

## Jérôme WALDISPÜHL

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### Research Interests

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Protein and RNA folding, formal language theory, statistical mechanics, evolution.

### Current position

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Sep. 2009    Assistant Professor of Computer Science, McGill University.  
Member of the McGill Centre for Bioinformatics.  
Research affiliate at the MIT Computer Science and AI Laboratory.

### Education

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Nov. 2004    **PhD in Computer Science** with honors.  
École Polytechnique (France)  
Title: "Modeling and Predicting the Structure of Transmembrane Proteins"  
Supervisor: Jean-Marc Steyaert.  
Referees: Peter Clote, Marie-France Sagot.  
Committee: Christian Choffrut (Chair), Alessandra Carbone, Philippe Dessen, Thomas Simonson.

Jul. 2000    **M.S. in Computer Science** with honors.  
University of Paris VII Denis Diderot (France)  
Majors: computer algebra, algorithm analysis, combinatorics.  
M.S. thesis: "Analysis of Combinatorial Properties of Protein Folding".  
Supervisor: Jean-Marc Steyaert.

Jun. 1999    **B.S. in Mathematics** with honors.  
University of Nice and Sophia-Antipolis (France)  
Algebra, complex analysis, differential calculus, geometry, numerical analysis, probability, statistics, topology.  
B.S. thesis: "Ehrhart Polynomial, Cooccurrence Matrices and Medical Imaging".  
Supervisor: Loïc Pottier.

### Experience

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2006-2009    Instructor, Applied Mathematics, M.I.T., USA.  
2005-2009    Postdoctoral Associate, Computer Science and AI Laboratory, M.I.T., USA.  
2005-2006    Postdoctoral Associate, Department of Biology, Boston College, USA.  
2003-2004    Instructor in Computer Science, University of Paris VII, France.  
2000-2003    Teaching assistant in Computer Science, École Polytechnique, France.

### Awards and Honors

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2000-2003    PhD Fellowship from the French Ministry for Research.  
2000-2003    Teaching Fellowship (monitorat) from the Academy of Versailles (France).  
1999-2000    Master Fellowship from the University of Paris VII (France).

## Most Significant Contributions

### Modeling and Predicting Transmembrane proteins

**Motivations:** Transmembrane proteins are an important class of proteins (i.e. major drug targets) which are difficult to predict because very few structures are available in databases.

**Results:** We designed a grammatical model that does not require and explicitly used long-range residue contacts to predict the structure of transmembrane  $\beta$ -barrels (6) and transmembrane  $\alpha$ -bundle (5). This work has been achieved during my PhD (11) and a web server is available (6).

### Modeling Ensembles of Protein Structures

**Motivations:** Classical protein structure predictor provide a limited list predictions that does not reflect the diversity of structures observed *in vivo*.

**Results:** We developed a Boltzmann model to compute statistical properties of the *ensemble* of structures that can be adopted by a protein, and make realistic predictions reproducing experimental results (9). These methods has been successfully applied on transmembrane  $\beta$ -barrels (2).

### Algorithms for exploring the RNA Mutations Landscape

**Motivations:** Tools for analyzing the effect of mutations on the structure of RNA molecules is essential for but also to study the principle of molecular evolution.

**Results:** We developed the first polynomial algorithm to compute the structural variations in the RNA mutational landscape (3; 7). A web server is available (1).

### Analysis of Kinetical Traps in the RNA Folding Landscape

**Motivations:** RNA molecule can misfold if they fall in a kinetic trap. The presence of such traps on folding pathways may explain why classical structure predictors fail.

**Results:** We implemented a algorithm to sample the distribution of kinetic traps in the RNA folding landscape. It enabled us to show the cooperativity of the Turner energy model and explain the folding of pseudo-knot structures (4).

### Simultaneous Alignment and Folding of Proteins

**Motivations:** Sequences with low identity (<30%) are difficult to align.

**Results:** We provided a method that efficiently use the structural information embedded in sequences to compute reliable alignments at low sequence identity (10). This method also enable us to improve the structure prediction accuracy.

