Transcranial Electrical Stimulation (tES) and also Cranial Nerve Stimulation

Marom Bikson
for CMU Neural Engineering (Bin He),
March 30, 2023

The plan

I am going to explain how **non-invasive electrical brain stimulation technology works**.

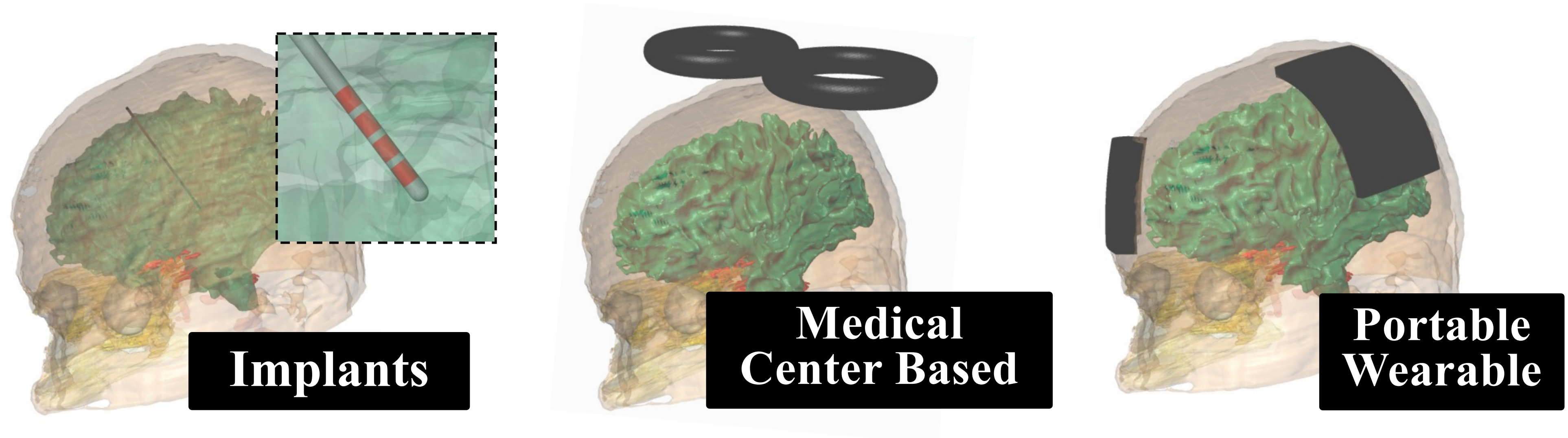
I will talk about the different **parts of an electrical stimulation stimulation device**.

I will assume you have very basic background in electrical engineering and some background on electrical stimulation, so will move quickly. But, **its important you stop me with questions as they come up.**

I am not going to talk about the clinical and wellness applications or mechanisms of brain stimulation. But I am happy to answer questions about that.

I will do a demo.

How neuromodulation technologies work: devices deliver targeted therapeutic energy.



Deep Brain Stimulation (DBS)

Spinal Cord Stimulation (SCS)

Transcranial Magnetic Stimulation (TMS)

Electroconvulsive Therapy (ECT)

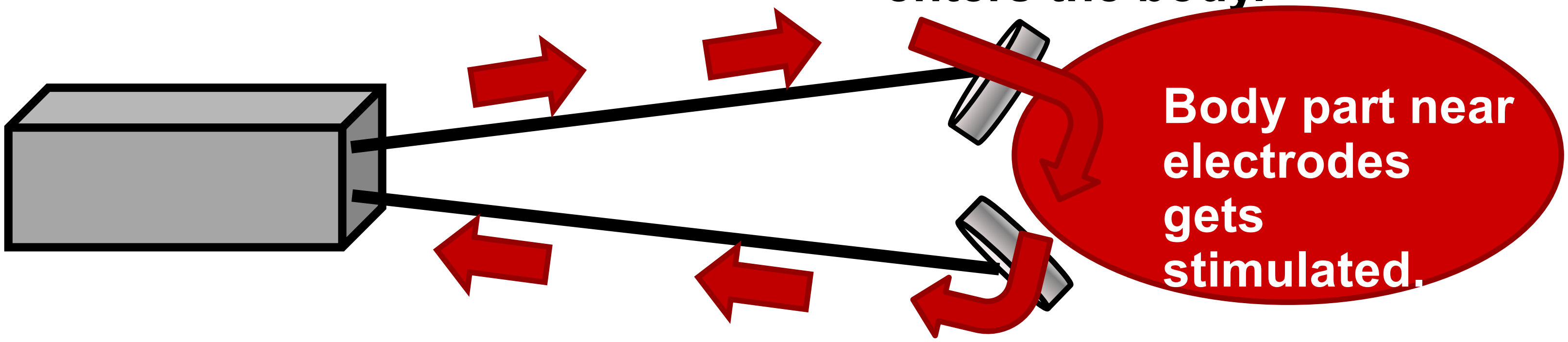
Transcranial Electrical Stimulation

Non-invasive cranial nerve stimulation.

Electrical stimulation (Neuromodulation) devices have two essential components. Together these two components determine the dose.

A The stimulation box includes the power source, controls, and generates (“plays”) the stimulation waveform.

B The electrodes are metal contacts where the stimulation waveform enters the body.



- Changes in the brain (cognition, behavior) are governed only by the dose (waveform & electrodes).
- Non-dose device features can be critical for usability and outcomes (e.g. battery life, shape, use instructions…)

Brain Stimulation (2012) 5, 435–53

BRAIN STIMULATION

www.brainstimjrnl.com

ELSEVIER

REVIEW ARTICLE

Fundamentals of transcranial electric and magnetic stimulation dose: Definition, selection, and reporting practices

Angel V. Peterchev,[a,b] Timothy A. Wagner,[c,d] Pedro C. Miranda,[e] Michael A. Nitsche,[f] Walter Paulus,[f] Sarah H. Lisanby,[a,g] Alvaro Pascual-Leone,[h] Marom Bikson[i]

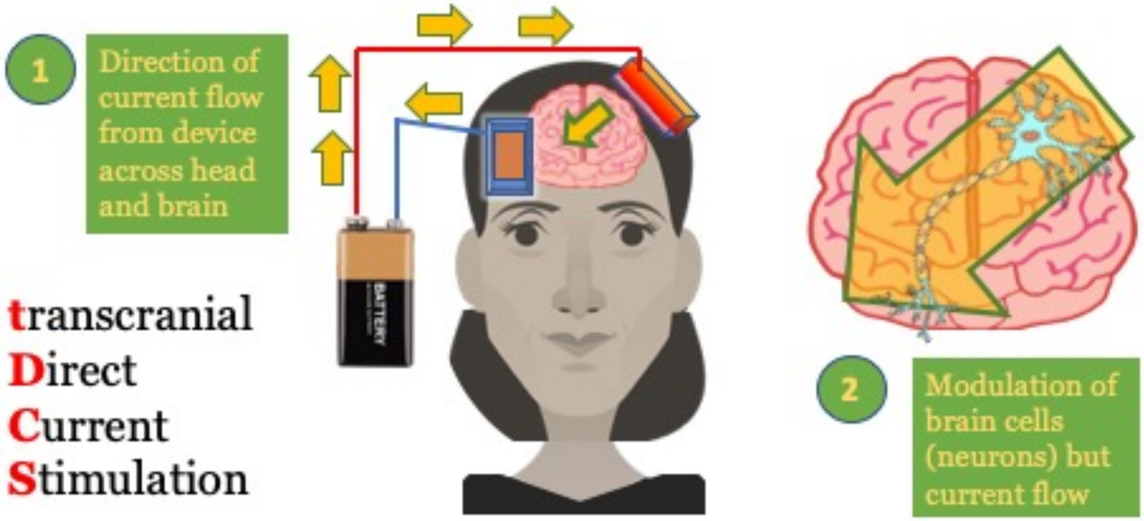
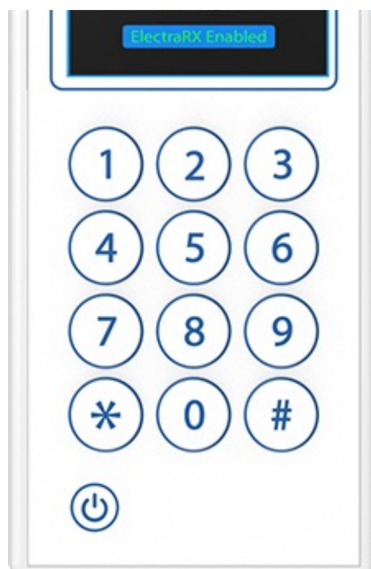
Explaining dose adjustment based on outcome (biomarker), is not a substitute for reporting dose.

“EM stimulation is be defined by all parameters of the stimulation device that affect the electric and current density fields generated in the body”

1) Stimulation electrode configuration parameters: shape, size, position, and electrical properties

2) Electrode current or voltage waveform parameters: pulse amplitude, width, polarity, repetition frequency, train duration, interval and number of stimulation sessions

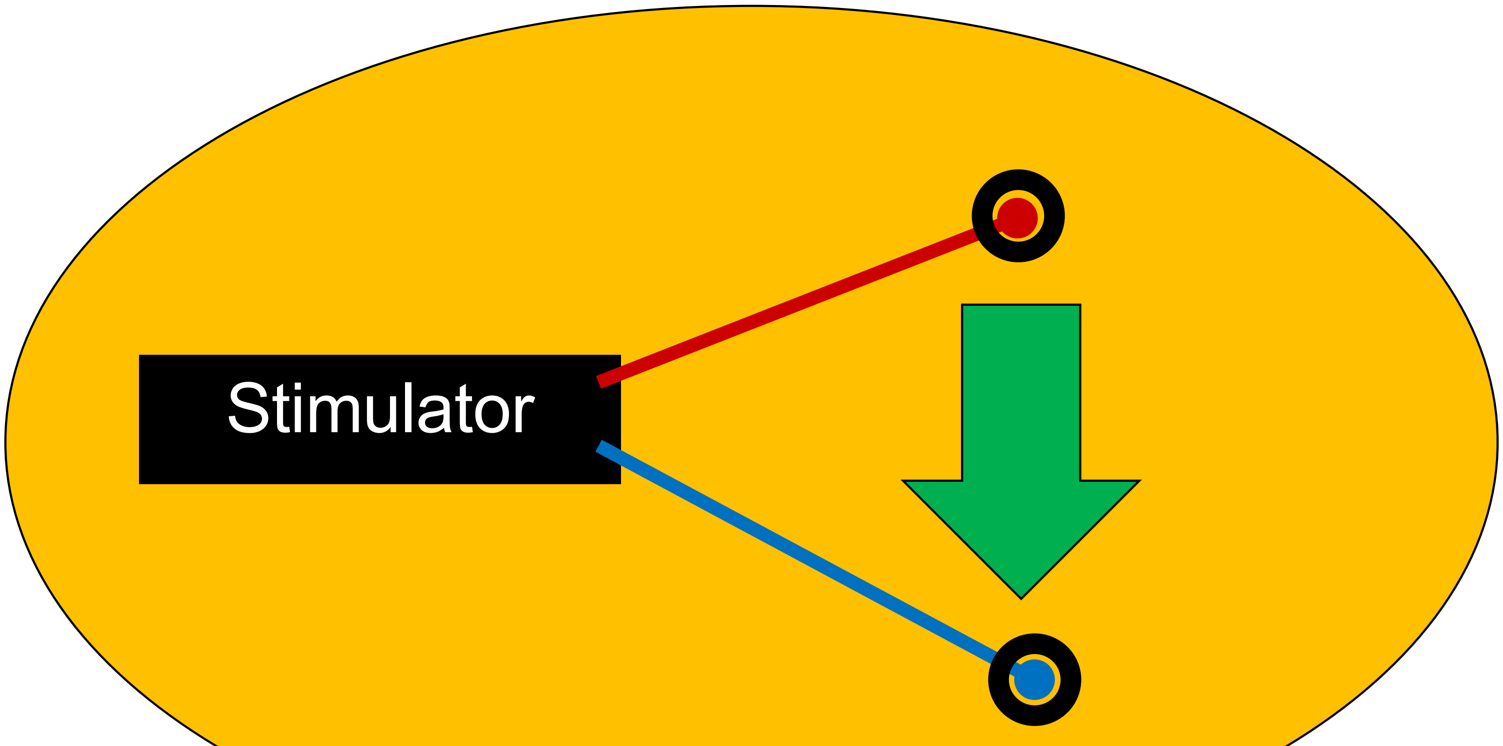
Fig. 1 Example of a tES device and a headgear used for electrical stimulation with sponge electrodes. In general, conventional sponges are soaked with a controlled volume of saline using a syringe. Rubber electrodes (electrochemical electrodes) are placed inside the sponge pockets. Lead wires connect to the device to the conductive rubber electrodes. Sponge electrodes are then secured on the scalp using a headgear. The rubber electrodes inside the saline-soaked sponge pockets are energized using a corresponding lead wire connected to the device


