ELEC ENG 3BB3:

Cellular Bioelectricity

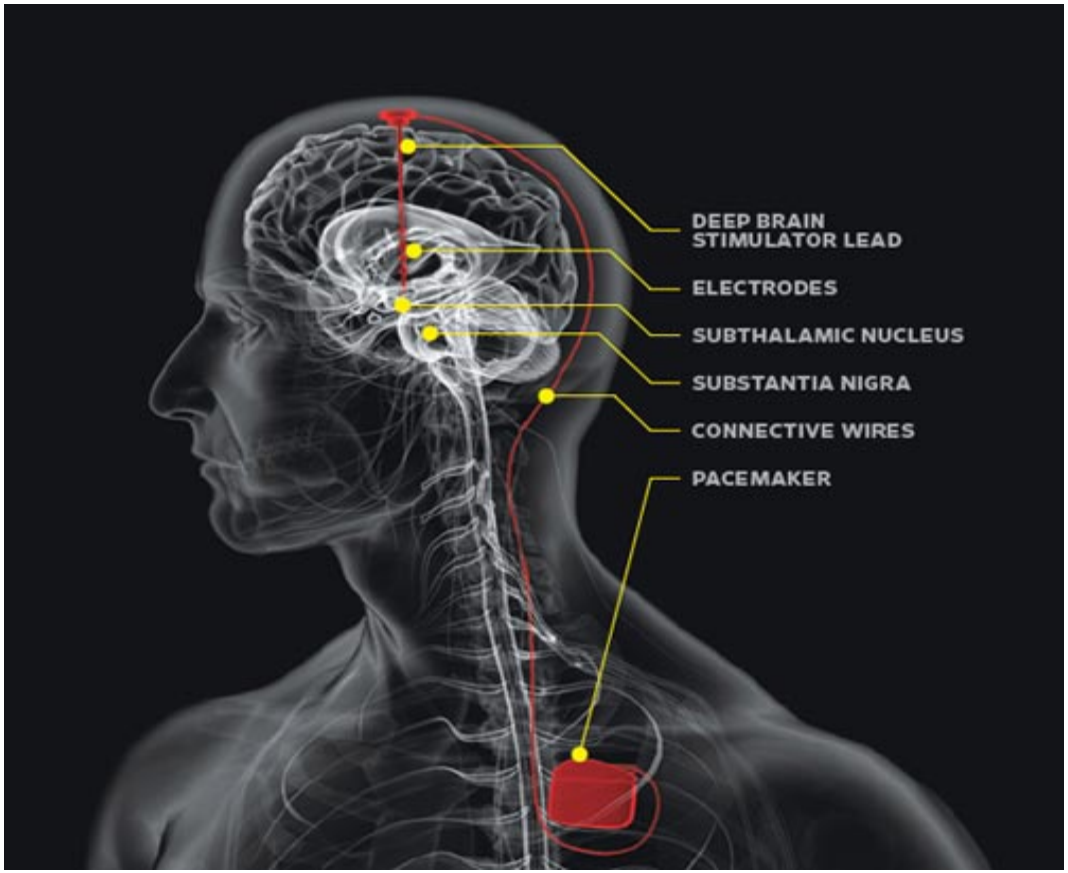
Notes for Lecture 32

Friday April 4, 2014

Other Forms of Brain Stimulation

- ECT (electroconvulsive therapy) does control MDD (major depressive disorder) when drugs fail
- Can we use less drastic forms of brain stimulation to manage depression?
- MDD is far more common than neurological problems such as Parkinsonism (third in economic costs and management)

System to Control Movement Disorders



Electrodes for Depression

EM Treatment of Depression

- Acute and Maintenance ECT “gold standard”? Maintenance (10 treatments) as effective as medication but 46% relapse
- Vagal Nerve Stimulation (implant) Mixed results
- Repetitive Transcranial Magnetic Stimulation (“non-invasive”) Mixed Results

VNS: Vagal Nerve Stimulation
Possible Mechanisms

- Alters CSF concentrations of neurotransmitters (e.g. GABBA) or their metabolites
- Alters functional activity of orbital frontal cortex, insula, thalamus, hypothalamus, etc.
- Anticonvulsants have been shown to have therapeutic value in mood disorders

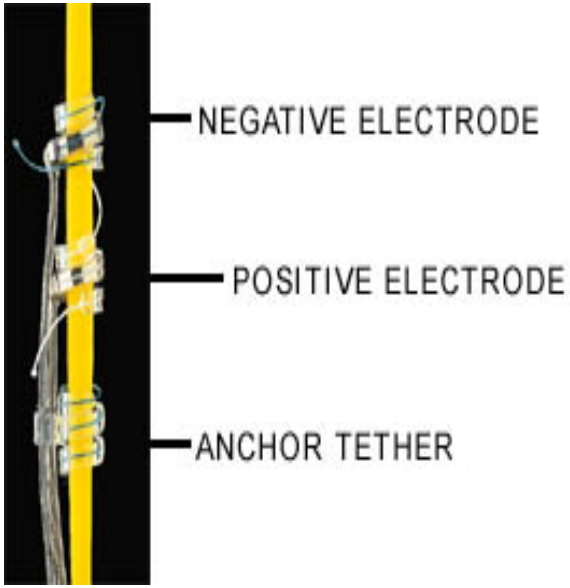
VNS: Vagal Nerve Stimulation Clinical Results

- Reduction in epileptic seizures (29,000 Cyberonics implants by 2005) few side effects
- 21 centre trial for major treatment-resistant depression 222 patients (Rush et al, Biol Psychiatry 2005)
- After 10 weeks 15% responded (≥ 50% improvement in HRSD) in treatment group vs 10% responded in sham group (not sig.)
- Longer term response rates more encouraging

Cyberonics VNS System

- Pacemaker similar to cardiac pacemaker
- Cuff electrodes on left vagal nerve
- Patient or caregiver parameter adjustment via magnetic field

Pacemaker and Electrodes



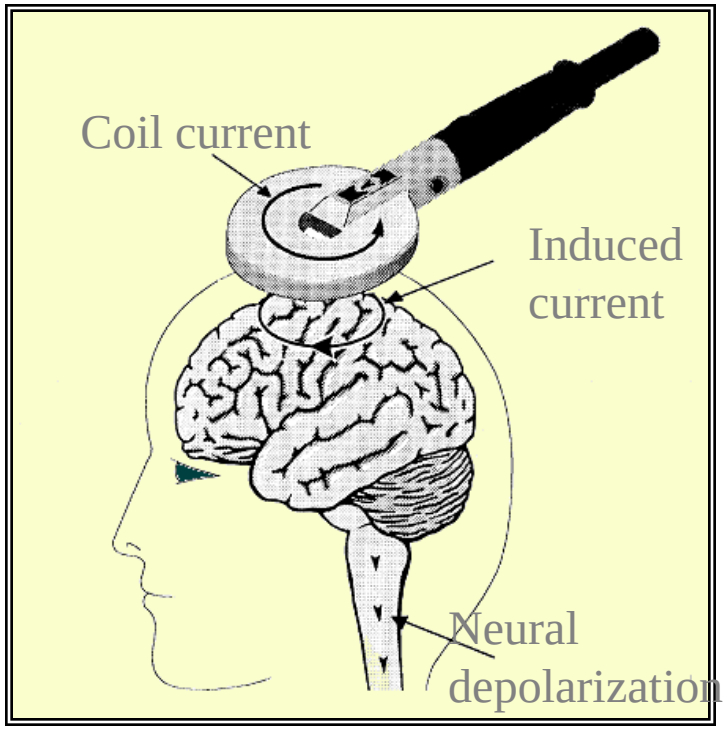
Treatment Settings

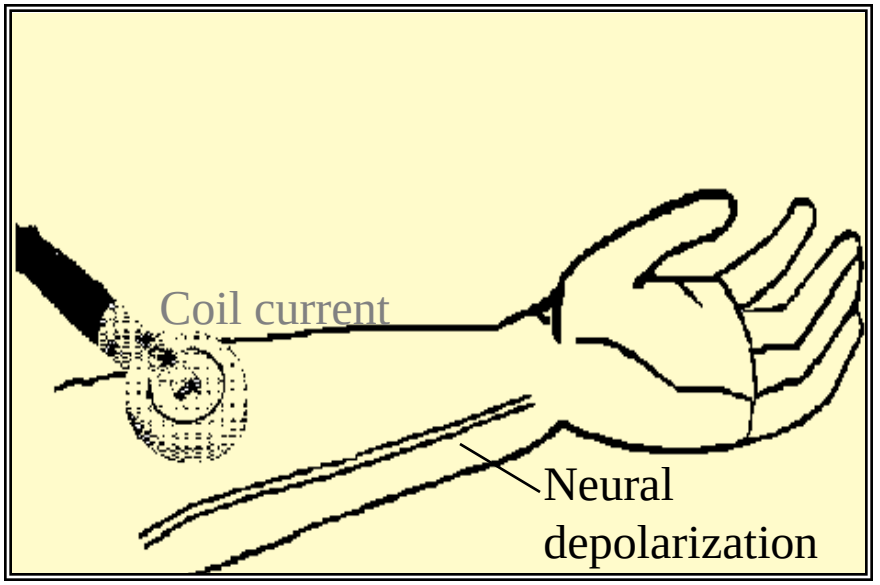
- Output current 0 -3.5mA: median last visit .75 ma, range .00 – 1.5 mA; start .25 mA (Rush)
- Signal frequency 1 – 30 Hz: median 20 Hz, range 10 – 20 Hz; start 20 Hz (Rush)
- Pulse width 130 – 1000 μsec: median 500 μsec, range 130 – 500 μsec; start 500 μsec (Rush)
- On time 7 – 60 sec, median 30 sec, range 14 – 30; start 30 sec (Rush)
- Off time .2 – 180 min: median 5 min; start 5 min (Rush)

rTMS: Repetitive Trans-Cranial Magnetic Stimulation

- Treat severely depressed patients who are resistant to pharmacology
- Alternative is periodic applications of electro-shock (ECT) treatment
- 30% of patients respond
- Would like to increase percentage of responders

Magnetic Nerve Stimulation (MNS)

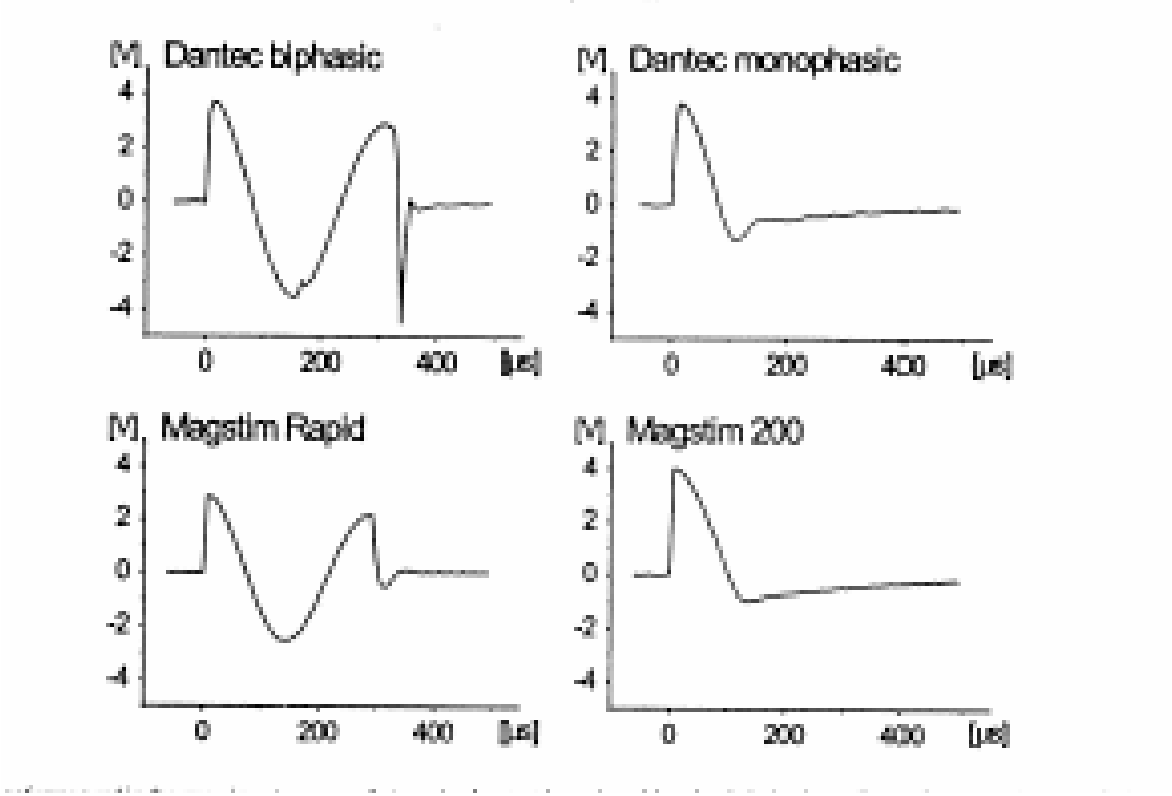




Current Commercial Machines

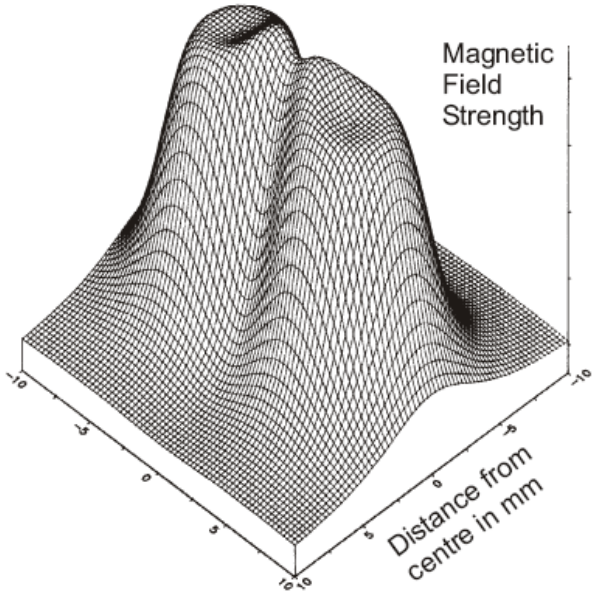
- Example Magstim

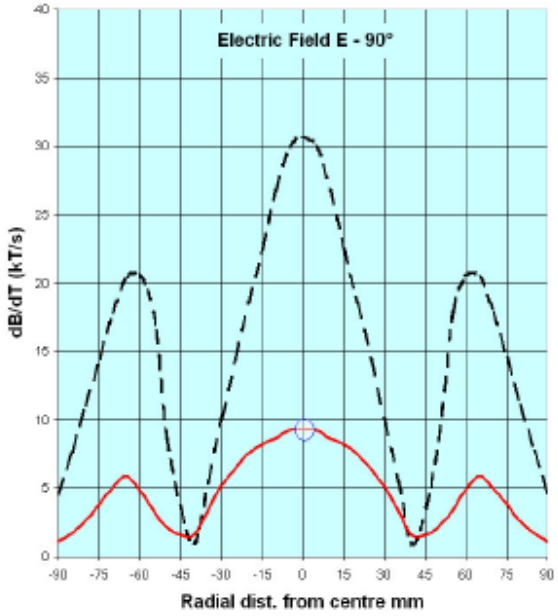
Stimulus Waveforms



Magnetic Field

Source: Medtronic, 2004





Source: Medtronic, 2004

Source: Medtronic, 2004

Treatment Protocol

- Find left thenar (abductor pollicis brevis) motor cortex stimulation point by monitoring M-wave of right thenar muscle
- Stimulate left frontal lobe (F3) at point 5 cm anterior to this site on a sagittal line
- Using a fixed % (80 – 120) of thenar threshold amplitude stimulate at 8 to 10 Hz for fixed periods up to 1800 stimuli; several clinics 3000 stimuli
- Repeat 4 to 5 times/week for 5 weeks

Clinical Treatment

Research Challenges (Objectives)

- Develop quantitative method for predicting which patients will respond to rTMS (use pre treatment EEG parameters, QEEG)
- Develop quantitative method for determining best site of stimulation
- Determine effects of changing stimulus amplitude and frequency

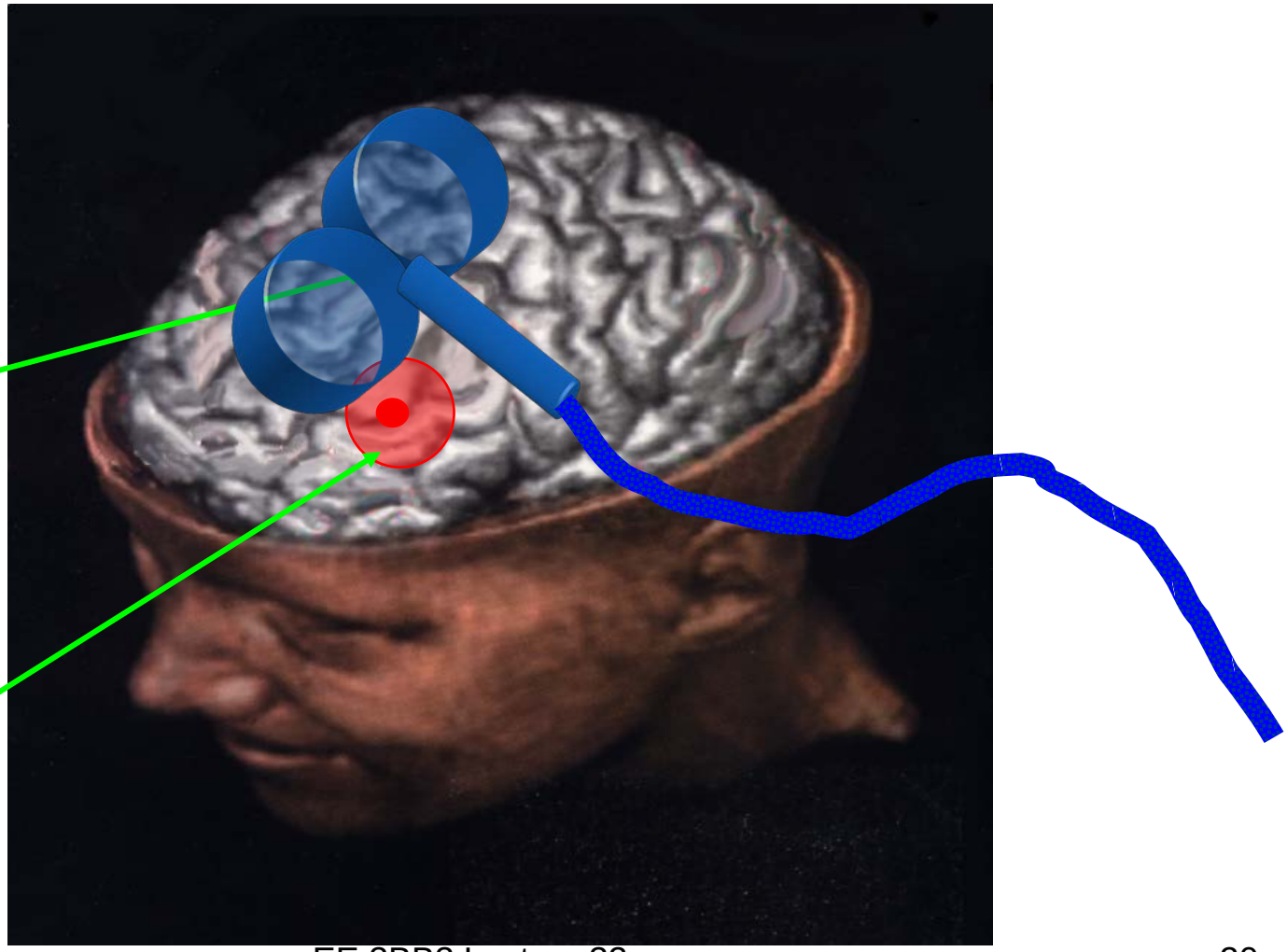
Can We Predict Who Will Respond?

	ACTUAL RESPONSE **Chi square = 4.866, p = .0227**	
PREDICTED RESPONSE	RESPONDER	NON-RESPONDER
RESPONDER	6	4
NON-RESPONDER	1	8

Those with correctable pathophysiology may not respond as standard methods place the coil in the wrong spot (we are not very good at predicting RESPONSE using QEEG)

Standard positioning Method incorrectly Places coil here. Magnetic energy is not delivered to the appropriate site

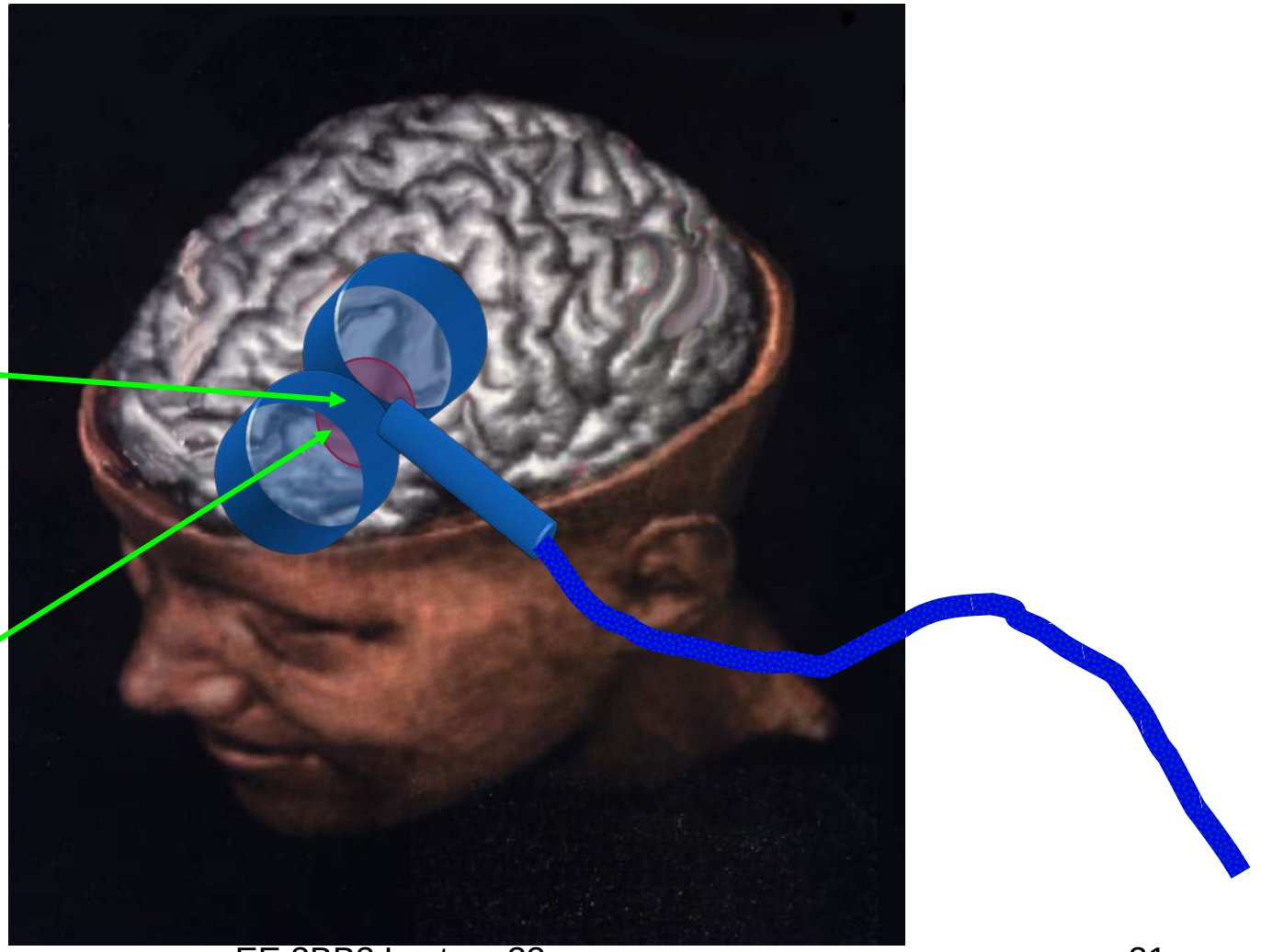
Possible site Of correctable dysfunction



Other subjects respond as their head size and brain anatomy is such that standard methods place the coil over the site of possible dysfunction (detectable using QEEG)

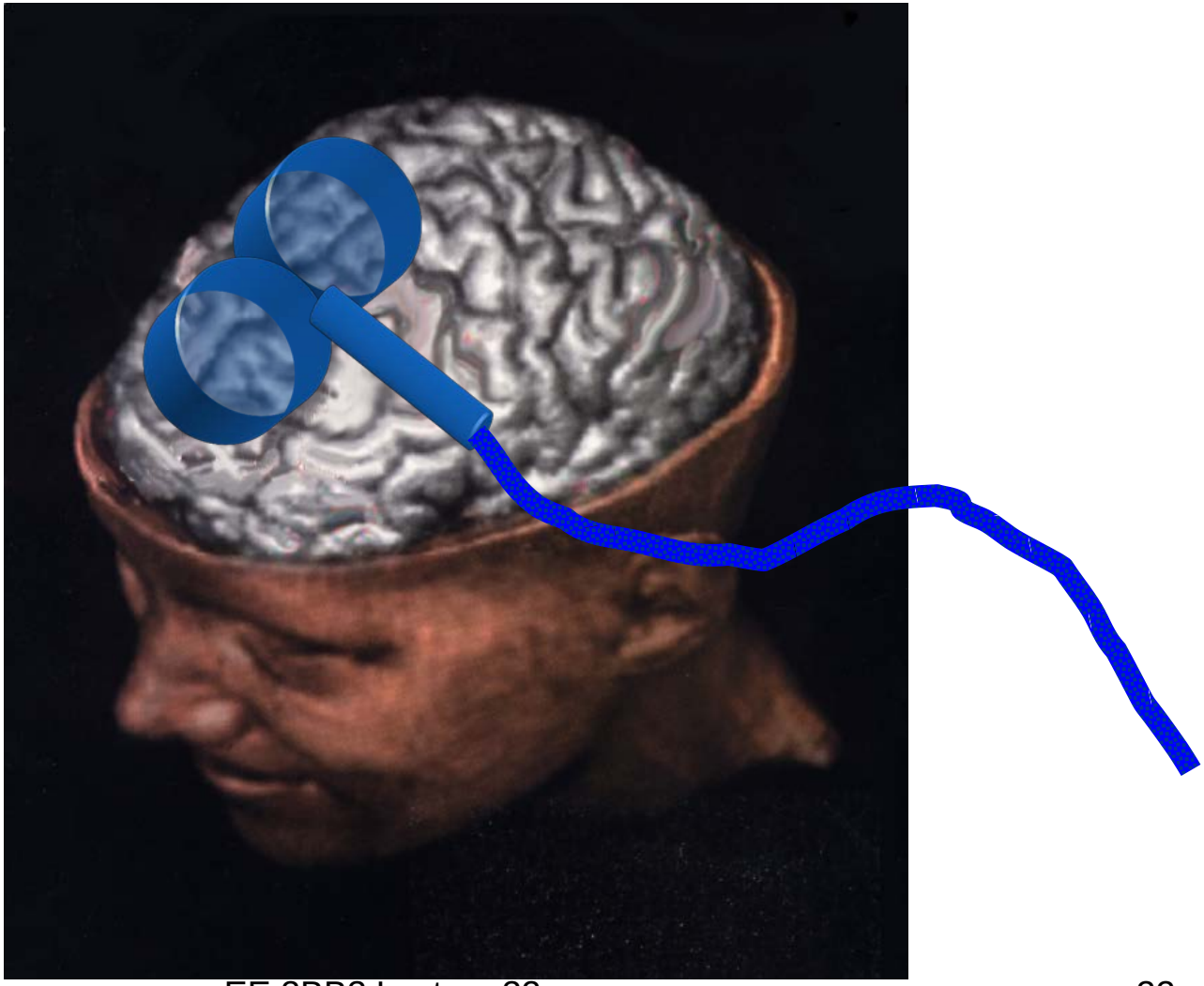
Standard positioning method correctly places coil at the appropriate site to effect an antidepressant response

Possible site of correctable dysfunction



Those without correctable pathophysiology will not respond no matter where we put the coil(we are quite good at predicting NON-RESPONSE using QEEG)

No rTMS correctable dysfunction present therefore coil positioning is not important



Current Status for EEG Processing

- Significant results for simple Alpha and Theta power ratios in determining potential responders (50 – 60%)
- Considerable improvement when using more EEG parameters in a learning algorithm (80%, N = 54)

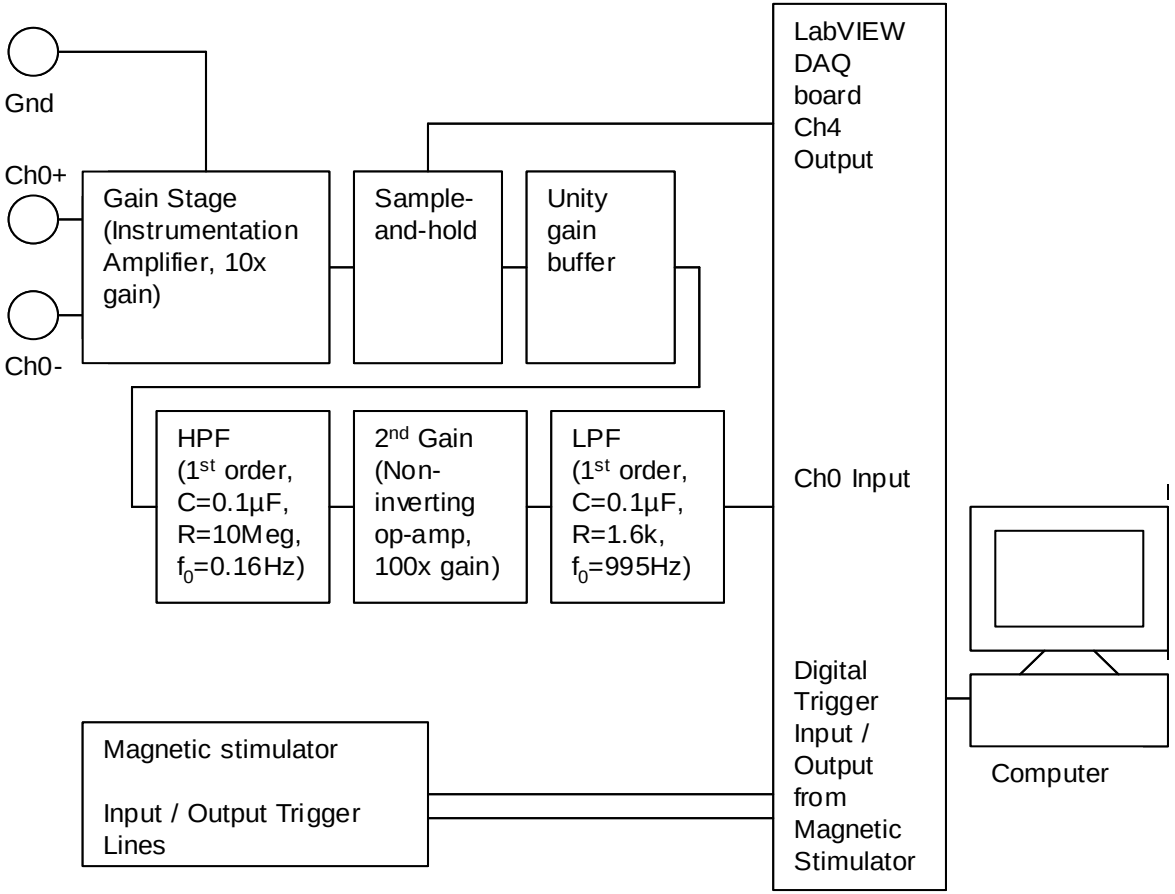
Magnetically Evoked Potentials (MEP)

- Assume the neural tissue is a stochastic system
- Require multiple stimuli and synchronous averaging of evoked potentials
- Heating of EEG electrodes during stimulus train
- Saturation of amplifiers by magnetic stimulus artifact

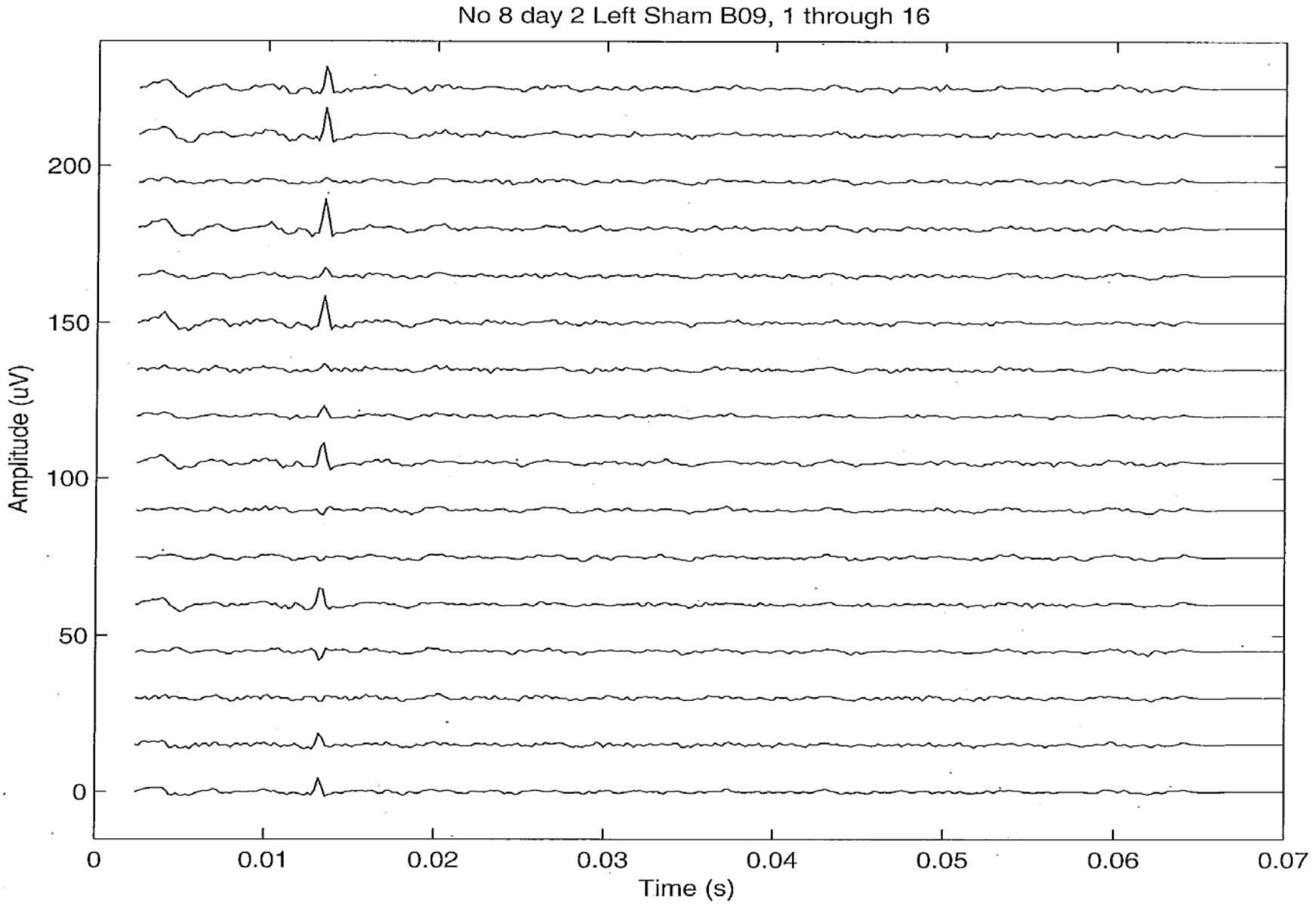
Artifact Blocking

- Various methods have been used:
  - Low slew rate amplifiers (Thut, 2005, Ives, 2006)
    - First 30ms of signal lost and bandwidth reduced
  - High bandwidth amplifiers (Fuggetta, 2005)
    - First 15ms of signal lost
  - Switching off the amplifiers (Shutter, 2006)
    - First 200ms of signal lost
  - Sample-and-hold circuit (Ilmoniemi, 1997)
    - Works, published results ignore or mask first 10 ms

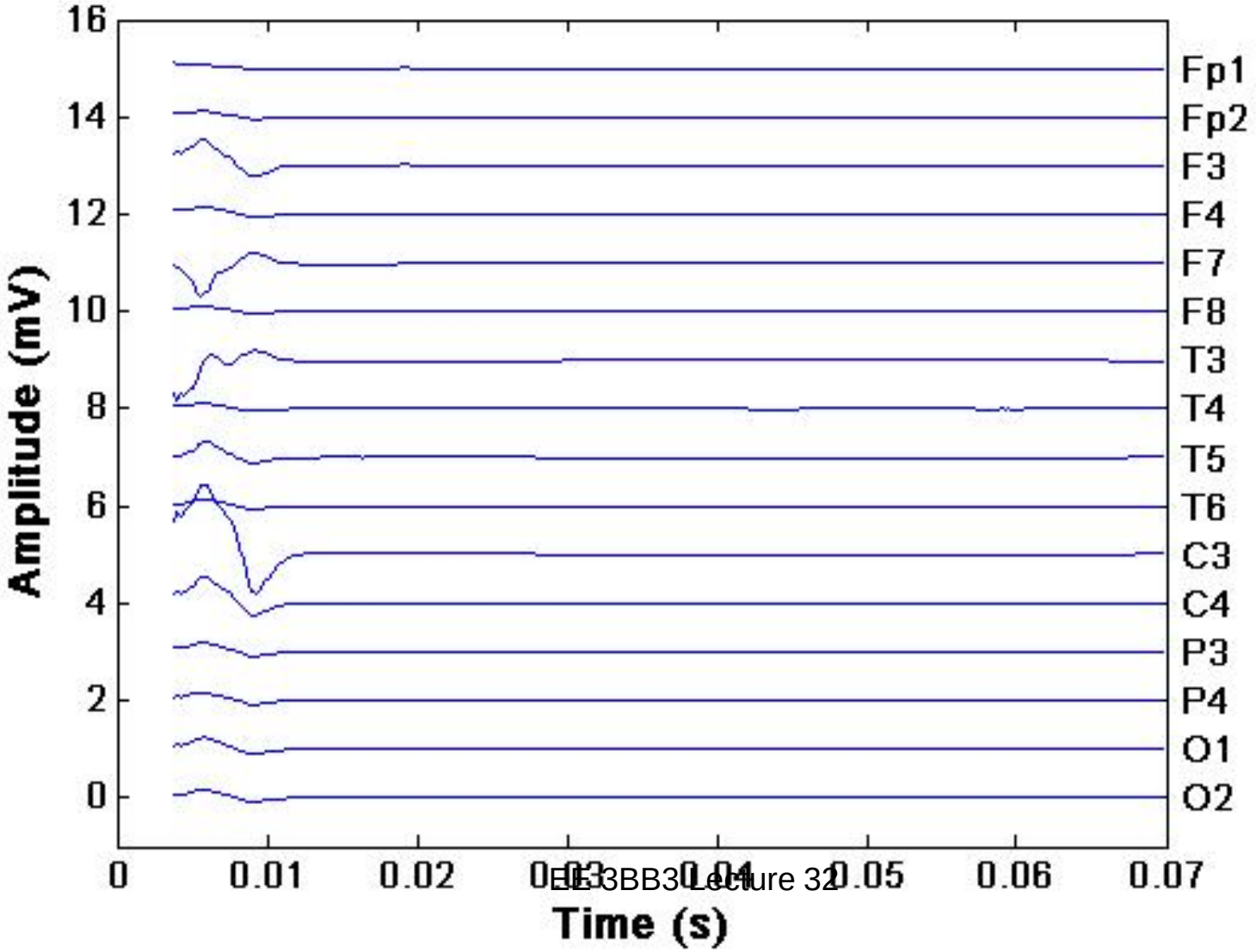
Systems Approach



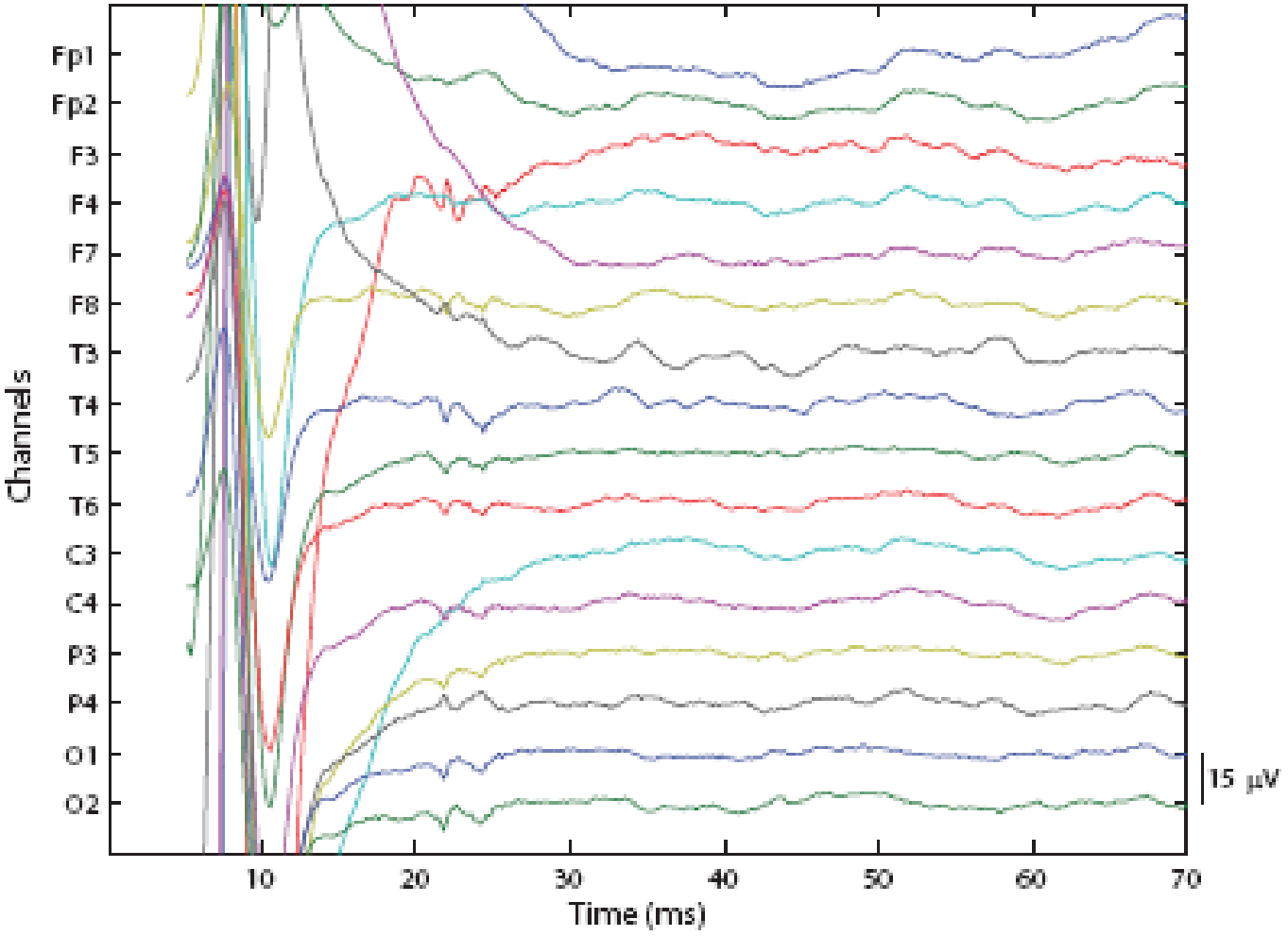
Typical Left 10 Hz Sham Response



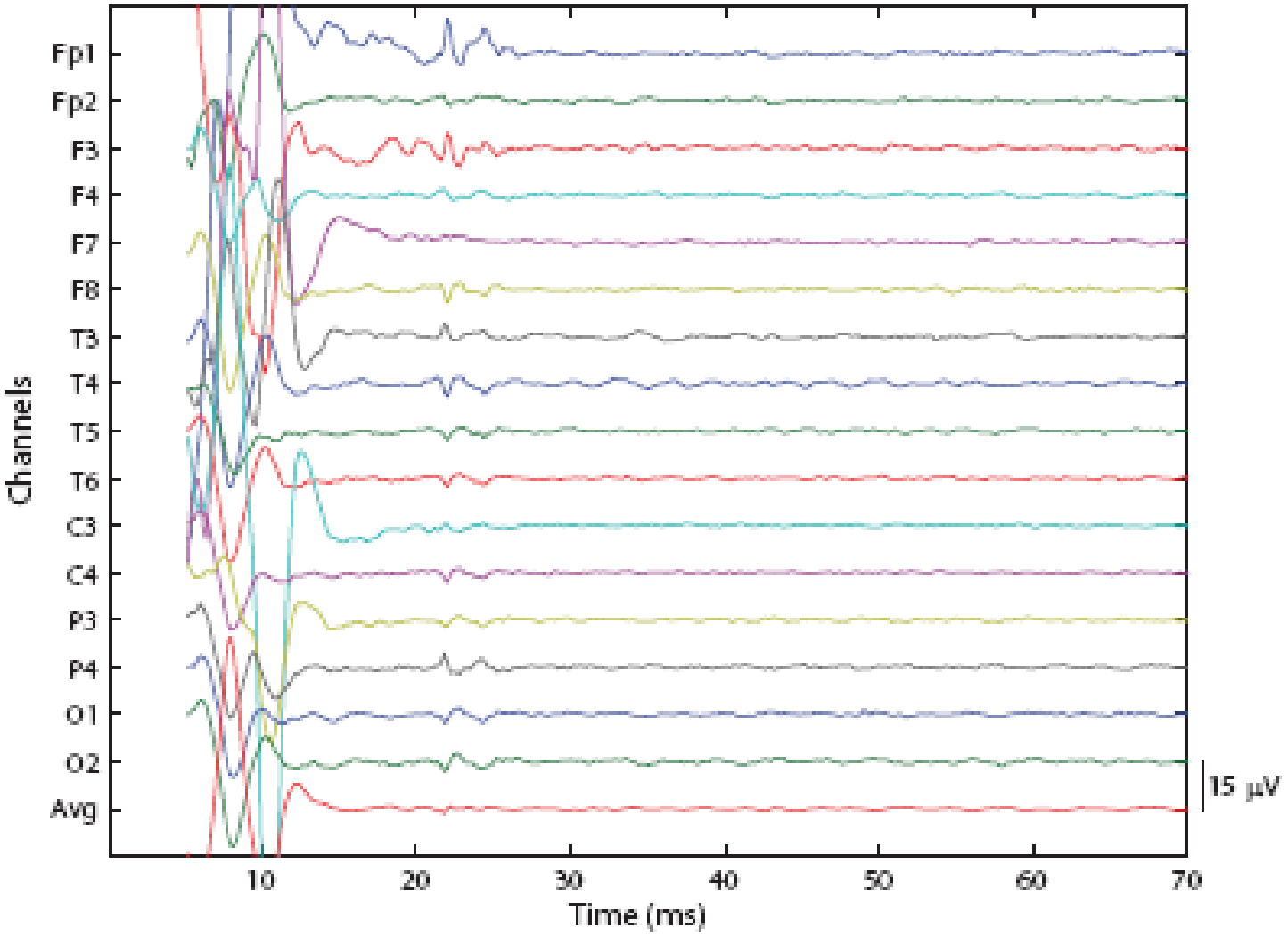
Scalp Muscle Response



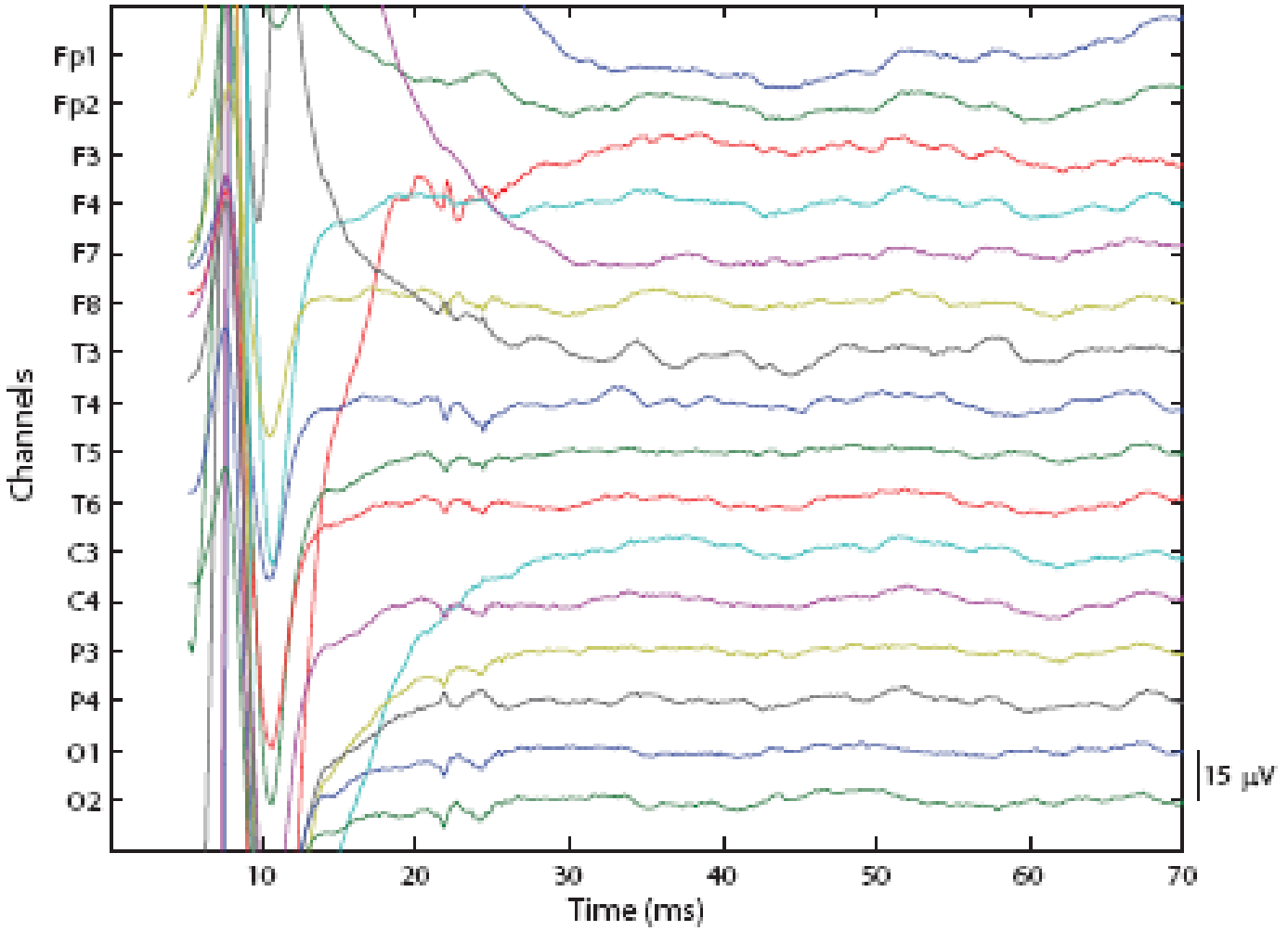
Unfiltered B10 Response to 10 Hz at B10, 80 Pulses



150 – 2 kHz Filtered Response for Slide 29



Brain Response Recorded on Scalp



Responses Following Processing

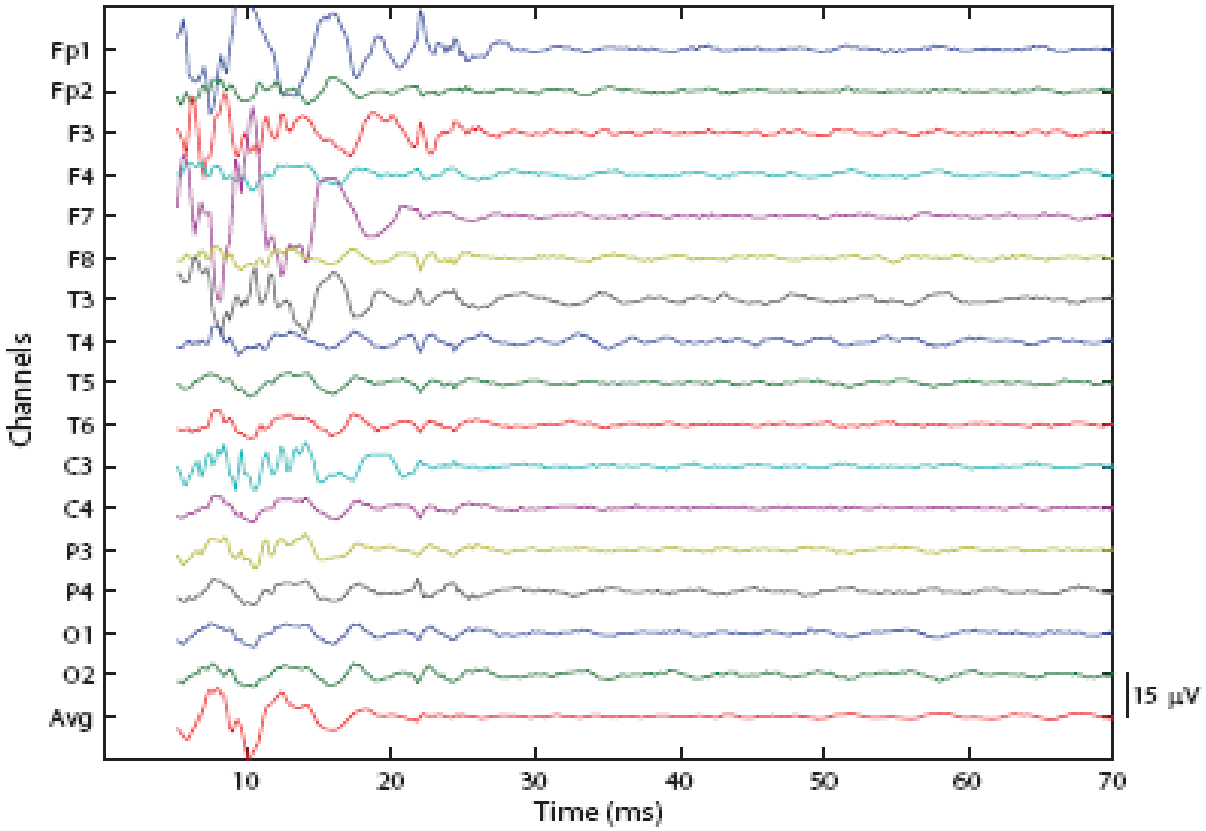
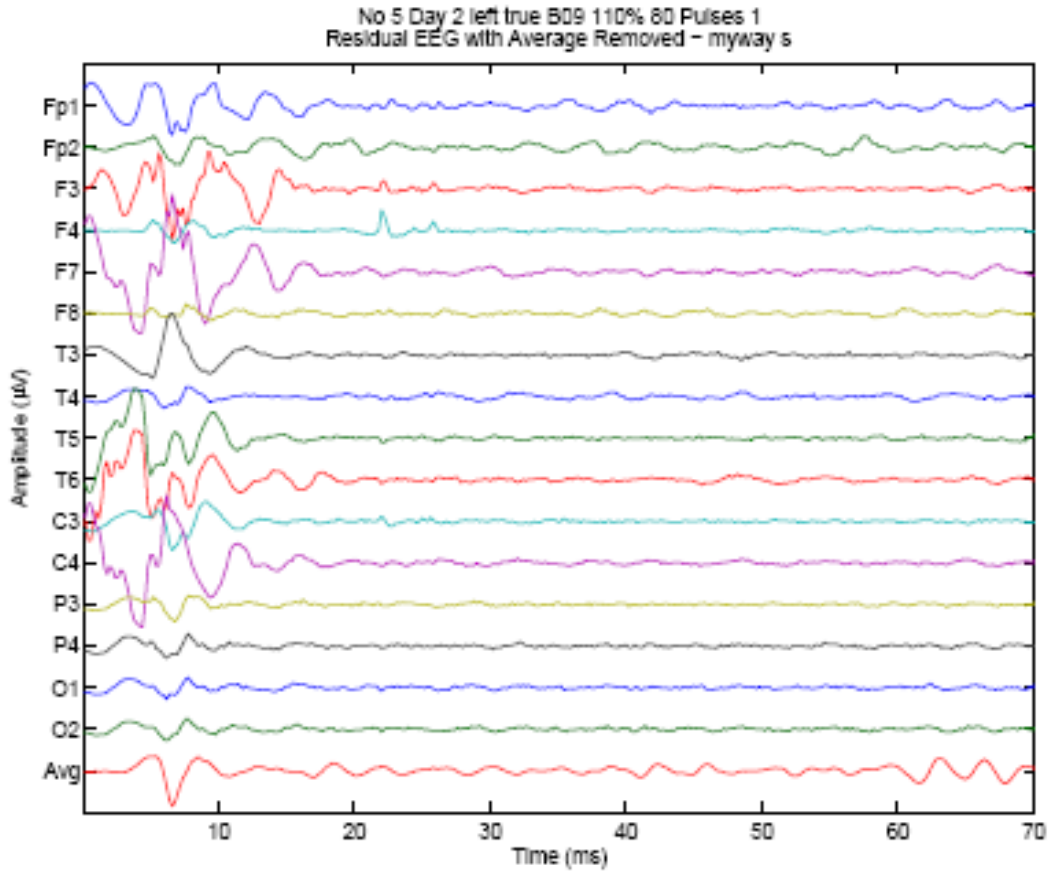


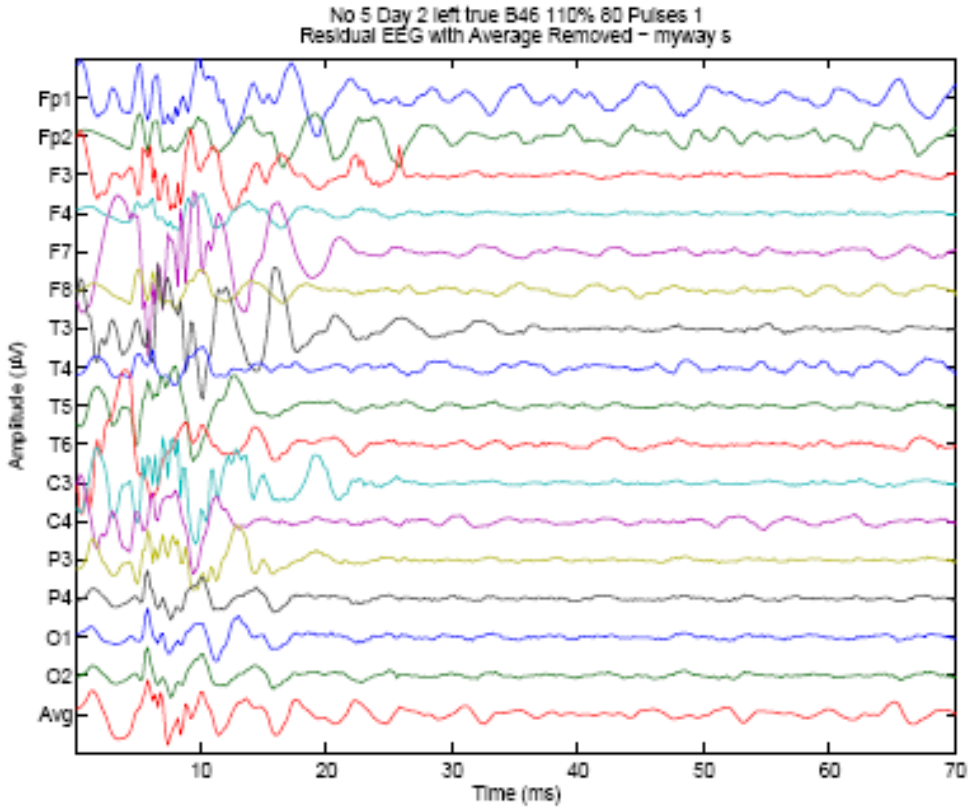
Fig. 3. Residual of wavelet denoising by soft thresholding

Left 10 Hz B09



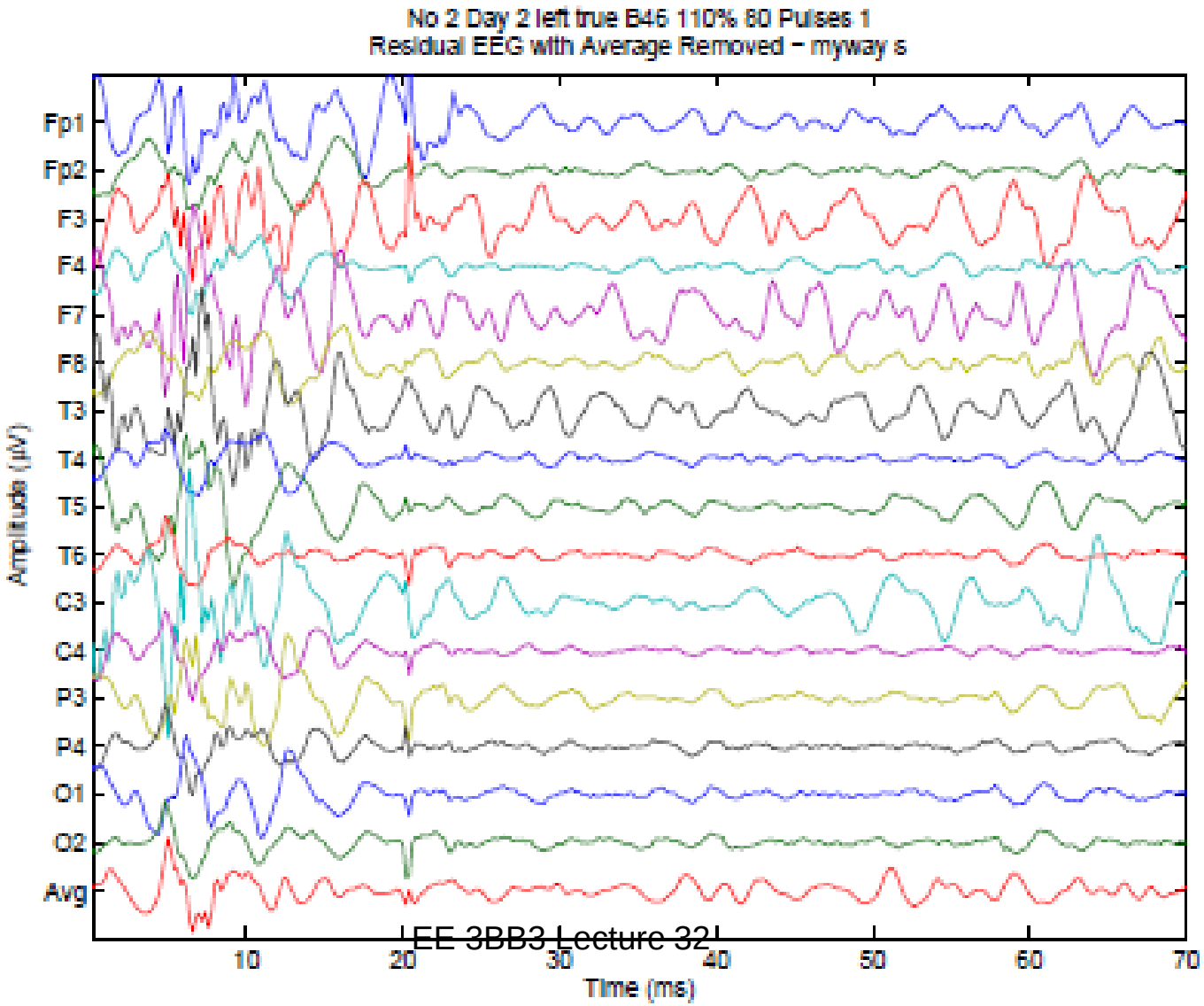
(b) Residual EEG, Soft Thresholding, Average Removed

Left 10 Hz B46



(b) Residual EEG, Soft Thresholding, Average Removed

Wavelet Denoised Response



Right Side Denoised Response