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Cryogenic Electron Microscopy for Energy Materials

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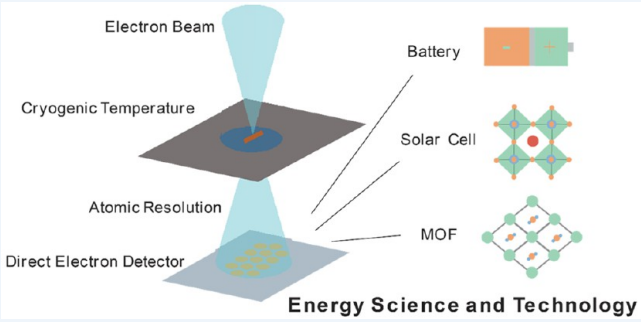
CONSPECTUS: The development of clean energy generation, transmission, and distribution technology, for example, high energy density batteries and high efficiency solar cells, is critical to the progress toward a sustainable future. Such advancement in both scientific understanding and technological innovations entail an atomic- and molecular-resolution understanding of the key materials and fundamental processes governing the operation and failure of the systems. These dynamic processes span multiple length and time scales bridging materials and interfaces involved across the entire device architecture. However, these key components are often highly sensitive to air, moisture, and electron-beam radiation and therefore remain resistant to conventional nanoscale interrogation by electron-optical methods, such as high-resolution (scanning) transmission electron microscopy and spectroscopy.



Fortunately, the rapid progress in cryogenic electron microscopy (cryo-EM) for physical sciences starts to offer researchers new tools and methods to probe these otherwise inaccessible length scales of components and phenomena in energy science. Specifically, weakly bonded and reactive materials, interfaces and phases that typically degrade under high energy electron-beam irradiation and environmental exposure can potentially be protected and stabilized by cryogenic methods, bringing up thrilling opportunities to address many crucial yet unanswered questions in energy science, which can eventually lead to new scientific discoveries and technological breakthroughs.

Thus, in this Account, we aim to highlight the significance of cryo-EM to energy related research and the impactful results that can be potentially spawned from there. Due to the limited space, we will mainly review representative examples of cryo-EM methodology for lithium (Li)-based batteries, hybrid perovskite solar cells, and metal−organic-frameworks, which have shown great promise in revealing atomic resolution of both structural and chemical information on the sensitive yet critical components in these systems. We will first emphasize the application of cryo-EM to resolve the nanostructure and chemistry of solid-electrolyte interphases, cathode-electrolyte interphase, and electrode materials in batteries to reflect how cryo-EM could inspire rational materials design and guide battery research toward practical applications. We then discuss how cryo-EM helped to reveal guest intercalation chemistry in weakly bonded metal−organic-frameworks to develop a complete picture of host−guest interaction. Next, we summarize efforts in hybrid perovskite materials for solar cells where cryo-EM preserved the volatile organic molecules and protected perovskites from any air or moisture contamination. Finally, we conclude with perspectives and brief discussion on future directions for cryo-EM in energy and materials science.

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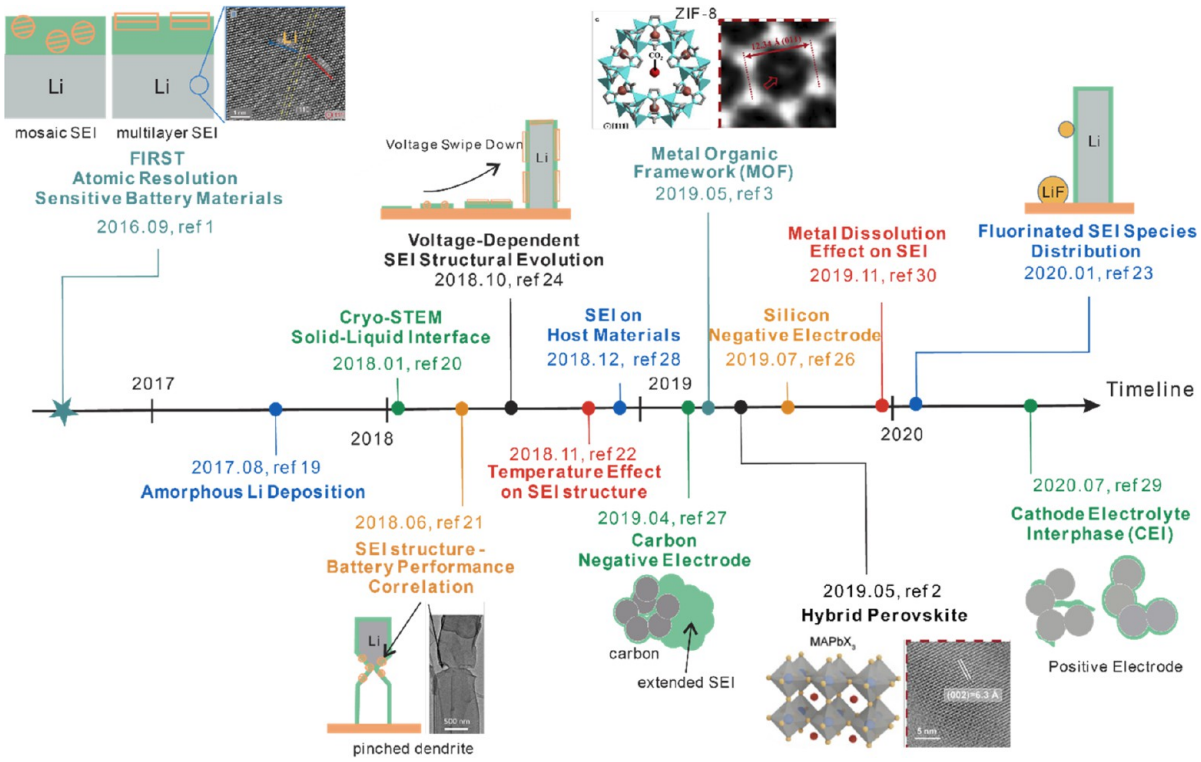

Figure 1. Significant milestones of cryo-EM development for energy research (sorted in the sequence of submission date).

Cryo-EM. *Joule* **2019**, *3*, 2854−2866.[2] This work preserved and stabilized hybrid perovskite materials for atomic-scale imaging. The nanoscale structural changes of hybrid perovskite under degradation were captured.

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1. INTRODUCTION

The evolution of civilization has always been fueled by humans' ability to harvest and harness energy.[4] Today, commercialized energy storage and conversion technologies, for example, secondary Li-ion batteries and Si-based solar cells, have significantly reshaped our life in many aspects.[5] Nevertheless, the state-of-the-art technology will be unlikely to meet the ever-growing demand for high energy density and high energy efficiency in the future. Continuous development of these renewable energy technologies plays an ever more significant role in the progress to a sustainable future. Such scientific discovery and technological innovations necessitate an atomic- and molecular-resolution understanding of the key materials and fundamental processes that governing the operation and the failure of the systems.[6]

In energy research, aberration-corrected (scanning) transmission electron microscopy ((S)TEM) is indispensable for atomic-resolution chemical and structural analysis of the materials. However, many key components in these energy conversion and storage systems are unstable and highly sensitive to air, moisture, and electron-beam radiation at room temperature and thus are incompatible with the room-temperature techniques. On the other hand, over the past decades, the development of cryogenic electron microscopy (cryo-EM) has revolutionized the life sciences already by resolving biomolecules with atomic resolution in their native state,[7−9] which featured continued development efforts in (1) sample preparation methods for freezing and stabilization of biomolecules in their hydrated state at cryogenic temperature in the TEM,[10,11] (2) direct electron detection for obtaining images under low electron dosages,[12] and (3) computational methods to calculate the structure of biomolecules.[13−15] These combined efforts allow the reconstruction of atomic biomolecular structures, establishing structure−property relationships of important biomolecules to guide the design and development of new drugs and medicines.

