

Recording spikes ... noninvasively?

1. Why to try spikes
2. Neurophysics of hf-EEG
3. The ‚workhorse‘: 600 Hz SEP
4. Technology for 1 kHz and above
5. DIY recipe

Gabriel Curio

gabriel.curio@charite.de

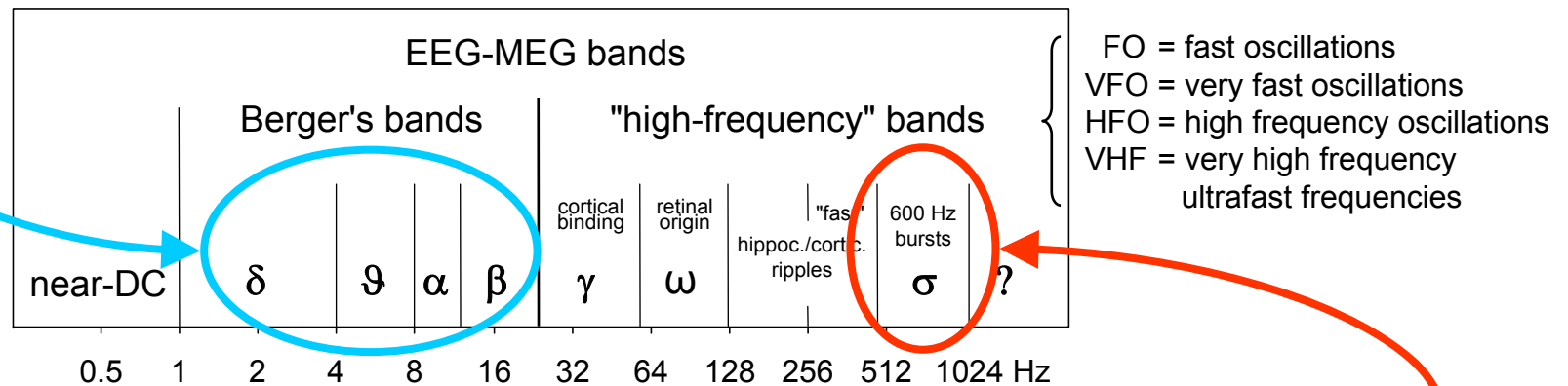
Neurophysics Group

Department of Neurology and Clinical Neurophysiology

CHARITÉ CAMPUS BENJAMIN FRANKLIN

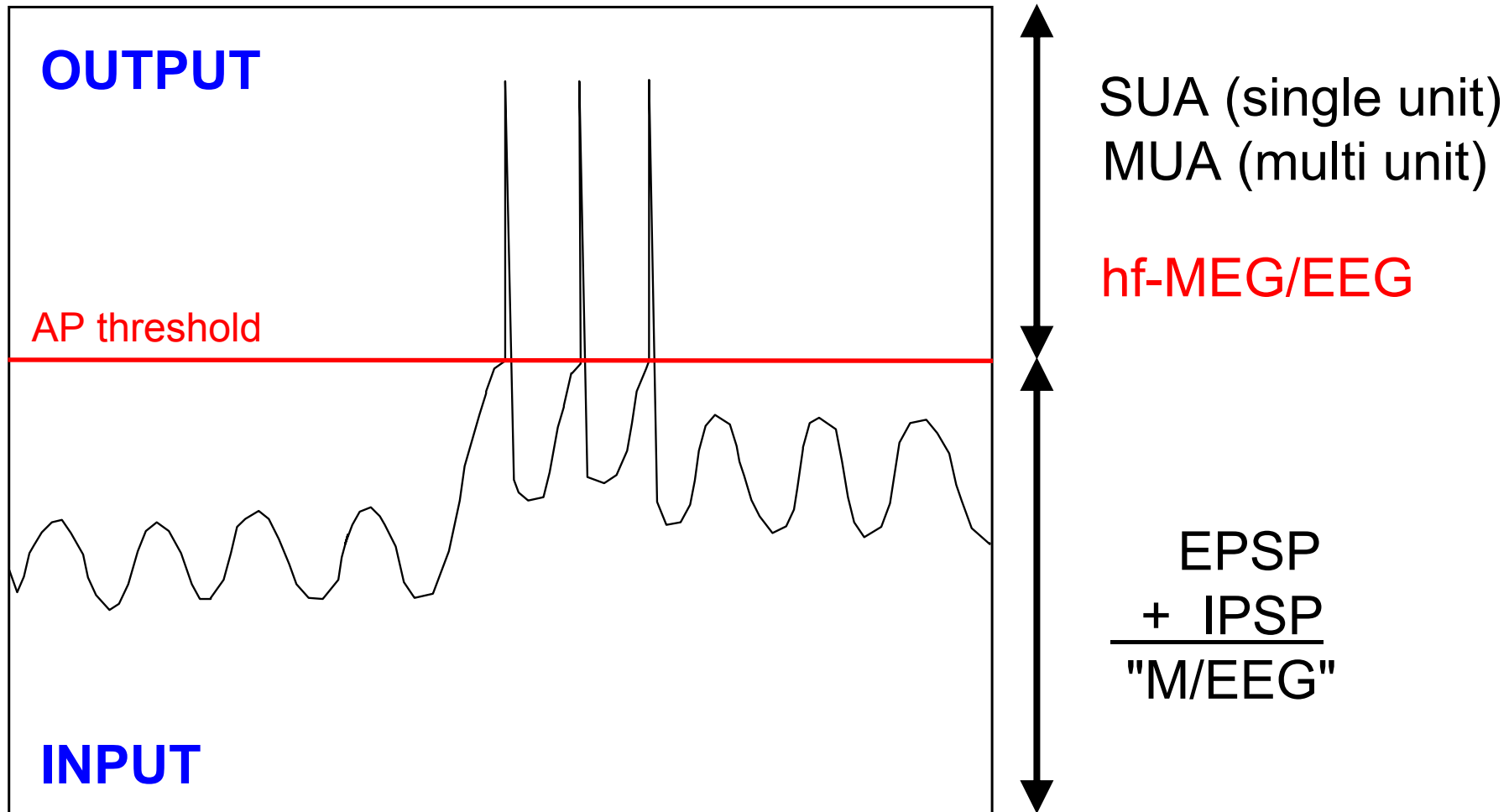
Berger's bands – and beyond

standard low-frequency EEG bands



**non-invasive analysis of
the timing of rapidly repeating population spike bursts
in the human somatosensory system**

Standard-MEG/EEG: Σ (EPSP + IPSP)



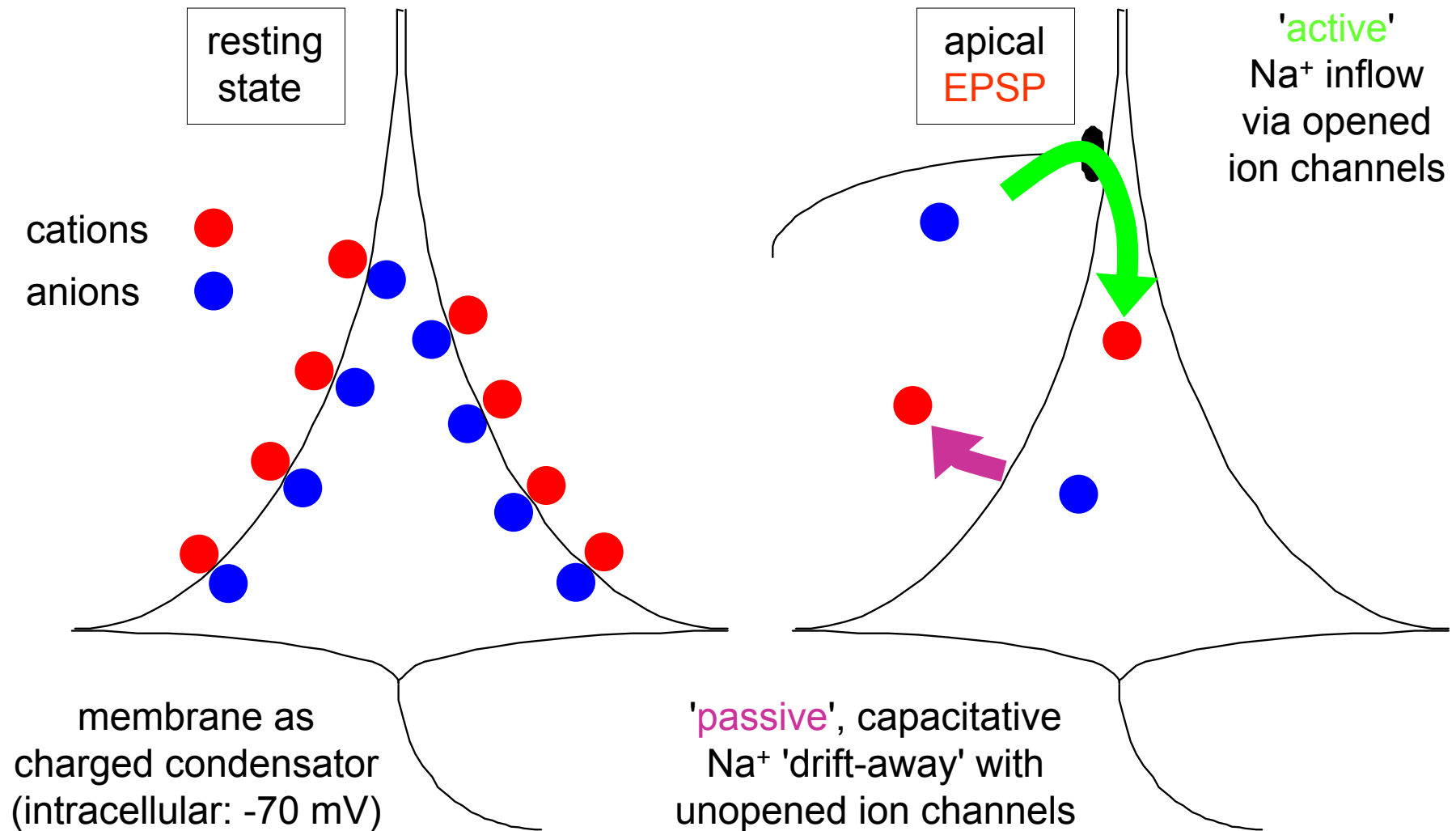
Neurophysics of hf-EEG (... and MEG)

1. Overview:

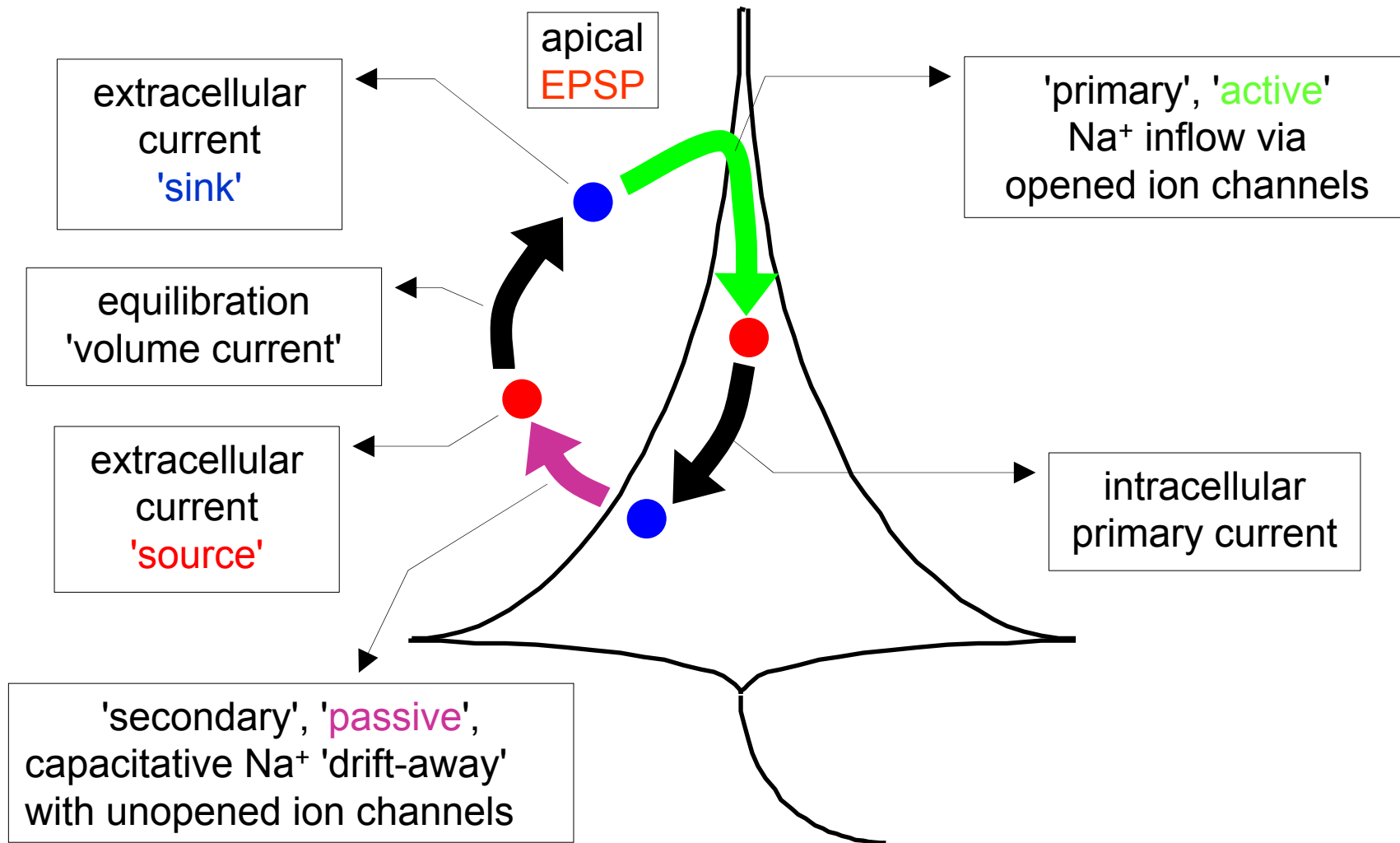
Terms of the Problem

near-fields	far-fields
real dipoles	virtual dipoles
primary sources	secondary sources
traveling peaks	stationary peaks
active current sources	junctional potentials

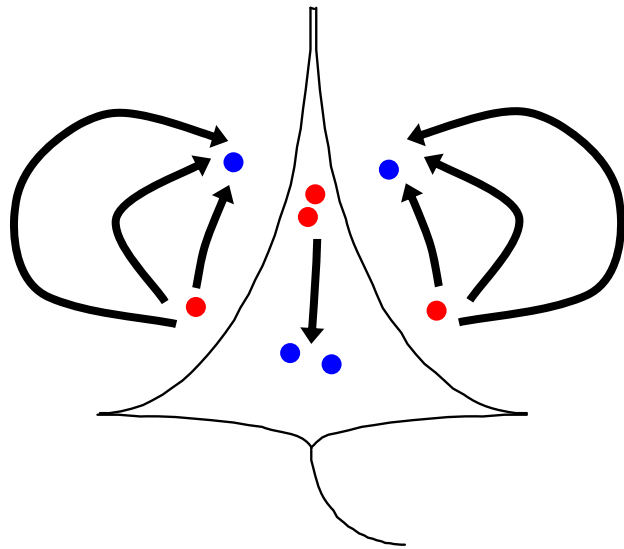
2. Ion currents and membrane potential



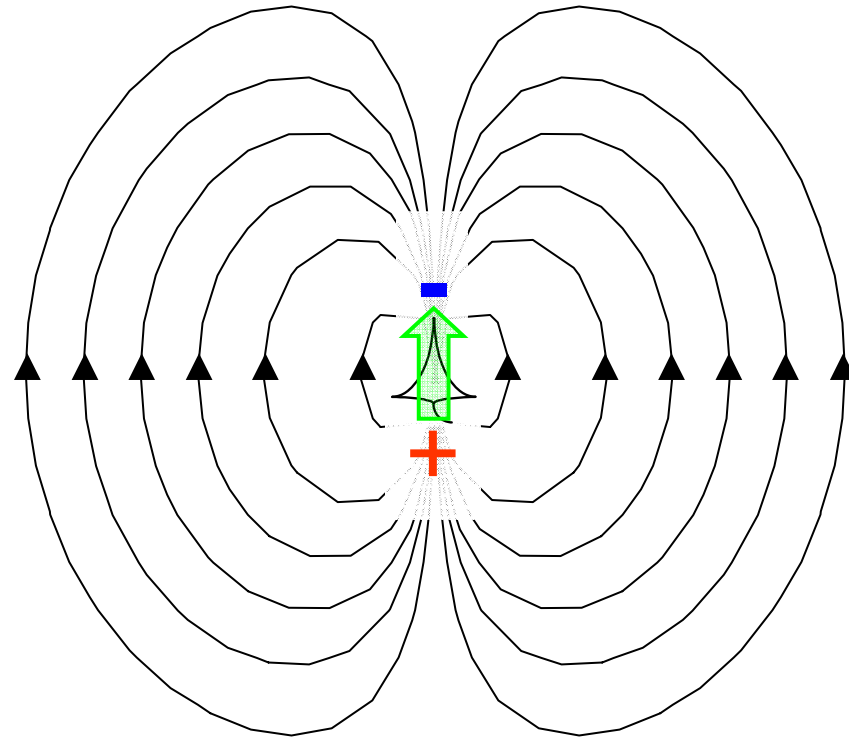
3. Closing the current loop



4. Equivalent Current Dipole (ECD)

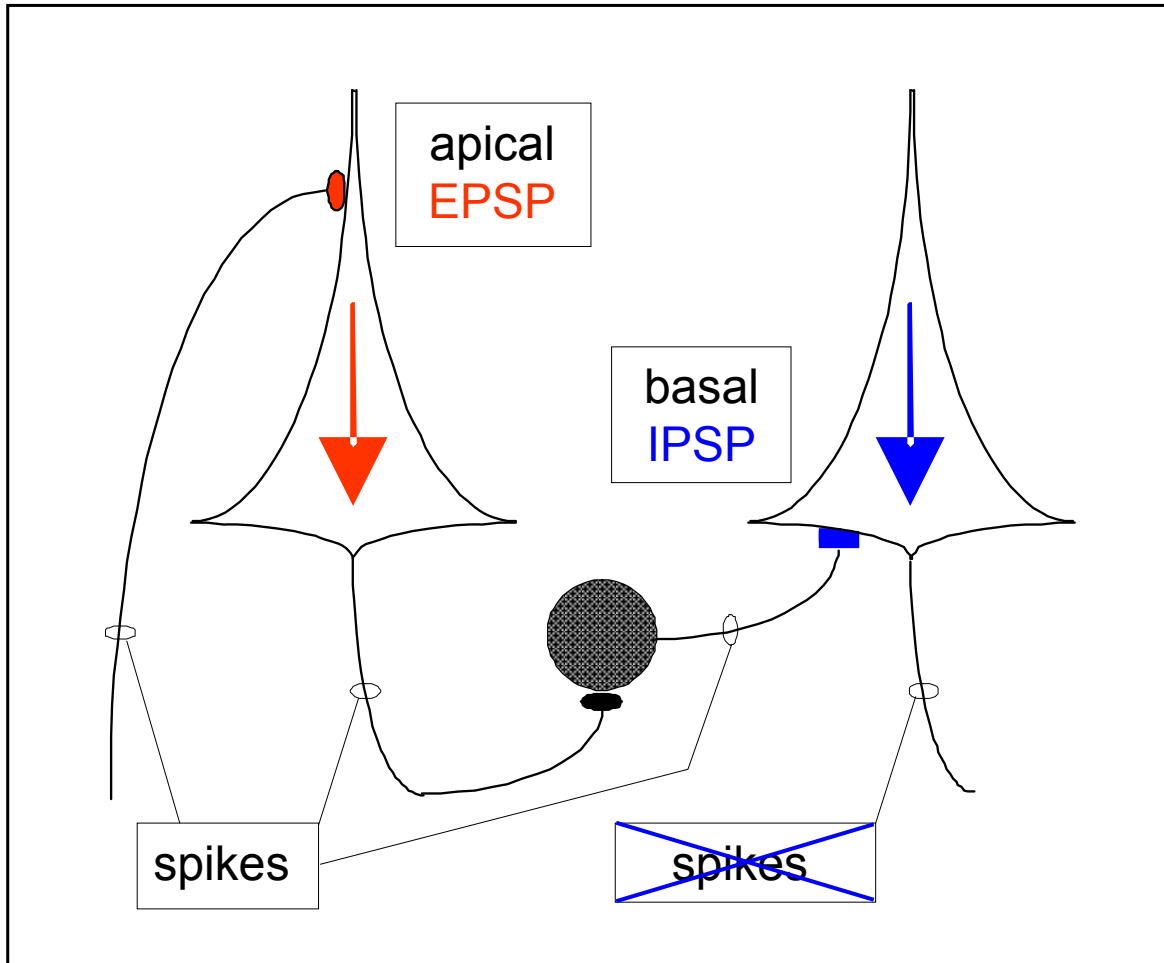


intra- and extracellular:
current sources → current sinks



EEG: extracellular volume currents

5. Synaptic events: EPSP and IPSP

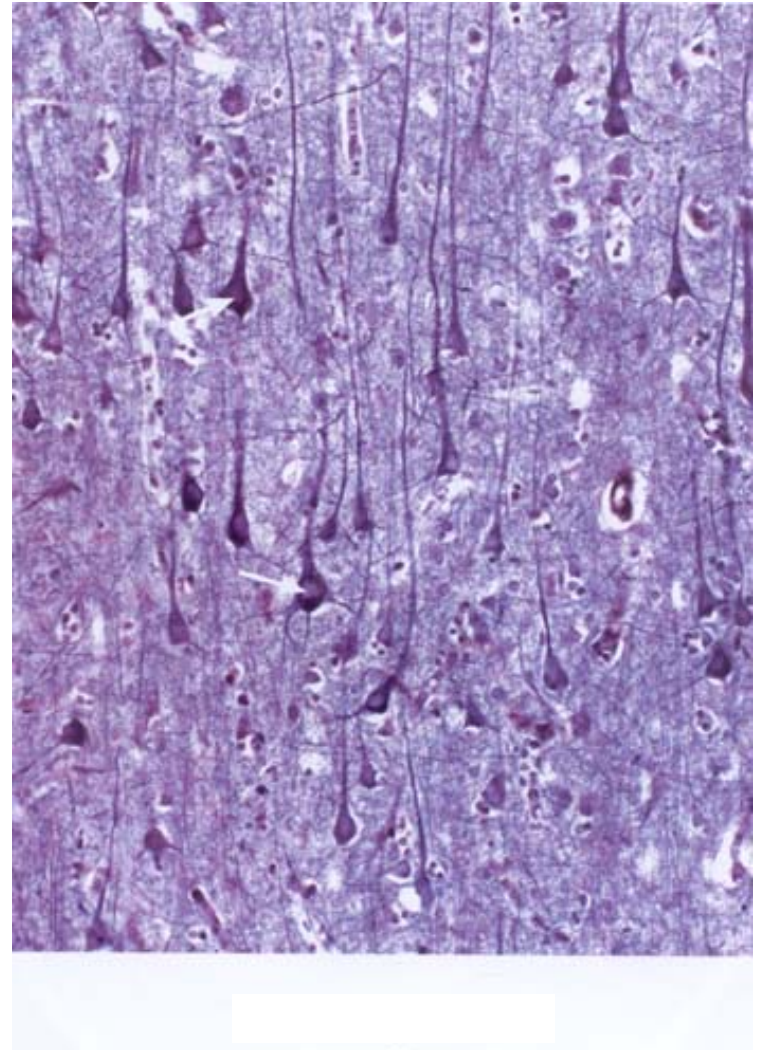
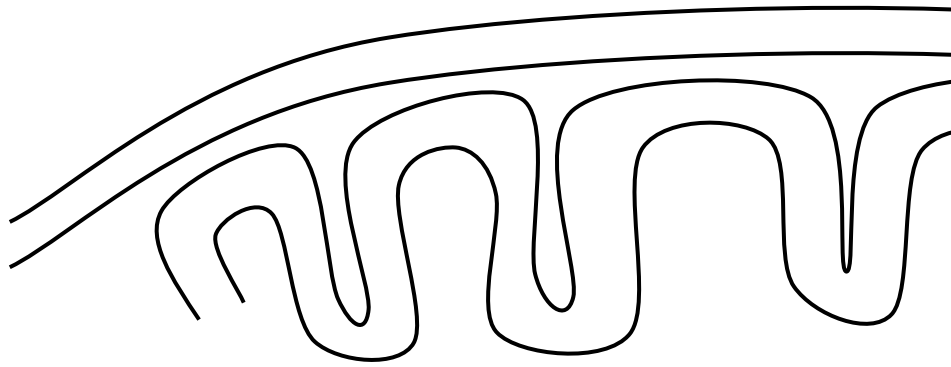


