

# BIostatISTICS (BIOS)

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## **BIOS 512. Basic Mathematical Statistics. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. The course builds the basics of probability theory and applications of probability theory toward statistical inference. Students will learn about the mathematical paradigm behind most statistical inference used in basic data analysis, estimation and hypothesis testing.

## **BIOS 513. Mathematical Statistics I. 3 Hours.**

Continuous course; 3 lecture hours. 3 credits. Prerequisite: MATH 307. Probability, random variables and their properties, distributions, moment generating functions, limit theorems, estimators and their properties; Neyman-Pearson and likelihood ratio criteria for testing hypotheses. Crosslisted as: STAT 513.

## **BIOS 514. Mathematical Statistics II. 3 Hours.**

Continuous course; 3 lecture hours. 3 credits. Prerequisite: STAT 513/BIOS 513. Probability, random variables and their properties, distributions, moment generating functions, limit theorems, estimators and their properties; Neyman-Pearson and likelihood ratio criteria for testing hypotheses. Crosslisted as: STAT 514.

## **BIOS 516. Biostatistical Consulting. 1 Hour.**

Semester course; 1 lecture hour. 1 credit. The principles dealing with the basic art and concepts of consulting in biostatistics. The nonstatistical course discusses role, responsibilities of biostatisticians, relationship between clients and consultants, method of writing reports, etc.

## **BIOS 524. Biostatistical Computing. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Techniques for biostatistical computing are presented by way of contemporary statistical packages. Students learn how to create and manage computer data files. Methods for data entry, preparation of data for analysis and summaritive procedures are covered. Students learn the basics of random number generation and its applications, numerical methods for statistical algorithms, and concepts of numerical accuracy and stability. Advanced topics include interactive matrix and macro languages. Emphasis is placed on computational methods and data management rather than on statistical methods and procedures.

## **BIOS 531. Clinical Epidemiology. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. This course is intended primarily for clinicians. Permission of the course coordinator is required for others interested in registering. Epidemiological concepts necessary for evidence based studies of medicine. Specific topics will include: cause and effect criteria, demographic rates, measures of association or effect, study designs, decision trees, meta-analysis, evaluation of the literature, sources of data, reliability and validity, bias, confounding and effect modification, screening and diagnostic tests, sensitivity, specificity, false positives, false negatives, applications of the above to diagnosis and treatment, treatment efficacy and improved patient care.

## **BIOS 543. Graduate Research Methods I. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Enrollment is restricted to students with graduate standing, or one course in statistics and permission of instructor. This course is intended for graduate students and researchers without formal training in the statistical and biostatistical sciences. Students enrolled in this course will study various aspects of the research process, from creating the research question to publication. Particularly, students will learn sampling theory, the roles of probability, chance and variability in measurement and decision-making, study design characteristics and validity, basic data management, visualization and summarization, simple techniques for analyzing categorical data (e.g., chi-square test, exact tests), common techniques for analyzing continuous data (t-tests, analysis of variance, correlation and simple linear regression), and statistical decision-making. These topics will be covered through a variety of approaches, including traditional lecture, group discussion and in-class activities, and students will be assessed on their ability to understand statistical considerations in the study design process, appropriately perform simple statistical procedures and report statistical findings using the IMRaD format. The appropriate use of data management and statistical procedures will be modeled using several commonly used software packages. Students may receive degree credit for only one of BIOS 543, STAT 441, STAT 541, STAT 543 or STAT 641. BIOS 543 is not applicable toward the M.S. degree in mathematical sciences or the M.S. degree in computer science.

## **BIOS 544. Graduate Research Methods II. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisite: BIOS 543 or STAT 543 or permission of instructor. This course is intended for graduate students and researchers without formal training in the statistical and biostatistical sciences. Students enrolled in this course will study various aspects of statistical model-building, including adjusting estimates for other measurements, creating multivariate models, analyzing noncontinuous outcomes and summarizing results. Particularly, students will learn multiple linear regression, multifactor analysis of variance, analysis of covariance, random and mixed effects models, repeated measure and longitudinal data analysis, logistic and Poisson regressions, and time-to-event analysis. These topics will be covered through a variety of approaches, including traditional lecture, group discussion and in-class activities, and students will be assessed on their ability to understand statistical considerations in the model-building process, appropriately perform intermediate statistical procedures and report statistical findings using the IMRaD format. The appropriate use of data management and statistical procedures will be modeled using several commonly used software packages. Students may receive degree credit for only one of BIOS 544 or STAT 544.

## **BIOS 546. Theory of Linear Models. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisites: BIOS 513 and BIOS 553. Review of linear algebraic concepts and matrix operations. Topics include generalized inverses and systems of equations; distribution of quadratic forms under normal theory; general linear model of full rank and less-than-full rank; least squares and maximum likelihood estimation; hypothesis testing; multiple linear regression; analysis of variance; balanced and unbalanced design.

