

MBX: A many-body energy and force calculator for data-driven many-body simulations

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ABSTRACT

Many-Body eXpansion (MBX) is a C++ library that implements many-body potential energy functions (PEFs) within the “many-body energy” (MB-nrg) formalism. MB-nrg PEFs integrate an underlying polarizable model with explicit machine-learned representations of many-body interactions to achieve chemical accuracy from the gas to the condensed phases. MBX can be employed either as a stand-alone package or as an energy/force engine that can be integrated with generic software for molecular dynamics and Monte Carlo simulations. MBX is parallelized internally using Open Multi-Processing and can utilize Message Passing Interface when available in interfaced molecular simulation software. MBX enables classical and quantum molecular simulations with MB-nrg PEFs, as well as hybrid simulations that combine conventional force fields and MB-nrg PEFs, for diverse systems ranging from small gas-phase clusters to aqueous solutions and molecular fluids to biomolecular systems and metal-organic frameworks.

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I. INTRODUCTION

Molecular dynamics (MD) and Monte Carlo (MC) simulations^{1,2} have been widely used for understanding and characterizing structural, thermodynamic, and dynamical properties of molecular systems, from small gas-phase clusters to extended materials and biomolecular systems.^{3–8} The potential energy function (PEF) used to represent the multidimensional potential energy surface associated with the molecular system being studied directly determines the level of realism as well as the predictive power of any MD and MC simulation.

In the early days of molecular simulations, due to limited computational resources, the only viable options for PEFs

were empirically parameterized force fields (FFs) that use relatively simple expressions to describe intramolecular distortions and pairwise-additive functions to describe intermolecular interactions.^{9,10} Although more advanced (nonpolarizable and polarizable) FFs developed over the past five decades^{11–15} remain the most commonly used PEFs in MD and MC simulations, machine-learning (ML) models trained on electronic structure data have become increasingly popular, promising higher accuracy than conventional FFs.^{16–19} Some examples of ML PEFs include neural network potentials (NNPs),^{20–29} equivariant graph neural network potentials,³⁰ Gaussian approximation potentials (GAPs),³¹ moment tensor potentials (MTPs),³² and spectral neighbor analysis potentials (SNAPs),³³ as well as PEFs based on the atomic cluster

expansion,³⁴ kernel ridge regression methods,³⁵ gradient-domain machine learning (GDML),³⁶ and support vector machines (SVM).³⁷ Permutationally invariant polynomials (PIPs) have also been used, either as standalone fitting functions^{38–62} or in combination with neural networks (PIP-NNs).^{63–66} Many ML PEFs are, however, limited in their transferability—those designed to mimic gas phase properties perform well under those conditions but may not be as accurate when applied to condensed-phase systems,^{67–69} and models that are trained to reproduce condensed-phase properties may not perform as well in the gas phase or at interfaces.^{70,71}

Ten years ago, Babin, Medders, and Paesani introduced MB-pol, a data-driven many-body PEF for water rigorously derived from “first principles.”^{72–74} MB-pol combines physics-based many-body models with data-driven machine-learned representations of individual many-body interactions that are expressed in terms of multidimensional PIPs. These machine-learned PIPs were shown to account for limitations in classical representations of molecular interactions that arise when overlapping electron densities lead to quantum-mechanical effects that do not have a classical counterpart, such as exchange-repulsion, charge transfer, and charge penetration.^{75–77} The PIPs of MB-pol were trained on large datasets of many-body energies calculated at the coupled cluster level of theory, including single, double, and perturbative triple excitations, i.e., CCSD(T), the current “gold standard” for chemical accuracy.⁷⁸ By construction, MB-pol is fully transferable across all phases,^{79,80} accurately reproducing the properties of small gas-phase clusters,^{81–92} liquid water,^{93–99} the air/water interface,^{100–104} and ice.^{105–110} Remarkably, MB-pol was shown to be the first and, currently, only water PEF able to correctly predict the phase diagram of water.¹¹¹ More recently, an updated version of MB-pol, MB-pol(2023), which was trained on larger training sets of many-body interactions, was shown to achieve even higher accuracy for simulations of water in both gas and liquid phases.¹¹²

Building on the accuracy and predictive power of MB-pol, many-body PEFs for various molecular systems were developed, including halide^{113–119} and alkali-metal^{120–124} ions in water, molecular fluids,^{125–128} small molecules in water,^{129,130} and generic covalently-bonded molecules in the gas phase.¹³¹ These many-body PEFs were developed within the many-body energy (MB-nrg) theoretical/computational framework,^{113,120} which effectively generalizes the MB-pol framework to arbitrary molecules. Briefly, the MB-nrg PEF of a system is built upon a baseline physics-based model describing permanent electrostatics, London dispersion forces, and many-body polarization, which is supplemented by explicit machine-learned n -body PIPs. As in MB-pol, the MB-nrg PIPs effectively represent quantum-mechanical many-body interactions arising from the overlap of the electron densities of individual monomers.^{113,120}

Here, we introduce MBX (Many-Body eXpansion),¹³² a modular C++ library that can either be used as a standalone software for calculating MB-nrg energies and forces for the molecular system of interest or interfaced with external MD and MC engines to perform classical and quantum simulations of the molecular system of interest across different thermodynamic states and phases, in both periodic and non-periodic conditions, using the corresponding MB-nrg PEFs. Importantly, MBX is interfaced with MB-Fit,¹³³ a Python software infrastructure that provides an integrated

suite of codes for the automated development of MB-nrg PEFs for generic molecules, from training set generation to PEF fitting and implementation.¹³⁴

II. THEORY: MB-NRG POTENTIAL ENERGY FUNCTIONS

The energy of a system containing N (atomic or molecular) monomers (hereafter referred to as 1-mers) can be rigorously expressed as a sum of n -body energy contributions ($1 \leq n \leq N$) according to the many-body expansion (MBE) of the energy,¹³⁵

$$E_N(1, \dots, N) = \sum_{i=1}^N \varepsilon^{1B}(i) + \sum_{i<j}^N \varepsilon^{2B}(i, j) + \sum_{i<j<k}^N \varepsilon^{3B}(i, j, k) + \dots + \varepsilon^{NB}(1, \dots, N), \quad (1)$$

where each 1-body energy, $\varepsilon^{1B}(i)$, is the energy of the isolated i th 1-mer, $E_1(i)$. For $n \geq 2$, the n -body energies, ε^{nB} are defined recursively according to the following expression:

$$\begin{aligned} \varepsilon^{nB}(1, \dots, n) &= E_n(1, \dots, n) - \sum_{i=1}^n \varepsilon^{1B}(i) \\ &\quad - \sum_{i<j}^n \varepsilon^{2B}(i, j) - \sum_{i<j<k}^n \varepsilon^{3B}(i, j, k) \\ &\quad - \dots - \sum_{i<j<k<\dots}^n \varepsilon^{(n-1)B}(i, j, k, \dots). \end{aligned} \quad (2)$$