EPSP =
excitatory
postsynaptic
potential
(glutamate: Na^+_{in})

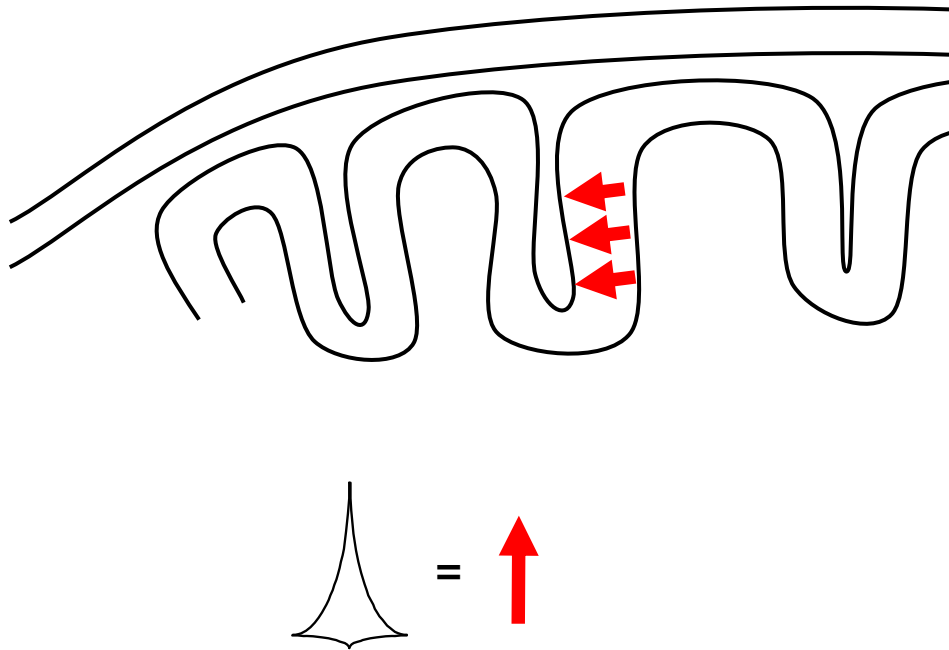
IPSP =
inhibitory
postsynaptic
potential
(GABA_A : Cl^-_{in})

net current flow: apical **EPSP** = basal **IPSP**

6. Far fields: **tangential** cortical dipoles

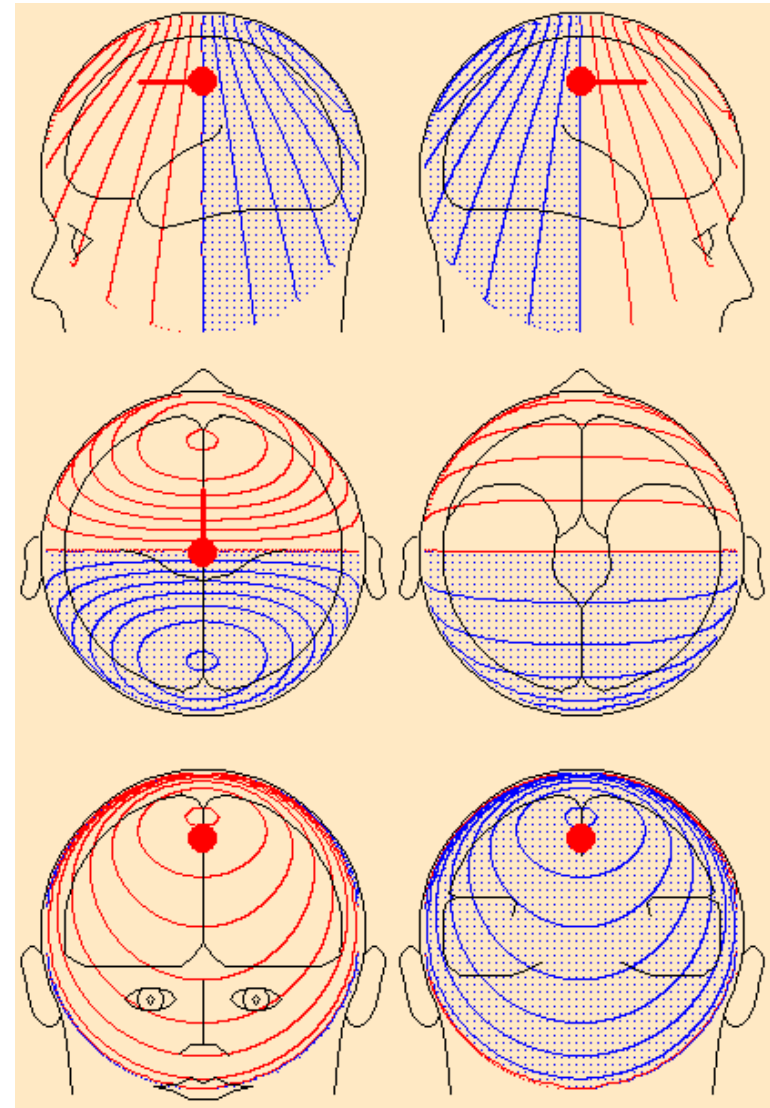


6. Far fields: **tangential** cortical dipoles



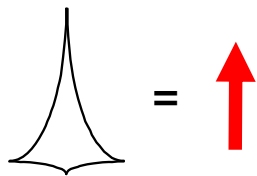
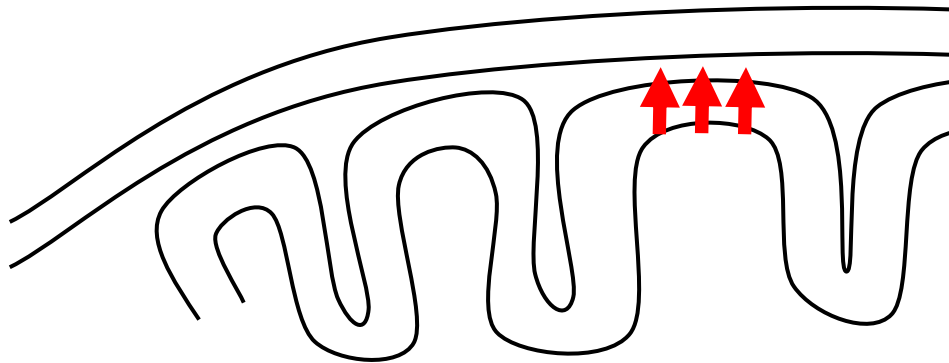
'open field' from pyramidal cells:

- elongated structure = apical dendrite
- parallel structure = summation due to 'palisade' arrangement



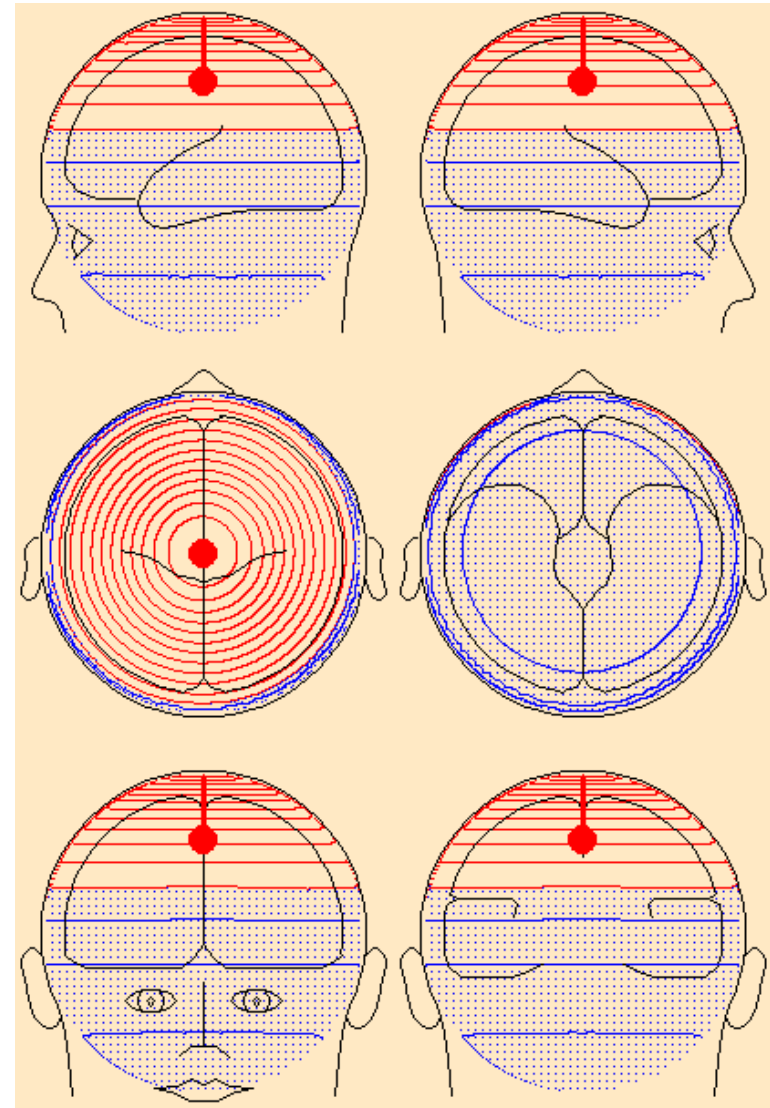
DipoleSimulator © P. Berg (2002)

7. Far fields: radial cortical dipoles



'open field' from pyramidal cells:

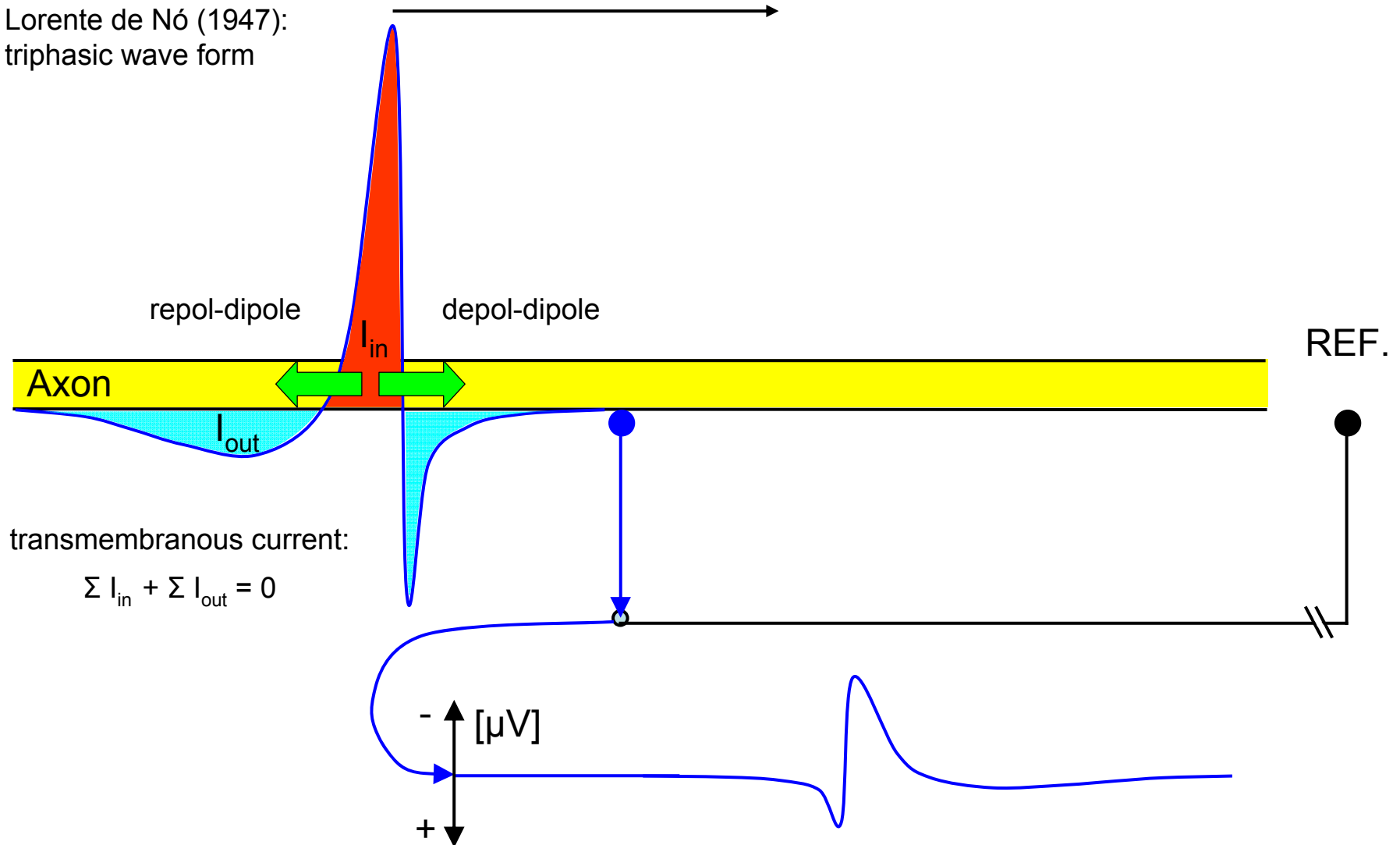
- elongated structure = apical dendrite
- parallel structure = summation due to 'palisade' arrangement



DipoleSimulator © P. Berg (2002)

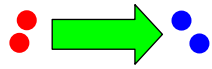
8. Propagating action potential

Lorente de Nó (1947):
triphasic wave form



9. Infinite vs. finite volume conductor

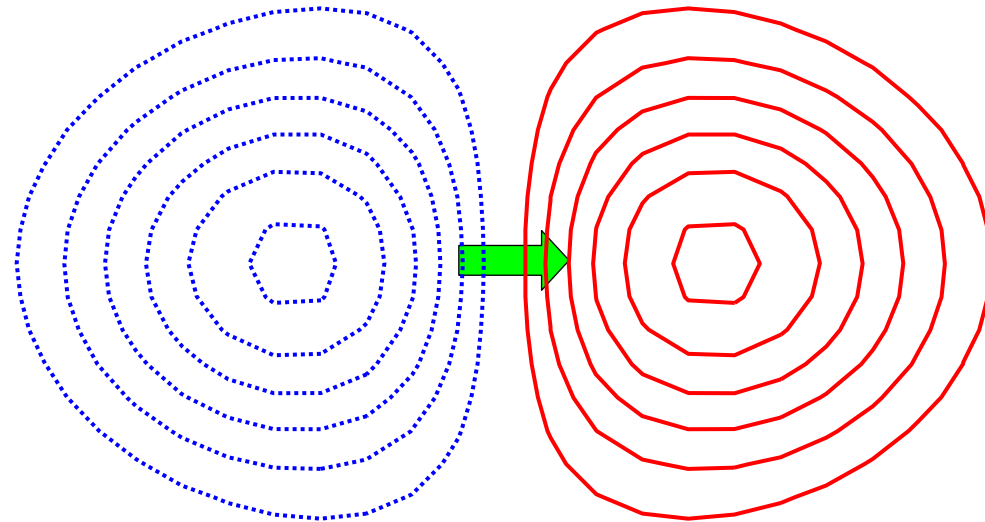
current dipole in
infinite volume conductor



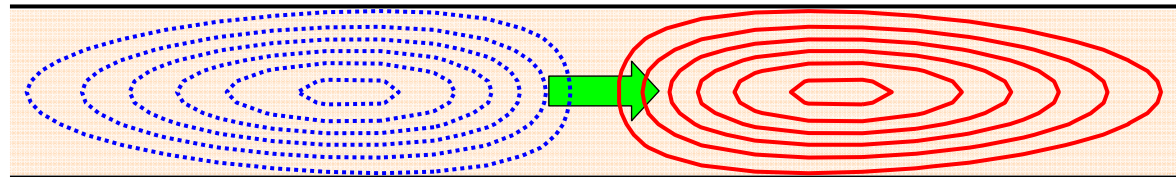
intracellular
current dipole



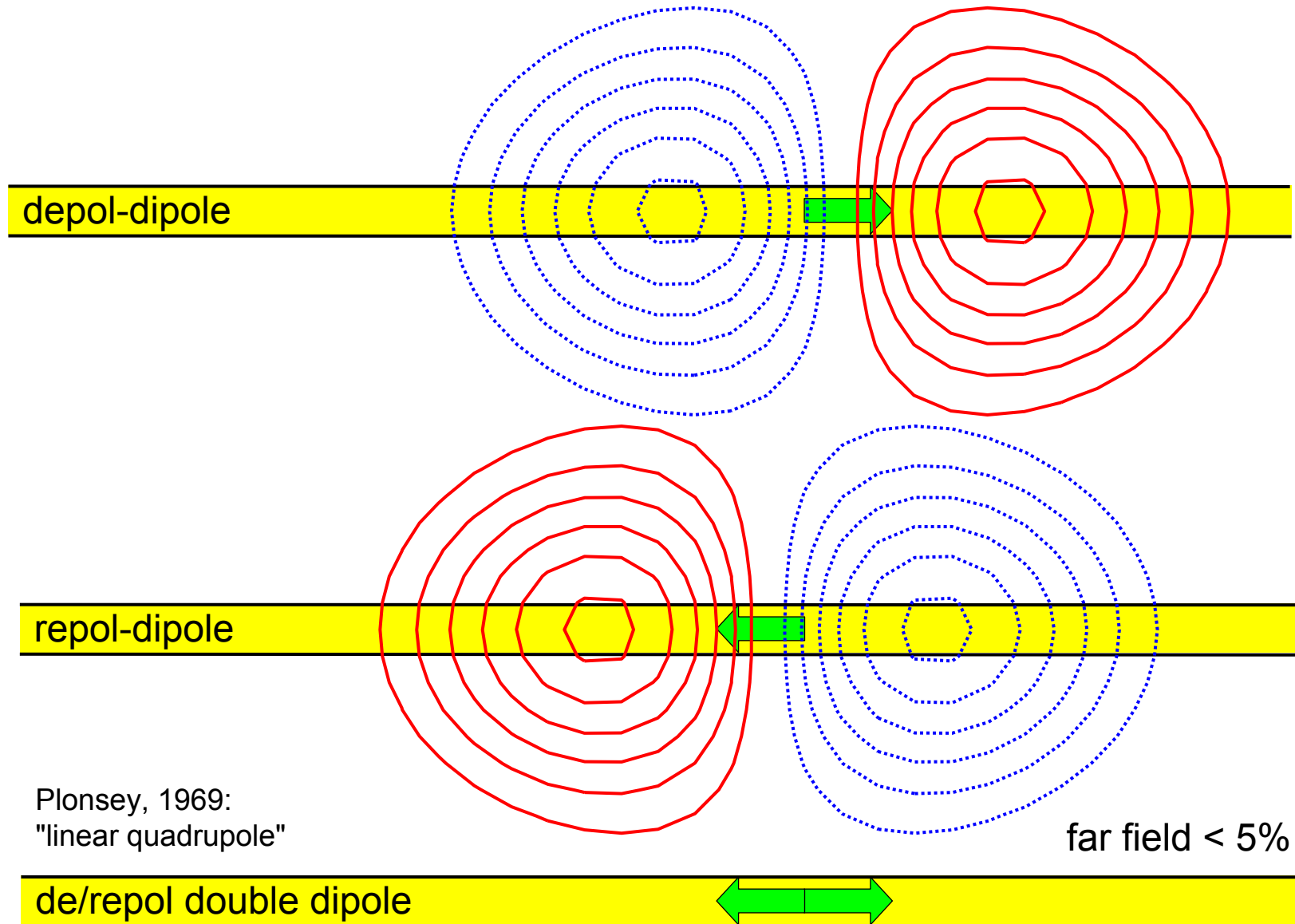
extracellular
potential distribution



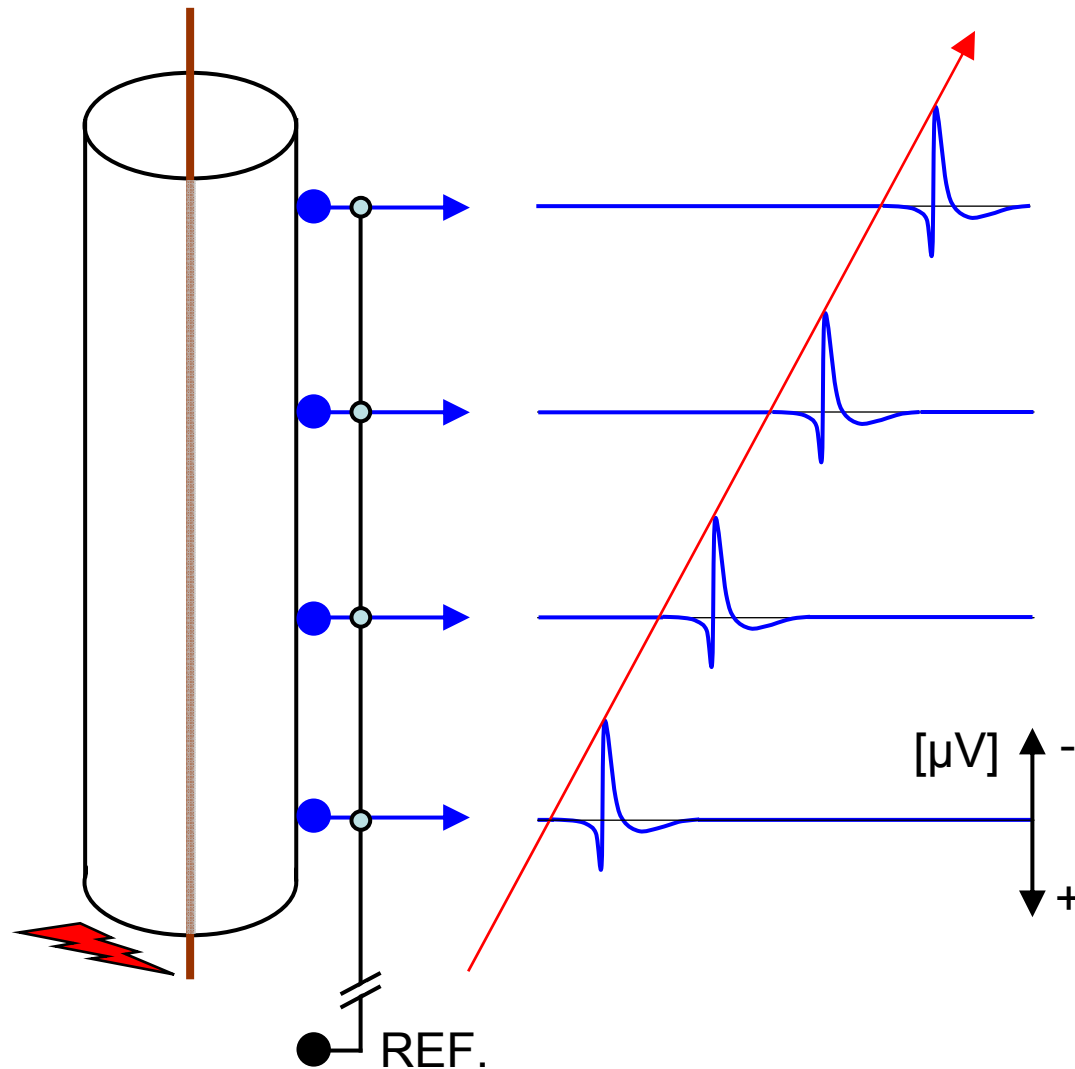
current dipole in
cylindrical volume conductor



