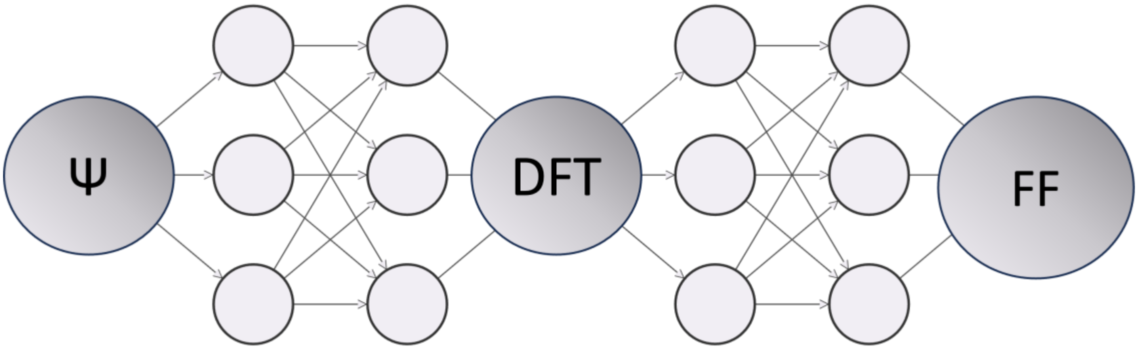
Density Functional Theory and Artificial Intelligence learning from each other



March 3, 2025 - March 6, 2025
CECAM-HQ-EPFL, Lausanne, Switzerland

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1. Description

The rapid progress of Artificial Intelligence (AI) is transforming nearly every facet of scientific research, with Quantum chemistry and electronic structure theory not being exceptions. Density Functional Theory (DFT) [1–5], the workhorse of these disciplines, is also undergoing substantial evolution under the influence of AI, leading to significant impacts on molecular and material simulations at various scales [6–13].

Specifically, AI's involvement in DFT serves two main purposes: Firstly, it is used to improve [1–9] and accelerate [2,10–13] DFT approximations, thereby striving to resolve or at least alleviate [14] the problems associated with functionals designed by humans. Secondly, AI is being employed to create surrogate models that reproduce DFT results [15–22,22–24]. In between these two strategies, there are also "Δ-machine learning" approaches, where (machine learning) ML is used to refine properties derived from DFT and bring them close to wavefunction accuracy [25–27]. Such models facilitate simulations on larger lengths and time scales [18,22]. The fusion of DFT and AI is also revolutionizing chemical research by accelerating high-throughput screenings by several orders of magnitude [20,28,29].

In this workshop, we will concentrate on the latest advancements at the intersection of AI and DFT, with a specific emphasis on two main areas: AI-powered improvements of DFT and the development of AI surrogate models aimed at reproducing DFT results. Our goal is to foster knowledge exchange between experts working on these interrelated areas and attempt to answer and better understand the implications of the following open challenges in the two fields:

1. When and how will AI-learned functionals attain the broad applicability that their human-designed counterparts already have?

2. Can the strong correlation problem in DFT [30–34] be mitigated or even solved by AI?

3. How is the lack of variety and reliability of benchmark data for extended systems, and for transition metal molecules [35–37], hampering the evolution of AI-based DFT methods? What solutions can be applied to rectify this?

4. Can AI enable further progress in handling dispersion interactions, beyond the standard heuristic corrections such as those introduced by Grimme [38,39]?

5. What strategies can be used to further advance ML-based DFT approximations beyond their current state-of-the-art? For example, what is next after DM21 [8]?

6. Can the use of novel DFT features advance ML-DFT [32,33]?

7. What are the key challenges in creating Machine Learning models for real-world applications (e.g., catalysts discoveries) that are based on the DFT data [28,40,41]? For this question, we aim to aim to distinguish and address the challenges that arise from DFT itself, and those that are related to the ML models. Moreover, we aim to distinguish and address the challenges that arise from DFT itself, and those that are related to the ML models.

8. In what way can ML models be informed by the "zoo" of DFT functionals rather than inheriting the bias of a single one?

Key References

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2. Program

Day 1 - Monday March 3rd 2025

Afternoon Session - moderator: Markus Meuwly

- 13:00 to 14:00 - Registration
- 14:00 to 14:15 - Welcome & Introduction
- 14:15 to 14:20 - Chair Session Introduction
- 14:20 to 14:55 - **Alexandre Tkatchenko**
  ML is an excellent student, but DFT can be a lousy teacher
- 14:55 to 15:10 - **Elias Polak**
  Real-space machine learning of correlation density functionals
- 15:10 to 15:50 - Coffee break
- 15:50 to 16:25 - **Fred Hamprecht**
  ML-powered orbital-free DFT
- 16:25 to 17:10 - Discussion Session 1
- 17:10 to 19:00 - Poster session & aperitif

Day 2 - Tuesday March 4th 2025

Morning session - moderator: Tim Gould

- 09:00 to 09:05 - Chair Session Introduction
- 09:05 to 09:40 - **Kieron Burke**
  Machine learning and finding XC functionals
- 09:40 to 09:55 - **Matteo Gori**
  Noncovalent interactions in density functional theory: all the charge density we do not see
- 09:55 to 10:35 - Coffee break
- 10:35 to 11:10 - **Michele Pavanello**
  Learning electronic structures via 1- and 2-RDMs
- 11:10 to 11:55 - Discussion Session 2
- 11:55 to 13:00 - Lunch

Afternoon Session 1 - moderator: Michael Herbst

- 13:00 to 13:05 - Chair Session Introduction
- 13:05 to 13:40 - **Tim Gould**
  Embedding physical and chemical variety through data
- 13:40 to 14:10 - Coffee break
- 14:10 to 14:45 - **Peter Nagy**
  Synergies of DFT, ML and accelerated wave function models for complex chemical processes
- 14:45 to 15:30 - Discussion Session 3
- 15:30 to 16:00 - Coffee break

