

IMPROVING THE SENSITIVITY OF TRACTOGRAPHY USING MICROSTRUCTURE MODELING AND PSEUDO-INVERSION

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Abstract. Tractography is a method to map white matter bundles within brain tissue based on diffusion MRI techniques. It seems to be a promising way of detecting white matter structure in vivo, however, method seems to be prone to false positives if standard methods of tractography are used. The paper promises to explore the possibilities of optimization techniques which would enable to include more informative models to the tractography procedure by filtering out false positives from a set of candidate tracts. To detect anatomically plausible tracts, inverse problem from matrix equation $y = Ax$ is solved with help of pseudo-inversion technique. However, pseudo-inversion seems to be inappropriate for system of such dimensions and conditioning.

Keywords: tractography, MRI, diffusion, optimization, pseudo-inversion, inverse problem

Mathematics subject classification: 49M04

1 Introduction

Tractography is a MRI based procedure which aims to map the structure of brain white matter in vivo. White matter is a special kind of neuronal tissue formed by axons, longitudinal cells which tend to cluster into bundles. Since the water diffusion within white matter follows tissue structure, and since it is possible to detect the directionality of diffusive motion by diffusion MRI techniques, we can derive structural information about tissue architecture from MRI data. Such assumption works well for white matter bundles with single population of parallel axons within voxel. However, experiments shown that voxels with strictly homogeneous fiber population are rather rare than in majority [1].

Modeling of the diffusive motion within white matter tissue is a process of per-voxel prediction of the diffusion signal by fitting some tissue model. The underlying architecture of the white matter can be surprisingly complex (multiple fiber populations within voxel etc.). If the more complex tissue model is applied, the more trustworthy the fit may be, however computational burden of such procedures critically grows.

Oversimplification of the real situation within neuronal tissue may often lead to untrustworthy results of tractography since the tractography builds the tracts on a basis of information about direction of

the diffusive motion within each voxel. False positive results may be detected. Improving reliability of tractography may be done by using more complex models and smart tracking algorithm (such algorithm appeared in recent literature [2]) or filter out false positive tracts built by standard simple tractography methods [6].

This paper deals with the option of determining anatomically plausible tracts by incorporating microstructural models to the analysis, as shown in [6], but via inverse problem solution.

2 Theoretical background

2.1 COMMIT

COMMIT, acronym for convex optimization modeling for microstructure informed tractography, is a post-processing tractography framework working in a top-down fashion. Given a tractogram computed by any of the conventional tractography methods, it selects the set of fibers describing the acquired DMRI data the best. The only prerequisite for the candidate set is that it contains true positives, possibly includes many false positives [6].

Once the candidate pathways have been estimated, DMRI signal contribution of every tract is mapped to each voxel of the image. For this purpose, multi-compartment model containing hindered, restricted and free diffusion compartment is included to characterize neuronal tissue [6].

For restricted compartment, each fiber has one column. Hypothetically, each fiber can be described by more columns if more fiber populations are considered. In case of hindered compartment, only one extraaxonal compartment is described for every fiber population, aiming to avoid redundancy.

The predicted signal $S(\mathbf{q})$ at q-space location \mathbf{q} , in a voxel can be expressed as a linear combination of the subsets of tracts, equation (1). In equation (1) standard biomedical labeling of the variables is used.

$$S(\mathbf{q}) = \sum_{\mathcal{F}_i \in \mathcal{F}} \mathbf{f}_i^{IC} R_i^{IC}(\mathbf{q}) + \sum_{\mathcal{F}_i \in \mathcal{F}} \mathbf{f}_i^{EC} R_i^{EC}(\mathbf{q}) + f^{ISO} R^{ISO}(\mathbf{q}) \quad (1)$$

