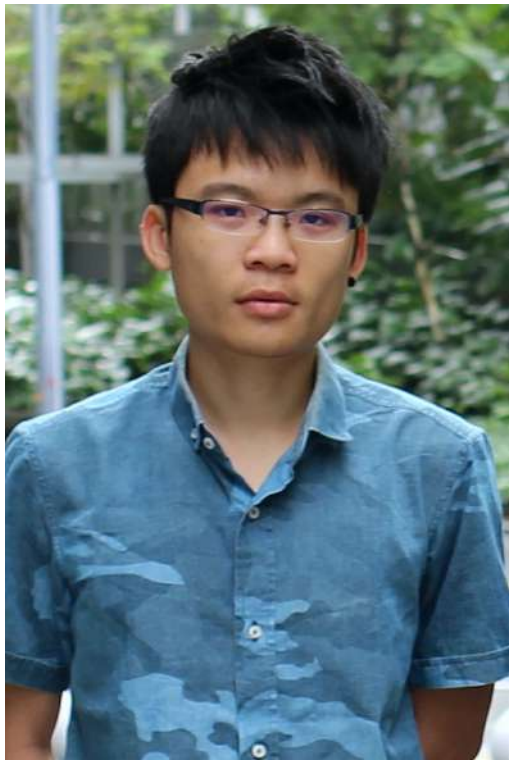
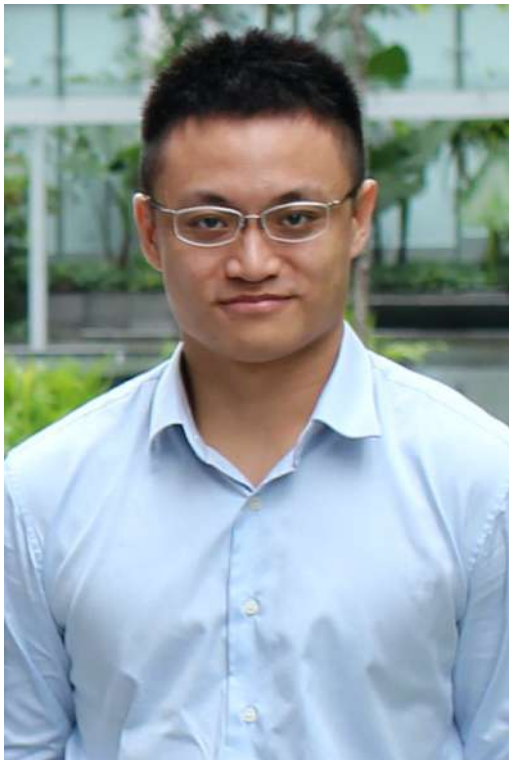
Berezovsky Group
Physics and Evolution of Biological Macromolecules

Bioinformatics Institute, A*STAR
April 21, 2021

Berezovsky Group
Physics and Evolution of Biological Macromolecules



Wei-Ven Tee



Melvin Yin

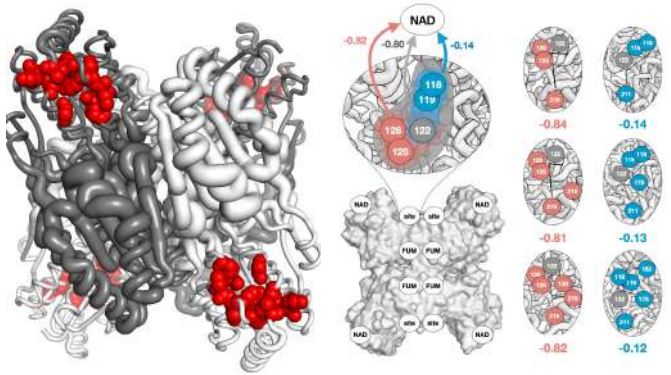
Enrico Guarnera

Zhen Wah Tan

Berezovsky Group
Physics and Evolution of Biological Macromolecules

Allostery

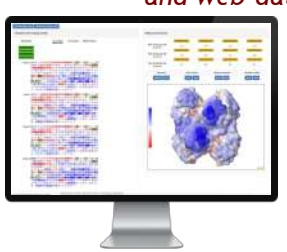
Paving the way to design of allosteric drugs and precision medicine



PLOS Comp Biol 12, e1004678 (2016)
Biochemistry 56, 228 (2017)
Trends Pharm Sci 39, 49 (2018)
PLOS Comp Biol 14, e1006228 (2018)

Structure 27, 866 (2019)
J Mol Biol 431, 3933 (2019)
Biophys J 119, 1833 (2020)

Outreach1: Highly acclaimed web-server AlloSigMA and web-database AlloMAPS



AlloSigMA server
http://allosigma.bii.a-star.edu.sg
Bioinformatics 33, 3996 (2017)
NAR 48, W116 (2020)
AlloMAPS database
http://allomaps.bii.a-star.edu.sg
NAR 47, D265 (2019)

*Outreach2: A*STAR Research Support Center*

Allostery Platform allows:

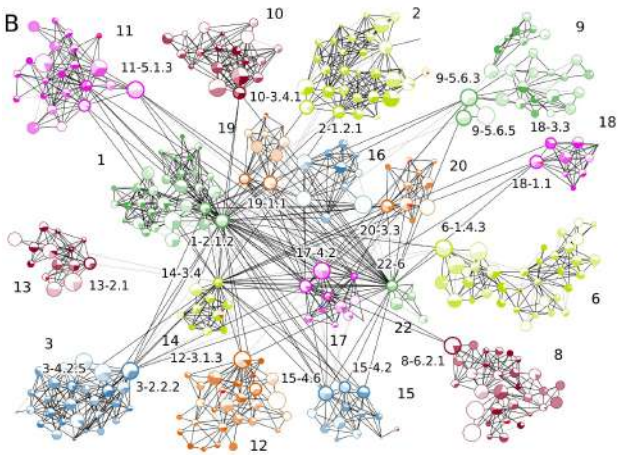
1. *Search/predict latent/new allosteric sites*
2. *Using allosteric regulation in protein design*
3. *Allosteric drug development*
4. *Exploring allosteric effect of mutations*

Collaboration:

BII: Peter Bond, Chandra Verma
Penn State University, USA, Prof. Anand,
SBS/NTU, Prof. Pervushin

