Creating life: the emergence of synthetic biology
A Duke University House Course

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Meeting Day/Time
Location

Course Description:

From curing genetic diseases to creating wholly artificial life forms, the new field of synthetic biology is rapidly redefining our understanding of life itself. Synthetic biology combines the vast knowledge of molecular biology developed over the last century with principles of forward design, giving new meaning and purpose to the concept of genetic engineering. The core philosophy of this movement can be summed up by the words of physicist Richard Feynman: "what I cannot create, I do not understand."

This course serves as an introduction to the synthetic biology movement, as well as a catalyst for dialogue about the potential applications of the young field and its implications for society. We will begin with an introduction to the biological and engineering principles required for an informed discussion on the topic, focusing on the Central Dogma, standard biological parts, and modular design. We will then discuss a variety of current and potential applications in the genres of basic research, gene therapies, and drug development, among others. Finally, we will analyze the potential impact of such technologies on human health, safety, intellectual property, and the environment. Students will have the opportunity to develop their own synthetic project ideas, assessing their implications on ethics and society.

Objectives:

The course will provide students with a foundation of understanding upon which they can critically evaluate developments in synthetic biology and society. As synthetic biotechnologies become more commonplace in our

world, it is critical that society's leaders have the necessary background to make crucial decisions regarding their development and use.

Upon completion of this course, students will have an understanding of the following:

- The synthetic biology movement, its origins, and its unique characteristics
- The molecular processes of gene expression according to the Central Dogma
- The characteristics that define a BioBrick or synthetic biological device
- The concept of forward engineering and its application to biology
- The importance of modeling and mathematics in design
- The relationship between basic and applied science

In addition, students will be equipped to critically evaluate the following:

- Intellectual property concerns in synthetic biology
- The benefits and concerns of synthetic gene therapies
- The environmental impact of biotechnologies
- Bioethical concerns involving synthetic biological parts and systems
- Strategies for the safe and ethical advancement of research

Required Readings:

This course includes weekly readings from a variety of sources, including popular and academic books, scientific journal articles, analysis reports, and literary works. All readings will be provided in .pdf format on Sakai. A detailed schedule of the readings is included within the course schedule below.

Books:

Atwood, M. (2003). *Oryx and Crake*. Chapters 1-4, pp. 3-58. New York: Anchor Books.

Church, G. (2012). *Regenesis: how synthetic biology will reinvent nature and ourselves.* New York: Basic Books.

Freemont, P. and Kitney, R. (2012). *Synthetic biology: a primer*. London: Imperial College Press.

National Research Council (2006). *Globalization, biosecurity, and the future of the life sciences.* Chapter 1, pp. 15-78. Washington, DC: National Academies Press.

Rutherford, A. (2013). *Creation: how science is reinventing life itself.* New York: Pearson.
Wang, X.,Chen, J., and Quinn, P. (eds). (2012). *Reprogramming microbial metabolic pathways.* Chapters 3 and 5, pp. 43-71, 95-114. New York: Springer.
Young S. (2006). *Designer Evolution: A transhumanist manifesto.* Forewords and Introduction, pp. 9-26. Amherst: Prometheus Books.

Articles and other readings:

Baker, M. (2014). "Gene editing at CRISPR speed." *Nature Biotechnology* 32(4), pp. 309-312.
Balmer, A. and Martin, P. (2008). *Synthetic biology: social and ethical challenges.* Biotechnology and Biological Sciences Research Council.
Bogdanove, A. and Voytas, D. (2011). "TAL Effectors: customizable proteins for DNA targeting." *Science* 333, pp. 1843-1846.
Elowitz, M. and Lim, W. (2010). "Build life to understand it." *Nature* 468 pp. 889-890.
Endy, D. (2005). "Foundations for engineering biology." *Nature* 438(24) pp. 449-453.
Gold, E. and Herder, M. (2007). *The role of biotechnology intellectual property rights in the bioeconomy of 2030.* OECD International Futures Programme.
Kelty, C. (2010). "Outlaws, hackers, victorian amateurs: diagnosing public participation in the life sciences today." *Journal of Science Communication* 9(1), pp. 1-8.
Kennedy, J. (2012). "The sources and uses of U.S. science funding." *The New Atlantis* 36, pp. 3-22.
Kumar, S. and Rai, A. (2007). "Synthetic Biology: The intellectual property puzzle." *Texas Law Review* 85, pp. 1745-1768.
Pennisi, E. (2012). "The Tale of the TALEs." *Science* 338, pp. 1408-1411.
Roberts, R. (2005). "How restriction enzymes became the workhorses of molecular biology." *Proc. Natl. Acad. Sci. USA* 102(17), pp. 5905-5908.
Rutz, B. (2009). "Synthetic biology and patents. A European perspective." *European Molecular Biology Organization Reports.* 10(Suppl 1), pp. S14-S17.
Sheridan, C. (2014). "First CRISPR-Cas Patent opens race to stake out intellectual property." *Nature Biotechnology* 32, pp. 599-601.

Tucker, J. and Zilinskas, R. (2006). "The promise and perils of synthetic biology." *The New Atlantis* 12, pp. 25-45.
Voosen, P. (2013). "Synthetic biology comes down to earth." *The Chronicle of Higher Education*, March 4, 2013.

Course Requirements:

Attendance: This is a primarily discussion-based course meant to foster dialogue about the issues surrounding the synthetic biology movement. As such, regular and prompt attendance at class meetings is expected. **Students are required to attend at least 11 classes to receive a passing grade.**

Participation and oral presentation: Students are expected to contribute thoughtfully to the dialogue of the course during each meeting. The instructors realize that the level of prior knowledge regarding molecular biology, engineering, and other aspects of the course will vary, and students are encouraged to help teach each other key concepts, both during and outside of scheduled class time. Participation in the course will culminate with **a brief, informal presentation of a synthetic biology project proposal.** The details of this proposal are outlined under Writing Project #2 below.

Readings: Approximately 50-60 pages of reading are assigned each week, listed within the course schedule below. This will include a combination of book chapters, journal articles, reports, and other writings, which will be of varying depth and scientific density. **It is required that students read the assigned pages before class.** While you may not understand all of the details, particularly in some of the more challenging readings, being familiar with each reading will allow you to ask questions and discuss confusing aspects with your peers during class, leading to a productive learning environment.

Writing Projects: This course requires two writing projects designed to make students consider the implications of a specific synthetic biology concept or project in detail.

Writing project #1: Current application.
Due: Week 10

Identify and research a particular application of synthetic biology tools or practices that has the potential to impact society in the near future. This should be an endeavor currently in development or recently proposed by members of the field, with a specific purpose and a clear utility. Write a 1500-word paper in which you critically analyze the application, its relationship to synthetic biology, and its implications for society. The paper should address the intended purpose of the application, how it is to be carried out, and possible side effects or setbacks the process may encounter.

Writing project #2: Future application.
Due: Week 15
Develop a proposal for a potential future application of synthetic biology tools or practices. A general model for how to develop the technology should be proposed, although intricacies of the design need not be finalized. Write a 1500-word paper outlining this new application, its relationship to synthetic biology, and its implications for society. The paper should address how the technology functions, its intended purpose, and possible side effects or setbacks that may encountered in its development. This proposal will be briefly presented to the class and discussed during the final class meeting.

Grading: House courses are graded on a satisfactory/unsatisfactory basis. A grade of satisfactory in this course requires satisfactory completion of all assignments of this course including written and oral assignments, attendance, and participation in class discussion.

