

THE BEST UNDERGRADUATE THESIS EVER! AND HERE IS
WHAT HAPPENS WHEN ITS TITLE IS LONG

by

My name goes here

January 29, 2010

A thesis

presented to the Department of Physics

in partial fulfillment of the

requirements for the degree of

Bachelor of Science

in the Program of

Medical Physics

at Ryerson University

Toronto, Ontario, Canada, 2010

© My name goes here 2010

Supervisor: Dr. Strangelove

Abstract

This is my wonderful abstract. I really like my abstract because it's so pretty. I've made sure it's less than 250 words, I've not included any references in it and if I really had to use symbols in my abstract I'd be sure to also explain right here what they stand for because I'm such a good student and I know all the thesis rules.

Acknowledgements

Many people have contributed to my work here at Ryerson University. First I thank my supervisor Dr. Strangelove for guiding my research, as well as providing many helpful suggestions throughout my time here. I would like to acknowledge the Natural Sciences and Engineering Research Council for providing funding for this work.

To

*my dog fluffy whom I love so very much, and my parents
too, I guess.*

Table of Contents

- 1 Introduction** **1**
 - 1.1 Background 1
 - 1.2 Goal 1

- 2 Materials and methods** **5**
 - 2.1 Example of a section 5
 - 2.1.1 Example of a subsection 5
 - 2.1.2 My alternate subsection title 5

- 3 Results and discussion** **7**
 - 3.1 Mathematical models of virus dynamics 7
 - 3.2 Shape of the viral titer curve 7

- 4 Conclusion** **9**

- A The title of my first appendix** **10**
 - A.1 The first section of my appendix 10
 - A.1.1 An appendix subsection if required 10

- B The second appendix chapter** **11**
 - B.1 A section in my second appendix chapter 11
 - B.1.1 Just making sure it all works 11

Bibliography	12
Glossary	14

List of Tables

3.1 Parameters used in our model.	8
---	---

List of Figures

3.1 Example figure file	8
-----------------------------------	---

Chapter 1

Introduction

1.1 Background

Although a wide body of knowledge exists for the study of novel, highly virulent influenza viruses, the reasons for the severity of these viruses are not well understood. In particular, while mathematical models have been developed to study the within-host dynamics of seasonal influenza viruses [1,2,5–7], no models have attempted to explain the underlying mechanisms which can bring about an increase in disease severity in some viral strains.

In this thesis, mathematical modelling is used to explore the effect of influenza infection within a population of cells containing two different types of cells. In Chapter 2, the biology of the influenza A virus will be discussed, including highly virulent influenza strains, such as the H5N1 strain, and the potential role differential cell tropism plays in disease severity. In Chapter 3, we use a mathematical model to test the hypothesis that cell tropism is sufficient to explain the increased severity of infection caused by certain strains of the influenza virus. It is shown that this model can lead to long-lasting influenza infections characterised by high viral loads. This will be justified through the use of a theoretical analysis, as well as with experimental data.

1.2 Goal

And here is some random text. Lorem ipsum dolor sit amet, consectetur adipiscing elit. Donec a tristique tellus. Duis ut risus risus, id mollis est. Curabitur gravida aliquam lacus sit amet malesuada. Aliquam lectus ipsum, sagittis ut ultrices eget, aliquet aliquet dui. Nullam vel sapien sit amet libero blandit bibendum. Nulla nec justo et odio hendrerit volutpat. Quisque tincidunt purus ut ante lacinia vel auctor nulla laoreet.

Mauris arcu felis, suscipit eget mollis a, lacinia et metus.

Nulla in nulla nec nunc vehicula porttitor sagittis id erat. Aliquam imperdiet urna pellentesque nibh vehicula tincidunt. In nulla lorem, viverra sed fringilla et, ultricies sed eros. Duis dictum pellentesque augue eget condimentum. Donec et ante vel velit facilisis molestie a nec nulla. Pellentesque euismod libero et sem gravida eleifend. Etiam nunc orci, laoreet nec euismod a, mollis quis nulla. Nullam vel odio tortor, eu dictum erat.

