

HELLO my name is

BARRY

bjgrant@ucsd.edu



ALEX

arsharp@ucsd.edu

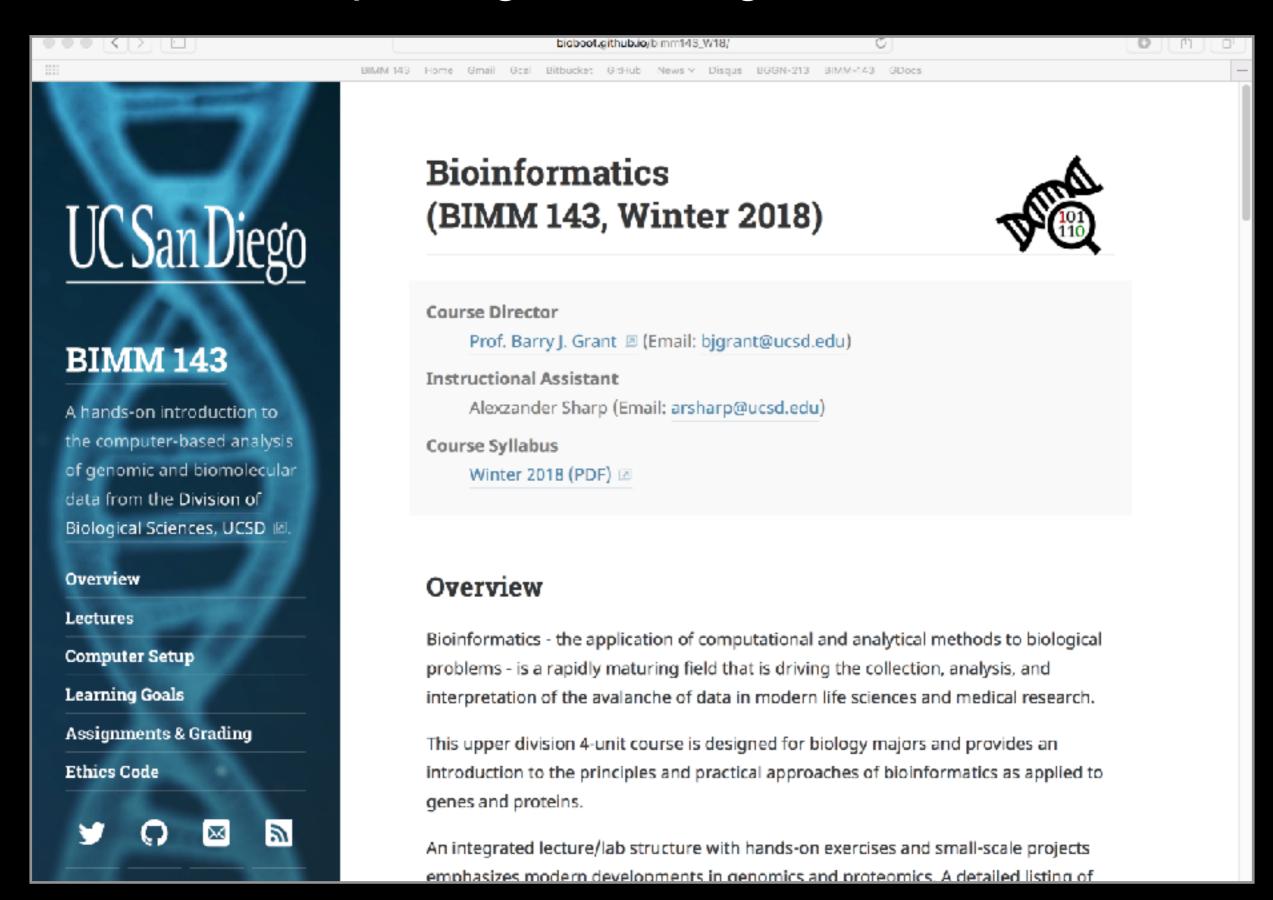
# Introduce Yourself!

Your preferred name,
Place you identify with,
Major area of study/research,
Favorite joke (optional)!

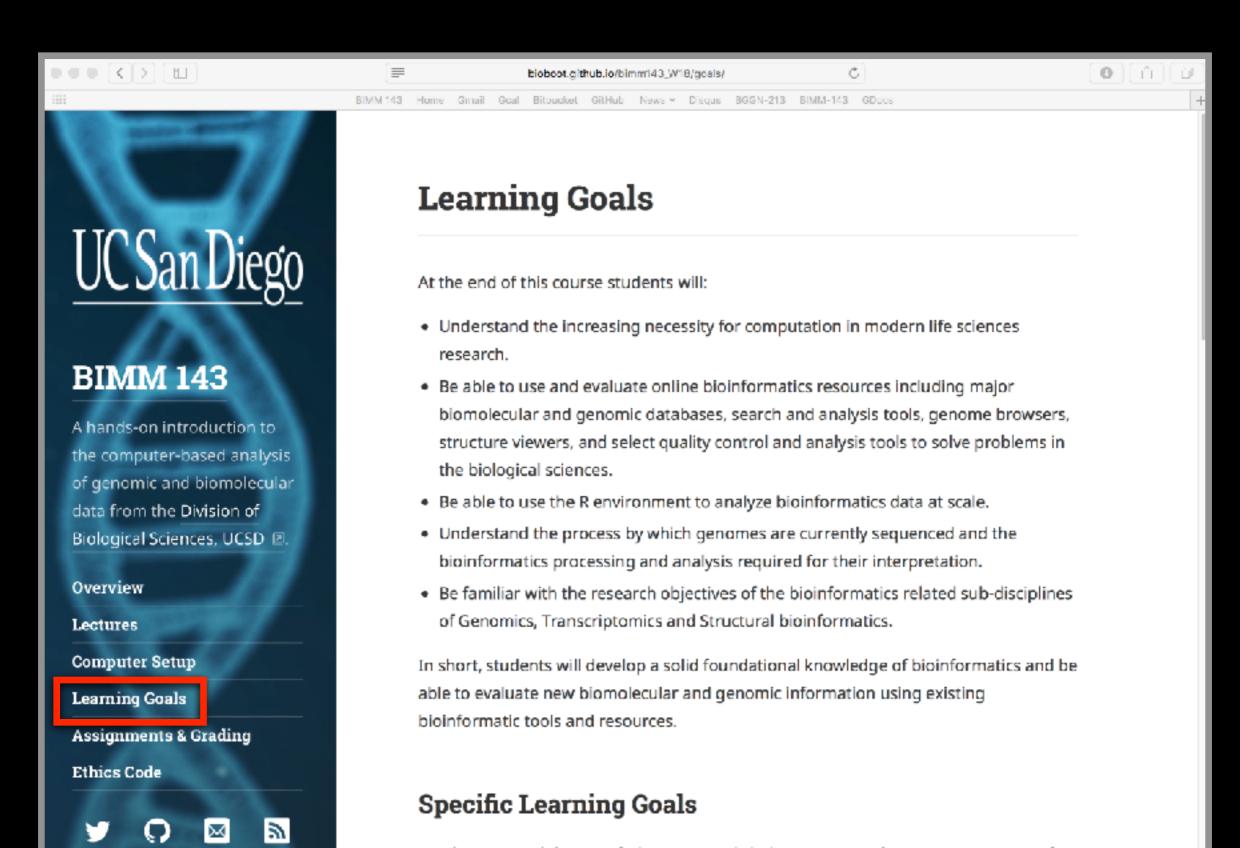
# Today's Menu

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 what, why and how of bioinformatics?
Bioinformatics Database	<b>Hands-on</b> exploration of several major databases and their associated tools.

### http://thegrantlab.org/bimm143/



# What essential concepts and skills should YOU attain from this course?



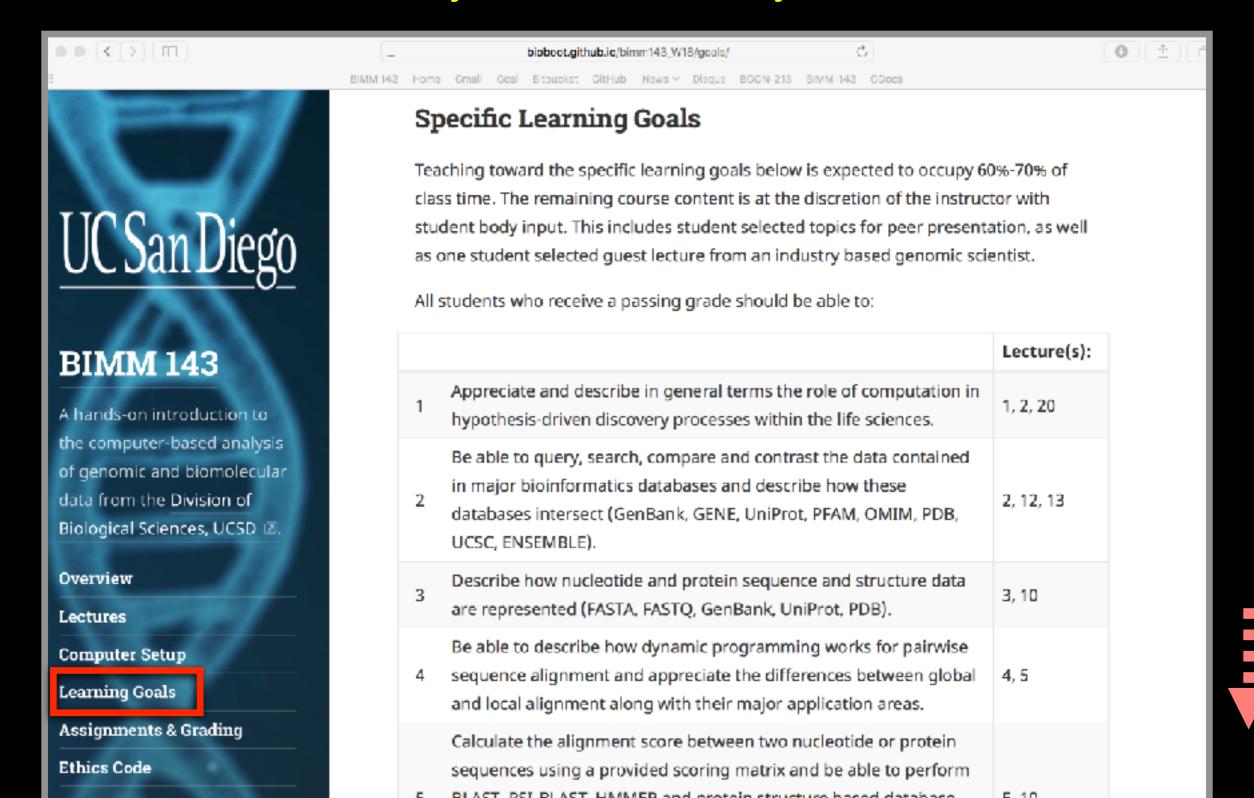
#### At the end of this course students will:

- 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**.

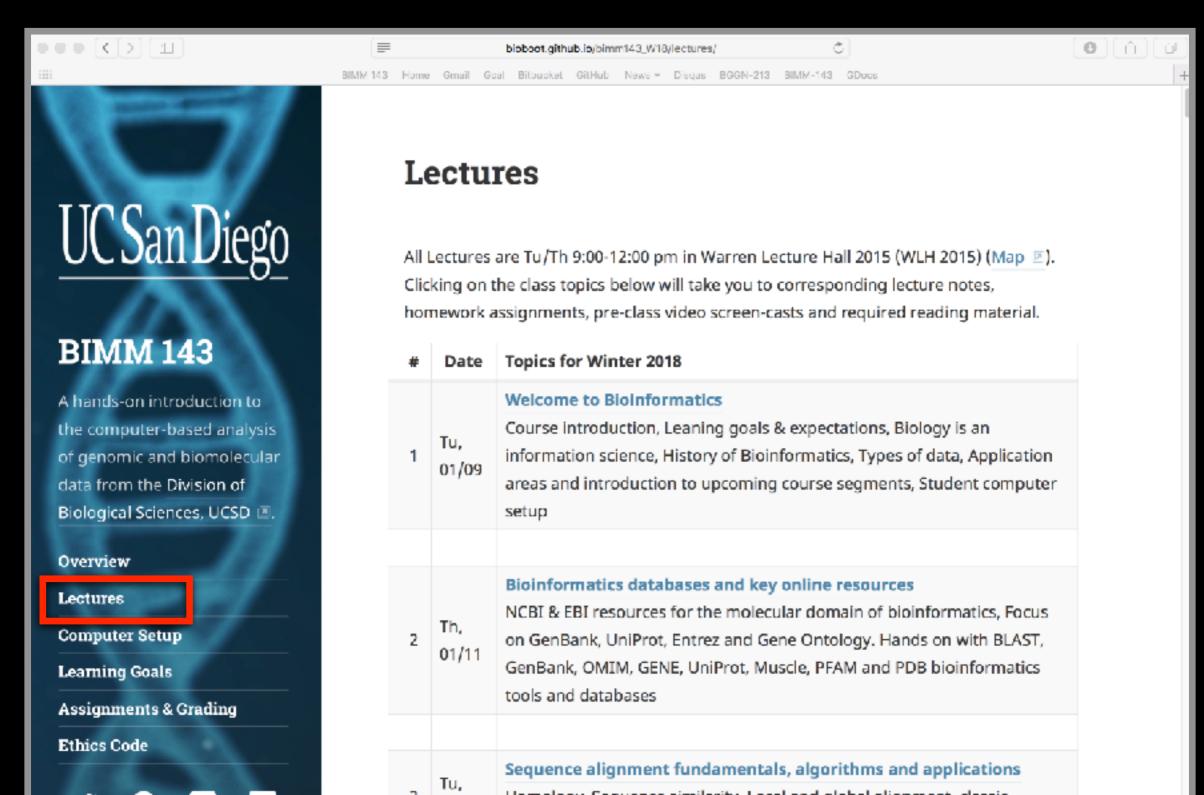
# Specific Learning Goals....