**BIOS 547. Applied Data Analysis in Public Health I. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Corequisite: EPID 547. This course is the first in a two-semester sequence in biostatistical methods for students in the Master of Public Health program. Basic probabilistic and statistical concepts will be introduced, such as probability theory and distributions, hypothesis testing, and sampling methodology. The course will also focus in detail on commonly used statistical methods for categorical and continuous measurements, including chi-square tests, t-tests, ANOVA and regression. The material will be motivated by data sets from public health studies.

**BIOS 548. Applied Data Analysis in Public Health II. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Corequisite: EPID 548. This course is the second in a two-semester sequence in biostatistical methods for students in the Master of Public Health program. Advanced statistical methods commonly used in public health research will be covered, including ANOVA, multiple linear regression, ANCOVA, mixed effects models, repeated measure designs, logistic regression and survival analysis. The material will be motivated by data sets from public health studies.

**BIOS 549. Spatial Data Analysis. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisites: BIOS 543 and BIOS 544 or permission of instructor. Introduces students to spatial data and the statistical methods to appropriately analyze them. Covers spatial data visualization and manipulation, spatial point pattern analysis, interpolation and geostatistics for point-referenced data, and spatial regression modeling of areal data. Includes the use of a statistical software package for data analysis.

**BIOS 553. Biostatistical Methods I. 4 Hours.**

Semester course; 4 lecture hours. 4 credits. Prerequisites: one course in statistics and permission of instructor. Introduces applied biostatistical concepts intended primarily for graduate students in the Department of Biostatistics. Topics include linear algebra for statistical algorithms, distributions of quadratic forms, simple and multiple linear regression, model selection and regression diagnostics, analysis of variance and covariance, and linear mixed effects models.

**BIOS 554. Biostatistical Methods II. 4 Hours.**

Semester course; 4 lecture hours. 4 credits. Prerequisite: BIOS 553. Continued study of applied biostatistical concepts intended primarily for graduate students in the Department of Biostatistics. Topics include categorical data analysis, generalized linear models, generalized linear mixed models, generalized additive models, non-linear regression and survival analysis.

**BIOS 567. Statistical Methods for High-throughput Genomics Data I. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisites: BIOS 524 and 546; and BIOS 544 or 554; or permission of instructor. Provides a detailed overview of all aspects pertaining to the preprocessing and analysis of data from high-throughput genomic experiments, such as normalization techniques, expression summaries, quality control assessments and data reduction methods. Presents strategies for class and identification of important molecular features. Includes hands-on experience using statistical software for processing and analyzing genomic data.

**BIOS 571. Clinical Trials. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Concepts of data management and statistical design and analysis in single-center and multicenter clinical trials. Data management topics include the collection, edition, and validation of data. Statistical design topics include randomization, stratification, blinding, placebo- and active-control groups, parallel and crossover designs, and power and sample size calculations. Statistical analysis topics include sequential and group sequential methods.

**BIOS 572. Analysis of Biomedical Data I. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisites: one course in statistics and permission of instructor. This course provides an overview of the analysis of continuous response data. The material begins with a brief review of theoretical tools used in inference and segues into common univariate and bivariate statistical methodologies for the analysis of continuous response data. Model-based statistical methodologies including linear regression, ANOVA, ANCOVA and mixed-effect models will also be covered. Practical consideration and usage of statistical methods, utilizing commonly used statistical software packages, will be emphasized over theoretical underpinnings of the methods.

**BIOS 573. Analysis of Biomedical Data II. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisite: BIOS 572. This course provides an overview of the analysis of categorical data. The course begins with a brief review of commonly used probability distributions for binary, ordinal, count and time-to-event measurements, then segues into chi-square and tabular testing. Model-based statistical methods including logistic regression, Poisson regression, log-linear modeling and survival analysis will be covered. Practical consideration and usage of statistical methods, utilizing commonly used software packages, will be emphasized over the theoretical underpinnings of the methods.

**BIOS 610. Research Processes and Methods for the Health Professions. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisite: BIOS 531 or permission of instructor. Focus on research processes, methods and research proposal (R01) writing for the health professions. Course will emphasize conceptual underpinnings of research; the continuum of methodologies, including qualitative data collection; and development of a relevant research question – all toward writing a fundable proposal. Topics include framing a relevant research question, writing a problem statements and aims, synthesizing and critiquing relevant literature, project management, developing project budget and justification, as well as critically reviewing grants and serving on a mock study section.

