Peer Review File

Implementing Reactivity in Molecular Dynamics Simulations with Harmonic Force Fields

REVIEWERS' COMMENTS:

Reviewer #1 (Remarks to the Author):

The authors have introduced a new interface force field with reactivity. The simulation results have shown that this potential has great accuracy and significantly faster then ReaxFF. However, there are queries that should be addressed before the manuscript is suggested for publication.

•The explanation for the selection of NPT over NVT and vice versa should be provided with a strong reason with supporting references.

•The variation of temperature is crucial in determining the accuracy of this force field and this aspect is still missing.

•Reactivity also allows the study of mechanical properties of nanomaterials such as CNT with various types of defects that are often found in real applications. Thus, it is suggested that this aspect is also studied.

Reviewer #2 (Remarks to the Author):

Classical non-reactive molecular dynamics (MD) computer simulations are the standard tool (in all its flavors) to access the microsopic (atomistic-level) properties of all kinds of matter. A major disadvantage is the lack of the inclusion of chemical reactivity, i.e. breaking and forming chemical bonds. Other methods, such as ab-initio MD can be used but are restricted to very small systems; the reactive MD (REAXFF) method has been pushed over years, but it is often cumbersome to parametrize and extend and still relatively slow in computation. Here, the authors suggest to replace non-reactive harmonic bond potentials in classical MD with reactive Morse potentials to add some reactivity into classical MD simulations. The authors describe a thorough and consistent mapping procedure; they illustrate applications to analyze bond scission in molecules and stress-strain curves for polymers, biopolymers, carbon nanostructures, and metals in good agreement with experimental measurements. The authors also demonstrate that their method is approximately 30 times faster and several times more accurate (in the presented applications) than ReaxFF.

While I totally welcome these efforts in the sense that an efficient reactive MD simulation

would be a huge methodical breakthrough, IMHO the presented method constitutes only a small step forward and has still large limitations. Hence, before I write about details I do not see the innovation needed to publish this in Nature Communication. More specialized journals, e.g., ACS JCTC, would be more appropriate.

The problem is that the 'only' thing that has been done is the change from a bounded harmonic potential to a dissociable Morse potential (while keeping consistently the harmonic expansion around the minimum, fair enough). Naturally, by fitting the Morse to DFT and/or experiments, this leads to the right stress and rupture behavior for quite rigid materials. This is now exactly the issue: for a single molecule or a rigid nanotube actually no MD simulation is really needed to get an accurate stress-strain or rupture behavior, this follows simply by adding an external force to the Hamiltonian and minimizing it (similar as in a zero temperature QM/MM). Not that the demonstrated applications in the MD are not nice and a step forward (because the reference MD force field still behaves OK) but the results are somewhat expected. But maybe this is something the authors should demonstrate, that the MD at finite temperature is qualitatively different and superior than simply adding an external force to the Hamiltonian.

A much more stringent and convincing application would be metastable molecules that dissociate upon thermal fluctuations or during molecular association or conformational changes. Desirably, like in REAXXF, is also the formation of bonds, which is not all discussed here. In particular, no efforts are presented how the breaking/forming of a bond can be consistently described for a force field; It is argued that at some empirical distance the bonds break and then the force fields (in particular, partial charges) are simply switched. But what happens to forces here (do they jump, are they continuous) and is electroneutrality conserved? Importantly, is there any microscopic reversibility (detailed balance) obeyed? I do understand that these are tough questions to answer and certainly approximations have to be made. However, in the current work this is hardly or not at all addressed and the innovation step for MD, in my opinion, interesting as promjsing first step but not that big. In particular, the current application range is limited to stressing rigid molecules and materials, but not really to chemical conversion, etc.

Reviewer #3 (Remarks to the Author):

This manuscript reports a new force field IFF-R for reactive molecular dynamics simulations by replacing the non-reactive harmonic bond potentials of INTERFACE Force Field with reactive Morse potentials. The IFF-R force field shows good performance in bond scission in molecules and stress-strain curves for various materials. Comparing with ReaxFF, IFF-R is much faster and more accurate. Though the work is of importance and potentially interesting, the demonstration is not convincing. Based on these, this work requires further study before it can be published in this journal. My suggestions and comments are detailed below.

1. In this manuscript, though the author has demonstrated the applicability and advantages of IFF-R force fields with some specific materials, the author has not conducted a benchmark over representative molecular or materials databases. Using single example of a type of materials to prove the applicability and advantages of a force field is not sufficient. The authors should give a more comprehensive benchmark.

2. It seems that the authors gave an empirical value of 200% of the equilibrium bond length for the bond length cutoff. I think the authors should give more reason or data to support the choice of this cutoff.

3. From all the supporting information given by the authors, I didn't get the complete Morse parameters file, but only Morse parameters for specific systems. I wonder if the authors have developed the IFF-R parameters for all the IFF force field atom types or just for the atom types of the material or molecules mentioned in this paper. If it is the latter, I think the applicability of this force field is limited. The authors should provide more information for the Morse parameters in the Supporting Information or in the main text. This makes it easier for the reader to use the force field.

4. There is a minor error in the last paragraph of Section 2.1 with an extra word "assigned".

Dear Referees,

We would like to bring a resubmitted manuscript to your attention, entitled "Implementing Reactivity in Molecular Dynamics Simulations with Harmonic Force Fields". Thank you very much for the appreciation and constructive criticisms, which we have now addressed. We carried out extensive further work to demonstrate applications, describe extensions of IFF-R for the simulation of bond forming reactions alongside bond breaking, including several examples, and made clarifications throughout the text and SI. We also provide a graphical user interface (GUI) as part of this reworked version in the SI, which aids in the automated generation of Morse parameters and input files for reactive simulations.

Please see the original comments below and the responses in blue font.

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The authors have introduced a new interface force field with reactivity. The simulation results have shown that this potential has great accuracy and significantly faster then ReaxFF. However, there are queries that should be addressed before the manuscript is suggested for publication.

Author reply: We thank the referee for the summary and encouragement.

•The explanation for the selection of NPT over NVT and vice versa should be provided with a strong reason with supporting references.

