Reactive dynamics and spectroscopy of hydrogen transfer from neural network-based reactive potential energy surfaces

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Abstract

The ‘in silico’ exploration of chemical, physical and biological systems requires accurate and efficient energy functions to follow their nuclear dynamics at a molecular and atomistic level. Recently, machine learning tools have gained a lot of attention in the field of molecular sciences and simulations and are increasingly used to investigate the dynamics of such systems. Among the various approaches, artificial neural networks (NNs) are one promising tool to learn a representation of potential energy surfaces. This is done by formulating the problem as a mapping from a set of atomic positions $x$ and nuclear charges $Z_i$ to a potential energy $V(x)$. Here, a fully-dimensional, reactive neural network representation for malonaldehyde (MA), acetoacetaldehyde (AAA) and acetylacetone (AcAc) is learned. It is used to run finite-temperature molecular dynamics simulations, and to determine the infrared spectra and the hydrogen transfer rates for the three molecules. The finite-temperature infrared spectrum for MA based on the NN learned on MP2 reference data provides a realistic representation of the low-frequency modes and the H-transfer band whereas the CH vibrations are somewhat too high in frequency. For AAA it is demonstrated that the IR spectroscopy is sensitive to the position of the transferring hydrogen at either the OCH- or OCCH$_3$ end of the molecule. For the hydrogen transfer rates it is demonstrated that the O–O vibration (at $\sim$ 250 cm$^{-1}$) is a gating mode and largely determines the rate at which the hydrogen is transferred between the donor and acceptor. Finally, possibilities to further improve such NN-based potential energy surfaces are explored. They include the transferability of an NN-learned energy function across chemical species (here methylation) and transfer learning from a lower level of reference data (MP2) to a higher level of theory (pair natural orbital-LCCSD(T)).

1. Introduction

Rapid progress of computer technology has given science new opportunities. With the possibility to carry out simulations in the broadest sense, the conventional approach to research consisting of experimental and theoretical/mathematical methods has been considerably extended. This is particularly true for the molecular sciences for which realistic, atomically-resolved simulations have become possible during the past two decades. Such ‘in silico’ approaches now constitute an integral part of the toolbox of molecular scientists to characterize, formulate and test hypotheses and make predictions about complex systems [1, 2].

A necessary requirement for carrying out such atomistic simulations—both, molecular dynamics (MD) and Monte Carlo (MC)—is the availability of a means to determine the total energy of the system for given positions $x$ of all the atoms. For MD simulations, the forces are required as well. The most rigorous approach would be to recompute the total energy for every new configuration using electronic structure methods, i.e. solving the electronic Schrödinger equation at the highest level of theory and with the largest basis set that is computationally affordable. However, this is impractical even for small systems due to a
number of reasons, in particular if a statistically significant number of trajectories is required. First, the computing time for high-level quantum methods is appreciable. Second, technical aspects such as accounting for basis set superposition errors or including multi-reference effects for highly distorted geometries can make ‘black box’ ab initio molecular dynamics simulations of arbitrary molecules inaccurate or unstable. Finally, for chemically demanding systems, e.g. those containing metal ions, it may even be difficult to converge the Hartree–Fock wavefunction to the desired state or converging it at all for arbitrary geometries. In such cases, human intervention is required which is not desirable.

As an alternative, the total energy can be computed for a number of conformations a priori on a grid. Then, the potential energy surface (PES) needs to be represented in a way that can be evaluated for arbitrary geometries. This can be done by either resorting to a fit of a parametrized function or by representing the PES, e.g. using reproducing kernel Hilbert space theory [3, 4]. Alternatively, machine learning (ML) methods have recently emerged as a possibility to represent the energetics of molecules and their intermolecular interactions [5]. Here, the energies are obtained from learning a representation of the potential energy surface (PES) of a system, which connects a set of nuclear charges and atomic positions to the energy [6]. A suitable tool for ‘learning’ molecular energies are so-called artificial neural networks (ANNs, henceforth NNs), which were shown to be general function approximators [7].

In the present work, an NN based on the PhysNet [6] architecture is used to generate and explore fully-dimensional, reactive PESs for three β-diketones, see figure 1. The structures all have an enol- and a keto-form, of which the enol form is more stable in the gas phase [8]. Malonaldehyde (MA, propandial) is a well-studied system (see below), both experimentally and by computation for hydrogen transfer (HT) which is one of the ubiquitous reaction mechanisms in chemistry [9]. The other two systems, acetoacetaldehyde (AAA, 3-oxobutanal) and acetylacetone (AcAc, pentan-2, 4-dion) examine the influence of methyl-substituents on the intramolecular HT for both, symmetric (AcAc) and asymmetric (AAA) substitution.

For MA, the infrared (IR) spectrum [10–13] and the ground state [14–16] and vibrationally excited state tunneling splittings [17] for hydrogen transfer have been determined experimentally. Calculations at different levels of theory have also been carried out to assign these spectra and to reproduce the tunneling splitting. In general, this requires classical or quantum dynamics simulations [18–23] on fully-dimensional, high level PESs. One such PES [24] has been constructed by computing energies from a compound energy scheme based on low-level calculations and limited explicit calculations at the highest (CCSD(T)) level of theory to infer energies at the basis set limit. This circumvents the problem of explicitly calculating several 10 000 energies required for covering the PES. These energies were subsequently fitted to an explicitly parametrized expansion (1633 parameters) into permutationally invariant polynomials depending on exponentially transformed intermolecular distances (similar to Morse functions). This PES has been found to provide very accurate tunneling splittings compared with experiments which underlines its high quality.

AcAc is structurally related to MA (see figure 1) through substitution of the symmetrical H-atoms by methyl groups. Given that the methyl torsion can couple to the O–O stretch and hence to the hydrogen motion along the H-bond, it constitutes a more challenging problem than HT in MA. In AAA, only one of the hydrogen atoms is replaced by methyl.

Contrary to MA, less information about activation barriers, structures and possible tunneling splittings in AcAc is available. Even the question whether its ground state assumes an asymmetric (C\text{\textsubscript{s}}) or a symmetric (C\text{\textsubscript{2v}}) structure is still debated [25–29, 72]. The ground state structure from neutron crystallography predicts a C\text{\textsubscript{s}} symmetry [72] whereas electron diffraction experiments suggest either a C\text{\textsubscript{s}} [25, 26] or a C\text{\textsubscript{2v}} structure [28]. The most recent study performed with ultrafast electron diffraction concluded that the lowest energy form of AcAc has C\text{\textsubscript{s}} symmetry [27]. In general, electronic structure calculations find an asymmetric minimum energy structure with C\text{\textsubscript{s}} symmetry for AcAc on the PESs excluding zero-point corrections, [30–35] while correcting for zero point vibrational energy leads to a slight preference of a C\text{\textsubscript{2v}} structure [35].
Conversely, high-resolution rotational spectra of AcAc and its singly substituted $^{13}$C-isotopologues in the frequency ranges 2–26.5 GHz ($\sim$0.1–1 cm$^{-1}$) and 60–80 GHz ($\sim$2–3 cm$^{-1}$) lead to a structure with C$_2h$ symmetry [29] possibly due to zero point vibration of the proton in systems with strong hydrogen bonds [36–38]. The double well potential in AcAc due to HT from one oxygen to another is responsible for the tunneling splitting [39, 40].

