Title	Time resolved chromatin architecture and transcription regulation during the yeast respiratory cycle
Sub Title	酵母の呼吸サイクルにおけるクロマチン構造の経時的変化と転写制御
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Abstract	Cellular rhythms, spanning from fast metabolic oscillators to circadian rhythms, are pervasive in many organisms. Their orchestration, crucial for the maintenance of cellular coherence, is poorly characterized due to difficulties in obtaining high-density time-series data where the cellular state is precisely defined. A system that overcomes these limitations is the continuous culture of Saccharomyces cerevisiae, in which cells auto- synchronize to produce respiratory oscillations that alternate between reductive and oxidative cellular states. This system has been used to investigate the interplay between the redox/energetic state and transcription, metabolite production and DNA replication, which revealed that the oscillation revolves around an alternation of anabolic and catabolic transcriptional programs leading to anabolic and catabolic phenotypes. This thesis investigates the role of chromatin architecture and its dynamics in the regulation of the transcriptional program. Previous datasets were analyzed with new computational tools developed for characterizing periodicities in high-throughput data, and the results pointed to an energy-dependent transcription regulation mechanism mediated by chromatin structure. Through CE-MS analyses of adenylate nucleotides, ChIP-qPCR and tiling array analyses of DNA occupancy, this study shows the existence of a global transcriptional "reset" point between the catabolic and anabolic transcriptional programs, characterized by a global nucleosome focusing event. The highly dynamic DNA occupancy correlates with changes in energy availability rather than transcriptional timing, suggesting that the initiation of anabolic and catabolic genes stems from differential effects of global remodeling events at gene promoters. An analysis of promoter regions revealed that a majority of genes are in close proximity, and many properties of gene transcription, i.e., average expression, noise, nucleosome occupancy, co-expression, correlate with the intergenic distance. These results point to global mechanisms underlying transcription regulation in eukaryotes, where the energetic state regulates global chromatin structure, and differential transcriptional outcomes stem from subtle differences in the promoter architecture.
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Time resolved chromatin architecture and transcription regulation during the yeast respiratory cycle

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Amariei Cornelia

Abstract

Cellular rhythms, spanning from fast metabolic oscillators to circadian rhythms, are pervasive in many organisms. Their orchestration, crucial for the maintenance of cellular coherence, is poorly characterized due to difficulties in obtaining high-density time-series data where the cellular state is precisely defined. A system that overcomes these limitations is the continuous culture of *Saccharomyces cerevisiae*, in which cells auto-synchronize to produce respiratory oscillations that alternate between reductive and oxidative cellular states. This system has been used to investigate the interplay between the redox/energetic state and transcription, metabolite production and DNA replication, which revealed that the oscillation revolves around an alternation of anabolic and catabolic transcriptional programs leading to anabolic and catabolic phenotypes. This thesis investigates the role of chromatin architecture and its dynamics in the regulation of the transcriptional program. Previous datasets were analyzed with new computational tools developed for characterizing periodicities in high-throughput data, and the results pointed to an energy-dependent transcription regulation mechanism mediated by chromatin structure. Through CE-MS analyses of adenylate nucleotides, ChIP-qPCR and tiling array analyses of DNA occupancy, this study shows the existence of a global transcriptional "reset" point between the catabolic and anabolic transcriptional programs, characterized by a global nucleosome focusing event. The highly dynamic DNA occupancy correlates with changes in energy availability rather than transcriptional timing, suggesting that the initiation of anabolic and catabolic genes stems from differential effects of global remodeling events at gene promoters. An analysis of promoter regions revealed that a majority of genes are in close proximity, and many properties of gene transcription, i.e., average expression, noise, nucleosome occupancy, co-expression, correlate with the intergenic distance. These results point to global mechanisms underlying transcription regulation in eukaryotes, where the energetic state regulates global chromatin structure, and differential transcriptional outcomes stem from subtle differences in the promoter architecture.

Keywords: Yeast respiratory cycle • Transcription regulation • Redox oscillation • Chromatin dynamics • Time-series computational analysis