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

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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: $\Sigma$ (EPSP + IPSP)

SUA (single unit)
MUA (multi unit)

hf-MEG/EEG

INPUT

OUTPUT

AP threshold

EPSP $+$ IPSP
"M/EEG"

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# Neurophysics of hf-EEG (… and MEG)

## 1. Overview:

### Terms of the Problem

<table>
<thead>
<tr>
<th>近场</th>
<th>远场</th>
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<tbody>
<tr>
<td>真实偶极子</td>
<td>虚拟偶极子</td>
</tr>
<tr>
<td>primary sources</td>
<td>secondary sources</td>
</tr>
<tr>
<td>traveling peaks</td>
<td>stationary peaks</td>
</tr>
<tr>
<td>active current sources</td>
<td>junctional potentials</td>
</tr>
</tbody>
</table>
2. Ion currents and membrane potential

resting state

membrane as charged condensator (intracellular: -70 mV)

cations
anions

apical EPSP

'active'
Na⁺ inflow via opened ion channels

'passive', capacitative
Na⁺ 'drift-away' with unopened ion channels

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3. Closing the current loop

- Extracellular current ('sink')
- Equilibration ('volume current')
- Extracellular current ('source')
- 'Secondary', 'passive', capacitative Na⁺ 'drift-away' with unopened ion channels
- Primary', 'active' Na⁺ inflow via opened ion channels
- Intracellular primary current

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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
7. Far fields: *radial* cortical dipoles

'open field' from pyramidal cells:
- elongated structure = apical dendrite
- parallel structure = summation due to 'palisade' arrangement
8. Propagating action potential

Lorente de Nó (1947): triphasic wave form

transmembranous current:
\[ \Sigma I_{in} + \Sigma I_{out} = 0 \]
9. Infinite vs. finite volume conductor

current dipole in infinite volume conductor

intracellular current dipole

extracellular potential distribution

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10. Action potential: quadrupole

Plonsey, 1969: "linear quadrupole"

far field < 5%
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

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12. Conductivity Change: Ohm's Law

\[ \sigma_2 > \sigma_1 \]

R \sim 1/\sigma

I_{AP} = \text{const.}

I_{AP} \cdot R_1 = V_1

I_{AP} \cdot R_2 = V_2

As \( V_1 > V_2 \):

stationary net dipole

(independent of direction of propagation)

propagating balanced quadrupole

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13. Conductivity Change: Polarity Switch

\[ \sigma_2 > \sigma_1 \]

\[ \sigma_2 < \sigma_1 \]
Comparable far field components due to step-like decrease of extracellular resistance through:

1) increase of conductivity

2) widening of conductor diameter
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

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17. Subcortical far field 'generators'

- distal n. acusticus
- meatus acusticus internus
- n. cochlearis
- corpus trapezoideum
- n. olivaris superior
- lemniscus lateralis
- colliculus inferior

- transition arm – trunk
- plexus brachialis
- dorsal horn
- transition trunk – neck
- dorsal column
- transition neck – head (foramen magnum)
- n. cuneatus
- lemniscus medialis
- n. ventroposterolateralis thalami
- radiatio thalamocorticalis

BAEP (brainstem auditory evoked potentials)

SEP (N. medianus) (somatosensory evoked potentials)
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 ⇔

(modified from Emerson et al. 1988)
MEG: **Cortical burst generator**


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

Gabriel Curio ***, Bruno-Marcel Mackert *, Martin Burghoff *, Roman Koetitz *, Klaus Abraham-Fuchs *** and Wolfgang Häker **
MEG: **Cortical** burst generator


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

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(A: 430-1500 Hz)  
B: 5-1500 Hz  
C: 5 - 430 Hz  
D: 430-1500 Hz

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Co-localisation of N20m and 600 Hz burst

(Curio et al., 1994)
Co-localisation of N20m and 600 Hz burst

N20m (<450 Hz)  HFOs (>450 Hz)  (modified from Hashimoto et al. 1996)

(Curio et al., 1994)
High-resolution (7 mm) somatotopy of burst generators in S-1

(Curio et al., 1997)
Burst components: stimulation rate

(normalized amplitude

stimulus rate (Hz)

instantaneous frequency (Hz)

interpeak interval

(modified from Klostermann, Nolte and Curio; 1999)

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Burst components: simultaneous MEG + EEG

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

C, D: MEG
tangential: area 3b

430-1500 Hz
5-1500 Hz

(Curio et al., 1994)
Thalamic SEP: Deep Brain Stimulation (DBS)

SEP > 428 Hz

SEP < 428 Hz

(Klostermann et al., 2003)

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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

Physiology in monkey S-1: burst neurons

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Physiology in monkey S-1: burst neurons

- Burst neurons exhibit a mode of 1.5 ms (≈ 660 Hz).

