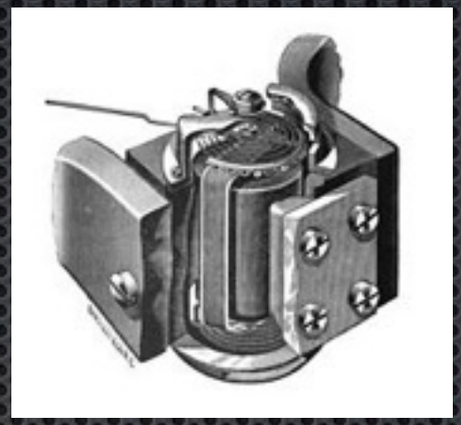
# Human Electrophysiology I

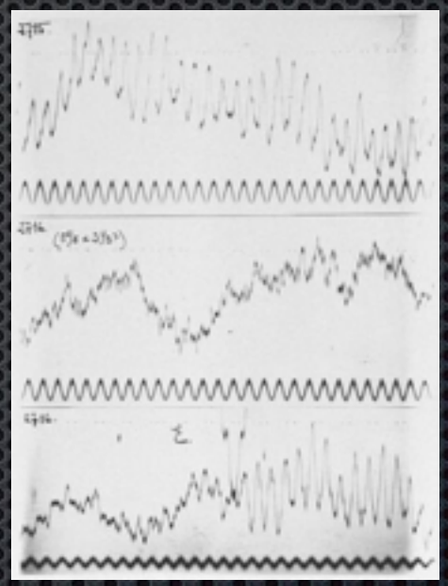
## Principles of Neuroimaging

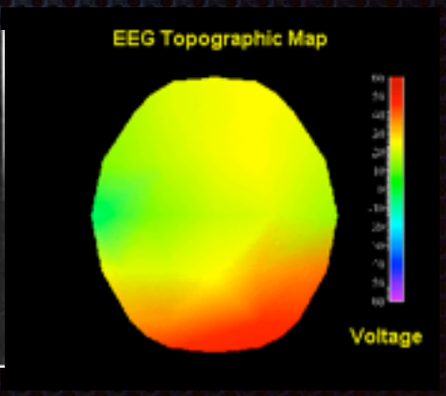
# History

- 1875 - Richard Caton measures electrical potential from exposed cortex of rabbits
  *(galvanometer used to record electrical impulses, replicated by Adolf Beck in 1891)*
- 1912 - Pravdich-Neminski *(photographic record of electrical activity in dog brain using galvanometer; electrocerebrogram)*
- 1929 - Hans Berger *(Lippman capillary electrometer; Edelman galvanometer; Electroencephalogram; methodologically weak, but observant of links between electrical impulses & "psychic phenomena"; psychiatrist)*
- 1950s - William Grey Walter *(improved range/speed of Berger's machine; develops topographic methods - spiral-scan CRTs attached to electrode pairs, arranged in geometrical array)*
- 1942/47 - UK/US EEG Societies formed

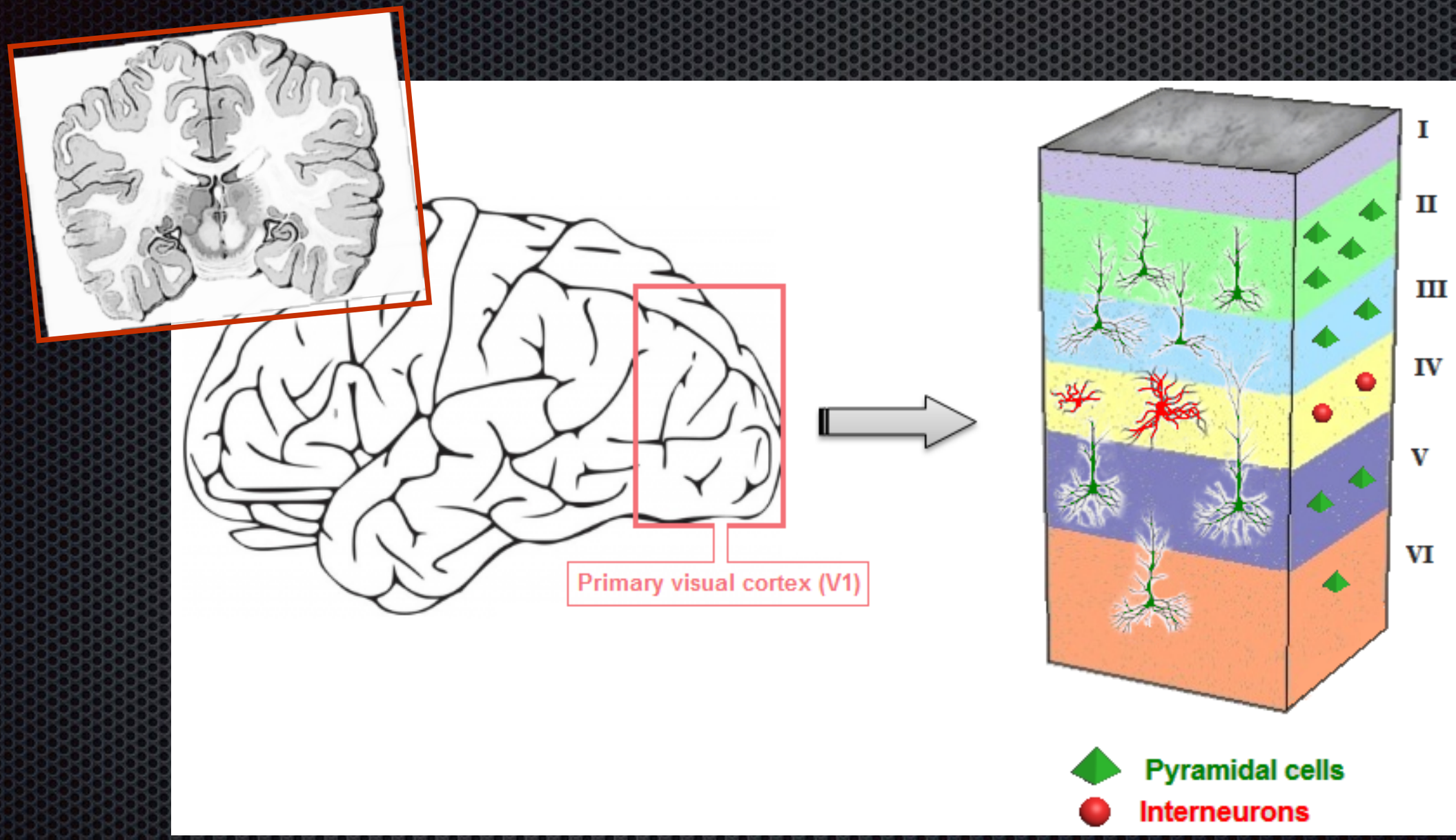


Galvanometer (pointer moves with detection of current in coil, within magnetic field)





# What is EEG?




Brain cortex is dominated by neuronal cells called Pyramidal cells. These are the primary source of EEG signals, we think.

# What is EEG?

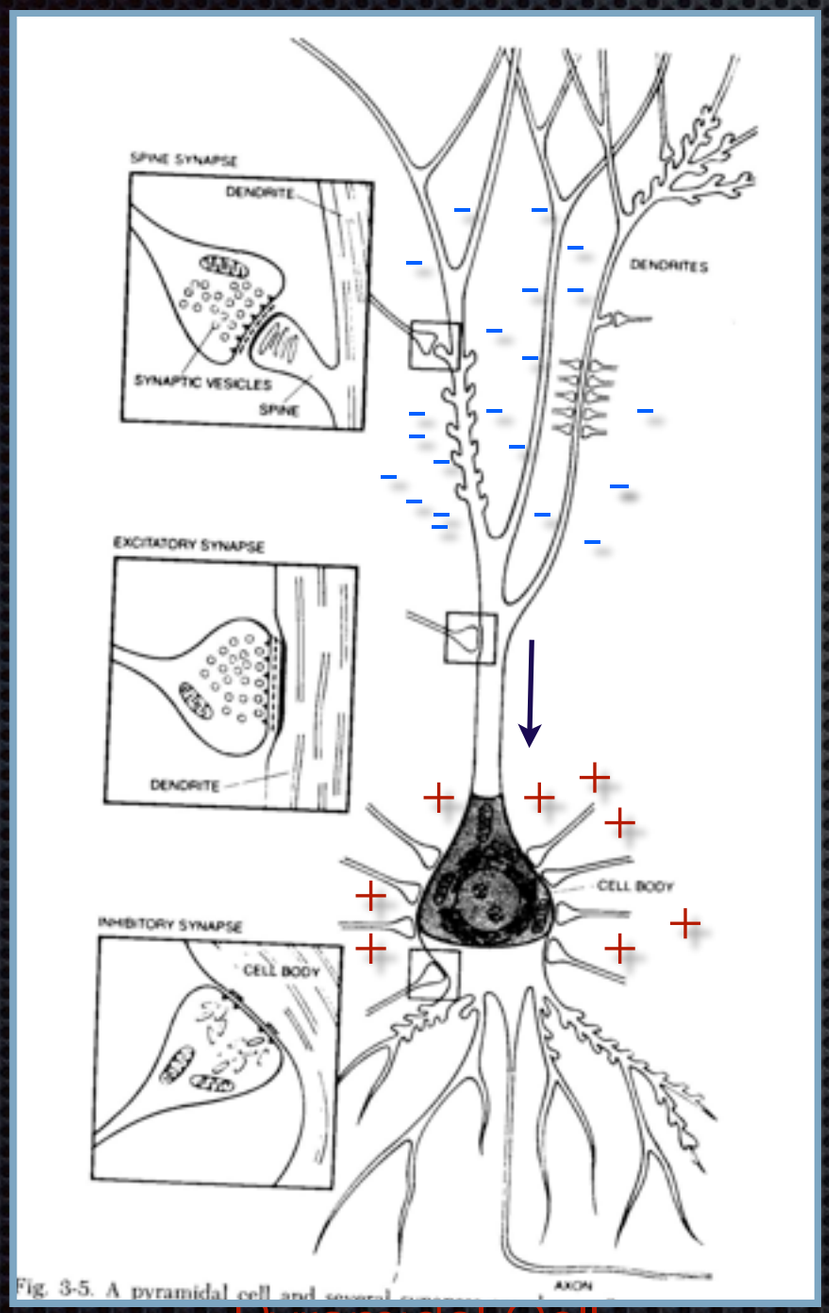
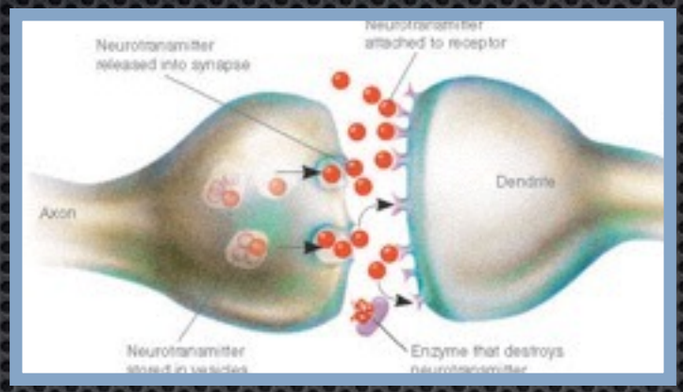
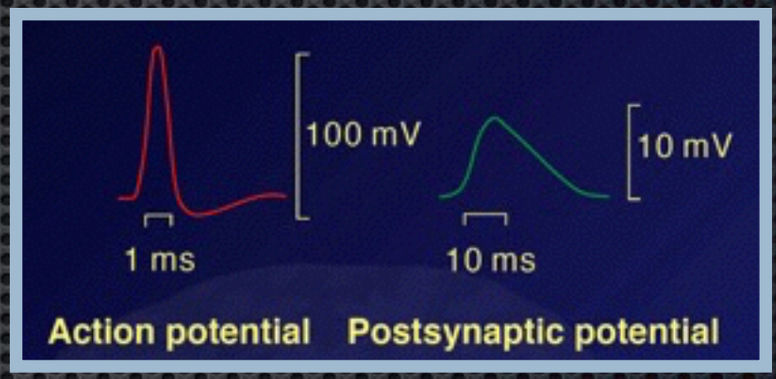


Fig. 3-5. A pyramidal cell and several

Pyramidal Cell



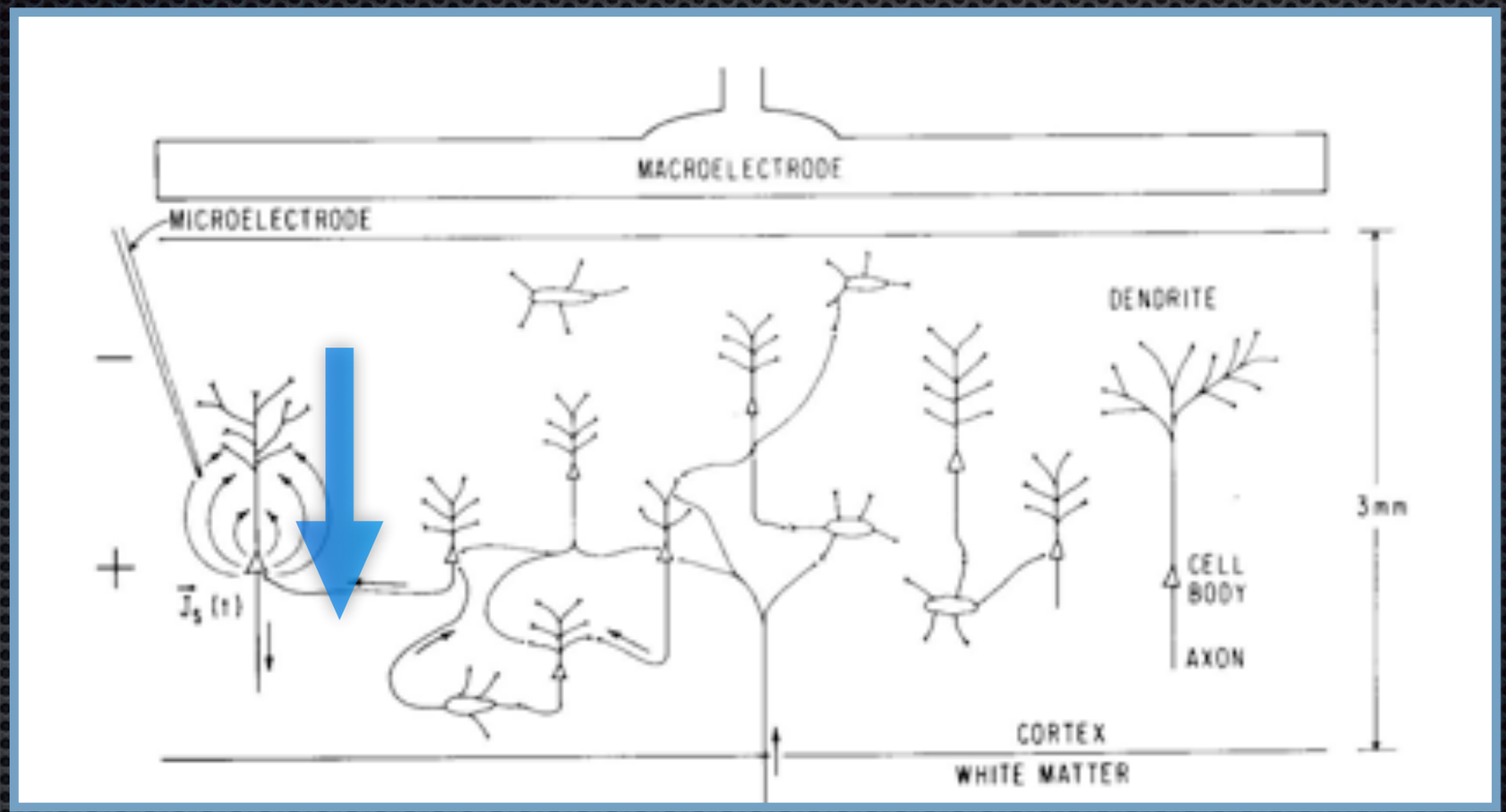




- communication involves synapses and action potentials

Inside Cell:
- post-synaptic potentials (PSPs, dendridic,100 ms)
- PSPs cause Na+ influx at dendrites
- action potentials (presynaptic, axonal & brief, <10 ms); this is the primary current

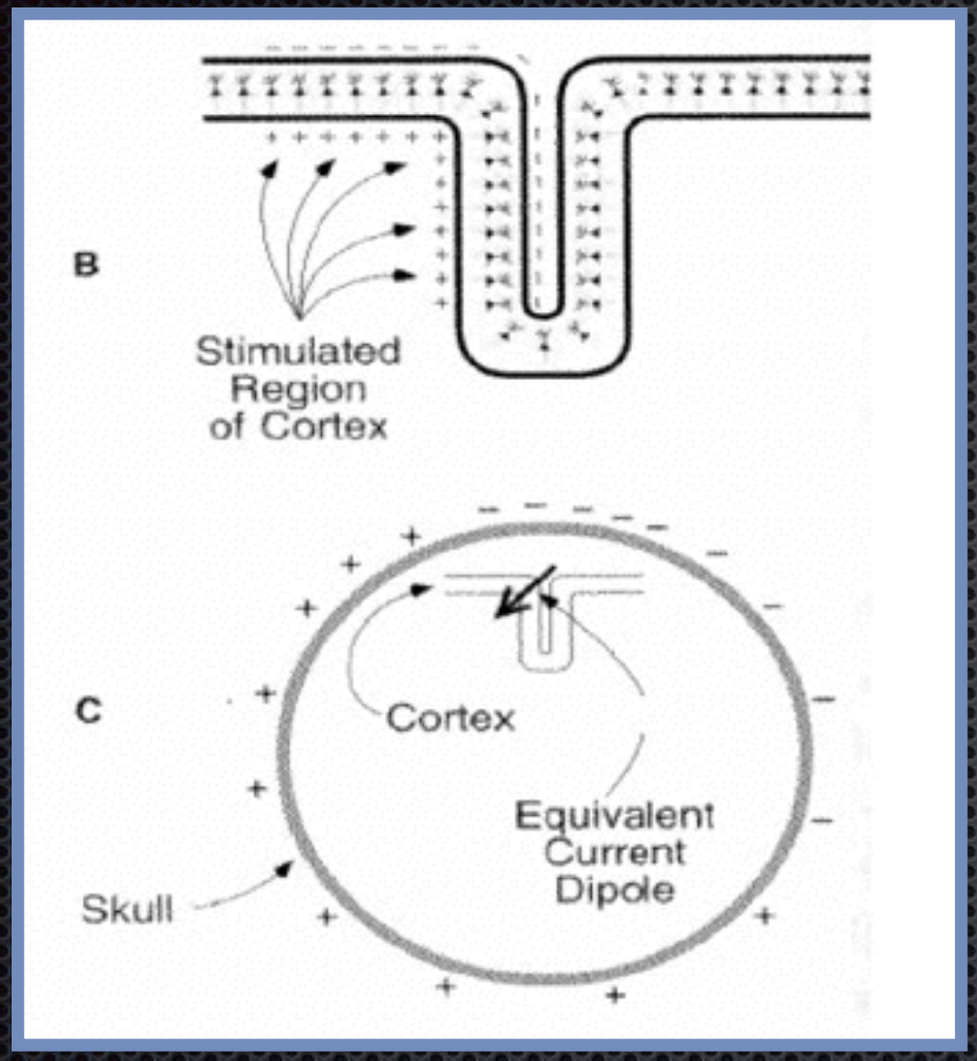
Outside Cell:
Result is a “sink” at dendrites (negative extracellular space) & “source” near body (positive extracellular space). Secondary current.

# What is EEG?




A dipole (flow of current from sink to source) is created with the electrical negativity towards cortex surface in extracellular space.

# What is EEG?




EEG measures spatially summed potentials - across neurons.

$10^5/mm^2$

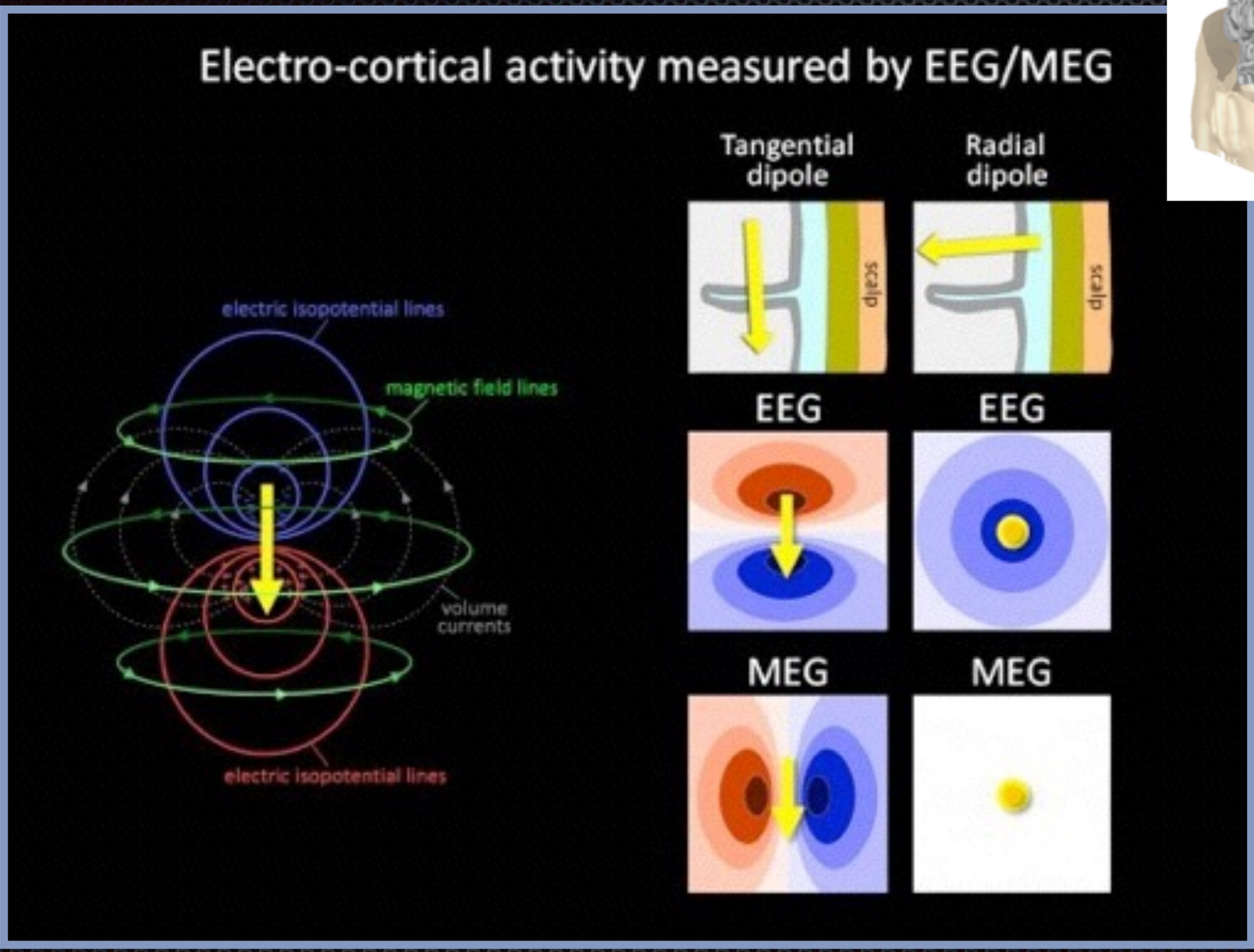
EEG measures spatially summed potentials - different cortical populations.

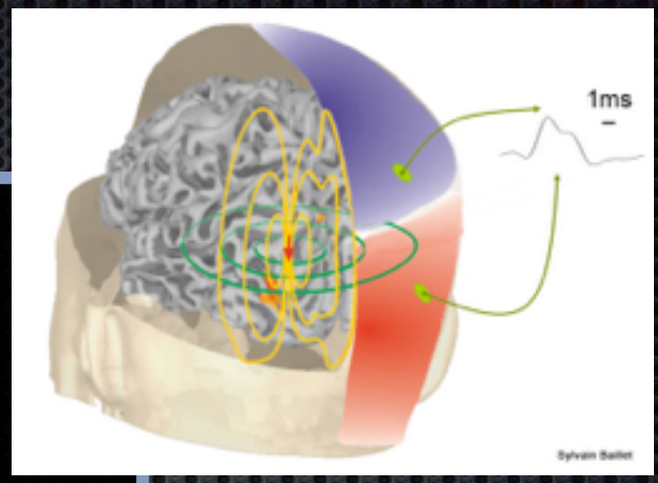
Spatial Distribution: Direction of dipole determines spatial distribution of potentials. Mixture if multiple dipoles (sum across spatial locations). Blurred.

Amplitude: Size of population, organization & depth determine strength.

What kind of obstacles might we encounter using EEG for sulcus activations?
How about thalamus?

# More on dipoles...



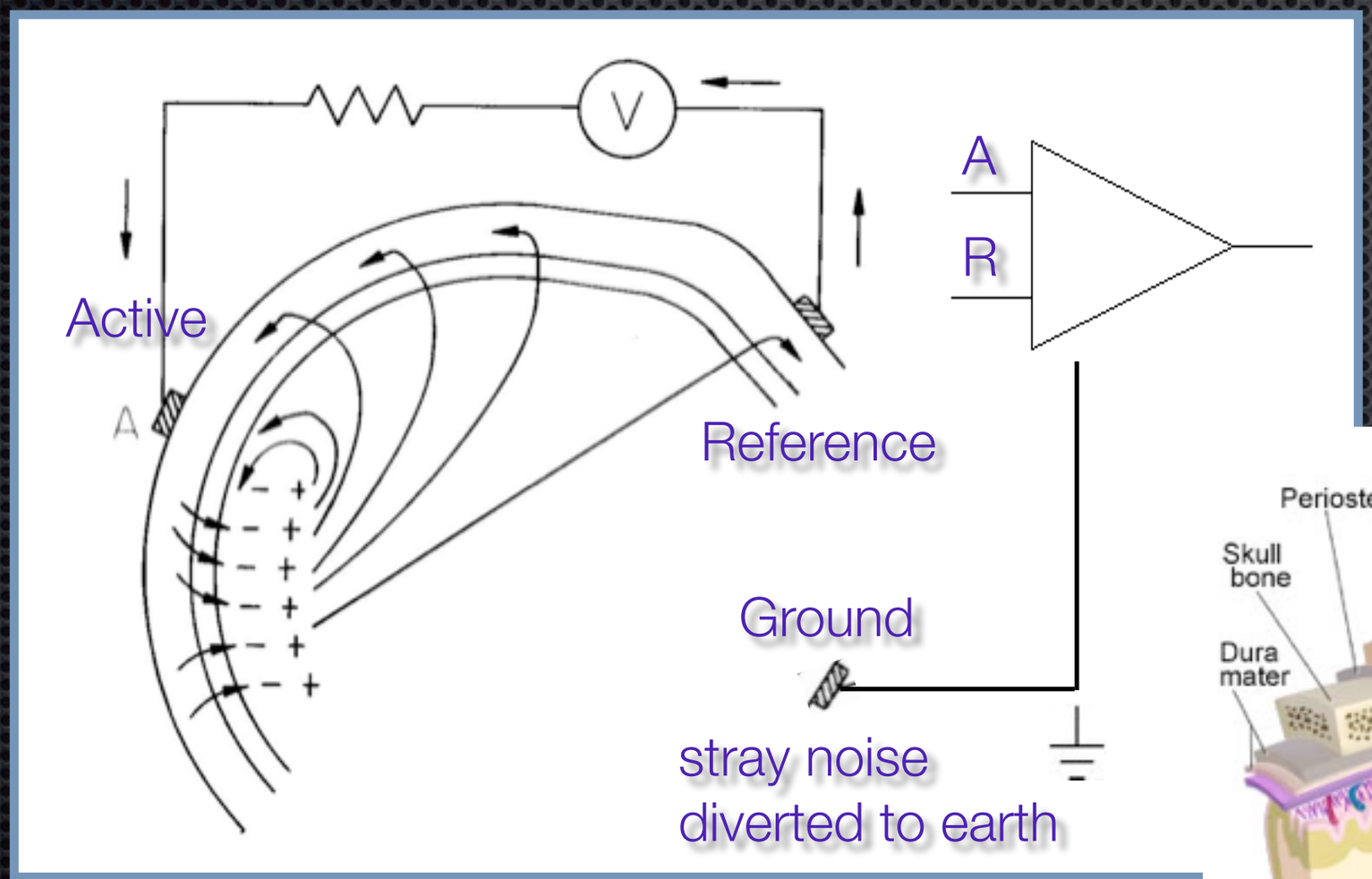




Sylvain Baillet

* *no obstruction from skull*
* *spatial resolution <1cmm*
* *better for source localization*
* *reference free*
* *more expensive*

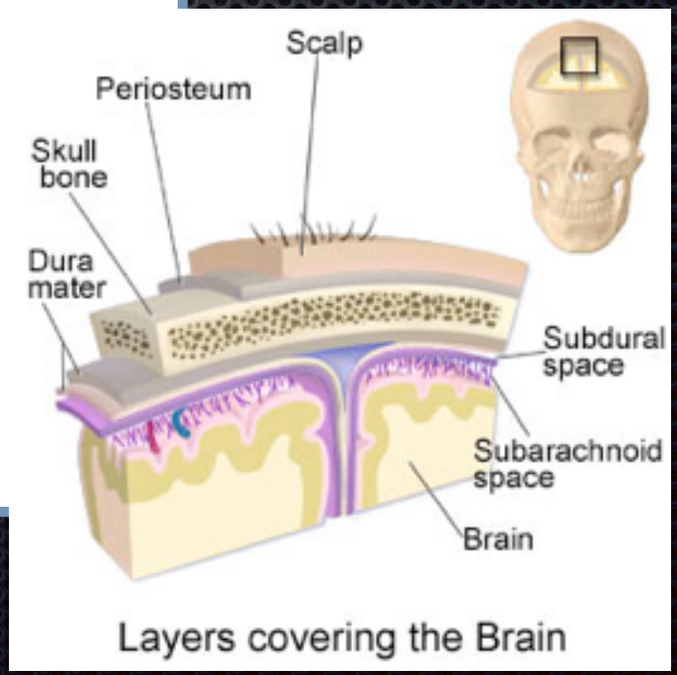
# How do we measure EEG?

Amplification
Gain x10, x50



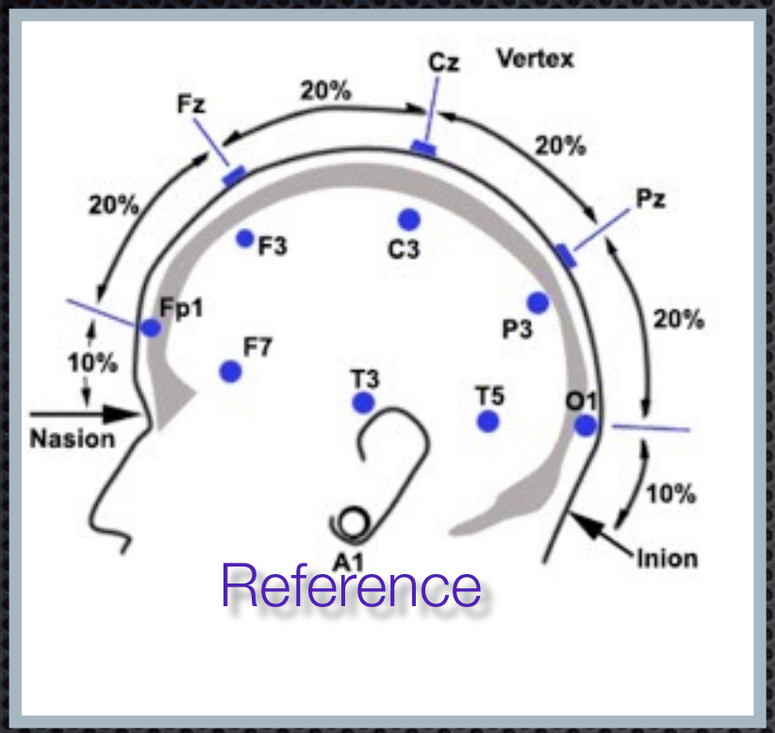

Signal Digitized

*Ref and active measured relative to a common electrode, isolated from ground.*




Layers covering the Brain

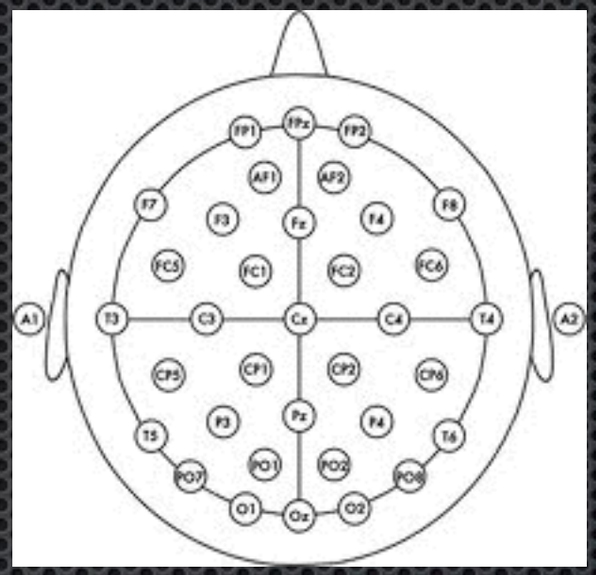
# Spatial Sampling



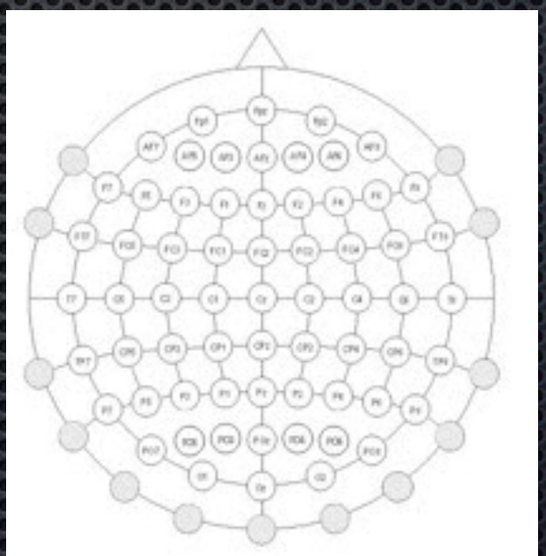

Reference

10/20 System for
Electrode Placement
Odd on Left, Even on Right
F, C, P, T, O designations
%distance to landmarks

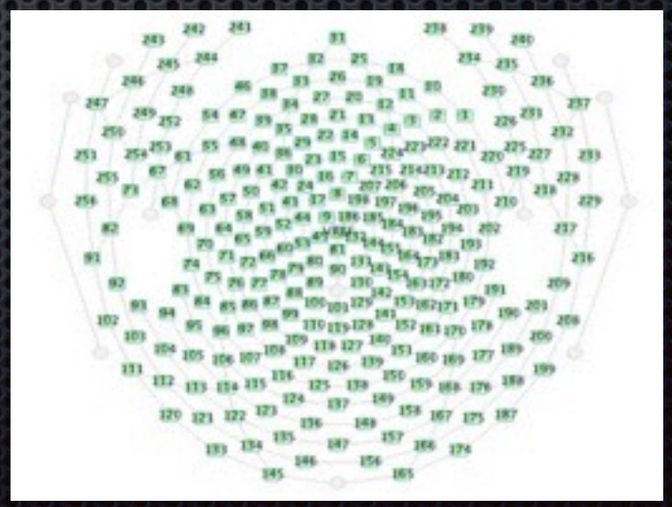
35 electrodes



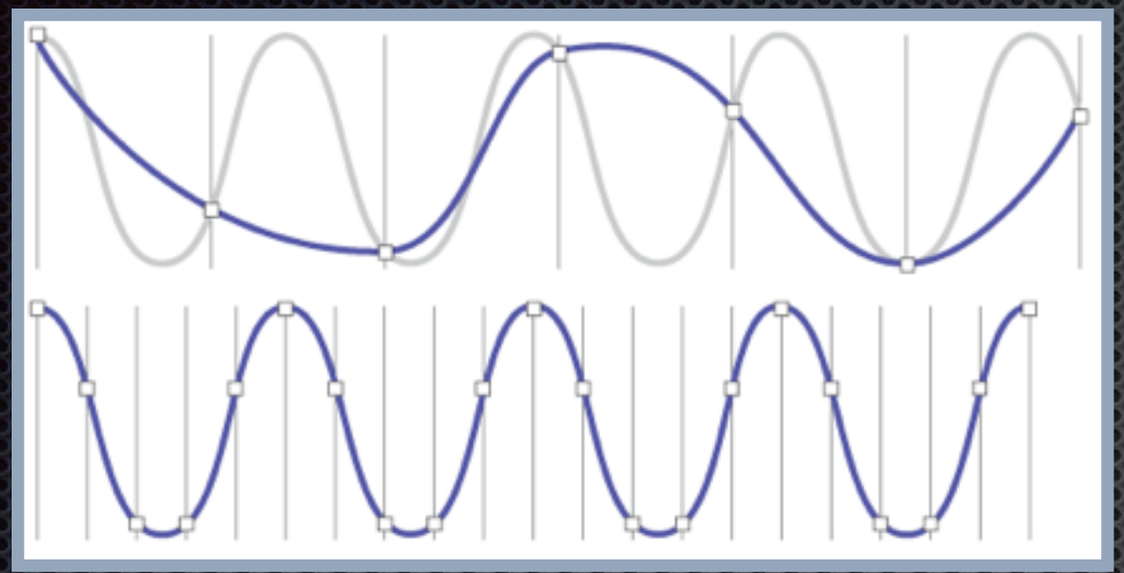

64 electrodes



256 electrodes

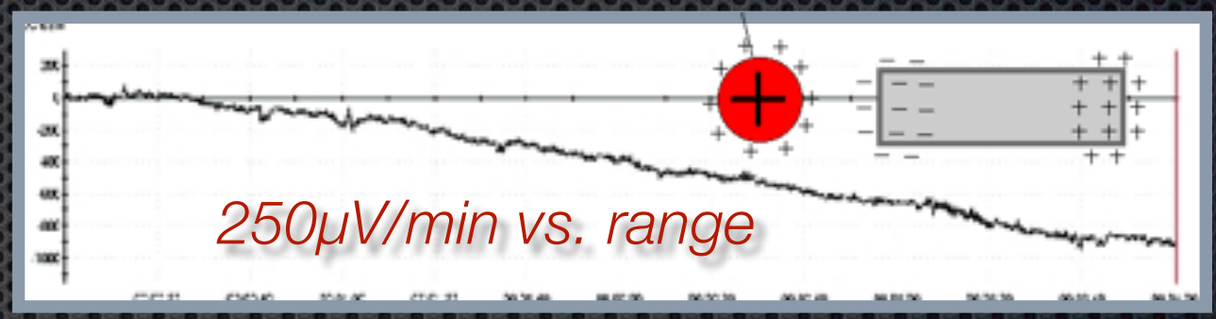


# Temporal Sampling



A/DC (Resolution)
samples / sec (Hz)
commonly 1000Hz, 250Hz
choice subject to Nyquist theorem

sampling range - 12 bits
($2^{12}$ = 4096 voltage values, impacts gain)




Amplitude (DC) Drift

Electrode Polarization = build up of charge at each electrode due to reaction with electrolyte = DC drift ("battery effect")

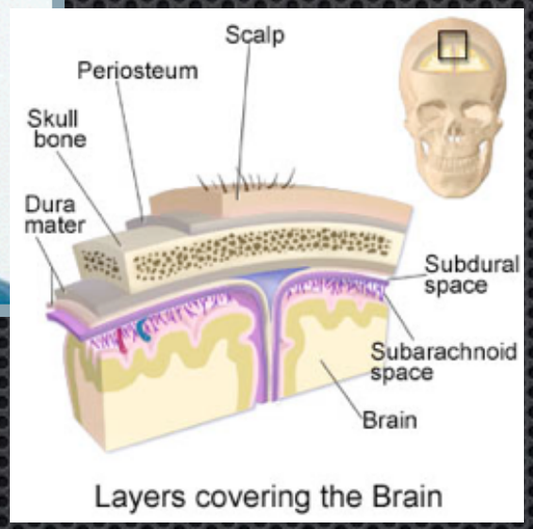
e.g., > .01Hz

*"DC amplifiers" will typically be coupled with sintered Ag/AgCl electrodes.*

# Different systems...

High-Impedance: e.g., HydroCel Nets (EGI) have a sponge attached to each electrode. The sponge is soaked in saline solution (no electrolyte gel required). High-input impedance on amplifier, slows current and minimizes voltage drop at electrode. Dry electrodes are an example of such a systems.

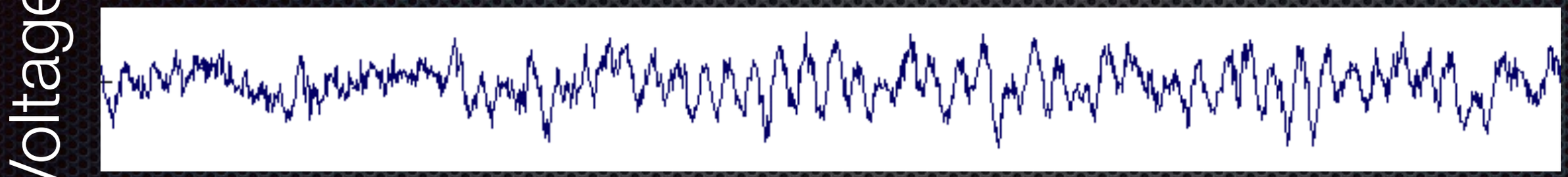
+ve - faster application for dense array nets.
-ve - the connection is not as stable as with gel application.



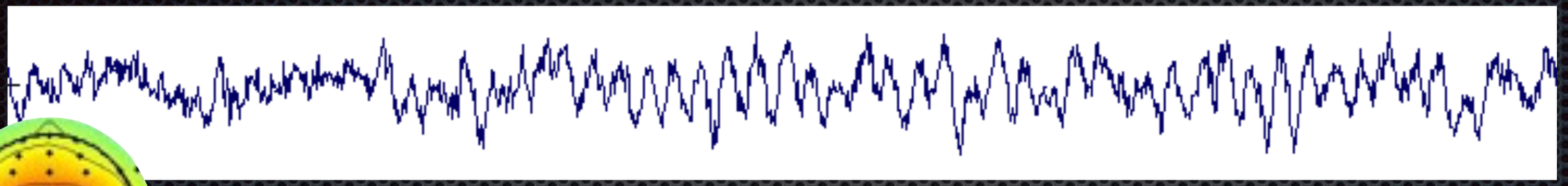
Layers covering the Brain

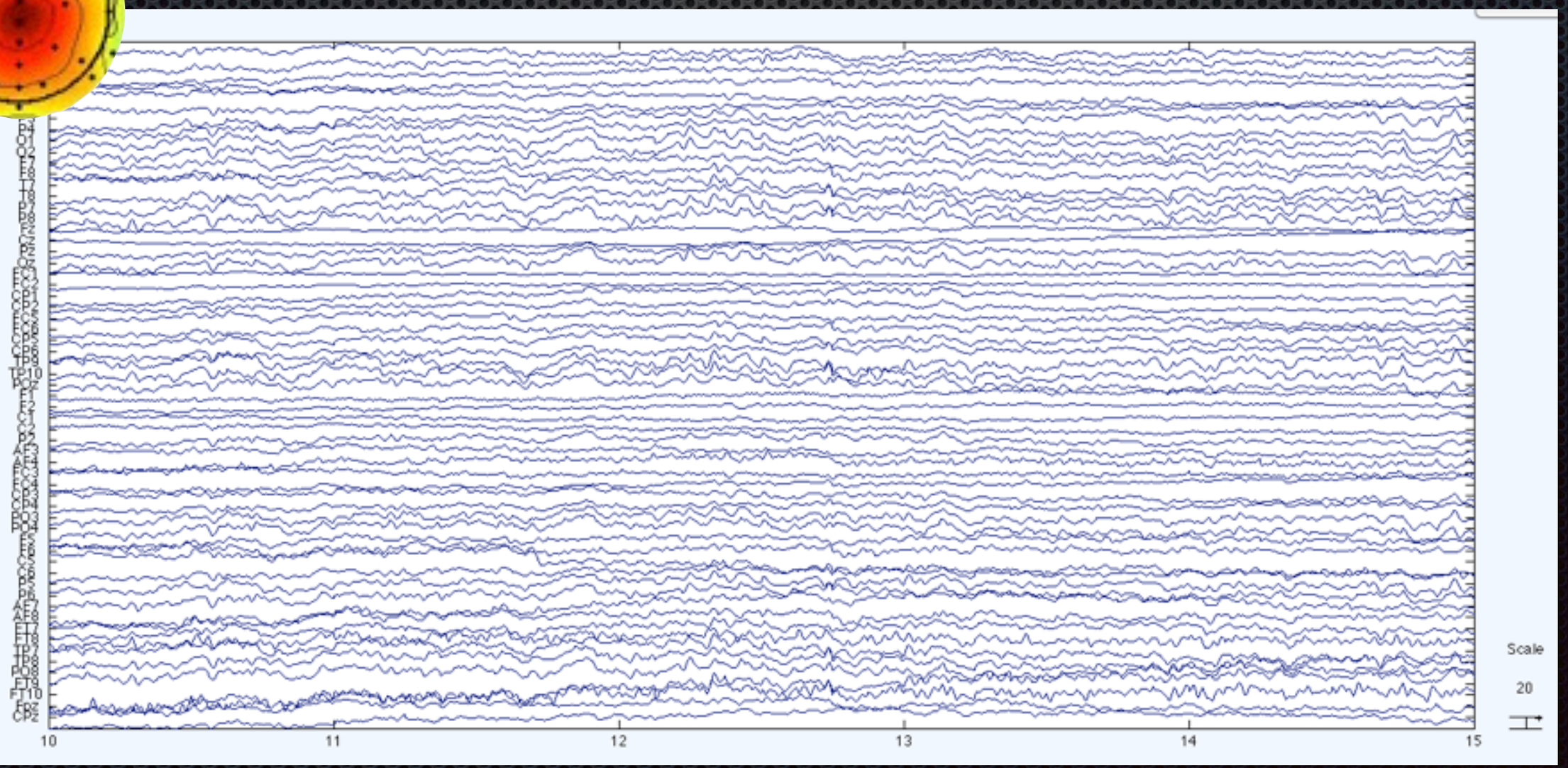
Low-Impedance: Use Ag/AgCl (Sintered) Electrodes. Electrolyte gel used to bridge electrode & scalp. Typically scrape the skin to remove dead skin cells (high-impedance).

# The data...



# The data...




Fp1
Fp2
F7
F3
Fz
F4
F8
FT9
FT7
FC5
FC1
FC2
FC6
FT8
FT10
T7
C3
Cz
C4
T8
TP9
CP5
CP1
CP2
CP6
TP10
P7
P3
Pz
P4
P8
PO9
O1
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O2
PO10
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AF3
AF4
AF8
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FC3
FC4
C5
C1
C2
C6
CP3
CP4
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Scale
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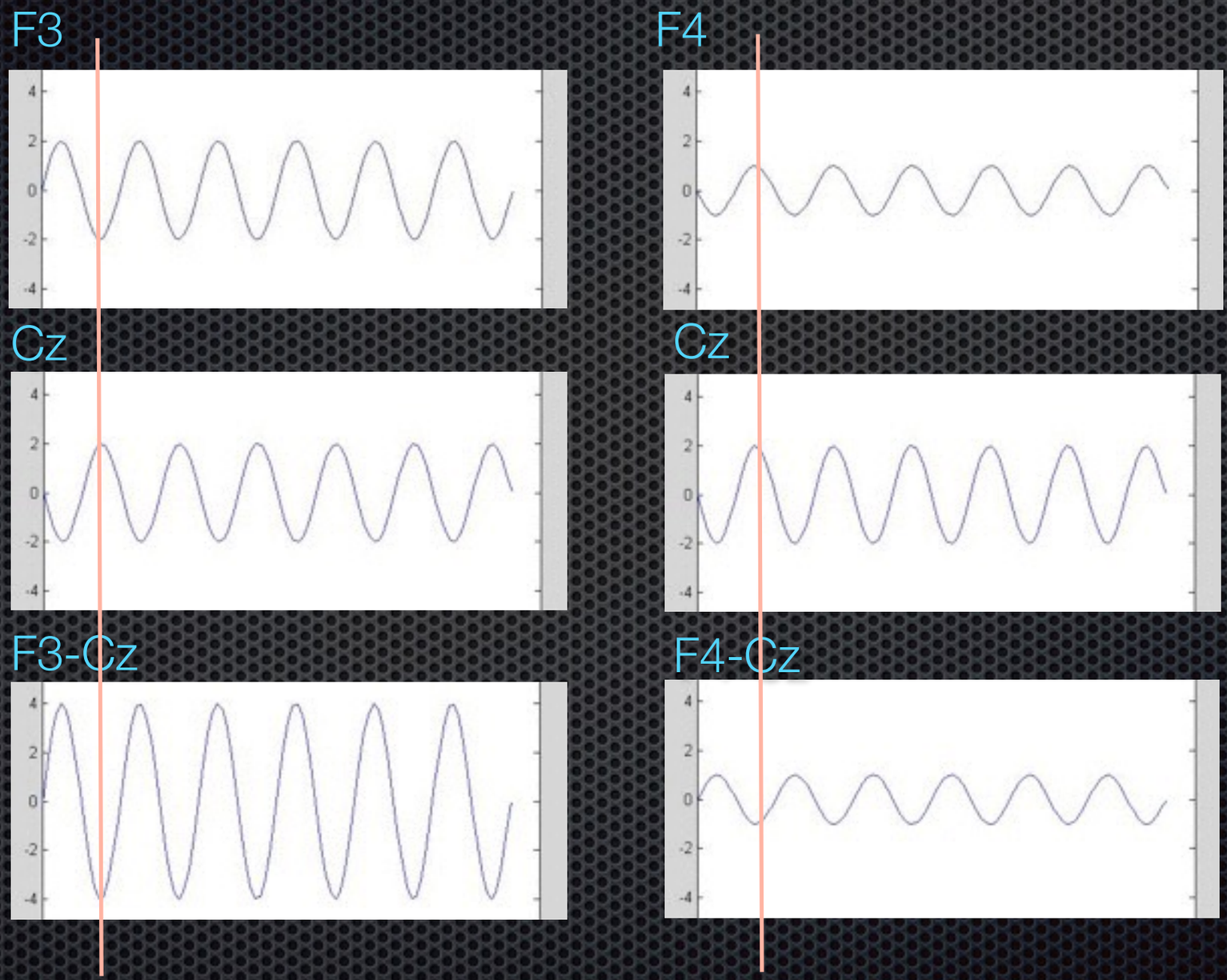
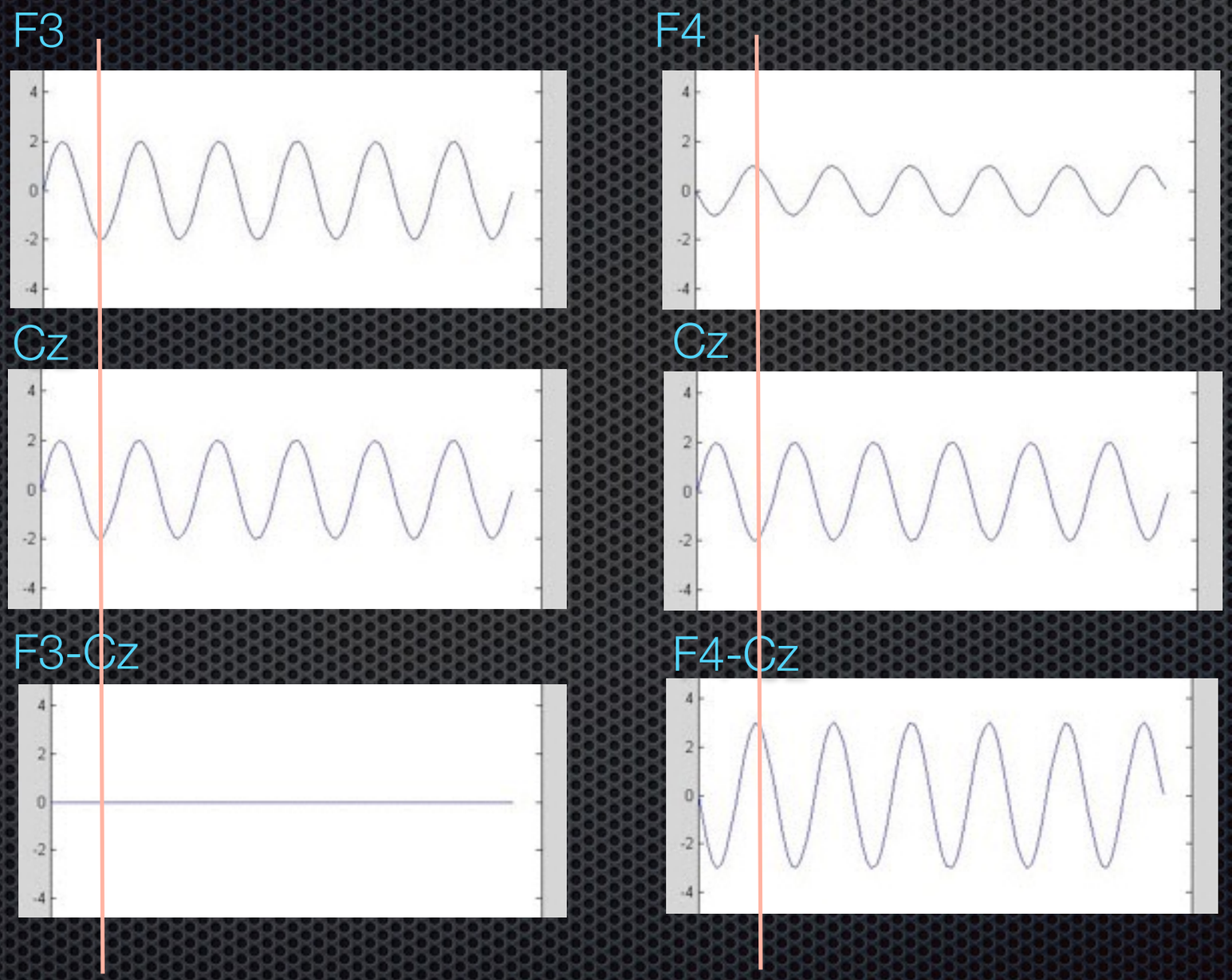
# Quick note on references.




