

Identifying Statistically Significant Frequent Single-cell Inter-chromosomal Interactions with Networks

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Abstract

Single-cell Chromatin Conformation Capture with High-throughput Sequencing (scHi-C) enables scientists to interrogate genome-wide chromatin interactions at single-cell resolution, which plays important roles in gene expression regulation, DNA replication and repair etc. With the advent of the popularity of this experimental approach, developing computational methods to unravel the patterns or mechanisms behind the data becomes critical. To the best of our knowledge, existing computational methods focus on the intra-chromosomal interactions and ignore the inter-chromosomal interactions because of many challenges, for example, low sequencing depth and signal-to-noise ratio, which may miss the opportunity for new discoveries. Therefore, we propose to analyze inter-chromosomal interactions by using networks to capture statistically significant frequent inter-chromosomal interactions at single-cell resolution. First of all, we construct an unweighted network for each cell respectively by dividing chromosomes into equal-size bins and connecting two bins with an edge if there is an inter-chromosomal interaction falling into them, then develop a statistical measurement to identify inter-chromosomal interactions frequently appear among these networks. At last, we visualize the identified inter-chromosomal interactions by using Circos [1] and analyze some statistically significant ones by literature review. In addition, to justify the results are robust to the selection of bin sizes and starting loci, we adopt different bin sizes and a sliding window approach. For a given mouse data set, we identify a highly interacted inter-chromosomal hub on the chromosome 11, which is corroborated by previous research [2]. Through the example, we demonstrate that our method can be used to identify statistically significant frequent inter-chromosomal interactions for scHi-C data.

References

- [1] Krzywinski, M. et al. Circos: An Information Aesthetic for Comparative Genomics. *Genome Res* 19:1639-1645, 2009.
- [2] Kaufmann, Stefanie, et al. Inter-chromosomal contact networks provide insights into Mammalian chromatin organization. *PloS one* 10.5: e0126125, 2015.