RUSH Epilepsy Translational Research Initiative:

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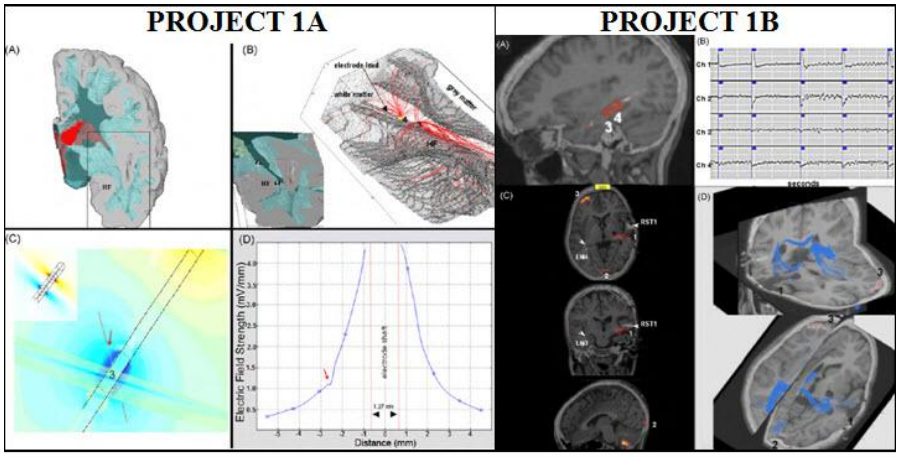
The overall goal of my research plan at RUSH is to establish a *Nanotechnology Translational Research Initiative* in association with the RUSH Epilepsy Center, and UIC Department of Bioengineering. The initiative is technology-based using disease-states, predominantly epilepsy, and primary high-grade central nervous system neoplasms, as problem-based platforms on which to build this technology.

The outcome objective that will benchmark a working infrastructure of such a research initiative is successful development of novel neural control nanotechnology. A patent was recently published by WIPO (see www.electroiq.com/index/display/mems-wire-news/1385462132.html).

Five projects are currently at different levels of development in our lab to further evolve this nanotechnology. The projects are listed as follows:

The objective of Project 1 is to develop a computationally intensive system to visualize the epileptic circuit. Two subprojects are included in Project 1.
Project 1a: A computational workflow will be developed to allow the ability to simulate interfacing intracranial depth electrodes with the pathological neural circuit before implanting investigational responsive direct stimulation technology used to abort a seizure and stabilize the seizure network (Rossi et al, 2010).

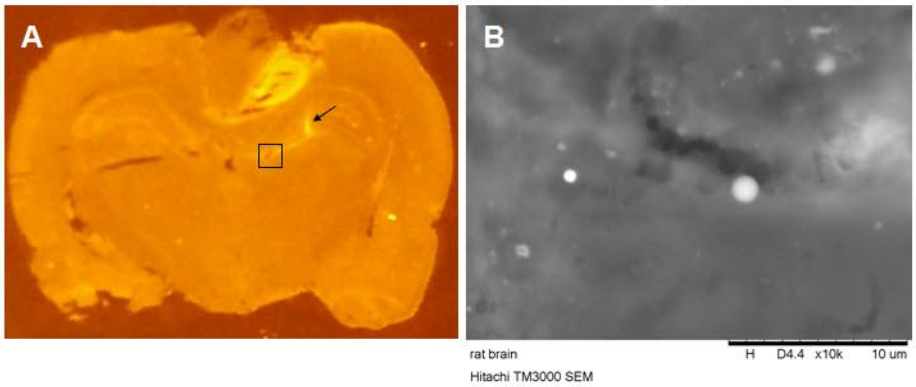
Project 1b: Two novel validation blood flow-related neuroimaging strategies conceived in our laboratory [(1) subtraction activated SPECT (Rossi et al, 2010), and (2) Dynamic SPECT Imaging (RUSH IRB ORA # 10031201)] are performed post-implantation of intracranial leads to validate influencing the predicted neural circuit. A new portable high-resolution SPECT scanner (NeuroLogica, Corp) is being actively developed at Rush for high resolution dynamic SPECT imaging. This technology will be implemented exclusively at RUSH through the development phase.



