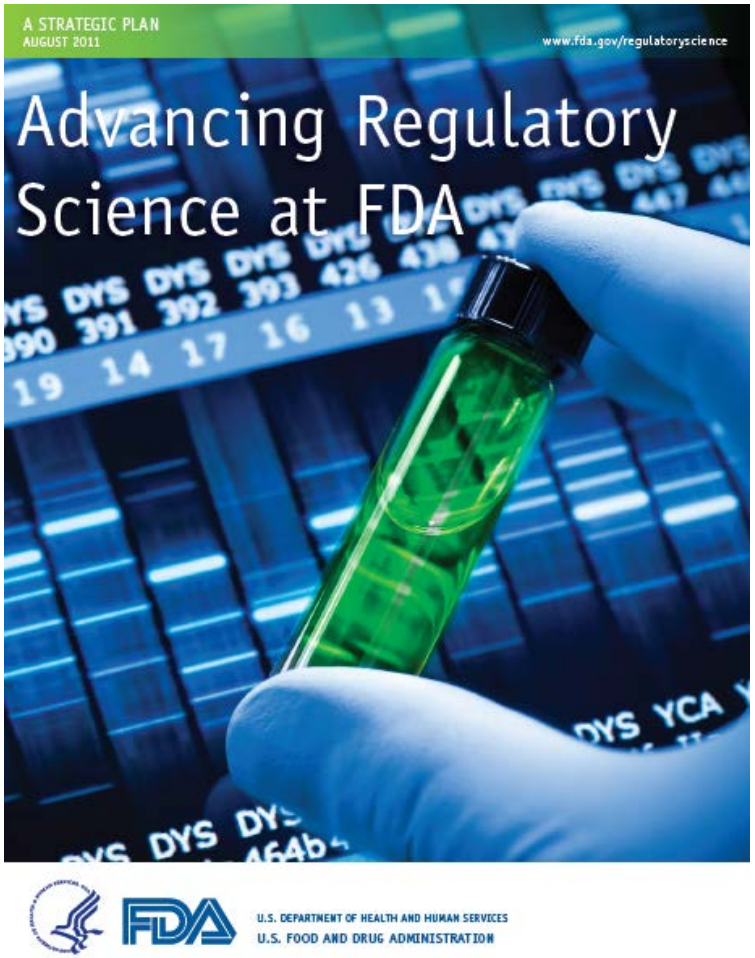
Modeling non-invasive neurostimulation in the human head: Regulatory Science Perspective

Leonardo Angelone, Ph.D.

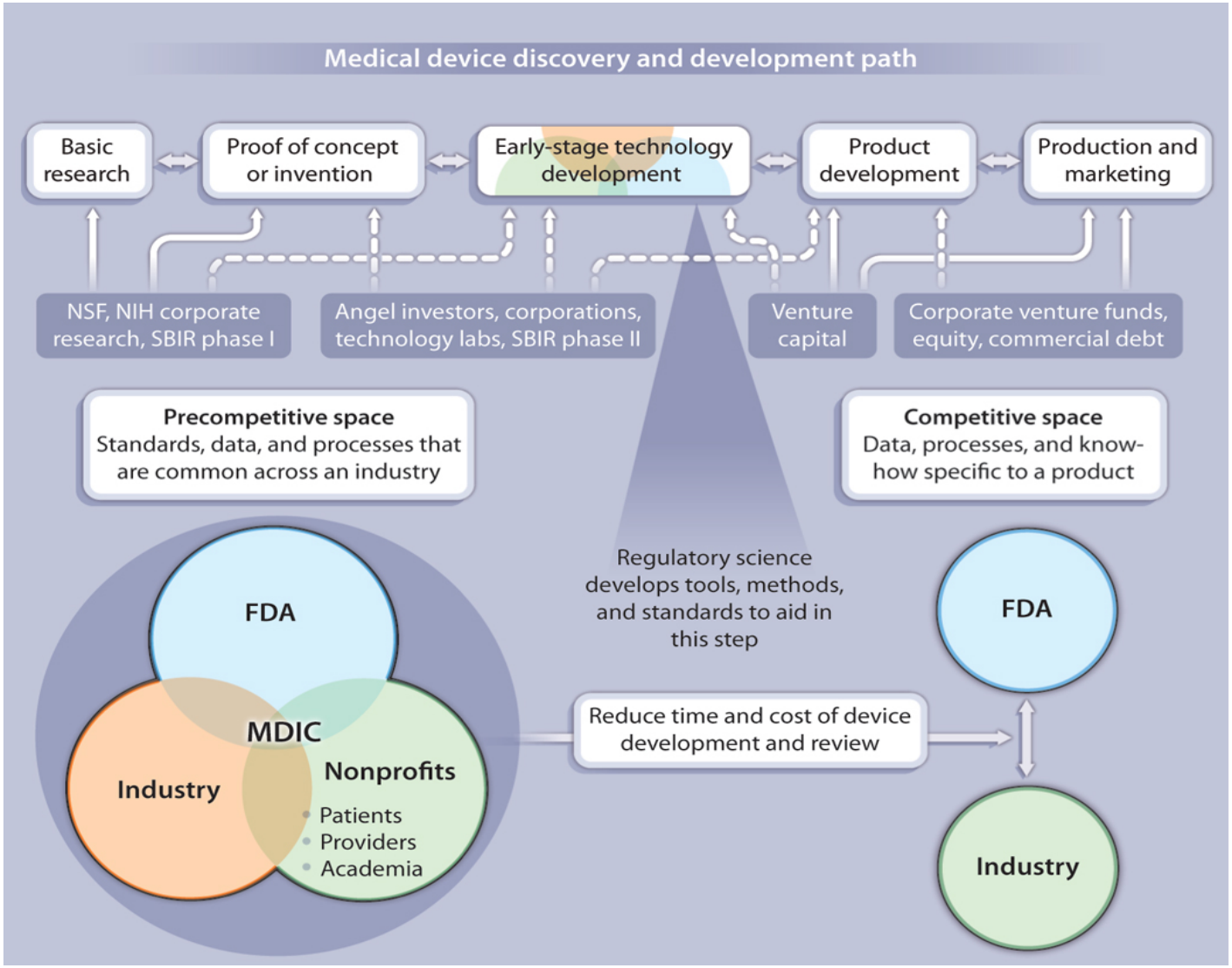
U.S. Food and Drug Administration,
Center for Devices and Radiological Health
Office of Science and Engineering Laboratories
November 20th, 2015

Regulatory Science

- Regulatory Science is the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products.



www.fda.gov/regulatoryscience



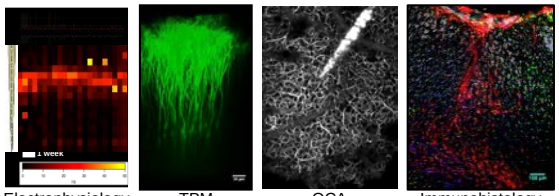
[M. McMurry-Heath and M. A. Hamburg Sci Transl Med 2012]

Regulatory Science in the FDA Division of Biomedical Physics

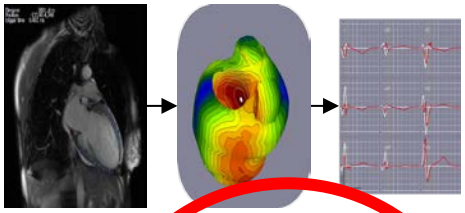
Regulatory science: development of new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA regulated products

Biophysics

Neural implant reliability



Clinical ECG outcome models



Electromagnetics

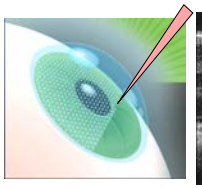
EMC, wireless coexistence

The Virtual Family

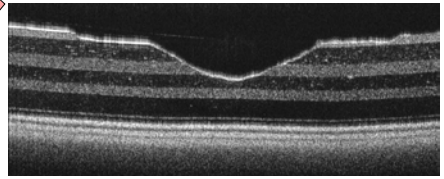
High resolution head model

Optics

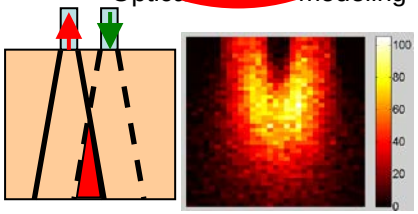
Laser Tx



Retina Phantom

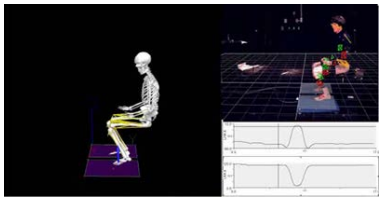


Optical thermal modeling



Functional Performance & Device Use

Functional Models

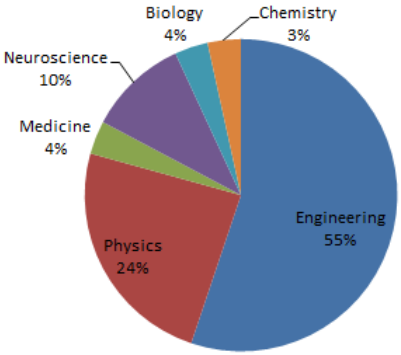


Human Factors

Who we are:

- 30 regulatory scientists
- 60 fellows, students, contractors

Field



Modeling non-invasive neurostimulation

Modeling electric field in the brain

- "Macroscopic" modeling (Organ level)
  - External source (e.g., TMS, tDCS, tACS)
  - Anatomical precision
  - Electrical properties of brain & anisotropy
- "Microscopic" level (Neuronal response)
  - What is the physiological response associated to a given electric field?
- Model Validation
- Regulatory Science: the "MIDA" model

Transcranial DC, then and now

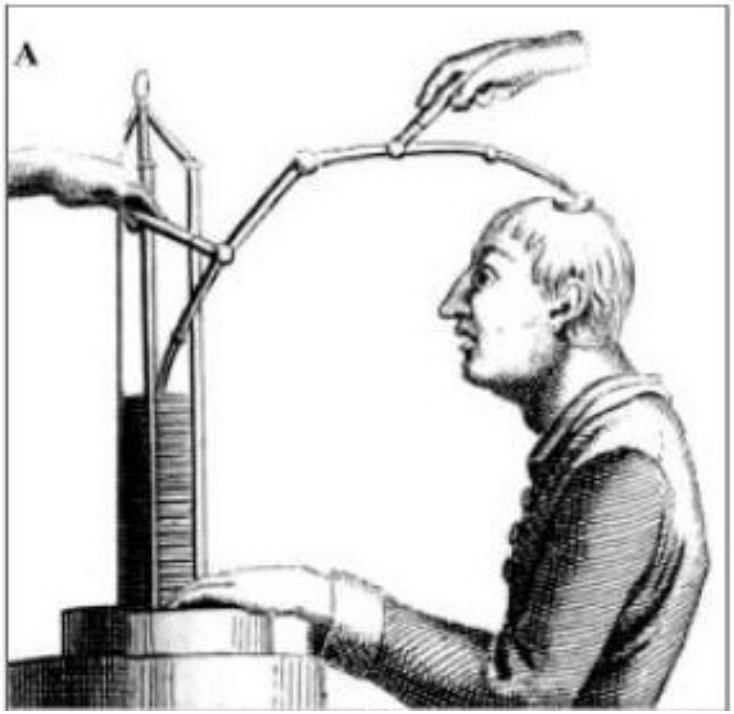
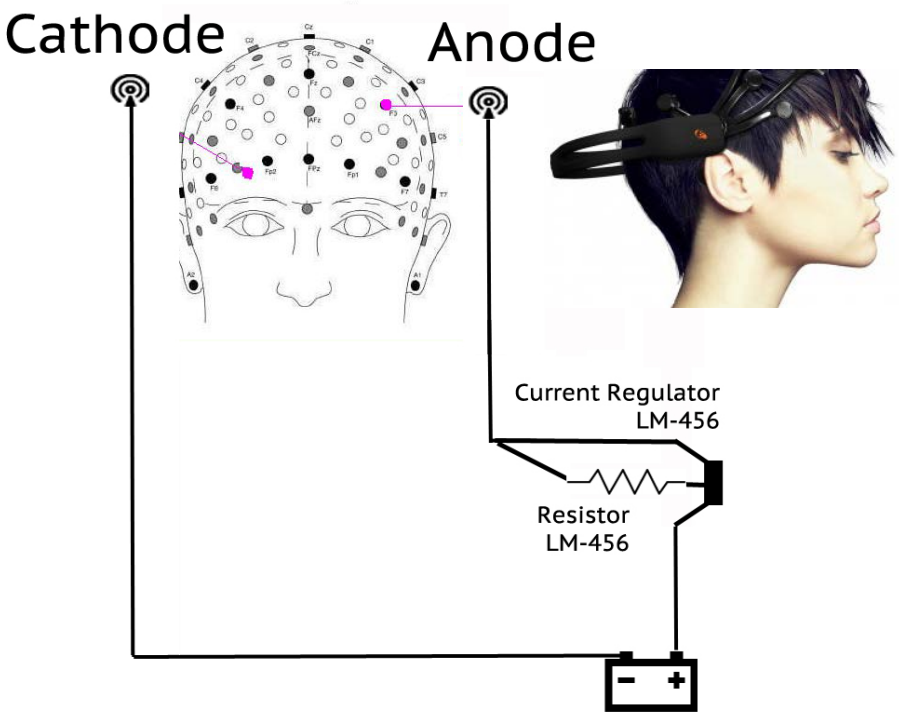


Plate V in Aldini J., Essai théorique et expérimental sur le galvanisme. Paris: Fournier Fils, 1804. Galvanism is being applied on the head of Luigi Lanzarini.

Parent, Can. J. Neurol. Sci. 2004; 31: 576-584

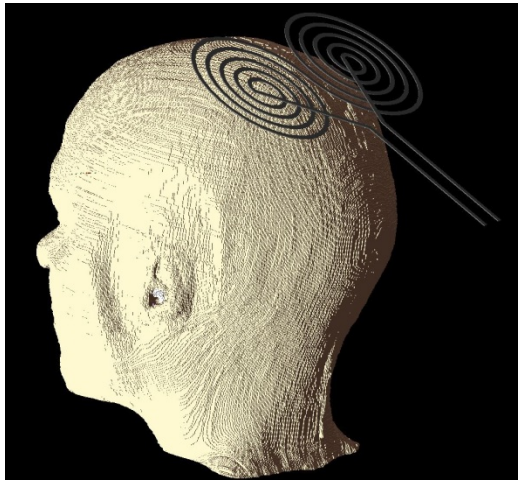


"DIY tDCS brain-boosting kit"

http://www.extremetech.com/extreme/121861-goflow-a-diy-tdcs-brain-boosting-kit

Macroscopic modeling

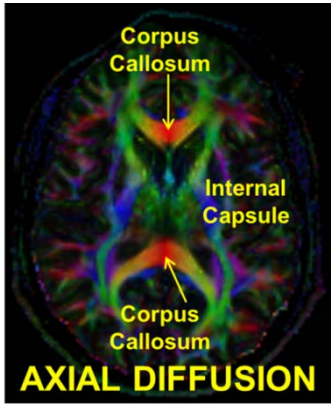
External source (TMS)

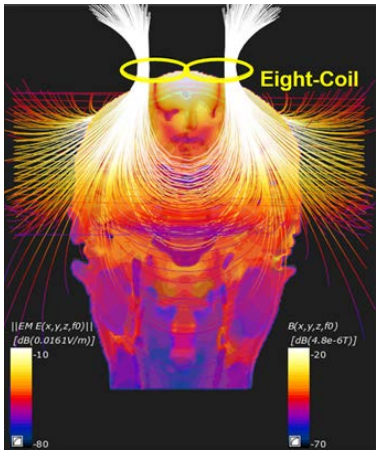


Electrical properties of brain (gray vs. white matter, anisotropy)