10. Action potential: quadrupole



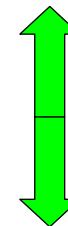
11. Homogenous volume conductor



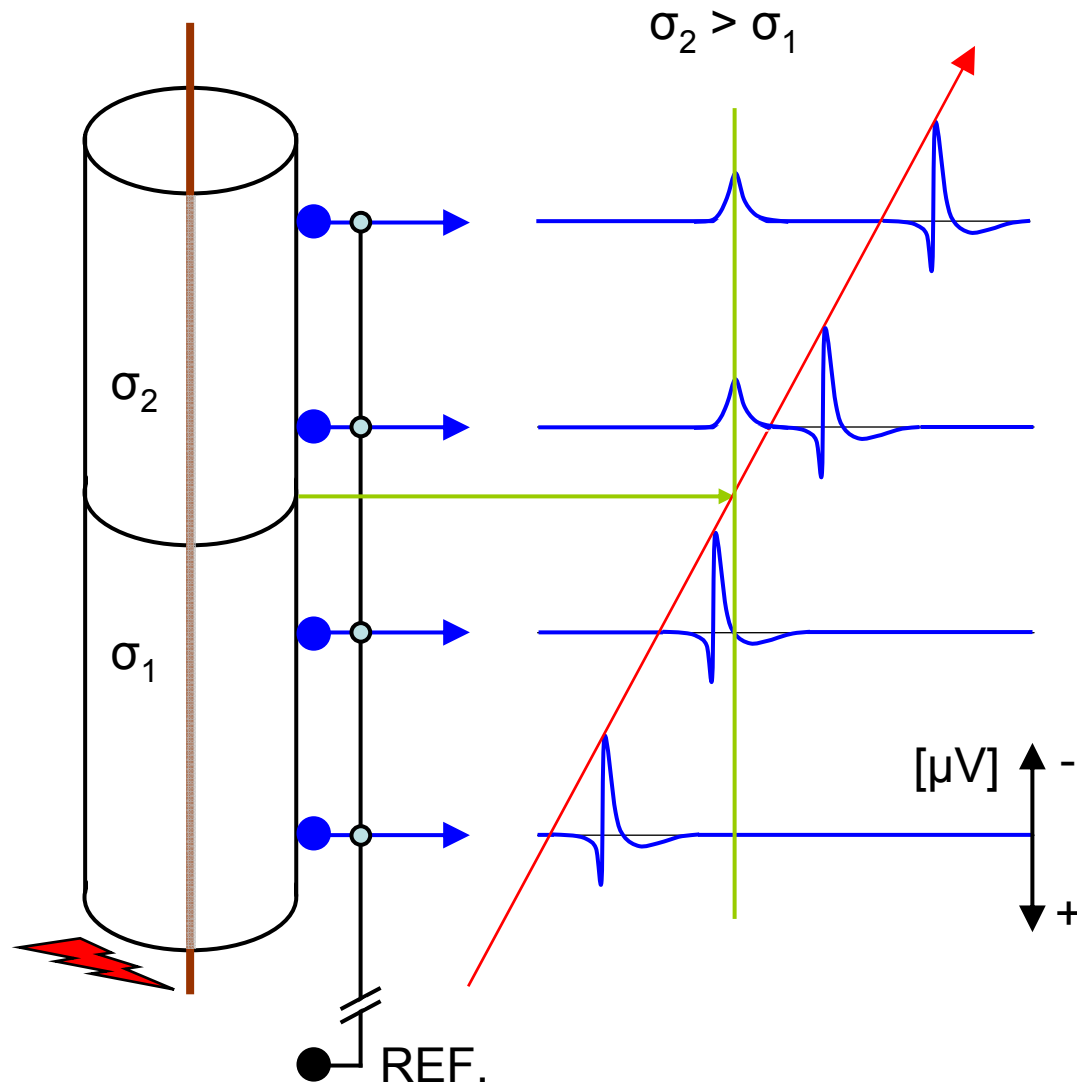
ONLY near-field components

NO far-field due to *balanced* quadrupole structure of the propagating action potential with almost complete cancellation of dipole fields from depol and repol currents

depol-dipole
repol-dipole



12. Conductivity Change: Ohm's Law

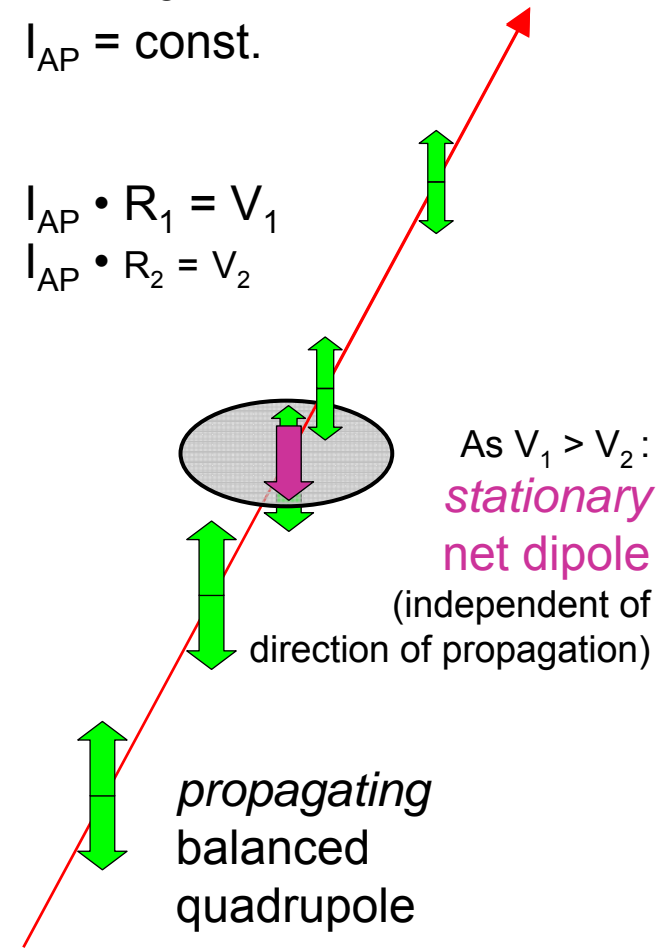


$$R \sim 1/\sigma$$

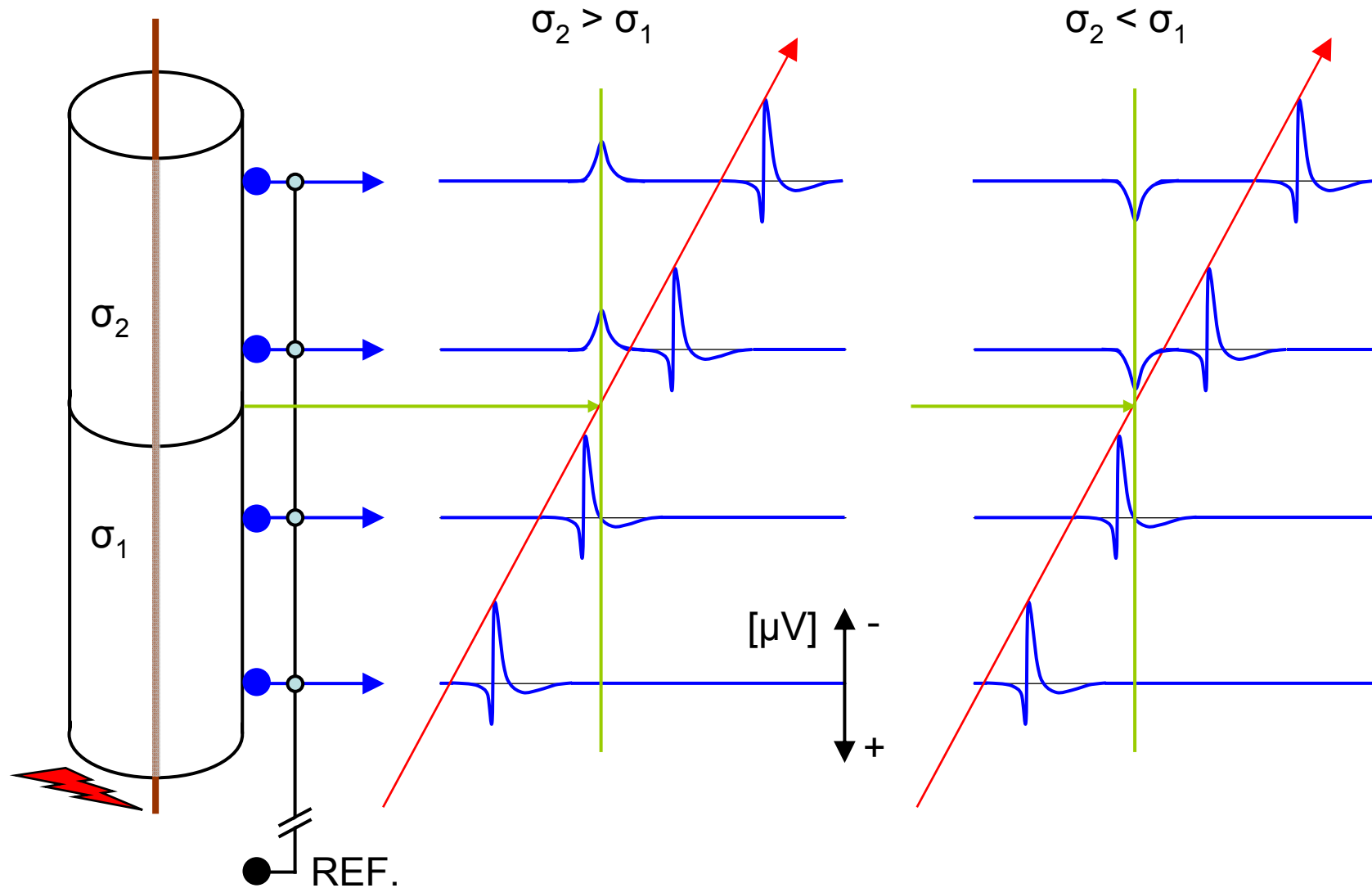
$$I_{AP} = \text{const.}$$

$$I_{AP} \cdot R_1 = V_1$$

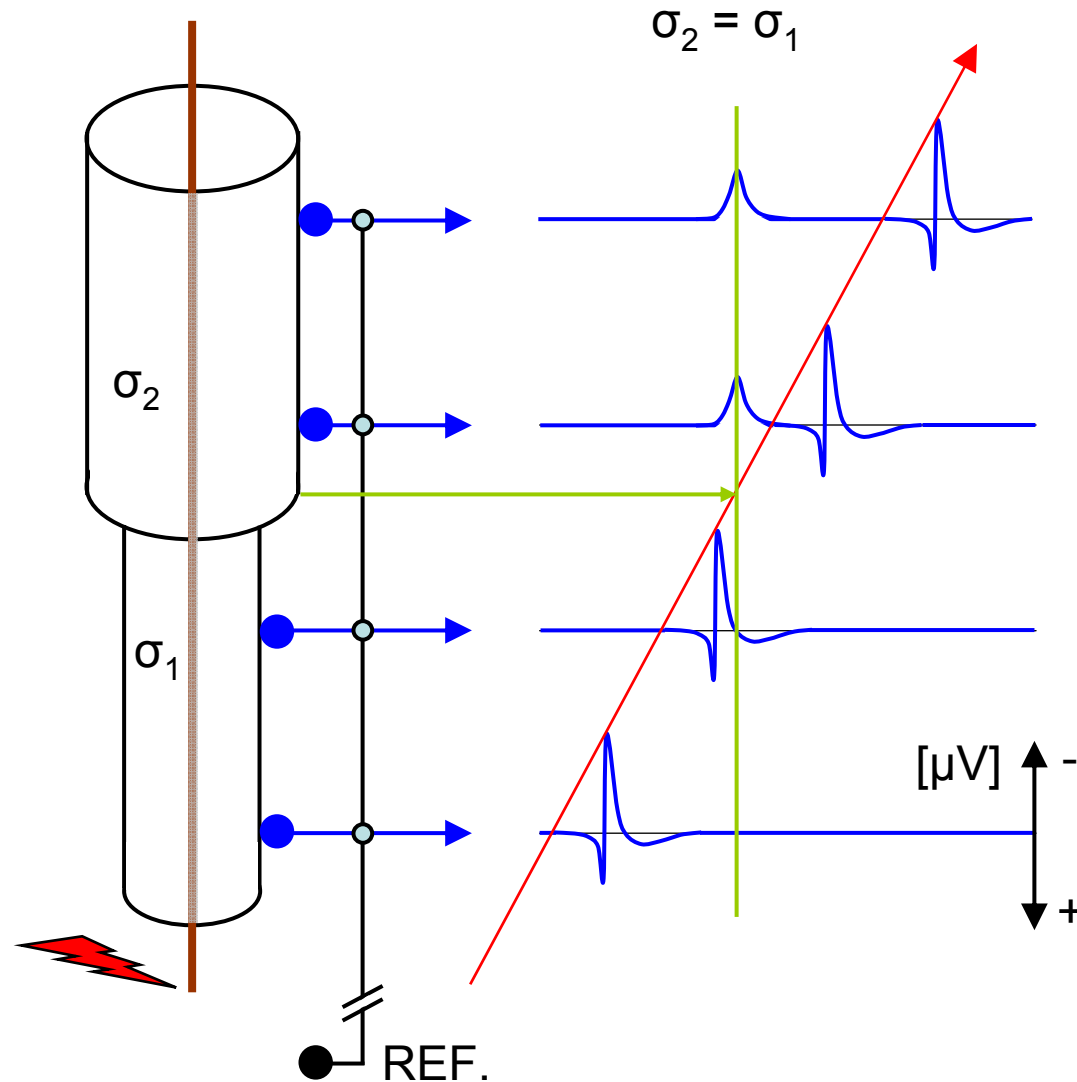
$$I_{AP} \cdot R_2 = V_2$$



13. Conductivity Change: Polarity Switch



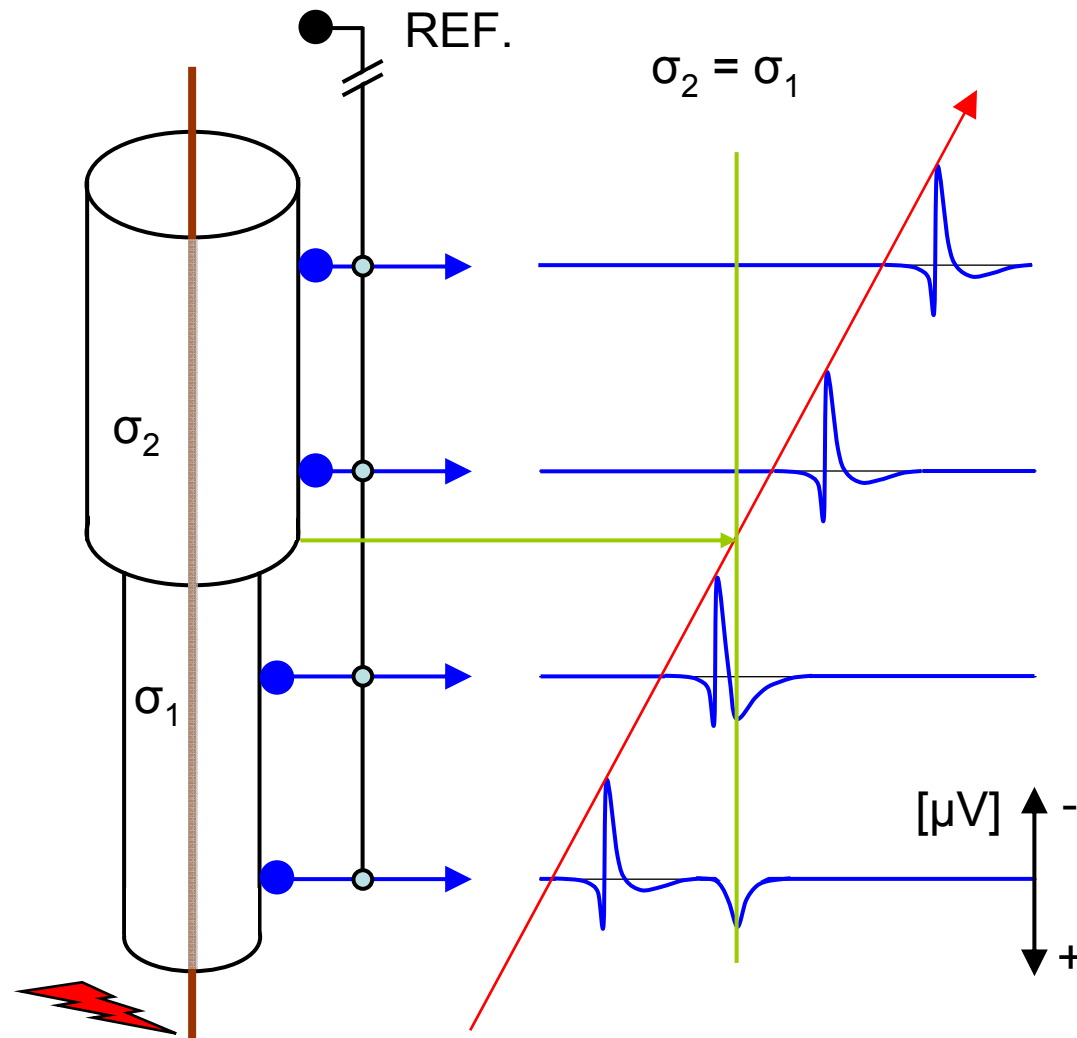
14. Geometry of volume conductor



Comparable far field components due to step-like decrease of extracellular resistance through:

- 1) increase of conductivity
- 2) widening of conductor diameter

15. Localisation of reference electrode

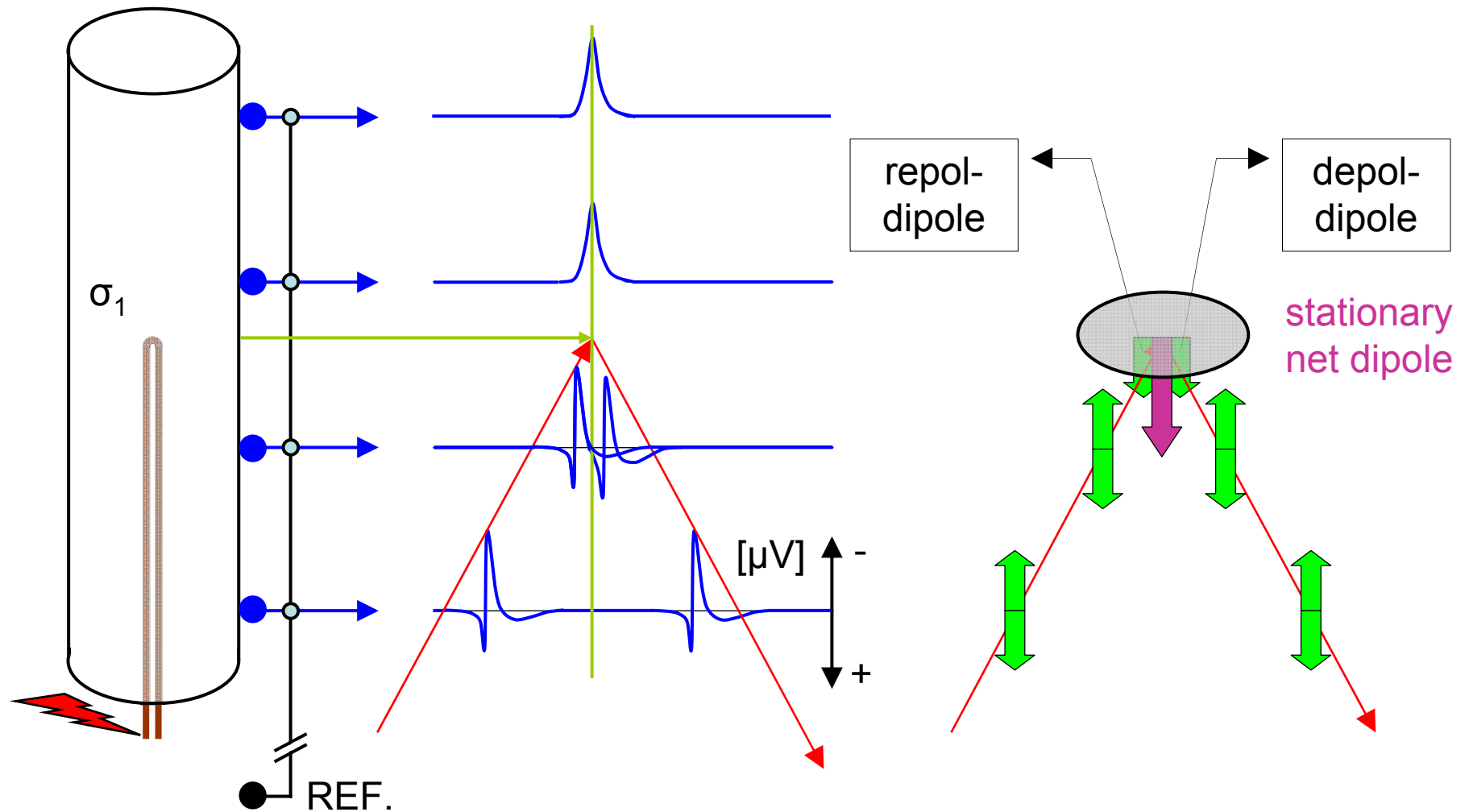


Polarity and site of a monophasic far field component depend on the placement of the reference electrode:

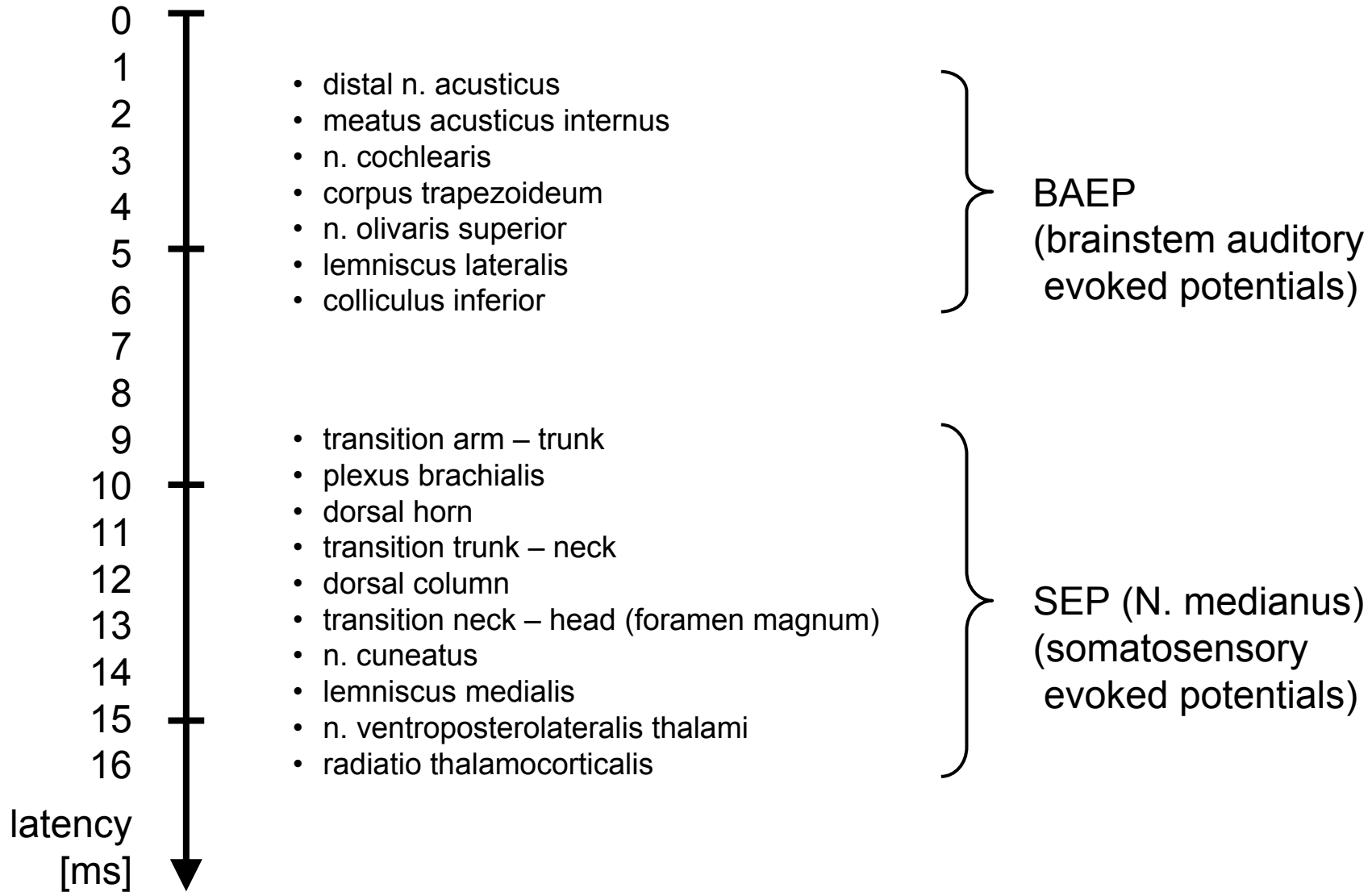
1) Far fields do NOT occur in the compartment of the reference electrode.

