Chemistry of the Origin of Life & Early Evolution

Summary of Class Meeting Topics

(as taught at Georgia Tech in Spring 2008, CHEM 2803)

1. Overview of the class and a discussion of expectations; Collection of the preconceptions of student in the class. Students are asked the following questions and their answers were compiled on the board. *1) What is life? 2) Where did life begin? 3) How long ago did life begin? 3) What were the first molecules of life? 4) In the history of origin of life studies, who are the prominent figures?*; Instructor read part of the preface from Schopf's book Life's Origin. Slides are shown of some of the people mentioned in the preface, along with commentaries by the instructor; Read out loud pages 108-113 from *Cradle of Life: The Discovery of Earth's Earliest Fossils* (J. William Schopf, Princeton University Press, 1999), illustrating the linage of scientific knowledge on the origin of life from Darwin to contemporary researchers. Slides were shown of Darwin and others, along with commentaries by the instructor. Assigned reading: Chapter 1, *Historical Understanding of Life's Beginnings, of Life's Origin - The Beginnings of Biological Evolution*, J. W. Schopf.
2. Discuss Chapter 1 of Schopf's book; Present very basic background material on the nature of biopolymers and lipids; Assigned reading: Chapter 2, *From Big Band to Primordial Planet: Setting the Stage for the Origin of Life, of Life's Origin - The Beginnings of Biological Evolution*, J. W. Schopf. Also handed out, but students were not required to submit written summary: Miller, S.L., Schopf, J.W., Lazcano, A., Oparin's ''origin of life'': Sixty years later, *Journal of Molecular Evolution* 44, 351-353, 1997; Leslie Orgel Obituary, G. Joyce, Nature 450, 627, 2007.
3. Discuss the life and achievements of Leslie Orgel; Discuss the paper Miller, S.L., Schopf, J.W., Lazcano, A., Oparin's ''origin of life'': Sixty years later, *Journal of Molecular Evolution* 44, 351-353, 1997; Discuss the philosophy and legacy of Trofim Lysenko; Discussed Chapter 2 of Schopf's book; Hand out table of amino acid structures; Discuss the concept of homochirality and how it is detected using circularly polarized light. Assigned reading: Chapter 3, *Formation of the Building Blocks of Life, of Life's Origin - The Beginnings of Biological Evolution*, J. W. Schopf.
4. Discuss Chapter 3 of Schopf's book; Introduce the RNA world hypothesis and discuss the significance of catalytic RNA. Assigned reading: Chapter 4, *From Building Blocks to the Polymers of Life, of Life's Origin - The Beginnings of Biological Evolution*, J. W. Schopf.
5. Discuss Chapter 4 of Schopf's book; Hand out and discuss an alternative approach to backbone formation, that of reversible linkages, X. Li, Z.-Y. J. Zhan, R. Knipe, and D. G. Lynn, DNA-Catalyzed Polymerization, *Journal of the American Chemical Society* 124, 746-747, 2002. (Paper emphasizes the potential selectivity of reactions when thermodynamics, not just kinetics, select product formation). Discuss Schiff base formation and their reduction. Assigned reading: Chapter 5, *The Origin of Biological Information, of Life's Origin - The Beginnings of Biological Evolution*, J. W. Schopf.
6. Discuss Chapter 5 of Schopf's book. Assigned reading: Chapter 6, *When Did Life Begin?, of Life's Origin - The Beginnings of Biological Evolution*, J. W. Schopf.
7. Discuss Chapter 6 of Shopf's book.; Handed out and discussed J. L. Bada and A. Lazcano, *Prebiotic Soup - Revisiting the Miller Experiment*, *Science* 300, 2003, 745-746. Noted significance of Miller and Urey's work, i.e. in addition to their discoveries, they started the era in which studying the origin of life became an experimental science. The paper by Bada et al. also emphasized that "the time had come", as no less than two other groups were starting experiments with model prebiotic atmospheres. Assigned reading:

Gave independent book assignment. Students directed to use reading time to start the process of choosing a book for the assignment.

