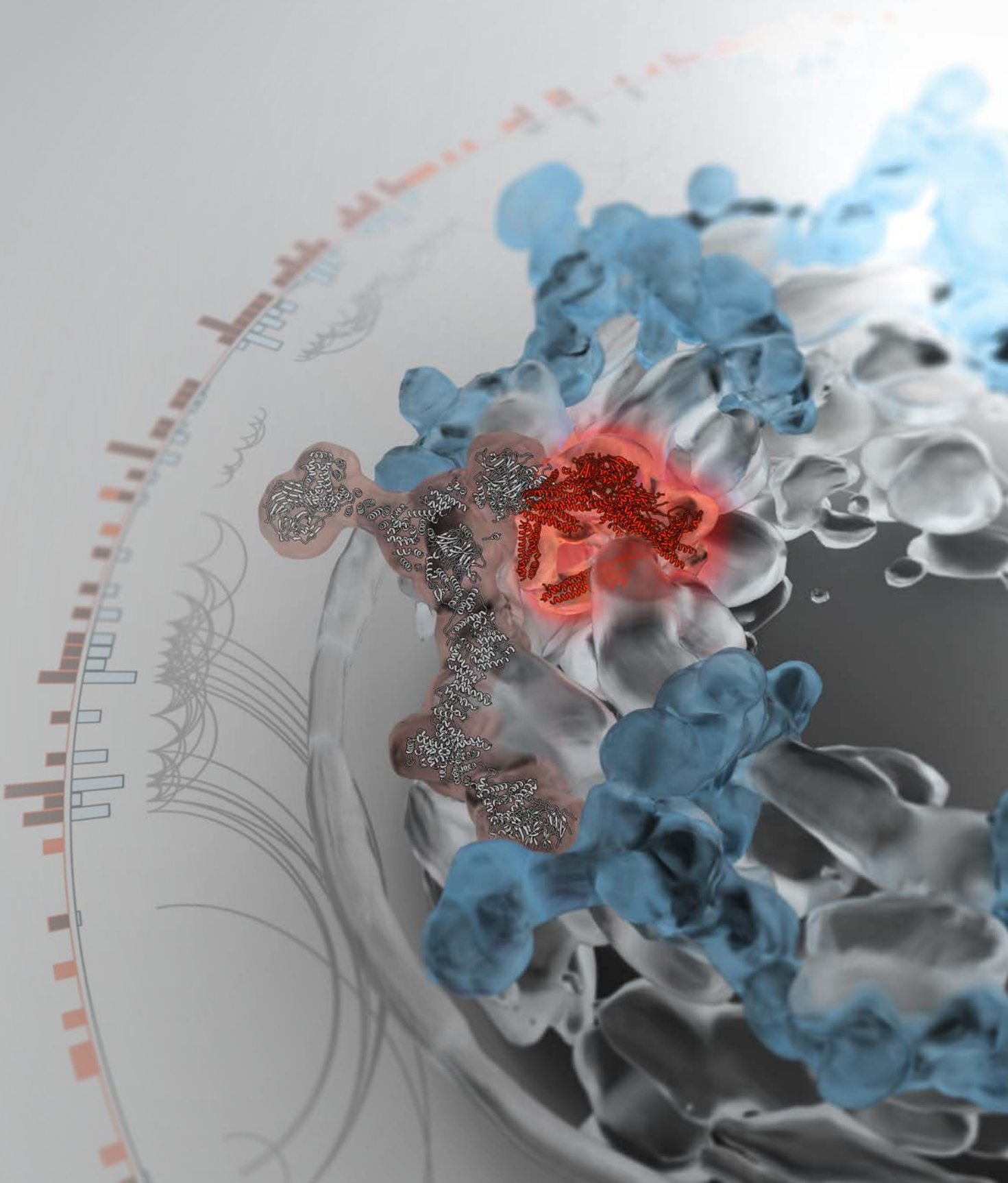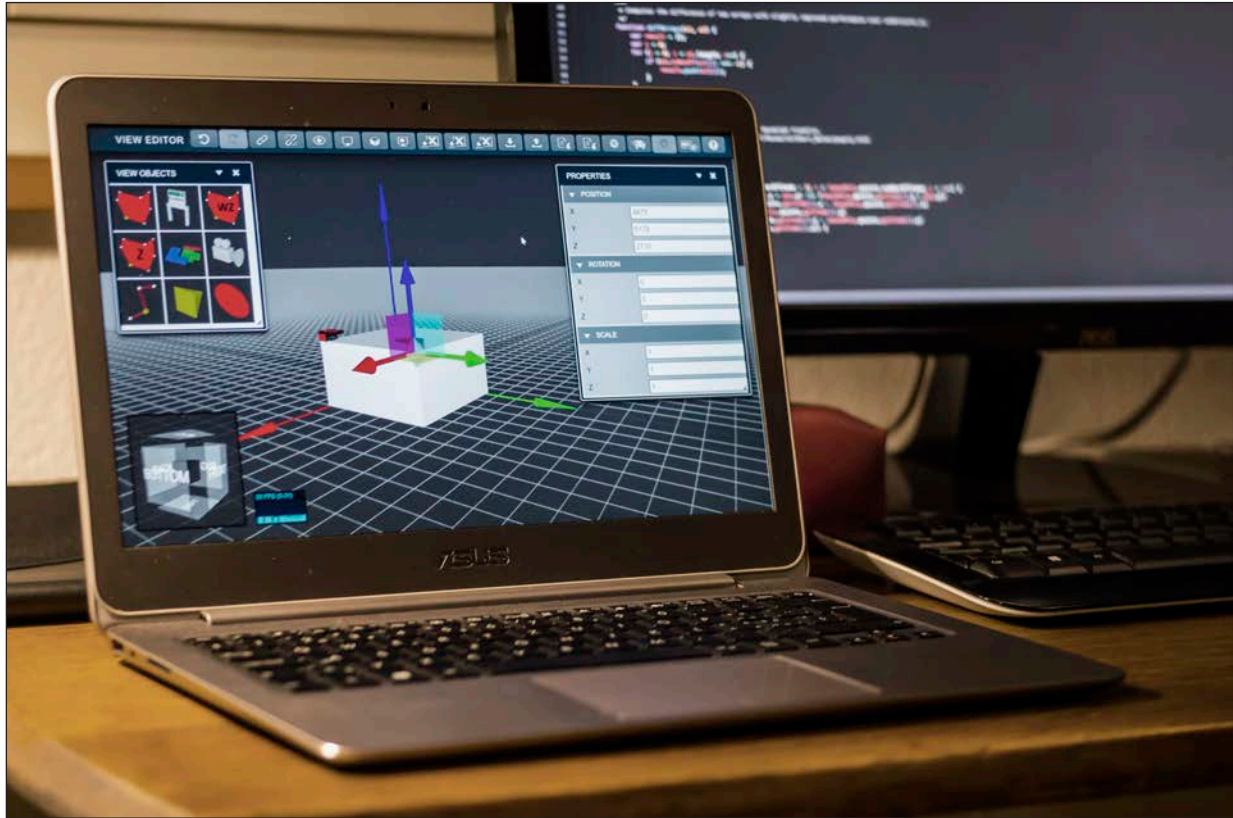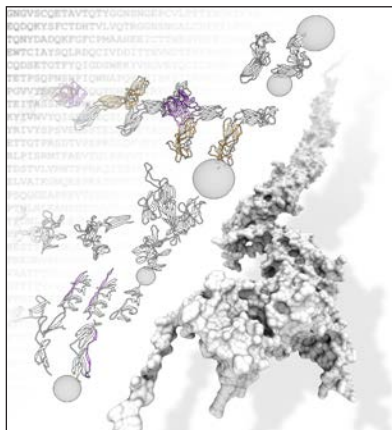# Sam Hertig

