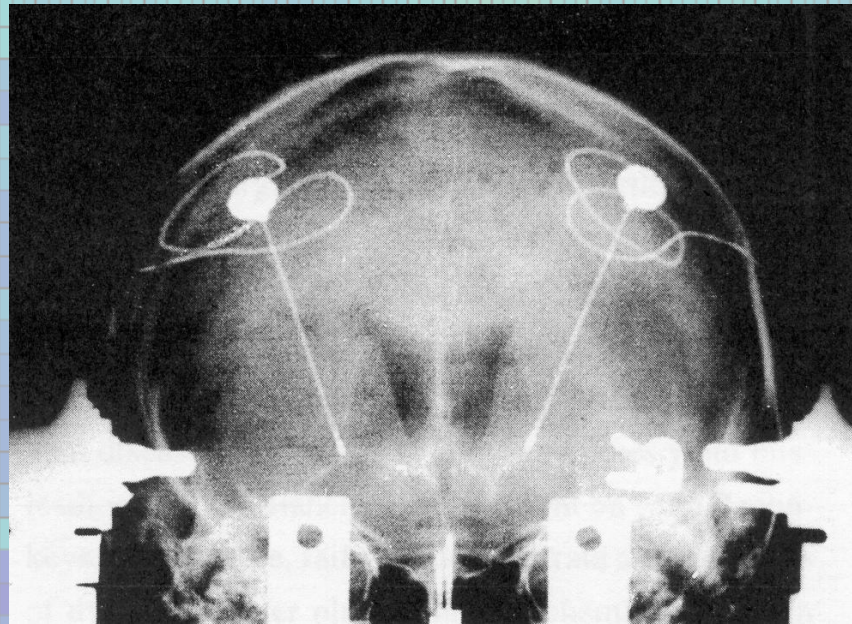


# Effects of nicotine on neuronal firing patterns in human subthalamic nucleus



Kim Scott

Mentor: Henry Lester

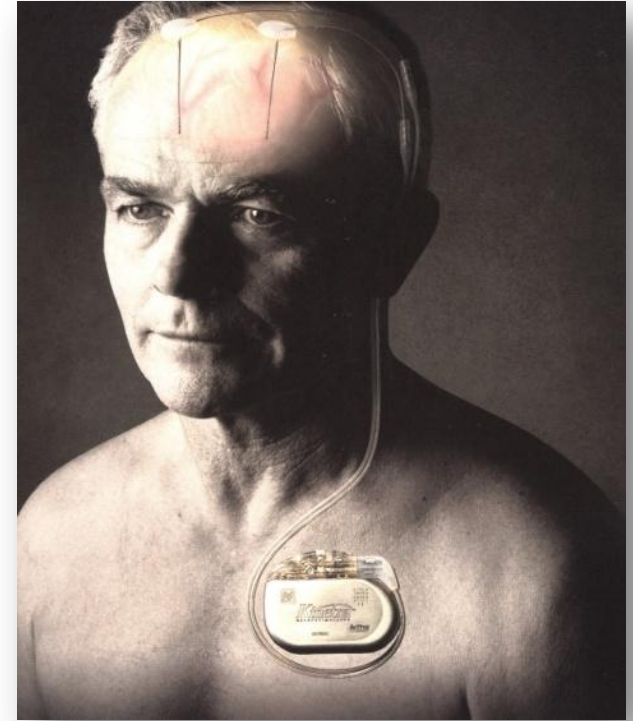
SURF seminar, January 15, 2009

# Smoking tobacco protects against Parkinson's Disease (PD).

- Identical twins: 10 pack-years' difference! (Tanner et al. 2002)
- Risk increases with years since quitting (Ritz et al. 2007)
- Nicotine has a protective effect in culture and animal models (Quik et al 2007)

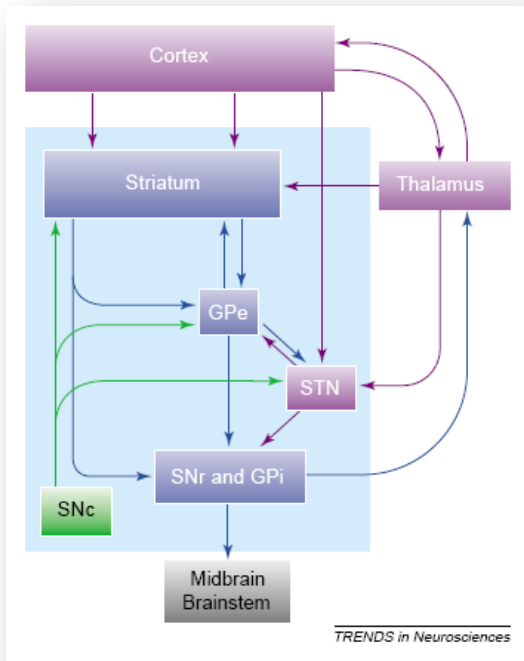
Conclusion: Chronic nicotine prevents the degeneration of dopaminergic neurons in the substantia nigra.

# Deep brain stimulation in PD

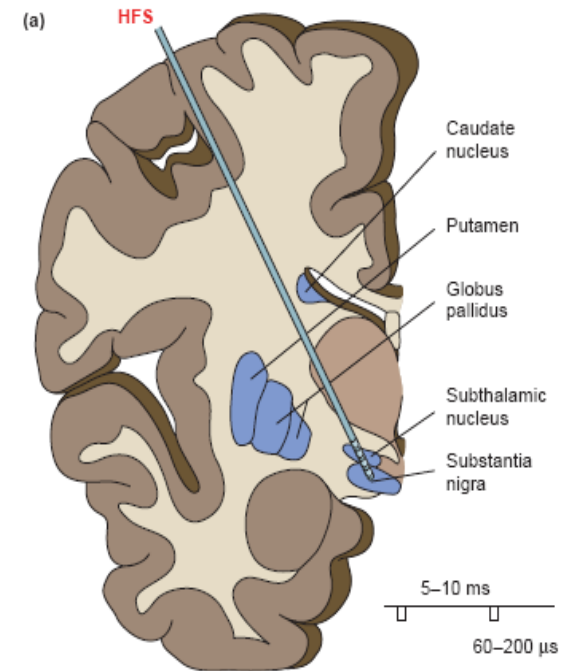


Electrical stimulation of the subthalamic nucleus (STN) at 120-180 Hz immediately relieves motor symptoms of PD.

# Deep brain stimulation in PD



Bevan et al. 2002



Garcia et al. 2005

Why is this important to *us*?

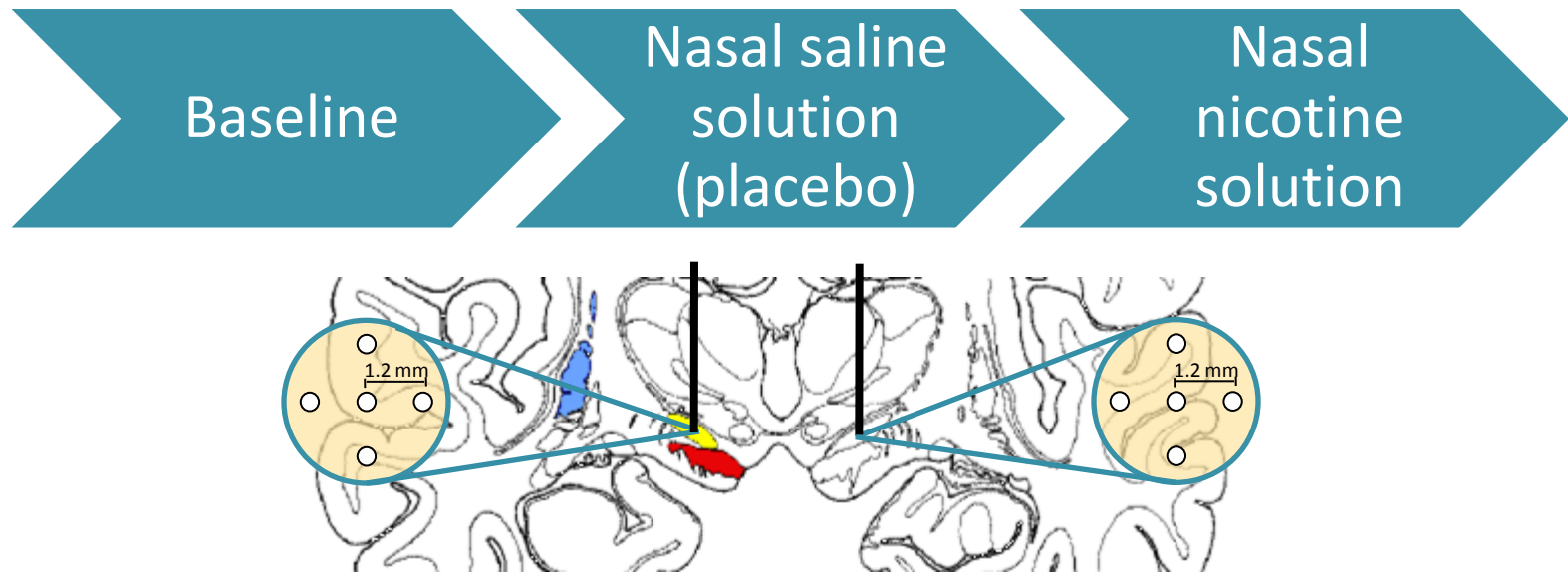
- It's an ethical reason to put electrodes in human brains
- Suggests a focus on subthalamic nucleus (STN)

