

# Nucleosome dynamics during the expression of the meiotic transcriptional programme in *Schizosaccharomyces pombe*



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## Background

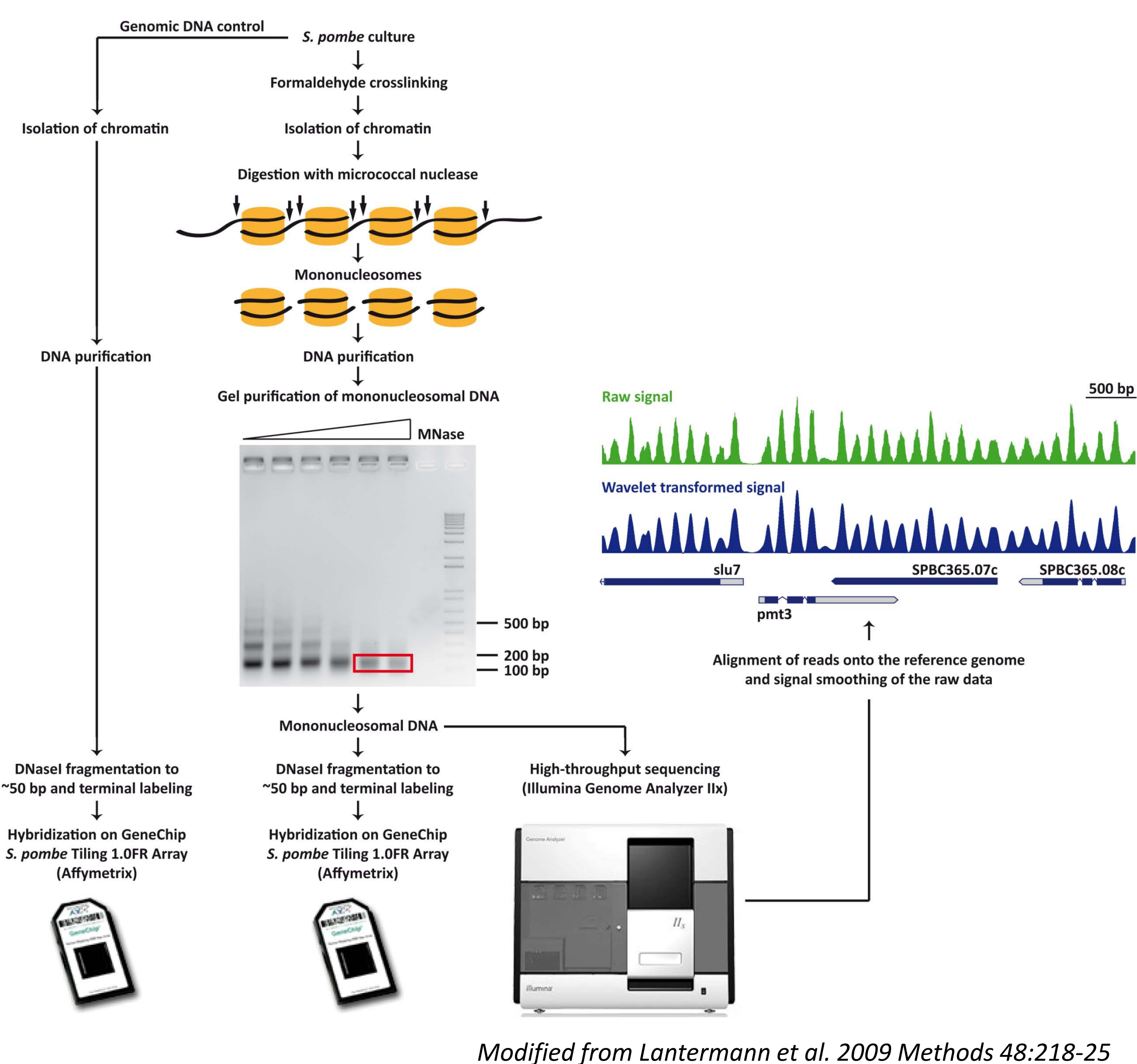
Nucleosomes play an essential role in the management of the eukaryotic genome by facilitating its packaging inside the nucleus. They also regulate basic genomic processes such as transcription, replication and recombination, either directly by controlling the physical access of regulators to DNA or indirectly by modulating their binding through a complex repertoire of histone modifications. Therefore, a detailed description of the nucleosomal organization under different transcriptional programmes is essential to understand their contribution to genomic regulation.