It should be noted that within the MB-nrg theoretical/computational framework the reference zero for the energy scale (where $E_N = 0$) corresponds to the molecular configuration in which all N 1-mers are separated by infinite distances and each 1-mer is in its minimum-energy geometry. As a consequence, $\varepsilon^{1B}(i)$ corresponds to the distortion energy of the i th 1-mer relative to its minimum-energy geometry. Since the MBE converges quickly for molecular systems with localized electron densities, i.e., molecular systems with large electronic band gaps,^{136–139} the MBE provides a rigorous and efficient theoretical/computational framework for the development of many-body PEFs where each n -body term of Eq. (1) is fitted to reproduce the corresponding n -body reference energies calculated from “first principles.”

As in MB-pol,^{72–74} the MB-nrg PEFs integrate physics-based many-body terms, representing contributions to molecular interactions that can be accurately represented by classical expressions (e.g., permanent electrostatics and polarization), with explicit machine-learned representations of individual n -body terms in the MBE, which effectively recover quantum-mechanical interactions arising from the overlap of 1-mer’s electron densities (e.g., exchange-repulsion, charge transfer, and charge penetration) that cannot be represented by classical expressions.¹⁴⁰ Specifically, the MB-nrg theoretical/computational framework approximates the MBE defined in Eq. (1) as

$$E_N = V^{1B} + V^{2B} + V^{3B} + \dots + V^{nB} + V_{\text{elec}}, \quad (3)$$

where $n \leq N$ and N is the total number of 1-mers in the system.

Each of the V^{nB} terms of an MB-nrg PEF includes an n -body machine-learned term (V_{ML}^{nB}) for each n -mer. Each V_{ML}^{nB} is expressed

as a product of a switching function and a PIP (i.e., $V_{\text{ML}}^{\text{nB}} = s^{\text{nB}} V_{\text{PIP}}^{\text{nB}}$). The switching function (s^{nB}) ensures that the contribution from the associated $V_{\text{ML}}^{\text{nB}}$ term goes to zero as any subset of the 1-mers in an n -mer is separated from the rest.

Following the original MB-pol PEF,^{72,73} a given n -body PIP takes the following form:

$$V_{\text{PIP}}^{\text{nB}}(M_1, M_2, \dots, M_n | v(M_1, M_2, \dots, M_n)) = \sum_{l=1}^L c_l \cdot \eta_l(\xi_1, \xi_2, \dots, \xi_\lambda), \quad (4)$$

where M_1, M_2, \dots, M_n are n 1-mers that compose an n -mer of type $v(M_1, M_2, \dots, M_n)$, L is the number of linear parameters, c_l are the linear parameters, η_l are the symmetrized monomials built from the variables, $\xi_{1-\lambda}$, each of which is an exponential of an interatomic distance with one of the following forms:

$$\xi^{\text{exp}}(R_{mn}) = e^{-k_{\tau(mn)} R_{mn}}, \quad (5a)$$

$$\xi^{\text{exp0}}(R_{mn}) = e^{-k_{\tau(mn)}(R_{mn} - d_{0,\tau(mn)})}, \quad (5b)$$

$$\xi^{\text{coul}}(R_{mn}) = e^{-k_{\tau(mn)} R_{mn}} / R_{mn}, \quad (5c)$$

$$\xi^{\text{coul0}}(R_{mn}) = e^{-k_{\tau(mn)}(R_{mn} - d_{0,\tau(mn)})} / R_{mn}, \quad (5d)$$

where m and n are the indices for the physical atoms or fictitious sites defined by the n -mer's geometry, and R_{mn} is the distance between two atoms/sites. $\tau(mn)$ maps the pair of atoms/sites into distinct classes, such that all atom/site pairs within the same class share the same nonlinear fitting parameters $k_{\tau(mn)}$ and $d_{0,\tau(mn)}$. There is one unique set of monomials (η_l), linear fitting parameters (c_l), and non-linear fitting parameters [$k_{\tau(mn)}$, $d_{0,\tau(mn)}$] for each unique n -mer type $[v(M_1, M_2, \dots, M_n)]$.

In Eq. (3), V^{1B} is the total 1-body energy given by

$$V^{\text{1B}} = \sum_{i=1}^N V_{\text{ML}}^{\text{1B}}(M_i | v(M_i)) (+ V_{\text{disp}}^{\text{1B}}). \quad (6)$$

Because a switching function is not used for the 1-body term, $V_{\text{ML}}^{\text{1B}}(M_i | v(M_i))$ is simply a machine-learned PIP representing the 1-body energy of the i th 1-mer with functional form as in Eq. (4),

$$V_{\text{ML}}^{\text{1B}}(M_i | v(M_i)) = V_{\text{PIP}}^{\text{1B}}(M_i | v(M_i)), \quad (7)$$

$V_{\text{disp}}^{\text{1B}}$ represents the 1-body dispersion energy, as a sum of interatomic pairwise contributions,

$$V_{\text{disp}}^{\text{1B}} = \sum_{i=1}^N \left[\sum_{\substack{k,l \in M_i \\ l \neq k}} -\Delta_{kl} f(\mathbf{b}_{kl} R_{kl}) \frac{C_{6,kl}}{R_{kl}^6} \right], \quad (8)$$

where R_{kl} is the distance between atoms k and l located on 1-mer M_i , $C_{6,kl}$ is the corresponding dispersion coefficient, and $\Delta_{kl} = 0$ if the atom pair is excluded or 1 otherwise. $f(\mathbf{b}_{kl} R_{kl})$ is the Tang-Toennies damping function,¹⁴¹

$$f(\mathbf{b}_{kl}, R_{kl}) = 1 - \exp(-\mathbf{b}_{kl} R_{kl}) \sum_{n=0}^6 \frac{(\mathbf{b}_{kl} R_{kl})^n}{n!}, \quad (9)$$

where \mathbf{b}_{kl} is a fitting parameter. By convention, all atom pairs that participate in a bond, angle, or dihedral angle are excluded

($\Delta_{kl} = 0$). Thus, for most 1-mers, all atom pairs are excluded and $V_{\text{disp}}^{\text{1B}} = 0$. However, for large 1-mers, this may not be the case.

