0.7 Å Resolution Electron Tomography Enabled by Deep-Learning-Aided Information Recovery

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The 3D determination of a nanomaterial’s atomic structure is crucial for understanding their physical, chemical, and electronic properties. Electron tomography, as an important 3D imaging method, offers a powerful method to probe the 3D structure of materials from nanoscale to atomic scale. However, the grand challenge—the missing-wedge-induced information loss and artifacts—has greatly hindered them from obtaining 3D atomic structures with high contrast, high precision, and high fidelity. Herein, for the first time, by combining atomic electron tomography with an artificially intelligent “deepfake” neural network, this work demonstrates that the resolution of 3D imaging can be improved down to 0.71 Å, which is a record high resolution achieved by electron tomography. It is also shown that the lost information in reconstructed tomograms can be effectively recovered by only acquiring data from −50 to +50 ° (44% reduction of dosage compared with −90 to +90 ° full tilt series). In contrast to conventional methods, the deep-learning model shows outstanding performance for both macroscopic objects and atomic features solving the long-standing dosage and missing-wedge problems in electron tomography. This work provides important guidance for the application of machine learning methods to tomographic imaging atomic-scale features in nanomaterials.

As the architectural complexity of integrated circuits and functional nanomaterials advances into the atomic-scale regimes, high-resolution transmission electron microscopy (TEM) has become an essential tool in validating the structure of nanomaterials and devices. In contrast to conventional TEM imaging, which only provides projected 2D information, electron tomography is a powerful tool that can probe the 3D internal structure and chemistry of materials at the nanoscale and the atomic scale. Due to its high resolution, it has been widely used in biological, physical, and materials science applications. Recently, with the development of discrete tomography and atomic-scale electron tomography, deciphering the structure of materials atom by atom has become possible. Electron tomography renders 3D reconstruction of an object by taking a series of 2D projections from a wide range of orientations. Ideally, projection images from −90° to +90° around a fixed axis are needed to render a perfect 3D reconstruction. However, due to the limited space in an electron microscope or shadowing from the holder/sample/support, it is hard to obtain projections for the full tilt range in many conditions. With a specialized tomography holder, images from −70° to +70° can be obtained in most TEMs, whereas in liquid-cell tomography, the tilt range is very limited to typically <30°, because the liquid flow holders are much bulkier. The limited tilt range unavoidably leads to a “missing wedge” of information, which renders artifacts in the reconstructed tomograms. These artifacts introduced by the missing wedge reduce the resolution and reliability of the reconstructed tomograms and, sometimes, can even lead to serious misinterpretations. So far, the missing-wedge problem has been the main source of systematic error that limits the application of electron tomography.

Mathematically speaking, when there are insufficient number of projections, the inverse problem of tomography is ill-posed, because the solution is non-unique. Therefore, to constrain the solution space, strong priors need to be used to regularize the problem. For example, total variance minimization (TVM) combines iterative reconstruction and regularization of total variance to recover the lost information and reduces the artifacts introduced by the missing wedge. This method is inspired by compressive sensing and it essentially deploys the sparsity constraint in the gradient domain of the tomogram. Some caveats of TVM are that it is not parameter-free and is also computationally expensive. Keeping these aside, the real problem of TVM or any generalized TVM approach is that they are bound to one regularization that promotes one prior constraint on the solution, which may or may not be suitable for the object of interest. For example, TVM promotes piecewise constants, rendering cartoon-like tomograms lacking gradient details.
Instead, it is highly suitable to treat this problem as a classification and inpainting problem, which involves the recognition of artifacts and the inpainting of the “correct” information.

Recently, the emerging and rapidly evolving deep-learning field has significantly contributed to the development of image processing and microscopy. In particular, convolutional neural networks (CNN), a class of deep neural networks, have been widely applied in multiple fields, including image and video recognition, super resolution, image segmentation, and medical image analysis.

By taking advantage of deep learning, for the first time, we introduce a deep-learning-based information-recovering model based on the U-Net++ neural network to recover the lost information and remove artifacts in the reconstructed tomograms of atomic electron tomography. Compared with the conventional methods, our deep-learning model has free parameters and shows outstanding performance on both macroscopic and atomic objects. In particular, we show that this method has improved the resolution of atomic electron tomography to 0.71 Å, which is the highest resolution achieved by any 3D imaging method thus far.

