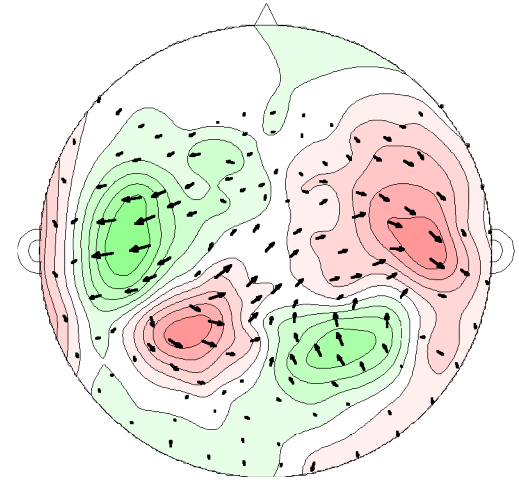
Neural Computation at the Femtotesla Scale: Visualizing Computations Inside the Human Brain



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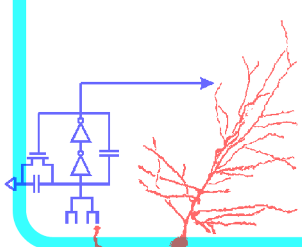
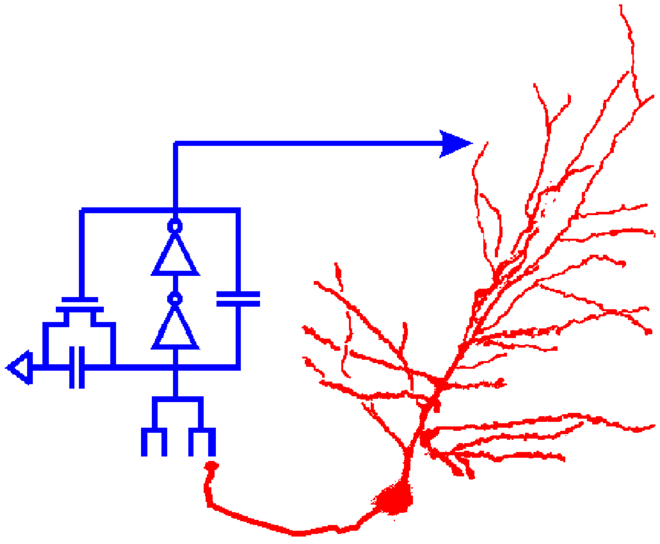


I.U. Physics Colloquium March 19, 2008

Computational Sensorimotor Systems Laboratory

Computational Sensorimotor Systems Laboratory



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NIH: NIDCD, NIBIB, NIA

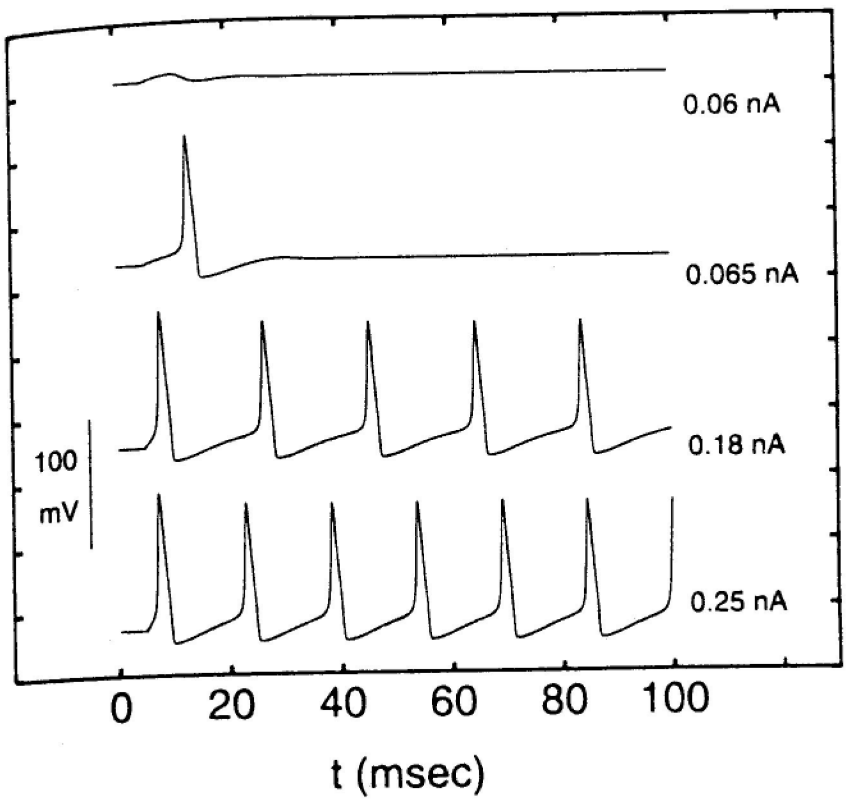
Luo, H., Y. Wang, D. Poeppel & J. Z. Simon (2006; 2007), J. Neurophysiology

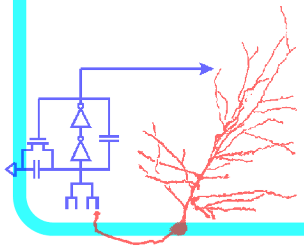
Outline

- The Brain and How It Works
- The Auditory System
- Magnetoencephalography (MEG)
- MEG in the Frequency Domain
- Using MEG to investigate Neural Coding

Universal Neural Code

- Neural signals = spikes in voltage
- Spikes are "all-or-none"
  - Digital in amplitude
  - Asynchronous in time
- Neural Input ≈ current





Primary Neural Current

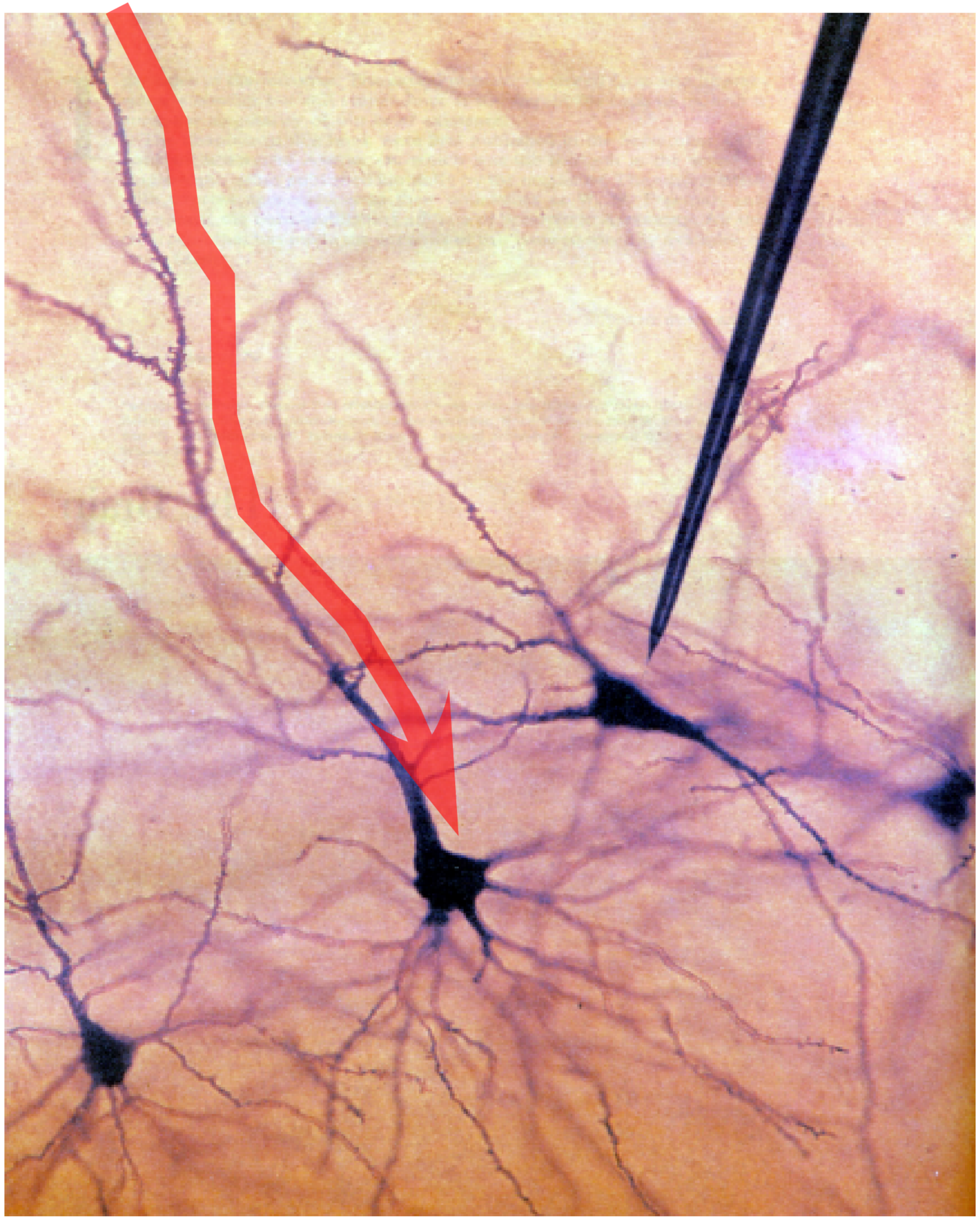


Photo by Fritz Goro

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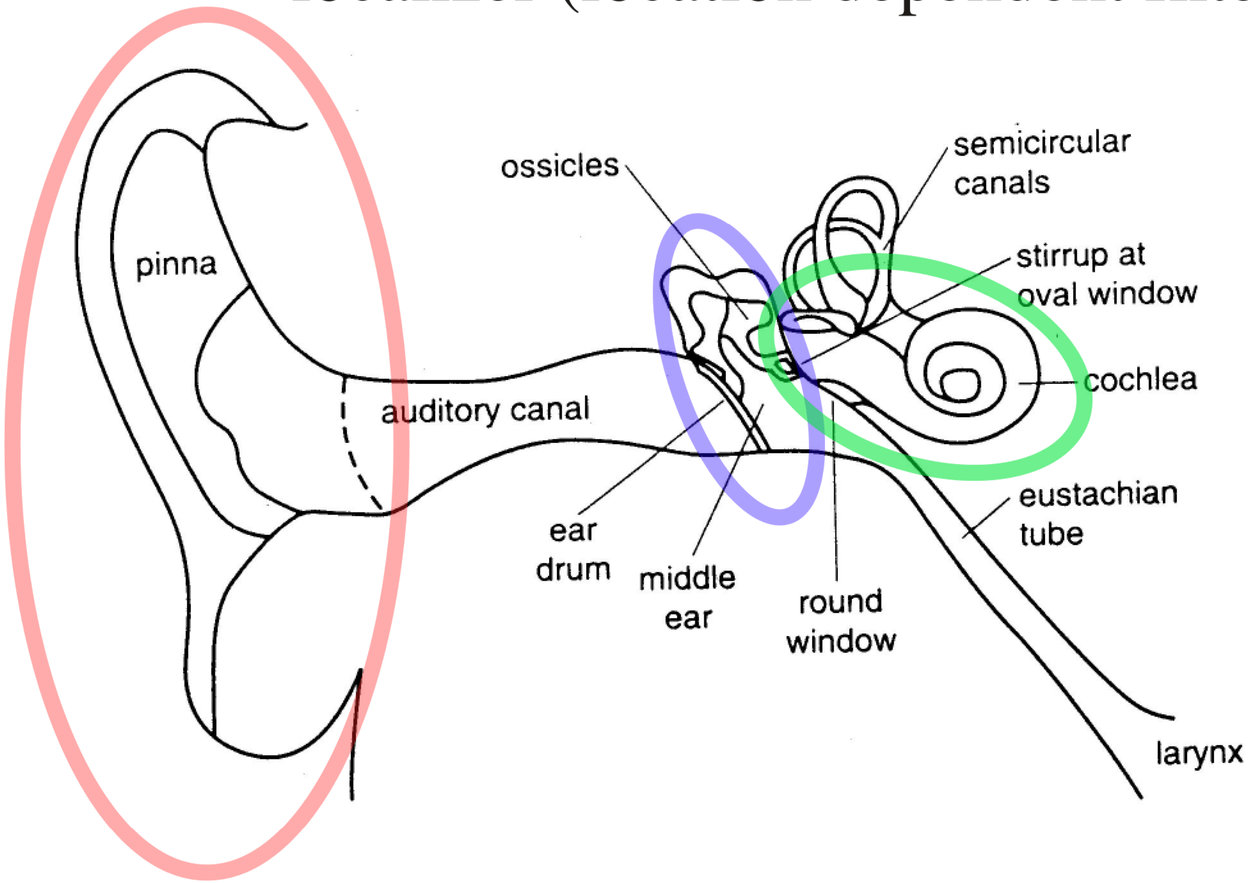
What Is Hearing?

Outer Ear (pinna) useful but not essential
- collector
- localizer (location dependent filtering)



Inner ear (cochlea)
- essential
  - neural "transducer"
  - turns *acoustic* signals into spikes
    = *auditory* signals

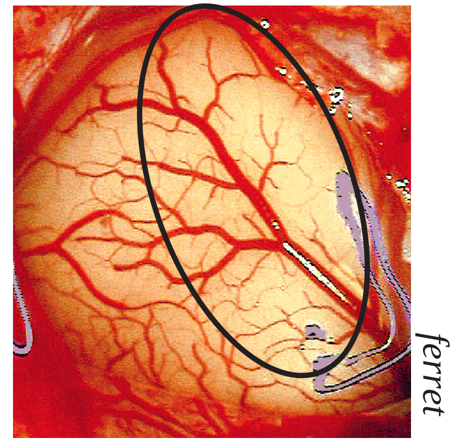
Only features conveyed as neural signals perceived
- e.g. masked sounds not conveyed neurally

Middle Ear useful but not essential
- impedance matching = minimized reflection

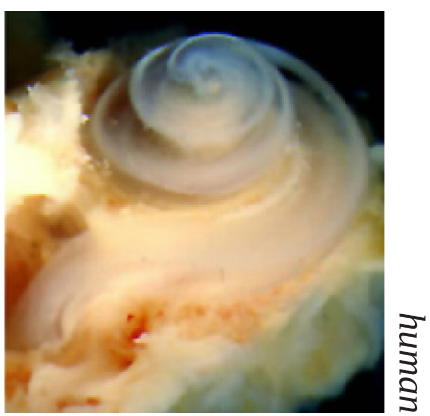
The Auditory Pathway (oversimplified)

Parallel and serial neural processing in multiple stages

Auditory Cortex



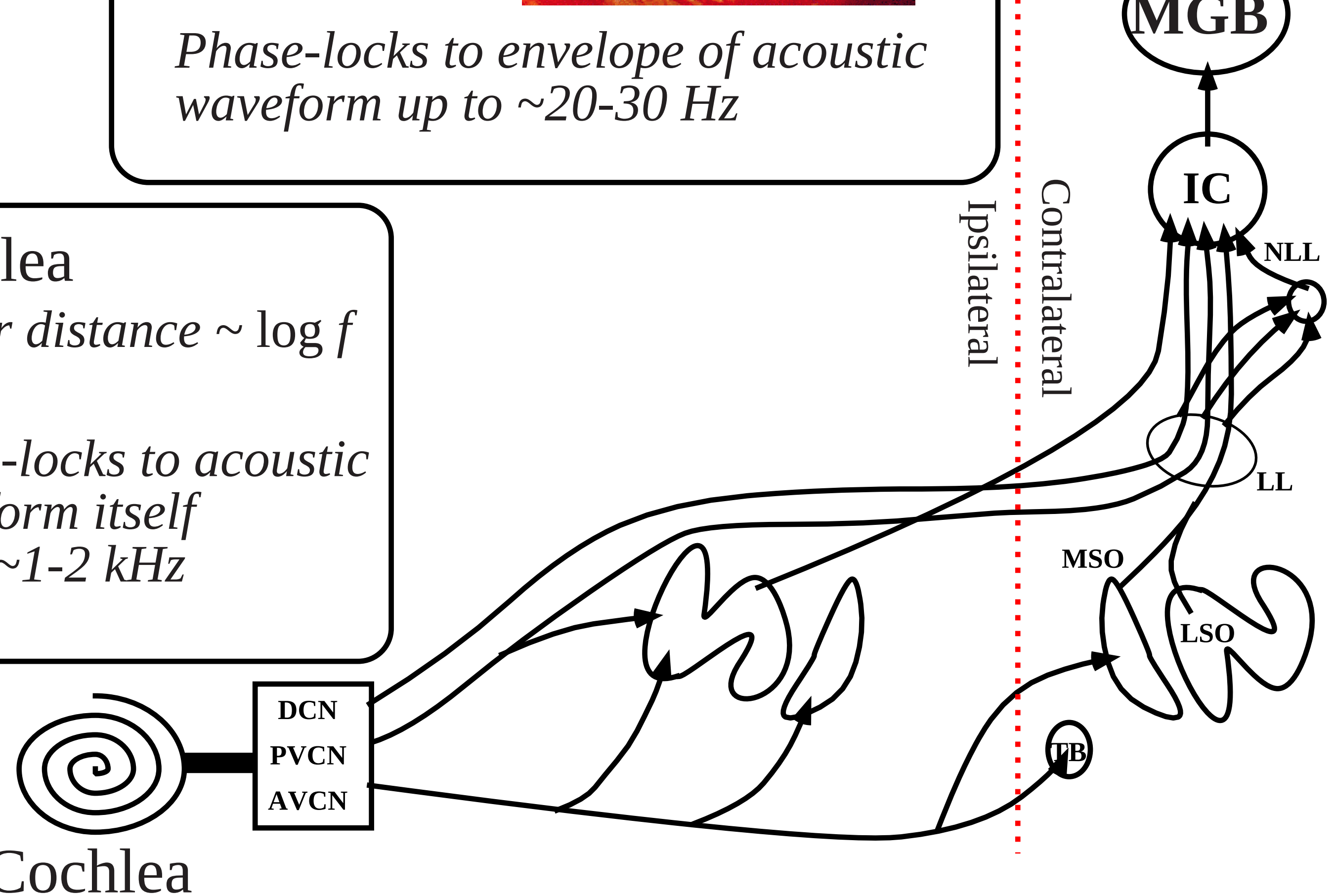
Phase-locks to envelope of acoustic waveform up to ~20-30 Hz



Cochlea

Linear distance ~ log *f*

Phase-locks to acoustic waveform itself up to ~1-2 kHz



What Is the Auditory Neural Code?

- **Neural code is essentially unknown** for almost all auditory features
  - Especially in auditory cortex
  - Much progress in coding near periphery, especially coding of sound location

- **Most important auditory features are acoustically non-trivial**
  - e.g. speech, speaker ID, emotional content, pitch, timbre, sound location, and many, many others

What Can We Hear?

