



# Chromosome walking with super-resolution imaging and modeling

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CNAG-CRG · ICREA

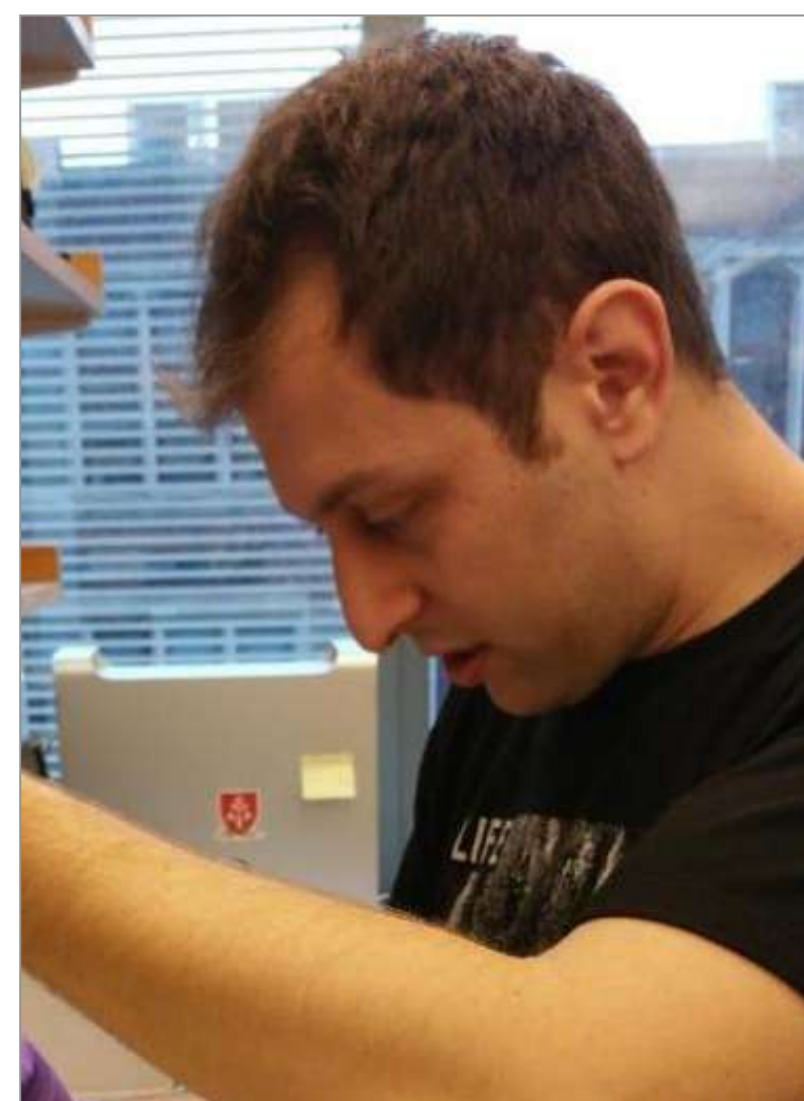
<http://marciuslab.org>  
<http://3DGenomes.org>  
<http://cnag.crg.eu>

**cnag** CRG<sup>®</sup> ICREA

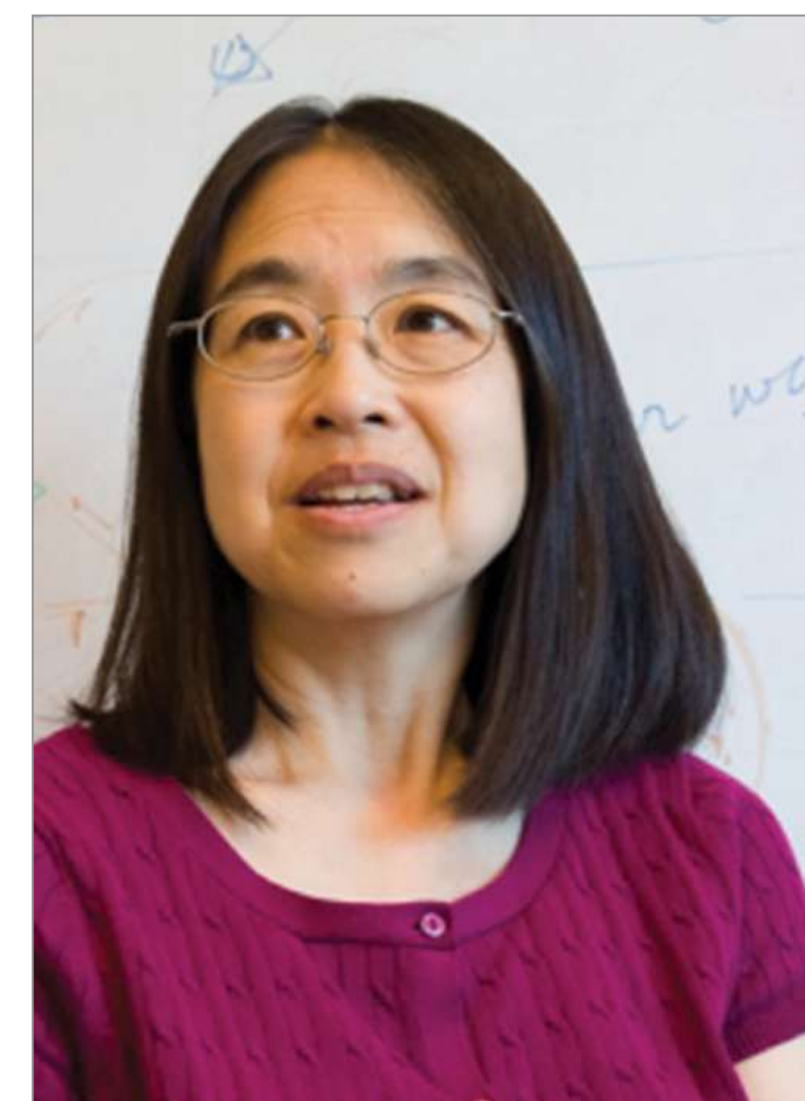




**Irene Farabella**  
CNAG-CRG



**Guy Nir**  
Harvard Med School



**Ting Wu**  
Harvard Med School

Can we walk the chromatin path in the nucleus?

by

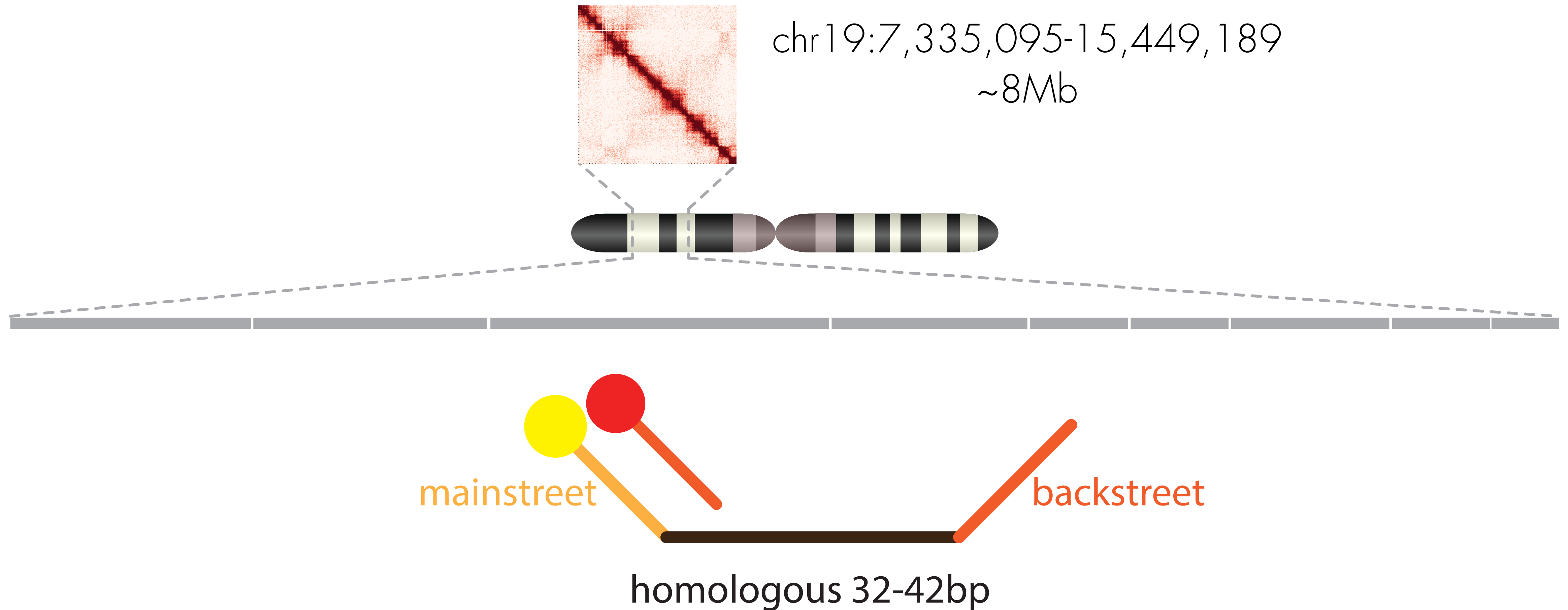
Integrating imaging and Hi-C maps with modeling.

by developing a method for

Oligopaint-based modeling of genomes

# High-resolution imaging

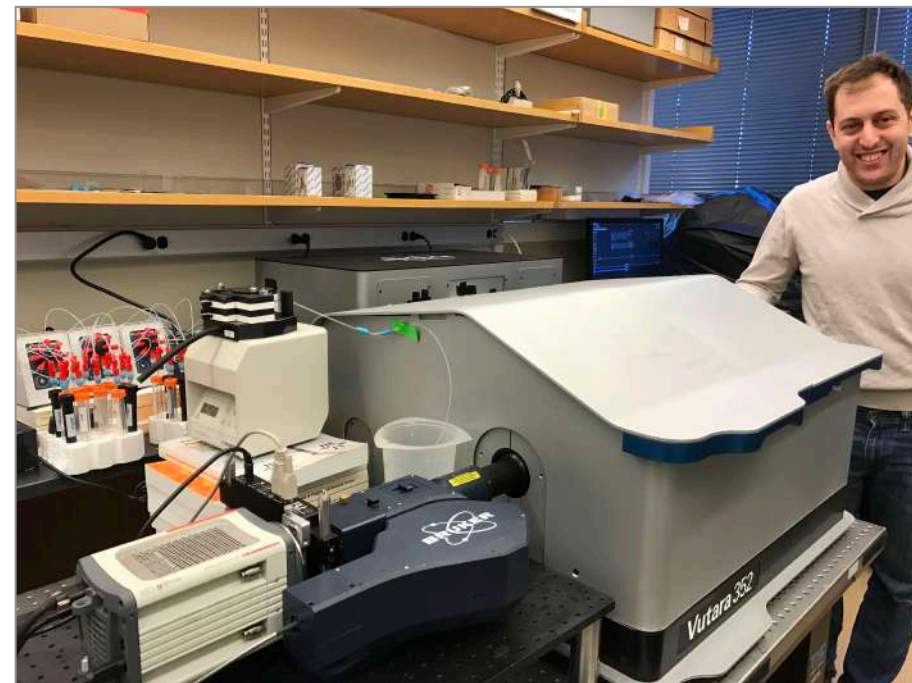
Tracing chromosomes with OligoSTROM & fluidics cycles in PGP1 cells





# High-resolution imaging

Tracing chromosomes with OligoSTROM & fluidics cycles in PGP1 cells



**Guy Nir** Harvard Med School

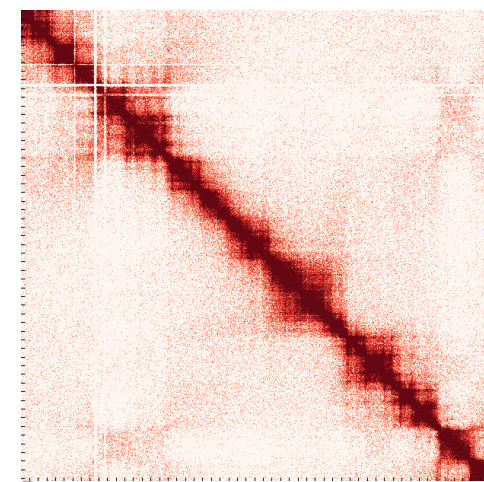
**Bodgan Bintu** Harvard

**Carl Ebeling** Bruker

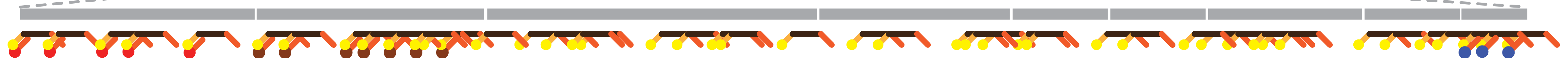
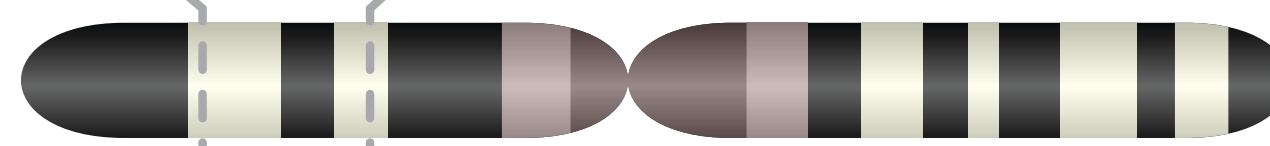
**Jeff Stuckey** Bruker

