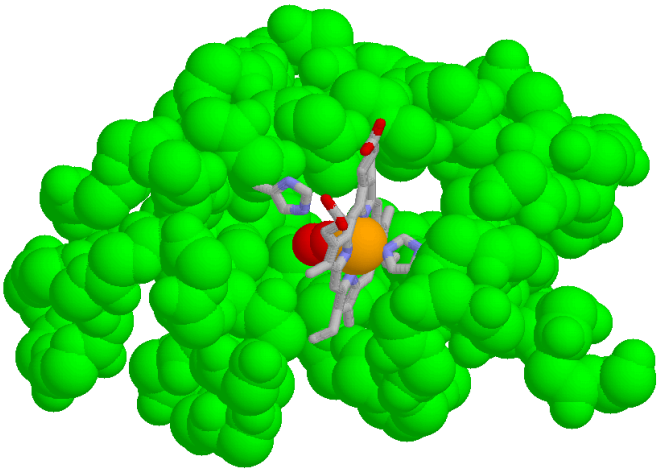
Department of Chemistry

CHEM*4630 Winter 2015

Bio-Inorganic Chemistry



Lecturer: Marcel Schlaf MACN 339, x 53002, mschlaf@uoguelph.ca

Prerequisites: CHEM 2580, CHEM 3640, CHEM 3650 (can be taken concurrently)

Objective of the course:

This course gives an introduction to the structural and functional roles of metals in biological systems with a particular emphasis on metalloproteins and the structure of and catalytic reactions at transition metal centres in those proteins.

Each student is expected to each give a ~ 12 min. presentation (maximum 10 slides, 10 minutes + 2 min. questions) on a specialized topic in bio-inorganic chemistry in the in the last 7-8 lectures of the course. The presentation must be in electronic format (i.e. PowerPoint/Impress/Prezi/ or equivalent software) and submitted to Professor Schlaf in electronic format (CD, email, server upload, memory stick) on the day of the lecture. See topic list below – topics will be assigned on a first-come-first-served basis. Each student will also select one review/account/perspective paper relevant to his/her presentation, which will be added to the required reading list given below.

You have to pick your presentation topic by 13/02/2015 !

The course also requires the use of programs such as RASTOP and/or CHIMERA used to display protein structures. Students will generate RASTOP and CHIMERA scripts and visualizations as an assignment.

Warning: *Without a good foundation in molecular bonding theories and transition metal chemistry as supplied by the prerequisite courses this course is probably not suitable for biochemistry students. However the prerequisites can be waived if you are a nano science or biochemistry/life science student and really want to take the course - at your own risk !*

Lecture & Lab times and dates:

MWF 08:30-09:20 h in MCKN 225

Start: 05/01/2013
End: 01/04/2013

No classes from 16/02-20/02/2013 (break week) and on 28/01/2015 (Schlaf away to give an invited lecture at UWO).

Dr. Schlaf's office hours:

Any time I am here (… and I am there a lot !). If I am too busy I may have to ask you to come back some other time. You can also ask questions by email (mschlaf@uoguelph.ca) ANYTIME. I will respond as soon as possible, but may not check my email on weekends or evenings. Emails that do not meet commonly accepted standards of communications between professionals will NOT be answered, neither will text messages, phone calls, tweets or similar nonsense.

Evaluation:

Midterm: In class, Monday, 02/03/2015
Final: Saturday, April 11/04/2015, 19:00-21:00 h, location TBA

Midterm: 25 %
Final: 35 %
Presentation: 35 %
RASTOP: 5 % (due date is the date of the Midterm, i.e. 02/03/2015 at12:00 h)

Course Materials:

Are available for download from the Schlaf Group Server at
https://schlafgroup.homeserver.com/Home/default.aspx
(login and password required – will be supplied in a separate email).

- All lecture notes as pdf files and various graphics and pdb files of protein structures.

