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WESTERN KENTUCKY UNIVERSITY
The Spirit Makes the Master

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October 11, 2005

Yves Brun,
Systems Biology/Microbiology Faculty Search,
Department of Biology,
Indiana University,
Jordan Hall 142, 1001 E 3rd St,
Bloomington IN 47405-7005

Dear Sir:

Thank you for considering my application for the position of Assistant Professor of Systems Biology in the Department of Biology at Indiana University. The members of the faculty of the department and the Biocomplexity Institute have broad and diverse interests, and I am certain that it would be an extremely stimulating place to work. I am particularly excited about the possibility of interacting and collaborating with Justen Andrews, Katy Börner, Ed Brodie, Matthew Grow, Thom Kauffman, Mike Lynch, Sun Kim, Rudy Raff, Santiago Schnell, Larry Yaeger, and many others. I had the privilege to be considered as a candidate for a faculty search at IU several years ago, and I remain very impressed with the students, faculty, and facilities at your institution.

I consider myself to be a broadly trained scientist with interests in both molecular and organismal biology. While I prefer not to pigeon-hole my interests, if pressed I describe my research specialty as evolutionary developmental genetics. I use the tools of genetics, genomics, molecular biology, computer simulation, and phylogenetics to understand how genetic pathways interact to produce patterns of cellular differentiation, and how these patterns are modulated to produce evolutionary novelty, particularly in insects. Current organisms being used in my laboratory are several species of Lepidopterans (butterflies and moths), and *Drosophila melanogaster*, and the laboratory is currently focusing on the origin and evolution of Lepidopteran color patterns. I am looking for a position where excellence in both research and teaching are valued, with access to high quality laboratory and library facilities, and where I will be able to attract talented PhD students to my research program.

I am enclosing a curriculum vitae, a research and teaching statement, and some representative publications and submitted manuscripts. I have also asked three individuals to serve as references in support of my application and their contact information is included below. I have not asked my former postdoctoral supervisor, Antónia Monteiro, to serve as a reference because she may also be on the job market this year and I want to avoid any possible conflict of interest.

Thank you for your time and consideration. Please let me know if there is any additional information that I can supply.

Very sincerely,

Jeffrey M. Marcus
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I have asked the following individuals to serve as references in support of my application:

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Research and Teaching Statement for Jeffrey M. Marcus

I consider myself to be a broadly trained scientist with interests in both molecular and organismal biology. I am particularly interested in the evolution of the molecular, genetic, and developmental processes responsible for producing phenotypes. I often use mathematical and computational techniques to study these processes and have worked in several experimental systems, including fish, brine shrimp, *Drosophila,* butterflies, and moths. A major component of my work thus far has examined the genetics and development of Lepidopteran (butterfly and moth) wing color patterns. These wing color patterns are among the most attractive model systems for understanding the relationship between development and evolution. Such patterns are suitable for study because they consist of clearly defined subunits, exist in two dimensions and are structurally very simple. Additionally, there is much interspecific and intraspecific variation in these patterns, and experimental perturbation of these patterns generally does not affect organismal survival under laboratory conditions. Finally, at least some patterns are clearly associated with fitness benefits associated with natural or sexual selection, providing an important opportunity to relate genetic and developmental processes to the ecology and evolution of an organism.

Much of the progress in Lepidopteran wing color pattern research thus far has involved the study of expression patterns of candidate genes identified primarily from *Drosophila* and the correlation of these expression patterns with the shape, size, and location of adult color patterns. However, this approach is limited by the supply of interesting candidate genes and does not provide any data regarding whether the gene products being studied are actually functional in the regions in which they are expressed. My own work has focused on developing methods to surmount these obstacles to further the field. One line of research that I have been pursuing is the comparative study of color patterns in different species of the moth family Saturniidae. This family contains the largest moths on earth; females of the largest species, *Atticus atlas,* can reach the size of dinner plates. This family is unique among the Lepidoptera because it includes both species that have eyespots in the typical position for these patterns and also includes species that have eyespot-like patterns in a second location where usually another pattern element is found: the discal spot. I have been rearing several species in this family and I have been able to determine that genes expressed in butterfly eyespots are also expressed in the eyespots of these moth species, regardless of whether these eyespots are found in the typical or the atypical location. Examining these patterns of gene expression in a phylogenetic context reveals that there appears to have been a shift in the regulation of one of the genes near the top of the eyespot development regulatory hierarchy so that it is expressed in the location of the incipient discal spot in those species (and only those species) with eyespots in that location.