**BIOS 615. Advanced Inference. 4 Hours.**

Semester course; 4 lecture hours. 4 credits. Prerequisite: BIOS/STAT 513, BIOS/STAT 514 or permission of instructor. Mathematical preliminaries: probability and expectation, modes of convergence, delta method, statistical limit theorems; ARE; asymptotic likelihood-based procedures. Decision theoretical approach to statistical inference; decision rules; admissibility. Bayes procedures. Point estimation; unbiasedness; efficiency. Hypothesis testing: the Neyman-Pearson theory; unbiasedness and invariant tests; conditional tests; likelihood-based tests. Nonparametric statistics: U statistics, rank-based tests, permutation test. Interval estimation; confidence sets; relationship between confidence sets and families of tests. Algorithms in statistical computation: EM algorithm, Newton Raphson method. Modern methods for controlling false discovery rate.

**BIOS 616. Advanced Inference. 4 Hours.**

Continuous courses; 4 lecture hours. 4 credits. Prerequisite: BIOS 514 or permission of instructor. Mathematical preliminaries: probability and measure; integration; modes of convergence. Decision theoretical approach to statistical inference; decision rules; admissibility. Bayes and minimax procedures, invariance; complete classes. Point estimation; unbiasedness; efficiency; M, L, and R estimators; U statistics. Hypothesis testing: the Neyman-Pearson theory; unbiasedness and invariant tests; conditional tests; permutation tests; rank tests; likelihood based tests. Interval estimation; confidence sets; relationship between confidence sets and families of tests; unbiased and invariant confidence sets. Asymptotics; stochastic convergence; statistical limit theorems; ARE; asymptotic likelihood based procedures. Overview of robust statistical procedures.

**BIOS 621. Nonparametric Statistical Methods. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisites: any two courses of statistics or permission of instructor. Estimation and hypothesis testing when the form of the underlying distribution is unknown. One-, two- and k-sample problems. Tests of randomness, Kolmogorov-Smirnov tests, analysis of contingency tables and coefficients of association. Crosslisted as: STAT 621.

**BIOS 625. Categorical Data Analysis and Generalized Linear Models. 4 Hours.**

Semester course; 4 lecture hours. 4 credits. Prerequisites: BIOS 514, 554 and 572. Introduction to the theory and methods of analysis of categorical data. Topics include exact and asymptotic analysis of contingency tables; measures of association and agreement; theory and applications of generalized linear models, maximum likelihood estimation and related numerical methods; linear models with different link functions and distributions; model fitting; and diagnostics.

**BIOS 631. Mixed Models and Longitudinal Data Analysis. 4 Hours.**

Semester course; 4 lecture hours. 4 credits. Prerequisites: BIOS/STAT 514, 546 and 554. Introduction to longitudinal data structures and statistical inference. Multivariate theory and applications of normal mixed models, generalized linear mixed models, mixed models for categorical data, nonlinear mixed models and multiple imputation methods for missing data.

**BIOS 632. Multivariate Analysis. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisites: BIOS/STAT 514 and 554. One- and two-sample multivariate tests; invariance: MANOVA, MANCOVA and multiple design models; nonparametric methods; inference with covariance matrices; principal components; factor analysis; discriminate analysis; clustering.

**BIOS 635. Structural Equation Modeling. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisites: two graduate-level statistics courses or permission of instructor. This course provides an overview of the principals and applications of the general statistical framework structural equation modeling. The course provides an introduction to the concepts, methods, problems and applications of SEM. Topics covered include the modeling of observed variables, consequences of measurement error, modeling of latent variables and longitudinal structural equation models.

**BIOS 638. Statistical Design and Analysis in Toxicology. 3 Hours.**

Continuous courses; 3 lecture hours. 3-3 credits. Prerequisites for BIOS students: BIOS 514 and 554. Prerequisite for non-biostatistics students (who can enroll on a Pass/Fail basis): BIOS 554. Classical bioassay, dose-response relationships, continuous and quantal data; probit and logit analysis; estimation of the ED50; combination experiments; low dose extrapolation and risk assessment; carcinogenicity, mutagenicity, and teratogenicity screening; overview of laboratory and experimental problems for the toxicologist. Non-biostatistics students may enroll on a pass/fail basis.

**BIOS 639. Statistical Design and Analysis in Toxicology. 3 Hours.**

Continuous courses; 3 lecture hours. 3-3 credits. Prerequisites for BIOS students: BIOS 514 and 554. Prerequisite for non-biostatistics students (who can enroll on a Pass/Fail basis): BIOS 554. Classical bioassay, dose-response relationships, continuous and quantal data; probit and logit analysis; estimation of the ED50; combination experiments; low dose extrapolation and risk assessment; carcinogenicity, mutagenicity, and teratogenicity screening; overview of laboratory and experimental problems for the toxicologist. Non-biostatistics students may enroll on a pass/fail basis.