Larry Greischar's Example

# Quick note on references.



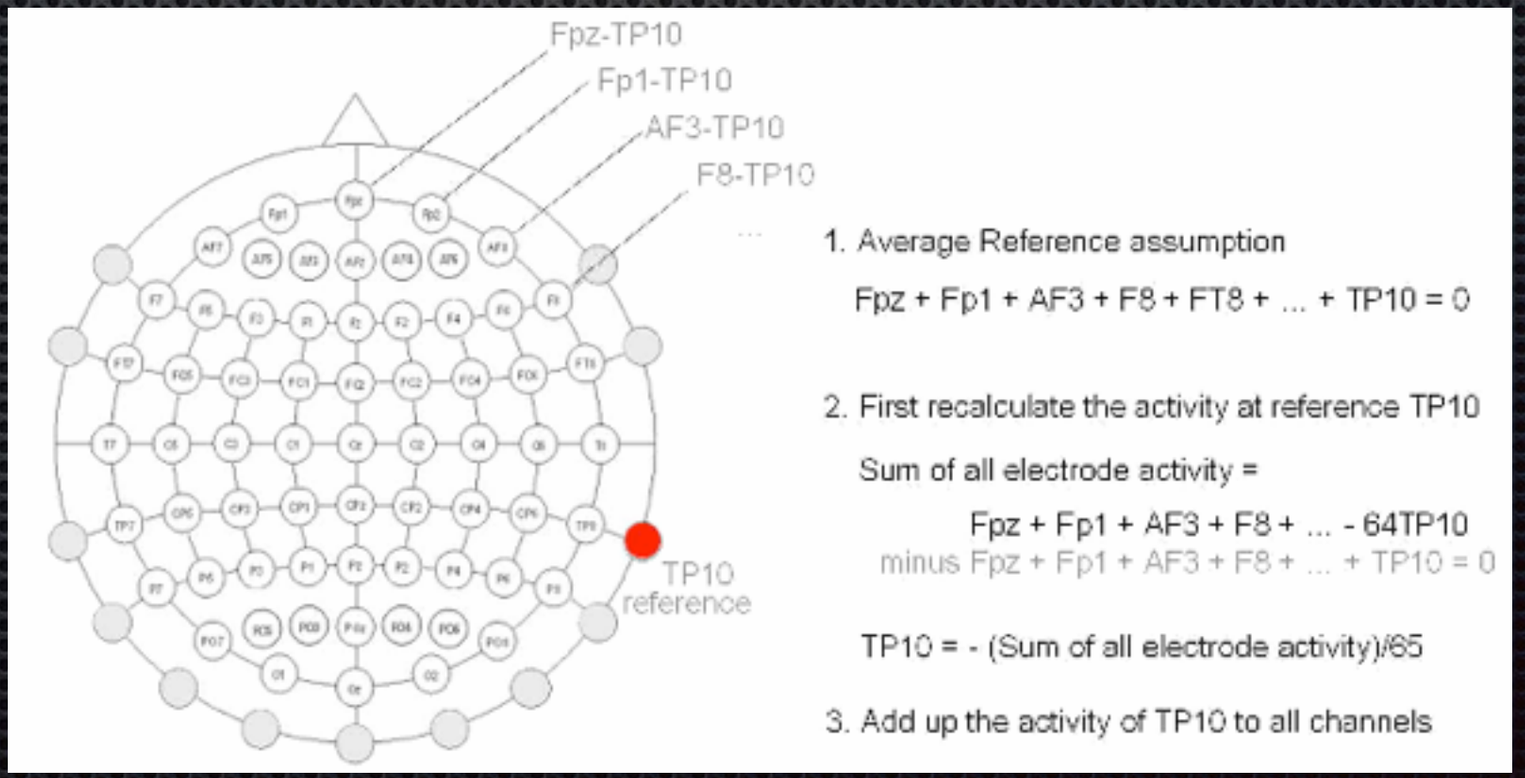

Larry Greischar's Example

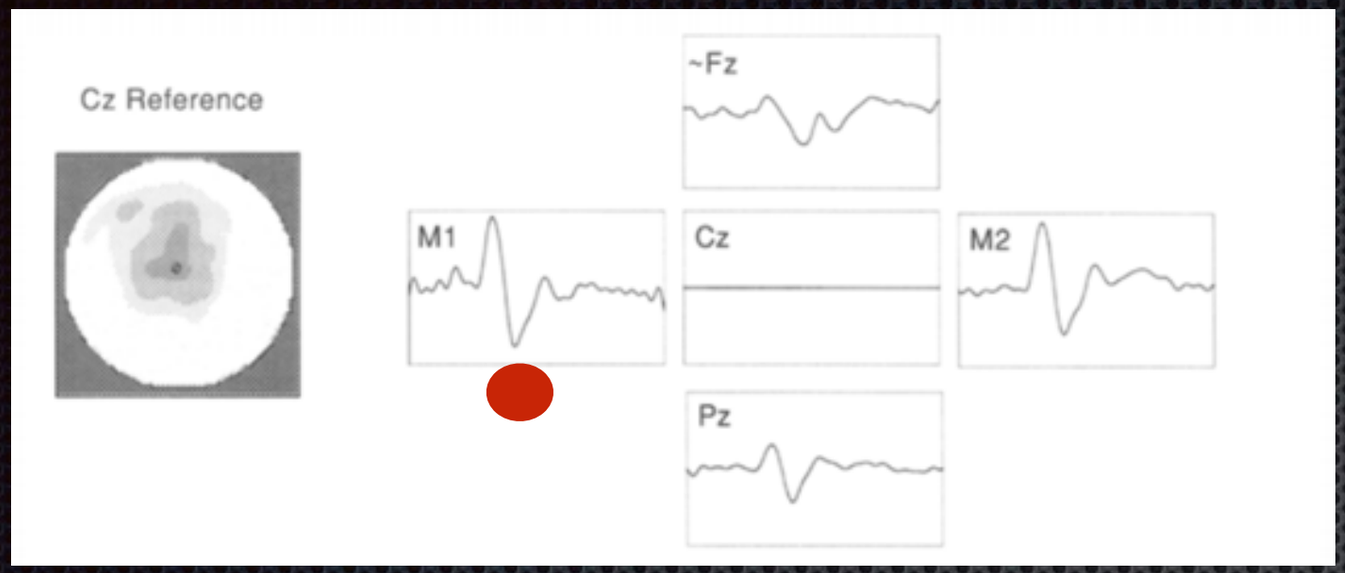
## YES!

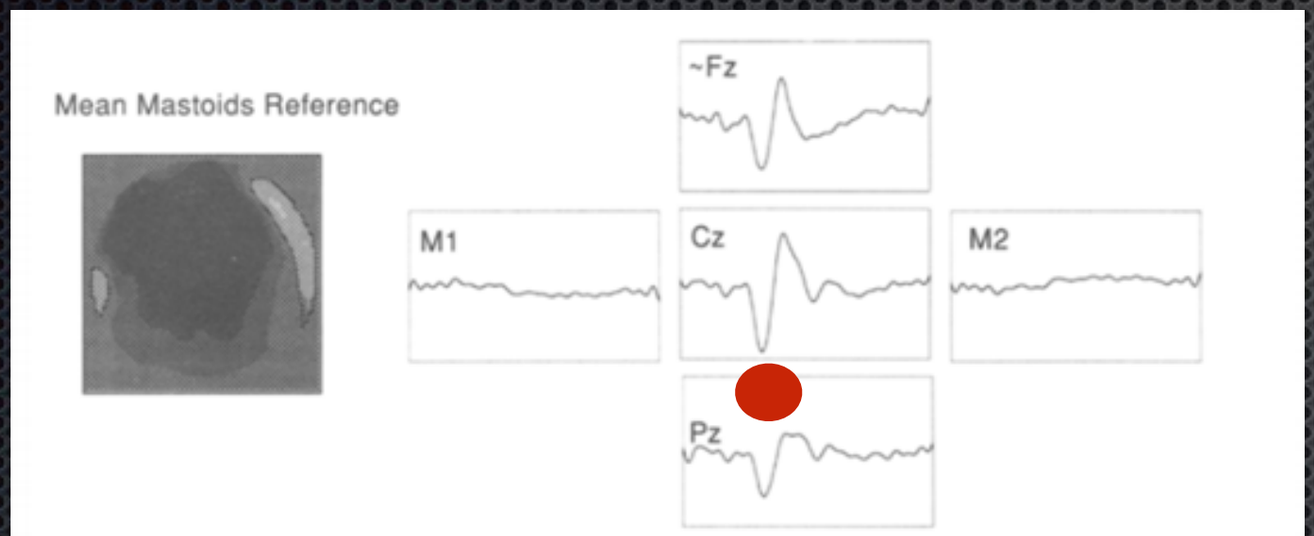
* will clearly change distribution of positive/negative values in topography
* must use “quiet” electrode (nose, earlobes etc)

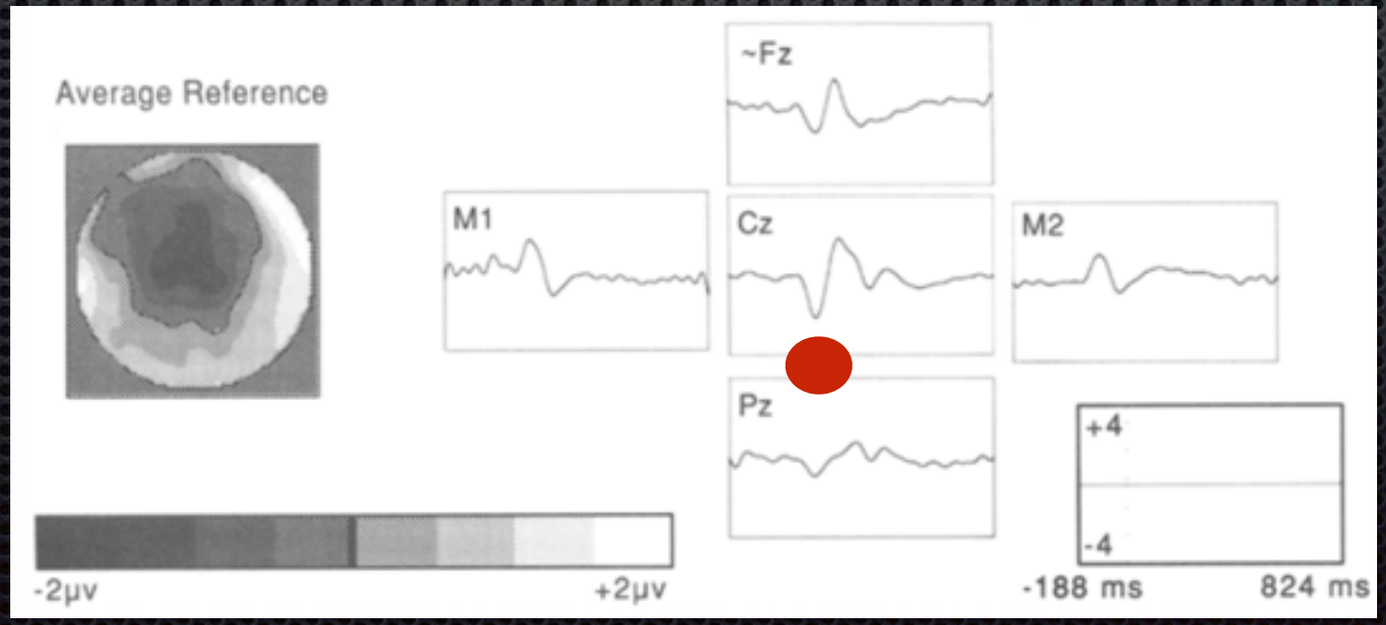
## NO!

* will not change isocontours of topography
* we can always re-reference (can use ANY electrode/sensor to re-reference)
* no evidence that scalp sensors better/worse than non-scalp reference like mastoid, nose tip etc.
* average reference is common solution but relies on pretty strong assumption (makes no sense if sampling of head sphere is low)





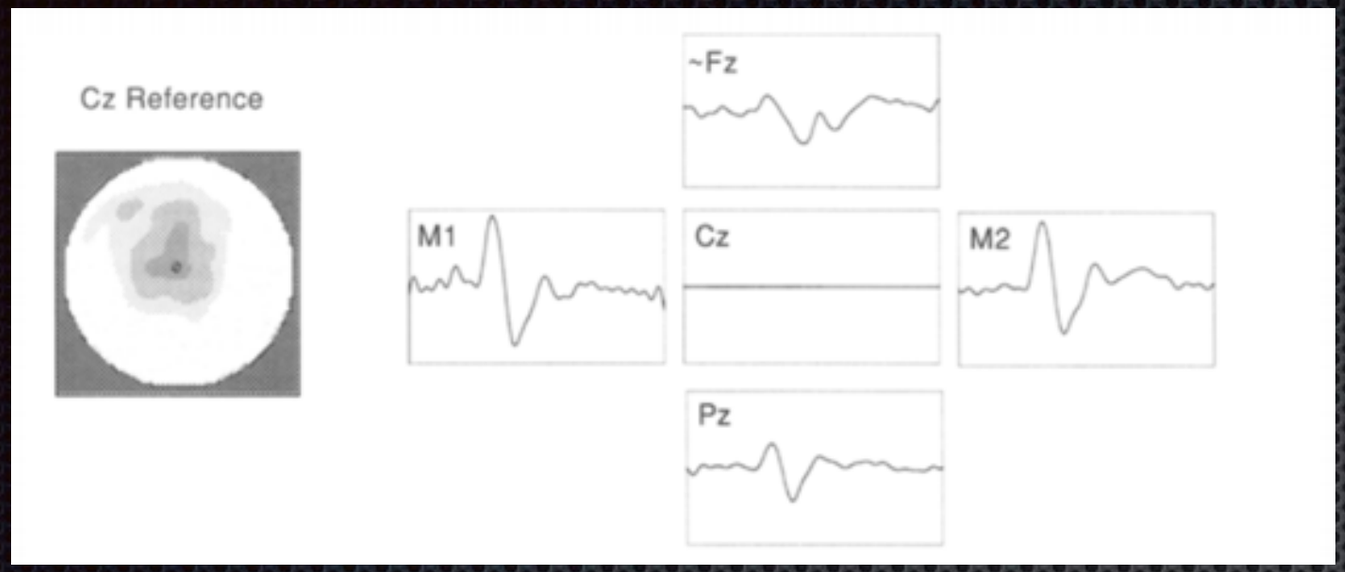



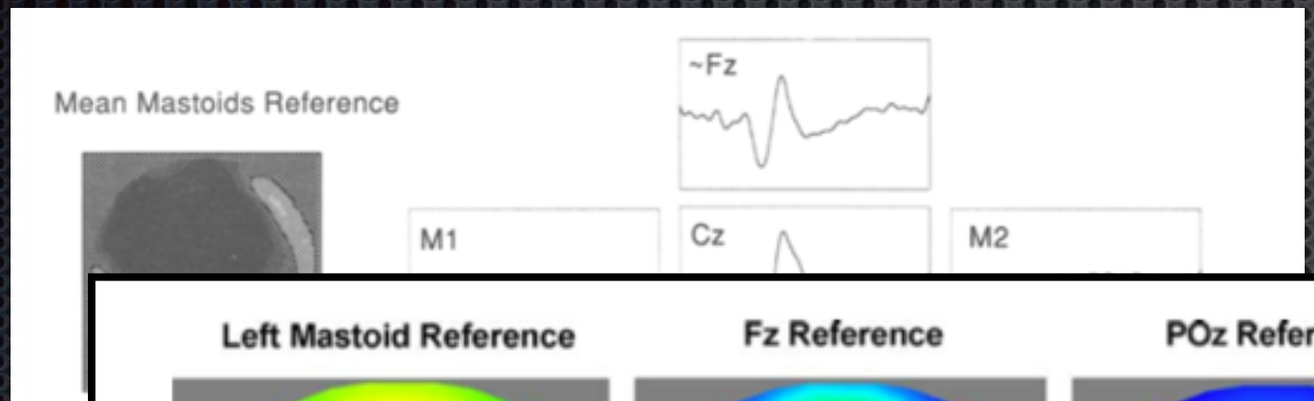




** reference will affect topography (here N1)*

** however temporally, the "event" of interest is unaffected and the isopotential lines of topographic distribution is constant*

*Dien 1998*

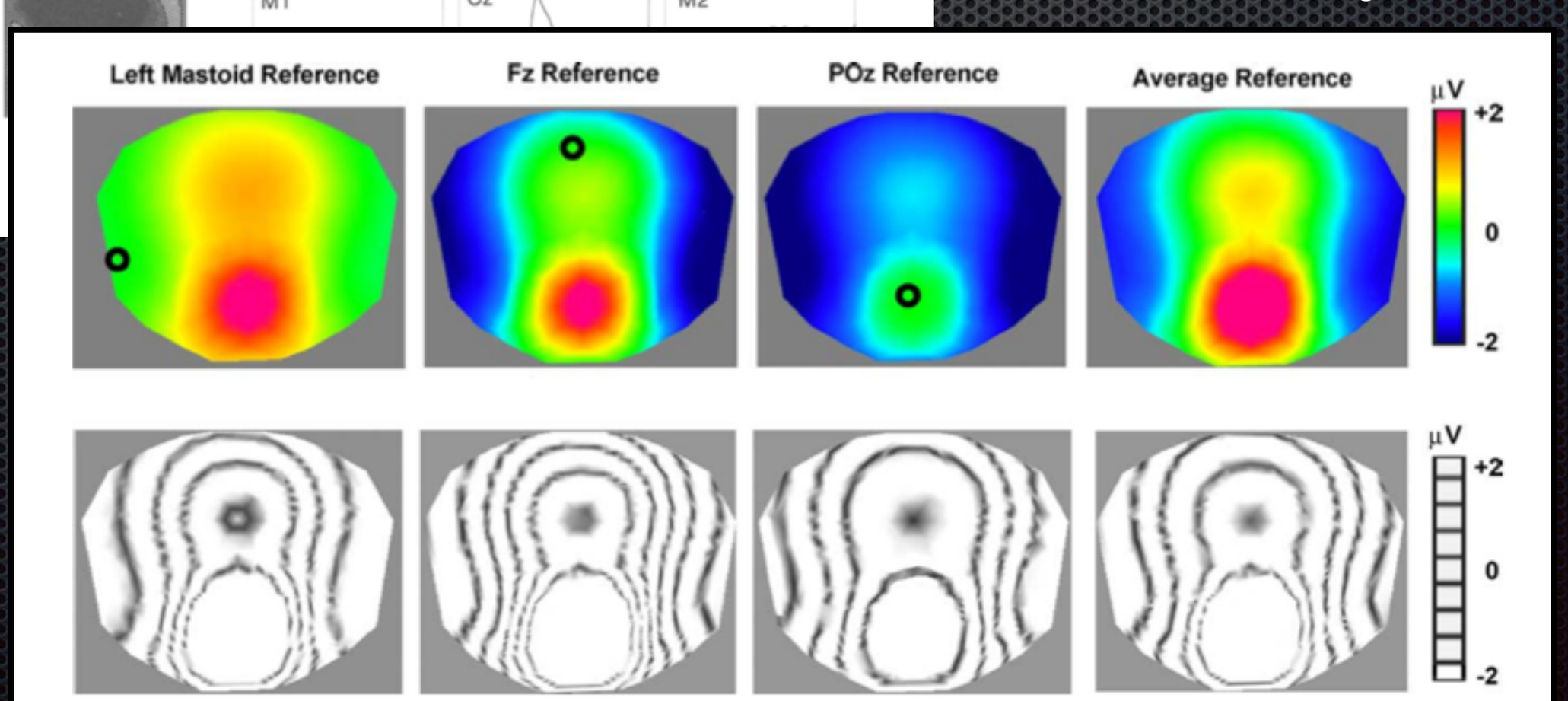



** reference will affect topography (here N1)*

** however temporally, the "event" of interest is unaffected and the isopotential lines of topographic distribution is constant*

*(1) to not rely on topography polarity and/or amplitudes to make interpretation but, rather, to examine temporal effects across the spatial "pattern" (multivariate) or unmix the signals, and, (2) use condition differences or parametric variability to interpret amplitude changes*



# Referencing…

A = a-c

B = b-c

C = c-c = 0

c = can be “quiet” or “active”

## electrode re-reference

A-B = (a-c) - (b-c) = a-b

C-B = (c-c)-(b-c) = c-b

## average reference

A+B…+Z = 0

C =-sum(A..Z) / #e-1

a=A+c

b=B+c

…

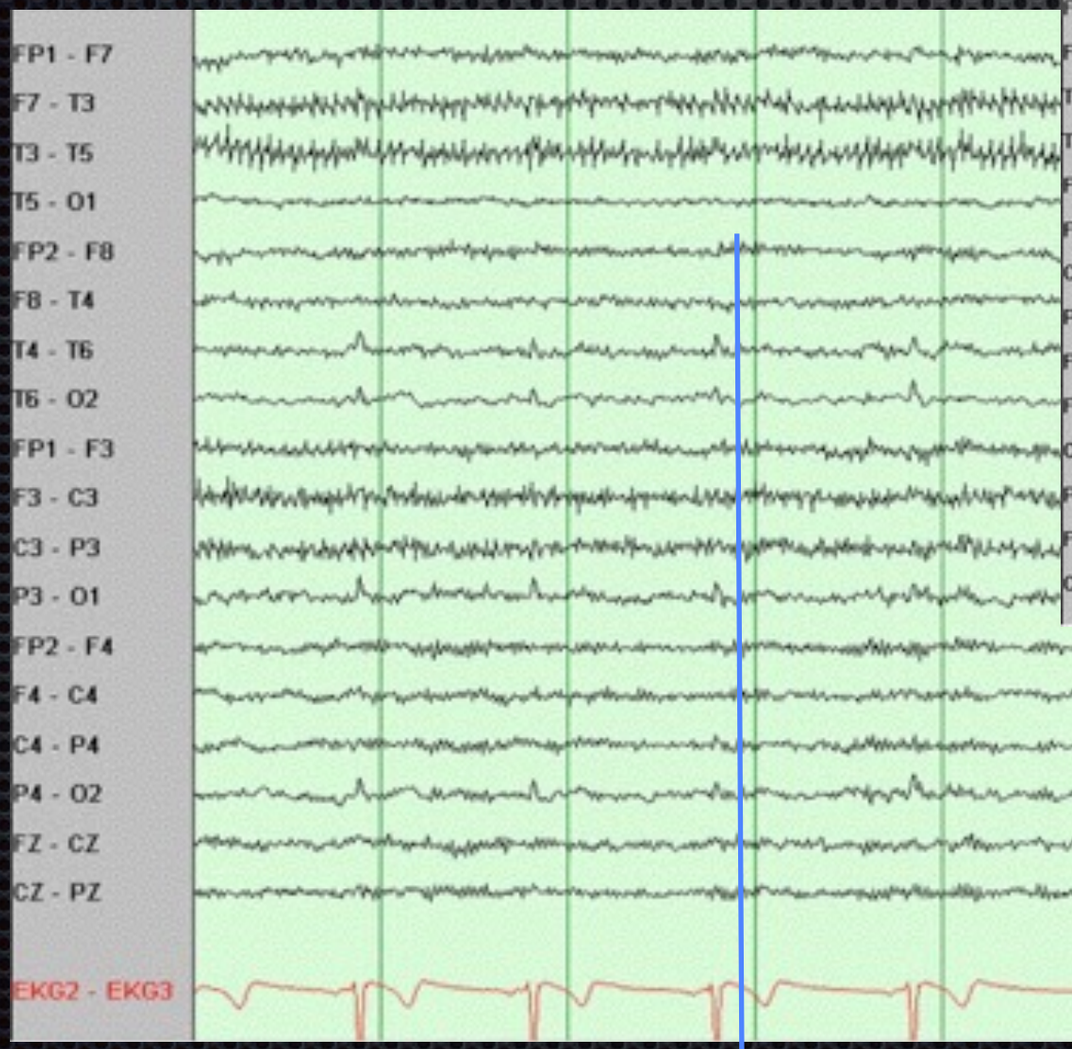
** assuming all electrodes referenced to the same ref (special case with bi-polar recording)*

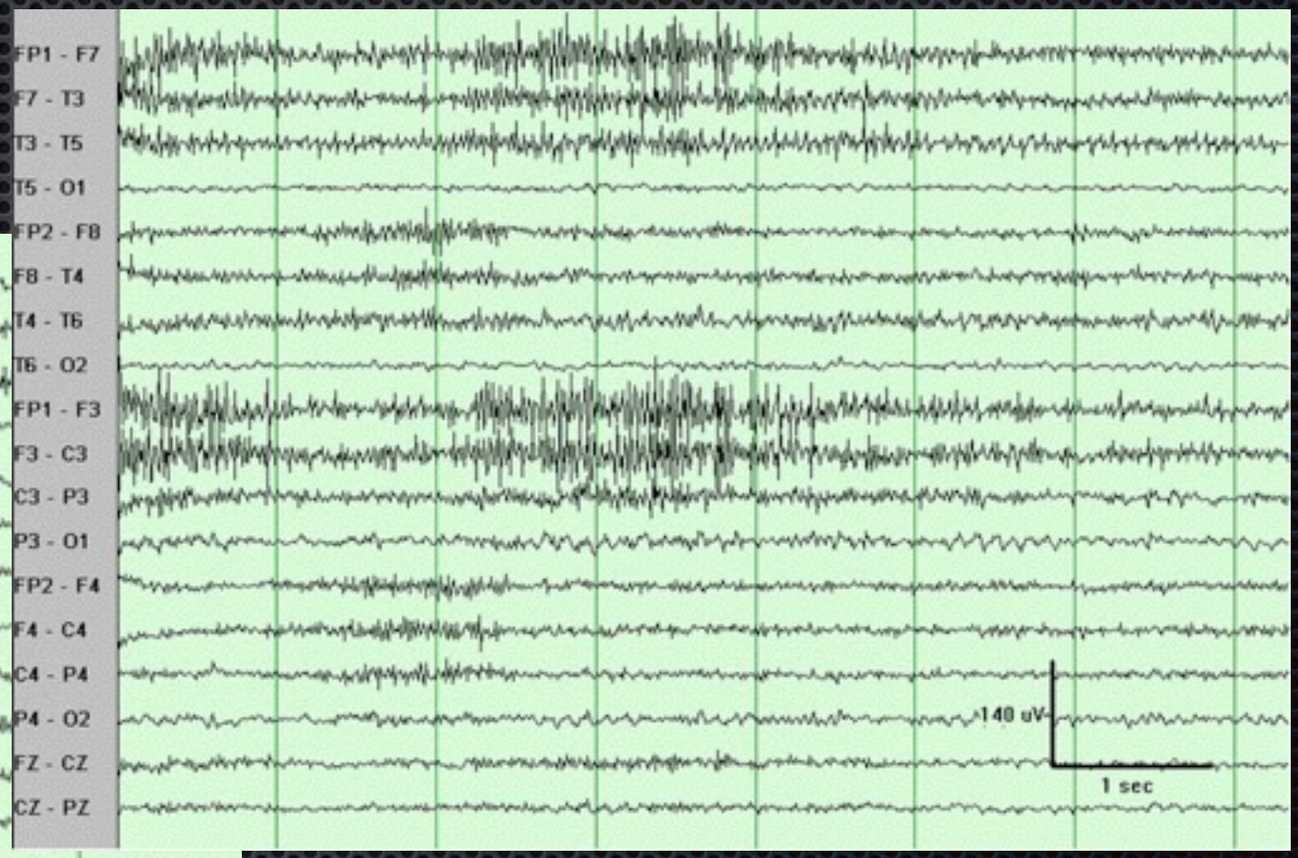
# Signal Sources...

# Non-brain contributions

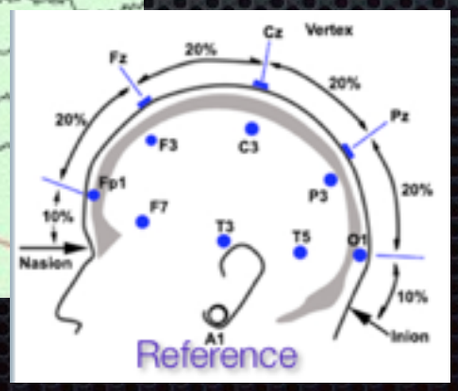
Electrodes pick up artefactual sources of electrical activity as well as neural sources.

PHYSIOLOGICAL: Muscle,
Eyes, Tongue, Skin, ECG

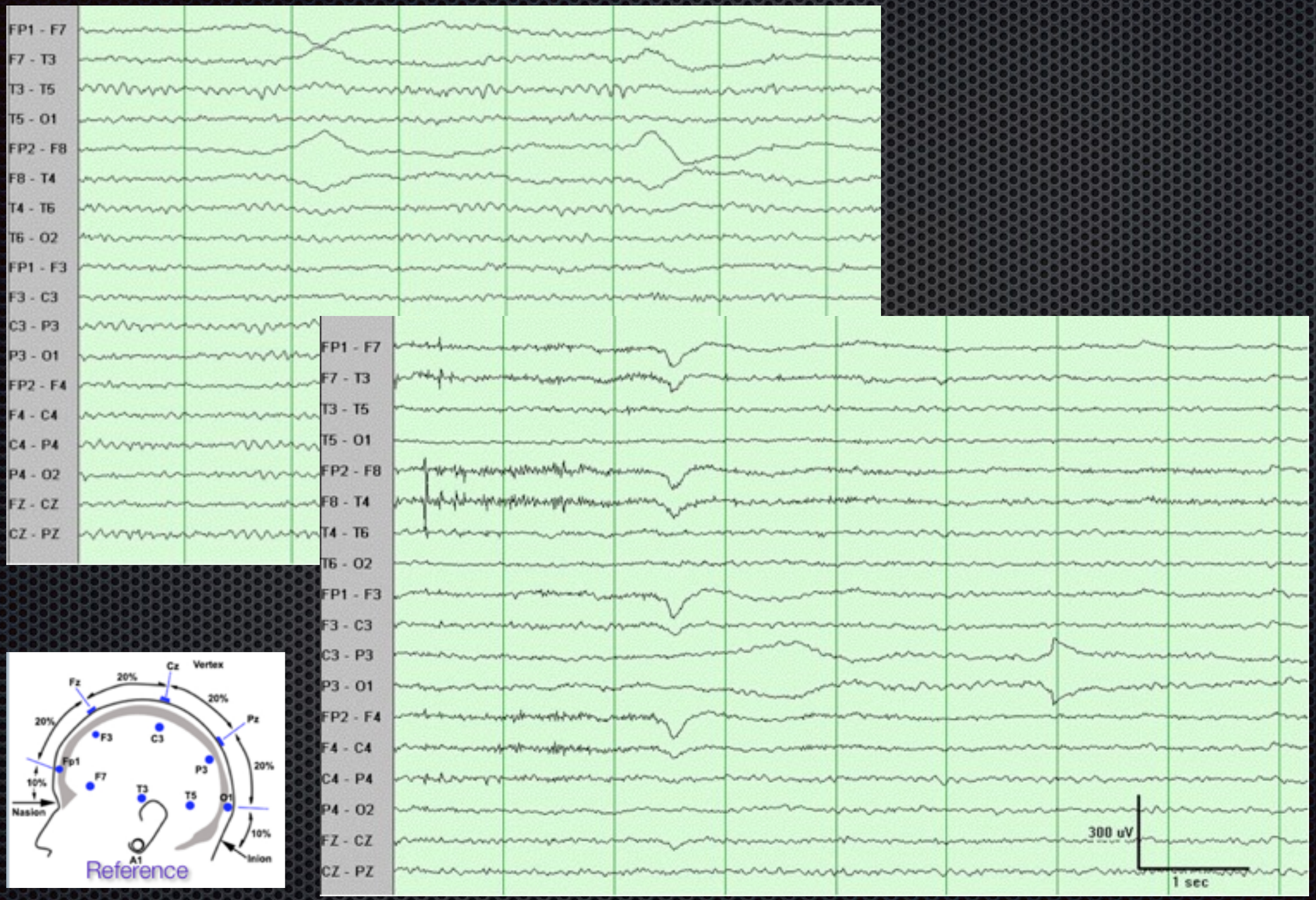



filter < 40Hz



# PHYSIOLOGICAL: Muscle, Eyes, Tongue, Skin, ECG

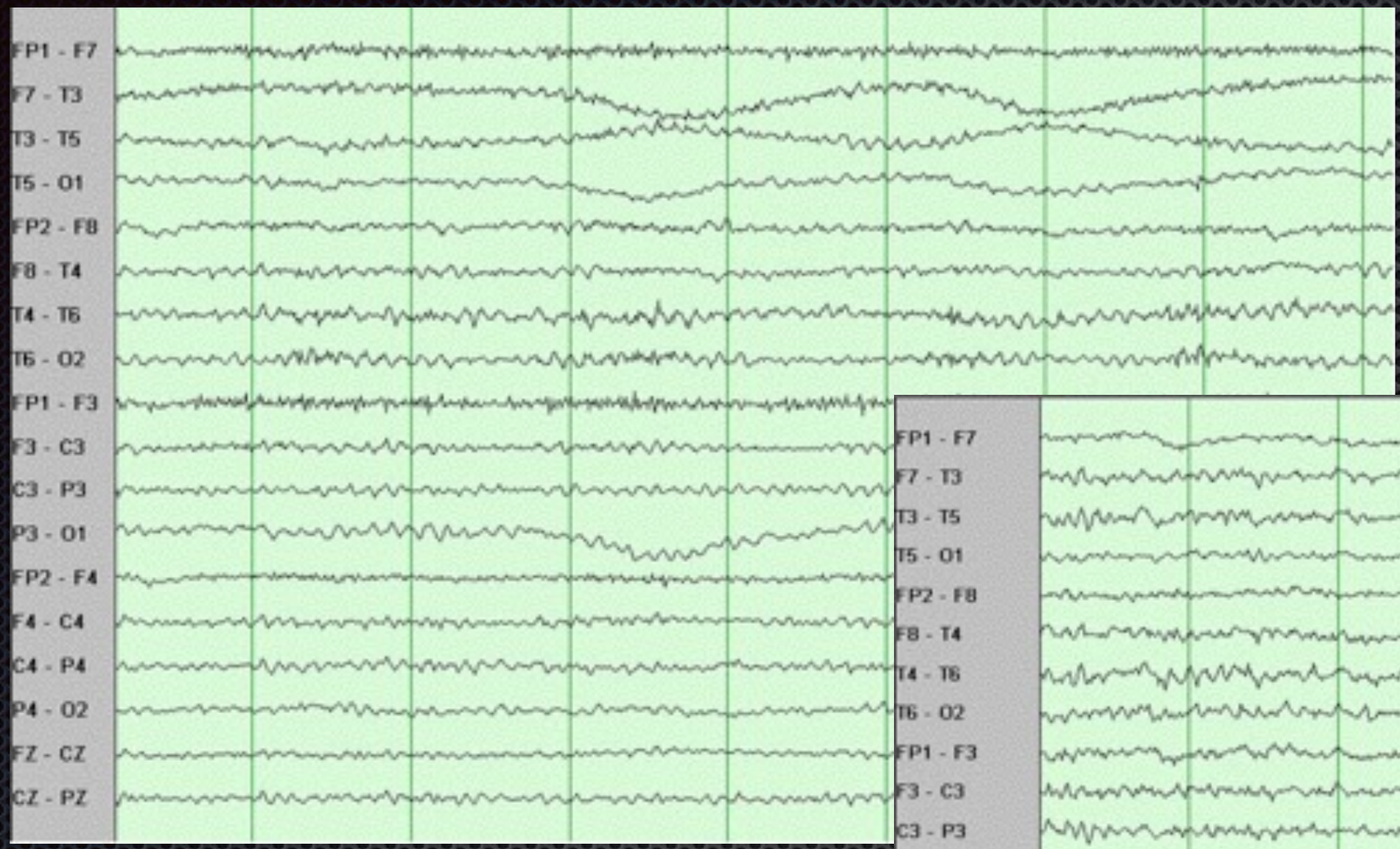




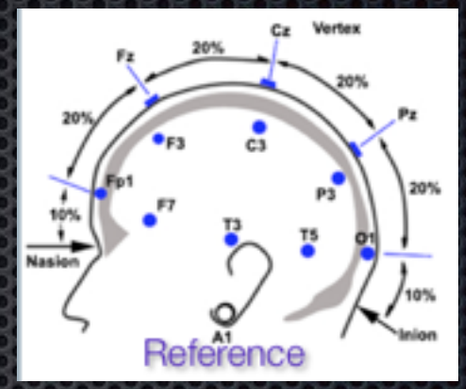


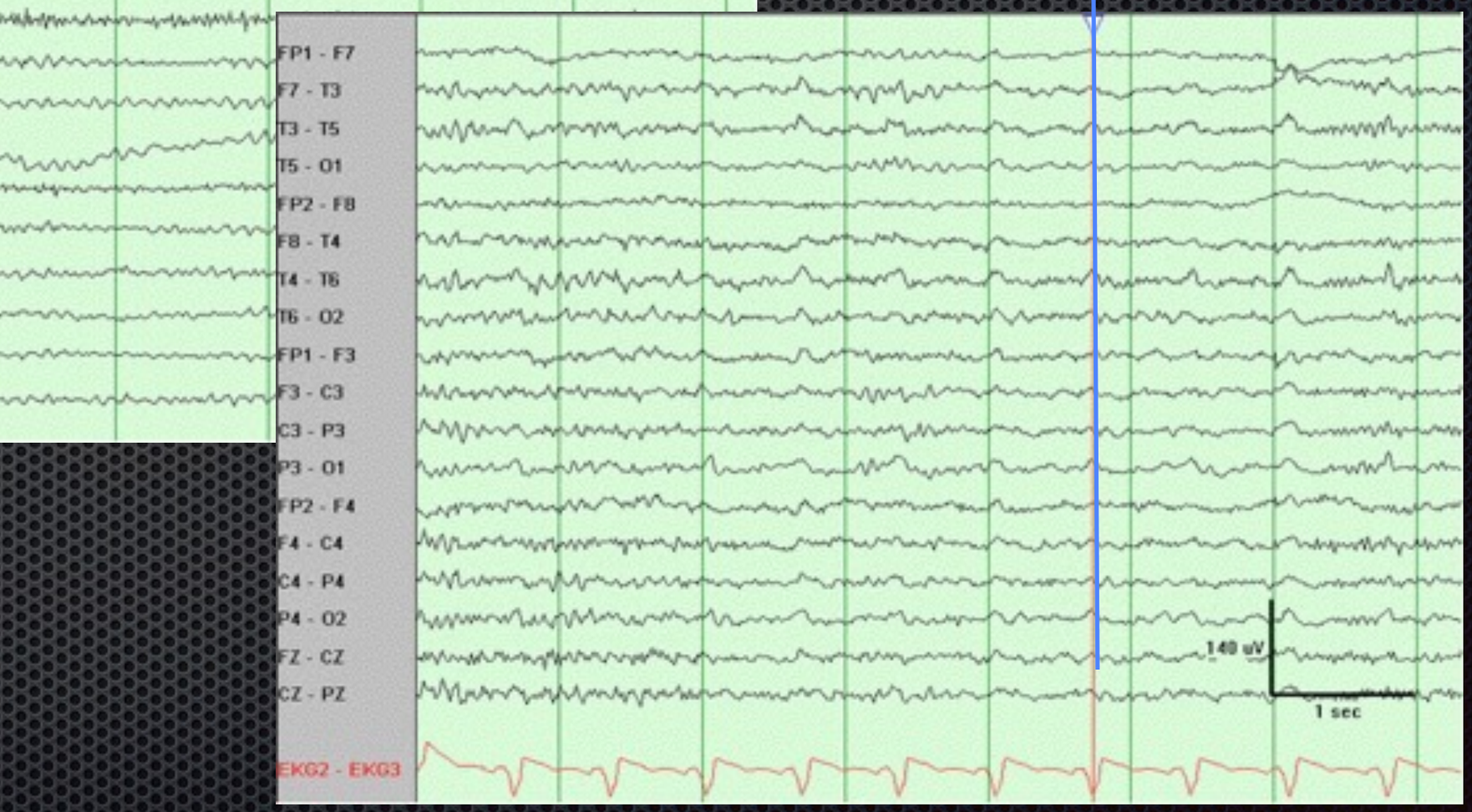
removal, template matching, ICA

# PHYSIOLOGICAL: Muscle, Eyes, Tongue, Skin, ECG



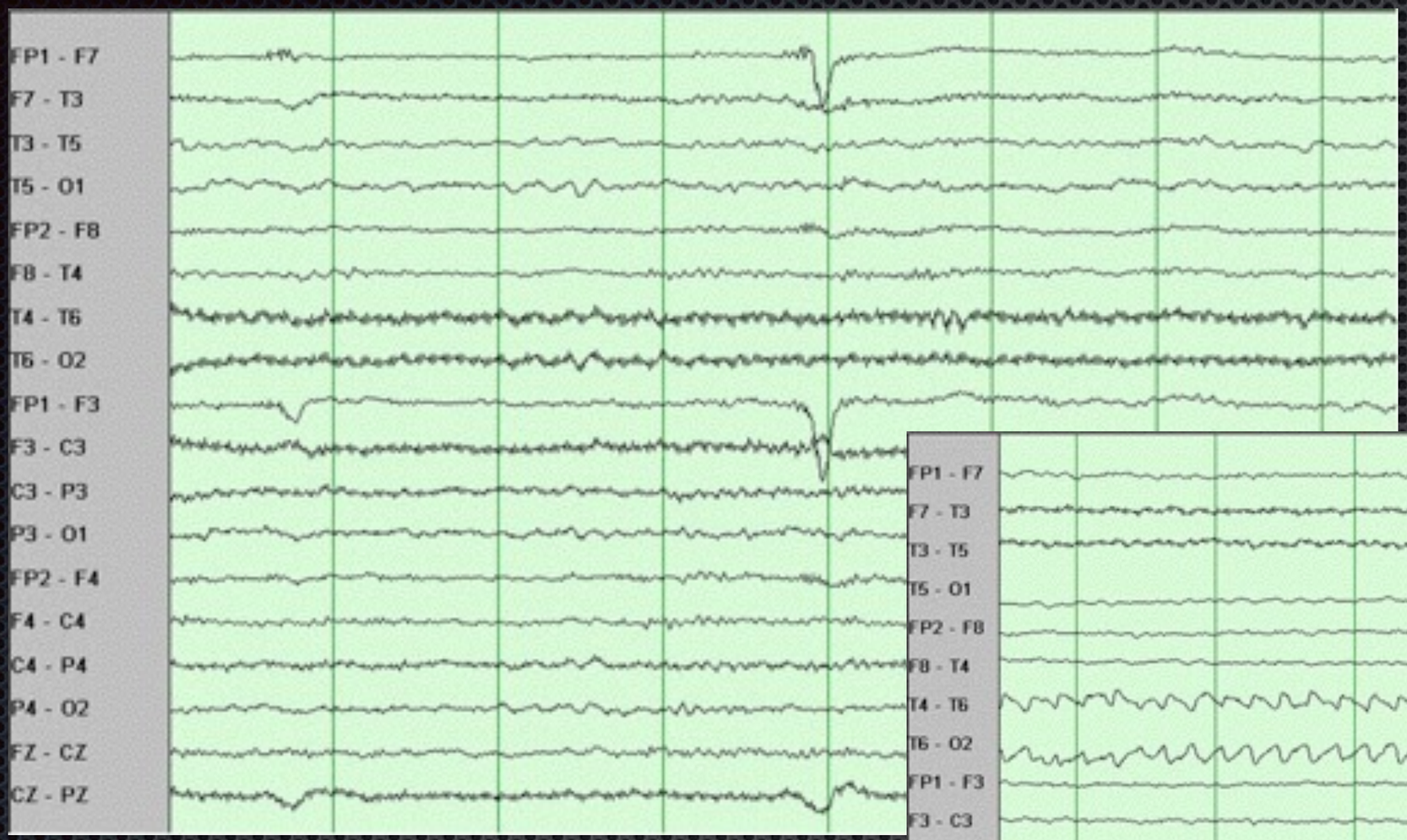

filter > 1Hz

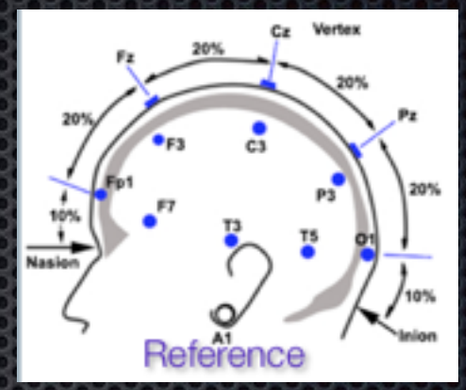


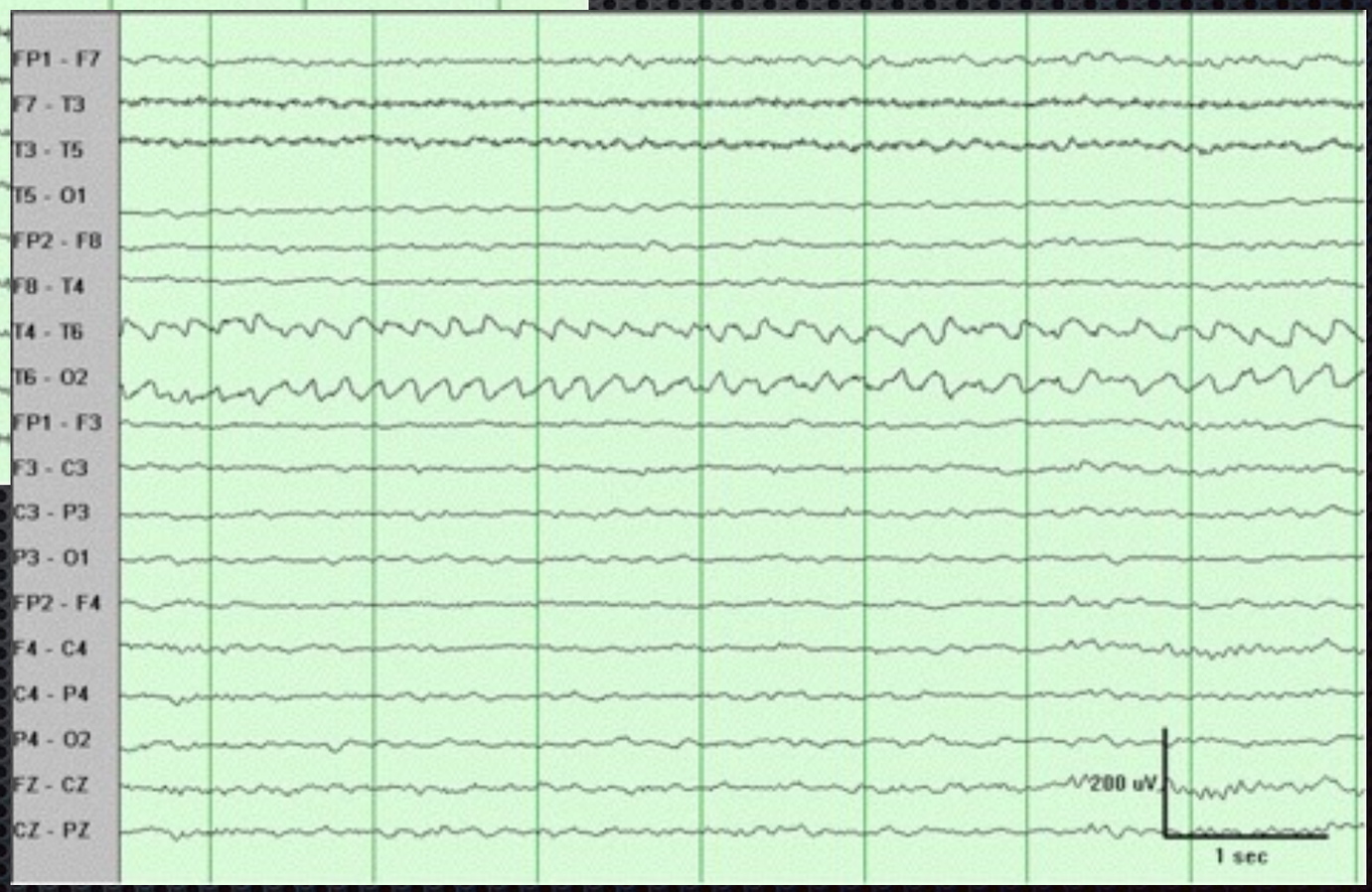

removal, template matching, ICA

Environmental: 60/50Hz,
electrode popping/slipping



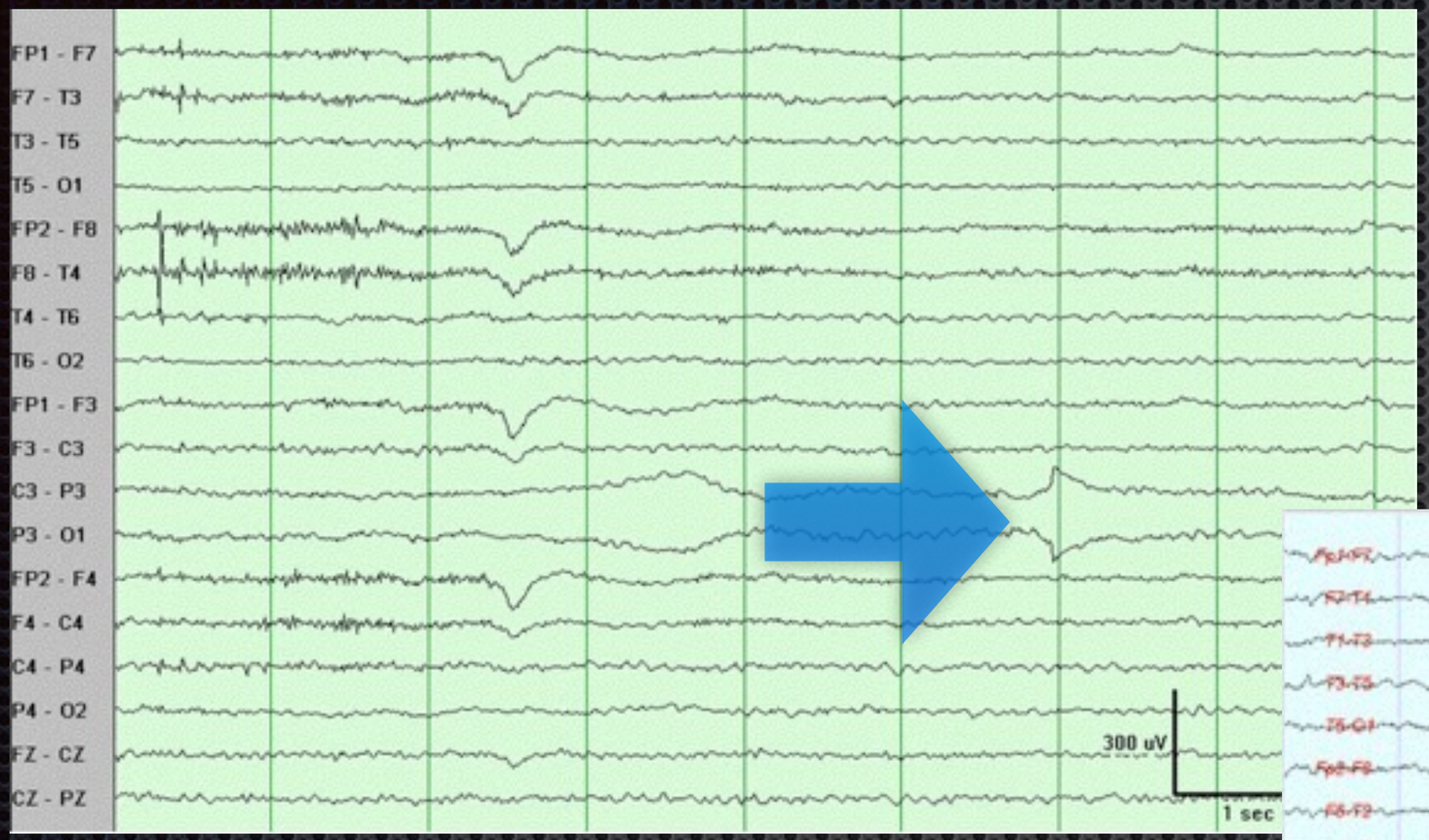



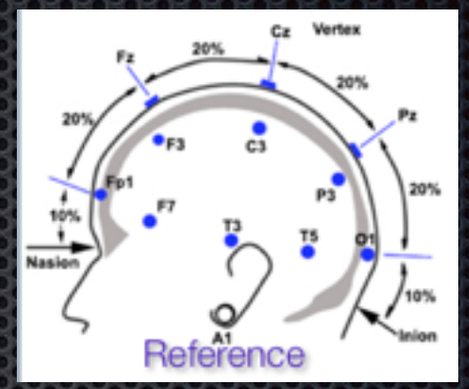

filter notch at narrow freq or <40Hz

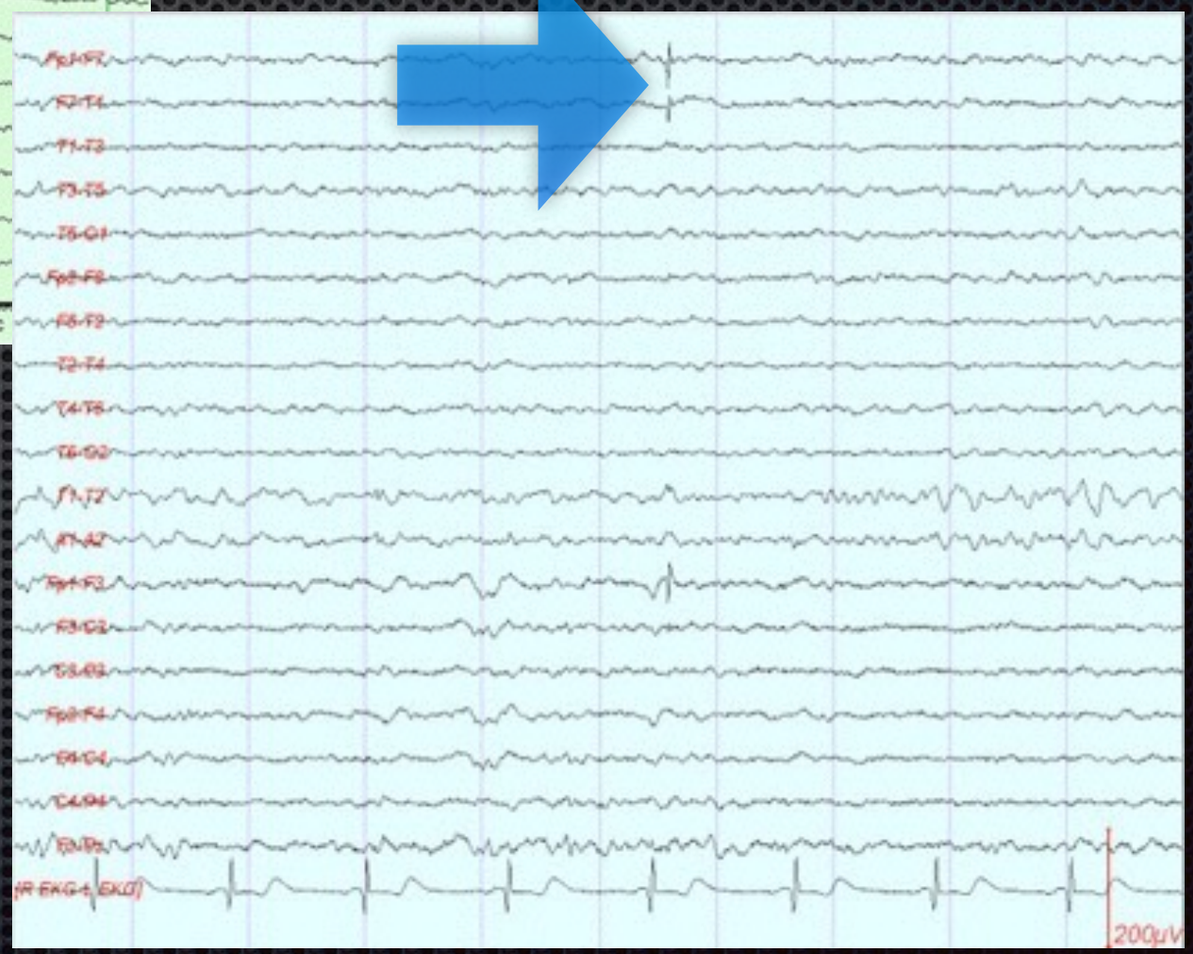



ICA, interpolation

# Environmental: 60/50Hz, electrode popping/slipping




ICA, interpolate, filter, exclude

# Preprocessing Decision Chart

*No correct set of steps - must be chosen based on needs of your analysis.*

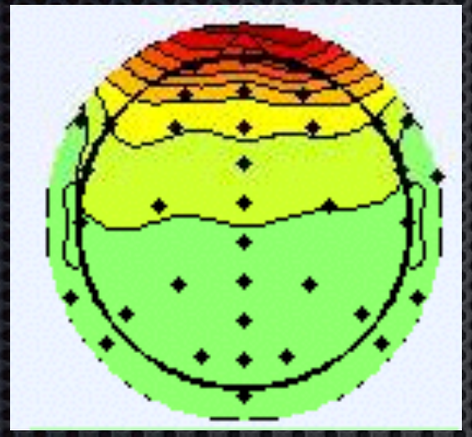
| High Pass Filter (>0.1/1Hz) | Low Pass Filter (<40/50Hz) | Interpolate Bad Electrodes |
|---|---|---|
| DC Recording: NO<br>Not DC Recording: YES | Study high-gamma: NO<br>ERPs or low freq: YES | Sparse Array: NO<br>Dense Array/Source Imaging: YES |
| Remove drift artifacts | Remove muscle, high freq electrical noise, electrode pops. | Maintains full montage |

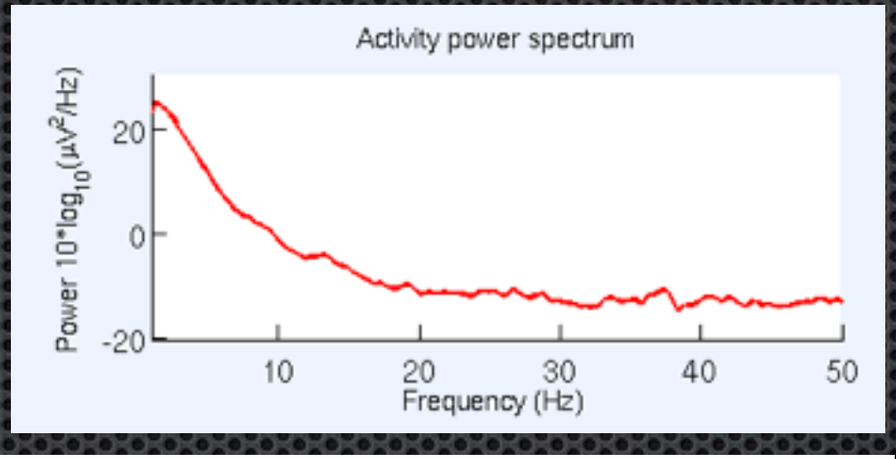
| Ocular Artifact Correction | Exclude bits of data |
|---|---|
| YES | Segmenting: YES<br>Continuous: MAYBE |
| Attenuates Noise Variance | Attenuates Noise Variance |

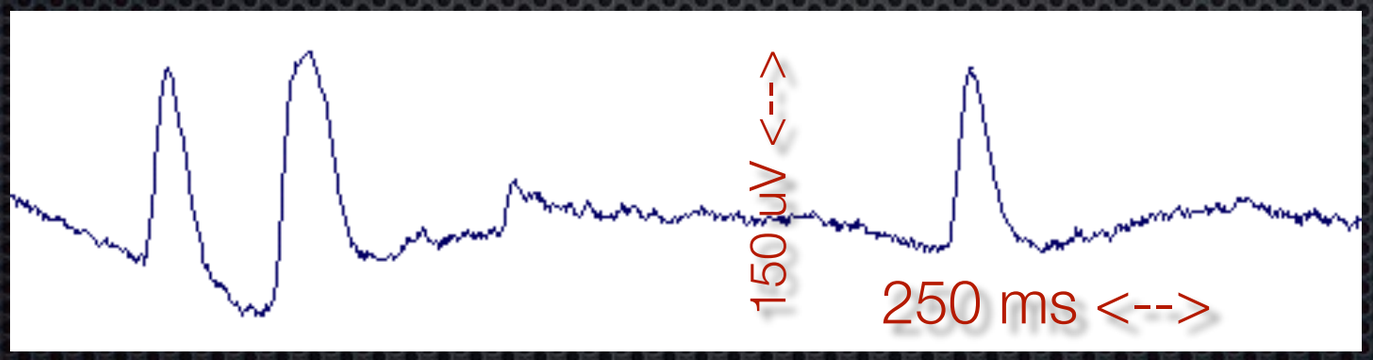
# Eye artifacts & ICA fun

1. Template based removal. Record from below/above eye and use the signals in these electrodes to ‘regress out’ similar activity in scalp leads (Gratton, Coles & Donchin, 1983).

