TMS Physics and Physiology

Targeting, Dosing, and Physiological Effects

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1 2/27/2026

1

COI Disclosure

- Potential conflicts of interest related to this presentation: None

2 2/27/2026

2

Outline

- ❑ Physics
- ❑ Physiology and physiological effects (spTMS)
- ❑ Targeting
- ❑ Intensity and Dosing

3

Key abbreviations

- ❑ B-field = Magnetic field (flux density) [Tesla]
- ❑ H = Magnetic field strength [A/m]
- ❑ E-field = Electric field [V/m]
- ❑ I = Electric current [Amperes]
- ❑ V = Electric voltage [Volts]
- ❑ AC = Alternating current
- ❑ DC = Direct current

4

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Physics

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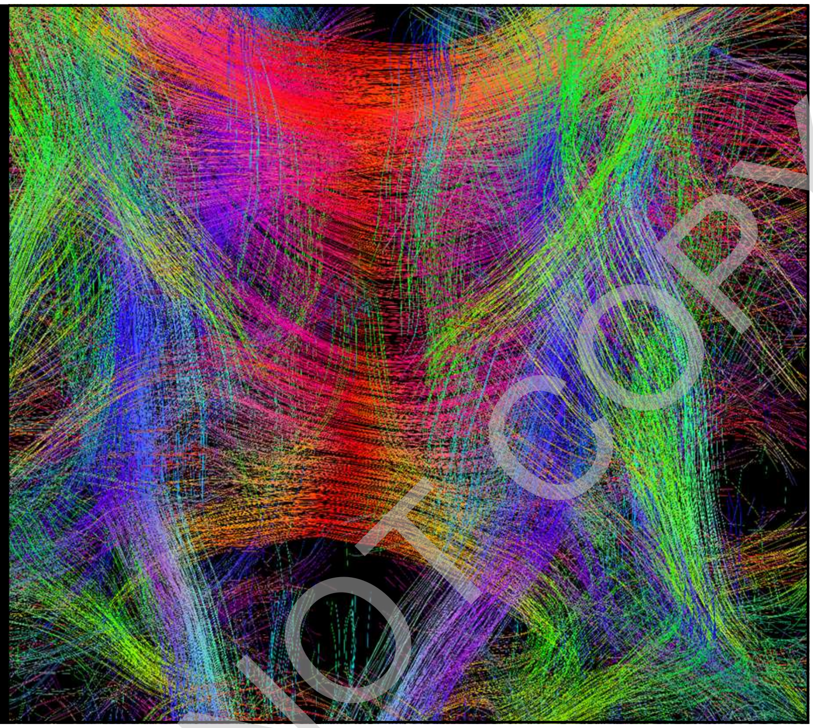

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Physics of TMS

1. Electricity

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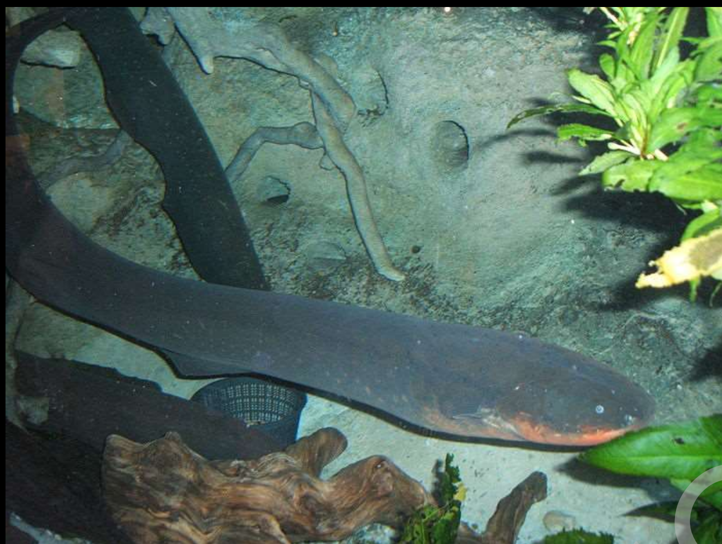
Old inventions



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Old inventions

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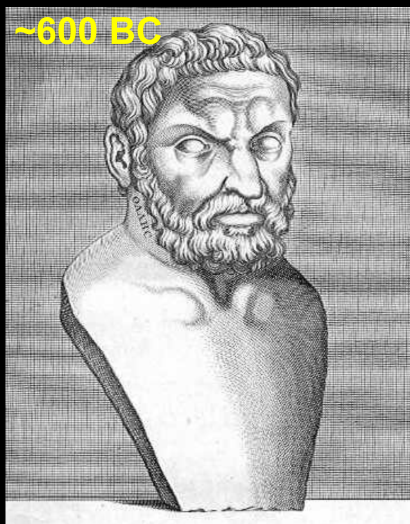
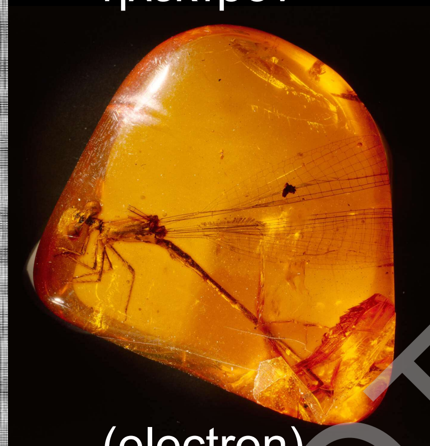
Old inventions: Static electricity



Thales of Miletus (c. 624 – 546 BC)

ἤλεκτρον



(electron)

αίλουρος

(aiélouros)

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Old inventions: Static electricity (non-human)

10

Old inventions: Static electricity (human)

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11

Physics of TMS

2. Magnetism

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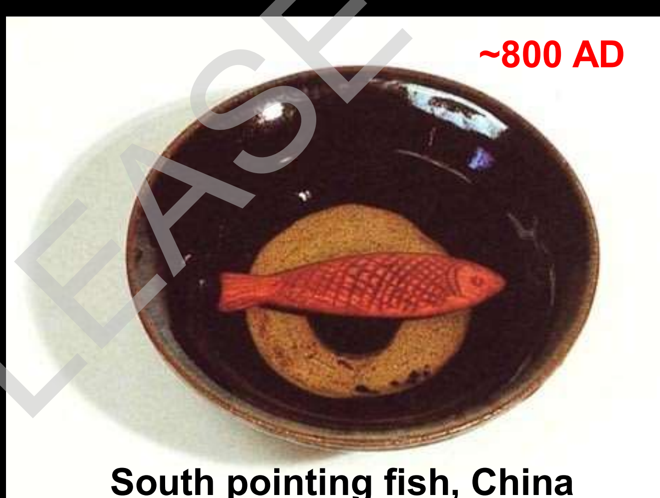
12

Old inventions

13

Old inventions



William Gilbert

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Gilbert (1600) De Magnete, Magneticisque Corporibus, et de Magno Magnete Tellure. Petrus Short (Publisher), London.

14

Physics of TMS

3. Electromagnetism

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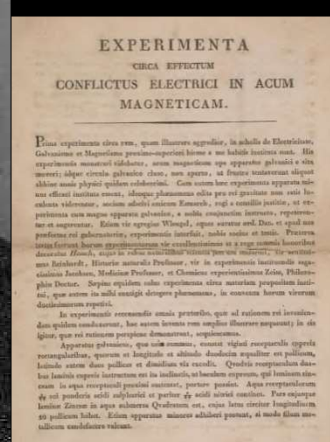
15

New inventions: Electricity and magnetism


EXPERIMENTA
CIRCA EFFECTUM
CONFLICTUS ELECTRICI IN ACUM
MAGNETICAM.

Hans Christian Ørsted

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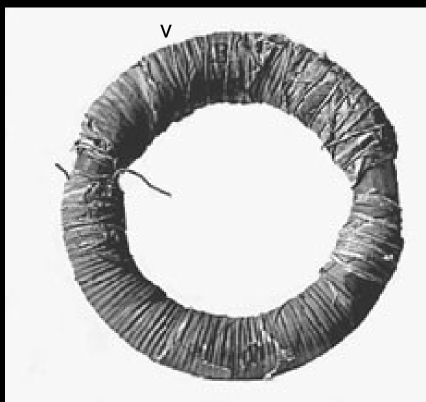
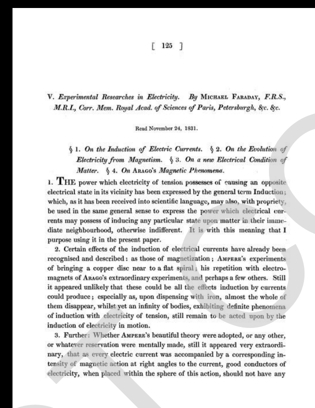
Ørsted (1820) Experimenta circa effectum conflictus electrici in acum magneticam. Self-publication, Copenhagen.

16

New inventions: Electromagnetic induction

1831





[125]

V. *Experimental Researches in Electricity.* *By* MICHAEL FARADAY, *F.R.S., M.R.I., Corr. Mem. Royal Acad. of Sciences of Paris, Petersburgh, &c. &c.*

Read November 24, 1831.

§ 1. *On the Induction of Electric Currents.* § 2. *On the Evolution of Electricity from Magnetism.* § 3. *On a new Electrical Condition of Matter.* § 4. *On* ARAGO's *Magnetic Phenomena.*

1. THE power which electricity of tension possesses of causing an opposite electrical state in its vicinity has been expressed by the general term Induction; which, as it has been received into scientific language, may also, with propriety, be used in the same general sense to express the power which electrical currents may possess of inducing any particular state upon matter in their immediate neighbourhood, otherwise indifferent. It is with this meaning that I purpose using it in the present paper.

