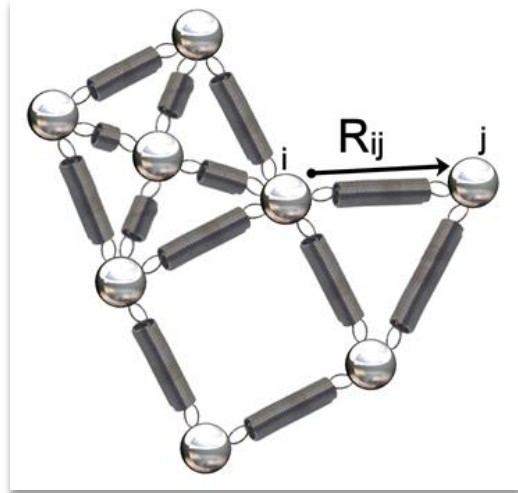


# Chromosomal dynamics

predicted by **Gaussian Network Model GNM**

explains genome-wide accessibility and  
long-range couplings



*She Zhang*

❖ **Bahar Lab**

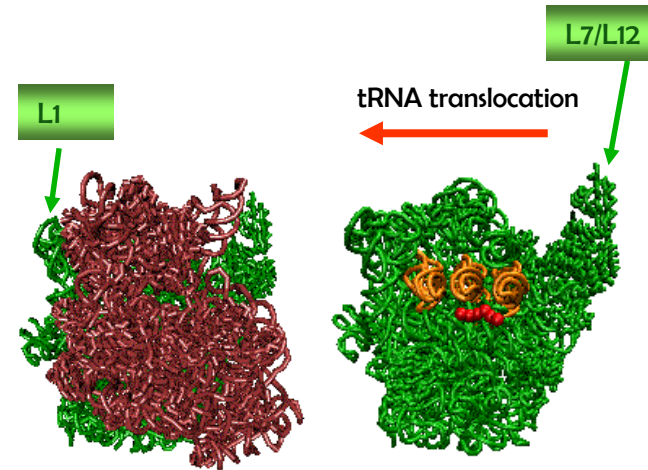
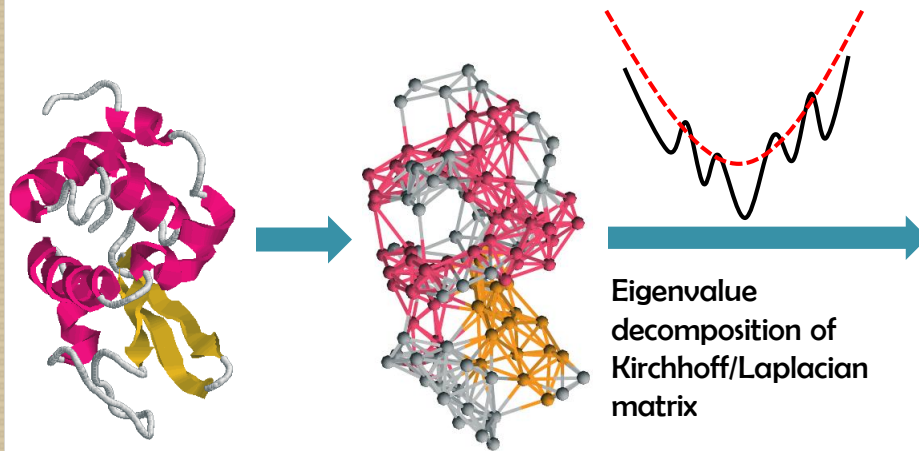
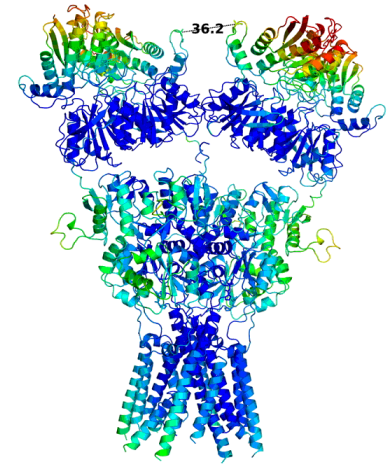
▪ She (John) Zhang

