Graphene enabling structural biology at the single particle level

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Abstract

To image an object by means of electron microscopy, it is normally placed onto a substrate. The signal from the object support, arising from the scattering of the impinging primary electrons in transmission electron microscopy or from the creation of secondary electrons in a scanning electron microscope, is spurious and efforts to reduce these signals have been accomplished since the development and implementation of the first electron microscopes. Ideally, for maximal contrast and resolution, one would like to have the thinnest substrate possible, made up of a low-atomic-number material, in order to reduce the interaction volume and the scattering cross-section of the incoming electrons. The idea of using freestanding single-layer graphene as the ultimate microscopic sample carrier in electron microscopy has been around since the isolation of single-layer graphene was achieved in 2004 by Geim and Novoselov. Significant efforts have been undertaken in the past few years to develop techniques for preparing either exfoliated or CVD grown graphene in a freestanding form. However, the cleanliness of the prepared graphene sheets has never been satisfactory with regard to their use as sample carrier in electron microscopy. We have recently demonstrated a simple method to prepare ultraclean freestanding graphene by platinum-metal catalysis. This method leads to large regions, extending up to several square microns, of ultraclean freestanding graphene suitable for electron microscopy applications.

Here, we will show that ultraclean graphene can be used as substrate for imaging individual biological particles by means of low-energy electron holography. In the range of electron kinetic energies 50-250eV, no radiation damage is imposed to the biomolecules by the electron radiation. This, combined with the fact that the de Broglie wavelengths associated with this energy range is between 0.8 and 1.7Å, makes low-energy electron microscopy a candidate for structural biology at the single molecule level. An illustration of the experimental scheme of in-line low-energy electron holography is presented in Figure 1a. We will report the imaging of individual tobacco mosaic viruses deposited onto ultraclean freestanding graphene. We will show that structural details arising from the helical structure of the viruses can be revealed (Figure 1 b-d) and that the agreement between our images and atomic model of the viruses available from the protein database is remarkable. We also describe our on-going efforts towards 2Å resolution by means of low-energy electron coherent diffraction imaging.

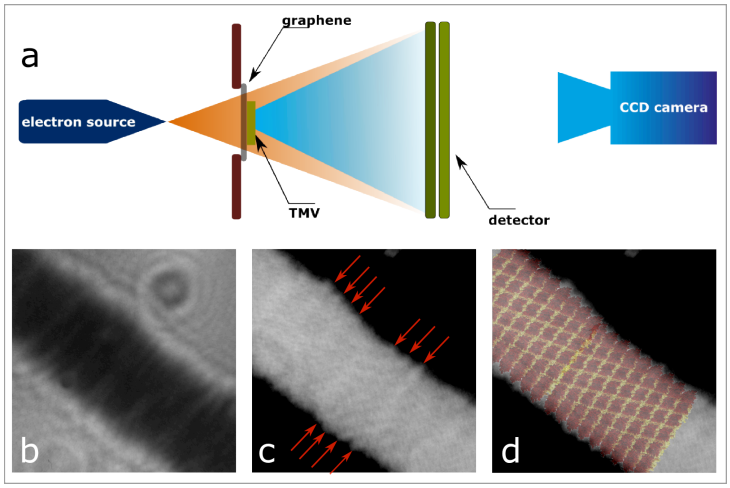

Figure 1: ***a*** *Scheme of the experimental setup of low-energy electron holography. The source-sample distance amounts to typically 100-1000nm which leads to kinetic electron energies in the range of 50-250eV.* ***b*** *high-magnification hologram of TMV recorded at 80eV.* ***c*** *reconstruction of the shape of TMV from* ***b*** *the red arrows mark the presence of details arising from the helical structure of TMV.* ***d*** *an atomic model for TMV is superimposed on the image presented in* ***c.***