

***Synthetic Biology and Comparative Genomics***  
***ZOO 4926 (Special topics)— Class Number: 20864***  
***(Spring Semester 2021)***

**Instructor Information:**

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***Brief Course Description:***

Synthetic biology is a field that merges genetics and engineering to: 1) redesign and fabricate existing biological systems; and 2) design and fabricate unnatural biological systems. This course has a strong focus on the use of comparisons among existing organisms to understand the results of synthetic biology experiments

***Textbook:***

*Synthetic Biology - A Primer: Revised Edition*, by Geoff Baldwin et al.

- **Publisher:** Imperial College Press; Revised edition (October 25, 2015)
- **Language:** English
- **ISBN-10:** 1783268794
- **ISBN-13:** 978-1783268795

<https://books.google.com/books?id=mTK6CgAAQBAJ>

Note: this is a relatively inexpensive textbook (approx. \$35 from various sources)

We will also do a number of readings from the peer-reviewed scientific literature. I provide examples in a selected bibliography at the end of this document.

***Additional Readings and Expanded Course Description:***

*Synthetic Biology and Comparative Genomics* is a stimulating and challenging survey of the field of synthetic biology. Synthetic biology is a diverse field that merges genetics and engineering and use methods from those fields to: 1) redesign and fabricate existing biological systems; and 2) design and fabricate biological systems that do not exist in the natural world. This course has a strong focus on the use of comparisons among existing organisms to understand the results of synthetic biology experiments. This course will comprise lectures, discussions, readings from the scientific literature, and a class project.

In addition to *Synthetic Biology - A Primer* we will read a number of papers from the peer-reviewed scientific literature. I vary the precise set of papers we read each year, but the general foci are: papers molecular genetics that illustrate principles important for synthetic biology (sometimes older than the “synthetic biology” era); and 2) papers on comparative and evolutionary genomics that can inspire the design of biological systems. A third focus is papers focused on the addition of “letters” to the two genetic “alphabets” (nucleic acids and proteins). Much of the discussion in class will focus on the yeast (*Saccharomyces cerevisiae*) as a “chassis” for building synthetics, augmented with examples from a variety of other organisms. The final topic has important implications for the early evolution of life and therefore a direct connection to the comparative and evolutionary foci of the course.

### ***Course Assignments and Grading:***

<b>Course component</b>	<b>Proportion of grade</b>
Participation	35%
Class project	35%
Take home exercises	30%

### ***Class participation***

I expect regular attendance. If you are sick, have a family emergency, or plan to participate in a university-sanctioned event just let me know; those absences are excused. Likewise, I will consider excusing you for any reasonable professional development activities; just discuss them with me. But otherwise I expect to see you in class and you will lose 1% of this portion of the grade for unexcused absences. Although some classes will be lectures many will include discussions; I expect everybody to participate. We will also be learning how to use specific computer programs during some classes and participating in those activities is important.

### ***Class project***

We will work on project to understand and analyze minimal genome projects, where synthetic biology is used to answer the question of “what is the minimum set of genes necessary for life?” This will involve extracting information from recent scientific papers, learning about the functions of specific proteins that appear to be necessary for life, and preparing a poster about your findings.

### ***Take home exercises***

There will be no tests, but I will expect you to produce short (1-2 paragraph) summaries of assigned readings.

## ***Grading scale***

The following grading scale will be used (values are percentages):

91-100 A	88-90.9 A-	
85-87.9 B+	81-84.9 B	78-80.9 B-
75-77.9 C+	68-74.9 C	65-67.9 C-
62-64.9 D+	58-61.9 D	

Below 58 is failing (E).

## ***Course policies***

\* Academic dishonesty will not be tolerated. If cheating or plagiarism is suspected, all persons involved will receive a zero on the affected assignment and it will be reported to the Dean of Students Office.

\* If you notice another student engaging in activities to you believe to constitute academic dishonesty please report the potential violation. I take all allegations seriously. However, remember that you are bound by the UF honor code, which states that *“in reporting an alleged Student Honor Code violation, a student shall not intentionally or in bad faith make a false or misleading statement.”* In other words, I view intentional false allegations as a type of academic dishonesty.

\*Attendance in class is required. However, if you cannot attend on specific days just email with the subject line “UNABLE TO ATTEND CLASS ON <DATE>” and provide a brief explanation. If you have concerns at any time just discuss them with me. My goal is to make the course enjoyable and informative so you will want to attend!