2. Certain effects of the induction of electrical currents have already been recognised and described: as those of magnetization; AMPERE's experiments of bringing a copper disc near to a flat spiral; his repetition with electro-magnets of ARAGO's extraordinary experiments, and perhaps a few others. Still it appeared unlikely that these could be all the effects induction by currents could produce; especially as, upon dispensing with iron, almost the whole of them disappear, whilst yet an infinity of bodies, exhibiting definite phenomena of induction with electricity of tension, still remain to be acted upon by the induction of electricity in motion.

3. Further: Whether AMPERE's beautiful theory were adopted, or any other, or whatever reservation were mentally made, still it appeared very extraordinary, that as every electric current was accompanied by a corresponding intensity of magnetic action at right angles to the current, good conductors of electricity, when placed within the sphere of this action, should not have any

Induction Ring

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Michael Faraday

The relationship between electricity and magnetism by induction

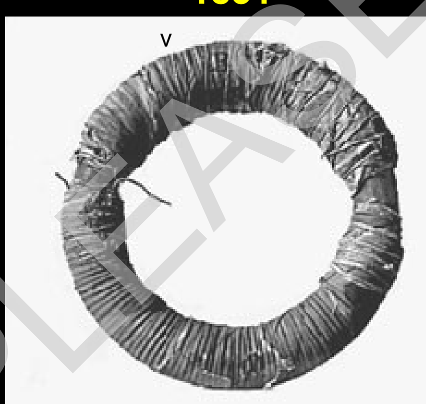
Faraday (1832) Experimental researches in electricity. Phil Trans R Soc Lond 122:125–62.

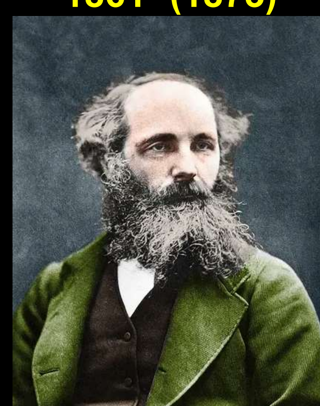
17

New inventions: Electromagnetic induction

1831

1861- (1873)





Induction Ring

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Michael Faraday

The relationship between electricity and magnetism by induction

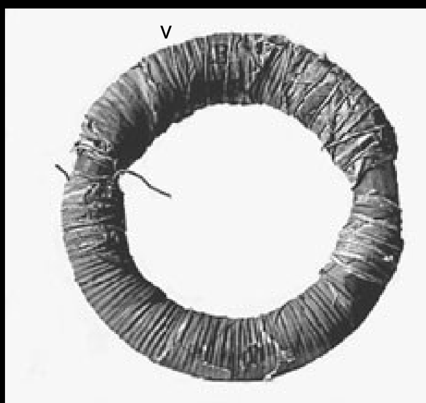
James Clerk Maxwell

Mathematical formulation

18

New inventions: Electromagnetic induction

1831



1861- (1873)

Induction Ring

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Michael Faraday

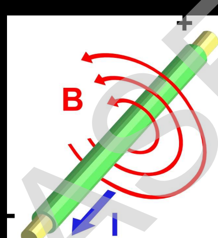
The relationship between electricity and magnetism by induction

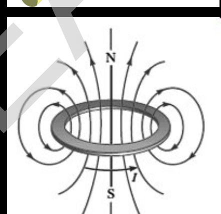
Maxwell (1873) A Treatise on Electricity and Magnetism. 2 vols. Oxford, Clarendon Press (publisher).

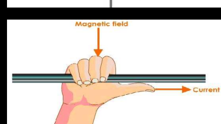
Heaviside (1885-1887) Electromagnetic Induction and Its Propagation. The Electrician (multi-volume publication).

19

New inventions: Electromagnetic induction







Current *I* flowing in a conductor wire will create a magnetic field ***B*** around the conductor (Ampère's Law)

Current *I* flowing in a circular conductor wire will create a shaped magnetic field ***B*** around the conductor (Biot–Savart Law)

Maxwell's right hand grip rule

20

Physics of TMS

4. Electromagnetic stimulation

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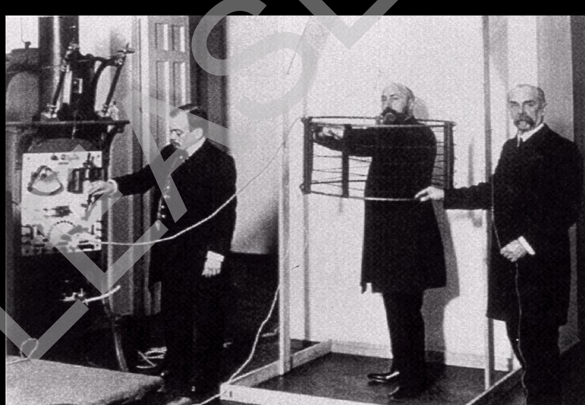
21

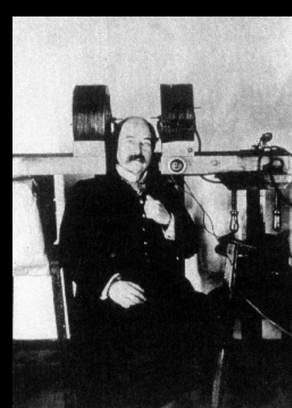
New inventions: AC current to coils (phosphenes)

1896



Arsene d'Arsonval

1910



Silvanius Thompson

d'Arsonval (1896) Dispositifs pour la mesure des courants alternatifs de toutes fréquences. C R Soc Biol (Paris) 3:450–7.

Thompson (1910) A physiological effect of an alternating magnetic field. Proc R Soc Lond (Biol) B82:396–9.

22

New inventions: AC current to coils (phosphenes)

1911

1947

VISUAL SENSATIONS AROUSED BY MAGNETIC FIELDS[1]

HORACE B. BARLOW, HENRY I. KOHN AND E. GEOFFREY WALSH

From the Department of Biology, Massachusetts Institute of Technology, Cambridge, and the Harvard Medical School, Boston, Massachusetts

Received for publication September 7, 1946

Visual sensations aroused by physical stimuli other than light are called phosphenes, and their production by the application of electric currents to the eye has long been known. Electromagnetic fields may also elicit phosphenes; a relatively obscure fact which d'Arsonval (1896) appears to have been the first to record. Thompson (1910) unaware of previous work, rediscovered this effect of magnetic fields using 1,000 Gauss at 50 c.p.s. and described the sensation as a colorless flicker which was brightest in the peripheral parts of the visual field. Dunlap (1911) and Magnusson and Stevens (1912) confirmed this description and made the additional observation that the 25 cycle field was more effective than the 60. For our work we used alternating magnetic fields of variable frequency and compared the properties of the sensations thereby produced with those produced by passing sinusoidal electric currents through the head.

METHODS. The magnet had 397 turns of number 16 copper wire. The dimensions were: internal diameter 10.5 cm., external diameter 20.3 cm., length 7.3 cm. A laminated iron core 5.3 x 2.9 x 37 cm. was placed inside the winding. Current was supplied by a generator, and the strength was adjusted by a variable transformer. The frequency was measured with a calibrated magneto and varied from 10 to 90 c.p.s. The field strength was calculated from the readings of an A.C. voltmeter connected to a small search coil, calibrated in a field of known strength and frequency. All values are in R. M. S. Gauss. Using 20 amperes we were able to obtain up to 900 Gauss. The subject was seated with his temple close to, but not necessarily in contact with, the core of the magnet; under optimal conditions the phosphene could be seen when the temple was several centimeters from the core. The subject fixated steadily on a white spot placed in the center of a dark grey background.

To produce phosphenes by electrical stimulation current from a beat frequency oscillator was applied between an electrode on the side of the forehead and one on the back of the forearm. These electrodes were copper discs 3 cm. in diameter, covered with cloth soaked in saturated sodium chloride solution, and were held in place with adhesive tape. Small changes in inter-electrode resistance should not affect the results since current, not voltage, was measured. The currents used never exceeded 1 milliampere and we were not troubled with pain at the site of the electrode.

[1] A preliminary note on this work appeared in Fed. Proc. 5: 110, 1946. We wish to thank Dr. K. S. Lion and Prof. F. O. Schmitt, Massachusetts Institute of Technology, for their helpful interest in this work, and the Baruch Committee on Physical Medicine for providing the laboratory equipment.

372

Magnusson & Stevens **Barlow et al: It is retinal…**

Magnusson & Stevens (1911) Visual sensation caused by changes in the strength of a magnetic field. Am J Physiol 29:124–36.
Barlow, Kohn, Walsh (1947) Visual sensations aroused by magnetic fields. Am J Physiol 148:372–5.