Afternoon Session 2 - moderator: Heather Kulik

- 16:00 to 16:05 - Chair Session Introduction
- 16:05 to 16:40 - **Michele Ceriotti**
  Physically uninspired models for atomistic machine learning
- 16:40 to 16:55 - **Danish Khan**
  Adaptive hybrid density functionals
- 16:55 to 17:30 - Discussion Session 4

Day 3 - Wednesday March 5th 2025

Morning Session - moderator: Stefan Vuckovic

- 09:00 to 09:05 - Chair Session Introduction
- 09:05 to 09:40 - **Matthias Ernzerhof**
  Using machine learning for the physics-guided construction of exchange-correlation functionals
- 09:40 to 09:55 - **Artur Wodynski**
  Position dependence of exact-exchange admixture as a central object in density functional development: escaping the zero-sum game and machine learning approaches
- 09:55 to 10:35 - Coffee break
- 10:35 to 11:10 - **Marivi Fernandez-Serra**
  Optimization of exchange and correlation functionals using Machine learning
- 11:10 to 11:55 - Discussion Session 5
- 11:55 to 13:00 - Lunch

Afternoon Session 1 - moderator: Augusto Gerolin

- 13:00 to 13:05 - Chair Session Introduction
- 13:05 to 13:40 - **Fang Liu**
  Size-transferable prediction of excited state properties for molecular assemblies with machine-learned exciton model
- 13:40 to 14:10 - Coffee break
- 14:10 to 14:45 - **Michael Herbst**
  Algorithmic differentiation in plane-wave DFT
- 14:45 to 15:30 - Discussion Session 6
- 15:30 to 16:00 - Coffee break

Afternoon Session 2 - moderator: Fang Liu

- 16:00 to 16:05 - Chair Session Introduction
- 16:05 to 16:40 - **Guillaume Maurin**
  Machine learning potentials for modelling MOFs
- 16:40 to 16:55 - **Yuri Cho**
  Benchmarking physics-based representations for predicting the properties of transition metal complexes with spin and charge diversity
- 16:55 to 17:30 - Discussion Session 7
- 19:00 to 21:30 - Social dinner

Day 4 - Thursday March 6th 2025

Morning Session - moderator: Alexandre Tkatchenko

- 09:00 to 09:05 - Chair Session Introduction
- 09:05 to 09:40 - **Anatole von Lilienfeld**
  Quantum machine learning in chemical space
- 09:40 to 09:55 - **Archa Santhosh**
  Developing machine learning models with ab-initio accuracy: applications in metal hydride materials
- 09:55 to 10:35 - Coffee break
- 10:35 to 11:10 - **M. Meuwly**
  Machine learning inter- and intramolecular interactions for chemical reaction dynamics
- 11:10 to 11:55 - Discussion Session 8
- 11:55 to 12:10 - Closing Word

3. Abstracts

Adaptive hybrid density functionals

Danish Khan, Alastair Price, Anatole von Lilienfeld
University of Toronto, Canada

Exact exchange contributions significantly affect electronic states, influencing covalent bond formation and breaking. Hybrid density functional approximations, which average exact exchange admixtures empirically, have achieved success but fall short of high-level quantum chemistry accuracy due to delocalization errors. We propose adaptive hybrid functionals, generating optimal exact exchange admixture ratios on the fly using data-efficient quantum machine learning models with negligible overhead. The adaptive Perdew-Burke-Ernzerhof hybrid density functional (aPBE0) improves energetics, electron densities, and HOMO-LUMO gaps in QM9, QM7b, and GMTKN55 benchmark datasets. A model uncertainty-based constraint reduces the method smoothly to PBE0 in extrapolative regimes, ensuring general applicability with limited training. By tuning exact exchange fractions for different spin states, aPBE0 effectively addresses the spin gap problem in open-shell systems such as carbenes. We also present a revised QM9 (revQM9) dataset with more accurate quantum properties, including stronger covalent binding, larger bandgaps, more localized electron densities, and larger dipole moments.

*[1] D. Khan, A. Price, B. Huang, M. Ach, O. von Lilienfeld, Sci. Adv., **11**, (2025)*

Algorithmic differentiation in plane-wave DFT

Michael Herbst, Niklas Schmitz
EPFL, Switzerland

Reliable algorithmic differentiation (AD) techniques offer great promise for the inverse design of materials and functionals as well as the propagating uncertainties from functionals to DFT quantities of interest.
Over the past years we spend considerable effort equipping the density-functional toolkit (DFTK, https://dftk.org) with AD capabilities. I will present some of our recent algorithmic developments, e.g. to efficiently compute DFT derivatives in numerically challenging metallic systems. Further I will hint at conceptional difficulties when applying AD to plane-wave DFT and provide some examples illustrating the current state of AD in DFTK.

Benchmarking physics-based representations for predicting the properties of transition metal complexes with spin and charge diversity

Yuri Cho, Yannick Calvino Alonso, Ksenia R. Briling, Ruben Laplaza, Clémence Corminboeuf
EPFL, Switzerland

Physics-based machine learning representations fall into two categories: those relying upon 3D structures and those incorporating both structural and electronic information. The latter aims at distinguishing molecular compounds with high charges and spin state diversity but their performances and relevance for improving the property predictions of transition metal (TM) complexes—characterized by diverse charges and spins—remain unestablished. This work systematically benchmarks the performance of a selection of physics-based representations in predicting the quantum chemical properties of TM complexes to assess the necessity of incorporating electronic information. The analysis is performed on two benchmark datasets, TM-GSspin [1] generated using cell2mol [2] and tmPHOTO [3, 4], which include diverse metal identity and differ in size and in ground-state spin, and charge distribution diversity. Target properties include spin-splitting energy, metal atomic charge, HOMO, LUMO, HOMO-LUMO gap, and dipole moment. The performance of both kernel-based statistical models and end-to-end equivariant neural networks (i.e., 3Dmol—a variant of 3Dreact [5]) is assessed.

