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Boris E. Shakhnovich

Research Interests

I am interested in co-evolution of regulation with sequence, structure and function. I am working on elucidating the impact of phenotypic constraints on the evolutionary dynamics driving sequence, structure and function divergence in proteins. In parallel, I am developing new computational tools for de-novo identification of transcription factor binding sites and cis-regulatory modules. The goal is to combine the two research areas by using evolution of open reading frames to guide investigations into the rewiring of upstream regulatory regions.

Education

2001 - 2004 Boston University Boston, MA

Ph. D in Bioinformatics

NSF Graduate Student Fellowship

1997 - 2001 University of Illinois Urbana-Champaign, IL

Bachelor of Science in Computational Biophysics

Cum Laude

Teaching Experience

- *Fall 2005* Developed curriculum and teaching a graduate course: Bioinformatics Applications (romi.bu.edu/bf527)
- *Spring 2003* Organized, designed curriculum, and co-presented a graduate seminar series: Biological Systematics (bioinfo.bu.edu/biosys)
- *2004-* Supervising two graduate, one masters student in Bioinformatics
- *2002-2004* Supervised two undergraduate summer students
- *2002* Teaching assistant for thermodynamics

Research Experience

2004-Present Boston University. Boston, MA

Research Assistant Professor on the Bioinformatics department. Main focus of research on molecular evolution, transcription factor binding site identification algorithms and reconstruction of system-level regulation models.

2001-2004 Boston University. Boston, MA

Graduate Student, research in structure-function relationship, molecular evolution and natural history of protein domains with Prof. DeLisi.

Summer 2001 Weizmann Institute Rehovot, Israel

Student, in Karyn Kupcinec International Science School. Worked under the guidance of Prof. Eytan Domany in the Weizmann Institute in Rehovot, Israel on applying super paramagnetic clustering to find co-regulated genes in the yeast genome.

2000-2001 Millenium Inc. Cambridge, MA

Research assistant, worked with Dr. Reich and Dr. Sander on creating an algorithm to find fast, close proximity alignments.

Summer 1999 Biogen Inc. Cambridge, MA
Research assistant, created an informatics tool for the local proteomics group and suggested improvements to hardware and software assemblies.

1998-1999 University of Illinois Urbana-Champaign, MA
Research assistant, involved in research with a cell biology lab doing experiments on Actin-Myosin transport.

Summer 1997 Beth-Israel Hospital Boston, MA
Research Assistant, designed and carried out experiments to explore the effects of hyper-tonicity on development of Xenopus embryos

Publications

- 1. Dokholyan NV, Shakhnovich B, Shakhnovich EI.**
Expanding protein universe and its origin from the biological Big Bang.
Proc Natl Acad Sci U S A. 2002 Oct 29;99(22):14132-6.
- 2. Shakhnovich BE**
Patent protection as a paradigm against bio-terrorism. The Journal of BioLaw & Business, Volume 6 Number 1 2003
- 3. Shakhnovich BE, Dokholyan NV, DeLisi C, Shakhnovich EI.**
Functional fingerprints of folds: evidence for correlated structure-function evolution.
J Mol Biol. 2003 Feb 7;326(1):1-9.
- 4. England JL, Shakhnovich BE, Shakhnovich EI.**
Natural selection of more designable folds: a mechanism for thermophilic adaptation. Proc Natl Acad Sci U S A. 2003 Jul 22;100(15):8727-31.
- 5. Shakhnovich BE, Harvey JM, Comeau S, Lorenz D, DeLisi C, Shakhnovich E.**
ELISA: structure-function inferences based on statistically significant and evolutionarily inspired observations. BMC Bioinformatics. 2003 Sep 2;4(1):34.
- 6. Tiana G, Shakhnovich BE, Dokholyan N, Shakhnovich EI.**
Imprint of evolution on protein structures, Proc Natl Acad Sci U S A. 2004 Mar 2;101(9):2846-51
- 7. Deeds E, Shakhnovich BE, Shakhnovich EI.**
Proteomic traces of speciation, J Mol Biol. 2004 Feb 10; 336(3): 695-706
- 8. Shakhnovich BE, Harvey JM.**
Quantifying Structure-Function uncertainty: A graph theoretical exploration into the origins and limitations of protein annotation, J Mol Biol. 2004 Apr 2;337(4):933-49.
- 9. Shakhnovich BE, Harvey JM, DeLisi C**
ELISA: A unified multidimensional view of the protein domain universe, Proc The Fourth International Workshop on Bioinformatics and Systems Biology, Genome Informatics 15(1): 213-220 (2004)
- 10. Shakhnovich BE, Reddy T, Galinsky K, Mellor J, DeLisi C**
Identification of co-expressed genes through module gene flow, Fourth International Workshop on Bioinformatics and Systems Biology, Genome Informatics 15(1): 221-228 (2004)
- 11. Shakhnovich BE, Deeds E, Delisi C, Shakhnovich E.**
Protein structure and evolutionary history determine sequence space topology.
Genome Res. 2005 Mar;15(3):385-92.
- 12. Reddy T, Delisi C, Shakhnovich BE.**
Assessing Transcription Factor Motif Drift From Noisy Decoy Sequences,
Workshop on Bioinformatics and Systems Biology, Genome Informatics 16(1)(In Press) (2005)
- 13. Shakhnovich BE.**
Improving the precision of the structure-function relationship by considering phylogenetic context. PLoS Comput Biol. 2005 Jun;1(1):e9. Epub 2005 Jun 24.
- 14. Shakhnovich BE**
Phenotypic determinants of molecular evolution (Submitted)