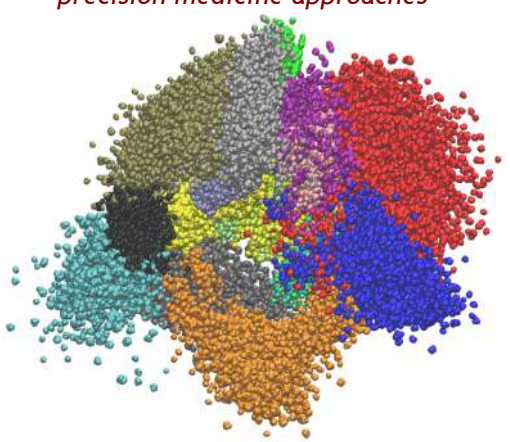
Chromatin

Whole-genome effective interactions and epigenetic regulation



PLOS Comp Biol 14, e1006686 (2018)

3D reconstruction and genome dynamics towards precision medicine approaches



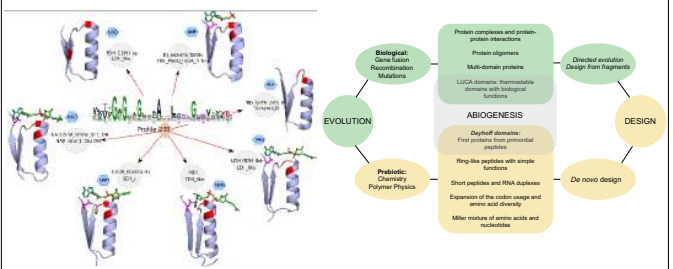
Structure, https://doi.org/10.1016/j.str.2021.01.008 *(2021)*

Collaboration:

SBS/NTU, Prof. Nordenskiöld; *Prof. Sanyal*

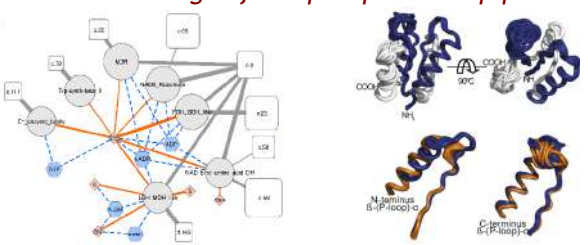
Evolution-based protein design

Emergence and evolution of protein function



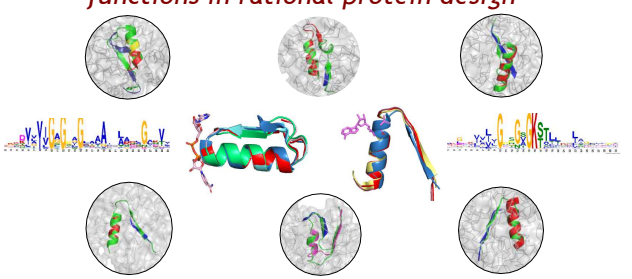
Curr Opin Struct Biol 58, 159 (2019)

De novo design of the phosphate-loop protein



PNAS USA 115, E11943 (2018)

Deriving and using descriptors of elementary functions in rational protein design



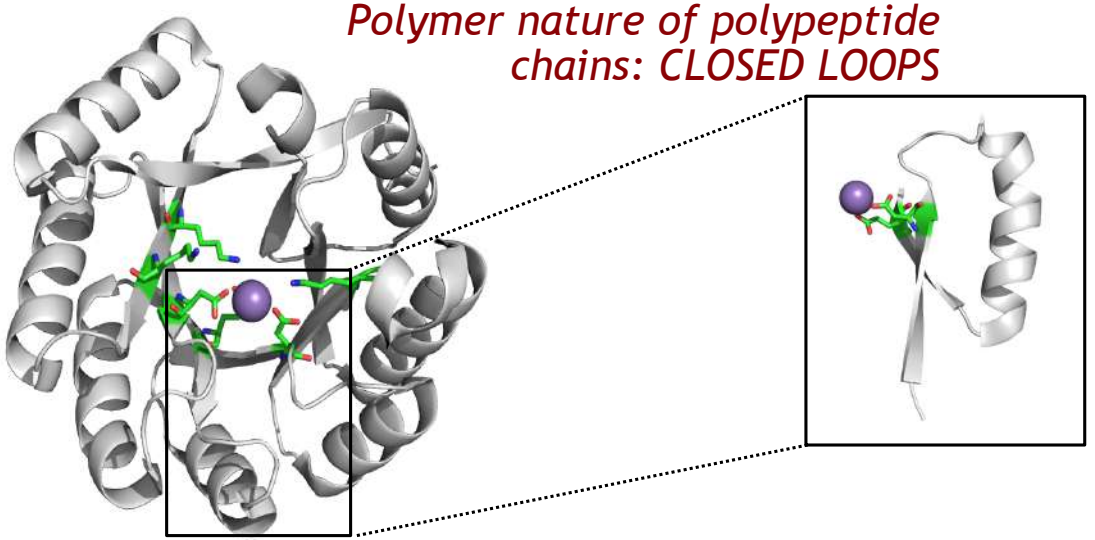
Frontiers in Bioinformatics 1, 657529 (2021)

Collaboration:

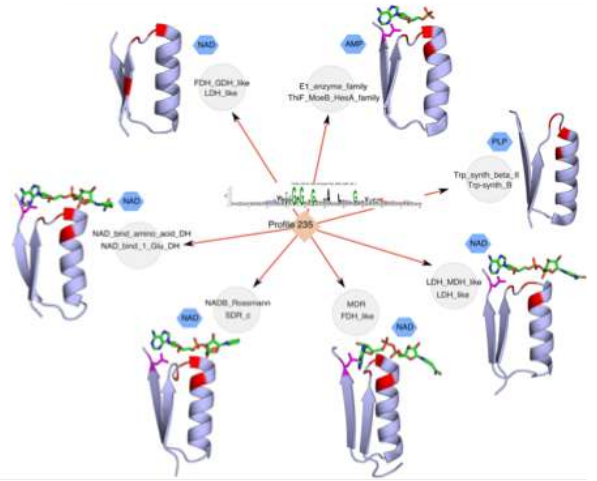
Weizmann Institute, IL, Prof. Dan Tawfik