Reproduced from Rossi et al (2010).

The core aim of Project 2 is to develop a mechanized inhibitory feedback system to augment direct stimulation therapy with on-demand pulsatile direct anti-epileptic drug (AED) delivery. The dual drug delivery recording/stimulating microprobe was developed for us in collaboration with NeuroNexus Technologies (Ann Arbor, MI). Recently presented preliminary data are promising (Mangubat & Rossi, 2010).

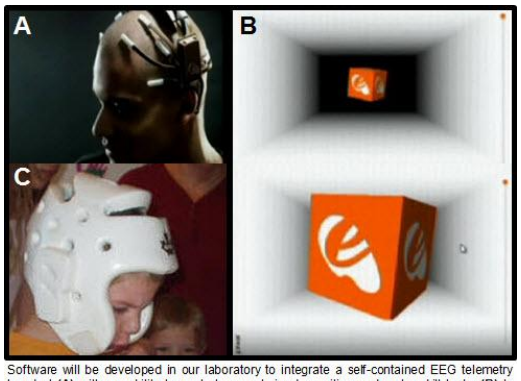
The objective of Project 3 is to develop electric field-guided delivery of AED encapsulated in charged biocompatible nanocarriers. The nanocarrier complexes can target tissue receptors by 'surfing' through brain in an induced electric field. Preliminary preclinical experiments are in progress.



(A) Fluorescein embedded chitosan nanoparticles delivered through fluidic microelectrode into right hippocampal formation at the level of the dentate gyrus (arrow). **(B)** Scanning electron micrograph of chitosan. Magnified field of interest (box) is shown in (A).

Project 4 is a project that crosses disciplines to synthesize biocompatible carbon nanotube-ligand complexes to target high-grade glioma cells. This project will be actively developed over the next 12 months. Preliminary data exist and made possible by the Rush Brain Tumor Philanthropy Fund and in collaboration with the Illinois Institute of Technology located in Chicago.

Project 5 is designed as a workbench for establishing a proof-of-concept to better understand the limitations of a patient with epilepsy to non-invasively interfere with the progression of a seizure. The task is custom-designed to engage brain circuitry shared by the patient's own seizure network to interfere with the progression of the seizure onset. We are developing signal processing algorithms to control a wireless/rechargeable self-contained EEG telemetry helmet.



Software will be developed in our laboratory to integrate a self-contained EEG telemetry headset **(A)** with capability to control computerized cognitive and motor-skill tasks **(B)** to potentially mediate the patient's seizure circuit. This integration will assess the limits of a patient to consciously control the progression of their seizure onset. In addition, the portable hardware platform will be modified to fit into a safety helmet **(C)** to assess and simulate engineering principles that will ultimately engage neural circuits with nano-scale control technology. See project 7 description.

Overall Student Goals: Participation in a 10-week 'project-based' seminar series developed and organized by Dr. Rossi is essential for grasping biophysics and nanotechnology concepts as implemented in our lab. In addition, each student working in the lab will choose a topic to develop over the summer experience. The student will present a weekly progress report. In addition, to accessing critical core resources and personnel available at Rush, collaboration with the UIC Department of Bioengineering, and Argonne National Laboratory will contribute toward completing the summer project. The results will be submitted in abstract form for presentation at a local or national meeting. Of note, each project has detailed tutorials written by the student researchers (as a requirement for working in the lab) to advance work already completed by previous students graduating from the lab.

Mangubat, EZ, **Rossi MA** (2010). On-demand pulsatile delivery of carisbamate concurrent with closed-loop direct neurostimulation therapy in a self-sustained limbic status epilepticus (SSLSE) rat model. **American Epilepsy Society Abstr 3.064.**

Rossi MA, Stebbins G, Murphy C, Greene D, et al (2010). Predicting white matter targets for direct neuro-stimulation therapy. **Epilepsy Res** 91(2-3):176-186.