Epigenetics - part 2

Doctoral Program in
Cell, Molecular, Developmental
Biology, and Biophysics

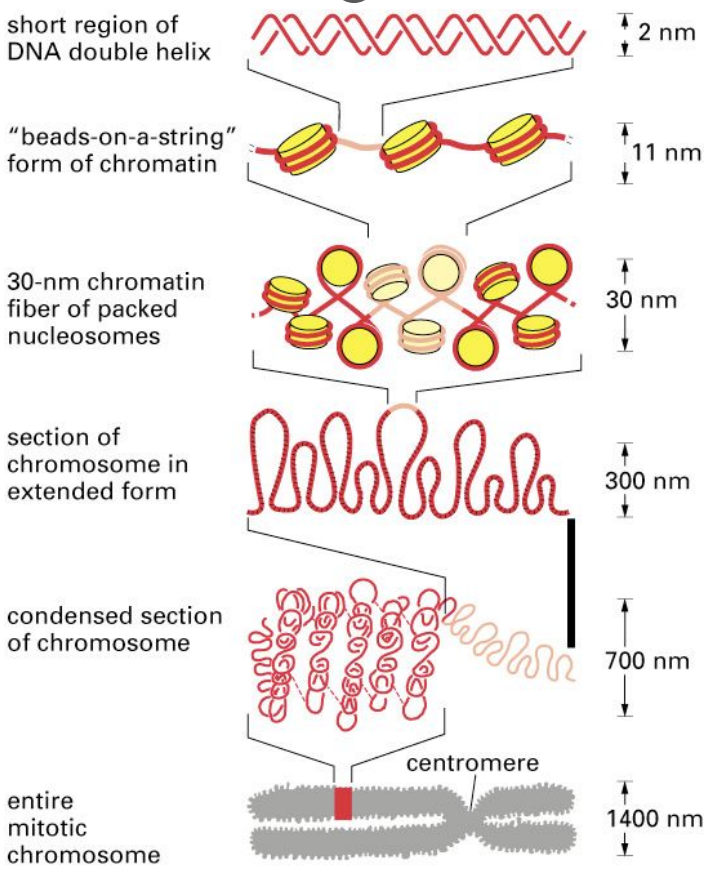
JOHNS HOPKINS
UNIVERSITY

Levels of epigenetic regulation

Chemical modification of histones

Chromatin folding

Non-coding RNAs



Chemical modification of bases

Histone density/ DNA accessibility

Nuclear compartmentalization

Figure 4–55. Molecular Biology of the Cell, 4th Edition.

Levels of epigenetic regulation

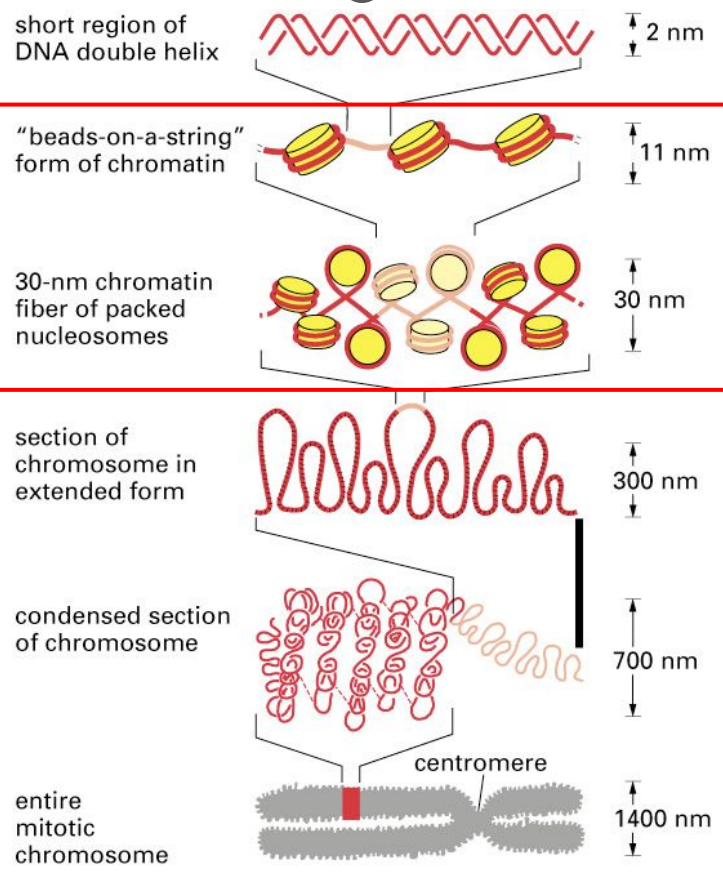
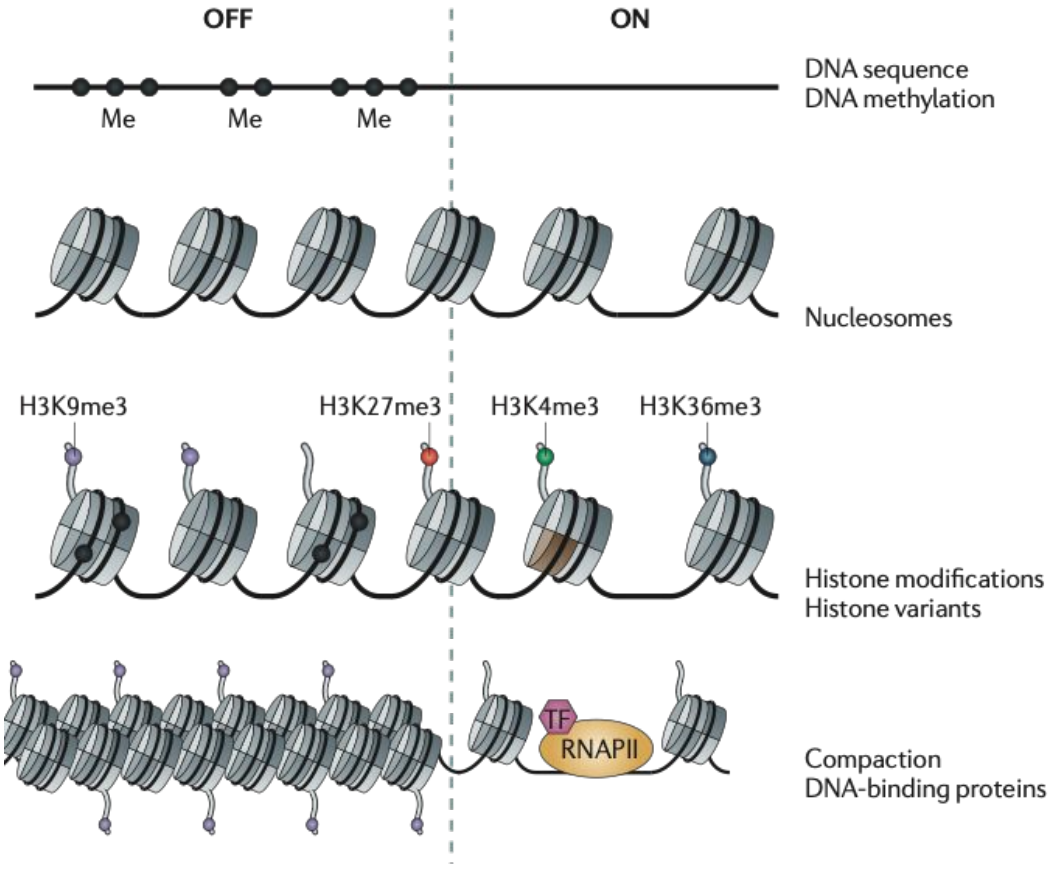