The explicit 2-body term of an MB-nrg PEF, V^{2B} in Eq. (3), is expressed as

$$V^{\text{2B}} = \sum_{\substack{i=1 \\ j>i}}^N V_{\text{ML}}^{\text{2B}}(M_i, M_j | v(M_i, M_j)) + V_{\text{disp}}^{\text{2B}}, \quad (10)$$

where $V_{\text{ML}}^{\text{2B}}(M_i, M_j | v(M_i, M_j))$ is a 2-body machine-learned term representing the 2-body energy of the 2-mer composed by the i th and j th 1-mers, constructed as a product of a switching function and a PIP with functional form as in Eq. (4),

$$V_{\text{ML}}^{\text{2B}}(M_i, M_j | v(i, j)) = s^{\text{2B}}(M_i, M_j | v(M_i, M_j)) \times V_{\text{PIP}}^{\text{2B}}(M_i, M_j | v(M_i, M_j)), \quad (11)$$

$V_{\text{disp}}^{\text{2B}}$ in Eq. (10) is the total 2-body dispersion energy calculated as a sum of pairwise additive contributions associated with each pair of atoms located on the two 1-mers in a 2-mer,¹⁴⁰

$$V_{\text{disp}}^{\text{2B}} = \sum_{\substack{i=1 \\ j>i}}^N \left[\sum_{k \in M_i} \sum_{l \in M_j} -f(\mathbf{b}_{kl} R_{kl}) \frac{C_{6,kl}}{R_{kl}^6} \right], \quad (12)$$

where R_{kl} is the distance between atoms k and l located on 1-mers M_i and M_j , respectively, $C_{6,kl}$ is the corresponding dispersion coefficient, and $f(\mathbf{b}_{kl} R_{kl})$ is the Tang-Toennies damping function [Eq. (9)]. In both Eqs. (8) and (12), the dispersion coefficients are calculated using the Exchange Dipole Moment (XDM) model.¹⁴²⁻¹⁴⁴

All other explicit many-body terms (V^{nB}) in Eq. (3) take the following form:

$$V^{\text{nB}} = \sum_{\substack{i=1 \\ j>i \\ l>k}}^N V_{\text{ML}}^{\text{nB}}(M_i, M_j, \dots, M_l | v(M_i, M_j, \dots, M_l)), \quad (13)$$

where each $V_{\text{ML}}^{\text{nB}}(M_i, M_j, \dots, M_l | v(M_i, M_j, \dots, M_l))$ is built as the product of a switching function and a PIP with functional form as in Eq. (4),

$$V_{\text{ML}}^{\text{nB}}(M_i, M_j, \dots, M_l | v(M_i, M_j, \dots, M_l)) = s^{\text{nB}}(M_i, M_j, \dots, M_l | v(M_i, M_j, \dots, M_l)) \times V_{\text{PIP}}^{\text{nB}}(M_i, M_j, \dots, M_l | v(M_i, M_j, \dots, M_l)). \quad (14)$$

Explicit n -body terms may be retained up to an arbitrary n -body level. Generally, it is sufficient to truncate these terms at the $n = 3$ or $n = 4$ level, depending on the system being studied. Specific details about the switching functions (s^{2B} , s^{3B} , and s^{4B}), including functional forms used by the MB-nrg PEFs available in MBX, are discussed in the supplementary material.

Finally, the electrostatics term, V_{elec} , in Eq. (3) is based on a modified version of the Thole model¹⁴⁵ introduced in Ref. 146 and further refined for the MB-pol PEF.^{72,73} V_{elec} represents permanent electrostatics by a sum of Coulomb interactions between smeared partial charges located on each 1-mer as well as induced

electrostatics (up to dipoles) by an implicit many-body polarization term. Within the MB-nrg theoretical/computational framework, the partial charges, which can have fixed or geometry-dependent values, are obtained by fitting the multipole moments calculated from “first principles” for each isolated 1-mer and can be placed on both physical atoms and fictitious sites.

In MBX, V_{elec} is represented by four terms describing charge-charge interactions (V_{qq}), charge-dipole interactions (V_{qm}), dipole-dipole interactions ($V_{\mu\mu}$), and the polarization energy (V_{pol}), respectively. Each of these terms is defined as follows:

$$V_{qq} = \sum_i^N \sum_{j>i}^N q_i \widehat{T}_{ij} q_j, \quad (15a)$$

$$V_{qm} = \sum_i^N \sum_{j>i}^N (\mu_i^\alpha \widehat{T}_{ij}^\alpha q_j - q_i \widehat{T}_{ij}^\alpha \mu_j^\alpha), \quad (15b)$$

$$V_{\mu\mu} = -\sum_i^N \sum_{j>i}^N \mu_i^\alpha \widehat{T}_{ij}^{\alpha\beta} \mu_j^\beta, \quad (15c)$$

$$V_{pol} = \frac{1}{2} \sum_{i=1}^N \mu_i^\alpha \widehat{\alpha}_i^{-1} \mu_i^\alpha, \quad (15d)$$

where the Einstein notation is used for repeated Greek letters (e.g., μ_i^α is a condensed form of $\sum_{\alpha=x,y,z} \mu_i^\alpha$). In Eqs. (15a)–(15d), N is the total number of electrostatic sites in the system, q_i is the charge of site i , μ_i is the dipole moment of site i , $\widehat{\alpha}_i$ is the polarizability of site i ($\widehat{\alpha}_i$ becomes a scalar if it is isotropic), and \widehat{T}_{ij} , \widehat{T}_{ij}^α , and $\widehat{T}_{ij}^{\alpha\beta}$ are the electrostatic tensors defined as follows:

$$\widehat{T}_{ij} = S_0(R_{ij}) \frac{1}{R_{ij}}, \quad (16a)$$

$$\widehat{T}_{ij}^\alpha = \nabla_\alpha \widehat{T}_{ij} = -S_1(R_{ij}) \frac{R_{ij}^\alpha}{R_{ij}^3}, \quad (16b)$$