**BIOS 647. Survival Analysis. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisites: BIOS 514 and 554 or permission of instructor. The analysis of survival (or failure time) data, with/without censoring. Actuarial and life-table methods, nonparametric and parametric estimation of survival functions, and comparison of survival curves; regression methods, such as the Cox proportional hazards model; competing risks; sequential models; applications to clinical trials.

**BIOS 649. Advanced Spatial Data Analysis. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisites: BIOS 543, BIOS 544, BIOS 549 or permission of instructor. This course focuses on the development and application of advanced statistical models for spatial and spatial-temporal data in a Bayesian hierarchical modeling framework. The data considered in this course include spatially referenced normal, binary, count and time-to-event health outcomes. Statistical methods covered include linear and Poisson regression, spatial survival analysis, spatial longitudinal analysis, multivariate disease modeling and spatio-temporal disease mapping. Students will gain practical experience in the application of the methods in commonly used software packages.

**BIOS 650. Design and Analysis of Response Surface Experiments. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Enrollment restricted to students with graduate status in mathematical sciences or systems modeling and analysis, or permission of the instructor. Philosophy, terminology and nomenclature for response surface methodology, analysis in the vicinity of the stationary point, canonical analysis, description of the response surface, rotatability, uniform information designs, central composite designs and design optimality. Crosslisted as: STAT 650.

**BIOS 660. Sequential Analysis and Advanced Design and Analysis of Clinical Trials. 3 Hours.**

3 lecture hours. 3 credits. Prerequisites: BIOS 514 and 554. Sequential methods versus fixed sample methods; the sequential probability ratio test with extensions and modifications; some applications of Cox's theorem; overview of analysis of clinical trials; closed and truncated tests; group sequential tests in clinical trials; sequential monitoring; sequential estimation; other topics with emphasis in clinical trials.

**BIOS 667. Statistical Learning and Data Mining. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisites: BIOS 514, 524 and 554. Provides a detailed overview of statistical methods used to discover the underlying structure of large complex datasets. Specific topics will include discrimination analysis, k-nearest neighbors, naive Bayes classifiers, classification and regression trees, ensemble methods, random forests, L1 penalized models, bootstrap and cross-validation methods. The course includes hands-on experience using statistical software for each method.

**BIOS 668. Statistical Methods for High-throughput Genomic Data II. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisite: BIOS 567. A continuation of BIOS 567 that will introduce methods of additional high-throughput genomic assays, including comparative genomic hybridization for copy number change analysis and next generation sequencing methods. Methods that will be addressed include issues in mapping reads, variability in representation of sequences, normalization of raw count data, ChIP-Seq analysis, and RNA-Seq analysis.

**BIOS 671. Nonlinear Models. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Prerequisite: BIOS 554. Nonlinear modeling is an important tool for biostatisticians working with clinical and pre-clinical applications of dose responsiveness. Addresses issues regarding estimation, inference and experimental designs associated with nonlinear models. Special attention is paid to sigmoid-shaped models and threshold or piecewise models. Both the generalized nonlinear least-squares and quasi-likelihood estimation criteria are developed for these models. In addition to the usual univariate data structure, nonlinear mixed models are described and illustrated with examples. Includes hands-on experience with available SAS software for data analyses.

**BIOS 688. Applied Bayesian Biostatistics. 3 Hours.**

Semester course; 3 lecture hours. 3 credits. Introduces the basic paradigm of Bayesian statistics along with the tools toward application of the methods in various data analysis situations. Covers Bayesian point estimation, interval estimation and model selection in univariate and multiparameter cases. Both conjugate and nonconjugate problems will be discussed. Modern Bayesian computation tools, such as rejection sampling, importance sampling, Gibbs sampling and Metropolis-Hastings algorithm, will be introduced with details of applied examples. A first introduction to Bayesian nonparametrics will also be done.

**BIOS 690. Biostatistical Research Seminar. 1 Hour.**

Semester course; 1 lecture hour. 1 credit. Talks by the students, faculty, and visitors describing recent research or reviewing topics of mutual interest.

**BIOS 691. Special Topics in Biostatistics. 1-4 Hours.**

Semester course; lecture and laboratory hours by arrangement. 1-4 credits. Lectures, tutorial studies, library assignments in selected areas of advanced study or specialized biostatistical procedures not available in other courses or as part of the research training.

**BIOS 692. Special Topics. 1-3 Hours.**

Semester course; 1-3 variable hours. 1-3 credits. Lectures, tutorials, library assignments in selected areas not available in other courses or as part of the research training. Graded as S/U/F.

**BIOS 697. Directed Research in Biostatistics. 1-15 Hours.**

Semester course; 1-15 credits. Research leading to the M.S. or Ph.D. degree and elective research projects for other students.