Several IR spectroscopic studies of AcAc are available in the vapor phase [41–44]. The OH–stretching transition is very broad, however, it is typically assigned in the region from 2750 cm$^{-1}$ to 2800 cm$^{-1}$ [41, 44]. The only near infrared (NIR) investigation of AcAc was performed in the liquid phase in 1929 as part of a study regarding carbonyl overtones [45]. Other than a tentative assignment of a carbonyl overtone at 1.91 μm, no further transitions for AcAc were assigned. More recently, the vapor phase IR and NIR spectra of AcAc were reported [70]. The experimental spectra were interpreted by using atomistic simulations combined with reactive force fields based on molecular mechanics with proton transfer (MMPT) [46]. To the best of our knowledge no spectroscopic data for AAA is available in the open literature.

In the present work fully-dimensional, reactive PESs for MA, AAA, and AcAc are constructed by training a single NN-representation using electronic structure data. The PESs are used in finite-temperature MD simulations to determine the IR spectra of the three compounds and the (classical) rates for HT. Machine learning of the PESs is also carried out in two further, complementary ways. First, the generalizability of such an NN-learned PES is tested by learning the AcAc PES based on reference data only from MA, AAA, and the underlying ‘amons’ [47]. Second, transfer learning [48] (TL) of an NN trained on lower-level ab initio data to a higher level of theory is attempted. The work is structured as follows. First, the methods are discussed. Then, the results from finite-temperature MD simulations for the three systems are presented and discussed in the context of previous experimental and computational work. This is followed by generalizations of the NN-learned PES and the results for TL. Finally, conclusions are drawn and an outlook is given.

2. Methods

2.1. Neural network PESs based on PhysNet

All PESs used in this work are constructed by fitting the parameters of the PhysNet [6] NN architecture to extensive reference ab initio data. The NN architecture, the data set [49] generation process and the training (fitting) procedure are described below.

Neural network architecture: PhysNet [6] is a high-dimensional NN [50] of the ‘message-passing’ [51] type. It predicts atomic energy contributions $E_i$ and partial charges $q_i$ from atomic feature vectors $x_i$ encoding information about the local chemical environment of each atom $i$ [52]. The features are initialized as $x_i^0 = e_{Z_i}$, where $e_{Z_i}$ is a parameter vector depending on the nuclear charge $Z_i$ of each atom (atoms of the same element have the same initial features). Structural information is encoded by iteratively passing ‘messages’ between atoms within a cut-off distance $r_{cut}$ (here $r_{cut} = 10 \text{ Å}$) according to a fixed rule

$$x_{i}^{l+1} = x_{i}^{l} + \sum_{r_{ij}<r_{cut}} \mathcal{F}^l(x_i, x_j, r_{ij})$$

(1)

where $x_i^l$ and $x_{i}^l$ are the features of atoms $i$ and $j$ at iteration $l$ and $r_{ij}$ is the distance between them. The ‘message-passing’ function $\mathcal{F}^l(x_i, x_j, r_{ij})$ is implemented as a separate neural network for each iteration (see reference [6] for details). Note that the functional form of equation (1) guarantees that atomic features are invariant with respect to translation, rotation, and permutation of atoms of the same element, as only pairwise distances $r_{ij}$ are used as structural information and summation is commutative. After each iteration, two quantities $E_i^l$ and $q_i^l$ are predicted for each atom from their features $x_i^l$ with a neural network (here a total of $L = 5$ iterations is performed) and accumulated to obtain atomic energy contributions $E_i = \sum_i E_i^l$ and partial charges $q_i = \sum_i q_i^l$. Finally, the charges are corrected to guarantee charge conservation by spreading the difference between the total charge $Q$ and $\sum_i q_i$ evenly over all atoms. The total potential energy $E$ of a system is calculated by summation of all atomic energy contributions and explicitly including long-range electrostatic and dispersion interactions according to

$$E = \sum_{i=1}^{N} E_i + k_e \sum_{i=1}^{N} \sum_{j>i}^{N} \frac{q_i q_j}{r_{ij}} + E_{D3}$$

(2)

where $k_e$ is Coulomb’s constant and $E_{D3}$ is the D3 dispersion correction [53]. To avoid numerical instabilities, the Coulomb term is damped at short distances $r_{ij}$ (not shown in equation (2) for simplicity, see reference [6] for details).
The forces $\mathbf{F}_i$ acting on each atom $i$, required for MD studies, can be obtained analytically by reverse mode automatic differentiation [54]. For computing the infrared (IR) spectra based on the MD simulations, the total molecular dipole moment is computed from the (fluctuating) partial charges $q_i$ (equation (3)):

$$\mathbf{\mu} = \sum_{i=1}^{N} q_i \mathbf{r}_i.$$  

(3)

During the NN training the parameters are fitted to reference ab initio energies, forces and dipole moments using the procedure described in reference [6]. The parameters for the D3 dispersion correction were initialized to standard values for the Hartree–Fock method [55] and then refined during training. Minimization was carried out using ‘adaptive moment estimation’ (Adam) [56] which combines momentum and root mean squared propagation.

**Data set generation:** the quality of the reference data set is crucial for generating an accurate and robust PES. Here, the general procedure followed reference [6] again. The data set for the present work is based on calculations at the MP2/aug-cc-pVTZ [57] level of theory. For a given geometry, the energy, forces and dipole moments are calculated using the MOLPRO software package [58]. The data set not only contained the structures of MA, AAA and AcAc, but included a total of 49 structures and substructures, given in figure S1 (https://stacks.iop.org/NJP/22/055002/mmedia), based on the ‘amon’ approach [47].

An initial ensemble of 49 000 molecular geometries was generated by running Langevin dynamics at 1000 K with a time-step of $\Delta t = 0.1$ fs using the atomic simulation environment (ASE) [59] and the semi-empirical PM7 method [60] as implemented in MOPAC [61]. For all these structures, reference data at the MP2/aug-cc-pVTZ level of theory was computed and initial NNs were trained on it. Based on the initial training, the data set was augmented using adaptive sampling [62, 63]. For this, Langevin dynamics are run with two NNs and the initial data set is extended with ab initio data if the energies predicted by the two NNs differed by more than 0.5 kcal mol$^{-1}$. Two rounds of adaptive sampling were carried out.

The final data set used to train the NNs contained energies, forces and molecular dipole moments for 71 208 structures including all three molecules and their amons. Choosing the MP2/aug-cc-pVTZ level of theory was motivated by the fact that it still provides good accuracy but is also computationally feasible for data sets of size $\sim 10^5$. As the number of required training points is a priori unknown when training a new NN the level of theory for the reference calculations should be chosen with circumspection. This is why a higher level method, such as CCSD(T), was not considered from the outset but rather used in TL. The training of the NN required about 24 h on a GeForce GTX TITAN graphics card. Energy and force predictions were performed on a machine equipped with Intel® Core™ i7-2600K CPUs (3.4 GHz × 4). One energy and energy/force evaluation for MA take ~ 4 and ~ 9 ms, respectively.

**Transfer learning to a higher level of theory:** in order to further improve the quality of the entire PES, TL [48] was used. In TL, instead of starting the training procedure of an NN from scratch, an NN trained on related data is used to initialize the parameters, which usually leads to a better model with less data. This approach can be useful when high-level reference data is scarce or expensive to generate, whereas data for ‘pre-training’ (in the present case based on a lower level of electronic structure theory) the NN is readily available [48]. As such, TL is a valuable tool to bypass the high computational cost of modern electronic structure calculations: first, an NN is pre-trained on a large number of low level ab initio data and then re-trained with a smaller number of high level ab initio data to slightly adjust its parameters [64].

Here, the model trained on the MP2 data is the base model and the pair natural orbital (PNO-)–LCCSD(T)–F12/cc-pVTZ-F12 method [65, 66] is the higher level of theory. A new data set at this level of theory is generated by extracting structures from MD simulations run with the NN trained on the MP2 reference data. The new data set contains a total of 49 000 structures, composed of 1000 structures per molecule in the reference set, see figure S1. Then, the data set is split into a training set of 44 100 and a test set of 4900 structures. TL is carried out with different, randomly chosen structures in the training set with sizes of 100, 1000, 5000, 15 000, 25 000 and 40 000 structures and all parameters of the NN were allowed to change. Since the reference data set only contains energies, the loss function only depends on those and the dependency on the forces and dipole moments was removed by setting the corresponding weights in the loss term to zero. For comparison, models with the same six training sets were also trained from scratch.

### 2.2. Molecular dynamics simulations

Molecular dynamics simulations are run using the NN-trained PESs to determine the IR spectrum and the rate for HT. All MD simulations, unless stated otherwise, were run as follows. Starting from an initial structure, random momenta drawn from a Boltzmann distribution at 300 K are used as initial conditions. The system is then equilibrated for 50 ps in the NVT ensemble followed by 50 ps in the NVE ensemble. This was followed by MD simulation in the NVE ensemble for a total of 1 ns, with a time step of...
0.5 fs. For each of the molecules (MA, AAA, and AcAc) a total of 1000 trajectories are run. Every second snapshot along the trajectory is recorded for analysis.

IR spectra are calculated from the dipole–dipole autocorrelation function of the MD simulations. For every configuration the molecular dipole moment \( \mathbf{\mu}(t) \) is calculated following equation (3). From this, the dipole moment autocorrelation function \( C(t) = \langle \mathbf{\mu}(0) \mathbf{\mu}(t) \rangle \) is determined. A fast Fourier transform of \( C(t) \) yields \( C(\omega) \) and a Blackman filter is employed to minimize noise. Finally, the IR-spectrum is Boltzmann averaged to yield

\[
A(\omega) = \omega \left[ 1 - \exp(-\hbar \omega / (k_B T)) \right] C(\omega).
\]

Here, \( \omega \) is the frequency, \( \hbar \) is reduced Planck’s constant, \( T \) is the temperature, and \( k_B \) is the Boltzmann constant.

HT rates are calculated from analyzing ‘hazards’ which are deduced from the residence times \( t_k \) of the \( k \)th transition [67, 68]. Here, the residence time is defined as the time interval the transferring hydrogen remains bound to one oxygen atom before changing to the other oxygen. This can be measured by defining a cutoff O–H separation, \( r_c \). Whenever \( r > r_c \), one transfer is considered completed and the transition time \( t_k \) is recorded. The Hazard for the \( k \)th transition [67]

\[
H_k = \sum_{i=1}^{k-1} \frac{1}{n-i}
\]

is determined from the \( n \) residence times, \( t_1, t_2, \ldots, t_n \), arranged in ascending order. From this, the rate can then be deduced from the slope of the hazard plot \( (H_k \text{ versus } t_k) \) [67].

3. Results and discussion

First, the quality of the fully-dimensional, reactive PESs for the three systems is discussed. This is followed by the analysis of the computed IR spectra and the HT rates. Then, possibilities to exploit chemical principles to reduce the number of required reference structures and that for quality improvement based on TL are examined.

3.1. Quality of the PESs

The performance of the NN is first validated on a separate test set which includes structures randomly chosen from all molecules and their amons. For the test set (9208 structures) a Pearson correlation coefficient of 1–2 \times 10^{-7}, a mean absolute error (MAE) in energy of 0.020 kcal mol^{-1} and a root mean squared error (RMSE) for the energy of 0.21 kcal mol^{-1} are obtained. The NN-predicted energies and those from the MP2 reference data are compared in figure S2. To test the reproducibility of these results, an independent second NN model was trained with an MAE and RMSE of 0.024 and 0.32 kcal mol^{-1}, respectively, close to the results for the first NN.

The three energy profiles along the minimum energy path (MEP) determined from the final NN-trained PESs are reported in figure 2. The barrier heights predicted by the NN increase from 2.17 kcal mol^{-1} for MA, to 2.59 kcal mol^{-1} for AAA and to 2.79 kcal mol^{-1} for MA, and compare with 2.18, 2.56, and 2.74 kcal mol^{-1} from the reference MP2 calculations. Compared with high-level calculations at the CCSD(T)/(aug-)cc-pVTZ level of theory, the barrier heights for MA [24] and AcAc [69] are underestimated by somewhat more than 1 kcal mol^{-1}, though. Further improvements of the barriers from the NNs can be achieved through TL, as will be discussed further below.

For AAA a 2D-projection of the PES along the HT coordinate \( q = r_{O1H} - r_{O2H} \) (x-axis) and the methyl rotation (y-axis) is shown in figure 3. As expected, a three-fold periodic pattern is found for the minima and the transition states along the rotation of the methyl group by 120° irrespective of the value of \( q \). With the hydrogen on the methylated side the minima are shifted by 60° compared with structures that have the hydrogen on the unmethylated side. Upon crossing the TS, a trajectory started from the isomer with the hydrogen atom on the methylated side ends up in the conformation of the second isomer for which the methyl is rotated by 60° relative to the starting structure.

