

Chemistry 544
The Inorganic Chemistry of Life
 Room 124 TTh 11:00 - 12:20
 Professors C. Dismukes and T. Spiro

Objective: To illustrate the chemical principles utilized by Nature for the organization of biological matter and its interconversion with energy sources. Inorganic physiology.

Readings and Assignments: About 35-40 pages per week

(1) Lippard and Berg, Principles of Bioinorganic Chemistry

(2) Review Articles from the primary literature will be assigned as reading material.

Grading: 10-12 study guides and two examinations.

WEEK	Tentative Topics	READINGS
Sept 14	Overview of Macromolecular Databases; Thermodynamic/structural description of molecular recognition	Ch 2 L&B, L,S&S ; SG1
19, 21, 26	Coordination chemistry:, kinetic and electronic factors controlling ligand binding equilibria; chelate effect;	SG2; Ch. 2 L&B; H,K&S section I, II A; L&Q
28	Electrostatics in biology: ion solvation, hydrogen bonding, ion transport, stereochemistry;	Electrostatics and H-bonding handouts
Oct 3, 5	Review of macromolecular structure (if needed): amino acids, 1° 2° and 3° structure of proteins, DNA, RNA, prosthetic groups, cofactors; interpretation of steady-state enzyme kinetics parameters	SG3; Ch 3 L&B H,K&S section II. B
10,12	Uptake, distribution and assembly of inorganics in biology; enrichment strategies; spontaneous self-assembly of metal clusters: iron -sulfur clusters; cofactors; Homeostasis: iron solubilization, transport and regulation	SG 4; Ch 5, 6.1-6.2 L&B
17, 19	Import and export of ions and molecules into cells: ionophores, siderophores; voltage-gated channels and membrane transport: K ⁺ Channel molecular structure and function;	Ch 6.4, L&B SG 5, Doyle et al.
24, 26	Redox Reactions/Atom Transfer Fundamentals Take-Home Midterm Examination	Ch 11.3, Holm, Mayer
28	Fall Break	
Nov 7,9	Metallo-hydrolases and hydride transfer enzymes	Ch 10, *
14, 16	Redox centers and electron transfer in proteins	Ch 9, *
21	B12 coenzyme reactions	Ch 11.5
28, 30	O ₂ , NO, CO - heme adducts Oxidative stress	Ch 11.1, *
Dec 5, 7	Fe Oxygenases	Ch 11.2, *
12, 14	Oxidases	*
Jan	Take-Home Final	

Useful secondary texts on reserve shelf:

1. Frausto-deSilva and R.J.P. Williams, *Biological Chemistry of the Elements*, 1991,
2. W. Kaim and B Schwederski, *Bioinorganic Chemistry*, 1994 Wiley Interscience.
3. "Bioinorganic Enzymology" editors: R.H. Holm, and E.I. Solomon. *Chemical Reviews* 96 (1996)

Reading Assignments and Study Guides:

SG1. Molecular Recognition: Determinants of Metal Binding Specificity to Proteins and Large Polydentate Ligands.

"Rationalization of the Strength of Metal Binding to Human Serum Transferrin" Li, H; Sadler, P.; Sun, H. (1996) *FEBS Lett.* 242, 387-393.

Handout: Chelation Study Guide

SG2. "Structural and Functional Aspects of Metal Sites in Biology"

R. H Holm, P. Kennepohl, E. I. Solomon in "Bioinorganic Enzymology" special edition of (editors: R.H. Holm, and E.I. Solomon) *Chemical Reviews* 96 (1996) p. 2239-2251 (sections I. and II assigned) H, K & S.

SG3. Based on student background.

Molecular Recognition: Determinants of Affinity and Specificity for Anion Binding to Proteins.

"High specificity of a phosphate transport protein determined by hydrogen bonds" Leucke and Quioco, *Nature* 347 (1990) 403-406.

SG4. TBD.

SG 5. Ion Transport Across Membranes: Ion Channels (Potassium, Calcium); Voltage-Gated Channels (Acetylcholine Receptor);

"The structure of the potassium channel: molecular basis of K^+ conduction and selectivity" Doyle, D. A. et al. *Science*, 280 (1998) 69-76; Armstrong, C. *Science*, 280 (1998) 56-57.

"Molecular Determinants of Ca^{2+} Selectivity and Ion Permeation in L-type Ca^{2+} Channels" J. A. Cowan, *Chemtracts: Inorganic Chemistry* 5, July/August 1993, P. 197-200; This article is a condensation of the original research by Yang, Elinor, Sather Zhang and Tsien (1993) *Nature*, 366, 158.

"Simulations of Ion Channels: Watching Ions and Water Move" M. P. S. Sanson; I Srivastava; K. Ranatunga and G. R. Smith, *TIBS* 25 (2000) 368-375.

SG6. Fundamentals of Redox Reactions/ Atom Transfer Reactions:

“Hydrogen atom abstraction by metal-oxo complexes: understanding the analogy with organic radical reactions” Mayer, J. M. *Accounts Chem. Res.* **1998**, 31, 441-450.

Holm, R.H. and J.P. Donahue, "A thermodynamic scale for oxygen atom transfer reactions." *Polyhedron*, 1993. **12**(6): p. 571-589.

*** Additional readings for the second half of the course to be distributed.**