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Perspective

Cryogenic Electron Microscopy for Characterizing and Diagnosing Batteries

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Most battery materials are beam sensitive, especially after cycling, which can be hardly characterized by electron microscopy (EM) with a high-energy beam. Inspired by structural biology, cryogenic EM (cryo-EM) offers a way to preserve the native state and image the battery materials at the nano/atomic scale. In this perspective, we highlight strategies on how to preserve the pristine intrinsic information of battery materials in terms of sample preparation, transformation, and imaging. Some key technical breakthroughs for the development of the cryo-EM are briefly illustrated to demonstrate its working principles. Recent achievements on cryo-EM characterization of battery materials are reviewed, especially Li metal. These profound observations demonstrate the increasing essential role of cryo-EM on diagnosing and characterizing the chemical, morphological, and atomic structure of battery materials. The new insights and knowledge obtained through this emerging new toolset will benefit the battery research field tremendously.

Introduction

The energy density of the state-of-the-art lithium (Li) ion batteries using transition metal oxides as cathode and graphite as anode have almost reached their theoretical specific energy density ($\sim$350 Wh/kg). To break this bottleneck and achieve higher energy density, such as the 500 Wh/kg requested by the Battery500 consortium, researchers consider the use of light elements (non-transition metals) replacing transition metals for the cathode, electrolyte, and anode. For example, lithium-sulfur (Li-S) and Li-oxygen (Li-O$_2$) are considered as next-generation batteries due to their high specific energy gravimetrically. Both the pristine materials and reaction intermediates, such as Li metal, lithium (poly)sulfides, and lithium (per)oxides are highly reactive and very sensitive to air and electron beams. This fragile nature requires the modification and improvement of the well-established characterization tools, which have been mainly dedicated to intercalation materials based on graphite or transition metal oxides. It is challenging to prepare a pristine and clean sample and obtain intrinsic information without any artifacts, especially for electron microscopy (EM).[1]

Recently, cryogenic EM (cryo-EM) has achieved great success in the materials research field,[2–9] such as nanoparticles, polymer, metal-organic frameworks, and battery materials, although the tool was originally developed for the biological community.[10,11] Cryo-protection not only helps to minimize damage from air and the beam, but also preserves the intrinsic structure of the samples, which enables us to image the structure of the light compounds at the nano/atomic scale, such as Li metal and its solid-state electrolyte interphase (SEI).[5] The new insights discovered using cryo-EM are intriguing and significant, such as the amorphous nucleation of