The two projections of the AcAc–PES containing the global minimum of the molecule are partially shown in figure 4(a) with \( q = r_{O1H} - r_{O2H} \) and the rotation angle \( \Phi \) of the left methyl group as the coordinates. In these projections the right-hand methyl group is frozen in an eclipsed (\( \Theta = 60° \)) or in a staggered (\( \Theta = 0° \)) geometry relative to the adjacent O-atom. The PESs shown here are again periodic (periodicity of 120°) with respect to the rotation angle \( \Phi \) of the methyl group. For \( q \approx -0.6 \) Å the rotation of the left methyl group involves a barrier of 1.37 kcal mol^{-1} which reduces to 0.25 kcal mol^{-1} for \( q \approx 0.6 \) Å. Finally, for \( q < -0.9 \) Å or \( q > 0.9 \) Å (i.e. along the O–O separation) the potential energy increases.
Figure 2. The MEP from the NN-trained model for MA (black), AAA (green), and AcAc (red). The solid part of the lines corresponds to translation of the hydrogen along the reaction coordinate \( q = r_{O1H} - r_{O2H} \), whereas the dotted part is for the rotation of a methyl group by 60° (see insets). The short horizontal lines indicate the barrier heights at higher levels of theory [24, 69]. The barrier heights on the NN PESs trained on the data from MP2/aug-cc-pVTZ calculations for MA, AAA, and AcAc are 2.79, 2.59, and 2.17 kcal mol\(^{-1}\), compared with higher-level calculations for MA (4.10 kcal mol\(^{-1}\) at frozen-core CCSD(T)/(aug-)cc-pVTZ level whereby only the basis set on the oxygen atoms was augmented) [24], and AcAc (3.20 kcal mol\(^{-1}\) at the CCSD(T)/cc-pVTZ level) [69].

Figure 3. Projection of the PES for AAA with \( q = r_{O1H} - r_{O2H} \) and the methyl rotation as the two coordinates. Contour lines are drawn every 0.3 kcal mol\(^{-1}\) and important structures are shown in ball-and-stick representation. The white solid line is the part of the MEP for the HT and the dashed white line that for the rotation of the methyl group (see also figure 2). The white crosses represent important extrema of the PES with the corresponding relative energies given in kcal mol\(^{-1}\). The red and black lines are averages over 300 independent trajectories for two possible rotation directions of the methyl group. Important features on the PES are labeled and energies are reported relative to the global minimum (in kcal mol\(^{-1}\)).

For visualization purposes, \( q, \Phi \) and \( \Theta \) are extracted from a trajectory used for the computation of the IR spectrum and the first 1 ps is shown in figure 4(a) as well as in a 3D representation in figure 4(b). Black dots represent early and white dots represent late points during the trajectory. The hydrogen atom is transferred twice and the left-hand side methyl rotates due to the lower rotational barrier for \( q > 0 \) (see figure 4(a)). When interpreting the trajectory it should, however, be taken into account that during the MD simulations both methyl groups are free to rotate whereas for the PES scan the right-hand methyl is frozen. The 3D trajectory illustrates that both methyl rotations (along the \( y \)- and \( z \)-axis) and HT (along the \( x \)-axis) occur during the course of an equilibrium dynamics and that they are coupled as the barrier for methyl rotation depends on whether the oxygen atom two bonds away from the methyl group carries the hydrogen or not.

Next, MEP and minimum dynamical path (MDP) for MA are compared. The MDP is defined as the path followed by a trajectory that passes the exact transition state with zero excess energy [70]. The MEP for MA is symmetrical (see figure 5) with a transition state at \( E_{TS} = 2.79 \) kcal mol\(^{-1}\) above the energy...
Figure 4. (a) 2D projections of the AcAc PES with $q = r_{O1H} - r_{O2H}$ and $\Phi$ as the two coordinates. The contours are drawn every 0.3 kcal mol$^{-1}$ with purple and red corresponding to low and high energies, respectively. They show the most extreme cases of the PES projections for $\Theta = 60^\circ$ ($\Theta = 0^\circ$) for which an H-atom of the right methyl group is in an eclipsed (staggered) geometry with the adjacent O-atom (see insets). Pairs of ($q, \Phi$)–values are extracted from the first picosecond of a trajectory run at 300 K and are shown as dots, where black dots are the beginning and white dots mark the end of the trajectory. The complete projections of the surfaces are shown in panel B where the missing parts are illustrated as transparent. (b) 3D representation of the same trajectory depending on $q = r_{O1H} - r_{O2H}$, $\Phi$, and $\Theta$ (see inset) with its $\Theta$-values illustrated modulo 120$^\circ$. The two PES projections including the global minimum ($\Theta = 60^\circ$ and $\Theta = 0^\circ$) are included and repeat every $\Theta = 120^\circ$. The contours are shown every 0.3 kcal mol$^{-1}$ and have the same energy scale as figure 4(a). The cluster of points in the upper right corner of the illustration (i.e. $q \approx 0.5 \text{Å}$, $\Phi \approx 300^\circ$ and $\Theta \approx 105^\circ$) correspond to structures close to the global minimum and the clustering is further amplified because ($\Theta \mod 120^\circ$) is used as the angle.

minimum. For both, MEP and MDP the O1–O2 distance and the reaction coordinate $q = r_{O1H} - r_{O2H}$ are considered. Moreover, snapshots at fixed intervals of the two paths are illustrated. Although the snapshots of the MDP and MEP are similar, the MEP lacks important dynamical information: first, the MDP reveals a strong oscillation of the O–O distance (see $r_{O1-O2}$ in figure 5), i.e. the O1–O2 distance is coupled to the HT coordinate. Even though both MEP and MDP indicate that the two oxygen atoms approach each other during HT, the strong counter-movement with O1–O2 distances up to 2.85 Å only manifests itself in the MDP. This could be essential in promoting HT and is not reflected in the MEP. A similar effect is seen for the translation of the hydrogen atom, see figure 5(b).

