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Form 201 - Application for an NSERC Scholarship or Fellowship

Reference number: 456431445

Applicant: Tyler Cassidy **NSERC PIN:** 439027

Program: Postdoctoral Fellowships - PDF

Application Title: Developing evolutionarily inspired treatment strategies to control and exploit tumor evolution

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Tyler Cassidy

Form 201 - Application for a Postgraduate Scholarship or Postdoctoral Fellowship

Electronic Attachments:

Outline of Proposed Research - Cassidy_Proposed_Research

Justification for Eligibility of Proposed Research - Cassidy_Research_Eligibility

Contributions/Statements - Cassidy_Research_Contributions

Transcripts - Direct - Cassidy_PhD_Transcripts

Natural Sciences and Engineering Research Council of Canada | Conseil de recherches en sciences naturelles et en génie du Canada

Application for a Postgraduate Scholarship or Postdoctoral Fellowship (FORM 201)

AID	
CTTEE	
Date	2020/10/19

Type of Award	Reference No.
PDF	456431445

Family name of applicant	Given name	Initial(s) of all given names	Personal identification no. (PIN)
Cassidy	Tyler	TT	**Valid** 439027

ADDRESSES. Changes to any of the information below must be sent to schol@nserc-crsng.gc.ca.

Current mailing address	Permanent address (if different from current mailing address)
Unit 313 950 West Cordova Rd Santa Fe, NM UNITED STATES 87505	11 Reighley Close Red Deer, AB CANADA T4P 3V7
If current mailing address is temporary, indicate leaving date: 2021/11/13	Telephone number at permanent address: 11 (403) 3432945

Telephone number	Facsimile number	E-mail address (NSERC will use this information as the initial point of contact.)
11 (505) 6902261		tyler.cassidy@mail.mcgill.ca

CITIZENSHIP

[X] Canadian citizen [ ] Permanent resident of Canada [ ] Other

Indicate date of landing as stated on official immigration document:

Indicate country of citizenship:

LANGUAGE OF CORRESPONDENCE

I wish to receive my correspondence in:

[X] English [ ] French

University responsible for the internal selection process (Not applicable for PGS applications submitted directly and PDF applications.)

Personal information collected on this form and appendices will be stored in the Personal Information Bank for the appropriate program.

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ACADEMIC BACKGROUND (include only current and past degree programs)

Degree	Name of discipline	Department, institution and country	Month and year started	Month and year awarded/expected
Bachelor's	Honors Applied Mathematics	Science, Faculty of Alberta, CANADA	9 / 2011	4 / 2015
Master's	Applied Mathematics	Mathematics and Statistics McGill, CANADA	9 / 2015	Transferred to Ph.D.
Doctorate	Applied Mathematics	Mathematics and Statistics McGill, CANADA	1 / 2017	10 / 2019

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ACADEMIC, RESEARCH AND OTHER RELEVANT WORK EXPERIENCE

Position held and nature of work (begin with current) Full Time - Part Time	Organization and department	Supervisor	Period (mm/yyyy-mm/yyyy)
Postdoctoral research associate - Full Time Researcher in theoretical biology	Los Alamos National Laboratory Theoretical Biology and Biophysics	Dr. Alan S. Perelson	11/2019 - 11/2021
Dynamical Systems Modeller - Full Time Quantitative systems biology scientist in the internal medicine research unit.	Pfizer Inc. Internal Medicine Research Unit	Dr. Cynthia J. Musante	6/2017 - 9/2017
Teaching Assistant - Part Time Teaching assistant for Calculus for Management, Calculus II	McGill University Mathematics and Statistics	Dr. Sidney Trudeau	9/2016 - 12/2017
Research Assistant - Full Time NSERC USRA research assistant	University of Alberta Mathematics and Statistics	Dr. Hassan Safouhi	5/2014 - 9/2014
Research Assistant - Full Time NSERC USRA research assistant	University of Alberta Mathematics and Statistics	Dr. Hassan Safouhi	5/2014 - 9/2015
Teaching Assistant - Part Time Teaching assistant for Statistics I, Calculus I, II and linear algebra I courses.	University of Alberta Campus Saint-Jean	Dr. Sarah Pelletier	1/2013 - 4/2015

Personal identification no. (PIN)	Family name, given name and initial(s) of applicant
Valid 439027	Cassidy, Tyler TT

AWARD APPLIED FOR

Type of award	Proposed starting date of award
Postdoctoral Fellowships - PDF	2021/09

Proposed degree program (e.g. Masters, Doctorate)	Proposed field of study/research	Research subject code
	APPLIED MATHEMATICS	2950

Title of proposed research

Developing evolutionarily inspired treatment strategies to control and exploit tumor evolution

List ten (10) key words that describe your proposed research.

Mathematical biology, Dynamical systems, Population dynamics, Mathematical oncology, Numerical analysis, Mathematical modelling,

PROPOSED LOCATION(S) OF TENURE (in order of preference)

Institution/organization	Department	Program of study	Proposed supervisor
University of Oxford,	Mathematical Institute	Evolutionarily inspired therapies in cancer treatment	Philip K. Maini

Are any of your proposed programs of study:

Clinically-oriented? [ ] Yes [X] No Joint programs with a professional degree (e.g., MD/PhD)? [ ] Yes [X] No

SECTION TO BE COMPLETED BY PGS APPLICANTS ONLY

Indicate the total number of months of graduate studies (master's and doctoral) you have completed as of December 31 of the year of application in the natural sciences and engineering.

_____ months of full-time studies _____ months of part-time studies

Indicate the number of months of studies you have completed, as of December 31 of the year of application, **in the program for which you are requesting funding.**

_____ months of full-time studies _____ months of part-time studies

Indicate if you are attending university at the time of application.

[ ] Attending full time [ ] Attending part time [ ] Not attending

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SCHOLARSHIPS AND OTHER AWARDS OFFERED (start with most recent and include NSERC awards)

Name of Award	Value (CDN$)	Level (Institutional, Provincial, National, International)	Type (Academic, Research, Leadership, Communication)	Location of tenure	Period held (yyyy/mm - yyyy/mm)
FRQNT Bourse au doctorat	21,000	Provincial	Research	McGill University	Declined
Mittag-Leffler Fellowship	10,000	International	Research	Institut Mittag-Leffler	2018/10 - 2018/12
Murata Family Fellowship	3,300	Institutional	Research	McGill University	2018/09 - 2019/04
Trottier Science Fellowship	5,000	Institutional	Research	McGill University	2018/09 - 2019/04
NSERC PGS-D	21,000	National	Research	McGill University	2018/05 - 2019/09
James Lougheed Award of	20,000	Provincial	Research	McGill University	2017/09 - 2018/04
CRM Applied Math	10,000	Provincial	Research	McGill University	2016/09 - 2018/09
CAMBAM Fellowship	12,500	Provincial	Research	McGill University	2015/09 - 2017/04
James Lougheed Award of	15,000	Provincial	Research	McGill University	2015/09 - 2016/04
NSERC USRA	7,500	Institutional	Research	University of Alberta	2014/05 - 2014/09

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THESIS COMPLETED OR IN PROGRESS

1. Degree	Supervisor	Date degree requirements completed
Doctor of philosophy	Antony R. Humphries, Morgan Craig	08/2019

Title of thesis
On the development and application of distributed delay equations to mathematical physiology

2. Degree	Supervisor	Date degree requirements completed

Title of thesis

SUMMARY OF THESIS MOST RECENTLY COMPLETED OR IN PROGRESS

Do not reproduce abstract of thesis.