Table 1.6. Approximate ranges of hearing

Species	Low	High (kHz)
Human	20 Hz	20
Chimpanzee	100 Hz	20
Rhesus monkey	75 Hz	25
Squirrel monkey	75 Hz	25
Cat	30 Hz	50
Dog	50 Hz	46
Chinchilla	75 Hz	20
Rat	1 kHz	60
Mouse	1 kHz	100
Guinea pig	150 Hz	50
Rabbit	300 Hz	45
Bats	3 kHz	120
Dolphin (*Tursiops*)	1 kHz	130
Galago	250 Hz	45
Tupaia	250 Hz	45
Sparrow	250 Hz	12
Pigeon	200 Hz	10
Turtle	20 Hz	1
Frog	100 Hz	3
Goldfish	100 Hz	2
Ostariophysi	50 Hz	7
Other teleosts	50 Hz	1

Data taken from Fay 1988

Human: 20 Hz to 20 kHz

Cat: 30 Hz to 50 kHz

Mouse: 1 kHz to 100 kHz

Bat: 3 kHz to 120 kHz

What Can We Hear?

- **Spectro-Temporal Features of Any Sound**

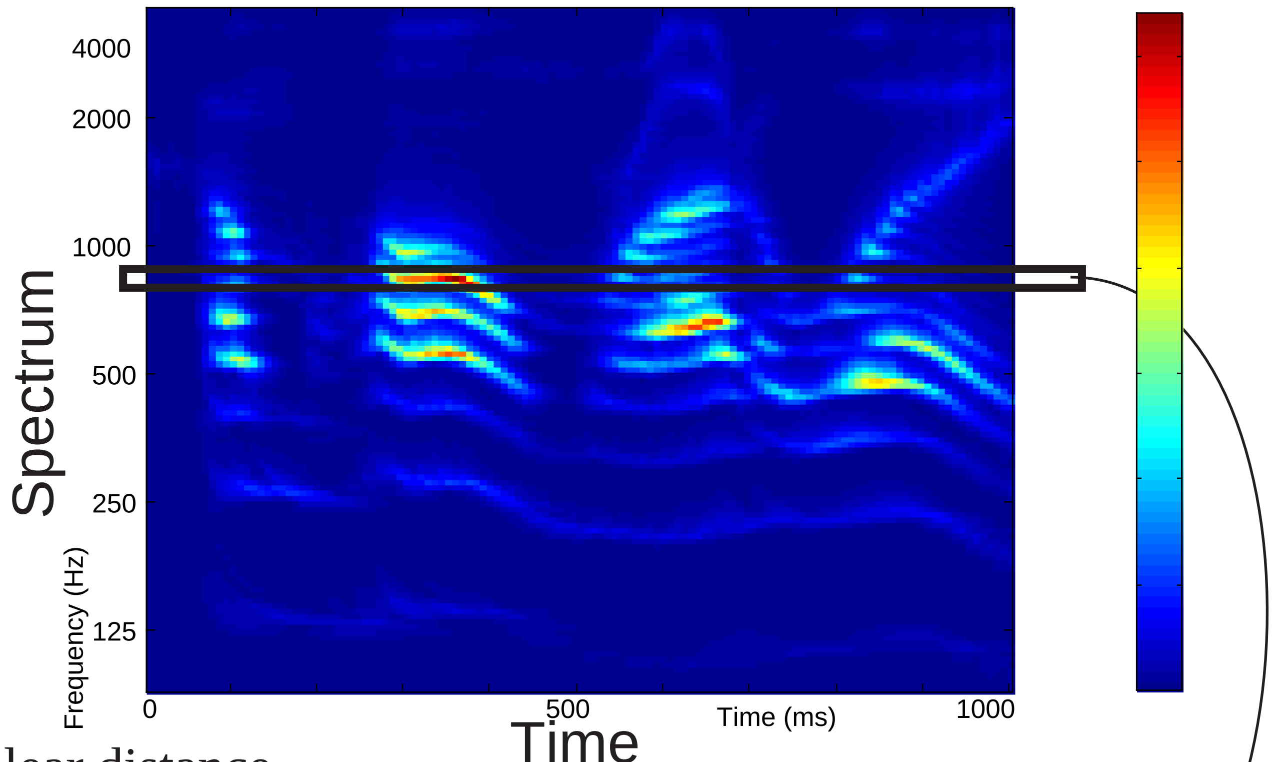
  Spectral content of sound as a function of time.

  Which spectral frequency bands have enhanced power?

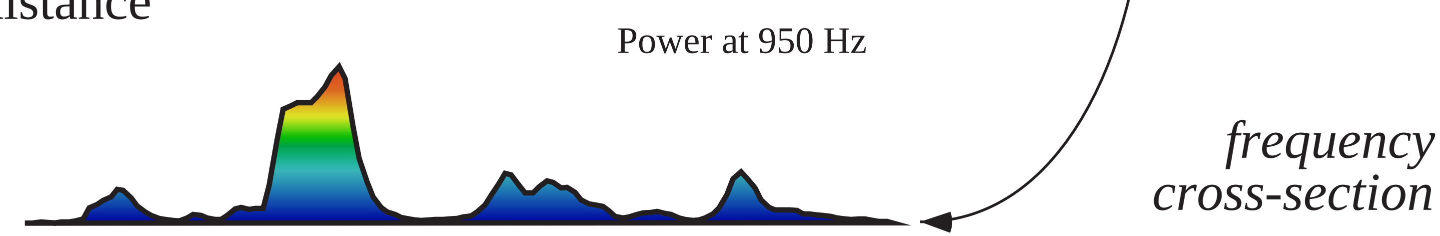
  Which spectral frequency bands have diminished power?

  How do these change as a function of time?

"Come home right away."



log *f* ~ linear cochlear distance



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Magnetoencephalography (MEG)

- Non-invasive, Passive, Silent Neural Recordings
- Simultaneous Whole-Head Recording (~200 sensors)
- Sensitivity

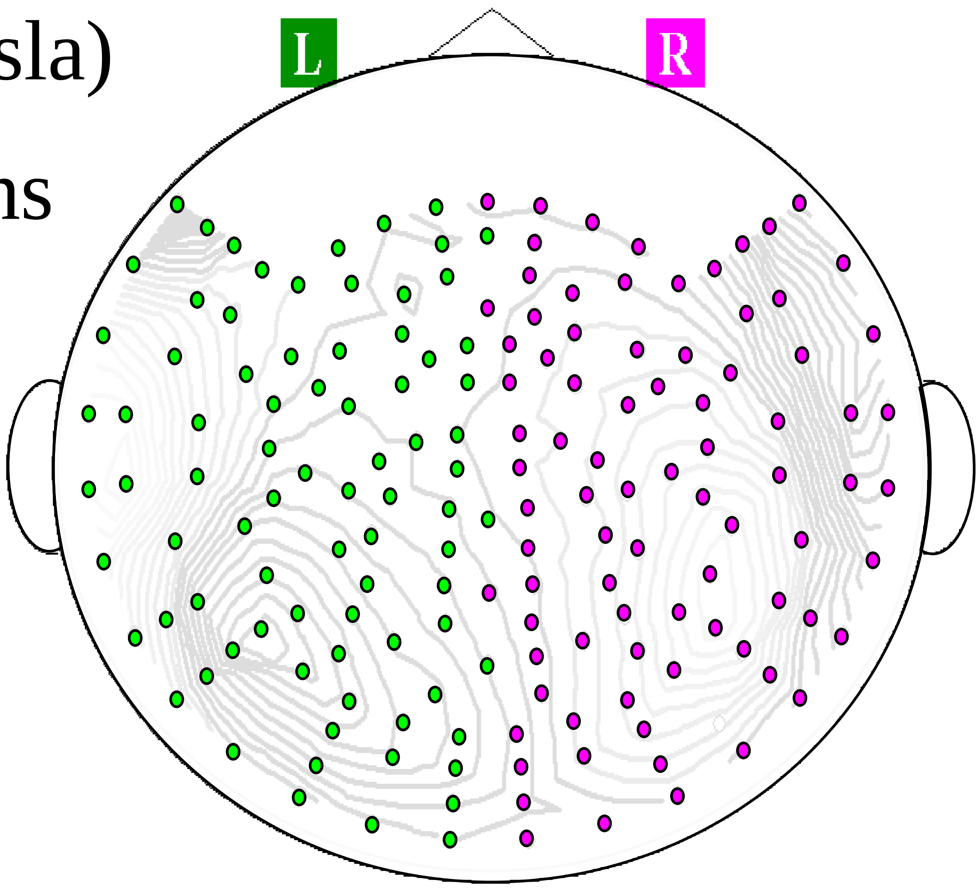
  high: ~100 fT (10^{-13} Tesla)

  low: ~10^4 – ~10^6 neurons

- Temporal Resolution: ~1 ms
- Spatial Resolution

  coarse: ~1 cm

  ambiguous

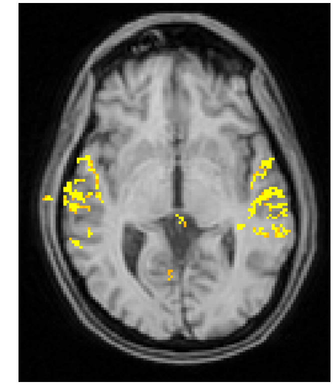


Functional Imaging

Non-invasive recording from human brain (Functional brain imaging)

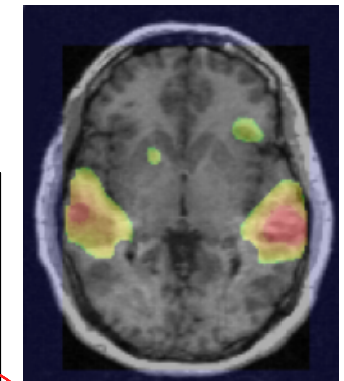
Hemodynamic techniques

Functional magnetic resonance imaging
fMRI



Excellent *spatial resolution*
(~ 1-2 mm)
Poor temporal resolution
(~ 1 s)

Positron emission tomography
PET

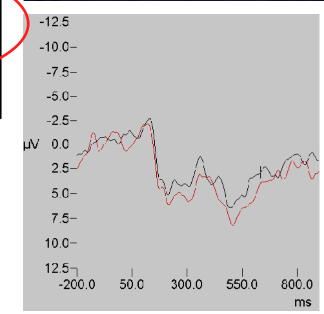


PET, EEG require across-subject averaging

fMRI and MEG can capture effects in single subjects

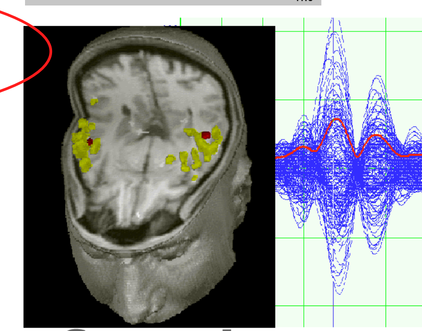
Electromagnetic techniques

Electroencephalography
EEG

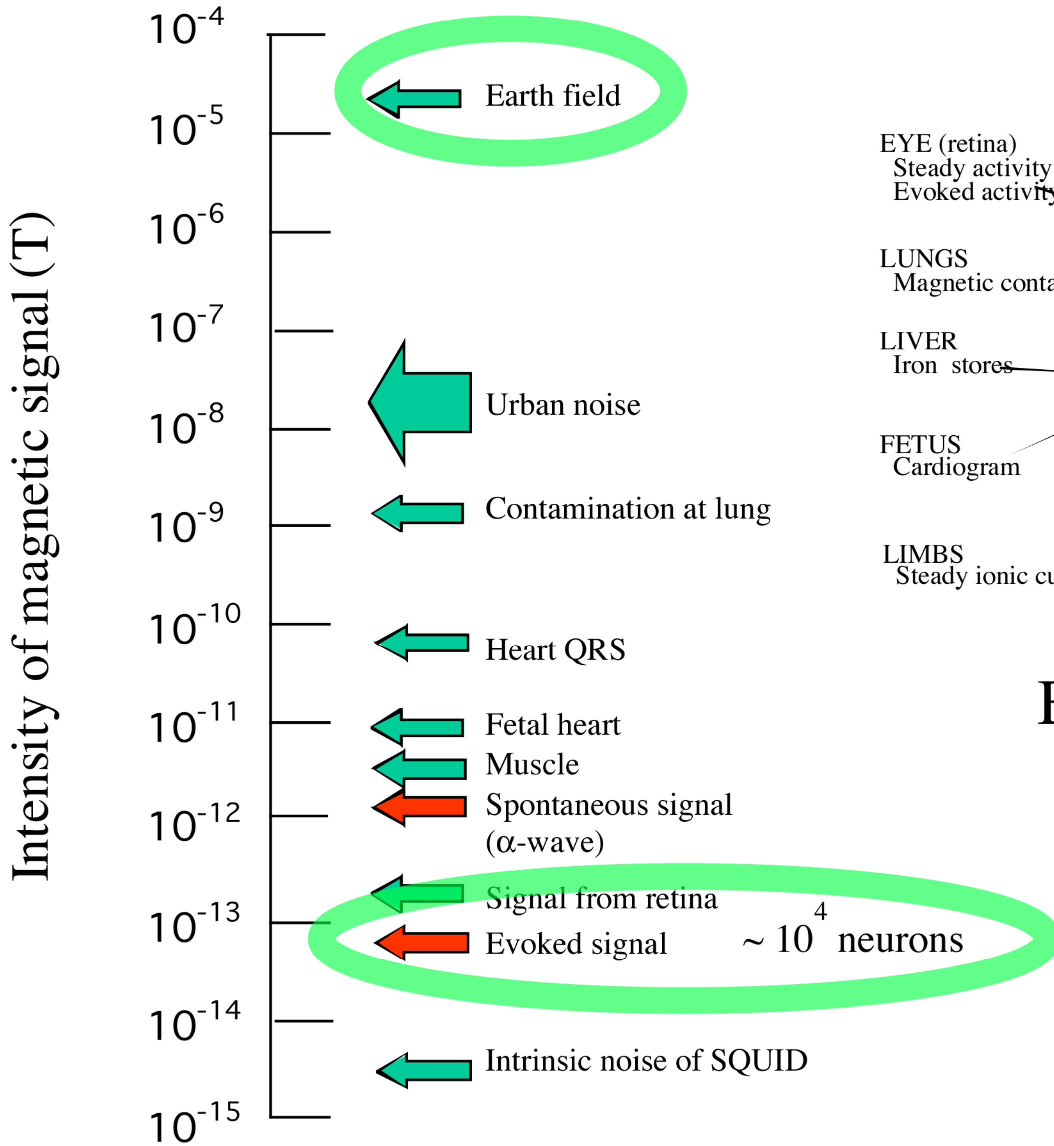


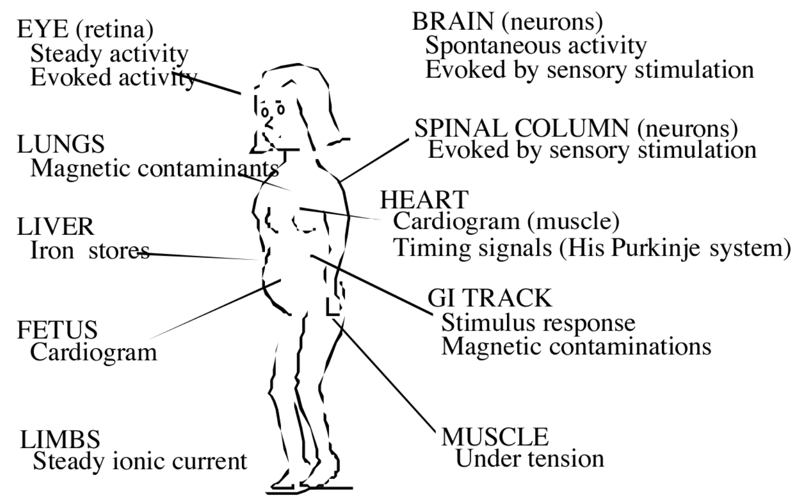
Poor spatial resolution
(~ 1 cm)
Excellent *temporal resolution*
(~ 1 ms)

