CS4220: Knowledge Discovery Methods in Bioinformatics
Course Briefing

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Recommended “Pre-requisites”

- **Completed modules on**
  - Programming
  - Algorithms
  - Basic molecular biology
  - **ST2334 Probability & Statistics**
  - **CS2220 Introduction to Computational Biology**

Objectives

- **Exposure to knowledge-discovery techniques**
- **Enhance flexible & logical problem-solving skill**
- **Understand bioinformatics problems and their solution in depth**
  - A modern network-based perspective

- **To achieve goals above, we expose students to case studies spanning gene expression and proteomic analysis, protein functional prediction, epistatic interaction analysis, etc.**

Contents of Course Overview

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- **Teaching Style**
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- **Assessment**

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

Time Table

- **Lecture**
  - – Wednesday 9am – 11am, COM1-208
- **“Tutorial” (it is actually integrated into lecture)**
  - – Wednesday 11am – 12nn, COM1-208

- **Emails**
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  - – nagarajann@gis.a-star.edu.sg

- **Consultation**
  - – Any time; just make appt

Course Syllabus

- **Essence of Biostatistics**
  - Statistical estimation
  - Hypothesis testing
  - Principle component analysis
- **Essence of Data Mining**
  - Clustering
  - Association rules
  - Classification
  - Class-imbalance learning
- **Gene Expression Analysis**
  - Basic gene expression analysis
  - Batch effect & normalization
  - Improving reproducibility
  - Dealing with small sample
- **Proteomic Profile Analysis**
  - Basic proteomic profile analysis
  - Improving consistency
  - Improving coverage
- **Protein Interaction Network**
  - Consistency, comprehensiveness of pathway databases
  - Integration of pathway databases
  - Reliability of PPI network
- **Protein Complex Prediction**
  - Basic approaches
  - Overlapping complexes
  - Low-density complexes
  - Small complexes
- **Network Perturbations in Disease Context**
- **Transcription Factor Interaction Identification**

Teaching Style

- **Bioinformatics is a broad area**

- **Need to learn a lot of material by yourself**
    - Reading books
    - Reading papers
    - Practise on the web

And do this before each lecture!

- **Don’t expect to be told everything**

Assignments, Project, & Exam

- **Assignments (30-40% of marks)**
  - 3 to 4 assignments
  - Some are simple programming assignments

- **Project (20-30% of marks)**
  - Based on a case study in the class
  - 8-10 pages of report / ppt slides expected

- **Exam (40% 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 & project 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

Background Readings

- **Every lecture will be accompanied by a small set of “must-read” and “good-to-read” articles**
  - The “must-read” articles are considered lecture notes and are examinable

Related Courses

- **CS2220 Introduction to Computational Biology**
  - Understand bioinformatics problems; interpretational skills
- **CS3225 Combinatorial Methods in Bioinformatics**
- **CS4220 Knowledge Discovery Methods in Bioinformatics**
  - Gene expression, proteomic profiling, protein interaction, transcription factor interaction, pathway perturbation
- **CS5238 Advanced Combinatorial Methods in Bioinformatics**
  - Seq alignment, whole-genome alignment, suffix tree, seq indexing, motif finding, RNA sec struct prediction, phylogeny reconstruction
- **CS6222 Computational frontier in precision medicine**
- **Etc …**

Any questions?

