

Dynamics of chromatin compactization in embryogenesis of *Drosophila melanogaster*



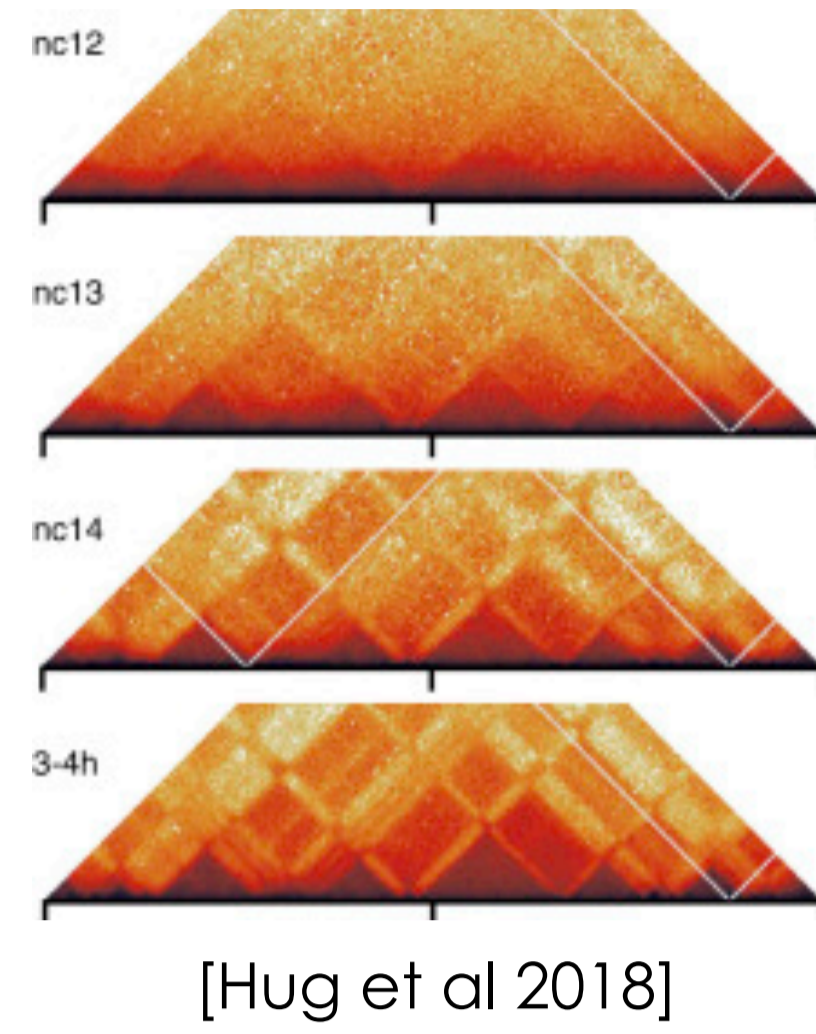
Динамика компактизации хроматина в эмбриогенезе *Drosophila melanogaster*

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Abstract

Хроматин - это ДНК-белковый комплекс. Укладка хроматина в домены связана с регуляцией экспрессии генов. Формирование доменов происходит в раннем эмбриогенезе, но динамика этого процесса мало изучена. В нашей работе мы изучали изменение укладки хроматина по четырем временным точкам в раннем эмбриональном развитии мухи *Drosophila melanogaster*.



[Hug et al 2018]

Chromatin is a DNA-protein complex. Folding of chromatin into domains (TADs) has been linked to the regulation of gene expression. Formation of domains occurs in early embryogenesis, but the dynamics of this process is poorly understood. Here, we have analysed the patterns of chromatin domains formation over four time points during early embryonic development of *Drosophila melanogaster*.

Results

Figure 1. General information on domain classes. (A) Domains clustered by their folding patterns. (B) Fragment of Hi-C map with several domains colored by class. (C) Gene density, lengths and number of genes in domains from different classes.

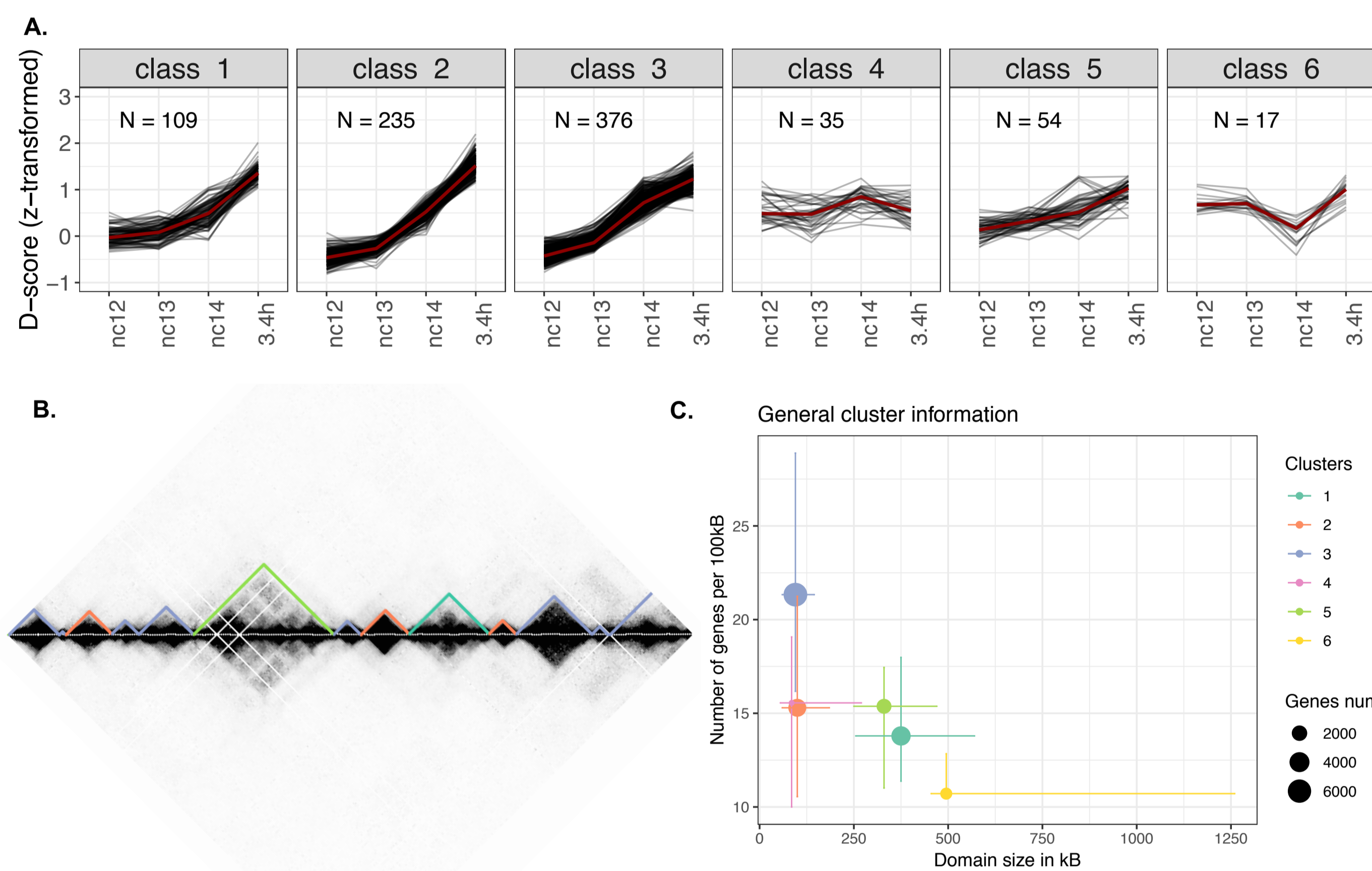
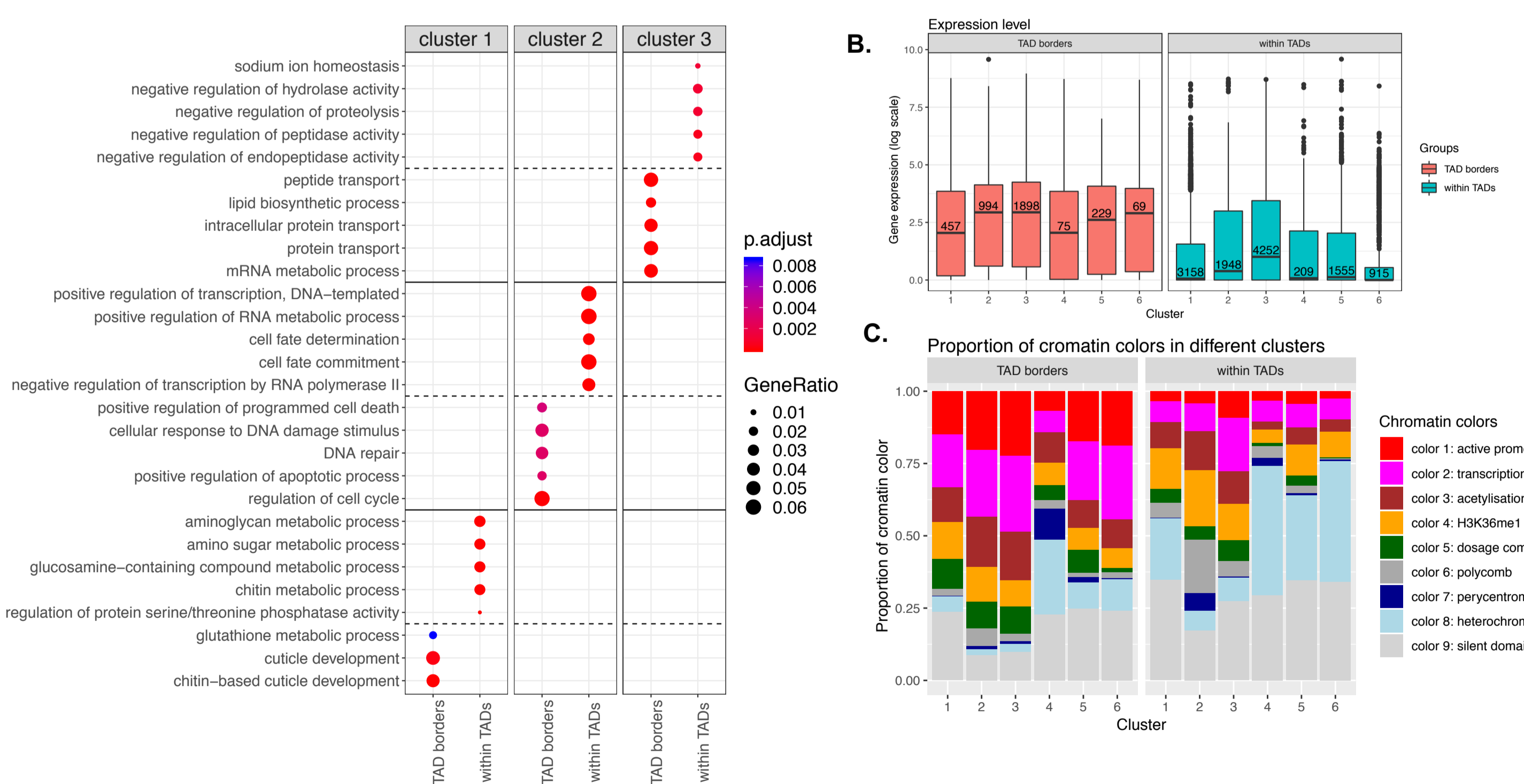