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Developing machine learning models with ab-initio accuracy: applications in metal hydride materials

Archa Santhosh, Kai Sellschopp, Thomas Klassen, Paul Jerabek, Claudio Pistidda
Helmholtz-Zentrum Hereon GmbH, Germany

Machine learning (ML) methods in computational material science offer immense potential in material design, discovery and engineering. In large-scale molecuar dynamics (MD), well trained ML interatomic models provide a much-desired balance between speed and chemical accuracy. In this work, this is demonstrated with succesfully trained deep neural network models (DNN) for two prominent metal hydride systems, TiFe and LaNi5. The DNN models for Ti-Fe-H and La-Ni-H systems are trained and validated with ab-initio molecular dynamics (AIMD) data. In performance, they far exceed the time and length-scales accessible with pure ab-initio methodology accomplishing 1000 times the speed of AIMD while retaining quantum chemical accuracy.
The Ti-Fe-H DNN model is utilized for exploring the dynamics of hydrogen interactions in the material lattice and performs very well for most common unary, binary and ternary phases in the Ti-Fe-H system. The DNN model for La-Ni-H system was built specifically for assessing the radiation tolerance of LaNi5 and its hydride phases for their potential hydrogen storage applications in cosmic environments. This model is used to understand defect generation and their evolution dynamics in relevant La-Ni-H phases, which in essence is unachievable with most ab-initio approaches. The accuracy necessary here also makes the use of empirical or semi-empirical potentials infeasible. These ML model thus provide a prime example as an ideal bridging tool for atomistic simulations. Furthermore, future prospects and potential diverse applications for ML methods with a focus on emerging materials are also explored.

Embedding physical and chemical variety through data

Tim Gould[1], Bun Chan[2], Stephen G. Dale[3], Stefan Vuckovic[4]
[1]Griffith University, Australia
[2]Nagasaki University, Japan
[3]National University Singapore, Singapore
[4]University of Fribourg, Switzerland

The most successful density functional approximations have employed a mix of physical constrains with minimal empiricism (to improve energies and constrain the final functional form). Data-driven density functional approximations have highly flexible functional forms, so risk swamping these constraints with excessive interpolation. The resulting approximations may therefore be more limited than their traditional counterparts in their ability to extrapolate (aka transfer) to new chemistry and physics, due to over-fitting. This talk will discuss strategies for embedding genuine diversity into training data, to ensure that data-driven approximations retain the accuracy of their predecessors, yet can harness the large benchmark databases available today.

Learning electronic structures via 1- and 2-RDMs

Michele Pavanello
Rutgers University-Newark, United States

Current quantum chemical models, while more robust and predictive than in past years, are often either too approximate to provide a faithful representation of reality or too computationally expensive to yield answers within a reasonable time. The talk introduces electronic structure models based on machine learning. It is argued that machine learning methods are best employed learning quantities rich in information, such as the electron density, density matrix or even the wavefunction, as these are inherently more useful than those targeting single quantities, such as energy, dipole, etc. We present models for the one-electron density matrix [1] of small to medium sized molecules. The crucial role of imposing N-representability conditions [2] is discussed. We also present methods to learn two-electron density matrices as a route for accounting for electronic correlation explicitly at low computational cost. The methods are available to the broader community as open-source Python implementations in the QMLearn software, http://qmlearn.rutgers.edu.

*[1] X. Shao, L. Paetow, M. Tuckerman, M. Pavanello, Nat. Commun., **14**, 6281 (2023)*

Machine learning and finding XC functionals

Kieron Burke
UC Irvine, United States

TBA

Machine learning inter- and intramolecular interactions for chemical reaction dynamics

M. Meuwly
Univ. Basel, Switzerland

Machine learning has gained considerable traction in the molecular sciences. One particularly relevant and useful domain of application has been the generation and representation of high-dimensional, global and reactive potential energy surfaces for molecular simulations. Here, I will discuss the current state-of-the art of such PESs and their application to dynamics studies of chemical reactivity. Specific examples that will be discussed concern quantitative studies of atmospheric photodissociation and recombination reactions, and tunneling splittings for H-transfer reactions.

Machine learning potentials for modelling MOFs

Guillaume Maurin
Université de Montpellier, France

Machine-learned potentials (MLPs) are transforming materials science by enabling accurate and efficient modeling of complex materials, such as metal-organic frameworks (MOFs). These data-driven approaches overcome the limitations of traditional methods like density functional theory (DFT), which are computationally prohibitive for large-scale simulations. MLPs offer a hybrid alternative by learning the potential energy surfaces from quantum mechanical data, thereby providing rapid and precise predictions of material properties across extended length and time scales. One area where MLPs prove especially valuable is in the modeling of flexible MOFs, which can exhibit phase transitions and mechanical deformations in response to external conditions (thermal, mechanical pressure). Using MLPs, we explore the MOF CALF-20's phase space with unprecedented efficiency, revealing distinct two-step elastic deformation and high fracture strain, which are critical for potential applications in flexible electronics and sensors. Furthermore, MLPs extend their utility to adsorption simulations, particularly for MOFs with open metal sites (OMS), where strong host-guest interactions are challenging for classical force fields to describe accurately. We demonstrate this by developing an MLP for H_2 adsorption in Al-soc-MOF-1d, an OMS-containing framework. The MLP accurately models H_2 binding and diffusion, offering insights into adsorption performance that can guide the design of MOFs for hydrogen storage applications. These examples illustrate the potential of ML-based approaches to advance the computational modeling of MOFs.

