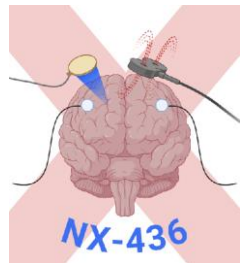


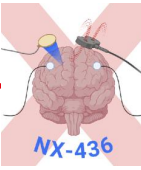
Introduction to
'Advanced methods for human
neuromodulation'
(Nx-436)

Prof. Friedhelm Hummel

Defitech Chair for Clinical Neuroengineering,
Neuro-X Institute (INX) & Brain Mind Institute (BMI)
Ecole Federale Polytechnique de Lausanne (EPFL)

Department of Clinical Neuroscience, University Hospital of Geneva





TIMELINE

Classes: Wednesday 8:15 – 10:00 – **14 Lectures** (recorded, slides moodle)

Exercises: Friday 15:15 - 17:00 – **14 Sessions**



Fall Semester

Examination:

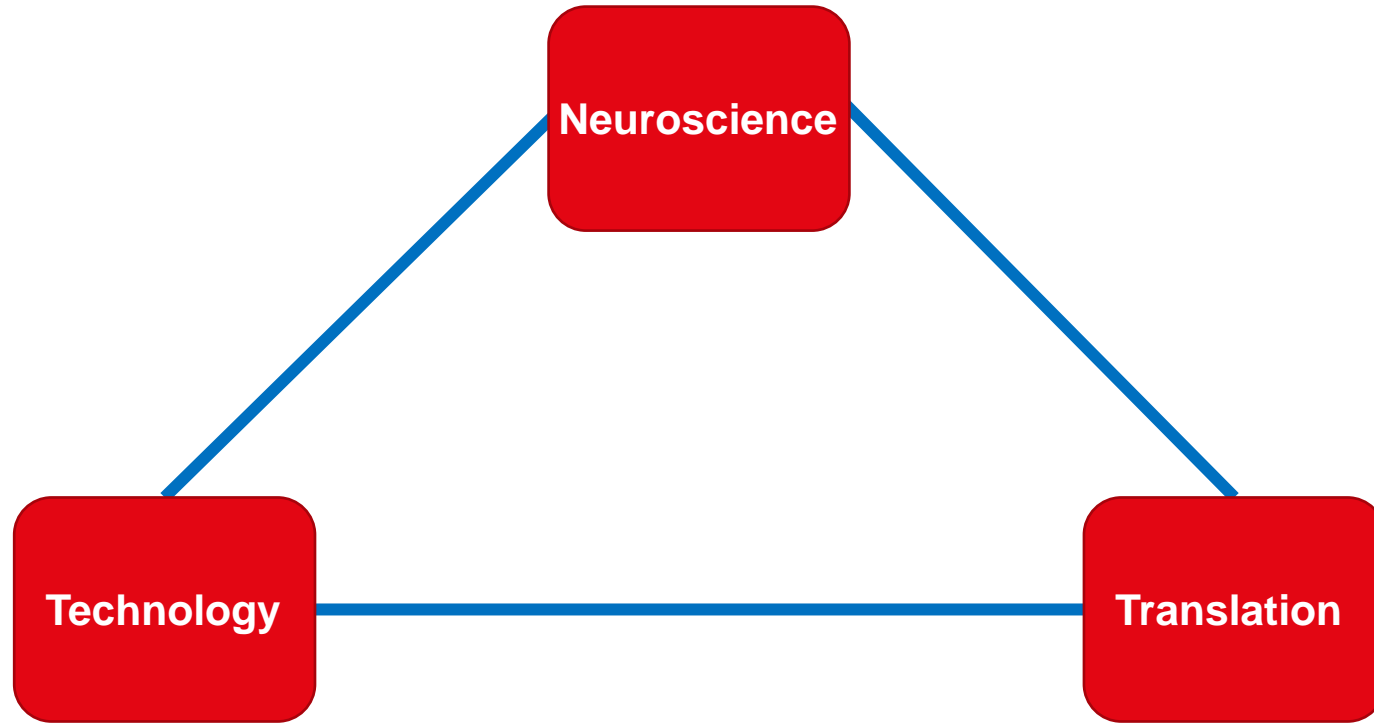
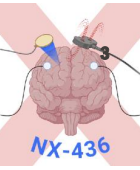
- Written MCQ Final Exam (50% of the grade)
- JC Presentation: 15 min Presentation + 10 min Questions (10% of the grade)
- Project Presentation : 20 min Presentation + 10 min Questions (40% of the grade)

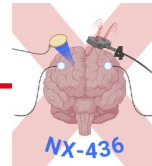
Link to **Coursebook**: <https://edu.epfl.ch/coursebook/en/advanced-methods-for-human-neuromodulation-NX-436>

Further **information** in moodle

- Guidelines JC and list of papers 4 JC
- Guidelines Project
- Guidelines MCQ

Literature suggestions in course book + JC papers in moodle





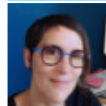
Week	Lecturer	Topic
Week1 10.09.2025	FH/TM	Introduction in the course (Organization, Requirements, Lectures-Exercises, Evaluation, Grading) Introduction into Neuromodulation. History of Neuromodulation
Week2 17.09.	FH	Neuromodulation of the vegetative system: Vagal nerve stimulation (VNS)
Week3 24.09.	FH	Neuromodulation of the peripheral nerve stimulation
Week4 01.10.	ER	Focused ultrasound neuromodulation
Week5 08.10.	FH	Spinal cord stimulation (invasive, non-invasive)
Week6 15.10.	FH	Transcranial magnetic stimulation (TMS) I (to determine brain functioning)
Week7 22.10.		no lecture
Week8 29.10.	FH	Transcranial magnetic stimulation (TMS) II (neuromodulation)
Week9 05.11.	FH	Transcranial electric stimulation (tES) I
Week10 12.11.	FH	Transcranial electric stimulation (tES) II
Week11 19.11.	VZ	Neuromodulation by optogenetics/chemogenetics
Week12 26.11.	FH	Deep brain stimulation (DBS) I: non-invasive
Week13 03.12.	MR	Deep brain stimulation (DBS) II: invasive
Week14 10.12.	FH	NIBS and multimodal imaging
Week15 17.12.	FH	Future outlook for neuromodulation: home-based, closed loop etc.

