

UNIVERSITY OF CALIFORNIA SAN DIEGO

Transcriptomic Analysis of Human Neurodevelopment

A thesis submitted in partial satisfaction of the requirements
for the degree Master of Science

in

Biology

by

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The thesis of Kevin Khai Chau is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

Co-Chair

Chair

University of California San Diego

2019

DEDICATION

To two, the loneliest number since the number one.

EPIGRAPH

*A careful quotation
conveys brilliance.*
—Smarty Pants

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Thanks to whoever deserves credit for Blacks Beach, Porters Pub, and every coffee shop in San Diego.

Thanks also to hottubs.

VITA

2002	B. S. in Mathematics <i>cum laude</i> , University of Southern North Dakota, Hoople
2002-2007	Graduate Teaching Assistant, University of California, San Diego
2007	Ph. D. in Mathematics, University of California, San Diego

PUBLICATIONS

Your Name, “A Simple Proof Of The Riemann Hypothesis”, *Annals of Math*, 314, 2007.

Your Name, Euclid, “There Are Lots Of Prime Numbers”, *Journal of Primes*, 1, 300 B.C.

ABSTRACT OF THE DISSERTATION

Transcriptomic Analysis of Human Neurodevelopment

by

Kevin Khai Chau

Master of Science in Biology

University of California San Diego, 2019

Professor Lilia Iakoucheva, Chair
Professor Scott Rifkin, Co-Chair

This dissertation will be abstract.

Chapter 1

Transcriptomic Analysis of Human Neurodevelopment

1.1 Background

Alternative splicing is the process by which the exons of a single gene may be differentially included or excluded in distinct mRNA transcripts to give rise to a plurality of distinct products. It is well known that much of the diversity in eukaryotic biology can be attributed to this alternative splicing of mRNA transcripts, and studies of high-throughput sequencing have shown 95-100% of human pre-mRNAs encompassing more than a single exon are processed to yield multiple mature mRNAs [1, 2]. The differential regulation and production of alternatively spliced mRNA transcripts can also be dictated by spatial or temporal cues, such as tissue specificity or developmental periods, respectively [3, 4], with the brain exhibiting higher numbers of alternative splicing events relative to other tissues[1, 5, 6].

While the specific functions of individual alternatively spliced isoforms are largely unexplored, these may be inferred through the use of isoform co-expression networks under the idea that, although co-regulation of a pair of isoforms may not necessarily imply that they are

related, large sets of isoforms that are co-expressed in a similar manner are likely to be enriched in a central function [7, 8].

1.2 Results

1.3 Materials and Methods

All analyses were performed using R version $\geq 3.5.1$. False discovery rate (FDR) adjustment was used to correct for multiple hypothesis testing with a significance threshold of 0.05.

1.3.1 Pre-processing of RNA-Seq data

We downloaded RNA-Seq quantification data from the BrainSpan Atlas of the Developing Human Brain [CITATION]. This resource consists of both gene-level and isoform-level counts and TPM matrices, with samples derived from post-mortem brain tissue from 57 donors aged between 8 weeks post-conception through 40 years, across a number of different brain regions, for a total of 606 initial samples. These matrices were filtered by applying a filter of $\text{TPM} \geq 0.1$ in at least 25% of samples in both data sets; we further restricted the data to only include genes with at least one retained isoform per the isoform-level filter and vice-versa.

1.3.2 Normalization and differential expression analysis

To normalize the isoform counts data for between-sample comparability, we first performed surrogate variable analysis to detect latent batch effects [CITATION], relying on evidence from a combination of principal components analysis, relative log expression and p-value distribution visualizations to determine the number of surrogate variables that minimizes latent batch

effects while avoiding the problem of overfitting (see figure []). Here, we proposed to use 11 surrogate variables for downstream analysis

Differential expression analysis of normalized isoform counts data was performed using the *limma* R package.

1.4 Discussion

Chapter 2

Single-Cell RNA-Seq of Mouse Models

something

2.1 16p11.2

2.2 Cul3 Knockout Mice

Chapter 3

Just a Test

This is only a test.

3.1 A section

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Nulla odio sem, bibendum ut, aliquam ac, facilisis id, tellus. Nam posuere pede sit amet ipsum. Etiam dolor. In sodales eros quis pede. Quisque sed nulla et ligula vulputate lacinia. In venenatis, ligula id semper feugiat, ligula odio adipiscing libero, eget mollis nunc erat id orci. Nullam ante dolor, rutrum eget, vestibulum euismod, pulvinar at, nibh. In sapien. Quisque ut arcu. Suspendisse potenti. Cras consequat cursus nulla.

3.1.1 A Figure Example

This subsection shows a sample figure.

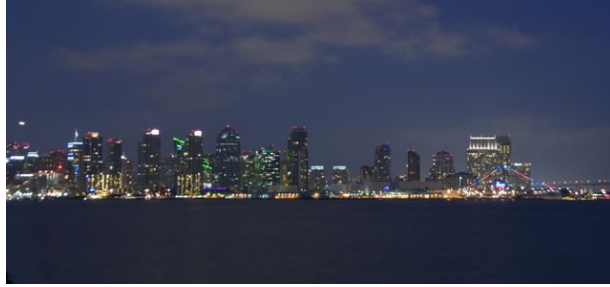


Figure 3.1: A picture of San Diego. Short figure caption must be < 4 lines in the list of figures and match the start of the main figure caption verbatim. Note that figures must be on their own line (no neighboring text) and captions must be single-spaced and appear *below* the figure. Captions can be as long as you want, but if they are longer than 4 lines in the list of figures, you must provide a short figure caption.

3.1.2 A Table Example

While in Section 3.1.1 Figure 3.1 we had a majestic figure, here we provide a crazy table example.

Table 3.1: A table of when I get hungry. Short table caption must be < 4 lines in the list of tables and match the start of the main table caption verbatim. Note that tables must be on their own line (no neighboring text) and captions must be single-spaced and appear *above* the table. Captions can be as long as you want, but if they are longer than 4 lines in the list of figures, you must provide a short figure caption.

Time of day	Hunger Level	Preferred Food
8am	high	IHOP (French Toast)
noon	medium	Croutons (Tomato Basil Soup & Granny Smith Chicken Salad)
5pm	high	Bombay Coast (Saag Paneer) or Hi Thai (Pad See Ew)
8pm	medium	Yogurt World (froyo!)

Appendix A

Final notes

Remove me in case of abdominal pain.

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