Brain GM

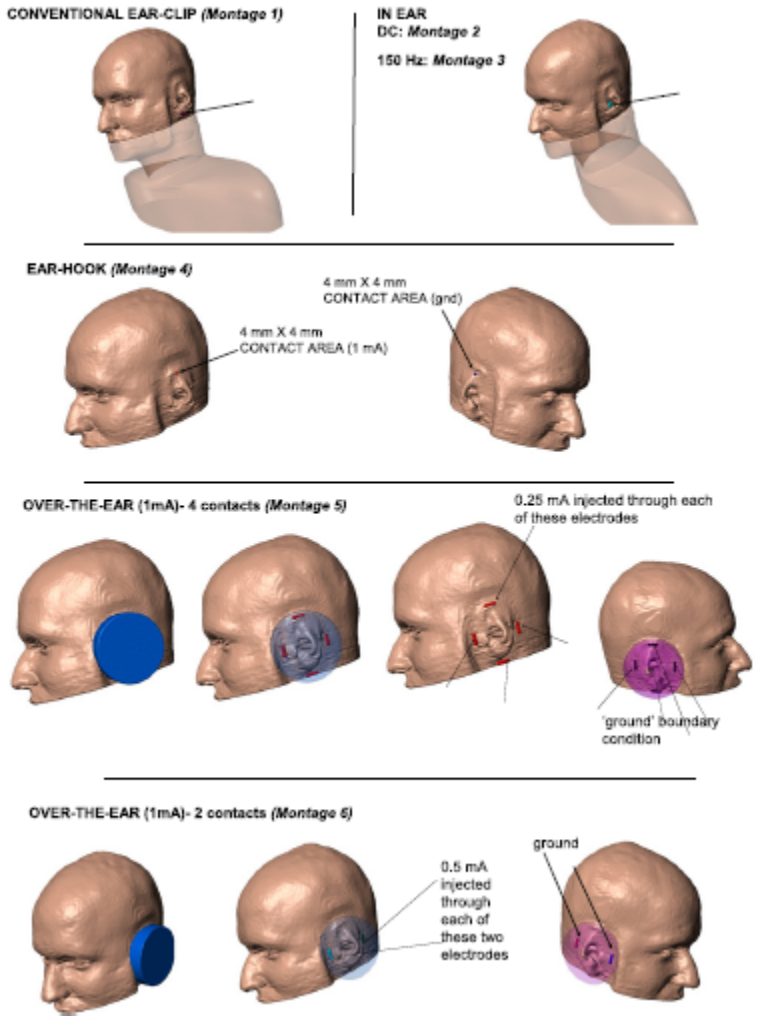
Brain WM

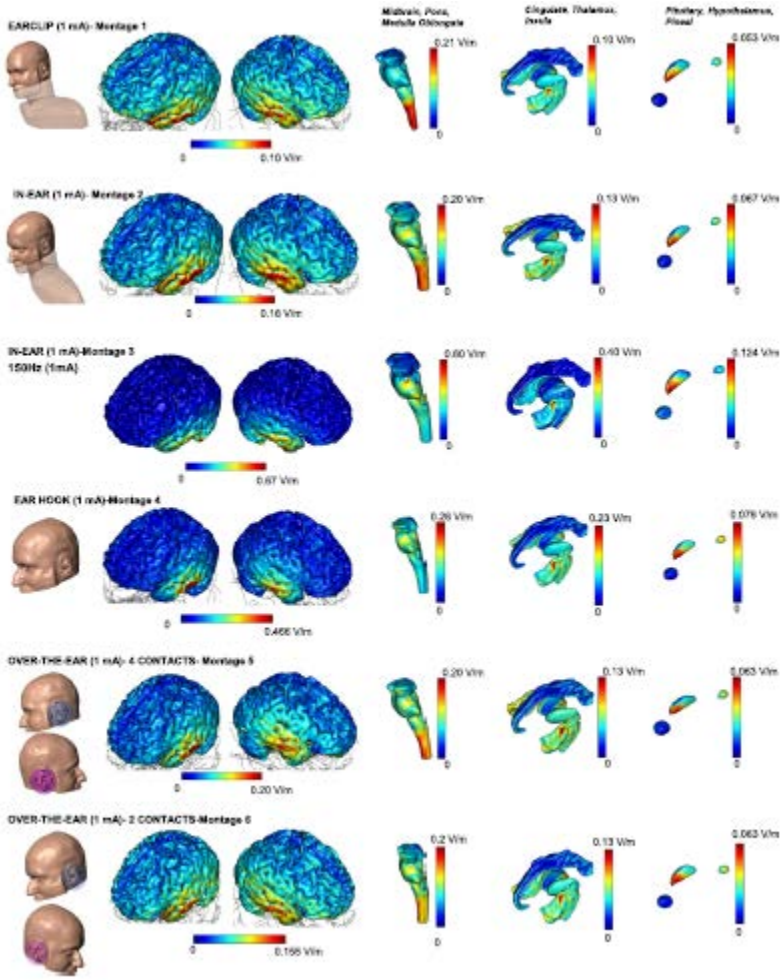




Anatomical precision: where is the electric field?

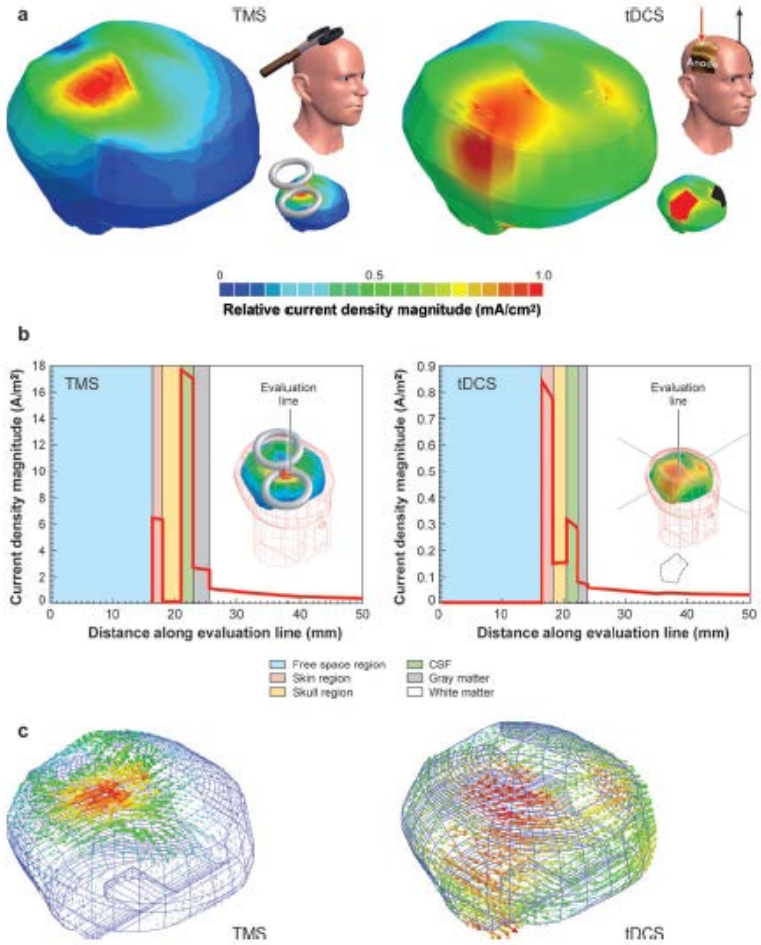
Electric field and source configuration





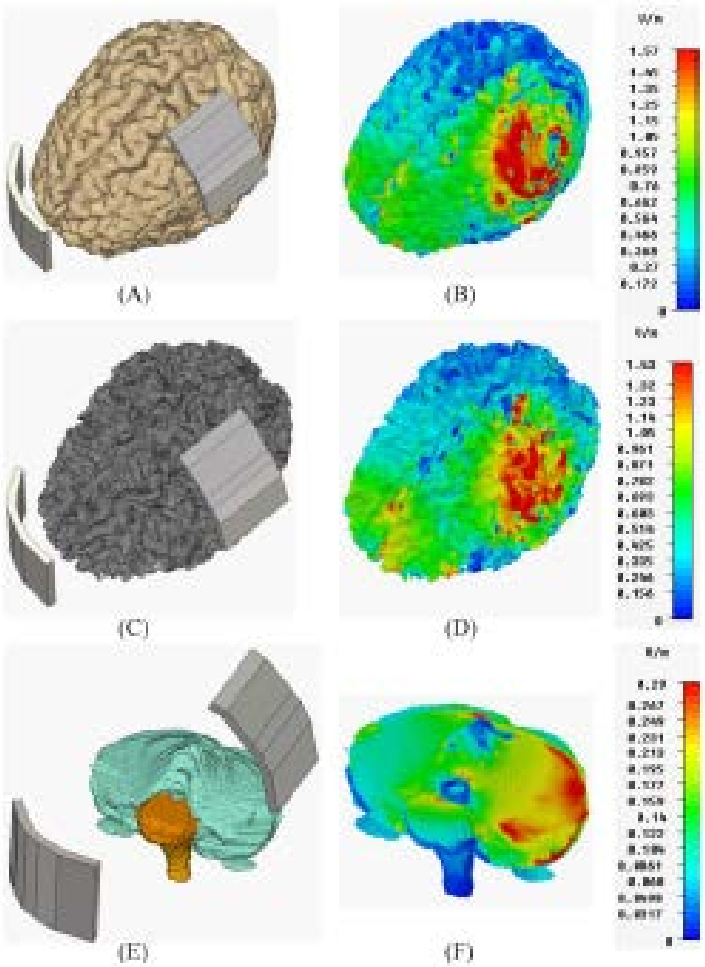
A. Datta et al., NeuroImage 65 (2013) 280–287