## ***University support services***

Resources are available on campus to help students meet academic goals and solve personal problems, which interfere with their academic performance. Resources include:

1. [UF Counseling and Wellness Center](#), 301 Peabody Hall and Radio Rd Facility, 392-1575, personal and career counseling.
2. [Career Resource Center](#), Reitz Union, 392-1601, career development assistance and counseling.
3. [CLAS Academic Advising Center](#), Farrior Hall, 100 Fletcher Drive, 392-1521, provides advise on course selection and course planning to meet graduation requirements

### ***Disability Notice***

Students with disabilities enrolled in this course and who may need disability-related classroom accommodations are encouraged to make an appointment to see me before the end of the second week of the term. All discussions will remain confidential, although the [Student Accessibility Services](#) office may be consulted to discuss appropriate implementation of any accommodation requested.

## Schedule

NOTE: an example bibliography is provided below; this is a fast-moving field and I anticipate changes in the readings over time

<b>Week</b>	<b>Topic and Reading</b>
1	<i>Review of Genetics and Molecular Biology</i> – Textbook (chapter 1)
2	<i>Conceptual Foundations of Biological Engineering, Orthogonality</i> – Textbook (chapter 2)
3	<i>Foundational technologies</i> – Textbook (chapter 3; also material in Appendix) <i>Reading the Peer-Reviewed Scientific Literature</i> – handout focusing on the best ways to see the “big picture” in scientific publications, using the Khorana (1979) paper as an example
4	<i>Definition of Essential Genes; Identifying and Characterizing Essential Genes</i> – Burns et al. (1994); Mnaimneh et al. (2004); Wishart et al. (2005)
5	<i>Definition of Minimal Genomes via Comparative Genomics</i> – Koonin (2000) <i>Yeast 2.0</i> – Richardson et al. (2017); Mitchell et al. (2017); Shen et al. (2017)
6	<i>Yeast 2.0 continued, Removal of “Selfish” Genetic Elements</i> – continue material from Richardson et al. (2017); Mitchell et al. (2017); Shen et al. (2017) <i>Perturbing Metabolic Systems</i> – Windram et al. (2017)
7	<i>“Swapability” of Orthologous Genes</i> – DeFeo-Jones et al. (1985); Kachroo et al. (2015); Kachroo et al. (2017)
8	<i>“Swapability” of Orthologous Genes continued</i> – DeFeo-Jones et al. (1985); Kachroo et al. (2015); Kachroo et al. (2017) <i>Design and Synthesis of Minimal Organisms</i> – Hutchison et al. (2015)
9	<i>Skills for Comparative Genomics</i> – Handout <i>Review Concepts for Minimal Organisms, Essential Genes, and Ortholog Swapping</i> – begin class project
10	<i>Importance of Codon Bias for Expression</i> –Gustafsson et al. 2004; Hershberg & Petrov (2008); Plotkin & Kudla (2011) <i>Gene Design Software</i> – Handout
11	<i>Redesigning the Genetic Code (also discussion of the need to contain synthetic organisms, which can be facilitated by unnatural codes)</i> – Calles et al. (2019)

12	<i>“Non-natural” (Non-canonical) Amino Acids and Modified Genetic Codes – Chin et al. (2003); Neumann et al. (2010); Nehring et al. (2012)</i>
13	<i>Expanding the Genetic Alphabet – Zhang et al. (2017)</i>
14	<i>Complete Project; Presentations</i>
15	<i>Complete Presentations</i>

### **Annotated Bibliography**

Burns, N., Grimwade, B., Ross-Macdonald, P. B., Choi, E. Y., Finberg, K., Roeder, G. S., & Snyder, M. (1994). Large-scale analysis of gene expression, protein localization, and gene disruption in *Saccharomyces cerevisiae*. *Genes & development*, 8(9), 1087-1105. *(example of large-scale gene disruption using TE insertions, a method used to identify essential genes)*

Calles, J., Justice, I., Brinkley, D., Garcia, A., & Endy, D. (2019). Fail-safe genetic codes designed to intrinsically contain engineered organisms. *Nucleic Acids Res*, gkz745. doi: 10.1093/nar/gkz745 *(computational methods to redesign the genetic code to ensure fidelity)*

Chin, J. W., Cropp, T. A., Anderson, J. C., Mukherji, M., Zhang, Z., & Schultz, P. G. (2003). An expanded eukaryotic genetic code. *Science*, 301(5635), 964-967. *(adding “unnatural” amino acids to the genetic code)*

DeFeo-Jones, D., Tatchell, K., Robinson, L. C., Sigal, I. S., Vass, W. C., Lowy, D. R., & Scolnick, E. M. (1985). Mammalian and yeast *ras* gene products: biological function in their heterologous systems. *Science*, 228(4696), 179-184. *(first example of “swapping” orthologs between yeast and mammals, near functional equivalence demonstrated)*

Gustafsson, C., Govindarajan, S., & Minshull, J. (2004). Codon bias and heterologous protein expression. *Trends in Biotechnology*, 22(7), 346-353. *(importance of codon bias for gene expression)*