To train a deep-learning model for information recovery and artifact removal, a training library with a range of missing wedge and a collage of spatial features is built. To train our deep-learning model, we constructed an information recovery and de-artifact model (IRDM) by combining generative adversarial network (GAN) and U-Net++. Figure 1a shows the training pipeline of IRDM, and Figure 1b shows the detailed structure of the generator and discriminator.

![Figure 1. a) The training pipeline of the IRDM. b) Structure of the generator and discriminator.](image-url)
keeps generating de-artifact images to deceive the discriminator, whereas the discriminator tries to judge whether the images are fake or ground truth. Then, the GAN loss for the generator, which is derived from the judgment of discriminator, will contribute to the backward propagation to improve the generator. In the meantime, a GAN loss for the discriminator will be calculated to strengthen the discriminator’s capability. In addition, condition GAN is used to stabilize the training and, thus, improve the GAN’s performance. Based on a training dataset (D2 in Table S1, Supporting Information), we trained and evaluated the performance of the IRDM. Figure 2 shows the reconstructions of a random “phantom face” using IRDM, weighted back-projection (WBP), simultaneous algebraic reconstruction technique (SART), and TVM, respectively. With missing wedges ranging from 40° to 80°, the reconstruction by the conventional WBP method shows severe information loss (blurring at top and bottom edges) and artifacts such as long tails and elongation along the vertical direction (see another example in Figure S1, Supporting Information). Although the SART and TVM methods can effectively suppress the long tail artifacts to some extent, the blur and elongation still exist. In contrast to SART and TVM, the tomograms processed by IRDM look almost identical to the ground truth with no obvious long tails, blurs, and elongation along the vertical direction, which indicates that our deep-learning model has outstanding information recovering and de-artifacting capabilities. With the missing wedge increased, both the information loss and artifacts become more prominent; however, the performance of IRDM still remains robust even with a missing wedge up to 80°. Besides “phantom face,” real medical images (i.e., brain CT images) are also used to further evaluate the effectiveness of IRDM. Figure 3 shows the reconstruction of a brain CT image with IRDM, WBP, SART, and TVM. In good agreement with the result in Figure 2, IRDM also shows robust capability of information recovering and de-artifacting of the brain image with a missing wedge up to 80°.

To test the influence of the composition of training features and the included range of missing wedges in the library on the performance of IRDM, datasets (see details in Table S2, Supporting Information) with different composition and ranges of missing wedge were created and tested. For D1–D3, the composition of the datasets is different, whereas the training ranges of missing wedges are kept the same (40°–60°). For datasets

