The overarching emphasis of my research is to examine the interactions of biogeography, demography, and evolutionary history on population responses to anthropogenic stressors. I apply the tools of population genetics, functional genomics including microarray analyses, and various toxicological biomarkers to problems in ecotoxicology. In the context of biomedical sciences, the individual is the unit of importance; whereas in the context of environmental health sciences, we tend to place the emphasis on the population as the unit of importance. Accordingly, one of the primary challenges of ecotoxicology is to design approaches to predict and evaluate effects of contaminants on populations. Integration of ecological and evolutionary theory, perspectives, and approaches are lacking in ecotoxicology, but essential for the future development of the field. My research has and will integrate these fields to provide a broader understanding of ecotoxicology. My undergraduate and Ph.D. training in ecotoxicology and my post-doctoral experience in evolutionary functional genomics uniquely prepares me to contribute towards the integration of ecology and evolutionary biology into traditional toxicology. My research experience has ranged from assessing the effects of anthropogenic impacts of logging and highway/railway developments on small mammal and large carnivore populations, to my Ph.D. research on the effects of contaminants on the genetic variation of exposed populations and post-doctoral research on the role of variation in gene expression for evolutionary adaptation to environmental change.

The focus of my Ph.D. research, under the direction of Dr. Susan Anderson in the UC Davis Genetic Ecotoxicology laboratory and funded by the US EPA, was to evaluate the effects of current and historical pesticide contamination on native fish populations in California. I coupled field with laboratory experimentation, and environmental chemistry with biochemical measures, to characterize proximate effects of pesticide runoff exposure on a native fish (Sacramento sucker, *Catostomus occidentalis*). I found that induction of genotoxicity from natural field exposures of *C. occidentalis* was strongly associated with agricultural pesticide runoff. The genotoxic effect was verified by laboratory exposures of *C. occidentalis* and mutagenicity studies in *Salmonella typhimurium.* Two molecular genotyping techniques (microsatellites and AFLPs) were used to examine the effects of long-term pesticide exposure on populations. My null hypothesis was that patterns of genetic variation among populations were primarily consistent with expectations based on biogeography and not primarily due to

environmental exposures. I found that biogeographical expectations matched the data set better than contaminant-related expectations. Although ecotoxicological impacts occur against a background of biogeography and history, few studies consider the influence of such alternate explanations for genetic patterns across polluted and un-polluted habitats. This research reinforced the power and importance of testing ecological expectations against a null model, which is important not only for assessing anthropogenic impacts on natural populations, but also for how natural ecological stressors influence populations over time. My post-doctoral research continues to draw on this philosophy, where in the context of evolutionary theory, random genetic drift is the null model.

My current research as a post-doctoral researcher in the University of Miami Marine Genomics Center under the direction of Dr. Douglas Crawford, and funded by NIH and NSF, is rounding out my training in evolutionary theory and genomic technologies. The overall goal of this research is to evaluate the role of variation in gene expression in evolutionary adaptation of killifish (*Fundulus heteroclitus*) to varying thermal regimes. The strength of our approach is that population differences in gene expression, characterized using cDNA microarrays, are evaluated within a phylogenetic context. *F. heteroclitus* populations are widely distributed along the Atlantic seaboard from Maine to Florida; one of the steepest thermal gradients in the world. Previous evidence indicates that differences in concentration of a few enzymes between northern and southern populations are likely adaptive. The purpose of my current investigations is to examine the role of variation in gene expression at thousands of loci simultaneously in a series of seven populations ranging from north to south. It is important to recognize that genetic distance between populations is a covariate with habitat temperature among populations. One may expect that patterns of gene expression would be most different between extreme north and extreme south populations. However, attributing those differences to evolutionary adaptation rather than the null hypothesis of random genetic drift is the primary challenge. Using phylogenetic autocorrelation, genetic distance is treated as a covariate to habitat temperature. Gene expression is regressed against genetic distance, and expression differences among populations accounted for by habitat temperature will be determined from the residuals. This is similar to how body weight is treated as a covariate in metabolic studies (i.e., the residuals of the measured physiological trait vs. body weight is analyzed). We currently have created a fully sequenced and annotated ~6000 gene cDNA microarray for killifish that is being applied in this research.

For statistically rigorous analyses, my microarray studies have included both replication at many different levels and the application of analysis of variance. Replication includes 32-fold technical replication encompassing spot, array, and dye variation, biological replication to account for natural polymorphism in gene expression, and multiple populations. To statistically analyze these data, I have written and tested MatLab scripts that perform nested ANOVA on large array datasets. The strength of this approach is the rigorous statistical design and analysis, and the test of hypotheses against the null model of neutral genetic drift.

Insights and tools gained from population genetics, evolutionary biology, classical toxicology, and functional genomics will contribute toward my goal of advancing the field of ecotoxicology. Toxicant exposure can affect survivorship, recruitment, reproductive success, mutation rates, and migration. How do different historical, phylogenetic, and biogeographic contexts influence how individuals and populations will respond to contemporary contaminant exposure? Is heritable physiological tolerance, in organisms such as Tubificid worms or mosquitofish, often achieved by selection operating on standing polymorphism in populations, or through general plasticity achieved by inherently flexible gene expression? I am interested in integrating ecological and phylogenetic factors and toxicant exposures to determine how different groups of organisms respond to environmental challenges.

My research program will involve examining the relationship between variation in gene expression and variation in individual, population, and species sensitivity to contaminant stress and relative ability to acclimate or adapt. My program would accordingly draw from evolution and ecology, classical toxicology, and environmental health, and could therefore be attractive to funding agencies such as NSF, NIH, and the EPA.