1
Direction of current flow from device across head and brain
BATTERY
transcranial
Direct
Current
Stimulation
2
Modulation of brain cells (neurons) but current flow

ElectraRX Enabled
1 2 3
4 5 6
7 8 9
* 0 #


As a stimulation engineers you have ”two levers to pull” (as far as Dose)

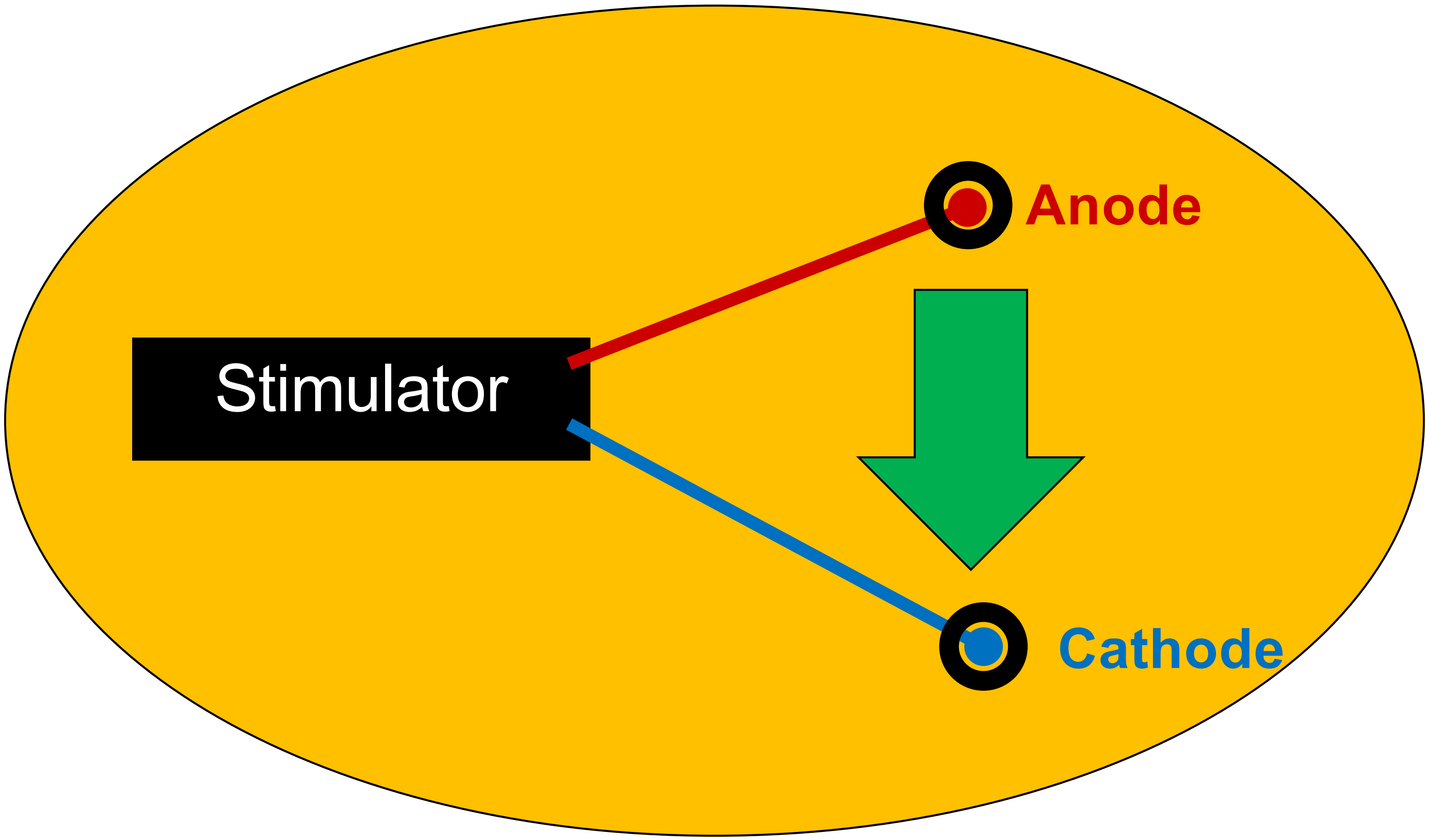
1. Where the electrodes are placed on the body (and their shape)
2. The electrical intensity and waveform applied through the electrodes in the body

Connecting an electrical stimulator to the body produces current flow through the body

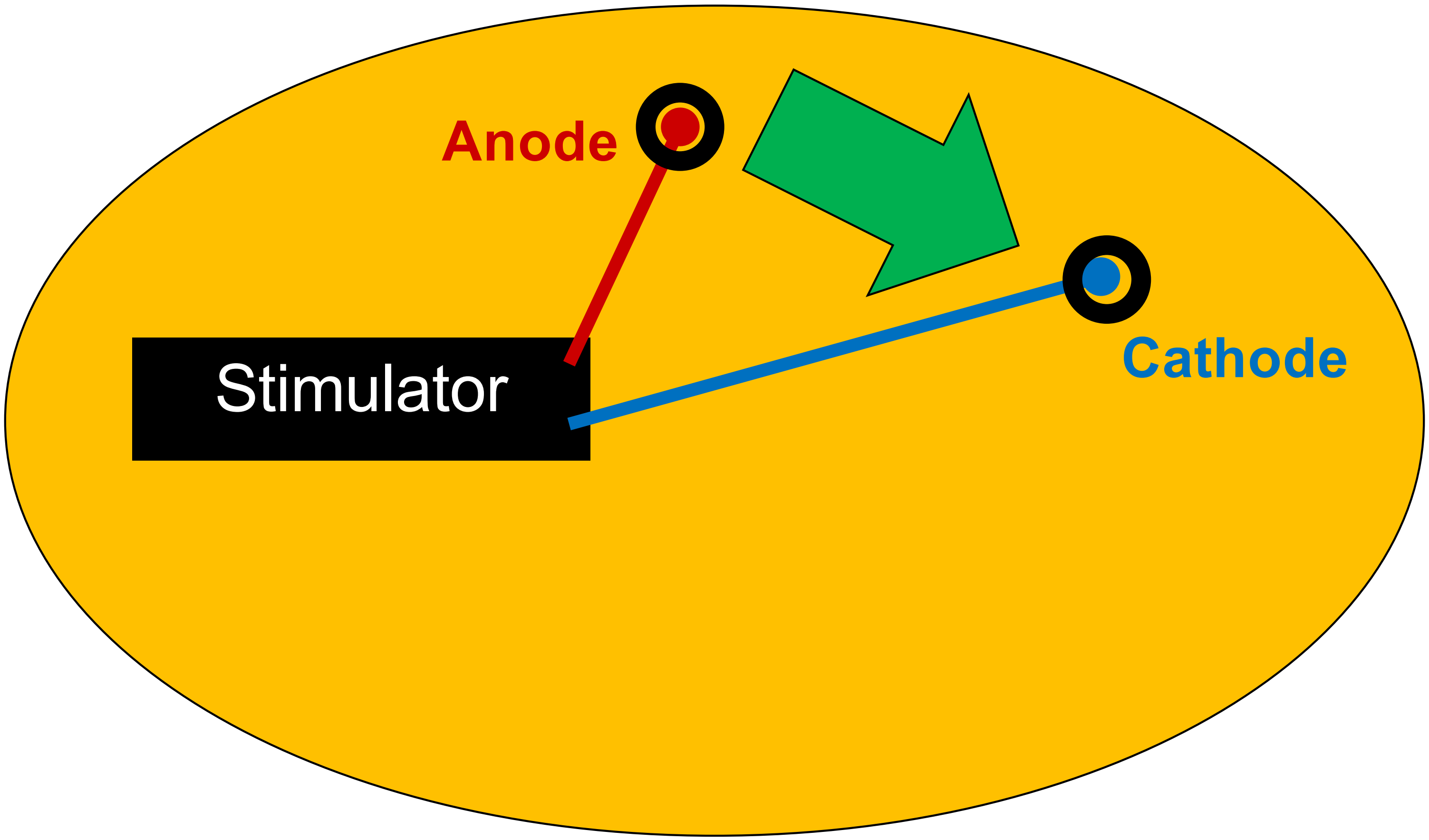


Current flows from the stimulator, through the wires (leads) and to exposed metal contacts (**Electrodes**)

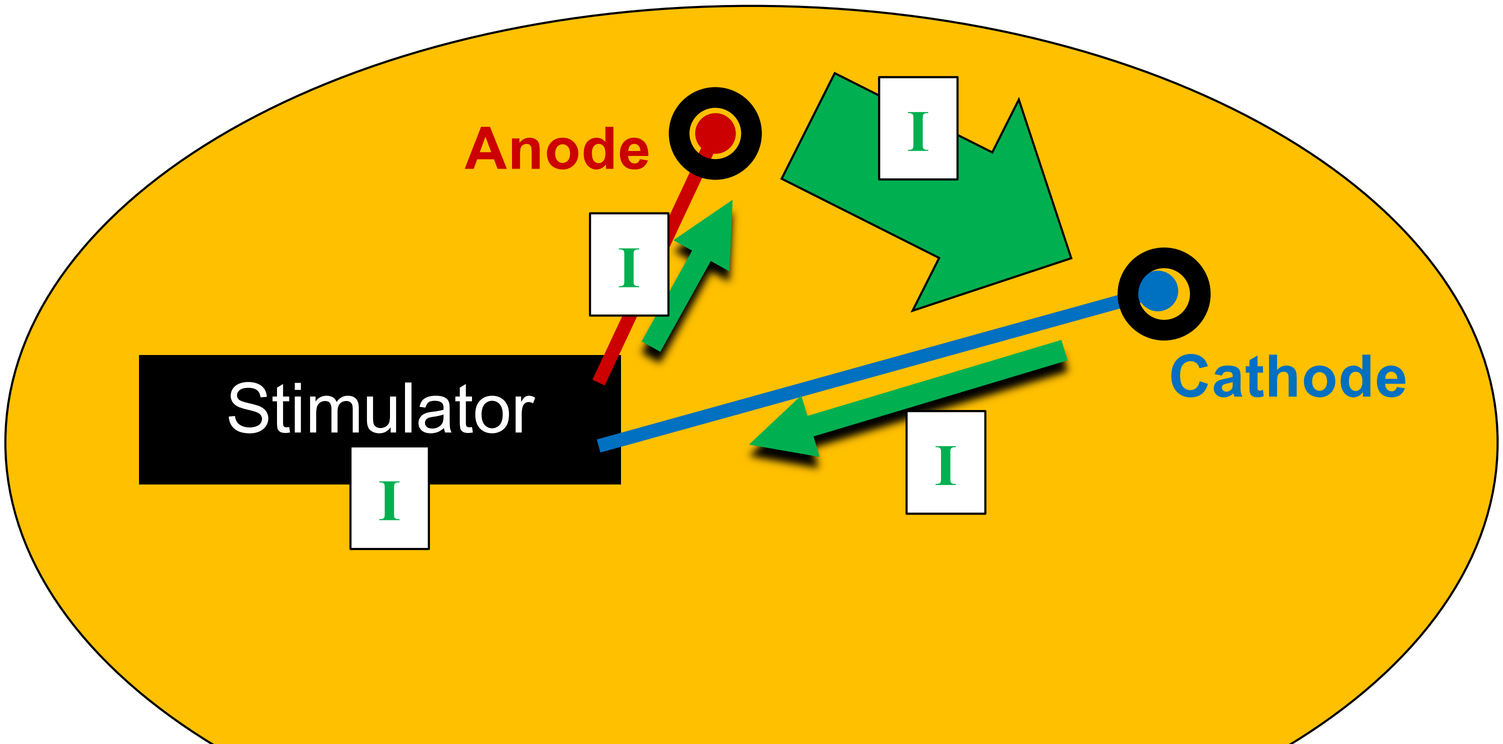
Current flows from the positive Electrode (Anode) to the negative Electrode (Cathode)



The position of the electrodes determines which parts of the body are exposed to current flow

