Predicting molecular dipoles by combining atomic partial charges and atomic dipoles

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The molecular dipole moment is a central quantity in chemistry. It is essential in predicting infrared spectra, sum-frequency generation spectra, and long-range electrostatic interactions. Furthermore, it can be extracted directly—via the ground state electron density—from high-level quantum mechanical calculations, making it an ideal target for machine learning. We choose to represent this quantity with a physically-inspired ML model that captures two distinct physical effects: local atomic polarization is captured within the symmetry-adapted Gaussian process regression (SA-GPR) framework, which assigns a (vector) dipole moment to each atom, while movement of charge across the entire molecule is captured by assigning a partial (scalar) charge to each atom. These “MuML” models are fitted together to reproduce molecular dipole moments computed by high-level coupled-cluster theory (CCSD) on the QM7b dataset, achieving more accurate results due to the physics-inspired combination of these complementary terms. The combined model shows excellent transferability to a showcase dataset of larger molecules, approaching the accuracy of DFT at a small fraction of the computational cost. The ultimate performance—and the optimal weighting of their combination—depend, however, on the details of the system at hand, with the scalar model being clearly superior when describing large molecules whose dipole is almost entirely generated by charge separation. These observations point to the importance of simultaneously accounting for the local and non-local effects that contribute to the molecular dipole moment; further, they define a challenging task to benchmark future models, particularly those aimed at the description of condensed phases.

I. INTRODUCTION

The dipole moment $\mu$ of a molecule is a measurement of its response to an applied electric field. It is a key ingredient in the calculation of infrared (IR) and sum-frequency generation (SFG) spectra, as well as in understanding intermolecular interactions.4 Despite its importance, the dipole moment presents a challenge for calculation, often depending significantly on the level of theory and the basis set used.5,6 Furthermore, while a molecular dipole moment gives information about the distribution of charge in the molecule, it is determined by the interplay of several physical effects, making it difficult to obtain physical insight from knowledge of $\mu$ alone. A number of methods for unravelling the different effects exist, generally based on a partitioning into localized atomic charges and dipoles (accounting for charge transfer and polarization). While these methods are attractive for understanding the underlying physics responsible for $\mu$, they are usually poorly transferable between different molecules or classes of molecules.

In this paper we design a new framework for the prediction of gas-phase dipole moments that unifies the atomic charge - atomic dipole description rooted in physics with the conformational and chemical sensitivity afforded by kernel-based machine learning. We begin in Section II with an overview of existing methods to describe and predict molecular dipoles. In Section III we formulate the different models we propose to learn and predict polarization: We use a general symmetry-adapted framework to give environment-centred dipole predictions,7 along with a partial-charge model in the vein of existing neural-network models8,9, to combine good chemical transferability with general conformational dependence. In Section IV, we train three models – only partial charges, only environment-centered dipoles, and a combination of the two – which we collectively refer to as MuML. The models are fitted to reference calculations from high-end linear response coupled-cluster calculations with single and double excitations (LR-CCSD), finding an accuracy comparable to that of hybrid density functional theory. Next, a showcase set of larger, more complex compounds is used to test these models rigorously. Finally, we make a critical comparison of the performance of the different models, revealing the interplay of the different terms that contribute to molecular polarization.

II. THEORY

The dipole moment of a molecule is defined as the first moment of the total electric charge density,

$$\mu = \int \rho_e(r) \, d^3r + \sum_i r_i Z_i,$$

where $\rho_e$ is the electronic charge density, $r_i$ the position of the $i$th nucleus, and $Z_i$ its charge. Usually we are concerned with the permanent dipole moment – that is, the first moment of the total charge density in the molecule’s

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ground-state. However, this expression remains valid for non-equilibrium geometries as well as for excited states. The expression can be simplified by making the approximation that the electron charge density is concentrated at individual atomic sites; that is, each atom \( i \), with coordinate \( \mathbf{r}_i \), has an associated partial charge \( q_i \) resulting from the difference between the nuclear charge and the partitioned electron density. The approximated total charge density is thus \( \rho(\mathbf{r}) = \sum_i q_i \delta(\mathbf{r} - \mathbf{r}_i) \) and we can write

\[
\mathbf{\mu} = \sum_i \mathbf{r}_i q_i, \tag{2}
\]

which is uniquely defined with respect to the origin of the molecular coordinate system only if the total molecular charge is zero. Charged molecules can be accommodated by setting the origin of the molecule to its centroid, such that \( \sum_i \mathbf{r}_i = 0 \); this makes the dipole moment insensitive to a collective shift of all the \( q_i \).

The problem then becomes the determination of the \( q_i \)s that best reproduce the molecular dipole – often in addition to other goals, such as modelling the electrostatic potential or characterizing chemical bonding. There are many existing methods to determine these charges, depending on the objectives of the model. Many methods are based directly on the ground-state charge density (or even the wavefunction), such as the Mulliken population analysis,\(^10\) the Hirshfeld decomposition\(^11\) (and its iterative\(^12\) extension), the atoms-in-molecules (AIM, also known as quantum chemical topology – QCT) theory,\(^13\) and iterative stockholder atoms (ISA).\(^14\)

Another major class of atomic charge assignment methods, known collectively as electrostatic potential fitting methods (ESP), focuses directly on reproducing the electrostatic potential of the molecule rather than simply decomposing its charge density. One can immediately see the relevance of such methods to Eq. (2), as the far-field limit of the electrostatic potential is dominated by the dipole term. ESP fitting methods were developed by Momany\(^15\), Cox and Williams\(^16\), Singh and Kollman\(^17\), and Breneman and Wiberg\(^18\); each of these methods finds the charges through a least-squares fit in order to reproduce the potential at a grid of sites fairly close to the molecule but well outside the van der Waals radius. Notably, Momany\(^15\) also fits the total molecular dipole moment in order to satisfy Eq. (2). Many subsequent methods incorporate similar information into a compromise fit between chemical information (the charge density) and far-field electrostatics, such as the DDEC\(^19\) and Hirshfeld-E\(^20\) methods. However, such an all-in-one compromise becomes a disadvantage when we are not interested in the chemical bonding information, but only in reproducing the molecular dipole moment.

