High Accuracy Semi-Empirical Quantum Models Based on a Reduced Training Set

Cong Huy Pham,*† Rebecca K. Lindsey,† Laurence E. Fried,† and Nir Goldman†

†Physical and Life Sciences Directorate, Lawrence Livermore National Laboratory,
Livermore, California 94550, United States
‡Department of Chemical Engineering, University of California, Davis, California 95616,
United States

E-mail: pham20@llnl.gov
Abstract

There exists a great need for computationally efficient quantum simulation approaches that can achieve an accuracy similar to high-level theories while exhibiting a wide degree of transferability. In this regard, we have leveraged a machine-learned force field based on Chebyshev polynomials to determine Density Functional Tight Binding (DFTB) models for organic materials. The benefit of our approach is two-fold: (1) many-body interactions can be corrected for in a systematic and rapidly tunable process, and (2) high-level quantum accuracy for a broad range of compounds can be achieved with $\sim0.3\%$ of data required for one advanced deep learning potential (ANI-1x). In addition, the total number of data points in our training set is less than one half of that used for a recent DFTB-neural network model (trained on a separate dataset). Validation tests of our DFTB model against energy and vibrational data for gas-phase molecules for additional quantum datasets shows strong agreement with reference data from either hybrid density-functional theory, coupled-cluster calculations, or experiments. Preliminary testing on graphite and diamond successfully reproduce condensed phase structures. The models developed in this work, in principle, can retain most of the accuracy of quantum-based methods at any level of theory with relatively small training sets. Our efforts can thus allow for high throughput physical and chemical predictions with up to coupled-cluster accuracy for materials that are computationally intractable with standard approaches.
Atomistic simulations are an essential tool for studies in physics, chemistry, biology, and materials science. These calculations can provide atomic level detail of physical phenomena and chemical reactions that can help to understand experimental observations. With modern computing advances, computationally intensive simulations using quantum mechanical methods such as hybrid density-functional theory (DFT), Møller-Plesset second-order perturbation theory (MP2), or coupled-cluster approaches can be performed to provide accurate descriptions of electronic and vibrational states, as well as thermodynamic quantities for a diverse set of systems. The high computational expense of these approaches, however, generally limits their application to static gas-phase clusters or small, sub-nanometer systems sizes. This can be far below the spatial scales of most experimental studies, which frequently probe nanometers or beyond and involve dynamic measurements. For example, the “gold standard” CCSD(T) (coupled-cluster considering single, double, and perturbative triple excitations) method scales as $O(N^7)$, where $N$ is the number of basis functions involved in the calculation. Consequently, it is generally only applicable to systems with tens of atoms or less, precluding its use for larger biomolecules or condensed phases. Neural network (NN) approaches can be used to completely parameterize the quantum mechanical interactions\cite{1,2} bypassing the need for direct electronic state calculation and thus yielding improved scaling and efficiency. However, NNs tend to require extremely large training sets and can perform poorly outside of their training regime\cite{3} This need for large data sets, in particular, makes such approaches challenging to implement and use effectively. Therefore, there is a widespread need for the development of computational methods that can maintain the accuracy of high level approaches while yielding substantial gains in training set size, computational costs, and scaling.

Semi-empirical methods, for example Density Functional Tight Binding (DFTB)\cite{4,5}, are a potential strong alternative quantum approach. The DFTB Hamiltonian is derived directly from an expansion of the Kohn-Sham DFT total energy, yielding a good balance between approximate quantum mechanics and empiricism. This can result in calculations requiring
only a small fraction of the computational cost compared to DFT or other high-level quantum approaches. Here, the DFTB total energy is written as:

\[ E_{\text{DFTB}} = E_{\text{BS}} + E_{\text{Coul}} + E_{\text{rep}}, \quad (1) \]