**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

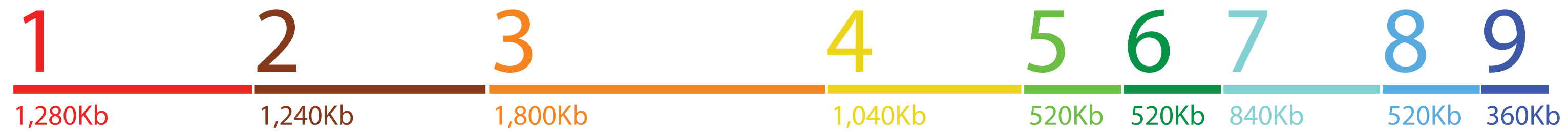
9

360Kb



# High-resolution imaging

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

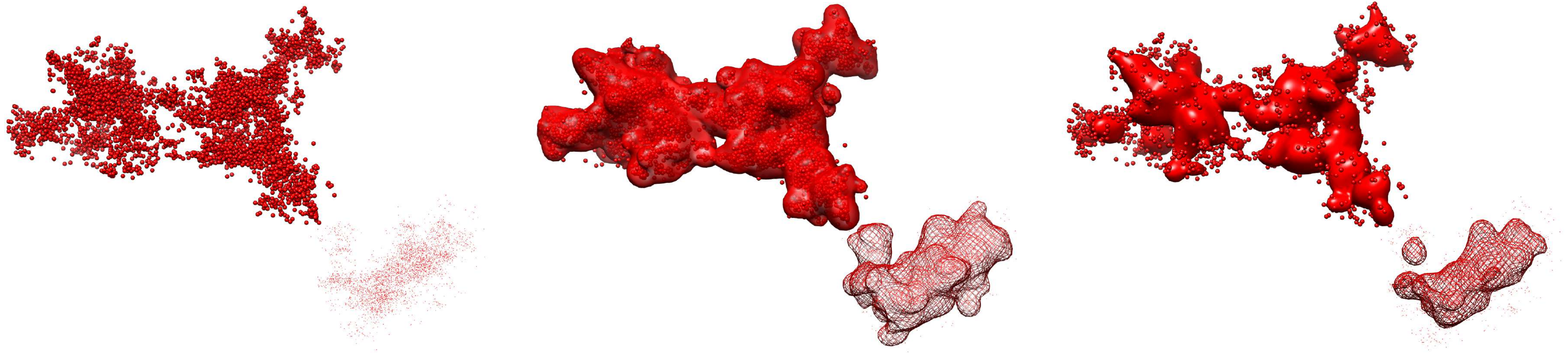




# High-resolution imaging

XYZ points convolution into a density map

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

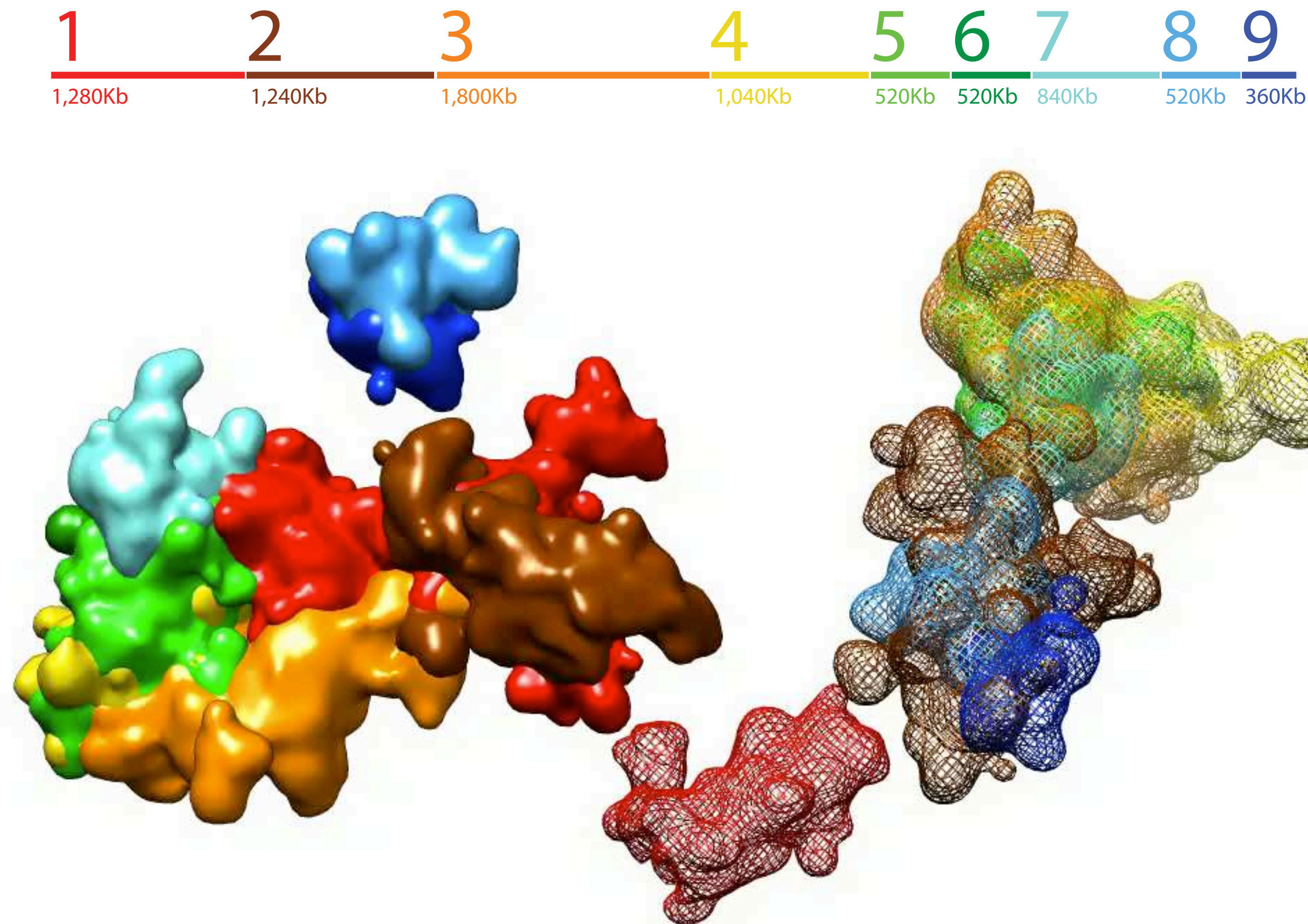


Cell-02 · Segment 1



# Density maps

Cell-02 · Density map @ 50nm



Area (nm<sup>2</sup>)

Volume (nm<sup>3</sup>)

Sphericity

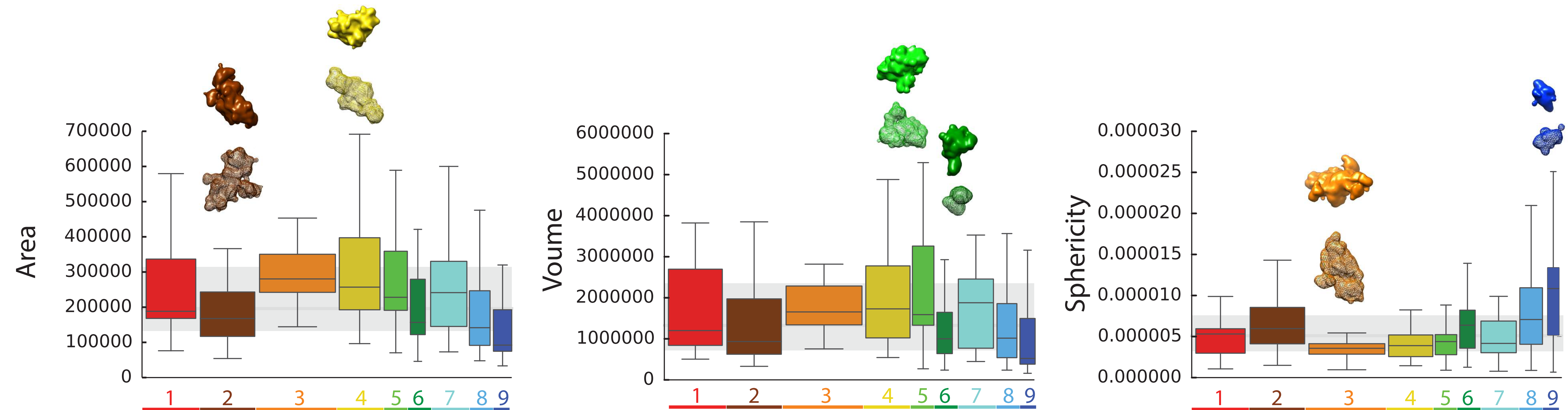
Overlap (%)

Distance (nm)



