Janna L. Fierst

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Dr. Juan Lopez-Bautista
Department of Biological Sciences
The University of Alabama

Dear Dr. Lopez-Bautista,

I am writing to apply for the Computational Biology position advertised in the Department of Biology. I am an evolutionary biologist, and I use a combination of modeling, bioinformatic analyses and computational genomics to study the influence of sex on genetic and genomic evolution. Currently, I am a postdoctoral researcher under the supervision of Patrick C. Phillips at the University of Oregon.

My research aims to take an innovative approach to integrating evolutionary theory and modern molecular data. Evolutionary theory has a rich conceptual and mathematical history, but until recently we could not generate the necessary data to test theoretical predictions and produce informed, biologically grounded theory. Biological technology is rapidly advancing on all fronts, and recent progress in computing, high-throughput sequencing, and molecular biology means that we are now poised to test many fundamental theoretical predictions regarding genetic evolution. I am currently pursuing two main areas of research: 1) The influence of reproductive mode on the evolution of genome structure; and 2) Sex and system-level evolution. In my research statement, I describe my current and future projects in greater detail.

Last year I had the opportunity to meet with Laura Reed, an assistant professor in your department, while she was visiting our Institute. She spoke very highly of your department, colleagues and the research environment and I am very excited by the opportunity to work in your department. My long-term goals are to build: 1) a research program integrating evolutionary theory with genetic data; and 2) a teaching and mentoring program that provides students with solid biological foundations and mathematical and computational skills. The University of Alabama has strong organismal, molecular, and genetic programs and I feel my research would complement the existing strengths by adding a computational component and the opportunity for productive collaborations.

I have attached my references to this document, and included a CV, research statement and teaching statement. If you would like any other information, please let me know. Thank you for your time and consideration.

Sincerely,

Janna Fierst

References

Professor Steven R. Dudgeon (MS Advisor)
Department of Biology, California State University, Northridge
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Northridge, CA 91330-8303
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Professor Thomas F. Hansen (PhD Advisor)
Center for Ecological and Evolutionary Synthesis
Department of Biology, University of Oslo
P.O. Box 1066, Blindern
0316 Oslo, Norway
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fax: +47 22 85 40 01
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Professor David Houle (PhD Advisor)
Department of Biological Sciences, Florida State University
4063 King Life Sciences
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ph: +1 850-645-0388
fax: +1 850-645-8447
dhoule@bio.fsu.edu

Professor and Associate Vice President for Research Patrick C. Phillips (Postdoctoral Advisor)
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Department of Biology, University of Oregon
Eugene, OR 97403-5289
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Research Statement

One of the central problems in biology is understanding how sex influences evolution. Sexual reproduction increases genetic variation through meiotic recombination, and that single difference results in a broad array of consequences at genetic and phenotypic levels. The division into two separate sexes results in different reproductive modes, mating systems, sexual dimorphism and sexual selection. Evolutionary theory predicts that populations and genomes should evolve differently depending on reproductive strategy, but theoretical predictions have been limited by a lack of biological details.

For example, nematode worms in the genus *Caenorhabditis* descended from an outcrossing ancestor (Kiontke et al., 2011). Three lineages independently evolved facultative hermaphroditism and these three species also have the smallest genomes. What accounts for these differences in genome size? Theory predicts that genome size evolution may be determined by effective population size (Lynch and Conery, 2003), transposable element activity (Bestor, 1999), selection for replication efficiency (Pagel and Johnstone, 1992), or purely neutral processes (Petrov et al., 2000). Until recently we could not go farther than these predictions because we lacked the data to test our theory, but advances in sequencing technology and computing power mean that it is now possible to answer these questions. My research capitalizes on modern technology and utilizes concept-driven modeling, bioinformatic analyses and computational genomics. I address the influence of sex on genetic and genomic evolution, and focus on two main areas: 1) Reproductive mode and the evolution of genome structure; and 2) Sex and system-level evolution.

Reproductive mode and the evolution of genome structure

Evolutionary theory predicts that patterns of selection, genetic variation and mutational accumulation will be determined by the relative rates of recombination and outcrossing that a population experiences. These differences should affect every aspect of an organisms genetic and genomic evolution, but these predictions were impossible to test prior to the development of modern genomics. Nematode worms present a perfect opportunity to study the influence of reproductive mode and mating system on genetic evolution as the Elegans group includes three self-fertile hermaphrodites, and at least seven species that retain the ancestral male-female mating system (a partial phylogeny is shown in Figure 1). The group includes the model organism *Caenorhabditis elegans*, and there is a wealth of genetic and genomic resources available because of this.

