



Chromosome walking with  
super-resolution imaging  
and modeling

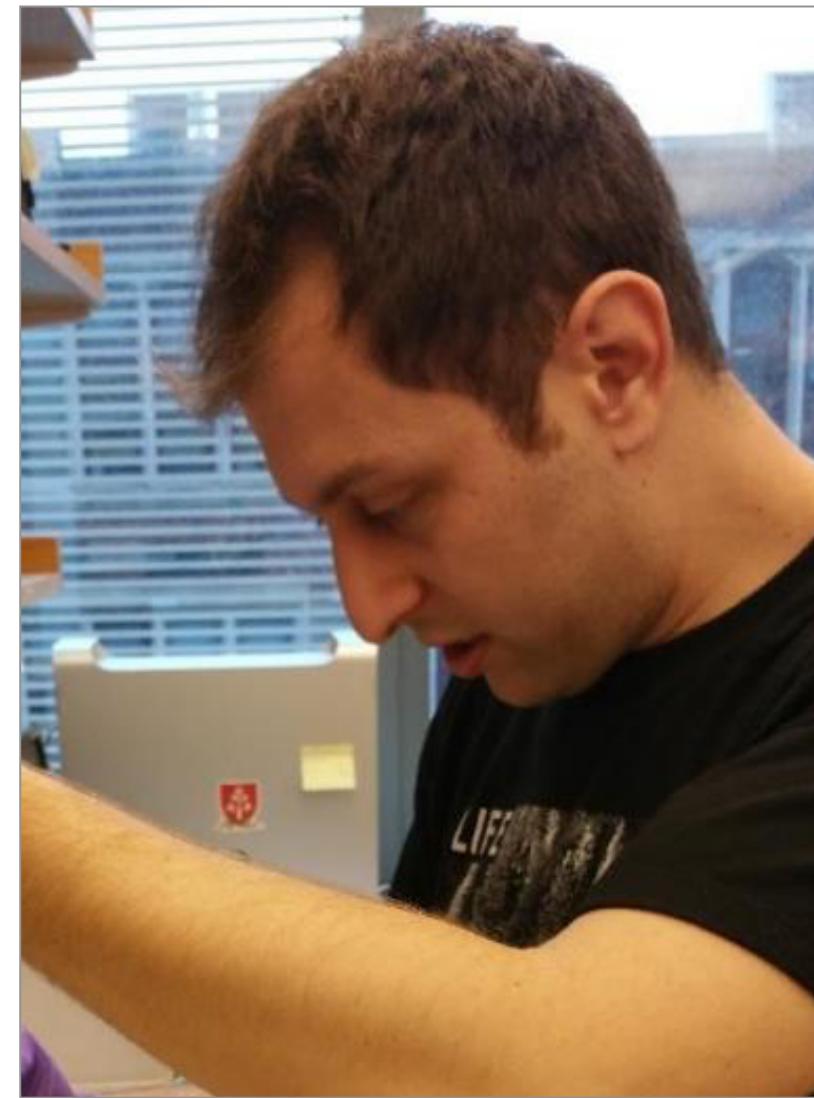
**Marc A. Marti-Renom**  
CNAG-CRG · ICREA

<http://marciuslab.org>  
<http://3DGenomes.org>  
<http://cnag.crg.eu>

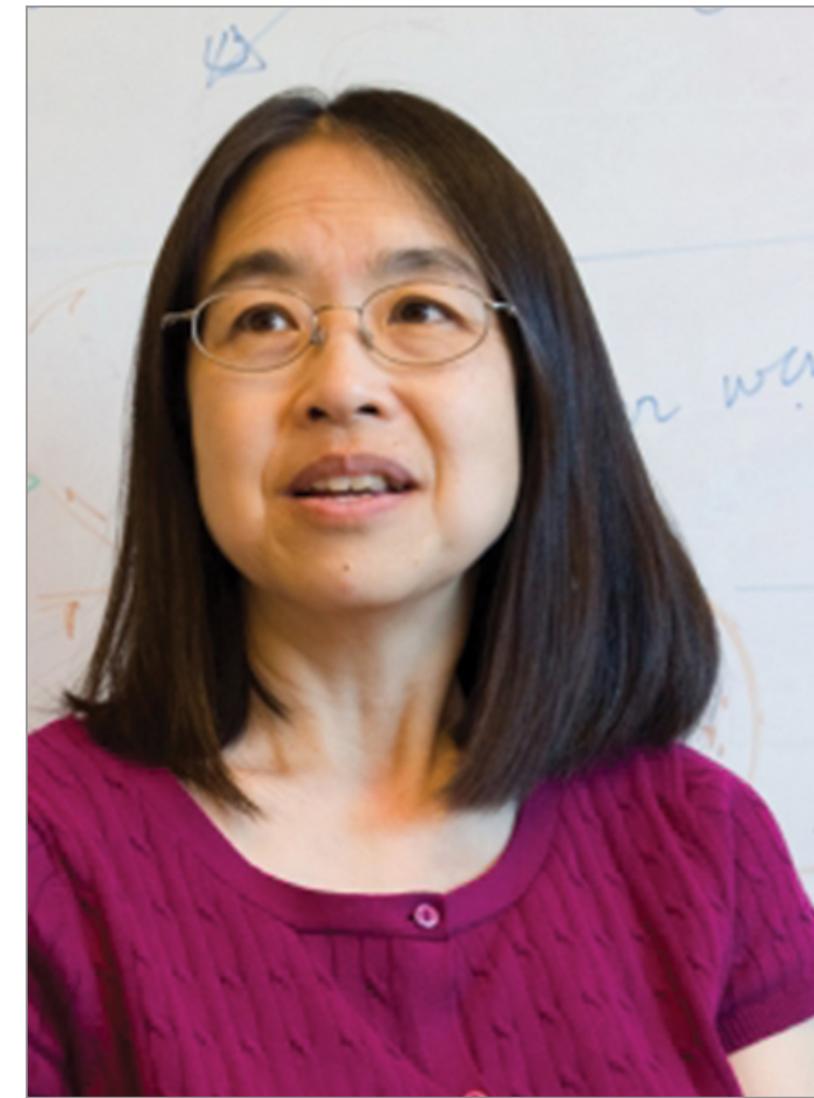
**cnag CRG<sup>R</sup>** ICREA



**Irene Farabella**  
CNAG-CRG



**Guy Nir**  
Harvard Med School



**Ting Wu**  
Harvard Med School

Can we walk the chromatin path in the nucleus?

by

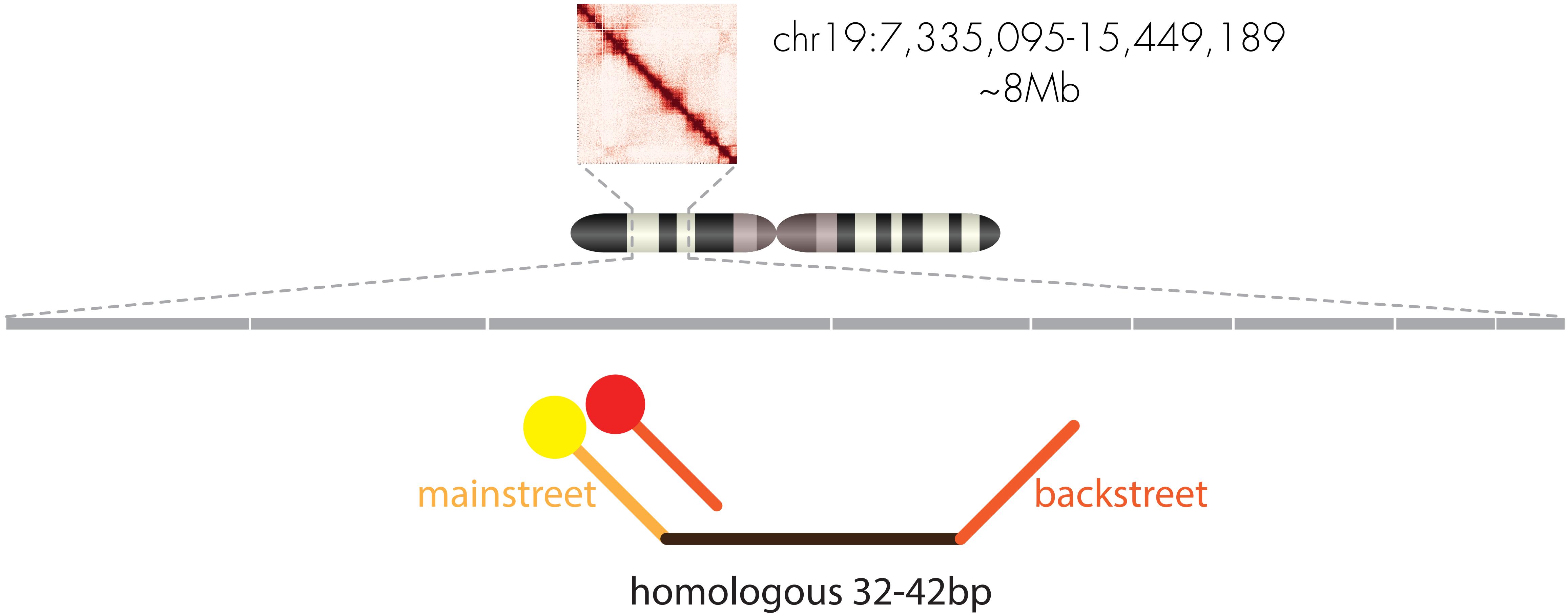
Integrating imaging and Hi-C maps with modeling.

by developing a method for

Oligopaint-based modeling of genomes

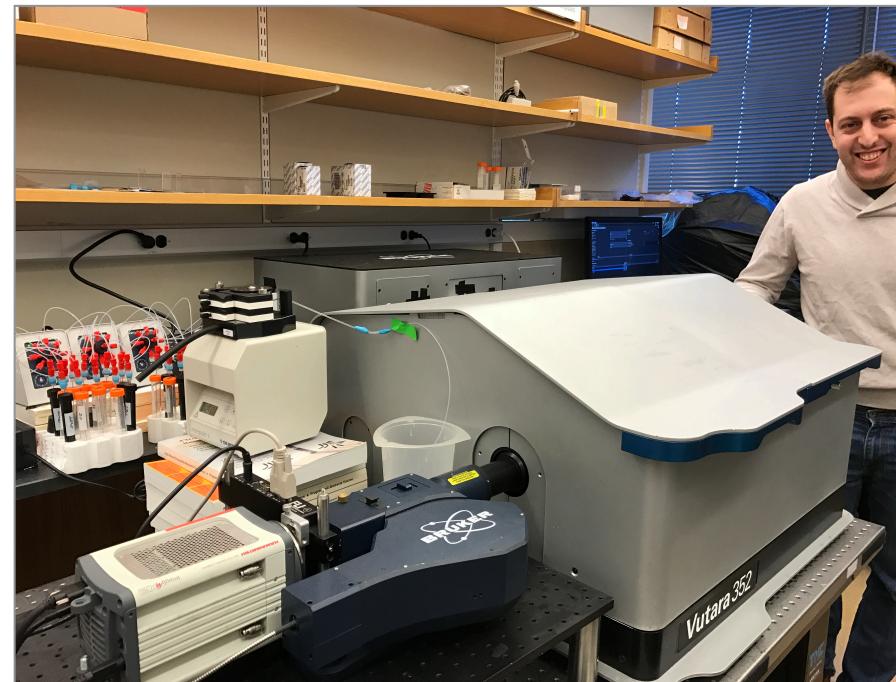
# High-resolution imaging

Tracing chromosomes with OligoSTROM & fluidics cycles in PGP1 cells



# High-resolution imaging

Tracing chromosomes with OligoSTROM & fluidics cycles in PGP1 cells



**Guy Nir** Harvard Med School

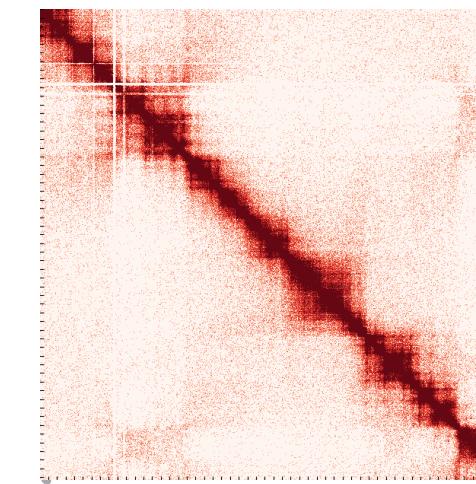
**Bodgan Bintu** Harvard

**Carl Ebeling** Bruker

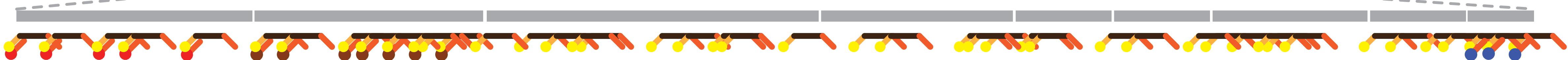
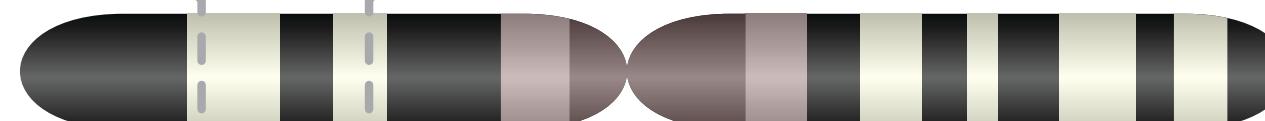
**Jeff Stuckey** Bruker