Context & Scale

Developing next-generation high-energy batteries requires the use of light elements (non-transition metals) for the cathode, electrolyte, and anode to achieve higher energy density, such as lithium-sulfur, lithium-oxygen, and solid-state electrolytes. However, both the pristine materials and reaction intermediates, such as Li metal, lithium (poly)sulfides, and lithium (per)oxides, etc., are highly reactive and very sensitive to air, moisture, and experimental probes (e.g., electron beam), bringing many challenges to characterize and diagnose these materials without any artifact. Inspired by structural biology, cryogenic electron microscopy (cryo-EM) offers a way to preserve the native state and image the cycled battery materials at the nano/atomic scale. In this perspective, we highlight strategies on how to preserve the pristine intrinsic information of the battery materials in terms of sample preparation, transformation, and imaging. We illustrate some key technical breakthroughs for the development of cryo-EM to show the working principles of cryo-EM compared with conventional EM. We review the recent
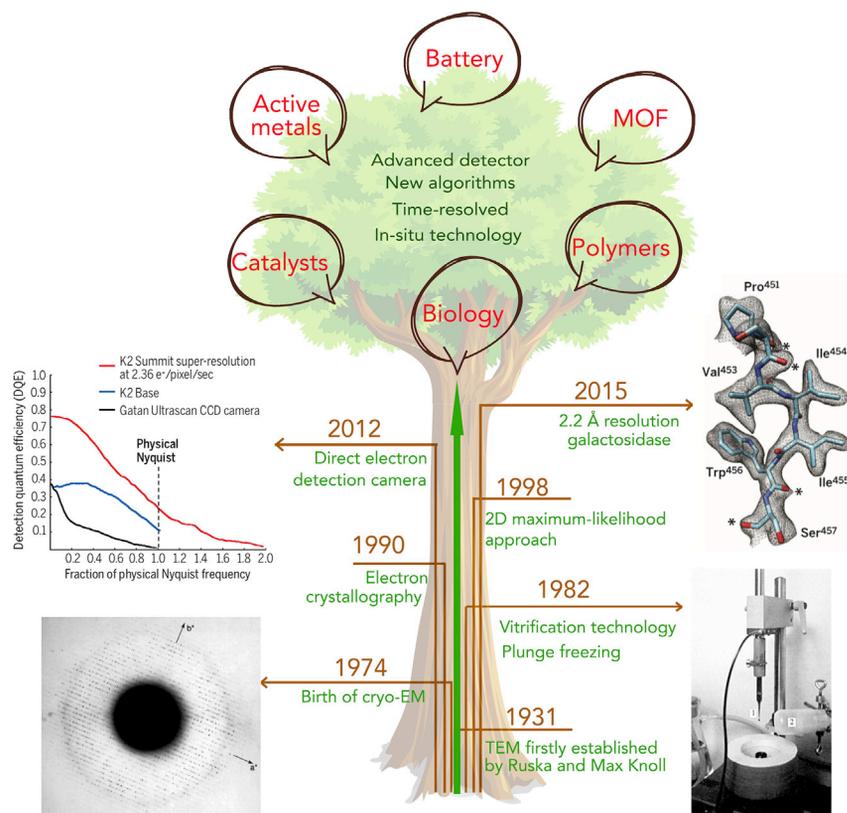
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achievements made using cryo-EM and propose some suggestions on the benefits of cryo-EM to future materials research. These profound observations demonstrate the increasingly essential role of cryo-EM on diagnosing and characterizing battery materials and inspire more researchers to use cryo-EM and make more unprecedented progress.

Figure 1. Schematic of the Development History of Cryo-EM—from Structural Biology to Materials Science

Li metal at the beginning of the electrochemical deposition.[5] These findings have inspired more researchers to use cryo-EM and make unprecedented progress in characterizing and diagnosing next-generation high-energy materials for batteries.

To introduce the cryo-EM technique to the materials researchers, this perspective focuses on how to acquire a real structural and chemical image by cryo-EM and what opportunities it will bring to the battery field. First, we briefly review the development of cryo-EM, and then transfer the knowledge from the biological material field to the battery material field (Figure 1). Sample preparation and evaluation is highlighted to maintain a pristine and clean sample and obtain intrinsic information using cryo-EM. We review the recent achievements made using cryo-EM and propose some suggestions on the benefit of cryo-EM to future battery research.

Development of Cryo-EM and Lessons Learned from Structural Biology

As one of the main structural techniques complementary to X-ray crystallography, transmission electron microscopy (TEM) was first developed in 1933 (Figure 1) on the basis of the electron-focusing magnetic lens, which overcomes the resolution barrier imposed by visible light.[12] To directly visualize biological macromolecules using TEM, three major methodological bottlenecks have been addressed. First, the samples need to be preserved under the ultra-high vacuum conditions of the TEM. Otherwise the vacuum will cause dehydration and destroy the sample's structural integrity. This difficulty was resolved by frozen hydration (vitrification), which was invented by Taylor and Glaeser,[13] who initiated the field of cryo-EM. This approach was further improved by Dubochet and colleagues for practical

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applications via cryo-plunging of thin solution into a potent cryogen such as liquid ethane,[10,14] which is still used today.

Subsequently, TEM images were used to produce 2D projections of the object but not its 3D structure. 3D reconstruction was thus developed.[15] For membrane proteins and other 2D crystals, Henderson and colleagues pioneered work on 2D electron crystallography, which combined all the images and electron diffraction patterns from different angles and achieved the atomic structure of bacteriorhodopsin (3.5 Å).[16] For a single particle with conformational or compositional heterogeneity, the maximum-likelihood (ML) approach was introduced by Sigworth for computational aligning and combining cryo-EM images from many randomly oriented biological molecules.[17] This ML approach endows the capability to capture the multiple structural states and provide insights into macromolecular dynamics. This approach is very useful when analyzing the heterogeneity of electrode materials and their SEI in porous 3D structures.

