An infeasible point method for minimizing the Lennard-Jones potential *

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Abstract

Minimizing the Lennard-Jones potential, the most-studied model problem for molecular conformation, is an unconstrained global optimization problem with a large number of local minima. In this paper, the problem is reformulated as an equality constrained nonlinear programming problem with only linear constraints. This formulation allows the solution to approached through infeasible configurations, increasing the basin of attraction of the global solution. In this way the likelihood of finding a global minimizer is increased. An algorithm for solving this nonlinear program is discussed, and results of numerical tests are presented.

1. Introduction

The molecular conformation problem consists of finding a configuration of atoms in a cluster or molecule whose potential energy is a minimum. This problem is important in the study of molecular dynamics, in which its solution is thought to provide the zero-temperature configuration or

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ground-state of the molecule. The solution of the molecular conformation problem is also of interest in the study of protein folding, in which the tertiary structure of the protein is sought.

In its simplest form, the potential energy of the molecule is modeled by the sum of the potential energies between pairs of atoms. Even in this case, the problem of finding a global minimum of the energy can be extremely difficult due to the excessive number of non-global minima. The characteristic difficulty of a true global optimization problem must be faced: while efficient algorithms are well-known which will converge to a local minimizer from almost any starting point, algorithms for finding a global minimizer are not so well-developed.

Researchers have therefore proceeded in one of three ways. Physical knowledge or intuition can be used to generate starting configurations which are likely to represent low-energy states. These configurations are then used as starting points for local minimization algorithms. The hope is that carefully chosen starting points will be more likely to lie in the region of convergence of a global minimizer. This approach, of course, is highly problem-specific in that it requires some knowledge of likely configurations.

At the other end of the spectrum are attempts to apply Monte-Carlo or stochastic algorithms, which can be expected to find the global minimizer with a high probability given enough random searches. Included in this category are the intelligent Monte-Carlo methods such as simulated annealing and genetic algorithms, as well as local minimization from multiple random starting points. These methods are general in the sense that they can be applied to any global optimization problem with; no specialized knowledge of the problem or its likely solutions is required.

Intermediate to these extremes are attempts to use the structure of the problem to reformulate the optimization problem into one which is somehow more tractable. These methods can be applied to other problems that have structure which can be exploited, although they provide no solution to the general global optimization problem. This current work falls into this last category; in it, the naturally unconstrained minimization problem is reformulated as a constrained problem. It will be shown by example that the global minimizer is somehow easier to find when approached through infeasible (i.e. physically impossible) configurations.

The outline of the paper is as follows. In section 2, we discuss various methods which have been used to find low-energy configurations and summarize some of the significant finding of these methods. Section 3 contains a description of our method for reformulating the problem. In section 4, we present an algorithm to solve the reformulated problem, with numerical results appearing in section 5. We discuss our conclusions in section 6.

2. Approaches to Molecular Conformation

For the purpose of finding the ground–state of a cluster of atoms, the potential energy is usually modeled by the sum of the pairwise energies. Although more complicated interactions (e.g. three-body forces) are ignored, it is believed that this assumption allows a reasonable approximation to the true state of affairs (see, for instance, [10]). Moreover, this simplification leaves some hope that the necessary computations can be carried out, although we shall see that even the simplified problem is very difficult.

The potential energy function we use is given by

$$E(X) = \sum_{j=1}^{m-1} \sum_{i=j+1}^{m} v_{LJ}(\|x_i - x_j\|), \tag{1}$$

where $x_1, x_2, \ldots, x_m$ are the positions of the m atoms, $X = (x_1, x_2, \ldots, x_m)$, and v_{LJ} is the Lennard-Jones 6-12 pair–potential:

$$v_{LJ}(r) = \frac{1}{r^{12}} - \frac{2}{r^6}. \tag{2}$$

Here $v_{LJ}(r)$ has been scaled so that it is minimized at $r = 1$ with minimum energy -1. This gives a crude lower bound of $-m(m-1)/2$ for $E(X)$. We take $x_1 = (0,0,0)$, $x_2 = (x_{21}, 0, 0)$, and $x_3 = (x_{31}, x_{32}, 0)$ in order to remove the translational and rotational degrees of freedom from the cluster. (It should be noted that there is still a great deal of symmetry left in the model, particularly in the representation of the atoms. Since, apart from the first three, the atoms are not distinguished except by enumeration, any physical configuration can be represented in $(m-3)!$ different ways simply by renumbering the atoms.) The review article [11] may be consulted for more information about the Lennard-Jones pair-potential and other pair-potentials which have been considered.

