

# Charles W. O'Donnell

## Curriculum Vitae

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## Education

- Exp. Spr. 2011 **Ph.D., EECS, Massachusetts Institute of Technology, Cambridge, MA.**  
Thesis: "Ensemble Modeling of  $\beta$ -sheet Proteins"  
Thesis committee: Bonnie Berger, Srinivas Devadas, Susan Lindquist, & Collin M. Stultz.  
Minor in Biology.
- 2005 **S.M., EECS, Massachusetts Institute of Technology, Cambridge, MA.**
- 2003 **B.S., Computer Engineering, Columbia University, New York, NY.**  
*Magna Cum Laude.* Major GPA: 3.91/4.0

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## Research Experience

- 2003–present Research Assistant, Computer Science and Artificial Intelligence Lab, MIT.  
*Bonnie Berger Group & Srinivas Devadas Group*
- 2007–present Research Assistant, Whitehead Institute for Biomedical Research.  
*Susan Lindquist Lab*

**Amyloid Modeling.** Proteins of all kinds have the ability to adopt amyloid structure: an aggregate state which is often difficult to characterize experimentally, and associated with both disease and beneficial biological function. To study this, I developed new algorithms that predict amyloid structure from sequence highly accurately ( $\sim 2\times$  existing methods) by computing an ensemble set of putative conformation variants, modeling *in vivo* structure variability. Further generalized technique to predict energetic landscape differences caused by sequence mutation, and allow simultaneous alignment and prediction of consensus structures given two sequences. Specifically modeled yeast Sup35 proteins to help guide wet experimentation probing structure, and investigated structural and sequence compositional properties of a genomic screen for prion proteins. Commenced inter-institute collaborations with McGill University and others.

**Inhibition of biofilms.** Created computational structure models of the functional amyloid Curli in *Enterobacteriaceae*, a protein of unknown structure necessary for biofilm formation. Predicted protein mutations which disrupt biofilm formation (confirmed experimentally by R. Krishnan) and putative inhibitory peptide fragments. Collaboration with R. Krishnan and T. K. Lu experimentally validated mutants and devised novel phage-display system which inhibits *E. Coli* biofilm formation, colony growth, and invasion of mammalian cells.

**Transmembrane  $\beta$ -barrel (TMB) Modeling.** Found in outer membranes of bacteria, mitochondria, and chloroplasts, TMB proteins are diversely involved in cell metabolism, but difficult to characterize structurally. For these, I developed algorithms for highly-accurate prediction of TMB structures based on similar ensemble techniques, and a technique for simultaneous alignment and structural prediction of two TMB sequences. Expanded system to include other classes of permuted  $\beta$ -sheet structures. Released web-based software tool (partiFold-TMB/Align), used by dozens of labs for experimentation and bacterial genome annotation. This work carried out jointly with J. Waldispühl.

**RNA/Protein structure energy models.** Studied methods for constructing pseudo-energy cost functions with minimal parameters. Applied constraint-based linear programming and SVM techniques to reduce the energy model for the RNAfold structure predictor from  $\sim 24k$  parameters to  $\sim 500$ , while maintaining similar-to-improved accuracy.

**SAT-based optimization for bioinformatics.** Designed classical structure prediction and alignment algorithm reductions to SAT instantiations to leverage the increasing power of SMT decision problem solvers.

**HMM-based secondary structure prediction.** Developed HMM-based protein secondary structure predictor utilizing an intuitive biophysically-motivated pseudo-energy model. Predicted  $\alpha$ -helix locations with accuracy unmatched by other tool with as few parameters.

**Computer architectures for secure processing.** Helped develop AEGIS custom FPGA processor, which enables secure execution under physical attack via physically unclonable functions (PUFs) and memory integrity verification algorithms. Designed models for partitioning application code into trusted and untrusted components while maintaining secrecy requirements. Introduced methods for secure virtual storage and execution using industry-standard TPM devices.

