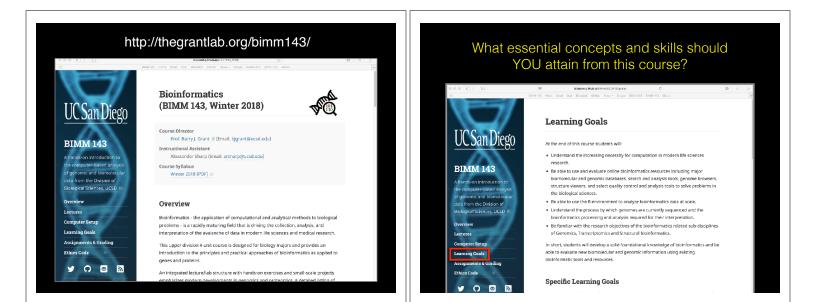


Today's Menu Website, screencasts, survey, ethics, **Course Logistics** assessment and grading. **Introduce Yourself!** What you need to learn to Learning Objectives succeed in this course. Your preferred name, Major lecture topics **Course Structure** and specific leaning goals. Place you identify with, Major area of study/research, Introducing the *what*, *why* and *how* of bioinformatics? Introduction to **Bioinformatis** Favorite joke (optional)! Bioinformatics Hands-on exploration of several major Database databases and their associated tools.



At the end of this course students will:

- Understand the increasing necessity for computation in modern life sciences research.
- Be able to use and evaluate online bioinformatics resources and analysis tools to solve problems in the biological sciences.
- Be able to use the R environment to analyze bioinformatics data at scale.
- Be familiar with the research objectives of the bioinformatics related sub-disciplines of Genome informatics, Transcriptomics and Structural informatics.

In short, you will develop a solid foundational knowledge of bioinformatics and be able to evaluate new biomolecular and genomic information using existing bioinformatic tools and resources.

Specific Learning Goals.... What I want you to know by course end!

Specific Learning Goals

UC San Diego

BIMM 143

ds-on introductio

Teaching toward the specific learning goals below is expected to occupy 60%-70% of class time. The remaining course content is at the discretion of the instructor with student body input. This includes student selected topics for peer presentation, as well as one student selected guest lecture from an industry based genomic scientist.

Lecture(s):

All students who receive a passing grade should be able to

- Appreciate and describe in general terms the role of computation in hypothesis-driven discovery processes within the life sciences.
- Be able to query, search, compare and contrast the data contained in major bioinformatics databases and desr/the how these databases interset (GenBanic, GENE, UniProt, PFAM, OMIM, FDB, USC, ENSENBLE).
- 3 Describe how nucleotide and protein sequence and structure data are represented (FASTA, FASTQ, GenBank, UniProt, PDB). 3, 10
- Be able to describe how dynamic programming works for pairwise sequence alignment and appreciate the differences between globa and local alignment along with their major application areas. ices between global 4, 5 Calculate the alignment score between two nucleotide or prote
- sequences using a provided scoring matrix and be able to perform

Course Structure Derived from specific learning goals

UCSanDiego BIMM 143 om the Division of

Lectures

All Lectures are Tu/Th 9:00-12:00 pm in Warren Lecture Hail 2015 (WLH 2015) (Mop \mathbb{Z}). Clicking on the class topics below will take you to corresponding lecture notes, homework assignments, pre-class video screen-casts and required reading material.

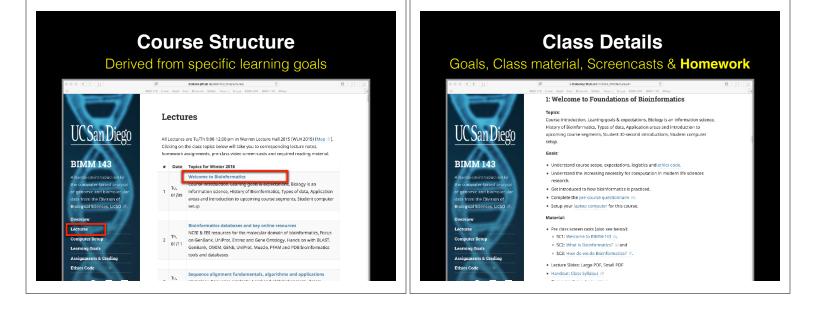
Date Topics for Winter 2018 Welcome to Bioinforma