Minimizing the radiation damage by the high-energy electron beam is always necessary to image biological samples without any artifacts. The incident electrons can ionize the samples, break the bond (referred to as primary damage), and produce free radicals and secondary electrons that cause further chemical reactions (referred to as secondary damage).[18] An effective solution is to limit the exposure of the specimen to incident electrons and cool the samples to reduce the primary and secondary damage, respectively. Low electron dose is used for biological samples to achieve a high-resolution image with optimal signal-to-noise ratios. To gain a good signal, numbers of images (up to thousands) from identical single particles need to be averaged by the aforementioned electron crystallography and ML approach. A breakthrough was made by applying direct electron detection cameras (e.g., a K2 camera) in 2012, which allows researchers to record images as movie stacks at high frame rates.[19] Most importantly, this enables the correction of the beam-induced image motion and partially mitigates the radiation damage, solving the two most difficult problems in cryo-EM.[20] With these approaches, cryo-EM is able to determine a protein structure at a resolution up to $\sim$2.2 Å[21] and becomes a dominant and powerful technique for structural biology.[11,22]

The success of cryo-EM for biological materials inspired the extension of its use for other beam-sensitive materials in other fields, such as catalysts, polymers, and batteries. Patterson and colleagues used cryo-EM to directly observe the morphology evolution in macromolecular self-assembly, inorganic nucleation and growth, and the cooperative evolution of hybrid materials.[9] Our group revealed the nanostructure of electrochemically deposited Li metal (EDLi) and its SEI by cryo-EM.[5,23] Compared with biological samples, much attention and additional procedures are needed to deal with the battery materials, especially after cycling, which is not only very beam sensitive but also extremely air sensitive. We would like to highlight sample preparation to mitigate the potential damage and avoid the artifacts, which are specific for high-energy battery materials.

Safe and Robust Sample Preparation

To prepare a pristine and clean battery material sample without any contamination, we have developed two typical methods to mount the sample on a grid, load the grid onto a holder, and transfer the holder into the TEM, as illustrated in Figure 2.

Compared with directly dispersing the particles on the TEM grid, using a focused ion beam (FIB) technique is able to mount the target particle of interest on the grid
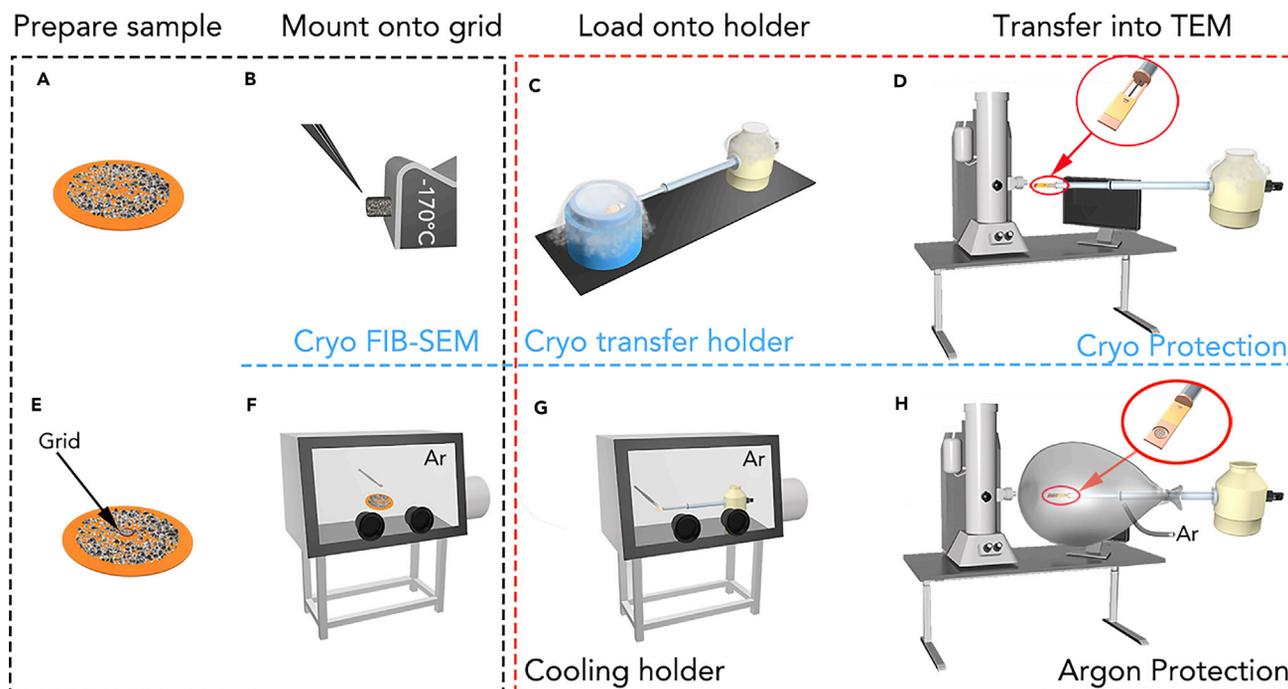
Figure 2. Schematic Images Showing the Processes to Prepare Sample, Mount to Grid, Load on Holder, and Transfer into the TEM Safely
(A) Sample dispersed on the subtract.
(B) Mount the sample on the grid by cryo-FIB-SEM.
(C) Load the grid onto the cryo transfer holder within the liquid N_2.
(D) Transfer the cryo transfer holder into the TEM with a closed shuttle.
(E) Samples directly deposited on the grid.
(F) Harvest the grid in the Ar-filled glovebox.
(G) Load the grid onto the cooling holder in the glovebox.
(H) Transfer the cooling holder into the TEM with Ar protection.

