Keio University

Thesis Abstract

No.

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Title of Thesis:

Development of an oscillation detection method and establishment of enzyme characterization system using mass spectrometry data

Summary of Thesis:

The big issue of systems biology is how to extract biological significance in *omics* datasets. In this thesis, I describe an algorithm to detect oscillating molecules in *omics* datasets for the study of circadian rhythms, and enzyme characterization of the orphan enzyme YhhY in *Escherichia coli* (*E. coli*) by mass spectrometry. In Chapter 1, I present a historical overview of research on circadian rhythms and show that it is essential to adopt a systematic approach in the research on circadian rhythms. In Chapter 2, I describe maximal information coefficient-based oscillation prediction (MICOP), which is an oscillation prediction method using mutual information coefficient. Owing to the development of parallel sequencers and mass spectrometers, classical methods are not suitable for *omics* datasets that have a low sampling rate and contain noise. From the results of numerical experiments, I show that MICOP demonstrates excellent performance for data with a low sampling frequency and noise, such as time-series *omics* data. Furthermore, upon the application of MICOP to a plurality of published mouse proteome data, novel oscillating molecules were identified, with the results being shown to be roughly in agreement with the transcriptome results. From these results, I assert that MICOP is an excellent oscillating molecule detection method. In Chapter 3, I describe a functional identification of the *E. coli* function-unknown gene *yhhY*. Although YhhY was predicted to be an acetyltransferase from its amino acid sequence, identification of the substrate and the obtainment of experimental proof of its function have not been conducted. Therefore, in this study, I aimed to clarify the function of YhhY by combining biochemical experiments and metabolome analysis using a mass spectrometer. The results suggested that YhhY is an enzyme that specifically acetylates some essential amino acids and that it is involved in metal stress *in vivo*. Finally, in Chapter 4, I summarize the contents of this paper.

Keywords

circadian rhythms, time-series data, mass spectrometry, YhhY