Protein design: learning form protein physics and evolution

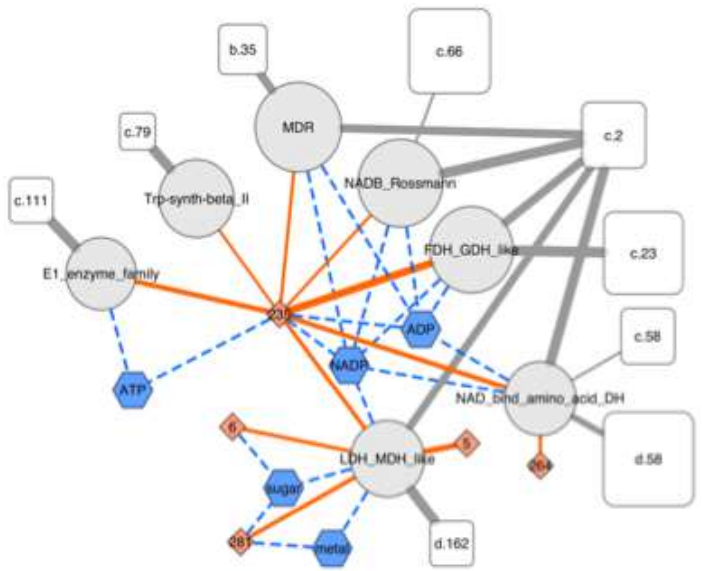
Polymer nature of polypeptide chains: CLOSED LOOPS



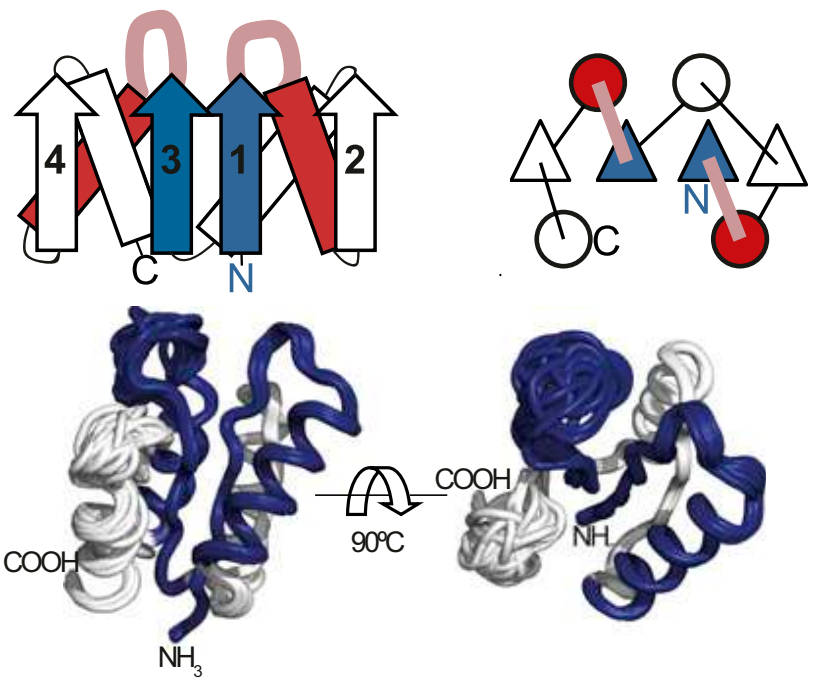
Sequence and functional signature: ELEMENTARY FUNCTIONAL LOOPS



Evolutionary connections between folds and functions



De novo design of the "phosphate-loop" protein

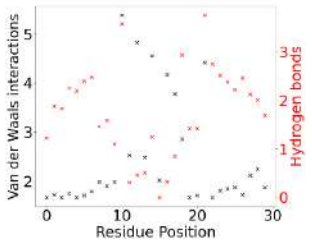


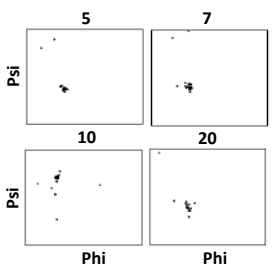
NBDB database; NAR 44, D301 (2016): http://nbdb.bii.a-star.edu.sg
Curr Opin Struct Biol 58, 159 (2019)

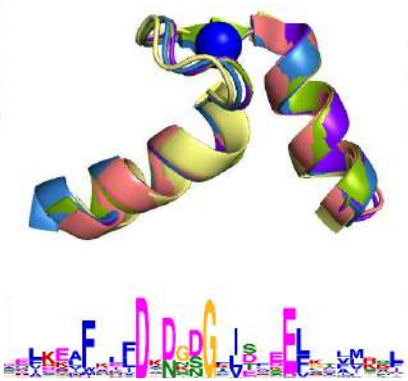
PNAS USA 115, E11943 (2018)

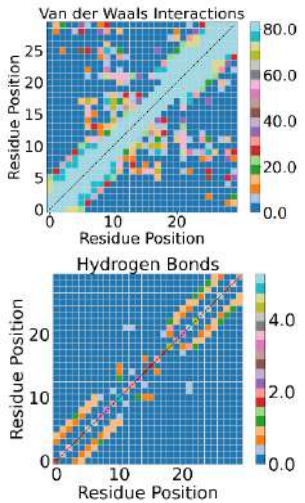
Protein design

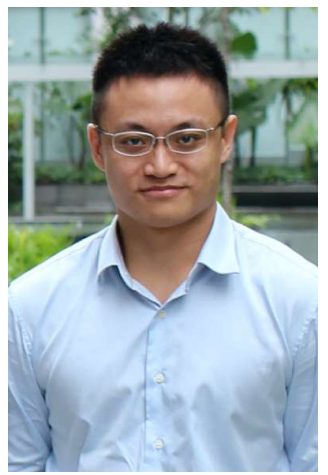
DEFINED-PROTEINS (Descriptor of Function IN Engineering and Design - PROTEINS) software package:
1. Derives the descriptor of elementary function 2. Provides the objective function for protein engineering and design



