



Course Syllabus

I. Course Information

3. January 18, 2016 - March 28, 2017 | Course Week runs from Wednesday to Tuesday.

4. Instructor's Name and Contact Information

- Alexandra Maertens, Ph.D.
- amaertens@brandeis.edu
- Office Hours/Availability - By Arrangement

Please send me an email to arrange a time to speak with me directly with questions or concerns or if you need help with the course material or assignments. You can also use the Private Forum in LATTE for any direct communications with me.

5. Document Overview

This syllabus contains all relevant information about the course: its objectives and outcomes, the grading criteria, the texts and other materials of instruction, and of weekly topics, outcomes, assignments, and due dates.

Consider this your roadmap for the course. Please read through the syllabus carefully and feel free to share any questions that you may have. Please print a copy of this syllabus for reference.

6. Course Description

Catalog Description and Course Outcomes

Microarrays are routinely used in genomic studies to detect changes in mRNA expression levels and have been key in developing biomarkers for several diseases. These experiments have fundamental statistical and data processing challenges associated with them. This course covers: the statistical aspects of experimental design, biological and technical replicates, preprocessing, quality assessment, parametric and non-parametric statistical tests, multiple-hypothesis testing, P-value correction and false discovery rates, visualization techniques (e.g. heatmaps, volcano plots), and biological significance (e.g. functional annotation, pathways, hypergeometric tests, gene set enrichment).

Upon completion of this course, students will be able to:

Course Outcomes:

1. Explain -omics technologies and biomarker study design;
2. Describe the different transcriptomic technologies and data availability;
3. Design a data workflow to use raw or processed transcriptomic data using R/Bioconductor;
4. Apply inferential, exploratory, and predictive statistical analysis of microarray data;
5. Apply functional annotation to transcriptomics data, understand the statistical procedures involved, and the limitations;
6. Perform network analysis of -omics technology using R and Cytoscape;
7. Create a data workflow for non-coding RNASeq data;
8. Identify microRNA biomarkers from microarrays and RNASeq data.

Welcome Note

Welcome to RBIFF 114! Over the next 10 weeks, we will walk through various data analysis techniques to find biomarkers in transcriptomic data, although the approaches and concepts are applicable to many types of data. We will survey several techniques ranging from the basic (t-test) to the more mathematically abstract (WGCNA). If you come from this class with a background in data mining, some of this will be new (for example, annotation-based analysis) but a lot should be familiar. If your background is in molecular biology, this is a great way to get started learning about some of the techniques to analyze Big Data!

Relevant Programs

Bioinformatics

Prerequisites

Programmers: Programming experience in any language

Non-programmers: Programming experience in R

Both programmers and non-programmers: Basic statistics and biology

7. Materials of Instruction

a. No required texts

b. Required Software and Other Supplies

- R/Bioconductor (latest version)
- Cytoscape v 3.02 or later
- R Studio (suggested, but not required)

c. Recommended Resources

- An excellent resource for bioinformatics and R questions in general: <https://www.biostars.org/>

d. Online Course Content

This course will be conducted completely online using Brandeis' LATTE site, available at <http://latte.brandeis.edu>. The site contains the course syllabus, assignments, discussion forums, links/resources to course-related professional organizations and sites, and weekly checklists, objectives, outcomes, topic notes, self-tests, and discussion questions. Access information is emailed to enrolled students before the start of the course.

To begin participating in the course, review the Welcome Message and the materials found in the Week 1 block.

8. Course Grading Criteria

Weighted Grading of Assignments	
Percent	Component
30%	Discussions/Online participation: 3% individual discussions (including original responses and replies)
40%	Assignments 1. Biomarkers (10%) 2. Microarray Data and Normalization (10%) 3. Data Analysis (10%) 4. Network Analysis (10%)
30%	Final Project -Microarray Data Analysis Project

Description of Assignments

1. Participation - Discussion Questions (30%, 3% per week)

Each week, students are required to post original responses to one or two discussion questions by Saturday (by 11:55pm in his/her time zone), and at least two substantive replies to the responses of others by Tuesday (by 11:55pm in his/her time zone).