Lecturer

FH: Friedhelm Hummel, EPFL (<https://www.epfl.ch/labs/hummel-lab/>) friedhelm.hummel@epfl.ch

**Guest Lecturer**

ER: Estelle Raffin, EPFL, (<https://ipnc.univ-grenoble-alpes.fr/fr/estelle-raffin>), Estelle.Raffin@univ-grenoble-alpes.fr

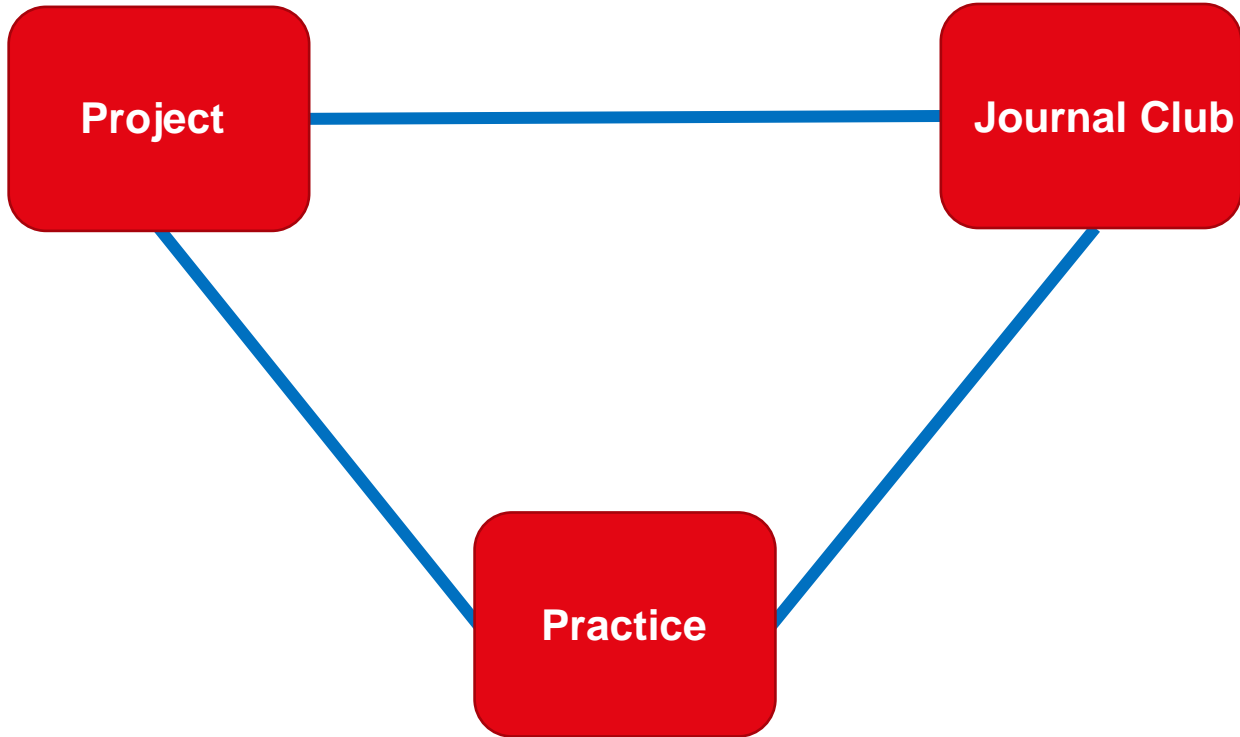
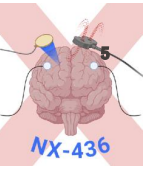


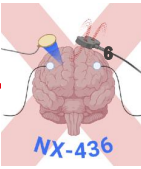
VZ: Valerio Zerbi, UNIGE, Valerio.Zerbi@unige.ch



MR: Martin Reich, UKW (https://www.ukw.de/neurologie/team/neurologie-detail/name/reich-martin/#reich_m1@ukw.de)

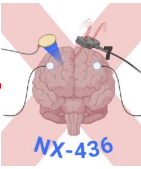




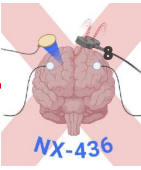


As one core component of the course, you will be tasked with developing an **innovative, disruptive, clinically** oriented project proposal involving a **novel** application or **improvement** of neuromodulation technology.

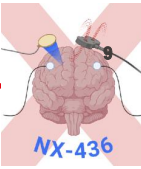
You will be provided with a **framework** to **guide** your **thinking**, including aspects such as targeting specific neural circuits, addressing unmet clinical needs, integrating neuroimaging or other advanced monitoring tools, and considering ethical, regulatory and entrepreneurial implications.



- **Innovation and Disruption:** Proposals should introduce **groundbreaking** ideas that challenge the status quo of current neuromodulation practices. You should feel free to propose ideas that may currently seem **speculative**, you are encouraged to propose **bold** and **unconventional** ideas, thinking **outside the box** to challenge existing paradigms in neuromodulation technology and its clinical applications.
- **Unlimited Budget Scenario:** While you should aim for practical and impactful solutions, you are encouraged to think expansively and creatively, imagining your projects with **no financial constraints**
- **Clinical Relevance:** Projects must have a **clinical focus**, addressing a specific neurological or psychiatric condition, cognitive function, or other health-related outcomes.
- **Feasibility and Impact:** While thinking big, you should consider the potential **feasibility** and **impact** of your proposed technology, including patient outcomes, scalability, and integration into current healthcare systems.



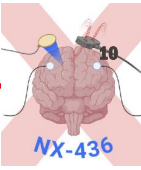
- **Group Collaboration:** You will form **groups** of three to **foster diverse perspectives** and **multidisciplinary** approaches to the project. **Collaborative** teamwork is essential to develop a comprehensive and innovative proposal.
- **Presentation and Defense:** At the end of the semester, you will present as a group your proposal in the course, simulating a pitch for funding or approval. You will need to defend your ideas in the view of the **current background** and demonstrate how your proposal could **transform** the field of neuromodulation.
- **Supervision and Guidance:** Throughout the semester, **each group** will receive supervision and guidance from a **teaching assistant (TA)**. The TA will provide support in refining ideas, ensuring scientific rigor, and offering feedback on project development. The exercise time and potential meetings with the TA will help groups navigate challenges, enhance their project proposals, and prepare for the final presentation.