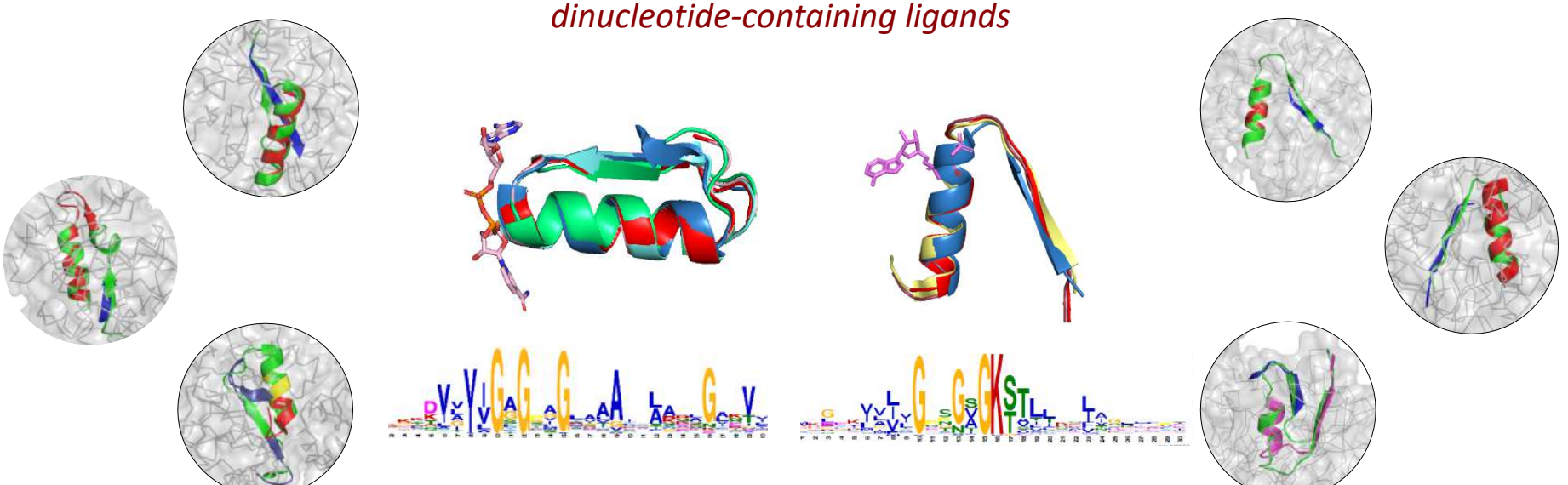








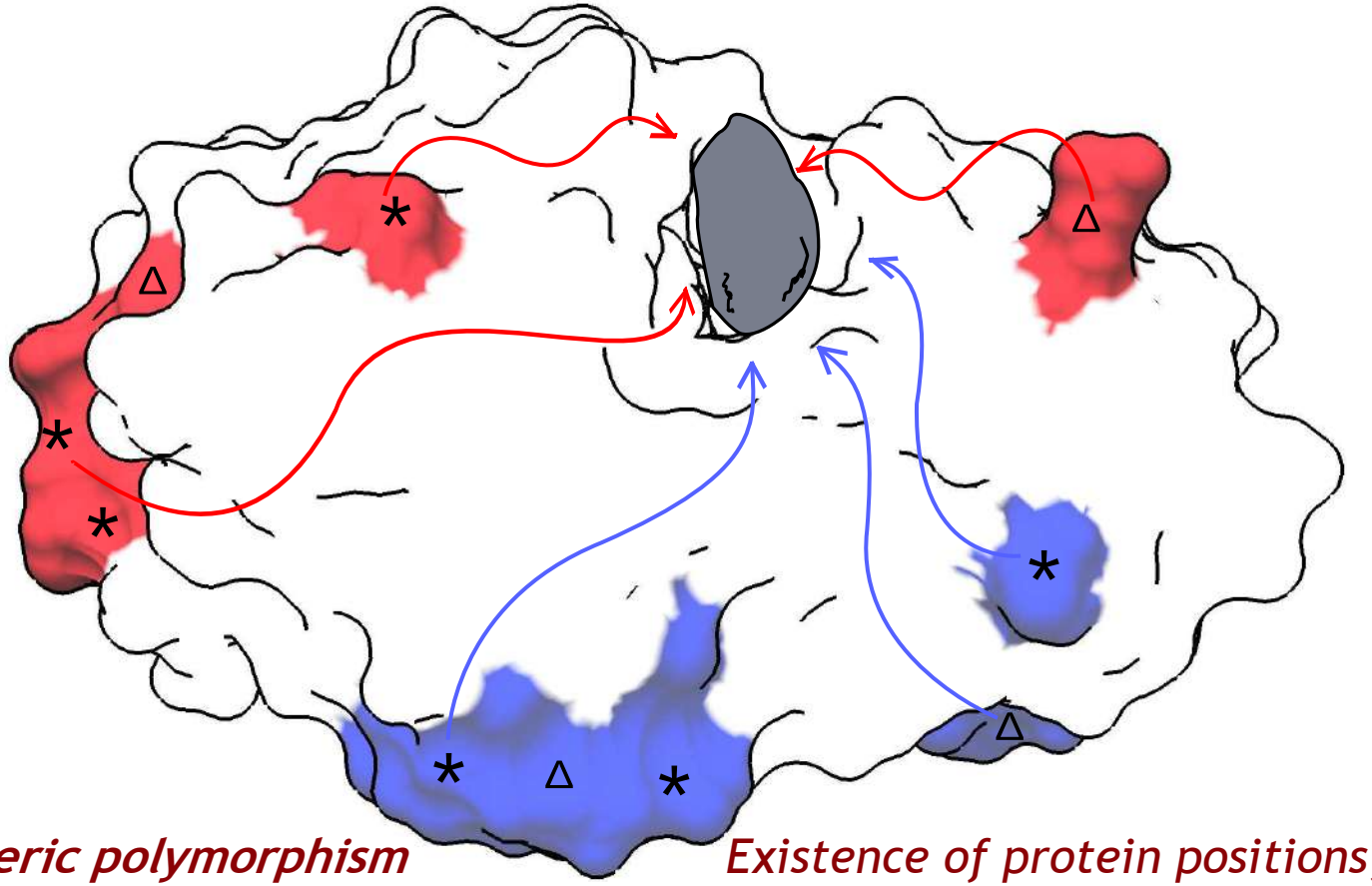
Realization of descriptors in the cross-grafting experiment between phosphate-binding signatures in the nucleotide- and dinucleotide-containing ligands