23

Physics of TMS

5. Electromagnetic stimulation of the BRAIN

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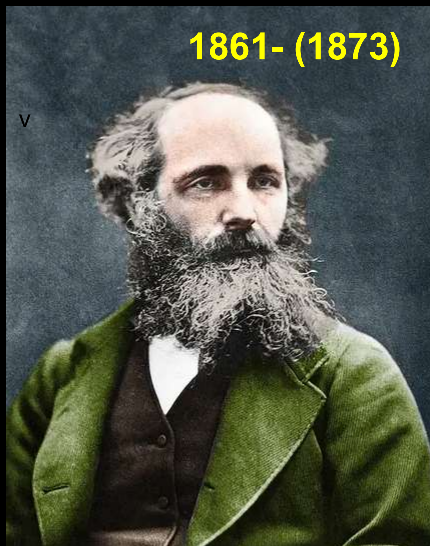
24

Newest inventions: Back to Maxwell



James Maxwell

Faraday-Maxwell Equation

$$\nabla \times E = -\frac{\partial B}{\partial t}$$

- Curl Operator
- Electric field
- Magnetic field
- Time
- Lenz sign

25

Newest inventions: TMS

Kolin et al. 1959: Alternating magnetic field (60 Hz/1 kHz) can stimulate nervous tissue

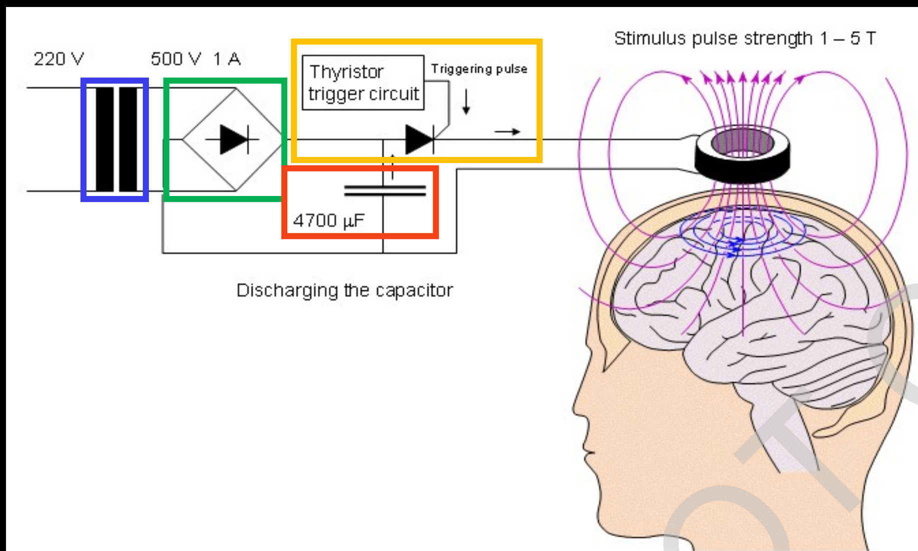
Bickford & Fremming 1965 used a magnetic pulse to stimulate muscle

Barker et al. 1985 stimulated the human brain transcranially with magnetic pulses (TMS)

Barker, Jalinous, Freeston (1985) Non-invasive magnetic stimulation of human motor cortex. The Lancet 325(8437):1106–7.

26

Newest inventions: TMS



27 *Picture from: Malmivuo and Plonsey (1995) Bioelectromagnetism. Oxford University Press.*

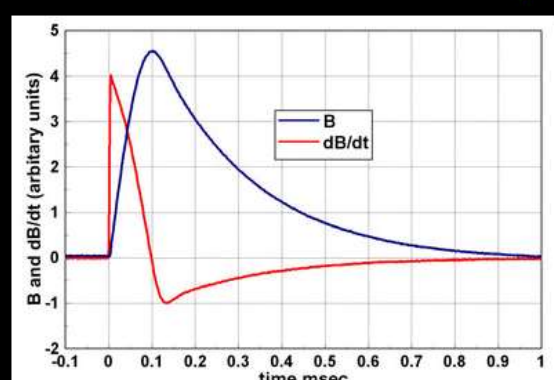
27

Newest inventions: TMS

Static 3T field (MRI) → no nerve stimulation

Fast change from 0 to ~3 T → TMS

The strength of the electric field is determined by the first derivative of the magnetic flux over time (dB/dt): The faster the change in magnetic field, the stronger the E-field and nervous stimulation



28 2/27/2026

28

Physics of TMS

6. Which brain areas do the laws of physics allow us to stimulate

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TMS coil shapes

- ❑ Circular (“pancake”) coils
- ❑ Figure-of-eight coils
- ❑ H-coils
- ❑ Other designs

Ueno et al., (1988) J Appl Phys 64:5862-5864; Zangen et al., (2005) Clin Neurophysiol 116(4):775-779; Ueno and Sekino (2021) Front Hum Neurosci 15:805971.

TMS coil shape and induced E-field shape

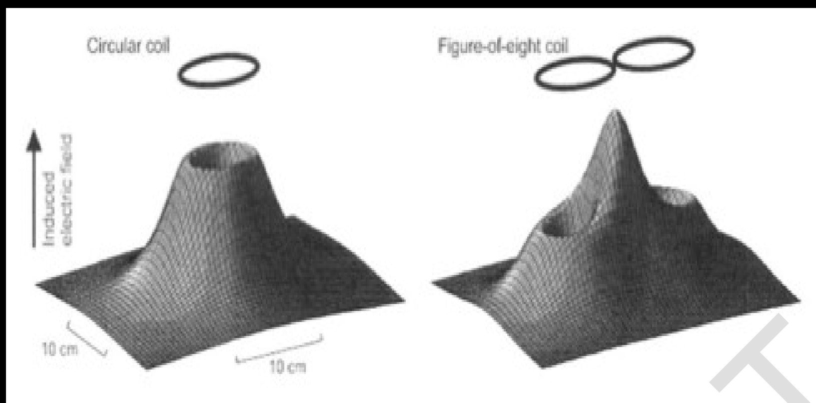


Fig. 2. The strength of the electric field induced in a spherical volume conductor below a circular (*left*) and a figure-of-eight coil (*right*). Reprinted from (Ilmoniemi *et al.*, 1999), with permission of Begell House, Inc.

Cohen & Cuffin (1991) J Clin Neurophysiol 8:102-11; Ilmoniemi et al. (1999) Crit Rev Biomed Eng 27(3-5):241-8

31

TMS coil shape and induced E-field shape

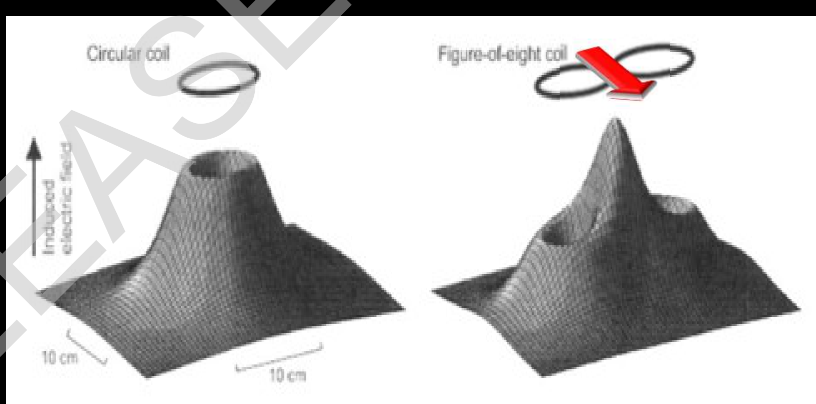


Fig. 2. The strength of the electric field induced in a spherical volume conductor below a circular (*left*) and a figure-of-eight coil (*right*). Reprinted from (Ilmoniemi *et al.*, 1999), with permission of Begell House, Inc.

Cohen & Cuffin (1991) J Clin Neurophysiol 8:102-11; Ilmoniemi et al. (1999) Crit Rev Biomed Eng 27(3-5):241-8

32

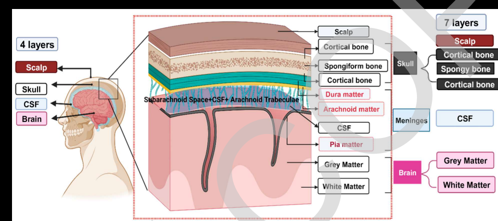
Volume conductor (Head): SKULL

The skull (bone in general) is an excellent electric insulator

Electric currents pass poorly

… but magnetic fields go right through!

Relevant to tDCS *vs.* TMS intensity (0.3-0.5 V/m *vs.* 50-100 V/m) and focality (tDCS focality is comparatively less)



Picture from: Daru et al (2024) Appl Sci 14:2495.

Cohen (1972) Science 175:664-6

Cohen & Cuffin (1991) J Clin Neurophysiol 8:102-11

Nummenmaa et al. (2013) Clin Neurophysiol 124:1995-2007

33 2/27/2026

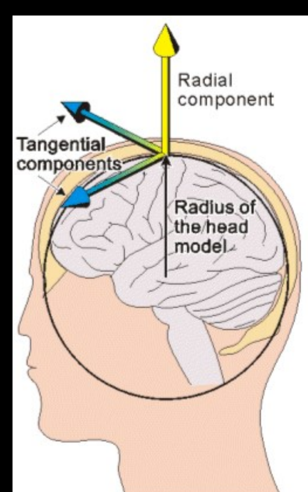
33

Volume conductor (Head): Geometry

In a spherically symmetric homogeneous isotropic volume conductor, TMS induced E-fields and currents at the center are ZERO

Since the head is not perfectly spherical or symmetrical or isotropic, in reality there may be some (weak) deep activations

Note the holes in the skull (e.g., foramen magnum)



Yonokuchi & Cohen (1991) J Clin Neurophysiol 8:112-20.