2006 [Summer Internship, IBM Research.](#)  
*Biomolecular Dynamics and Scalable Modeling Group*

**BlueMatter molecular dynamics simulator.** Applied concepts from relational databases to massively-parallel scientific MD software, implementing a translation layer that effects data structures and data movements within 16k node BlueGene/L supercomputer. Developed relational primitives described by C annotations providing physical representation flexibility.

2002–2003 [Undergraduate Research Assistant, Computer Science, Columbia University.](#)  
*Steven Nowick Group, Asynchronous Circuits and Systems Group*

**Asynchronous boolean logic theory.** Solved open question concerning the existence of hazard-free logic circuits given an arbitrary Boolean function; proving a minimal set of requirements. Designed “extended burst-mode” logic verifier and logical hazard simulator, integrated into CAD tool MINIMALIST.

2003–2003 [Undergraduate Research Assistant, Electrical Engineering, Columbia University.](#)  
*Ken Shepard Group, Integrated Systems Laboratory*

**Signal processing.** Designed digital core and adders for an asynchronous continuous-time sampling digital FIR filter ASIC.

- 2001–2002 Undergraduate Research Assistant, Computer Science, Columbia University.  
*Salvatore Stolfo Group, Intrusion Detection Systems*  
**Statistical data-mining.** Devised real-time OS information monitoring techniques for intrusion detection systems and sparse sequence models.
- 2001–2002 Summer Internship, AT&T Research.  
*Intelligent Network Services Solutions Group*  
**Decentralized network platform for VoIP.** Developed pluggable modules for computational control of voice calls and Voice-XML dialogues on “ECLIPSE” platform.
- 2000–2002 Internship, Lincoln Electric.  
*Machine Research and Development*  
**Embedded weld-precision software.** Assisted design of simulation algorithms and embedded communication software for precision welding.

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## Publications & Presentations

### Peer-Reviewed Conferences and Journals

- R. Halfmann, S. Alberti, R. Krishnan, N. Lyle, **C. W. O’Donnell**, O. D. King, B. Berger, R. Pappu, S. Lindquist,  
*Opposing effects of glutamine and asparagine govern prion formation by intrinsically disordered proteins*, *Molecular Cell*, to appear.
- **C. W. O’Donnell**, J. Waldispühl, M. Lis, R. Halfmann, S. Devadas, S. Lindquist, B. Berger,  
*A method for probing the mutational landscape of amyloid structure*. Accepted to the 19<sup>th</sup> Annual International Conference on Intelligent Systems for Molecular Biology & 10<sup>th</sup> European Conference on Computational Biology (ISMB/ECCB 2011), Vienna, Austria. *Bioinformatics*, to appear.
- S. Shenker, **C. W. O’Donnell**, S. Devadas, B. Berger., J. Waldispühl,  
*Efficient traversal of protein folding pathways using ensemble models*. To appear in the Proc. of the 15<sup>th</sup> Annual International Conference on Research in Computational Molecular Biology (RECOMB 2011) to appear, Vancouver, BC, Canada.
- J. Waldispühl, **C. W. O’Donnell**, S. Will, S. Devadas, R. Backofen, B. Berger,  
*Simultaneous Alignment and Folding of Protein Sequences*, Proc. of the 13<sup>th</sup> Annual International Conference on Research in Computational Molecular Biology (RECOMB 2009), Tucson, AZ.
- J. Waldispühl\*, **C. W. O’Donnell\***, S. Devadas, P. Clote, B. Berger (**\*equal contrib.**),  
*Modeling Ensembles of Transmembrane  $\beta$ -barrel Proteins*, *PROTEINS: Structure, Function, and Bioinformatics*, 71(3):1097–1112, 2008.