- A collection of recent original papers and reviews in the field of bio-inorganic chemistry ordered by topic as pdf files. This collection includes the thematic issue of Chemical Reviews on Bioinorganic Enzymology from November 1996.

- Decompressed copies of the protein display programs RASTOP with help and tutorial files, which may or may not work on your computer.

- Compressed original download copies of these programs, which should work on your computer when decompressed and the CHIME plug-in for the real-time display of chemical structures in Firefox and Internet Explorer.

All software provided is public-domain and free, but subject to certain licence restrictions as specified in their respective "About" menu items !

Recommended textbooks:

There is no actual textbook for this course – instead there will be a list of reading assignments from the primary and secondary scientific literature.

If you are interested there a few books out there:

"Principles of Bioinorganic Chemistry" (S. Lippard & J. Berg, 1994, University Science Books).

"Bioinorganic Chemistry: Inorganic Elements in the Chemistry of Life" (W. Kaim, B. Schwerderski, 1994, John Wiley & Sons) (probably the better choice)

"Bioinorganic Enzymology" Chemical Reviews Thematic Issue, Vol. 96 (1996). (A lot more advanced – the quality of the articles varies. Can be ordered from the ACS for about 35 $ US, IF they still have some left over). **Also available on-line and at the library and in its entirety on the server.**

Bio-inorganic chemistry, A.J. Thomson, H.B. Gray (Ed.) in Current Opinion on Chemical Biology, Vol 2, No. 2, April 1998. (Available in electronic format on the web via the library website.)

"Biochemistry", Voet & Voet, John Wiley & Sons, Toronto, 2nd Edition 1990 or any later edition.

... or any other biochemistry textbook that you like.

Reading List for CHEM 4630

Most of these papers are available as pdf files available on the server.

Lecture 1: The Elements of Life

The Trinity of Life: The Genome, the Proteome, and the Mineral Chemical Elements
R.J.P. Williams, *J. Chem. Ed.*, **2004**, *81*, 738-749.

The Chemical Elements of Life
R.J.P. Williams, *Dalton Trans.*, **1991**, 539-546.

Lecture 2: Biomolecules as Ligands, Macrocycles & Self-assembly

Structural and Functional Aspects of Metal Sites in Biology
R.H. Holm *et al*., *Chem. Rev.*, **1996**, *96*, 2239-2314. (first 10 pages)

A Thermodynamic "Vocabulary" for Metal Ion Interactions in Biological Systems
M.T. Rodgers and P.B. Armentrout, *Acc. Chem. Res.*, **2004**, *37*, 989-998.

Lecture 3: Uptake, Transport, Storage, and Regulation of Metal-Ions in vivo I

Magnesium transport in prokaryotes
M.B.C. Moncrief and M.E. Maguire, *J. Biol. Inorg. Chem.*, **1999**, *4*, 523–527

X-ray structure of a ClC chloride channel at 3.0 Å reveals the molecular basis of anion selectivity
R. Dutzler *et al.*, *Nature*, **2004**, *415*, 287-294.

Lecture 4: Uptake, Transport, Storage, and Regulation of Metal-Ions in vivo II

Ferritins: Dynamic Management of Biological Iron and Oxygen Chemistry
X. Liu and E.C. Theil, *Acc. Chem. Res.*, **2005**, *38*, 167-175.

Transferrin as a Metal Ion Mediator
H. Sun, H. Li, and P.J. Sadler, *Chem. Rev.*, **1999**, *99*, 2817-2842

Lecture 5: Metal Binding to DNA and RNA

Zinc Fingers
D. Rhodes and A. Klug, *Sci. Am.*, **Feb. 1993**, 56-65.

Molecular Recognition and Chemistry in Restricted Reaction Spaces. Photophysics and Photoinduced Electron Transfer on the Surfaces of Micelles, Dendrimers, and DNA
N.S. Turro, J.K. Barton and D. Tomalla, *Acc. Chem. Res.*, **1991**, *24*, 332-340.

