

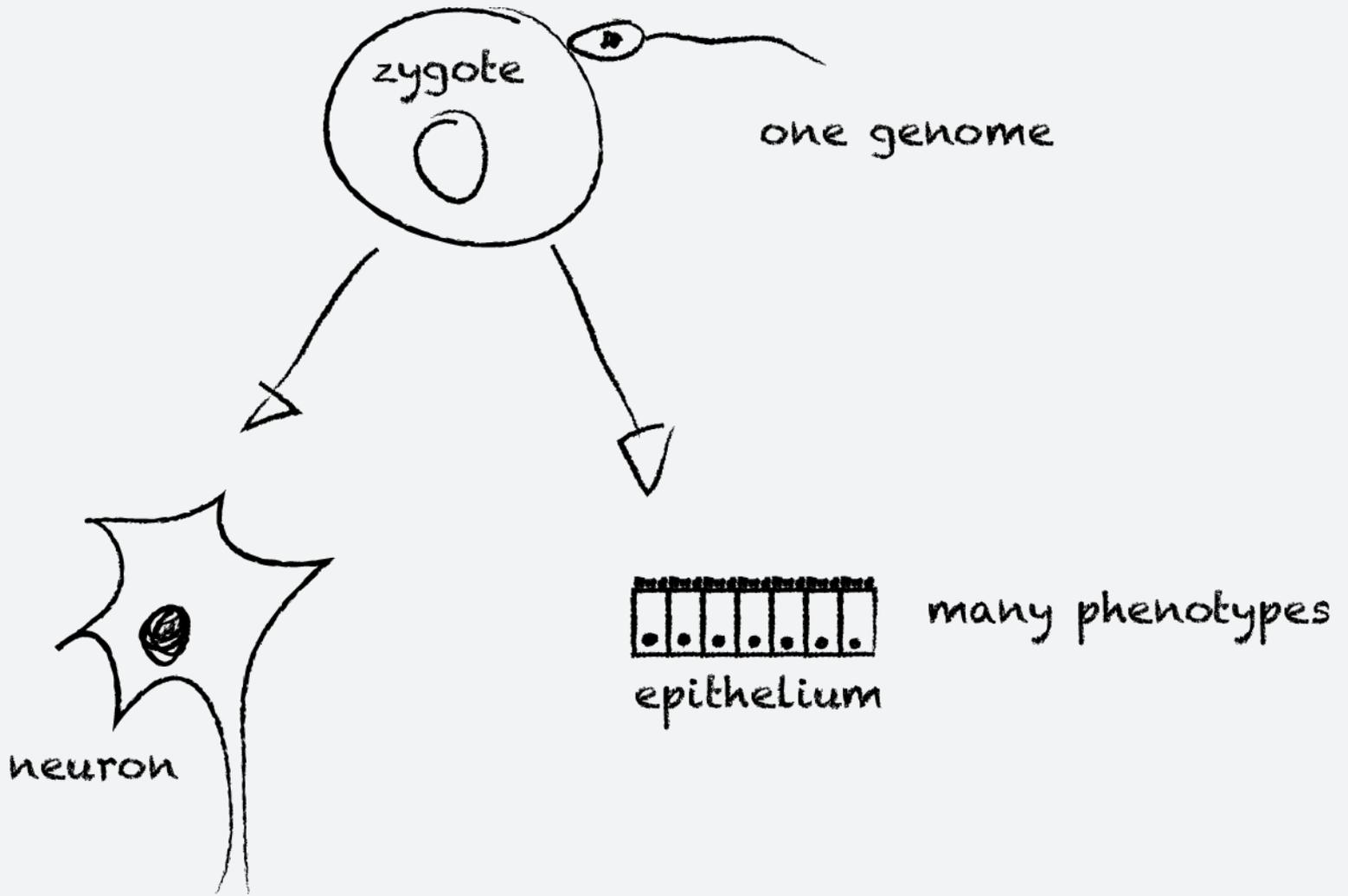
Computational Epigenomics in health and disease

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neuron

epithelium

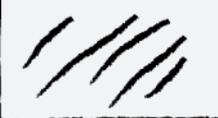
gene A

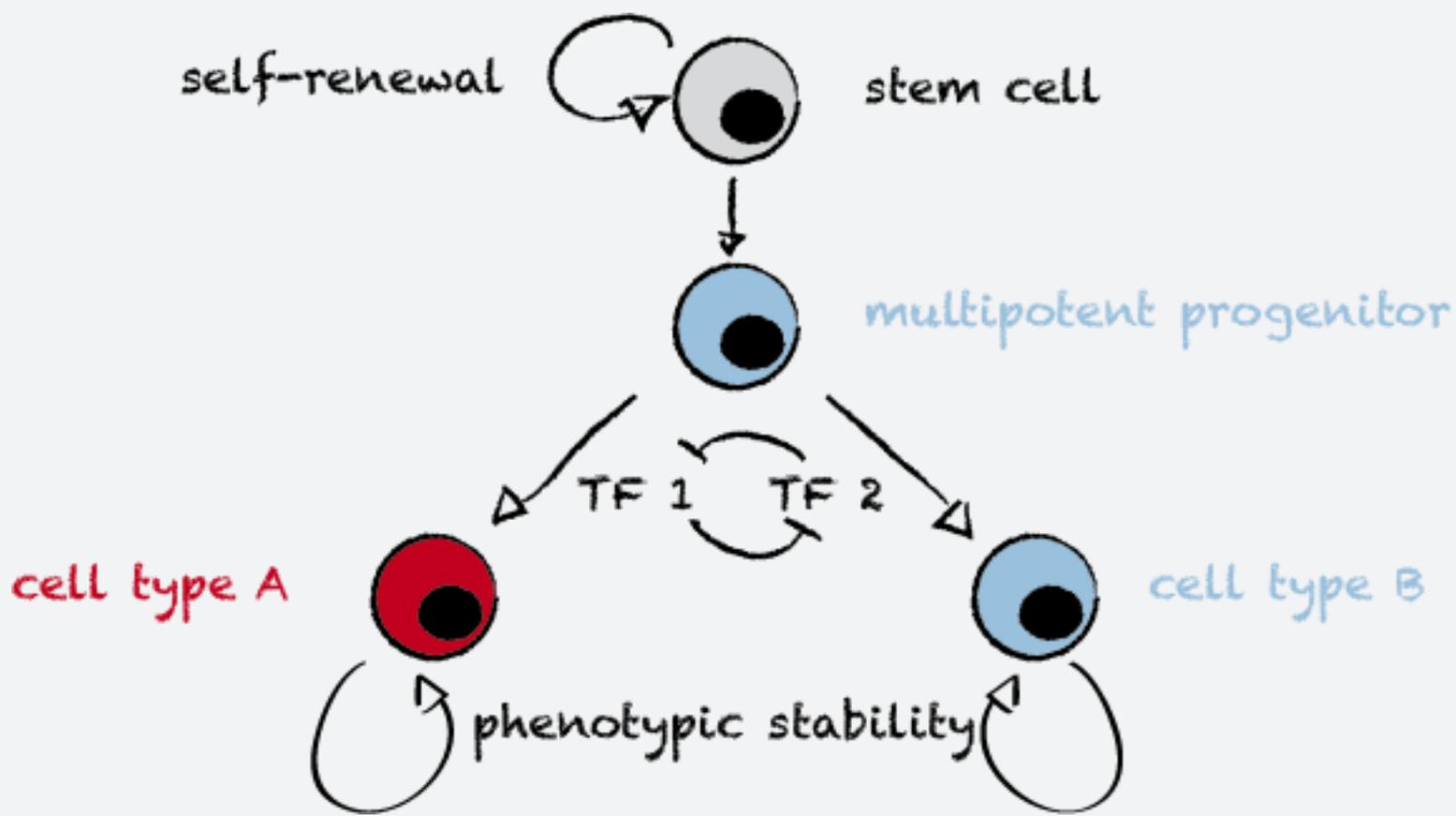
gene B

gene C

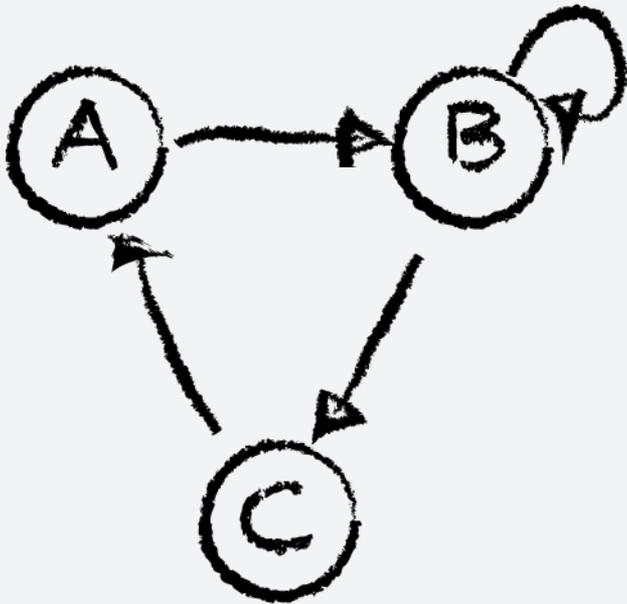
gene D

gene E

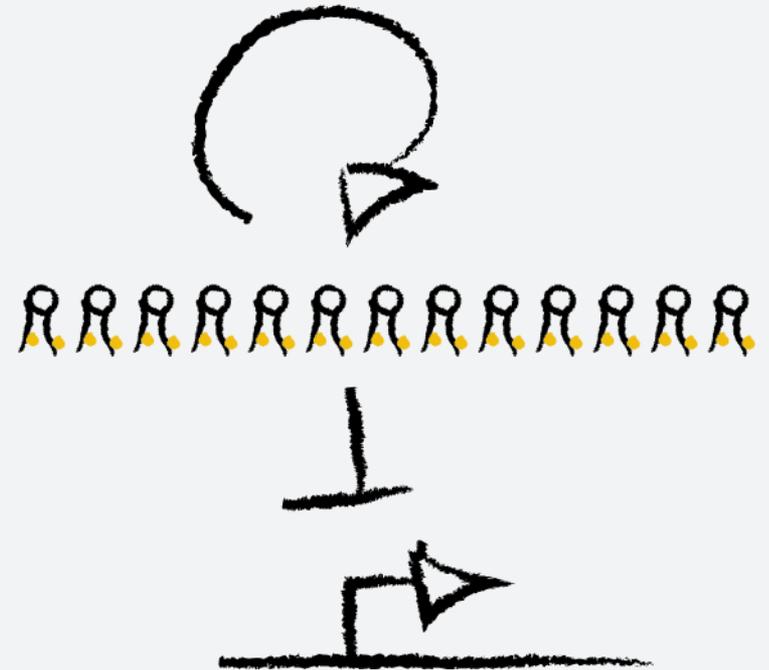
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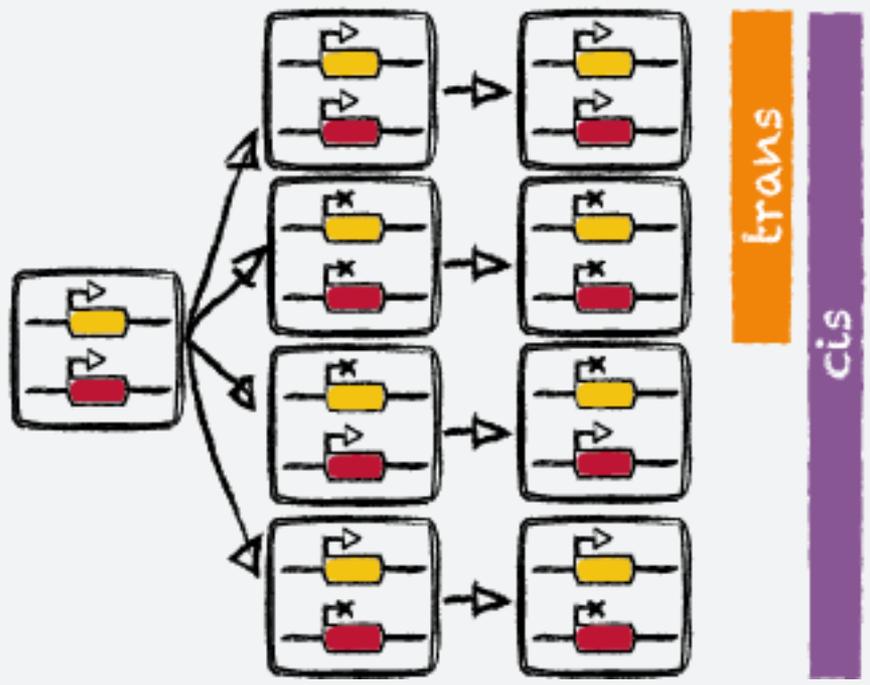


Regulatory network
"trans" epigenetics



Chromatin state
"cis" epigenetics

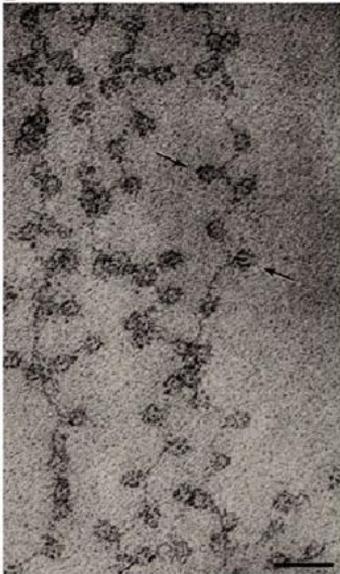




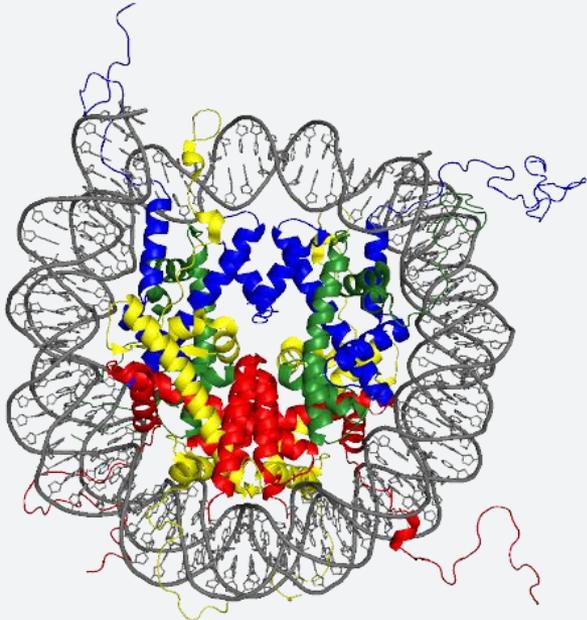
30 nm fiber



beads on the string



nucleosome



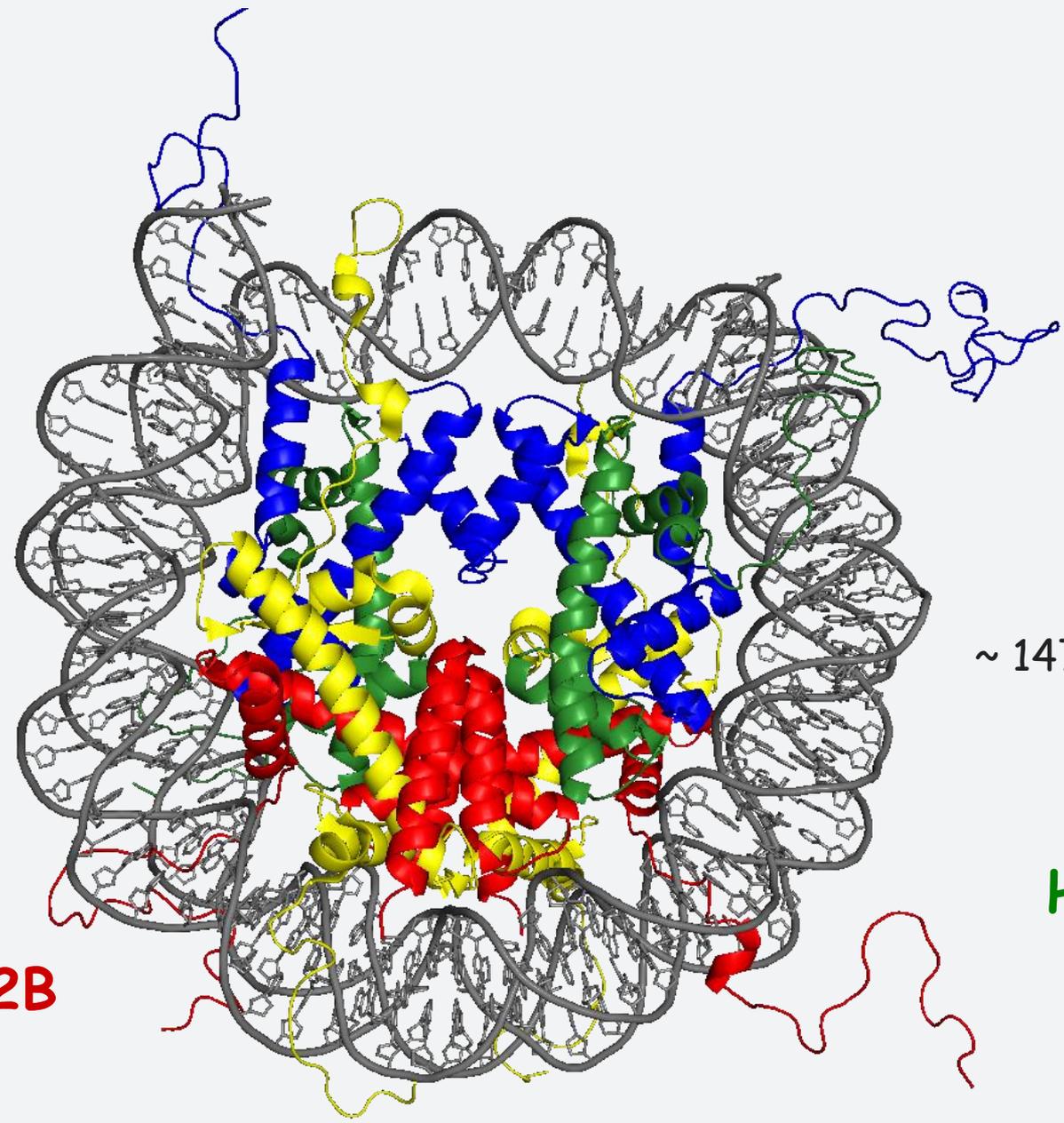
H2A

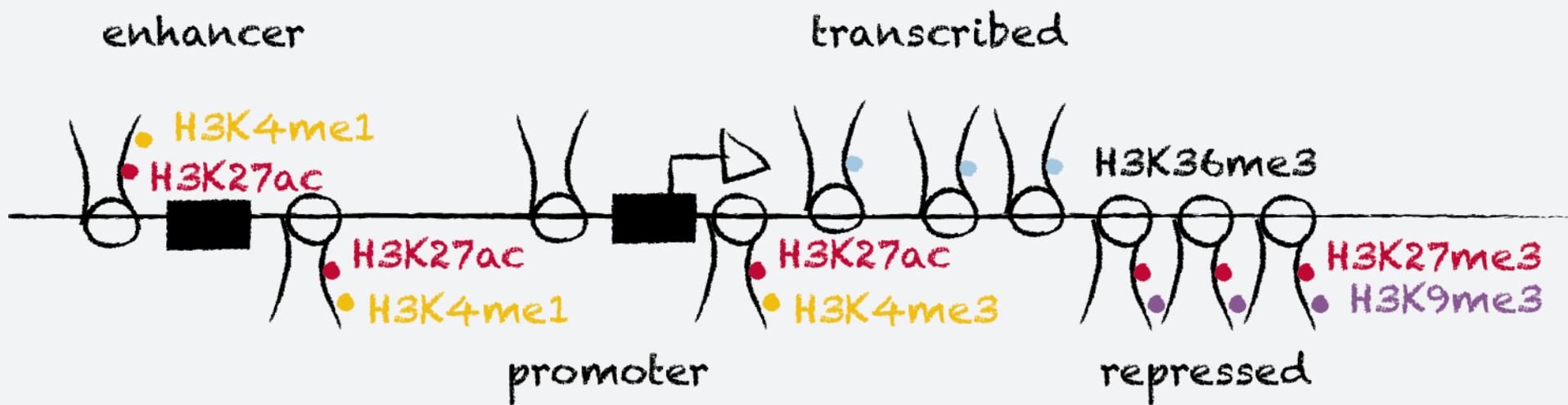
H3

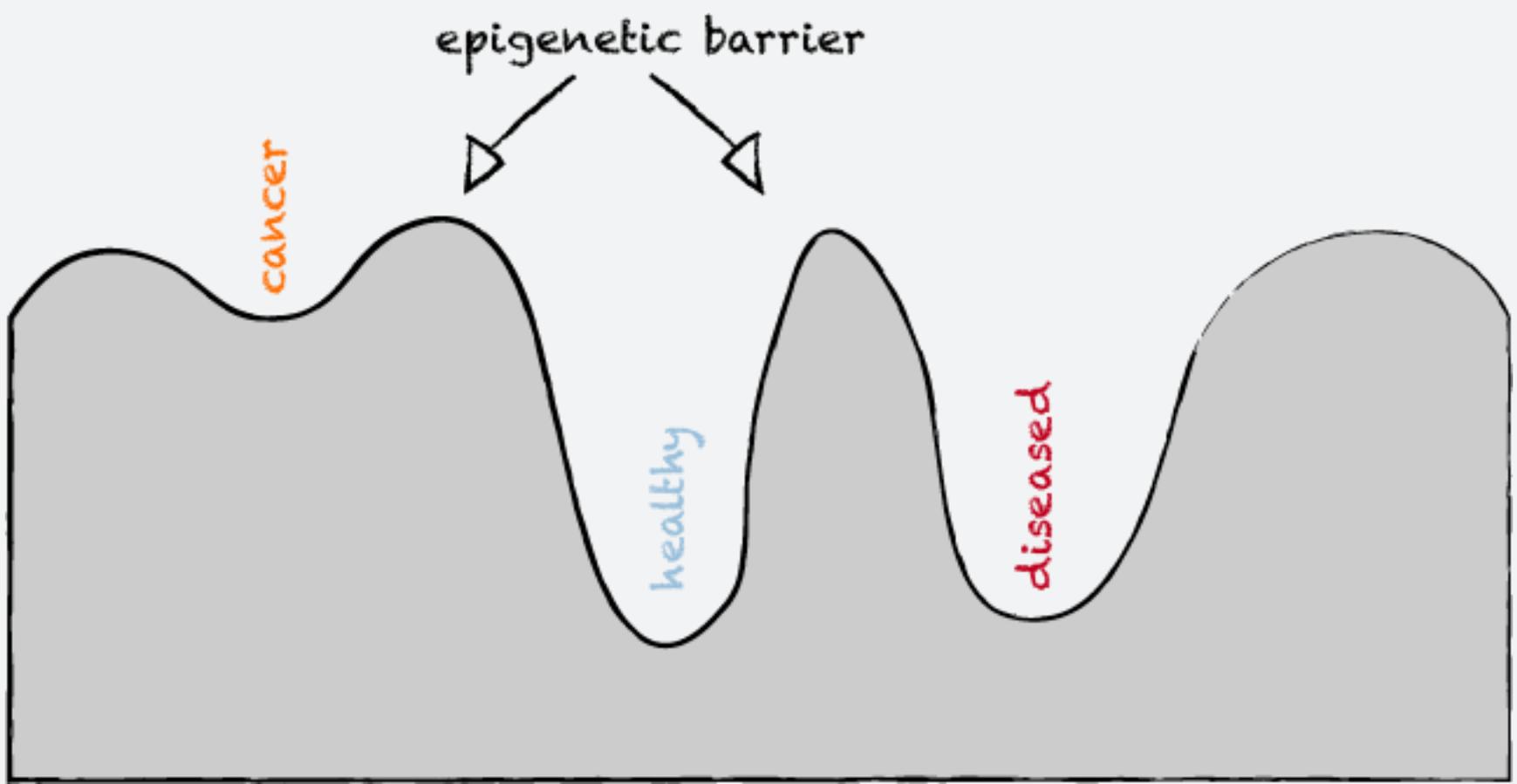
~ 147 bp DNA

H4

H2B

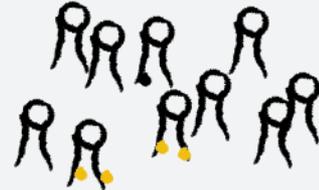








crosslink cells
with formaldehyde



sonicate to release
chromatin fragments



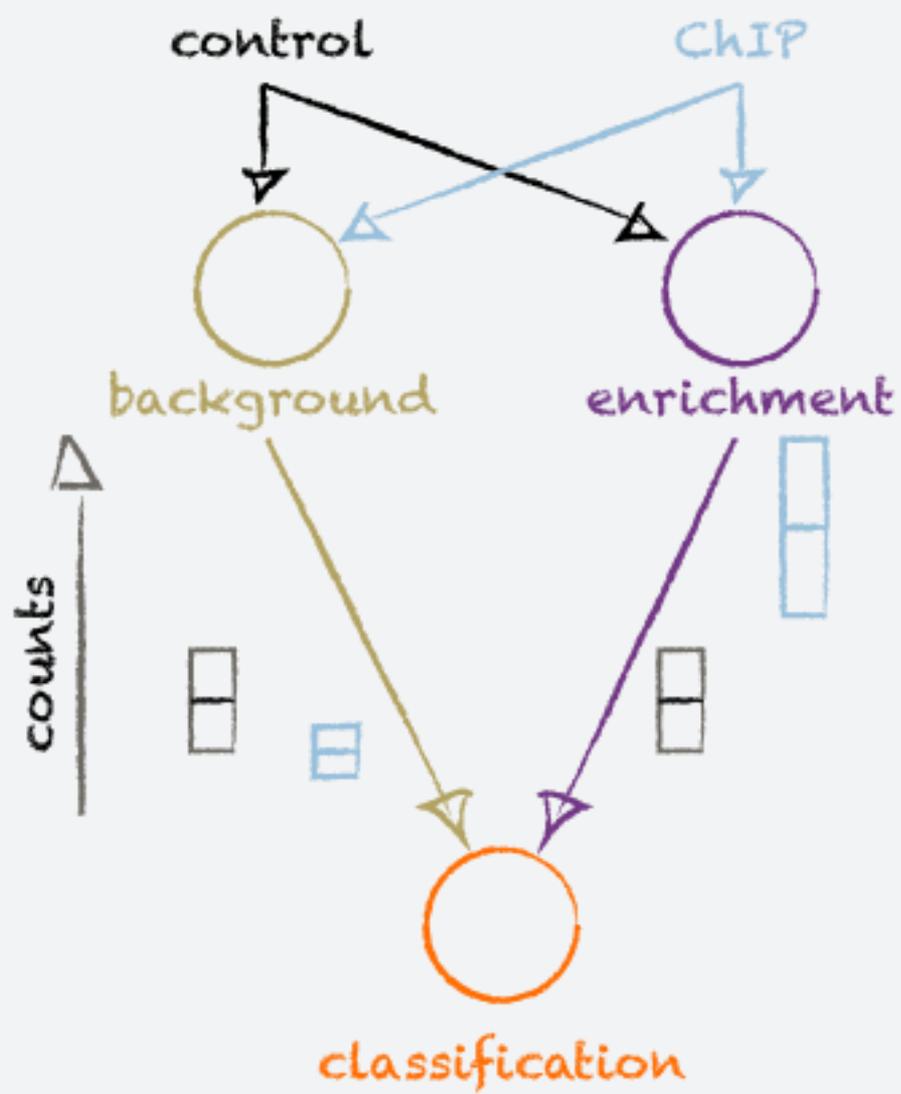
add histone modification
specific antibody



immunoprecipitate



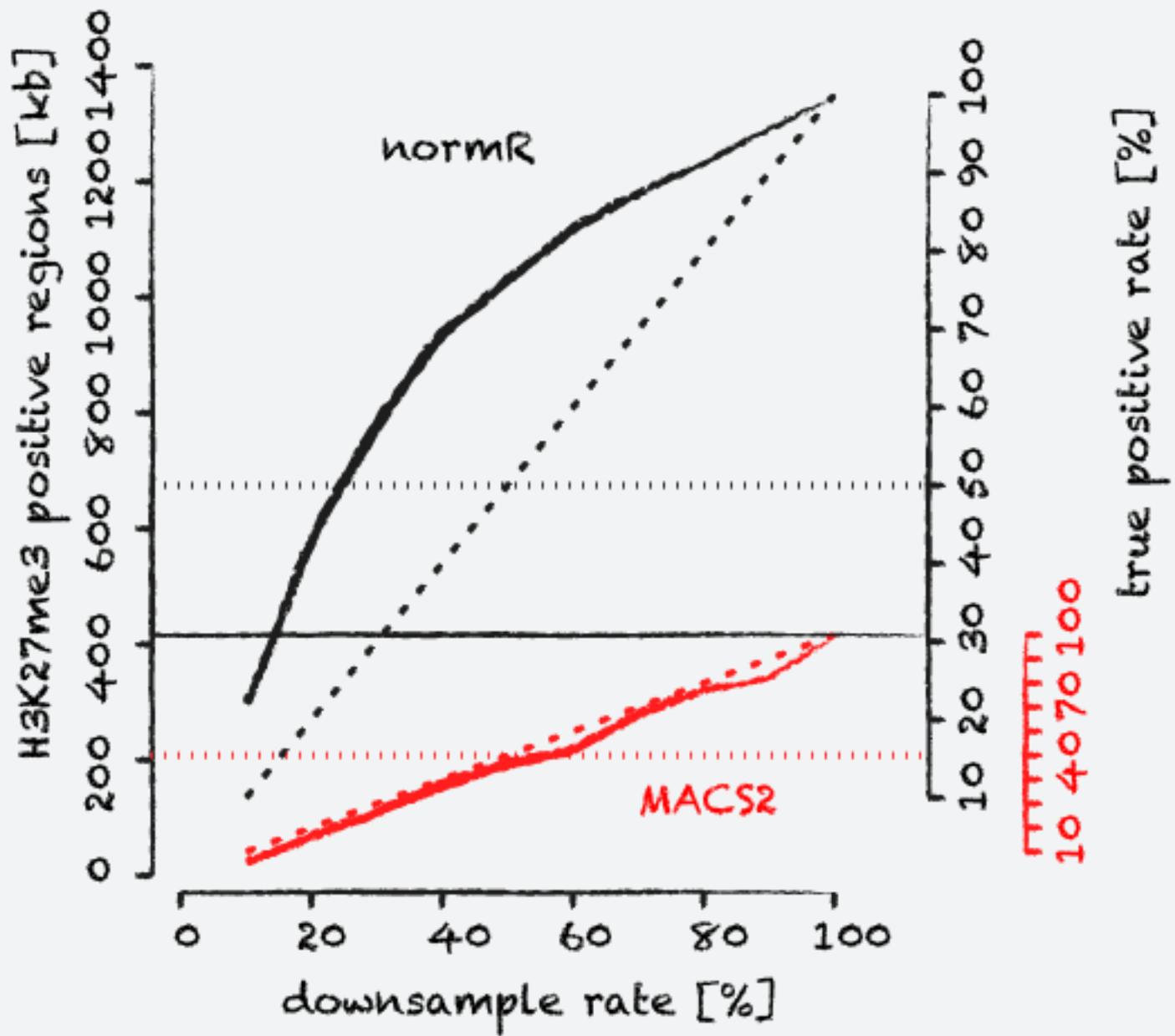
sequence

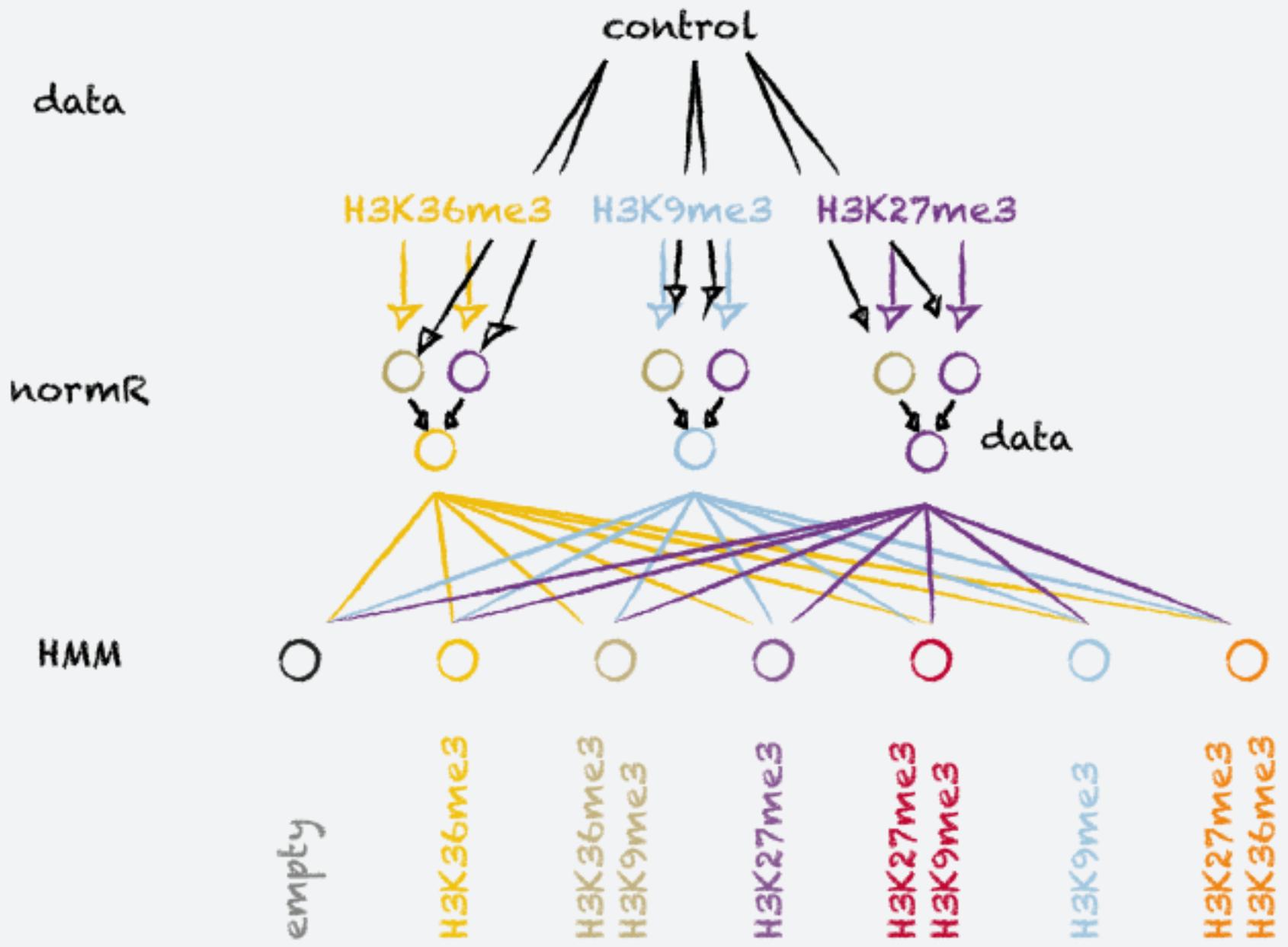


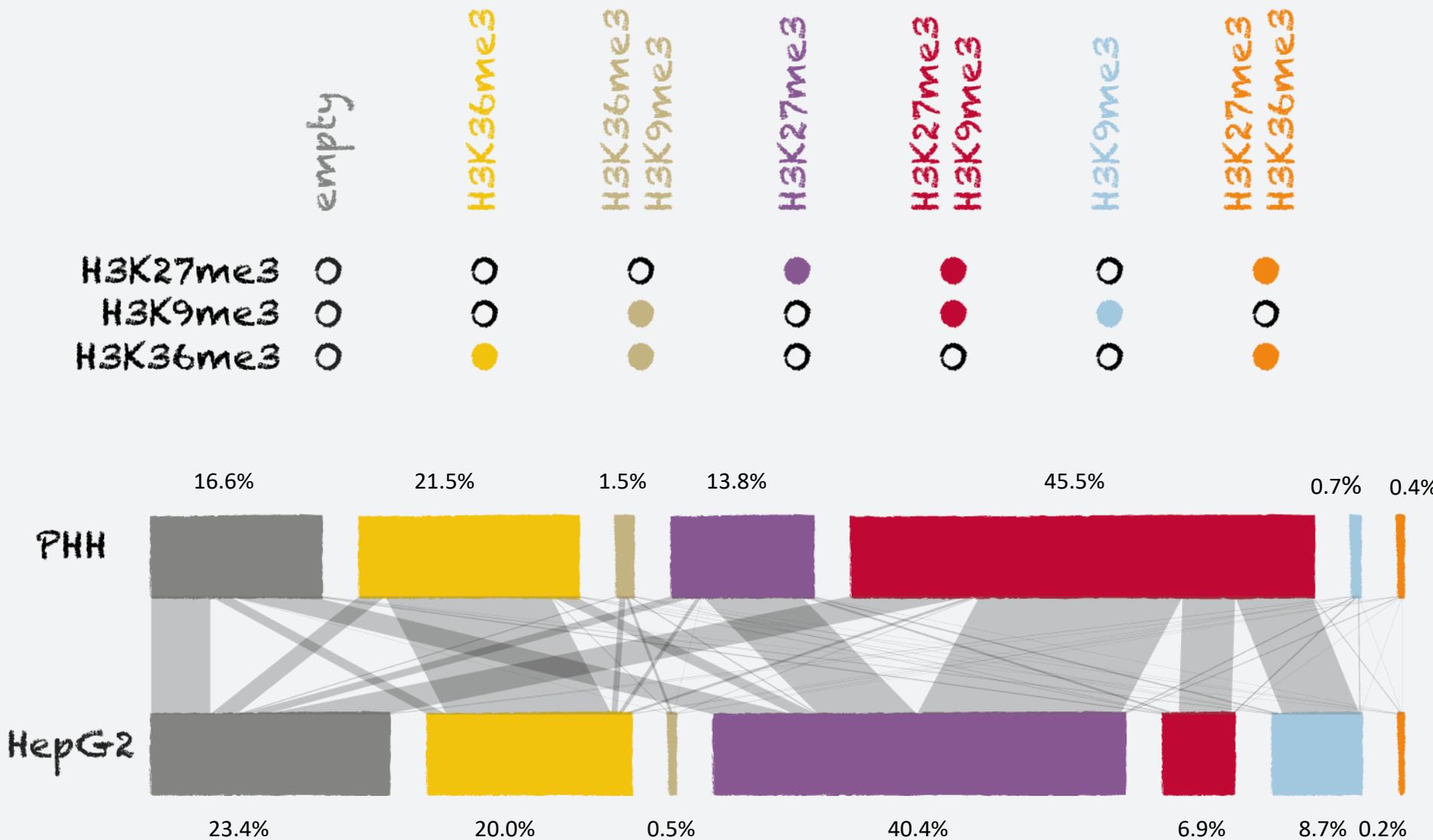
data

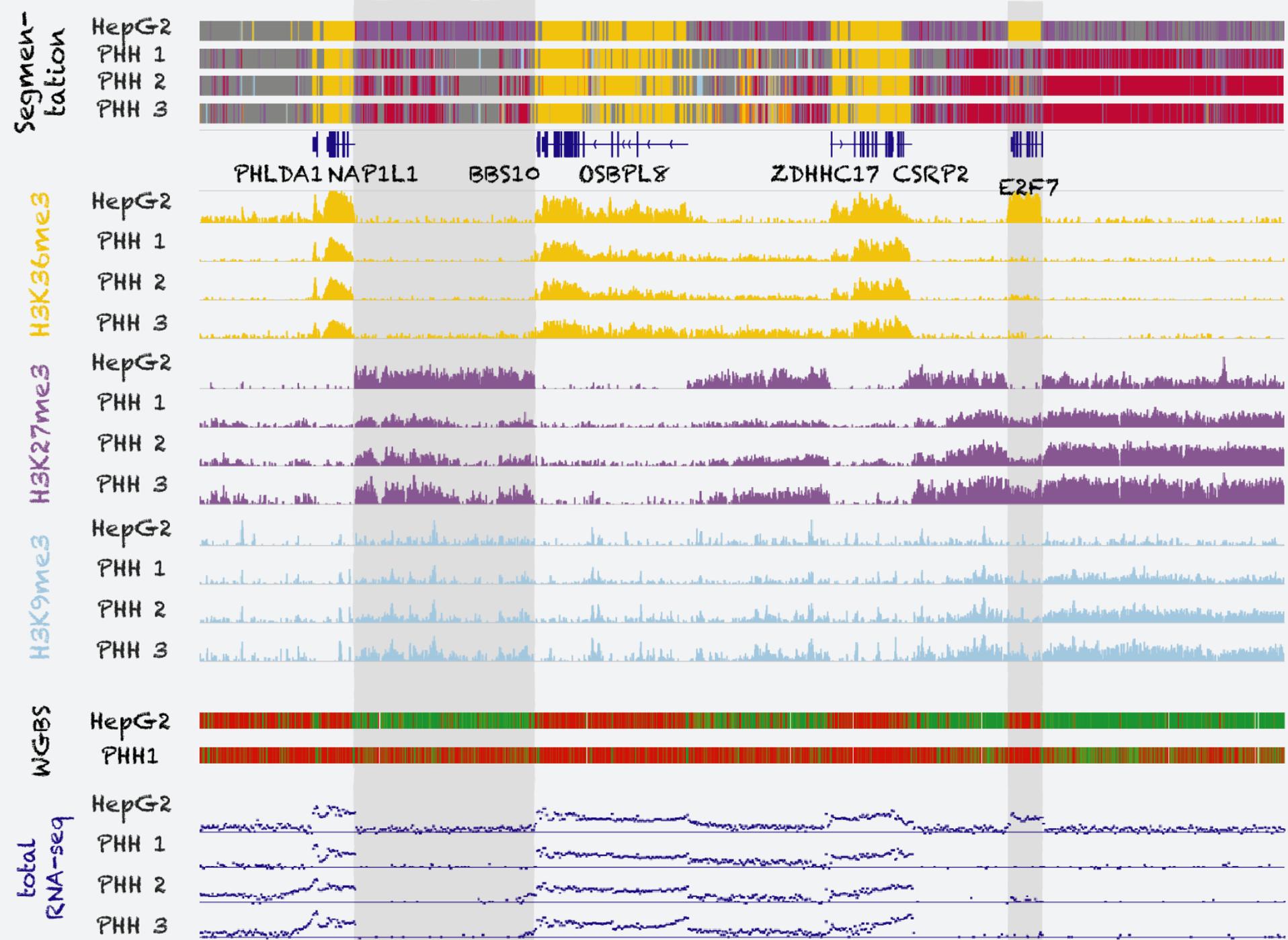
binomial
mixture model

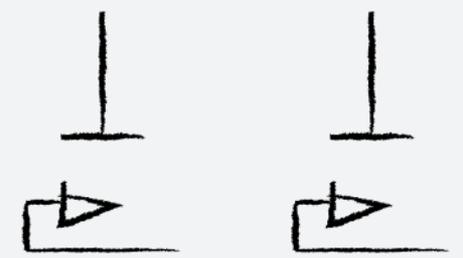
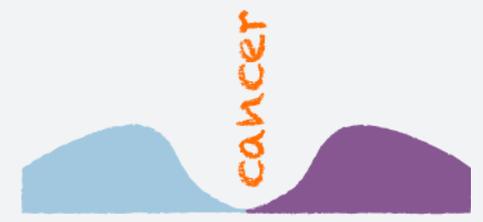
WOTMR

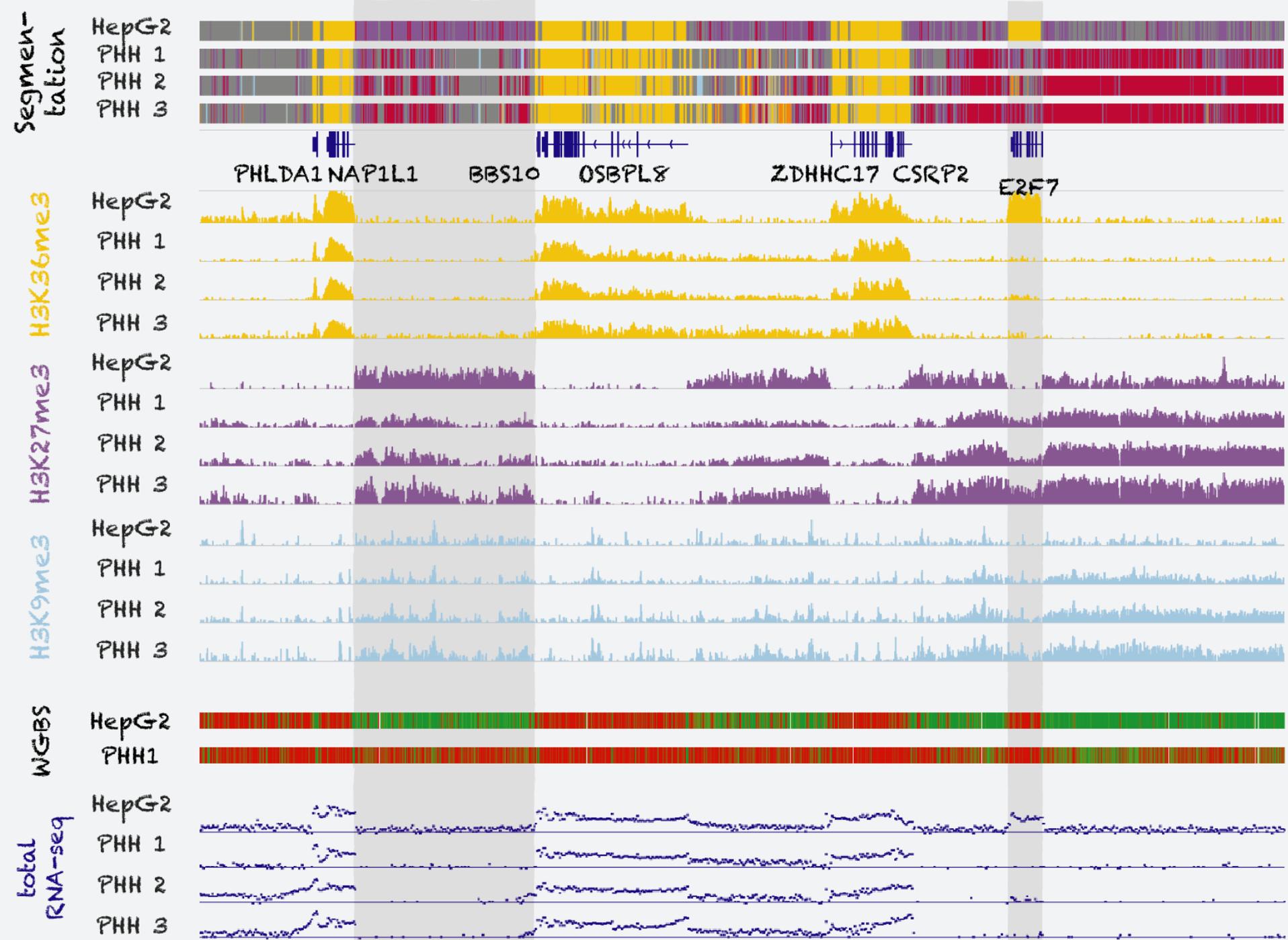




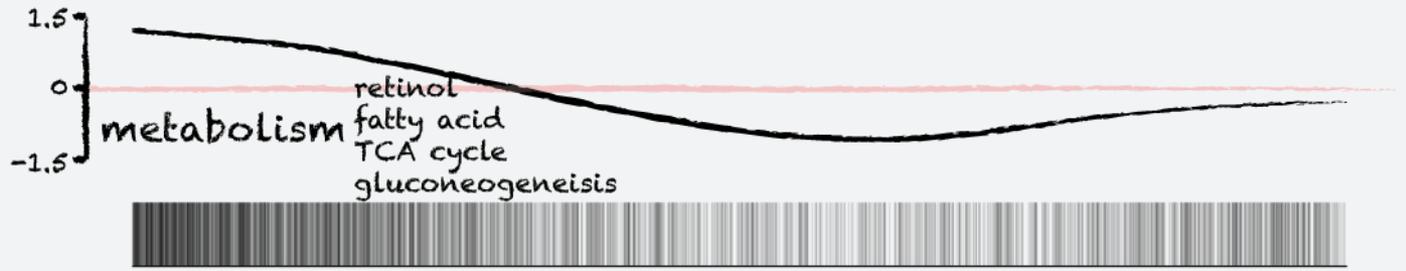








genes gaining heterochromatin in HepG2



genes loosing heterochromatin in HepG2



genes staying H3K36me3 in HepG2

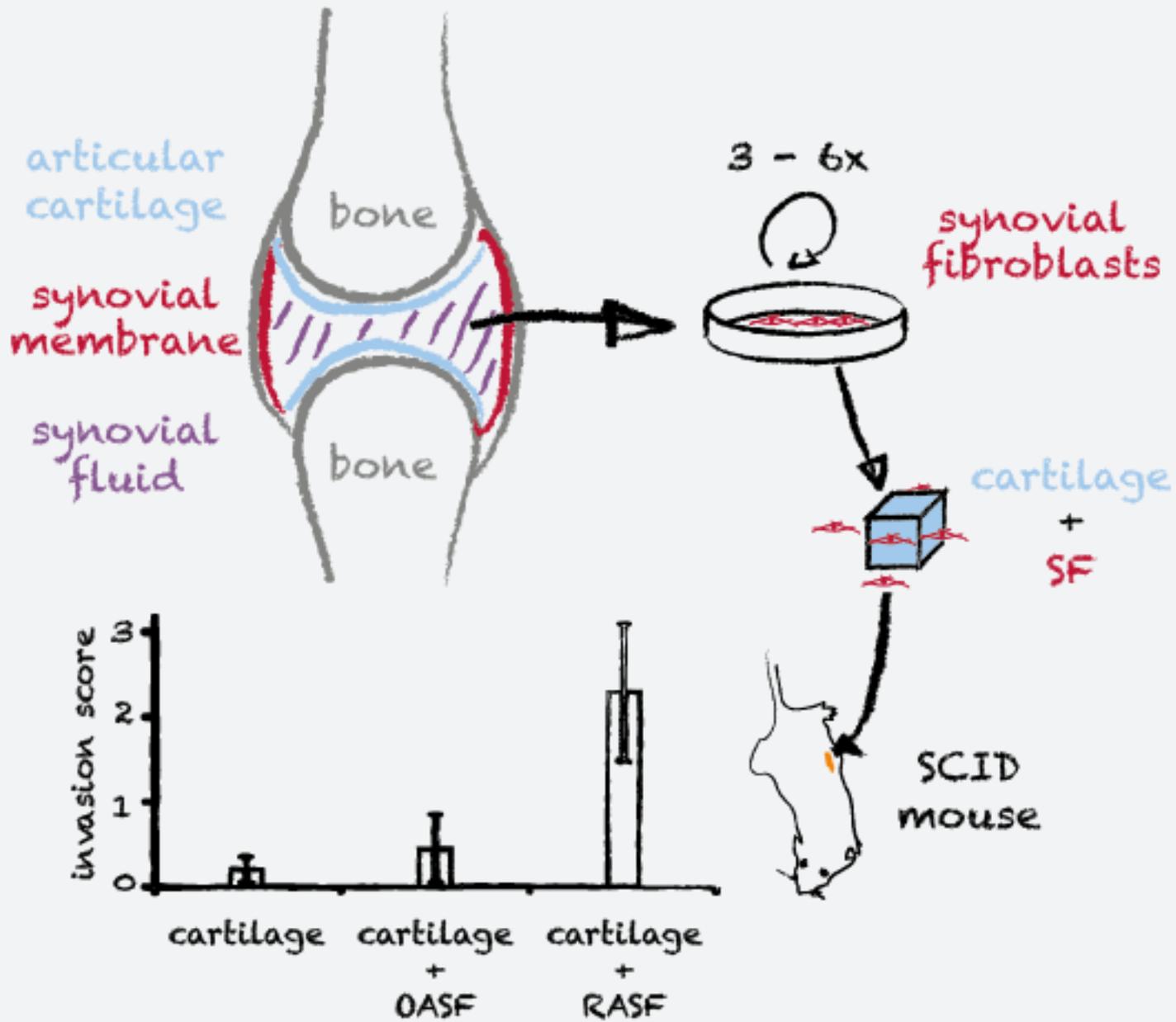


genes staying heterochromatic in HepG2



gene expression change

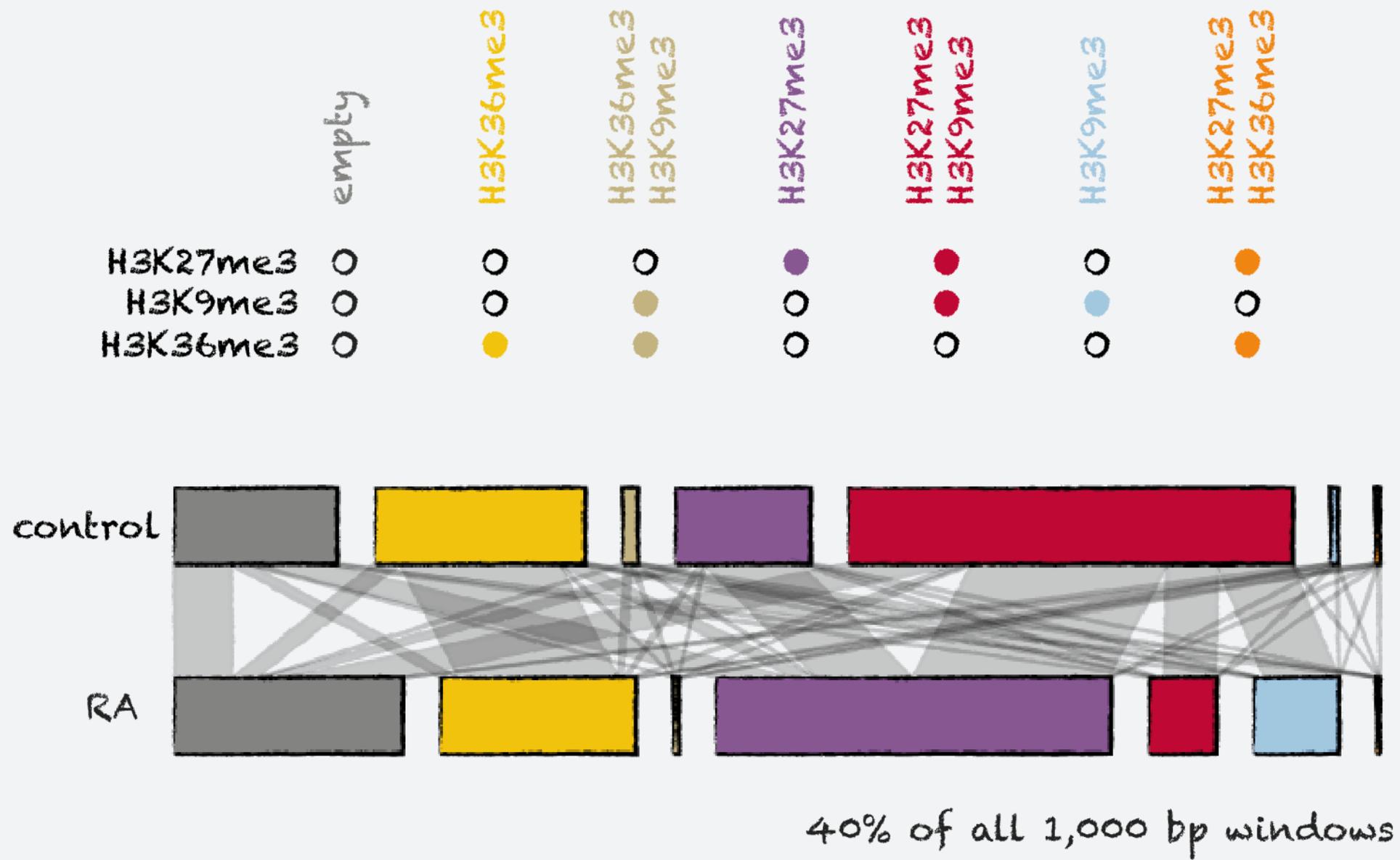




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Xinyi Yang
Claudia Schade
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Vera Rykalina

Marcos Torroba
Yelizaveta Mochalova
Johannes Helmuth
Gina Renschler
Guofeng Meng
Alessandro Mammana
Juliane Perner
Na Li
Ilona Dunkel
Rosa Karlic





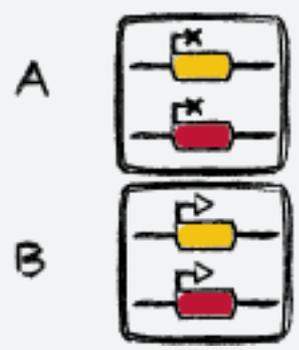
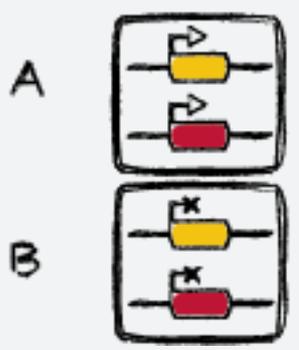
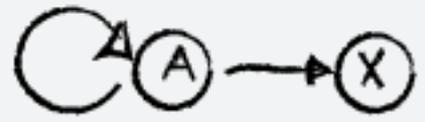
Heterochromatic in control to (partially) expressed in RA

| Pathways | Adjusted p-value | matches |
|--------------------------|------------------|---------|
| Immune System | 5.85e-8 | 38/150 |
| Innate Immune System | 2.05e-5 | 26/150 |
| Neutrophil degranulation | 4.37e-5 | 19/150 |

Expressed in control to (partially polycomb) repressed in RA

| Pathways | Adjusted p-value | Matches |
|--|------------------|---------|
| Extracellular Matrix organization | 1.74e-8 | 26/388 |
| Collagen formation | 1.79e-6 | 13/388 |
| Signaling by PDGF | 1.04e-5 | 11/388 |
| Signaling by receptor tyrosine kinases | 3.24e-5 | 28/388 |
| Integrin cell surface interactions | 4.44e-5 | 12/388 |
| YAP1- and WWTR1 (TAZ)-stimulated gene expression | 2.06e-4 | 5/388 |

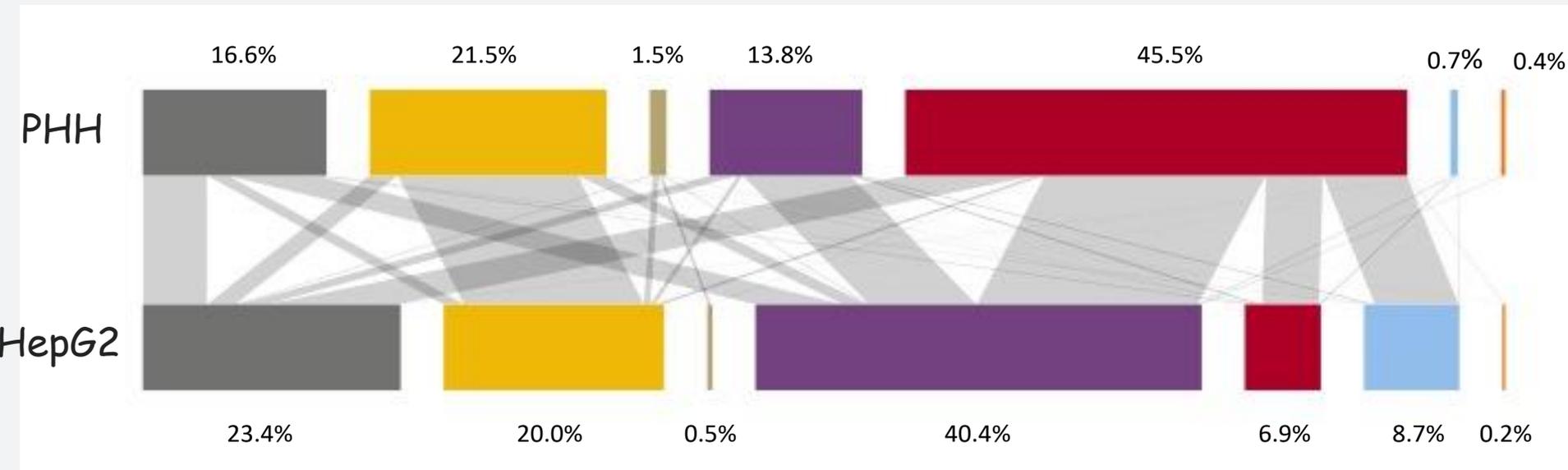
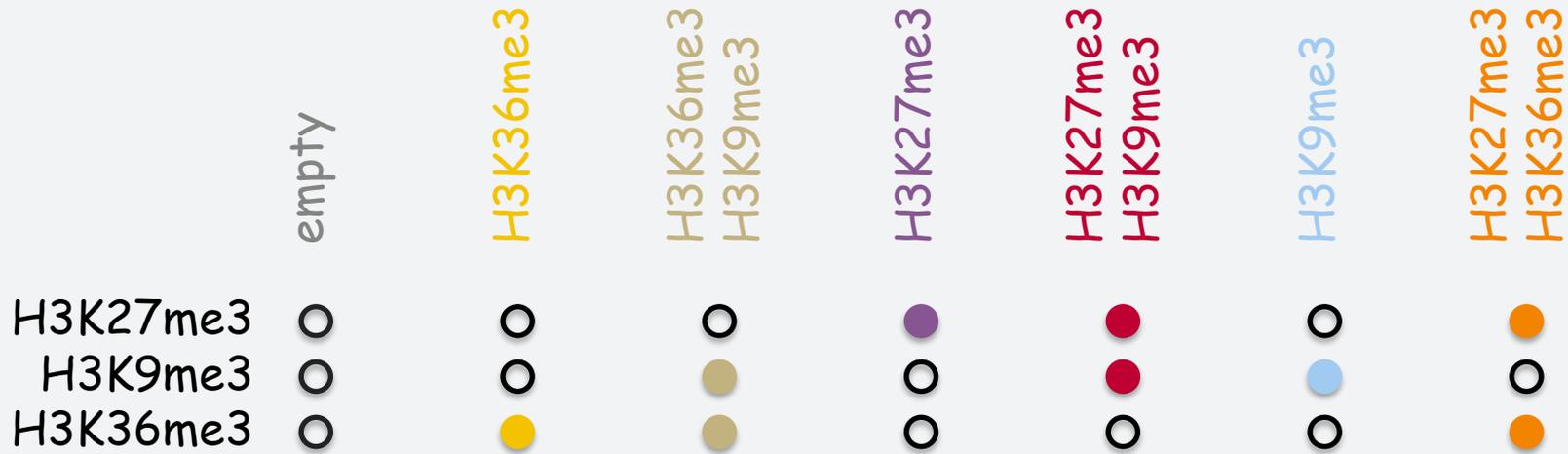
stable transformation

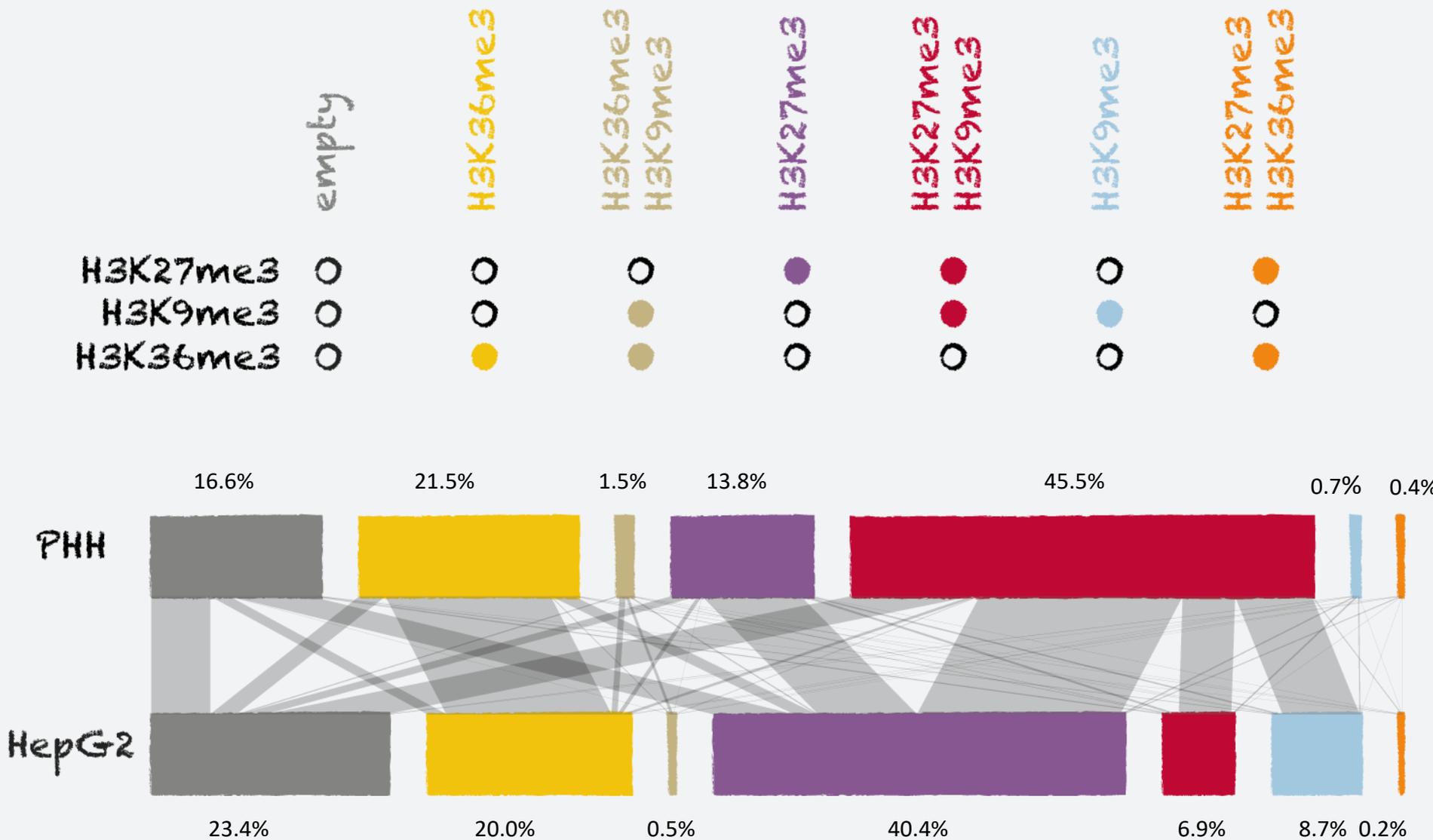


gene regulatory layer



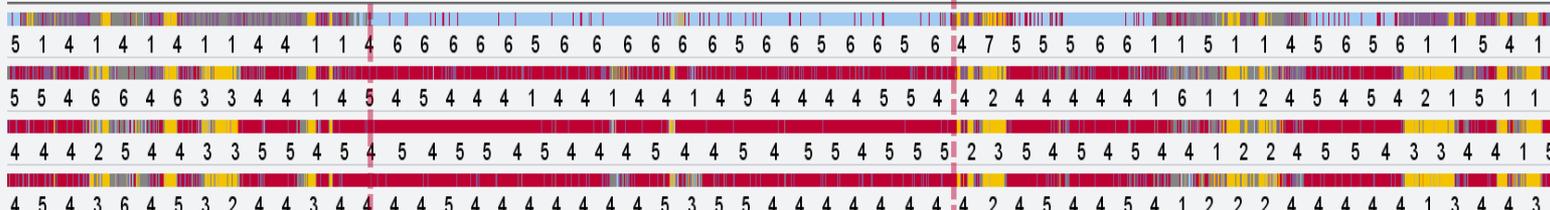
cis-epigenetic layer





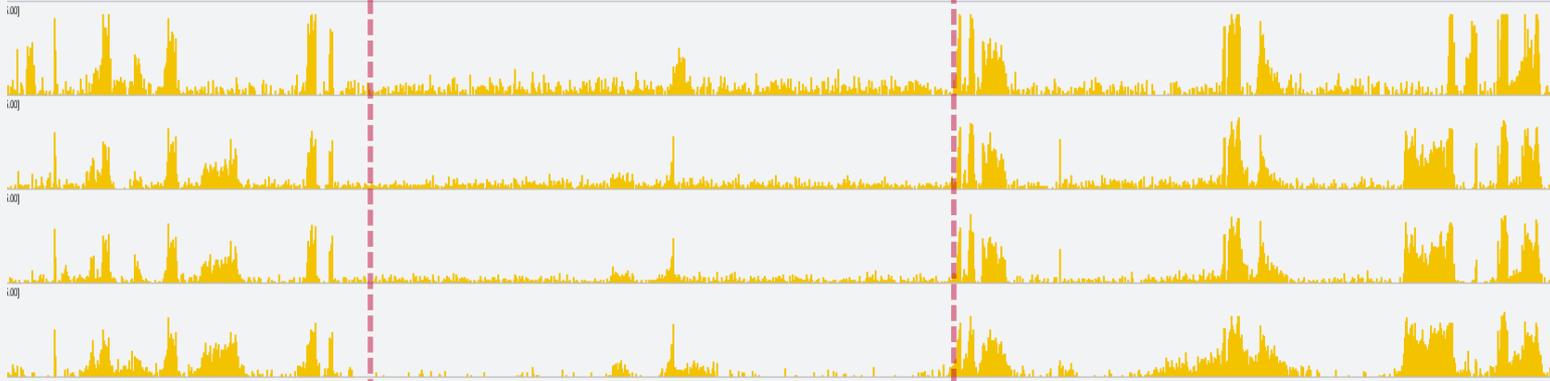
Segmentation

HepG2
PHH 1
PHH 2
PHH 3



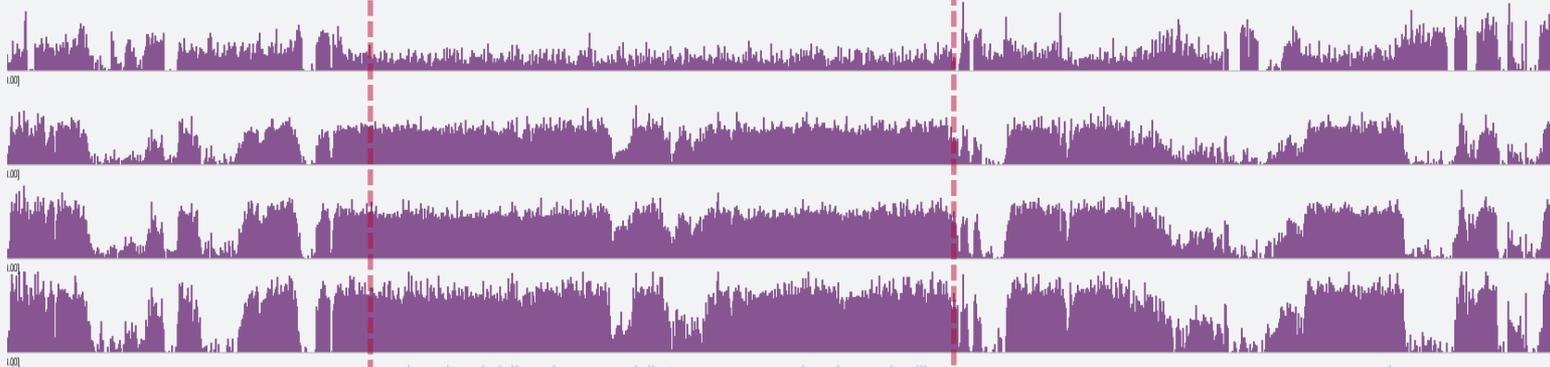
H3K36me3

HepG2
PHH 1
PHH 2
PHH 3



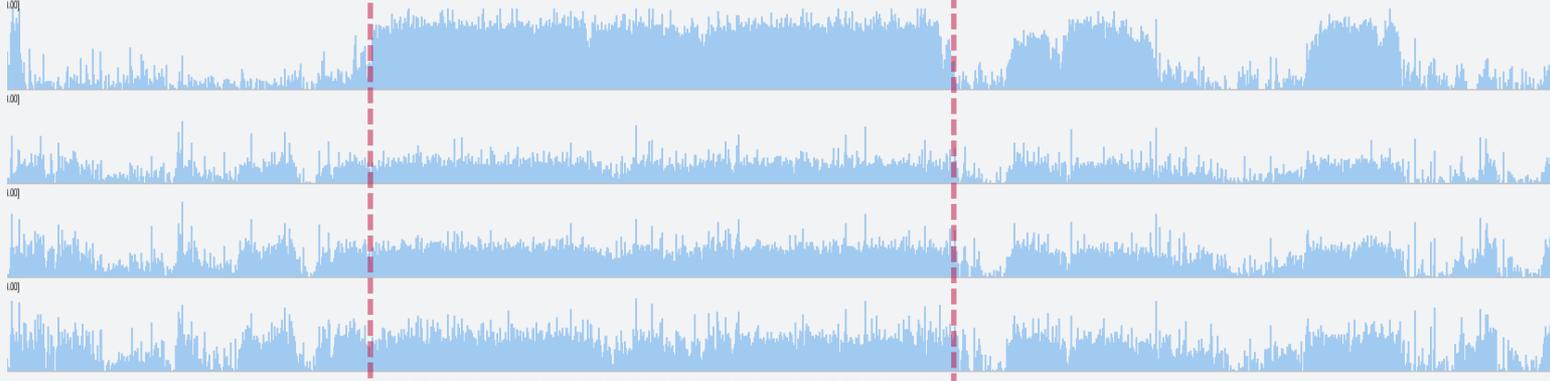
H3K27me3

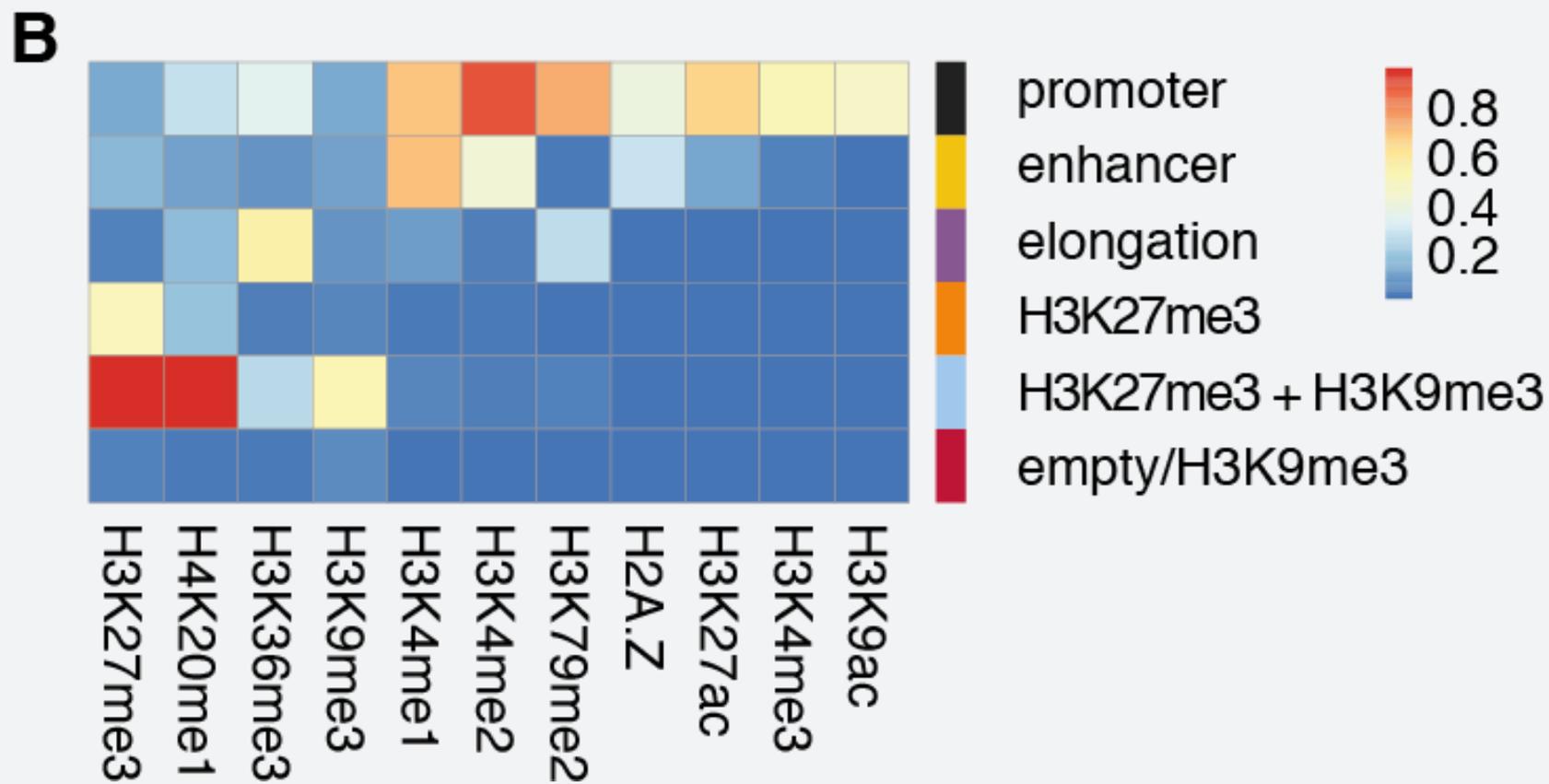
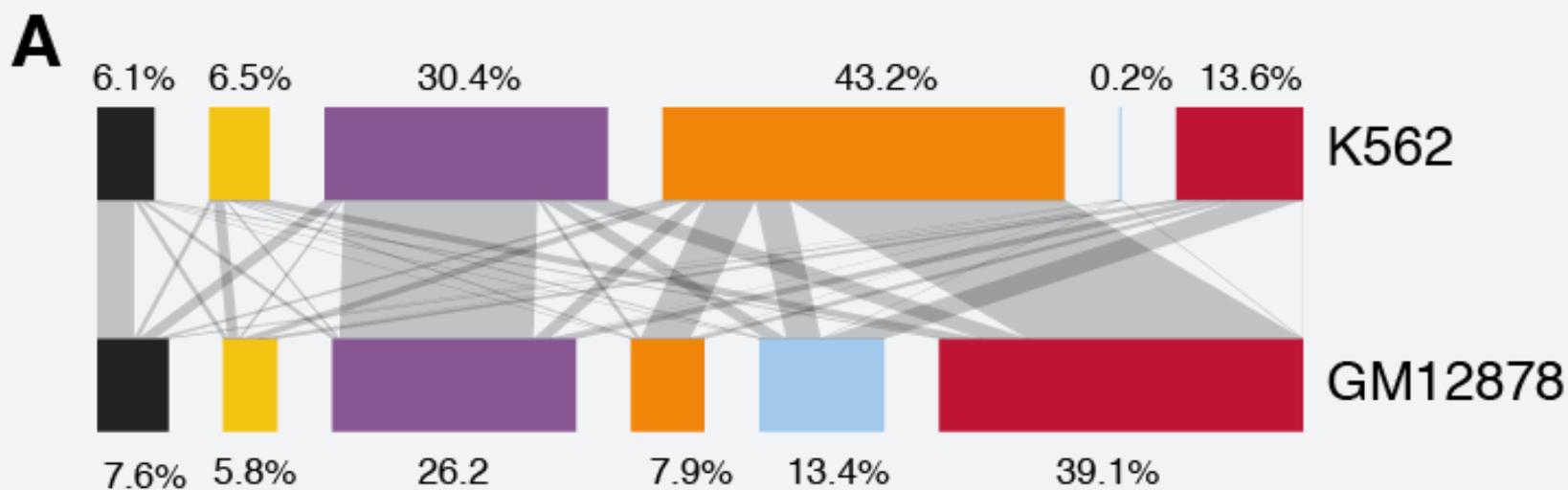
HepG2
PHH 1
PHH 2
PHH 3



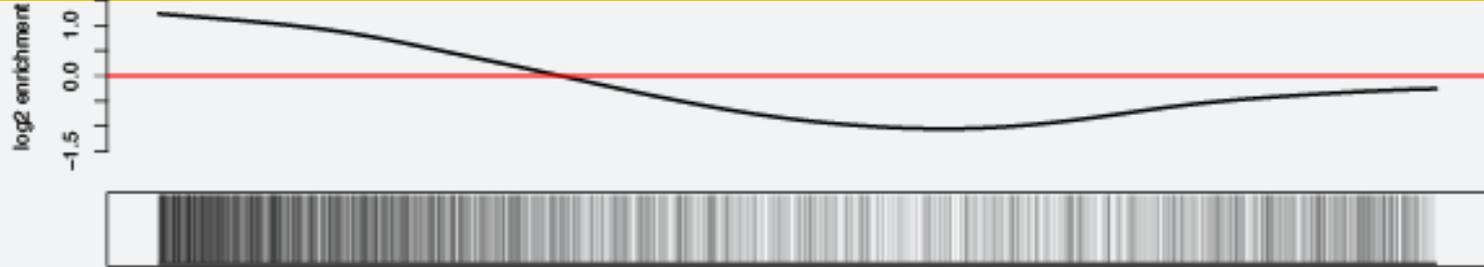
H3K9me3

HepG2
PHH 1
PHH 2
PHH 3

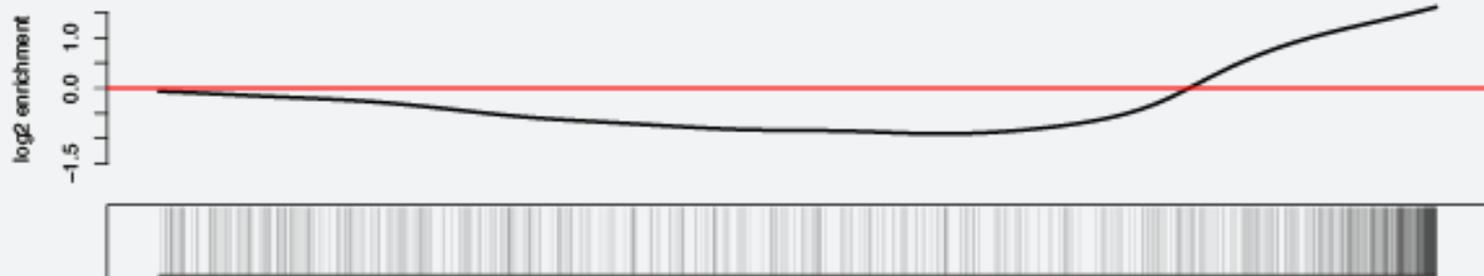




genes gaining
heterochromatin
in HepG2



genes loosing
heterochromatin
in HepG2



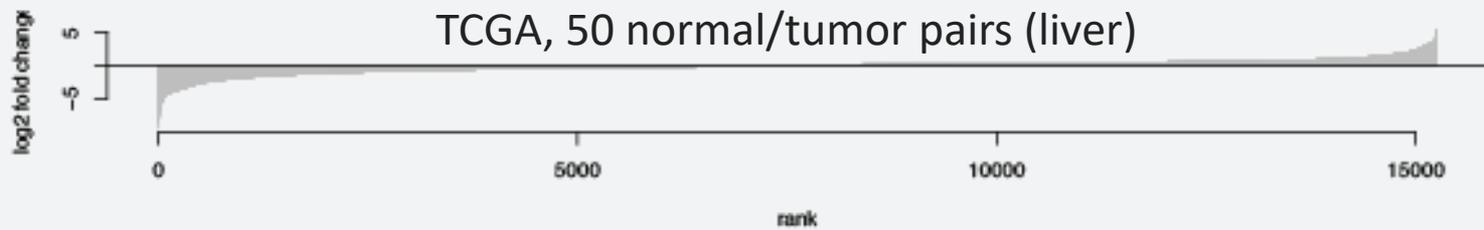
genes staying
expressed
in HepG2

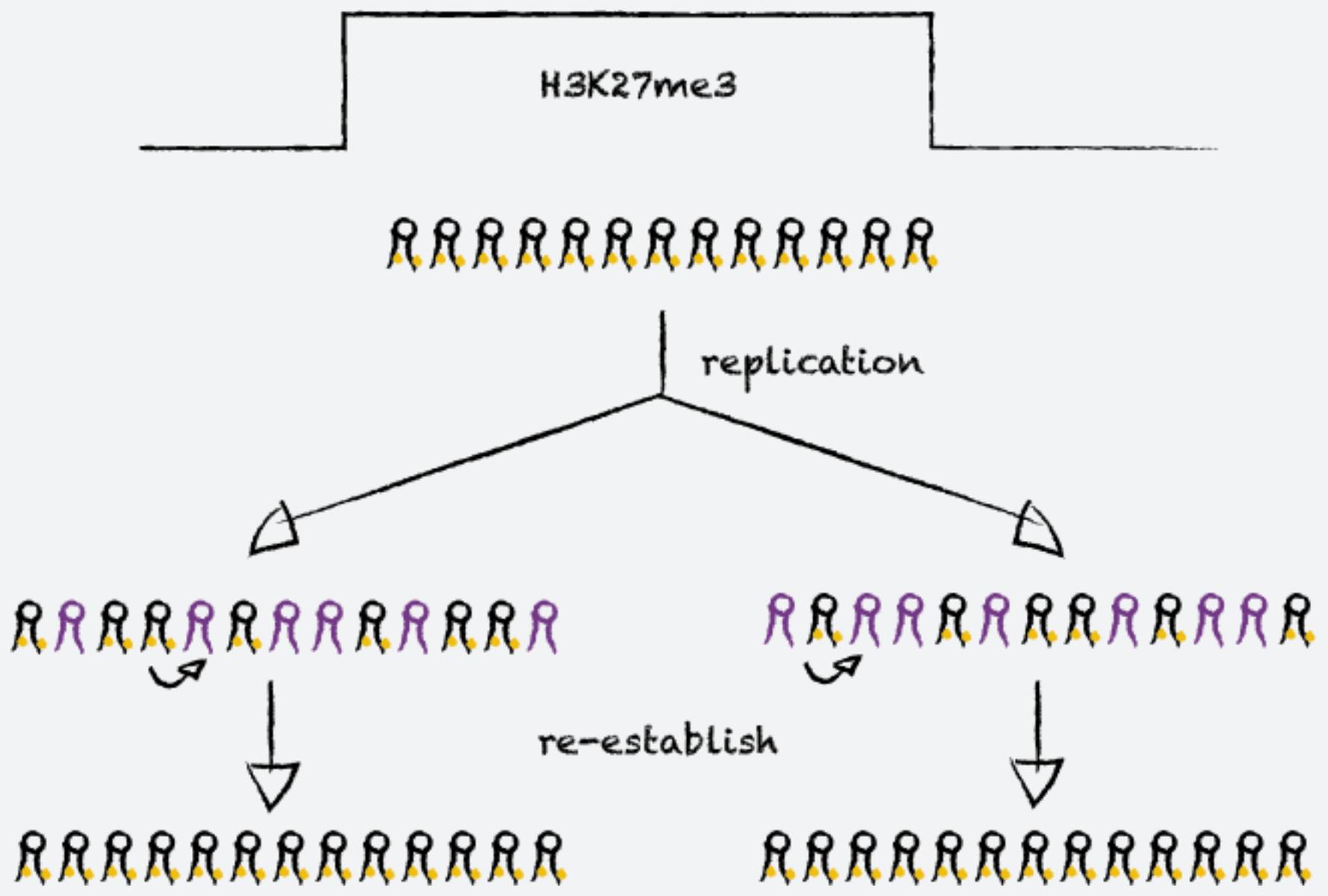


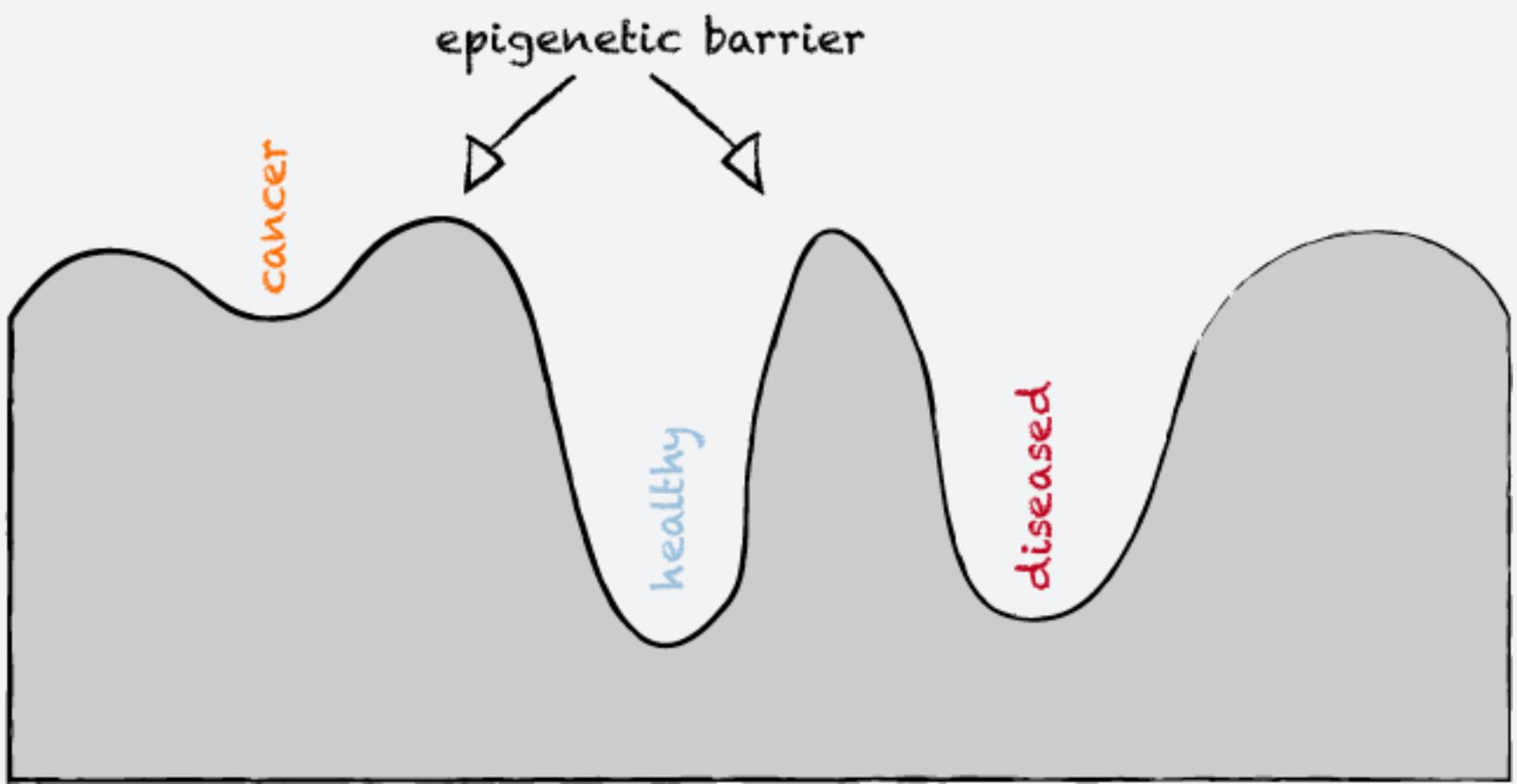
genes staying
heterochromatic
in HepG2



TCGA, 50 normal/tumor pairs (liver)

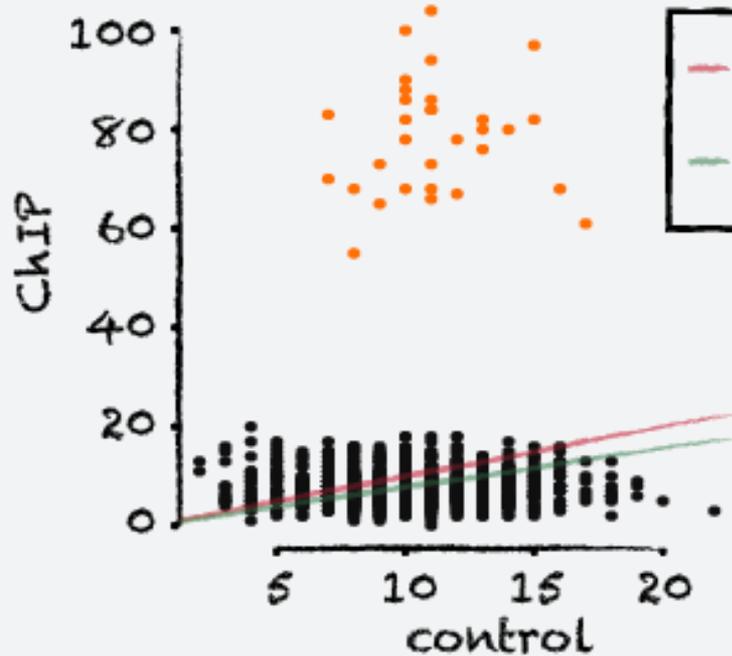
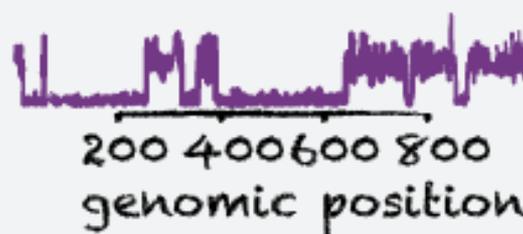
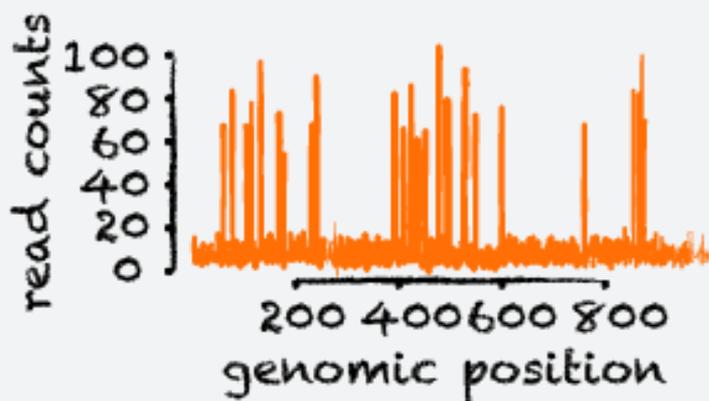






punctuate, H3K4me3

broad, H3K27me3



— sequencing-depth normalization
— normalization based on known background regions