- B. Gassend, **C. W. O'Donnell**, W. Thies, A. Lee, M. van Dijk, S. Devadas, *Learning Biophysically-Motivated Parameters for Alpha Helix Prediction*, BMC Bioinformatics, 8(Suppl. 5):S3, 2007.
- B. Gassend, **C. W. O'Donnell**, W. Thies, A. Lee, M. van Dijk, S. Devadas, *Predicting Secondary Structure of All-Helical Proteins Using Hidden Markov Support Vector Machines*, Proc. of the 2006 Workshop on Pattern Recognition in Bioinformatics, Volume 4146 of LNCS pp. 93-104 (PRIB 2006), Hong Kong, China.
- G. E. Suh, **C. W. O'Donnell**, S. Devadas, *AEGIS: A Single-Chip Secure Processor*, IEEE Design & Test, 24(6):570–580, 2007.
- **C. W. O'Donnell**, G. E. Suh, M. van Dijk, S. Devadas, *Memoization Attacks and Copy Protection in Partitioned Applications*, Proc. of the 2007 IEEE Workshop on Information Assurance (IAW 2007), West Point, NY.
- L. F. G. Sarmenta, M. van Dijk, **C. W. O'Donnell**, J. Rhodes, S. Devadas, *Virtual Monotonic Counters and Count-Limited Objects using a TPM without a Trusted OS*, Proc. of the 2006 Workshop on Scalable Trusted Computing (STC 2006), Fairfax, VA.
- G. E. Suh, **C. W. O'Donnell**, S. Devadas, *Design and Implementation of the AEGIS Single-Chip Secure Processor Using Physical Random Functions*, Proc. of the 32<sup>nd</sup> Annual International Symposium on Computer Architecture (ISCA 2005), Madison, WI.
- **C. W. O'Donnell**, V. Vaikuntanathan, *Information Leak in the Chord Lookup Protocol*, Proc. of the 4<sup>th</sup> Annual IEEE International Conference on Peer-to-Peer Computing (P2P 2004), Zurich.
- S. M. Nowick, **C. W. O'Donnell**, *On the Existence of Hazard-Free Multi-Level Logic*, Proc. of the 9<sup>th</sup> Annual IEEE International Conference on Advanced Research in Asynchronous Circuits and Systems (ASYNC 2003), Vancouver.

## Posters

- **RECOMB 2010**, *A Method for Probing the Mutational Landscape of Amyloid Structure*, Lisbon, Portugal, August 2010.
- **GRC Protein Folding Dynamics 2010**, *Hypothesis-Driven Ensemble Modeling of Amyloids*, Ventura, CA, January 2010.
- **IMA Protein Folding 2008**, *Modeling Structure Ensembles of Conserved  $\beta$ -sheet Folds*, Minneapolis, MN, January 2008.
- **GRC Protein Folding Dynamics 2008**, *Modeling Structure Ensembles of Conserved  $\beta$ -sheet Folds*, Ventura, CA, January 2008.
- **ISMB/ECCB 2007**, *Modeling Ensembles of Transmembrane  $\beta$ -barrel Proteins*, Vienna, Austria, July 2007.
- **RECOMB 2006**, *Learning Biophysically-Motivated Parameters for Alpha Helix Prediction*, Venice, Italy, April 2006.

## Other Reports

- **C. W. O'Donnell**,  
*Secure Application Partitioning for Intellectual Property Protection*, MIT EECS S.M. Thesis (August 2005).
- G. E. Suh, **C. W. O'Donnell**, S. Devadas  
*AEGIS: A Single-Chip Secure Processor*, Elsevier Information Security Technical Report, 10(2):63-73, 2005.
- **C. W. O'Donnell**, G. E. Suh, S. Devadas  
*PUF-Based Random Number Generation*, MIT CSAIL CSG Technical Memo 481, 2004.