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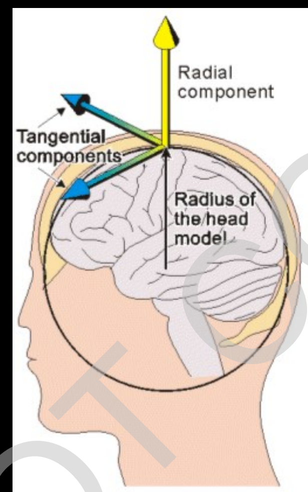
34

Volume conductor (Head): Orientations

In a spherically symmetric homogeneous isotropic volume conductor, TMS induces only tangential E-fields and currents (nothing radial)

Since the head is not perfectly spherical or homogeneous or isotropic, in reality there may be some (weak) radial components

Relevant to activation of sulci vs. gyri



Cohen & Cuffin (1991) J Clin Neurophysiol 8:102-11.

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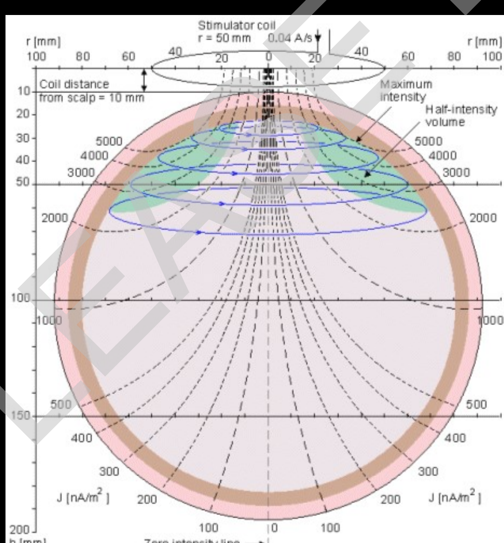
35

How deep can we stimulate?



TMS is fundamentally a <u>superficial</u> brain stimulation technique

To reach effective stimulation intensities <u>a little</u> deeper, we can use a larger coil and/or increase the stimulator intensity

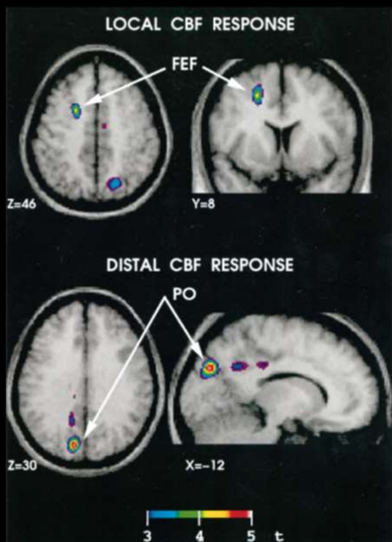
However, then we
- Sacrifice focality on the surface
- Stimulate the surface VERY strongly

Picture from: Malmivuo and Plonsey (1995) Bioelectromagnetism. Oxford University Press.

Deng et al. (2013) Electric field depth-focality tradeoff in transcranial magnetic stimulation: Simulation comparison of 50 coil designs. *Brain Stimul 6:1-13.*

36

If we must stimulate a deep structure:



Our best (~only) approach is to leverage connectivity (indirect stimulation):

Stimulate a surface area accessible to TMS that is connected to the remote / deep target

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Paus et al. (1997) J Neurosci 17(9):3178-84; Ilmoniemi et al. (1997) Neuroreport 8:3537-40.

37

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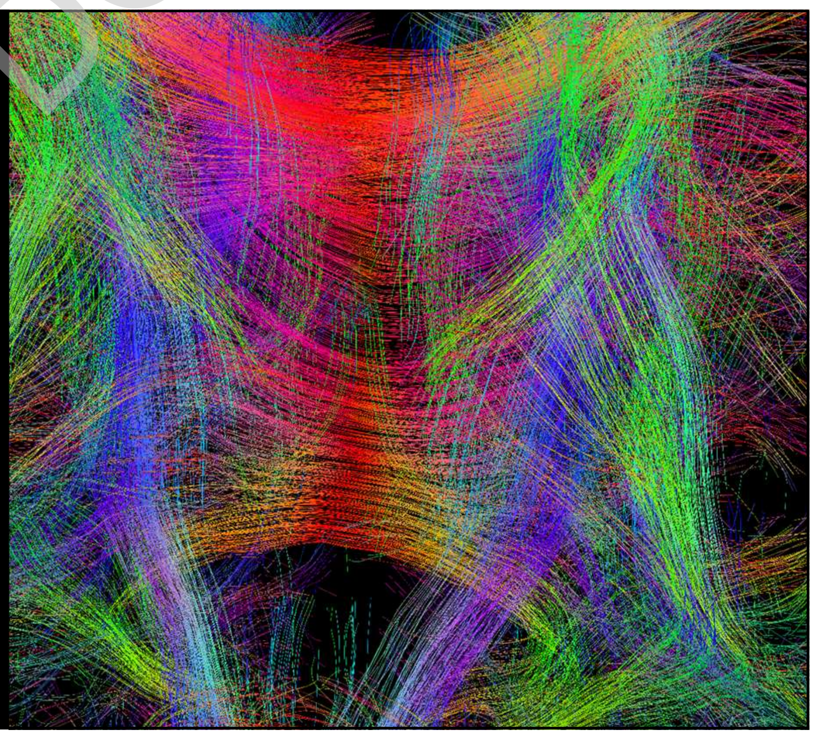
Physiology and Physiological Effects (spTMS)

38 2/27/2026



38

Physiology of TMS

How does TMS activate neurons?

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How does TMS activate neurons?

How does TES activate (tDCS/tACS bias) neurons?

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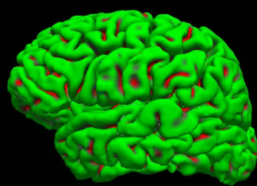
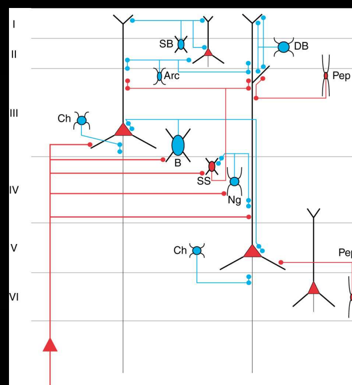
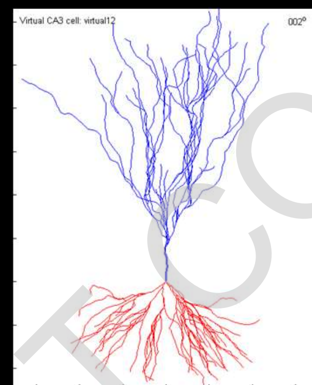
… approached at different spatial resolutions:

Macroscopic | **Mesoscopic** | **Microscopic**







Source:
http://www.krasnow.gmu.edu/alexei/cinema/virt3/intro.html

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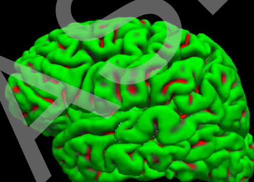
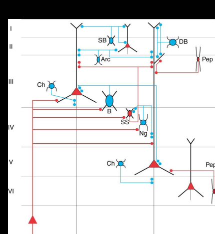
Nummenmaa et al. (2013) Clin Neurophysiol 124:1995-2007; Mountcastle (1998) Perceptual Neuroscience; Diana et al., (2017) Nat Rev Neurosci 18(11):685-93

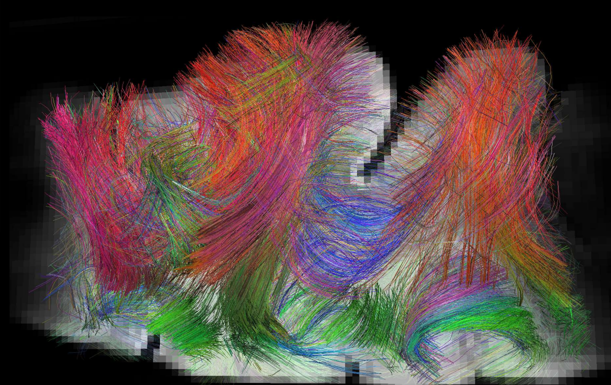
41

… in two different compartments:

Grey matter | **White matter**







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Nummenmaa et al. (2013) Clin Neurophysiol 124:1995-2007; Mountcastle (1998) Perceptual Neuroscience; Diana et al., (2017) Nat Rev Neurosci 18(11):685-93

42

What does TMS do?

Magnetic field pulse (0.2 ms)

→

Electric field pulse (0.2 ms)

→

Electric current pulse in tissue (0.2 ms)

→

Initiation of action potentials in interneurons and/or or pyramidal neurons

43 2/27/2026

43

What does TES do?

Electric field pulse (0.2 ms)

→

Electric current pulse in tissue (0.2 ms)

→

Initiation of action potentials in interneurons and/or or pyramidal neurons

44 2/27/2026

44

What do tDCS/tACS do?