## Aims

To study the extent of nucleosome remodelling in *Schizosaccharomyces pombe*, we have generated high-resolution nucleosome maps to visualize the dynamics of individual nucleosomes during mitosis and meiosis.

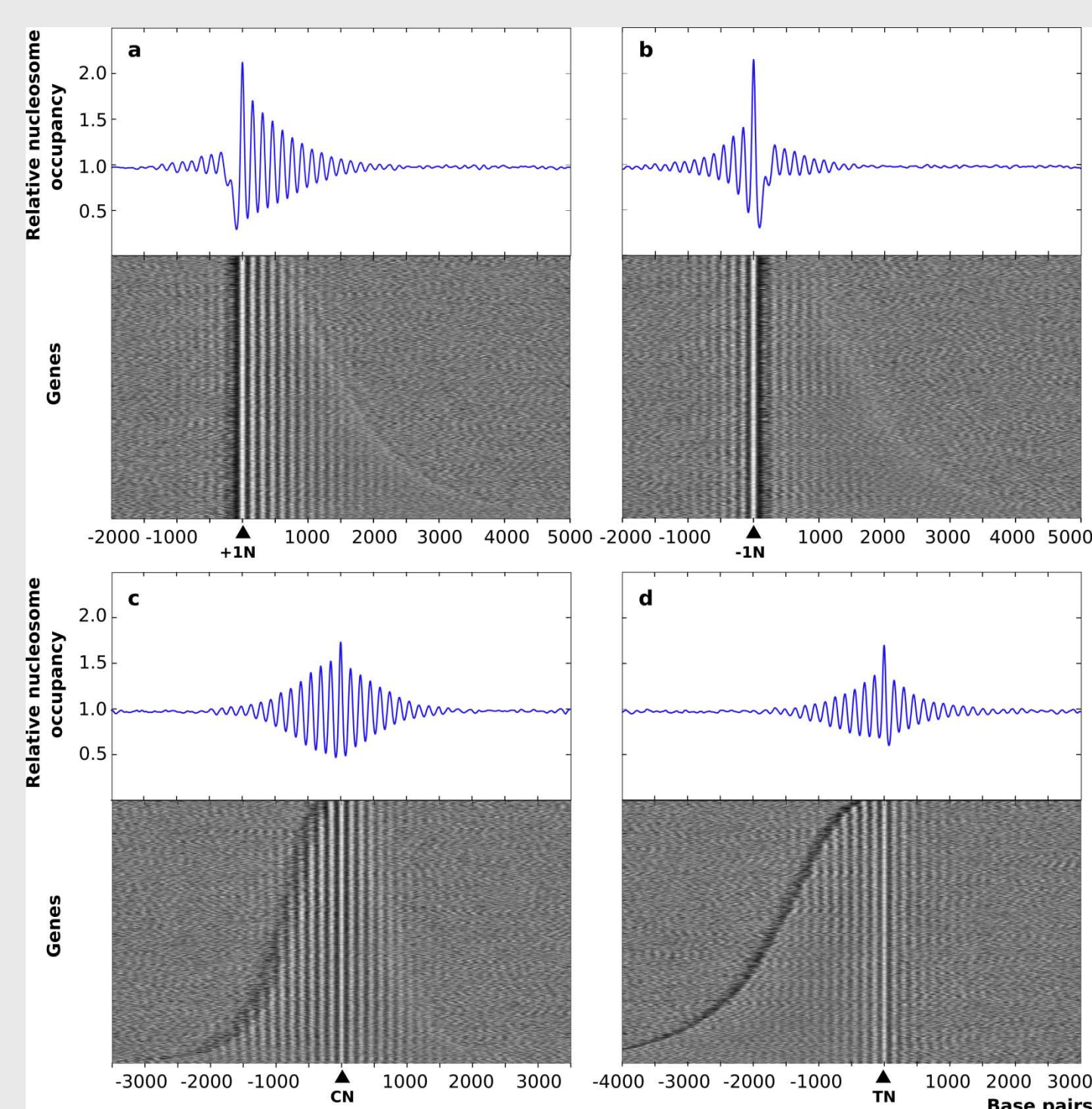
## Methods

### Genome-wide nucleosome mapping



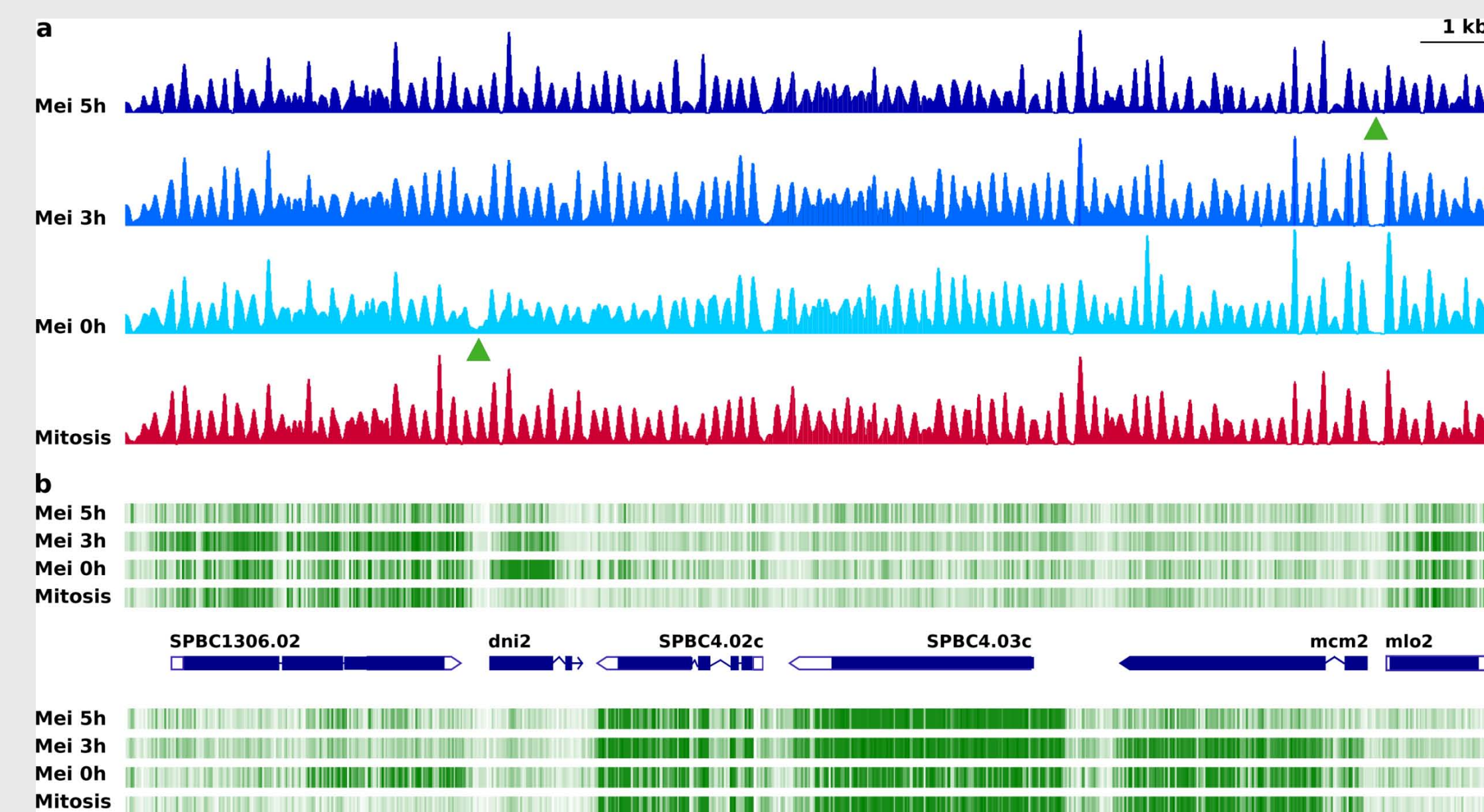
## Results

### Genome-wide nucleosome positioning in *S. pombe*



Nucleosomal arrays are present downstream (a) and upstream (b) from the NDR at the 5' position of the genes. Nucleosomes on the 5' and 3' halves of transcription units are equally positioned (c) and nucleosomal positioning extends beyond the transcription termination site (d).