Hershberg, R., & Petrov, D. A. (2008). Selection on codon bias. *Annual review of genetics*, 42, 287-299. *(importance of codon bias for expression)*

Hutchison, C. A., Chuang, R. Y., Noskov, V. N., Assad-Garcia, N., Deerinck, T. J., Ellisman, M. H., et al. (2016). Design and synthesis of a minimal bacterial genome. *Science*, 351(6280), 1414 (aad6253). *(first example of designed minimal organism)*

Kachroo, A. H., Laurent, J. M., Akhmetov, A., Szilagyijones, M., McWhite, C. D., Zhao, A., & Marcotte, E. M. (2017). Systematic bacterialization of yeast genes identifies a near-universally swappable pathway. *Elife*, 6, e25093. (example of gene swapping using CRISPR-Cas9)

Kachroo, A. H., Laurent, J. M., Yellman, C. M., Meyer, A. G., Wilke, C. O., & Marcotte, E. M. (2015). Systematic humanization of yeast genes reveals conserved functions and genetic modularity. *Science*, 348(6237), 921-925. (example of gene swapping using other methods)

Khorana, H. G. (1979). Total synthesis of a gene. *Science*, 203(4381), 614-625. (first example of complete gene synthesis)

Koonin, E. V. (2000). How many genes can make a cell: the minimal-gene-set concept. *Annu Rev Genomics Hum Genet*, 1, 99-116. (review of efforts to define the minimal cell using comparative and functional genomics)

Mitchell, L. A., Wang, A., Stracquadanio, G., Kuang, Z., Wang, X., Yang, K., et al. (2017). Synthesis, debugging, and effects of synthetic chromosome consolidation: synVI and beyond. *Science*, 355(6329), eaaf4831. (introduces the idea of the need to "debug" a synthetic yeast chromosome to make it work)

Mnaimneh, S., Davierwala, A. P., Haynes, J., Moffat, J., Peng, W. T., Zhang, W., et al. (2004). Exploration of essential gene functions via titratable promoter alleles. *Cell*, 118(1), 31-44. (description of large-scale placement of engineered tet promoters that can be controlled using doxycycline)

Nehring, S., Budisa, N., & Wiltschi, B. (2012). Performance analysis of orthogonal pairs designed for an expanded eukaryotic genetic code. *PloS one*, 7(4), e31992. (building orthogonal sets of proteins and tRNAs to expand the genetic code)

Neumann, H., Wang, K., Davis, L., Garcia-Alai, M., & Chin, J. W. (2010). Encoding multiple unnatural amino acids via evolution of a quadruplet-decoding ribosome. *Nature*, 464(7287), 441-444. (alternative method for expanding the amino acid set)

Plotkin, J. B., & Kudla, G. (2011). Synonymous but not the same: the causes and consequences of codon bias. *Nature Reviews Genetics*, 12(1), 32-42. (comparative genomics of codon bias)

Richardson, S. M., Mitchell, L. A., Stracquadanio, G., Yang, K., Dymond, J. S., DiCarlo, J. E., et al. (2017). Design of a synthetic yeast genome. *Science*, 355(6329), 1040-1044. (overview of the "yeast 2.0" redesign project)

Shen, Y., Wang, Y., Chen, T., Gao, F., Gong, J., Abramczyk, D., et al. (2017). Deep functional analysis of synII, a 770-kilobase synthetic yeast chromosome. *Science*, 355(6329), eaaf4791. (use of synthetic biology to analyze a yeast chromosome)

Windram, O. P., Rodrigues, R. T., Lee, S., Haines, M., & Bayer, T. S. (2017). Engineering microbial phenotypes through rewiring of genetic networks. *Nucleic acids research*, 45(8), 4984-4993. *(illustrates the use of synthetic biology to perturb yeast expression system to maximize production of a compound)*

Wishart, J. A., Hayes, A., Wardleworth, L., Zhang, N., & Oliver, S. G. (2005). Doxycycline, the drug used to control the *tet*-regulatable promoter system, has no effect on global gene expression in *Saccharomyces cerevisiae*. *Yeast*, 22(7), 565-569. *(illustrates the importance of controls – in this case the need to determine whether the doxycycline used to control the tet promoter has undesirable off-target effects)*

Zhang, Y., Lamb, B. M., Feldman, A. W., Zhou, A. X., Lavergne, T., Li, L., & Romesberg, F. E. (2017). A semisynthetic organism engineered for the stable expansion of the genetic alphabet. *Proceedings of the National Academy of Sciences*, 114(6), 1317-1322. *(description of system to expand the number of DNA nucleotides from four to six in vivo)*