

Interplay between the Gentlest Ascent Dynamics Method and Conjugate Directions to Locate Transition States

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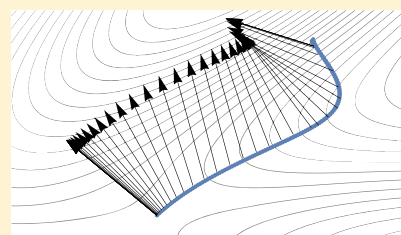
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Supporting Information

ABSTRACT: An algorithm to locate transition states on a potential energy surface (PES) is proposed and described. The technique is based on the GAD method where the gradient of the PES is projected into a given direction and also perpendicular to it. In the proposed method, named GAD-CD, the projection is not only applied to the gradient but also to the Hessian matrix. Then, the resulting Hessian matrix is block diagonal. The direction is updated according to the GAD method. Furthermore, to ensure stability and to avoid a high computational cost, a trust region technique is incorporated and the Hessian matrix is updated at each iteration. The performance of the algorithm in comparison with the standard ascent dynamics is discussed for a simple two dimensional model PES. Its efficiency for describing the reaction mechanisms involving small and medium size molecular systems is demonstrated for five molecular systems of interest.



1. INTRODUCTION

An extensive mathematical literature has been accumulated in the last 50 years for the location of saddle points of index one on continuous and differentiable functions of several variables. The interest for this type of points lies on the fact that they correspond to transition states (TSs), which are the cornerstone of all chemical reaction rate theories and hence are essential in establishing the mechanism of any chemical transformation. A saddle point of index one is a stationary point on a surface and the corresponding Hessian matrix, the matrix of second-order partial derivatives with respect to the coordinates, has one and only one negative eigenvalue. Many different methods have been proposed in the literature that are based on few common approximations, thus, in many cases, it is difficult to establish the effectiveness and differences among them. As it will be shown, the proposed gentlest ascent dynamics-conjugate directions (GAD-CD) method takes into account, in different ways, the achievements and particularities of many previous methods to locate TSs. In this way, we expect to have a robust and efficient method to locate such points. In contrast to the original GAD method,¹ we will demonstrate that GAD-CD allows for a second-order expansion of the coordinates, thus making the method more robust.

The structure of the article is as follows. We will first provide in Section 2, a brief historical review describing the nature of some of the most widely used methodologies for TS location in order to put the proposed method in the appropriate

context. We will then introduce the mathematical basis of the GAD-CD method and also the flowchart of the associated algorithm in Section 3. The performance and behavior of the method is discussed and analyzed in Section 4. Conclusions are given in Section 5.

2. BRIEF HISTORICAL REVIEW OF THE METHODS TO LOCATE TS

The most primitive method to locate TSs is the so-called *grid search* on a potential energy surface (PES).^{2,3} In this method the PES is evaluated on a spatial grid of points that is assumed to span the saddle point of interest whose position is found by a polynomial fit. The accuracy of the method depends on the resolution of the multidimensional grid, which makes it prohibitive for moderate molecular systems.

Another widely used approach is the *reaction coordinate* method.^{4,5} Usually, in this method one selects a specific internal coordinate—or a subset of them—as a reaction coordinate. Step by step, the remaining coordinates are optimized between the reactant and product minima. The procedure can be seen as a predictor–corrector method. As a result, one obtains a reaction pathway and the corresponding energy profile where the maximum of which would occur at the saddle point. A more recent generalization of the reaction

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coordinate is the reduced gradient following or Newton trajectory.^{6–10} In this generalization of the reaction coordinate, the reaction pathway is built by the set points that fulfill that the gradient vector points to a constant direction. The curve passes through consecutive stationary points. In general, these methods involve the prediction of the selected variable and optimization for the last $N - 1$ variables taken as correctors, where N is the number of internal coordinates. The optimization involves the calculation of the Hessian matrix in an exact or approximated way. Note that different choices of the reaction coordinate, or which is the same, a constant search direction of the gradient, produce different reaction pathways; some of them have little or no chemical significance. Other types of reaction pathways have been proposed like the following of a valley ground along a gradient extremal.^{11–15} However, their computational demand limits their applicability.

In the early years, where the development of methods to locate TSs starts, the most common one was the minimization of the square of the gradient norm of the PES. This method was originally proposed by McIver and Komornicki^{16,17} and consists of the minimization of the function $\mathbf{g}^T(\mathbf{x})\mathbf{g}(\mathbf{x})$, where $\mathbf{g}(\mathbf{x})$ is the gradient vector at the point \mathbf{x} of the PES function $V(\mathbf{x})$, that is, $g_i(\mathbf{x}) = \partial V(\mathbf{x})/\partial x_i$ for $i = 1, \dots, N$. It is used as a standard least square minimization technique. Normally, the least squares algorithms show a poor rate of convergence. The main disadvantage of these methods is that while the square of the gradient norm must necessarily be zero at the TS, it is also zero at a local minimum or maximum of the PES function and hence there may be other nonzero minima on the square of the gradient norm surface for so-called shoulders. Thus, except in the case where one has an a-priori knowledge of the PES and starts from a point sufficiently close to the position of the TS, there is no guarantee that this method will converge to a TS. Nonetheless, a least squares minimization algorithm has been proposed and applied to locate other types of points on the PES with some degree of success.¹⁸

Other methods to locate TSs have been proposed to follow a reaction path from the minimum of the PES uphill to the TS. These methods can be labeled *uphill walk*. The Crippen–Scheraga¹⁹ algorithm was the pioneer for climbing out of the minimum basin of attraction. The method starts from the minimum point, \mathbf{x}_{\min} . At the iteration step i , the system is translated along the pre-established direction \mathbf{d} to yield $\mathbf{x}_i = \mathbf{x}_{\min} + \rho_i \mathbf{d}$, where ρ_i is a suitable step length. This is followed by an energy minimization on a hyperplane perpendicular to \mathbf{d} , $\text{HP}_i = \{(\mathbf{x} - \mathbf{x}_i)^T \mathbf{d} = 0\}$, to obtain $\mathbf{x}_{i+1} = \text{argmin}_{\mathbf{x} \in \text{HP}_i} V(\mathbf{x})$. The iterative process is repeated until the system reaches a saddle point. More recently proposed algorithms of this family for exploring high dimensional PES are based upon realizing that evaluating the eigenmodes of the Hessian is central to the convergence to a TS.²⁰ Another algorithm was suggested by Cerjan and Miller.²¹ It requires the selection of a trust region around a point on the multidimensional PES and it approximates the energy of the system within this trust region by a quadratic expression. An optimal direction to translate the system is then determined by evaluating the extremum of the energy on the boundary of the trust region. The key for a reliable evaluation of the optimal direction relies in the proper selection of the trust region. Within the same class of methods, Henkelman and Jónsson²² proposed the dimer algorithm where the dimer consists of two points separated by a small

distance. The dimer moves toward the TS by the modification of the $-\mathbf{g}(\mathbf{x})$ vector, namely, $-\mathbf{g}(\mathbf{x}) + 2\mathbf{v}(\mathbf{v}^T \mathbf{g}(\mathbf{x}))$, where the direction \mathbf{v} is the dimer direction being determined by minimizing the dimer energy. Related to this type of methods, there is also the algorithm proposed by Ohno and Maeda²³ and Shang and Liu.²⁴ More recently it has been proposed by the so-called GAD¹ method that goes a step back and reformulates the procedure of uphill walking through a set of ordinary differential equations whose solutions converge to saddle points.^{25–30} The set of equations that governs the GAD is

$$\frac{d\mathbf{x}}{dt} = -[\mathbf{I} - 2\mathbf{v}\mathbf{v}^T]\mathbf{g}(\mathbf{x}) \quad (1a)$$

$$\frac{d\mathbf{v}}{dt} = -[\mathbf{I} - \mathbf{v}\mathbf{v}^T]\mathbf{H}(\mathbf{x})\mathbf{v} \quad (1b)$$

where $\mathbf{H}(\mathbf{x})$ is the Hessian matrix, that is, $H_{ij}(\mathbf{x}) = \partial^2 V(\mathbf{x})/\partial x_i \partial x_j$ and t is the parameter characterizing the GAD curve. Equation 1a means that the gradient is used by two different components, one in the ascent direction of the \mathbf{v} -vector subspace and the second in the descent direction of the set of directions perpendicular to the \mathbf{v} -vector. Equation 1b defines the update of the ascent direction represented by the \mathbf{v} -vector. The right-hand side of eq 1b ensures that the \mathbf{v} -vector converges to an eigenvector associated with the smallest eigenvalue of $\mathbf{H}(\mathbf{x})$, and we have to make sure that the \mathbf{v} -vector is normalized. At the starting point, the norm of the $\mathbf{v}(t_0)$ -vector is equal to 1. We remark that the GAD algorithm can be seen as a Zermelo-like navigation model on the PES to reach TSs in some optimal way, see refs 29 and 30 for a demonstration. For this reason, the \mathbf{v} -vector is also called the control vector.

Another family of very important methods is known as quasi-Newton type. In these methods the position of a local stationary point on the PES is located by an iterative procedure briefly outlined as follows. At the i -th iteration, a direction $\Delta \mathbf{x}^{(i)}$ is calculated according to the equation $\Delta \mathbf{x}^{(i)} = -\mathbf{H}^{-1(i)} \mathbf{g}^{(i)}$, where $\mathbf{H}^{-1(i)}$ is an approximation to the inverse Hessian matrix and $\mathbf{g}^{(i)}$ is the gradient vector at the point $\mathbf{x}^{(i)}$. The Hessian matrix is computed at the first iteration and subsequently updated during the procedure. The various quasi-Newton methods differ in the way in which the Hessian matrix (or its inverse) is updated. The new estimate of the stationary point $\mathbf{x}^{(i+1)}$ is usually taken as $\mathbf{x}^{(i+1)} = \mathbf{x}^{(i)} + \Delta \mathbf{x}^{(i)}$.³¹ There may seem to be no reason why this type of method, just outlined, could not be used for locating TSs, so long as at each iteration the Hessian matrix has one and only one negative eigenvalue. A quasi-Newton like method was devised by Schlegel for the first time.^{32,33} The quasi-Newton methods, however, suffer from the disadvantage that there is no way of preventing the Hessian matrix from becoming positive definite, which would cause the method to locate a local minimum rather than a TS. We note that quasi-Newton methods to find TSs can be seen as uphill walk methods from a minimum toward a saddle point of index one, achieved by maximizing the quadratic approximation of the PES along a direction and minimizing it along the other directions. The problem to avoid a positive Hessian matrix in the quasi-Newton search of TSs was considered by Banerjee et al.^{34,35} and others.^{36–39} This is achieved using the Levenberg–Marquardt technique³¹ consisting of a parametric modification of the second order term in the quadratic expansion, such that the resulting “perturbed”

Hessian matrix has a negative eigenvalue in one direction and positive eigenvalues in the remaining directions.