# How does nicotine affect firing patterns in STN: “What changes?”

- Experimental protocol
- Spike detection and sorting
- 1-2 Hz oscillation
- Hope for the future



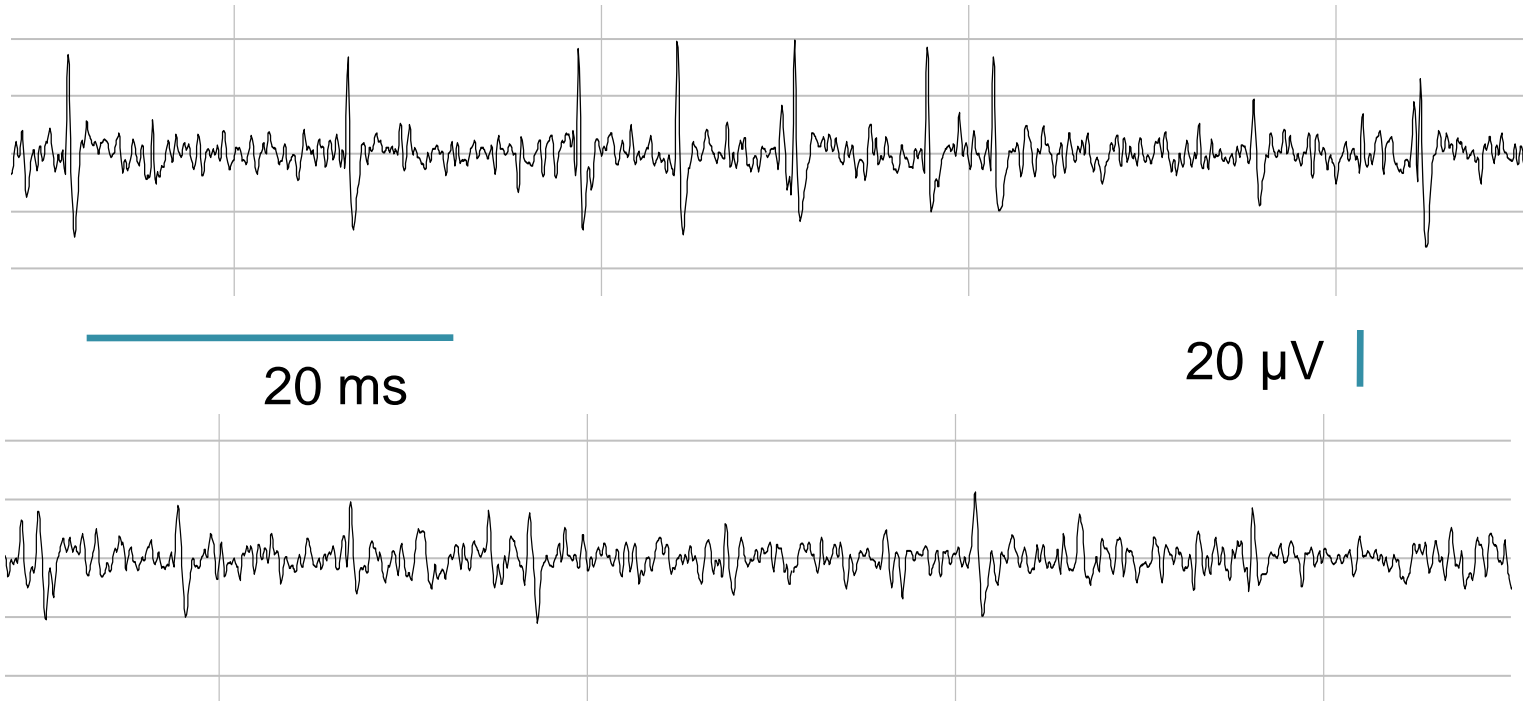
# Recording procedure



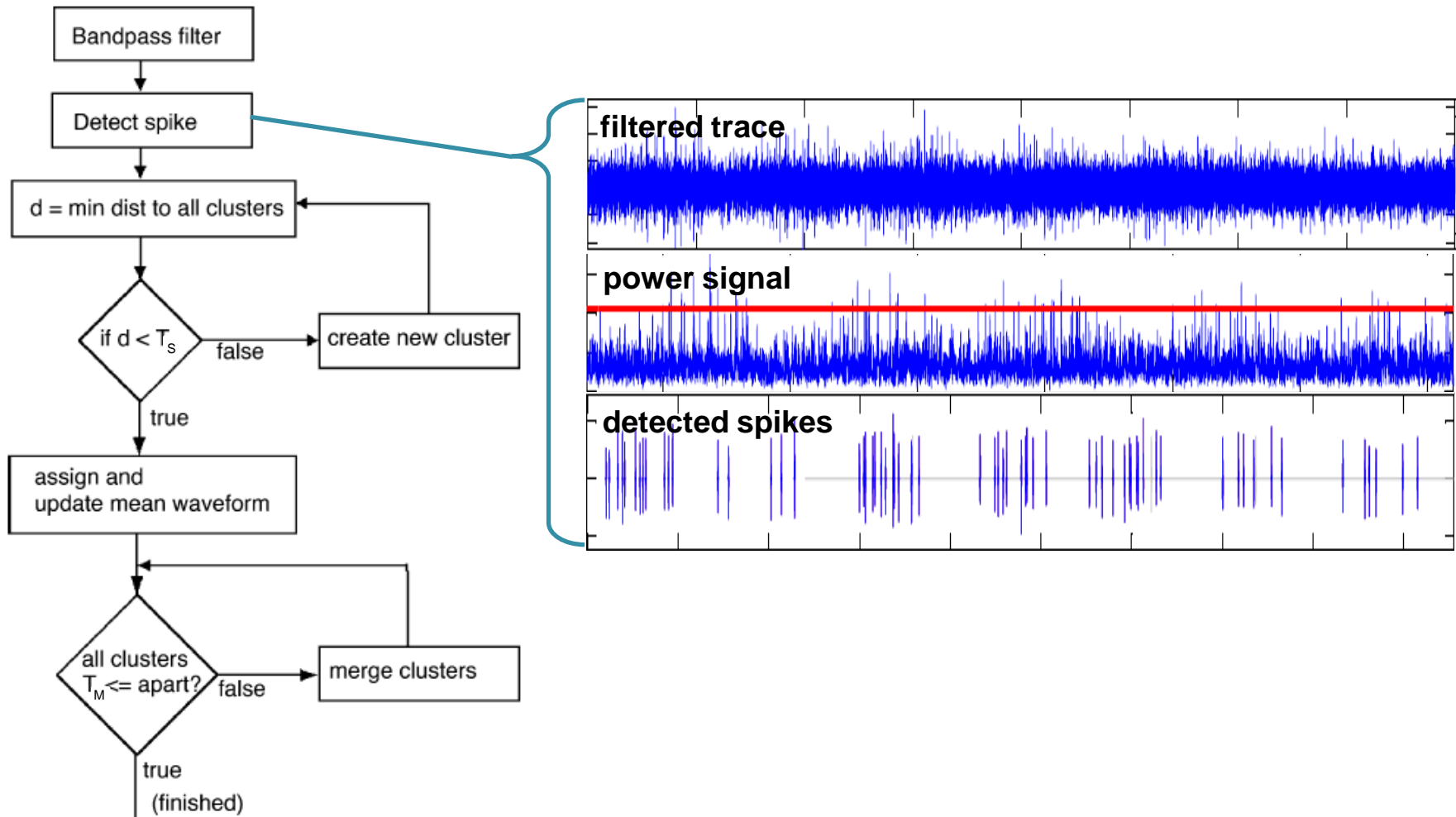
Currently available STN recordings:

- 8 patients (2 smokers)
- Placebo recordings in all but first two patients. Active placebo in newest patient!
- Variable lengths of recording, ~5 minutes total.

