

The Microbiome

MCB 4320C/ MCB 6670C

3 credit hours

Prerequisite: MCB 3020 or MCB 3023 or equivalent

Course Description:

Increase knowledge, appreciation and use of genomics pertaining to the breadth of microbial diversity across a wide variety of organisms and habitats using methods that do not require culturing of the myriad of inhabitants. Students will use tools, practice analysis and interpretation of genomic data sets to analyze different microbiomes.

Instructor:

Prof. Eric W. Triplett
Microbiology and Cell Science Department
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352-392-5430
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Twitter: @ewtriplett

Teaching assistants: PhD students and post-doctoral fellows will also contribute to the lecture material and guide students through the computer based activities and microbiome data analysis.

The best ways to contact us are via E-learning mail or we can set up a time for individual phone calls or Skype sessions.

Brief Background:

What is the microbiome? The collection of microorganisms that inhabit a specific environment is referred to as the microbiome. The microbiome includes all microbial life: bacterial, archaeal, fungal, and viral. Microbiomes exist on and within plants, mammals, insects, amphibians, birds, etc. They also exist in niches to themselves in a wide variety of terrestrial, marine, and aquatic environments. Many of these environments are extreme including hot springs, deep ocean thermal vents, and subsurface rock formations.

Given the many environments in which microbiomes thrive, no single course or group of courses can hope to cover them adequately. But this course intends to teach students many of the modern tools available to analyze the microbiome and its role in a given environment. As a result, this course will provide students with experience using many

of the molecular tools used in microbiome analysis including 16S rRNA sequencing, whole genome sequencing, epigenomics, transcriptomics, small RNA analysis, proteomics, and metabolomics. Some lessons learned on experimental design will also be included.

The course will be entirely web-based. The reading assignments, course lecture materials and online computer based lab activities will be posted each week. There will be a quiz every two weeks and four exams.

Course Objectives:

1. Students can explain how “microbial-omics” data are used to understand the human microbiome and its role in human health.
2. Students are familiar with and can use and apply modern technologies used in microbiome research.
3. Students can compile “omics” datasets and execute a microbiome analysis.
4. Students will be able to explore genome mining and can characterize a genome sequence from sample data containing many genomes.
5. Students can communicate the importance of the microbiome in many environments is able to perform analysis of microbial communities in a particular ecosystem.
6. Students can compare epigenomics, transcriptomics, and proteomics and can explain how they are used to address questions of interest.
7. Students participate in an on-going microbiome experiment and work in groups to write a manuscript on their results including the analysis and interpretation of the data.

Textbook: There is no required or recommended textbook.

e-Learning system: The course will be managed entirely through the e-Learning in the Canvas system (one of two big orange button at <https://elearning.ufl.edu/>). If you are not familiar with this system, you need to become acquainted with it for this course. The LSS homepage contains tips and tutorials for students as well as [computer requirements](#). It is your responsibility to become familiar with e-Learning in Canvas and to ensure that you have the appropriate browsers, settings, internet speed, etc. For any technical questions regarding Canvas, please visit the e-Learning site (https://elearning.ufl.edu/help/Student_Faq) and/or the UF Help desk (<http://helpdesk.ufl.edu/>). They can address technical issues such as not being able to view course materials, not being able to access the quizzes, not being able to send mail, etc. **All technical issues/questions/comments should go to the Help Desk first (352-392-HELP)**. They are the experts. The Help Desk suggests that if you encounter any problem (error messages, etc.) that you take a screen shot of the problem and save it. This will help the Help Desk in fixing your problem.

If you encounter a problem that the HELP DESK cannot fix, please send a help request to the Technical Support Center of the Microbiology & Cell Science Department. Please fill out your request at <http://microcell.ufl.edu/support/index.php>. The form will ask for your name, number, email and location. In the location field, please indicate “online course.”

Office Hours: Since this is a web-based course, office hours will be online. The office hours will be conducted via the Meetings function in e-Learning in Canvas or via Skype. Office hours are difficult to schedule since our students have such varied schedules. We will always be available to answer questions by email or to set up an individual phone or Skype conversation. Just contact us to arrange.

