ab initio electrostatic potentials for transmission electron microscopy

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Abstract

The simulation of transmission electron microscopy (TEM) images or diffraction patterns is often required to interpret their contrast and extract specimen features. This is especially true for high-resolution phase-contrast imaging of materials, but model-based reconstructions in TEM are widely used across the physical and biological sciences. Since electron scattering is dominated by the nuclear cores, the scattering potential is typically described by the widely applied independent atom model. This approximation is fast and accurate, especially for annular dark-field contrast, but it completely neglects valence bonding and its effect on the transmitting electrons. However, an emerging trend in electron microscopy is to use new instrumentation and methods to extract the maximum amount of information from each electron. This is evident in the increasing popularity of techniques such as 4D-STEM combined with ptychography in materials science, and cryogenic microcrystal electron diffraction in structural biology, where subtle differences in the scattering potential may be both measurable and contain additional insights. Thus, there is increasing interest in electron scattering simulations based on electrostatic potentials obtained from first principles, mainly via density functional theory. In this Review, we discuss the motivation and basis for these developments, survey the pioneering work that has been published thus far, and give our outlook for the future. We

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argue that a physically better justified \textit{ab initio} description of the scattering potential is both useful and viable for an increasing number of systems, and we expect such simulations to steadily gain in popularity and importance.

\textit{Keywords:} HRTEM, holography, DPC, 4D-STEM, ptychography, DFT

1. Introduction

Transmission electron microscopy (TEM) has become an invaluably versatile tool for materials science and structural biology. Improvements in instrumentation, data analysis methods, and the development of new imaging techniques and detectors continue at a rapid pace, further expanding its capabilities. Simultaneously, retracing the early development of cryogenic electron microscopy, the data obtained from specimens is shifting from being resolution-limited to being dose-limited. This has prompted increasing interest in obtaining the maximum amount of information from each transmitted electron.

In TEM, information about the sample is encoded in changes in the momentum and phase of the electron waves that are scattered by the specimen. At typical kinetic energies of the electron beam, that interaction is dominated by the Coulomb attraction between the negatively charged probe electrons and the positively charged screened nuclei of the atoms of the material, with a weaker contribution arising due to the Coulomb repulsion between the probe electrons and the electrons within the sample. The electrostatic potential responsible for the scattering thus properly includes both the contribution of the screened nuclear cores as well as the valence electron density of the specimen.

However, since nuclear scattering typically dominates, it is common to ignore the contribution of valence bonding and instead approximate the scattering potential as a superposition of isolated atomic potentials in the so-called independent atom model (IAM). This approximation has been shown to be accurate to within 10\% for low $Z$-number materials \cite{1} and is accepted to be within about 5\% in typical cases \cite{2}, although the influence of valence electrons is more pronounced at the lower electron energies that are becoming ever more popular \cite{3}.
Further, however large that remnant is, it contains all of the chemistry of the specimen and is thus of great potential interest. Finally, more advanced imaging methods are able to directly reconstruct the electrostatic potential of the sample, whose theoretical description obviously requires valence bonding to be correctly accounted for.

1.1. Measuring the electrostatic potential

The contrast in high-resolution TEM (HRTEM) is typically produced by the intentional introduction of lens aberrations to alter the relative phases of the different spatial frequencies. The resulting interference causes an image with contrast depending strongly on the choice of aberrations, but which has been used to detect local changes in charge density [4].

More commonly, however, holography is instead employed to study local electromagnetic fields. In this technique, a reference wave in vacuum is used to interfere with the wave that is transmitted through the sample, which is called the image wave [5]. Off-axis holography uses a biprism to interfere the reference and image waves and is presently the most popular electron holography method. Although the detector recording the resulting interference can only provide an intensity image, the fringes that appear in this intensity provide a way of determining both the phase and amplitude of the image wave. For a thin and light, weakly diffracting sample, the phase is proportional to the projected potential plus a contribution from any magnetic field present, making it possible to measure local variations in both fields from the measured phase. However, the requirement of the reference wave typically limits this to regions of the sample close to vacuum. Holography also requires a high degree of coherence, and background images are needed to remove artifacts such as the influence of imperfections in the positively charged wire used for the biprism.

Multiple modes of phase imaging also exist for scanning TEM (STEM), which offers the added advantage of simultaneously available compositionally sensitive signals such as annular dark-field contrast [6]. For resolving electromagnetic fields, differential phase contrast (DPC) has been a popular choice.
The first proposed DPC detector consisted of four quadrants \[7\], providing modest sensitivity to shifts of the bright field (BF) disk. If the beam is initially illuminating all segments equally, when it encounters an electric or magnetic field with components perpendicular to the beam direction, it will be deflected by the Coulomb or Lorentz forces, causing an imbalance in the illumination of the segments. By determining the difference in the signals on the segments, one can calculate a deflection vector, and from this, a field vector. This allows DPC to map electric and magnetic fields at medium resolution, for example in devices such as \textit{p-n} junctions \[8\].

With such measurements, one is essentially measuring shifts in the center of “mass” (CoM) of the BF disk \[9\]. Especially at higher resolutions where the field varies on a scale similar to or smaller than the size of the probe itself, the BF disk does not always shift rigidly \[10\]. In such cases, the redistribution of intensity within the BF disk itself needs to be measured, and it becomes advantageous to have additional segments. This led researchers Shibata and co-workers to develop a 16-segment DPC detector \[11\], which was used to demonstrate atomic-resolution DPC imaging for the first time \[12\], followed later by electric field imaging of atomic columns as well as individual atoms \[13, 14\]. With the ability to map the local electric field also comes the ability to deduce the charge density via Maxwell’s equations \[15\]. The quality of such maps correlates with the ability to determine the CoM of the scattered intensity, and DPC detectors with even more segments are thus beneficial. We note that the University of Tokyo recently developed a 40-segment version of their DPC detector, which starts to resemble a small pixelated detector, albeit with a small number of curved “pixels”.