$$\widehat{T}_{ij}^{\alpha\beta} = \nabla_\alpha \widehat{T}_{ij}^\beta = S_2(R_{ij}) \frac{3R_{ij}^\alpha R_{ij}^\beta}{R_{ij}^5} - S_1(R_{ij}) \frac{\delta_{\alpha\beta}}{R_{ij}^3}, \quad (16c)$$

$$\begin{aligned} \widehat{T}_{ij}^{\alpha\beta\gamma} = \nabla_\alpha \widehat{T}_{ij}^{\beta\gamma} = & -S_3(R_{ij}) \frac{15}{R_{ij}^7} R_{ij}^\alpha R_{ij}^\beta R_{ij}^\gamma + S_2(R_{ij}) \frac{3}{R_{ij}^5} \\ & \times (R_{ij}^\alpha \delta_{\beta\gamma} + R_{ij}^\beta \delta_{\alpha\gamma} + R_{ij}^\gamma \delta_{\alpha\beta}), \end{aligned} \quad (16d)$$

where α, β, γ define any of the Cartesian directions (x, y , or z), R_{ij} is the distance between atoms i and j , and δ is the Kronecker delta. The functions $S_i(r)$ are the screening functions designed to smear the charges over space, which can be recursively derived from Eq. (18a) as

$$S_k(r) = S_{k-1} - \frac{r}{2k-1} \frac{\partial}{\partial r} S_{k-1}(r). \quad (17)$$

As in MB-pol,^{72,73} the screening functions for the MB-nrg PEFs are given by

$$S_0(r) = 1 - e^{-a(\frac{r}{A})^4} + \frac{a^{1/4} r}{A} \Gamma\left(\frac{3}{4}, a\left(\frac{r}{A}\right)^4\right), \quad (18a)$$

$$S_1(r) = 1 - e^{-a(\frac{r}{A})^4}, \quad (18b)$$

$$S_2(r) = S_1(r) - \frac{4a}{3} \left(\frac{r}{A}\right)^4 e^{-a(\frac{r}{A})^4}, \quad (18c)$$

$$S_3(r) = S_2(r) - \frac{4a}{15} \left(\frac{r}{A}\right)^4 e^{-a(\frac{r}{A})^4} \left(4a\left(\frac{r}{A}\right)^4 - 1\right), \quad (18d)$$

where a is the Thole damping, which can be different for charge-charge, charge-dipole, and dipole-dipole interactions, $A = (\alpha_i \alpha_j)^{1/6}$, with i and j being the two sites involved, $r = R_{ij}$, and α is the polarizability factor that is usually set to be the same as the polarizability. The interested reader is referred to Ref. 147 for specific details about the derivation of Eqs. (14)–(17).

III. SOFTWARE STRUCTURE

The C++ source code of MBX is organized into four modules, each of which handles specific functions: **building block** is responsible for maintaining the state of the system; **potential** evaluates the various components of the MB-nrg PEFs; **I/O** manages inputs, outputs, and interfaces with MD drivers; and **utilities** contains functions to execute miscellaneous support tasks. The **potential** module is further divided into sub-modules to calculate each of the energy contributions described in Eq. (3): n -body PIPs, 2-body dispersion, permanent electrostatics, and many-body polarization. The general workflow for an energy calculation step performed by MBX is shown in Fig. 1.

A. Input

Since all PEF parameters are directly compiled into MBX, the user only needs to provide minimal information that is passed to MBX through two files: the NRG file, which contains information about all 1-mers in the system and their initial coordinates, and the JSON file, which specifies details about the calculation to be performed, such as enabling or disabling n -body terms for certain n -mers, and assorted settings, such as the algorithm for the calculation of many-body polarization and convergence threshold

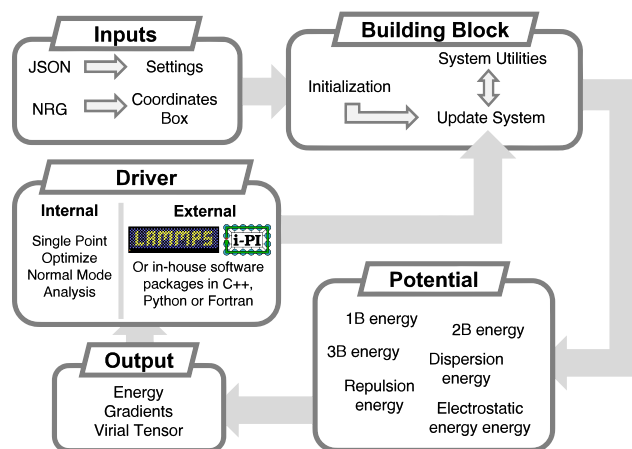


FIG. 1. General workflow for an energy and force calculation step in MBX.

for the induced dipole moments. More information about the format and contents of the NRG and JSON files are discussed in the supplementary material.

B. Building block

The building block module contains the `System` class, which stores all the information about the 1-mers in the system. `MBX` provides a function that reads the NRG file, and creates and initializes a `System` instance. The initialized `System` can then be configured using the JSON parameters that control the energy calculation. Initializing a `System` object requires multiple memory allocation calls and is therefore not instantaneous, but it is performed only once per system of interest.

While MD and MC software implementations for force fields typically treat atoms as the smallest unit, `MBX` considers 1-mers, each consisting of a few atoms, as the smallest unit of the system since the n -body PIPs, which form the backbone of MB-nrg PEFs, are evaluated on these 1-mers. For this reason, the `System` class stores data on a per-1-mer basis.

For each 1-mer type defined in a MB-nrg PEF, the parameters defining all relevant atomic quantities (e.g., charges, polarizabilities, and dispersion coefficients) are automatically compiled into `MBX`. Because the n -body PIPs of a given MB-nrg PEF are fitted over the underlying representation of electrostatics and dispersion, the parameters entering the expressions for $V_{\text{disp}}^{2\text{B}}$ [Eq. (10)] and V_{elec} [Eqs. (15a)–(15d)] are intertwined with each MB-nrg PEF. As a consequence, if the user wishes to adopt a different set of electrostatic or dispersion parameters, all n -body PIPs will need to be refitted using `MB-Fit`.¹³³

The `System` class oversees the calculations of each contribution to the total energy by delegating to the appropriate functions within the `potential` module (see below). Each function returns the energy and associated gradients of a particular energy contribution with respect to the coordinates of the atoms. Once the `System` object is initialized, it is not possible in the current version of `MBX` to add new 1-mers or change the type of existing ones without rebuilding the `System` instance. The atomic coordinates can be updated at any time as long as they are in the same order as the initial set of coordinates. Similarly, any parameters specifying the type of calculation to be performed (e.g., algorithm for many-body polarization, convergence threshold for the induced dipoles, and box size and shape for calculations in periodic boundary conditions) can be changed at any time.

