

Jonathan P. Bollback

ADDRESS

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CURRENT POSITION

2010 - Assistant Professor Institute of Science and Technology Austria

ACADEMICS

Degrees

2004	Ph.D. (Evolutionary Genetics)	University of Rochester, New York
2000	M.Sc. (Evolutionary Genetics)	University of Rochester, New York
1995	B.Sc. (Biology)	University of Maryland, Maryland

History

2008 - 2010	Postdoctoral Research Associate	University of Edinburgh
2004 - 2008	Postdoctoral Research Associate	University of Copenhagen
1998 - 2004	Doctoral Student	University of Rochester
1995 - 1998	Masters Student	University of Maryland
1993 - 1995	Undergraduate Studies	University of Maryland
1990 - 1993	Undergraduate Studies	SUNY College at Purchase

Fellows

1995 - 1998	Predoctoral Fellow, Laboratory of Molecular Systematics, Smithsonian Institution
1997	NSF Biology of Small Populations RTG Fellow, University of Maryland - College Park

Grants

2007 - 2008	Danish Agency for Science, Technology and Innovation The Danish Natural Science Research Council Forskningsrådet for Natur og Univers, FNU (Ref. No. 272-06-0316), 1.498.528 DKK
2006 - 2007	Danish Agency for Science, Technology and Innovation Danish Medical Research Council Forskningsrådet for Sundhed og Sygdom, FSS (Ref. No. 271-05-0599), 576.000 DKK

Post-docs

2010 -	Dr. Anne Kupczok
2010 -	Dr. Rodrigo A. F. Redondo

RESEARCH OVERVIEW

Microbes — viruses, bacteria, archaea, and protists — account for half of all the biomass and the majority of organismal diversity on planet earth. Microbes gave rise to higher organisms and have left their genomic calling cards in the form of organelles, genes, and so called junk DNA. In addition, microbes are the source of the majority of human diseases. For these reasons alone microbes are worthy of scientific study. Yet, they are also important in another, not so obvious, way: microbes are an extraordinarily powerful model system for understanding, in very fine detail, how evolution operates. To this end, experimental microbial evolution offers one the most powerful approaches to (1) understanding microbial evolution and (2) evolutionary principles in general. This power arises from a number of important features of microbes. First, they can be easily propagated in the laboratory. Second, they have short generation times allowing for many generations of evolution to be documented and analyzed. Third, due to their relatively small genomes we can track many if not all of the genetic changes occurring during evolution and then easily determine their selective affects. Lastly, we can easily manipulate important evolutionary parameters such as population size, recombination, and mutation rates to understand the role these forces

play in evolution.

Thus the research in my group focuses on three fundamental areas — microbial evolution, experimental evolution, and statistical phylogenomics — in evolutionary biology to better understand the selective forces shaping microbial genomes, evolutionary interactions between hosts and parasites, the evolution of bacterial immunity, and the genetics of adaptation.

RESEARCH — CURRENT PROJECTS

Currently, my group is working in three focal areas of microbial and experimental evolution:

- 1) Evolution of a bacterial immune system,
- 2) Adaptation in asexuals and sexuals, and
- 3) Selective barriers to horizontal gene exchange in bacteria.

The Evolution of an Adaptive Heritable Immune System in Bacteria

It has been known since the 1970s that bacteria have an innate antiviral defense system (i.e., the restriction modification system). Bacteria, and the Archaea, also have an adaptive heritable immune system called CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats). CRISPR is found in Eubacteria and Archaea. The system consists of a number of CRISPR associated (CAS) proteins and an array of repeats and spacers - the later represent the viral/plasmid targeting sequence and the system functions in an analogous way to the eukaryotic siRNA system. The length and content of the spacer array varies considerably among individuals within species (suggesting a rapid arms race) and it has been suggested that there is a selective cost, in the absence of parasites, associated with maintaining these arrays. This immunity is then inherited by the daughter cells. Dr. Rodrigo Redondo (a post-doc in my group) and I are currently working on a project of collecting spatial and population time-series data from the common soil bacterium *Stenotrophomonas maltophilia* and its viruses. The goal is to address questions about the evolutionary dynamics of host-parasite interactions and local adaptation at the phenotypic and genotypic level. This study is focusing on the genetic changes in the CRISPR repeat array and concurrent changes (escape mutations) in the associated viral populations. By collecting time-series genetic data we will be able to observe the gains and losses (rate of turnover) in the repeat array and the changes in allele frequencies through time to estimate selection (a method for estimating $2N_e s$ from time-series data was previously developed by myself and colleagues [9]). In addition, we will address questions about local adaptation in the bacterial and viral population in the lab by performing challenges to determine levels of resistance (sensitivity) to local and spatially isolated phages.