## Research Contributions and Practical Applications

### Articles in Refereed Publications

- [1] Jérôme Waldispühl, Srinivas Devadas, Bonnie Berger, and Peter Clote. RNAmutants: a web server to explore the mutational landscape of RNA secondary structures. *Nucleic Acids Res*, 37(Web Server issue):W281–6, Jul 2009.
- [2] Jérôme Waldispühl, Charles W O'Donnell, Srinivas Devadas, Peter Clote, and Bonnie Berger. Modeling ensembles of transmembrane beta-barrel proteins. *Proteins*, 71(3):1097–112, May 2008.
- [3] Jérôme Waldispühl, Srinivas Devadas, Bonnie Berger, and Peter Clote. Efficient algorithms for probing the RNA mutation landscape. *PLoS Comput Biol*, 4(8):e1000124, 2008.
- [4] Jérôme Waldispühl and Peter Clote. Computing the partition function and sampling for saturated secondary structures of RNA with respect to the turner energy model. *J Comput Biol*, 14(2):190–215, Mar 2007.
- [5] Jérôme Waldispühl, Bonnie Berger, Peter Clote, and Jean-Marc Steyaert. Predicting transmembrane beta-barrels and interstrand residue interactions from sequence. *Proteins*, 65(1):61–74, Oct 2006.
- [6] Jérôme Waldispühl, Bonnie Berger, Peter Clote, and Jean-Marc Steyaert. transFold: a web server for predicting the structure and residue contacts of transmembrane beta-barrels. *Nucleic Acids Res*, 34(Web Server issue):W189–93, Jul 2006.
- [7] Peter Clote, Jérôme Waldispühl, Behshad Behzadi, and Jean-Marc Steyaert. Energy landscape of k-point mutants of an RNA molecule. *Bioinformatics*, 21(22):4140–7, Nov 2005.
- [8] Jérôme Waldispühl and Jean-Marc Steyaert. Modeling and predicting all-alpha transmembrane proteins including helix-helix pairing. *Theor. Comput. Sci.*, 335(1):67–92, 2005.

### Other Refereed Contributions

- [9] Bonnie Berger and Jérôme Waldispühl. Novel perspectives on protein structure prediction. In Lenwood S. Heath and Naren Ramakrishnan, editors, *The Problem Solving Handbook for Computational Biology and Bioinformatics*. Springer, 2010.
- [10] Jérôme Waldispühl, Charles W O'Donnell, Sebastian Will, Srinivas Devadas, Rolf Backofen, and Bonnie Berger. Simultaneous alignment and folding of protein sequences. In *RECOMB*, pages 339–355, 2009.
- [11] Jérôme Waldispühl. *Modeling and Predicting the Structure of Transmembrane Proteins*. PhD thesis, École Polytechnique, Nov 2004.
- [12] Jérôme Waldispühl, Behshad Behzadi, and Jean-Marc Steyaert. An approximate matching algorithm for finding (sub-)optimal sequences in s-attributed grammars. In *ECCB*, pages 250–259, 2002.