Vivamus rhoncus, ipsum sit amet hendrerit consetetur, risus eros ultricies massa, ut dignissim lorem libero in augue. Proin varius molestie vehicula. Vestibulum a turpis vitae lorem facilisis aliquam tincidunt eget ligula. Maecenas mi arcu, adipiscing at lobortis vitae, porta vitae lacus. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Sed dui leo, tempus id congue eu, convallis eget orci. Suspendisse lobortis, leo quis euismod tincidunt, sem nibh commodo orci, nec bibendum neque purus nec augue. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Nam tellus ipsum, tincidunt sit amet convallis eget, tristique vitae massa. Proin turpis risus, placerat a molestie sit amet, gravida id metus. Maecenas eu velit metus. Donec eget varius nunc. Proin pellentesque facilisis elit non hendrerit. Curabitur condimentum euismod auctor. Nullam porttitor, mi in pellentesque dictum, libero lacus condimentum ante, sit amet faucibus velit tortor sit amet diam.

Vivamus nisi metus, semper ut hendrerit id, suscipit a metus. Fusce et ligula leo. Etiam id hendrerit neque. Nam consequat tempor hendrerit. Cras suscipit dignissim odio eget commodo. Phasellus tortor dolor, congue et ornare sed, mattis quis nisl. Sed elementum est quis velit lacinia blandit. Aliquam erat volutpat. Nam facilisis, mi et bibendum molestie, arcu tortor fermentum enim, id venenatis orci est id nisl. Suspendisse vitae dui et lacus euismod consetetur nec sed lorem. Nam placerat ipsum sapien, et condimentum neque. Maecenas tincidunt ipsum mollis leo consetetur sagittis.

Maecenas et sem non dui pharetra venenatis. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Sed sit amet orci ac elit consequat accumsan vel at nibh. Nulla sed mauris a nibh convallis iaculis vitae in eros. Nam ipsum neque, rutrum vitae mollis nec, rutrum eu libero. Curabitur non elit in dui tincidunt tincidunt. Vestibulum vitae odio vitae mauris consequat adipiscing.

Lorem ipsum dolor sit amet, consetetur adipiscing elit. Donec a tristique tellus. Duis ut risus risus, id mollis est. Curabitur gravida aliquam lacus sit amet malesuada. Aliquam lectus ipsum, sagittis ut ultrices eget, aliquet aliquet dui. Nullam vel sapien sit amet libero blandit bibendum. Nulla nec justo et odio hendrerit volutpat. Quisque tincidunt purus ut ante lacinia vel auctor nulla laoreet. Mauris arcu felis, suscipit eget mollis a, lacinia et metus.

Nulla in nulla nec nunc vehicula porttitor sagittis id erat. Aliquam imperdiet urna pellentesque nibh vehicula tincidunt. In nulla lorem, viverra sed fringilla et, ultricies sed eros. Duis dictum pellentesque augue eget condimentum. Donec et ante vel velit facilisis molestie a nec nulla. Pellentesque euismod libero et sem gravida eleifend. Etiam nunc orci, laoreet nec euismod a, mollis quis nulla. Nullam vel odio tortor, eu dictum erat.

Vivamus rhoncus, ipsum sit amet hendrerit consetetur, risus eros ultricies massa, ut dignissim lorem libero in augue. Proin varius molestie vehicula. Vestibulum a turpis vitae lorem facilisis aliquam tincidunt eget ligula. Maecenas mi arcu, adipiscing at lobortis vitae, porta vitae lacus. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Sed dui leo, tempus id congue eu, convallis eget orci. Suspendisse lobortis, leo quis euismod tincidunt, sem nibh commodo orci, nec bibendum neque purus nec augue. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Nam tellus ipsum, tincidunt sit amet convallis eget, tristique vitae massa. Proin turpis risus, placerat a molestie sit amet, gravida id metus. Maecenas eu velit metus. Donec eget varius nunc. Proin pellentesque facilisis elit non hendrerit. Curabitur condimentum euismod auctor. Nullam porttitor, mi in pellentesque dictum, libero lacus condimentum ante, sit amet faucibus velit tortor sit amet diam.