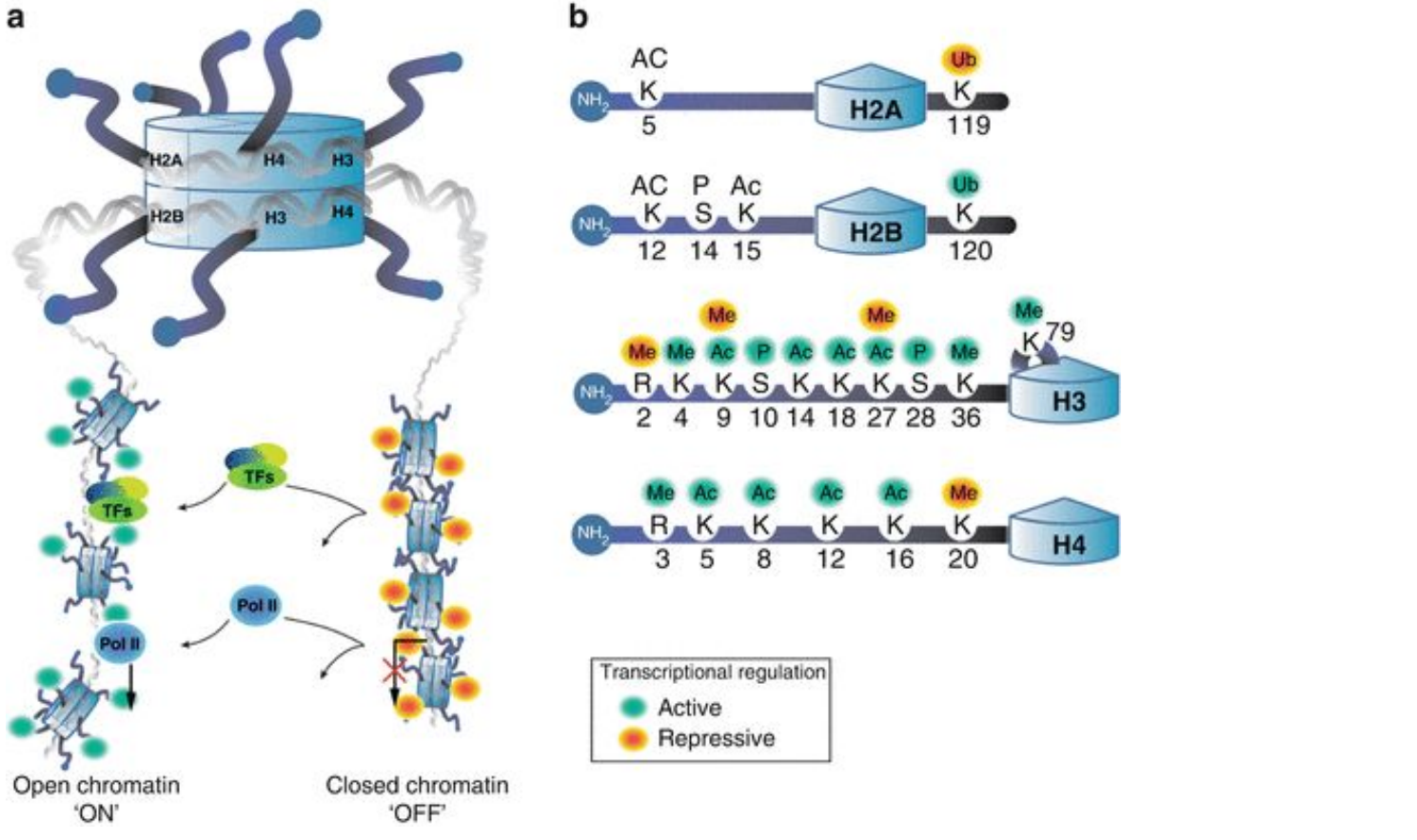
Figure 4–55. Molecular Biology of the Cell, 4th Edition.