# Spike detection isn't automatic



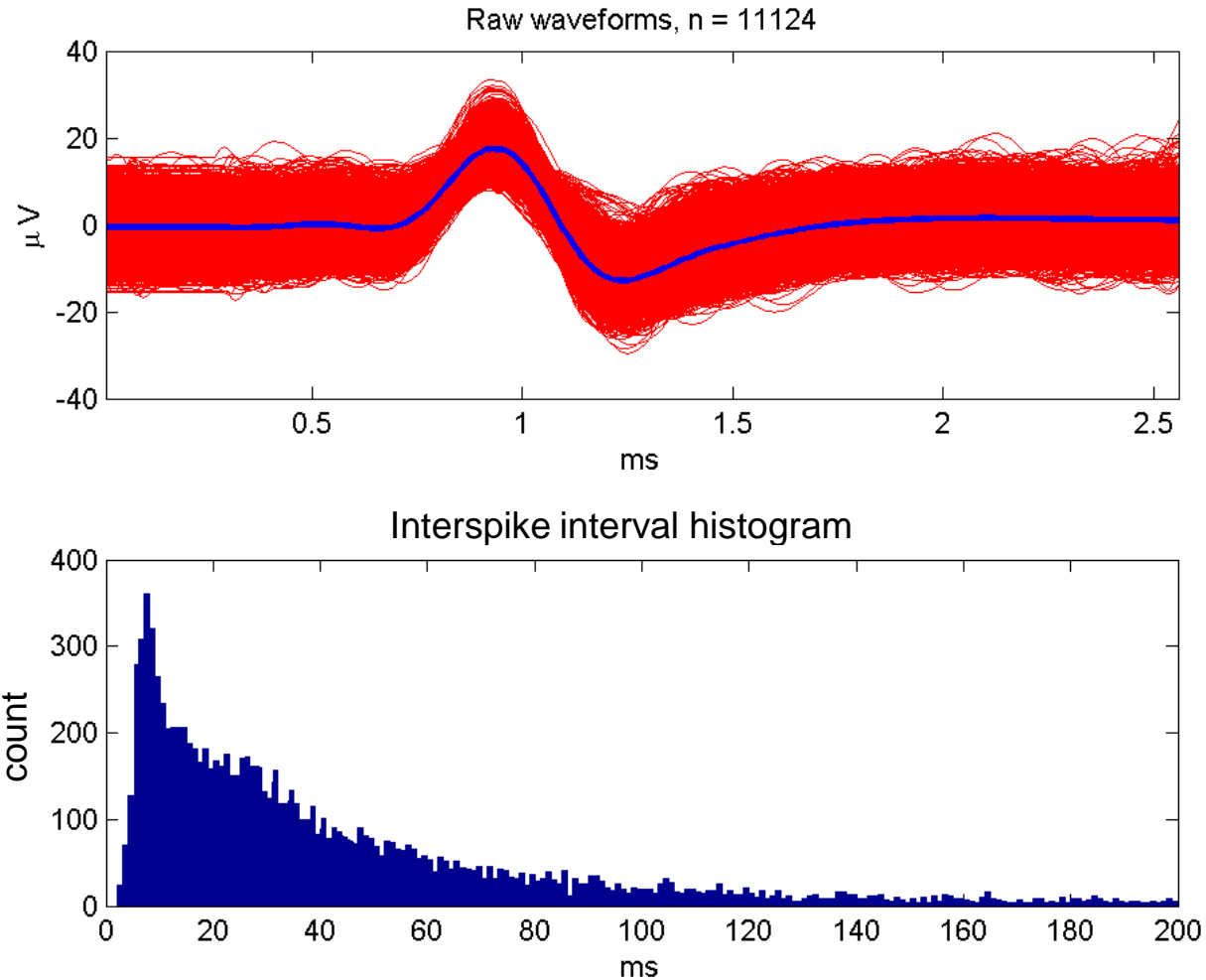
# Osort: spike detection and sorting



Rutishauser et al. 2006



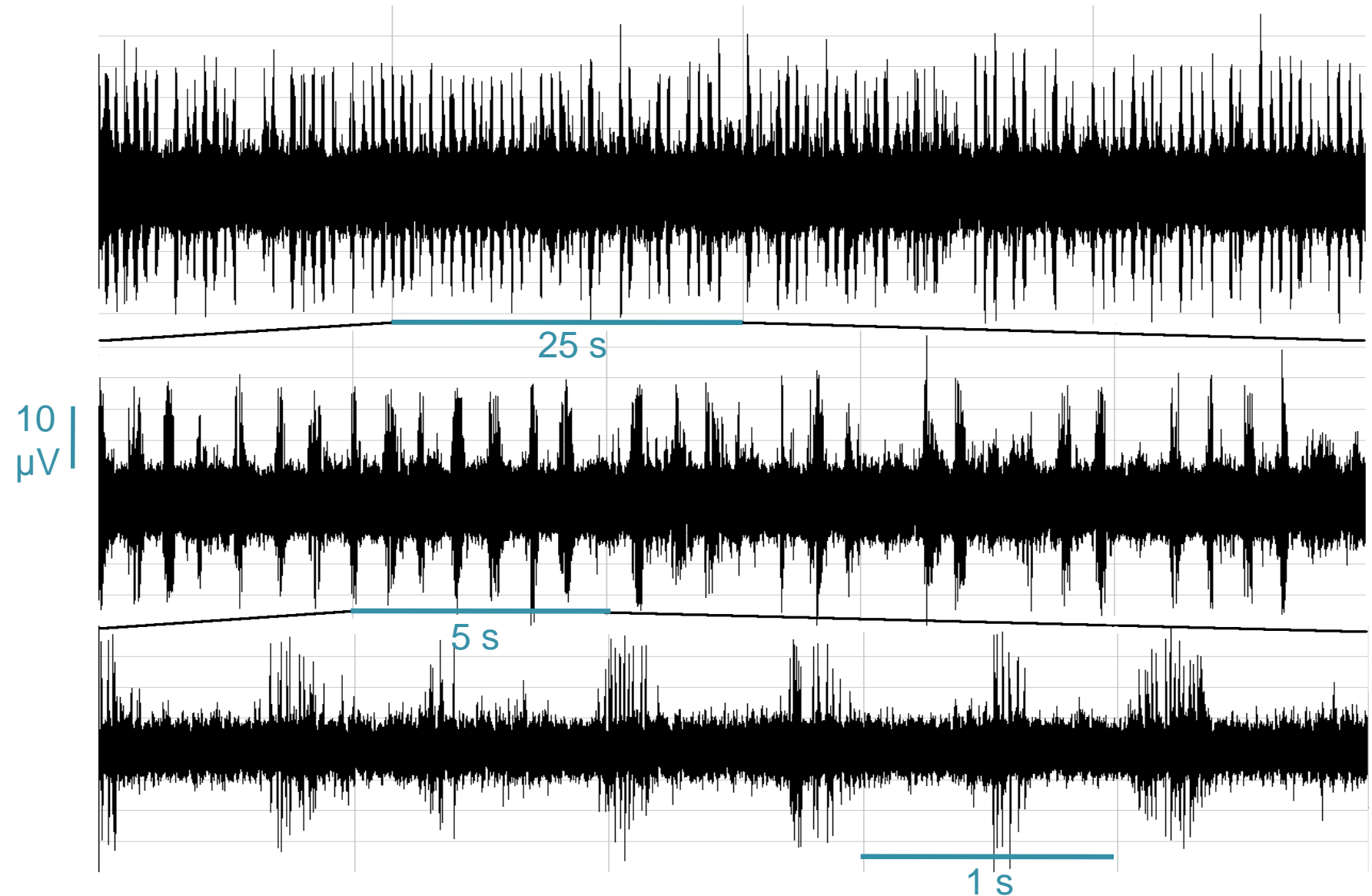
# Sample sorted cluster: LUD ch. 2



# Nothing obvious changes.

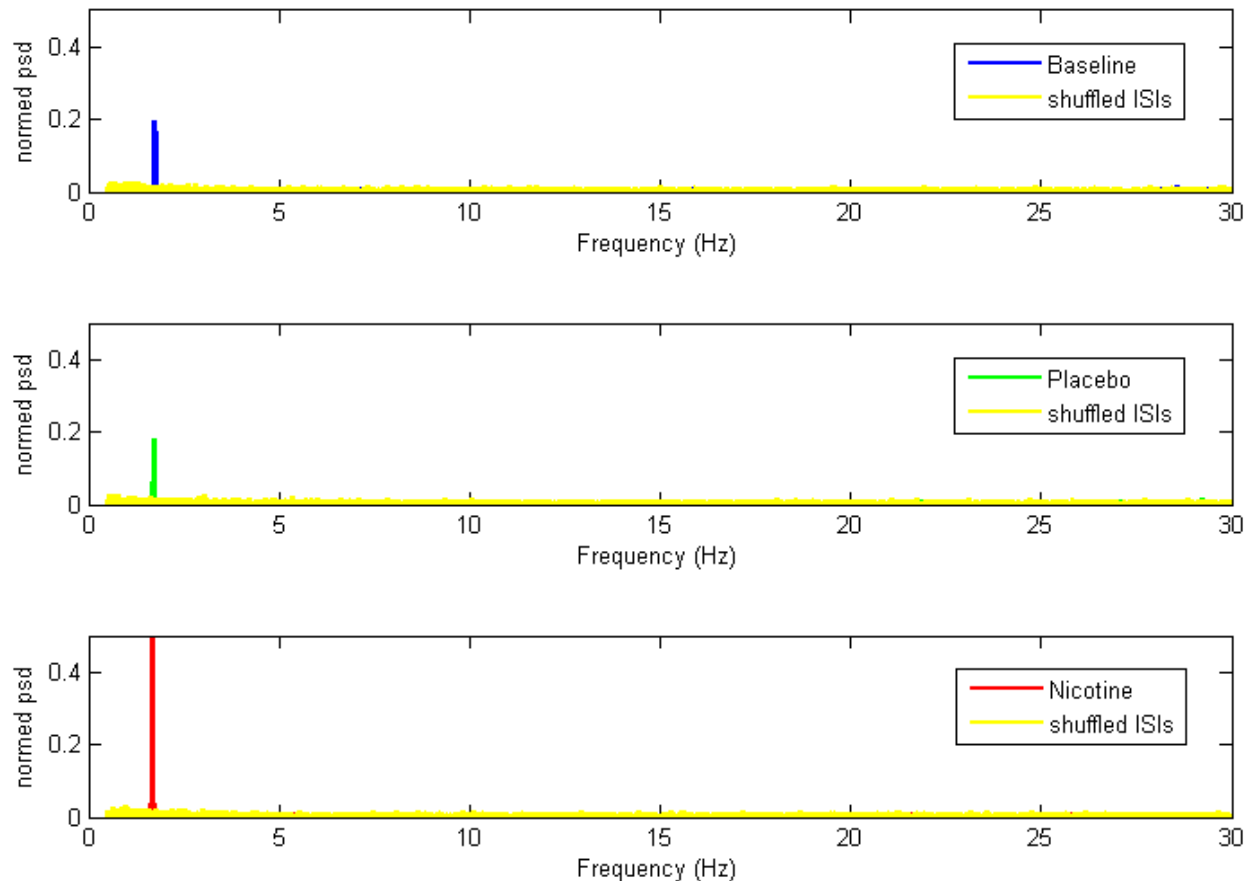
- Peak amplitude, variation therein, variation in shape of waveform
- Firing rate, coefficient of variation
- Burst propensity
- Connections among these factors