Although the methods above are all motivated by physical principles, different methods can give quite different results for the partial charges;\(^4,21\) even worse, the results of a single method may be very sensitive to the details of the underlying electronic structure calculation, such as the basis set used.\(^16,17,22,23\)

Furthermore, collapsing the charge density to a set of points is often too severe an approximation to obtain an accurate description of the electrostatic potential.\(^4,21\) We can therefore augment our approximation to include information on the atom-localized anisotropy or, informally, local polarization of the charge distribution, by adding dipoles or higher moments onto atomic sites. This is the idea behind the distributed multipole analysis (DMA) theory,\(^24\) which gives for the total dipole

\[
\mathbf{\mu} = \sum_{j \in \mathcal{C}} (\mathbf{r}_j q_j + \mathbf{\mu}_j), \tag{3}
\]

where \( \mathcal{C} \) is a list of centres that includes both atoms and interatomic positions. \( q_j \) is the partial charge associated with the \( j \)th centre and \( \mathbf{\mu}_j \) its associated partial dipole, with higher multipole moments making no contribution to the total dipole moment.

Several other methods use this idea of representing the field with both charges and higher multipole moments assigned to atomic sites, like the FOHI-D model\(^25\) and the fullerene polarization model of Mayer\(^26\), the latter recently modified and incorporated into a QM/MM context (where accurate reproduction of the far-field electrostatic potential is essential) as the FqF\(\mu\) model.\(^27\) The authors of FOHI-D in particular separate intrinsic atomic polarization, which can be calculated directly for isolated atoms in the same iterative spirit as the classic iterative Hirshfeld method, from atomic charge transfer, which is described using the point-charge model. However, they note that the agreement of their model with the electrostatic potential is generally worse when dipoles are included, although this could have been due to their choice of grid points much closer to the molecule than is usually used for ESP-fitting methods. Mayer\(^26\), on the other hand, discusses the physical idea from the opposite perspective, that of adding atomic charges, derived from a procedure similar to the electronegativity equalization (EEQ) known in chemistry, to an atomic-dipole model in order to describe nonlocal polarization. The polarization of carbon nanostructures (nanotubes and fullerenes) is much better described by adding atomic charges to the description, as they can describe the large-scale flow of charge across the conjugated \( \pi \)-systems typical of these nanostructures.

A key limitation of most of these methods is their inability to describe the dependence of electrostatic quantities across conformational and chemical space without performing additional \textit{ab initio} calculations or fitting empirical parameters, which severely limits their ability to model experimental spectra and make transferable predictions for new molecules. A natural way to incorporate the required conformational and chemical sensitivity is to draw on the large body of work over the last two decades that uses machine learning to predict molecular properties\(^9,28–35\) or molecular potential energy surfaces.\(^36–41\)

Many existing methods are explicitly targeted to reproduce the molecular dipole moment, or produce it as
a side effect. The earliest of these is the neural network
method of Darley, Handley, and Popelier28 (see also Ref.
29), where a neural network is fitted to reproduce the
multipole moments of a molecule or fragment computed
via quantum chemical topology (QCT, a.k.a. atoms-in-
molecules theory)13. The two main drawbacks of this
strategy, common to many of the other methods dis-
cussed here, are (1) the need to define a local reference
frame, which limits the method’s transferability to other
chemical compounds, and (2) the need to fit to a precom-
puted set of atomic charges and multipoles, the choice
of which is ultimately arbitrary. The QCT charges and
multipole moments, in particular, are known to be poorly
convergent due to the irregular shapes of the partitioned
atomic volumes.4

The techniques for fitting local electrostatic properties
have evolved considerably since then, but most of the
proposed methods retain these two key drawbacks. For
example, the IPML model of Bereau et al.32 predicts in-
termolecular interaction energies accurately by system-
atically treating several different physical energy con-
tributions. The dipole moments themselves, on the other
hand, are not as well predicted, given that their accu-
rate reproduction is not the primary goal of the model.
Part of the error may come from using environment-local
axis systems to predict the higher-order multipole mo-
ments, which is a less general and robust approach than
the symmetry-adapted regression introduced in Grisafi
et al.7; furthermore, the model retains the same draw-
back of being fitted to a specific partitioning scheme –
in this case, the minimal-basis iterative stockholder
method42, which was chosen for its accuracy in mod-
elling electrostatic interactions and not for reproducing
the total dipole.

The neural network model of Gastegger, Behler, and
Marquetand8, on the other hand, does explicitly target
the total molecular dipole moment. It predicts the set
of environment-dependent partial charges that best re-
produce the total dipole moment, thereby bypassing the
need to choose an arbitrary charge partitioning scheme,
and uses the conformational sensitivity gained through
the neural network to accurately predict infrared spec-
tra. The PhysNet model of Unke and Meuwly9 uses the
same idea and additionally uses a new representation to
span a large swath of chemical space, as does the HIP-NN
model of Sifain et al.43, which also incorporates enough
conformational dependence to be able to predict infrared
spectra. However, all three of these models only predict
scalar atomic properties (no atomic polarization), which
we will see is important to achieving the best accuracy
and transferability.