2.1. Generation of Likely Configurations

A number of researchers have searched for global minimizers of the Lennard-Jones potential by constructing configurations which are expected to represent low energy states and using these as starting points for local minimization routines. In particular, Hoare and Pal ([10]) found all the local minimizers for a small value of m and used the corresponding configurations as 'seed' structures; that is, they began with the minimal energy configurations for $m = 6$ and added one atom at a time to gradually build starting configurations for larger clusters. The configurations they produced were then relaxed by local minimization into locally minimal energy configurations. In this way they produced low–energy configurations for m from 6 to 46. Northby ([18]) searched through various lattice-based configurations and used the lowest–energy configurations thus found as starting points for local minimizations. He found low–energy configurations in the range $m = 13, \ldots, 147$.

It should be emphasized that in none of the work cited above or below is there any assertion that a global minimum has been found. Instead, low–energy configurations are compared with one another and with the lowest given in the literature. Indeed, Xue ([24]) has recently given a parallel version of Northby's algorithm and used it to improve on several of Northby's solutions.

In an investigation by Hoare and McInnes ([12]), problems with m varying from 6 to 13 were exhaustively studied, with the result that 2,4,8,18,57,145,366, and 988 physically distinct local minimizers were discovered for m = 6, 7,8,9,10,11,12, and 13 atoms, respectively. This gives some idea of the difficulty of the problem, especially when it is noted that many of the minimal energy configurations have energy very close to the globally minimal energy, and that a realistic problem may have 1000 to 10000 atoms.

2.2. Stochastic Methods

For problems of realistic size, exhaustively searching for the global minimizer is so computationally intensive as to be out of the question. A popular alternative is to use some type of random search strategy. Numerous researchers have applied some variant of the simulated annealing algorithm (see, e.g. [21], [22], [13], [15]). Various degrees of success have been reported. Wille ([21]) found the putative global minimizer in problems of size up to $m = 25$. Li and Scherage ([15]) and Judson et al. ([13]) have applied simulated annealing to other forms of the molecular conformation problem with mixed success at finding the best–known minimizers. The last reference also contains results of applying two genetic algorithms to the problem studied by Judson et al.

Byrd et al. ([1], [2]) have developed a general parallel algorithm for global optimization. It consists of multiple local minimizations from random starting points, together with refinements of the local minimizers via low–dimensional perturbations and further local minimization. They report a high rate of success in finding the best–known minimizer for problems with $m \leq 30$, but their algorithm is unable to find the minimizer in many problems with a larger number of atoms.

2.3. Reformulation of the Problem

The approach taken in this paper is to reformulate the problem in order to make the global minimizers more accessible to local minimization. Several researchers have taken similar approaches. Piela et al. ([19], [14]) have applied the time–dependent diffusion equation to the potential energy surface to smooth it, in hopes that the global minimum will be the last minimum to survive. In this way a problem with a unique minimum can be produced. Using a homotopy–like method, this minimum can then be traced back to a minimum (hopefully global) of the original problem. In the second reference above, a good rate of success in finding the putative global solution is reported.

Coleman et al. ([4], see also [23]) have implemented another method for smoothing the potential energy surface. A parameterized integral transform (similar to convolution with a Gaussian) is applied to the Lennard-Jones potential in a similar attempt to smooth out the local minima while leaving the global minima intact. The method also involves a homotopy–like aspect. Once a smoothed version of the problem has been solved, it is necessary to follow a path as the problem is transformed back to the original. By combining this idea of reformulating the energy function with a version of simulated annealing and local minimization, the global minimum has been found in a large proportion of attempts for problems with $m \leq 27$ (see [4]).

Crippen and Havel ([5]) reformulate the problem by allowing the atoms to move in a higher–dimensional Euclidean space. A constraint which enforces the condition that the atoms are actually in 3–space is then added, and the constrained problem is then solved by an augmented Lagrangian algorithm. Although this approach does not always find the global solution, it is reported that it tends to find low-energy configurations consistently (see [5] and the references therein).

