Dr. Niles Lehman (SB1-540) email: niles@pdx.edu

Chemistry 460/560 – Prebiotic Chemistry
Portland State University, Spring 2008

General Information

Class meetings (**required**): Wednesday evenings 5:30 pm – 9:30 pm in SB1-304
Dr. Lehman's Office Hours: Mon 9:00 am – 10:00 am; Fri 10 – 11 am; and by appt.
Best way to contact Dr. Lehman: by email! (niles@pdx.edu)

Prerequisites

The prerequisite for enrollment in CH 460/560 is completion of, or concurrent enrollment in, CH 492 (or equivalent), or consent of the instructor. Essentially you must have had a full year of majors' level biochemistry. **CH 350 is not sufficient**. I will also expect passage of a full year of organic chemistry.

Course Overview

Chem 460/560 is an introduction to prebiotic chemistry that has been approved to satisfy partially the Chemistry Ph.D. core course requirement at Portland State University. It also partially satisfies a 400-level elective requirement for undergraduates majoring in Chemistry or Biochemistry. We will meet one night per week during the term. In the first 5 lectures I will provide an overview on the current theories of the chemical origins of life on the Earth some 4 billion years ago. For the last 5 weeks we will read papers in the primary literature and discuss them via students' oral presentations to the class.

Grading

There will be 100 points possible in the course, and grades will be assigned on a straight scale: (>85% = A range; >75% = B range; >65% = C range; <65 % = F). Plus and minus grades will only be given for students whose total points fall near a grade boundary but clearly outside the statistical "bubble" of the other students (*i.e.*, for outliers). Grades will be assigned for student presentations (20%), the midterm examinations (4 x 10%), and the final exam (40%). Each student will be the primary presenter for some literature readings we will have after the first five of weeks of class. The student will summarize assigned papers using overheads or PowerPoint presentations, and give this presentation to the rest of the class. I will expect each presentation to last approximately 45 minutes per paper. Undergraduate students (CH 460) will be assigned one paper each to present during the term; graduate students (CH 560) will be assigned two papers each to present. After the first week, each class session will be divided into three segments. First, I will lecture for about 2.5 hours on the topics of the week. Then, we will take a short 15-minute break. After exactly 15 minutes, I will hand out midterm exams that cover the material presented in the previous week. Students will be given exactly 45 minutes to complete these exams. Each exam will be worth a total of 10 points maximum. After the 10th and final week of the class I will give all students a final exam worth 40% of their grade, covering the entire course, including the student presentations. In addition, because there will only be ten class meetings, I will expect all students to attend all class sessions and actively participate in the discussions. Two points (2%) will be deducted from each class session a student misses; one point will be deducted for each lateness, regardless of reason. This policy absolutely applies to the student presentations as well.

Course Policies

I will expect all students to conduct themselves responsibly during class periods and observe academic honesty during exams. Students may assist each other with the in-class presentations but must work entirely independently on the exams. All cell phones are to be turned off during class!

Lecture Schedule

Date	Reading	Presenter(s)	Topics
Wed, Apr 2	Zubay, Ch. 2, 5 & 10	NL	life / atoms / water / atmospheres
Wed, Apr 9**	Zubay, Ch. 10 & 15	NL	Oparin / Haldane / amino acids
Wed, Apr 16**	Zubay, Ch. 12 & 18	NL	sugars / lipids / protocells
Wed, Apr 23**	Zubay, Ch. 13 & 14	NL	nucleotides / RNA / DNA / TNA
Wed, Apr 30**	Zubay, Ch. 10 again & TBA	NL	extra topics: FeS, thioesters, fossils
Wed, May 7	Zubay, Ch. 5 & 10 (again)	students:	TBD
Wed, May 14	Zubay, Ch. 2 & 15 (again)	students:	TBD
Wed, May 21	Zubay, Ch. 12 & 18 (again)	students:	TBD
Wed, May 28	Zubay, Ch. 13 & 14 (again)	students:	TBD
Wed, Jun 4	Sullivan, Ch. 8 (handout)	students:	TBD
Wed, Jun 11??	final exam, covering entire course		

**45 minute Midterm exam on previous week's lecture material

Textbook
We will be using the book *Origins of Life on the Earth and in the Cosmos* (2nd Edition, 2000) by Geoffrey Zubay. This is a required textbook, and we will cover about two chapters per week during the first five weeks. To get a head-start on the class, buy the book and read chapters 2, 5 & 10 before the first lecture. You will be tested on this material during week #2. Other readings will be provided later.

Presentations
Students will work in teams to give oral (PowerPoint) presentations on literature readings.

Week #6 team: topics covered during week #1
Week #7 team: topics covered during week #2
Week #8 team: topics covered during week #3
Week #9 team: topics covered during week #4
Week #10 team: topics covered during week #5

The Ten Reactions that Define the Field

1. $CH_4 + H_2 + H_2O + NH_3 \rightarrow HCN + HCOOH \rightarrow$ glycine (Miller)
2. 5HCN + UV light $\rightarrow$ adenine (Oró)
3. $FeS + H_2S \rightarrow CH_3{-}CH_3, CH_2{=}CH_2$ (Wächtershäuser)
4. $R_1{-}S{\sim}CO{-}R_2 + X{-}OH + Y{-}OH \rightarrow X{-}Y + H_2O$ (deDuve)
5. nImATP + clay $\rightarrow (AMP)_n$ (Ferris)
6. A + B + AB $\leftrightarrow$ A•B•AB $\rightarrow$ AB•AB $\leftrightarrow$ 2AB (von Kiedrowski)
7. A + B $\leftrightarrow$ C; C + A + B $\rightarrow$ C (Rebek)
8. HCHO + $Pb(OH)_2 \rightarrow$ ribose (Orgel)
9. ribose-5P + $NH_3 + NH_2CN + HC{\equiv}C{-}CN \rightarrow$ cytidine (Orgel)
10. RNA + $(NTP)_n \rightarrow$ 2RNA (Bartel)

Chem 460/560 Spring 2008 – Potential Reading List Pool

Prebiotic Synthesis of Small Molecules

Oró J (1961). Mechanism of synthesis of adenine from hydrogen cyanide under possible primitive Earth conditions. *Nature* **191:** 1193-1194.

Sanchez RA, Ferris JP, Orgel LE (1966). Cyanoacetylene in prebiotic synthesis. *Science* **154:** 784-785.

Lohrman R, Orgel LE (1968). Prebiotic synthesis: phosphorylation in aqueous solution. *Science* **161:** 64-66.

Fuller WD, Sanchez RA, Orgel LE (1972). Studies in prebiotic synthesis. VI. Synthesis of purine nucleotides. *J. Mol. Biol.* **67:** 25-33.

van Trump JE, Miller SL (1972). Prebiotic synthesis of methionine. *Science* **178:** 859 – 860.

Wolman Y, Haverland WH, Miller SL (1972). Non-protein amino acids from spark discharges and their comparison with the Murchison meteorite amino acids. *Proc. Natl. Acad. Sci. USA* **69:** 809-811.

Hawker JR Jr, Oró J (1981). Cyanamide mediated synthesis of peptides containing histidine and hydrophobic amino acids. *J. Mol. Evol.* **17:** 285-294.

Weber AL (1982). Formation of pyrophosphate on hydroxyapatite with thioesters as condensing agents. *BioSystems* **15:** 183-189.

Weber AL (1985). Alanine synthesis from glyceraldehyde and ammonium ion in aqueous solution. *J Mol Evol* **21:** 351-355.

Schwartz AW, deGraaf RM (1993). The prebiotic synthesis of carbohydrates: a reassessment. *J. Mol. Evol.* **36:** 101-106 (theory and discussion only).

Larralde R, Robertson MP, Miller SL (1995). Rates of decomposition of ribose and other sugars: Implication for chemical evolution. *Proc. Natl. Acad. Sci. USA* **92:** 8158-8160.

Robertson MP, Miller SL (1995). An efficient prebiotic synthesis of cytocine and uracil. *Nature* **375:** 772-774.

Weber AL (2004). Kinetics of organic transformations under mild aqueous conditions: Implications for the origin of life and its metabolism. *Orig. Life Evol. Biosphere* **34:** 473-495.

Abo-Riziq A, Grace L, Nir E, Kabelac M, Hobza P, deVries MS (2005). Photochemical selectivity in guanine-cytosine base-pair structures. *Proc. Natl. Acad. Sci. USA* **102:** 20-23.

Pasek MA, Lauretta DS (2005). Aqueous corrosion of phosphide minerals from iron meteorites: a highly reactive source of prebiotic phosphorus on the surface of the early Earth. *Astrobiology* **5:** 515-535.

Anastasi C, Buchet FF, Crowe MA, Parkes AL, Powner MW, Smith JM, Sutherland JD (2007). RNA: prebiotic product or biotic invention? *Chemistry & Biodiversity* **4:** 721-739 (theory and review paper).

Baaske P, Weinert FM, Duhr S, Lemke KH, Russell MJ, Braun D (2007). Extreme accumulation of nucleotides in simulated hydrothermal pore systems. *Proc. Natl. Acad. Sci. USA* **104:** 9346-9351.

Brack A (2007). From interstellar amino acids to prebiotic catalytic peptides: a review. *Chemistry & Biodiversity* **4:** 665-679 (theory and review paper).

The Encapsulation Problem

Fox S, Harada K, Kendrick J (1959). Production of spherules from synthetic proteinoid and water. *Science* **129:** 1221-1222.

Fox SW (1965). A theory of macromolecular and cellular origins. *Nature* **205:** 328-340.

Deamer DW, Boatman DE (1980). An enzymatically driven membrane reconstruction from solubilized components. *J. Cell Biology* **84:** 461-467.

Weber AL, Miller SL (1981). Reasons for the occurrence of the twenty coded protein amino acids. *J. Mol. Evol.* **17:** 273-284. (theory and discussion only)

Chakrabarti AC, Breaker RR, Joyce GF, Deamer DW (1994). Production of RNA by a polymerase protein encapsulated within phospholipid vesicles. *J. Mol. Evol.* **39:** 555-559

Deamer DW (1997). The first living systems: a bioenergetic perspective. *Microbiology and Molecular Biology Reviews* **61:** 239-261 (theory and review only).

Apel CL, Deamer DW, Mautner MN (2002). Self-assembled vesicles of monocarboxylic acids and alcohols: conditions for stability and for the encapsulation of biopolymers. *Biochim. Biophys. Acta* **1559**:1-9.

Sacerdote MG, Szostak JW (2005). Semipermeable lipid bilayers exhibit diastereoselectivity favoring ribose. *Proc. Natl. Acad. Sci. USA* **102:** 6004-6008.

Rajamani S, Vlassov A, Benner S, Coombs A, Olasagasti F, Deamer D (2008). Lipid-assisted synthesis of RNA-like polymers from mononucleotids. *Orig. Life Evol. Biosphere* (in press: DOI 10.1007/s11084-007-9113-2).

<u>Metabolism-first Experiments</u>

de Duve C. (1987). Selection by differential molecular survival: a possible mechanism of early chemical evolution. *Proc. Natl. Acad. Sci. USA* **84:** 8253-8256.

de Duve C (1991). “Chapter Seven: Harnessing Energy” Pp. 147-170 *in* de Duve, C *Blueprint for a Cell*. Carolina Biological Supply Publishers, Burlington NC. (theory and discussion only)

Blöchl E, Keller M, Wächtershäuser G, Stetter KO (1992). Reactions depending on iron sulfide and linking geochemistry with biochemistry. *Proc. Natl. Acad. Sci. USA* **89:** 8117-8120.

Huber C, Wächtershäuser G (1998). Peptides by activation of amino acids with CO on (Ni, Fe)S surfaces: implications for the origin of life. *Science* **281:** 670-672.

Huber C, Eisenreich W, Hecht S, Wächtershäuser G (2003). A possible primordial peptide cycle. *Science* **301:** 938-940.

<u>Self-replicating and Autocatalytic Chemical Systems</u>

Tjivikua T, Ballester P, Rebek J Jr. (1990). A self-replicating system. *J. Am. Chem. Soc.* 112: 1249-1250.

Feng Q, Park TK, Rebek J Jr. (1992). Crossover reactions between synthetic replicators yield active and inactive recombinants. *Science* **256:** 1179-1180.

von Kiedrowski G, Wlotzka B, Helbing J, Matzen M, Jordan S (1991). Parabolic growth of a self-replicating hexadeoxynucleotide bearing a 3´-5´-phosphoamidate linkage. *Angew. Chem. Int. Ed. English* **30:** 423-426.

Terfort A, von Kiedrowski G (1992). Self-replication by condensation of 3-amino-benzamidines and 2-formylphenoxyacetic acids. *Angew. Chem. Int. Ed. English* **31:** 654-656.

Sievers D, von Kiedrowski G (1994). Self-replication of complementary nucleotide-based oligomers. *Nature* **369:** 221-224.

Lee DH, Severin K, Yokobayahsi Y, Ghadiri MR (1997). Emergence of symbiosis in peptide self-replication through a hypercyclic network. *Nature* **390:** 591-594.

Severin K, Lee DH, Martinez JA, Ghadiri MR (1997). Peptide self-replication via template-directed ligation. *Chem. Eur. J.* **3:** 1017-1024.

Luther A, Brandsch R, von Kiedrowski G (1998). Surface-promoted replication and exponential amplification of DNA analogues. *Nature* **396:** 245-248.

Paul N, Joyce GF (2002). A self-replicating ligase ribozyme. *Proc. Natl. Acad. Sci. USA* **99:** 12733-12740.

Kim D-E, Joyce GF (2004). Cross-catalytic replication of an RNA ligase ribozyme. *Chem. Biol.* **11:** 1505-1512.

Polymers and Ribozymes

Weber AL, Caroon JM, Warden JT, Lemmon RM, Calvin M (1977). Simultaneous peptide and oligonucleotide formation in mixtures of amino acid, nucleoside triphosphate, imidazole, and magnesium ion. *BioSystems* **8:** 277-286.

Lahav N, White D, Chang S (1978). Peptide formation in the prebiotic era: thermal condensation of glycine in fluctuating clay environments. *Science* **201:** 67-69.

Inoue T, Orgel LE (1983). A nonenzymatic RNA polymerase model. *Science* **219:** 859-862.

Zielinski WS, Orgel LE (1987). Autocatalytic synthesis of a tetranucleotide analogue. *Nature* **327:** 346-347.

Doudna JA, Szostak JW (1989). RNA-catalyzed synthesis of complementary-strand RNA. *Nature* **339:** 519-522.

Beaudry AA, Joyce GF (1992) Directed evolution of an RNA enzyme. *Science* **257:** 635-641.

Bartel DP, Szostak JW (1993). Isolation of new ribozymes from a large pool of random sequences. *Science* **261:** 1411-1418.

Ferris JP, Hill AR, Liu R, Orgel LE (1996). Synthesis of long prebiotic oligomers on mineral surfaces. *Nature* **381:** 59-61.

Unrau PJ, Bartel DP (1998). RNA-catalyzed nucleotide synthesis. *Nature* **395:** 260-263.

Johnston WK, Unrau PJ, Lawrence MS, Glasner ME, Bartel DP (2001). RNA-catalyzed RNA polymerization: accurate and general RNA-templated primer extension. *Science* **292:** 1319-1325.

Dworkin JP, Lazcano A, Miller SL (2003). The roads to and from the RNA world. *J. Thoer. Biol.* **222:**127-134 (theory and discussion only).

Zaher HS, Unrau PJ (2007). Selection of an improved RNA polymerase ribozyme with superior extension and fidelity. *RNA* **13:** 1017-1026.

Chen X, Li N, Ellington AD (2007). Ribozyme catalysis of metabolism in the RNA world. *Chemistry & Biodiversity* **4:** 633-655 (theory and review paper).

Yang Y-W, Zhang S, McCullum EO, Chaput JC (2007). Experimental evidence that GNA and TNA were not sequential polymers in the prebiotic evolution of RNA. *J. Mol. Evol.* **65:** 289-295.

The Chirality Problem

Cairns-Smith AG (1986). Chirality and the common ancestor effect. *Chemistry in Britain* **22:** 559-561 (discussion only).

Joyce GF, Schwartz AW, Miller SL, Orgel LE (1987). The case for an ancestral genetic system involving simple analogues of the nucleotides. *Proc. Natl. Acad. Sci. USA* **84:** 4398-4402.

Prabahar KJ, Ferris JP (1997). Adenine derivative as phosphate-activating groups for the regioselective formation of 3', 5'-linked oligoadenylates on montmorillonite: possible phosphate-activating groups for the prebiotic synthesis of RNA. *J. Am. Chem. Soc.* **119:** 4330-4337.

Berstein MP, Dworkin JP, Sandford SA, Cooper GW, Allamandola LJ (2002). Racemic amino acids from the ultraviolet photolysis of interstellar ice analogs. *Nature* **416:** 401-403.

Shinitzky M, Nudelman F, Barda Y, Haimovitz, Chen E, Deamer DW (2002). Unexpected differences between D- and L-tyrosine lead to chiral enhancement in racemic mixtures. *Orig. Life Evol. Biosphere* **32:** 285-297.

Avalos M, Babiano R, Cintas P, Jimenez JL, Palacios JC (2004). Symmetry breaking by spontaneous crystallization. *Orig. Life Evol. Biosphere* **34:** 391-405.

McDonald GD, Storrie-Lombardi MC (2006). Amino acid distribution in meteorites. *Astrobiology* **6:** 17-33.

Klussmann M, *et al*. (2006). Thermodynamic control of asymmetric amplification in amino acid catalysis. *Nature* **441**: 621-623.

Viedma C (2007). Chiral symmetry breaking and complete chiral purity by thermodynamic-kinetic feedback near equilibrium: implications for the origin of biochirality. *Astrobiology* **7:** 312-319.

Scorei RI, Cimpoiasu VM, Popa R (2007). TD-^{1}H-NMR measurements show enantioselective dissociation of ribose and glucose in the presence of $H_2{}^{17}O$. *Astrobiology* **7:** 733-744.

Goldberg SI (2007). Enantiomeric enrichment on the prebiotic earth. *Orig. Life Evol. Biosphere* **37:** 55-60.

Noorduin WL, *et al*. (2008). Emergence of a single solid chiral state from a nearly racemic amino acid derivative. *J. Am. Chem. Soc.* **130:** 1158-1159.

Crystals and Other Possible Life Forms

Cairns-Smith AG (1985). *Seven Clues to the Origin of Life*. Cambridge University Press.

Arrhenius GO (2003). Crystals and Life. *Helvetica Chimica Acta* **86:** 1569-1586.

Cairns-Smith AG (2008). Chemistry and the missing era of evolution. As of March 8, 2008, this is in press in *Chem. Eur. J.* doi: 10.1002/chem.200701215.

Extraterrestrial Origins

Stoks PG, Swartz AW (1979). Uracil in carbonaceous meteorites. *Nature* **282:** 709-710.

Dworkin JP, Deamer DW, Sandford SA, Allamandola LJ (2001). Self-assembling amphiphilic molecules: synthesis in simulated interstellar/precometary ice. *Proc. Natl. Acad. Sci. USA* **98:** 815-819.

Glaser R, Hodgen B, Farrelly D, McKee E (2007). Adenine synthesis in interstellar space: mechanisms of prebiotic pyrimidine ring-formation in monocyclic HCN-pentamers. *Astrobiology* **7:** 455-470.

Hoehler TM, Amend JP, Shock EL (2007). A “follow the energy” approach for Astrobiology. *Astrobiology* **7:** 819-823.