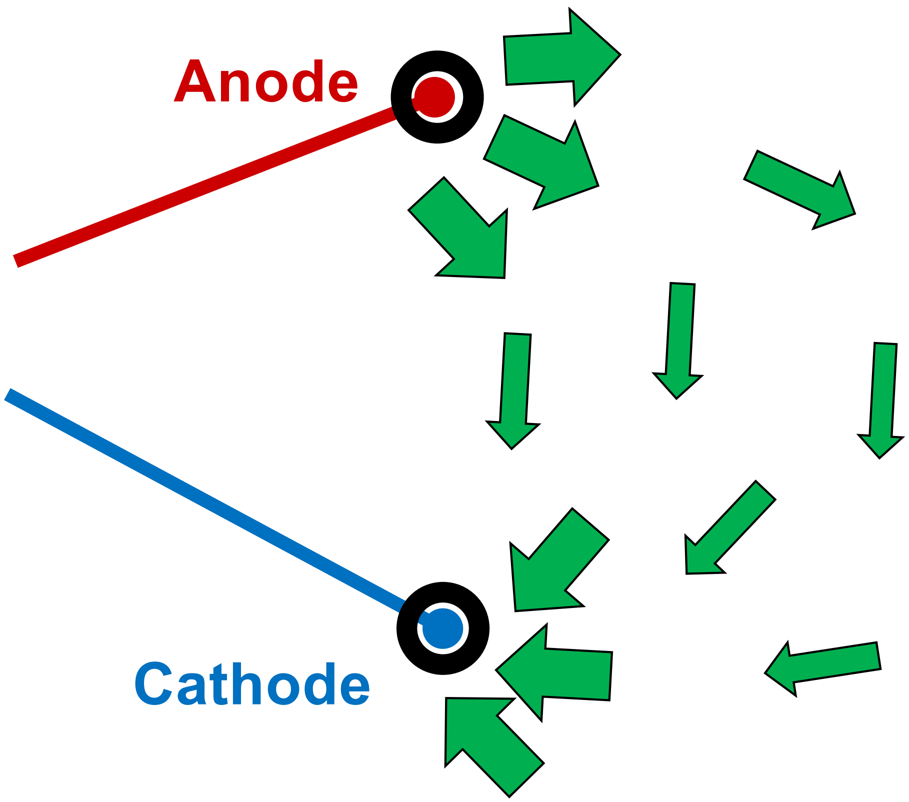


The position of the electrodes determines which parts of the body are exposed to current flow



The total current produced by the stimulator (I in mA) is passed through the body

But the current flow through the body is not even, some part get more **Current Density** then others

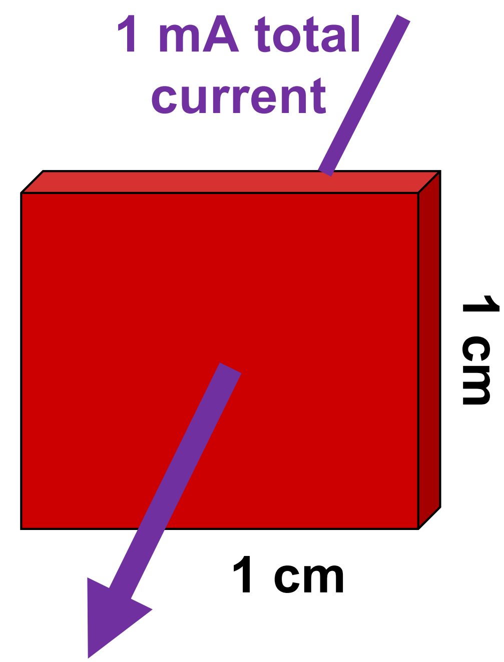


Current does not flow in a straight thin line between electrodes, but is **diffused** through the tissue.

The parts of the body near the electrodes get (much) more **Current Density.**

Current Density is current per area
(unit of mA per cm^2)

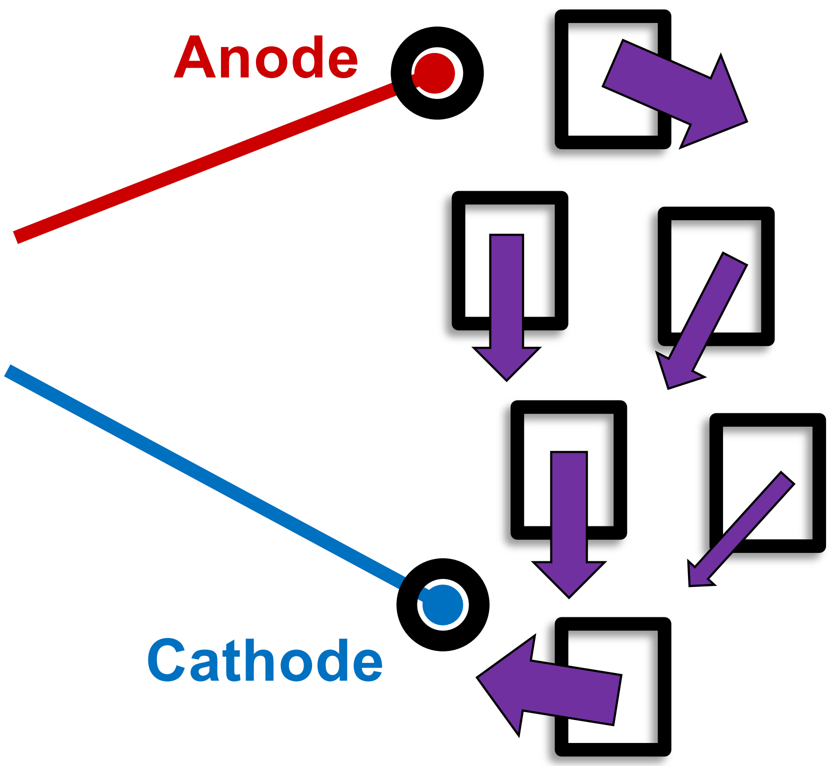
For example, an electrode has an area of 1 cm^2 with 1 mA of current passed through it.
What is the electrode Current Density*?



1 mA current / 1 cm^2 area = 1 mA / cm2

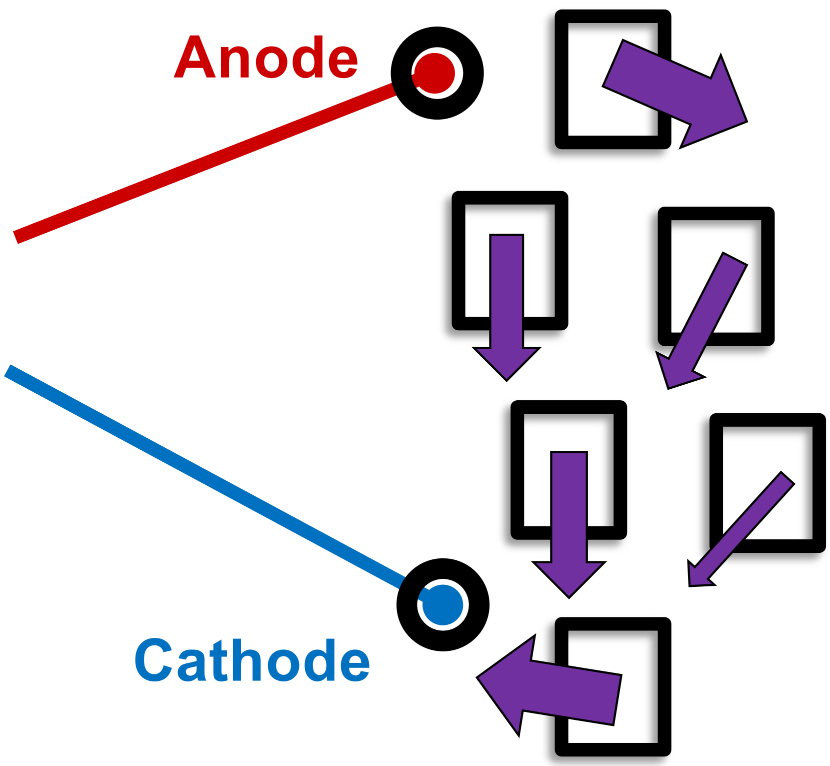
*Assume uniform current density on the electrode surface (no hot spots)

But the current flow through the body is not even, some part get more **Current Density** then others



In each part of the tissue we can describe the local **Current Density**

The arrow size illustrates variation in current density at each location



Current Density has a magnitude in each location, but it also has a direction

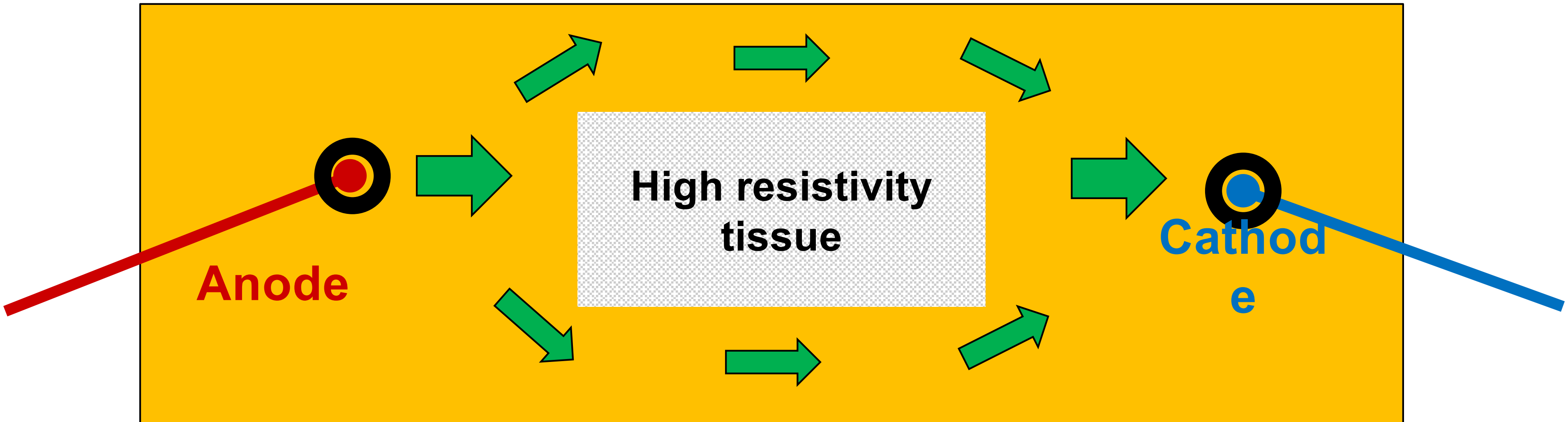
Current Density is related to **Electric Field** by a simple equation.

Current Density * **Resistivity** of Tissue = **Electric Field**

Resistivity is a property of tissue.

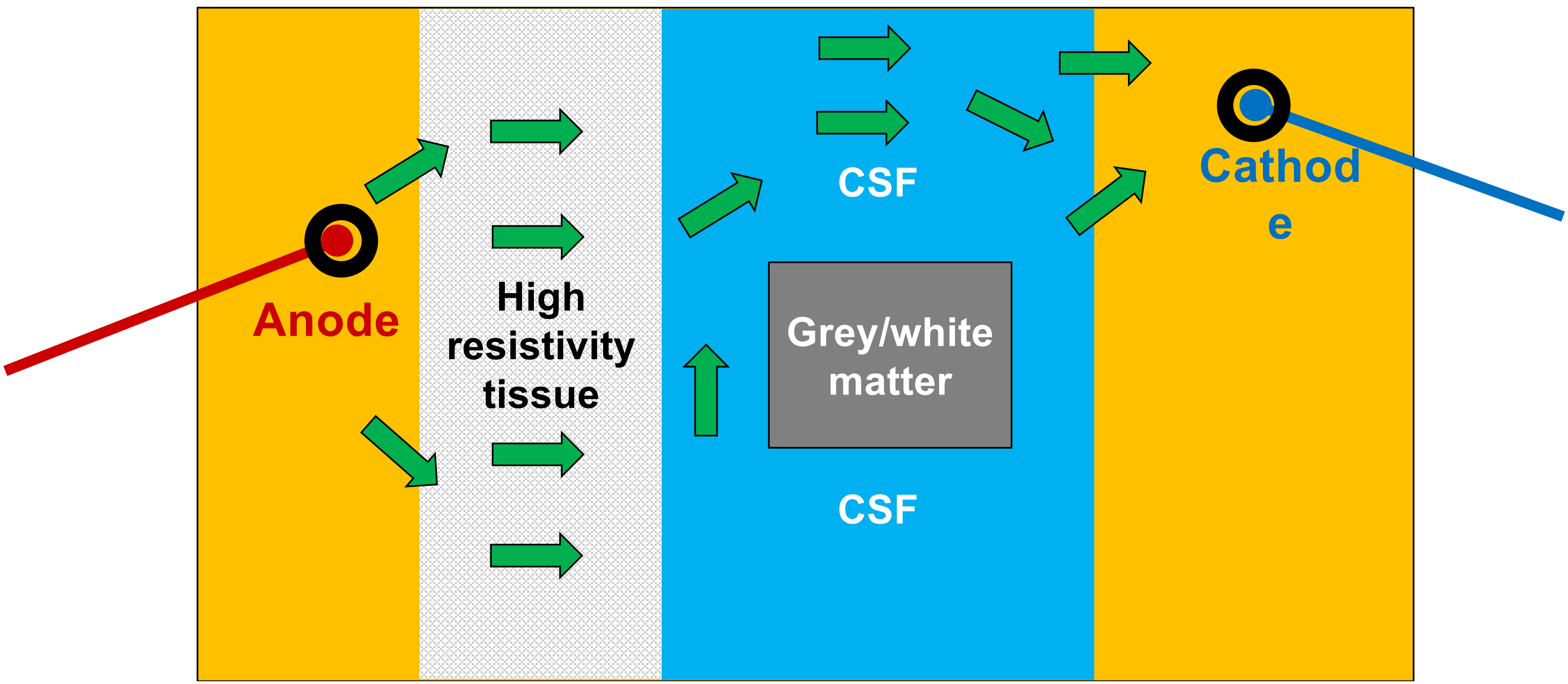
(units of ohm meter)

Some tissue has high resistivity like bone or fat. Some tissue has low resistivity like CSF. Grey and white brain matter has intermediate resistivity.