where \( E_{\text{BS}} \) corresponds to the band structure energy, \( E_{\text{Coul}} \) is the charge fluctuation term, and \( E_{\text{rep}} \) is the repulsive energy. \( E_{\text{BS}} \) is calculated as a sum over occupied electronic states from the DFTB Hamiltonian. In practice, DFTB Hamiltonian matrix elements are computed from pre-tabulated Slater-Koster tables derived from reference calculations with a minimal basis set. The repulsive energy, \( E_{\text{rep}} \), corresponds to ion-ion repulsions, as well as Hartree and exchange-correlation double counting terms. This term can be expressed as an empirical function where parameters are fit to reproduce high-level quantum or experimental reference data. A pairwise potential energy function is often used for the repulsive energy term,\(^8\)\(^9\) though many-body interaction terms are required in some cases.\(^10\)\(^11\) DFTB is approximately three orders of magnitude more efficient than DFT calculations and exhibits \( O(N^3) \) scaling. Its combination of approximate quantum mechanics with empirical functions can allow for a high degree of flexibility in terms of optimization approaches, desired accuracy, and transferability across element types and diverse conditions.\(^12\)\(^13\) DFTB models have been created for a broad range of materials, though the repulsive energy largely has been tuned to relatively low-level DFT data for condensed phases.\(^14\)\(^15\)\(^16\)

Recent efforts have been made to enhance the accuracy of DFTB through creation of more sophisticated and systematic approaches for determining the repulsive energy term.\(^14\)\(^20\)\(^22\) Kranz et al. added general polynomial forms to the standard DFTB repulsive energy to describe different bond types and various chemical environments.\(^20\) By training to energies and atomic forces of \( \sim 150,000 \) structures of 2100 unique C, H, N, O, and F containing molecules in both equilibrium and distorted configurations, their model can reproduce reference atomization energies of an \( \sim 130,000 \) molecule test set. Gaussian Process Regression\(^21\)
and the Curvature Constrained Splines methodology have been used to create strictly pair-wise additive repulsive energies for several organic and inorganic systems. However, these methods can struggle for systems where greater than two-body interactions in $E_{\text{rep}}$ are needed. NNs have been proposed as a promising method to include many-body interactions into the DFTB repulsive energy. The resulting DFTB-NN models have the capability of predicting molecular properties for a wide range of compounds and element types. However, the drawback of utilizing NNs for $E_{\text{rep}}$ is similar to their use for classical force fields in that they require large amounts of training data and can have slow parameterization due to the presence of quasi-degenerate local minima, making their development exceedingly challenging.

Here, we explore the possibility of creating DFTB models that can leverage the relative simplicity of linear regression machine learning in the recently developed Chebyshev Interaction Model for Efficient Simulation (ChIMES) method. ChIMES is a many-body force field based on linear combinations of Chebyshev polynomials. It has been shown that ChIMES models yield good agreement with DFT reference method for a wide range of properties and materials under both ambient and extreme conditions. The main advantage of ChIMES is that it is completely linear in fitted coefficients, allowing for rapid parameterization to a global minimum. The reliance on Chebyshev polynomials, which are orthogonal, allows the complexity of a ChIMES model to be systematically tuned to an arbitrary degree of accuracy and transferability, while also providing straightforward methods for regularization to minimize overfitting. In this study, we determine an optimal DFTB/ChIMES model for C, H, N, O-containing systems using high level quantum chemical reference data. We use an iterative scheme to systematically expand our training set where at each iteration, a small fraction of the force configurations with largest deviation in our validation set are included in the next training set iteration. The accuracy and transferability of the resulting model are investigated for a wide variety of gas-phase clusters as well as some carbon solids. We find that use of a small fraction of our chosen data set (∼0.3% of similar NN efforts) yields
DFTB/ChIMES models that maintain close to hybrid functional, coupled-cluster, and/or experimental accuracy for the gas-phase clusters studies here, and compares favorably to previous DFTB-NN efforts for similar systems.

For our DFTB/ChIMES models, the total energy is determined as the sum of the standard DFTB energy with an additional ChIMES contribution:

\[
E_{\text{DFTB/ChIMES}} = E_{\text{BS}} + E_{\text{Coul}} + E_{\text{rep}} + E_{\text{ChIMES}},
\]

(2)