Participation Evaluation Criteria:

Question Responses	60% of weekly participation grade	Max. Points per criteria
	Includes your own insights into the topics, sharing your professional experiences as appropriate and your own conclusions	16
	Includes references to weekly required readings and/or other external sources, cited appropriately. All original responses must draw on external references	16
	Answers the question posed completely; poses questions or points of consideration to elicit responses from classmates	16
	Consists of at least 250-300 words	6
	Well written , with no spelling or grammatical errors, and with the care normally exercised for the student's professional communications	6
<i>One day late: -15 out of 30 possible raw points; more than one day late: no credit</i>		
Discussion Replies	30% of Weekly Participation Grade	Max. Points per criteria

	Substantive (beyond an "I agree" or complimentary post) with: <ul style="list-style-type: none"> ○ Follow-on points from your related experiences and/or from the readings ○ Consists of at least 200 words ○ Follow-up questions of others to extend the conversation (encouraged, but not required) 	24
	Grammar/spelling/format/sources noted as appropriate	6
Posting Activity	10% of Participation Grade	Max. Points
	Post the minimum number of required posts on three or more days of the course week	
	Post the minimum number of required posts on two days of the course week (5 pts max)	10
	Post any number of posts on one day of the course week (1 pt max)	

Thoughts on Discussions

Keep in mind that these postings to the forums will be as rich as we make them; not having a traditional classroom in which to discuss topics, we can have some interesting discussions and share our experiences during the 10 weeks. They are required to encourage you to share your knowledge and ideas while gaining from the experiences of your peers as well. You will quickly adjust to the weekly requirements and become familiar with the review criteria, and I look forward to some rich discussions.

Also, part of your participation grade will be determined by asking good questions of either your instructor or fellow students - being inquisitive and willing to ask is part of being a good scientist.

2. Weekly Assignments

The assignments listed in the table above create the opportunity for students to begin to apply what they are learning in this course towards the analysis of microarray or RNASeq data. For the weekly assignments, you will be required to submit your own original data analysis. Please note that you may work collaboratively on trouble-shooting computer problems - in fact, you should - but the analysis should be your own.

All graded assignments will be evaluated on a 100 point scale, and will be weighted toward your final grade according to the Course Grading Criteria section above. Grading criteria unique to each assignment will be included where it is posted on the course page in LATTE.

3. Final Project

The final project required you to synthesize the knowledge and techniques that you learned over the course. Focus on originality and thoughtful data analysis rather than a lengthy write-up or a lot of graphs. Please make sure your final project is well-documented - what software you use, your data source, etc.

II. Weekly Information

Week 1	Introduction to -Omics Technologies for Biomarker Discovery
Learning Objectives	<ul style="list-style-type: none"> • Define a biomarker of disease, treatment, and exposure • Calculate sensitivity and specificity in biomarkers • Discuss how -omics technologies have aided in the discovery of biomarkers
Readings	<ul style="list-style-type: none"> • Topic Note One • Anderson D.C., Kodukula K. (2014) Biomarkers in pharmacology and drug discovery. <i>Biochemical Pharmacology</i> 87(1):172-88.
Discussions	<ul style="list-style-type: none"> • Introduce Yourself Forum • Private Forum • Week 1 Discussion: original responses no later than Saturday, replies no later than Tuesday
Assignments/ Assessments	<ul style="list-style-type: none"> • Academic Integrity Agreement: by Tues Week 1 • Biomarker Assignment Available

