

UNIVERSITY COLLEGE LONDON

UPGRADE REPORT

Deep learning and genome-wide analysis to identify novel mechanisms in diabetic retinopathy progression

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*A report submitted in fulfillment of the requirements for upgrading to
candidate status for the degree of Doctor of Philosophy*

in the

Institute for Global Health



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Declaration of Authorship

I, Rolando Silva Jorquera, declare that this thesis titled, Deep learning and genome-wide analysis to identify novel mechanisms in diabetic retinopathy progression and the work presented in it are my own. I confirm that:

- This work was done wholly or mainly while in candidature for a research degree at this University.
- Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated.
- Where I have consulted the published work of others, this is always clearly attributed.
- Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work.
- I have acknowledged all main sources of help.
- Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself.

Signed:

Date:

“Thanks to my solid academic training, today I can write hundreds of words on virtually any topic without possessing a shred of information, which is how I got a good job in journalism.”

Dave Barry

UNIVERSITY COLLEGE LONDON

Abstract

Faculty of Population Health Sciences

Institute for Global Health

Doctor of Philosophy

Deep learning and genome-wide analysis to identify novel mechanisms in diabetic retinopathy progression

by Rolando Silva Jorquera

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam quis accumsan ante. Quisque lorem metus, varius id urna eget, lacinia dapibus sem. Etiam laoreet, quam ac mollis congue, arcu leo dictum neque, nec euismod sem enim luctus odio. Donec condimentum tortor sit amet mollis volutpat. Donec ornare libero vel velit malesuada consectetur. Vestibulum in sem non justo dignissim congue at quis erat. Integer quis erat vitae mi maximus fringilla tristique nec odio. Morbi non ipsum sapien. Vestibulum tortor est, ultricies in eros et, bibendum iaculis justo. Cras pellentesque enim quam, id pretium lacus lacinia non. Integer velit neque, ultrices a malesuada vel, imperdiet quis enim. Quisque eu facilisis urna, ut faucibus lorem. Donec mollis turpis sed arcu venenatis interdum. Nulla facilisis tortor ac scelerisque consequat.

Acknowledgements

Integer id risus vel lorem laoreet commodo lobortis quis purus. Cras cursus leo vel dui laoreet pulvinar. Nunc tincidunt metus et ante fermentum lacinia. Proin quam magna, tristique ut viverra at, dapibus eget elit. Quisque eu leo id nisi semper laoreet at ac nulla. Fusce volutpat, metus sed dictum mattis, nisl elit dapibus velit, non porttitor urna urna vel diam. Praesent tortor nulla, rutrum ac magna a, tempor sagittis enim. Praesent pharetra ipsum libero, eu malesuada libero blandit ut. Sed sed venenatis ligula, nec convallis turpis. Nulla iaculis felis eros, eget pharetra lorem cursus quis. Nunc iaculis lobortis magna at malesuada. Nullam elementum elit at urna congue aliquam.

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List of Abbreviations

LAH List Abbreviations **H**ere
WSF **W**hat (it) **S**tands **F**or

List of Symbols

a	distance	m
P	power	W (J s ⁻¹)
ω	angular frequency	rad

For Elsa

Chapter 1

Chapter 1 Title

1.1 Welcome and Thank You

Welcome to this L^AT_EX Thesis Template, using the L^AT_EX typesetting system and **Quarto** and based on the L^AT_EX thesis template MastersDoctoralThesis version 2.0 downloaded from **LaTeXTemplates**. This LaTeX document class was authored by Vel (vel@latextemplates.com) and Johannes Böttcher based on a style file by Steve R. Gunn from the University of Southampton (UK), department of Electronics and Computer Science.

1.2 A Short Math Guide for L^AT_EX

If you are writing a technical or mathematical thesis, then you may want to read the document by the AMS (American Mathematical Society) called, **A Short Math Guide for L^AT_EX**. It can be found online at [AMS] (<http://www.ams.org/tex/amslatex.html>) under the "Additional Documentation" section towards the bottom of the page.

1.2.1 Common L^AT_EX Math Symbols

There are a multitude of mathematical symbols available for L^AT_EX and it would take a great effort to learn the commands for them all. The most common ones you are likely to use are shown on **this page**.

You can use this page as a reference or crib sheet, the symbols are rendered as large, high quality images so you can quickly find the L^AT_EX command for the symbol you need.

1.3 About this Template

This L^AT_EX Thesis Template is originally based and created around a L^AT_EX style file created by Steve R. Gunn from the University of Southampton (UK), department of Electronics and Computer Science. You can find his original thesis style file at his site, here: <http://www.ecs.soton.ac.uk/~srg/softwaretools/document/templates/>.

Steve's `ecsthesis.cls` was then taken by Sunil Patel who modified it by creating a skeleton framework and folder structure to place the thesis files in. The resulting template can be found on Sunil's site here: <http://www.sunilpatel.co.uk/thesis-template>.

Sunil's template was made available through **LaTeXTemplates** where it was modified many times based on user requests and questions. Version 2.0 and onwards of this template represents a major modification to Sunil's template and is, in fact,

hardly recognisable. The work to make version 2.0 possible was carried out by Vel (vel@latextemplates.com) and Johannes Böttcher.

1.4 What this Template Includes

1.4.1 Folders

- Appendices – this is the folder where you put the appendices. Each appendix should go into its own separate qmd file. An example and template are included in the directory.
- Chapters – this is the folder where you put the thesis chapters. Each chapter should go in its own separate qmd file.
- Figures – this folder contains static figures for the thesis, i.e. figures that are not generated by code in the chapters.

1.4.2 Files

- example.bib – this is file that contains all the bibliographic information and references that you will be citing in the thesis for use with BibTeX. You can write it manually, but there are reference manager programs available that will create and manage it for you. Zotero is popular and integrates with RStudio IDE if you use that.
- MastersDoctoralThesis.cls – this is the class file that tells L^AT_EX how to format the thesis.
- pdf in docs folder – this is your typeset thesis.
- Frontmater folder – this has the files for the various front matter elements.

1.5 Filling in Your Information

Most of the personal information is found on in the `_quarto.yml` file.

- author – you; optionally add url
- supervisor – your supervisor; optionally add url.
- university – your university
- department – your department
- faculty – faculty name
- group – research group name (optional)
- abstract

1.6 The `tex\before-body.tex` File Explained

The `tex\before-body.tex` file contains the structure of the thesis and is a mix of Pandoc template and L^AT_EX code. The bits that look like `$book.university$` say are Pandoc and are referencing variables in the `_quarto.yml` file. Knowing that, you should be able to figure out what is happening.

There are plenty of written comments that explain what pages, sections and formatting the L^AT_EX code is creating. Each major document element is divided into commented blocks with titles in all capitals to make it obvious what the following

bit of code is doing. Initially there seems to be a lot of L^AT_EX code, but this is all formatting, and it has all been taken care of so you don't have to do it.

Many of the sections have `$if(...)$` so that the section is only included if you included information for that in `_quarto.yml`.

In the `_quarto.yml`, `pdf: toc: false` is used so that Quarto/Pandoc doesn't add a table of contents. This template puts the table of contents before the abbreviations and symbols pages and Quarto/Pandoc doesn't let us control where it puts the table of contents. So we have to add the TOC manually for pdf and pass in `toc: false`.

The list of figures and tables are all taken care of for you and do not need to be manually created or edited. The next set of pages are more likely to be optional and can be deleted since they are for a more technical thesis: insert a list of abbreviations you have used in the thesis, then a list of the physical constants and numbers you refer to and finally, a list of mathematical symbols used in any formulae. Making the effort to fill these tables means the reader has a one-stop place to refer to instead of searching the internet and references to try and find out what you meant by certain abbreviations or symbols.

The list of symbols is split into the Roman and Greek alphabets. Whereas the abbreviations and symbols ought to be listed in alphabetical order (and this is **not** done automatically for you) the list of physical constants should be grouped into similar themes.

The next page contains a one line dedication. Who will you dedicate your thesis to?

1.7 Adding Your Chapters and Appendices

Add your chapters and appendices to `_quarto.yml`. Note that the spacing is important as is the leading `-`.

1.8 Bibliography and Citations

Citations will be added and formatted automatically for you.

If you use the RStudio IDE, then you can link Zotero to RStudio and Quarto will find your citations for you when you enter `@`. This is in the visual editor mode. Make sure to search for videos on how to do this as using Zotero libraries will make your citation and bibliography management much much easier.

In the text use `@smith2000` to produce Smith (2000) add use `[@smith2000, @jones1999]` to produce (Smith 2000; Jones 1999). See the natbib cheatsheet for how to do other types of formatting for your in text citations. The bibliography style (`classoption: "authoryear"`) is used for the bibliography and is a fully featured style that will even include links to where the referenced paper can be found online.

1.8.0.1 A Note on bibtex

The bibtex backend used in the template by default does not correctly handle unicode character encoding (i.e. "international" characters). You may see a warning about this in the compilation log and, if your references contain unicode characters, they may not show up correctly or at all. One solution to this is to use the biber backend instead of the outdated bibtex backend. This is done by finding this in `tex/in-header.tex`:

`backend=bibtex` and changing it to `backend=biber`. Google a bit to find information on this.

1.9 Thesis Features and Conventions

To get the best out of this template, there are a few conventions that you may want to follow.

1.9.1 Printing Format

This thesis template is designed for double sided printing (i.e. content on the front and back of pages) as most theses are printed and bound this way. Switching to one sided printing is as simple as adding `"oneside"` to `classoptions:` in the `_quarto.yml` file. The headers for the pages contain the page number on the outer side (so it is easy to flick through to the page you want) and the chapter name on the inner side.

The text is set to 11 point by default with single line spacing, again, you can tune the text size and spacing should you want or need to using the class options. The spacing can be changed similarly by replacing the `"singlespacing"` with `"onehalfspacing"` or `"doublespacing"` in the class options.

1.9.2 Using US Letter Paper

The paper size used in the template is A4, which is the standard size in Europe. If you are using this thesis template elsewhere and particularly in the United States, then you may have to change the A4 paper size to the US Letter size. This can be by editing `geometry:` in `_quarto.yml` in the pdf format section.

1.10 Tables

When you render your Quarto thesis to PDF, it will process \LaTeX table code just fine. However, if you are doing that, I am guessing you would be writing your thesis in \LaTeX not Quarto. So I will not discuss \LaTeX tables. Instead here is how you create tables using R. Python and Julia users, you'll have your own table packages but the idea will be similar.

```
```{r}
#| label: tbl-cars
#| tbl-cap: This is my caption.
knitr::kable(head(mtcars))
```
```

The `#|` is what sets up our cross-references and you can then reference the table as `@tbl-cars`. Note in order for table numbering to work in Quarto, you **must** label your tables with the `tbl-` prefix.

TABLE 1.1: This is my caption.

| | mpg | cyl | disp | hp | drat | wt | qsec | vs | am | gear | carb |
|-----------|------|-----|------|-----|------|-------|-------|----|----|------|------|
| Mazda RX4 | 21.0 | 6 | 160 | 110 | 3.90 | 2.620 | 16.46 | 0 | 1 | 4 | 4 |

| | mpg | cyl | disp | hp | drat | wt | qsec | vs | am | gear | carb |
|------------|------|-----|------|-----|------|-------|-------|----|----|------|------|
| Mazda RX4 | 21.0 | 6 | 160 | 110 | 3.90 | 2.875 | 17.02 | 0 | 1 | 4 | 4 |
| Wag | | | | | | | | | | | |
| Datsun 710 | 22.8 | 4 | 108 | 93 | 3.85 | 2.320 | 18.61 | 1 | 1 | 4 | 1 |
| Hornet 4 | 21.4 | 6 | 258 | 110 | 3.08 | 3.215 | 19.44 | 1 | 0 | 3 | 1 |
| Drive | | | | | | | | | | | |
| Hornet | 18.7 | 8 | 360 | 175 | 3.15 | 3.440 | 17.02 | 0 | 0 | 3 | 2 |
| Sportabout | | | | | | | | | | | |
| Valiant | 18.1 | 6 | 225 | 105 | 2.76 | 3.460 | 20.22 | 1 | 0 | 3 | 1 |

This is Table 1.1.

See the Quarto manual for full examples and instructions.

1.11 Figures

Again we write in Quarto (markdown) not \LaTeX for our figures. You can write in \LaTeX if you really want but it would only be interpreted for the PDF output.

```
```{r}
#| label: fig-cars
#| fig-cap: This is my caption.
plot(mtcars[,1:4])
```
```

The `#|` is what sets up our cross-references and you can then reference the table as `@fig-cars`.