Course Schedule:

Week 1 ***Introduction: What is Synthetic Biology?***
MM/DD Lecture/Discussion:

- Introduction to the course
  - Syllabus, expectations, assignments, and readings
- Overview of synthetic biology
  - Arrive at a working definition
  - Similarities and differences to genetic engineering
  - Goals of synthetic biology
  - The forward-engineering approach
- Origins of synthetic biology

- Advances that made it possible
- Seminal papers
- Paradigm shifts

Readings (50 pages):

Rutherford, A. (2013). *Creation: how science is reinventing life itself.*
Chapters 7-8, pp. 135-160 (26 pp)

Church, G. (2012). *Regenesis: how synthetic biology will reinvent nature and ourselves.*
Prologue, pp. 1-13 (13 pp)

Voosen, P. (2013). "Synthetic biology comes down to earth."
(11 pp)

Week 2 ***Molecular Genetics: what you need to know***

MM/DD Lecture/Discussion:

- The Central Dogma: DNA to RNA to protein
- The parts of a gene
- Cloning vs. synthesis
- Standardization and characterization of parts
- The BioBrick

Activities:

- Partner/small group session: peer teaching
- Analyze sample Biobricks with DNA software

Readings (55 pages):

Freemont, P. and Kitney, R. (2012). *Synthetic biology: a primer*.
Chapter 1, pp. 1-18 (18 pp)
Chapter 5, pp. 73-88 (16 pp)

Church, G. (2012). *Regenesis: how synthetic biology will reinvent nature and ourselves.*
Chapter 1, pp. 15-35 (21 pp)

Week 3 ***iGEM and synthetic biology as a movement***

MM/DD Lecture/Discussion:

- The iGEM competition
- The BioBricks foundation and the registry
- Open-source collaboration
- "Garage bio"

Activities:

- Analyze a biobrick in the registry

- Find an iGEM team wiki and discuss their project

Readings (50 pages):

Rutherford, A. (2013). *Creation: how science is reinventing life itself.*
Chapter 10, pp. 183-194 (12 pp)

Freemont, P. and Kitney, R. (2012). *Synthetic biology: a primer*.
Chapter 8, pp. 119-129 (10 pp)

Church, G. (2012). *Regenesis: how synthetic biology will reinvent nature and ourselves.*
Chapter 8, pp. 179-201 (23 pp)

Endy, D. (2005). "Foundations for engineering biology."
pp. 449-453 (5 pp)

Week 4 ***Gene circuits and modeling molecular systems***

MM/DD ***Guest Lecturer: Nicolas Buchler***

Lecture/Discussion:

- What is a gene circuit?
- Circuits in nature
- Synthetic circuits
- What can we do with circuits?
  - Genetic computing
  - Complex, predictable systems
- Analog vs. digital
- What is modeling? Why is it useful?

Readings (55 pages):

Rutherford, A. (2013). *Creation: how science is reinventing life itself.*
Chapter 9 (21 pp)

Freemont, P. and Kitney, R. (2012). *Synthetic biology: a primer*.
Ch. 2, pp. 29-40 (12 pp)
Ch. 6, pp. 89-105 (17 pp)

Week 5 ***Applications of synthetic biology: overview***

MM/DD Lecture/Discussion:

- Metabolic engineering and drug development
- Directed evolution
- Biological computing
- Experimental and basic science applications
- Gene therapies

Activities:

- Brainstorm potential applications

- Discuss viability of potential applications

Assignments:

- Introduce writing project #1: Current applications.

Readings (64 pages):

Freemont, P. and Kitney, R. (2012). *Synthetic biology: a primer*.
Ch. 7, pp. 109-118 (10 pp)

Church, G. (2012). *Regenesis: how synthetic biology will reinvent nature and ourselves.*
Chapters 2-3, pp. 37-90 (54 pp)

Week 6 ***Metabolic engineering and drug development***

MM/DD ***Guest Lecturer: Michael Lynch***

Lecture/Discussion:

- Metabolic pathways
- Insulin production and the beginning of bio-engineering
- Drug development
- Biofuels
- Challenges to design and implementation
- How are synthetic biology techniques changing this field?
- What are other applications of these techniques?