Magnetoencephalography
MEG



Magnetic Field Strengths





Biomagnetism

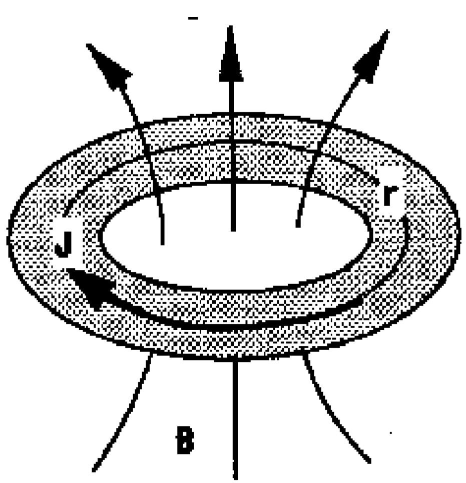
Magnetic Flux Detectors

Superconductivity →

Magnetic flux quantization →

Josephson Effect →

SQUID = Superconducting Quantum Interference Device

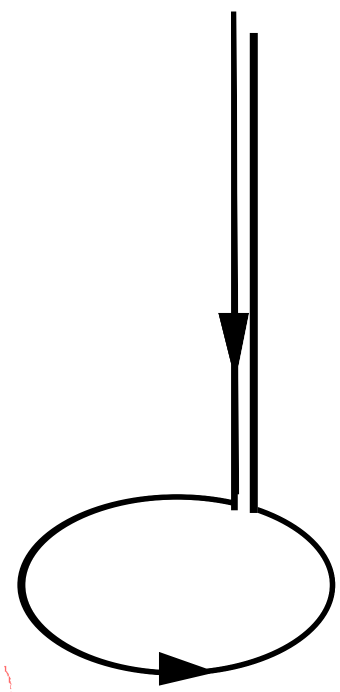


$$\Phi = n \frac{h}{2e} = n\,\Phi_0$$

$$\Phi_0 = \frac{h}{2e} = 2.07 \times 10^{-15}\ \mathrm{Wb}$$

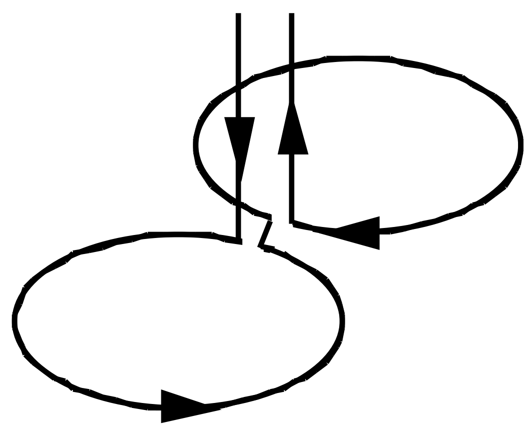
MEG SQUIDs

SQUID Magnetometer

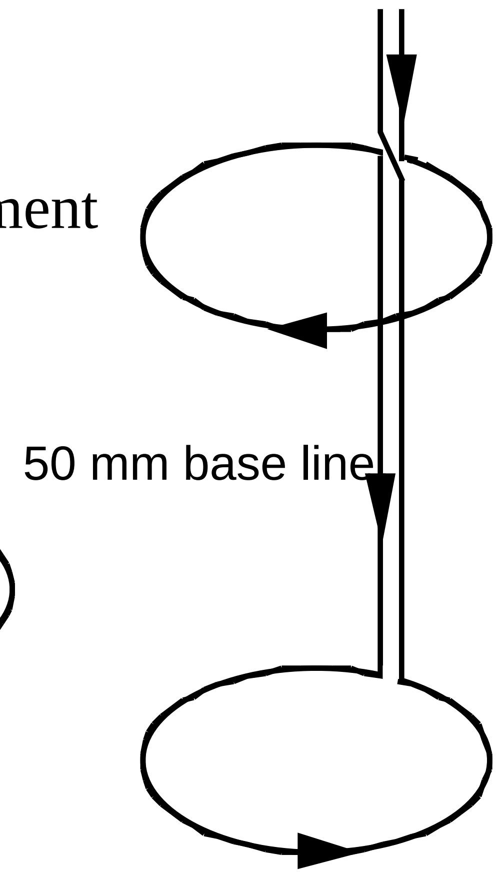


SQUID Gradiometer

Noise reduction from
Differential measurement



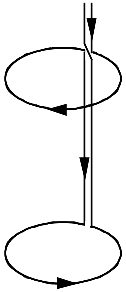
Planar type

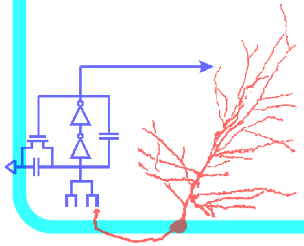


Axial type

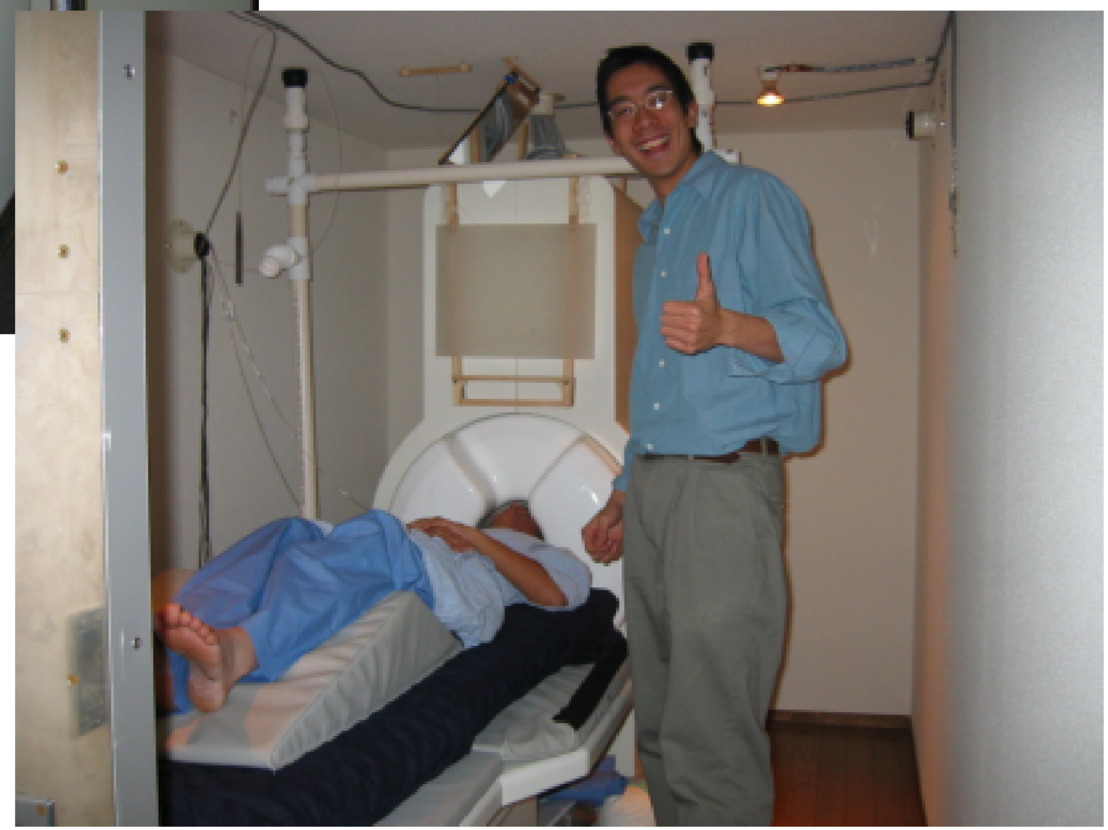
Shielding

+

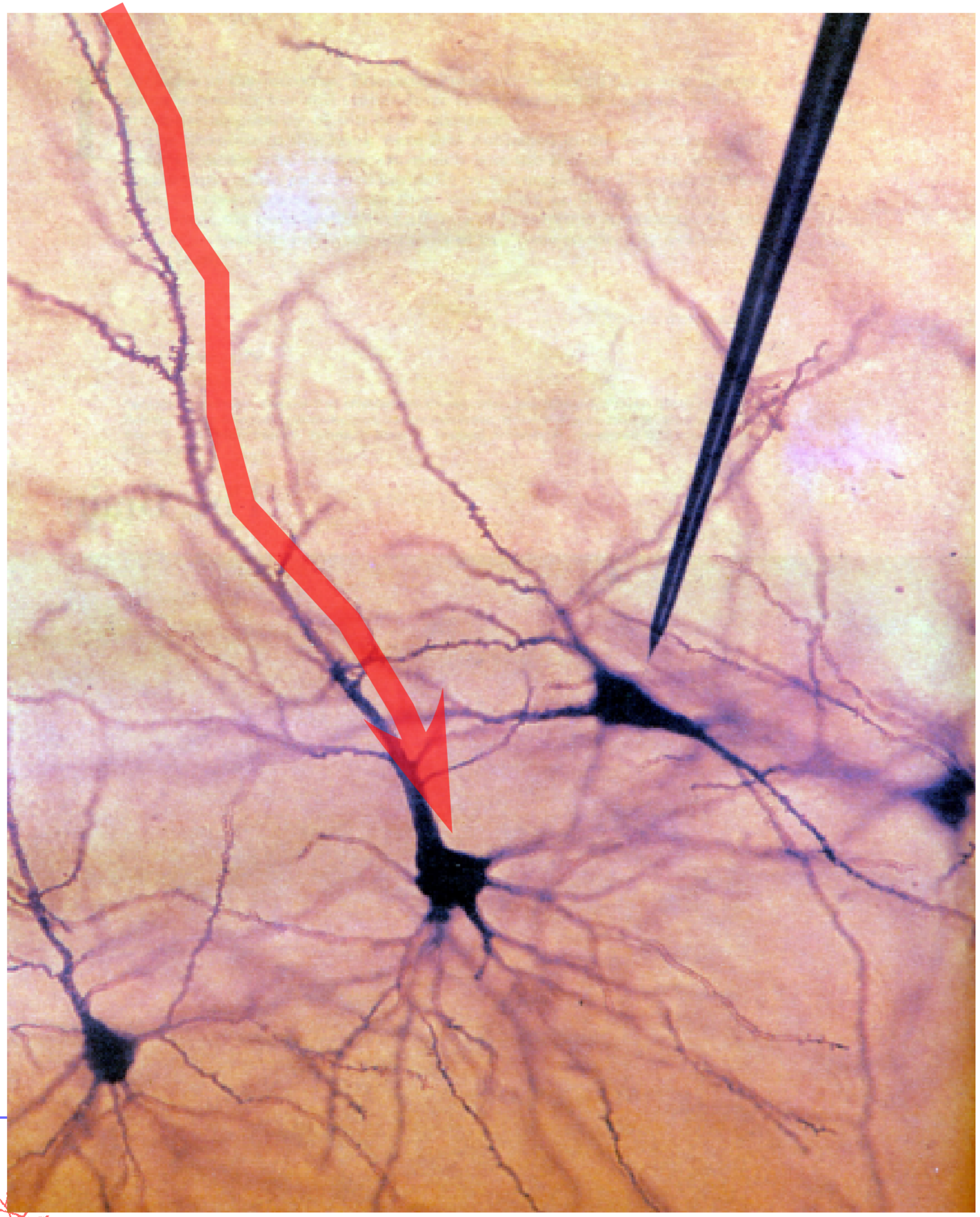


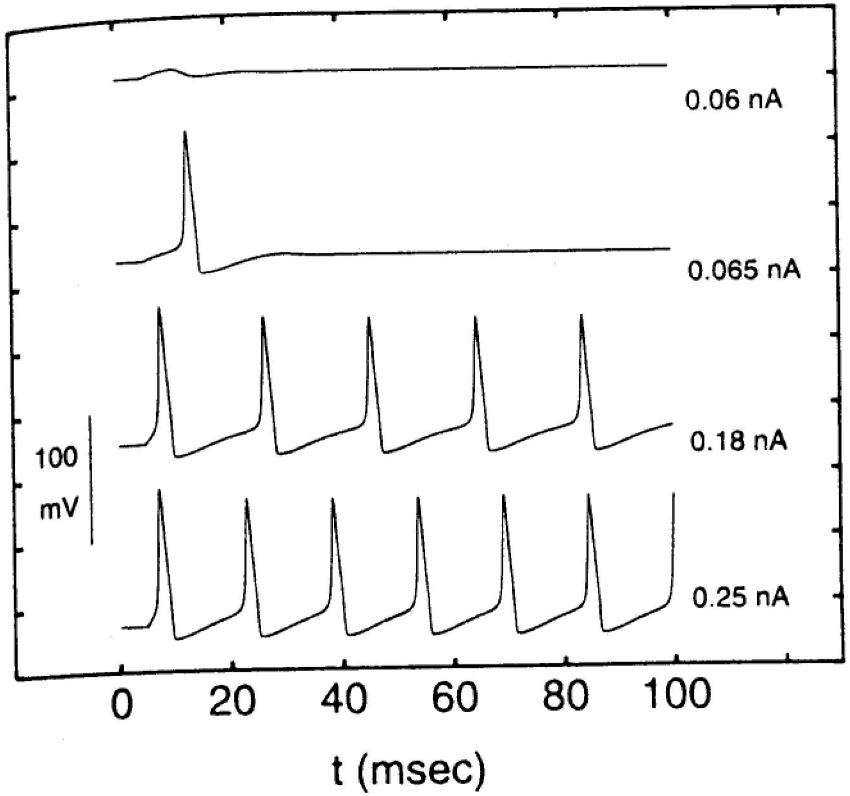


MEG Snapshots

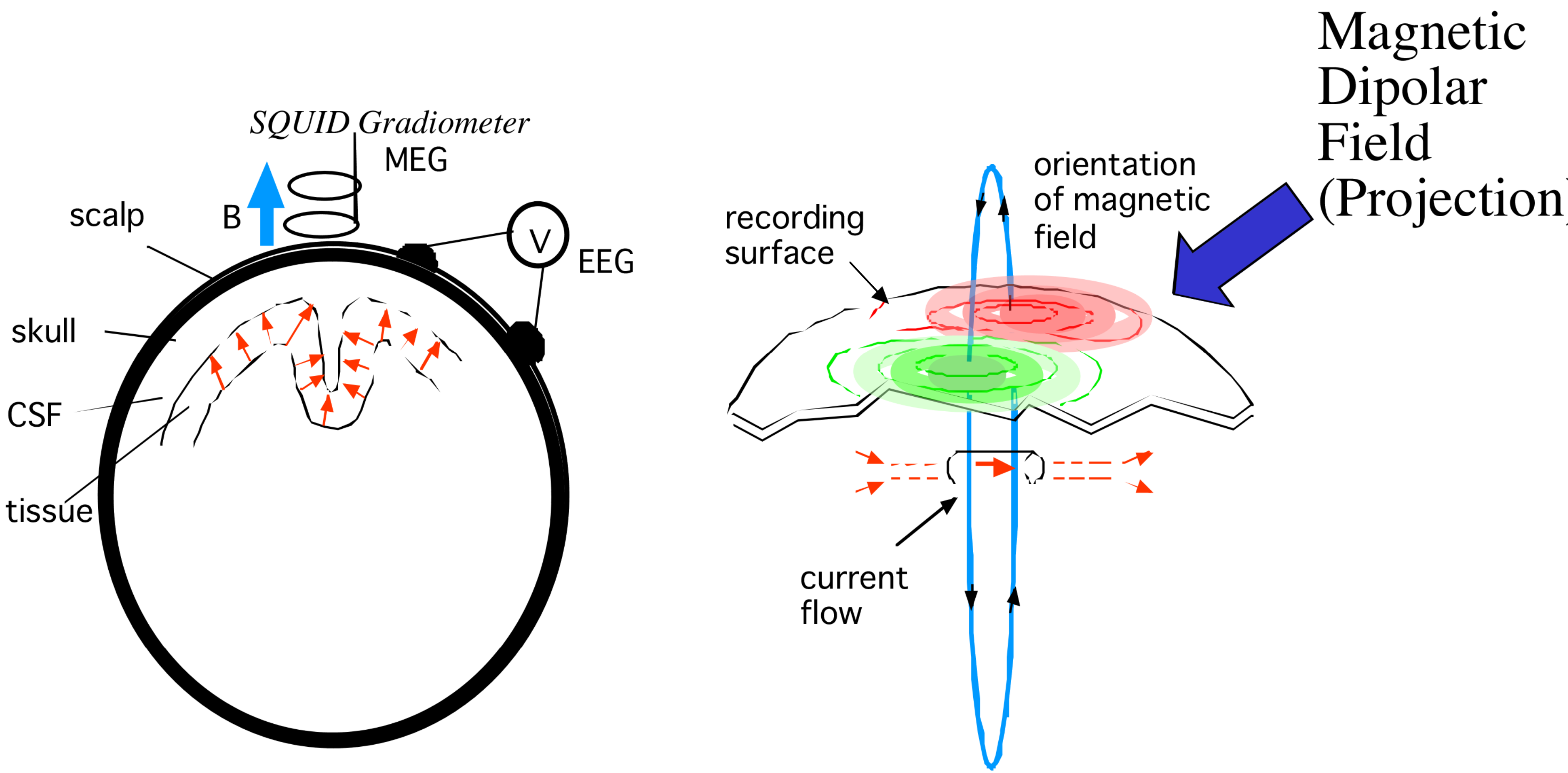


Neural Activity = Neural Current





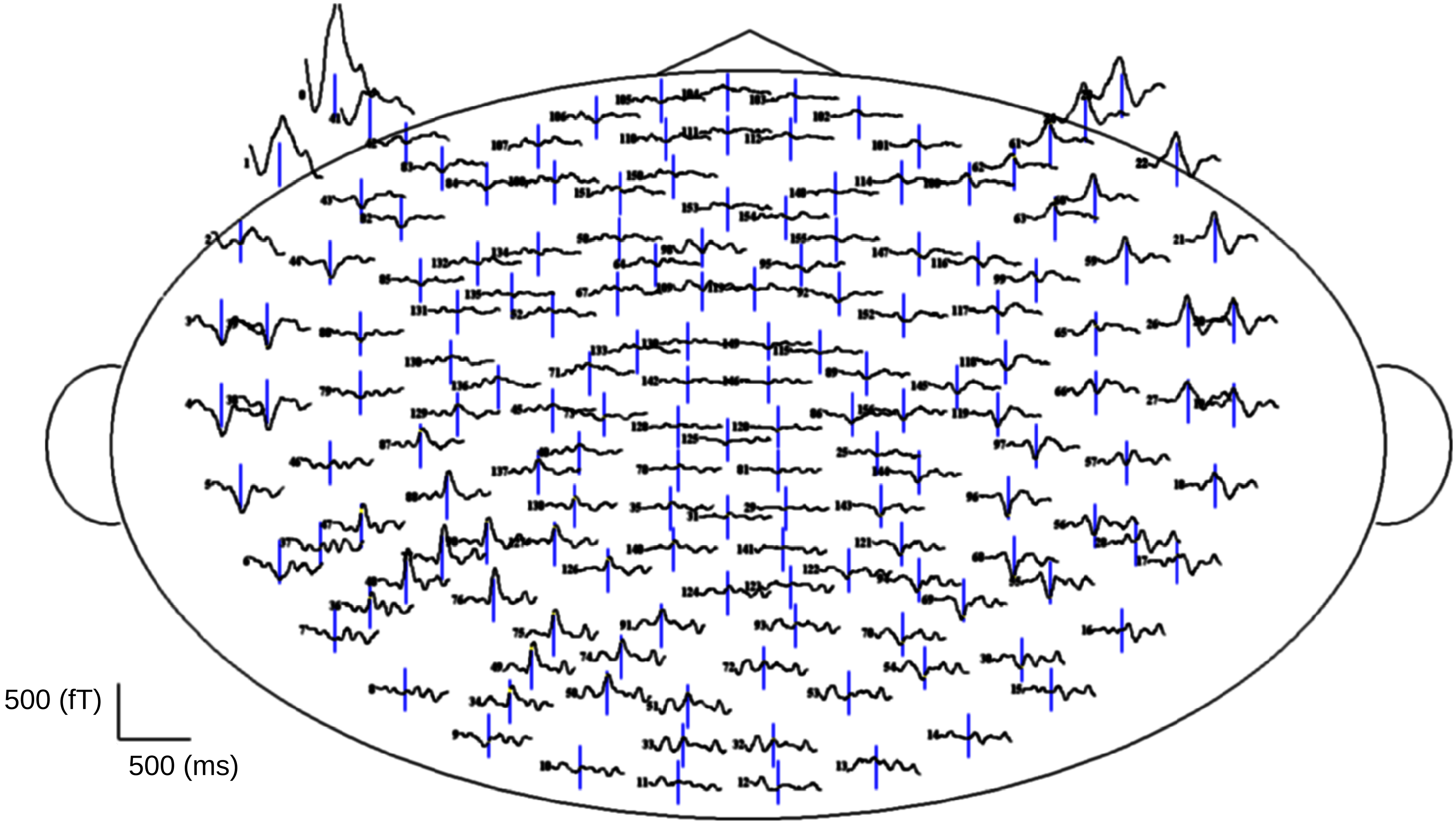
MEG Magnetic Signal

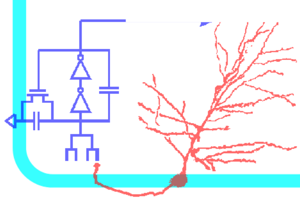


- Direct electrophysiological measurement
  - not hemodynamic
  - real-time
- No unique solution for distributed source

