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Minima hopping guided path search: An efficient method for finding complex chemical reaction pathways

Bastian Schaefer,1,a) Stephan Mohr,1,2 Maximilian Amsler,1 and Stefan Goedecker1,b)
1Department of Physics, University of Basel, Klingelbergstrasse 82, CH-4056 Basel, Switzerland
2University Grenoble Alpes, CEA, INAC-SP2M, F-38000 Grenoble, France
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The Minima Hopping global optimization method uses physically realizable molecular dynamics moves in combination with an energy feedback that guarantees the escape from any potential energy funnel. For the purpose of finding reaction pathways, we argue that Minima Hopping is particularly suitable as a guide through the potential energy landscape and as a generator for pairs of minima that can be used as input structures for methods capable of finding transition states between two minima. For Lennard-Jones benchmark systems we compared this Minima Hopping guided path search method to a known approach for the exploration of potential energy landscapes that is based on deterministic mode-following. Although we used a stabilized mode-following technique that reliably allows to follow distinct directions when escaping from a local minimum, we observed that Minima Hopping guided path search is far superior in finding lowest-barrier reaction pathways. We, therefore, suggest that Minima Hopping guided path search can be used as a simple and efficient way to identify energetically low-lying chemical reaction pathways. Finally, we applied the Minima Hopping guided path search approach to 75-atom and 102-atom Lennard-Jones systems. For the 75-atom system we found pathways whose highest energies are significantly lower than the highest energy along the previously published lowest-barrier pathway. Furthermore, many of these pathways contain a smaller number of intermediate transition states than the previously published lowest-barrier pathway. In case of the 102-atom system Minima Hopping guided path search found a previously unknown and energetically low-lying funnel. © 2014 AIP Publishing LLC. [http://dx.doi.org/10.1063/1.4878944]

I. INTRODUCTION

The exploration of potential energy landscapes requires two important aspects to be considered. On the one hand, the geometries of stable ground-states are of large interest. For this reason powerful global optimization methods such as several genetic algorithms,1–5 Basin Hopping,6 the Activation Relaxation Technique (ART),7–11 and Minima Hopping (MH)8,12–14 have been developed during the last two decades. On the other hand, processes like protein folding, catalysis, chemical reactions in solutions and surfaces, or the formation of stable phases in solids often force the reacting systems to undergo rarely occurring complex transformations between long-lived states. Actively stabilizing or destabilizing long-lived states by inhibiting or promoting reaction pathways responsible for certain events allows to synthesize new materials or substances with specifically tailored properties.15–17 Unfortunately, the sole knowledge of the global minimum and a collection of local minima provided by global optimization methods is not sufficient for being able to influence reaction pathways specifically. Instead, an accurate knowledge of the atomistic details of reaction pathways is needed. For this reason, in addition to local minima also transition states and the information which minima are connected by which transition states are of great importance. As soon as these data are available, various methods like the master equation approach, the discrete path formulation of Discrete Paths Sampling, or Kinetic Monte Carlo allow to compute dynamic properties.18–21 Using graph-theoretic methods it is possible to extract reaction pathways from databases containing the just mentioned data. Since pathways with energetically high barriers have a vanishingly small contribution to properties like rate constants, it is important not to investigate just any pathways but to sample preferably those that have low overall barriers.

As shown in Ref. 22, such a kind of sampling can in principle be accomplished by mode-following methods coupled to an acceptance-rejection criterion that provides a bias to low-energy configurations. However, in a study by Doye et al.23 a systematic sampling approach was considered not to be able to find even a single pathway connecting both lowest lying minima of the 75-atom Lennard-Jones system within a feasible computation time. Instead of using a completely unbiased search, they had to use a method which optimizes an initially given input pathway. The method of constructing an initial pathway which connects two states of interest and subsequently finding lower energy pathways by perturbing the initial path has been used and refined in various ways in later studies conducted by Wales et al. Apparently, this approach seems to be an efficient procedure for constructing reaction pathways since, in a nutshell, this is the method of choice in the often applied Discrete Path Sampling approach.18,20,24,25

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a)bastian.schaefer@unibas.ch
b)stefan.goedecker@unibas.ch
Conventional methods for computing Hessian eigenvectors (modes) that are based on an iterative minimization of the curvature tend to converge to the lowest Hessian eigenvector, only. Therefore, deterministic methods using mode-following approaches based on these conventional eigenvector computation methods run into the risk of being non-ergodic, because the number of available escape directions away from a local minimum is very limited. In Sec. II D, we show a stabilized mode-following technique that allows to converge reliably to the closest Hessian eigenvector. This somewhat alleviates the problem of converging only to the lowest eigenvector. Therefore, it can be used to follow more reliably the full number of $6N - 12$ search directions available in a $N$-atomic system (free boundary conditions assumed).

Besides for global optimization, the powerful ART nouveau\(^9\)–\(^{11}\) of Mousseau and co-workers can also be used for computing reaction pathways. In this method, the problem of the restricted number of escape-directions is solved by using random displacements away from the initial local minimum. ART nouveau has evolved from ART\(^7\),\(^8\) and has successfully been applied to different systems, for example, amorphous\(^{26}\) and crystalline silicon,\(^{27,28}\) the diffusion of interstitials and vacancies,\(^{29–31}\) and peptides and proteins.\(^{32–37}\)

A further method that has been applied for the calculations of reaction pathways is Transition Path Sampling (TPS) which generalizes importance sampling to trajectory space.\(^{38–44}\) However, as has been shown by Miller and Predescu, TPS with shooting and shifting moves becomes trapped in high-energy structures of LJ\(_{38}\) and thus fails to find the global minimum funnel of this system. They thus developed a double-ended transition path sampling method, named Sliding and Sampling, which could find pathways between both funnels.\(^{45}\) However, the main drawbacks of their method are the non-ergodicity of their simulation for LJ\(_{38}\) and the high computational cost which is several orders of magnitude higher than that of the above mentioned method by Doye \etal.\(^{32}\)

