https://doi.org/10.1038/s42254-023-00615-x

Advancing molecular simulation with equivariant interatomic potentials

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Deep learning has the potential to accelerate atomistic simulations, but existing models suffer from a lack of robustness, sample efficiency, and accuracy. Simon Batzner, Albert Musaelian, and Boris Kozinsky outline how exploiting the symmetry of Euclidean space offers a new way to address these challenges.

Elucidating the behaviour of molecules and materials at the atomic scale is a core goal throughout the physical sciences. The fine-grained control over thermodynamic conditions as well as the spatial and temporal resolution that computations can provide has rapidly made molecular dynamics simulation an important pillar of modern science, complimenting experiment and theory. Traditionally, however, computational chemists and materials scientists have had to choose between expensive first-principles methods — that accurately and explicitly describe the quantum-mechanical electronic structure and properties — and computationally efficient approaches that only approximately model atomic interactions. Machine learning, however, can now provide a way to study large systems at long timescales while still capturing with high fidelity the underlying potential energy surface as a function of atomic positions.

Neural equivariant interatomic potentials (NequIP)[1] are a recent neural network approach for learning interatomic potentials from ab initio calculations for molecular dynamics simulations. Following their initial success, equivariant interatomic potentials — a new class of deep learning-based interatomic potentials — emerged as a promising paradigm that has been shown to significantly improve accuracy, robustness, transferability, and sample efficiency, establishing the new state-of-the-art in the field[1–5].

Graph neural networks

Deep learning methods based on graph neural networks, more broadly, have proven to be a powerful modelling paradigm for atomistic systems and for many other domains in the physical sciences. In the context of modelling molecules and materials at the atomic level, graph neural networks typically represent the atomistic structure by associating each atom with a node in the graph. When modelling 3D geometry, edges between these nodes are then drawn for all pairs of atoms that are closer than some physically motivated interaction distance. Over a series of layers in the graph neural network, information is then propagated along the graph and thereby iteratively refined (Fig. 1). Nodes in later layers of the neural network can thus 'learn' about correlations among nodes in their environment, corresponding to learning many-body interactions among atoms.

Since physical systems in 3D space obey the symmetries of the Euclidean group E(3), namely translation, rotation, and mirroring, their representations should transform predictably under the actions of this group. Conventional graph neural networks have achieved this by operating on predetermined geometric invariants of the atomic geometry such as distances and angles[6]. Such 'featurizations' are invariant with respect to E(3) symmetry transformations, making the output of a function acting on them again E(3)-invariant. Atomic forces — which are equivariant quantities — are typically obtained as the negative gradient of this invariant energy (to construct conservative force fields), thus by construction making them equivariant.

Symmetry

At the core of equivariant potentials, and equivariant neural networks more broadly, lies the idea of generalizing this invariant representation: exploiting the knowledge of symmetry operations in 3D space rather than just respecting it[7,8]. Instead of operating on these predefined invariant descriptors or features, equivariant potentials process relative interatomic positions directly, enabling more expressive functions of that geometry. Internally, equivariant models' states (also termed latent features or representations) are collections of (invariant) scalars, (equivariant) vectors, and (equivariant) higher-order geometric tensors. Equivariant models combine these mathematical objects in a symmetry-preserving fashion, in particular by restricting all allowed operations inside the neural network to those that commute with actions of the Euclidean group and can thus learn powerful representations reflected in the accuracy and sample efficiency of these models that far exceed previous approaches.

Equivariant interatomic potentials have led to several advances in molecular modelling. Starting from the NequIP framework[1], order-of-magnitude improvements in accuracy and sample efficiency compared to traditional methods have been observed. In the most striking example so far, the NequIP model was able to improve on the accuracy of a previous leading approach[9] despite being trained on 1,000 times fewer reference data generated from accurate density functional theory (DFT) calculations. Practitioners are also observing large improvements in transferability, that is, the model's ability to extrapolate to physical configurations outside the training set, and robustness (the numerical stability in long dynamics simulations)[3,4]. A particularly interesting example was demonstrated in ref. 4, in which an equivariant potential under the right normalization of the energy targets was able to extrapolate far beyond the training distribution of near-equilibrium structures, both under dissociation of an atom and under the sampling of normal modes. These enhanced attributes make equivariant potentials a powerful new tool for a diverse set of applications where approximations were previously difficult to develop. Software codes are generally publicly available (examples include Allegro, NequIP, SchNetPack), integrated with high-performance molecular dynamics software, and are easy to use, which has enabled applications ranging from heterogeneous catalysis to ionic diffusion, metal–organic frameworks, and biomolecular systems[2,5,10].