2) The monophasic far field is POSITIVE if the reference electrode is placed on the volume conductor part with LOWER resistance.

16. Changing direction of propagation



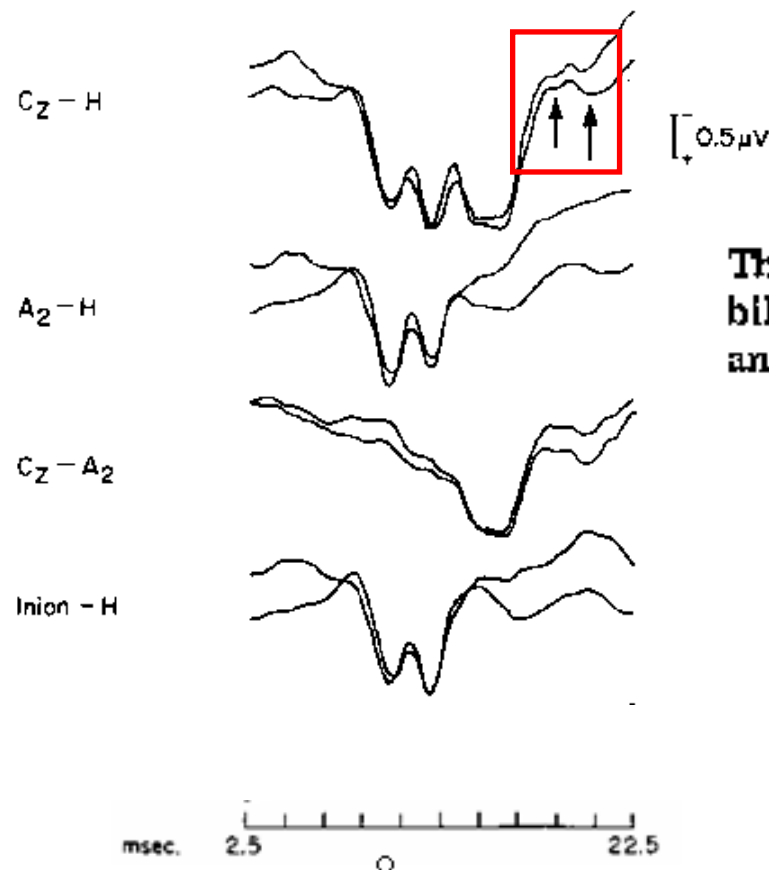
17. Subcortical far field 'generators'



SOMATOSENSORY EVOKED POTENTIAL IN MAN: FAR FIELD POTENTIALS *

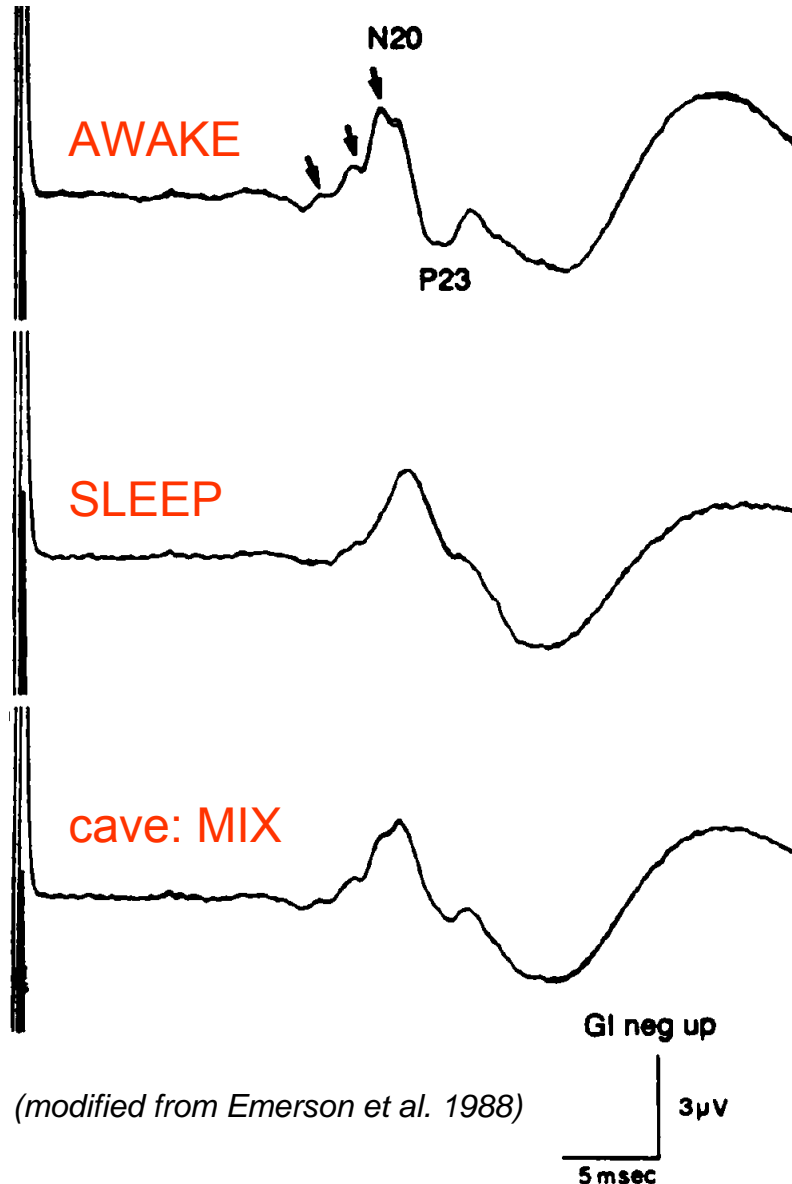
ROGER Q. CRACCO and JOAN B. CRACCO

*Department of Neurology, State University of New York, Downstate Medical Center, Brooklyn,
 N.Y. 11203 (U.S.A.)*



These potentials are followed by a poorly defined bilobed positive component with peaks at about 18.5 and 20 msec (arrows).

Early EEG studies (1976-1988)



generator hypotheses:

Cracco and Cracco (1976):
brainstem and diencephalic structures

Abbruzzese et al. (1978):

N14–P15: *n. cuneatus, medial lemniscus*

N16: *thalamus*

N17: *thalamocortical radiation*

Stöhr and Riffel (1982):

P16-P18: 1.4 ms = 714 Hz; *volley ascending in thalamocortical afferents*

Maccabee et al. (1983, 1986):

N16 *caudal thalamocortical radiation*

N18 *rostral thalamocortical radiation*

functional dissociation:

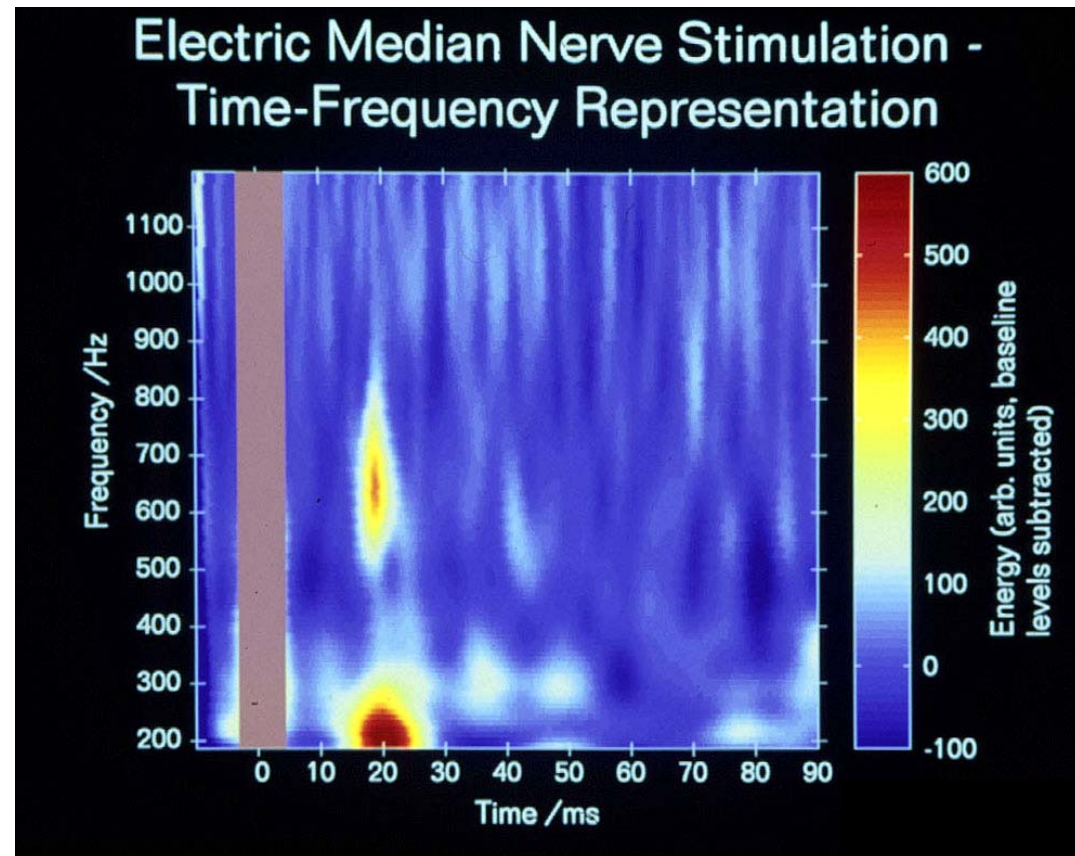
Emerson et al. (1988), Yamada et al. (1988):
during sleep: hf-oscillation ↓ vs. N20 ⇔

MEG: **Cortical** burst generator

Electroencephalography and clinical Neurophysiology, 91 (1994) 483–487

Localization of evoked neuromagnetic 600 Hz activity in the cerebral somatosensory system

Gabriel Curio ^{a*}, Bruno-Marcel Mackert ^a, Martin Burghoff ^b, Roman Koetitz ^b,
Klaus Abraham-Fuchs ^c and Wolfgang Härer ^c

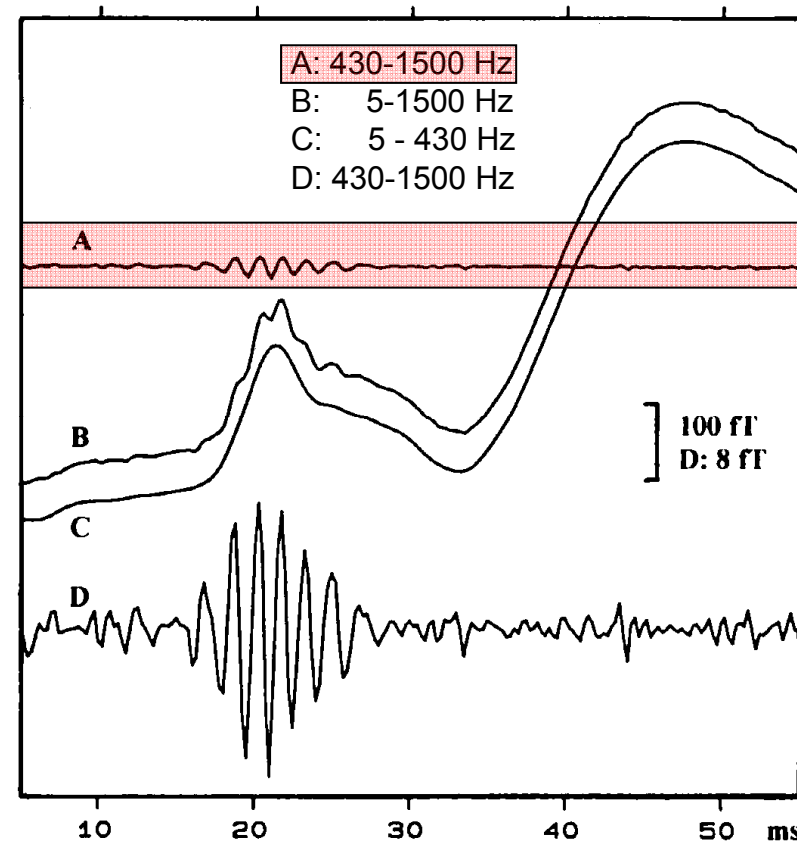


MEG: Cortical burst generator

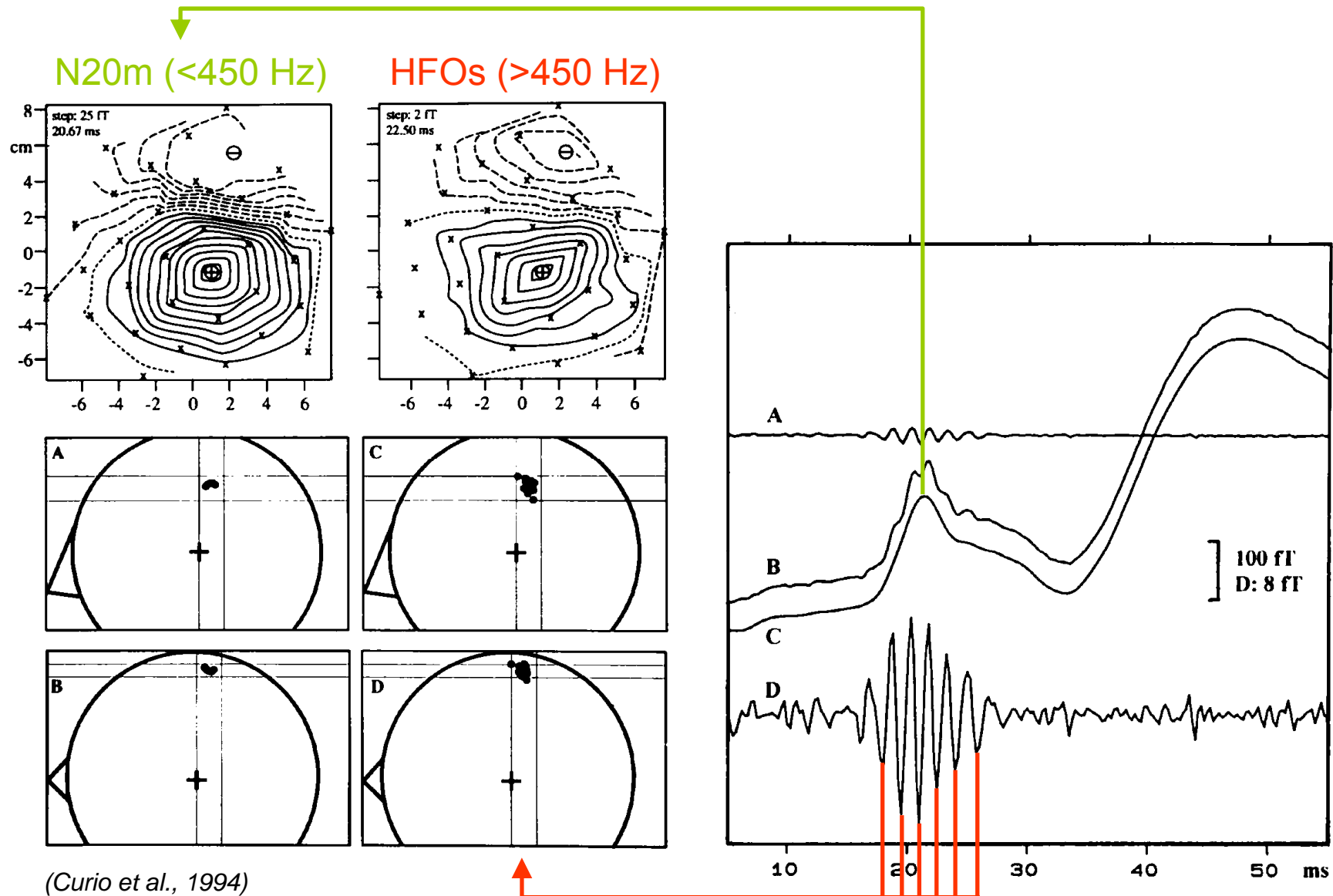
Electroencephalography and clinical Neurophysiology, 91 (1994) 483–487

Localization of evoked neuromagnetic 600 Hz activity in the cerebral somatosensory system

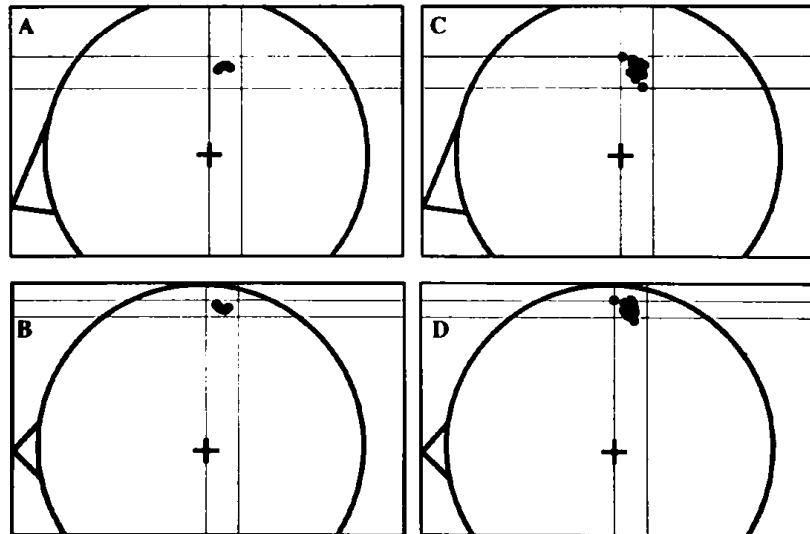
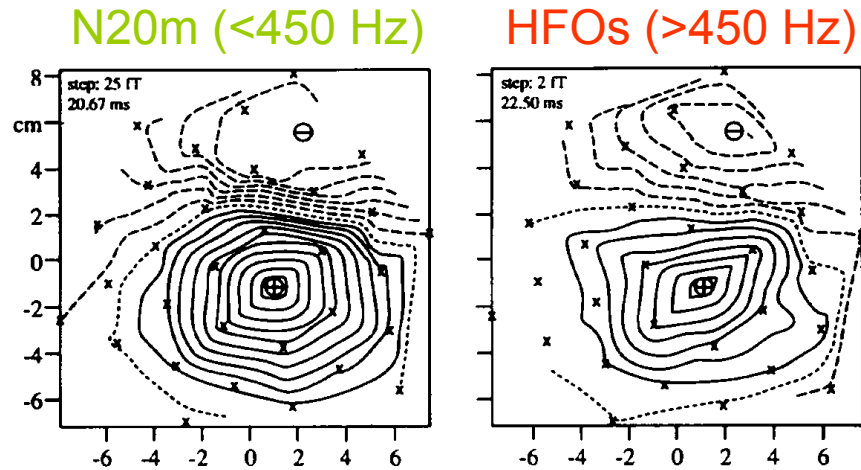
Gabriel Curio ^{a*}, Bruno-Marcel Mackert ^a, Martin Burghoff ^b, Roman Koetitz ^b,
Klaus Abraham-Fuchs ^c and Wolfgang Härer ^c