Chemical reaction pathways can be partitioned into a sequence of stationary point crossings. Therefore, many methods that are intended for predicting chemical reaction pathways necessarily must use techniques for converging to stationary points. However, the main focus of this work is not to compare the efficiency of methods that converge to individual stationary points, but to discuss and benchmark a new scheme for generating sequences of stationary points from which low-barrier pathways leading over many barriers can be extracted. To do so, we re-examine a systematic potential energy landscape exploration method that has been outlined in Ref. 22. In contrast to Ref. 22, we use a stabilized mode-following method which is introduced in Sec. II D. Although, this stabilized mode-following method alleviates the problem of preferentially escaping a minimum along the lowest Hessian eigenvector only, we come to similar results as previous investigations.\(^{9,23}\) We conclude that in general this systematic potential energy landscape exploration approach is not optimal and occasionally fails to find lowest-barrier pathways for even moderately sized systems like LJ\(_{38}\).

By virtue of the explosion condition\(^{12,46}\) MH is guaranteed to escape from any potential energy funnel and due to the molecular dynamics (MD) based moves the minima along the MH trajectory are separated by low energy barriers. Furthermore, the consecutive minima are structurally not too different from each other, because the MD moves consist of a few steps, only. These properties make MH particularly suitable to serve as a guide for searching low-energy reaction pathways. These pathways can connect parts of the potential energy landscape that are far away from each other and that are possibly separated by high energy barriers. Combining MH and a suitable method for finding transition states between two input geometries leads to the novel Minima Hopping guided path search (MHGPS) approach presented in Sec. II G. Using MHGPS we mapped out the energy landscape of LJ\(_{75}\) and LJ\(_{102}\). Despite numerous published investigations of the Lennard-Jones clusters, we were able to detect many pathways that are significantly lower in energy and shorter with respect to the integrated path length and number of intermediate transition states than previously known pathways for LJ\(_{75}\),\(^{23}\) For LJ\(_{102}\) we found a third, previously unknown and energetically low-lying funnel at the bottom of which a new structural motif is located. The pathways found between both lowest minima of LJ\(_{102}\) are also significantly shorter in terms of the number of intermediate transition states and in terms of the integrated path length when compared to previously presented pathways.\(^{47}\)

II. METHODS

A. Lennard-Jones potential

All interactions in this study were modeled by the Lennard-Jones (LJ) potential\(^{48,49}\)

$$E = 4\epsilon \sum_{i<j} \left\{ \left( \frac{\sigma}{r_{ij}} \right)^{12} - \left( \frac{\sigma}{r_{ij}} \right)^{6} \right\},$$

where $\epsilon$ defines the pair-well depth and $2^{1/6}\sigma$ is the pair-well equilibrium distance. All energies and distances are reported in units of $\epsilon$ and $\sigma$, respectively.

B. Transition states, their connectivity, and stationary point databases

We follow the usual definition of a transition state being a first order saddle point of the energy function.\(^{19}\) Steepest descent paths connect transition states to two stationary points. In most cases these stationary points are local minima. We adapt the terminology of Wales\(^{18–20}\) and denote sequences of minima and transition states connected by steepest descent paths as “discrete paths.” A collection of local minima, transition states, and the information which transition states connect which minima is called a “stationary point database.”\(^{18–20}\)

Building stationary point databases requires the identification or distinction of atomic configurations with or from each other. For this purpose we utilized the recently developed fingerprints which are based on the eigenvalues of a s-orbital overlap matrix.\(^{50}\) For the calculation of the fingerprints, we used $2^{1/6}\sigma$ as the covalent radius of the LJ atoms. We considered two conformers to be identical if their energy difference
was smaller than $10^{-5}\epsilon$ and their fingerprint distance less than $2 \times 10^{-2}$.

Extracting from a stationary point database all lowest-barrier paths with the least number of intermediate transition states between two given minima poses a problem that is closely related to the so-called shortest-widest$^{51}$ path problem. This can be solved by applying Dijkstra’s algorithm$^{52}$ twice.$^{51}$ In the first step Dijkstra’s algorithm searches for all paths that connect both minima with the lowest possible energy barrier $E_{\text{bar}, \text{lowest}}$. The stationary point database then is truncated by removing all transition states with energies higher than $E_{\text{bar}, \text{lowest}}$. Next, Dijkstra’s algorithm passes through the truncated database and searches for the path with the smallest possible number of intermediate transition states.

To determine the connectivity in all sampling approaches presented below, we stepped away from a transition state by adding to and subtracting from the transition state one-100th of the normalized Hessian eigenvector that corresponds to the negative curvature. Using Euler’s method with a maximum step size of $10^{-2}\sigma$, approximate steepest descent paths were computed until the Euler integrator entered the quadratic region surrounding a minimum. In this Euler integration scheme steps were rejected and the step size was decreased if either the angle between the gradients of two successive steps was larger than $60^\circ$ or if the energy increased. Inside the quadratic region the Euler method was replaced by the fast inertial relaxation engine (FIRE)$^{53}$ in order to speed up the geometry optimization. For the FIRE integrator itself it is not of any relevance whether it operates inside the quadratic region or not. However, compared to non-quadratic regions it seems less likely that inside the quadratic region the FIRE method will converge to a different minimum than Euler’s method. Because dynamic properties computed from stationary point databases are unlikely to depend strongly on whether the connectivity of the potential energy landscape is established by using approximate steepest descent paths or paths from advanced minimization algorithms,$^{19,21}$ for example, FIRE or the Broyden–Fletcher–Goldfarb–Shanno (BFGS) algorithm,$^{54–58}$ the time used for relaxations to local minima could have shortened significantly when omitting the Euler integration and using advanced minimization algorithms throughout. However, because we introduce a new reaction pathway search method, we decided to use the conservative Euler integration approach in order to sample connectivity information that is in accordance with the connectivity defined by the widely accepted intrinsic reaction coordinate.$^{59}$ Although we do not report any results based on FIRE-only minimization, we compared the differences of pathways obtained from FIRE-only and Euler integration plus FIRE optimization. We only observed changes in the number of intermediate transition states. In all cases the energetically lowest transition state between two states found by FIRE-only runs was identical to the lowest transition state found by connections established by approximate steepest descent paths.