ML is an excellent student, but DFT can be a lousy teacher

Alexandre Tkatchenko
University of Luxembourg, Luxembourg

ML methods for atomistic systems must learn at the highest possible level of quantum mechanics. As a tradeoff, they are instead taught approximate DFT (DFA) data. How good (or bad) is DFA data, where it works and where it fails? In this talk, I will provide a few examples where we train ML models close to the exact solution of Schroedinger's equation, and use them to assess DFA-trained models. Certain DFAs that include non-locality of both exchange and correlation effects can be remarkably accurate at times and in general seem to provide very reasonable baselines for delta-learning or transfer-learning. However, there are chemical systems where even the "gold standard" methods of quantum mechanics disagree, and we should be mindful of the ultimate accuracy we can claim. I will conclude by discussing the ongoing work in developing both better DFA and better ML methods that aim to obtain "the right answer for the right reason".

ML-powered orbital-free DFT

Fred Hamprecht, Roman Remme, Tobias Kaczun, Christof Gehrig, Marc Ickler, Tim Ebert, Dominik Geng, Gerrit Gerhartz, Manuel Klockow, Peter Lippmann, Johannnes Schmidt, Simon Wagner, Andreas Dreuw
Heidelberg University, Germany

We learn a kinetic energy functional, realizing an entirely orbital-free prediction pipeline. Trained on Kohn-Sham ground truth, our atomistic message passing neural network achieves chemical accuracy and fully convergent variational density optimization on all of QM9.

[1] R. Remme, T. Kaczun, M. Scheurer, A. Dreuw, F. Hamprecht, The Journal of Chemical Physics, ***159****, (2023)*

Noncovalent interactions in density functional theory: all the charge density we do not see

Matteo Gori, Almaz Khabibrakhmanov, Alexandre Tkatchenko
University of Luxembourg, Luxembourg

Exact determination of the electronic density of molecules and materials would provide direct access to accurate bonded and non-bonded interatomic interactions by virtue of the Hellman-Feynman theorem. However, density-functional approximations (DFA) -- the workhorse methods for the electronic structure of atomistic systems -- only provide approximate and sometimes unreliable electron densities. Here we show that long-range van der Waals (vdW) dispersion interactions can visibly modify the charge density, scale nontrivially with system size, and in some cases cause polarization of charge density that exceeds that of the underlying semi-local density functional. We use the fully-coupled Many-Body Dispersion model to compute the vdW charge density by an appropriate real-space projection of the collective fluctuations of optimally-tuned coupled harmonic oscillators that constitute the model. Our analysis highlights the potential unreliability of post-hoc methods for vdW dispersion interactions, has implications for detecting interacting regions in large (bio)molecules, and enables the construction of more accurate DFAs and machine-learned force fields based on the electron density.

Optimization of exchange and correlation functionals using Machine learning

Marivi Fernandez-Serra
Stony Brook University, United States

Density Functional Theory (DFT) is the standard formalism to study the electronic structure of matter
at the atomic scale. The balance between accuracy and computational cost that DFT-based simulations provide allows researchers to understand the structural and dynamical properties of increasingly large and complex systems at the quantum mechanical level.
The fundamental theorems of density functional theory ensure that there exists an exact functional which provides the exact energy of a system from its exact density. This functional is minimized at a fixed electron number and a fixed external potential by the exact electron density, hence providing both the density and and energy. However, doing this exactly comes at a colossal computational cost. It is, however, possible to approximate the exact functional, providing a balance between accuracy and computational cost.
I will show different approaches to use machine learning methods to construct approximations of the exact functional.

I will also show how to implement general methods to facilitate their incorporation in available electronic structure codes.
In addition, inherent limitations to differentiable methods -which have shown to be necessary to increase accuracy- will be highlighted.

Physically uninspired models for atomistic machine learning

Michele Ceriotti
EPFL, Switzerland

Machine-learning techniques have proven tremendously effective at replacing electronic-structure calculations of matter, both to estimate the interatomic potential energy function, and to compute functional properties and electronic excitations. Much of the work in the field has focused on incorporating physical priors, such as equivariance to rotations, symmetry and conservation laws. Recently, however, models have been proposed that relax these physical constraints and - perhaps surprisingly - achieve competitive or better accuracy in several benchmark tasks. I will discuss critically the behavior of these "physically uninspired" models that attempt to incorporate approximate symmetry or energy conservation through training. I will present some examples of the risks associated with neglecting symmetry and conservation laws, but also discuss the advantages of the unconstrained models, and how to use them safely in the context of atomistic simulations.

Position dependence of exact-exchange admixture as a central object in density functional development: escaping the zero-sum game and machine learning approaches

Artur Wodynski
Technische Universität Berlin, Germany

Kohn–Sham density functional theory remains the dominant electronic-structure method due to its balance between computational efficiency and accuracy. However, the ongoing challenge of simultaneously minimizing delocalization and static correlation errors often results in a zero-sum game, where improvements in one aspect lead to deterioration in the other. Local hybrid (LH) functionals and range-separated local hybrids (RSLHs) [1,2] provide a promising framework to break this trade-off by utilizing a real-space-dependent exact exchange (EXX) admixture, which is also used as an ingredient in the DM21 functional.
Local mixing functions (LMFs), which control the position dependence of exact-exchange admixture, serve as the central object in constructing these advanced functionals, offering a direct pathway to systematically control delocalization and static correlation errors in a spatially resolved manner. Early LMF constructions relied on the heuristic use of inhomogeneity factors, but recent advances demonstrate the power of machine learning in optimizing LMFs. In particular, the training of neural-network-based LMFs (n-LMFs) [3] has led to substantial improvements in general thermochemistry, kinetics, and noncovalent interactions, as evidenced by the LH24n-D4 functional. Unlike black-box neural network functionals such as DM21, which can be interpreted as a variant of RSLH, training LMFs within a well-defined functional framework preserves interpretability and allows for graphical analysis.
This presentation highlights the role of LMFs as a key element in DFT functional design and their transition from heuristic models to machine-learning-driven approaches. By integrating ML-trained LMFs, we enhance accuracy while maintaining interpretability. Future research will focus on addressing the zero-sum game in data-driven approaches through more systematic studies and optimization strategies.