<u>Author reply:</u> We thank the referee for asking for clarification. We updated the Methods section, included new references, and more details to explain the selection of the NPT ensemble and the NVT ensemble, see p. 38:

"We employed the NPT ensemble, except for CNTs that include some vacuum in the simulation box where the NVT ensemble is more suitable, and the Nose-Hoover barostat for pressure control at 1 atm. The tensile strain was increased continuously during molecular dynamics simulations in a strain program from zero until after failure. The maximum strain varied depending on the material from 0.4 for CNTs to 6.0 for polymers. The strain rate was between 0.04 and 0.10 per 100 ps, equal to between 0.4 ns^{-1} and 1.0 ns^{-1}. All components of the stress tensor were measured using the NPT ensemble for polymers and metals,[112-114] and using the NVT ensemble for CNTs. In the case of CNTs, the engineering stress in the tensile direction was calculated using the cross-sectional area of the CNTs in relation to the total cross-sectional area of the box that included some vacuum (Section S1.2 in the Supporting Information)."

Previously this information was already contained in the Supporting Information sections S1.2 and S1.4, and we revised the details in the SI for more clarity on p. S26/S27 (please see marked up copy).

•The variation of temperature is crucial in determining the accuracy of this force field and this aspect is still missing.

<u>Author reply:</u> We thank the referee for this comment. The influence of temperature on the performance of IFF-R was recently validated in another publication that examines the thermomechanical properties of epoxy resins and shows good agreement with laboratory data. We included the citation in the main text on p. 26:

"Further validation of IFF-R for predicting the thermomechanical properties of amorphous epoxy resins has recently been reported by Odegard et al.[102]"

The reliability for different temperatures has also been examined for IFF since inception (ref. 5), and it is expected that energy differences as a function of temperature are at least as good with IFF-R (slightly better since the Morse potential is more realistic and includes the nonlinearity). Typically, we expect very good performance within +/- 200 K, and often far outside this temperature range. For example, earlier studies showed that computed melting points of metals such as Pt (around 1700 ºC) was better reproduced by IFF than by EAM models, within about 100 K (see Zhou, J.; Yang, Y.; Yang, Y.; Kim, D. S.; Yuan, A.; Tian, X.; Ophus, C.; Sun, F.; Schmid, A. K.; Nathanson, M.; Heinz, H.; An, Q.; Zeng, H.; Ercius, P.; Miao, J., Observing Crystal Nucleation in Four Dimensions Using Atomic Electron Tomography. *Nature* **2019**, *570* (7762), 500-503.) We are confident that the Morse potential, due to its more realistic curve shape compared to the harmonic potential, and compatibility would perform even better at higher temperatures than IFF (as shown for the epoxies in ref. 102).

•Reactivity also allows the study of mechanical properties of nanomaterials such as CNT with various types of defects that are often found in real applications. Thus, it is suggested that this aspect is also studied.

Author reply: We thank the referee for this suggestion and included calculations for a series of CNTs with defects in the Supporting Information. Please see new Figure S8 and Section S5 (Figure S8 also shown below).
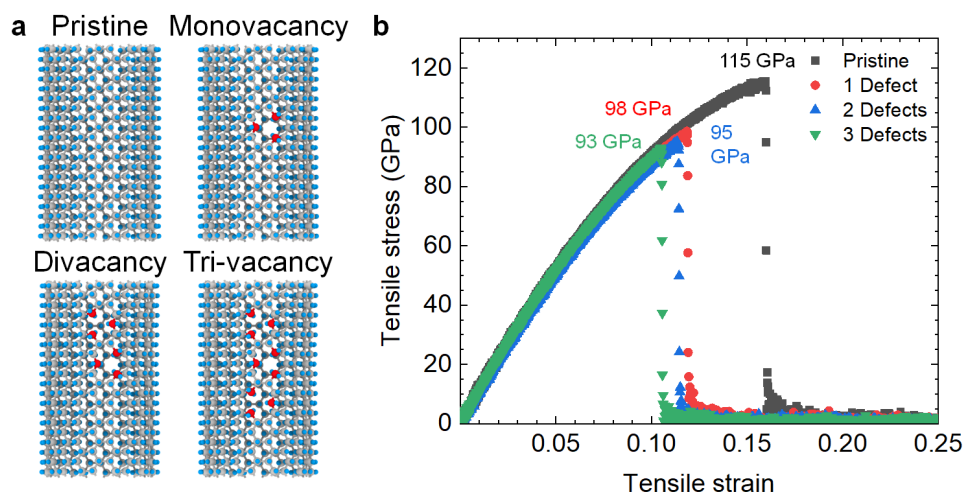

Figure S8. Demonstration of the variability of the stress-strain curves and failure mechanisms of single-wall carbon nanotubes containing defects as seen in MD simulations with IFF-R. (a) Models of 2.0 nm diameter (15,15) SWCNTs with increasing number of missing atoms from 0 (pristine) to 3 (tri-vacancy). Sites of missing atoms are highlighted in red. (b) Stress-strain curves for the carbon nanotubes in (a). A limit for the influence of missing atoms on the reduction of tensile strength and ultimate strain can be seen. A single missing atom from a pristine SWCNT structure causes the greatest reduction in tensile strength of -14.7%, i.e., from 115 GPa to 98 GPa. Subsequent removal of atoms leads to reductions of -3.1% and -2.1%, respectively.

In addition, an extensive data set of pristine and defective CNTs was created with IFF-R in a recent separate study to create an experimentally-inspired database for machine learning of mechanical properties (see: Zhao, Q.; Winetrout, J. J.; Wang, Y.; Heinz, H., Prediction of Carbon Nanotube and Carbon Fiber Mechanical Properties Using Reactive Simulations and Machine Learning. *arXiv preprint* **2021**, arXiv:2110.00517., under re-review for publication).

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Author reply: We thank the referee for detailed summary.

While I totally welcome these efforts in the sense that an efficient reactive MD simulation would be a huge methodical breakthrough, IMHO the presented method constitutes only a small step forward and has still large limitations. Hence, before I write about details I do not see the innovation needed to publish this in Nature Communication. More specialized journals, e.g., ACS JCTC, would be more appropriate.

