Rafael F. Guerrero

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Education

Current   Indiana University
Postdoctoral researcher with Dr. Matthew Hahn

2013   University of Texas at Austin
Ph.D. Ecology, Evolution and Behavior, with Dr. Mark Kirkpatrick

2006   Universidad de los Andes – Bogota, Colombia
M.S. Biology

2003   Universidad de los Andes – Bogota, Colombia
B.S. Biology (Honors)

Publications

-   **Guerrero RF** and MW Hahn. Quantifying the risk of hemiplasy in phylogenetic inference. *pending minor revision at* PNAS. (BioRxiv doi:10.1101/391391)

-   Ogbunugafor CB, **Guerrero RF**, and MJ Eppstein. Genotypic context modulates fitness landscapes: Effects on the speed and direction of evolution for antimicrobial resistance. *In review at* PLoS Computational Biology. (BioRxiv doi:10.1101/427328)

18   Berrio A, **Guerrero RF**, Aglyamova GV, Okhovat M, Matz MV, and SM Phelps (2018). Complex selection on a regulator of social cognition: Evidence of balancing, epistatic, and spatially varying selection at the prairie vole Avpr1a locus. Molecular Ecology 27:419-431.

17   **Guerrero RF** and MW Hahn (2017). Speciation as a sieve for ancestral polymorphism. Molecular Ecology 26:5362-5368.

16   **Guerrero RF**, Muir CD, Josway S, and LC Moyle (2017). Pervasive antagonistic interactions among hybrid incompatibility loci. PLoS Genetics 13:e1006817.

15   Des Marais DL, **Guerrero RF**, Lasky JR, and SV Scarpino (2017). Topological features of gene regulatory networks predict patterns of natural diversity in environmental response. Proceedings of the Royal Society B 284:20170914.

14   Broz AK*, **Guerrero RF***, Randle AM, Baek YS, Hahn MW, and PA Bedinger (2017). Transcriptomic analysis links gene expression to unilateral pollen-pistil reproductive barriers. BMC Plant Biology 17:81. (*equal contributors)

13   **Guerrero RF**, Posto AL, Moyle LC, and MW Hahn (2016). Genome-wide patterns of regulatory divergence revealed by introgression lines. Evolution 70:696-706.

12   Pease JB, **Guerrero RF**, Sherman NA, Hahn MW, and LC Moyle (2016). Transcriptome-wide analysis of gene expression changes that accompany post-mating prezygotic reproductive isolation. Molecular Ecology, 25:2592-2608.

11   **Guerrero RF**, and M Kirkpatrick (2014). Local adaptation and the evolution of chromosome fusions. Evolution 68:2747-2756.

10   Kirkpatrick, M and **RF Guerrero** (2014). Signatures of sex-antagonistic selection on recombining sex chromosomes. Genetics 197:531-541.

9   Hopkins R, **Guerrero RF**, Rausher MD and M Kirkpatrick (2014). Strong reinforcement in a Texas wildflower. Current Biology 24:1995-1999.

8   Rousset F, Kirkpatrick M and **RF Guerrero** (2014). Matrix inversions for chromosomal inversion: A method to construct summary statistics in complex coalescent models. Theoretical Population Biology 97:1-10.

7   Peischl S, Koch E, **Guerrero RF**, and M Kirkpatrick (2013). A sequential coalescent algorithm for chromosomal inversions. Heredity 111:200-209.

6   Ayala D*, **Guerrero RF*** and M Kirkpatrick* (2013). Reproductive isolation and local adaptation quantified for a chromosome inversion in a malaria mosquito. Evolution 67:946-958. (*equal contributors)

5   **Guerrero RF**, Kirkpatrick M, and N Perrin (2012). Cryptic recombination in the ever-young sex chromosomes of European tree frogs. Journal of Evolutionary Biology 25:1947-1952.

4   McTavish EJ, Smith GK, **Guerrero RF**, and EJ Gering (2012). Flight morphology variation in a damselfly with female-limited polymorphism. Evolutionary Ecology Research 14:325-341.

3   **Guerrero RF**, Rousset F, and M Kirkpatrick (2012) Coalescent patterns of chromosomal inversions in divergent populations. Philosophical Transactions of the Royal Society B 367:430-438.