When current flows from one electrode to the other through the body, the pattern of current flow favors going through tissues with low resistivity.

Details of body anatomy and associated tissue **resistivity** can lead to **current patterns** that are hard to guess.



Computational models predict the current flow generated in the brain for a specific stimulation configuration/settings

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Electrical activity (efficacy and safety) is determined by current flow at tissue

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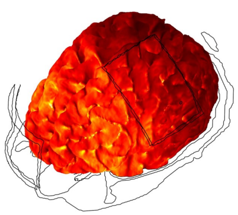
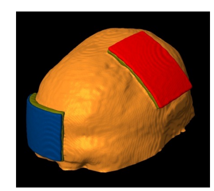
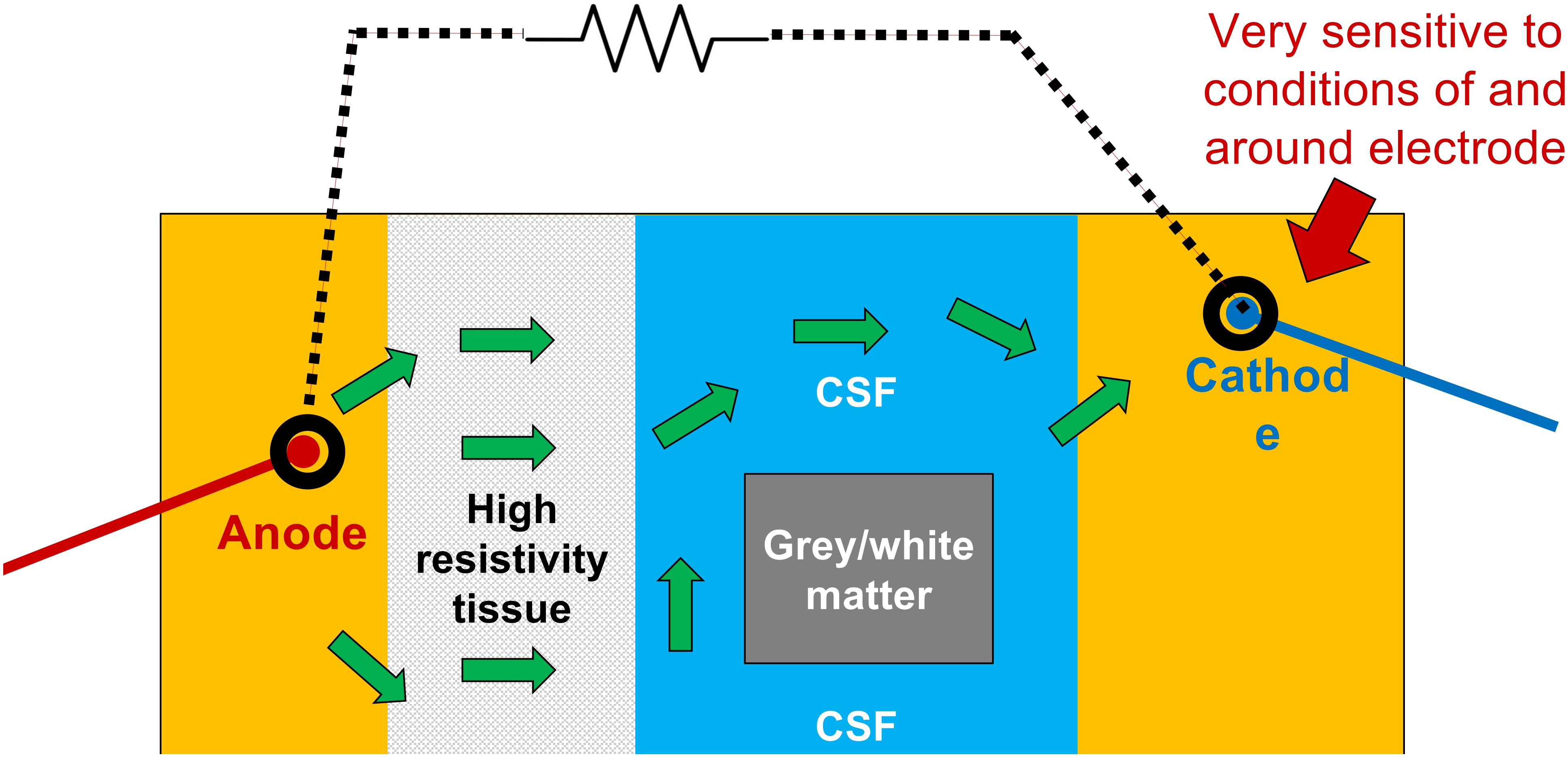
tES dose is set by surface application (stimulators and pads/coils)





Resistance / Impedance (Ohms) is a single number (between a pair of electrodes) that reflects all tissues.

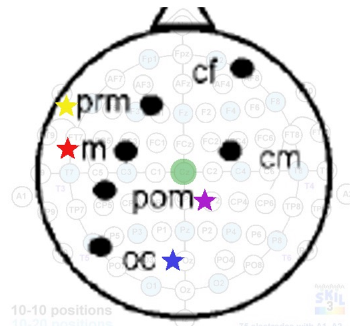


As a stimulation engineers you have ”two levers to pull” (as far as Dose)

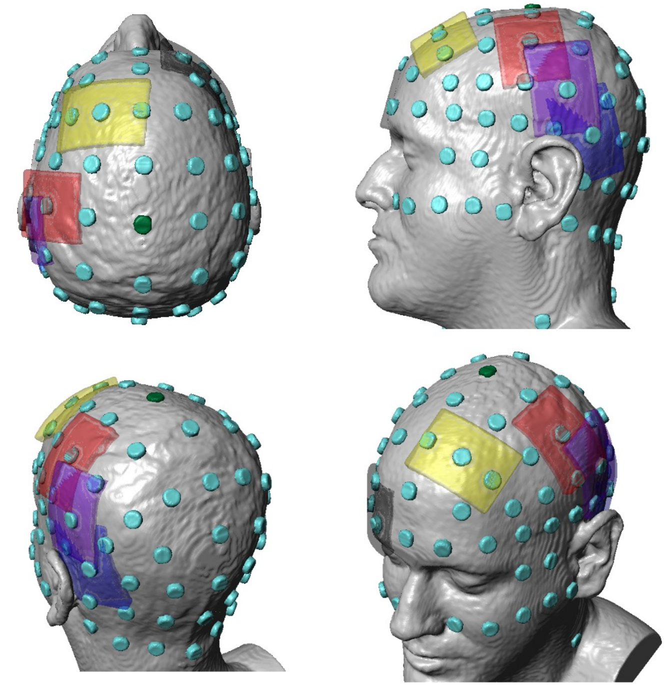
1. Where the electrodes are placed on the body (and their shape)
2. The electrical intensity and waveform applied through the electrodes in the body

Anatomical targeting with tES

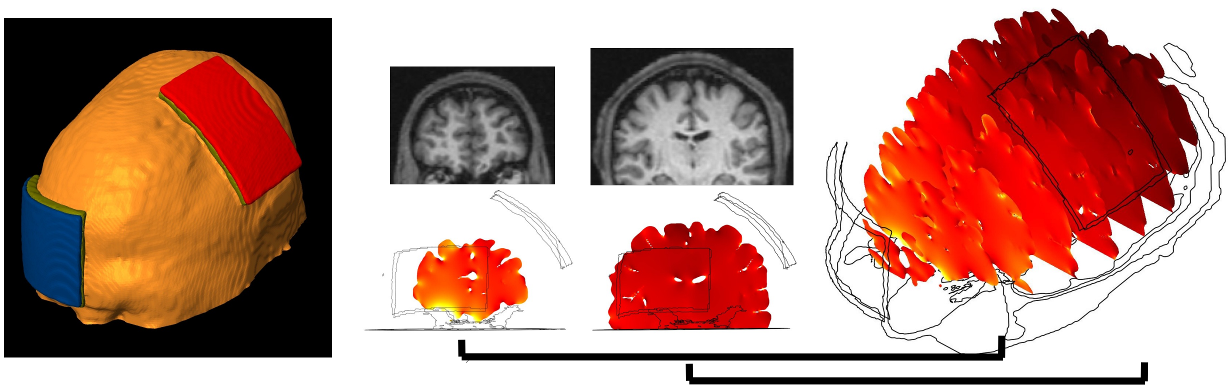
"Conventional" tES varies the position of two large electrodes.



Contralateral Forehead:	AF8
PreMotor:	F1
Motor:	C3
PostMotor:	CP5
Occipital:	P7



Conventional bipolar large electrodes



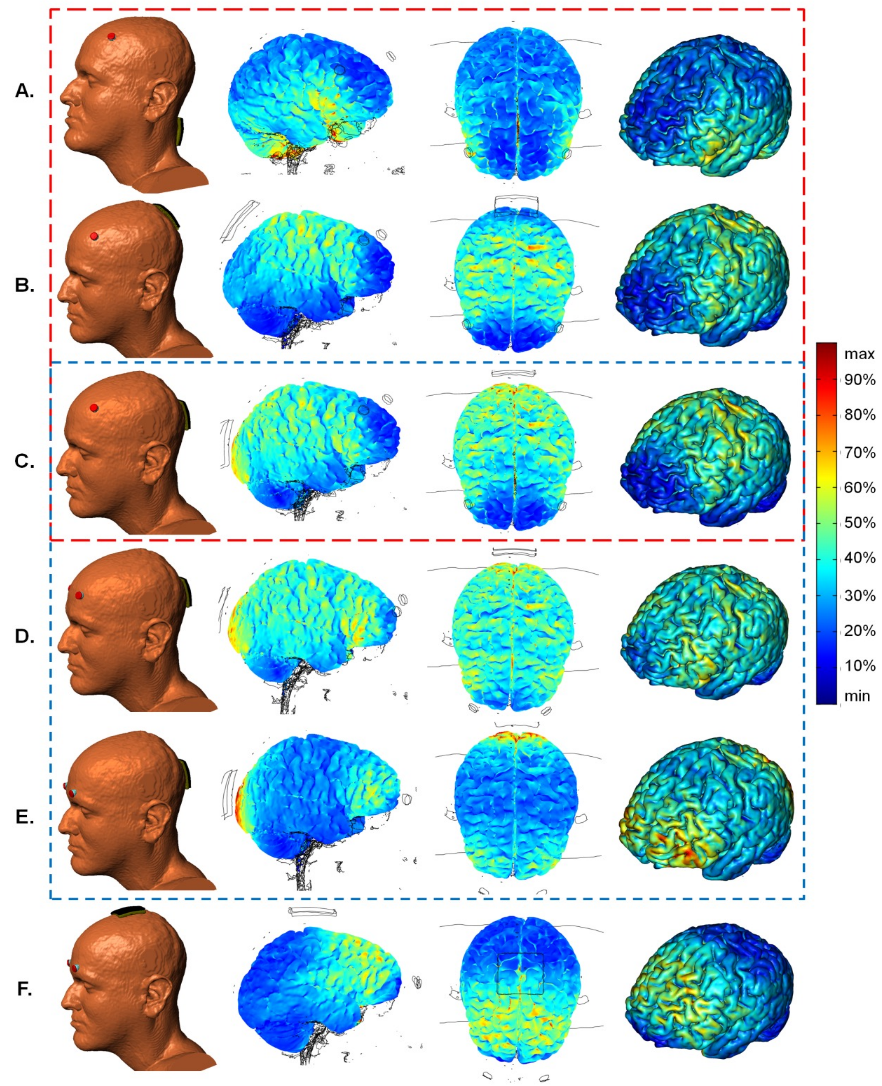
Current flow model

Selecting the right montage is not trivial.

There are many montage variations.