8. Discussion of three important concepts for understanding the origin of life, the special properties of water, the nature of the genetic code and the concept of the last common ancestor. Give demo of a simulation of the Miller-Urey experiment: http://www.ucsd.tv/miller-urey/. Do not give solution, but one failed simulation. Tell students to try it after reading assigned paper. Assigned reading: S. L. Miller, *A Production of Amino Acids under Possible Primitive Earth Conditions*, *Science* 117, 528-529, 1953.
9. Book selection due. Discuss Miller's 1953 paper, with additional discussion of previous Bada et al. paper; Discuss α versus ß amino acids, and the significance of Miller finding both; Go over chemistry of the ninhydrin reaction. Start introduction to nucleic acid structure. Handed out and discussed J. D. Watson and F. H.C. Crick, *Molecular Structure of Nucleic Acids*, *Nature* 171, 737-738, 1953, and R. Olby, *Quiet debut for the double helix*, *Nature* 421, 403-403, 2003; Discuss the magnitude of the discovery of DNA structure, but the apparent lag time for appreciation; Discuss the accomplishments and personalities of Watson, Crick and others of the time. Assigned reading: Chapter 9, *Storage, Replication, and Utilization of Biochemical Information from Origins of Life on the Earth and in the Cosmos*, 2nd ed., Geoffrey Zubay, Academic Press, 2000. Assigned problems at end of chapter instead of summary, but original questions still required.
10. Discuss Chapter 9 of Zubay and went over problems from chapter. Assigned reading: Chapter 16, *Chemistry of Translation*, from Zubay. Assigned problems at end of chapter.
11. Discuss chapter 16 and went over problems; Discuss tRNA; Show animation of the Ribosome: http://pubs.acs.org/cen/coverstory/85/8508cover.html; Discuss DNA replication and the special case of telomeres, which have a protein-RNA complex (telomerase) that carries out their replication. Assigned reading: S. W. Fox, K. Harada, *Production of Spherules from Synthetic Proteinoid and Hot Water*, *Science* 129, 1221-1222, 1959 and D. L. Rohlfing, *Thermal Polyamno Acids: Synthesis at Less Than 100°C*, Science 193, 1976, 68-69.
12. Discuss Fox and Rholfing protenoid papers. Discuss dextran and Sephadex columns. Handed out and discussed Fox and Harada, *Science* 128, 1958, 1214 (has recipe for hot production of protenoids); Go over chemistry of biuret test for proteins. Assigned reading: Chapter from Biochemistry book on introduction to protein structure.
13. Discuss chemical properties of amino acids, hydrophobic effect and protein folding. Assigned reading: A. Brack and G. Spach, *Enantiomer Enrichment in Early Peptides*, *Origins of Life and Evolution of the Biosphere* 11, 1981, 135-142.
14. Discuss Brack and Spach paper. Discuss other proposed theories for the origin of amino acid homochirality. Hand out and discuss L. E. Orgel and F. H. C. Crick, *Anticipating an RNA World - Some Past Speculations on the Origin of Life: Where are They Today*, *FASEB Journal* 7, 1993, 238-239. (Orgel and Crick paper gives a good re-introduction of the RNA world hypothesis, and emphasizes that speculation without experiment is not very effective in moving science forward.) Assigned reading: *Hud and Anet, Intercalation-Mediated Synthesis and Replication: A New Approach to the Origin of Life*, *J. theor. Biol.* 205, 2000, 543-562.
15. Discuss Hud and Anet paper. Compare and contrast to mineral hypothesis presented in Schopf book. Hand out and discuss Jain et al., *Enzymatic Behavior of Intercalating Molecules in a Template-Directed Ligation Reaction*, *Angew. Chem. Int. Ed*. 43, 2004, 2004-2008. Assigned reading: Bean et al., *Glyoxylate as a Backbone Linkage for a Prebiotic Ancestor of RNA*, *Origins of Life and Evolution of Biospheres* 36, 2006, 39-63.