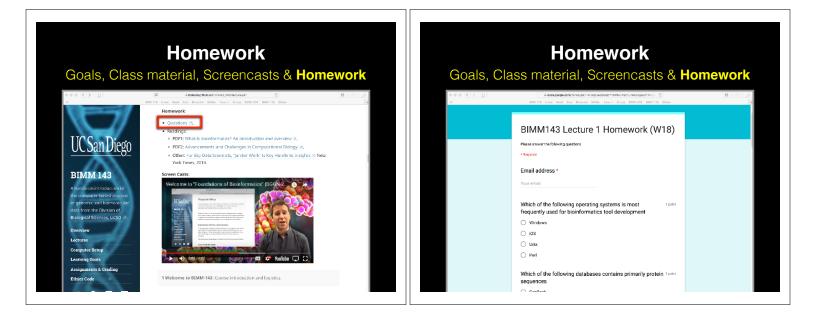
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 Veccome to unonnormatics
 Tu, Course introduction, Lening goals & expectations, Biology is an
 information science, History of Bioinformatics, Types of data, Application
 or Ap9 areas and introduction to upcoming course segments, Student computer
 setup

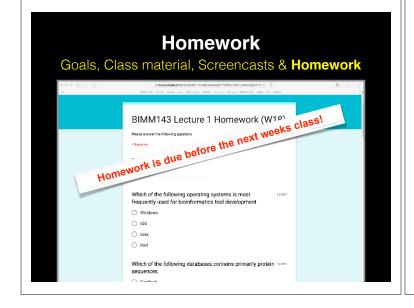
tics databases and key online re

Tr,
 On GenBank, UniProt. Entrez and Care Ontology, Hands on with BLAST,
 Of Jill
 GenBank, OMIM, GENE, UniProt. Muscle, PFAN and PDB bioinformatics

Tu, Sequence alignment fundamentals, algorithms and applications







Side Note: Why stick with this course?

Provides a hands-on practical introduction to major bioinformatics concepts and resources.

Covers modern hot topics and the intimate coupling of informatics with biology - highlighting the impact of computing advances and 'big data' on biology!

Designed for biology majors with no programing experience or high level math skills.

Provides a hook for increasing computational and data science competencies in the biosciences - valuable high demand translational skills!

Side Note: Why stick with this course?

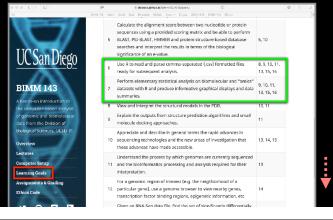
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BIMM-143 Learning Goals.... Data science R based learning goals



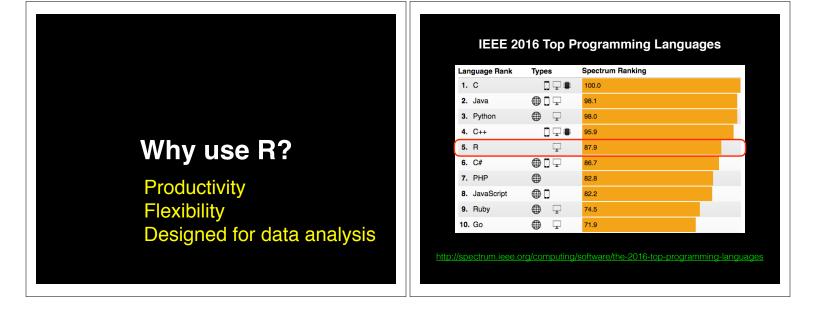
BIMM-143 Learning Goals.... Delve deeper into "real-world" bioinformatics

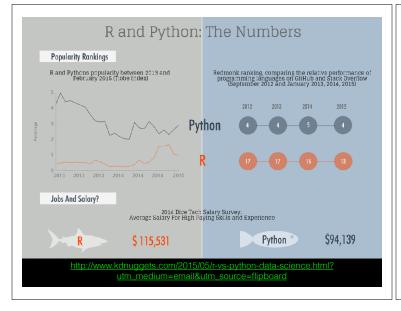


These support a major learning objective

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- R is the "lingua franca" of data science in industry and academia.
- · Large user and developer community.
 - As of Jan 8th 2018 there are 12,039 add on R packages on <u>CRAN</u> and 1,473 on <u>Bioconductor</u> - more on these later!
- Virtually every statistical technique is either already built into R, or available as a free package.
- Unparalleled exploratory data analysis environment.