Vivamus nisi metus, semper ut hendrerit id, suscipit a metus. Fusce et ligula leo. Etiam id hendrerit neque. Nam consequat tempor hendrerit. Cras suscipit dignissim odio eget commodo. Phasellus tortor dolor, congue et ornare sed, mattis quis nisl. Sed elementum est quis velit lacinia blandit. Aliquam erat volutpat. Nam facilisis, mi et bibendum molestie, arcu tortor fermentum enim, id venenatis orci est id nisl. Suspendisse vitae dui et lacus euismod consetetur nec sed lorem. Nam placerat ipsum sapien, et condimentum neque. Maecenas tincidunt ipsum mollis leo consetetur sagittis.

Maecenas et sem non dui pharetra venenatis. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Sed sit amet orci ac elit consequat accumsan vel at nibh. Nulla sed mauris a nibh convallis iaculis vitae in eros. Nam ipsum neque, rutrum vitae mollis nec, rutrum eu libero. Curabitur non elit in dui tincidunt tincidunt. Vestibulum vitae odio vitae mauris consequat adipiscing.

Lorem ipsum dolor sit amet, consetetur adipiscing elit. Donec a tristique tellus. Duis ut risus risus, id mollis est. Curabitur gravida aliquam lacus sit amet malesuada. Aliquam lectus ipsum, sagittis ut ultrices eget, aliquet aliquet dui. Nullam vel sapien sit amet libero blandit bibendum. Nulla nec justo et odio hendrerit volutpat. Quisque tincidunt purus ut ante lacinia vel auctor nulla laoreet. Mauris arcu felis, suscipit eget mollis a, lacinia et metus.

Nulla in nulla nec nunc vehicula porttitor sagittis id erat. Aliquam imperdiet urna

pellentesque nibh vehicula tincidunt. In nulla lorem, viverra sed fringilla et, ultricies sed eros. Duis dictum pellentesque augue eget condimentum. Donec et ante vel velit facilisis molestie a nec nulla. Pellentesque euismod libero et sem gravida eleifend. Etiam nunc orci, laoreet nec euismod a, mollis quis nulla. Nullam vel odio tortor, eu dictum erat.

Vivamus rhoncus, ipsum sit amet hendrerit consectetur, risus eros ultricies massa, ut dignissim lorem libero in augue. Proin varius molestie vehicula. Vestibulum a turpis vitae lorem facilisis aliquam tincidunt eget ligula. Maecenas mi arcu, adipiscing at lobortis vitae, porta vitae lacus. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Sed dui leo, tempus id congue eu, convallis eget orci. Suspendisse lobortis, leo quis euismod tincidunt, sem nibh commodo orci, nec bibendum neque purus nec augue. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Nam tellus ipsum, tincidunt sit amet convallis eget, tristique vitae massa. Proin turpis risus, placerat a molestie sit amet, gravida id metus. Maecenas eu velit metus. Donec eget varius nunc. Proin pellentesque facilisis elit non hendrerit. Curabitur condimentum euismod auctor. Nullam porttitor, mi in pellentesque dictum, libero lacus condimentum ante, sit amet faucibus velit tortor sit amet diam.

Vivamus nisi metus, semper ut hendrerit id, suscipit a metus. Fusce et ligula leo. Etiam id hendrerit neque. Nam consequat tempor hendrerit. Cras suscipit dignissim odio eget commodo. Phasellus tortor dolor, congue et ornare sed, mattis quis nisl. Sed elementum est quis velit lacinia blandit. Aliquam erat volutpat. Nam facilisis, mi et bibendum molestie, arcu tortor fermentum enim, id venenatis orci est id nisl. Suspendisse vitae dui et lacus euismod consectetur nec sed lorem. Nam placerat ipsum sapien, et condimentum neque. Maecenas tincidunt ipsum mollis leo consectetur sagittis.

Maecenas et sem non dui pharetra venenatis. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Sed sit amet orci ac elit consequat accumsan vel at nibh. Nulla sed mauris a nibh convallis iaculis vitae in eros. Nam ipsum neque, rutrum vitae mollis nec, rutrum eu libero. Curabitur non elit in dui tincidunt tincidunt. Vestibulum vitae odio vitae mauris consequat adipiscing.

