# Convection-Enhanced Delivery of Macromolecules to the Brain Using Electrokinetic Transport

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## Introduction

Conventional pressure-driven infusion of molecules into the brain has recently shown promise, however it has drawbacks such as lack of control of infusions and damage from neuronal distortion and mass effect. By using electrokinetic transport as the driving force for local delivery of macromolecules to the brain, many of these issues can be circumvented. Herein, this body of work demonstrates proof-of-principal that electrokinetic convection-enhanced delivery is a viable means for delivery of locally high concentrations of macromolecules to the brain.

## Methods

All protocols were approved by the Institutional Animal Care and Use Committee. Rats were anesthetized and infusion and counter cannulas were inserted into the bilateral rat thalamus. Direct electrical currents ranging from 25 to 75 microAmps were utilized to trigger electrokinetic infusions via the cannulas, which is less than that of electroporation or deep brain stimulation. The infusions were conducted for one hour and the rat brains were then rapidly harvested, fixated, and sectioned for imaging analysis using fluorescence microscopy. A series of molecules of varying charge and size were analyzed.

## Results

Robust infusion profiles were observed for small, positively charged molecules; however, larger molecules also were delivered to brain tissue. Electrokinetic transport occured along current paths in vitro and in vivo, which often coincided with white matter tracts. Infusions may also be conducted along a tissue surface via a doped hydrogel with applied current. No appreciable cell death from the electrical current was observed in any of our experiments. Based upon our observations, a theoretical framework model was developed to predict the infusion profile.

## Conclusions

Electrokinetic convection-enhanced delivery is a new methodology that may be used to reproducibly deliver macromolecules to the brain. Understanding the electrical current path and properties of brain tissue imparts the ability to predict infusion profiles. This work provides an exciting adjunct to convection-enhanced delivery using pressure.

## Learning Objectives

By the conclusion of this session, participants should be able to: 1) describe the importance of convection-enhanced delivery (CED) in functional neurosurgery, 2) describe the limitations of current CED techniques, 3) understand basic principles of electrokinetic transport, 4) understand how electrokinetic transport may service to address key limitations or traditional CED.

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