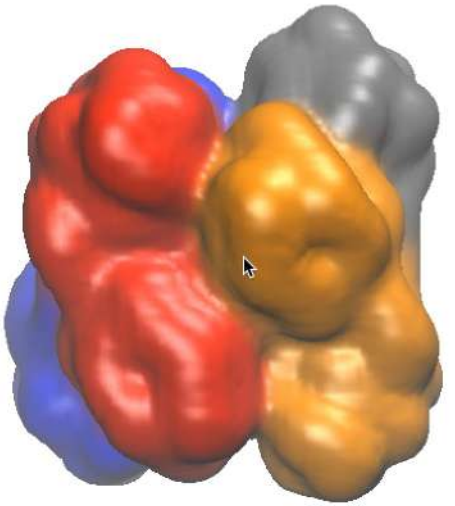


Curr Opin Struct Biol 58, 159 (2019)

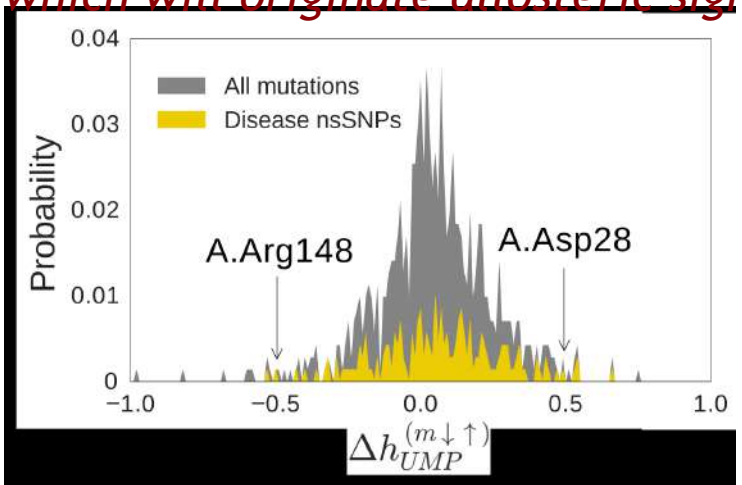
Frontiers in Bioinformatics 1, 657529 (2021)

Allosteric effect of nsSNPs and allosteric polymorphism

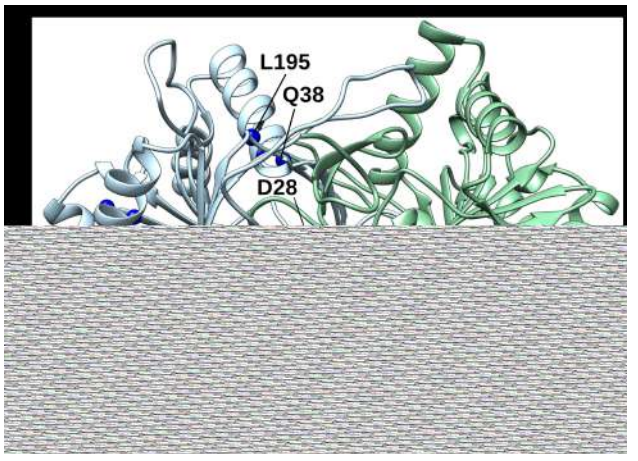




Allosteric polymorphism *Existence of protein positions, mutations of which will originate allosteric signals similar to those observed for known SNPs*

