MCS New Course Proposal Form

Course Title: Metals in Biology: Function and Reactivity

Instructors: Yisong Guo

Course Number: 09-521/09-721    Cross Listing:

Prerequisites/Corequisites: (09344 and 09-345) or 09214 or 09-347; and 09-348; or approval of the instructor.

Semesters Offered:

☒ Fall    ☐ Spring    ☐ Summer-All    ☐ Summer 1    ☐ Summer 2

Semester Length:

☐ Mini 1    ☐ Mini 2    ☐ Mini 3    ☐ Mini 4    ☒ Full Semester

Location    ☒ Pittsburgh    ☐ Doha

Course Offering Frequency: Every other year

Suggested Days and Times: Two 80 minute lectures per week; days and times TBD

Learning Format    ☒ In Person    ☐ Online    ☐ Combination

Course Evaluation type:    ☒ Letter Grade    ☐ Pass/Fail

Course Unit Justification:    Total Units 12 units (09-721), 9 units (09-521)

In Class Hours: 3    Recitation Hours: 0

Lab Hours: 0    Out of Class Hours: 9 (09-721), 6 (09-521)

Target Population: Seniors and graduate students in chemistry, biological sciences, and chemical engineering.

Anticipated Enrollment: 10-15

Rationale for Course (Background): Many fundamental processes of life require metal ions, including photosynthesis, respiration, global nitrogen cycle, carbon
cycle, gene regulation, bio-signal sensing and DNA/RNA repair. These metal ions are usually covalently bound to protein scaffold to form well-defined metal sites in order to perform chemical transformations that are essential in supporting the biological processes mentioned above with high efficiency. Some of the chemical transformations are highly relevant in renewable energy research and human health, such as photosynthetic water oxidation, carbon dioxide fixation, nitrogen fixation, hydrocarbon formation, antibiotics biosynthesis, and toxic aromatic compound degradation. The knowledge on how the metal sites in proteins function can provide valuable guidelines for designing efficient and inexpensive catalysts to perform some of these important yet challenging chemical reactions. This course is designed to illustrate this knowledge to students. The focus is to introduce the properties of the geometric and electronic structures of metal sites in proteins using transition metal chemistry principles, and the interactions between metal sites and their surrounding protein environments, as well as how these properties and interactions define functions of these metal containing proteins (metalloproteins). The research tools used in this research area will also be introduced. This course is a expansion to the existing course – Bioinorganic Chemistry (09-521/721). The newly added sections are related to biomimetic/bioinspired chemistry and metalloprotein engineering (See Topic 5 and 6 in Topic Covered section). This course will attract students from different research areas, including biochemistry, physical chemistry, catalysis, and chemical engineering.

Special Facilities Needed: None

Assessment: Problem sets, final exam, original research proposal (for graduate students only), research proposal defence (for graduate students only) and journal review presentation (for undergraduate students).

Topics Covered: (1) Introduction of bioavailable metals that are essential to life, their distribution in nature, the mechanisms used to selectively transport these metal ions into living organisms, and the strategies utilized for the storage of these metals in living organisms. (2) The fundamentals of protein structures and the modes of metal binding in proteins. In this topic, principles of coordination chemistry related to bioinorganic chemistry will be introduced. The focus is on discussing the different coordination modes that metal ions adopt when bound to protein, the amino acid residues used for metal binding, and the geometric/electronic properties of metal binding sites in proteins. (3) Introduction of physical methods used in bioinorganic chemistry to detect and characterize metal sites in proteins and their interaction with the surrounding protein environment. The methods will be introduced include optical techniques, such as optical absorption spectroscopy, vibrational techniques, such as Infrared and Raman spectroscopies, magnetic techniques, such as Mössbauer, electron paramagnetic resonance (EPR), and X-ray techniques, such as X-ray absorption, X-ray diffraction. (4) Introduction of chemical reactivities exhibited by metal sites in proteins. This is
the major part of the course. In this topic, different types of chemical reactions catalyzed by metal containing enzymes (metalloenzymes) will be introduced, the factors determine the native reactivities of these enzymes will be discussed. The reactions will be included are hydrolytic reactions, electron transfer and respiration, photosynthesis, oxygen metabolism that focuses on O2-transport and O2-activation chemistry, hydrogen metabolism that focuses on H2 generation and oxidation, nitrogen fixation and nitrification/denitrification, carbon metabolism that focuses on the reduction of carbon dioxide to methane, racial chemistry utilized by metalloenzymes. (5) Introduction of biomimetic and bioinspired chemistry. In this topic, recent literature examples of inorganic model complexes and catalysts that are designed by utilizing chemical principles discovered from enzyme studies and introduced in the previous topics will be discussed. (6) Introduction of metalloenzyme design and engineering. In this topic, recent literature examples of artificial metalloenzymes will be discussed. The focus is on how to integrate the chemical principles learnt from the studies on native enzymes to design and engineer metalloenzymes in order to mimic reactivities of native enzymes and also explore novel chemical reactivities on the naturally occurring protein scaffolds.

Course Catalog Description: Metal ions play important roles in many biological processes, including photosynthesis, respiration, global nitrogen cycle, carbon cycle, antibiotics biosynthesis, gene regulation, bio-signal sensing, and DNA/RNA repair, just to name a few. Usually, metal ions are embedded in protein scaffold to form active centers of proteins in order to catalyze a broad array of chemical transformations, which are essential in supporting the biological processes
mentioned above. These metal containing proteins, or metalloproteins, account for half of all proteins discovered so far. In this course, the relation between the chemical reactivity and the structure of metalloproteins will be discussed in detail. The main focus is to illustrate the geometric and electronic structure of metal centers and their interactions with the protein environment in governing the chemical reactivity of metalloproteins. The applications of these principles in designing biomimetic/bioinspired inorganic catalysts and in engineering metalloproteins bearing novel chemical reactivity will also be discussed. The basic principles of the frequently utilized physical methods in this research area will also be introduced, which include optical absorption spectroscopy, Infrared (IR) and Raman spectroscopies, Mössbauer spectroscopy, electron paramagnetic resonance (EPR), X-ray absorption and diffraction techniques.

**Learning Objectives:** Students should be able to: understand the general strategies used to transport and store metals in living organisms, and the basic coordination chemistry of metal ions in protein scaffolds; understand the basic principles of physical methods introduced in this course, and know what kind of information can be extracted by using different spectroscopic techniques; understand the effects of the geometric and electronic structure of metal centers and their interactions with the protein environment in governing the chemical reactivity of metalloproteins; and utilize this knowledge to design research projects to study metalloprotein functions.

**Departmental Approval Date:** Click here to enter text.

**CUA Recommendation Date:** Click here to enter text.
College Council Approval Date: Click here to enter text.

Date Sent to Enrollment Services: Click here to enter text.

Comments: Click here to enter text.

* Please attach a copy of the proposed syllabus
Carnegie Mellon University
Department of Chemistry
09-521/721 Metals in Biology: Function and Reactivity
Fall 2017

Instructor: Yisong Guo
Office: Mellon Institute 552, ext: 8-1704
Email: ysguo@andrew.cmu.edu

Class Schedule: M, W 10:30 am – 11:50 am in Mellon Institute 448
Office Hours: By appointment

Prerequisites: (09-344 and 09-345) or 09-214 or 09-347, AND 09-348 or approval of the instructor.

Overview
Metal ions play important roles in many biological processes, including photosynthesis, respiration, global nitrogen cycle, carbon cycle, antibiotics biosynthesis, gene regulation, bio-signal sensing, and DNA/RNA repair, just to name a few. Usually, metal ions are embedded in protein scaffold to form active centers of proteins in order to catalyze a broad array of chemical transformations, which are essential in supporting the biological processes mentioned above. These metal containing proteins, or metalloproteins, account for half of all proteins discovered so far. In this course, the relation between the chemical reactivity and the structure of metalloproteins will be discussed in detail. The main focus is to illustrate the geometric and electronic structure of metal centers and their interactions with the protein environment in governing the chemical reactivity of metalloproteins. The applications of these principles in designing biomimetic/bioinspired inorganic catalysts and in engineering metalloproteins bearing novel chemical reactivity will also be discussed. The basic principles of the frequently utilized physical methods in this research area will also be introduced, which include optical absorption spectroscopy, Infrared (IR) and Raman spectroscopies, Mössbauer spectroscopy, electron paramagnetic resonance (EPR), X-ray absorption and diffraction techniques.

Learning Objectives
By the end of this course, you should be able to:
(i) understand the general strategies used to transport and store metals in living organisms, and the basic coordination chemistry of metal ions in protein scaffolds;
(ii) understand the basic principles of physical methods introduced in this course, and know what kind of information can be extracted by using different spectroscopic techniques;
(iii) understand how the geometric and electronic structure of metal centers and their interactions with the protein environment can tune the chemical reactivity of metalloproteins;
(iv) utilize the knowledge learnt to design research projects to study metalloprotein functions.