# Structural features

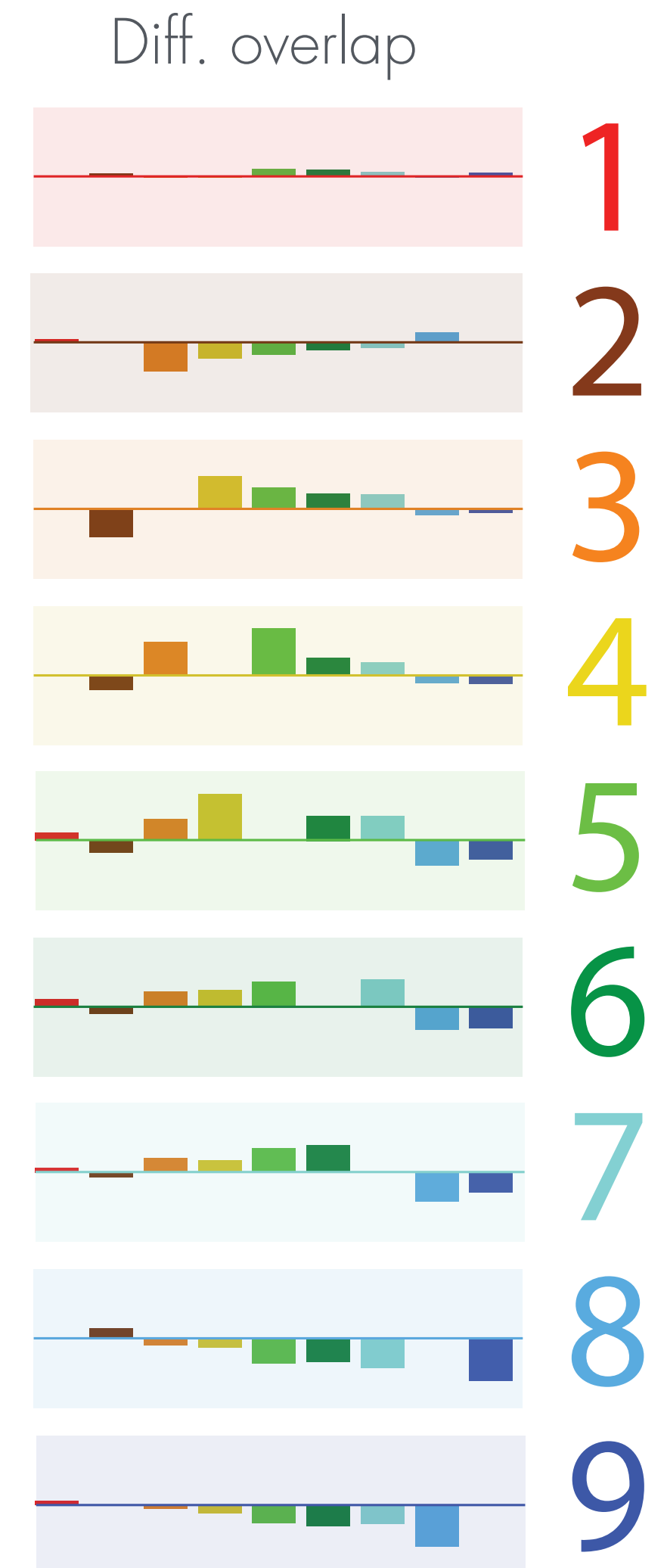
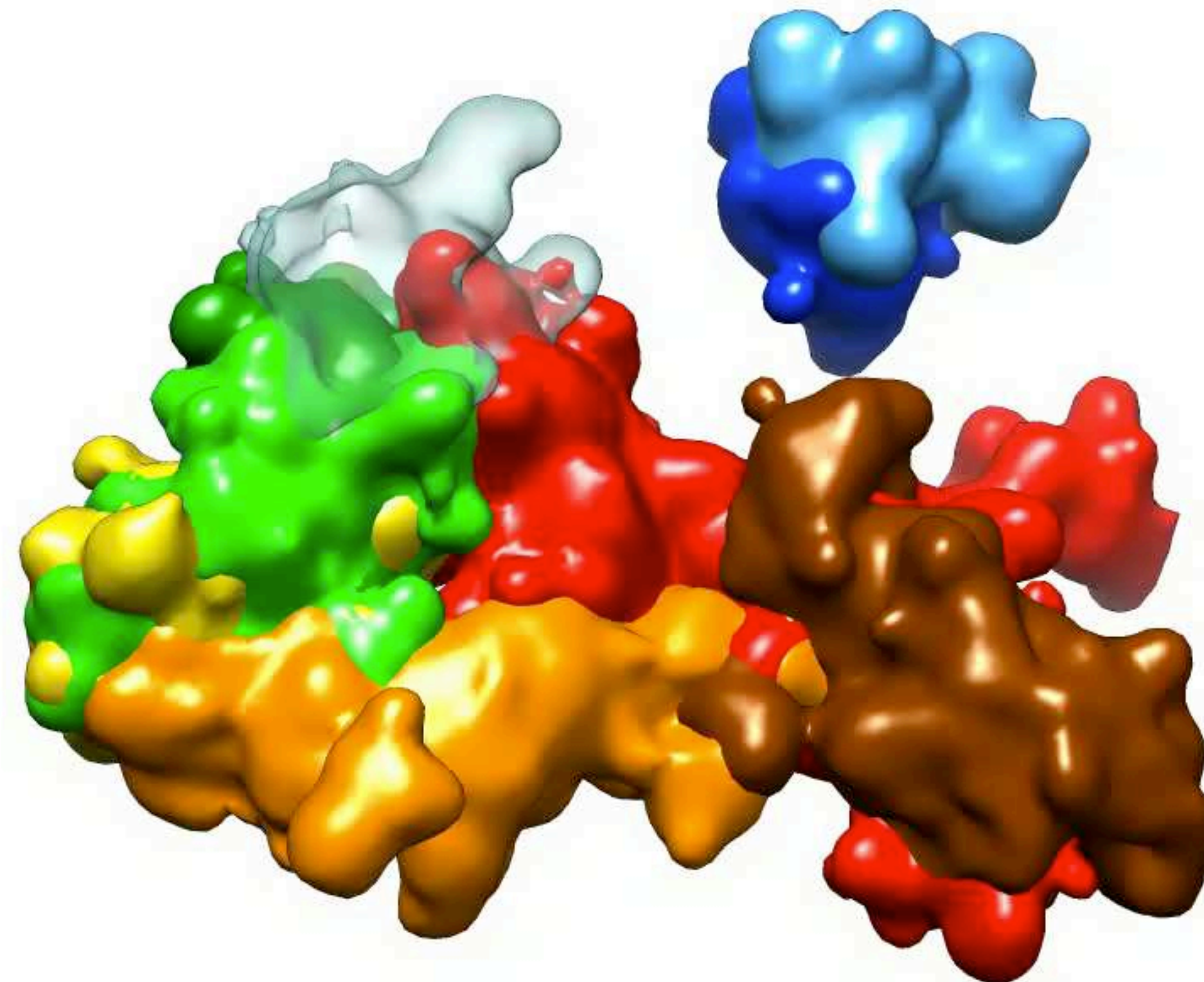
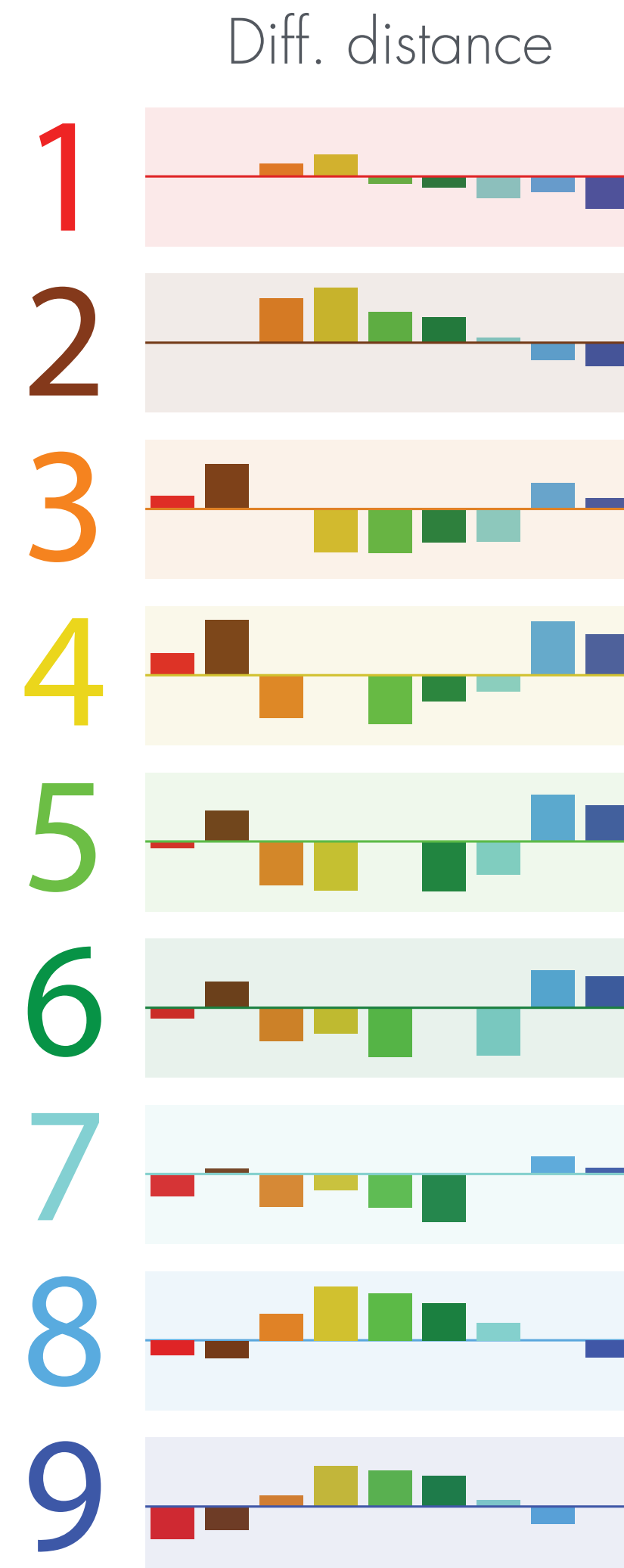
Area, Volume and Sphericity of 19 cells each with 2 homologous resolved





# Spatial arrangement

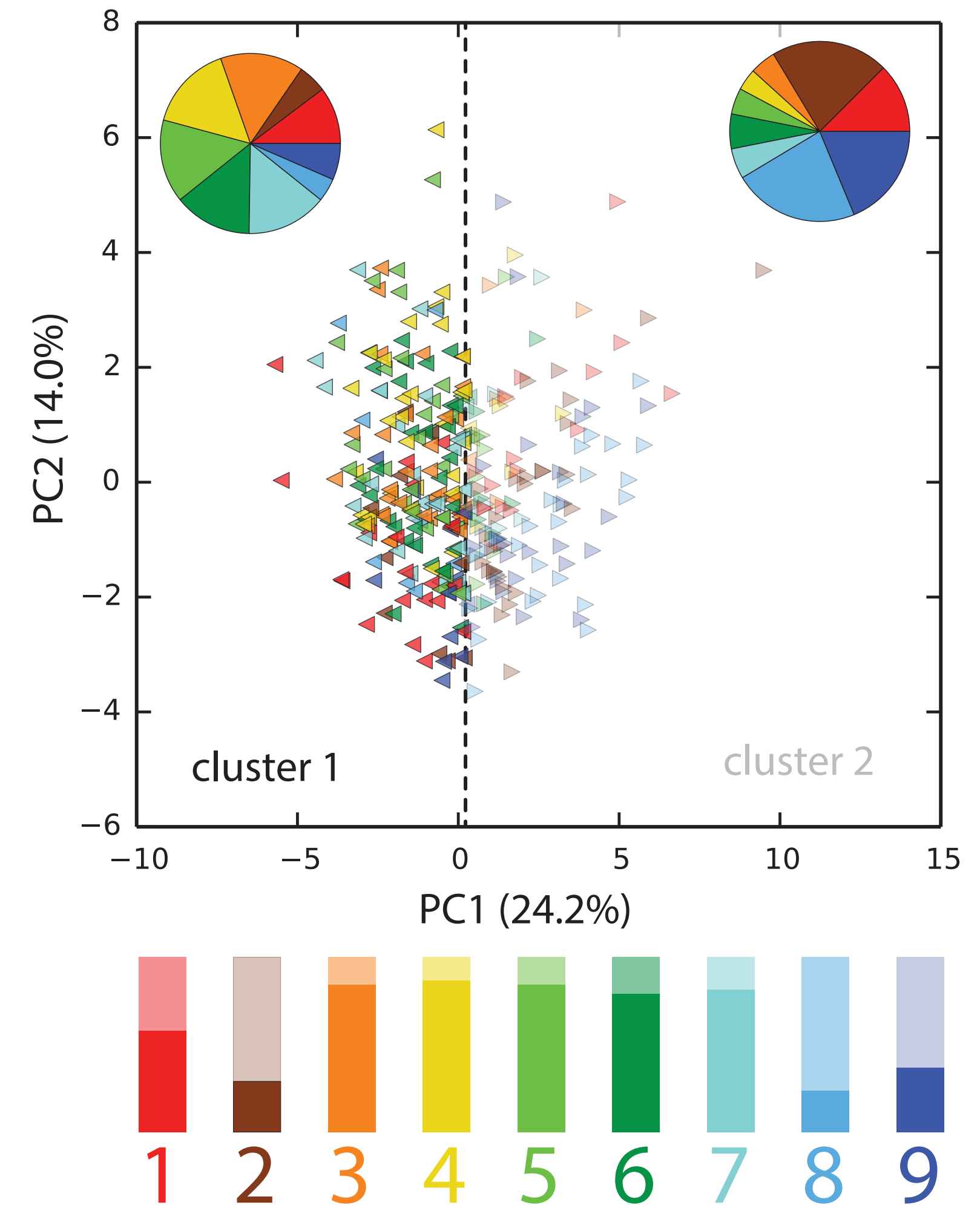
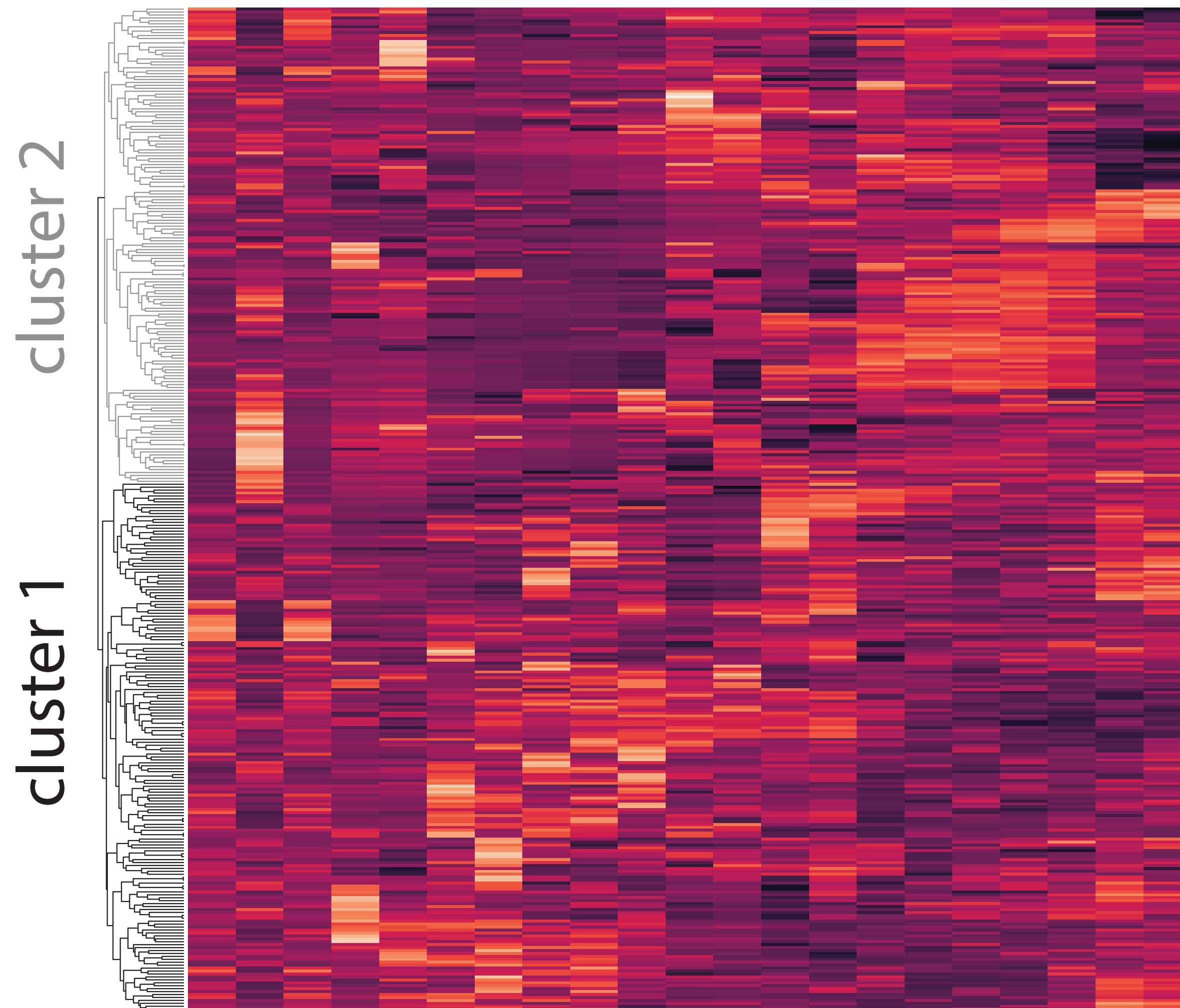
Distance and overlap of 19 cells each with 2 homologous resolved