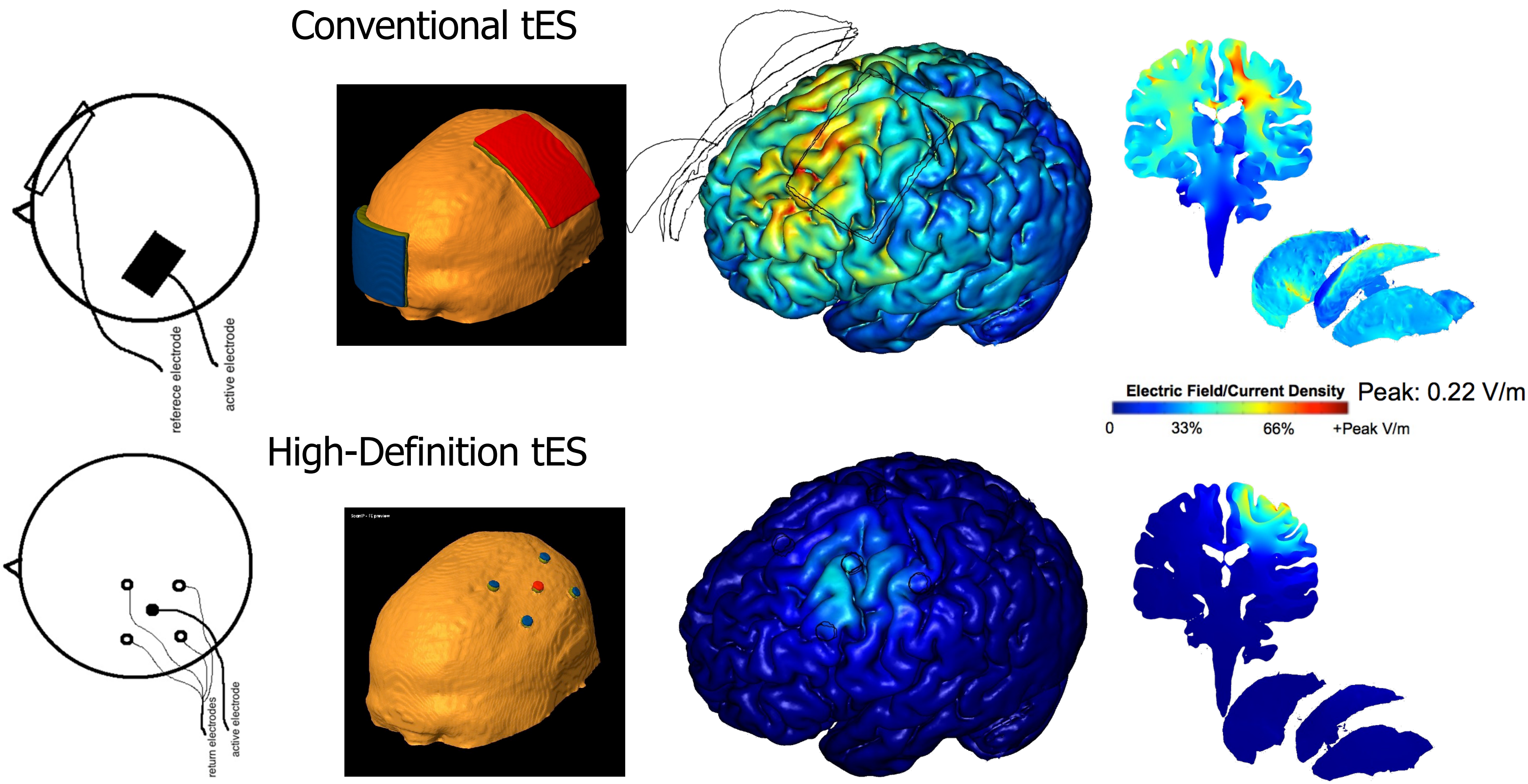
Poor choice can result in missing the target.

The position and size of the active AND of the return influence brain current flow



Neuromodulation with diffuse vs. focused tES

Kuo et. al. Brain Stim 2013



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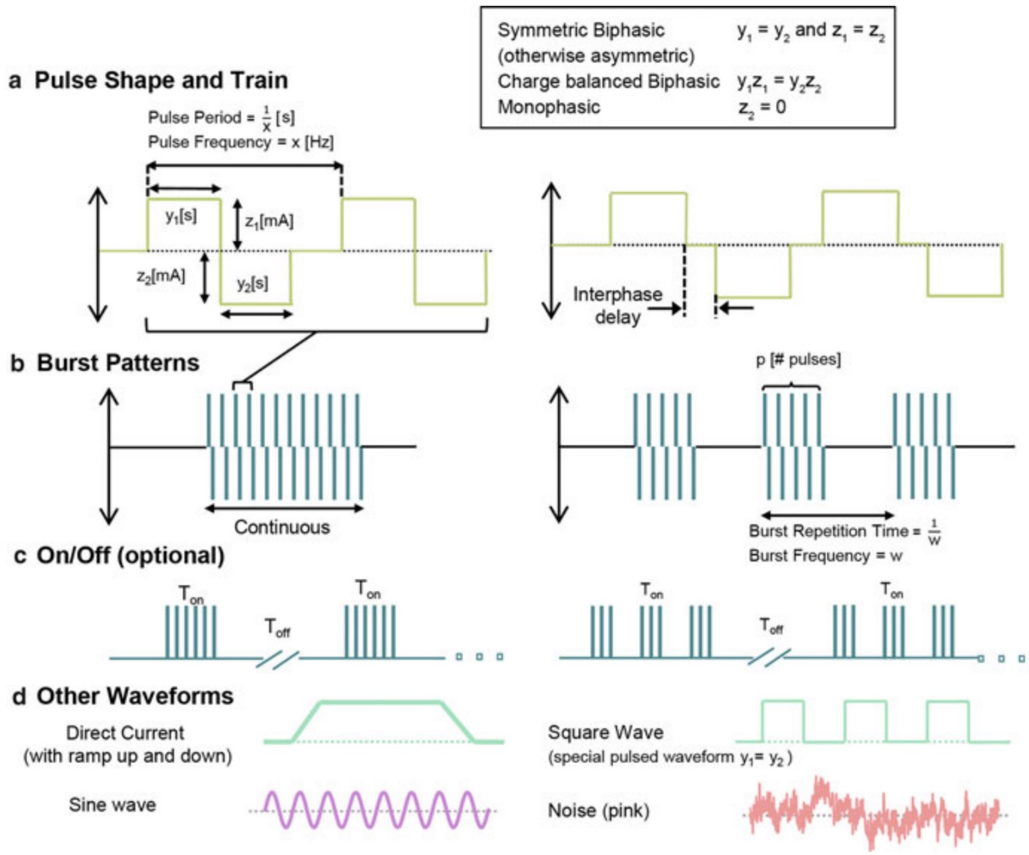
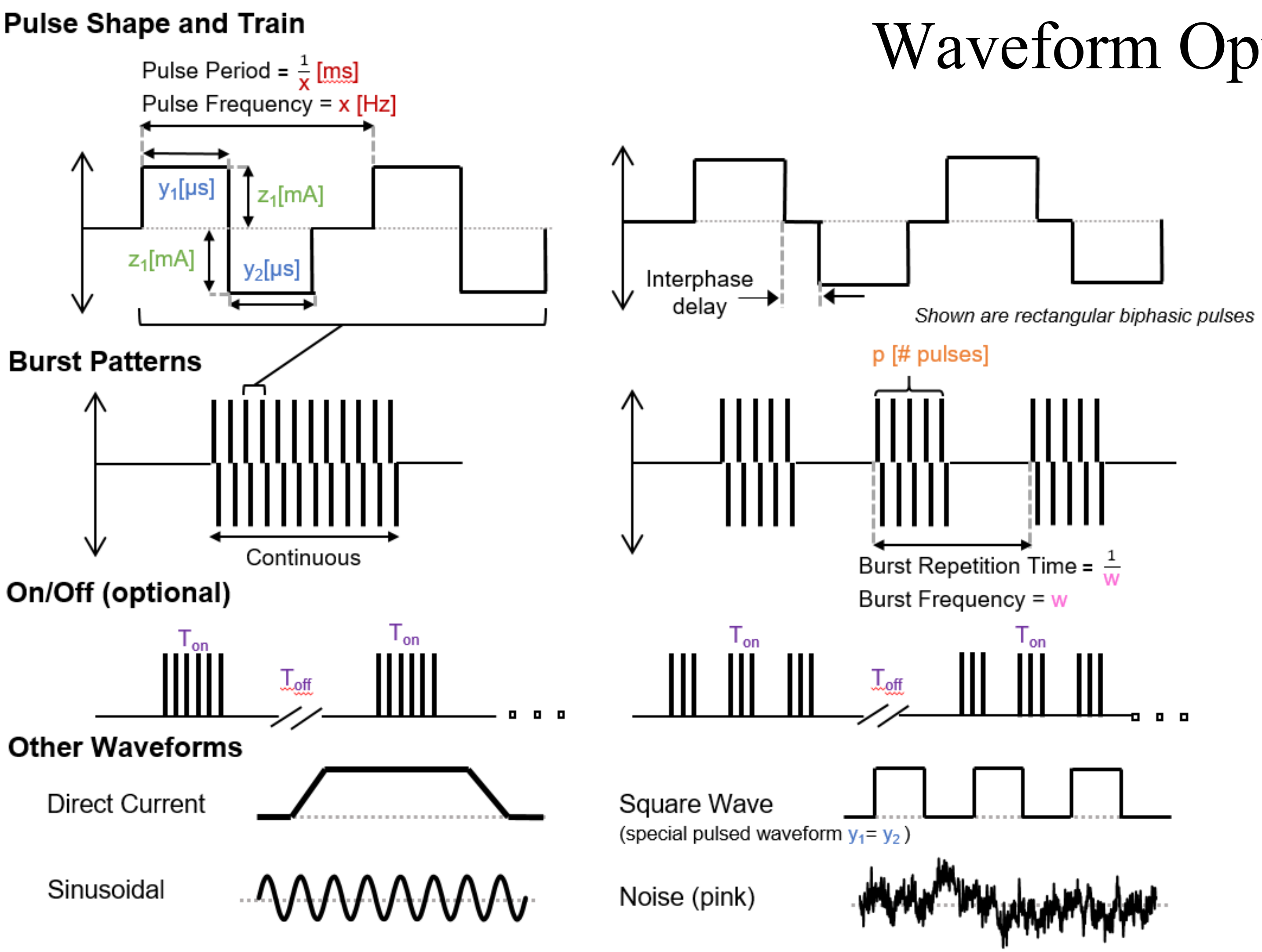


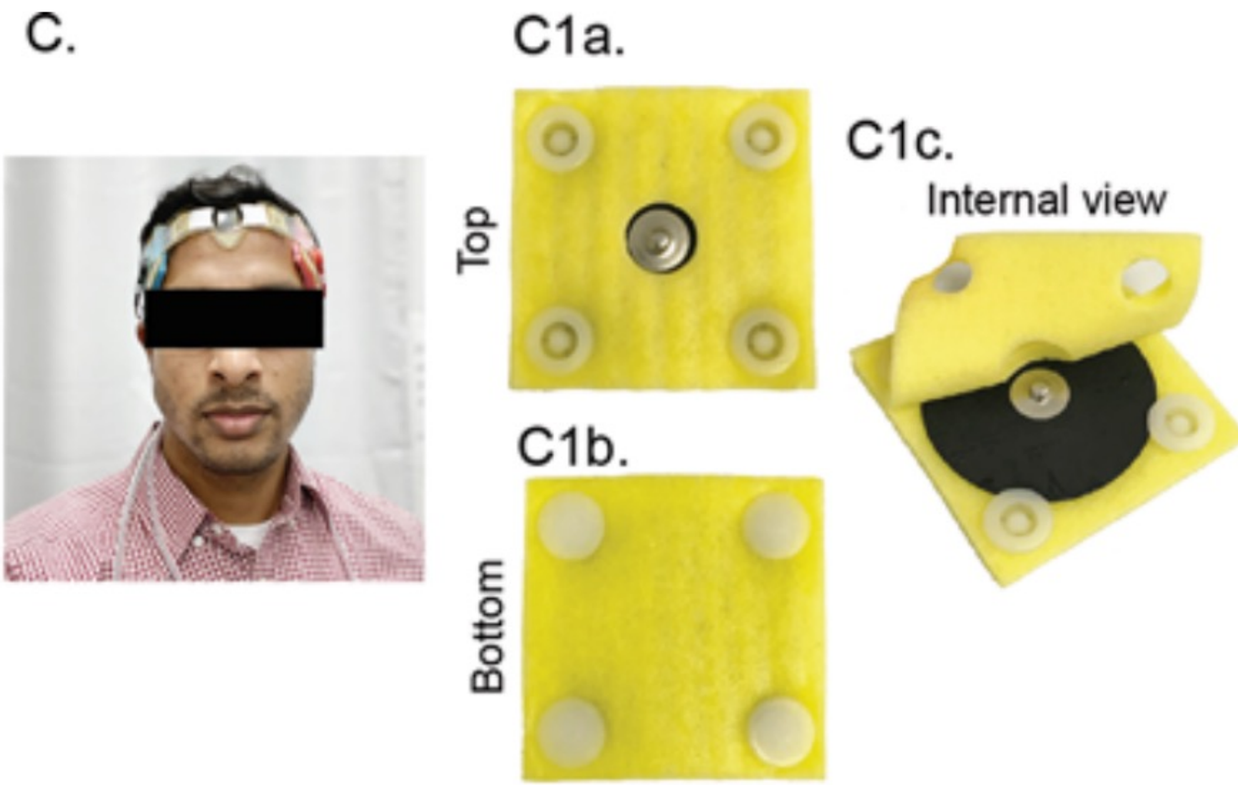
Fig. 2 Different types of waveforms used in tES and their parameters. (**a**) Represents rectangular biphasic pulses with frequency "x in Hz," period "1/x in sec," amplitude "$Z_1=Z_2$ in mA," and pulse width "$y_1=y_2$ in sec." (**b**) Illustrates continuous and discrete burst patterns of pulses where "p" is number of pulses, "w" is the burst frequency, and "1/w" is the burst repetition time. (**c**) Represents monophasic burst on (T_{on}) and burst off (T_{off}). Other waveforms such as DC, square wave, sinusoidal, and pink noise are shown in D

Waveform Optimization



Electrodes

Electrodes: Sponge kind



Understanding what tES electrode are and what they do.

