BIOMATERIALS

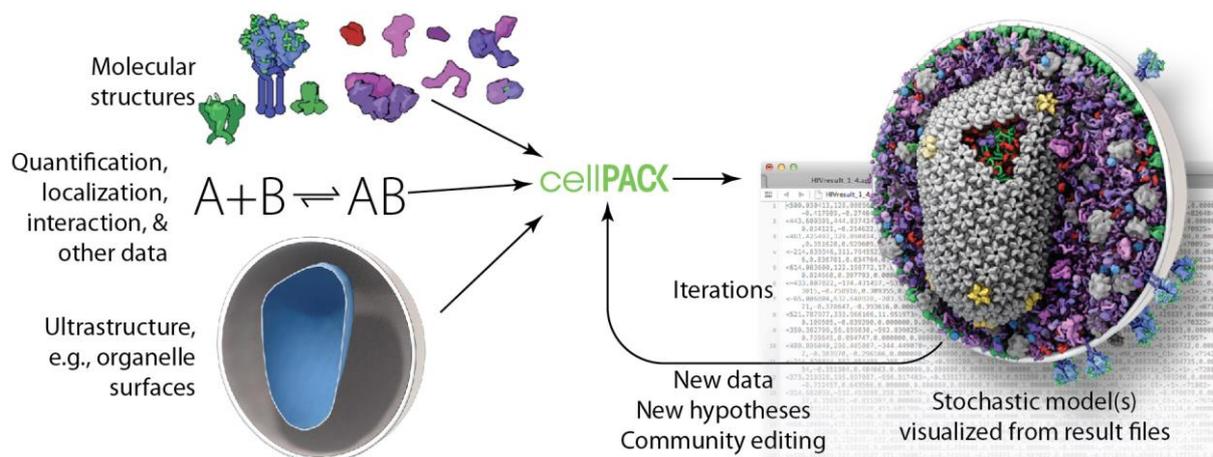**Forces in Biomolecular Systems** **SFB 863**

Towards Whole Cells Modeled in 3D Molecular Detail and Community Curated with cellPACK

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Abstract:

Two central questions that biology strives to answer are: How do complex functions and behaviors arise from the molecular building blocks of life? and similarly, How does such a variety of functionality arise from different interactions among the same underlying molecular structures? A virus with cell-like structural properties such as HIV-1 provides an ideal system to begin to study these questions. Although thousands of studies provide details on the molecules that make up HIV, there had been no tools to assemble complete models that enable researchers to study the larger system of this entire virus in molecular detail. Our open-source cellPACK software is uniquely able to assemble full virus models that can assist researchers in developing systems-scale hypotheses, testing models, and in validating and communicating the results1. We have used cellPACK to build models of mature HIV-1 as well as blood plasma and a few subcellular systems, but cellPACK needs further development and community input to accurately model larger or more complex structures, such as immature HIV, entire bacteria, or eukaryotic cells. The current version of cellPACK is also labor-intensive and difficult for non-experts, which is a major bottleneck to the community participation required for consensus modeling on this scale. As we continue improve and extend the core packing and analysis capabilities of cellPACK, a new project under development is making cellPACK easier to use and more robust as an online web tool with an integrated database, intuitive web browser interface, and support for community curation. By leveraging social-networking technologies, the scientific community will be able to analyze, critique and edit the models in an effort to produce confidence-voted community
consensus models and to iteratively improve the recipes. We anticipate that cellPACK will serve as a structural and informatics foundation for broader projects such as 3dvcell.org and the new Allen Institute for Cell Biology, which aim to generate dynamic whole-cell models for predictive experimentation.

Molecular structures

Quantification, localization, interaction, & other data

$A + B \rightleftharpoons AB$ — cellPACK →

Ultrastructure, e.g., organelle surfaces

Iterations

New data
New hypotheses
Community editing

Stochastic model(s) visualized from result files

1. Johnson, G.T. Johnson, G. T., Autin, L., Al-Alusi, M., Goodsell, D. S., Sanner, M. F., Olson, A. J. cellPACK: a virtual mesoscope to model and visualize structural systems biology. Nat Methods 12, 85-91 (2015).

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