# Structural clustering

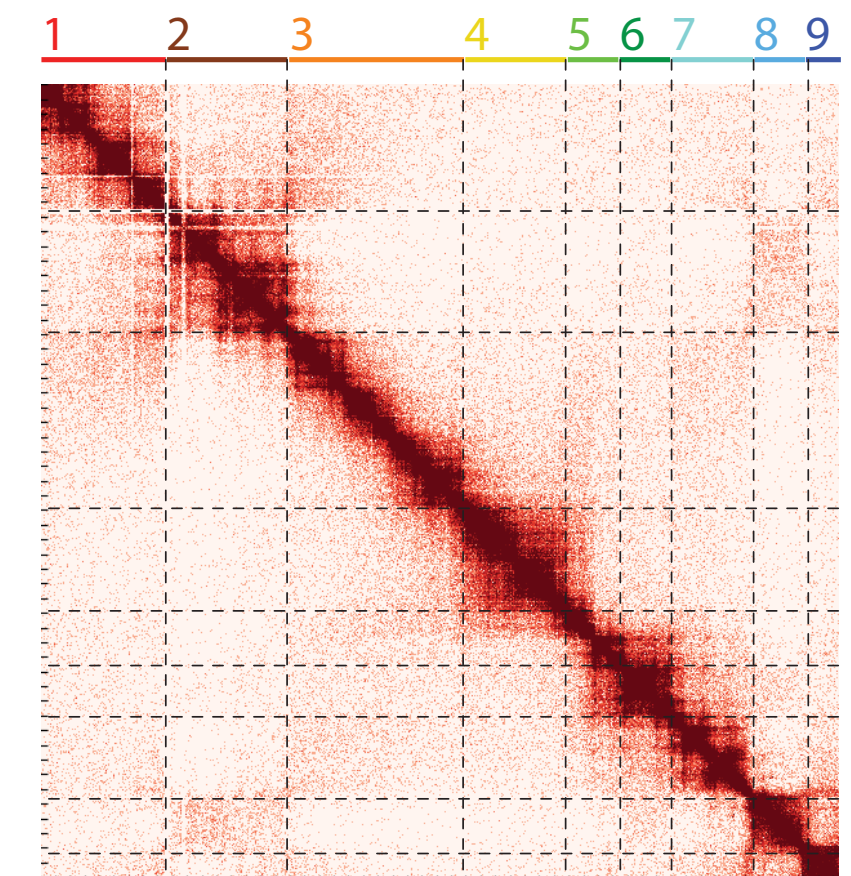
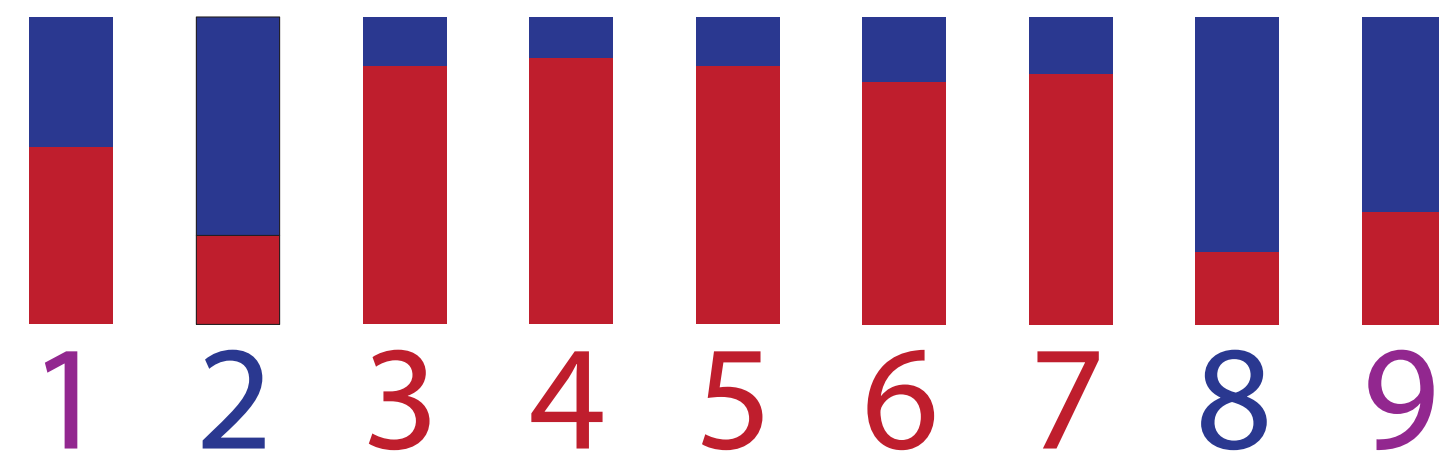
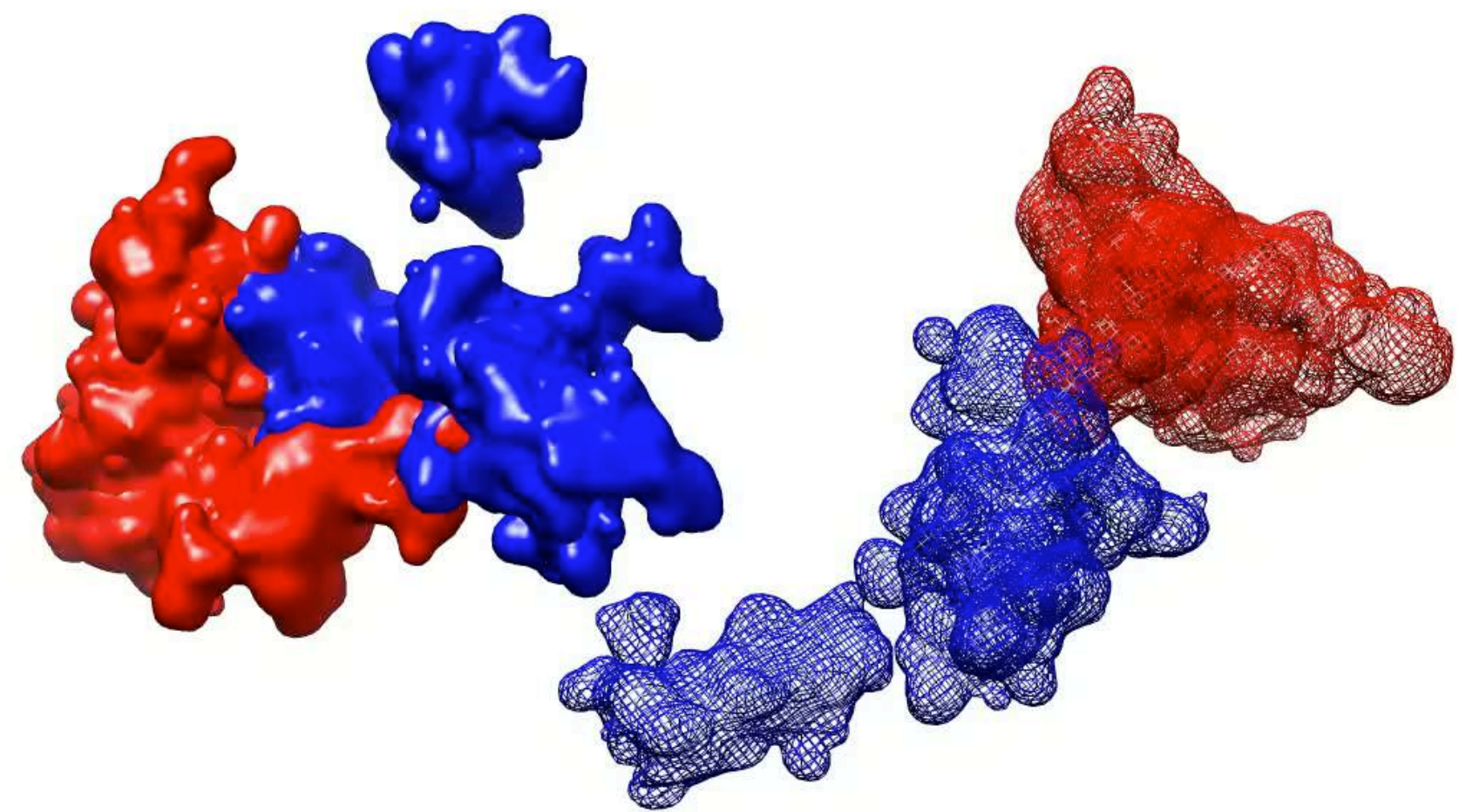
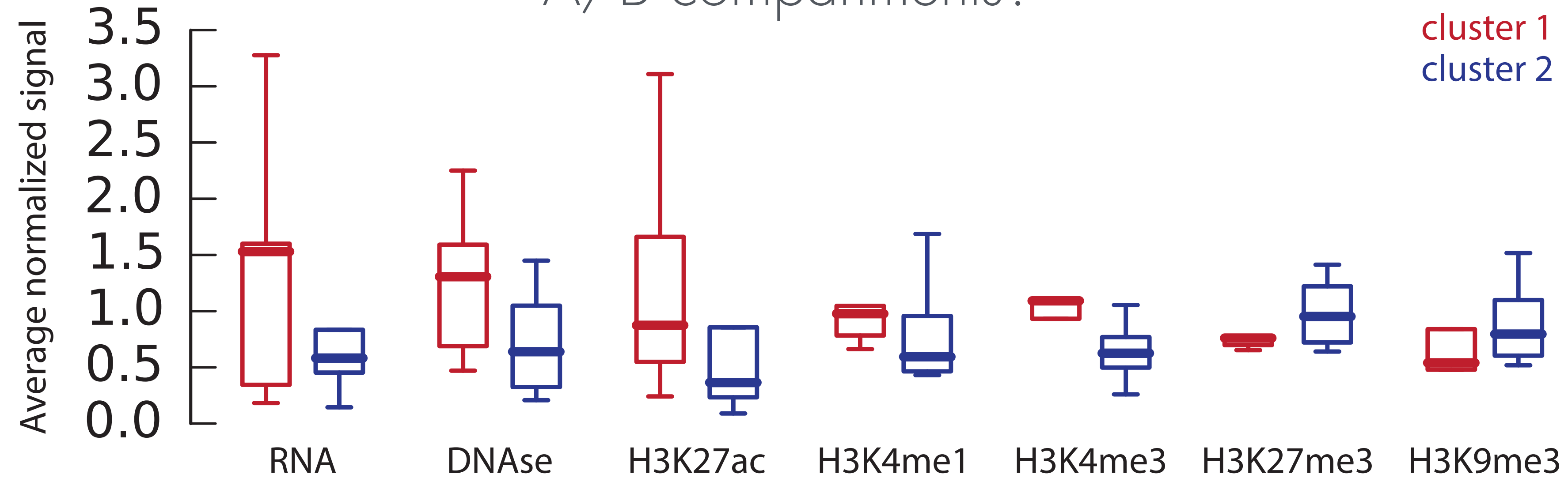
19 cells each with 2 homologous and 9 segments each (342)





# Cluster properties

A/B compartments?

