

Bio 4337 Seminal papers in Molecular Biology

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Fall, 2008, MW 11:30 AM-12:45 PM, Room FO 3.222

Seminal Papers is a history course. Selected theoretical and experimental papers in the history of Molecular Biology will be assigned to be read by all students. They will be discussed and analyzed in class. The topics will be covered roughly in the order in which they are discussed by Horace Judson in *The Eighth Day of Creation: Maker's of the Revolution in Biology* (Expanded Edition, 1996, CSHL Press). Judson's book, a widely acclaimed history of molecular biology, is based on the interviews of 111 scientists. The first Edition was published in 1978, the twenty fifth anniversary of the Watson and Crick paper on the structure of DNA. In his 1988 book, *What Mad Pursuit*, Francis Crick stated that in comparison with other accounts, *The Eighth Day of Creation* "is more vivid, since it contains lengthy verbatim quotations from most of the participants. His story begins nearer in time to the discovery of the double helix and continues for another dozen years or so until the genetic code was unraveled provid[ing] the most complete and the most balanced accounts so far of the beginnings of classical molecular biology" (p. 81). Readings in Judson will serve as a background narrative for the selected papers. The Expanded Edition has important additions: an Epilogue, "*On the transformation of Molecular Biology, 1970-1995*", Afterword I, *In defense of Rosalind Franklin*, and Afterword II, *What Did Erwin Chargaff Contribute?*

Most papers are covered in two sessions: the first session is devoted to background reading in Judson and the second to reading of the seminal paper. Outlines are provided for both readings in the Learning Module.

Topics to be covered

DNA

The genetic material (DNA): (Avery, and Chase)

DNA Structure: (Chargaff; Watson and Crick; Franklin; Wilkins)

DNA Replication (Meselson and Stahl)

Proteins

Protein Structure: (Pauling)

Protein Synthesis:

Adaptor hypothesis: tRNA (Crick; Zamecnik et al; Chapeville et al.)

The genetic code: (Nirenberg and Matthaei; Crick, Barnett, Brenner and Watts-Tobin)

Messenger RNA: (Brenner, Jacob and Meselson)

Regulation: The Lac Operon (Jacob and Monod)

Allostery: (Monod, Changeux and Jacob)

Format, Student Participation and Grading

Text: : *The Eighth Day of Creation, Makers of the Revolution in Biology, Expanded Edition*, Horace Judson, 1996, Cold Spring Harbor Laboratory Press.

Seminal Papers: Journals, eJournals or reprint collections on reserve in the library.

The reading assignments and Exam schedule:

Date	Day	Exam	Reading Assignments Judson (pp.)/Seminal Paper
August 25	M		Introduction: Syllabus, Course Format
August 27	W		1. DNA is the hereditary material, pp. 11-24
September 3	W		<i>Avery, McCleod and McCarty paper</i>
September 8	M		2. Demise of the Tetranucleotide, pp. 73-75; 631-637
September 10	W		<i>Chargaff paper</i>
September 15	M		3. The alpha helix, pp. 51-65.
September 17	W		<i>Pauling and Corey paper</i>
September 22	M	EXAM I	
Septembr 24	W		4. Double Helix, I pp. 77 - 97
September 29	M		II pp. 97-123
October 1	W	 III pp. 125-150 <i>Watson and Crick papers</i>
October 6	M		5. DNA Replication, pp. 161-166
October 8	W		<i>Meselson and Stahl paper</i>
October 13	M		6. tRNA, pp. 236-245,287-295; 312-313; 333-336
October 15	W		<i>Chapeville et al. paper</i>
October 20	M	EXAM II	
October 22	W		7. The lac Operon, pp. 369-374, 390-403
October 27	M		<i>Jacob and Monod Review I</i>
October 29	W		<i>Jacob and Monod Review II</i>
November 3	M		8. UUU is phenylalanine, 453-464-
November 5	W		<i>Nirenberg and Matthaei paper</i>
November 10	M		9. Allostery, "The 2 nd secret of life", 545-557
November 12	W		<i>Monod, Changeux and Jacob</i>
November 17	M		<i>Monod, Changeux and Jacob</i>
November 19 - December 3	W W		Student Presentations
December 8	M	Exam III	Topics 7-9

Attendance and Class Participation: In a small class seminar format, attendance and class participation are essential. The readings should be completed before class. Come to class and be prepared!

Term paper: Students must submit a term paper which meets the University writing requirement (i.e. 15 pages of text).

First Draft: Each student must submit a draft of the paper on a previously approved topic.