MEG Response

Spatial Map of Time Series





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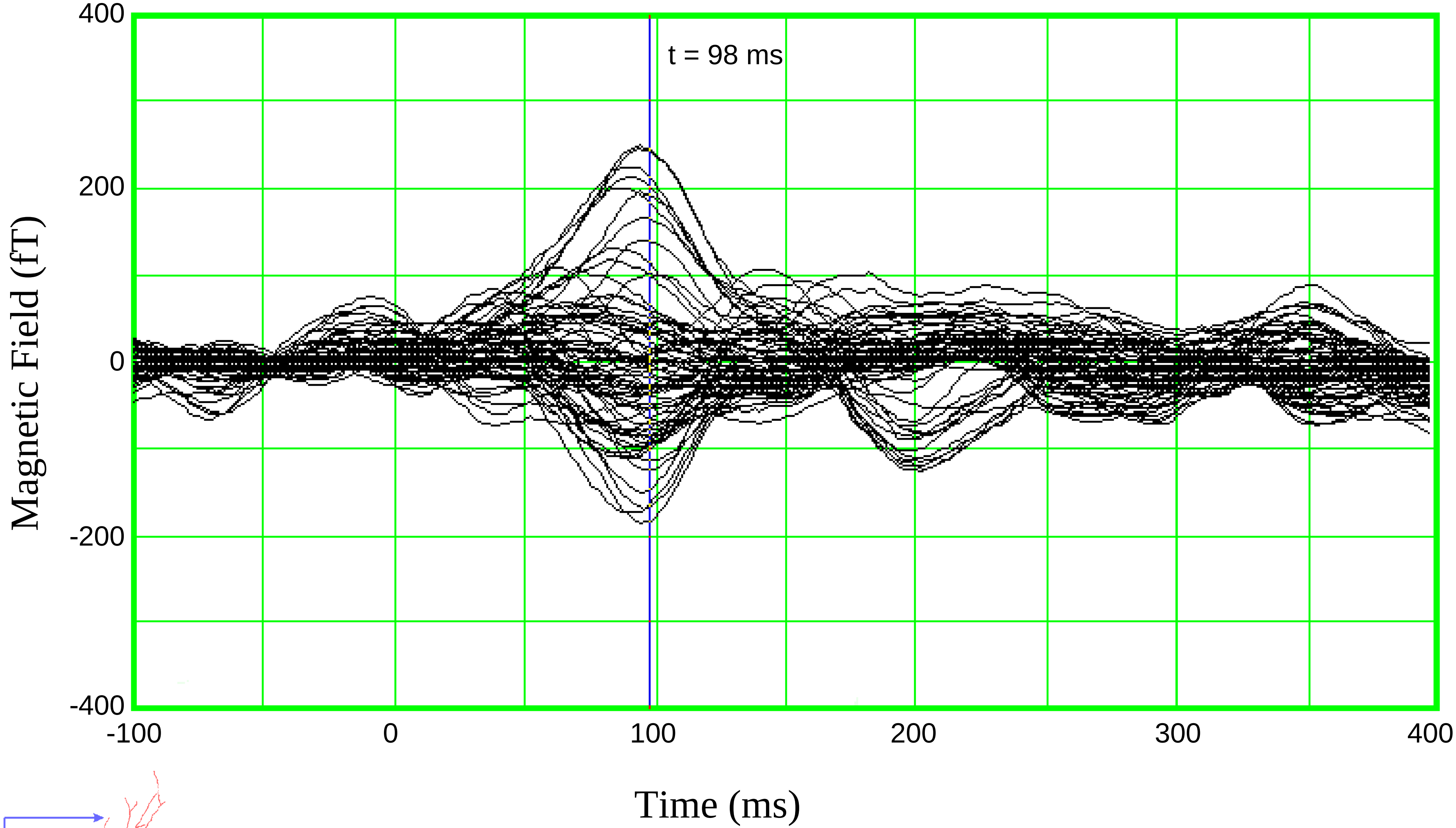
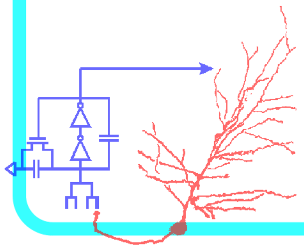
MEG Response

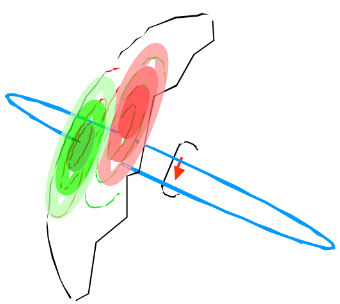
Butterfly Plot

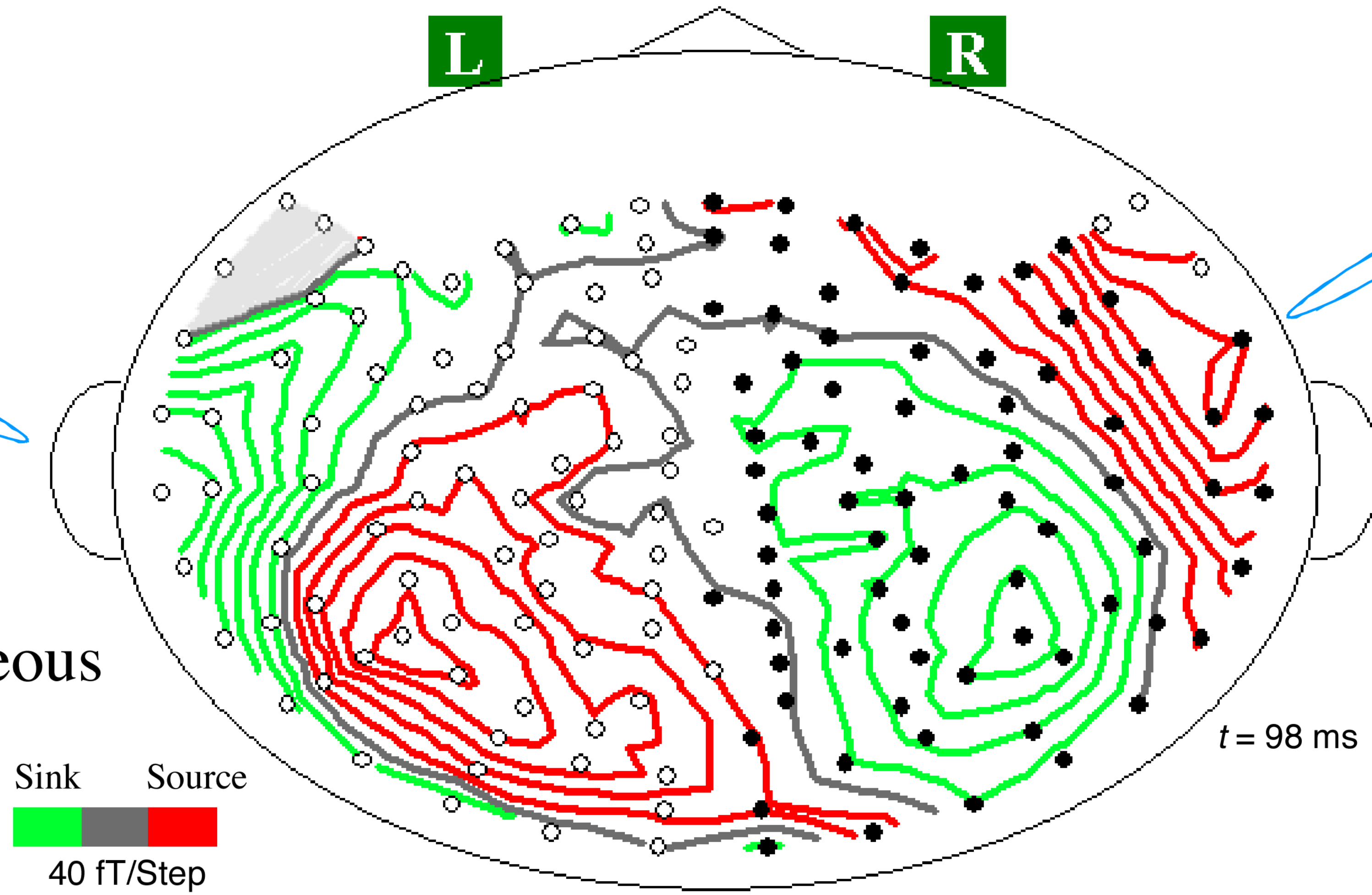


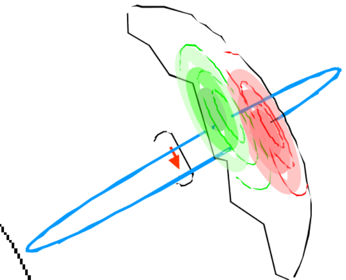


MEG Response

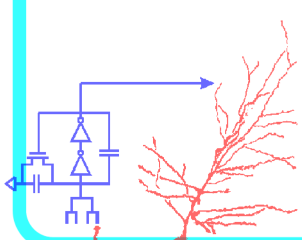
Flattened Isofield Contour Map







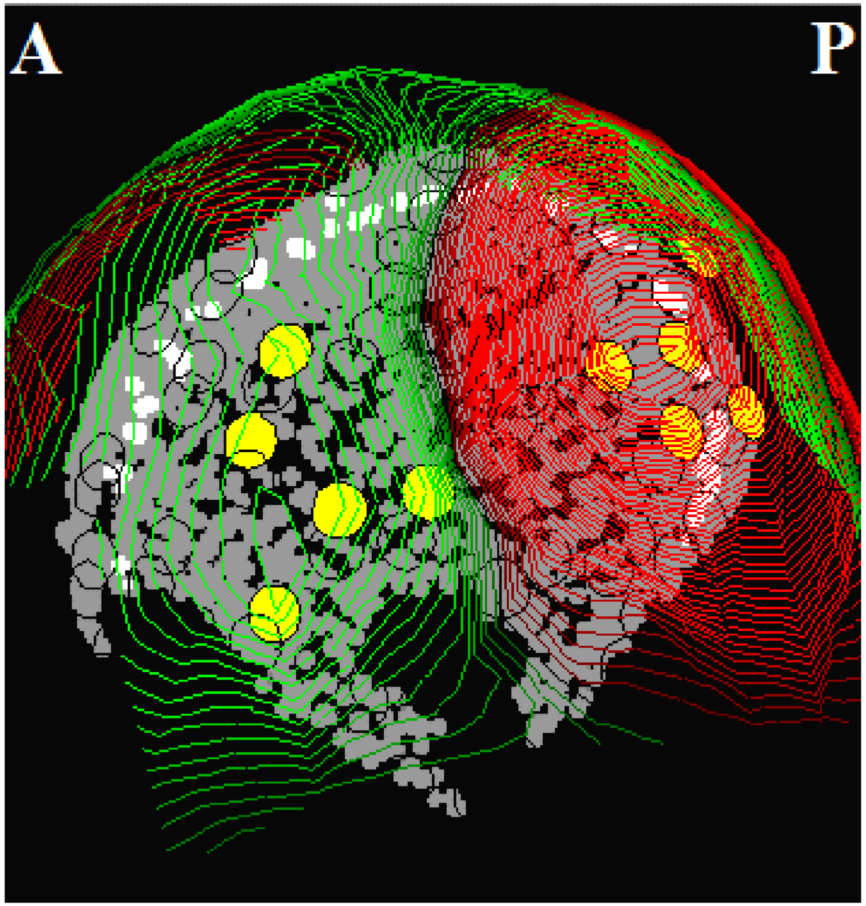
Instantaneous
Magnetic
Field



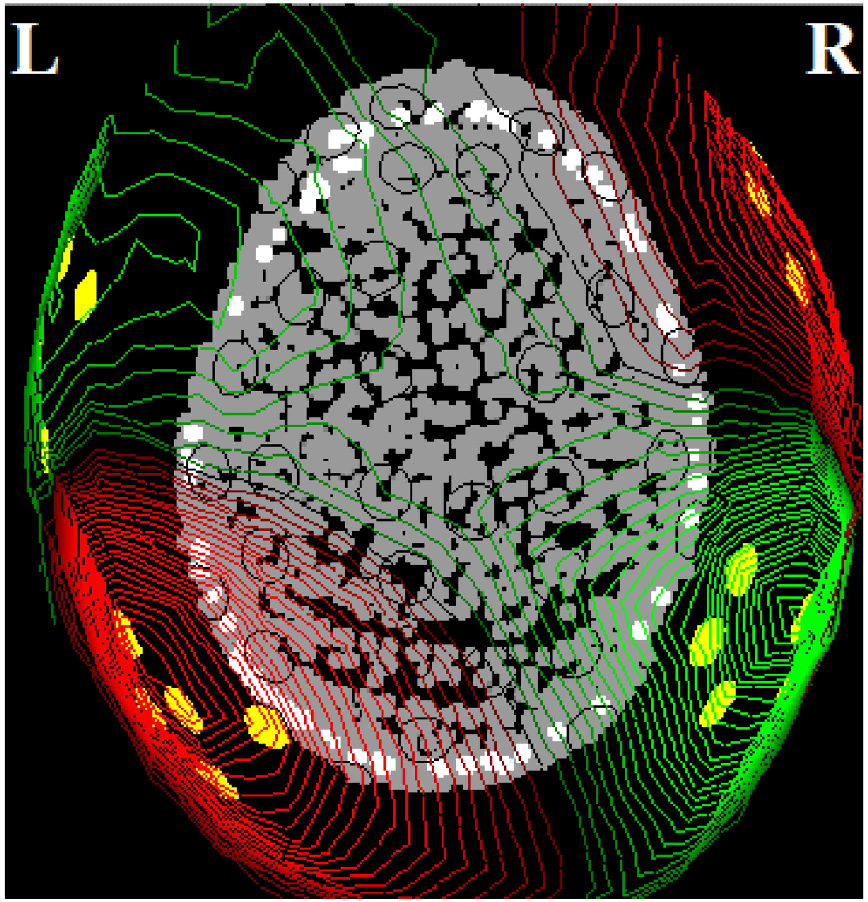
MEG Response

3-D Isofield Contour Map

Sagittal View



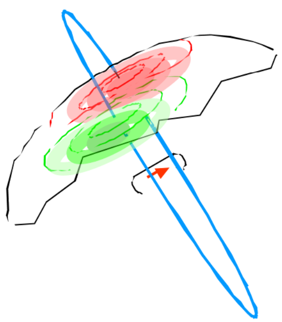
Axial View



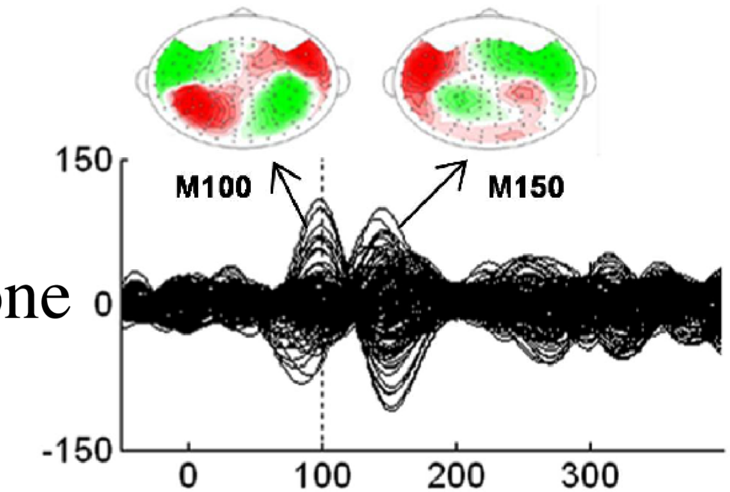
Chait, Poeppel and Simon, Cerebral Cortex 2006

Time Course of MEG Responses

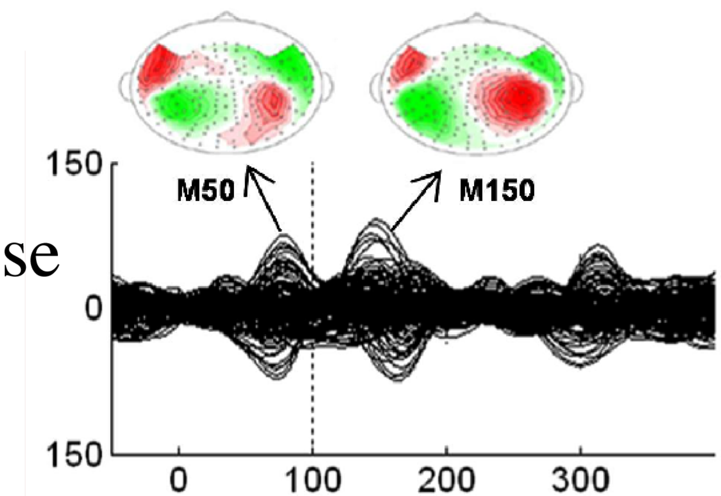
Evoked Responses
MEG Events Time-Locked
to Stimulus Event



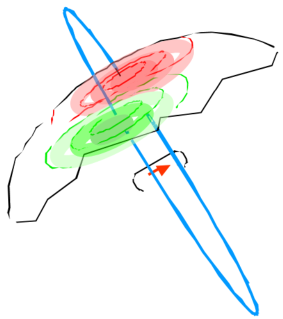
Pure Tone



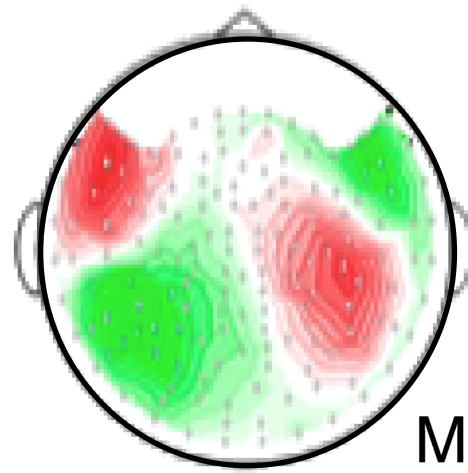
Broadband Noise



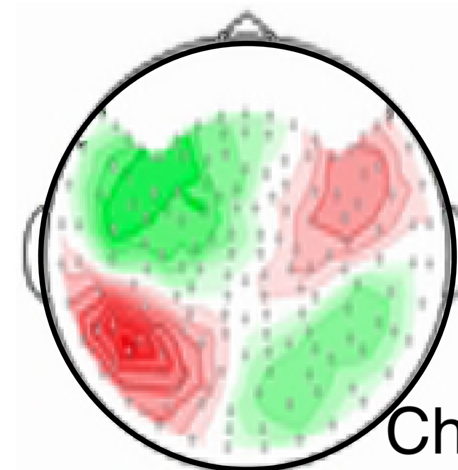
Spatial Auditory MEG Responses



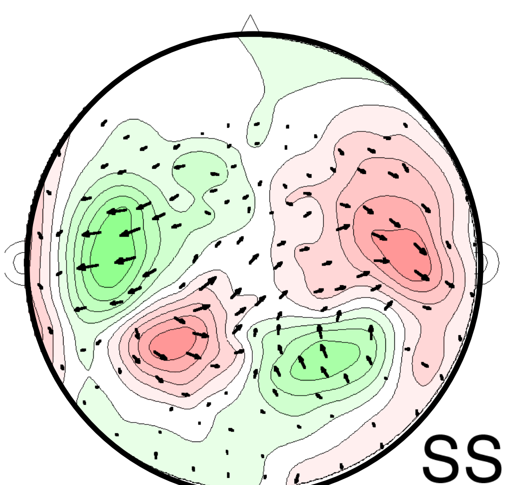
Auditory Responses
Robust
Strongly Lateralized