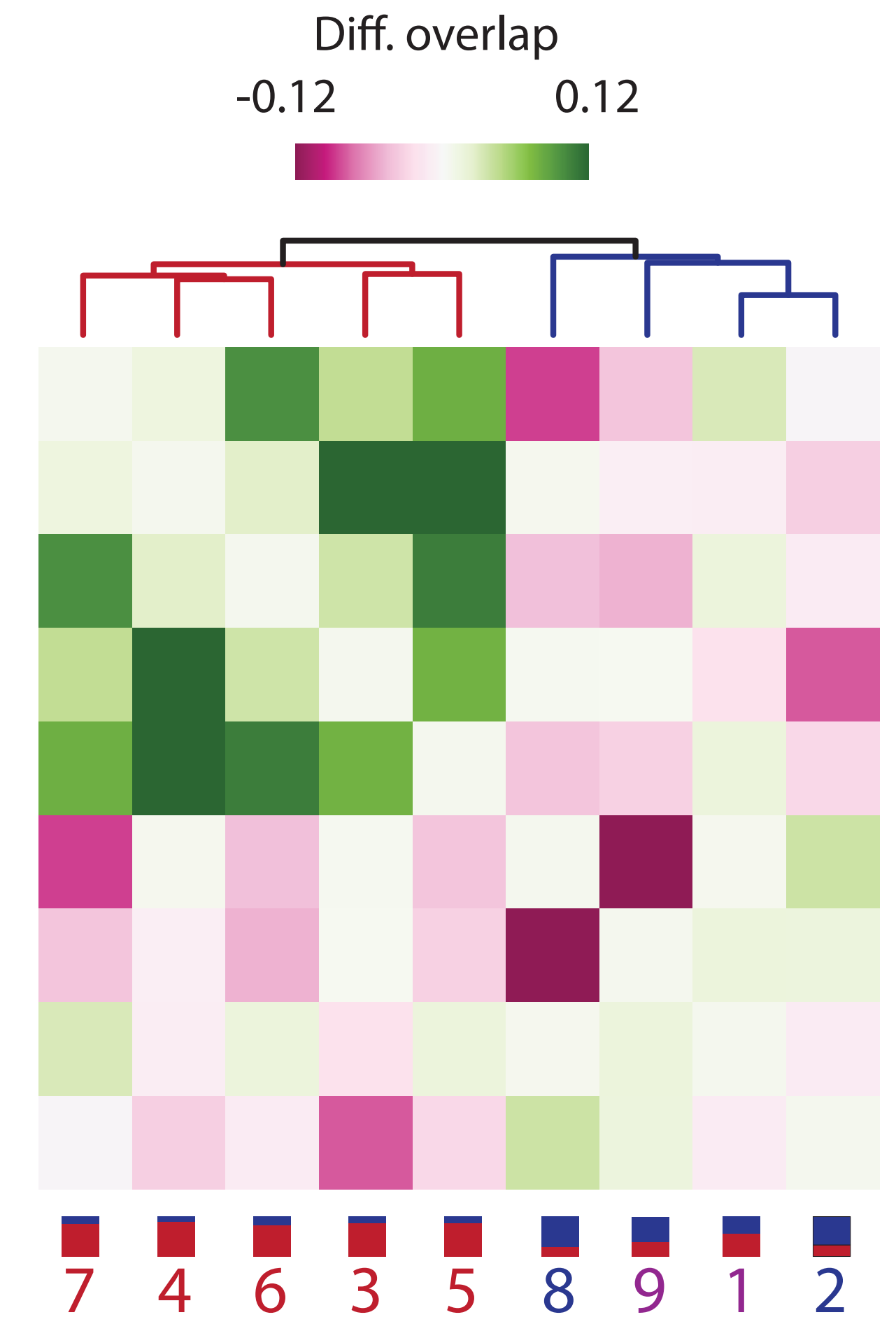
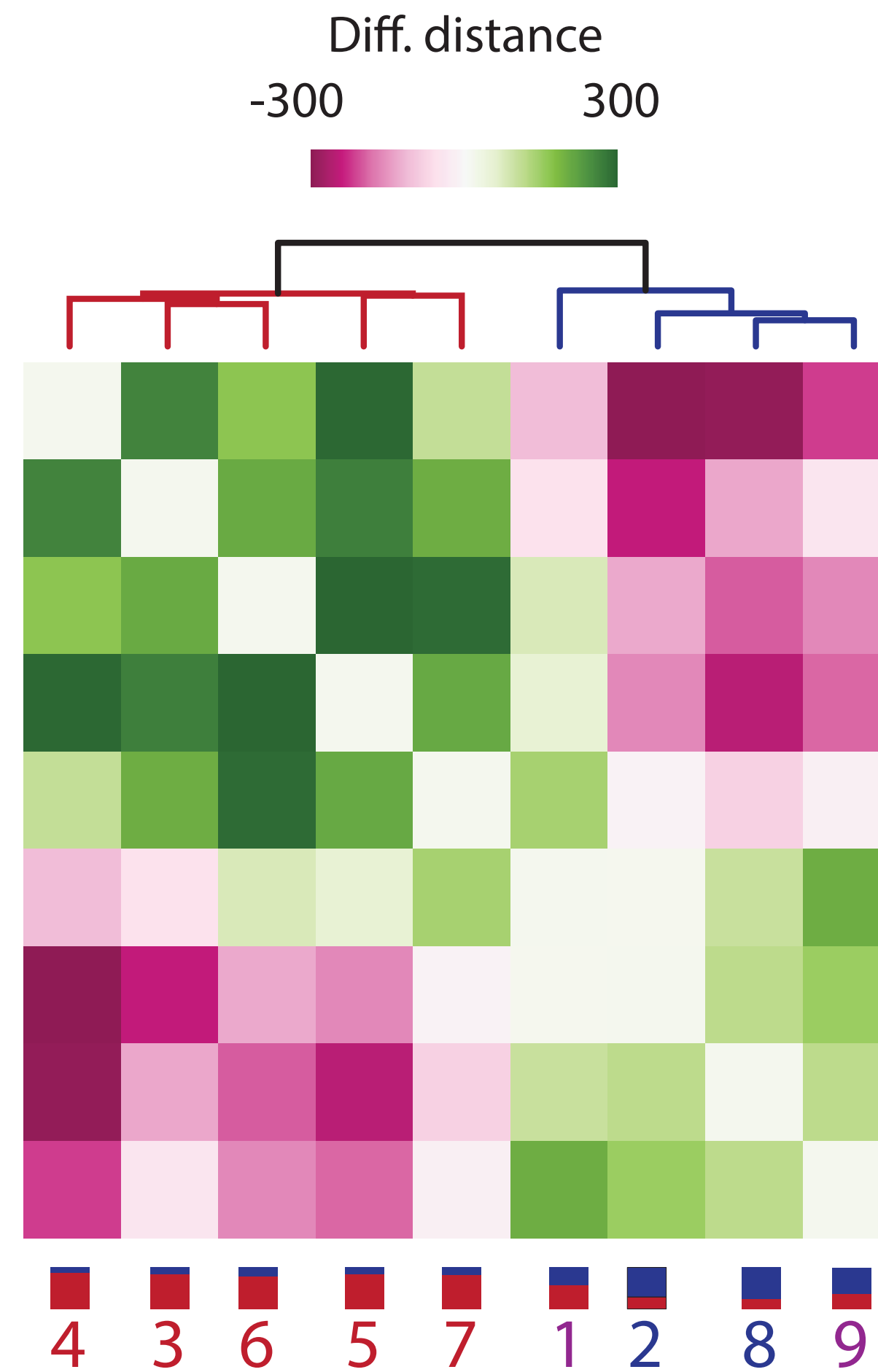
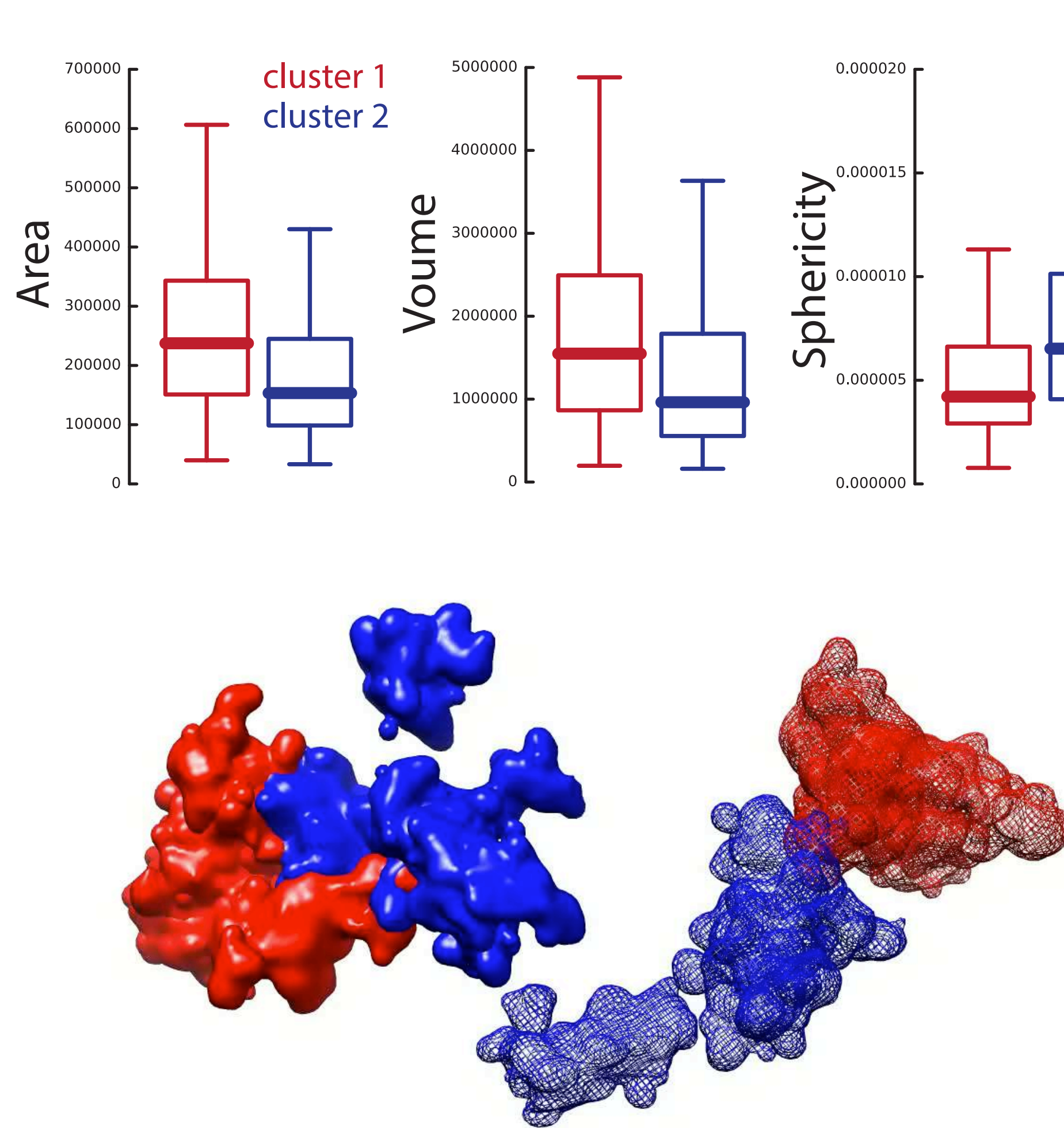


PGP1 ChIP-seq and Hi-C data from ENCODE and Lieberman-Aiden Lab, respectively



# Cluster properties

## A/B compartment properties





Can we walk the chromatin path in the nucleus?

YES!

