

## **Holocentric *Bombyx mori* chromosomes segregate into three genome-wide compartments**

Gil Jr., J.<sup>1</sup>, Rosin, L.<sup>2</sup>, Chowdhury, N.<sup>3</sup>, **Navarrete, E.**<sup>3</sup>, Abraham, S.<sup>3</sup>, Cornilleau, G.<sup>1</sup>, Lei, E.<sup>4</sup>, Mozziconacci, J.<sup>5</sup>, Mirny, L.<sup>1,3</sup>, Muller, H.<sup>1\*</sup>, Drinnenberg, I.<sup>1\*</sup>

Affiliations:

1 Institut Curie, PSL University, Sorbonne Université, CNRS, Nuclear Dynamics, 75005 Paris, France

2 Unit on Chromosome Dynamics, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD 20892 USA

3 Institute of Medical Engineering and Science, Massachusetts Institute of Technology, Cambridge, MA 02139 USA

4 Nuclear Organization and Gene Expression Section; Laboratory of Biochemistry and Genetics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892 USA

5 Structure and Instability of Genomes Lab, UMR 7196, Museum National d'Histoire Naturelle, Paris, France.

The 3D genome contains a hierarchy of structures: chromosome territories, compartmentalization of active and inactive chromatin, and topologically associating domains (TADs). While the *B. mori*'s genome architecture encompasses all three, it is distinct in its implementation of these classical features.

Most prominently, *B. mori* chromosomes segregate into three compartments. In addition to previously described active (A) and inactive (B) compartments, Hi-C maps reveal a third compartment that we term X. Unlike all previously documented compartments, X compartments do not prefer to interact with other X compartments. By modeling *B. mori* compartments as a block copolymer, we find compartment affinities alone cannot form X compartments.

Unlike most of the genome, X compartments also contain TADs. Loop extrusion, which forms TADs, weakens compartmentalization through active mixing of chromatin. Though loop extrusion is insufficient to form X compartments on its own, we find that adding extrusion to a three-compartment model successfully forms X compartments.

Finally, we find local compaction is associated with the histone mark H4K20me1. This mark has previously been linked to condensin activity in other organisms, hinting that *B. mori* TADs may be condensin, rather than cohesin-mediated.

Taken together, our modeling and analyses demonstrate how unique chromosome folding structures can arise through conserved biophysical mechanisms.