Figure 2. Functional annotations of domain classes. (A) Gene ontology enrichment of classes 1-3. (B) Expression levels of genes at TAD boundaries (less than 10 kb to the boundary) and within TADs. (C) Distribution of chromatin colors in domains of different classes at domain boundaries and within domains.



The Fisher tests: We performed Fisher tests on 275 transcription factors to check whether any TFs are enriched at domain boundaries of particular classes. No TFs showed significant odds ratios after the Benjamini-Hochberg correction.

Conclusions

- TADs form distinct clusters by their folding patterns during embryogenesis
- Genes in domains of different classes have different functional enrichment
- Domains of different classes have different chromatin color enrichments.
- Transcription factors behave similarly on domain boundaries, though there are differences in the binding profiles within domains

Questions

- Do different domains have different folding patterns during embryogenesis?
- Do domains with similar dynamics co-localize?
- For domains of different classes:
 - Does the gene functional enrichment differ?
 - Does the activity of transcription factors differ at TAD boundaries and within TADs?
 - Is there any difference in chromatin colors annotation?

Methods

- Pre-processing: TAD calling (Armatus from the lavaburst Python package), domain score and insulation score calculations
- Clustering
- Gene ontology enrichment analysis, functional annotations
- Distribution of genes and transcription factor binding sites as related to TAD profiles
- Statistics: the Fisher test, the Chi-squared test
- Hilbert curves

Figure 3. Distribution of genes and transcription factor binding sites as related to TAD profiles. (A) Housekeeping and non-housekeeping genes; (B) Ubiquitous transcription factors; (C) Tissue-specific transcription factors.

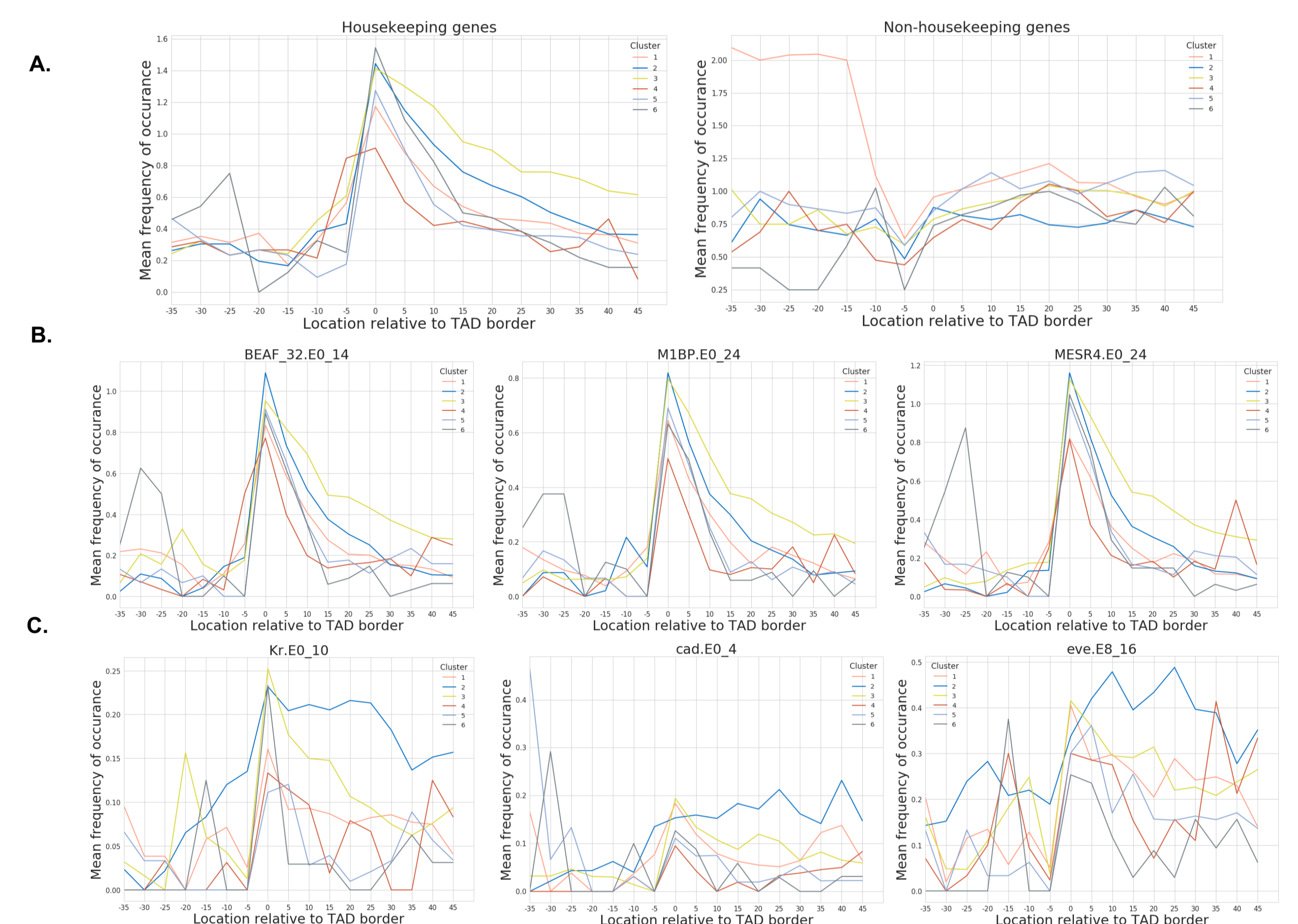
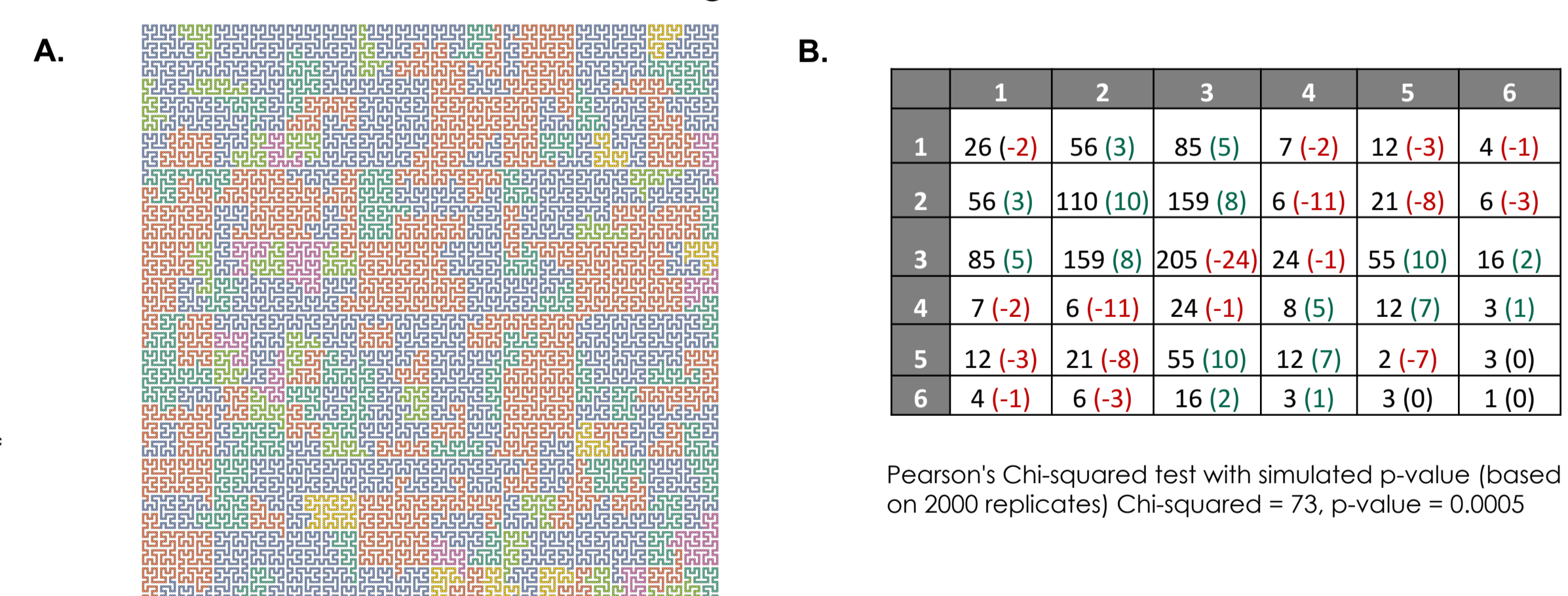


Figure 4. Co-localization of domains of different classes. (A) Contingency matrix of domain neighborhoods. Differences between observed and expected values (chi-squared test) are shown in brackets. (B) Chromosome 3 visualized with the Hilbert curve. Colors correspond to classes; color code is the same as in Figure 1C. All domains are resized to the same length.



Pearson's Chi-squared test with simulated p-value (based on 2000 replicates) Chi-squared = 73, p-value = 0.0005

Figure 5. Dynamics of insulation scores as related to TAD profiles. Profiles of insulation score (IS) at the boundaries are different for the classes retrieved by the D-score clustering. Dynamics of IS at the TAD boundaries corresponds to the dynamics of clusters by D-score. Boundaries of TADs are prominent at nc12 for class 4 and 5.