**John Schreiner** Zero Epsilon

**Steve Callahan** Zero Epsilon



chr19:7,335,095-15,449,189  
~8Mb



**1**

1,280Kb

**2**

1,240Kb

**3**

1,800Kb

**4**

1,040Kb

**5**

520Kb

**6**

520Kb

**7**

840Kb

**8**

520Kb

**9**

360Kb



# High-resolution imaging

Tracing chr19:7,335,095-15,449,189 ~8Mb

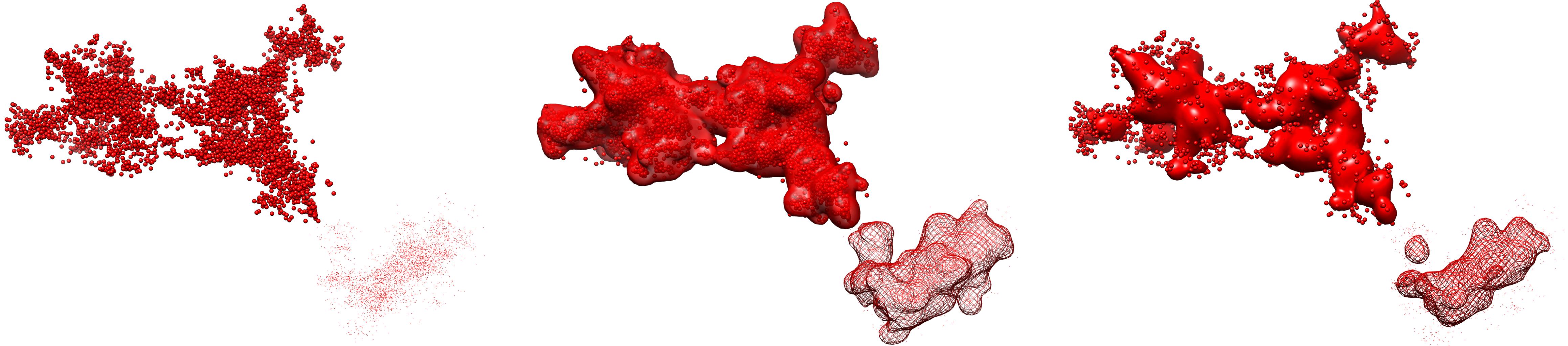


Cell-02

# High-resolution imaging

## XYZ points convolution into a density map

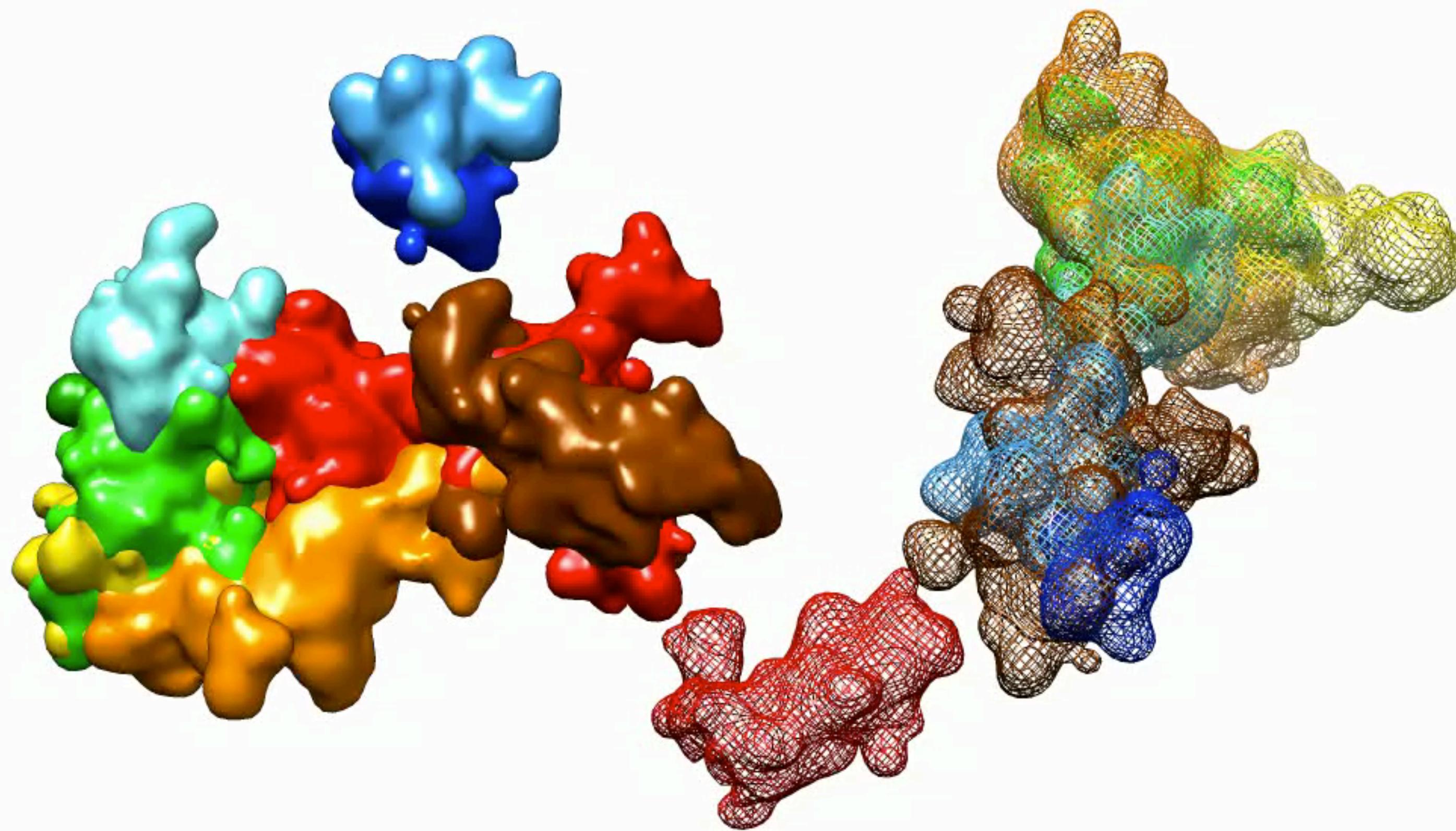
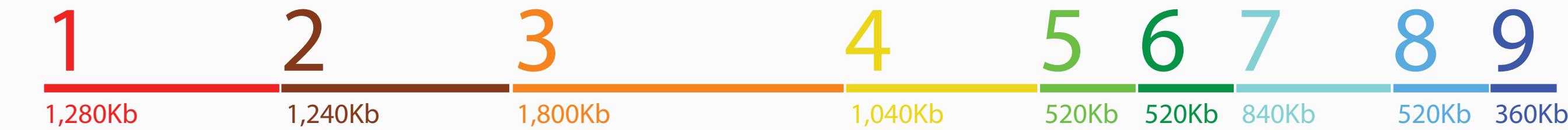
$$\rho(x, y, z) = \sum_N \frac{Z_N}{(\sigma\sqrt{2\pi})^3} e^{-\frac{(x-x_n)^2 + (y-y_n)^2 + (z-z_n)^2}{2\sigma^2}}$$



Cell02 · Segment 1

# Density maps

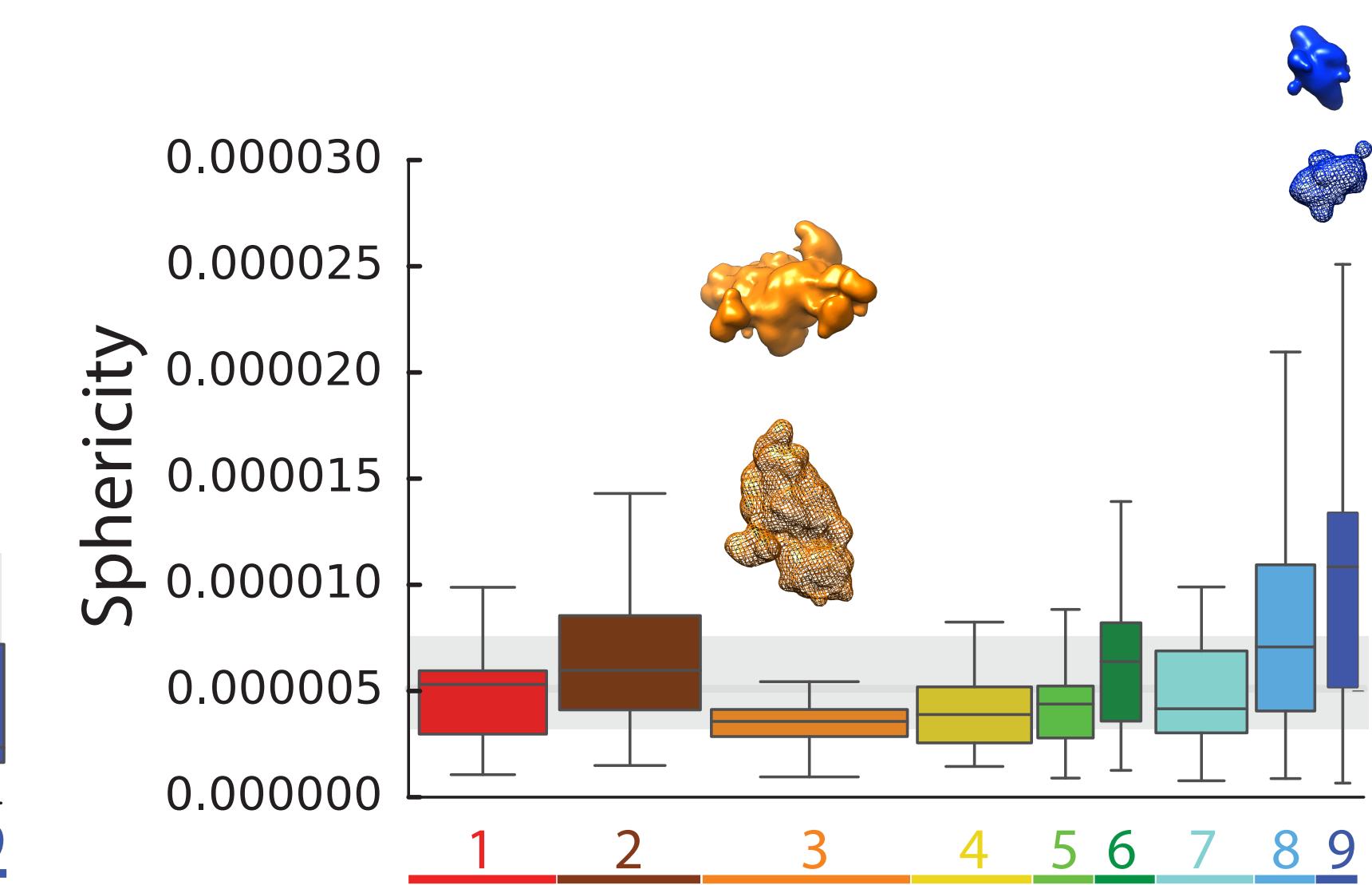
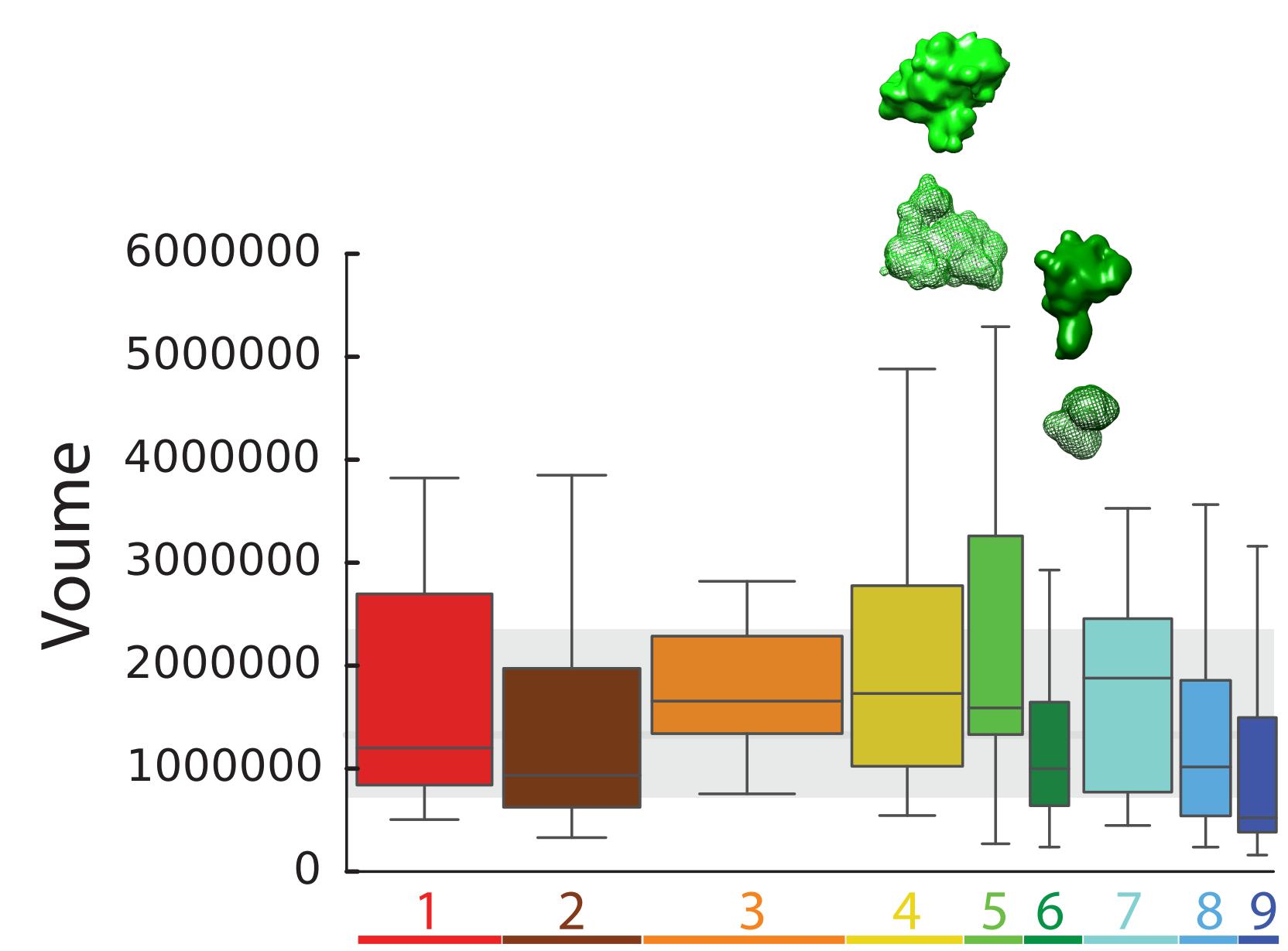
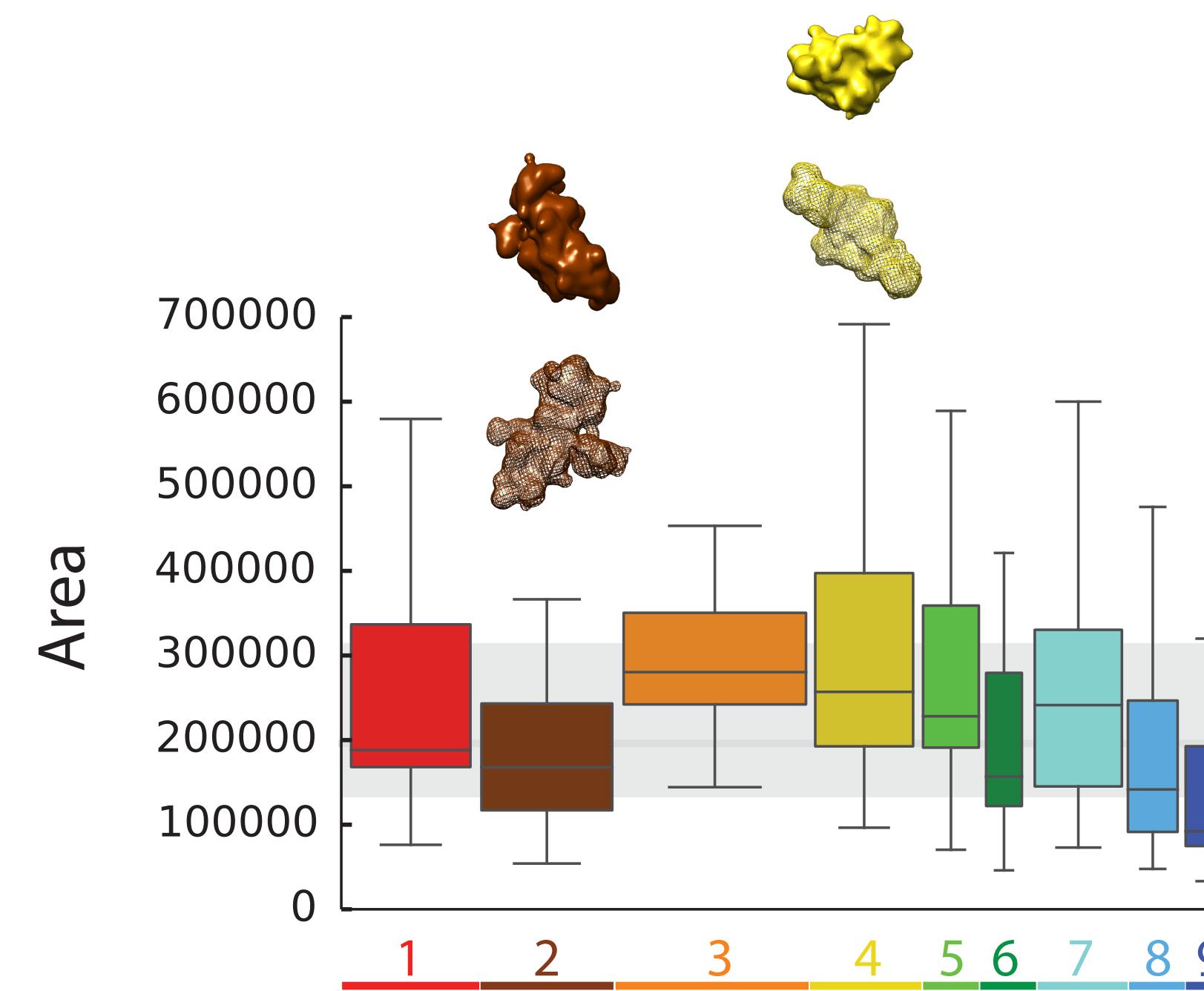
Cell-02 · Density map @ 50nm



