On a Global Optimization Technique for Solving a Nonlinear Hyperboloid Least Squares Problem

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ABSTRACT
We present a numerical experimentation of the global optimization algorithm presented by Velázquez et. al. [3] applied to a nonlinear hyperboloid least squares problem. This problem arises when beta sheet residues from an allosteric enzyme are fitted onto a hyperboloid by using Newton type methods. The results show that the algorithm performs well on three testcases. An important side result of this study is that the nonlinear fitting procedure is vastly superior to the linear least squares procedures traditionally used for this type of problems.

Categories and Subject Descriptors
G.1.6 [**Numerical Analysis**]: Optimization – global optimization, least squares methods, nonlinear programming.

General Terms
Algorithms, Experimentation.

Keywords
Global optimization, least squares methods, and Levenberg-Marquardt method.

1. INTRODUCTION
We studied a nonlinear least squares problem that arises in a process of hyperbola fitting to the Carbon alpha (Ca) atoms positions of selected beta sheets in proteins. Beta sheets are one of the most dominating secondary structure elements and they can be approximated by the hyperbola.

Especially interesting problems arises when we study allosteric enzymes. Those are responsible for controlling cell function and change differentially the activity in response to external effectors. Our purpose is to describe the conformational changes of the beta sheets between the active (R-state) and inactive (T-state) of allosteric enzymes.

1. PROBLEM DATA AND FORMULATION
First, we study the data obtained from a protein with a clear barrel structure to test the effectiveness of the algorithms. It is convenient to use this data since we expect the mapped atoms to arrange themselves in a barrel shape around the calculated hyperboloid.

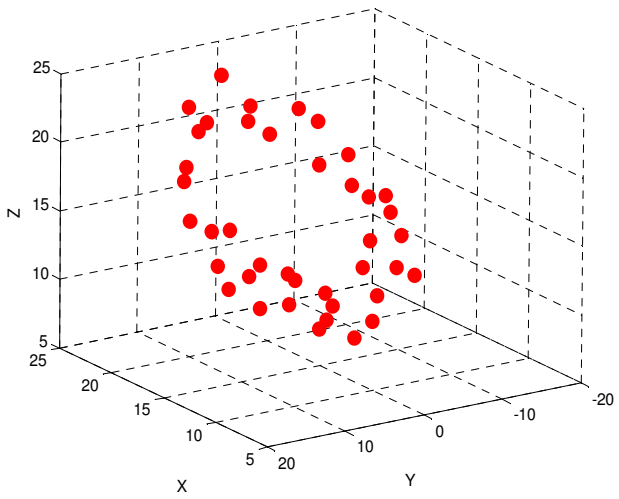

Figure 1. TIM Barrel atom positions.

The model used to map the atoms is given by the equation of a one-sheeted hyperboloid oriented along the z-axis. In order to map the atom positions (x_i, y_i, z_i) for $i = 1, \ldots, m$ onto the hyperboloid, three steps must be followed: First, the data must be rotated, then translated, and finally the best hyperboloid must be found to match the new position of the atoms in $\Re^3$. For the rotation of the atom positions, we use the following matrix $A \in \Re^{3x3}$:

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$$A=\begin{bmatrix} -\cos\theta\sin\varphi\sin\gamma+\cos\varphi\cos\phi & \cos\theta\text{ocs}\phi\sin\gamma+\cos\gamma\sin\phi & \sin\gamma\sin\theta \\ -\cos\theta\sin\phi\cos\gamma-\sin\gamma\cos\phi & \cos\theta\cos\phi\cos\gamma\text{-}\sin\gamma\sin\phi & \cos\gamma\sin\theta \\ \sin\theta\sin\phi & \text{-}\sin\theta\cos\phi & \cos\theta \end{bmatrix}.$$

Then, the new position of the atoms is calculated by

$$\begin{bmatrix} \hat{x}_i \\ \hat{y}_i \\ \hat{z}_i \end{bmatrix} = A \begin{bmatrix} x_i \\ y_i \\ z_i \end{bmatrix} + \begin{bmatrix} t_1 \\ t_2 \\ t_3 \end{bmatrix}$$

where the vector (t_1, t_2, t_3) represents the translation in the x, y, z coordinates, respectively.

Now we pose the data fitting problem as an unconstrained minimization problem

$$\text{minimize } f(w)$$

where the objective function $f:\Re^n \to \Re$ is a twice continuously differentiable nonlinear least squares function given by

$$f(w) = \sum_{i=1}^{m} r_i(w)^2$$

where

$$r_i = \left(\frac{\hat{x}_i^2}{a^2} + \frac{\hat{y}_i^2}{b^2} - \frac{\hat{z}_i^2}{c^2} \right)$$

and $(\phi,\theta,\gamma,a,b,c,t_1,t_2,t_3)^T \in \Re^9$ is the vector of unknown parameters.

Then for each atom $i = 1, \ldots, m$, the residual function $r_i(w)$ determines how well the observed data approximates the calculated data.

We are interested in finding the global minimum solution w^* that is $f(w^*) \le f(w)$ for all $w \in \Re^9$, and $m > n$.

In this problem, the objective function value at the global minimum w^* is never zero, i.e. $f(w^*) > 0$. The first and second derivatives of f are

$$\nabla f(w) = \sum_{i=1}^{m} r_i(w)\nabla r_i(w) = J(w)^T R(w)$$

where $J(w) = \nabla R(w)$ and $R(w) = \left[\text{r}_1(w),\ldots,r_m(w)\right]^T$ and

$$\nabla^2 f(w) = J(w)^T J(w) + \sum_{i=1}^{m} r_i(w)\nabla^2 r_i(w),$$

respectively. On the technique used the second order information of the residual function is approximated by $\tau\|R(x_k)\|$ and $\tau \ge 0$.

2. ALGORITHM

We apply the global optimization algorithm presented by [1] for solving nonzero or small residual nonlinear least squares problems. This strategy compared favorably with the classical damped Levenberg-Marquardt, Gauss-Newton method, tunneling and simulated annealing techniques on problems of significant sizes. Therefore, we use this technique for solving the hyperboloid least squares problem. The algorithm is as follows

Algorithm

Set initial point x_0 provided by the chemist, and a maximum number of iterations $k_{\max}$ allowed. Choose a tolerance $\varepsilon > 0$ and parameter $\tau \ge 0$.

Until $\|R(x_k)\|^2 < \varepsilon$ or $k > k_{\max}$

Do

(a) Compute $\nabla f(x_k) = J^T(x_k)R(x_k)$.

(b)Compute $\nabla^2 f(x_k) = J(x_k)^T J(x_k) + \tau\|R(x_k)\| I_m$.

(c) Compute $s_k = -\nabla^2 f(x_k)\nabla f(x_k)$.

(d) Set $x_{k+1} = x_k + s_k$ and increment k.

End

In our implementation, the following parameter values were chosen: $k_{\max} = 2000$, ε=10^{-9}, τ=0.1 and I_m is a diagonal matrix $m \times m$.

It was observed that this algorithm tends to repulse the closest local minimizer from any given starting point. (See [3]).

3. NUMERICAL EXPERIMENTATION

We conducted a numerical experimentation on the following test problems: TIM Barrel (Triose Phosphate Isomerase) data, and the R and T States of Fructose 1,6 bisphosphatase data. We use the coordinates of particular atoms of selected beta sheets at the (R) and (T) states from an allosteric enzyme. This information is obtained from published macromolecular structures archived at the Protein Data Bank (PDB) online.

The main objective of the experiments is to show how the algorithm proposed by [3] performs on the three test cases with the initial point provided by the chemists.

In Figure 2, we plot the solution obtained on the calculated hyperboloid for the TIM Barrel with $\nabla f(w^*) = 2.54e-7$, $f(w^*) = 1.77$, and CPU time of 4.67 seconds.

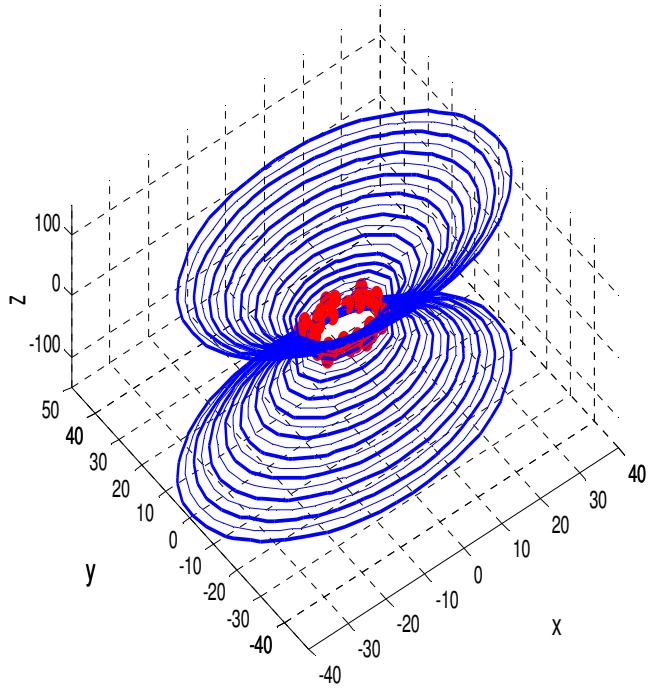

Figure 2 Mapped solution into hyperboloid for the TIM Barrel

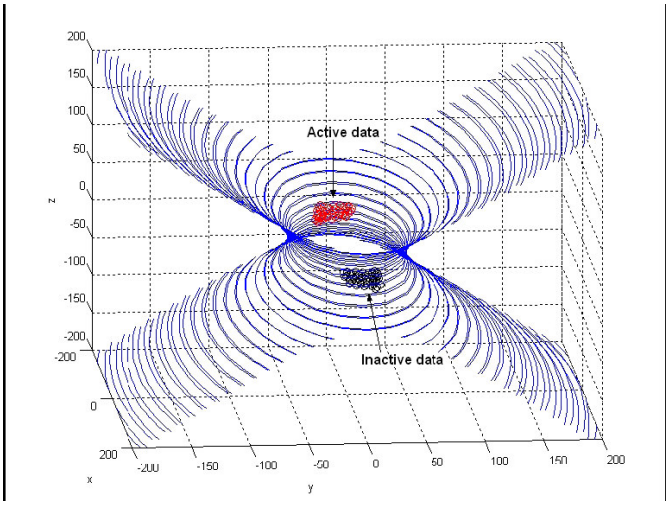

Figure 3. Mapped solutions into the hyperboloid for the active and inactive testcases.

Figure 3 shows the graphical results obtained on the Fructose 1,6 Bisphosphatase allosteric enzyme on the R and T states, respectively.

Furthermore, we calculated the root-mean-square (RMS) error for each approximate solution given by the nonlinear and linear fitting as $e_{RMS} = \sqrt{\frac{1}{m}\sum_{i=1}^{m} R_i^2}$ for $i = 1, \ldots, m$. Table 1 shows the results for the three testcases that indicates that the nonlinear fitting is superior than the linear fitting.

Table 1 indicates that using a linear fitting procedure is highly inaccurate in determining an optimal fit. For the TIM Barrel testcase, the solution obtained by the linear fitting yield a small RMS error, but it did not provide with a solution approved by the chemists. In the contrary, by using a nonlinear method of fitting that incorporates first and approximated second derivative information provided reasonable optimal solutions and a close agreement between the active and inactive results as expected.

Table 1. Comparison of RMS error between a linear vs nonlinear fitting of the three testcases.

Testcase	Linear Fitting	Nonlinear fitting
TIM Barrel	1.1506	1.5206
Active (R-state)	20.6658	1.2081
Inactive (T-state)	25.9421	1.0086

4. CONCLUSIONS

The numerical results indicates that the strategy is a promising approach for solving the particular nonlinear hyperboloid least-squares problems.

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