What I want you to know by course end!



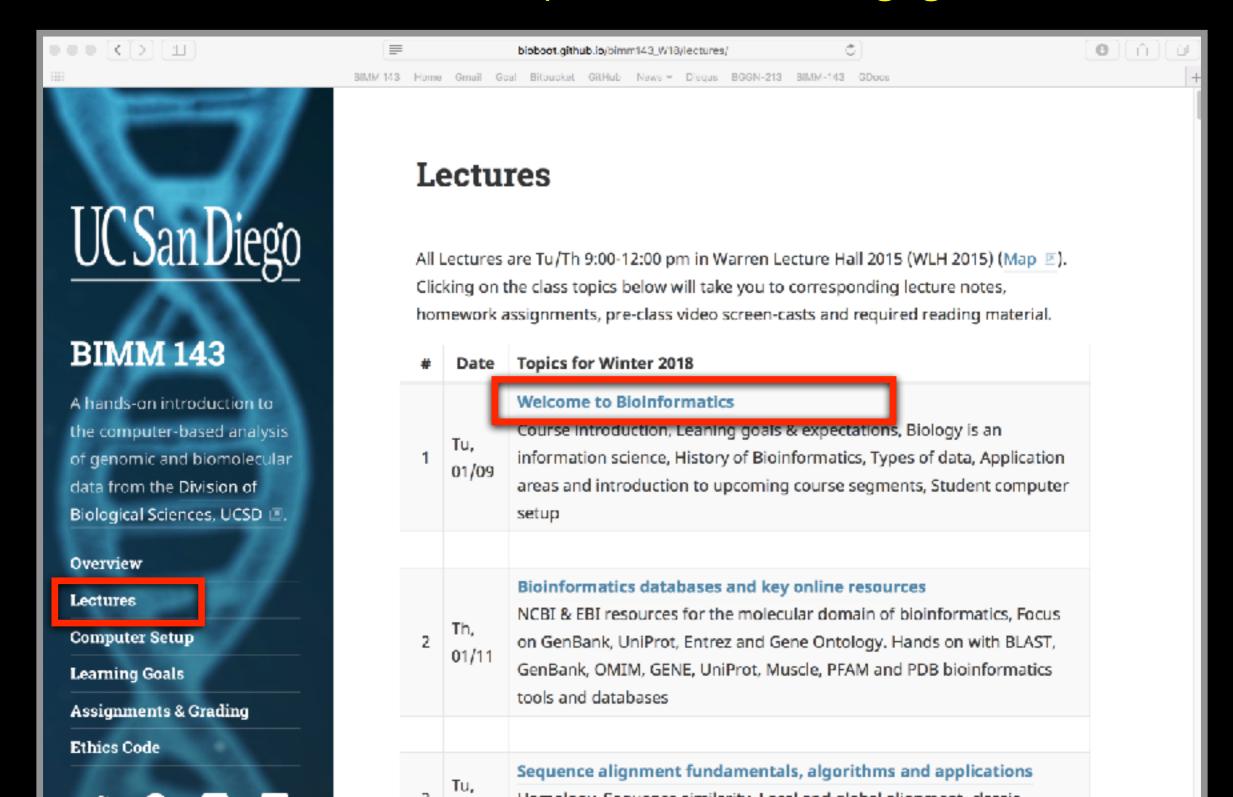
# Course Structure

## Derived from specific learning goals

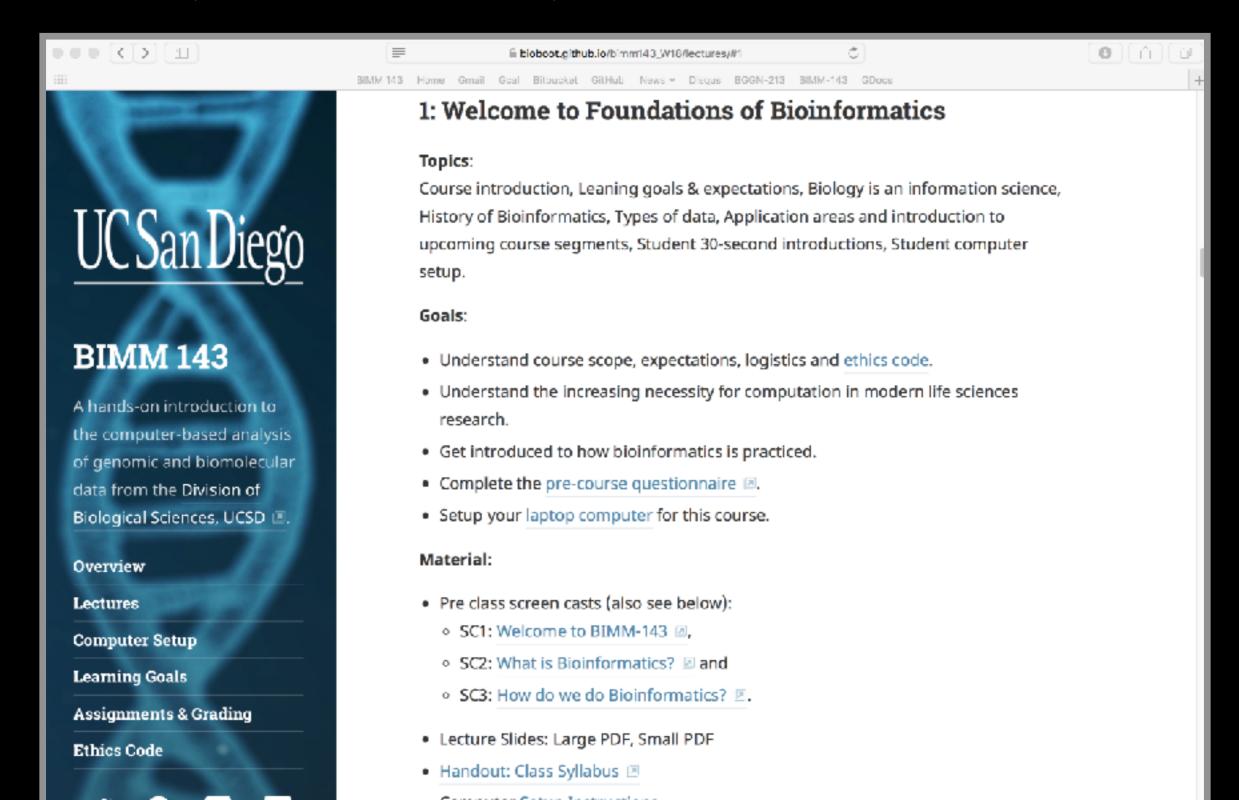


# Course Structure

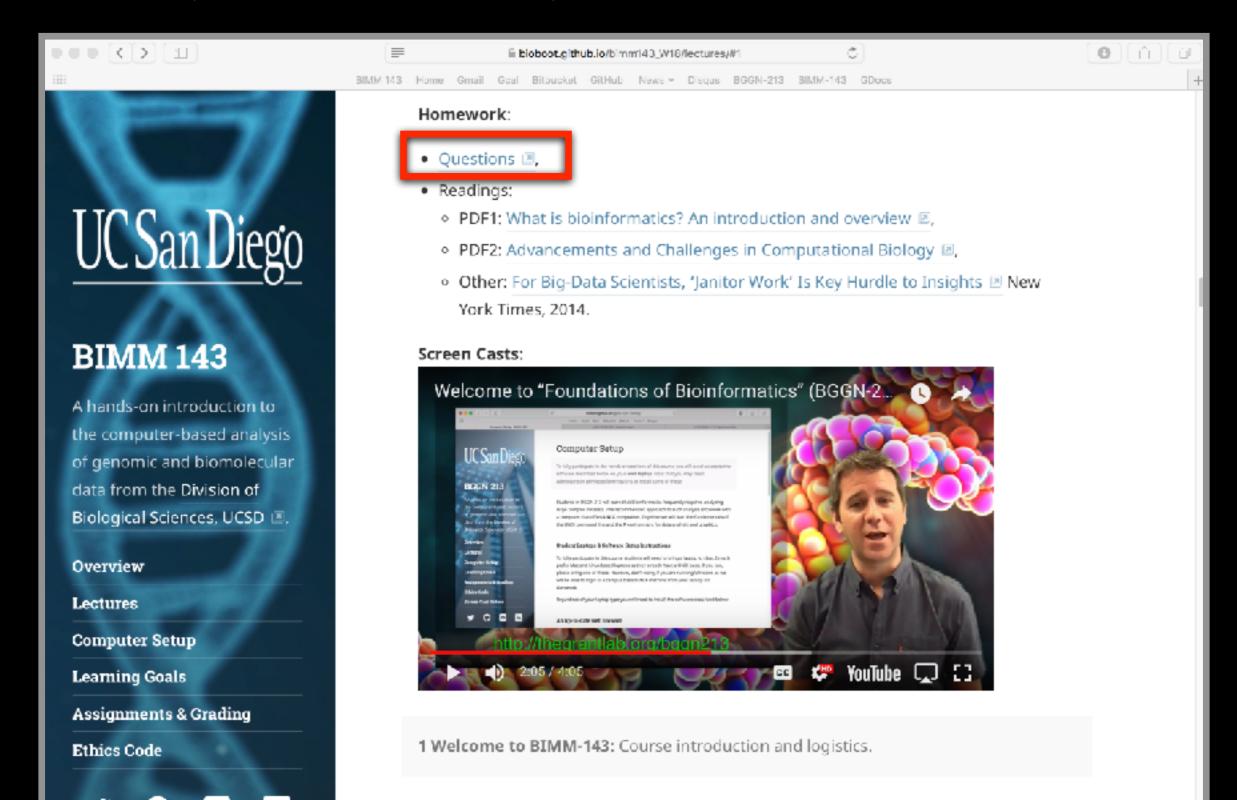
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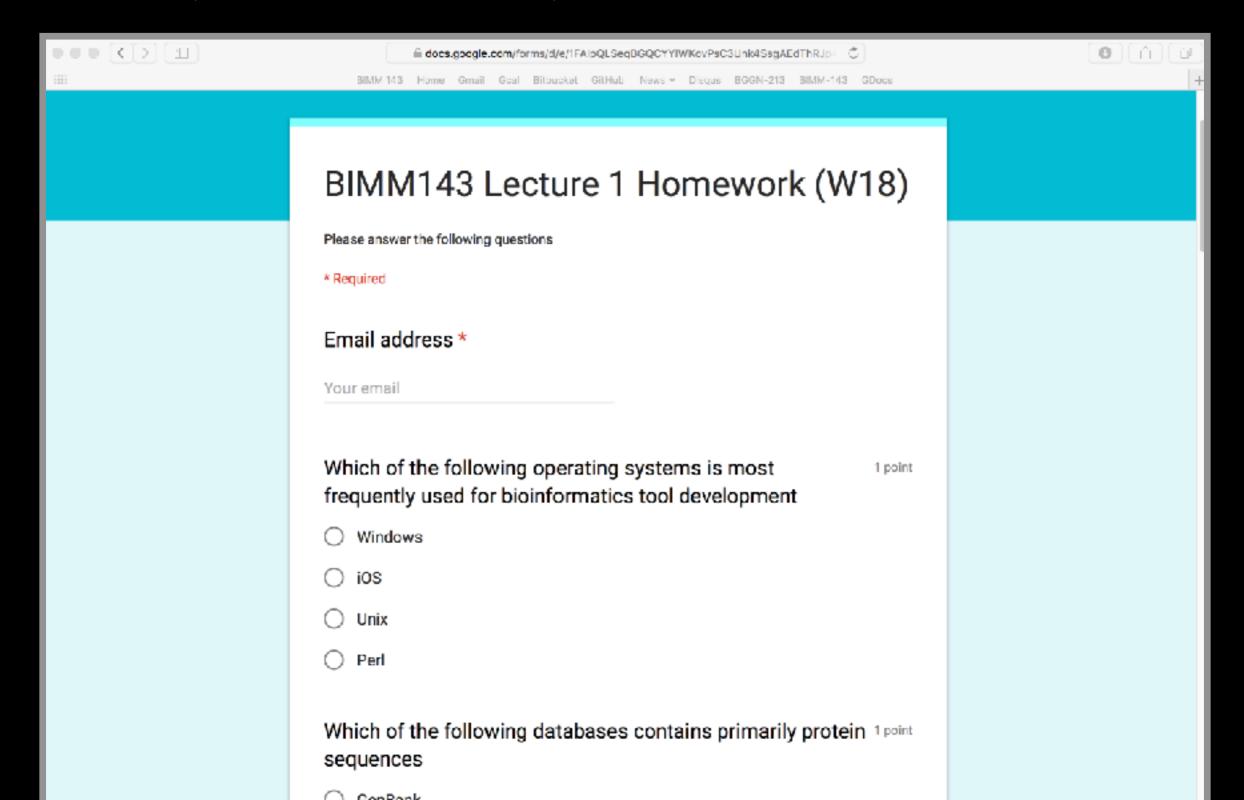
# **Class Details**