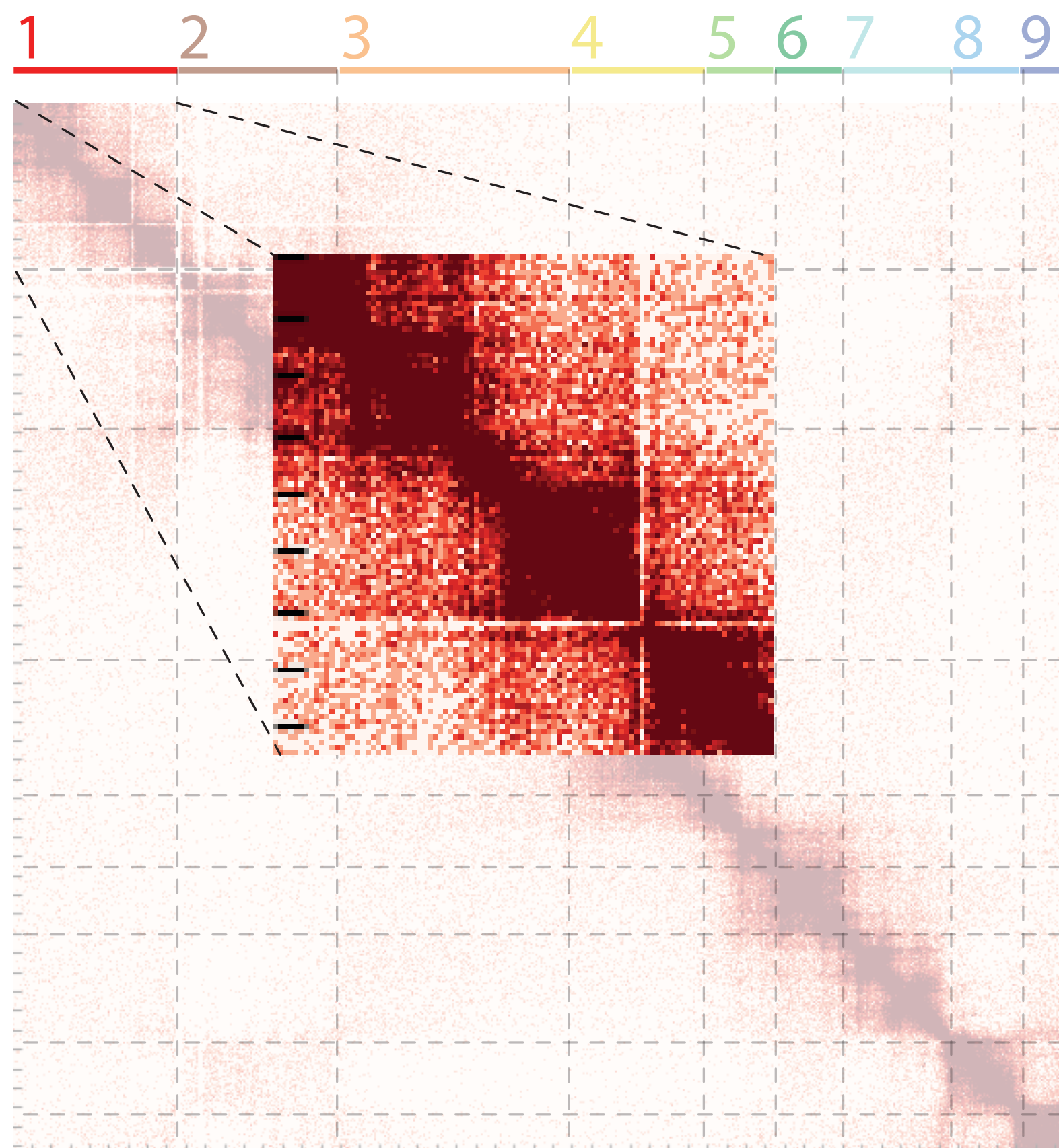
Can we increase the resolution of our data?

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

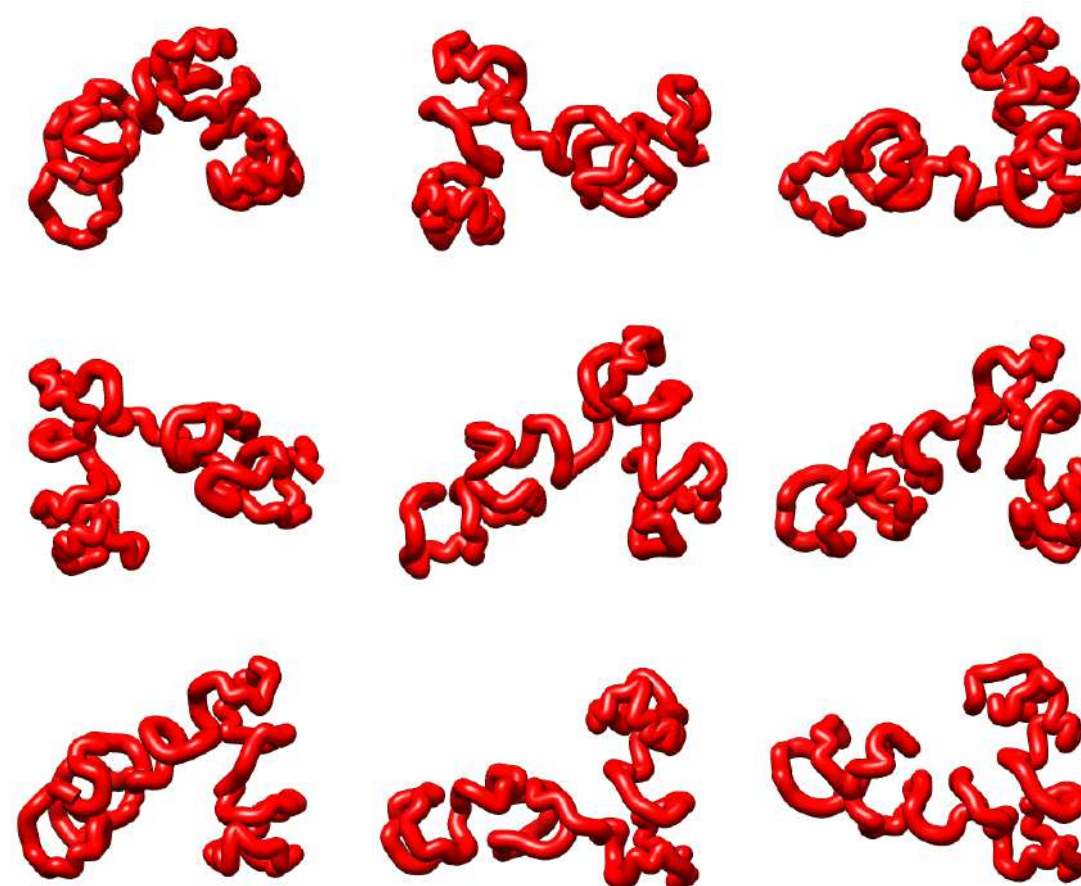


# Increasing resolution

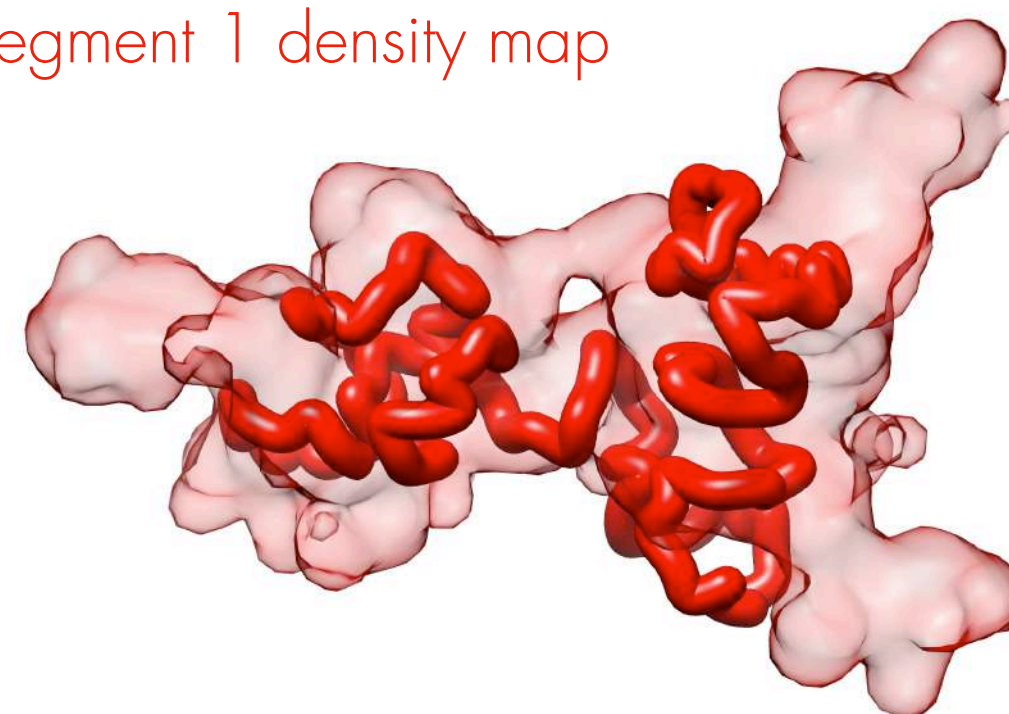
Rigid body fitting 3D structures based on Hi-C data



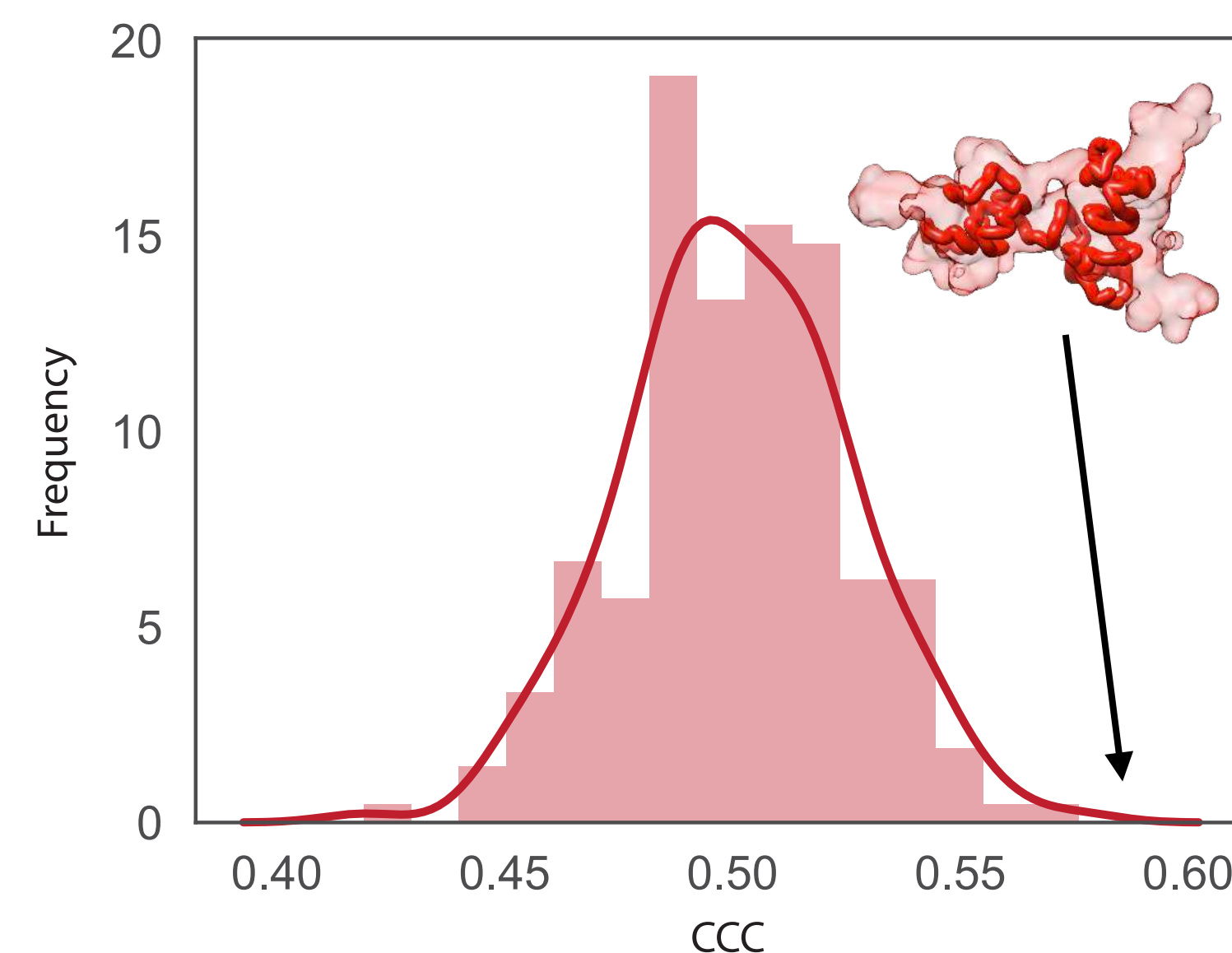
Segment 1 3D models



Segment 1 density map



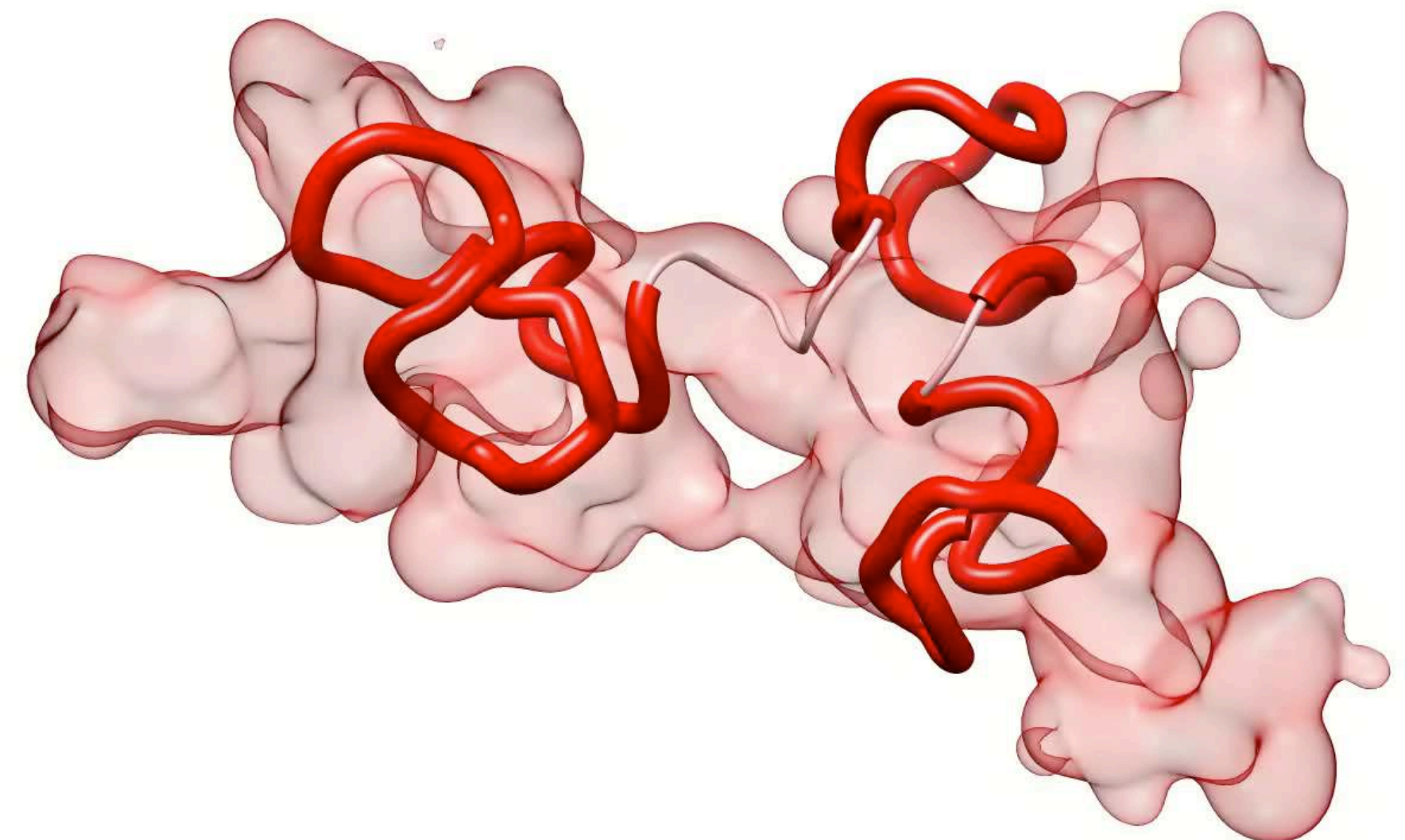
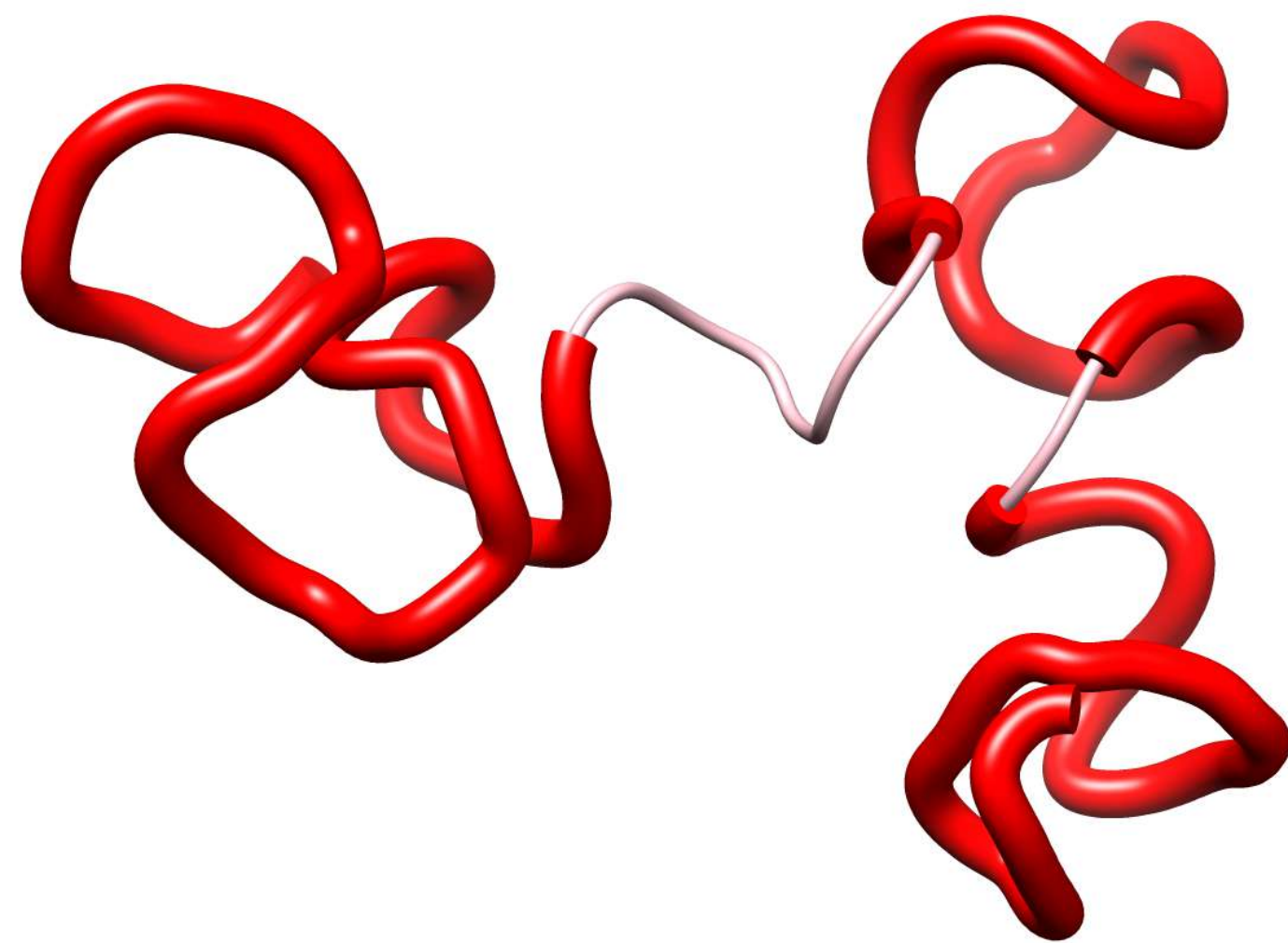
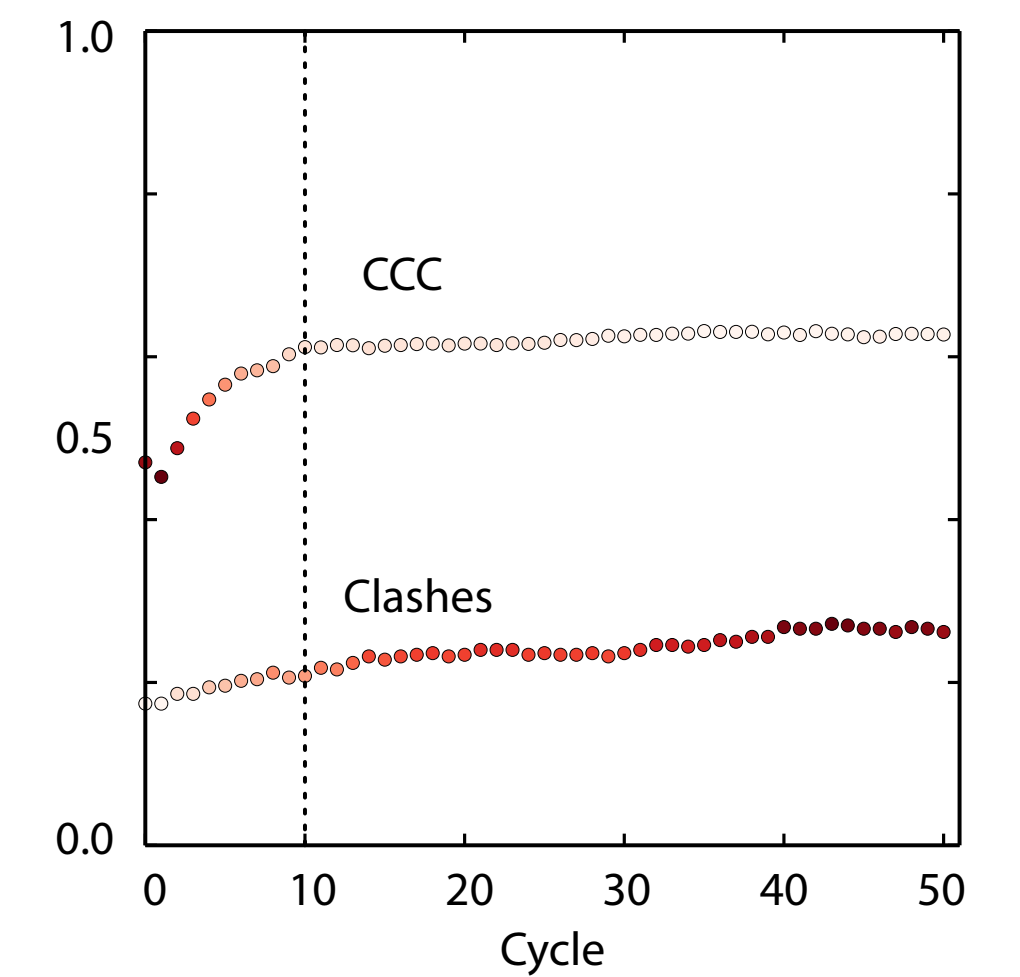
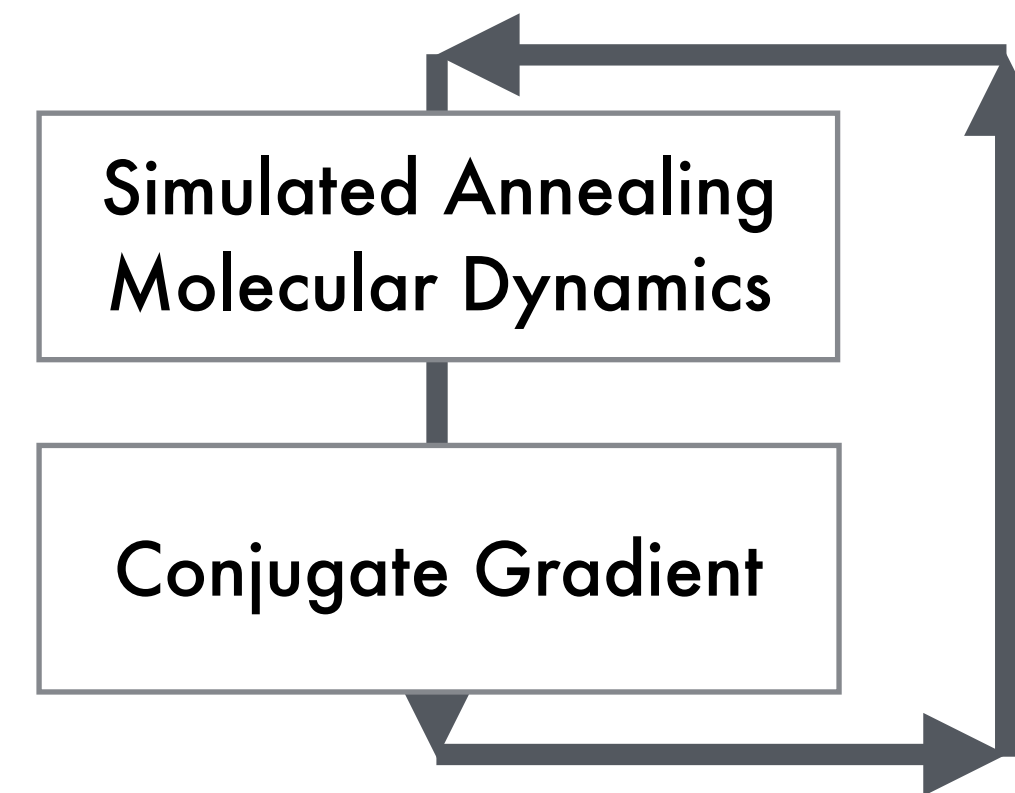
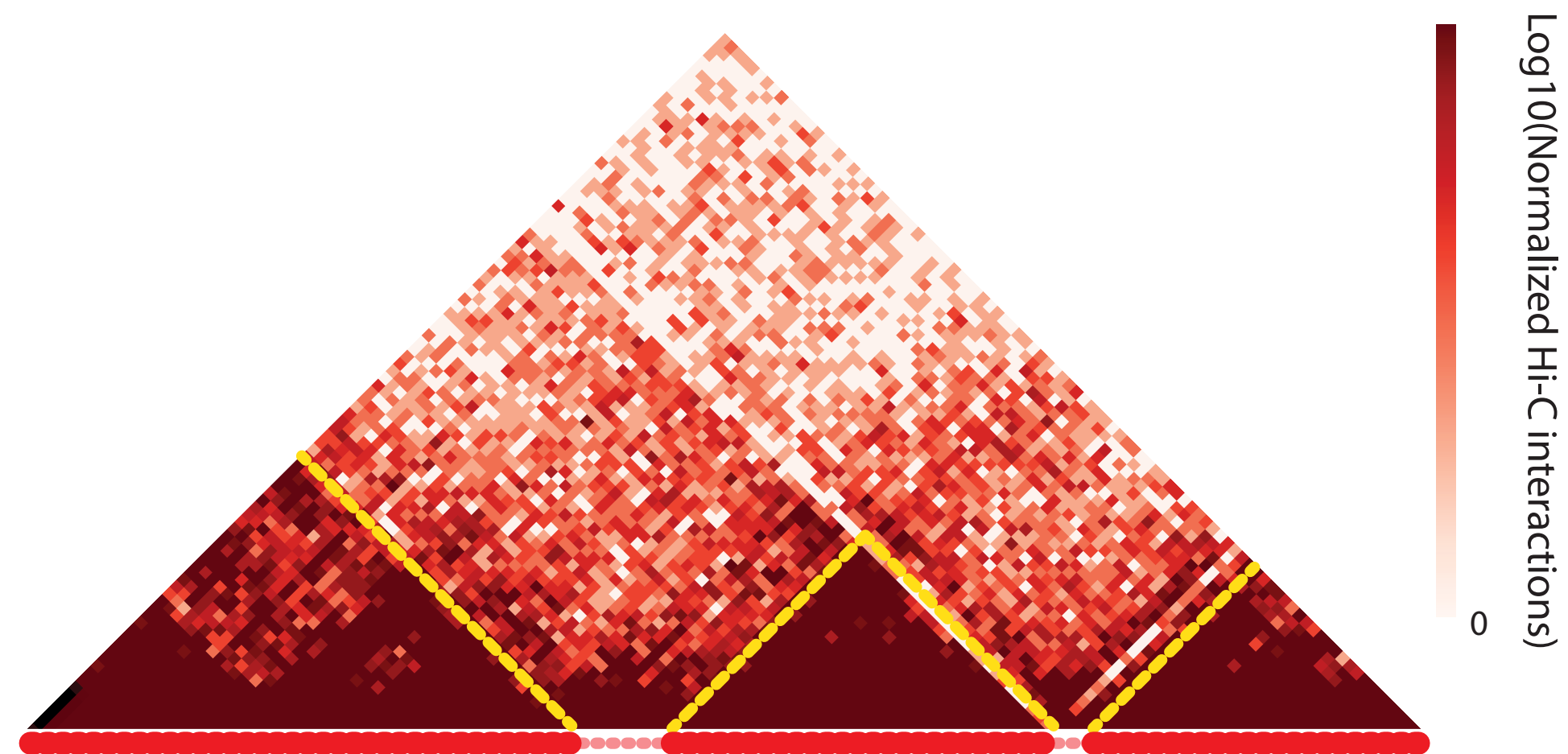
$$CCC = \frac{\sum_{i=1}^M [\rho_i^{EM} - \bar{\rho}^{EM}] [\rho_i^P - \bar{\rho}^P]}{\sqrt{\sum_{i=1}^M [\rho_i^{EM} - \bar{\rho}^{EM}]^2 \sum_{i=1}^M [\rho_i^P - \bar{\rho}^P]^2}}$$