In addition to the conservative combination of Euler’s method and FIRE, all new pathways explicitly reported in this study (Figures 6 and 7) were double-checked in a post-processing step. In order to obtain quasi-exact intrinsic reaction pathways, steepest descent paths were recomputed using only Euler’s method with a maximum displacement of $10^{-6}\sigma$ in each integration step. Before this steepest descent relaxation the structures had been pushed away from the transition state one-10 000th of the normalized eigenvector belonging to the negative Hessian eigenvalue.

It has to be emphasized that, similar to all commonly used global optimization algorithms, the methods presented in this work do not rigorously guarantee that an optimal solution has been found. That is, all presented structures and lowest-barrier pathways should be denoted as “putative lowest structures” or “putative lowest-barrier pathways.” However, for convenience we sometimes omit the word “putative.”

C. Disconnectivity graphs

Disconnectivity graphs introduced by Becker and Karplus$^{60}$ and frequently used and illustrated by Wales et al.$^{19,21,61,62}$ can be used to visualize stationary point databases of multidimensional potential energy landscapes. They therefore allow to obtain a rough, intuitive insight into dynamic properties. In this section, we briefly recapitulate the theory of disconnectivity graphs.

Disconnectivity graphs illustrate which minima are convertible into each other by following reaction pathways without ever exceeding a given threshold energy. Such mutually accessible regions are called “superbasins.”$^{21}$ The number of superbasins depends on the threshold energy. The vertical axis of a disconnectivity graph is partitioned into a predefined and freely chosen number of energy thresholds. At each threshold energy the superbasins are represented by nodes on the graph and are arranged along the horizontal axis. At threshold energies at and above which superbasins are mutually accessible, the corresponding nodes below this threshold energy are connected by lines. Finally, all the single minima at the bottoms of the superbasins are represented separately by drawing lines down to the energy of each minimum. The horizontal position of the nodes and minima is arbitrary. Typically, there are too many minima to visualize, hence only the lowest $n$ minima are usually plotted. Nevertheless, all minima and transition states contained in the underlying stationary point database contribute to the superbasin and barrier analysis.

The number and positions of the chosen threshold energies can heavily influence the appearance of a disconnectivity graph and hence these parameters have to be well chosen in order to obtain a suitable trade-off between a detailed and coarse grained visualization of the topological information contained in the underlying stationary point database.$^{21}$ The plots of all disconnectivity graphs in this work were generated using the connectionDPS$^{62}$ software.

D. A stabilized mode-following method

As the name suggests, the basic idea of mode following methods is to find the path from a minimum to a first-order saddle point by following an eigenmode of the Hessian.$^{19,63–65}$ In practice, the determination of the eigenmodes via a diagonalization is too costly and one therefore
has to resort to iterative methods, meaning that the mode to be followed is found by a minimization problem.

In our approach the Hessian eigenmodes are found using a version of the dimer method. The dimer consists of two images \( \mathbf{R}_1 \) and \( \mathbf{R}_2 \) in the 3\( N \)-dimensional search space, separated by a short distance \( 2\epsilon \):

\[
\mathbf{R}_1 = \mathbf{R}_0 + \epsilon \mathbf{N},
\]

\[
\mathbf{R}_2 = \mathbf{R}_0 - \epsilon \mathbf{N},
\]

where \( \mathbf{N} \) is the normalized dimer direction and \( \mathbf{R}_0 \) is the dimer midpoint. The dimer method first rotates the dimer in order to align it with a Hessian eigenmode and then translates it along this mode. This procedure is repeated until the transition state is reached. As explained below, conventional methods that compute Hessian eigenvectors by an iterative minimization tend to converge preferentially to the eigenvector corresponding to the lowest Hessian eigenvalue. However, in order to escape from a minimum to many different transition states, it is desirable to follow as many different escape directions as possible in the beginning of the mode-following procedure. The ability to converge reliably to the closest Hessian eigenvector, and thus being able to systematically follow many different directions is the original contribution of the method presented in this section.

1. Rotating the dimer

The essential point of the dimer method is to find an efficient prescription for the rotational part. The quantity that has to be minimized is the curvature along the dimer direction, \( C_{\mathbf{R}_0}(\mathbf{N}) = \mathbf{N}^T \mathbf{H}_{\mathbf{R}_0} \mathbf{N} \), where \( \mathbf{H}_{\mathbf{R}_0} \) is the Hessian evaluated at the dimer midpoint. Since the computation of the exact Hessian is in general too costly, the curvature is approximated using finite differences computed from the forces that act on the two images of the dimer:

\[
C_{\mathbf{R}_0} = \frac{(\mathbf{F}_2 - \mathbf{F}_1) \cdot \mathbf{N}}{2\epsilon}.
\]

There are ways to locally approximate the curvature by a short Fourier series and then to directly minimize this expression. However, we chose a more straightforward approach by working directly with the torsional force:

\[
\mathbf{F}^\perp = (\mathbf{F}_1 - \mathbf{F}_2) - ((\mathbf{F}_1 - \mathbf{F}_2) \cdot \mathbf{N})\mathbf{N}.
\]

This formula can be used for the translation as well as for the rotation. The translation can be performed by using the Lanczos method, as described in Ref. 68.