Evaluation Guidelines:

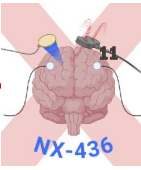
- **Percentage of the project for the final grade: 40%**
- **Evaluation criteria for the presentation:**
 - Background knowledge
 - Proposed solution
 - Innovation, disruptiveness
 - Feasibility
 - Readiness/responses to answers
 - Presentation skills and slides

- **Please see also moodle**

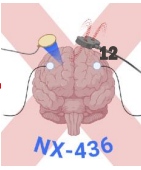


As part of the course, you will participate in a **Journal Club** to enhance your ability to critically **evaluate scientific** literature and effectively **communicate research** findings. This exercise is designed to develop skills in **scientific analysis, presentation, and discussion.**

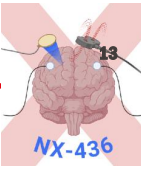
Furthermore, the presented scientific papers are related to the following weeks' lecture.



- **Paper to present:** Each group will receive a recent scientific manuscript related to the course and the lecture of the following week. Groups will be responsible for **thoroughly reading** and **analyzing** the manuscript, focusing on understanding the **background**, **novelty**, **limitations**, **challenges**, and **open questions** presented by the study.
- **Duration presentation:** Each group will deliver a **15-minute presentation** followed by a **10-minute Q&A** session.
- **Content:** Presentations should cover the following aspects of the manuscript:
 - **Background:** Provide an overview of the study's context, including key concepts, objectives, and the significance of the research question. Summarize the methodological approach.
 - **Novelty:** Highlight the unique contributions and innovative aspects of the study. Discuss what sets this research apart from previous work in the field.
 - **Limitations:** Critically assess the study's limitations, such as methodological constraints, sample size, potential biases, or areas where the data may be lacking.
 - **Challenges:** Identify any challenges encountered in the research process, including technical difficulties, ethical considerations, or interpretative complexities.
 - **Open Questions:** Discuss any unresolved issues or questions that arise from the study, suggesting possible directions for future research.



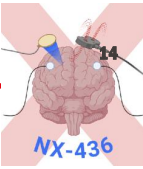
- **Preparation:** Groups should thoroughly understand the manuscript and be prepared to discuss it in depth. This includes anticipating potential questions from peers and preparing thoughtful, evidence-based responses.
- **Q&A Session:** Following each presentation, a 10-minute Q&A session will allow other students and instructors to ask questions. Presenters should be prepared to engage in a constructive discussion, demonstrating a deep understanding of the study and its broader implications.
- **Participation:** Each student should participate in the JC and should have read the paper to profit from the presentation and to be able to participate in the informed discussion. This will allow relevant learning with the JC.



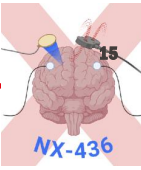
Evaluation Guidelines:

- **Percentage of the JC for the final grade: 10%**
- **Evaluation criteria for the presentation:**
 - Background knowledge, critical thinking, depth of analyses
 - Clarity of the presentation incl. slides
 - Readiness/responses to answers

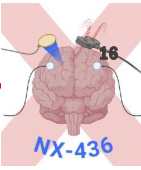
- **Please see also moodle**



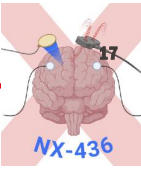
To Discuss



At the end of the course, you will complete a **comprehensive** Multiple Choice Questionnaire (**MCQ**) exam to **assess** their **understanding** of the course content. This exam will cover **all topics** discussed throughout the semester, including the principles of neuromodulation, underlying mechanisms of neuromodulation technologies, and their clinical applications. The MCQ exam is designed not only to test recall but also to assess your ability to apply your knowledge and think critically about the course content.

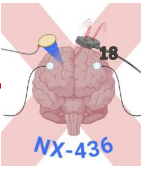


- **Format:** The MCQ exam will consist of questions that may have **single or multiple correct** answers. You should read each question carefully and select the most appropriate response(s). Some questions may require students to select a combination of answers to reflect the complexity and nuanced understanding of the course material. It is important to consider all options carefully to choose the most accurate responses.
- **Content Coverage:** Questions will encompass the topics covered in the course, including:
 - Fundamental principles and mechanisms of action for various neuromodulation techniques.
 - Recent advancements and research findings in neuromodulation.
 - Clinical applications of neuromodulation in neurological and psychiatric disorders.
 - Key concepts discussed during lectures, journal clubs, and project presentations.
- **Preparation and Expectations:**
 - **Study Materials:** you are encouraged to review lecture notes, assigned readings, suggested literature, JC discussions, and key points from the group projects to prepare for the exam.



Evaluation Guidelines:

- **Percentage of the MCQ exam for the final grade:** 50%
- **Evaluation criteria:**
 - Wrong answers are not punished
 - If combination of answers is required, only the correct combination will be accepted as correct
- **Mock MCQ Questions:** moodle



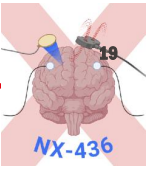
N Students: ~ 40 Students

JC: 13 JCs -> ~ 2-3 Students/JC

Projects: ~ 12 Project groups (1 Project/ TA; ~ 3 Students/Project)

Projects

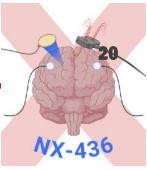
1. Apathy deep brain stimulation
2. Freezing of Gait Parkinson
3. Digital Bridge
4. Minimal-invasive tTIS
5. Optogenetic neuromodulation
6. Multifocal Neuromodulation



Questions?

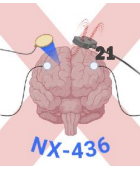
Email to:

paul.cadetdefontenay@epfl.ch

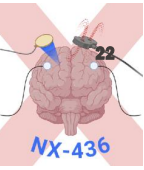


Background knowledge/Classes

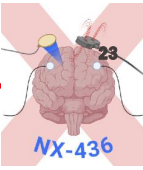
Neuroscience?
Translational Neuroengineering?
Imaging?



Expectations to the course?



Brainstorming - Neuromodulation



Learning Goals

- Brief overview about the **history** of brain stimulation
- Know the **current methods** for neuromodulation (**non-invasive** and **invasive**)
- Know the **technological** background, **mechanisms of actions** of them
- Know **safety** and **regulatory** aspects of them
- Know the **challenges, limitations** of these technologies that have to be addressed
- Know about **non-personalized** vs. **personalized** neuromodulation, **heterogeneity** of response and how to address this
- Know the concept of **state-dependent, closed-loop** neuromodulation, challenges and opportunities
- Know the use of **ML, AI** for neuromodulation.
- Know about **clinical** applications, challenges and opportunities
- Know about **next steps**: e.g., home-based self-application, technological requirements, challenges, opportunities.

