Evolution of a single-cell predictive model for packaging and budding of viruses based on TEM based measurements

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Although detailed experimental investigations would provide insight into viral infections and vaccine production, building a computational framework is necessary to identify the parameters that regulate the budding and packaging of nucleocapsids. This study shows that a predictive model for the complete infection cycle can be built using nonlinear coupled ODEs and parameter estimation using a Genetic algorithm. Specifically, we have used a dataset containing the occluded virus information, budded virus in infected cells obtained by transmission electron microscopy (TEM). A novel parameter estimation strategy is proposed based on the k-medoid clustering of infected cells. Firstly, we show that the parameter estimation framework can be used for model evolution and selection of the feedback structure. Secondly, we show that the model was capable of capturing the distribution of packaged and unpackaged nucleocapsids in the nucleus, cytoplasm, and plasma membrane, the number of packaged and unpackaged ODV, and polyhedra in the nucleus. The proposed framework assumes importance in generating data for achieving quality by design in the optimization of vaccine/recombinant protein yield.

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