`MBX` initializes a `System` object through the following steps:

1. Create a new `System` object with default parameters corresponding to those used for a gas-phase calculation.
2. Add 1-mers to the `System` using the `AddMonomer` member function. The coordinates, atom labels, and 1-mer type for each 1-mer are stored in the `System` object.
3. After all 1-mers have been added, initialize the `System`. This involves storing the properties for each 1-mer and reordering the 1-mers for optimization of parallelization. The reordering process groups 1-mers of the same type together and orders the types by increasing number of 1-mers. For example, the input for a system of 250 CO_2 molecules (i.e., 1-mers of type CO_2) and 300 H_2O molecules (i.e., 1-mers of type H_2O) can be provided in any order, but `MBX` will

reorder it such that the CO_2 molecules come before the H_2O molecules.

4. Set the physical properties of the atoms, such as charges, polarizabilities, and dispersion coefficients, using helper functions.
5. Parse the JSON file containing information about box size and shape for calculations in periodic boundary conditions, cut-offs, and type of MB-nrg PEFs, as well as other options that control and determine the type of calculation and energy calls to be performed. If a JSON file is not found or not present, the defaults are used.

C. Machine-learned 1-body term: $V_{\text{ML}}^{1\text{B}}$

Since different MD and MC engines have different conventions regarding storage of atom coordinates, `MBX` first translates the atoms in the 1-mer to obey the minimum-image convention before evaluating the 1-body PIPs. This is only necessary when performing a calculation in periodic boundary conditions. `MBX` selects the first atom of each 1-mer as the reference atom to identify the minimum images of the other atoms in the 1-mer. This reference atom is then placed in the principal box and the closest images of other atoms in the 1-mer are selected through an algorithm that operates in fractional coordinates.

D. Machine-learned n -body terms ($n > 1$): $V_{\text{ML}}^{n\text{B}}$

`MBX` supports n -body PIPs with arbitrary values for n , which can be generated with `MB-Fit`,^{133,134} and currently already provides functions to evaluate 2-body, 3-body, and 4-body PIPs. Adding n -body PIPs with larger values of n is trivial and does not require any significant refactoring of the source code. In order to efficiently evaluate all $V_{\text{ML}}^{n\text{B}}$ terms [Eq. (4)], `MBX` first identifies all n -mers for which it is possible that the associated n -body switching function ($s^{n\text{B}}$) is non-zero. An n -mer is accepted and passed to the polynomial evaluation if and only if some 1-mer within the n -mer is within a predefined n -body cutoff ($r_{\text{cutoff}}^{n\text{B}}$) of all other 1-mers in the n -mer. In other words, there must be a “central” 1-mer, and all other 1-mers must be within the n -body cutoff of the “central” 1-mer. This idea is formalized in the following criterion:

CENTER-NEIGHBOR CRITERION: *Using the first atom of each 1-mer to define the position of the 1-mer, the center-neighbor criterion for a given n -mer is satisfied if and only if there exists at least one 1-mer (“center”) such that the distances between the “center” 1-mer and all other $n - 1$ 1-mers (“neighbors”) in the n -mer are smaller than the n -body cutoff $r_{\text{cutoff}}^{n\text{B}}$.*

The value for each $r_{\text{cutoff}}^{n\text{B}}$ used by the CENTER-NEIGHBOR CRITERION is specified by the user in the JSON file. As a consequence, `MBX` only needs to collect n -mers for which the CENTER-NEIGHBOR CRITERION is satisfied and pass this information to the PIP evaluator. The rules for setting appropriate values for $r_{\text{cutoff}}^{n\text{B}}$ are discussed in the supplementary material.

`MBX` uses a K-D Tree to search for n -mers that satisfy the CENTER-NEIGHBOR CRITERION, after which the evaluation of the n -body PIPs with $n > 1$ is effectively the same as for the 1-body PIPs. Using a K-D Tree allows `MBX` to quickly identify relevant n -mers and avoid the need for a double or triple loop over all 1-mers,

which would be extremely slow. The Nanoflann library¹⁴⁸ is used to implement the K-D Tree and perform the radial search. It should be noted that, although not negligible, the Central Processing Unit (CPU) time required to create the tree and perform the search is still a small fraction of the CPU time required to calculate the n -body PIP contributions. The K-D Tree implementation in MBX is as follows: first, a tree is built using the first atom of each 1-mer as a point in the tree. Once the tree containing all the 1-mers is completed, MBX loops over all the 1-mers, which will be the candidate “center” 1-mer in the current loop, and performs a radial search of all other 1-mers that are within r_{cutoff}^{nB} , which will be the candidate “neighbor” 1-mers. Then, n -mers are constructed from the “center” 1-mer and each combination of $n-1$ “neighbors.” By construction, each of the constructed n -mers necessarily satisfies the CENTER-NEIGHBOR CRITERION. However, it is possible that the same n -mer can be selected several times, with different 1-mers acting as the “center.” To avoid double counting, the candidate n -mer is considered valid only if the 1-mer index of the “center” is the smallest among all valid “center” 1-mers.

Although K-D Trees were not originally designed for use in periodic boundary conditions, MBX has implemented a patch that allows for their use in such cases by replicating the box in space. This implies that instead of building a tree for a single copy of the system as done in the gas phase, MBX builds a tree for 27 copies: the original one and the 26 adjacent boxes. Only images within the main simulation box are eligible “center” 1-mers. Future versions of MBX will implement more advanced solutions to address the potential memory cost of this process when the target number of 1-mers is large. After obtaining the lists of n -mers, MBX sends batches of multiple n -mers of the same type to the PIP functions, which then transform the coordinates into PIP variables and calculate the corresponding PIP values.