Co-localisation of N20m and 600 Hz burst

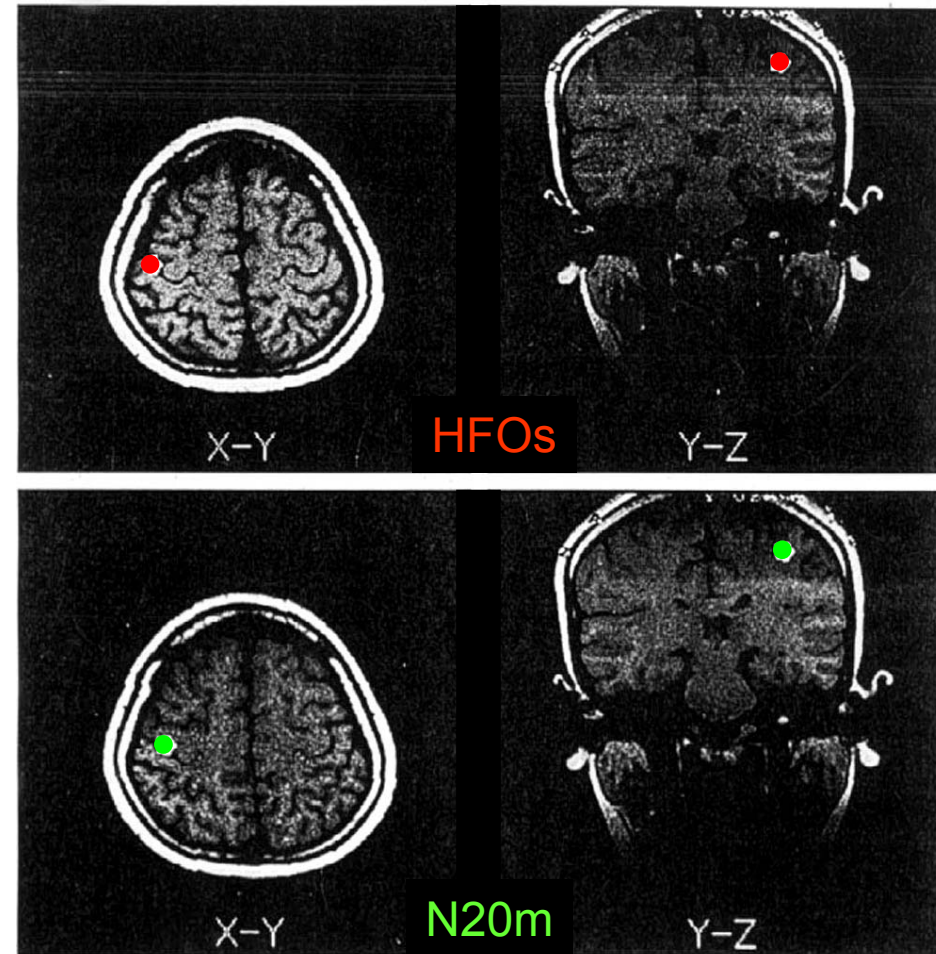


Co-localisation of N20m and 600 Hz burst

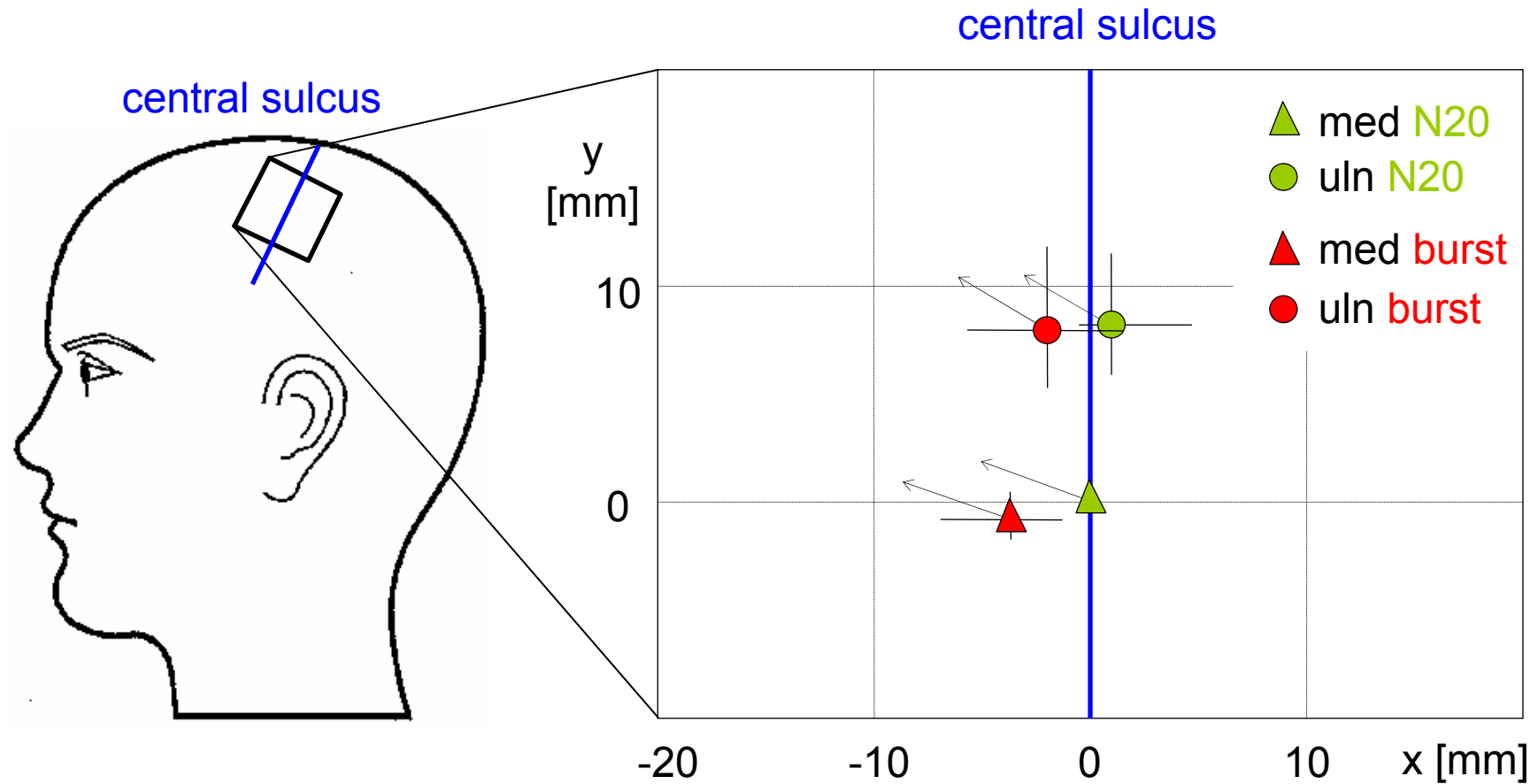


(Curio et al., 1994)

(modified from Hashimoto et al. 1996)



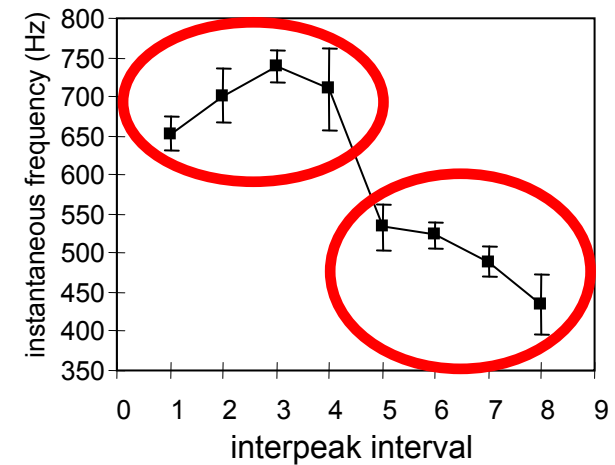
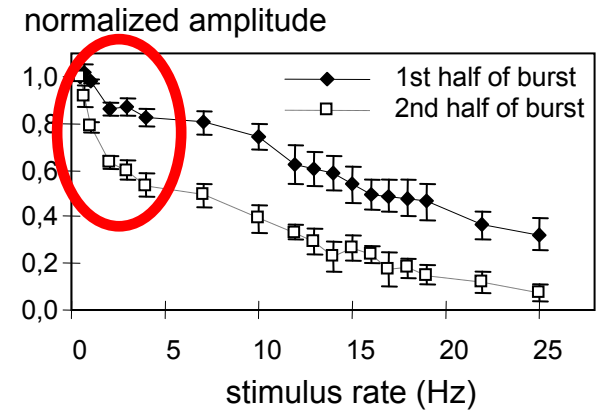
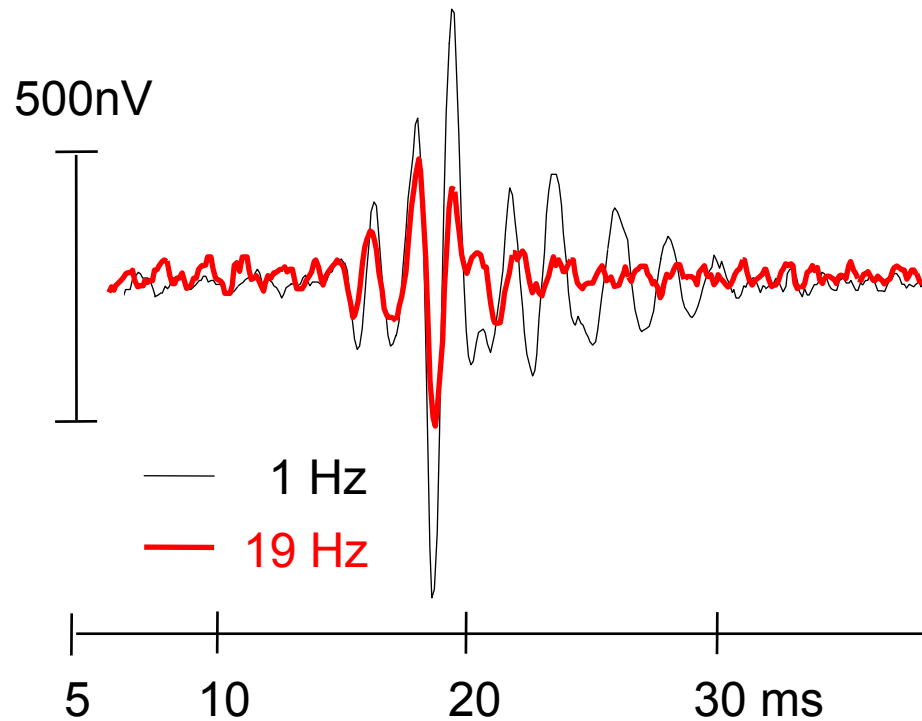
Somatotopy



High-resolution (7 mm) **somatotopy** of burst generators in S-1

(Curio et al., 1997)

Burst components: stimulation rate

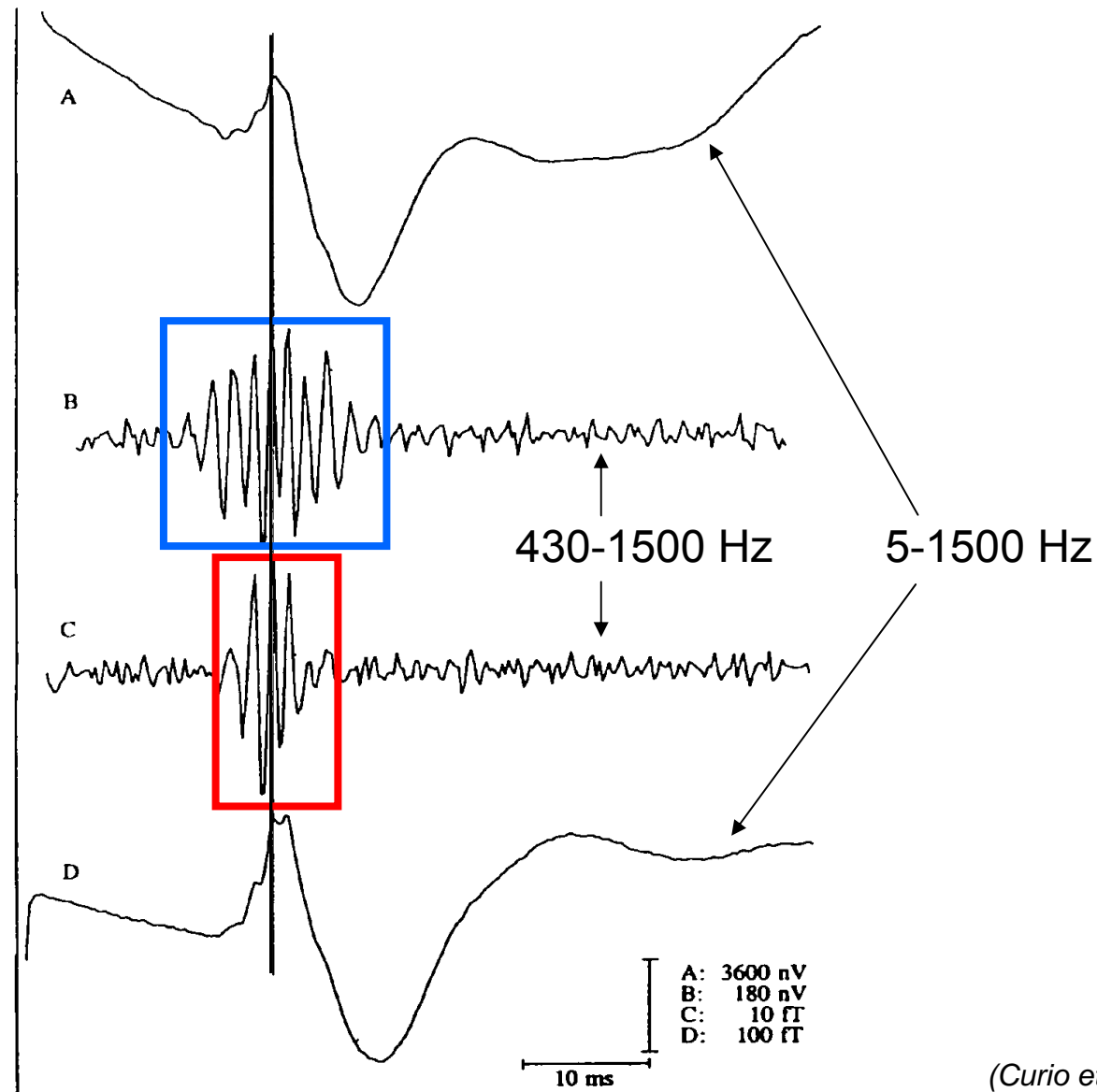


(modified from Klostermann, Nolte and Curio; 1999)

Burst components: simultaneous **MEG** + **EEG**

A, B: **EEG**
early **radial**: TC aff.
late **radial**: area 1

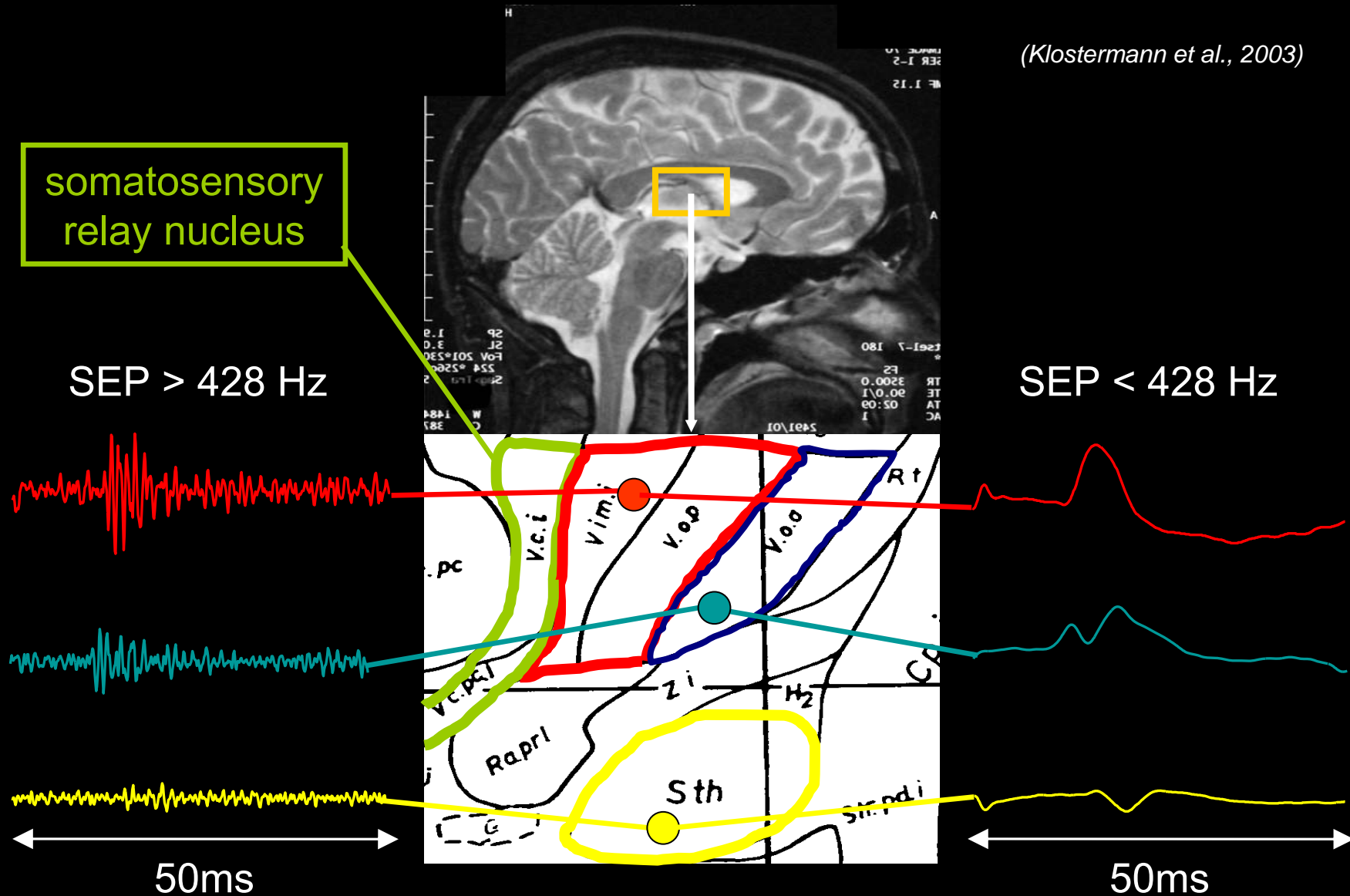
C, D: **MEG**
tangential: area 3b



(Curio et al., 1994)

Thalamic SEP: Deep Brain Stimulation (DBS)

(Klostermann et al., 2003)



Physiology in LGN: Intensity

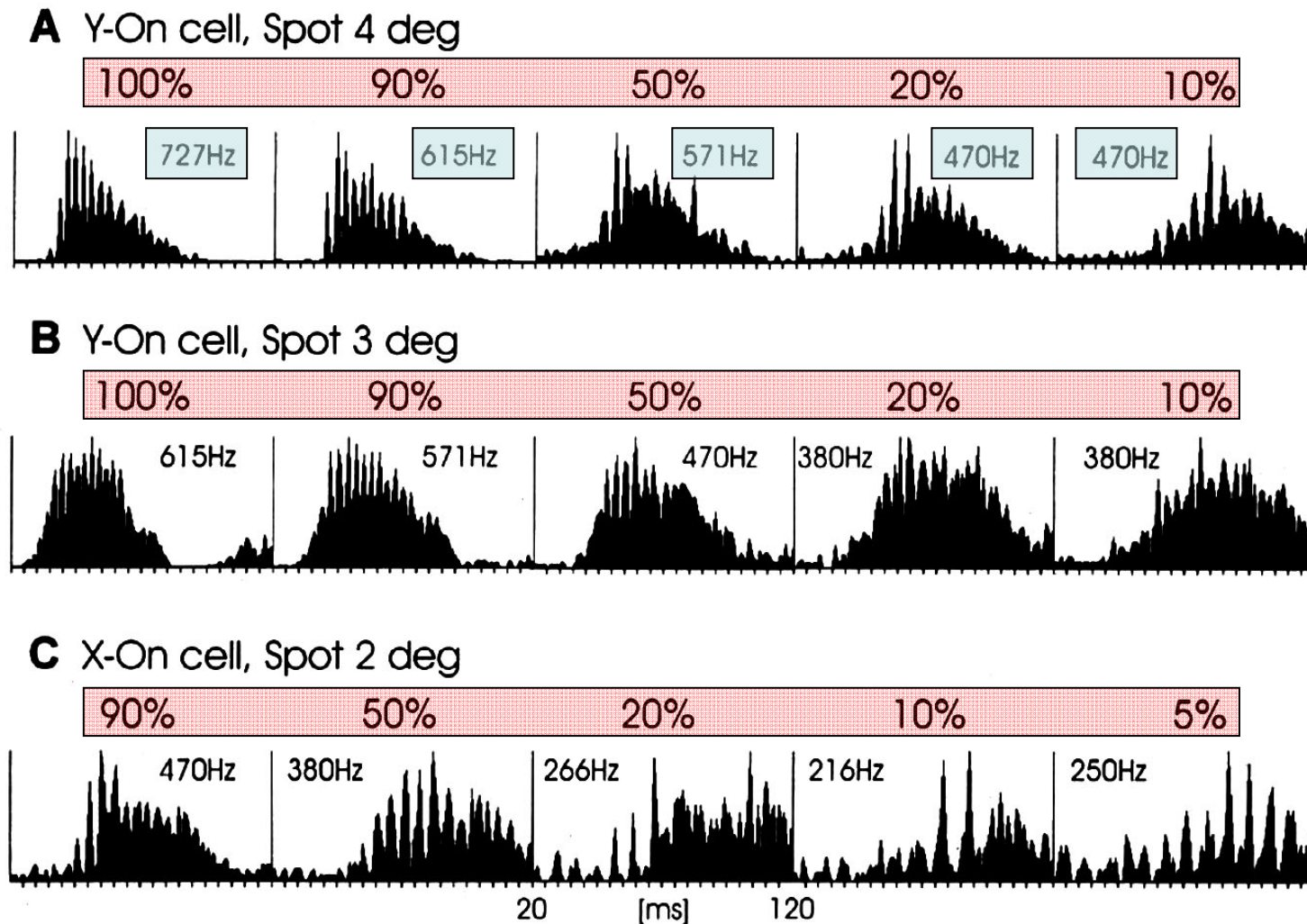
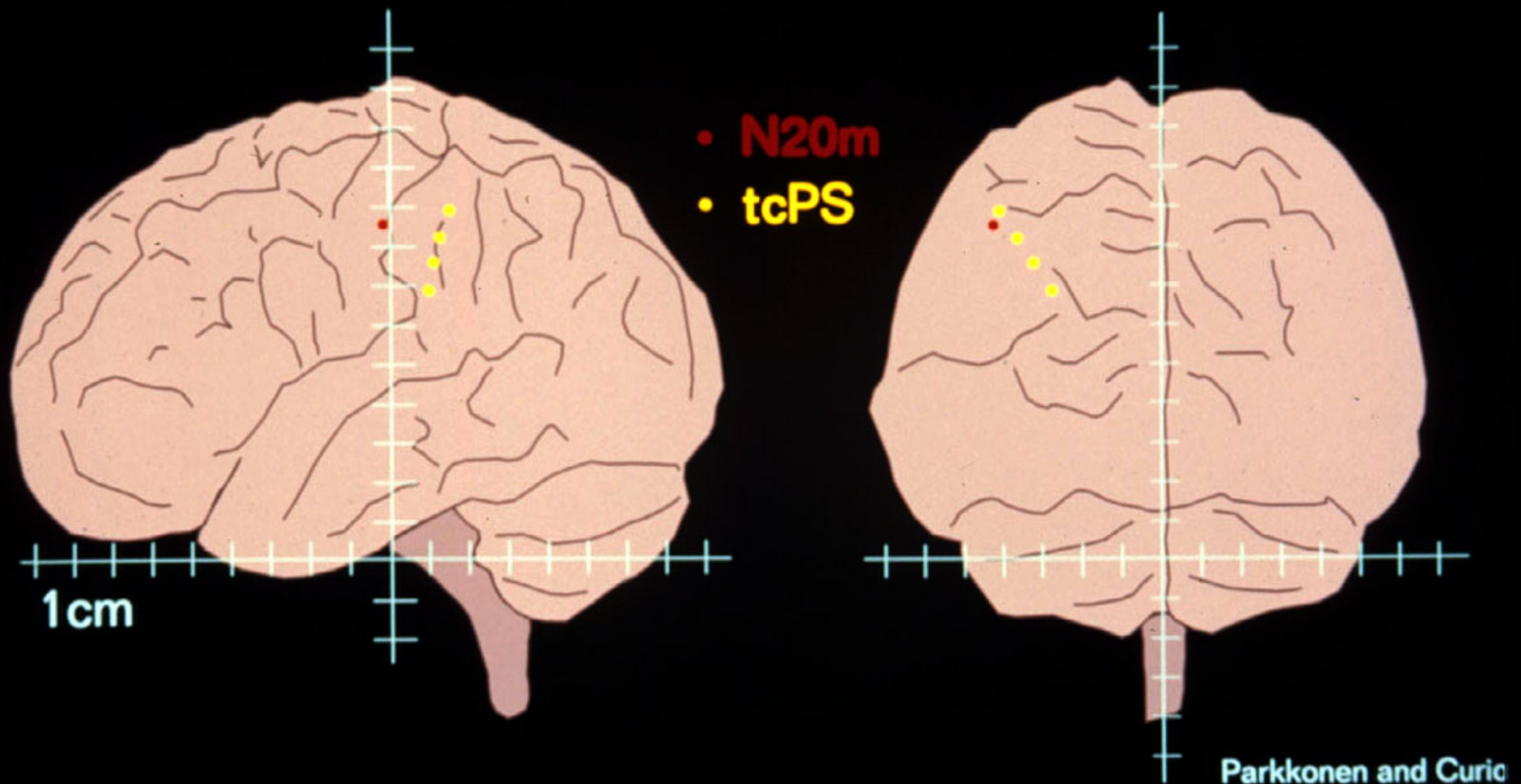


Figure 4. Initial light responses of two Y-cells (A, B) and one X-cell (C) elicited by light spots of constant size but varied intensity, resulting in 100, 90, 50, 20, 10 and 5% contrast to background. Frequency of the oscillation declines with decreasing stimulus contrast.