Fully-fledged pixelated detectors generally provide higher resolution images of scattering and can thus provide an even more accurate determination of the CoM \[10, 16, 17\]. This is particularly true with the development of direct detection cameras that avoid the use of a scintillator to convert electron hits into light \[18, 19\], making them far more efficient than conventional cameras. Direct electron detection cameras also generally offer far less noisy images, and their speed has been increasing rapidly. Such cameras have spurred interest in
so-called 4D-STEM \[20], in which the 2D scattering intensity is recorded at each probe position in a 2D scan. Speed, which is important because too slow a scan can cause motion blur in the data due to drift, has so far been an advantage of scintillator-based DPC detectors. However, as cameras increase in speed, the higher resolution maps of scattering available from 4D-STEM are increasingly advantageous for a higher-quality determination of the CoM.

4D-STEM provides the ability to computationally recreate any desired imaging mode after taking the data \[21\]. However, it also enables more advanced processing methods such as electron ptychography, which is a highly efficient means of computational phase imaging that harnesses redundancies available in 4D datasets. Various ptychographic algorithms exist. Iterative methods such as ePIE \[22, 23\] or mixed-state electron ptychography \[24, 25\] make use of redundancy contained in diffraction patterns taken from significantly overlapping regions of the sample to constrain the solution. Such iterative methods can be applied both with a defocused or in-focus probe, and often provide the possibility of removing the effect of the probe \[23\] or superresolution \[26\].

Direct non-iterative in-focus probe methods that rely on the interference of diffracted convergent beam electron diffraction (CBED) disks to determine the amplitude and relative phases of the transferred spatial frequencies also exist. Such direct methods include the single side-band method \[27–30\] or Wigner distribution deconvolution method \[31–33\], which also offer the possibility of post-acquisition aberration correction \[32\] or superresolution \[34\]. Ptychographic imaging also shows greater resilience to temporal incoherence than HRTEM, and does not require vacuum for a reference wave as holography does \[30\]. In-focus ptychography also provides the benefits of simultaneous Z-contrast annular dark-field images, complementing phase images by easing the discrimination of effects due to the total charge density and atomic number. Therefore, with both center of mass and ptychographic imaging benefiting, the development of fast and efficient cameras for 4D-STEM is enhancing our ability to study the local charge density in materials, albeit at the cost of significantly greater data volumes and computational effort.
1.2. Beyond independent atoms

These developments underline the increasing need for an accessible and reliable method to describe the full electrostatic potential of real materials for use in transmission electron microscopy scattering simulations. In this Review, we first survey the existing work that has been done towards this end, and then highlight recent exciting developments, especially concerning the use of the projector-augmented wave method of density functional theory instead of earlier more demanding all-electron approaches, making much bigger systems accessible for ab initio simulations without compromising accuracy. Finally, we finish with a brief look at what is becoming possible in terms of modeling and the experiment/theory interface in modern transmission electron microscopy.

2. State of the art

2.1. Description of the ab initio electrostatic potential

The electron density and thus electrostatic potential of a collection of atoms is described by their quantum mechanical ground-state wave function. However, due to the complicated many-body interactions of the electron states, that wave function cannot be analytically solved except for a few simple molecules. Different approximations have thus been developed to overcome this fundamental difficulty, with density functional theory (DFT) unarguably being the most popular and widely used framework [35]. In DFT, the many-body problem of $N$ electrons with $3N$ spatial coordinates is reduced to a variational solution for the three spatial coordinates of the electron density. This reduction is in principle exact, up to a term that describes electron exchange and correlation that is not analytically known.

While it is possible to solve the ground-state electron density for all electrons, including those in the core levels and in the valence, the numerical description of the orthogonal electron wave functions rapidly oscillating near the nuclei is computationally extremely expensive. Thus, some partition of the treatment of the cores and the valence is typically used to make calculations practical.
One of the most popular such approaches, originally developed by Slater [36], is the augmented plane wave (APW) method, where the electron density in non-overlapping volumes around each atom is described by atomic-like functions, which are smoothly connected by plane waves in the interstitial regions.

Most modern implementations have adopted the efficient linearized form of the APW method originally developed by Andersen [37], where the density near the atoms is described as a linear variation of atomic-like functions. In its so-called full-potential form (FLAPW), no assumptions about the shape of the potential inside the spheres are made (contrary to the early ‘muffin-tin’ approaches). This results in a highly precise description of the all-electron density, including any core relaxation effects. However, while accurate, this method is still computationally highly demanding, limiting its use to a few dozen or at most around one hundred atoms. For specimens of interest to TEM, especially in a realistic slab geometry, this is a severe limitation in capability.

More recently, so-called pseudopotential [38] and projector-augmented wave (PAW) methods [39] have become popular due to their greater computational efficiency. In these approaches, the core electrons are not described explicitly, but rather replaced either by a smooth pseudo-density near the nuclei or by analytical projector functions, which are also smooth in the core region. Both approaches are valid and useful, but the PAW method has the distinct advantage that the real (frozen) core electron density can be analytically recovered by inverting the projector functions. As such, it is arguably the most suitable approach for obtaining efficient and accurate ab initio electrostatic potentials for electron scattering simulations. This approach was pioneered by Pennington and co-workers who highlighted that the mean inner potentials of group-IV and group-III–V materials were up to 10% lower for PAW-based DFT calculations than those derived from IAM scattering factors [40], and in good agreement with FLAPW values found in the literature. Recently, Susi and co-workers further directly compared the spatial variation of the electrostatic potential obtained using the PAW method to a reference FLAPW calculation, finding them (unsurprisingly) essentially identical [41].
Table 1: ab initio simulations of the electrostatic potential of materials for TEM. In these works, electron scattering was not modelled, but the measured electrostatic potential or electric field was explicitly compared to the simulation. Core electrons have been treated in several ways: FLAPW denotes the accurate but expensive full-potential linearized augmented plane wave all-electron approach; PAW is the projector-augmented wave method, where the exact frozen core orbital density is described by analytic projector functions; and in the pseudopotential approach, the core density is instead replaced by a smooth pseudo-density.

| DFT code | Core electrons | Material         | Refs. |
|----------|----------------|------------------|-------|
| FLAPW    | FLAPW          | Si, Ge, MgO      | 42    |
| WIEN2K   | FLAPW          | Mg               | 43    |
| WIEN     | FLAPW          | MgB₂             | 44    |
| WIEN2K   | FLAPW          | amorphous C      | 45    |
| WIEN2K   | FLAPW          | Si, Ge, III-V    | 46    |
| GPAW     | PAW            | films, nanowires | 40    |
| VASP     | PAW            | graphene         | 14    |
| VASP     | PAW            | MoS₂             | 47    |
| VASP     | PAW            | Al₂O₃            | 48    |
| VASP/ELK | PAW, FLAPW     | MoS₂, WS₂        | 19    |
| VASP     | PAW            | SrTiO₃, BiFeO₃   | 49    |
| VASP     | PAW            | MoS₂, WS₂        | 50    |
| VASP     | PAW            | MoS₂             | 51    |

In Tables 1 and 2 we list published studies that have used DFT to calculate the electrostatic potential of a specimen in the context of transmission electron microscopy. We have chosen to limit ourselves to studies that have explicitly compared the potential or field itself, or a resulting image or diffraction pattern, to an experimental measurement, leaving out the numerous works where DFT has been used to model any specimen properties (such as strain) that indirectly influence image contrast. In many cases, only the mean inner potential (MIP) — the zeroth-order term in the Fourier expansion of the full Coulomb potential — of the material was computed, as this was sufficient to describe the experimental results, and no explicit electron scattering simulation was made (Table 1).
others, image simulations were performed based on the DFT potentials to go beyond the independent atom model (Table 2).

Since scattering simulations and 4D-STEM are explicitly real-space methods, there are some advantages, at least in terms of simplicity, in using a real-space DFT code. Furthermore, the description of vacuum regions that are typically required for TEM simulations is as computationally expensive as that of the interstitial regions between atoms when using plane waves, and Fourier transforms are required to recover the real-space electron densities. Of the methods that have been used to date, most FLAPW and vasp-based PAW approaches use reciprocal-space plane-wave bases for the wave functions. Instead, as arguably the most popular PAW-based real-space code [64, 65], gpaw is ideally suited for describing the scattering potential for TEM simulations. Furthermore, its excellent parallel scaling [65] and the option of using a highly efficient localized basis set [66] allow large systems with vacuum to be effectively treated.

Table 2: ab initio simulations of the electrostatic potential of materials for explicit TEM electron scattering simulations. See the caption of Table 1 for a description of the different treatments of core electrons.

| DFT code          | Core electrons | Material       | Refs. |
|-------------------|----------------|----------------|-------|
| WIEN2K            | FLAPW          | MgO            | 52    |
| WIEN2K            | FLAPW          | graphene, hBN  | [4] 53|
| SIESTA            | pseudo         | graphene       | 54    |
| QUANTUM ESPRESSO  | pseudo         | AlN            | 55    |
| EXCITING          | FLAPW          | graphene       | 56    |
| ABINIT/ELK        | pseudo         | WSe2           | 57    |
| WIEN2K            | FLAPW          | GaN            | 58    |
| VASP              | pseudo         | SrTiO3         | 59    |
| GPW               | PAW            | graphene, hBN  | [41] 60|
| CASTEP/WIEN2K     | pseudo, FLAPW  | hBN            | 61    |
| FPLO-18           | FLAPW          | graphene, hBN  | 62    |
| GPW               | PAW            | GaP            | 63    |
2.2. Simulation of electron scattering

Simulations are often required to interpret measurements obtained via different TEM imaging modalities, or to test ideas for a study. Notably, a significant number of 4D-STEM works rely heavily on simulations \[67\]–\[70\]. These are typically performed using either Bloch wave calculations \[71\]–\[72\], or the multislice algorithm \[73\]–\[74\]. Bloch wave methods do not scale favorably with system size, and thus 4D-STEM simulation studies usually employ the multislice method. This consists of two main steps: first, the electrostatic potential of all atoms is calculated and distributed into a series of 2D slices; and second, the electron wave is initialized and propagated through the potential slices.

In several published works that have used the \textit{ab initio} approach, only a single propagation through a projected 2D potential within the weak phase object approximation (WPOA) was performed \[4\]–\[53\], \[54\]–\[56\], \[62\]. Although this is a good approximation for very thin and light specimens, even for truly 2D materials composed of light elements, there seem to be small quantitative differences \[41\]. However, for thicker specimens, the projected potential is not sufficient for the description of dynamical diffraction. Accordingly, several recent works have performed full multislice simulations based on a 3D \textit{ab initio} electrostatic potential \[41\]–\[52\], \[57\]–\[61\], \[63\]–\[75\].

The multislice method is quite efficient for plane-wave or single-probe diffraction simulations; however, STEM experiments may record images with thousands or even millions of probe positions. Large 4D-STEM simulations thus require parallelization over multiple central processing units (CPUs) or use one or more graphics processing units (GPUs). Recently, Ophus developed the PRISM algorithm \[76\], which is a hybrid of the Bloch wave and multislice methods that offers a substantial speed-up for STEM simulations.

There are a large number of codes implementing multislice simulations with varying degrees of support and features; however, not all of these can output the full 4D signal. In Table \[3\] we list some prominent open-source codes that can model 4D-STEM signals. All of the listed codes currently use the IAM to calculate the electrostatic potential, apart from the recently released \textit{abTEM} code,
which was built to directly support simulations with \textit{ab initio} potentials through integration with the GPAW code. Heimes and co-workers also recently reported on the latter’s upcoming integration with the STEMsalabim code [63].

In terms of programming languages, simulation codes have typically been written in C++ or Fortran for high numerical performance, making them somewhat rigid with respect to the types of simulation modes that are readily available. We argue that the rapid recent growth of novel imaging techniques calls instead for flexible simulation tools that are easy to develop and adapt. The Python language has been gaining significant popularity in scientific computing in recent years, as it provides a low barrier to entry, easy code modification due to being an interpreted programming language, and an extensive list of open source projects to draw on.