2. Isolate eye related artefacts by blind-source separation methods (ICA).



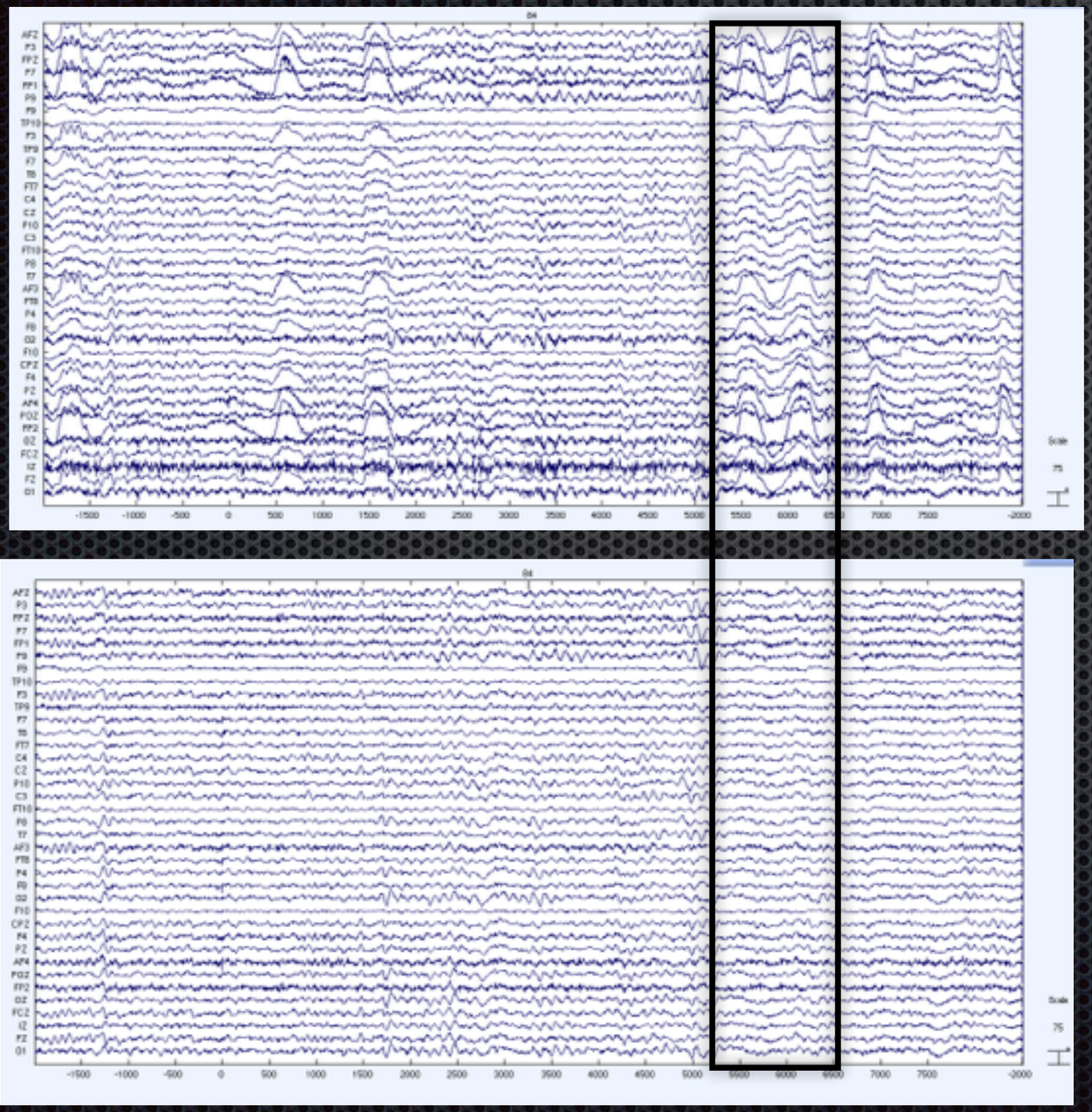



# X = W’S

extended Infomax (Lee, Girolami, Sejnowski, 1999)

# Eye artifacts & ICA fun

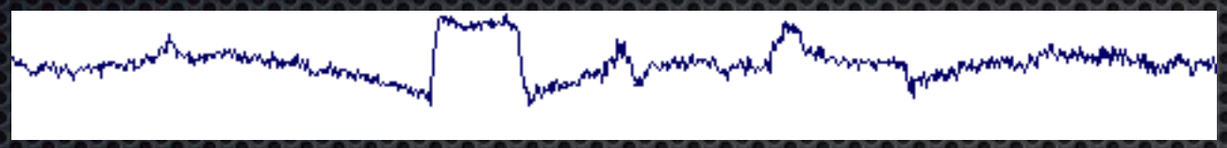


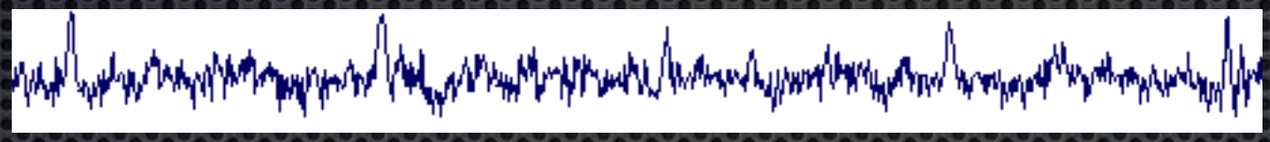
Which is pre-IC removal?
Which is post-IC removal?

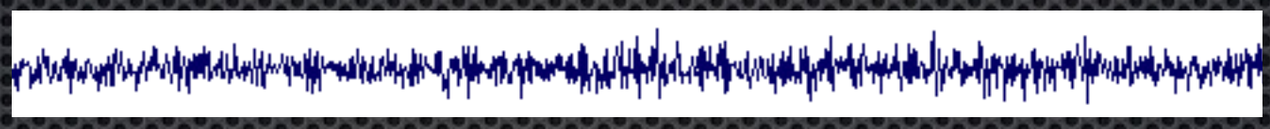
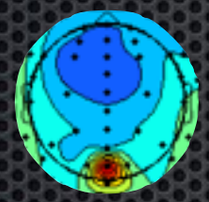
It works quite well (Hoffman & Falkenstein, 2008)!

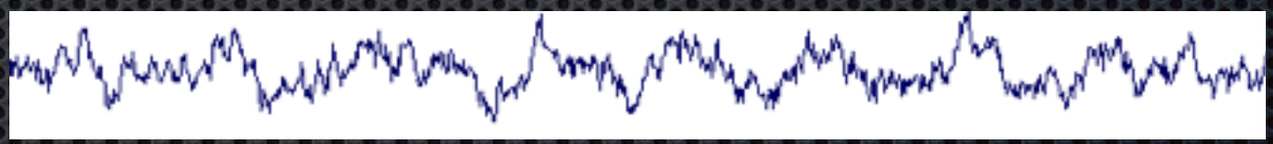
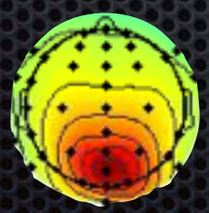
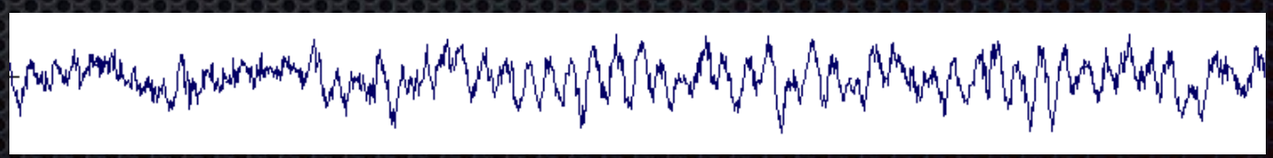
Caveats
- it helps to do a little bit of pre-cleaning (remove drift and bad electrodes, bad segments)
- infomax not so good with muscle - amica does work well with muscle (but experimental)
- ultimately seeks temporal independence (stationarity assumption)

# Other artifacts & ICA fun

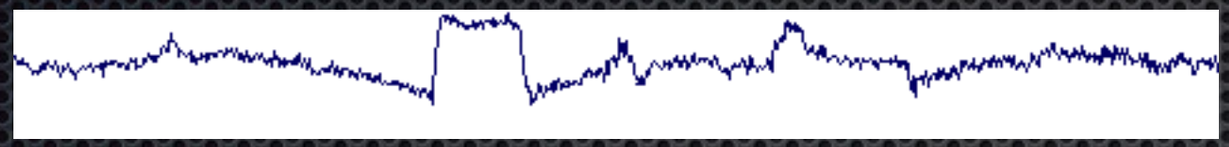



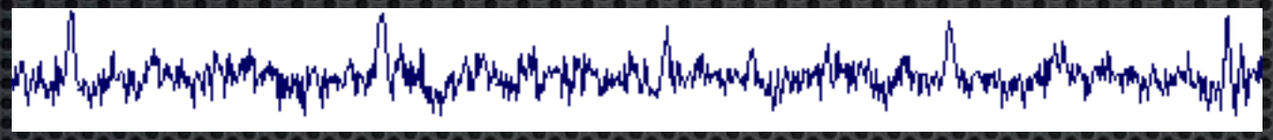


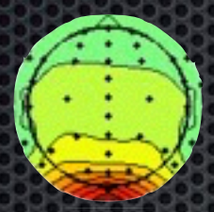



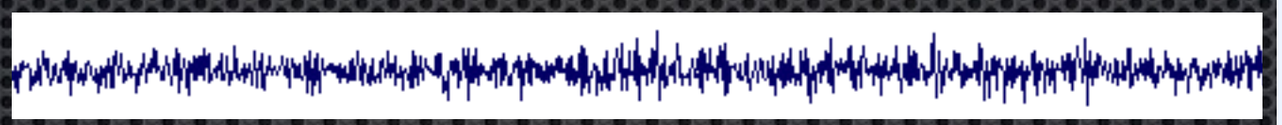





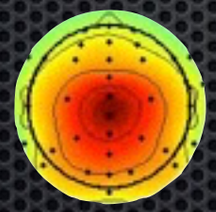
# Other artifacts & ICA fun

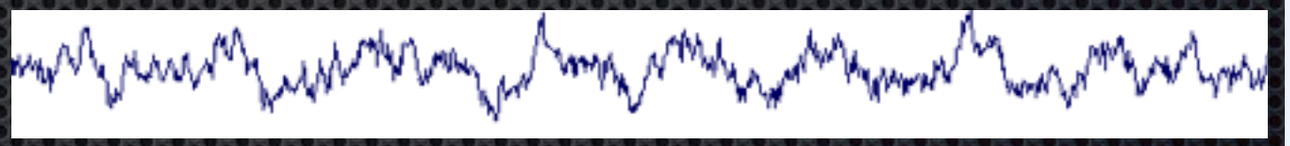


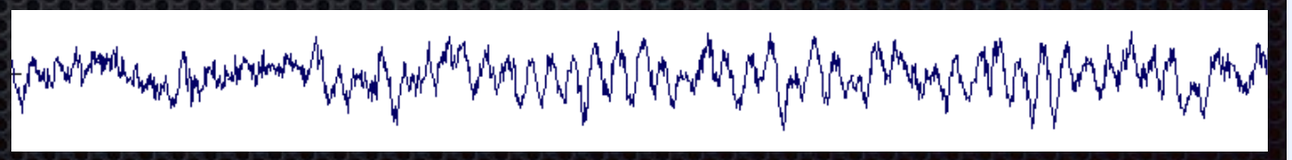


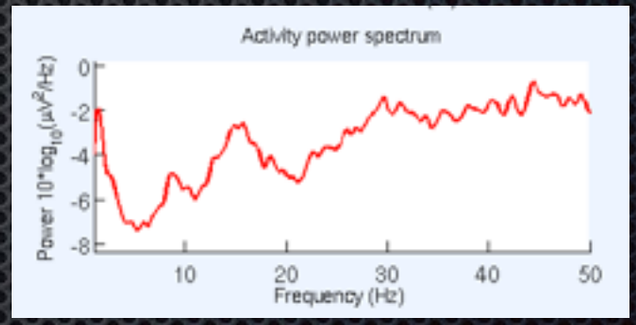


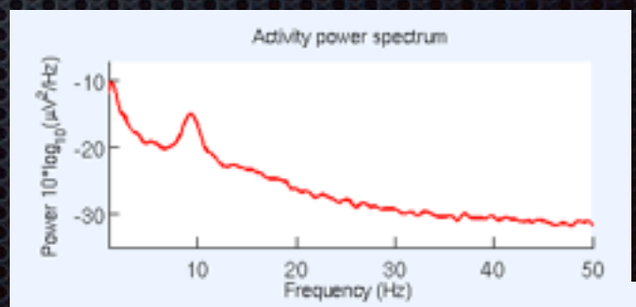


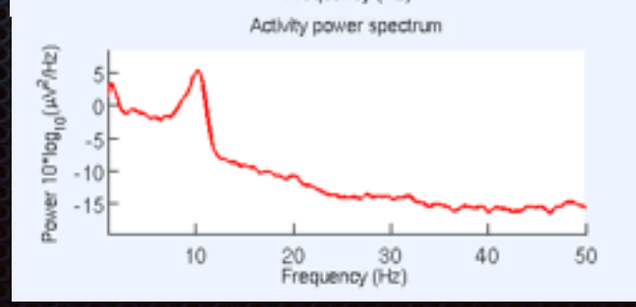








How can we use EEG data to learn something about brain function?

Brain States

Timing of Neurocognitive Processes

Neural/Network Dynamics

# Brain States

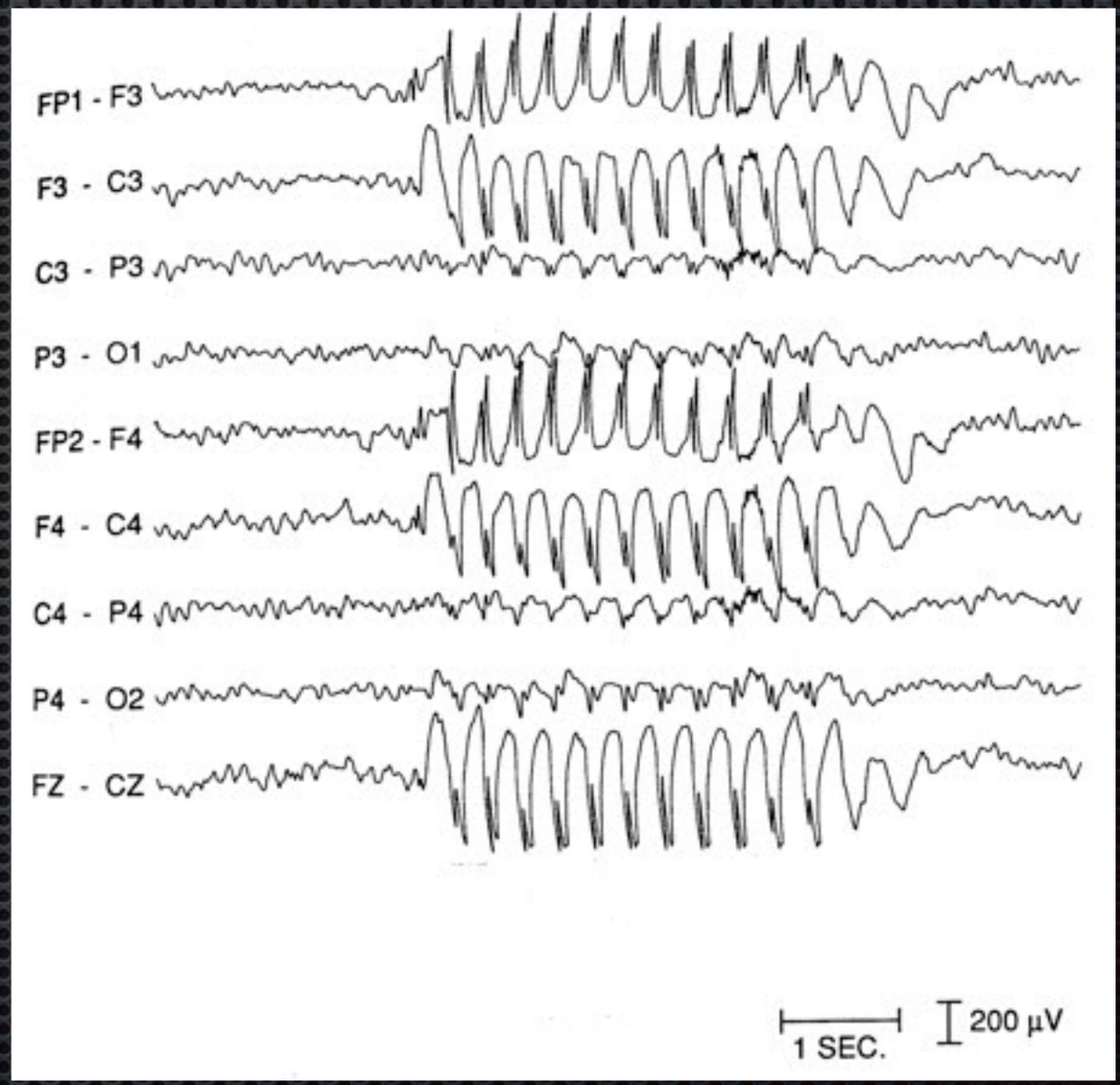
- initial EEG experiments examined *unique events* and *spectral content* across *entire recording and electrode set*

*qEEG (quantitative EEG)*
*clinical term to indicate quantitative (typically spectral) description of data in contrast to qualitative description*

- focus is on neural event of functional significance, not on neural mechanisms (recall Hans Berger)

# Brain States

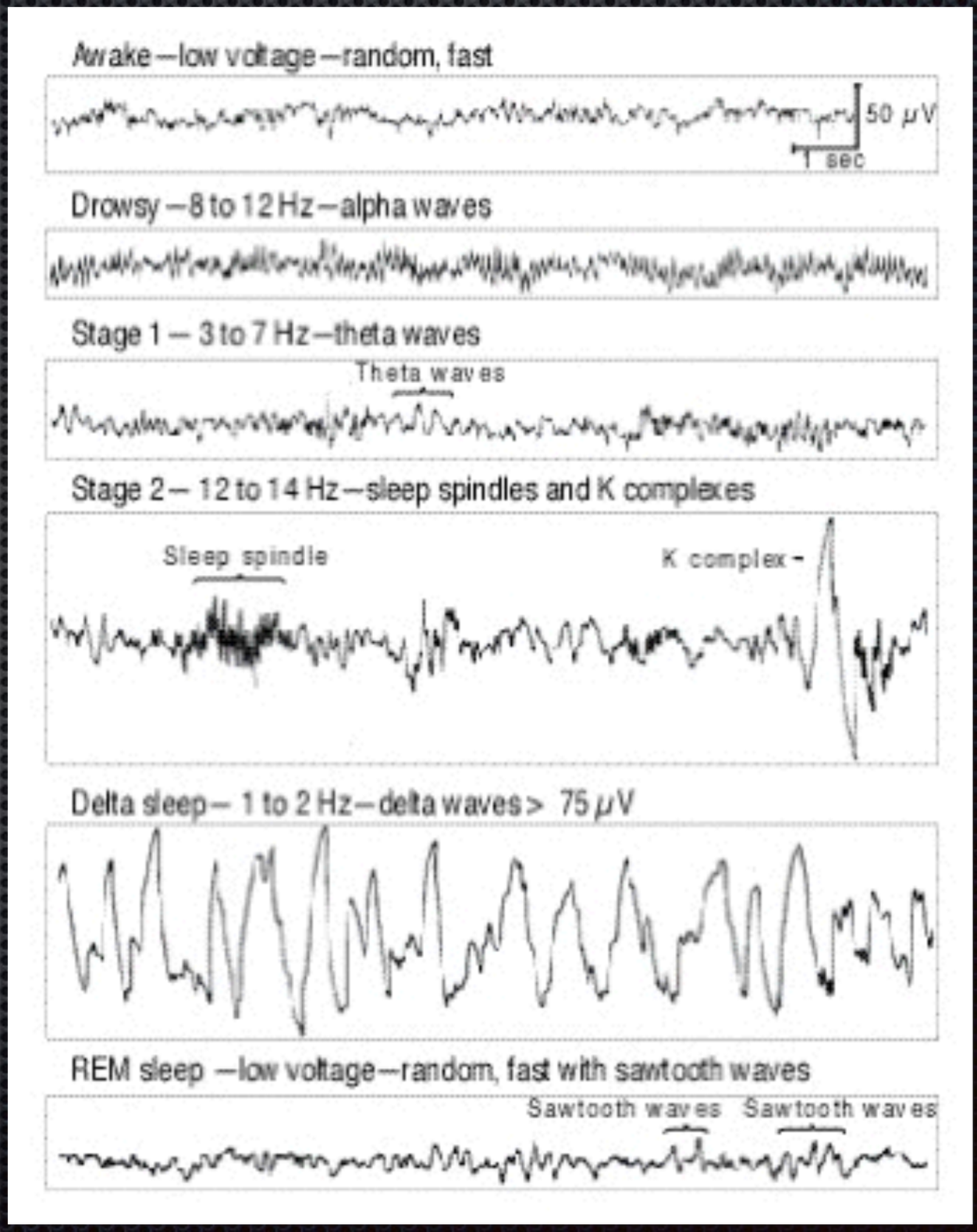
- epilepsy



# Brain States

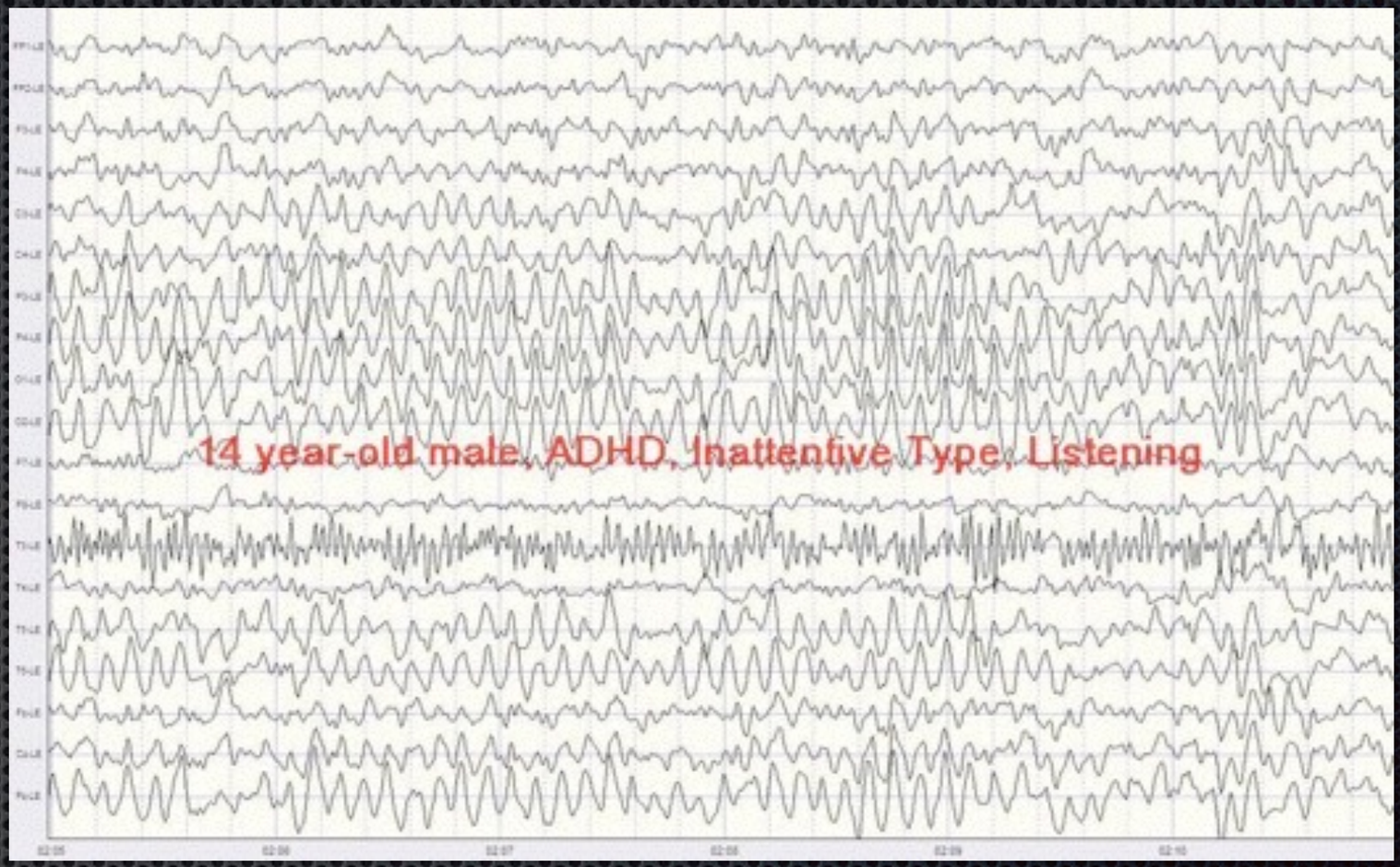
- epilepsy
- sleep

progression from fast to slow oscillation with increasing sleep



# Brain States

- epilepsy
- sleep
- psychiatry




e.g., theta (3-7Hz)/beta (12-30Hz) ratio increases interpreted as “less active” brain states being dominant

# Brain States

These are robust measures - visible to the naked eye, require relatively little data, easy to compute (qEEG). Non-qEEG requires training.

They are non-specific correlates of gross changes in brain state as they tell us nothing about underlying brain sources. This can be a problem for obtaining specificity in attempting to use these measures as diagnostics (types of epileptic event, psychiatric diagnosis).

***Note: This is not to say that one couldn't figure out sources of these gross changes, though it's surprising how little of that we have achieved.***

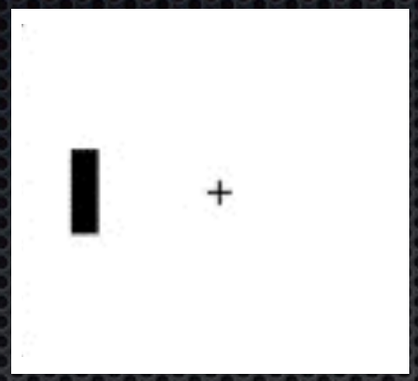
# Brain States

## Timing of Neurocognitive Processes

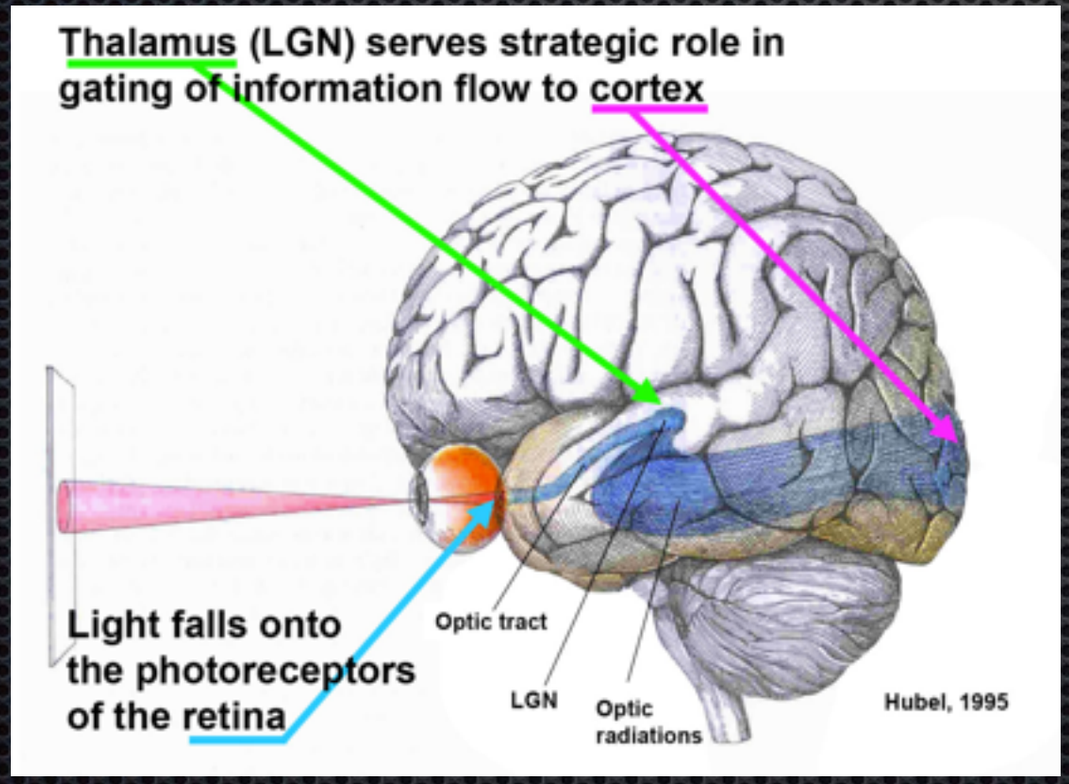
bipolar
montage

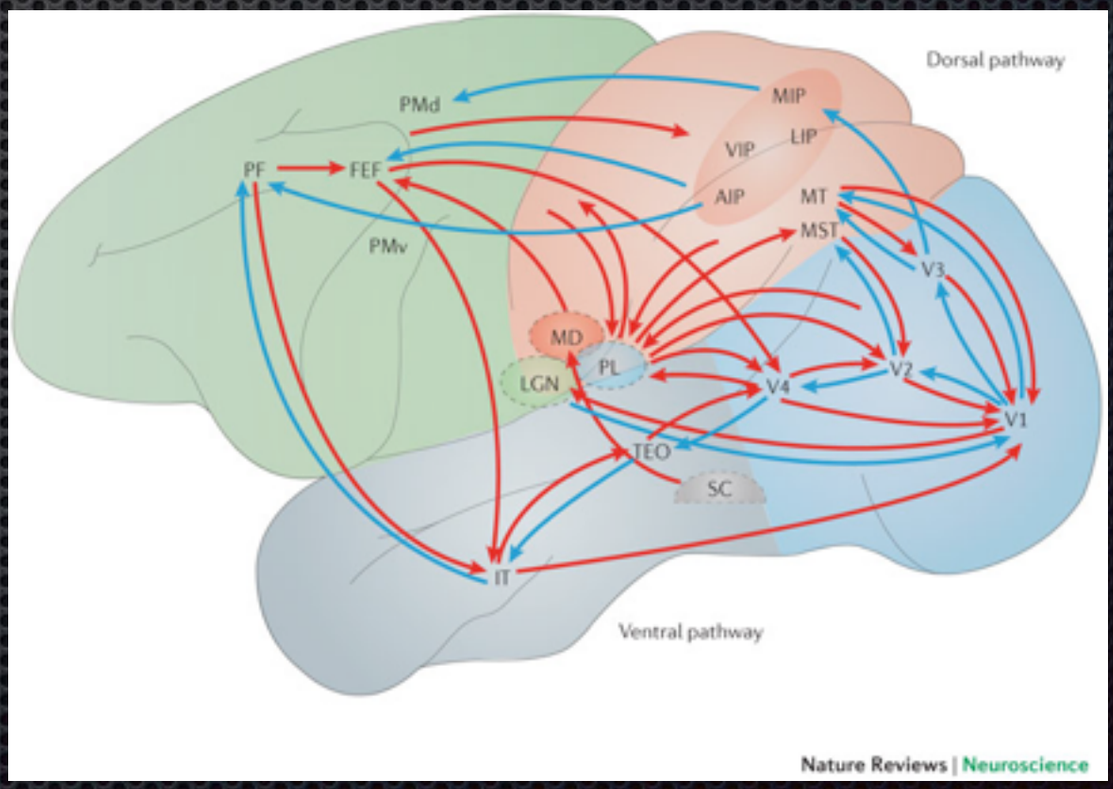
# Human Electrophysiology II

## Principles of Neuroimaging

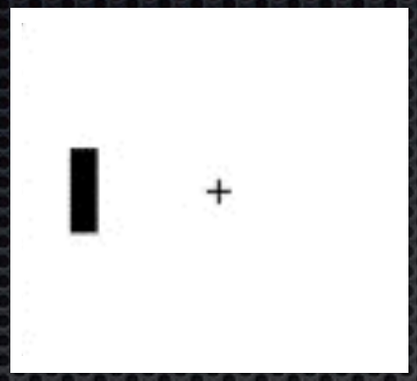


Q. At what time in the neural processing cascade do effects of attention impact visual processing?

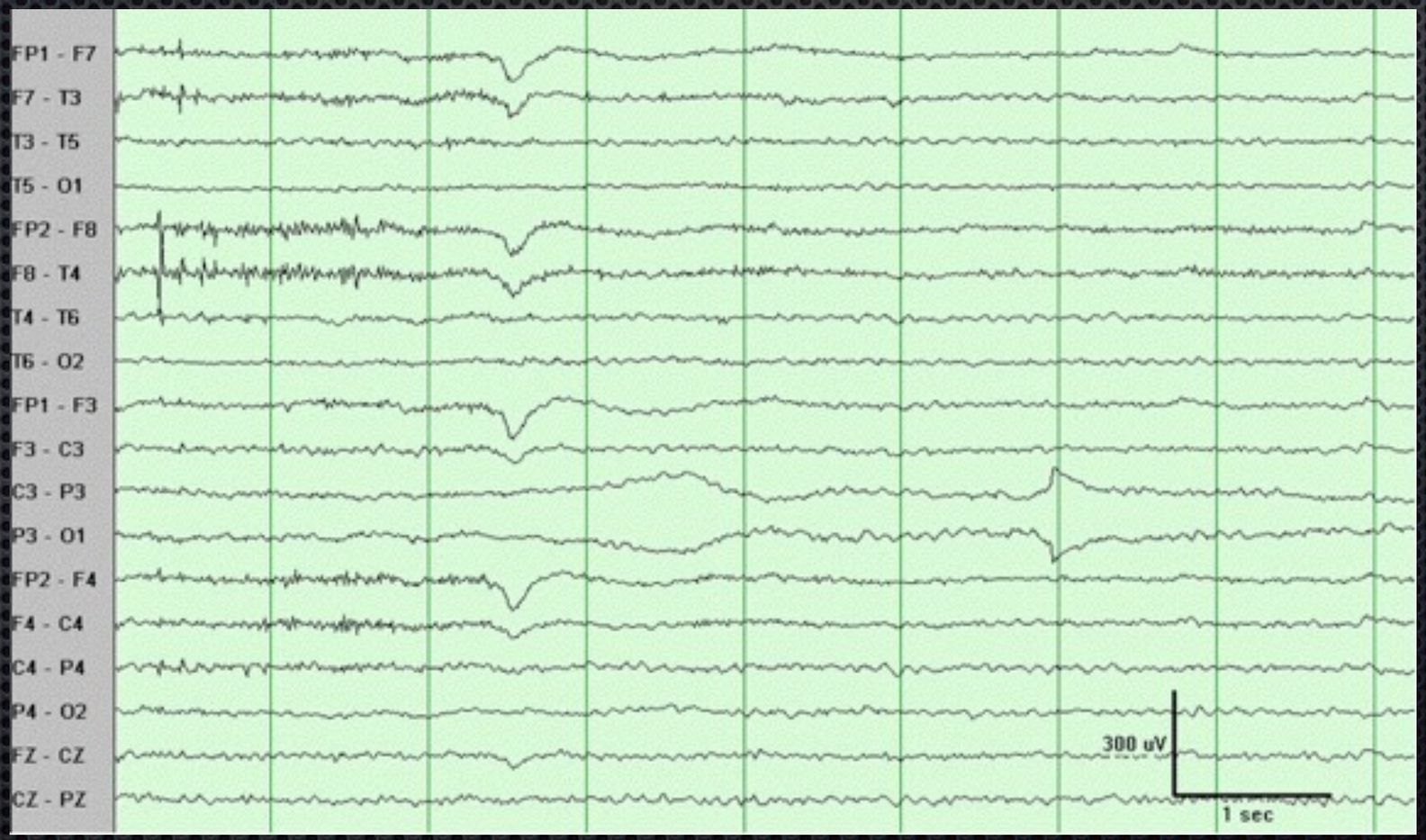


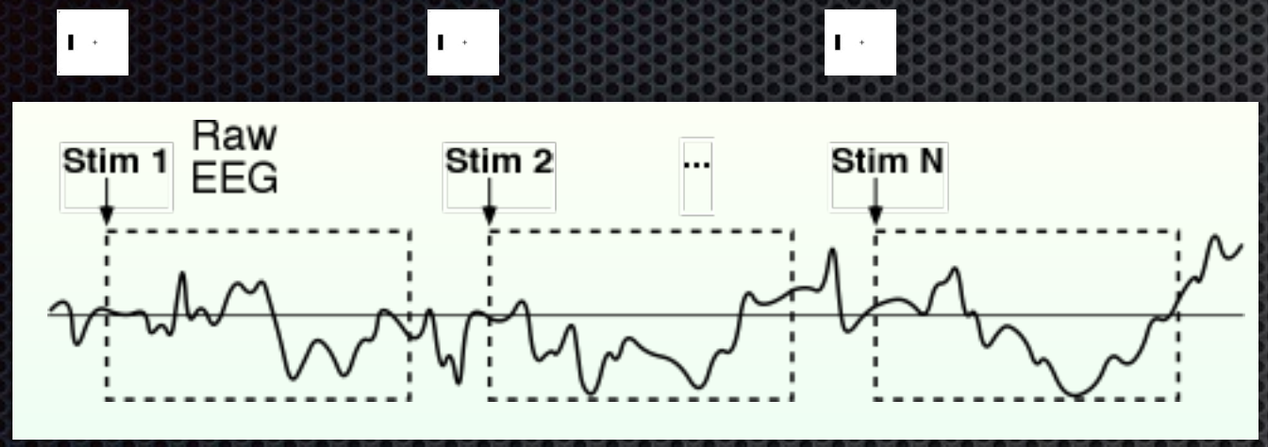

Gilbert & Li, 2013

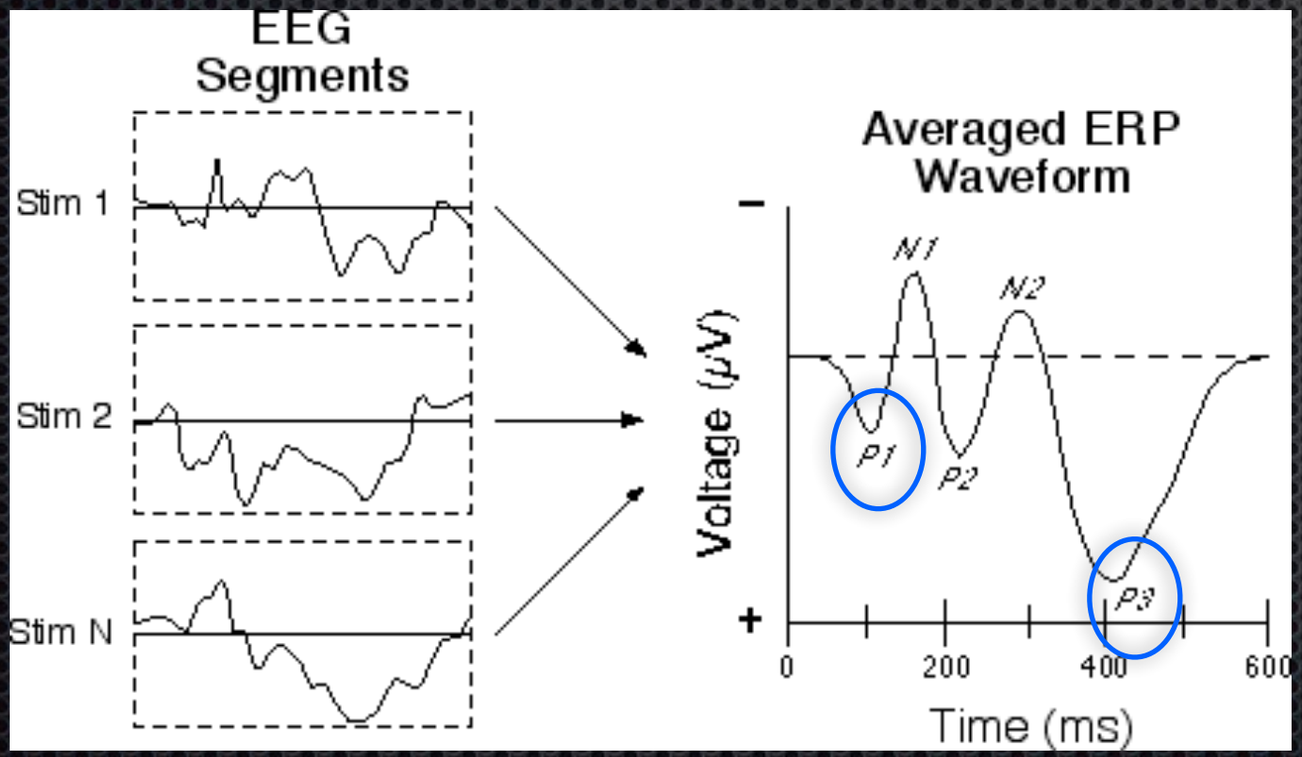


Q. At what time in the neural processing cascade do effects of attention impact visual processing?



# EEG: Event Related Potential




Define "event" - identify onset-locked responses for a window of interest. Average across events to produce a stereotypical waveform describing the timing of key processes following that event.

Assume that we minimize "noise" through averaging.

Typically pre-stimulus interval is subtracted to provide reference.

**-- ERP = event-related potential**

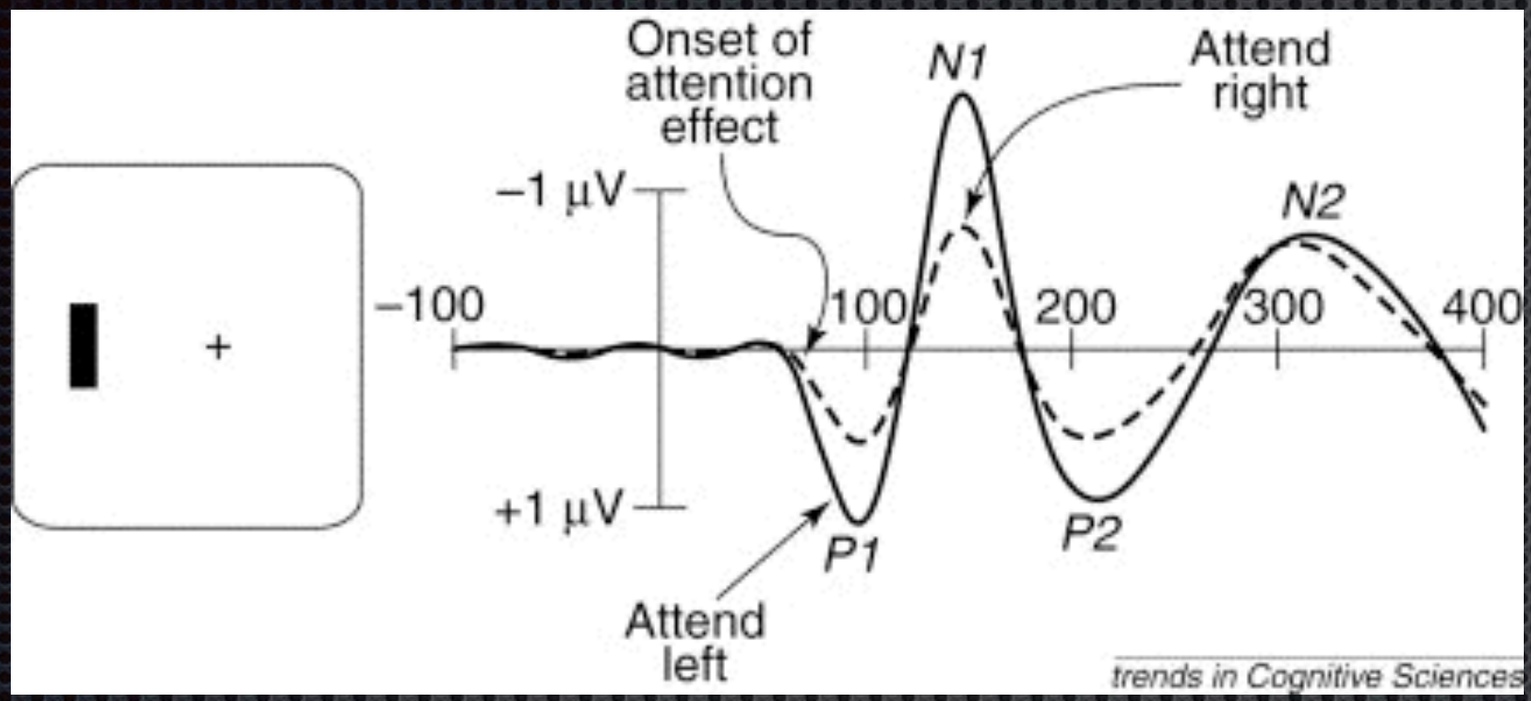
-- sign is not meaningful

-- P = positive, N = negative

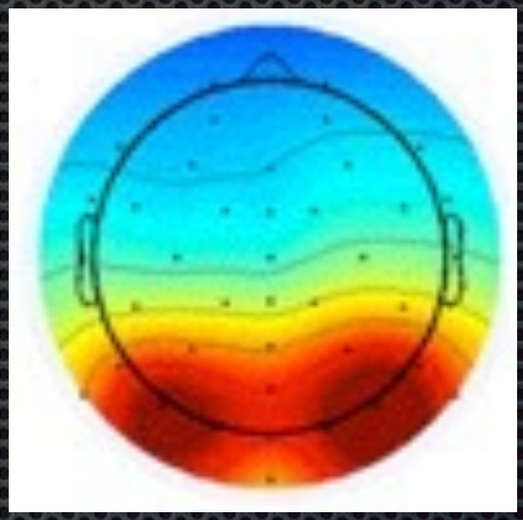
-- XX = latency indicator

# Extracting timing...

Luck (review), TiCS 2007




scale = <10 uV



rinse and repeat at each electrode to plot the scalp topography of the effect

A. Within the first 100 ms of stimulus effects apparent in sensory cortex. In anticipatory paradigms will see this pre-stimulus. Not clear if effects present in thalamus. Can occur at different levels of processing depending on level of “competition”.