3. An Infeasible Point Approach

3.1. Motivation

The incredible multiplicity of minima of the Lennard–Jones potential is due to the fact that each atom interacts with every other atom. The pair-potential itself is relatively simple, having a unique minimum (see Figure 1). The difficulty arises when all of the atom–atom interactions are included.

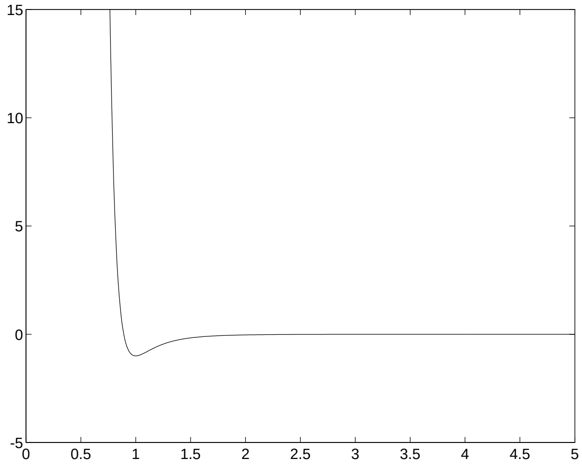

Figure 1: Lennard-Jones pair potential v_{LJ}

Our approach is to directly address the difficulty described above by decoupling the interactions of the atoms. We split each atom into $m-1$ 'artificial' atoms, and then designate exactly one of the $m-1$ atoms spawned by the ith physical atom to interact with a corresponding representative of the jth physical atom. Specifically, let $\tilde{x}_{ij}$ be the coordinates of the artificial atom which is spawned by the ith original atom and which interacts with an atom spawned by the jth original atom (so $\tilde{x}_{ij}$ interacts with $\tilde{x}_{ji}$). We let $\tilde{X}$ represent the collection of all $\tilde{x}_{ij}$'s and define $\tilde{E}$ by

$$\tilde{E}(\tilde{X}) = \sum_{j=1}^{m} \sum_{i>j} v_{LJ}(\|\tilde{x}_{ij} - \tilde{x}_{ji}\|).$$

It is easy to find the global minimum of $\tilde{E}$; any configuration $\tilde{X}$ in which $\|\tilde{x}_{ij} - \tilde{x}_{ji}\| = 1$ for all i and j satisfies $\tilde{E}(\tilde{X}) = -m(m-1)/2$.

In order to recover the original problem, we must impose the constraint that all of the artificial atoms corresponding to any one of the original atoms have the same coordinates, that is, that

$$\tilde{x}_{ij} = \tilde{x}_{ik}, 1 \leq j < k \leq m, i = 1, \ldots, m. \tag{3}$$

We let W be a linear operator with the property that the only configurations $\tilde{X}$ in the null space of W are those satisfying constraint (3).

An equivalent formulation of the original problem is the following:

$$\begin{aligned} \text{minimize} \quad & \tilde{E}(\tilde{X}) \\ \text{s.t.} \quad & W\tilde{X} = 0 \end{aligned} \tag{4}$$

The advantage of this formulation, as discussed below, is that it seems to be easier to approach the global minimizer along a path of infeasible configurations.

Of course, the approach we outline above involves a great increase in the number of variables. After removing the rotational and translational degrees of freedom, $3m - 6$ variables describe the coordinates of m particles in 3-dimensional space. Our approach requires $3m(m-1) - 6$ variables for the same problem. However, the increase in problem size is somewhat mitigated by the fact that both the Hessian of $\tilde{E}$ and the constraint matrix W are very sparse. In the algorithm we present below, we take advantage of this sparsity.

This method of reformulating the problem is inspired by *Differential Semblance Optimization* (DSO), which was introduced by Symes ([20]) to address difficulties in the standard approach to seismic velocity inversion. The goal of seismic velocity inversion is the estimation of parameters which represent the material properties of the subsurface, particularly seismic wave velocities, by means of measurements made at the surface. The standard formulation of a typical application takes the following abstract form:

$$\begin{array}{rl} & \text{minimize} \quad \sum_{i \in I} \|S_i(x, y) - D_i\|_{L^2}^2 \\ x \in X, y \in Y & \end{array} \tag{5}$$

where x and y represent the parameters to be determined. The difficulty arises because the parameters must be chosen to fit data from multiple experiments (indexed by i). The natural objective function is observed to be very nonconvex with multiple minima (see, for example, [8]).

