CS2220: Intro to Computational Biology
Course Briefing

Limsoon Wong

Recommended “Pre-requisites”

- **CS1020 Data Structures and Algorithms I**
- **CS2010 Data Structures and Algorithms II**

- **LSM1101 Biochemistry of Biomolecules**
- **LSM1102 Molecular Genetics**

Objectives

- **Develop flexible and logical problem solving skill**
- **Understand bioinformatics problems**
- **Appreciate techniques and approaches to bioinformatics**

- **To achieve goals above, we expose students to case studies spanning gene feature recognition, gene expression and proteomic analysis, gene finding, sequence homology interpretation, phylogeny analysis, etc.**

Contents of Course Overview

- **Time Table**
- **Course Syllabus**
- **Course Homepage**
- **Teaching Style**
- **Project, Assignments, Exams**
- **Readings**
- **Assessment**

- **Quick Overview of Themes and Applications of Bioinformatics**

Time Table

- **Lecture**
  - Thursday 9am – 11am, SR@LT19
- **Tutorial**
  - Thursday11am – 12nn, SR@LT19
- **Email**
  - wongls@comp.nus.edu.sg

- **Consultations**
  - Any time; just make appt to make sure I am in
  - Pls email my PA, tanps@comp.nus.edu.sg

Course Syllabus

- **Intro to Bioinformatics**
  - molecular biology basics
  - tools and instruments for molecular biology
  - themes and applications of bioinformatics
- **Essence of Knowledge Discovery**
  - Classification performance measures
  - Feature selection techniques
  - Supervised & unsupervised machine learning techniques
- **Gene Feature Recognition from Genomic DNA**
  - Feature generation, selection, & integration
  - Translation initiation site (TIS) recognition
  - Transcription start site (TSS) recognition
- **Gene Expression Analysis**
  - Microarray basics
  - Gene expression profile normalization
  - Classification of gene expression profiles
  - Clustering of gene expression profiles
  - Molecular network reconstruction
- **Essence of Seq Comparison**
  - Dynamic programming basics
  - Sequence comparison and alignment basics
  - Needleman-Wunsh global alignment algorithm
  - Smith-Waterman local alignment algorithm
- **Seq Homology Interpretation**
  - protein function prediction by sequence alignment
  - protein function prediction by phylogenetic profiling
  - active site and domain prediction
  - key mutation sites prediction
- **Gene Finding**
  - Overview of gene finding
  - GRAIL
  - Handling of frame shifts and in-dels
- **Phylogenetic Trees**
  - Phylogeny reconstruction method basics
  - origin of Polynesians & Europeans
  - Large-scale sequencing basics
- **Some hot current topics like PPI, miRNA, etc.**

Course Homepage

- **IVLE**
  - https://ivle.nus.edu.sg/module/student/?CourseID=8114af75-4c4b-42af-a4d4-2acd299014b6

- **Lecture Slides & etc**
  - http://www.comp.nus.edu.sg/~wongls/courses/cs2220/2013

Teaching Style

- **Bioinformatics is a broad area**
- **Need to learn a lot of material by yourself**
  - Reading books
  - Reading papers
  - Practice on the web
- **Don’t expect to be told everything**

Assignments, Project, & Exam

- **Assignments (35% of marks)**
  - 3 assignments
  - Some simple programming required
- **Project (15% of marks)**
  - Based on material associated with e-learning
  - 8-10 pages of report / ppt slides expected
- **Exam (50% of marks)**
  - 1 final open-book exam

Be Honest

- **Exam**
  - Absence w/o good cause results in ZERO mark
  - Cheating results in ZERO mark
- **Discussion on assignments is allowed**
- **Blatant plagiarism is not allowed**
  - Offender gets ZERO mark for assignment or exam
  - Penalty applies to those who copied AND those who allowed their assignments to be copied

Returning Exam Scripts

- **We will return the exam scripts to students. So adopt different procedure from the usual university exam**

- **For the exam**
  - Treated as an “extra CA” for the course
  - Held in reading week @ the normal lecture slot in normal lecture room