2. Translating the dimer

In contrast to the rotation of the dimer, the translation is rather straightforward, following the approach outlined in Ref. 66. If the saddle point search was started from a local minimum, then there are two cases to distinguish. First, the dimer has to be brought out of the convex region around
the minimum. To this end it is moved upwards along the
dimer direction using the most simple prescription, i.e., \( \mathbf{R}_0^{i+1} = \mathbf{R}_0^i + \alpha \mathbf{F}_{eff}^i \) with \( \mathbf{F}_{eff}^i = -\left(\mathbf{F}_0^i \cdot \mathbf{N}^0(i)\right) \mathbf{N}^0(i) \), \( \alpha > 0 \). This is
the method of choice until the curvature along the dimer axis
becomes negative. As soon as this happens, the effective force
is altered to \( \mathbf{F}_{eff}^i = \mathbf{F}_0^i - \lambda \left(\mathbf{F}_0^i \cdot \mathbf{N}^0(i)\right) \mathbf{N}^0(i) \), where \( \lambda \) was
typically set to 10. In this way the dimer will be guided towards
the saddle point. However, the procedure can be become in-
efficient as soon as the dimer is close to the stationary point.
In this case it is advisable to switch to a convergence accel-
erator; in our case we were using DIIS, an approach which is
also employed in ART nouveau.\(^{31}\)

\section*{E. Generating stationary point databases using
the mode-following approach}

In Ref. 22, Doye et al. presented an algorithm that al-
 lows mode-following techniques to be used for the explora-
tion of the potential energy landscape. In order to map out
the potential energy landscape, we used this algorithm in con-
junction with our stabilized mode-following method. Based
on the method used for the transition state search, we hence-
forth will denote the potential energy landscape exploration
method of Ref. 22 as the eigenvector following exploration
(EFE) method. For the convenience of the reader we here-
after shortly recapitulate the EFE method. Concisely spoken,
the walker of the EFE method starts at a local minimum and
follows the lowest Hessian eigenvector until a transition state
is found. If this transition state leads to a minimum with an
energy that is less than or equal to the energy of the current
minimum, the new minimum is accepted and a new transition
state search is initiated from this minimum. If a transition state
leads to a minimum that is higher in energy, or if the transition
state is not connected to the current minimum, the move is
discarded and a further transition state search is begun at the
current minimum, either by following the negative direction
of the just followed mode, or if this already has been done,
by following the direction of the eigenvector belonging to the
next higher Hessian eigenvalue. For each minimum, only a
maximum number of transition state searches is performed
(less or equal than \( 6N - 12 \), where \( N \) is the number of atoms).
If this number is exceeded, no new transition state searches
are initiated from this minimum and the algorithm jumps to the
minimum that is next higher in energy and for which the
maximum number of transition state searches have not been
accomplished yet.

\section*{F. Bar-Saddle}

In the presence of friction, a ball released from a high alti-
itude mountainside would roll downhill and lead to a close-by
local minimum. The Bar-Saddle method presented here uses
the idea that, in contrast to the rolling ball, a solid, horizontal
bar would roll to the closest saddle point if its point of contact
with the surface is kept at its center. In our implementation a
bar is represented by two endpoints \( A \) and \( B \) at the coordinates
\( \mathbf{R}_A \) and \( \mathbf{R}_B \) in the high-dimensional configuration space. The
length of a bar is evaluated as \( h = |\mathbf{R}_{AB}| = |\mathbf{R}_B - \mathbf{R}_A| \). Al-
though the Bar-Saddle formalism derived below is formally
closely related to the dimer method,\(^{46}\) it follows a different
usage paradigm. The Bar-Saddle formalism can be used to
find transition states connecting two given minima. To do
so, it starts from a configuration that is geometrically in be-
tween the two input minima and high in energy. In prin-
ciple, the highest energy configuration along the linear inter-
polation path between two minima can be used. However, in
order to avoid colliding atoms we prefer the freezing string
method in Cartesian coordinates for identifying a high energy
geometry.\(^{71}\) In all computations we used a new-node inter-
polation distance corresponding to 1/10th of the Euclidean
distance of the given two minima. Perpendicular relaxations
were stopped as soon as the perpendicular force fell below
\( 5\sqrt{\epsilon} \) or as soon as the iteration counter for the perpendicular
relaxations was equal to four. Configurations in between the
nodes generated by the freezing string method were interpola-
ted using a cubic spline interpolation. A maximum energy
configuration along this interpolated path was searched using
Brent’s method\(^{72}\) in between each pair of nodes and then se-
lecting the energetically highest configuration that was found.
Section \( \text{II G} \) describes how to obtain two suitable local min-
ima which serve as input for the freezing string method.

Having identified a suitable starting configuration from
which the bar can roll down, the bar is moved iteratively such
that the maximum energy along the direction of the bar is at
its center (corresponding to the point of contact) and such that
the energy at its center is minimized along all directions per-
pendicular to the bar. In each iteration, the energies and the
forces are evaluated at the bar ends. The forces are then de-
composed into a component parallel to the bar \( F^\parallel_{i} \) \( = (\mathbf{F}_i \cdot \hat{h}) \hat{h} \) and a component perpendicular to the bar \( F^\perp_{i} \) \( = \mathbf{F}_i - F^\parallel_{i} \),
where \( i = A, B \) and \( \hat{h} = \hat{R}_{TT} \) is the unit vector along the bar.

For the translation of the bar its energy and force along
the bar is defined by a cubic interpolation at the center of the
bar, such that

\[
E_{h/2} = \frac{1}{8} (4E_A + 4E_B + (f_B - f_A)h),
\]

and

\[
F^\parallel_{h/2} = \frac{6E_A - 6E_B - (f_A + f_B)h}{4h},
\]

where \( f_i = F_i \cdot \hat{h} \).