Human physiology is filled with examples of time-delayed feedback. In certain cases, such as the hematopoietic system, the time lag between signal and response is variable and distributed around a mean delay. In my dissertation, I derived a physiologically realistic method of modelling these delays, developed new techniques for analyzing physiologically structured equations, and applied these techniques to model tumour growth in the presence of immune surveillance.

I began by deriving a general model of population renewal that includes an arbitrary maturation period. I used an age structured partial differential equation to model a population with a randomly distributed maturation period and variable maturation rate. I then reduced the age structured partial differential equation to a state dependent distributed delay differential equation (DDE). This general setting encompasses the common state dependent discrete DDE and generalizes the linear chain technique to include variable transition rates and concatenated ageing processes. To illustrate the utility of the distributed DDE framework, I simplified two published models of hematopoiesis to their equivalent state dependent distributed DDE and analysed their resulting form.

Next, I developed and analyzed a mathematical model of tumour-immune interaction that explicitly incorporates heterogeneity in tumour cell cycle duration by using a distributed DDE. Through linear stability analysis, I completely characterised the importance of tumour-immune interaction by deriving a necessary and sufficient condition for disease remission. Consistent with the immunoediting hypothesis, bifurcation analysis of the mathematical model shows that decreasing tumour-immune interaction leads to tumour expansion through a transcritical bifurcation. By incorporating a model of viral therapy, I showed that immune involvement is crucial in determining long-term treatment outcomes.

To understand the effects of genetic variability in treatment outcome, I performed a virtual clinical trial of viral therapy and immunotherapy. I quantified the synergistic interaction between these two treatments by simulating viral and immunostimulatory combination therapy. Finally, I exploited this synergy by using a genetic algorithm to create an optimal dosing regimen that reduces treatment burden and improves virtual prognosis.

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JUSTIFICATION FOR LOCATION OF TENURE

Provide a rationale for your choice(s) for location of tenure. See instructions for further details.

I intend to perform my postdoctoral research at the Wolfson Center for Mathematical Biology in the Mathematical Institute at the University of Oxford. I have already identified a mentor, Prof. Philip K. Maini, and received approval to join the Institute.

The Wolfson Center for Mathematical Biology provides a dynamic and collaborative atmosphere for my postdoctoral research. In particular, the Wolfson Center is home to a number of mathematical biologists studying cancer. Prof. Helen Byrne's research has illuminated the mechanisms underlying angiogenesis in tumour development, and Prof. Ruth Baker has focused on cellular migration and invasion which are critical to understanding tumour growth. The Center is also home to the Quantitative Biology Network which connects quantitative researchers with experimentalists and clinicians with the goal of driving interdisciplinary research into biology and medicine. The Center hosts weekly seminars with researchers from around the world.

At Oxford, I will work in close collaboration with Prof. Philip K. Maini. Prof. Maini is a world leader in mathematical biology and has a proven track record of productivity with over 80 published articles since 2016. He is a Fellow of the Royal Society, the Society of Industrial and Applied Mathematics, and the Society of Mathematical Biology. His ability to translate mathematical results into medical insight was recognized with his election to the Academy of Medical Sciences.

His research has focused on collective cell dynamics and has elucidated the mechanisms leading to cancer. In particular, he has proposed models that bridge scales between single cell and population-level dynamics. These techniques are particularly important in understanding non-genetic evolution in tumours, as recent experimental work has shown that epigenetic regulation is influenced by local behavior and the life history of the parent cell. Recently, his research in mathematical oncology has identified strategies for combination cancer therapies. Accordingly, he is an ideal supervisor and collaborator for my proposed research into the physiological mechanisms underlying epigenetic evolution and the development of evolutionarily inspired therapeutic strategies.

Prof. Maini has existing collaborations with experimentalists throughout Oxford and the world. In particular, he works closely with researchers and students at the Integrated Mathematical Oncology (IMO) group at the Moffitt Cancer Center in the USA. Moffitt Cancer Center is the host institution for a stage I adaptive therapy trial in prostate cancer. I will therefore be able to continue my collaboration with the IMO while having access to clinicians and experimentalists who are testing our mathematical predictions.

All told, collaborating with Prof. Philip Maini at the Wolfson Center for Mathematical Biology at the University of Oxford offers a exceptional atmosphere for my postdoctoral research.

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DIVERSITY CONSIDERATIONS IN RESEARCH DESIGN

Are diversity considerations including, but not limited to, sex and gender taken into account in the research design, methods, analysis and interpretation, and/or dissemination of findings?

☐ Yes ☒ No

NOTE

If you answer “yes” to the question above, please ensure that diversity considerations are incorporated throughout your proposal (i.e. research design, methods, analysis and interpretation, and/or dissemination of their findings).

If you answer “no” to the question above, please use the text box provided to explain why diversity considerations are not relevant to your research design.

My research concerns the development and analysis of mathematical models. These mathematical models represent idealized systems and their analysis forms a significant proportion of my work. The mathematical models will be parametrized using in vitro data derived from genetically engineered cancer cell lines. These cancer cell lines are expanded in vitro and form the in vitro systems that will be used to parametrize the mathematical model. However, sex or race differences present in culture, possibly due to hormonal influence in cell culture serum, are not relevant to the development and analysis of the mathematical models. These influences will be critical when translating my work to the clinic, but that is not a goal of the current work.

The development of new anti-cancer drugs can be expected to take over a decade and cost over $1 billion USD. Despite advances in targeted and precision medicine, most patients with advanced cancer will experience drug resistance, treatment failure and, ultimately, disease recurrence [1, 2]. This resistance, long thought to result from genetic heterogeneity and evolution, is increasingly understood as the result of non-mutational evolutionary adaptations to therapy [3, 4]. ***Accordingly, my proposed research will develop mathematical models to understand the physiological mechanisms underlying this epigenetic resistance, and use these models to develop evolutionarily-inspired and clinically-actionable therapeutic strategies that mitigate the development of treatment resistance.***

Typically, drug-resistant populations co-exist in a dynamic equilibrium with drug-sensitive populations [1], but therapeutic interventions upset this equilibrium by imposing evolutionary pressures that confer a fitness advantage to the drug-resistant populations. This treatment-induced selection of drug-resistant cells is a natural consequence of conventional maximally-tolerated cytotoxic therapy, which aims to kill as many drug-sensitive cells as possible, and therefore induces strong selection pressure against the drug-sensitive population [5]. Thus, the accepted standard of care may be leading to the competitive release of drug-tolerant populations and contributing to the inevitability of treatment failure and disease progression [4].