- **For returning the script**
  - Lecturer records mark on IVLE Gradebook
  - Lecturer returns marked script to students in exam week 1 or 2
  - Student checks mark in IVLE after receiving script for correctness
  - Student may make appointment with lecturer to discuss the script till end of exam week 2. After that, no appeal will be entertained
    - **Lecturer photostats scripts. If a student appeals, his script will be compared against its copy. If modified, the student will be considered to have cheated**

Background Readings

- **Limsoon Wong, *The Practical Bioinformatician*, WSPC, 2004**
- **Wing-Kin Sung, *Algorithms in Bioinformatics: A Practical Introduction*, CRC, 2010**
- **Marketa Zvelebil and Jeremy Baum, *Understanding Bioinformatics*, Garland, 2007**

What comes after CS2220

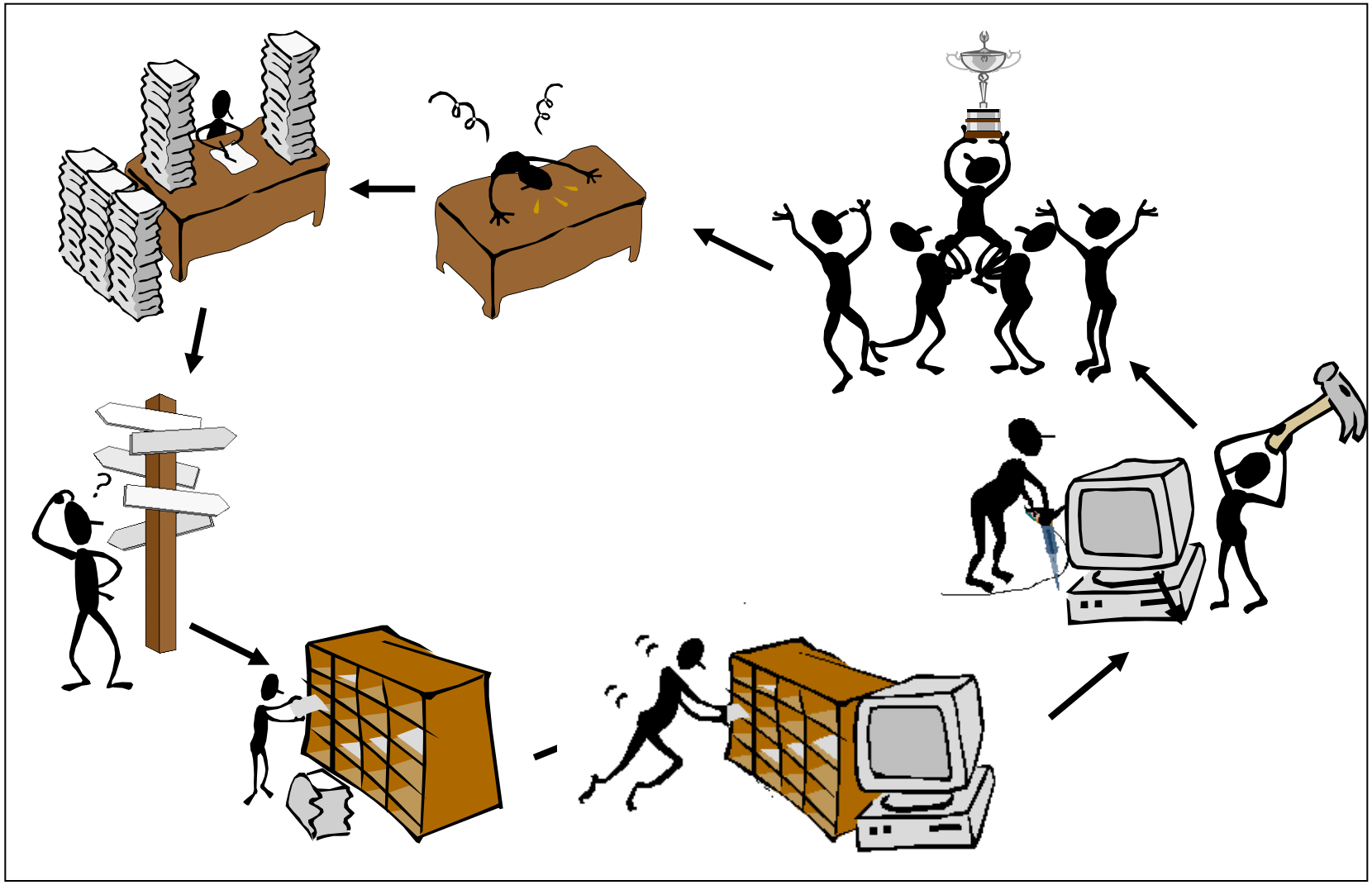
- **CS2220 Introduction to Computational Biology**
  - Understand bioinformatics problems; interpretational skills
- **CS3225 Combinatorial Methods in Bioinformatics**
- **CS4220 Knowledge Discovery Methods in Bioinformatics**
  - Clustering; classification; association rules; SVM; HMM; Mining of seq, trees, & graphs
- **CS5238 Advanced Combinatorial Methods in Bioinformatics**
  - Seq alignment, whole-genome alignment, suffix tree, seq indexing, motif finding, RNA sec struct prediction, phylogeny reconstruction
- **CS6221 Modeling & Analysis Techniques in Systems Biology**
  - Dynamics of biochemical and signaling networks; modeling, simulating, & analyzing them
- **Etc …**

Any questions?

I hope you will enjoy this class ☺

Themes and Applications of Bioinformatics

What is Bioinformatics?



Themes of Bioinformatics
Themes of This Course

Bioinformatics involves

Data Mgmt +

Knowledge Discovery +

Sequence Analysis +

Physical Modeling + ...

Knowledge Discovery =

Statistics + Algorithms + Databases

The Promises of Bioinformatics

To the patient:

Better drug, better treatment

To the pharma:

Save time, save cost, make more $

To the scientist:

Better science

Fulfilling the Promise via Drugs

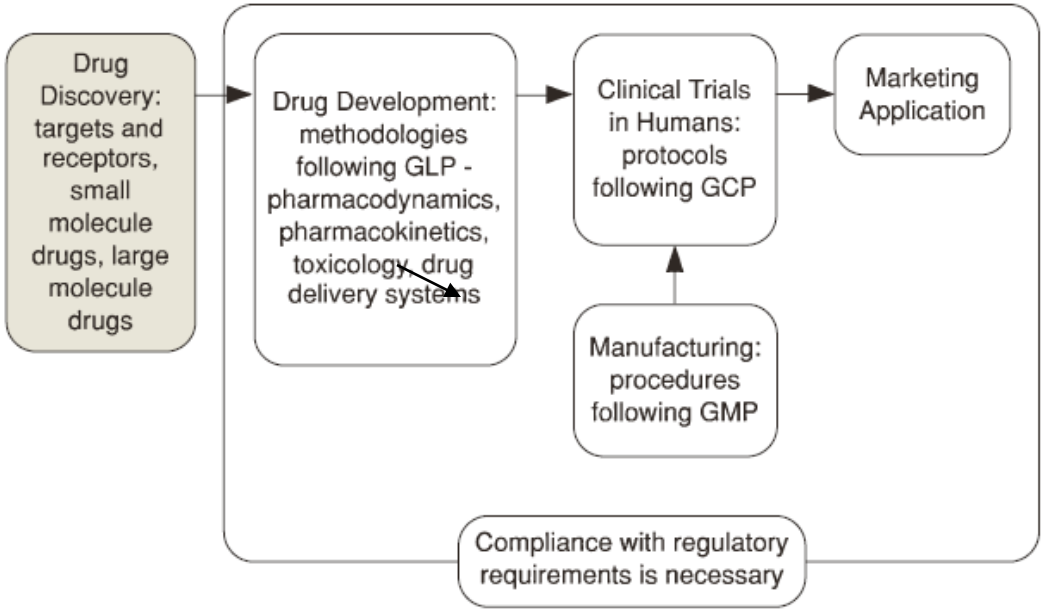


Figure from Rick Ng, *Drugs: From Discovery to Approval*

- **Bioinformatics is applicable to drug development**
- **Drug discovery: Design small molecules that bind target proteins**
  - Which proteins?
  - What should binding accomplish?
- **Biomarkers**