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*[2] M. Kaupp, A. Wodyński, A. Arbuznikov, S. Fürst, C. Schattenberg, Acc. Chem. Res., **57**, 1815 (2024)*
*[3] A. Wodyński, K. Glodny, M. Kaupp, J. Chem. Theory Comput., **21**, 762 (2025)*

Quantum machine learning in chemical space

Anatole von Lilienfeld
University of Toronto, Canada

Many of the most relevant observables of matter depend explicitly on atomistic and electronic structure, rendering physics-based approaches to chemistry and materials necessary. Unfortunately, due to the combinatorial scaling of the number of chemicals and potential reaction settings, gaining a holistic and rigorous understanding through exhaustive quantum and statistical mechanics-based sampling is prohibitive --- even when using high-performance computers. Accounting for explicit and implicit dependencies and correlations, however, will not only deepen our fundamental understanding but also benefit exploration campaigns (computational and experimental). I will discuss recently gained insights from my lab elucidating such relationships thanks to alchemical perturbation density functional theory and supervised machine learning.

Real-space machine learning of correlation density functionals

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University of Fribourg, Switzerland

Machine learning (ML) is increasingly playing a pivotal role in extending the reach of quantum chemistry methods for both molecules and materials. However, in density functional theory — the primary workhorse for quantum simulations—using ML to address the limitations of human-designed density functional approximations (DFAs) remains elusive, as ML-based approximations suffer from severely limited transferability to unseen chemical systems. The presentation will explore the application of real-space ML to DFAs to address this challenge, where energies are learned point-by-point in space through energy densities. This specialized training strategy optimizes the learning process of deep neural networks for energy model functions. Central to the real-space learning approach is the derivation and implementation of correlation energy densities from regularized perturbation theory [1], enabling two distinct directions for real-space ML of DFAs. First, the Local Energy Loss (LES) model trains energy densities against their implemented counterparts at each point in space. By expanding each system's single energy data point into thousands of spatial data points, LES dramatically enhances the transferability of ML DFAs compared to traditional global energy training. Second, the spin-resolved correlation energy density allows the derivation of real-space, ML-based, and regularized extensions of Spin-Component-Scaled second-order Møller-Plesset perturbation theory. The resulting model opens new avenues for constructing transferable ML DFAs.

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Size-transferable prediction of excited state properties for molecular assemblies with machine-learned exciton model

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Computational modeling of the excited states of molecular aggregates faces significant computational challenges and size heterogeneity. Current machine learning (ML) models, typically trained on specific-sized aggregates, struggle with scalability. We found that the exciton model Hamiltonian of large aggregates can be decomposed into dimer pairs, allowing an ML model trained on dimers to reconstruct Hamiltonians for aggregates of any size. We also systematically addressed the phase-correction problem by introducing coupling terms' approximations. Our model accurately predicted the excitation energies of trimer and tetramer of perylene and tetracene and estimated S_1 oscillator strengths of perylene aggregates. Leveraging our ML model, the optical gaps of nanosized perylene aggregates with up to 50 monomers are analyzed, qualitatively revealing the role of different couplings on their size-dependency. Future work will explore transferability across different monomers to predict optical properties in heterogeneous assemblies.

Synergies of DFT, ML and accelerated wave function models for complex chemical processes

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Accurate modeling of complex electronic structures in large molecular and material systems benefits from blending high-level wave function theory with the efficiency of DFT and ML methods. New synergies are enabled by our accelerated coupled-cluster (CC) methods, including frozen and local natural orbital (FNO & LNO) approaches, optimized parallel closed- and open-shell implementations, linear-scaling MP2, LNO-CCSD(T), and general-order LNO-CC, as well as (so far conventional) CCSD gradients. [1,2]

On one hand, our CC approaches provide to DFT/ML high-fidelity energies, densities, and forces; direct CCSD(T) energy corrections; and accelerated double-hybrid DFT components. Conversely, CC methods are further enhanced by DFT-based basis set convergence acceleration, multi-level CC-in-DFT embedding, and cost-effective DFT/ML-based sampling and free energy corrections.

We showcase these synergies in modeling supramolecular and protein-ligand complexes, as well as homogeneous, surface, and enzymatic catalysis, scaling up to 100s-1000 of CC-level atoms. [1,3,4] Additionally, our efficient CC methods are designed for high-throughput computation, [1,2] significantly reducing the bottleneck of generating benchmark data. This advances the validation, refinement, and training of lower-cost DFT and ML models and supports the development of CC-quality ML PESs.[5]

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Using machine learning for the physics-guided construction of exchange-correlation functionals

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The development of improved exchange-correlation (XC) functionals involves multiple steps, many of which can be accelerated using machine learning techniques. To be specific, in our work, we improve functionals through the introduction of additional physical constraints. Typically, we build models for the exchange-correlation hole $n_{XC}(\mathbf{r},u)$, where the reference charge is located at **r** and u is the electron–electron separation. With mathematical intuition, a given set of physical constraints can be expressed in a formula, yielding an approximation to $n_{XC}(\mathbf{r},u)$ and the corresponding E_{XC}. In an attempt to automate this process, we adapt [1] machine learning algorithms to partially construct X and XC holes.