and control the thickness by milling (Figure 2B). The ion flux used for milling contains plenty of the high-energy Ga ions, which easily causes sample damage, including local heating, surface reconstruction, and Ga implantation, etc.[24] Both Li metal and S (sulfur) cathodes are subjected to melt and sublimation.[25] Even worse, the Li metal can react with Ga to form a Li-Ga alloy.[26] To reduce the above damage, cryo-FIB is essential to enable sample preparation for EM. By means of cryo-FIB, the slices containing the whole interfaces between deposited Li metal and the liquid electrolyte,[8] and between Li metal and artificial SEI,[27] were successfully acquired. It is worth mentioning that, even at the cryo temperature used, we still need to adjust the Ga flux for etching to minimize the potential damage based on the chemical components of the samples.[28]

For electrochemically deposited samples such as EDLi, we can directly plate it on the TEM sample grid (e.g., Cu with lacey carbon) in a coin cell (Figure 2E), which helps to maintain the intrinsic nature of the EDLi and mitigate any possible contamination or damage during sample preparation.[5,7,23] Since the grid is in the working cell, its effect on the growth of EDLi should be checked as well as its stability in the cell.[29] For the cycled samples, especially those with a SEI, we should pay much attention on the washing process (Figure 2F), which can dissolve and remove some of the SEI and lead to artifacts as demonstrated by X-ray photoelectron spectroscopy.[30]

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Once the samples are on the grid, it is still challenging to load the grid on the holder and transfer the holder into the TEM chamber without any air exposure. This process is much related with the type of the holder used for cryo-TEM. There are two commercially available holders developed for cryo-TEM: the cryo transfer holder (Figures 2E and 2D) and the cooling holder (Figures 2G and 2H). The former is to cool down the holder prior to loading the grid with sample onto the holder in liquid N_2, which is widely used for the biological samples. This method allows to keep the sample frozen at the cryo state and reduce the sample reactivity, but inevitably introduces some crystalline water on the grid during loading the grid onto the holder. Besides, the surface species, such as the SEI on the sample may be dissolved and washed away by the liquid N_2.

Alternatively, the cooling holder (Figure 2G) allows to cool the sample after inserting the holder into the TEM system, which requires protection by an inert gas, such as argon (Ar), in the glovebox or glovebag, as illustrated in Figures 2G and 2H.[23] This method is easier to access than that with a cryo transfer holder, but more care is needed to make sure that the sample is always protected by Ar. In this regard, developing a holder with a self-sealing function and faster cooling will be a new direction for developers of holders for cryo-EM.

