



GRADUATE SCHOOL OF BIOMEDICAL SCIENCES BIOINFORMATICS AND COMPUTATIONAL BIOLOGY

Ph.D. THESIS DEFENSE

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MENTOR: Job Dekker, PhD

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"Computational approaches for analysis of chromosome conformation capture data and their application to study long-range gene regulation"

Over the last decade, development and application of a set of molecular genomic approaches based on the chromosome conformation capture method (3C), combined with increasingly powerful imaging approaches have enabled high resolution and genome-wide analysis of the spatial organization of chromosomes. The aim of this thesis is two-fold; 1), to provide guidelines for analyzing and interpreting data obtained from genome-wide 3C methods such as Hi-C and 3C-seq and 2), to leverage the 3C technology to solve genome function, structure, assembly, development and dosage problems across a broad range of organisms and disease models.

First, through the introduction of cWorld, a toolkit for manipulating genome structure data, I accelerate the pace at which *C experiments can be performed, analyzed and biological insights inferred. Next I discuss a set of practical guidelines one should consider while planning an experiment to study the structure of the genome, a simple workflow for data processing unique to *C data and a set of considerations one should be aware of while attempting to gain insights from the data.

Next, I apply these guidelines and leverage the cWorld toolkit in the context of two dosage compensation systems. The first is a worm condensin mutant which shows a reduction in dosage compensation in the hermaphrodite X chromosomes. The second is an allele-specific study consisting of genome wide Hi-C, RNA-Seq and ATAC-Seq which can measure the state of the active (Xa) and inactive (Xi) X chromosome. Finally I turn to studying specific gene – enhancer looping interactions across a panel of ENCODE cell-lines.

These studies, when taken together, further our understanding of how genome structure relates to genome function.

Mentor(s)

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