For this work, DFTB calculations are performed using the 3ob-3-1 parameter set, which contains a third-order expansion about the charges and is considered an optimal DFTB starting point for most organic system.\(^{22,29}\) The ChIMES energy is written as a many-body expansion:

\[
E_{\text{ChIMES}} = \sum_{i=1}^{n_a} E_i + \sum_{i=1}^{n_a} \sum_{j=1}^{i-1} E_{ij} + \sum_{i=1}^{n_a} \sum_{j=1}^{i-1} \sum_{k=1}^{j-1} E_{ijk} + \sum_{i=1}^{n_a} \sum_{j=1}^{i-1} \sum_{k=1}^{j-1} \sum_{l=1}^{k-1} E_{ijkl} + \cdots,
\]

(3)

where \(n_a\) is the number of atoms in the system. The atomic energies \(E_i\) are constants used to match energies from reference data, and two-body (pairwise) energies are expressed as linear combinations of Chebyshev polynomials of the first kind.\(^{30,31}\) Higher-bodied interactions are determined through products of a cluster’s constituent pair-wise polynomials.\(^{32}\) ChIMES parameters are determined by fitting to the difference between the reference energies and atomic forces and those computed from DFTB alone using the following objective function:

\[
F_{\text{obj}} = \sum_{i=1}^{n_g} \left[ \sum_{j=1}^{n_a(i)} \sum_{k=1}^{n_a(i)} 3 w_{F_{ijk}}^2 (\Delta F_{ijk})^2 + w_{E_i}^2 (\Delta E_i)^2 \right] / N_d,
\]

(4)

where \(N_d\) is the total number of data entries, given by \(N_d = n_g + \sum_{i=1}^{n_g} 3n_a(i)\). Here the number of gas phase molecular conformations in the training set is given by \(n_g\) and \(n_a(i)\) indicates the number of atoms in the configuration \(i\). \(F_{ijk}\) is the \(k^{\text{th}}\) Cartesian component of the force acting
on atom \( j \) in configuration \( i \), while \( E_i \) is the energy per atom of configuration \( i \). The term \( \Delta X \) is equal to \( X_{\text{ref}} - X_{\text{DFTB}} - X_{\text{ChIMES}} \) (where \( X \equiv F_{ijk}, E_i \)). The subscripts “ref”, “DFTB”, and “ChIMES” indicate the predicted quantity \( X \) from reference method, DFTB, and the present ChIMES correction, respectively. Further details about our DFTB calculations, the ChIMES functional form, the fitting procedure and ChIMES hyper-parameter selection (including radial ranges, polynomial orders, and other pertinent details) can be found in the Supporting Information.

The dataset used to develop the DFTB/ChIMES model here is a subset of the ANI-1x dataset which we will refer to as ‘sub_ANI-1x’. It contains only molecular conformations from ANI-1x computed using CCSD(T)/CBS, \( \text{wB97X/def2-TZVPP} \), and \( \text{wB97X/6-31G*} \) levels of theory. This corresponds to \( \sim 10\% \) of the full ANI-1x data set, and resulted in 459,464 molecular conformations of 1895 unique molecules, including transition states of some chemical reactions. Since there are no data for atomic forces at the CCSD(T)/CBS level of theory in the ‘sub_ANI-1x’, for our fitting purposes we use the \( \text{wB97X/def2-TZVPP} \) reference data only. We note here that fitting a DFTB/ChIMES model using a whole ‘sub_ANI-1x’ set directly would utilize \( \sim 19\text{M} \) data points, resulting in a slow parameterization. In addition, it is of great benefit to create semi-empirical quantum approaches that do not require the traditionally vast amounts of training data needed by most machine learning approaches. As a result, our first objective is to determine how much data is needed from ‘sub_ANI-1x’ to train a good DFTB/ChIMES model. Starting from this dataset, we randomly selected only 1\% of the total possible configurations (4594 molecular geometries) with the remainder kept for validation purposes. The performance of this iteration is labeled “circle 0” in figure II panel (a) and (d) for the comparison of energies and forces, respectively. The largest deviations in energies and forces come from molecular configurations where short-ranged interactions are not adequately sampled, i.e., the smallest atom pair distances in non-equilibrium molecular conformations are somewhat poorly sampled in the initial training set. We then used an iterative fitting scheme to generate the next set of
DFTB/ChIMES models.