Subsequent Drafts: The corrected First Draft will be returned within a week with indications of whether it is acceptable as a Final Paper, after corrections, or must be resubmitted

as a subsequent draft. More than one draft may be necessary until an acceptable Final Paper is submitted.

Final Paper: Upon final approval of a Final Draft, a final Paper must be submitted ***no later than*** the last day of class.

Exams:: There will be 3 non-cumulative exams.

Course grade: Determined *approximately* as follows:

1) Exams (3 x 25%)	75 %
2) Term paper: (10+5)	15 % *
3) Oral Presentation	5 %
4) Participation and attendance	5 %

I tend to send many e-mails with comments on the reading or reminders of upcoming deadlines. ***Please read your e-mails every day.***

2008 Seminal Papers

Avery, Oswald, T., Colin M. MacLeod and Maclyn McCarty 1944 Studies on the chemical nature of the substance inducing transformation of pneumococcal types. Induction of transformation by a desoxyribonucleic acid fraction isolated from Pneumococcus Type III. *Journal of Experimental Medicine*, 79, 137-158.(T)

Chargaff, Erwin 1950 Chemical specificity of nucleic acids and mechanism of their enzymatic degradation. *Experientia*, 6, 201-209. (T)

Pauling, Linus and Robert B. Corey 1950 "Two Hydrogen Bonded Spiral Configuraton of the Polypeptide Chain. *Journal of the American Chemical Society* 72, 5349

Pauling, Linus, Robert Corey and H. R. Branson 1951 The structure of proteins: Two hydrogen-bonded helical configurations of the peptide chain. Proceedings of the National Academy of Sciences, USA, 37, 205-211.

Pauling, Linus and Robert Corey 1951, The pleated sheet, a new layer configuration of polypeptide chains. . Proceedings of the National Academy of Sciences, USA, 37, 251.

Watson, James, D. and Francis H. C. Crick 1953, Molecular structure of nucleic acids. Nature 171, 737-738. Judson: pp. 170-171

**Watson, James, D. and Francis H. C. Crick 1953, Genetical implications of the structure of deoxyribonucleic acid. Nature, 171, 964-967
Judson: pp. 171-173**

Meselson, Mathew and Franklin W. Stahl 1958, The replication of DNA in Escherichia coli, Proceedings of the National Academy of Sciences, USA, 44, 671-682. (T)

Hoagland, Mahlon B. , Paul C. Zamecnik and Mary L. Stephenson 1957, Intermediates in protein synthesis, Biochimica et Biophysica Acta, 24, 215-216.

Chapeville, Francois, Fritz Lipmann, Gunter von Ehrenstein, Bernard Weisblum, William J. Ray, Jr., and Seymour Benzer 1962, Proceedings of the National Academy of Sciences, USA, 48, 1086-1092.

Brenner, Seymour, Francois Jacob and Mathew Meselson 1961, An unstable intermediate carrying information from genes to ribosomes for protein synthesis. Nature 190, 576-581. (T)

Jacob, Francois, David Perrin, Carmen Sanchez and Jacques Monod 1960, Compte Rendus des Seances de l'Academie des Sciences, 250, 1727-1729. (Translated from the French) (A)

Jacob, Francois and Jacques Monod 1961, Genetic regulatory mechanisms in the synthesis of proteins. Journal of Molecular Biology 3, 318-356. (T)

Crick, F.H., Leslie Barnett, Sidney Brenner and R. J. Watts-Tobin 1962, General Nature of the Genetic code for proteins. Nature 192, 1227-1232.

Nirenberg, Marshall, W., and J. Heinrich Matthaei 1961, The dependence of cell-free protein synthesis in E. coli upon naturally occurring or synthetic

polyribonucleotides. Proceedings of the National Academy of Sciences, USA, 47, 1588-1602. (T)

Monod, Jacques, Jean-Pierre Changeux and Francois Jacob 1963, Allosteric proteins and cellular control systems. Journal of Molecular Biology, 6, 306-329.

*T: J. H. Taylor, 1965 *Selected Papers on Molecular Genetics*, Academic Press, NY

*A: E. A. Adelberg , 1960 *Papers on Bacterial Genetics*, Little Brown and Co., Boston.

Note on copying papers

***Because of copyright regulations, copies of the papers cannot be distributed to students and purchasing copies through the University Copy Center is prohibitively expensive. Therefore, students must make their own copies from books on reserve or journals in the library. Papers, marked with a T or A, above, are in collections of reprints on Reserve. All other papers must be copied directly from the library Journals or e-Journals...**