Of note, the merit of cryogenic temperature is not simply counteracting the heating effect of the electron beam. The main damage mechanisms in TEM could be classified into two categories: displacement damage (knock-on) and ionization damage (radiolysis), where the knock-on damage dominates in conductive materials and the ionization damage is of prime importance in semiconductor and insulators. By cooling down the temperature, the electron-beam sputtering and atomic displacement in knock-on damage are not eliminated, and the bond breakage and rearrangement in radiolysis still occur. However, the subsequent diffusion processes that cause structural rearrangements and mass loss, like vacancy agglomeration, free radicals, and radiation-scissioned molecular group diffusion, are greatly suppressed. The positions of atomic nuclei remain largely unaltered, enabling the measurement of structures that are characteristic of the undamaged materials.[16−18]

Recently, cryo-EM has begun to offer thrilling opportunities in energy research. The potential impact that cryo-EM could

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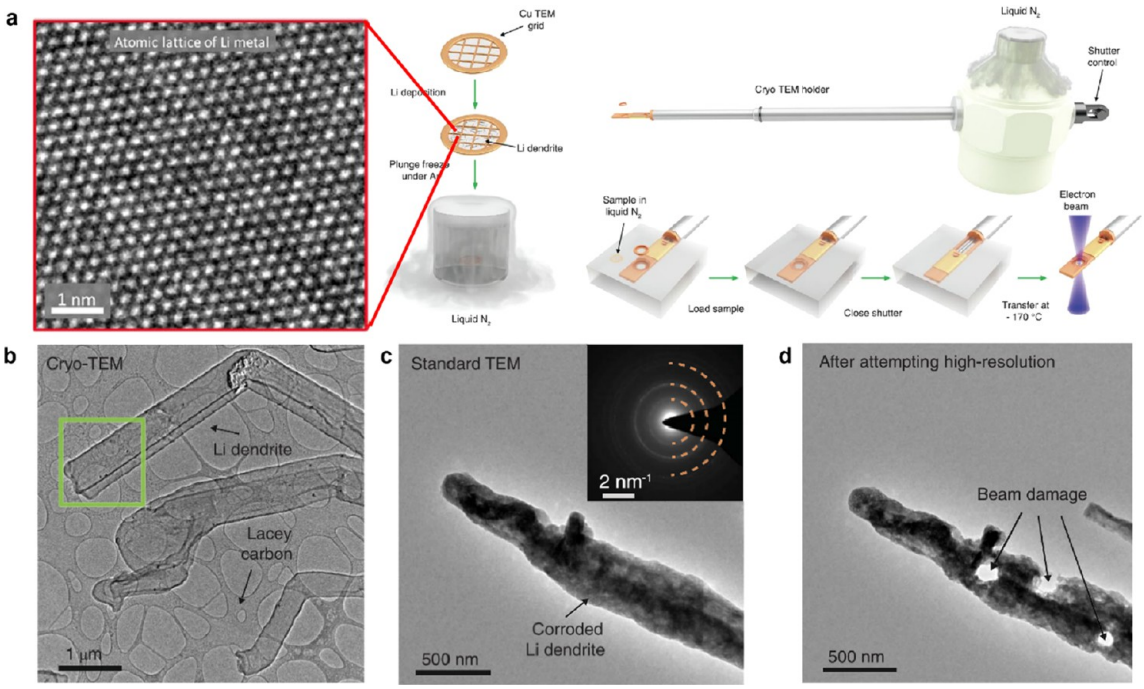

Figure 2. (a) Schematic of cryo-transfer procedure developed for energy materials and first atomic resolution TEM image resolving individual Li atom columns along the [111] zone axes. (b) Cryo-EM images of Li dendrites plated in EC/DEC electrolyte. (c) Standard room temperature TEM image of Li dendrites plated in EC/DEC. (d) Standard room temperature TEM image of Li dendrites from panel b after exposure to electron dose rate of 500 ($e^-/Å^2$)/s for about 1 s. Adapted with permission from ref 1. Copyright 2017 AAAS.

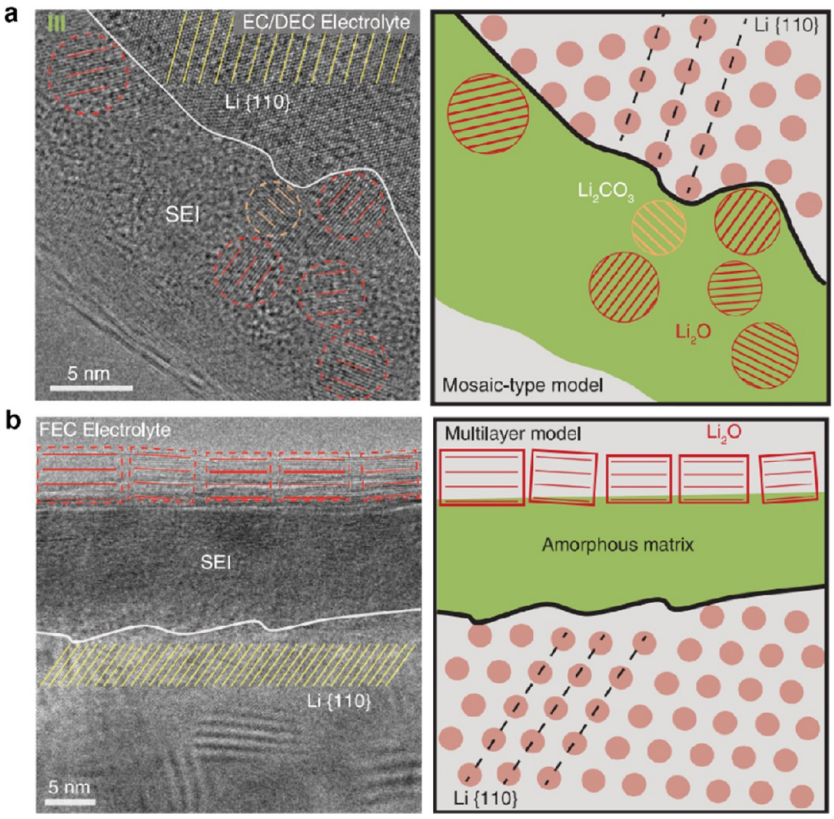

Figure 3. (a, b) Cryo-EM images and schematic of (a) mosaic SEI on Li metal and (b) multilayer SEI on Li metal in EC/DEC and EC/DEC with FEC additive electrolytes. Adapted with permission from ref 1. Copyright 2017 AAAS.

have on energy research is heralded by the significant breakthrough from our group in 2017, where we pioneered cryo-EM with cryo-analytical TEM to stabilize reactive battery materials and discover new atomic structures at key interfaces.[1] Together with findings in the following studies, these unprecedented results demonstrate the huge research oppor-

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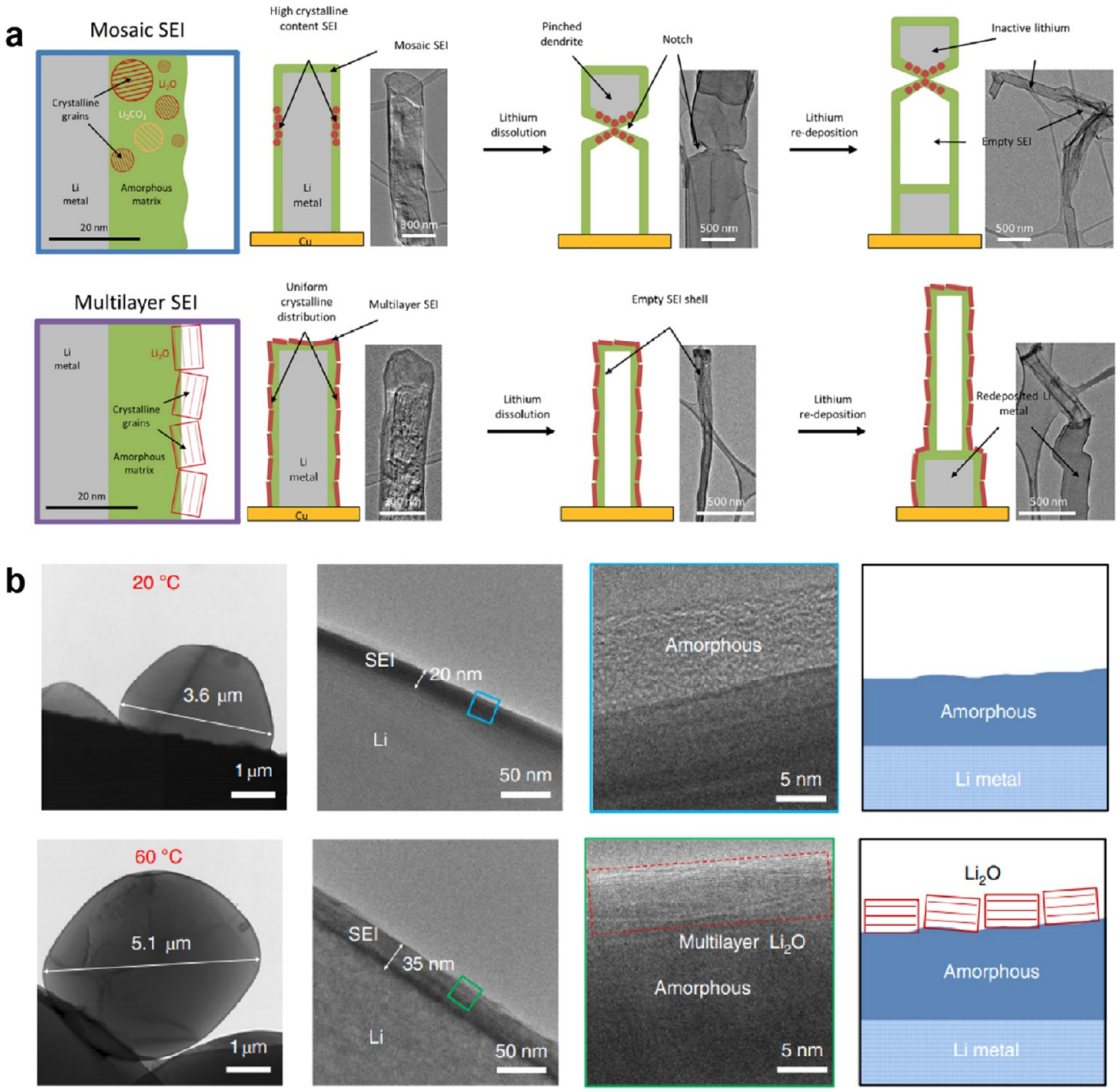

Figure 4. (a) Cryo-EM images and schematic of Li dendrite, stripping, and re-deposition with mosaic SEI or multilayer SEI nanostructure on Li metal in EC/DEC and EC/DEC with FEC additive electrolytes. Adapted with permission from ref 24. Copyright 2018 Elsevier. (b) Cryo-EM images and schematics of Li metal plate and corresponding SEI in DOL/DME electrolyte with $LiNO_3$ additives at room temperature of 20 °C and elevated temperature of 60 °C. Adapted with permission from ref 25. Copyright 2019 Nature Publishing Group.

tunities brought up by cryo-EM to investigate previously inaccessible aspects of energy science and technology (Figure 1). This Account aims to summarize the critical role of cryo-EM methodologies in energy science and materials, highlighting representative examples from our group and collaborators as anode materials and solid-electrolyte interphases (SEIs) in batteries, hybrid perovskite materials in solar cells, and metal–organic frameworks in gas storage, separation for fuel cells, and electrocatalysis. Then we briefly discuss the future development of cryo-EM and relevant techniques for energy science.

2. CRYO-EM FOR BATTERIES

Over the past decades, batteries have revolutionized energy storage technology and enabled the mobile revolution, making possible a variety of electrically driven tools and vehicles. The stable operation and failure mode is often determined by the interfaces between various components in the battery (e.g., cathode, anode, current collector, and electrolyte), which govern the ionic and electronic pathways of the electrochemical reactions.[19] To meet the ever-growing demand in energy density and cycle life for future needs, it is critical to resolve the atomic structures and chemistries of key interfaces inside a battery and reveal how they evolve with operation conditions. However, these key components in batteries, such as SEI, can be highly sensitive to ambient conditions, making it hard to resolve them in their native state. Fortunately, cryo-EM offers exciting new opportunities here.

Sample preparation protocols were central to the first successful application of cryo-EM in battery research: by air-free transfer and rapid sample freezing in liquid nitrogen, battery material was kept in its native environment without air exposure and side reactions (Figure 2a). More importantly, the fact that imaging at cryogenic temperature greatly reduces electron beam damage makes the high-resolution characterization of these sensitive materials possible (Figure 2b). Atomic resolution of Li metal anode and its SEI, an interfacial layer formed on the electrode surface due to electrolyte decomposition, was obtained for the first time. Single-crystalline growth of Li metal dendrites through electrochemical deposition was captured (Figure 2c). Additionally, two distinct, interfacial

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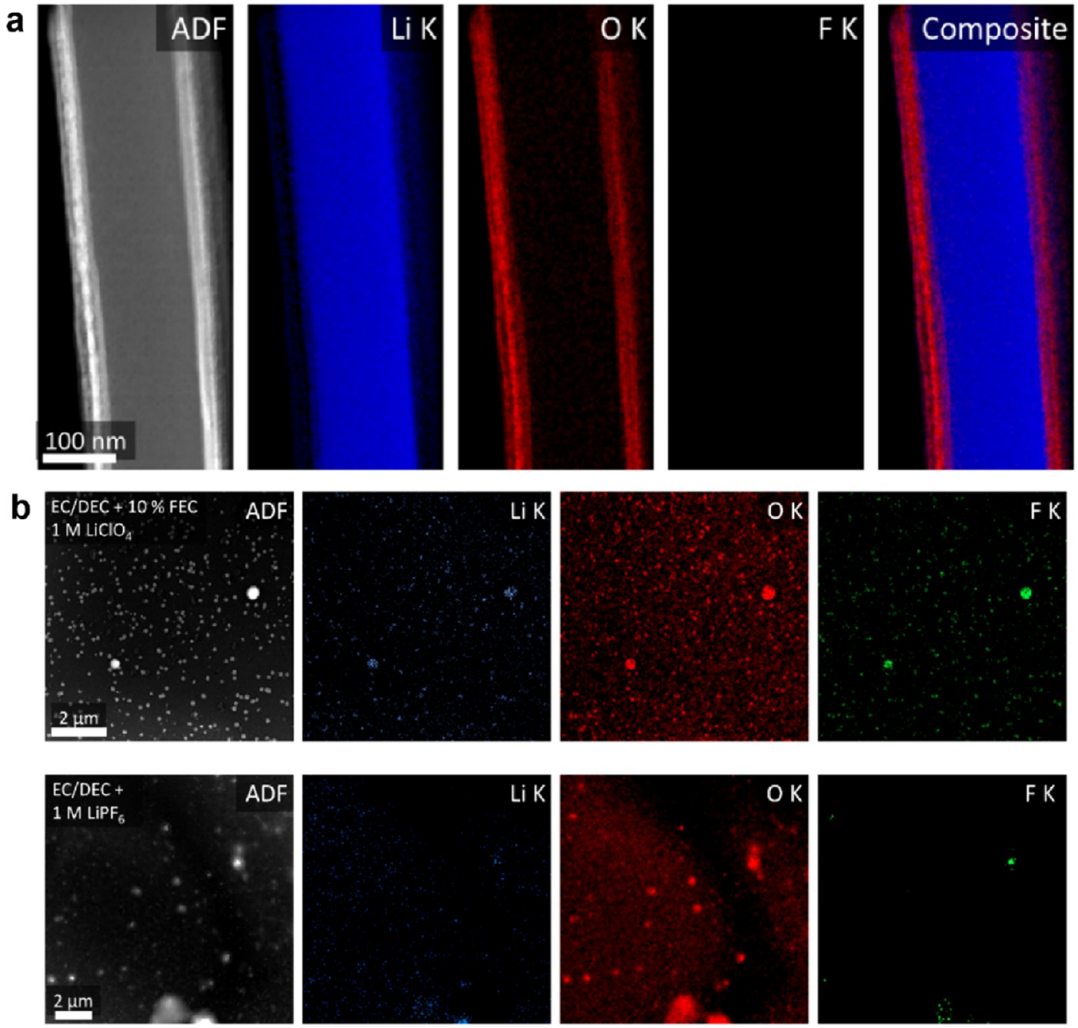