Pervasiveness of Bioinformatics

- **Bioinformatics is mandatory for large-scale biology**
  - e.g., High-throughput, massively-parallel measurements, or “lab on a chip” miniaturization
- **Computational data analysis is mandatory for indirect experimental methods**
  - e.g., reconstruction based on phase contrast or wave diffraction
- **What about the rest of biology (and medicine) ?**
- **Limitless opportunities!**

Some Bioinformatics Problems

- **Biological Data Searching**
- **Biological Data Integration**
- **Gene/Promoter finding**
- **Cis-regulatory DNA**
- **Gene/Protein Network**
- **Protein/RNA Structure Prediction**
- **Evolutionary Tree reconstruction**
- **Infer Protein Function**
- **Disease Diagnosis**
- **Disease Prognosis**
- **Disease Treatment Optimization, ...**

Biological Data Searching

- **Biological Data is increasing rapidly**
- **Biologists need to locate required info**
- **Difficulties:**
  - Too much
  - Too heterogeneous
  - Too distributed
  - Too many errors
  - Need approximate searches because of errors, mutations, etc.

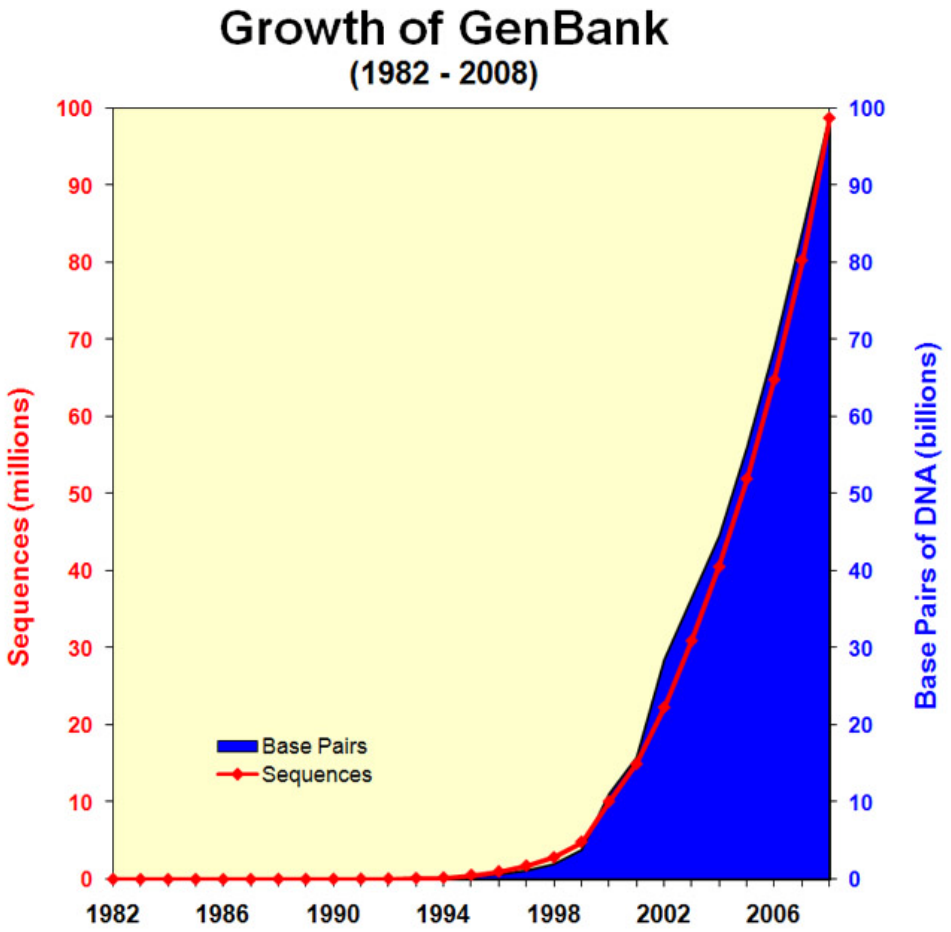


Image credit: NCBI

Cis-Regulatory DNAs

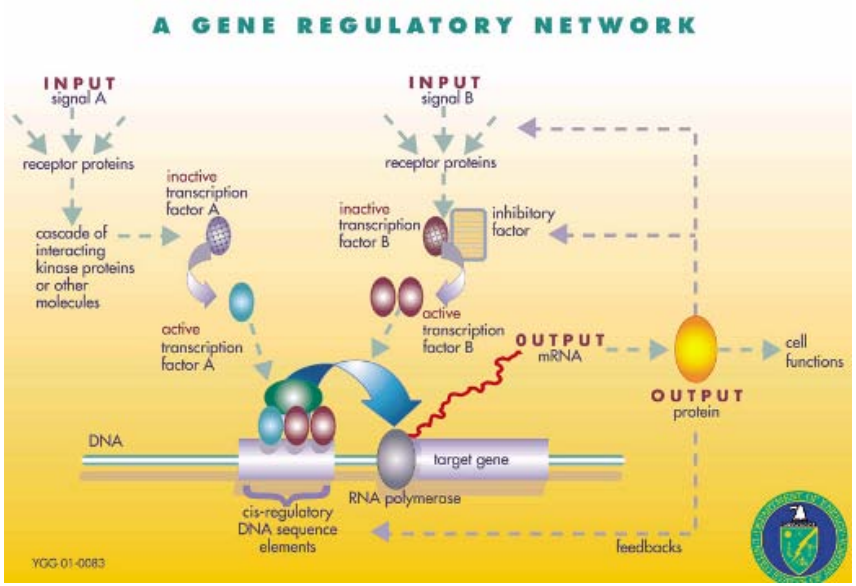
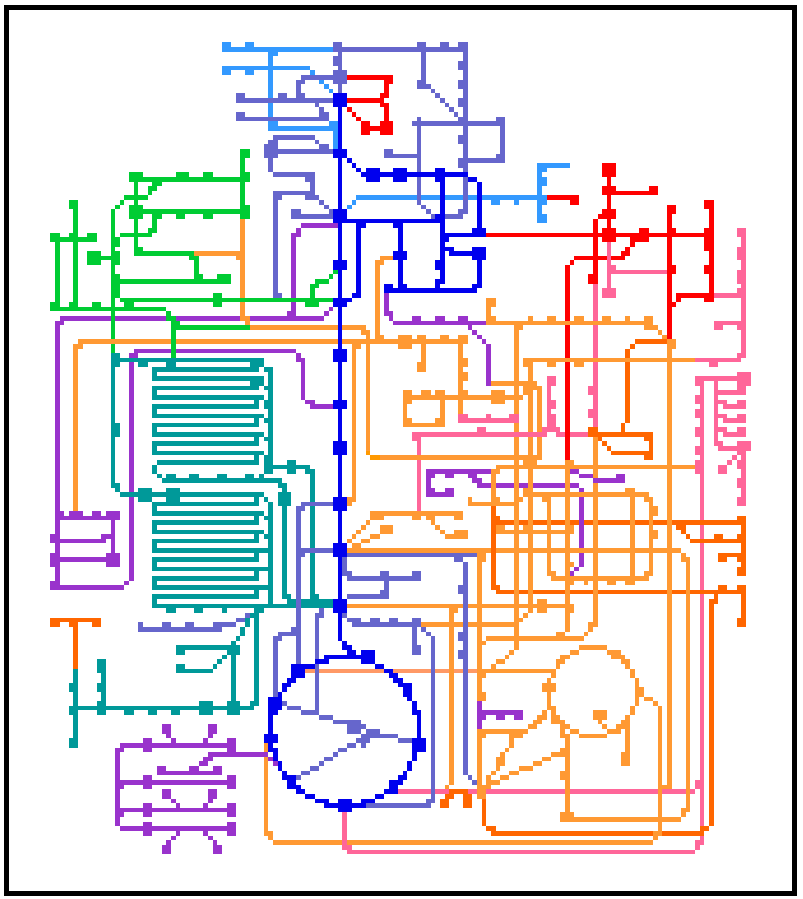


Image credit: US DOE

- **Cis-regulatory DNAs control whether genes should express or not**
- **Cis-regulatory DNAs may locate in promoter region, intron, or exon**
- **Finding & understanding cis-regulatory DNAs is one of the key problem in coming years**

Gene Networks

- **Cell is a complex system**
- **Expression of one gene depends on expression of another gene**
- **Such interactions can be form gene network**
- **Understanding such networks helps identify association betw genes & diseases**