Chapter 2

Materials and methods

2.1 Example of a section

2.1.1 Example of a subsection

The influenza virus is transmitted between hosts primarily through the inhalation of aerosols containing the influenza virus, which is expelled from the infected host by coughing or sneezing, though it can also enter through direct contact of the virus with the eyes, mouth or nose [4]. And I could go on, but I won't.

Example of a subsubsection

This is my first subsubsection. As you may have noticed, it does not appear in my Table of Contents, but I can change that if I wish.

Paragraphs are the division level just below subsubsections. Aren't they fun. If you'd like paragraphs to appear in your Table of Contents, there is an option for that.

2.1.2 Eh, another subsection but its title is too long so I provide an alternate one for the Table of Content

This here is another subsection. It is one way I can separate out the content of my subsection and cite some more authors [8,9].

And some more random text. Lorem ipsum dolor sit amet, consectetur adipiscing elit. Donec a tristique tellus. Duis ut risus risus, id mollis est. Curabitur gravida aliquam lacus sit amet malesuada. Aliquam lectus ipsum, sagittis ut ultrices eget, aliquet aliquet dui. Nullam vel sapien sit amet libero blandit bibendum. Nulla nec justo et odio

hendrerit volutpat. Quisque tincidunt purus ut ante lacinia vel auctor nulla laoreet. Mauris arcu felis, suscipit eget mollis a, lacinia et metus.

Nulla in nulla nec nunc vehicula porttitor sagittis id erat. Aliquam imperdiet urna pellentesque nibh vehicula tincidunt. In nulla lorem, viverra sed fringilla et, ultricies sed eros. Duis dictum pellentesque augue eget condimentum. Donec et ante vel velit facilisis molestie a nec nulla. Pellentesque euismod libero et sem gravida eleifend. Etiam nunc orci, laoreet nec euismod a, mollis quis nulla. Nullam vel odio tortor, eu dictum erat.

Vivamus rhoncus, ipsum sit amet hendrerit consectetur, risus eros ultricies massa, ut dignissim lorem libero in augue. Proin varius molestie vehicula. Vestibulum a turpis vitae lorem facilisis aliquam tincidunt eget ligula. Maecenas mi arcu, adipiscing at lobortis vitae, porta vitae lacus. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Sed dui leo, tempus id congue eu, convallis eget orci. Suspendisse lobortis, leo quis euismod tincidunt, sem nibh commodo orci, nec bibendum neque purus nec augue. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Nam tellus ipsum, tincidunt sit amet convallis eget, tristique vitae massa. Proin turpis risus, placerat a molestie sit amet, gravida id metus. Maecenas eu velit metus. Donec eget varius nunc. Proin pellentesque facilisis elit non hendrerit. Curabitur condimentum euismod auctor. Nullam porttitor, mi in pellentesque dictum, libero lacus condimentum ante, sit amet faucibus velit tortor sit amet diam.

Vivamus nisi metus, semper ut hendrerit id, suscipit a metus. Fusce et ligula leo. Etiam id hendrerit neque. Nam consequat tempor hendrerit. Cras suscipit dignissim odio eget commodo. Phasellus tortor dolor, congue et ornare sed, mattis quis nisl. Sed elementum est quis velit lacinia blandit. Aliquam erat volutpat. Nam facilisis, mi et bibendum molestie, arcu tortor fermentum enim, id venenatis orci est id nisl. Suspendisse vitae dui et lacus euismod consectetur nec sed lorem. Nam placerat ipsum sapien, et condimentum neque. Maecenas tincidunt ipsum mollis leo consectetur sagittis.

Maecenas et sem non dui pharetra venenatis. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Sed sit amet orci ac elit consequat accumsan vel at nibh. Nulla sed mauris a nibh convallis iaculis vitae in eros. Nam ipsum neque, rutrum vitae mollis nec, rutrum eu libero. Curabitur non elit in dui tincidunt tincidunt. Vestibulum vitae odio vitae mauris consequat adipiscing.