Electric field and technology (e.g., TMS vs. tDCS)



Wagner et al., Annu. Rev. Biomed. Eng. 2007. 9:527–65

Computational modeling in support of clinical studies



doi:10.1093/brain/awu343
BRAIN 2015: 138; 428–439 | 428
BRAIN
A JOURNAL OF NEUROLOGY

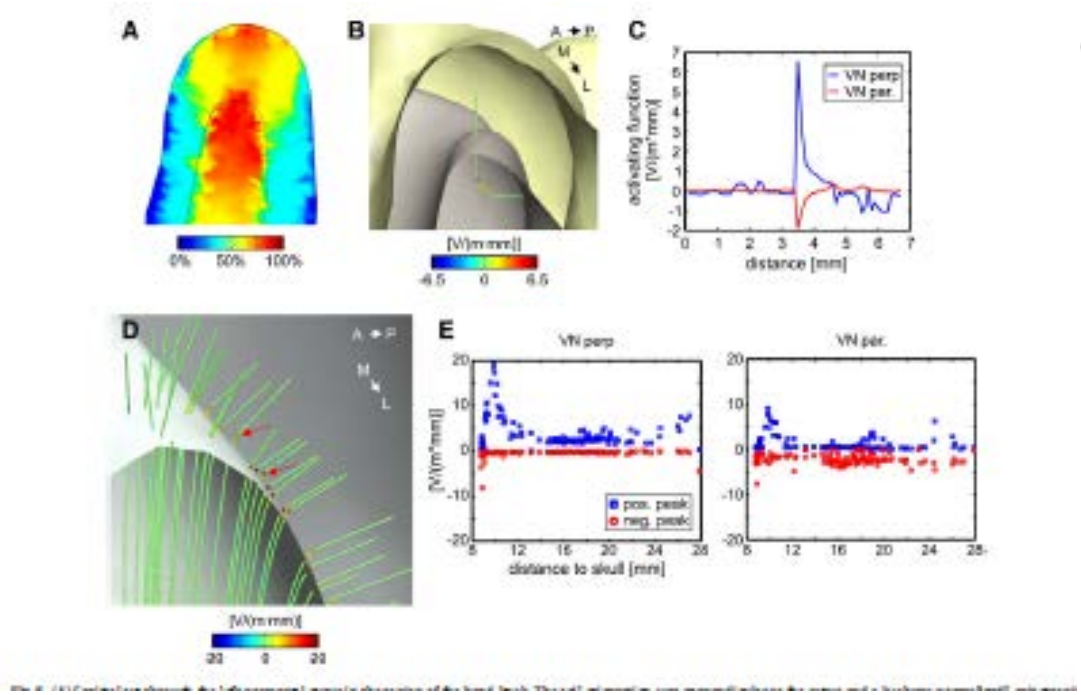
Improving ideomotor limb apraxia by electrical stimulation of the left posterior parietal cortex

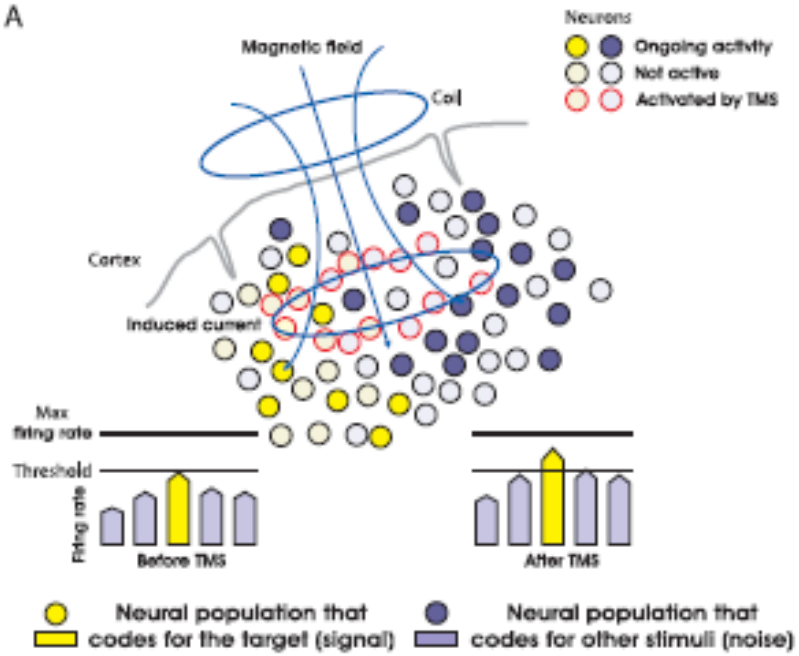
Nadia Bolognini,[1,2] Silvia Convento,[1] Elisabetta Banco,[2,3] Flavia Mattioli,[4] Luigi Tesio[3,5] and Giuseppe Vallar[1,2]

- Clinical and technological "pull & push"
- Modeling can help to understand underlying mechanisms

Parazzini et al., IEEE TransBiomEng 2011

From Macroscopic to Neuronal response

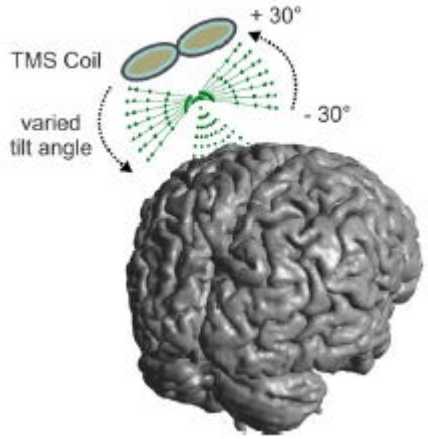


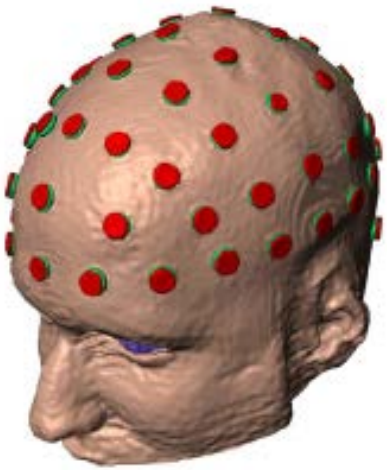


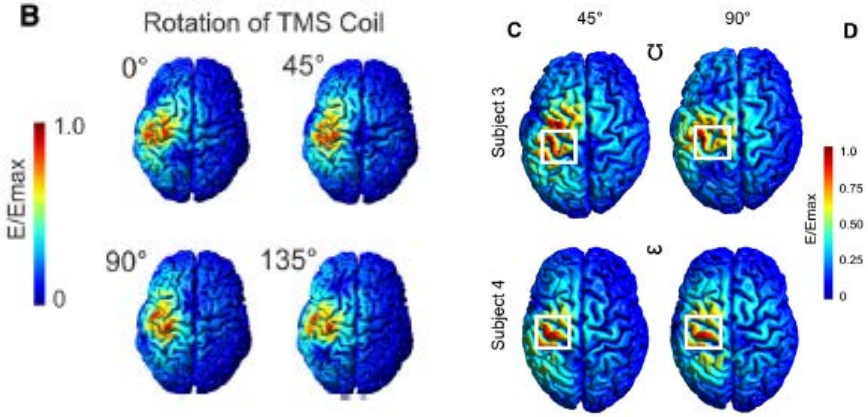
A. Opitz et al., NeuroImage 58 (2011) 849–859