Protein/RNA Structure Prediction

- **Structure of Protein / RNA is essential to its functionality**
- **Impt to predict structure of a protein / RNA given its seq**
- **Problem is considered a "grand challenge" problem in bioinformatics**

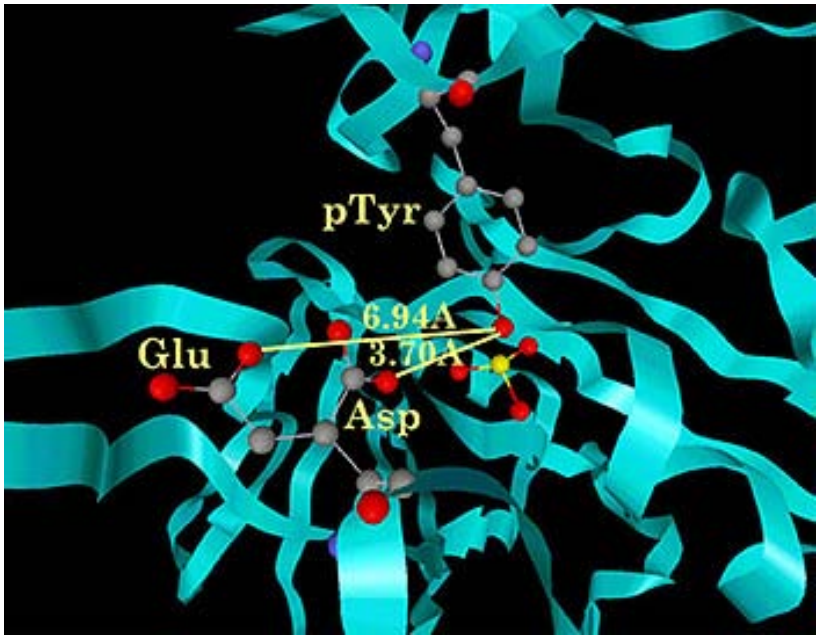
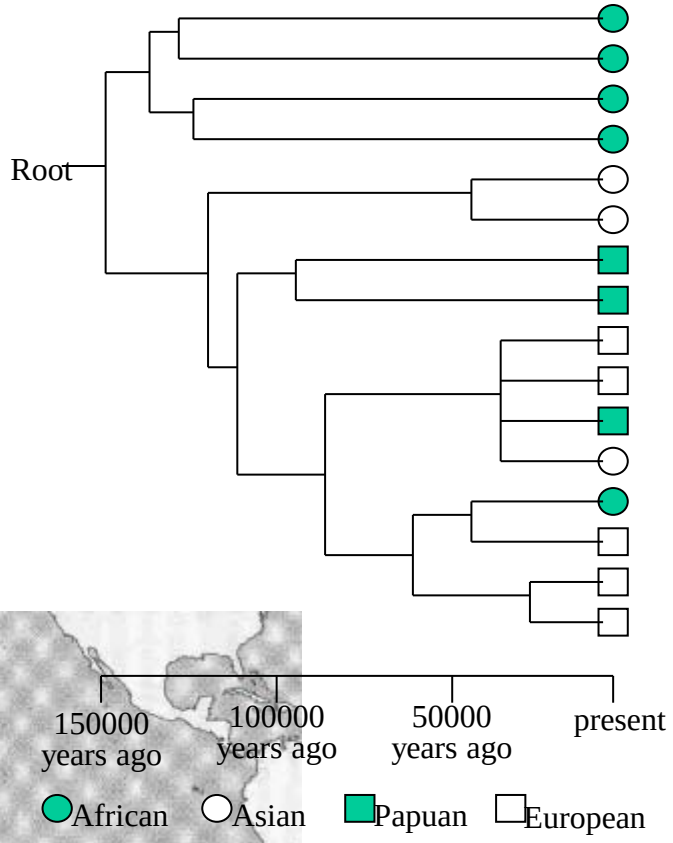


Image credit: Kolatkar

Evolutionary Tree Reconstruction

- **Protein /RNA / DNA mutates**
- **Evolutionary tree studies evolutionary relationship among set of protein / RNA / DNAs**
- **Origin of species**