### Nucleosome dynamics and transcription during mitosis and meiosis

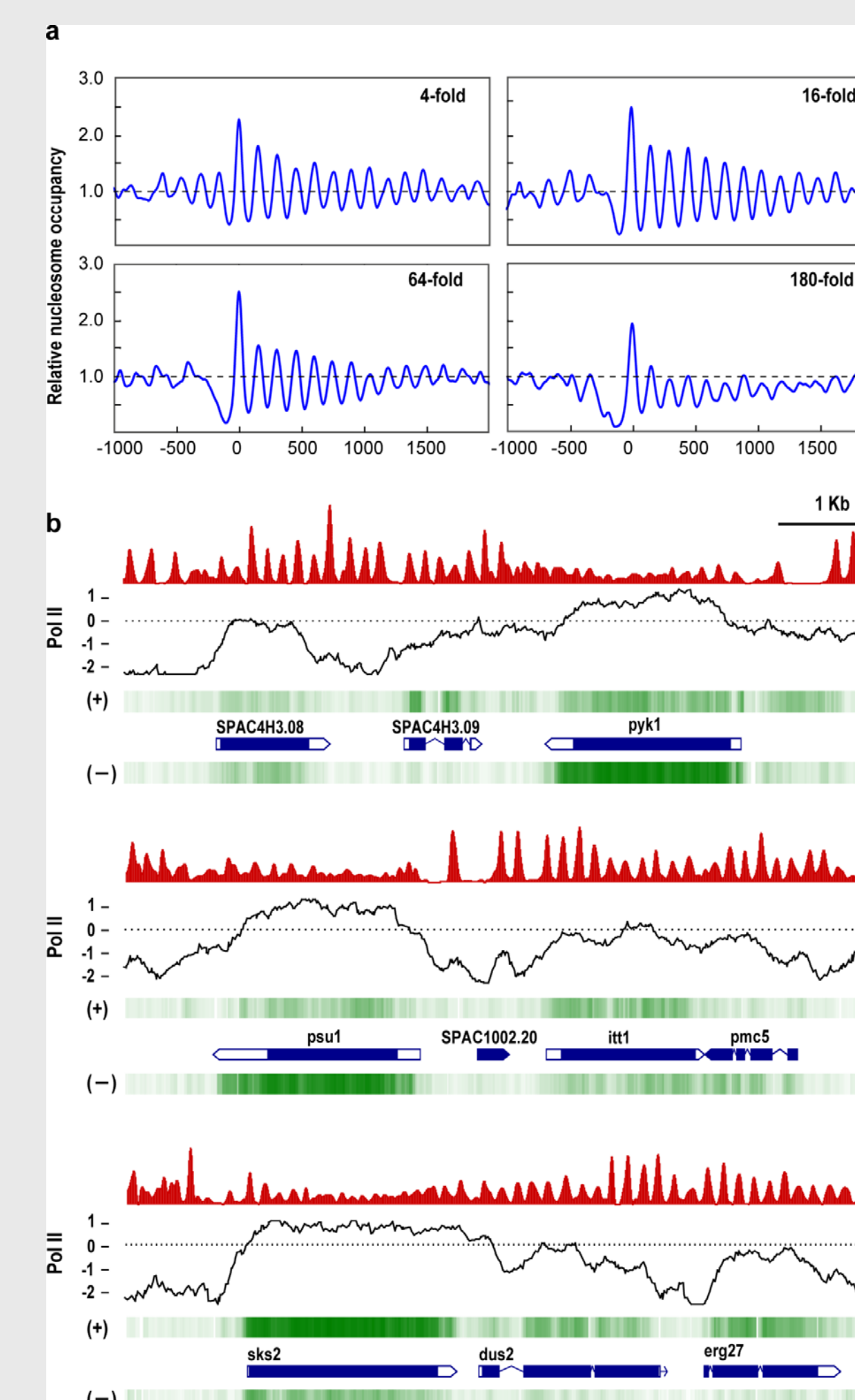


Global transcription analyses (b) revealed nucleosome remodelling at the promoters of genes differentially expressed during meiosis. In general, remodelling was associated with the eviction or appearance of one or two nucleosomes in some promoter