I hope you will enjoy this class ☺

Themes and Applications of Bioinformatics

These slides are for those who have not taken CS2220 to read at your own leisure

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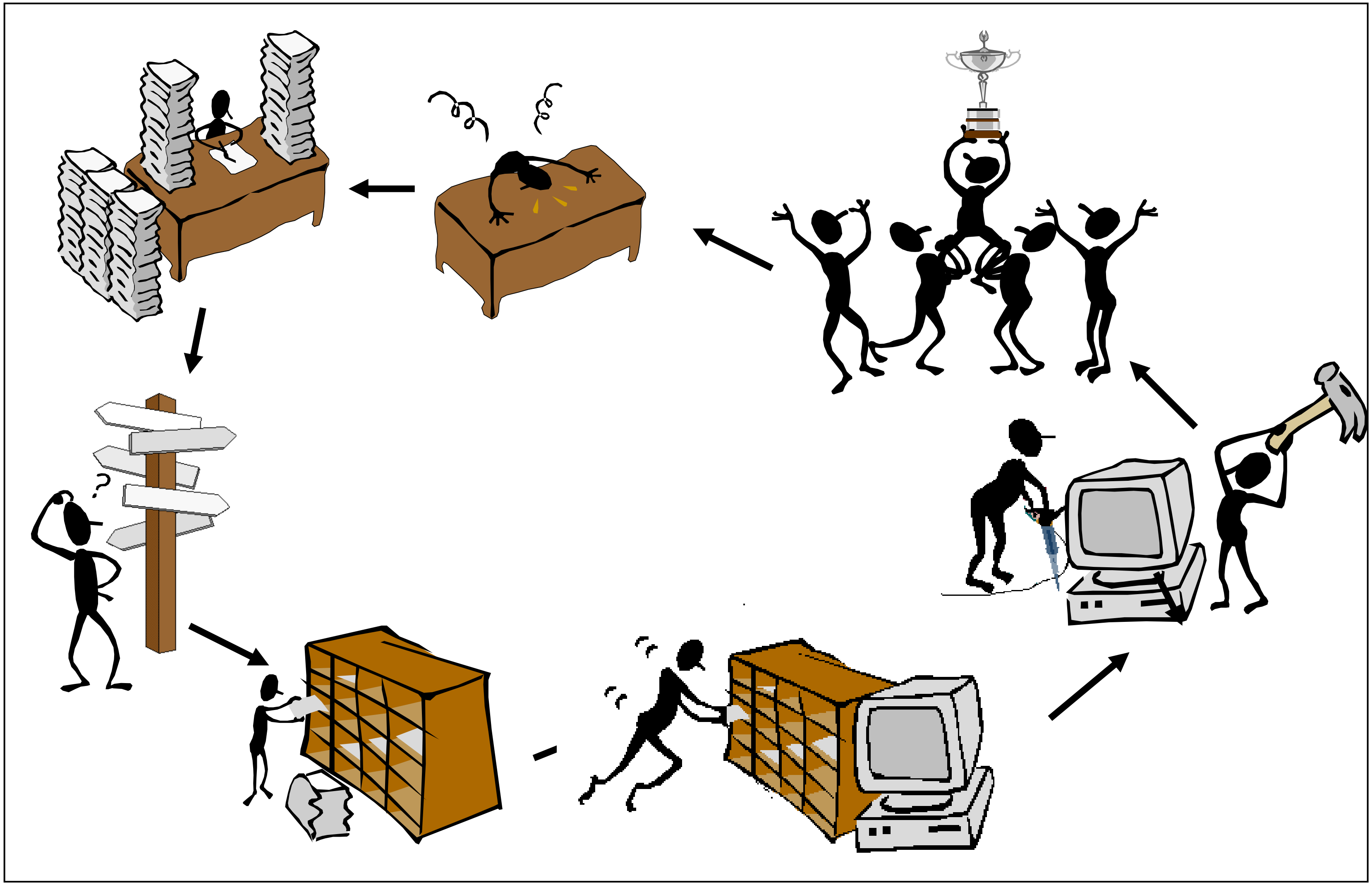
What is Bioinformatics?



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

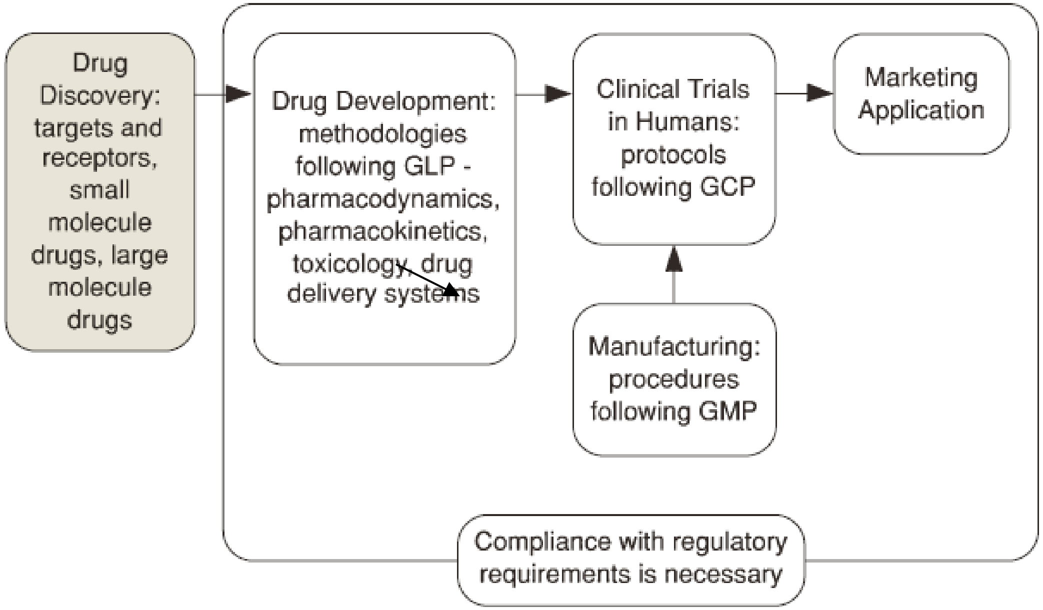


Figure from Rick Ng, *Drugs: From Discovery to Approval*

- **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, ...**

Commonly Used Data Sources

These slides are for those who have not taken CS2220 to read at your own leisure

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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

Introductory References

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

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

- **Materials from CS2220, http://www.comp.nus.edu.sg/~wongls/courses/cs2220/2015**