

Chemistry of the Origin of Life and Early Evolution  
*An undergraduate biochemistry seminar course*

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Overview and course objectives: The purpose of this course is to introduce students to the current scientific theories pertaining to the origin of life and early evolution. An intrinsically interdisciplinary topic, this course includes material as varied as the use of atmospheric physics to model the early Earth, to the use of genetics to map evolution and the tree of life. The material chosen for the course helps the instructor demonstrate to the students how we can use our current knowledge of biology, chemistry and physics to place limits on possible scenarios for the origin of life, and eventually solve the problem of how life began on Earth. An equally important objective of this course, particularly when taught at the undergraduate level, is to help students develop critical thinking skills, the ability to read scientific literature and to inspire them to pursue answers to big questions/challenges in science and society.

Prerequisites: Most students may enter this course with very little knowledge of origin of life research. The course has been designed such that students of any major that have completed at least one year of college level chemistry and one semester of organic chemistry will be able to follow the material presented, sometimes with the aid of additional background sources.

Course textbooks: The course begins with the reading of *Life's Origin - The Beginnings of Biological Evolution*, J. W. Schopf, University of California Press, 2002. This book is written at an introductory level for the popular press, which provides the students with a common level of knowledge, as well as a relatively quick overview of the field. Selected chapters of the text *Origins of Life on the Earth and in the Cosmos*, 2<sup>nd</sup> ed., Geoffrey Zubay, Academic Press, 2000, are also used over the course of the semester, but the text is usually listed as "recommended" to the students taking the course.

Lecture structure teaching pedagogy: At Georgia Tech, this course has usually met twice a week, with 75 minutes per class. Students were given a reading assignment at the end of each class. The students were required to turn in a typed summary (one to two paragraphs) and three questions or discussion points at the beginning of the next class. It is recommended that the students bring two copies of their summary and questions to class, one to turn in and one to keep for reference and note taking. At the beginning of the class a volunteer is requested to read his or her summary of the reading assignment. After the initial summary, other students in the class are encouraged to add to the summary any points that they felt were important but not expressed. When the students are satisfied that the important points and concepts of the reading have been expressed, the question and discussion portion of the class begins. Students are then welcomed to ask the questions that they had prepared before class. Because there are many concepts and experimental techniques introduced in this course, certainly more than one of each per lecture, the instructor may need to take considerable time in each class to provide background information to the students. It is also helpful to bring extra material, such as handouts and slides, to each class in anticipation of questions from the class.

Reading and discussing Schopf's *Life's Origins* has typically required six to seven class periods. The students are required to begin reading one additional book on the origin of life or early evolution from a list of recommended titles (see below). The purpose of having the students read a book of their choice is to both allow the students to explore a particular aspect of origin of life research that is of personal interest, and to expose the rest of the class to concepts and proposals that might not be introduced over the course of the assigned reading material.

After the class has finished reading and discussing Schopf's *Life's Origins*, a series of papers are assigned from the primary literature. Typically, one scientific paper is assigned for reading at the end of the class. The discussion of some papers will require an entire class period, whereas others may only require 45 min. For those papers requiring less discussion time it has worked well to pass out a second paper on the same topic as supplementary material. The instructor then provides a summary and leads the discussion on the second paper for the remainder of the class.

Major assignments: Students are required to prepare two written reports and to make brief oral presentations of these reports to the class. The first report is based upon a book selected by each student. Students are provided with a list of suggested titles, but may select a book not on the list. In either case, book selection requires instructor approval. To minimize redundancy in class reports and to maximize exposure of student to new concepts, no two students are allowed to select the same book in a class of twelve or fewer students, and now two students are allowed to select the same book for a larger class. Book selection is typically required before the class has finished Schopf's *Life's Origins*, so that students can begin their independent reading soon after. Students are required to submit a *critical* written report on their chosen book. In addition to presenting concepts not covered in the class, the students are to critically assess the validity of arguments presented by the book authors in support of hypotheses relating to the origin of life and early evolution. Three class periods are usually set aside for students to present short oral presentations of their book. Like the written portion of this assignment, the presentations are not be book summaries, but the presentation of new concepts and critical review of hypotheses championed by the book authors.