All best practices mentioned above may guarantee a pristine battery material sample with minimum damage and contamination, and acquire intrinsic information without significant artifacts. To ensure the reproducibility of the data and comparison of observations among different research groups, detailed experimental conditions are of vital importance, and need to be mentioned in the experimental details section, especially the electron dose received in the sample. As cryo-EM is an emerging new tool for the materials science field, such data reporting will help the field to build a reliable and robust database.

Insights of Battery Materials from Cryo-EM

Although cryo-EM is still a new technique for battery materials, much profound progress has been made (summarized in Table 1), which may lead to new discoveries and breakthroughs in the future in materials science using cryo-EM.

Li metal is the most attractive anode material for rechargeable batteries due to its low electrode potential (−3.04 V versus a standard hydrogen electrode) and high theoretical specific capacity (3,860 mAh g^{-1}). However, little is known about the nanostructure and its correlation with electrochemical performance, or the proposed strategies to prevent dendritic growth and increase its columbic efficiency. This is because Li metal is so reactive and brittle that a slight harsh environment (e.g., exposure to air and a strong beam) can contaminate and damage the samples, leading to artifacts and controversial conclusions. Conventional TEM at room temperature fails to image the Li metal at the nanoscale because it will quickly drift, melt, and evaporate once the beam focuses on the sample. In contrast, at a cryo temperature, the Li metal is very stable under the same e exposure dose and is able to tolerate the higher electron dose needed for high-resolution imaging.[5] By means of cryo-TEM, our group firstly revealed the nanostructure of the EDLi and its SEI on the surface (Figures 3A and 3B). It is interesting to find out that the EDLi nucleates as an amorphous state (Figure 3B) and grows into crystalline ribbons.[5] The atomic structure of EDLi was further revealed (Figure 3C), which matches well with the cubic structural Li (*bcc*).[7] We also found that the SEI is unevenly distributed on the surface of EDLi, which contains crystalline LiF, Li_2O, and Li_2CO_3. Combining cryo-FIB and cryo-TEM, the Kourkoutis group was able to maintain the complete interface

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Table 1. Summary of the Recent Work on Cryo-EM in Battery Research

Objective	Transfer Protection Holder Type	Characterization Techniques	Important Findings	Reference
Plated Li metal	Ar and vacuum	cryo-TEM cryo-XRD	amorphous Li crystalline LiF	Wang et al.[5]
Plated Li metal	Ar cooling holder	cryo-TEM	LMC coated on the Li metal	Liu et al.[23]
Plated Li metal	cryo cryo transfer holder	cryo-TEM	atomic structure of Li mosaic and multilayer SEI model	Li et al.[7]
Plated Li metal	cryo cryo transfer holder	cryo-TEM	bilayered SEI configuration	Liu et al.[31]
Stripped Li metal	cryo cryo transfer holder	cryo-TEM	correlate the SEI structure with stripping process	Li et al.[32]
Li metal-liquid electrolyte interface	cryo cryo transfer holder	cryo-FIB cryo-TEM	LiH presence $\sim$300–500 nm SEI	Zachman et al.[8]
Li metal-Sn interface	cryo	cryo-FIB	uniform Sn coating on Li metal	Tu et al.[33]
Li metal-ionomer interface	cryo	cryo-FIB	uniform ionomer coating on Li metal	Tu et al.[27]
Li metal-Al_2O_3 interface	cryo	cryo-FIB	ultrathin Al_2O_3 coating on Li metal	Tu et al.[34]
C/S composite	cryo cryo transfer holder	cryo-STEM	not all the S in the porous carbon	Levin et al.[35]
TiS_2/S composite	cryo cryo transfer holder	cryo-STEM	S incorporated into the TiS_2	Liu et al.[36]
Fe_3O_4/S composite	cryo cryo transfer holder	cryo-STEM	S embedded in the Fe_3O_4 nanosphere	Zhang et al.[37]
Cathode interphase	Ar cooling holder	cryo-TEM	uniform CEI on LNMO	Alvarado et al.[38]
Aromatic amine	cryo cryo transfer holder	cryo-STEM	quantification elemental ratio	Deunf et al.[39]
Na metal-NaBr interface	cryo	cryo-FIB	uniform NaBr coating on Na anode	Choudhury et al.[40]

between EDLi and liquid electrolyte (Figures 3D–3F), where LiH is present, which is very surprising because LiH can react with water and organic solvents.[8] Besides the electron energy loss spectroscopy spectrum, more solid evidence is needed to confirm the presence of LiH instead of LiOH, which is commonly found in previous literature.[41]