❖ **Kingsford Lab**

▪ Natalie Sauerwald



# Collective motions using elastic network models

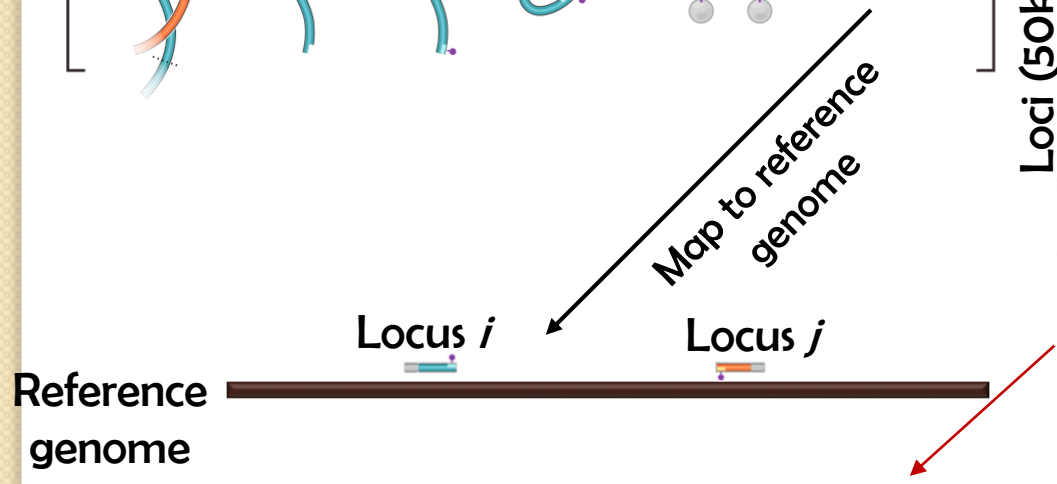
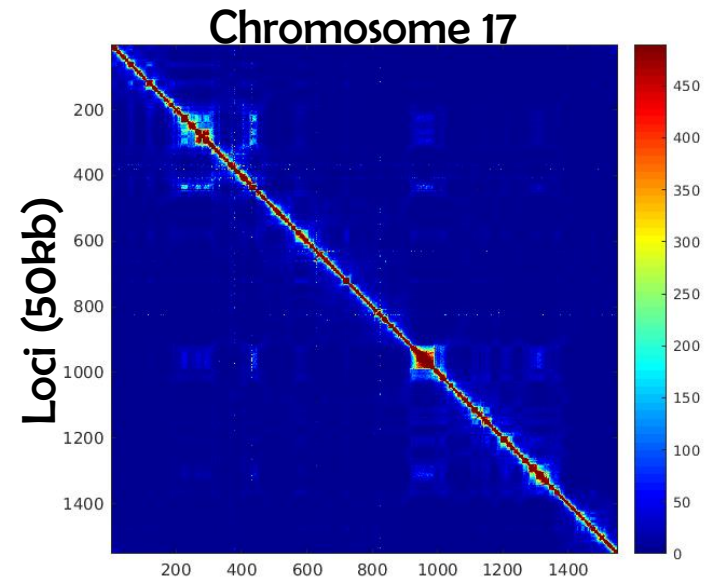
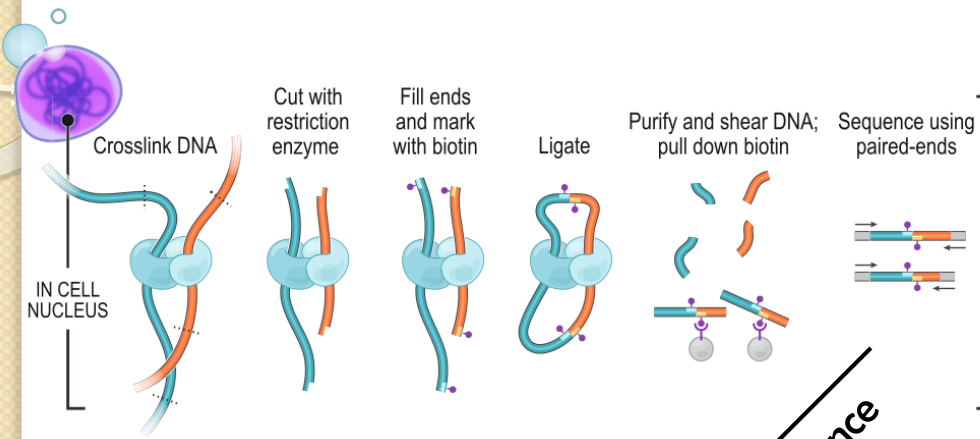


Wang et al *JSB* (2004)

GNM: Bahar et al *Fold & Des* 1996; Haliloglu et al. *Phys Rev Lett* 1997  
ANM: Doruker et al. *Proteins* 2000; Atilgan et al, *Biophys J* 2001

Based on theory of elasticity for polymer networks by Flory, 1976

# Chromosome Conformation Capture (e.g. Hi-C)



$$M_{ij} = \# \text{ reads mapped to locus } i \text{ and } j$$

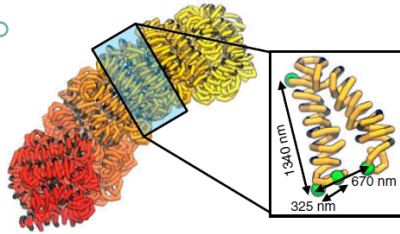
$$= \# \text{ interactions between locus } i \text{ and } j$$

Loci (50kb)

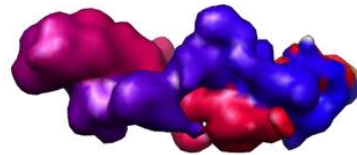
Contact map ( $M$ )  
determined by  
experiments ( $n \times n$ )

Rao, S. S., ... Aiden, E. L. (2014). A 3D map of the human genome at kilobase resolution reveals principles of chromatin looping. *Cell*, 159(7), 1665–1680.