In the DSO technique, the data from different experiments are fitted using different parameters (so that the experiments are decoupled). The requirement that all the data be explained by the same parameters is then enforced by a constraint. Specifically, the parameter $y \in Y$ is replaced by a parameter $\tilde{y} \in Y^I$ (so that each experiment is being explained independently). Then the constraint $W\tilde{y} = 0$ is imposed, where the null space of W is the diagonal of Y^I (that is, $W\tilde{y} = 0$ implies that $\tilde{y}_i = \bar{y} \in Y$ for all $i \in I$).

In this way, the original problem (5) is reformulated as the following equality constrained nonlinear program:

$$\begin{array}{rc} \text{minimize} & \sum_{i \in I} \|S_i(x, \tilde{y}_i) - D_i\|_{L^2}^2 \\ \text{s.t.} & W\tilde{y} = 0. \end{array} \tag{6}$$

The similarity between the DSO approach to velocity inversion and our reformulation of the Lennard-Jones problem should be clear. In both cases, the original objective function is expressed in terms of an expanded parameter set and a linear constraint is imposed to recover the original problem.

3.2. The Quadratic Penalty Function

In velocity inversion applications, the advantage of the constrained version of the problem becomes evident when it is solved by the quadratic penalty method. In certain cases ([9]), it can be shown that for sufficiently small values of the penalty parameter, the penalty function has a unique minimum. Moreover, it is possible to follow a path, parameterized by the penalty constant, to the global constrained minimum.

The quadratic penalty function for the general equality constrained nonlinear program

$$\begin{array}{rc} \text{minimize} & f(x) \\ \text{s.t.} & g(x) = 0 \end{array} \tag{7}$$

(where $g(x)$ is d–dimensional) is

$$P(x; r) = f(x) + \frac{1}{2}\sigma^2 g(x)^T g(x). \tag{8}$$

The theory for such penalty functions is well-known (see [7]). Under appropriate conditions, given any local minimizer x^* of (7), there exists a positive number Σ such that a path $x(\sigma)$ exists for $\sigma \in [\Sigma, \infty)$ with $x(\sigma) \in \operatorname{argmin}\{P(x; \sigma)\}$ and $x(\sigma) \to x^*$ as $\sigma \to \infty$. In particular it should be noted that the standard theory addresses only the case where σ is large. The novel aspect of Differential Semblance Optimization is that it demonstrates that allowing infeasible iterates can sometime expand the basin of attraction of the global minimizer.

Our approach to the Lennard-Jones problem is modeled after the above discussion. We attempt to find the global minimum of the constrained problem (4) by allowing infeasible iterates and following a path as $\sigma \to \infty$.

4. Algorithm

The penalty function for problem (4) is

$$P(\tilde{X};\sigma) = \tilde{E}(\tilde{X}) + \frac{1}{2}\sigma^2 \tilde{X}^T W^T W \tilde{X}.$$

We take a starting configuration, embed it in the larger dimensional space, and minimize $P(\tilde{X};\sigma)$ for some value of σ. This finds a point on a path of minimizers parameterized by σ. We then use a predictor-corrector method for following the path. After increasing σ to a 'large enough' value, we project the current configuration onto the smaller dimensional (feasible) subspace, and perform an unconstrained minimization on the original Lennard-Jones potential E. As is typical in penalty function methods, there are no firm rules upon which to base the choice of the starting or ending value of σ. The numerical results presented in the following section show, however, that even simple choices can lead to good results.

The initial minimization (to find a point on the path) is accomplished with the limited memory BFGS algorithm of Nocedal ([17]). The predictor-corrector algorithm is based on following the solution of

$$\nabla P(\tilde{X};\sigma) = 0.$$

Differentiating with respect to σ, we obtain the following ordinary differential equation:

$$\left\{\nabla^2 \tilde{E}(\tilde{X}) + \sigma^2 W^T W\right\} \frac{d\tilde{X}}{d\sigma} = -2\sigma W^T W \tilde{X}.$$

As discussed above, the existence of a solution is guaranteed provided the initial value of σ is sufficiently large.