![Figure 2](image-url). Evaluation of IRDM in comparison with conventional methods by “phantom face” reconstruction. The “phantom face” with different missing wedges is reconstructed by WBP, SART, TVM, and IRDM, respectively. The lower panels show enlarged images of the boxed regions in upper panels.
D3–D6, the composition of the datasets is exactly the same, whereas the training ranges of missing wedge are different. Figure 4a shows the average peak-signal-to-noise ratio (PSNR) and structural similarity index measure (SSIM)\(^{(45)}\) of SART, TVM, and IRDM trained on datasets with different compositions but the same missing wedge from 40° to 60°. PSNR, which is a ratio between the maximum possible power of a signal and the power of corrupting noise that affects the fidelity of its representation, is mainly used to evaluate the denoise performance of different algorithms on tomographic reconstructions. SSIM is used for measuring the similarity (profiles of the subobjects) between the reconstructed tomogram and the corresponding ground truth. The results show that the IRDM exhibits evidently improved PSNR and SSIM compared with WBP and SART. However, it does not show much improvement in PSNR and SSIM compared with TVM. To further evaluate the performance of TVM and IRDM, normalized root-mean-square deviation (NRMSE) is calculated and plotted. NRMSE is an index to evaluate the overall difference between the reconstructed image and the original image. The smaller the value is, the closer the reconstructed image is to the original image. Figure 4b shows the average NRMSE of TVM and IRDM trained on datasets with the same data composition but different ranges of missing wedge. Compared with dataset D1, which only comprises of “phantom face” data, the more diverse dataset D2, which includes “phantom faces” as well as tumor and brain data, shows lower NRMSE, thereby improving information recovery and de-artifact capability. However, by adding more complexity to the training dataset with ImageNet data labeled with dogs, the IRDM trained on D3 yields higher NRMSE, thereby reducing information recovering and de-artifacting capability for data with a missing wedge from 40° to 60°. Notably, for data with a larger missing wedge beyond the training range, e.g., more than 65°, IRDM trained on D3 shows much lower NRMSE than that trained on D2, which means although adding diversity to the training datasets may slightly degrade the performance of IRDM on data within the range of trained missing-wedge angles, it will certainly improve the robustness of IRDM in a larger range of missing wedge. Furthermore, we explored the influence of the training range of missing wedge on the performance of the IRDM. From D5 → D4 → D3 → D6, the training ranges of missing wedge are gradually widened. Figure 4c,d shows the NRMSE of IRDM trained on D3–D6 and the TVM method. The result shows that IRDM trained on dataset D5 with the narrowest training range of missing wedge shows lowest NRMSE, thereby showing best performance in range of missing wedge from 50° to 53°; however, at higher missing wedge beyond the training range (47.5°–52.5°), the performance of IRDM trained on D5 deteriorates rapidly. In contrast, for IRDM trained on D6 with the broadest training range of missing wedge (35°–65°), although its NRMSE is slightly higher than that trained on D5 and D4, it shows lowest NRMSE for data with

![Figure 3. Evaluation of IRDM in comparison with conventional methods by brain image reconstruction. The brain image with different missing wedges is reconstructed by WBP, SART, TVM, and IRDM, respectively. The lower panels show enlarged images of the boxed regions in upper panels.](image-url)
missing wedge beyond 62.5°. In addition, it is worth noting that IRDM trained on D6 always shows much lower NRMSE than that of conventional TVM methods.

To confirm the validity and robustness of our deep-learning model, for the first time, we applied IRDM to information recovery and de-artifact for atomic electron tomography with a missing wedge of approximately 40°. Figure 5a shows a representative view of the 3D atomic reconstruction of a gold crystal (see details in Experimental Section) using the conventional WBP method. The power spectrum (lower panel of Figure 5a) in Fourier space shows Bragg spots corresponding to [220] planes of the crystal (higher order Bragg spots represent higher resolution) with a resolution of approximately 1.42 Å. It is easy to see that a missing-information wedge outlined by blue dot lines evidently exists in the diffractogram of the reconstruction. By applying IRDM to the WBP reconstruction, the artifacts introduced by missing wedge and the noise in the reconstruction are effectively eliminated. As a result, some of the higher order Bragg spots corresponding to [242] and [440] planes (indicated by ovals in Figure 5b), which are not resolved in the WBP reconstruction (Figure 5a), are recovered by the IRDM algorithm. The [242] and [440] Bragg spots correspond to a resolution of 0.83 and 0.71 Å, respectively. Note that a resolution anisotropy is identified in the reconstruction, which is believed to be caused by the anisotropic information for different planes of a plane family obtained during sample tilting along a chosen tilting axis, which does not reflect an anisotropic information recovering by the IRDM. In addition, a detailed analysis was also carried out on the power spectrum along the [112] zone axis (Figure S4, Supporting Information), and the result agrees well with that shown in Figure 5.

