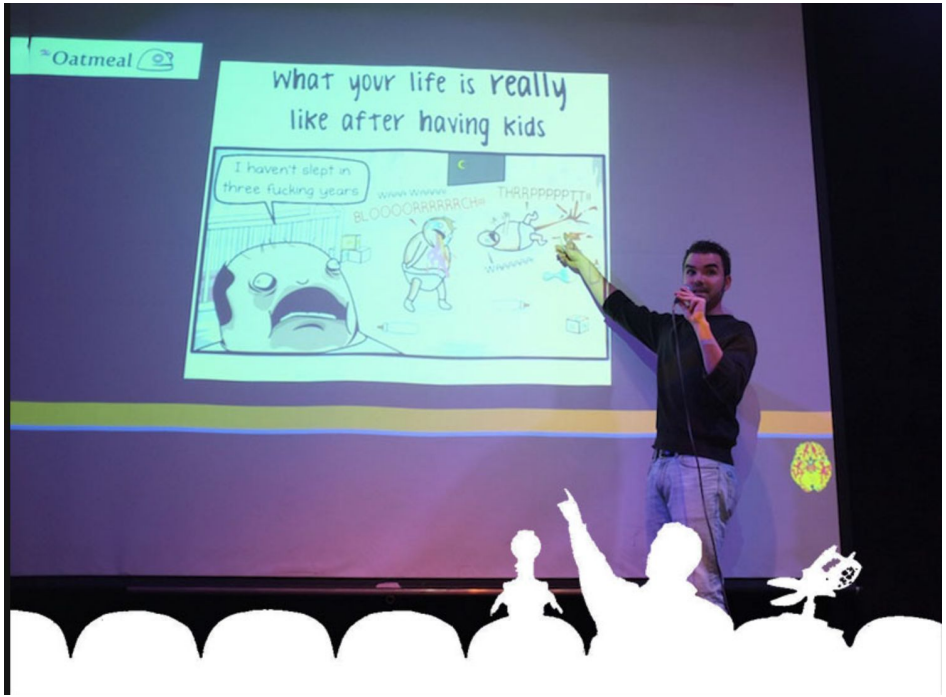
Acknowledgements

Voytek lab

- Richard Gao
- Tammy Tran
- Tom Donoghue
- Erik Peterson
- Roemer van der Meij
- Torben Noto

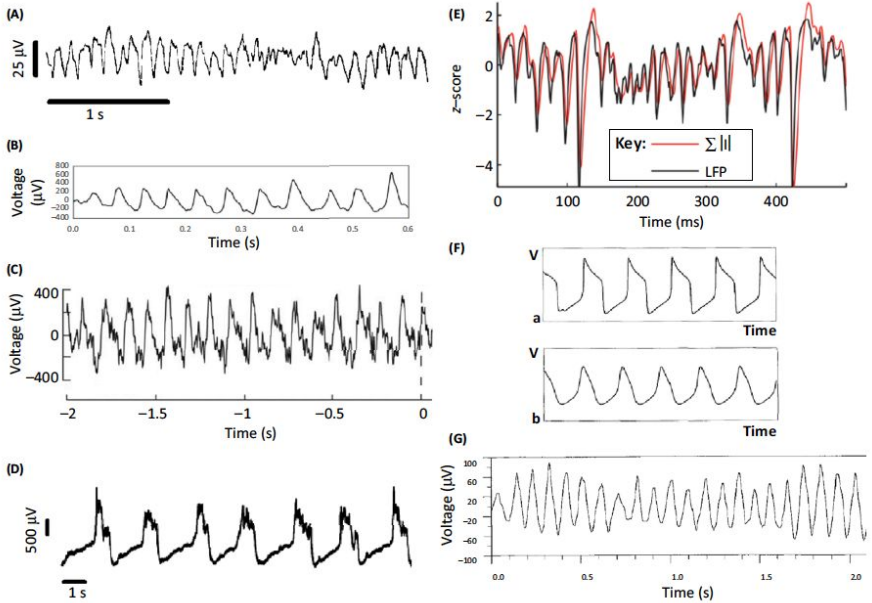
Thesis committee

- Eran Mukamel
- Eric Halgren
- Lara Rangel



NSF GRADUATE RESEARCH FELLOWSHIP PROGRAM

Questions?