The curvature Q of the spherically averaged exchange hole is one of the crucial variables for the construction of approximations to E_{XC}, as exemplified by the Becke–Roussel model [2]. We consider the next higher nonzero derivative of the spherically averaged X hole, the fourth-order term T, and employ it to approximate hybrid functionals [3]. To this end, a new functional is constructed using machine learning; having identified a physical correlation between T and the nonlocality of the X hole, we employ a neural network to express this relation.

The approximation of an XC hole is a complex process, often resulting in functionals without a closed analytic form. To simplify the application of functionals, we use neural networks to represent them as an analytical expression. We discuss the implementation and the limitations of this approach.

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4. Posters

A neural expert functional for water

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In density functional theory, simpler exchange-correlation (XC) approximations such as the local density approximation (LDA) are favoured for computational speed but entail a loss of information, leading to a trade-off between accuracy and generality. Here, we train a neural LDA using a differentiable Kohn–Sham solver, imparting system-specific expertise for molecular water and sacrificing generality for accuracy. Our model achieves chemical accuracy on CCSD(T) ionization and atomization energies, and improves predictions of spectral lines, electron density distribution, and equilibrium geometry while curing LDA overbinding. This result opens the door for expert functionals to be trained on different systems, enhancing predictions while maintaining low computational costs. Finally, use of neural networks to simply modify LDA-XC affords an unusual degree of explainability.

Adaptive energy reference for machine-learning models of the electronic density of states

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The electronic density of states (DOS) provides information regarding the distribution of electronic energy levels in a material, and can be used to approximate its optical and electronic properties and therefore guide computational materials design. Given its usefulness and relative simplicity, it has been one of the first electronic properties used as a target for machine-learning approaches going beyond interatomic potentials. A subtle but important point, well appreciated in the condensed matter community but usually overlooked in the construction of data-driven models, is that for bulk configurations the absolute energy reference of single-particle energy levels is ill-defined. Only energy differences matter, and quantities derived from the DOS are typically independent of the absolute alignment. We introduce an adaptive scheme that optimizes the energy reference of each structure as part of the training process and show that it consistently improves the quality of machine-learning models compared to traditional choices of energy reference for different classes of materials and different model architectures. On a practical level, we trace the improved performance to the ability of this self-aligning scheme to match the most prominent features in the DOS. More broadly, we believe that this paper highlights the importance of incorporating insights on the nature of the physical target into the definition of the architecture and of the appropriate figures of merit for machine-learning models, translating into better transferability and overall performance.

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Adaptive gaussian basis for quantum chemistry calculation

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We propose a new adaptive Gaussian basis for quantum chemistry calculation. Compared with classical basis sets such as contracted Gaussian basis set, we replace the polynomial parts by Gaussian profiles with arbitrary covariance matrices. Heuristically, the covariance matrices can also control the shape of the wave functions, playing the similar role, that polynomials are used to account for angular momentum. Thanks to the Gaussian product theorem and various Gaussian integral, the basis integration appearing int the Hartree-Fock calculation can be reduced to analytic formula easily. To handle the electron-nucleus and electron-electron Coulomb energy, we further approximate the Coulomb kernel via a series of Gaussian modes and leverage the analytic formula of the Gaussian

integral. Following the total energy minimization framework, we can also parametrize the means and covariances of Gaussian basis and optimize simultaneously with the orbital coefficients. We demonstrate the effectiveness of the proposed method on the Hartree-Fock calculation of water and methane molecules.

We compare the scalability of the double-electron four-center integral, which is the computational bottleneck of most quantum chemistry calculation, with classical recursive based method, e.g. MD, HPG, Rys.

Algorithmic differentiation in plane-wave DFT

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Algorithmic Differentiation (AD) holds the promise of a unifying framework for arbitrary parameter derivatives in DFT. Applications include uncertainty propagation, property derivatives, numerical error estimation, and machine learning DFT functionals. I will present ongoing work on AD in DFTK (dftk.org), a flexible open-source plane-wave DFT framework in Julia.

An evaluation of local double hybrid density functionals

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Double hybrid density functionals, which combine exact exchange with a perturbative second-order correlation contribution, represent rung 5, the highest rung of density functional approximations [1]. This work introduces range-separated local double hybrid (RSLDH) functionals, where the fraction of exact exchange (EXX) is varied in real space. Our attempts of optimizing them using standard human-designed local mixing functions (LMFs) [2] led either (1) to a vanishing perturbative correlation contribution or (2) to a vanishing position-dependence of EXX admixture (constant LMF). The latter case provided a new range-separated double hybrid functional, ωDH25. When combined with D4 dispersion corrections, ωDH25-D4 achieves a WTMAD-2 of 2.13 kcal/mol on the GMTKN55 benchmark set, the lowest so far for a “gDH”.

To overcome the limitations of human-designed LMFs, we employ a shallow neural network (n-LMF) [3] to generate a data-driven LMF, leading to the first RSLDH functionals evaluated in a post-SCF framework [4]. This approach results in a decreased WTMAD-2 value of 1.88 kcal/mol and a well-structured n-LMF. Logical next steps to further improve the functional are a self-consistent implementation, improved machine-learned LMFs and the use of full-range EXX admixture.

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Analysis of intrinsic errors in orbital dependent exchange-correlation approximations.