Therapeutic strategies have been proposed to exploit the competition between drug-sensitive and tolerant cells. These strategies aim to prolong the time to disease progression by inhibiting the emergence of drug-tolerant populations [5]. These adaptive strategies in cancer treatment make extensive use of the theoretical framework of evolutionary game theory. In these evolutionary games, the oncologist controls the environment through treatment while tumour sub-populations, or the players, strategize to maximize their reproductive ability by modulating their frequency inside the tumour. In the resulting game, drug-resistant cells exploit their treatment-induced fitness advantage to increase in frequency at the expense of drug-sensitive cells. This treatment-driven evolution is typically modelled as a multi-species replicator equation describing clonal dynamics on a fixed genetic landscape so the population dynamics are entirely determined by clonal frequency and pre-determined sensitivity to therapy. Thus, while the theoretical framework underlying adaptive therapy exploits both the competition between genetically distinct tumour sub-populations and the relatively slow timescales for genetic evolution [6], these evolutionary games do not consider the role of non-mutational factors in treatment resistance [3].

However, we are beginning to appreciate that genetic resistance may not be the principle driver of therapeutic resistance, and recent studies have identified the important role of non-mutational, or epigenetic, adaptations in treatment resistance [3, 4, 7]. For example, epigenetic regulation of genetically identical non-small cell lung cancer (NSCLC) cells induces a reversible drug-tolerant phenotype that expands during cytotoxic chemotherapy [7]. This non-mutational resistance, where genetically identical cells transiently adopt a drug-resistant phenotype to avoid the treatment imposed selection pressure, may thwart therapeutic strategies that rely on Darwinian evolution over a fixed genetic landscape. Consequently, it is presently unclear how to adapt evolutionarily inspired therapies to the address the difficulties posed by reversible non-genetic mechanisms that change on a faster timescale than Darwinian evolution.

To this end, recent experimental work suggests that this phenotypic heterogeneity can be modulated by a number of complex physiological factors, including the current state of the population, tumour microenvironment, and the life history of the parental cell [8, 9]. Accordingly, as systems-level experiments of these complex and non-linear interactions are currently intractable, standard experimental techniques are unable to probe the physiological determinants of non-genetic heterogeneity. ***Therefore, mathematical modelling offers an unparalleled opportunity to identify the physiological mechanisms underlying non-mutational drug resistance and to use this understanding to extend adaptive therapies to non-genetic drug resistance***.

My research will address the systemic determinants of epigenetic resistance through the development of mechanistic mathematical models of tumour evolution in response to therapy. I will explicitly include the physiological mechanisms underlying phenotypic heterogeneity through the use of physiologically-structured population models. Unlike most game theoretical models, these mechanistic models take the form of partial

differential equations that are explicitly designed to study intra-clonal population heterogeneity. By using a combination of single cell RNA-sequencing and population level data arising from *in vitro* and *in vivo* experiments [8] in concert with sophisticated parameter estimation techniques and parameter identifiability analysis, I will calibrate and validate my mathematical models. After these steps, I will leverage these models to predict the epigenetic response to therapy, and to understand the mechanisms underlying treatment resistance and drug failure.

These models will serve as the basis of the development of evolutionarily inspired therapies that explicitly address non-mutational resistance. I have recently shown that it is possible to derive therapeutic strategies that exploit the epigenetic regulation of phenotypic resistance and drive extinction of a NSCLC population resistant to standard chemotherapies by combining techniques from infinite dimensional dynamical systems with physiologically based pharmacokinetic models. Effectively, my results show that oncologists can preserve a significant proportion of drug-sensitive cells while simultaneously driving tumour contraction by carefully choosing dose size and frequency to modulate selection pressure on drug-sensitive cells.

The theme of selectively applying treatment pressure to an evolving population underlies the main contribution of my proposal. I will use biologically-relevant and physiologically-structured mathematical models to understand how therapeutic selection shapes epigenetic evolution of malignant tumours. With this understanding in hand, I will use techniques from dynamical systems, pharmacometrics, and numerical analysis to develop rational and clinically-actionable treatment schedules to steer this epigenetic evolution towards desired clinical outcomes. This rational use of drug-interventions will be particularly important when considering large heterogeneous tumours where single drug therapies are unlikely to be successful. There, evolutionary steering may involve drug cycling to maintain a drug-sensitive population of cells and thus limit treatment failure, or strategies to induce collateral sensitivity wherein resistance to the first therapy increases sensitivity to subsequent therapeutics [10]. Finally, I will demonstrate the robustness of these clinically actionable strategies through the use of *in silico* clinical trials [11].

Most importantly, I will utilize my experience in the pharmaceutical industry and existing collaborations with experimentalists and clinicians to translate my mathematical results into new biological knowledge. Specifically, the mathematical models developed during this work will make predictions that will first be tested in *in vitro* experiments before being applied to patient-derived organoid models [12]. In this way, my research will inform a multi-disciplinary approach to rational personalized medicine and allow for these evolutionary steering techniques to be translated into clinically actionable strategies.

Despite significant progress in anti-cancer drug development, therapeutic success is often transient with treatment failure being driven by the emergence of resistant populations. These resistant populations then form the "minimal residual disease" that almost inevitably act as a reservoir of drug-resistant cells that drive refractory tumour growth. Therapeutic strategies have been developed to combat pre-existing genetic resistance and a recent pilot clinical trial in metastatic castrate-resistant prostate cancer has illustrated the possible clinical benefits of these so-called "adaptive therapies" [13]. My work is critical to extending these strategies to account for non-mutational evolutionary adaptations to therapy. My research will develop evolutionarily-inspired treatment strategies that will permit re-purposing of existing anti-cancer drugs, decrease treatment toxicity and burden, and ultimately support efforts towards improving clinical outcomes.

[1] Russo, M. et al. (2019) *Science (80-.).* **366(6472)**.
[2] McGranahan, N. and Swanton, C.(2017) *Cell* **168(4)**.
[3] Marine, J.-C., Dawson, S.-J., and Dawson, M. A., (2020) *Nat. Rev. Cancer* **In press**.
[4] Bell, C. C. and Gilan, O. (2020) *Br. J. Cancer* **122(4)**.
[5] Gatenby, R. A. and Brown, J. S.(2020) *Nat. Rev. Clin. Oncol.*
[6] Gluzman, M., Scott, J. G., and Vladimirsky, A. (2020) *Proc. R. Soc. B Biol. Sci.* **287(1925)**.
[7] Sharma, S. V. et al. (2010) *Cell* **141(1)**.
[8] Shaffer, S. M. et al. (2020) *Cell* **182(4)**.
[9] Yang, H. W., Chung, M., Kudo, T., and Meyer, T. (2017) *Nature* **549(7672)**.
[10] Acar, A. et al., (2020) *Nat. Commun.***11(1)**.
[11] Cassidy, T. and Craig, M. (2019) *PLOS Comput. Biol.* **15(11)**.
[12] Vlachogiannis, G. et al. (2018) *Science (80-.).* **359(6378)**.
[13] Zhang, J., Cunningham, J. J., Brown, J. S., and Gatenby, R. A. (2017) *Nat. Commun.* **8(1)**.

The goal of the proposed research is to develop physiologically-structured and biologically relevant models of epigenetic resistance to anti-cancer therapies. While this work is translational and therefore interdisciplinary, my proposed research is entirely mathematical. In broad terms, my research aims to

> develop(ing) new mathematical or statistical models, theories, methodologies, or analytical tools that may lead to potential future applications in human health [1]

Specifically, my work will involve

1. The development of physiologically-structured mechanistic models of evolutionary selection in a heterogeneous population. These infinite dimensional models will either be systems of non-local partial differential equations or delay differential equations. The development, analysis, and simulation of these types of models is an active area of research in mathematics. For example, the extension of well-known linearisation techniques and bifurcation analysis from finite dimensional systems to these infinite dimensional dynamical systems is non-trivial and will require the development of new mathematical techniques.

2. The simulation of the mathematical models will require either the development of new numerical techniques or the derivation of mathematical equivalences with simpler models for which numerical techniques exist.

3. The parametrization and validation of these mathematical models will require the adaptation of existing statistical techniques to available data and model predictions. This will include the development of local sensitivity analysis techniques, optimization routines for parameter fitting, and practical identifiability analysis.

Accordingly, the proposed research will contribute to the advancement of knowledge in mathematical biology, dynamical systems, and numerical methods, all of which fall under the mandate of NSERC and its programmes.

[1] Taken from: Addendum to the guidelines for the eligibility of applications related to health, https://www.nserc-crsng.gc.ca/nserc-crsng/policies-politiques/addendum-addenda_eng.asp, Accessed: 10/17/2020.

I Contributions to research and development

a) Articles published or accepted in peer-reviewed journals

1) **Cassidy, T.**, Humphries, A.R., Craig, M., and Mackey, M.C. (2020) Characterizing chemotherapy-induced neutropenia and monocytopenia through mathematical modelling, Bulletin of Mathematical Biology, **82**: 1-26. (Ph.D. Work)

2) **Cassidy, T.** and Craig, M., (2019) Determinants of combination GM-CSF immunotherapy and oncolytic virotherapy success identified through in silico treatment personalization, PLOS Computational Biology, **15**: 1-16. (Ph.D. Work)

3) **Cassidy, T.**, Craig, M. and Humphries, A.R. (2019) Equivalences Between Age Structured Models and State Dependent Distributed Delay Differential Equations, Mathematical Biosciences and Engineering, **16**: 5419-5450. (Ph.D. Work)

4) **Cassidy, T.** and Humphries, A.R., (2019) A Mathematical Model Of Viral Oncology As An Immuno-Oncology Instigator, Mathematical Medicine and Biology: A Journal of the IMA, **37**: 117-151. (Ph.D. Work)

5) De Souza, D.C, Craig, M., **Cassidy, T.**, Li, J., Nekka, F., Humphries, A.R. (2018) Transit and lifespan in neutrophil production: implications for drug intervention, Journal of Pharmacokinetics and Pharmacodynamics, **45**: 59-77. (Ph.D. Work)

6) **Cassidy, T.**, Gaudreau, P. and Safouhi, H. (2017) On the Computation of Eigenvalues of the Anharmonic Coulombic Potential, Journal of Mathematical Chemistry, **56**: 477-492. (B.Sc work)

b) Articles submitted to peer-reviewed journals

1) **Cassidy, T.**, Distributed Delay Differential Equation Representations of Cyclic Differential Equations, SIAM Journal on Applied Mathematics, Submitted: July 9th, 2020, Submission ID: M135160, 19 pp. (Postdoctoral Work)

2) Jenner, A.L., **Cassidy, T.**, Belaid, K., Bourgeois-Daigneault, M.C., and Craig, M. In silico trials predict that combination strategies for enhancing vesicular stomatisis oncolytic virus are determined by tumour aggressivity, Journal of ImmunoTherapy for Cancer, Submitted: July 7th, 2020, Submission ID: jitc-2020-001387, 33 pp. (Postdoctoral Work)

d) Non-peer-reviewed contributions

1) **Cassidy, T.,***, Transit compartmental representations of functional differential equations, Los Alamos National Laboratory Theoretical Biology and Biophysics Seminar, National institutional oral presentation, 2020 (Postdoctoral work)

2) **Cassidy, T.,***, Nichol, D., Robertson-Tessi, M., Craig, M. and Anderson, A.R.A., Insights from phenotype and age structured equations to avoid chemotherapeutic drug resistance, SIAM/CAIMS Joint Annual Meeting, International conference oral presentation, 2020, (Postdoctoral work)

3) **Cassidy, T.,***, Nichol, D., Robertson-Tessi, M., Craig, M. and Anderson, A.R.A., Using Structured Equations to Control Tumour Evolution and Avoid Chemotherapeutic Resistance, York University Laboratory of Industrial and Applied Mathematics Seminar, International institutional oral presentation, 2020, (Postdoctoral work)

4) **Cassidy, T***, Humphries, A.R., Craig, M. and Mackey, M.C., Innate Immune System Regulation in Health and Disease, Society for Mathematical Biology Annual Meeting, International conference oral presentation, 2019, (Ph.D. work)

5) **Cassidy, T***, Craig, M. and Humphries, A.R., The Linear Chain Trick in Modelling Drug Effects on Neutrophil Response, CAIMS Annual Meeting, International conference oral presentation, 2019, (Ph.D. work)

6) **Cassidy, T***, Craig, M. and Humphries, A.R., A Recipe for State Dependent Distributed Delay Dif-

ferential Equations, SIAM Meeting on Dynamical Systems, International conference oral presentation, 2019, (Ph.D. work)
7) **Cassidy, T***, Craig, M. and Humphries, A.R., Understanding and Exploiting Immune Support of Cancer Virotherapy, Pfizer Inc. Quantitative Systems Pharmacology in Early Clinical Development Seminar, International institutional oral presentation, 2019, (Ph.D. work)
8) **Cassidy, T***, Craig, M. and Humphries, A.R., Modelling and Optimizing Immune Support of Cancer Virotherapy, Helmholtz Center for Infection Research Systems Immunology Seminar, International institutional oral presentation, 2019, (Ph.D. work)
9) **Cassidy, T*** and Humphries, A.R., A Mathematical Model of Viral Oncology, 10th Swedish Meeting on Mathematics in Biology, International conference oral presentation, 2018, (Ph.D. work)
10) **Cassidy, T*** and Humphries, A.R., Viruses as Instigators of Cancer Immunotherapy, SIAM Life Sciences Meeting, International conference oral presentation, 2018, (Ph.D. work)
11) **Cassidy, T.,***, Humphries, A.R. and Mackey, M.C, Mathematical Modelling of Cyclic Neutropenia, CAMBAM Seminar National institutional oral presentation, 2017 (M.Sc work)
12) **Cassidy, T.,***, Humphries, A.R. and Mackey, M.C, Understanding, Treating and Avoiding Hematological Disease: Better Medicine Through Mathematics, SIAM Life Sciences Meeting, International conference oral presentation, 2016 (Ph.D. Work)

f) Contributions resulting from your participation in industrially relevant RD activities

1) **Cassidy,T.,***, Rieger, T. and Baraldi, R., Modelling Lipoprotein Dynamics during PCSK-9 Inhibition, Pfizer Internal Medicine Research Unit Quantitative Research Group Seminar (Institutional oral presentation and technical report), 2017.

II Most significant contributions to research and development

1) A significant portion of my research has involved the development and analysis of mathematical models of hematopoiesis during immunosuppressive chemotherapy. In 2018, we compared three different mathematical models of granulopoiesis and showed that the "gold standard" Quartino model misspecifies the neutrophil precursor maturation stage as an additional proliferative stage[1] and published this work in the official journal of the International Society of Pharmacometrics. I showed that such misspecifications can be avoided by explicitly modelling the proliferative stage as a physiologically-structured partial differential equation. I established the equivalence between the common transit compartment ordinary differential equation models of hematopoiesis that include pharmacological interventions and a system of delay differential equations where the delay is both state dependent and distributed[2]. This equivalence links the three major classes of physiologically based mathematical models of hematopoiesis and was published in a special issue dedicated to Advances in Mathematical Population Dynamics. I derived and validated a novel physiologically-structured model of monocytopoiesis to characterize the relationship between monocytopenia and neutropenia during chemotherapy. Our results suggest using monocyte concentrations as a early warning sign for chemotherapy induced neutropenia[3]. We published this work in the official journal of the Society of Mathematical Biology.

2) I developed a physiologically based mathematical model of tumour growth and oncolytic viral therapy[4]. Using a system of distributed delay differential equations, I explicitly incorporated intra-tumour heterogeneity in a model of tumour growth. I demonstrated that intra-tumour heterogeneity acts to destabilize the disease-free state and characterized the importance of immune recruitment in cancer

[1]de Souza et al. *Journal of Pharmacokinetics and Pharmacodynamics* (2018)
[2]Cassidy, Craig, and Humphries, *Mathematical Biosciences and Engineering* (2019)
[3]Cassidy, Humphries, Craig, and Mackey, *Bulletin of Mathematical Biology* (2020)
[4]Cassidy and Humphries, *Mathematical Medicine and Biology: A Journal of the IMA* (2019)

progression. I extended the model to include oncolytic viral therapy and showed that the resulting immune involvement is critical for determining treatment outcome. By parametrizing the mathematical model to late stage melanoma and performing an *in silico* clinical trial, I showed the mathematical model can replicate the population-level results of the OPTiM clinical trial that led to FDA approval of the first oncolytic viral therapy[5]. I then investigated the synergy between standard immunotherapies and an oncolytic virus and thus tailored therapeutic strategies for our virtual population. I leveraged these individualized schedules to propose a clinically actionable combination therapy schedule that significantly improves virtual prognosis while minimizing treatment burden in a paper published in a special issue on Targeted Anticancer Therapies and Precision Medicine in Cancer. We recently extended this model to study combination oncolytic virus treatment[6]. We worked closely with an experimental collaborator to identify optimal combination strategies that exploit the different immunological characteristics of candidate oncolytic viruses. This work illustrates the use of computational techniques in pre-clinical development and contains broad results that are of interest to clinical researchers. We therefore submitted this work to the official journal of the Society of Immunotherapy for Cancer where it is currently under review.

3) Structured population models allow for the explicit study of intra- and inter-patient heterogeneity. However, their implementation has been limited due to difficulties in analysis and simulation. I have addressed these difficulties by establishing the mathematical equivalence between these physiologically-structured models and simpler differential equation models. This work has broad implications in model development as researchers can use the model formulation best suited to their needs[2]. It is common to use compartmental models to mimic time delays arising naturally in structured population models. I have recently formalized this relationship by establishing the equivalence between general compartmental models and functional differential equations. Using techniques from infinite dimensional dynamical systems and functional analysis, I developed new tools to simplify the study of these compartmental models[7]. Given the ubiquity of compartmental models throughout applied mathematics, I submitted this work to the founding journal of the Society of Industrial and Applied Mathematics where it is currently under review.

Part III Applicant's statement

Research experience: My academic career began with a NSERC-USRA funded summer research project at the University of Alberta. My undergraduate research involved the development of novel numerical techniques for Sturm-Liouville problems that arise in quantum mechanics. This work led to my first publication.

I then moved to McGill University for my doctoral training in applied mathematics. Broadly speaking, my research focused on using mathematics to address problems in medicine. My doctoral work, supported by a NSERC PGS-D award, was primarily centered on the development of physiologically-based structured population models to study the role of intra- and inter-patient heterogeneity in disease progression and therapeutic scheduling. This work led to five publications.

During my Ph.D., I spent 4 months working in the quantitative systems pharmacology group at Pfizer Inc. where I extended a mechanistic model of circulating lipoprotein dynamics to include the effects of a novel monoclonal antibody in monotherapy and in combination with statin treatment. We used the model to elucidate the mechanism leading to their synergistic function and impact on familial cholesteroalaemia. At Pfizer, I learned to effectively translate mathematical insights into actionable results through my collaboration with experimentalists and clinicians. This experience confirmed the importance of mathematical

[5]Cassidy and Craig, *PLOS Computational Biology* (2020)

[6]Jenner et al. *Journal of ImmunoTherapy for Cancer*, Submitted: July 7th, 2020

[7]Cassidy, *SIAM Journal on Applied Mathematics*, Submitted: July 9th, 2020

modelling for understanding disease progression and pre-clinical treatment development.
In the final year of my Ph.D., I was awarded a postdoctoral fellowship (now called junior fellowships) to attend the thematic semester in mathematical biology at the Institut Mittag-Leffler in Stockholm, Sweden. There, I began a collaboration with scientists from the Institute for Cancer Research in the UK and the Moffitt Cancer Center in the USA that has deepened my interest in non-genetic mechanisms of cancer drug resistance, and further entrenched my belief that mathematical modelling is critical in revealing important insights into disease progression and treatment resistance.
My postdoctoral work with Alan Perelson at the Los Alamos National Laboratory has involved the development of mathematical models to understand the evolution of treatment resistance in HIV. In particular, I have worked in close collaboration with clinical scientists to illuminate the dynamic pathways leading to HIV resistance against a broadly neutralizing antibody in a recently completed phase I clinical trial. I have also used mathematical modelling to identify the immunological mechanisms underlying post-treatment control of HIV infection. This work will submitted in the near future.

Relevant activities

Teaching: I was the teaching assistant for *Calcul élémentaire I* (2013), *Calcul élémentaire* (2013, 2014), *Calcul élémentaire* II (2013, 2014), *Algebre linéaire* I (2012, 2013, 2014) and *Statistiques* I (2012) at the University of Alberta–Campus Saint Jean. These tutorials were given in French. At McGill University, I was the teaching assistant for Calculus for Management (2016) and Calculus II (2017, 2018). I was awarded the departmental teaching assistant award in 2017 and 2018.
In 2020, I organized a day-long workshop titled *Problems and solutions in lifting individual behaviour to population level dynamics* during the Centre de Recherches Mathématiques-Center for Applied Mathematics in Biology and Medicine Workshop Series in Mathematical Biology. I developed the syllabus and lectured half of the workshop. The workshop had approximately 60 attendees and we covered the use of structured equations in the context of graduate-level mathematical biology.

Supervision and Mentorship:

Supervision: I supervised two undergraduate final projects at McGill, and the summer research of two undergraduate researchers. In all cases, I defined the research question, organized and guided their research and participated in writing manuscripts.
Mentorship: During my doctoral studies, I was an active mentor to the other graduate students in our research group by leading group discussions and student driven presentations. I was elected to the McGill mathematics graduate student government in 2017.

Activities Related to the Dissemination of Results:

Seminar organization: I organized a series of undergraduate research seminars at the University of Alberta–Campus Saint Jean. Undergraduate researchers presented their work to a multi-disciplinary audience during lunch. The seminar series included professional development presentations and social activities to promote interdisciplinary communication. I also organized a Montreal-wide student computational biology seminar during my time at McGill. The seminar involved presentations from student researchers in a variety of quantitative biology sub-fields.
Session organization: I organized a session titled *Quantitative approaches to unravel immune function and immunity* at the Society for Mathematical Biology's 2019 annual meeting.
Peer review: I am currently a reviewer for five journals.
Awards: I was awarded the best poster prize at the McGill Physiology Department Research Day in 2018 and at the 2019 Fields Institute Workshop on Mathematical Ecology. I received travel awards to attend the SIAM Life Sciences meeting (2018), SIAM Dynamical Systems meeting (2019), CAIMS Annual Meeting (2019), and the Fields Institute Workshop on Mathematical Ecology.

Natural Sciences and Engineering Research Council of Canada | Conseil de recherches en sciences naturelles et en génie du Canada

Application for a Postgraduate Scholarship or Postdoctoral Fellowship (FORM 201)

Type of Award	Personal identification no. (PIN)	Family name, given name and initial(s) of applicant
PDF	Valid 439027	Cassidy, Tyler TT

SPECIAL CIRCUMSTANCES

McGill UNIVERSITY

INCLUDING / Y COMPRIS
MACDONALD CAMPUS
MONTRÉAL, CANADA

DATE OF BIRTH / DATE DE NAISSANCE: Jul 27

STUDENT No / No MATRICULE: 260666464

REFERENCE / RÉFÉRENCE:

DATE ISSUED / DATE D'ÉMISSION: 2019/10/18

STUDENT NAME / NOM DE L'ÉTUDIANT

Cassidy, Tyler

COURSE NUMBER / NUMÉRO DE COURS	TITLE / TITRE	CR / C.E.U / CR / U.E.C	GRADE / NOTE	REMARKS / REMARQUES	EARNED / OBTENUS	CLASS AVG / MOY. DU GROUPE

PREVIOUS EDUCATION
Quebec Univ (incl. McGill)
Alberta University/College
University of Alberta - Bachelor of Science 2014

Fall 2015
Master of Science
Thesis Full-time
Mathematics and Statistics (Thesis) - Thesis

MATH	564	Advanced Real Analysis 1	4	A-	4	
MATH	578	Numerical Analysis 1	4	A	4	
MATH	580	Partial Differential Equat's 1	4	A	4	

					Att Cr	Earned Cr	GPA Cr	Points
TERM GPA:	3.90	Advanced Standing Transfer Credits:	0.00	TERM TOTALS:	12.00	12.00	12.00	46.80
CUM GPA:	3.90	TOTAL CREDITS:	12.00	CUM TOTALS:	12.00	12.00	12.00	46.80

Standing: Satisfactory

Winter 2016
Master of Science
Thesis Full-time
Mathematics and Statistics (Thesis) - Thesis

		Inter-University Transfer			
MATH	579	Numerical Differential Eqns	4	A	4
MATH	761	Adv Topics in Applied Math 1	4	A	4

Credits/Exemptions

From: Concordia University - 4 credits
COMP 6XX 4 cr

					Att Cr	Earned Cr	GPA Cr	Points
TERM GPA:	4.00	Advanced Standing Transfer Credits:	4.00	TERM TOTALS:	8.00	8.00	8.00	32.00
CUM GPA:	3.94	TOTAL CREDITS:	24.00	CUM TOTALS:	20.00	20.00	20.00	78.80

Standing: Satisfactory

Summer 2016
Master of Science
Thesis Continuing
Mathematics and Statistics (Thesis) - Thesis

Standing: Satisfactory

Fall 2016
Master of Science
Thesis Full-time
Mathematics and Statistics (Thesis) - Thesis

Standing: Satisfactory

MATHEMATICS AND STATISTICS
BURNSIDE HALL
805 SHERBROOKE ST. WEST
QC

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Gillian Nycum

Gillian Nycum, Registrar

McGill UNIVERSITY

INCLUDING / Y COMPRIS
MACDONALD CAMPUS
MONTRÉAL, CANADA

DATE OF BIRTH / DATE DE NAISSANCE: Jul 27

STUDENT No / No MATRICULE: 260666464

REFERENCE / RÉFÉRENCE:

DATE ISSUED / DATE D'ÉMISSION: 2019/10/18

STUDENT NAME / NOM DE L'ÉTUDIANT

Cassidy, Tyler

COURSE NUMBER / NUMÉRO DE COURS	TITLE / TITRE	CR / C.E.U / CR / U.E.C	GRADE / NOTE	REMARKS / REMARQUES	EARNED / OBTENUS	CLASS AVG / MOY. DU GROUPE
Change of Degree						
Winter 2017						
Doctor of Philosophy						
Thesis Full-time						
Mathematics and Statistics (Thesis) - Thesis						
	Standing: Satisfactory					
Summer 2017						
Doctor of Philosophy						
Leave of Absence						
Mathematics and Statistics (Thesis) - Thesis						
	Leave of Absence-Grad Studies					
	Standing: Satisfactory					
Fall 2017						
Doctor of Philosophy						
Thesis Full-time						
Mathematics and Statistics (Thesis) - Thesis						
MATH 700	Ph.D. Preliminary Exam Part A	0	P		0	
	Standing: Satisfactory					
Winter 2018						
Doctor of Philosophy						
Thesis Full-time						
Mathematics and Statistics (Thesis) - Thesis						
MATH 701	Ph.D. Preliminary Exam Part B	0	P		0	
	Standing: Satisfactory					
Summer 2018						
Doctor of Philosophy						
Thesis Continuing						
Mathematics and Statistics (Thesis) - Thesis						
	Standing: Satisfactory					
Fall 2018						
Doctor of Philosophy						
Thesis Full-time						
Mathematics and Statistics (Thesis) - Thesis						
MATH 761	Adv Topics in Applied Math 1	4	A		4	

TERM GPA: 4.00
CUM GPA: 4.00

Advanced Standing
Transfer Credits: 0.00
TOTAL CREDITS: 4.00

	Att Cr	Earned Cr	GPA Cr	Points
TERM TOTALS:	4.00	4.00	4.00	16.00
CUM TOTALS:	4.00	4.00	4.00	16.00

Standing: Satisfactory

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McGill UNIVERSITY

INCLUDING / Y COMPRIS
MACDONALD CAMPUS
MONTRÉAL, CANADA

DATE OF BIRTH / DATE DE NAISSANCE: Jul 27

STUDENT No / No MATRICULE: 260666464

REFERENCE / RÉFÉRENCE:

DATE ISSUED / DATE D'ÉMISSION: 2019/10/18

STUDENT NAME / NOM DE L'ÉTUDIANT

Cassidy, Tyler

COURSE NUMBER / NUMÉRO DE COURS	TITLE / TITRE	CR / C.E.U / CR / U.E.C	GRADE / NOTE	REMARKS / REMARQUES	EARNED / OBTENUS	CLASS AVG / MOY. DU GROUPE

Winter 2019
Doctor of Philosophy
Thesis Full-time
Mathematics and Statistics (Thesis) - Thesis

Credits/Exemptions

From: McGill University - 20 credits

MATH	564	4 cr
MATH	578	4 cr
MATH	579	4 cr
MATH	580	4 cr
MATH	761	4 cr

TERM GPA:	0.00	Advanced Standing Transfer Credits:	20.00
CUM GPA:	4.00	TOTAL CREDITS:	24.00

	Att Cr	Earned Cr	GPA Cr	Points
TERM TOTALS:	0.00	0.00	0.00	0.00
CUM TOTALS:	4.00	4.00	4.00	16.00

Standing: Satisfactory

Summer 2019
Doctor of Philosophy
Thesis Continuing
Mathematics and Statistics (Thesis) - Thesis

Standing: Satisfactory

Doctoral Thesis Title
On the development and application of distributed delay equations to mathematical physiology

Doctor of Philosophy Granted: October 2019
Mathematics and Statistics (Thesis) - Thesis

END OF TRANSCRIPT

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GRADING – Effective September 1980

Dentistry (effective 1987)	Graduate Grades	Undergraduate Grades	Grade Points	Numerical Scale of Marks
A	A	A	4.0	85 - 100 %
A-	A-	A-	3.7	80 - 84 %
B+	B+	B+	3.3	75 - 79 %
B	B	B	3.0	70 - 74 %
B-	B-	B-	2.7	65 - 69 %
C+		C+	2.3	60 - 64 %
		C	2.0	55 - 59 %
		D	1.0	50 - 54 %
F (0-59%)	F (0-64%)	F (0-49%)	0.0	

Medicine (January 1970 to date):
S = Satisfactory U = Unsatisfactory

Prior to September 2002, numerical grades as well as letter grades were recorded for some courses.

'D' is a passing grade, but is not sufficient if the course is a pre-requisite for other courses or is required by the student's program.

Information about grading policies in effect prior to 1980 (Law prior to 1985, Dentistry prior to 1987) is available at www.mcgill.ca/students/records/transcripts.

Grade Point Average (GPA)
All credits attempted are used in the calculation of the Grade Point Average, including courses with a grade of 'D' or failed courses that are repeated or for which supplemental examinations are taken.

Other Grades
CR ..... Credit granted based on equivalent qualifications
EX ..... Exemption
FN ..... Failure, may not write a supplemental examination
HH ..... To be continued
IP ..... In progress
J ..... Absent
K ..... Incomplete
KE or K* ..... Further extension granted
KF ..... Incomplete - Failed
KK ..... Completion requirement waived
L ..... Deferred
LE or L* ..... Deferred - extension granted
N ..... Withdrew without approval
NA or && ..... Grade not yet available
NC ..... No evaluation
NE ..... No evaluation
NR ..... No grade reported by the instructor (recorded by the Registrar)
P ..... Pass
Q ..... Course continues in following term
R ..... Course credit
S ..... Satisfactory
U ..... Unsatisfactory
W ..... Withdrew
WF ..... Withdrew - failing
WL ..... Faculty Permission to withdraw from a deferred examination
W-- or -- ..... No grade: student withdrew from the University

Administrative Statuses
(applicable to the Academic Integrity Tutorial)
CO ..... Completed
IC ..... Incomplete

Remarks
A ..... included in the GPA calculation but not credits
E ..... excluded from the GPA and credit calculation
I ..... included in the GPA and credit calculation
EXC ..... excluded from the GPA and credit calculation, normally at the time of a change in the student's degree program

Remarks – Prior to September 2002
G ..... credit not normally allowed but permitted in this case
H ..... pass at undergraduate level
Ø ..... completion from earlier year
R ..... course repeated to meet program time limit
T ..... credit by exam only
U ..... extra
V ..... course for non McGill DCS
X ..... extra
Y ..... not for credit, not calculated in the GPA
Z ..... course for McGill DCS

Class Average
Where appropriate, a class average expressed as the letter grade most representative of the class performance, appears in the class average column.

Credits
Since September 1971, most courses have carried a credit weight. Generally, a one-term course taught for 3 hours a week carries 3 credits. The number of credits completed is shown for most programs.

