Development and Prospect of Neuromodulation Technology

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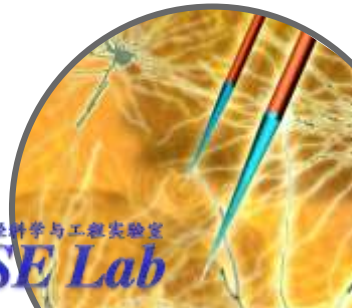
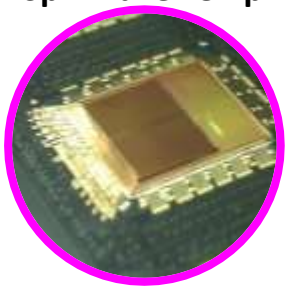


Why Study the Brain?

SpiNNaker Chip



80-90 billion Neurons

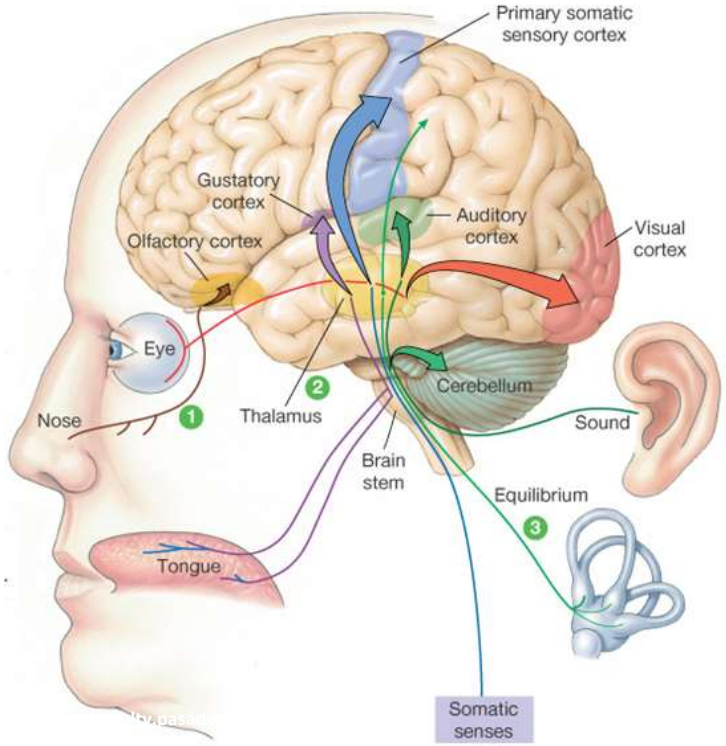
Robot

Brain Disease

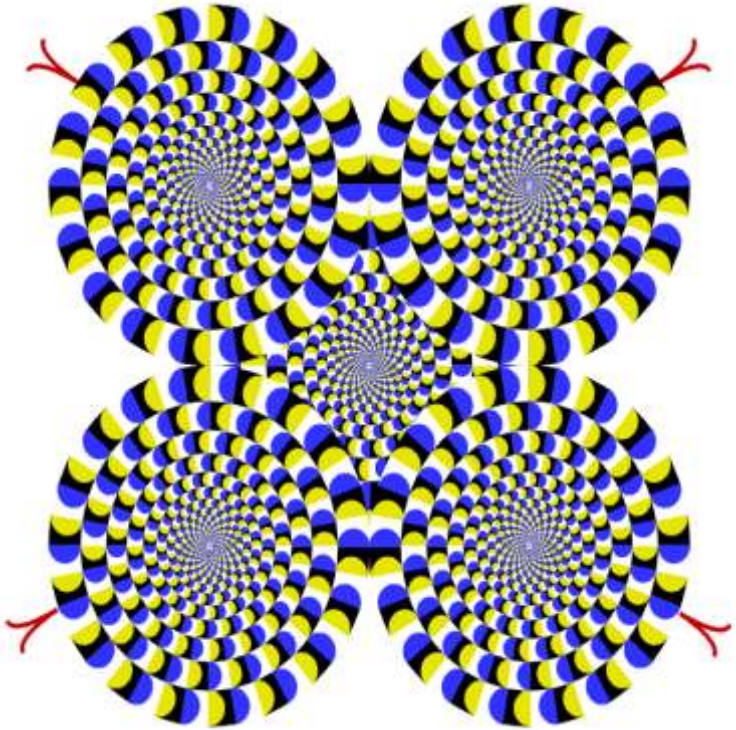
- Understanding Human Mind and Brain Function
- Neuroscience-inspired Artificial Intelligence
- New Diagnosis and Treatments for Brain Disease

Brain

Sensations, Memory, Emotion…

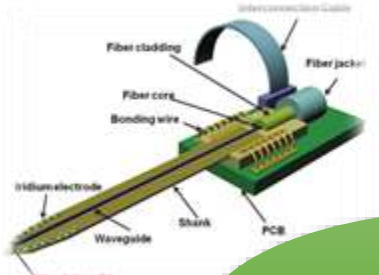


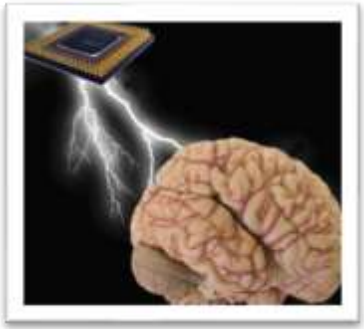
Vision



How to Study the Brain?