Two recent codes, \textsc{abTEM} [60] and \textsc{py_multislice} [83], take advantage of Python to offer users increased customizability, while retaining high performance via the use of modern CPU- and GPU-accelerated software libraries such as PyTorch [84], CuPy [85], and Numba [86]. Other important open source projects for TEM include the Atomic Simulation Environment [87] for building atomic structures and interacting with atomistic simulation codes that are integral to

| Simulation code   | Language  | Features         | Refs. |
|-------------------|-----------|------------------|-------|
| EMSoft            | Fortran   | GPU              | 77    |
| \(\mu\text{STEM}\) | C++       | GPU, EELS        | 78    |
| MULTEM            | C++, Matlab| GPU, EELS        | 79    |
| STEMsalabim       | C++       | Multi CPU        | 80    |
| PRISMATIC         | C++       | Multi CPU/GPU, PRISM | 81    |
| Dr. Probe         | C++       | GPU              | 82    |
| \textsc{abTEM}    | Python    | GPU, PRISM, \textit{ab initio} | 60    |
| \textsc{py_multislice} | Python   | GPU, PRISM, EELS | 83    |

Table 3: Simulation codes that output the full four-dimensional scanning transmission electron microscopy (4D-STEM) signal that are open source and currently maintained.
abTEM, and py4DSTEM [88], which is being developed for the analysis of 4D-STEM data and includes integration into the open-source Python electron microscopy software, Nion Swift.

2.3. Experimental works

Finally, we wish to highlight some illustrative recent examples that clearly demonstrate how going beyond the independent atom model has been vital for describing experimental data in a quantitatively correct manner. Most commonly thus far, the mean inner potential of materials has been measured with electron holography and compared to an \textit{ab initio} calculation (see Table 1). After pioneering work by Kim on Si, Ge and MgO [42], several groups have extended such studies to other semiconductors, borides, oxides and carbon materials [43–46, 52]. Whenever an explicit comparison to the independent atom model was made, \textit{ab initio} values were consistently found to be lower and in better agreement with experiment. This tendency of the IAM to overestimate potential values was highlighted by very recent work on the mean inner potential of water [89], which compared it to several experimental measurements (see Fig. 1).

In terms of spatially resolved studies, hexagonal boron nitride (hBN) has arguably been the clearest example of a system where valence bonding plays an important role for electron scattering. In contrast to independent B and N atoms, where the stronger nuclear scattering from the N sites would be expected to lead to their greater image intensity, the greater electronegativity of N in the bonded ionic compound leads to significant charge transfer from the B atoms, enhancing the screening of the N nucleus. This almost completely negates the contrast difference between the two sites in HRTEM [4] (see Fig. 2) and ptychography [61], and can only be reproduced using an \textit{ab initio} electrostatic potential. This phenomenon was also responsible for the visibility of substitutional nitrogen sites in defocused HRTEM images of chemically doped graphene, again requiring an \textit{ab initio}-based potential to reproduce the experimental image contrast [4, 53].
As we have shown, details of the electronic configuration and potential derived from density functional theory (DFT) can be detected in TEM images with a high signal-to-noise ratio. The neutral-atom (IAM) charge distribution, which predicts a separation of the electronic charge in different regions with the same thickness. This means that the ionic distributions in the hexagon and the atom sites, on the basis of comparisons of experimental measurements, thereby the charge densities, which might not be deduced from the earlier calculations. Nevertheless, we successfully distinguish between two candidate models.

Errors. The neutral-atom (IAM) charge distribution, which predicts a separation of the electronic charge in different regions with the same thickness. This means that the ionic distributions in the hexagon and the atom sites, on the basis of comparisons of experimental measurements. Red-solid line corresponds to an independent atom model (IAM) calculation. For detail on the experiments and the cited references, please see the original article. Reproduced with permission from Ref. 89, Copyright © 2020, American Physical Society.

Figure 1: Comparison of mean inner potential (MIP) values of water from several experimental measurements. Red-solid line corresponds to an independent atom model (IAM) calculation. For detail on the experiments and the cited references, please see the original article. Reproduced with permission from Ref. 89, Copyright © 2020, American Physical Society.

Figure 2: Comparison of high-resolution transmission electron microscopy (HRTEM) images simulated with the independent atom model (IAM) to those simulated with an electrostatic potential derived from density functional theory (DFT). The overlaid red and green lines in panels (a) and (c) correspond to the line profiles plotted in panel (e). Reproduced with permission from Ref. 4, Copyright © 2011, Springer Nature.
Table calculations are listed alongside our experimental results in parameter optimization. It should be noted here that a parameter optimization considering the phase image wave convolution when the phase yielded identical parameters for the sample tilt and the experimental and simulated phase images for bilayer WSe$_2$. It should be noted that aberration correction has no influence on the averaged electron phases presented here.

Table I. Spatially averaged electron phase shifts for WSe$_2$ structures and several samples. The experimental spatially averaged phase for a monolayer is determined from an extrapolation of values acquired for thicker layers.  It should be noted that a calculated phase image obtained with the DFT method lies within the confidence interval for the experimental value. For the WSe$_2$ bilayer, the spatially averaged phase obtained using the DFT method yields the lowest average phase, while the IA methods deviate significantly more from the experimental values.

Another recent example is the comparison of atomically resolved off-axis holography of mono- and bilayer specimens of the transition metal dichalcogenide WSe$_2$ to simulations. An ab initio electrostatic potential was again required to accurately reproduce electron-optical phase images of the material, and near-perfect agreement with experimental data was obtained (see Fig. 3). Electron diffraction intensities are likewise highly sensitive to the inclusion of valence bonding, as was recently demonstrated for graphene and hBN, where only a scattering simulation with an ab initio potential could correctly reproduce the intensity ratio of the first two diffraction orders. While many of these examples are from two-dimensional materials, that is not due to any fundamental limitation; modern PAW-based DFT simulations can handle thousands of atoms, even when including an explicit description of van der Waals interactions.
3. Outlook

The rapid ongoing development of transmission electron microscopy instrumentation, imaging modalities, and analysis methods continues to expand its already impressive capabilities at a remarkable pace. At the same time, an intimate interplay with modeling is becoming ever more important, especially for techniques such as 4D-STEM and ptychography that aim at extracting novel physical information from each detected electron with the help of model-based reconstructions. Although these increase the computational cost and complexity of cutting-edge TEM work, such effort is still modest compared to the cost of density functional theory.

Advances in first-principles modeling codes and high-performance computing facilities are making ever-larger system sizes amenable for a physically more accurate description. Further, emerging developments in machine learning and instrument automation can be expected to drive a trend towards closer software integration, which is a need that new TEM simulation packages based on Python are particularly well-placed to meet.

While established simulation methods based on the independent atom model will continue to play an important role in routine work, we anticipate that the importance of accessing the full ab initio electrostatic potential will grow ever more significant over time. Overall, the sustained increase in the power and versatility of transmission electron microscopy as a tool of choice for materials science and structural biology shows no sign of abating, and modern simulation methods and software tools are poised to make an important contribution to advancing both our scientific research and technological development.