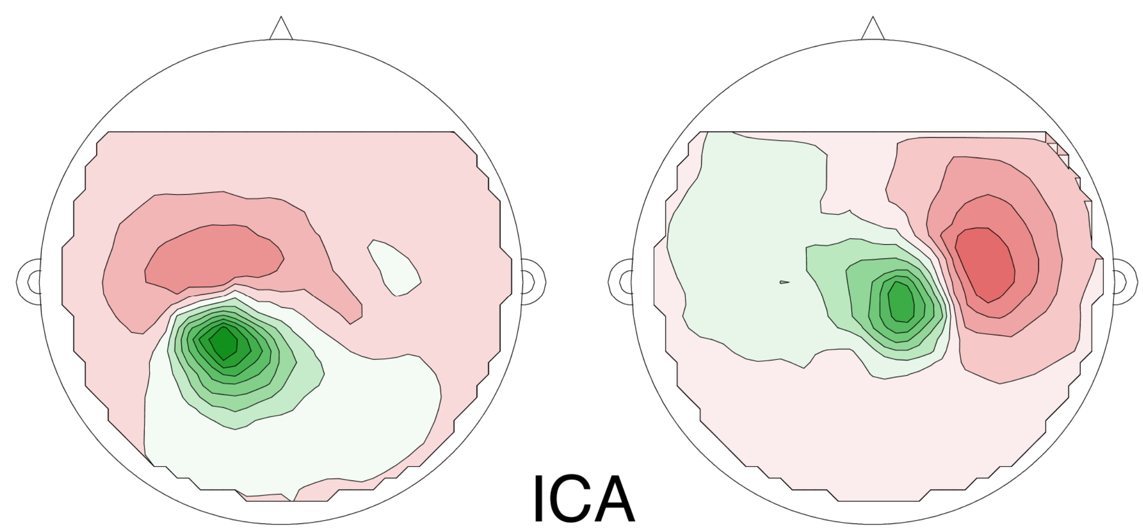
M50



Change
Onset



SSR



ICA

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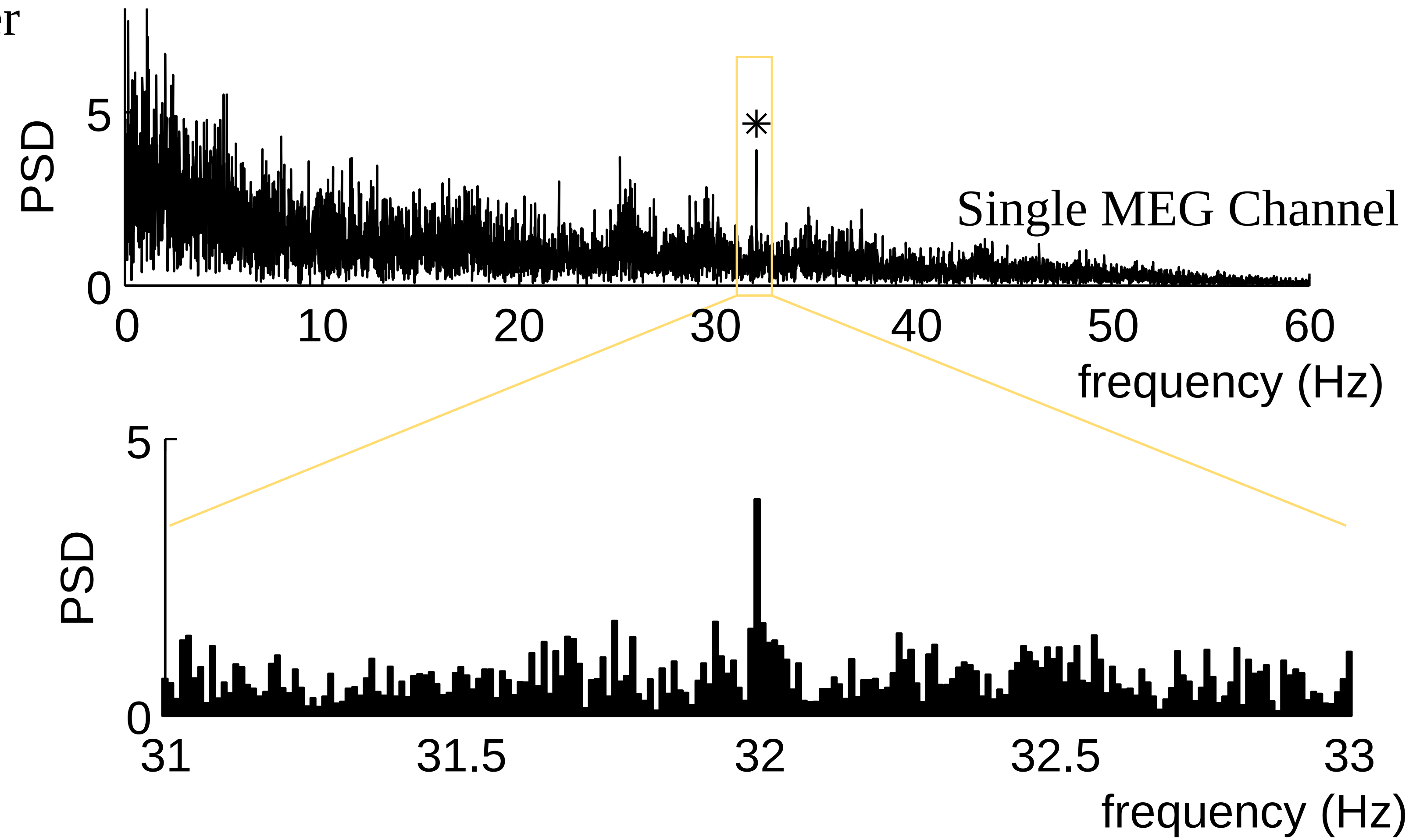
An Alternative to Time: Frequency

- Use Stimuli localized in Frequency rather than time
- Examine Response at Same Frequency
- Steady State Response (SSR)
- Frequency Response/Transfer Function

Frequency Response

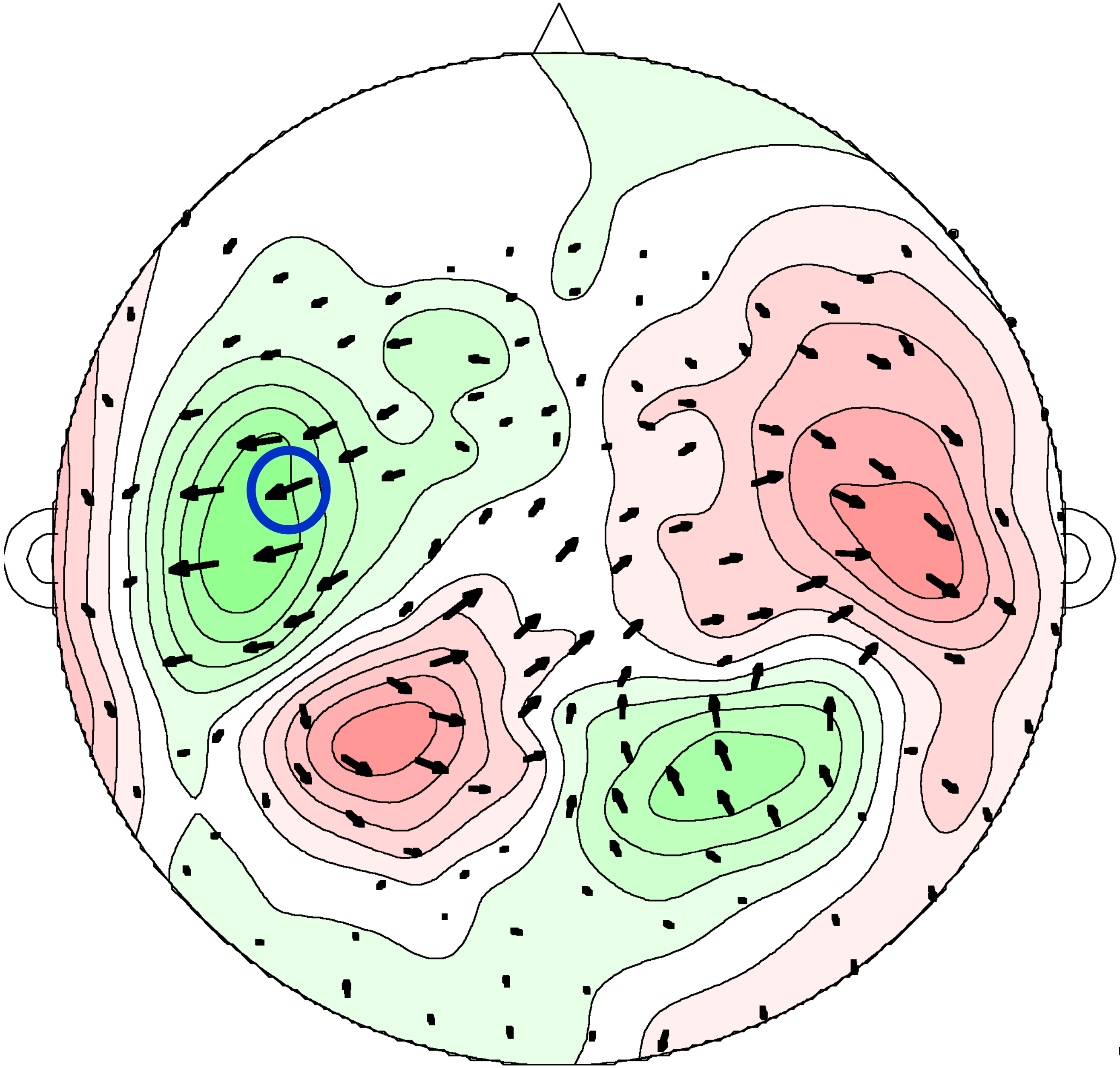
32 Hz Modulation
400 Hz tone carrier
100 trials @ 1 s
(concatenated)

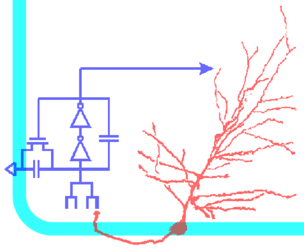


Precise Phase-Locking: 0.01 Hz
Little trial-to-trial jitter

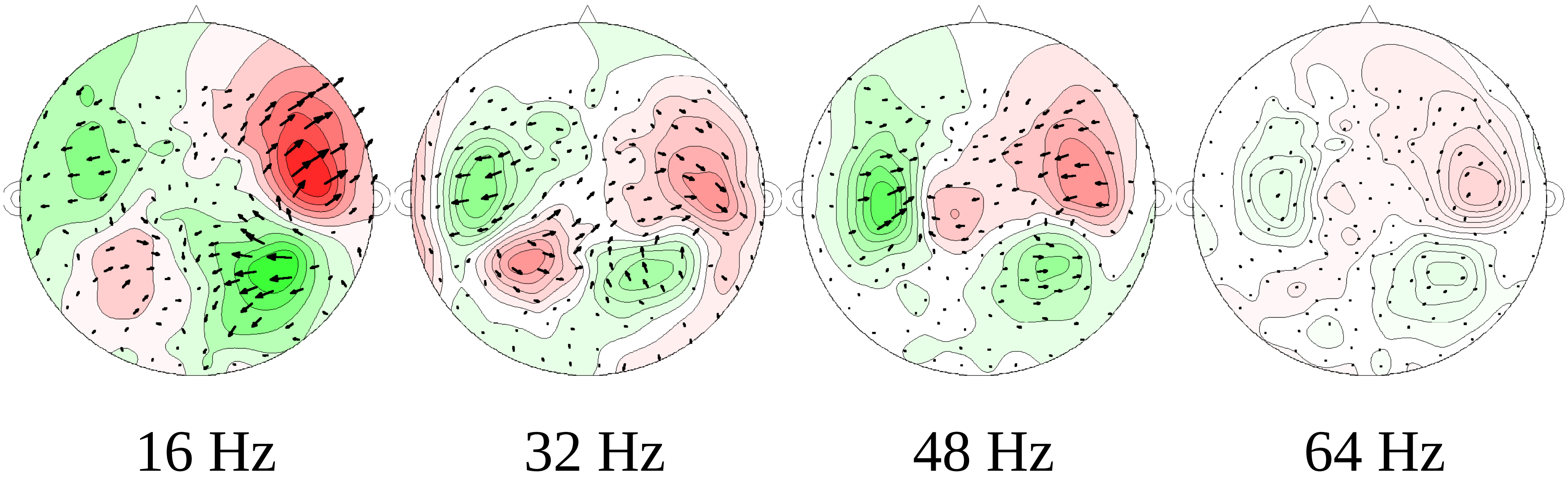
Amplitude + Phase...

Whole Head Steady State Response

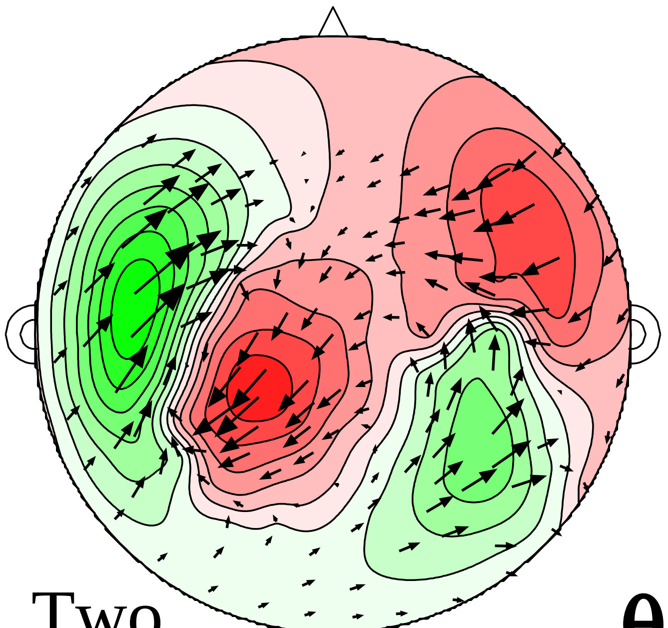




Whole Head Transfer Function



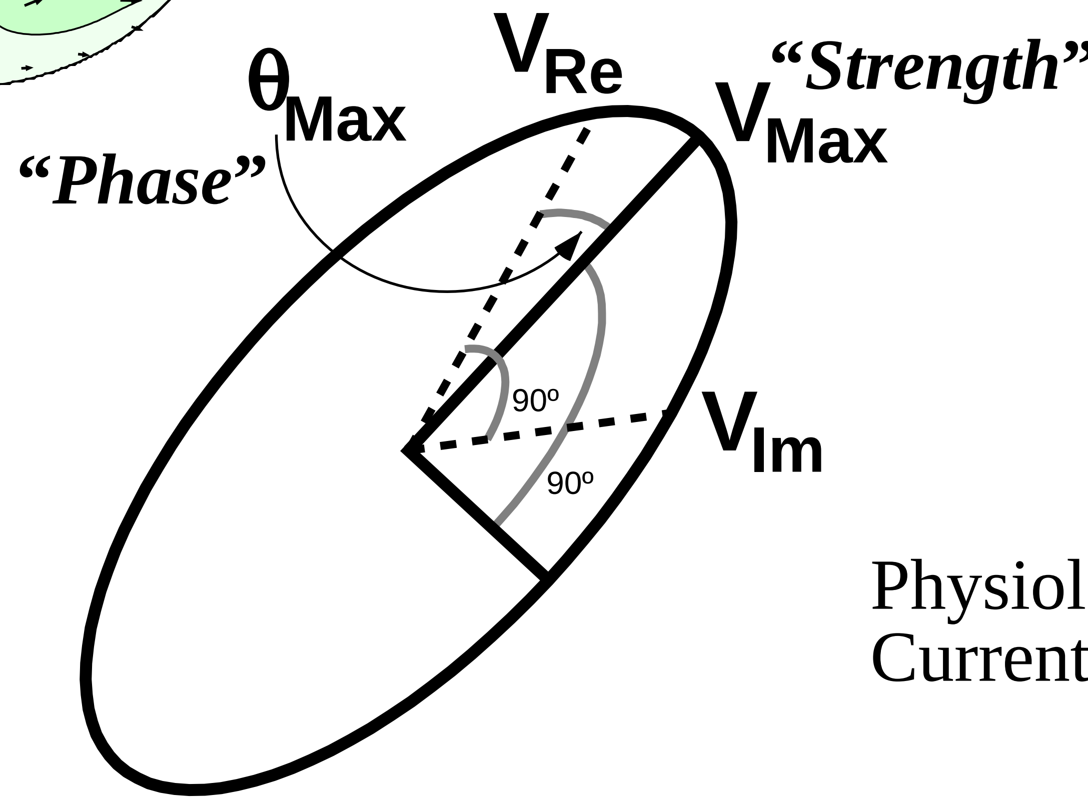
Complex Neural Current Sources



Two Dipole Fit

$$\vec{V} = \vec{V}_{Re} + i\,\vec{V}_{Im}$$

$$\vec{V}(\theta) = \vec{V}_{Re}\cos(\theta) + \vec{V}_{Im}\sin(\theta)$$



$\hat{V}_{Max}, \hat{V}_{Min}$

Orientations

"Sharpness"