High-quality genome sequences are available for the hermaphrodites *C. elegans* and *C. briggsae*, but high levels of genetic polymorphism have made it difficult to obtain accurate genome sequences for the sexual members of the Elegans group (Barriere et al., 2009). For example, current estimates of molecular diversity in *C. brenneri* are higher than any other plant or animal species yet studied (Dey et al., 2013). New molecular techniques and freely available assembly software make it possible to produce high-quality draft genomes for these nematodes. In my postdoctoral research, I have constructed a pipeline for *de novo* genome assembly, validation and annotation and am currently working to produce high-quality draft genomes for three strains of the outcrossing *C. remanei*.

The next steps in this research are: 1) Testing fundamental evolutionary theory; and 2) Computational methods development. First, completing these genome sequences allows us to address questions regarding the evolution of genome size and structure, and the influence of reproductive mode on
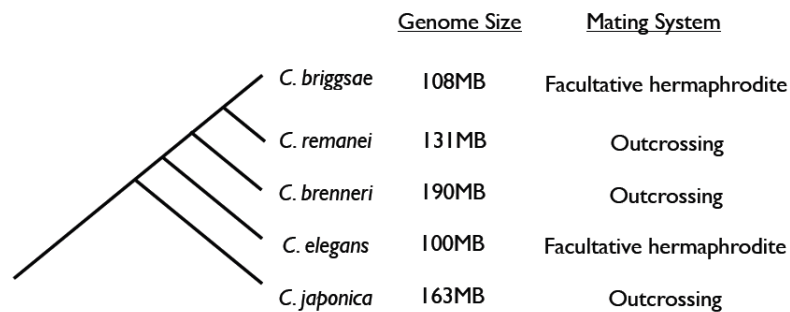
	Genome Size	Mating System
C. briggsae	108MB	Facultative hermaphrodite
C. remanei	131MB	Outcrossing
C. brenneri	190MB	Outcrossing
C. elegans	100MB	Facultative hermaphrodite
C. japonica	163MB	Outcrossing

Figure 1: Hermaphrodites in the genus *Caenorhabditis* have smaller genomes than related outcrossing species. There are at least 16 species in the Elegans group; data are shown for those species with genomic data available on Ensembl.

organismal evolution. Comparing patterns of insertions and deletions, gene duplications, transposable element proliferation and genetic diversity allows us to test important theoretical predictions regarding genome evolution. The next steps in this research will be to place these findings in a comparative context, and analyze genome sequences across populations within these highly diverse species, across related species, and different taxonomic groups. For example, angiosperm genomes vary in size from 63MB to 150GB (approximately fifty times the size of the human genome; Bennett and Leitch, 2011) and the bulk of research on reproductive mode and genome evolution has been done with self-fertile and outcrossing plant species.

Second, inexpensive, accurate genome sequencing is possible with current molecular techniques and freely available software packages but implementation remains very difficult as it requires navigating between complex molecular biology protocols and multiple bioinformatic platforms. Major genome projects like the Beijing Genome Institute's 10,000 Genomes Project are sequencing single members of species of interest, but researchers who are interested in evolutionary variation or unique species are still left without genomic resources. To this end, I am mentoring a group of computer science students to produce a software package that integrates the major steps in genome assembly. The package recommends specific sequencing strategies to address the relative genome size, gene density and repetitive content of different phylogenetic groups, filters raw data for assembly, utilizes machine-learning algorithms for validation, produces visualization files for verification and analysis, and integrates with the gene annotation software MAKER2. The next step in this research is developing this package into a freely available platform that can be utilized by the scientific research community.

Sex and system-level evolution

Biological systems must be robust in order to function despite mutations and environmental change but at the same time evolvable, or able to change. A fundamental question is how a system produces both a robust phenotype and the variance necessary for evolutionary change (Wagner, 2005). Sexually dimorphic characters often show rapid rates of change, and are an excellent system for studying the balance between evolvability and robustness. Many sexually dimorphic traits are subject to sexual selection. There are several different hypotheses that explain the evolution of female mate preferences

and these vary in their proposed beneficial or detrimental effects. For example, the Fisher process posits that female mate preferences and male traits evolve through neutral associations while sexual conflict proposes that males and females conflict over some aspect of mating and population fitness declines as a consequence (Andersson, 1994). Examples of phenotypic differences due to sexual selection, like the peacock's tail, abound in natural populations and many studies have documented genetic changes in single genes or pathways (reviewed in Andersson and Simmons, 2006). It is still unclear how sexual dimorphism and sexual selection affect fitness (e.g., Hollis et al., 2009), and we do not know how these processes affect the evolution of system-level properties like evolvability and mutational robustness.