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References

[1] E. J. Kirkland, Advanced Computing in Electron Microscopy, Springer-Link: Springer e-Books, Springer US, 2010.

[2] L. M. Peng, S. L. Dudarev, M. J. Whelan, High Energy Electron Diffraction and Microscopy, Monographs on the Physics and Chemistry of Materials, Oxford University Press, Oxford, New York, 2011.

[3] U. Kaiser, J. Biskupek, J. C. Meyer, J. Leschner, L. Lechner, H. Rose, M. Stöger-Pollach, A. N. Khlobystov, P. Hartel, H. Müller, M. Halder, S. Eyhusen, G. Benner, Transmission electron microscopy at 20 kV for imaging and spectroscopy, Ultramicroscopy 111 (2011) 1239–1246.

[4] J. C. Meyer, S. Kurasch, H. J. Park, V. Skakalova, D. Künzel, A. Groß, A. Chuvilin, G. Algara-Siller, S. Roth, T. Iwasaki, U. Starke, J. H. Smet, U. Kaiser, Experimental analysis of charge redistribution due to chemical bonding by high-resolution transmission electron microscopy, Nat. Mater. 10 (2011) 209–215.

[5] R. E. Dunin-Borkowski, A. Kovács, T. Kasama, M. R. McCartney, D. J. Smith, Electron Holography, in: P. W. Hawkes, J. C. H. Spence (Eds.), Springer Handbook of Microscopy, Springer Handbooks, Springer International Publishing, Cham, 2019, pp. 767–818.

[6] S. J. Pennycook, P. D. Nellist (Eds.), Scanning Transmission Electron Microscopy: Imaging and Analysis, Springer-Verlag, New York, 2011.

[7] N. H. Dekkers, H. de Lang, Differential phase contrast in a STEM, Optik 41 (2015) 452–256.

[8] N. Shibata, S. D. Findlay, H. Sasaki, T. Matsumoto, H. Sawada, Y. Kohno, S. Otomo, R. Minato, Y. Ikuhara, Imaging of built-in electric field at a p-n junction by scanning transmission electron microscopy, Sci. Rep. 5 (2015) 10040.
[9] N. Shibata, Atomic-resolution differential phase contrast electron microscopy, J. Ceram. Soc. Jpn. 127 (2019) 708–714.

[10] K. Müller, F. F. Krause, A. Béché, M. Schowalter, V. Galioit, S. Löffler, J. Verbeeck, J. Zweck, P. Schattschneider, A. Rosenauer, Atomic electric fields revealed by a quantum mechanical approach to electron picodiffraction, Nat. Commun. 5 (2014) 5653.

[11] N. Shibata, Y. Kohno, S. D. Findlay, H. Sawada, Y. Kondo, Y. Ikuhara, New area detector for atomic-resolution scanning transmission electron microscopy, J. Electron Microsc. 59 (2010) 473–479.

[12] N. Shibata, S. D. Findlay, Y. Kohno, H. Sawada, Y. Kondo, Y. Ikuhara, Differential phase-contrast microscopy at atomic resolution, Nat. Phys. 8 (2012) 611–615.

[13] N. Shibata, T. Seki, G. Sánchez-Santolino, S. D. Findlay, Y. Kohno, T. Matsumoto, R. Ishikawa, Y. Ikuhara, Electric field imaging of single atoms, Nat. Commun. 8 (2017) 15631.

[14] R. Ishikawa, S. D. Findlay, T. Seki, G. Sánchez-Santolino, Y. Kohno, Y. Ikuhara, N. Shibata, Direct electric field imaging of graphene defects, Nat. Commun. 9 (2018) 3878.

[15] G. Sánchez-Santolino, N. R. Lugg, T. Seki, R. Ishikawa, S. D. Findlay, Y. Kohno, Y. Kanitani, S. Tanaka, S. Tomiya, Y. Ikuhara, Y. Ikuhara, N. Shibata, Probing the Internal Atomic Charge Density Distributions in Real Space, ACS Nano 12 (2018) 8875–8881.

[16] K. Müller-Caspary, F. F. Krause, T. Grieb, S. Löffler, M. Schowalter, A. Béché, V. Galioit, D. Marquardt, J. Zweck, P. Schattschneider, J. Verbeeck, A. Rosenauer, Measurement of atomic electric fields and charge densities from average momentum transfers using scanning transmission electron microscopy, Ultramicroscopy 178 (2017) 62–80.
[17] G. Argentero, A. Mittelberger, M. Reza Ahmadpour Monazam, Y. Cao, T. J. Pennycook, C. Mangler, C. Kramberger, J. Kotakoski, A. K. Geim, J. C. Meyer, Unraveling the 3D Atomic Structure of a Suspended Graphene/hBN van der Waals Heterostructure, Nano Lett. 17 (2017) 1409–1416. Publisher: American Chemical Society.

[18] J. A. Mir, R. Clough, R. MacInnes, C. Gough, R. Plackett, I. Shipsey, H. Sawada, I. MacLaren, R. Ballabriga, D. Maneuski, V. O’Shea, D. McGrouther, A. I. Kirkland, Characterisation of the Medipix3 detector for 60 and 80 keV electrons, Ultramicroscopy 182 (2017) 44–53.

[19] S. Fang, Y. Wen, C. S. Allen, C. Ophus, G. G. D. Han, A. I. Kirkland, E. Kaxiras, J. H. Warner, Atomic electrostatic maps of 1D channels in 2D semiconductors using 4D scanning transmission electron microscopy, Nat. Commun. 10 (2019) 1127.

[20] C. Ophus, Four-Dimensional Scanning Transmission Electron Microscopy (4D-STEM): From Scanning Nanodiffraction to Ptychography and Beyond, Microsc. Microanal. 25 (2019) 563–582.

[21] J. A. Hachtel, J. C. Idrobo, M. Chi, Sub-Ångstrom electric field measurements on a universal detector in a scanning transmission electron microscope, Adv. Struct. Chem. Imaging 4 (2018) 10.

[22] A. M. Maiden, J. M. Rodenburg, An improved ptychographical phase retrieval algorithm for diffractive imaging, Ultramicroscopy 109 (2009) 1256–1262.