regions as in the case of *dni2* and *mcm2/mlo2* genes (a) rather than in long-range changes. We estimate that only 1.5% of the approximately 78000 nucleosomes in the genome are remodelled during the expression of the meiotic transcriptional programme.

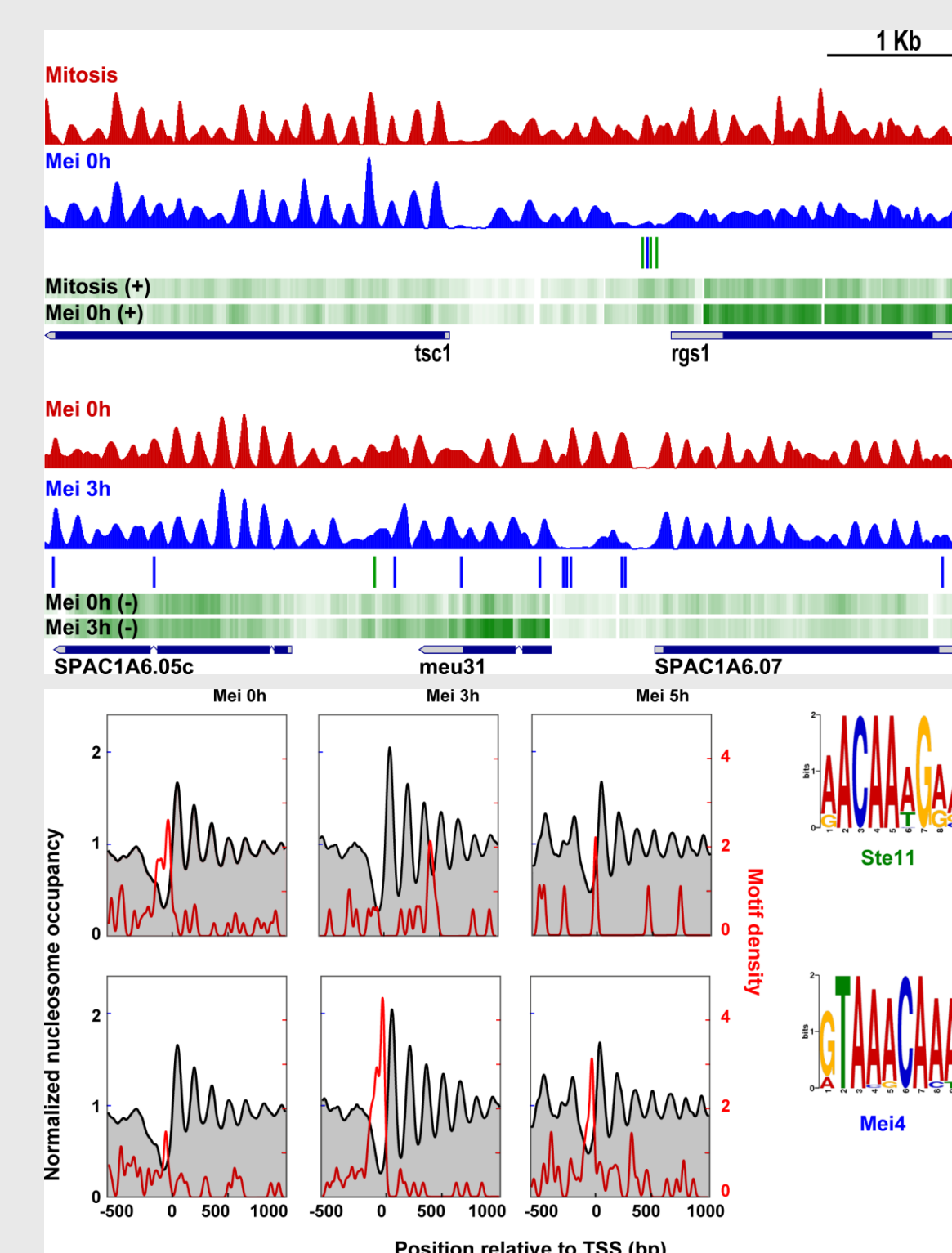
### Nucleosome positioning across differentially transcribed genes

(a) Nucleosome positioning is stably maintained under a wide range of transcription rates. Only in the case of genes expressed over 180-fold above the background (1.2% of all the genes in the genome), the highly organized nucleosomal pattern was disturbed.

(b) This is probably due to a high rate of nucleosome repositioning as a result of the high density of RNA polymerase II molecules (Pol II) traversing the gene. This possibility is supported by the strong correlation between genes expressed at a very high rate, the loss of nucleosome positioning and the high level of RNA polymerase II occupancy. The profile of Pol II occupancy has been reported by Wilhelm et al. (Genome Biol 2011, 12: R82).

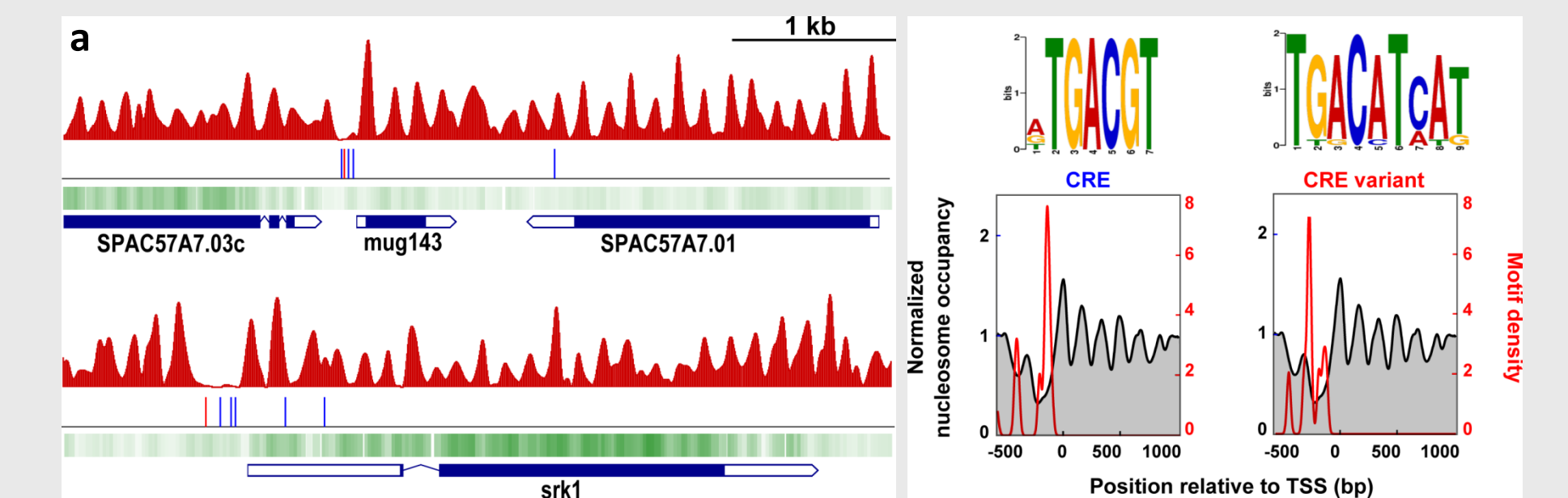


### Meiosis-specific NDRs are enriched in binding sites for meiosis-specific transcription factors

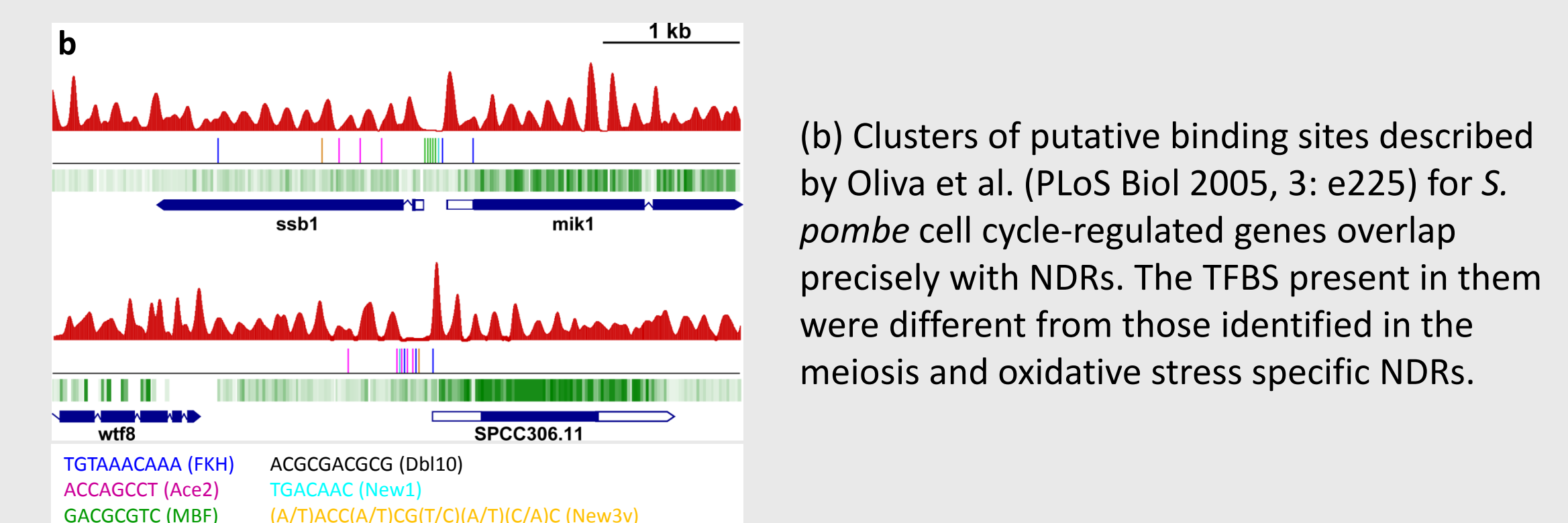


By using the MEME algorithm (Multiple EM for Motif Elicitation), we have found two consensus sequences in the meiosis-specific NDRs of genes specifically transcribed at 0 h, 3 h and 5 h during meiosis. The first of them, AACAAAG[AG]A (green lines), is the binding site for the Ste11 transcription factor and was enriched in the NDRs specific of meiosis at 0 h. However, it was not overrepresented in those specifically generated at 3 and 5 h of meiosis. The second motif, GTAAACAAA (blue lines), is the binding site for the Mei4 transcription factor and, contrary to the Ste11 binding sites, was enriched in the NDRs of genes expressed at 3 h and 5 h but not in those expressed at 0 h.

### NDRs of different functional classes of genes colocalized with clusters of different TFBS

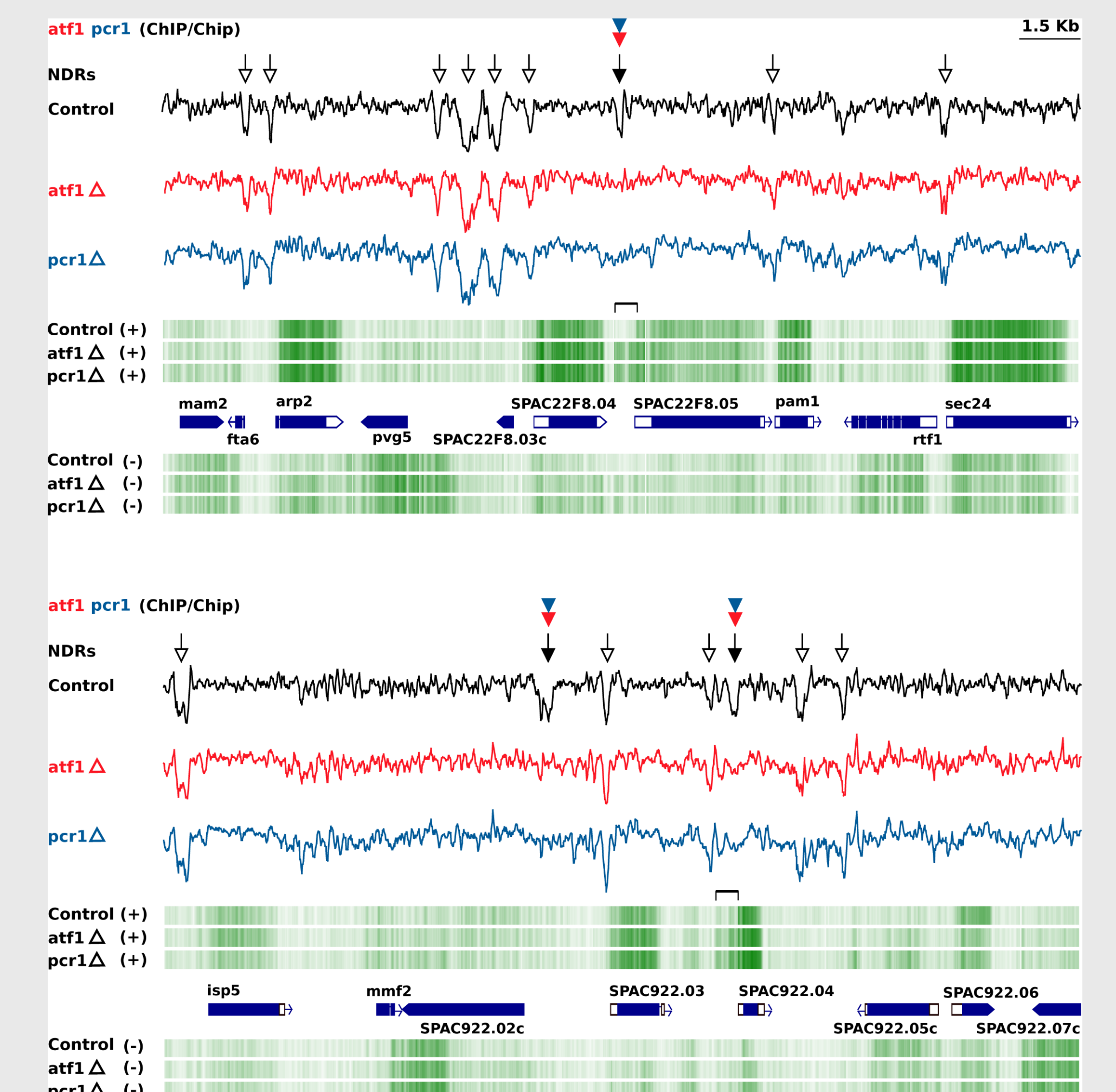


(a) NDRs localized at the promoters of genes showing the highest overexpression under conditions of oxidative stress contained clusters of the consensus CRE (TGACGT) (blue lines) and CRE variant (TGACATCAT) elements (red lines).



(b) Clusters of putative binding sites described by Oliva et al. (PLoS Biol 2005, 3: e225) for *S. pombe* cell cycle-regulated genes overlap precisely with NDRs. The TFBS present in them were different from those identified in the meiosis and oxidative stress specific NDRs.

### Transcription factors are required for the maintenance of NDRs



Deletion analyses of the transcriptional regulators Atf1 and Pcr1 revealed that only a small fraction of all the NDRs to which they bind *in vivo* disappear (as in the cases shown in the figure). This suggests that transcription factors collectively cooperate in the generation of NDRs.

## Conclusions

1. Nucleosome remodelling during meiosis is limited to approximately 1100 nucleosomes (1.5% of the genome) localized at a subset of meiosis-specific genes. The remaining 98.5% of the genome is organized into a pattern of highly positioned nucleosomes that remain virtually invariable under conditions where chromosomes undergo major structural and functional changes.
2. The highly ordered nucleosome pattern across transcribed and intergenic regions is stably maintained under a wide range of transcription rates.
3. Nucleosome-depleted regions (NDRs) at the 5' end of genes overlap precisely with clusters of binding sites for transcription factors specific for different functional classes of genes.