For the predictor step, we use the RKF45 code developed by Watts and Shampine in single step mode; this uses a Runge–Kutta–Fehlberg 4th/5th order scheme to achieve automatic step size control. The corrector step is performed using Newton's method. It is important to note that in our formulation of the problem, the potential energy function has an extremely sparse Hessian. Moreover, the matrix $W^T W$ is also sparse, so both the predictor step and the Newton correction step involve the solution of sparse linear systems. We used a sparse Choleski algorithm to solve these systems.

In order to generate reasonable starting points, we took the solutions to the problems and replaced each coordinate c by $c + \rho u c$, where u is taken from a (pseudo-)random uniform distribution on $[-0.5, 0.5]$ and ρ measures the relative size of the perturbation.

Algorithm 1

1. Choose $\sigma_1 > 0$ and $\sigma_{final} > \sigma_0$
2. Choose $\tilde{X}_0$
3. Find $\tilde{X}_{\sigma_1} \in \text{argmin}\{P(\tilde{X}; \sigma_1)\}$
4. repeat until $\sigma_k > \sigma_{final}$
    1. Set $k := k + 1$
    2. Predict $\tilde{X}_{\sigma_k}$ by a call to RKF45
    3. Correct $\tilde{X}_{\sigma_k}$ using s steps of Newton's method
5. Project $\tilde{X}$ onto the feasible set by setting $x_i := \frac{1}{m-1} \sum_{j \neq i} \tilde{x}_{ij}$ for $i = 1, \ldots, m$, obtaining X_0
6. Find $X^* \in \text{argmin}\{E(X)\}$ using X_0 as the starting point

In order to provide a basis for comparison, we also attempted to minimize $E(X)$ directly. One difficulty was encountered when starting a local algorithm from a random starting point. If the starting point corresponded to a high energy state, frequently a long step was taken in an early iteration, which led to one or more atoms 'escaping' from the cluster (referring back to Figure 1, it is clear that once the distance between a particular atom and the rest of the cluster is large, there is almost no interaction which will tend to pull it back). Therefore, we used the following two-step algorithm. The first step includes a penalty on the size of the coordinates, so that atoms cannot escape the Lennard-Jones forces.

Algorithm 2

1. Choose X_0 and $\epsilon > 0$
2. Find $X_{reg} \in \text{argmin}\{E(X) + \frac{1}{2}\epsilon^2 X^T X\}$ using X_0 as the starting point
3. Find $X^* \in \text{argmin}\{E(X)\}$ using X_{reg} as the starting point

5. Numerical Results

We tested Algorithm 1 on problems corresponding to $m = 5, \ldots, 30$ atoms, running the algorithm 10 times on each problem beginning from 10 different perturbations of the global solutions. To define the perturbations, we used $\rho = 0.75$, that is, the coordinates were perturbed by up to 37.5% each. The following version of the constraint $W\tilde{X} = 0$ was used

$$\left.\begin{array}{rcl} x_{i1} & = & x_{i2} \\ x_{i2} & = & x_{i3} \\ & \vdots & \\ x_{i,i-2} & = & x_{i,i-1} \\ x_{i,i-1} & = & x_{i,i+1} \\ & \vdots & \\ x_{i,m-1} & = & x_{im} \end{array}\right\} i = 1, \ldots, m. \tag{9}$$

For comparison purposes, Algorithm 2 was applied to each problem using the same starting points. We used $\epsilon = 0.01$ in Algorithm 2.

All computations were performed on a Sun SPARCstation 10 in IEEE double precision (64 bit) arithmetic. Machine epsilon ϵ_M is about 2.2×10^{-16}. The minimizations using limited memory BFGS were halted when the relative norm of the gradient was reduced to 10^{-8}.

In Table 1, the results of the numerical experiments are summarized. We record the number of times each algorithm finds the putative global minimum versus the number of attempts, and the mean energy at the solution for each algorithm. Also listed is the value of the putative global minimum. Note that Algorithm 1 succeeded in locating the global minimum in every attempt, while in 15 of the problems, Algorithm 2 did not succeed in any attempt.

We interpret these results to mean that the infeasible formulation increases the size of the basin of attraction of the global minimizer. It is possible that this ability to expand the basin of attraction, together with good starting points provided by chemical knowledge, could be used to solve larger Lennard-Jones problems.