For AAA the MEP is shown as a projection in figure 3 (white solid and dotted trace). It demonstrates that hydrogen translation along $q$ is not coupled to the methyl rotation. To obtain insight into the dynamics of a representative trajectory, MD simulations are run from structures close to the TS with an energy of $E = E_{TS} + 3$ kcal mol$^{-1}$, following the approach presented in reference [70]. Overall, 300 independent trajectories were run and fall into two groups, depending on the direction of the rotation of the methyl group after HT. Between $q \approx -0.5$ to $q \approx 0.5$ Å the MEP (white) and the path traced by the trajectories...
Figure 5. The MEP and MDP for MA. The O1–O2 distance $r_{O1-O2}$ (a) and the reaction coordinate $q = r_{O1H} - r_{O2H}$ (b) for the MDP (black) and the MEP (red) are shown. The MEP lacks important dynamical information such as the oscillation of the O1–O2 distance (a) or the oscillation of the O–H bond (b). These aspects present in the MDP play an important role for promoting the reaction. The snapshots shown in (c) illustrate the atomic displacements for the two paths. The $x$-axis for the MEP (red) corresponds to the transfer of the H-atom progressing from the initial minimum energy structure (0) to the TS (0.5) and to the final optimum structure with the H-atom completely transferred (1). Conversely, the MDP progresses in time (black $x$-axis).

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(red and black traces) follow comparable paths across the barrier. Once they reach the TS around $q = 0.6$ Å the coupling between HT and methyl rotation leads to differences between MEP and the averaged trajectories. However, this coupling is rather dynamical in nature and not conveyed by the shape of the PES. Due to the finite kinetic energy the motion continues beyond the TS with energy 0.42 kcal mol$^{-1}$ above the minimum into regions with $q > 0.6$ where coupling between $q$ and $\Phi$ sets in. Coupling of HT and methyl rotation is also consistent with results from neutron scattering experiments [71].

3.2. Infrared spectroscopy
All IR spectra shown in this work are calculated from NN–MD simulations. The IR spectrum for MA, AcAc and AA2Ac are discussed in the following.

Malonaldehyde (MA). The calculated IR spectrum from MD simulations at 300 K along with the normal modes from the NN is shown in figure 6. The center frequencies of the IR spectrum show good overall agreement with the normal modes, although single peaks are shifted due to anharmonicity and couplings. Most importantly, the broad absorption between 2000 and 3000 cm$^{-1}$ in the IR spectrum is due to the transferring hydrogen. There are 149 073 HT events in the 1000 independent trajectories, each 1 ns in length, from which the spectra were determined. To examine the accuracy of the NN normal mode predictions, they are compared with those computed directly from MP2 calculations, see table 1. The largest deviation is 8.3 cm$^{-1}$ for mode 11. The normal modes from the MP2 calculations and the NN trained on them also compare well with higher-level calculations using CCSD(T)/(aug-)cc-pVTZ [24]. As a comparison of the accuracy of the NN, the RMSD for the normal modes from the CCSD(T) calculations and the fitted surface using permutationally invariant polynomials based on them is 21.3 cm$^{-1}$ which compares with 3.6 cm$^{-1}$ from the NN-trained PES. For the TS the overall RMSD increases to 8.7 cm$^{-1}$ (see table S1) which confirms the high accuracy of the NN-trained PES.

A detailed comparison and interpretation of the infrared spectrum with that from experiment is outside the scope of the present work. Instead, a few features are highlighted and the experimental line positions for the fundamentals [10] are provided as a guide in figure 6. The C–H stretching vibrations $\nu_{CH}$ are assigned to peaks in the 3000 cm$^{-1}$ region although experimentally, they are around or even below
Figure 6. IR spectrum of MA at 300 K averaged over 1000 independent runs, each 1 ns in length (top panel). The normal modes determined from the NN PES are given in the lower panel (red) together with normal modes determined from MP2 reference calculations (green) and the center frequencies from experiment (black) [10]. HT leads to broadening of the spectrum between 2000 and 3000 cm$^{-1}$ [69]. The experimental spectrum shows a peak at 650 cm$^{-1}$ which is not covered by the theoretical normal modes, however, its presence can be guessed in the IR-spectrum. The peak at 650 cm$^{-1}$ is attributed to a ring bend, but the frequency was not clearly assigned to a fundamental vibration [69]. Moreover, the position of the $\nu_{CH}$ is at lower frequencies than predicted by the theoretical values.

3000 cm$^{-1}$. However, it is well known that harmonic frequencies from $ab\ initio$ calculations need to be scaled when comparing them with experiments [72]. For the MP2/aug-cc-pVTZ the scaling is 0.953 which brings the frequencies to values between 2897 and 3110 cm$^{-1}$. The broad absorption between 2000 and 3000 cm$^{-1}$ in the IR spectrum is due to the transferring hydrogen. This region is spectroscopically empty when considering the normal modes. Around 1600 cm$^{-1}$ the C–O stretch vibrations follow which are at 1693 and 1640 cm$^{-1}$, respectively. At yet lower frequency, framework modes follow which are highly mixed. Their assignment is outside the scope of the present work. Finally, the O–O stretch vibration in the IR spectrum is at 243 cm$^{-1}$ whereby the assignment was made by analyzing the normal modes computed on the NN-trained PES.

Acetoacetaldehyde (AAA). The calculated IR spectrum for AAA from MD simulations is reported in figure 7 together with the normal modes for the two isomers. Depending on the position of the transferring hydrogen the normal mode frequencies can change appreciably. Because in the finite-temperature simulations both isomers are sampled due to HT, the IR spectrum contains signatures from both isomers. The normal mode frequencies of both isomers are directly compared in the upper right inset in figure 7 for the NN-predicted (red) and the MP2 (green) values. Although the two sets of frequencies correlate, slight deviations from the diagonal occur which are due to differences in the intramolecular interactions. Similar to MA, the O–O vibration is assigned to the IR frequency of 249 cm$^{-1}$ by examining the normal modes of the two isomers (261 and 277 cm$^{-1}$).

Acetylacetone (AcAc). The calculated IR spectrum of AcAc is shown in figure 8, complemented with the normal modes predicted by the NN. Again, the normal modes are well represented by the IR spectrum, with slight shifts due to the anharmonicity. Moreover, good agreement can be found with experiment and theory [69]. Some prominent peaks and regions are assigned as follows: the broad band between 2000 and 3000 cm$^{-1}$ is assigned to $\nu_{OM}$, which is caused by the transferring hydrogen. The C–H vibrations are slightly higher in wavenumber and are around and above 3000 cm$^{-1}$. Similar to MA, the CH stretch vibrations in the experiment are rather around 3000 cm$^{-1}$ whereas those from computations are shifted to the blue.
order to test whether the findings depend on the choice of is a ‘dwell’ time scale caused by partial equilibration of the hydrogen in one of the two potential wells. In the smaller barrier heights for HT it is expected that some of the rates increase compared with those in 

\[ \frac{r_{\text{c}}}{E_{\text{r}}} = \frac{91 \text{ kcal mol}^{-1}}{2.79 \text{ kcal mol}^{-1}} \]

This is explained by the exclusion of a set of HTs which immediately re-transfer without leaving the TS region completely. The slow reaction rate was not influenced by the change in \( r_{\text{c}} \).