The perpendicular force is evaluated by \( F^\perp_{h/2} = \frac{1}{2}(F^\perp_A + F^\perp_B) \), such that the total translational forces on the bar ends result to \( F^\text{trans}_A = F^\text{trans}_B = -\gamma (f^\perp_A + f^\perp_B) \), where \( \gamma > 0 \). In our implemen-
tation we chose \( \gamma = 2 \).

In addition, a rotational force is applied to the bar in or-
der to approximately align it along the lowest curvature direc-
tion. This additional force is given by \( F^\text{rot}_A = \frac{1}{2}(F^\perp_A - F^\perp_B) \) and

\[
F^\text{rot}_B = \frac{1}{2}(F^\perp_B - F^\perp_A).
\]

Finally, following a steepest descent approach, the bar
ends are moved along the effective forces \( F^\text{eff} = \alpha F^\text{trans} + \beta F^\text{rot} \), where \( \alpha > 0 \) and \( \beta > 0 \) de-
note the translational and rotational step sizes. After each step, the bar length is rescaled such that the new bar length remains the same in each iteration \( |\mathbf{R}_{\text{New}} - \mathbf{R}_{\text{New}}| = h \).

In comparison to Bar-Saddle, the dimer method estimates
both the parallel and perpendicular components of the trans-
lational force by the arithmetic mean of the forces at the dimer
endpoints. The force responsible for the rotation acts only on
one endpoint in case of the dimer method and the rotation is
implemented by using the parametrization of a circle in a 2-
dimensional plane and rotating the dimer in a single step by an
angle estimated using a modified one-dimensional Newton
method.

Figure 2 shows the trajectories of the Bar-Saddle method
on a model energy landscape. Note that, although the method
works most efficiently if the initial point is energetically
higher than the saddle point, it will still converge when the
search is started close to a local minimum.

The efficiency of the method can be improved by applying
an energy or gradient feedback to the step sizes \( \alpha \) and \( \beta \).
In practice, we used a hybrid method where the first few itera-
tions were obtained from steepest descent with gradient feed-
back, followed by a BFGS minimization with respect to the
translational force \( F^\text{trans} \) only and applying the rotational
forces separately in each iteration.

In our implementation we considered a Bar-Saddle com-
putation as converged if the force norm at the center of the
bar fell below \( 10^{-3} \) and the curvature in bar direction was
negative. Typically, only on the order of 0.1% of all saddle
computations used for the simulations reported in this
study could not meet these convergence criteria within 15 000
iterations.

G. Generating stationary point databases using the
minima hopping guided path search approach

Searching for reaction pathways and the exploration of
the connectivity of energy landscapes requires an algorithm
that moves efficiently inside one funnel and between several
funnels. An algorithm that has proven its efficiency in exp-
either decreases the kinetic energy by a factor $\beta_n$ or increases it by a factor $\beta_n$, depending on whether the new minimum has been visited before or not. This introduces a feedback which promotes cooling down in unexplored regions and heating up in well explored regions of the potential energy landscape and thus ensures that the algorithm quickly samples the bottom of a funnel and at the same time does not get trapped.

Based on a Metropolis-like criterion MHGPS decides whether it should connect the current minimum $M_{\text{curr}}$ and the new minimum $M$ by a discrete path. If the energy of the new minimum $E$ is lower than the energy $E_{\text{curr}}$ of the current minimum, a connection attempt is always made. If its energy is higher than the energy of the current minimum, an attempt is made with a probability of

$$\exp\left(-\frac{E - E_{\text{curr}}}{E_{\text{diff}}}\right). \quad (8)$$

The parameter $E_{\text{diff}}$ resembles the energy $k_BT$ of an ordinary Metropolis simulation. However, in contrast to an ordinary Metropolis simulation, $E_{\text{diff}}$ constantly gets adjusted. If the decision is made to connect $M_{\text{curr}}$ and $M$, $E_{\text{diff}}$ is decreased by a factor $\alpha_s < 1$, otherwise it is increased by a factor $\alpha_s > 1$.

The connections are made by recursively applying Bar-Saddle and following approximate steepest descent paths from emerging intermediate transition states. Establishing the connection between the two Bar-Saddle input minima $M_{\text{curr}}$ and $M$ in a recursive or iterative fashion is essential, because there is no guarantee that the two minima $M_{\text{curr}}$ and $M$ can be connected with each other by exactly one transition state. Hence, during a connection intermediate transition states can appear which might not be connected to one or to both of the two input minima. In such a case the minima to which the intermediate transition states are connected also have to be connected to the corresponding Bar-Saddle input minima in order to obtain a discrete path that properly connects $M_{\text{curr}}$ and $M$.

After connecting $M_{\text{curr}}$ and $M$ by a discrete path, the new minimum becomes the current one and the algorithm starts a new MD trajectory at this minimum. The whole procedure is stopped as soon as a given number of distinct minima are identified. In all simulations presented in this study the standard minima hopping parameters ($\beta_s = \beta_a = 1/\beta_n = \alpha_s = 1/\alpha_a = 1.05$) were used.

MHGPS is not limited to using Bar-Saddle for connecting minima. In principle, any saddle search method that can find transition states between two given minima, for example, the Nudged Elastic Band method or the Splined Saddle method can be used. We decided to use the Bar-Saddle method, because it was the most reliable implementation available to us.

It must be emphasized that, when used alone, methods like the Nudged Elastic Band method or the Splined Saddle method are not suitable for finding lowest-barrier pathways or pathways between structurally very different configurations. These methods often fail to find a connection between distant minima and, in the best case, can only find some pathway, but not a path having a low overall-barrier.