Non-Refereed Contributions

- [13] Jérôme Waldispühl, Srinivas Devadas, Bonnie Berger, and Peter Clote. Efficient algorithms for probing the RNA mutation landscape and prediction of deleterious mutations. Poster at the RNA in Biology, Bioengineering and Nanotechnology IMA workshop, 2007.
- [14] Jérôme Waldispühl, Charles W O'Donnell, Nathan Palmer, Srinivas Devadas, Peter Clote, and Bonnie Berger. Modeling ensemble of transmembrane beta-barrels. Poster at the 15th Annual International Conference on Intelligent Systems for Molecular Biology (ISMB 2007), 2007.
- [15] Jérôme Waldispühl, Bonnie Berger, Peter Clote, and Jean-Marc Steyaert. Predicting transmembrane beta-barrels and inter-strand residue interactions from sequence: Application to OmpA of *E. Coli*. Poster at Merck/MIT annual meeting, 2006.
- [16] Jérôme Waldispühl and Peter Clote. A study of the folding energy spectrum of RNA. Poster at the Ninth Annual International Conference on Research in Computational Molecular Biology (RECOMB 2005), 2005.
- [17] Jérôme Waldispühl, Behshad Behzadi, and Jean-Marc Steyaert. Can RNA super-optimal structure improve prediction? Poster at the fourth Belgium Bioinformatics Conference (BBC 2003), 2003.
- [18] Jérôme Waldispühl and Jean-Marc Steyaert. Modeling and predicting all-alpha transmembrane proteins. Poster at the second European Conference on Computational Biology (ECCB 2003), 2003.
- [19] Jérôme Waldispühl and Jean-Marc Steyaert. Modeling membrane protein with s-attribute grammars. Poster at the "troisièmes Journées Ouvertes en Biologie Informatique et Mathématiques" (JOBIM 2002), 2002.
- [20] Jérôme Waldispühl. A study of combinatorial properties of protein folding. Master's thesis, École Polytechnique, June 2000.
- [21] Jérôme Waldispühl. Erhart polynomial, cooccurrence matrices and applications to medical imaging. B.S. thesis, July 1999.

Contributions to practical applications of knowledge

- [22] Jérôme Waldispühl. *RNAmutants*. Software and Web Server, 2008.
- [23] Jérôme Waldispühl. *partiFoldTMB*. Software and Web Server, 2006.
- [24] Jérôme Waldispühl. *RNA<sub>sat</sub>*. Software, 2005.
- [25] Jérôme Waldispühl. *amsag2c*. Software, 2002.

## Contributions to the Community

### Selected invited talks (Conferences, Symposiums, Workshops):

- MonBUG symposium, Montreal, Canada, September 2009.
- Symposium of the Cluster of Excellence "Multimodal Computing and Interaction", Saarland University, Saarbrücken, Germany, March 2009.
- Thirteenth Annual Meeting of the RNA society, Berlin, Germany, July 2008
- IMA Workshop on Protein Folding, Minneapolis, USA, January 2008.

### Program Committee:

- Program Committee Member of the Fourteenth Annual International Conference on Research in Computational Molecular Biology (RECOMB 2010), Lisbon, April 2010.
- Program Committee Member of the Eighteenth Annual International Conference on Intelligent Systems for Molecular Biology (ISMB 2010), Boston, July 2010.

### Organizing Committees:

- Organizing committee of the McGill System Biology training program open house, Montreal, February 4th, 2010.
- Organizing committee of the LIX symposium: "Bioinformatics: algorithms, structures and statistics", Palaiseau, December 2005.
- Chief of the technical staff of the South West European Regional programming Contest of ACM, École Polytechnique, Palaiseau, France, November 2004.
- Member of the technical staff of the South West European Regional programming Contest of ACM, École Polytechnique, Palaiseau, France, November 2003.

### Administrative duties:

- SOCS PhD committee, School of Computer Science (SOCS), McGill, Since 2009.
- PhD student representative at the computer science department council, École Polytechnique, Palaiseau, France, 2003-2005.
- PhD student representative at the Academy of Versailles council, France, 2001-2002.

### Teachings:

- McGill (Since 2010): 1 Undergraduate Class (Lecturer).
- MIT (2006-2009): 3 Graduate Classes (Lecturer), 3 Undergraduate Classes (TA).
- University Paris VII (2002-2004): 2 Graduate Classes (Lecturer), 4 Undergraduate Classes (1 as Lecturer & 3 as TA).
- École Polytechnique (2000-2004): 9 Undergraduate Classes (TA).

## Training of Highly Qualified Personnel

### Masters

- Philippe Antoine, "Using NMR data for Transmembrane  $\beta$ -barrel structure prediction", M.S. École Polytechnique, France, 2007.

### Undergraduates

- Solomon Shenker, "Ensemble Modeling of  $\beta$ -structures", McGill, 2010.
- Kelley Bailey, "Analysis of Protein Loop Flexibility", MIT, 2008.
- Natasha Plotkins, "Reconstruction of Transmembrane  $\beta$ -barrel from contacts", MIT, 2008.