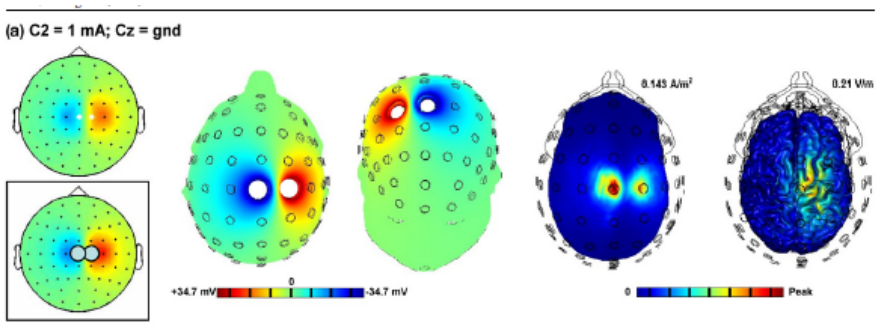
C. Miniussi et al. / Neuroscience and Biobehavioral Reviews 37 (2013) 1702–1712

Model validation





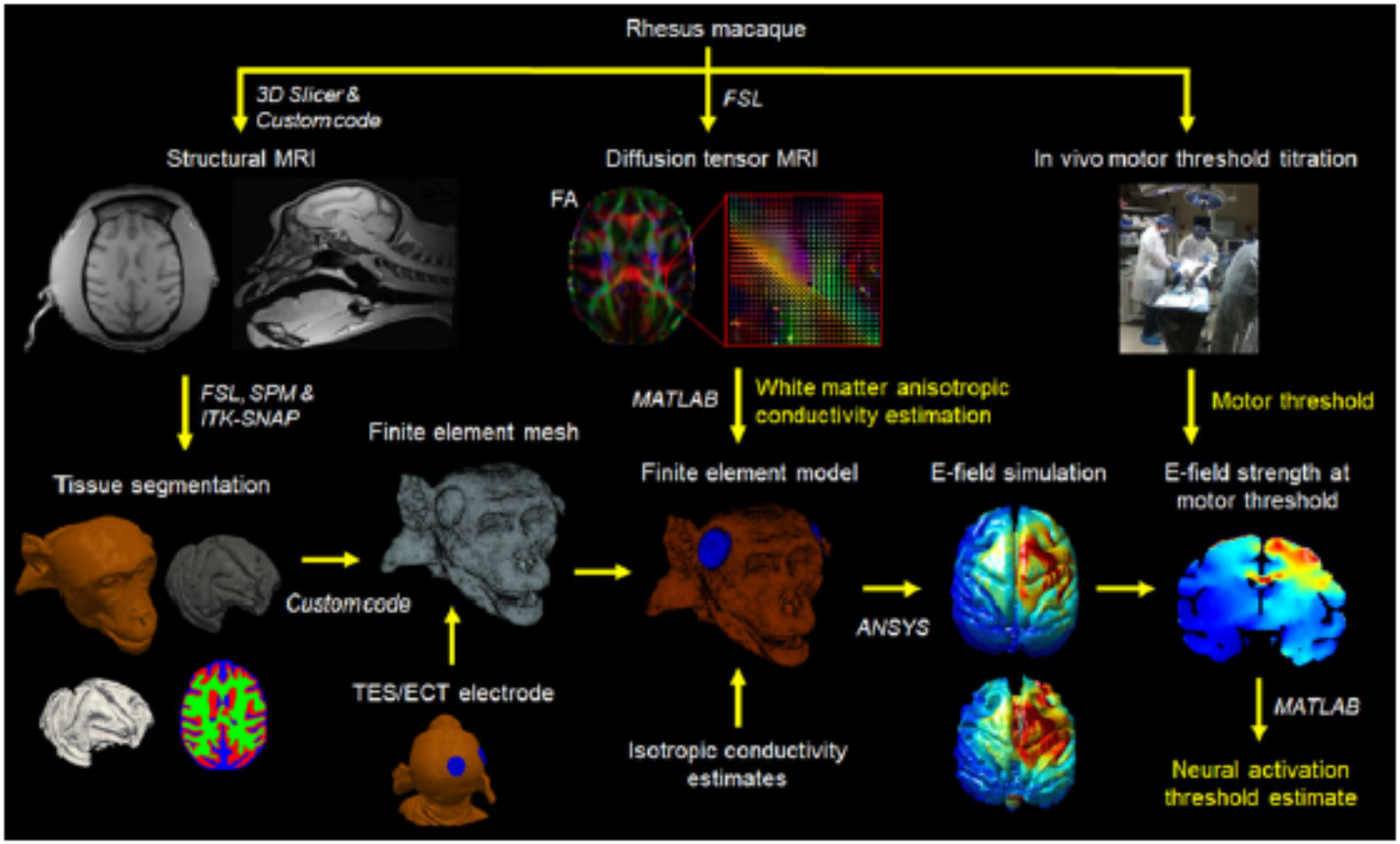




A. Opitz et al. / NeuroImage 81 (2013) 253–264

A. Datta et al. J. Neural Eng. 10 (2013) 036018

Model validation



Hee Lee, IEEE TBME 62 (9) (2015) 2095-2105, 2015

Modeling non-invasive neurostimulation: Regulatory Science Research in the Office of Science and Engineering Laboratories

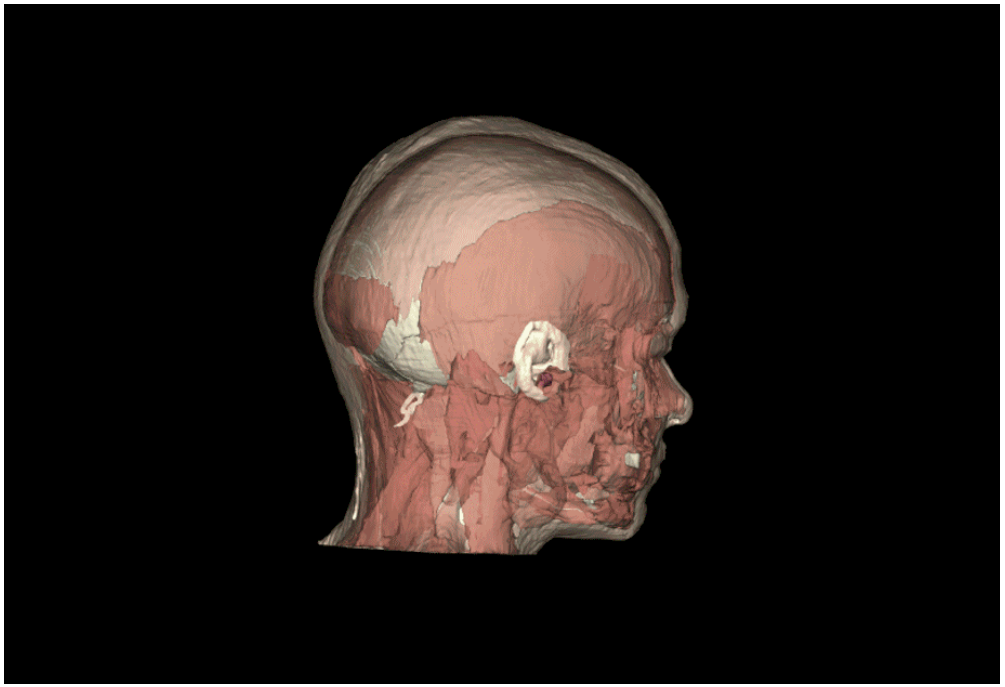
PLOS | ONE

MIDA: A Multimodal Imaging-Based Detailed Anatomical Model of the Human Head and Neck

Maria Ida Iacono, Esra Neufeld, Esther Akinnagbe, Kelsey Bower, Johanna Wolf, Ioannis Vogiatzis Oikonomidis, Deepika Sharma, Bryn Lloyd, Bertram J. Wilm, Michael Wyss, Klaas P. Pruessmann, Andras Jakab, Nikos Makris, Ethan D. Cohen, Niels Kuster, Wolfgang Kainz, Leonardo M. Angelone [view less]

Published: April 22, 2015 • DOI: 10.1371/journal.pone.0124126

Model of human head and neck freely available for the scientific community



FDA Staff:

- Maria Iacono
- Kelsey Bower
- Esther Akinnagbe
- Ethan Cohen
- Wolfgang Kainz (PI)
- Leonardo Angelone (PI)

Collaborators:

- IT'IS Foundation (Zurich)
- Massachusetts General Hospital (Boston, MA)
- University of Vienna
- ETH Zurich (Switzerland)