Brain Machine Interface

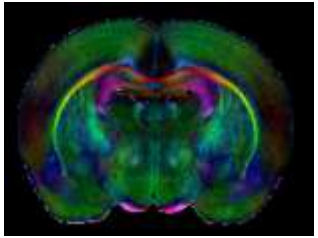




Recording Technology

Neuromodulation Technology

Brain Research
Medical Science
Diagnosis and Therapy



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Neuromodulation Technology

Electrical (DBS)
Chemical
Thermal
Cryogenic
Optical
Magnetic (TMS)
Mechanical (FUS)

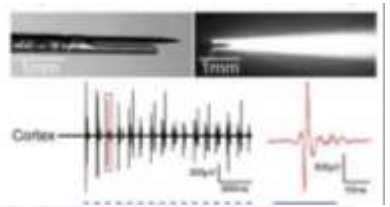
Invasive Neuromodulation

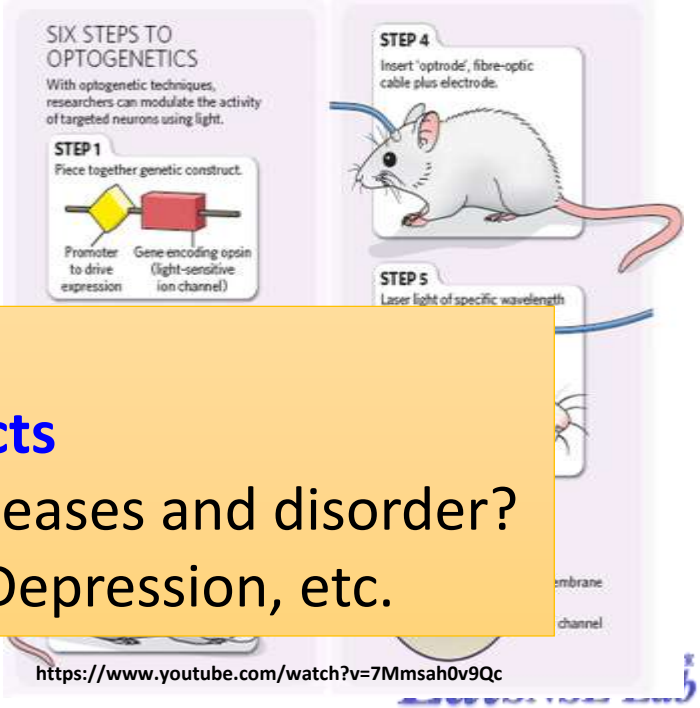
Microinjection

http://www.tritechresearch.com/IMS-3.html

Deep brain stimulation (DBS)

Optical stimulation





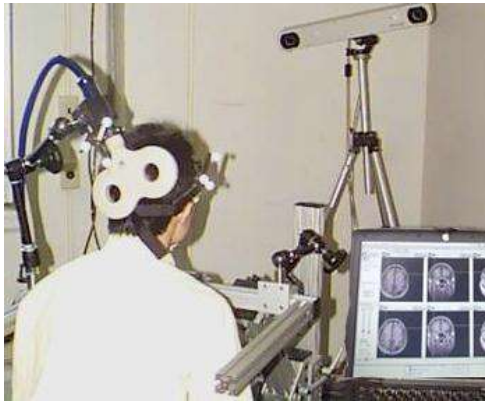
https://www.youtube.com/watch?v=7Mmsah0v9Qc

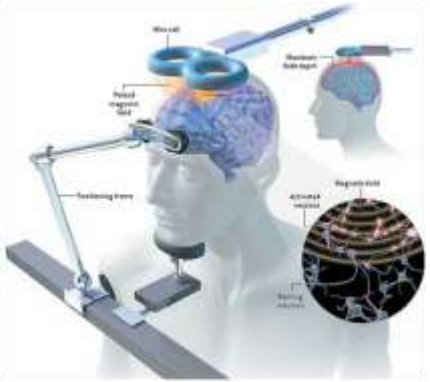
- targeting accuracy
- **brain tissue damage, adverse side effects**
- Any new applications for other brain diseases and disorder?
  Ex: Epilepsy, Dysmyotonia, Obsessive, Depression, etc.

Sumner et al., Nat Neuroscience, 2008

Noninvasive Neuromodulation

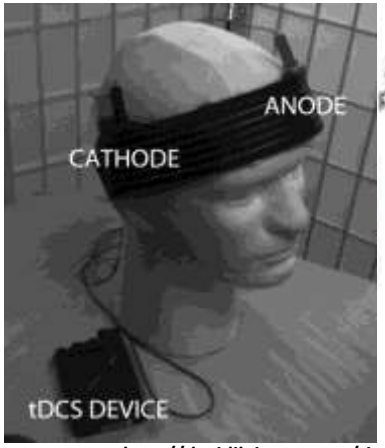
Transcranial magnetic stimulation (TMS)

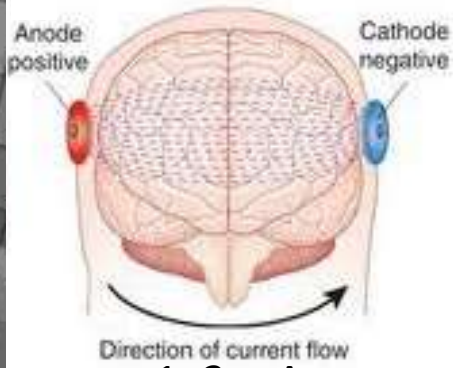




http://www.drchugh.com/rtms.html

Transcranial direct current stimulation (tDCS)