Readings (66 pages):

Church, G. (2012). *Regenesis: how synthetic biology will reinvent nature and ourselves.*
Chapter 4, pp. 91-107 (17 pp)

Wang, X.,Chen, J., and Quinn, P. (eds). (2012). *Reprogramming microbial metabolic pathways.*
Chapter 3, pp. 43-71 (29 pp)
Chapter 5, pp. 95-114 (20 pp)

Week 7 ***Synthetic biology relies on basic science***

MM/DD Lecture/Discussion:

- The tools of synthetic biology
  - Restriction enzymes
  - Zinc fingers, CRISPR and TALEs
- Other examples of basic science benefits
  - The foundations of the field itself
  - Sequencing
  - Mathematics and modeling

- The long timeline of scientific benefits
- Research priorities
  - Results-based funding
  - Accountability
  - Funding of basic and applied research

Readings (51 pages):

Freemont, P. and Kitney, R. (2012). *Synthetic biology: a primer*.
Ch. 3, pp. 41-59 (19 pp)
Bogdanove, A. and Voytas, D. (2011). "TAL Effectors: customizable proteins for DNA targeting."
pp. 1843-1846 (4 pp)
Pennisi, E. (2012). "The Tale of the TALEs."
pp. 1408-1411 (4 pp)
Roberts, R. (2005). "How restriction enzymes became the workhorses of molecular biology."
pp. 5905-5908 (4 pp)
Kennedy, J. (2012). "The sources and uses of U.S. science funding."
pp. 3-22 (20 pp)

Week 8 ***Basic science learns from synthetic biology***

MM/DD Lecture/Discussion:

- Minimal systems
  - "What I cannot create, I do not understand"
- Recreating systems from the ground up
- Probing systems through modification
- Have geneticists been doing synthetic biology all along?
- New tools make it easier
- Standard characterization helps too
- The mathematicization of biology

Readings (49 pages):

Rutherford, A. (2013). *Creation: how science is reinventing life itself.*
Afterword, pp. 233-250 (18 pp)
Freemont, P. and Kitney, R. (2012). *Synthetic biology: a primer*.
Ch. 4, pp. 61-71 (11 pp)
Church, G. (2012). *Regenesis: how synthetic biology will reinvent nature and ourselves.*
Chapter 6, pp. 133-150 (18 pp)
Elowitz, M. and Lim, W. (2010). "Build life to understand it."

(2 pp)

Week 9 ***Gene therapies and synthetic biology in medicine***
MM/DD ***Guest Lecturer: Charles Gersbach***

Lecture/Discussion:

- Identifying gene errors
  - The genomic information revolution
  - Personalized genomic medicine
- Fixing faulty genes
  - CRISPR tools
- Delivery mechanisms
- Difficulties in achieving gene therapies
  - Consistent results in a noisy cellular environment
  - Different from person to person
- Existing and upcoming therapies
- If it ain't broke, should we fix it?

Readings (52 pages):

Church, G. (2012). *Regenesis: how synthetic biology will reinvent nature and ourselves.*

Chapter 5, pp. 109-132 (24 pp)
Chapter 9, pp. 203-223 (24 pp)

Baker, M. (2014). "Gene editing at CRISPR speed."
pp. 309-312 (4 pp)

Week 10 ***Synthetic biology in industry***
MM/DD

Lecture/Discussion:

- What are companies currently doing?
  - DNA synthesis
  - Sequencing
  - Providing standard parts
  - Enzyme development
- What might companies do in the future?
  - Drug companies
- From bench to biotech: challenges in scaling up

Assignments:

- **Writing project #1 due**
- Introduce Writing project #2: Future applications.

Readings (58 pages):

Church, G. (2012). *Regenesis: how synthetic biology will reinvent nature and ourselves.*

Chapter 7, pp. 151-178 (28 pp)

Balmer, A. and Martin, P. (2008). *Synthetic biology: social and ethical challenges.*

pp. 3-32 (30 pp)

Week 11 Public Health and the Environment

MM/DD <u>Lecture/Discussion:</u>

- Introduction: the Asilomar meetings
- Regulations
  - Current
  - Proposed?
- GMOs
  - Are they a legitimate concern?
  - How synthetic biology could radically change the scope of genetic modification
- Environmental change
  - Spread of synthetic organisms in the environment
  - Resistance to herbicides/antibiotics
  - Targeting invasive species
  - Resurrecting extinct species, saving endangered ones

<u>Readings (58 pages):</u>

Rutherford, A. (2013). *Creation: how science is reinventing life itself.*

Chapter 11, pp. 202-231 (30 pp)

Freemont, P. and Kitney, R. (2012). *Synthetic biology: a primer*.