Prior to Fall 2002 an asterisk (*) appears next to the credit value of courses not counted in the total credits earned.

Non-Credit Courses
Courses offered by the School of Continuing Studies which are non-credit are assigned Continuing Education Units (CEU). One CEU represents 10 hours of participation.

Multi-Term Courses
A multi-term course is indicated by a ◇ following the course number.

DCS/DEC
Since 1969, Quebec high school graduates must complete a two-year college (CEGEP) program leading to a Diploma of Collegial Studies (DCS/DEC) before entering university.

Graduation Honours – Effective September 2009
Distinction The notation of *Distinction* is awarded to students who have completed the required number of McGill credits for graduation and whose cumulative grade point average is in the top 25%, but below the top 10%, of their Faculty's graduating class.

Dean's Honour List A graduand identified as being on the *Dean's Honour List* must have earned a cumulative grade point average within the top 10% of their Faculty's graduating class.

NOTATION – depuis septembre 1980

Médecine dentaire (depuis1987)	Notes de 2e/3e cycle	Notes de 1er cycle	Notes pondérées	Échelle numérique des notes
A	A	A	4.0	85 - 100 %
A-	A-	A-	3.7	80 - 84 %
B+	B+	B+	3.3	75 - 79 %
B	B	B	3.0	70 - 74 %
B-	B-	B-	2.7	65 - 69 %
C+		C+	2.3	60 - 64 %
		C	2.0	55 - 59 %
		D	1.0	50 - 54 %
F (0-59%)	F (0-64%)	F (0-49%)	0.0	

Médecine (janvier 1970 à aujourd'hui) :
S = satisfaisant U = insatisfaisant

Avant septembre 2002, les notes numériques et les notes graphiques étaient indiquées pour certains cours.

« D » est une note de passage, mais qui ne suffit pas si le cours est exigible pour d'autres cours ou si le cours est obligatoire dans le cas du programme de l'étudiant.

On trouvera des données sur les politiques de notation en vigueur avant 1980 (pour le droit, avant 1985 et la médecine dentaire, avant 1987) à l'adresse http://www.mcgill.ca/students/records/fr/transcripts/key.

Moyenne pondérée (MP)
Toutes les unités visées servent au calcul de la moyenne pondérée, y compris les cours auxquels l'étudiant obtient un « D » ou les cours auxquels l'étudiant a échoué et qu'il redouble ou pour lesquels il subit un examen de reprise.

Autres notes
CR ..... Unité accordée en fonction de qualifications équivalentes
EX ..... Dispense
FN ..... Échec, sans droit de passer un examen de reprise
HH ..... À suivre
IP ..... En cours
J ..... Absent
K ..... Incomplet
KE ou K* ..... Autre prolongation consentie
KF ..... Incomplet - échec
KK ..... Dispense d'achèvement
L ..... Reporté
LE ou L* ..... Reporté - prolongation accordée
N ..... Abandon sans autorisation
NA ou && ..... Note pas encore disponible
NC ..... Sans évaluation
NE ..... Sans évaluation
NR ..... Aucune note déclarée par le chargé de cours (consignée par le registraire)
P ..... Réussite
Q ..... Cours poursuivi au trimestre suivant
R ..... Unité de cours
S ..... Satisfaisant
U ..... Insatisfaisant
W ..... Abandonné
WF ..... Abandonné - échec
WL ..... Autorisation de la faculté de ne pas subir un examen reporté
W-- ou -- ..... Pas de note : l'étudiant a quitté l'Université

Statuts administratifs
(applicables au tutoriel d'intégrité académique)
CO ..... Terminé
IC ..... Incomplet

Remarques
A ..... inclus dans le calcul de la MP, mais sans unités
E ..... exclu de la MP et du calcul des unités
I ..... inclus dans la MP et le calcul des unités
EXC ..... exclu de la MP et du calcul des unités, normalement au moment d'un changement dans le programme de l'étudiant sanctionné par un grade

Remarques – avant septembre 2002
G ..... Unité normalement interdite, mais autorisée dans ce cas
H ..... Réussite au niveau du 1er cycle
Ø ..... Terminé au préalable
R ..... Cours redoublé pour respecter l'échéance du programme
T ..... Unité accordée sur examen seulement
U ..... Extra
V ..... Cours valant pour un DEC hors McGill
X ..... Extra
Y ..... Sans unité, non calculé dans la MP
Z ..... Cours valant pour le DEC de McGill

Moyenne de la classe
Lorsqu'il y a lieu, la moyenne de la classe, exprimée comme la note alphabétique la plus représentative des résultats de la classe, figure dans la colonne de la moyenne de la classe.

Unités
Depuis septembre 1971, la plupart des cours ont un coefficient exprimé en unités. En général, un cours d'un trimestre enseigné trois heures par semaine vaut 3 unités. Le nombre d'unités obtenues est indiqué pour la plupart des programmes.

Avant l'automne 2002, un astérisque (*) figure en regard du coefficient d'unités des cours qui ne sont pas comptabilisés dans le total des unités obtenues.

Cours sans unités
Les cours dispensés par l'École d'éducation permanente pour lesquels l'étudiant n'a pas reçu d'unités donnent droit à des unités d'éducation permanente (UEC). Une UEC représente 10 heures de participation à un cours.

Cours échelonnés sur plusieurs trimestres
Un cours échelonné sur plusieurs trimestres est indiqué par un ◇ suivi du numéro du cours.

DCS/DEC
Depuis 1969, les diplômés des écoles secondaires du Québec doivent suivre un programme collégial de deux ans sanctionné par un diplôme d'études collégiales (DEC/DCS) avant d'être admis à l'Université.

Mentions d'honneur pour les diplômés – depuis septembre 2009
Distinction La mention de *Distinction* sera attribuée aux étudiants qui ont réussi le nombre exigé d'unités de McGill en vue de l'obtention du diplôme et qui se classent parmi les meilleurs 25 % (mais sous le seuil des 10 %) de l'effectif de dernière année dans chaque faculté, selon leur moyenne pondérée cumulative.

Tableau d'honneur du doyen Un étudiant en passe d'obtenir son diplôme et sélectionné en vue du *Tableau d'honneur du doyen* devra être du nombre des étudiants de dernière année dans chaque faculté se classant parmi les meilleurs 10 %, selon leur moyenne pondérée cumulative.

Address McGill University | Enrolment Services | 3415 McTavish St.
Montreal, QC | H3A 0C8 | Canada | www.mcgill.ca/students/records/transcripts

July 2017

Adresse Université McGill | Gestion de l'effectif étudiant | 3415, rue McTavish
Montréal (Québec) | H3A 0C8 | Canada | www.mcgill.ca/students/records/fr/transcripts

Juillet 2017