Chapter 3

Results and discussion

3.1 Mathematical models of virus dynamics

The basic model of virus dynamics can be written as follows [3, 12, 15]:

$$\begin{aligned}\frac{dT}{dt} &= -\beta TV \\ \frac{dI}{dt} &= \beta TV - \delta I \\ \frac{dV}{dt} &= pI - cV .\end{aligned}$$

where T is something something.

3.2 Shape of the viral titer curve

The virus spread and kills everything. This is well illustrated in Figure 3.1 where the kinetics of the infection are shown for three different viral production rates of the secondary cell population for the case where these cells are 1,000-fold harder to infect than cells of the default type. When secondary cells produce only 10-fold more virus than cells of the default type, the infection is mostly limited to the default cell population as the amount of virus produced is not sufficient for the infection to spread to the secondary cell population. Increasing the production rate to 100-fold more than cells of the default type results in a sufficient amount of virus being produced to sustain a slow growing infection within the secondary cell population, leading to long-lasting, high-levels of viral titer. Finally, increasing the viral production rate to 1,000-fold more than the default cell type allows the infection to successfully infect and decimate both cell populations

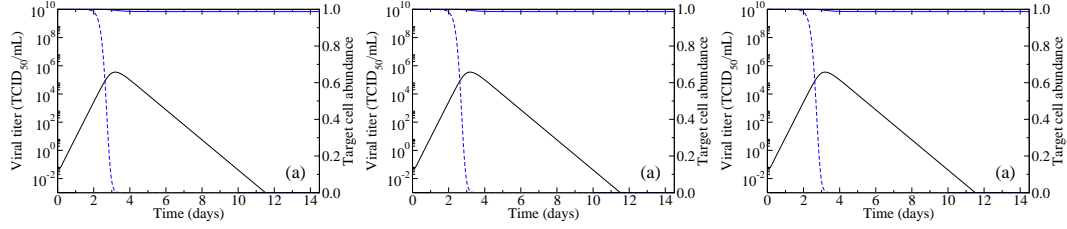


Figure 3.1: **An example illustrating how to include figure files.** I can not only display figures, but I can resize them so they look just right to appear side-by-side. This is how you produce multiple-panel images as a single figure. In addition, if your figure file is generated from some sort of model, you can refer to the table where the data or model parameters are listed. For example, you could say: All parameters are as in Table 3.1.

Parameter	Value
α	$3.4 \pm 0.1 \text{ m}$
β	$3.4 \times 10^{-2} \text{ kg}$

Table 3.1: Parameters used in our model.

rapidly. From these results, we see that there appears to be a relationship between the secondary cells' susceptibility to infection and their viral production rate which leads to a severe and sustained infection.

Note that all parameters use to produce our simulations can be found in Table 3.1.

Chapter 4

Conclusion

While differences in severity between human- and avian-derived influenza strains likely depend on several factors, we have demonstrated that a difference in cell tropism alone can be sufficient to explain or at least to capture the important differences in severity between these two strain subtypes. This makes the two target cell model a useful tool for studying delayed antiviral treatment of infections characterized by sustained viral production. In addition, since our model is a simple extension of the classic viral dynamics model used to capture in-host infection with a variety of other diseases such as HIV [16, 17], and Hepatitis viruses [10, 11, 13, 14], our conclusions also apply to these other diseases where different cell types can be affected by the virus.

Appendix A

The title of my first appendix

A.1 The first section of my appendix

blah blah

A.1.1 An appendix subsection if required

blah blah blah.

Appendix B

The second appendix chapter

B.1 A section in my second appendix chapter

blah blah.

B.1.1 Just making sure it all works

blah blah blah.

