

Manolis Kellis

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RESEARCH GOALS

I am interested in applying computational methods to understanding biological signals. My specific interests are: (1) in the area of genome interpretation, developing comparative genomics methods to identify genes and regulatory elements in the human genome; (2) in the area of gene regulation, deciphering the combinatorial control of gene expression and cell fate specification, and understanding the dynamic reconfiguration of genetic sub-networks in changing environmental conditions; (3) in the area of evolutionary genomics, understanding the emergence of new functions, reconfiguration of regulatory motifs, and the coordinated evolution of functionally interconnected cellular components. My goal is to pursue academic research in these areas in an interdisciplinary way, working together with computer scientists and biologists.

EDUCATION

- Massachusetts Institute of Technology** 2000-2003
Doctor of Philosophy (Ph.D.) in Computer Science
Dissertation title: Computational Comparative Genomics: Genes, Regulation, Evolution.
Supervisors: Eric Lander and Bonnie Berger.
Thesis earned MIT Sprowls award for best Ph.D. thesis in Computer Science
- Massachusetts Institute of Technology** 1999-2000
Masters of Engineering (M.Eng.) in Electrical Engineering and Computer Science.
Dissertation title: Imagina: A cognitive abstraction approach to sketch-based image retrieval
Supervisor: Patrick Winston
- Massachusetts Institute of Technology** 1995-1999
Bachelor of Science (B.S.) in Computer Science and Engineering
Coursework includes Machine Learning, Robot Vision, Artificial Intelligence, Distributed Algorithms, Complexity, Probability, Statistics, Software Engineering, Programming Languages, Signal Processing, Computer Graphics, Microprocessor Design, Computer Architecture.
GPA: 5.0 / 5.0.

DISSERTATION

My thesis focused on the computational foundations of genomics. I pioneered new methods for discovering biological signals using multiple species comparisons. My contributions are in four areas: (1) the automatic alignment of multiple genomes, using a graph theoretic framework to determine orthologous genes as well as gene duplication and loss events, (2) the identification of protein-coding genes, using a classification approach based on their patterns of nucleotide change, (3) the de-novo discovery of genome-wide regulatory motifs that does not require prior biological knowledge, and (4) the elucidation of combinatorial interactions between regulatory motifs. I applied these methods to analyze four complete species of yeast, leading to (a) the largest re-annotation of the yeast genome since its original sequencing, (b) the discovery of nearly all previously known regulatory motifs and a similar number of novel motifs, and (c) the first global analysis of eukaryotic evolution across multiple species revealing specific regions of rapid evolutionary change.

HONORS & AWARDS

- MIT Sprowls award for the best Ph.D. thesis in Computer Science, 2003.
First annual Paris Kanellakis Fellowship, 2000.
NTT Fellowship for graduate studies, 1999.
Chorafas Foundation Award, 1999.
MassGrant Award for academic excellence, 1998.
Member of National Scientific and Engineering Honor Societies Sigma Xi, Tau Beta Pi and Eta Kappa Nu.
First prize in the TBP Engineering Design Competition, representing MIT, Spring 1997.
French Baccalauréat with the Congratulations of the Jury, the highest distinction in France, June 1995.
First prize in South France in a country-wide math competition, 1993.
First prize in Saint Eutrôpe chess tournament for two consecutive years, 1991 and 1992.

TEACHING EXPERIENCE

- MIT Department of Mathematics - Fall 2001 - Lecturer**
Co-lectured the department's graduate-level introductory course on computational biology with Prof. Bonnie Berger.
Lectures covered the algorithmic, statistical, technological, and biological foundations of computational genomics.
Introduced lectures on computational genomics, designed the homework and lab assignments and advised final projects.

RESEARCH EXPERIENCE

MIT/Whitehead Institute Center for Genome Research - 2000-2003 - Biological Signal Discovery (*)

Evolutionary genomics: proof of yeast genome duplication and emergence of new functions, Fall 2003
Gene identification using cross-species comparison and re-annotation of the yeast genome, Fall 2002
Regulatory motif discovery using genome-wide conservation criteria, with Nick Patterson, Spring 2002
Automatic genome correspondence and alignment in a graph-theoretic framework, Spring 2001
Gene spacing constraints in the mammalian Hox developmental gene cluster, with Ken Dewar, Fall 2000
Projects supervised by Prof. Eric Lander and Prof. Bonnie Berger, in collaboration with Dr. Bruce Birren.

MIT Learning and Vision Group - Fall 99 - Handwritten character recognition (*)

Introduced a curve-based representation for handwritten characters that facilitates online recognition and classification. The geometry-based representation matches shapes rather than pixels and is invariant to scaling and rotation. Wavelet-based smoothing reduces noise and facilitates recognition. Project supervised by Prof. Paul Viola, MIT AI Lab.