Metal ions in the structure and function of RNA
A.M. Pyle, *J. Biol. Inorg. Chem*., **2002**, *7*,679–690.

Lecture 6 & 7: Bioinorganic Enzymology – An Overview/ Hydrolases – The Special Role of Zinc

How to Hide Zinc in a Small Protein
C. Blindauer and P.J. Sadler, *Acc. Chem. Res.*, **2005**, *38*, 62-69.

Why Zinc in Zinc Enzymes ? From biological roles to DNA base-selective recognition
E. Kimura and E. Kikuta, *J.Biol. Inorg. Chem.*, **2000**, *5*, 139-155.

Model Studies for Molecular Recognition of Carbonic Anhydrase and Carboxypeptidase
E. KIMURA, *Acc. Chem. Res.*, **2001**, *34*, 171-179.

70 Years of Crystalline Urease: What Have We Learned ?
P. A. Karplus and M.A. Pearson, *Acc. Chem. Res.*, **1997**, *30*, 330-337.

Lecture 8:

a) Electron Transfer Proteins – Iron Sulfur Cores

X-ray Crystallography and Biological Metal Centers: Is Seeing Believing ?
M. Sommerhalter, R.L. Lieberman and A.C. Rosenzweig, *Inorg. Chem.*, **2005**, *44*, 770-778.

Chemical Applications of Extended X-ray Absorption Fine Structure (EXAFS) Spectroscopy
T. Boon-Keng, *Acc. Chem. Res.*, **1980**, *13*, 412-419.

Determination of the iron-sulfur distances in rubredoxin by x-ray absorption spectroscopy
R. G. Shulman *et al.*, *Proc. Nat. Acad. Sci.*, **1975**, *72*, 4003-4007

b) Blue Copper Proteins

Use of EPR Spectroscopy in Elucidating Electronic Structures of Paramagnetic Transition Metal Complexes
P. Basu, *J. Chem. Ed.*, **2001**,*78*, 666-669.

Electronic structure contributions to electron transfer in blue Cu and CuA
D.W. Randall et. al., J. Biol. Inorg. Chem., **2000**, *5*, 16-19.

c) Cytochromes as Electron Carrier and the Respiratory Chain

… relevant chapters in any biochemistry textbook – e.g. Voet & Voet.

Lecture 9: Photosynthesis

The Complex Architecture of Oxygenic Photosynthesis
N. Nelson and A. Ben-Shem, *Nature Reviews*, **2004**, *5*, 1.

Electron Transfer between Membrane Complexes and Soluble Proteins in Photosynthesis
M. Hervää *et al., Acc. Chem. Res.*, **2003**, *36*, 798-805.

Photosynthetic O_2 Formation Tracked by Time-Resolved X-ray Experiments
M. Haumann *et al*., *Science*, **2005**, *310*, 1019-1021.

Where Water Is Oxidized to Dioxygen: Structure of the Photosynthetic Mn_4Ca Cluster
J. Yano *et al.*, Science, **2006**, *314*, 821-824.

Lecture 10: Oxygen Transport and Activation

The Dark Side of Dioxygen Biochemistry
J. Selverstone Valentine, Curr. Op. Chem. Biol., **1998**, *2*, 253-262.

Bioinspired Hydrogen Bond Motifs in Ligand Design: The Role of Noncovalent Interactions in Metal Ion Mediated Activation of Dioxygen
A. S. Borovik, *Acc. Chem. Res.*, **2005**, *38*, 54-61.

Mechanisms of Ligand Discrimination by Heme Proteins
R. Jain and M.K. Chan, *J. Biol. Inorg. Chem*., **2003**, *8*, 1–11.