Chapter 9, pp. 131-136 (7 pp)

Tucker, J. and Zilinskas, R. (2006). "The promise and perils of synthetic biology."

pp. 25-45 (21 pp)

Week 12 Garage bio, bio-hacking, and bioterrorism

MM/DD <u>Lecture/Discussion:</u>

- The dawn of Bio-hacking and garage bio
- What it would take to make a synthetic biology start-up
  - The challenges facing start-ups
- Killer viruses
- Anthrax scares
- How easy would it be to make a bio-terror weapon?

    - Smallpox research
  - Deliberate versus accidental threats
    - Can we make " a truly fail-safe fail-safe?"
  - What precautions are being taken?
  - What precautions and regulations should be considered?

Readings (72 pages):

Kelty, C. (2010). "Outlaws, hackers, victorian amateurs: diagnosing public participation in the life sciences today.".

pp. 1-8 (8 pp)

National Research Council (2006). *Globalization, biosecurity, and the future of the life sciences.*

pp. 15-78 (64 pp)

Week 13 Intellectual property in SynthBio

MM/DD Lecture/Discussion:

- Introduction to intellectual property
  - Copyrights, trademarks, patents
  - Purpose of IP law
  - Is it effective? Are there limitations?
- Recent court cases
- The problem of judicial process in a rapidly changing field
- Open-source movements
- Patenting of gene sequences
- Is there a fair way to spur innovation?

Readings (49 pages):

Rutherford, A. (2013). *Creation: how science is reinventing life itself.*

Chapter 10, pp. 194-199 (5 pp)

Freemont, P. and Kitney, R. (2012). *Synthetic biology: a primer*.

Chapter 9, pp. 136-139 (4 pp)

Sheridan, C. (2014). "First CRISPR-Cas Patent opens race to stake out intellectual property."

pp. 599-601 (3 pp)

Gold, E. and Herder, M. (2007). *The role of biotechnology intellectual property rights in the bioeconomy of 2030.*

pp. 4-12 (9 pp)

Kumar, S. and Rai, A. (2007). "Synthetic Biology: The intellectual property puzzle."

pp. 1745-1768 (24 pp)

Rutz, B. (2009). "Synthetic biology and patents. A European perspective."
pp. 14-17 (4 pp)

Week 14 Ethical and moral concerns

MM/DD <u>Lecture/Discussion:</u>

- How far should we go?
- Cloning
- Gene therapies and human engineering
  - Dangers vs. promise
  - How do they affect the entire population?
- Genetic exploitation
- The right to change your own body
- The emerging philosophy of transhumanism
- How to proceed as a society and as leaders
  - Is there a way to maximize the benefits while limiting the costs?

<u>Readings (55 pages):</u>

Freemont, P. and Kitney, R. (2012). *Synthetic biology: a primer*.
Chapter 9, pp. 139-146 (8 pp)

Church, G. (2012). *Regenesis: how synthetic biology will reinvent nature and ourselves.*
Epilogue, pp. 225-253 (29 pp)

Young S. (2006). *Designer Evolution: A transhumanist manifesto.*
Forewords and Introduction, pp. 9-26 (18 pp)

Week 15 Future Directions

MM/DD <u>Activity/Discussion:</u>

- Short presentations of student proposals
- Student-led discussion on the plausibility and societal implications of each proposal

<u>Assignments:</u>

- **Writing project #2 due**

<u>Readings (56 pages):</u>

Atwood, M. (2003). *Oryx and Crake*.
pp. 3-58 (56 pp)