Email and Announcements: All email communication regarding this course will be done through the mail function of E-learning in Canvas. This mail system is private and secure. It is your responsibility to check your E-learning Mail and Announcements **frequently** to stay updated on the course. Please check the course a minimum of two times per week to be certain that you are not missing any important communications. As the instructors, we will respond to your questions and emails promptly. By maintaining all email communication through Canvas instead of other email domains, it reduces the chance that discussions will get lost among outside accounts. When sending an email through e-Learning in Canvas, you have the option to also forward the email to the recipient's UFI account. Please use this option if you have an urgent message. If you receive a course email (from Canvas) to your UFI account, please note that you cannot simply hit "reply" to the email. You must login to Canvas to respond through the mail function.

Topical outline of weekly modules:

Wk	Dates	Lecture topic:	Lab/Computer activity
1	Jan 4 - 13	Introduction to Course History of the study of the microbiome	
2	Jan 17 - 20	Describing the organisms present in the microbiome: 16S rRNA sequencing	
3	Jan 23 - Jan 27	Analysis and interpretation of 16S rRNA sequencing	RDP pipeline for microbial classification R Studio for analyzing RDP results
4	Jan 30 - Feb 3	Extracting whole genomes from the microbiome - genome sequencing through PacBio	Assembling PacBio sequence data using SMRT Analysis software
5	Feb 6 - 10	Culturing organisms of interest from the microbiome: bacterial, archaeal, fungal, and yes, viral.	

		Exam 1, February 8, available 5-10 PM	
6	Feb 13 - 17	Environmental influences on bacterial genomes: bacterial epigenome and its analysis	Epeigenetic analysis of assembled genome using SMRT Analysis software
7	Feb 20 - 24	Learning the metabolic potential of the microbiome: metagenomics	MG-RAST to annotate and analyze metagenomic data
		Exam 2, February 22, available 5-10 PM	Deadline for project.....
8	Feb 27 - Mar 3	Which functions are expressed in the microbiome - transcriptomics	RNA Rocket software to assemble, map, and quantify gene expression
9	Mar 13 - 17	RNA influencing gene expression: sRNA sequencing	Trim, assemble, and map sRNA reads to reference using tools available in Galaxy
10	Mar 20 - 24	Functions available in the microbiome - metaproteomics	Other tools to introduce include PAREsnip, iMir, and MiRCAT
11	Mar 27 - Mar 31	Microbiome experiment - description and analysis	TPP (transproteomic) pipeline to interpret mass spec data, identify, validate, quantify, and assign proteins to reference
		Exam 3, March 29, available 5-10 PM	
12	Apr 3 - 7	Microbiome experiment - data analysis and interpretation	
13	Apr 10 - 14	Microbiome experiment - writing the paper	
			Deadline for project
14	Apr 17 - 19	Microbiome experiment - writing the paper	
15	April 27	Exam 4, draft of paper due 10 PM	

Content for the 6xxx-level course:

Graduate students will be asked weekly to read and review a recent peer-reviewed paper from the current microbiome literature. On each exam day, they will be asked to submit a summary of each paper read in a Canvas assignment. Recent papers will be chosen from Elizabeth Bik's Microbiome Digest (<https://microbiomedigest.com>). This site provides daily updates on virtually all of the microbiome papers published.

For the final exam, the graduate students will be expected to write a paper on the dataset provided (just as are all of the undergraduates in the course), write a two page summary of the most important findings they learned from the original papers read this semester. Students will be asked to discuss the future of microbiome research.

Example papers from previous semesters include:

Module 1: Intro to genome sequencing

- Loman, N. J., & Pallen, M. J. (2015). Twenty years of bacterial genome sequencing. *Nature Reviews Microbiology*.