Lecture 11: Activation & Metabolic control of O_2

Structure and Chemistry of Cytochrome P450
I.G. Denisov *et. al.*, *Chem. Rev.*, **2005**, *105*, 2253-2277

The 2-His-1-carboxylate Facial Triad: A Versatile Platform for Dioxygen Activation by Mononuclear Non-Heme Iron(II) Enzymes
K.D. Koehntop, J.P. Emerson, L. Que Jr, *J. Biol. Inorg. Chem.*, **2005**, *10*, 87–93.

Design principles of proton-pumping haem-copper oxidases
P. Brzezinski, P. Ädelroth, *Curr. Op. Struct. Biol.*, **2006**, *16*, 465-472.

Copper-Zinc Superoxide Dismutase: Theoretical Insights into the Catalytic Mechanism
V. Pelmenschikov and P.E. M. Siegbahn, *Inorg. Chem.*, **2005**, *44*, 3311-3320.

Lecture 12: Molybdenum Enzymes

The active sites of molybdenum- and tungsten-containing enzymes.
J. McMaster & J.H. Ememark, *Curr. Op. Chem. Biol.*, **1998**, *2*, 201.

Lecture 13: The Methane Problem

Beyond Oil and Gas: The Methanol Economy.
G.A. Olah, *Angew. Chem. Int. Ed.*, **2005**, *44*, 2636-2639.

Platinum Catalysts for the High-Yield Oxidation of Methane to a Methanol Derivative.
R.A. Periana *et al.*, *Science*, **2005**, *280*, 560-564.

Correlating Structure with Function in Bacterial Multicomponent Monooxygenases and Related Diiron Proteins.
M.H. Sazinsky & S.J. Lippard, *Acc Chem. Res.*, **2006**, *39*, 558-566.

ENDOR of Metallonezymes
B.M. Hoffmann, *Acc Chem. Res.*, **2003**, *36*, 522-529.

Lecture 14: Hydrogenase

Chemistry and the Hydrogenases.
David J. Evans and Christopher J. Pickett, *Chem. Soc. Rev.*, 2003, **32**, 268–275.

Hydrogenase Sophistication.
R. Cammack, *Nature*, **1999**, *397*, 214-215.

Lecture 15: Nitrogenase

Breaking the N_2 Triple Bond: Insights into the Nitrogenase Mechanism.
B.M. Barney *et al.*, *Dalton*, **2006**, 2277-2284.

Exploring New Frontiers of Nitrogenase Structure and Mechanism.
J.W. Peters & R.K. Szilagyi, *Curr. Op. Chem. Biol.*, **2006**, *10*, 101-108.

How Many Metals Does It Take to Fix N_2 ? A Mechanistic Overview of Biological Nitrogen Fixation.
J.B. Howard & D.C. Rees, *PNAS*, **2006**, *103*, 17088-17093.

Lecture 16: The Nitrogen Cycle

Nitrogen Cycle Enzymology
S.J. Ferguson, *Curr. Op. Chem. Biol.*, **1998**, *2*, 182-193.

… plus all the papers relevant to the individual student presentations as selected by you peers !

Software:

The original software packages contained on the server provided along with lot's of information are also available at:

RASTOP: http://www.geneinfinity.org/rastop/

CHIMERA: http://www.cgl.ucsf.edu/chimera/

Data:

Most important and comprehensive site:

Protein Data Bank: http://www.rcsb.org/pdb/

Some specialized sites:

Cytochrome Oxidase: http://www-bioc.rice.edu/~graham/CcO.html

Calcium-binding proteins data library: http://structbio.vanderbilt.edu/cabp_database/

Instructions on the RasTop/CHIMERA Demo Assignment:

You can load the RasTop/CHIMERA software on your own computer or use the CPES computer labs. Both programs should be installed on these computers. The server also contains a collection of representative pdb (Protein Database) files of proteins of general interest in the context of the course, all of which have been featured on the PDB website (http://www.rcsb.org/pdb/) as a "Molecule of the Month". You are of course welcome to select a more recent metallo protein structure of bioinorganic relevance for your presentation – please consult me before you make your choice and start working on it !