The Evolution of CRISPR in *Staphylococcus pseudintermedius*

The CRISPR loci appears to be absent in *S. aureus* (based on surveying 30 completed genomes). However, our collaborator, Dr. J. Ross Fitzgerald (Royal Infirmary, Edinburgh), has discovered the presence of CRISPR in the first sequenced genome (currently unpublished) of the related species, *Staphylococcus pseudintermedius*. My group is sequencing the CRISPR repeat loci and the associated CAS proteins in 70 isolates of this species. Dr. Anne Kupczok (a post-doctoral scientist in my group) and I have recently developed a statistical model of evolution of the CRISPR repeat locus enabling us to estimate the rate of evolution (gains/losses) for repeats originating from different sources (viruses, plasmids, etc.). We are currently applying this method to published data across a variety of bacterial species to understand the differences in rates among them. Our approach will be applied to the *S. pseudintermedius* data set. We will extend the model to incorporate information from the population study in soil bacteria described above to calibrate the rates of gains/losses to their expected selective values. Bringing together these different levels of analysis is an important step towards bringing together population genetics and comparative statistical genomic approaches.

Selective Barriers to Horizontal Gene Exchange

Horizontal gene exchange represents one of the important sources of novel gene function in bacteria and Archaea. It has been estimated that nearly all bacterial genes have experienced at least one successful horizontal gene transfer during its evolutionary history. This observation coupled with the many single gene studies of horizontal gene transfer have led others to adopt a largely genomic approach to better understanding the barriers to horizontal exchange. This rich body of work has identified such forces as divergence, dosage, and the location of the new gene within the new genomic backgrounds gene network as important factors. Yet we still lack a fundamental global understanding of these factors and the selective affects of a newly acquired gene during the

first phase of gene acquisition. To address this question we have adopted an experimental evolutionary approach. Using a clone library from *Salmonella typhimurium* LT2 covering 98% of the genome we will introduce these approximately 1,000 genes into a novel *E. coli* genomic background that can express the new genes at varying levels. Using competition assays between the HGE lines and the ancestral genome (i.e., those lacking the new gene) we will be able to estimate the distribution of mutational effects at different levels of gene expression and different environments. With this information, coupled with information about the functional role of the introduced genes, we will be able to address questions about the relative magnitude of different barriers to horizontal gene acquisition (e.g., importance of dosage effects, location in the gene network, environmental dependency, etc.).

SCIENTIFIC IMPACT

Invited Lectures

- 1) November, 2010. Symposium, EvolVienna, Vienna, Austria
- 2) September, 2009. Symposium, ICHAIR Annual Workshop, Interdisciplinary Centre for Avian and Human Influenza Research, Edinburgh, Scotland
- 3) April, 2007. Mathematical Genetics of Selection and Adaptation — University of Aarhus
- 4) October, 2005. Reunión Anual Sociedad de Biología de Chile, Sociedad de Ecología - Sociedad de Botánica
- 5) May, 2005. Evolutionary Biology Center, Uppsala Universitet, Uppsala, Sweden
- 6) March, 2005. Symposium: Using Ancestral Sequence Reconstruction to Understand Protein Function, Kristineberg, Sweden
- 7) November, 2003. Journées de la Société Française de Systématique, Muséum National d'Historie Naturelle, Paris, France
- 8) August, 2002. Bayesian inference of phylogeny and molecular evolution, Ph. D. Student course — Department of Systematic Zoology, Uppsala University, Uppsala, Sweden.
- 9) December, 2001. Department of Biologie II, Evolutionary Biology, Ludwig-Maximilians-University, Munich, Germany
- 10) Fall, 1996. Department of Plant Biology, University of Maryland

Journal Reviewer

I participate as peer reviewer for the following international scientific journals: *Evolution*, *Journal of General Virology*, *Journal of Molecular Evolution*, *Molecular Biology and Evolution*, *Molecular Phylogenetics and Evolution*, and *Systematic Biology*.

Software

SIMMAP: Stochastic Mutational Mapping on Phylogenies.

Program Description: A program for stochastically mapping the evolutionary history of discrete molecular and morphological characters. Program evaluates the posterior history of characters facilitating addressing questions in molecular and phenotypic evolution. SIMMAP uses predictive distributions to test a variety of hypotheses of character evolution.

Current version: 1.5

Download Source: <http://www.simmap.com>

PUBLICATIONS

Citations: 1408

- 1) Caitriona M. Guinane, Nouri L. Ben Zakour, Maria A. Tormo-Mas, Lucy A. Weinert, Bethan V. Lowder, Robyn A. Cartwright, Davida S. Smyth, Cyril J. Smyth, Jodi Lindsay, Katherine A. Gould, Adam Witney, Jason Hinds, **J. P. Bollback**, Andrew Rambaut, Jos Penads, and J. Ross Fitzgerald. (2010) Evolutionary genomics of *Staphylococcus aureus* reveals insights into the origin and molecular basis of ruminant host adaptation. *GBE*. 2:454-466.
- 2) **Jonathan P. Bollback** and John P. Huelsenbeck. (2009) Parallel genetic evolution within and among species of varying degrees of divergence. *Genetics*. 181: 225–234.
- 3) **Jonathan P. Bollback**, Tom York, and Rasmus Nielsen. (2008) A likelihood method for estimating 2Ns from serially sampled di-allelic data. *Genetics*. 179: 497–502.