(A)
25 µV
1 s
(B)
Voltage (µV)
Time (s)
(C)
Voltage (µV)
Time (s)
(D)
500 µV
1 s
(E)
z-score
Key: ∑|i|
LFP
Time (ms)
(F)
V
a
Time
V
b
Time
(G)
Voltage (µV)
Time (s)


WRAP
INTEGRITY
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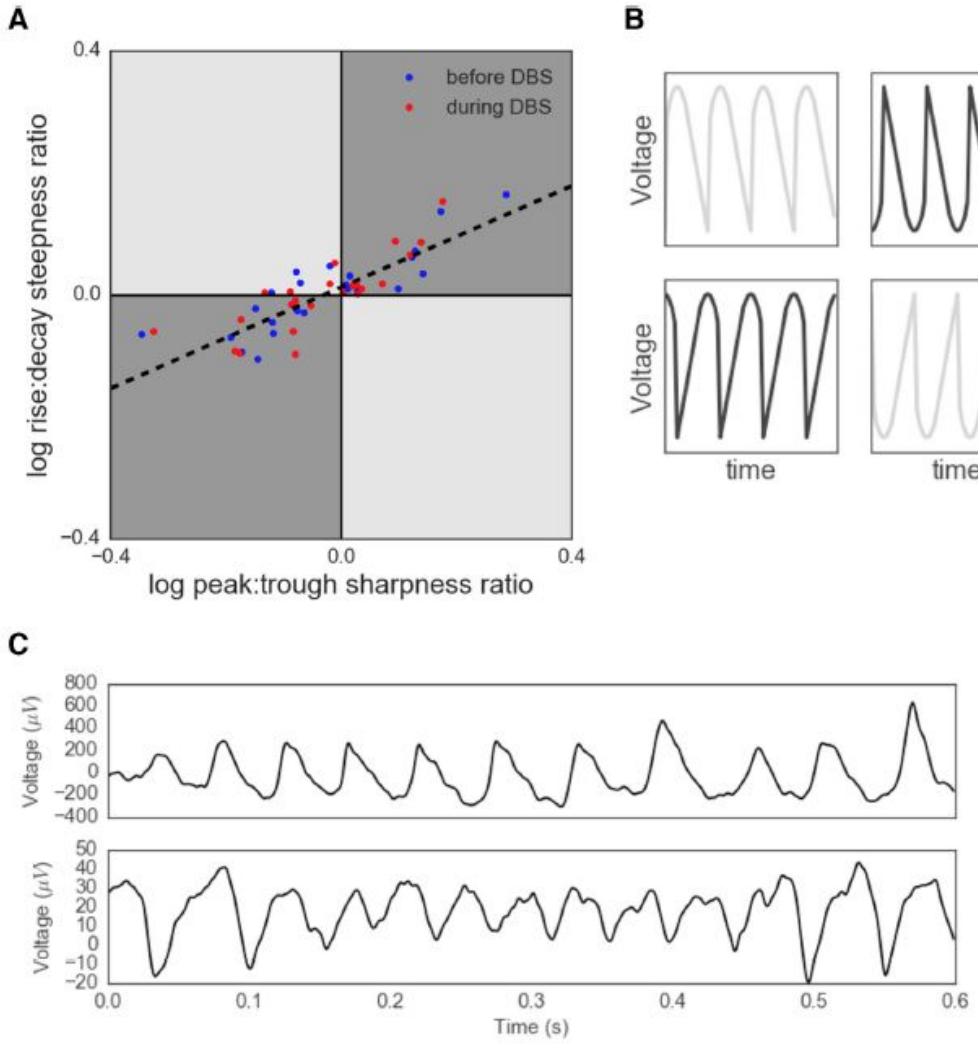
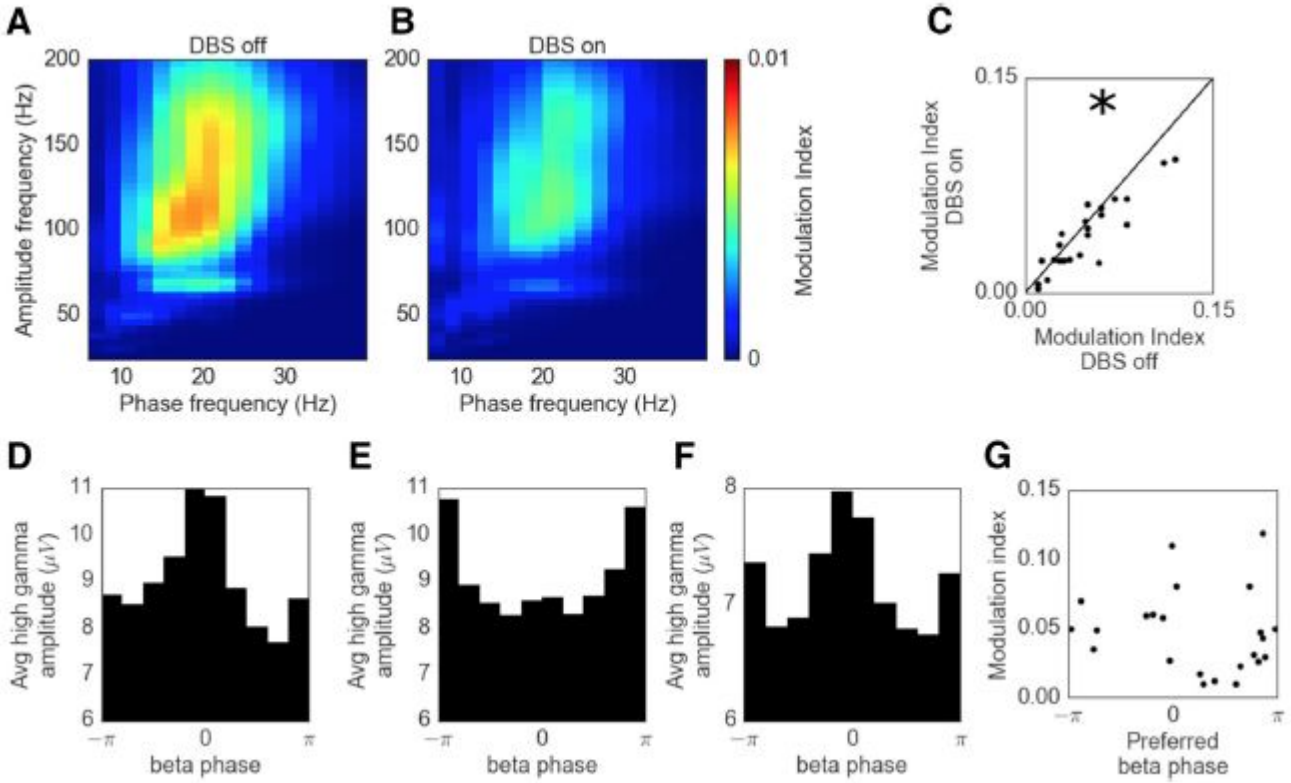