The second major assignment, typically assigned immediately after book reports are completed, is a scientific critique of a current theory regarding the origin of life or early evolution. Each student is to choose a unique topic, which may be as focused as the problem concerning the abiotic synthesis of ribose, to as broad as the role of oxygen in evolution. Students are required to use at least three original sources from the scientific literature to support their position of support or dissent of a current hypothesis. This report, both written and oral, typically serves as the final exam grade for the course.

Grading system used at Georgia Tech:

25% is based on the quality of written summaries of assigned reading and questions/discussion points. No late assignments are accepted.

25% is based on class participation. This grade includes class attendance, participation in discussions, and volunteering to present reading summaries and introduce discussion points.

25% is based on the written and oral report of a book chosen for individualized reading.

25% is based on the end-of-term written and oral report on a selected theory regarding the origin of life or early evolution.

List of course topics:

Historical perspective of the search for the origin of life  
The molecules of contemporary life  
The cosmos and the nature of the early Earth  
The formation of the building blocks of life  
Prebiotic polymer formation  
The origin of biological information  
Compartmentalization, from membranes to the first cells  
Determining the age of life  
Energy as a constraint on life  
The appearance of photosynthesis  
The biological source and effects of O<sub>2</sub>  
Early microbial colonies  
The origin of eukaryotes  
The search for the last common ancestor  
The Precambrian explosion  
The origin of the genetic code  
Synthetic biology

Summary of class meeting topics, new concepts and assigned papers from Georgia Tech CHEM 2803, spring semester 2008

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 lineage 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 Bang 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 [www.ucsd.tv/miller-urey/](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  $\alpha$  versus  $\beta$  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*, 2<sup>nd</sup> 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. Rohlfsing, Thermal Polyamino Acids: Synthesis at Less Than 100°C, *Science* 193, 1976, 68-69.
12. Discuss Fox and Rohlfsing proteinoid papers. Discuss dextran and Sephadex columns. Handed out and discussed Fox and Harada, *Science* 128, 1958, 1214 (has recipe for hot production of proteinoids); 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  $\beta$ -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. Rivera 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.

Additional papers in Supplementary Reading that have some times been used in this class.

J. Raymond, O. Zhaxybayeva, J. P. Gogarten, S. Y. Gerdes, R. E. Blankenship, Whole-Genome Analysis of Photosynthetic Prokaryotes, *Science* 298, 2002, 1616-1620.

G. W. Hodgson and C. Ponnamperna, Prebiotic Porphyrin Genesis: Porphyrins from Electric Discharge in Methane, Ammonia, and Water Vapor, *Proc. Natl. Acad. Sci. USA* 59, 1968, 22-28.

H. Urey, On the Early Chemical History of the Earth and the Origin of Life, *Proc. Natl. Acad. Sci. USA* 38, 351-363.

P. Rothemund, A New Porphyrin Synthesis. The Synthesis of Porphin, *J. Am. Chem. Soc.* 58, 1936, 625-627.

D. Fitz, H. Reiner, K. Plankensteiner and B. M. Rode, Possible Origins of Biohomochirality, *Current Chemical Biology*, 2007, 1, 41-52.

Examples of recommended books for individual reading and written/oral report:

Acquiring Genomes: The Theory of the Origins of the Species, Lynn Margulis, Dorion Sagan, 256 pages, Basic Books, 2003.

The Blind Watchmaker: Why the Evidence of Evolution Reveals a Universe Without Design, Richard Dawkins, W. W. Norton & Company, 1996, 358 p.

Cradle of Life: The Discovery of Earth's Earliest Fossils, J. William Schopf, Princeton University Press, 1999, 367 p.

Five Kingdoms: An Illustrated Guide to the Phyla of Life on Earth (3rd edition), Lynn Margulis, Karlene V. Schwartz, Owl Books, 1997, 544 p.

Microcosmos: Four Billion Years of Evolution from Our Microbial Ancestors, Lynn Margulis, Dorion Sagan, University of California Press, 1997, 300 p.

Origin and Early Evolution of Life, Tom Fenchel, Oxford University Press, 2003, 224 p.

The Selfish Gene, Richard Dawkins, Oxford University Press; 2nd Ed edition, 1990, 368 p.