Week 2	Microarray Study Design, Data Quality, and Data Availability
Learning Objectives	<ul style="list-style-type: none"> • Differentiate between biological vs technical replicates • Calculate an appropriate sample size for a given biological question • Find and download publicly available microarray data and load into R • Document code
Readings	<ul style="list-style-type: none"> • Topic Notes • “DNA Microarrays: a Powerful Genomic Tool for Biomedical and Clinical Research,” in <i>Molecular Medicine</i> (V. Trevino, F. Falciani, H.A. Barrera-Saldana, 2007) • “Design of Microarray Experiments,” Genomics and Bioinformatics Group (discover.nci.nih.gov)
Discussions	<ul style="list-style-type: none"> • Week 2 Discussion: original responses no later than Saturday, replies no later than Tuesday
Assignments/ Assessments	<ul style="list-style-type: none"> • Biomarker Assignment Due • Begin Microarray Data and Normalization Assignment

Week 3	Microarray Data Preprocessing
Learning Objectives	<ul style="list-style-type: none"> • Explain sources of noise in microarray data and how to compensate • Perform normalization for Agilent and Affymetrix technologies using limma in R • Detect batch effects • Extract a normalized expression matrix
Readings	<ul style="list-style-type: none"> • Topic Notes • “How high is the level of technical noise in microarray data?” Biology Direct (L. Klebanov, A. Yakovlev, 2007)
Discussions	<ul style="list-style-type: none"> • Week 3 Discussion: original responses no later than Saturday, replies no later than Tuesday
Assignments/ Assessments	<ul style="list-style-type: none"> • Continue Microarray Assignment

Week 4	Inferential Statistics
Learning Objectives	<ul style="list-style-type: none"> • Calculate fold-change and p-value • Apply different methods of correction for multiple hypothesis testing • Compare t-test vs SAM
Readings	<ul style="list-style-type: none"> • Topic Notes • “Fold change and p-value cutoffs significantly alter microarray interpretations” BMC Bioinformatics (Dalman, Deeter, Nimishakavi, Duan, 2012)
Discussions	<ul style="list-style-type: none"> • Week 4 Discussion: original responses no later than Saturday, replies no later than Tuesday
Assignments/ Assessments	<ul style="list-style-type: none"> • Microarray Data and Normalization Due • Begin Microarray Data Analysis Assignment

Week 5	Exploratory Statistical Analysis/Predictive Statistical Analysis
Learning Objectives	<ul style="list-style-type: none"> • Explore a data set using Hierarchical Clustering and k-means clustering • Classify a dataset with Random Forest
Readings	<ul style="list-style-type: none"> • Topic Notes • “Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling” Nature (A. Alidazeh, etal., 2000)
Discussions	<ul style="list-style-type: none"> • Week 5 Discussion: original responses no later than Saturday, replies no later than Tuesday
Assignments/ Assessments	<ul style="list-style-type: none"> • Continue Microarray Data Analysis Assignment

Week 6	Genes in Context: Functional Analysis
Learning Objectives	<ul style="list-style-type: none"> • Find annotations for microarray platforms • Apply Overrepresentation Analysis • Perform Quantitative Enrichment Analysis
Readings	<ul style="list-style-type: none"> • Topic Notes • Timmons, James A., Krzysztof J. Szkop, and Iain J. Gallagher. "Multiple sources of bias confound functional enrichment analysis of global-omics data." Genome biology 16.1 (2015): 1-3.
Discussions	<ul style="list-style-type: none"> • Week 6 Discussion: original responses no later than Saturday, replies no later than Tuesday
Assignments/ Assessments	<ul style="list-style-type: none"> • Microarray Data Analysis Assignment due

Week 7	Network Analysis
Learning Objectives	<ul style="list-style-type: none"> • Derive a de novo network from microarray data using Weighted Gene Correlation Network method • Detect module significance using a permutation test
Readings	<ul style="list-style-type: none"> • Topic Notes • Horvath, S., et al. "Analysis of oncogenic signaling networks in glioblastoma identifies ASPM as a molecular target." <i>Proceedings of the National Academy of Sciences</i> 103.46 (2006): 17402-17407.
Discussions	<ul style="list-style-type: none"> • Week 7 Discussion: original responses no later than Saturday, replies no later than Tuesday
Assignments/ Assessments	<ul style="list-style-type: none"> • Begin Network Analysis Assignment

