RAPID imaging provides numerous opportunities with deep learning

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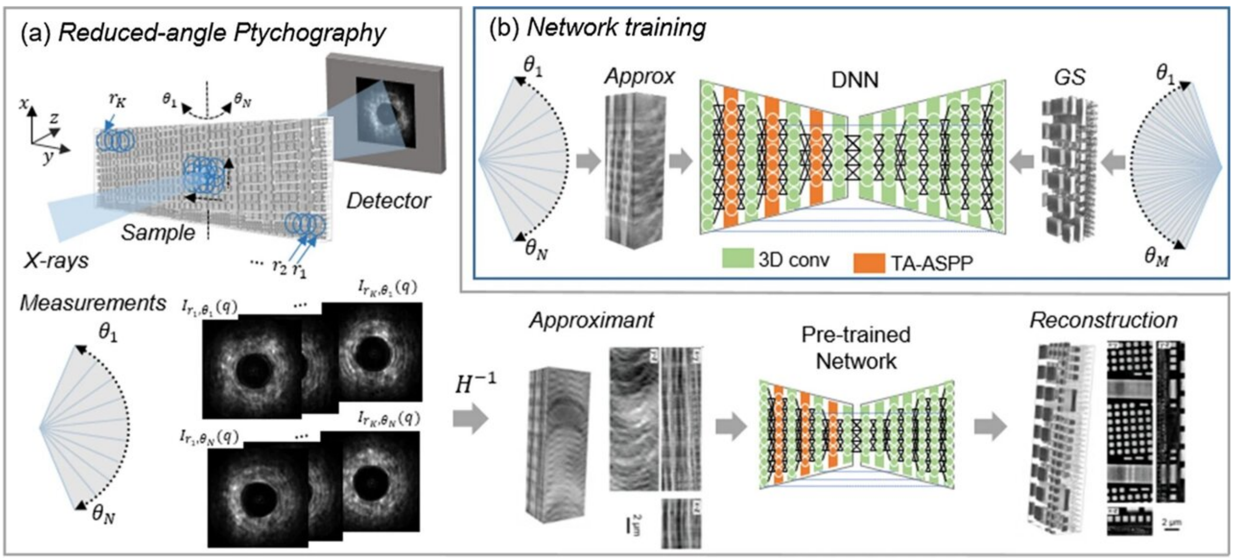

Schematic of the proposed RAPID framework. **a** Reduced-angle ptycho-tomography experiment to collect diffraction pattern measurements via translational and rotational scanning. Raw diffraction patterns are pre-processed to generate the approximant as the input to the pre-trained network, and volumetric distribution are obtained as the final output. **b** Network training process. Diffraction patterns acquired from reduced-angle ptycho-tomography are pre-processed to get the approximant as the network input, and a two-step conventional approach is employed to generate the high-resolution golden standard (GS) as the ground truth to train the DNN. Credit: *eLight* (2023). DOI: 10.1186/s43593-022-00037-9

Three-dimensional (3D) imaging at the nanometer scale enables important insights in biology and material behaviors, including virus function, structural damage, and nanoelectronics.

One way is to do this destructively. Researchers would immobilize their specimen, etch the top layer finely with a particle beam, image the revealed features with a scanning electron microscope or similar high-resolution methods, and repeat this process until the entire specimen volume has been consumed. However, in many instances, it is preferable to operate non-destructively, and then a form of tomography is necessary.

In a new paper published in *eLight*, a team of scientists led by Professor Ziling Wu from the Massachusetts Institute of Technology, developed a new reconstruction method for 3D imaging.

The research team used integrated circuits (IC) as an exemplar because they presented some practical conveniences. ICs are rigid and, thus, require no fixing. They are also very useful in manufacturing process verification, failure analysis and counterfeits detection. On the other hand, the challenge of 3D IC imaging grows with time due to Moore's law.

For nondestructive 3D IC imaging at the nanoscale, hard X-rays are ideal probes because of their long penetration depth and short wavelength. Unlike medical X-ray tomography, however, which operates almost always on the intensity of the projections, in the nanoscale case it is common to seek the complex field via ptychography first, and then do tomography. This combined scheme is also known as X-ray ptychographic tomography (ptycho-tomography).

There are several reasons to do this. For example, if the projection approximation is still applicable, then scientists can perform two tomographic reconstructions in parallel. Most materials exhibit phase variations by 10 times larger than their respective absorption changes.

X-ray ptycho-tomography reconstructions are performed in the same sequence as experimental acquisition, in a two-step approach. First, 2D projections are retrieved from far-field diffraction patterns using phase-retrieval algorithms, and then, tomographic reconstructions are implemented to recover the real and/or imaginary parts of a 3D object from 2D projections.

Many applications have been successfully demonstrated with this two-step approach. These applications include IC imaging, microscopic organism imaging and studies of material properties such as fracture, percolation and hydration. However, both ptychography and tomography demand large redundancy in the data, leading to long acquisition and processing times generally.

One way to reduce the acquisition time is through high-precision scanners that can reliably work with efficient scanning schemes and at high scanning velocities. Reducing the data redundancy requirements in ptycho-tomography is an alternate way to speed up data acquisition but introduces ill-posedness. However, with reduced data, the conventional reconstruction algorithms are likely to produce artifacts and a general loss of fidelity.

Supervised learning approaches often is a cause for concern regarding the generalization ability to new and unseen data. The researchers proposed a strategy to train on a subset of the sample, where a trustable but otherwise very slow alternative method can be used to obtain ground truths; and then use the train network on the rest of the sample, significantly speeding up the entire operation. This approach is appealing for integrated circuits or other large 3D specimens.

It is possible that transfer learning might alleviate the efforts for training RAPID anew for new experiments. For even more general specimens, like viruses and nanoparticles, comparable performance may be expected, but most likely at the cost of some redesign in the learning architecture.

More information: Ziling Wu et al, Three-dimensional nanoscale reduced-angle ptycho-tomographic imaging with deep learning (RAPID), *eLight* (2023). DOI: 10.1186/s43593-022-00037-9

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