Author reply: We appreciate this critique. We made significant extensions, including reactions for bond formation and bond dissociation in the same simulation. We think that the manuscript is a critical first step towards reversible modeling of chemical reactions using interpretable potentials and a low number of empirical fit parameters. The breadth of application is very wide, as now demonstrated for proteins, polymer/CNT composites, metals, and self-healing polymers. The approach is suitable for any material types and works with the widely used IFF as well as the very widely used biomolecular force fields such as CHARMM, which we now explicitly demonstrate in our manuscript as well (spider silk fibroin).

First, considering the introduced method for bond dissociation by itself, we think this work is a large step forward since there has been no clarity and no validated examples in the community on how to smoothly interface a Morse potential with a typical energy expression like PCFF, IFF, or CHARMM. The feasible accuracy in terms of bond curves and failure properties is very high and has not been demonstrated before, and a discussion of important bond cutoffs was not previously available.

Importantly, the path to modeling chemical reactions also requires continuous energy curves upon bond dissociation and bond formation, and our approach with IFF-R is the first to accomplish this challenge for bond energies with a minimum of parameters. Morse potentials have been used previously, as acknowledged by us and referees, however, without validation of critical bulk and interfacial properties, and without energy continuity.

We introduce energy continuity through a shift of the Morse potential to zero energy at the bond cutoff distance, which is a groundbreaking step for all reaction modeling to follow, and this step has not been made in prior studies to-date.

The problem is that the 'only' thing that has been done is the change from a bounded harmonic potential to a dissociable Morse potential (while keeping consistently the harmonic expansion around the minimum, fair enough). Naturally, by fitting the Morse to DFT and/or experiments, this leads to the right stress and rupture behavior for quite rigid materials. This is now exactly the issue: for a single molecule or a rigid nanotube actually no MD simulation is really needed to get an accurate stress-strain or rupture behavior, this follows simply by adding an external force to the Hamiltonian and minimizing it (similar as in a zero temperature QM/MM). Not that the demonstrated applications in the MD are not nice and a step forward (because the reference MD force field still behaves OK) but the results are somewhat expected. But maybe this is something the authors should demonstrate, that the MD at finite temperature is qualitatively different and superior than simply adding an external force to the Hamiltonian.

Author reply: We agree that the use cases reported in the original submission are somewhat simple and not hugely practical. We agree with the referee that more "useful" or practical applications should be shown, and we have included several new examples and comparisons to experiments, to the extent available, to demonstrate the applicability of the IFF-R approach.

We agree that bond formation is very important, too (see next comment), and in the revision, we updated our work to include bond formation using template-based reaction methods in LAMMPS (Reacter). We show a path for simulating the formation and dissociation of bonds in a single, continuous simulation using IFF-R as an extension of classical force fields.

The added capabilities are described in new Figures 5 and 6, along with a new section 2.8 on p. 28-34. We include two examples, of which the first includes reversible bond dissociation and reformation (self-healing) in polyacrylonitrile (Figure 5). The approach can be used to describe a variety of chemically responsive polymers. The second example involves cross-linking of epoxy/CNT composites using the REACTER tool, followed by stress-strain curves up to failure to analyze the mechanical properties (Figure 6).

We also added more complex examples of stress-strain curves closer to applications, including the use of CHARMM36-R for failure of spider silk protein (spidroin) at different temperatures (new Figure S9 in the Supporting Information), and a series of defective CNTs, showing the impact of various defects on the mechanical properties (new Figure S8 in the Supporting Information).

By describing the fundamental advance, benchmarks, and significantly expanded examples in the revision, a lot of future efforts can be built upon this work. Most notably, the suite of widely used biomolecular force fields can be expanded to become reactive in this manner. We are already comfortable using these tools and other groups started picking up

the methods. Arguably, the proposed approaches are currently the most interpretable and fastest to simulate reactions. Alternatives are hardly available, and the impact will be high.

We also discuss limitations, for example, the need to define reaction templates (as reactions often involve atomic rearrangements and multiple steps) and the need for further efforts to reduce energy discontinuities upon bond breaking (hereby, not the IFF-R Morse potential but energy terms other than the Morse potential still cause energy discontinuities).

Overall, the new capabilities of computing reliable stress-strain curves and failure mechanisms for any type of organic and inorganic materials is already a major advance for thousands of potential users, and can be combined with reactivity.

Before describing the additions, also, we would like to emphasize that demonstrating unchanged structural and energetic properties in equilibrium (lattice parameters, density, surface energy/vaporization energy, mechanics) after adding Morse parameters to the parent force field is very important for these techniques to be able to advance and shape the field of reaction modeling going forward. Without such verification, the entire development of interpretable bonded force fields towards describing reactivity in transparent and fast approaches may not proceed.

In the following, we describe the updates for specific materials types and new use cases:

1) We added simulations of failure and self-repair of semicrystalline polyacrylonitrile (new Figure 5, new section 2.8). We assume here, for simplicity, easy criteria to reconnect bonds (else, it could be an entire work of its own)

2) We added simulations of cross-linking reactions of an amine/epoxy resin with and without a CNT, and the subsequent failure mechanisms of these systems upon tensile strain (new Figure 6 and new section 2.8); the strength agrees well with experimental data.

3) We reported IFF-R stress-strain curves of a set of CNTs with various defects (new Figure S8 in the SI).

4) We computed stress-strain curves of spidroin (spider silk protein) at room temperature and at a low temperature, where by the modulus and strength correlate with experimental data (Figure S9 in the SI).

5) Additions to the methods sections (main text and SI) were made accordingly.

Hereby, the cross-linking of the epoxy resin and subsequent stress-strain and failure characteristics were run in a single, continuous simulation. It is also expected that temperature will change the mechanical properties, e.g., if the system is heated closer to the melting point. Therefore, the suggested protocols for reactive MD simulations using IFF-R are helpful due to few limitations regarding temperature, stress, and allowing rather long relaxation times (milliseconds when employing large supercomputing as of ten years ago, see ref. 6, which other methods have still difficulties with today).