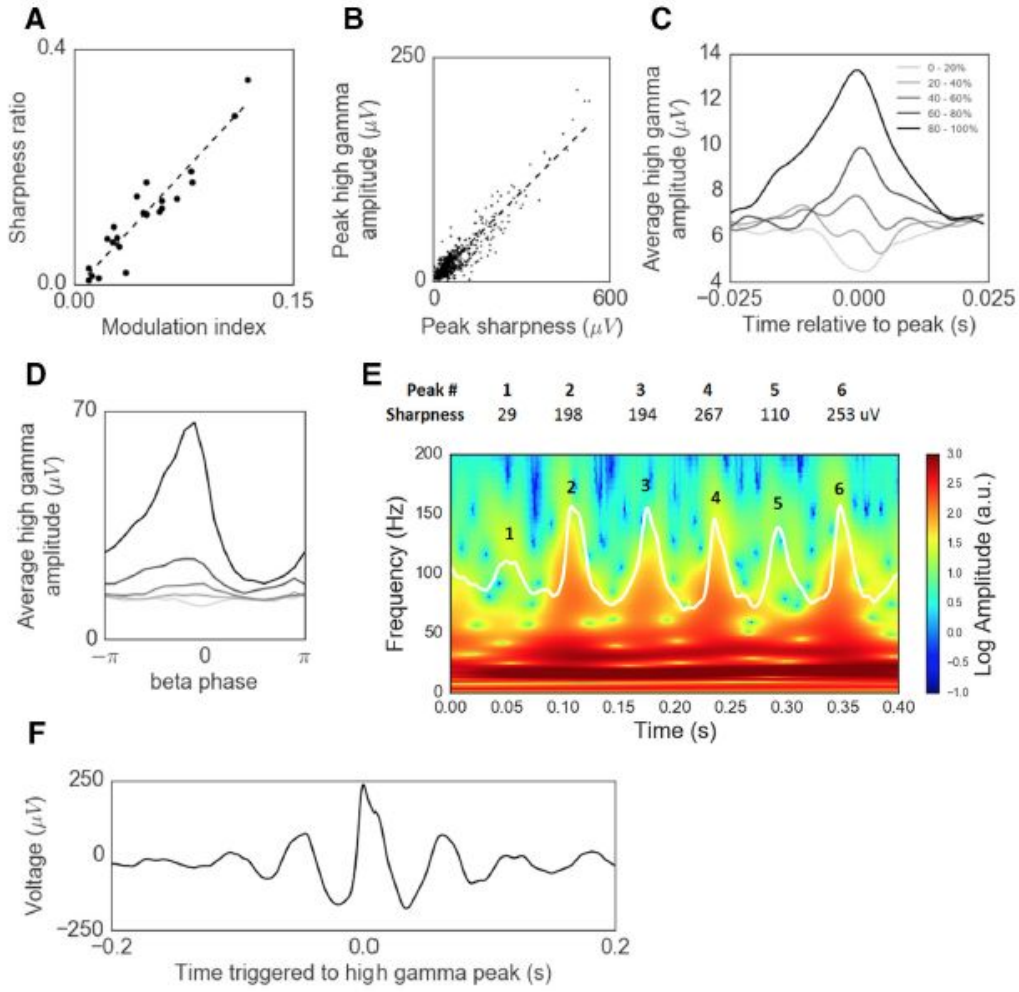
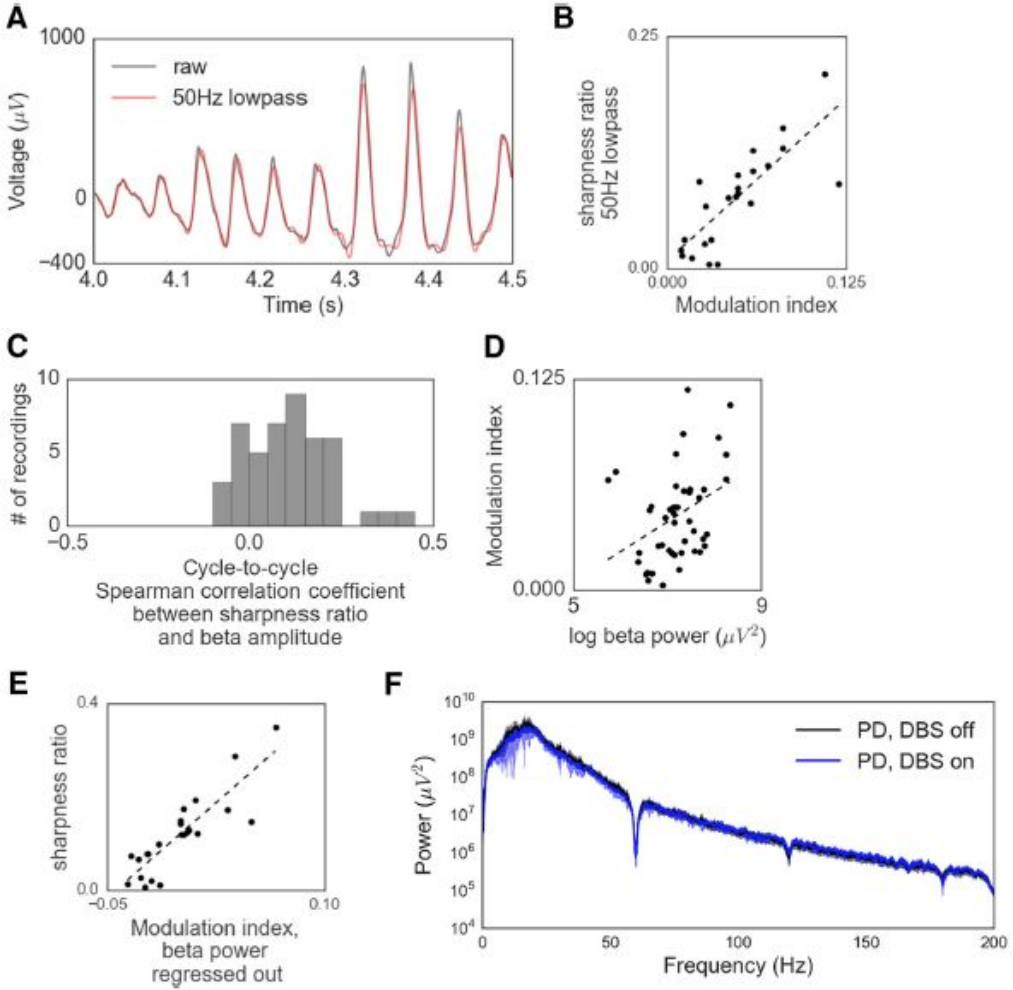
Y