E. Physics-based terms

MBX defines two distinct classes that are dedicated to calculating the following non-bonded interactions: dispersion (Dispersion class) and permanent and induced electrostatics (Electrostatics class). As in conventional force fields and discussed in Sec. II, MBX excludes these non-bonded interactions for atom pairs that are part of a bond, angle, or dihedral angle. However, MBX does not scale these interactions as common force fields do—for a particular atom pair, they are either entirely enabled or entirely disabled [hence, Δ_{kl} in Eq. (8)]. Generally, all atom pairs within a 1-mer are excluded, but in the event that a 1-mer contains non-excluded pairs both classes calculate the contributions from 1-mer dispersion and electrostatics [i.e., dispersion energy as in Eq. (8) and 1-body contributions to V_{elec} in Eq. (3), respectively] in a first step, ignoring any pair in the excluded pairs list. Then, the intermolecular contributions are calculated in a double-loop over the 1-mer types. For each pair of 1-mer types, the contributions to the dispersion and electrostatics energies are calculated. Before evaluation, the coordinates and associated properties (e.g., atomic charges and polarizabilities, dispersion coefficients, etc.) are reordered to maximize speedup from vectorization through single-instruction multiple-data (SIMD) operations.

1. Dispersion

As shown in Eq. (12), the dispersion energy of a MB-nrg PEF is calculated in real space as a pairwise-additive potential using

pair-defined dispersion coefficients ($C_{6,kl}$) that are calculated using the XDM model.^{142–144} If the molecular system of interest is in periodic boundary conditions, the long-range contribution to the dispersion energy is calculated in reciprocal space using the particle mesh Ewald (PME) algorithm as implemented in the helpME library.^{149,150} PME uses atom-defined C_6 that are then combined using the usual geometric mean combination rule to obtain pair coefficients (i.e., $C_{6,kl} = \sqrt{C_{6,kk}C_{6,ll}}$). A discontinuity in the energy and its gradients can occur if the $C_{6,kl}$ pair coefficients used to calculate the dispersion energy in real space are abruptly changed to the values used by the PME algorithm at the cutoff distance. To avoid this discontinuity, MBX applies a switching function of the same form as that used for the 2-body PIP switching function (see the supplementary material), enabling a smooth transition from the $C_{6,kl}$ used in real space to the $C_{6,kl}$ used in the PME calculation.

2. Electrostatics

The electrostatics calculation involves several steps, including the computation of the permanent electric field, the calculation of the long-range electric field using the PME algorithm as implemented in the helpME library,^{149,150} and the determination of the induced dipoles using one of three algorithms: iterative, conjugate gradient, or always stable predictor-corrector.¹⁵¹ The permanent contribution to the electrostatic energy is straightforward to calculate and relatively fast. However, the bottleneck of the electrostatics calculation is to obtain the induced dipoles on each site. While the analytical solution of the induced dipole moments is possible, it is not efficient for large systems,¹⁴⁷ and it has not been implemented in MBX. A detailed description of the possible methods to solve for the induced dipole moments can be found in Ref. 147.

F. Output

Once all energy and gradient contributions have been calculated, they are summed and stored in the System object, ready to be retrieved by the user or a MD/MC driver. After this step is completed, external modifications to the coordinates of the system such as progression to the next MD/MC step can be performed. The new coordinates are set in the same System instance, which can then be used to perform another energy/force calculation.

While energies and forces are the most commonly retrieved information by MD and MC drivers, MBX provides interfaces to retrieve any of the system’s properties, including but not limited to, charges, permanent and induced dipole moments, and the virial tensor.

IV. DRIVERS

MBX has three built-in drivers to perform single point calculations, geometry optimizations, and normal-mode analyses, all written in C++. A simple example on how to use MBX to read an NRG file and set up the system with a JSON file is shown in Fig. 2.

Besides the internal drivers discussed above, the current version of MBX also provides an efficient interface to popular software packages Large-scale Atomic/Molecular Massively Parallel Simulator (LAMMPS)¹⁵² and i-PI¹⁵³ for both classical MD and quantum path-integral molecular dynamics (PIMD) simulations.² MBX acts as a

```
1 // Needed to read the NRG file
2 #include "io_tools/read_nrg.h"
3 // Needed to use the system class
4 #include "bblock/system.h"
5 #include <vector>
6 #include <string>
7 int main() {
8     // Declare systems vector
9     std::vector<bblock::System> systems;
10    // Read systems from NRG file
11    std::string input = "input.nrg";
12    tools::ReadNrg(&input[0], systems);
13    // Set up from json file
14    std::string json_file = "input.json";
15    systems[0].SetUpFromJson(&json_file[0]);
16    // Compute energy
17    double e = systems[0].Energy(true);
18    // Retrieve gradients
19    std::vector<double> grads = systems[0].GetRealGrads();
20    return 0;
21 }
```

FIG. 2. Example of a C++ main function to use the MBX library with a NRG and a JSON file.

client that returns MB-nrg energies and forces, while the actual MD steps are controlled by the MD engine. In the case of i-PI, the communication between MBX and i-PI can be established in two ways: Internet and Unix domain sockets. For LAMMPS, MBX is connected through the combination of specific FIX and PAIR_STYLE commands in the LAMMPS input. The MBX/LAMMPS and MBX/i-PI interfaces have already been used to study the water vapor/liquid equilibrium,¹⁰⁴ CH₄/H₂O^{126,128} and CO₂/H₂O^{125,127} mixtures, and ions in solution.^{118,119,122} In the current version of MBX, all of the computationally expensive functions are parallelized using Open Multi-Processing (OpenMP) to maximize use of large many-core compute nodes. This design readily enables other “driver” codes, serial or parallel, to couple with MBX and perform advanced calculations, such as MD and PIMD simulations using LAMMPS or i-PI.

The pure driver-only nature of i-PI makes the interface with MBX very simple. A single driver code that communicates with the i-PI socket is enough to allow both packages to communicate. The driver code receives the coordinates and the simulation cell from i-PI through a socket, sets them into MBX, and performs the energy calculation for those coordinates. Gradients and energies are then retrieved from MBX and sent through the socket to i-PI that performs the time evolution for each time step, updating both atom coordinates and simulation cell, which are then sent back to the driver.

In the case of LAMMPS, MBX is tightly coupled to enable large-scale parallel simulations with minimal overhead. LAMMPS is parallelized using a spatial domain decomposition algorithm whereby the simulation is partitioned into sub-domains and individual Message Passing Interface (MPI) ranks are responsible for computing all tasks within the sub-domain to which they have been assigned. In MBX, minimal changes were necessary to enable the calculation of the real-space interactions within each LAMMPS sub-domain containing local and ghost particles. Local particles are contained within the sub-domain owned by an MPI rank and ghost particles are replicated from neighboring sub-domains owned by other MPI ranks.