The simulation of failure of spider silk provides an example of the temperature dependent mechanical properties, which illustrates that property estimates at zero temperature by QM/MM are not transferable to conditions at room temperature or other finite temperatures.

A much more stringent and convincing application would be metastable molecules that dissociate upon thermal fluctuations or during molecular association or conformational changes. Desirably, like in REAXXF, is also the formation of bonds, which is not all discussed here. In particular, no efforts are presented how the breaking/forming of a bond can be consistently described for a force field;

Author reply: We agree with the referee that bond dissociation of metastable molecules would be desirable and we made extensions additions to demonstrate these capabilities, at least at a basic level (see reply to previous comment for bond forming and breaking in the same simulation). We introduced bond forming reactions via reaction templates, as implemented in the REACTER framework. The use of Morse bonds hereby introduces a physically more justified bond energy function.

We allow for thermal dissociation when using Morse bonds and include the new example for spider silk which examines T-dependent and conformation-dependent dissociation behavior, which is associated with the role of T-dependent entanglements and relaxation times. See the new Figure S9 and Section S5 in the Supporting Information. For a full examination, more detailed separate studies are necessary.

We hope, hereby, and with the 4 added detailed examples, we have addressed the concerns and we welcome additional feedback.

It is argued that at some empirical distance the bonds break and then the force fields (in particular, partial charges) are simply switched. But what happens to forces here (do they jump, are they continuous) and is electroneutrality conserved?

Author reply: We thank the referee for bringing this aspect to our attention. We updated our work to emphasize electroneutrality conservation as well as the behavior of the interatomic forces after bond dissociation in the main text.

Part of these questions were already answered in the SI before, and we made further additions and clarifications in Figures S2, S3, S4, and S5 (please see highlighted copy). See also Section S3, p. S36 to S44.

In essence, the forces do not jump, but energy discontinuities still occur. Hereby, the bond energy has no energy discontinuity anymore, which we eliminate by shifting the Morse potential. Other energy contributions still exhibit discontinuities, which we discuss (e.g., changing angle, torsion , and nonbond interactions due to the cutoff). Yet, we observed that the forces and failure mechanisms are essentially unaffected as long as the cut off is chosen at around 200% of the equilibrium bond length (or at least 170%, if desired, and less than 300%), see Figure S2b-d.
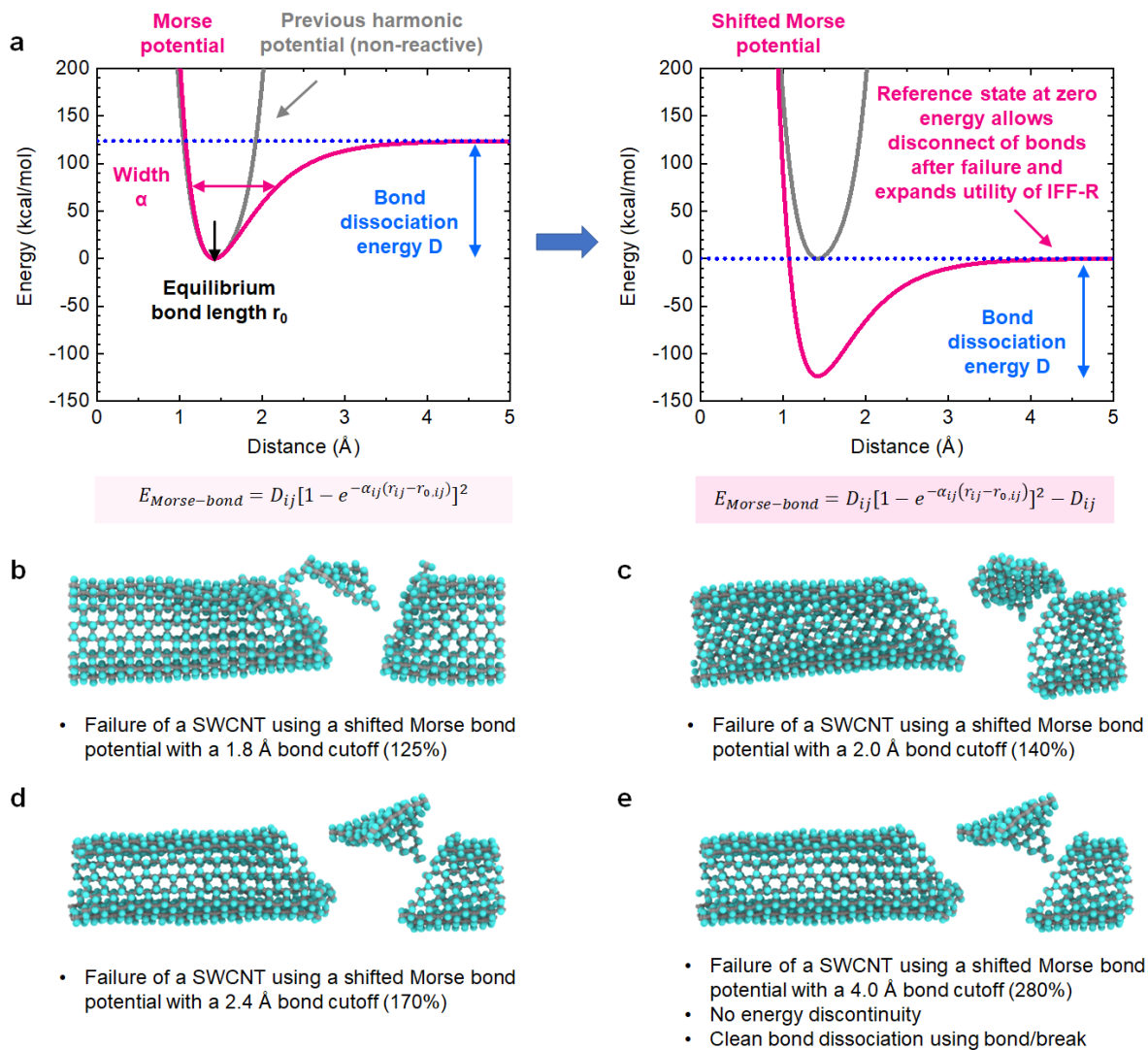
a