- Area ( $\text{nm}^2$ )
- Volume ( $\text{nm}^3$ )
- Sphericity
- Overlap (%)
- Distance (nm)

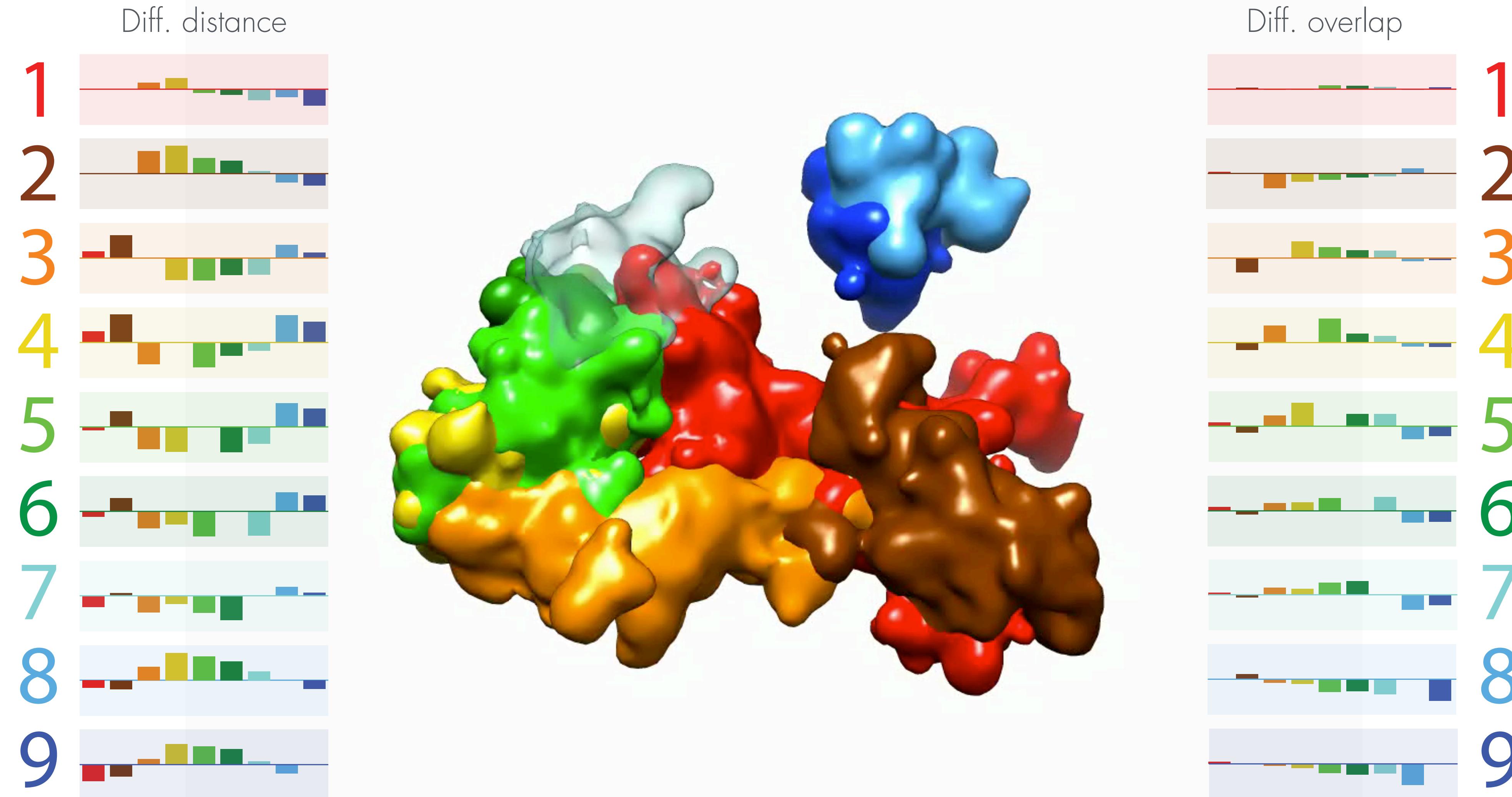
# Structural features

Area, Volume and Sphericity of 19 cells each with 2 homologous resolved



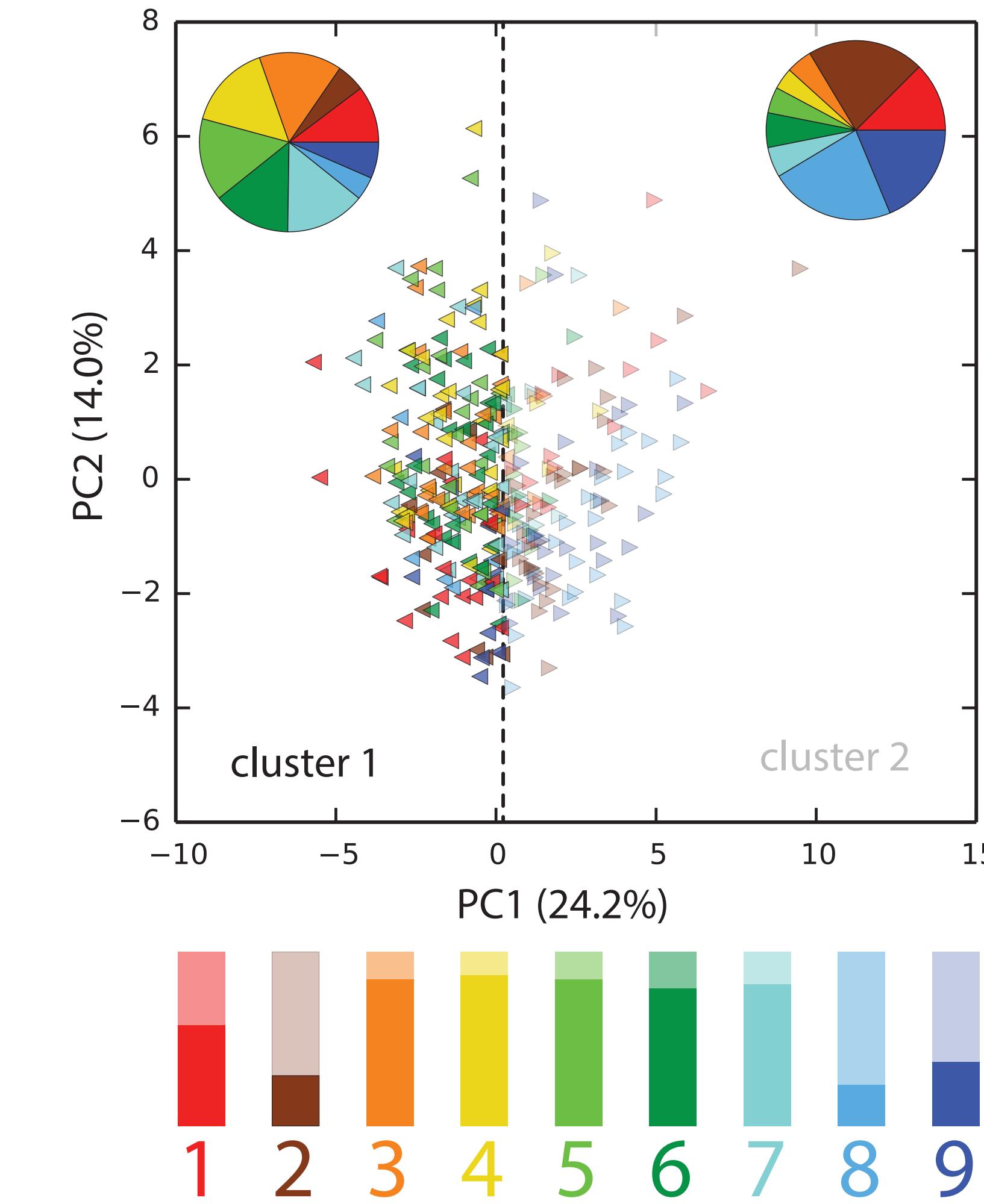
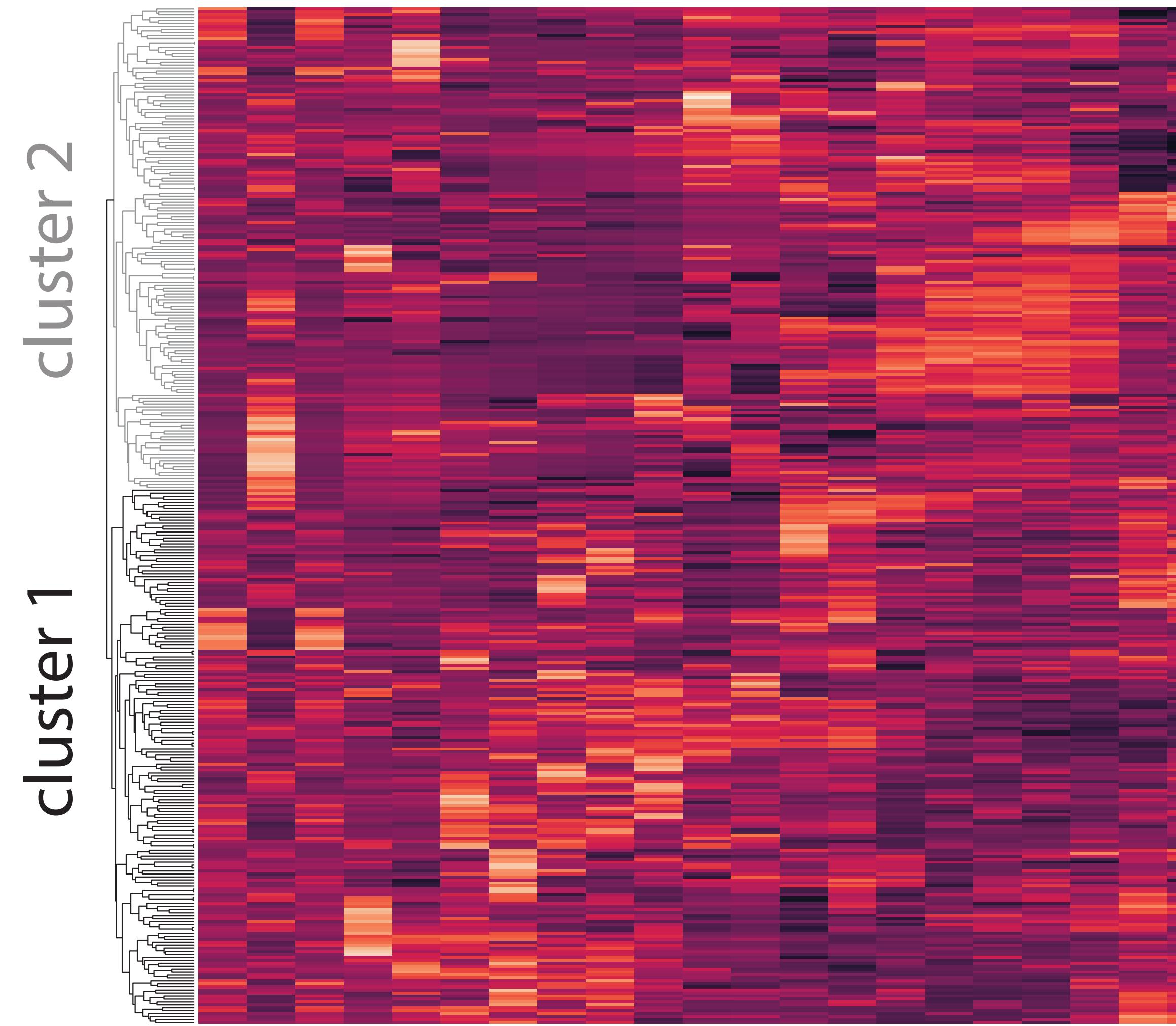
# Spatial arrangement