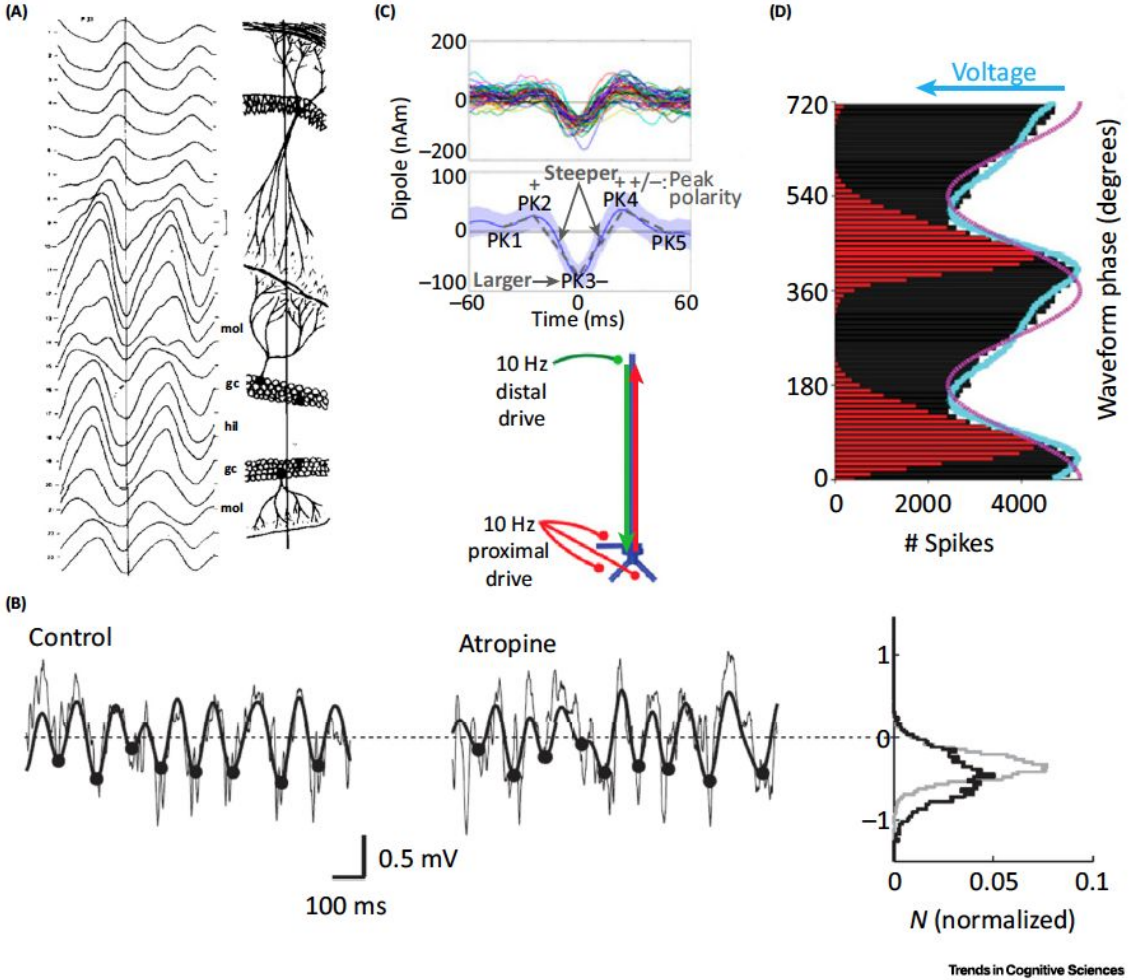
Appendix

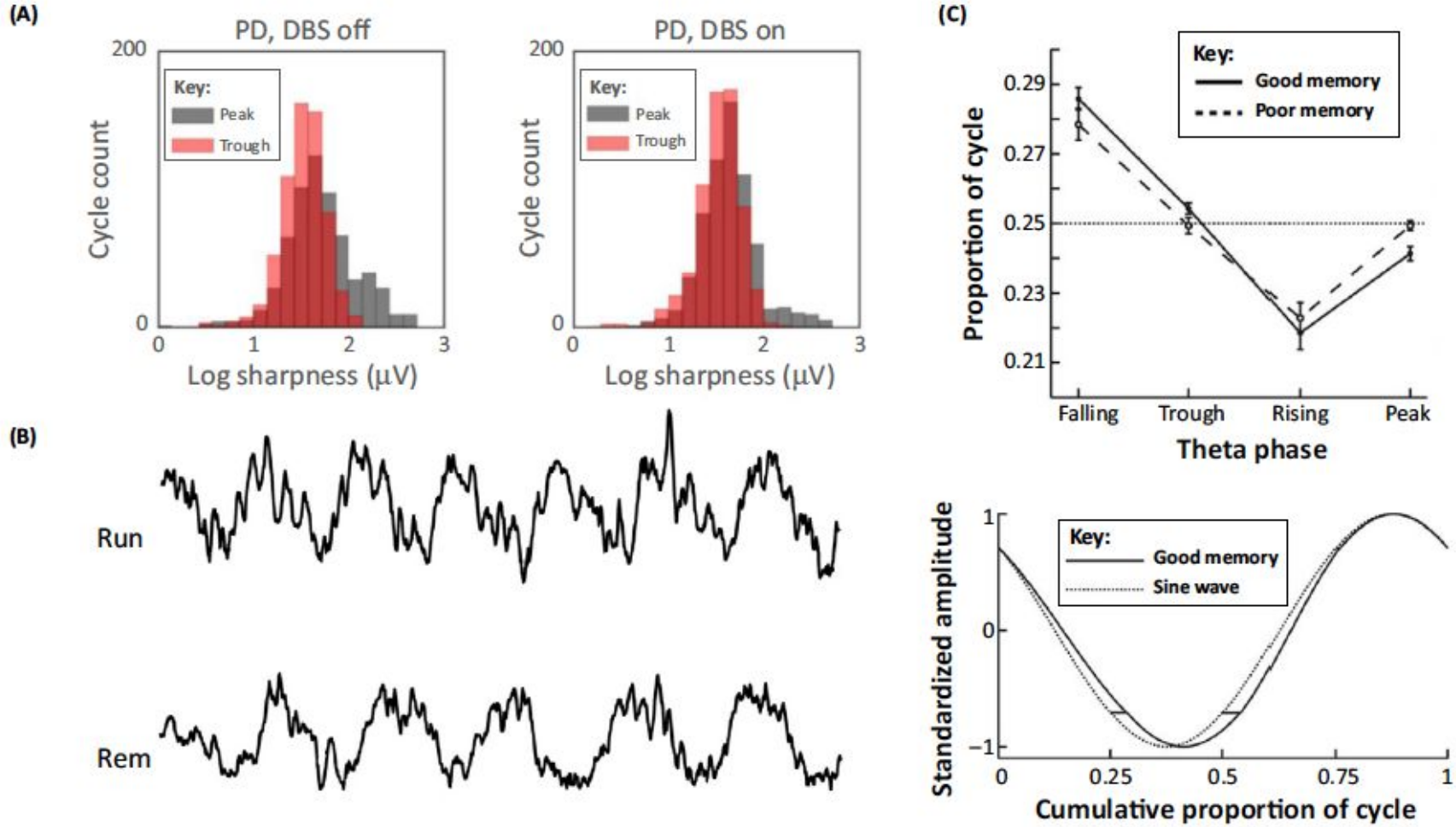

A
0.4
0.0
−0.4
−0.4
0.0
0.4
before DBS
during DBS
log rise:decay steepness ratio
log peak:trough sharpness ratio
B
Voltage
Voltage
time
time
C
800
600
400
200
0
−200
−400
Voltage (μV)
50
40
30
20
10
0
−10
−20
Voltage (μV)
0.0
0.1
0.2
0.3
0.4
0.5
0.6
Time (s)


A
DBS off
200
150
100
50
Amplitude frequency (Hz)
10
20
30
Phase frequency (Hz)
B
DBS on
200
150
100
50
10
20
30
Phase frequency (Hz)
0.01
0
Modulation Index
C
0.15
0.00
Modulation Index
DBS on
0.00
0.15
Modulation Index
DBS off
*
D
11
10
9
8
7
6
Avg high gamma amplitude (μV)
−π
0
π
beta phase
E
11
10
9
8
7
6
Avg high gamma amplitude (μV)
−π
0
π
beta phase
F
8
7
6
Avg high gamma amplitude (μV)
−π
0
π
beta phase
G
0.15
0.10
0.05
0.00
Modulation index
−π
0
π
Preferred
beta phase