Bibliography

- [1] P. Baccam, C. Beauchemin, C. A. Macken, F. G. Hayden, and A. S. Perelson. Kinetics of influenza A virus infection in humans. *J. Virol.*, 80(15):7590–7599, August 2006.
- [2] C. Beauchemin, J. McSharry, G. Drusano, J. Nguyen, G. Went, R. Ribeiro, and A. Perelson. Modeling amantadine treatment of influenza A virus in vitro. *J. Theor. Biol.*, 254:439–451, 2008.
- [3] S. Bonhoeffer, R. M. May, G. M. Shaw, and M. A. Nowak. Virus dynamics and drug therapy. *Proc. Natl. Acad. Sci. U. S. A.*, 94(13):6971–6976, 24 June 1997.
- [4] C. B. Hall. The spread of influenza and other respiratory viruses: Complexities and conjectures. *Clin. Infect. Dis.*, 45(3):353–359, 1 August 2007.
- [5] A. Handel, I. M. Longini Jr., and R. Antia. Neuraminidase inhibitor resistance in influenza: Assessing the danger of its generation and spread. *PLoS Comput. Biol.*, 3(12):e240, December 2007.
- [6] A. Handel, I. M. Longini Jr., and R. Antia. Towards a quantitative understanding of the within-host dynamics of influenza A infections. *J. R. Soc. Interface*, 7(42):35–47, 6 January 2010.
- [7] H. Y. Lee, D. J. Topham, S. Y. Park, J. Hollengaugh, J. Treanor, T. R. Mosmann, X. Jin, B. M. Ward, H. Miao, J. Holden-Wiltse, A. S. Perelson, M. Zand, and H. Wu. Simulation and prediction of the adaptive immune response to influenza virus infection. *J. Virol.*, 83(14):7151–7165, July 2009.
- [8] M. N. Matrosovich, T. Y. Matrosovich, T. Gray, N. A. Roberts, and H.-D. Klenk. Neuraminidase is important for the initiation of influenza virus infection in human airway epithelium. *J. Virol.*, 78(22):12665–12667, November 2004.

- [9] M. A. Mohsin, S. J. Morris, H. Smith, and C. Sweet. Correlation between levels of apoptosis, levels of infection and haemagglutinin receptor binding interaction of various subtypes of influenza virus: Does the viral neuraminidase have a role in these associations. *Virus Res.*, 85(2):123–131, 10 May 2002.
- [10] A. U. Neumann, N. P. Lam, H. Dahari, D. R. Gretch, T. E. Wiley, T. J. Layden, and A. S. Perelson. Hepatitis C viral dynamics in vivo and the antiviral efficacy of interferon- α therapy. *Science*, 282(5386):103–107, 2 October 1998.
- [11] M. Nowak, S. Bonhoeffer, A. Hill, R. Boehme, H. Thomas, and H. McDade. Viral dynamics in hepatitis B viral infection. *Proc. Natl. Acad. Sci. USA*, 93:4398–4402, April 1996.
- [12] M. A. Nowak and R. M. May. *Virus Dynamics: Mathematical Principles of Immunology and Virology*. Oxford University Press, Oxford, 2000.
- [13] R. J. H. Payne, M. A. Nowak, and B. S. Blumberg. Analysis of a cellular model to account for the natural history of infection by the hepatitis B virus and its role in the development of primary hepatocellular carcinoma. *J. Theor. Biol.*, 159(2):215–240, 21 November 1992.
- [14] R. J. H. Payne, M. A. Nowak, and B. S. Blumberg. A cellular model to explain the pathogenesis of infection by the hepatitis B virus. *Math. Biosci.*, 123(1):25–58, September 1994.
- [15] A. S. Perelson. Modelling viral and immune system dynamics. *Nature Rev. Immunol.*, 2(1):28–36, 2002.
- [16] A. S. Perelson, P. Essunger, Y. Cao, M. Vesanen, A. Hurley, K. Saksela, M. Markowitz, and D. D. Ho. Decay characteristics of HIV-1 infected compartments during combination therapy. *Nature*, 387(6629):188–191, 8 May 1997.
- [17] A. S. Perelson, A. U. Neumann, M. Markowitz, J. M. Leonard, and D. D. Ho. HIV-1 dynamics *in vivo*: Virion clearance rate, infected cell life-span, and viral generation time. *Science*, 271(5255):1582–1586, 15 March 1996.

Glossary

ABM Agent-based model.

AUC Area under the curve (units: TCID₅₀/mL).

ODE Ordinary differential equation.

PDE Partial differential equation.