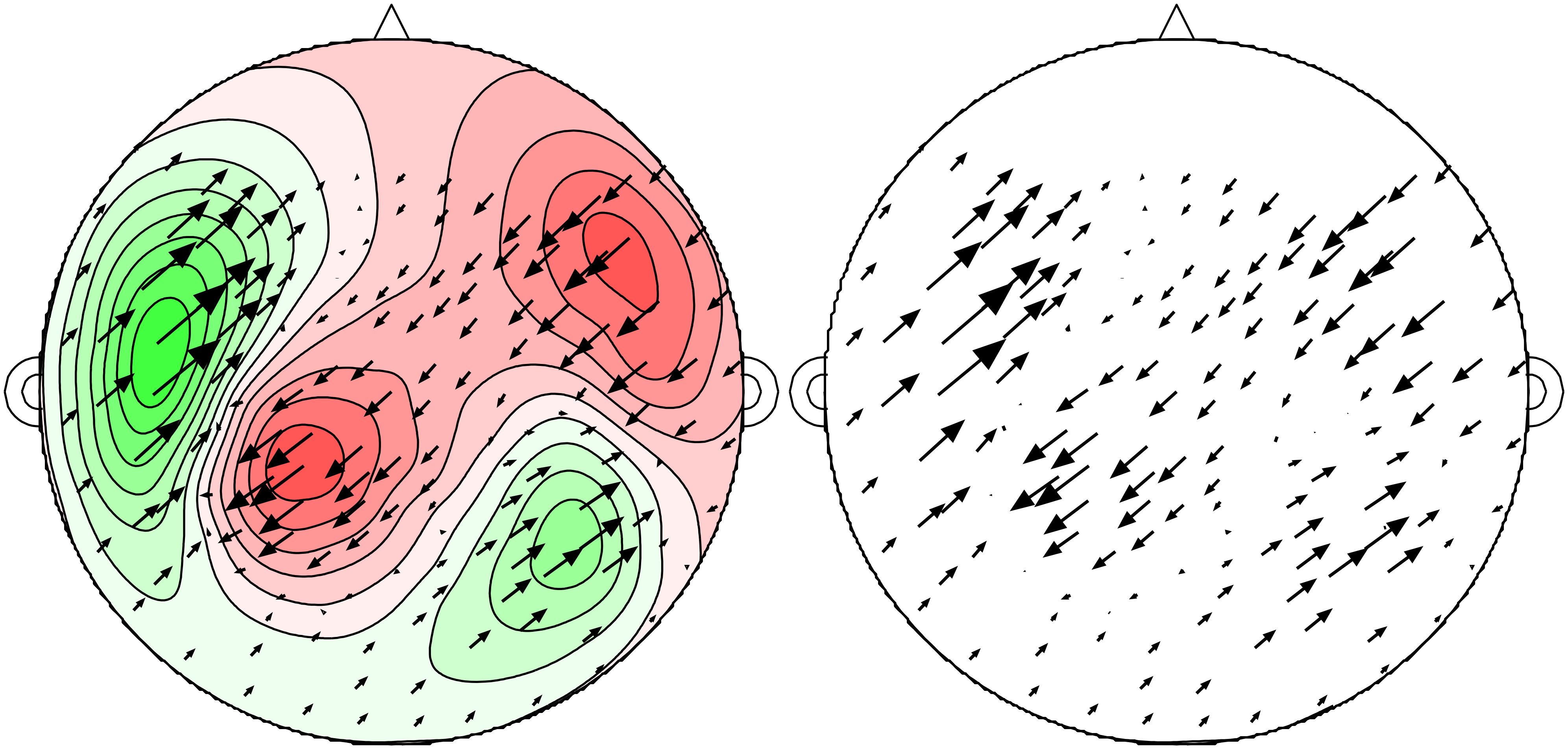
$$\eta = \frac{|V_{Min}|}{|V_{Max}|}$$

$$0 < \eta < 1$$

Physiologically Simple Current Sources: $\eta = 0$

Simon and Wang, J. Neurosci. Methods 2005

Single Orientation Current Sources



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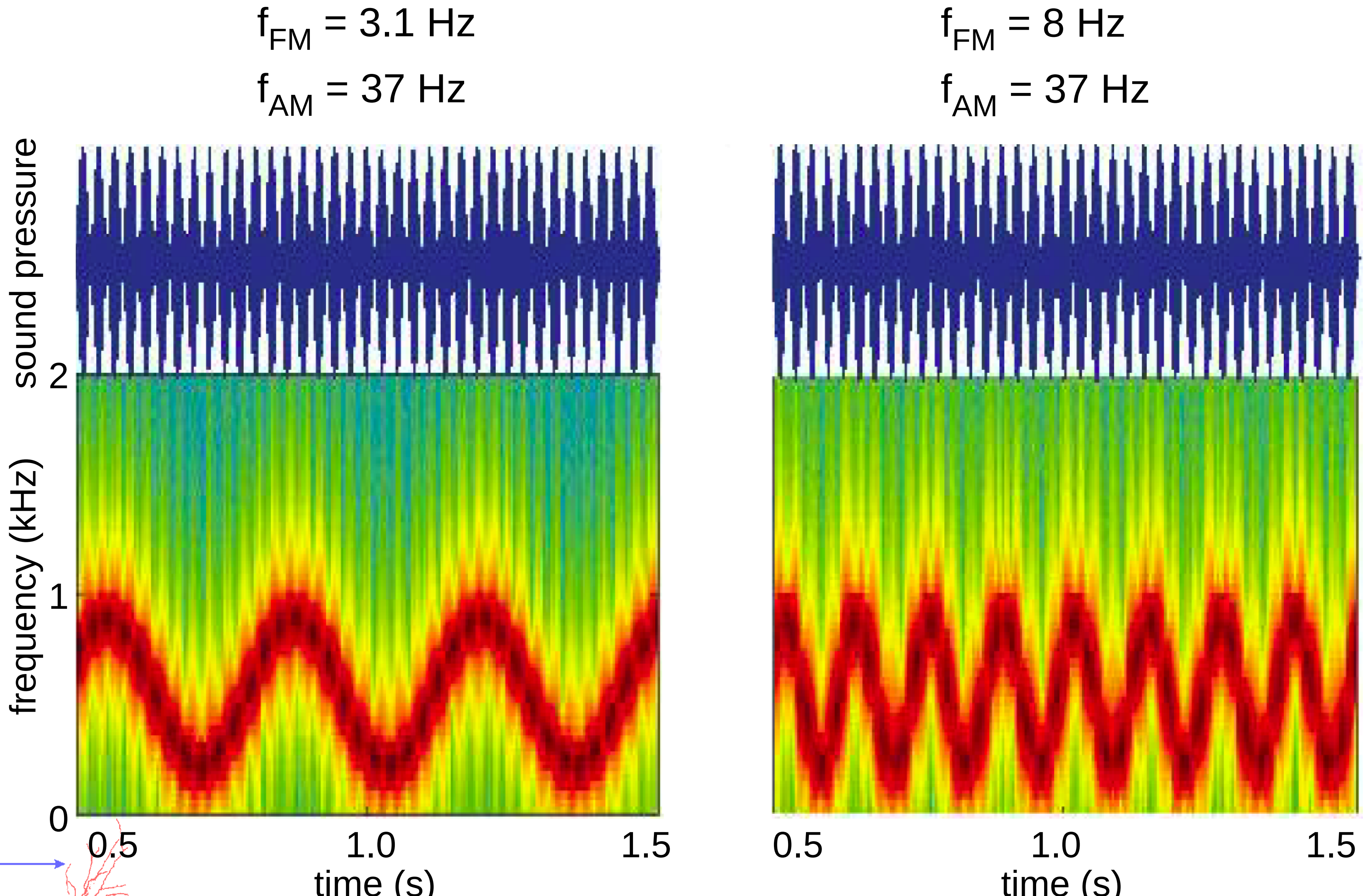
Modulation Encoding

- Simple Modulations → Simple Cortical Encoding
  - *Amplitude Modulation* coding often used for *slower* modulations
  - *Rate* coding (invisible to MEG) often used for *faster* modulations

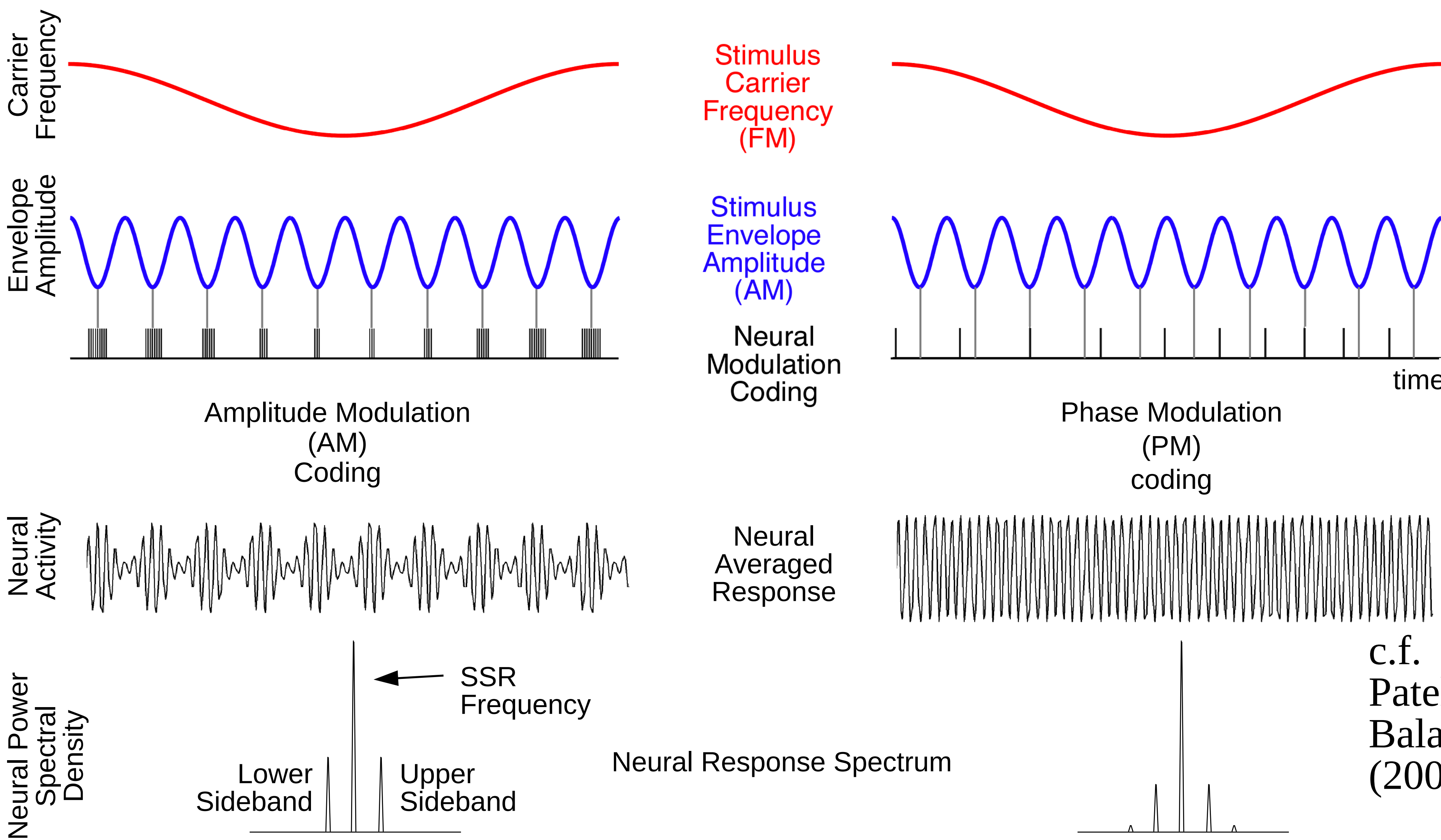
- Applies to general modulations: AM, FM, other

- Amplitude Modulation coding is easily detectable in Fourier/Spectral domain
  - Spectral Peak at Modulation Frequency

Sample Dual Modulation Stimuli



Neural Modulation Models



c.f. Patel & Balaban (2004)

$$\alpha = (\varphi_{upper} - \varphi_{\mathrm{SSR}}) - (\varphi_{\mathrm{SSR}} - \varphi_{lower})$$

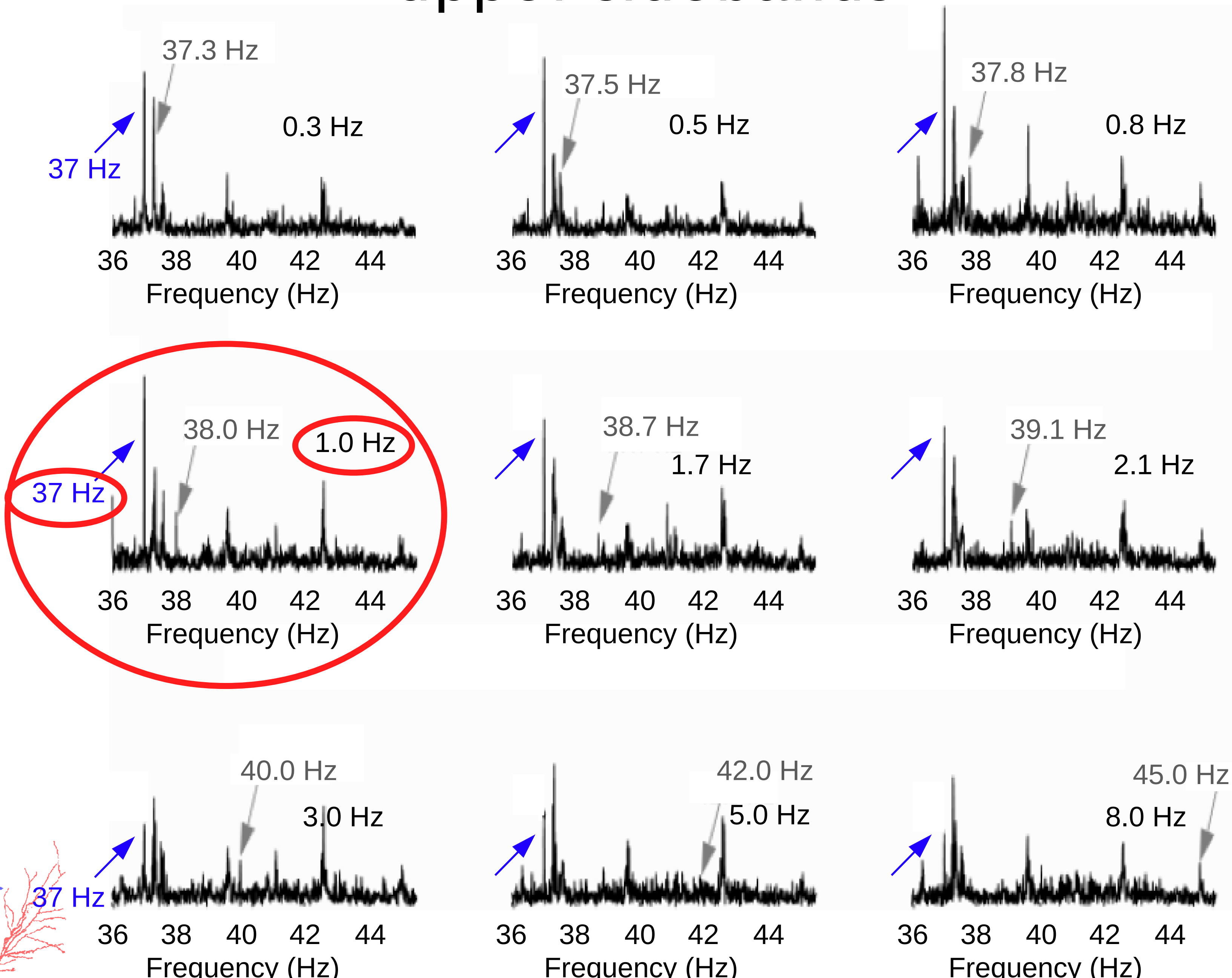
$\alpha_{\mathrm{AM}} = 0 \text{ or } 2\pi$

Neural Response Phase Encoding Parameter

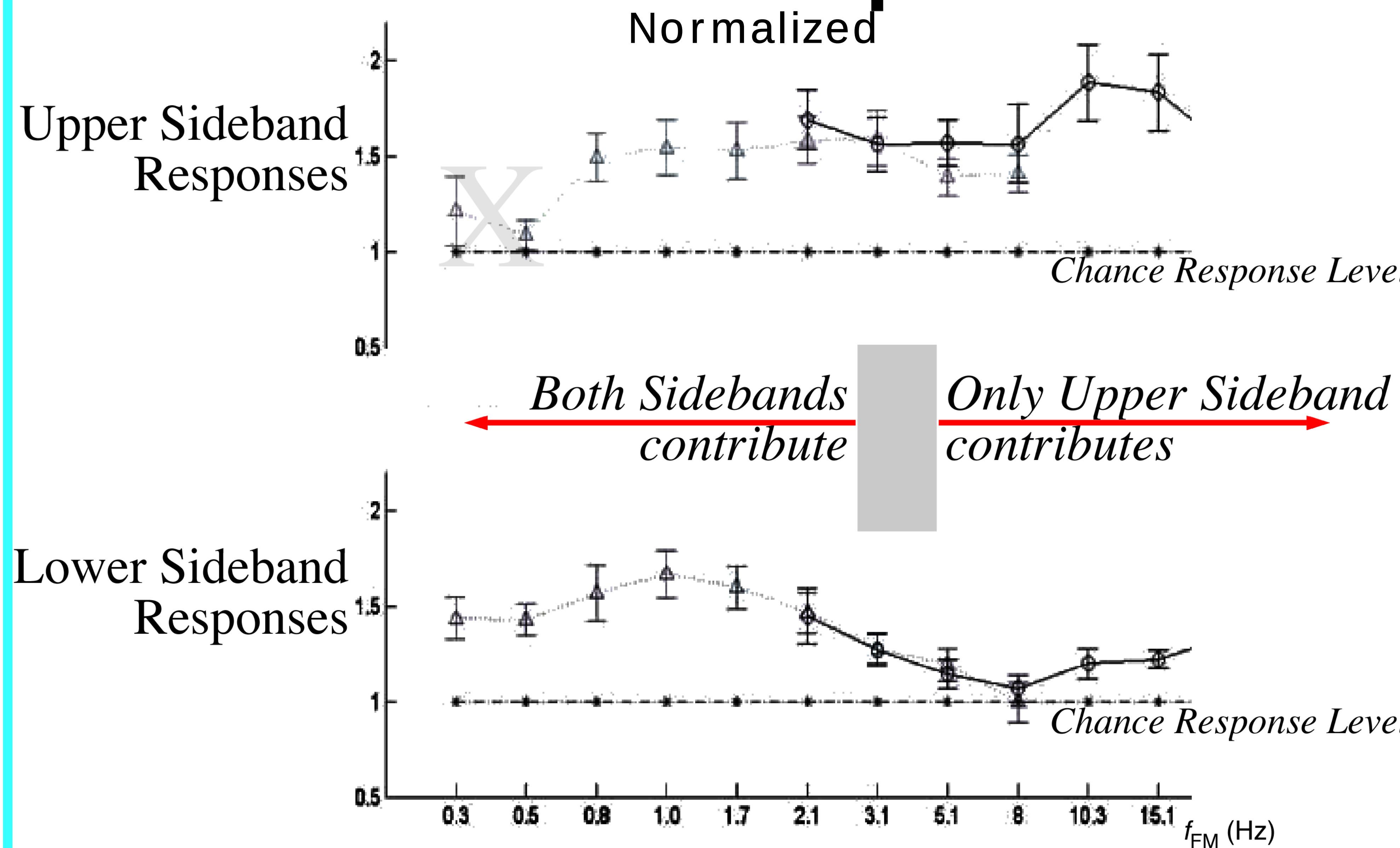
$\alpha_{\mathrm{PM}} = \pi$

Spectral Sideband Responses

upper sidebands



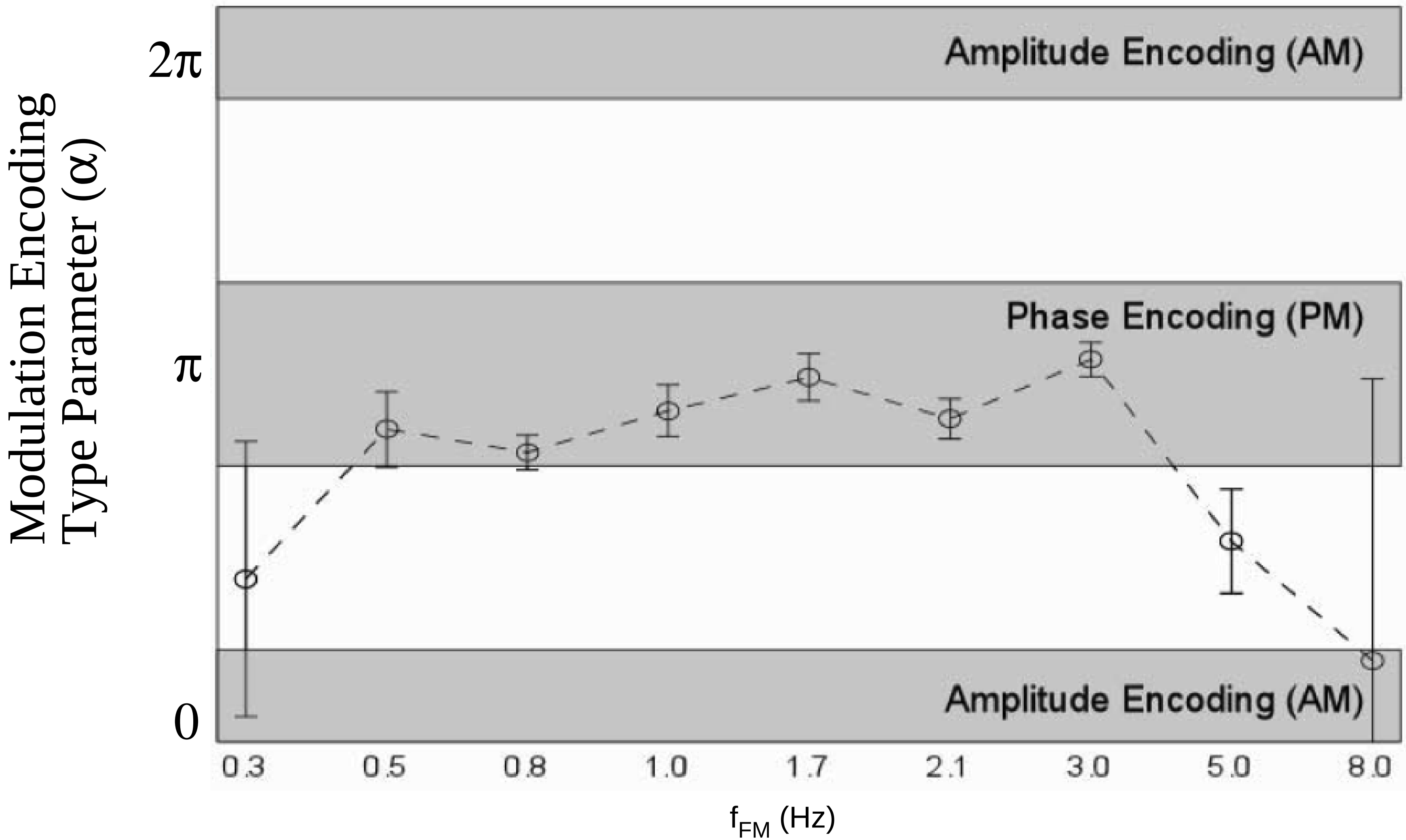
Sideband Responses



Modulation Encoding, with coding transition at f_{FM} ~ 5 Hz

Luo, Wang, Poeppel and Simon (2007)