Module 2: 16S rRNA sequencing

- Davis-Richardson, A. G., Ardisson, A. N., Dias, R., Simell, V., Leonard, M. T., Kempainen, K. M., ... & Ilonen, J. (2014). *Bacteroides dorei* dominates gut microbiome prior to autoimmunity in Finnish children at high risk for type 1 diabetes. *Frontiers in microbiology*, 5, 678.
- Karamitros, T., & Magiorkinis, G. (2015). A novel method for the multiplexed target enrichment of MinION next generation sequencing libraries using PCR-generated baits. *Nucleic acids research*, 43(22), e152-e152.
- Loman, N. J., Quick, J., & Simpson, J. T. (2015). A complete bacterial genome assembled de novo using only nanopore sequencing data. *Nature methods*.

Module 3: 16S sequencing analysis

- No papers were assigned for this module

Module 4: PacBio genome sequencing

- Korem, T., Zeevi, D., Suez, J., Weinberger, A., Avnit-Sagi, T., Pompan-Lotan, M., ... & Sirota-Madi, A. (2015). Growth dynamics of gut microbiota in health and disease inferred from single metagenomic samples. *Science*, 349(6252), 1101-1106.

Module 5: Annotation of bacterial genomes

- No papers were assigned for this module

Module 6: Bacterial epigenome

- Leonard, M. T., Davis-Richardson, A. G., Ardisson, A. N., Kempainen, K. M., Drew, J. C., Ilonen, J., ... & Hyöty, H. (2014). The methylome of the gut microbiome: disparate Dam methylation patterns in intestinal *Bacteroides dorei*. *Frontiers in microbiology*, 5, 361.
- Kumar, R., & Rao, D. N. (2013). Role of DNA methyltransferases in epigenetic regulation in bacteria. In *Epigenetics: Development and Disease* (pp. 81-102). Springer Netherlands.

Module 7: Metagenomics

- No papers were assigned for this module

Module 8: Transcriptomics

- Croucher, N. J., & Thomson, N. R. (2010). Studying bacterial transcriptomes using RNA-seq. *Current opinion in microbiology*, 13(5), 619-624.
- Warren, A. S., Aurrecochea, C., Brunk, B., Desai, P., Emrich, S., Giraldo-Calderón, G. I., ... & Mao, C. (2015). RNA-Rocket: an RNA-Seq analysis resource for infectious disease research. *Bioinformatics*, btv002.

Module 9: sRNA sequencing

- Gottesman, S., McCullen, C. A., Guillier, M., Vanderpool, C. K., Majdalani, N., Benhammou, J., ... & FitzGerald, D. J. (2006, January). Small RNA regulators and the bacterial response to stress. In *Cold Spring Harbor Symposia on Quantitative Biology* (Vol. 71, pp. 1-11). Cold Spring Harbor Laboratory Press.
- Storz, G., Vogel, J., & Wassarman, K. M. (2011). Regulation by small RNAs in bacteria: expanding frontiers. *Molecular cell*, 43(6), 880-891.
- Raabe, C. A., Tang, T. H., Brosius, J., & Rozhdestvensky, T. S. (2014). Biases in small RNA deep sequencing data. *Nucleic acids research*, 42(3), 1414-1426.
- Folkes, L., Moxon, S., Woolfenden, H. C., Stocks, M. B., Szittyá, G., Dalmay, T., & Moulton, V. (2012). PAREsnip: a tool for rapid genome-wide discovery of small RNA/target interactions evidenced through degradome sequencing. *Nucleic acids research*, 40(13), e103-e103.
- Giurato, G., De Filippo, M. R., Rinaldi, A., Hashim, A., Nassa, G., Ravo, M., ... & Weisz, A. (2013). iMir: an integrated pipeline for high-throughput analysis of small non-coding RNA data obtained by smallRNA-Seq. *BMC bioinformatics*, 14(1), 362.

Module 10: Proteomics

- Deutsch, E. W., Mendoza, L., Shteynberg, D., Farrah, T., Lam, H., Tasman, N., ... & Eng, J. K. (2010). A guided tour of the Trans-Proteomic Pipeline. *Proteomics*, 10(6), 1150-1159.