Studying system-level evolution is inherently complex, but recent computational advances in processor speed and parallel architectures have opened up the field of computational modeling and evolutionary simulations. In my dissertation research I studied the evolution of sexual dimorphism and
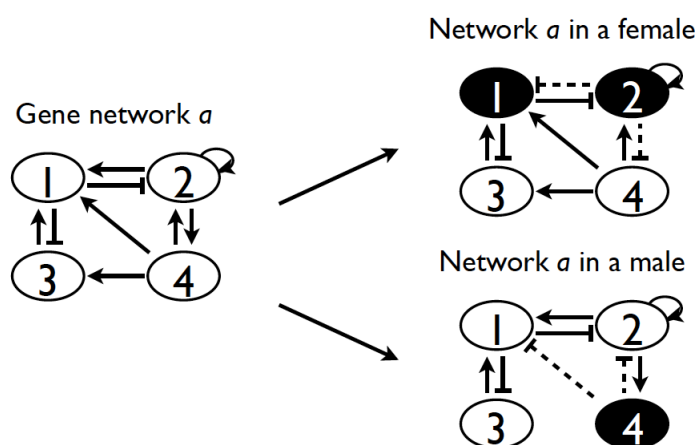
Figure 2: Gene networks receive different patterns of activation and repression in males and females, and these patterns trigger different network connections in males and females.

sexual selection through female mating preferences with a computational network model (the model formulation is shown in Figure 2). I found that genetic regulatory networks that produced sexually dimorphic characters evolved higher levels of evolvability and robustness, and that sexual selection uniformly acted to reduce evolvability and robustness (Fierst, 2011, 2013). The next steps in this research are: 1) Developing measures that describe the evolutionary potential of different genetic networks; and 2) Studying genetic networks in sexually dimorphic organisms.

One of the major challenges in network studies is that we do not know how to measure the biologically relevant features of a network. Currently, there are no metrics that describe the evolutionary properties of genetic networks and we measure these properties through intensive computational simulations. In addition, we know how very few existing network descriptors relate to evolutionary properties (Fierst, 2012). For example, Liu et al. (2011) developed a method to measure network 'controllability' and found that biological networks have a diffuse control structure that differs from social or information networks. Are these differences are causal or a by-product of evolutionary processes? To address these questions, I am mentoring a graduate student project modeling the evolution of networks with different control structures, and measuring how controllability changes over network evolution. The next steps in this research are to identify significant allelic distributions, patterns of

gene function, and network features in order to develop quantitative measures of evolutionary potential. Developing these measures is the key to making progress in our understanding of the evolution of biological networks because it will allow us to link system-level network theory with empirical systems.

Theory plays a major role in guiding biological research. Ultimately, theory must be tested in empirical systems to be useful. To this end, a major goal in my research is to study the evolution of genetic networks involved in sexual dimorphism and subject to sexual selection by coupling theory and modeling with empirical biology. Two systems, sex combs in the fruitfly *Drosophila melanogaster* and eye stalks in the stalk-eyed fly *Teleopsis dalmanni*, are excellent models for these questions. The developmental and genomic resources for these systems are still developing, but in the near future it will be possible to manipulate these organisms in the lab through artificial selection and genome engineering techniques like CRISPR. High-throughput sequencing will facilitate the analysis of genetic changes, and the identification of alterations to transcriptional networks through protein-DNA chromatin immunoprecipitation assays like ChIP-Seq and gene expression assays like RNA-Seq. These emerging technologies will allow us to empirically test the conceptual theory that structures our understanding of biological systems.

References

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Andersson, M. and L. W. Simmons, 2006. Sexual selection and mate choice. Trends in Ecology and Evolution 21:296–302.

Barriere, A., S.-P. Yang, E. Pekarek, C. G. Thomas, E. S. Haag, and I. Ruvinsky, 2009. Detecting heterozygosity in shotgun genome assemblies: Lessons from obligately outcrossing nematodes. Genome Research 19:470–480.

Bennett, M. D. and I. J. Leitch, 2011. Nuclear DNA amounts in angiosperms: targets, trends and tomorrow. Annals of Botany 107:467–590.