Based on the insights obtained from cryo-EM, one can formulate strategies to improve the electrochemical performance of the EDLi, e.g., using electrolyte additives and constructing an artificial protective film on Li metal. Cryo-TEM provides a useful way to bridge the gap between the nanostructure of EDLi and these approaches. The results show that the electrolyte additives, such as Cs^+, Zn^{2+}, and fluoroethylene carbonate, mainly influence the component and distribution of the SEI rather than the bulk Li metal.[5,7,31] Artificial films, such as Al_2O_3, ionomer, and CH_3OCO_2Li are uniformly coated on the Li metal and protect the EDLi from the electrolyte corrosion.[23,27,34]

For the cathode side, a stable cathode-electrolyte interphase (CEI) is also important to inhibit the continuous reaction between cathode material and electrolyte, especially at a high working voltage. A combination of lithium bis(fluorosulfonyl)imide (LiFSI) salt and sulfolane solvent was found to form a conformal CEI ($\sim$0.612 nm)
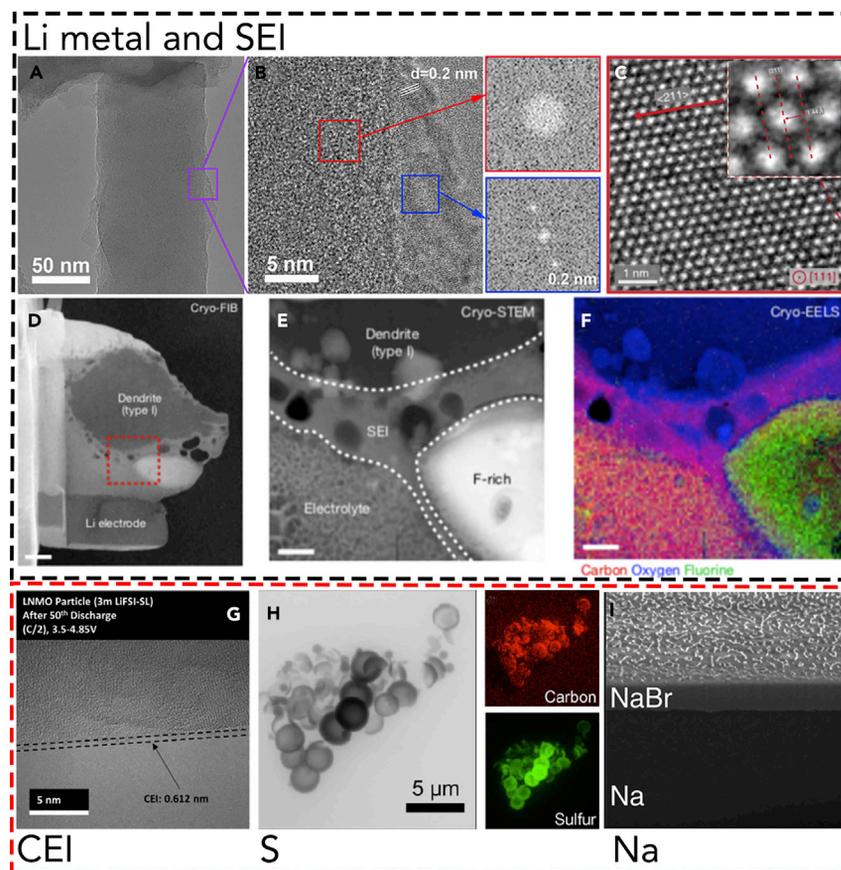
Figure 3. Cryo-EM Images on the Battery Materials

(A and B) Nanoscale image (A) and its regional zoomed-in image (B) with the bulk and surface fast Fourier transform result of the EDLi at 0.5 mA/cm² for 5 min.[5]

(C) Atomic structure of EDLi at 2.0 mA/cm² for 30 min.[7]

(D–F) Electron transparent cryo-FIB lift-out lamellae (D), the cryo-STEM imaging (E), and electron energy loss spectroscopy elemental mapping (F) of EDLi with electrolyte. Scale bar, 300 nm.[8]

(G) Cryo-TEM image of $LiMn_{1.5}Ni_{0.5}O_4$ after 50 cycles.[38]

(H) STEM image of carbon spheres/S composite and the elemental distribution of C and S.[35]

(I) Cross-sectional SEM image of NaBr-coated Na metal.