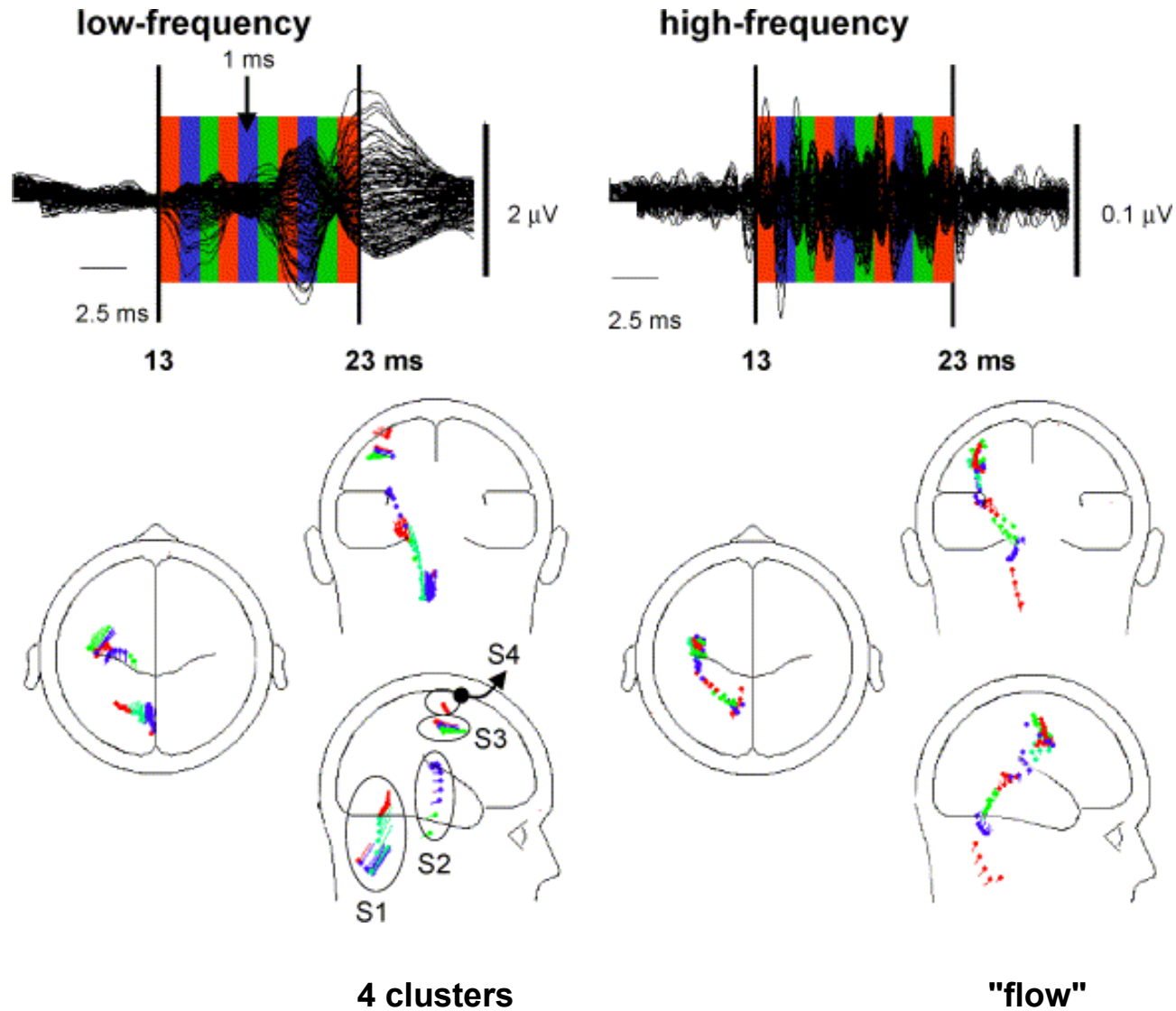
(modified from Funke and Kerscher, 2000)

Early Median Nerve Somatosensory Evoked Responses



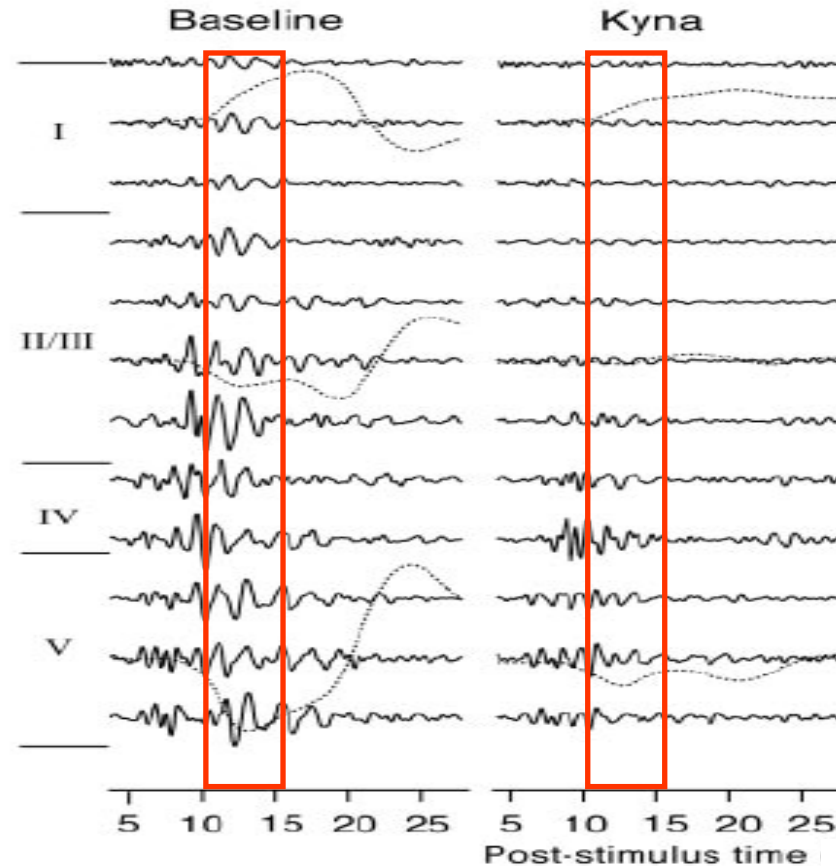
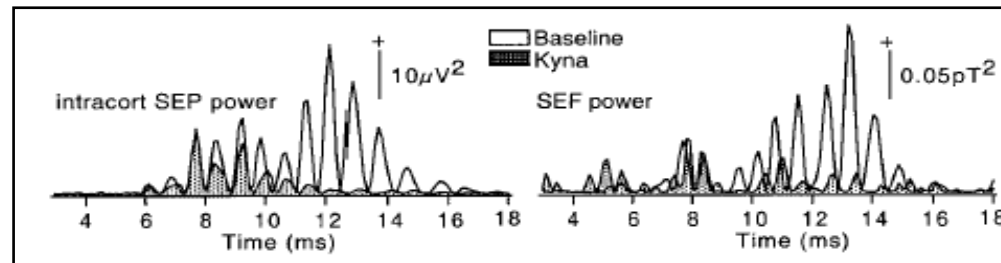
306 channel MEG helmet
(102 magnetometers)

EEG source analysis



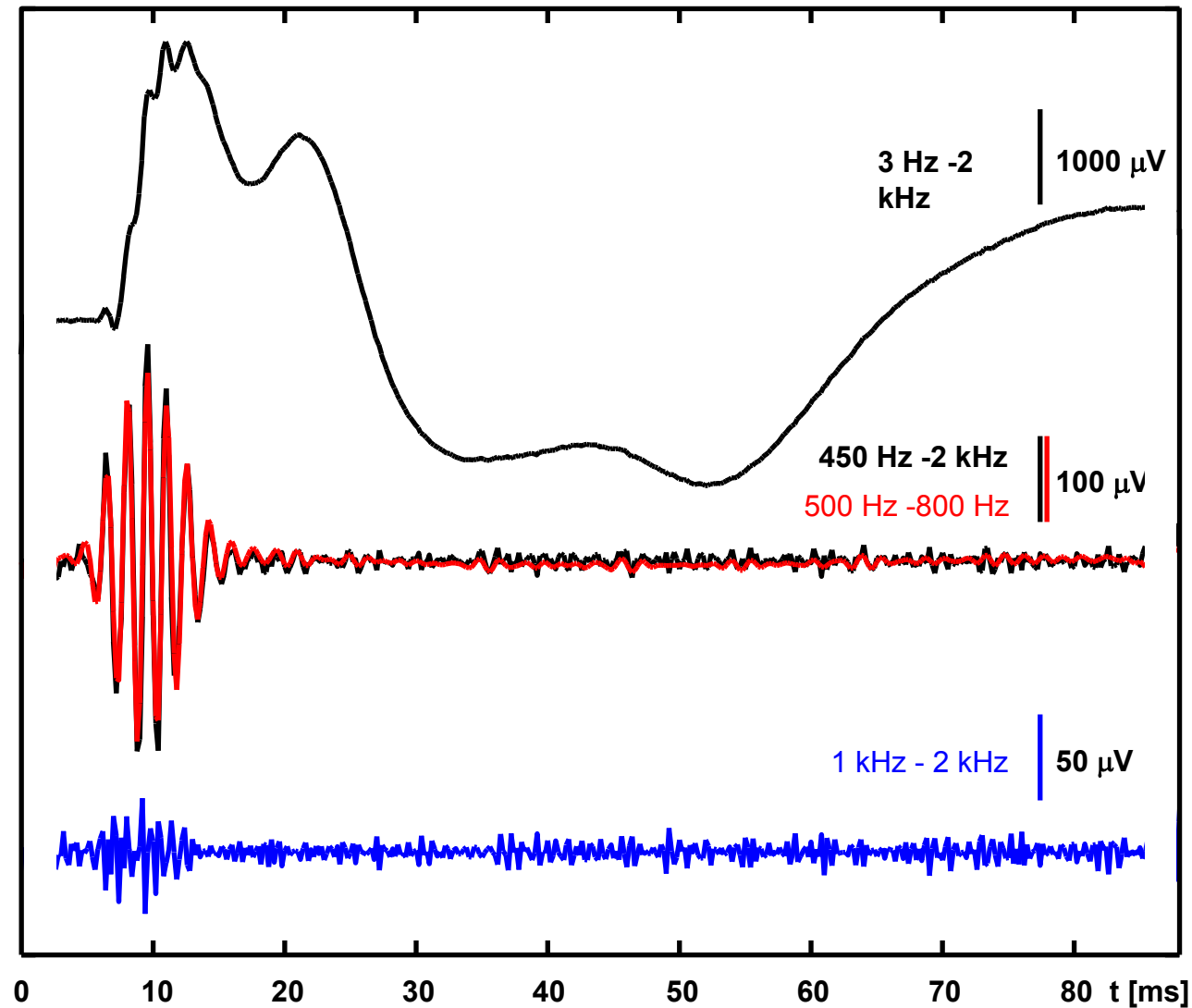
(Gobbelé et al., 2004)

Early burst survives cortical glutamate antagonisation



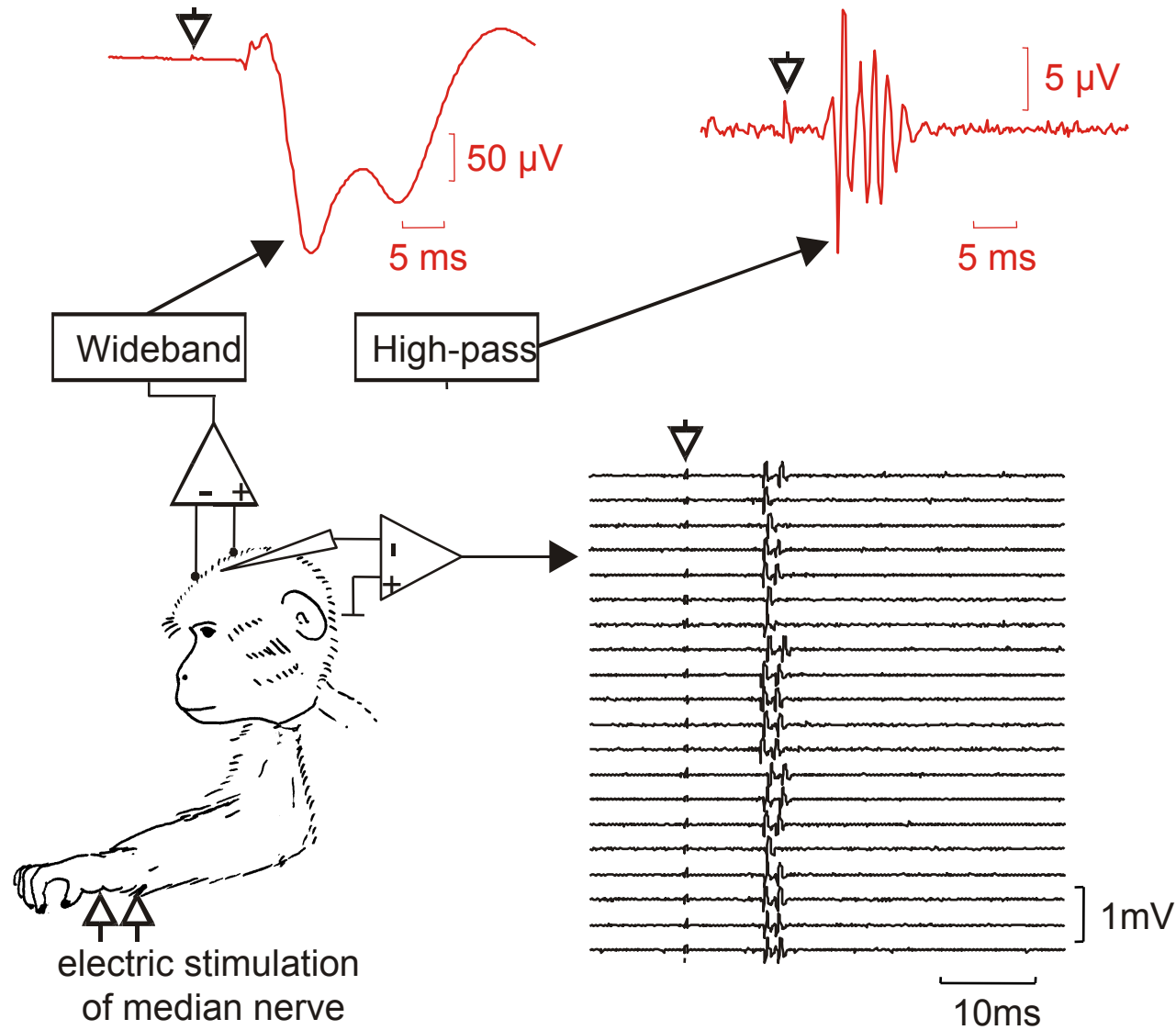
(Ikeda et al, 2002)

Epidural SEP from monkey S-1



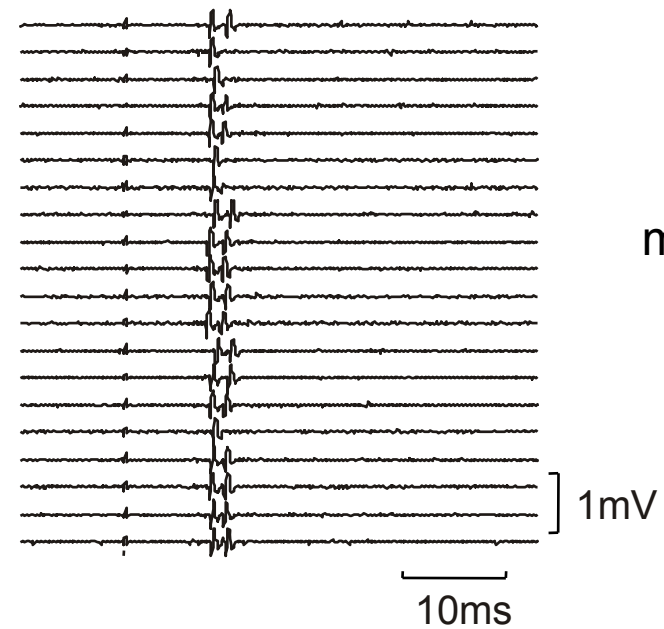
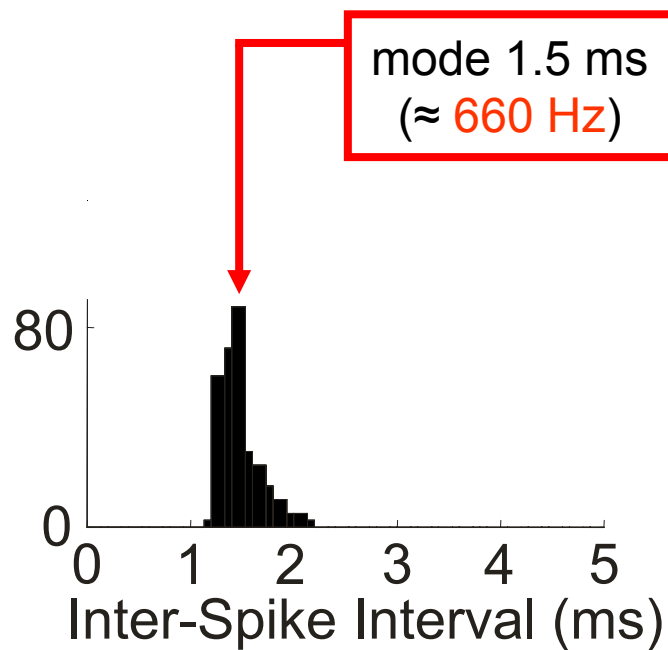
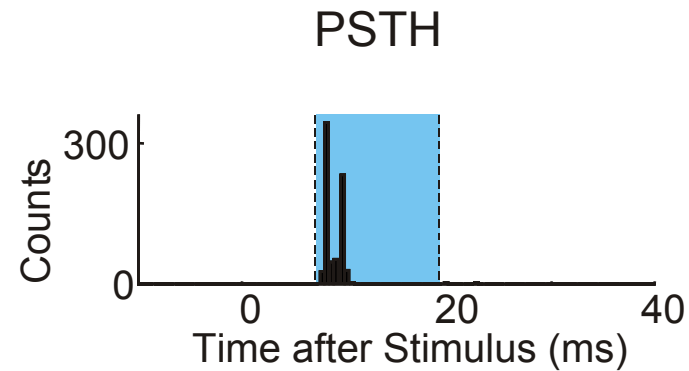
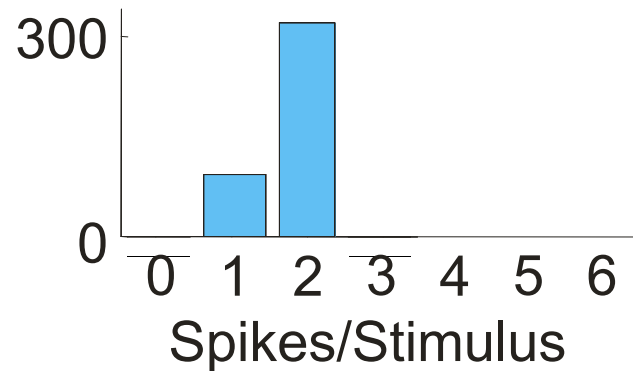
(Baker, Curio, Lemon, *J Physiol.*, 2003)

Physiology in monkey S-1: **burst neurons**



(Baker, Curio, Lemon, *J Physiol.*, 2003)

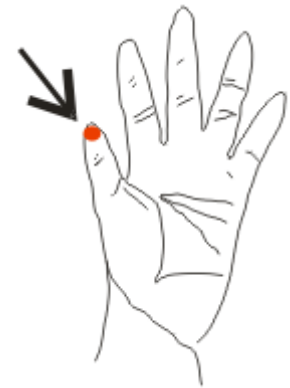
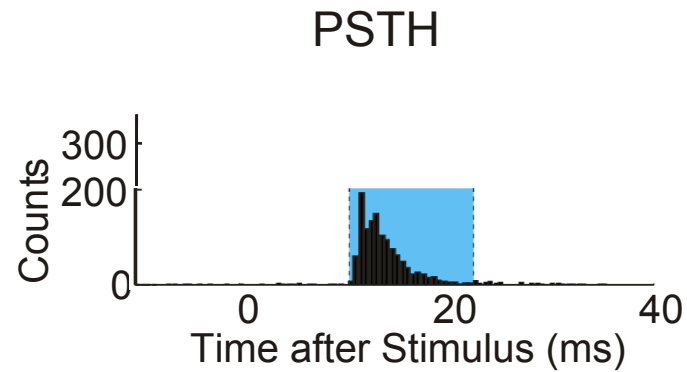
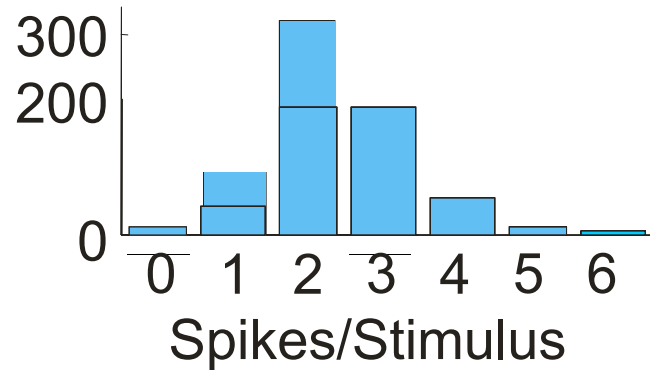
Physiology in monkey S-1: **burst neurons**