The first algorithm proposed for locating TSs based on the conjugate gradient optimization method was due to Sinclair and Fletcher.⁴⁰ This type of method allows for the use of line searches without the generation of zero-curvature search directions. The basic concept of these methods is the so-called conjugacy. Let us assume an N -dimensional quadratic PES with the Hessian matrix \mathbf{H} . Then, we say that two vectors, $\mathbf{v}^{(i)}$ and $\mathbf{v}^{(j)}$, are H -conjugate when they have the property that $\mathbf{v}^{(i)\text{T}}\mathbf{H}\mathbf{v}^{(j)} = 0$.³¹ If the Hessian matrix has only one negative eigenvalue and if the $\mathbf{v}^{(i)}$ -vector is a direction of negative curvature, that is $\mathbf{v}^{(i)\text{T}}\mathbf{H}\mathbf{v}^{(i)} < 0$, then the remaining conjugate vectors, $\mathbf{v}^{(j)}$ ($j \neq i$), have necessarily non-negative curvature. Briefly, the structure of these methods to locate a TS is described as follows. We start at a point, $\mathbf{x}^{(1)}$, assumed to be in the midpoint between two minima, and with a $\mathbf{v}^{(1)}$ -vector which depicts the straight-line joining these minima. The first iteration consists in searching the maximum $\mathbf{x}^{(2)}$ along the line $\mathbf{v}^{(1)}$. A conjugate vector, $\mathbf{v}^{(2)}$, is then computed as the component of $-\mathbf{g}^{(2)}$, H -conjugate to $\mathbf{v}^{(1)}$, resulting in

$$\begin{aligned}\mathbf{v}^{(2)} &= -\mathbf{g}^{(2)} + \frac{\mathbf{g}^{(2)\text{T}}(\mathbf{g}^{(2)} - \mathbf{g}^{(1)})}{\mathbf{v}^{(1)\text{T}}(\mathbf{g}^{(2)} - \mathbf{g}^{(1)})}\mathbf{v}^{(1)} \\ &= -\mathbf{g}^{(2)} + (\mathbf{g}^{(2)\text{T}}\mathbf{h}^{(1)})\mathbf{v}^{(1)}\end{aligned}\quad (2)$$

Thus, the $\mathbf{v}^{(2)}$ conjugate vector is found only using the gradients $\mathbf{g}^{(1)}$ and $\mathbf{g}^{(2)}$, and the original vector $\mathbf{v}^{(1)}$. A search for a minimum is made along this new vector. In a similar way in the subsequent iterations new H -conjugate vectors are generated, say $\mathbf{v}^{(i+1)}$, using only the gradient $\mathbf{g}^{(i+1)}$, the vectors $\mathbf{h}^{(1)}$, $\mathbf{v}^{(1)}$, and $\mathbf{v}^{(i)}$. The new H -conjugate vectors are obtained through the expression $\mathbf{v}^{(i+1)} = -\mathbf{g}^{(i+1)} + (\mathbf{g}^{(i+1)\text{T}}\mathbf{h}^{(1)})\mathbf{v}^{(1)} + \|\mathbf{g}^{(i+1)}\|/\|\mathbf{g}^{(i)}\|\mathbf{v}^{(i)}$, and linear searches are in turn carried out along each of these directions. After each iteration, it is necessary to make a test to ensure that the current gradient along the initial vector, $\mathbf{v}^{(1)}$, is still close to zero. If the current gradient, $\mathbf{g}^{(i+1)}$, along the $\mathbf{v}^{(1)}$ -vector is too large then the algorithm is restarted by replacing, $\mathbf{x}^{(1)}$, with the current point, $\mathbf{x}^{(i+1)}$. The algorithm continues until the gradient norm is less than a given tolerance. We note that if the exact line searches are performed on a quadratic function then the magnitude $\mathbf{v}^{(1)\text{T}}\mathbf{g}^{(i)}$ would remain zero throughout. Also, the algorithm would never need to restart. In other words, using this method on a quadratic PES, the TS would be found in at most N iterations, N being the number of variables. On the other hand, on a nonquadratic PES it is always necessary to check the projection of the current gradient along the $\mathbf{v}^{(1)}$ -vector to ensure that the algorithm converges to the TS. The main disadvantage of these methods is that the convergence rate is rarely well behaved. Even on a quadratic PES there is no guarantee that a conjugate gradient method will converge in N iterations, whereas the quasi-Newton method will converge in one iteration given the exact Hessian matrix. It is, in fact, well known that the quasi-Newton methods will converge to stationary points much faster than any general conjugate direction methods, in particular the conjugate gradient.

It is worth mentioning that the algorithm proposed by Bell et al.^{41,42} works well on PESs that are not far from being quadratic. This algorithm commences, as above, by finding a maximum along a $\mathbf{v}^{(1)}$ -vector that is known to have a negative curvature. Furthermore, a quasi-Newton minimization is then

made in a space of $(N - 1)$ linearly independent vectors which is the H -conjugate to the $\mathbf{v}^{(1)}$ -vector. If the PES is quadratic then the gradient component along this vector would remain zero during the minimization in the $(N - 1)$ -space H -conjugate to the $\mathbf{v}^{(1)}$ -vector. In nonquadratic PESs, this gradient could be different from zero. For this reason, conjugate gradient methods require a test to check the value of this gradient and, if necessary, another search along the $\mathbf{v}^{(1)}$ vector for a maximum. Thereafter, a new minimization on the $(N - 1) - H$ -conjugate space is carried out. This ensures that the algorithm is stable and converges to a TS. We note that the algorithm of Bell et al.^{41,42} is based on an interplay between the conjugate gradient and quasi-Newton methods. The conjugate gradient performs the maximization, whereas the quasi-Newton method performs the minimization to find the TS. The main difficulty of this algorithm appears when the TS is very far from the line characterized by the $\mathbf{v}^{(1)}$ -vector and frequently the H matrix ceases to have a negative curvature after some minimizations. These difficulties were partially solved in a later improvement of the method.⁴²

The so-called *synchronous transit* method proposed by Halgren and Lipscomb⁴³ has inspired a large number of algorithms. The synchronous transit methods consist, like the conjugate gradient method, in alternating maximum and minimum searches, starting with a search for a maximum along the line joining two known minima of the PES, the linear synchronous transit. A minimization is then carried out along directions orthogonal to the linear synchronous transit followed by the maximum search along a parabolic path containing the two minima and the current estimate of the TS. This minimization and maximization search process is repeated until the TS is obtained. Schlegel et al.⁴⁴ improved the original algorithm of Halgren and Lipscomb⁴³ by performing a combination of synchronous transit and quasi-Newton minimizations. Other algorithms that can be classified within this set of methods are those given in the refs.^{45–51} It is worth mentioning a recent improvement within this type of methods due to Zimmerman.⁵²

The algorithm presented in this work, the GAD-CD method, is designed as an interplay between the conjugate direction,^{31,53} quasi-Newton,³¹ and GAD methods.¹ In part, the algorithm is based on the results from Bell et al.,⁴¹ GAD¹ and also the restricted step technique³¹ to improve the stability of the entire procedure to locate TSs on general PESs. In the following section, we explain and summarize the basic mathematical points of the algorithm and its implementation.

3. GAD-CD METHOD

3.1. Mathematical Basis. We will find a stationary point say, \mathbf{x}_{TS} , on a PES, $V(\mathbf{x})$, by successive quadratic expansions of this surface, denoted by $q(\mathbf{x})$. The dimension of the \mathbf{x} vector is N . Let \mathbf{v}_1 be a given normalized direction vector such that the energy increases in this direction. Let \mathbf{x}_0 be a point where the quadratic expansion is centered and $q(\mathbf{x}_0 + \mathbf{v}_1 a_1)$ is maximized over a_1 . We expect to construct a \mathbf{V}_{N-1} matrix of dimension $N \times (N - 1)$ with $N - 1$ independent column vectors, $\mathbf{V}_{N-1} = [\mathbf{v}_2 | \dots | \mathbf{v}_N]$, such that $\mathbf{V}_{N-1}^{\text{T}}\mathbf{H}_0\mathbf{v}_1 = \mathbf{0}_{N-1}$, where \mathbf{H}_0 is the Hessian matrix at \mathbf{x}_0 and $\mathbf{0}_{N-1}$ the zero vector of dimension $N - 1$. Under these conditions, we can say that the direction $\mathbf{x}' - \mathbf{x}_0 = \mathbf{V}_{N-1}\mathbf{a}_{N-1}$ is the H_0 -conjugate to the \mathbf{v}_1 direction vector, where $\mathbf{a}_{N-1} = (a_2, \dots, a_N)^{\text{T}}$, is a vector of dimension $N - 1$ and it is different from the zero vector. More specifically, $(\mathbf{x}' - \mathbf{x}_0)^{\text{T}}\mathbf{H}_0\mathbf{v}_1 = \mathbf{a}_{N-1}^{\text{T}}\mathbf{V}_{N-1}^{\text{T}}\mathbf{H}_0\mathbf{v}_1 = \mathbf{a}_{N-1}^{\text{T}}\mathbf{0}_{N-1} = 0$, which is the

conjugacy conditions. Then, from the theory of conjugate directions it can be shown that the matrix $\mathbf{V} = [\mathbf{v}_1 | \mathbf{V}_{N-1}]$ is nonsingular and hence that $\mathbf{V}^T \mathbf{H}_0 \mathbf{V}$ can be chosen in such a way that the resulting matrix has a negative curvature on $\mathbf{v}_1^T \mathbf{H}_0 \mathbf{v}_1$ and $\mathbf{V}_{N-1}^T \mathbf{H}_0 \mathbf{V}_{N-1}$ is positive definite. In this way, $q(\mathbf{x}_0 + \mathbf{V}_{N-1} \mathbf{a}_{N-1}) = V(\mathbf{x}_0) + \mathbf{g}_0^T \mathbf{V}_{N-1} \mathbf{a}_{N-1} + 1/2 \mathbf{a}_{N-1}^T \mathbf{V}_{N-1}^T \mathbf{H}_0 \mathbf{V}_{N-1} \mathbf{a}_{N-1}$ has a unique minimizing point

$$\mathbf{x}' = \mathbf{x}_0 - \mathbf{V}_{N-1} (\mathbf{V}_{N-1}^T \mathbf{H}_0 \mathbf{V}_{N-1})^{-1} \mathbf{V}_{N-1}^T \mathbf{g}_0 \quad (3)$$

where \mathbf{g}_0 is the gradient of the PES at \mathbf{x}_0 . If $\mathbf{g}(\mathbf{x}')$, the gradient of the PES at \mathbf{x}' , satisfies that $\mathbf{V}^T \mathbf{g}(\mathbf{x}') = \mathbf{0}$, then \mathbf{x}' is a saddle point of index one or a TS on $q(\mathbf{x}')$ and also on the PES.

Now the task to write an algorithm is reduced first to find a suitable \mathbf{V}_{N-1} matrix and second to search a way to find the \mathbf{v}_1 direction vector. The \mathbf{V}_{N-1} matrix can be constructed and obtained from an elementary Householder orthogonal matrix $\mathbf{Q} = \mathbf{I} - 2\mathbf{w}(\mathbf{w}^T \mathbf{w})^{-1} \mathbf{w}^T$, where \mathbf{w} is a vector of dimension N such that $\mathbf{Q}\mathbf{t} = \pm \|\mathbf{t}\| \mathbf{e}_1$, and $\mathbf{t} = \mathbf{H}_0 \mathbf{v}_1$, \mathbf{e}_1 is the first column of the unit matrix \mathbf{I} of dimension $N \times N$ and $\|\mathbf{t}\| = (\mathbf{t}^T \mathbf{t})^{1/2}$.⁴¹ Thus, the symmetric orthogonal matrix $\mathbf{Q} = [\mathbf{q}_1 | \mathbf{Q}_{N-1}]$ constructed in this way is such that $\mathbf{t}^T \mathbf{Q} = \mathbf{v}_1^T \mathbf{H}_0 \mathbf{Q} = (\mathbf{v}_1^T \mathbf{H}_0 \mathbf{q}_1, \mathbf{v}_1^T \mathbf{H}_0 \mathbf{Q}_{N-1}) = (\mathbf{v}_1^T \mathbf{H}_0 \mathbf{q}_1, \mathbf{0}_{N-1}^T) = (\pm \|\mathbf{t}\|, \mathbf{0}_{N-1}^T) = \pm \|\mathbf{t}\| \mathbf{e}_1^T$. \mathbf{Q}_{N-1} is then an $N \times (N-1)$ matrix of independent columns satisfying $\mathbf{Q}_{N-1}^T \mathbf{H}_0 \mathbf{v}_1 = \mathbf{0}_{N-1}$ and thus a representation of the \mathbf{V}_{N-1} matrix, $\mathbf{Q}_{N-1} = \mathbf{V}_{N-1}$. The \mathbf{Q} matrix is a rank-one matrix with the unit matrix \mathbf{I}

$$\mathbf{Q}\mathbf{t} = (\mathbf{I} - 2\mathbf{w}(\mathbf{w}^T \mathbf{w})^{-1} \mathbf{w}^T) \mathbf{t} = \pm \|\mathbf{t}\| \mathbf{e}_1 \quad (4)$$

If we take $2(\mathbf{w}^T \mathbf{w})^{-1} \mathbf{w}^T \mathbf{t} = 1$, then the vector $\mathbf{w} = \mathbf{t} \pm \|\mathbf{t}\| \mathbf{e}_1$ and $2(\mathbf{w}^T \mathbf{w})^{-1} = (\mathbf{w}^T \mathbf{t})^{-1} = (\mathbf{t}^T \mathbf{t} \pm \|\mathbf{t}\| t_1)^{-1}$, where t_1 is the first component of the \mathbf{t} vector. The resulting matrix \mathbf{Q} is

$$\mathbf{Q} = \mathbf{I} - 2\mathbf{w}(\mathbf{w}^T \mathbf{w})^{-1} \mathbf{w}^T = \mathbf{I} - (\mathbf{t} \pm \|\mathbf{t}\| \mathbf{e}_1)(\mathbf{t}^T \mathbf{t} \pm \|\mathbf{t}\| t_1)^{-1} (\mathbf{t} \pm \|\mathbf{t}\| \mathbf{e}_1)^T \quad (5)$$

The last $N-1$ columns of this matrix form the \mathbf{Q}_{N-1} matrix, $\mathbf{V} = [\mathbf{v}_1 | \mathbf{V}_{N-1}] = [\mathbf{v}_1 | \mathbf{Q}_{N-1}]$. We note that the idea underlying the above results is a theorem due to Powell on the parallel subspace property of conjugate directions.^{31,53} This theorem establishes that on a quadratic surface, for $a_1 \neq 0$ the relation $\Delta \mathbf{g}_0 = \mathbf{g}(\mathbf{x}_0 + \mathbf{v}_1 a_1) - \mathbf{g}(\mathbf{x}_0) = \mathbf{H}_0 \mathbf{v}_1 a_1$ always holds. If the gradient difference vector, $\Delta \mathbf{g}_0$, has a null projection into the subspace spanned by the set of linear independent vectors, \mathbf{V}_{N-1} , then these vectors are H_0 -conjugate with respect to the vector \mathbf{v}_1 . In other words, $\mathbf{V}_{N-1}^T \Delta \mathbf{g}_0 = \mathbf{V}_{N-1}^T \mathbf{H}_0 \mathbf{v}_1 a_1 = \mathbf{0}_{N-1}$ implies the H_0 -conjugacy because by hypothesis $a_1 \neq 0$. Notice that the set of vectors, \mathbf{V}_{N-1} , can be H_0 -conjugate within them or not, the only requirement is their linear independence. This theorem permits us to propose an extension to quadratic order in $\Delta \mathbf{x}$ of the GAD method, by minimizing the energy surface in the subspace spanned by the set of vectors H_0 -orthogonal to the direction of the control vector \mathbf{v}_1 . Now, we only need a correction to the second order expansion and the way to update the \mathbf{v}_1 -vector. As will be shown below, the first question is addressed through the restricted step technique.³¹

The quadratic approximation of the PES, $V(\mathbf{x})$, around \mathbf{x}_0 takes the form

$$\begin{aligned} V(\mathbf{x}_0 + \Delta \mathbf{x}_0) &\approx q(\mathbf{x}_0 + \Delta \mathbf{x}_0) = q(\mathbf{x}_0 + \mathbf{V}\mathbf{a}) = V(\mathbf{x}_0) + \mathbf{a}^T \mathbf{V}^T \mathbf{g}_0 \\ &+ 1/2 \mathbf{a}^T \mathbf{V}^T \mathbf{H}_0 \mathbf{V} \mathbf{a} = V(\mathbf{x}_0) + a_1 \mathbf{v}_1^T \mathbf{g}_0 + 1/2 a_1^2 \mathbf{v}_1^T \mathbf{H}_0 \mathbf{v}_1 \\ &+ \mathbf{a}_{N-1}^T \mathbf{V}_{N-1}^T \mathbf{g}_0 + 1/2 \mathbf{a}_{N-1}^T \mathbf{V}_{N-1}^T \mathbf{H}_0 \mathbf{V}_{N-1} \mathbf{a}_{N-1} = V(\mathbf{x}_0) \\ &+ q_+(a_1) + q_-(\mathbf{a}_{N-1}) \end{aligned} \quad (6)$$

where $\Delta \mathbf{x}_0 = \mathbf{x} - \mathbf{x}_0$, $\mathbf{a}^T = (a_1, \mathbf{a}_{N-1}^T)$, and $\Delta \mathbf{x}_0 = \mathbf{V}\mathbf{a}$. The confidence in the quadratic approximation is warranted by a restricted step method characterized by a trust radius r defined as $\mathbf{a}^T \mathbf{a} = \|\mathbf{a}\|^2 \leq r^2$. The TS search is performed via the maximization of the quadratic approximation $q_+(a_1)$ along the subspace \mathbf{v}_1 , and the minimization of the approximation $q_-(\mathbf{a}_{N-1})$ in the \mathbf{V}_{N-1} subspace. Both subspaces are H_0 -conjugate, because $\mathbf{V}_{N-1}^T \mathbf{H}_0 \mathbf{v}_1 = \mathbf{0}_{N-1}$.

The mathematical formalization of the above problem can be written as

$$\begin{aligned} q_{\text{optimal}}(\mathbf{x}_0 + \mathbf{V}\mathbf{a}) &= V(\mathbf{x}_0) + \text{MaxMin}\{q_+(a_1) + q_-(\mathbf{a}_{N-1}) \\ &\text{la}^T \mathbf{a} \leq r^2 \text{ and } \mathbf{a} \in \mathbb{R}^N\} = V(\mathbf{x}_0) + \text{Min}_a\{-q_+(a_1) + q_-(\mathbf{a}_{N-1}) \\ &\text{la}^T \mathbf{a} \leq r^2 \text{ and } \mathbf{a} \in \mathbb{R}^N\} \end{aligned} \quad (7)$$

where r is a positive scalar. A solution of this problem can be found using the Lagrangian multipliers method

$$L(\mathbf{a}, \lambda) = -q_+(a_1) + q_-(\mathbf{a}_{N-1}) + \lambda/2(\mathbf{a}^T \mathbf{a} - r^2) \quad (8)$$

Differentiation with respect to \mathbf{a} and λ yields, after some rearrangements, the equations

$$\mathbf{a} = -(\mathbf{M}_0 + \lambda \mathbf{I})^{-1} \mathbf{h}_0 \quad (9a)$$

$$\mathbf{a}^T \mathbf{a} - r^2 = 0 \quad (9b)$$

where $\mathbf{h}_0^T = (-\mathbf{g}_0^T \mathbf{v}_1, \mathbf{g}_0^T \mathbf{V}_{N-1})$ and \mathbf{M}_0 is the block diagonal matrix

$$\mathbf{M}_0 = \begin{pmatrix} -\mathbf{v}_1^T \mathbf{H}_0 \mathbf{v}_1 & \mathbf{0}_{N-1}^T \\ \mathbf{0}_{N-1} & \mathbf{V}_{N-1}^T \mathbf{H}_0 \mathbf{V}_{N-1} \end{pmatrix} \quad (10)$$

of dimension $N \times N$. Substituting eq 9a into eq 9b, we obtain the secular function

$$f(\lambda) = \mathbf{h}_0^T (\mathbf{M}_0 + \lambda \mathbf{I})^{-2} \mathbf{h}_0 - r^2 \quad (11)$$

the zeros of which are to be computed. To solve the max–min problem, the parameter λ is chosen to satisfy $f(\lambda) = 0$ and the two conditions:

1. $(\mathbf{v}_1^T \mathbf{H}_0 \mathbf{v}_1 - \lambda) < 0$ to obtain an uphill direction of $q(\mathbf{x})$ in the subspace spanned by \mathbf{v}_1 ,
2. $\det(\mathbf{V}_{N-1}^T \mathbf{H}_0 \mathbf{V}_{N-1} + \lambda \mathbf{I}_{N-1}) > 0$ to obtain a downhill direction of $q(\mathbf{x})$ in the subspace spanned by the set of columns of \mathbf{V}_{N-1} .

Here, \mathbf{I}_{N-1} is the unit matrix of dimension $(N-1) \times (N-1)$. If the \mathbf{H}_0 has the expected structure and the quasi-Newton step lies within the boundary of the trust region, $\mathbf{a}^T \mathbf{a} < r^2$, then the quasi-Newton step is taken. Otherwise the step is chosen in the boundary of the trust region, $\mathbf{a}^T \mathbf{a} = r^2$, by finding the λ that satisfies $f(\lambda) = 0$ and the above conditions 1 and 2.

Now, we propose an algorithm that solves the secular function $f(\lambda) = 0$ of eq 11. To this end, we multiply this equality by the quantity, $\mathbf{h}_0^T \mathbf{b} r^{-2}$, where \mathbf{b} is a vector different from zero of dimension N and not orthogonal to the \mathbf{h}_0 vector. The resulting expression is

$$\mathbf{h}_0^T [\mathbf{b} - (\mathbf{M}_0 + \lambda \mathbf{I})^{-2} \mathbf{h}_0 \mathbf{h}_0^T \mathbf{b} r^{-2}] = 0 \quad (12)$$

Because $\mathbf{h}_0 \neq \mathbf{0}$ then we can write, $(\mathbf{M}_0 + \lambda \mathbf{I})^2 \mathbf{b} - \mathbf{h}_0 \mathbf{h}_0^T \mathbf{b} r^{-2} = \mathbf{0}$. By defining a new vector, $\mathbf{p} = (\mathbf{M}_0 + \lambda \mathbf{I}) \mathbf{b}$, the latter equation can be written in the form $(\mathbf{M}_0 + \lambda \mathbf{I}) \mathbf{p} - \mathbf{h}_0 \mathbf{h}_0^T \mathbf{b} r^{-2} = \mathbf{0}$. The above two equalities can be written in a compact form as an eigenvalue equation

$$\begin{pmatrix} -\mathbf{M}_0 & \mathbf{I} \\ r^{-2}\mathbf{h}_0\mathbf{h}_0^T & -\mathbf{M}_0 \end{pmatrix} \begin{pmatrix} \mathbf{b} \\ \mathbf{p} \end{pmatrix} = \lambda \begin{pmatrix} \mathbf{b} \\ \mathbf{p} \end{pmatrix} \quad (13)$$

Let us denote the real solutions of this real nonsymmetric eigenvalue eq 13 by the triples, $\{(\lambda_i, \mathbf{b}_i^T, \mathbf{p}_i^T)\}_{i=1}^{n_{\text{real}}}$, where λ_i are given in increasing order and $n_{\text{real}} \leq 2N$. Substituting any real triple in the eigenvalue eq 13 and using eq 9a, we obtain

$$\mathbf{a}_i = -\mathbf{p}_i^T (\mathbf{h}_0^T \mathbf{b}_i)^{-1} r^2 \quad i = 1, \dots, n_{\text{real}} \quad (14)$$

If we multiply eq 14 from the left by $-\mathbf{h}_0^T (\mathbf{M}_0 + \lambda \mathbf{I})^{-1}$ and if we take into account eq 9a and the fact that $\mathbf{h}_0^T (\mathbf{M}_0 + \lambda \mathbf{I})^{-1} \mathbf{p}_i = \mathbf{h}_0^T \mathbf{b}_i$, then we conclude from eq 13 that all these solutions satisfy the relation $\mathbf{a}_i^T \mathbf{a}_i = r^2$ for $i = 1, \dots, n_{\text{real}}$. Within these real solutions, we have to find the solution that satisfies the above considerations 1 and 2. It is easy to check that the triple solution whose λ_i is located in the interval, $]\max\{\mathbf{v}_1^T \mathbf{H}_0 \mathbf{v}_1, -h_{\text{min}}, 0\}, +\infty[$, where h_{min} is the lowest eigenvalue of $\mathbf{V}_{N-1}^T \mathbf{H}_0 \mathbf{V}_{N-1}$, satisfies these two requirements. We take the triple whose λ_i has the lowest value in the interval, that is, $(\lambda_i, \mathbf{b}_i^T, \mathbf{p}_i^T)$, corresponding to the tuple $(\lambda_i, \mathbf{a}_i^T)$, through eq 14. The selected tuple, $(\lambda_i, \mathbf{a}_i^T)$, is called from now, (λ, \mathbf{a}^T) . We emphasize that this tuple is the solution of eqs 9a,9b and in addition satisfies the conditions 1 and 2. With this choice, $q_{\text{optimal}}(\mathbf{x} + \mathbf{V}\mathbf{a})$ has the minimum value because λ is the lowest eigenvalue. Note that

$$\begin{aligned} q_{\text{optimal}}(\mathbf{x} + \mathbf{V}\mathbf{a}) - V(\mathbf{x}_0) &= 1/2(\mathbf{a}^T \mathbf{I}_- \mathbf{h}_0 - \lambda \mathbf{a}^T \mathbf{I}_- \mathbf{a}) \\ &= 1/2(\mathbf{a}^T \mathbf{I}_- \mathbf{h}_0 + \lambda(2a_1^2 - r^2)) \end{aligned} \quad (15)$$

where

$$\mathbf{I}_- = \begin{pmatrix} -1 & \mathbf{0}_{N-1}^T \\ \mathbf{0}_{N-1} & \mathbf{I}_{N-1} \end{pmatrix} \quad (16)$$

and a_1 is the first component of the \mathbf{a} vector. In the derivation of eq 15, we have used the equality, $r^2 = \mathbf{a}^T \mathbf{a} = a_1^2 + \mathbf{a}_{N-1}^T \mathbf{a}_{N-1}$, where, $\mathbf{a}_{N-1} = (a_2, \dots, a_N)^T$. The trust radius is updated according to the following simple algorithm. First, the new $V(\mathbf{x})$ is computed where $\mathbf{x} = \mathbf{x}_0 + \Delta \mathbf{x}_0 = \mathbf{x}_0 + \mathbf{V}\mathbf{a}$ obtained from the tuple with λ . Second, we compute the quotient $c = (V(\mathbf{x}) - V(\mathbf{x}_0)) / (q_{\text{optimal}}(\mathbf{x}_0 + \mathbf{V}\mathbf{a}) - V(\mathbf{x}_0))$. Now, if $c \leq c_{\text{min}}$ or $c \geq (2 - c_{\text{min}})$, then we set $r/c_f \rightarrow r$. Contrarily, if $c \geq c_{\text{accept}}$ and $c \leq (2 - c_{\text{accept}})$ and $\mathbf{a}^T \mathbf{a} < r^2$, then \mathbf{a} is evaluated according to a pure Newton step, that is, if $\mathbf{a} = -\mathbf{M}_0^{-1} \mathbf{h}_0$, then $r c_f^{1/2} \rightarrow r$. Throughout, we take $c_{\text{min}} = 0.75$, $c_{\text{accept}} = 0.80$ and $c_f = 2$. The displacement $\Delta \mathbf{x}_0$ is accepted if $0 < c < 2$. Otherwise, a new set of triples is computed with the new r but the same \mathbf{x}_0 and a new c is obtained and tested. This is repeated until $0 < c < 2$.

If for the new \mathbf{x} , $\|\mathbf{g}(\mathbf{x})\|$ is lower than a threshold, then the process has converged and \mathbf{x} is a TS. Otherwise, we first update the \mathbf{v}_1 vector, the control vector, according to the second GAD formula, eq 1b

$$\mathbf{v}_1 = s[\mathbf{v}_1 - m(\mathbf{I} - \mathbf{v}_1 \mathbf{v}_1^T) \mathbf{H}_0 \mathbf{v}_1] \quad (17)$$

where s is the normalization factor such that $\mathbf{v}_1^T \mathbf{v}_1 = 1$ and $m = (\Delta \mathbf{x}_0^T \Delta \mathbf{x}_0)^{1/2}$. Second, with the new gradient $\mathbf{g}(\mathbf{x})$ the vector $\mathbf{j}_0 = \mathbf{g}(\mathbf{x}) - \mathbf{g}(\mathbf{x}_0) - \mathbf{H}_0 \Delta \mathbf{x}_0$ is built and the Hessian matrix is updated according to the general Greenstadt variational formula⁵⁴

$$\mathbf{H} = \mathbf{H}_0 + \mathbf{j}_0 \mathbf{u}_0^T + \mathbf{u}_0 \mathbf{j}_0^T - (\mathbf{j}_0^T \Delta \mathbf{x}_0) \mathbf{u}_0 \mathbf{u}_0^T \quad (18)$$

where $\mathbf{u}_0 = \mathbf{W} \Delta \mathbf{x}_0 / (\Delta \mathbf{x}_0^T \mathbf{W} \Delta \mathbf{x}_0)$, \mathbf{W} being the inverse of a symmetric positive weighted matrix. In order to use the Murtagh–Sargent–Powell update formula, in the present algorithm we take $\mathbf{W} = \phi \Delta \mathbf{x}_0 \Delta \mathbf{x}_0^T + (1 - \phi) \mathbf{j}_0 \mathbf{j}_0^T$ where $\phi = (\mathbf{j}_0^T \Delta \mathbf{x}_0)^2 (\Delta \mathbf{x}_0^T \Delta \mathbf{x}_0 \mathbf{j}_0^T \mathbf{j}_0)^{-1}$.^{31,54–59} Notice that $\mathbf{u}_0^T \Delta \mathbf{x}_0 = 1$ and thus the condition, $\mathbf{H} \Delta \mathbf{x}_0 = \mathbf{g}(\mathbf{x}) - \mathbf{g}(\mathbf{x}_0)$, is satisfied. Finally, we reveal the potential energy, vectors, and matrices, $V(\mathbf{x}) \rightarrow V(\mathbf{x}_0)$, $\mathbf{x} \rightarrow \mathbf{x}_0$, $\mathbf{g}(\mathbf{x}) \rightarrow \mathbf{g}(\mathbf{x}_0)$, $\mathbf{v}_1 \rightarrow \mathbf{v}_1$, and $\mathbf{H} \rightarrow \mathbf{H}_0$ and a new iteration begins constructing the \mathbf{Q} matrix, eq 5, and solving the problem given in eq 7.

As a final comment, we remark some basic equivalences between the GAD algorithm^{1,25–30} and the GAD-CD presented in this work. In the original GAD model, the trajectory optimally transverses the set of equipotential surfaces while evolving toward the TS, see eq 17 in ref 30. The trajectory is guided by the \mathbf{v} -vector. Alternatively, in the GAD-CD method, each point of the trajectory satisfies an optimal max–min solution of a quadratic approximation to the PES, see eq 7. This optimal solution does also depend on the \mathbf{v}_1 -vector. In both methods, the \mathbf{v} -vector is found at each point under the condition that it minimizes the Rayleigh–Ritz quotient, $\mathbf{v}_1^T \mathbf{H}_0 \mathbf{v}_1 / (\mathbf{v}_1^T \mathbf{v}_1)$, given in eq 1b for the GAD method and eq 17 for the GAD-CD.

3.2. Description of the Algorithm. The above-detailed GAD-CD method can be practically implemented according to an operational algorithm that can be schematically described according to the flowchart below. The sub-index, i , and the super-index, (i) , refer to the iteration number. This algorithm has been interfaced with the Turbomole package.⁶⁰

1. Initialization.

- Choose a guess \mathbf{x}_0 and an initial trust radius r_0 .
- Calculate the potential energy, V_0 , the gradient vector, \mathbf{g}_0 , and the Hessian matrix, \mathbf{H}_0 .
- Select the normalized $\mathbf{v}_1^{(0)}$ -vector, usually an eigenvector of the \mathbf{H}_0 matrix.
- Set $i = 0$.

2. Hessian and gradient transformation.

- Compute the element $\mathbf{v}_1^{(i)T} \mathbf{H}_i \mathbf{v}_1^{(i)}$.
- Evaluate the vector $\mathbf{w}^{(i)} = \mathbf{t}^{(i)} - \|\mathbf{t}^{(i)}\| \mathbf{e}_1$, where $\mathbf{t}^{(i)} = \mathbf{H}_i \mathbf{v}_1^{(i)}$, and hence calculate $\mathbf{Q}^{(i)}$ according to eq 5. Obtain the $\mathbf{V}_{N-1}^{(i)}$ matrix from $\mathbf{Q}^{(i)}$ by taking the last $N - 1$ columns.
- Calculate $\mathbf{V}_{N-1}^{(i)T} \mathbf{H}_i \mathbf{V}_{N-1}^{(i)}$ and $\mathbf{h}_i = [-\mathbf{v}_1^{(i)T} \mathbf{V}_{N-1}^{(i)}]^T \mathbf{g}_i$.
- Build the \mathbf{M}_i -matrix according to eq 10 taking into account that $\mathbf{v}_1^{(i)T} \mathbf{H}_i \mathbf{v}_1^{(i)}$ should be multiplied by -1 , $\mathbf{v}_1^{(i)T} \mathbf{H}_i \mathbf{v}_1^{(i)} \rightarrow -\mathbf{v}_1^{(i)T} \mathbf{H}_i \mathbf{v}_1^{(i)}$.

3. Solution of the restricted step problem, mainly defined in eq 7

- Compute the Newton step, $\mathbf{a}^{(i)} = -\mathbf{M}_i^{-1} \mathbf{h}_i$. If $\mathbf{a}^{(i)T} \mathbf{a}^{(i)} \leq r_i^2$, $\mathbf{v}_1^{(i)T} \mathbf{H}_i \mathbf{v}_1^{(i)} < 0$, and $\det(\mathbf{V}_{N-1}^{(i)T} \mathbf{H}_i \mathbf{V}_{N-1}^{(i)}) > 0$ then the problem of eq 7 is solved. If $\mathbf{a}^{(i)T} \mathbf{a}^{(i)} < r_i^2$ then $r_i = (\mathbf{a}^{(i)T} \mathbf{a}^{(i)})^{1/2}$ is taken as the current trust radius. Compute the predicted energy change $q_{\text{optimal}}^{(i)} - V(\mathbf{x}_i) = -1/2 \mathbf{h}_i^T \mathbf{M}_i^{-1} \mathbf{h}_i$, otherwise,
- solve the nonsymmetric eigenproblem eq 13, take the real triple of lowest $\lambda_i^{(i)} = \lambda^{(i)}$. Using eq 14 compute $\mathbf{a}_i^{(i)}$ and evaluate $q_{\text{optimal}}^{(i)} - V(\mathbf{x}_i)$ through eq 15. Set $\mathbf{a}_1^{(i)} = \mathbf{a}^{(i)}$.

4. Trust region verification.

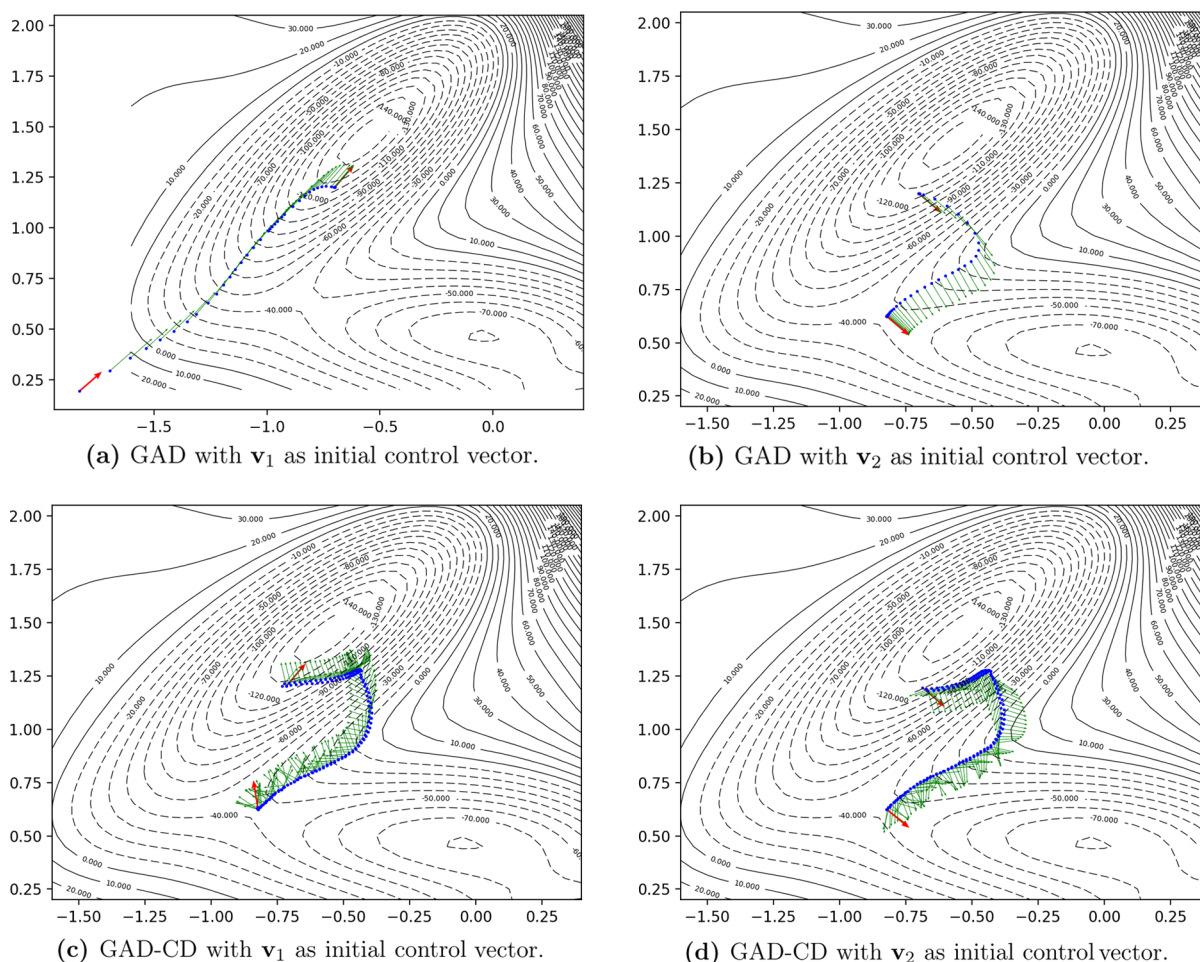


Figure 1. Behavior of GAD (a,b) and GAD-CD (c,d) methods on the two-dimensional Müller–Brown PES.⁶¹ The two curves are depicted in blue color. The set of arrows showing the evolution of the control \mathbf{v} -vector according to eq 17 is depicted in green color. The two red arrows are the initial and final control vectors. In both methods the starting point of the curve is $(-0.7, 1.2)$. The initial control vector, \mathbf{v}_1 , corresponds to the eigenvector with the lowest eigenvalue of the Hessian matrix evaluated in this point, whereas the initial control vector, \mathbf{v}_2 , is the eigenvector with the highest eigenvalue of this Hessian matrix. The achieved TS in the cases (b–d) is that located at the point $(-0.822, 0.624)$. In the case (a) the GAD method does not converge to a TS.

- Calculate the potential energy at the new point, $V_{\text{new}}^{(i)} = V(\mathbf{x}_i + \mathbf{V}^{(i)}\mathbf{a}^{(i)})$ where $\mathbf{V}^{(i)} = [\mathbf{v}_1^{(i)} | \mathbf{V}_{N-1}^{(i)}]$.
- Evaluate $c_i = (V_{\text{new}}^{(i)} - V(\mathbf{x}_i)) / (q_{\text{optimal}} - V(\mathbf{x}_i))$.
- If $c_i \leq c_{\text{min}}$ or $c_i \geq (2 - c_{\text{min}})$ then $r_{i+1} = r_i / c_i$.
- If $c_i \geq c_{\text{accep}}$ and $c_i \leq (2 - c_{\text{accep}})$ and $\mathbf{a}^{(i)\text{T}}\mathbf{a}^{(i)} < r_i^2$, then a pure Newton step leads to $r_{i+1} = r_i(c_i)^{1/2}$.

5. Acceptation of the current step.

- If $c_i < 2$ or $c_i > 2$ compute the new change $\Delta\mathbf{x}_i = \mathbf{V}^{(i)}\mathbf{a}^{(i)}$ at the same point \mathbf{x}_i but using the updated $r_{i+1} \rightarrow r_i$ and go back to 3. Otherwise,
- check the convergence criteria on $\{|\Delta\mathbf{x}_i|_{\mu}\}_{\mu=1}^N \leq \epsilon_x$ and $\{|\mathbf{g}_i|_{\mu}\}_{\mu=1}^N \leq \epsilon_g$. If they are fulfilled, the process has converged and the point \mathbf{x}_i is the first-order saddle point. Otherwise,
- make $\mathbf{x}_{i+1} = \mathbf{x}_i + \Delta\mathbf{x}_i$, $V_{\text{new}}^{(i)} = V(\mathbf{x}_{i+1})$, and compute $\mathbf{g}(\mathbf{x}_{i+1}) = \mathbf{g}_{i+1}$. Using eq 17 to update the \mathbf{v}_1 and set $\mathbf{v}_1^{(i+1)}$ to the new vector. Finally update the approximate Hessian matrix using eq 18. Set $i = i + 1$ and go back to 2.

4. APPLICATIONS AND PERFORMANCE OF THE GAD-CD ALGORITHM

4.1. Comparison between GAD and GAD-CD Algorithms.

The performance of the GAD-CD algorithm has been tested and compared with the results obtained using the GAD algorithm on the Müller–Brown PES,⁶¹ a simple two-variable model PES. The behavior of both methods is shown in Figure 1. In both cases, we consider the starting point, $(-0.7, 1.2)$, located near the minimum of the deep valley of the PES. The initial \mathbf{v} -vectors are, in each case, the eigenvector corresponding to the lowest eigenvalue, \mathbf{v}_1 , and the highest eigenvalue, \mathbf{v}_2 , of the Hessian matrix evaluated at this initial point. The components of these two vectors are $\mathbf{v}_1 = (0.651, 0.759)$ and $\mathbf{v}_2 = (0.759, -0.651)$. The TS achieved by both methods is that located at the point $(-0.822, 0.624)$. The integration of the GAD equations, eqs 1a,1b, is carried out using the Runge–Kutta-4,5 with adaptive size control and the Cash–Karp parameters.⁶² The Hessian matrix was computed analytically at each step of integration as required by the second GAD equation, namely, eq 1b. The step size of integration taken was very small, $h = 1 \times 10^{-6}$, otherwise the algorithm does not converge. The reason of this small step size is due to the fact that the initial point is located in a very deep valley. When the

initial control vector is \mathbf{v}_1 , the GAD does not reach the TS. The curve evolves toward the Müller–Brown plateau region, see Figure 1a.

However, if we take the \mathbf{v}_2 -vector as the initial control vector, the GAD method converges to the above indicated TS. The total number of energy, gradient, and Hessian evaluations in this integration was 252 evaluations. On the other hand, the GAD-CD method, based on eqs 7 and 17, is solved following the algorithm described in Section 3.2. The initial radius r_0 taken was very small, 5×10^{-3} , for the same reasons as explained above. Except for the initial Hessian matrix, the rest of Hessian matrices required in both GAD-CD equations at each step of the process is updated according to the formula given in eq 18. The total number of energy and gradient calculations needed for GAD-CD to reach the TS was 154 when the starting control vector is \mathbf{v}_1 -vector and 150 when the initial vector is \mathbf{v}_2 . We recall that, in contrast to the GAD method, only the initial Hessian was evaluated analytically and updated during the process. This two-dimensional example shows the efficiency of the GAD-CD method compared to the GAD method. Using an update rather than the analytic Hessian matrix, the GAD-CD achieves the TS with a lower number of energy and gradient calls than the GAD method. Furthermore, the GAD-CD method converges to the TS independently of the initial control vector. Notice that both curves do not evolve in the same way in what the evolution of the control vector is concerned.

The different behavior of GAD and GAD-CD methods is due to a different type of optimization in their evolution, whereas GAD evolves satisfying an optimal transversality,^{29,30} the GAD-CD evolves solving the optimization of both eq 7 and the Rayleigh–Ritz quotient, $\mathbf{v}^T \mathbf{H} \mathbf{v} / (\mathbf{v}^T \mathbf{v})$, through eq 17.

In terms of computational efficiency, robustness, and stability, the GAD-CD algorithm is superior to GAD with a lower time step. In addition, GAD-CD shows low dependence on the guess structure and the control vector to reach the TS. Notice that the search starts far from the TS and very close to the deep minimum.

4.2. Behavior on Molecular Systems. The GAD-CD algorithm was interfaced with the Turbomole package⁶⁰ in order to assess its performance in molecular systems. Five different reactions were employed to test the performance of the GAD-CD algorithm:

1. The simple S_N2 reaction between Cl^\ominus and CH_3F to produce F^\ominus and CH_3Cl (Figure 2a.1,a.2 show one of the initial configurations considered and the TS configuration, respectively),
2. The simple S_N2 reaction between Br^\ominus and methylammonium, ($\text{CH}_3\text{NH}_3^\oplus$) to produce BrCH_3 and NH_3 (Figure 3a.1,a.2 show the initial configuration considered and the TS configuration, respectively),
3. The [1,5]-hydrogen shift in 1,3-cyclopentadiene ($c\text{-C}_5\text{H}_6$),⁶³ which is an example of a sigmatropic rearrangement (Figure 4a.1,a.2 show one of the initial configurations considered and the TS configuration, respectively),
4. The electrocyclic ring opening of a *gem*-dichlorocyclopropane molecule, which occurs via a disrotatory mechanism (according to the Woodward–Hoffmann rules⁶⁴) accompanied by a chlorine-atom migration⁶⁵ (Figure 5a.1,a.2 show one of the initial configurations considered and the TS configuration, respectively),

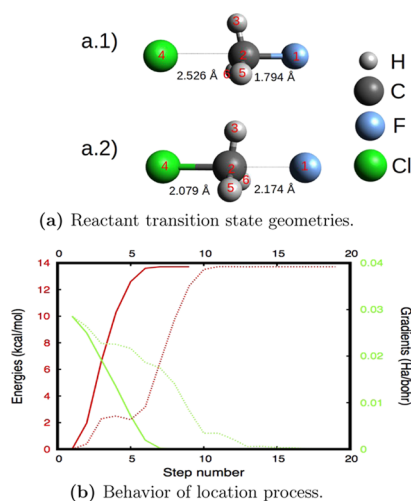


Figure 2. Performance of GAD-CD for the $sn2$ reaction, $\text{Cl}^\ominus + \text{CH}_3\text{F} \rightarrow \text{ClCH}_3 + \text{F}^\ominus$, ($sn2.2.1$ and $sn2.2.2$ runs; see Table 1 for the setup employed in these runs). The distances between F and C and between C and Cl are shown for the initial structure (a.1) and the converged TS (a.2). The evolution of the energy (in kcal/mol) and maximum component in the absolute value of the gradient (in Ha/bohr), $\max\{|\mathbf{g}_\mu|\}_{\mu=1}^N$, as a function of the step number during the TS search for $sn2.2.1$ (solid lines) and for $sn2.2.2$ (dashed lines) are shown in (b).

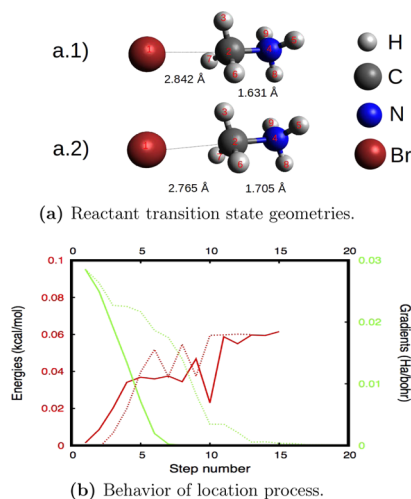


Figure 3. Performance of GAD-CD for the $sn2b$ reaction, $\text{Br}^\ominus + \text{CH}_3\text{NH}_3^\oplus \rightarrow \text{BrCH}_3 + \text{NH}_3$, ($sn2b.1.3$ and $sn2b.1.4$ runs; see Table 2 for the setup employed in these runs). Br and C and between C and N are shown for the initial structure (a.1) and the converged TS (a.2). The evolution of the energy (in kcal/mol) and the maximum component in the absolute value of the gradient (in Ha/bohr), $\max\{|\mathbf{g}_\mu|\}_{\mu=1}^N$, as a function of the step number during the TS search for $sn2b.1.3$ (solid lines) and for $sn2b.1.4$ (dashed lines) are shown in (b).

5. The electrocyclic ring opening of *cis*-1,2-dimethylbenzocyclobutene, which proceeds by a concerted conrotatory pathway to furnish an E,Z -diene^{64,66,67} (Figure 6a.1,a.2 show one of the initial configurations considered and the TS configuration, respectively).

These reactions will hereafter be identified with the following labels: $sn2$, $sn2b$, sig , dcc , and bcb , respectively. Three different starting configurations were considered for the $sn2$, sig , dcc , and bcb reactions in order to study the behavior of GAD-CD as a function of the initial guess \mathbf{x}_0 . All the starting

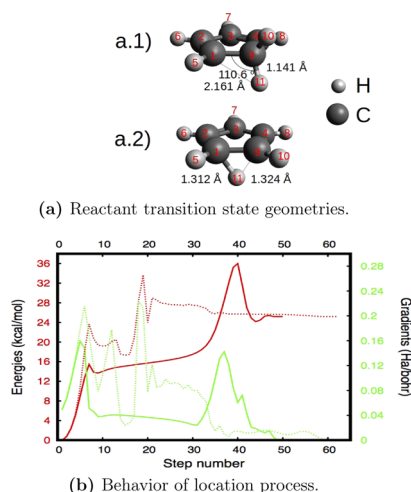


Figure 4. Performance of GAD-CD for the *sig* reaction, [1,5]-H shift in 1,3-cyclopentadiene (**sig.3.1** and **sig.3.4** runs; see Table 3 for the setup employed in these runs). The distances between C9 and H11 and between C1 and H11 are shown for the initial structure (a.1) and the converged TS (a.2). The evolution of the energy (in kcal/mol) and maximum component in the absolute value of the gradient (in Ha/bohr), $\max\{|\mathbf{g}_\mu|\}_{\mu=1}^N$, as a function of the step number during the TS search for **sig.3.1** (solid lines) and for **sig.3.4** (dashed lines) are shown in (b).

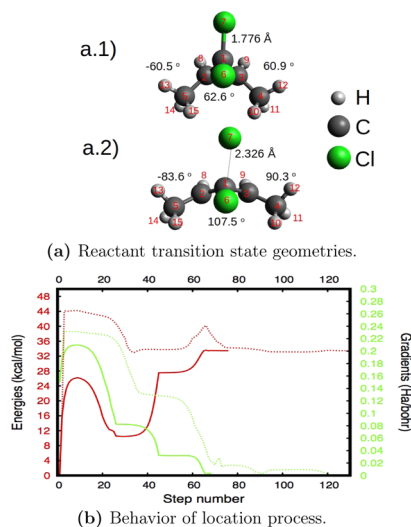


Figure 5. Performance of GAD-CD for the *dcc* reaction, 1,1-dichloro-2,3-dimethylcyclopropane \rightarrow 1,2-dichloro-1,3-dimethylpropene (**dcc.3.3** and **dcc.3.6** runs; see Table 4 for the setup employed in these runs). The distance between C1 and Cl7, angle between C3, C1, and C2 and dihedrals between H12, C4, C3, and H9, and between H13, C5, C2, and H8 are shown for the initial structure (a.1) and the converged TS (a.2). The evolution of the energy (in kcal/mol) and maximum component in the absolute value of the gradient (in Ha/bohr), $\max\{|\mathbf{g}_\mu|\}_{\mu=1}^N$, as a function of the step number during the TS search for **dcc.3.3** (solid lines) and for **dcc.3.6** (dashed lines) are shown in (b).

configurations for these reactions were taken from the set of configurations sampled along the corresponding IRCs. The three starting configurations considered for each reaction feature the following properties:

1. The first starting configuration was taken from a point lying close to the TS along the IRC. The Hessian matrix of all these configurations has a single negative

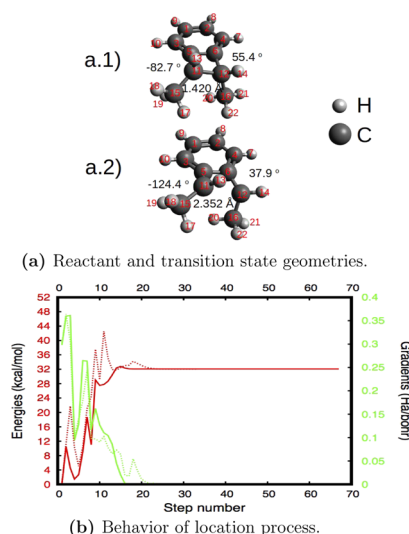


Figure 6. Performance of GAD-CD for the *bcb* reaction, *cis*-1,2-dimethyl-benzocyclobutene \rightarrow *E,Z*-diene (**bcb.3.3** and **bcb.3.6** runs; see Table 5 for the setup employed in these runs). The distance between C11 and C12, the dihedral between C3, C5, C11, and C15, and that between C4, C6, C12, and C16, are shown for the initial structure (a.1) and the converged TS (a.2). The evolution of the energy (in kcal/mol) and maximum component in the absolute value of the gradient (in Ha/bohr), $\max\{|\mathbf{g}_\mu|\}_{\mu=1}^N$, as a function of the step number during the TS search for **bcb.3.3** (solid lines) and for **bcb.3.6** (dashed lines) are shown in (b).

eigenvalue whose associated eigenvector has a large overlap with the TS eigenvector (in the particular case of *bcb*, H_0 has two negative eigenvalues, one of which is vanishingly small and is associated with a rotation of a methyl group).

2. The second starting point lies further away from the TS along the IRC. In some cases, the eigenvalues of the corresponding Hessian matrix are all positive (*sig* and *dcc* cases), while in some cases H_0 has a single negative eigenvalue (*sn2* and *bcb*).
3. The third starting configuration was taken from a point lying very close to the reactants' configuration. The Hessian matrix of all these configurations is positive definite (in the particular case of *bcb*, the first eigenvector has a slightly negative value and is associated with a rotation of a methyl group).

In the case of the *sn2b* reaction, only one starting configuration was considered. This configuration, which does not belong to the IRC of the reaction, was manually generated from the reactant configuration by shortening the C...Br bond by 0.02 au and stretching the C–N bond by 0.02 au. The purpose of this specific reaction was to test the performance of GAD-CD in the case with a very small energy difference between the TS and reactant configurations (for the *sn2b* reaction, the TS is only 0.07 kcal mol⁻¹ above in energy with respect to the reactants). Because one single starting configuration lying close to the reactants was sufficient to carry out this test, no further starting configurations were considered for *sn2b*. All the starting configurations (written both in Cartesian and internal coordinates), together with the TS configurations of all reactions, are provided in the Supporting Information.

In all the GAD-CD runs on molecular systems, the calculation of energies, Cartesian gradients, and Hessians was

carried out using the B3LYP density functional⁶⁸ in its VWN(V) version and the def-SVP basis set⁶⁹ (the def-SVPD basis set was used for the *sn2* reaction because the overall charge of the system was -1). The location of the TSs for all reactions was done using internal coordinates. The Cartesian coordinates, gradients, and Hessians were transformed on the fly to their internal coordinate representation (bond lengths, bending angles, and torsional dihedrals). The initial trust radius, maximum and minimum step lengths of 0.15, 0.30, and 1×10^{-3} Å/rad are considered, respectively. The convergence thresholds for the maximum component in the absolute value of the gradient, ϵ_g , and displacement, ϵ_x , were set to 5×10^{-4} , 2×10^{-3} a.u., respectively. Finally, the values c_{\min} , c_{accept} and c_f are taken as 0.75, 0.80, and 2.0, respectively.

Several setups were used for each reaction and each starting point in order to evaluate the performance of GAD-CD depending on the choice of the initial \mathbf{v}_1 control vector and on the type of calculation of the Hessian. In some runs, the Hessian was computed analytically at each step of the optimization, while in some other runs the Hessian was computed analytically at the starting configuration and updated using the Murtagh–Sargent–Powell equation from then on. All the GAD-CD runs will hereafter be identified using a code with the following general scheme: *reaction-ID.X.Y*. The first label of the code (*reaction-ID*) refers to the reaction studied (*sn2*, *sn2b*, *sig*, *dcc*, or *bcc*). The second label of the code (*X*) is a number referring to the starting configuration (1 for a configuration close to the TS, 2 for a configuration further away from the TS, and 3 for a configuration very close to reactants). The third label of the code (*Y*), in turn, is a number that allows us to distinguish different simulation setups (different guesses for the \mathbf{v}_1 vector and different types of Hessian calculation) for a given reaction and starting configuration.

The results of the multiple runs carried out to test the GAD-CD algorithm are summarized in Tables 1–5. Besides, the evolution of the energy of the system and the evolution of the maximum component in the absolute value of the gradient throughout the TS search for some selected runs are shown in Figures 2b, 3b, 4b, 5b, and 6b.

The first important conclusion of the results gathered in Tables 1–5 is that GAD-CD has been able to locate the TS for all the reactions and starting configurations studied. Remarkably, GAD-CD works efficiently even when the starting configuration is very close to the reactant minimum energy configuration. It should be also stressed that GAD-CD always works very efficiently in conjunction with the Murtagh–Sargent–Powell updating protocol for the Hessian. This demonstrates that GAD-CD is a powerful method for locating TSs of medium size systems at a moderate computational cost. In fact in Figures 4b and 5b the behavior of the update Hessian algorithm is much smoother than the analytical Hessian algorithm. Note the flattening of the peak around iteration 35. The presence of the peak is maybe due to a turning point in the GAD-CD curve. We recall that GAD presents in some cases a turning point behavior.²⁵

We will now turn our attention to the performance of the scheme use to update the \mathbf{v}_1 -vector according to eq 17. In some cases, the exclusive use of eq 17 was found not to be the optimal choice in terms of the convergence rate. The specific examples of the *sig.2.2*, *sig.3.2*, *sig.3.5*, *dcc.1.2*, and *dcc.1.5* reactions (compared to *sig.2.1*, *sig.3.1*, *sig.3.4*, *dcc.1.1*, and *dcc.1.4* reactions, respectively) show that resetting the \mathbf{v}_1 -

Table 1. Performance of the GAC-CD Algorithm for the *sn2* Reaction

reaction ^a	<i>s</i> ^b	$\mathbf{v}_1^{(0)c}$	overlap ^d	Hessian ^e	update of \mathbf{v}_1^f	# steps ^g
sn2.1.1	0.58	\mathbf{H}_0	0.99	analytical	eq 17	7
sn2.1.2	0.58	\mathbf{H}_0	0.99	updated	eq 17	13
sn2.2.1	0.76	\mathbf{H}_0	0.99	analytical	eq 17	9
sn2.2.2	0.76	\mathbf{H}_0	0.99	updated	eq 17	19
sn2.3.1	0.95	\mathbf{H}_0	0.88	analytical	eq 17	-
sn2.3.2	0.95	no \mathbf{H}_0	1.00	analytical	eq 17	-
sn2.3.3	0.95	\mathbf{H}_0	0.88	analytical	eq 17 + EF(1)	14
sn2.3.4	0.95	\mathbf{H}_0	0.88	updated	eq 17	109
sn2.3.5	0.95	no \mathbf{H}_0	1.00	updated	eq 17	26
sn2.3.6	0.95	\mathbf{H}_0	0.88	updated	eq 17 + EF(1)	26

^aLabels used to identify the reactions studied and the initial conditions employed to locate the TS configurations. ^bArc length (Å) along the IRC associated with the initial configuration. Smaller *s* values are associated with configurations that are closer to the TS configuration. ^cThe initial control vector can be defined by taking one of the eigenvectors of the \mathbf{H}_0 matrix or it can be manually built based on the coordinates expected to be relevant in the location of the TS. If the entry is “ \mathbf{H}_0 ”, it means that the initial control vector is the eigenvector with the smallest eigenvalue of the \mathbf{H}_0 matrix. If the entry is “no \mathbf{H}_0 ”, it means that the initial control vector was manually built. ^dOverlap between the initial \mathbf{v}_1 vector and the eigenvector associated with the imaginary frequency at the TS configuration. ^eIf the entry is “analytical”, it means that the Hessian was evaluated by means of an analytical calculation at each iteration of the optimization procedure. If the entry is “updated”, it means that the Hessian was analytically solved only at the initial configuration and that the Hessian was updated following eq 18 from then on. ^fProtocol used to update the \mathbf{v}_1 vector. If the entry is “eq 17”, it means that \mathbf{v}_1 was updated according to eq 17. If the entry is “eq 17 + EF(*n*)”, it means that at a given step of the optimization, the update of \mathbf{v}_1 following eq 17 was interrupted and that the eigenvector with the smallest eigenvalue was taken as the new \mathbf{v}_1 vector (EF stands for the Eigenvector-Following). *n* refers to the number of times in which the evolution of \mathbf{v}_1 according to eq 17 was interrupted along the optimization procedure. ^gNumber of steps needed to reach convergence. If the entry is “-”, it means that convergence was not achieved due to any of the following reasons: (i) the maximum number of steps (150) was reached; (ii) the algorithm failed to progress after reaching a specific configuration (i.e., the molecular structure barely changed from a certain point on); (iii) the optimization led to a high-energy configuration for which the SCF calculation did not converge.

Table 2. Performance of the GAC-CD Algorithm for the *sn2b* Reaction

reaction ^a	<i>s</i> ^b	$\mathbf{v}_1^{(0)c}$	overlap ^d	Hessian ^e	update of \mathbf{v}_1^f	# steps ^g
sn2b.1.1	-	\mathbf{H}_0	0.97	analytical	eq 17	-
sn2b.1.2	-	\mathbf{H}_0	0.97	analytical	eq 17+ EF(1)	10
sn2b.1.3	-	no \mathbf{H}_0	1.00	analytical	eq 17	15
sn2b.1.4	-	no \mathbf{H}_0	0.99	updated	eq 17	13

^aSee footnote a of Table 1. ^bIn this particular case, only one starting configuration was tested. This configuration does not belong to the IRC path of the reaction. Instead, it was manually generated from the reactant configuration by shortening the C··Br bond by 0.02 au and stretching the C–N bond by 0.02 au, to test the performance of the method in a very flat PES. ^cSee footnote c of Table 1. ^dSee footnote d of Table 1. ^eSee footnote e of Table 1. ^fSee footnote f of Table 1. ^gSee footnote g of Table 1.

Table 3. Performance of the GAC-CD Algorithm for the *sig* Reaction

reaction ^a	s ^b	v ₁ ^{(0)c}	overlap ^d	Hessian ^e	update of v ₁ ^f	# steps ^g
sig.1.1	0.33	H ₀	0.94	analytical	eq 17	6
sig.1.2	0.33	H ₀	0.94	updated	eq 17	7
sig.2.1	1.30	no H ₀	0.89	analytical	eq 17	37
sig.2.2	1.30	no H ₀	0.89	analytical	eq 17+ EF(1)	14
sig.2.3	1.30	no H ₀	1.00	analytical	eq 17	-
sig.2.4	1.30	no H ₀	0.89	updated	eq 17	43
sig.3.1	2.67	no H ₀	0.82	analytical	eq 17	50
sig.3.2	2.67	no H ₀	0.82	analytical	eq 17+ EF(1)	26
sig.3.3	2.67	no H ₀	1.00	analytical	eq 17	-
sig.3.4	2.67	no H ₀	0.82	updated	eq 17	62
sig.3.5	2.67	no H ₀	0.82	updated	eq 17+ EF(1)	45
sig.3.6	2.67	no H ₀	1.00	updated	eq 17	-

^aSee footnote a of Table 1. ^bSee footnote b of Table 1. ^cSee footnote c of Table 1. ^dSee footnote d of Table 1. ^eSee footnote e of Table 1. ^fSee footnote f of Table 1. ^gSee footnote g of Table 1.

Table 4. Performance of the GAC-CD Algorithm for the *dcc* Reaction

reaction ^a	s ^b	v ₁ ^{(0)c}	overlap ^d	Hessian ^e	update of v ₁ ^f	# steps ^g
dcc.1.1	0.96	H ₀	0.79	analytical	eq 17	81
dcc.1.2	0.96	H ₀	0.79	analytical	eq 17+ EF(1)	19
dcc.1.3	0.96	no H ₀	1.00	analytical	eq 17	-
dcc.1.4	0.96	H ₀	0.79	updated	eq 17	115
dcc.1.5	0.96	H ₀	0.79	updated	eq 17+ EF(2)	18
dcc.2.1	1.96	no H ₀	0.58	analytical	eq 17	-
dcc.2.2	1.96	no H ₀	0.58	analytical	eq 17+ EF(1)	95
dcc.2.3	1.96	no H ₀	0.59	analytical	eq 17+ EF(2)	38
dcc.2.4	1.96	no H ₀	0.32	analytical	eq 17+ EF(6)	66
dcc.2.5	1.96	no H ₀	0.59	updated (5)	eq 17	-
dcc.2.6	1.96	no H ₀	0.59	updated (5)	eq 17+ EF(1)	171
dcc.2.7	1.96	no H ₀	0.59	updated (5)	eq 17+ EF(2)	80
dcc.2.8	1.96	no H ₀	0.32	updated (5)	eq 17+ EF(15)	79
dcc.3.1	5.25	no H ₀	0.58	analytical	eq 17	-
dcc.3.2	5.25	no H ₀	0.58	analytical	eq 17+ EF(2)	42
dcc.3.3	5.25	no H ₀	0.32	analytical	eq 17+ EF(7)	76
dcc.3.4	5.25	no H ₀	0.58	updated (5)	eq 17	-
dcc.3.5	5.25	no H ₀	0.58	updated (5)	eq 17+ EF(1)	120
dcc.3.6	5.25	no H ₀	0.32	updated (10)	eq 17+ EF(12)	128

^aSee footnote a of Table 1. ^bSee footnote b of Table 1. ^cSee footnote c of Table 1. ^dSee footnote d of Table 1. ^eSee footnote e of Table 1. If the entry is “updated (*n*)”, it means that the Hessian was computed analytically every *n* steps. ^fSee footnote f of Table 1. ^gSee footnote g of Table 1.

vector when the Hessian has the right inertia and/or the gradient is below a certain threshold can lead to a large acceleration of the convergence rate. In these examples, the reset of the v₁-vector at a given step *i* was done by replacing v₁ with the eigenvector of the Hessian with the largest overlap with the v₁-vector at step *i* – 1 (which turned out to be the eigenvector of the Hessian with the smallest eigenvalue). Note that this scheme of resetting is equivalent to an eigenvector following protocol applied at a given step of the whole optimization procedure. The slower rate of convergence when using exclusively eq 17 is due to the fact that this equation entails a linear integration of the second equation of the GAD algorithm (eq 1b), while the first equation of GAD (eq 1a) is integrated up to the second order. Note that an integration of eq 1b up to second order would improve the performance of the algorithm but at the expense of a large computational cost associated with the evaluation of the third order energy derivatives. For this reason, we have opted for the protocol for resetting v₁-vector as the simplest and cheapest method to accelerate convergence.

In some other cases (sn2.3.1, sn2b.1.1, dcc.2.1, dcc.3.1, dcc.3.4, bcb.2.3, bcb.3.1, bcb.3.4), the exclusive use of eq 17 was found to be unstable and the algorithm failed to locate the TS. In these cases, resetting the v₁-vector once (or twice in one specific case) proved to be an efficient way to achieve convergence (see sn2.3.3 vs. sn2.3.1, sn2b.1.2 vs. sn2b.1.1, dcc.2.2 vs. dcc.2.1, dcc.3.2 vs. dcc.3.1, dcc.3.5 vs. dcc.3.4). Besides, the runs of the dcc.2.4, dcc.2.8, dcc.3.3, and dcc.3.6 reactions demonstrate that an updating protocol in which the v₁-vector is automatically reset every 10 steps results in a good performance in terms of the convergence rate.

In a few cases of the *bcb* reaction (bcb.2.3, bcb.3.1, and bcb.3.4 reactions), the v₁-vector featured an unexpected evolution. Specifically, it was observed that this vector becomes very different with respect to the desired eigenvector of the Hessian matrix as the TS search goes on. This resulted in a “corrupted” control vector with large weights on components that are not chemically relevant to drive the reaction, thus leading to failure to locate the TS. Freezing the v₁-vector during the initial steps of the search proved to be an efficient

Table 5. Performance of the GAC-CD Algorithm for the *bc*b Reaction

reaction ^a	s ^b	v ₁ ^{(0)c}	overlap ^d	Hessian ^e	update of v ₁ ^f	# steps ^g
bc b .1.1	0.75	H ₀	0.93	analytical	eq 17	13
bc b .1.2	0.75	H ₀	0.93	updated	eq 17	13
bc b .2.1	1.51	no H ₀	0.89	analytical	eq 17	49
bc b .2.2	1.51	no H ₀	1.00	analytical	eq 17	-
bc b .2.3	1.51	no H ₀	0.89	updated	eq 17	-
bc b .2.4	1.51	no H ₀	0.89	updated	v ₁ frozen	47
bc b .2.5	1.51	no H ₀	0.89	updated	v ₁ frozen + eq 17 ^h	40
bc b .3.1	4.15	no H ₀	0.90	analytical	eq 17	-
bc b .3.2	4.15	no H ₀	0.90	analytical	v ₁ frozen + eq 17 ⁱ	67
bc b .3.3	4.15	no H ₀	0.90	analytical	v ₁ frozen	39
bc b .3.4	4.15	no H ₀	0.90	updated	eq 17	-
bc b .3.5	4.15	no H ₀	0.90	updated (5)	v ₁ frozen + eq 17 ^h	33
bc b .3.6	4.15	no H ₀	0.90	updated (30)	v ₁ frozen	65
bc b .3.7	4.15	no H ₀	0.85	updated (5)	v ₁ frozen	24

^aSee footnote a of Table 1. ^bSee footnote b of Table 1. ^cSee footnote c of Table 1. ^dSee footnote d of Table 1. ^eSee footnote e of Table 1. If the entry is "updated (*n*)", it means that the Hessian was computed analytically every *n* steps. ^fSee footnote f of Table 1. If the entry is "v₁ frozen", it means that v₁ was kept constant throughout the optimization. ^gSee footnote g of Table 1. ^hIn this particular run, the v₁ vector was kept frozen until the 25th step and from then on the vector was allowed to change according to eq 17. ⁱIn this particular run, the v₁ vector was kept frozen until the 10th step and from then on the vector was allowed to change according to eq 17.

Table 6. Assessment of the Performance of the GAD-CD Method for the *bc*b Reaction as a Function of the Initial v₁-Vector^a

reaction ^b	v ₁ relevant components ^c						angle ^d	# steps ^e
	v ₁ (26)	v ₁ (29)	v ₁ (33)	v ₁ (36)	v ₁ (39)	v ₁ (42)		
bc b .3.6	0.31	0.31	0.62	0.21	0.05	0.62	28.9	65
bc b .3.7	0.39	0.39	0.59	0.00	0.00	0.59	31.6	24
bc b .3.8 ^f	0.38	0.42	0.47	0.25	0.21	0.44	0.00	23
bc b .3.9	0.38	0.38	0.57	0.25	0.06	0.57	25.8	30
bc b .3.10	0.32	0.32	0.63	0.00	0.00	0.63	33.8	34
bc b .3.11	0.26	0.26	0.66	0.00	0.00	0.66	36.0	57
bc b .3.12	0.22	0.22	0.67	0.00	0.00	0.67	37.8	27
bc b .3.13	0.17	0.17	0.68	0.00	0.00	0.68	40.4	-
bc b .3.14	0.48	0.48	0.48	0.24	0.06	0.48	24.9	20
bc b .3.15	0.50	0.50	0.00	0.00	0.50	0.50	30.8	21
bc b .3.16	0.57	0.57	0.38	0.25	0.06	0.38	28.1	17
bc b .3.17	0.59	0.59	0.39	0.00	0.00	0.39	33.6	-
bc b .3.18	0.63	0.63	0.31	0.10	0.05	0.31	33.7	35
bc b .3.19	0.65	0.65	0.26	0.09	0.04	0.26	37.0	47
bc b .3.20	0.69	0.69	0.22	0.07	0.04	0.22	39.6	-

^aThe starting configuration was the same for all the calculations and was taken from the IRC (the arc length along the IRC associated with the starting configuration is 4.15). In all the calculations, the Hessian was analytically evaluated every five steps of the search. The Hessian was updated via eq 18 using the Murtagh–Sargent–Powell option in between the steps in which an analytical evaluation was carried out. The v₁ vector was kept frozen throughout the optimization in all calculations. ^bLabels used to identify the reactions that were studied and the initial conditions that were employed to locate the TS configurations. ^cThe components of the initial v₁ vector with a non-negligible weight are (see Figure 6 for the atom labels): v₁ (26) = angle {11 5 3} (i.e., the angle formed between atoms 11, 5, and 3, atom 5 being the apex atom). v₁ (29) = angle {12 6 4}. v₁ (33) = dihedral {13 11 5 6} (i.e., the dihedral angle formed between atoms 13, 11, 5, and 6). v₁ (36) = dihedral {14 12 6 4}. v₁ (39) = dihedral {15 11 5 3}. v₁ (42) = dihedral {16 12 6 5}. ^dAngle between the initial v₁ vector and the eigenvector associated with the imaginary frequency at the TS configuration. ^eNumber of steps needed to reach convergence. If the entry is "-", it means that convergence was not achieved due to any of the reasons mentioned in footnote g of Table 1. ^fIn this particular case, the v₁ vector has other components with a non-negligible weight. The full list of components is given in the Supporting Information.

way to overcome this problem and achieve convergence (see **bc**b2.5, **bc**b3.2, **bc**b3.5) and in some cases the algorithm converges even if the v₁-vector is kept frozen during the whole process (see **bc**b2.4, **bc**b3.3, **bc**b3.6 and **bc**b3.7).

Another important aspect of the GAD-CD algorithm is its performance as a function of the initial choice for the v₁-vector. In order to assess such performance, we took the third starting configuration (i.e., the one lying closer to the reactants configuration) of the *bc*b system, and we carried out multiple GAD-CD runs with different initial definitions of the v₁-vector

for the same starting configuration. As shown in Table 6, there is a wide range of initial v₁ vectors that lead to the same TS. This demonstrates that GAD-CD is a robust and versatile method for locating TS in molecular systems (see section 5 of Supporting Information for further evidence).

Finally, we focus on the strong and weak points of the new proposed method compared to other methods existing in the literature. As explained in Section 2, the family of techniques based on an eigenvector-following philosophy is one of the most widely used families to locate TSs. One of the algorithms

that fall within this set is the TRIM algorithm⁷⁰ (implemented, for instance, in the Turbomole⁶⁰ code). From a conceptual point of view, TRIM is, within the family of the eigenvector following techniques, the closest one to GAD-CD. The main difference between these two techniques is the way in which the guiding vector is updated during the location process. A numerical comparison between GAD-CD and the standard TRIM methods is reported in Section 6 of the [Supporting Information](#). When considering initial configurations close to the TS, the performance of GAD-CD is quite similar to that of TRIM. In some of the tested cases, GAD-CD takes a few extra iterations (less than 10) to converge compared to TRIM. This is not surprising if one takes into account that TRIM was specifically designed for situations in which the initial configuration is close to the TS. However, the main advantage of GAD-CD over TRIM emerges when considering initial configurations that are very close to reactants. Indeed, GAD-CD is able to locate the TS of all systems considered in this study when starting close to reactants (see [Tables 1–4](#)), while TRIM fails to do so in the most complex systems (*dcc* and *bc*) even when the full Hessian is evaluated at each point.

Let us stress again that GAD-CD behaves well even when the Hessian is updated and not analytically computed, thus making the technique very efficient. The limitations of TRIM when starting far away from the TS stem from the fact that this method was not designed to locate TSs in such cases. In fact, it is usually recommended (see, e.g., the manual of Turbomole⁶⁰) to use a “double-ended” method to generate an initial guess structure prior to using TRIM to ensure the convergence to the desired TS. In contrast, GAD-CD does not need the preliminary calculation and works well even when starting from just one of the minima of the PES. Overall, we conclude that the GAD-CD algorithm possesses good numerical stability and computational efficiency. Finally, the control over the initial v_1 -vector together with the low computational cost associated with the updated Hessian protocol renders GAD-CD a very powerful method for the automatic exploration of complex PESs by parallel runs with different initial v_1 vectors from a given basin of the PES.

5. CONCLUSIONS

We have reported an algorithm, called GAD-CD, to locate saddle points of index one on multidimensional PESs. This method can be considered an extension of the GAD method to the quadratic order using a restricted step technique and a set of conjugate directions with respect to the Hessian matrix. It is shown that the GAD-CD method is more robust than the GAD method, requiring not only a smaller number of energy and gradient calculations, but also achieving converged results independently of the initial control vector in situations where the GAD method fails to capture the corresponding TS. Although the present form of the GAD-CD has a higher computational cost than GAD (due to an extra diagonalization at each step), there may be different ways to make GAD-CD more efficient. This is currently being investigated.

The GAD-CD method is easily interfaced with standard quantum-chemistry software such as the widespread Turbomole package,⁶⁰ and provides converged results within a relatively small number of iteration steps. This has been proven by means of five medium-sized molecular systems for which GAD-CD works efficiently even when starting close to the reactant minima. Its performance remains optimal even when

fast updating Hessian protocols are employed. This opens the door to an automatic exploration of complex PESs.

Hence, we envision our GAD-CD method as being implemented in standard quantum-chemistry packages and become a useful tool for the localization of TS in multidimensional PESs, especially in situations where the high complexity of the associated topographies make it difficult for defining an educated guess structure, close enough to the TS to be located by standard algorithms.

■ ASSOCIATED CONTENT

📄 Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: [10.1021/acs.jctc.8b01061](https://doi.org/10.1021/acs.jctc.8b01061).

Sets of internal coordinates employed in the calculations of molecular systems, initial configurations given in both cartesian and internal coordinates, TS configurations given in both cartesian and internal coordinates, initial v_1 vectors for all runs, extra assessments of the performance of GAD-CD as a function of the initial v_1 -vector, 6, comparison between the GAD-CD and TRIM algorithms, and code including the interface between GAD-CD and Turbomole⁶⁰ (PDF)

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Notes

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■ DEDICATION

Dedicated to Professor Jean Paul Malrieu on occasion of his 80 birthday.

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