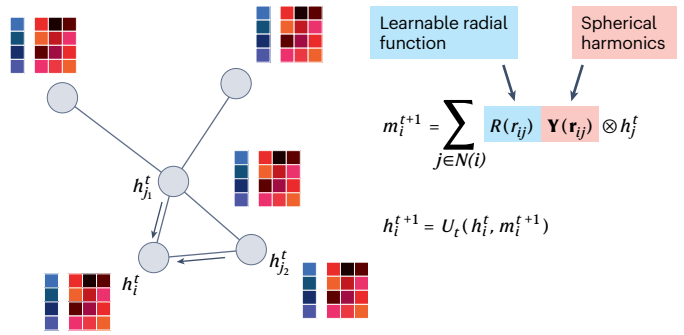

Fig. 1 | Equivariant message passing interatomic potentials. Each atom i at layer t carries a feature vector h_i^t made up of a set of scalar (4 blue squares per atom, each with 1 scalar), vector (4 × 3 red squares, denoting 4 vectors with 3 spatial dimensions), or higher-order tensor features. These are updated over a series of layers using E(3)-equivariant operations. Right: first a message m_i^{t+1} is created as a function of atom i's neighbourhood, operating on the neighbouring atom feature h_j as well as the relative interatomic position to the neighbouring atom $\mathbf{r}_{ij}$ and distance r_{ij}. In a second step, the atom features h_i^t are then updated using a learned updated function U_t acting on the previous node state and the newly computed message. The blue arrows indicate the direction that messages are being passed along the graph.

Towards large-scale simulations

Although equivariant potentials have enabled significant progress on these diverse molecular and materials systems, their increased accuracy initially came at the cost of increased computational expense. In practice, operating on geometric tensors (as is the case for equivariant graph neural networks) is more expensive than operating on scalars, for which software and hardware has been optimized for many years. Recently, algorithmic approaches have emerged that surpass these limitations: the Allegro architecture, in particular, appears to retain the state-of-the-art characteristics of equivariant potentials while being orders of magnitude more scalable across hundreds to thousands of GPUs, thus greatly enhancing the time-to-solution and ability to simulate large structures of tens of millions of atoms with near-quantum mechanical accuracy[2,5]. This is achieved through a combination of strictly local interactions (making computation highly parallel) as well as through a separation of the network into interacting scalar and tensor 'tracks' so that computationally efficient operations on scalars can be added to the model independently from more expensive computation on tensors, allowing most of the the network's capacity to be shifted into scalar operations that are more efficient on GPUs[2].

Simulating large-scale biomolecular dynamics

Recently, this combination of scalability and accuracy has been used for a first-of-its-kind demonstration in large biomolecular dynamics simulations. In ref. 2 an Allegro model was trained on a dataset of approximately 1 million structures of inter- and intra-molecular interactions across a very diverse set of organic biomolecules at DFT accuracy. This transferable potential was then used without any further modification to run molecular dynamics on a variety of different proteins and biomolecular assemblies that did not appear in the training set, including an all-atom, explicitly solvated model of the HIV capsid totalling 44 million atoms.

Outlook

Further developments in algorithms and software are required to advance these promising initial efforts towards the scientific impact they could provide. At present, all machine learning interatomic potentials still present a trade-off between accuracy and computational efficiency. In addition, although equivariant machine learning interatomic potentials appear to demonstrate improved robustness[2–4], current methods still can lead to unphysical or diverging simulations when evaluated on samples far beyond their training distribution. Finally, and possibly most importantly, all machine learning interatomic potentials, equivariant or not, are now fundamentally limited by the level of theory that their training data was obtained from. Given the increasing accuracy of learned interatomic potentials, this limitation puts a heightened focus on improving quantum-chemical methods, through machine learning itself, or other techniques.

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Published online: 19 July 2023

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Acknowledgements

The authors are indebted to many contributions from A. Johansson, L. Sun, M. Geiger, and T. Smidt in developing the ideas and their software implementation.

Competing interests

The authors declare no competing interests.