Today's Menu

Course Logistics	Website, screencasts, survey, ethics, assessment and grading.	
Learning Objectives	What you need to learn to succeed in this course.	
Course Structure	Major lecture topics and specific leaning goals.	
Introduction to Bioinformatis	Introducing the <i>what</i> , <i>why</i> and <i>how</i> of bioinformatics?	
Computer Setup	Ensuring your laptop is all set for future sections of this course.	

OUTLINE

Overview of bioinformatics

- The <u>what</u>, <u>why</u> and <u>how</u> of bioinformatics?
- · Major bioinformatics research areas.
- · Skepticism and common problems with bioinformatics.

Online databases and associated tools

- · Primary, secondary and composite databases.
 - Nucleotide sequence databases (GenBank & RefSeq).
 - Protein sequence database (UniProt).
 - Composite databases (PFAM & OMIM).

Database usage vignette

· How-to productively navigate major databases.

Q. What is Bioinformatics?

"Bioinformatics is the application of computers to the collection, archiving, organization, and analysis of biological data."

... Bioinformatics is a hybrid of biology and computer science

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Computer based management and analysis of biological and biomedical data with useful applications in many disciplines, particularly genomics, proteomics, metabolomics, etc...

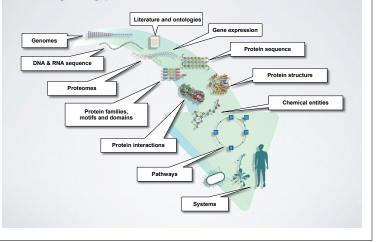
MORE DEFINITIONS

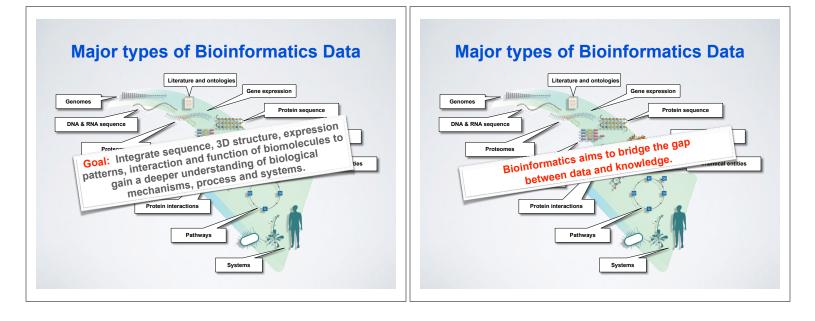
- "Bioinformatics is conceptualizing biology in terms of macromolecules and then applying "informatics" techniques (derived from disciplines such as applied maths, computer science, and statistics) to understand and organize the information associated with these molecules, on a large-scale. Luscombe NM, et al. Methods Inf Med. 2001;40:346.
- "Bioinformatics is research, development, or application of computational approaches for expanding the use of biological, medical, behavioral or health data, including those to acquire, store, organize and analyze such data." National Institutes of Health (NIH) (http://tinyurl.com/l3gxr6b)

MORE DEFINITIONS

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- "Bioinformatic Bioinformatic Advelopment, or application of computer point" popoaches for expanding the use of bi Key medical, behavioral or health data, including those to quire, store, organize and analyze such data."
 National Institutes of Health (NIH) (http://tinyurl.com/l3gxr6b)

Major types of Bioinformatics Data





BIOINFORMATICS RESEARCH AREAS

Include but are not limited to:

- Organization, classification, dissemination and analysis of biological and biomedical data (particularly '-omics' data).
- · Biological sequence analysis and phylogenetics.
- · Genome organization and evolution.
- Regulation of gene expression and epigenetics.
- · Biological pathways and networks in healthy & disease states.
- · Protein structure prediction from sequence
- Modeling and prediction of the biophysical properties of biomolecules for binding prediction and drug design.
 Design of biomolecular structure and function.

With applications to Biology, Medicine, Agriculture and Industry

Where did bioinformatics come from?