III. BENCHMARKS AND COMPARISONS

In contrast to global minimum searches, a performance analysis of stationary point database generation algorithms is
TABLE I. Results of performance test for LJ38. Averages for \( \langle n_{ts, \text{diff}} \rangle \) and \( \langle n_{\text{ts}} \rangle \) are taken over 1000 – \( n_{\text{f}} \) independent and successful runs.

<table>
<thead>
<tr>
<th>Method</th>
<th>( n_{\text{ts}} )^a</th>
<th>( \langle n_{ts, \text{diff}} \rangle )^b</th>
<th>( \langle n_{\text{ts}} \rangle )^c</th>
<th>( n_{\text{Ed}} )</th>
<th>( n_{\text{diff}} )^d</th>
</tr>
</thead>
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<td>MHGPS</td>
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<td>14 580</td>
<td>3464</td>
<td>0</td>
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<tr>
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<td>10</td>
<td>64 611</td>
<td>168 688</td>
<td>3384</td>
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<td>72 977</td>
<td>192 097</td>
<td>3508</td>
<td>8</td>
</tr>
<tr>
<td>EFE</td>
<td>40</td>
<td>91 313</td>
<td>268 422</td>
<td>3492</td>
<td>1</td>
</tr>
</tbody>
</table>

- ^aNumber of lowest eigenvectors along which transition states were searched in positive and negative direction.
- ^bAverage number of distinct transition states needed to be found before identifying a lowest-barrier pathway.
- ^cAverage number of transition states computations needed before identifying a lowest-barrier pathway.
- ^dNumber of totally performed energy evaluations divided by the number of totally performed transition state computations. The number of energy evaluations includes the evaluations used for transition state searches, minimizations, softening, and MD.
- ^eNumber of runs in which lowest-barrier pathways could not be found before identifying \( 5 \times 10^5 \) distinct minima.

not straightforward since there is no obvious stopping criterion. One possible stopping criterion can be defined by checking whether a putative lowest-barrier pathway between two minima has been found. Because of the computational cost of Dijkstra’s algorithm, this check is not feasible if it has to be performed between every pair of minima for a given system. Therefore, a suitable test system should contain two outstanding and well defined minima for which pathways that connect them can be examined. The global minimum of LJ38 is located inside a small funnel containing fcc-like structures, the second-lowest minimum of LJ38 is contained inside a comparatively large icosahedral funnel. Both funnels are separated by a high energy barrier. Furthermore, the number of atoms in LJ38 is small enough to perform a sufficient number of runs within a feasible amount of time. Therefore, LJ38 fulfills all requirements on being a suitable benchmark system.

Table I shows the results of a performance test based on 1000 independent runs for LJ38. Each run was started using a random non-fcc structure as input geometry and, depending on what happened earlier, was either stopped as soon as the putative lowest-barrier pathway between the global minimum and the second lowest local minimum of LJ38 was identified, or if \( 5 \times 10^5 \) distinct local minima were found. For all methods and all runs the same convergence criteria for the stationary points were used.

EFE needed roughly between a factor of 12 to 18 more transition state computations than the MHGPS method before encountering a lowest-barrier pathway of LJ38. Because the number of energy evaluations per transition state computation \( n_{\text{Ed}} \) are similar for both methods, similar factors are obtained when measuring the computational cost in terms of energy evaluations.

For the EFE method we could observe a small number of runs that failed to find a lowest-barrier pathway at all. Since the number of failure runs decreased with increasing number of followed mode directions these failures can be explained by the limited number of search directions available to the EFE method. Assuming free boundary conditions, the EFE method can follow at maximum \( 6N – 12 \) directions per minimum for a \( N \)-atom system. However, the number of transition states connected to a minimum can exceed the number of \( 6N – 12 \) directions by far. For example, it is known that the global minimum of LJ13 is surrounded by 535 local minima which are connected to the global minimum by 911 transition states. It is, therefore, possible to miss stationary points that potentially lie on the lowest-barrier pathway. This general restriction of the EFE-method and similar deterministic mode-following methods has been mentioned before by Malek and Mousseau. By using random displacements away from the initial minimum, they showed that it is possible to avoid this problem in advanced mode-following techniques like the Activation Relaxation Technique.

The average number of distinct transition states \( \langle n_{\text{ts, diff}} \rangle \) divided by the average number of computed transition states \( \langle n_{\text{ts}} \rangle \) was between 66% and 87% larger for the MHGPS method than corresponding ratios of the EFE method.

The average CPU time required before MHGPS identified the lowest-barrier pathways between both lowest structures of LJ38 was measured to be roughly 8 min (on a single core of an Intel Xeon E5-2665 CPU clocked at 2.40 GHz). This timing should be compared to the \( 10^5 \) CPU hours that were required for the Sliding and Sampling computations reported in Ref. 45. These timings differ by several orders of magnitude and therefore allow to give a rough idea on the performance differences between the different methods. They are particularly noteworthy when noting that Ref. 45 only presents pathways that are higher in energy than the known lowest-barrier pathway. As well as MHGPS, the EFE method is also several orders of magnitudes faster than Sliding and Sampling. On average, our implementation of EFE needed just under 3 CPU hours to find the lowest barrier path for LJ38 \( (n_{\text{ts}} = 10, \text{average taken over successful runs}) \). As the CPU time depends very strongly on the computer hardware and the implementation of an algorithm, one should compare methods that do not exhibit such a distinct timing difference by using more suitable quantities like those given in Table I.