2   Otto SP, Pannell JR, Peichel CL, Ashman T, Charlesworth D, Chippindale AK, Delph LF, **Guerrero RF**, Scarpino SV, and BF McAllister (2011). About PAR: The distinct evolutionary dynamics of the pseudoautosomal region. Trends in Genetics 27:358-367.

1   Kirkpatrick M, **Guerrero RF**, and S Scarpino (2010). Patterns of neutral genetic variation on recombining sex chromosomes. Genetics 184:1141-1152.

Teaching

2016	Instructor, Applied Evolutionary Theory Workshop. Gulbenkian Institute, Portugal.
2014	Guest lecturer, SNP discovery and population genetics. Indiana U.
2008	Teaching Assistant, Introduction to Biology. U Texas.
2008	Teaching Assistant, Biostatistics. U Texas.
2007	Teaching Assistant, Introduction to Biology. U Texas.
2006	Teacher. 7th grade Biology. San Carlos School, Bogota.
2003–2005	Teaching Assistant, Animal Physiology lab. U Andes, Bogota.
2001–2003	Teacher. 9th grade Biology. San Carlos School, Bogota.

Invited Seminars

2018   North Carolina State University, Department of Genetics
2018   University of California – Irvine, Department of Ecology & Evolutionary Biology
2018   University of Arizona, Department of Ecology & Evolutionary Biology
2017   University of Missouri, Division of Biological Sciences
2017   University of Vermont, Department of Biology
2016   Instituto Gulbenkian de Ciencia (Portugal)
2016   University of Massachusetts – Lowell, Department of Biology
2014   Indiana University, Common Themes in Reproductive Diversity
2012   University of California – Berkeley, Center for Theoretical Evolutionary Genomics
2012   Universitat Autonoma de Barcelona, Departament de Genetica i de Microbiologia

Fellowships and Awards

2008   ESI Texas EcoLab Research Grant
2008   Zoology Scholarship Endowment for Excellence, University of Texas
2006   Degree *cum Laude*, Universidad de Los Andes
2005   Graduate Student Research Fellowship. Universidad de Los Andes

Recent Presentations

2018   Guerrero RF and M Hahn. Quantifying the risk of hemiplasy in phylogenetic inference (*Poster*). GSA PEQG meeting, Madison WI.
2017   Guerrero RF. Complex hybrid incompatibilities inferred from widespread pairwise interactions among sterility loci. Spotlight symposium, SSE meeting, Portland OR.
2016   Guerrero RF, Nakazato T, and L Moyle. Antagonistic interactions among sterility QTL. SSE meeting, Austin TX.
2014   Guerrero RF, Hahn M, and L Moyle. Pervasive misexpression in tomato introgression lines is unrelated to low-fitness hybrid phenotypes (*Poster*). SMBE meeting, San Juan, PR.

Service and Professional Activities

Reviewer for *Genetics*, *Evolution*, *Nature Ecology & Evolution*, *Proc Roy Soc B*, *Molecular Ecology*, *American Naturalist*, *New Phytologist*, *Journal of Evolutionary Biology*, *Phil Trans Roy Soc B.*, among others.
Member of the Society for the Study of Evolution, Genetics Society of America, Society for Molecular Biology and Evolution, Society for the Advancement of Chicanos, Hispanics, and Native Americans in Science.
Graduate student representative. IB postdoctoral fellowship search committee. University of Texas, 2012
Organizer. Integrative Biology Graduate Research Symposium. University of Texas, 2009–2013
Coordinator. Biology booth at ExpoCiencia, a science outreach fair in Bogota, Colombia. 2004

Last updated: October 22, 2018

October 30, 2018

Evolutionary or Ecological Theory Faculty Search Committee
Department of Biological Science
Florida State University

Dear committee,

I am writing to apply for the position of Assistant Professor in Evolutionary Theory. I believe my research, integrating computational and theoretical approaches in evolutionary genetics, complements the current strengths of your Department and makes me an ideal candidate for the position.