Proteins interacting with DNA



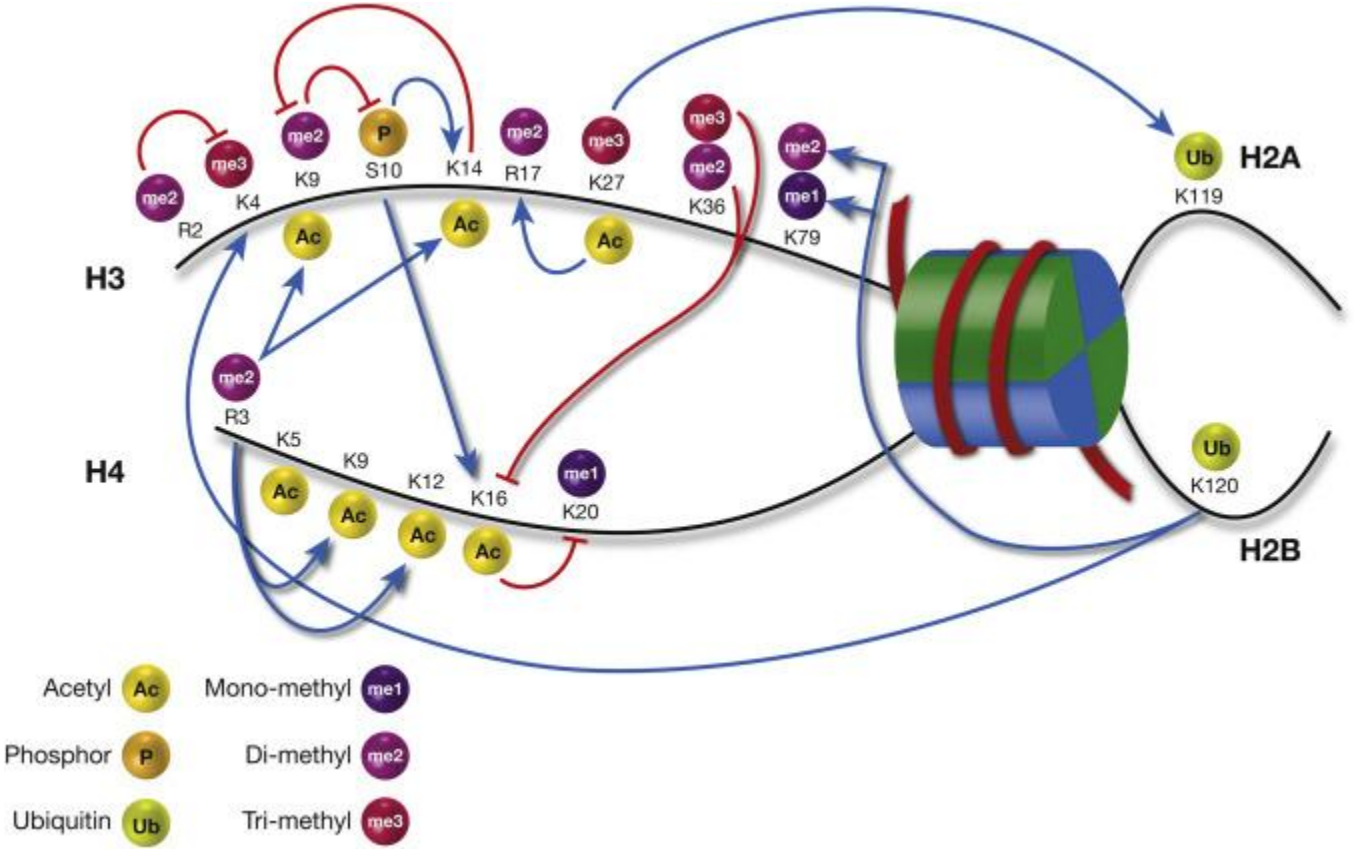
Furey, T. S. (2012). *Nat. Rev. Genet., 13*, 840-852

The Histone Code



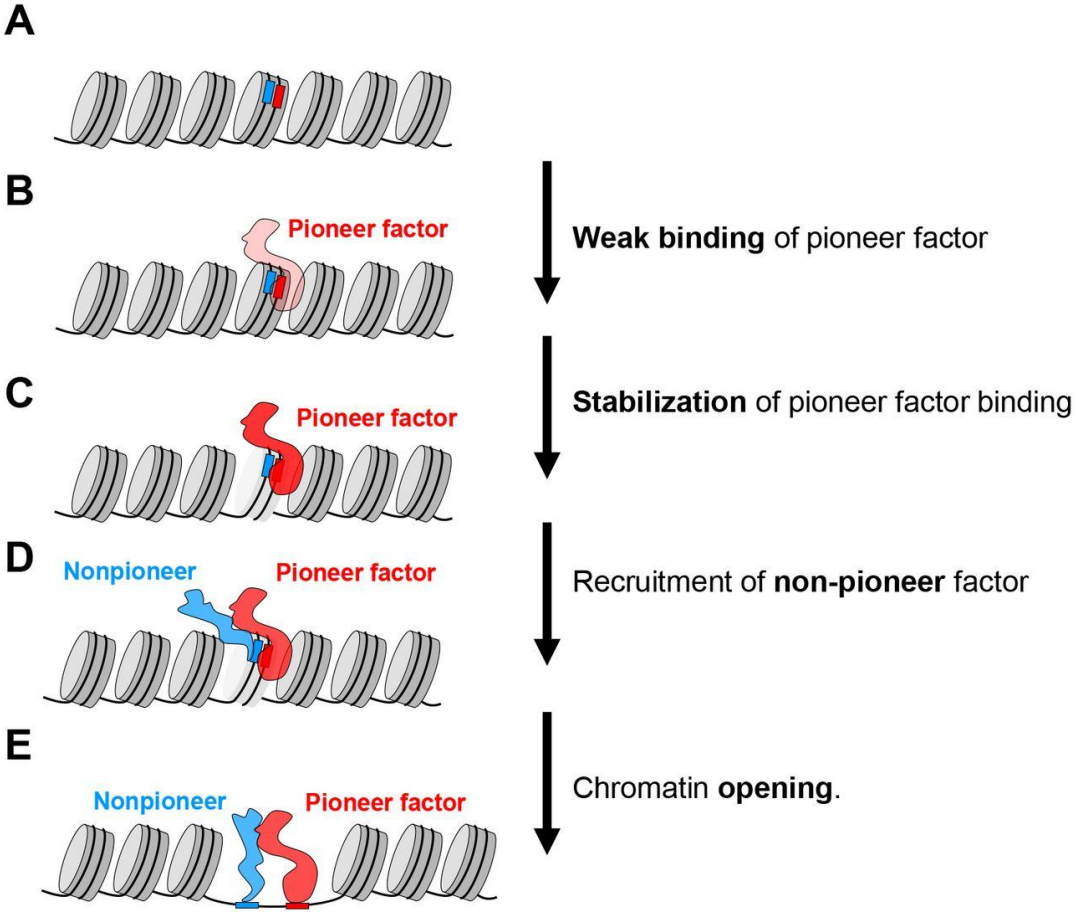
Kim, H.-D., Call, T., Magazu, S., & Ferguson, D. (2017). Drug Addiction and Histone Code Alterations. In R. Delgado-Morales (Ed.), *Neuroepigenomics in Aging and Disease* (pp. 127–143). Springer International Publishing.

Cross-talk between histone modifications



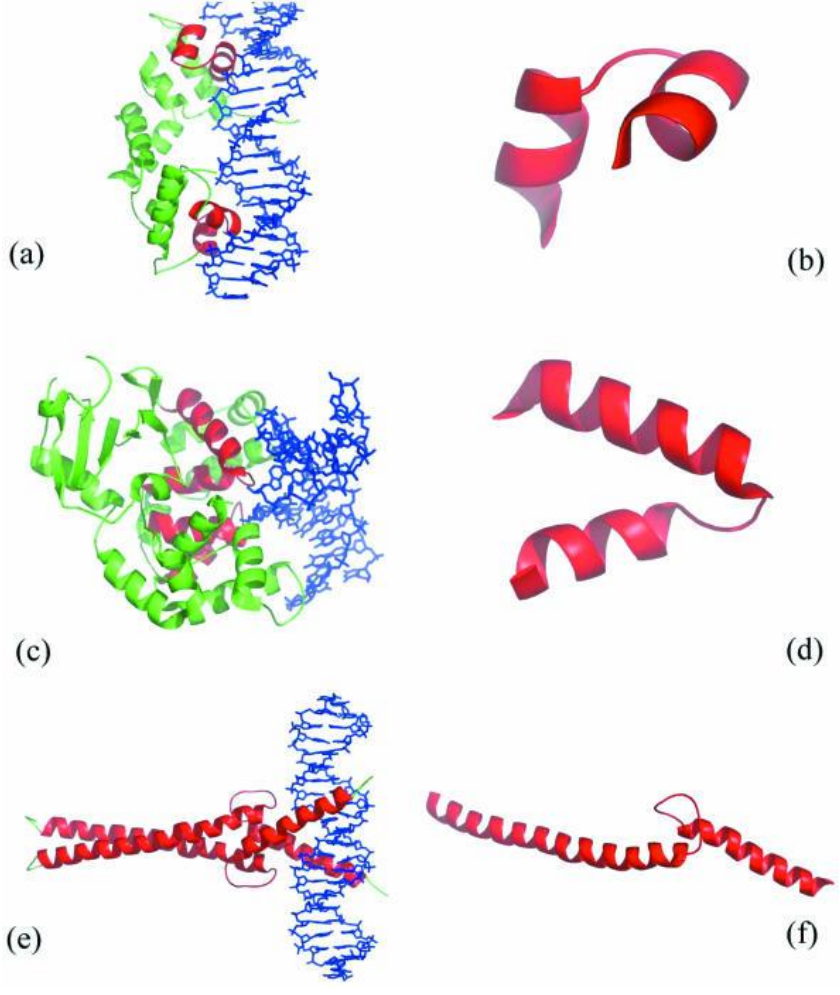
Simonet, N. G., Rasti, G., & Vaquero, A. (2016). Chapter 21 - The Histone Code and Disease: Posttranslational Modifications as Potential Prognostic Factors for Clinical Diagnosis. In J. L. García-Giménez (Ed.), *Epigenetic Biomarkers and Diagnostics* (pp. 417–445). Academic Press.

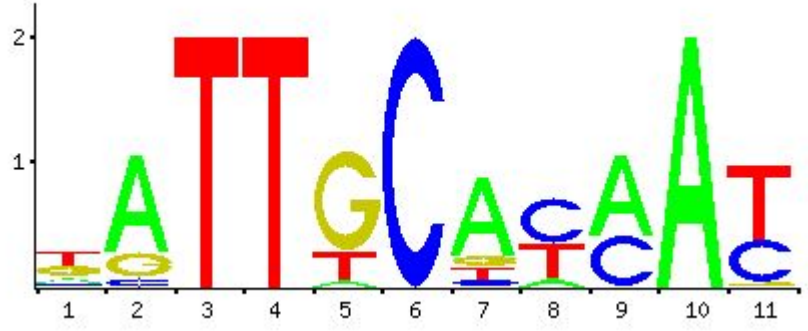
Transcription factor binding



Mayran, A., Sochodolsky, K., Khetchoumian, K., Harris, J., Gauthier, Y., Bemmo, A., Balsalobre, A., & Drouin, J. (2018). Pioneer and nonpioneer factor cooperation drives lineage specific chromatin opening. In *bioRxiv* (p. 472647). https://doi.org/10.1101/472647