There are several approaches to fitting properties, such
as the dipole moment, that transform as tensors – in par-
icular, that are covariant to rotation rather than invari-
ant. The local-axis approach used in Bereau et al.32 has
already been mentioned; another approach is the covari-
ant kernels introduced in Glielmo, Sollich, and De Vita34
and developed into a general symmetry-adapted regres-
sion method for any tensor order in Grisafi et al.7. (Co-
variant kernels were tried in Bereau et al.32 but found
to perform about as well as the local-axis method, al-
though this is not the same formulation as used in Grisafi
et al.7.) The symmetry-adapted regression method was
successfully tested on dipole moments of small molecules
and clusters, as well as accurately predicting higher-order
tensors such as the polarizability35.

Finally, Christensen, Faber, and von Lilienfeld45 have
developed a formalism (OQML) for incorporating elec-
tric field gradients into a machine learning fit. They
use a system of arbitrary, though usually realistic, par-
tial charges in order to define an implicit local reference
frame for each atomic environment, which can then be
used to fit local dipole moments. While their formul-
ation is quite different from the method we will develop
below, we believe it is fundamentally similar to assigning
an environment-dependent partial dipole to each atom,
as described in Section III B.

III. METHODS

A. Partial-Charge Model

We begin by building a machine-learning model that
incorporates local environment sensitivity into the simple
partial-charge model of Eq. (2) using Gaussian process
regression (GPR)46. To do this, we exploit the fact that
GPR uses a linear fit in kernel space, and so can be used
to fit the result of any linear operator applied to atomic
quantities47. The vector of weights w is required that
minimizes the regularized loss function,

$$L^2 = \|K_PM w - y\|_{\Lambda}^2 + \|w\|_K^2$$

(4)

where $\Lambda$ is a diagonal matrix whose entries $\sigma^2_i$ are chosen
to optimize the error of the fit along with its transferabil-
ty to new molecular databases, and $L$ a linear operator, then:

$$w = (K_{MM} + (K_{PM})^T \Lambda^{-1} K_{PM})^{-1} \Lambda^{-1} y.$$  

(5)

The fit uses an “active set” of $M$ basis functions (which
in practice is a small fraction of the total number $P$ of
atoms in the database). In principle, any sufficiently rep-
resentative set of configurations could be used to form
the active set of basis functions, but in practice they are
almost always chosen from the environments present in
the molecules in the training set using an algorithm such
as FPS or CUR.48. The entries of the kernel matrix are
$(K_{ij})_{ij} = k(\chi^{(i)}, \chi^{(j)})$, where the SOAP kernel49 is
used as the similarity function $k(\cdot, \cdot)$ between two atomic
environments.

To build up a model for the dipole moment, we predict
partial charges $q(A_i)$ for atom $i$ in molecule $A$ such that

$$\mu(A) = \sum_{i \in A} r_i q(A_i),$$

(6)
where

$$q(A_i) = \sum_{j \in M} w_j k(X^{(i)}, X^{(j)}), \quad (7)$$

with $X^{(j)}$ a basis point, i.e. an environment in the active set. We can then define the linearly transformed kernel matrix as

$$(L'K_{PM})_{M,j} = \sum_{i \in M} r_i k(X^{(i)}, X^{(j)}), \quad (8)$$

allowing us to use Eq. (5) to determine the weights.

The matrix in Eq. (8) has $3N$ rows, where $N$ is the number of molecules; one for each Cartesian component of the dipole moment of each molecule $M$ in the training set. The $r_i$ are defined with respect to the coordinate system in which the dipole is given, centred on the centroid of the respective molecule so that the prediction is insensitive to a shift in total charge. The target data $y$ are then defined as a concatenation of all the Cartesian components of the given dipole moments of the molecules in the training set.

The insensitivity of the model to the total charge of the molecule is an advantage because then the model’s total charge, $Q_M = \sum_{i \in M} q_i$, need not be constrained to reproduce exactly the total charge of a molecule. As noted in Unke and Meuwly, applying this constraint to the training set would not guarantee that the model gives the correct charges for prediction on a new molecule. Furthermore, we found that including exact total-charge constraints into the fit via Lagrange multipliers severely reduced the quality of the fit – in most cases simply giving all partial charges as zero – because the procedure used to select the sparse active set of $M$ environments also discarded the basis functions necessary to satisfy this constraint whilst also satisfactorily reproducing the dipole moment.

However, it is usually beneficial to include some sort of restraint on total charge, as a model insensitive to this quantity can predict unreasonably large total charges, ultimately compromising its transferability to other datasets. We therefore include the total charge as extra information to the fit, by appending to $y$ the list of total charges of the molecules in the training set, and appending to the transformed kernel matrix $LK_{PM}$ the extra $N$ rows representing the sums of the model’s partial charges:

$$(L'K_{PM})_{M,j} = \sum_{i \in M} k(X^{(i)}, X^{(j)}) \quad (9)$$

and extending the diagonal regularization matrix $\Lambda$ with an extra $N$ entries $\sigma^2_\beta$ in order to be able to regularize the two target quantities separately.

### B. Partial Dipole Model

An alternative method for predicting the dipole moment of a molecule is to build up the prediction as a sum of atom-centred dipole moment predictions using symmetry-adapted Gaussian process regression (SA-GPR), a modification of standard GPR that allows tensor properties to be learned. A SA-GPR prediction of the dipole moment $\mu$ of a test molecule $A$ is given by:

$$\mu(A) = \sum_{j \in M} \sum_{i \in A} k^V(X^{(i)}, X^{(j)}) w_j, \quad (10)$$

where $k^V(X_i, X_j)$ is an element of an extended kernel matrix, being the tensor (concretely a $3 \times 3$ matrix) whose components $k^V_{\alpha \beta}(X_i, X_j)$ give the coupling between the Cartesian component $\mu^{(i)}_{\alpha}$ associated with environment $X_i$ with the $\mu^{(j)}_{\beta}$ component associated with $X_j$. Each environment $j$ in the active set now requires a set of three weights (represented by the vector $w^{(j)}$) to represent the three independent components of the vector quantity assigned to each atom.

Since the dipole moment is a vector quantity that is related by a linear transformation to the spherical harmonics with $L = 1$, the vector kernel $k^V(X, X')$ can be obtained directly from the $\lambda = 1$-order $\lambda$-SOAP kernel of SA-GPR, $k^{\lambda=1}(X, X')$ by the transformation,

$$k^V(X, X') = M^1 k^{\lambda=1}(X, X') M, \quad (11)$$

where $M$ transforms from the Cartesian basis to the basis of $\lambda = 1$ spherical tensors (see e.g. Ref. 4 for an explicit formula).

As has been shown by recent work, SA-GPR performs very well for response properties of different orders in a wide variety of systems. Further, one can see from the atom-centred formulation of Eq. (10) that the atom-centred dipoles, analogous to the atomic partial charges of Eq. (7), can easily be extracted:

$$\mu(A_i) = \sum_{j \in M} k^V(X^{(i)}, X^{(j)}) w^{(j)}. \quad (12)$$

Although an SA-GPR prediction of the dipole moment does not require charge constraints, it is computationally more expensive than a partial-charge model, requiring the inversion of a square matrix with three times the number of rows ($3M$ rows, where $M$ is the number of basis functions in the active set).

### C. Combined Model

We now consider the partial-charge model and partial-dipole model as two separate models for the same system, encoding two different physical effects. It should then be possible to get a better prediction simply by fitting the sum of the two models to the training data. We call the matrix of Eq. (8) the “transformed scalar kernel”:

$$K^S_{N,M} := LK_{PM}, \quad (13)$$
Table I. Optimal hyperparameters for the pure scalar and pure vector models, found using a Nelder-Mead optimization. Symbols are: $\theta_a$: Gaussian width for SOAP atom smearing, $r_0$ and $m$: radial scaling parameters (see Ref. 50), $\sigma_{\mu}$: dipole regularization, $\sigma_Q$: total charge regularization. All numbers truncated to three significant figures.

| Model          | $\theta_a$/Å | $r_0$/Å | $m$    | $\sigma_{\mu}$/10^{-3} D | $\sigma_Q$/10^{-3} e |
|----------------|---------------|---------|--------|---------------------------|---------------------|
| Scalar (CCSD)  | 0.375         | 2.32    | 4.41   | 11.1                      | 18.8                |
| Scalar (B3LYP)| –             | –       | –      | –                         | –                   |
| Vector (CCSD)  | 0.256         | 2.75    | 3.34   | 3.75                      | –                   |
| Vector (B3LYP)| –             | –       | –      | –                         | 2.94                |

Table II. Convergence parameters for the scalar and vector kernels: $n_{max}$ is the number of radial basis functions and $l_{max}$ is the angular momentum band limit for the SOAP kernel, $N_F$ is the number of selected sparse features, and $M$ is the number of selected sparse environments for each model. Note that the scalar and tensor power spectrum components of the vector SOAP kernel use the same parameters.

| Model          | $n_{max}$ | $l_{max}$ | $N_F$ | $M$  |
|----------------|-----------|-----------|-------|------|
| Scalar         | 8         | 6         | 200   | 2000 |
| Vector         | 4         | 2         | 200   | 2000 |

and the analogous “transformed vector kernel” $K_{NM'}^V$, whose rows are the atom-wise summations of the kernel from Eq. (10):

$$K_{NM'}^V = \sum_{i=1}^{N} k^V(x_i, x_j).$$

(14)

Because the models are of different dimension and model different physical effects, we assign each a different weight vector: $w_S$ for the scalar weights and $w_V$ for the vector weights. Note also that this means we do not need to use the same set of basis functions for the scalar and vector models: they can be chosen independently. Then, in order to find the best combined sum model, we optimize

$$L^2 = \|\delta_2^S K_{NM}^S w^S + \delta_2^V K_{NM'}^V w^V - y\|^2_{\Lambda^{-1}} + \delta_2^S \|w^S\|^2_{K_{MM}^S} + \delta_2^V \|w^V\|^2_{K_{MM'}^V},$$

(15)

with respect to both sets of weights $x^S$ and $x^V$ simultaneously. (The $K_{MM}^S$ and $K_{MM'}^V$ are the matrices of non-transformed kernels of all the basis functions with each other.) The result can be expressed using the inversion of a square matrix whose size is $M \times M'$, where $M'$ is the number of vector weights (three times the number of vector basis functions). Since the number of basis functions is usually kept the same for both scalar and vector models, the matrix to be inverted has $4M$ rows, making the combined model the most expensive of the three models discussed here. In practice, however, the cost is typically manageable.

Furthermore, the charge restraint can be incorporated just as discussed in Section III A, where the transformed scalar kernel is appended with the matrix from Eq. (9) and the transformed vector kernel is appended with the same number of rows of zeros, the vector model contributing nothing to the total molecular charge. Note also that we have introduced weights $\delta_S$ and $\delta_V$ to modify the overall relative amount that the scalar and vector components each contribute to the combined model. The $\delta$-weights effectively allow for different regularizations of the scalar and vector components of the model, which is equivalent to assuming different variances for the dipole components modelled by the scalar and vector models.}

IV. RESULTS AND DISCUSSION

We optimize and train scalar, vector and combined models on the QM7b data set, containing 7211 small organic molecules with up to 7 non-hydrogen atoms (specifically C, N, O, S, and Cl) with varying degrees of H saturation. The dipoles were computed using the methods described in Yang et al., using both density functional theory (DFT) with the B3LYP functional and linear response coupled-clusters theory with single and double excitations (LR-CCSD), hereafter just ‘CCSD’), using in both cases a doubly augmented double zeta (d-aug-cc-pVDZ, hereafter called ‘daDZ’) basis set. We then demonstrate the transferability of this model on the QM9 data set, comparing with state-of-the-art results from Ref. 45, and on a “MuML showcase” data set of larger molecules. Finally, we push the models to their limits by studying polymers based on the amino acid glycine.

A. Model Optimization

We first optimize the models for space and computational requirements by subsampling the SOAP feature matrices (which are multiplied and raised to an integer entry-wise power to obtain the SOAP kernel) using the FPS selection algorithm described in Imbalzamno et al. Descriptors are first subsampled in the feature space dimension, allowing for fewer SOAP components ($N_F$) to be used in calculating the kernel, then in environment space dimension, allowing for fewer representative environments ($M$) to be used in performing the fit. The convergence of the final fitting error with respect to these parameters, as well as other kernel convergence parameters such as the number of radial channels ($n_{max}$) and
the maximum angular momentum number \((l_{\text{max}})\) of the expansion, is shown in the Supplementary Information.

We choose the model’s overall distance-based cutoff at 5 Å, to encompass all atom pairs in the QM7b dataset. The actual radial dependence of the kernels, however, is optimized using the radial-scaling function from Willatt, Musil, and Ceriotti\(^{50}\). Together with the SOAP atom width and the regularization parameters, this leaves us with several continuous hyperparameters whose optimal values are to be found. In a Bayesian approach these would be considered priors; they would ideally be integrated over using a previously-known prior distribution. Here, however, we do not have much prior knowledge about the distribution of these parameters – in contrast to the study of potential energy surfaces, where good values can be guessed quite accurately based on prior experience and physical knowledge\(^{59}\). Instead, we use optimization to find the best values of these parameters for our problem, along with cross-validation (CV) to guard against the problem of overfitting that is otherwise introduced by hyperparameter optimization techniques.

First, the hyperparameters for the scalar and vector models are each independently optimized on a randomized four-fold CV split of 5400 randomly-selected molecules of the QM7b test set\(^{52}\). The results of this optimization can be found in Table I. The combined model is then obtained as follows: Since there are only three free parameters between the overall scalar weight \(\delta_S\), the overall vector weight \(\delta_V\), the dipole regularization \(\sigma_\mu\), and the total charge regularization \(\sigma_Q\), we set the dipole regularization to 1 and scale the rest of the parameters accordingly: \(\delta_S \mapsto \frac{1}{\sigma_\mu^S}\) (since \(\delta_S\) for the pure scalar model is set to 1; \(\sigma_\mu^S\) is the dipole regularization found by optimizing the scalar model alone), \(\sigma_Q \mapsto \frac{\sigma_Q^S}{\sigma_\mu^S}\), and \(\delta_V \mapsto \frac{1}{\sigma_\mu^V}\). Further details of the optimization procedure are discussed in the SI.

**B. Error measures**

We use two different error measures. The “per-atom” RMSE (root-mean-squared error)

\[
\text{RMSE} = \sqrt{\frac{1}{N_{\text{test}}} \sum_{j \in \text{test}} \left\| \frac{\mu_{\text{predicted}}^{(j)} - \mu_{\text{actual}}^{(j)}}{N_j} \right\|^2} , \quad (16)
\]

reports on both the magnitude and the orientation of the predicted dipoles. The residuals are normalized by the number of atoms \(N_j\) in the respective molecule before taking the RMSE. This scaling posits a generally linear trend of the dipole moment norm as a function of the number of atoms. Such a trend would be expected from an additive model where each atom contributes a certain, locally-dependent amount. This is the case with the vector model, but not with the scalar model, where the contribution additionally depends on its distance from the molecular origin, making the scaling depend on the molecular geometry. Therefore, to provide an alternate assessment of the error of the total dipole, and to facilitate comparison with other studies, we additionally plot the MAE (mean absolute error) of the norm of the total dipole moment:

\[
\text{MAE} = \frac{1}{N_{\text{test}}} \sum_{j \in \text{test}} \left\| \frac{\mu_{\text{predicted}}^{(j)}}{\mu_{\text{actual}}^{(j)}} - 1 \right\|^2 . \quad (17)
\]

For the QM7b dataset, the two measures provide similar information, but for transferability testing on other datasets these measures provide complementary information.

**C. Training on QM7b**

Figure 1 shows the learning curves of the models, with the kernel parameters fixed to the values optimized on 5400 points. Errors are computed on a test set of 1811 randomly-selected molecules from the QM7b dataset\(^{52}\).
Note that the pure scalar and pure vector models both achieve similar performance in the limit of a large amount of data, while the combined model clearly outperforms both (by a factor of about 20%) in the same regime.

The figure reports results for models trained on CCSD/daDZ dipoles. Results for B3LYP-trained models are analogous (see SI). For reference, the discrepancy between B3LYP and CCSD dipoles amounts to RMSE = 0.011 D per atom, or MAE = 0.087 D. It should be stressed that, contrary to the case of the polarizability,

\[ \delta \]

DFT performances for dipoles are usually satisfactory. When trained on 5400 QM7b structures the combined model delivers better accuracy (RMSE = 0.0086 D per atom, MAE = 0.054 D), at a dramatically reduced computational cost.

D. Testing on QM9

In order to test the extrapolation capabilities of the model, we have selected 1000 random samples from the QM9 dataset and computed the dipole moments following the same protocol we used for the QM7b dataset. Due to the very high computational cost of evaluating response properties at the CCSD level, for this test we use B3LYP/daDZ calculations as reference, and the corresponding models trained on QM7b at the B3LYP level. The learning curves of these models are shown in Figure 2. The combined model outperforms both the scalar and the vector model in terms of the per-atom RMSE measure, but performs worse than the vector model using the norm MAE. It appears that the scalar model has a tendency to overfit, with both RMSE and MAE degrading as the number of training points approaches the full train set size, which is also carried over to the combined model.

A simple, ad hoc method to address this overfitting problem, and the resulting loss of transferability, is to adjust the mixing weights \(\delta_S\) and \(\delta_V\): the model labelled “adjusted” in the plot is identical to the combined model, except with \(\delta_S\) reduced by a factor of ten. The weights \(w\) are again recomputed for each training set size. This model outperforms both the scalar and vector models using both error measures. This adjustment also serves to highlight the sensitivity of the combined model to the mixing weights, and shows that the optimal combination may not be the same for all datasets. We will comment further on the interplay between the two contributions in Section IVF.

E. Comparison with OQML

It is interesting to compare the performance of our models to that of the operator quantum machine learning (OQML) scheme in Ref. 45. In OQML, a formal dependence on an applied electric field is included in the definition of the (scalar) kernel, by assigning fictitious charges to each atom. This makes it possible to define derivatives of the kernels relative to an applied field that are naturally covariant and serve as a basis to fit molecular dipoles. It should be stressed that, even though the scheme relies on formal atomic charges, it amounts effectively to learning local dipoles, and is therefore similar to our vector model. Whereas in OQML energy and dipole regression models are coupled through a scalar constant, in our case every property can be trained independently.

As can be seen in Figure 2 the vector and the adjusted model outperform the FCHL* OQML model by approximately 20%. This is particularly remarkable, because the model of Ref. 45 was trained on 5000 structures from QM9, while our models are only trained on the smaller QM7b structures, and are therefore function-
ing in a much more challenging extrapolative regime.

F. MuML showcase set

Similar to Ref. 35, we now turn from standard, systematically generated benchmark datasets to a showcase set in which molecules have been selected because of their relevance and/or to test the sensitivity of the model to subtler variations in chemical structure and bonding. To this end, we assembled a MuML showcase dataset, depicted in Fig. 3, that comprises the first 29 molecules of the AlphaML showcase set\textsuperscript{53,60} (including nucleotides, amino acids, sugars, and common drugs). The C\textsubscript{8}H\textsubscript{n} isomers from AlphaML were discarded (because they all have very small dipole moments), and substituted with 31 C\textsubscript{3}H\textsubscript{n}NH\textsubscript{2}COOH amino acid derivatives, with dipole moments spanning a broad range from 0.5 D to 6 D. The new geometries were optimized using the same protocol described in Refs.\textsuperscript{30,35} For reference, the dipole moment norms computed with CCSD/daDZ on the MuML showcase are shown in the top panel of Figure 4b.

The learning curves of the three dipole models on the MuML showcase are shown Figure 4a. All three models achieve an accuracy comparable, in absolute terms, to that on QM9. The (unadjusted) combined model narrowly outperforms both the scalar and vector models. Even in this extrapolative regime, the accuracy of MuML is competitive with that of B3LYP: for the largest train set size, MuML achieves errors (RMSE = 0.029 D per atom, MAE = 0.24 D) that are only 30\% larger (in RMSE, 56\% larger in MAE) than those of B3LYP relative to CCSD (RMSE = 0.019 D per atom, MAE = 0.19 D). Figure 4 shows the breakdown of the errors of the model trained on the largest amount of QM7b data (5400 molecules) across the molecules of the AlphaML showcase. No systematic patterns are apparent, though there are some outliers. The scalar model performs particularly poorly on Molecule 14 (cysteine): one may be tempted to interpret this observation as a consequence of the highly-polarizable nature of sulfur, given that a poor relative performance of the scalar model is also seen in the case of methionine, the only other S-containing molecule in the MuML showcase set. On the other hand, the vector model performs poorly on Molecule 21 (caffeine), 24 (metformin) and 30-33 (isomers of aminopentanedienoic acid). All of these molecules contain conjugated systems, and possess a relatively large dipole moment. The heterogeneous nature of the MuML showcase, and its relatively limited size, however, do not allow for a definitive interpretation of the performance of the models.

In order to provide a more systematic, and far more stringent, test of our models’ extrapolation capabilities, we designed three new “challenge” test sets each consisting of a series of linear molecules with polar groups and large separation of charge, thereby giving rise to large dipole moments. We consider polymers of glycine, in both \(\alpha\)-helix and \(\beta\)-strand configurations, and amino polyenoic acids, with an amino and a carboxylic groups separated by a polyacetylene spacer. Because of the large size of these molecules (up to 122 atoms, of which 69 non-H for the longest \(\alpha\) helical configuration) we used B3LYP/daDZ references and models. Figure 5 contrasts the growth of the dipole with chain length, which is roughly linear, with the predictions of the scalar, vector, and combined model. In the case of polyglycine, the three models capture at least qualitatively the trend, with the vector model usually under-predicting the slope, and the combined model performing substantially better than either the scalar or the vector model. In the case of amino polyenoic acids, however, the vector model breaks down completely, predicting a constant dipole as a function of chain length. The scalar model approaches most closely the correct slope, and the combined model shows the correct trend, but with a smaller slope than the pure scalar model.

In order to gain a deeper insight into the performance of the different models, and the physical effects that determine the breakdown of the vector model, we compute atomic contributions to the dipole moment – both the vector predictions and the partial charges (for the models that use them) for each atom – and represent them together with the molecular structure in Figure 6. We discuss only the \(\beta\)-strands and the amino polyenoic acids here, as the observations for the \(\alpha\)-helical structures are very similar to those for the \(\beta\)-strands. The per-atom breakdown for the \(\alpha\)-helices can be found in the SI. In the case of polyglycine each monomeric unit is polar. Since the total dipole is made up almost entirely of these local monomeric contributions, a model based on local atomic dipoles captures the correct scaling behavior with system size. A scalar model also captures the correct behavior, as each molecular unit is (approximately) neutral and contributes a roughly constant term (even though individual atomic dipoles grow larger for atoms that are farther away from the molecular centre). The case of amino polyenoic acids reveals the shortcomings of a local vector model. The nonpolar spacer is (correctly) predicted to contribute very little to the total dipole, while the amino and carboxylic acid groups bear each a (roughly) constant dipole, which results in a prediction that is independent on the length of the spacer. The scalar model, on the other hand, predicts net positive and negative scalar charges on the amino and carboxylic acid groups, and as a consequence predicts a total dipole that scales linearly with the length of the spacer. Even if it underpredicts the total dipole, the combined model most closely reflects the conventional chemical wisdom: it predicts negligible charges along the polyacetylene spacer with only the polar end groups contributing to the total dipole. Since the end groups carry a net positive and negative charge, the total dipole increases with their separation.

These observations reflect the shortcomings of a local model, similar to what was observed in Ref. 35 for the molecular polarizability of conjugated hydrocarbons. SOAP features are computed with a cutoff of 5 Å, and
Figure 3. List of molecules included in the MuML showcase set. The numerical key is used to identify the various compounds in other figures.

Figure 4. Performance of the models on the MuML showcase set: a) learning curves by per-atom RMSE (top) and MAE (bottom), b) per-molecule breakdown of the model trained on 5400 molecules: Norms of the reference dipole moments computed with CCSD/daDZ on the new MuML showcase set (top) and error of the norms of the dipole moment predictions across the same set (bottom). The molecule ID is in reference to Figure 3.

cannot therefore describe structure-property correlations beyond this limit. The scalar model circumvents this limitation by assuming that atomic charges are local, and that the non-locality of the dipole moment is entirely captured by the spatial separation of the atomic charges. As shown in the SI, the radial scaling functions of the two models, which reflect how quickly the influence of far-away atoms decay, is consistent with the greater non-locality of the vector model. The radial scaling of the scalar models decays rapidly, well before the neighbor list cutoff, while that of the vector model indicates that correlations beyond 5 Å would be needed to describe...
molecular dipoles as a sum of local contributions.

Finally, while the local partial charges and dipoles provided by this analysis bear some similarities to the electron density decomposition schemes discussed in Section II, they should not be confused. The partitioning scheme shown here does not use the electron density; rather, it provides an interpretable description of how the machine-learning model arrives at its prediction of the total dipole, allowing us to verify whether or not it includes the appropriate physics.

V. CONCLUSIONS

We have introduced a set of models for molecular dipoles that we collectively refer to as "MuML". These models rely on a local, atom-centred description of molecular structure that fulfills the symmetries of the target property. We compare a vector model that predicts atom-centred dipolar contributions with a scalar model that predicts atomic charges entering into a physics-based expression for the contribution to the total dipole moment. Training on a set of small organic molecules, both models can achieve a similar accuracy of around 0.1 D, which is comparable to the accuracy of density functional theory, with a slight improvement made possible by combining the two models. The difference between the models is more noticeable – up to 40% RMSE – when considering the transferability to larger molecules. The vector model seems to be more robust while the scalar model appears to overfit, with a model trained on 5000 small molecules giving a worse performance than one trained on only 500. Although the optimal combination of models, determined by cross-validation on the train set, suffers from the poor transferability of the scalar model, a simple adjustment of the relative weight of the two contributions leads to an improvement over the vector model. This adjusted model outperforms a state-of-the-art model based on the FCHL* framework. This result is particularly remarkable given that the FCHL* model is trained on a dataset containing the same type of large molecules being tested, and is therefore operating in the interpolative regime, whilst MuML is applied here in a more challenging extrapolative regime. State-of-the-art performance for MuML is also observed for a showcase set of even larger molecules, where the scalar model shows improved performance relative to the vector model.

We push MuML to its breaking point by performing predictions on a set of polymers of increasing length, that extend far beyond the cutoff radius of the atom-centred features used to describe the molecules. The vector model can predict reasonably well the molecular dipole of polyglycine, for which each monomeric unit contributes a dipolar term. It fails dramatically, however, for the amino polyenoic acid series, where the increase of molecular dipole arises because of charge separation by nonpolar spacer units. The scalar model, on the other hand, recovers this effect correctly because the geometric separation between atoms is built into the form of the kernel, introducing an element of non-locality.

The combination of the two models makes it possible to improve the performance of MuML, even though the optimal combination weights depend rather strongly on the nature of the test molecules. This suggests that, even when taken together, local vector and scalar models of the dipole only partially capture the physics of polarization, affecting the overall model's transferability. An explicit treatment of long-range effects using a charge equilibration scheme, or incorporating long-range co-
Figure 6. A representation of the per-atom contributions to the total dipole for two of the challenge systems: polyglycine in the $\beta$-strand conformation (top), amino polyenoic acids, in the all-trans conformation (bottom). Vector per-atom dipoles are defined in Eq. (12), and plotted exaggerated by a factor of 5 for visibility; atoms are colored according to the atom type. Scalar per-atom dipoles are defined as the partial charges multiplied with the displacement vectors (referenced to the molecule’s centre of geometry), as in Eq. (6); atomic charges are also represented as the atom colors, according to the displayed color scale. Per-atom dipoles for the combined model are the (appropriately weighted) sums of the respective scalar and vector per-atom dipole predictions. The total dipoles, in each case equal to the sum of the per-atom predictions, are shown below each molecule along with (in black) the reference dipole moment computed from B3LYP/daDZ. The per-atom arrows for the vector model are exaggerated by a factor of 5 for visibility. The scale bar shows the maximum range of sensitivity (5 Å) of the partial charges and atomic dipoles to their environments. Visualizations created with Ovito.\textsuperscript{61}
relations by long-distance equivariant features might improve even further the accuracy of MuML, which is already competitive with that of hybrid DFT calculations while being dramatically less computationally expensive.