Scientific Visualization

Interactive

Web-based 3D-visualization app to render and simulate warehouses in real-time, in collaboration with Comerge AG, Zurich, 2016. Tools: Blender, HTML5, CSS, JavaScript, jQuery, and Three.js WebGl library.

*> https://www.comerge.net/en/work/swisslog*

*During my postdoc at University of California, San Francisco, I contributed to the molecular graphics software UCSF Chimera by adding an extension to faciliate modeling and visualization of large multidomain proteins using Python and various libraries:
"S. Hertig, T. D. Goddard, G. T. Johnson, T. E. Ferrin. Multidomain Assembler (MDA) Generates Models of Large Multidomain Proteins. Biophysical Journal 108(9) (2015), 2097–2102."*

> https://www.rbvi.ucsf.edu/chimera/
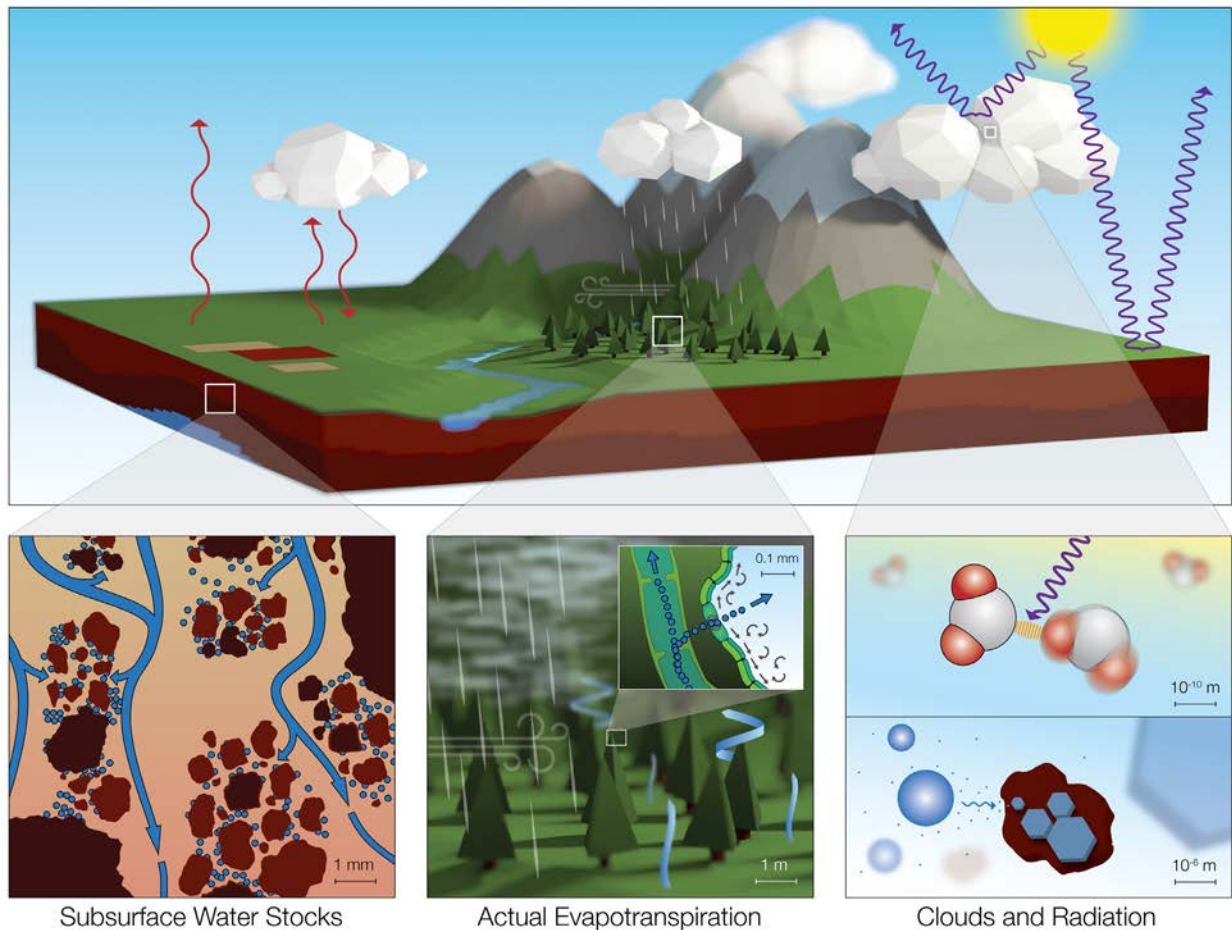
Graphics

Infographics illustrating several projects in a proposed research collaboration in climate physics. Created in 2017 for a grant proposal for a group of scientists at Karlsruhe Institute of Technology, using Blender, scanned hand-drawn sketches, Adobe Illustrator, and Photoshop.

Cover image: *3D rendering showing how a team of researchers at Rockefeller University determined the structure of the protein complex Nup82/84 (orange), which acts as a RNA export platform, and its relative position and orientation within the nuclear pore complex (grey/blue). The circular plot symbolizes the interactions between different proteins in the complex. Created in 2016 with UCSF Chimera, Cheetah 3D and Adobe Photoshop.*

Assembly and visualization of immature HIV

Samuel Hertig, Graham T. Johnson, Thomas D. Goddard, Thomas E. Ferrin

University of California, San Francisco

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

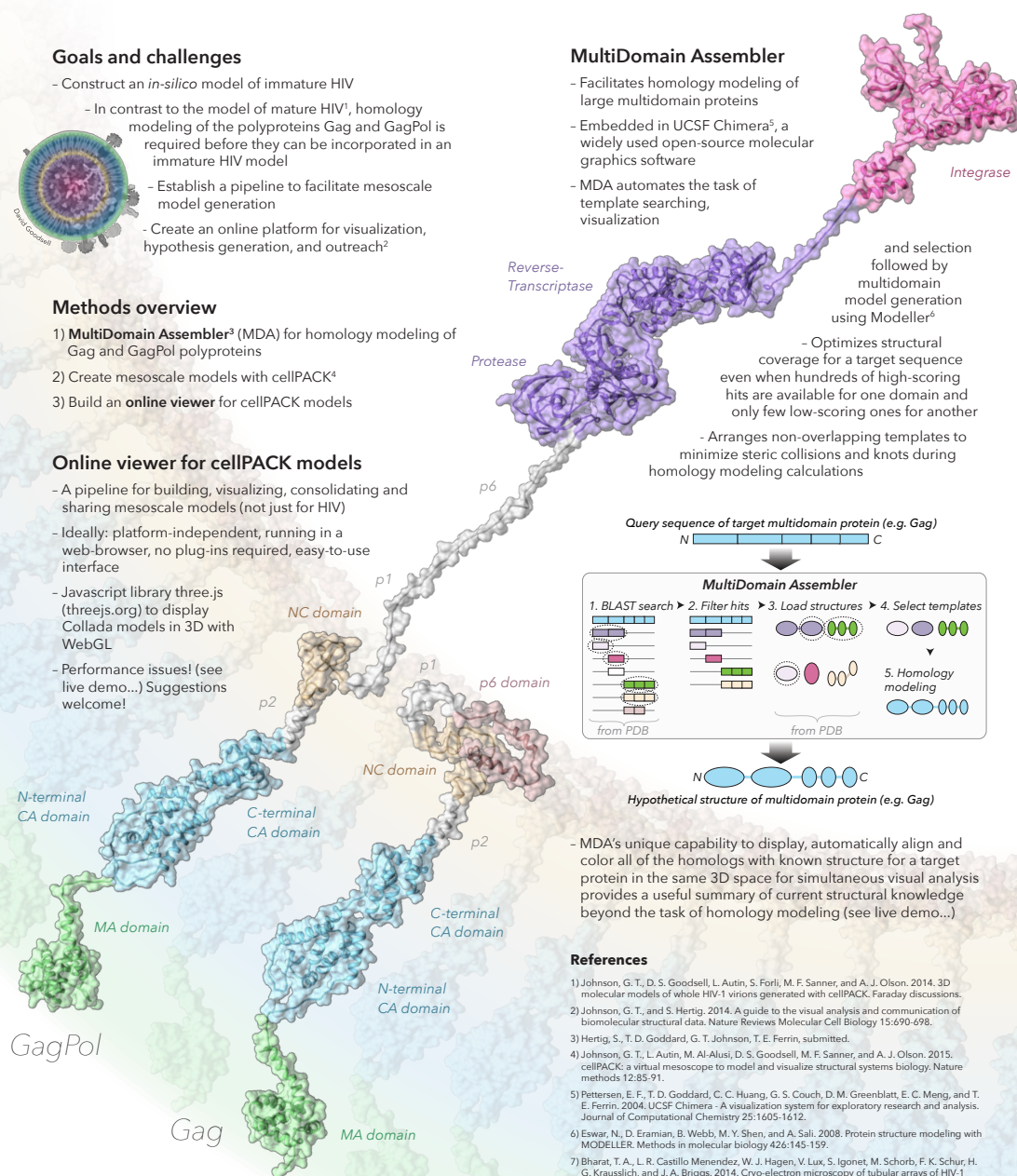– Create an online platform for visualization, hypothesis generation, and outreach[2]
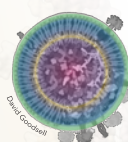
Methods overview

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!

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

Integrase

Reverse-Transcriptase

Protease

p6

p1

NC domain

p1

p2

p6 domain

N-terminal CA domain

C-terminal CA domain

NC domain

MA domain

C-terminal CA domain

GagPol

N-terminal CA domain

Gag

p2

MA domain

Query sequence of target multidomain protein (e.g. Gag)

N [ ] C

MultiDomain Assembler

1. BLAST search ▶ 2. Filter hits ▶ 3. Load structures ▶ 4. Select templates

5. Homology modeling

from PDB   *from PDB*

N [ ] C

Hypothetical structure of multidomain protein (e.g. Gag)

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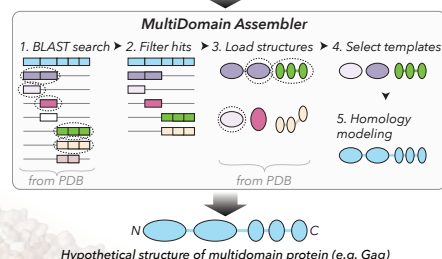
The viral polyproteins Gag and GagPol govern the assembly of HIV, and are composed of multiple domains connected by flexible linkers. These models were created using MDA with additional distance restraints, for example obtained by EM studies of the immature virion[7].

References

1) Johnson, G. T., D. S. Goodsell, L. Autin, S. Forli, M. F. Sanner, and A. J. Olson. 2014. 3D molecular models of whole HIV-1 virions generated with cellPACK. Faraday discussions.

2) Johnson, G. T., and S. Hertig. 2014. A guide to the visual analysis and communication of biomolecular structural data. Nature Reviews Molecular Cell Biology 15:690-698.

3) Hertig, S., T. D. Goddard, G. T. Johnson, T. E. Ferrin, submitted.

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

5) Pettersen, E. F., T. D. Goddard, C. C. Huang, G. S. Couch, D. M. Greenblatt, E. C. Meng, and T. E. Ferrin. 2004. UCSF Chimera - A visualization system for exploratory research and analysis. Journal of Computational Chemistry 25:1605-1612.

6) Eswar, N., D. Eramian, B. Webb, M. Y. Shen, and A. Sali. 2008. Protein structure modeling with MODELLER. Methods in molecular biology 426:145-159.

7) Bharat, T. A., L. R. Castillo Menendez, W. J. Hagen, V. Lux, S. Igonet, M. Schorb, F. K. Schur, H. G. Krausslich, and J. A. Briggs. 2014. Cryo-electron microscopy of tubular arrays of HIV-1 Gag resolves structures essential for immature virus assembly. Proc Natl Acad Sci U S A 111:8233-8238.

Conference poster presented at the conference on Visualization of Biological Data in Boston in 2015, which earned the best poster award. Crafted with UCSF Chimera, Adobe Illustrator and Photoshop.

Videos

Movie of a human immunodeficiency virus (HIV) in blood plasma. Created with Lego bricks, a camera and iMovie. Received a honorary mention in a scientific visualization challenge hosted on cgsociety.org, 2013.

> *https://youtu.be/1WZH0y16Yww*
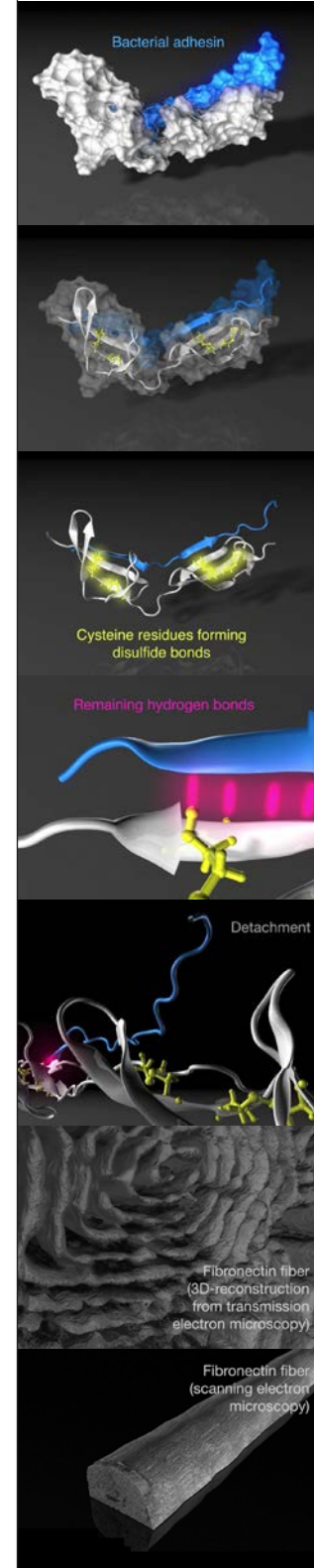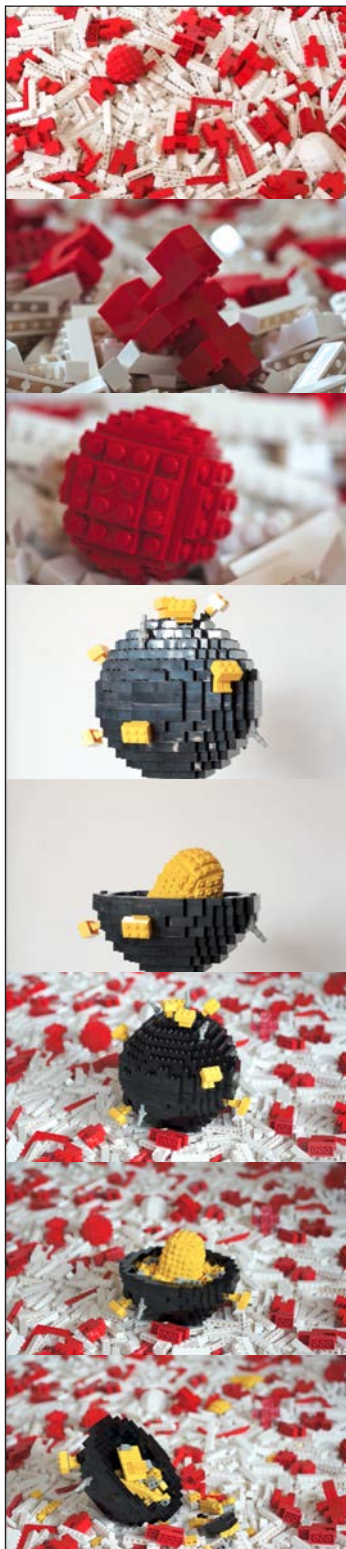
Animation describing a molecular dynamics simulation of a protein complex in the context of its environment. Made with Autodesk Maya, VMD, various scripts and Adobe AfterEffects. Featured in "G. T. Johnson and S. Hertig: A guide to the visual analysis and communication of biomolecular structural data. Nature Reviews Molecular Cell Biology 15 (2014), 690-698."

> *https://youtu.be/yeIOTrbIx_2*

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