[23] F. Hüb, J. M. Rodenburg, A. M. Maiden, P. A. Midgley, Extended ptychography in the transmission electron microscope: Possibilities and limitations, Ultramicroscopy 111 (2011) 1117–1123.

[24] P. Thibault, A. Menzel, Reconstructing state mixtures from diffraction measurements, Nature 494 (2013) 68–71.
[25] Z. Chen, M. Odstrcil, Y. Jiang, Y. Han, M.-H. Chiu, L.-J. Li, D. A. Muller, Mixed-state electron ptychography enables sub-angstrom resolution imaging with picometer precision at low dose, Nat. Commun. 11 (2020) 2994.

[26] Y. Jiang, Z. Chen, Y. Han, P. Deb, H. Gao, S. Xie, P. Purohit, M. W. Tate, J. Park, S. M. Gruner, V. Elser, D. A. Muller, Electron ptychography of 2D materials to deep sub-Ångström resolution, Nature 559 (2018) 343–349.

[27] J. M. Rodenburg, B. C. McCallum, P. D. Nellist, Experimental tests on double-resolution coherent imaging via STEM, Ultramicroscopy 48 (1993) 304–314.

[28] T. J. Pennycook, A. R. Lupini, H. Yang, M. F. Murfitt, L. Jones, P. D. Nellist, Efficient phase contrast imaging in STEM using a pixelated detector. Part 1: Experimental demonstration at atomic resolution, Ultramicroscopy 151 (2015) 160–167.

[29] H. Yang, T. J. Pennycook, P. D. Nellist, Efficient phase contrast imaging in STEM using a pixelated detector. Part II: Optimisation of imaging conditions, Ultramicroscopy 151 (2015) 232–239.

[30] T. J. Pennycook, G. T. Martinez, P. D. Nellist, J. C. Meyer, High dose efficiency atomic resolution imaging via electron ptychography, Ultramicroscopy 196 (2019) 131–135.

[31] J. M. Rodenburg, R. H. T. Bates, The theory of super-resolution electron microscopy via Wigner-distribution deconvolution, Philos. Trans. R. Soc. A 339 (1992) 521–553.

[32] H. Yang, R. N. Rutte, L. Jones, M. Simson, R. Sagawa, H. Ryll, M. Huth, T. J. Pennycook, M. L. H. Green, H. Soltau, Y. Kondo, B. G. Davis, P. D. Nellist, Simultaneous atomic-resolution electron ptychography and Z-contrast imaging of light and heavy elements in complex nanostructures, Nat. Commun. 7 (2016) 12532.
[33] H. Yang, I. MacLaren, L. Jones, G. T. Martinez, M. Simson, M. Huth, H. Ryll, H. Soltau, R. Sagawa, Y. Kondo, C. Ophus, P. Ercius, L. Jin, A. Kovács, P. D. Nellist, Electron ptychographic phase imaging of light elements in crystalline materials using Wigner distribution deconvolution, Ultramicroscopy 180 (2017) 173–179.

[34] P. D. Nellist, B. C. McCallum, J. M. Rodenburg, Resolution beyond the 'information limit' in transmission electron microscopy, Nature 374 (1995) 630–632.

[35] W. Kohn, Nobel Lecture: Electronic structure of matter— wave functions and density functionals, Rev. Mod. Phys. 71 (1999) 1253.

[36] J. C. Slater, Wave Functions in a Periodic Potential, Phys. Rev. 51 (1937) 846–851.

[37] O. K. Andersen, Linear methods in band theory, Phys. Rev. B 12 (1975) 3060–3083.

[38] P. Schwerdtfeger, The Pseudopotential Approximation in Electronic Structure Theory, ChemPhysChem 12 (2011) 3143–3155.

[39] P. E. Blöchl, Projector augmented-wave method, Phys. Rev. B 50 (1994) 17953.

[40] R. S. Pennington, C. B. Boothroyd, R. E. Dunin-Borkowski, Surface effects on mean inner potentials studied using density functional theory, Ultramicroscopy 159 (2015) 34–45.

[41] T. Susi, J. Madsen, U. Ludacka, J. J. Mortensen, T. J. Pennycook, Z. Lee, J. Kotakoski, U. Kaiser, J. C. Meyer, Efficient first principles simulation of electron scattering factors for transmission electron microscopy, Ultramicroscopy 197 (2019) 16–22.

[42] M. Y. Kim, J. M. Zuo, J. Spence, Ab-initio LDA calculations of the mean Coulomb potential \( V_0 \) in slabs of crystalline Si, Ge and MgO, Phys. Status Solidi A 166 (1998) 445–451.
[43] J. Friis, G. K. H. Madsen, F. K. Larsen, B. Jiang, K. Marthinsen, R. Holmestad, Magnesium: Comparison of density functional theory calculations with electron and x-ray diffraction experiments, J. Chem. Phys. 119 (2003) 11359–11366.

[44] L. Wu, Y. Zhu, T. Vogt, H. Su, J. W. Davenport, J. Tafto, Valence-electron distribution in MgB$_2$ by accurate diffraction measurements and first-principles calculations, Phys. Rev. B 69 (2004) 064501.

[45] M. Schowalter, J. T. Titantah, D. Lamoen, P. Kruse, Ab initio computation of the mean inner Coulomb potential of amorphous carbon structures, Appl. Phys. Lett. 86 (2005) 112102.

[46] P. Kruse, M. Schowalter, D. Lamoen, A. Rosenauer, D. Gerthsen, Determination of the mean inner potential in III–V semiconductors, Si and Ge by density functional theory and electron holography, Ultramicroscopy 106 (2006) 105–113.

[47] K. Müller-Caspary, M. Duchamp, M. Rösner, V. Migunov, F. Winkler, H. Yang, M. Huth, R. Ritz, M. Simson, S. Ihle, H. Soltau, T. Wehling, R. E. Dunin-Borkowski, S. Van Aert, A. Rosenauer, Atomic-scale quantification of charge densities in two-dimensional materials, Phys. Rev. B 98 (2018) 121408.

[48] A. Auslender, M. Halabi, G. Levi, O. Diéguez, A. Kohn, Measuring the mean inner potential of Al$_2$O$_3$ sapphire using off-axis electron holography, Ultramicroscopy 198 (2019) 18–25.

[49] W. Gao, C. Addiego, H. Wang, X. Yan, Y. Hou, D. Ji, C. Heikes, Y. Zhang, L. Li, H. Huyan, T. Blum, T. Aoki, Y. Nie, D. G. Schlom, R. Wu, X. Pan, Real-space charge-density imaging with sub-Ångström resolution by four-dimensional electron microscopy, Nature 575 (2019) 480–484.

[50] Y. Wen, C. Ophus, C. S. Allen, S. Fang, J. Chen, E. Kaxiras, A. I. Kirkland, J. H. Warner, Simultaneous Identification of Low and High Atomic Num-
ber Atoms in Monolayer 2D Materials Using 4D Scanning Transmission Electron Microscopy, Nano Lett. 19 (2019) 6482–6491.

[51] V. Boureau, B. Sklenard, R. McLeod, D. Ovchinnikov, D. Dumcenco, A. Kis, D. Cooper, Quantitative Mapping of the Charge Density in a Monolayer of MoS$_2$ at Atomic Resolution by Off-Axis Electron Holography, ACS Nano 14 (2020) 524–530.

[52] B. Deng, L. D. Marks, J. M. Rondinelli, Charge defects glowing in the dark, Ultramicroscopy 107 (2007) 374–381.

[53] S. Kurasch, J. C. Meyer, D. Künzel, A. Groß, U. Kaiser, Simulation of bonding effects in HRTEM images of light element materials, Beilstein J. Nanotechnol. 2 (2011) 394–404.

[54] W. L. Wang, E. Kaxiras, Efficient calculation of the effective single-particle potential and its application in electron microscopy, Phys. Rev. B 87 (2013) 085103.

[55] M. L. Odlyzko, B. Himmetoglu, M. Cococcioni, K. A. Mkhoyan, Atomic bonding effects in annular dark field scanning transmission electron microscopy. I. Computational predictions, J. Vac. Sci. Technol. A 34 (2016) 041602.

[56] L. Pardini, S. Löffler, G. Biddau, R. Hambach, U. Kaiser, C. Draxl, P. Schattschneider, Mapping Atomic Orbitals with the Transmission Electron Microscope: Images of Defective Graphene Predicted from First-Principles Theory, Phys. Rev. Lett. 117 (2016) 036801.

[57] S. Borghardt, F. Winkler, Z. Zanolli, M. J. Verstraete, J. Barthel, A. H. Tavabi, R. E. Dunin-Borkowski, B. E. Kardynal, Quantitative Agreement between Electron-Optical Phase Images of WSe$_2$ and Simulations Based on Electrostatic Potentials that Include Bonding Effects, Phys. Rev. Lett. 118 (2017) 086101.
[58] K. Müller-Caspary, F. F. Krause, T. Grieb, S. Löffler, M. Schowalter, A. Bech, V. Galioit, D. Marquardt, J. Zweck, P. Schattschneider, J. Verbeek, A. Rosenauer, Measurement of atomic electric fields and charge densities from average momentum transfers using scanning transmission electron microscopy, Ultramicroscopy 178 (2017) 62–80.

[59] M. P. Oxley, A. Y. Birenbaum, T. Pandey, V. R. Cooper, M. Chi, Accurate Calculation of CBED Patterns for 4D STEM Using Electron Densities Calculated by Density Functional Theory., Microsc. Microanal. 24 (2018) 116–117.

[60] J. Madsen, T. Susi, abTEM: ab Initio Transmission Electron Microscopy Image Simulation, Microsc. Microanal. (2020) 1–4.

[61] G. T. Martinez, T. C. Naginey, L. Jones, C. M. O’Leary, T. J. Pennycook, R. J. Nicholls, J. R. Yates, P. D. Nellist, Direct imaging of charge redistribution due to bonding at atomic resolution via electron ptychography, 2019. arXiv:1907.12974.

[62] F. Kern, M. Linck, D. Wolf, N. Alem, H. Arora, S. Gemming, A. Erbe, A. Zettl, B. Büchner, A. Lubk, Autocorrected Off-axis Holography of 2D Materials, 2020. arXiv:2006.13855.

[63] D. Heimes, J. Belz, A. Beyer, K. Volz, Measuring Interatomic Bonding and Charge Redistributions in Defects by Combining 4D-STEM and STEM Multislice Simulations, Microsc. Microanal. (2020) 1–3.

[64] J. Mortensen, L. Hansen, K. Jacobsen, Real-space grid implementation of the projector augmented wave method, Phys. Rev. B 71 (2005) 035109.

[65] J. Enkovaara, C. Rostgaard, J. J. Mortensen, J. Chen, M. Dulak, L. Ferrighi, J. Gavnholm, C. Glinsvad, V. Haikola, H. A. Hansen, H. H. Kristoffersen, M. Kuisma, A. H. Larsen, L. Lehtovaara, M. Ljungberg, O. Lopez-Acevedo, P. G. Moses, J. Ojanen, T. Olsen, V. Petzold, N. A. Romero, J. Stausholm-Møller, M. Strange, G. A. Tritsaris, M. Vanin, M. Walter,
B. Hammer, H. Häkkinen, G. K. H. Madsen, R. M. Nieminen, J. K. Nørskov, M. Puska, T. T. Rantala, J. Schiøtz, K. S. Thygesen, K. W. Jacobsen, Electronic structure calculations with GPAW: a real-space implementation of the projector augmented-wave method, J. Phys. Condens. Matter 22 (2010) 253202.

[66] A. H. Larsen, M. Vanin, J. J. Mortensen, K. S. Thygesen, K. W. Jacobsen, Localized atomic basis set in the projector augmented wave method, Phys. Rev. B 80 (2009) 195112.

[67] A. C. Liu, M. J. Neish, G. Stokol, G. A. Buckley, L. A. Smillie, M. D. De Jonge, R. T. Ott, M. J. Kramer, L. Bourgeois, Systematic mapping of icosahedral short-range order in a melt-spun Zr$_3$Cu$_6$ metallic glass, Phys. Rev. Lett. 110 (2013) 205505.

[68] J. M. LeBeau, S. D. Findlay, L. J. Allen, S. Stemmer, Position averaged convergent beam electron diffraction: Theory and applications, Ultramicroscopy 110 (2010) 118–125.