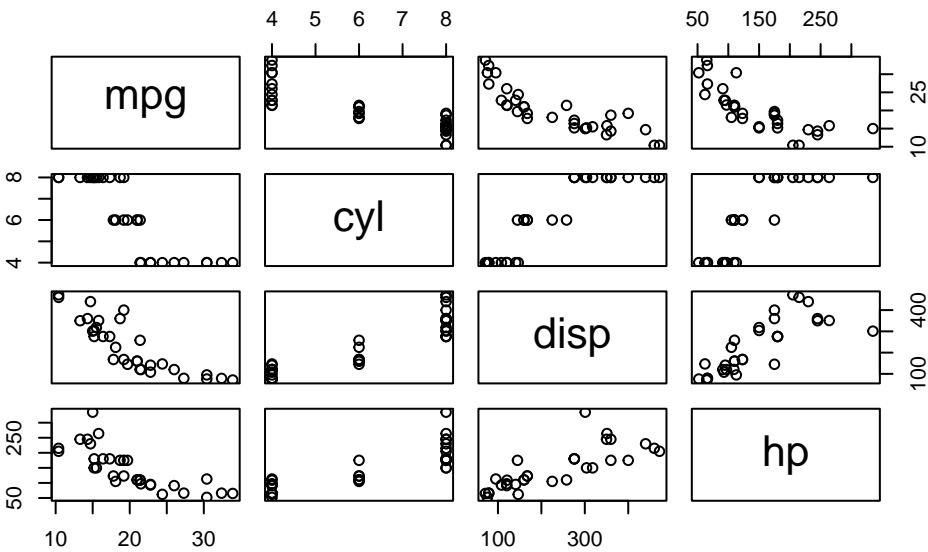


FIGURE 1.1: This is my caption.

This is Figure 1.1.

See the Quarto manual for full examples and instructions.

1.11.1 Typesetting mathematics

If your thesis is going to contain heavy mathematical content, \LaTeX will make it look beautiful, for HTML or PDF output.

The [Not So Short Introduction to LaTeX](#) should tell you everything you need to know for most cases of typesetting mathematics. If you need more information, a much more thorough mathematical guide is available from the AMS called, [A Short Math Guide to LaTeX](#).

1.12 In Closing

Good luck and have lots of fun!

This guide was written originally by

Sunil Patel: [{www.sunilpatel.co.uk}](http://www.sunilpatel.co.uk)

and Vel: <http://www.LaTeXTemplates.com>

and heavily shortened and adapted for [Quarto](#) by [Eli Holmes](#).

Chapter 2

Chapter 2 Title

2.1 Main Section 1

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam ultricies lacinia euismod. Nam tempus risus in dolor rhoncus in interdum enim tincidunt. Donec vel nunc neque. In condimentum ullamcorper quam non consequat. Fusce sagittis tempor feugiat. Fusce magna erat, molestie eu convallis ut, tempus sed arcu. Quisque molestie, ante a tincidunt ullamcorper, sapien enim dignissim lacus, in semper nibh erat lobortis purus. Integer dapibus ligula ac risus convallis pellentesque.

$$\int_{A_i} \lambda(\boldsymbol{\mu}) \quad (2.1)$$

$$\int_{A_i} \lambda(\mathbf{x}) \quad (2.2)$$

2.1.1 Subsection 1

Nunc posuere quam at lectus tristique eu ultrices augue venenatis. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Aliquam erat volutpat. Vivamus sodales tortor eget quam adipiscing in vulputate ante ullamcorper. Sed eros ante, lacinia et sollicitudin et, aliquam sit amet augue. In hac habitasse platea dictumst.

2.1.2 Subsection 2

Morbi rutrum odio eget arcu adipiscing sodales. Aenean et purus a est pulvinar pellentesque. Cras in elit neque, quis varius elit. Phasellus fringilla, nibh eu tempus venenatis, dolor elit posuere quam, quis adipiscing urna leo nec orci. Sed nec nulla auctor odio aliquet consequat. Ut nec nulla in ante ullamcorper aliquam at sed dolor. Phasellus fermentum magna in augue gravida cursus. Cras sed pretium lorem. Pellentesque eget ornare odio. Proin accumsan, massa viverra cursus pharetra, ipsum nisi lobortis velit, a malesuada dolor lorem eu neque.

2.2 Main Section 2

Sed ullamcorper quam eu nisl interdum at interdum enim egestas. Aliquam placerat justo sed lectus lobortis ut porta nisl porttitor. Vestibulum mi dolor, lacinia molestie gravida at, tempus vitae ligula. Donec eget quam sapien, in viverra eros. Donec

pellentesque justo a massa fringilla non vestibulum metus vestibulum. Vestibulum in orci quis felis tempor lacinia. Vivamus ornare ultrices facilisis. Ut hendrerit volutpat vulputate. Morbi condimentum venenatis augue, id porta ipsum vulputate in. Curabitur luctus tempus justo. Vestibulum risus lectus, adipiscing nec condimentum quis, condimentum nec nisl. Aliquam dictum sagittis velit sed iaculis. Morbi tristique augue sit amet nulla pulvinar id facilisis ligula mollis. Nam elit libero, tincidunt ut aliquam at, molestie in quam. Aenean rhoncus vehicula hendrerit.

References

Appendix A

Frequently Asked Questions

A.1 How do I change the colors of links?

Pass in `urlcolor:` in yaml. Or set these in the include-in-header file.

If you want to completely hide the links, you can use:

`{\hypersetup{allcolors=.}}`, or even better:

`{\hypersetup{hidelinks}}`.

If you want to have obvious links in the PDF but not the printed text, use:

`{\hypersetup{colorlinks=false}}`.