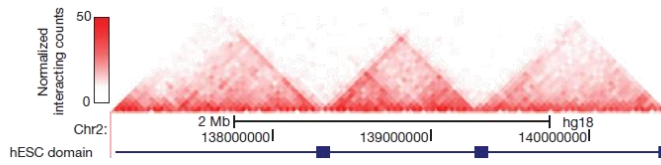
# Chromosome Conformation Capture (e.g. Hi-C)



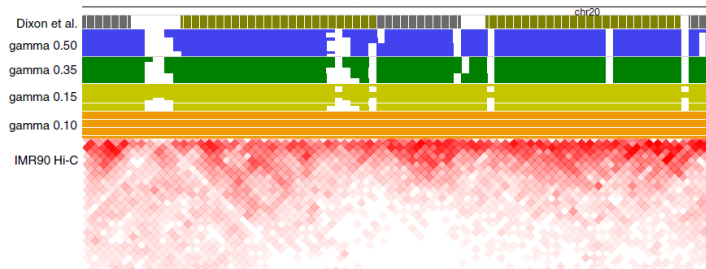
Zhang and Wolynes  
(2015)



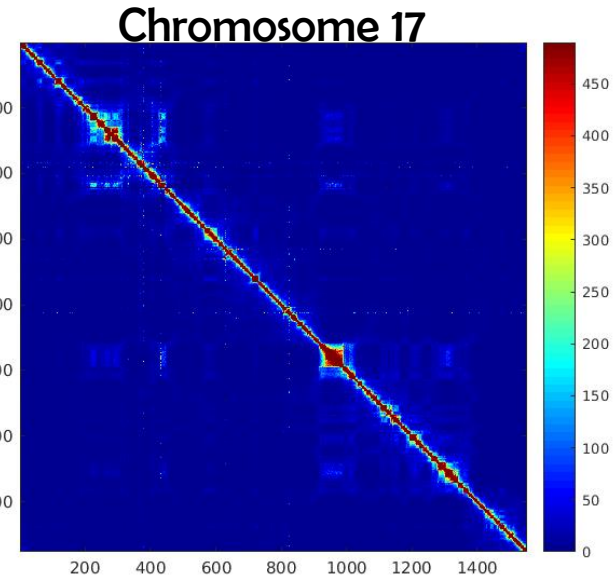
Umbarger et al.  
(2011)



Dixon et al. (2012)



Carl's Lab: Filippova et  
al. (2014)