Another direction I have taken is an elaboration of the candidate gene approach, which I like to describe as the candidate morphology approach. In a candidate gene approach, a gene product that is suspected to play a role in a process of interest because of knowledge from its role in another model system is examined in the species of interest. In the candidate morphology approach, the study of the genetics and development of a structure of interest in one species is furthered by the study of a homologous structure in another species more amenable to manipulation. Genes shown to play a role in the development of the structure in the model are then selected as candidates to be examined in the original species. One of the characteristics of discal spots on the wings of lepidopterans is that they develop around the incipient crossveins.

Therefore, an understanding of the development of crossveins may provide insight into how discal spots (and eyespot-like discal spots) form and how they are positioned with respect to other structures on the wing. I therefore studied the genetics and development of the homologous crossveins of *Drosophila* and was able to develop a model for how different signal transduction pathways participate in the development of these structures. I have also used this model to begin to generate testable hypotheses for how the pathways involved in crossvein formation and discal spot formation may interconnect. While doing my crossvein work in *Drosophila,* I found it necessary to develop a new genetic technique called Female Site-Specific Transposase-Induced Recombination (FaSSTIR) mapping to fine-map genetic intervals on the X-chromosome. This method is a great improvement over existing alternatives, with as much as a several hundred fold increase in efficiency over conventional meiotic mapping over short intervals. I am continuing to characterize genes that are essential for crossvein formation in *Drosophila.*

I have also been working to develop a transposon-based method for the germ-line transformation of butterflies. I successfully transformed the butterfly *Bicyclus anynana* during my postdoc, and I am extending this success in my own laboratory by transforming another butterfly species, *Junonia (Precis) coenia.* Ultimately, this will allow for both the introduction of genetic constructs designed to allow the misexpression of gene products, and also allow marked transposons to be used for mutagenesis and the subsequent molecular characterization of the mutagenized loci. Together, these two techniques will for the first time permit us to test in-vivo the functional relationships between gene products that have been implicated in color pattern formation. In turn, this will permit functional genomic comparisons between genetic networks from flies and butterflies. Germ-line transformation will also open the door to the introduction of other genetic techniques into butterflies such as mosaic analysis, enhancer trapping, and transposon-based mapping methods. I am also beginning the process of creating an AFLP linkage map for *Junonia (Precis) coenia* by crossing it with its congener *Junonia (Precis) evarete.* Once this map is constructed and mutations can be assigned to linkage groups, understanding the genomic organization of color pattern genes will be much easier. The addition of these techniques will allow butterflies to become a fully-fledged genetic and developmental model organism.

In addition, I have worked to develop computational models for proposed genetic regulatory hierarchies thought to underlie Lepidopteran color patterns in order to see if these hierarchies are capable of produces observed patterns of gene expression. By using these simulations, we have been able to improve our models considerably, and they have suggested specific additional experiments in established butterfly mutant stocks that will allow us to test between alternative regulatory hierarchies, and improve our models still further.

Finally, I am interested in using these tools to answer both basic and applied research questions. I am in the initial stages of creating a molecular phylogeny of the genus *Junonia,* I have started to look at *Junonia coenia* genetic population structure in the wild, and I recently received a 5 year grant from the NIH to conduct a mutagenesis screen in *J. coenia* in order to find mutations in the wingless signal transduction pathway, a pathway that is not only involved in butterfly color pattern formation, but also appear to play a role in the majority of human colon cancers. Since my arrival at Western Kentucky University, I have had eight undergraduate students and one high school student work with me in my laboratory on research projects. Thus far, five of my students have coauthored manuscripts with me. I am enthusiastic about working with research students at both the graduate and undergraduate level in the future.

For my future work, I would like to continue to pursue each of these lines of research to gain a more complete understanding of the genetics, development, and evolution of lepidopteran wing color patterns. I plan to continue to involve students (both graduate and undergraduate) in my research program, and to bring elements of that research into the classroom and the teaching laboratory. Teaching well, and getting students excited about what they are learning is very important to me. In particular, I am very much interested in using experiential learning techniques, where students learn by doing. Since arriving at Western Kentucky University, I have redesigned the laboratory experience for the undergraduate genetics course, including a series of exercises in which the students map transposon insertion mutations in *Drosophila*. Since none of these mutations have been genetically mapped before, the students have the opportunity to make a small but real contribution to the field of genetics. The data collected by the students in my Fall 2003 Genetics class were published in a paper in the Drosophila Information Service. The results gathered from classes since then are described in a paper published in 2004 in the Drosophila Information Service and co-authored by an undergraduate who conducted many of the crosses in parallel with the Genetics students as an independent research project. Since coming to WKU I have also taught a course in the History of Biology (as a 2 week study abroad course in London) as a faculty member. While in Graduate school, I served as a teaching assistant for Genetics, Cell Biology, Microbiology, and Introductory Biology at Cambridge University, Duke University, and Elon College. In addition to these courses, I would feel comfortable teaching courses in Evolutionary Biology, Developmental Biology, Entomology, and the Evolution of Development. For additional information about my teaching philosophy, please refer to my enclosed article published in the Chronicle for Higher Education's Career Network.

As work progresses on genome sequencing of insect species, there will be increasing opportunities for the use of microarray technology for the study of gene expression in color pattern development, which I hope to use at every opportunity. With the genome sequence of the silk moth essentially completed, the creation of BAC libraries for several other Lepidopteran species underway, and the creation of EST libraries for still other species, it is an exciting time to be working with butterfly color patterns. However, these technologies are far more powerful when used in combination with modern genetic tools for the manipulation of gene expression such as those that I have been developing. The new genomic information and genetic techniques in butterflies may also allow the use of these organisms as models for studying basic cellular processes that may have biomedical applications which will be a very interesting avenue of research to explore. Finally, by using transformation technology in *J. coenia,* we will be able to make comparisons between the genetic networks that underlying wing pigmentation formation in this species and *Bicyclus*. *Junonia coenia* also has patterns that are very similar to the discal spots found in Saturniid moths, while *Bicyclus* lacks these patterns entirely, making this a particularly interesting species pair to examine in the context of my other lines of research. More generally, functional genomic comparisons between these butterfly species could tell us a great deal about the mechanisms by which color patterns and their underlying genetic regulatory hierarchies have evolved.

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A Teaching Statement

http://www.chronicle.com/jobs/2001/10/2001100901c.htm

By JEFFREY MARCUS

FIRST PERSON
Personal experiences on the job market

Previous articles

The spring semester was almost over when the instructor distributed our last assignment for the "Graduate Seminar in Teaching Biology." The class was offered by our department to equip graduate students with more-effective teaching skills and to prepare us for the academic job market. Despite the departmental support, no faculty member was willing to teach the course, so Paula, a postdoc in our department who had recently started job hunting, volunteered. The workload was light, the classes were congenial, and Paula made sure that we always had snacks. However, this last assignment was the toughest of the course: to write a statement about our philosophy of teaching.

The difficulty was that, even after many teaching assistantships, nobody had ever asked us why we wanted to teach. Yet here was the assignment, and Paula explained that not only teaching institutions, but even research universities, now request such a teaching statement from applicants. We had one week.

I racked my brain for inspiration. Why do I want to teach? When did I decide that I wanted to teach? I couldn't remember. This was even harder than I had anticipated. If I was having trouble just writing a short paper about teaching, did that mean I wasn't cut out to be a professor? Were there any exceptional learning experiences that had inspired me to teach? I was at a loss for answers and it was getting depressing.

The truth is, I felt miserable anyway. My mother had passed away a few months earlier at the age of 53, due to a brain tumor. Her illness had progressed very quickly, so there was not enough time for me to say all of the things that needed to be said, to ask her all of the questions I needed to ask. My inability to do this assignment just added to my despondency. I missed class and didn't turn in the assignment. The course was not graded so it didn't count against me, but my type-A personality and matching type-A ego would not let me give up. Paula said she would read my statement whenever I finished it.

