DIVIDE AND CONQUER: COMBINING STRUCTURED ILLUMINATION MICROSCOPY WITH MACHINE LEARNING FOR LARGE SCALE STRUCTURAL ANALYSIS OF VIRUSES

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ABSTRACT: Super-resolution microscopy has enabled the study of molecular assembly at the nanoscale. Previously, we showed that super-resolution and model-based fitting enable the structural analysis of viruses at near Ångström precision [1]. Here, we generalize the method to large heterogenous virus populations by combining this approach with machine learning classification [2]. We design a pipeline that identifies, classifies and analyses the structures of viruses from Structured Illumination Microscopy (SIM) images and demonstrate the potentials of the techniques on samples of Newcastle Disease Virus (NDV) and Influenza viruses. These viruses are central to many pharmaceutical developments, from vaccines to oncolytic viriotherapy drugs. Our approach demonstrates the potentials of Artificial Intelligence applied to microscopy for high-throughput analysis.

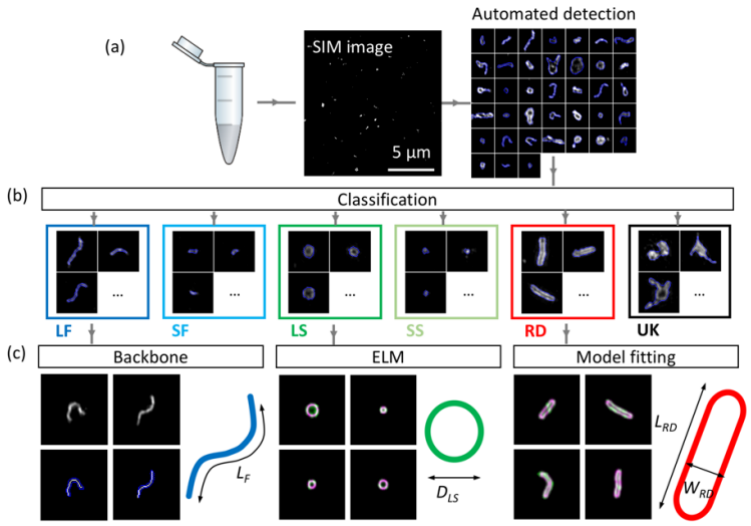

Figure 1: Workflow of the method. Individual virus particles are automatically detected from the SIM images (a), classified using machine learning (b) and analysed for full structural description (c). Images of individual particles cover a field of view of 1.6 µm x 1.6 µm.

[1] Laine, R. F. et al. Structural analysis of herpes simplex virus by optical super-resolution imaging. Nat. Commun. 6, 5980 (2015).
[2] Laine, R. F. et al. Structured illumination microscopy combined with machine learning enables the high throughput analysis and classification of virus structure. Elife 7, (2018).