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Density Functional Theory has long struggled to obtain the exact exchange-correlation (XC) functional. Numerous approximations have been designed with the hope of achieving chemical accuracy. However, the traditional design of functionals involves numerous methodologies, which has a greater possibility of error accumulation if the functionals are poorly formulated. In this spirit, the machine learning (ML) technique holds the promise of finding more reliable exchange-correlation functional approximations. Usually, the ML construction integrates physical constraints, such as scaling relations and asymptotic behavior of XC energy density and XC potentials, into deep neural networks, ensuring physically consistent predictions. In this study, we investigate the accuracy of orbital-dependent XC functionals via functional-, orbital- and eigenvalue-driven error decomposition and provide deeper insights into the factors governing the accuracy of these functionals, thereby guiding future functional development in the context of ML.

Conceptual DFT descriptors for drug-like molecules

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Conceptual Density Functional Theory (CDFT) has been shown to be a powerful interpretative and computational tool to understand chemical reactivity using conceptual tools and descriptors such as e.g. electronegativity, hardness, Fukui functions, etc.[1] At the core of CDFT lies the description of the energy of molecular systems as a functional of number of electrons (N) and the external potential (V(r)). By taking the partial derivatives of the energy functional with respect to N and V(r), various CDFT descriptors emerge naturally. Given the success of CDFT in qualitative chemical analysis, an interest has recently been shown in developing machine learning (ML) models for chemical reactivity with CDFT descriptor-based input featurization. In this work, we present C-Mugs, a dataset comprising of CDFT descriptors computed for nearly 120 k molecules. Descriptors such as electronegativity, hardness, Fukui function and dual descriptor are extracted at the density functional level of theory (wB97X-D/def2-SVP) by performing calculations for cationic and anionic species on the existing QMugs dataset.[2] A subset of these descriptors is recalculated employing different charge partition schemes and analytical expressions using coupled perturbed Kohn Sham approach to establish relative errors. This dataset is intended to facilitate the inclusion of CDFT descriptors in downstream reactivity prediction ML models. I will also present our recent investigation on the performance and validity of an electronic structure principle related with hardness called Maximum Hardness Principle.[3] This involves the examination of hardness criteria for chemically diverse existing reaction datasets including the BH9 dataset of 449 reactions belonging to 9 reaction types by Prasad et al.[4] and a cycloaddition reaction dataset of 5000 reactions by Stuyver et al.[5]

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Crash testing machine learning force fields for molecules, materials, and interfaces

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Accurate and efficient force fields (FFs) are crucial for reliable atomistic simulations. Machine learning (ML) integration has enabled FFs to achieve quantum-chemical accuracy while maintaining high computational efficiency. In our study [1, 2], we systematically evaluate state-of-the-art MLFF models—MACE, SO3krates, sGDML, SOAP/GAP, and FCHL19*—by assessing their ability to predict potential energy surfaces, accurately compute forces, and maintain stable long-time simulations across four diverse challenges. The test systems include two biomolecular structures (alanine tetrapeptide and N-acetylphenylalanyl-pentaalanyl-lysine), a 1,8-naphthyridine/graphene interface, and a methylammonium lead iodide perovskite, each designed to probe different aspects of MLFF performance. While the biomolecular systems evaluate the models' ability to reproduce FFs under varying levels of training set incompleteness, the latter two test their capability to capture molecule-surface interactions and the complex interatomic forces in perovskites, with additional challenges arising from the sluggish motion of Pb and I atoms relative to H, C, and N, as well as the rotational freedom of MA within the PbI3 cage.

Our results demonstrate significant progress, particularly with equivariant neural networks like MACE and SO3krates, setting the new standard for force prediction accuracy in the 0.2–0.5 kcal/(mol·Å) range. Also, we found that MLFFs trained on well-curated datasets exhibit strong mutual agreement, a significant advance in the reliability of MLFF simulations. Yet many challenges persist. All models display substantial atomistic force error heterogeneity (worst-to-best mean absolute error (MAE) ratio of 5:1 to 6:1), with maximum errors often exceeding the MAE by two orders of magnitude. Dataset quality and completeness are other critical factors that affect MLFF predictions. Based on our comprehensive benchmarking of different models, we identified key pitfalls and provided guidelines to enhance the safe and effective deployment of MLFFs in atomistic simulations.

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Density-corrected DFT: dispersion and dipoles

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Density-corrected density functional theory (DC-DFT) targets density-driven errors by substituting the self-consistent density with a "borrowed" density from another calculation. Practically, substituting Hartree Fock (HF) densities can mitigate density-driven errors in a targeted fashion. DC-DFT methods have strong potential to provide high-accuracy training data for ML methods. We present D2C-DFT, an improved parameterization of the D4 dispersion correction specially designed for HF-DFT calculations. D2C-DFT provides more accurate energies for a wide range of molecules and reactions. Benchmarking results on the GMTKN55 database show that D2C-DFT significantly improves results for 6 different semilocal functionals and their hybrids. We also extend the methodology of DC-DFT to the calculation of dipole moments. Analytical results for a model system show that DC-DFT systematically provides a more accurate dipole moment than traditional methods.

Diagonalization without diagonalization: a direct optimization approach for solid-state density functional theory

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We present a novel approach to address the challenges of variable occupation numbers in direct optimization of solid-state density functional theory (DFT).[1] By parameterizing both the eigenfunctions and the occupation matrix, our method minimizes the free energy with respect to these parameters. As the stationary conditions require the occupation matrix and the Kohn-Sham Hamiltonian to be simultaneously diagonalizable, this leads to the concept of "self-diagonalization," where, by assuming a diagonal occupation matrix without loss of generality, the Hamiltonian matrix naturally becomes diagonal at stationary points. Our method incorporates physical constraints on both the eigenfunctions and the occupations into the parameterization, transforming the constrained optimization into a fully differentiable unconstrained problem, which is solvable via gradient descent.

