Veit Schwämmle
Department of Biochemistry and Molecular Biology, University of Southern Denmark, Campusvej 55, DK-5230 Odense M, Denmark
e-mail: veits@bmb.sdu.dk
Kim Sneppen
Center for Models of Life, Niels Bohr Institute, University of Copenhagen, Blegdamsvej 17, 2100 Copenhagen Ø, Denmark
Ole Nørregaard Jensen
Department of Biochemistry and Molecular Biology, University of Southern Denmark, Campusvej 55, DK-5230 Odense M, Denmark

The formation of histone modification domains

Histones proteins are key players in the gene regulation of eukaryotes. Many of their with post-translational modifications decorated isoforms are organized in spatial domains along the DNA string of a chromosome. For instance, a large part of the transcriptionally inactive genome is densely packed and forms large domains. This heterochromatin has its histones modified by methylation of the ninth amino acid (a lysine) of histone type H3 (H3K9me). We propose a simple computer model that simulates the distribution of heterochromatin over the human chromosomes by assuming a competition between H3K9 methylation and H3K4 methylation, the latter being an abundant activating modification. Both marks are related to nucleation sites on the genome and spread from these sites due to simple mechanisms. Furthermore, both marks are mutually exclusive [2] and therefore compete against each other. With this model, we are able to explain why heterochromatin does not occupy the entire chromosomes and could reproduce the distribution measured in the ChIP-seq experiments from [1]. The further extension of the model to a large number of histone modifications allows the simulation of complex switch-like behavior.

References

[1] A. Barski et al., *High-resolution profiling of histone methylations in the human genome.* Cell, **129** 823–837 2007.

[2] K. Nishioka et al., *Set9, a novel histone H3 methyltransferase that facilitates transcription by precluding histone tail modifications required for heterochromatin formation.* Genes Dev. **16** 479–489 2002.