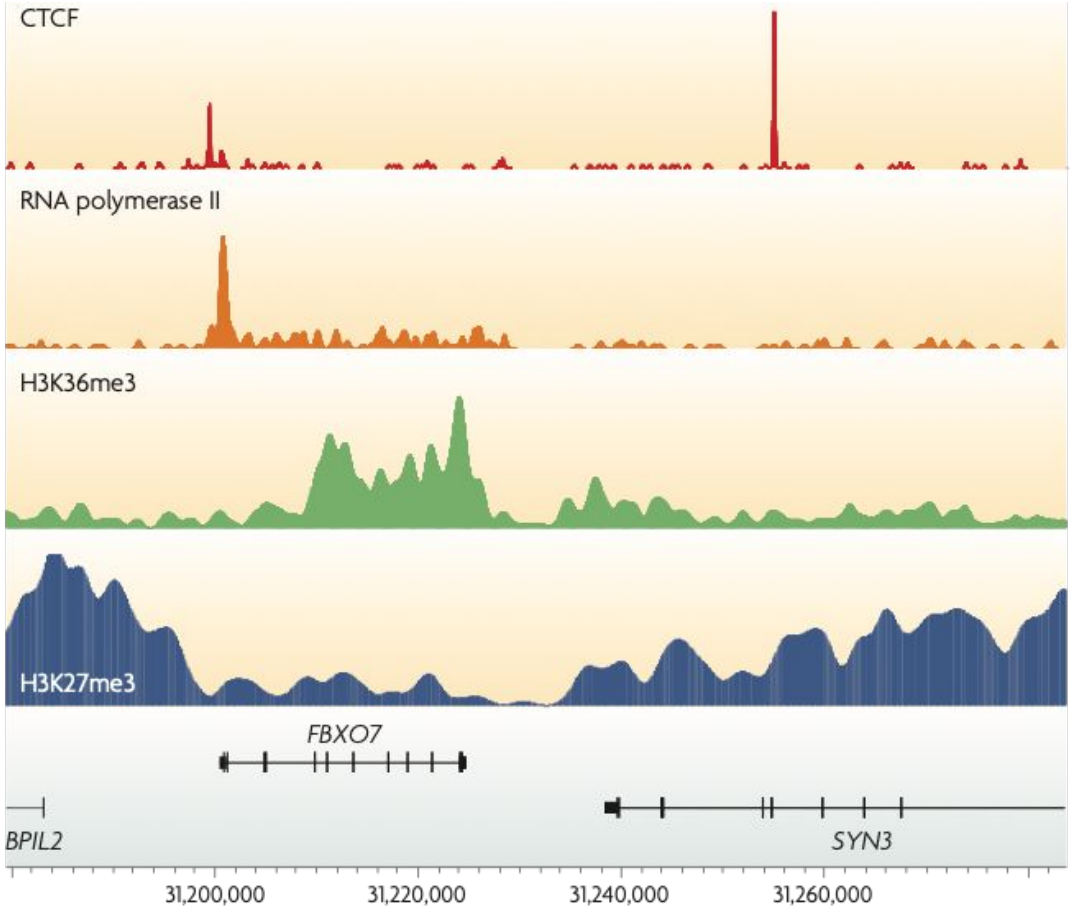
Binding motifs





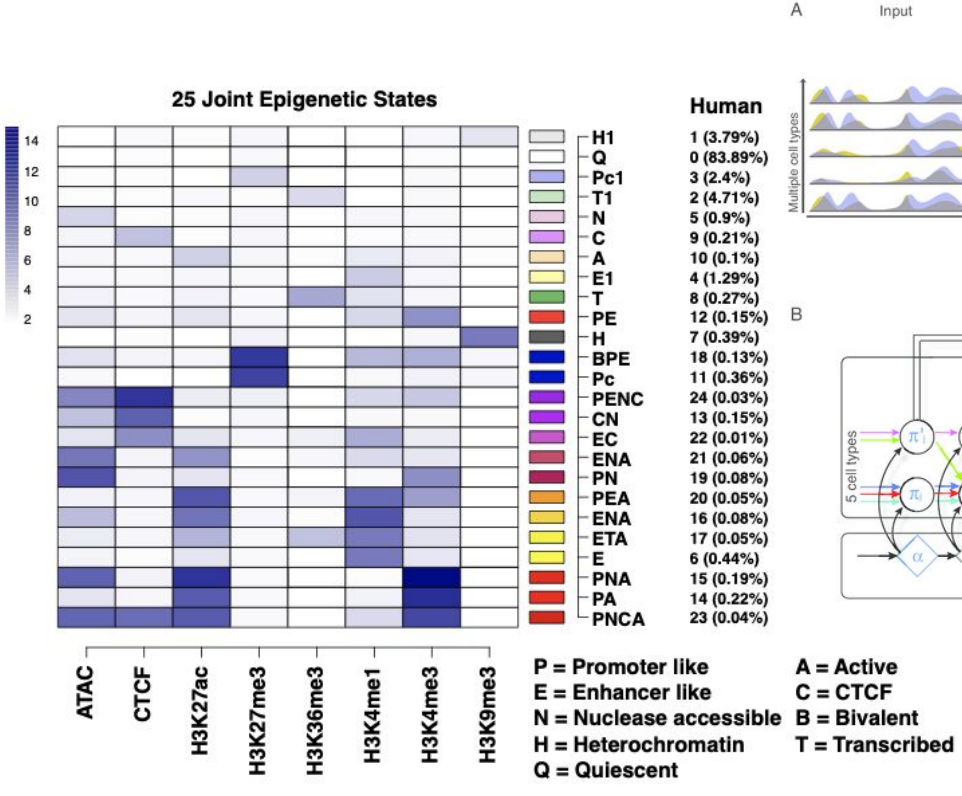
Shanahan, H. P., Garcia, M. A., Jones, S., & Thornton, J. M. (2004). Identifying DNA-binding proteins using structural motifs and the electrostatic potential. *Nucleic Acids Research*, *32*(16), 4732–4741.

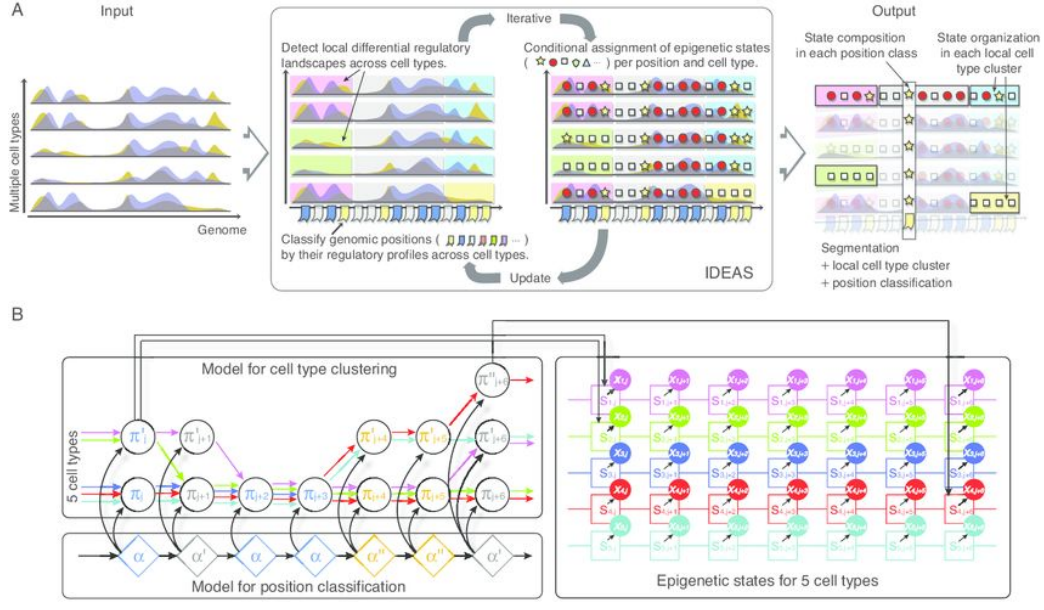
Coordination of features



Park, P. J. (2009). *Nat. Rev. Genet*, *10*, 669-680.

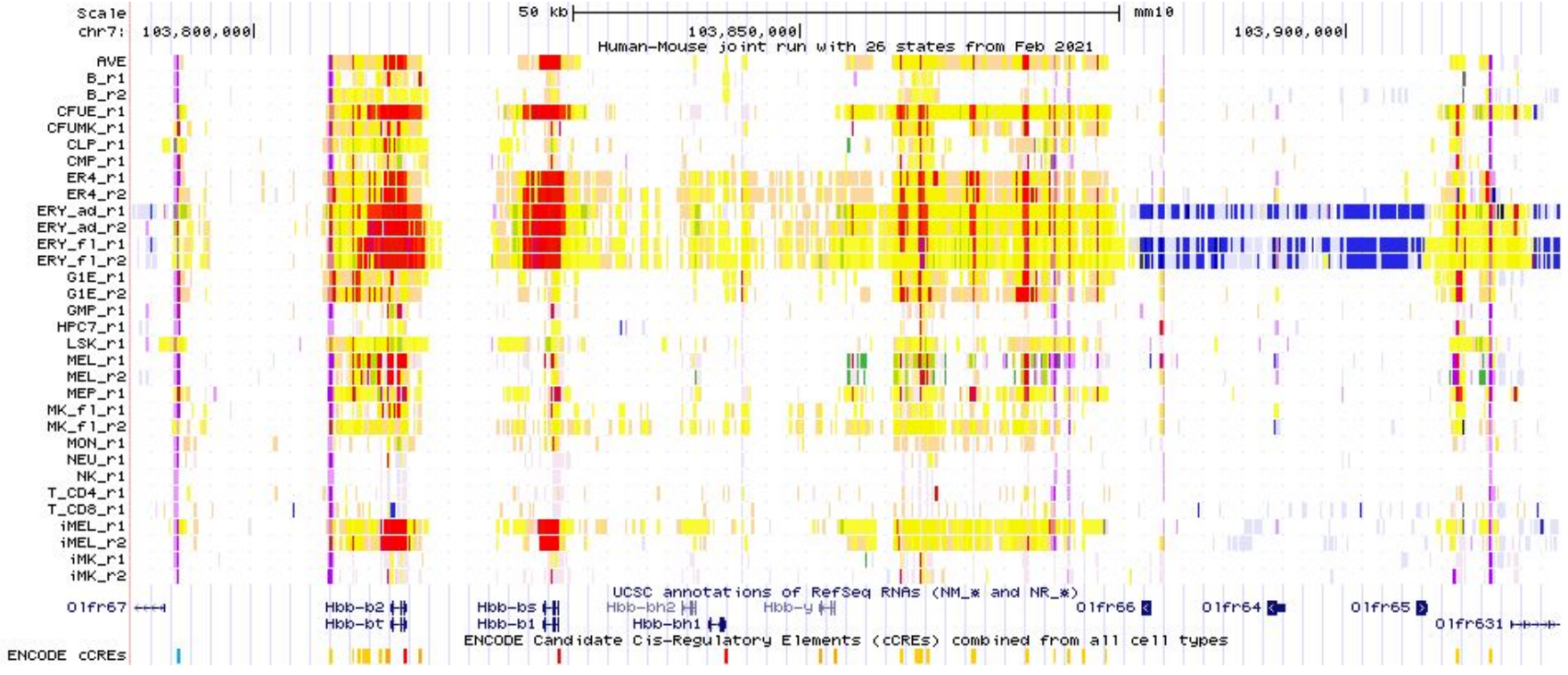
Epigenetic segmentation





Zhang, Y., An, L., Yue, F., & Hardison, R. C. (2016). Jointly characterizing epigenetic dynamics across multiple human cell types. *Nucleic Acids Research*, *44*(14), 6721–6731.

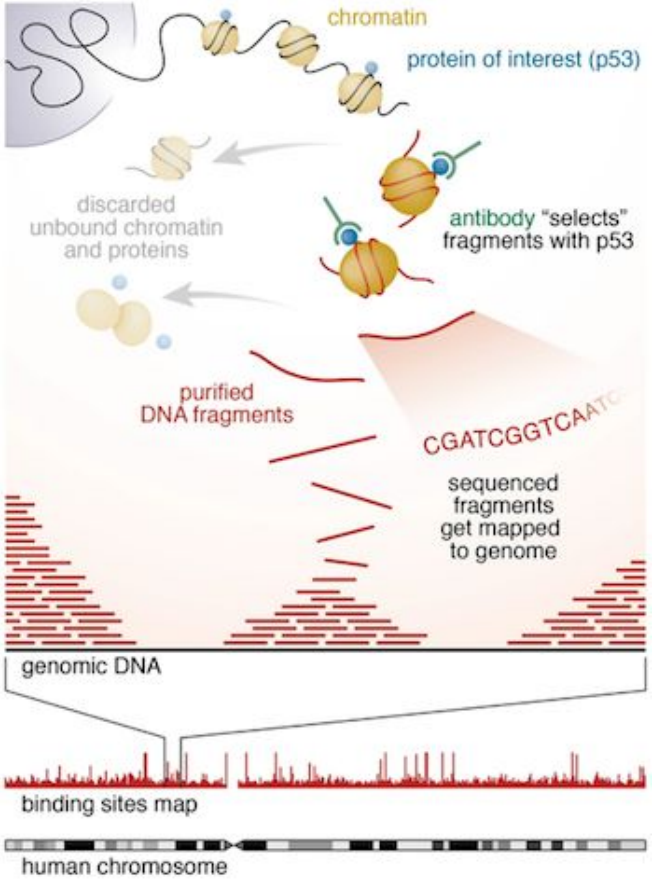
Tissue-specific expression



ChIP-seq, DNASE-seq, ATAC-seq

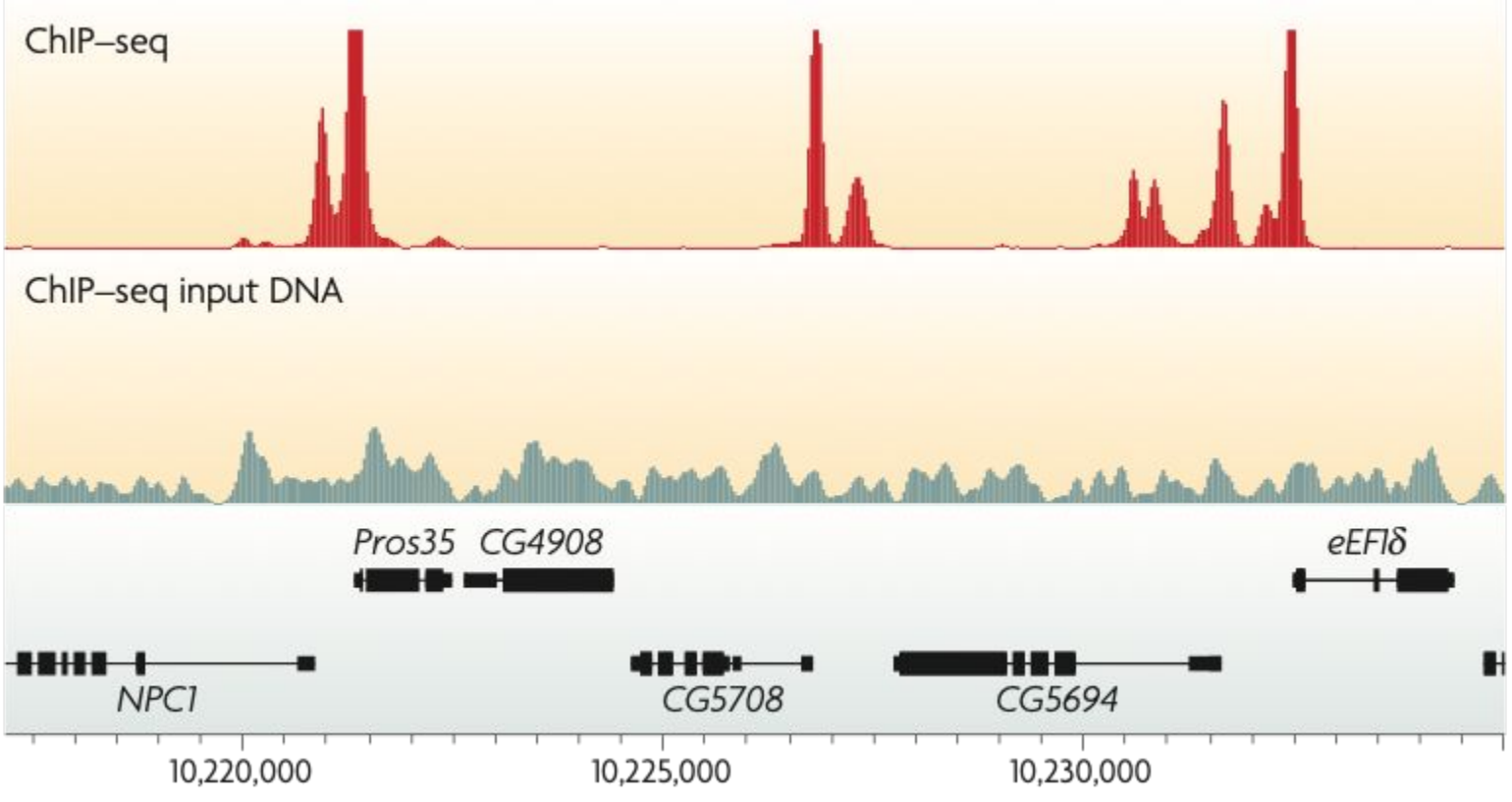
Chromatin immunoprecipitation

1. Fragment DNA
2. Bind target with antibodies
3. Immunoprecipitate bound fragments
4. Sequence purified fragments
5. Map fragments to genome
6. Find significant regions of enrichment



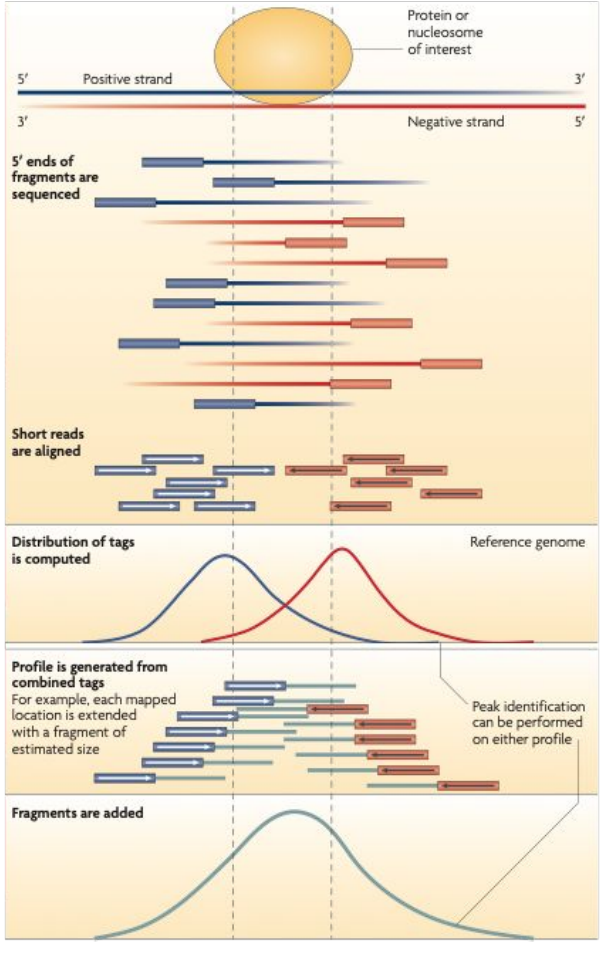
https://hbctraining.github.io/Intro-to-ChIPseq/lessons/01_Intro_chipseq_data_organization.html

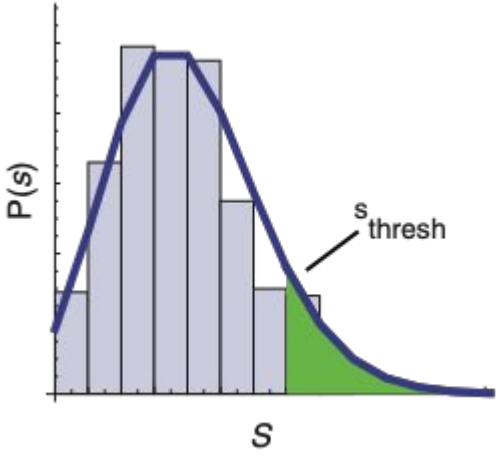
ChIPseq signals



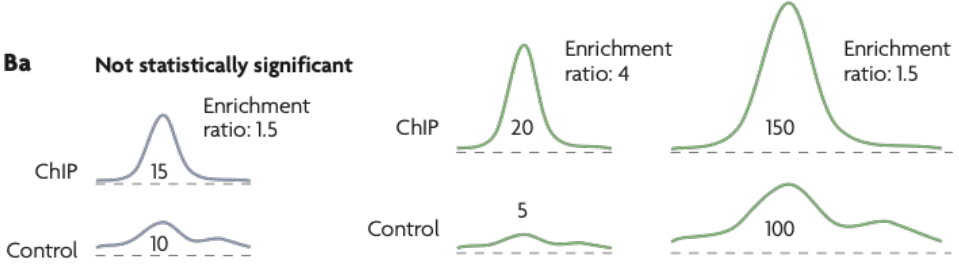
Park, P. J. (2009). *Nat. Rev. Genet*, *10*, 669-680.

Adjusting for single-end sequencing



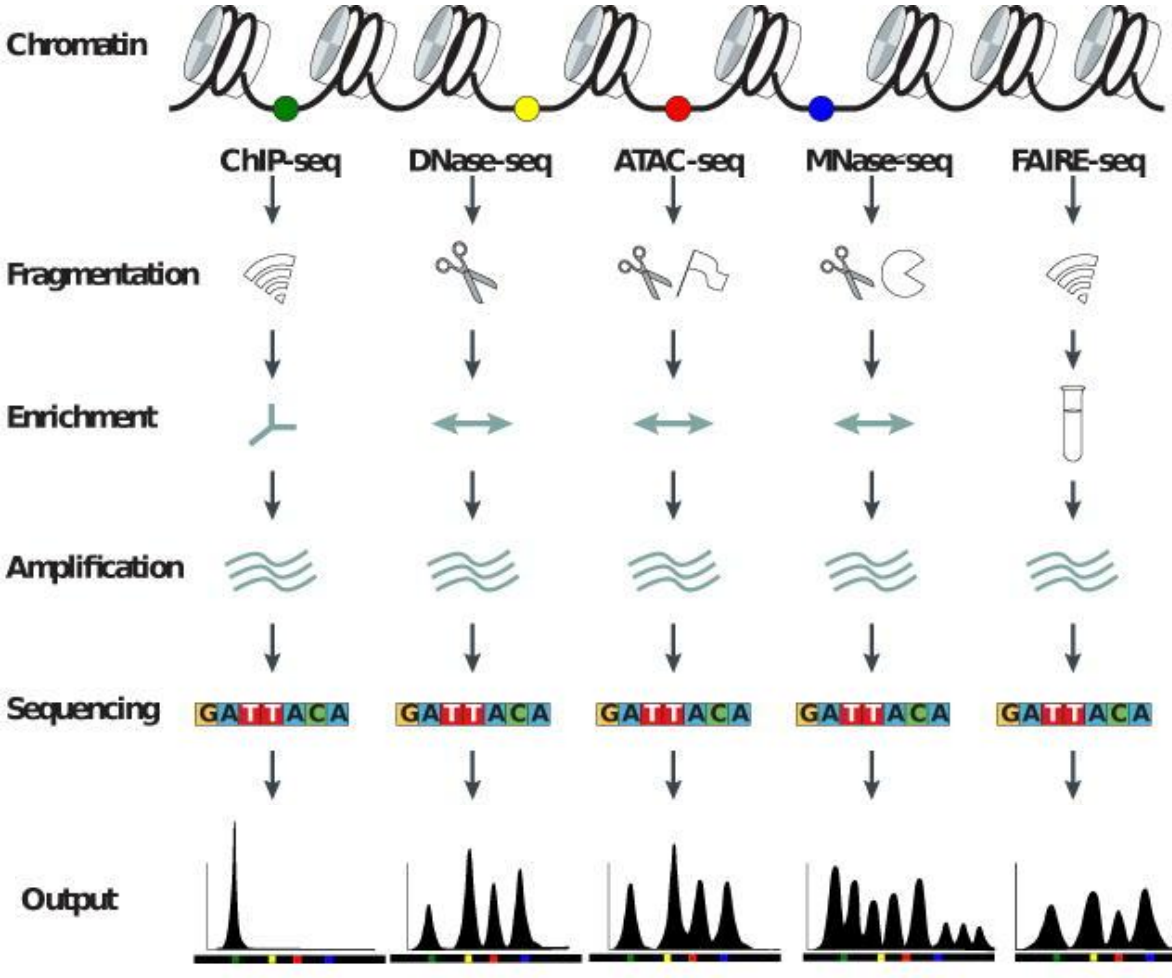


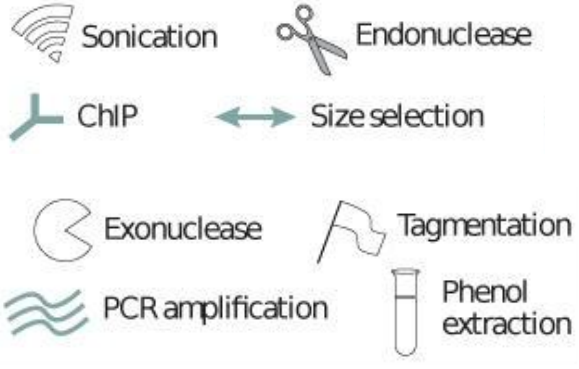
Bb **Statistically significant**



Park, P. J. (2009). *Nat. Rev. Genet*, *10*, 669-680.

Other assays





Meyer, C. A., & Liu, X. S. (2014). Identifying and mitigating bias in next-generation sequencing methods for chromatin biology. *Nature Reviews. Genetics*, *15*(11), 709–721.