I am a population geneticist interested in bridging the gap between theory and data analysis in evolutionary biology. I have focused on understanding how **antagonistic interactions** shape the **evolution of chromosomes** and **population divergence**. I have developed models that provide a foundation for complex population-genomic studies, and implemented statistical methods to quantify a variety of evolutionary forces in natural populations. During my postdoctoral training, I have used transcriptome and phenotypic data to study the evolution of reproductive isolation, and I am currently generating *de novo* genome assemblies in the study of new sex chromosomes. Some of my current work is in **evolutionary medicine**, inferring genetic interactions relevant to the evolution of antibiotic resistance and exploring the potential role of parent-offspring conflict in gestational diabetes.

A great part of my research has been possible through close collaborations. As an Assistant Professor, I will develop a research program that continues to be close to empirical questions that motivate new theoretical and statistical work. I believe that my interests are complementary to the outstanding research done at Florida State, and I am confident that this will lead to fruitful collaborations with faculty in the Department and beyond.

Please find attached my *curriculum vitae*, as well as research and teaching statements. I am particularly pleased to submit this application, since I know FSU has a great deal to offer, and I believe I have much to contribute in return. I hope I have the opportunity to do so.

Sincerely,

Rafael F. Guerrero

Teaching Statement

My teaching philosophy revolves around two goals. First, to convince students that science is not a finished body of knowledge, but a way of seeing the world. Second, to equip students with the tools to critically analyze the impact science has in our lives. In my experience, while these goals in science education are constant from middle school Biology to undergraduate classes, teaching itself is an ever-changing endeavor. Effective educators must adapt their teaching style to the background and experience of students, and incorporate the latest discoveries into their material. Below, I provide brief descriptions of how I will approach teaching in courses of various levels.

Introductory courses – Through my experience as a teaching assistant, I realized introductory courses need to emphasize on the relevance and ubiquity of the science being taught. Using workshops, concept maps, critical summaries and in-class activities I will develop critical analysis skills that students to evaluate concepts such as replication, use of controls, and correlation-causation issues in press articles. To engage students, I will use contemporary topics such as flu epidemics, vaccination, and genetic modification of crops to demonstrate that biology is an exciting, current field affecting students' everyday lives.

Advanced undergraduate courses – At this level, the goal must be to prepare students for entering the work force or going on to an advanced degree. To that end, my courses will include a strong component of reading and presenting of scientific articles, and carrying out a semester-long project through which students learn how to design experiments and write a report about them. By doing so, students will learn to critically evaluate primary scientific literature, acquire observation-based hypothesis testing and experimental design, and learn to present their results.

Graduate courses – At the graduate level, classes have two purposes: 1) to provide a context for thinking about the unanswered questions in biology, and 2) to teach the skills to answer those questions. For courses aimed at the first objective, lectures and discussion of papers on current issues in the field – anchored by a historical perspective – are effective approaches. For the second type of courses, I will design courses where students get hands-on practice with analytical and computational methods (for example, identifying SNPs in genomic data, reconstructing phylogenies, and carrying out evolution experiments with available simulation platforms).

Mentoring students is a fundamental component of teaching science. I will encourage students of all levels to engage in research in my lab. As a graduate student, I guided undergraduates doing research that lead to publications. As a postdoc, I maintain close communication with graduate students, leading a weekly group meeting – without our adviser – to discuss and troubleshoot everyone's ongoing research. This meeting has been a wonderful way of harnessing the diverse skills of lab members, and has contributed to a healthy, collaborative lab environment. As and adviser, I will strive to provide students with the support they need while leaving them the freedom to develop their own intellectual direction.

Courses of Interest: I would be interested in teaching a range of introductory and advanced courses in subjects such as (but not limited to): 1. **Evolution**, 2. **Theoretical and/or Statistical Population Genetics**, 3. **Biostatistics**, 4. **Mathematical Modeling in Biology**, and 5. **Introductory Bioinformatics**. I would also be interested in developing a hands-on course on **Computational Ecology and Evolution**, where students create their own pipelines (by extending available software) to analyze data. This course would involve students writing a mini-thesis in the form of a scientific paper.

Theory and inference of antagonism in evolution
Rafael F. Guerrero

I aim to understand the evolutionary forces that shape natural diversity within and between populations, by developing new population genetic theory and using novel statistical methods to analyze complex data. As a population geneticist, I have focused on phenomena driven by antagonistic genetic interactions, such as the evolution of sex chromosomes, regulatory divergence, and hybrid incompatibilities. In my work I combine an array of mathematical and computational methods, from classic population genetic models to transcriptome analysis and genome assembly.