Bestor, T. H., 1999. Sex brings transposons and genomes into conflict. Genetica 107:289–295.

Dey, A., C. K. W. Chan, C. G. Thomas, and A. D. Cutter, 2013. Molecular hyperdiversity defines populations of the nematode *Caenorhabditis brenneri*. Proceedings Of The National Academy Of Sciences 110:11056–11060.

Fierst, J. L., 2011. Sexual dimorphism increases evolvability in a genetic regulatory network. Evolutionary Biology 38:52–67.

———, 2012. Variance in epistasis links gene regulation and evolutionary rate in the yeast genetic interaction network. Genome Biology and Evolution 4:1080–1087.

———, 2013. Female mating preferences determine system-level evolution in a gene network model. Genetica 141:157–170.

Hollis, B., J. L. Fierst, and D. Houle, 2009. Sexual selection accelerates the elimination of a deleterious mutant in *Drosophila melanogaster*. Evolution 63:324–333.

Kiontke, K. C., M.-A. Felix, M. Ailion, M. V. Rockman, C. Braendle, J.-B. Penigault, and D. H. Fitch, 2011. A phylogeny and molecular barcodes for Caenorhabditis, with numerous new species from rotting fruits. BMC Evolutionary Biology 11:339.

Liu, Y.-Y., J.-J. Slotine, and A.-L. Barabási, 2011. Controllability of complex networks. Nature 473:167–173.

Lynch, M. and J. S. Conery, 2003. The origins of genome complexity. Science 302:1401–1404.

Pagel, M. and R. A. Johnstone, 1992. Variation across species in the size of the nuclear genome supports the junk-DNA explanation for the c-value paradox. Proceedings Of The Royal Society Of London Series B-Biological Sciences 249:119–124.

Petrov, D. A., T. A. Sangster, J. S. Johnston, D. L. Hartl, and K. L. Shaw, 2000. Evidence for DNA loss as a determinant of genome size. Science 287:1060–1062.

Wagner, A., 2005. Robustness and Evolvability in Living Systems. Princeton University Press Princeton New Jersey.

Teaching Statement

Teaching Philosophy

I believe the objective of university teaching is to aid in each student's intellectual and personal development. We achieve this through lectures, assignments and tests, as vehicles for teaching students to organize and process information, develop critical thinking and analysis, communicate effectively, balance work and other pressures, and operate as community members. One of the reasons I enjoy teaching is because it also requires me to develop my own skills in these areas. I started my teaching career at the high school level, after I had finished my undergraduate degree. I had no plans to go on to graduate school, but teaching forced me to learn the material in-depth in a way I never had as a student. I developed an appreciation for science and research, and that led me to graduate school. Integrating teaching and research keeps me motivated in both areas, and provides me with a broader, deeper perspective on research questions.

I find that biology is interesting to students because it addresses the world around them, and this motivates them to engage with class material. Biology, and evolution in particular, involves complex concepts, mathematics, and diverse material. In order to succeed, students must develop a conceptual framework and practical skills and both of these are valuable for future education and work. I have found the most effective way to help students succeed is to keep them engaged. Students develop as they connect with primary literature and the broader scientific community through reading scientific papers, organize findings through oral and written presentations, and develop ideas through discussions and collaborative work. In small, advanced classes these activities happen within one semester but at introductory levels these are spread over several classes through a mix of large lectures, smaller labs, and tutorials and study sessions.

As a teacher, my primary goal is to provide a framework for students to develop critical thinking and analysis. As a biology teacher, my primary goal is to convey the excitement and wonder of science. Science has a long, developed history and an exciting future. I incorporate historical perspectives and modern research into lectures to give students a sense of perspective and continuity, and I try to spark students' excitement by relating classroom topics to modern science and research.

Mentoring

Mentoring student research projects is very rewarding for me. I believe that independent research provides students with a creative experience that is very different from the rest of their education. For undergraduate students this experience may be what inspires them to go on to graduate studies and for graduate students, undertaking independent research is essential. I use a combination of structure, with weekly meetings, readings and specific goals, and flexibility, with projects designed and altered according to students needs and interests, to provide students with positive, productive research experiences. I enjoy mentoring a wide range of research projects ranging from mathematical

modeling and computational simulations to purely empirical projects requiring specific statistical or bioinformatics analyses. In the future, I look forward to continuing this range of mentorship and I hope to build a lab with students pursuing a wide variety of independent research projects.