1–2 mA

http://davidileitman.com/time-causality-and-perception-tcp/

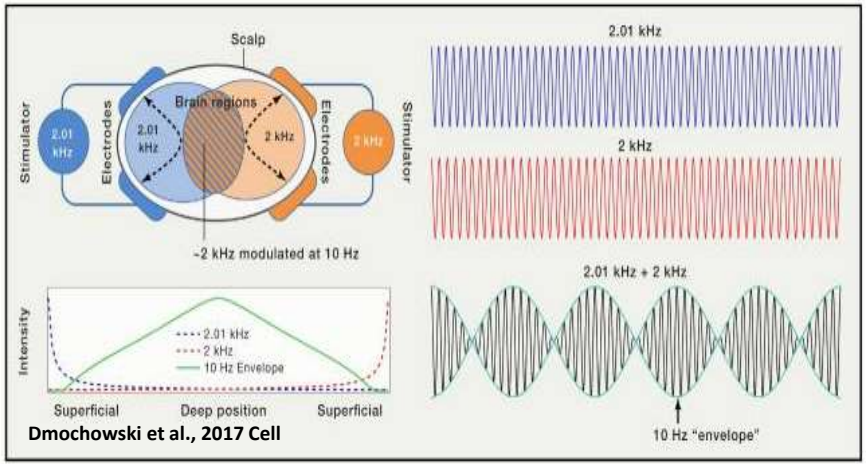
neurology and mental health

cognitive functions

Limitation of spatial resolution !!!

Noninvasive Neuromodulation

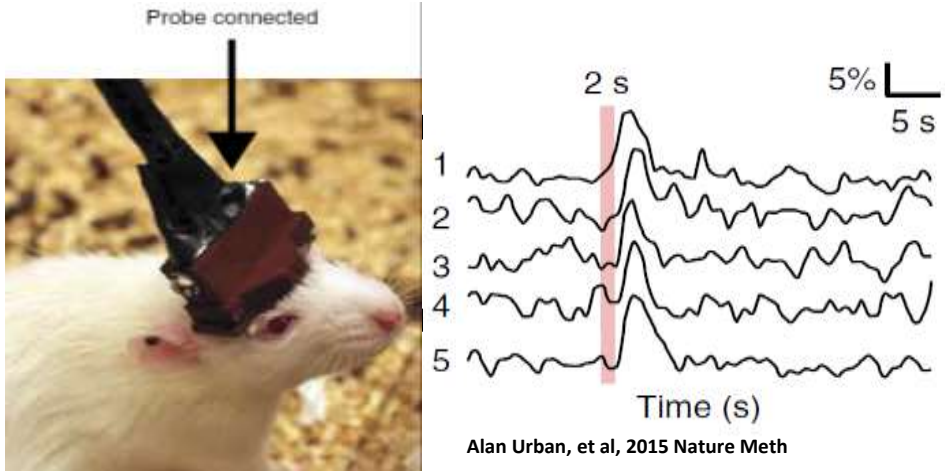
Temporal interference stimulation (TIS)



Dmochowski et al., 2017 Cell

TIS in humans is a challenging and promising technique.

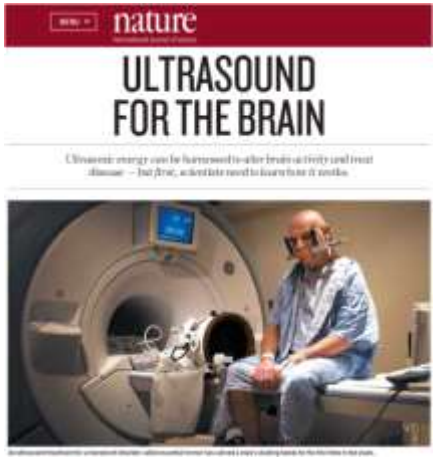
Focused ultrasound (FUS)

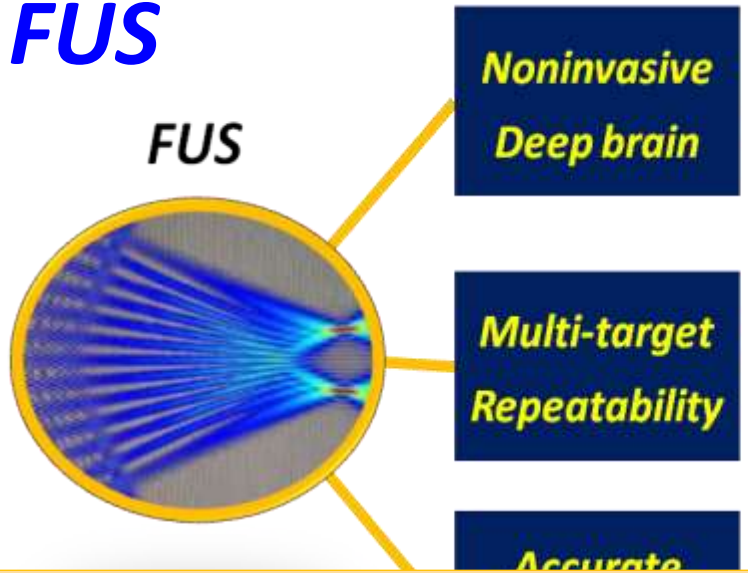


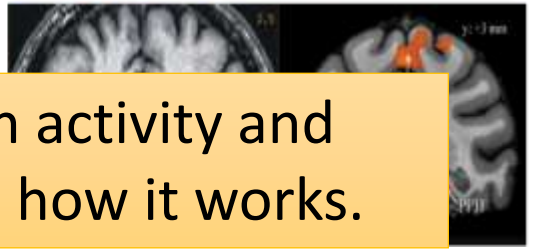
Alan Urban, et al, 2015 Nature Meth

- high spatial selectivity
- penetration depth
- excite or inhibit neural activity

