Discovery of Transport and Reaction Properties by Problem Inversion

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Summary:
Invasive drug delivery overcomes the blood brain barrier (BBB) [Nicholson, 1985] by directly inserting therapeutic drug molecules into the porous tissue of target areas of the brain. Thus, the design of the drug therapy constitutes a challenging transport problem with kinetic drug-cell metabolic reaction. The efficiency of the treatments depends strongly on the drugs properties (e.g. diffusivity and reaction constant) and its metabolic interaction with the brain tissue. Until now, it is very difficult to obtain accurately transport and metabolic reaction properties for large drug molecules injected into the porous brain matter. This presentation proposes rigorous mathematical approach to extract crucial physical and chemical properties from advanced imaging data quantifying drug concentration in three dimensional high specialized and segmental brain treatment targets. We will demonstrate a novel computational approach to infer the unknown diffusivity and metabolic uptake of the drug from clinically concentration measurement. We solve a large scale transport and kinetic inversion problem (*TKIP*) using a trust region method implemented with sparse matrix technique (i.e. GMRES). The papers will discuss how to overcome a diverse array of technological challenges on image processing, quantification of component concentration and computational fluid mechanics needed to tackle transport and kinetic inversion problems. One strong point of the novel approach is its ability to determine the most consistent transport mechanism among competing approaches based on the clinical data. Those optimal properties will allow doctors to develop and improve those therapeutic approaches e.g. the penetration depth and penetration location of catheters, initial concentration of drug and injection policies.

Scope:
This presentation will propose a mathematical methodology called trust region method [Biegler, et al., 1997; Conn, et al., 2000; Dennis and Schnabel, 1996] to solve this large scale optimization problem resulting from *TKIP*. While this algorithm has successfully been used for the lumped system, *TKIP* for distributed system is still new. We deploy the first and second order sensitivity map of transport properties to improve convergence and robustness of the proposed algorithm. The generalized curvilinear transformation will help us to solve the transport problem in complex geometries (i.e. human brain) with complicated directional properties (i.e. anisotropy in white matter and isotropy in grey matter). The advanced devices in medical area (e.g. MRI) provide us a way to measure the drug concentration in three dimensional human brain. Once we get the data, we are

capable of obtaining those sophisticated directional diffusivities and metabolic reaction constants of drug by solving *TKIP* in the distributed system. This distributed system will be implemented by discretizing the transport equations to a set of linear or nonlinear equations with help of the finite volume approach [Patankar, 1980] in the generalized curvilinear coordinate. In the discussions, we will demonstrate proposed methodology to extract the optimal transport and reaction properties from clinical data in the following cases: (i) a steady state diffusion-convection with different boundaries, (ii) a steady state diffusion-convection with reaction along different boundaries, (iii) a dynamic state diffusion convection with different boundaries, and (iv) a dynamic state diffusion-convection with reaction along different boundaries. Comparison of different cases can provide a quantitative measure for the important degree of different properties of drug in human brain.

Significance:

The proposed methodology applies advanced optimization techniques to solve the transport kinetic inversion problem of distributed system with complex inhomogeneous geometry. Optimal diffusivity of drug in the human brain and reaction constant of drug will be obtained by this methodology. With the help of those accurate properties, therapeutic equipment (e.g. catheters) used to inject the drug into the brain can be improved with no extra painful experiments. The proposed optimization algorithm is capable to solve a large scale problem very effectively with the help of sparse matrix techniques which was developed in the Laboratory for Product and Process Design at the University of Illinois at Chicago. The kinetic inversion problem in the transport distribution system for human brain has not been reported so far.

References:

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