**Course Director:**  Dr. Barry Grant (DCM&B, bjgrant@med.umich.edu)

**Description:**  BIOINF524 is a three credit three module course covering (1) *Foundations of Bioinformatics*, (2) *Statistics in Bioinformatics*, and (3) *Systems Biology*.  BIOINF525 allows for each one credit module to be registered for separately.

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| **Module 1**: | January 10 – February 2 | (four lectures and four labs). |
| **Module 2**: | February 7 – March 16 | (five lectures and five labs). |
| **Module 3**: | March 21 – April 13 | (four lectures and four labs). |

**Schedule:**

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| **Lectures**: | Tuesdays 2:30 - 4:00 PM, Rm. 2062 Palmer Commons Bldg. |
| **Labs**: | Thursdays 2:30 - 4:00 PM, Rm. 2062 Palmer Commons Bldg. |

**Prerequisites**: A familiarity with basic biomedical concepts and basic knowledge of computer usage.  No programing skills are needed.  You MUST bring your own wifi enabled laptop to lectures and labs to fully participate in this class.

**Grading**: Satisfactory/unsatisfactory grading will be based on a combination of lecture and lab involvement together with weekly homework and quiz assignment performance.

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**Module 1** (1 credit)**:   Foundations of Bioinformatics**
**Module 1 Director:**   Dr. Barry Grant (DCM&B, bjgrant@med.umich.edu)

Bioinformatics is driving the collection, analysis and interpretation of big data for biomedicine and the biosciences.  This module provides an introduction to practical issues of computer-based handling and interpretation of biomolecular and genomic datasets.  We specifically target bioinformatics software and data resources freely available on the Internet.

**Lecture (1-1)**: *Introduction to bioinformatics*
**Instructor:**   **Dr. Barry Grant**
**Time:**          Jan 10 (Tuesday), 2:30 - 4:00 PM
**Topics:**
What are bioinformatics and computational biology?  Major NCBI and EBI bioinformatics resources.  How do we actually do bioinformatics?  Major areas of research and application.

**Lab (1-1)**:     **Bioinformatics databases and major online resources**
**Instructor:**   **Dr. Barry Grant**
**Time:**          Jan 12 (Thursday), 2:30 – 4:00 PM
**Topics:**
The purpose of this lab session is to introduce a range of core bioinformatics databases and associated online services whilst investigating the molecular basis of several common human disease.

**Lecture (1-2):** *Sequence alignment and database searching*
**Instructor:** **Dr. Barry Grant**
**Time:** Jan 17 (Tuesday), 2:30 - 4:00 PM
**Topics:**
Homology and sequence alignments, Dynamic programming, Sequence similarity and database searching, Interpreting search results – E value, Needleman and Wunsch, Smith and Waterman, The BLAST algorithm.

**Lab (1-2):** **Sequence alignment algorithms and applications**
**Instructor:** **Dr. Barry Grant**
**Time:** Jan 19 (Thursday), 2:30 – 4:00 PM,
**Topics:**
Aligning novel sequences with previously characterized genes or proteins provides important insights into their common attributes and evolutionary origins. In this lab session we will explore the principles underlying the computational tools that can be used to compute and evaluate sequence alignments.

**Lecture (1-3):** *Structural bioinformatics*
**Instructor:** **Dr. Barry Grant**
**Time:** Jan 24 (Tuesday), 2:30 - 4:00 PM
**Topics:**
Major goals, current research challenges, and application areas of structural bioinformatics. Key concepts covered include: Sequence-structure-function relationships; Energy landscapes; Physics and knowledge based modeling approaches for describing the structure, energetics and dynamics of biomolecules computationally.

**Lab (1-3):** **Protein structure visualization, analysis and small molecule docking**
**Instructor:** **Dr. Barry Grant**
**Time:** Jan 26 (Thursday), 2:30 - 4:00 PM
**Topics:**
The RCSB PDB resource.  Interactive biomolecular structure visualization with VMD.  Structural analysis of protein families and prediction of protein flexibility with Bio3D.  *In silico* docking and virtual screening strategies for drug design.

**Lecture (1-4):** *Genome informatics*
**Instructor:** **Dr. Ryan Mills**
**Time:** Jan 31 (Tuesday), 2:30 - 4:00 PM
**Topics:**
High throughput sequencing technologies, biological applications and bioinformatics analysis methods.  Web interfaces to genome databases at Ensembl and UCSC.

**Lab (1-4):** **Web resources for analyzing genomic data**
**Instructor:** **Drs. Ryan Mills and Barry Grant**
**Time:** Feb 2 (Thursday), 2:30 - 4:00 PM
**Topics:**
The Galaxy web-based platform for genomic data analysis. Manipulation and analysis of next generation sequencing data sets.

**Module 2** (1 credit):   <u>**Introduction to Statistics in Bioinformatics**</u>
**Module 2 Director**:   Dr. Niko Kaciroti (Biostatistics, nicola@umich.edu)

Basic statistics as used in bioinformatics, especially standard statistical tests of significance and when they apply. Applications to genetics, experimental and observational medical data, as well as exploration of multiple testing issues that arise in bioinformatics and other experimental settings. NOTE: Dr. Kaciroti is the instructor for all Module 2 lectures and labs.

