Active chromatin regions are sufficient to define borders of topologically associated domains in D. melanogaster interphase chromosomes

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In *Drosophila*, interphase chromosomes are organized in topologically associated domains (TADs) within which chromatin-chromatin interactions are frequent, while interactions across domain borders are rare [1]. TAD positions on chromosomes appear to be conservative between cells of different lineages, and even between animal species [2]. However, molecular mechanisms underlying partitioning of chromosomes in TADs are poorly understood. Insulator elements have been proposed [1-3] to play a key role in definition of TAD borders but recently experimental evidences against this hypothesis have appeared [4]. Here we used Hi-C method [5] to map TADs in four drosophila cell lines of different origin. The cell lines share up to 80% TAD positions, while cell type specific TAD borders correlate with transcription changes between cell lines. TADs appear to be self-organizing condensed chromatin domains depleted in active chromatin marks (Fig. 1A). Active chromatin regions that cannot be organized in compact structures separate TADs, being sufficient to establish TAD borders without contribution of insulator proteins, such as Su(Hw) or CTCF (Fig. 1B).

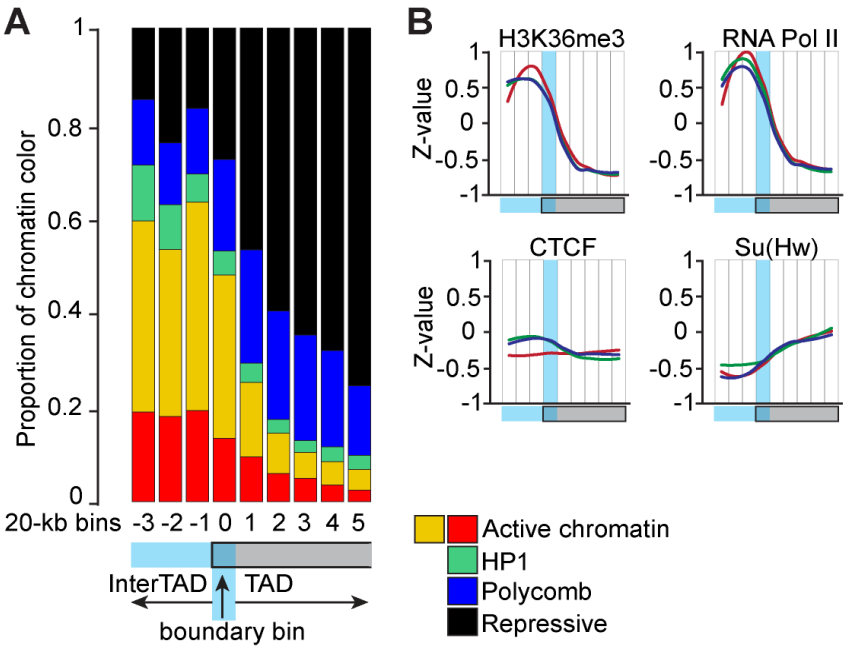

Fig. 1. Distribution of active chromatin marks and insulator protein sites in 20 kb bins surrounding aligned TAD boundaries. A. Proportion of chromatin colors in TADs and inter-TADs calculated as an average proportion of chromatin colors (as annotated in [6]) in aligned bins. B. Enrichment of chromatin marks and insulator protein binding sites in TADs and inter-TADs. The enrichment was calculated as the median proportion of ChIP-seq peaks (provided in modENCODE database [7]) in aligned bins, multiplied by the peak scores, and Z-transformed to make different chromatin features comparable. Blue lines correspond to Kc167 cells, green lines – to ML-DmBG3 cells, and red lines – to S2-DRSC cells.

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