For performance reasons, the iterative electrostatic solver in MBX was enabled with MPI and does not need to interact with LAMMPS during intermediate steps. In current CPU-only data-driven many-body simulations with MBX+LAMMPS, the performance bottleneck functions include evaluation of the *n*-body PIP terms, and calculation of the long-range portion of the electrostatic and dispersion interactions that include evaluation of distributed 3D Fast Fourier Transforms (FFTs). The electrostatic solver involves an iterative calculation of induced dipole moments requiring repeated communication with neighboring MPI ranks and evaluation of multiple 3D FFTs. These terms of the MB-nrg PEF along with all the others can be evaluated independently of one another and in arbitrary order.

The LAMMPS interface also enables hybrid FF/MB-nrg simulations where some interactions are described by conventional force fields [e.g., Assisted Model Building with Energy Refinement (AMBER),¹⁵⁴ Chemistry at Harvard Molecular Mechanics (CHARMM),¹⁵⁵ and Optimized Potentials for Liquid Simulations (OPLS)¹⁵⁶] and other interactions are described by MB-nrg PEFs. In these hybrid simulations, the electrostatic energy is exclusively computed by MBX, while the remaining non-bonded interactions between FF and MB-nrg molecules are represented by Lennard-Jones potentials that can be derived using standard Lorentz-Berthelot mixing rules. In the case of FF molecules solvated in MB-pol water, the recommended effective Lennard-Jones parameters for MB-pol are listed in Table I.

Importantly, given its modularity and portability, MBX can be used in combination with any software package (e.g., in-house software developed within a research group) that supplies atom

TABLE I. Effective Lennard-Jones parameters for MB-pol water.

Atom	σ (Å)	ϵ (kcal/mol)
O	3.263 93	0.269 48
H	2.683 54	3.7×10^{-10}

coordinates and expects energies and forces. MBX modules and sub-modules can be included by other C++ codes and `System` objects can be instantiated and used like any other C++ class. MBX also provides wrapper interfaces in C, FORTRAN and Python. The `System` class by itself is too big to be automatically adapted to other languages. However, for each one of the main `System` member function, there is a wrapper that enables calls from other programming languages. While not all of the member functions are wrapped, implementing a wrapper to retrieve a property that is currently not available is a simple and straightforward process.

V. PARALLELIZATION

In order to perform calculations on large systems, it is necessary to parallelize the evaluation of the various contributions to the total potential energy and forces. MBX exploits two sources of parallelization. Internally, MBX parallelizes the calculation of the various PEF contributions using OpenMP. Externally, MBX can exploit MPI parallelization schemes implementing domain decomposition which may be available in the interfaced molecular simulation software. For example, since LAMMPS is able to partition the simulation box into sub-domains overseen by individual MPI ranks, the MBX/LAMMPS interface allows each LAMMPS MPI rank to use one or more MBX OpenMP threads. This implies that both sources of parallelization (OpenMP in MBX and MPI in LAMMPS or other software) can be used together.

As a showcase of the OpenMP parallelization, Fig. 3 reports the mean runtime of an energy calculation for a box of 2048 water molecules as a function of the number of cores. The timings observed suggest that the OpenMP parallelization is efficient up to about 16 threads, after which MBX is not currently able to take full advantage of further parallelization through OpenMP. Also shown in Fig. 3 is the runtime when the calculations are performed within LAMMPS using a single MPI rank (and the indicated number of OpenMP threads). As expected, the scaling for both MBX as a standalone code and when interfaced with LAMMPS using a single MPI rank is essentially identical, since the OpenMP parallelization is

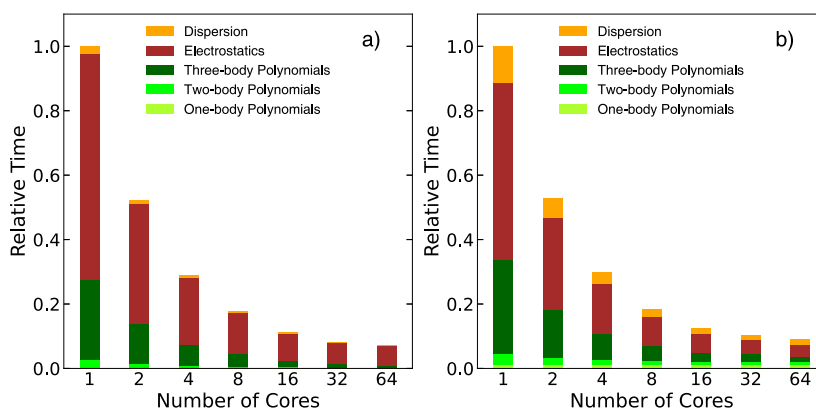


FIG. 3. Relative time to calculate all energies and gradients for a cubic box of 2048 water molecules in MBX in periodic boundary conditions. Calculations were each performed 100 times, and the average was taken. The relative times are presented as a function of the number of OpenMP threads used with MBX as a standalone code (a) and with LAMMPS using a single MPI rank (b), being the reference time the average time taken when using 1 OMP thread. All the calculations were performed on a compute node with two sockets each with 64 2.6 GHz AMD 7H12 Rome processors.

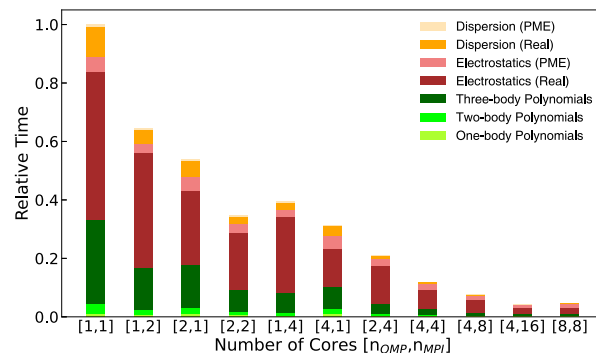


FIG. 4. Relative time to calculate all energies and gradients for a cubic box of 2048 water molecules in periodic boundary conditions using MBX interfaced with LAMMPS. Calculations were each performed 100 times, and the average was taken. The relative times are presented as a function of the number of OpenMP threads (n_{OMP}) per MPI rank and the number of MPI ranks (n_{MPI}), being the time corresponding to 1 OMP thread and 1 MPI rank the reference. Calculations were performed on a compute node with two sockets each with 64 2.6 GHz AMD 7H12 Rome processors.

internal to MBX. It should be noted here that, as is generally the case, the electrostatics represents the most expensive energy contribution to calculate. Since the i-PI interface utilizes no additional source of parallelization, the relative times profile of MBX in i-PI is essentially identical to that obtained when MBX is interfaced with LAMMPS in Fig. 3.