Figure 5. (a) Large area cryo-STEM EELS mapping of Li dendrite and its SEI in EC/DEC with FEC additive electrolyte. (b) Cryo-STEM EELS mapping of the current collector. Adapted with permission from ref 26. Copyright 2020 American Chemical Society.

nanostructures, the mosaic SEI and the multilayer SEI, were identified in two different battery electrolyte systems (Figure 3). Specifically, in standard carbonate electrolyte, ethylene carbonate/diethylene carbonate (EC/DEC) with 1 M $LiPF_6$, small crystalline domains (mostly Li_2O and Li_2CO_3) randomly distributed in the amorphous matrix. This patchy SEI nanostructure is in good agreement with the mosaic SEI model proposed by Peled.[20] In EC/DEC with fluoroethylene carbonate (FEC) additives, a bilayer SEI structure, with an inner amorphous matrix layer and an outer more ordered crystalline layer, is observed. This bilayer structure is consistent with the multiplayer SEI model brought up by Aurbach et al.[21] Further cryo-EM work showed interesting and surprising results: Meng and colleagues observed amorphous Li metal nucleation and deposition with cryo-EM,[22] while using cryogenic scanning transmission electron microscopy (cryo-STEM) coupled with electron energy loss spectroscopy (EELS), Kourkoutis and colleagues detected two types of deposited Li dendrites with their own unique SEI compositions and nanostructures in carbonate electrolyte, Li metal dendrites with a thick organic SEI and LiH dendrites with a thin inorganic SEI (Figure 3b−e).[23]

These initial discoveries have spawned numerous novel fundamental understandings about battery materials and interfaces that were inaccessible before. Most importantly, cryo-EM provides a direct correlation between nanoscopic structure of battery components and macroscopic battery performance. Specifically, on Li metal anode, the crystalline grain distribution in the SEI was identified as the critical feature to differentiate mosaic SEI from multilayer SEI in carbonate electrolytes (Figure 4a).[24] This subtle difference in nanostructure leads to a dramatic performance enhancement. More uniform Li stripping was observed for the more ordered multilayer SEI in EC/DEC with FEC electrolyte, which corresponds to a large decrease in Li loss during battery operation.

The origin of temperature effect on the battery cycling was also revealed to be the structural change in SEI with cryo-EM.[25] By cycling at an elevated temperature of 60 °C in ether-based electrolyte (1 M LiTFSI in DOL/DME with $LiNO_3$ as an additive), much-improved cycling stability of Li metal anode was achieved. This can be attributed to a drastically different SEI nanostructure revealed by cryo-EM, where a more crystalline outer shell on SEI that was absent in room temperature cycling conditions formed at the elevated temperature (Figure 4b). This new SEI nanostructure provides mechanical stability, inhibits continuous side reactions, and leads to good cycling stability.

The atomic resolution picture of SEI nanostructure and local chemistry obtained from cryo-EM generates novel under-

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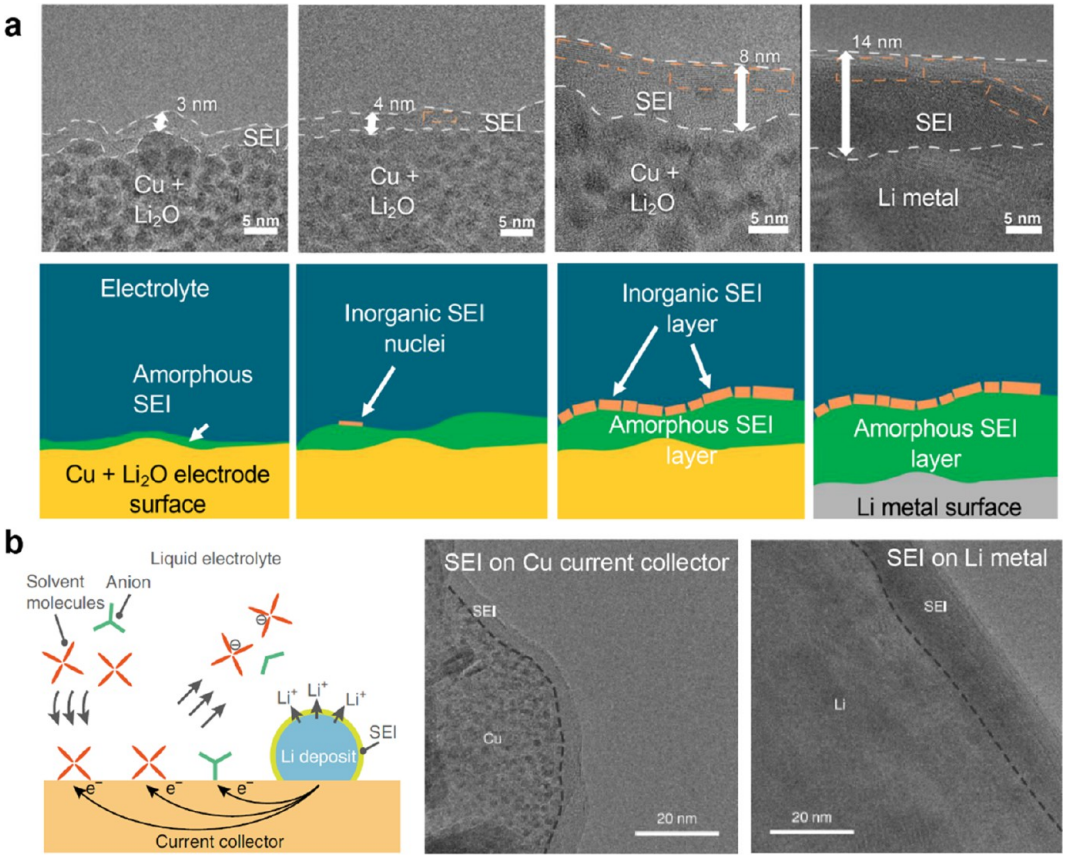

Figure 6. (a) Cryo-EM images and schematics of structural evolution of multilayer SEI nanostructure in EC/DEC with FEC additive electrolyte. Adapted with permission from ref 27. Copyright 2019 American Chemical Society. (b) Schematic of galvanic corrosion mechanism for Li metal anode and cryo-EM images of SEI on copper current collector and Li metal. Adapted with permission from ref 28. Copyright 2019 Nature Publishing Group.

standing about the function of critical SEI species. Specifically, LiF is widely believed to be an important SEI component that benefits the Li metal anode stripping and plating processes. However, with high resolution cryo-TEM and cryo-STEM EELS mapping, LiF was not found in the intimate coating SEI layer on the Li metal dendrite surface plated in both EC/DEC and EC/DEC with FEC electrolytes (Figure 5a), instead fluorine-rich inorganic particles were observed on the electrode surface (Figure 5b).[26] The fact that LiF species lie outside the compact SEI layer leads to the conclusion that LiF cannot be a dominant contributor to the SEI passivation and cannot influence Li^+ transport through the compact SEI film. This nanoscopic picture of SEI species distribution is otherwise inaccessible with traditional characterization methods with poor in-plane resolution.

The investigation of SEI nanostructure with cryo-EM shed light on the evolution of the SEI at different time scales. In the initial discharge cycle on the anode side, voltage-dependent SEI nanostructure evolution was mapped with cryo-EM using CuO nanowire as a platform.[27] In carbonate electrolyte, a thin amorphous SEI film formed at 1.0 V vs Li^+/Li, while the crystalline component emerged at 0.5 V vs Li^+/Li, and then the SEI became thicker as the electrode potential approached zero and further to lithium plating potential (Figure 6a). These findings depict a complete sequence of SEI formation and pinpoint the critical voltages for different components in SEI. The nuanced structural difference also gave rise to the Kirkendall-type corrosion mechanism of the Li metal anode upon aging (e.g., on-shelf storage or resting).[28] The SEI on the Cu current collector was found to be much thinner and have less crystalline domains than that on the Li metal anode in the same system. The shorter diffusion length for ions and solvent and less compact SEI nanostructure led to a much higher corrosion rate on the Cu substrate than on Li metal, which eventually results in the Kirkendall-type corrosion mechanism (Figure 6b).

Furthermore, the SEI evolution along with battery cycling could be tracked and analyzed with cryo-EM and analytical cryo-STEM. Within a charge−discharge cycle, the SEI can evolve with depth of charge; this is also known as the dynamic behavior of the SEI. Cryo-EM study of a Si nanowire anode revealed such dynamic behaviors in the SEI on the Si anode and revealed the origin of the Si SEI instability in ethylene carbonate (EC) electrolytes, resulting in a highly reversible SEI (Figure 7a).[29] The SEI on lithiated Si was rich in carbon, mainly from electrolyte decomposition, while it became less carbon-rich in the delithiated state. This fluctuation in carbon content reflected the reported reversibility of SEI species during charge and discharge cycles.[30,31] Furthermore, the critical electrolyte additive FEC is illustrated to extend the cyclability of the Si anode through deposition of an electrochemically irreversible polycarbonate layer on the anode surface.

On the carbonaceous anode, the SEI nucleation in the first cycle was found to result in a thin and primarily amorphous layer of around 2−5 nm.[32] Upon further cycling, two distinct SEI morphologies were found to exist on the carbonaceous anode, a compact layer of similar thickness as the initial SEI formed with more inorganic components that effectively passivates the surface and an extended layer with hundreds of nanometers

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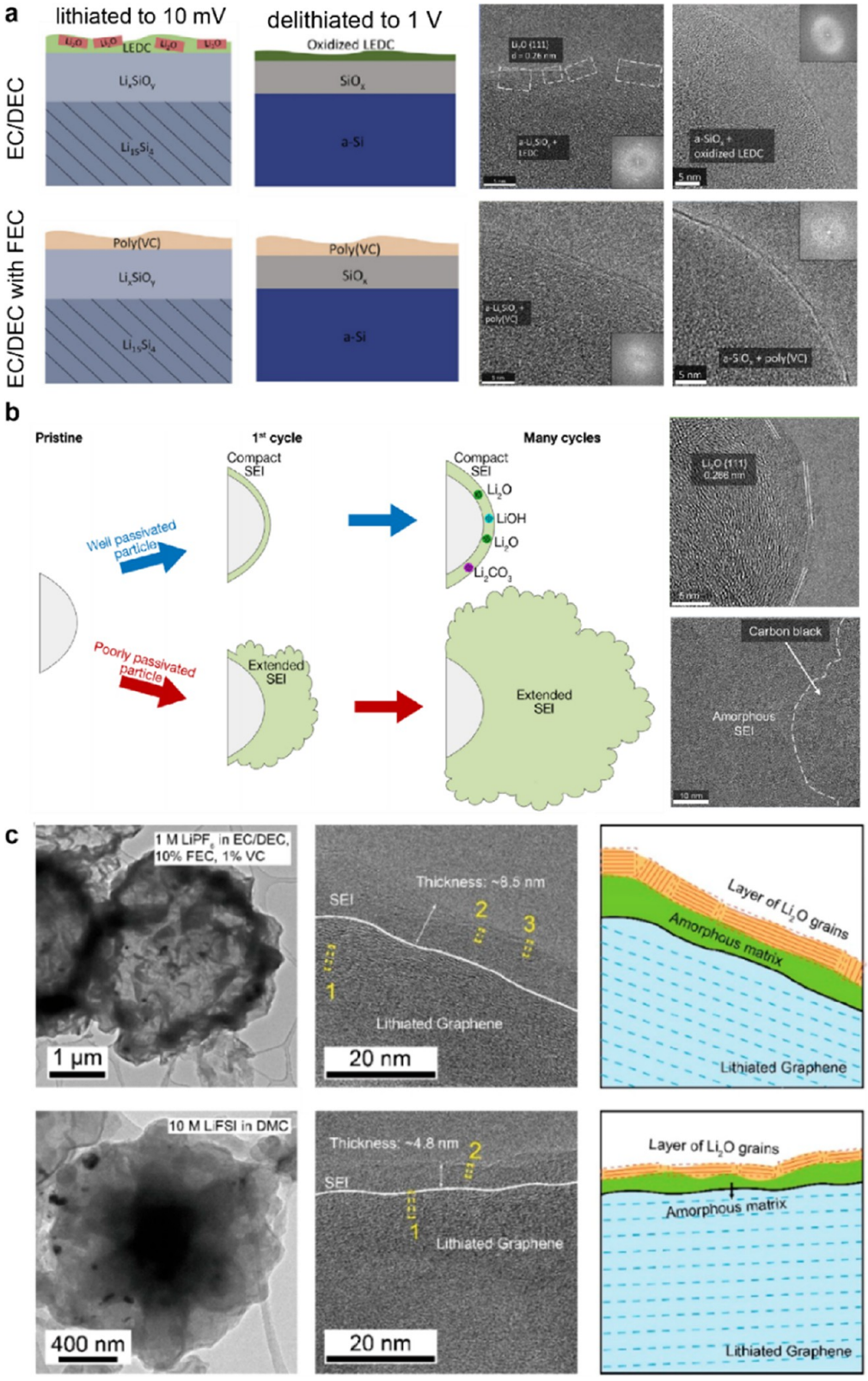

Figure 7. (a) Schematic and cryo-EM images of dynamic SEI behavior in the first charge−discharge cycling in carbonate electrolyte on Si negative electrode. Adapted with permission from ref 29. Copyright 2019 Elsevier. (b) Schematic and cryo-EM images of SEI formation and evolution upon cycling in commercial carbonate electrolyte on carbonaceous negative electrode. Adapted with permission from ref 32. Copyright 2019 American Chemical Society. (c) Schematic and cryo-EM images of SEI formation on wrinkled graphene cage host for Li metal anode. Adapted with permission from ref 33. Copyright 2019 American Chemical Society.

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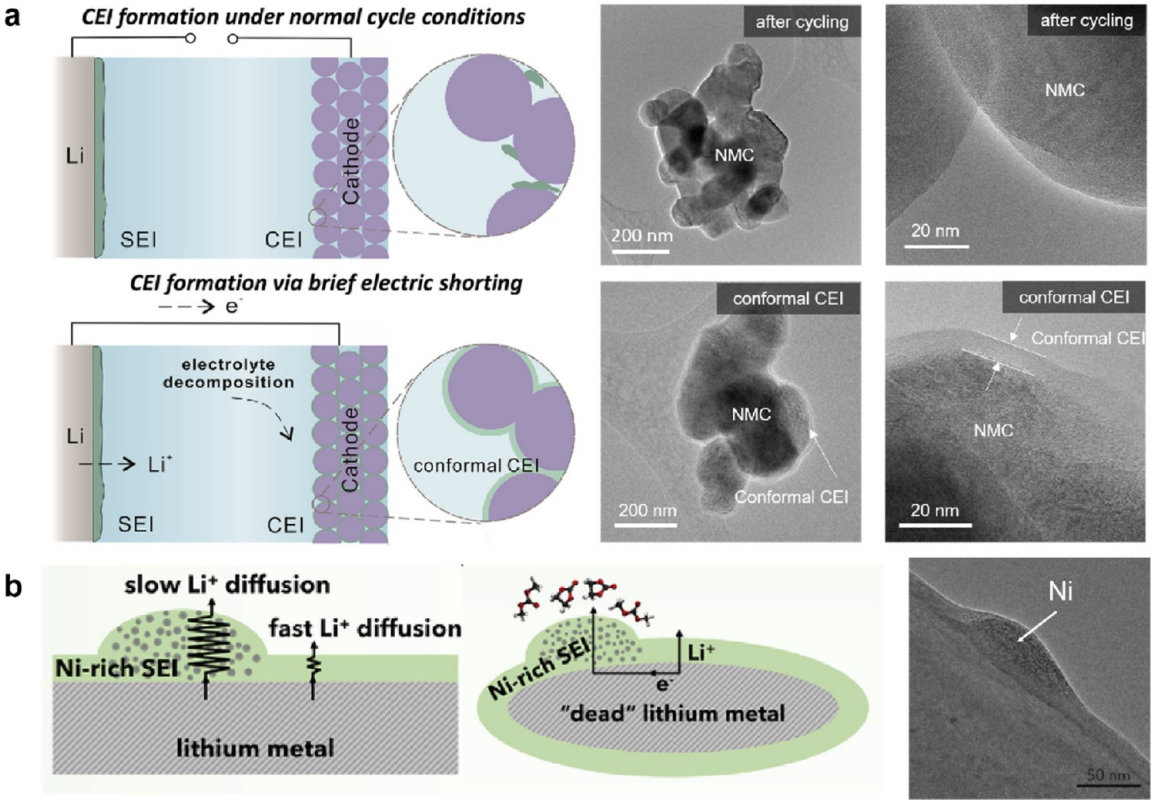

Figure 8. (a) Schematic and cryo-EM images of CEI in commercial carbonate electrolyte under normal cycling conditions and conformal CEI formation on an NMC532 electrode. Adapted with permission from ref 34. Copyright 2021 Elsevier. (b) Schematic and cryo-EM images of SEI in nickel-contaminated electrolyte on Li metal. Adapted with permission from ref 35. Copyright 2020 Elsevier.

thickness that is more organic (Figure 7b). This is direct evidence of SEI growth after initial formation cycles and should be correlated with capacity loss upon cycling.

Another important research aspect for lithium metal anode is the host material design for high energy density battery materials, such as Li metal anode and Si anode, where a stable electrode framework is employed to mitigate the huge volume fluctuation during charge and discharge cycles. Cryo-EM investigation of the host materials reveal another important function of the host. The SEI formed on the wrinkled graphene cage is much thinner than the SEI formed on the Li metal surface in the same electrolyte system (Figure 7c).[33] The difference here corresponds to a reduced Li loss from SEI formation during cycling.

The SEI on the cathode side, known as the cathode electrolyte interphase (CEI), is critical to the cathode performance especially at high voltages, yet it has also been elusive to the battery community due to its complex chemistry origin. Contrary to common beliefs, the close examination of CEI in its native state with cryo-EM reveals that an intimate coating layer does not exist on the cathode particles after cycling up to 4.8 V in commercial carbonate electrolyte, which means the CEI does not resemble the nanostructure of its counterpart on the anode side (Figure 8a).[34] However, a conformal CEI could be formed via brief electrochemical shorting followed by normal cycling to better protect the cathode−electrolyte interface.

The interplay between cathode and anode also plays an important role in long-term battery cycle stability. Chemical and structural changes in anodes and cathodes during battery operation can influence each other synergistically or destructively. Most prominent of these processes is metal dissolution from cathode materials, where transition metal ions (Mn^{2+}, Ni^{2+}) in the cathode materials structure dissolve into the electrolyte and get reduced on the anode surface. Nickel is found to be reduced into small metallic clusters of a few nanometers and incorporated into the SEI on the Li metal anode (Figure 8b), which alters the local SEI chemistry into a more organic-rich region as indicated by the increase of carbon atomic ratios shown in cryo-TEM EDS measurement.[35]

Chemistries beyond Li-ion and Li metal have also been explored. Sodium-based batteries have long been investigated as a cheaper and more environmentally friendly alternative to its Li counterparts. Although sodium-based batteries have a lower energy density compared to their lithium counterparts, the higher availability of raw materials for sodium anodes and cathodes could make them commercially competitive. Using cryo-EM, Zhang and colleagues reported a stable SEI in ether-based electrolyte for sodium metal anode.[36] Dai and colleagues demonstrated the use of chloroaluminate based ionic liquid electrolyte for rechargeable sodium metal battery, where NaCl as an SEI component is revealed with cryo-EM that forms uniform coating on the electrode.[37] Zhang and colleagues investigated SEI on the Sn-based anode for sodium ion batteries in both ether-based electrolyte and carbonate-based electrolyte.[38]

Beyond the liquid electrolyte batteries, solid-state technology holds great promise for next generation energy storage as featured by its high theoretical energy density and much reduced safety concerns. Few solid-state electrolytes are stable against typical anode operation potential, leading to the formation of SEI in solid state batteries. Unlike liquid electrolyte with high mobility, solid-state electrolyte remains relatively rigid and any

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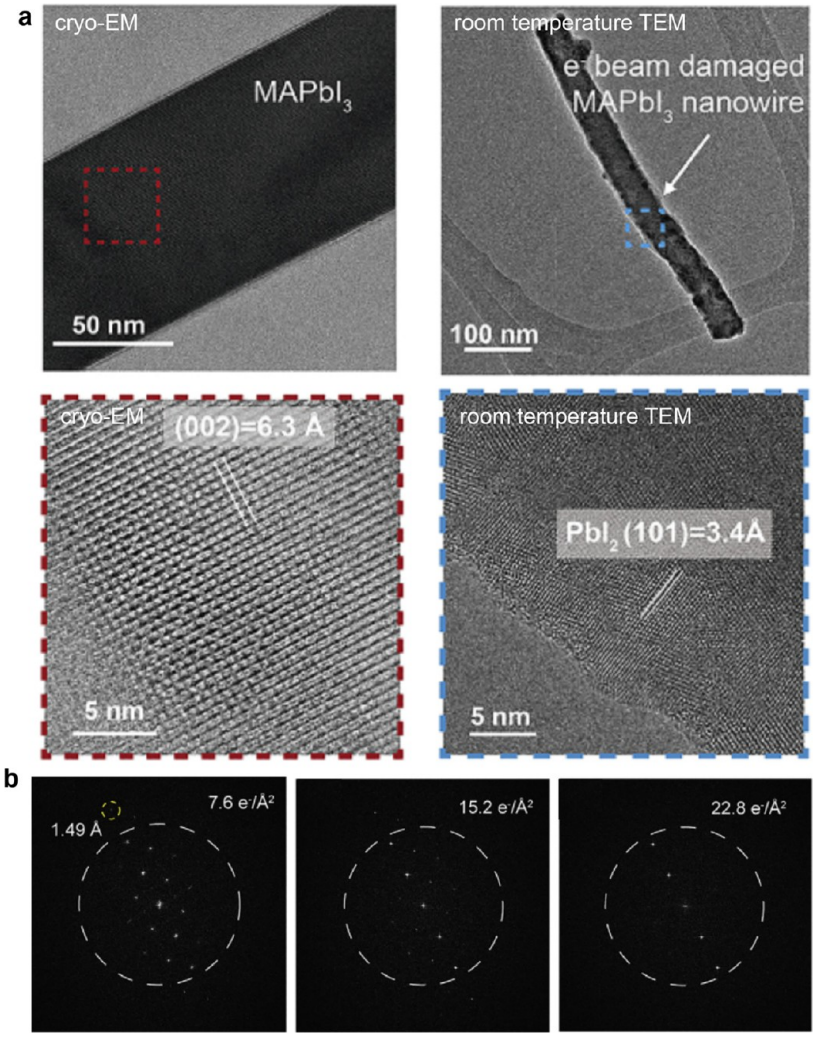

Figure 9. (a) TEM images of hybrid perovskite solar cell materials ($MAPbI_3$) with standard TEM at room temperature and cryo-EM. (b) Radiation damage measurement and quantification of hybrid perovskite materials. Adapted with permission from ref 2. Copyright 2019 Elsevier.

local disconnection between two solid phases would cause electrochemical inactivity and capacity loss. Therefore, the interfacial properties at the solid−solid interfaces buried inside batteries can be more critical to the battery performance. Using cryo-EM, it is possible to correlate the nanoscale evolution of the Li/solid-state electrolyte interface with capacity loss, which will eventually help the rational design of interface engineering in solid-state batteries. The key for cryo-EM in solid-state batteries is sample preparation method development. Some recent efforts started to show interesting results: Tao and colleagues investigated the SEI in polymer-based solid-state batteries to show that LiF-rich SEI stabilized the Li/poly(ethylene oxide) (PEO) interface to enable stable cycling,[39] while Meng and colleagues utilized cryo-FIB to get thin lamella of Li/LiPON for cryo-EM study to unravel the origin of interfacial stability in commercialized solid-state thin-film batteries.[40] Jung and colleagues demonstrated high resolution cryo-EM characterization of sensitive sulfide-based solid-state electrolyte.[41]

Such studies will help researchers understand the fundamental processes and key components in the batteries spanning multiple length and time scales and inspire further investigations. The adoption of cryo-EM makes it feasible to access the pristine state of important solid−liquid interfaces and solid−solid interfaces buried in batteries, which will uncover fundamental aspects of battery Li-based chemistry and beyond. Together these unexplored areas and dimensions would contribute to future advances in battery technology.

3. CRYO-EM FOR SOLAR CELLS

Solar cells are among the most efficient and practical ways to harness solar energy as a renewable energy source by converting sunlight into electricity.[42] The photovoltaics of hybrid metal halide perovskite materials have shown rapid improvements in solar cell performance, where the power conversion efficiency (PCE) of organic−inorganic hybrid perovskite solar cells (PSCs) has been increased from the initial 3.81% to more than 24%, surpassing the top efficiency of semiconductor compounds such as CdTe and CIGS (copper indium gallium selenide) used in solar cells in just about a decade.[43] Other favorable characteristics such as low synthesis cost and potential to deliver efficient and scalable solar energy have contributed to the burgeoning research activity in this field. Despite the rapid progress in PCE, the fundamental operating mechanisms of such high efficiency (>24%) and long carrier lifetimes are still not well understood.

TEM has been used for macroscopic morphology study of hybrid perovskite PSCs;[44−46] however high-resolution investigation has been hindered by rapid structural degradation under

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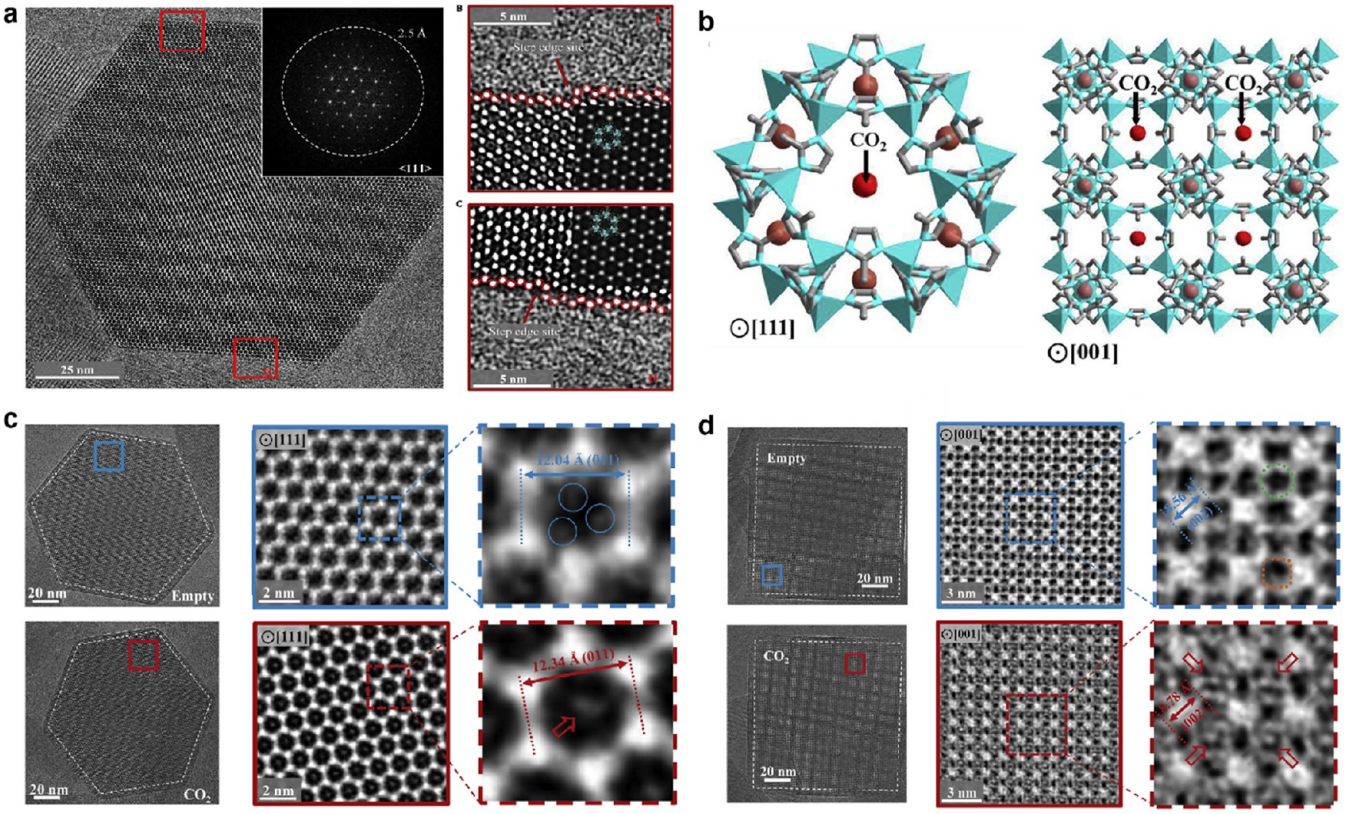

Figure 10. (a) High-resolution cryo-EM images of ZIF-8 and sharp surface resolved with atomic resolution. (b) Simulated structure of ZIF-8 with DFT-predicted binding site of CO_2 (simplified as red spheres) along the ⟨111⟩ and ⟨001⟩ projection. (c) Atomic resolution cryo-EM image of both empty and CO_2-filled ZIF-8 particle at ⟨111⟩ projection. (c) Atomic resolution cryo-EM image of both empty and CO_2-filled ZIF-8 particle at ⟨111⟩ projection. (d) Atomic resolution cryo-EM image of both empty and CO_2-filled ZIF-8 particle at ⟨001⟩ projection. Adapted with permission from ref 3. Copyright 2019 Elsevier.