As an independent researcher, I will establish a program that continues to expand on these topics by applying different aspects of my expertise. For instance, current work on sex chromosome evolution involves large-scale genomic analysis, while questions regarding regulatory divergence require a considerable mathematical and statistical effort. Below, I briefly describe my previous contributions and outline future research plans.

The evolution of nascent sex chromosomes

Sex is arguably the largest source of variance within species. Consequently, sex chromosomes are key elements of the biology and evolution in species with genetic sex determination. Sex chromosomes follow a fascinating evolutionary trajectory, involving the accumulation of sex-antagonistic genes followed by the suppression of recombination–often by chromosome inversions (Otto et al. 2012). The lack of recombination leads to high levels of divergence between the homologous pair and the degeneration of one of the chromosomes (e.g, the Y chromosome of mammals). However, many questions about this trajectory remain open, for example regarding the mode and tempo of sexual antagonism or the evolutionary forces that interact to favor or prevent the spread of chromosome inversions. I have contributed to some of these issues, specifically by generating models that predict levels of sequence divergence in sex chromosomes (Kirkpatrick et al. 2010) and chromosome inversions (Guerrero et al. 2012), describing the expected signatures of sex-antagonistic selection (Kirkpatrick & Guerrero 2014), and developing methods to estimate extremely low levels of recombination (Guerrero et al. 2012). Currently, I am working towards the application of these models to the study of a recently evolved sex-chromosome system. 'Young' sex chromosomes offer a unique perspective on the origin of sex and the dynamics of sex-linked genomic regions, and can tell us about the conditions that affect the evolution of recombination suppression, subsequent sex-chromosome divergence and potential degeneration.

Roadmap 1: A new system for the study of young sex chromosomes

Current — Assemble the genome of the nightshades Solanum polygamum and S. appendiculatum, which represent two independently evolved sex-determination systems, and characterize sex-linked regions (collaboration with G. Anderson at U Connecticut). Using mapping coverage differences between male and female samples I will infer the sex-linked sequence, providing a foundation for tests of the models of sex chromosome evolution. Through this project, I am mentoring Meng Wu, a fifth-year PhD student.

Mid-term — Test sex-linked regions S. polygamum and S. appendiculatum for signatures of sex-antagonistic selection predicted by Kirkpatrick & Guerrero (2014). Using sequence diversity and allele frequency data, I will fit coalescent models to identify loci under sexual conflict in this young sex determination system.

Examine gene expression patterns across the genome of S. appendiculatum, testing the hypothesis that the resolution of sex antagonism leads to an excess of genes with sex-biased expression in the sex chromosomes.

Future grant	I propose to study the tempo of sex chromosome divergence, using the genus Solanum as a unique system with existing genomic resources and multiple recent independent origins of dioecy. Using a comparative approach, I will contrast the sequence diversity and gene expression patterns in the sex chromosomes of S. polygamum, S. appendiculatum and S. dioicum to their monoecious relatives. While the genomes of at least six Solanum species are available, this project will require assembling the genome of S. dioicum, and developing a novel pipeline for the phylogenetic analysis of patterns in orthologous sequences. This work will be in collaboration with L. Moyle at Indiana U, who would carry out the greenhouse and wet-lab component of the experiment.

Regulatory divergence & hybrid incompatibilities

As populations evolve, chance and natural selection drive them apart. These divergence processes uncover the dramatic extent to which genetic interactions are present throughout the genome. In inter-specific hybrids, antagonistic interactions are manifest in their misregulation of gene expression (e.g, Guerrero et al. 2016), sterility, or inviability (e.g, Guerrero et al 2017). Recently, I found evidence of widespread antagonistic interactions among multiple loci involved in genetic incompatibility (Guerrero et al. 2017; Fig.1). This antagonism could have critical consequences for the tempo of speciation by decoupling the accumulation of isolation loci and isolation phenotypes, therefore attenuating the rate of accumulation of hybrid infertility among lineages. I will continue to work
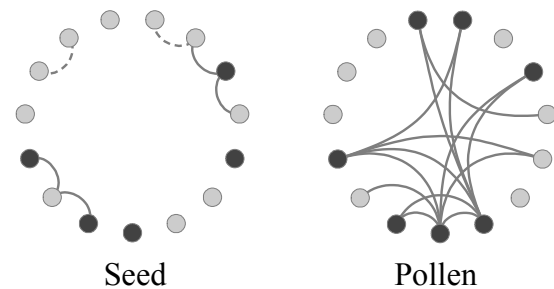

