## Bioinformatics: Biology X

### Bud Mishra

Room 1002, 715 Broadway, Courant Institute, NYU, New York, USA

Model Building/Checking, Reverse Engineering, Causality

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## Main theses

"There are seven main propositions in the text. These are:

- The world is everything that is the case.
- What is the case (a fact) is the existence of states of affairs.
- A logical picture of facts is a thought.
- A thought is a proposition with sense.
- A proposition is a truth-function of elementary propositions.
- The general form of a proposition is the general form of a truth function, which is:  $\langle \bar{p}, \bar{\xi}, \neg \bar{\xi} \rangle$
- Where (or of what) one cannot speak, one must pass over in silence."
- -Ludwig Wittgenstein, Tractatus Logico-Philosophicus, 1921.









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## Administrivia

- Instructor: Bud Mishra
- Room 1002, 715 Broadway
- email: mishra@nyu.edu
- phone: 212-998-3464
- Office Hours: Tuesdays, 1:30 pm

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## Administrivia

- Course Details: G22.3033-010 || Bioinformatics
- Time and Place: Tuesdays, 5:00-6:50 pm EST
   || Room 1221, 719 Broadway
- Number of Credits: 3 credits
- Course Work: Software Project, Analyzing Gene Expression Data
- Diseases (Cancer, Diabetes, Autism, CFS, Mortality)
- Languages of Choice: Python, Matlab, Mathematica, R (No Perl please)

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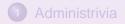
- Uri Alon || An Introduction to Systems Biology: Design Principles of Biological Circuits || Chapman & Hall/CRC, 2006.
- Edmund M Clarke, Orna Grumberg, Doron A Peled || Model Checking, The MIT Press, 2001.
- Patrick Suppes || A probabilistic theory of causality, 1970. (Available at:

http://suppes-corpus.stanford.edu/
article.html?id=106-1)

 Jon Williamson || Bayesian Nets and Causality: Philosophical and Computational Foundations, Oxford University Press, 2005.

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## Automating Biology

### Main Thesis

- A computational biologist is one who thinks about how biologists think about what they think is biology.
- Biology of the future will be done by a biologist and his dog: The biologist to ensure that large-scale high-throughput experiments and computational analysis of the resulting data are carried out properly, and the dog to bite him if he ever touches the experiments or the computers.
- How should time-course biological data be anlayzed? Mathematical Models?
  - How can we find causal connections among biological processes?
  - What are the most important applications of such data?

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## Areas we wish to touch on...

- Systems Biology
- Statistical Algorithms for Data Analysis
- Model Selection
- Model Checking

Let us think about these inter-connected questions from a single global perspective... CAUSALITY

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# Why is the study of biology intrinsically a causal pursuit?

### Part I

- Overview and known biology (Genome, etc)
- What do biologists mean by A causes B?
- Pathways, metabolic processes, computational biology
- Gene expression and regulatory networks
- The search for biological mechanisms (Knockout experiments, association studies, etc.)

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What does it mean for one thing to cause another?

### Part II

- Overview of causality (Regularities, Counterfactuals, and Processes)
- Probabilistic Causality and the common cause principle
- Review of probability, statistics and information theory background.
- Type and Token causality

## How can we identify causes?

### Part III

- Overview of graphical models
- Temporal Logic and Model Checking
- Statistical testing and Empirical Bayes Methods
- Causality and time
- Temporal logic and causality
- Back to biology: experiment design, clinical trials, personal genomics



### Heated Discussions on the Suggested Topics... Resulting in a New and Better Syllabus... That EVERYONE Loves!

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## Some Reading

- Nir Friedman, Michal Linial, Iftach Nachman, and Dana Pe'er. Using Bayesian Networks to Analyze Expression Data. Journal of Computational Biology, 7(3-4): 601–620, 2000.
- Stuart Glennan. Rethinking mechanistic explanation. Philosophy of Science, 69(3):S342–S353, 2002. ISSN 00318248. URL

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 D. Deutscher, I. Meilijson, S. Schuster, and E. Ruppin. Can single knockouts accurately single out gene functions?
 BMC Systems Biology, 2(1):50, 2008.



 Stuart S. Glennan. Mechanisms and the nature of causation. Erkenntnis (1975-), 44(1):49–71, 1996. ISSN 01650106. URL

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- John Leslie Mackie. *The Cement of the Universe*. Clarendon Press, 1974.
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- Ellery Eells. Probabilistic Causality. Cambridge University Press, 1991.
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- Jon Williamson. Bayesian nets and causality: philosophical and computational foundations. Oxford University Press, 2005.
- Hans Hansson and Bengt Jonsson. A logic for reasoning about time and reliability. Formal Aspects of Computing, 6(5): 512–535, 1994.

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- E.M. Clarke, O. Grumberg, and D.A. Peled. *Model checking*. Springer, 1999.
- Bradley Efron. Large-Scale Simultaneous Hypothesis Testing: The Choice of a Null Hypothesis. Journal of the American Statistical Association, 99(465):96–105, 2004.
- Clive W.J. Granger. Testing for Causality: A Personal Viewpoint. Journal of Economic Dynamics and Control, 2: 329–352, 1980.
- C. J. Langmead. Towards inference and learning in dynamic bayesian networks using generalized evidence. Technical Report CMU-CS-08-151, Carnegie Mellon University, 2008.

## [End of Lecture #1]

### See you next week!

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