# Increasing resolution

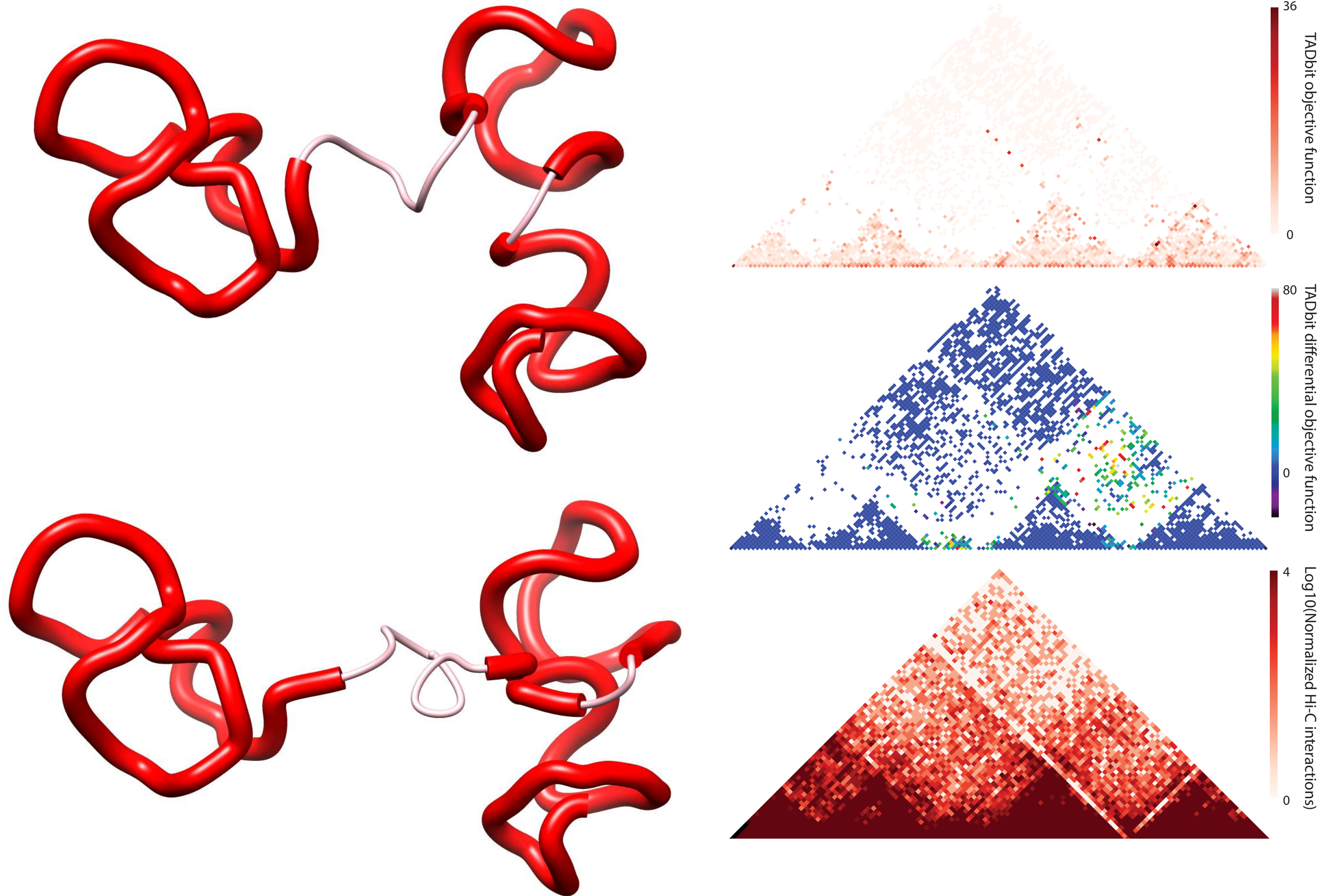
Flexible fitting 3D structures based on Hi-C data





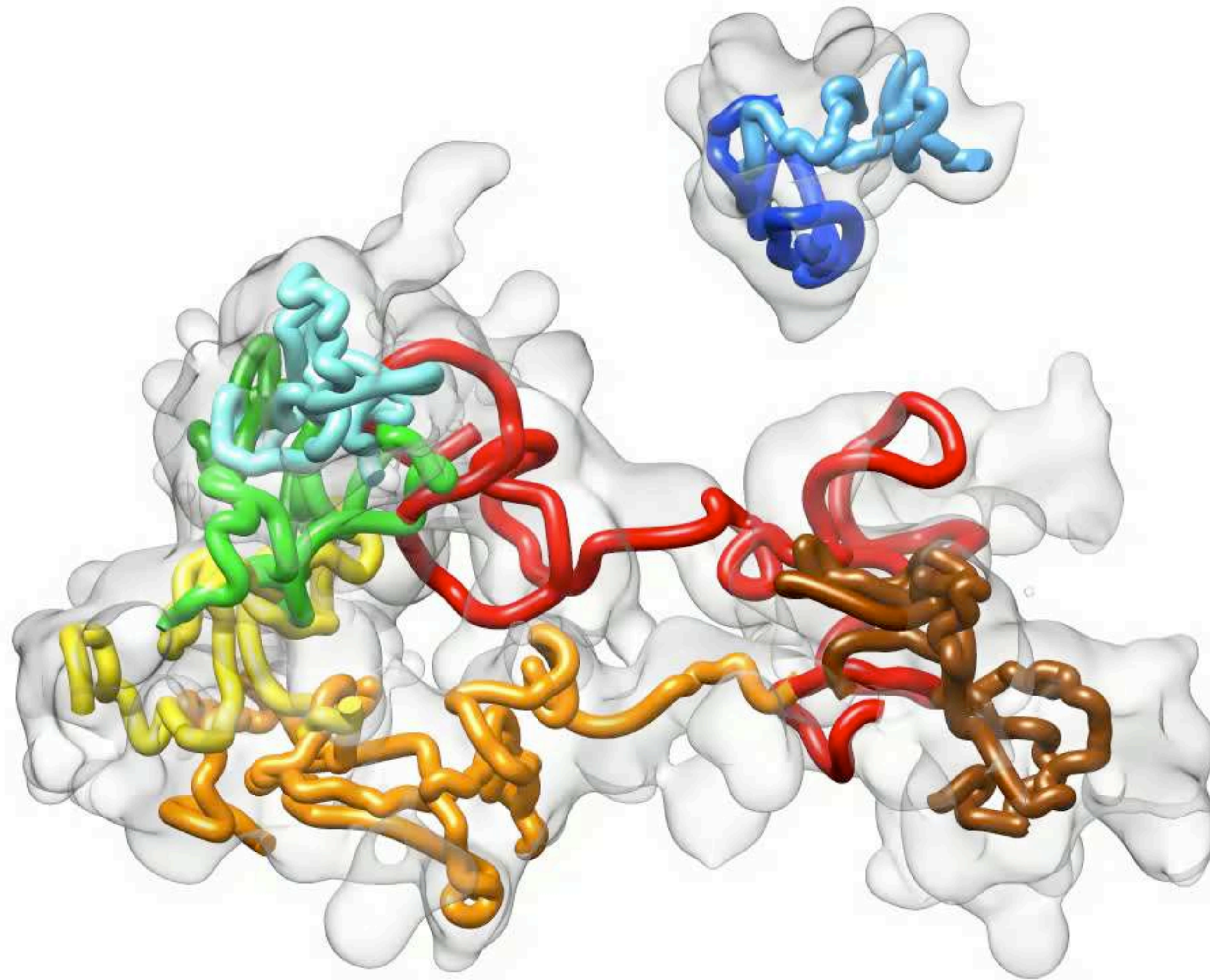
# Increasing resolution

Flexible fitting 3D structures based on Hi-C data





# Chromosome walking path @10Kb resolution





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

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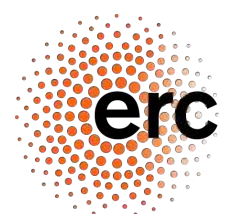
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Paula Soler

Aleksandra Sparavier



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