- PSTH (post-stimulus time histogram) shows spiking activity.

- Electric median nerve stimulation is used.

Physiology in monkey S-1: burst neurons

mode 1.5 ms
(≈ 660 Hz)

Physiology in monkey S-1: burst neurons

- Somatosensory evoked response
- High-frequency oscillations (HFO)
- Post-stimulus time histogram of a single cell

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Physiology in monkey S-1: burst neurons

**Monkey 33**

- Epidural EEG
- Summed single unit PSTHs
- n=17

**Monkey 32**

- Epidural EEG
- Summed single unit PSTHs
- n=15

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Single-cell spike burst patterns: 111 vs 110

(Telenczuk et al., J Neurophysiol., 2011)
Physiology in cat V-1: burst neurons

A  regular spiking

B  intrinsic burster

C  fast spiking

D  chattering cells

(Gray and McCormick, 1996)
SEP bursts can be recovered during fMRI (n=49)
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

<table>
<thead>
<tr>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>8</th>
<th>16</th>
<th>32</th>
<th>64</th>
<th>128</th>
<th>256</th>
<th>512</th>
<th>1024 Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>δ</td>
<td>θ</td>
<td>α</td>
<td>β</td>
<td>γ</td>
<td>ω</td>
<td>σ</td>
<td>?</td>
<td></td>
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</tr>
</tbody>
</table>

**EEG-MEG bands**
- Berger's bands
- "high-frequency" bands

- cortical binding
- retinal origin
- "fast" hippoc./cortic. ripples
- 600 Hz bursts

**FO = fast oscillations**
**VFO = very fast oscillations**
**HFO = high frequency oscillations**
**VHF = very high frequency ultrafast frequencies**

**standard low-frequency EEG bands**

**non-invasive analysis of multi-unit activity**
MEG noise analysis: amplitude spectra

Curio, Burghoff (unpubl.)

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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

<table>
<thead>
<tr>
<th>Channel</th>
<th>Impedance (Ω)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ch1</td>
<td>215</td>
</tr>
<tr>
<td>Ch2</td>
<td>150</td>
</tr>
<tr>
<td>Ch3</td>
<td>130</td>
</tr>
<tr>
<td>Ch4</td>
<td>205</td>
</tr>
<tr>
<td>Ch5</td>
<td>120</td>
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<td>Ch6</td>
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<td>Ch7</td>
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<td>Ch8</td>
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<td>Ch9</td>
<td>205</td>
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<tr>
<td>Ch10</td>
<td>120</td>
</tr>
<tr>
<td>Ch11</td>
<td>150</td>
</tr>
<tr>
<td>Ch12</td>
<td>240</td>
</tr>
</tbody>
</table>

30 sites: 700 Ω ≤ |Z| ≤ 900 Ω

coherence at 1 kHz: no physical cross-talk

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White noise level of EEG spectra

1 = m. masseter innervation
2 = relaxed, 12 nV/√Hz amplifier
3 = relaxed, 4.8 nV/√Hz amplifier

2011 Physiol. Meas. 32 N73

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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 nV/√Hz)
b) electrode-skin impedances a.l.a.p. (<1 kOhm)

**RESULT:**

a) non-invasive detection of SEP components > 1 kHz
b) multi-channel **mappings** delineate cortical/subcortical sources

**PERSPECTIVE for „MUA“:**

non-invasive monitoring of **Multi-Unit spike Activity**

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M. Burghoff  B.-M. Mackert  L. Trahms
T. Fedele  G. Nolte  A. Villringer
R. Gobbelé  L. Parkonnen  G. Waterstraat

**DIY: σ-burst recipe**
- montage: CP3-F3
- impedance: \( \leq 1 \ \Omega \)
- bandpass: 5-1500 Hz
- averages: 2000
- stim. freq.: 1.1/s + 8.1/s