the intense electron beam. Cryogenic temperature imaging and low dose techniques combined with a direct electron detector have been proposed to reduce the electron-beam damage and total electron dose required for high resolution imaging.[47,48] Nonetheless, atomically resolved imaging of pristine state hybrid perovskites remains challenging due to their sensitivity to ambient conditions (e.g., moisture); even a short air exposure during sample transfer and insertion into TEM columns can cause side reactions on delicate hybrid perovskite materials (Figure 9a). Additionally, the sublimation of volatile organic species under high vacuum in a TEM chamber at room temperature is almost unavoidable. $MAPbI_3$ nanowires loaded at room temperature show clear surface degradation, even though the samples were only exposed to air for a few seconds during the loading process. In this regard, our group first proposed a cryo-EM protocol to reveal the atomic structure of $MAPbI_3$ by combining low-dose imaging with plunge-freezing and cryogenic sample loading.[2] We established that the standard for critical electron dose for $MAPbI_3$ at cryogenic condition is 12 $e^-/Å^2$ at 1.49 Å spatial resolution (Figure 9b). Moreover, the intermediate states of $MAPbI_3$ were successfully preserved under ultraviolet (UV) and moisture exposure to unravel degradation phenomena at the atomic scale. Later, Gu and colleagues reported high resolution cryo-EM imaging of the stacking faults in $MAPbI_3$ to which the enhanced charge separation and reduced photon-generated recombination in hybrid perovskite materials were attributed.[49]

Current study on hybrid PSCs mainly focuses on perovskite materials themselves. Future development of sample preparation techniques such as cryogenic focused ion beam milling (cryo-FIB) and cryo-ultramicrotome would enable detailed investigation of the interfaces in PSCs at a device level, which would promote the understanding of the working mechanism as well as the failure mode to guide future development of more efficient and stable PSCs.

4. CRYO-EM FOR METAL−ORGANIC FRAMEWORKS

Metal−organic frameworks (MOFs) are a class of highly porous extended structures assembled by bonding metal-containing building blocks with organic linker molecules through reticular chemistry.[50] Building block chemistry and framework topology can be tuned for various applications in energy technology such as fuel storage, gas capture and separation, catalysis, and electrochemistry.[51−54] Atomic scale understanding of the interactions between the host framework and guest molecule is critical to their practical application but remains limited. Commonly used characterization techniques, such as powder or single crystalline X-ray diffraction and nitrogen adsorption/desorption isotherms, are useful for resolving the average crystallinity, pore size, particle size, and chemistry of MOFs at equilibrium state. TEM can provide atomic-scale insight into MOF structure, defects, and host−guest interactions. Nonetheless, high resolution single particle MOF structure and guest molecules in pristine state is hard to obtain. Volatile guest molecules loaded into MOFs can desorb in the high vacuum of the TEM column and radiation damage from the electron beam causes the framework to collapse before any atomic-scale information can be obtained.

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Acc. Chem. Res. 2021, 54, 3505−3517

Initial work with cryo-EM for MOFs showed that imaging at cryogenic temperatures can reduce electron beam damage and keep the adsorbed state of the guest molecules.[3] Plunge freezing of MOFs kinetically confines guest molecules in the framework, and the low vapor pressure at cryogenic temperature prevents the desorption in the high-vacuum environment of the TEM. Additionally, direct electron detectors with high detection quantum efficiencies can reduce the overall dosage required for high-fidelity phase imaging in the TEM. Combining these three techniques (plunge freezing, cryo-TEM, and high DQE detectors) our group was able to capture the first atomic-scale images of guest molecules loaded into a MOF, zeolitic imidazolate framework-8 (ZIF-8) frozen during CO_2 adsorption (Figure 10).

Microcrystal electron diffraction (microED) at cryogenic temperatures is an exciting technique that can be used to resolve crystal structure on particles much smaller than are typically needed for single crystal X-ray crystallography.[55] The structure of ZIF-8 was resolved using microED to a resolution of 0.87 Å, which is comparable to the resolution obtained from single crystal X-ray diffraction.[56] Small crystal sizes have limited the number of resolved 2D π-conjugated MOF structures. In the work by Duo and colleagues, they were able to resolve the structure of Cu_3(2,3,7,8,12,13-hexahydroxytetraazanaphthotetraphene) using microED in combination with high-resolution cryo-TEM imaging.[57] In addition to MOFs, other highly porous extended frameworks such covalent organic frameworks,[58] cyclophane-protein cage frameworks,[59] and homochiral porous nanosheets[60] have benefited from the use of cryo-TEM, demonstrating the success of radiation damage minimization in porous extended frameworks.

5. PERSPECTIVES

Despite various exciting results obtained with cryo-EM in batteries, solar cells, and MOFs, cryo-EM is still in its initial states for energy material research. The development of sample preparation protocols, imaging conditions, and data processing techniques will benefit the wider adoption of cryo-EM for energy research. In general, the main goal in sample preparation for cryo-EM is to enable fast freezing or plunge freezing while avoiding ambient condition exposure. Slowly cooling from room temperature to liquid nitrogen temperature could cause phase transitions, while exposure to ambient conditions could result in side reactions. Both scenarios might alter the native state of the targeted materials system. Thus, room temperature TEM holder insertion with liquid nitrogen cooling afterward should be avoided. It is desirable to submerge the sample directly in cryogens (liquid ethane or liquid nitrogen) to freeze and then transfer or store the samples in liquid nitrogen all the time. Additionally, a side-entry cryo-holder with a shutter at the tip or a cryo-TEM autoloader system is recommended.[30,31] Lessons can be learned from structural biology to facilitate the process. We also need to notice that cryo-EM for structural biology mainly focused on structural information. For energy research, chemical information should be equally as important. In this regard, analytical TEM techniques such as EDS and EELS at cryogenic conditions can better support cryo-EM. Additionally, several related techniques, such as cryo-FIB, cryo-ultramicrotome, cryogenic microED, and cryo-ET should also get researcher's attention.

Notably, current cryo-EM study for energy research mainly benefits from cryoprotection of samples, from both ambient environment exposure and high energy electron beam radiation, to enable high resolution microscopy and spectroscopy. Another significant yet unexplored aspect of cryogenic temperature is the possibility to capture the intermediate states or species in the complex chemical, electrochemical, and photochemical processes. Such intermediate states or species at the interfaces in the energy devices would affect the reaction pathways and can be tuned by external excitations. The reactions will be kinetically slowed or even halted at low temperature and rapid quenching of ongoing processes will prevent the relaxation to equilibrium state and enable time-resolved analysis. The development of sample preparation apparatus capable of fast freezing while applying external excitations, such as electric field, magnetic field, or light, would be highly important.

Lastly, it is still important to notice that careful interpretation of cryo-EM results is required to rule out suspicious conclusions, where special care for critical dose determination should be taken to avoid artifacts and the analysis of multiple regions, samples, or batches to report unbiased observation is particularly critical. Standardized workflow and protocols for cryo-EM in energy research should be established for various systems.

6. CONCLUSIONS

In this Account, we have surveyed the recent developments in cryo-EM for energy science and technology. Representative research directions, batteries for energy storage, solar cells for energy conversion, and MOFs as gas storage materials for fuels cells and electrocatalysis, have been summarized. Fast freezing in cryogens and cryo-transfer protocols prevent undesired side reactions and maintain the sensitive materials in their native states. Imaging at liquid nitrogen temperature great reduces electron beam damage. Unprecedented high-resolution structural and chemical information were therefore obtained for extremely sensitive materials in the pristine state, such as Li metal and SEI in batteries, hybrid perovskite in solar cells, and MOFs for gas storage and catalysis. The valuable atomic and molecular resolution understanding of these key components will facilitate the future development of these energy technologies. In summary, cryo-EM starts to bring exciting opportunities in energy research, offering powerful tools to probe the phenomena at time and length scales that are otherwise inaccessible and guide the development of future energy solutions.

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