Seed   Pollen

Figure 1. Networks of epistatic interactions (edges) among loci (nodes) involved in hybrid sterility between S. lycopersicum and S. pennellii. Pollen sterility interactions are more frequent than ones involving seed sterility, and tend to occur more between loci of large effect (dark nodes). From Guerrero et al (2017).

on this area by taking a networks approach to the study of hybrid incompatibilities and the evolution of gene regulation.

Roadmap 2: Interacting genes in diverging populations

Current	Develop new theory to understand how topological properties of gene networks (e.g., size, modularity or connectivity; Fig.1) can affect the rate of accumulation of hybrid incompatibilities and the expected degree of these epistatic interactions. McKenzie Givens, a first-year PhD student who I mentor, is involved in this project.
Mid-term	Model the evolution of regulatory divergence in a network framework, testing the hypothesis that network topology drives the saturation of observable differences, determining the relative importance of cis- vs. trans-regulatory divergence.
Future grant	I propose to map genome-wide changes in gene expression across the genus Solanum on their phylogeny, inferring the contribution of trans-regulation in the evolution of gene expression. I will use gene trees to inform the construction of gene coexpression networks, to obtain a phylogenetic view of gene-gene interactions and explore a novel perspective on the evolution of gene networks.

Applications to disease and public health

We can leverage insights from evolutionary biology to better understand and prevent disease. For instance, we can gain power in the computational prediction of the pathogenicity of mutations by incorporating comparative and demographic data (I took such an approach at the most recent 'Critical Assessment of Genome Interpretation' challenge, in which my submission ranked first). In turn, many diseases represent fascinating cases to study genetic interactions. Abnormal pregnacy outcomes (such as preterm birth, pre-

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eclampsia, and heart disease) have been linked to an antagonistic interaction between maternal and fetal genes called maternal-fetal genotype incompatibility (MFGI). I am currently involved in multiple projects that apply evolutionary genetics in medicine, specifically studying epistatic interactions in the genetic basis of antibiotic resistance and metabolic diseases.

Roadmap 3: Antagonistic interactions in evolutionary medicine

Current	Characterize the interactions between SNPs associated with resistance to antibiotics in an essential bacterial enzyme (dihydrofolate reductase or DHFR), differing DHFR species backbone sequences (Escherichia coli, Chlamydia muridarum, and Listeria grayi) and different protein quality control genetic backgrounds, with regards to their effect on traits that contribute to microbial survival in the presence of antibiotic (in collaboration with B. Ogbunugafor at Brown U).
Mid-term	Study the genetic basis of gestational diabetes, taking a genome-wide association approach that includes rigorous analysis of the effect of fetal genotype on the maternal phenotype. This is an ancillary study of the NuMom2B consortium (a cohort of 10 thousand mother-child pairs), in collaboration with D. Haas (IU School of Medicine) and P. Radivojac (Northeastern U).
Future grant	I propose develop an approach to detect loci that are putatively under parent-offspring conflict in the human genome, which would allow us to better infer epistatic interactions involved in disease. By narrowing the search space for potential interactions, I propose an alternative to traditional genome-wide association studies (which usually require very large sample sizes to detect interactions) with which we can tackle hypotheses involving intergenerational gene-gene interactions.

Future directions

My research program is centered around the study of increasingly complex interactions, which are ubiquitous in nature. Higher-order interactions are present between sex-determining genes and hundreds of genes throughout the genome, among loci involved in genetic incompatibilities. Understanding this complexity is paramount to the study biological systems, and I aim to develop a research program that leads the field in that regard by developing tools to study these intricate processes in natural populations. Collaborations are a large component of my work, allowing me to study a wide diversity of taxa (including vertebrates, insects, and plants) and data (from mendelian traits to whole transcriptomes). I plan to continue this highly collaborative work, always deeply rooted in population genetic theory. In the long term, I want to establish a dry lab that strives for rigor, training students as critical scientists in empirical and theoretical research.