Xerox Palo Alto Research Center (PARC) - Summer 99 - Video Analysis using Human Motion Primitives

Developed new angle-based representations for whole-body human motion, enabling time-warping of three-dimensional motion capture data and facilitating matching of gates across individuals. Worked towards an alphabet of human motions to be used in activity recognition and in combination with video data. Digital Video Analysis Area, Dr. Michael Black.

MIT AI Lab - Masters Thesis - Spring 99 - Imagina: Sketch-based Image Retrieval (*)

Developed a system for content-based image retrieval from a sketch of the desired image. Matching focused on regions instead of global pixel metrics. Representation captured geometry and spatial organizations of regions within images, using a combination of shape and color representations at multiple levels of abstraction. Advisor: Prof. Patrick Winston.

MIT Microprocessor Lab - Fall 98 - RoboLogo: Programming Environment for Interactive Robots (*)

Co-developed an environment that enables children to program interactive robots in a high-level language that extends Logo. Compiler written in javacc, low-level routines written in A51 assembly, printed circuit board designed on Protel.

Xerox PARC Smart Matter Area - Summer 98 - PolyBot: Distributed Control Architecture for Reconfigurable Robots

Worked on a new control architecture to allow many identical robotic modules to communicate, share state information, and arbitrate decisions based on local rules, message-passing, and environmental stimuli. Supervised by Dr. Mark Yim.

MIT AI Lab - Spring 98 - Mood: Music Classification using Patterns of Attentional State (*)

Co-developed a new architecture for music classification, integrating a low-level note observer with a music classifier that observes high-level patterns in the routines used by the note observer. Supervised by Prof. Patrick Winston.

AI in Practice Project - Spring 98 - Invest: Applications of Artificial Intelligence to Stock Market Prediction (*)

Applied Artificial Intelligence methods to the study of the stock market. Co-developed neural network, pattern saliency, and nearest neighbor predictors and applied them to real stock market data. Supervised by Prof. Tomás Lozano-Perez.

MIT Machine Vision Project - Fall 97 - EciMorph: Curve Morphing in Extended Gaussian Projection Space (*)

Developed a morphing method for convex two-dimensional curves, as projected in their Extended Gaussian Image representation, originally used in machine vision for object recognition. Supervised by Prof. Berthold Horn.

MIT Lab for Computer Science - Fall 97 - 3DMorph: Polygon Model Morphing (*)

Co-developed a morphing algorithm for three-dimensional models, which directly alters the surface mesh to interpolate shapes rather than pixels or volumes. Matching methods are general and applicable beyond morphing. Prof. Seth Teller.

Xerox PARC Computer Science Lab - Summer 97 - Crust: Voronoi-Based 3D Surface Reconstruction (*)

Co-developed the Crust algorithm for 3D reconstruction of surfaces from unorganized sample points. Algorithm runs on a desktop rather than movie studio supercomputers and has provable guarantees of its performance. ACM Siggraph publication has been influential in the field, cited in 78 papers. Internship with Dr. Marshall Bern and Prof. Nina Amenta.

World Wide Web Consortium - Summer 96 - WebBot: Constraint Model for a Web Robot (*)

Proposed and implemented a modular rule-based constraint language for automatic web traversal. The model allows a recursive definition of arbitrarily complex rules and constraints. Project supervised by Henrik Frystyk Nielsen.

(*) = Further details for these projects can be found in papers linked on my web page at web.mit.edu/manoli

EXPERIMENTAL BACKGROUND

Cold Spring Harbor Laboratory - Summer 03 - Yeast Genetics Course

Experiments included immunofluorescence microscopy and cell staining, mutant isolation and complementation, tetrad analysis, recombinant DNA transformation, genome-wide synthetic lethal screens, targeted gene disruption, pathway suppressor analysis, transposon mutagenesis, two-hybrid protein-protein interactions, DNA precipitation and sequencing. Daily guest lectures covered current research topics. In-depth lectures treated the foundations and principles of genetics.

