From the Editor

Nobel Prize

The Royal Swedish Academy of Sciences awarded the 2017 Nobel Prize for Chemistry to Jacques Dubochet, Joachim Frank, and Richard Henderson "for developing cryo-electron microscopy for the high-resolution structure determination of biomolecules in solution." It is interesting to note that each of these awardees was previously honored by the Microscopy Society of America with its Distinguished Scientist Award (Biological Science): Dubochet (2009), Frank (2003), and Henderson (2005).

Two facts have long been known: biological molecules exist in a water environment, and the transmission electron microscope has the potential to image atoms. But there were two major problems. Biological molecules are easily damaged by the electron beam, and the microscope vacuum makes imaging in liquid water impractical.

The first problem was surmounted by Richard Henderson's group in 1975 by imaging a regular array of molecules with as few electrons as possible. By averaging a repeating motif, the "electron dose" given to each motif was reduced, and summed motif images produced a higher-resolution image. Henderson's group achieved near-atomic resolution in 1990. Henderson's early work was with the protein bacterial rhodopsin, which is embedded in a membrane as an array of identical molecules. While Henderson knew in principle that his approach could be extended to isolated, asymmetric molecules, the method to do it resulted from Frank's work.

Joachim Frank's group developed a computational method (1975) to identify and "classify" many different views of the same molecule. Next, Frank's group came up with a computational method that assigned a viewing angle to each example of the molecule (1987) so that the different views could be projected into an averaged 3D reconstruction of the molecule.

But it was the work of Jacques Dubochet that made possible electron microscopy of molecules in their native water environment. Normally, when water freezes ice crystals form, which damage the molecule and interfere with imaging. In 1981 Dubochet's group published a method to freeze the water in a "vitreous" (glass-like) state, which preserves native biological structure, facilitates electron imaging, and avoids the need for chemical treatment or staining. In Henderson's first EM work, water was replaced by a glucose solution, and he did not achieve near-atomic resolution until he used vitrified frozen samples. Dubochet's comprehensive paper describing the states of water in the electron microscope was published in 1988.

While the pioneering work was largely carried out in the 1970s and 1980s, the introduction of direct-electron-detector cameras for the electron microscope in 2013 (partly carried out in association with Richard Henderson) made possible reconstructions with resolution better than 2 Ångströms. This camera improved the signal-to-noise ratio and recorded each image as a series of frames, allowing correction for movement of the molecule during exposure.

Content for this editorial was provided by MSA Archivist Mike Marko and the Nobel Prize for Chemistry official website.

Charles Lyman
Editor-in-Chief

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