Advantages of FUS





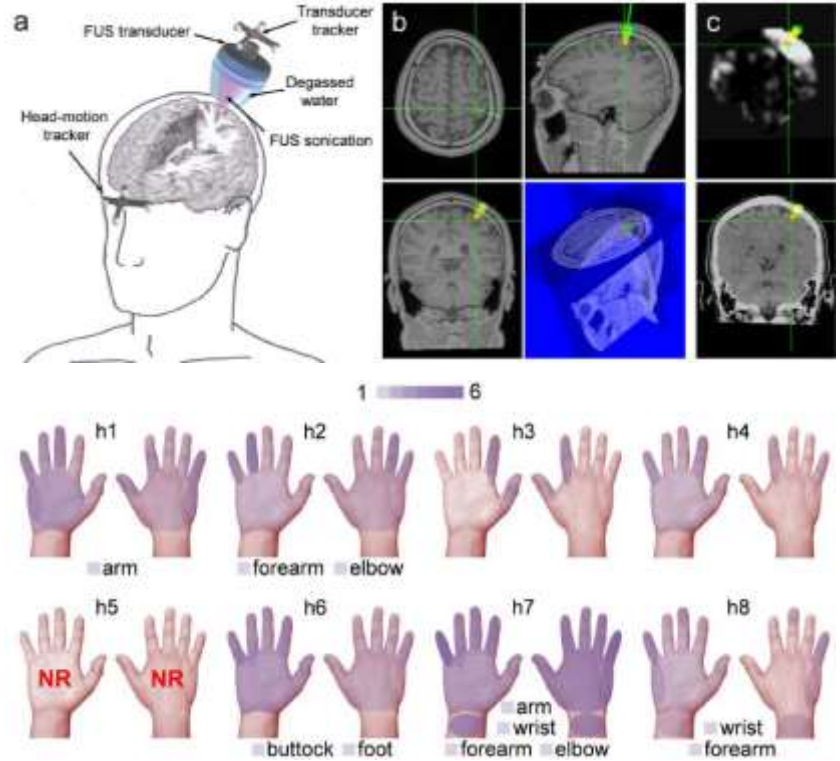


Ultrasonic energy can be harnessed to alter brain activity and treat disease — but first, scientists need to learn how it works.

- **High Intensity Focused Ultrasound (HIFU)**
- **FUS Neuromodulation**
- **FUS Blood-Brain Barrier (BBB) opening**

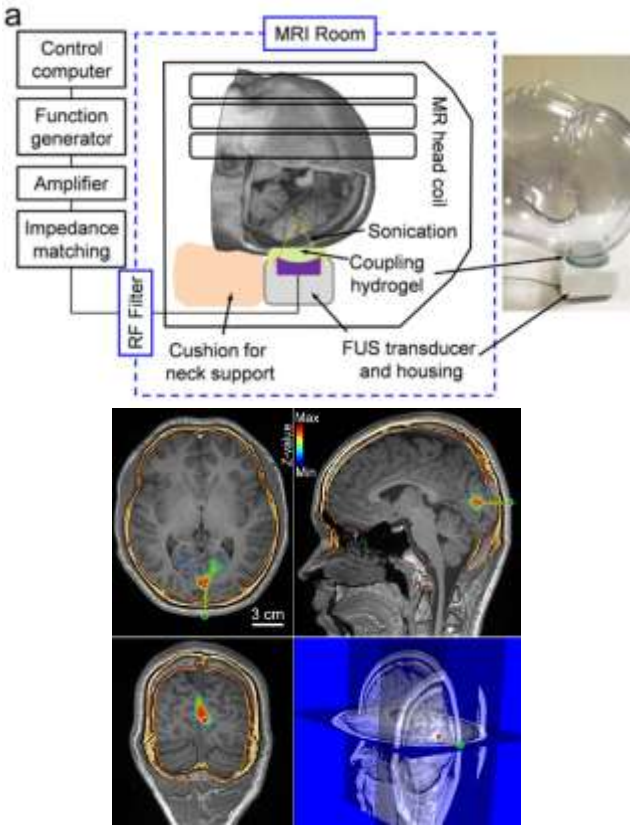
FUS Neuromodulation

Somatosensory cortex



Lee et al., Sci Rep, 2015

Visual cortex



Lee et al., Sci Rep, 2016

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FUS Neuromodulation

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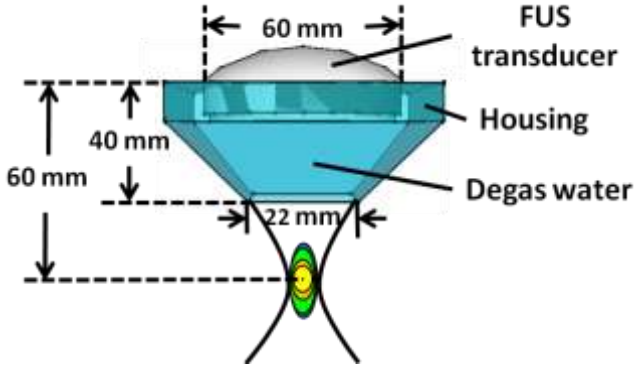

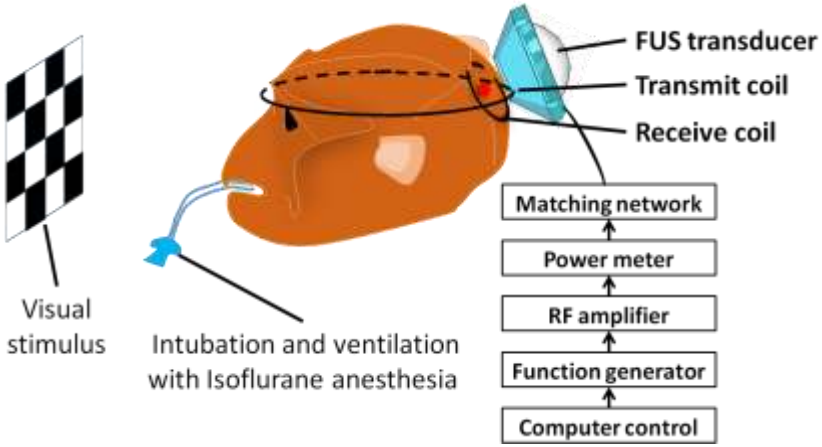

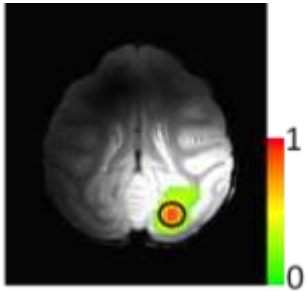

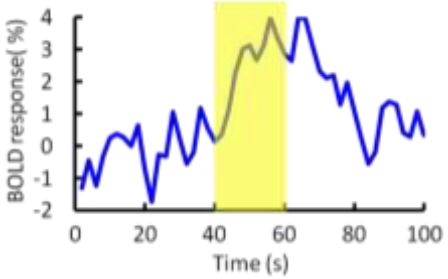

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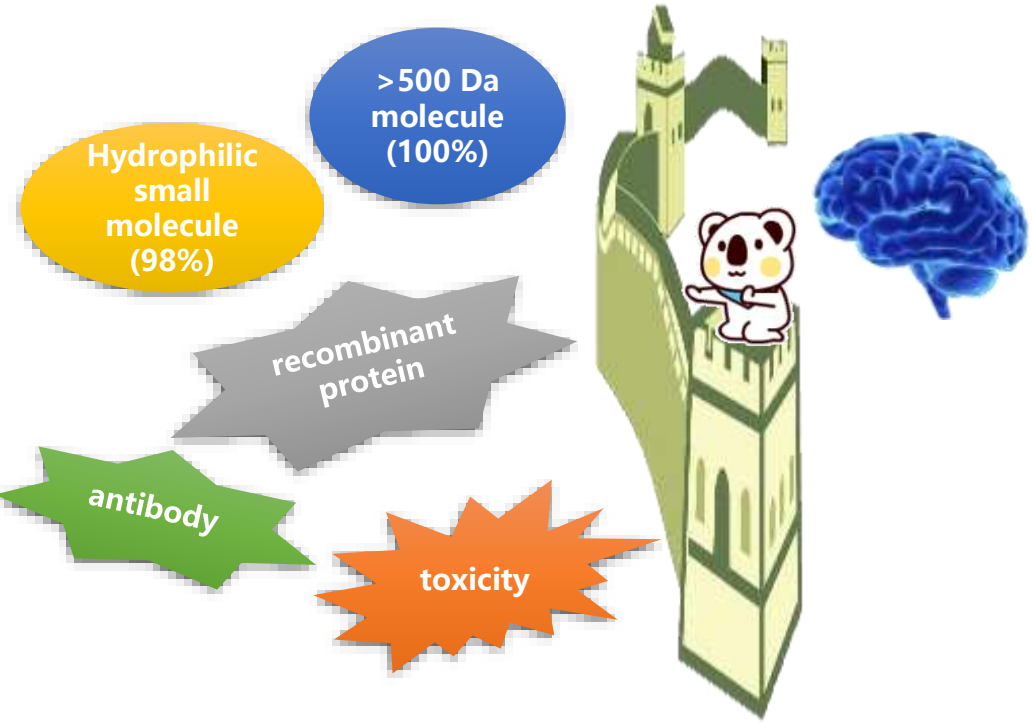
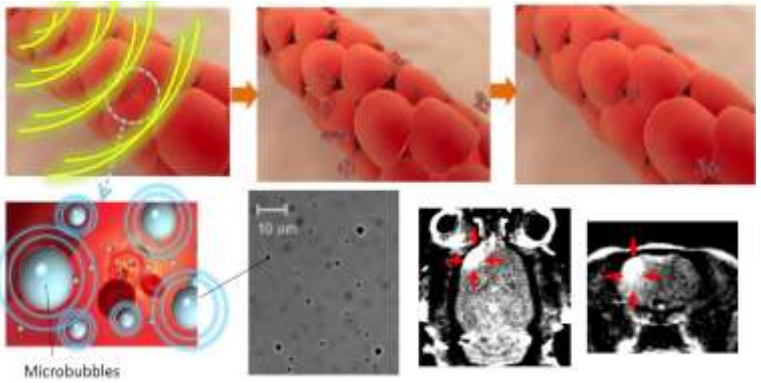
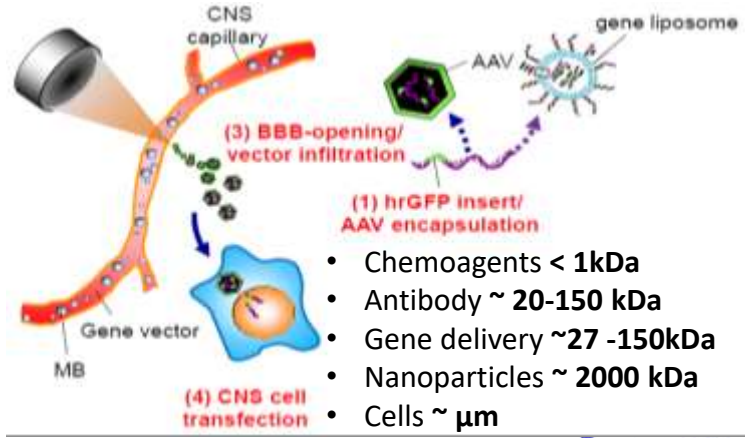
FUS with Intravenous Microbubble-Induced BBB Opening