16. Discuss Bean et al. Hand out and discuss Bean et al., *Formation of a ß-Pyrimidine Nucleoside by a Free Pyrimidine Base and Ribose in a Plausible Prebiotic Reaction*, *Journal of the American Chemical Society* 129, 2007, 9556-9557. Assigned reading: Joyce et al., *Chiral selection in poly(C)-directed synthesis of oligo(G)*, *Nature* 310, 602-603, 1984.
17. Discuss Joyce et al. Hand out and discuss V. Avetisov and V. Goldanskii, *Mirror symmetry breaking at the molecular level*, *Proceedings of the National Academy of Sciences* 93, 1996, 11435-11442, a rather complex paper that students need to be slowly lead through. Avetisov and V. Goldanskii bring up questions regarding the results by Joyce et al. Both papers are good for introducing a more general discussion of the difficulties associated with the incorporation of racemic monomers into protein and nucleic acid polymers. No assigned reading, as written reports due next class period.
18. Written book reports due. Because no reading assignment was given, papers are handed out for discussion to be lead by instructor. Papers from a mixture of topics are given that address questions that had arisen during previous class periods. For example: 1) Dworkin, Lazcano and Miller, *The roads to and from the RNA world*, *Journal of Theoretical Biology* 222, 2003, 127-134, which argues that RNA is older than DNA. Show with this paper the complex mechanism used by ribonucleotide reductase to convert NMPs into dNMPs.; The following two papers question the conclusion by some scientists that the Earth's atmosphere would have been too oxidizing (or at least not reducing enough) to support the chemistry observed by Miller. 2) H. J. Cleaves, J. H. Chalmers, A. Lazcano, S. L. Miller and J. L. Bada, *A Reassessment of Prebiotic Organic Synthesis in Neutral Planetary Atmospheres*, *Origins of Life and Evolution of the Biosphere* 38, 2008, 105-115. This paper demonstrates that prebiotic compounds can be formed in a neutral atmosphere. 3) Tian et al., *A Hydrogen-Rich Early Earth Atmosphere*, *Science* 308, 2005, 1014-1017. This paper revisits models for hydrogen loss from the atmosphere and the new models conclude that a reducing atmosphere would have been possible. No assigned reading, as oral reports given over next four class periods.
19. Oral book reports 1.
20. Oral book reports 2.
21. Oral book reports 3.
22. Oral book reports 4. Assign term research project. Assigned reading: F. Westheimer, *Why nature chose phosphates*, *Science* 235, 1173-1177.
23. Discussed Westheimer paper; Discussed additional examples of phosphorylation in living organisms; Showed animation of ATP synthase; Discussed saponification. Assigned reading: D. W. Deamer and J. P. Dworkin, *Chemistry and Physics of Primitive Membranes*, *Topics in Current Chemistry* 259, 2005, 1-27.
24. Project proposals due. Discussed Deamer and Dworkin paper; Additional discussions about the nature of cell membranes, nucleus membranes and cell walls. Assigned reading: R. M. Hazen, T. R. Filley, and G. A. Goodfriend, *Selective adsorption of L- and D-amino acids on calcite: Implications for biochemical Homochirality*, *Proceedings of the National Academe of Sciences USA* 98, 2001, 5487-5490. Also handed out chapter from crystallography book on crystal forms.
25. Discuss Hazen's paper and general topics about crystals; Discussed nucleation and suppression of crystal growth by the binding of organic molecules; Showed figures Bart Kahr's website: http://faculty.washington.edu/annkurth/dyeingcrystals.html. Assigned Reading: A. L. Weber and S. Pizzarello, *The peptide-catalyzed stereospecific synthesis of tetroses: A possible model for prebiotic molecular evolution*, *Proceedings of the National Academe of Sciences USA* 103, 2006, 12713-12717.; M. Bolli, R. Micural and A. Eschenmoser, *Pyranosyl-RNA: chiroselective self-assembly of base sequences by ligative*

oligomerization of tetranucleotide-2',3'-cyclophosphates (with a commentary concerning the origin of biomolecular homochirality), *Chemistry* and Biology 1997. (Students directed to focus only on the commentary on the origin of biomolecular homochirality, and to consider the different possible efficiencies of these two theories with Hazen's paper.)

26. Discuss Eschenmoser's paper and Weber's paper. Assigned reading: R.F. Fox, *Origin of Life and Energy*, *Encyclopedia of Energy*, Volume 4 (2004).

27. Discuss Fox paper, and provide background on chemical principles introduced by Fox. Assigned reading: *Aminoacyl-tRNA synthetases: potential markers of genetic code development*, *TRENDS in Biochemical Sciences* 26, 2001, 591-596.; L. Ribas de Pouplana and P. Schimmel, *Two Classes of tRNA Synthetases Suggested by Sterically Compatible Dockings on tRNA Acceptor Stem*, *Cell* 104, 2001, 191-193. (Papers are similar, but helpful to give both.)
28. Discuss expansion of code theory; handed out and discussed E. Szathmáry, *Why are there four letters in the genetic alphabet?*, *Nature Reviews Genetics* 4, 2003, 995-1001. (Includes introduction to Synthetic Biology). Assigned reading: W. F. Doolittle, *Phylogenetic Classification of the Universal Tree*, *Science* 284, 1999, 2124-2128.
29. Written final reports due. Discussed Doolittle's paper; Handed out and discussed M. C. Rivera1 and J. A. Lake, *The ring of life provides evidence for a genome fusion origin of eukaryotes*, *Nature* 431, 2004, 152-155, along with other theories for the origin of eukaryotes.
30. Oral final reports 1.
31. Oral final reports 2.