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## Patents

- T. K. Lu, R. Krishnan, **C. W. O'Donnell**, S. Devadas, B. Berger, J. Collins, S. Lindquist,  
*Bacteriophages Expressing Amyloid Peptides and Uses Thereof*, Provisional applications 61/229,703 (filed July 29, 2009), 61/233,697 (filed August 13, 2009). International Serial Number: PCT/US2010/043770. Published February 3, 2011.

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## Software

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|-----------------|--|
| AmyloidMutants  | Sequence-based ensemble structure prediction and mutational analysis of amyloid proteins. Webserver to be announced.   |
| partiFold-TMB   | Sequence-based ensemble structure prediction of transmembrane proteins. Webserver: <a href="http://partifold.csail.mit.edu/TMB/">http://partifold.csail.mit.edu/TMB/</a> |
| partiFold-Align | Simultaneous alignment and structure prediction of transmembrane proteins. Webserver: <a href="http://align.csail.mit.edu/TMB/">http://align.csail.mit.edu/TMB/</a>      |
| MINIMALIST      | Contributed to CAD package for the synthesis and optimization of asynchronous burst-mode controllers.  |

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## Teaching Experience

- December 2010 **Guest Lecturer**, *Tufts University, Dept. of Computer Science*.  
COMP 150-PBT: Protein Bioinformatic Topics. Guest lecture for Prof. Lenore Cowen on the experimental and computational analysis of amyloid and prion proteins.
- Spring 2009 **Co-Lecturer**, *Massachusetts Institute of Technology, Dept. of Mathematics*.  
18.417: Introduction to Computational Molecular Biology (graduate level). Taught introductory algorithms for bioinformatic analysis of proteins and RNAs. Mentored individual students on topics and techniques throughout semester-long research projects.
- Spring 2009 **Teaching Assistant**, *Massachusetts Institute of Technology, Dept. of Mathematics*.  
18.418: Topics in Computational Molecular Biology (graduate level). Managed and advised students on end-of-term research presentations. Presented seminar on protein structure prediction.

- Fall 2005 **Teaching Assistant**, *Massachusetts Institute of Technology, Dept. of EECS.*  
6.170: Software Engineering (undergraduate level). Led weekly group recitations, conducted weekly one-on-one student meetings, assisted full-class lecturing, designed and graded problem sets, mentored 4-person student groups in semester-long research projects, and maintained course infrastructure for homework and project source code.
- Spring 2002 **Teaching Assistant**, *Columbia University, Dept. of CS.*  
CS3824: Computer Organization (undergraduate level). Helped manage and grade course homework material. Held semi-weekly office hours for general computer science assistance.

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## Awards and Honors

- 2006 **Sigma Xi Scientific Research Society.**
- 2003 **Theodore R. Bashkow Award**, *Columbia University, Computer Science.*  
Awarded to senior who has excelled in independent research
- 2003 **Prentis Scholarship**, *Columbia Engineering School Alumni Association.*
- 2003 **John E. Bertram Memorial Honorary Scholarship**, *Columbia University.*
- 1999-2003 **Dean's List**, *Columbia University.*
- 1999-2003 **Scholarship Winner**, *Slovene National Benefits Society.*
- 2002 **Tau Beta Pi Engineering Honor Society.**
- 2002 **Golden Key International Honour Society.**
- 2001 **Ralph Haines Honorary Scholarship**, *Columbia University.*
- 2000,2001 **A. Peers Montgomery Memorial Honorary Scholarship**, *Columbia University.*
- 1999 **Scholarship Winner**, *American Mutual Life Association.*
- 1998 **Eagle Scout**, *Boy Scouts of America.*

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## Service

- Reviewer for RECOMB, ISMB, and HPCA conferences, and IEEE TCBB, IEEE TSP, IEEE TPDS, IEEE TACO, IEEE TOCS journals.
- Organizational Committee for the 4<sup>th</sup> Annual MIT CSAIL Computer Architecture Workshop (2004).

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## Miscellaneous

Citizenship: United States

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## References

**Prof. Bonnie Berger**

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