Morse potential | Previous harmonic potential (non-reactive)

Width α

Bond dissociation energy D

Equilibrium bond length r_0

$E_{Morse-bond} = D_{ij}[1 - e^{-\alpha_{ij}(r_{ij}-r_{0,ij})}]^2$

Shifted Morse potential

Reference state at zero energy allows disconnect of bonds after failure and expands utility of IFF-R

Bond dissociation energy D

$E_{Morse-bond} = D_{ij}[1 - e^{-\alpha_{ij}(r_{ij}-r_{0,ij})}]^2 - D_{ij}$

b
- Failure of a SWCNT using a shifted Morse bond potential with a 1.8 Å bond cutoff (125%)

c
- Failure of a SWCNT using a shifted Morse bond potential with a 2.0 Å bond cutoff (140%)

d
- Failure of a SWCNT using a shifted Morse bond potential with a 2.4 Å bond cutoff (170%)

e
- Failure of a SWCNT using a shifted Morse bond potential with a 4.0 Å bond cutoff (280%)
- No energy discontinuity
- Clean bond dissociation using bond/break

Figure S2. Illustration of the shifted Morse bond potential in IFF-R and implications on failure (see Supporting File "user-morse-2Aug23.tgz"). The Morse potential benefits from energy conservation, i.e., a shift to zero energy upon bond dissociation. (a) The default Morse bond potential (left) and the shifted Morse bond potential (right) for graphitic carbon-carbon bonds with an equilibrium bond length of 1.42 Å. The unmodified Morse bond potential has an energy minimum at $r_{0,\ ij}$ and 0 kcal/mol and a high potential energy upon bond dissociation, which causes an energy discontinuity (energy drop) when elongated Morse bonds are disconnected or reassigned, respectively. In comparison, the shifted Morse bond potential has an energy minimum at $r_{0,\ ij}$ and $-D_{ij}$. Using a shift so that the bond energy approaches 0 kcal/mol as the bond dissociates avoids energy discontinuities in molecular dynamics simulations arising from the Morse potential during bond scission. At the same time, the shift does not change the force as a function of distance and has no visible effect on the failure mechanism. (b-e) Another key parameter is the bond cutoff distance. If the bonds are not disconnected at a certain distance past dissociation, "ghost" contributions from remaining angle, dihedral, and other energy contributions taint the potential energy. On the other hand, cutoff distances too close to the equilibrium bond

length are unphysical. Examples of the fracture pattern of a SWCNT are shown using the shifted Morse potential with bond cutoff distances of 1.8 Å (b), 2.0 Å (c), 2.4 Å (d), and 4.0 Å (e). The simulation protocol was the same. The failure mechanism was affected when the cutoff distances were chosen too small and became independent of the cutoff distance when chosen larger than 2.4 Å, equal to ~170% of the equilibrium bond length.

Electroneutrality is always observed in IFF-R (and in IFF too). Regarding chemical reactions, we need to consider that many chemical reactions involve the motion of multiple atoms, or multiple steps, so that the question of energy discontinuities remains open and needs to be addressed in future studies. We explain the origin of discontinuities here, for the first time to our knowledge, with specific details and identification of the contributions (Figures S3-S5). In addition to the bonds to be ultimately disconnected, neighbor bonds and other parts of the molecule, such as angles and torsions are stretched, and related contributions from LJ and electrostatic energies occur. To eliminate discontinuities, all energy terms need a solution, which goes beyond the scope of this work.

One possibility is a temporary attenuation of these additional interactions in the vicinity of the bond to be broken to zero values, and then switching on these contributions after bond break with new force field types. Hereby, the central Morse bond, as proposed, is already ergodic. However, it is beyond this discussion to demonstrate all the follow-up steps and required tests. We focus on showing the utility and interpretability of the Morse potential for bond dissociation, use of proper shift to zero and cutoff distance to minimize energy gaps. We explain the origin of energy discontinuities, the combination with template-based methods to form new bonds in the same simulation, and how these approaches are ready to use for a variety of materials systems.

A future full treatment of discontinuities in energy could include (1) an introduction and validation of new methods to reduce energy discontinuities (in local angle, torsion, improper and nonbonded energy contributions), (2) a discussion how to handle reactions that have complex mechanisms with multiple atom transfers and timelines beyond MD simulations. Heuristic assumptions, even with discontinuities in energy, may remain a practical solution as long as the reaction products and reaction templates concur with the proposed reaction mechanism.

Importantly, is there any microscopic reversibility (detailed balance) obeyed? I do understand that these are tough questions to answer and certainly approximations have to be made. However, in the current work this is hardly or not at all addressed and the innovation step for MD, in my opinion, interesting as promjsing first step but not that big. In particular, the current application range is limited to stressing rigid molecules and materials, but not really to chemical conversion, etc.

Author reply: We agree with the referee that the simulations should show a clear demonstration of microscopic reversibility, and we updated our work accordingly.
The example in Figure 5 and section 2.8 for bond breaking and subsequent bond formation in polyacrylonitrile approximates microscopic reversibility. The simulations overall obey the potential functions and allow both bond breaking and reformation in the same simulation. Thus, in the big picture, the proposed methods have this capability.

In the details, due to discontinuities in the energy in both directions, some problems need to be solved in future work (see answers to previous comments). As a critical first step proposed here, the shifted Morse potential eliminates energy discontinuities upon bond breaking and bond formation.

The role of the other energy contributions near the reaction centers has been documented (Figure S3 to S5) and needs to be addressed to achieve full ergodicity in follow-on work. A temporary smoothing function to zero (e.g., over 100 fs) to switch off local energies near reaction centers before bond breaking, and gradually switching them on after formation of a new bond could be an interpretable and relatively parameter-free solution. Full details for a given type of reaction depend on orbital symmetry and stereoelectronic effects, which can be challenging to represent in MD simulations with classical or reactive potentials (i.e. torsion and angle potentials would then have to be informed by theory or QM calculations for every type of reaction, even when atoms are not rearranging). ReaxFF does not capture such specifics currently, too.

