**BIOS 4225/BIOL 7111 Molecular Evolution**

**Fall 2018 Tues/Thursday 9:30am-10:45 am, Location: CE 204**

**Instructor:** Soojin Yi, School of Biological Sciences, Georgia Tech. EBB 2111

Office hour: by appointment (email)

[soojinyi@gatech.edu](mailto:soojinyi@gatech.edu), 404-385-6084

**Instructional Goals:** This class is designed to accomplish the following specific goals:

* Learn key molecular evolutionary models and be able to apply appropriate models to different types of data (from lectures and discussions)
* Learn new knowledge in the field of molecular and genome evolution and be able to integrate findings in different fields of modern –omics research into evolutionary context (from lectures and discussions and paper reading/critiques)
* Build up deep knowledge in a couple of specific research areas of molecular/genome evolution
* Being able to give a professional scientific presentation and lead peer discussion

**Background knowledge:** To accomplish the above instructional goals, some background knowledge is required.

* Understand basic concepts of statistics (mean, variance, co-variance, normal distribution, chi-square distribution, binomial probability)
* Basic arithmetic skills (e.g., Taylor approximation)
* Basic knowledge on genetics and evolution (e.g. Hardy-Weinberg equilibrium allele frequencies)

These should have been covered in the prerequisite classes (Evolution, Genetics, other prerequisite classes). I strongly recommend the students to brush up these points beforehand.

**Summary of the class:** This class is composed of two main activities.

*The first* is traditional ‘lectures’. I will work with you to go over classical models used in molecular evolutionary analyses. We will also touch upon some population genetic principles, which are critical to understanding molecular evolution.

*The second* activity is your participation. In addition to participating in class discussions, you are required to provide a few presentations (the exact number of presentations will depend on the size of the class). An important goal of this class is to build on your knowledge of classical and up-to-date literature, ability to provide scientific presentation and lead discussion, and write a paper. To this end, you are required to present a paper, and lead discussion. The list of recommended papers for presentations is provided at the end of this syllabus and will be available as a google doc. The list is designed to include classical literature as well as some up-to-date topics. Students should check the list of recommended papers and sign up for presentations. You are welcome to provide recommendations according to your own research interests as well. The presentations will start by the fourth week of the class, and will become more and more frequent as the semester progresses. Students are recommended to consult the instructor prior to the presentation with a draft presentation. I will also provide written and graded feedback after the presentation. Other students will also provide written feedbacks.

*Expected number of presentations and presentation lengths*: Based on the current enrollment, graduate students are expected to give at least two presentations, and undergraduate students are expected to give one presentation. Some of the recommended papers are short and relatively straightforward. In such cases, a 15 min presentation is sufficient. Some of the papers require more time, and in such cases a 25 min presentation might be necessary.

*Paper Summaries:* To facilitate discussion, ALL students are required to read the paper prior to the class. Each student is to submit a summary of the paper(s) to be discussed each day. The summaries should be at most one page per paper. I will accept printed and/or electronic submission of paper summaries before the start of each class. These will be graded according to the following scheme:

* Timely submission (before the start of each class): 1 point
* Late submission: 0 point
* Submission that are copy and pastes of introduction: 0 point

*Exams*: There will be TWO graded exams in this class. A mid-term, currently scheduled for Oct. 11, and the final exam, currently scheduled for Dec. 6th. Both will be open-books, but online search is not allowed, and no laptop/phone/other electronic devices are allowed, except a calculator. Students who use any electronic device other than a calculator will be automatically given a zero. The exams are to cover ALL concepts discussed in the class (lectures, papers, and other discussion). If exams appear very similar, both students will get zeros and failing grades. Both students will be reported to the administration.

Problem sets, quizzes: There will be a few problem sets and quizzes. These will NOT be graded, and are intended to provide supplementary material.

Guest lectures: We have several exciting guest lectures scheduled! See the syllabus for the quest speakers this semester.

**Grading Scheme:** Undergraduate and graduate students will be graded separately.

* Paper summaries: 20%
* mid-term: 25%
* Presentation: 25%
* Final-exam: 30%

Your final grade will be assigned as a letter grade according to the following scale:

A 90-100%

B 80-89%

C 70-79%

D 60-69%

F 0-59%

## Missed Exam Policy

There will be no make up exam. However, in case of emergency or other excused absence, the student will have an opportunity to perform additional work to receive partial credit. The partial credit for the missed exam will not exceed 50% of the total credit accounted by the missed exam.