This builds on our previous work in which the traditional self-consistent field (SCF) approach (i.e. solving the Kohn-Sham equation to self-consistency) is converted to a direct-gradient-descent minimization of the total energy with respect to one-electron orbitals and an occupation function, subject to orthogonality constraints. [2-3]

At the heart of our method is a novel reparameterization of the orthogonality constraint by QR decomposition.[2] Our programs are written using Google's JAX deep-learning framework and are designed to be end-to-end differentiable to provide additional tools that are essential for discovery and design of advanced materials. Ultimately any available input variable can be targeted by the direct-gradient-descent optimization function, enabling; alchemical analysis by making nuclear charge a variable; on-the-fly adjustment of density functional parameters; and incorporation of neural networks to train a wide range of solutions.

Experiments are carried out to demonstrate the efficacy of our approach on representative systems, an example of optimization from randomly initialized occupations to the expected Fermi Dirac distribution is presented in Figure 1. Finally, we discuss some of the cutting-edge applications we are actively working towards.

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Finding molecular minima and transition-states with reverse diffusion

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Molecular relaxation and transition state finding are essential components of computational chemistry to understand reactivity. Focusing on the former, neural network force field models require large labeled datasets encompassing both equilibrium and non-equilibrium structures. As a remedy, we propose MoreRed [1], molecular relaxation by reverse diffusion where non-equilibrium structures are treated as “noisy” instances of their corresponding equilibrium states. We extend this framework to also denoise structures to generate transition states. Notably, MoreRed learns a simpler pseudo potential energy surface instead of the complex physical potential energy surface, thereby requiring much less and unlabeled data. We compare MoreRed to classical force fields, equivariant neural network force fields trained on a large dataset of equilibrium and non-equilibrium data, as well as a semi-empirical tight-binding model. Lastly, we show the potential for elucidating chemical reaction networks by chaining a relaxation and a transition state model.

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Molecular simulations with a pretrained neural network and universal pairwise force fields

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Machine Learning Force Fields (MLFFs) promise to enable general molecular simulations that can simultaneously achieve efficiency, accuracy, transferability, and scalability for diverse molecules, materials, and hybrid interfaces. A key step toward this goal has been made with the GEMS approach to biomolecular dynamics [Sci. Adv. 10, eadn4397 (2024)]. This work introduces the SO3LR method that integrates the fast and stable SO3krates neural network for semi-local interactions with universal pairwise force fields designed for short-range repulsion, long-range electrostatics, and dispersion interactions. SO3LR is trained on a diverse set of 4 million neutral and charged molecular complexes computed at the PBE0+MBD level of quantum mechanics, ensuring a comprehensive coverage of covalent and non-covalent interactions. Our approach is characterized by computational and data efficiency, scalability to 200 thousand atoms on a single GPU, and reasonable to high accuracy across the chemical space of organic (bio)molecules. SO3LR is applied to study units of four major biomolecule types, polypeptide folding, and nanosecond dynamics of larger systems such as a protein, a glycoprotein, and a lipid bilayer, all in explicit solvent. Finally, we discuss the future challenges toward truly general molecular simulations by combining MLFFs with traditional atomistic models.

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Performance of DFT+U method with Wannier functions-based projectors for Ce-oxide systems.

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Due to their unique electronic properties stemming from the partially filled 4f orbitals, lanthanide oxides are of interest for catalysis, fuel cells and nuclear materials. However, accurate computation of these materials is a challenge for density functional theory (DFT). The Hubbard U correction (DFT+U method) with the U parameter derived from first principles improves description of electron localization, ionic structure and thermochemical parameters of these materials [1]. On the other hand, previous studies claim that the DFT+U approach is not able to correctly describe the electronic structure of Ce oxides and more sophisticated, G_0W_0 method has to be applied to cure for these shortcommings [2]. We will show that the XPS spectra of Ce-oxides can be accuratelly reproduced when strongly localized Wannier functions are used for projection of occupancies of f state in the DFT+U scheme. Our results demonstrate that selection of projectors that realistically reproduce actual shape of f orbitals in the investigated material is an important aspect of the DFT+U approach and that the DFT+U+Wannier functions scheme leads to significant improvement of the predictive power of DFT+U method.

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Reconstructing xc functionals with differentiable DFT

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Machine-learning (ML) based exchange-correlation (XC) functionals are increasingly used for Density Functional Theory (DFT) calculations, offering an attractive alternative to established functional approximations. Although often accurate, these functionals typically rely on vast amounts of training data, including electron density distributions. In this work, we use Differentiable DFT with Kohn-Sham regularization to reconstruct PW-LDA and PBE using synthetic data generated from DFT calculations, demonstrating the method's ability to learn underlying exchange and correlation interactions. Achieving high accuracy, even without using electron density data during training, paves the way towards the development of custom neural XC functionals based on experimental data or high-accuracy quantum chemical calculations.

Regularization in adaptive density functionals: from accuracy to transferability

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Machine learning (ML) bridges physical rigor and data-driven optimization in density functional theory (DFT) by enabling adaptive parameterization of functionals. We present an ML framework where neural networks (NNs) automate parameter optimization while ensuring transferability. First, we use NNs to refine parameters on-the-fly for the Møller-Plesset Adiabatic Connection (MPAC) functional, achieving robust accuracy across diverse non-covalent interactions without manual fitting bias. Building on this foundation, we extend this framework by introducing a regularization strategy to penalize non-robust predicted parameters during training, resulting in an adaptive XYG-type double hybrid functionals with improved accuracy across various test sets. By integrating data-driven parameter tuning with regularization, our approach balances system-specific accuracy and broad applicability, advancing DFT functionals that adapt without overfitting.

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