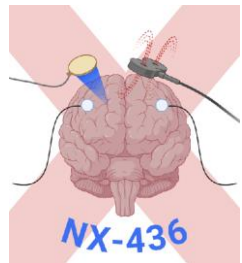


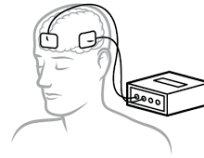
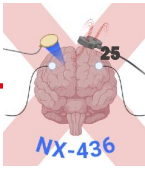
A short (long) history of neuromodulation (Nx-436)

Prof. Dr. med. Friedhelm Hummel

Defitech Chair for Clinical Neuroengineering,
Neuro-X Institute (INX) & Brain Mind Institute (BMI)
Ecole Federale Polytechnique de Lausanne (EPFL)

Department of Clinical Neuroscience, University Hospital of Geneva





Brain Stimulation

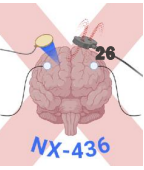
... modulating the activity of specific brain structures to understand their function, to handle and influence their dysfunction, has been and is a timeless mission for basic and translational neuroscientists and neurologists/psychiatrists....



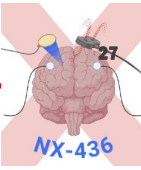
Training



Drugs



Quiz



Claudius Galen – treatment of headache

‘...the whole torpedo, and I mean the sea-torpedo, is said by some to cure headache ...

I indeed tried both of these things and found neither to be true. Therefore I thought the torpedo should be applied alive to the person who has headache, and it could be that this remedy is anodyne and could free the patient from pain as other remedies, which numb the senses: this is found to be so.

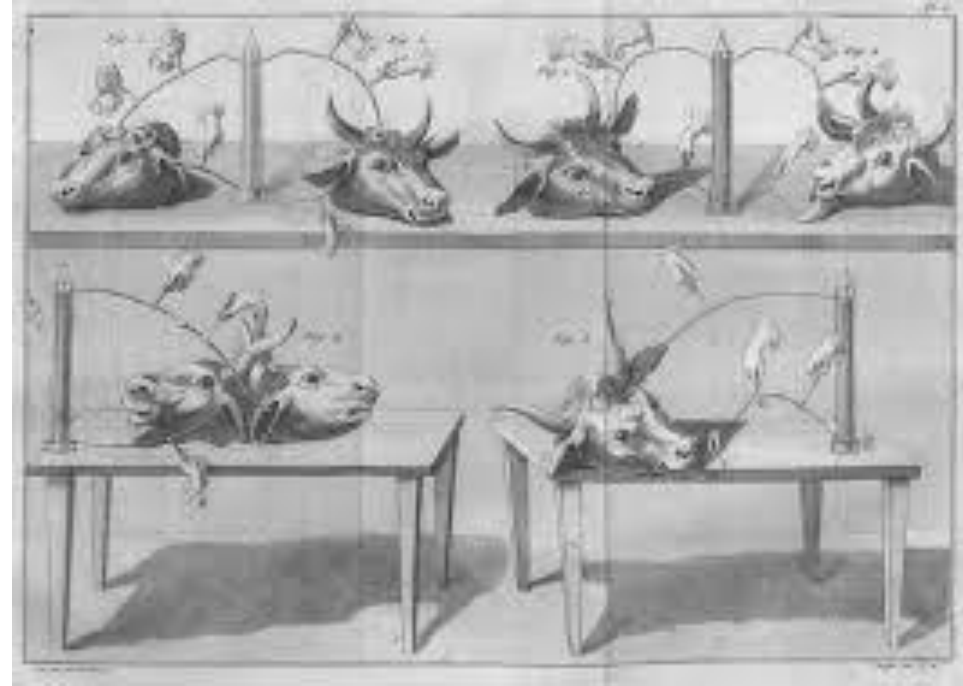
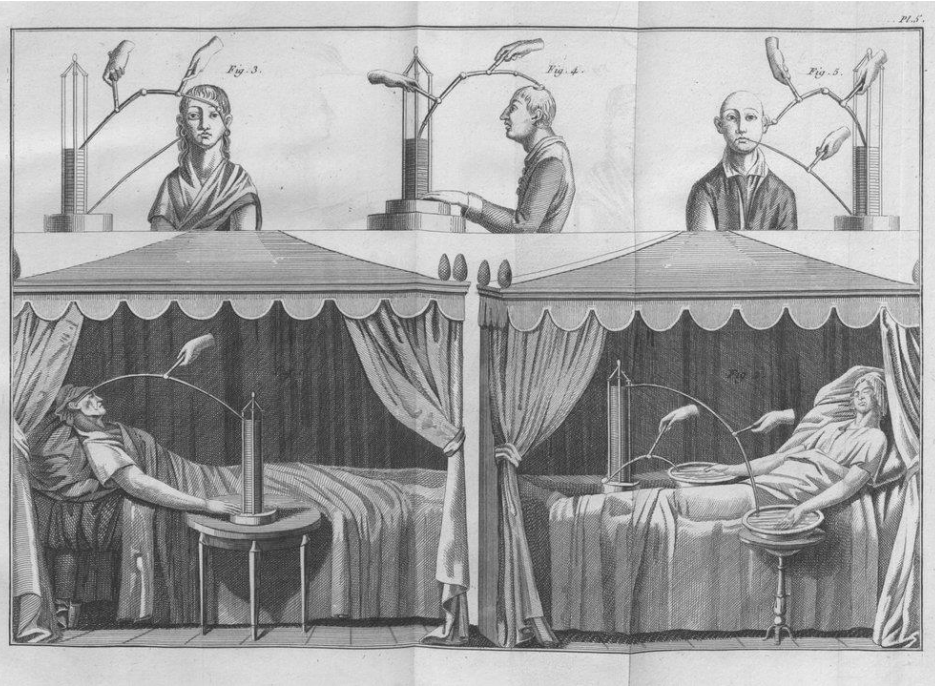
And I think that he who first tried this did so for the above-mentioned reason...’