## Academic Integrity

Georgia Tech aims to cultivate a community based on trust, academic integrity, and honor. Students are expected to act according to the highest ethical standards. For information on Georgia Tech's Academic Honor Code, please visit http://www.catalog.gatech.edu/policies/honor-code/ or <http://www.catalog.gatech.edu/rules/18/>.

Any student suspected of cheating or plagiarizing on a quiz, exam, or assignment will be reported to the Office of Student Integrity, who will investigate the incident and identify the appropriate penalty for violations.

## Accommodations for Students with Disabilities

If you are a student with learning needs that require special accommodation, contact the Office of Disability Services at (404)894-2563 or <http://disabilityservices.gatech.edu/>, as soon as possible, to make an appointment to discuss your special needs and to obtain an accommodations letter. Please also e-mail me as soon as possible in order to set up a time to discuss your learning needs.

**Texts (recommended):**

* *Fundamentals of Molecular Evolution* by Dan Graur, Wen-Hsiung Li. Sinauer Associates, ISBN: 0878932666 (available from the Instructor and also in the GT library)
* *Molecular and Genome Evolution* by Dan Graur, Sinauer Associates, ISBN: 9781605354699 (available from the instructor)
* *Population Genetics: A Concise Guide* by John Gilespie. Johns Hopkins University Press. ISBN: 0801857554 (available from the Instructor and also in the GT library)

Supplementary Texts:

* *Molecular Evolution and Phylogenetics* by Masatoshi Nei, Sudhir Kumar. Oxford University Press. ISBN: 0195135849 (available from the Instructor)
* *Molecular Evolution* by Wen-Hsiung Li. Sinauer Associates, ISBN: 0878934634 (available from the Instructor)

**Detailed topics:** this list is tentative and subject to change.

Note: this list and the paper list are drafts as of 8/21/2018. The syllabus WILL CHANGE according to the input from the students. Updated list of topics and papers will be shared as a google doc.

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|  | **Date** | **Topic** | **Suggested Reading** |
| Week 1 | Aug. 21 | (Brief) history of molecular evolution Models of nucleotide substitution I. | G&L Ch. 2, 3 Supplementary Material |
|  | Aug. 23 | Models of nucleotide substitution II. | G&L Ch. 2, 3 |
| Week 2 | Aug. 28 | Other methods of multiple hit corrections Patterns and rates of nucleotide substitutions | G&L Ch. 3 |
|  | Aug. 30 | Examples of neutral rate variation Hominoid-rate slowdown Male-driven evolution | G&L Ch. 3,4 |
| Week 3 | Sep. 4 | Problem Set |  |
|  | Sep. 6 | Guest Lecture Dr. Isabel Mendizabal Human evolution |  |
| Week 4 | Sep. 11 | Protein-coding sequence evolution Ka, Ks, dN and dS | G&L Ch. 3, 4 |
|  | Sep. 13 | protein-coding sequence evolution continued  **Student presentations/discussion 1, 2, 3: examples of evolutionary rate variation Presenter: TBA** | G&L Ch. 3, 4  see paper list paper critiques due |
| Week 5 | Sep. 18 | Rates and patterns of nucleotide substitution continued  Purifying selection versus positive selection When genes evolve slow and fast Usage of statistical methods in molecular evolutionary studies | G&L Ch. 4 JG Ch.3 |
|  | Sep. 20 | Molecular population genetics I. selection Deterministic models of natural selection Balancing selection, positive selection, purifying selection, disruptive selection | G&L Ch. 4 JG Ch.3 |
| Week 6 | Sep. 25 | **Student presentations/discussions 4, 5, 6: Selection in protein-coding sequences Presenters: TBA** | JG Ch.2, see paper list paper critiques due |
|  | Sep. 27 | Molecular population genetics II. genetic drift Definition of genetic drift Some mathematical facts Consequences of genetic drift | Supplementary Material |
| Week 7 | Oct. 2 | Molecular population genetics III. Effective population size. | Supplementary Material |
|  | Oct. 4 | **Student presentations/discussions 7, 8, 9 Presenters: TBA** | Supplementary Material, Paper Critiques Due |
| Week 8 | **Oct. 9** | **Fall Recess** | Have Fun! |
|  | **Oct. 11** | **Exam I (open book)** |  |
| Week 9 | Oct. 16 | Molecular population genetics continued: Combining population genetics and divergence. Molecular Phylogenetics I. | G&L Ch. 5 |
|  | Oct. 18 | Discussing FOXP2 case: **Discussion of papers 10, 11, 12, 13. Presenters: Soojin Yi and TBA** | Paper Critiques Due |
| Week 10 | Oct. 23 | Molecular Phylogenetics II. | Supplementary Material  G&L Ch. 6 |
|  | Oct. 25 | Human molecular evolution | Supplementary Material |
| Week 11 | Oct. 30 | **Student presentation/discussion 10, 11** Gene duplication and chromosomal evolution | Paper Critiques Due |
|  | Nov. 2 | **Student presentation/discussion 12, 13** Gene duplication and chromosomal evolution continued | Paper Critiques Due |
| Week 12 | Nov. 6 | **Student presentation/discussion 14, 15, 16** | Paper critiques due |
|  | Nov. 8 | Guest speaker: King Jordan, Transposable Elements and Genome Evolution |  |
| Week 13 | Nov. 13 | **Student presentations/discussion 17** Experimental Evolution | Paper critiques due |
|  | Nov. 15 | **Student presentation/discussion 18, 19** Gene duplication and chromosomal evolution Evolution of Genome Information | Paper Critiques Due |
| Week 14 | Nov. 20 | Regulatory Evolution, Information content of the genome. What's the deal with the ENCODE? | Supplementary Material |
|  | Nov. 22 | **School Holiday** |  |
| Week 15 | Nov. 27 | **Student Presentation 20, 21, 22** | Supplementary Material  Paper critiques due |
|  | Nov. 29 | **Student Presentation 23, 24, 25,** General discussion | Supplementary Material  Paper critiques due |
| Week 16 | Dec. 4 | **Student Presentation 26, 27, 28,** General discussion. Problem sets | Supplementary Material  Paper critiques due |
|  | Dec. 6 | **Final Exam** |  |

