

General information

Course: CHEM 498U
Section: 01
Term: Fall 2016
Credits: 3.0
Location: CJ-1.121
Time: Wed and Fri 10:15-11:30

Instructor: Prof. Dajana Vuckovic
Department: Chemistry and Biochemistry
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Office hours: **Wed 1-2 pm, Fri 12-1 pm or by appointment**

Course Description

Calendar course description: Prerequisite: CHEM 271 AND 312 or permission from the instructor. This course presents the concepts, tools and common instrumental techniques employed in modern bioanalytical chemistry for the quantitative analysis of drugs, metabolites, toxins, environmental contaminants, biomarkers, proteins, biotherapeutics and/or DNA in biological samples. The main topics covered will include sample preparation; mass spectrometry; immunoassays; biosensors; microfluidics; bioanalytical method validation and discussion of emerging bioanalytical techniques and trends. The applications discussed will encompass toxicology, forensics, pharmacokinetics, metabolism, clinical chemistry, environmental analysis and biotechnology. Lectures and discussion-style tutorials.

Expanded course description: The main objective of this course is to teach students how to select or develop an analytical method for a given analyte in a given biological matrix. The students will be expected to understand the main principles of the stated techniques, and subsequently be able to compare/contrast different instrumental and non-instrumental approaches to select the most appropriate choice for a given analysis. To guide such critical interpretation, this course will heavily emphasize critical thinking and problem-solving skills through class discussions, problem-solving assignments and detailed exploration of case studies encompassing bioanalytical problems of current relevance such as newborn screening, clinical analysis of vitamin D, quality control of biotherapeutics and biosimilars and glucose monitoring.

Grading scheme

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|---------------------------------------|---|------------------------|
| Assignment 1 | October 14, 2016 | 10% |
| Assignment 2 | November 16, 2016 | 10% |
| Participation | Throughout the course | 10% |
| 5-page critical evaluation term paper | November 25, 2016 | 25% |
| Final exam | TBD, during exam period Dec 7-21, 2016 | 45% (comprehensive) |

Due dates and late policy:

→ Assignment due dates: **Assignments are due by 10:15 am before the beginning of the class on the stated dates.**

→ Late policy on assignments: **No late assignments will be accepted unless** medical note is provided. Any assignments that are not handed in by due date and time will be assigned a mark of **zero**. Assignments will **not** be accepted by email. Only printed or hand-written solutions to the assignment will be accepted. Please hand in complete solution to the assigned problems, not just the final answers.

Textbook:

→ Course notes and references described in weekly schedule for deeper information

→ Discussion papers – see page 4

→ FDA Bioanalytical Method Validation Guidelines:

<http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm368107.pdf>

<http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidance/ucm070107.pdf>

→ EMA Bioanalytical Method Validation Guidelines:

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/08/WC500109686.pdf

Textbooks (optional):

- **Bioanalytical Chemistry, Mikkelsen and Corton, 2nd edition, Wiley, 2016**
- Handbook of LC-MS Analysis, Li, Zhang and Tse, Wiley, 2013

MOODLE

All assignments and relevant course notes will be posted on Moodle course website. Please check the course website periodically to access these online materials. For any issues in terms of Moodle use please consult Helpdesk at extension 7613.

PARTICIPATION

Participation grade will be assigned at the end of the term based on the quality and quantity of your exchanges with your instructor and your peers in the class. You are expected to come prepared to the class which includes reading the materials before class and being prepared to discuss and critique the assigned readings. Please note that participation and attendance are not equal. Attendance at every class will not result in full marks for participation unless you actively engage in class and group discussions of the material. Participation for this class may involve various forms throughout the term including: i-clickers, class discussions, group discussions and brainstorming, asking questions based on lecture material and short in-class quizzes to assess whether you performed assigned readings.

GOOD ADVICE

→ do all questions on distributed assignments

→ do all assigned readings

→ prepare for discussion-style tutorials by reading the assigned journal article and critically thinking about it ahead of class time

→ seek assistance well before the exam

SCHEDULE:

| Week | Topic | References/readings |
|-------------------------|--|--|
| Week 1 Sep 7 | Biological samples Total protein, DNA, RNA and sugars spectroscopic methods | Li, Zhang and Tse, Chapter 12, Assessment of whole blood stability and blood/plasma distribution of drugs Mikkelsen and Corton, Chapter 2, Spectroscopic Methods for the Quantitation of Classes of Biomolecules |
| Week 2 Sep 14 | Centrifugation and separation | Mikkelsen and Corton, Chapter 15, Centrifugation Methods |
| Week 3 Sep 21 | Immunoassays | Mikkelsen and Corton, Chapter 6, Antibodies Mikkelsen and Corton, Chapter 7, Quantitative Immunoassays with Labels |
| Week 4 Sep 28 | Immunoassays (discussion paper) Sample preparation - classical | Li, Zhang and Tse, Chapter 13, Best practice in biological sample collection, processing and storage for LC-MS in bioanalysis of drugs Li, Zhang and Tse, Chapter 14, Best practice in biological sample preparation for LC-MS bioanalysis |
| Week 5 Oct 5 | Sample preparation – classical and microextraction | |
| Week 6 Oct 12 | Please note on Oct 12 there is guest lecture that you will be expected to attend on metabolomics Sample preparation - dried blood spots | Li, Zhang and Tse, Chapter 30, Best practices in LC-MS method development and validation for dried blood spots |
| Week 7 Oct 19 | Liquid chromatography-Mass Spectrometry | Mikkelsen and Corton, Chapter 16, Chromatography of biomolecules Mikkelsen and Corton, Chapter 17, Mass Spectrometry of Biomolecules |
| Week 8 Oct 26 | Bioanalytical method validation and regulatory requirements | FDA and EMA Bioanalytical Method Validation Guidelines Li, Zhang and Tse, Chapter 20, Evaluation and elimination of matrix effects in LC-MS bioanalysis Vogesser and Segel, Pitfalls Associated with the Use of Liquid Chromatography–Tandem Mass Spectrometry in the Clinical Laboratory Mikkelsen and Corton, Chapter 19, Validation of New Bioanalytical Methods |
| Week 9 Nov 2 | LC-MS of drugs, toxins and metabolites LC-MS of endogenous biomarkers | Quantitative determination of endogenous compounds in biological samples using chromatographic techniques, Nico Merbel, TrAC, 2008, http://www.sciencedirect.com/science/article/pii/S016599360800191X |
| Week 10 | LC-MS of proteins and | Lange et al. Selected reaction monitoring for quantitative |

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|--------------------------|-------------------|---|
| Nov 9 | biotherapeutics | proteomics: a tutorial http://msb.embopress.org/content/msb/4/1/222.full.pdf Tackling the increasing complexity of therapeutic monoclonal antibodies with mass spectrometry Sara Rosati, Natalie J. Thompson, Albert J.R. Heck, http://www.sciencedirect.com/science/article/pii/S0165993613000988 |
| Week 11 Nov 16 | Microfluidics | The present and future role of microfluidics in biomedical research, Eric K. Sackmann, Anna L. Fulton & David J. Beebe, <i>Nature</i> , 2014, http://www.nature.com/nature/journal/v507/n7491/pdf/nature13118.pdf |
| Week 12 Nov 23 | Biosensors | Glucose monitoring and pregnancy test Glucose Biosensors: An Overview of Use in Clinical Practice, Eun-Hyung Yoo and Soo-Youn Lee 2, <i>Sensors</i> 2010 , 10, 4558-4576; doi:10.3390/s100504558 Mikkelsen and Corton, Chapter 8, Biosensors |
| Week 13 Nov 30 | Final exam review | Slides will be posted on Moodle website |

DISCUSSION PAPER SCHEDULE

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|--------|---|
| Sep 23 | Sandwich Assay for Tacrolimus Using 2 Anti-Tacrolimus Antibodies T.Q. Wei, Y.F. Zheng, M. Dubowy, and M. Sharma, <i>Clinical Chemistry</i> , 2014, www.clinchem.org/content/60/4/621.full |
| Sep 28 | False Biomarker Discovery due to Reactivity of a Commercial ELISA for CUZD1 with Cancer Antigen CA125, Prassas I, Brinc D, Farkona S, Leung F, Dimitromanolakis A, Chrystoja CC, Brand R, Kulasingam V, Blasutig IM, Diamandis EP. <i>Clinical Chemistry</i> , 2014 http://www.clinchem.org/content/60/2/381.full.pdf+html |
| Oct 19 | Multifunctional CoreShell Nanoparticles: Discovery of Previously Invisible Biomarkers, Davide Tamburro, Claudia Fredolini, Virginia Espina, Temple A. Douglas, Adarsh Ranganathan, Leopold Ilag, Weidong Zhou, Paul Russo, Benjamin H. Espina, Giovanni Muto, Emanuel F. Petricoin, Lance A. Liotta, and Alessandra Luchini*, <i>JACS</i> , 2011, http://pubs.acs.org/doi/pdf/10.1021/ja207515j |
| Nov 11 | Quantitative Insulin Analysis Using Liquid Chromatography–Tandem Mass Spectrometry in a High-Throughput Clinical Laboratory, Chen Z , Caulfield MP , McPhaul MJ , Reitz RE , Taylor SW , Clarke NJ . <i>Clinical Chemistry</i> , 2014, http://www.clinchem.org/content/59/9/1349.full.pdf+html |
| Nov 23 | Analysis on the Go: Quantitation of Drugs of Abuse in Dried Urine with Digital Microfluidics and Miniature Mass Spectrometry Andrea E. Kirby, Nelson M. Lafrenière, Brendon Seale, Paul I. Hendricks, R. Graham Cooks, and Aaron R. Wheeler, <i>Analytical Chemistry</i> , 2014, http://pubs.acs.org/doi/pdf/10.1021/ac5012969 |

RIGHTS AND RESPONSIBILITIES**Plagiarism:**

The most common offense under the Academic Code of Conduct is plagiarism which the Code defines as “the presentation of the work of another person as one’s own or without proper acknowledgement.” This could be material copied word for word from books, journals, internet sites, professor’s course notes, etc. It could be material that is paraphrased but closely resembles the original source. It could be the work of a fellow student, for example, an answer on a quiz, data for a lab report, a paper or assignment completed by another student. It might be a paper purchased through one of the many available sources. Plagiarism does not refer to words alone - it can also refer to copying images, graphs, tables, and ideas. “Presentation” is not limited to written work.

It also includes oral presentations, computer assignments and artistic works. Finally, if you translate the work of another person into French or English and do not cite the source, this is also plagiarism.

In Simple Words: Do not copy, paraphrase or translate anything from anywhere without saying where you obtained it! (Source: The Academic Integrity Website:

<http://provost.concordia.ca/academicintegrity/plagiarism/>)

MANDATORY QUIZ AND SEMINAR

As part of this course, you are **required** to i) attend a Chemistry and Biochemistry Departmental Seminar on the academic conduct code and the appropriate use of information sources and ii) pass the online quiz associated with this seminar (the passing grade for the quiz is 100%). (**Note:** This is **not** the University's quiz you may have been asked to take when you first registered and logged into the myConcordia portal; the one you must take is similar, but graded by the Department of Chemistry and Biochemistry, and you cannot take it until after you have attended the seminar.) The aim of this seminar is to clarify the academic conduct code in terms of what practices will be considered unacceptable with regards to work submitted for grading in Chemistry and Biochemistry courses. **You are only exempt from repeating the seminar and the quiz if you have done both in Fall 2011 or more recently,*** otherwise you are required to repeat both this term. This short seminar (1 hour) will be held at the following times (note that late-comers will not be admitted):

| Date | Time | Place |
|---------------------|-------------|--------|
| Monday, Sept. 26 | 16:45-17:45 | CC-308 |
| Tuesday, Sept. 27 | 16:45-17:45 | HB-130 |
| Wednesday, Sept. 28 | 16:45-17:45 | CC-308 |
| Wednesday, Sept. 28 | 20:45-21:45 | HC-157 |
| Thursday, Sept. 29 | 16:45-17:45 | CC-204 |
| Thursday, Sept. 29 | 20:45-21:45 | HC-157 |
| Friday, Sept. 30 | 16:45-17:45 | CC-310 |

As space for each of the seminars is limited by the room size, please sign up to your preferred time. Sign-up sheets are available outside SP 201.01 (Departmental office).

If you do not complete this course requirement, your final grade for the course may be lowered by one full letter grade with an incomplete (INC) notation until such time as this requirement is completed. Please refer to the undergraduate calendar (section 16.3.6) for details on removal of an incomplete notation.

* You are exempt if you can locate your ID in the pdf file located on the CHEM 101 Moodle site (for guest login, go to: <http://moodle.concordia.ca/moodle>, Arts and Science, Chemistry and Biochemistry, Specialized Chemistry Sites, CHEM 101, look under FAQ).

PLAGIARISM AND OTHER FORMS OF ACADEMIC DISHONESTY:

The academic code of conduct can be found in section 17.10 of the academic calendar (<http://www.concordia.ca/academics/undergraduate/calendar/current/17-10.html>). Any form of unauthorized

collaboration, cheating, copying or plagiarism found in this course will be reported and the appropriate sanctions applied. The mandatory seminar is a clear and fair opportunity to learn what our faculty regards as academic misconduct. Failure to take part in this learning opportunity and thus ignorance of these regulations is no excuse and will not result in a reduced sanction in any case where academic misconduct is observed.