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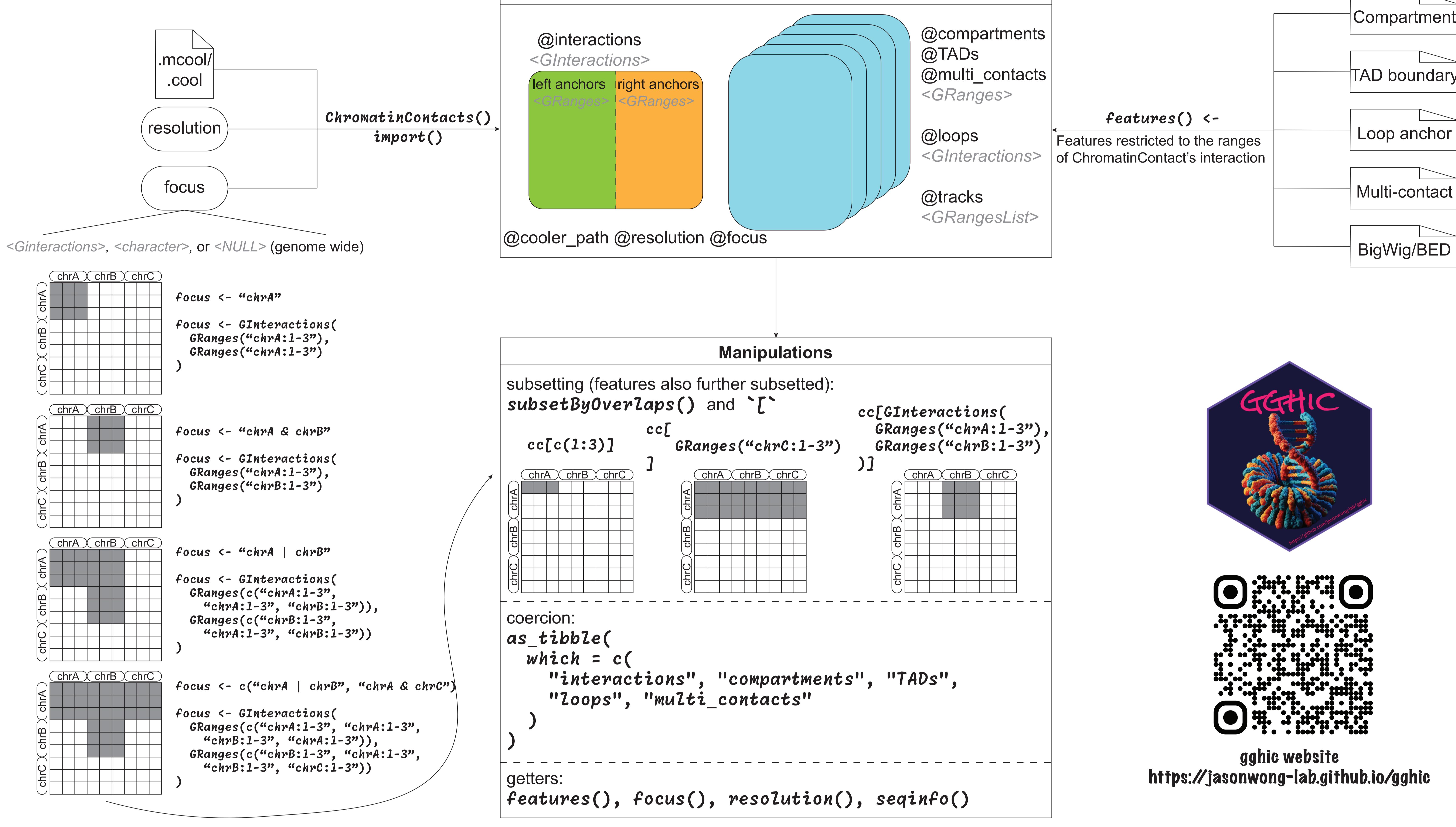
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## 1. INTRODUCTION

**Motivation:** The three-dimensional (3D) organization of the genome plays a critical role in regulating gene expression and maintaining cellular homeostasis. Disruptions in chromatin architecture can lead to aberrant interactions between genomic regions, contributing to the pathogenesis of various diseases, including cancer. Recent advances in chromosome conformation capture technologies, particularly Hi-C and Pore-C, have enabled genome-wide mapping of chromatin interactions at increasingly high resolution. However, visualizing and interpreting these complex datasets remains challenging, especially when integrating multiple data types such as genomic annotations, structural features, inter-chromosomal interactions, and multi-way contacts. There is a pressing need for flexible tools that can generate publication-quality visualizations while supporting both pairwise and multi-way contact data.

**Results:** We present gg hic, an R package that extends the ggplot2 framework to provide intuitive and customizable visualization of 3D genome organization data from experiments of both pairwise and multi-way contacts. The package introduces the ChromatinContacts S4 class for efficient management of genomic interaction data, featuring streamlined data import, flexible region focusing, and integration of genomic features such as compartments, topologically associating domains (TADs), chromatin loops, and multi-contact regions. For Pore-C and other multi-way contact data, gg hic implements hypergraph-based analysis, enabling sophisticated filtering, weighting, and visualization of complex multi-way interaction patterns. gg hic provides specialized geom layers for creating triangular heatmaps of pairwise chromatin contacts, hypergraph plots showing multi-way interactions, and rich annotations including chromosome ideograms, TAD boundaries, loop calls, gene models, genomic signal tracks, and concatemer reads. The package seamlessly supports both intra- and inter-chromosomal interaction visualization across multiple resolutions. We demonstrate gg hic's capabilities using acute lymphoblastic leukemia Pore-C multi-way contact data, generating publication-ready figures that reveal translocation breakpoints and higher-order chromatin organization. By combining powerful 3D genome analysis with ggplot2's expressive and familiar syntax, gg hic makes the exploration and communication of chromatin architecture data—from simple pairwise interactions to complex multi-way contacts—both accessible and reproducible.

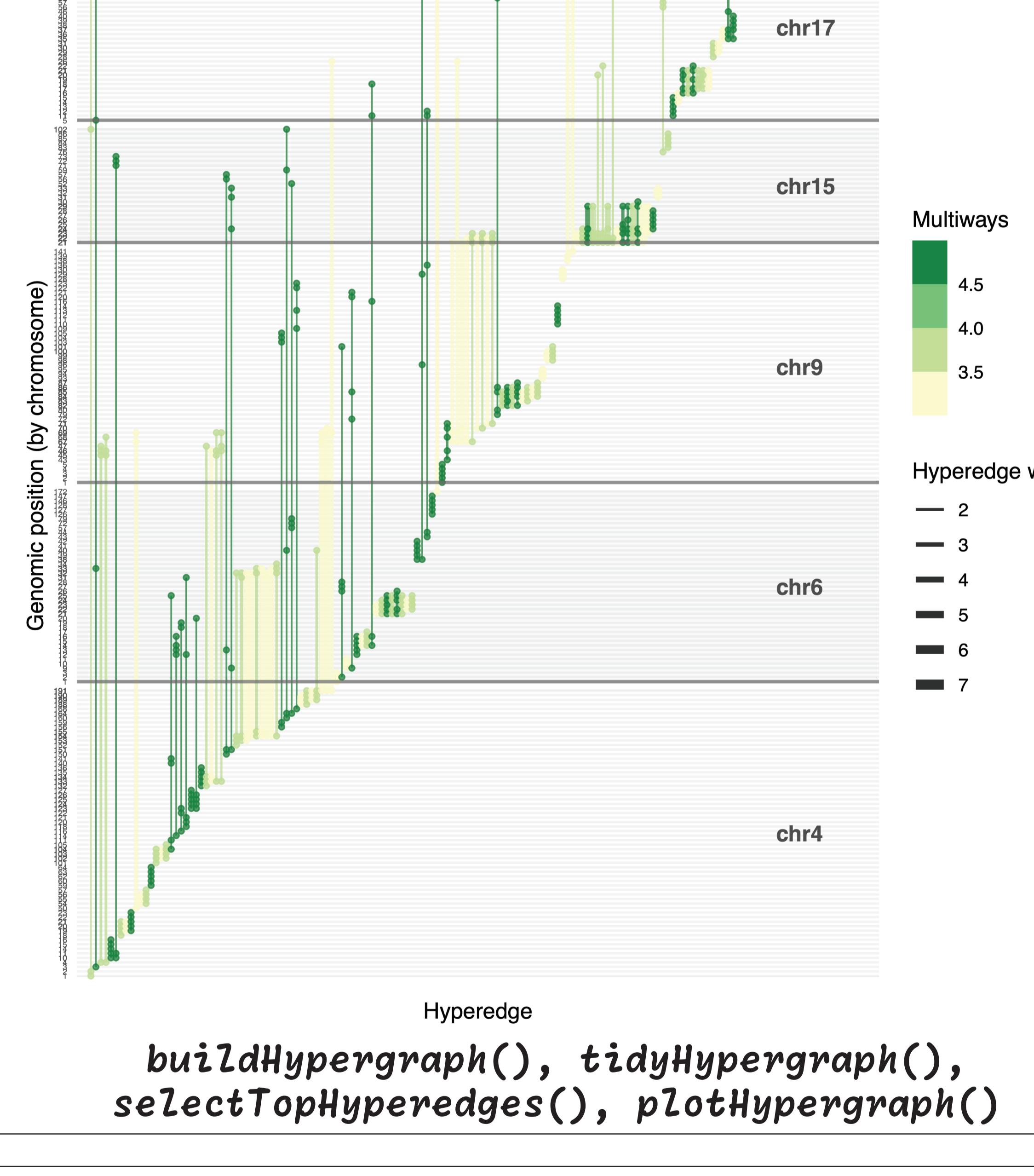
## 2. MANIPULATING DATA OF CHROMATIN CONTACTS IN R



## 3. VISUALIZATION OF 3D GENOME STRUCTURES USING GGHIC

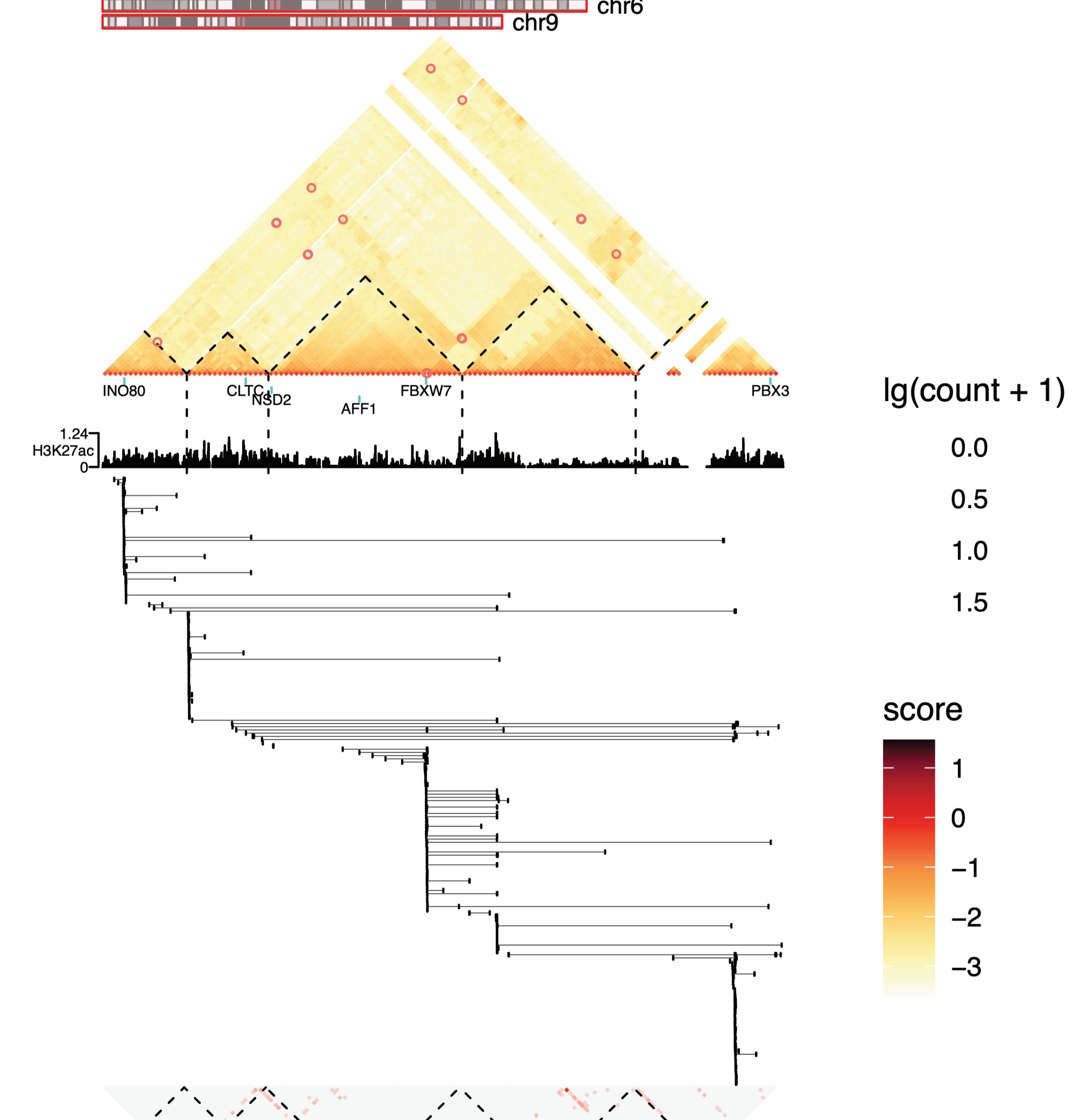
### A. Multi-way Chromatin Contact Hypergraph

Hypergraph analysis of Pore-C data shows reads with  $\geq 3$  contacts across chr4, 6, 9, 15, and 17. Multi-way Contacts: 5 chromosomes (bin size: 1,000,000)



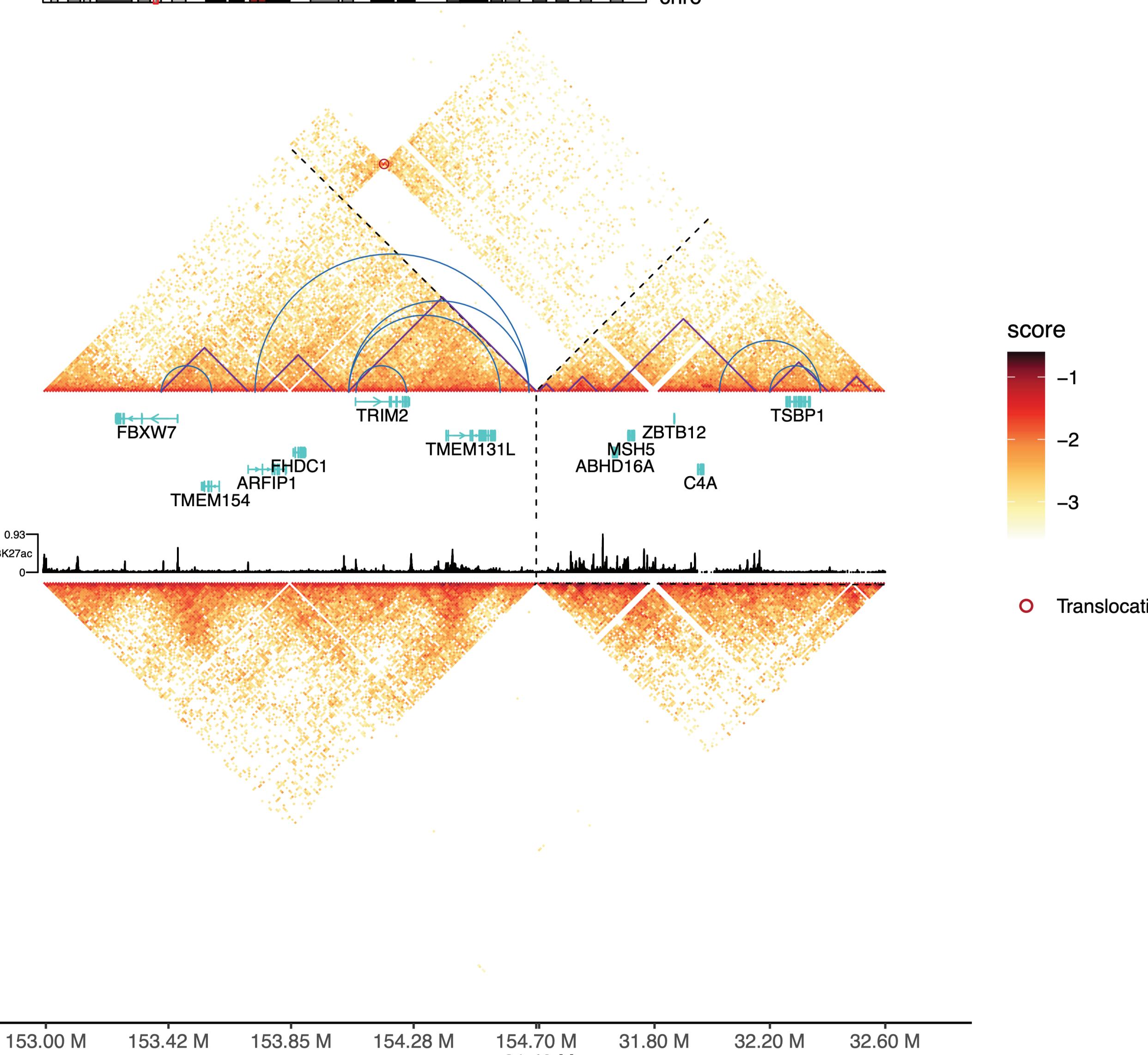
### B. Multi-scale Chromatin Architecture with Pore-C Multi-contacts

Individual Pore-C concatemers show multi-way contacts between five chromosomes, overlaid on the pair-wise contact map with chromatin loops (pink circles), gene annotations, and H3K27ac signal. Bottom heatmap: aggregated Pore-C contact frequency.



### C. Inter-chromosomal Translocation at FBXW7 Locus

Pair-wise contact map shows translocation between chr4:153-154.7 Mb and chr6:31.4-32.6 Mb. Red circle: translocation breakpoint; blue circle: chromatin loops; purple lines: TAD boundaries. Bottom heatmap: normal tissue control.



All figures presented are unprocessed results generated by gg hic, with no post-processing or editing.

## 4. REFERENCES

- Jiang, M., Jing, D. & Wong, J. W. gg hic: A Versatile R Package for Exploring and Visualizing 3D Genome Organization. *arXiv preprint arXiv:2412.03005* (2024).
- Serizay, J., Matthey-Doret, C., Bignaud, A., Baudry, L. & Koszul, R. Orchestrating chromosome conformation capture analysis with Bioconductor. *Nat Commun* **15**, 1072 (2024). <https://doi.org/10.1038/s41467-024-44761-x>
- Dekker, J. et al. The 4D nucleome project. *Nature* **549**, 219-226 (2017). <https://doi.org/10.1038/nature23884>