



Ministry of Science and Higher Education of the Russian Federation
Institute of Gene Biology Russian Academy of Sciences

# Single-nucleus Hi-C analysis of the Drosophila genome folding

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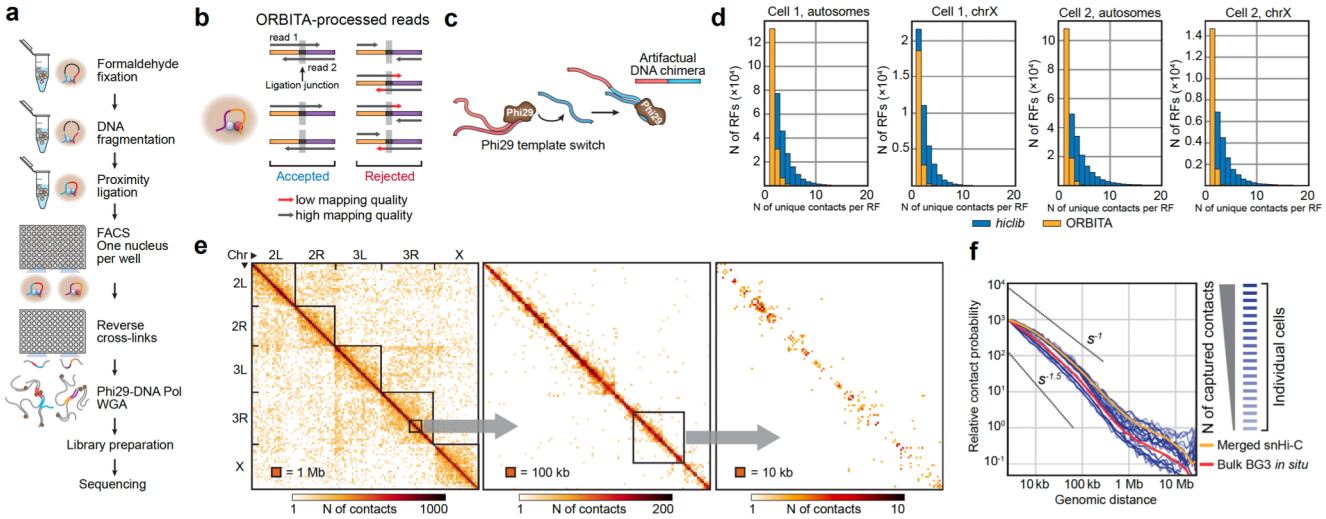
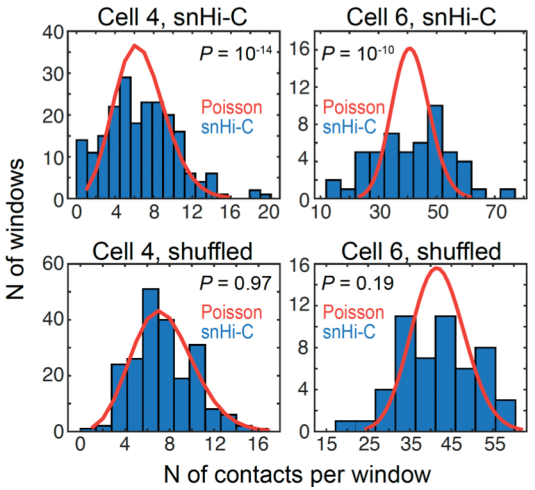
# ORBITA-processed Hi-C data from single *Drosophila* nuclei



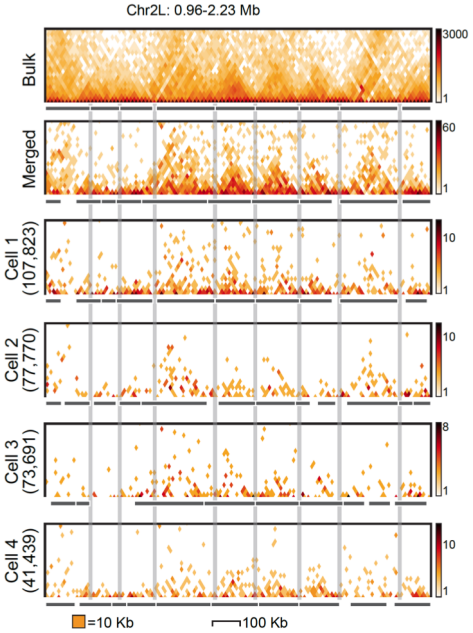

**a** Single-nucleus Hi-C protocol scheme.
**b** Workflow of ORBITA function for detection of unique Hi-C contacts. ORBITA processes only chimeric reads with good mapping quality containing ligation junction marked by the cleavage site for restriction enzyme used for the snHi-C map construction.
**c** Scheme of an artefactual DNA chimera formation by Phi29-DNA-polymerase.
**d** Number of unique contacts per restriction fragment (RF) captured by ORBITA (orange) and *hiclib* (blue) for autosomes and the X chromosome.
**e** Visualization of a single-nucleus Hi-C map at 1-Mb, 100-kb, and 10-kb resolution for the cell with 107,823 captured unique contacts.
**f** Dependence of the contact probability $P_c(s)$ on the genomic distance s for single nuclei (shades of blue reflect the number of unique contacts captured in individual nuclei), merged snHi-C data (orange), and bulk *in situ* BG3 Hi-C data (red). Black lines show slopes for $P_c(s) = s^{-1.5}$ and $P_c(s) = s^{-1}$.