Distance and overlap of 19 cells each with 2 homologous resolved



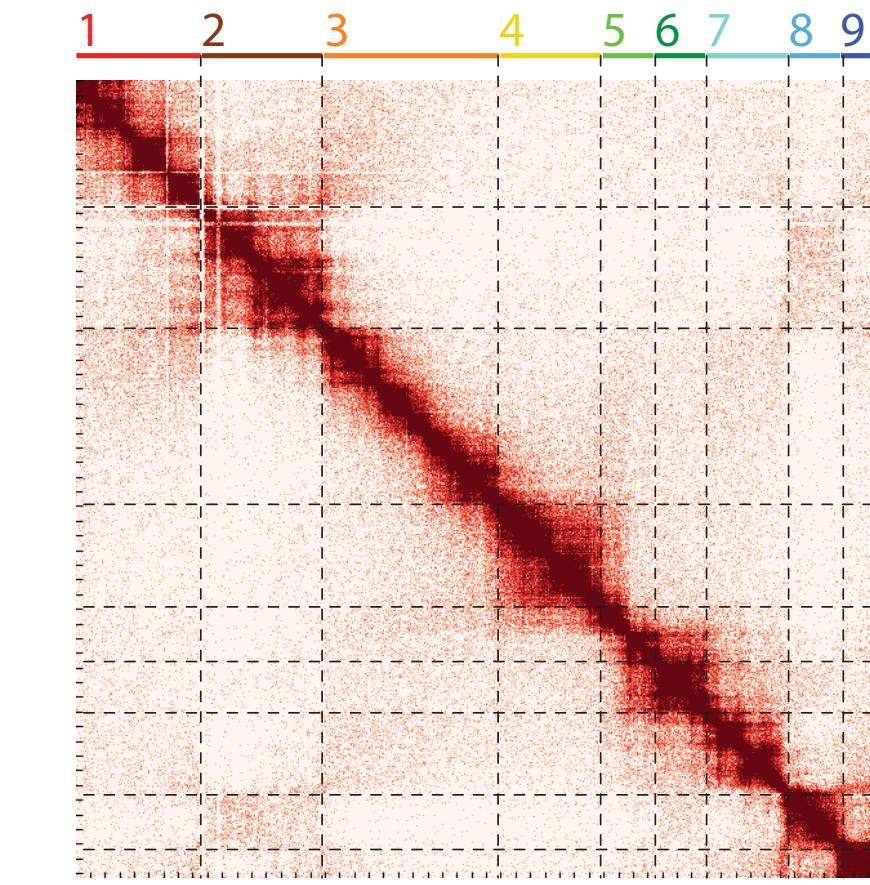
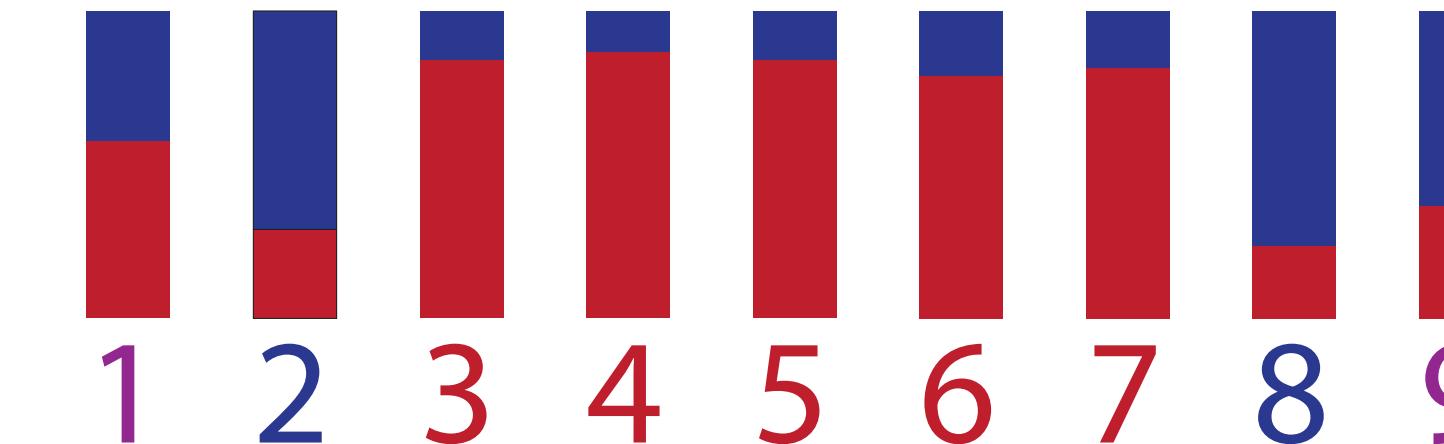
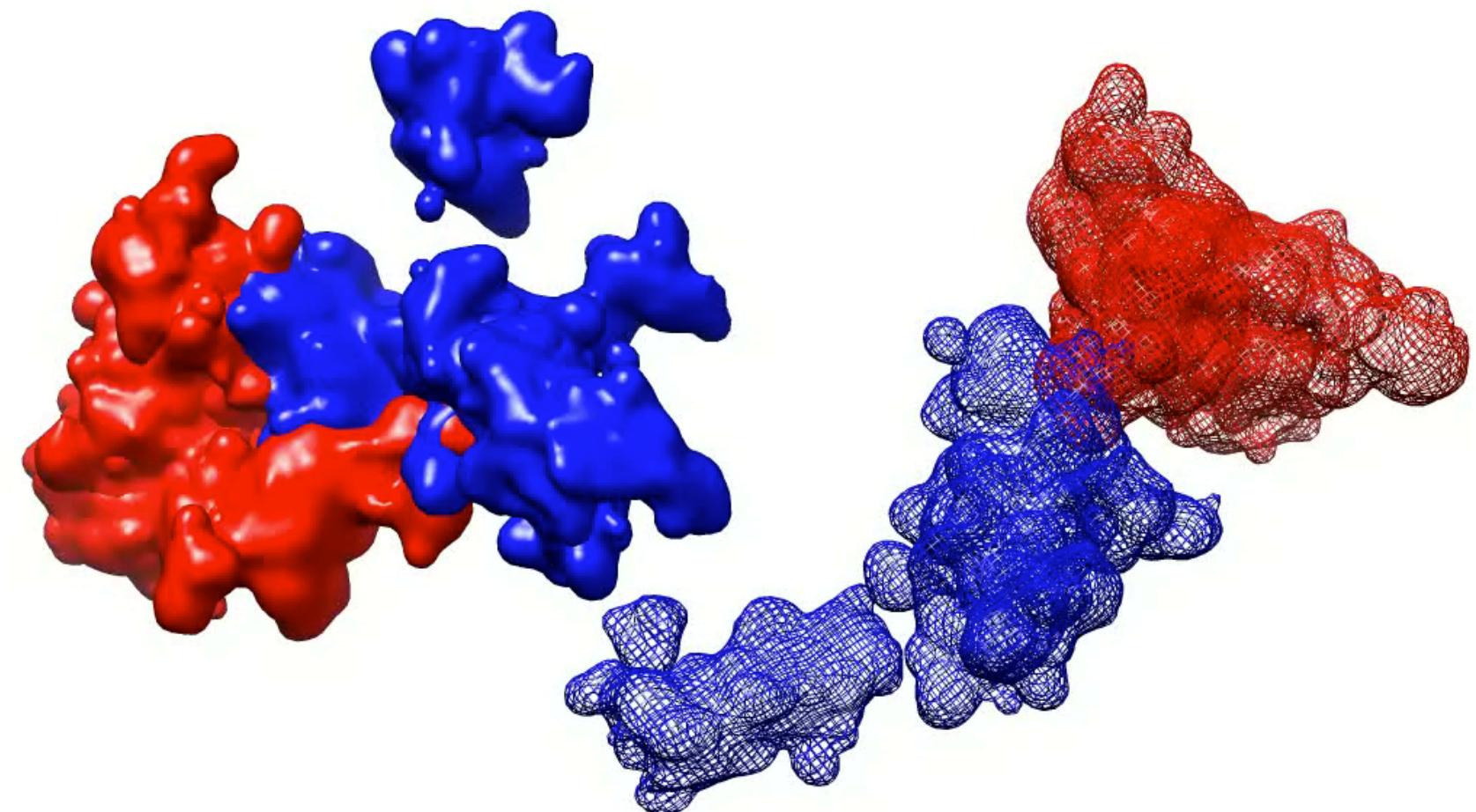
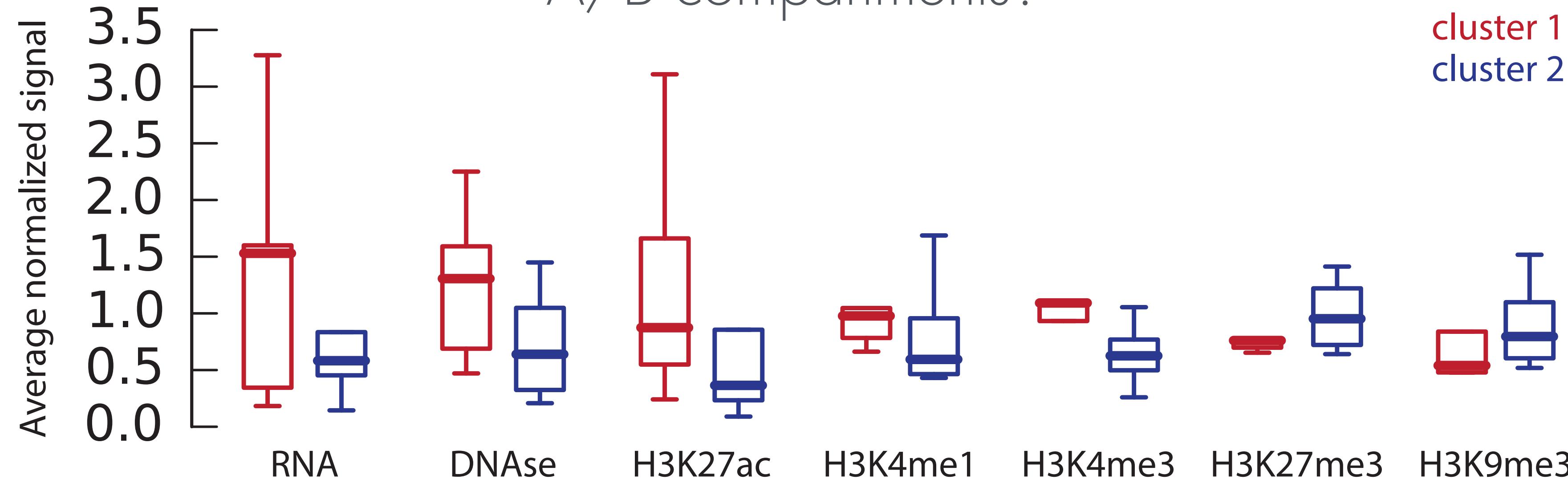
# Structural clustering

19 cells each with 2 homologous and 9 segments each (342)



