Significance. Targeted delivery of therapeutics to diseased sites within the brain is critical in order to effectively treat neurodegenerative diseases and brain cancers. Two of these diseases, Alzheimer’s and Parkinson’s, collectively affect approximately 40 million people worldwide with an annual cost exceeding $375 billion [ADI, 2010 and NPF, 2010]. Insufficient drug targeting can lead to disease progression, tumor metastasis and systemic toxicity.

Need. The increasing prevalence of neurodegenerative diseases and brain cancer, along with the continued difficulty in targeting diseased sites with therapeutics, heightens the importance of developing improved targeted drug delivery methods within the central nervous system (CNS). Due to the anisotropic properties of brain tissue, drug distribution is difficult to control. Magnetic guidance of therapeutically functionalized nanoparticles offers a potential means of controlling the drug distribution.

Objective. The main goal of this research is to determine if and how magnetic nanoparticles can be magnetically driven through the brain and CNS in order to increase the targeting efficacy and volume distribution of therapeutics.

Proposed Research. In order to achieve our overall objective, the following will be done:

1) In vitro and in vivo experiments which use an external magnetic field to guide magnetic nanoparticles (shown in Fig. 1) to a specific site within brain tissue phantoms and rat brain tissue.
2) Computational modeling and analysis of the in vitro and in vivo experiments.
3) Development of improved therapeutic nanoparticle delivery techniques utilizing the knowledge gained from the experiments and computational models.

Deliverables. Through the use of in vitro and in vivo experiments along with computational analysis, we will acquire new insight into particle physics within the brain. The knowledge we gain from our proposed research will ultimately lead to improved treatment options for people suffering from neurological disorders, and will aid in elucidating some of the mysterious properties of the human brain.
**Governing Equations used in the Computational Models.** The flow of the fluid carrying the nanoparticles is assumed to be laminar and incompressible with a dilute amount of nanoparticles present in the fluid. The continuity and momentum equations, Eq. (1) and Eq. (2) respectively, are shown below for the infusate.

\[ \nabla \cdot \vec{u} = 0 \]
\[ \frac{\partial \vec{u}}{\partial t} + \vec{u} \cdot \nabla \vec{u} = -\frac{1}{\rho} \nabla p + \nabla \cdot \left[ \nu \nabla \vec{u} \right] \]

Where, \( \rho \) is the density, \( \vec{u} \) is the velocity vector and \( \nu \) is the kinetic viscosity. The mass conservation equation for nanoparticle transport, shown in Eq. (3), can be written as,

\[ \frac{\partial C}{\partial t} + \nabla \cdot (\vec{u}C) = \nabla \cdot (D _p \nabla C) - \nabla \cdot (\vec{u} _p C) \]

Where, \( C \) is the nanoparticle concentration, \( D _p \) is the particle diffusivity and \( \vec{u} _p \) is the nanoparticle drift velocity due to external forces such as magnetic, gravitational and drag forces. The last term in Eq. (3) represents the nanoparticle drift flux which is caused by effects other than convection. The drift velocity of the nanoparticles can be found using a force balance on the nanoparticles as shown in Eq. (4).

\[ \frac{d\vec{u} _p}{dt} = \sum \vec{F} \]

The magnetic force exerted by an induced magnetic field, \( \vec{B} \), and drag force on a magnetic nanoparticle can be calculated using Equations (5) and (6), respectively, as,

\[ \vec{F} _p = V _p (\chi _p - \chi _\text{media}) (\vec{B} \cdot \nabla) \vec{B} \]
\[ \vec{F} _\text{drag} = (6 \pi \mu r _p ) (\vec{u} _p - \vec{u}) \]

Where, \( V _p \) and \( r _p \) are the average volume and radius of the nanoparticle, respectively. \( \chi _p \) is the volume susceptibility of the magnetic particle, \( \chi _\text{media} \) is the volume susceptibility of the surrounding medium, \( \mu \) is the viscosity of the fluid and \( \mu _0 \) is the permeability of the free space.

The fluid phase is treated as a continuum by solving the time average Navier-Stokes equations while the dispersed phase is solved using the species transport equation including the additional drift fluxes caused by external forces.

**References**