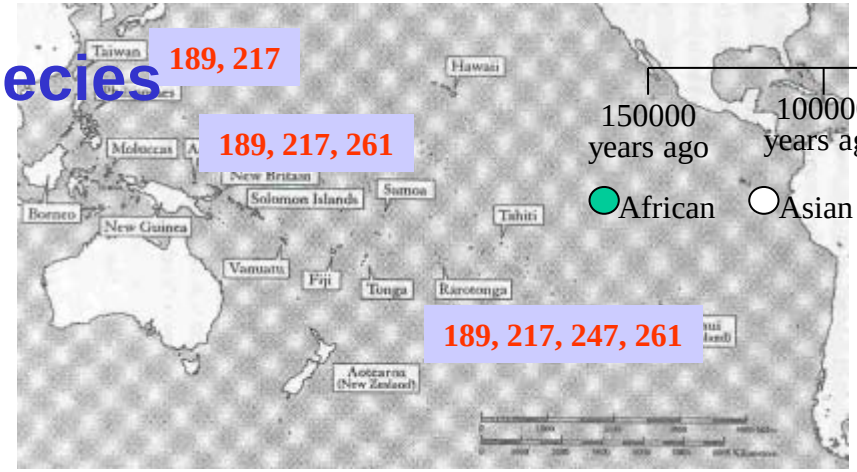


Image credit: Sykes

Breast Cancer Outcome Prediction

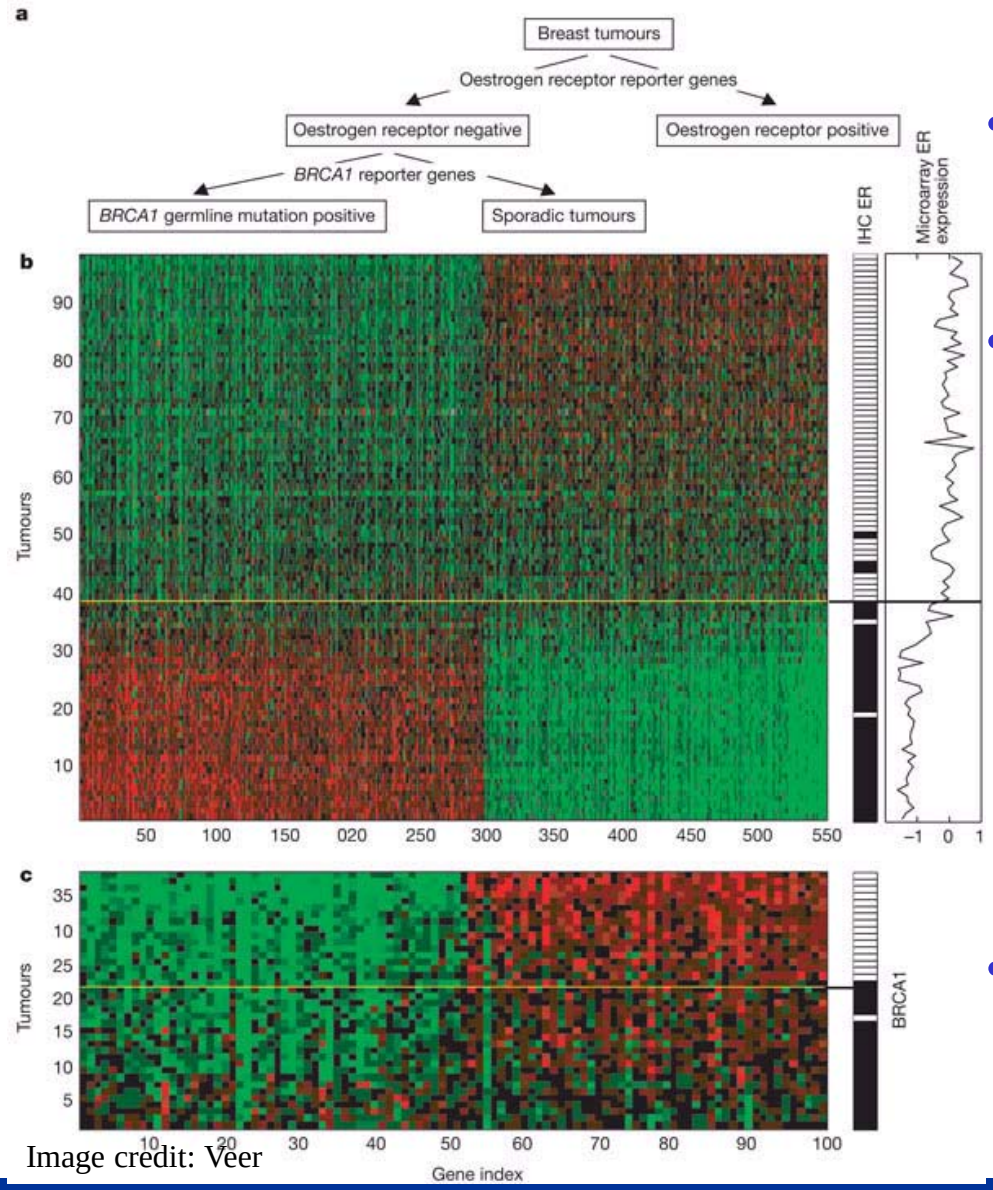


Image credit: Veer

- **Van't Veer et al., *Nature* 415:530-536, 2002**
- **Training set contains 78 patient samples**
  - 34 patients develop distance metastases in 5 yrs
  - 44 patients remain healthy from the disease after initial diagnosis for >5 yrs
- **Testing set contains 12 relapse & 7 non-relapse samples**

Commonly Used Data Sources

Type of Biological Databases

- **Micro Level**
  - Contain info on the composition of DNA, RNA, Protein Sequences
- **Metadata**
  - Ontology
  - Literature

- **Macro Level**
  - Contain info on interactions
    - **Gene Expression**
    - **Metabolites**
    - **Protein-Protein Interaction**
    - **Biological Network**

Exercise: Name a protein seq db and a DNA seq db

Transcriptome Database

- **Complete collection of all possible mRNAs (including splice variants) of an organism**
- **Regions of an organism's genome that get transcribed into messenger RNA**
- **Transcriptome can be extended to include all transcribed elements, including non-coding RNAs used for structural and regulatory purposes**

Exercise: Name a transcriptome database

Gene Expression Databases

- **Detect what genes are being expressed or found in a cell of a tissue sample**

- **Single-gene analysis**
  - Northern Blot
  - In Situ Hybridization
  - RT-PCR

- **Many genes: High throughput arrays**
  - cDNA Microarray
  - Affymetrix GeneChip® Microarray

Exercise: Name a gene expression database

Metabolites Database

- **A metabolite is an organic compound that is a starting material in, an intermediate in, or an end product of metabolism**