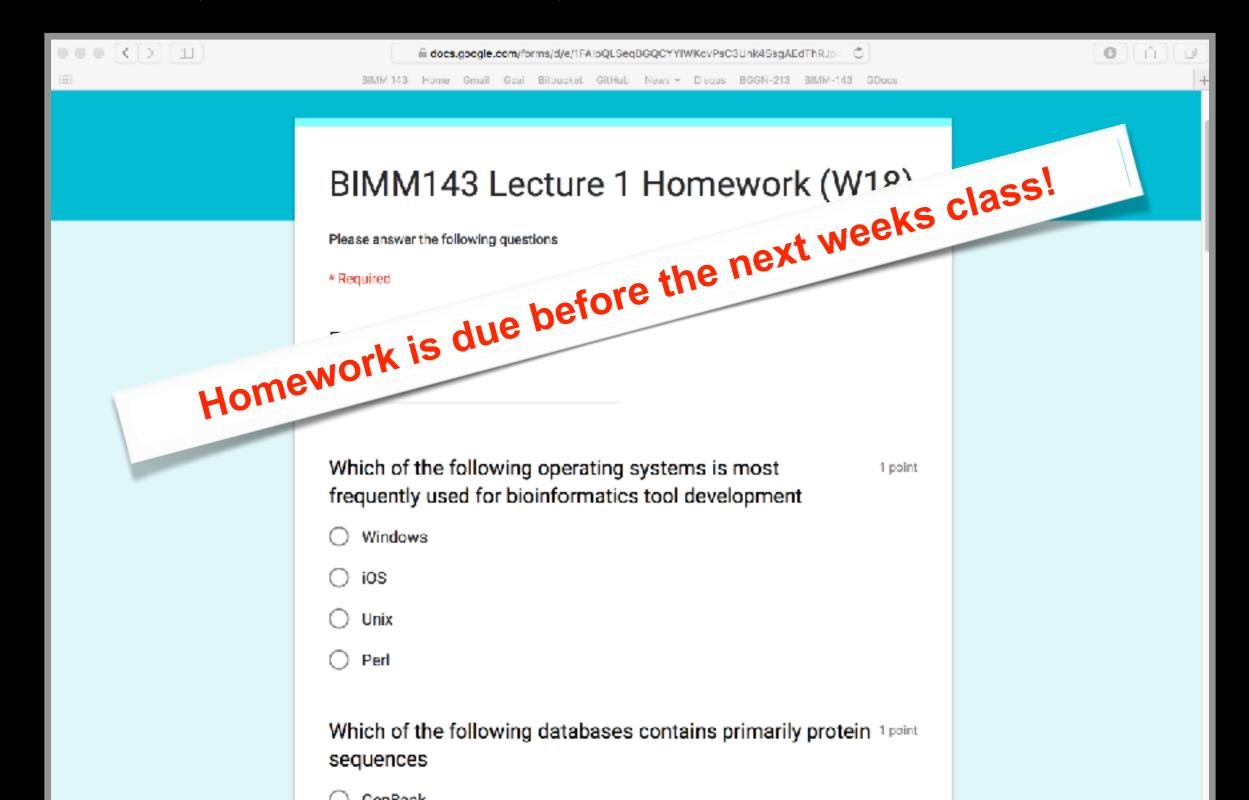
# Homework



# Homework



# Homework



# 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!

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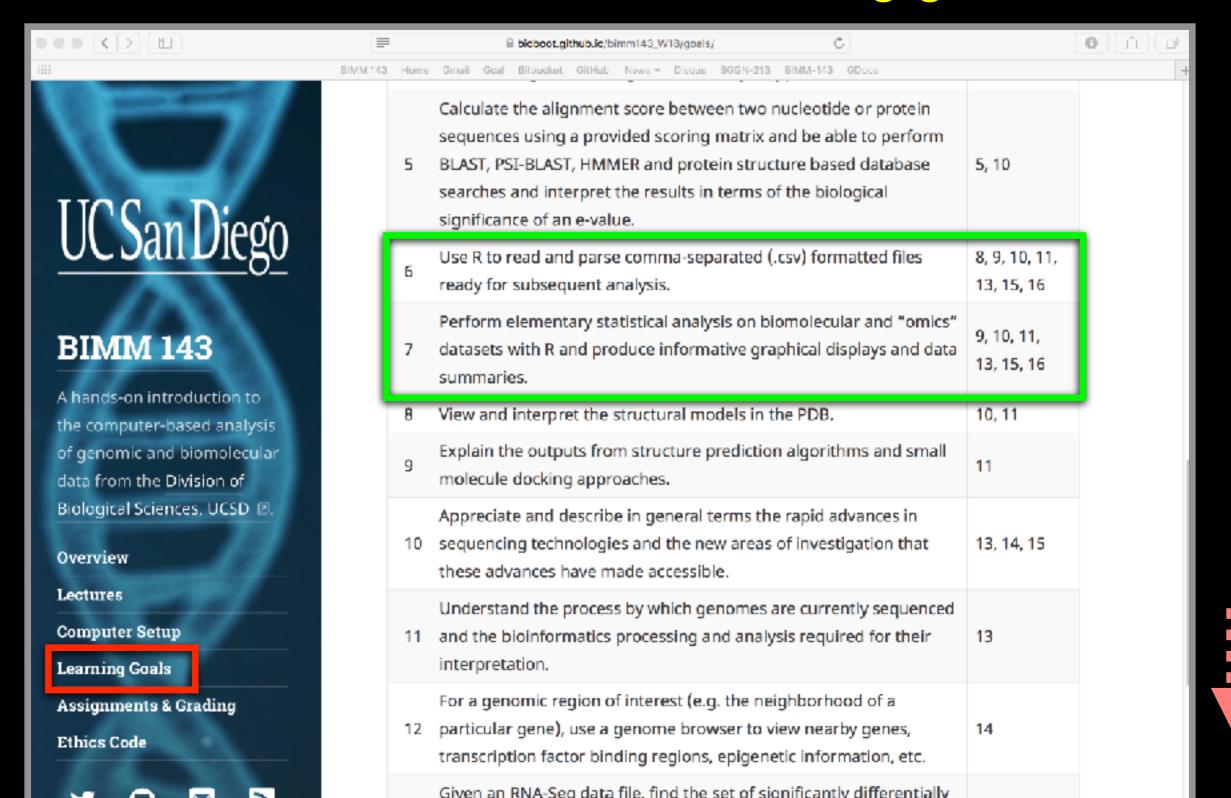
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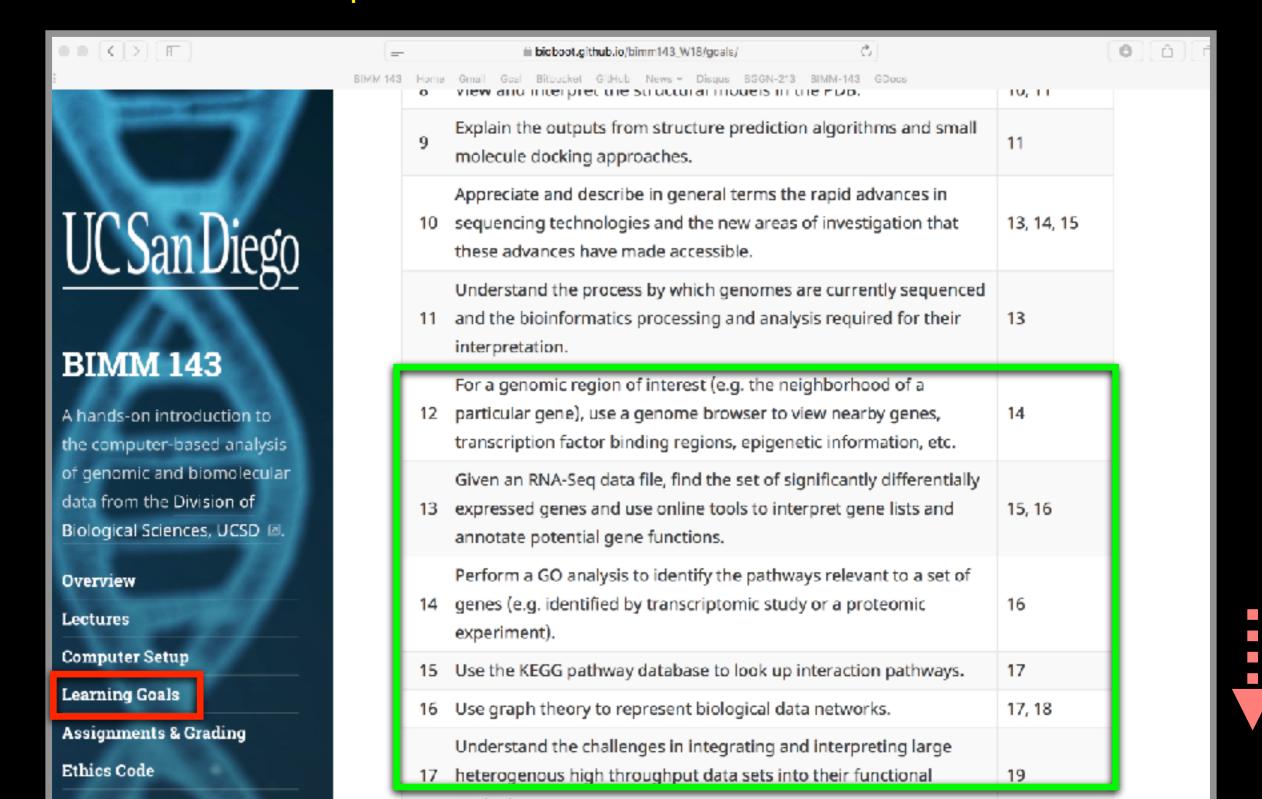
# BIMM-143 Learning Goals....

## 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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# Why use R?

Productivity
Flexibility
Designed for data analysis

## **IEEE 2016 Top Programming Languages**

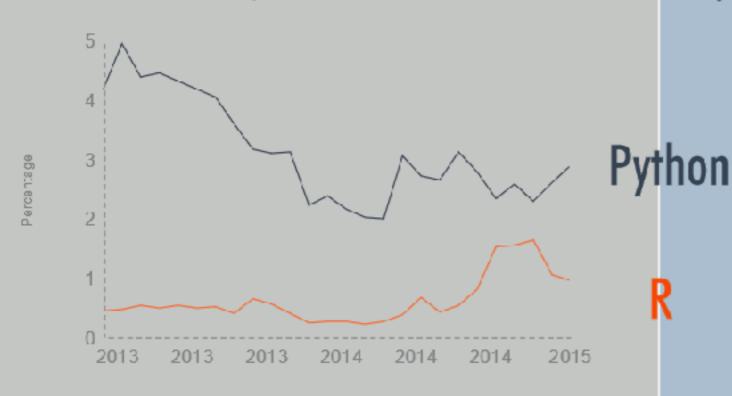
Language Rank	Types	Spectrum Ranking
1. C		100.0
2. Java	$\bigoplus$ $\square$ $\neg$	98.1
3. Python	₩ ፲	98.0
<b>4.</b> C++		95.9
<b>5.</b> R	Ţ	87.9
6. C#	₩ 🗓 🖵	86.7
<b>7.</b> PHP		82.8
8. JavaScript		82.2
9. Ruby	$\oplus$ $\Box$	74.5
<b>10.</b> Go	⊕ ፲	71.9

http://spectrum.ieee.org/computing/software/the-2016-top-programming-languages

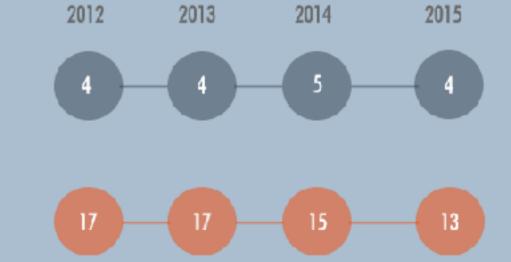
## R and Python: The Numbers



R and Pythons popularity between 2013 and February 2015 (Tiobe Index)



Redmonk ranking, comparing the relative performance of programming languages on GitHub and Stack Overflow (September 2012 and January 2013, 2014, 2015)



Jobs And Salary?