- 4) Petersen, L., **J. P. Bollback**, M. Dimmic, M. Hubisz, R. Nielsen. (2007) Genes under positive selection in *Escherichia coli*. *Genome Research*. 17: 1336–1343.
- 5) **Jonathan P. Bollback** and John P. Huelsenbeck. (2007) Clonal interference is alleviated by high mutation rates in large populations. *Molecular Biology and Evolution*. 24(6):1397–1406.
- 6) Jonas Binladen, M. T. P. Gilbert, **Jonathan P. Bollback**, F. Panitz, C. Bendixen, R. Nielsen, E. Willerslev. (2007) The use of coded PCR primers enables high-throughput sequencing of multiple homolog amplification products by 454 parallel sequencing. *PLoS ONE*. 2(2): e197.
- 7) Eva Freyhult, **Jonathan P. Bollback**, and Paul P. Gardner. (2007) Exploring genomic dark matter: homology search for non-coding RNA. *Genome Research*. 17:117–125.
- 8) Sheila M. Reynolds, Katie Dryer, **Jonathan P. Bollback**, J. Albert C. Uy, Gail L. Patricelli, Timothy Robson, Gerald Borgia, and Michael J. Braun (2007) Behavioral paternity predicts genetic paternity in satin bowerbirds, a species with a non-resource-based mating system. *The Auk*. 124(3):857–867.
- 9) **Jonathan P. Bollback**, Paul P. Gardner, and Rasmus Nielsen. (2007) Estimating the history of mutations on a phylogeny. In “Ancestral Sequence Reconstruction” (Liberles, D. Ed.) Oxford University Press, UK.
- 10) **Jonathan P. Bollback** (2006) SIMMAP: Stochastic character mapping of discrete traits on phylogenies. *BMC Bioinformatics*. 7:88.
- 11) Jan E. Conn, Joseph H. Vineis, **Jonathan P. Bollback**, David Y. Onyabe, Richard C. Wilkerson and Marinete M. Póvoa. (2006) Population structure of the malaria vector *Anopheles darlingi* in a malaria-endemic region of eastern Amazonian Brazil. *Am. J. Trop. Med. Hyg.* 74(5): 798–806.
- 12) Andrea J. Betancourt and **Jonathan P. Bollback**. (2006) The mutational landscape model in experimental evolution. *Current Opinions in Genetics and Development*. 16:618–623.
- 13) **Jonathan P. Bollback**. (2005) Posterior mapping and predictive distributions. In “Statistical methods in Molecular Evolution” (Nielsen, R. Ed.) Springer Verlag New York, Inc. New York, USA.
- 14) John Harshman, Christopher J. Huddleston, **Jonathan P. Bollback**, Thomas J. Parsons, and Michael J. Braun. (2003) True and false gavials: A nuclear gene phylogeny of Crocodylia. *Systematic Biology* 52(3): 386–402.
- 15) John P. Huelsenbeck, Rasmus Nielsen, **Jonathan P. Bollback**. (2003) Stochastic mapping of morphological characters. *Systematic Biology* 52(2):131–158.
- 16) **Jonathan P. Bollback** (2002) Bayesian model adequacy and choice in phylogenetics. *Molecular Biology and Evolution*. 19 (7): 1171–1180.
- 17) John P. Huelsenbeck, **Jonathan P. Bollback**, and Amy Levine. (2002) Inferring the root of a phylogenetic tree. *Systematic Biology*. 51 (1): 32–43.
- 18) John P. Huelsenbeck, Frederick Ronquist, Rasmus Nielsen and **Jonathan P. Bollback**. (2001) Bayesian inference of phylogeny and its impact on evolutionary biology. *Science*. 294: 2310–2314.
- 19) Jan E. Conn, **Jonathan P. Bollback**, Davide Y. Onyabe, Tessa N. Robinson, Richard C. Wilkerson, and Marinete M. Póvoa. (2001) Isolation of polymorphic microsatellite markers from the malaria vector *Anopheles darlingi*. *Molecular Ecology Notes*. 1 (4): 223–225.
- 20) John P. Huelsenbeck and **Jonathan P. Bollback**. (2001) Empirical and hierarchical Bayesian estimation of ancestral states. *Systematic Biology*. 50 (3): 351–366.
- 21) John P. Huelsenbeck and **Jonathan P. Bollback**[†]. (2001) Application of the likelihood function in phylogenetic analysis. In “Handbook of Statistical Genetics” (Balding. D.J., Bishop, M., and Cannings, C., Eds.) Chapter 15, pp. 415–439. John Wiley and Sons, Inc. New York, USA.
- 22) **Jonathan P. Bollback** and John P. Huelsenbeck. (2001) Phylogeny, genome evolution, and host specificity of single-stranded RNA bacteriophage (Family Leviviridae). *Journal of Molecular Evolution*. 52: 117–128.