In this contribution, we demonstrate a working approach that yields quantitative results for bond breaking and can use reaction templates to allow reconnection of bonds with a given probability, and can represent correctly the stoichiometry of the reaction and changes in bond connectivity.

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Author reply: We appreciate the referee's suggestion. The new reactive form of the force field (IFF-R) is physics-based and extends validated force fields (IFF, CHARMM, PCFF, CVFF, etc) for a broad range of compounds (see revisions on pages 3 and 4). Benchmarking against molecular databases is not common for these potentials, especially when they are all compatible with each other (it would be a gigantic task).

Selecting several examples of different types of materials is more feasible and sufficient here since we are not changing the overall format or scope of these force fields, but just adding a new, physics-based reactive representation of the bond potential. If this works for one type of bond, it works for another, too.

We added further demonstrations for IFF (epoxies, composites) and for CHARMM36 (spider silk) in the revision, which covers the entire space of proteins, DNA. We demonstrated that the methodology of adding reactive Morse bonds maintains accurate material properties and updated our work to be more user-friendly and generalizable to any class of system. We also made clarifications to help understand the interpretable and physics-based nature of the reactive simulations, which is unlike most existing reactive force fields.

We added Python code and a full graphical user interface (GUI) that can automatically assign Morse parameters to most organic bonds and expanded as needed (see p. 10 and Figure S1 in the SI). Using these tools, the physically justified parameters can be applied to a wide variety of organic molecules. For any bonds not currently covered, we provide the rationale to add parameters (updated Figure 1 and p. 9-11). The process, as demonstrated in Figure 1, requires limited effort as data on equilibrium bond lengths, bond dissociation energies, and vibration constants are readily available from the cited databases, or can be computed using QM.

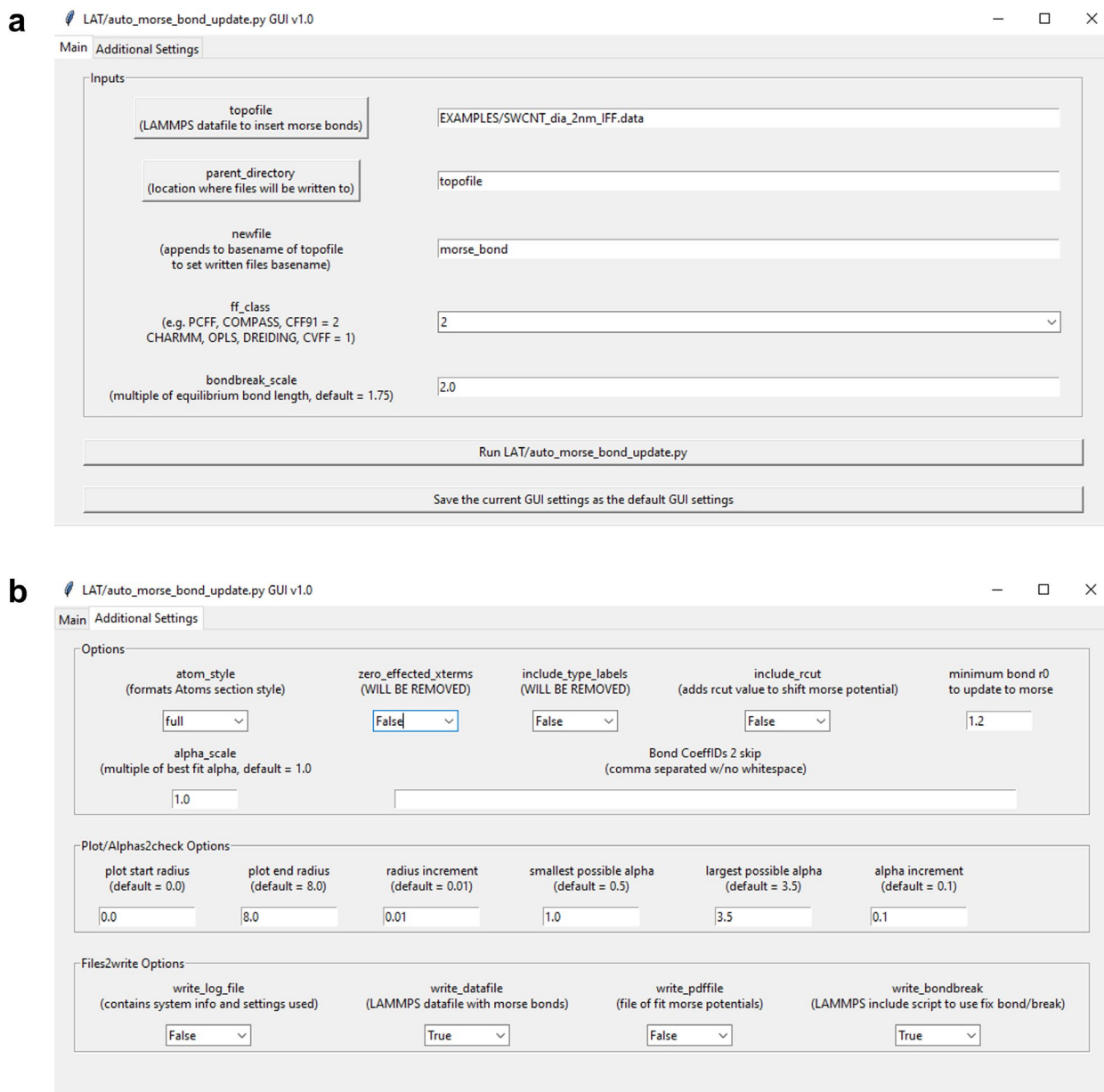We also added a list of parameters, which can be generated by the GUI, in Table S1.