Modulation Encoding Type



Phase Modulation Encoding below f_{FM} ~ 5 Hz

Luo, Wang, Poeppel and Simon
J. Neurophysiol. 2006

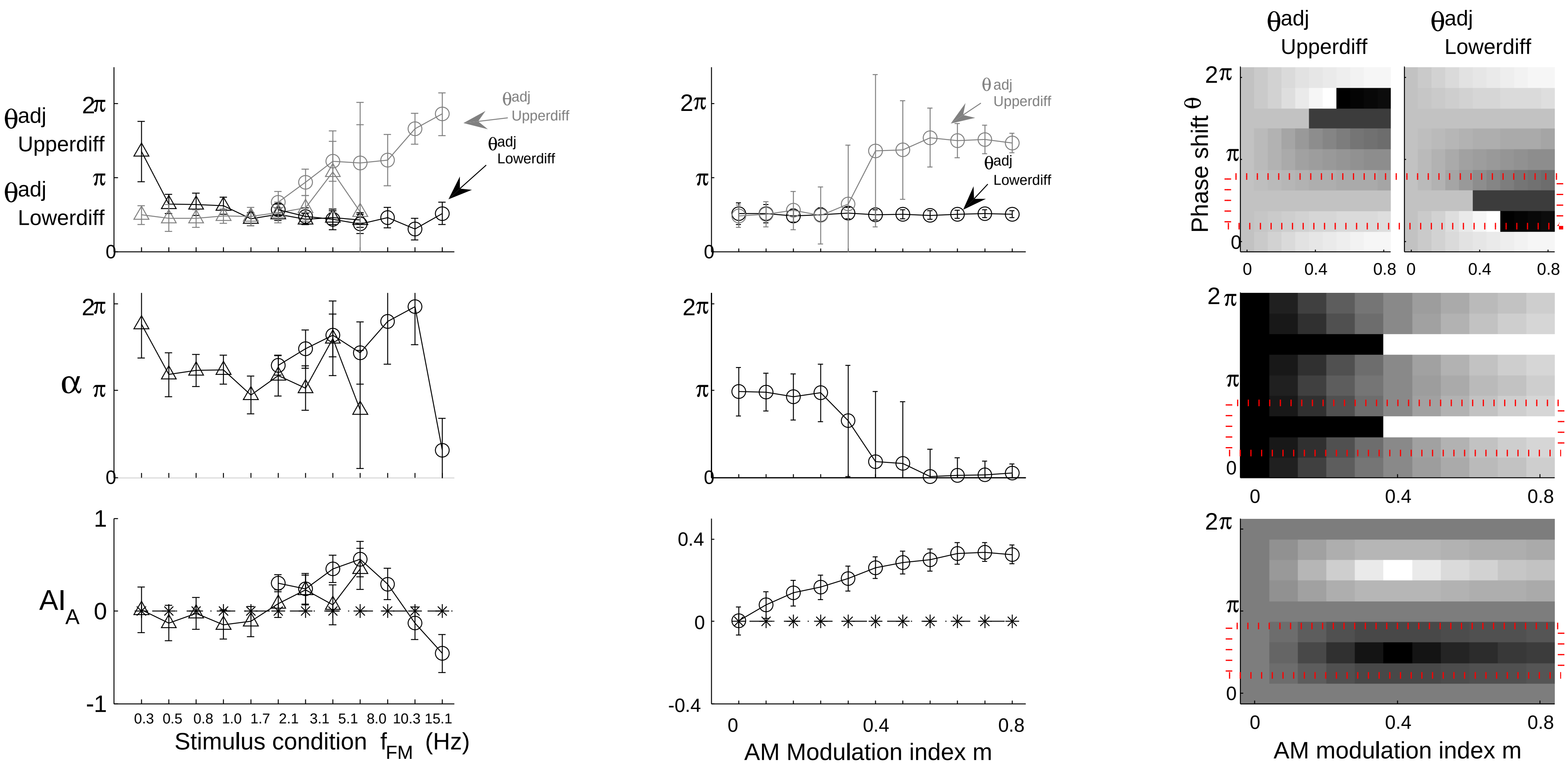
Neural Population Model

$$
\begin{aligned}
S(t) = {} & \underbrace{\left(1 + m\cos(2\pi f_{FM} t + \theta)\right)}_{Amplitude\ \ Modulation} \\
& \times \underbrace{\cos\left(2\pi f_{AM} t + \frac{\pi}{8}\cos(2\pi f_{FM} t)\right)}_{Phase\ \ Modulation} \\
& + GWN
\end{aligned}
$$

Model Results

Experimental Results

Model Results



$$S(t)= \underbrace{(1+m\cos(2\pi f_{FM}t+\theta))}_{Amplitude\ Modulation} \times \underbrace{\cos(2\pi f_{AM}t+\frac{\pi}{8}\cos(2\pi f_{FM}t))}_{Phase\ Modulation} + GWN$$

AM in quadrature with PM *Why?*

Summary

- Combined AM/FM modulations are encoded in Auditory Cortex
  - Phase Modulation seen at lowest FM rates
  - Modulation Encoding changes at higher rates
- Single Sideband Modulation unexpected
  - Speculate: Single Modulation Encoding type?
  - Or: Two populations of AM and PM encoding neurons whose phase happens to cancel in lower sideband?
- Magnetoencephalography (MEG)

  Directly generated by neural currents

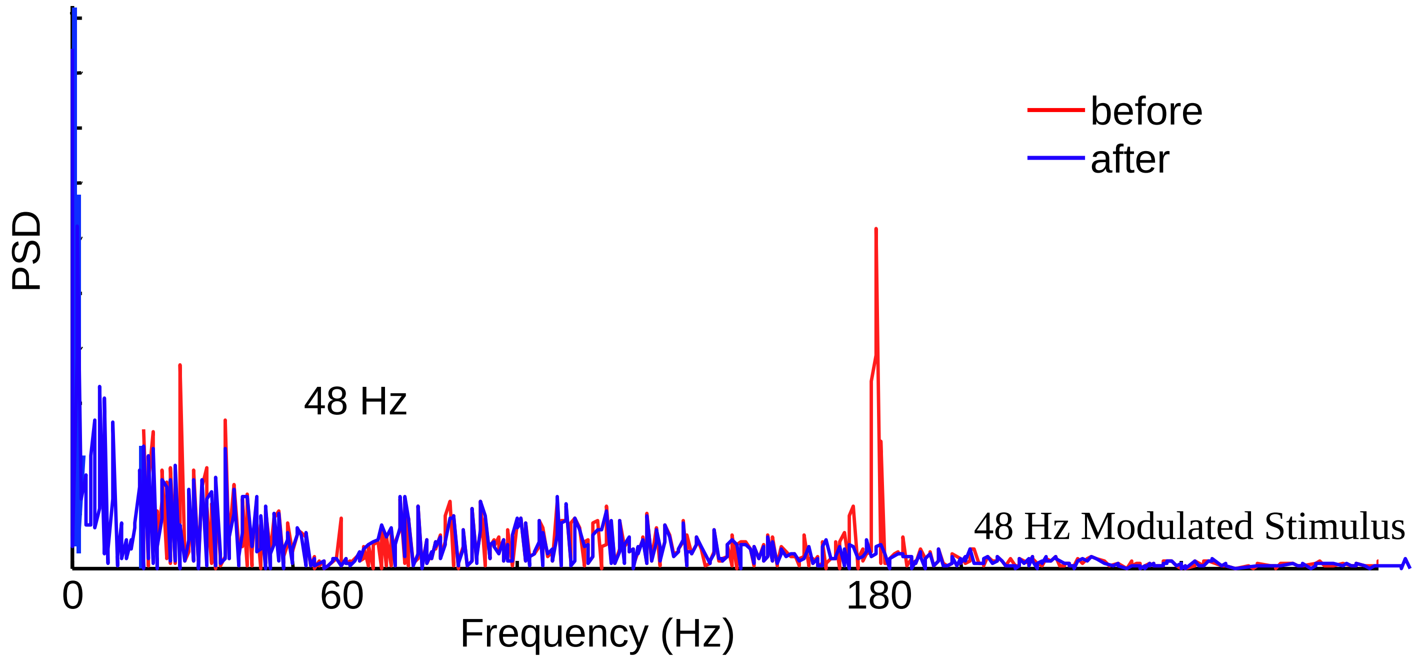
  Excellent time/frequency resolution

  Spatial Localizability an open question

Thank You

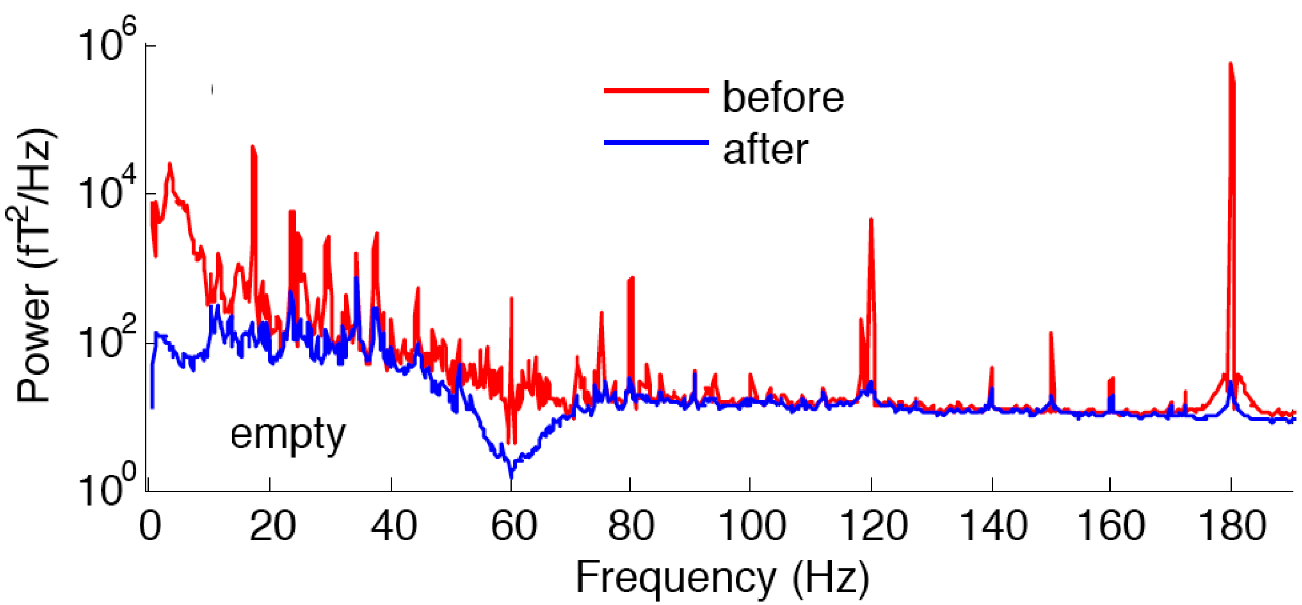
Noise Reduction in Software

Cleaned with
Fast-LMS
+ 3 Reference
channels



Ahmar and Simon, Neural Engineering 2005

Cleaned with
TSPCA
+ 3 Reference
channels



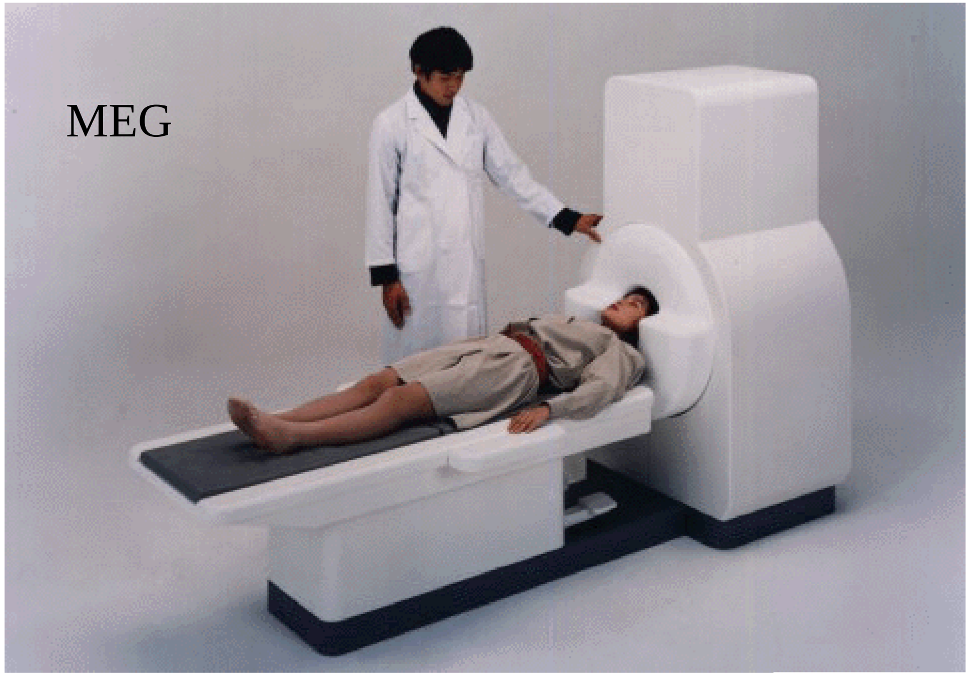
de Cheveigné, Le Roux, and Simon, ICASSP 2007.

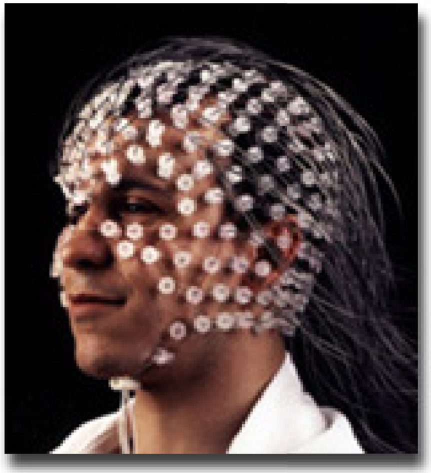
MEG compared to EEG

Temporal resolution high as EEG
Fast, easy set-up
Magnetic fields are not attenuated
or distorted, unlike electric fields
Higher spatial resolution

Expensive
Inverse problem worse? better?