# EEG: Event Related Potential

*we can now come up with a buffet of ERP delights to understand the relative timing of different types of neuro-cognitive events*

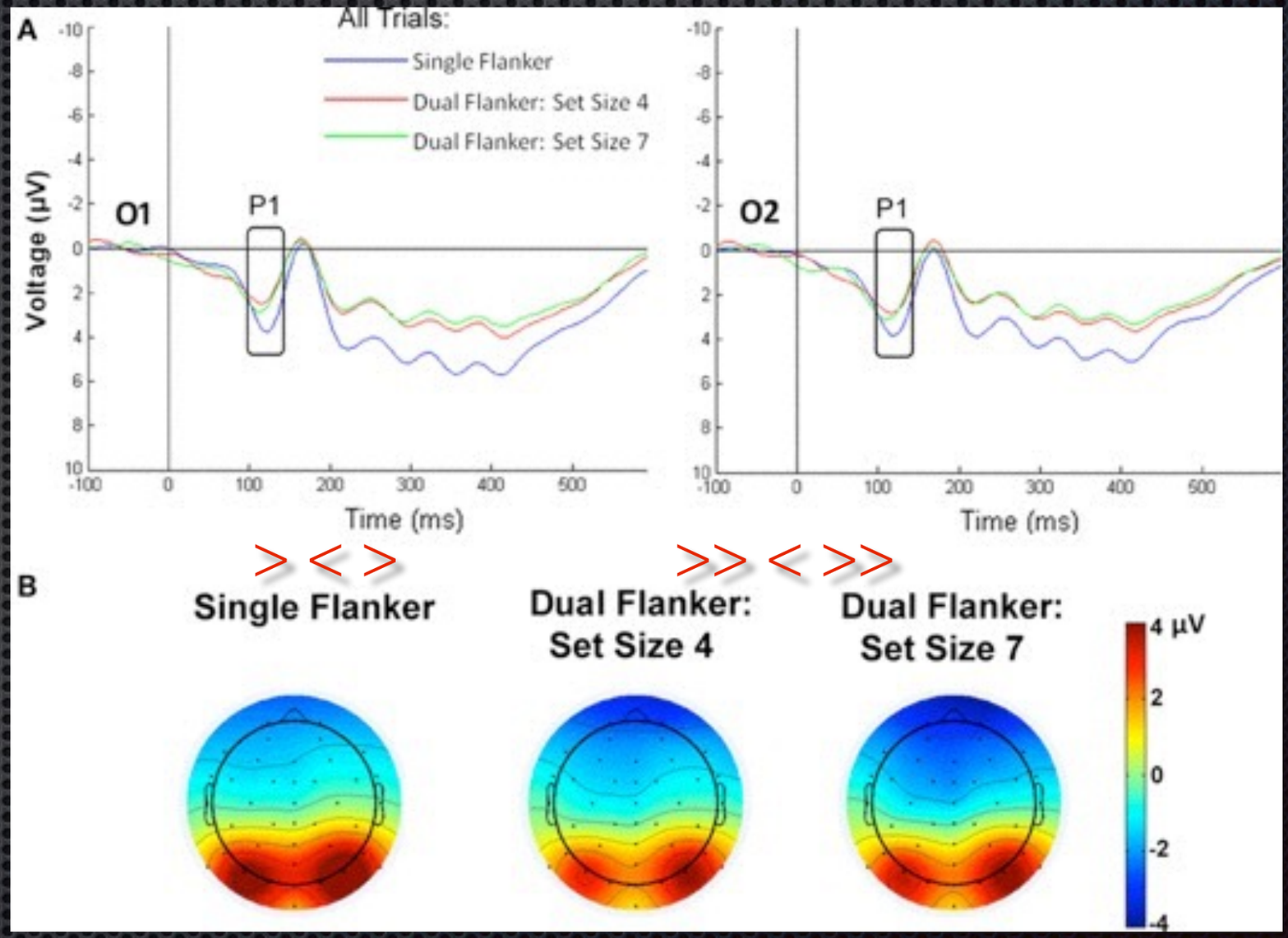
# Steve Hillyard's 6 families of cognitive ERPs:

## 1.Sensory/Perceptual <200ms

P1, N1, N2(faces), Mismatch Negativity (N2), N2Pc

inferred processes:
* automatic stimulus responses
* early attentional selection
* sensory memory

*Perceptual response is present within 100 ms of stimulus onset, and is reduced in presence of visual distractors. Competition thus occurs at this level (visual cortex).*




Pratt et al (2011) Frontiers

# Steve Hillyard's 6 families of cognitive ERPs:

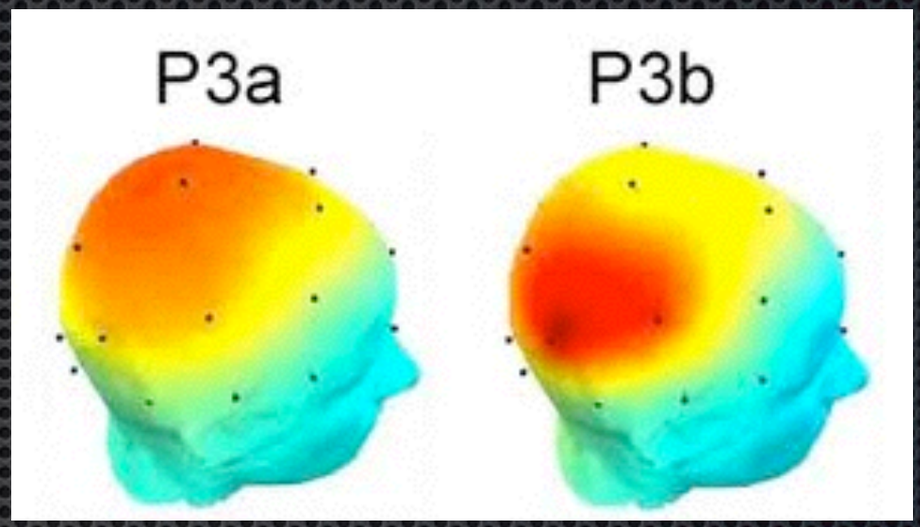
2. Discrimination/Recognition
150-500ms

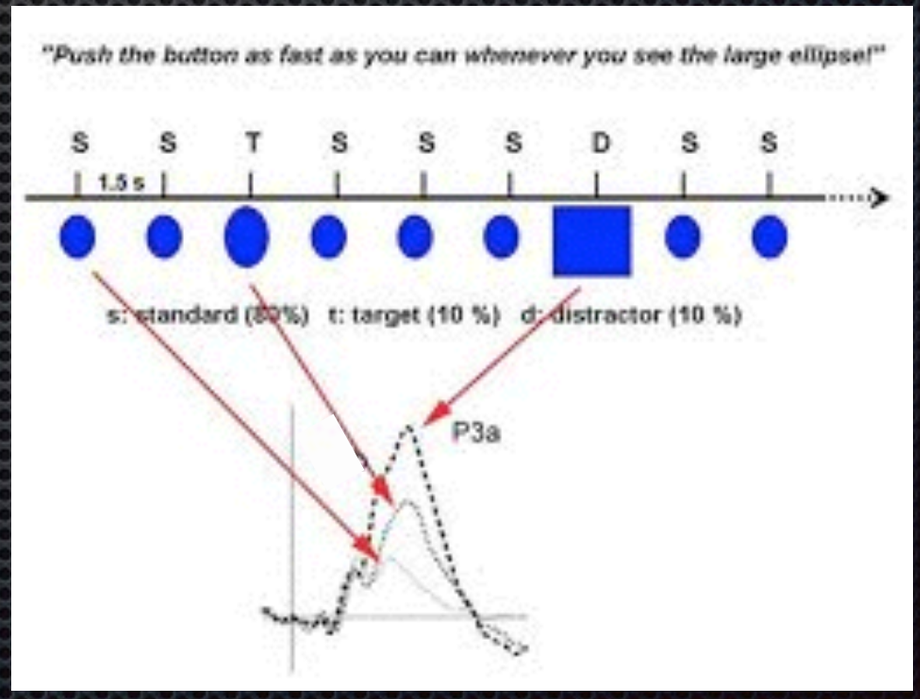
N2, P2, selection negativity, P3's

inferred processes:
* late attentional selection (updating)
* orienting to novelty (vs familiar)
* pattern recognition

*"comparison of signals to internal model"*

*P1 is unaffected by detection instructions, but P3 is affected, suggesting that this is the time at which visual signals are compared against internal template.*



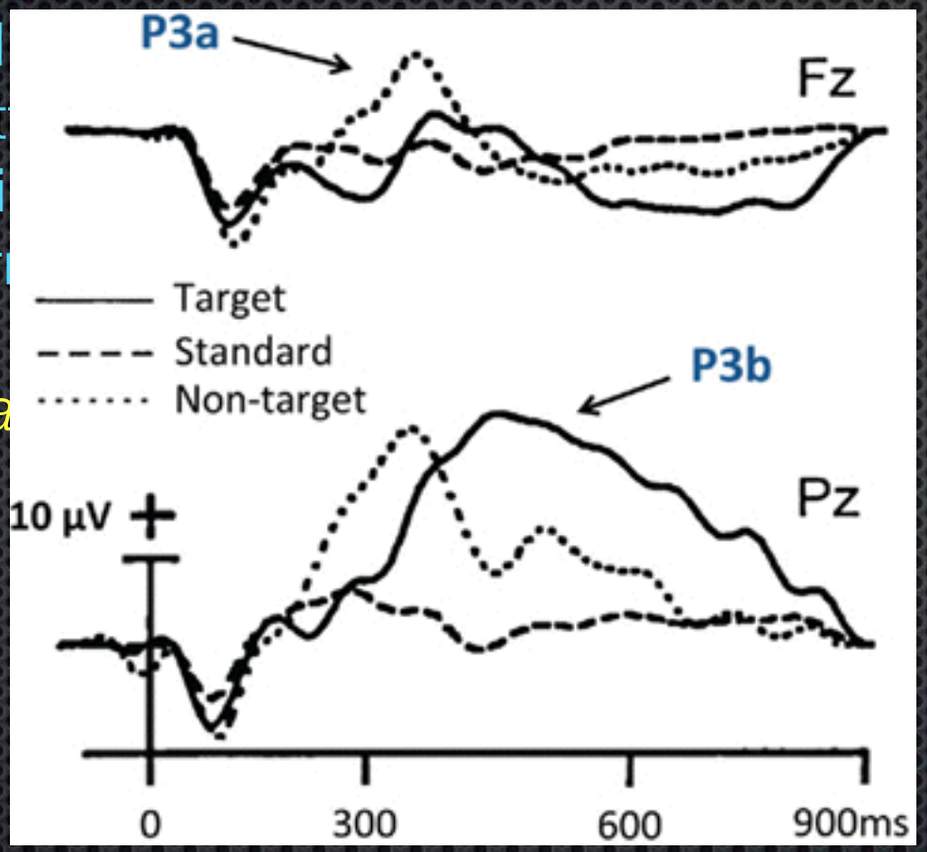
# Steve Hillyard's 6 families of cognitive ERPs:

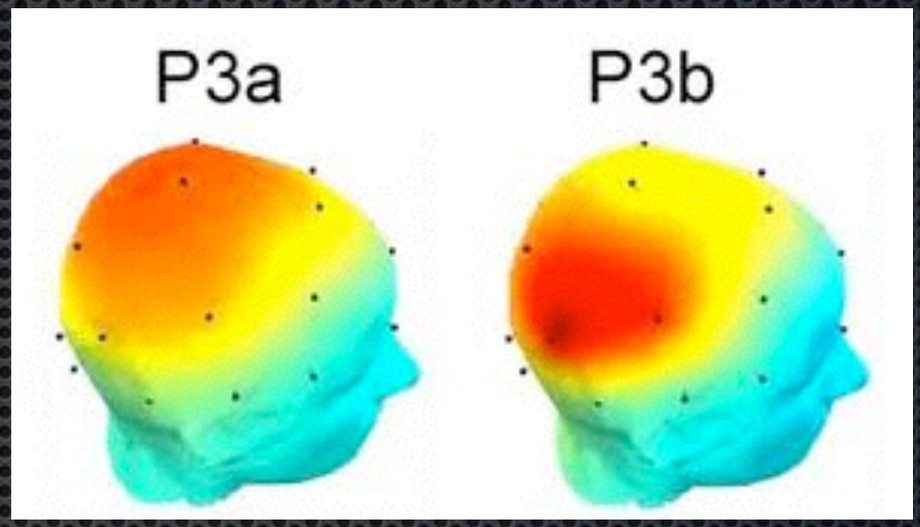
## 2. Discrimination/Recognition 150-500ms

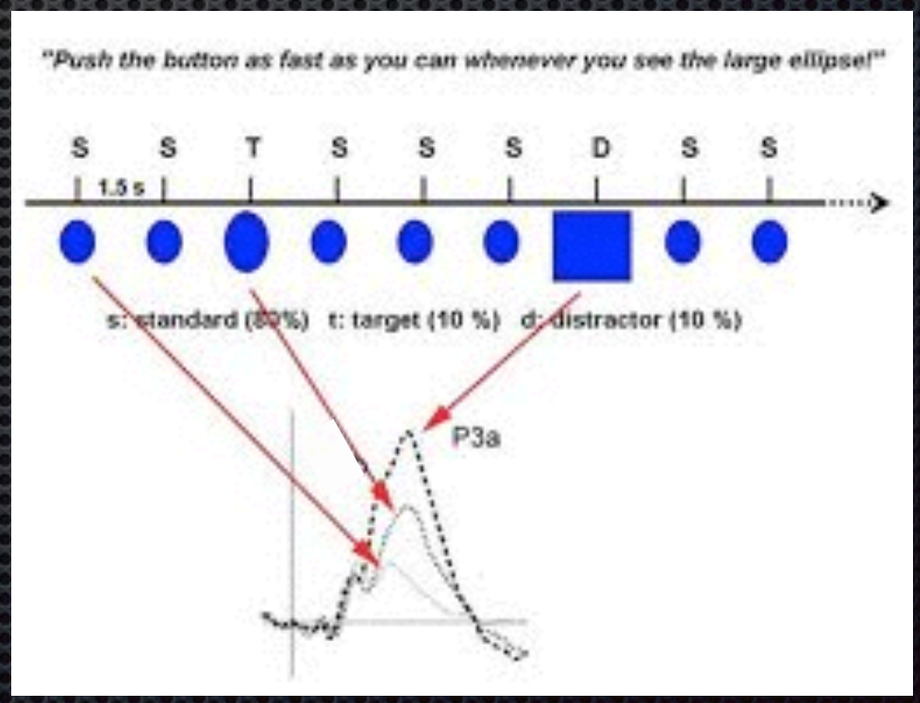
N2, P2, selection negativity, P3's

inferred
* late at
* orienti
* patter

*"compa*




*Template comparison involves different processes for task-related and task-unrelated, but salient, inputs. The latter is a faster process (capacity to interrupt?).*

# Steve Hillyard's 6 families of cognitive ERPs:

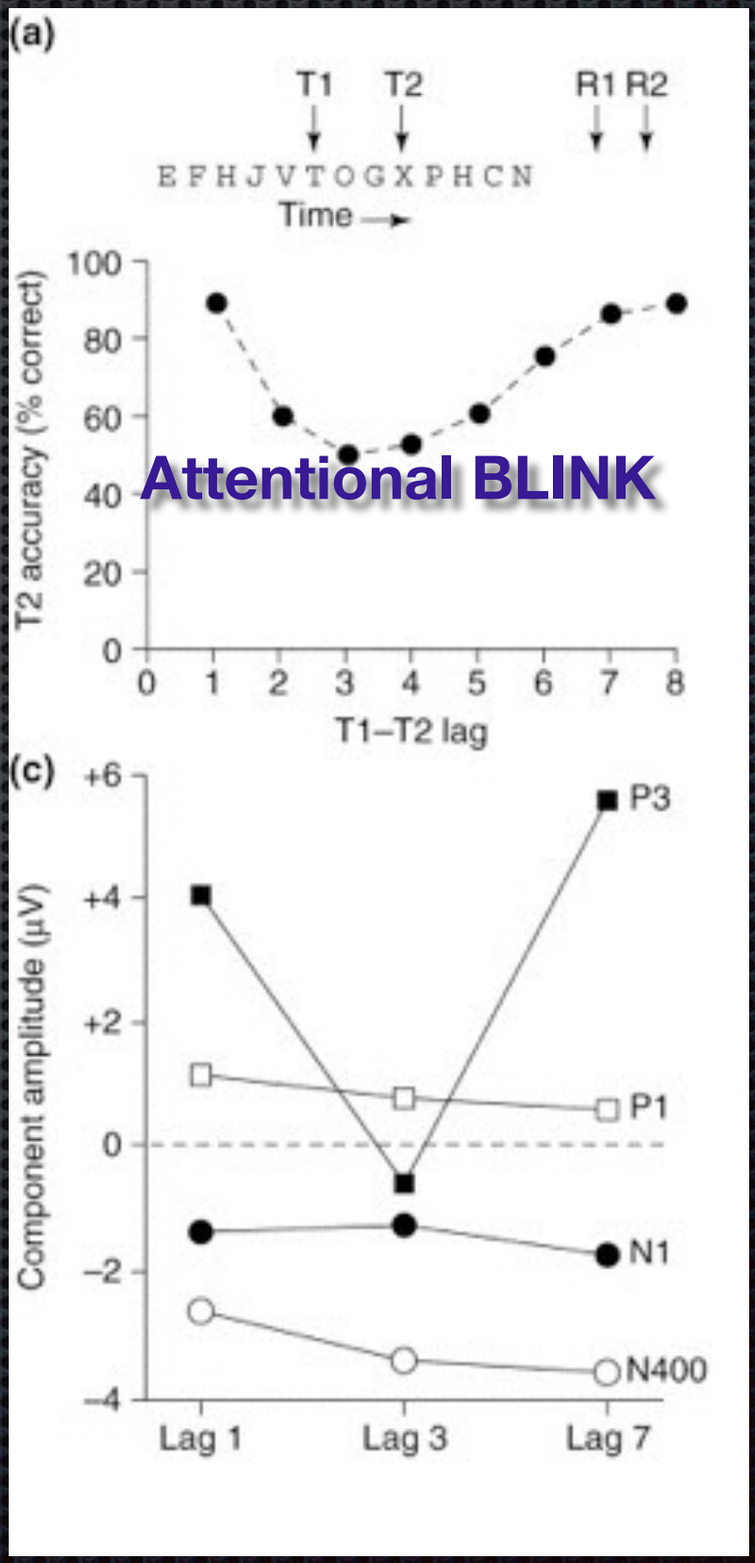
2. Discrimination/Recognition
150-500ms

N2, P2, selection negativity, P3's

inferred processes:
* late attentional selection (updating)
* orienting to novelty (vs familiar)
* pattern recognition

*"comparison of signals to internal model"*

*Template comparison tie-ups "resources" that translate a visual input (P1, N1) into a label.*

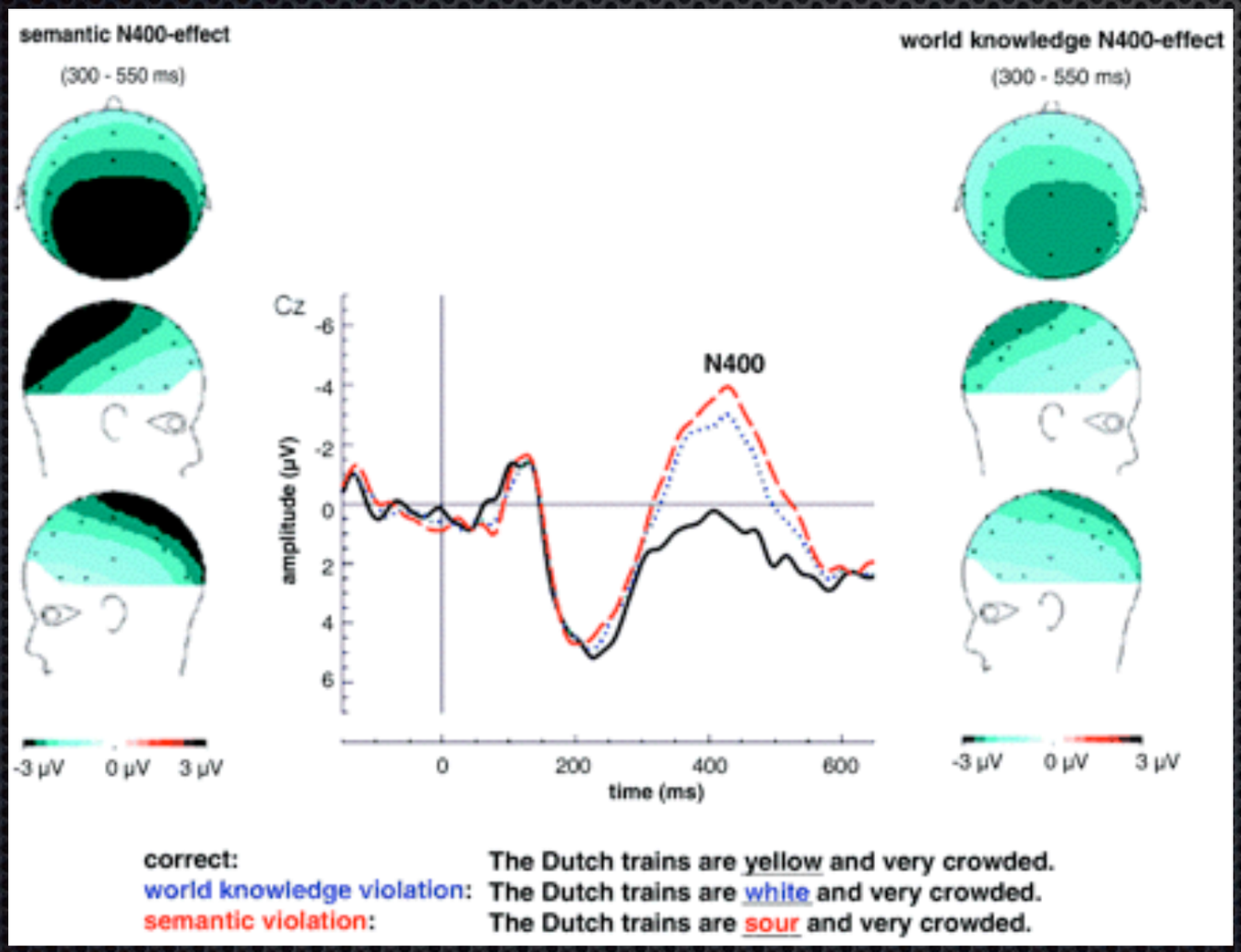



Luck (review), TiCS 2007

# Steve Hillyard's 6 families of cognitive ERPs:

**3. Memory Related (2-600 ms)** — Late positivities, negativities.

**4. Language Related (2-600 ms)** — N400, Syntactic positive shift, lexical processing negativity, left anterior negativity.




*Like template comparison (visual P3-like potentials), syntactic/content matching has a latency of >200 ms. Slower than visual.*

Hagoort et al (2004) *Science*

# Steve Hillyard's 6 families of cognitive ERPs:

## 5. Readiness Potentials

Lateralized Readiness Potential (LRP) [c3-c4]
Bereitschaftspotential (BP) [c3 or c4]
Cognitive Negative Variation (CNV) [frontal midline]

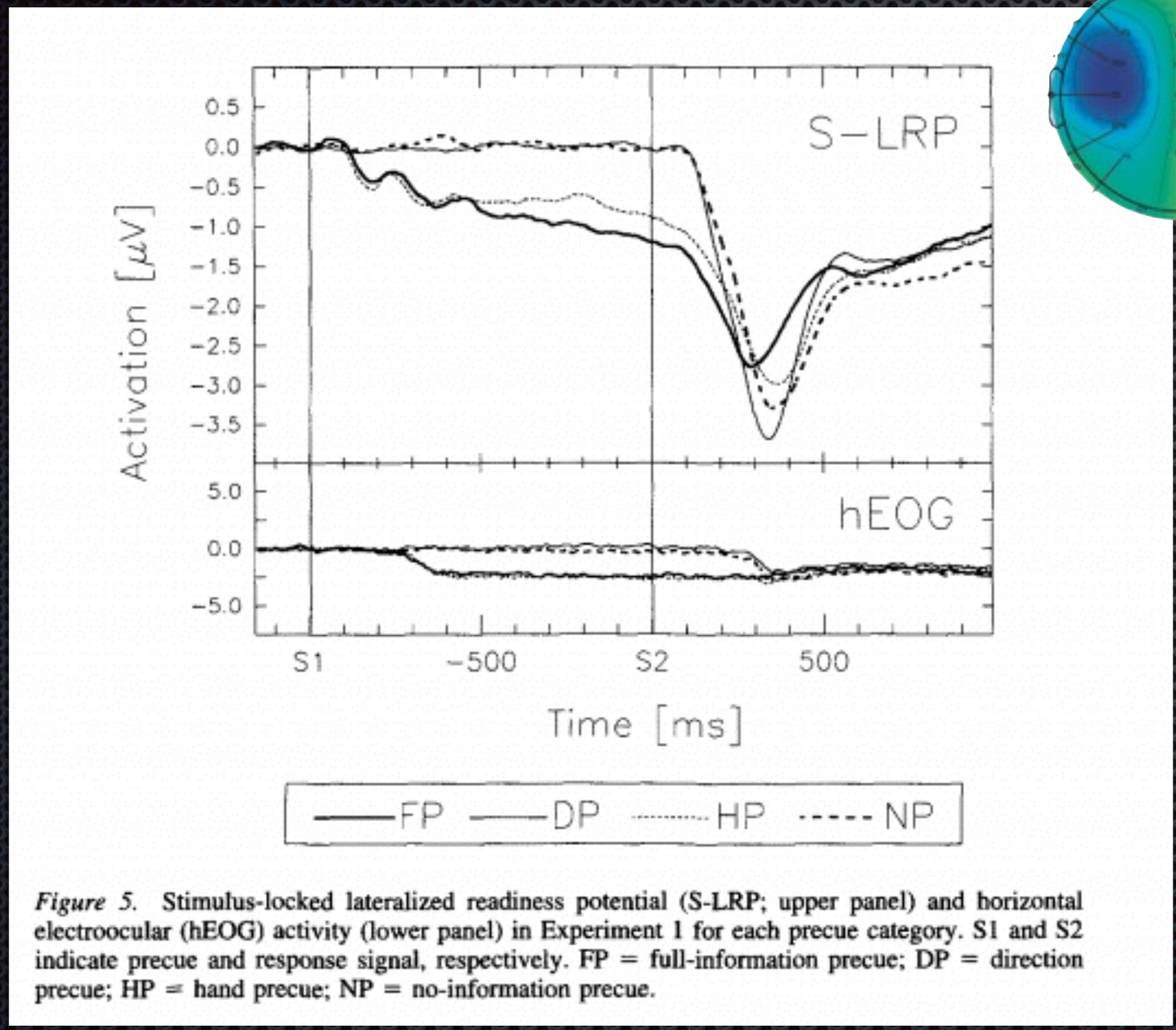
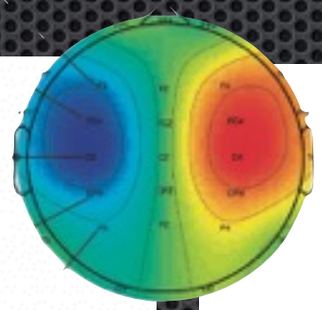
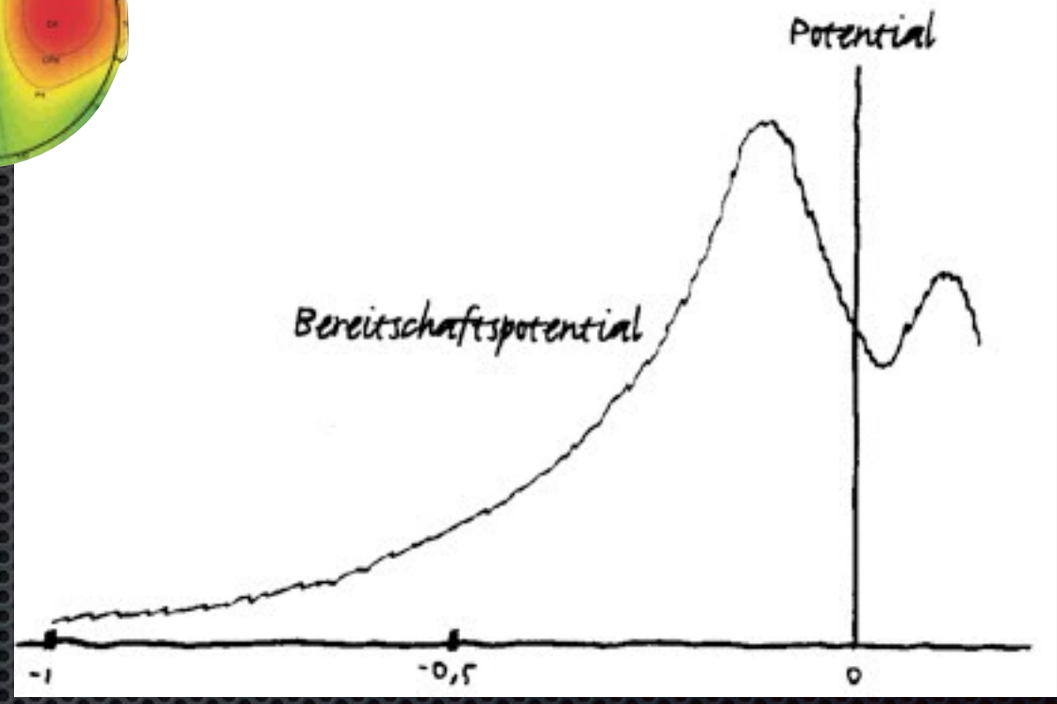



*Figure 5.* Stimulus-locked lateralized readiness potential (S-LRP; upper panel) and horizontal electrooocular (hEOG) activity (lower panel) in Experiment 1 for each precue category. S1 and S2 indicate precue and response signal, respectively. FP = full-information precue; DP = direction precue; HP = hand precue; NP = no-information precue.

Leuthold et al., (1996) *JEP: General*






*Motor cortex** (hand/eye) activates to anticipate movement based on spatial knowledge.*

Steve

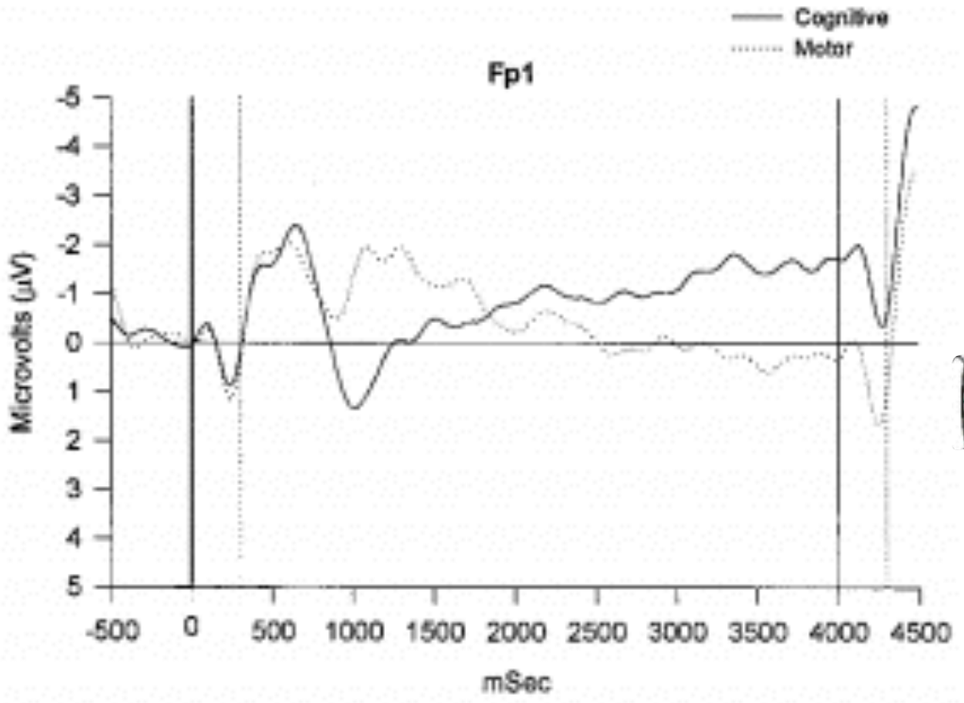
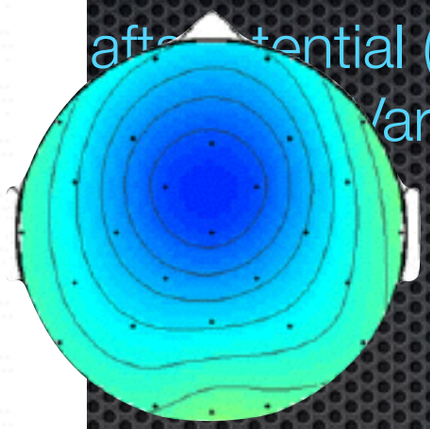
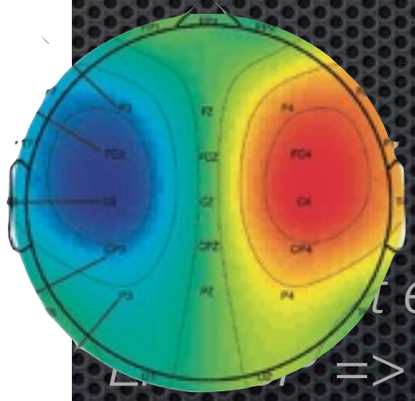



Fig. 3. Grand average ERP activity collapsed across type of task (cognitive and motor) at Fp1 and C3 electrode sites. This figure clearly illustrates the difference in ERP topography across these two general types of tasks.

ed Readiness Potential (LRP)
aft tential (BP)
Variation (CNV)



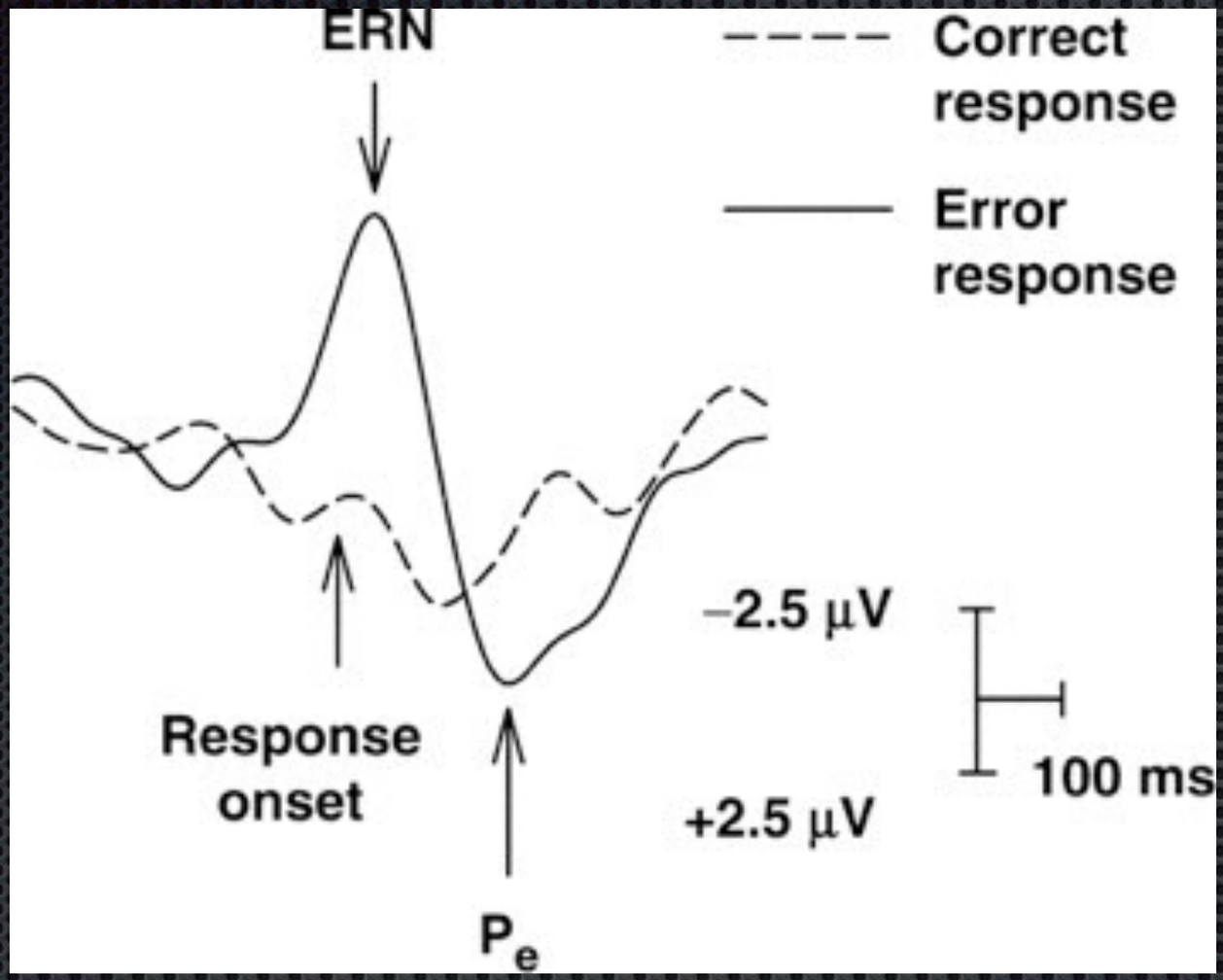
Leynes et al., (1998) *International Journal of Psychophys*



*t equal to LRP/BP*
*=> Motor Cortex*
*CNV => Something else - may or may not result in movement*

# Steve Hillyard's 6 families of cognitive ERPs:

## 6. Error-Related Potential




*A cortical response is present immediately following erroneous responses - what does this tell us? (Ne regardless of awareness, Pe with awareness)*

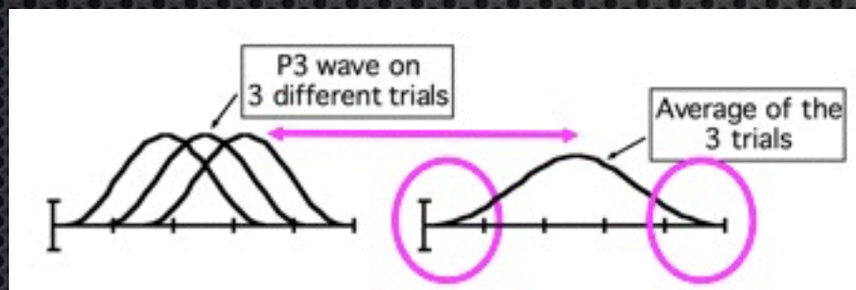
# Steve Luck's (alum of Hillyard) caveats

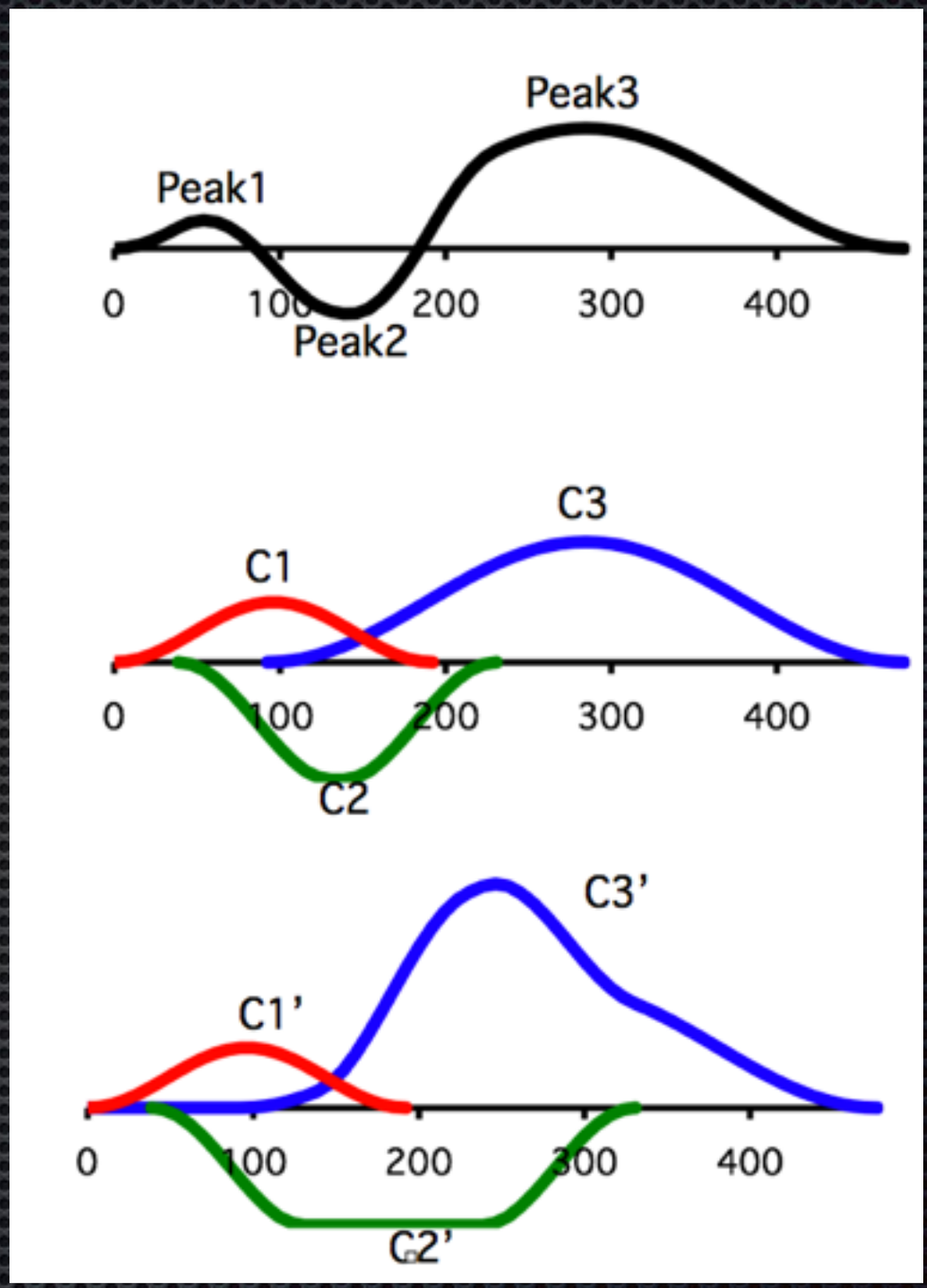
*component = "source/process"*

1. Peaks ≠ Components

2. Peaks ≠ Modulation, Size, Timing of Components

3. Onsets/Offsets represent range across individuals.




*ERPs tell us something about stages of processing, assuming some underlying neuro-cognitive module. They may or may not inform neuronal dynamics. We are recording mixtures of signals.*

Brain States

Timing of Neurocognitive Processes

Neural/Network Dynamics

What do ERPs tell us?

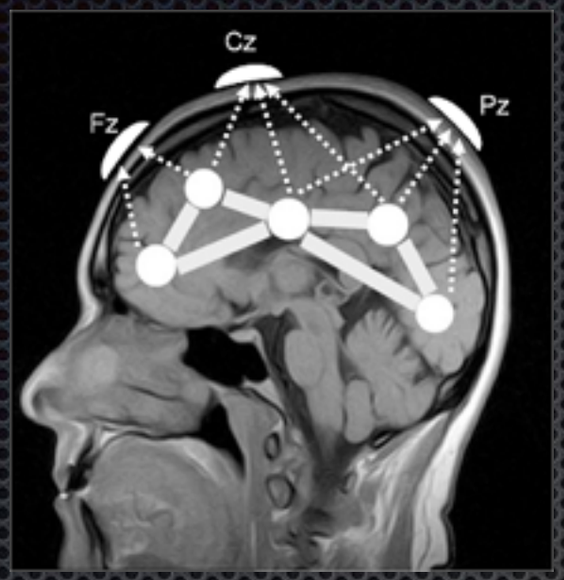
Flow of Information in Cognition and Perception

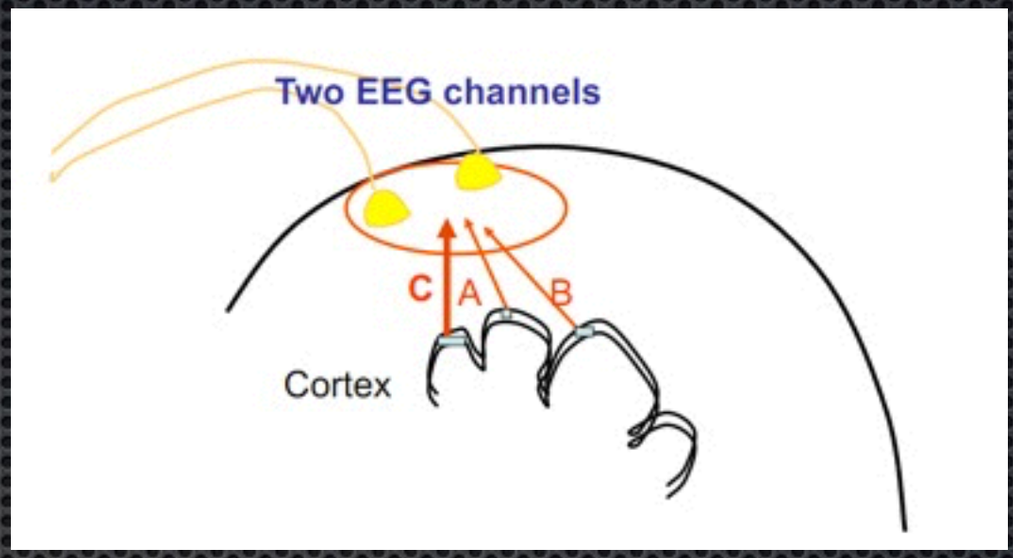
1. Latency of neurocognitive events.
2. Define stages of processing (sensory, template comparison, response).

What do ERPs not tell us?

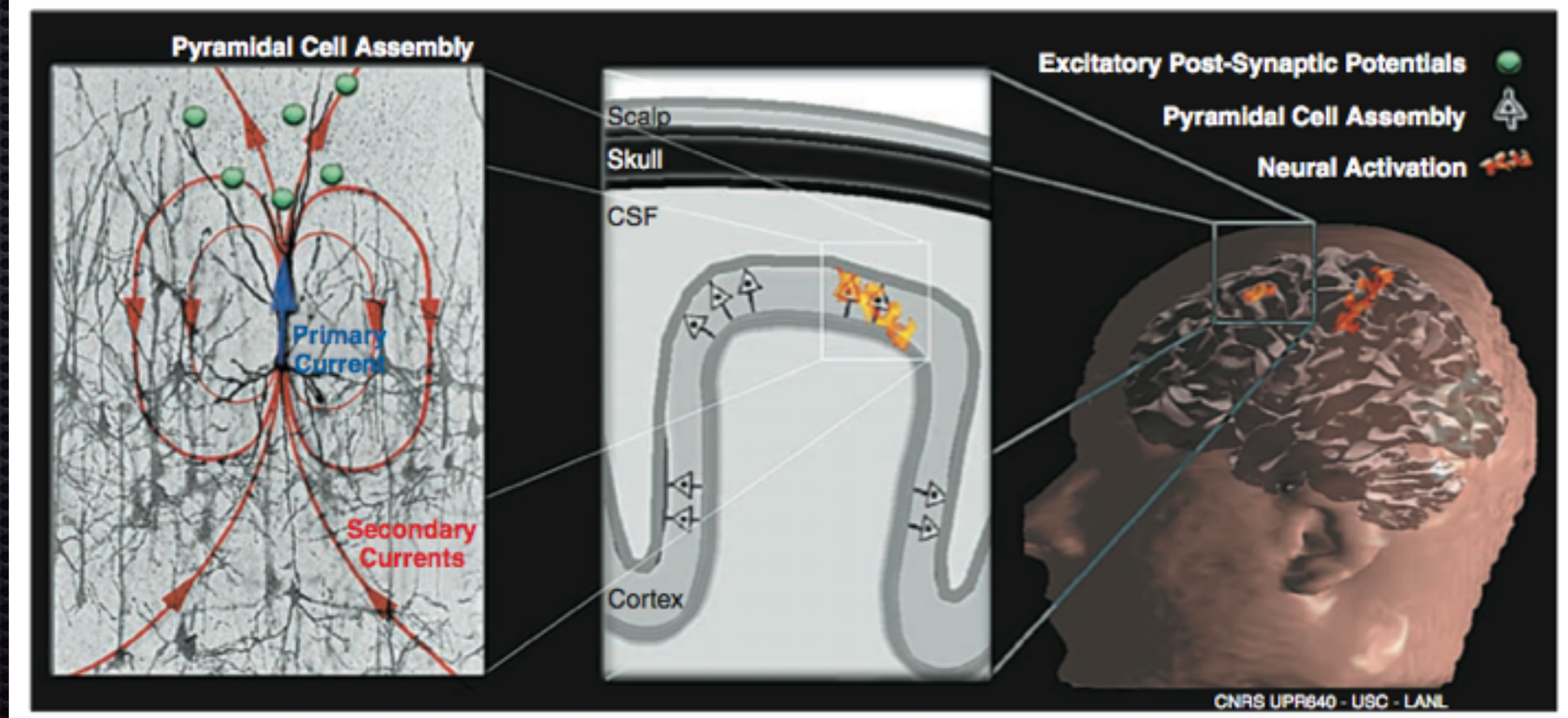
Spatial Sources of the Latency Effects
Connectivity (Flow of Information Within Circuit)/Network Dynamics

# Sources




Scott Makeig's Rendering

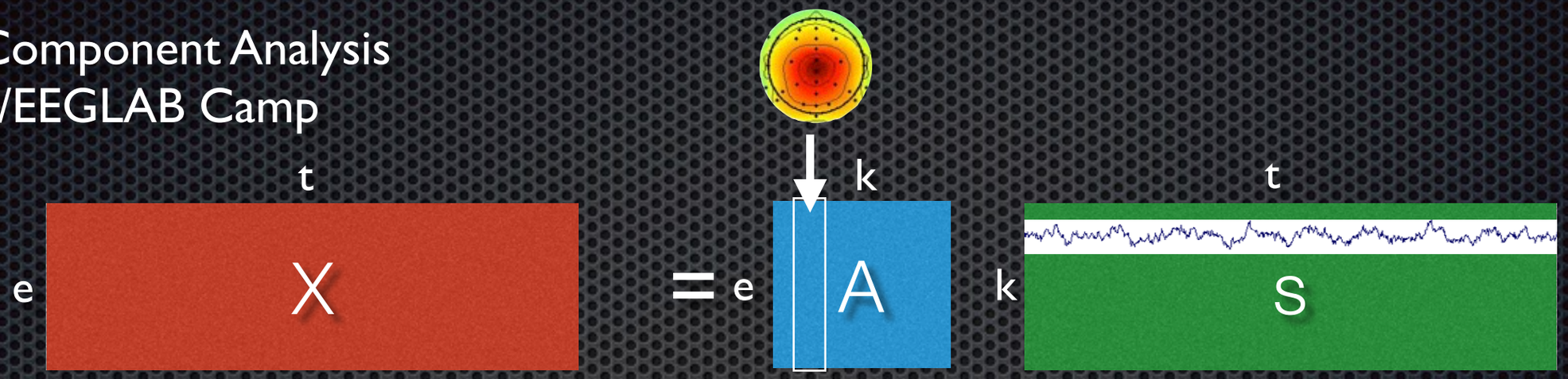


# Approaches

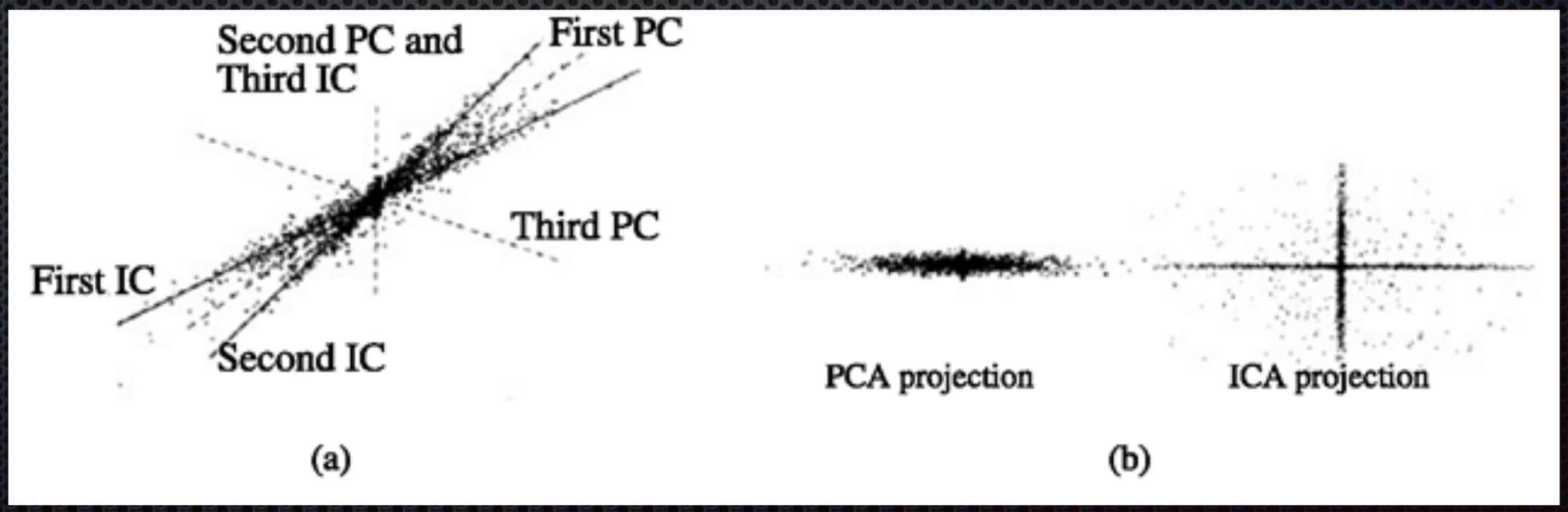
1. Statistical separation of signal into components.
2. Modeling of cortical generators of EEG.