- **Metabolites dataset are also generated from mass spectrometry which measure the mass the these simple molecules, thus allowing us to estimate what are the metabolites in a tissue**

- **Starting metabolites**
  - Small, of simple structure, absorbed by the organism as food
  - E.g., vitamins and amino acids
- **Intermediary metabolites**
  - The most common metabolites
  - May be synthesized from other metabolites, or broken down into simpler compounds, often with the release of chemical energy
  - E.g., glucose
- **End products of metabolism**
  - Final result of the breakdown of other metabolites
  - Excreted from the organism without further change
  - E.g., urea, carbon dioxide

Protein-Protein Interaction Databases

- **Proteins are true workhorses**
  - Lots of cell's activities are performed thru PPI, e.g., message passing, gene regulation, etc.
- **Function of a protein depends on proteins it interacts with**
- **Methods for generating PPI db**
  - biochemical purifications, Y2H, synthetic lethals, in silico predictions, mRNA-co-expression
- **Contain many false positives & false negatives**

Exercise: Name a PPI database

Any Question?

Acknowledgements

- **Most of the slides used in this lecture are based on original slides created by**
  - Ken Sung
  - Anthony Tung

- **But you should blame me for any errors**

References

- **S.K. Ng, "Molecular Biology for the Practical Bioinformatician", *The Practical Bioinformatic*ian, Chapter 1, pages 1-30, WSPC, 2004**

- **DOE HGP Primer, http://www.ornl.gov/sci/techresources/Human_Genome/publicat/primer/index.shtml**

- **Lots of useful videos, http://www.as.wvu.edu/~dray/Bio_219.html**