Solution Multiplicity of Inversion Problems in Distributed Systems
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Summary
The treatment of certain diseases of the central nervous system (Alzheimer, Huntington disease, etc) require the insertion of therapeutic drug molecules directly into the porous tissue of target areas deep in the brain. The design of invasive drug delivery therapies [Nicholson, 1985] constitutes a challenging transport problem with complex metabolic drug-neural interaction. The efficiency of the treatments depends strongly on the drugs’ molecular properties and its metabolic uptake into the brain tissue. However, it is very difficult to experimentally measure transport and metabolic reaction properties of large drug molecules in the brain tissue with high accuracy. The discovery of those transport and metabolic properties constitutes large-scale transport and kinetic inversion problems (TKIP). However, the complexity of the underlying transport mechanism and the measurement noise in the advanced imaging data through magnetic resonance imaging (MRI), computer tomography (CT) or ultrasound render challenges for finding multiple solutions to this inversion problem. This presentation proposes to identify all the possible solutions to the inversion problem from the advanced imaging data.

Methodology
We will propose to use sequential niche techniques based on genetic algorithms [Beasley et al, 1993, Zhang et al, 2006] and global terrain methods [Lucia and Feng, 2002] to quantify unknown diffusion and convection phenomena as well as metabolic reaction rates of drug molecules from clinically observed two-dimensional drug distributions within the highly specialized and segmented treatment targets in the brain. This approach involves obtaining all the solutions to the inversion of large-scale transport and kinetic inversion problems (TKIP) in generalized curvilinear coordinates and unstructured computational grids. The global terrain methodology is based on intelligent movement along the valleys and ridges of an appropriate objective function using downhill, local minimization calculations defined in terms of a trust region method and uphill integration of the Newton-like vector field combined with intermittent SQP corrector steps. The sequential niche technique is a modified genetic algorithm that uses the concept of fitness sharing to avoid re-searching regions in the parameter space that are already explored. This dramatically increases the likelihood of discovering a new solution at each iteration. Thus, we are able to identify all possible solutions for the TKIP in human brain.
Significance

The proposed methodology advances mathematical programming techniques to solve large-scale transport and kinetic inversion problems of distributed systems in complex multi-dimensional geometry of the human brain. It investigates the possibility of multiple solutions to the TKIP and devises a method to find out all the physically relevant solutions. The approach infers apparent directional diffusion, convection and metabolic reaction phenomena of drug distribution in the human brain from highly accurate imaging data obtained by MRI, CT and ultrasound. The goal of this research is to systematically design invasive devices (e.g. catheters, osmotic pumps, etc) for effective drug delivery of large molecules into the central nervous system. The solution of simultaneous transport and kinetic inversion problem for optimal drug distribution in the human brain using sequential niche techniques and global terrain methods is a first to the best of our knowledge.

References:


