

RosettaAntibodyDesign (RAbD)

Talk by: Benjamin Mueller
Meiler Lab, Vanderbilt University

RosettaAntibodyDesign (RAbD)

This talk is focused on the publication:

RESEARCH ARTICLE

RosettaAntibodyDesign (RAbD): A general framework for computational antibody design

Jared Adolf-Bryfogle^{1,2,3}, Oleks Kalyuzhniy^{3,4}, Michael Kubitz³, Brian D. Weitzner^{5,6}, Xiaozhen Hu³, Yumiko Adachi⁴, William R. Schief^{3,4}, Roland L. Dunbrack, Jr.^{1*}

1 Institute for Cancer Research, Fox Chase Cancer Center, Philadelphia, PA, United States of America, **2** Program in Molecular and Cell Biology and Genetics, Drexel University College of Medicine, Philadelphia, PA, United States of America, **3** The Scripps Research Institute, La Jolla, CA, United States of America, **4** IAVI Neutralizing Antibody Center at TSRI, La Jolla, CA, United States of America, **5** Department of Biochemistry, University of Washington, Seattle, WA, United States of America, **6** Institute for Protein Design, University of Washington, Seattle, WA, United States of America

April 2018, PLOS Comp Bio

Rosetta Design

Rosetta has been used extensively for protein design and docking + design

For example, from earlier this year:

Transferrin receptor targeting by de novo sheet extension

Danny D. Sahtoe^{a,b,c}, Adrian Coscia^{d,1}, Nur Mustafaoglu^{e,1}, Lauren M. Miller^{a,b,1}, Daniel Olal^d, Ivan Vulovic^{a,b}, Ta-Yi Yu^{b,f}, Inna Goreshnik^{a,b}, Yu-Ru Lin^{a,b}, Lars Clark^d, Florian Busch^{g,h}, Lance Stewart^{a,b}, Vicki H. Wysocki^{g,h}, Donald E. Ingber^{e,i,j}, Jonathan Abraham^{d,k,l,2}, and David Baker^{a,b,c,2}

^aDepartment of Biochemistry, University of Washington, Seattle, WA 98195; ^bInstitute for Protein Design, University of Washington, Seattle, WA 98195; ^cHHMI, University of Washington, Seattle, WA 98195; ^dDepartment of Microbiology, Blavatnik Institute, Harvard Medical School, Boston, MA 02115; ^eWyss Institute for Biologically Inspired Engineering at Harvard University, Boston, MA 02115; ^fDepartment of Bioengineering, University of Washington, Seattle, WA 98195; ^gDepartment of Chemistry and Biochemistry, The Ohio State University, Columbus, OH 43210; ^hResource for Native Mass Spectrometry Guided Structural Biology, The Ohio State University, Columbus, OH 43210; ⁱDepartment of Surgery and Vascular Biology Program, Harvard Medical School and Boston Children's Hospital, Boston, MA 02115; ^jHarvard John A. Paulson School of Engineering and Applied Sciences, Harvard University, Cambridge, MA 02539; ^kDivision of Infectious Diseases, Department of Medicine, Brigham and Women's Hospital, Boston, MA 02115; and ^lBroad Institute of MIT and Harvard, Cambridge, MA 02142

Rosetta Design

However that publication developed a bespoke protocol for that system, which may not be amenable to your specific needs

RAbD, while specific to antibodies, offers a flexible, general framework with which to design antibodies for your needs

It can be used for many design projects, including

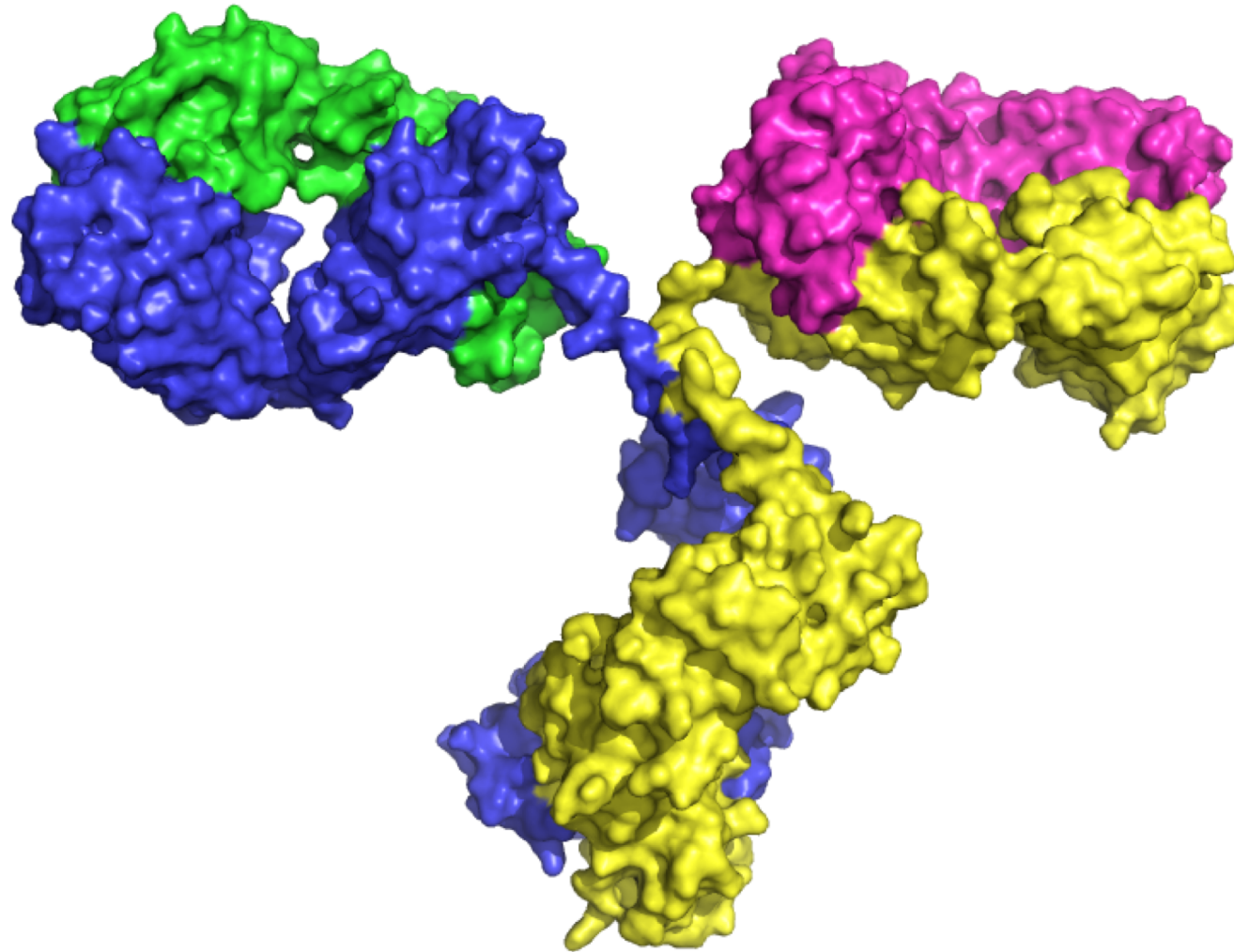
- Affinity Maturation

- Homologous Redesign

- Stability Improvement

- De Novo* Design

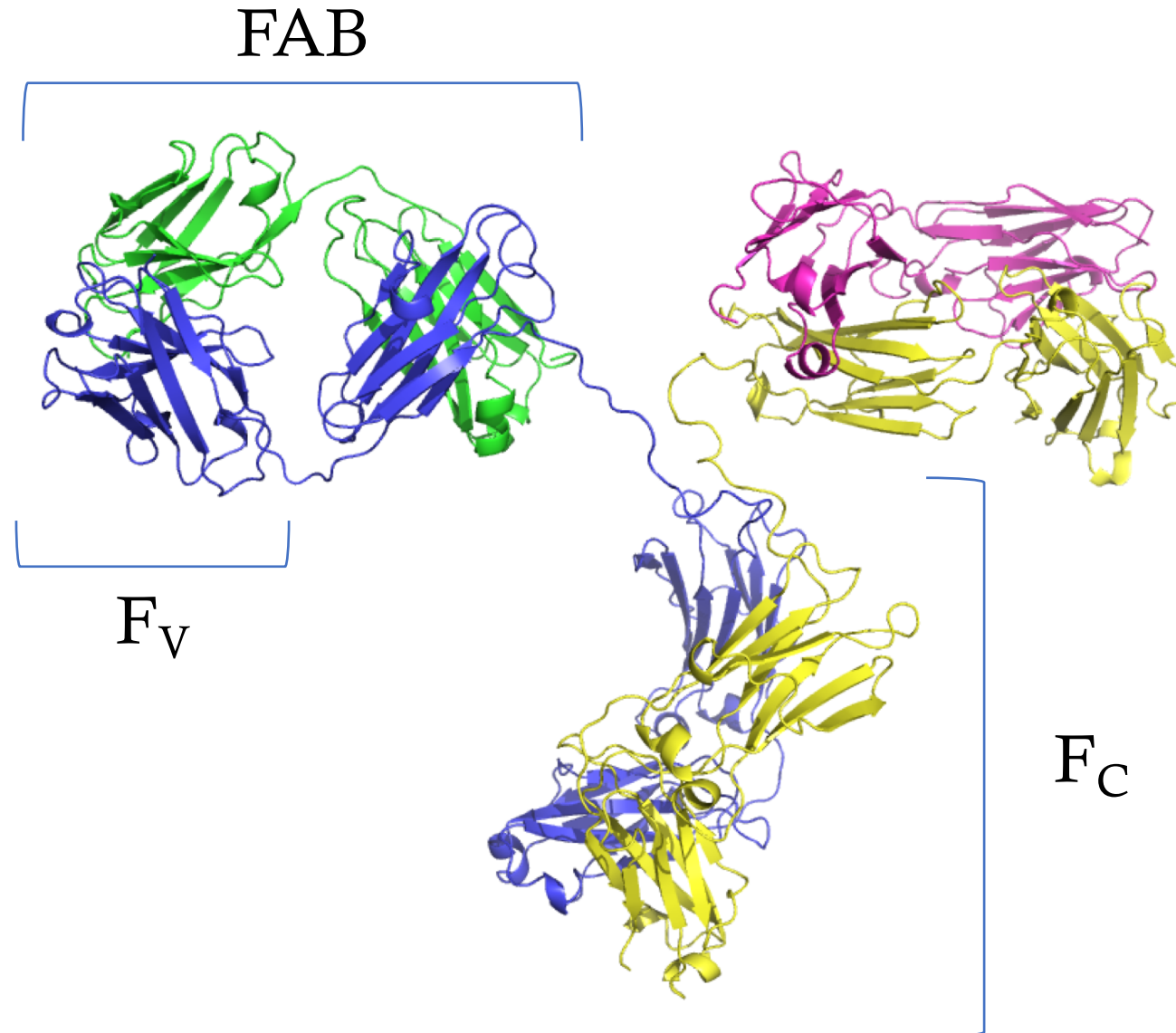
Quick Antibody Overview



Yellow / Blue –
Heavy Chain

Green / Pink –
Light Chain

Quick Antibody Overview

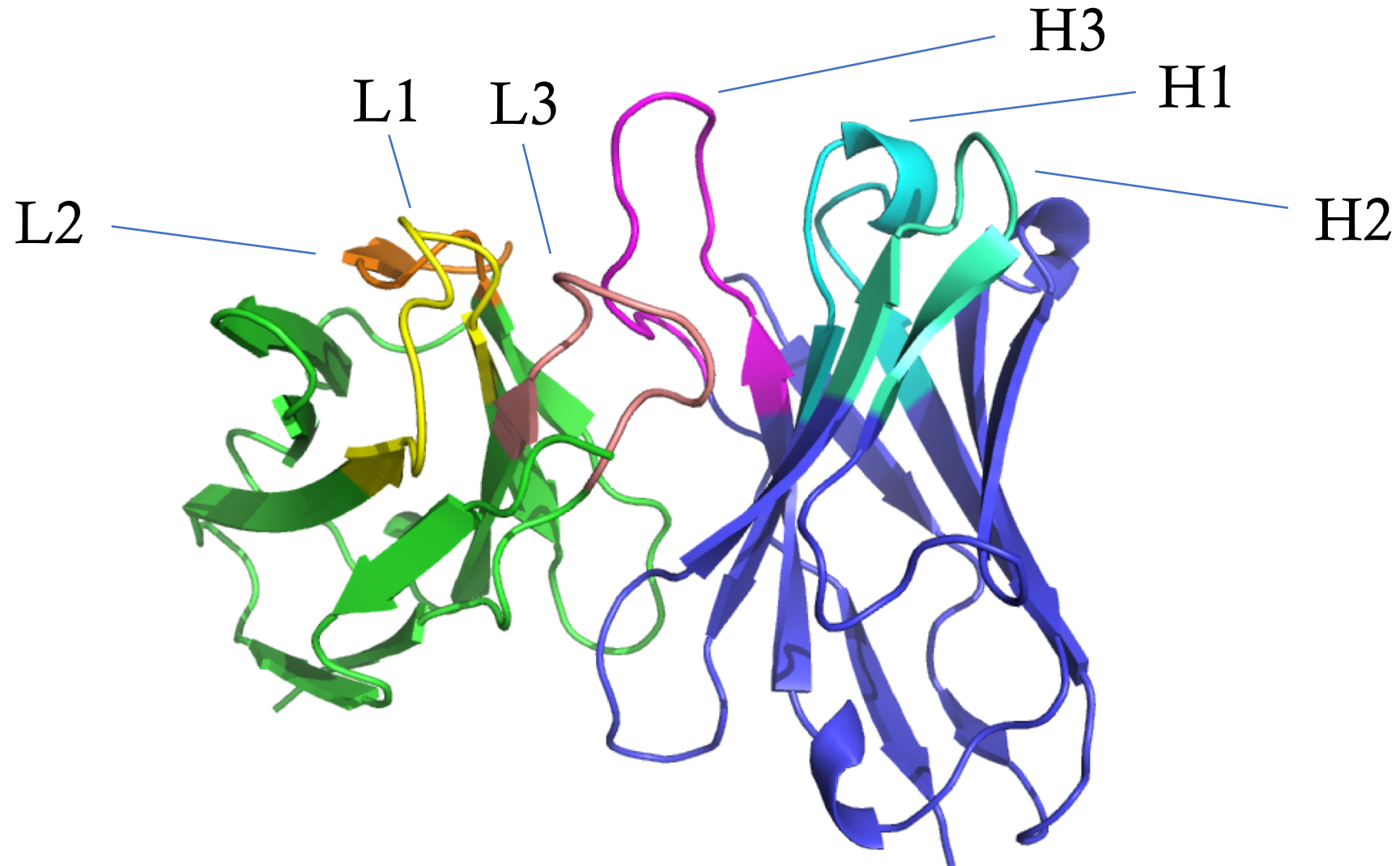


FAB – antigen binding fragment

F_v – variable fragment

F_c – crystallizable fragment

Quick Antibody Overview – F_V region



6 CDR loops – 3 on the heavy chain, 3 on the light chain

CDR Clustering

A new clustering of antibody CDR loop conformations

Benjamin North, Andreas Lehmann, and Roland L. Dunbrack Jr.

Institute for Cancer Research Fox Chase Cancer Center 333 Cottman Avenue Philadelphia PA 19111 USA

2011, J Mol Bio.

PylgClassify: a database of antibody CDR structural classifications

Jared Adolf-Bryfogle^{1,2}, Qifang Xu¹, Benjamin North¹, Andreas Lehmann¹ and Roland L. Dunbrack, Jr^{1,*}

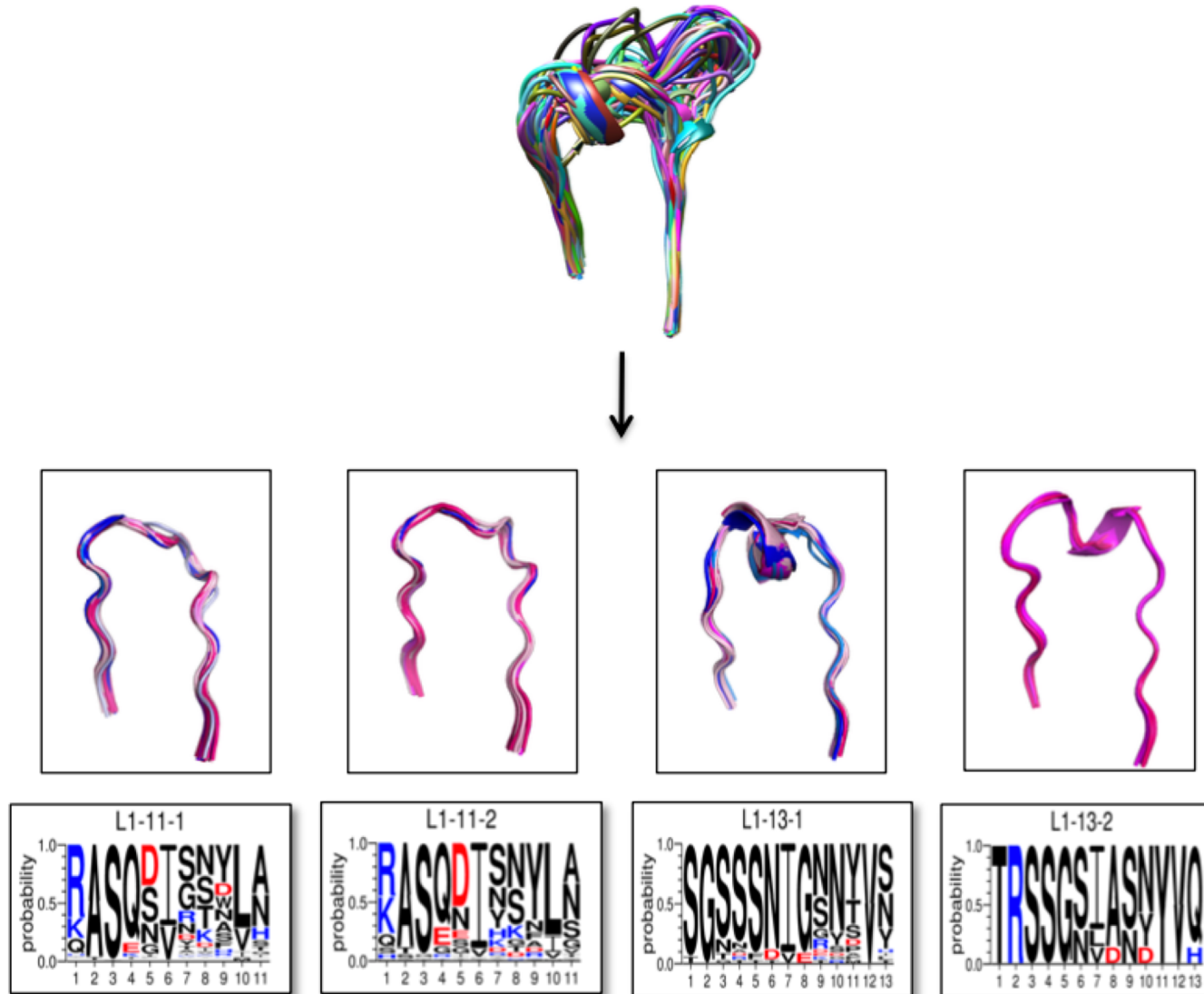
¹Institute for Cancer Research, Fox Chase Cancer Center, 333 Cottman Avenue, Philadelphia, PA 19111, USA and

²Program in Molecular and Cell Biology and Genetics, Drexel University College of Medicine, 245 N. 15th St. Philadelphia, PA 19102, USA

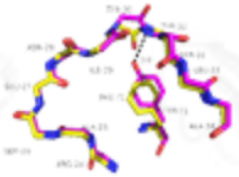
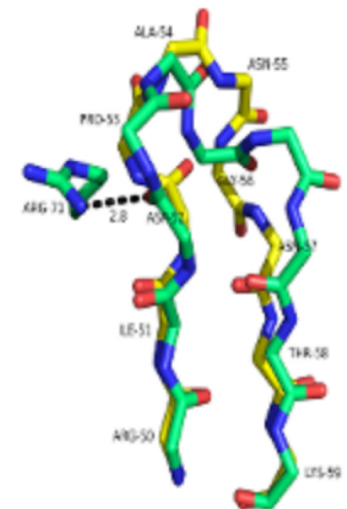
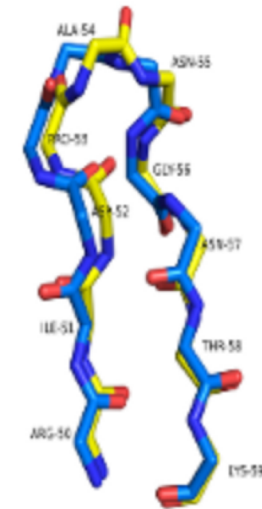
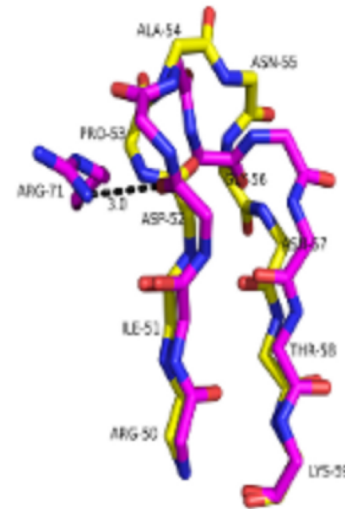
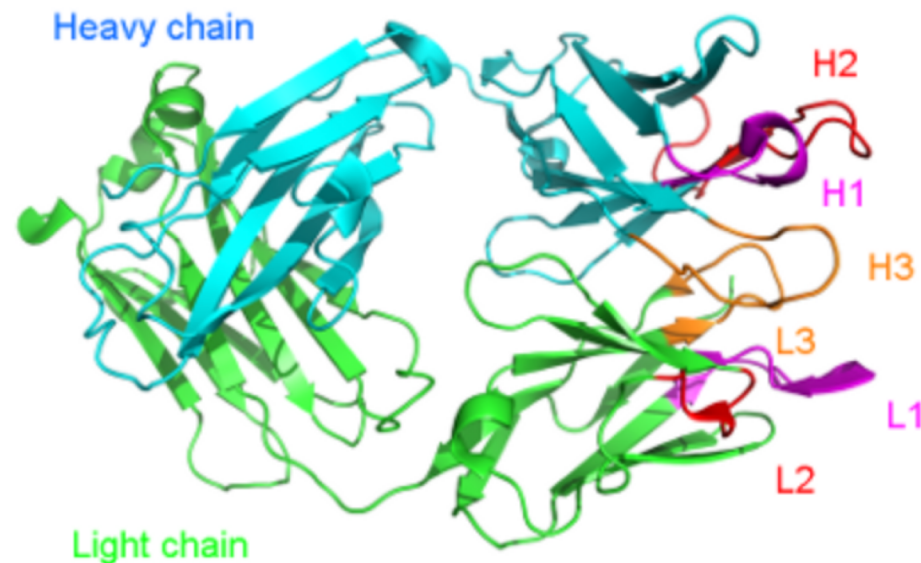
Received August 15, 2014; Revised October 20, 2014; Accepted October 23, 2014