2014 Dice Tech Salary Survey: Average Salary For High Paying Skills and Experience



\$ 115,531



\$94,139

- 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.

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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."

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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...

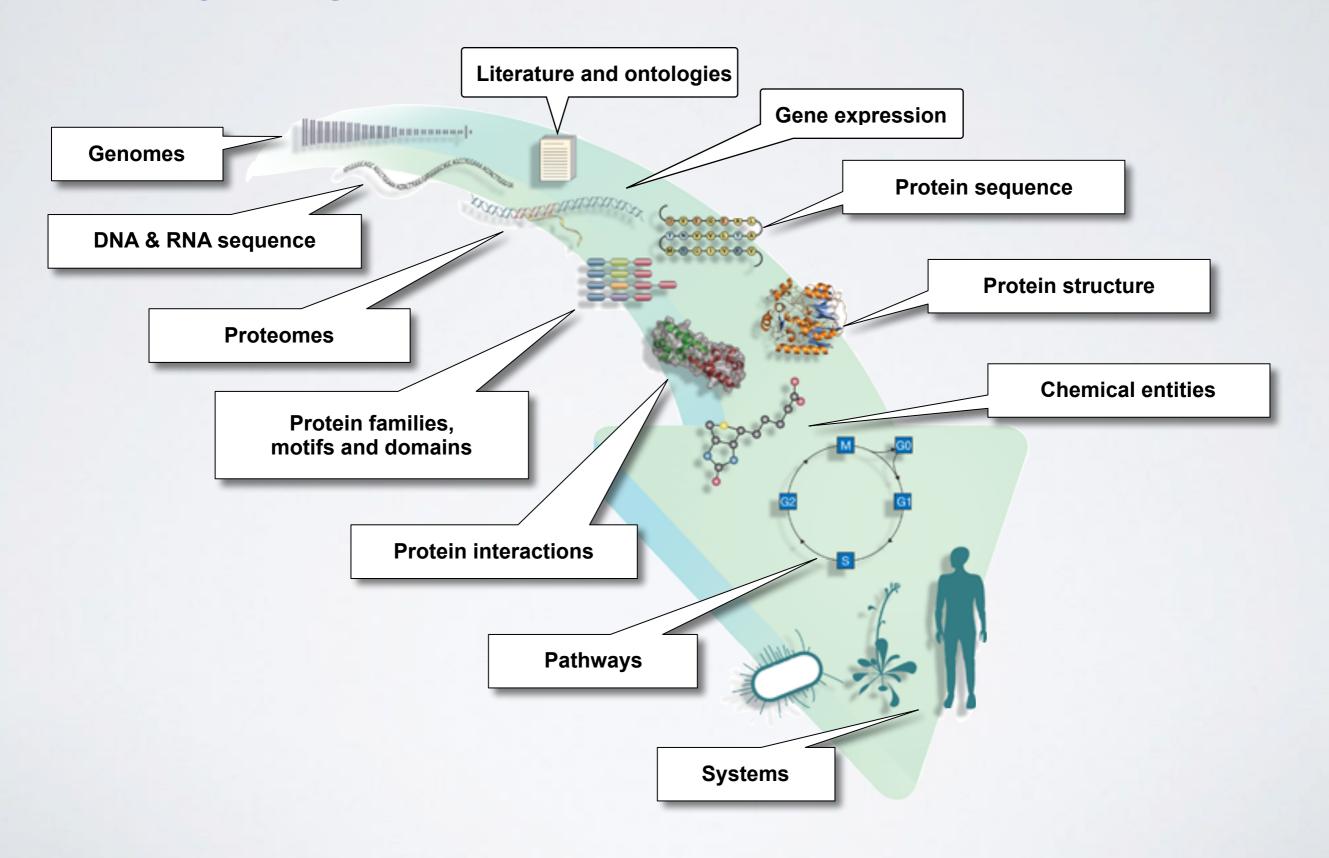
# MORE DEFINITIONS

- "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)

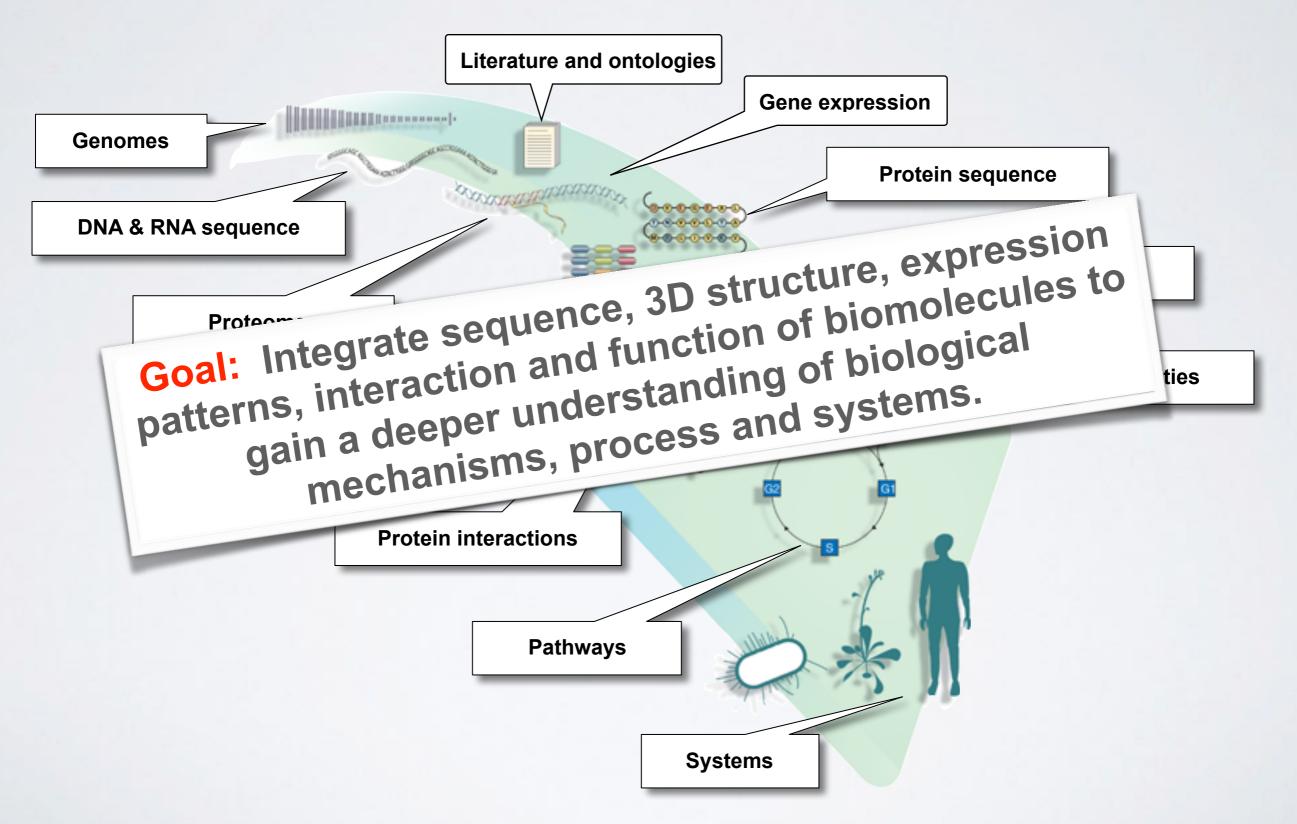
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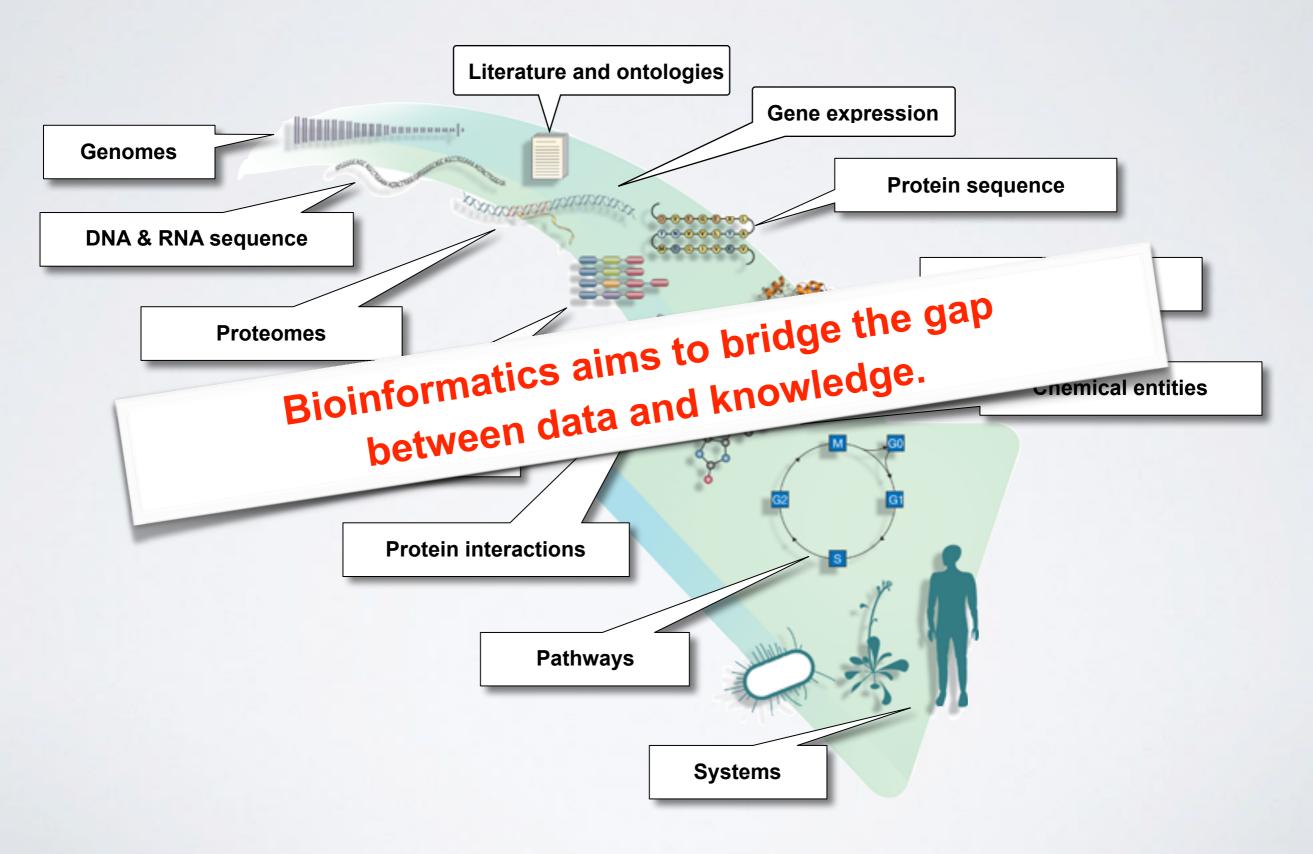
# **Major types of Bioinformatics Data**



# Major types of Bioinformatics Data



# **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

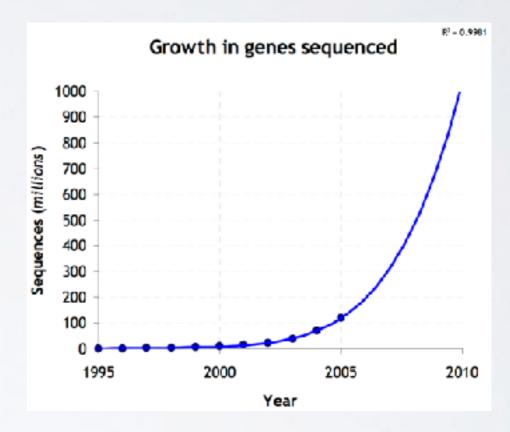
- DNA sequence determines protein sequence.
- Protein sequence determines protein structure.
- Protein structure determines protein function.
- Regulatory mechanisms (e.g. gene expression) determine the amount of a particular function in space and time.

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

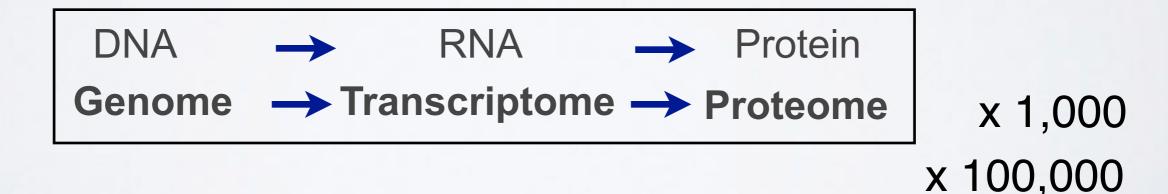
- Bioinformatics provides methods for the efficient:
  - storage
  - annotation
  - search and retrieval
  - data integration
  - data mining and analysis



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...