At each “circle”, an additional 1% of configurations from the validation set with the highest force deviations is added to the previous training set to generate our next iteration of the model. Model performance evaluation (based on the MAE/RMSE for energies and forces) is done on the new validation set. The process is repeated until changes in the MAE/RMSE converge. Surprisingly, we found that our approach converges quickly, since at “circle 2” the changes in MAE/RMSE for energies and forces are relatively small (less than 0.1 kcal/mol for energy and 0.1 kcal/mol-Å for force, see Supporting Information). This means that by using only 3% of the ‘sub_ANI-1x’ data, DFTB/ChIMES is able to reproduce the reference data in the remaining 97% of the configurations. The required training set size for this DFTB/ChIMES model (only 0.3% of ANI-1x dataset) is therefore significantly less than that of previous ANI potentials, which generally have used at least 5M molecular conformations in the training data. This can be attributed in part to the relative accuracy of the approximate quantum mechanics in DFTB as well as the flexibility of ChIMES. Our method also leverages previous efforts in generating high accuracy and highly diverse quantum-mechanical ANI-1x dataset. We note here that our final DFTB/ChIMES model contains approximately two orders of magnitude fewer parameters than a similar NN effort (5546 for DFTB/ChIMES vs. 389376 for ANI-1x), also helping to reduce the needed amount of training data. The final total size of our training set (∼372K data points) is also less than the ∼800K data points used for a recent DFTB-NN model with deep tensor neural networks.

To further test the transferability of our model, we compute comparisons from DFTB/ChIMES to three additional high-level quantum chemical data sets for organic materials, with reference energies/forces at the level of wB97X (the same as in the training data) or coupled-cluster calculations (higher level of accuracy). The GDB-10to13 data set consists of the molecular energies and forces at the DFT (wB97X) level of nearly 3000 molecules containing 10-13 C, N, or O atoms. For each molecule in this data set, 12 to 24 non-equilibrium geome-
tries are generated from displacements along normal modes, yielding a total number of 47,670
configurations. Table 1 provides MAE and RMSE for DFTB and DFTB/ChIMES models on
the GDB-10to13 benchmark. The standard DFTB method predicts relatively large values for
MAE/RMSE. Our DFTB/ChIMES model exhibits a 60% and 45% decrease in MAE/RMSE
of the energies and forces, respectively, over standard DFTB. We note that the predicted
MAE/RMSE using DFTB/ChIMES is similar to values from the ANI-1 and ANI-1x poten-
tials, though here we have only trained our model on ~14k molecular geometries compared
to 22M and 5M molecular conformations used to train ANI-1 and ANI-1x, respectively.
Our computed MAE/RMSE (3.57/4.72 kcal/mol for energies and 3.62/5.33 kcal/mol-Å for
forces) are smaller than the variations between wB97X-DFT itself and higher levels such as
CCSD(T) and MP2 (4.9/5.9 kcal/mol for energies and 4.6/5.9 kcal/mol-Å for forces).

The performance of DFTB/ChIMES in comparison to coupled-cluster reference data is
also provided in Table 1. Here, we have selected the ISO34 data set which consists of
computed energies only of 34 isomers containing the elements C, H, N, and O. The reference
isomerization energies are at the CCSD(T) level of theory or contain experimental reac-
tion enthalpies with the removal of vibrational and thermal effects. This data set has been
widely used for benchmarking different computational methods, including DFT, DFTB
and DFTB-NN (DFTB-NN with deep tensor neural networks). One can see that the
accuracy of DFTB/ChIMES is much better than that for standard DFTB, is slightly im-
proved over that from DFTB-NN, and approaches the PBE0 data given in Reference

To test the performance of our model on high accuracy force data specifically, we compare
DFTB/ChIMES with the CCSD(T)/cc-pVTZ data for 2000 configurations of ethanol in the
GDML data set (54,000 data points total). Again our DFTB/ChIMES gives an improve-
ment over standard DFTB as MAE and RMSE are both reduced by ~40%. A direct force
comparison to DFTB-NN or the ISO34 reference was unavailable.