Figure S1. Snapshot of the graphical user interface (GUI) for Morse bond conversion from a classical, harmonic force field (auto_morse_bond_update.py). The input to the code is a LAMMPS data file with classical bond parameters. The outputs include a data file with Morse bond parameters, a LAMMPS input script file containing "fix bond/break" commands for the newly assigned Morse bonds, a pdf file showing Morse bond parameterization graphically, and a logfile with system information that can be useful for tracking parameter assignment. (a) The main tab used for automatic Morse bond conversion. The "topofile" button is used for selecting the LAMMPS data file for Morse bond conversion. The "parent_directory" button is the default path that determines the directory for the outputs, and "topofile" is the path of the LAMMPS data file (topofile). If "topofile" is not used for the "parent_directory" option, the full path to the desired output directory should be given. The "newfile" section is an additional descriptor appended to

the "topofile" name to identify the new data file with Morse bonds and avoids overwriting the "topofile" if it's in the same output directory. The auto_morse_bond_update.py code will work with class I and class II force fields, and the "ff_class" section needs to designate 1 or 2 as acceptable inputs, accordingly. The "bondbreak_scale" is used cutoff distances for the new Morse bonds (used with the "fix bond/break" command), and the unit is the multiple of the equilibrium bond length. We recommend this parameter to be 2.0, e.g., creating a bond/break cutoff for a C-C single bond with r_0 = 1.54 Å at 3.08 Å. (b) Image of the "Additional Settings" tab. This tab is included so the user has customizability over the outputs from the auto_morse_bond_update.py code. The "Options" section provides capabilities for the user to modify the information written to the output datafile. The "Plot/Alphas2check Options" section allows the user to change variables associated with the automatic parameterization of a Morse bond. Finally, the "Files2write Options" section allows the users to specify which files should appear in the output directory with "False" meaning the file will not be written to the output directory and "True" meaning the file will be written to the output directory. Using this menu of additional settings is optional.

2. It seems that the authors gave an empirical value of 200% of the equilibrium bond length for the bond length cutoff. I think the authors should give more reason or data to support the choice of this cutoff.

Author reply: We explain this choice in Section S3 in the SI and we made some additions and revisions (see updated Figure S2b-e and p. S38/S39). In short, a bond cutoff greater than 170% of the equilibrium bond length no longer influences the energy and is often larger than the reliable range of bond scans by DFT calculations (Figure 2). A cutoff larger than 170% also leads to convergent fracture patterns (Figure S2b-e in the SI, and shown below), while a shorter cutoff would not. Choosing a cutoff of less than 140% even demonstrates a "premature" bond failure and different (non-convergent) fracture patterns (Figure S2b-e and Figures S3 and S4). On the other hand, a cutoff too large, e.g., beyond 250%, introduces stronger energy discontinuities for other-than-bond terms and the bond energy at this distance is more of a vdW energy because no localized bonding/orbital overlap is left (according to QM calculations, and Figures S3 and S4).

Therefore, the value of 200% +/- 20% adds a safe margin to premature bond failure at shorter cutoff distances and avoids large distances that would be dominated by non-covalent bonding. It is a reasonable recommendation, and we updated the main text and SI for clarity. From the user perspective, results are essentially identical whether 180% or 220% would be used (Figures S2 to S5 in the SI).

We introduced a new custom LAMMPS command for the shifted Morse potential in IFF-R, which lets the user define the cutoff distance and automatically shift the bond energy to zero at the user-defined cutoff distance. Please see new Section S3.5 in the SI on pages S43-S44, and the Supporting Files.
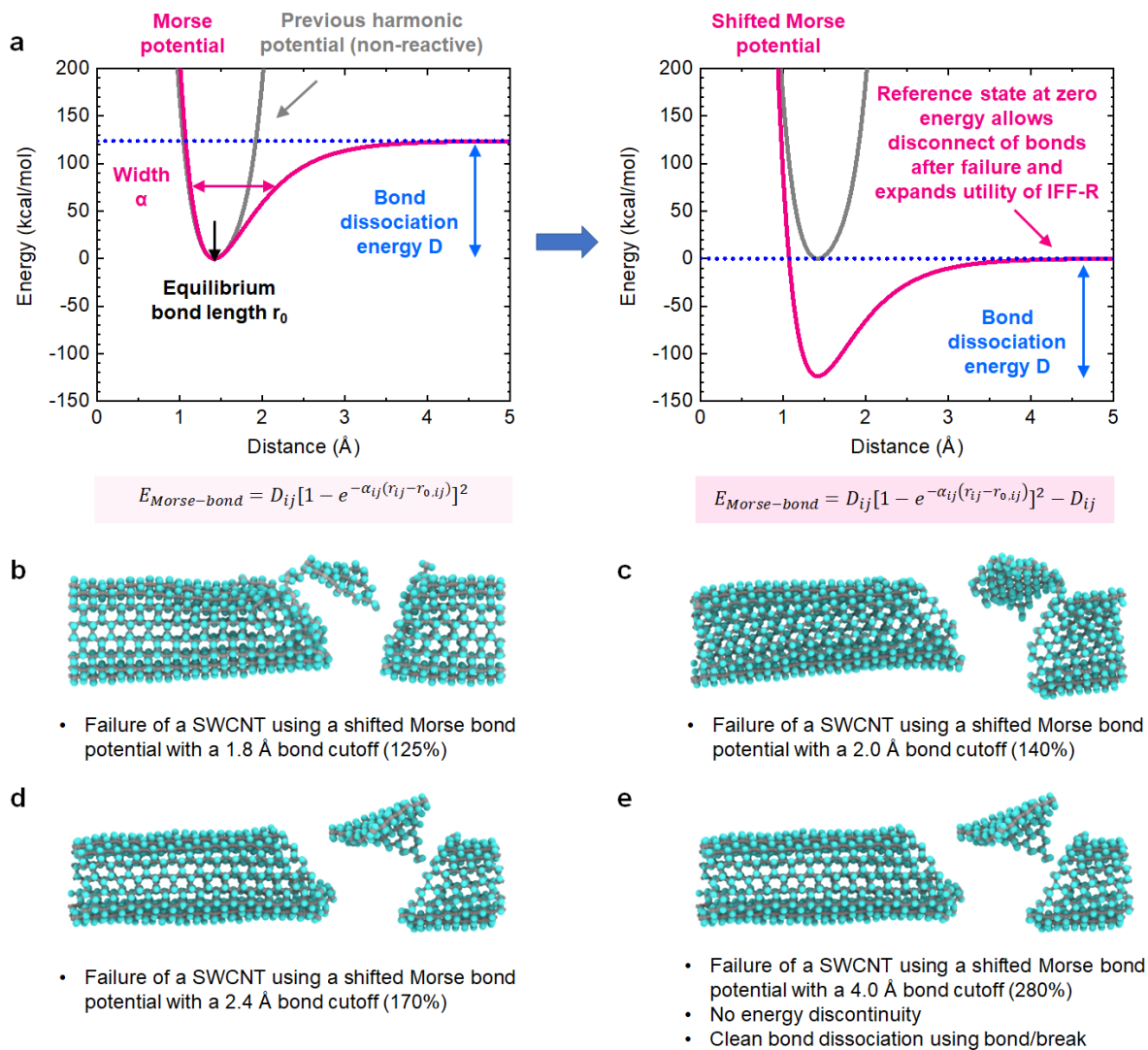
Figure S2. Illustration of the shifted Morse bond potential in IFF-R and implications on failure (see Supporting File "user-morse-2Aug23.tgz"). The Morse potential benefits from energy conservation, i.e., a shift to zero energy upon bond dissociation. (a) The default Morse bond potential (left) and the shifted Morse bond potential (right) for graphitic carbon-carbon bonds with an equilibrium bond length of 1.42 Å. The unmodified Morse bond potential has an energy minimum at $r_{0, ij}$ and 0 kcal/mol and a high potential energy upon bond dissociation, which causes an energy discontinuity (energy drop) when elongated Morse bonds are disconnected or reassigned, respectively. In comparison, the shifted Morse bond potential has an energy minimum at $r_{0, ij}$ and $-D_{ij}$. Using a shift so that the bond energy approaches 0 kcal/mol as the bond dissociates avoids energy discontinuities in molecular dynamics simulations arising from the Morse potential during bond scission. At the same time, the shift does not change the force as a function of distance and has no visible effect on the failure mechanism. (b-e) Another key parameter is the bond cutoff distance. If the bonds are not disconnected at a certain distance past dissociation, "ghost" contributions from remaining angle, dihedral, and other energy contributions taint the potential energy. On the other hand, cutoff distances too close to the equilibrium bond