# 1-2 Hz bursting oscillation is real.

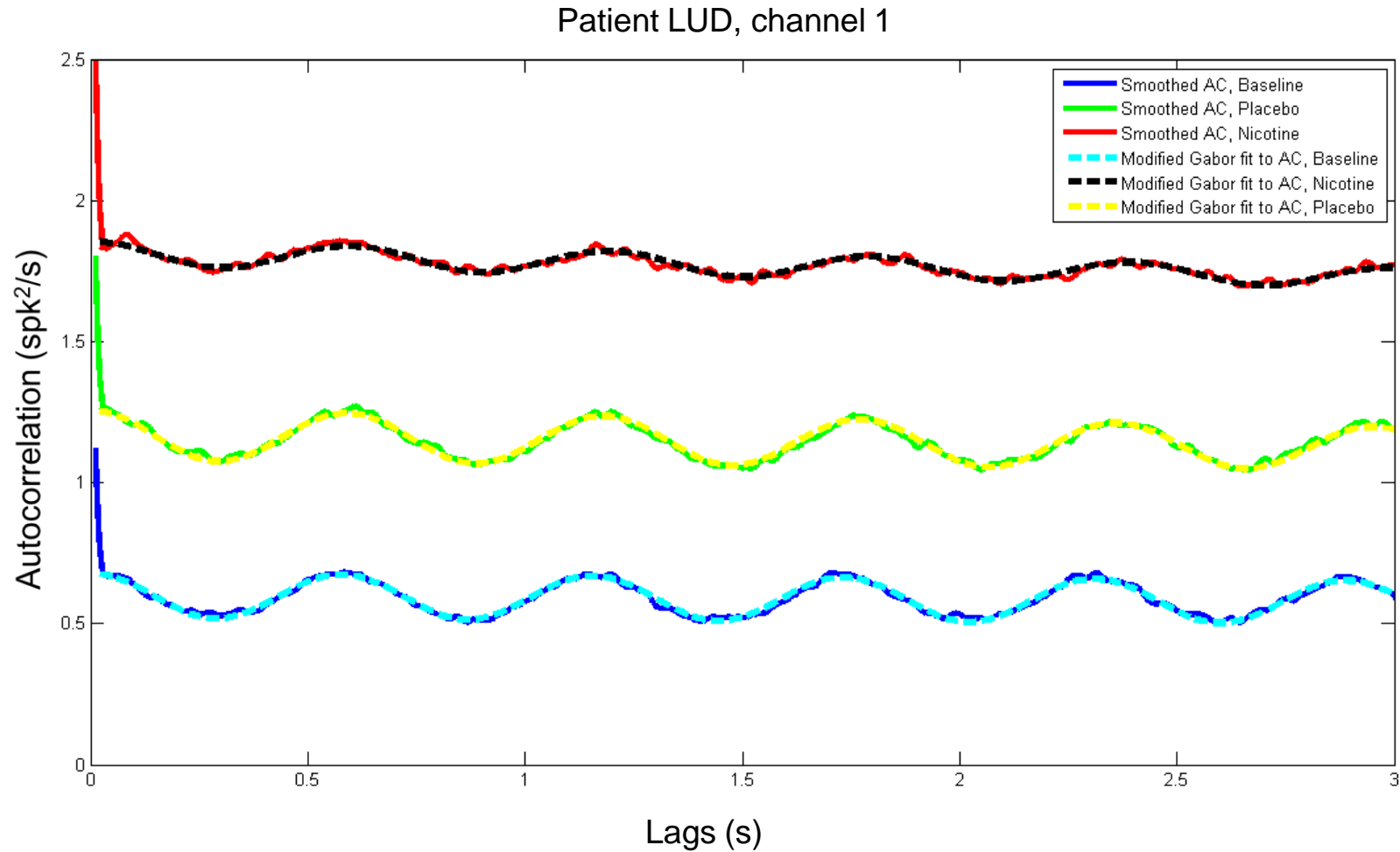


# Firing of an STN neuron isn't a renewal process.

Power spectral density, PDLUD, cluster 1616



# The autocorrelation function

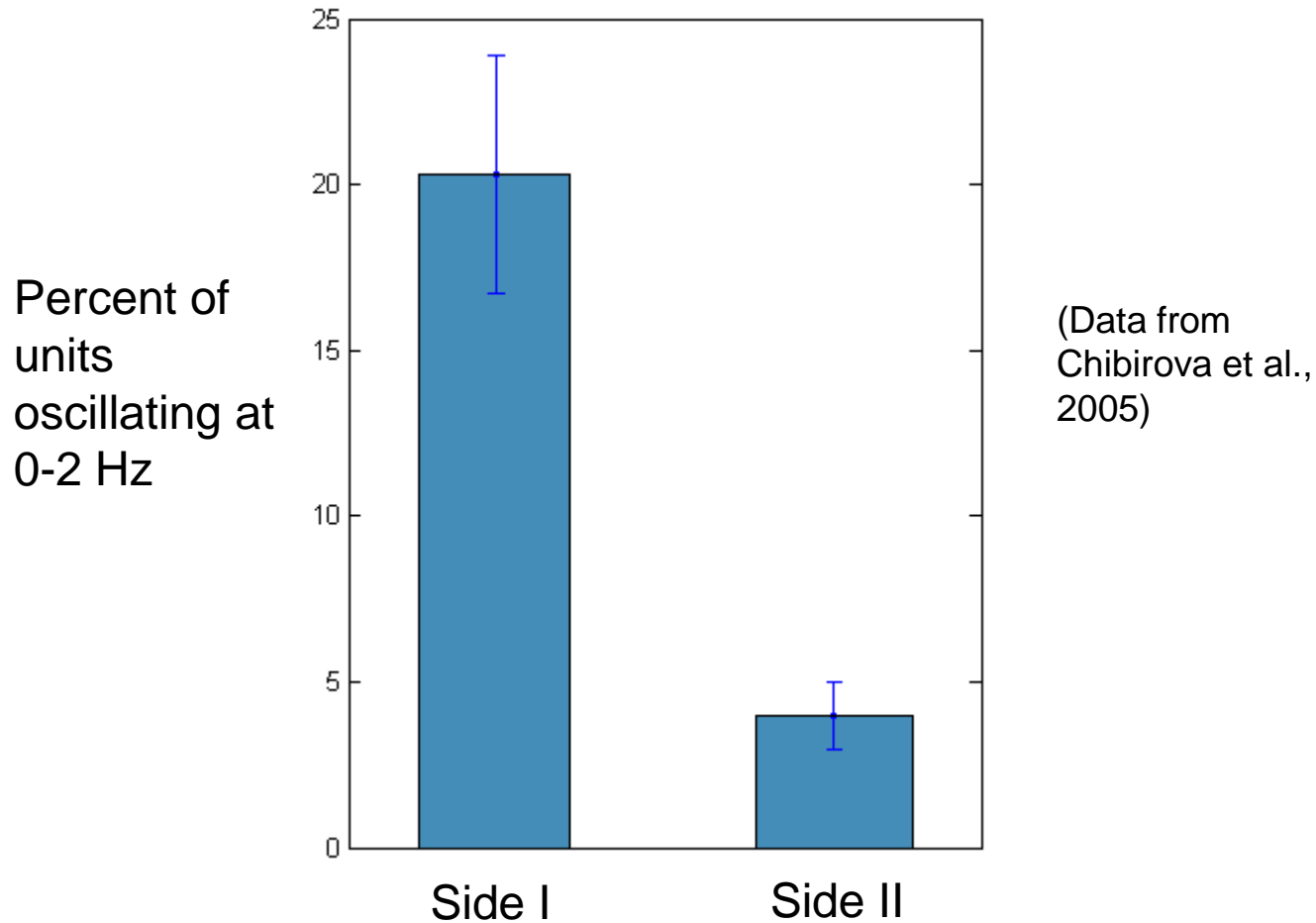


# Properties of 1-2 Hz oscillation

- Statistically significant oscillation detected in 30 of 47 clusters
- Tightly clustered frequencies across channels in the same patient: average variance 0.0022 Hz
- Consistent changes across channels with placebo and nicotine
- Units tend to synchronize in or out of phase
- Almost unique to our group

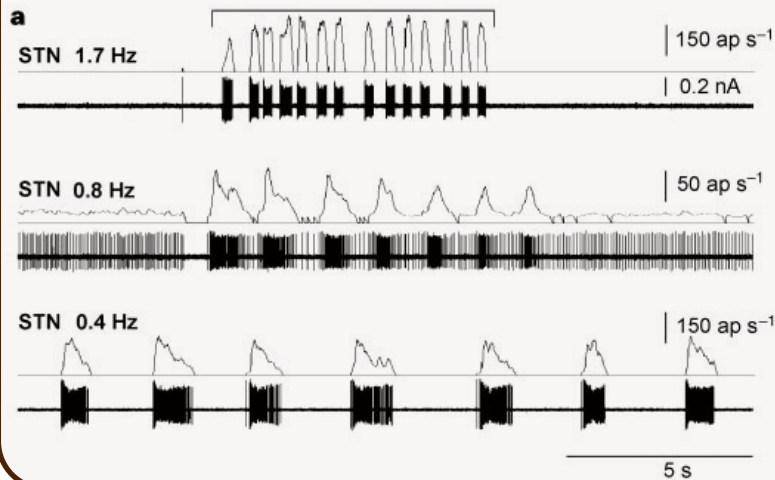


# Brief contralateral stimulation abolishes 1-2 Hz oscillation



# Possible sources of oscillation

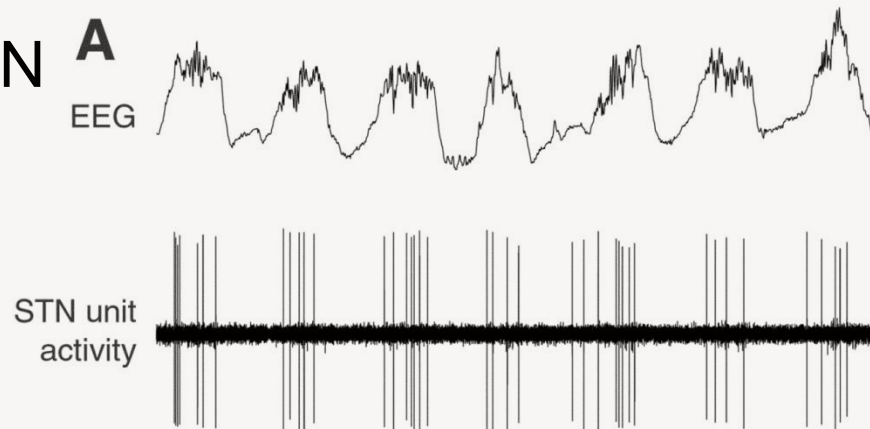
Plenz & Kital 1999:



- STN oscillates in culture!
- STN-GPe cut: abolishes synchronization and oscillation
- STN-cortex cut: centers frequency at 0.8 Hz

Magill et al. 2001:

- ~ 1 Hz oscillation in STN phase-locked to slow-wave activity in cortex
- Bursting is more intense in dopamine depletion

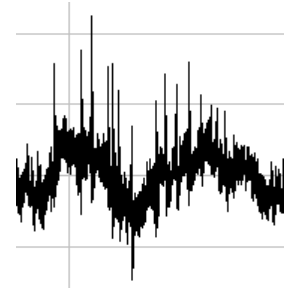


# Nothing obvious changes.

- Peak amplitude, variation therein, variation in shape of waveform
- Firing rate, coefficient of variation
- Burst propensity
- Strength of oscillation (several measures)
- Variation in oscillation timing
- Frequency of oscillation
- Phase variance, strength, or frequency of synchronization
- Connections among these

# Next steps in analysis

- Measures of synchrony across all clusters
- Higher-order features: clustering of bursts
- Connections between low-frequency components of raw trace and burst timing