On the other hand, \( t_{\text{p}} \) depends quite sensitively on the range over which the data is fitted for long residence times. Values ranging from 0.006 to 0.008 crossings/ps are obtained depending on the range over which the fit is carried out. Within transition state theory (and using a frequency factor of \( 10^{12} \text{s}^{-1} \)) [73], a transition rate of 0.0076 ps\(^{-1}\) corresponds to a barrier height of \( E_{\text{b}} = 2.91 \text{ kcal mol}^{-1} \), consistent with 2.79 kcal mol\(^{-1}\) from the NN PES, see figure 2. Finally, in previous work, the hopping rate for MA was determined to be 0.0024 crossings/ps from simulations using a scaled MP2 PES with a barrier of 4.3 kcal mol\(^{-1}\), consistent with higher-level CCSD(T) calculations [21]. This compares with an increased rate for HT (0.0076 crossings/ps) on the MP2 NN-PES due to its lower barrier height.

The same analysis was carried out for AAA and AcAc using \( r_{\text{c}} = 1.23 \text{ Å} \), see figures S4 and S5. Due to the smaller barrier heights for HT it is expected that some of the rates increase compared with those in

### Table 1

| Mode Number | NN (cm\(^{-1}\)) | MP2 (cm\(^{-1}\)) | PES [24] (cm\(^{-1}\)) | CCSD(T) [24] (cm\(^{-1}\)) |
|-------------|-----------------|-----------------|-----------------|-----------------|
| 1           | 277.8           | 277.5           | 268.6           | 252.9           |
| 2           | 294.7           | 286.6           | 295.4           | 283.3           |
| 3           | 393.8           | 394.3           | 383.2           | 373.8           |
| 4           | 512.7           | 514.0           | 522.1           | 504.2           |
| 5           | 787.9           | 789.4           | 760.6           | 780.6           |
| 6           | 888.7           | 888.6           | 888.3           | 887.5           |
| 7           | 937.6           | 937.6           | 897.4           | 899.1           |
| 8           | 1016.9          | 1012.3          | 995.7           | 992.9           |
| 9           | 1025.0          | 1023.8          | 998.0           | 1004.1          |
| 10          | 1049.8          | 1048.7          | 1023.1          | 1032.3          |
| 11          | 1118.0          | 1109.7          | 1105.4          | 1102.2          |
| 12          | 1289.5          | 1288.3          | 1280.8          | 1276.2          |
| 13          | 1405.1          | 1403.1          | 1393.6          | 1403.1          |
| 14          | 1413.5          | 1408.0          | 1419.5          | 1409.9          |
| 15          | 1478.6          | 1482.0          | 1490.2          | 1473.2          |
| 16          | 1640.4          | 1641.5          | 1647.2          | 1636.0          |
| 17          | 1692.8          | 1692.9          | 1713.5          | 1698.3          |
| 18          | 3037.1          | 3039.0          | 3020.7          | 3009.1          |
| 19          | 3114.4          | 3107.1          | 3196.8          | 3183.3          |
| 20          | 3216.5          | 3217.9          | 3251.4          | 3236.9          |
| 21          | 3269.1          | 3267.3          | 3348.9          | 3266.4          |
| RMSD        | 3.6 cm\(^{-1}\) |                 | 21.3 cm\(^{-1}\) |                |

The reason for this is unclear. For the signatures in the 1000 to 2000 cm\(^{-1}\) region the agreement between the normal modes and the IR-spectrum is quite apparent. At yet lower frequencies it is found that certain normal modes do not appear in the infrared spectrum as the dipole moment along these motions does not change and, hence, no IR-activity is expected. The normal mode frequency of the O–O stretch vibration is at 234 cm\(^{-1}\) compared with the corresponding peak in the IR spectrum at 226 cm\(^{-1}\).
Figure 7. IR spectrum of AAA at 300 K averaged over 1000 independent MD runs (top panel) together with the normal modes of the two isomers predicted by the NN. Some peaks of the IR spectrum are due to sampling both isomers. The inset in the upper right corner illustrates the correlation between the two sets of normal modes for both isomers from the NN (red) and MP2 calculations (green).

MA. For AAA, the fast and slow rates are \( t_1 = 1.56 \) crossings/ps and \( t_2 = 0.015 \) crossings/ps. Similar to MA, the distribution of the transition times \( p(\tau) \) shows a periodicity of \( \approx 0.135 \) ps, which corresponds to a frequency of \( 247 \) cm\(^{-1}\) which is again close to the frequency for the O–O motion at \( 249 \) cm\(^{-1}\). For AcAc the fast and slow rates are \( t_1 = 1.45 \) crossings/ps and \( t_2 = 0.036 \) crossings/ps and the periodicity of \( p(\tau) \) yields a frequency of \( 222 \) cm\(^{-1}\). This is in good agreement with the IR frequency at \( 226 \) cm\(^{-1}\). In conclusion, the fast time scale for all three systems is between \( 1.5 \) and \( 1.8 \) crossings/ps whereas the long time scale \( t_2 \) differs appreciably and ranges from \( 0.008 \) crossings/ps to \( 0.036 \) crossings/ps, commensurate with a difference in the barrier height by almost a factor of two between MA and AcAc.

An independent test for the applicability of a hazard analysis is to consider the total number of hazards as a starting population and to follow its decay using first order kinetics. Then, the residence time is the time for a 'state' to decay. For MA such an analysis yields 1.69 crossings/ps compared with 1.81 crossings/ps from the hazard analysis and confirms its validity. In all these considerations it is important to note that this approach using classical trajectories is expected to give a lower limit for the rate because quantum effects, such as tunneling or zero-point energy are not included and typically increase the rate.

3.4. Generalizability of the NN

High-quality PESs are often difficult to obtain due to the computational cost in calculating a sufficiently large number of \textit{ab initio} reference energies at a sufficiently high level of theory. It would be desirable to minimize the number of such high-level calculations that need to be carried out while retaining the quality of the high-level calculations in the represented PES. Two possibilities are explored in the following. The first examines whether it is possible to infer the PES for a larger chemical compound from information about a smaller one (transferability). The second one attempts to learn a high-level PES from a fully-dimensional PES at a lower level of theory together with information about selected points of the higher-level PES (TL).

To assess how the NN generalizes on unseen structures, an NN PES for AcAc (two CH\(_3\)) is determined by learning on a training set with structures for MA (no CH\(_3\)), AAA (one CH\(_3\)) and the amons only. This model is called NN\(^*\) in the following. The performance of NN\(^*\) is reported in figure 10 where the unknown energies of 5000 AcAc structures are predicted from NN\(^*\) and compared with the reference
energies at the MP2/aug-cc-pVTZ level of theory. The Pearson correlation coefficient is \( r^2 = 0.9984 \), the mean absolute error (MAE) is 0.98 and the root mean squared error (RMSE) is 1.25 kcal mol\(^{-1}\). The data shows only a small, uniform dispersion without evident outliers. It is noteworthy that the MAE is below 1 kcal mol\(^{-1}\), i.e. ‘chemical accuracy’ is achieved for this H → CH\(_3\) replacement over a range of energies exceeding 100 kcal mol\(^{-1}\).