Week 8	Network Properties and Visualization
Learning Objectives	<ul style="list-style-type: none"> • Calculate network statistics • Visualize a network using Cytoscape or Vizant
Readings	<ul style="list-style-type: none"> • Topic Notes • Continue previous week's article
Discussions	<ul style="list-style-type: none"> • Week 8 Discussion: original responses no later than Saturday, replies no later than Tuesday
Assignments/ Assessments	<ul style="list-style-type: none"> • Network Analysis due

Week 9	Introduction to RNASeq
Learning Objectives	<ul style="list-style-type: none"> Describe how sequence by synthesis works. Using either an R pipeline or Galaxy, create a list of differentially expressed genes from RNASeq data.
Readings	<ul style="list-style-type: none"> Topic Notes Wang, Zhong, Mark Gerstein, and Michael Snyder. "RNA-Seq: A Revolutionary Tool for Transcriptomics." <i>Nature reviews. Genetics</i> 10.1 (2009): 57-63. PMC. Web. 6 Jan. 2016.
Discussions	<ul style="list-style-type: none"> Week 9 Discussion: original responses no later than Saturday, replies no later than Tuesday
Assignments/ Assessments	<ul style="list-style-type: none"> RNA-Seq workflow (part of participation grade) Final Project description available

Week 10	Network Properties and Visualization
Learning Objectives	<ul style="list-style-type: none"> Discuss the advantages and disadvantages of microRNA for biomarker discovery Analyze a noncoding RNA dataset Apply DIANA mirPATH to understand biological significance of microarray
Readings	<ul style="list-style-type: none"> Topic Notes Etheridge, Alton, et al. "Extracellular microRNA: a new source of biomarkers." <i>Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis</i> 717.1 (2011): 85-90. Meyer, Swanhild U., Michael W. Pfaffl, and Susanne E. Ulbrich. "Normalization strategies for microRNA profiling experiments: a 'normal' way to a hidden layer of complexity?." <i>Biotechnology letters</i> 32.12 (2010): 1777-1788.
Discussions	<ul style="list-style-type: none"> Week 10 Discussion: original responses no later than Saturday, replies no later than Tuesday
Assignments/ Assessments	<ul style="list-style-type: none"> Final Project Due

III. Course Policies and Procedures

1. Late Policies

If you have an illness or other major life event and need an extension, please contact the instructor as soon as possible. You are allowed a one-time late day for any one assignment without penalty. After that, you will lose 5 percent of your grade per day

2. Grading Standards

Students are responsible to explore each week's materials and submit required work by their due dates. On average, a student can expect to spend approximately 3-5 hours per week reading and approximately 5-8 hours per week completing assignments and posting to discussions. The calendar of assignments and due dates is located at the end of this syllabus, and all assignments are due by the close

100-94	A	76-73	C
93-90	A-	72-70	C-
89-87	B+	69-67	D+
86-83	B	66-63	D
82-80	B-	62-60	D-
79-77	C+	59 or <	F

3. Feedback

Feedback will be provided on all assignments within one week.

4. Confidentiality

We can draw on the wealth of examples from our organizations in class discussions and in our written work. However, it is imperative that we not share information that is confidential, privileged, or proprietary in nature. We must be mindful of any contracts we have agreed to with our companies. In addition, we should respect our fellow classmates and work under the assumption that what is discussed here (as it pertains to the workings of particular organizations) stays within the confines of the classroom.

For your awareness, members of the University's technical staff have access to all course sites to aid in course setup and technical troubleshooting. Program Chairs and a small number of Graduate Professional Studies (GPS) staff have access to all GPS courses for oversight purposes. Students enrolled in GPS courses can expect that individuals other than their fellow classmates and the course instructor(s) may visit their course for various purposes. Their intentions are to aid in technical troubleshooting and to ensure that quality course delivery standards are met. Strict confidentiality of student information is maintained.