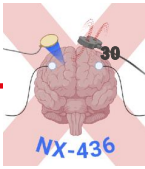
Claudius Galen (130-210 AD)
physician, writer and philosopher, most famous doctor in the Roman Empire

Scribonius largus (43-48 AC)



Non-invasive brain stimulation: G. Aldini 18th century





transcranial electric stimulation (tES)



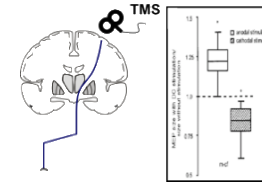
Scribonius laryus
Pain

Ibn-Sidah
Epilepsy

Luigi Galvani
Bioelectricity

Robert Bartholow
'Epidural stimulation'

Bindman
Animal work



Nitsche & Paulus
tDCS motor cortex +
electrophysiology



Treatment of
neuropsychiatric
diseases

Claudius Galen
Medical Pope of
the Middle ages

Dawud al-Antaki
Famous Syrian
physician /
philosopher,
headache and vertigo

Giovanni Aldini

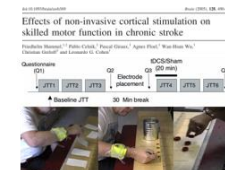


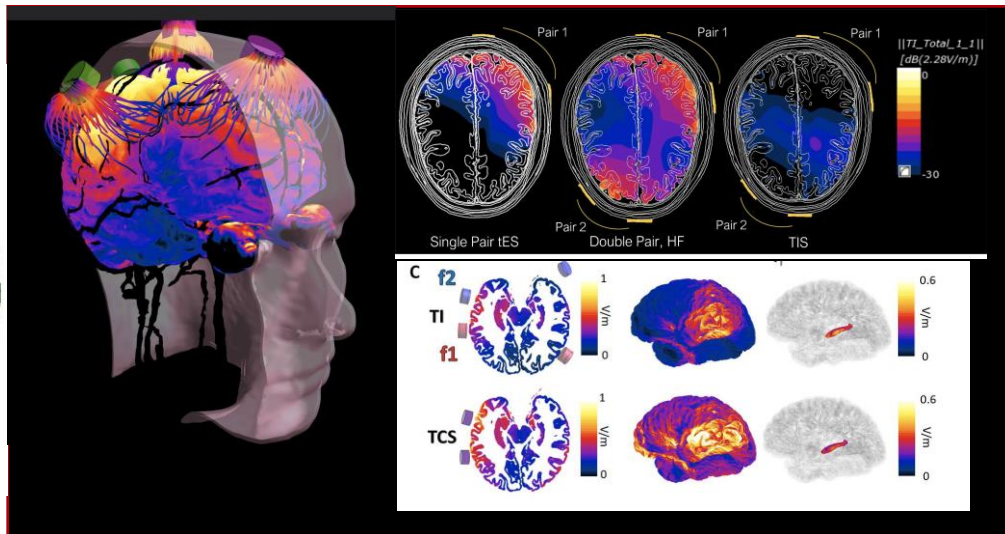
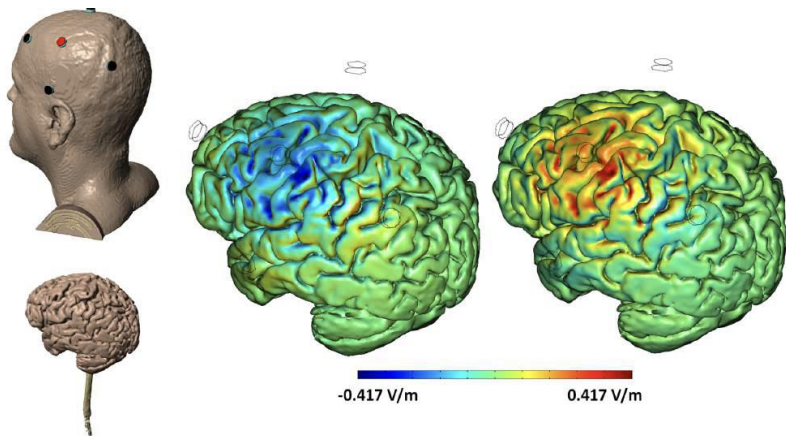
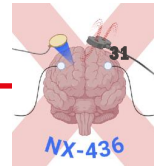
Cerletti and Bini
Electroconvulsive
Therapy