Interests

I enjoy teaching a range of classes because this deepens my understanding of a wider range of subjects. I would like to teach two areas of courses, one focused on ecology, evolution, genetics, introductory biology and other foundation courses, and a second focused on developing skills in computing, mathematics, and statistics. Below, I describe the content of example classes in these areas.

Evolution

Evolution is the unifying factor in biology, and explains the patterns of biological diversity we see in nature. This course presents the historical roots of evolutionary biology, the key principles of evolution, and evolutionary patterns and processes. We will read and discuss primary scientific literature to understand the problems that evolutionary biologists today are working to solve.

Practical Computing for Biologists

This class will provide you with a foundational set of computational skills. Topics we will cover include operating within a Unix shell, high performance computing and cloud systems, understanding operating system architecture, writing Python programs utilizing loops and text input/output, scripting and text manipulation with regular expressions. The class will operate through a combination of lectures, individual and group assignments, and individual projects.

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EDUCATION

2010	**The Florida State University**	**Tallahassee, FL**

PhD, Biological Science, Section for Ecology and Evolution
Dissertation: *Genetic Interactions in Evolutionary Processes*
Advisors: David Houle and Thomas F. Hansen
Committee: Peter Beerli, Alice Winn and Richard Bertram

2004	**California State University, Northridge**	**Los Angeles, CA**

MS, Biology
Thesis: *Ecological Factors Separating Life Histories in the Red Alga, Mastocarpus papillatus*
Advisor: Steven R. Dudgeon

1998	**Pomona College**	**Los Angeles, CA**

BA, Biology

PROFESSIONAL POSITIONS

2012-Present	**The University of Oregon**	**Eugene, OR**

Postdoctoral Research Associate, Institute for Ecology and Evolution
Computational genomics of *Caenorhabditis remanei*
Sponsor : Patrick C. Phillips

2010-2012	**The University of Oregon**	**Eugene, OR**

NSF Postdoctoral Fellow in Biological Informatics
Evolution of the *Saccharomyces cerevisiae* genetic interaction network
Sponsor: Patrick C. Phillips

2008-2009	**The University of Oslo**	**Oslo, Norway**

Leiv Eiriksson Mobility Fellow, Center for Ecological and Evolutionary Synthesis
Evolution of genetic regulatory networks
Sponsor: Thomas F. Hansen

PUBLICATIONS

2013	**Fierst, J.L.** Female mating preferences determine system-level evolution in a gene network model. Genetica 141: 157-170.
2013	Houle, D. and **J.L. Fierst**. Properties of spontaneous mutational variance and covariance for wing size and shape in *Drosophila melanogaster*. Evolution 67: 1116-1130.
2012	**Fierst, J.L.** and P.C. Phillips. Variance in epistasis links gene regulation and evolutionary rate in the yeast genetic interaction network. Genome Biology and Evolution 4: 1080- 1087.
2011	**Fierst, J.L.** A history of phenotypic plasticity accelerates evolution to a new environment. Journal of Evolutionary Biology 24: 1992-2001.

2011	**Fierst, J.L.** Sexual dimorphism increases evolvability in a genetic regulatory network. Evolutionary Biology 38: 52-67.
2010	**Fierst, J.L**., and T.F. Hansen. 2010. Genetic architecture and post-zygotic reproductive isolation: Bateson-Dobzhansky-Muller incompatibilities in a polygenic model. Evolution 64: 675-693.
2010	**Fierst, J.L**., J.E. Kubler and S.R. Dudgeon. 2010. Spatial distribution and reproductive phenology of sexual and asexual *Mastocarpus papillatus* (Rhodophyta). Phycologia 49: 274-282.
2010	Hollis, B., **J.L. Fierst**, and D. Houle. 2009. Sexual selection accelerates the elimination of a deleterious mutant in *Drosophila* m*elanogaster*. Evolution 63: 324-333.
2005	**Fierst, J.**, C. Terhorst, J.E. Kubler and S.R. Dudgeon. 2005. Fertilization success can drive patterns of phases dominance in complex life histories. Journal of Phycology 41: 238-249.

Manuscripts in Preparation and Review

Fierst, J.L. The network model family tree. In prep.