The performance of NN* is further examined by computing the IR spectrum and comparing it with that from the NN PES trained on the data set including AcAc. The results are summarized in figure 11, where the IR spectrum from using the NN PES is shown in the bottom and the spectrum from using NN*
Figure 10. Performance of NN* from analyzing 5000 AcAc structures from training on MA, AAA, and amons. The energies predicted by NN* are compared with those from the reference MP2/aug-cc-pVTZ calculations and demonstrate that the H → CH₃ replacement can be predicted with ‘chemical accuracy’. The MAE is 0.9775 kcal mol⁻¹, and NN* achieves a Pearson correlation coefficient of \( r^2 = 0.9984 \). The zero of energy is the optimized AcAc structure.

Figure 11. Comparison of the IR-spectra from MDs for AcAc from models NN* (top panel, red) and from NN (bottom panel, black). The red and black impulse lines in the middle panel show the positions of the most prominent peaks. They differ by at most 14.6 cm⁻¹. In the top panel. The stick spectrum in the middle panel are the peak positions of the IR spectrum in the corresponding colors. The IR spectra calculated from NN and NN* are very similar with a maximum difference of the peak positions of 14.6 cm⁻¹ for the line at 366.6 (381.2) cm⁻¹. The average difference is, however, only 5.4 cm⁻¹ (see table 2). Moreover, one additional peak was found in the IR-spectrum calculated by the final model. A normal mode analysis for NN and NN* shows that all the major differences are caused by vibrations involving the additional methyl group, see figure S6.
Table 2. Comparison of the most prominent IR peaks for AcAc from NN and NN*, see figure 11.

| NN* (cm⁻¹) | NN (cm⁻¹) | Absolute difference (cm⁻¹) |
|------------|-----------|---------------------------|
| 381.2      | 366.6     | 14.6                      |
| 407.0      | 396.7     | 10.3                      |
| 510.1      | 506.6     | 3.5                       |
| 644.8      | 646.4     | 1.6                       |
| 784.7      | 791.5     | 6.8                       |
| 939.4      | 930.9     | 8.5                       |
| 1015.0     | 1011.4    | 3.6                       |
| —          | 1032.4    | —                         |
| 1176.0     | 1187.1    | 11.1                      |
| 1277.7     | 1275.7    | 2.0                       |
| 1378.0     | 1379.9    | 1.9                       |
| 1459.7     | 1460.5    | 0.8                       |
| 1571.7     | 1571.6    | 0.1                       |
| 1642.6     | 1650.4    | 7.8                       |
| 1682.4     | 1677.0    | 5.4                       |
| 3072.9     | 3077.3    | 4.4                       |
| 3185.9     | 3189.2    | 3.3                       |

average = 5.36 cm⁻¹

Figure 12. Learning curve for the NNs based on PNO–LCCSD(T)–F12 (blue) and for the TL models (red). The MAE (solid) and the RMSE (dashed) are shown in kcal mol⁻¹ for all models. All models were evaluated on the same test set consisting of 4900 structures. The black lines show the performance of the MP2 model trained on 71 208 structures on the same test set.

The results discussed above show that an NN can generalize to unknown structures for an H → CH₃ substitution with an error of < 1 kcal mol⁻¹ for energies and for normal modes with a mean average error of 5.4 cm⁻¹. Hence, PhysNet appears to be a suitable model to further explore the possibility to generalize fully dimensional, reactive PESs based on smaller reference structures which may increase the speed with which such models can be trained.

3.5. Transfer learning to a higher level of theory

Transfer learning for the present application requires reference calculations at a higher level of theory. For this, energies for a total of 49 000 geometries for MA, AAA, AcAc and the amons were calculated at the PNO–LCCSD(T)–F12 level of theory. TL from the lower (MP2) to the higher (PNO–LCCSD(T)–F12) level of theory was carried out with different training set sizes (100, 1000, 5000, 15 000, 25 000, 40 000) drawn randomly from the higher-level data set. All models were then evaluated for the same test set containing 4900 randomly chosen structures, again including MA, AAA, AcAc and their amons. The MAE and the RMSE for predicting the energies of the 4900 test structures are reported in figure 12. The black lines correspond to the performance of the MP2 model trained on 71 208 structures on the same test set.

Evidently, the TL models outperform the models trained from scratch. Their performance is superior for small data set sizes, because the training already starts with a good guess for the weights and biases. For
larger sizes, the errors of models trained from scratch converge toward the TL models, however, even for the largest training set size the TL models reach higher accuracy. These results suggest that pre-training on lower level data leads to higher-accuracy models when TL is applied. Already adding 100 structures from the higher level of theory to the original MP2 training data set yields a significantly lower RMSE. With 5000 reference structures the TL model performs again with chemical accuracy whereas the model learned from scratch is inferior by a factor of two.

It is also of interest to consider particular features of the transfer learned PES, such as the barrier heights for HT. First, this barrier was determined at the PNO–LCCSD(T)–F12 level for the three systems. As no gradients are available for this method, the energies for the minima and transition state geometries were determined at the optimized MP2 structures which yields barrier heights for MA, AAA, and AcAc of 4.04, 3.81, and 3.25 kcal mol\(^{-1}\), respectively, which compare with 4.1 kcal mol\(^{-1}\) (MA) \cite{24} and 3.2 kcal mol\(^{-1}\) (AcAc) \cite{69} at the CCSD(T) level of theory. Hence, compared with the MP2 calculations and the NN learned on MP2 energies all TS energies are in very good agreement with the highest level of theory (CCSD(T)).

Next, the barrier heights \(E_b\) from the TL models are considered. The minimum and TS geometry of each compound are optimized with the respective model before computing \(E_b\). Barrier heights based on the MP2 optimized geometries are given in table S2 for completeness. TL with different numbers of randomly chosen structures (between 100 and 40 000) from the training set shows that between 15 000 (for AcAc) and 25 000 (for MA and AAA) structures are required to obtain barrier heights within fractions of one kcal mol\(^{-1}\) of the PNO–LCCSD(T)–F12 values. This is primarily due to the fact that the structures for TL were randomly chosen and that it is not guaranteed that the training set contains sufficient information about the property (here TS energy) of interest. If particular features of a PES need to be improved, better choices will be possible, see further below.

