Academic Year	2020/21	**Semester**	2
Course Coordinator	Richard D. WEBSTER and ZHANG Zhengyang		
Course Code	CM4011		
Course Title	Advanced Analytical Chemistry		
Pre-requisites	{CM2011 and CM2062 and CM3062} or by permission		
No of AUs	3		
Contact Hours	On-line or face to face lectures - 35 hours Mid-term assessments - 4 hours		

Course Aims

The lectures provide an advanced account of modern analytical methods and instruments that are used to quantify chemical and biological samples and to monitor the progress of reactions. Students will understand the principles of advanced electrochemical, spectroscopic and chromatographic techniques applied to chemical analysis. The students will be able to use their in-depth knowledge of analytical chemistry to devise experiments that can quantify a range of diverse chemical components. The students will learn problem solving skills where they apply their theoretical knowledge to real life problems in the environment.

Intended Learning Outcomes (ILO)

By the end of this course, you (as a student) would be able to:

1. **Quality Assurance and Calibration Methods**
    a. Explain the steps in Quality Assurance (Use objectives, Specifications and Assessment).
    b. Describe how method validation is performed.
    c. Calculate the limit of detection (LOD) and limit of quantification (LOQ) and understand how they differ.
    d. Explain how and why standard additions are performed and how to calculate the concentration.
    e. Describe the principles of internal standards.

2. **Automated Measurements of Priority Pollutants**
    a. Explain how $PM_{2.5/10}$ levels are determined, first by separation into their respective sizes (by impactors or cyclones), and then their quantification by (direct weighing, beta attenuation monitoring, or with a tapered element oscillating microbalance).
    b. Describe how the gases SO_2 (fluorescence), O_3 (absorbance or chemiluminescence) and CO (infrared) are measured.
    c. Explain the equilibria between the major nitrogen/oxygen containing gaseous pollutants.
    d. Explain how NO, NO_X (fluorescence) and NO_2 (chemiluminescence) are measured.

3. **Electrolytic Methods**
    a. Describe why flowing current affects the cell potentials.
    b. Explain IR drop and polarisation (concentration and kinetic).
    c. Calculate “charge” and describe how it relates to electron count and mols of compounds (Faraday’s law).
    d. Explain how electrochemical electrolysis cells are constructed.
    e. Describe how the Karl Fischer (KF) titration works and how to calculate the water content from the measurements.
    f. Explain the principles of ion chromatography.

g. Describe the pros and cons of ion chromatography (IC) and ion-selective electrodes (ISE) measurements and when you would use the techniques.

4. Voltammetric Analysis

a. Describe the concepts of voltammetry.
b. Explain the different ways that voltammetric excitation signals can be applied and the advantages and disadvantages of the different voltammetric techniques.
c. Explain how a potentiostat functions and what is the purpose of having 3 electrodes.
d. Explain the difference between hydrodynamic and stationary electrode voltammetry.
e. Describe why current-voltage curves have a specific shape in hydrodynamic voltammetry.
f. Explain how pH effects voltammograms for reactions that involve protons.
g. Explain the differences and similarities in pulsed voltammetric methods.
h. Describe how the oxygen and glucose voltammetric sensors function.

5. Cyclic voltammetry

a. Explain how cyclic voltammetry is performed.
b. Explain why comproportionation reactions occur.
c. Explain the use of cyclic voltammetry to determine electrochemical mechanisms.

6. EPR spectroscopy

a. Describe the Zeeman effect.
b. Explain what hyperfine interactions are and why they occur in a magnetic field.
c. Describe how the nuclear spin quantum number affects the hyperfine pattern.
d. Explain the important rules for predicting hyperfine coupling patterns for all nuclei ($2nI + 1$) and the binomial expansion (Pascal's triangle) for $I = {}^1/_2$ nuclei.
e. Describe why isotopes affect the line intensities.
f. Explain the methods of preparing radicals.
g. Describe the difference between spin traps and spin labels.

7. Optical Sensors

a. Describe the scientific concepts of absorbance and fluorescence.
b. Explain how optical fibres transmit light and the importance of the “cone of acceptance” and “critical angle”.
c. Explain the different ways that optodes can function in sensing, including through absorbance (transmission and reflectance) and fluorescence and be able to draw simple schematic diagrams.

8. Capillary Electrophoresis

a. Explain how ions are separated in capillary zone electrophoresis.
b. Describe how charge is related to electrophoretic mobility.
c. Explain how the solution is transported from anode to cathode.
d. Describe the arrival of species in the detector.
e. Describe what is apparent mobility.
f. Explain how zone dispersion arises in capillary zone electrophoresis.
g. Describe how stacking of solute ions in the capillary occurs.
h. Describe electroosmotic flow under low pH.
i. Explain how covalent coatings reduces electroosmosis and wall adsorption.
j. Describe hydrodynamic and electrokinetic sample injection.
k. Describe common detection methods in capillary electrophoresis.

l. Explain how micellar electrophoretic chromatography separates neutral molecules and ions.
m. Explain how capillary gel electrophoresis separates macromolecules and discuss the speed of separation with molecular exclusion chromatography.
n. Discuss how microfluidic devices function.

9. Mass spectrometry

a. Explain how ions are created in mass spectrometer.
b. Describe how magnetic sector mass spectrometer separates gaseous ions.
c. Describe how ions are detected.
d. Explain the high resolution obtained by double-focusing mass spectrometer.
e. Explain the operations of transmission quadrupole and time-of-flight mass spectrometer.
f. Describe how resolving power is defined.
g. Describe how to determine molecular ion from the mass spectrum.
h. Explain how to predict the relative intensities of isotopic peaks for a given composition.
i. Interpret the fragment ions arising from bond cleavage to determine the molecular structure.
j. Calculate the molecular composition from the rings + double bonds equation.
k. Explain how electrospray ionization creates ions in liquid chromatography.
l. Describe how atmospheric pressure chemical ionization crate gaseous ions.
m. Explain how collisionally activated dissociation produce fragmented ions.
n. Describe the working principle of matrix-assisted laser desorption/ionization.
o. Describe the peaks obtained in reconstructed total ion chromatogram and extracted ion chromatogram.
p. Describe the working principle in selected ion monitoring.
q. Explain how molecules can be ionized from the surface of an object in ambient atmosphere.
r. Explain how ion mobility spectrometer separates gas-phase ions.

Course Content

S/N	Topic	Approx. Lecture Hours
1	**Quality Assurance and Calibration Methods:** Method blanks, standard operating procedures, method validation, limits of detection and quantification, calibration curves, standard additions and internal standards.	3
2	**Automated Measurements of Priority Pollutants:** Air quality index and pollutant standards index, $PM_{2.5}$ and PM_{10} and methods of separation and quantification, inorganic gases including SO_2, NO_X, O_3, CO and their methods of detection and quantification though absorbance, luminescence and infrared measurements.	2
3	**Electrolytic Methods:** The effect of current on cell potentials, concentration and kinetic polarisation, controlled potential electrolysis, coulometry, Karl Fischer (KF) titrations and ion chromatography.	3
4A	**Voltammetric Analysis:** Linear sweep voltammetry, electrode materials, microelectrodes, hydrodynamic effects, differential pulse voltammetry, square-wave voltammetry, stripping methods and voltammetric sensors.	3

4B	**Cyclic voltammetry:** Diagnostic features, scan rate dependence, electrochemical mechanisms, comproportionation, reduction of aromatic halides, hydroquinones, quinones, phenols, disproprtionation, reversible dimerization and the square scheme mechanism.	3
5	**EPR spectroscopy:** Basic theory, rules for interpreting spectra of organic radicals, examples of spectra, methods or preparing paramagnetic compounds and spin traps.	3
6	**Optical Sensors:** Beer-Lambert law, optodes, total internal reflection, absorbance (transmission, reflectance) and fluorescence	2
6	**Capillary Electrophoresis:** Principles of capillary electrophoresis, electrophoresis, electroosmosis, mobility, theoretical plates and resolution, conducting capillary electrophoresis, controlling the environment inside the capillary, sample injection and composition, conductivity effects (stacking and skewed peaks), detectors, micellar electrokinetic chromatography, capillary gel electrophoresis, method development, lab-on-a-chip.	8
7	**Mass spectrometry:** Molecular mass and nominal mass, separation of masses by magnetic field, electron ionization, resolving power, molecular ion and isotope patterns, high-resolution mass spectrometry, rings and double bonds, identifying molecular ion peak, interpreting fragmentation patterns, types of mass spectrometers, transmission quadrupole mass spectrometer, time-of-flight mass spectrometer, orbitrap mass spectrometer, chromatography-mass spectrometry interfaces, electrospray ionization, atmospheric pressure chemical ionization, direct electron ionization, photoionization, chromatography-mass spectrometry techniques, selected ion monitoring and extracted ion monitoring, selected reaction monitoring, electrospray of proteins, electron-transfer dissociation for protein sequencing, open-air sampling for mass spectrometry, direct analysis in real time, desorption electrospray ionization, ion mobility spectrometry.	8

Assessment (includes both continuous and summative assessment)

Component	Course LO Tested	Related Programme LO or Graduate Attributes	Weighting	Team/Individual	Assessment Rubrics
Mid-term Test 1	1-5b	Competence and Creativity	20%	Individual	See Appendix 1
Mid-term Test 2	6-7		20%	Individual	
Final Examination	All		60%	Individual	
Total			100%		

Formative feedback

You will be given feedback in four ways:

1. By response to postings on the course discussion board.
2. Through the marking of the mid-terms.
3. Through one-on-one discussions via appointment with the course instructor

4. General feedback will be provided to the students following the final exam.

Learning and Teaching approach

Approach	How does this approach support students in achieving the learning outcomes?
Blend of online and face-to- face lectures.	The bulk of the content will be delivered online. This allows (a) extensive use of animations and laboratory videos and (b) use of interactive questions so that students may immediately test their learning. Face to face lectures and experimental demonstrations will be employed for selected topics.

Reading and References

D. A. Skoog, D. M. West, F. J. Holler and S. R. Crouch "Fundamentals of Analytical Chemistry (9th Edition)", Brooks/Cole, Cengage Learning, 2014. ISBN: 9780495558286

Reference textbook: D. C. Harris and C. A. Lucy “Quantitative Chemical Analysis (9th Edition)", W. H. Freeman and Company, 2016. ISBN: 9781319154141

Course Policies and Student Responsibilities

(1) General

You are expected to complete all online activities in good time.

(2) Absenteeism

If you miss a lecture, you are expected to make up for the lost learning activities. If you miss one of the mid-term tests with a valid reason and approval (such as a medical certificate), then the total CA will come from the other mid-term test. If you miss both mid-term tests with a valid reason then an additional make-up test will be set to obtain the total CA mark.

Academic Integrity

Good academic work depends on honesty and ethical behaviour. The quality of your work as a student relies on adhering to the principles of academic integrity and to the NTU Honour Code, a set of values shared by the whole university community. Truth, Trust and Justice are at the core of NTU’s shared values.

As a student, it is important that you recognize your responsibilities in understanding and applying the principles of academic integrity in all the work you do at NTU. Not knowing what is involved in maintaining academic integrity does not excuse academic dishonesty. You need to actively equip yourself with strategies to avoid all forms of academic dishonesty, including plagiarism, academic fraud, collusion and cheating. If you are uncertain of the definitions of any of these terms, you should go to the academic integrity website for more information. Consult your instructor(s) if you need any clarification about the requirements of academic integrity in the course.

Course Instructors

Instructor	Office Location	Phone	E-mail
Richard WEBSTER	SPMS-CBC-04-06	6316 8793	webster@ntu.edu.sg
ZHANG Zhengyang	SPMS-CBC-03-02	6513 6059	zhang.zy@ntu.edu.sg

Planned Weekly Schedule

Week	Topic	Course LO	Readings/ Activities
1	Quality Assurance / Air Quality Measurements	1	Lecture and online
2	Air Quality Measurements / Electrolysis	2	Online content
3	Electrolysis	3	Online content
4	Voltammetry	4	Online content
5	Voltammetry	5	Online content
6	Mid-term Test 1 / EPR Spectroscopy	6a to 6d	Lecture and online content
7	EPR Spectroscopy / Optical Sensors	6e to 6g, 7	Online content
8	Capillary Electrophoresis	8a to 8f	Lecture and online
9	Capillary Electrophoresis	8g to 8l	Lecture and online
10	Capillary Electrophoresis / Mass spectrometry	8n to 8n, 9a to 9d	Lecture and online
11	Mass spectrometry	9e to 9h	Lecture and online
12	Mid-term Test 2 / Mass spectrometry	9i to 9l	Lecture and online
13	Mass spectrometry	9m to 9r	Lecture and online
The above schedule is for illustrative purposes and is subject to the exigencies of the calendar			

Appendix 1: Assessment Criteria for all components

Mid-term Test 1 and 2 – MCQ questions (two tests worth 20 marks each).

Standards		
Fail standard (0-7 marks)	**Pass standard (8-15 marks)**	**High standard (16-20 marks)**
Answers to the questions are mostly incorrect.	Answers to the questions are mostly correct.	Answers to the questions are almost always correct.

Final Examination – short answer questions and calculations (exam worth 60 marks).

Standards		
Fail standard (0-24 marks)	**Pass standard (25-48 marks)**	**High standard (49 -60 marks)**
Answers demonstrate the ability to repeat factual knowledge but not to apply it outside of the lecture context. Answers do not have a strong logical underpinning or maybe attempts to answer both ways at the same time.	Answers to the standard level question are correct and show the ability to apply concepts from the course, but a high level of critical thinking is absent. Answers are reasonably logical, but with gaps.	Answers to all questions show a high and consistent level of critical analysis of the information presented and creative solutions to the problems. Answers are highly logical and demonstrate strong reasoning. Answers are concise and to the point.

CBC Programme Learning Outcome

The Division of Chemistry and Biological Chemistry (CBC) offers an undergraduate degree major in Chemistry that satisfies the American Chemical Society (ACS) curricular guidelines and equips students with knowledge relevant to the industry. Graduates of the Division of Chemistry and Biological Chemistry should have the following key attributes:

1. Competence

Graduates should be well-versed in the foundational and advanced concepts of chemical science, be able to evaluate chemistry-related information critically and independently, and be able to use complex reasoning to solve emergent chemical problems.

2. Creativity

Graduates should be able to synthesize and integrate multiple ideas across the curriculum, and propose innovative solutions to emergent chemistry-related problems based on their training in chemistry.

3. Communication

Graduates should be able to demonstrate clarity of thought, independent thinking, and sound scientific analysis and reasoning through written and oral reports to audiences with varying technical backgrounds. They should also be able to effectively engage other professional chemists in collaborative endeavours.

4. Character

Graduates should be able to act in responsible ways and uphold the high ethical standards that the society expects of professional chemists.

5. Civic-mindedness

Graduates should be aware of the impact of chemistry on society, and how chemistry can be applied to benefit mankind. They should also be aware of and uphold the best chemical safety practices.