# Statistical Separation of EEG into Components

Independent Component Analysis
Mostly Makeig/EEGLAB Camp

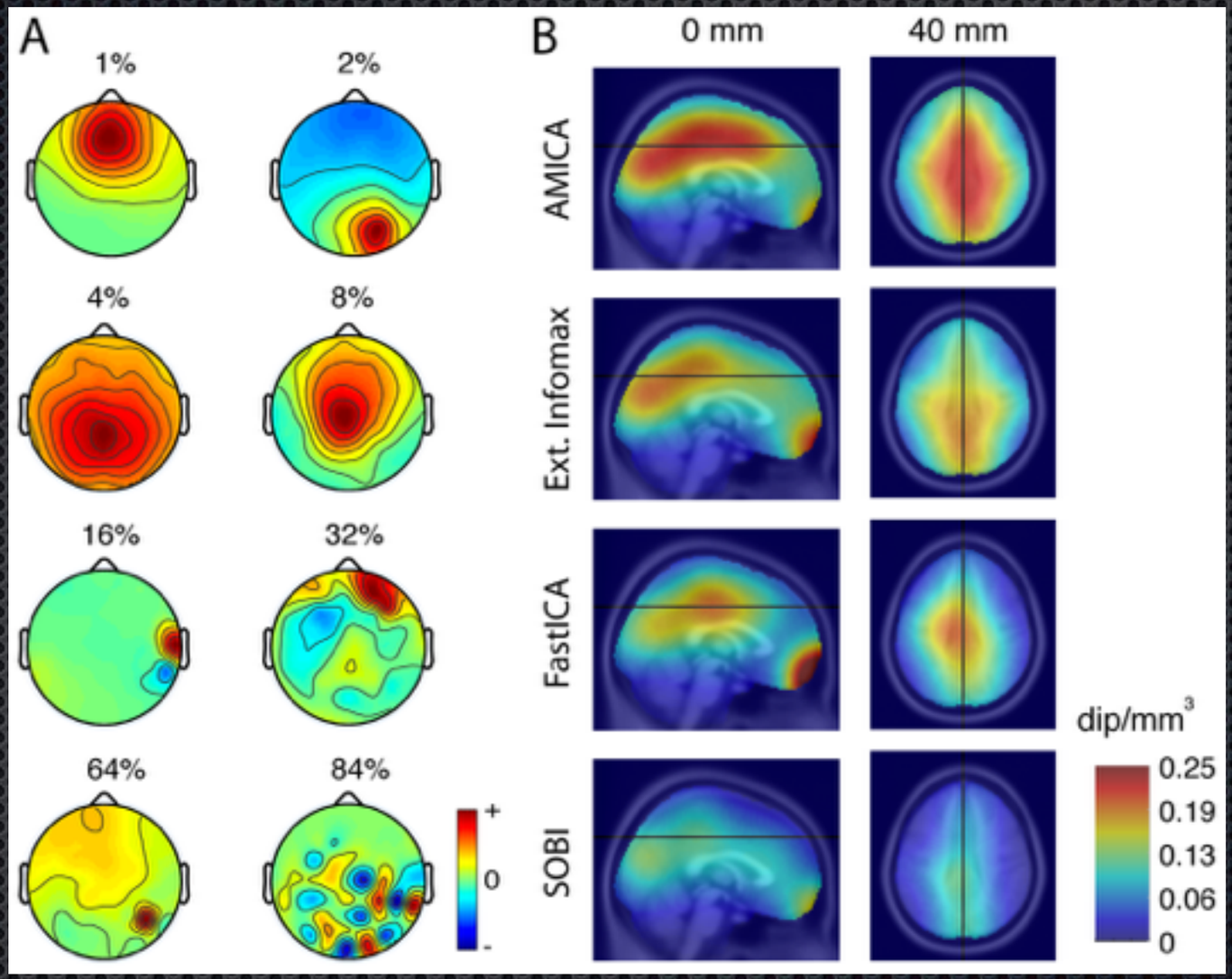



X=As
X=data (electrodes x time)
A=mixing matrix (electrodes x K)
s =statistically independent components (X * time)



# Statistical Separation of EEG into Components

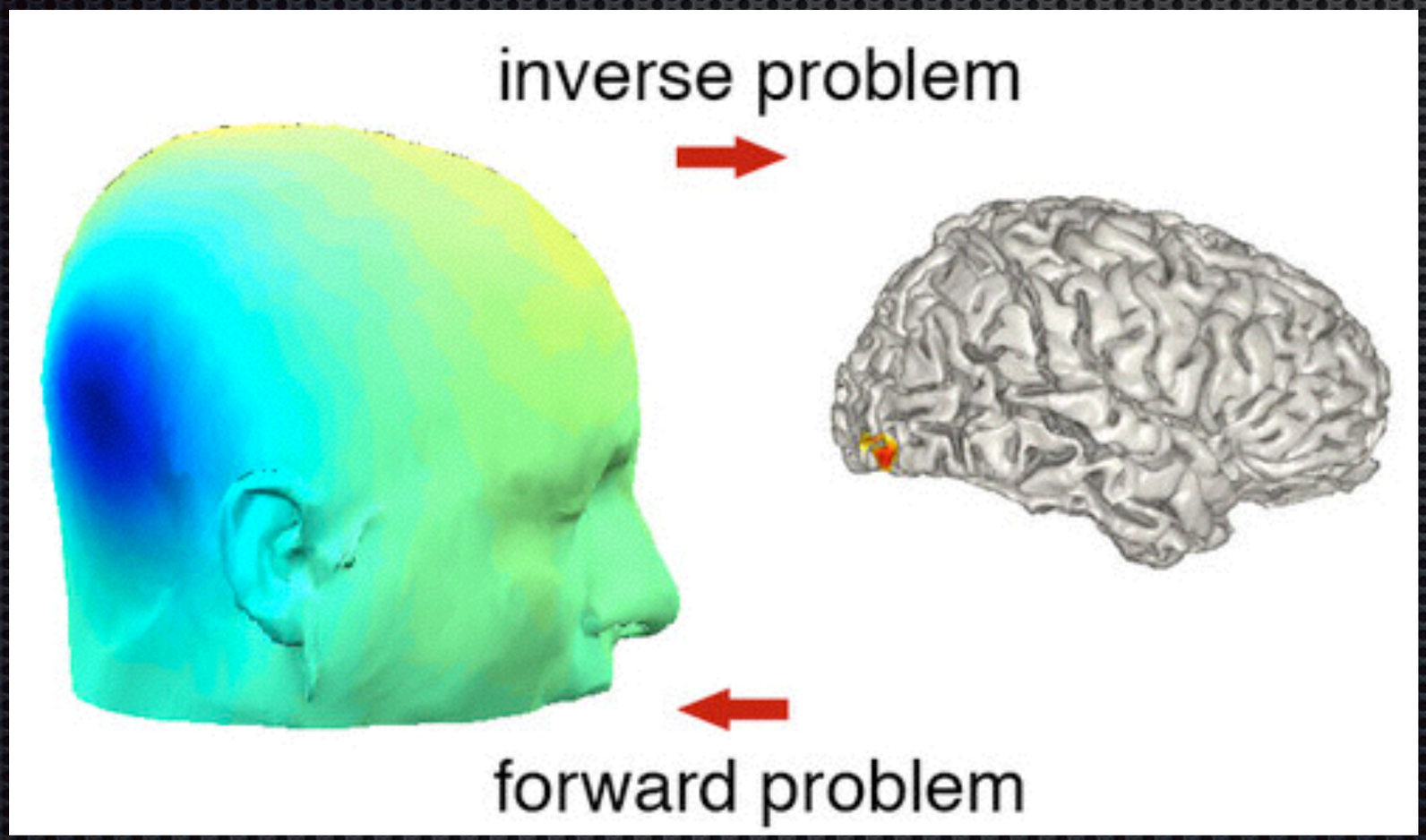
Independent Component Analysis
Mostly Makeig/EEGLAB Camp




*Independent EEG Sources Are Dipolar*
*Arnaud Delorme , Jason Palmer, Julie Onton, Robert Oostenveld, Scott Makeig*
*Published: February 15, 2012http://dx.doi.org/10.1371/journal.pone.0030135*

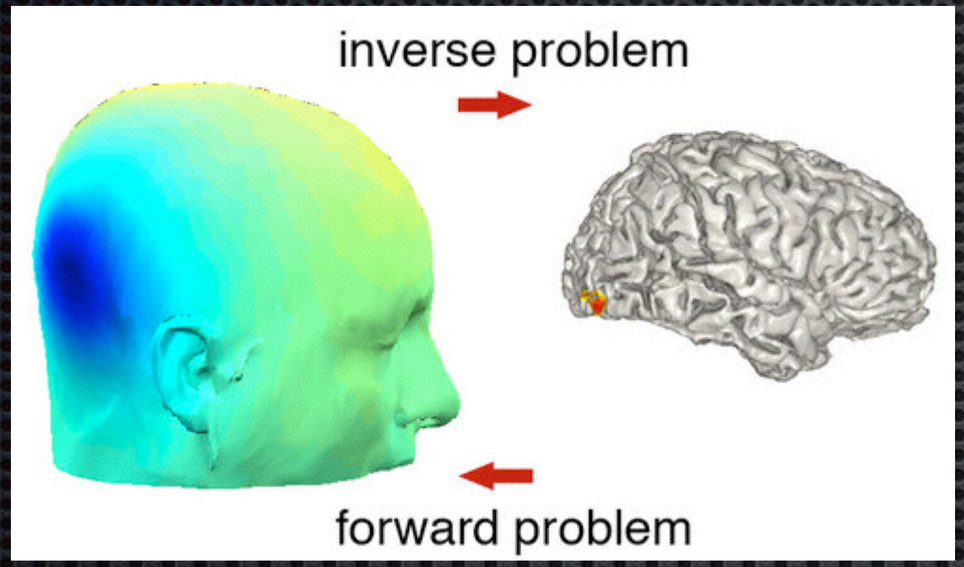
# Modeling cortical generators of EEG:

- inverse problem (map scalp to cortex)
- forward problem (map cortex to scalp)

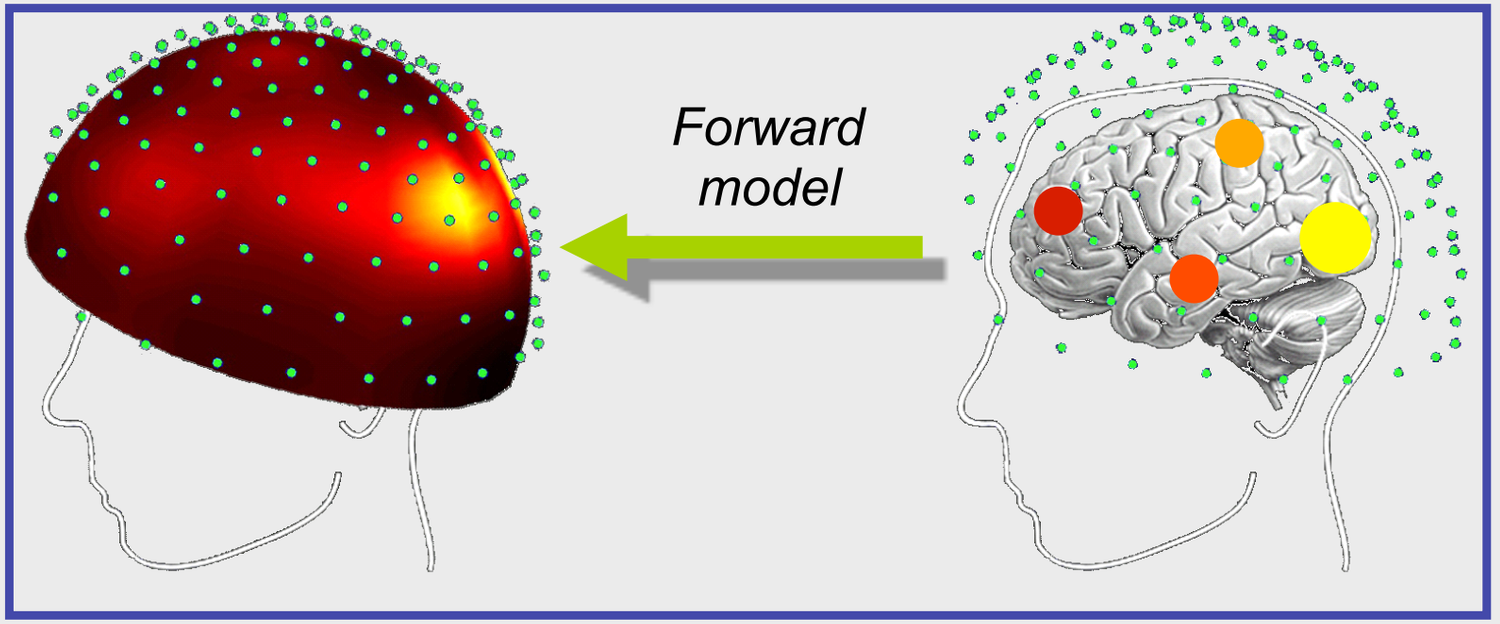


# Algorithm:

- inverse problem (map scalp to cortex)
- forward problem (map cortex to scalp)




1. take a guess at cortical source(s)
2. project to surface via forward solution
3. check accuracy (least-squares)
4. revise initial guess




$$Y = f(J) + E$$

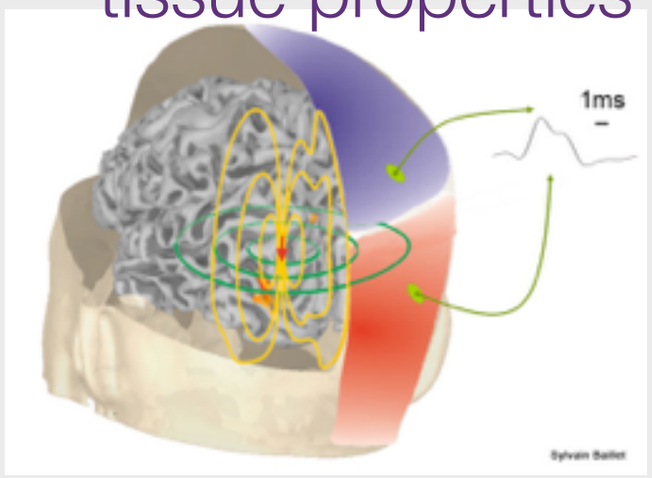
data

forward operator

source parameters

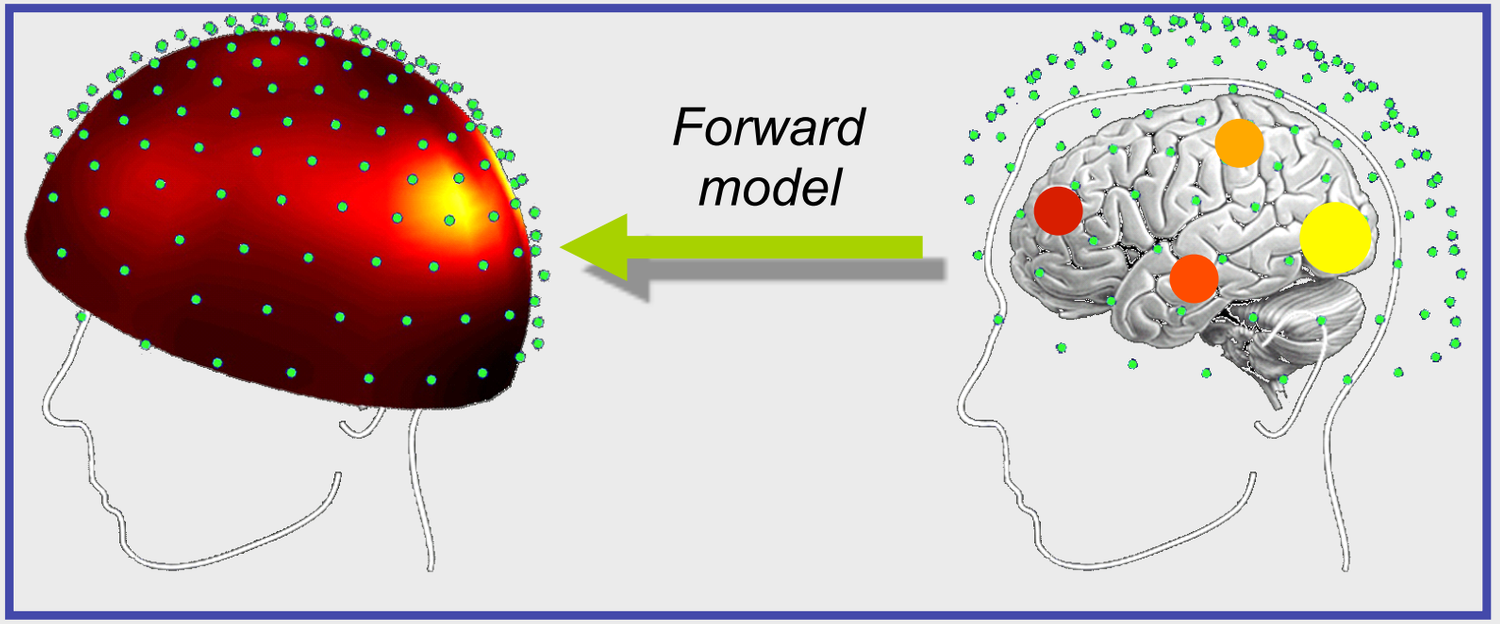
noise

tissue properties



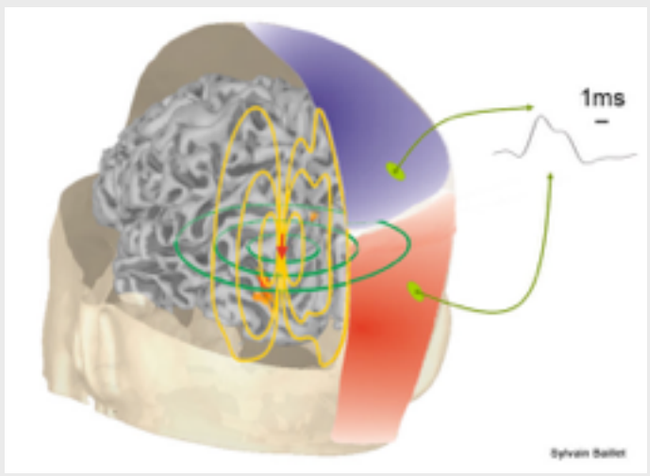

location (x,y,z)
direction
amplitude
current density vector

**Jérémie Mattout, Christophe Phillips**



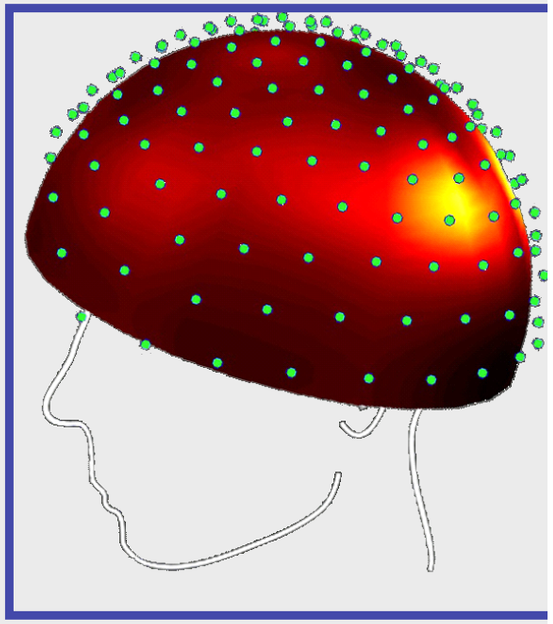

$$Y = f\left(J\right) + E$$

data — forward operator — source parameters — noise

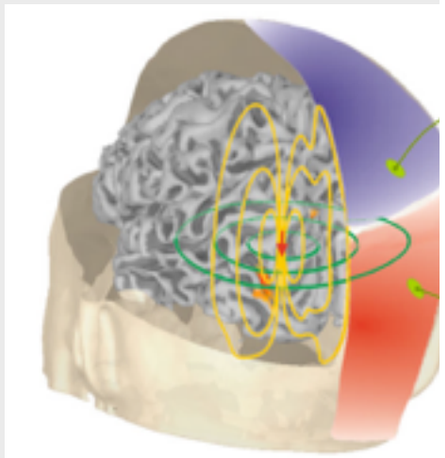



**Equivalent Current Dipole** (1-5 dipoles, estimate location and orientation and amplitude)
**Distributed Models** (many dipoles, fixed location, estimate orientation, amplitude)

**Jérémie Mattout, Christophe Phillips**



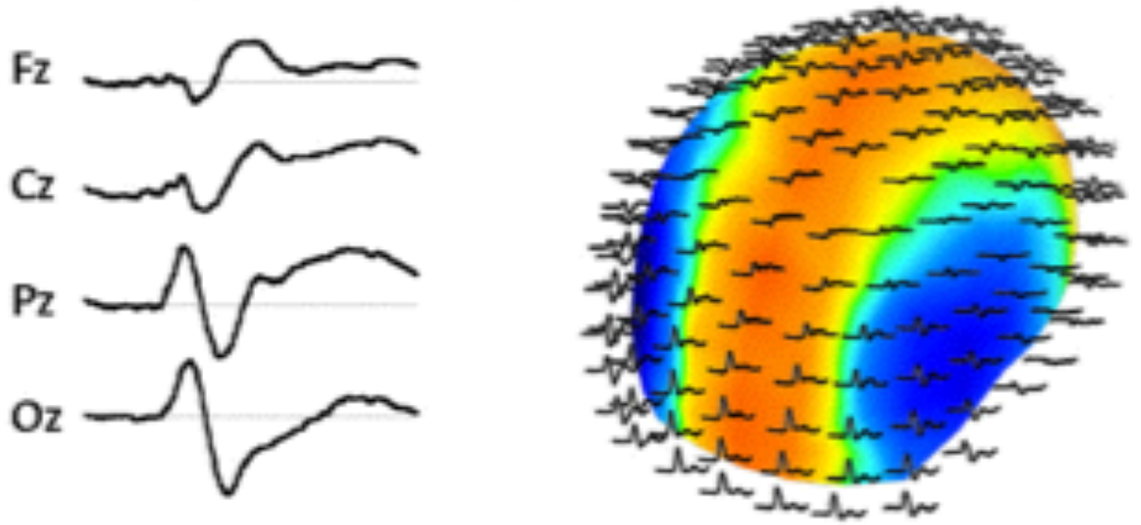
$$Y = \quad \text{data} \qquad \text{forward operator}$$



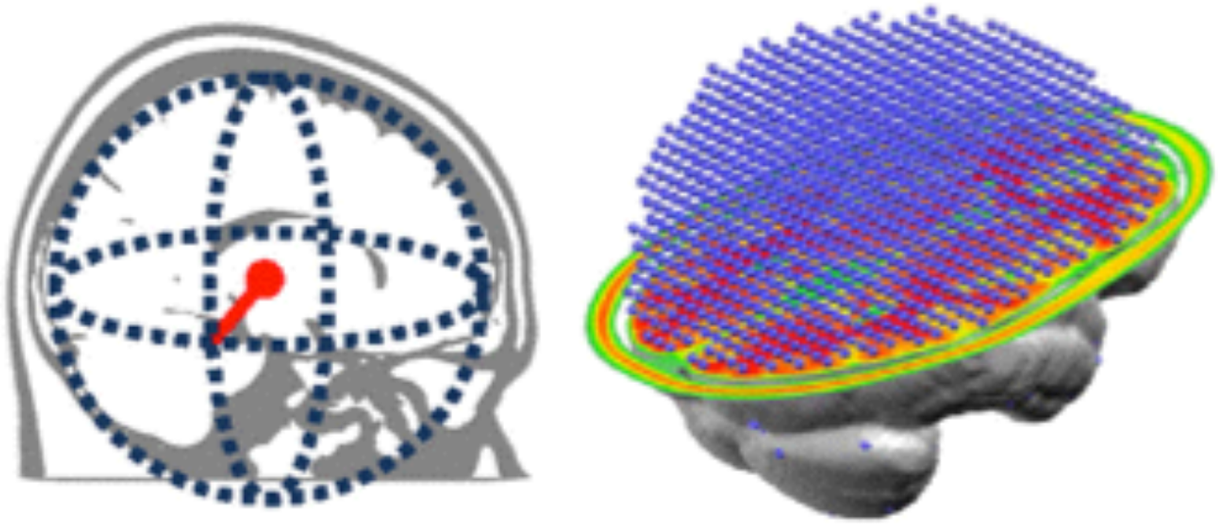


**A.** From low-density to high-density montages

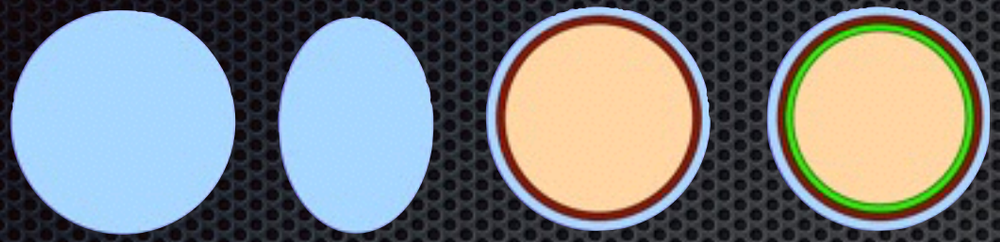
**B.** From voltage waveforms to topographic representations




**C.** From equivalent current dipole to distributed source models

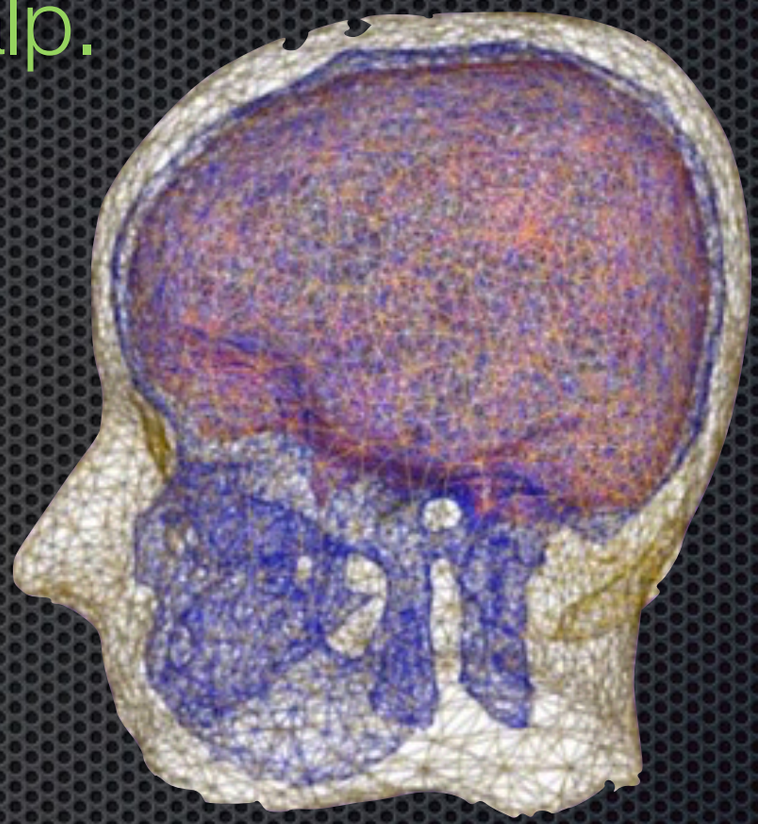


Forward operator = “Lead Field Matrix” = electromagnetic (permeability and conductivity) and geometric properties of tissue between source and scalp.



sphere, homogenous spheroid, 3-layer (scalp, skull, brain), 4-layer (scalp, skull, CSF, brain)

unique estimates of tissue conduction



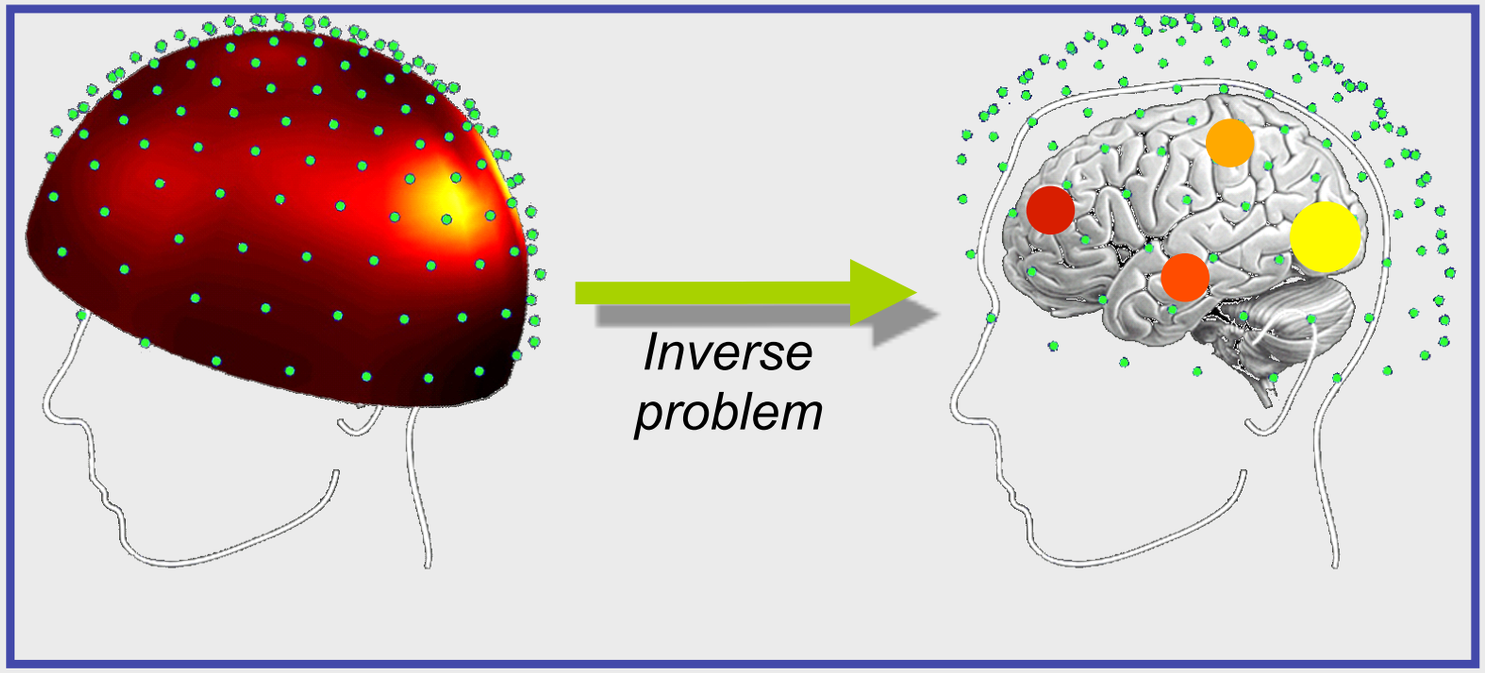
BEM (boundary element model)

surface triangulation of interfaces between compartments of equal isotropic conductivities to provide more accurate model

FEM (fine element model)

volume tesselation, handles anisotropic (directionally dependent) conductivities within each element

*use MRI to constrain surfaces*



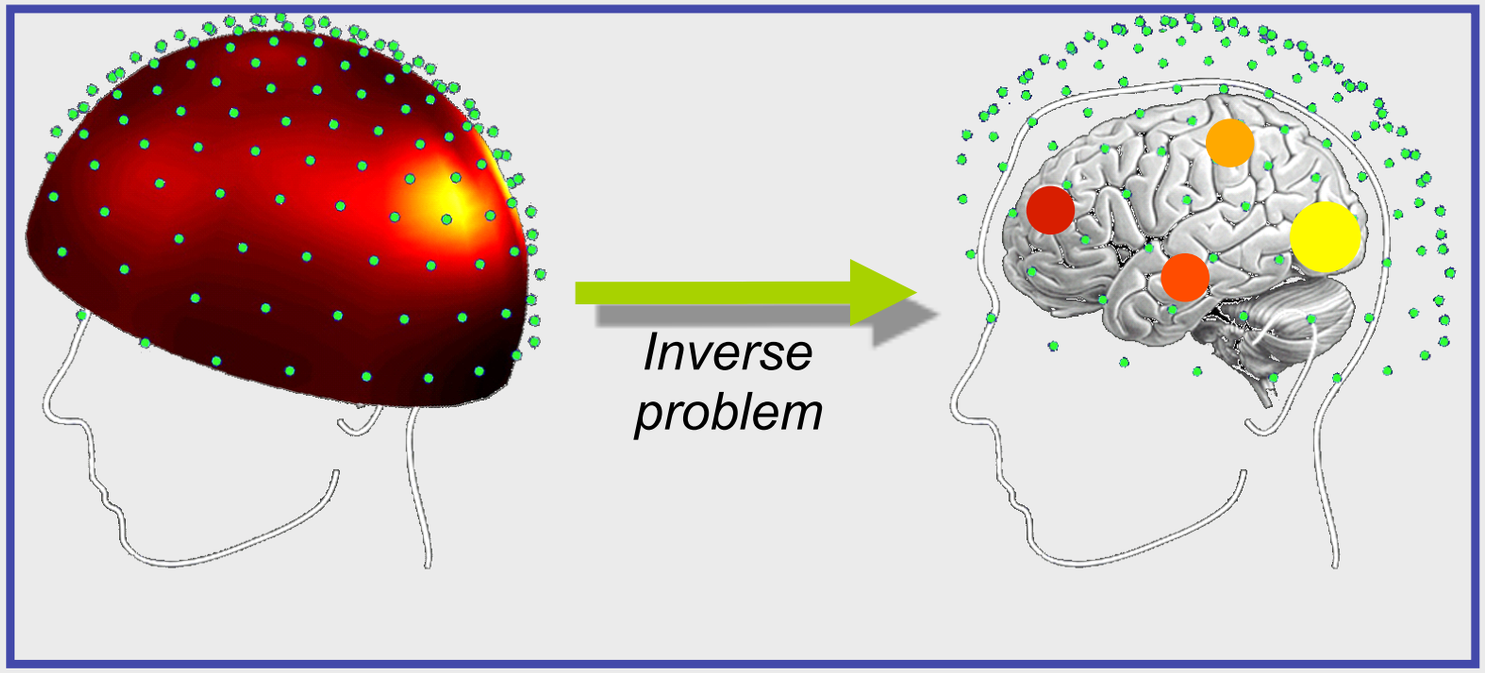

*f*(J)

$$U(\mathbf{J}) = \|\mathbf{Y} - \mathbf{K}\mathbf{J}\|^2 + \alpha \|\mathbf{W}\mathbf{J}\|^2$$

$$\hat{\mathbf{J}} = \underset{\mathbf{J}}{\operatorname{argmin}}[U(\mathbf{J})]$$

K = gains (lead field matrix)
J = current density vector
Y = scalp data
W/alpha = regularization parameters

**Jérémie Mattout, Christophe Phillips**




*f*(J)

$$U(\mathbf{J}) = \|\mathbf{Y} - \mathbf{K}\mathbf{J}\|^2 + \alpha \|\mathbf{W}\mathbf{J}\|^2$$

$$\hat{\mathbf{J}} = \underset{\mathbf{J}}{\operatorname{argmin}}[U(\mathbf{J})]$$

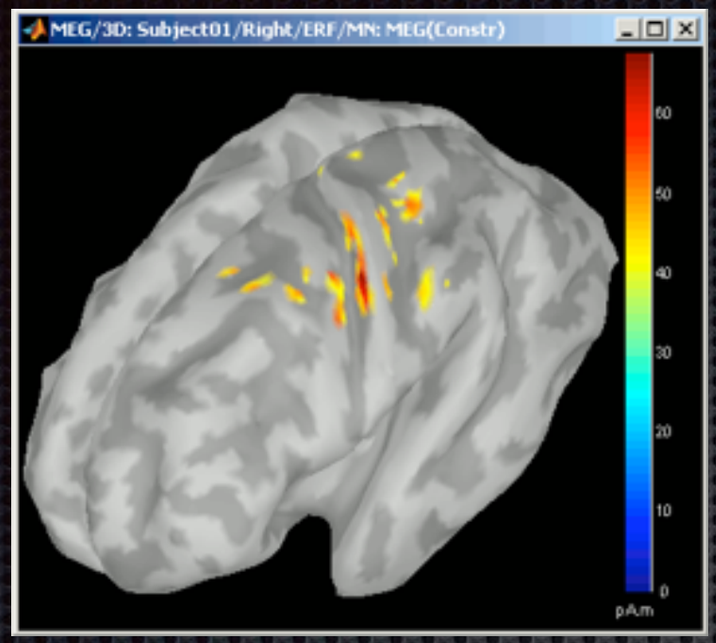
$\mathbf{W} = \mathbf{I}$ : minimum norm *min(overall intensity) favors weak/superficial sources*

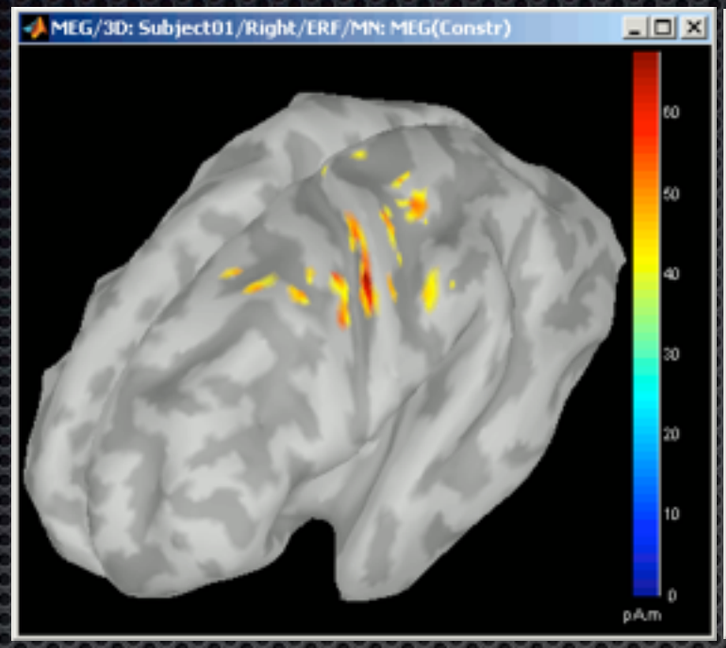
$\mathbf{W} = \Delta$ : maximum smoothness (LORETA) *favors smooth sources*

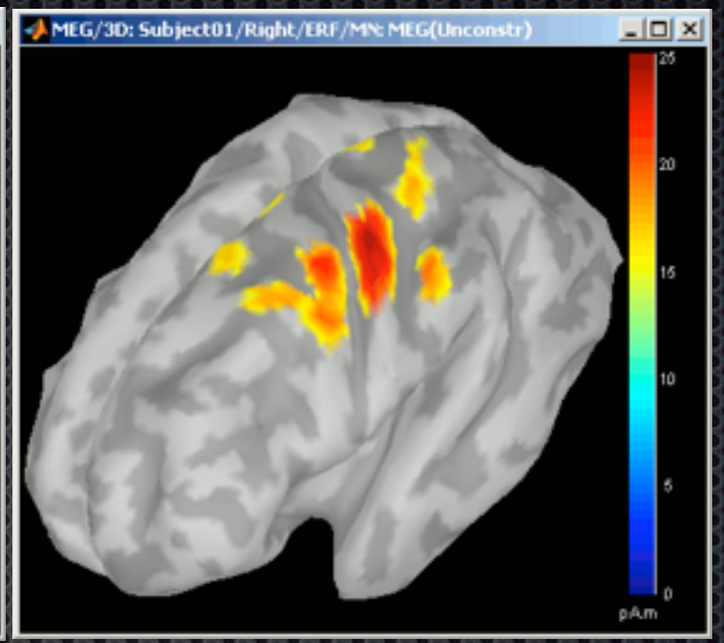
*other methods exist*

**Jérémie Mattout, Christophe Phillips**

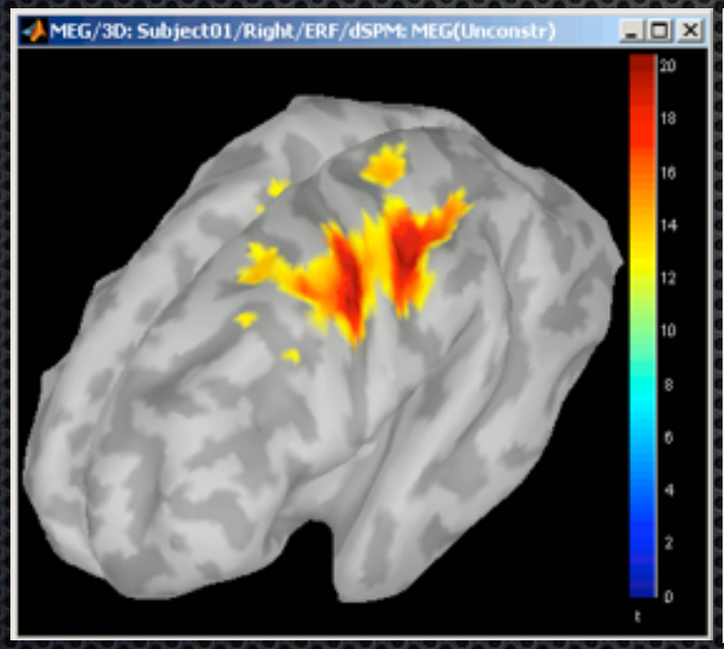
# wMNE (constrained kernel, full, and unconstrained)