To probe the smoothness in the potential energy surface from DFTB/ChIMES, we have
also computed the potential energy profile for rotation around the dihedral angles in alka-
The torsional profile for $n$-butane is shown in Figure 2 as a test case. The reference data are at the level of $w$B97X/def2-TZVPP, where the C-C-C-C dihedral angles are fixed at corresponding values and the other degrees of freedom are fully optimized. Comparison was then made to DFTB or DFTB/ChIMES single point calculations at the DFT optimized geometries. As shown, both DFTB and DFTB/ChIMES predict the relative energy of the metastable minimum (at $\pm 70^\circ$) in good agreement with $w$B97X reference data with deviations of less than 0.5 kcal/mol. DFTB, however, underestimates the torsional barriers by 0.9 and 1.7 kcal/mol for the lower-energy (at $\pm 120^\circ$) and main barrier (at $0^\circ$), respectively. DFTB/ChIMES is more accurate overall, with deviations of less than 0.5 kcal/mol for predicting all energy barriers discussed here.

Next, we compare the vibrational frequency predictions of DFTB and DFTB/ChIMES on 342 gas phase molecules from the Computational Chemistry Comparison and Benchmark Database or CCCBDB (https://cccbdb.nist.gov/). The reference data is at the MP2/cc-pVTZ level of theory. We also make comparisons with several DFT methods. The functionals chosen here are $w$B97XD, which is the same as $w$B97X with an additional dispersion correction, and the Perdew-Burke-Ernzerhof (PBE) functional. The predicted vibrational frequencies for those DFT functionals are also taken from CCCBDB. Figure 3 shows the distribution of frequencies for each computational method. $w$B97XD gives good agreement with MP2 reference data with MAE/RMSE = 20/36 cm$^{-1}$. DFTB and PBE underestimate the vibrational stretching frequencies by about 100 cm$^{-1}$ on average, where the MAE/RMSE are 77/114 and 61/79 cm$^{-1}$, respectively. DFTB/ChIMES yields smaller errors in the frequency prediction with MAE/RMSE = 36/61 cm$^{-1}$, showing notable improvement over PBE and comparable accuracy to $w$B97XD.

Though the DFTB/ChIMES model developed here is trained on molecular (gas phase) data, we have also tested its performance in reproducing the structural properties of graphite and diamond. These systems were chosen due to the fact that they contain a single element only while still probing different types of chemical bonds. Figure 4 shows the potential-
energy landscape in the $a$-$c$ plane of graphite ($a = b$) with DFTB (top) and DFTB/ChIMES (bottom). The standard DFTB method is insufficient for obtaining the experimental cell geometry and the potential energy surface is very flat along the $c$-direction, indicative of the severe underestimation of dispersion interactions. The ChIMES correction, which was fitted to hybrid DFT reference data, captures the interlayer interactions of graphite, leading to a minimum that is in excellent agreement with experiment. The predicted density and lattice parameters of graphite and diamond using DFTB, DFTB/ChIMES, and PBE-DFT in comparison with experiment are provided in Table 2. For graphite, all computational models considered here give an accurate description of the in-plane lattice parameters. DFTB and PBE overestimate the interlayer separation ($c/2$) by over 25% and 30%, respectively, and therefore underestimate the density by over 20%. DFTB/ChIMES predicts the lattice parameters and density in excellent agreement with the experimental value, with a deviation of less than 1%. For diamond, the computed values using DFTB, DFTB/ChIMES, and PBE-DFT differ by $\sim$1% for lattice parameters and $\sim$3% for density from experimental values.

In conclusion, we have shown that ChIMES can be used to extend DFTB to hybrid functional accuracy or greater. ChIMES parameters are determined rapidly through linear optimization, creating a beyond-pairwise interaction potential for DFTB. DFTB/ChIMES has the capability of reproducing vast quantities of high-level reference data while requiring only a small fraction of it for training. The accuracy of DFTB/ChIMES is discussed for total energies, atomic forces, isomerization energies, and vibrational frequencies across the vast conformational diversity of organic molecules in several popular datasets, as well as for the dihedral rotation energy profile of $n$–butane. Preliminary testing on solid carbon allotropes at ambient conditions show that DFTB/ChIMES is able to reproduce the experimental structure of graphite (a well-known challenge for standard DFT) as well as bulk diamond properties, while having been determined from gas-phase cluster data, only. On the basis of the results presented here, DFTB/ChIMES represents a promising direction for
developing general purpose quantum models that are applicable to a wide range of materials and conditions. The small training set required by our approach, as shown in this study, could yield significant advantages for future development of computational models with a coupled cluster accuracy, significantly improved scaling, and high efficiency. The utility and ease of parameterization of DFTB/ChIMES allows for high-level quantum theory accuracy in the systems where traditional methods are far too computationally intensive for use.