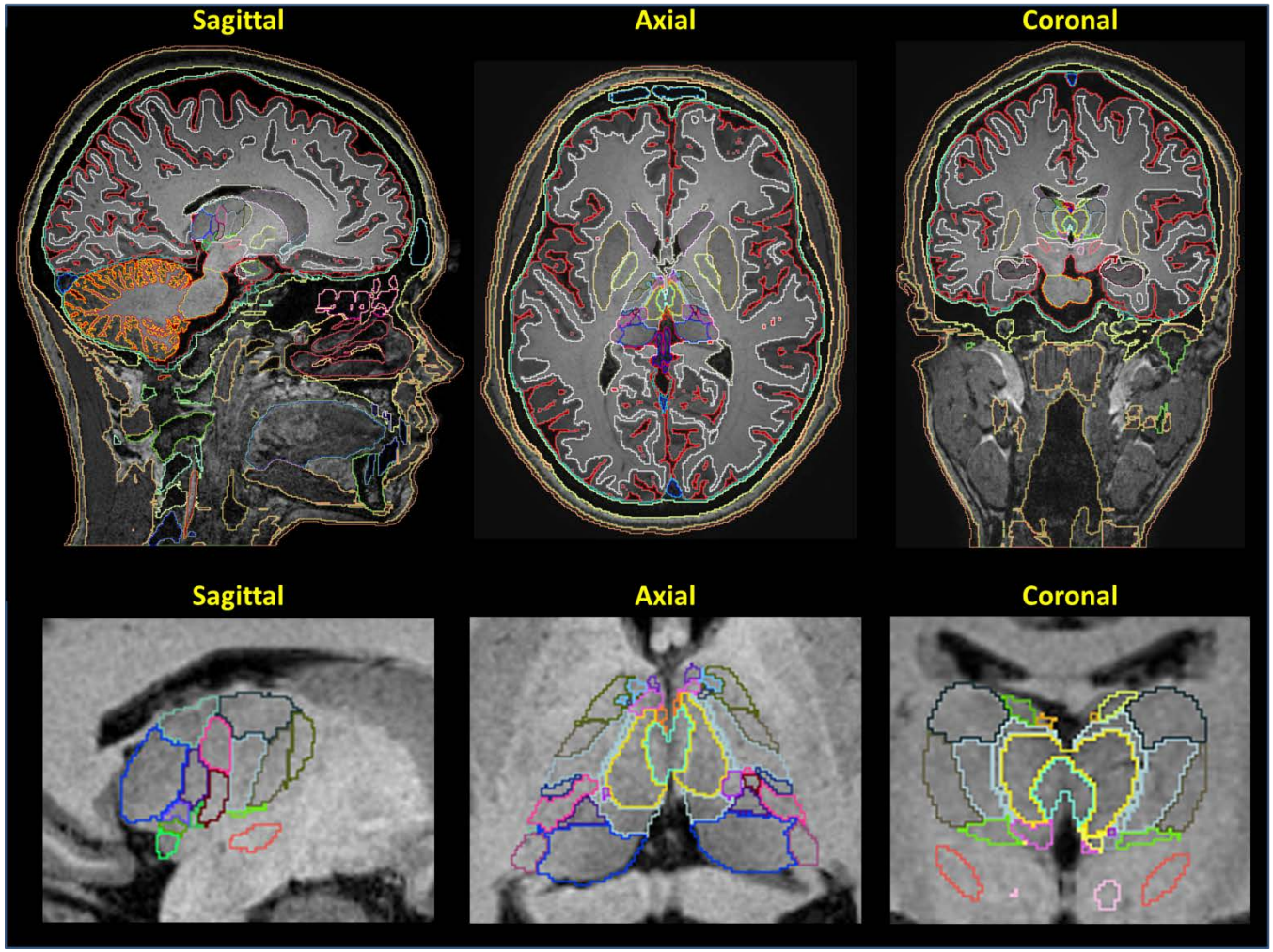
FDA Critical Path Initiative

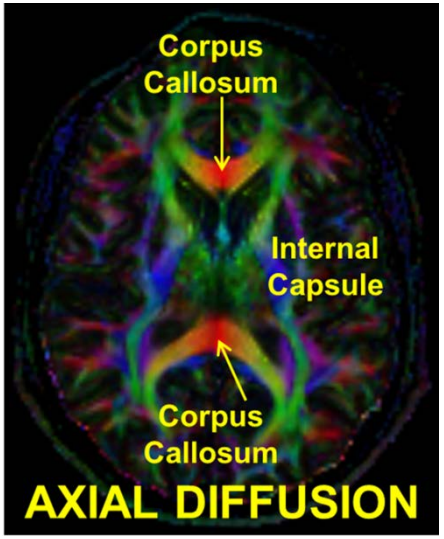
NIH- NIBIB (1R21EB016449-01A1),

ORISE Research Participation Program

CTI (14930.1 PFLS-LS)