## Future recordings



# Acknowledgments

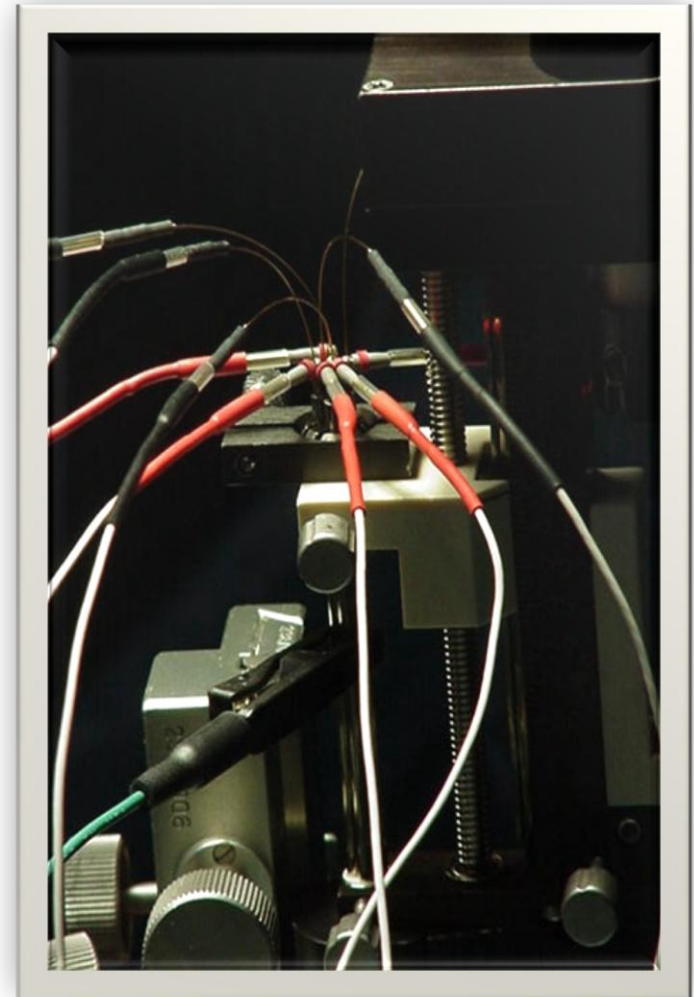
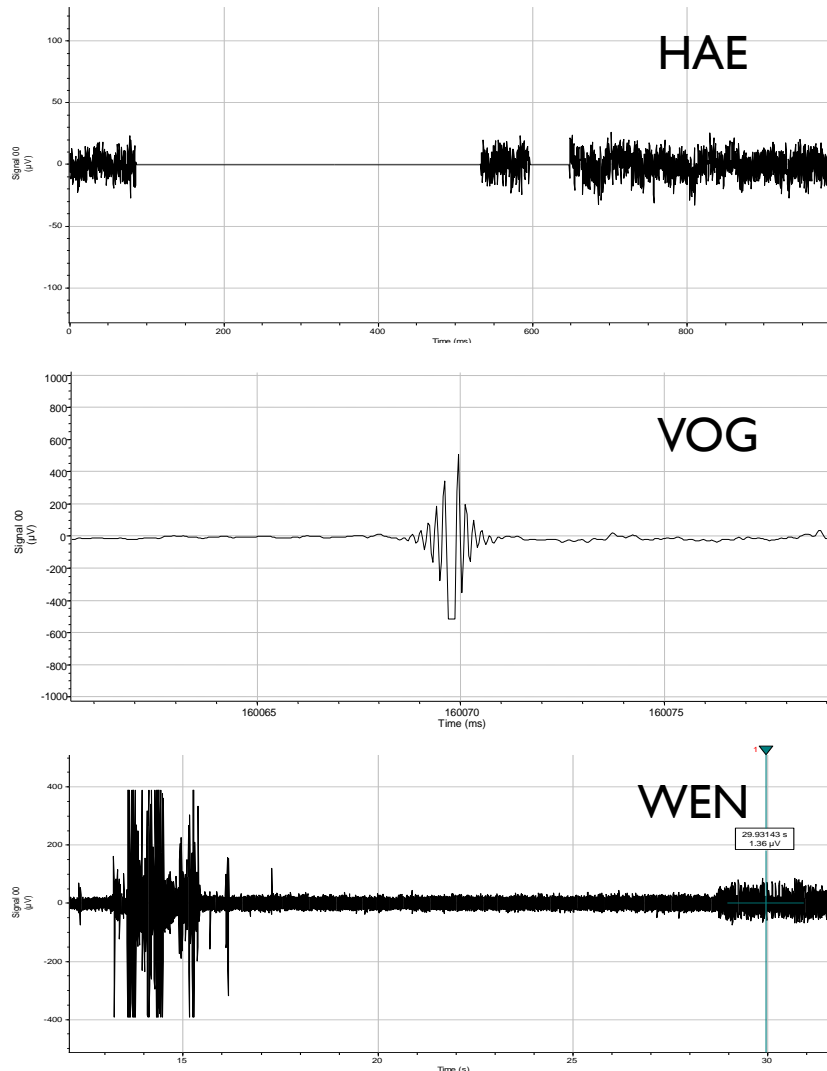
- Henry Lester
- Johannes Schwarz (Universität Leipzig)
- Shawna Frazier
- Ueli Rutishauser
- Pam Fong
- Lester lab
- the Caltech SURF program and Richter Memorial Fund