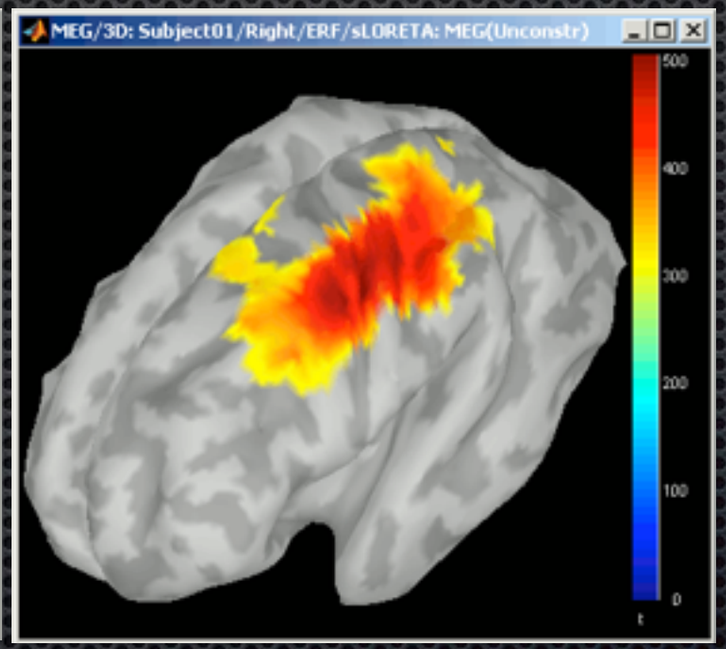




dSPM

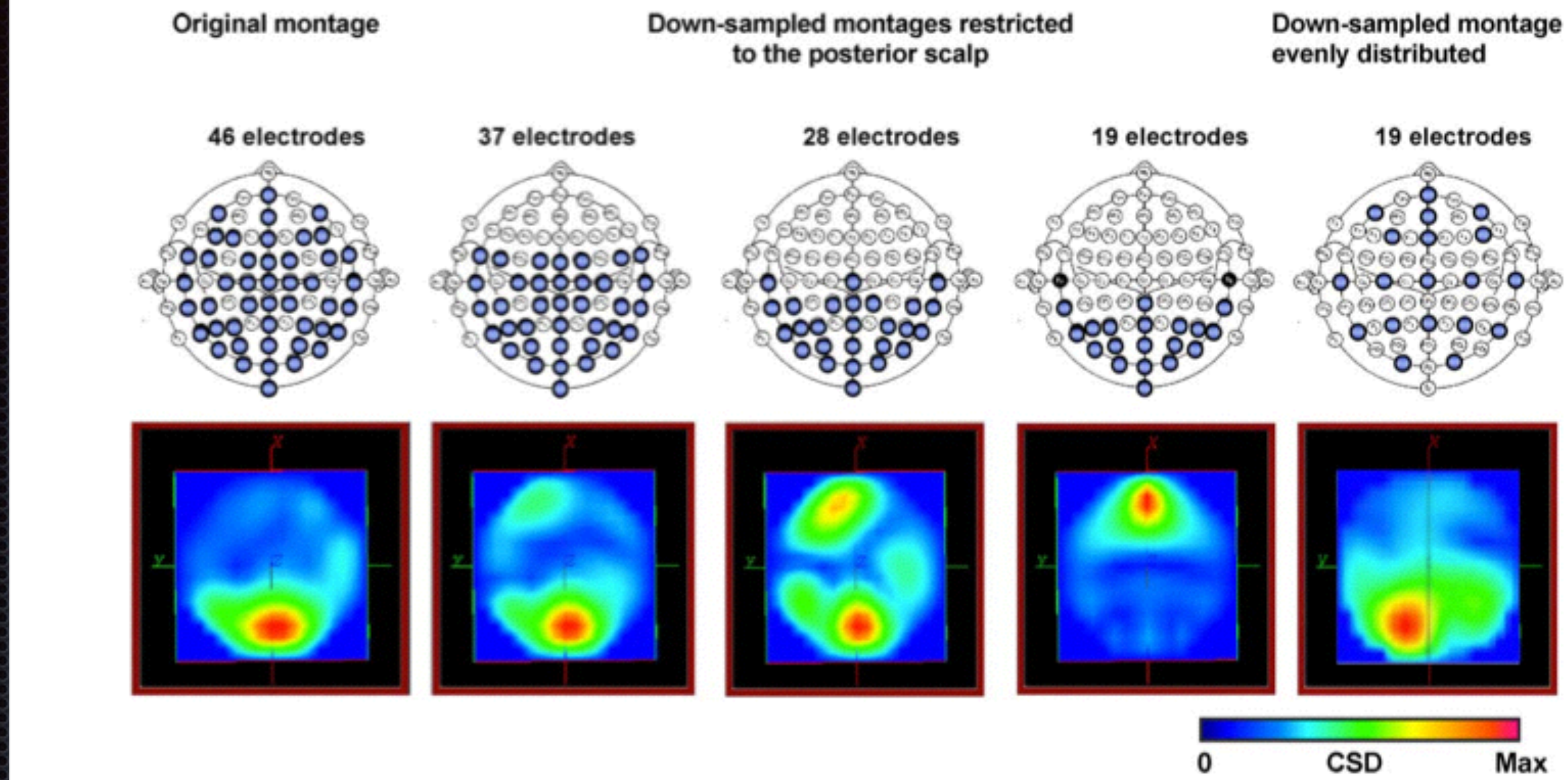



sLORETA




*solution space needs to consider space of plausible sources*

http://neuroimage.usc.edu/brainstorm/Tutorials/TutSourceEstimation



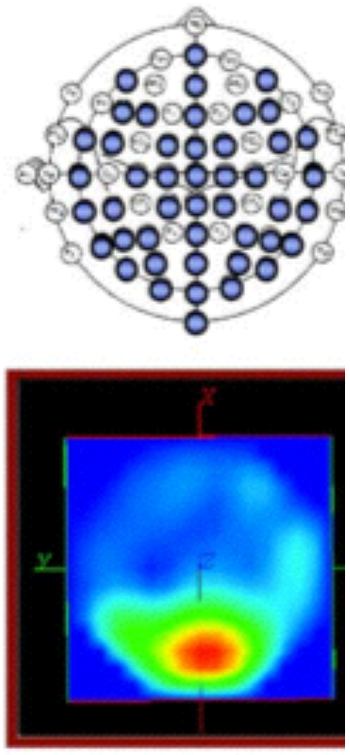

source localization is impacted by spatial sampling

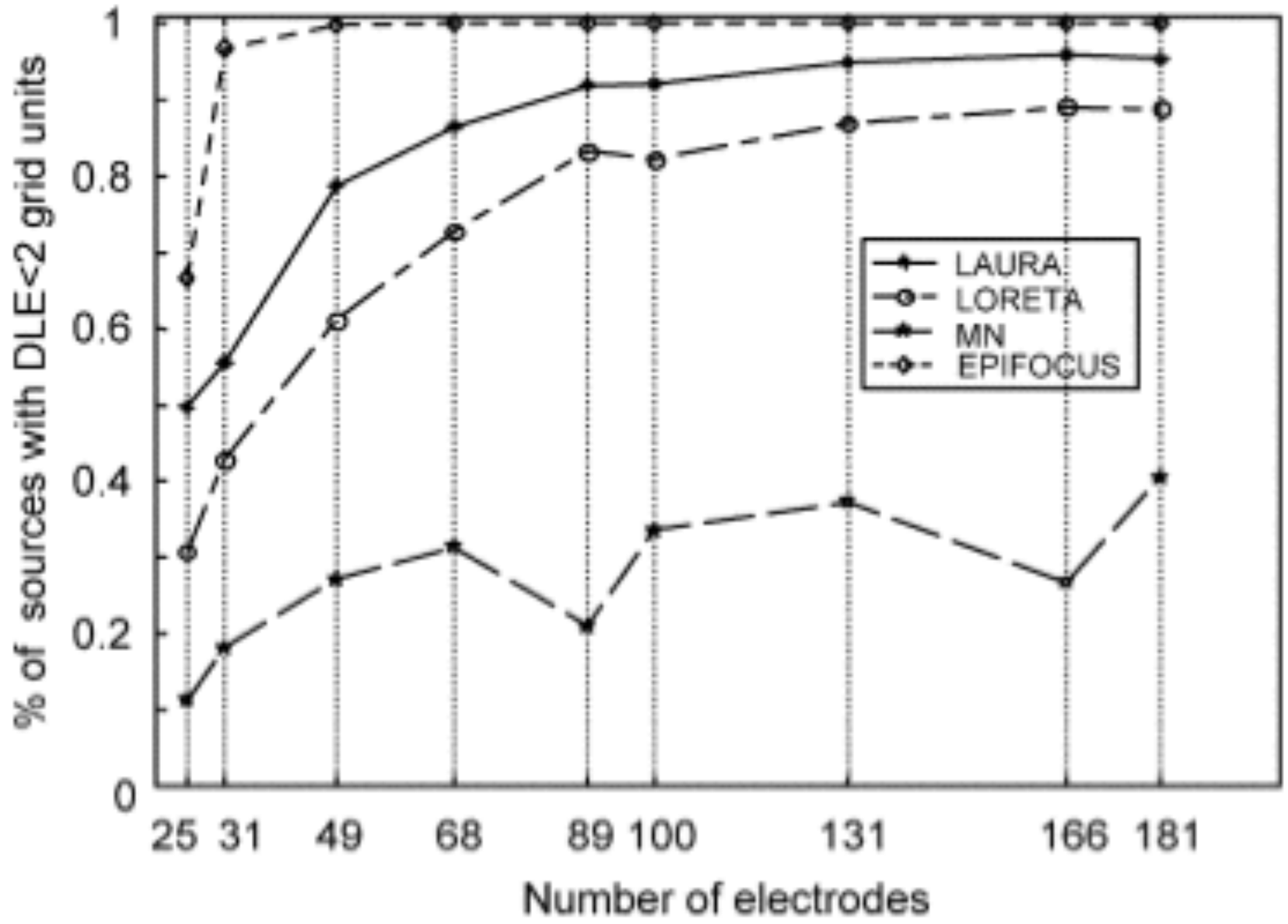
Original montage

Down-sampled montages restricted to the posterior scalp

Down-sampled montage evenly distributed

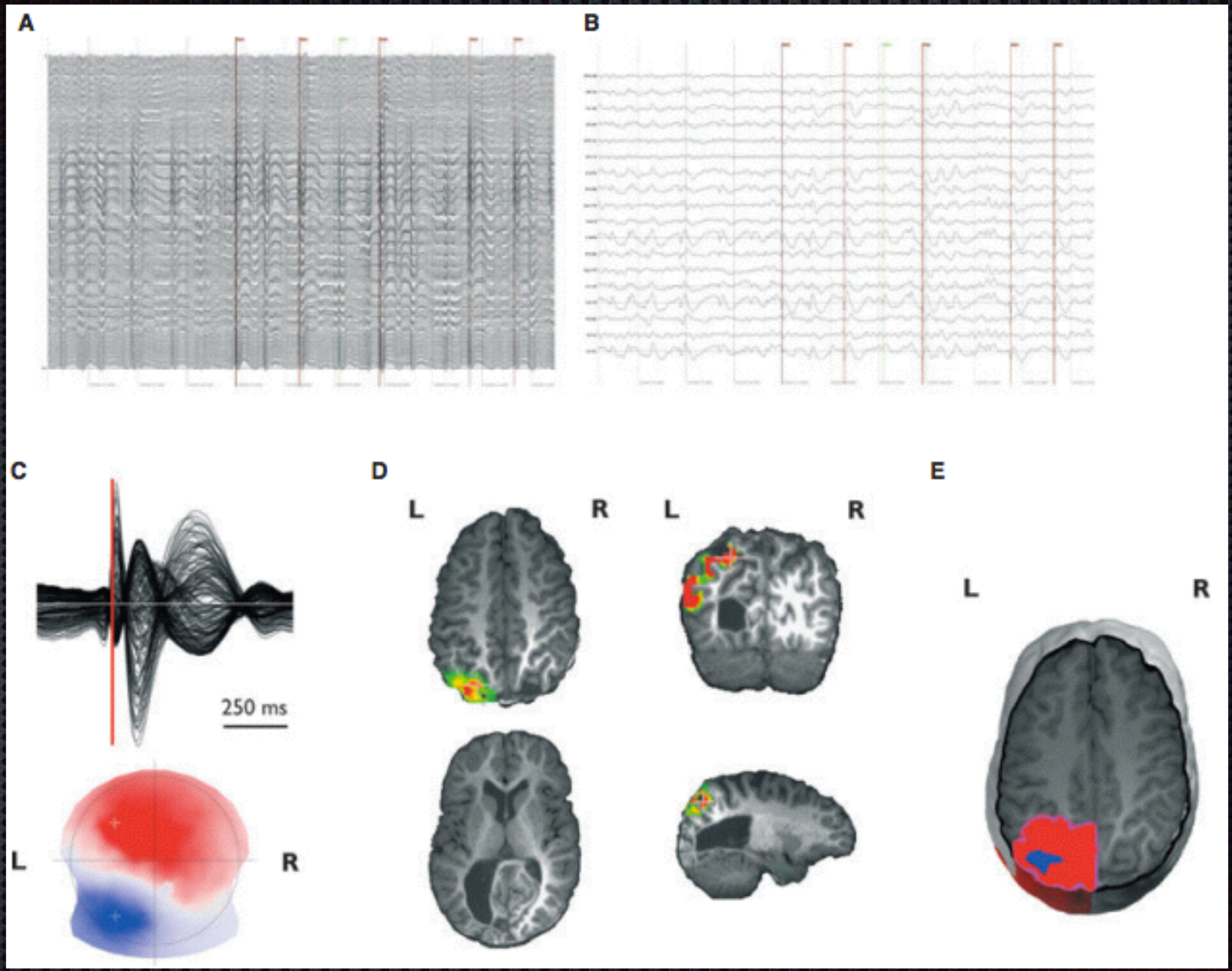
46 electrodes





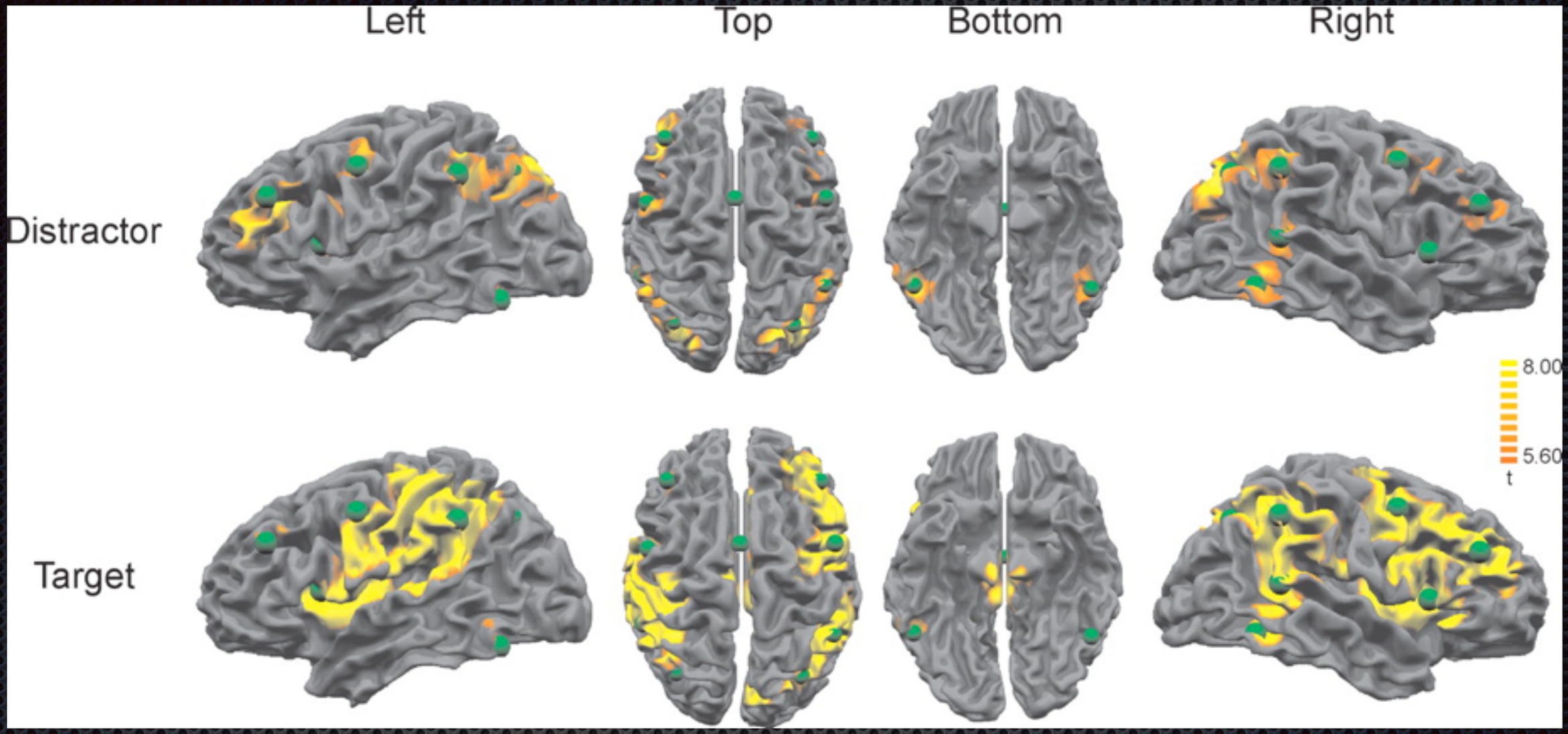

source local
spa

# Example: Interical Epileptiform Discharges

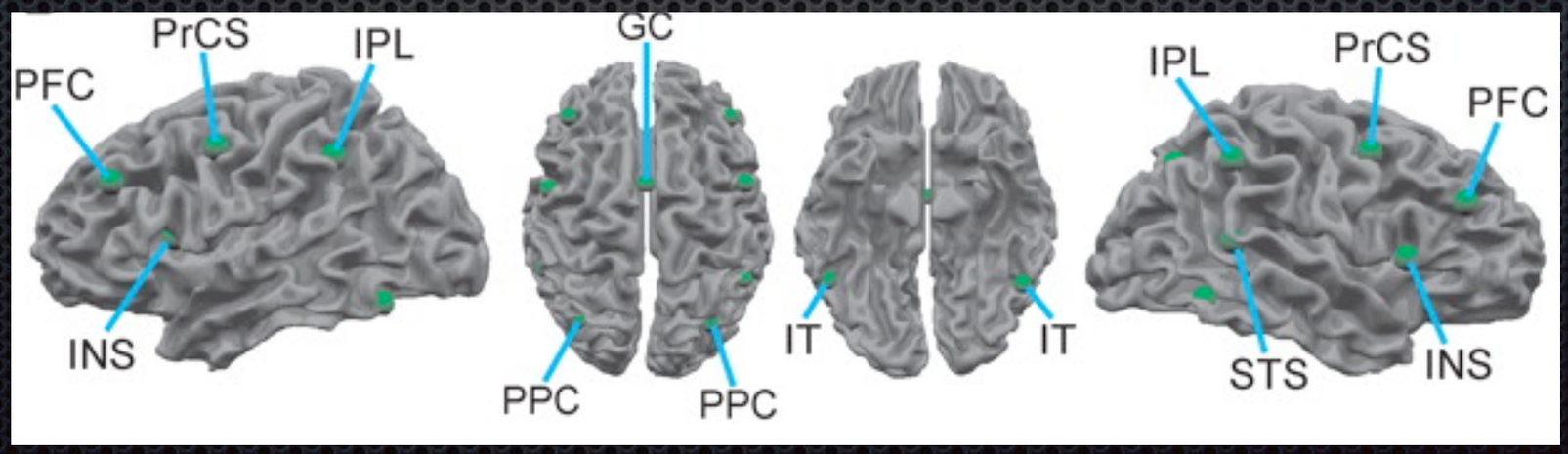


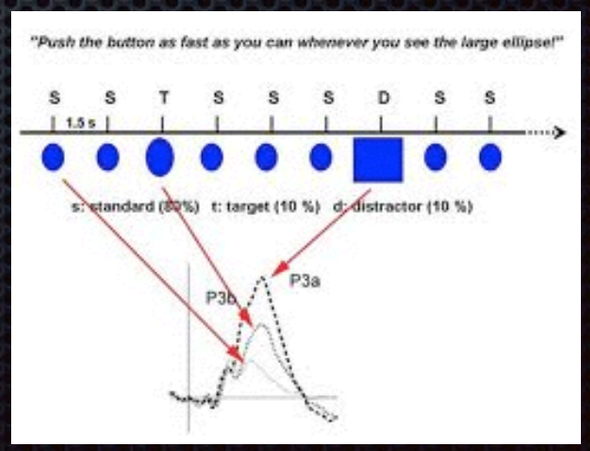

*Vulliemoz et al., 2009, Epilepsia*

# Example: P3a versus P3b

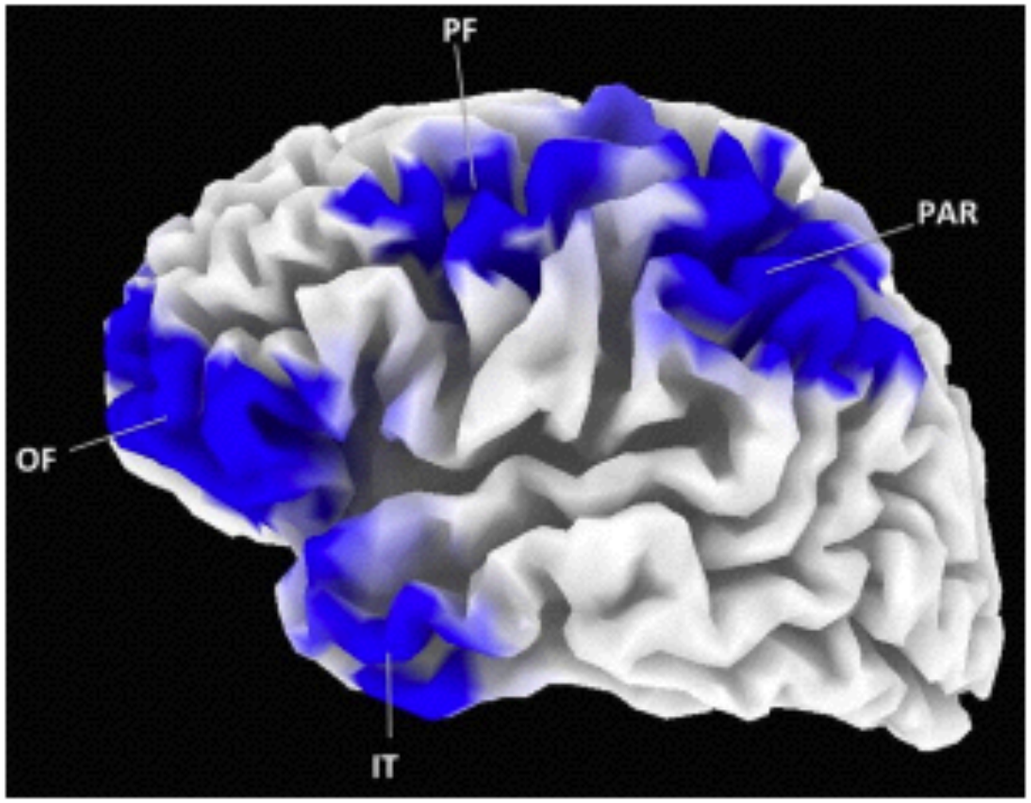



*Bledowski et al., 2004, J Neurosci*

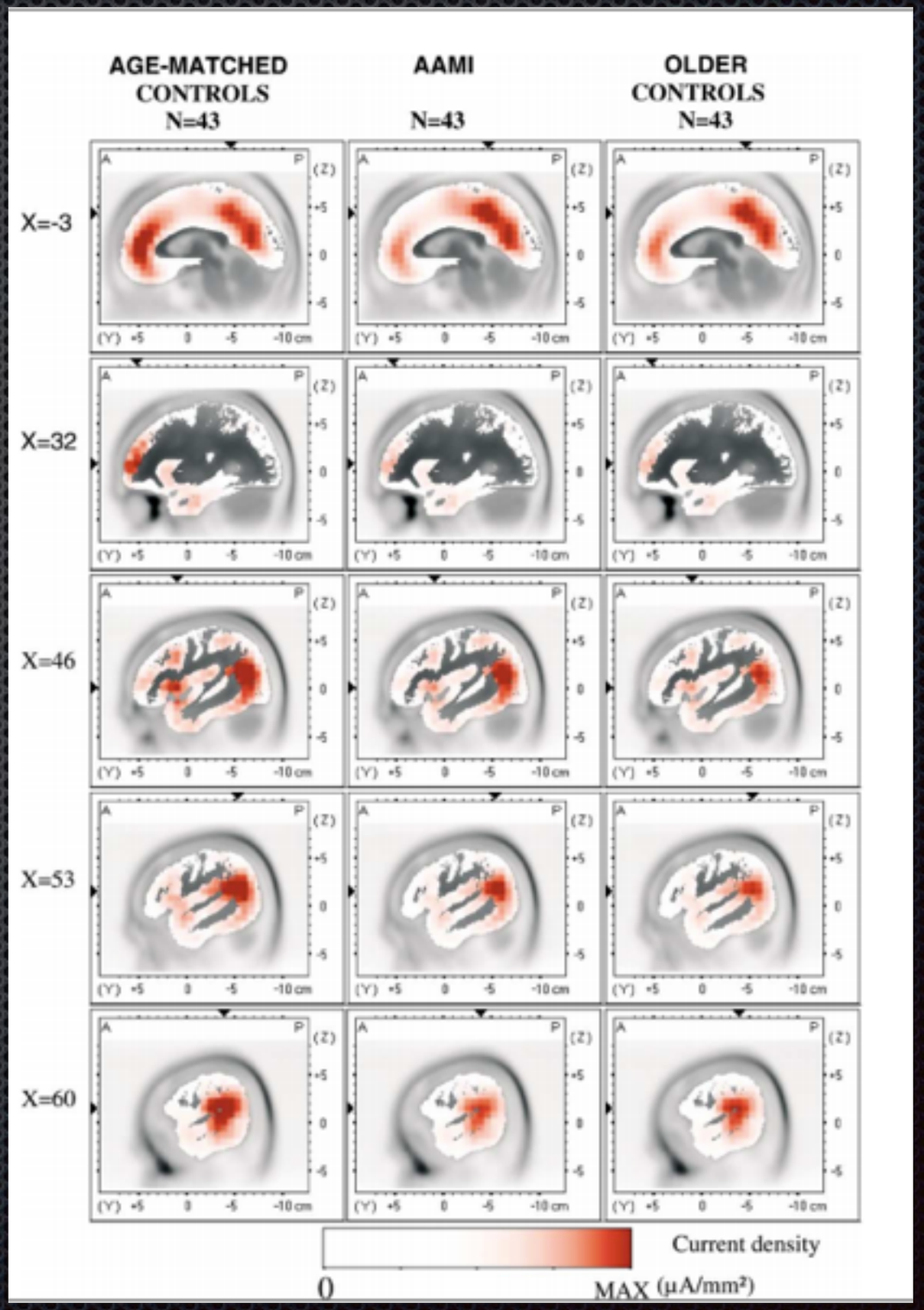


# Example: P3 source localizations (LORETA)

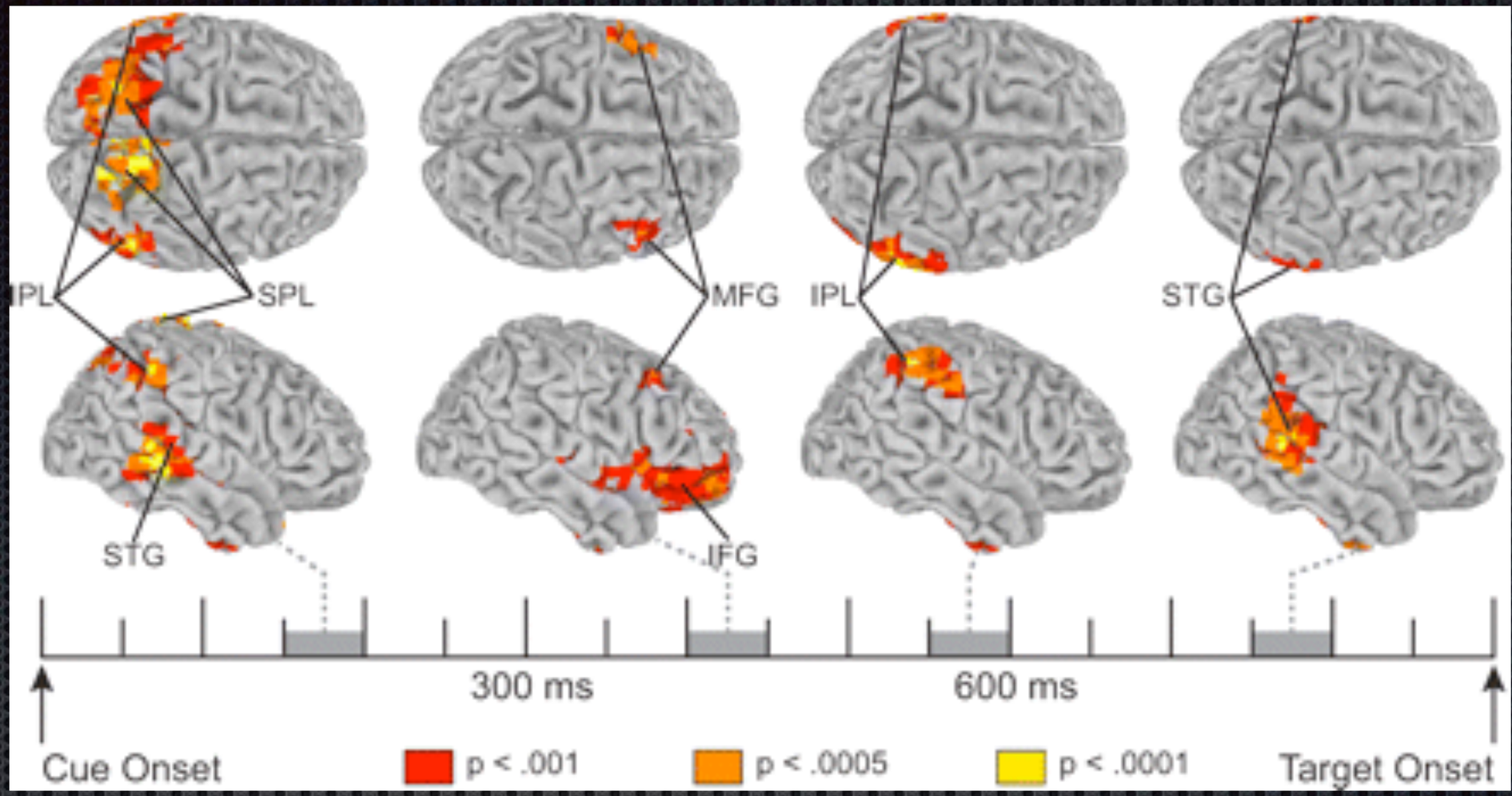



*Andreou et al., 2013 J Neuro*

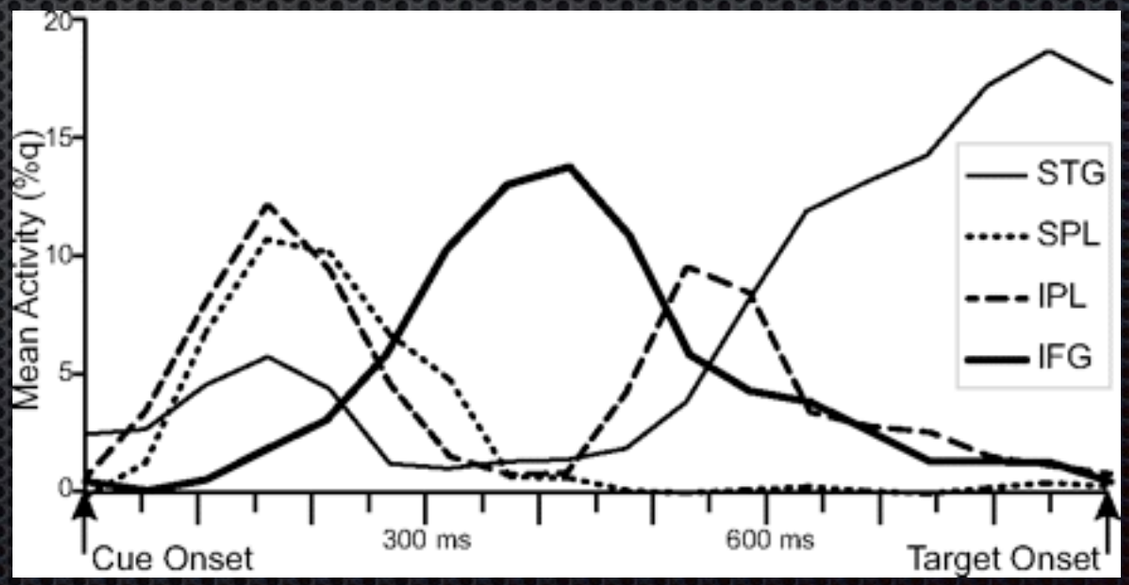



*Anderer 2003, Neurobiology of Aging*

# Example: Auditory Anticipatory Attention Deployment (Shifting)

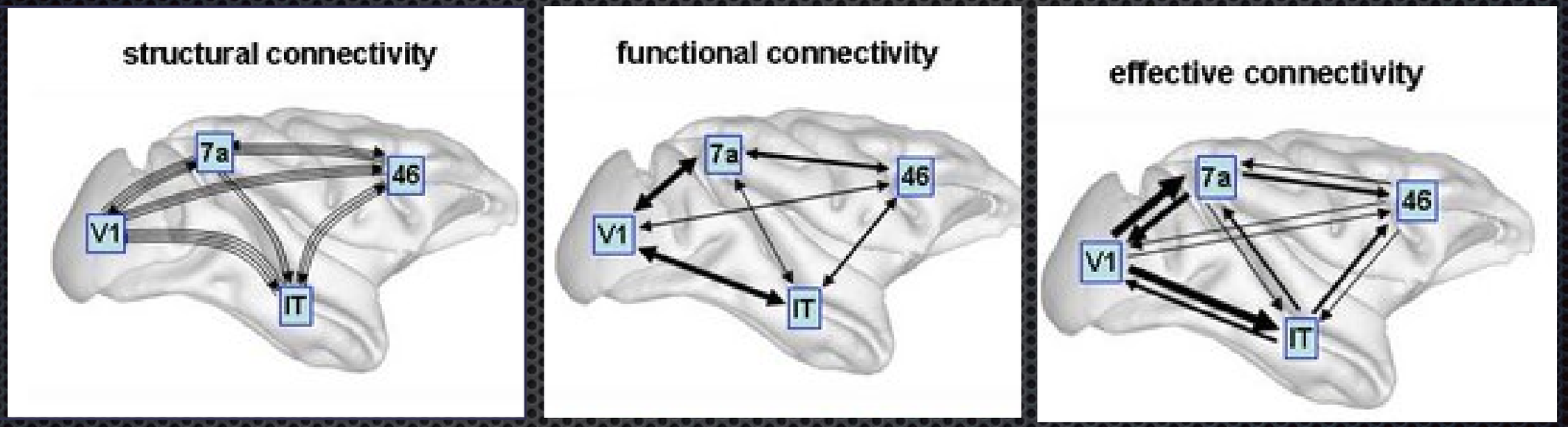



*Green & McDonald, 2011, JNeuro*

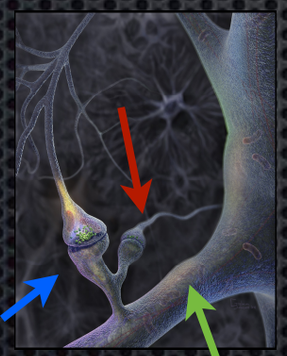


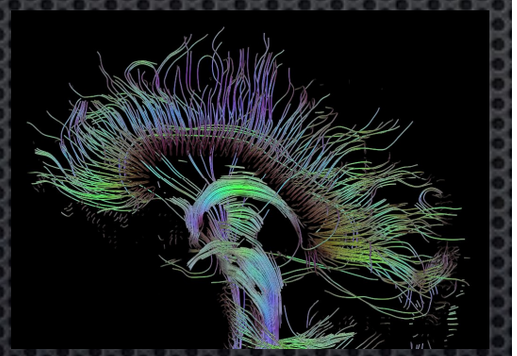
# Source localization gives EEG access to connectivity

- the holy grail of neural study is to model brain circuits
- effective connectivity requires temporal resolution (M/EEG only)
- source localization provides necessary spatial resolution



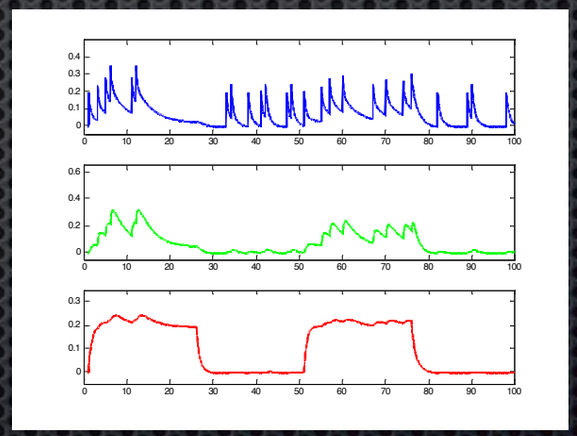

*Sporns 2007 (Scholaropedia, 2 (10):4695)*



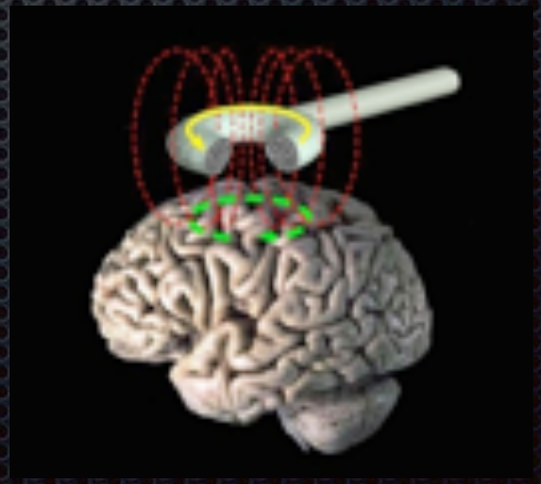


*Thanks to SPM group for slide images.*

tracers, dissection



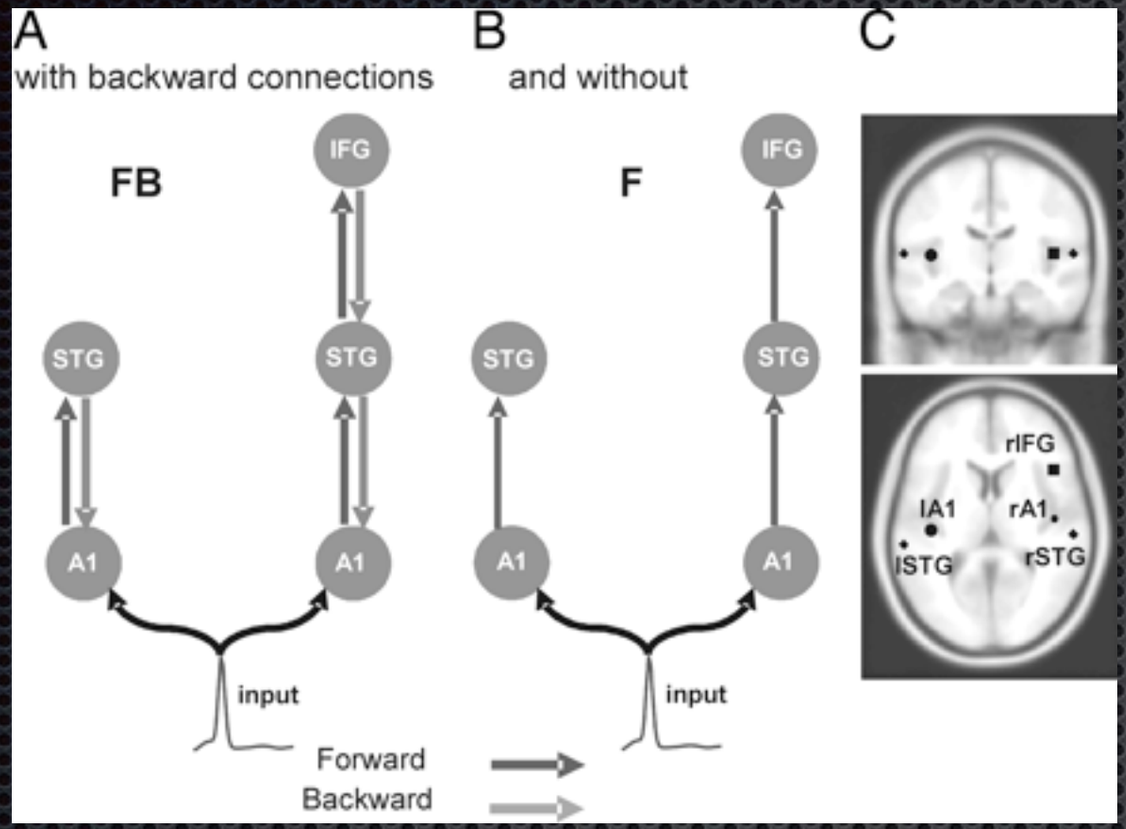

association measures

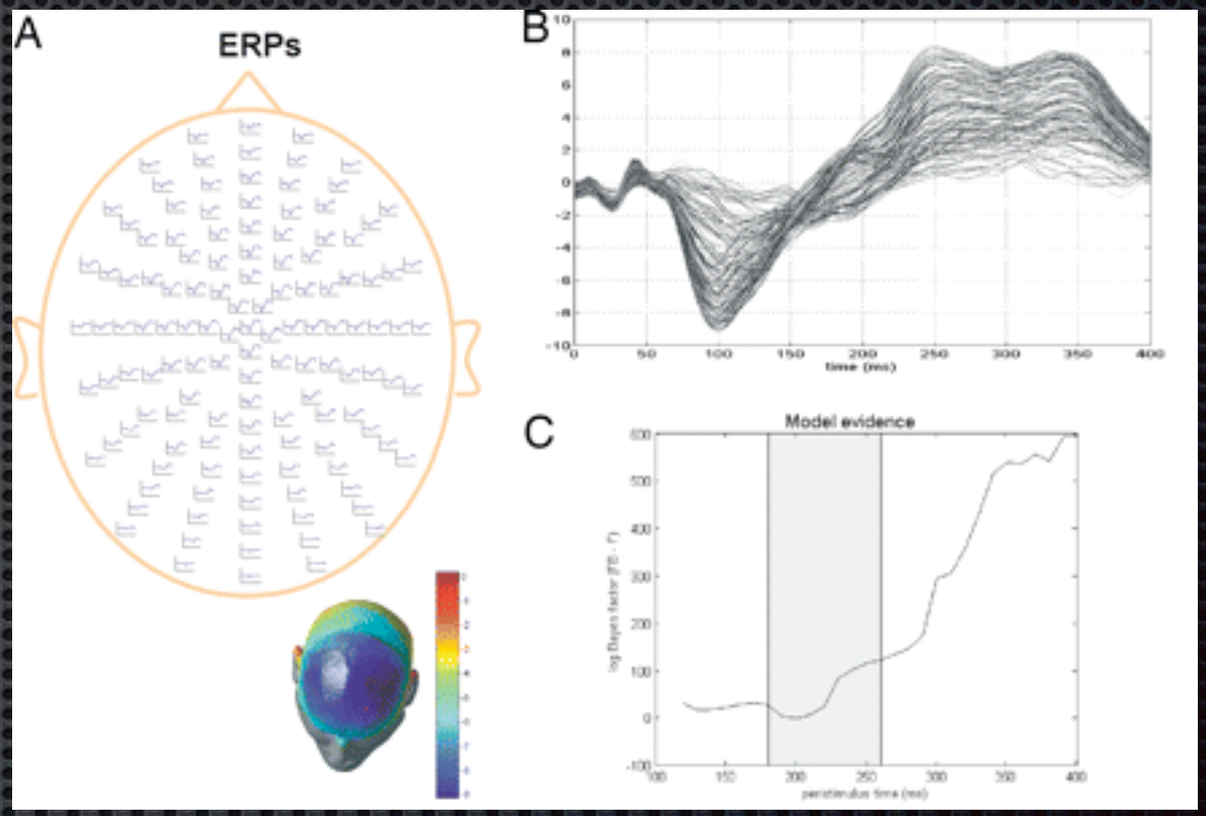


ablation, disruption, modeling

# Effective/Causal Connectivity in EEG

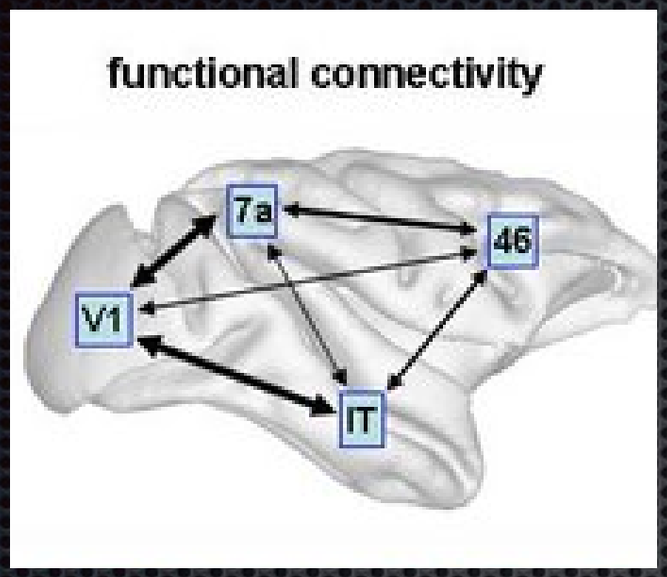
*Garrido et al, PNAS 2007*




*forward connections contribute to evoked potential and late potentials (auditory MMN), whereas backward connections contribute to late potentials*
*dynamic causal modeling*

# Small list of methods

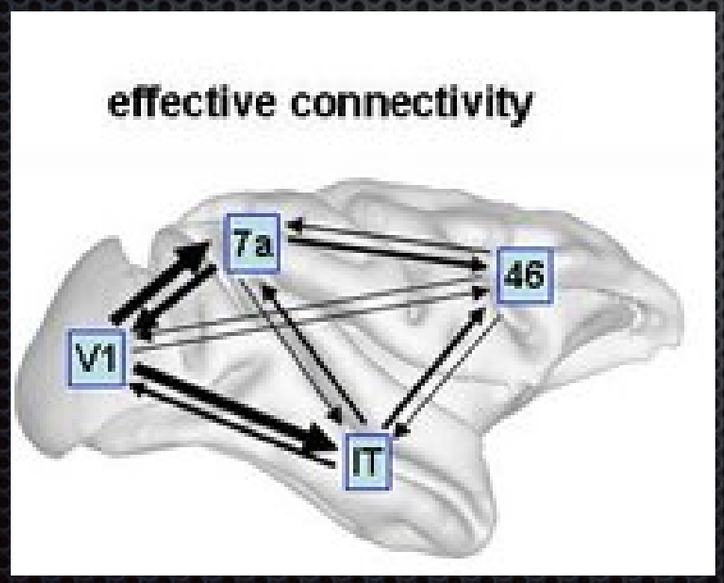



*Functional Connectivity*

*e.g., correlation, coherence, phase locking value, imaginary part of coherency, phase lag index, pairwise phase consistency, mutual information*

$$coh_{xy}(\omega) = \frac{|S_{xy}(\omega)|}{\sqrt{S_{xx}(\omega)S_{yy}(\omega)}}$$

$$\mathrm{cor}(X,Y) = \frac{\mathrm{cov}(X,Y)}{\mathrm{sd}(X)\mathrm{sd}(Y)}$$




*Effective Connectivity*

*e.g., dynamic causal modeling, granger causality (also partial directed coherence, direct transfer function), transfer entropy, phase slope index*

*if previous state of x improves prediction of current activity in y, more than the previous state of y, we say that x is Granger causal of y*

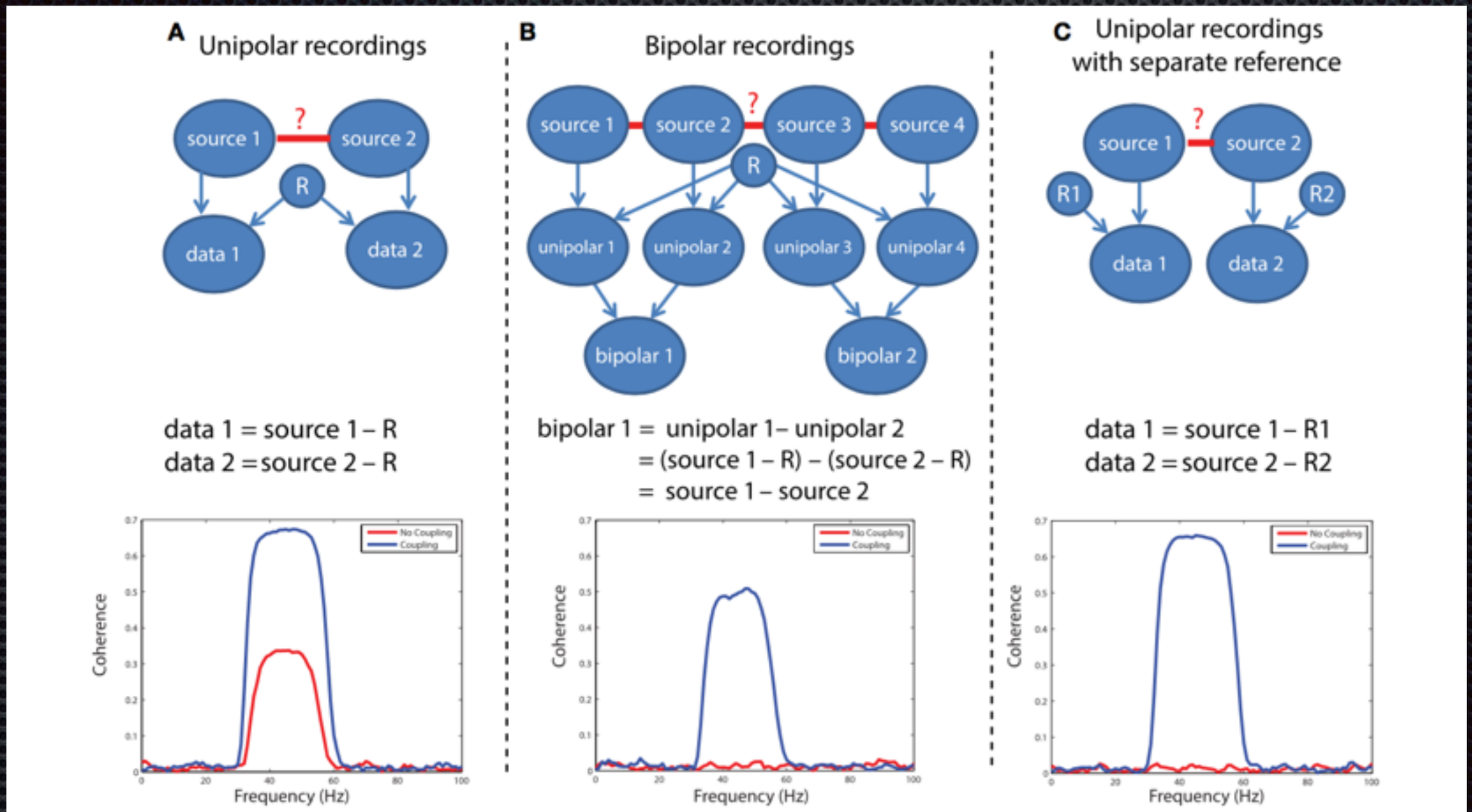
# Human Electrophysiology III

## Principles of Neuroimaging

# Problems with connectivity measures in EEG

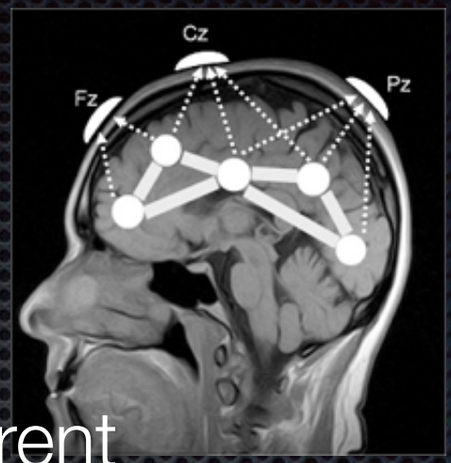
*Images from Bastos & Schoffelen 2016 Frontiers Review*

- common reference problem




**GURE 5 | Illustration of different referencing schemes and how each effects the calculation of coherence with and without true neuronal coupling.**
**)** The case of unipolar recordings, which introduce spurious coherence values in the absence of coherence. **(B)** The bipolar derivation technique, which largely solves the common reference problem. **(C)** The separate reference scheme, which also is not sensitive to common reference problems.

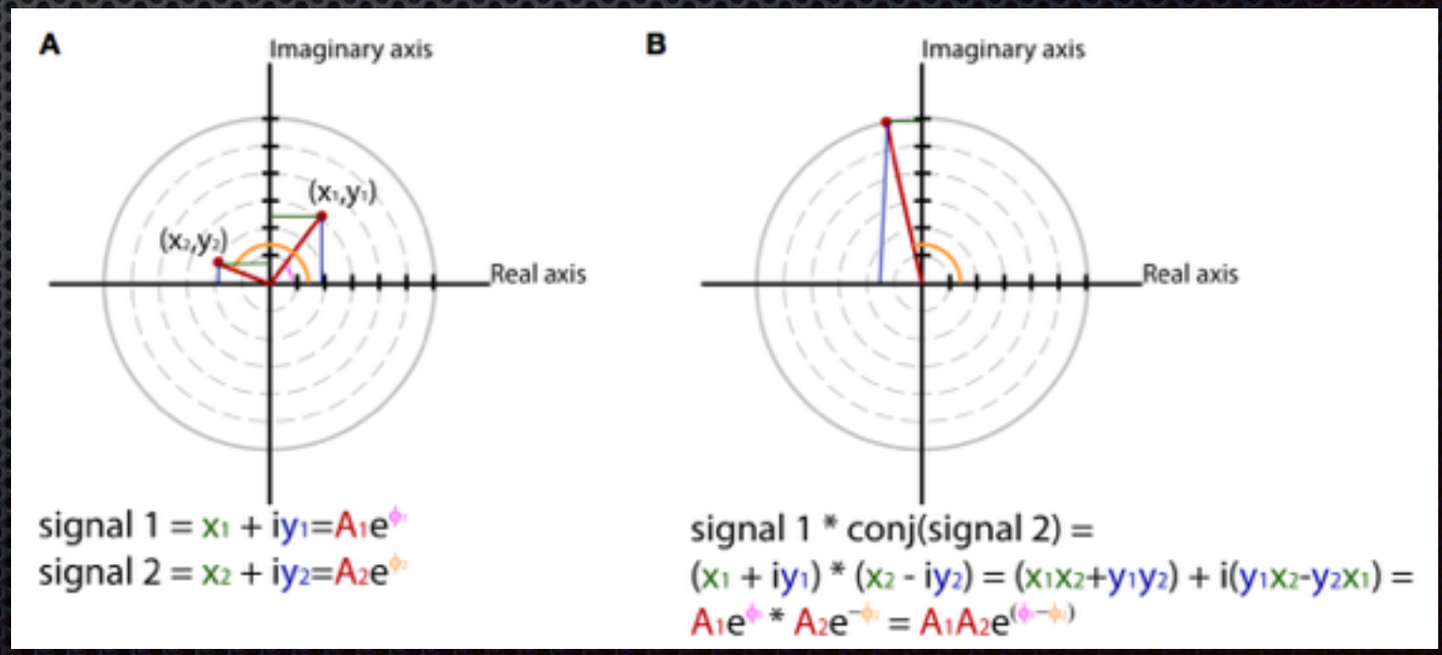
- volume conduction problem



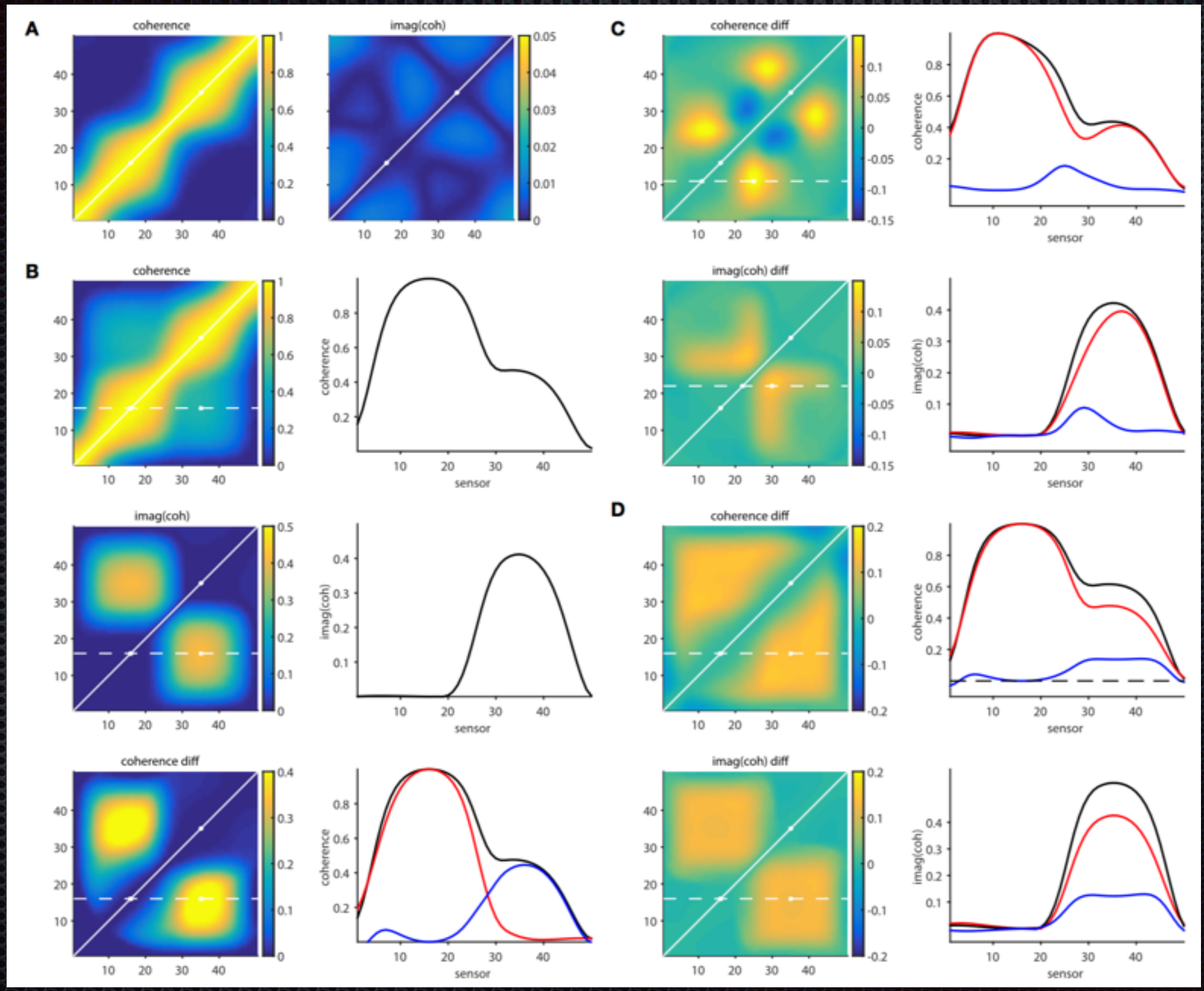

- field spread results in mixing of signals which can inflate apparent functional connectivity
- some “fixes” exist (below) but these are not complete*

**Schoffelen, J.-M., and Gross, J. (2009). Source connectivity analysis with MEG and EEG. Hum. Brain Mapp. 30, 1857–1865. doi: 10.1002/hbm.20745*

- unmix signals (source analysis, ICA)*
- use experimental contrasts*
- use measures that ignore zero-phase relationships (e.g., imaginary part of coherency, phase lag index, phase slope index)*



- volume conduction problem



- signal to noise problem

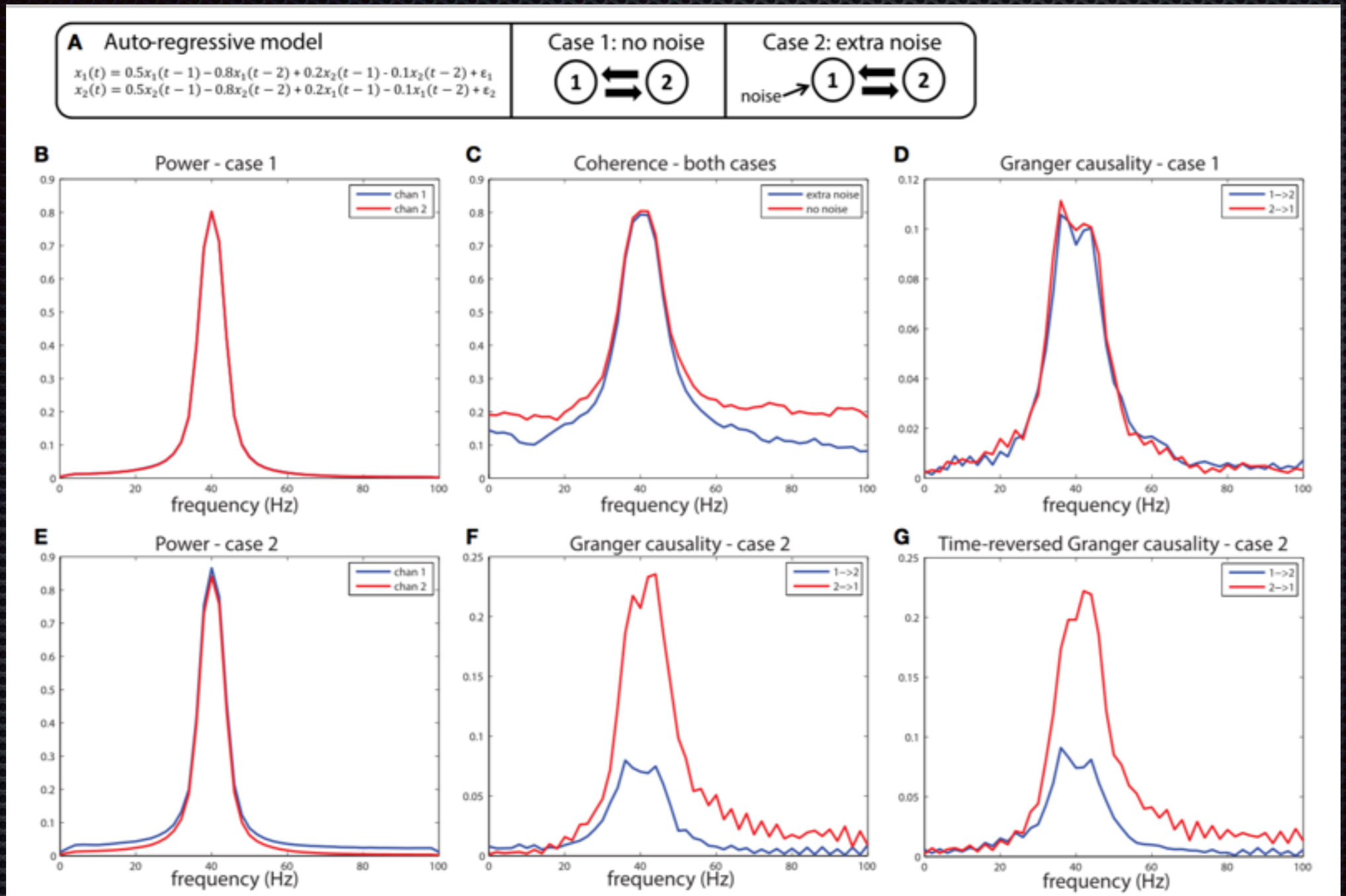
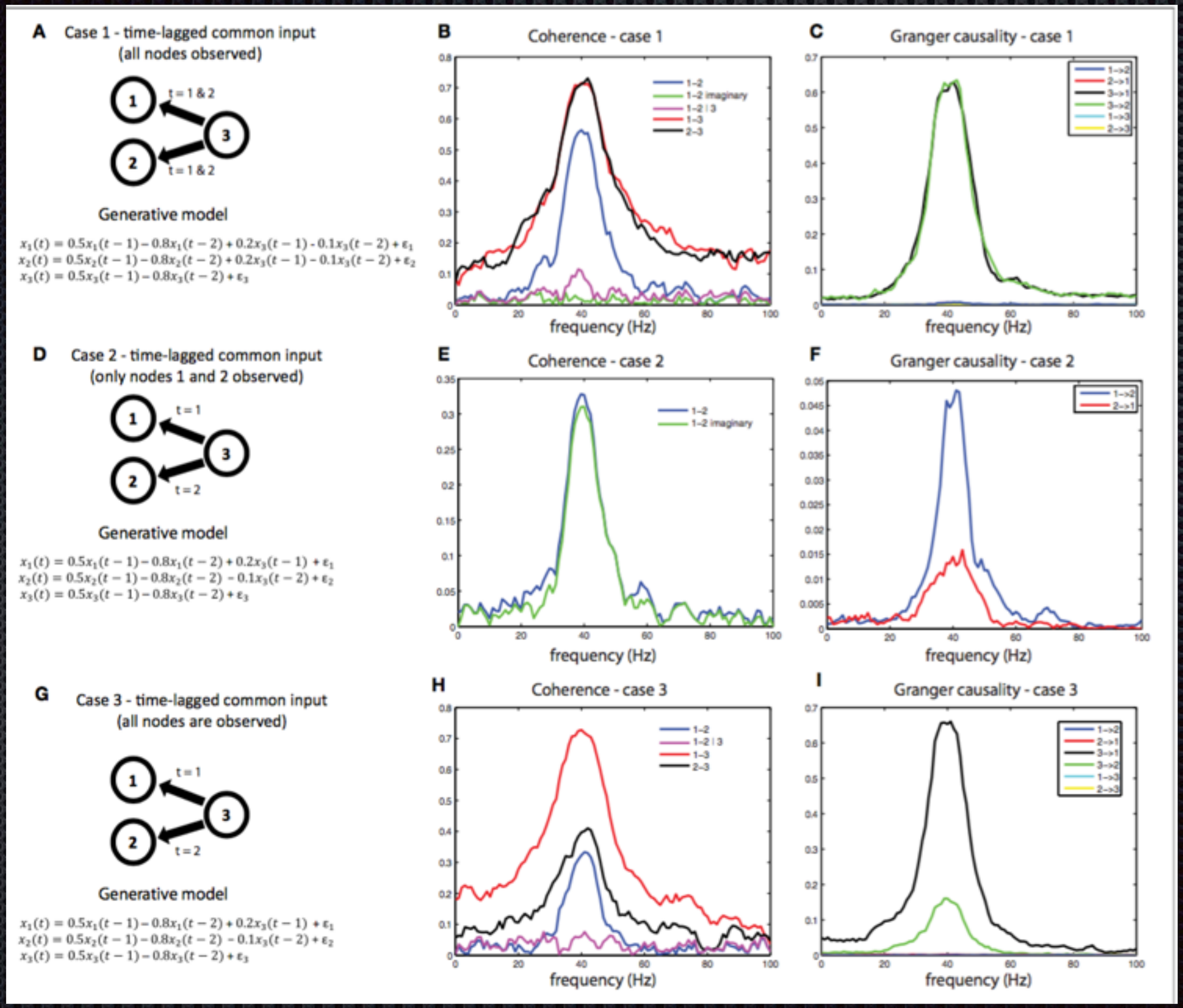



**FIGURE 7 | A simulation of the signal to noise ratio problem. (A)** Two nodes interact bidirectionally with equal connectivity strengths in the two directions, and the data is observed without (case 1) or with (case 2) measurement noise. **(B)** Power for case 1, **(C)** Coherence for case 1 and 2, and **(D)** Granger causality estimates for case 1. **(E)** Power, **(F)** Granger causality estimates for case 2. **(G)** Granger causality estimates after time-reversing the data produced by case 2.

** mitigate by keeping noise constant across sources (e.g., impedances), using time reversed model, DCM*

- common input problem (also “all” input problem)




** problem for DCM too (all directed models)*

- sample size problem

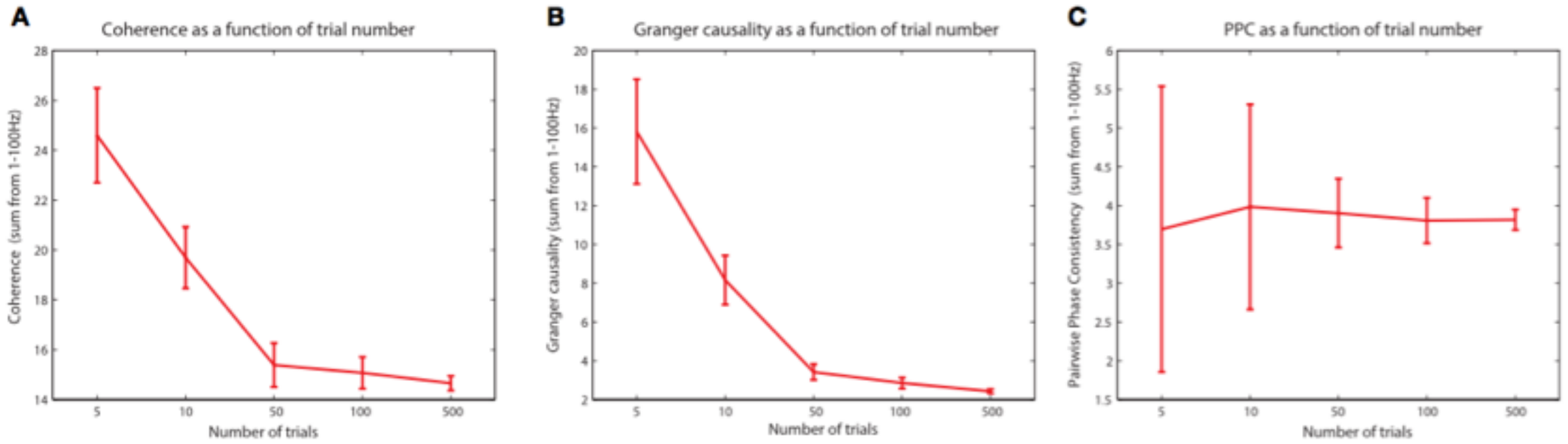



**FIGURE 10 | Sample size bias for coherence and Granger causality estimates. (A–C)** For each respective metric, simulations based on 5, 10, 50, 100, and 500 trials were run, and coherence **(A)**, Granger causality **(B)**, and PPC **(C)** were calculated. Each panel reflects the average ± 1 standard deviation across 100 realizations.

