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**

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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

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

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

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Time Table

- **Lecture**
  - Thursday 9am – 11am, COM1-208
- **"Tutorial"**
  - Thursday 11am – 12nn, COM1-208

- **Emails**
  - wongls@comp.nus.edu.sg
  - nagarajann@gis.a-star.edu.sg

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

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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**

Course Homepage

- **IVLE**
  - https://ivle.nus.edu.sg/v1/Module/Student/default.aspx?CourseID=b8292ca8-7ade-4c10-b72f-50d7a6f008c3

- **Lecture Slides & etc**
  - http://www.comp.nus.edu.sg/~wongls/courses/cs4220/2016

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)**
  - 2 to 3 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 …**

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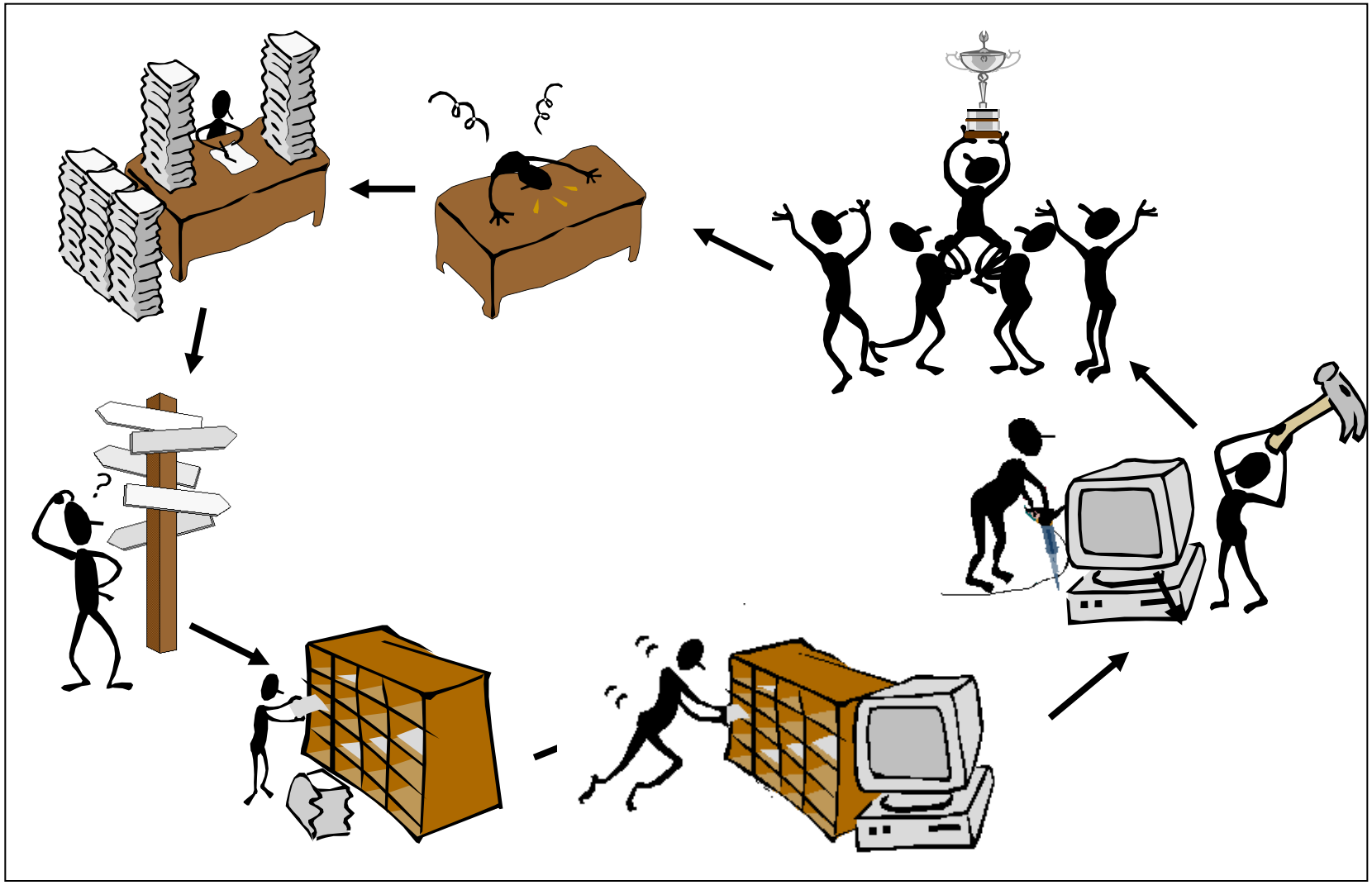
Any questions?

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

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

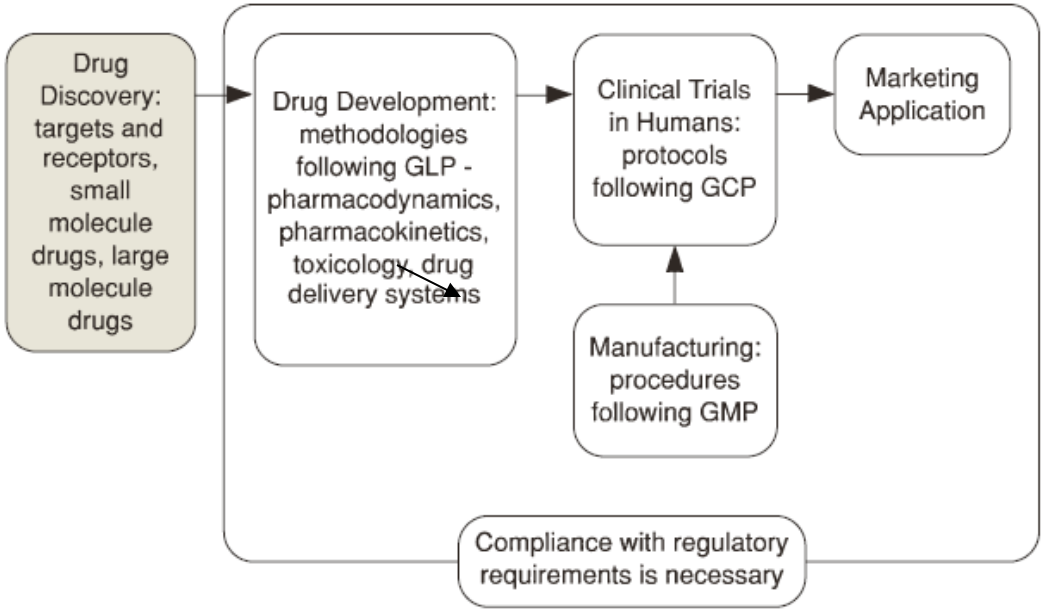


Figure from Rick Ng, *Drugs: From Discovery to Approval*

- **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

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 Bioinformatic*ian, 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