GRANTS AND AWARDS

2010	Biological Informatics Postdoctoral Fellowship	National Science Foundation
2008	Leiv Eiriksson Mobility Fellowship	Norwegian Research Council
2003	Grant in Aid of Research	PADI Project Aware
2002	Grant in Aid of Research	Sigma Xi
2002	Grant in Aid of Research	Phycological Society of America

TEACHING AND MENTORING EXPERIENCE

Teaching

2003-2010	**The Florida State University**	**Tallahassee, FL**
	Graduate Teaching Assistant	
	Study sections, lectures and lab sessions for Introductory Biology, Animal Diversity and Evolution	
2000-2004	**California State University, Northridge**	**Los Angeles, CA**
	Graduate Teaching Assistant	
	Lectures and lab sessions for Introductory Biology, Anatomy and Physiology, Marine Ecology and Biometry	
1998-2000	**Immaculate Heart High School**	**Los Angeles, CA**
	Science Teacher	
	9th grade Introductory Science and 10th grade Biology and Honors Biology	

Student advising

2012-2013	**Computer and Information Sciences research projects**
	Undergraduate students: Zeyu Feng, Katerina Ko, Jiazhang Liu, Erick Rogers, Alexandra Weston and Ran Zhang
	Graduate students: Azad Abbasi, Daniel Everson, Mahshid Yar Mohammadi, Yunfeng Zhang
2012-2013	**Graduate student rotation projects (Institute of Ecology and Evolution):** Christine O'Connor, Andrew Nishida, Allison Fuiten

SPECIAL PROGRAMS

2011	**Pacific-American Studies Institute**	**Valparaiso, Chile**
	Scientific Computing: The Challenge of Massive Parallelism in the Americas	
2006	**Santa Fe Institute**	**Beijing, China**
	Complex Systems Summer School	
1997	**Semester Abroad in Zimbabwe**	**Harare, Zimbabwe**
	Pitzer International Programs	

SERVICE

2013	Organizing Committee, University of Oregon Postdoctoral Association
2012-2013	Constitution and Bylaws Committee, University of Oregon Faculty Union
2006-2008	Graduate representative, Integrating Genotype and Phenotype faculty search committee, Florida State University
2004-2005	President, Ecology and Evolution Discussion Group, Florida State University
2002-2003	President, Biology Graduate Student Association, CSU Northridge

Articles reviewed for: *Ecology, Evolution, Genetics, J. of Evol. Biol., PLoS Genetics, Proc. of the Royal Society, Series B*

INVITED PRESENTATIONS

2012	Evolutionary systems biology. University of Colorado at Denver.
2011	Nucleosome occupancy mediates transcription, gene expression, and epistatic fitness effects. Workshop on Systems Biology, Luebeck, Germany.
2010	Studying evolutionary processes with models of gene regulatory networks. University of Pretoria, Pretoria, South Africa.
2010	Sexual selection determines robustness and evolvability in a computational model of a genetic regulatory network. Gothenburg University, Gothenburg, Sweden.

SELECTED CONFERENCE PRESENTATIONS

2012	Evolution of genome structure in Caenorhabditis remanei. Cold Spring Harbor Laboratory, Evolution of Caenorhabditid worms and their relatives, New York.
2011	A history of phenotypic plasticity accelerates adaptation. Western Society of Naturalists, Vancouver, WA.
2010	Sexual dimorphism increases both robustness and evolvability. Society for Integrative and Comparative Biology, Seattle, USA.
2009	Genetic architecture in reproductive isolation: Evolution of Bateson-Dobzhansky-Muller incompatibilities in a polygenic model. Society for the Study of Evolution Annual Meeting, Moscow, USA.
2008	Genetic architecture in reproductive isolation. Society for Molecular Biology and Evolution Annual Meeting, Barcelona, Spain.
2006	Good genes and sexual conflict. Society for the Study of Evolution Annual Meeting, Stonybrook, NY.
2004	Multilinear epistatic interactions in the Bateson-Dobzhansky-Muller model. Society for the Study of Evolution Annual Meeting, Fort Collins, CO.

RESEARCH SKILLS

- Mathematical and computational modeling of genetic networks, evolution and systems biology
- Bioinformatics for next-generation sequence data, analysis of large datasets, and statistical analysis
- Programming Languages: Perl, Python, C/C++, Java, Ruby, UNIX/Command Line
- Bioinformatics Tools: ALLPATHS-LG, Abyss, Velvet, GMAP-GSNAP, Bowtie2, BWA, Tophat, Cufflinks, Trinity, BLAT, MUMmer, MAKER2, Augustus, OrthoMCL
- Statistical Tools: R, SAS, Matlab

MEMBERSHIPS

Society for the Study of Evolution, Society for Integrated and Applied Mathematics, Society for Integrative and Comparative Biology

REFERENCES

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