** not unique to these measures - true for most measures of association (functional connectivity), with exception of pairwise phase consistency (developed to mitigate sample size bias - looks at distribution across trials clustering around value)*

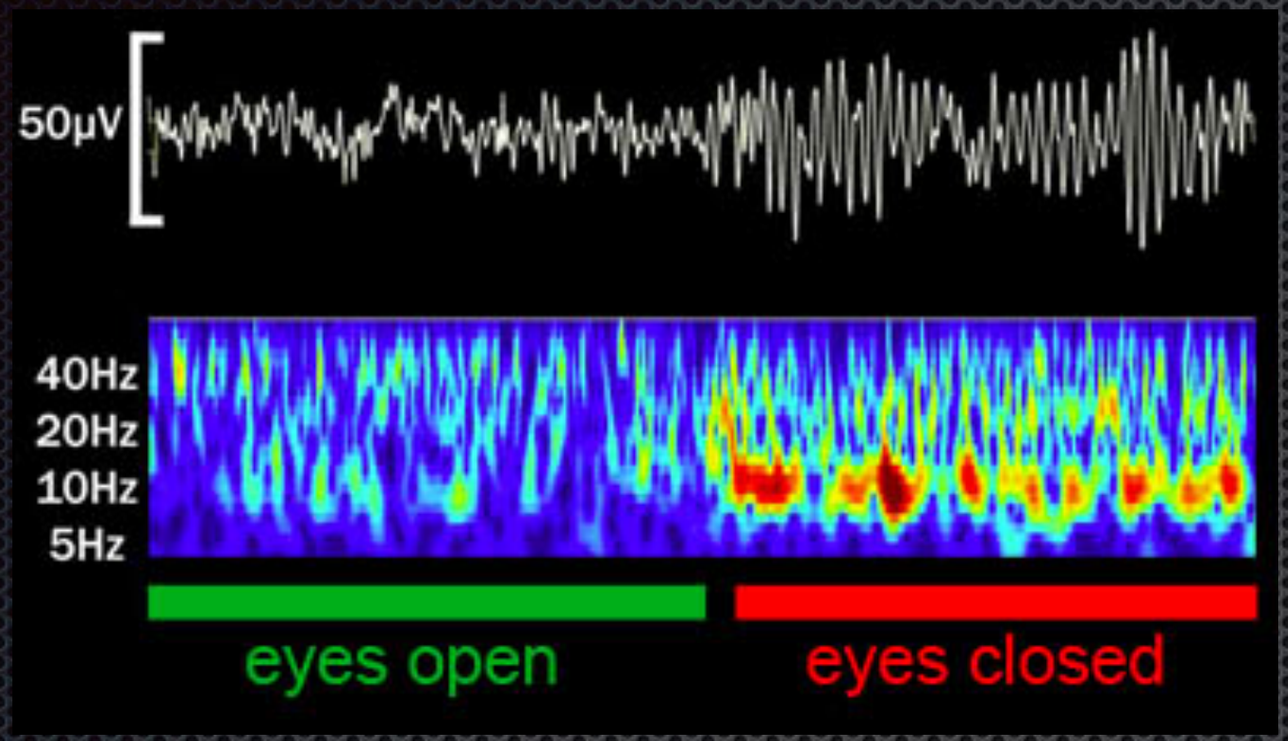
# Problems with connectivity measures in EEG

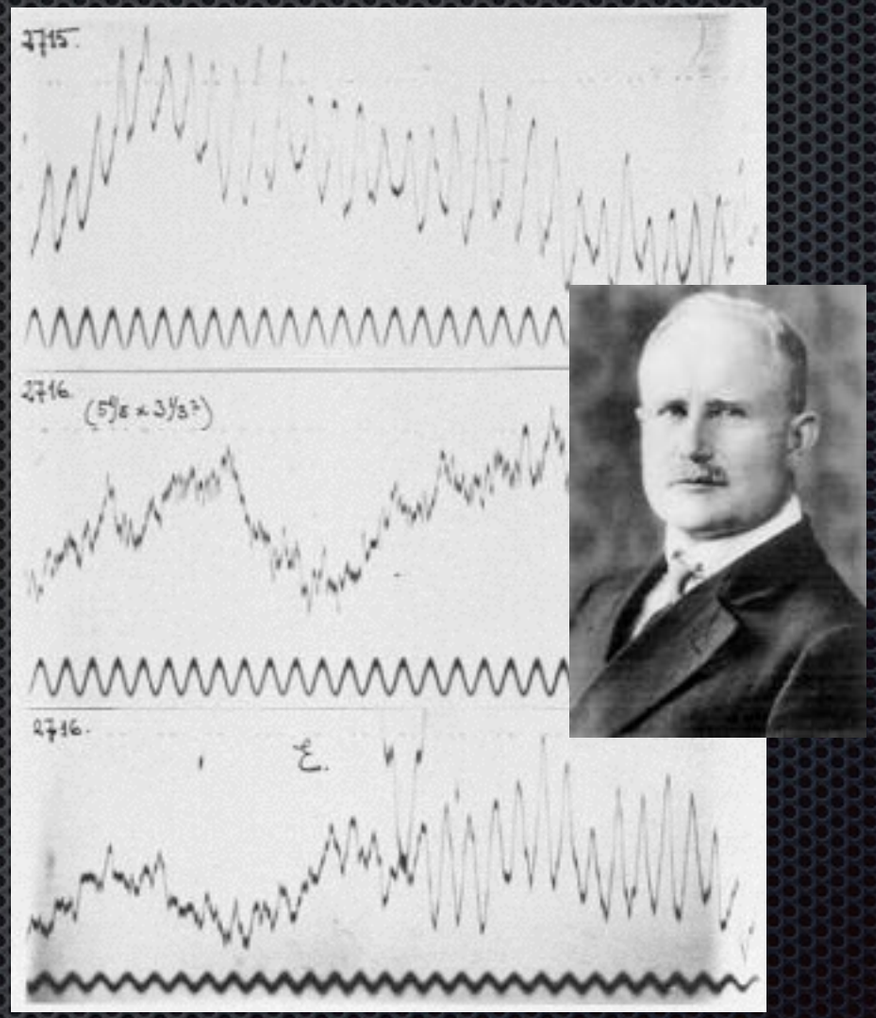
- estimating connectivity is not trivial
- no magic bullet

- good practice considerations
  - *use reference condition (eliminate spurious effects due to common reference)*
- *keep noise constant across sources*
- *keep trials constant across sources*
- *must consider measures immune to volume conduction*
- ***and/or** unmix sources*
- *assume model is wrong*

# Oscillations in EEG Signals

*Berger 1924*



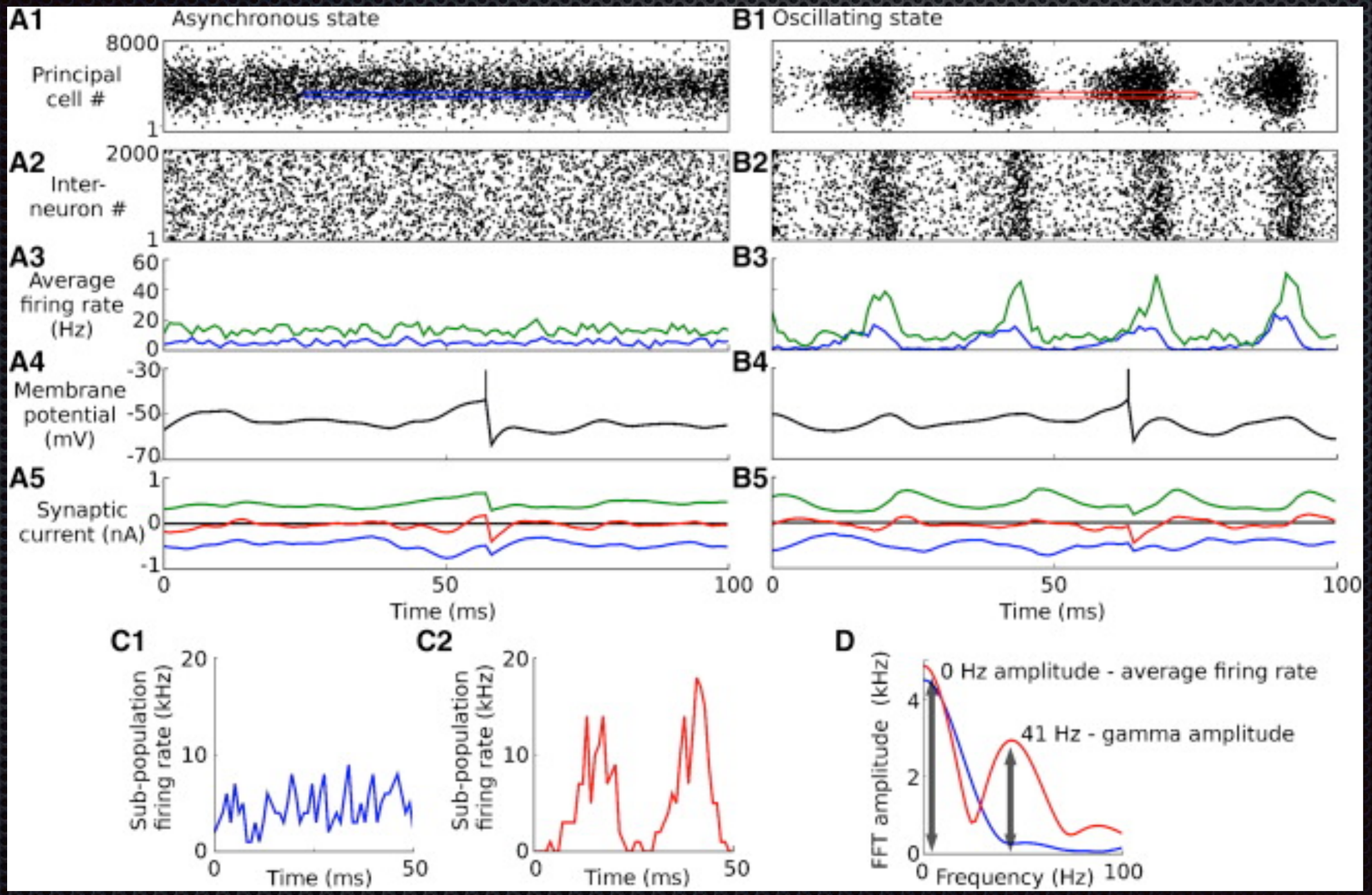

*A different approach to "connectivity/dynamics"*

*A different approach to finding "sources"*

*A different approach to "temporal profiling" events/states*

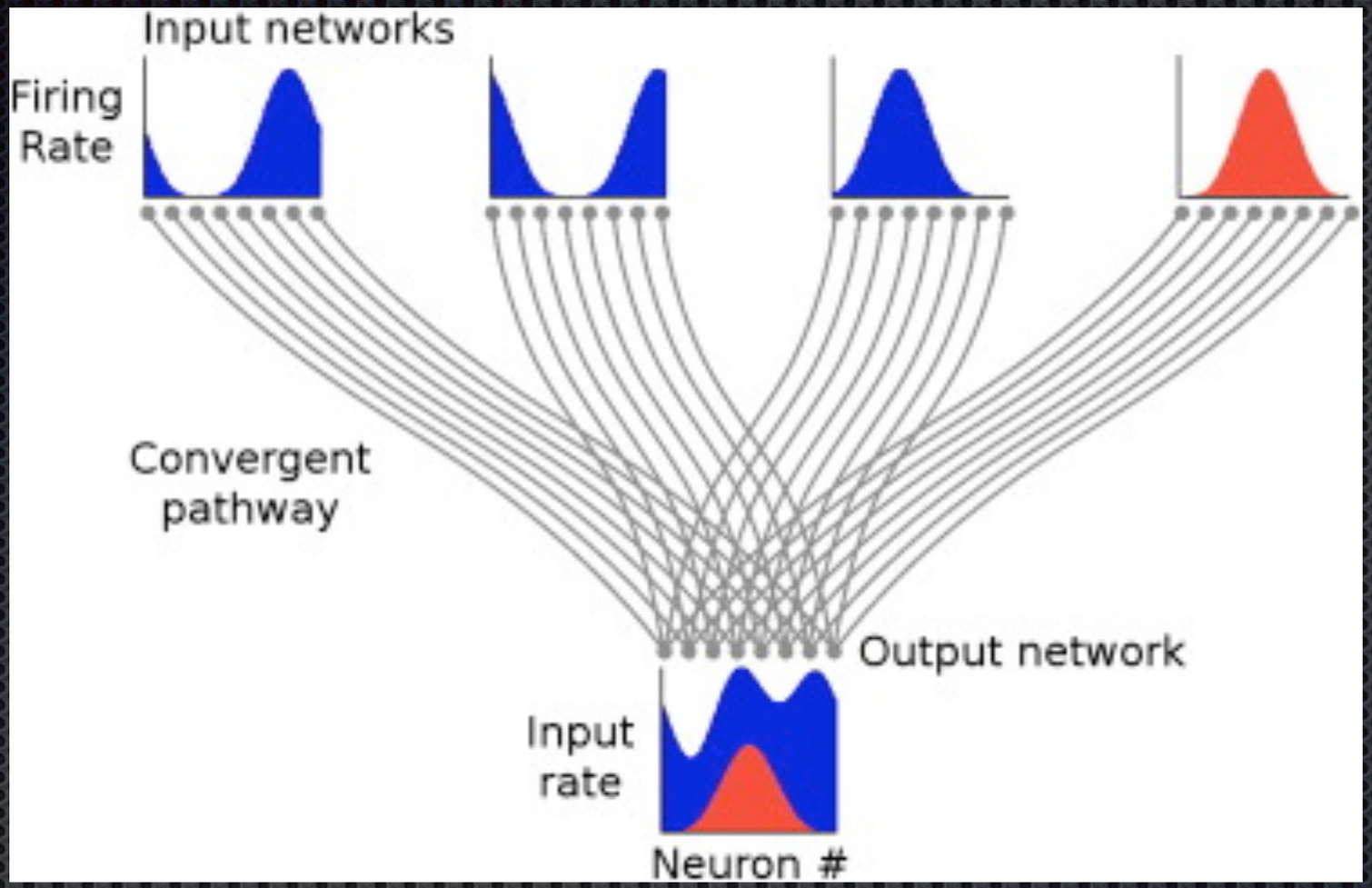
# What are oscillations?

** synchrony among neuronal populations in fluctuation of neuronal excitability (de/polarization)*




*Akam & Kullman 2010 Neuron*

# Why do oscillations exist?

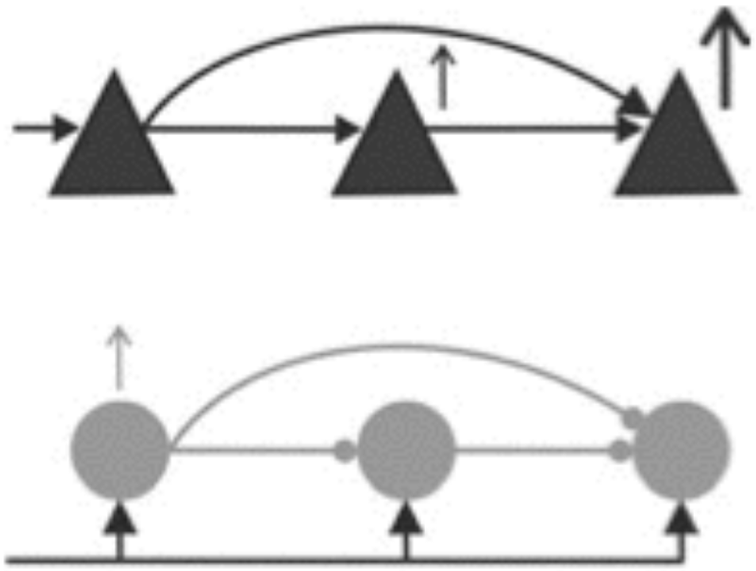



*Akam & Kullman 2010 Neuron*

*Within cell, energy efficient mechanism of ensuring that neurons respond to inputs without being oversensitive to noise (Buzsaki).*

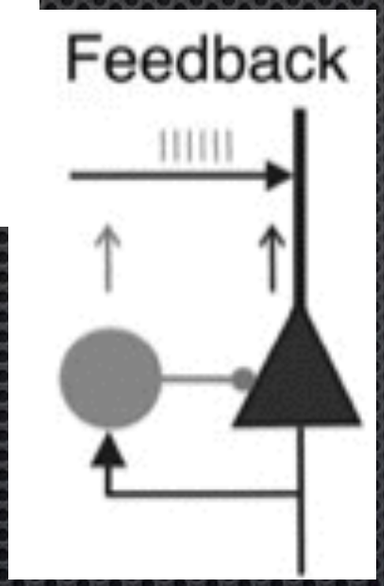
*Between cells, means of binding of functional ensemble of neurons (red - synchronous state population) via driving of output network spatial frequency/firing pattern (Akam & Kullman).*

# Types of Oscillatory Mechanisms



*feedforward excitation produces activity; oscillations can arise from biophysical time constants on pyramidal cells (e.g., neurotransmitters, epilepsy hypersynchronization)*

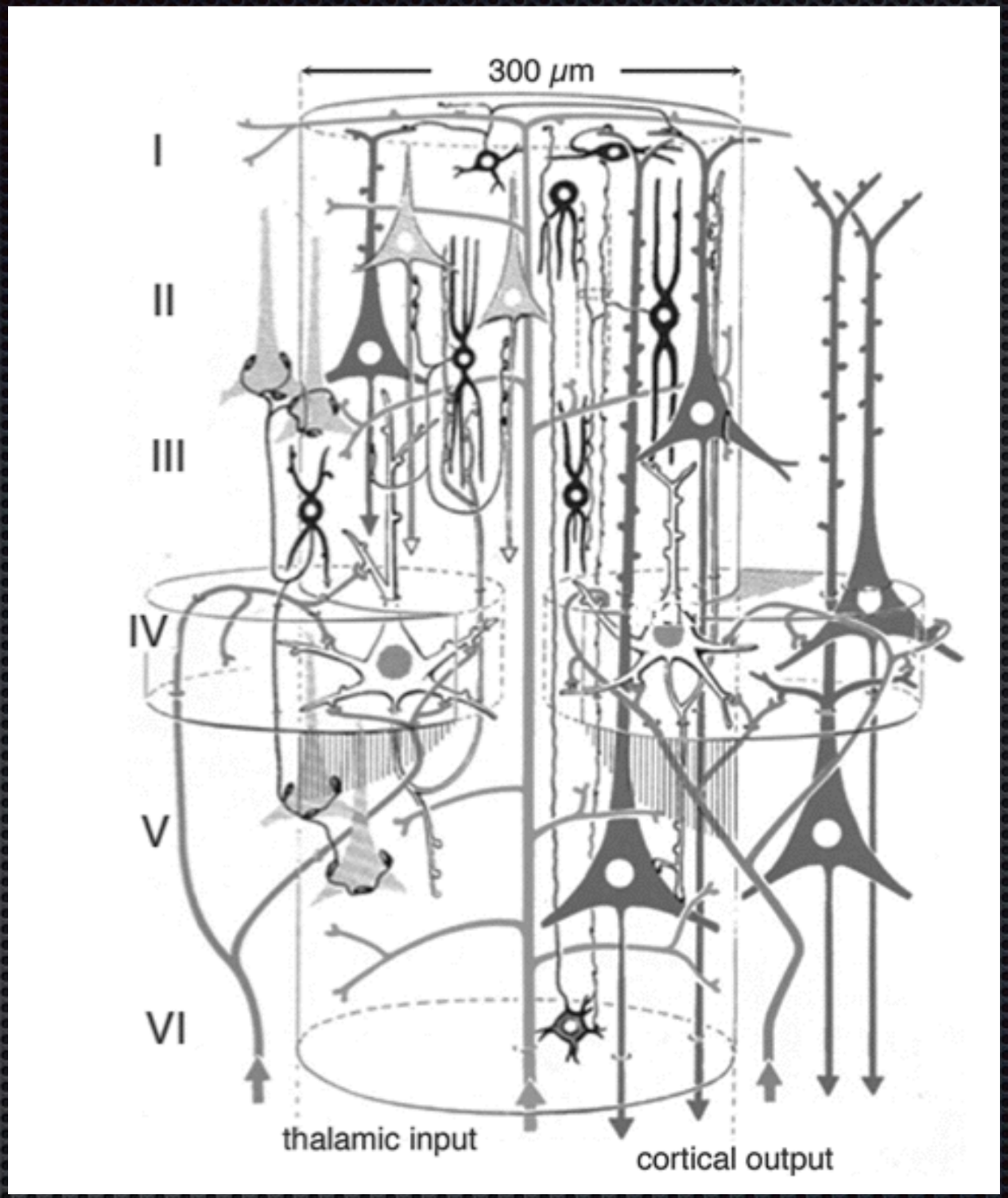
*feed forward inhibition with ambient activation can produce unstable oscillation; in this inhibition based oscillation, frequency is dependent on GABA-ergic time constants, e.g., fast-acting GABAa receptors => 40-100Hz (one of the most common rhythms throughout cortex)*




*inhibition with excitation produces stable oscillation*

oscillations = circuitry

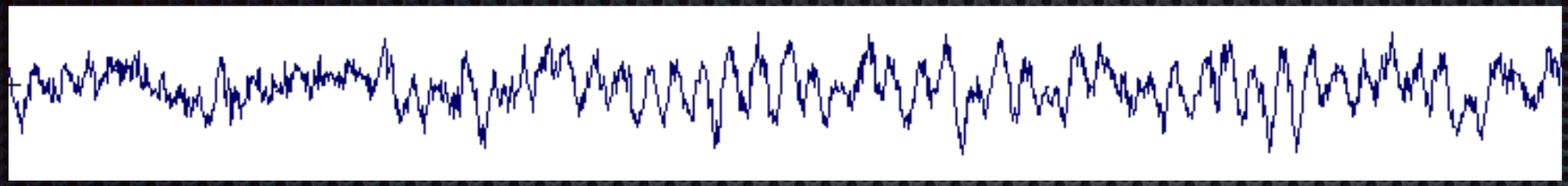
frequency = biophysics of oscillators => localization?

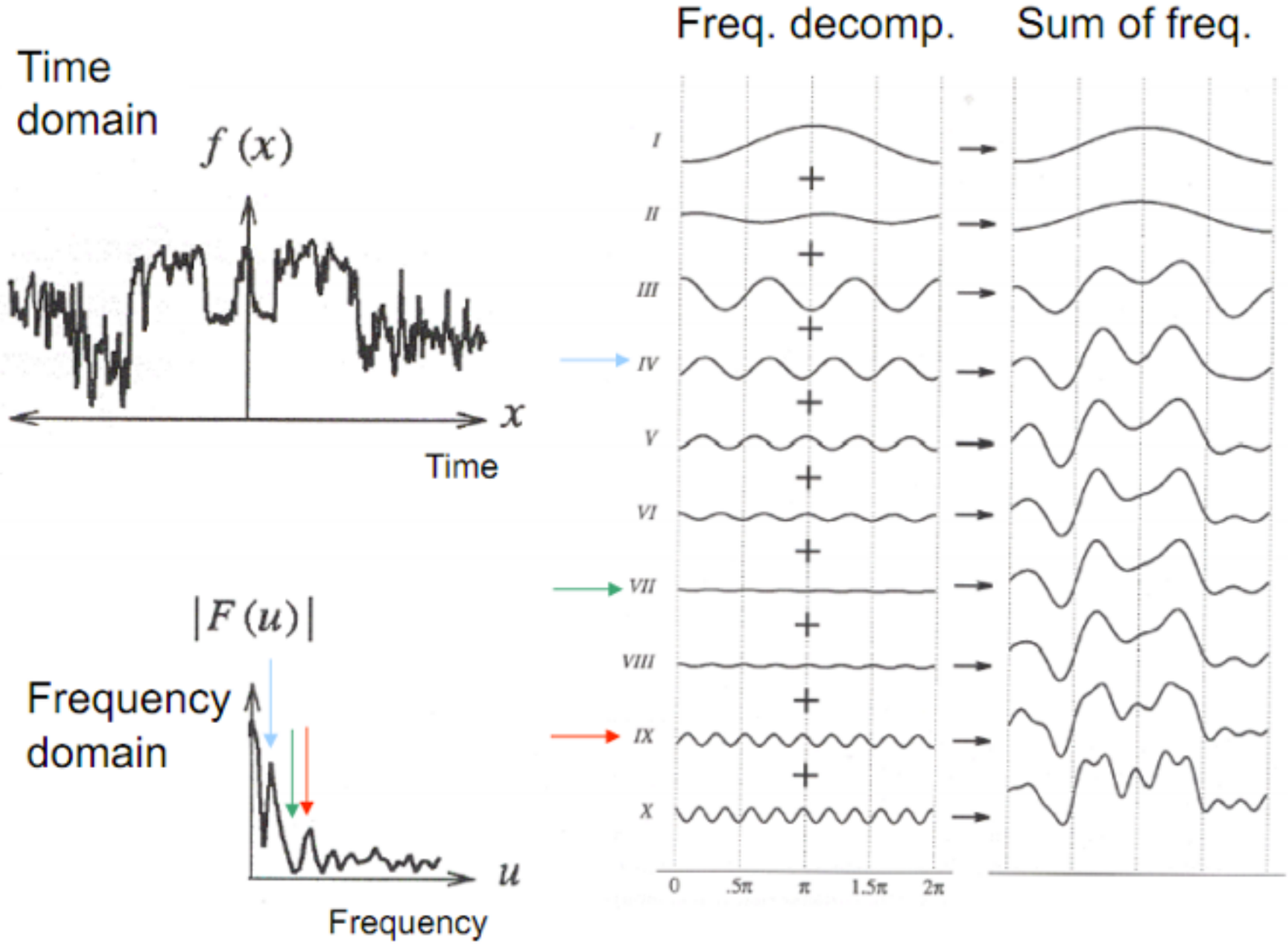



*Buzsaki (Rhythms of the Brain)*

** interaction between excitatory (pyramidal) and inhibitory (GABAa-ergic interneurons) neurons*

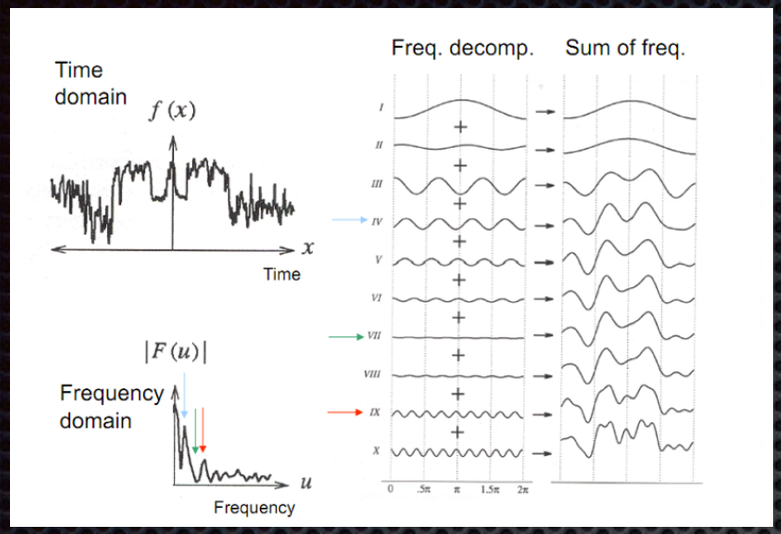
# Measuring Oscillations



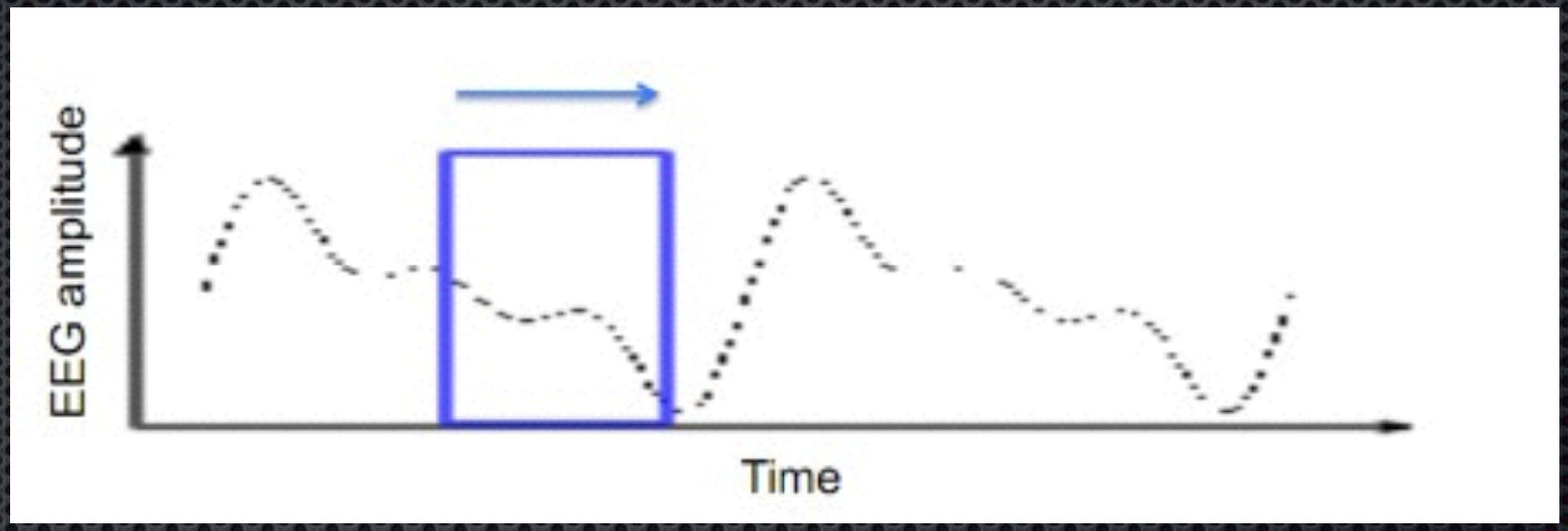



Arnauld Delorme

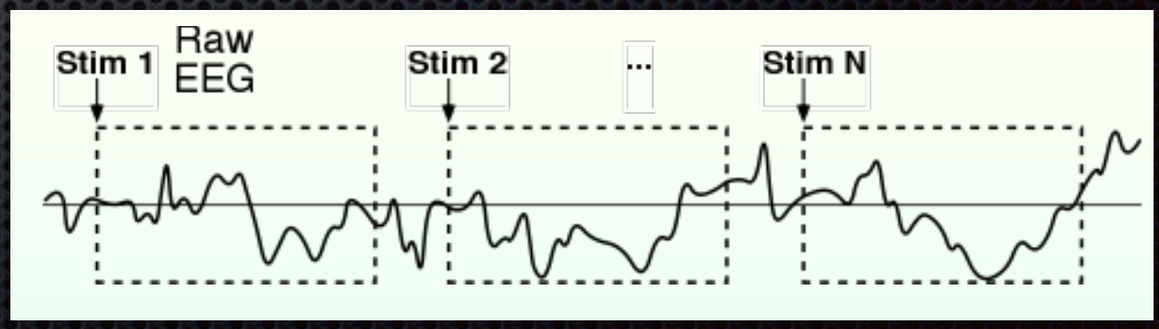
# Extracting temporal flow of oscillatory effects




*FFT, wavelets, Hilbert transform etc.*

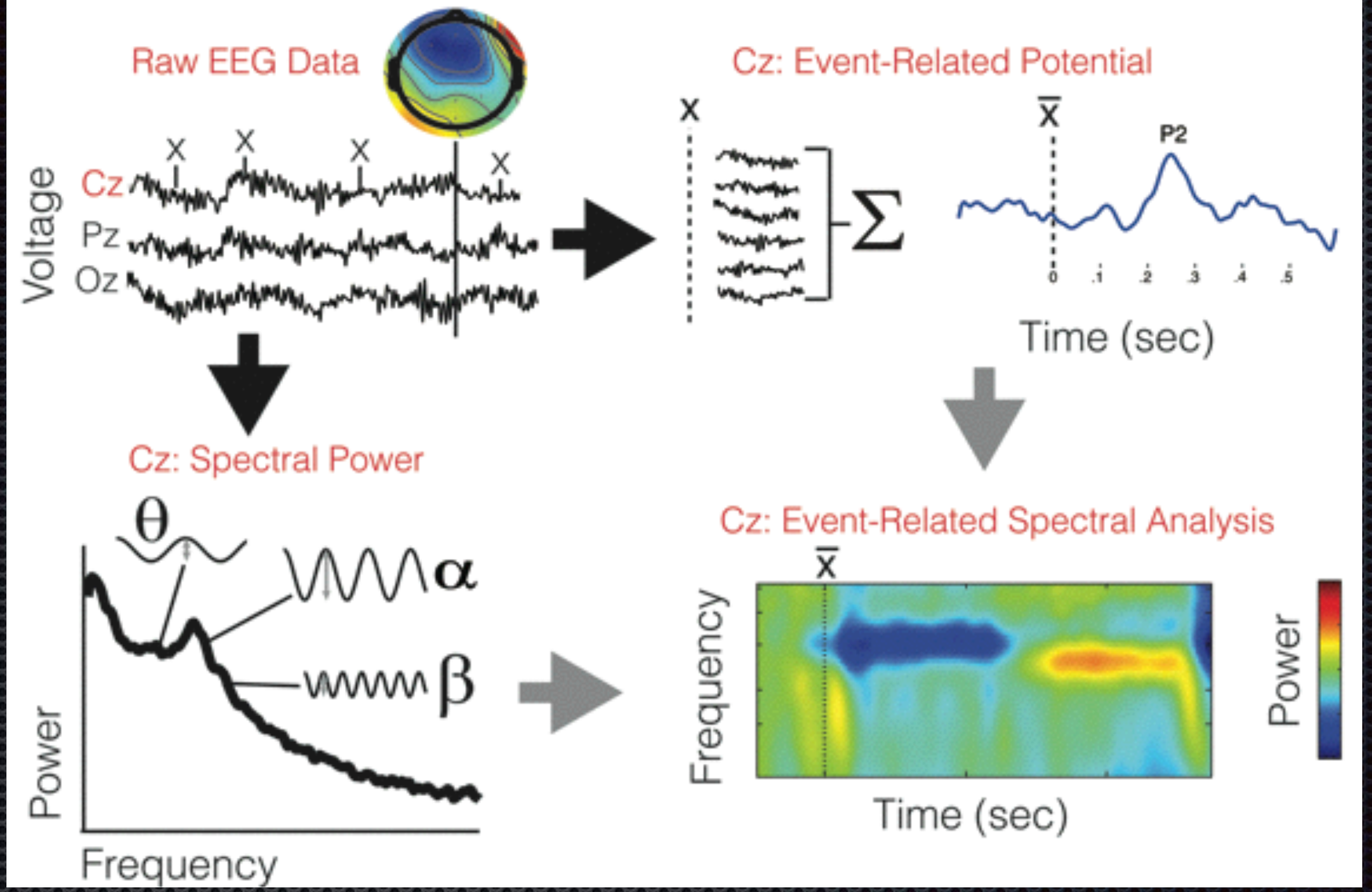



*Time x Amp => Time x Freq x Power*




*Event Related Spectral Perturbation (ERSP)*

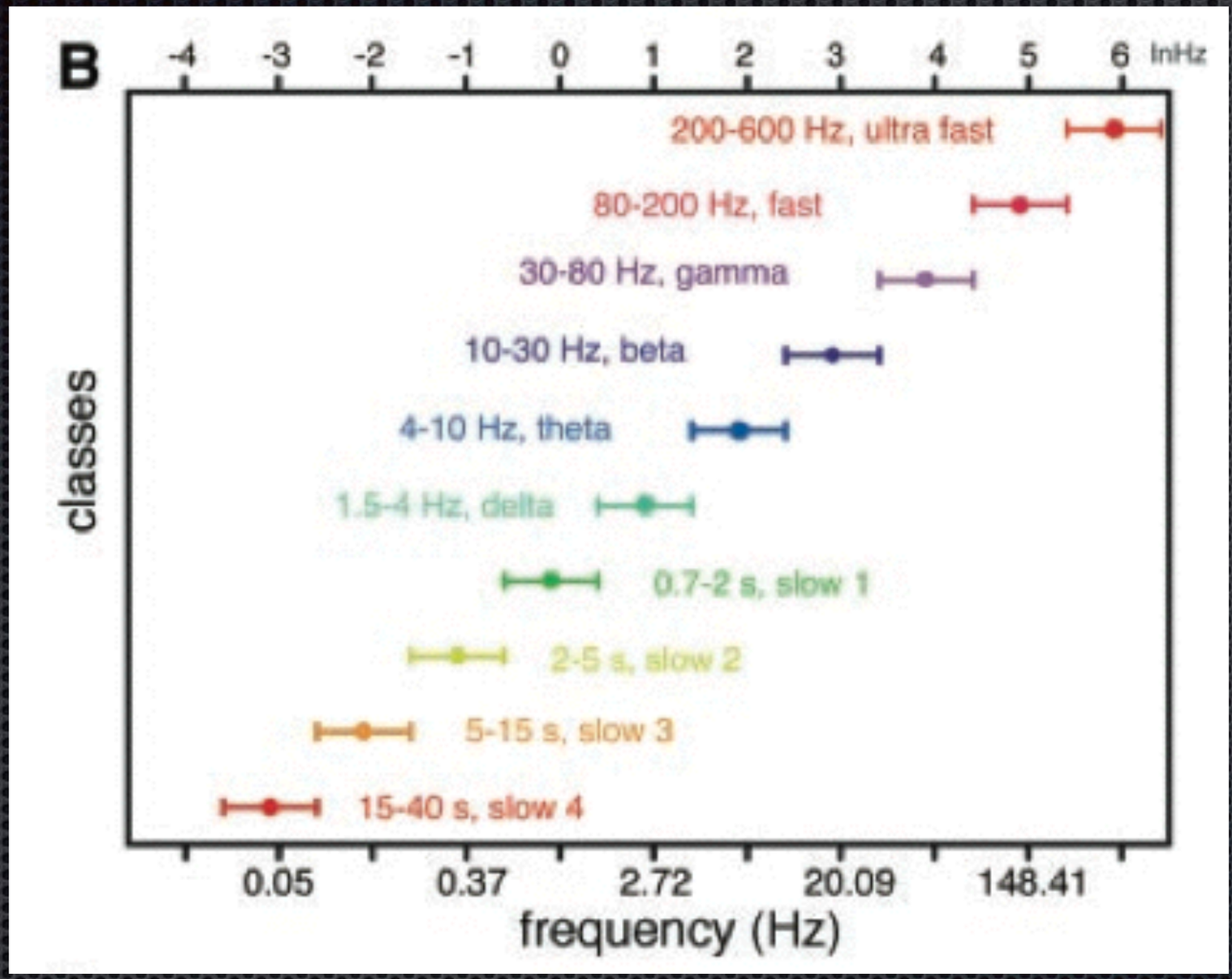
*ERP*




*qEEG*

*Event Related Spectral Perturbation (ERSP)*
*event related changes in frequency content of signal*

# Classes of Oscillations in Rat Cortex

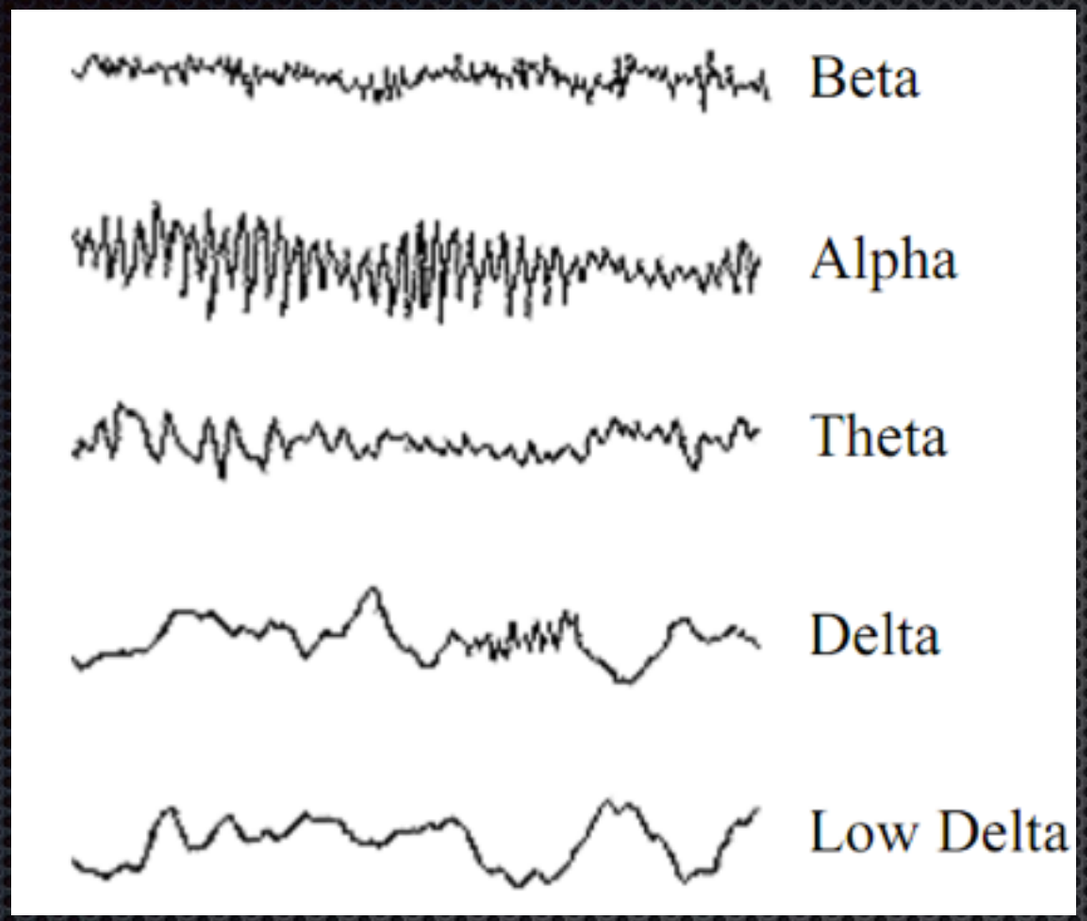


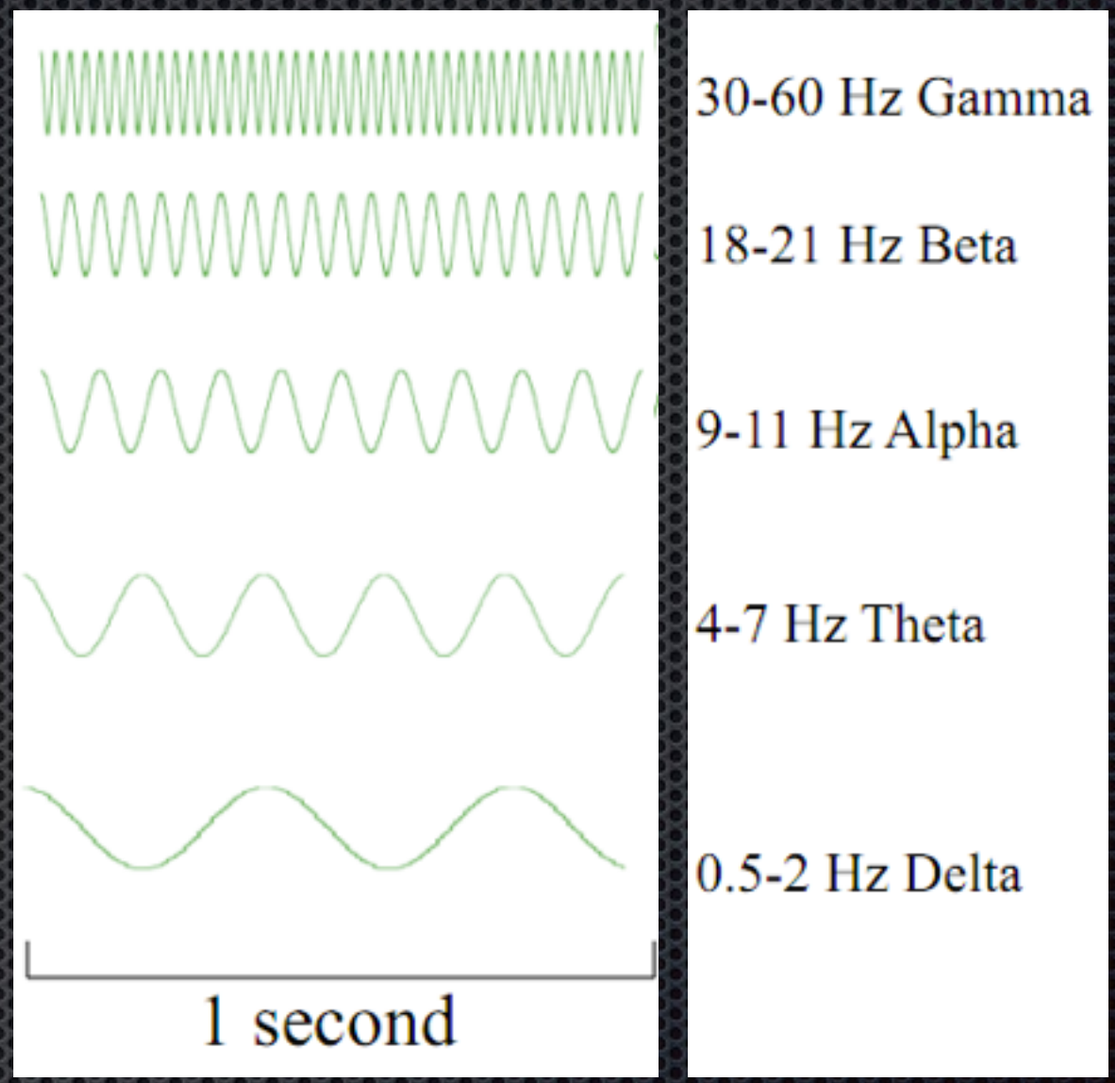

*Buzsaki Science 2004*

*linear progression on logarithmic scale with constant ratio between neighboring frequencies*
*typically different neighboring classes compete with one another within single network*
*multiple frequencies can exist temporally within network and interact*

# Classes of Oscillations in Human EEG

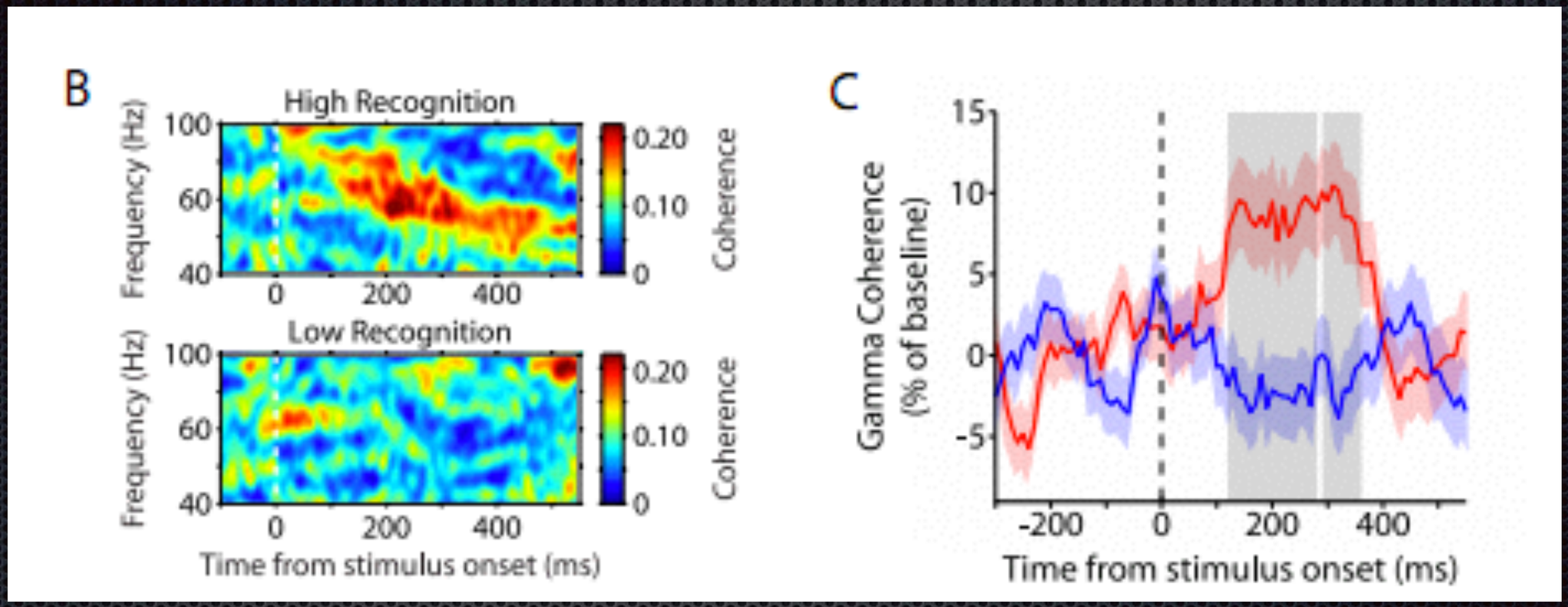
?