Where R_i^{IC} , R_i^{EC} , R_i^{ISO} are the predicted signal profiles for each compartment, these can be estimated from the data or synthetically generated with analytic models. It is assumed that microstructure parameters remain the same along the bundle. Variables f^{IC} , f^{EC} and f^{ISO} are the corresponding fractal volumes. \mathcal{F}_i is the i^{th} fiber, in equation (1) meaning global contribution of the diffusion arising from all traced fibers. In other words, if the fiber does not cross a voxel there is no signal contribution from it in that voxel [6].

$$y = \mathbf{A}\mathbf{x} + \eta \quad (2)$$

Figure 1 pictures the COMMIT model, which can be also expressed by equation (2). Where $y \in R_+^{n_d n_v}$ is the vector containing the n_d q-space samples acquired in all n_v voxels, η means acquisition noise and modeling errors, $\mathbf{A} \in R^{n_d n_v \times n_c}$ is the observation matrix, a result of multi-compartment model in every voxel, $\mathbf{x} \in R^{n_c}$ are the contributions of the n_c basis functions in \mathbf{A} .

Schematic representation of COMMIT formulation. Vector \mathbf{y} is the set of acquired data, every colored block means a different voxel (the number of rows of each block depends on a number of diffusion measurements). \mathbf{A} is a block matrix filled with data computed by microstructure model. Each column

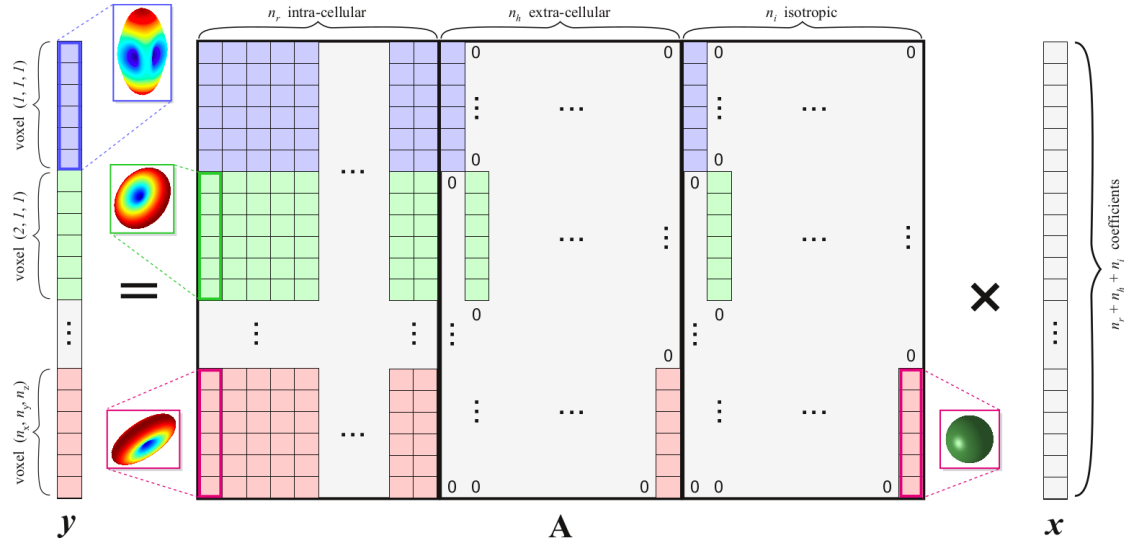


Fig. 1. Schematic representation of COMMIT formulation [6].

for every compartment in matrix \mathbf{A} corresponds to the fiber from the set of candidates. If the fiber does not cross the voxel, there is no signal contribution from it. The single fibre crosses only few voxels within the dataset, hence the matrix \mathbf{A} is sparse. Vector \mathbf{x} is a positive weights vector and is solved by optimization method, non-negative least squares in this case [6].

The goal is to find the optimal vector \mathbf{x} , hence to weight fibers with respect to how much their features are consistent alongside each fiber. In other words the goal is to detect anatomically correct fibers, if the assumption that fiber parameters are consistent alongside anatomically valid fibers is made.

3 Solution of linear systems

Task described by COMMIT algorithm can be understood as a typical inverse problem. Inverse problem is mathematical framework that is used to obtain information about a physical object or system from observed measurements. It is useful because it provides information about physical parameter that we can not measure directly (anatomical correctness of the axon fiber, parameters consistency, in this case).

If the linear operator \mathbf{A} was regular matrix, finding of solution vector \mathbf{x} would not be problematic. However, for singular systems (which arise often from the practical applications), finding the solution becomes an optimization problem.

To find optimal vector \mathbf{x} from a solution space, we tend to minimize the equation (3),

$$\underset{\mathbf{x} \geq 0}{\operatorname{argmin}} \|\mathbf{Ax} - \mathbf{y}\|, \quad (3)$$

where $\|\cdot\|$ is a l_p norm defined as

$$\|\mathbf{x}\| = \sqrt[p]{\sum_i |x_i|^p}, \quad p \in \mathbb{R}. \quad (4)$$

Even though every l_p norm look similar, their mathematical properties and applications are very different, figure 2.

The case of $p = 2$ is the most important norm in practice. All norms are convex functions, which makes optimization a convex problem. Other l_p norms are however problematic to optimize because of the computational complexity of the problem (l_0 optimization gives interesting results, but it is NP-hard problem to solve).

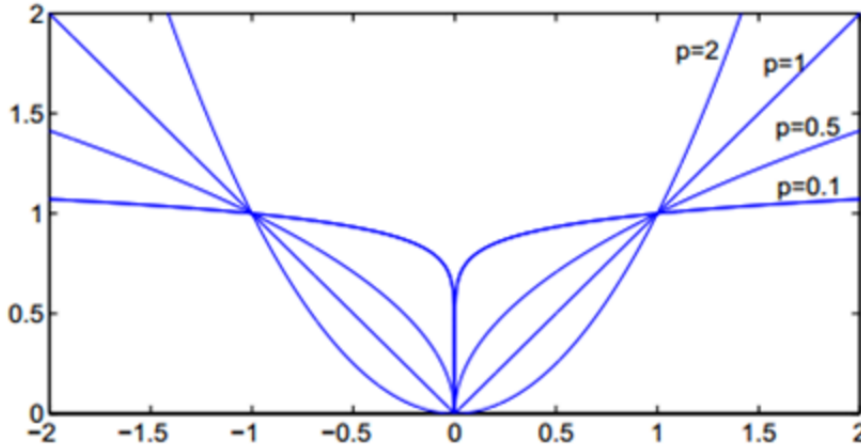


Fig. 2. The functions of various p norms.

The pursuit for solutions of

$$\mathbf{Ax} = \mathbf{y} \quad (5)$$

is then the minimization of error $\|\mathbf{r}\|_p = \|\mathbf{Ax} - \mathbf{y}\|_p$ for some suitable choice of p . For example l_2 norm is computationally the easiest to reach. Different norms render different optimum solutions.

Minimization of the l_2 norm is widespread in various fields of engineering and is called least squares problem. It is preferred due to uniqueness of the solution (in contrast with other p-norms).

4 Problem formulation

The problem to be optimized is expressed by figure 1. The linear operator \mathbf{A} can be understood as a dictionary of atoms (columns). The aim is to produce representation of the signal \mathbf{y} by expressing it as a linear combination of atoms from \mathbf{A} by retrieveing the best solution vector \mathbf{x} by minimizing the support of

$$\mathbf{x} \text{ subject to } \mathbf{y} = \mathbf{Ax}. \quad (6)$$

Than it is possible to use the indices of nonzero components of \mathbf{x} to identify the atoms (fibers) that are significant for reproducing the signal.

The shape of the linear system strongly depends on the size of the candidate set, model used and even on the acquisition scheme. In vast majority of applications, we are dealing with rectangular matrix whith tremendous dimensions (it is problematic to store the linear operator if no special format

exploiting sparseness of the matrix is used). Fortunately, since each tract crosses only few voxels of the full volume, the matrix is sparse.

Linear operator \mathbf{A} based on a real data is also extremely ill-conditioned. The condition number of the system is close to infinity (computed by `numpy.linalg.cond` method on the most dense fragment of the linear operator, size (1000 x 1000)).

5 Solution design

Problem solved is known to be large, sparse, singular (or close to singular) and ill-conditioned. Since it is known that singular problems are prone to roundoff errors when iterative methods are used, we decided to choose direct method of computation. Direct methods also enables to reach optimal solution without iterative procedure. Pseudo-inversion provides the optimal solution in means of l_2 optimization.

5.1 Pseudo-inversion by normal equations

In pursuit of finding a solution vector \mathbf{x} , it is very intuitive to rearrange the inverse problem equation as in (7). This solution was proposed because it is theoretically the simplest one. Also, the solution theoretically guarantees reaching global optimum in terms of $\|\mathbf{Ax} - \mathbf{y}\|_2$, hence least squares, minimization [4].

$$\begin{aligned}\mathbf{Ax} &= \mathbf{y} \\ \mathbf{x} &= \mathbf{A}^{-1}\mathbf{y}\end{aligned}\tag{7}$$

Since we are dealing with rectangular matrix, it is not possible to compute \mathbf{A}^{-1} by inversion, but it is necessary to use pseudo-inversion, \mathbf{A}^+ . More approaches how to reach pseudo-inverse of the matrix \mathbf{A} exist. First, let's mention normal equations (8).

$$\begin{aligned}\mathbf{Ax} &= \mathbf{y} \\ \mathbf{A}^T\mathbf{Ax} &= \mathbf{A}^T\mathbf{y} \\ \mathbf{x} &= (\mathbf{A}^T\mathbf{A})^{-1}\mathbf{A}^T\mathbf{y}\end{aligned}\tag{8}$$

Normal equations are no doubt elegant analysis, since the product of $\mathbf{A}^T\mathbf{A}$ is always symmetric matrix. However, we are dealing with badly ill-posed system, and the condition number of $\mathbf{A}^T\mathbf{A}$ product is the condition number of the original matrix \mathbf{A} squared. Such process make the solution of the system even more prone to the roundoff errors [5].

The computational instability of the pseudo-inversion is shown on well-conditioned and ill-conditioned problem by comparison of defined vector of solution and vector of solution obtained by pseudo-inverse. If we define matrices \mathbf{A} and \mathbf{y} , process is as in (9).

$$\begin{aligned}\mathbf{y} &= \mathbf{Ax} \\ \mathbf{x} &= \mathbf{A}^+\mathbf{y}\end{aligned}\tag{9}$$

First of all, analysis is shown on a well-conditioned matrix $\mathbf{A1}$ (condition number = 7.3, with solution vector \mathbf{x}).

$$\mathbf{A1} = \begin{pmatrix} 1 & 2 & 3 \\ 3 & 2 & 1 \\ 1 & 2 & 1 \end{pmatrix}, \mathbf{x} = \begin{pmatrix} 3 \\ 2 \\ 1 \end{pmatrix} \quad (10)$$

As shown in figure 3, solution vector \mathbf{x} reached by pseudoinversion is identical with the original one.

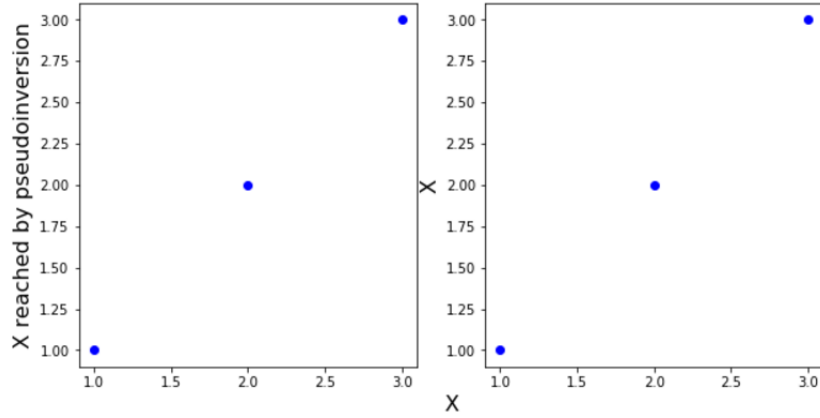


Fig. 3. Pseudo-inverse of the well-conditioned system.

Now, let's analyze ill-conditioned matrix $\mathbf{A2}$ (conditional number $2 * 10^{16}$) with solution vector \mathbf{x} .

$$\mathbf{A2} = \begin{pmatrix} 1 & 0 & 1 \\ 1 & 1 & 1 \\ 1 & 2 & 1 \end{pmatrix}, \mathbf{x} = \begin{pmatrix} 3 \\ 2 \\ 1 \end{pmatrix} \quad (11)$$

In figure 4 comparison of vector of solution \mathbf{x} reached by pseudo-inversion is not identical to the vector \mathbf{x} defined previously. Such error is caused by roundoff errors during the process of computation.

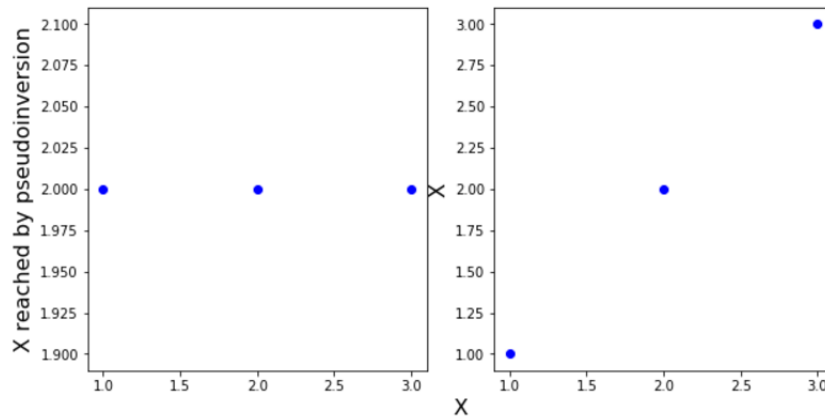


Fig. 4. Pseudo-inverse of the ill-conditioned system.

Note that the condition number of matrix $\mathbf{A2}$ is still very low in comparison with condition number of system built from neurological data. What is more, the pseudo-inverse of the sparse system is a very dense matrix, which throws off potentially beneficial feature of the matrix in terms of data

storage and computational demands. In fact, solution of large ill-posed systems is very challenging task, sparseness brings a dramatic simplification if used in a sophisticated way.

6 Conclusion

It is not possible to use direct inversion matrix method because linear operator \mathbf{A} is not square.

The method of pseudo-inversion is suitable for rectangular matrices, however it seems to be extremely prone to roundoff errors and comes with innegligible computational and memory burden if standard methods [3]) are used.

Method of pseudo-inversion also is not suitable for such task because it does not exploit the sparseness of the linear operator, which comes with significant memory issues. What is more, let be kept in mind that COMMIT algorithm is just a postprocessing step of improving the sensitivity of the modelling. Incorporation of the more complex models could be computationally more feasible task, if the candidate dataset would be build based on more precise information. Hence, in COMMIT case, the task lays a great deal on how the computation is time and space consuming.

Using pseudo-inversion without exploiting the sparseness of the linear operator leads at least to very multi-dimensional problem resulting in ridiculous time estimations if standard methods and material was used (months of computation time if standard PC used). What is more, results reached by pseudo-inversion seems to be non-valid due to ill-posed nature of the problem.

Optimization of a matrix equation $\mathbf{y} = \mathbf{Ax}$ for real neurological data is challenging task due to dimensions of the data and also due to errors which arises from measurement itself. Let assume this problematics as open problem and find the right way to solve it.

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