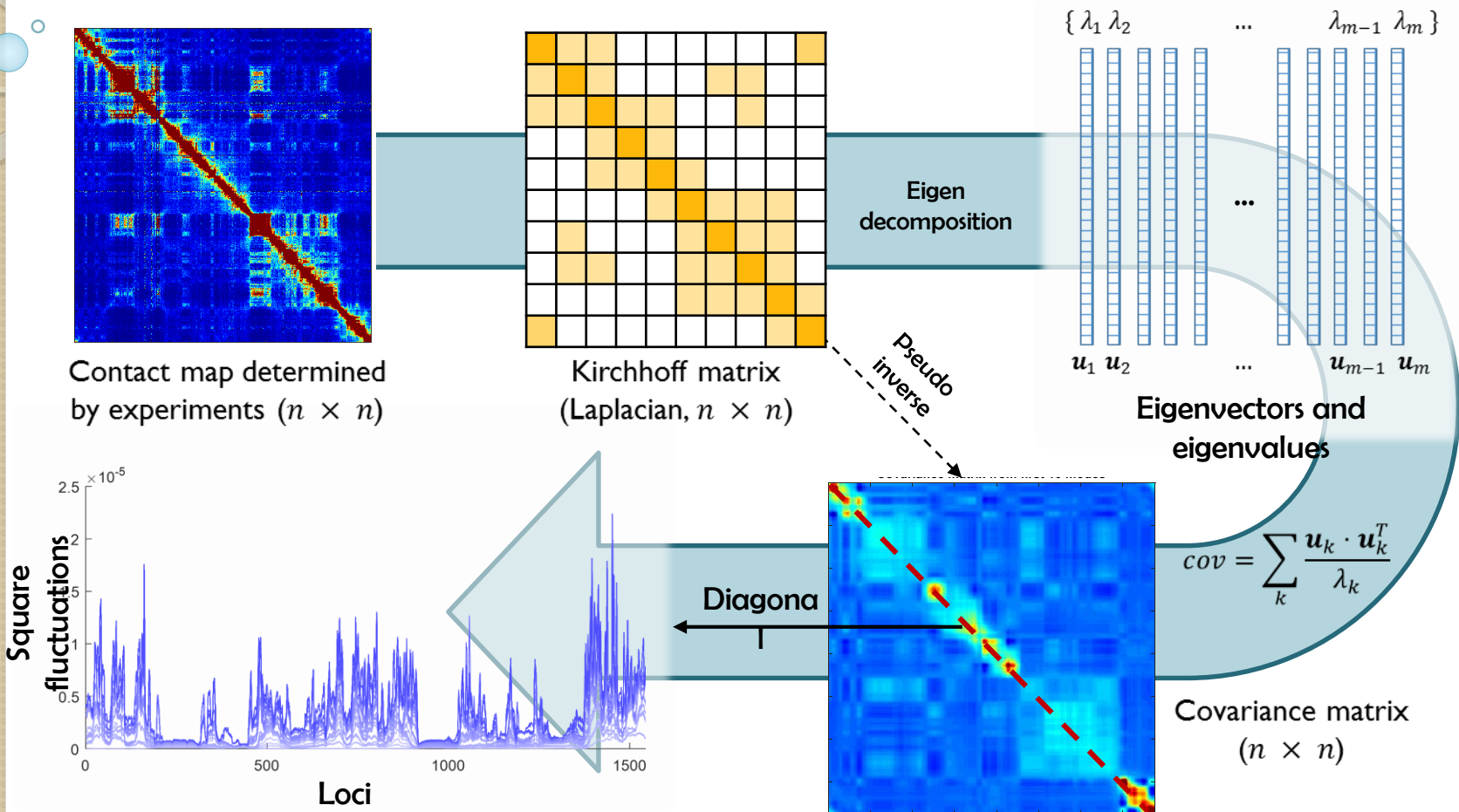


Loci (50kb)