# Cluster properties

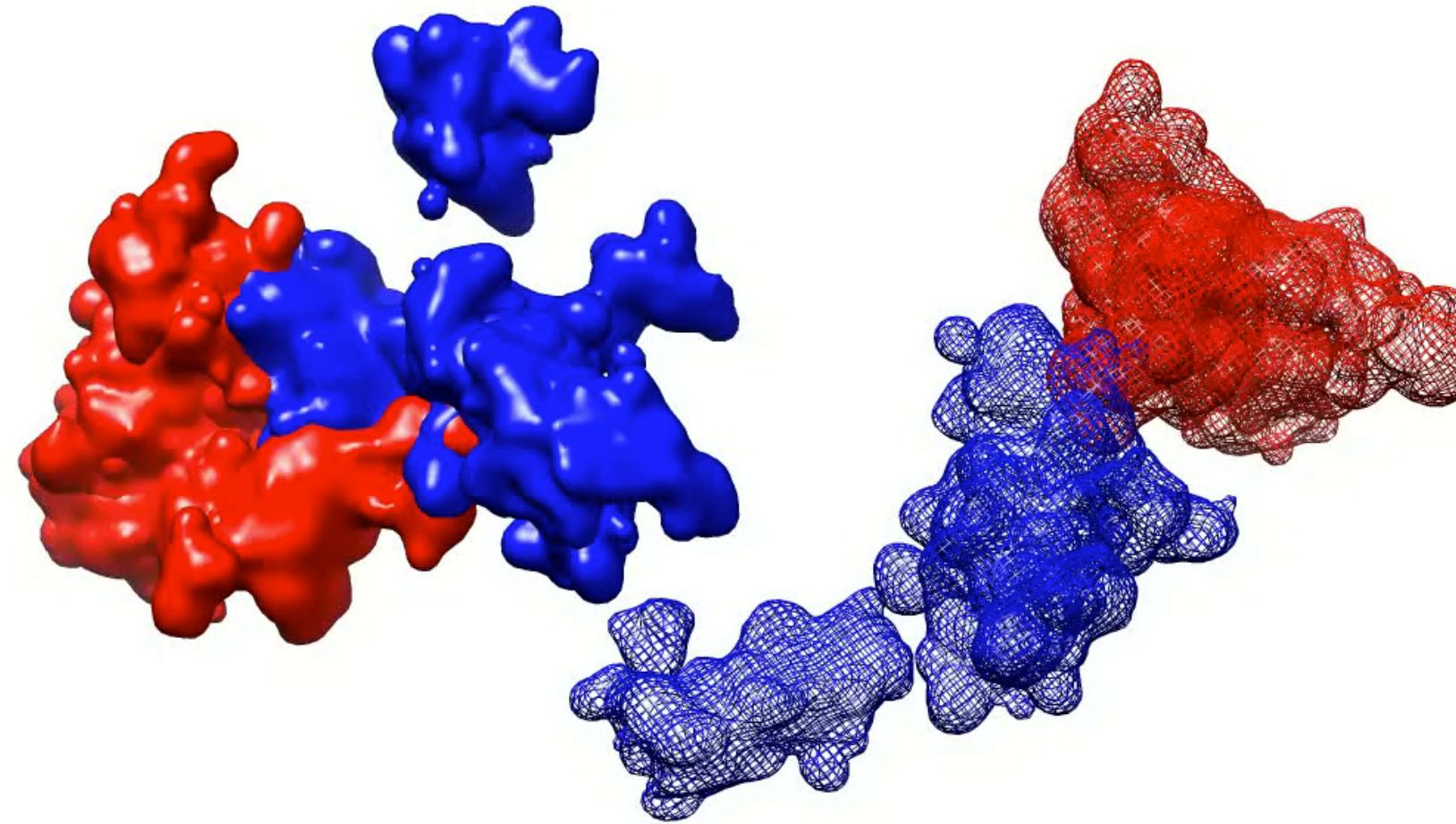
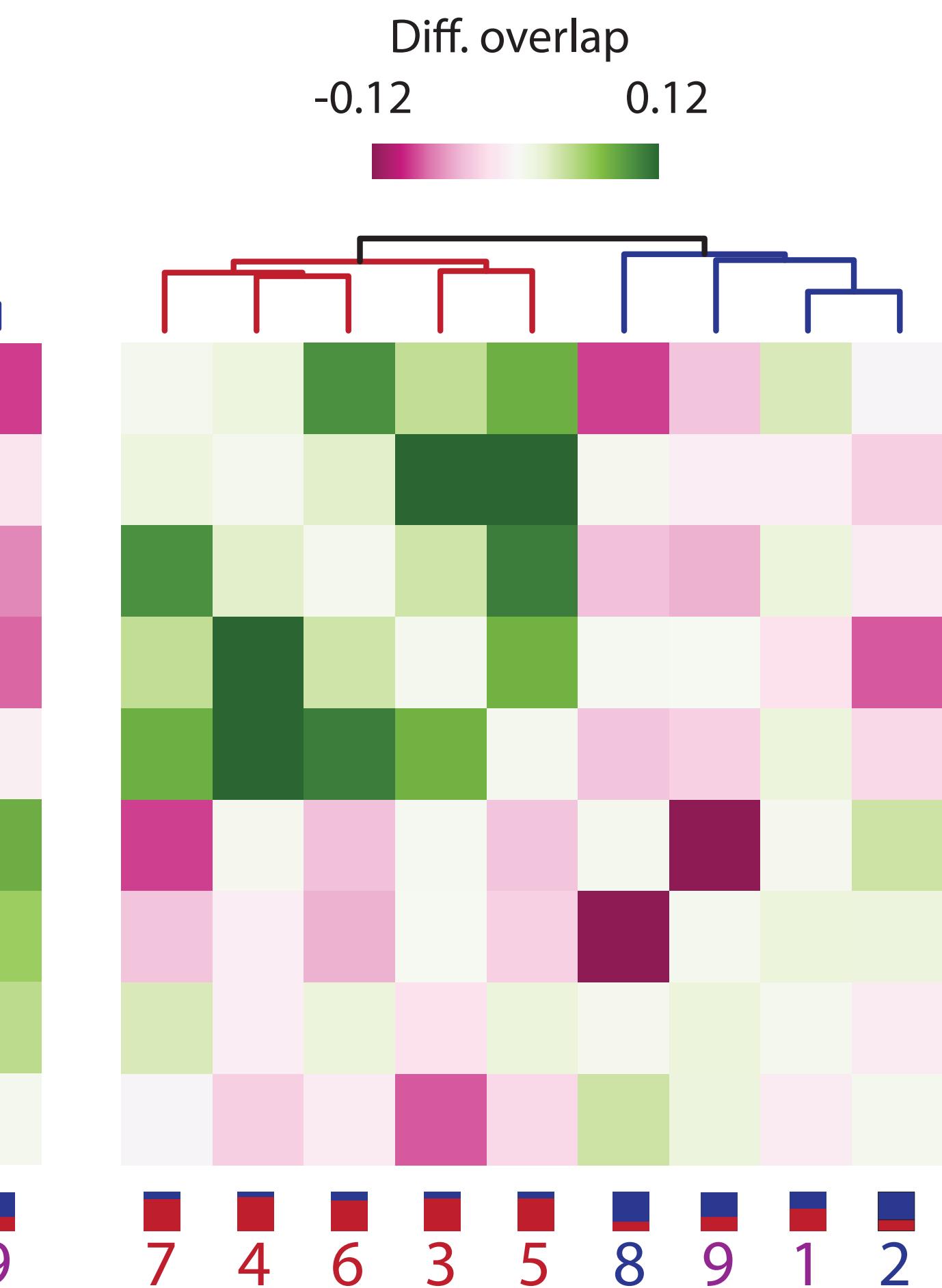
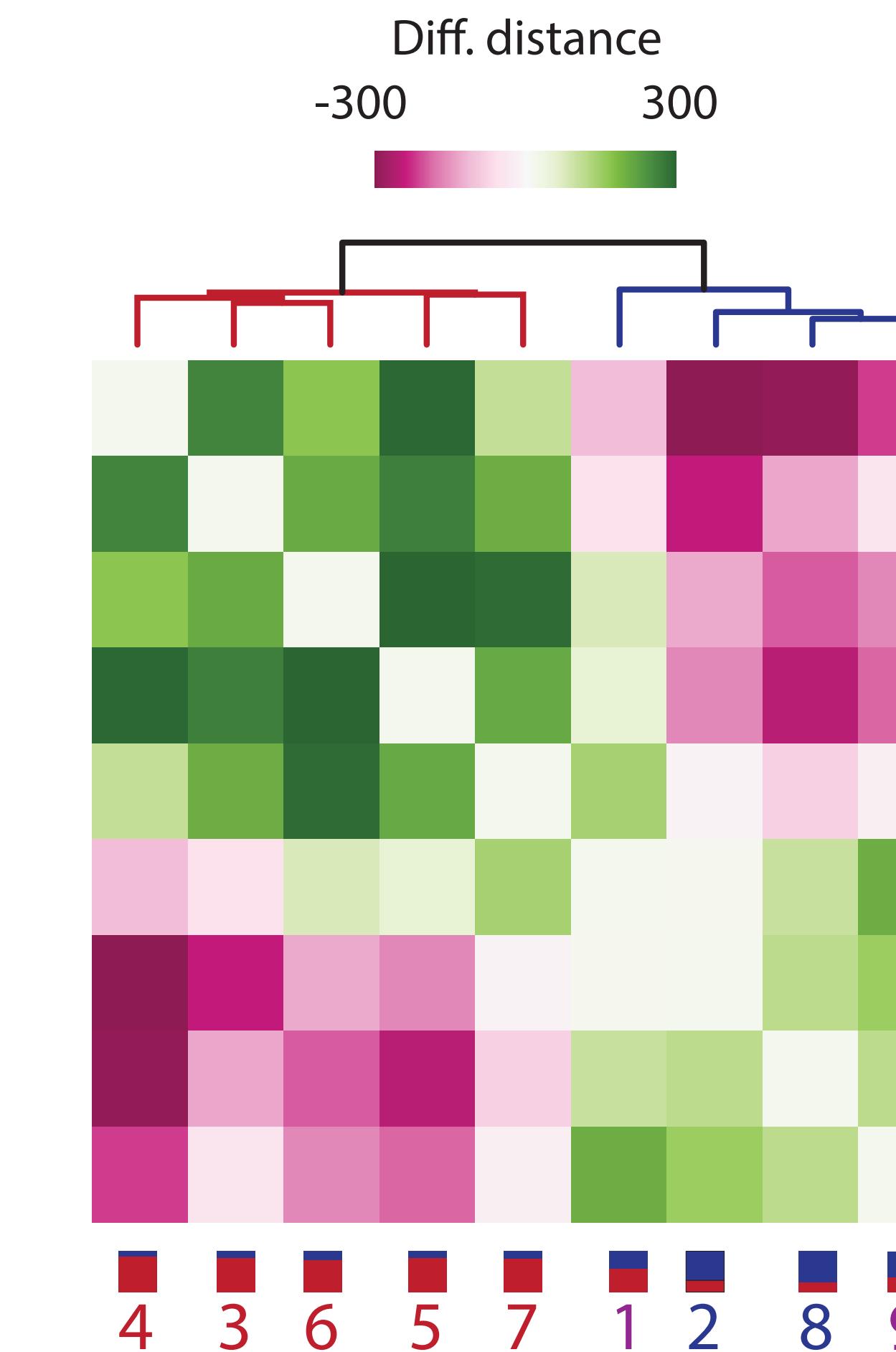
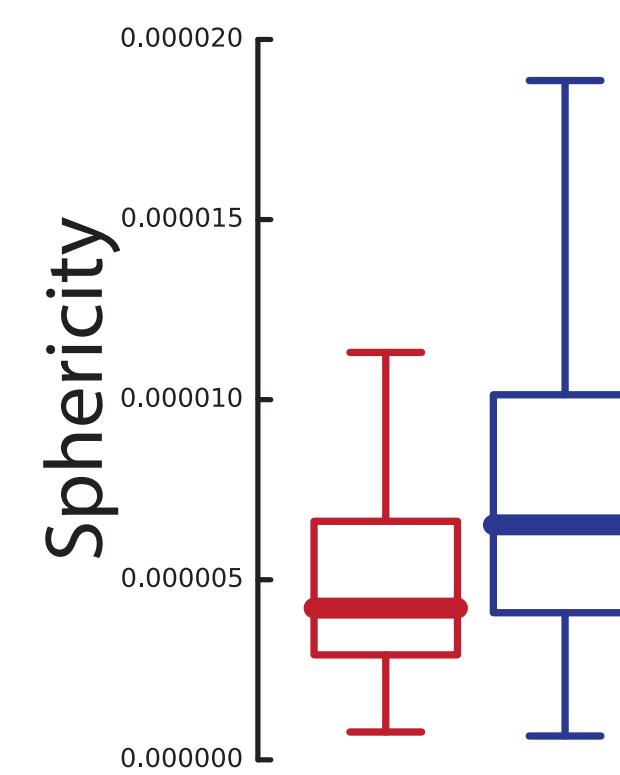
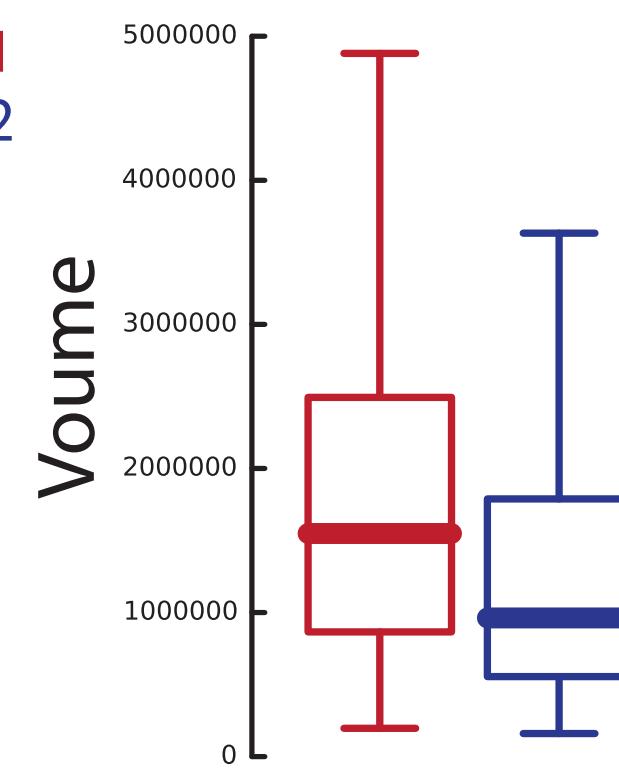
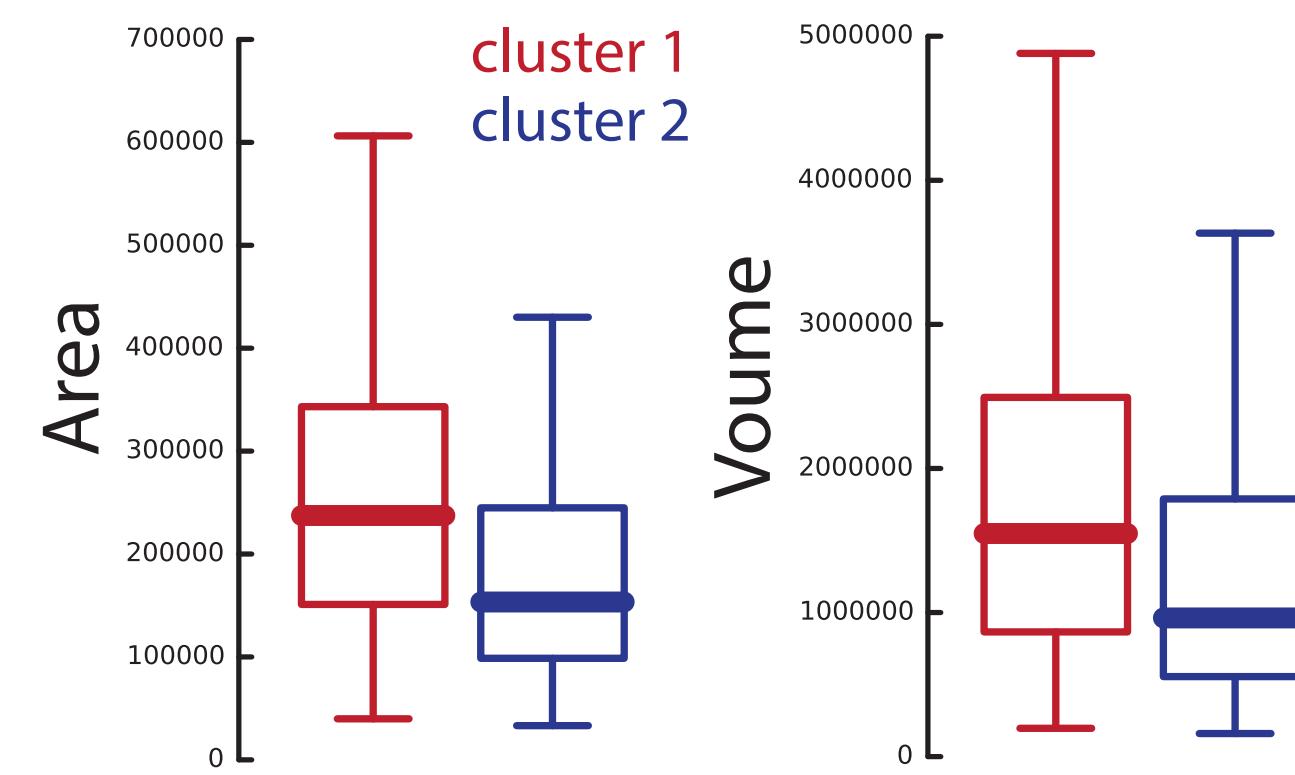
A/B compartments?