Scale bar, 5 μm.[40]

on the surface of the $LiMn_{1.5}Ni_{0.5}O_4$ after 50 cycles by cryo-scanning TEM (Figure 3G), which enables to operate a high-voltage (4.85 V) $LiMn_{1.5}Ni_{0.5}O_4$/graphite full cell for 1,000 cycles.[38]

Various nanostructured sulfur (S) cathodes have been developed to achieve the high-performance Li-S battery. However, the S distribution in these cathodes is barely known because S sublimates in the conventional EM. The cryogenic protection helps to stabilize the S and map the S distribution at a micro scale, as shown in Figure 3H.[35–37] Further imaging the S and its intermediate polysulfides at the nanoscale is required to understand its reaction mechanism in the future, such as the formation and adsorption principles of the polysulfides. However, this may be more difficult than Li metal since the S is an insulator and is easier to evaporate by local heat. We tried but failed to obtain high-resolution images of both S and Li_2S at the temperature of liquid nitrogen with an acceleration voltage of 300 kV. Further cooling the sample to a lower temperature using liquid helium or using a lower acceleration voltage down to 80 kV may work for the insulated S and sulfides.

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Besides Li ion/metal batteries, researchers extend the application of cryo-EM for other metal batteries, such as Na. Archer's group used cryo-FIB to study in-depth interface information of the Na electrode and found that NaBr is evenly coated on the surface of the Na anode with a thickness of 2 μm (Figure 3I).[40] Compared with Li metal, other metals have heavier atomic weight and thus higher EM contrast, which also enables to probe their distribution by energy-dispersive X-ray spectroscopy. Noting that some metals such as Na and K are more reactive than Li metal, more care and caution should be paid to mitigate the contaminations and radiation damage while transferring and imaging the samples.

Future Perspective

The great achievements described above demonstrate the increasingly important role of cryo-EM, which will no longer be just a complementary technique but a dominant one to understand the dynamic structure and reaction mechanism of battery materials. Emphasis should be put on the battery materials containing light and reactive non-transition metals elements, such as Li, C, O, F, P, and S. For example, the structural evolution of EDLi and its SEI will be recognized as a function of different operation conditions by cryo-EM, elucidating the roles of electrolyte component and concentration, current density, and cell stack pressure. It is conceivable to capture and visualize the distribution of some reaction intermediates in the electrolyte, such as lithium superoxide, lithium polysulfides, and soluble redox mediates. Cryo-EM also provides another way to identify the structure and spatial distribution of the organic battery materials, such as organic cathode and solvation structure of the electrolyte.[39] A combination of cryo-FIB and TEM is beneficial for exploring the interfaces between electrode and electrolyte, such as SEI on anode materials, CEI on cathode materials, and the interface in solid-state batteries.[42] We may be able to detect the presence of the O-O dimer and O^{n-} species on the surface of the charged cathode with anionic electrochemical activity.[43] Cryo-EM opens a new way to revisit the previous issues for deeper understanding and address the new challenges for gaining new insights and knowledge on battery materials. Operando experiments based on cryo-EM are hoped to be fulfilled soon. For instance, developing a cryo bias holder allows to probe the dynamic nucleation and growth of EDLi, which is urgently required to explore the growth mechanism of EDLi. We also expect the employment of advanced artificial intelligence to acquire and analyze the cryo-EM images automatically.[44,45]

A prerequisite to apply cryo-EM is that the cryo-cooled structures are representative of the original physiological state, which should be validated at least by cryo X-ray diffraction.[5] Materials undergoing phase transition during the cooling process are not suitable for cryo-EM. It is worth mentioning that cryo-EM is still a technique most sensitive to crystalline materials at a local area of the sample. Other complementary techniques, including X-ray photoelectron spectroscopy, X-ray diffraction, nuclear magnetic resonance spectroscopy, and chemical titration, are necessary to identify and quantify the content of different species and provide sample information with better statistics and more thorough understanding.

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