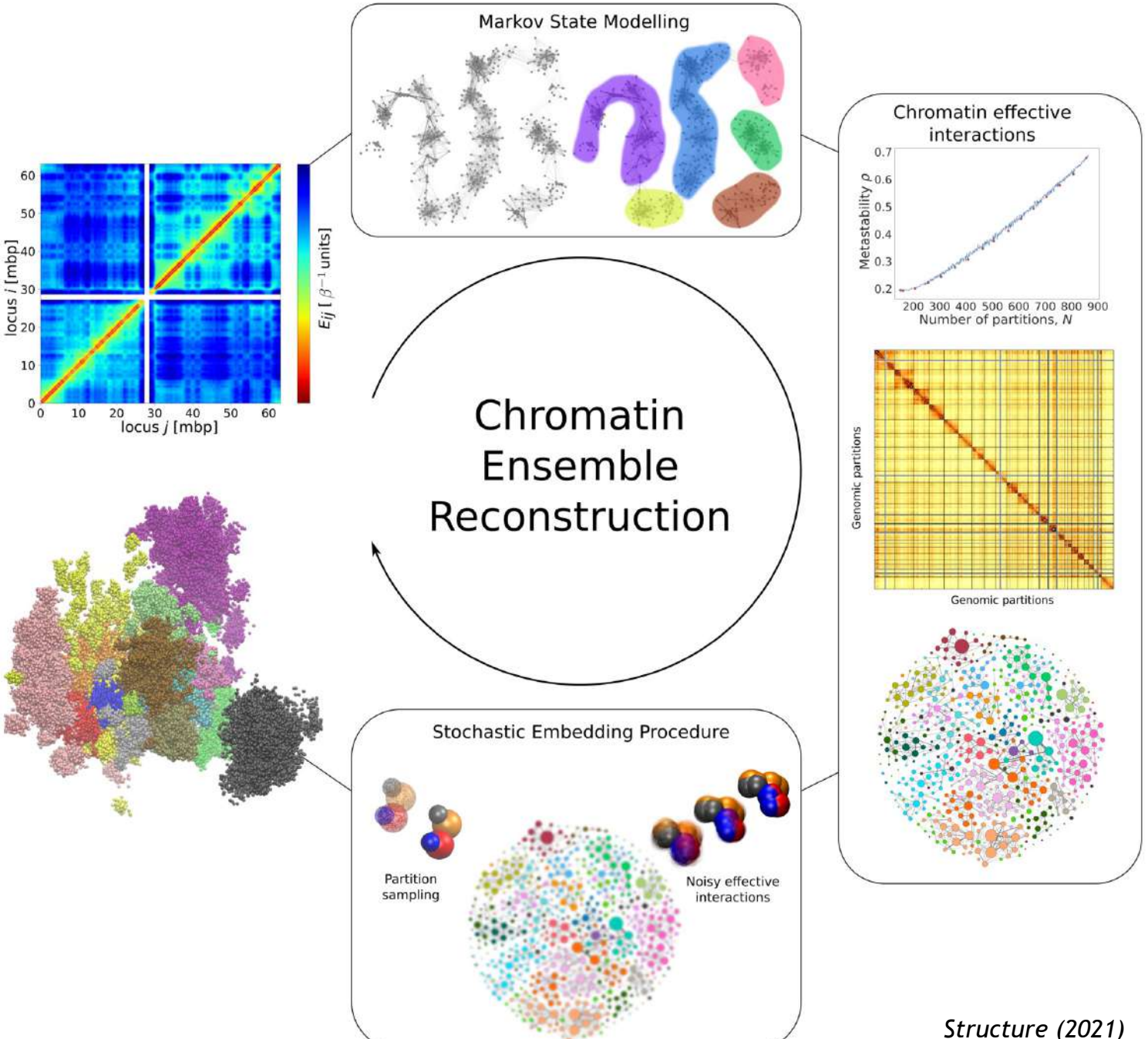


Galactose 1-phosphate uridyltransferase



J Mol Biol 431, 3933 (2019)
Curr Opin Struct Biol 62, 149 (2020)

Chromatin structure, dynamics, and epigenetic regulation

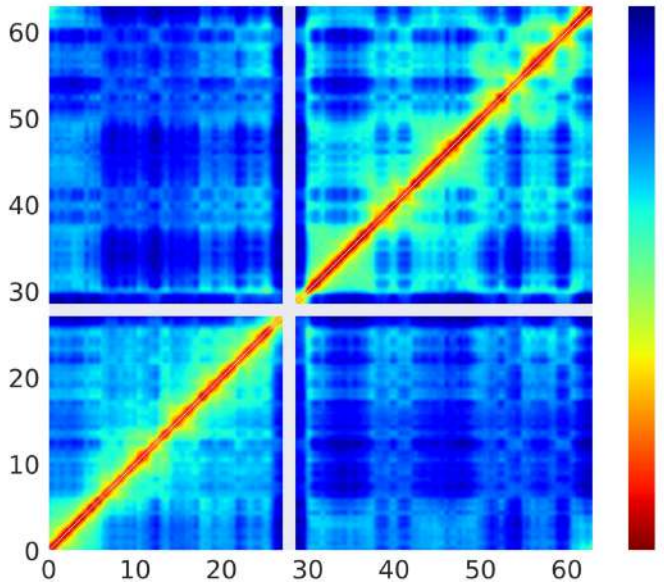


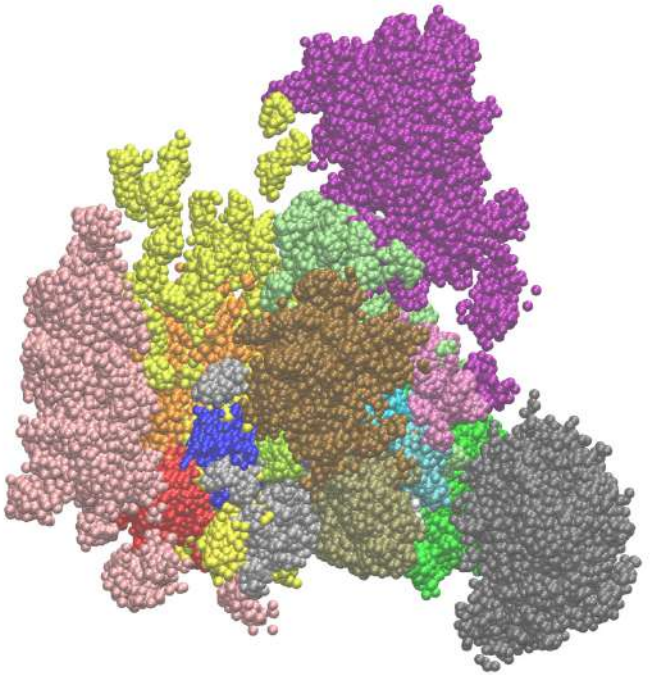
PLOS Comp Biol 14, e1006686 (2018)

Structure (2021)
https://doi.org/10.1016/j.str.2021.01.008

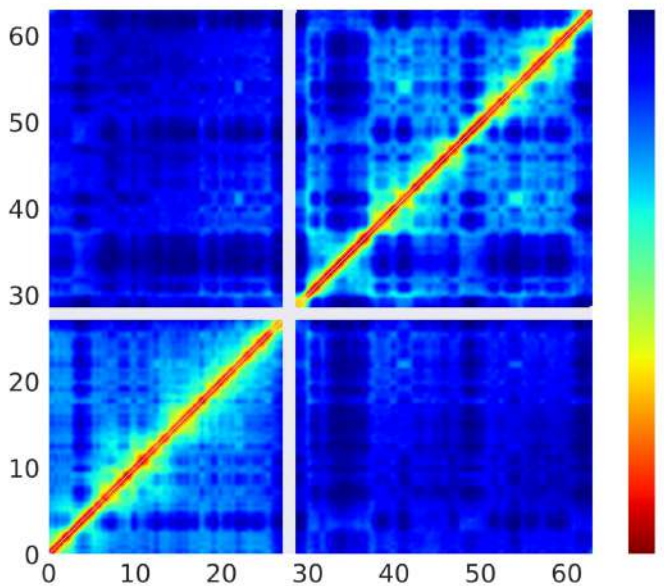
3D Whole-Genome Reconstruction from the Hi-C Data