- BBB temporally opened 0.5 – 4 hrs
- Reversibility, targetability
- molecules delivery

FUS BBB opening for molecules delivery



- Chemoagents **< 1kDa**
- Antibody **~ 20-150 kDa**
- Gene delivery **~27 -150kDa**
- Nanoparticles **~ 2000 kDa**
- Cells **~ µm**

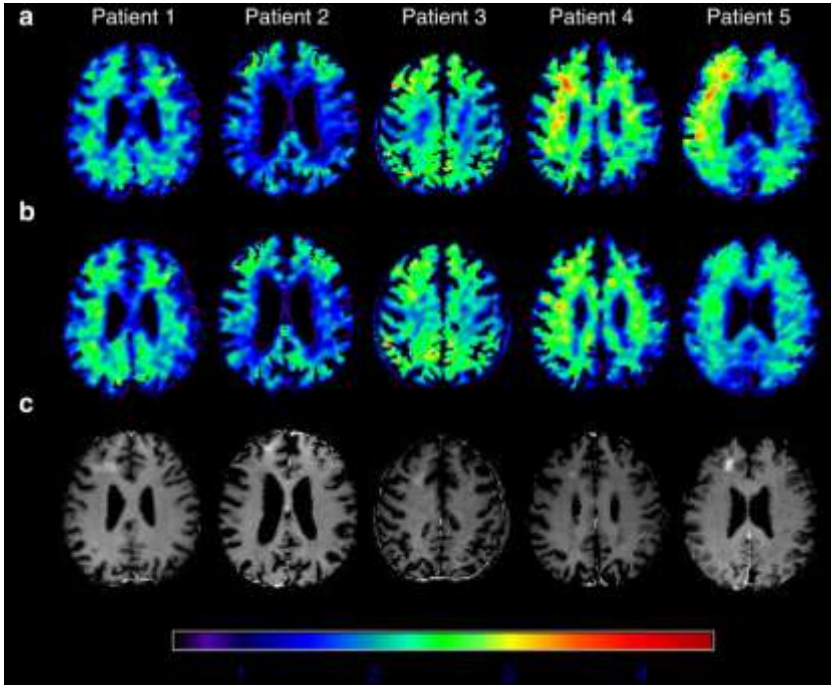
FUS with Intravenous Microbubble-Induced BBB Opening for Treatment of Patient with Alzheimer's disease