# How do we actually do Bioinformatics?

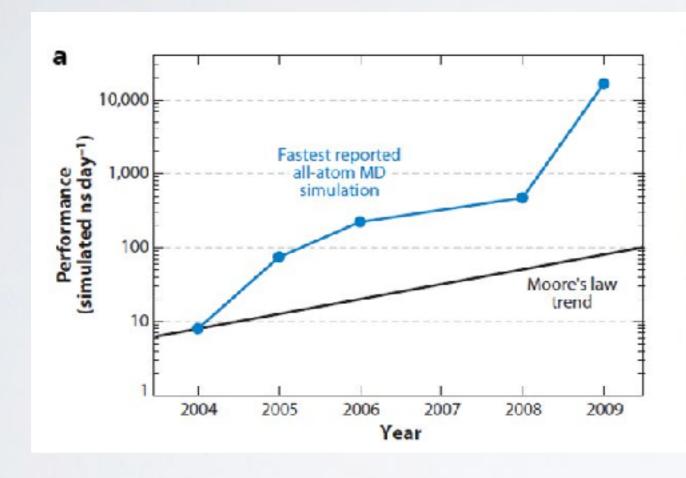
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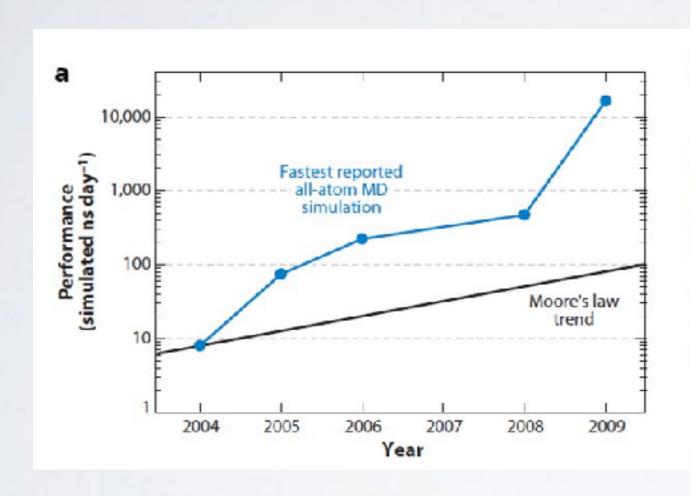
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## SIDE-NOTE: SUPERCOMPUTERS AND GPUS





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# HOW COMPUTERS HAVE CHANGED

DATE	CONT	SEED HENDRY		
1967	1408	0.1 MH	1 M8	MAT
1013	14,000	164	10 GB	LAPTOP
CHANGE	10,000	10,000	10,000	10,000

It cars were the computers then a new Volice would cost \$3, would have a top speed of 1,000,000 km/hr, would carry \$0,000 adults and would park in a shocker.

# **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

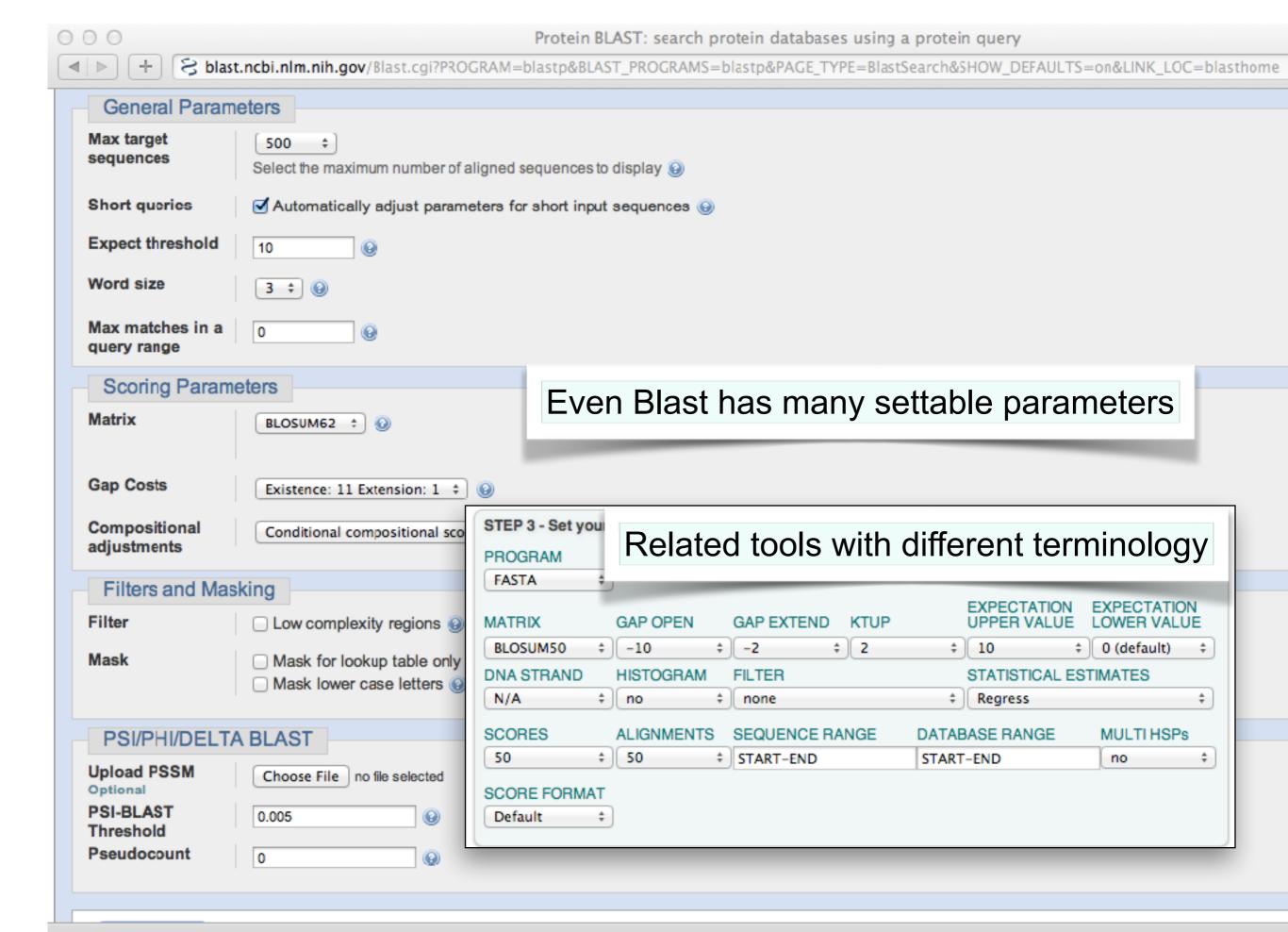
Most tools and databases are written by and for nerds

Same is true of documentation - if any exists!

Most are developed independently

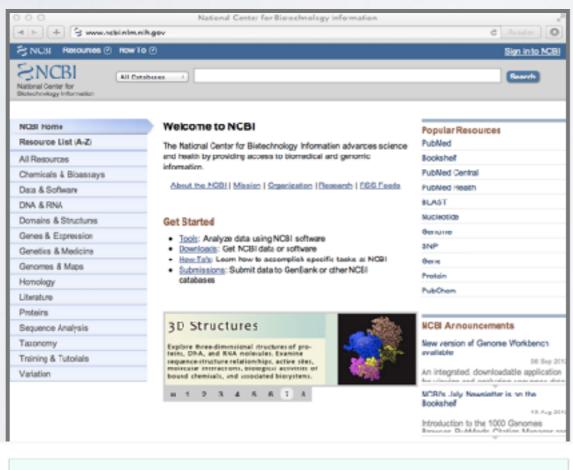
Notable exceptions are found at the:

- EBI (European Bioinformatics Institute) and
- NCBI (National Center for Biotechnology Information)

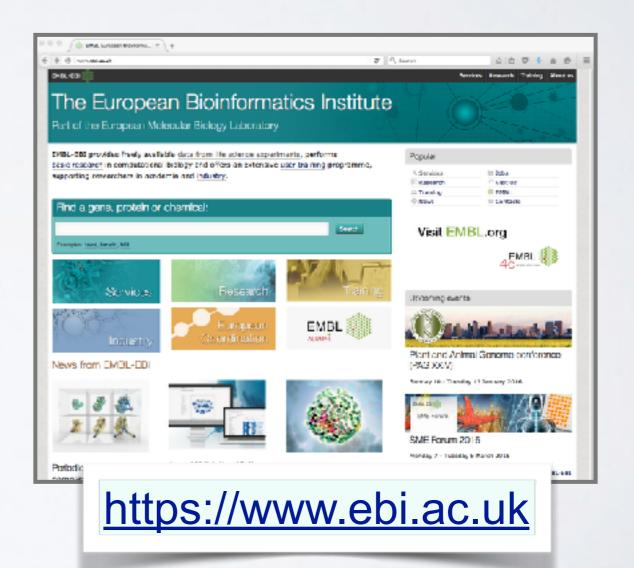


# **Key Online Bioinformatics Resources: NCBI & EBI**

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



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



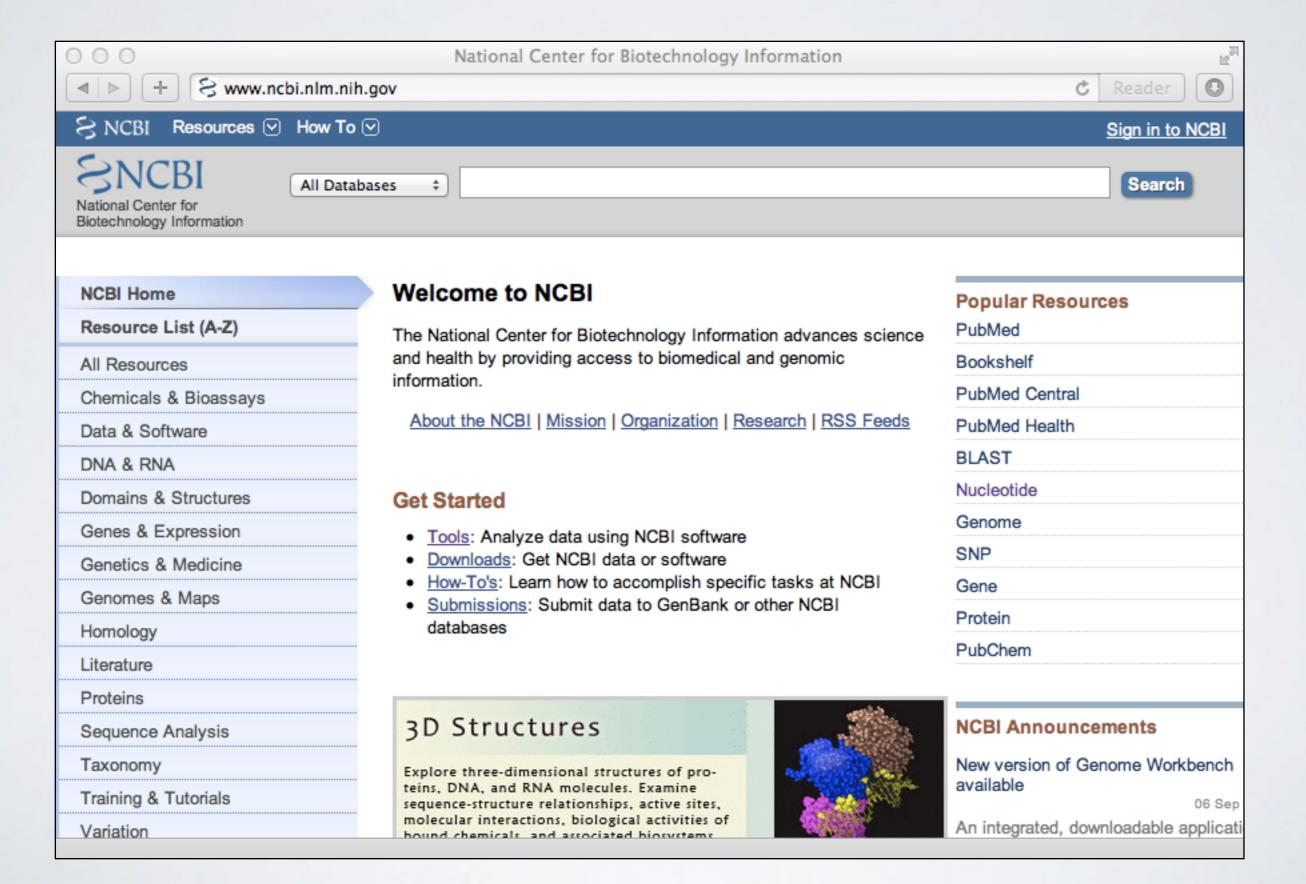
# National Center for Biotechnology Information (NCBI)