Course Material
Department of Chemistry, Carnegie Mellon University
Text:
Principles of Bioinorganic Chemistry, Lippard and Berg
Biological Inorganic Chemistry – Structure and Reactivity, ed. Bertini, Gray, Stiefel, Valentine

Additional references:
Physical Methods in Bioinorganic Chemistry, cd. Que
The Biological Chemistry of the Elements, Frausto da Silva, Williams
Bioinorganic Chemistry, Rehder
Physical Methods for Chemists, Drago
Physical Inorganic Chemistry, Kettle

Topic Covered
1. Introduction of bio available metals, their distribution, uptake and storage
2. Metal coordination chemistry in bioinorganic chemistry
3. Fundamentals of protein structures
4. Introduction of physical methods in bioinorganic chemistry
5. Introduction of chemical reactivities by metal sites in metalloproteins
6. Introduction of biomimetic/bioinspired chemistry
7. Introduction of metalloenzyme design and engineering

Tentative Class Schedule
Lecture 1. Biologically relevant metals and biomolecule overview
Lecture 2-3. Metal coordination chemistry
Lecture 4. The fundamentals of protein structure and metal cofactors
Lecture 5-8. Introduction of various physical methods
Lecture 9. Metal uptake and storage
Lecture 10. The fundamental of electron transfer and electron transfer proteins
Lecture 11. Hydrolytic, non-redox enzymes
Lecture 12-13. Photosynthesis
Lecture 14. O₂-transport proteins
Lecture 15-16. O₂-activating enzymes and their catalytic functions
Lecture 17-18. Metalloenzymes in the global nitrogen cycle
Lecture 19. Metalloenzymes in the reduction of one-carbon compounds
Lecture 20-21. Protein tuning of metal properties
Lecture 22-23. Examples of biomimetic/bioinspired chemistry
Lecture 24-26. Examples of artificial metalloenzymes and their novel reactivities
Lecture 27-28. Original research proposal defense and journal review presentation

Course Work and Grading
The final grade will be based on the following point distribution. For graduate students, the final grade is the sum of items 1 - 4 (total points of 120), and for undergraduate students, the final grade is the sum of items 1-2, and 5 (total points of 100). 90-100% A; 80-89% B, 70-79% C, 60-69% D, 50-59% R.

Department of Chemistry, Carnegie Mellon University
1. **Problem Sets (50%)**. Each problem set will be due in two weeks from the initial assigned date.

2. **Final Exam (20%)**. A comprehensive final exam will be given in the final exam week, which will include all the materials covered in this course.

3. **Original Research Proposal (30%) [for graduate students only]**. Create a written research proposal based on the topic of your choice. The proposal must focus on transition metals in biological systems. You can propose to study the function of a metalloenzyme of your choice using the physical methods introduced in this course or propose to explore new function of a metalloenzyme through protein engineering.

   **Length**: 1 page abstract including the title, 1 page specific aims, 6 page research narrative including figures, but excluding abstract and references.

   **Due Date**: Nov. 27th, 2017

   **Format of the proposal**:
   
   Title
   Abstract
   Specific Aims: List the long-term objectives of the research. From those objectives, state the specific research hypotheses that are to be tested in this proposal.
   Background and Significance: Review and critically evaluate the existing literature, identify the gaps that this project is intended to fill.
   Research Design and Methods: Describe the research design and procedures to be used to accomplish the specific aims of the project. Include the means by which the data will be collected, analyzed, and interpreted. Discuss the potential difficulties and limitations of the proposed research and alternative procedures.

4. **Original Research Proposal Defense (20%) [for graduate students only]**. Each student will deliver an oral presentation (20 min) to the instructor and all other students. Then the work will be reviewed by your peers in a convened panel following the NIH review guidelines. All feedbacks will be used to assign a score for your presentation.

5. **Journal Review (30%) [for undergraduate students only]**. A review of journal articles that has appeared within the last 3 years. You will present the review to the class. The instructor and all other students will give formal feedbacks to your presentation. All these feedbacks will be used to assign a score for your presentation. The powerpoint presentation should be approximately 20 minutes in duration with 5-10 min Q&A. The research must be concerned with transition metals in biological systems. Please refer to one of the following journals for your topic: Science, Nature, Nature Chemistry, Proceedings of the National Academy of Sciences, Journal of the American Chemical Society, Angewante Chemie – International Edition, Chemical Science, Inorganic Chemistry, Chemistry – a European Journal, Dalton Transactions, Biochemistry, Journal of Biological Chemistry, Journal of Biological Inorganic Chemistry.

*Finally, do your best to maintain a healthy lifestyle this semester by eating well, exercising, avoiding drugs*

Department of Chemistry, Carnegie Mellon University
and alcohol, getting enough sleep and taking some time to relax. This will help you achieve your goals and cope with stress.

All of us benefit from support during times of struggle. You are not alone. There are many helpful resources available on campus and an important part of the college experience is learning how to ask for help. Asking for support sooner rather than later is often helpful.

If you or anyone you know experiences any academic stress, difficult life events, or feelings like anxiety or depression, we strongly encourage you to seek support. Counseling and Psychological Services (CaPS) is here to help: call 412-268-2922 and visit their website at http://www.cmucounseling.edu. Consider reaching out to a friend, faculty or family member you trust for help getting connected to the support that can help.