Leinenga and Gotz, 2015 Sci Transl Med

Safety

Long-term side effect

[18F]-Florbetaben PET scans



baseline

7 days post-FUS

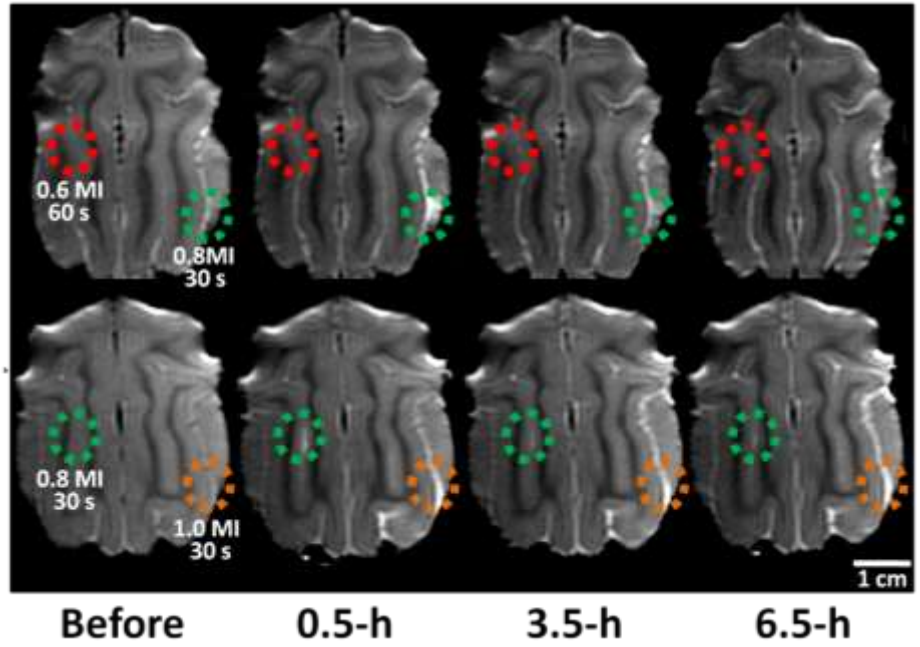
post-FUS

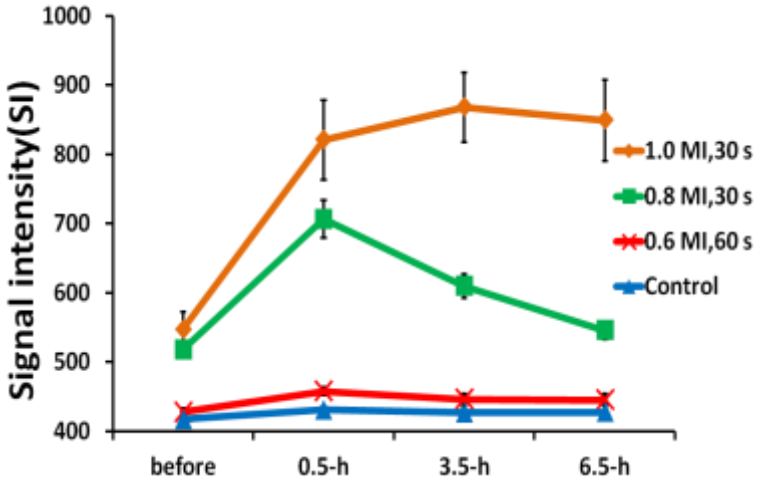
Nir Lipsman et al., 2018 Nature Commun

It Remains Unclear whether FUS-induced BBB Opening Induces Neuromodulation

MR-Guide FUS-induced BBB opening in large animals

LaiSNSE Lab (Unpublished)