Bioinformatics arose as molecular biology began to be transformed by the emergence of molecular sequence and structural data

Recap: The key dogmas of molecular biology

- DNA sequence determines protein sequence.
- Protein sequence determines protein structure.
- Protein structure determines protein function.
- Regulatory mechanisms (e.g. gene expression) determine the amount of a particular function in space and time.

Bioinformatics is <u>now</u> essential for the archiving, organization and analysis of data related to all these processes.

Why do we need Bioinformatics?

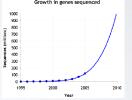
Bioinformatics is necessitated by the rapidly expanding quantities and complexity of biomolecular data

 Bioinformatics provides methods for the efficient:

data integration

data mining and analysis

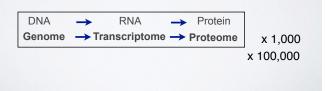
- storage
- annotation
 search and retrieval



E.G. data from sequencing, structural genomics, proteomics, new high throughput assays, *etc...*

How do we do Bioinformatics?

• A "bioinformatics approach" involves the application of computer algorithms, computer models and computer databases with the broad goal of understanding the action of both individual genes, transcripts, proteins and large collections of these entities.



How do we actually do Bioinformatics?

Pre-packaged tools and databases

- Many online
- Most are free to use
- Time consuming methods require downloading...

Advanced tool application & development

- Mostly on a UNIX environment
- Knowledge of programing languages frequently required (*e.g.* **R**, Python, Perl, C, Java, Fortran)
- May require specialized high performance computing...

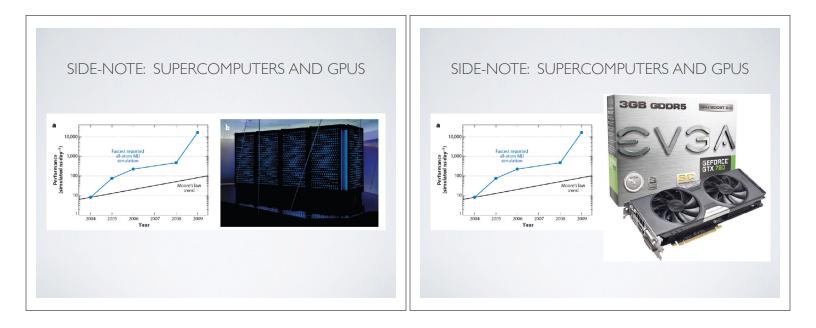
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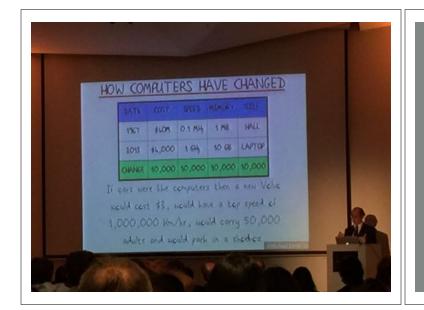
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Skepticism & Bioinformatics

We have to approach computational results the same way we do wet-lab results:

- Do they make sense?
- Is it what we expected?
- Do we have adequate controls, and how did they come out?
- Modeling is modeling, but biology is different... What does this model actually contribute?
- Avoid the miss-use of 'black boxes'

Skepticism & Bioinformatics

Gunnar von Heijne in his old but quite readable treatise, Sequence Analysis in Molecular Biology; Treasure Trove or Trivial Pursuit, provides a very appropriate conclusion:

- "Think about what you're doing; use your knowledge of the molecular system involved to guide both your interpretation of results and your direction of inquiry; use as much information as possible; and do not blindly accept everything the computer offers you".
- Key-Point: Avoid the miss-use of 'black boxes'!

Common problems with Bioinformatics

Confusing multitude of tools available • Each with many options and settable parameters

Most tools and databases are written by and for nerds Same is true of documentation - if any exists!