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Supporting Information Available

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Figure 1: Comparison of energies per atom (top panels) and forces (bottom panels) predicted by DFT (\(\omega\)B97X) and DFTB/ChIMES for all configurations in the validation set. The dataset used here is ‘sub_ANI-1x’, \(\sim\)10% of the full ANI-1x. The black line shows perfect correlation.
Table 1: Performance of DFTB and DFTB/ChIMES in predicting reference energies and/or atomic forces in the GDB-10to13, ISO34, and GDML data set. MAE \( E \)/RMSE \( E \) and MAE \( F \)/RMSE \( F \) are in kcal/mol and kcal/mol-Å, respectively. Reference molecular energies and atomic forces in the GDB-10to13 data set are at the \( \omega \)B97X/6-31G* level of theory. Isomerization energies in the ISO34 data set are a mixture of experimental- and CCSD(T) extrapolation energies. The CCSD(T)/cc-pVTZ atomic forces of 2000 configurations of ethanol in the GDML data set are used for comparison.

| method           | GDB-10to13      | ISO34   | GDML   |
|------------------|-----------------|---------|--------|
|                  | MAE \( E \)/RMSE \( E \) | MAE \( F \)/RMSE \( F \) | MAE \( E \)/RMSE \( E \) | MAE \( F \)/RMSE \( F \) |
| DFTB             | 9.10/11.70      | 6.34/9.85 | 3.69/4.96 | 4.52/6.12 |
| DFTB/ChIMES      | 3.57/4.72       | 3.62/5.33 | 2.06/2.56 | 2.72/3.61 |
| ANI-1\(^{[2]}\)  | 3.12/4.74       | 3.96/7.09 | -       | -          |
| ANI-1x\(^{[2]}\) | 2.30/3.21       | 3.67/6.01 | -       | -          |
| DFTB-NN\(_{rep}\)^{[22]} | -               | -       | 2.21/3.30 | -          |
| PBE0\(^{[22]}\)  | -               | -       | 1.82/2.48 | -          |

Table 2: Comparison of predicted density and lattice parameters of graphite and diamond for DFTB, DFTB/ChIMES, PBE-DFT with experimental data.

| phase | method          | density (g/cm\(^3\)) | \( a \) (Å) | \( c/2 \) (Å) |
|-------|-----------------|-----------------------|--------------|---------------|
| graphite | Expt\(^{[44]}\) | 2.26                  | 2.462        | 3.356         |
|        | PBE-DFT\(^{[42]}\) | 1.71                  | 2.470        | 4.420         |
|        | DFTB/ChIMES     | 2.25                  | 2.461        | 3.379         |
|        | DFTB            | 1.77                  | 2.474        | 4.248         |
| diamond | Expt\(^{[43]}\) | 3.51                  | 3.567        |               |
|        | PBE-DFT\(^{[6]}\) | 3.48                  | 3.580        |               |
|        | DFTB/ChIMES     | 3.42                  | 3.600        |               |
|        | DFTB            | 3.42                  | 3.600        |               |

Graphical TOC Entry
Figure 2: One dimensional potential energy profile for C-C-C-C dihedral angles of \( n \)-butane. The molecular configurations are fully relaxed at fixed dihedral angles in the DFT (\( \omega \text{B97X} \)) calculations. The single point energy calculations at DFT optimized geometries are performed for DFTB and DFTB/ChIMES.
Figure 3: The distribution of the calculated frequency values using DFTB and DFTB/ChIMES for 342 neutral molecules taken from the CCCBDB database. The MP2 and DFT (PBE and ωB97XD) calculations using cc-pVTZ basis set in the CCCBDB are selected for comparison.
Figure 4: Potential-energy surfaces (in kcal/mol) for the $a$-$c$ plane of graphite obtained using: DFTB (top) and DFTB/ChIMES (bottom). Experimental lattice parameters are marked by a cross.