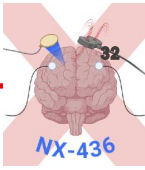


Elbert & Birbaumer
Human work

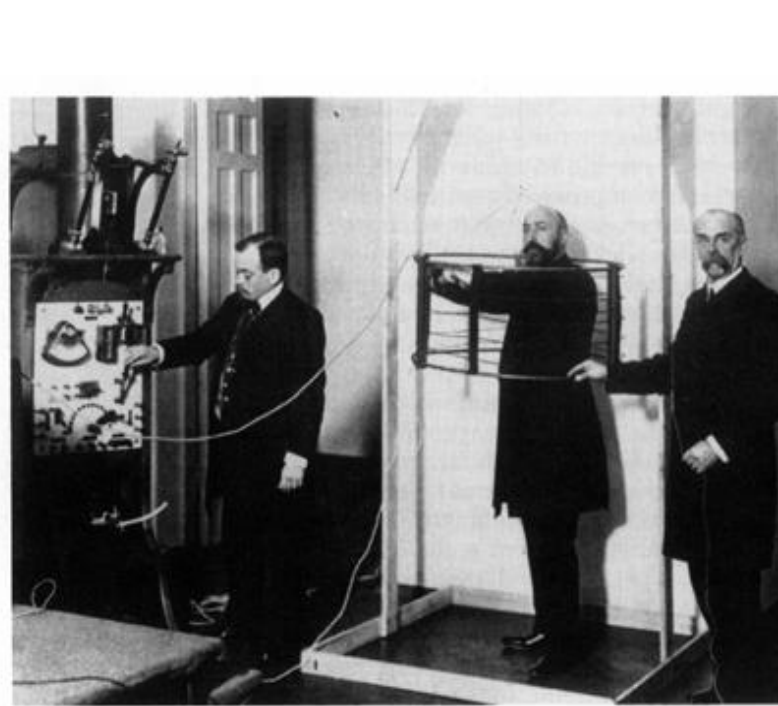
Hummel
Stroke







Transcranial Magnetic Stimulation

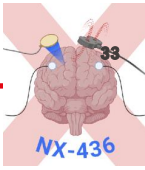


d'Arsonval 1896/1911

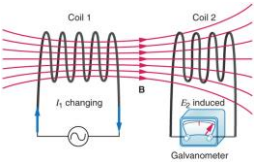


Magnusson & Stevens, 1911





Transcranial Magnetic Stimulation



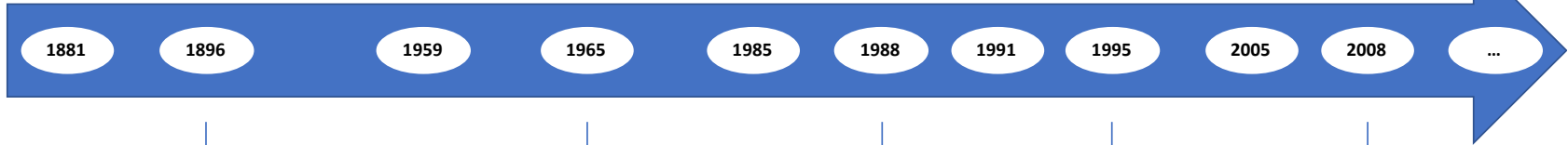
Faraday
Electro-magnetic coupling

Kolin
Stimulated nerves magnetically

Barker
Transcranial Magnetic Stimulation

Pascual-Leone
Virtual lesion, rTMS

Mansur&Takeuchi
Stroke



Treatment of neuropsychiatric diseases

d'Arsonval
Phosphenes, Vertigo

Bickford & Fremming
Human nerves magnetically

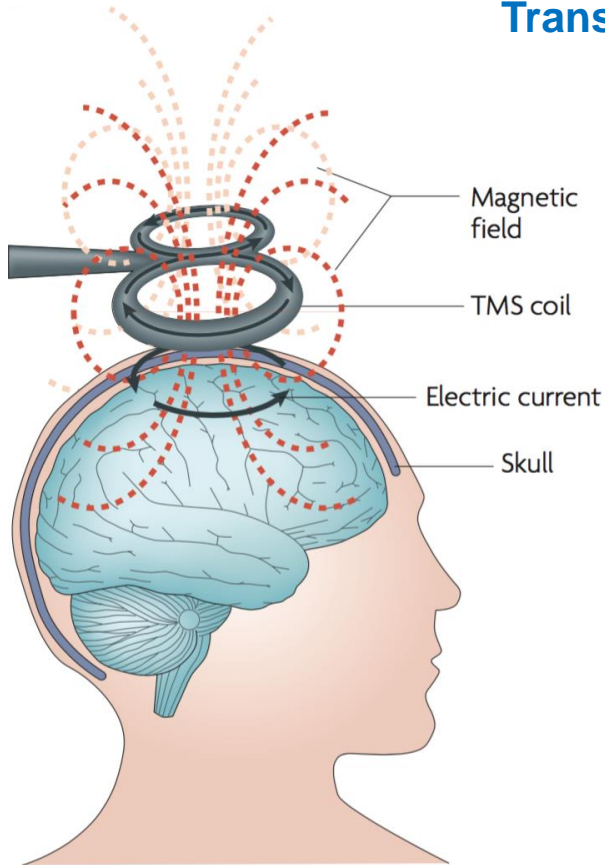
Cohen&Ueno
Figure of Eight Coil

Kolbinger
Depression

FDA Approval
Depression



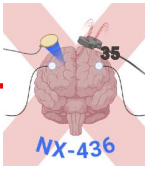
Transcranial Magnetic Stimulation



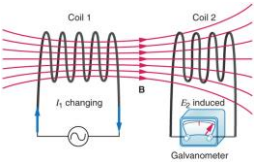
Ridding & Rothwell 2007 Nat Rev Neurosci



Barker et al.



Transcranial Magnetic Stimulation



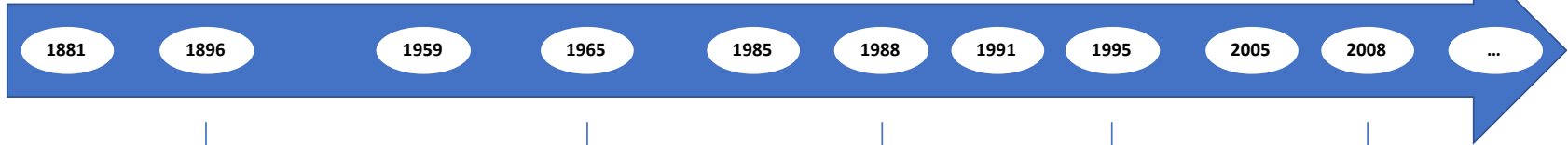
Faraday
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Mansur&Takeuchi
Stroke



Treatment of neuropsychiatric diseases

d'Arsonval
Phosphenes, Vertigo

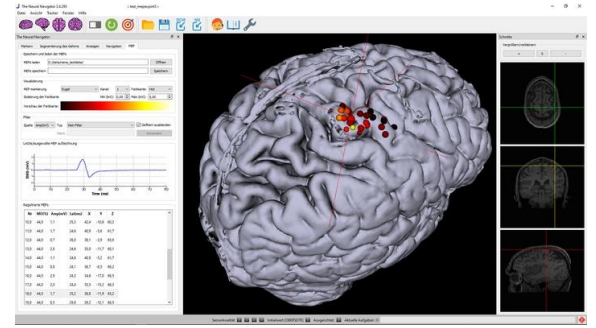
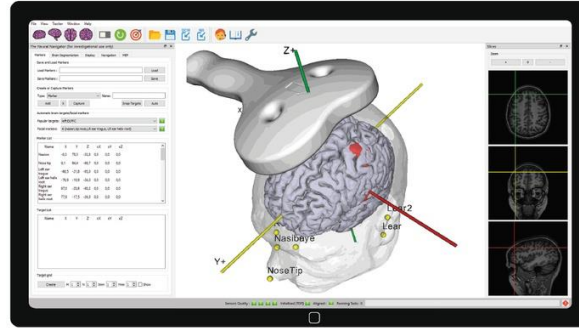
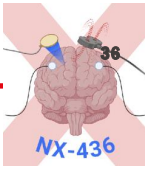
Bickford & Fremming
Human nerves magnetically