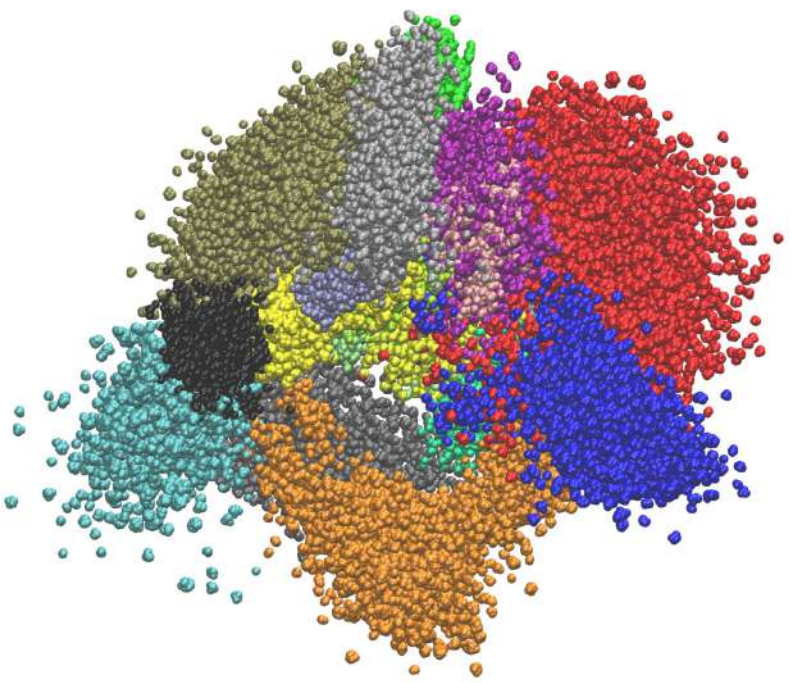
GM12878





IMR90

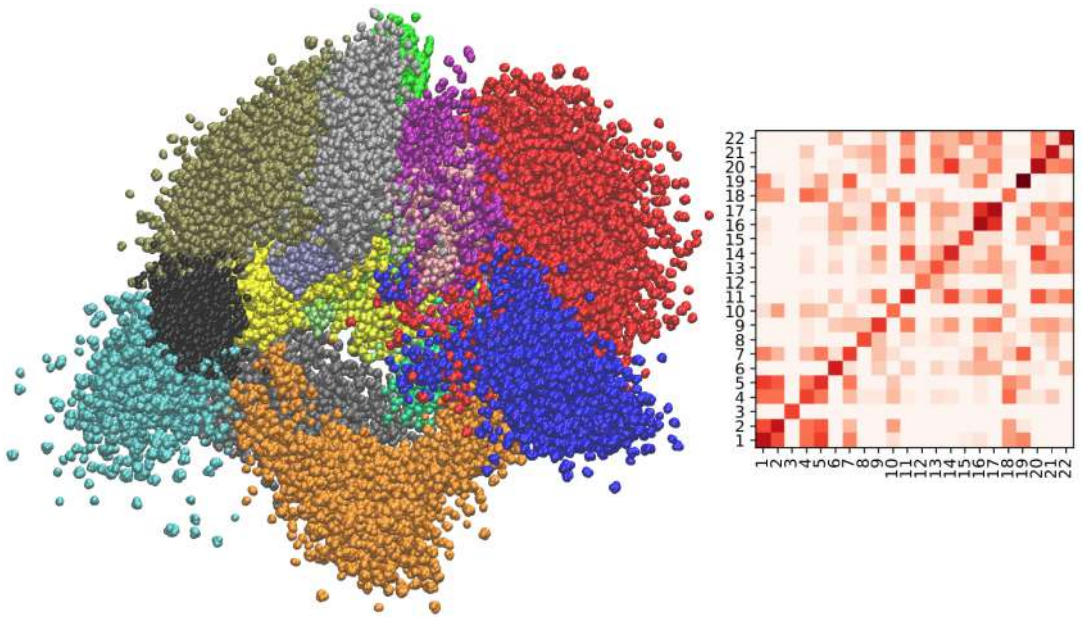




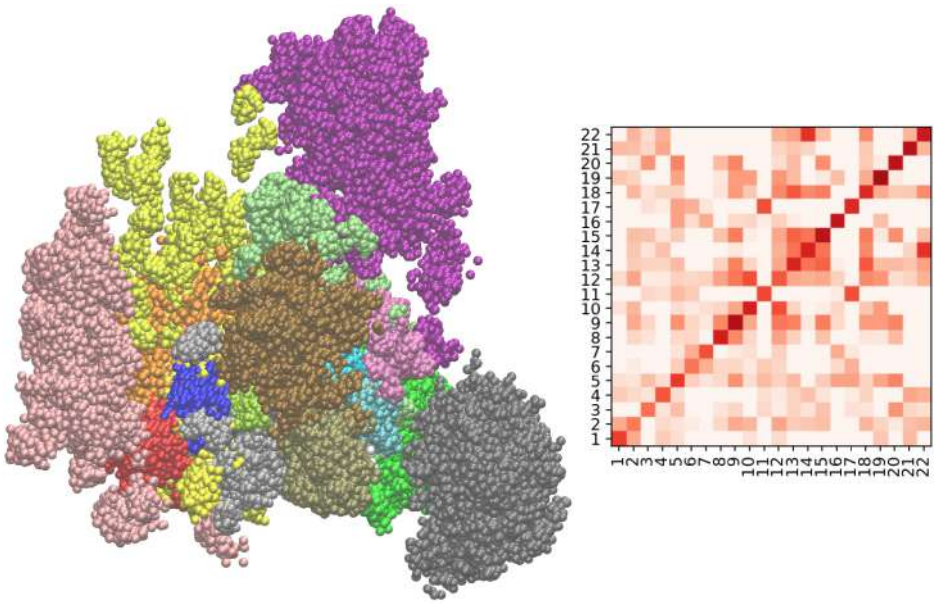
Structure (2021)
https://doi.org/10.1016/j.str.2021.01.008