Figure 4 shows the histories of all transition state energies of two typical MHGPS (panel (a)) and EFE (panel (b)) runs that were performed on the LJ38 system. Both runs were started at non-fcc structures and thus are residing inside the large icosahedral funnel during the first transition state computations. Figure 4 illustrates the differing transition state sampling behavior of both methods. In the very beginning the EFE method is able to sample low-energy transition states. However, with an increasing number of totally sampled transition states, the energies of the lowest transition states that are being sampled also rises. This means the EFE-method explores the energy landscape in a bottom-up fashion. In conjunction with the limited number of search directions per minimum, this is a severe problem in particular for multi-funnel systems. As can be seen from Fig. 4, in the beginning of the sampling procedure the bottom-up sampling forces a very detailed exploration of the icosahedral funnel. The EFE method is, therefore, not able to escape from the icosahedral to the fcc funnel until roughly 5000 transition states have been computed. In very long runs, the same bottom-up sampling of the EFE method will lead at some point to the
IV. APPLICATION OF MHGPS TO LJ75 AND LJ102

Due to its advantages presented in Sec. III we applied MHGPS to LJ75 and LJ102. Concerning the task of sampling relevant stationary points, in particular LJ75 is known to be a very difficult system. This is explained by the frustration of its potential energy landscape and the large geometrical differences of both structures located at the bottoms of two major funnels.23

For each system we started 10 independent runs at the corresponding global minimum structures. For every run different random seeds were used. A run was stopped, as soon as \(2 \times 10^6\) distinct local minima were found. For the analysis of the potential energy landscapes the stationary point databases resulting from all runs were merged into a single database for each system. For LJ75 this procedure resulted in a stationary point database containing roughly \(12.0 \times 10^6\) distinct transition states connecting \(7.0 \times 10^6\) distinct local minima. In case of LJ102 we obtained by this procedure a database containing roughly \(10.9 \times 10^6\) distinct transition states which connect \(7.5 \times 10^6\) distinct local minima. The disconnectivity graphs of both system are shown in Fig. 5. Figures 6 and 7 show plots of the energy along the reaction pathways in dependence of the integrated path length \(S\) which is defined by the arc length of the steepest descent reaction path in the \(3N\)-dimensional coordinate space.63 Numerically, the integrated path length is computed by summing up all the lengths \(|\Delta R|\) of all steepest descent steps:

\[
S = \sum_{\text{steps}} |\Delta R|. \tag{9}
\]
FIG. 5. Disconnectivity graphs of LJ75 [panel (a)] and LJ102 [panel (b)]. Panel (a) shows the new putative lowest barrier between both funnels. The blue dashed line indicates the previously known lowest barrier connecting both funnels. Panel (b) shows a third, previously unknown, funnel with an energetically low bottom structure (minimum b.3) and a high barrier connecting it to the other two funnels. Both graphs show the 250 lowest minima that were found for each system. The bottom structures of each major funnel are labeled and highlighted using red color.

A. LJ75

As shown in panel (a) of Fig. 5, the highest barriers along the lowest-barrier pathways connecting the two major funnels of LJ75 that were found by MHGPS are significantly lower in energy than those of the previously known lowest-barrier pathways. Using Dijkstra’s algorithm as outlined in Sec. II B, we could identify roughly 20,000 pathways all having the same highest-barrier energies of 7.51\(\epsilon\) and 6.30\(\epsilon\) and the same number of 51 intermediate transition states. Compared to this, the previously known lowest-barrier pathway has significantly higher highest-barrier energies of 8.69\(\epsilon\) and 7.48\(\epsilon\) and possesses 65 intermediate transition states. In order to illustrate typical differences between alternative lowest-barrier pathways, panels (a)–(c) of Fig. 6 explicitly show the steepest descent reaction paths of three lowest-barrier pathways. In order to check whether there might exist further pathways which are energetically in-between the previously known lowest-barrier pathway and the putative lowest-barrier pathways found by MHGPS, we successively removed the highest energy transition state along the lowest-barrier pathway from the stationary point database and applied Dijkstra’s algorithm. Pathways resulting from this removal are shown in panels (d) and (e) of Fig. 6. For the pathway shown in panel (d) the barriers are 7.52\(\epsilon\) and 6.31\(\epsilon\), for the pathway of panel (e) the barriers are 7.54\(\epsilon\) and 6.33\(\epsilon\). They are only slightly higher in energy than the highest barriers along the putative lowest-barrier pathway. This suggests that there exists a whole range of pathways that are energetically between the putative lowest pathways presented in this study and the previously known lowest pathway. This conjecture seems to be reinforced by the pathway shown in panel (f) of Fig. 6. This pathway was found in a preliminary single-run test in which only roughly \(6 \times 10^5\) distinct local minima and roughly \(9 \times 10^5\) distinct transition states were sampled. The highest barriers along this pathway are 7.78\(\epsilon\) and 6.57\(\epsilon\).

B. LJ102

As shown in panel (b) of Fig. 5, MHGPS could find a previously unknown funnel for LJ102.47 An illustration of the bottom structure of this funnel is given in Fig. 8. The new bottom structure possesses icosahedral elements and its surface is dominated by buckled hexagonal patches. It has an energy of \(-568.388773\epsilon\).

Lowest-barrier pathways connecting the new structure to the global minimum and to the second lowest minimum are shown in panels (a) and (b) of Fig. 7. The lowest-barrier pathways connecting this new structure and the global minimum contain 40 intermediate transition states and the highest barriers are 7.97\(\epsilon\) and 7.89\(\epsilon\). The highest barriers of the lowest-barrier pathways that connect the second lowest minimum to the bottom of the new funnel are 7.97\(\epsilon\) and 7.00\(\epsilon\). These pathways contain 53 intermediate transition states. Furthermore, MHGPS could confirm the energy of the highest barrier along the putative lowest-barrier pathway connecting the global minimum to the second lowest minimum.47 However, both in terms of the number of intermediate transition states and in terms of the integrated path length, the pathway found by MHGPS is significantly shorter than the
FIG. 6. Pathways found by MHGPS connecting the bottom-structures of both LJ75 funnels (configurations a.2 and a.1 of Fig. 5). The dashed horizontal lines indicate the highest energy along the previously known lowest-barrier pathway. Panels (a)–(c) show three alternative putative lowest-barrier pathways. Panels (d)–(f) show pathways that have been obtained by successively removing the highest energy transition state along the lowest-barrier pathway from the stationary point database [panels (d) and (e)] or from a preliminary test run [panel (f)]. They only have slightly higher barriers than the pathways of panels (a) to (c) and thus show that there exist a variety of pathways lying energetically between our best results and the previously presented lowest-barrier pathways for LJ75.