- **Components of tES electrodes**
  - **"Electrode" (metal or conducting rubber)**
  - **Electrolyte (salty fluid or gel)**
    - **Fluid may be suspended in a Sponge**
    - **Gel may be held in a plastic Holder**
  - **Lead (wire)**

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In circuits (tDCS current sources, computers, wires) current is carried only by electrons

In the body current is carried by only ions like Na+, K+, Cl- (e.g. Na+ current for Action Potentials)

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Where the wire (metal) touches the body = ELECTRODE

In circuits (tDCS current sources, computers, wires) current is carried only by electrons

e- e- e- .... ->

Wire (metal)

Cl- Cl- Cl- ->

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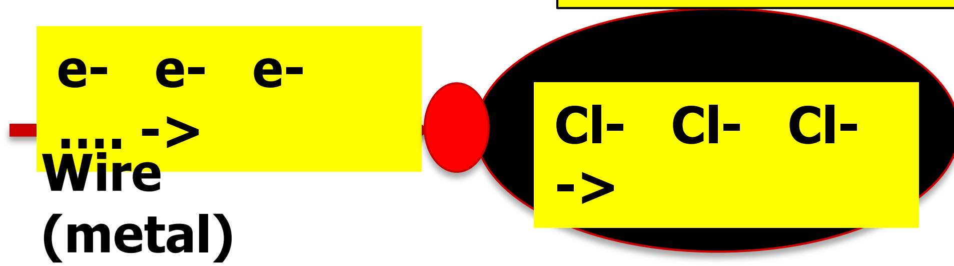

- BAD things happen at the electrode (oxidation / reduction chemical reactions that form chemicals right at the skin that are bad for the body (and for the electrode).
- Especially during "bad" waveforms like Direct Current stimulation there is NOTHING you can do to stop this.

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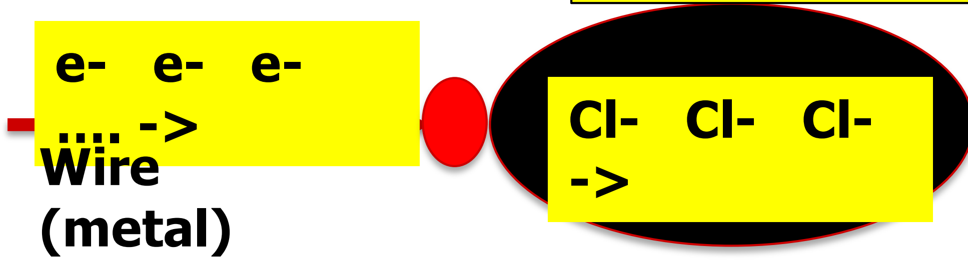

- Solution: Put "something" between the electrode and the body that is an Electrolyte (an "extension" of the body in that sense).
- All the BAD things happen in the Electrolyte (and so AWAY at the skin*)
- *Hence maintain minimum distance between electrode and skin.

Understanding what tES electrode are and what they do.

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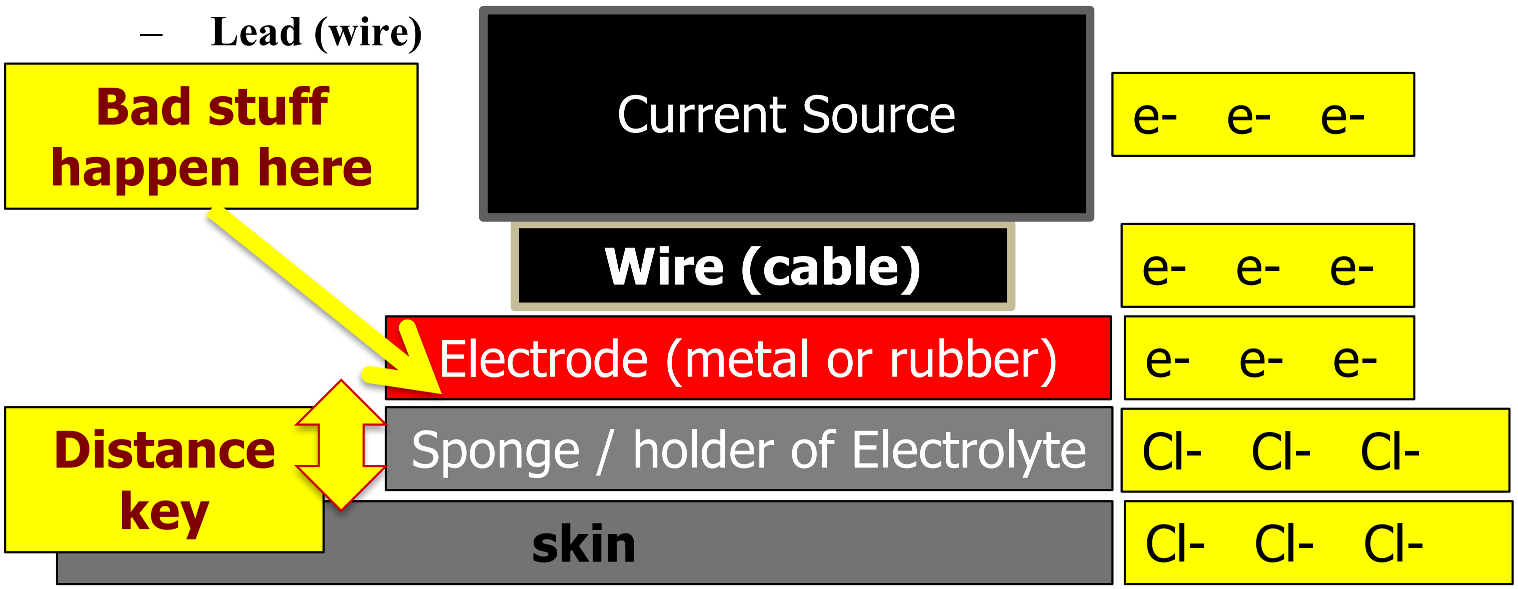


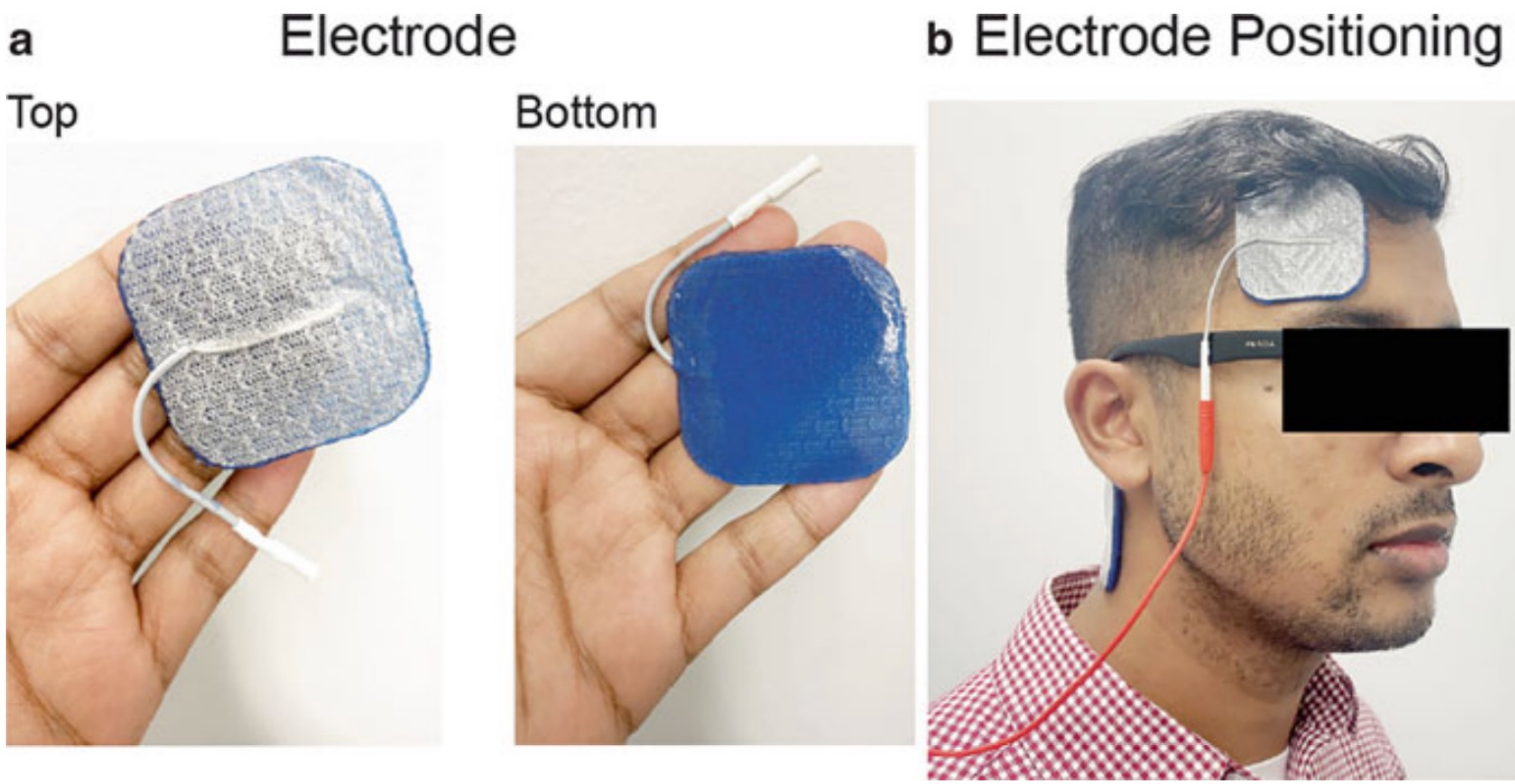


Fig. 5 Illustration of adhesive hydrogel electrode. (**a**) Top and bottom view of the adhesive electrode. (**b**) Placement of square adhesive electrodes on the subject's right temples on the back of neck. Generally, adhesive electrodes are restricted to placement below the hairline

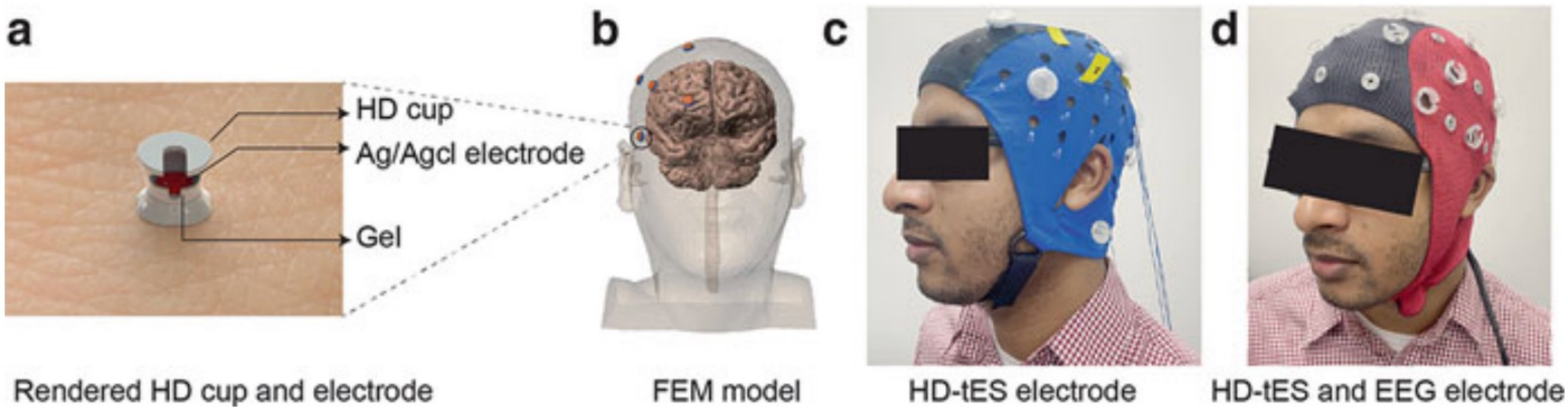
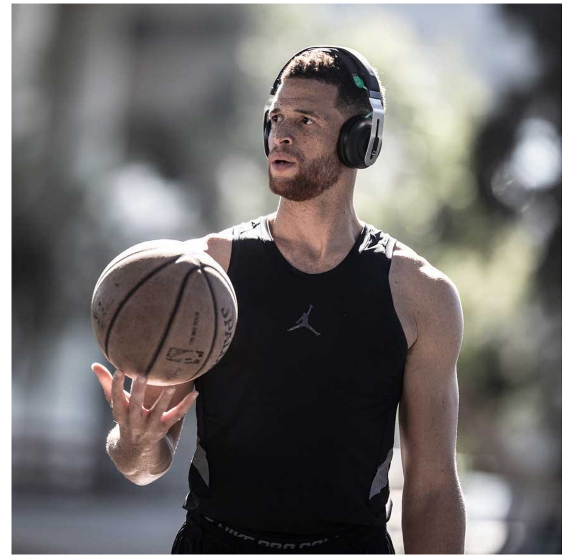