- 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

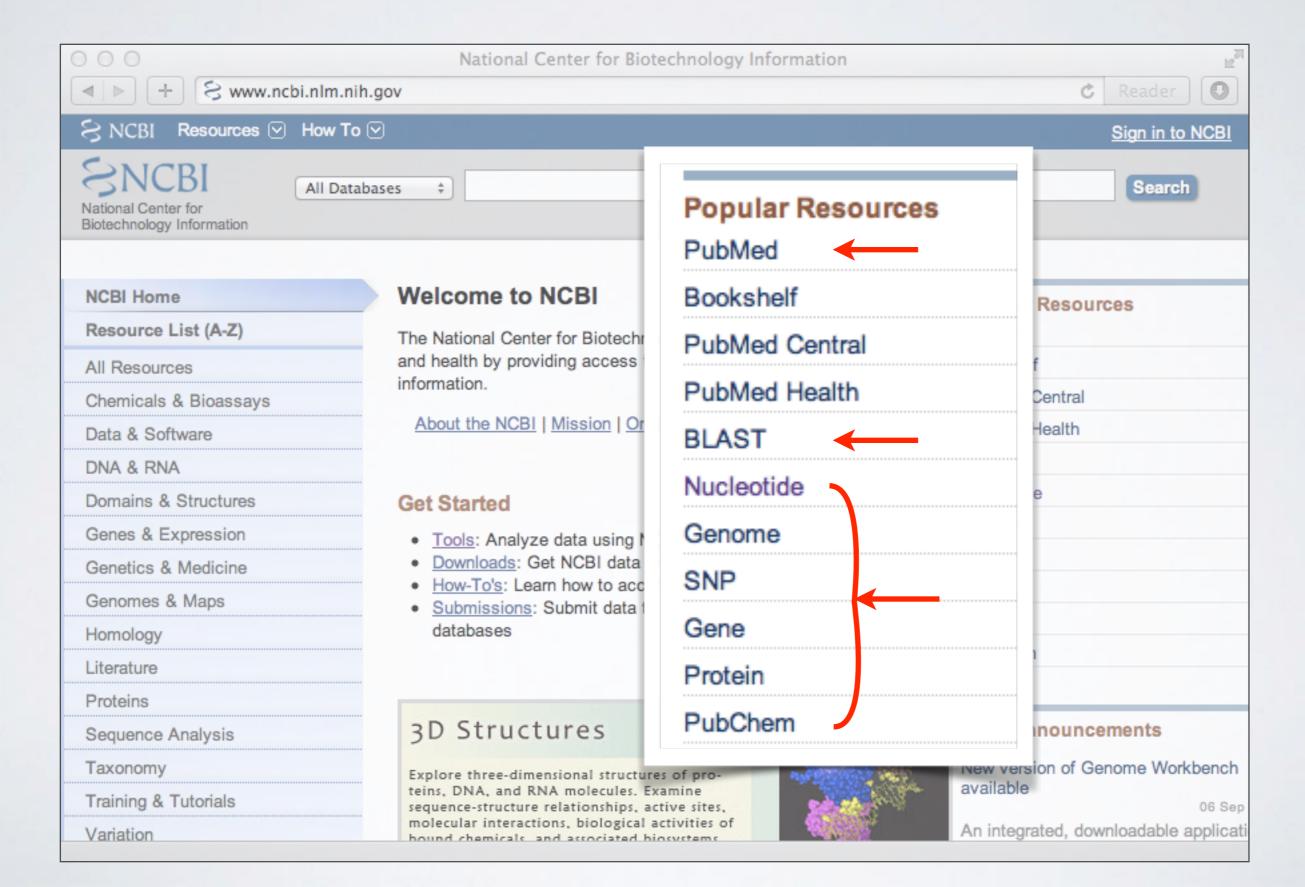


 We will cover a number of core NCBI databases and software tools in the lecture

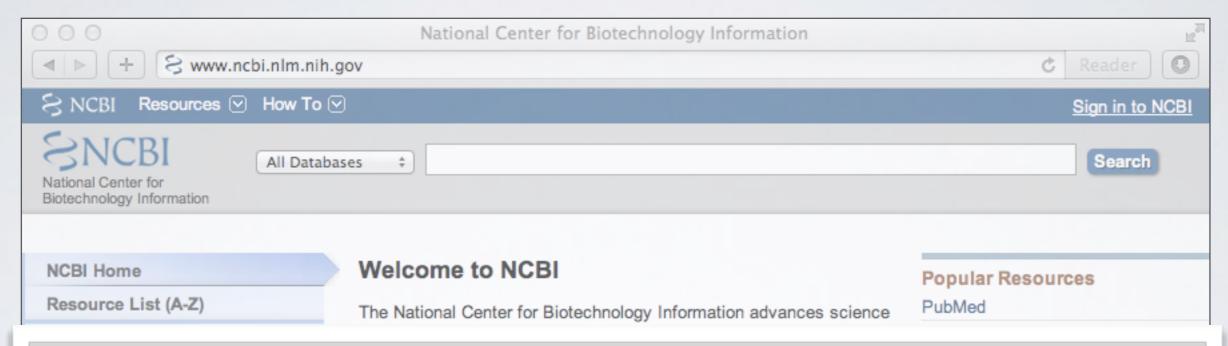
## http://www.ncbi.nlm.nih.gov



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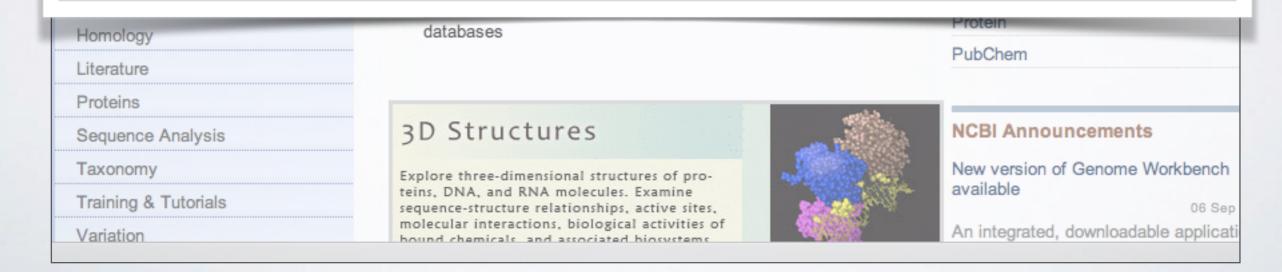


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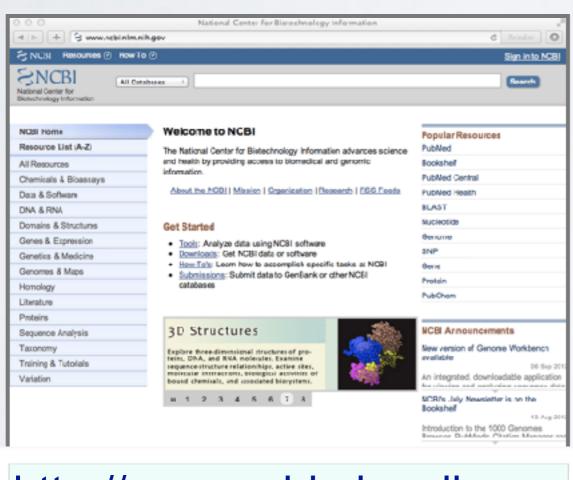
# Notable NCBI databases include: **GenBank**, **RefSeq**, PubMed, dbSNP

and the search tools **ENTREZ** and **BLAST** 

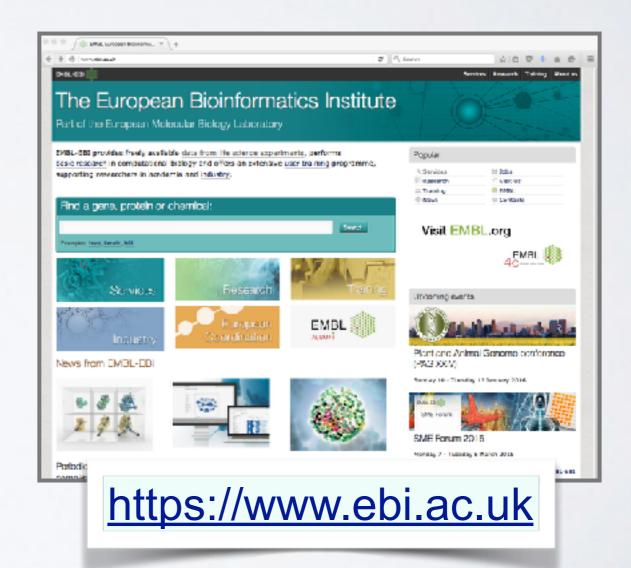


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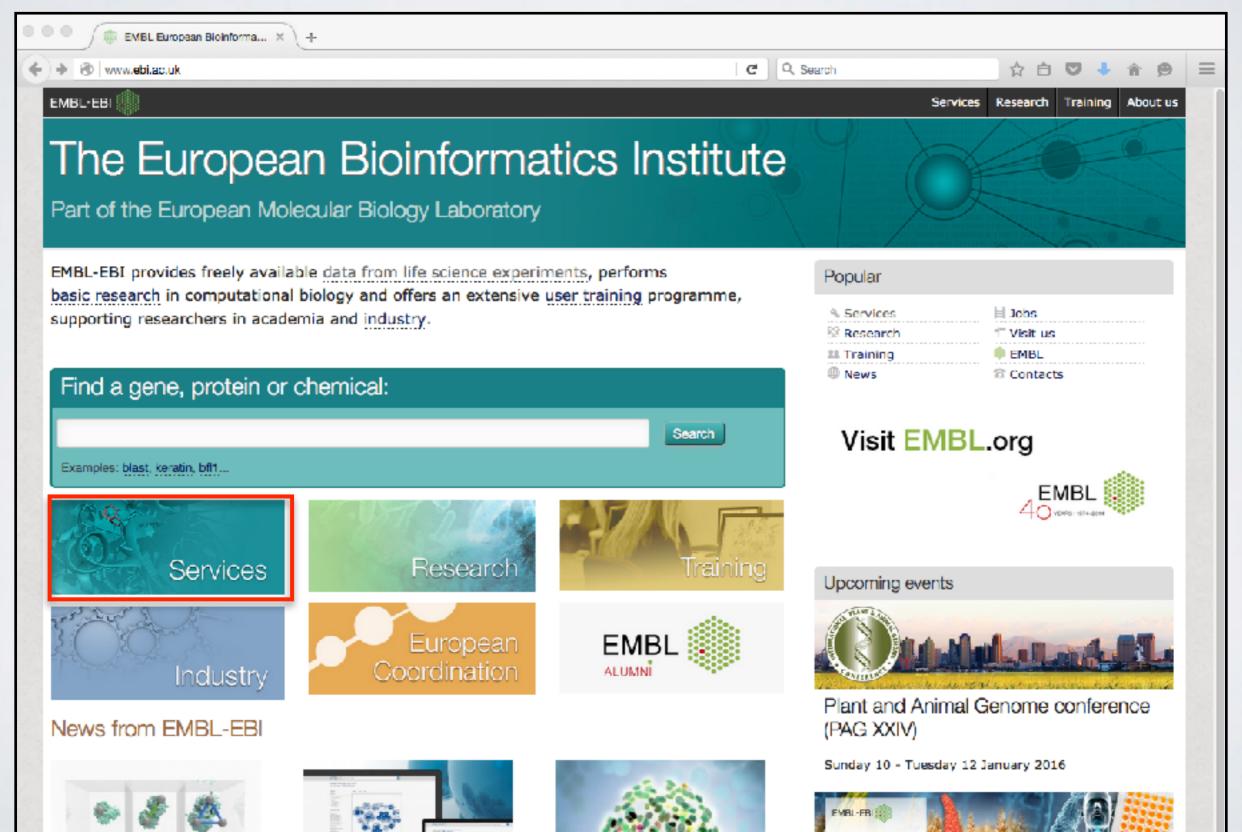
# European Bioinformatics Institute (EBI)

- Created in 1997 as a part of the European Molecular Biology Laboratory (EMBL)
- EBI's mission includes:
  - providing freely available data and bioinformatics services
  - and providing advanced bioinformatics training