FIG. 7. Putative lowest-barrier pathways that were found by MHGPS for LJ102. Panel (a) shows a putative lowest-barrier pathway connecting the putative global minimum (configuration b.1 of Fig. 5) to structure b.3 of Fig. 5. A lowest-barrier pathway connecting the second-lowest minimum of LJ102 (configuration b.2 of Fig. 5) and configuration b.3 of Fig. 5 is shown in panel (b). The parts of the reaction pathways shown in panels (a) and (b) that coincide with each other are highlighted by using dashed lines. Panel (c) shows a putative lowest-barrier pathway connecting the second-lowest configuration of LJ102 (configuration b.2 of Fig. 5) to the putative global minimum (configuration b.1 of Fig. 5).
previously known pathway. It contains only 16 intermediate transition states compared to 30 transition states contained in the pathway published earlier.\textsuperscript{37} The integrated path length is roughly 11\% shorter (difference of paths length was estimated using the plot of Ref.\textsuperscript{47}).

\section{V. CONCLUSION}

MH is a practical guide for the search of low-barrier reaction pathways, because it uses short MD moves for the exploration of potential energy surfaces and an energy feedback that satisfies the explosion condition.\textsuperscript{12,46} As a consequence of the short MD moves, consecutive minima along the MH trajectory are structurally not too different from each other and thus are well suited as input structures for methods that can find transition states between two given input geometries. Furthermore, energy conservation assures that the maximum barrier energy between two consecutive minima is bounded from above. The explosion condition assures that the MH guide does not get stuck in deep funnels. As a consequence, MHGPS must perform computationally expensive transition states computations only between minima that are particularly promising for the exploration of the potential energy landscape. MHGPS needs no human intuition and its MH based exploration of the potential energy surface is completely unbiased. It, therefore, does not fail to explore unforeseen and unexpected features of potential energy landscapes. In comparison to the EFE mode-following approach, MHGPS detects a significantly larger number of distinct transition states when performing the same number of transition state computations. MHGPS reduces the cost of sampling stationary points and their connectivity information by over one order of magnitude compared to the EFE mode-following approach. In contrast to other methods, MHGPS could successfully find the lowest-barrier pathways of LJ\textsubscript{35} in all tests. The efficiency of our new method is also confirmed by new results that were found for LJ\textsubscript{75} and LJ\textsubscript{102}, systems that have been thoroughly examined for more than a decade.

\section{ACKNOWLEDGMENTS}

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\section*{APPENDIX: STABILITY OF THE MODES}

The curvature along an arbitrary vector $x$, evaluated at the position $x_0$, is defined as

$$C_{x_0}(x) = \frac{x^T H_{x_0} x}{x^T x}, \quad (A1)$$

where $H_{x_0}$ is the Hessian at $x_0$. If $x$ was an eigenvector $v_1$, this would give the corresponding eigenvalue $\lambda_1$. Furthermore, calculating the gradient with respect to $x$ under the constraint of normalization gives

$$\frac{1}{2} \frac{d}{dx} \frac{x^T H_{x_0} x}{x^T x} \bigg|_{x^T x=1} = H_{x_0} x - (x^T H_{x_0} x) x. \quad (A2)$$

This expression vanishes in case $x$ is an eigenvector, showing that the eigenmodes are stationary points of $C_{x_0}(x)$.

The next point is to show that among all these stationary directions, only the lowest mode is actually a minimum and thus stable, meaning that rotating a slightly misaligned dimer according to its torsional force will lead back to this mode. Since the eigenvectors form a complete set, any vector can be written as a linear combination of them, i.e., $x = \sum_i c_i v_i$, with the normalization condition $\sum_i c_i^2 = 1$. Plugging this into Eq. (A1) and using the orthonormality of the eigenvectors gives

$$C_{x_0}(x) = \sum_i c_i^2 \lambda_i = c_1^2 \lambda_1 + c_m^2 \lambda_m + c_n^2 \lambda_n + \sum_{i \notin \{1,m,n\}} c_i^2 \lambda_i. \quad (A3)$$

There are three cases to consider:

- $m$ corresponds to the lowest eigenvalue: Eq. (A3) is minimal for the set $\{c_1 = 0, c_m = 1, c_n = 0, c_i = 0\}$, proving that the lowest mode corresponds to a minimum.
- $m$ corresponds to the highest eigenvalue: Eq. (A3) is maximal for the set $\{c_1 = 0, c_m = 1, c_n = 0, c_i = 0\}$, proving that the highest mode corresponds to a maximum.
- $m$ corresponds neither to the lowest nor the highest eigenvalue: assuming $\lambda_1 < \lambda_m < \lambda_n$, then choosing $c_1 = 1, c_m = 0, c_n = 0, c_i = 0$ results in $C < \lambda_m$, whereas choosing $c_1 = 0, c_m = 0, c_n = 1, c_i = 0$ results in $C > \lambda_m$. Together this shows that all these modes are saddle points.

\textsuperscript{1}J. Holland, Adaptation in Natural and Artificial Systems an Introductory Analysis with Applications to Biology, Control, and Artificial Intelligence (MIT Press, Cambridge, MA, 1992).