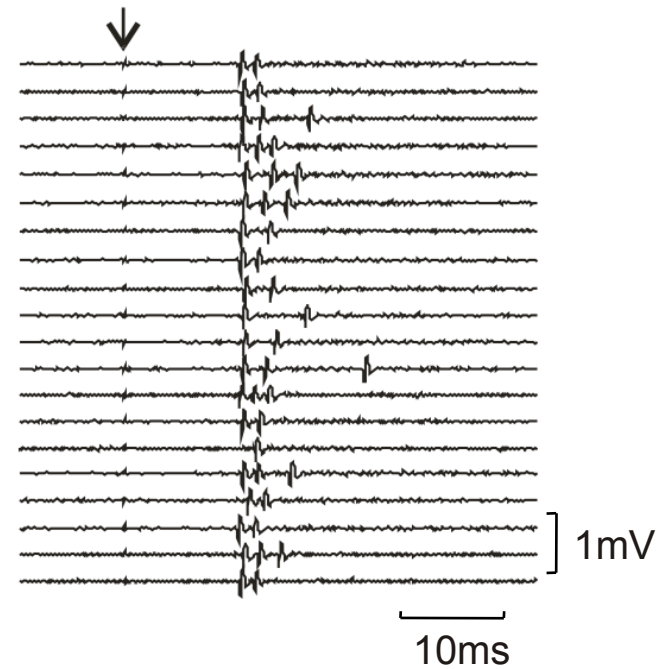
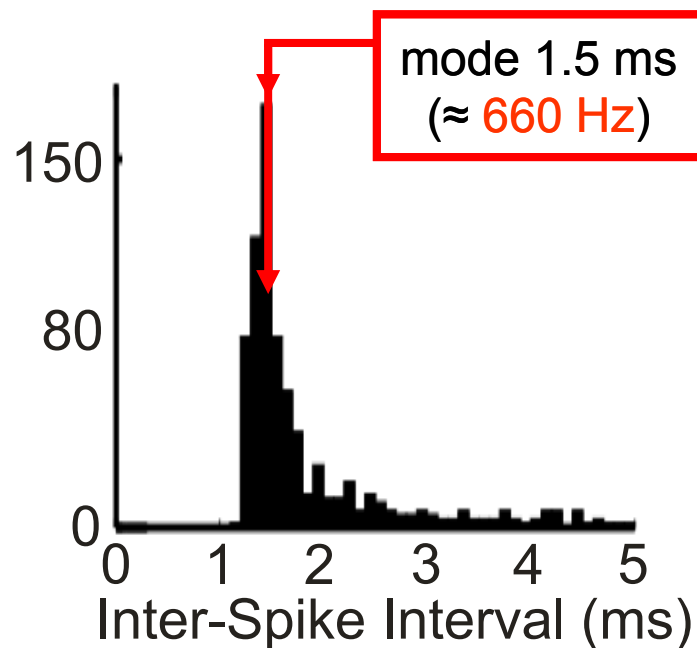
electric
median nerve
stimulation

(Baker, Curio, Lemon, *J Physiol.*, 2003)

Physiology in monkey S-1: **burst neurons**

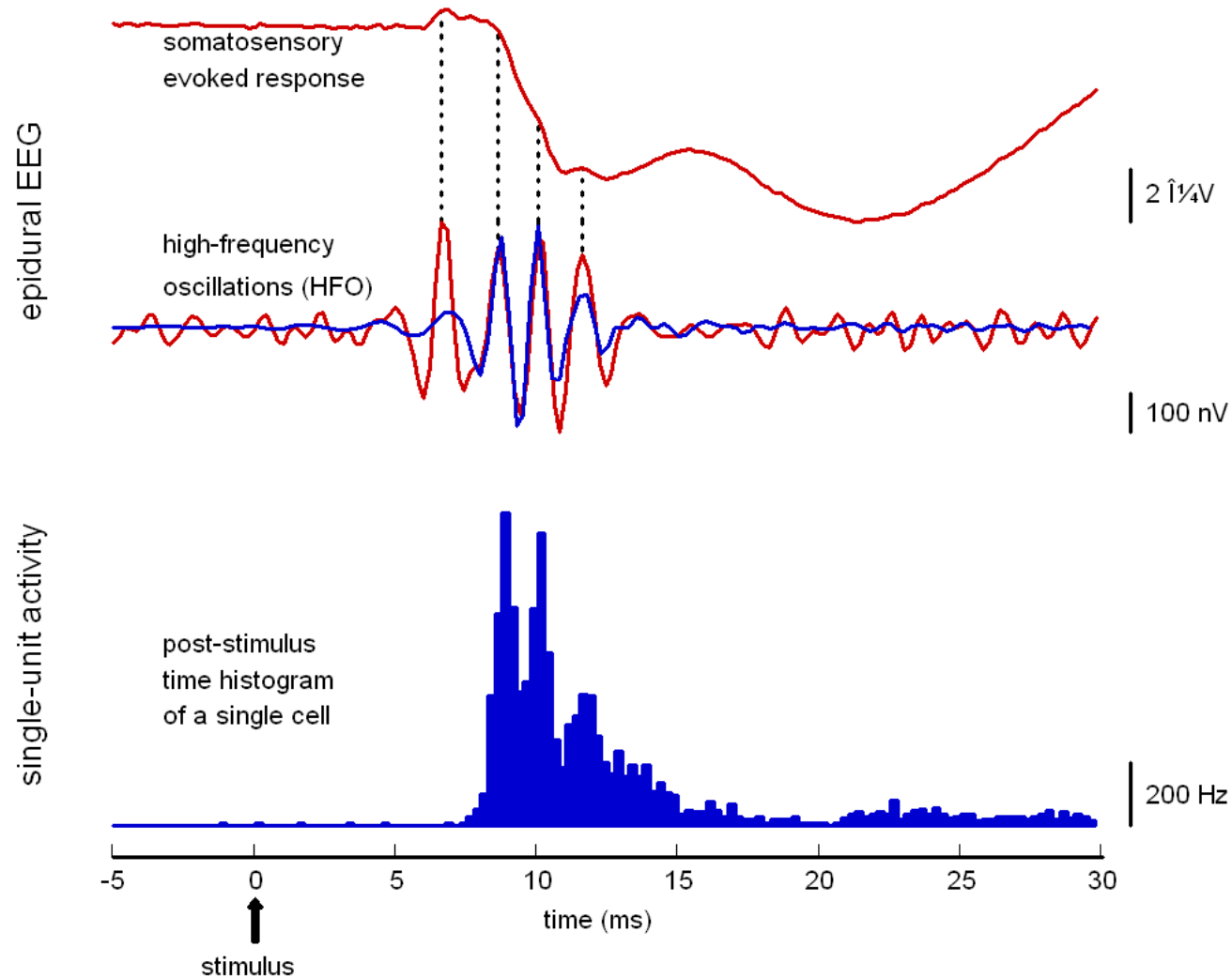


stylus tap
natural RF
stimulation



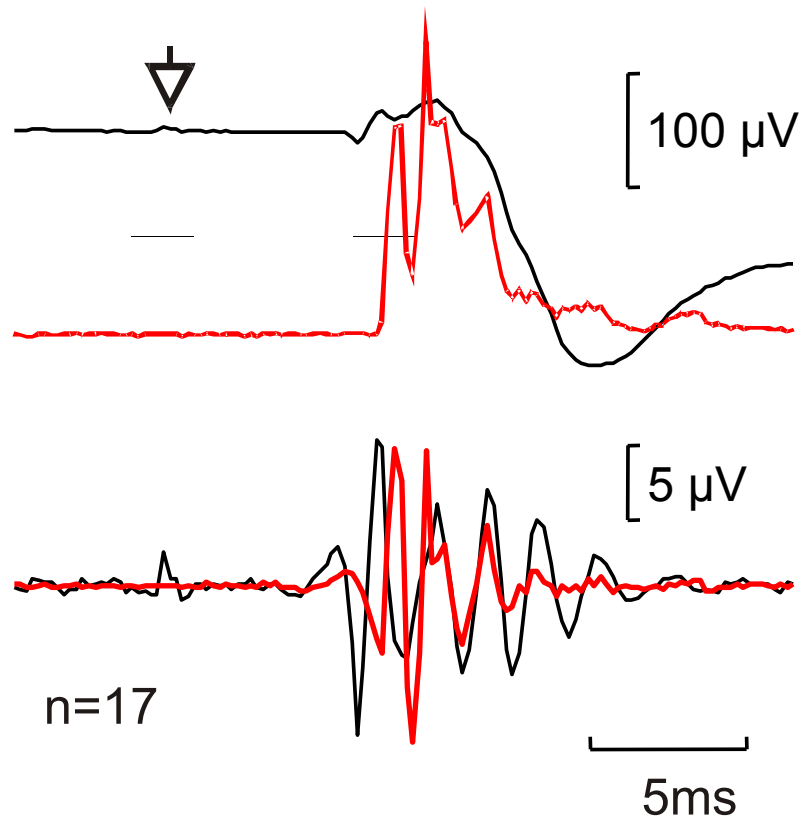
(Baker, Curio, Lemon, *J Physiol.*, 2003)

Physiology in monkey S-1: **burst neurons**

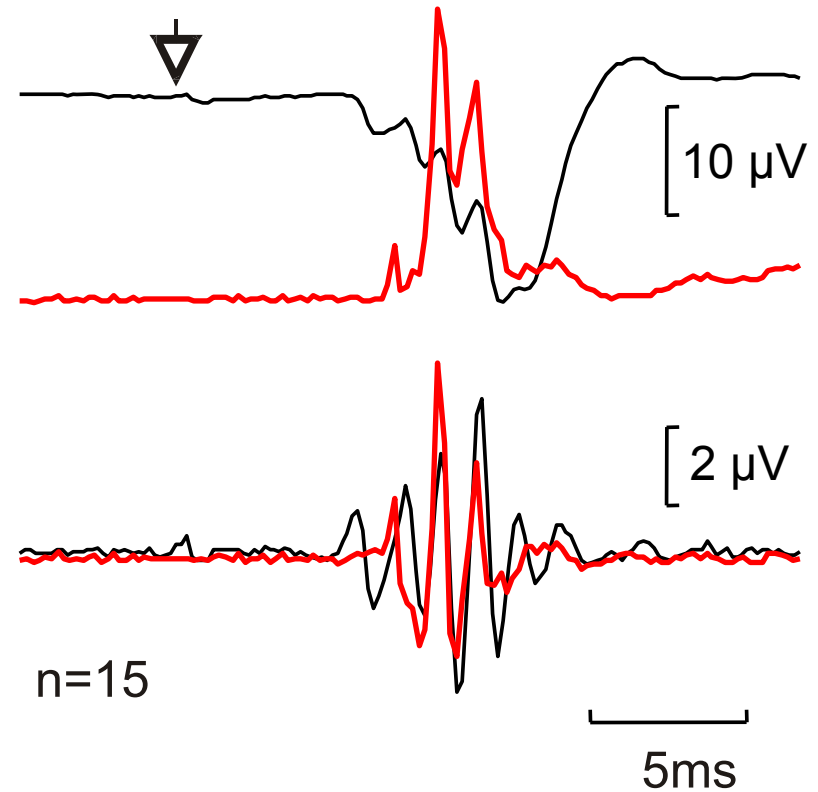


Physiology in monkey S-1: **burst neurons**

Monkey 33



Monkey 32

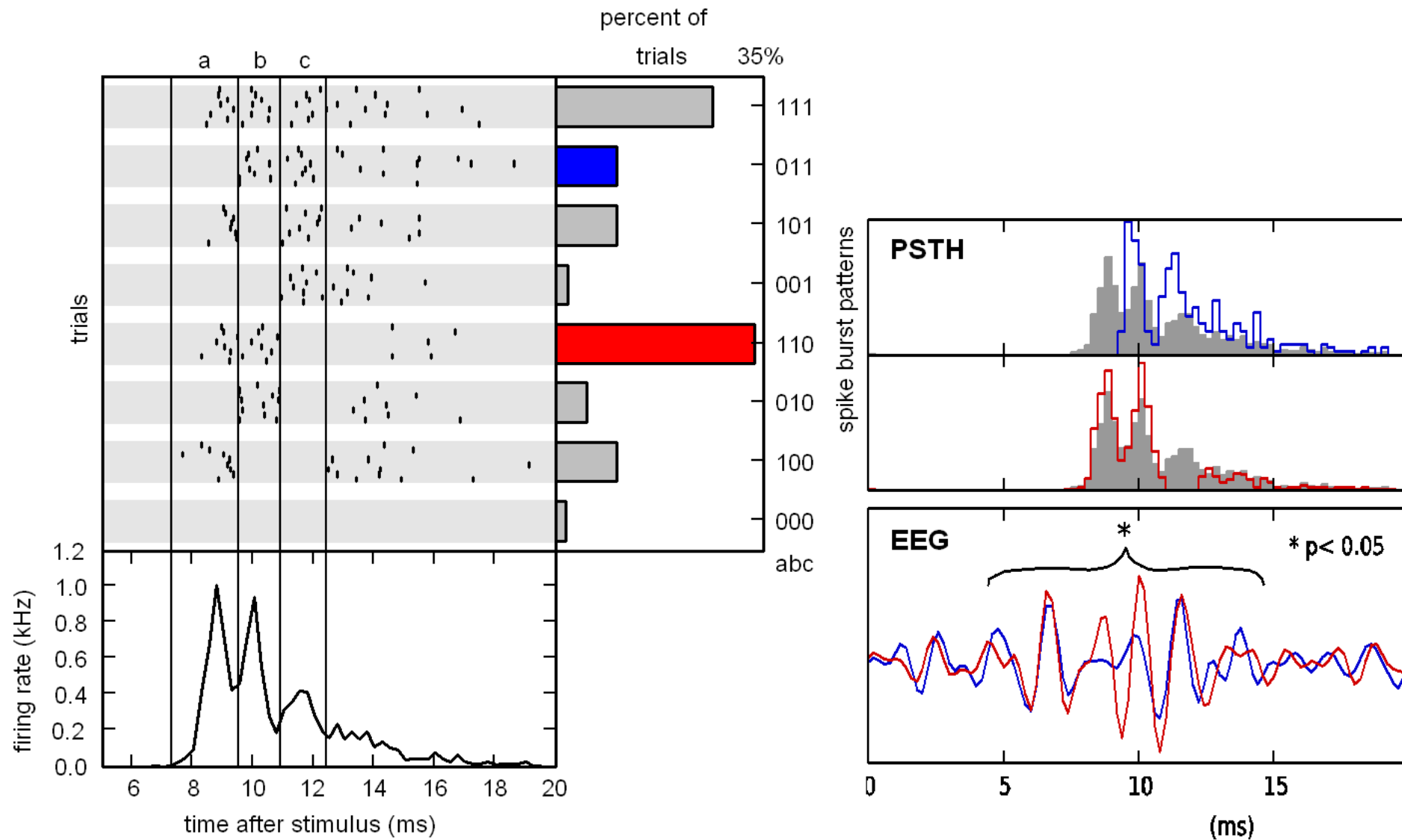


epidural EEG

summed single unit PSTHs

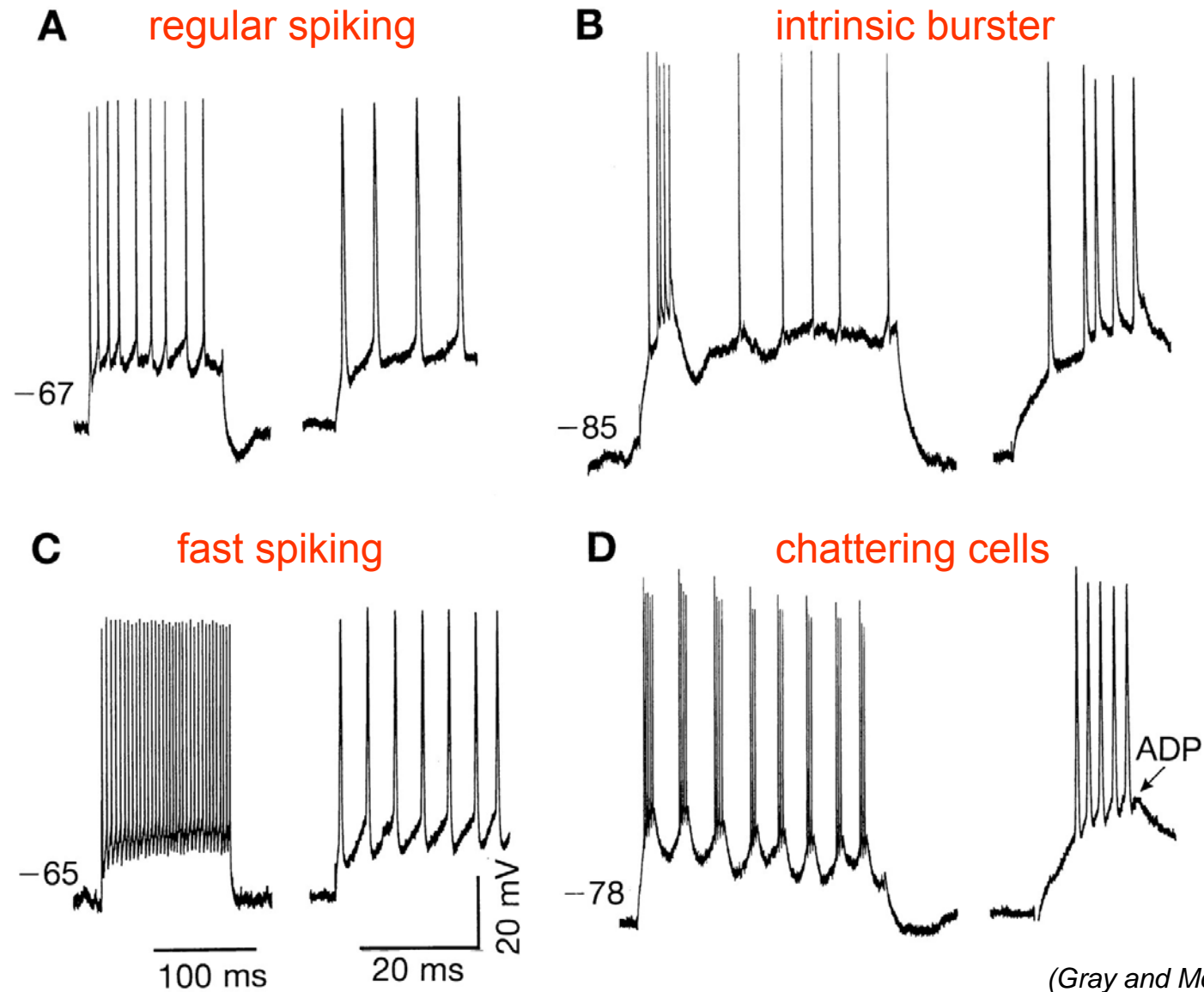
(Baker, Curio, Lemon, *J Physiol.*, 2003)

Single-cell spike burst patterns: 111 vs 110

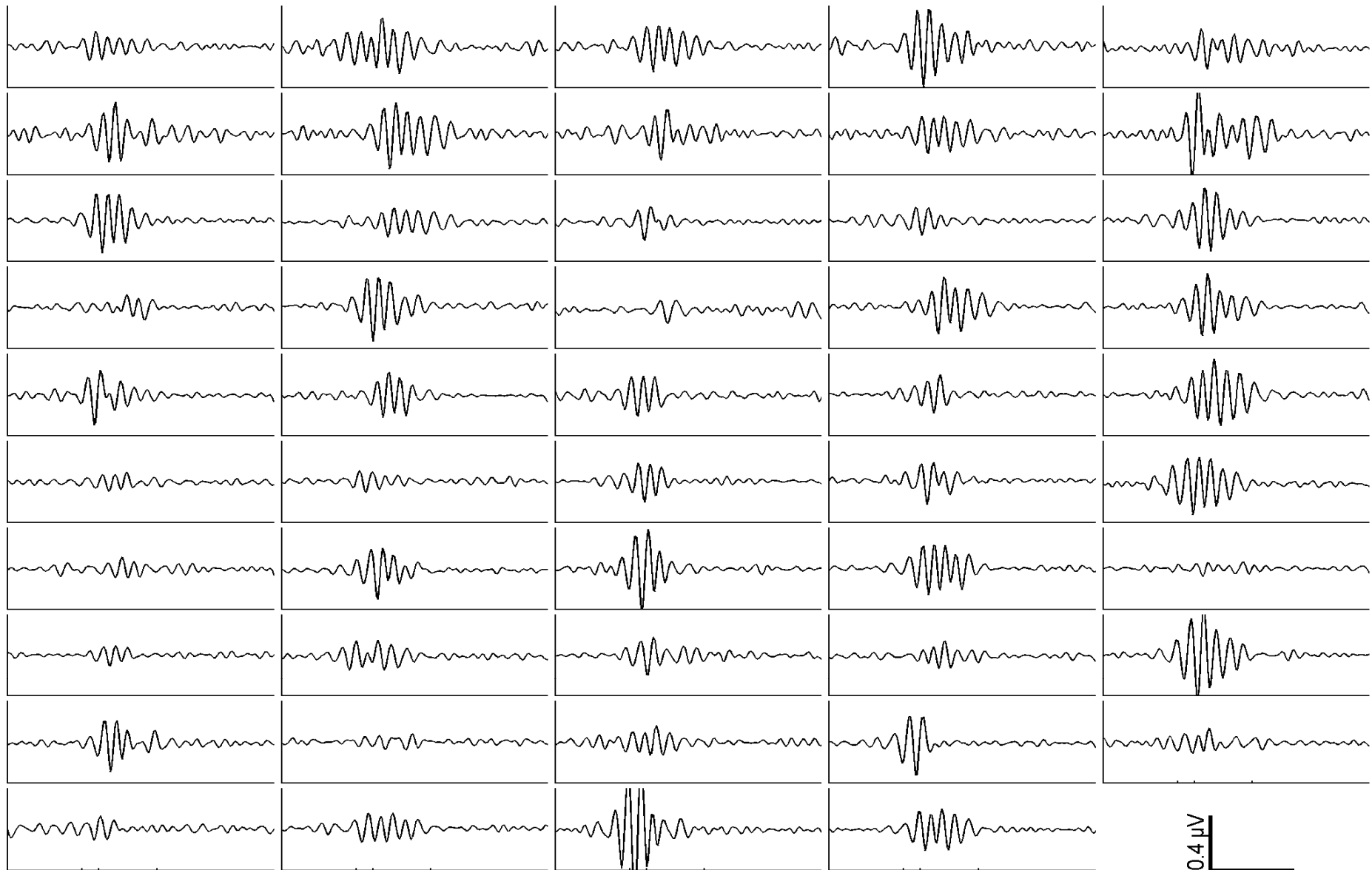


(Telenczuk et al., J Neurophysiol., 2011)

