Imaging of SARS-CoV-2 infected Vero E6 Cells by Helium Ion Microscopy

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The Helium Ion Microscope (HIM) utilizes a focused beam of helium ions to image and modify materials with high spatial resolution, large depth of field, and chemical sensitivity [1]. HIM images show stronger chemical and topographical contrasts than images from the related scanning electron microscope, and the HIM is capable to resolve sub-nanometer features. Due to its charge compensation capability, the HIM can image insulating biological samples without additional conductive coatings [2]. In this contribution, the first HIM images of uncoated SARS-CoV-2 infected Vero E6 cells are presented. Interactions between cells and virus particles, as well as among virus particles, could be imaged [3]. The HIM pictures show the three-dimensional appearance of SARS-CoV-2 and the surface of Vero E6 cells at a multiplicity of infection (MOI) of approximately 1 with great morphological detail. The absence of a conductive coating allows a distinction between virus particles bound to the cell membrane and virus particles lying on top of the membrane.

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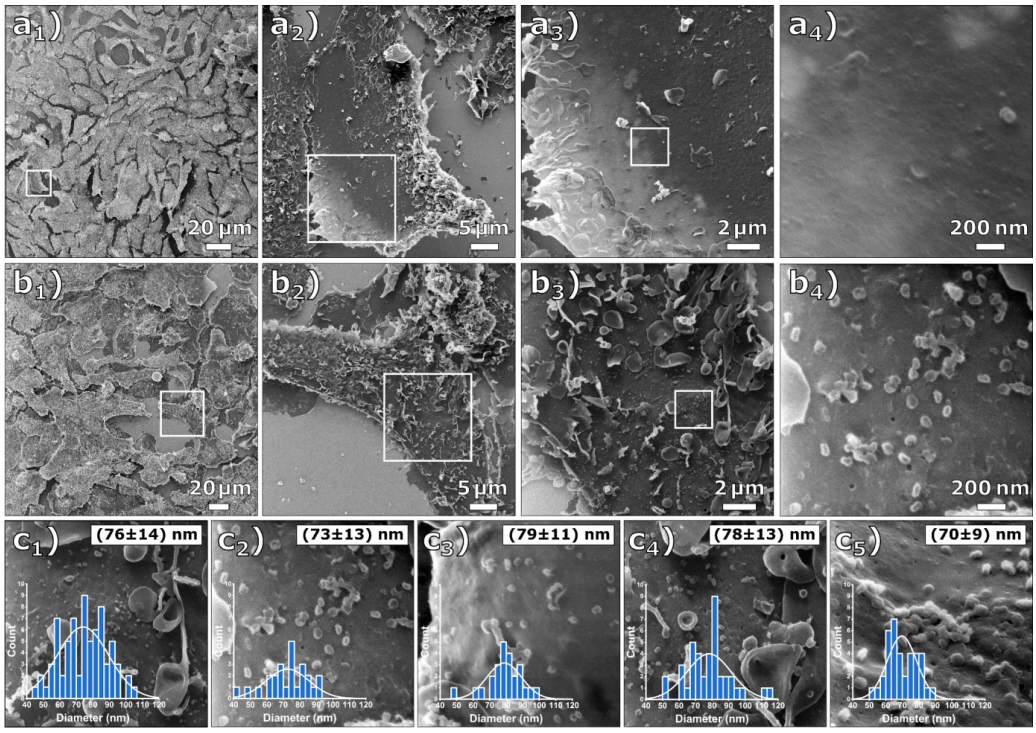

Fig. 1: Comparative HIM images of non-infected and infected Vero E6 cells: $a_{1\text{-}4}$) Non-infected cell at different magnifications (FOV 200 µm, 45 µm, 15 µm, 1.7 µm) and $b_{1\text{-}4}$) MOI 1 infected cells at different magnifications (FOV 250 µm, 45 µm, 15 µm, 1.7 µm). The cell membrane is covered with the virus particles. $c_{1\text{-}5}$) Virus particle diameter distributions determined. The inserted histograms show the respective image evaluation, the average particle diameter of all evaluated images is 75 ± 13 nm.

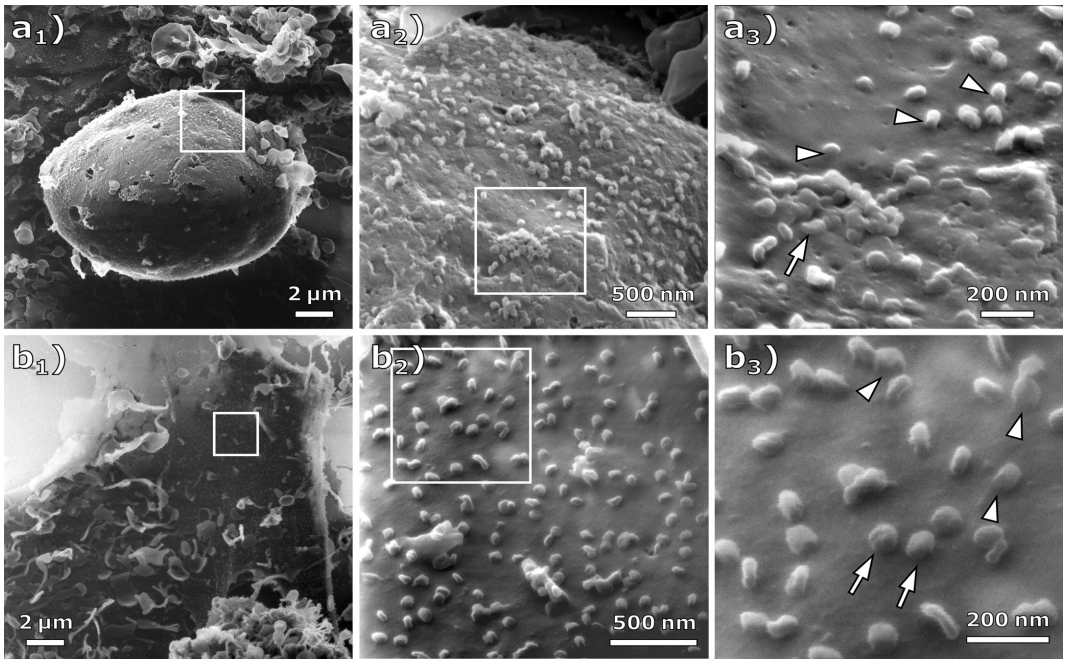

Fig. 2: HIM images of infected cells imaged with charge compensation. $a_{1\text{-}3}$) Different magnifications of a MOI 1 infected cell (FOV 17 µm, 3.5 µm, 1.3 µm). At high magnification clusters of virus particles (arrow) and junctions (arrowheads) between virus particles and the cell membrane become visible. $b_{1\text{-}3}$) Different magnifications of a MOI 1 infected cell (FOV 18 µm, 2 µm, 850 nm). While some of the virus particles appear to be bound to the cell membrane (arrowheads), others seem to just lie on top (arrow).