Another direction for further research involves the modelling of condensed phases. The presence of periodic boundary conditions makes the position operator ill-defined. As a consequence, an expression like Eq. (2) cannot be used to define the polarization in the condensed phase, which makes the scalar and, by extension, the combined models inapplicable. One way around this limitation is to instead model the position of Wannier function centers, so that each point in the unit cell is an integer multiple of the electron charge, thereby preserving the lattice condition for polarization in a periodic medium (see e.g. Spaldin or Resta). Current implementations of the idea, however, predict the position of centers attached to an atom, so that the framework is effectively equivalent to learning atom-centred dipoles. Indeed, a vector model can be readily applied to bulk systems, and has already been used successfully to predict the infrared spectrum of liquid water. It is not obvious, however, that this methodology will work well in systems where there is significant delocalization of charge. Incorporating ideas from the modern theory of polarization, learning the Born effective charge tensors, or taking a more decidedly data-driven approach by using long-range features without explicitly incorporating a physical description of electrostatics all provide possible strategies to apply to condensed phases a model that can capture, like MuML, the different phenomena that give rise to permanent of transient polarization.

SUPPORTING INFORMATION

The supplementary material contains further details about the derivation, implementation and benchmarks of the method, including: • Convergence of the scalar and vector models on QM7b • Kernel optimization procedure • Radial scaling function for scalar and vector models • QM7b Learning curves for B3LYP dipoles • Comparison of B3LYP, CCSD, and SCAN0 dipole moment predictions on the MuML showcase • Per-atom breakdown of the alpha-helix predictions

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## Supplementary Information

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The scalar and vector kernels both depend on several discrete parameters that affect their predictive performance. These are the radial ($n_{\text{max}}$) and angular ($l_{\text{max}}$) band limits of the spherical expansion; the number of sparse feature components ($N_F$) selected, and the number of sparse environments ($M$) selected for the fit. Of these, $n_{\text{max}}$, $l_{\text{max}}$, $N_F$, and $M$ are varied to observe their effect on the kernel performance.

Figure 1. Convergence of the scalar and vector kernels as four parameters are varied. The error for the scalar kernels is computed over a six-fold cross-validation partitioning randomly selected from the 5400 QM7b training molecules used in the main paper; the vector kernel error is computed over a four-fold CV partitioning taken from the same set. Each plot shows the dependence of the CV-error as the labelled parameter is varied around the final, chosen values (indicated by orange dots). The error bars show the standard deviation of the cross-validation error. All other kernel parameters were set to the final optimized values.
and $N_F$ affect the speed of kernel building, and hence prediction. $M$, on the other hand, is the size of the matrix to be inverted; therefore, the time of the fitting (weight-computing) step depends cubically on $M$. The prediction also depends on $M$, but only linearly.

Figure 1 shows the dependence of the fitting error on these four parameters for both the scalar and vector kernels. (For the vector kernel, the $\lambda = 0$ power spectrum is constrained to use the same parameters as the $\lambda = 1$ power spectrum, to limit the size of the optimization space.) Both $n_{\text{max}}$ and especially $l_{\text{max}}$ are too noisy to show any clear dependence, so sensible standard values were chosen (marked in orange in the plots) – the vector kernel values being lower due to the increased computational cost of computing this kernel. The $N_F$ dependence is pronounced only for the scalar kernel, so the value of 200 was chosen to give reasonable performance for both kernels. Finally, the number of sparse environments $M$ is the only parameter to have a real, pronounced effect on the final CV-error; the value of 2000 was chosen for both as a good compromise between lowering the final error and keeping the computational cost within bounds.

II. KERNEL OPTIMIZATION

The remaining, continuous parameters are optimized, again on the 5400 training molecules of QM7b but this time with four-fold CV for both scalar and vector kernels. The optimization consists of two layers: an outer Nelder-Mead (simplex) optimization of the atom width ($\theta_w$) and the radial scaling parameters $r_0$ and $m$, initialized with the simplex in Table I, coupled with an inner optimization of the regularization parameters (which have a much simpler dependence for the final error). For the vector kernels, where only one regularization parameter is used, the inner optimization uses Brent’s algorithm for one-dimensional optimization problems (the default in SciPy 1.4.1). For the scalar kernels there are two regularization parameters, which are optimized again using the Nelder-Mead method. Both regularizer optimizations are performed in log-space to follow the typical logarithmic dependence of the results on the regularizers. All Nelder-Mead optimizations are terminated once the absolute value of change of the parameter vector is less than 0.01.

| Point | $\theta_w$ | $r_0$ | $m$  |
|-------|-----------|-------|------|
| 0     | 0.3       | 3.0   | 5.0  |
| 1     | 0.3       | 4.0   | 5.0  |
| 2     | 0.3       | 2.0   | 3.0  |
| 3     | 0.5       | 3.0   | 6.0  |

Table I. Initial simplex for the parameters of the outer kernel optimization

A. Radial scaling

The radial scaling function resulting from the optimized kernel parameters (shown in Table I of the main paper) are plotted in Figure 2.
Figure 2. The radial scaling functions found through separate optimizations of the scalar and vector kernels. The final cutoff at 5 Å is sharp.
III. OTHER FIGURES

Figure 3. Learning curves on QM7b, analogous to Figure 1 of the main paper but using B3LYP/daDZ$^2$–4 dipole data instead. Note the results are very similar, with the B3LYP fits being slightly less accurate.
Figure 4. Comparison of the norms of the dipole moments computed on the MuML showcase set by three different methods: B3LYP, SCAN0, and CCSD. Note the norms are largely consistent, with the exception of the conjugated amino acids (Molecules 30-33) where the DFT norms are up to 17% larger than the CCSD ones.

Figure 5. Per-atom breakdown of the MuML predictions on the α-helix challenge series. The results are broadly similar to the β-strands, but with much larger dipoles (in part due to the much larger molecular size). Reference dipoles computed with B3LYP/daDZ.
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