5. Calendar of Class Dates and Assignment Schedule

Week	Weekly Start/End Dates Wednesday - Tuesday	Assignments (listed in weeks when available)	Due
1	January 20-26	1 - Biomarkers	Tuesday, Week 2
2	January 27-February 2	1 - Biomarkers 2 - Microarray Data and Normalization	Tuesday, Week 2 Tuesday, Week 4
3	February 3-9	2 - Microarray Data and Normalization	Tuesday, Week 4
4	February 10-16	2 - Microarray Data and Normalization 3 - Microarray Data Analysis	Tuesday, Week 4 Tuesday, Week 6
5	February 17-23	3 - Microarray Data Analysis	Tuesday, Week 6
6	February 24-March 1	3 - Microarray Data Analysis	Tuesday, Week 6
7	March 2-8	4 - Network Analysis Assignment	Tuesday, Week 8
8	March 9-15	4 - Network Analysis Assignment	Tuesday, Week 8
9	March 16-22	Final Project	Tuesday, Week 10
10	March 23-29	Final Project	Tuesday, Week 10

IV. University and Division of Graduate Professional Studies Standards

Please review the policies and procedures of Graduate Professional Studies, found at <http://www.brandeis.edu/gps/current-students/academic-information/student-handbook.html>. We would like to highlight the following.

Learning Disabilities

If you are a student who needs accommodations because of a documented disability, you may present your letter of accommodation from the Rabb School Disability Coordinator to me, as soon as possible and ideally before the course begins. If you have questions about documenting a disability or requesting academic accommodation you should contact the Rabb School Disabilities Coordinator directly (781-736-8787)

Academic Honesty and Student Integrity

Academic honesty and student integrity are of fundamental importance at Brandeis University and we want students to understand this clearly at the start of the term. As stated in the Brandeis Rights and Responsibilities handbook, "Every member of the University Community is expected to maintain the highest standards of academic honesty. A student shall not receive credit for work that is not the product of the student's own effort. A student's name on any written exercise constitutes a statement that the work is the result of the student's own thought and study, stated in the student's own words, and produced without the assistance of others, except in quotes, footnotes or references with appropriate acknowledgement of the source." In particular, students must be aware that material (including ideas, phrases, sentences, etc.) taken from the Internet and other sources MUST be appropriately cited if quoted, and footnoted in any written work turned in for this, or any, Brandeis class. Also, students will not be allowed to collaborate on work except by the specific permission of the instructor. Failure to cite resources properly may result in a referral being made to the Office of Student Development and Judicial Education. The outcome of this action may involve academic and disciplinary sanctions, which could include (but are not limited to) such penalties as receiving no credit for the assignment in question, receiving no credit for the related course, or suspension or dismissal from the University.

Students may be required to submit work to TurnItIn.com software to verify originality. TurnItIn is a tool that compares student assignment submissions to internet sources and a comprehensive database of other papers. It creates a report that provide a link to possible matches and a "similarity score". TurnItIn does not determine whether a paper has been plagiarized; individual faculty will make that judgment. All papers submitted to TurnItIn are kept in a separate reference database of Brandeis work, to be used solely for the purpose of detecting plagiarism in the future. Students retain copyright on their original course work. Allegations of alleged academic dishonesty will be forwarded to the Director of Academic Integrity. Sanctions for academic dishonesty can include failing grades and/or suspension from the university. Citation and research assistance can be found at [LTS - Library guides](#)

Further information regarding academic integrity may be found in the following publications: "In Pursuit of Excellence - A Guide to Academic Integrity for the Brandeis Community", "(Students') Rights and Responsibilities Handbook", AND " Graduate Professional Studies Student Handbook". You should read these publications, which all can be accessed from the Graduate Professional Studies Web site. A student that is in doubt about standards of academic honesty (regarding plagiarism, multiple submissions of written work, unacknowledged or unauthorized collaborative effort, false citation or false data) should consult either the course instructor or other staff of the Rabb School Graduate Professional Studies.

University Caveat

The above schedule, content, and procedures in this course are subject to change in the event of extenuating circumstances.