# References

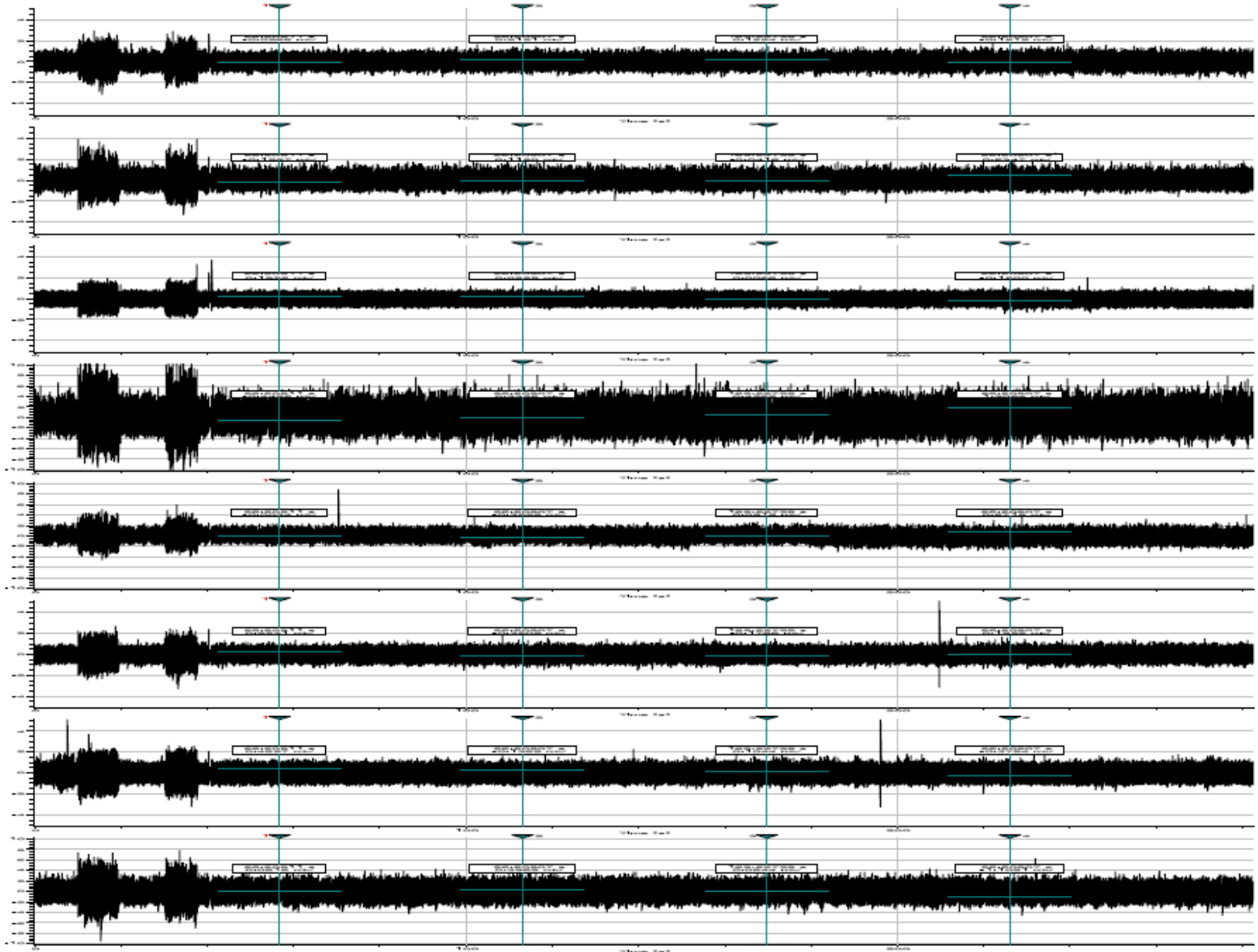
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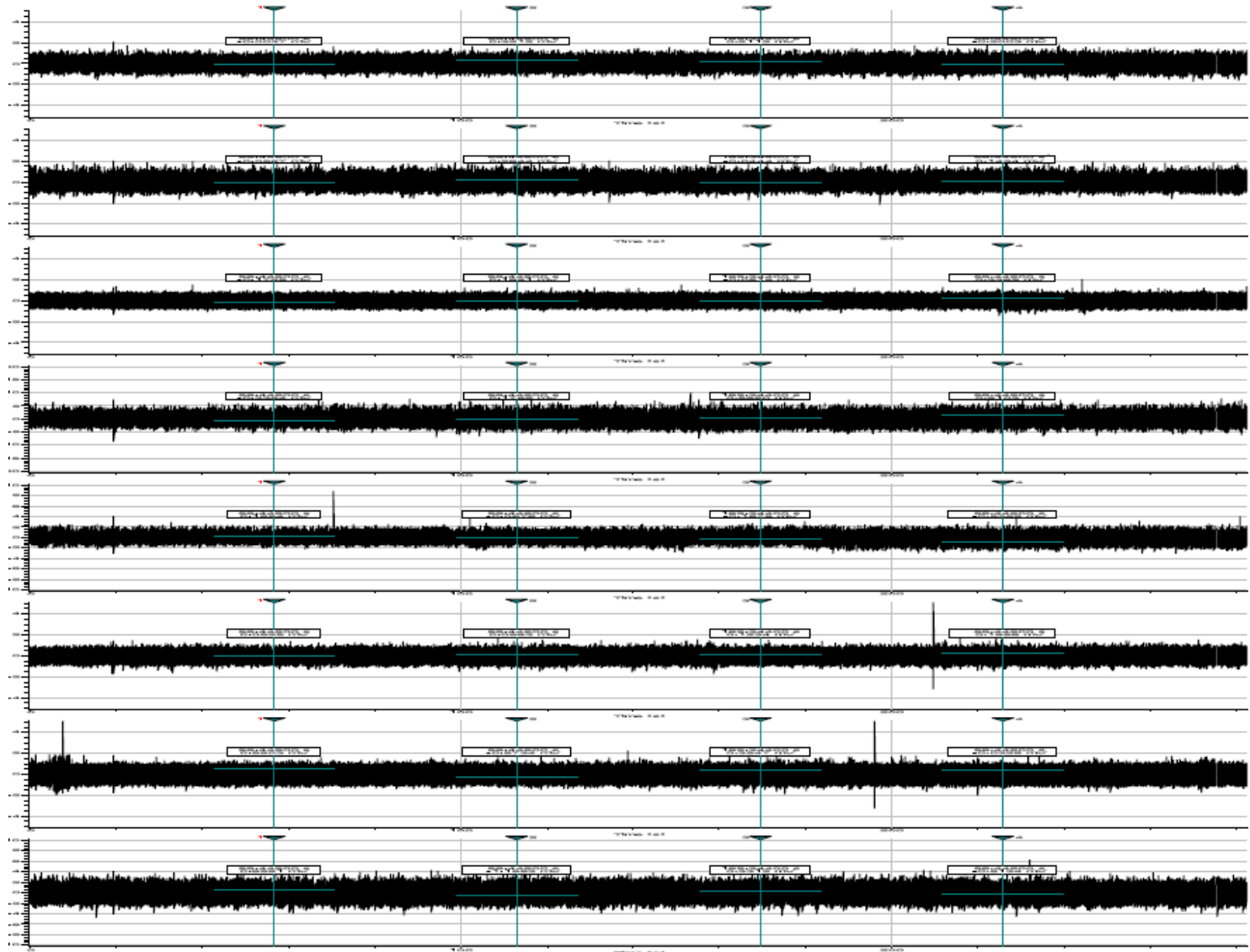
# Challenge: artifact ID & correction



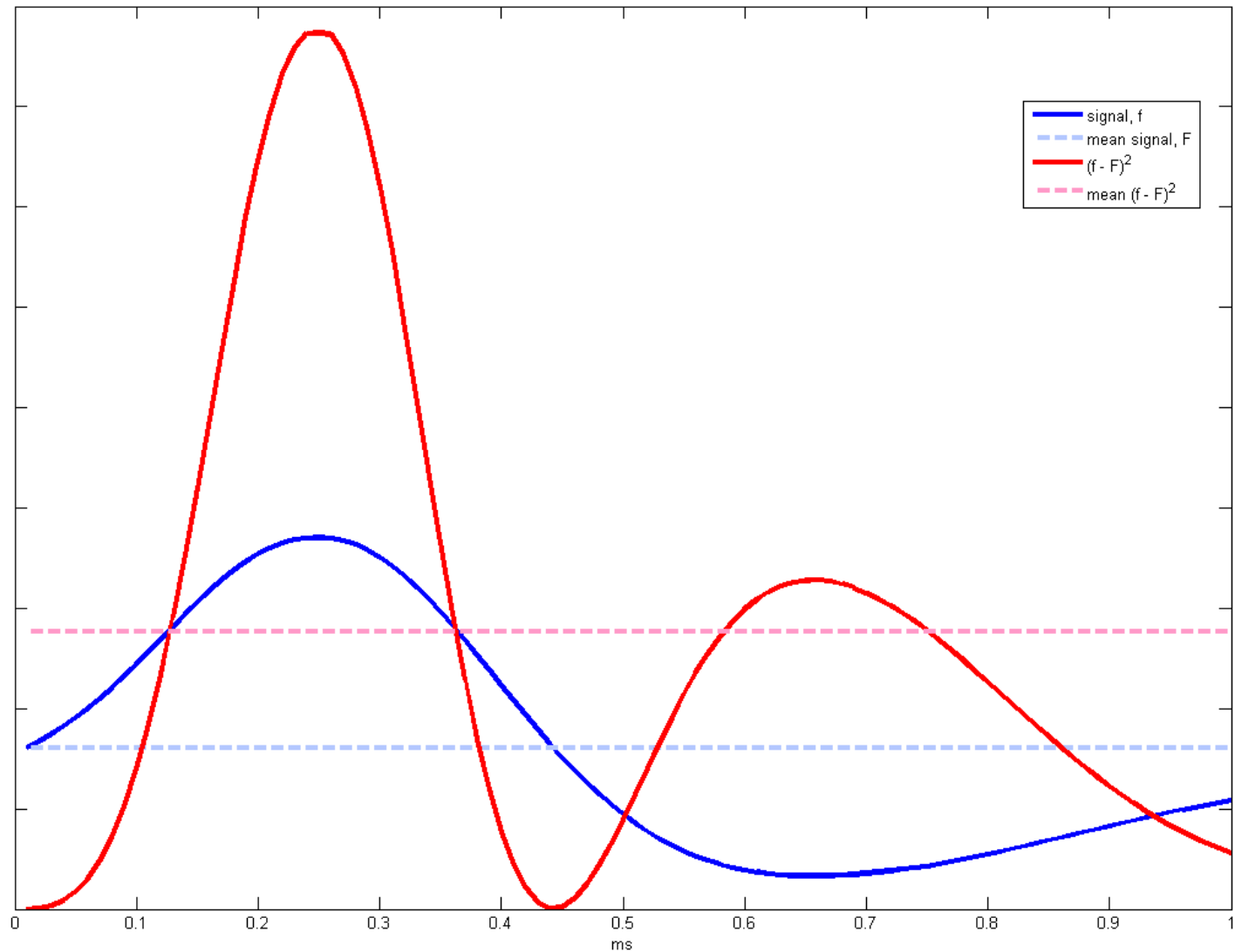
# Gain changes during recording



... are removable!