3D Whole-Genome Reconstruction

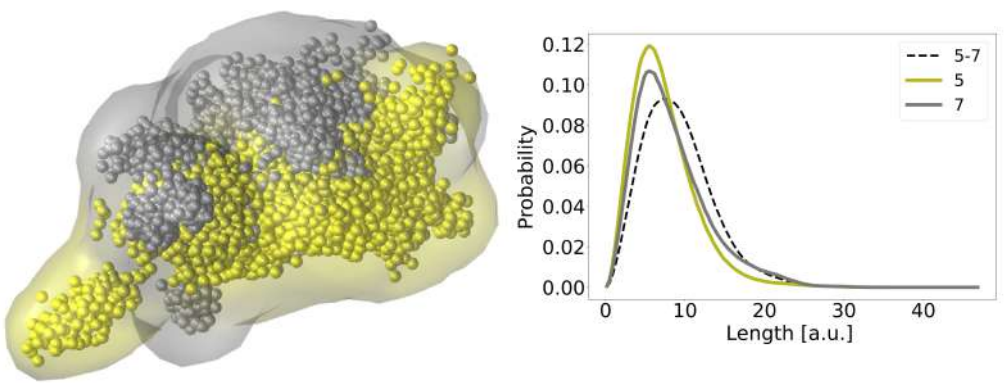
GM12878

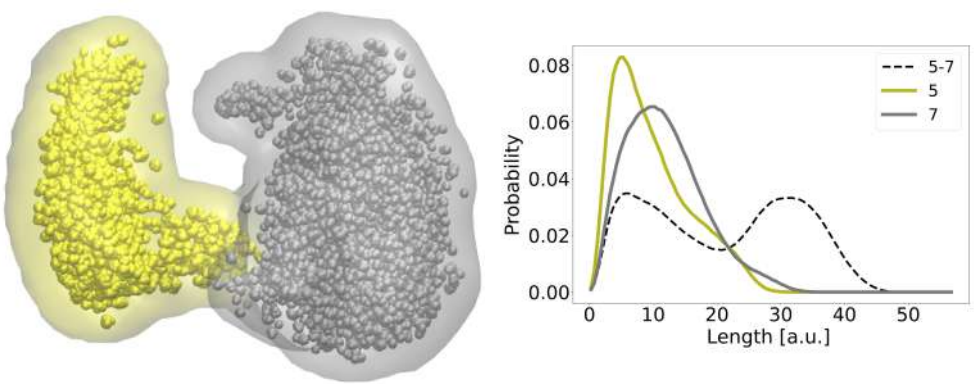


IMR90



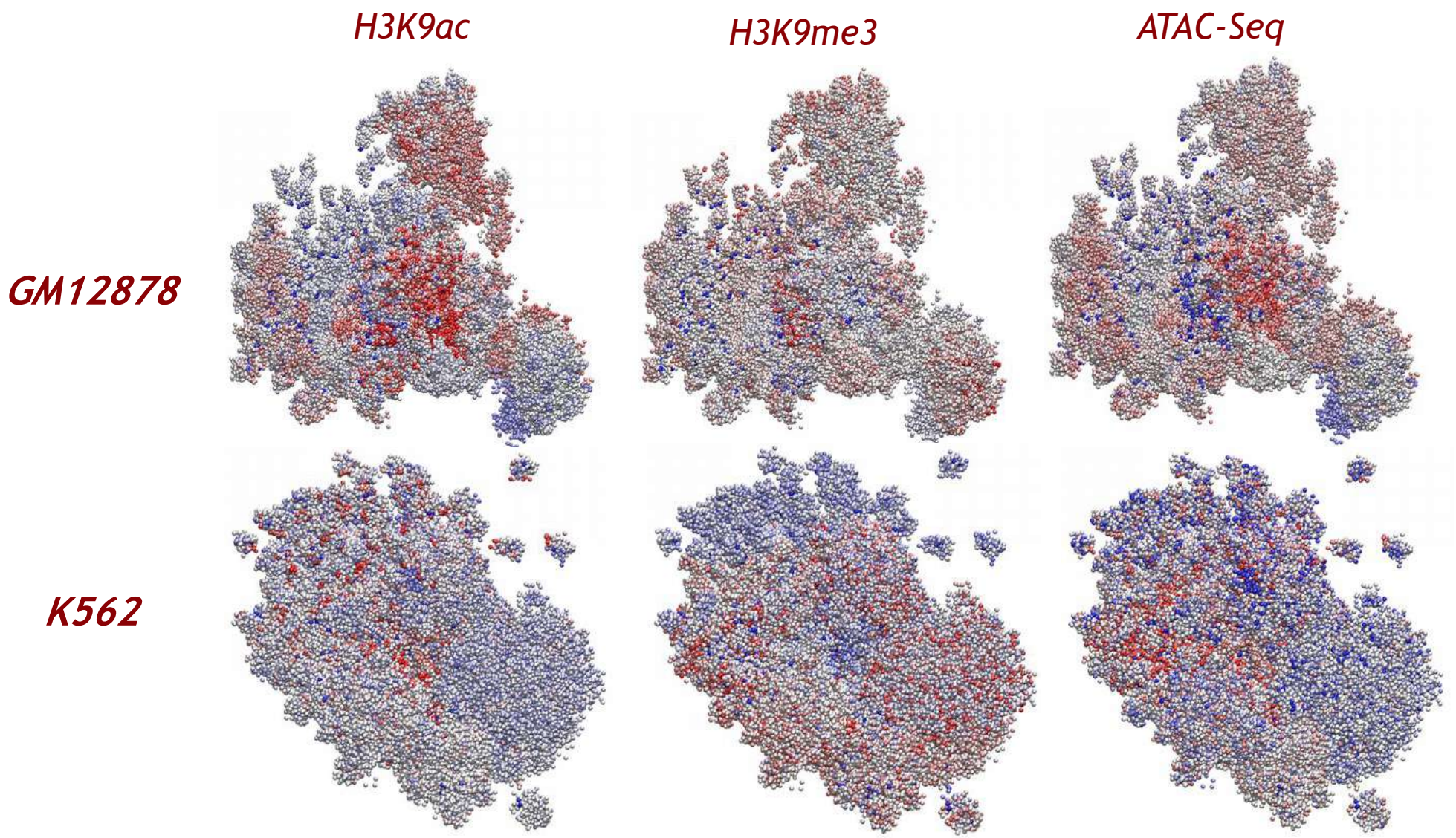
Chromosomal territories and intermingling





Structure (2021)
https://doi.org/10.1016/j.str.2021.01.008

Current and future work: spatial distribution of epigenetic markers; chromatin dynamics and epigenetic regulation



Structure (2021)
https://doi.org/10.1016/j.str.2021.01.008

Thank you

AlloSigMA server
http://allosigma.bii.a-star.edu.sg

AlloMAPS database
http://allomaps.bii.a-star.edu.sg

NBDB database
http://nbdb.bii.a-star.edu.sg

Allostery Platform at the Research Support Center
https://www.rsc.a-star.edu.sg/technologyplatforms/scientific-side-menu/scientific-information/bioinformatics/allostery-platform

Physics and Evolution of Biological Macromolecules, BMAD/BII
https://www.a-star.edu.sg/bii/research/bmad/pebmth

Wei-Ven Tee *teewv@bii.a-star.edu.sg*

Zhen Wah Tan *tanzw@bii.a-star.edu.sg*

Igor N. Berezovsky *igorb@bii.a-star.edu.sg*