**Lecture (2-1)**: *Framework for statistical analysis of biomedical data*
**Time:**          Feb 7 (Tuesday), 2:30 - 4:00 PM
**Topics:**
Probability distributions, quantifying central values and variability, quantifying association, graphical displays of data

**Lab (2-1)**:      **Descriptive statistics and summarizing data**
**Time:**          Feb 9 (Thursday), 2:30 - 4:00 PM
**Topics:**
Probability distributions, quantifying central values and variability, quantifying association, graphical displays of data

**Lecture (2-2)**: *Approaches to statistical estimation and testing*
**Time:**          Feb 14 (Tuesday), 2:30 - 4:00 PM
**Topics:**
Estimation and standard errors, standard errors for means, correlations, and log odds ratios, formal hypothesis testing, tests involving means, correlations, and log odds ratios, power.

**Lab (2-2)**:      **Statistical estimation and hypothesis testing**
**Time:**          Feb 16 (Thursday), 2:30 - 4:00 PM
**Topics:**
Estimation and standard errors, standard errors for means, correlations, and log odds ratios, formal hypothesis testing, one and two sample tests involving means, power.

**Lecture (2-3)**: *Analyses involving associations*
**Time:**          Feb 21 (Tuesday), 2:30 - 4:00 PM
**Topics:**
Pearson correlation, t-test, odds ratios, discussion of a research article

**Lab (2-3)**:      **Pearson correlation, t-test, and log odds ratios**
**Time:**          Feb 23 (Thursday), 2:30 - 4:00 PM
**Topics:**
Tests based on Pearson correlation t-test, and log odds ratios

**Lecture (2-4)**: *Linear regression*
**Time:**          Mar 7 (Tuesday), 2:30 - 4:00 PM
**Topics:**
Single and multiple variable linear regression, Bonferroni correction, power for regression analysis

**Lab (2-4):**      **Regression models**
**Time:**        Mar 9 (Thursday), 2:30 - 4:00 PM
**Topics:**
Fitting regression models for prediction and effect estimation, inference for regression effects, $R^2$, diagnostics, comparing models


**Lecture (2-5):** *Introduction to graphical methods for multivariate data analysis*
**Time:**        Mar 14 (Tuesday), 2:30 - 4:00 PM
**Topics:**
Clustering methods, Multidimensional scaling and Principal component analysis

**Lab (2-5):**      **Clustering and principal component analysis**
**Time:**        Mar 16 (Thursday), 2:30 - 4:00 PM
**Topics:**
Multivariate data, Heat maps and dendrograms, clustering methods, principal component analysis

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**Module 3** (1 credit):    **Bioinformatics and Systems Biology**
**Module 3 Director**:    Dr. Peter Freddolino (Biological Chemistry,  petefred@umich.edu)

Computational analysis of OMICs data (genomics, transcriptomics, proteomics).  Analysis of protein-protein interactions and gene expression data. Pathways and networks, machine learning. Example applications from translational medicine and cell biology.


**Lecture (3-1):** *Introduction to systems biology*
**Instructor:**    **Dr. Gerry Higgins**
**Time:**        Mar 21 (Tuesday), 2:30 - 4:00 PM

**Lab (3-1):**      **Network analysis for systems biology**
**Instructors:**  **Marci Brandenburg and Dr. Viji Nair**
**Time:**        Mar 23 (Thursday), 2:30 - 4:00 PM
**Topics:**
Representation of data as graphs.  Pathway and network exploration and visualization with Cytoscape, including the MetScape app, in addition to ConceptGen.


**Lecture (3-2):** *Computational approaches to clinical decision support systems*
**Instructor:**    **Dr. Kayvan Najarian**
**Time:**        Mar 28 (Tuesday), 2:30 - 4:00 PM
**Topics:**
Introduction to computational clinical decision support systems. Machine learning and its application to biomedical informatics.

**Lab (3-2):**      **WEKA for machine learning and feature analysis**
**Instructors:**  **Dr. Kayvan Najarian**
**Time:**        Mar 30 (Thursday), 2:30 - 4:00 PM

**Topics:**
Introduction to WEKA, using machine learning methods such as SVM, Random Forest, Neural Networks for simple examples in systems biology, using WEKA for feature extraction and analysis.

**Lecture (3-3):** *Epigenome data mining to understand disease predisposition*
**Instructor:** Dr. Steven Parker
**Time:** Apr 4 (Tuesday), 2:30 - 4:00 PM
**Topics:**
For decades, substantial research efforts have focused on the <2% of the human genome that encodes proteins. Recent epigenome-based functional genomic analyses and genome-wide association studies (GWAS) together implicate non-coding DNA regulatory elements as critical regions influencing gene expression, risk for common diseases, variation in physiological traits, and evolution across species. Because they represent the convergent point of evolutionary, genetic, developmental, and environmental inputs, basal epigenomic signatures and their dynamic changes are central to understanding biological function. This lecture will explore epigenomic assays and bioinformatic analyses and how these approaches can help untangle disease mechanisms.

**Lab (3-3):** **Epigenome profiling and disease links**
**Instructors:** Dr. Steven Parker
**Time:** Apr 6 (Thursday), 2:30 - 4:00 PM
**Topics:**
Students will learn how to computationally process epigenomic data, create interactive displays of these profiles, and then use the profiles to interpret disease associated genetic variations.

**Lecture (3-4):** *Application of systems biology to translational medicine*
**Instructor:** Dr. Matthias Kretzler
**Time:** Apr 11 (Tuesday), 2:30 - 4:00 PM
**Topics:**
Integrating genome wide data sets with high-resolution clinical phenotypes, molecular marker definition, regulatory network generation in patient samples.

**Lab (3-4):** **Systems biology resources for translational medicine**
**Instructor:** Dr. Felix Eichinger
**Time:** Apr 13 (Thursday), 2:30 - 4:00 PM
**Topics:**
Introduction to web based systems biology resources including Oncomine and Nephromine.
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