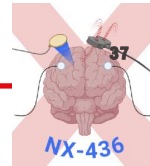
Cohen&Ueno
Figure of Eight Coil

Kolbinger
Depression

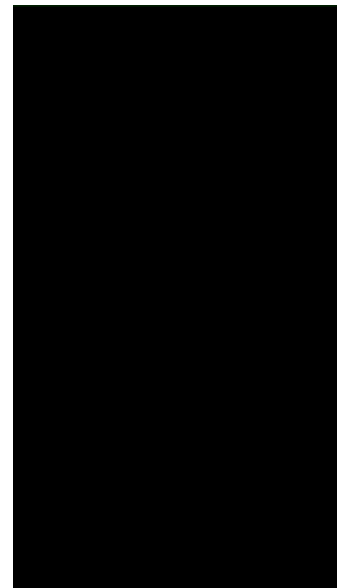
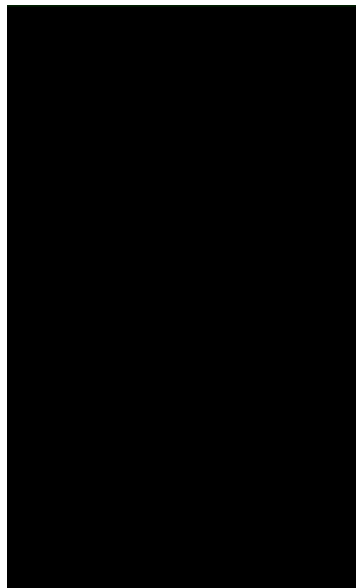
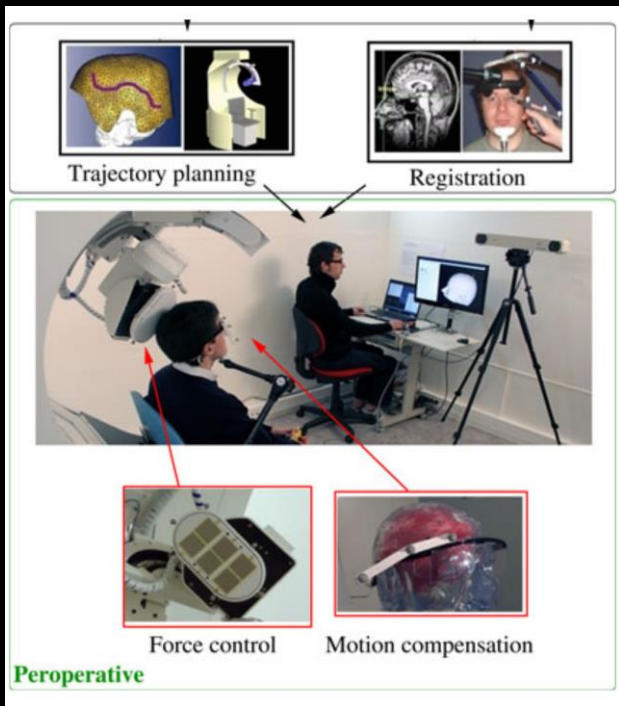
FDA Approval
Depression

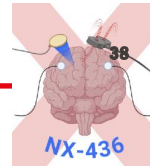




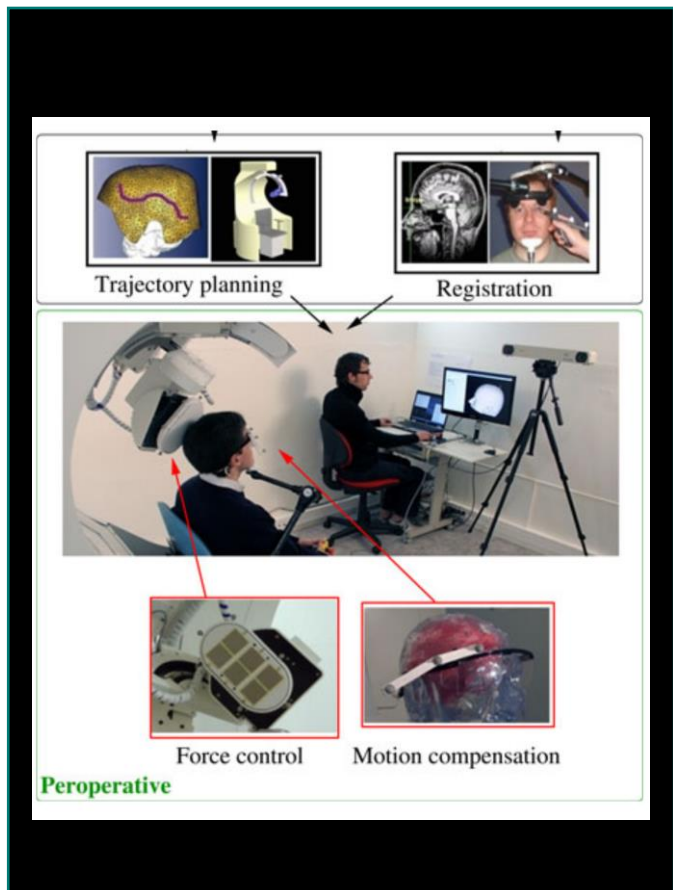
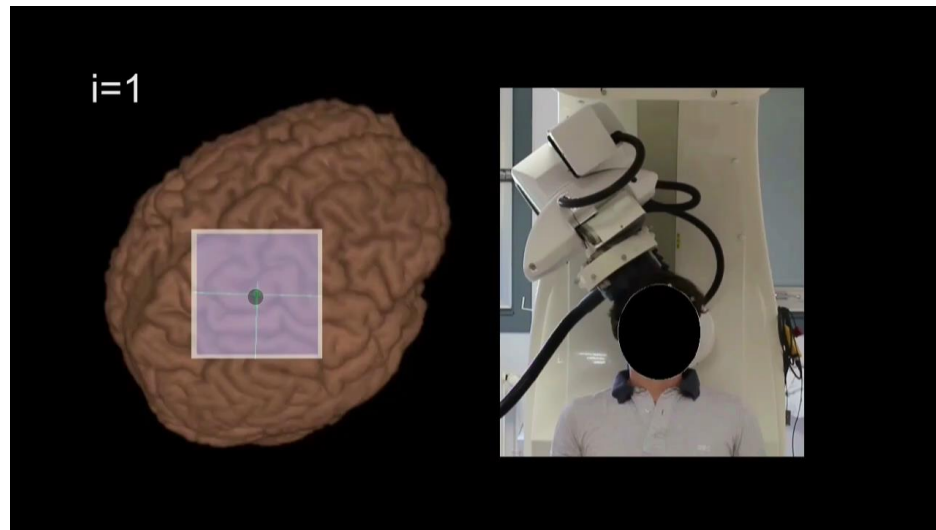