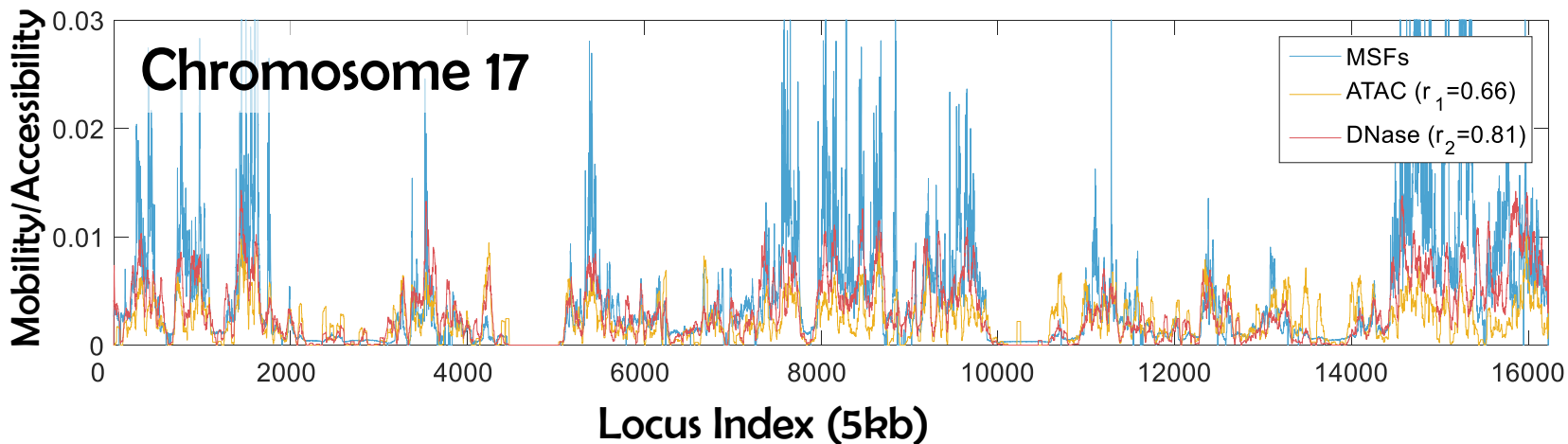
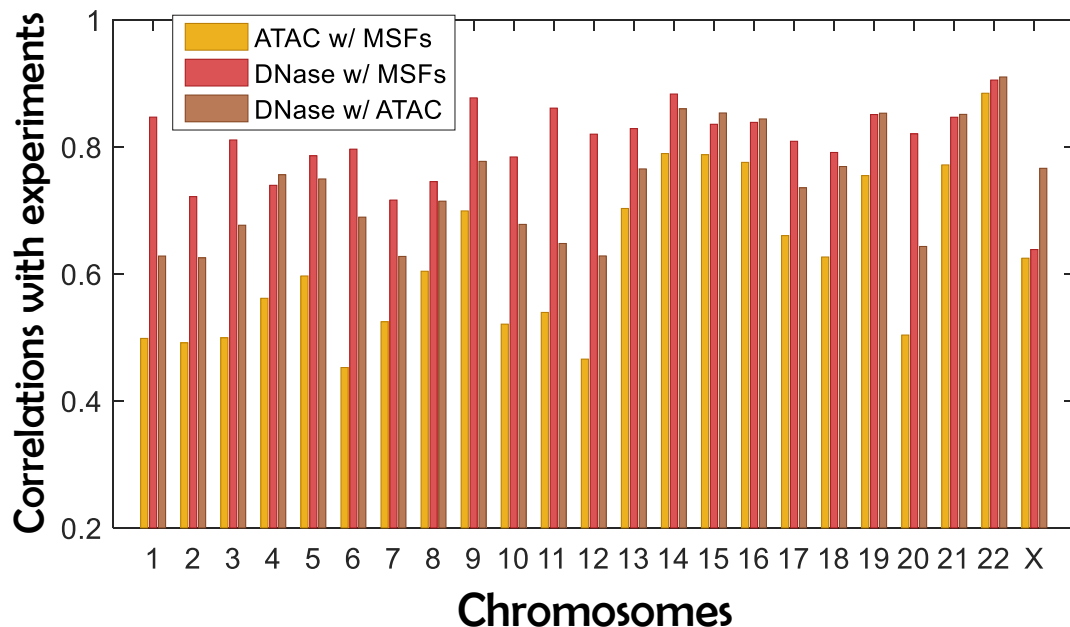
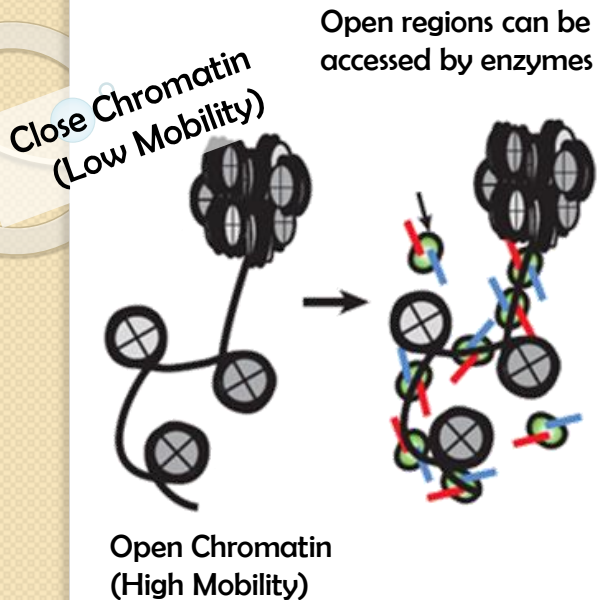
Resolve 3D  
structures

