

**Stony Brook University  
The Graduate School**

**Doctoral Defense Announcement**

**Abstract**

Temporal and spatial regulation of the *Caenorhabditis elegans lin-4* microRNA gene

By

**Kelly Hills-Muckey**

Development is a stepwise process that is controlled by gene regulatory networks (GRNs) that generate sequential patterns of cell divisions and execute these programs at the appropriate times. In *Caenorhabditis elegans* (*C. elegans*), development progresses through four larval stages (L1-L4) where stage-specific patterns of cell division and cell fate are established in order. Transitions between patterns of development are mediated by the sequential expression of multiple microRNAs (miRNAs) that function in dosage-dependent fashions as “molecular switches” to repress the expression of temporal selector genes.

We show that the dosage of *C. elegans* miRNA *lin-4* is controlled, temporally and spatially, through a combinatorial mechanism involving shadow enhancers and repetitive transcriptional cycles. More specifically, we show that these shadow enhancers regulate the amplitude of expression in a spatially restricted manner directly through modulating the duration of the transcriptional period. Through analysis of transcriptional patterns and modeling of expression dynamics of *lin-4* miRNAs, we suggest that *lin-4* functions across development to regulate the sequential down-regulation of multiple developmental targets in a manner analogous to the function of morphogens that control spatial gene regulation. Like the spatial gradients establishing body plan in *Drosophila* development, *lin-4* establishes a temporal gradient to set the temporal plan of *C. elegans* development. It is likely that different transcription factors function through the enhancer elements to establish this temporal gradient in a tissue specific manner and that each larval stage contains different targets for *lin-4*.

**Date:** May 03, 2022

**Program:** Genetics

**Time:** 1:30 PM

**Dissertation Advisor:** Christopher Hammell

**Place:** Plimpton Conference Room, Beckman Building, Cold Spring Harbor Laboratory