Assembly and visualization of immature HIV

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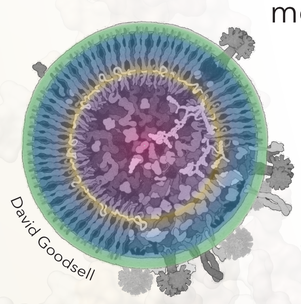
Goals and challenges

– Construct an *in-silico* model of immature HIV

– In contrast to the model of mature HIV[1], homology modeling of the polyproteins Gag and GagPol is required before they can be incorporated in an immature HIV model

– Establish a pipeline to facilitate mesoscale model generation

- Create an online platform for visualization, hypothesis generation, and outreach[2]



Methods overview

1) **MultiDomain Assembler**[3] (MDA) for homology modeling of Gag and GagPol polyproteins

2) Create mesoscale models with cellPACK[4]

3) Build an **online viewer** for cellPACK models

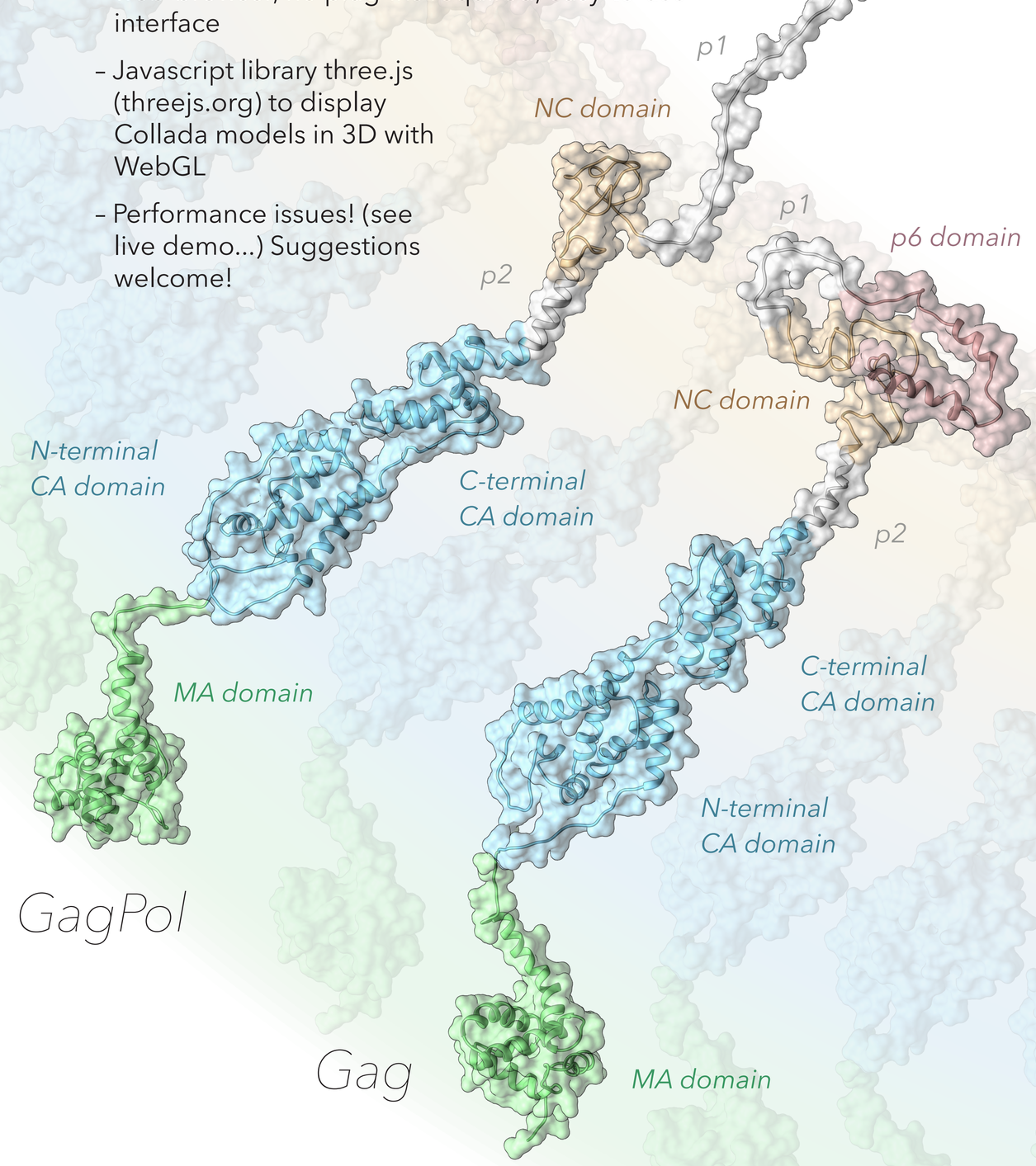
Online viewer for cellPACK models

– A pipeline for building, visualizing, consolidating and sharing mesoscale models (not just for HIV)

– Ideally: platform-independent, running in a web-browser, no plug-ins required, easy-to-use interface

– Javascript library three.js (threejs.org) to display Collada models in 3D with WebGL

– Performance issues! (see live demo...) Suggestions welcome!



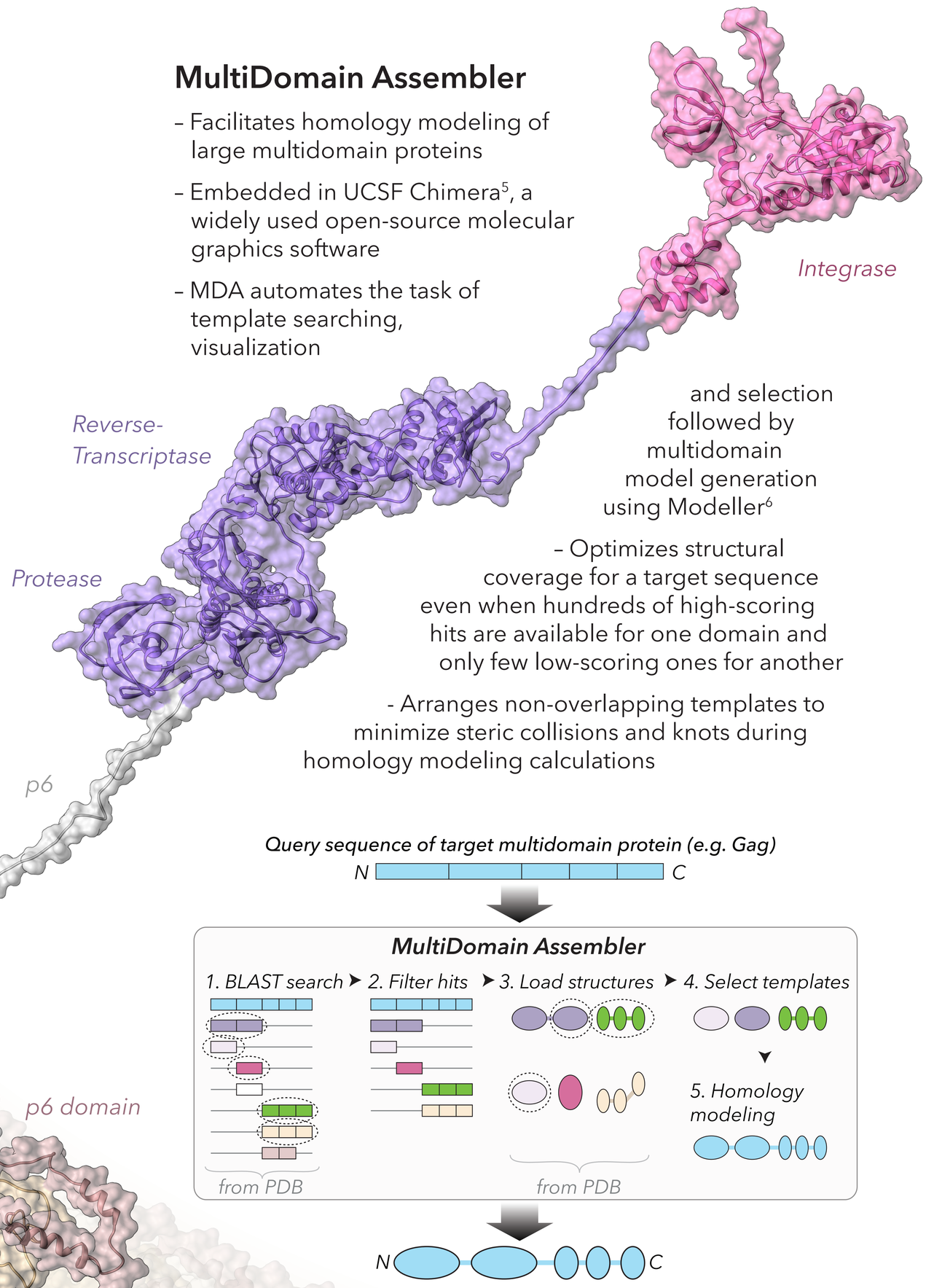
The viral polyproteins Gag and GagPol govern the assembly of HIV, and are composed of multiple domains connected by flexible linkers. These models were created using MDA with additional distance restraints, for example obtained by EM studies of the immature virion[7].

MultiDomain Assembler

– Facilitates homology modeling of large multidomain proteins

– Embedded in UCSF Chimera[5], a widely used open-source molecular graphics software

– MDA automates the task of template searching, visualization and selection followed by multidomain model generation using Modeller[6]



– Optimizes structural coverage for a target sequence even when hundreds of high-scoring hits are available for one domain and only few low-scoring ones for another

- Arranges non-overlapping templates to minimize steric collisions and knots during homology modeling calculations

– MDA's unique capability to display, automatically align and color all of the homologs with known structure for a target protein in the same 3D space for simultaneous visual analysis provides a useful summary of current structural knowledge beyond the task of homology modeling (see live demo...)

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Acknowledgments

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UCSF Chimera cellPACK