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Local states of chromatin compaction at transcription start sites control transcription levels.

Chromatin that is generally classified as open or compact is associated with transcription, but individual genes produce their transcripts at various levels. This suggests that transcriptional output is controlled by structural variations in chromatin, rather than a simple open-compact conversion. However, what structure in chromatin is responsible for transcription levels remains elusive. We established a method to fractionate chromatin according to its degree of three-dimensional compaction within several nucleosomes, which is represented as structures higher than nucleosome arrays. Nucleosomes were evenly detected through all of the fractions, but histone H1 was more highly enriched in the more compact chromatin fractions. Similarly, HP1a and MBD2b were more abundant in more compact chromatin, while the levels of tri-methylated histone H3 (Lys9) and 5-methyl cytosine subtly increased. Via genome-wide analyses, nearly the entire genome was found to exist in compact chromatin without variations between repeat and non-repeat sequences; however, active transcription start sites (TSSs) were rarely found in compact chromatin. Based on a correlation between weak compaction and RNA polymerase binding at TSSs, it appears that local states of chromatin compaction determine transcription levels.

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