Identifying  
topological  
domains

# Method Pipeline

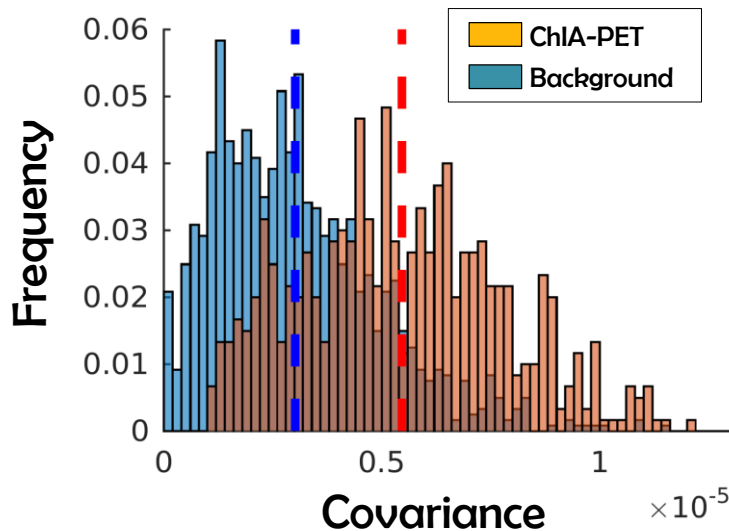
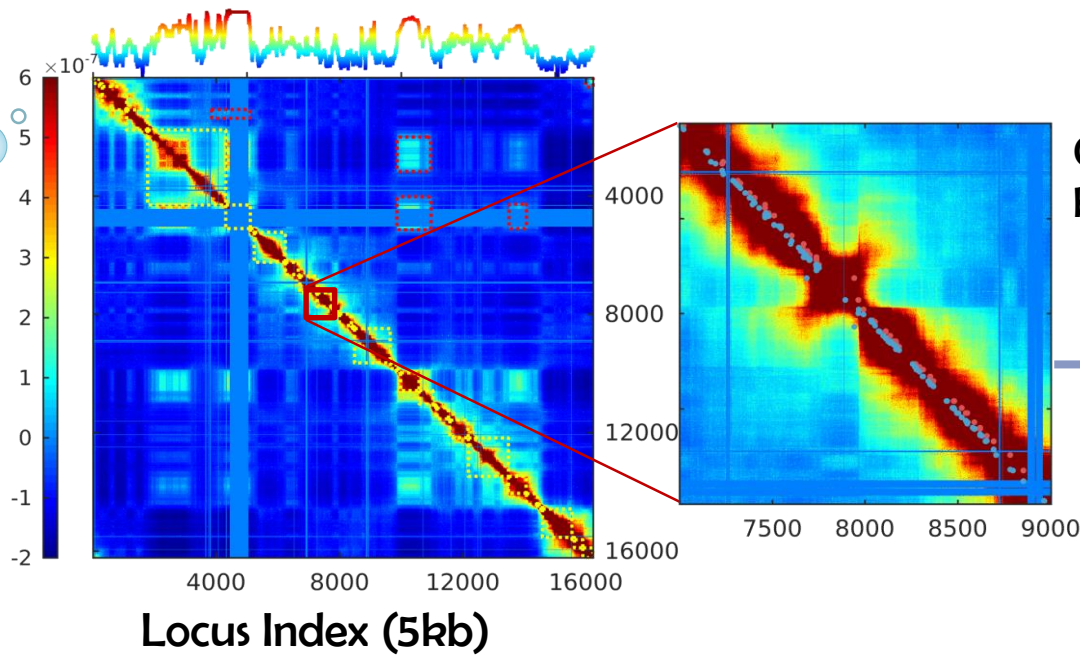


# Square fluctuations *vs* chromatin accessibility



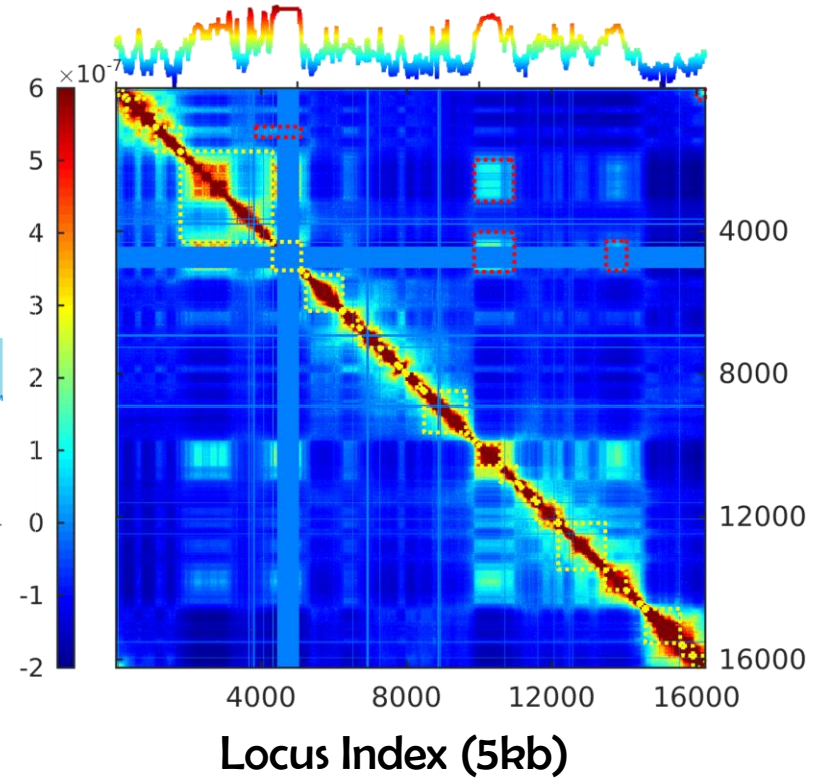
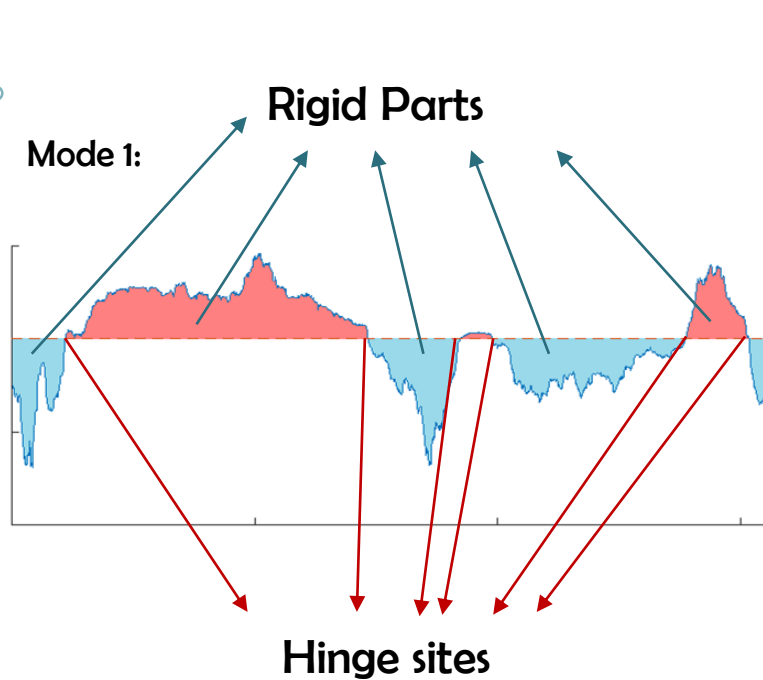
Buenrostro JD et al. (2013) Transposition of native chromatin for fast and sensitive epigenomic profiling of open chromatin, DNA-binding proteins and nucleosome position. *Nat Methods* 10(12):1213-+.