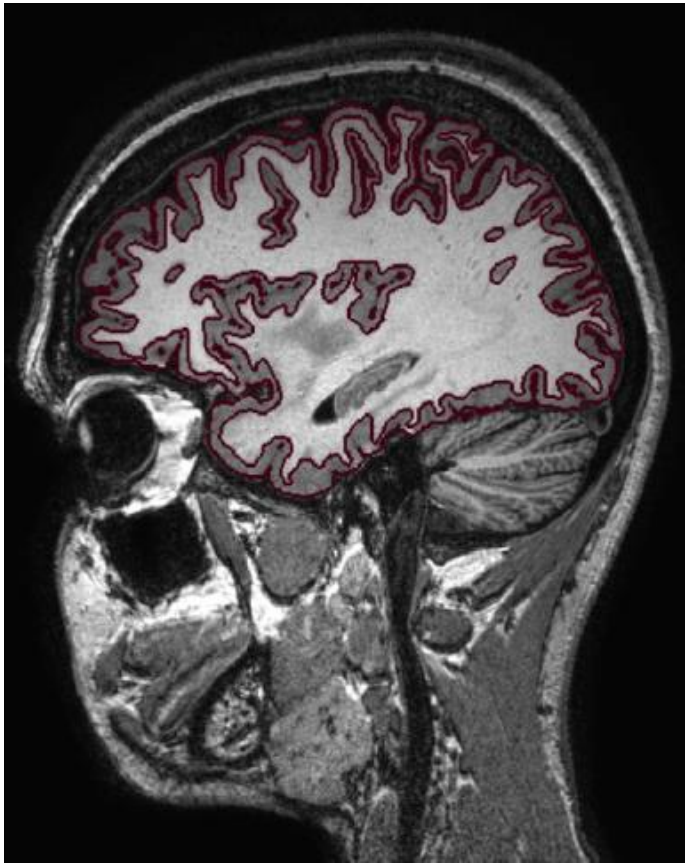
MIDA model – MRI and DTI



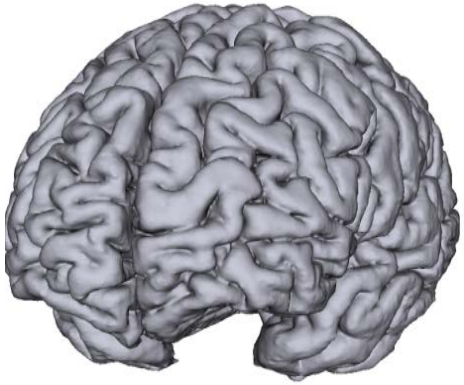


Iacono et al., IEEE EMBS 2014

Gray Matter and White Matter

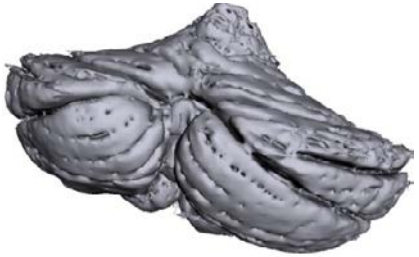


Brain GM

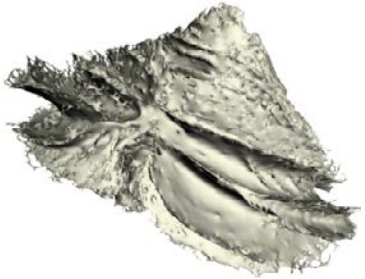


Brain WM

Cerebellar GM



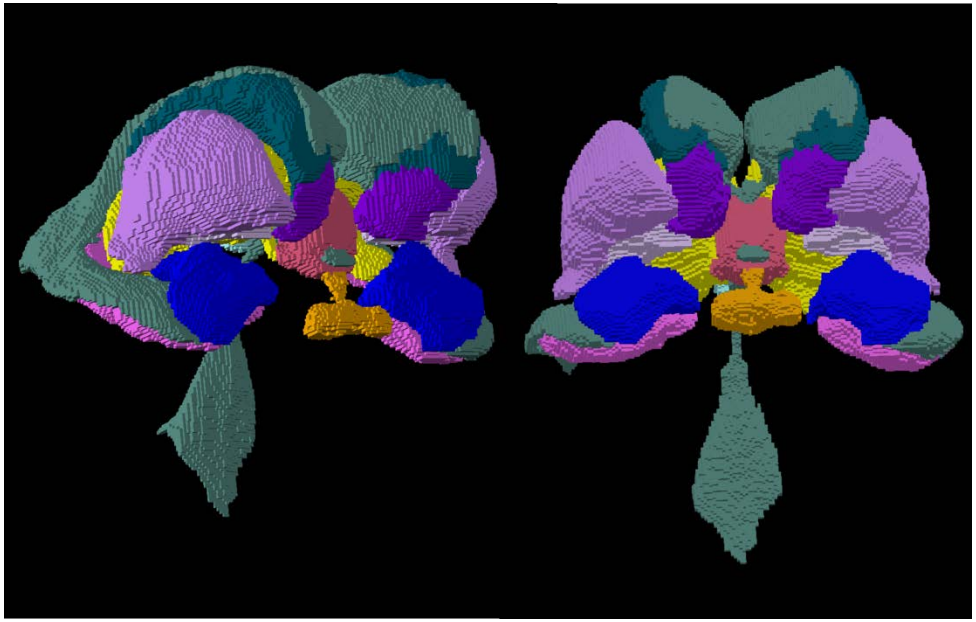
Cerebellar WM



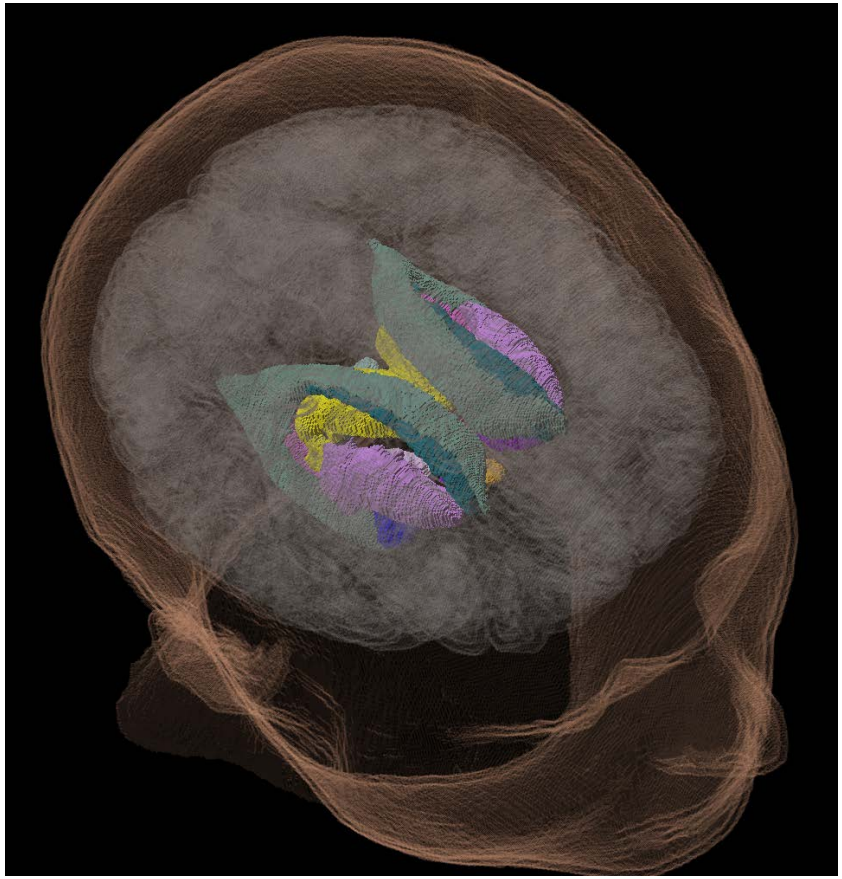
Iacono et al., MIDA Model, PlosOne 2015

Deep Brain

Basal Ganglia, Thalamus, & Limbic System

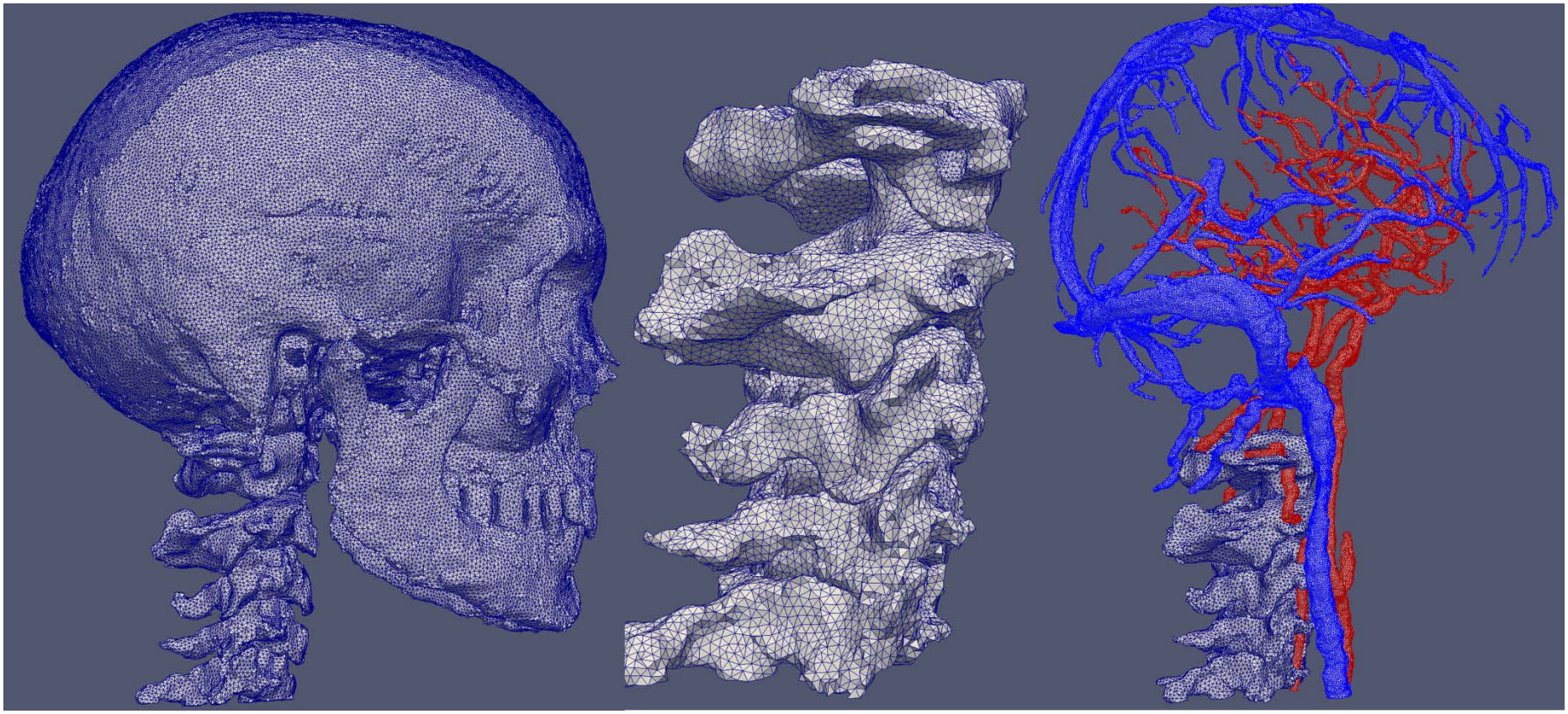


MIDA model



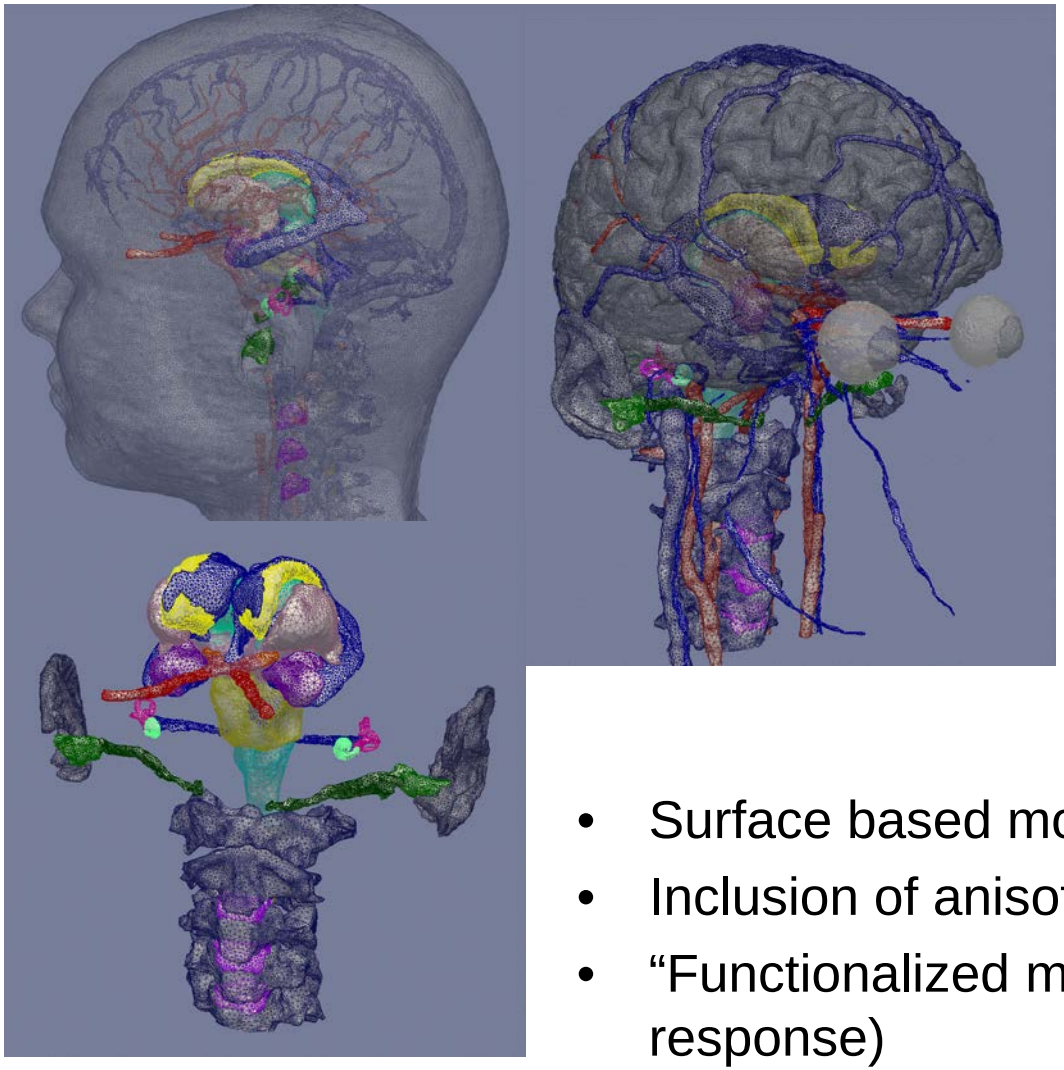
Iacono et al., MIDA Model, PlosOne 2015

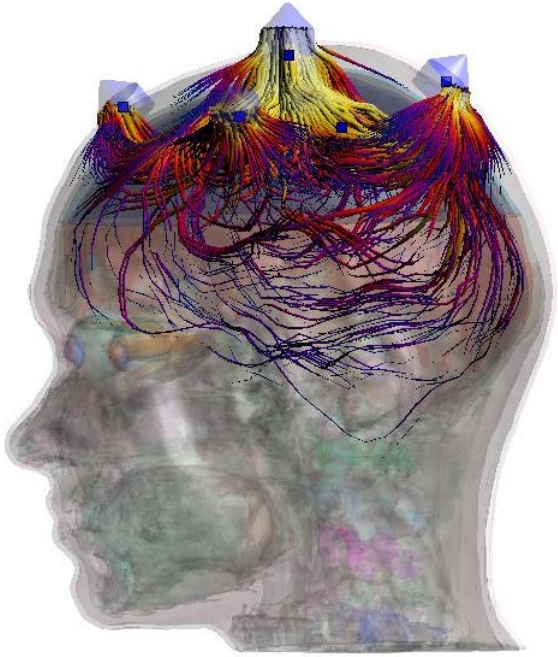
Bones and Vessels



Iacono et al., MIDA Model, PlosOne 2015

Case study – tACS