# snHi-C datasets in *Drosophila* are not random matrices

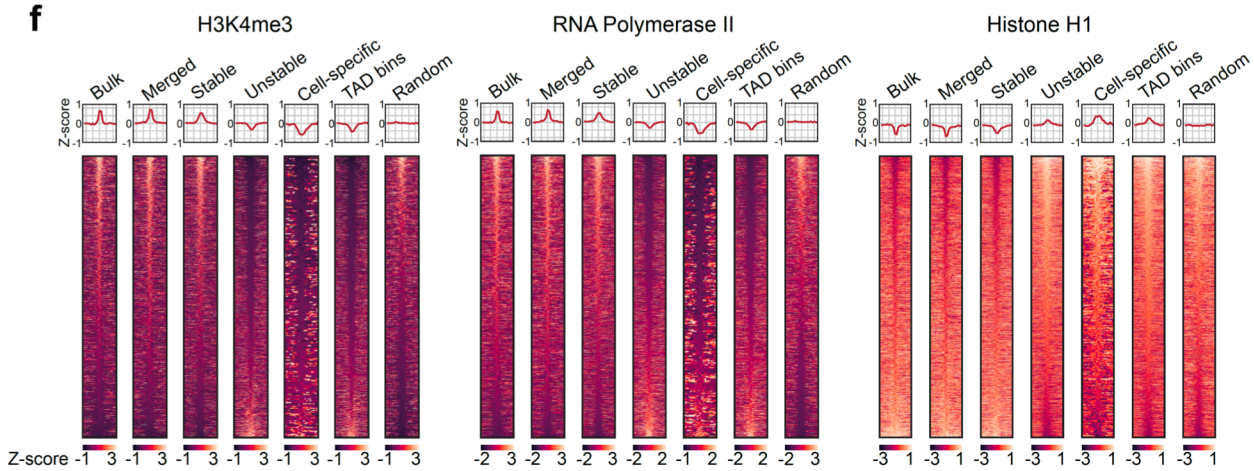



Distributions of the number of contacts in windows of fixed size (100 kb for the Cell 4, and 400 kb for the Cell 6; chr2R) in snHi-C data and shuffled maps for two individual cells (blue bars). The red curve shows the Poisson distribution expected for an entirely random matrix with the same number of contacts.

# Stable TAD boundaries are defined by high level of active epigenetic marks

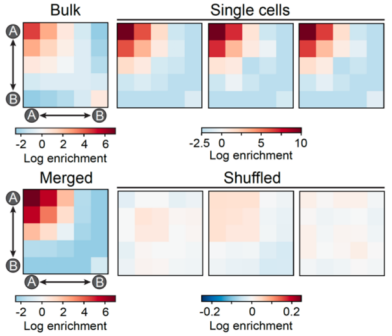



Example of a genomic region on Chromosome 2L with a high similarity of TAD profiles (black rectangles) in individual cells and bulk BG3 *in situ* Hi-C data. Number of unique captured contacts is shown in brackets. Positions of TAD boundaries identified in bulk BG3 *in situ* Hi-C data (top panel) are highlighted with grey lines




Heatmaps of active (H3K4me3, RNA Polymerase II) and inactive (H1 histone) chromatin marks centered at single-cell TAD boundaries from different groups (+/- 100 kb). Bulk – conventional BG3 *in situ* Hi-C; merged – aggregated snHi-C data from all individual cells; stable and unstable – boundaries found in more and in less than 50% of cells, respectively; cell-specific – boundaries identified in any one individual cell; TAD bins – genomic bins from TAD interior; random – randomly selected genomic bins.

## Compartments in individual cells



# Our team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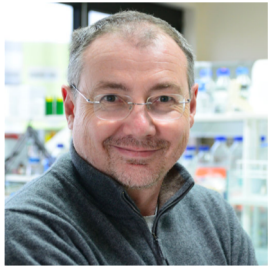
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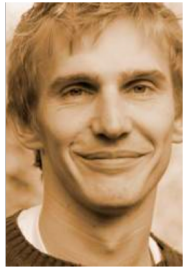
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