Complementary Techniques

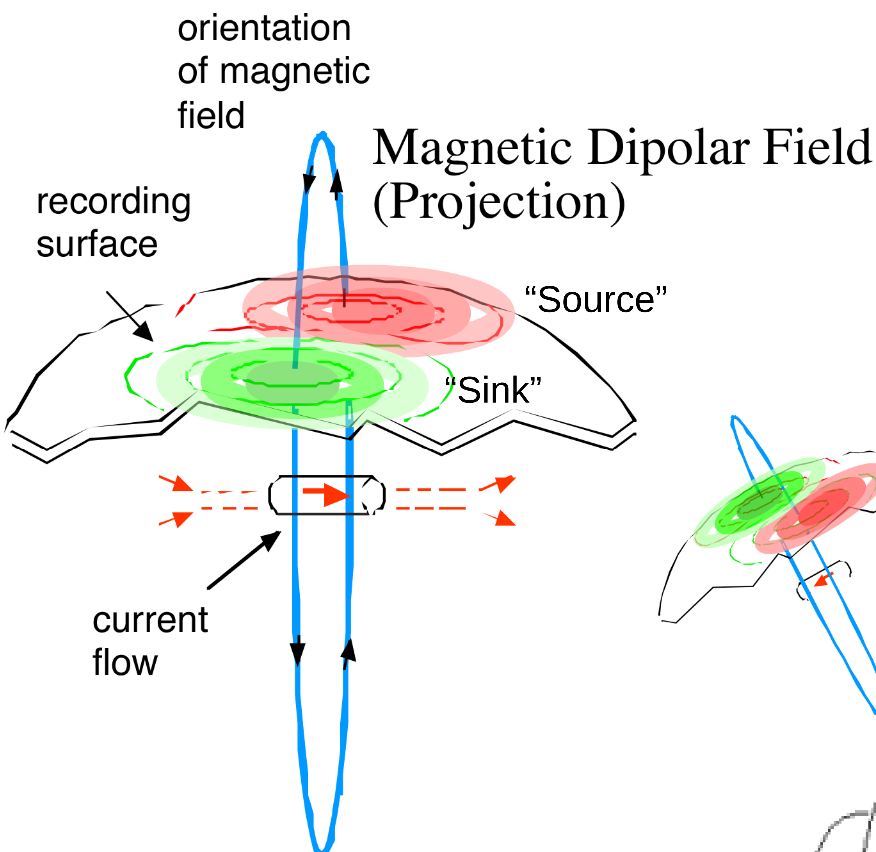


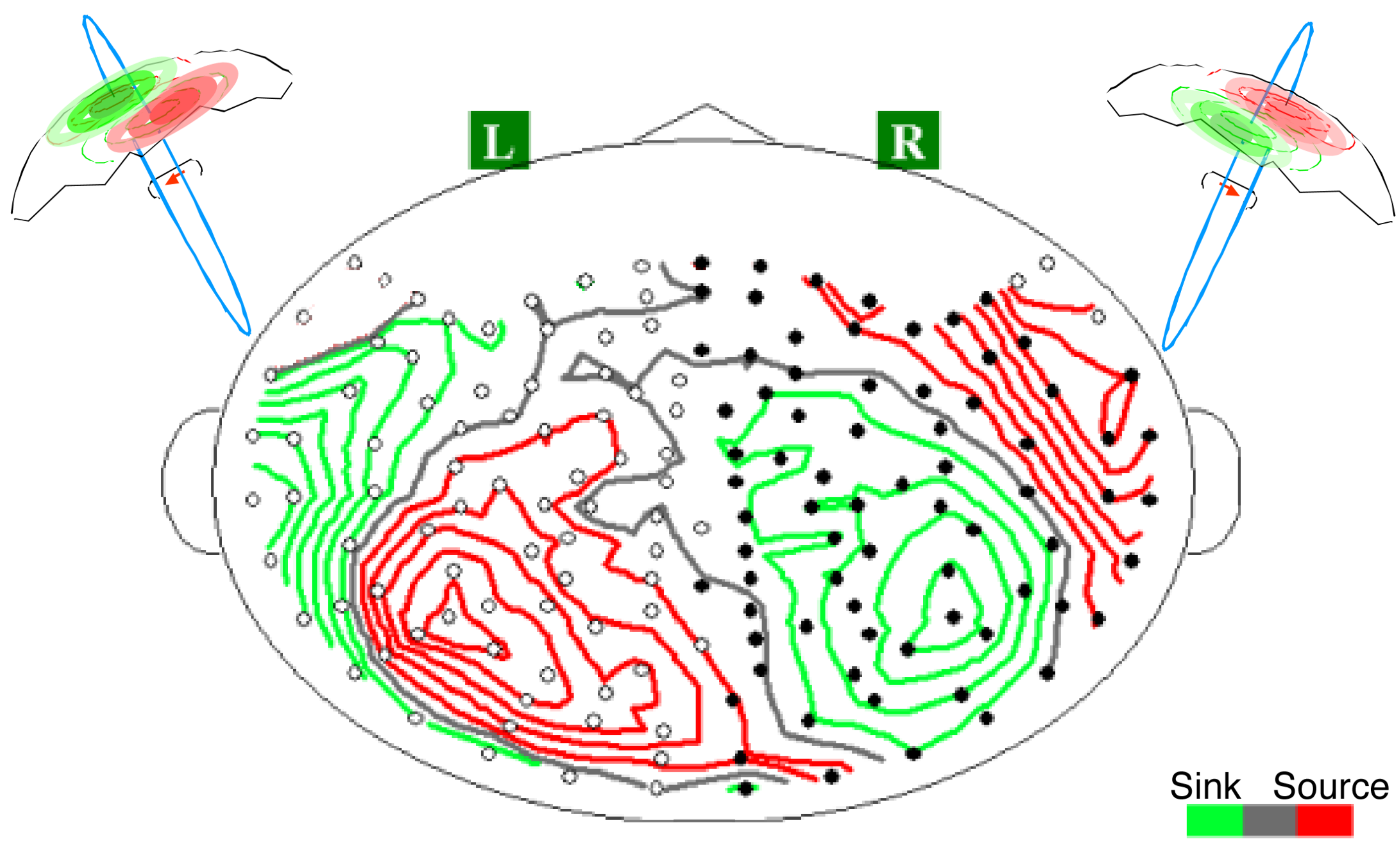


EEG

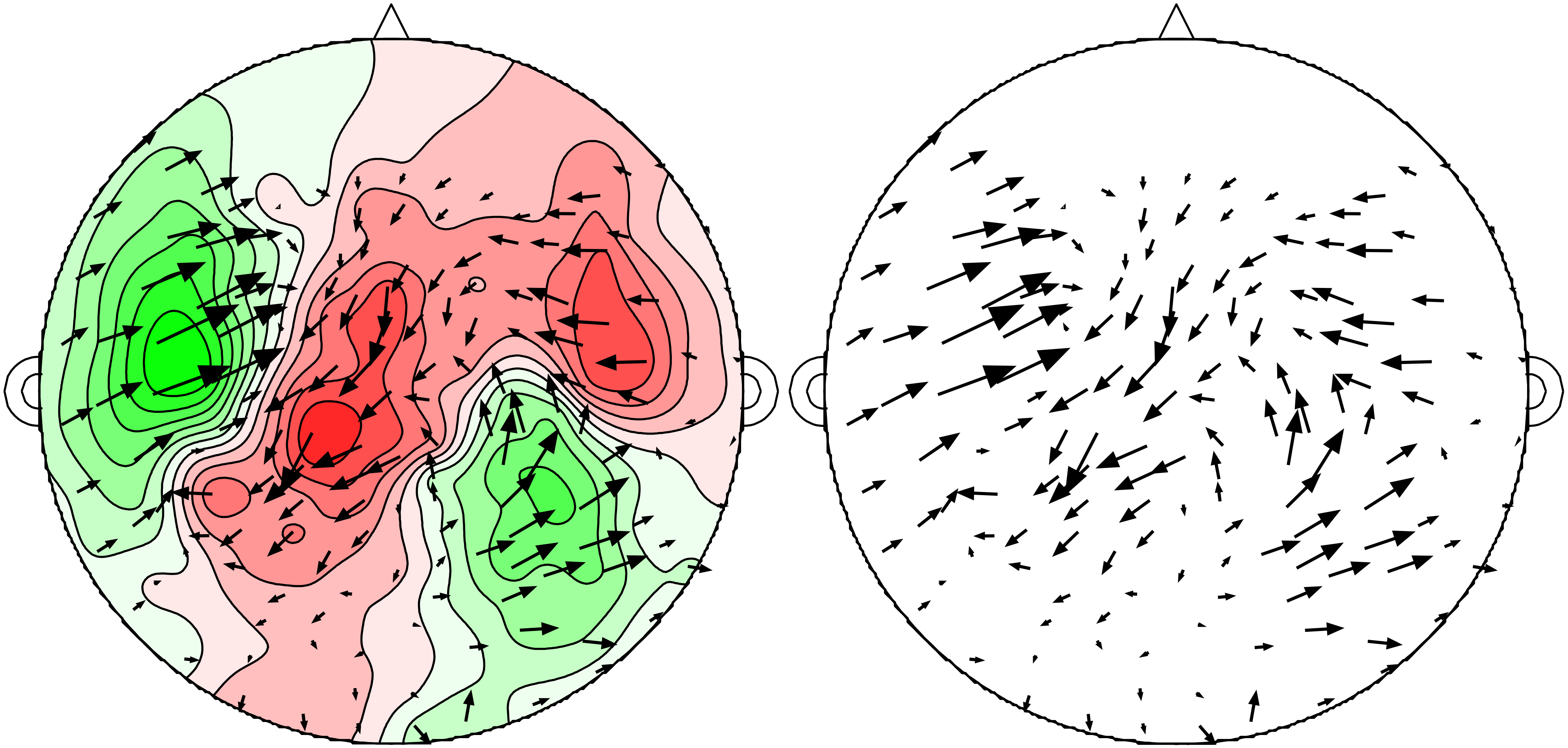
MEG Measures Neural Currents

- Direct electrophysiological measurement
  - not hemodynamic
  - real-time
- No unique solution for distributed source



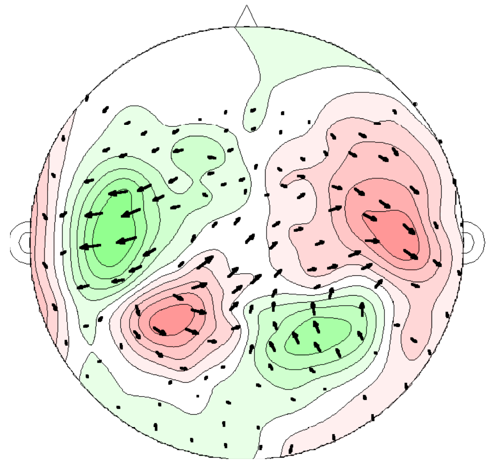


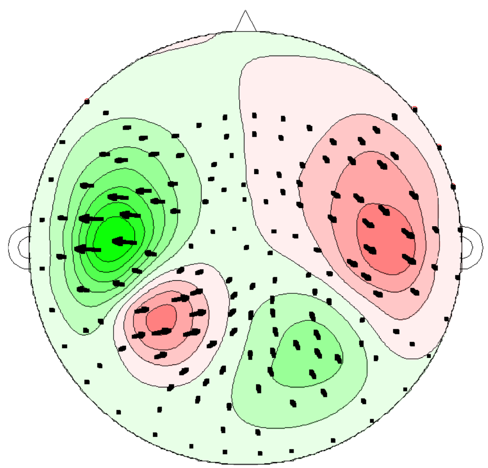
Complex Magnetic Field



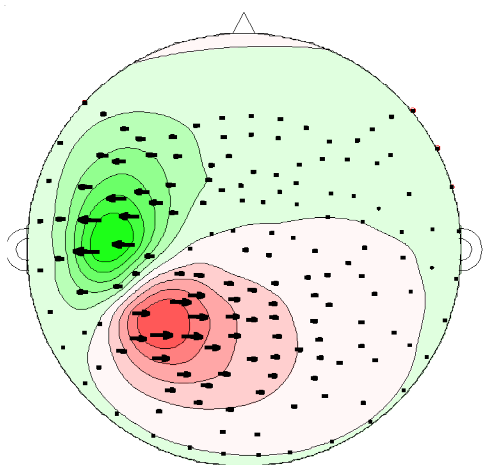
Data Reduction via Equivalent Dipoles

Raw Data

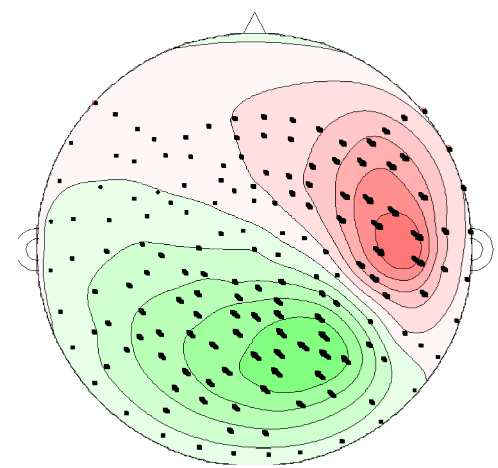




Two Dipole Fit



Left Dipole



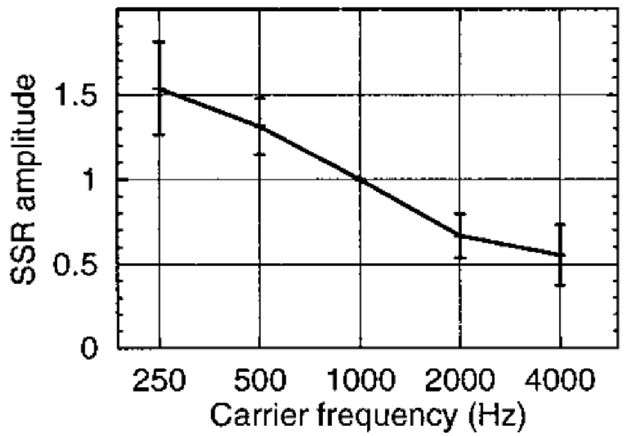
Right Dipole

Dipoles are Complex

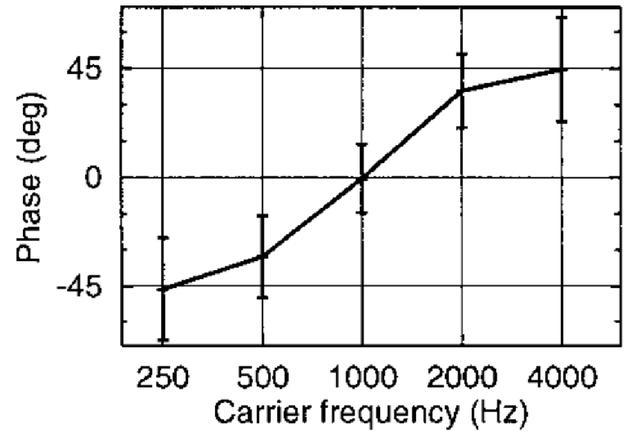
32 Hz

SSR Carrier Dependence

SSR Amplitude

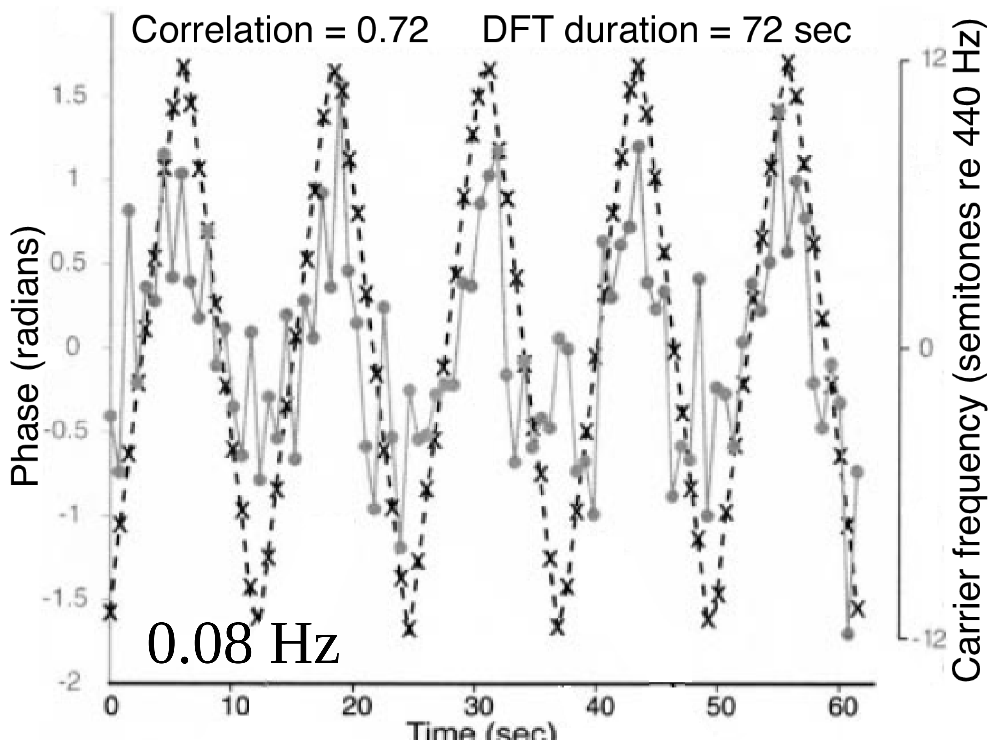


SSR Phase



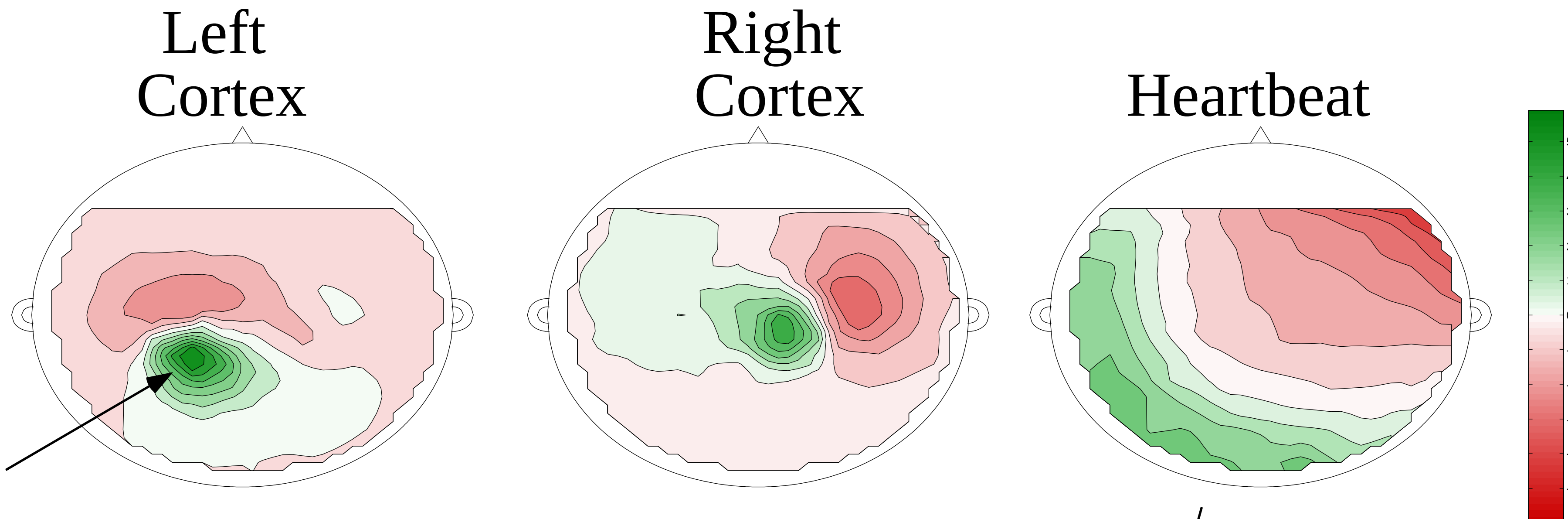
Ross et al. (2000)

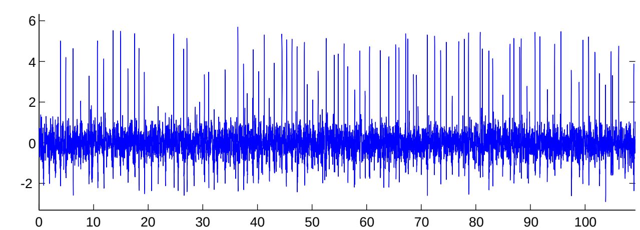
SSR Phase Follows Carrier
⬇
Phase Modulation Encoding

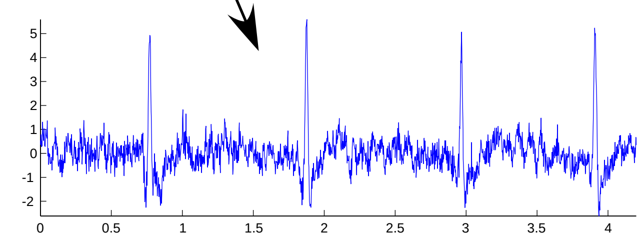


Patel & Balaban (2004)

Independent Component Analysis







ICA finds:

Independent Neural Sources in *Auditory* areas

Independent Neural Sources in *non-Auditory* areas

Independent non-Neural Sources