**Suggested papers for presentations for BIOL 7111 A**

Here’s a list of suggested papers for presentations. Please think about which papers you would like to present. Note that we may add/remove specific papers in later dates. If you have suggestions for specific papers, please contact the instructor.

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| **Number in the Syllabus** | **Paper** | ***Recommendation*** | **Presenter(s)** |
| 1 | *Bohossian HB, Skaletsky H, Page DC, 2000, Unexpectedly similar rates of nucleotide substitution found in male and female hominids. Nature, 406:622-625.* |  |  |
| 2 | *Makova, K.D., and Li, W.-H. 2002. Strong male-driven evolution of DNA sequences in humans and apes. Nature 416, 624-626.* |  |  |
| 3 | King, M.-C., & Wilson, A. C. 1975. Evolution at two levels in humans and chimpanzees. Science 188: 107-116. |  |  |
| 4 | *Clark, A. G., S. Glanowski, R. Nielsen, P. D. Thomas, A. Kejeriwal, M. A. Todd, D. M. Tanenbaum, D. Civello, F. Lu, B. Murphy, S. Ferriera, G. Wang, X. Zheng, T. J. White, J. J. Sninsky, M. D. Adams, and M. Gargill. 2003. Inferring nonneutral evolution from human-chimp-mouse orthologous gene trios. Science 302, 1960-1963.* |  |  |
| 5 | *Haygood R, Fedrigo O, Hanson B, Yokoyama K-D, Wray GA. 2007. Promoter regions of many neural- and nutrition-related genes have experienced positive selection during human evolution. Nature Genet 39(9): 1140-1144.* | ***G*** |  |
| 6 | Drummond, D. A., A. Raval, and C. O. Wilke. 2006. A single determinant dominates the rate of yeast protein evolution. Mol. Biol. Evol. 23:327-337. (Note: the presenter may also check Kim, S-H. and Yi, S. (2007). Understanding relationship between sequence and functional evolution in yeast proteins. Genetica, 131: 151-156). | ***G*** |  |
| 7 | Lynch, M., and Conery, J.S. (2003). The origins of genome complexity. Science 302, 1401-1404. | ***G*** |  |
| 8 | Bundle: Charlesworth B, Barton N: Genome size: does bigger mean worse? Curr Biol 2004, 14:R233-R235. |  |  |
| 9 | Yi, S., and J. T. Streelman. 2005. Genome size is negatively correlated with effective population size in ray-finned fish. Trends Genet. 21, 643-646. |  |  |
| 10 | *Enard, W., Przeworski, M., Fisher, S.E., Lai, C.S.L., Wiebe, V., Kitano, T., Monaco, A.P., and Paabo, S. 2002. Molecular evolution of FOXP2, a gene involved in speech and language. Nature 418, 869-872.* |  | Soojin Yi |
| 11 | *Krause, K., Lalueza-Fox, C., Orlando, L., Enard, W., Green, R. E., Burbano, H. A., Hublin, J. J., Hänni, C., Fortea, J., de la Rasilla M., Bertranpetit, J., Rosas, A., Páábo, S., 2007. The derived FOXP2 variant of modern humans was shared with Neanderthals. Curr. Biol. 17: 1908-1912.;* |  |  |
| 12 | *Coop, G., Bullaughey, K., Luca, F., and M. Przeworski 2008. The timing of selection at the human FOXP2 gene. Mol. Biol. Evol. 25: 1257-1259* |  |  |
| 13 | *Atkinson, E. G., Audesse, A. J., Palacios, J. A., Bobo, D. M., Webb., A. E., Ramachandra, S., and B. M. HEnn. 2018. No evidence for recent selection at FOXP2 among diverse human populations. Cell 174: 1-12.* | ***G*** |  |