# Dynamical coupling consistent with ChIA-PET measurements



“Long range” (~100 kBp) interactions identified by ChIA-PET were found to show higher covariance in their movement calculated by GNM than the background pairs.

# Structural Domains Identified by GNM modes



Collective GNM domains can be identified by combining hinge sites from different modes



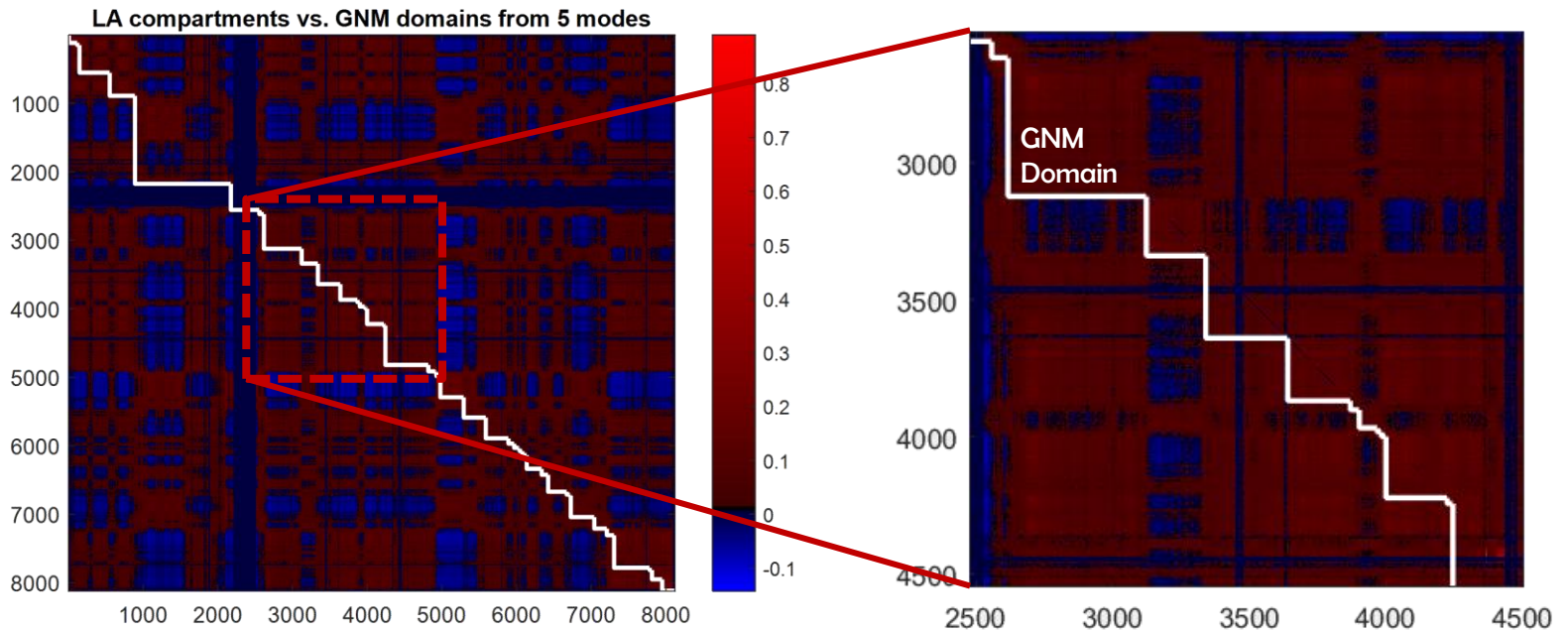
GNM Domains



Cross-Correlated Distal Domains (CCDDs)