Weak electric fields on scalp, static or fluctuating

→

Corresponding electric currents on scalp

→

Small changes is resting potentials of neurons

→

Changed likelihood of action potentials

45

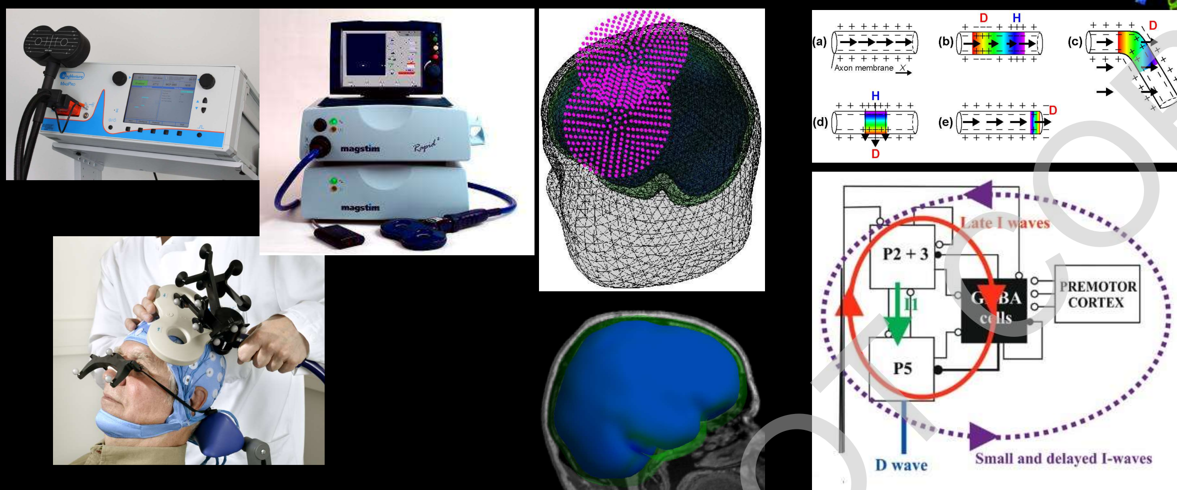
One common currency to bind them all:

Intracranial Electric field (E-field)

46

Three components to unravel mechanisms

Instruments ← **Biophysics** → **Physiology**



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Ilmoniemi et al. (1999) Crit Rev Biomed Eng 27:241-84; Nummenmaa et al. (2013) Clin Neurophysiol 124:1995-2007

47

Biophysics

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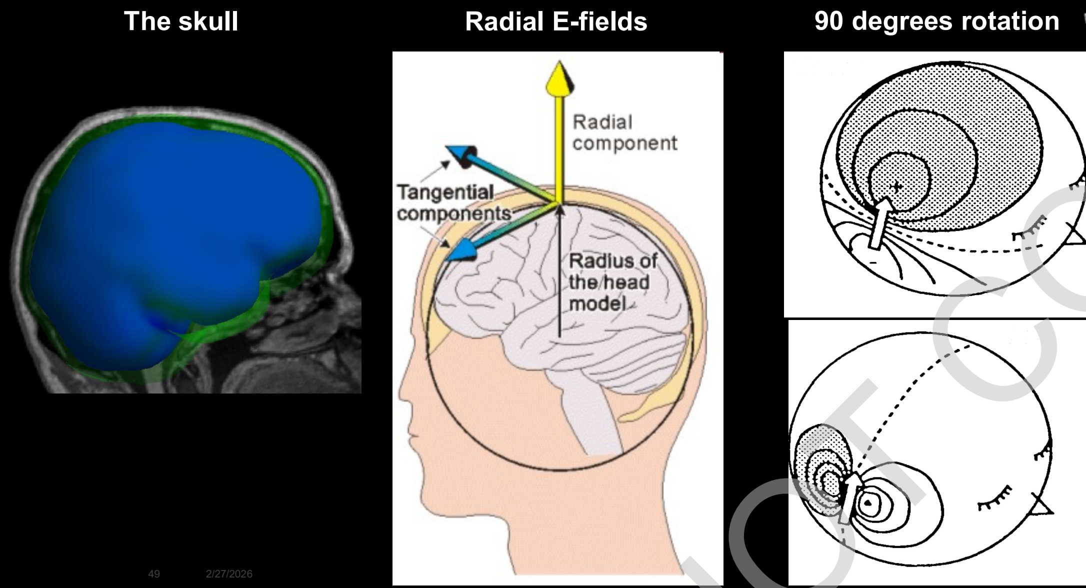
48

Key differences for magnetic *vs.* electrical stimulation



Ilmoniemi et al. (1999) Crit Rev Biomed Eng 27:241-84; Nummenmaa et al. (2013) Clin Neurophysiol 124:1995-2007

49

Physiology: Macroscopic level

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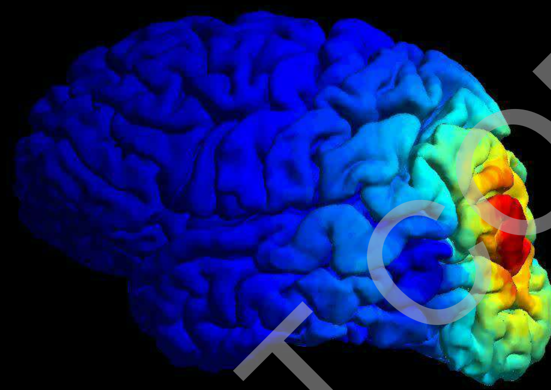
E-field calculations

Where am I stimulating this patient?

What is the intracranial E-field intensity ("dose") of my stimulation?

= "Proof" of target engagement

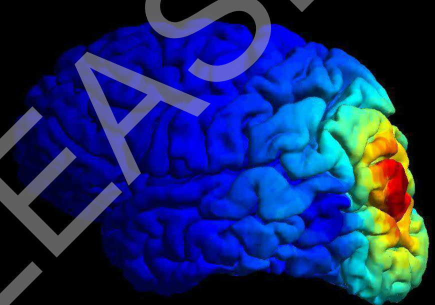


Nummenmaa, Stenroos, Ilmoniemi, Okada, Hamalainen, and Raij (2013) Clin Neurophysiol 124:1995-2007

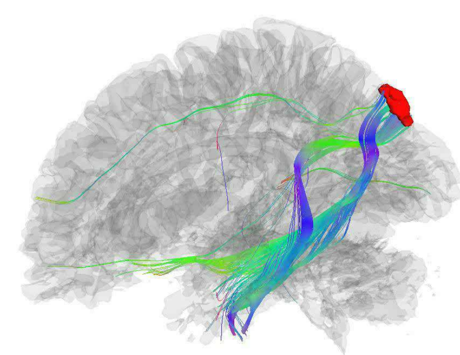
51

E-field calculations and network effects

Primary activations



Secondary activations



Nummenmaa, Stenroos, Ilmoniemi, Okada, Hamalainen, and Raij (2013) Clin Neurophysiol 124:1995-2007

52

Physiology: Microscopic level

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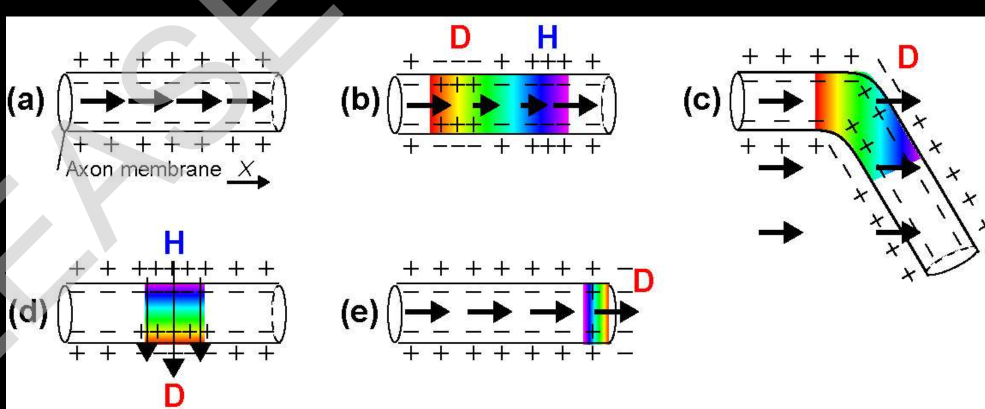
53 2/27/2026

53

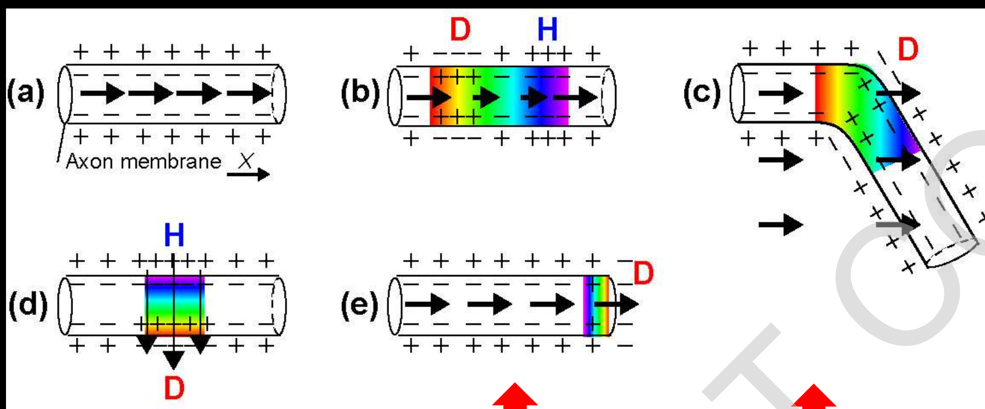
Microscopic effects in GM and WM axons: Passive



Ilmoniemi et al. (1999) Crit Rev Biomed Eng 27:241-84

54

Microscopic effects in GM and WM axons: Passive



Ilmoniemi et al. (1999) Crit Rev Biomed Eng 27:241-84

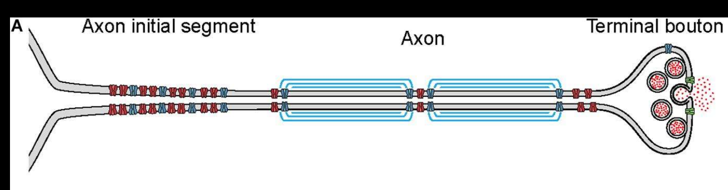
55

Microscopic effects in GM and WM axons: Active

The density of voltage-gated channels varies across the neuron

Thus, E-field evoked action potentials are initiated preferentially at:

- ❑ Axon hillock
- ❑ Nodes of Ranvier
- ❑ Axonal curves
- ❑ Axon terminals (synapses)



Siebner et al., (2022) Clin Neurophysiol 140:59-97.