Neufeld et al., IEEE NER 2015

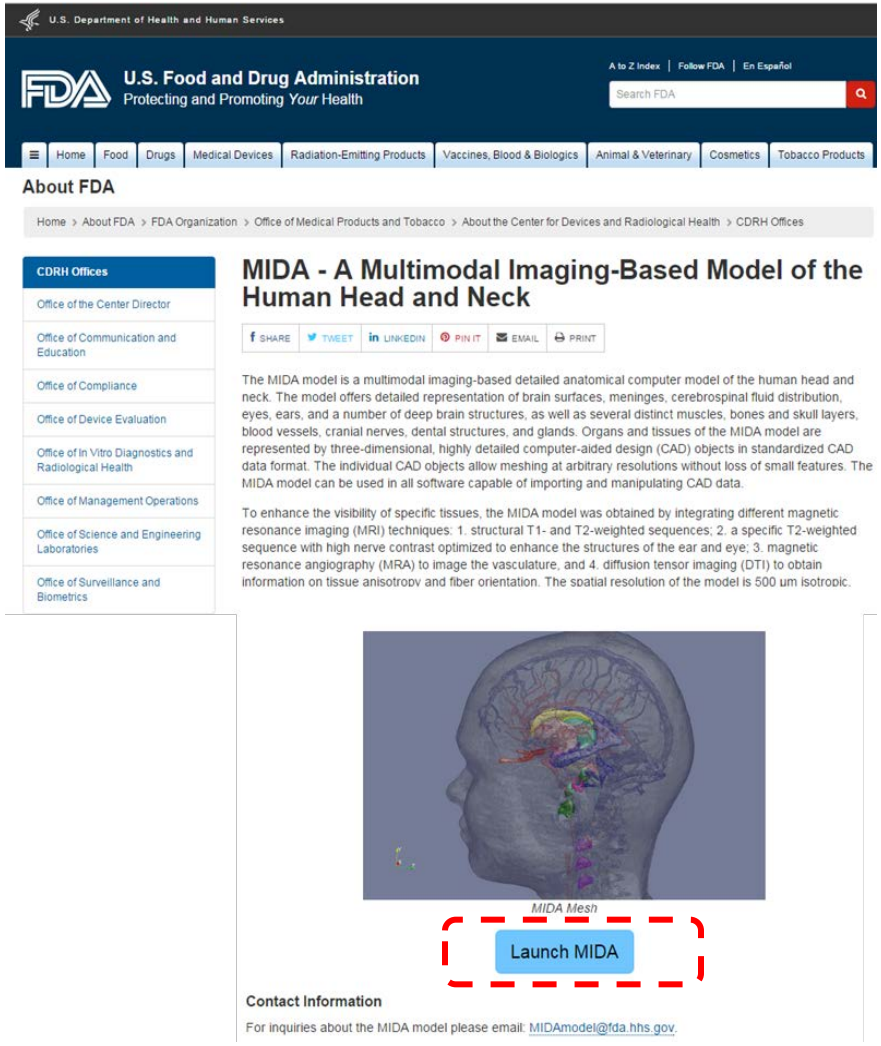
- Surface based models
- Inclusion of anisotropic properties
- “Functionalized model” (Neuronal response)

Iacono et al., MIDA Model, PlosOne 2015

Summary

- "Macroscopic" modeling (Organ level)
  - External source (e.g., TMS, tDCS, tACS)
  - Anatomical precision
  - Electrical properties of brain & anisotropy
- "Microscopic" level (Neuronal response)
  - What is the physiological response associated to a given electric field?
- Model Validation
- Regulatory Science: the "MIDA" model

MIDA Model: released to the public



Apr 22, 2015 (publication date) through Nov 19, 2015:

- PlosOne paper views: 3137
- PlosOne paper downloads: 418
- MIDA model downloads: 44

Thank you!