

1. Course Information

BCH4415B: Applications of Synthetic Biology and Chemical Genetics in Medicine

Winter Term 2022

This course provides an introduction to the emerging fields of Synthetic Biology and Chemical Genetics and how work in these areas is being applied to medicine. We will explore how metabolic pathways are being re-engineered in microorganisms to produce drugs that are otherwise difficult to manufacture. The potential to manipulate complex signal transduction pathways in humans will also be investigated. Chemical genetic approaches to define drug targets will be introduced and methods for expanding the genetic code plus applications of an expanded genetic code will be described. Emerging tools for genome-wide editing and genome construction will also be presented.

Lectures:

PAB-106 (in-person) plus Zoom Synchronous sessions,
Monday/Wednesday 1:30-2:30 pm

Friday Lectures:

B&GS 1056 (in-person) plus Zoom Synchronous sessions,
Friday 11:30am - 12:30 pm (dates as indicated)

Requisites:

Prerequisite(s): Either (Biochemistry 3381A and Biochemistry 3382A) or (Biochemistry 2280A and one of Chemistry 3393A/B or Chemistry 4493A/B)

Corequisite(s)

Antirequisite(s) Chemistry 4415b

Senate regulation regarding the student's responsibility regarding requisites:

Unless you have either the requisites for this course or written special permission from your Dean to enroll in it, you may be removed from this course and it will be deleted from your record. This decision may not be appealed. You will receive no adjustment to your fees in the event that you are dropped from a course for failing to have the necessary prerequisites.

Accessibility Statement

Please contact the course instructor if you require material in an alternate format or if you require any other arrangements to make this course more accessible to you. You may also wish to contact Services for Students with Disabilities (SSD) at 661-2111 x 82147 for any specific question regarding an accommodation.

2. Instructor Information

Instructors	Email	Office	Phone
Dr. Patrick O'Donoghue Course Coordinator	patrick.odonoghue@uwo.ca	MSB 388	82373
Dr. Brian Shilton	bshilton@uwo.ca	MSB 332	519-661-4124
Dr. Christopher Garnham	chris.garnham@agr.gc.ca	Agriculture and Agri-Food Canada, 1391 Sandford Street, London, ON	519-953-6643

OWL: BIOCHEM 4415B 001 FW21

Students with OWL issues should see: <https://owl.uwo.ca/portal/site/owldocs>

3. Course Syllabus

Topics and Learning Outcomes

Course Overview: Dr. P. O'Donoghue (Jan 3)

Chemical Genetics Part 1: Manipulating the genetic code

Dr. P. O'Donoghue - 4 lectures (Jan 5, 10, 12, 17)

- Expanding the genetic code: overview of engineering techniques to make proteins with > 20 canonical amino acids – applications in hardwiring posttranslational modifications in bacteria, yeast and mammalian cells
- Expanding the nucleotide alphabet: overview of chemical synthesis of non-canonical DNA and RNA bases and possible applications

Synthetic Biology Part 1: Introduction to recombineering:

Dr. P. O'Donoghue - 4 lectures (Jan 19, 24, 26, 31)

- Tools for genome-wide editing: multiplex genome engineering [MAGE] and phage assisted continuous evolution [PACE]
- Applications of “designer organisms” for biofuels, biocontainment and de-extinction

Learning Outcomes:

After completing this section, students should have gained knowledge/understanding of:

- how an interdisciplinary effort in chemistry and biochemistry decoded the genetic code

- chemical biology methods to expand the chemical space of genetically encoded amino acids and nucleotides
- methods for genome editing
- concepts and ethical implications related to synthetic cells and organisms
- how to read critically and assess historical and current scientific literature

O'Donoghue section Friday Lecture dates: Jan 14, Jan 28, Exam take-up March 4

O'Donoghue section Exam date: due Feb 4

Chemical Genetics Part 2: Combining Chemistry and Genetics for Synthetic Biology

Dr. B. Shilton – 8 lectures (Feb 2, 7, 9, 14, 16, 28; March 2, 7)
Friday Lectures (TBD)

Feb 19 – 27 - Spring Reading week

“Genetics is the study of genes and tries to explain what they are and how they work. Genes are how living organisms inherit features or traits from their ancestors. Genetics tries to identify which traits are inherited, and explain how these traits are passed from generation to generation.”¹ At the molecular level, most genes code for proteins that execute one or more functions. The goal of this section of the course is to understand how protein function can be modulated using chemicals or light, and how these approaches can be used in synthetic biological systems. In other words, chemical genetics and optical genetics incorporate synthetic biology to control and/or investigate protein (and by extension gene) function in a cellular or organismal context. In these 8 lectures, we will study chemical- and optical-genetic approaches that have been used to control biological systems, understand protein function, find new drugs, and characterize off-target interactions.

Learning outcomes:

After completing this section, students should have gained knowledge/understanding of:

- concepts underlying forward and reverse chemical genetics approaches,
- small molecule library design, screening (in vivo and in vitro), and target identification,
- function, design, and examples of optical biosensors and effectors

Shilton section Friday Lecture dates: TBD

Synthetic Biology Part 2: Metabolic engineering

Dr. C. Garnham – 7 lectures (March 9, 14, 16, 21, 23, 28, 30);
Friday lectures (March 18, April 1)

April 1 - last day of classes

¹ https://en.wikipedia.org/wiki/Introduction_to_genetics

- Understanding and engineering the biosynthesis of microbial secondary metabolites
- Screening for microbes capable of degrading secondary metabolites
- Engineering enzymes for improved performance (increased activity, altered specificity, enhanced thermostability)

Learning Outcomes:

After completing this section, students should have gained knowledge/understanding of:

- Understand how biosynthetic gene clusters (BGCs) are organized to produce secondary metabolites within bacteria and fungi
- Methods to engineer microbial BGCs to produce known metabolites and screen for novel metabolites with unknown function
- Methods to screen for microbes and enzymes capable of degrading secondary metabolites
- Methods to select for and characterize enzymes with improved biochemical and biophysical traits

Garnham section Friday lecture dates: March 18, April 1

5. Tutorial Sessions

- Held biweekly (or as directed by instructor – see above).
- Sessions will be run by either the course TA or an instructor.
- Material presented in the tutorial sessions is examinable.

6. Course Materials

Research papers provided as citations in lecture notes on course OWL web site.

7. Evaluation:

Component	Date	% of Final Mark
O'Donoghue section		
Rapid fire presentation	Fridays as indicated	5
Take home test	Feb 4, 2020	30
Shilton section		
In-class quizzes (~10 minutes)	TBD	15
“News and Views” article	TBD	20
Garnham section		
Final exam, take-home format	TBA	30

8. Additional Information/Statements

Statement on Final Marks

Final grades in this course, irrespective of the number of decimal places used in marking individual assignments and tests, will be calculated to one decimal place and rounded to the nearest integer (e.g., 74.4 becomes 74, while 74.5 becomes 75). Marks WILL NOT be bumped to the next grade or GPA level (e.g., an 84 will NOT be bumped up to an 85). The mark attained is the mark you achieved and the mark assigned; requests for mark bumping will be denied, in accordance with Bachelor of Medical Science Undergraduate Education policy.

Statement on Use of Electronic Devices

No electronic devices may be used for in-class quizzes or the final exam.

Statement on Academic Offences

“Scholastic offences are taken seriously and students are directed to read the appropriate policy, specifically, the definition of what constitutes a Scholastic Offence, at the following website: http://www.uwo.ca/univsec/handbook/appeals/scholastic_discipline_undergrad.pdf.”

“All required papers may be subject to submission for textual similarity review to the commercial plagiarism detection software under license to the University for the detection of plagiarism. All papers submitted for such checking will be included as source documents in the reference database for the purpose of detecting plagiarism of papers subsequently submitted to the system. Use of the service is subject to the licensing agreement, currently between The University of Western Ontario and Turnitin.com (<http://www.turnitin.com>).”

Absence from course commitments

Students must complete the following course evaluations (1 take-home test, 3 of 4 in-class quizzes, 1 research proposal, 1 exam) – there will be no re-weighting of marks due to a missed evaluation. The take-home test and research proposal (hard copy) are to be handed in at the beginning of class on the due date and an e-copy of the test/proposal is to be submitted on the course web site any time on the date the test/proposal is due. For the take-home test and the research proposal you will be lose 10% of the total value of the assignment per day handed in late.

A. Absence for medical illness:

Students must familiarize themselves with the Policy on Accommodation for Medical Illness for Undergraduate Students, located at:

http://www.uwo.ca/univsec/pdf/academic_policies/appeals/accommodation_medical.pdf

The policy is also accessible from the Medical Accommodation Policy link at

<https://studentservices.uwo.ca/secure/index.cfm>

Statement from the Academic Counselling Office, Faculty of Science (for Science and BMSc students)

If you are unable to meet a course requirement due to illness or other serious circumstances, you must provide valid medical or other supporting documentation to the Academic Counselling Office as soon as possible and contact your instructor immediately. It is the student's responsibility to make alternative arrangements with their instructor once the accommodation has been approved by the Academic Counselling Office and the instructor has been informed. In the event of a missed final exam, a

"Recommendation of Special Examination" form must be obtained from the Academic Counselling Office immediately. For further information please see:

http://www.uwo.ca/univsec/pdf/academic_policies/appeals/accommodation_medical.pdf

A student requiring academic accommodation due to illness, should use the Student Medical Certificate when visiting an off-campus medical facility or request a Record's Release Form (located in the Dean's Office) for visits to Student Health Services.

The form can be found at:

<https://studentservices.uwo.ca/secure/index.cfm>

B. Absence for non-medical reasons:

Students who are in emotional/mental distress should refer to Mental Health@Western

<http://www.uwo.ca/uwocom/mentalhealth/> for a complete list of options about how to obtain help.

C. Special Examinations

A Special Examination is any examination other than the regular final examination, and it may be offered only with the permission of the Dean/Academic Counselling Office of the Faculty in which the student is registered, in consultation with the instructor and Department Chair. Permission to write a Special Examination may be given on the basis of compassionate or medical grounds with appropriate supporting documents.

A Special Examination must be written at the University or an Affiliated University College no later than 30 days after the end of the examination period involved. To accommodate unusual circumstances, a date later than this may be arranged at the time permission is first given by the Dean/Academic Counselling Office of the Faculty. The Dean/Academic Counselling Office will consult with the instructor and Department Chair and, if a later date is arranged, will communicate this to the Office of the Registrar.

If a student fails to write a scheduled Special Examination, permission to write another Special Examination will be granted only with the permission of the Dean/Academic Counselling Office in exceptional circumstances and with appropriate supporting documents. In such a case, the date of this Special Examination normally will be the scheduled date for the final exam the next time the course is offered.

When a grade of Special (SPC) or Incomplete (INC) appears on a student's record, the notations will be removed and replaced by a substantive grade as soon as the grade is available.

Support Services:

Registrarial Services: <http://www.registrar.uwo.ca>

Academic Counselling (Science and Basic Medical Sciences):

http://www.uwo.ca/sci/undergrad/academic_counselling/index.html

USC Student Support Services: <http://westernusc.ca/services/>

Student Development Services: <http://www.sdc.uwo.ca>

Student Health Services: <http://www.shs.uwo.ca/>

Students who are in emotional/mental distress should refer to Mental Health@Western

<http://www.uwo.ca/uwocom/mentalhealth/> for a complete list of options about how to obtain help.