Burke and Bender (2019) Front Cell Neurophysiol 13:221.

56

TMS physics vs. physiology

Neurons are active elements!

- The physiological output (neuronal action potentials) is not linearly correlated with the physical input (TMS or biological). This nonlinearity is bigger at the level of individual neurons that at populations of neurons.
- The duration of the pulse / stimulation, orientation of the electric field *vs.* the neuron's axis -> all matter!

Software packages (e.g., NEURON) can be used to model the active membrane properties. Not routinely done.

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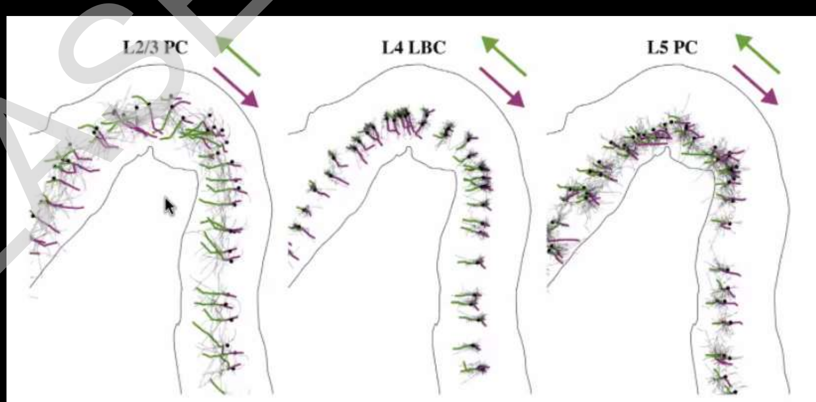
57 2/27/2026

57

E-field microscopic effects in GM axonal arbors

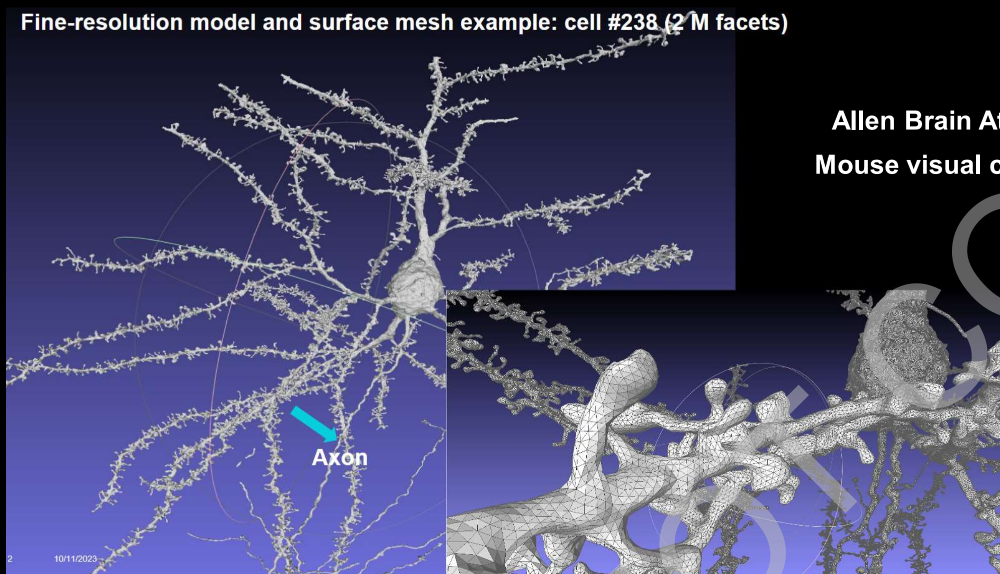


TMS activates axonal terminations aligned to local E-field direction

Aberra et al., (2020) Brain Stimul 13:175-189

58

Microscopic effects in GM



Allen Brain Atlas:
Mouse visual cortex

Qi et al. (2025) Brain Stimul 18(1):77-93

59

Physiology: Mesoscopic level

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60

Physiology: Mesoscopic level

Grey Matter (GM)

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61

Cortical columns and intracortical circuits

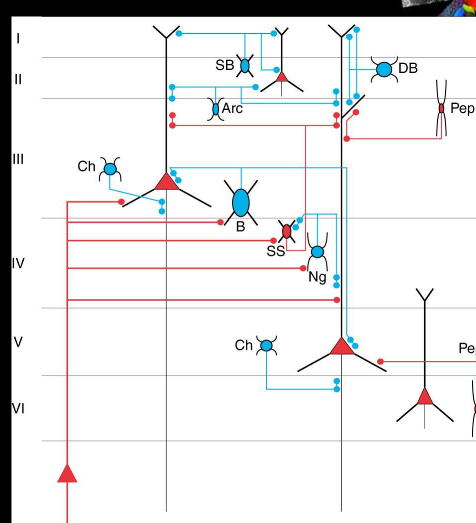
Pyramidal neurons (output units)

Interneurons

TMS/TES induced electric currents permeate the entire scene, causing local hyper- and depolarizations

This triggers cascades of action potentials from all cell types

However, typical recordings detect pyramidal neuron outputs (*e.g.*, MEPs) only



Mountcastle (1998) Perceptual Neuroscience

62

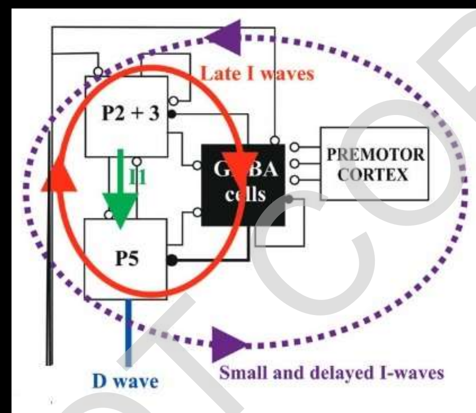
D-waves and I-waves

D-waves: Direct activation of pyramidal neurons

I-waves: Interneurons are activated, leading to indirect activation of pyramidal neurons

Pyramidal neurons and interneurons have different activation thresholds and preferred orientations for the activating current

➔ We can somewhat separately evoke D-waves or I-waves, to study some clinically relevant features (*e.g.,* grey matter abnormalities, white matter lesions)



Terao & Ugawa (2002) J Clin Neurophysiol 19:322-43; Douglas et al., (1989) Neural Comp 1:480-488; Di Lazzaro (2013) Handbook of Clinical Neurology 116: Brain Stimulation

63

D-waves and I-waves (monophasic TMS)

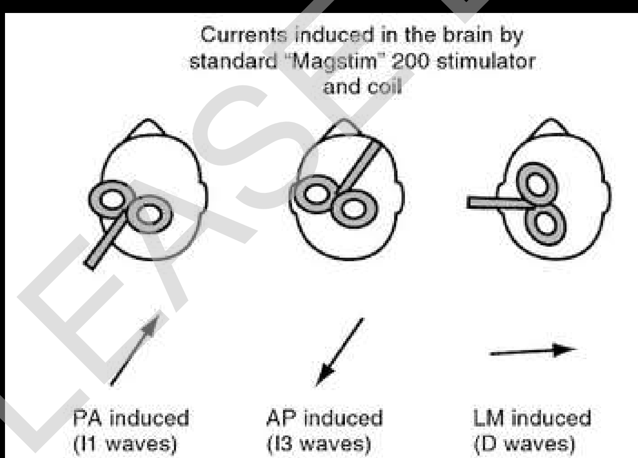
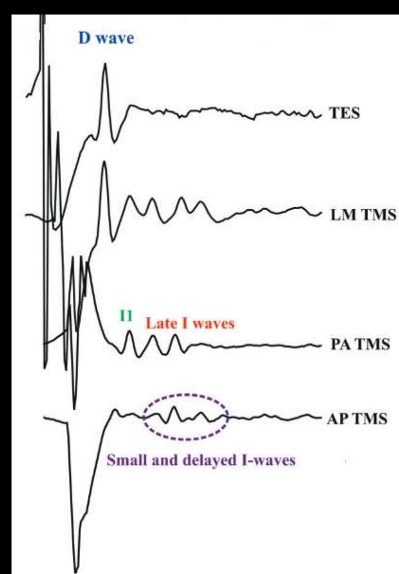


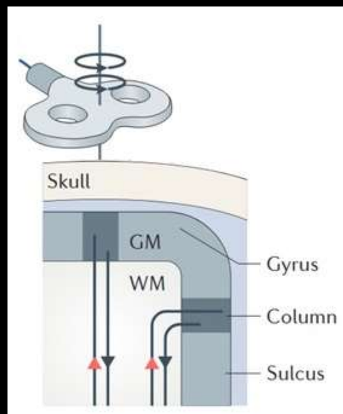
Figure 4–6 Stimulation of the hand area of the motor cortex with different directions of monophasic TMS pulses.