PUBLICATIONS

- Sequencing and Comparison of Yeast Species to Identify Genes and Regulatory Motifs.
Kellis, Patterson, Endrizzi, Birren, Lander. *Nature* May 15, v. 423 p. 241-254, 2003.
Cited in 40 publications in the last six months, and featured in numerous reviews, magazines and newspapers.
- Direct Proof and Evolutionary Analysis of Ancient Genome Duplication in Yeast.
Kellis, Birren, Lander. *Nature*, article accepted for publication, 2004.
- Methods in Comparative Genomics: Genome Correspondence, Gene Identification, Regulatory Motif Discovery.
Kellis, Patterson, Birren, Berger, Lander. *Journal of Computational Biology*, in press, 2004.
- Whole-Genome Comparative Annotation and Motif Discovery in Yeasts.
Kellis, Patterson, Birren, Berger, Lander. *Proceedings of ACM Recomb (Res. in Comp. Mol. Biol.)*, p. 157-166, 2003.
- Phylogenetically and Spatially Conserved Word Pairs Associated with Gene-Expression Changes in Yeasts.
Chiang, Moses, Kellis, Lander, Eisen. *Genome Biology*, 4(7):R43, Jun 26, 2003. Also *ACM Recomb*, p. 84-93, 2003.
- Position Specific Variation in the Rate of Evolution in Transcription Factor Binding Sites.
Moses, Chiang, Kellis, Lander, Eisen. *BMC Evolutionary Biology*, 3:19, Aug 28, 2003.
- Biological Signal Discovery: The Power of Multiple Genomes.
Kellis. *Fungal comparative genomics*, Springer Verlag, invited book chapter, 2004.
- Comparative Gene Identification: Lessons from Yeast.
Kellis. *Encyclopedia of Genetics, Genomics, Proteomics*, John Wiley & Sons, invited review, 2004.
- Computational Comparative Genomics: Genes, Regulation, Evolution.
Kellis. *MIT Ph.D. Thesis*, 2003.
- The Genome Sequence of the Filamentous Fungus *Neurospora crassa*.
Galagan et al. *Nature*, Apr 24, v. 422, p. 859-868, 2003.
- Imagina: Sketch-based Image Retrieval using Cognitive Abstraction.
Kamvysselis. *MIT Masters Thesis*, 1999.
- Crust: A new Voronoi-Based Surface Reconstruction Algorithm.
Amenta, Bern, Kamvysselis. *ACM Siggraph Proceedings*, v. 32, p. 415-421, 1998.

CONFERENCE TALKS

- CSHL 2002 - Genome Sequencing and Biology - 5/02 - Cold Spring Harbor, New York
AGBT 2003 - Advances in Genome Biology and Technology - 2/03 - Marco Island, Florida
RECOMB 2003 - Int. Conf. on Research in Computational Molecular Biology - 4/03 - Berlin, Germany
Yeast 2003 - International Meeting on Yeast Genetics - 7/03 - Göteborg, Sweden
AGBT 2004 - Advances in Genome Biology and Technology - 2/04 - Marco Island, Florida
Human Genome Discovery and Gene Functional Analysis conference (invited) - 3/04 - San Francisco, California
HMS Conference on Analysis of Genomic Data (invited) - 5/04 - Cambridge, Massachusetts
Gordon Conference - Plenary Lecture on Phylogenomics (invited) - 6/04 - Plymouth, New Hampshire

INVITED LECTURES

- Whitehead Institute First Symposium on Genomics - June 18, 2002
WICGR/Harvard Institute of Proteomics Joint Colloquium - Aug 29, 2002
MIT Department of Mathematics Computational Biology Colloquium - Nov 15, 2002
Boston Area Yeast Meeting Monthly Lecture - Dec 11, 2002
Harvard Center for Genomics Research, Genomics Talks - March 05, 2003
MIT Artificial Intelligence Lab Computational Biology seminar - April 05, 2003

SCIENTIFIC COMMITTEES

- NIH/NHGRI** - Invited member and speaker for the planning meeting of Project ENCODE, Jun 2002 and Jun 2003.
SGD advisory board - Invited member for annual planning meeting in the yeast community, Aug 2002.
NIH Genomic Institute - Invited lecturer for the annual council meeting, Feb 2004.

PEER REVIEW

- Referee for peer-reviewed journals including *Genome Research*, *Genome Biology*, *Bioinformatics*, *Yeast*.
Member of the RECOMB program committee for the First Annual Satellite workshop on Gene Regulation, Apr 04.

BACKGROUND INFORMATION

Citizenship: Dual US and Greek citizenship with right to work in the US and in the European Union.

Education: Primary school in Greece. Secondary school in France. University in the United States.

Languages: Fluent English, French, Greek speaker. Proficient in Spanish. German studies.

Computers: Python, Java, C, C++, Scheme (LISP), Tcl/Tk, Open Inventor, CLU, Assembly.

Social: President, International Students Association. Group leader, Traditional Greek Dancing troupe.

Activities: Skiing, sailing, hiking, rollerblading, biking, dancing, scuba diving, photography.

REFERENCES

Prof. Eric S. Lander

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Prof. Gerald J. Sussman

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MIT Lab for Computer Science and Artificial Intelligence
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Prof. Patrick H. Winston

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Prof. Bonnie Berger

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