# Gamma (>40Hz)

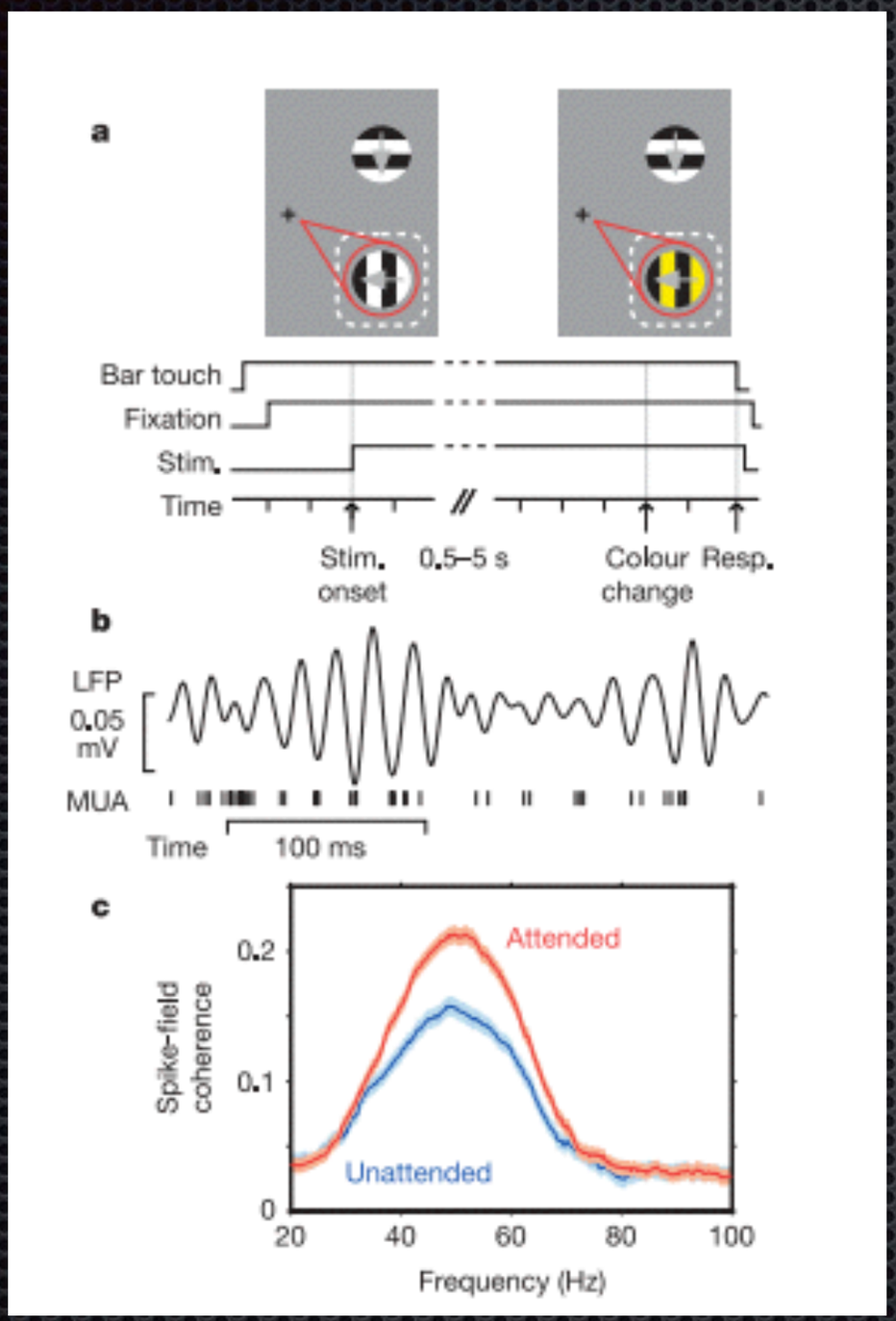
Hippocampus & Entorhinal Cortex, *Fisahn et al., 1998, Gamma 40Hz*
Neocortex Gamma (Visual Cortex), *Gray & McCormick 1996, Gamma 70Hz+*

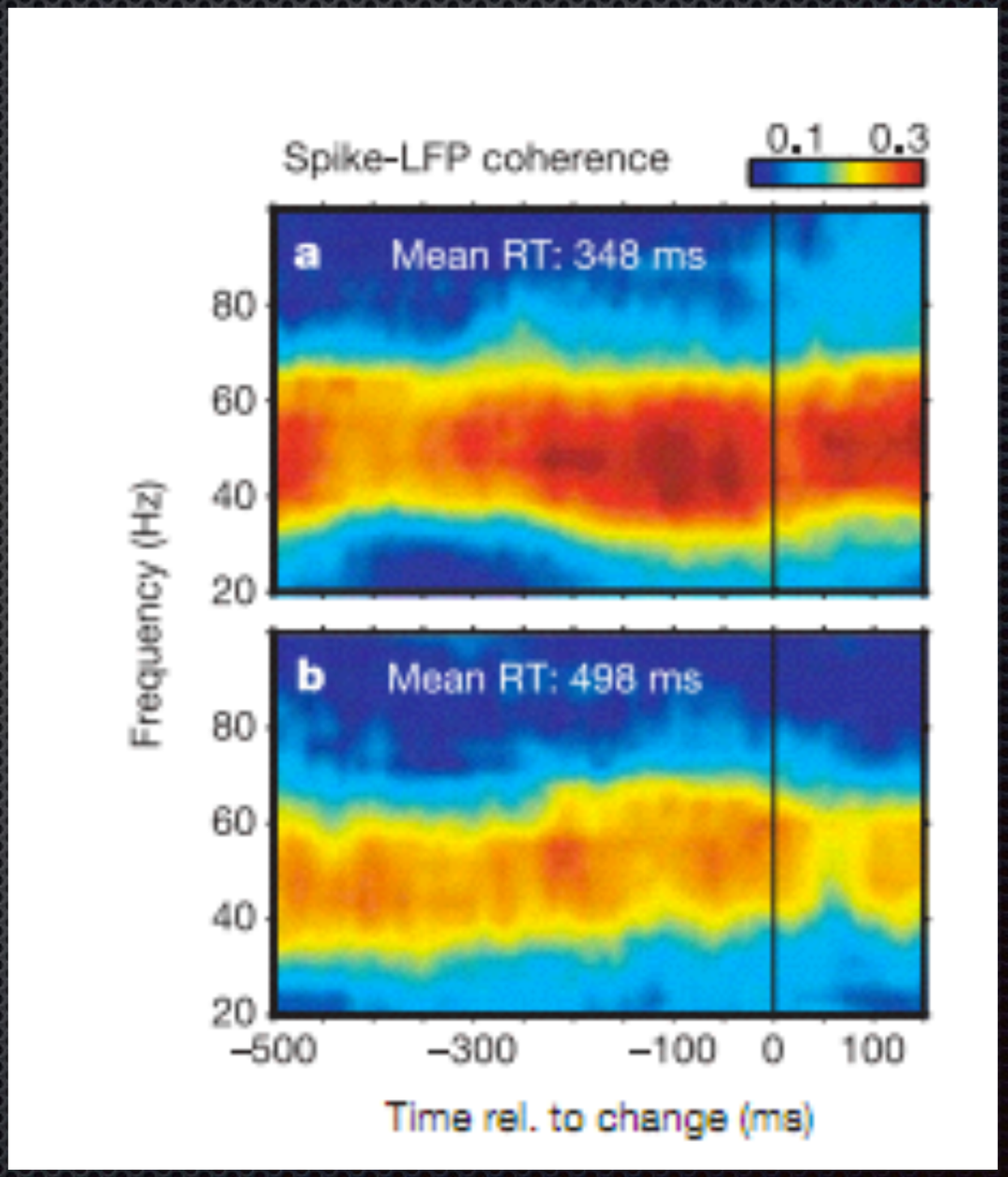




Jutras, Fries & Buffalo (2009) JNeuro
Gamma in Hi predicts recognition
spike synchrony intracortical recordings

Womelsdorf, Fries, Mitra & Desimone (2006) Nature
gamma in visual cortex predict attention & RT (and perception)
spike synchrony intracortical recordings

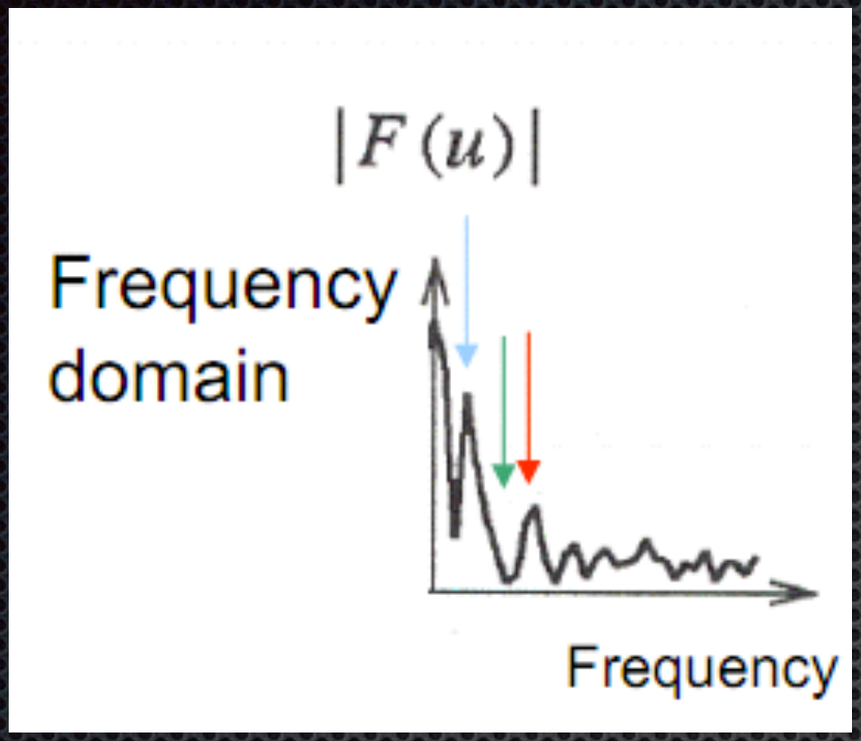


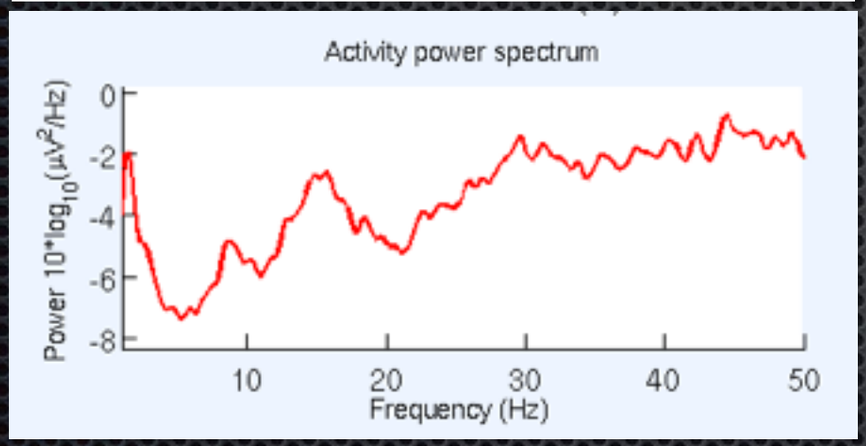



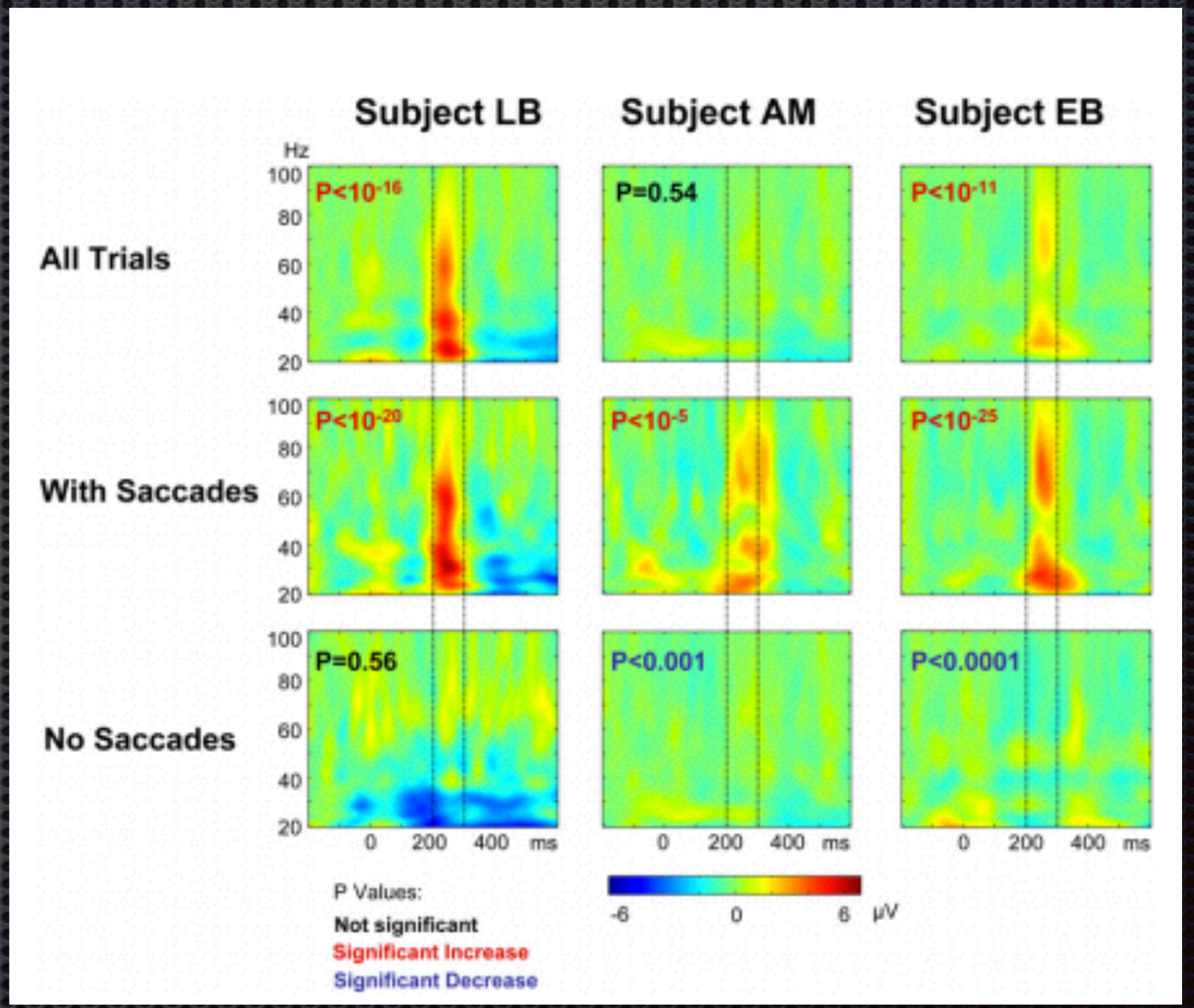

*Gamma seems to correlate with processing efficacy of neuronal populations or perhaps activation of a neuronal ensemble.*

Gamma is hard to image with EEG/MEG:

- lower power
- in 'artifact' range (muscle, microsaccades, high-freq noise)
- most human gamma recording are intracortical



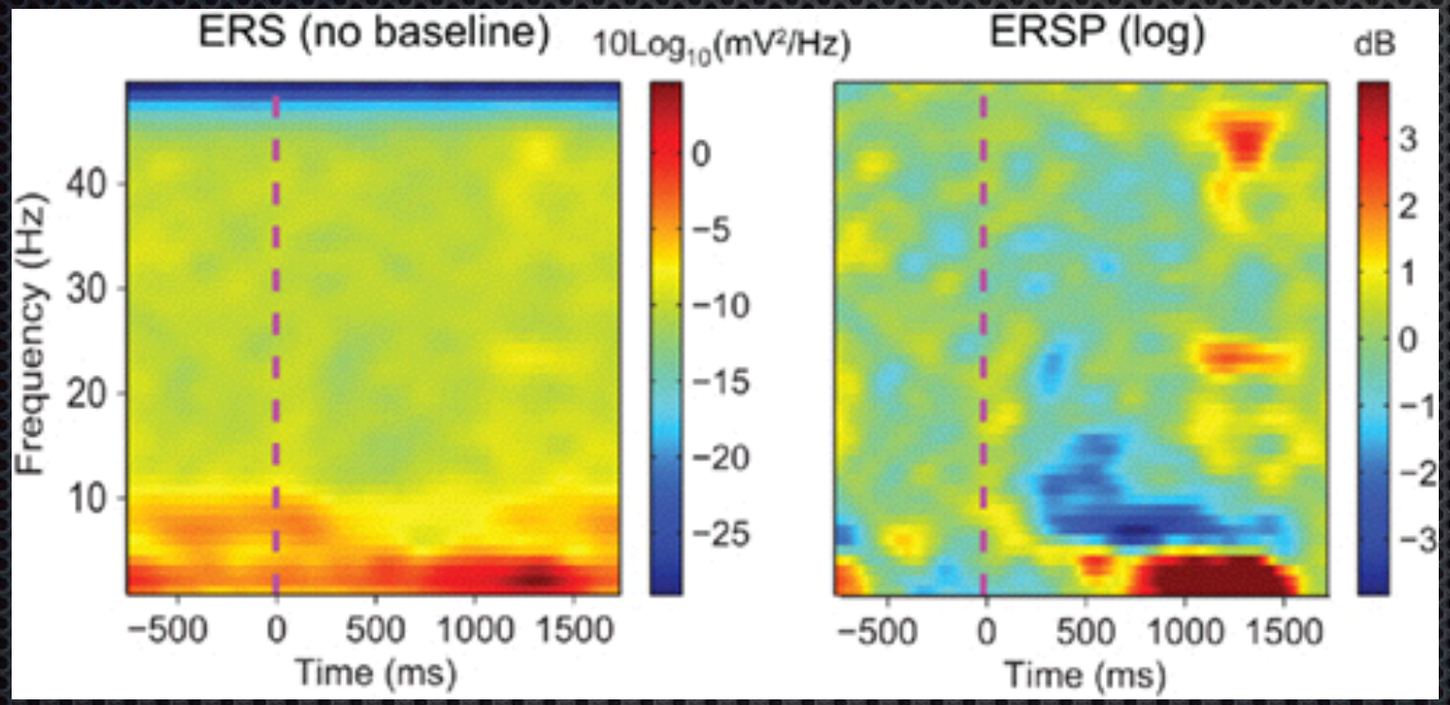



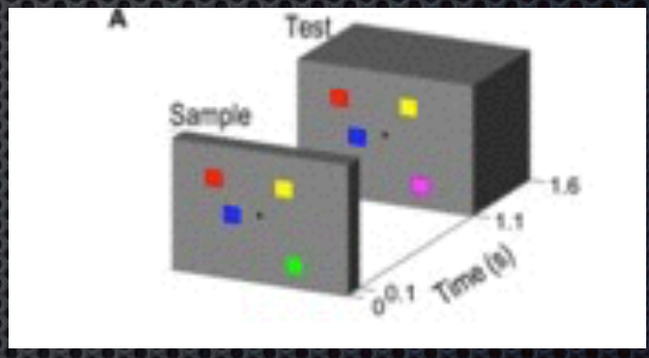

The most prominent oscillations in scalp EEG fall in lower frequency range (4-7Hz, 8-12Hz, 13-30Hz).

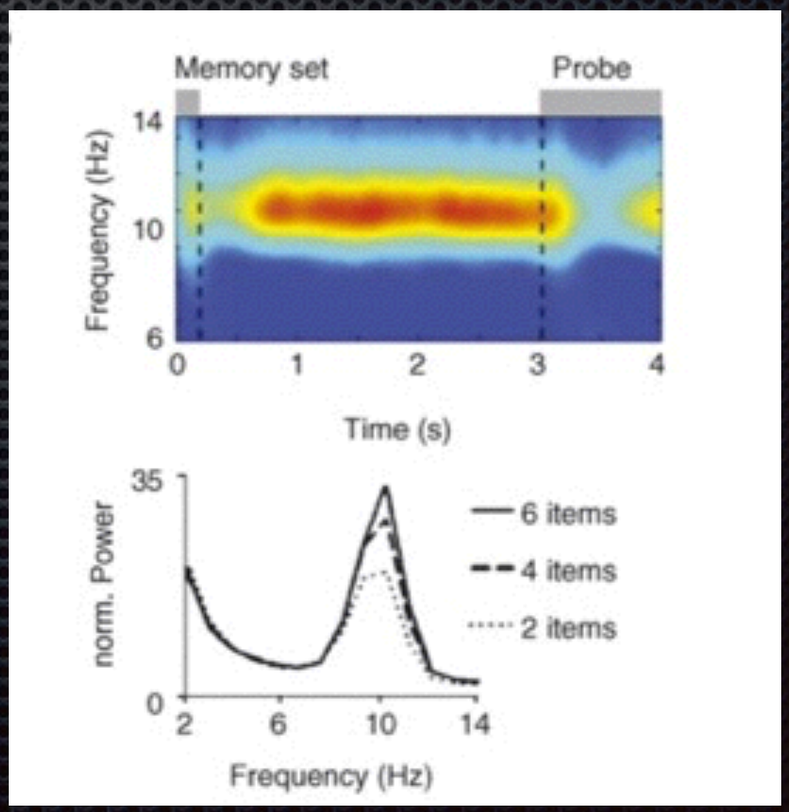
# EEG: Alpha (8-12 Hz)

- described by Hans Berger in 1929 (but not task related)
- decreases during stimulus processing (ERD), typically over occipital electrodes and localized to occipito-parietal sources
- increases also observed (ERS)
- Klimesch (1999; 2007) gating/inhibition theory of alpha



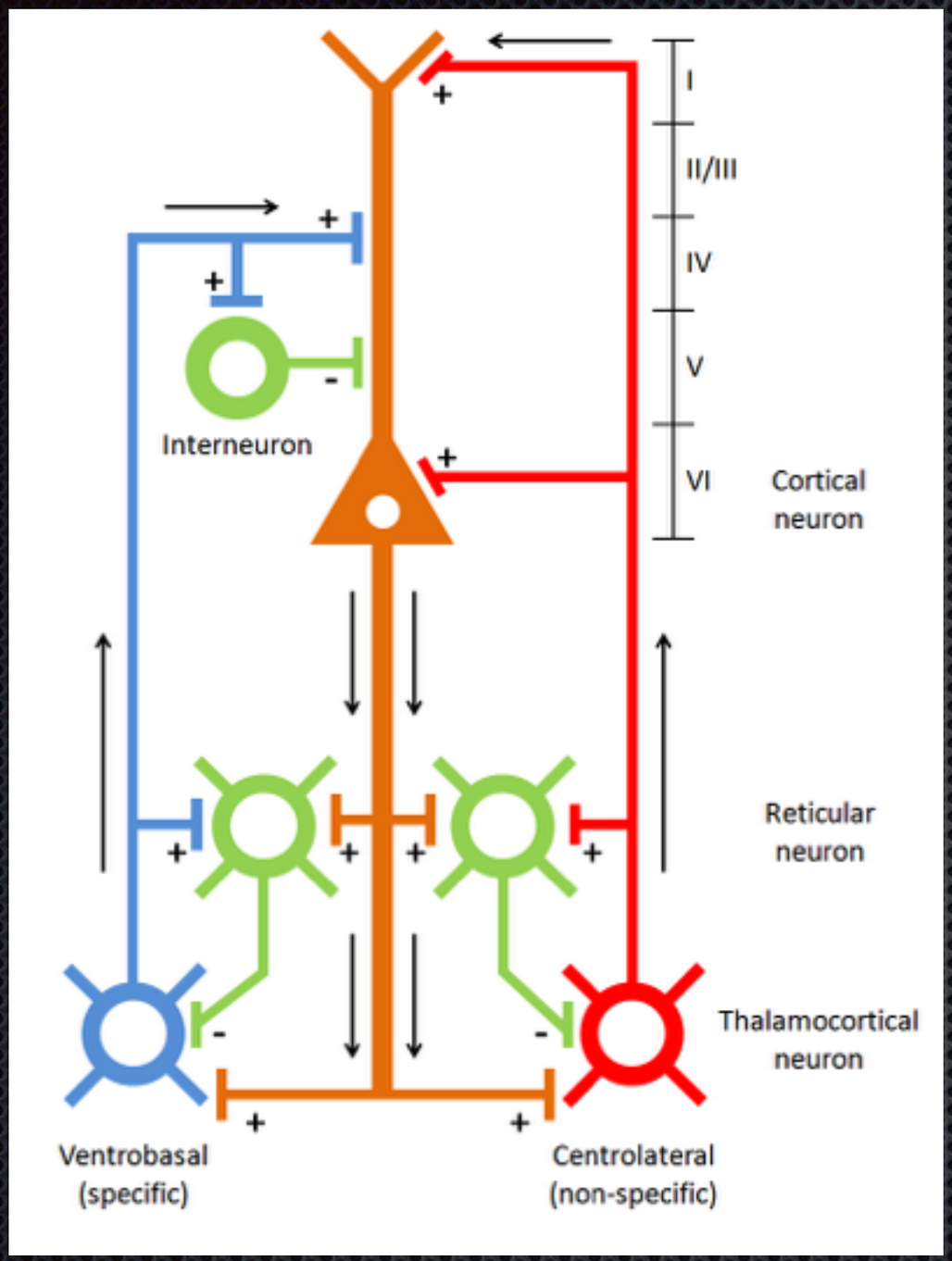

Granchamps & Delorme (2011), Frontiers
animal/non-animal categorization




Palva (2011)

# EEG: Alpha (8-12 Hz)




* thalamo-cortical relay neurons contribute to oscillations in alpha range

* circuit of excitatory and inhibitory neurons (GABAergic neurons of reticular nucleus and TC relay neurons)

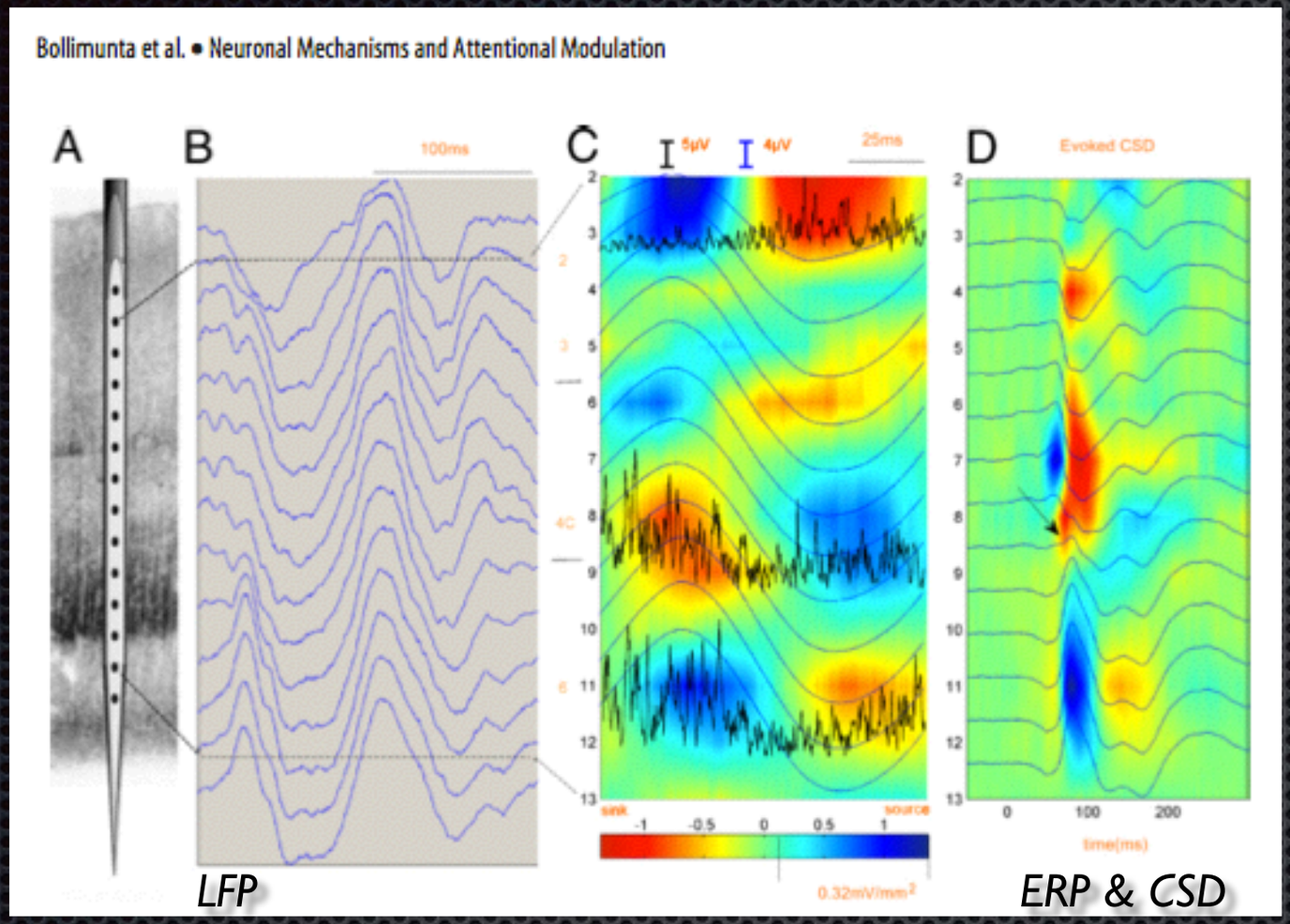
* frequency depends on degree of hyperpolarization at inhibitory synapses, which varies with which ionic currents are open (10Hz vs 3Hz)

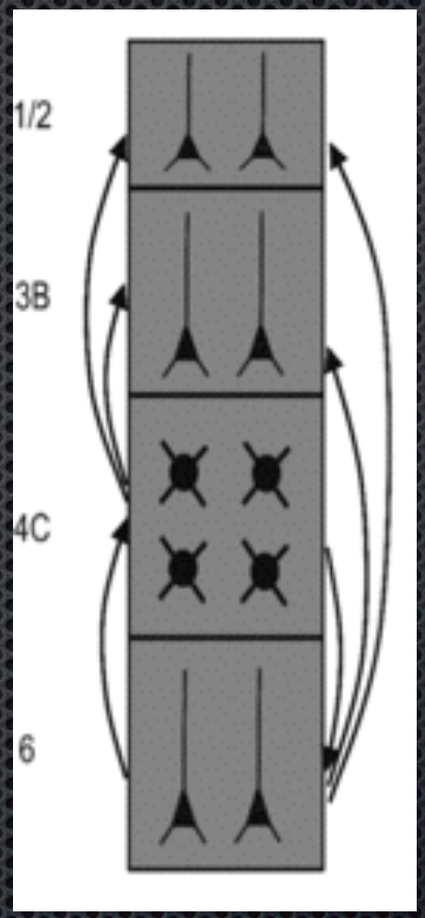
*Llinas, 1984*

*Lopes da Silva 1974*

# EEG: Alpha (8-12 Hz)

*Bollimunta et al., 2011, J Neuro*



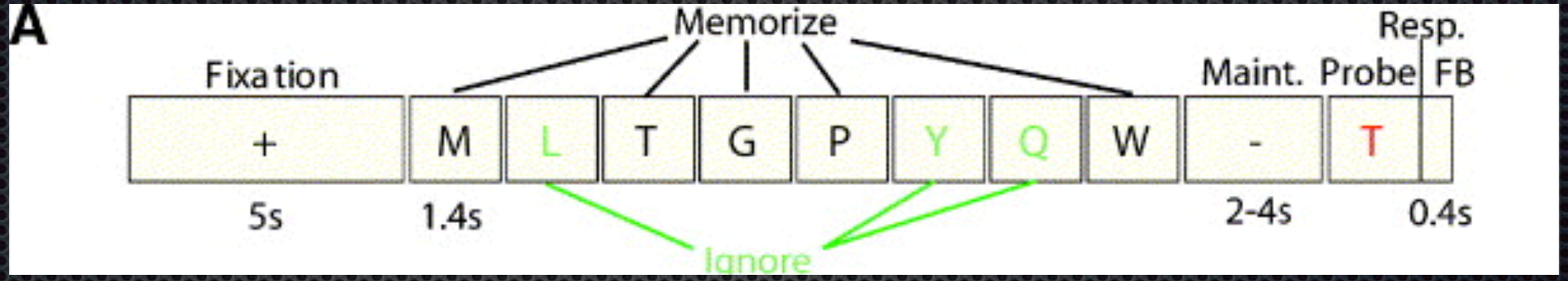

6 => LGN => 4c => 6

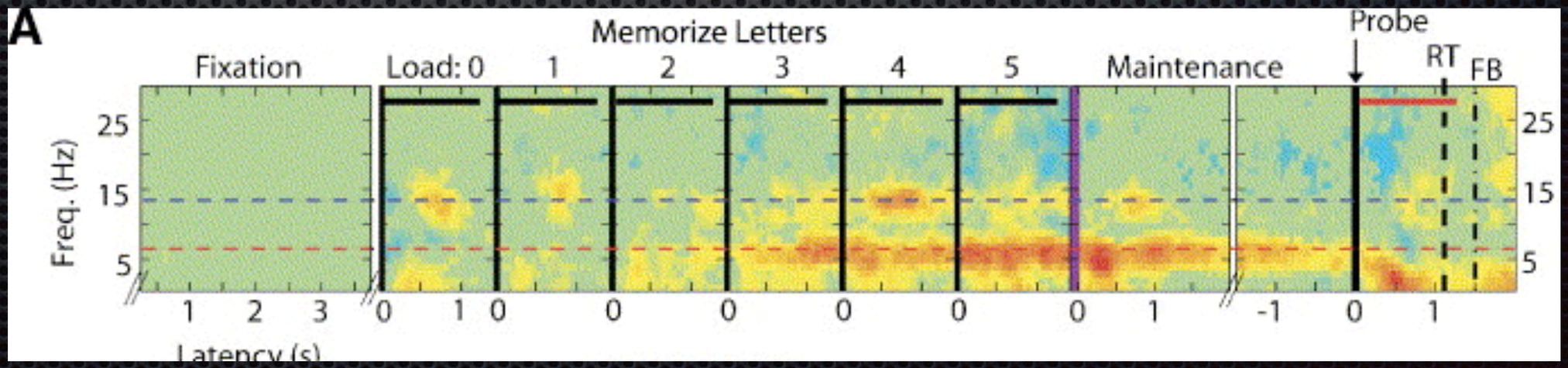
Granger Causality analysis to model alpha generation across layers
- layer 4 generators to superficial layers with additional drivers of alpha in deep layers 5/6
- suggest thalami-cortical signal contributes to generation of alpha in visual cortex
- found also that attention can suppress alpha rhythms in cortex (modulator inputs)

# EEG: Theta (4-7 Hz)

Onton, Delorme, Makeig (2005), NeuroImage

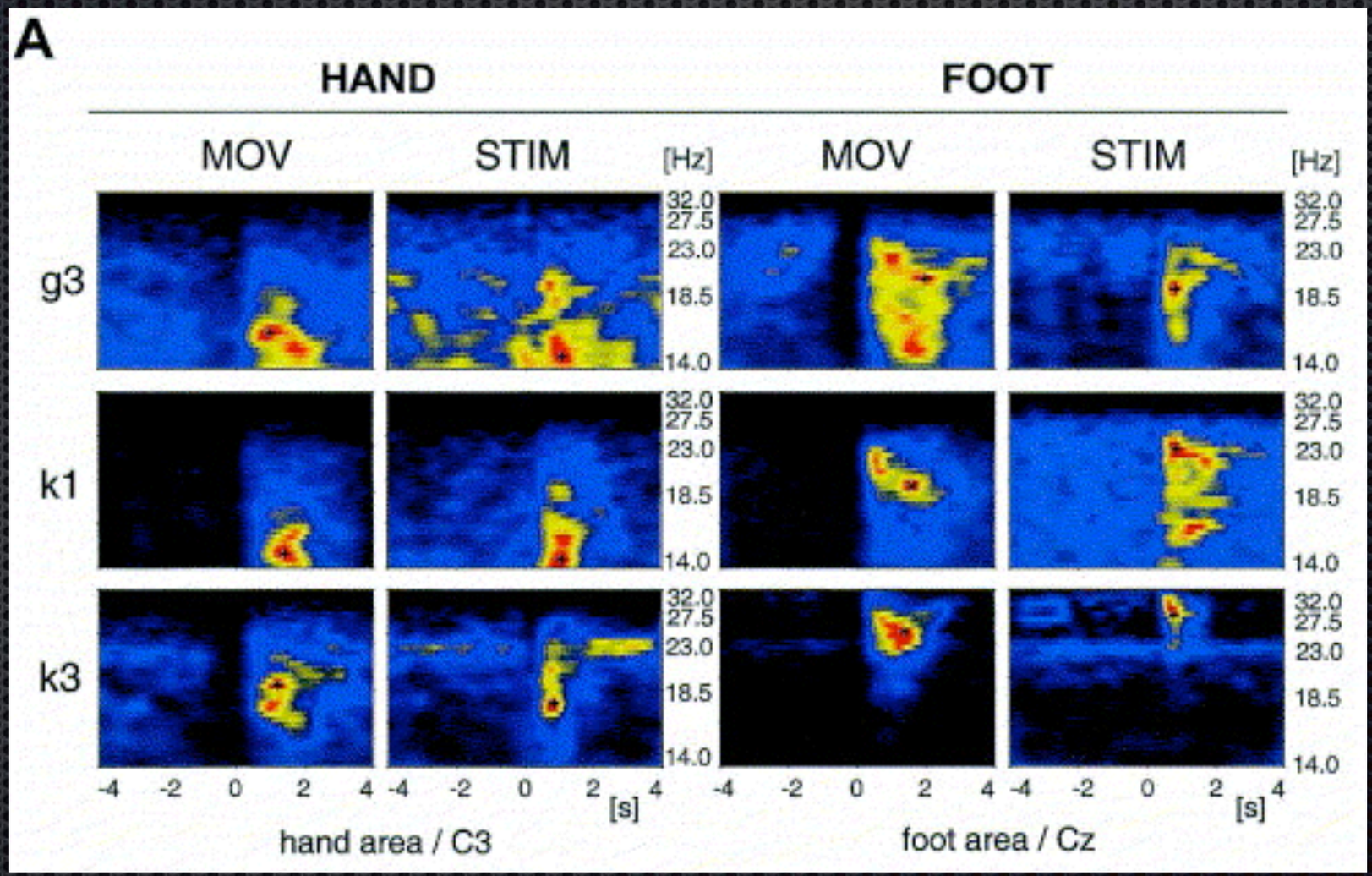
- observed locked to stimulus and during maintenance (increases with load), typically localized to medial frontal sources, observed over frontal electrodes
- associated with memory formation
- long history of study in entorhinal cortex



# EEG: Beta (13-30 Hz)

- has not been as commonly studied in event-related studies as alpha/theta
- qEEG decreases during movement (with post movement rebound), increases during "active states", observed across scalp




Neuper et al., (2001)
*Clinical Neurophys, 112 (2084-2097)*

# Cross-Frequency Interactions

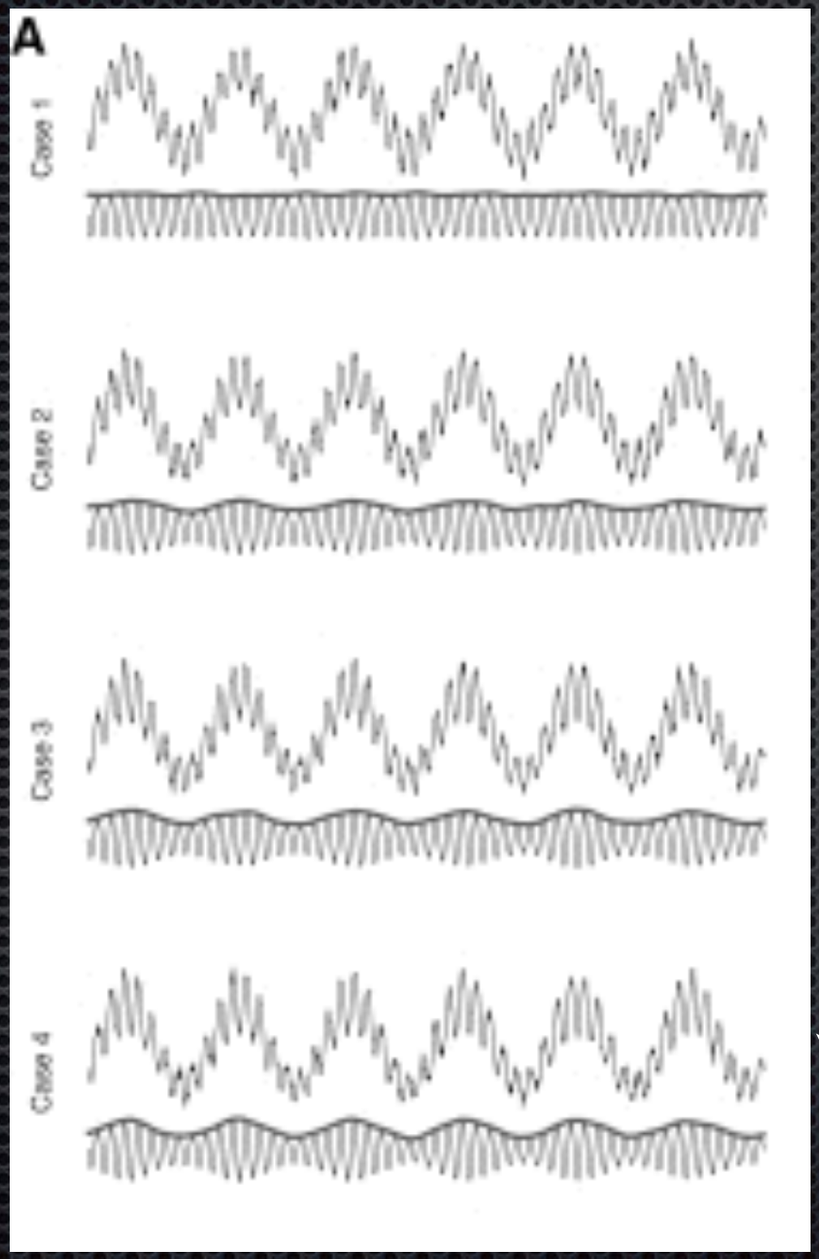
* like gamma, lower frequencies associated with "stability" of a neural representation; perhaps also stability of neural ensemble
* however low/high frequencies differ in critical ways:
    * higher frequencies associated with a smaller spatial extent (smaller point spread function) whereas lower frequencies associated with broader spatial extent
    * higher frequencies associated with degree of population response whereas lower frequencies associated with excitability (gain => modulatory characteristic)
    * higher frequency amplitude coupled to lower frequency phase

Slow oscillatory influences reflect modulatory influences on local processing?

...von Stein & Sarnthein (2000), Bressler (2005), Palva & Palva (2007), Doesburg (2009), Buzsaki (1998; 2010; 2012), Varela (2001), Shroeder & Lakatos (2008) etc.

# Quantifying Frequency Coupling

The phase of lower frequencies tends to modulate the amplitude of higher frequencies (cross-frequency phase-amplitude coupling).

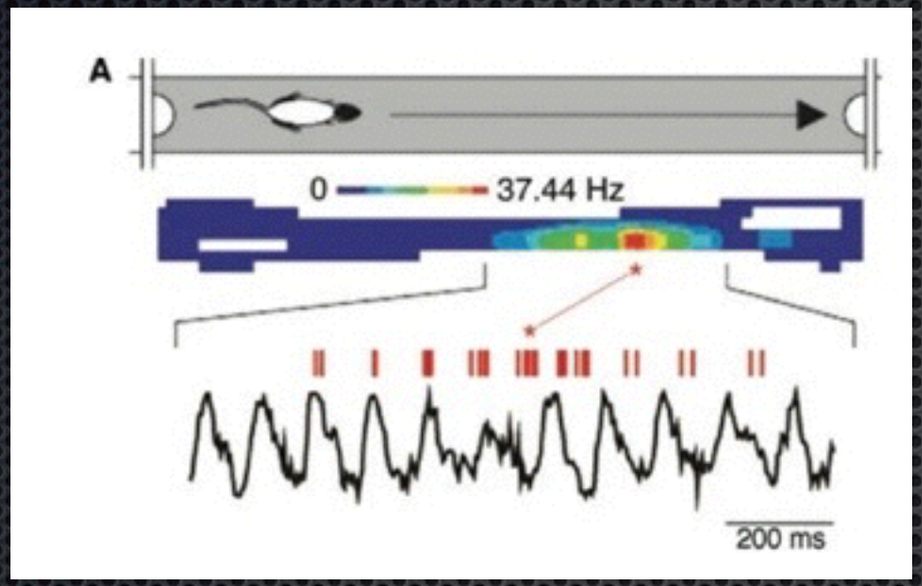



Phase-Amplitude Coupling

# Coupling for Memory Encoding

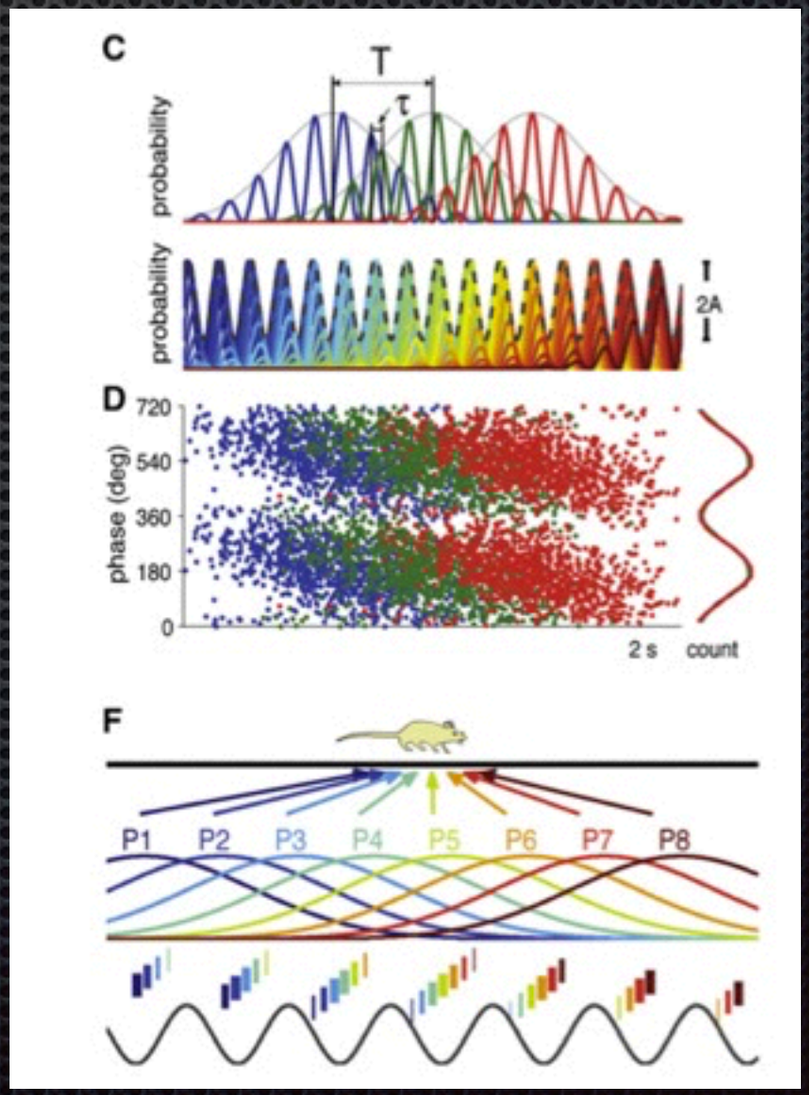
learning & consolidation (memory, sleep)
e.g., hippocampus pulse trains delivered at trough of theta
population response; trains produce LTP (vs LTD)

2004 Buzsaki




*the type of response (fast/slow, size of place field) varies across Hippocampus*

*"neural syntax"*

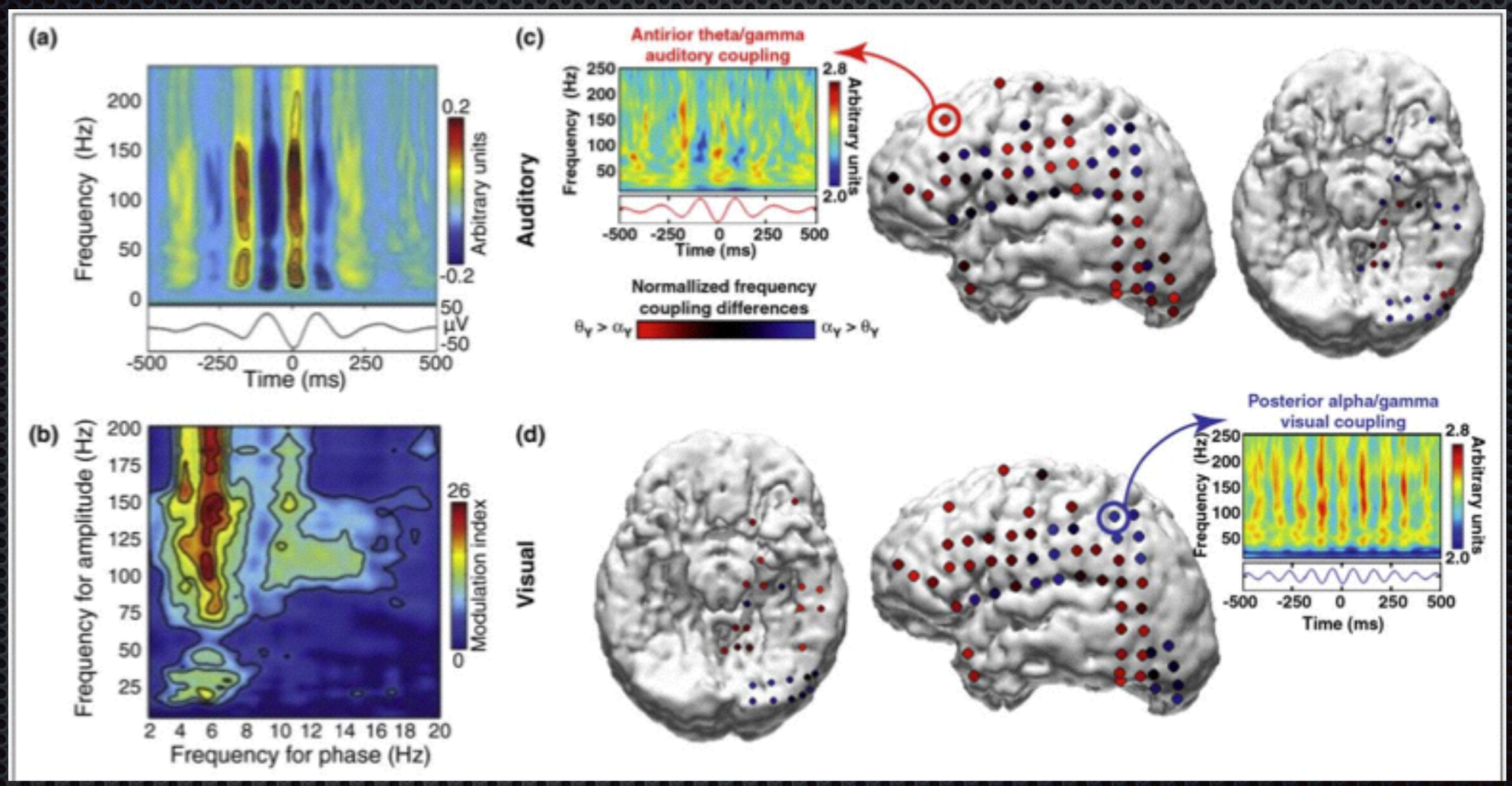



Buzsaki 2010 *Neuron 68, 382-385*

# Theta/Alpha Modulation in Neocortex

working memory

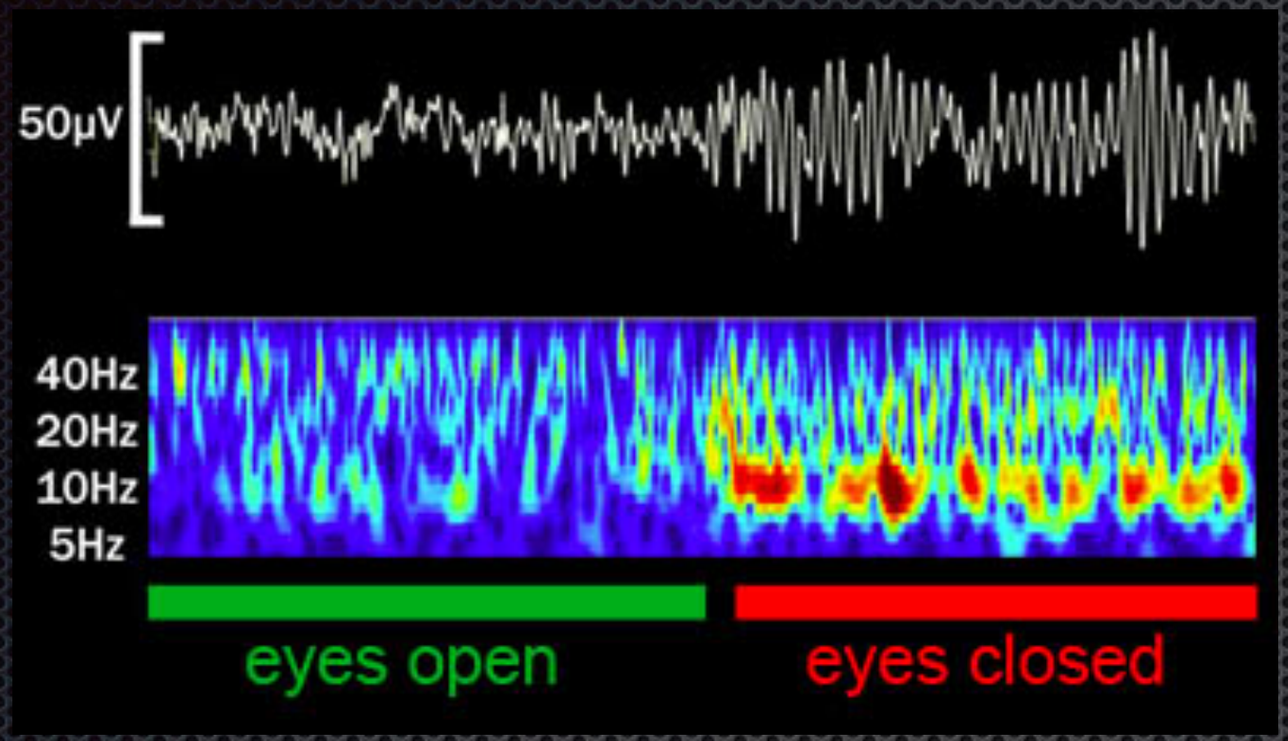
e.g., auditory task anterior theta/gamma coupling, visual task posterior alpha/gamma coupling

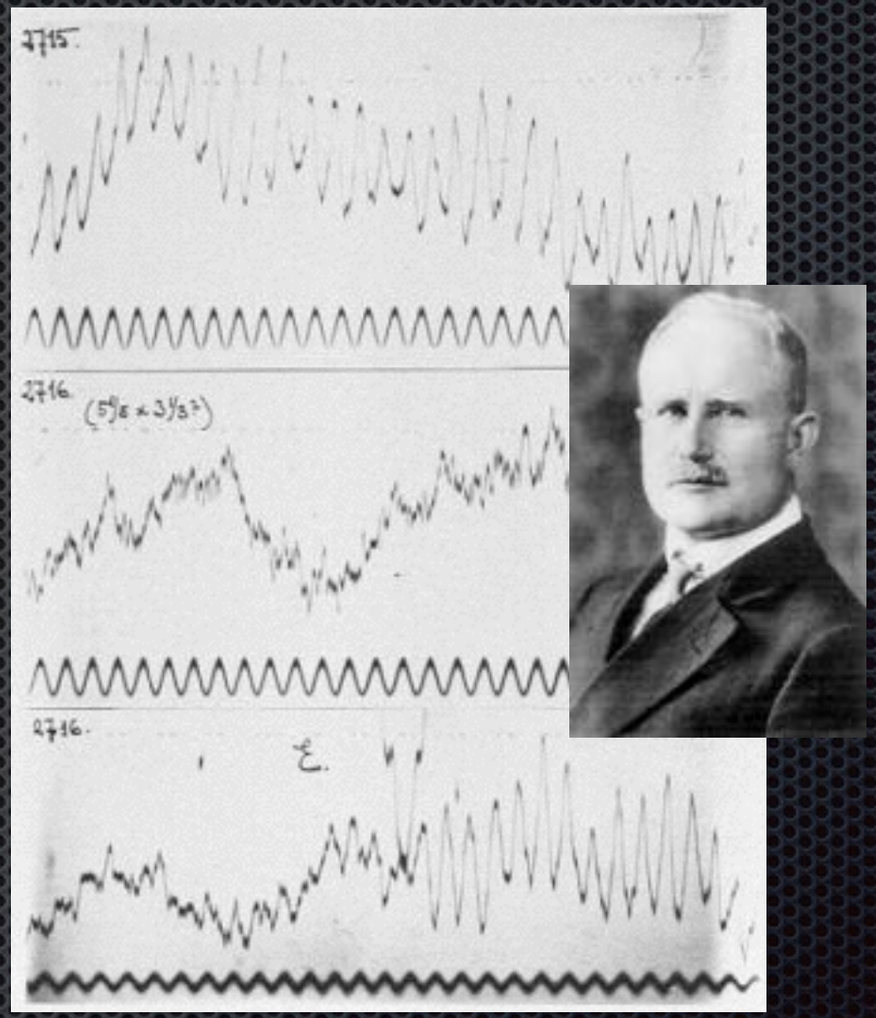



Canolty & Knight (2010) TiCS

# Oscillations in EEG Signals

*Berger 1924*




*A different approach to "**connectivity/dynamics**"*

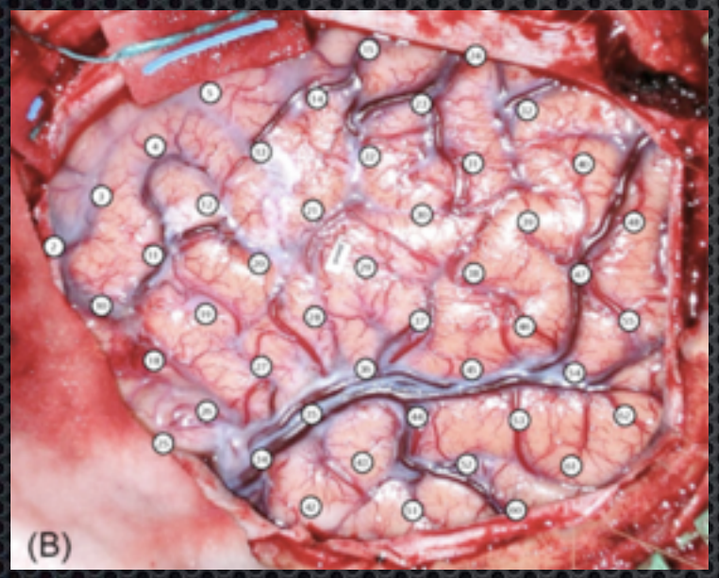
*A different approach to finding "**sources**"*

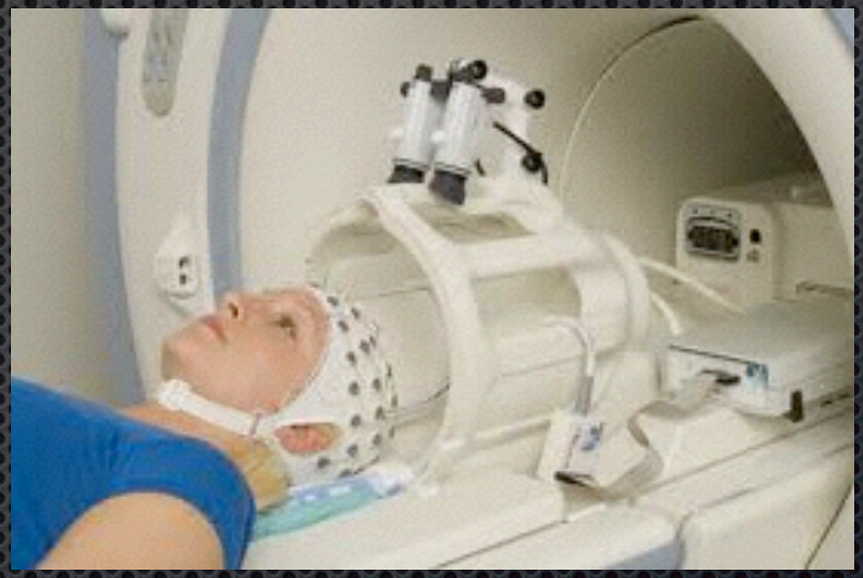
*A different approach to "**temporal profiling**" events/states*

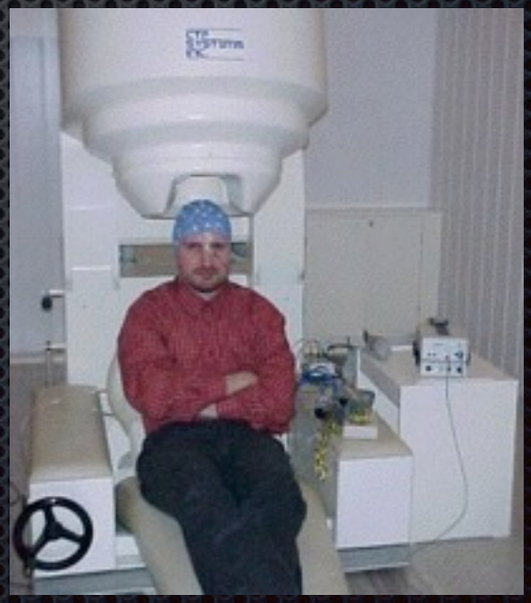
# EEG Future?

- Need stronger tools for source analysis
- Continued integration with other modalities
- Portable adaptations

- Combines well with other methods
  - EEG & ECoG, EEG & fMRI, EEG & MEG
  - but need continued analytics development



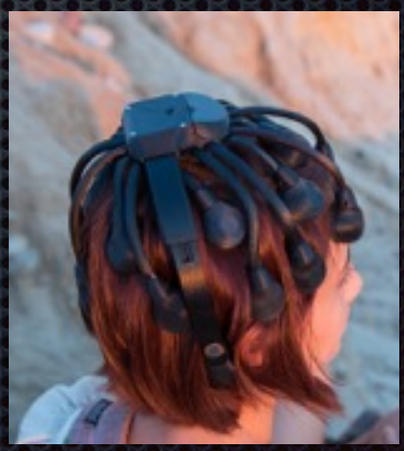


- Adaptable & Practical
  - Dry electrodes, portable devices, motion

Neurofocus
Berkeley/Knight

UCSD Tzyy-Ping
Jung

Mobile Brain/Body
Imaging @ UCSD



Cognionics

# Happy EEG-ing.