When the simulations are driven by LAMMPS, MBX can also take advantage of parallelization over MPI ranks. Figure 4 shows the relative times associated with the MBX energy and gradient calculations when interfaced with LAMMPS, utilizing several different combinations of MPI ranks and OpenMP threads. Comparing columns [1, 2] and [1, 4] with columns [2, 1] and [4, 1], it is clear that the OpenMP parallelization is more effective when the total number of available threads is small. However, as n_{OMP} gets

larger and approaches the parallelization limit observed in Fig. 3, the use of MPI ranks is more effective in achieving the best performance. The optimal combination of OpenMP threads and MPI ranks depends on various factors, including the system's size and topology (i.e., cluster, bulk, or interface). It should be noted that the evaluation of all individual contributions to the energy scales relatively well with both MPI and OpenMP parallelization, with the exception of the PME part of the electrostatics, which will be the focus of further optimizations in the subsequent releases of MBX. The actual timings associated with the MBX energy and gradient calculations shown in Figs. 3 and 4 are reported in the supplementary material.

All timings reported in Figs. 3 and 4 were obtained for simulations of 2048 water molecules in a periodic cubic box carried out on a compute node with two sockets each with 64 2.6 GHz AMD 7H12 Rome processors using a convergence threshold (ϵ) for the atomic induced dipole moments of 10^{-16} , which corresponds to each component of the induced dipole moment of each atom being converged up to the eighth decimal digit. The convergence criterion is met when the squared difference between successive iterations (k and $k + 1$) of each induced dipole moment component (α) for each atom i , $\mu_{\text{ind},i,\alpha}$, is smaller than the tolerance ϵ ,

$$\left(\mu_{\text{ind},i,\alpha}^{(k+1)} - \mu_{\text{ind},i,\alpha}^{(k)}\right)^2 < \epsilon, \quad \forall i, \alpha. \quad (19)$$

A threshold $\epsilon = 10^{-16}$ corresponds to a conservative and safe convergence criterion for all systems that we have simulated with our MB-nrg PEFs to date. However, it is worth noting that larger values up to $\epsilon = 10^{-8}$ are sufficient for systems with weaker responses to electric fields (e.g., neat H₂O, CO₂, CH₄ solutions). A systematic analysis of the energy conservation and associated energy fluctuations for simulations of 2048 water molecules in a periodic cubic box carried out in the microcanonical (NVE = constant number of molecules, volume, and energy) ensemble as a function of the convergence tolerance is reported in the supplementary material.

VI. CONCLUSIONS

Over the past decade, data-driven many-body MB-nrg PEFs have been shown to accurately predict the properties of various molecular systems from the gas to the condensed phase. By integrating an underlying many-body polarizable model with explicit machine-learned representations of individual n -body interactions, MB-nrg PEFs achieve chemical accuracy in the representation of molecular interactions at both short and long range, and at all n -body orders.

In this work, we introduced MBX, a C++ modular library that enables MB-nrg energy and forces calculations. MBX is divided into modules responsible for particular tasks. The potential module is divided into sub-modules, each handling one specific energy contribution: n -body PIPs, dispersion energy, and electrostatics. Other modules are responsible for input/output, interfacing with drivers (e.g., software for MD and MC simulations), and constructing the System class that stores the state of the molecular system.

While MBX can be used as a standalone software, it also provides interfaces to common MD packages such as i-PI and LAMMPS

along with interfaces written in Fortran and Python that can be seamlessly used in combination with third-party software (e.g., in-house software developed by a research group). Both interfaces have already been used to study various molecular systems, including liquid water, CO₂/H₂O mixtures, CH₄/H₂O mixtures, hydrated alkali-metal ion clusters, and ionic solutions.

MBX includes an internal OpenMP parallelization that is more efficient when the number of threads is small. When interfaced with external software that provides its own MPI parallelization (e.g., LAMMPS), MBX enables efficient MB-nrg energy and force calculations that take advantage of both OpenMP and MPI parallelizations. Future versions of MBX will include improved parallelization schemes as well as the implementation of the extended MB-nrg framework introduced in Ref. 131 for covalently bonded molecules, with the goal of enabling fast MB-nrg energy/force calculations that, in turn, will enable chemically accurate large-scale computer simulations of generic molecular systems.

SUPPLEMENTARY MATERIAL

Description of the MBX input file formats and functional form of the switching functions for the MB-nrg PEFs.

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AUTHOR DECLARATIONS

Conflict of Interest

The authors have no conflicts to disclose.

Author Contributions

Marc Riera: Conceptualization (equal); Investigation (equal); Methodology (equal); Software (lead); Validation (equal); Visualization (equal); Writing – original draft (equal); Writing – review & editing (equal). **Christopher Knight:** Funding acquisition (supporting); Investigation (equal); Software (equal); Validation (equal); Writing – original draft (equal); Writing – review & editing (equal). **Ethan F. Bull-Vulpe:** Investigation (equal); Methodology (equal); Software (supporting); Validation (supporting); Visualization (supporting); Writing – original draft (equal); Writing – review & editing (equal). **Xuanyu Zhu:** Investigation (equal); Methodology (equal); Software (supporting); Validation (supporting); Visualization (supporting); Writing – original draft (equal); Writing – review & editing (equal). **Henry Agnew:** Investigation (supporting); Methodology (supporting); Software (supporting); Validation (supporting); Visualization (supporting); Writing – review & editing (supporting). **Daniel G. A. Smith:** Funding acquisition (supporting); Software (supporting); Writing – review & editing (supporting). **Andrew C. Simmonett:** Funding acquisition (supporting); Software (supporting); Writing – review & editing (supporting). **Francesco Paesani:** Conceptualization (equal); Funding acquisition (equal); Investigation (equal); Methodology (equal); Project administration (equal); Resources (equal); Software (equal); Supervision (equal); Writing – original draft (equal); Writing – review & editing (equal).

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request. MBX can be downloaded from <https://github.com/paesani/MBX>.

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