On the problem with 21, 25 and 30 atoms, Algorithm 2 performed unusually well, locating the optimal structure on every attempt. To explore this anomaly, we ran both algorithms on this problem, while increasing the relative perturbation ρ. The results are shown in Table 2, Table 3 and Table 4. Algorithm 2 began to fail when ρ reached 0.85 (42.5% perturbation), while Algorithm did not fail until ρ reached 1.35 (62.5% perturbation). Thus, although the basin of attraction of the optimal configuration is relatively large for $m = 21$, these results show that it is still much larger for the infeasible approach.

6. Conclusions

We have presented a reformulation of the Lennard-Jones problem as a linearly constrained nonlinear program. This reformulation is an attempt to improve the global characteristics of of the problem, thereby making it easier to locate a global minimizer. The basic idea is that it may be easier to approach global minimizers through infeasible points.

In order to test this idea, we have conducted experiments using a naive implementation of an infeasible point algorithm (the quadratic penalty function method). For the purpose of comparison, a straightforward feasible point method has also been implemented and tested. The results show that the infeasible point approach is biased toward very low energy configurations, and, in particular, that it is more likely to locate a global minimizer.

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References

[1] R. H. Byrd, E. Eskow, R. B. Schnabel, S. L. Smith, *Parallel Global Optimization: Numerical Methods, Dynamic Scheduling Methods, and Application to Molecular Conformation,* in "Parallel Computation," B. Ford and A. Fincham, eds., Oxford University Press, 1993, pp. 187-207

[2] R. H. Byrd, E. Eskow, R. B. Schnabel, *A New Large–Scale Global Optimization Method and its Applicationto Lennard-Jones Problems,* Technical Report CU-CS-630-92, University of Colorado at Boulder, Department of Computer Science, Boulder, CO 80309, 1992.

[3] T. Coleman, D. Shalloway, Z. Wu, *Isotropic Effective Energy Simulated Annealing Searches for Low Energy Molecular Cluster States,* Journal of Computational Optimization and Applications, 2, 145–170, 1993.

[4] T. Coleman, Z. Wu, *Parallel Continuation–Based Global Optimization for Molecular Conformation and Protein Folding* Technical Report MCS–P443–0694, Mathematics and Computer Science Division, Argonne National Laboratory, Argonne, IL, 1994.

[5] G. M. Crippen and T. F. Havel. *Distance Geometry and Molecular Conformation*, John Wiley & Sons, New York, 1988.

[6] J. E. Dennis and R. B. Schnabel, *Numerical Methods for Unconstrained Optimization and Nonlinear Equations,* Prentice–Hall: Englewood Cliffs, NJ, 1983.

[7] A. Fiacco and G. McCormick, *Nonlinear Programming: Sequential unconstrained minimization techniques,* John Wiley, New York, 1968.

[8] M. S. Gockenbach, *"An abstract analysis of Differential Semblance Optimization",* Ph.D. thesis, Department of Computational and Applied Mathematics, Rice University, Houston, TX 77251.

[9] M. S. Gockenbach, W. W. Symes, R. A. Tapia, *"Seismic velocity via regularization of a related problem,* To appear in Inverse Problems.

[10] M. R. Hoare, P. Pal, *"Physical Cluster Mechanics: Statics and Energy Surfaces for Monatomic Systems,"* Adv. Phys., Vol. 20, pp. 161-196, 1971.

[11] M. R. Hoare, *"Structure and Dynamics of Simple Microclusters,"* Adv. Chem. Phys., Vol. 40, pp. 49-135, 1979.

[12] M. R. HOARE, J. A. MCINNES, *"Morphology and statistical statics of simple microclusters,"* Adv. Phys., Vol. 32, pp. 791-821, 1983.

[13] R. S. JUDSON, M. E. COLVIN, J. C. MEZA, A. HUFFER, D. GUTIERREZ, *Do Intelligent Configuration Search Techniques Outperform Random Search for Large Molecules?,* Sandia Report 91-8740, Sandia National Laboratories, Albuquerque, NM 87185, 1991.

[14] J. KOSTROWICKI, L. PIELA, B. J. CHERAYIL, H. A. SCHERAGA, *" Performance of the Diffusion Equation Method in Searches for Optimum Structures of Lennard-Jones Atoms,"* J. Phys. Chem., Vol. 95, pp.4113-4119, 1991.

[15] Z. LI, H. A. SCHERAGA, *"Monte Carlo Minimization Approach to the Multiple-Minima Problem in Protein Folding,"* Proc. Natl. Acad. Sci. USA, Vol. 84, pp. 6611-6615, 1987.

[16] D. C. LIU AND J. NOCEDAL, *"On the Limited Memory BFGS Method for Large Scale Optimization,"* Math. Prog., 45, pp.503-528, 1989.

[17] J. NOCEDAL, *"Updating Quasi-Newton Matrices with Limited Storage,"* Mathematics of Computation, Vol. 35, pp.773–782, 1980.

[18] J. A. NORTHBY, *"Structure and Binding of Lennard-Jones Clusters: 13 $<=$ n $<=$ 147,"* J. Chem. Phys., Vol. 6, pp. 599-616, 1987.

[19] L. PIELA, J. KOSTROWICKI, H. A. SCHERAGA, *"The Multiple–Minima Problem in the Conformational Analysis of Molecules. Deformation of the Potential Energy Hypersurface by the Diffusion Equation Method,"* J. Phys. Chem., Vol. 93, pp. 3339-3346, 1989.

[20] W. W. SYMES, *"Velocity Inversion: A Case Study in Infinite-Dimensional Optimization,"* Math. Prog., Vol. 48, pp. 71-102, 1990.

[21] L. T. WILLE, *"Minimum–Energy Configurations of Atomic Clusters: New Results Obtained by Simulated Annealing,"* Chem. Phys. Lett., Vol 133, pp. 405-410, 1987.

[22] S. R. WILSON, W. CUI, *"Applications of Simulated Annealing to Peptides,"* Biopolymers, Vol. 29, pp. 225-235, 1991.

[23] Z. WU, *The Effective Energy Transformation Scheme as a General Continuation Approach to Global Optimization with Applications to Molecular Conformation,* Technical Report CTC93TR143, Advanced Computing Research Institute, Cornell University, Ithaca, NY, 1992.

[24] G. L. XUE, *Improvement on the Northby Algorithm for Molecular Conformation: Better Solutions* Pre-print 92-055, Army High Per-

formance Computing Research Center, University of Minnesota, Minneapolis, 1992.

m	success/try(IPM)	mean energy(IPM)	success/try(LM)	mean energy(LM)	putative min.
5	10/10	-9.10385	10/10	-9.10385	-9.10385
6	10/10	-12.7121	0/10	-12.7121	-12.7121
7	10/10	-16.5054	4/10	-16.5054	-16.5054
8	10/10	-19.8215	4/10	-19.2084	-19.8215
9	10/10	-24.1134	0/10	-22.9690	-24.1134
10	10/10	-28.4225	1/10	-26.8424	-28.4225
11	10/10	-32.7656	0/10	-31.5629	-32.7656
12	10/10	-37.9676	3/10	-36.3692	-37.9676
13	10/10	-44.3268	1/10	-41.1379	-44.3268
14	10/10	-47.8452	1/10	-44.3883	-47.8452
15	10/10	-52.3226	2/10	-49.7777	-52.3226
16	10/10	-56.8157	0/10	-54.5608	-56.8157
17	10/10	-61.3180	0/10	-57.6631	-61.3180
18	10/10	-66.5309	1/10	-62.4705	-66.5309
19	10/10	-72.6598	0/10	-68.7679	-72.6598
20	10/10	-77.1770	0/10	-71.5516	-77.1770
21	10/10	-81.6846	10/10	-81.6846	-81.6846
22	10/10	-86.8098	0/10	-80.5738	-86.8098
23	10/10	-92.8445	0/10	-85.4309	-92.8445
24	10/10	-97.3488	0/10	-90.5833	-97.3488
25	10/10	-102.3727	0/10	-98.6382	-102.3727
26	10/10	-108.3156	2/10	-102.0618	-108.3156
27	10/10	-112.8736	0/10	-104.4727	-112.8735
28	10/10	-117.8224	0/10	-111.2948	-117.8224
29	10/10	-123.5874	0/10	-115.0656	-123.5874
30	10/10	-128.2866	0/10	-123.2344	-128.2866

Table 1: Comparison of Infeasible Point Algorithm (IPM) with Local Minimization (LM) with a starting point equal to global solution with % 75 percent perturbation to each coordinate

ρ	success/try(IPM)	mean(IPM)	success/try (LM)	mean(LM)	putative minim um
.70	10/10	-81.6846	10/10	-81.6846	-81.6846
.75	10/10	-81.6846	10/10	-81.6846	-81.6846
.80	10/10	-81.6846	10/10	-81.6846	-81.6846
.85	10/10	-81.6846	9/10	-81.2645	-81.6846
.90	10/10	-81.6846	3/10	-77.9603	-81.6846
.95	10/10	-81.6846	0/10	-75.0916	-81.6846
1.00	10/10	-81.6846	0/10	-75.7976	-81.6846
1.05	10/10	-81.6846	0/10	-75.2229	-81.6846
1.10	10/10	-81.6846	0/10	-76.2532	-81.6846
1.15	10/10	-81.6846	0/10	-76.1845	-81.6846
1.20	10/10	-81.6846	0/10	-75.0138	-81.6846
1.25	10/10	-81.6846	0/10	-76.1396	-81.6846
1.30	10/10	-81.6846	0/10	-75.6178	-81.6846
1.35	8/10	-81.3678	0/10	-76.1242	-81.6846
1.40	9/10	-81.6796	0/10	-76.7100	-81.6846
1.45	4/10	-81.5004	0/10	-76.5249	-81.6846
1.50	0/10	-81.0764	0/10	-76.7679	-81.6846

Table 2: Comparison of Infeasible Point Algorithm (IPM) with Local Minimization (LM) on problem $m = 21$ with varing perturbation to each coordinate

ρ	success/try(IPM)	mean(IPM)	success/try (LM)	mean(LM)	putative minim um
.70	10/10	-102.373	10/10	-102.373	-102.373
.75	10/10	-102.373	10/10	-102.373	-102.373
.80	10/10	-102.373	0/10	-101.829	-102.373
.85	10/10	-102.373	1/10	-101.533	-102.373
.90	10/10	-102.373	0/10	-101.193	-102.373
.95	10/10	-102.373	0/10	-101.507	-102.373
1.00	10/10	-102.373	0/10	-100.185	-102.373
1.05	10/10	-102.373	0/10	-100.798	-102.373
1.10	10/10	-102.373	0/10	-100.195	-102.373
1.15	10/10	-102.373	0/10	-100.022	-102.373
1.20	10/10	-102.373	0/10	-101.421	-102.373
1.25	10/10	-102.373	0/10	-101.829	-102.373
1.30	10/10	-102.373	0/10	-100.888	-102.373
1.35	0/10	-101.971	0/10	-100.742	-102.373
1.40	8/10	-102.289	0/10	-100.081	-102.373
1.45	7/10	-102.089	0/10	-100.823	-102.373
1.50	0/10	-100.321	0/10	-99.9988	-102.373

Table 3: Comparison of Infeasible Point Algorithm (IPM) with Local Minimization (LM) on problem $m = 25$ with varing perturbation to each coordinate

ρ	success/try(IPM)	mean(IPM)	success/try (LM)	mean(LM)	putative minim um
.70	10/10	-128.287	8/10	-128.202	-128.287
.75	10/10	-128.287	0/10	-127.619	-128.287
.80	10/10	-128.287	0/10	-127.772	-128.287
.85	10/10	-128.287	0/10	-127.431	-128.287
.90	10/10	-128.287	0/10	-126.529	-128.287
.95	10/10	-128.287	0/10	-126.758	-128.287
1.00	10/10	-128.287	0/10	-126.324	-128.287
1.05	10/10	-128.287	0/10	-126.419	-128.287
1.10	10/10	-128.287	0/10	-126.275	-128.287
1.15	10/10	-128.287	0/10	-126.129	-128.287
1.20	10/10	-128.287	0/10	-125.943	-128.287
1.25	10/10	-128.287	0/10	-125.874	-128.287
1.30	0/10	-127.341	0/10	-125.805	-128.287
1.35	0/10	-127.524	0/10	-126.155	-128.287
1.40	0/10	-127.456	0/10	-126.423	-128.287
1.45	1/10	-127.349	0/10	-126.221	-128.287
1.50	0/10	-126.863	0/10	-125.172	-128.287

Table 4: Comparison of Infeasible Point Algorithm (IPM) with Local Minimization (LM) on problem $m = 30$ with varing perturbation to each coordinate