Hallet and Chokroverty (2005) Magnetic Stimulation in Clinical Neurophysiology; Di Lazzaro (2013) Handbook of Clinical Neurology 116: Brain Stimulation

64

TMS coil orientations over gyri *vs.* sulci

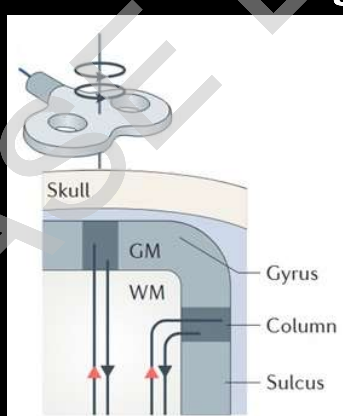


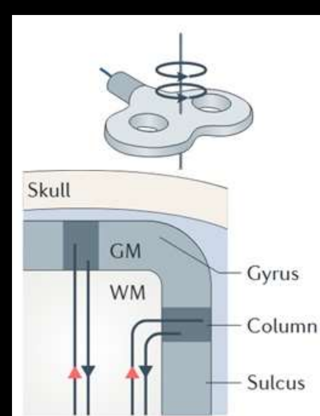
- TMS coil orientation over a gyrus has only a limited effect on motor evoked responses (both D- and I-waves)

Diana, Raij, Melis, Nummenmaa, Leggio, Bonci (2017) Nat Rev Neurosci 18(11):685-93

65

TMS coil orientations over gyri *vs.* sulci





- TMS coil orientation over a gyrus has only a limited effect on motor evoked responses (both D- and I-waves)
- TMS coil orientation over a sulcus has a strong effect on motor evoked responses (both D- and I-waves)

Diana, Raij, Melis, Nummenmaa, Leggio, Bonci (2017) Nat Rev Neurosci 18(11):685-93

66

Physiology: Mesoscopic level

White Matter (WM)

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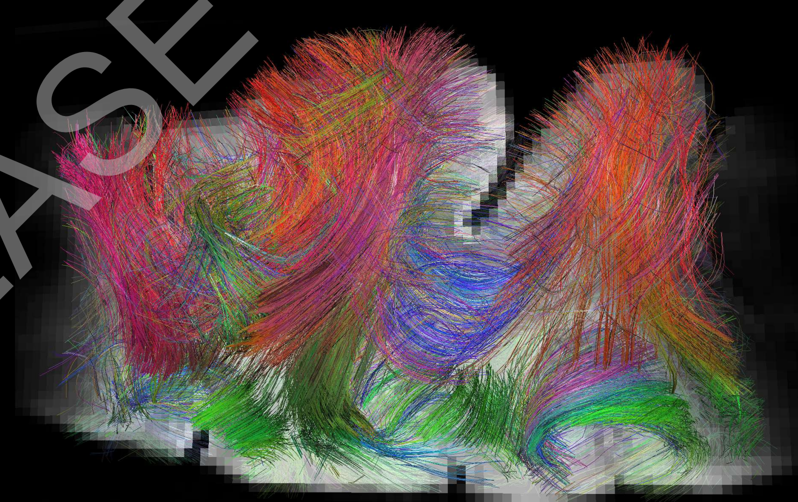
67

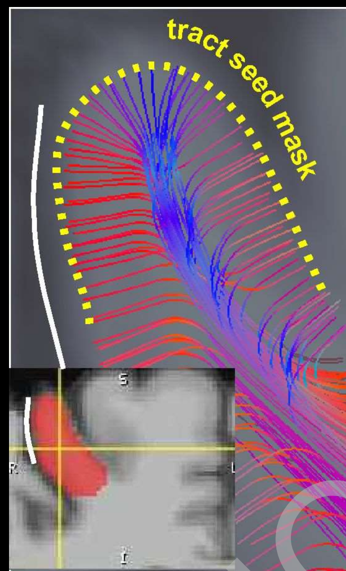
Effects in WM



Nummenmaa, McNab, Savadiev, Okada, Hamalainen, Wang, Wald, Pascual-Leone, Wedeen, and Raij (2014) Brain Stimulation 7(1):80-4.

68

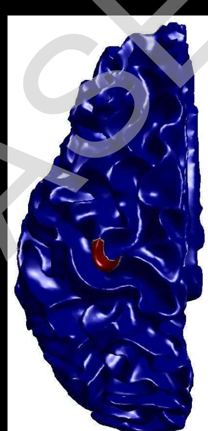
Effects in WM

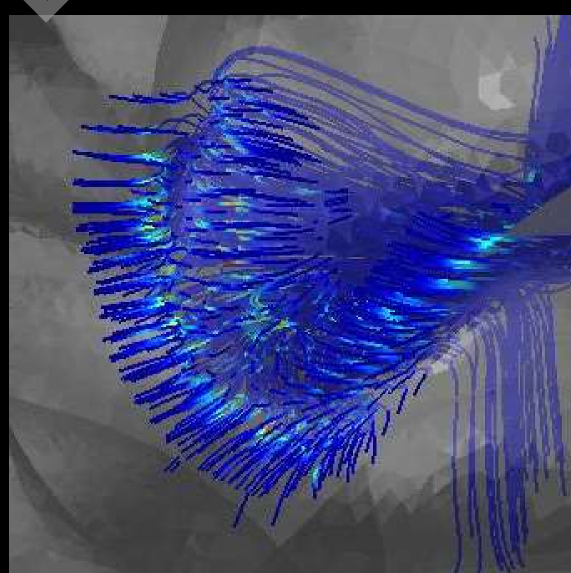


Nummenmaa, McNab, Savadiev, Okada, Hamalainen, Wang, Wald, Pascual-Leone, Wedeen, and Raij (2014) Brain Stimulation 7(1):80-4.

69

Effects in WM

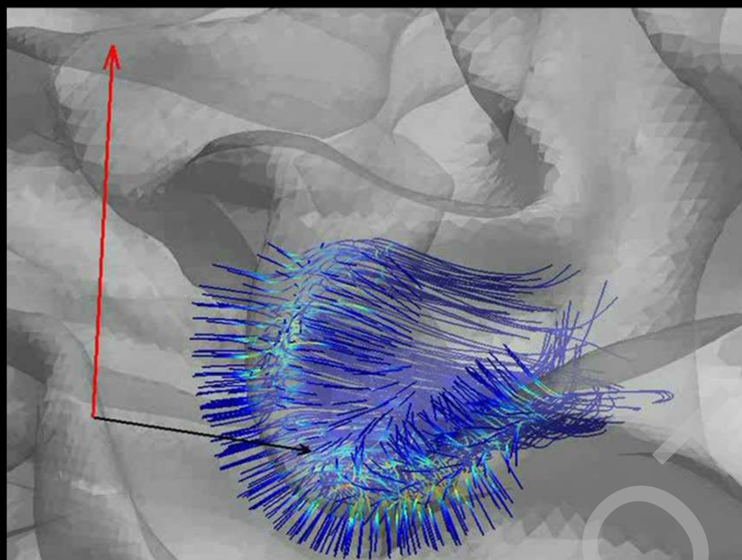




Nummenmaa, McNab, Savadiev, Okada, Hamalainen, Wang, Wald, Pascual-Leone, Wedeen, and Raij (2014) Brain Stimulation 7(1):80-4.

70

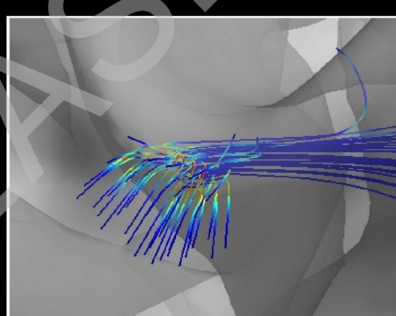
Effects in WM

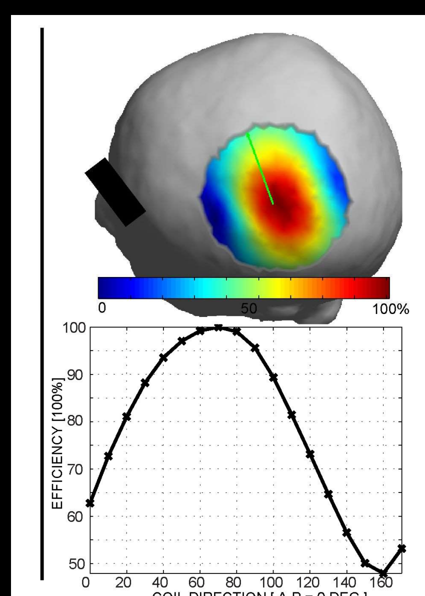


Nummenmaa, McNab, Savadiev, Okada, Hamalainen, Wang, Wald, Pascual-Leone, Wedeen, and Raij (2014) Brain Stimulation 7(1):80-4.

71

Effects in WM





Nummenmaa, McNab, Savadiev, Okada, Hamalainen, Wang, Wald, Pascual-Leone, Wedeen, and Raij (2014) Brain Stimulation 7(1):80-4.

72

Issues in putting this knowledge into clinical practice

- ❑ TMS neuronavigators
- ❑ Individual MRIs
- ❑ TMS coil orientation and the hand knob
- ❑ TMS coil center and tilt
- ❑ TMS intensity *vs.* specificity

73

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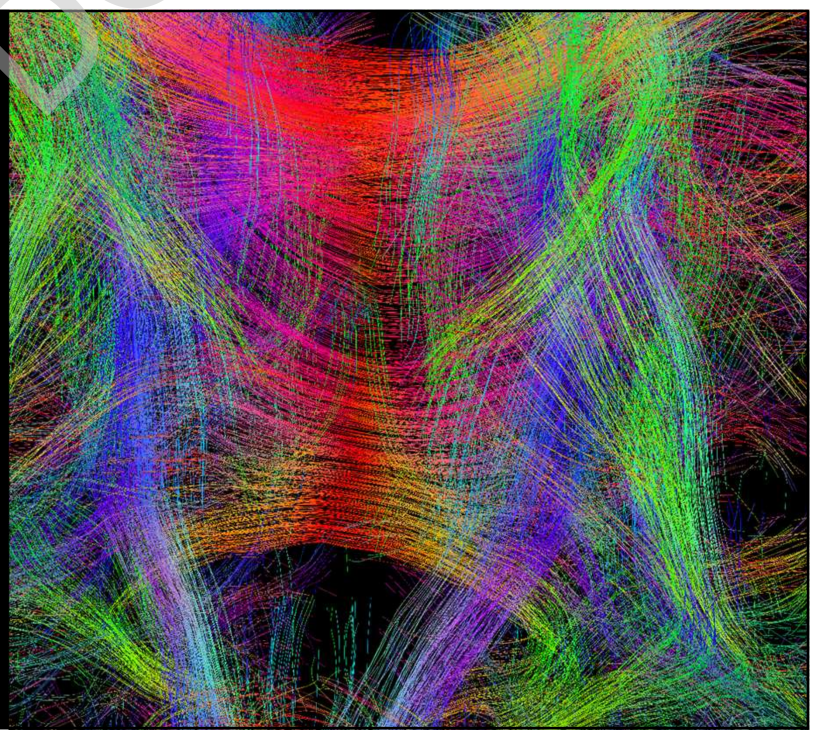
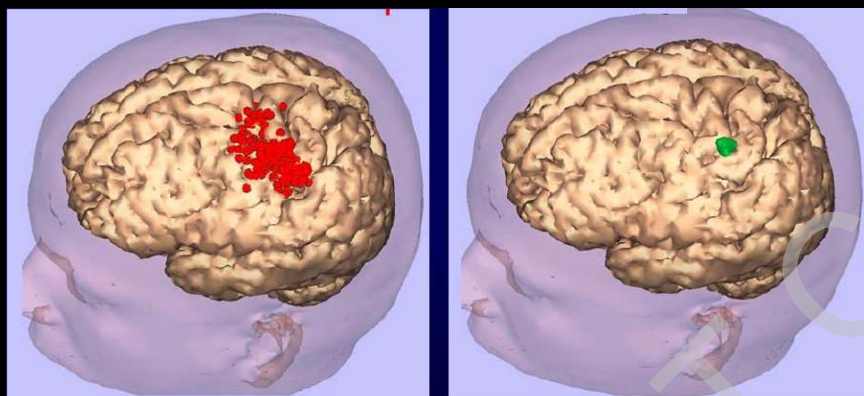
Targeting

74 2/27/2026



74

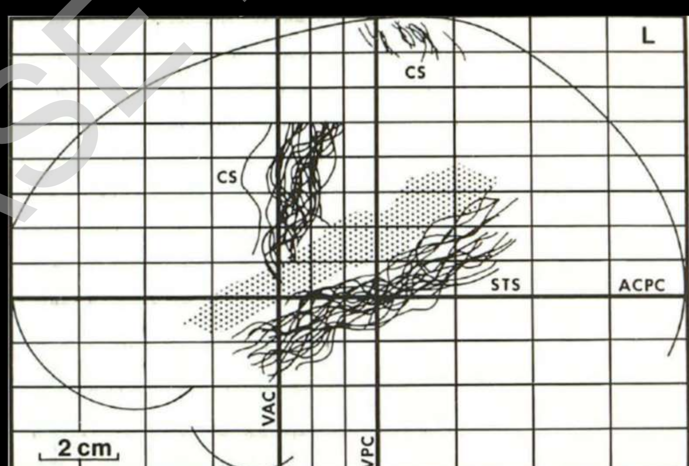
Do we need TMS navigators?



Gugino et al (2001) Clin Neurophysiol 112:1781-92

75

Do we need individual MRIs for the TMS navigators?



Szikla et al (1977) in Tamraz & Comair (2000); Ono et al (1990)

Steinmetz, Fürst, Freund (1990) AJNR Am J Neuroradiol 11:1123-30

Pascual-Leone, Bartrez-Faz, Keenan (1999) Philos Trans R Sec Lond B Biol Sci 354:1229-38

Fox, Buckner, Liu, Chakravarty, Lozano, Pascual-Leone (2014) PNAS 111:E4367-75

76

TMS coil orientation over M1 and the hand knob

Nummenmaa, McNab, Savadiev, Okada, Hamalainen, Wang, Wald, Pascual-Leone, Wedeen, and Raij (2014) Brain Stimulation 7(1):80-4.

77

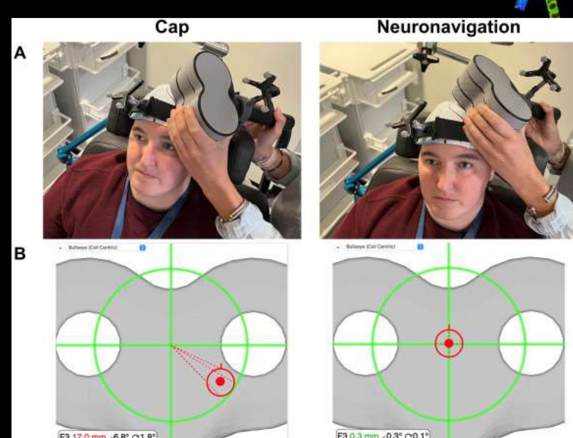
TMS coil center and tilt

TMS coil center should be on the scalp tangential to the local head curvature.

Common mistakes:

- ❑ Gap
- ❑ Incorrect roll
- ❑ Incorrect pitch

These influence the E-field maximum location and intensity, leading to loss of activation, or activation of different areas and mechanisms than intended.



Caulfield et al., (2022) Brain Stimulation 15(5):1192-

78

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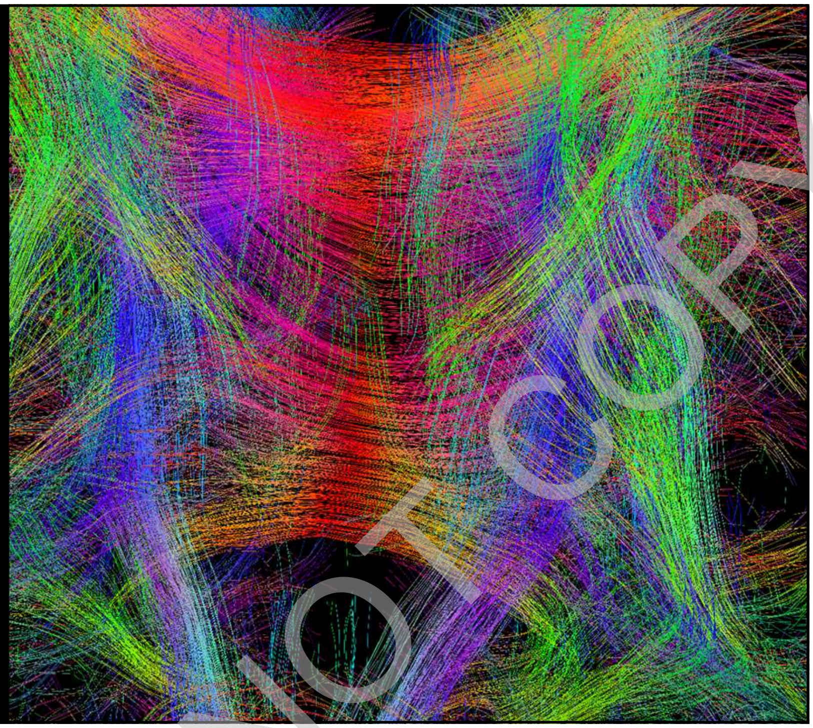
Intensity and Dosing



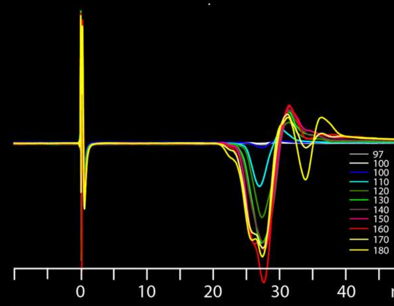
TMS intensity

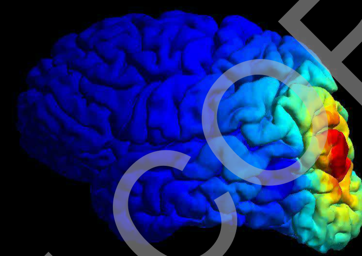
Activation thresholds are quite individual

→ Intensity needs to be individualized

Benchmarks
- Motor threshold (MT). Most widely used. Resting or active MT.
- Phosphene threshold
- Outside M1 & visual cortex: EEG-based activation thresholds ?
- Note: Thresholds might not be the same across all brain areas

TMS intensity *vs.* TMS dose





MSO (%) **Motor Threshold MT (%)** **Dose (E-field V/m)**

81

D-waves and I-waves (biphasic TMS)

[Currently unpublished data removed here]

Raij et al., (2026) In Preparation

82

TMS intensity vs. specificity: A fine dance

Probing neurophysiology with TMS requires a balance between:

- ❑ Location
- ❑ Orientation
- ❑ Intensity (dose)

If your location and/or orientation are inaccurate, you will overestimate the required intensity.

Too large intensities may be problematic, because they stimulate large areas and activate (too) many mechanisms.

83

Thank you

- ❑ Aapo Nummenmaa (MGH)
- ❑ Sergey Makaroff (WPI/MGH)
- ❑ Padma Sundaram (MGH)

Questions or comments

- ❑ raij@nmr.mgh.harvard.edu

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P41EB015896 (BR)

NIH National Institute of Neurological Disorders and Stroke

84