length are unphysical. Examples of the fracture pattern of a SWCNT are shown using the shifted Morse potential with bond cutoff distances of 1.8 Å (b), 2.0 Å (c), 2.4 Å (d), and 4.0 Å (e). The simulation protocol was the same. The failure mechanism was affected when the cutoff distances were chosen too small and became independent of the cutoff distance when chosen larger than 2.4 Å, equal to ~170% of the equilibrium bond length.

3. From all the supporting information given by the authors, I didn't get the complete Morse parameters file, but only Morse parameters for specific systems. I wonder if the authors have developed the IFF-R parameters for all the IFF force field atom types or just for the atom types of the material or molecules mentioned in this paper. If it is the latter, I think the applicability of this force field is limited. The authors should provide more information for the Morse parameters in the Supporting Information or in the main text. This makes it easier for the reader to use the force field.

Author reply: We thank the referee for this note. We have provided Morse parameters for a wide range of bonds (much beyond the systems covered in this paper, including the newly added ones), but not for every possible bond (there is effectively an unlimited number due to using various force field types).

To remedy, we now provide Python code that can automatically assign Morse bond parameters to most harmonic organic bonds and generates LAMMPS input scripts so users can easily access the capabilities of IFF-R irrespective of the provided force field. Please see Figure S1 shown further above and in the SI.

For any new bonds, as mentioned on p. 9-11, it is relatively easy to obtain Morse parameters. Only the equilibrium bond length, the bond dissociation energy, and the vibration constant need to be retrieved from the cited databases, be computed using QM, or initially assigned using chemical analogy to existing Morse parameters for chemically similar bonds. It is a straightforward and interpretable approach with little potential for error in the Morse bond parameters (to avoid errors in the implementation to generate files for simulations, it is helpful to use the provided GUI).

4. There is a minor error in the last paragraph of Section 2.1 with an extra word "assigned".

Author reply: Fixed, thank you.

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REVIEWERS' COMMENTS

Reviewer #1 (Remarks to the Author):

I am satisfied with the provided responses and the manuscript is now suggested for publication.

Reviewer #2 (Remarks to the Author):

As I mentioned in my previous report, an efficient reactive force field, as introduced here, would be very important to have for the modeling community. I expressed some doubts because the applications in the first version were too limited, excluding bond formation and a critical discussion of the physics happening during reaction. In a tremendous effort, the authors have now addressed my concerns and substantially added new methods and results, as well as many new details in the supporting Information. From my point of view, all looks sound and is well presented. The paper presents an important first step now in the establishment of an efficient reactive force field (outpowering the REAXFF standard by an order of magnitude) and I am convinced it will be appreciated by the community and spark many new developments, extensions, and unprecedented applications. Hence, I do not hesitate to recommend publication now as is.

Dear Referees,

Now both referees recommended publication as is and for completeness we provide brief responses below.

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REVIEWERS' COMMENTS

Reviewer #1 (Remarks to the Author):

I am satisfied with the provided responses and the manuscript is now suggested for publication.

Author response: We thank the referee to approve publication in the present form.

Reviewer #2 (Remarks to the Author):

As I mentioned in my previous report, an efficient reactive force field, as introduced here, would be very important to have for the modeling community. I expressed some doubts because the applications in the first version were too limited, excluding bond formation and a critical discussion of the physics happening during reaction. In a tremendous effort, the authors have now addressed my concerns and substantially added new methods and results, as well as many new details in the supporting Information. From my point of view, all looks sound and is well presented. The paper presents an important first step now in the establishment of an efficient reactive force field (outpowering the REAXFF standard by an order of magnitude) and I am convinced it will be appreciated by the community and spark many new developments, extensions, and unprecedented applications. Hence, I do not hesitate to recommend publication now as is.

Author response: We thank the referee for the summary and agree that the work is ready for publication. We carried out final proofreading and minor edits throughout the text for utmost clarity, and extensive editorial revisions following the checklist.

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