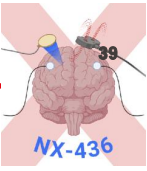
Robotized TMS



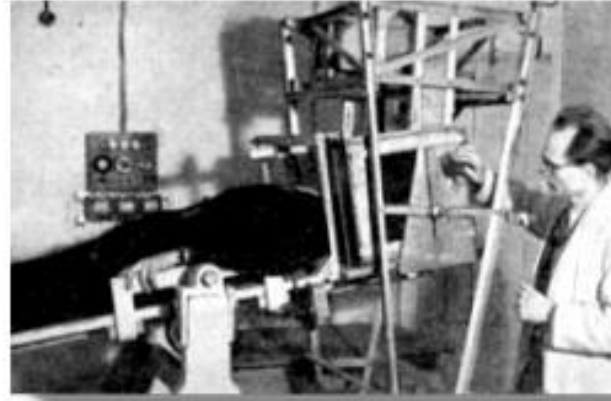


Robotized TMS

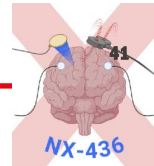




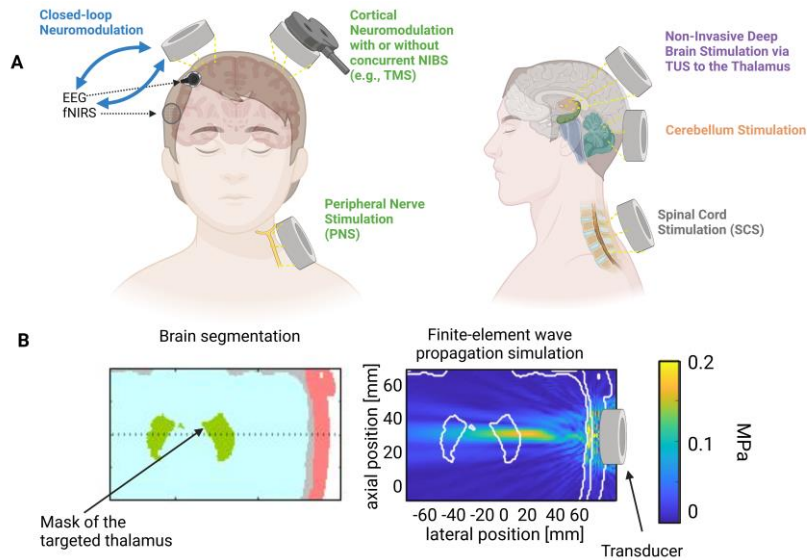
<https://www.iuslondon.co.uk/>



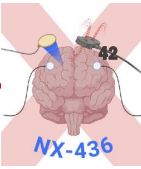
<https://www.ob-ultrasound.net>



Beisteiner 2020



Yüksel et al. , 2024 IEEE EMB



****Timeline of the History of Optogenetics****

Discovery of light-sensitive proteins
(1970s-1990s)

First optogenetic control of mice spread adoption and novel applications
(2005) (2010-Present)



Identification of channelrhodopsins and halorhodopsins
(late 1990s)

Expansion of optogenetic tools and applications
(2005-2010) Current and future directions
(Present)

1975

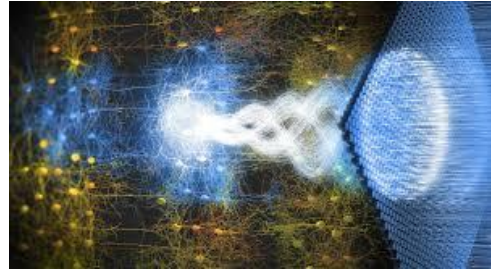
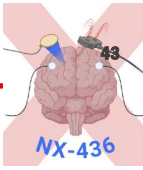
1995

2005

2010

2015

2024



****Timeline of the History of Sonogenetics****

Inspiration from optogenetics and ultrasound applications
(2000s - 2010s)

Pioneering experiments in nematodes using ultrasound
(2015)

Current research and potential clinical applications
(2020s - Present)



Exploring effects of ultrasound on expansion and refinement of techniques in various models
(early 2010s)

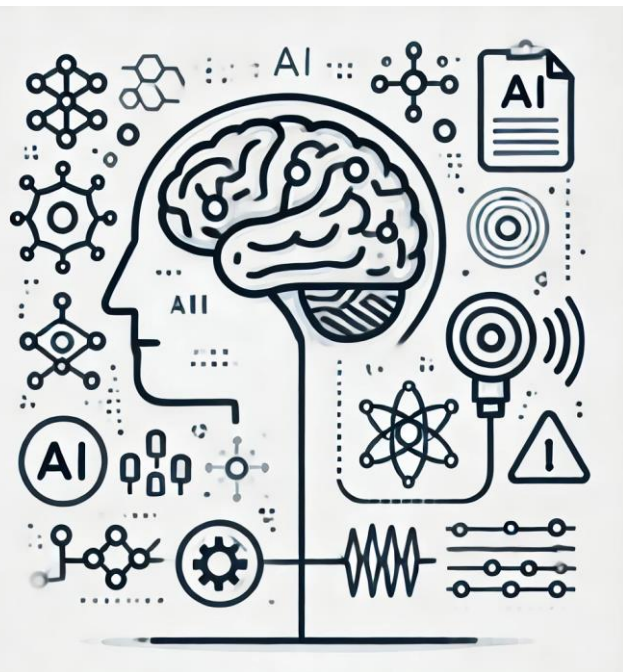
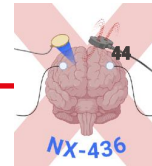
2005

2012

2015

2018

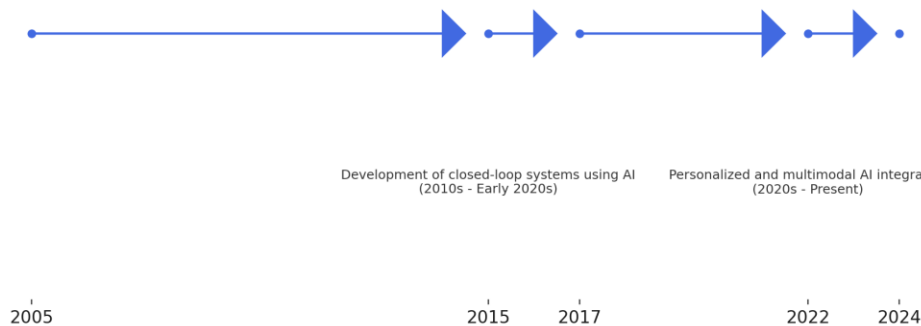
2024

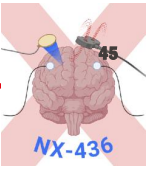


Timeline of the History of AI-Inspired Neuromodulation

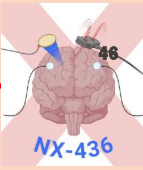
Foundations and early integration of AI in neuromodulation
(2000s - 2010s)

Advances in machine learning for pattern recognition
Ethical considerations and future applications
(2015 - Present)





Questions?



Which ideas unify different neuromodulation techniques?

Overview over the timelines, core developments of the current brain stimulation?

- Transcranial electrical stimulation (tES)
- Transcranial Magnetic Stimulation (TMS)
- Transcranial focused Ultrasound (tUS)