PGP1 ChIP-seq and Hi-C data from ENCODE and Lieberman-Aiden Lab, respectively

# Cluster properties

## A/B compartment properties



Can we walk the chromatin path in the nucleus?

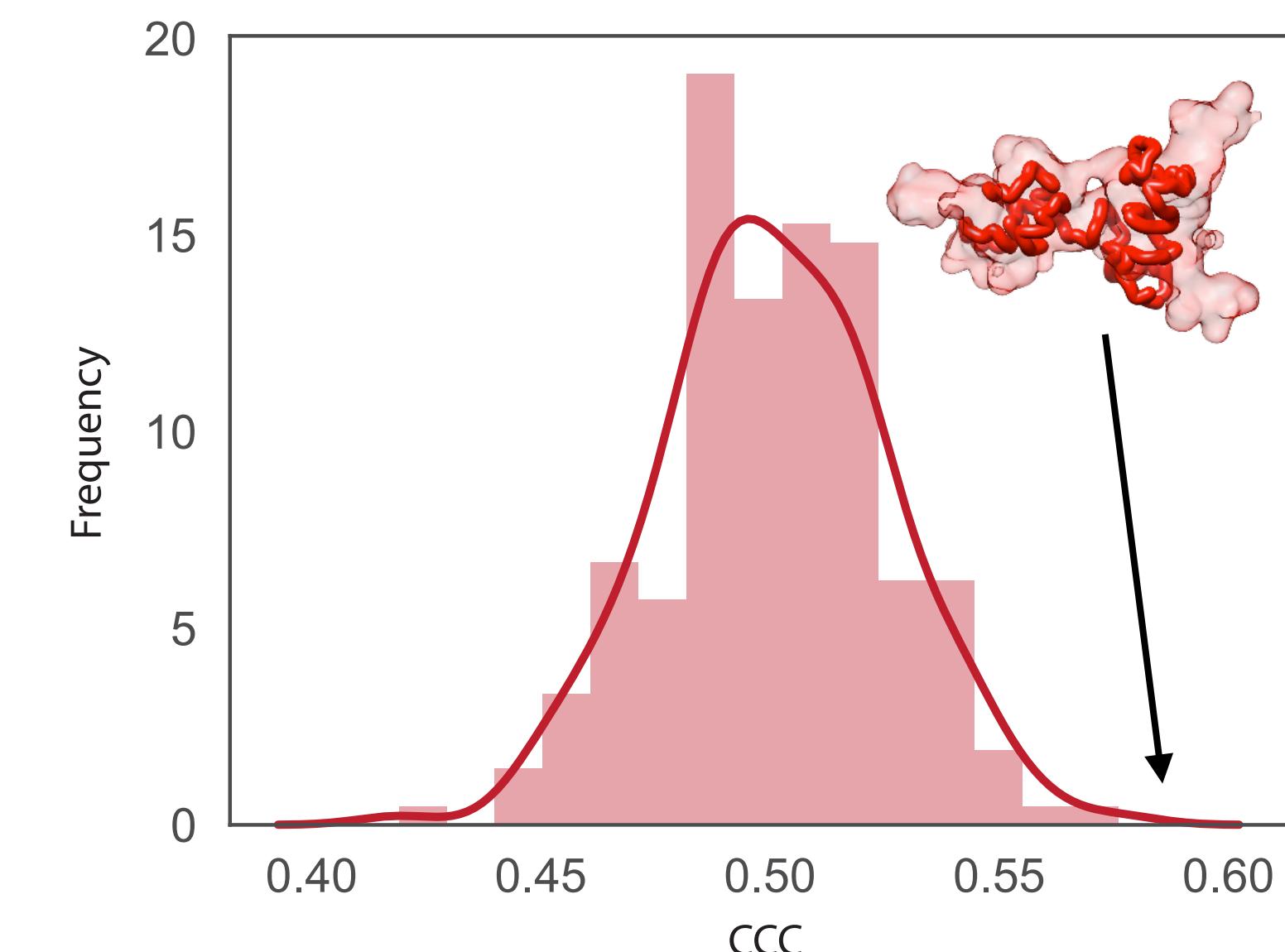
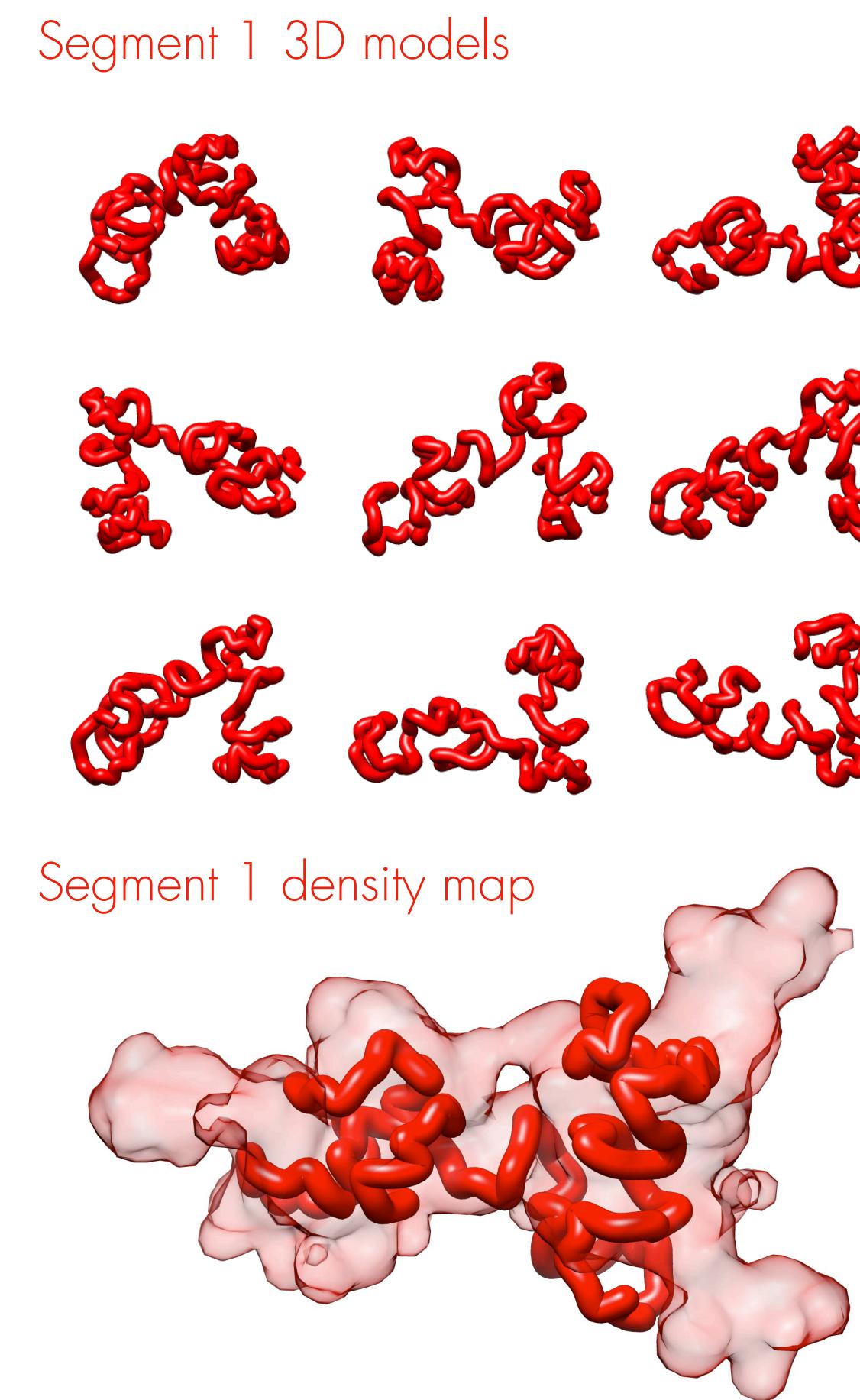
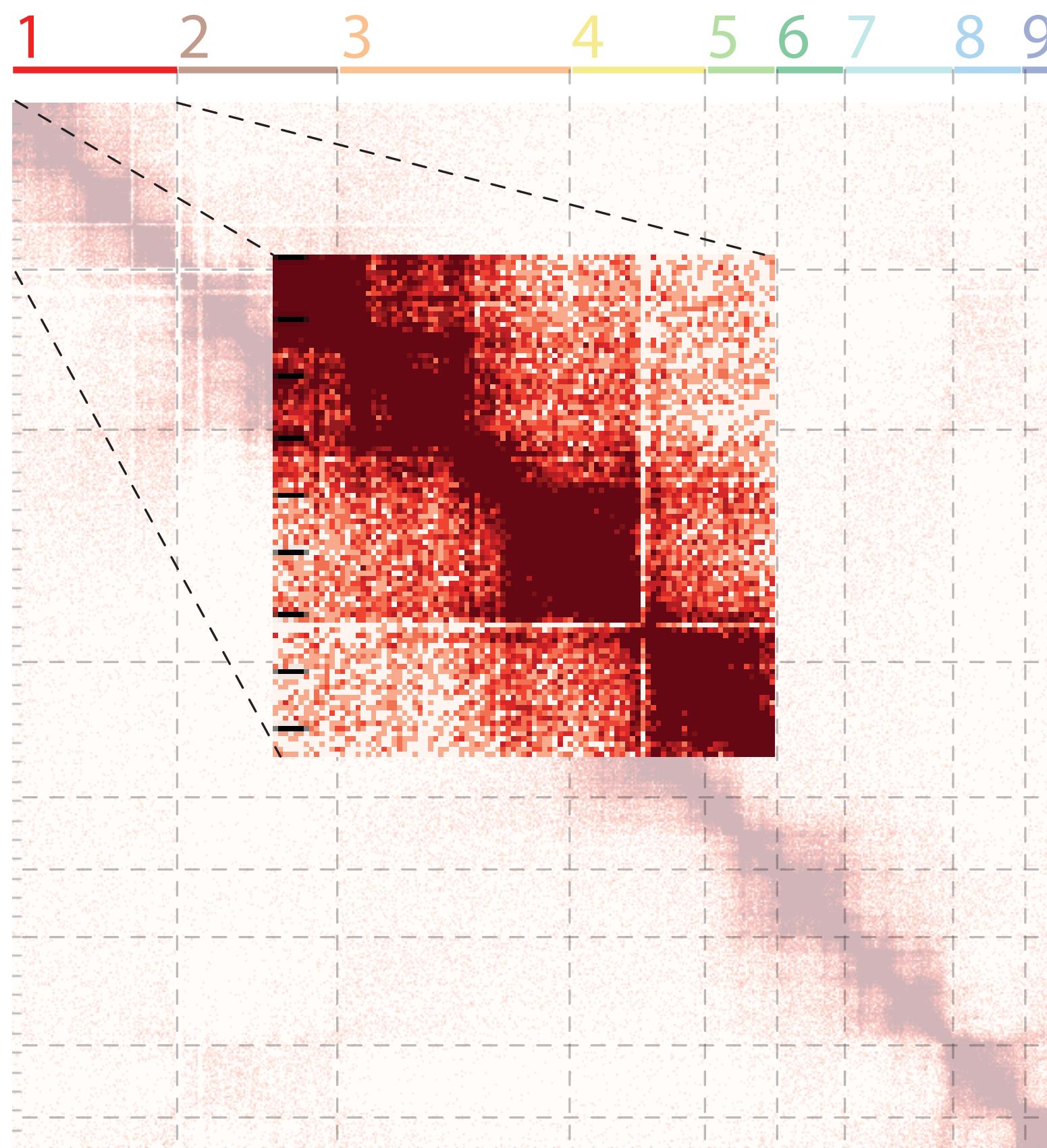
YES!

Can we increase the resolution of our data?

by fitting 3D models based on Hi-C interaction maps

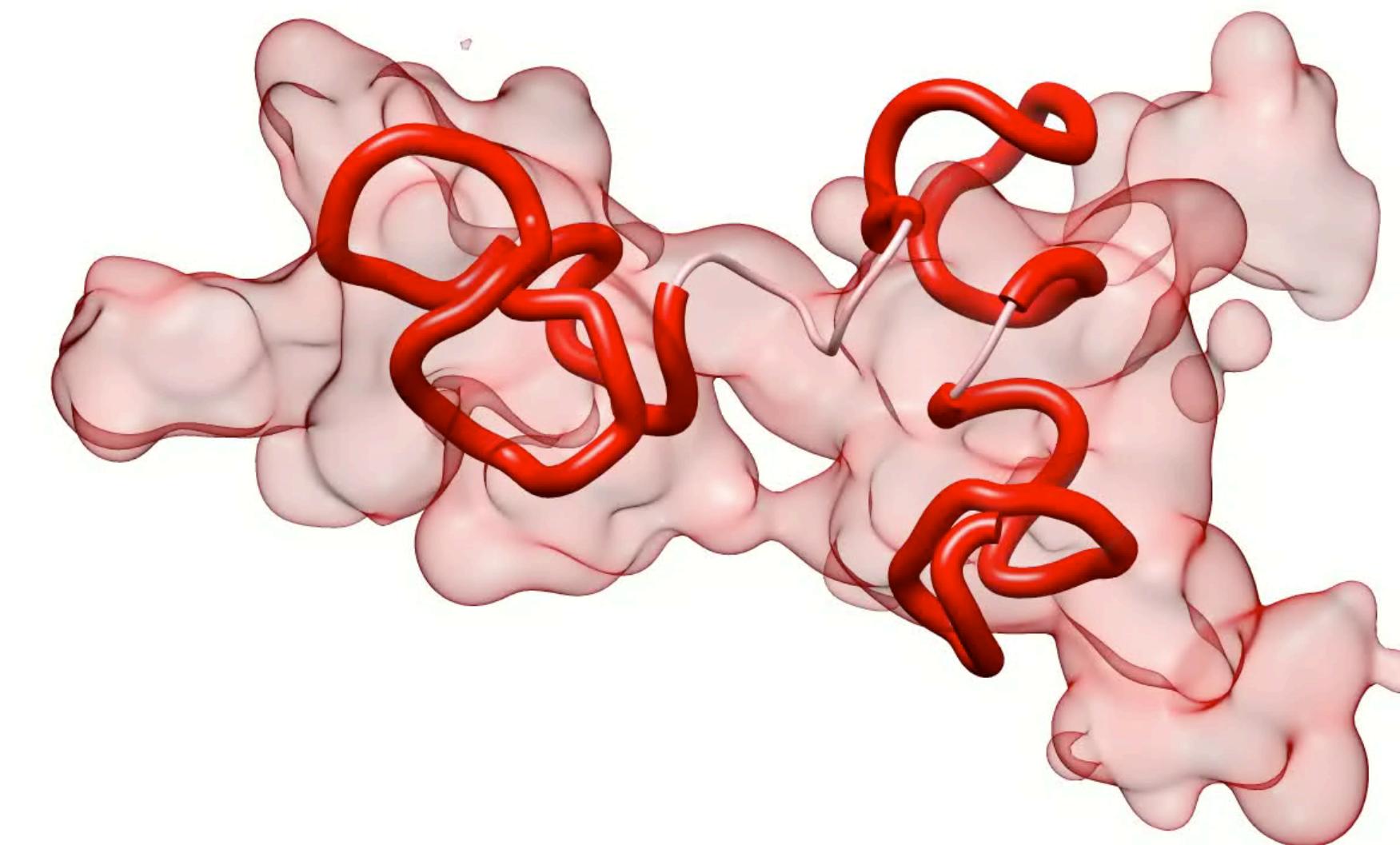
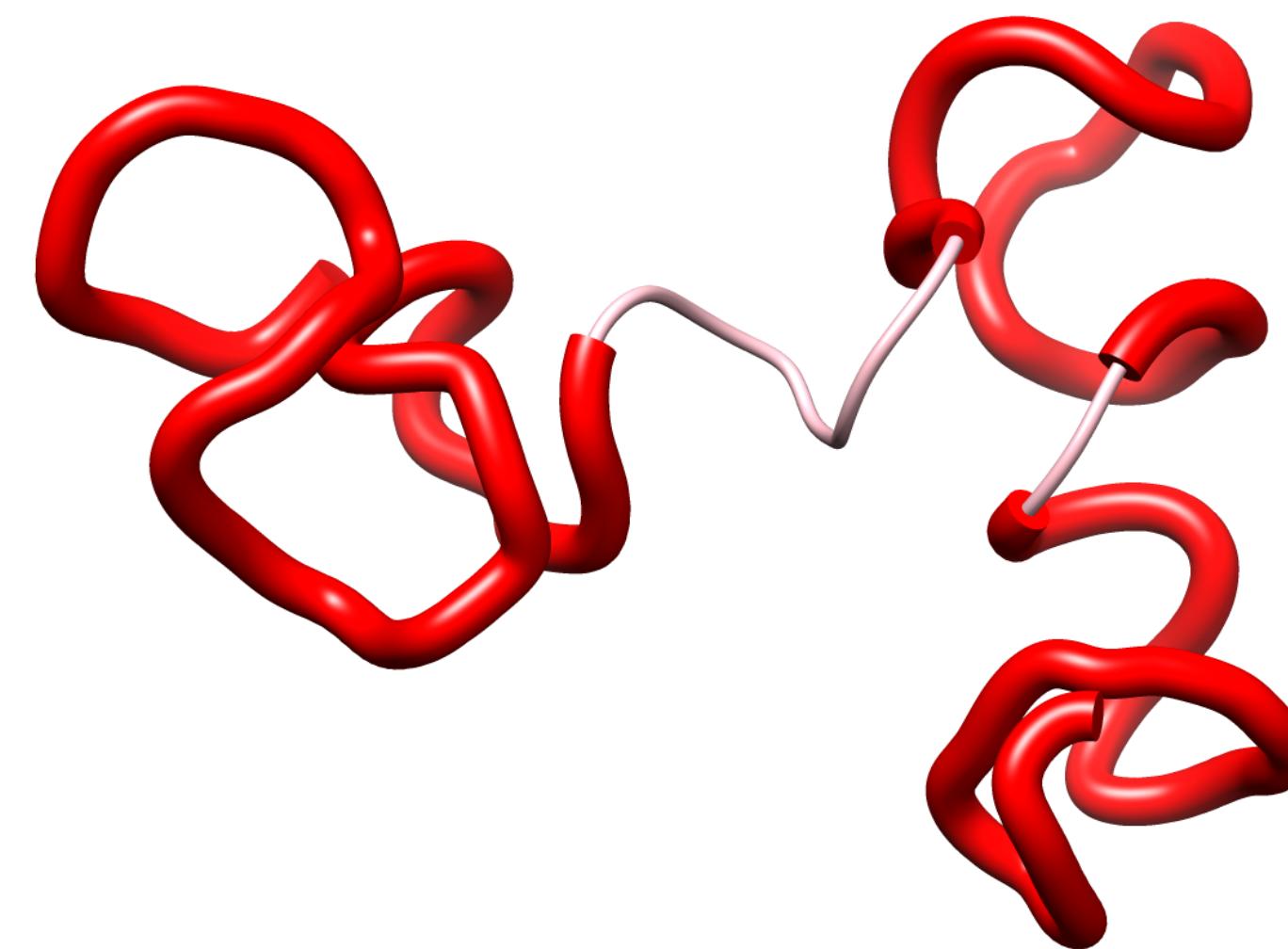
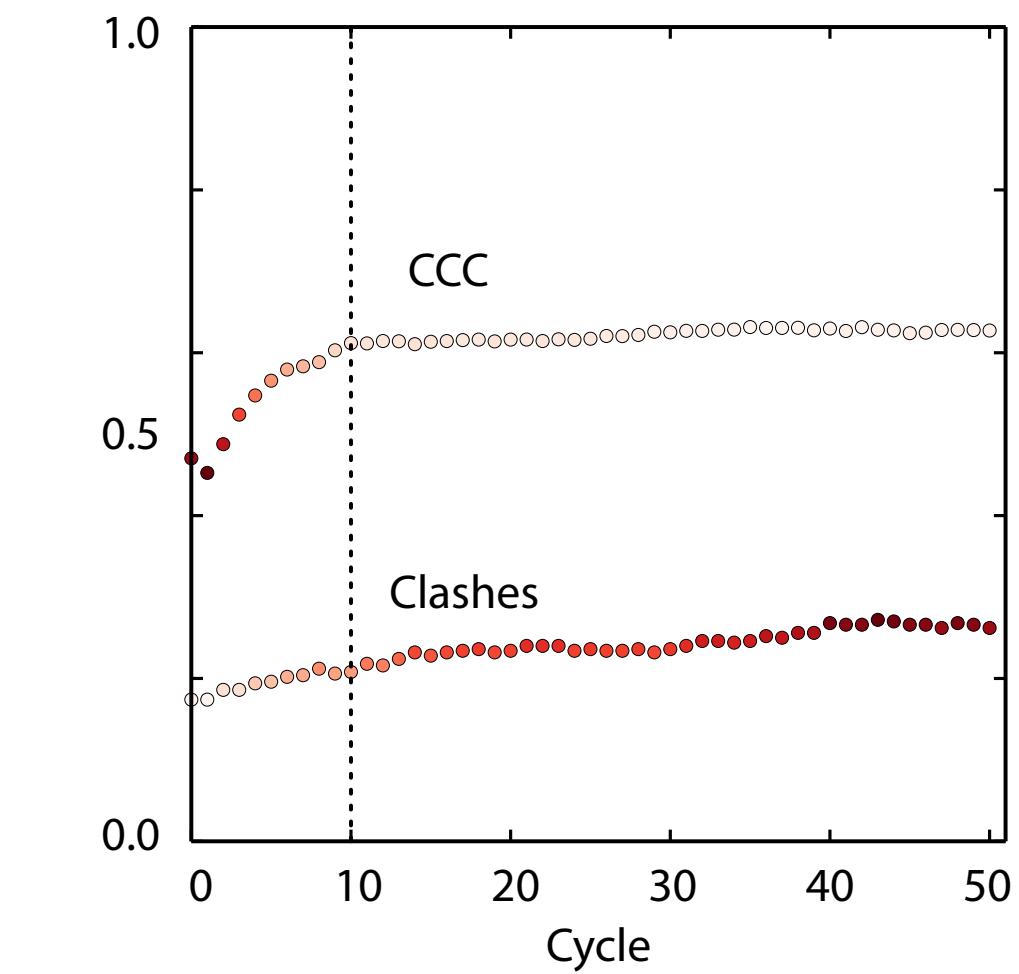
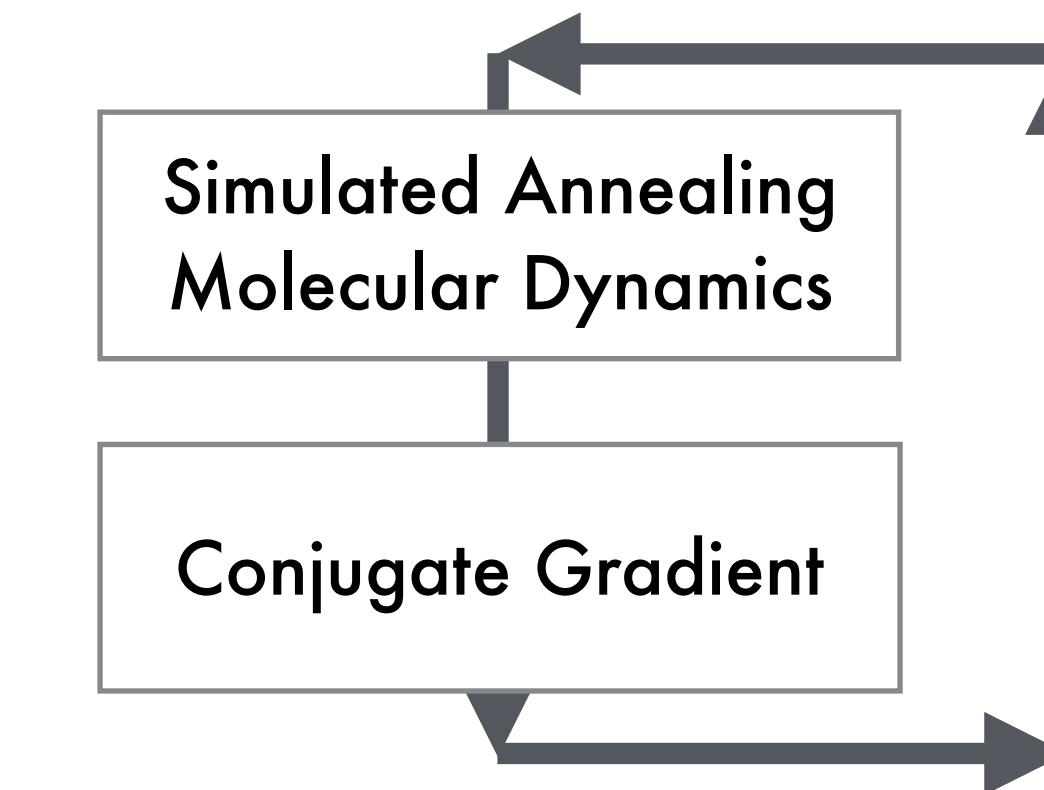
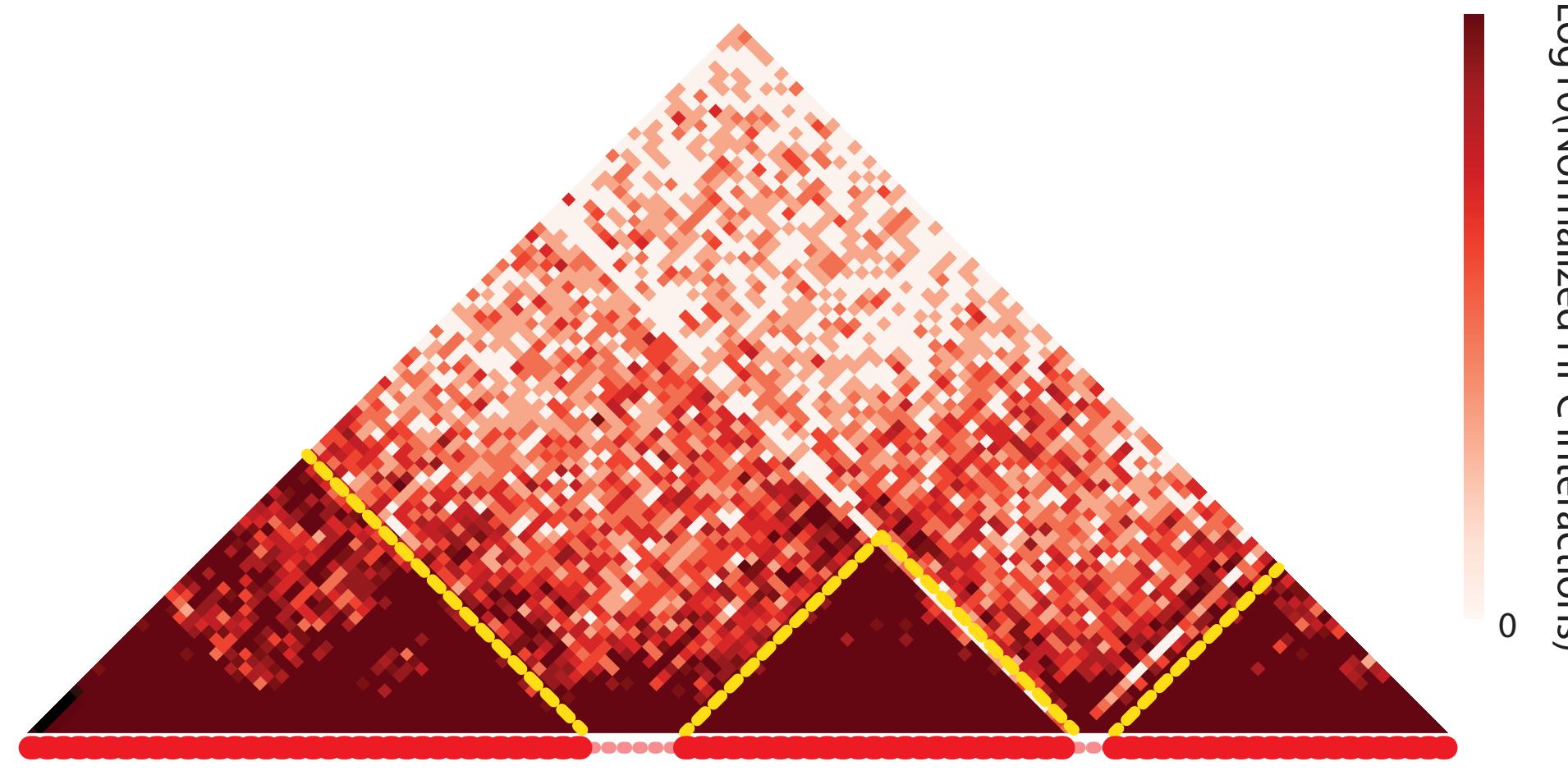
# Increasing resolution

## Rigid body fitting 3D structures based on Hi-C data



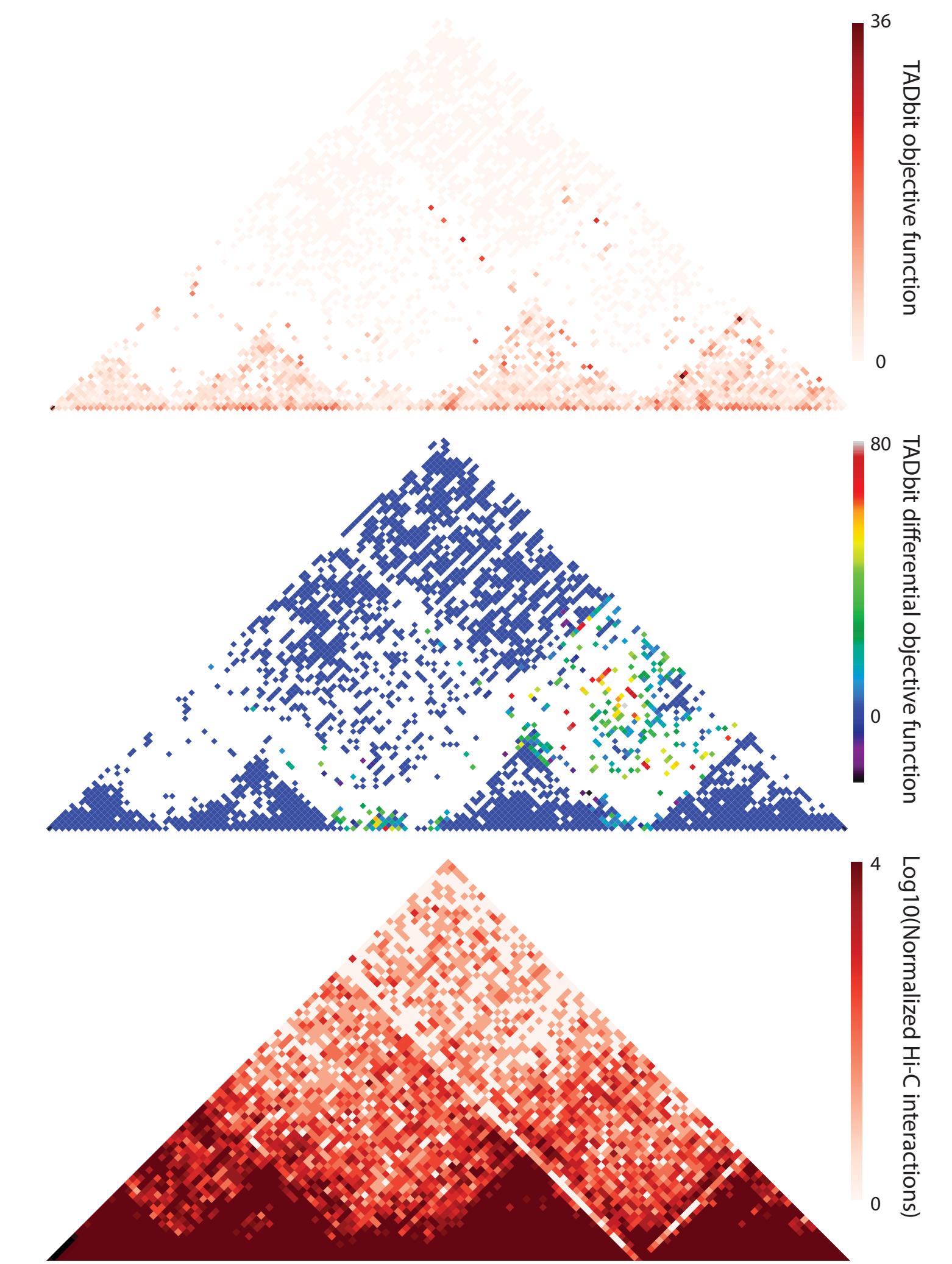
# Increasing resolution

## Flexible fitting 3D structures based on Hi-C data

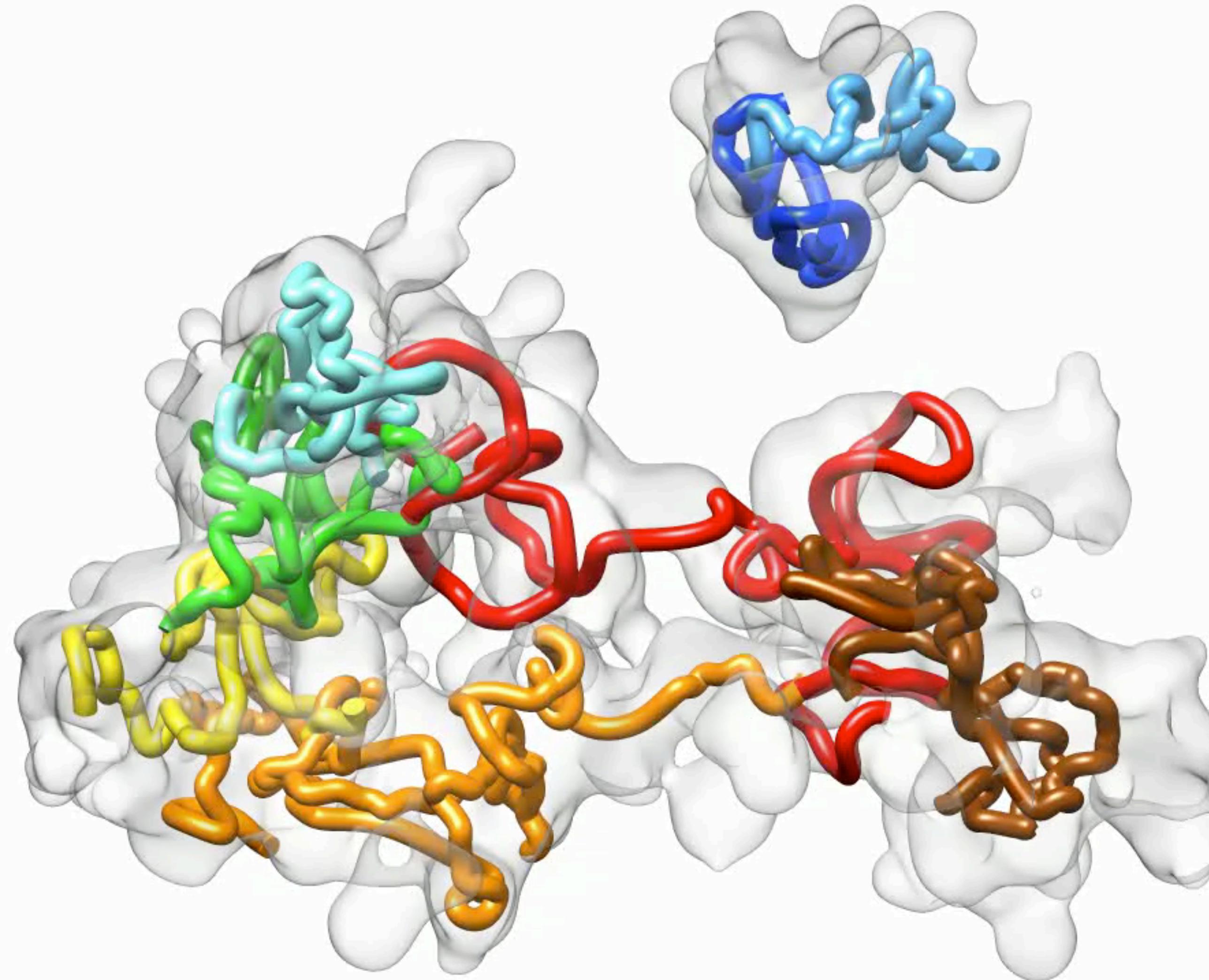


# Increasing resolution

Flexible fitting 3D structures based on Hi-C data



# Chromosome walking path @10Kb resolution



David Castillo  
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Irene Farabella  
Silvia Galan  
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