Your RASTOP/CHIMERA assignment cannot be on the same topic as your presentation – you have to choose a different type of system and molecule !

Your tasks for the RasTop/CHIMERA assignment are:

- Teach yourself what the program is all about and how to use it – **this is an integral part of the assignment ! RTFM !!!** (= Read The F…ine Manual !!!)
  (Important hint: In order to access the all important help and tutorial files for RASTOP you must set the path to /RasTop/help/index.htm under the File ® Preferences menu in the program to match your installation on your own machine).

- Pick one of the "Molecules of the Month" containing a metal or any other metallo-protein and inform me of your choice by email (PDB code) – selections are mutually exclusive, first come first served.

- Generate several RasTop/CHIMERA pictures and scripts that

  a) display the whole structure as a ribbon/cartoon and the active site in a space filling model using the CPK color scheme.

  b) show the active site, ligands and hetero atoms only in a space-filling/stick/ball-and-stick representation. If the are multiple identical chains show one chain only.

  c) identify all amino acid residues connected to the active site by name and residue number.

- Save and e-mail your views and scripts to me. Your evaluation will be based on these files. If we have time and the physical resources (computer room & projector) you may also get a chance to present your graphics to your peers on screen.

CHEM*4630 Bioinorganic Chemistry – Proposed Lecture Schedule

Topic
The Elements of Life (Essential and toxic elements)
Biomolecules as Ligands, Macrocycles & Self-assembly (The chelate effect, Ahrlandt-Chatt-Davies classification and the Irving-Williams series)
Uptake, Transport, Storage, and Regulation of Metal-Ions in vivo I (Alkali metals, the Na/K pump, ion channels, patch clamping)
Uptake, Transport, Storage, and Regulation of Metal-Ions in vivo II (Iron metabolism, Siderophores, Moessbauer Spectroscopy, Calcium)
Metal Binding to DNA and RNA (Telomers, Zinc Fingers)
Bioinorganic Enzymology – An Overview (Structure explains function - RASTOP as a visualization tool)
Hydrolases – The Special Role of Zinc (General & specific acid/base catalysis)
Electron Transfer Proteins – Iron Sulfur Cores (Basic phenomena and structures, cyclic voltammetry, aconitase)
Blue Copper Proteins (structral models and EPR)
Cytochromes as Electron Carrier and the Respiratory Chain (Marcus Theory)
Photosynthesis (light harvesting, reaction models, XPS)
Oxygen Transport and Activation (MO and binding modes of O_2, hemo/myoglobin, hemeerythritin hemocyanin)
Activation & Metabolic control of O_2 (Cytochrome P450, SOD and Non-heme Oxygenases)
Mo Oxygenases
The methane problem (MMO, Catalytica Process, Olah's vision, MeOH as a fuel chlathrates and climate change)
Hydrogenase
Nitrogen Fixation (The Cage Match ! Nitrogenase vs the Haber-Bosch process)
The Nitrogen Cycle (The Enzymes for Nitrification and Denitrification)

CHEM*4630 Bioinorganic Chemistry
Possible Topics for Student Lectures
(Not in temporal order – dates to be assigned later !)

Student lectures 1-4 1) Sulfur S_8 oxidizing enzymes 2) Contrast agents in MRI 3) Contrast agents in PET 4) Contrast agents in CT and X-ray
Student lectures 5-8 5) Au arthritis drugs 6) V as an insulin mimic 7) Platinum anti-cancer drugs 8) Non-Platinum metallo anti-cancer drugs
Student lectures 9-12 9) Iron biominerals – how to find your way home … 10) Biomineralization I: Silicon 11) Biomineralization II: Phosphorus 12) Biomineralization III: Carbon
Student lectures 13-16 13) Boron Neutron Capture Therapy 14) Fluorine, Bromine and Iodine in vivo 15) Selenium in vivo 16) The molecular basis of the toxicity of Cadmium and Mercury
Student lectures 17-20 17) Tungstoenzymes 18) Chromium, Bismuth and Lithium *in vivo* and in medical applications. 19) Vanadium in vivo (exclusive diabetes treatment) 20) Cobalt in vivo: Vitamin B_{12}
Student lectures 21-24 21) Cytochrome C Nitrite Reductase 22) Artificial Hydrogenases 23) Artificial Hydrolytic Enzymes: DNAses 24) Artificial Hydrolytic Enzymes: Proteases
Student lectures 25-28 25) Artificial Nitrogenases and Nitrogenase Models 26) Artificial Oxygen Carriers: Models for Hemoglobin 27) Artificial Photosynthesis 28) Non-Heme Rieske Oxygenases
Student lectures 29-32 29) Calcium Mediated Bioluminescence 30) Formate Dehydrogenase 31) Is DNA a molecular wire ? 32) Copper Transport Proteins
Student lectures 33-36 33) Copper metabolism related diseases

34) Dopamine Monooxygenase and the role of dopamin *in vivo* 35) Quantum phenomena in Photosystem I & II and other living systems. 36) Lanthanides *in vivo* ? What role do they play ?

… or any other relevant & interesting topic you can come up with. Ask !

The LEGAL CRAP:

E-mail Communication
As per university regulations, all students are required to check their <mail.uoguelph.ca> e-mail account regularly: e-mail is the official route of communication between the University and its students.

When You Cannot Meet a Course Requirement
When you find yourself unable to meet an in-course requirement because of illness or compassionate reasons, please advise the course instructor (or designated person, such as a teaching assistant) in writing, with your name, id#, and e-mail contact. See the undergraduate calendar for information on regulations and procedures for Academic Consideration.

Drop Date
The last date to drop one-semester courses, without academic penalty, is INSERT DATE HERE. For regulations and procedures for Dropping Courses, see the Undergraduate Calendar.

Copies of out-of-class assignments
Keep paper and/or other reliable back-up copies of all out-of-class assignments: you may be asked to resubmit work at any time.

Accessibility
The University of Guelph is committed to creating a barrier-free environment. Providing services for students is a shared responsibility among students, faculty and administrators. This relationship is based on respect of individual rights, the dignity of the individual and the University community's shared commitment to an open and supportive learning environment. Students requiring service or accommodation, whether due to an identified, ongoing disability or a short-term disability should contact the Centre for Students with Disabilities as soon as possible.

For more information, contact CSD at 519-824-4120 ext. 56208 or email csd@uoguelph.ca or see the website: http://www.uoguelph.ca/csd/

Academic Misconduct
The University of Guelph is committed to upholding the highest standards of academic integrity and it is the responsibility of all members of the University community –

faculty, staff, and students – to be aware of what constitutes academic misconduct and to do as much as possible to prevent academic offences from occurring. University of Guelph students have the responsibility of abiding by the University's policy on academic misconduct regardless of their location of study; faculty, staff and students have the responsibility of supporting an environment that discourages misconduct. Students need to remain aware that instructors have access to and the right to use electronic and other means of detection.

Please note: Whether or not a student intended to commit academic misconduct is not relevant for a finding of guilt. Hurried or careless submission of assignments does not excuse students from responsibility for verifying the academic integrity of their work before submitting it. Students who are in any doubt as to whether an action on their part could be construed as an academic offence should consult with a faculty member or faculty advisor.

The Academic Misconduct Policy is detailed in the Undergraduate Calendar.

Recording of Materials

Presentations which are made in relation to course work—including lectures—cannot be recorded or copied without the permission of the presenter, whether the instructor, a classmate or guest lecturer. Material recorded with permission is restricted to use for that course unless further permission is granted.

Resources

The Academic Calendars are the source of information about the University of Guelph's procedures, policies and regulations which apply to undergraduate, graduate and diploma programs.