| 14 | *Bundle: Cann, R., Stoneking, M., and Wilson, A. C. 1987. Mitochondrial DNA and human evolution. Nature 325: 31-36.; Vigilant, L., M. Stoneking, H. Harpending, K. Hawkes, and A. C. Wilson. 1991. African populations and the evolution of human mitochondrial DNA. Science 253,1503-1507.* | ***G*** |  |
| 15 | *Huerta-Sánchez, et al. 2014. Altitude adaptation in Tibetans caused by introgression of Denisovan-like DNA. Nature 512, 194-197.* | ***G*** |  |
| 16 | *Presgraves DC, Yi S. 2009. Doubts about complex speciation between humans and chimpanzees. Trends Ecol Evol 24, 533-540.* |  |  |
| 17 | *Patterson N, Richter DJ, Gnerre S, Lander ES, Reich D. 2006. Genetic evidence for complex speciation of humans and chimpanzees. Nature 441, 1103-1108.* | ***G*** |  |
| 18 | Wolfe, K., H., and D. C. Shields, 1997. Molecular evidence for an ancient duplication of the entire yeast genome. Nature 387: 708-713. | ***G*** |  |
| 19 | *Lynch M and JS Conery, 2000. The evolutionary fate and consequences of duplicate genes. Science 290, 1151-1155* |  |  |
| 20 | Kellis, M., Birren, B., and E. S. Lander, 2004. Proof and evolutionary analysis of ancient genome duplication in the yeast Saccharomyces cerevisiae. Nature 428: 617-624. | ***G*** |  |
| 21, 22 | Lior Patcher’s blog post on May 26, 2015 titled “Patcher’s P-value Prize” and comments therein. Because this is a long post and even longer comments, I am willing to let two students to share this presentation. For example, two students, preferably those who are interested and experienced in genomics/statistics, may consult with each other beforehand to decide on which comments to take. It will be impossible to talk about all comments, I will leave it to the presenters’ discretion to choose a few notable ones to discuss in depth during the class. | ***G*** |  |
|  | Note: papers below are at no particular order and subject to change according to students' and the instructor's interest. My comments for why I think they could be read and discussed are attached. |  |  |
|  | *Baym, M. et al. 2016. Spatiotemporal microbial evolution on antibiotic landscapes. Science 353, 1147-1151.* | ***Short but really cool paper about fundamental processes.*** |  |
|  | Good, B. H., McDonald, M. J., Barrick, J. E., Lenski, R. E., and M. M. Desai. 2017. The dynamics of molecular evolution over 60,000 generations. Nature 551: 45-50 | ***definintely dense, but will be a must-read for graduate students interested in experimental evolution.*** |  |
|  | Lien et al. 2016, The Atlantic salmon genome provides insights into rediploidization. Nature 533, 200-205. | ***This paper and the next paper started a debate on statistical analyses of gene duplication, and the relative prevalence of subfunctionalization and neofunctionalization. These papers may be substituted for other gene duplication papers in the syllabus.*** |  |
|  | Brasch et al., 2016, The spotted gar genome illuminates vertebrate evolution and facilitates human-teleost comparisons. Nature Genetics, 48, 427-437. |  |  |
|  | Sandve, et al., 2018, Subfunctionalization versus neofunctionalization after whole-genome duplication. Nature Genetics, 50: 908-909 |  |  |
|  | Braasch et al., 2018, Reply to: 'Subfunctionalization versus neofunctionalization after whole-genome duplication' Nature Genetics 50, 906-911 |  |  |