Module 11: Microbiome experiment

- Fagen, J. R., Leonard, M. T., McCullough, C. M., Edirisinghe, J. N., Henry, C. S., Davis, M. J., & Triplett, E. W. (2014). Comparative genomics of cultured and uncultured strains suggests genes essential for free-living growth of *Liberibacter*. *PloS one*, 9(1), e84469.
- Leonard, M. T., Fagen, J. R., Davis-Richardson, A. G., Davis, M. J., & Triplett, E. W. (2012). Complete genome sequence of *Liberibacter crescens* BT-1. *Standards in genomic sciences*, 7(2), 271.

Grading Scale:

	<u>Percentage</u>
A	90 or above
A-	87-89
B+	84-86
B	80-83
B-	77-79
C+	74-76
C	70-73
C-	67-69

D+	64-66
D	60-63
D-	57-59
E	56 or below

For more information on grade points and UF grading policies, see <https://catalog.ufl.edu/ugrad/current/regulations/info/grades.aspx>

Assessment Breakdown Undergraduate students

Exams: Four proctored exams will be administered during the semester. Exams are worth 50% (12.5% each) of your grade. Specific details regarding the exam and proctoring will be given closer to the exam dates.

Quizzes: 7 quizzes will be worth 10%

Projects: Computer based microbiome analysis projects will be worth 40%

Assessment Breakdown Graduate students

Exams: Four proctored exams will be administered during the semester. Exams are worth 40% (10% each) of your grade. Specific details regarding the exam and proctoring will be given closer to the exam dates.

Quizzes: 7 quizzes will be worth 10%

Projects: Computer based microbiome analysis projects will be worth 40%

Research Paper: 10%

Tentative exam date/times:

Exam 1	Wednesday, February 8	5-10 PM
Exam 2	Wednesday, February 22	5-10 PM
Exam 3	Friday, March 29	5-10 PM
Exam 4	Thursday, April 27	5-10 PM

(Exam 4 if based on the draft of the paper written by the students.)

All exams are open for a 5h window but students have to complete the exam within 60 minutes.

Quizzes: Brief quizzes will be given that cover every two weeks of material. These short quizzes will be open for one week and need to be completed by **Friday evening BY 9 PM** of every other week. Following the lectures and taking these quizzes ensures timely participation and progress in the course. These quizzes are a *learning tool* so you may take each quiz up to **three times each** and only your last score of each week's quiz attempt will be recorded. Your quiz average will count for **10%** of your final grade. There will be a total of 7 quizzes (one for every two weeks of course material). You can drop your 2 lowest quiz scores. Your dropped quiz grades will include any quizzes you miss for **any** reason. This includes minor illness, travel, meetings, and **technical problems** etc. Rarely, technical issues may occur while you are taking the timed quiz, and any quizzes affected by

technical problems will count against your drops. A quiz will not be re-opened or reset if it is interrupted by technical difficulties. (NOTE: A slow Internet connection may affect timed quizzes, but it is your responsibility to use a connection at the speed suggested in the E-learning homepage.)

Plan to take each quiz and save up your dropped quizzes for unexpected events like illness or technical problems. Only quizzes that have been submitted by students can be accessed for studying for exams. Therefore, even if you choose to use a week as a drop and do not study, try to take the quiz anyway by the deadline so you can still access the quiz questions at later date. If you do not take a quiz during the open quiz window, then you are shut out of the quiz, and it cannot be reopened for you.

Following the close of each quiz and exam window, you have 10 calendar days to contest your quiz/exam grade in an email to me (i.e., a student cannot request a grade correction on quiz 2 during the last week of the course). Please note that you can ask a question about or discuss any quiz/exam question at any time during the semester for the purposes of understanding and education.

Make up and attendance policy: Please contact me directly regarding any serious illnesses, family emergencies, or prolonged absences that result in missed work.

Excused absences are consistent with university policies in the undergraduate catalog (<https://catalog.ufl.edu/ugrad/current/regulations/info/attendance.aspx>) and require appropriate documentation.

Course structure: The course is structured as 14 Lessons – one each week of the semester. Each week will cover a different topic. The topics build on each other so in order to understand a topic in week 6, for example, it is necessary that you understand the material from week 1. The first 4 weeks of the course lay the foundation for the remaining weeks.

Each week begins on Monday morning, which is the day by which a new week's worth of material will be posted. Every effort on my part will be made to post material prior to Mondays, but that may not always happen. Start by navigating to the Lessons page. Then, click on the appropriate week. For each week's lesson, there will be several items to complete. Click on the link for each item. The first item will be the **learning objectives** for the week. Keep the learning objectives in mind as you learn the week's material. If you meet the learning objectives, you should do very well on the quiz and the exams. After reading the learning objectives, please go through the week's material in the order presented. The next item in the list will usually be the reading assignment (a handout) followed by the lectures, and links to any online tutorials or modules. After you go through the material in the order presented, you are always free to return and visit any of the content. The introductory lecture will give an example of the types of course content and

how it will be presented. The pdf of the lecture slides will also be posted each week for your convenience. This convenience is for students who wish to print out the slides and follow along with the lecture, study the notes later, etc. The lectures slides will only be available in pdf format.

Each quiz will be based on the content of two weeks of material. The quiz window will be open for one week at the end of those two weeks and will close at **9 PM Friday** night every other week. If you only attempt a quiz once before 9 PM on Friday, that score is the one that will count for that week's quiz grade.

Academic Honesty: As a student at the University of Florida, you have committed yourself to uphold the Honor Code, which includes the following pledge: "We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honesty and integrity." You are expected to exhibit behavior consistent with this commitment to the UF academic community, and on all work submitted for credit at the University of Florida, the following pledge is either required or implied: "On my honor, I have neither given nor received unauthorized aid in doing this assignment."

It is your individual responsibility to know and comply with all university policies and procedures regarding academic integrity and the Student Honor Code. Violations of the Honor Code at the University of Florida will not be tolerated. Violations will be reported to the Dean of Students Office for consideration of disciplinary action. For more information regarding the Student Honor Code, please see: <http://www.dsoufl.edu/SCCR/honorcodes/honorcode.php>.

Software Use: All faculty, staff, and students of the University are required and expected to obey the laws and legal agreements governing software use. Failure to do so can lead to monetary damages and/or criminal penalties for the individual violator. Because such violations are also against University policies and rules, disciplinary action will be taken as appropriate.

Campus Helping Resources: Students experiencing crisis or personal problems that interfere with their general well being are encouraged to utilize the university's counseling resources. The Counseling & Wellness Center provides confidential counseling services at no cost for currently enrolled students. Resources are available on campus for students having personal problems or lacking clear career or academic goals, which interfere with their academic performance.

② *University Counseling & Wellness Center, 3190 Radio Road, 352-392-1575, www.counseling.ufl.edu/cwc/*

- Counseling Services
- Groups and Workshops
- Outreach and Consultation
- Self-Help Library

- Training Programs
- Community Provider Database

☒ *U Matter, We Care:* If you or a friend is in distress, please contact umatter@ufl.edu or 352-392-1575 so that a team member can reach out to the student.

☒ *Career Resource Center,* First Floor JWRU, 392-1601, www.crc.ufl.edu/

Students Requiring Accommodations: Students requesting class accommodation must first register with the Dean of Students Office. The Dean of Students Office will provide documentation to the student who must then provide this documentation to the Instructor when requesting accommodation.

The Disability Resource Center coordinates the needed accommodations of students with disabilities. This includes registering disabilities, recommending academic accommodations within the classroom, accessing special adaptive computer equipment, providing interpretation services and mediating faculty-student disability related issues. 0001 Reid Hall, 352-392-8565, www.dso.ufl.edu/drc/

Statement on Distance Education Courses

Should you have any complaints with your experience in this course, please visit <http://www.distance.ufl.edu/student-complaints>.

Course Evaluation

Students are expected to provide feedback on the quality of instruction in this course by completing online evaluations at <https://evaluations.ufl.edu>. Evaluations are typically open during the last two or three weeks of the semester, but students will be given specific times when they are open. Summary results of these assessments are available to students at <https://evaluations.ufl.edu/results/>.