15. Lerman G, Shakhnovich BE

Local manifold embedding for exploring the functional annotation landscape
(Submitted)

16. Shakhnovich BE

Properties of the multidimensional Protein Domain Universe Graph (Submitted)

17. Reddy TE, Shakhnovich BE, Delisi C, Russek S,

De-novo identification of novel functional sites in upstream regions of human GABA receptor genes (In preparation)

18. Reddy TE, Delisi C, Shakhnovich BE

GibTigs: A position centric algorithm for identification of transcription factor binding sites (In preparation)

19. Harvey JM, Tanella A, Reddy T, Shakhnovich BE,

Detailing regulation in yeast via Cis-Regulatory module identification (In preparation)

20. Hu Z, Wu J, Okuda S, Niu T, Shakhnovich BE, DeLisi C, Detecting evolutionary order: Genomic Fusion Flux and it's application in rooting the Universal Tree of Life (In preparation)

Presentations

Talks:

- Invited Talk: Bioinformatics: Novel challenges for computer science in the new millenium, October 2002, *ACM Conference, UIUC*
- Contributed Talk: On the natural history of protein domains, August 2003, *Dresden International Conference on Bioinformatics.*
- Contributed Talk: Divergent evolution of proteins: Pressures, Structure-Function relationship and the uncertainty principle, March 2004, *Bioinformatics Seminar Series Boston University*
- Invited Talk: Effect of structural designability on viral mutability, May 2004, *CVRD Seminar series Brown University*
- Invited Talk: Pushing the limits of computation: examples from computational biology, May 2004, *Siebel Invitational Seminar Series, UIUC*
- Contributed Talk: ELISA: A unified multidimensional view of the protein domain universe, June 2004, *Fourth International Workshop on Bioinformatics and Systems Biology Goto, Japan*
- Contributed Talk: A graph theoretical treatment of protein evolution: Fitness characteristics and natural selection, June 2004, *Bioinformatics 2004 -- Linköping, Sweden*
- Invited Talk: Role of lethality in molecular evolution: A conversation between Darwin and Kimura, Oct. 2004, *Bioinformatics Boston University*
- Invited Talk: Lethality: Interplay between molecular and Darwinian evolution, Oct. 2004, *CGR, Harvard University*
- Invited Talk: Interface of molecular and organismal evolution, March 2005, *NCBI National Institutes of Health*
- Contributed Talk: Evolutionary and physical constraints on molecular evolution, July 2005, *2nd Moscow Conference on Computational Molecular Biology (MCCMB'05)*
- Contributed Talk: Impact of phenotypic constraints on dynamics of duplication and divergence, November 2005, *Fifth Georgia Tech Conference on Bioinformatics*

Posters:

- Poster: Origin of the Protein Domain Universe Graph Feb. 2003 *DIMACS Workshop on Protein Domains*
- Poster: Functional Fingerprints of Folds and co-evolution of Structure and Function. Feb. 2003 *DIMACS Workshop on Protein Domains*
- Poster: Functional Fingerprints of Folds and co-evolution of Structure and Function. March 2003, *RECOMB2003*
- Poster: Natural selection of more designable folds: a mechanism for thermophilic adaptation. March 2003, *RECOMB2003*
- Poster: Protein structure and evolutionary history determine sequence space topology. November 2003, *The Fourth International Georgia Tech Conference on Bioinformatics*
- Poster: Protein structure and evolutionary history determine sequence space topology. March 2004, *RECOMB 2004 – **Best Poster Award***
- Poster: Protein structure and evolutionary history determine sequence space topology. March 2004, *RECOMB 2004*
- Poster: Improving the precision of the structure-function relationship by considering phylogenetic context. June 2005, Gordon Conference on Structural, Functional & Evolutionary Genomics
- Poster: Detailing regulation in yeast via computational identification of cis-regulatory modules. October 2005, Sixth International Conference on Systems Biology (ICSB 2005)

Distinctions and Fellowships

- NSF Pre-doctoral fellow
- Paper selected for cover art in the March, 2005 issue of *Genome Research*
- Papers voted for Faculty of 1000 “must read”
- Two of the papers designated “most read” on PNAS for that month
- Best Poster Award at RECOMB 2004
- Outstanding teaching award for Biological Systematics
- Fellow of Karyn Kupciner International Science School, Rehovot Israel

Other Relevant Experience

- Organized the first student invitational series of lectures for the Bioinformatics program
- Served as a student advisor to the Bioinformatics curriculum committee
- Supervised undergraduate students as part of a university-wide mentoring program (UROP Undergraduate Research Opportunities)