CASE21: Uniting Non-Empirical and Semi-Empirical Density Functional Approximation Strategies using Constraint-Based Regularization

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In this work, we present a general framework that unites the two primary strategies for constructing density functional approximations (DFAs): non-empirical (NE) constraint satisfaction and semi-empirical (SE) data-driven optimization. The proposed method employs B-splines—bell-shaped spline functions with compact support—to construct each inhomogeneity correction factor (ICF). This choice offers several distinct advantages over a polynomial basis by enabling explicit enforcement of linear and non-linear constraints as well as ICF smoothness using Tikhonov regularization and penalized B-splines (P-splines). As proof of concept, we use this approach to construct CASE21—a Constrained And Smoothed semi-Empirical hybrid generalized gradient approximation that completely satisfies all but one constraint (and partially satisfies the remaining one) met by the PBE0 NE-DFA and exhibits enhanced performance across a diverse set of chemical properties. As such, we argue that the paradigm presented herein maintains the physical rigor and transferability of NE-DFAs while leveraging high-quality quantum-mechanical data to improve performance.

Kohn-Sham density functional theory (KS-DFT) is the de facto standard for electronic structure calculations in chemistry, physics, and materials science due to its favorable trade-off between accuracy and computational cost.[1] While there now exist hundreds of density functional approximations (DFAs) of varying complexity across all rungs of Perdew’s popular Jacob’s ladder,[2] most have been designed using either non-empirical (NE) or semi-empirical (SE) strategies.[3] NE strategies seek to construct DFAs by proposing simple ansätze designed to satisfy well-defined physical constraints (e.g., the uniform electron gas (UEG) limit), second-order gradient responses,[4,5] or exchange-correlation (xc) energy is sometimes ignored as it often results in inaccurate DFAs for real systems.[6] On the other hand, striving for the best-performing functional using only an SE-DFA strategy often goes hand-in-hand with sacrificing exact physical constraints.[7–9] Furthermore, some SE-DFAs suffer from non-physical “bumps” or “wiggles” in the inhomogeneity correction factor (ICF), which violate an implicit smoothness constraint and can require significantly larger quadrature grids for accurate integration.[10–12] Consequently, there is no guarantee that the target constraint is satisfied during the data-driven optimization process has remained difficult to date. To address the smoothness problem in SE-DFAs, the BEEF[13] and Minnesota[14] functionals have adopted an explicit smoothness penalty in the regression procedure with reasonable success; the resulting ICFs are significantly smoother than previous generations, albeit not always completely devoid of spurious features. Furthermore, the recent MCML approach[15] has made efforts to combine NE-DFA and SE-DFA strategies by algebraically enforcing three linear constraints during the SE-DFA optimization process (an approach originally used in the M05 family[16]). While successful in enforcing the targeted constraints, the polynomial basis used in MCML (and the vast majority of SE-DFAs to date) prevents explicit enforcement of non-linear constraints (such as inequalities), and makes satisfying new constraints non-trivial as each regression coefficient appears in every algebraic constraint.

In this work, we present a general framework that unites NE-DFA and SE-DFA strategies by enabling straightforward enforcement of both physical constraints and ICF smoothness while leveraging high-quality quantum-mechanical data. The proposed DFA strategy uses B-splines, compact bell-shaped piece-wise functions,[17] to construct the ICF, which allows for a tunable trade-off between ICF smoothness and flexibility using penalized B-spline (P-spline) regularization,[18] while still allowing for explicit enforcement of both linear and non-linear constraints via generalized Tikhonov

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regularization. As proof of concept, we use this framework to construct a hybrid generalized gradient approximation (GGA): CASE21—Constrained And Smoothened semi-Empirical 2021, which completely satisfies all but one constraint (and partially satisfies the remaining one) met by the PBE0 NE-DFA. When compared to PBE0 (and the popular B3LYP SE-DFA), CASE21 attains higher accuracy across a diverse set of chemical properties without sacrificing transferability or requiring large numerical quadrature grids. As such, we argue that the CASE paradigm presented herein maintains the physical rigor and transferability of NE-DFAs while leveraging high-quality quantum-mechanical data to remove the arbitrariness of ansatz selection.