Physiology in cat V-1: **burst neurons**



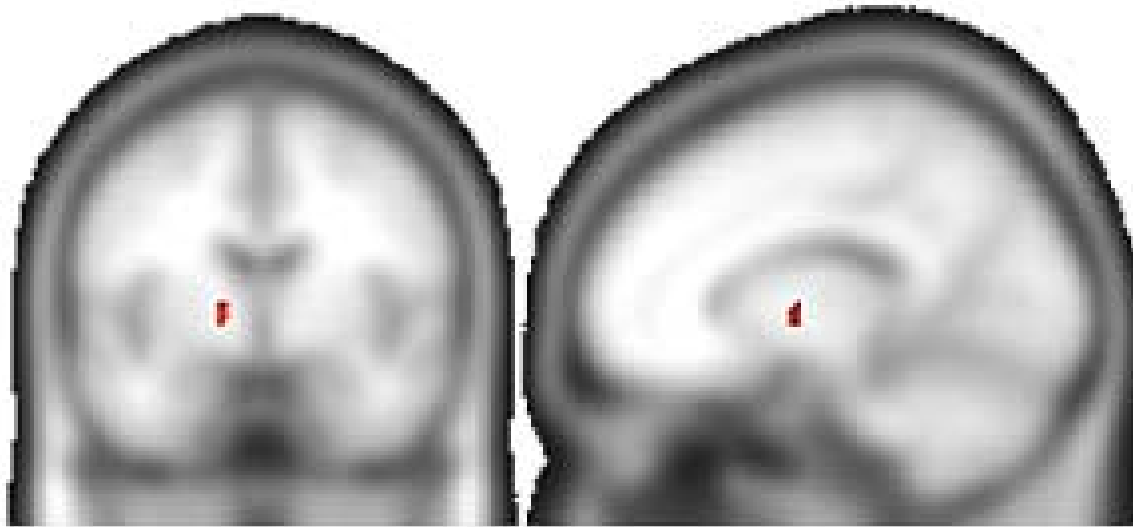
SEP bursts can be recovered during fMRI (n=49)



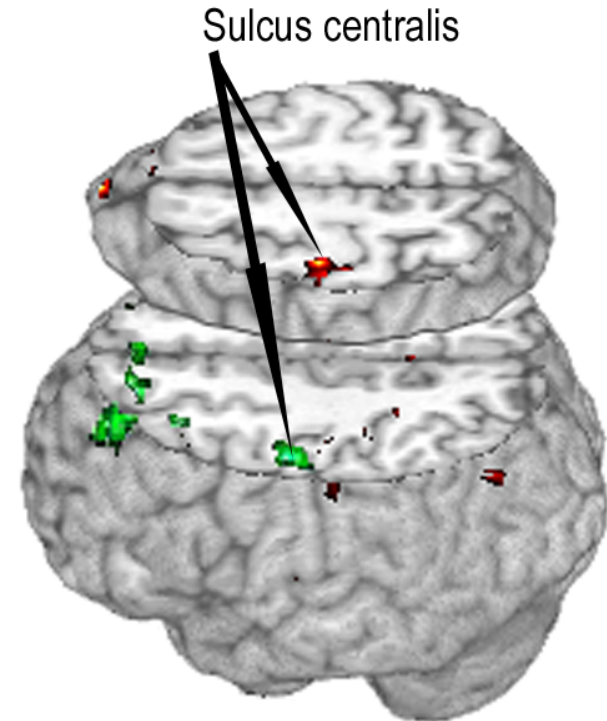
Cp5; 400-1000 Hz

0.4 μV
10 ms

BOLD covariation with SEP components



Thalamic BOLD covariation
with **early** burst

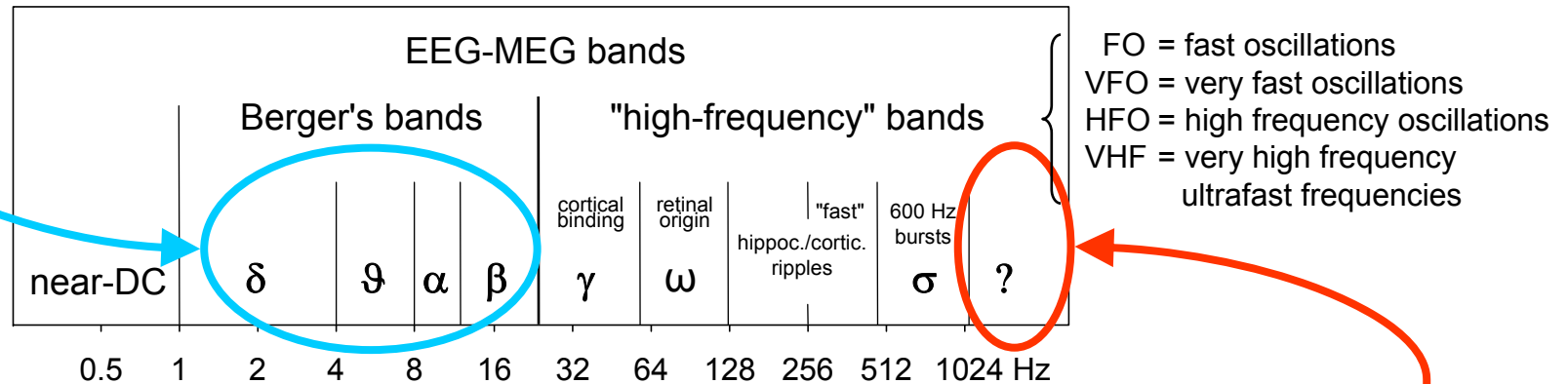


S-1 BOLD covariation
with **N20**
and **late** burst

(Ritter et al., NeuroImage, 2008)

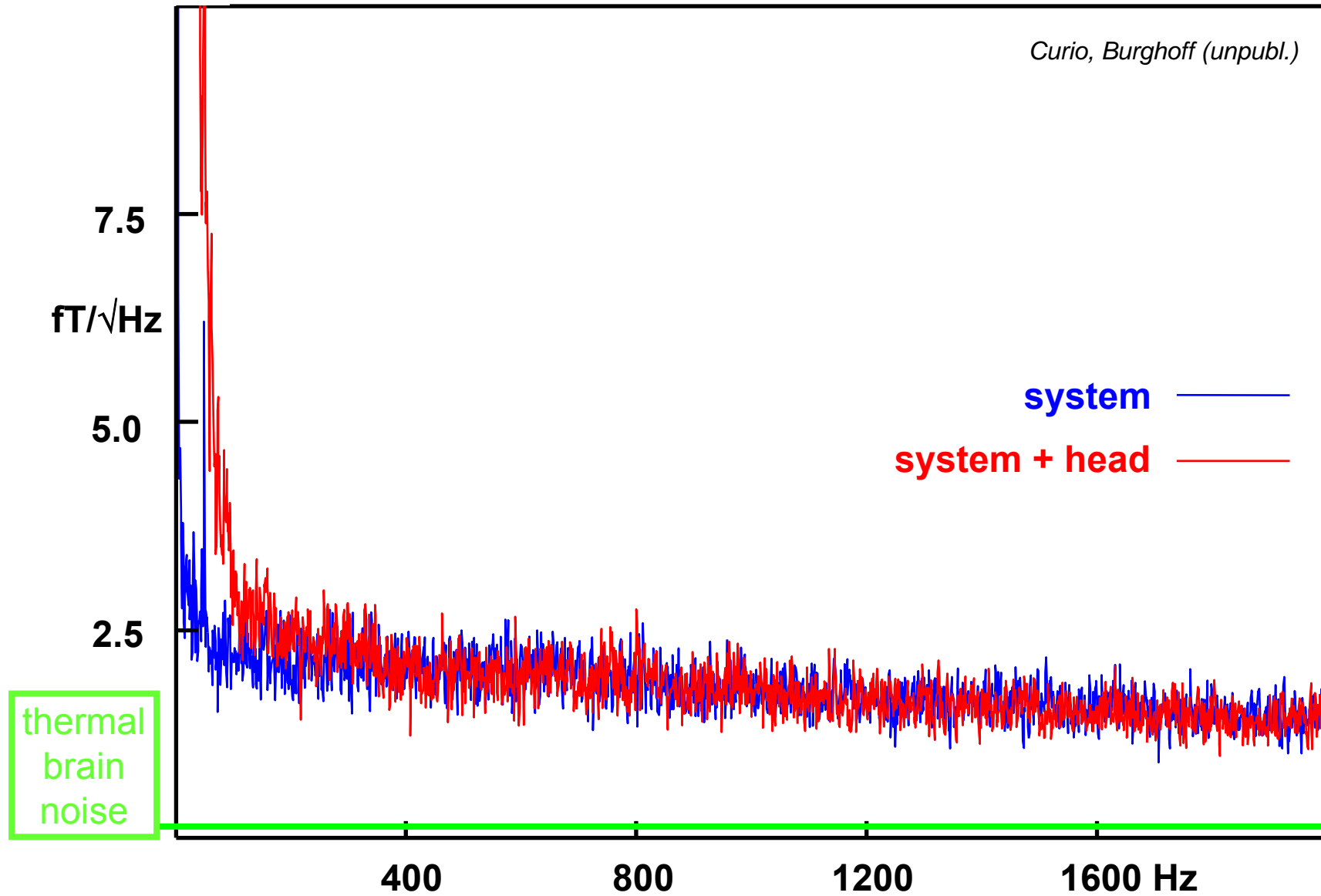
Berger's bands – and far beyond

standard low-frequency EEG bands



non-invasive analysis of multi-unit activity

MEG noise analysis: amplitude spectra



THERMAL AGITATION OF ELECTRICITY IN CONDUCTORS

BY J. B. JOHNSON

Thermal **Johnson–Nyquist noise** (electrode-skin impedance)

$$V(t) = \sqrt{4k_B \cdot T \cdot R \cdot \Delta f}$$

$$k_B = 1.38 \cdot 10^{-23} \text{ J/K}$$

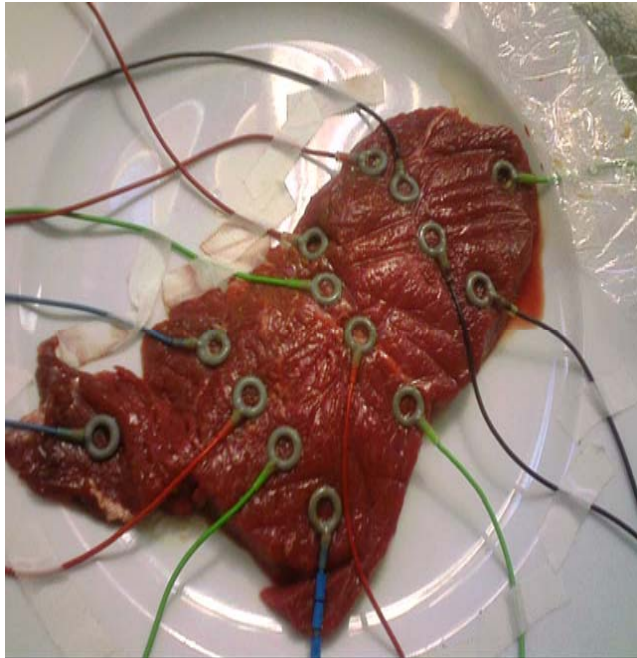
$$T = 310 \text{ K (37° C)}$$

$$R = 1 \text{ kOhm}$$

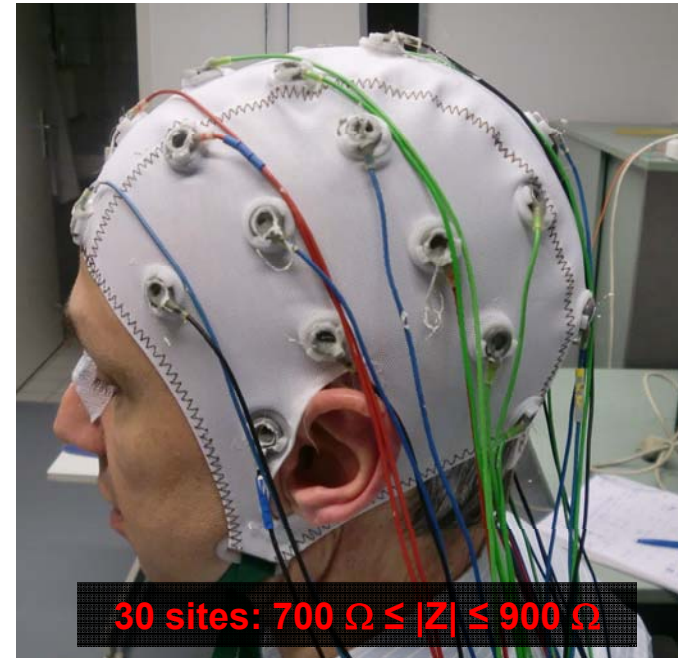
$$\Delta f = 1 \text{ Hz}$$

$$\approx 4.1 \text{ nV} / \sqrt{\text{Hz}}$$

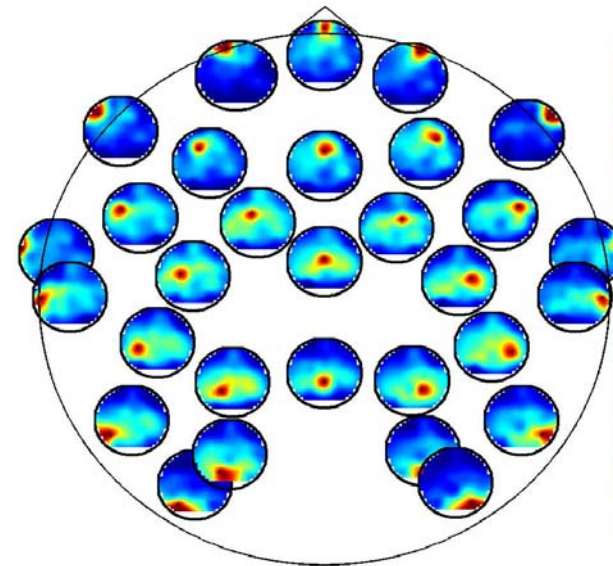
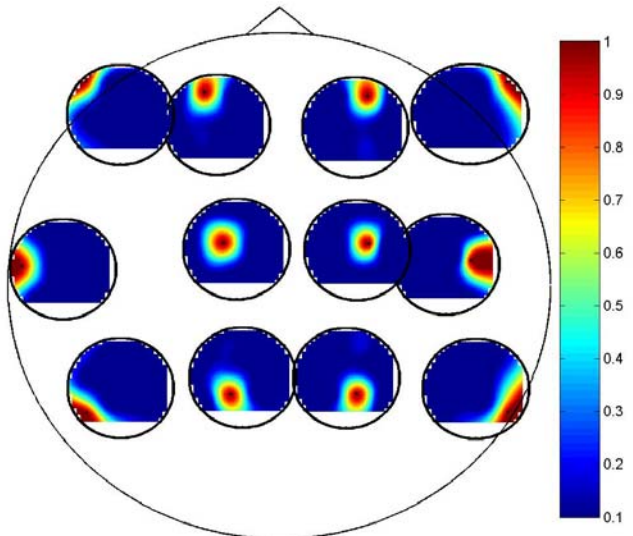
Impedances – checking the limits



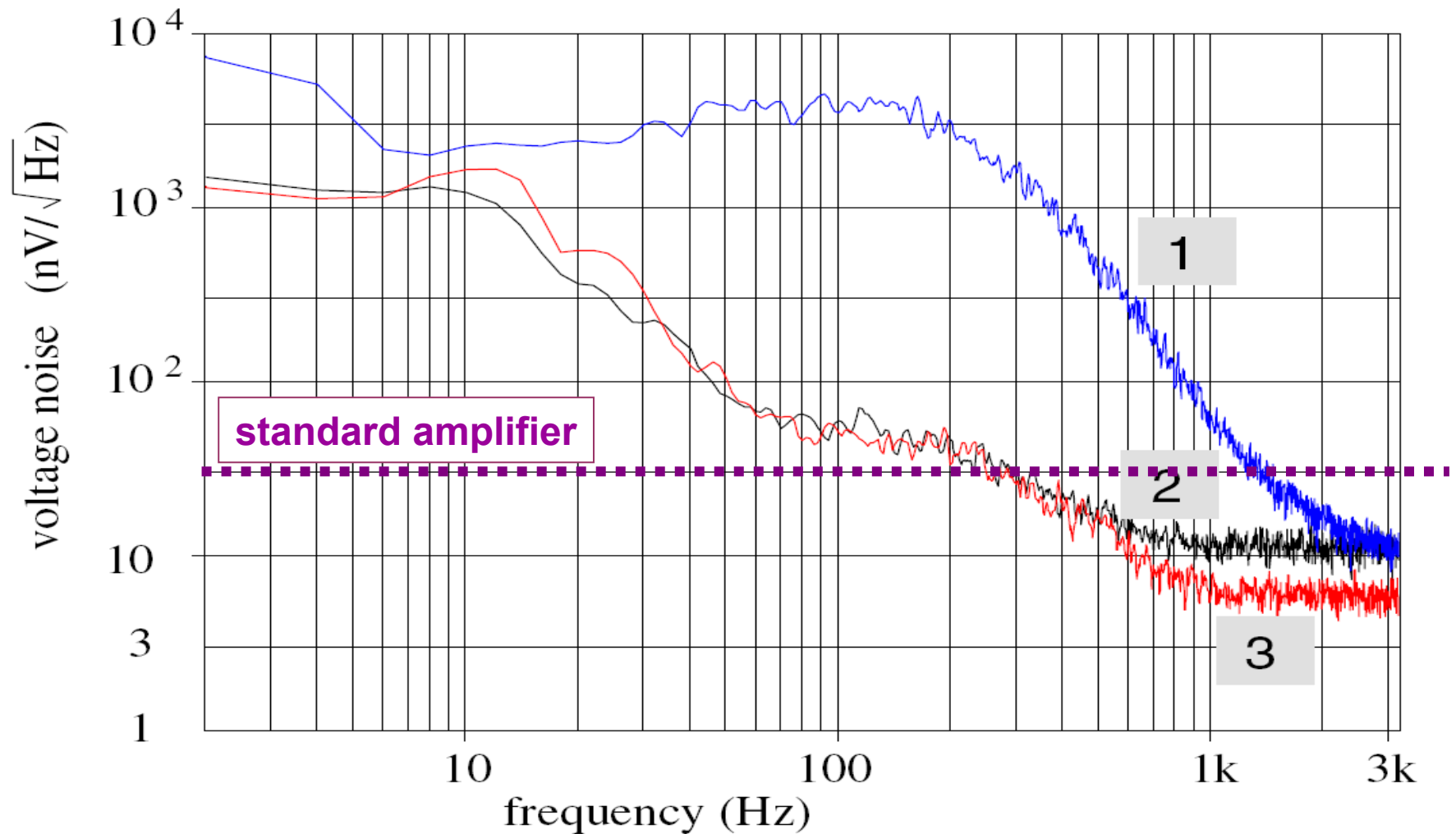
Ch1	215 Ω
Ch2	125 Ω
Ch3	205 Ω
Ch4	95 Ω
Ch5	150 Ω
Ch6	205 Ω
Ch7	95 Ω
Ch8	155 Ω
Ch9	215 Ω
Ch10	120 Ω
Ch11	150 Ω
Ch12	240 Ω



30 sites: $700 \Omega \leq |Z| \leq 900 \Omega$



White noise level of EEG spectra

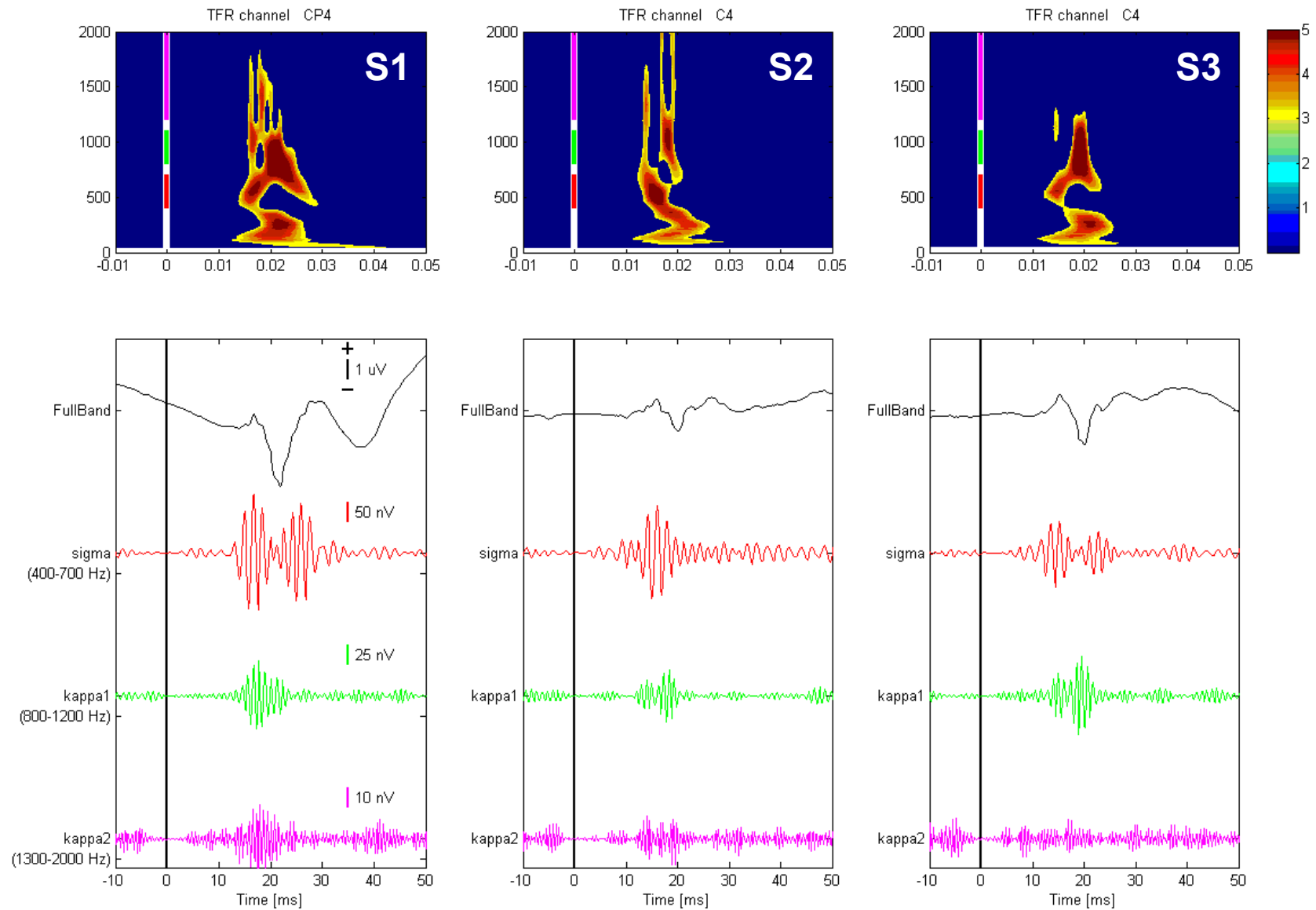


1 = m. masseter innervation

2 = relaxed, $12 \text{ nV}/\sqrt{\text{Hz}}$ amplifier

3 = relaxed, $4.8 \text{ nV}/\sqrt{\text{Hz}}$ amplifier

Averaged SEP: Stockwell transform (time-freq.)



(Fedele et al., 2012)

**Yesterday's noise may be tomorrow's signal:
Where are today's limits for
high-resolution high-frequency surface EEG?**

RECIPE: a) dedicated low-noise amplifier ($< 5 \text{ nV}/\sqrt{\text{Hz}}$)
b) electrode-skin impedances a.l.a.p. ($< 1 \text{ k}\Omega$)

RESULT: a) non-invasive detection of SEP components $> 1 \text{ kHz}$
b) multi-channel **mappings** delineate cortical/subcortical sources

**PERSPECTIVE for „MUA“:
non-invasive monitoring of **Multi-Unit spike Activity****



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DIY: σ -burst recipe

- montage: CP3-F3
- impedance: $\leq 1 \text{ k}\Omega$
- bandpass: 5-1500 Hz
- averages: 2000
- stim. freq.: 1.1/s + 8.1/s