[69] H. Yang, I. MacLaren, L. Jones, G. T. Martinez, M. Simson, M. Huth, H. Ryll, H. Soltau, R. Sagawa, Y. Kondo, C. Ophus, P. Ercius, L. Jin, A. Kovács, P. D. Nellist, Electron ptychographic phase imaging of light elements in crystalline materials using Wigner distribution deconvolution, Ultramicroscopy 180 (2017) 173–179.

[70] M. P. Oxley, O. E. Dyck, The importance of temporal and spatial incoherence in quantitative interpretation of 4D-STEM, Ultramicroscopy 215 (2020) 113015.

[71] C. J. Humphreys, The scattering of fast electrons by crystals, Rep. Prog. Phys. 42 (1979) 1825–1887.

[72] H. Bethe, Theorie der Beugung von Elektronen an Kristallen, Ann. Phys. (Berl.) 392 (1928) 55–129.
[73] J. M. Cowley, A. F. Moodie, The scattering of electrons by atoms and crystals. I. A new theoretical approach, Acta Crystallogr. 10 (1957) 609–619.

[74] P. Goodman, A. F. Moodie, Numerical evaluations of N-beam wave functions in electron scattering by the multi-slice method, Acta Crystallogr. A 30 (1974) 280–290.

[75] M. L. Odlyzko, J. T. Held, K. A. Mkhoyan, Atomic bonding effects in annular dark field scanning transmission electron microscopy. II. Experiments, J. Vac. Sci. Technol. A 34 (2016) 041603.

[76] C. Ophus, A fast image simulation algorithm for scanning transmission electron microscopy, Adv. Struct. Chem. Imaging 3 (2017) 1–11.

[77] M. D. Graef, M. Jackson, J. Kleingers, C. Zhu, joseph tessmer, wlenthe, saransh13, M. Atkinson, S. Wright, H. Ånes, EMsoft-org/EMsoft: EMsoft Release 5.0.0, 2019. doi:10.5281/ZENODO.3489720

[78] L. J. Allen, A. J. D’Alfonso, S. D. Findlay, Modelling the inelastic scattering of fast electrons, Ultramicroscopy 151 (2015) 11–22.

[79] I. Lobato, D. Van Dyck, MULTEM: A new multislice program to perform accurate and fast electron diffraction and imaging simulations using Graphics Processing Units with CUDA, Ultramicroscopy 156 (2015) 9–17.

[80] J. O. Oelerich, L. Duschek, J. Belz, A. Beyer, S. D. Baranovskii, K. Volz, STEMsalabim: A high-performance computing cluster friendly code for scanning transmission electron microscopy image simulations of thin specimens, Ultramicroscopy 177 (2017) 91–96.

[81] A. Pryor, C. Ophus, J. Miao, A streaming multi-GPU implementation of image simulation algorithms for scanning transmission electron microscopy, Adv. Struct. Chem. Imaging 3 (2017) 1–14.
[82] J. Barthel, Dr. Probe: A software for high-resolution STEM image simulation, Ultramicroscopy 193 (2018) 1–11.

[83] H. Brown, P. Pelz, C. Ophus, J. Ciston, A Python Based Open-source Multislice Simulation Package for Transmission Electron Microscopy, Microsc. Microanal. (2020) 1–3.

[84] A. Paszke, S. Gross, F. Massa, A. Lerer, J. Bradbury, G. Chanan, T. Killeen, Z. Lin, N. Gimelshein, L. Antiga, A. Desmaison, A. Kopf, E. Yang, Z. DeVito, M. Raison, A. Tejani, S. Chilamkurthy, B. Steiner, L. Fang, J. Bai, S. Chintala, PyTorch: An imperative style, high-performance deep learning library, in: H. Wallach, H. Larochelle, A. Beygelzimer, F. d’Alché Buc, E. Fox, R. Garnett (Eds.), Advances in Neural Information Processing Systems 32, Curran Associates, Inc., 2019, pp. 8024–8035.

[85] R. Okuta, Y. Unno, D. Nishino, S. Hido, C. Loomis, CuPy: A NumPy-compatible library for NVIDIA GPU calculations, in: Proceedings of Workshop on Machine Learning Systems (LearningSys) in The Thirty-first Annual Conference on Neural Information Processing Systems (NIPS), 2017.

[86] S. K. Lam, A. Pitrou, S. Seibert, Numba: A LLVM-based python JIT compiler, in: Proceedings of the Second Workshop on the LLVM Compiler Infrastructure in HPC, LLVM ’15, Association for Computing Machinery, New York, NY, USA, 2015.

[87] A. H. Larsen, J. J. Mortensen, J. Blomqvist, I. E. Castelli, R. Christensen, M. Dulak, J. Friis, M. N. Groves, B. Hammer, C. Hargus, E. D. Hermes, P. C. Jennings, P. B. Jensen, J. Kermode, J. R. Kitchin, E. L. Kolshbjerg, J. Kubal, K. Kaasbjerg, S. Lygaard, J. B. Maronsson, T. Maxson, T. Olsen, L. Pastewka, A. Peterson, C. Rostgaard, J. Schiøtz, O. Schütt, M. Strange, K. S. Thygesen, T. Vegge, L. Vilhelmsen, M. Walter, Z. Zeng, K. W. Jacobsen, The atomic simulation environment—a Python library for working with atoms, J. Phys. Condens. Matter 29 (2017) 273002.
[88] B. H. Savitzky, L. Hughes, K. C. Bustillo, H. D. Deng, N. L. Jin, E. G. Lomeli, W. C. Chueh, P. Herring, A. Minor, C. Ophus, py4DSTEM: Open Source Software for 4D-STEM Data Analysis, Microsc. Microanal. 25 (2019) 124–125.

[89] M. N. Yesibolati, S. Laganà, H. Sun, M. Beleggia, S. M. Kathmann, T. Kasama, K. Mølhave, Mean Inner Potential of Liquid Water, Phys. Rev. Lett. 124 (2020) 065502.

[90] A. H. Larsen, M. Kuisma, J. Löfgren, Y. Pouillon, P. Erhart, P. Hyldgaard, libvdwxc: a library for exchange–correlation functionals in the vdW-DF family, Model. Simul. Mat. Sci. Eng. 25 (2017) 065004.