Functional Form. We write CASE21 as the sum of exchange and correlation contributions,

\[ E_{xc}^{\text{CASE21}} = \frac{3}{4} E_x[\rho_t, \rho_u] + \frac{1}{4} E_{xx} + E_c[\rho, \zeta], \]

(1)

where the exchange contribution uses 25% exact exchange \((E_{xx})\), as generally recommended for global hybrid GGA\(^2\). The semi-local exchange is defined using the exchange spin scaling relationship\(^3\)

\[ E_x[\rho_t, \rho_u] = \frac{1}{2} (E_x[2\rho_t] + E_x[2\rho_u]), \]

(2)

in which

\[ E_x[\rho] = \int \rho \frac{\xi^{\text{LDA}}(\rho)}{\xi^{\text{LDA}}(\rho)} F_x(u_{x,\sigma}) \, dr, \]

(3)

\(\rho_\sigma\) is the spin density (with spin \(\sigma \in \{\uparrow, \downarrow\}\)), \(\xi^{\text{LDA}}(\rho)\) is the exchange energy density per particle within the local density approximation (LDA), and \(F_x(u_{x,\sigma})\) is the yet to be determined CASE21 exchange ICF. We employ \(0 \leq u_{x,\sigma} = (\gamma_x s^4_x)/(1 + \gamma_x s^4_x) < 1\) (as originally proposed by Becke\(^4\)) as the finite-domain parameterization of the PBE dimensionless spin density gradient, \(s_x = |\nabla \rho_\sigma|/\sqrt{2/3(2\rho_\sigma)^{4/3}}\). Here, we note that the PBE exchange ICF can be written as a linear function of \(u_{x,\sigma}\) if \(\gamma_x = \mu/\kappa \approx 0.273022\) (where \(\mu\) and \(\kappa\) are the NE parameters in PBE), which we denote by \(F_x(u_{x,\sigma}) = 1 + \kappa u_{x,\sigma}\). Hence, we argue that this is an appropriate choice for \(\gamma_x\) since the UEG exchange limit\(^5\) and the Lieb-Oxford bound\(^6\) and the PBE limit\(^7\) and second-order gradient expansion for correlation\(^8\)\(^9\) Namely, we propose \(0 \leq u_c = (\phi^2)/(\phi^2 + \gamma_c \zeta^{\text{LDA}}(\rho)) < 1\), where \(\phi = \frac{1}{2} [(1 + \zeta)^{2/3} + (1 - \zeta)^{2/3}]\) is a spin scaling factor\(^10\), \(\gamma_c = 1/\beta \approx 14.986886\) (where \(\beta\) is another parameter in PBE), and \(t\) is a dimensionless spin-separated density gradient,

\[ t \equiv \sqrt{\alpha_0} \left( \frac{\pi}{3} \right)^{1/6} \frac{|\nabla \rho_\uparrow| + |\nabla \rho_\downarrow|}{4\rho^{1/6}\phi}, \]

(5)

which reduces to the PBE dimensionless density gradient \((t_{\text{PBE}})\), which has \(|\nabla \rho|\) instead of \(|\nabla \rho_\uparrow| + |\nabla \rho_\downarrow|\) in the numerator) when \(|\nabla \zeta| = 0\) (which was assumed during the construction of PBE correlation, and is a relationship that allows DFAs based on \(t\) to satisfy PBE correlation constraints). We note in passing that the use of \(t_{\text{PBE}}\) yields qualitatively similar results to \(t\) (which might be expected, given that \(t\) and \(t_{\text{PBE}}\) are equivalent for closed-shell systems), although \(t\) slightly outperforms \(t_{\text{PBE}}\) quantitatively. Importantly, \(u_c\) increases monotonically with \(t\), suggesting a one-to-one mapping between \(t\) and \(u_c\) for a given \(\epsilon^{\text{LDA}}\); hence, \(u_c\) is an appropriate finite-domain transformation of \(t\). While Eq. 6 with this definition of \(u_c\) does not fully satisfy uniform scaling to the high-density limit for correlation\(^11\); it does completely cancel the \(\epsilon^{\text{LDA}}\) logarithmic singularity\(^12\) and allows for satisfaction of all other PBE correlation constraints. However, such partial satisfaction of this constraint is not a restriction of the presented method—in principle, an (albeit more complex) functional form that completely satisfies all PBE correlation constraints could have also been used.

We write the CASE21 exchange and correlation ICFs as linear combinations of \(N_{sp}\) compact piece-wise bilinear cubic \((k = 3)\) uniform B-spline basis functions \((\{B_i\})\)

\[ F_x(u_{x,\sigma}) = \sum_{i} \phi_{x,i} B_i(u_{x,\sigma}) = \phi_x \cdot B_{x,\sigma} \]

(6)

\[ F_c(u_c) = \sum_{i} \phi_{c,i} B_i(u_c) = \phi_c \cdot B_c, \]

which is equivalent to constructing each ICF using a cubic spline\(^13\) (see Supporting Information SI for more details). With the choice of knot vector employed herein\(^14\) the \(B_i(u_{x,\sigma})\) and \(B_i(u_c)\) are uniformly spaced with all points in \(0 \leq u_{x,\sigma} \leq 1\) and \(0 \leq u_c \leq 1\) supported by three non-zero B-splines. As depicted in Fig. 1(a), setting \(\phi_x = 1 = \phi_c\) in Eq. 6 results in \(F_x(u_{x,\sigma}) = 1 = F_c(u_c)\); in this limit, CASE21 exchange and correlation reduce to LSDA exchange and LDA correlation, respectively.

Having defined the CASE21 functional form, we now discuss a general framework that unites NE-DFA and SE-DFA strategies. Namely, we determine \(\phi = (\epsilon_x, \epsilon_c)\) using generalized Tikhonov regularization\(^15\), i.e., by minimiz-
FIG. 1. (Top) B-spline basis functions \( \{B_i\}_{i=1,19} \), rainbow) used to represent the exchange and correlation ICFs in this work. When all expansion coefficients are set to unity, the resulting B-spline curve \( F(u) = \sum c_i B_i(u) \), black) is uniform in \( 0 \leq u \leq 1 \) and recovers the LSDA/LDA limit. (Bottom) B-spline curve with non-uniform coefficients. Note again how the coefficients closely align with the curve for \( 0 \leq u \leq 1 \).

Linear combinations of \( \xi \), with \( \xi \) obtained after applying Eqs. (1) to \( \xi_{\nu} \) in Eq. (8), allows us to write:

\[
\Delta E_{xc} = \sum_j \nu_j (c \cdot \xi_j) = c \cdot \sum_j \nu_j \xi_j \equiv c \cdot x, \tag{9}
\]

in which \( \nu_j \) is the stoichiometric coefficient for the \( j \)-th component in \( \Delta E_{xc} \) (i.e., the energy of a molecule or atom) and \( x \) is a single row of \( X \). \( y \) is the corresponding vector of reference energy differences \( \Delta E_{xc}^{\text{ref}} \), and our choice for \( W \) (a square diagonal matrix of weights \( w_i \equiv 1/\Delta E_{xc}^{\text{ref}} \)) is motivated by the fact that the \( c \)-minimizing the goodness of fit term only (i.e., weighted least squares) is the best linear unbiased estimator (under some common assumptions) if the \( w_i \) are inversely proportional to the variance in each measurement \({}\text{ref}\). Since \( E_{xc} \) is the only inexact term in KS-DFT, both bias- and variance-type DFA errors should scale linearly with \( E_{xc} \), making this a natural choice for \( W \).

Here, we argue that the piece-wise nature of a B-spline curve offers more flexibility than the low-order polynomial expansions often used to represent SE-DFA ICFs (e.g., the B97 family), with the ability to conform to more subtle shapes, a B-spline ICF should be able to better leverage the reference data.

Regularization/Smoothness. For the second term in \( L \), we note that B-splines can be regularized by explicitly penalizing deviations from smoothness (i.e., ICF “wiggles”) using P-splines, a regularization technique suggested by Eilers and Marx \cite{10.1016/0167-8406(96)80039-4} based on the observation that B-spline coefficients closely resemble the B-spline curve (see Fig. 1(b)). As such, smoothness can be explicitly enforced via a finite-difference penalty on \( c \); in this work, we interpret non-smoothness as non-linearity in the ICF, and construct \( A \) from the second-derivative finite-difference matrix (see SI). \( \lambda \) is a hyperparameter that governs the relative importance of the regularization/smoothness and goodness of fit contributions to \( L \), and interpolates (assuming \( \eta \gg 1 \), vide infra) between linear ICFs (i.e., \( F_{\nu}(u) \) and \( F_{\nu}(u) \)) that are completely constraint-driven (as \( \lambda \rightarrow \infty \)) and wiggly ICFs that are data-driven to the maximal amount possible in this framework (as \( \lambda \rightarrow 0 \)). As such, any non-linearity in the final optimized CASE21 ICFs can be attributed to the data. Here, we note that alternative interpretations of smoothness would result in penalizing other derivatives (e.g., \( F''(u) \)). Separately penalizing the exchange and correlation ICFs (i.e., using two \( \lambda \)-hyperparameters) is also possible if the regularization/smoothness contributions to \( L \) from \( F_{\nu}(u) \) and \( F_{\nu}(u) \) strongly differ. In this work, we found that P-spline regularization (which is uniquely enabled by the choice of a B-spline basis) yields ICFs devoid of any spurious “wiggles” via single-\( \lambda \) penalization of \( F''(u) \) (vide infra). In contrast, an excessively large penalty (which results in decreased performance) is usually required to remove all non-physical “bumps” or “wiggles” in polynomial ICFs regularized via Tikhonov (or ridge) regression \cite{10.1021/acs.jcim.5b00849}. Furthermore, although such polynomial-based smoothness penalties are somewhat effective in reducing DFA
grid dependence, these approaches have been largely ineffective when enforced alongside constraints. On the other hand, we find no issues when simultaneously enforcing ICF smoothness as well as numerous linear and non-linear constraints.

**Constraint Satisfaction.** During CASE21 construction, we fully enforce the following 10 constraints: exchange spin scaling \( \delta \), uniform density scaling for exchange \( \delta \), UEG exchange limit \( \delta \), UEG linear response \( \delta \), Lieb-Oxford bound \( \delta \), exchange energy negativity, UEG correlation limit \( \delta \), second-order gradient expansion for correlation \( \delta \) rapidly varying density limit for correlation \( \delta \) and correlation energy non-positivity \( \delta \). We also partially enforce uniform scaling to the high-density limit for correlation \( \delta \) (vide supra). In the constraint satisfaction term in \( \mathcal{L} \), the \( \{ Q_i \} \) are chosen to measure constraint-specific deviations of \( c \) from \( c_0 \), the coefficients corresponding to \( \bar{F}_c(\psi_{i,\sigma}) \) and \( \bar{F}_c(\psi_{i}) \). Each \( Q_i \) corresponds to a constraint on \( F(u) \) or \( F' (u) \), and is constructed such that any constraint-satisfying \( c \) yields \( \| c - c_0 \|_Q = 0 \) (see SI for details on \( Q_i \) construction). \( \eta \) is a hyperparameter that governs the relative importance of the constraint satisfaction contribution to \( \mathcal{L} \), and was chosen to be large enough (\( \eta = 10^8 \)) for strict constraint satisfaction, but small enough to avoid conditioning issues. Since each B-spline has compact support, each \( Q_i \) only enforces the constraint on a small subset of \( c \) (e.g., the \( c \) corresponding to non-zero B-splines at the \( u = 0 \) limit); in contrast, each constraint would generally involve every parameter in a polynomial-based ICF (e.g., MCMI). Another important consequence of this local support is that the B-spline curve will lie within the range of \( c \) (cf. Fig. 1b)). Hence, inequality constraints can be enforced via an iterative update to the corresponding \( Q_i \) using the shape constraint algorithm (SCA) of Bollaerts et al. which fixes all inequality-violating \( c_i \) to the constraint boundary. In contrast, there is no straightforward way to explicitly apply inequality constraints on a polynomial-based ICF as each basis function is unique and has global support. This highlights another benefit provided by a B-spline basis in the construction of smooth and constraint-satisfying SE-DFAs.

**Training Procedure.** Our self-consistent training procedure (Scheme 1) leverages three distinct data sets (see SI): training \( (X_{\text{train}}, y_{\text{train}}) \), validation \( (X_{\text{val}}, y_{\text{val}}) \), and testing \( (X_{\text{test}}, y_{\text{test}}) \). In a given iteration, the training set (a single database of heavy atom transfer reaction energies, HAT70\footnote{Preliminary fits using \( \{ \psi_i \} \) suggested that the effective degrees of freedom (DoF) (see SI for derivation) change slowly starting around \( N_{\text{sp}} = 10 \), and the performance of the corresponding (non-self-consistently optimized) DFA was representative of those with \( N_{\text{sp}} > 10 \). Hence, we used \( N_{\text{sp}} = 10 \) in Scheme 1 to generate the self-consistently optimized CASE21 DFA (six iterations; convergence criterion: \( | \Delta c | < 10^{-5} \); see SI for \( c^* \)). Even with a finite \( \eta \), CASE21 nearly exactly satisfies all enforced constraints, i.e., \( F_c(0), F_c'(0), F_c''(0), \) and \( F_c'''(0) \) differ from their corresponding exact values by \( \sim 10^{-5} \), \( F_c(1) \) differs by \( \sim 10^{-6} \), and all other constraints are exactly satisfied. We therefore conclude that the proposed CASE framework (i.e., Tikhonov regularization in conjunction with P-splines) successfully enforced all constraints without sacrificing smoothness, which still remains a challenge for other DFA training procedures). To confirm that CASE21 remains representative of DFAs trained with other \( N_{\text{sp}} \) values, we (non-self-consistently) optimized \( c \) for select \( N_{\text{sp}} \in [6, 40] \) using the CASE21 \( \{ \psi_i \} \). As depicted in Fig. 2, the resulting ICFs and their first derivatives were all smooth and very similar (particularly for \( N_{\text{sp}} \geq 10 \)), thereby providing an a posteriori justification for our choice of \( N_{\text{sp}} = 10 \) for CASE21.

### SCHEME 1. Self-consistent DFA training procedure.

1. **Generate Initial Orbitals**
   
   \[
   X_{\text{train}}, y_{\text{train}}, \{ Q_i \} \rightarrow \{ \psi_i \} \rightarrow \{ \psi_i \} \rightarrow \mathcal{L}(c; \{ \lambda \}) \rightarrow \text{Optimize} \ w\text{RMSE}(\lambda) \text{ Eq. (10)}
   \]

2. **Generate New Orbitals**
   
   \[
   c^* \rightarrow \{ \psi_i \} \rightarrow \mathcal{L}(c; \{ \lambda^* \}) \rightarrow \text{Optimize} \ w\text{RMSE}(\lambda) \text{ Eq. (10)}
   \]

3. **Final Testing**
   
   \[
   \text{X}_{\text{test}}, y_{\text{test}} \rightarrow \text{Minimize} \mathcal{L}(c; \{ \lambda^* \}) \text{ Eq. (7)} \rightarrow \text{Minimize} \mathcal{L}(c; \{ \lambda^* \}) \text{ Eq. (7)} \rightarrow \lambda^* = \arg \min_{\lambda} w\text{RMSE}(\lambda)
   \]