Fig. 6 High-definition (HD) electrodes. (**a**) In contrast to other types of tES electrode, HD electrodes are relatively small. (Render) A HD cup is placed on the skin and contained the metal electrodes (Ag/AgCl) and the electrolyte gel. (**b**) Because HD electrodes are smaller, they can be arranged in variation configurations on the head. Shown is the 4x1 ring configuration of electrode placement where four electrodes of matched polarity are positioned around a central electrode of opposite polarity. The render shows placement of the electrodes over the targeted brain region. (**c**) Image of a HD electrode assembly on a subject head. (**d**) HD-tES can be integrated readily with EEG in a single headgear

Fig. 8 Formed sponge electrode with stimulator integrated into headgear. (**a**) Rectangular electrode with formed pre-salinized foam spikes. (**b**) Electrodes are incorporated in the headset with built-in stimulator. Prior to positioning, the pre-salinated electrodes are saturated with water. The foam spike design of the electrode ensures good contact between the electrode and skin, even in the region with hairs. (**c**) Headset with saturated and salinated foam spikes positioned over brain region

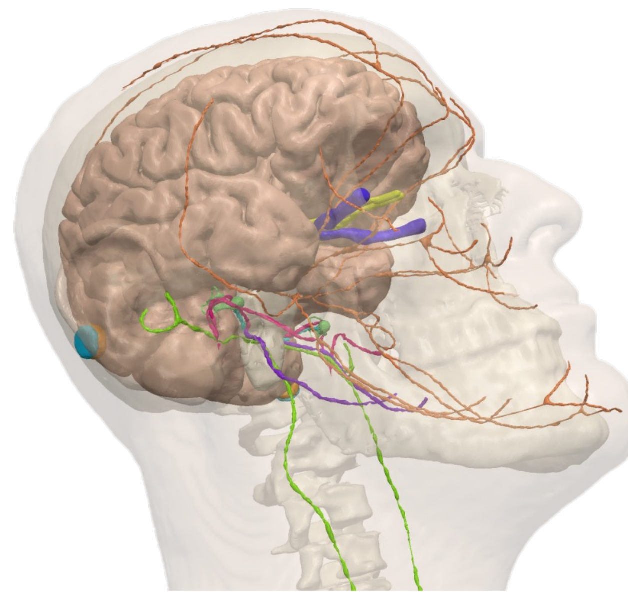


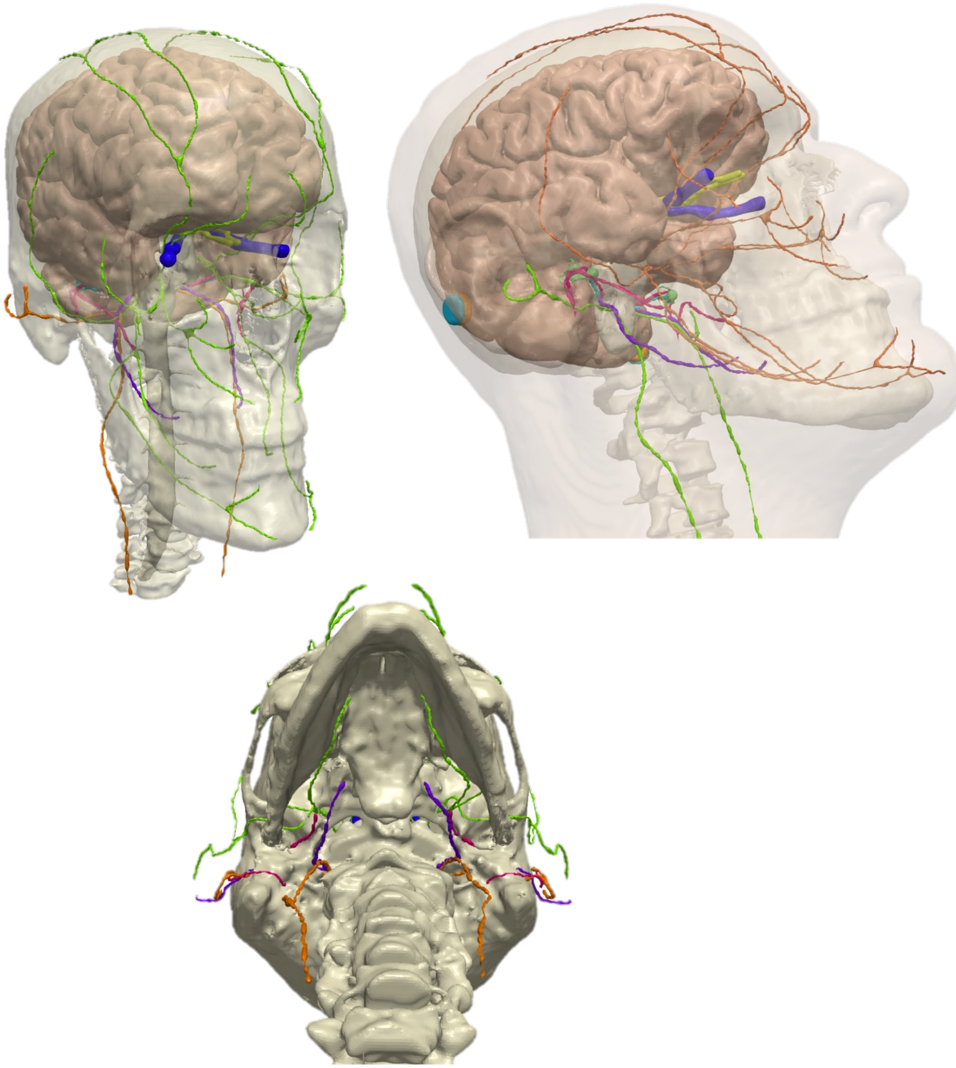
Brain Stimulation 13 (2020) 717–750

Electrical stimulation of cranial nerves in cognition and disease

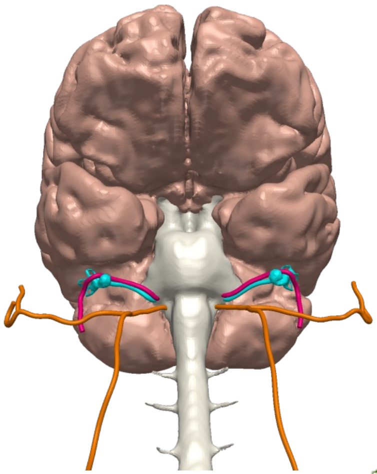
Devin Adair [a], Dennis Truong [a], Zeinab Esmaeilpour [a, *], Nigel Gebodh [a], Helen Borges [a],
Libby Ho [a], J. Douglas Bremner [b, c], Bashar W. Badran [d], Vitaly Napadow [e],
Vincent P. Clark [f, g, h], Marom Bikson [a, **]

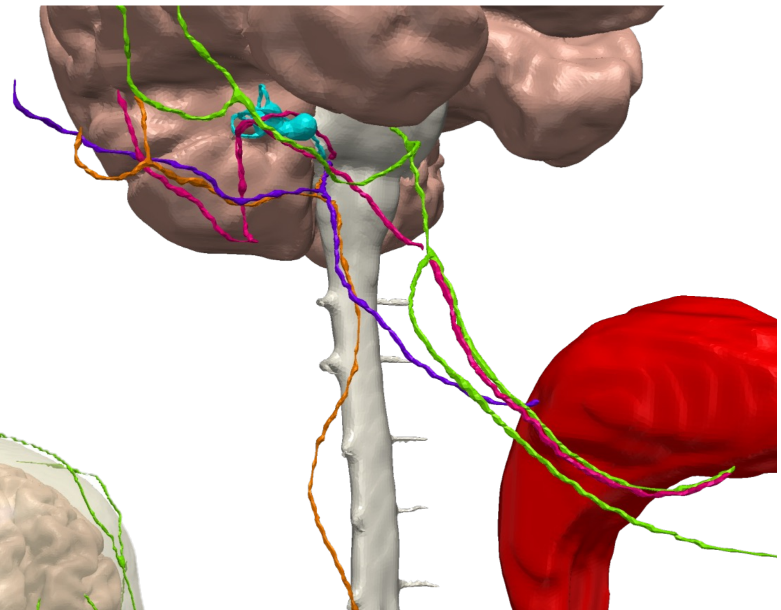
- The cranial nerves are the pathways through which environmental information (sensation) is directly communicated to the brain, leading to perception, and giving rise to higher cognition.
- Because cranial nerves modulate brain function, cranial nerve electrical stimulation has applications in the clinical, behavioral, and cognitive domains.
- Among other neuromodulation approaches, cranial nerve stimulation is unique in allowing axon pathway-specific engagement of brain circuits, including thalamocortical networks.
- Cranial nerve stimulation is not simply sensory substitution.

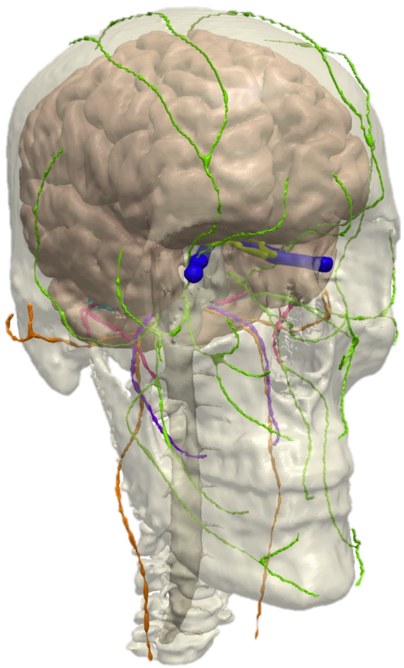


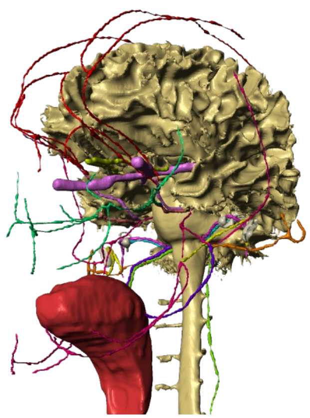


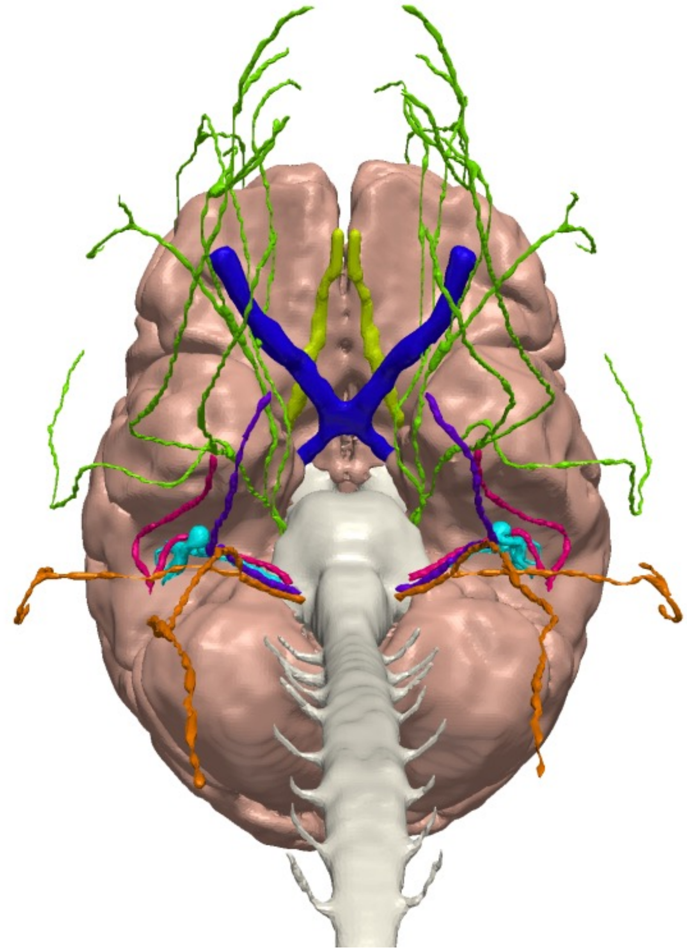
Fiber Type	Cranial Nerves	Function
Special somatic afferent (SSA)	**II** **VIII**	Vision Balance, hearing
Special visceral afferent (SVA)	**I** **VII**, **IX**, **X**	Smell Taste
General somatic afferent (GSA)	**V**, **VII**, **IX**, **X**	Proprioception (touch)
General visceral afferent (GVA)	**VII**, **IX**, **X**	Sensation from viscera
Special visceral efferent (SVE)	**V**, **VII**, **IX**, **X**	Motor control of the pharyngeal arches
General visceral efferent (GVE)	III, **VII**, **IX**, **X**	Autonomic motor and smooth muscles of the gut
General somatic efferent (GSE)	III, IV, VI XII	Motor control of eye muscles Motor control of the tongue