The performance of the IRDM is dependent on both the type and composition of the training data. As shown in Figure 4b, the performance of D1, which only contains “phantom faces,” is not as robust as D2, which contains three types of data, including “phantom faces, brain, and tumor CT images,” even though they have the same size of training data. Compared with D1, D2 is a more diverse dataset comprised of different types of data, but still shares some similarities. Therefore, the robustness of IRDM trained on D2 is much higher than that trained on D1. Moreover, by adding more diverse data, i.e., images of dogs, with distinct features from the data in D2, D3 shows a slightly reduced performance in the range of lower missing wedge; however, it shows higher robustness for higher missing wedge up to approximately 75°. It indicates that, in general, the robustness and stability of the IRDM will be improved in wider missing wedges, if trained on a dataset with high complexity. Nevertheless, it should be noted that when missing wedge goes far beyond the missing-wedge range in which the model is trained, for example approximately 75°,
the performance of the model becomes somewhat limited and unpredictable. The possible explanation is that only a relatively small missing-wedge range, i.e., from 40° to 60°, is covered by D1–D3 during training. Therefore, for data with large missing wedge, the IRDM trained with similar missing wedge should produce the best performance. Moreover, it is worth noting that in this work, although the training datasets are not directly related to tilt series of atomic images, excellent information recovery performance was obtained. The rationale behind the success is that compared with the objects in the training datasets, i.e., “phantom faces” and images of brains, tumors, and dogs, the features of atomic images are much simpler with regard to the shape of atomic columns as well as their brightness and contrast distributions. That is to say, similar features, although in different scales, are fully covered by the current training datasets. In this way, the features of atomic images can still be effectively recognized via generalization of the IRDM trained by current training datasets.

With widening of the missing wedge, the feature of the objects will be significantly changed by artifacts. For example, the reconstruction of the brain images with a missing wedge of 40° shows a rounded shape similar to the original one. In contrast, with the missing wedge increased to 80°, the bottom of the brain turns into a sharp ridge, which significantly deviates from the original shape of the brain. Different from Gaussian noise, the distribution of this kind of artifacts introduced by missing wedge will remarkably change with missing-wedge angles, and it cannot be effectively eliminated by applying the IRDM trained on a dataset with missing wedge far different from that of the data. Therefore, to achieve the best performance, training data sets with missing wedges similar to that of the experimental data should be applied.

To make our deep-learning model universally applicable to different types of objects and sceneries, the training database should be as large, diverse, and complex as possible, which, however, will require massive computing resources and data sources. In practice, if the database is not big and diverse enough, the optimal strategy to achieve the best information recovery and de-artifact effect is to try to find a minimum inclusion matrix (training dataset), which shares the highest feature similarity with the data. For example, for “phantom faces” with missing wedge between 40° and 60°, training dataset (shown in Figure 6a) as indicated in Figure 6 is the most appropriate training dataset. If we expect the model works for both brain images and “phantom faces,” training dataset shown in Figure 6b (for missing wedge between 40° and 60°) and training dataset shown in Figure 6c (for missing wedge around 80°) are appropriate choices. Data size is another factor, which has influence on the performance of IRDM. For example, if the size of training dataset (shown in Figure 6b) is limited, the performance of IRDM on brain images or “phantom face” data will degrade. Then, as an alternative, a more diverse training dataset, e.g., dataset (shown in Figure 6d) with dog images added in, could be used to improve the robustness of IRDM.

The missing-wedge (or missing cone) problem is not unique in electron tomography, but has been observed in other imaging systems.
modalities, such as X-ray CT, optical diffraction tomography (ODT), and magnetic resonance imaging (MRI). Addressing the missing-wedge or missing-cone problem is one of the major research thrusts in these fields. Similar to that in ODT, regularization techniques such as TVM have also been applied in electron tomography. However, the main drawback of regularization techniques is that they are bound to one regularization that promotes one prior constraint on the solution, which may or may not be suitable for the object of interest. So far, regularization techniques for electron tomography have proved useful for data with small missing wedge; however, they fall short in solving the large missing-wedge problem. Although designing a more complex regularization formulation may alleviate this problem to some extent, to design such a better regularization formulation still remains a grand challenge to date. In contrast to conventional regularization techniques, the deep-learning approach proposed in this work effectively solve the missing-wedge problem through deep learning of the regularization properties of the data itself. Compared with the regularization methods, the advantages of the deep-learning model are: 1) no regularization formulation is needed; 2) the reconstruction no longer requires multiple iterations, which involves hyper-parameter tuning; 3) performance improvements can be easily achieved by annotating more data and building larger models; and 4) the model design of deep learning is flexible and can be extended to other similar tasks. Therefore, the deep-learning model described in this work can be deployed to other fields, such as CT, ODT, and MRI.