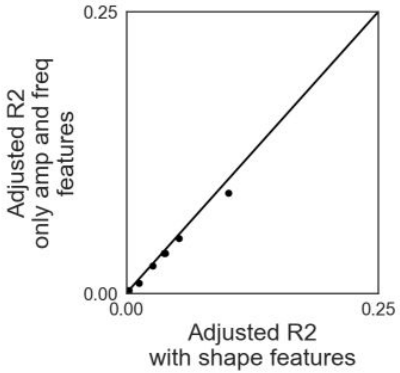

A
0.4
0.0
0.00
0.15
Sharpness ratio
Modulation index
B
250
0
0
600
Peak high gamma amplitude (μV)
Peak sharpness (μV)
C
14
12
10
8
6
4
−0.025
0.000
0.025
Average high gamma amplitude (μV)
Time relative to peak (s)
0 - 20%
20 - 40%
40 - 60%
60 - 80%
80 - 100%
D
70
0
−π
0
π
Average high gamma amplitude (μV)
beta phase
E
Peak #
1
2
3
4
5
6
Sharpness
29
198
194
267
110
253 uV
200
150
100
50
0
Frequency (Hz)
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.35
0.40
Time (s)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
Log Amplitude (a.u.)
F
250
0
−250
−0.2
0.0
0.2
Voltage (μV)
Time triggered to high gamma peak (s)

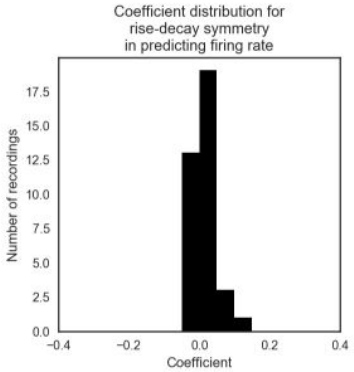

A
1000
raw
50Hz lowpass
Voltage (μV)
0
−400
4.0
4.1
4.2
4.3
4.4
4.5
Time (s)
B
0.25
sharpness ratio
50Hz lowpass
0.00
0.000
0.125
Modulation index
C
10
# of recordings
5
0
−0.5
0.0
0.5
Cycle-to-cycle
Spearman correlation coefficient
between sharpness ratio
and beta amplitude
D
0.125
Modulation index
0.000
5
9
log beta power (μV²)
E
0.4
sharpness ratio
0.0
−0.05
0.10
Modulation index,
beta power
regressed out
F
10¹⁰
10⁹
10⁸
10⁷
10⁶
10⁵
10⁴
Power (μV²)
PD, DBS off
PD, DBS on
0
50
100
150
200
Frequency (Hz)

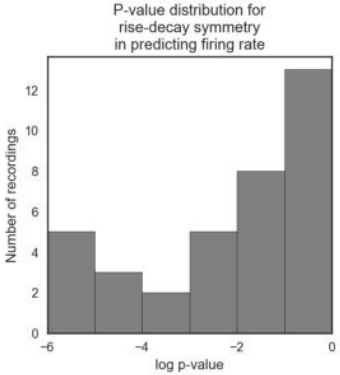

(A)
mol
gc
hil
gc
mol
(C)
200
0
−200
Dipole (nAm)
100
0
−100
Steeper
+
PK2
PK4
+ + /− : Peak polarity
PK1
PK5
Larger
PK3−
−60
0
60
Time (ms)
10 Hz distal drive
10 Hz proximal drive
(D)
Voltage
720
540
360
180
0
Waveform phase (degrees)
0
2000
4000
Spikes
(B)
Control
Atropine
0.5 mV
100 ms
1
0
−1
0
0.05
0.1
N (normalized)
Trends in Cognitive Sciences


(A)
PD, DBS off
PD, DBS on
Key:
Peak
Trough
Cycle count
200
0
0
1
2
3
Log sharpness (μV)
(B)
Run
Rem
(C)
Key:
Good memory
Poor memory
Proportion of cycle
0.29
0.27
0.25
0.23
0.21
Falling
Trough
Rising
Peak
Theta phase
Key:
Good memory
Sine wave
Standardized amplitude
1
0
−1
0
0.25
0.5
0.75
1
Cumulative proportion of cycle

3. Does waveform shape and CA1 pyramidal firing rate







Feature set	R^2 (adjusted)
Amplitude, frequency	.027
+ Rise-decay symmetry	.030
All shape features (symmetry, sharpness)	.049