This was explored in two ways. First, four additional, independent models were trained, each for a training set size of 1000 and 15 000 structures and the barrier heights were determined from their average. For the averaged model based on 1000 training structures (\(\langle m_{1000} \rangle\)) an \(E_b = 4.66\) kcal mol\(^{-1}\) is determined with a range from 4.31 to 5.08 kcal mol\(^{-1}\) for the individual models, see table 3. For \(m_{15000}\) this increases to 6.42 kcal mol\(^{-1}\) (range from 6.00 to 6.87 kcal mol\(^{-1}\)). Hence, the larger training set size did not lead to an improved energy barrier. For AAA, the barriers range from 2.74 to 4.20 kcal mol\(^{-1}\) for \(m_{1000}\) and \(\langle m_{15000} \rangle\), respectively, compared with 3.81 kcal mol\(^{-1}\) from PNO–LCCSD(T)–F12. The energy barriers of the HT for AcAc were also determined and averaged values of 1.80 and 3.32 kcal mol\(^{-1}\) were found for \(m_{1000}\) and \(\langle m_{15000} \rangle\), respectively. The value of 3.32 kcal mol\(^{-1}\) compares well with the PNO–LCCSD(T) value of 3.25 kcal mol\(^{-1}\).

Specifically the failure of \(\langle m_{15000} \rangle\) to qualitatively describe the H-transfer barrier height for MA is a motivation to consider enrichment of the training data set with specific information about this property. Hence, four additional models each are transfer learned based on a) 100 structures from the MEP for H-transfer in MA and b) the remaining structures randomly drawn from (MA, AAA, AcAc, and the amons) as before, for training set sizes of 1000 and 15 000, respectively. Table 3 shows averages of the TL

| \(E_b\) MA | \(E_b\) AAA | \(E_b\) AcAc |
|---|---|---|
| no MEP | MEP | no MEP | MEP | no MEP | MEP |
| \(m_{100}\) | 3.18 | | 1.99 | | 0.92 | |
| \(m_{1000}\) | 5.08 | 3.00 | | 2.40 | | |
| \(\langle m_{1000} \rangle\) | 4.66 | 3.91 | 2.74 | 3.35 | 1.80 | 2.72 |
| \(m_{2000}\) | 4.94 | 3.80 | | 2.66 | | |
| \(m_{4000}\) | 6.28 | 4.32 | | 3.31 | | |
| \(\langle m_{15000} \rangle\) | 6.42 | 4.04 | 4.20 | 3.97 | 3.32 | 3.34 |
| \(m_{25000}\) | 4.09 | 3.84 | | 3.28 | | |
| \(m_{5000}\) | 4.00 | 3.83 | | 3.29 | | |
| MP2 | 2.79 | 2.46 | | 2.17 | | |
| P-LC-F12 | 2.74 | 2.47 | | 2.18 | | |
| CCSD(T) | 4.1 \cite{24} | — | | 3.2 \cite{69} | | |
models including the MEP structures for all three systems. Now $E_b$ for MA is 3.91 and 4.04 kcal mol\(^{-1}\) for $\langle m_{1000}\rangle$ and $\langle m_{5000}\rangle$, respectively, which compares well with the PNO--LCCSD(T)--F12 reference value of 4.04 kcal mol\(^{-1}\). Even though no dedicated MEP-data was included for AAA and AcAc, these barrier heights are now also accurately predicted. Barrier heights of 3.35 (2.72) and 3.97 (3.34) kcal mol\(^{-1}\) are found for AAA (AcAc) for the two training set sizes, respectively, and compare with a PNO--LCCSD(T)--F12 value of 3.81 (3.25) kcal mol\(^{-1}\). Hence, including structures along the MEP for HT in MA not only improves the trained NNs for MA but for AAA and AcAc, too.

In summary, TL from a fully-trained NN at the MP2 level of theory by using additional information of the higher PNO--LCCSD(T)--F12 level of theory yields improved PESs for the three systems considered at the level of mean absolute and root mean squared error when using randomly selected reference data, see figure 12. However, when evaluating particular local features of the TL--NNs, such as the barrier height for hydrogen transfer or the relative stabilization of two structural isomers, the results are not particularly accurate and may even lack convergence toward the correct value with increasing size of the training set. Including specific information about the property of interest was shown to considerably improve this. This is reminiscent of the ‘morphing potential’ approach [74] which aims at reshaping a fully-dimensional PES calculated at a lower level of theory by means of a generalized coordinate transformation and reference data at a higher level of theory.

4. Conclusion and outlook

The PESs of MA, AAA and AcAc are modeled successfully with a single NN, which predicts the energies of a test set containing 9208 structures, including MA, AAA, AcAc and substructures, with an MAE of $\approx 0.020$ kcal mol\(^{-1}\) and an RMSE of $\approx 0.21$ kcal mol\(^{-1}\). The NN based on MP2/aug-cc-pVTZ calculations is able to predict the energy barriers for the three HT reactions with deviations $\leq 0.05$ kcal mol\(^{-1}\) in comparison to the MP2/aug-cc-pVTZ values. The model can be used to run simulations, calculate IR spectra or reaction rates. Both the IR spectra and the rates were found to agree with the literature. The generalizability of the NN was examined with a prospect to simplify future research in terms of modeling. It was shown that the NN is able to generalize fairly well to structures with an extra methyl group, although not all properties will be predicted perfectly. Depending on what the aim of the theoretical investigation is, this approach could be used to circumvent considerable amounts of computing time.

Finally, the method of TL was explored and the MP2 NN was transfer learned to the PNO--LCCSD(T)--F12 level of theory. First, models with different training set sizes are used to predict the energies of the test set containing 4900 structures. The TL models outperform the models trained from scratch in terms of learning curve and accuracy. Second, the energy barriers of the HT reactions are examined and it is found that between 15 000 (for AcAc) and 25 000 (for MA and AAA) random structures are required to obtain barrier heights within fractions of one kcal mol\(^{-1}\) of the PNO--LCCSD(T)--F12 values. Including structures along the MEP for HT in MA considerably improves the barrier heights found in the TL models for MA, AAA, and AcAc, with a maximal difference of 0.26 kcal mol\(^{-1}\) between the NN and the reference calculations.

In summary, a comprehensive NN model for MD studies of the spectroscopy and HT dynamics for MA, AAA, and AcAc was trained at the MP2 level of theory. The findings suggest that TL will provide an efficient route forward for high-level, fully dimensional and reactive models to investigate the dynamics of chemical systems. Also, generalizations to different chemical substitutions (here H $\rightarrow$ CH$_3$) appear to be possible but more systematic studies on this aspect are required.

Data and code availability

All data required to train the NNs has been made available on zenodo (https://doi.org/10.5281/zenodo.3629239) and the code for training the PhysNet model is available at https://github.com/MMunibas/PhysNet.

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