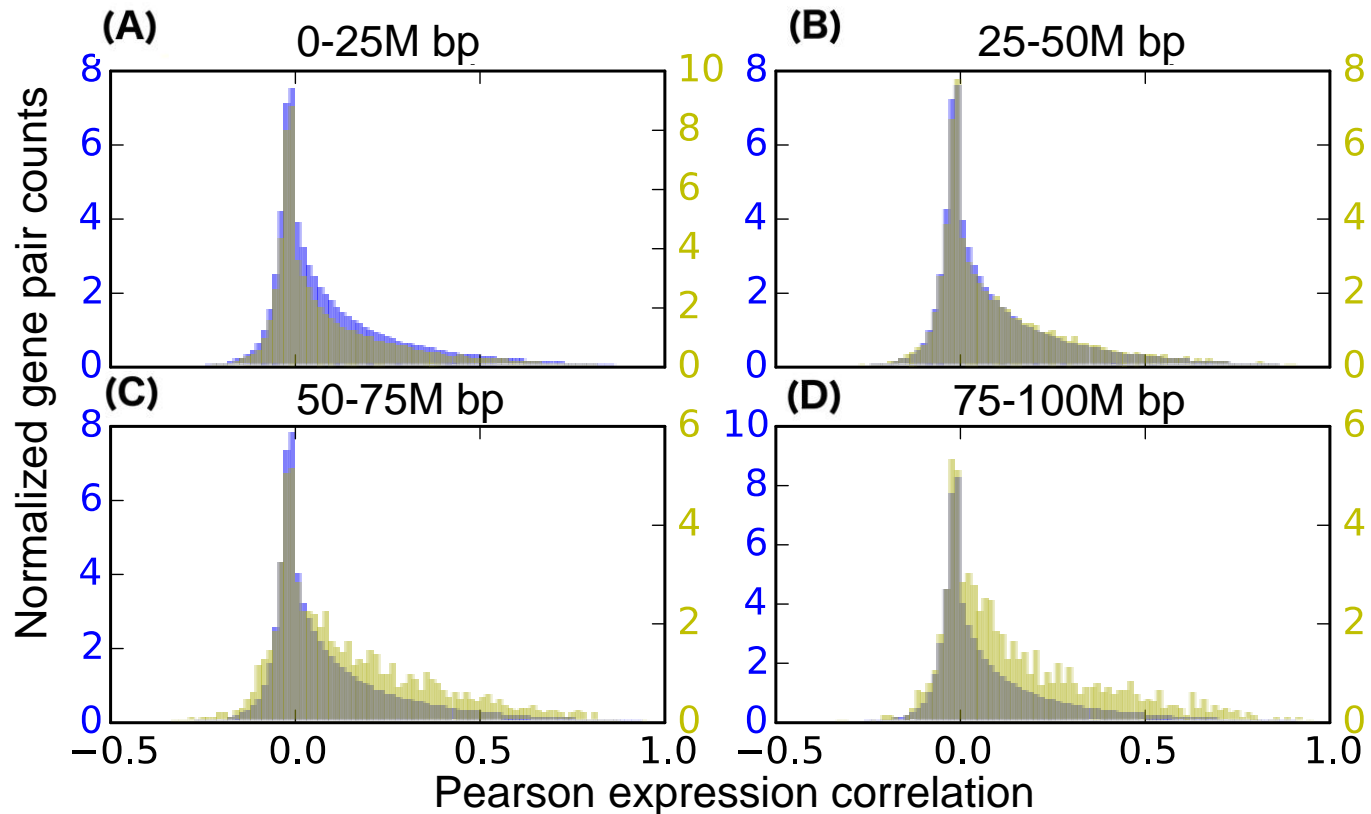


# Structural Domains Identified by GNM modes



GNM domains agree with Lieberman-Aiden compartments. The loci-correlation matrix is computed by Lieberman-Aiden et al. **Red** and **blue** represents **positive** and **negative** correlations respectively. White lines denotes the GNM domains.

# Distal domains with strong cross-correlations are co-expressed



Genes located in the high value region of the covariance matrix are found to be co-expressed. **Yellow**: expression correlations of dynamically coupled gene-pairs identified by GNM. **Blue**: those of background gene-pairs.