In this work, we demonstrate a deep-learning-based inpainting method, which enables us to achieve 3D imaging of nanosized metals with significantly improved resolution and quality. The 0.71 Å resolution achieved in this work will significantly improve our capabilities to localize and differentiate atoms with different atomic numbers and local coordination environment, and thus opens the possibility of 3D visualization and quantification of a variety of materials atom by atom.

**Experimental Section**

**Structure of Generator and Discriminator.** The IRDM is trained by the GAN structure with U-Net++ as a generator. U-Net++ is an encoding-decoding structure with cross-layer connections to compensate the feature information loss during the encoding–decoding process. The cross layers between encoder and decoder are DenseNet blocks, which can enhance the flow of information and the efficiency of parameters utilization. Each Conv Layer in Figure S2, Supporting Information, contains two alternating stacks of convolution layer, batch normalization, and SELU activation function. A max pooling is used to reduce the dimension, which is similar to an encoder. After max pooling for four times, we use Conv Layer with upsampling as a decoder to recover the dimension. The input of U-Net++ is a WBP iradon transform from a sinogram with missing wedge, and the output is an image after information recovering and de-artificing. For discriminator, as shown in Figure S3, Supporting Information, we use a normal stack convolution layer structure similar to the network structured developed by the Visual Geometry Group. We stack convolution layer, batch normalization, LeakyReLU activation function, and max pooling as a Conv Layer in the first four layers. For the fifth layer, we replace max pooling with average pooling to reduce information loss. A single convolution layer is used as the last output layer without activation function.

**Loss Function:** In our model, different from the joint loss in standard U-Net++, we only use the output from right layer to compute loss. Least squares generative adversarial network (LSGAN) is used to compute the loss for generator and discriminator, as least squares loss is stable and straightforward with lower computational cost, and it can eliminate gradients vanishing. Furthermore, by replacing the absolute discriminator loss with relativistic discriminator loss, we get relativistic average LSGAN (RaLSGAN) loss functions shown as follows

\[
L_{RaLSD} = \left[ |D(x_{\text{real}}) - E[D(x_{\text{fake}})]| - 1 \right]^2 + |D(x_{\text{fake}}) - E[D(x_{\text{real}})] + 1|^2
\]

\[
L_{RaLSG} = \left[ |D(x_{\text{real}}) - E[D(x_{\text{fake}})]| + 1 \right]^2 + |D(x_{\text{fake}}) - E[D(x_{\text{real}})] - 1|^2
\]

\[
x_{\text{fake}} \rightleftharpoons G(x_{\text{input}})
\]
Equation (1) and (2) are the loss functions for the discriminator and generator, respectively. $x_{\text{input}}$ and $x_{\text{output}}$ are the input and output data of the generator and discriminator, respectively. $x_{\text{real}}$ is the ground truth. $E[I]$ is the average operation of minibatch when loading from the dataset.

**Training Strategy:** The training parameters for IRDM are summarized in Table S5, Supporting Information. The total training epochs are 60. The training frequency ratio of discriminative and generative is 1:1. We set the learning rate as $1e^{-4}$ and the rate decays at the 45 and 55 epochs by multiplying 0.1. The training weight decay is $1e^{-4}$. We set minibatch size as 32 and use four Nvidia 1080TI graphics processing units.

Atomic Electron Tomography Experiments: Electron tomography experiments were performed on an aberration-corrected field-emission instrument operated at 300 kV. High-angle annular dark-field scanning transmission electron microscopy (HAADF-STEM) imaging was conducted with a probe semi-convergence angle of 24.9 mrad and a camera length of 90 mm. Nanoporous gold sample (some sample preparation details in the previous study) containing interconnected nanoligaments was used for the electron tomography experiments. Tilt series of HAADF-STEM images were obtained within a tilting range of ±70° with an interval of 1°–2°, using Fischione 2020 advanced tomography holder. The tilt series were aligned by cross-correlation function and reconstructed by custom-written Matlab scripts. The 3D reconstructions are visualized by Avizo.

**Supporting Information**

Supporting Information is available from the Wiley Online Library or from www.advancedsciencenews.com.

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**Conflict of Interest**

The authors declare no conflict of interest.

**Keywords**

3D imaging, artificial intelligence, atomic structures, electron tomography, machine learning, sub-angstrom

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