\( \dagger \) Subject to inequality constraints enforced by the SCA.
Effective degrees of freedom (DoF) for select properties, with improvements as large as \(0.81\) kcal/mol and \(0.82\) kcal/mol for bond dissociation energies and electron affinities, respectively. In the testing set, CASE21 improves upon PBE0 in 7/8 properties by an average of 0.38 kcal/mol. On the other hand, PBE0 only outperforms CASE21 for ionization potentials. CASE21 also outperforms B3LYP (a popular SE-DFA for chemical applications) on 8/11 properties; in the testing set, CASE21 improves upon B3LYP in 6/8 properties by an average of 0.41 kcal/mol (while B3LYP only offers a marginal \(-0.07\) kcal/mol improvement on the remaining 2/8). We therefore conclude that CASE21 preserves the physical rigor and transferability of the PBE0 NE-DFA while still outperforming the B3LYP SE-DFA. Although the CASE21 ICFs are clearly smooth (cf. Fig. 2), we also investigated the grid dependence of this DFA for completeness. Since Lebedev-Treutler grids with 50 radial and 194 angular grid points (i.e., \((50, 194)\)) are typically large enough to obtain accurate energetics with standard hybrid GGAs (such as PBE0) \([20]\) we compared the performance of CASE21 using this grid to the larger grids employed during the training procedure (see Computational Methods). Using all points in the training, validation, and testing data sets \((N = 2,263)\), we find nearly identical mean absolute deviations of \(1.84 \times 10^{-2}\) kcal/mol for CASE21 and \(1.83 \times 10^{-2}\) kcal/mol for PBE0, thereby indicating that CASE21 does not require larger quadrature grids than PBE0 for accurate integration.

In this work, we presented the CASE (Constrained And Smoothed semi-Empirical) framework for uniting NE-DFA and SE-DFA construction paradigms. By employing a B-spline representation for the ICFs, this approach has several distinct advantages over the historical choice of a polynomial basis, namely, explicit enforcement of linear and non-linear constraints (using Tikhonov regularization) as well as explicit penalization of non-physical ICF “bumps” or “wiggles” (using P-splines). As proof of concept, we used this approach to construct CASE21, a hybrid GGA that completely satisfies all but one constraint (and partially satisfies the remaining one) met by the PBE0 NE-DFA. Despite being trained on only a handful of properties, CASE21 outperforms PBE0 and B3LYP (arguably the most popular SE-DFA for chemical applications) across a diverse set of chemical properties. As such, we argue that the CASE framework can be used to design next-generation DFAs that maintain the physical rigor and transferability of NE-DFAs while leveraging
benchmark quantum-mechanical data to remove the arbitrariness of ansatz selection and improve performance. Future work will extend this approach to more sophisticated DFAs (e.g., meta-GGAs, range-separated hybrids) as well as explore the use of B-splines in constructing robust features for machine-learning chemical properties.

COMPUTATIONAL METHODS

All electronic structure calculations were performed using in-house versions of Psi4 (v1.3.2) and LibXC (v4.3.4) modified with a self-consistent implementation of the CASE21 DFA (including functional derivatives analytically computed using Mathematica v12.1). All self-consistent field (SCF) calculations were performed using density fitting (DF) in conjunction with the def2-QZVPP-JKFIT basis sets and an energy convergence threshold of $e_{\text{convergence}} = 1e-12$. During DFA training, all calculations employed (99,990) Lebedev-Treutler grids except for the calculations of the absolute energies in AE18 which used (500,974). Minimization of $L$ in Eq. (7) and optimization of wRMSE($\lambda$) in Eq. (10) were performed in Mathematica v12.1.

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SUPPORTING INFORMATION AVAILABLE:

Supporting Information (SI) includes:

- B-spline definitions: Enforcement of ICF constraints; Training, validation, and testing data sets; Derivation of optimal coefficients and effective degrees of freedom for weighted generalized Tikhonov regularization; Optimized CASE21 ICF coefficients.

TOC GRAPHIC

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