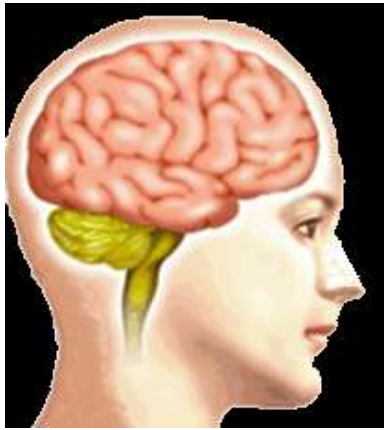




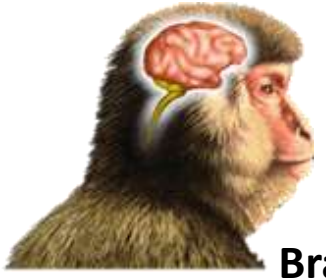
Challenge & Opportunity

Multimodality
Multiscale
Multispecies

Human



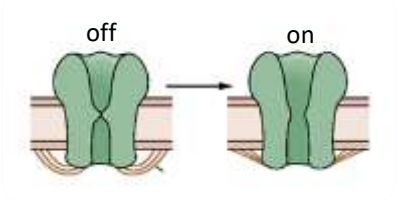
Monkey



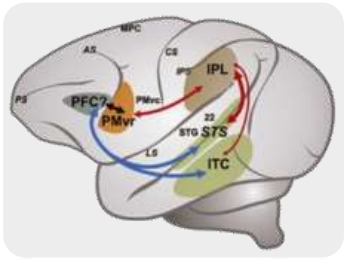
Rodent

cell

Ion channel,
Molecular mechanisms

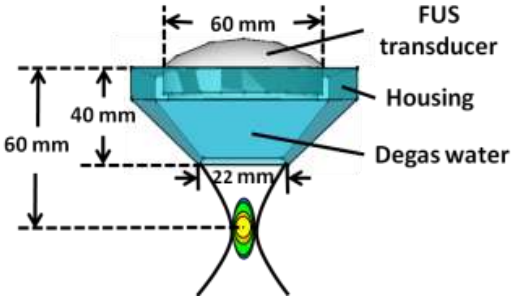


Neural Circuit ,
Functional network



Brain Disease

Technology Issue

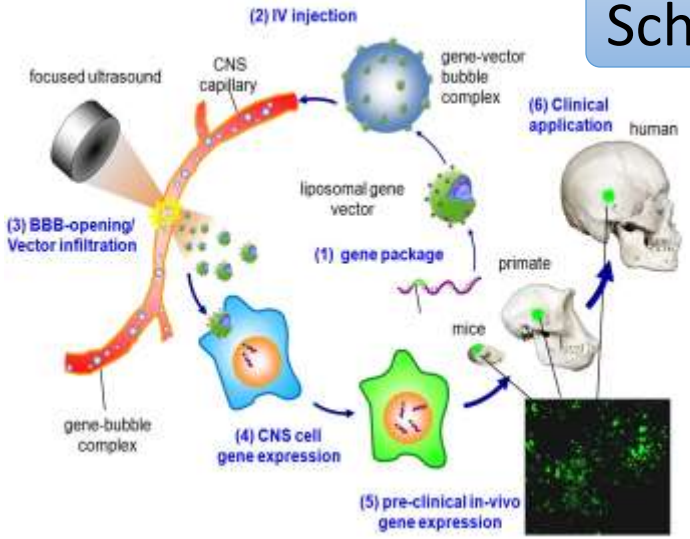


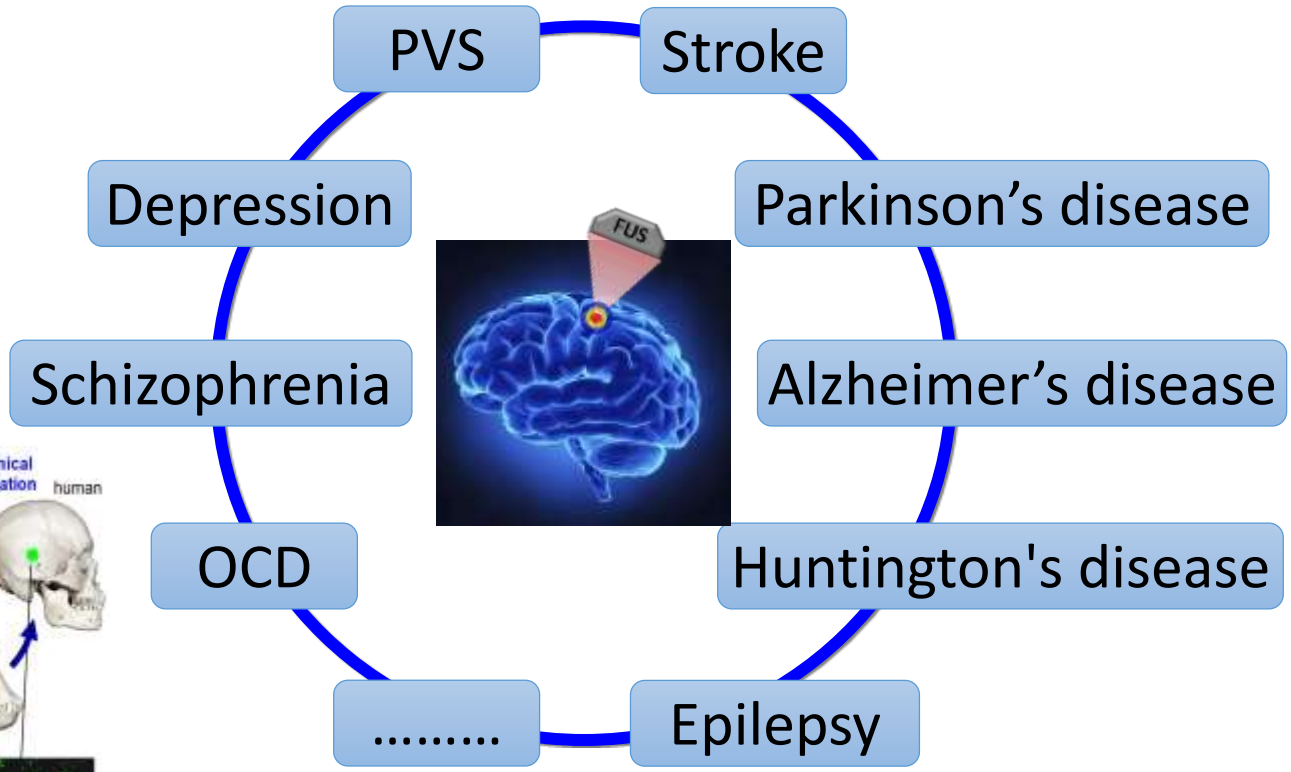
- Material of FUS transducer
  - small size
- Circuit of low-frequency high-power amplifier
  - small size, low power loss
- Nanomaterial coating with drug or gene
  - chronic drug delivery system
  - non-viral gene vectors

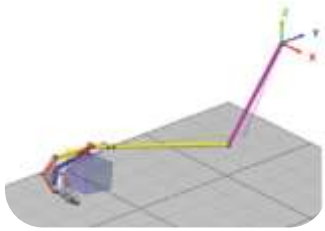
linearly PA

Potential Applications Using FUS technology

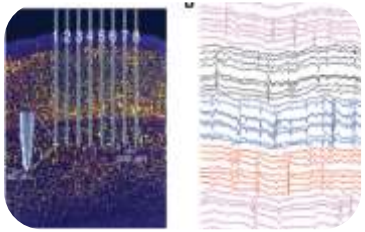
Home care
Rehabilitation
Skill Improvement
Smart Control







Interdisciplinary Research



Computer

Equipment

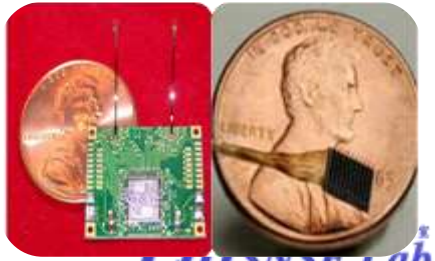
Neuromodulation

Robot Control

Medical Science

BioMEMS Chip

……



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Looking forward to future collaborations…