2015, Nucleic Acids Research

CDR Clustering

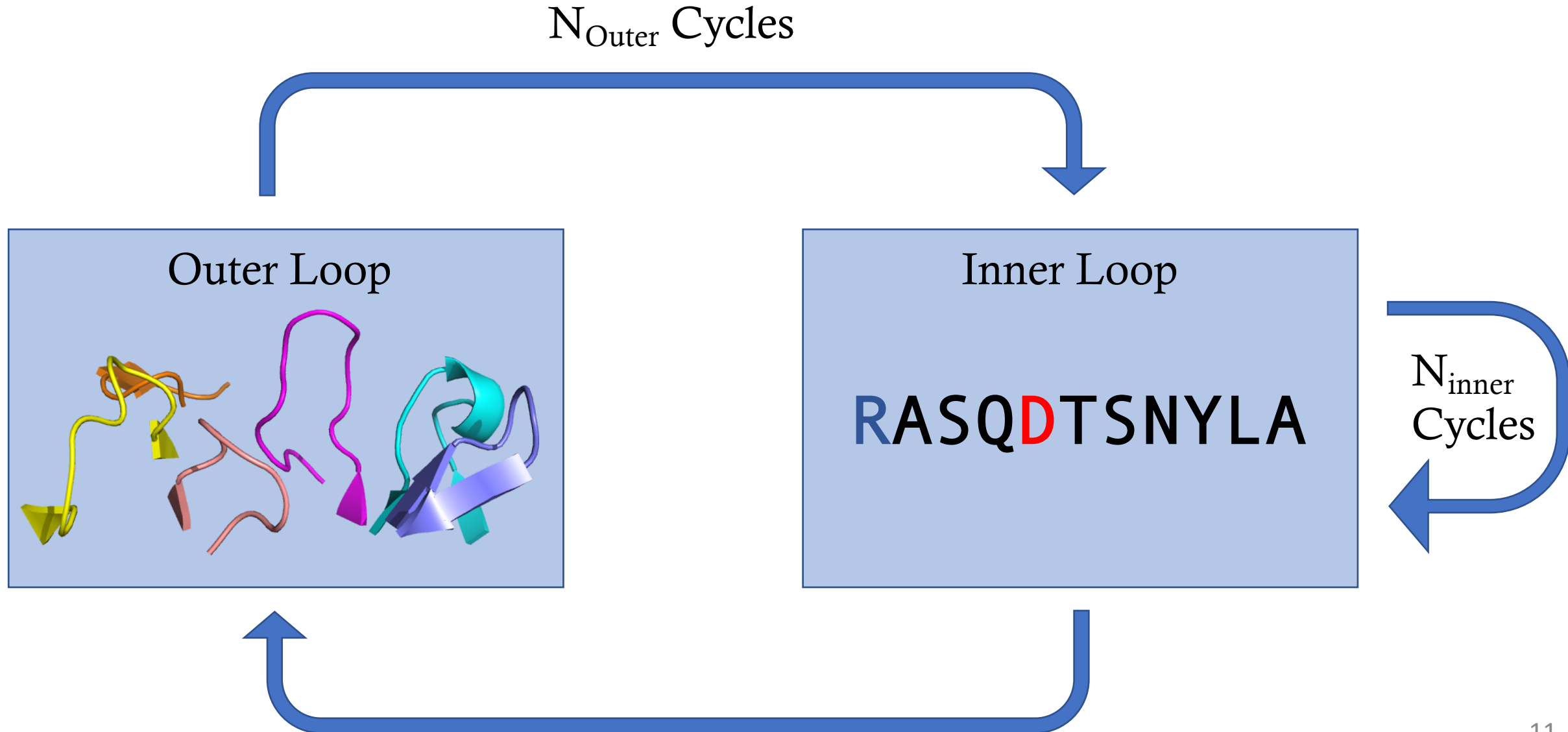


Clusters of Antibody CDR Loop Conformations

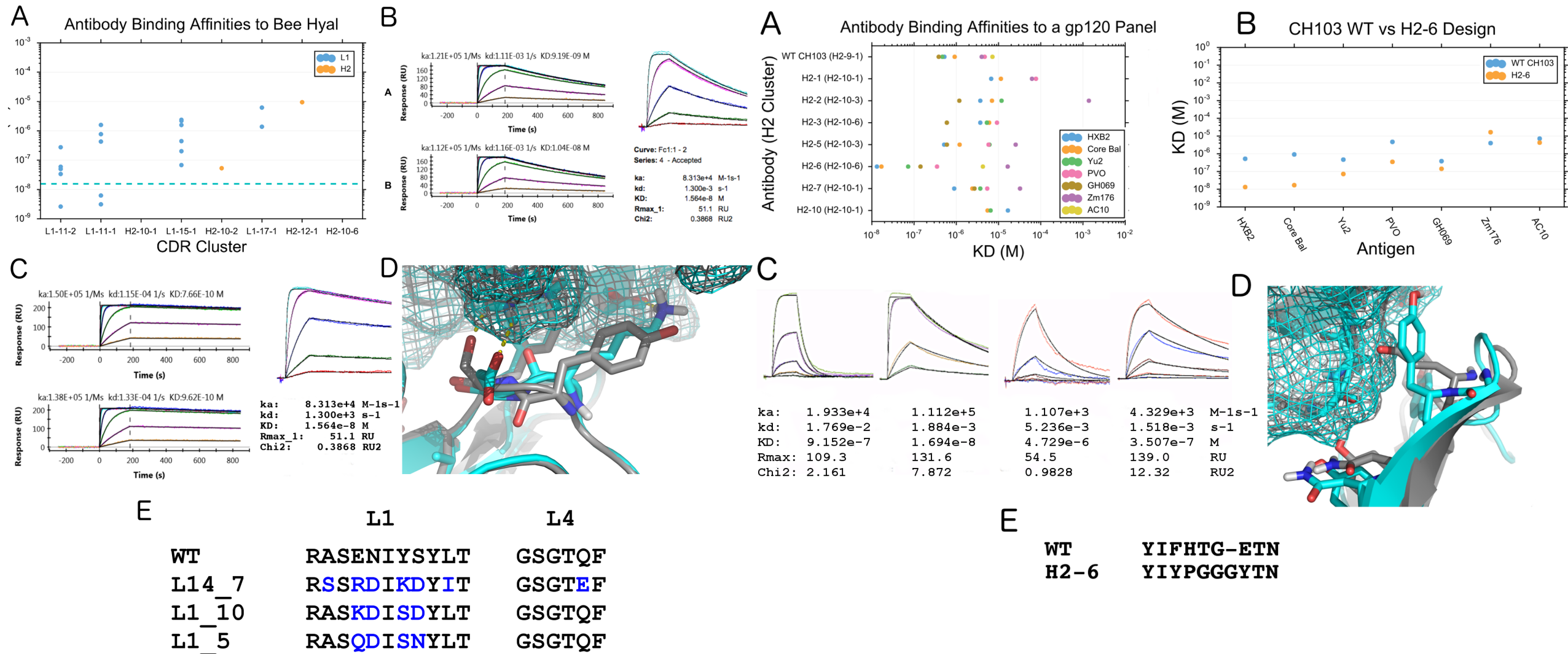
[Home](#)[Search](#)[Submit](#)[Statistics](#)[Download](#)[Help](#)[About](#)

PyIgClassify (Last updated on November 1, 2019) is a monthly-updated web server primarily providing the clusters and associated information of the antibody complementarity determining regions (CDRs) in the Protein Data Bank (PDB). The current database contains 3,065 PDB antibody entries. The list of PDB entries can be browsed [here](#).

RAbD Algorithm Overview



Results



Tutorials

1. Sequence Design Only
2. CDR replacement and Sequence Design
3. De Novo Design
4. Custom Protocol Creation using RosettaScripts