Most are developed independently

Notable exceptions are found at the: • EBI (European Bioinformatics Institute) and • NCBI (National Center for Biotechnology Information)

General Parar	neters	
Max target sequences	Select the maximum number of a	aligned sequences to display 🥹
Short queries	Automatically adjust param	ieters for short input sequences 😡
Expect threshold	10	
Word size	3 : 0	
Max matches in a query range	0	
Scoring Paran	eters	Even Diest has many asttable reconstant
Matrix	BLOSUM62 :	Even Blast has many settable parameters
Gap Costs	Existence: 11 Extension: 1 +	
Compositional adjustments	Conditional compositional sco	PROGRAM Related tools with different terminology
Filters and Ma	sking	FASTA 4
Filter	Low complexity regions 🥹	MATRIX GAP OPEN GAP EXTEND KTUP UPPER VALUE LOWER VALUE
Mask	Mask for lookup table only Mask lower case letters	BLOSUMS0 : 10 : 2 : 10 : 0 (default) : DNA STRAND HISTOGRAM FILTER STATISTICAL ESTIMATES : N/A : none : Regress :
	ABLAST	SCORES ALIGNMENTS SEQUENCE RANGE DATABASE RANGE MULTI HSPs
PSI/PHI/DELT	Choose File no file selected	S0 ÷ S0 ÷ START-END START-END no ÷
PSI/PHI/DELT Upload PSSM Optional		Default +
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Key Online Bioinformatics Resources: NCBI & EBI

The NCBI and EBI are invaluable, publicly available resources for biomedical research

WOR FORM	Welcome to NCDI	Popular Resources
Resource List (A-Z)	The National Center for Biotechnology Information advances science	Public
il Gauna ana	and health by providing access to blomatical and genomic	Instated
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National Center for Biotechnology Information (NCBI)

- Created in 1988 as a part of the National Library of Medicine (NLM) at the National Institutes of Health
- NCBI's mission includes:
 - Establish public databases
 - Develop software tools
 - Education on and dissemination of biomedical information



• We will cover a number of core NCBI databases and software tools in the lecture

http://www.ncbi.nlm.nih.gov



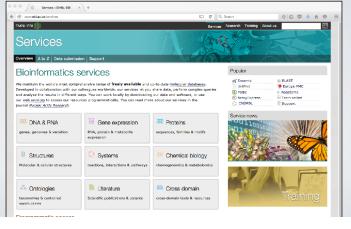
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SNCBI National Center for Biotechnology Information	Databases 0	Popular Resources	Search	National Conter for Biotechnology Information	Search
NCBI Home	Welcome to NCBI	Bookshelf	Resources	NCBI Home Welcome to NCBI	Popular Resources
Resource List (A-Z)	The National Center for Biotech	PubMed Central		Resource List (A-Z) The National Center for Biotechnology Information as	
All Resources	and health by providing access		F		
Chemicals & Bioassays	information.	PubMed Health	Central	Notable NCBI database	es include:
Data & Software	About the NCBI Mission Or	BLAST	Health		
DNA & RNA				GenBank, RefSeq, Publ	Med, dbSNP
Domains & Structures	Get Started	Nucleotide	e		
				and the search tools ENTR	E7 and BLACT
Genes & Expression	 Tools: Analyze data using I 	Genome			
	Downloads: Get NCBI data				EZ anu BLAST
Genetics & Medicine		SNP			
Genetics & Medicine Genomes & Maps	Downloads: Get NCBI data How-To's: Learn how to acc			Homology databases	Protein
Genetics & Medicine Genomes & Maps Homology	Downloads: Get NCBI data How-To's: Learn how to acc Submissions: Submit data	SNP			Protein PubChem
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Genes & Expression Genetics & Medicine Genomes & Maps Homology Librature Proteins Sequence Analysis Taxonomy Training & Tutonals	Ocwinada: Get NOBI data How/Tog: Leam how to acc Submissions: Submit data databases 3D Structures	SNP Gene Protein PubChem		Homology databases Literature Proteins Sequence Analysis 3D Structures	PubChem NCBI Announcements

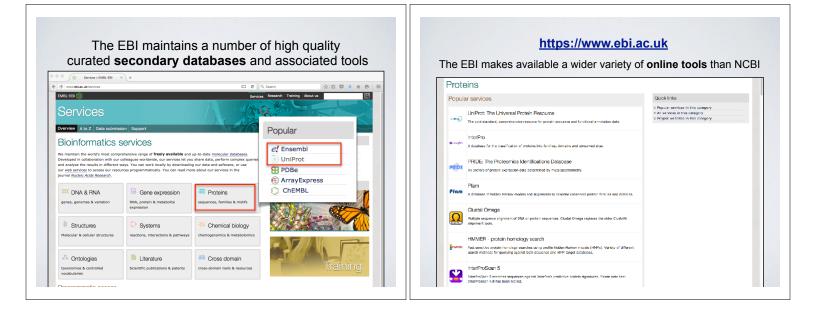
Key Online Bioinformatics Resources: NCBI & EBI The NCBI and EBI are invaluable, publicly available resources for biomedical research	European Bioinformatics Institute (EBI) • Created in 1997 as a part of the European Molecular Biology Laboratory (EMBL)
<complex-block><complex-block></complex-block></complex-block>	 EBI's mission includes: providing freely available data and bioinformatics services and providing advanced bioinformatics training We will briefly cover several EBI databases and tools that have advantages over those offered at NCBI

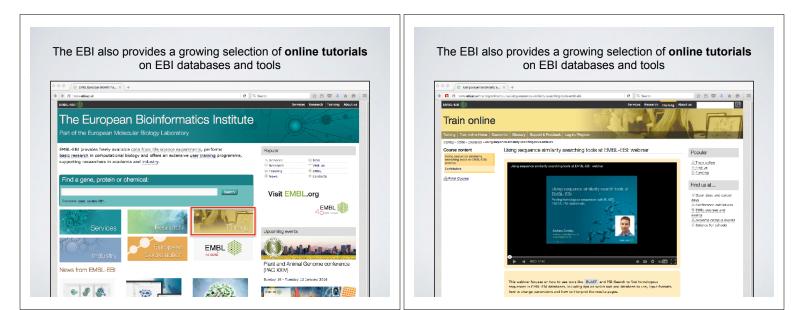
The EBI maintains a number of high quality curated **secondary databases** and associated tools

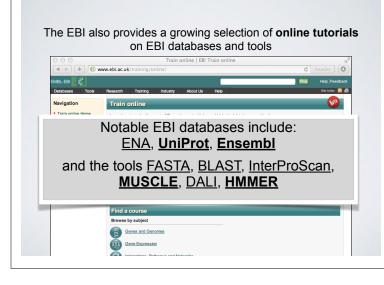


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Next Class...

MAJOR BIOINFORMATICS DATABASES AND ASSOCIATED ONLINE TOOLS

Bioinformatics Databases

AATDB, AceDb, ACUTS, ADB, AFDB, AGIS, AMSdb, ARR, AsDb, BBDB, BCGD, Beanref. Biolmage, BioMagResBank, BIOMDB, BLOCKS, BovGBASE, BOVMAP, BSORF, BTKbase, CANSITE, CarbBank, CARBHYD, CATH, CAZY, CCDC, CD4OLbase, CGAP, ChickGBASE, Colibri, COPE, CottonDB, CSNDB, CUTG, CyanoBase, dbCFC, dbEST, dbSTS, DDBJ, DGP, DictyDb, Picty_cDB, DIP, DOGS, DOMÓ, DPD, DPInteract, ECDC ECGC, EC02DBASE, EcoCyc, EcoGene, EMBL, EMD db, ENZYME, EPD, EpoDB, ESTHER, FlyBase, FlyView, GCRDB, GDB, GENATLAS, Genbank, GeneCards, Genlilesne, GenLink, GENOTK, GenProtEC, GIFTS, GPCRDB, GRAP, GRBase, gRNAsdb, GRR, GSDB, HAEMB, HAMSTERS, HEART-2DPAGE, HEXAdb, HGMD, HIDB, HIDC, HIVdb, HotMolecBase, HOVERGEN, HPDB, HSC-2DPAGE, ICN, ICTVDB, IL2RGbase, IMGT, Kabat, KDNA, KEGG, Klotho, LGIC, MAD, MaizeDb, MDB, Medline, Mendel, MEROPS, MGDB, MGI, MHCPEP5 Micado, MitoDat, MITOMAP, MJDB, MmtDB, Mol-R-Us, MPDB, MRR, MutBase, MycDB, NDB, NRSub, 0-lycBase, OMIA, OMIM, OPD, ORDB, OWL, PAHdb, PatBase, PDB, PDD, Pfam, PhosphoBase, PigBASE, PIR, PKR, PMD, PPDB, PRESAGE, PRINTS, ProDom, Prolysis, PROSITE, PROTOMAP, RatMAP, RDP, REBASE, RGP, SBASE, SCOP, SeqAnaiRef, SGD, SGP, SheepMap, Soybase, SPAD, SRNA db, SRPDB, STACK, StyGene,Sub2D, SubtiList, SWISS-2DPAGE, SWISS-3DIMAGE, SWISS- MODEL Repository, SWISS-PROT, TeIDB, TGN, tmRDB, TOPS, TRANSFAC, TRR, UniGene,

Bioinformatics Databases



Side-note: Databases come in all shapes and sizes



Databases can be of variable quality and often there are multiple databases with overlapping content.

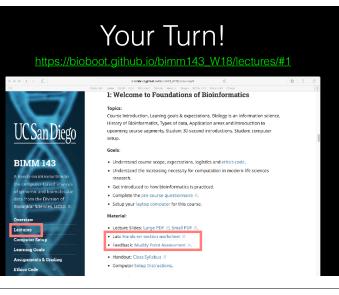
Primary, secondary & composite databases

Bioinformatics databases can be usefully classified into *primary*, *secondary* and *composite* according to their data source.

- Primary databases (or <u>archival databases</u>) consist of data derived experimentally.
 - GenBank: NCBI's primary nucleotide sequence database.
 PDB: Protein X-ray crystal and NMR structures.
- Secondary databases (or *derived databases*) contain information derived from a primary database.
 - RefSeq: non redundant set of curated reference sequences primarily from GenBank
 - PFAM: protein sequence families primarily from UniProt and PDB
- Composite databases (or metadatabases) join a variety of different primary and secondary database sources.
 - OMIM: catalog of human genes, genetic disorders and related literature
 GENE: molecular data and literature related to genes with extensive links to other databases.

Today's Menu

Course Logistics	Website, screencasts, survey, ethics, assessment and grading.
Learning Objectives	What you need to learn to succeed in this course.
Course Structure	Major lecture topics and specific leaning goals.
Introduction to Bioinformatis	Introducing the <i>what, why</i> and <i>how</i> of bioinformatics?
Bioinformatics Database	Hands-on exploration of several major databases and their associated tools.



BIMM-143: INTRODUCTION TO BIOINFORMATICS (Lecture 1) Bioinformatics Databases and Key Online Resources https://bioiod.github.jobimm153_W18/bio/unsi/1 Dr. Bany Grant	YOUR TURN! • There are five major hands-on sections including:
Lan 2018 Centralize: The purpose of this lab essation is to introduce a range of bioinformatics databases and associated enviros available on the Web while intersigning the molecular basis of a common human disease. Sections 1 and 2 data Swith quarking and sectioning CanBack (GBHE and CMM dipotential and a databases). Sections and visualizing protein structures. Thraining section 5 provides an opportunity to expire these and other databases further with additional examples. Side-note: The Web is a dynamic environment, where information is constantly added and the databases further with additional examples. Side-note: The Web is a dynamic environment, where information is constantly added and the databases further with additional examples. Side-note: The Web is a dynamic environment, where information is constantly added and the databases further with additional examples. Side-note: The Web is a dynamic environment, where information is constantly added and the accord p and the sector engine using terms related to the page you are trying to access. Section 1 The following transcript was found to be abundant in a human patient's blood sample. Page 1 Anstructure Content Cont	 BLAST, GenBank and OMIM @ NCBI [~35 mins] GENE database @ NCBI [~15 mins] — BREAK — UniProt & Muscle @ EBI [~25 mins] PFAM, PDB & NGL [~30 mins] — BREAK — Extension exercises [~30 mins] Please do answer the last review question (Q19). We encourage <u>discussion</u> and <u>exploration</u>!

YOUR TURN!	SUMMARY
 There are five major hands-on sections including: End times: BLAST, GenBank and OMIM @ NCBI GENE database @ NCBI BREAK — UniProt & Muscle @ EBI PFAM, PDB & NGL BREAK — BREAK — BREAK — Extension exercises Please do answer the last review question (Q19). We encourage discussion and exploration! 	 Bioinformatics is computer aided biology. Bioinformatics deals with the collection, archiving, organization, and interpretation of a wide range of biological data. There are a large number of primary, secondary and tertiary bioinformatics databases. The NCBI and EBI are major online bioinformatics service providers. Introduced Gene, UniProt, PDB databases as well as a number of 'boutique' databases including PFAM and OMIM.