Spring 2014 Chemistry 741
Bioorganic Chemistry
TR 3:30-4:45 PM CHM 197
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Bioorganic Chemistry is a fairly broad area, distinct from Biochemistry in its focus on the chemical mechanisms and transformations of biology, rather than the pathways and biological consequences of those transformations. In this course, we will cover the structures and activities of biomolecules from an Organic Chemical perspective. We will discuss some biosynthesis and enzymatic mechanism, but more of the course will deal with biomimetic chemistry, the study of model compounds that mimic the structures and activities of the more complex biomolecules.

We will not use a text for this course, though sections of various texts will be useful, and will be mentioned at the appropriate junctures. Much of the material will be presented as readings from the primary literature. It is critical that you read these assigned papers before class, and be ready to discuss them, even if you are auditing the course. Class discussion is a very important part of the course. We will bring out details and comparisons in class that go beyond the readings assigned, but which will not be meaningful without adequate preparation. At the end of this course, you should be well prepared to read a journal article in the field of Bioorganic Chemistry, and to critically evaluate its contents.

Grading will be based on class discussion (40%), 2 exams (20% each), and a final paper (20%). It is very important that you do the readings, as you will be called upon to contribute to the discussion.

I am hopeful that class discussions will include significant contributions from the entire class. In the event that discussion is insufficient, final papers will be expanded to include an oral presentation and the class discussion grade will be partially based on this.

Topics to be covered:

Enzymatic Catalysis:

Energy flow in enzymatic pathways. Structure and mechanism, elementary kinetics, cofactors, and biosynthesis. Model compounds.

Synthesis of biomolecules:

Peptide synthesis, DNA synthesis.

Molecular Recognition:

Crown ethers, ionophore antibiotics (conformational analysis and stereochemical contributors to activity), Hydrogen bonding in natural and synthetic assemblies, hydrophobic effect, cation-π effect, polyvalency, relevance to drug design.

Combinatorial chemistry and biochemistry:

Peptides, peptoids, small molecules, aptamers.

Artificial Enzymes:

Designed structures, catalytic antibodies, ribozymes, artificial evolution.

Some of the papers we will cover early in the semester:
1. Cofactor mechanisms Any Biochemistry text.
2. Westheimer "Why Nature chose phosphates" Science 1987, 235, 1173-1178.
3. Energy flow: Benner "Biomimetic Biotechnological Process…" J. Am. Chem. Soc. 1992, 114, 6980-6978.
4. Effective Molarities (Kirby Adv. Phys Org. Chem., Jencks Catalysis in Chemistry and Enzymology)
5. Crown Ethers (Nobel lectures) Angew. Chem. Int. Ed. 1988, 27, 1009-1020; ACIEE 1988, 27, 1021-1027; ACIE 27, 89-112; Resolving machine: J. Am. Chem. Soc., 1979, 101, 4941-5947.
6. Stereochemical control and explanation. Still Lect. Het. Chem. 1987, 9, S33-S42; J. Am. Chem. Soc. 1992, 114, 4128-4137.
7. Understanding crown ether binding affinity by studying related sulfides, ultimately yielding insight into the role of methionine in proteins.
J. Am. Chem. Soc. 1991, 113, 8663-8671; ibid1990, 112, 4321-4324; ibid 1991, 113, 703-706; perspective: Biochem. 1991, 30, 6633-6636.
8. Hydrogen bonding receptors J. Am. Chem. Soc., 1987, 109, 6549-6551.
9. Why are some receptors much better? J. Am. Chem. Soc., 1992, 114, 4010-4011.
10. Hydrophobic binding Koga J. Am. Chem. Soc., 1980, 102, 2504-2505