I thought about my mother, about why I wanted to teach biology, and about whether graduate school was a pointless endeavor. I also spent a lot of time thinking about my childhood, my early learning experiences, and what my mother looked like when she smiled as she answered one of my many questions. Slowly, I realized that much of my enthusiasm for biology could be traced back to my first biology teacher, my mother.

She had a bachelor's degree in biology and worked for the Department of Public Health in New York City, investigating cases of food poisoning. Even when I was little, she helped me learn the names of the birds that came to our backyard feeder, to understand why marigolds in the vegetable garden kept the bugs away, and to discover the red-striped salamanders that lived under the logs at the edge of the woods. She and my father took me regularly to the Bronx Zoo, the New York Botanical Gardens, and the American Museum of Natural History. We used to spend part of every summer on a dairy farm, where I learned how to milk cows and hauled bales of hay up to the loft for storage. My mother encouraged me to read Stephen Jay Gould's articles in *Natural History* magazine when I was 10 and encouraged me to take all of the hardest science classes at school.

Yet despite her obvious interest and enthusiasm for biology, my mother was fond of saying, "Ninety percent of all biology courses is just vocabulary."

My mother's opinions were influenced by the fact that she was part of the baby boom, which overwhelmed the resources of her university's biology department. She told stories about professors who wrote textbooks, and proceeded to read the relevant pages to auditoriums full of students. In one large course, none of the exams were ever graded, and students were evaluated solely on the basis of their class standing: Seniors got A's, and freshmen received D's. More typical exams, which were graded, stressed the recollection of facts, definitions, and jargon, but did not really require students to understand the fundamental concepts underlying the material. Above all, my mother was disappointed by the lack of mechanisms to help students come to appreciate the beauty and wonder of living things.

Biology instruction has progressed since my mother was in school. I never had a course in which the teacher read to me from the textbook, but in many ways my learning experiences have been similar to hers. I took many courses that were almost entirely devoid of general principles, underlying themes, or problem-solving skills.

In my undergraduate biochemistry course, I was expected to know, among other things, the entire chemical pathways for aerobic respiration and photosynthesis, including the names and structures of all of the chemical intermediates and cofactors, the names and cellular locations of all of the enzymes, and the mechanisms of their catalysis. The course was so focused on memorization that it included no lectures at all. There were no labs, either. We purchased a textbook and a "reader's guide," and were expected to learn the material on our own, coming to a test center periodically to be quizzed on our progress.

This approach to teaching has nothing in common with what I enjoy or value about biology, but many of my classmates loved it because they didn't really have to understand anything. It was only an exercise in mnemonics.

The classes that I value the most were experiential, like the rambling walks I used to take with my mother and younger brother. There was always a goal in mind, but also room for improvisation, and you never knew what you might discover along the way. Unfortunately, the list of classes like that is very short: The ecology courses in which we took long field trips to strange habitats just a few miles from campus; the molecular-genetics class in which students worked for months on independent projects; and the marine-invertebrates course in which students were forced to seriously engage the primary literature to write term papers. Yet these classes always suffered from low enrollments or were not offered at all, because few students were willing to commit the time they required, or do work that involved more than memorization.

I see an essential ambivalence about teaching in science departments at research universities. A lot of lip service is devoted to providing high-quality teaching, while the undergraduates demand good professors. However, what gets rewarded is excellence in research, and most students seem to think that the best professors are the ones who teach the easiest classes. As a result, undergraduate courses are designed so that they require minimal effort from both the professors and the students.

All along, my mother knew something that I have only just realized -- scientific discovery is essentially an experiential process. Scientists discover new things by doing experiments, making observations, and immersing themselves in their subject. If we hope to inspire students to become scientists or even to respect what scientists do, we have to find a way to show them the excitement of discovering something new, of experiencing the acquisition of new scientific knowledge.

I aspire to challenge students to truly engage with the subject matter and give them firsthand experience with the magnificence of life on earth. Maybe enrollments in my courses will be small, maybe it will demand a lot of my time and effort, but I now have a mission and a teaching philosophy: By using experiential learning, I hope to prove my mother wrong and create courses that are not just 90-percent vocabulary. I think my Mom would be proud.

Jeffrey Marcus is in his final year of the Ph.D. program in biology at Duke University and hopes to land a postdoctoral fellowship while beginning his search for a