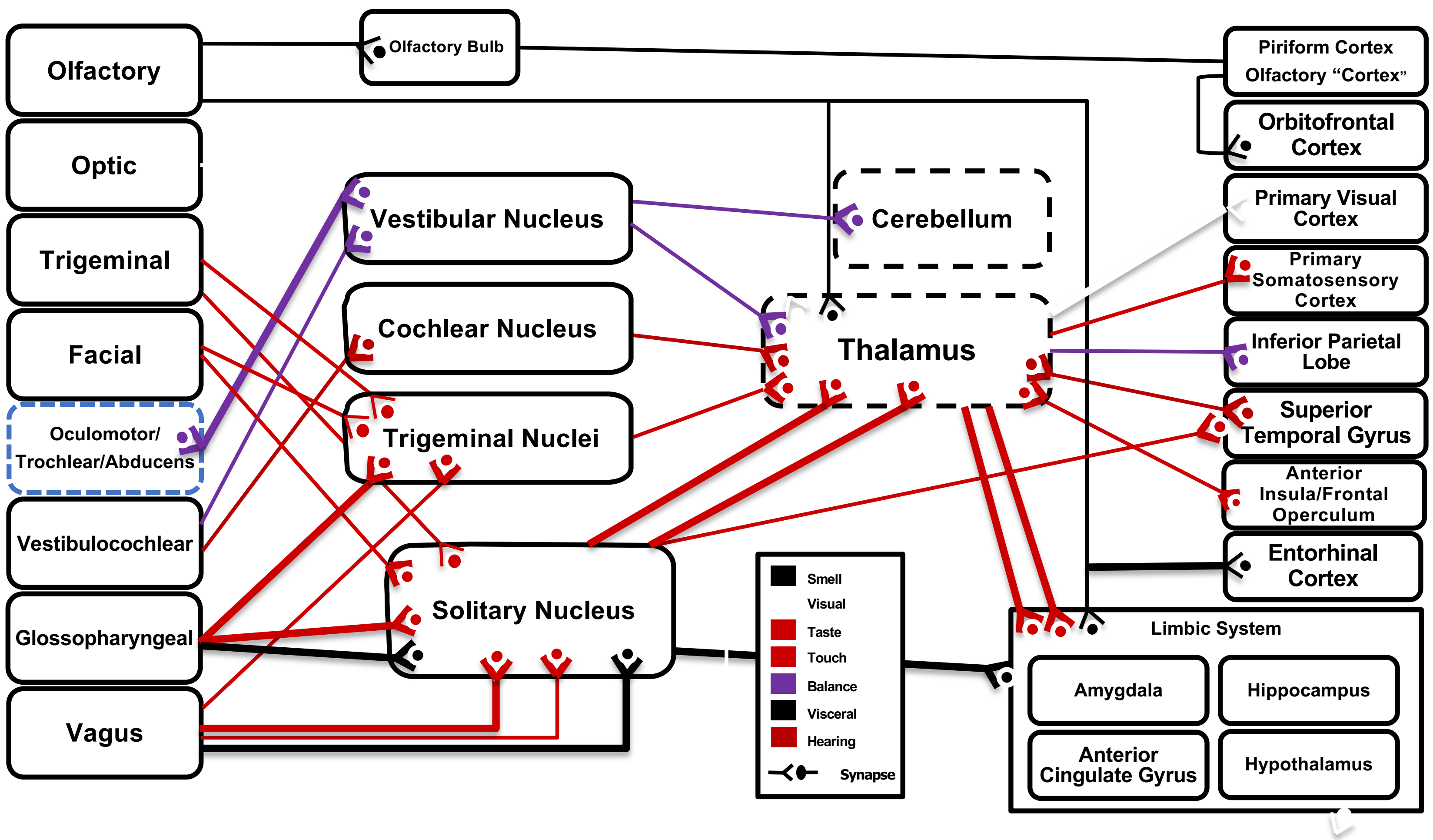








Connectivity of afferent cranial nerves to the brain. Cranial nerves activity modulates cognition and behavior at sub-cortical and cortical levels.



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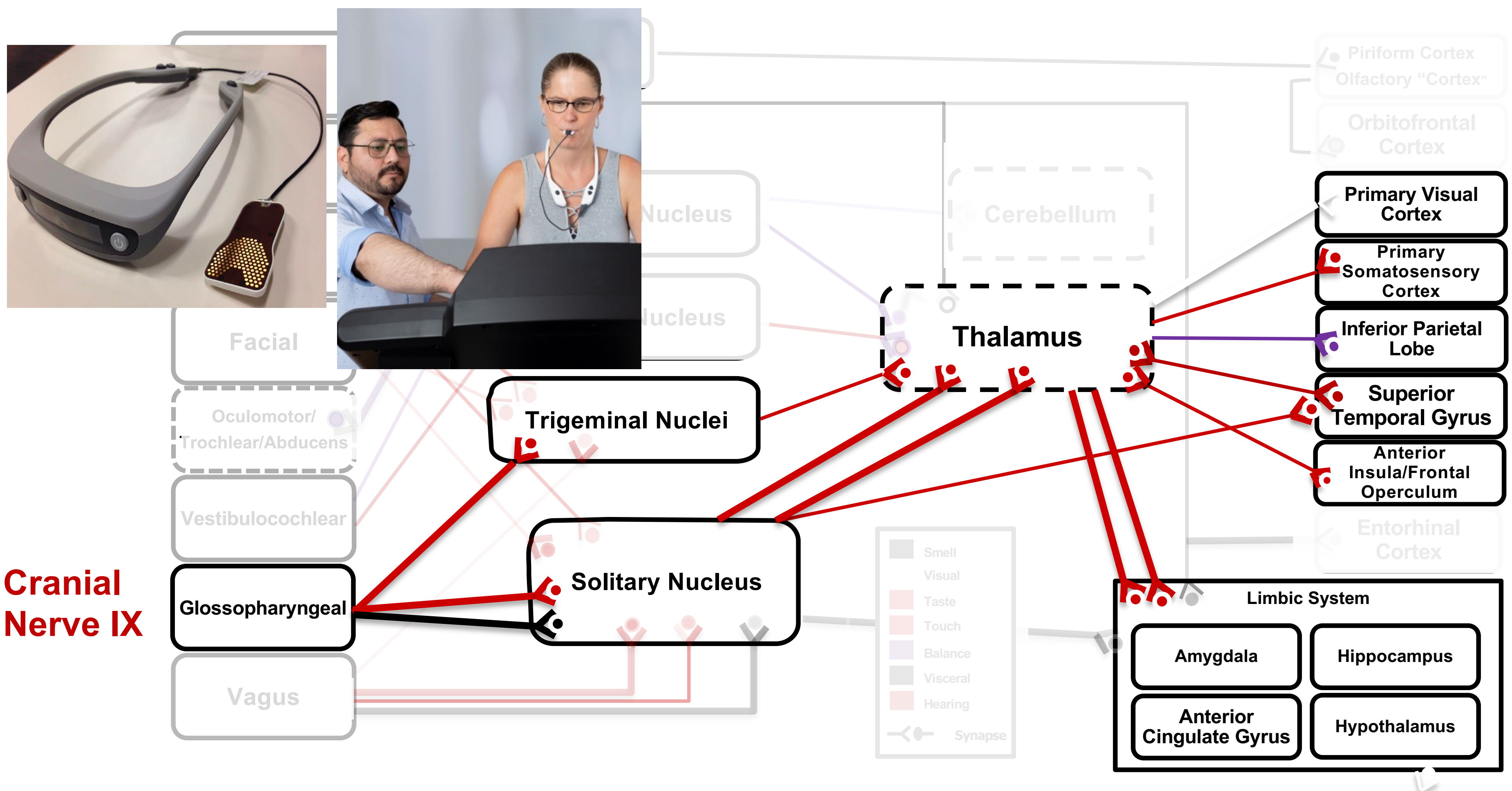

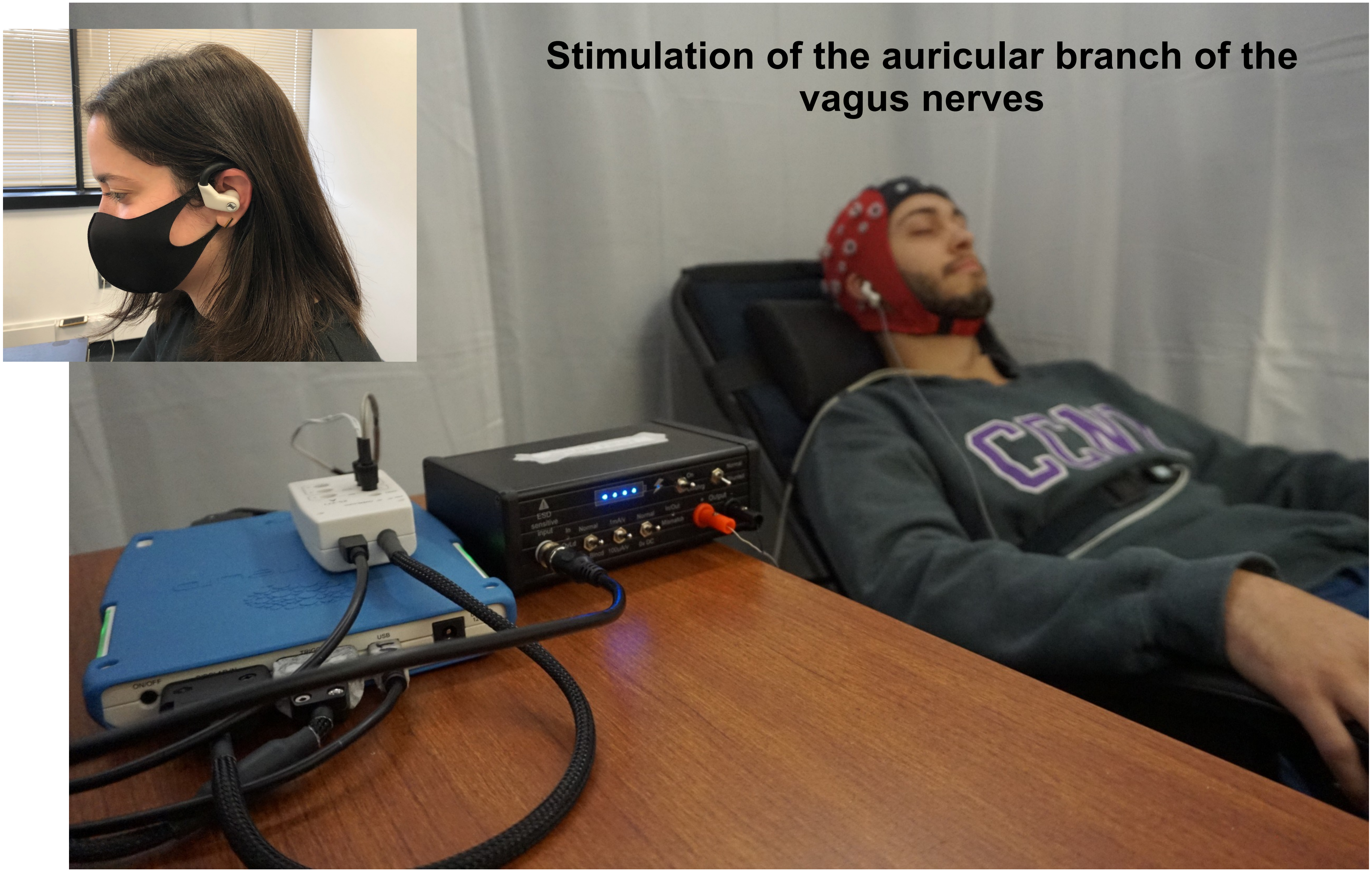
Stimulation of the auricular branch of the
vagus nerves

Connectivity of afferent cranial nerves to the brain. Cranial nerves activity modulates cognition and behavior at sub-cortical and cortical levels.