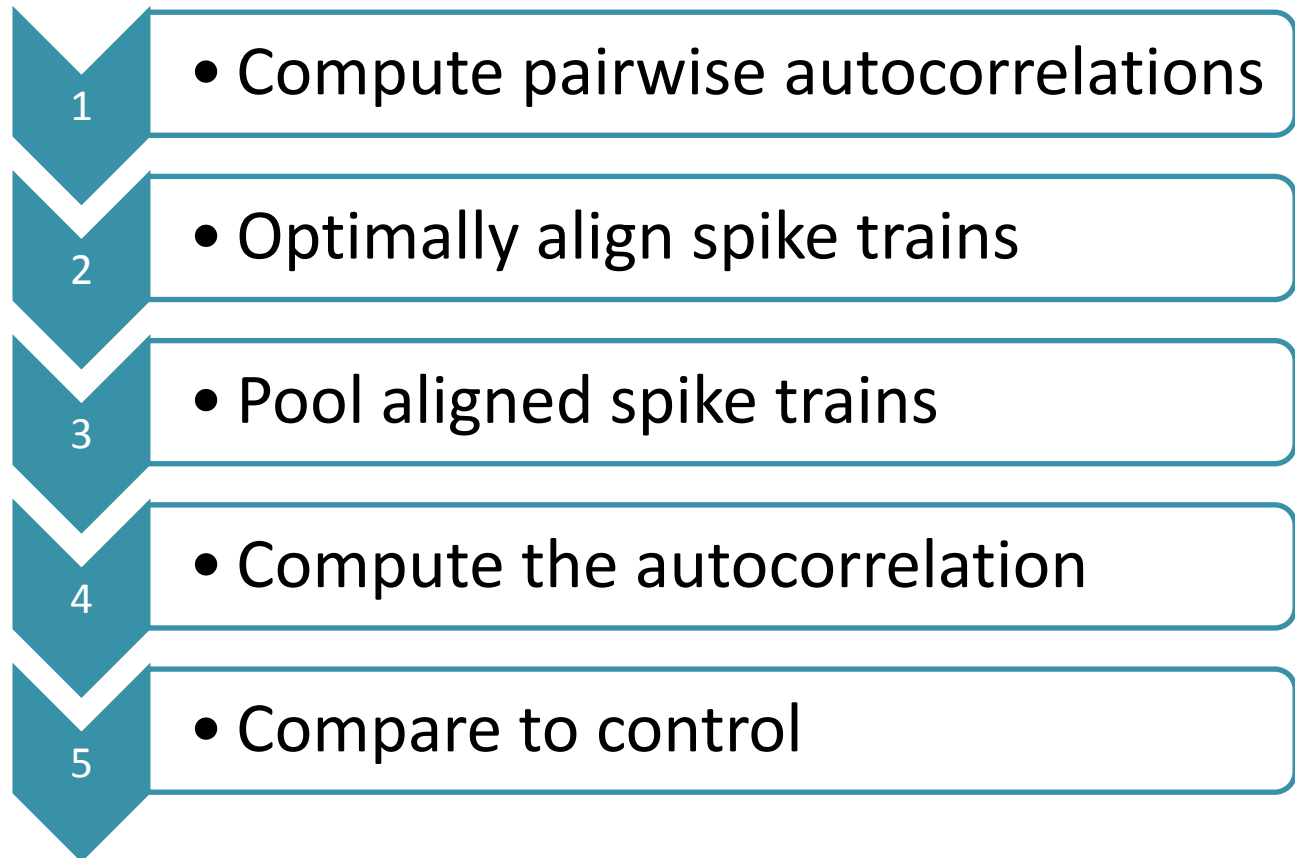


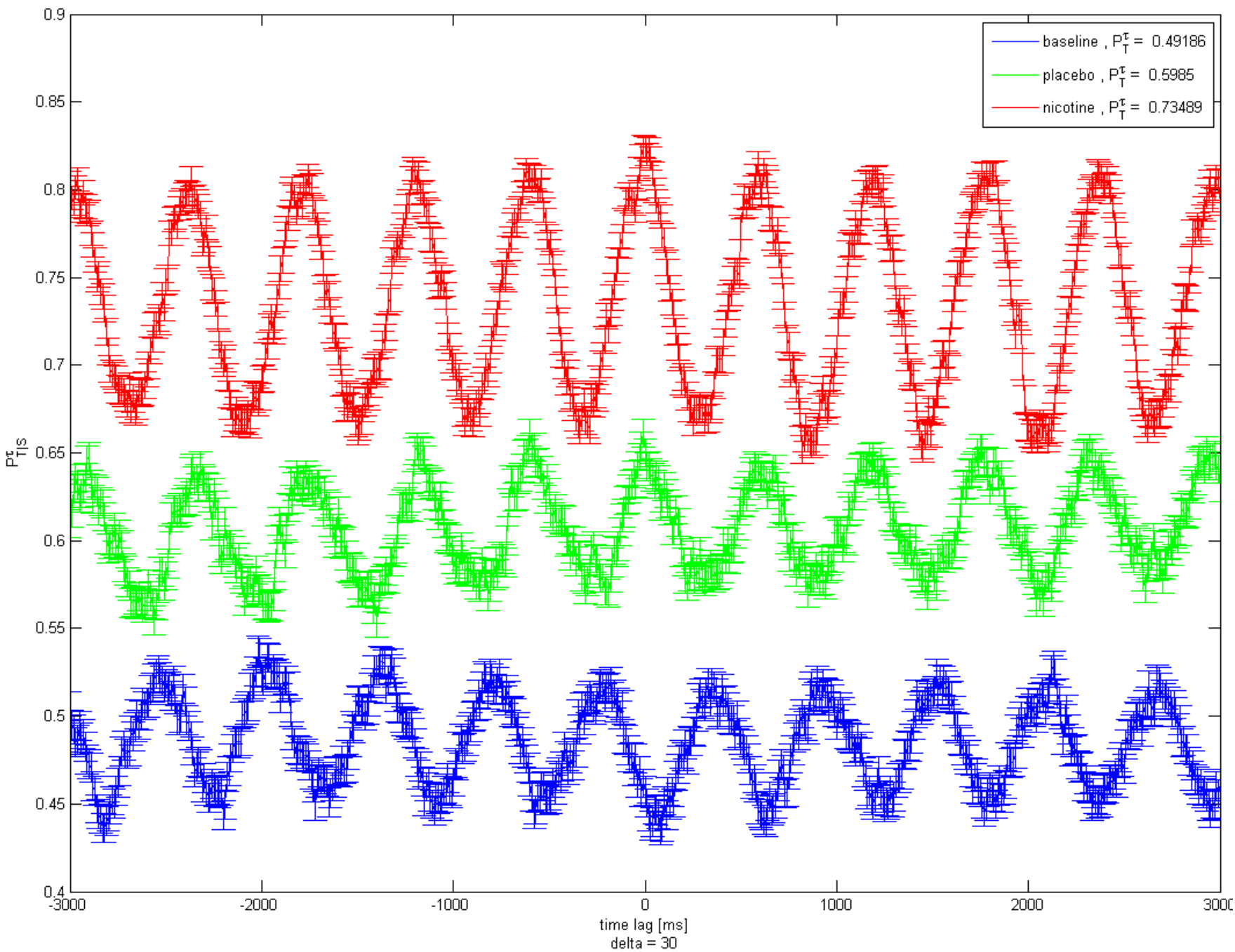
# Power thresholding



# We're not limited to studying pairs of clusters

- The cross-correlation is only defined for two signals, but:







- Direct pathway: striatum inhibits Gpi/SNr inhibits thalamus
- Indirect pathway: striatum inhibits Gpe inhibits STN excites Gpi/SNr inhibits thalamus.
- STN is part of the indirect pathway
- Dysfunction leads to impulsivity
- B.G. possibly participate in action selection.