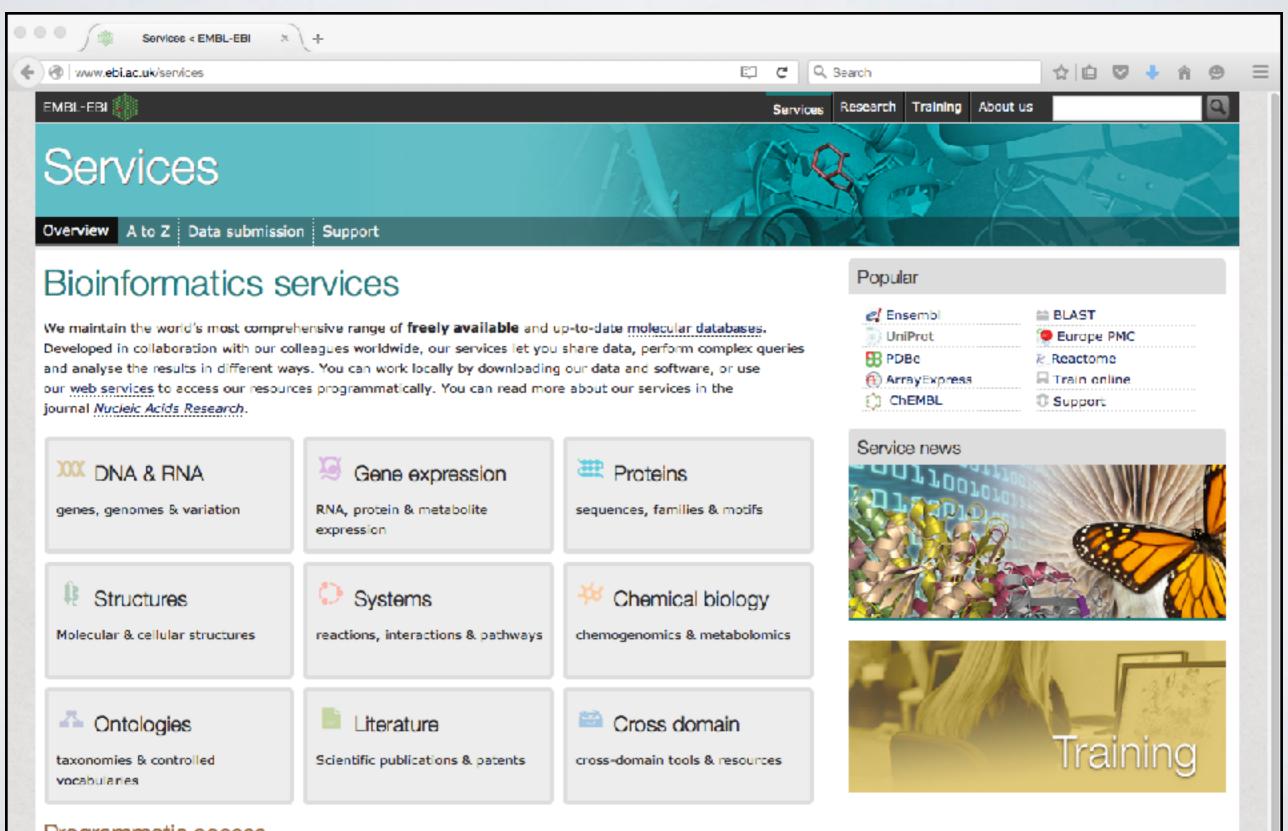


 We will briefly cover several EBI databases and tools that have advantages over those offered at NCBI

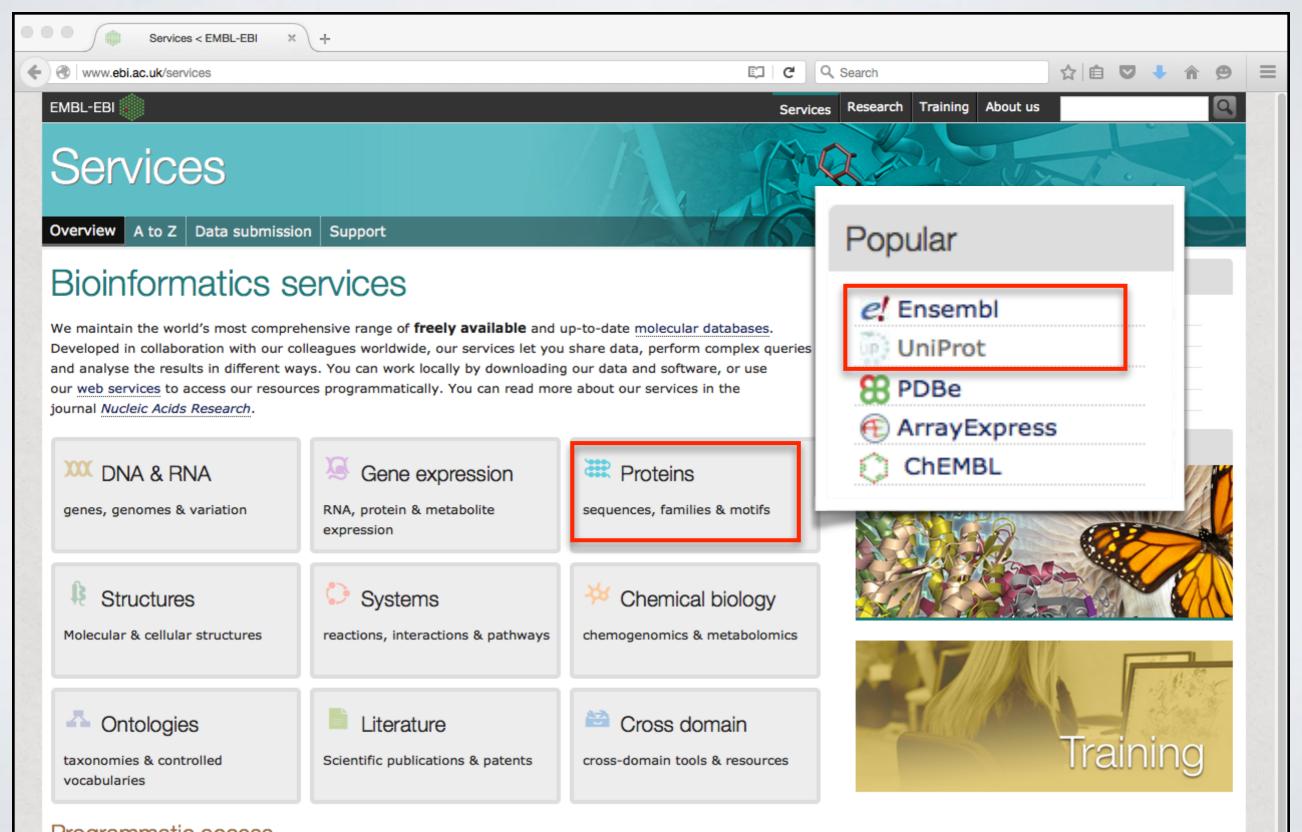
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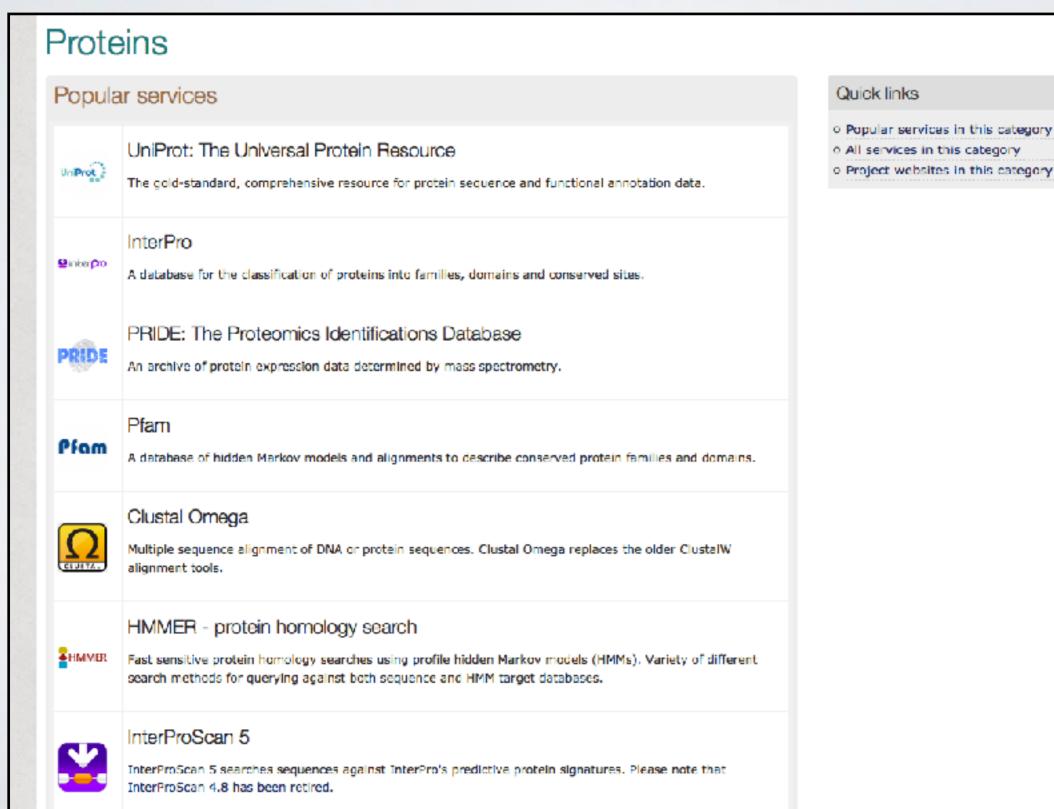


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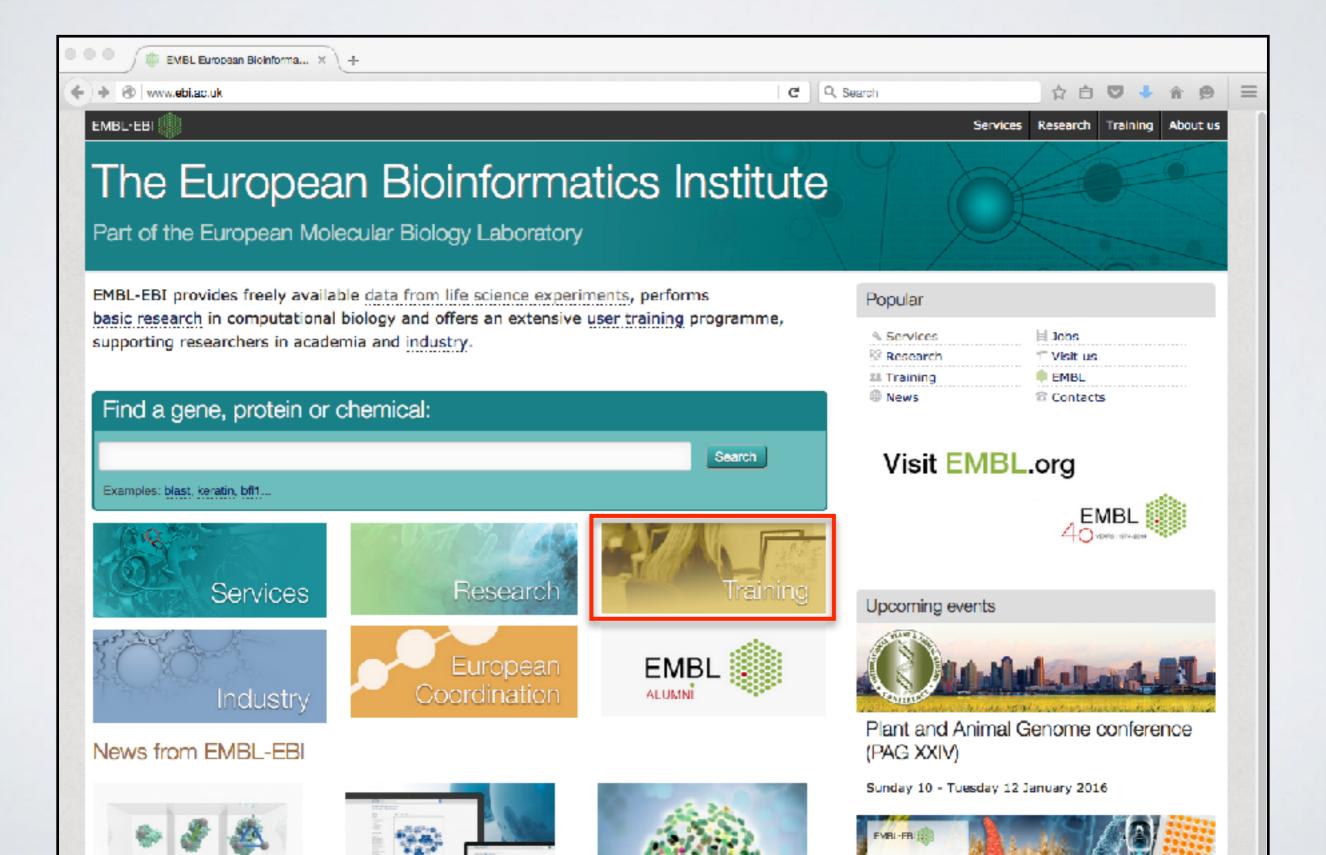
## https://www.ebi.ac.uk

### The EBI makes available a wider variety of online tools than NCBI

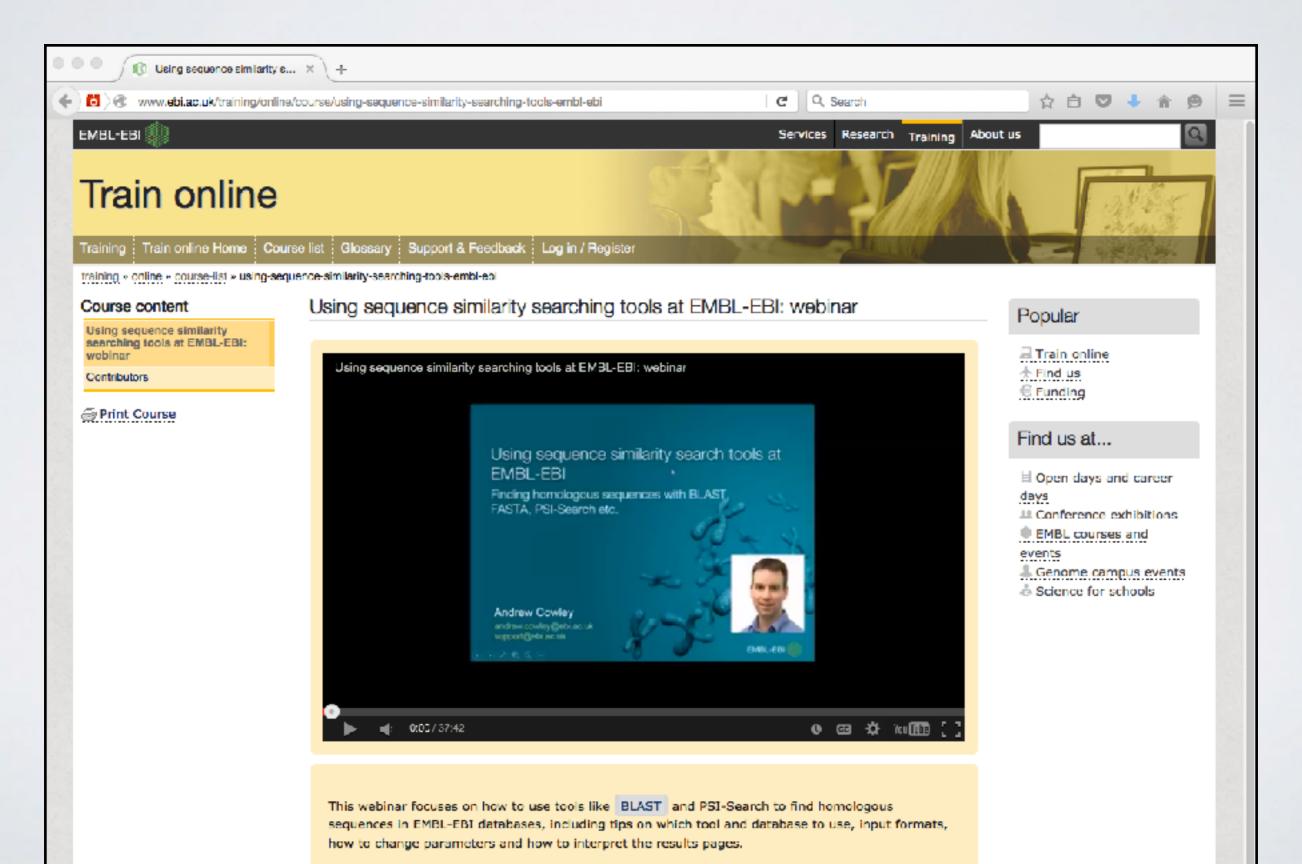


#### Quick links Popular services in this category All services in this category

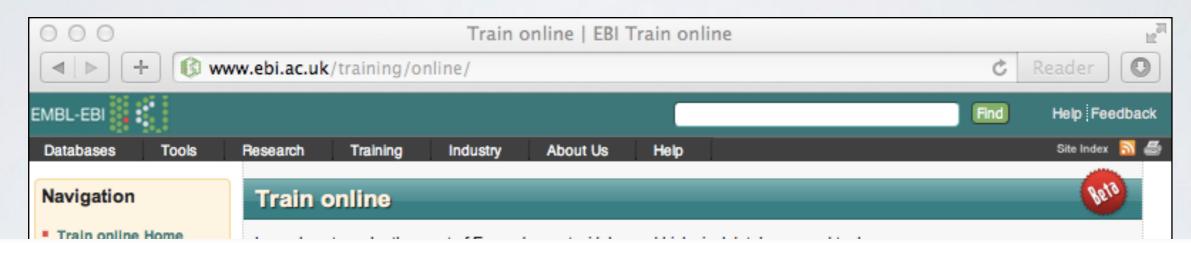
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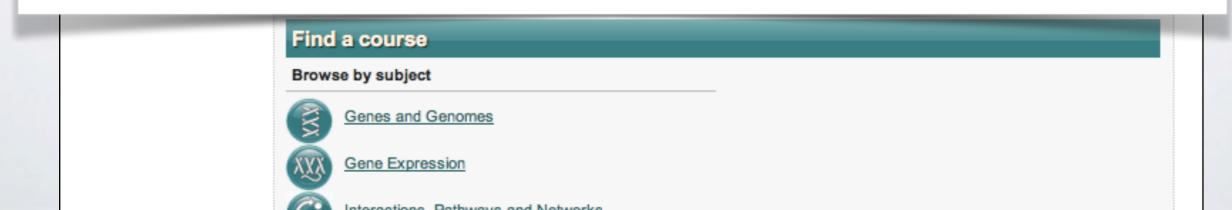


# The EBI also provides a growing selection of **online tutorials** on EBI databases and tools



# Notable EBI databases include: ENA, <u>UniProt</u>, <u>Ensembl</u>

and the tools <u>FASTA</u>, <u>BLAST</u>, <u>InterProScan</u>, <u>MUSCLE</u>, <u>DALI</u>, <u>HMMER</u>



# **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, DOMO, 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, TelDB, TGN, tmRDB, TOPS, TRANSFAC, TRR, UniGene, URNADB, V BASE, VDRR, VectorDB, WDCM, WIT, WormPep, etc ..... !!!!

# **Bioinformatics Databases**

```
AATDB, AceDb, ACUTS, ADB, AFDB, AGIS, AMSdb, ARR, AsDb, BBDB, BCCT
                                                                   Beanref,
        There are lots of Bioinformatics Databases
 Biolmage, BioMagResBank, BIOMDB, BLOCKS, BovGBASE, BOVAN
                                                                   TKbase,
     CANSITE, CarbBank, CARBHYD, CATH, CA7Y
                                                                   AP,
       For a annotated listing of major bioinformatics
  ChickGBASE, Colibri, COPE, CottonDR
                                                                    bEST,
           databases please see the online handout
 dbSTS, DDBJ, DGP, DictyDb D'
                                                                     CDC.
ECGC, EC02DBASE
                                                                      THER,
FlyBase F
                                                                      \Link,
                      < Major Databases.pdf >
                                                                     IAEMB.
                                                KGbase, IMGT, Kabat,
                                   Medline, Mendel, MEROPS, MGDB, MGI,
                            MAP, MIDB, MmtDB, Mol-R-Us, MPDB, MRR, MutBase,
MHC
                   o, O-TycBase, OMIA, OMIM, OPD, ORDB, OWL, PAHdb, PatBase,
 Myd
        Pfam, PhosphoBase, PigBASE, PIR, PKR, PMD, PPDB, PRESAGE, PRINTS,
 ProDom, Prolysis, PROSITE, PROTOMAP, RatMAP, RDP, REBASE, RGP, SBASE, SCOP,
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   Repository, SWISS-PROT, TelDB, TGN, tmRDB, TOPS, TRANSFAC, TRR, UniGene,
     URNADB, V BASE, VDRR, VectorDB, WDCM, WIT, WormPep, etc ..... !!!!
```

# 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.

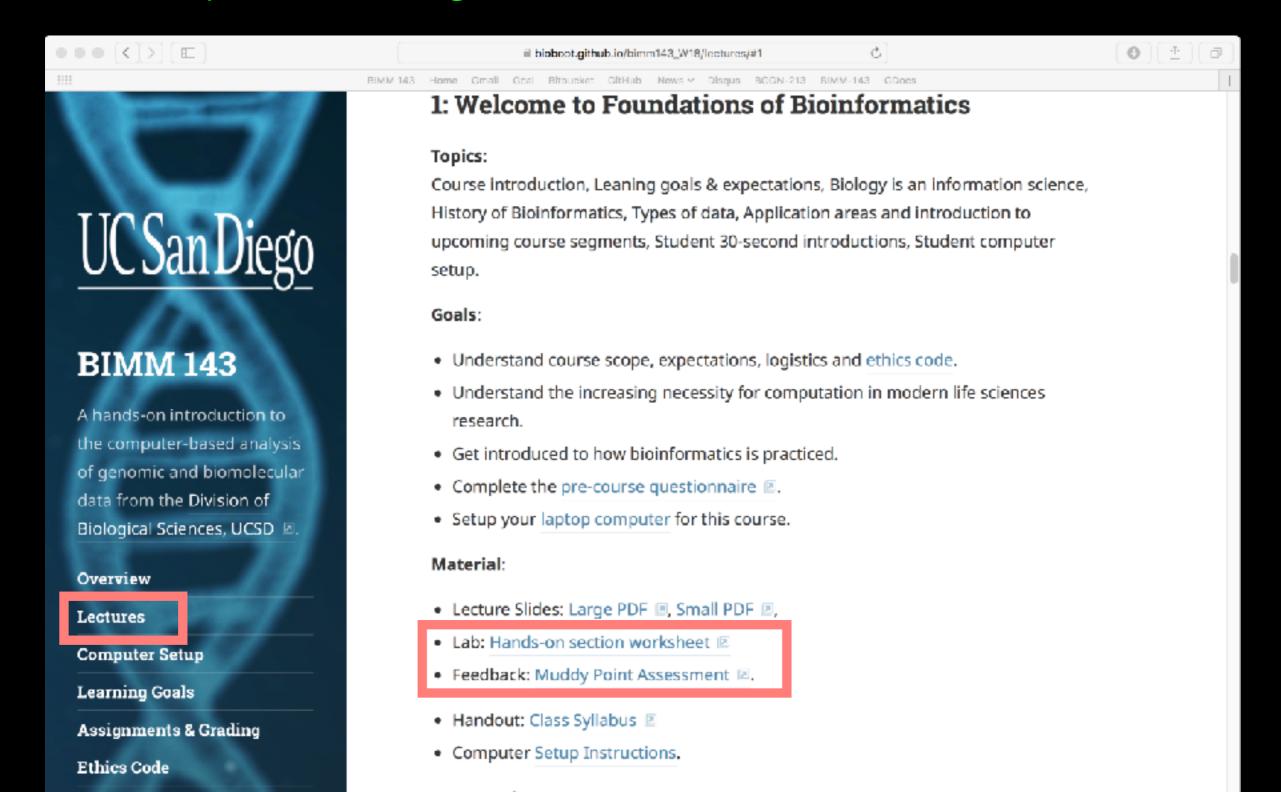
- Primary databases (or <u>archival databases</u>) consist of data derived experimentally.
  - GenBank: NCBI's primary nucleotide sequence database.
  - PDB: Protein X-ray crystal and NMR structures.
- Secondary databases (or <u>derived databases</u>) contain information derived from a primary database.
  - 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.

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# Your Turn!

https://bioboot.github.io/bimm143\_W18/lectures/#1



#### BIMM-143: INTRODUCTION TO BIOINFORMATICS (Lecture 1)

#### Bioinformatics Databases and Key Online Resources

https://bioboot.github.io/bimm143\_W18/lectures/#1

Dr. Barry Grant

Jan 2018

**Overview:** The purpose of this lab session is to introduce a range of bioinformatics databases and associated services available on the Web whilst investigating the molecular basis of a common human disease.

Sections 1 and 2 deal with querying and searching GenBank, GENE and OMIM databases at NCBI. Sections 3 and 4 provide exposure to EBI resources for comparing proteins and visualizing protein structures. Finally, section 5 provides an opportunity to explore these and other databases further with additional examples.

**Side-note:** The Web is a dynamic environment, where information is constantly added and removed. Servers "go down", links change without warning, etc. This can lead to "broken" links and results not being returned from services. Don't give up - give it a second go and try a search 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.

#### >example1

The only information you are given is the above sequence so you must begin your investigation with a sequence search - for this example we will use NCBI's **BLAST** service at: http://blast.ncbi.nlm.nih.gov/

Note that there are several different "basic BLAST" programs available at NCBI (including nucleotide BLAST, protein BLAST, and BLASTx).

## YOUR TURN!

There are five major hands-on sections including:

1.	BLAST, GenBank and OMIM @ NCBI	[~35 mins]
2.	GENE database @ NCBI	[~15 mins]
	— BREAK —	
3.	UniProt & Muscle @ EBI	[~25 mins]
4.	PFAM, PDB & NGL	[~30 mins]

— BREAK —

5. Extension exercises [~30 mins]

- Please do answer the last review question (Q19).
- We encourage <u>discussion</u> and <u>exploration</u>!

## YOUR TURN!

There are five major hands-on sections including:

- BLAST, GenBank and OMIM @ NCBI
- 2. GENE database @ NCBI

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— BREAK —
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- 3. UniProt & Muscle @ EBI
- 4. PFAM, PDB & NGL

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— BREAK —
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5. Extension exercises

- Please do answer the last review question (Q19).
- We encourage <u>discussion</u> and <u>exploration</u>!

# **SUMMARY**

- 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.

# HOMEWORK

https://bioboot.github.io/bimm143 W18/lectures/#1

- **Complete the initial course questionnaire**:
- Check out the "Background Reading" material online:
- Complete the lecture 1 homework questions:

