

Annual Report for Period:09/2007 - 08/2008**Submitted on:** 06/16/2008**Principal Investigator:** Schatz, Bruce R.**Award ID:** 0425852**Organization:** U of Ill Urbana-Champaign**Submitted By:**

Schatz, Bruce - Principal Investigator

Title:

FIBR: BeeSpace - An Interactive Environment for Analyzing Nature and Nurture in Societal Roles

Project Participants**Senior Personnel****Name:** Schatz, Bruce**Worked for more than 160 Hours:** Yes**Contribution to Project:****Name:** Robinson, Gene**Worked for more than 160 Hours:** Yes**Contribution to Project:****Name:** Fahrbach, Susan**Worked for more than 160 Hours:** Yes**Contribution to Project:****Name:** Rodriguez-Zas, Sandra**Worked for more than 160 Hours:** Yes**Contribution to Project:****Name:** Zhai, ChengXiang**Worked for more than 160 Hours:** Yes**Contribution to Project:****Name:** Bruce, Bertram**Worked for more than 160 Hours:** Yes**Contribution to Project:**

Project Lead for Education and Outreach.

Senior graduate student in education supported on grant, plus summer salary for Biology Teacher at University Laboratory High School.

Post-doc**Name:** Sen Sarma, Moushumi**Worked for more than 160 Hours:** Yes**Contribution to Project:**

Biology Advisor for software functionality and user testing

Graduate Student**Undergraduate Student****Technician, Programmer**

Name: Buell, Jim

Worked for more than 160 Hours: Yes

Contribution to Project:

project coordinator for user community and education/outreach

Name: Arcoleo, David

Worked for more than 160 Hours: Yes

Contribution to Project:

Lead programmer for system infrastructure and user interface.

Name: Sanders, Barry

Worked for more than 160 Hours: Yes

Contribution to Project:

Informatics Programmer for database integration and interface design

Other Participant

Research Experience for Undergraduates

Organizational Partners

Georgetown University

Computational annotation of the honey bee genome, working with BeeBase researchers

CORNELL UNIVERSITY

fulltext digitalization of the beekeeping literature

Indiana University

FlyBase curator site, working to evaluate our analysis software

Harvard University

FlyBase curator site, working to evaluate analysis software

Kansas State University

Community organization of Arthropod Base Consortium, working with BeetleBase researchers

Other Collaborators or Contacts

Chris Elsik, Department of Biology, Georgetown University

Nan Hyland, Mann Biology Library, Cornell University

Kathy Mathews, Department of Biology, Indiana University

Bill Gelbart, Department of Biology, Harvard University

Susan Brown, Department of Genetics, Kansas State University

At University of Illinois at Urbana-Champaign:

May Berenbaum, Department of Entomology

Saurabh Sinha, Department of Computer Science

Sheng Zhong, Department of Bioengineering

Matthew Hudson, Department of Crop Sciences

John MacMullen, School of Library and Information Science

Activities and Findings

Research and Education Activities: (See PDF version submitted by PI at the end of the report)

See attached file with details of our substantial efforts into Research (Informatics and Biology) and Education (including Outreach).

Findings:

For Biology Research, the nature-nurture dissection has been completely planned, the honey bees have been collected from each experimental situation, and the microarray expression pipeline has been established. The expression experiments are now proceeding. Analysis of findings has begun with the first publications and will rapidly increase this coming year.

For Informatics Research, the first fully fledged analysis environment has been developed. This supports concept navigation of community collections, with all collections and indexing being dynamically computed. Each individual component has been evaluated and published. The integrated system is beginning user testing with local users and will be released to the Arthropod Genome Consortium this year.

Training and Development:

Graduate Students. Work closely with 15 postdocs and PhDs for judging results and helping their research, in departments ranging from neuro science to computer science.

Building early adopter community at external sites, notably the Arthropod Base Consortium and the North Carolina honey bee consortium.

Undergraduate Students. Developed freshman bioinformatics course based on BeeSpace at Wake Forest. Taught for second time this year, including lectures by project investigators.

High School Students. Paying biology teacher at University High School to plan and teach summer workshop for 15 Uni students, who will leverage the materials into national science competition projects.

Outreach Activities:

We support an extensive website of slides and videos of our research. The educational materials are packaged for external distribution. See <http://www.beespace.uiuc.edu>

We set up a computer laboratory for outreach partners at University Laboratory High School and at Campus Middle School for Girls. Our project coordinator salvaged and refurbished all these machines.

Journal Publications

Gene Robinson, "Beyond Nature and Nurture", *Science*, p. 397, vol. 304, (2004). Published,

Honey Bee Genome Sequencing Consortium, "The genome sequence of the honey bee, *Apis mellifera*, a highly social animal", *Nature*, p. , vol. 443, (2006). Published,

R. Velarde, G. Robinson, S. Fahrback, "Nuclear receptors of the honey bee: Annotation and Expression in the Adult Brain", *Insect Molecular Biology*. Honey bee genome special issue., p. , vol. 15, (2006). Published,

A. Hummon, T. Richmond, P. Verleyen, G. Baggerman, J. Huybrechts, M. Ewing, E. Vierstraete, S. Rodriguez-Zas, L. Schoofs, G. Robinson, J. Sweedler, "From the Genome to the Proteome: Uncovering Peptides in the *Apis* Brain", *Science*, p. , vol. 314, (2006). Published,

S. Rodriguez-Zas, B. Southey, C. Whitfield, G. Robinson, "Characterization of unique gene expression trajectories across behavioral maturation in honey bees using a semiparametric model", *Genome Research*, p. , vol. , (). Submitted,

C. Whitfield, Y. Ben-Shahar, C. Brillet, I. Leoncini, D. Crauser, Y. LeConte, S. Rodriguez-Zas, G. Robinson, "Genomic dissection of behavioral maturation in the honey bee", *PNAS*, p. , vol. 103, (2006). Published,

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- J. Jiang, C. Zhai, "Exploiting Domain Structure for Named Entity Recognition", Proceedings of HLT/NAACL, p. , vol. , (2006). Published,
- Q. Mei, C. Zhai, "A Mixture Model for Contextual Text Mining", Proceedings 2006 ACM SIGKDD International Conference on Knowledge Discovery and Data Mining, (KDD'06), p. , vol. , (2006). Published,
- Q. Mei, C. Liu, H. Su, C. Zhai, "A Probabilistic Approach to Spatiotemporal Theme Pattern Mining on Weblogs", Proceedings of the World Wide Web Conference 2006 (WWW'06), p. , vol. , (2006). Published,
- Q. Mei, D. Xin, H. Cheng, J. Han, C. Zhai, "Generating Semantic Annotations for Frequent Patterns with Context Analysis", Proceedings 2006 ACM SIGKDD International Conference on Knowledge Discovery and Data Mining (KDD '06), p. , vol. , (2006). Published,
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- Yue Lu, Xin He, Sheng Zhong, "Cross-species microarray analysis with the OSCAR system suggests an INSR->Pax6->NQO1 neuro-protective pathway in ageing and Alzheimer's disease", Nucleic Acids Research, p. , vol. , (). Accepted,
- S. Sinha, X. Ling, C. Whitfield, C. Zhai, G. Robinson, "Genome scan for cis-regulatory DNA motifs associated with social behavior in honey bees", PNAS, p. , vol. 103, (2006). Published,
- C. Whitfield, Y. Ben-Shahar, C. Brillet, I. Leoncini, D. Crauser, Y. LeConte, S. Rodriguez-Zas, G. Robinson, "Thrice Out of Africa: ancient and recent expansions of the honey bee", Science, p. , vol. 314, (2006). Published,
- T. Tao, X. Wang, Q. Mei, C. Zhai, "Language Model Information Retrieval with Document Expansion", Proceedings of HLT/NAACL, p. , vol. , (2006). Published,
- G. Robinson, J. Evans, R. Maleszka, H. Robertson, D. Weaver, K. Worley, R. Gibbs, G. Weinstock, "Sweetness and Light: Illuminating the Honey Bee Genome", Insect Molecular Biology, p. , vol. 15, (2006). Published,
- Y. Lu, X. Ling, X. He, C. Zhai, "Language Models for Genomics Information Retrieval", TREC Genomics Track, p. , vol. Jun, (2007). Published,
- J. Jiang, C. Zhai, "Instance Weighting for domain adaptation in NLP", Proc 45th Annual Meeting of Association for Computational Linguistics (ACL), p. 264, vol. Jun, (2007). Published,
- X. Ling, Q. Mei, B. Schatz, C. Zhai, "Mining multifaceted overviews of arbitrary topics in a text collection", Proc ACM KDD Knowledge Discovery and Data Mining, p. , vol. Aug, (2008). Published,
- B. Schatz, "Interactive Functional Analysis of Arthropod Genome Databases", Arthropod Genomics Symposium annual meeting, p. , vol. April, (2008). Published,
- X. Ling, J. Jiang, Q. Mei, M. Sen Sarma, C. Zhai, B. Schatz, "Gene Summarizer: Software for Automatically Generating Structured Summaries from Biomedical Literature", 2nd International Biocuration Meeting, p. , vol. Oct, (2007). Published,
- B. Sanders, D. Arcoleo, B. Schatz, "BeeSpace: Interactive Analysis of Genome Databases", BOSC Bioinformatics Open Source Conference, p. , vol. Jul, (2008). Published,

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- M. Sen Sarma, C. Whitfield, G. Robinson, "Species differences in brain gene expression profiles in honey bees", *BMC Genomics*, p. 202, vol. 8, (2007). Published,
- C. Alaux, G. Robinson, "Releaser pheromone provokes immediate-early gene and slow behavioral response", *J. Chemical Ecology*, p. 1346, vol. 33, (2007). Published,
- R. Kantorovitz, G. Robinson, S. Sinha, "A statistical method for alignment-free comparison of regulatory sequences", *Proc 15th Intl Conf Intelligent Systems for Molecular Biology (ISMB)*, p. , vol. Jul, (2008). Published,
- A. Toth, K. Varala, T. Newman, J. Simons, M. Egholm, J. Hunt, M. Hudson, G. Robinson, "Wasp brain gene expression supports an evolutionary link between maternal behavior and eusociality", *Science*, p. 441, vol. 318, (2007). Published,
- A. Toth, G. Robinson, "Evo-Devo and the evolution of social behavior", *Trends in Genetics*, p. 334, vol. 23, (2007). Published,
- N. Ismail, S. Christine, G. Robinson, S. Fahrbach, "Pilocarpine improves recognition of nestmates in young honey bees", *Neuroscience Letters*, p. , vol. , (2008). Accepted,
- C. Smith, A. Toth, A. Suarez, G. Robinson, "Genetic and genomic analyses of division of labour in the insect societies", *Nature Reviews Genetics*, p. , vol. , (2008). Accepted,

Books or Other One-time Publications

Web/Internet Site

URL(s):

<http://www.beespace.uiuc.edu>

Description:

- The project website.
- Contains detailed information on the background behind the project.
- Contains slides and videos of the lectures given during the project.
- Contains prototype software system for biology users.
- Contains scientific publications and educational materials.

Other Specific Products

Product Type:

Audio or video products

Product Description:

Slides and Videos of Project. Overviews and Training.

Sharing Information:

Freely available on project website.

Product Type:

Software (or netware)

Product Description:

BeeSpace analysis environment supporting concept navigation.

Sharing Information:

available from website <http://www.beespace.uiuc.edu>

Contributions**Contributions within Discipline:**

Informatics Research is pioneering conceptual navigation of biological literature and distributing related software to the Arthropod Base Consortium of NSF-funded biologists. We gave big demonstration and plenary talk at annual Arthropod Genomics Symposium.

coPI Gene Robinson was awarded a Swanlund Chair at the University of Illinois, the most prestigious university endowed chair

Contributions to Other Disciplines:

Collaboration with FlyBase is leading towards automatic support for biology curation. Important for future of biology as genome sequencing becomes routine and each community must provide their own annotations. We gave plenary talk at International Biocuration Meeting this year.

Contributions to Human Resource Development:

Established research facility in new Institute for Genomic Biology at University of Illinois, training new generation of integrative biologists across wet lab biology and dry lab informatics.

Contributions to Resources for Research and Education:

PI Schatz is the campus leader to develop new interdisciplinary PhD program in informatics at University of Illinois, with special focus on biomedical informatics. He chaired the campus committee this year to establish the new degree.

coPI Zhai is the campus chair of the Bioinformatics MS degree.

Contributions Beyond Science and Engineering:

BeeSpace-catalyzed genomics research being used to study agricultural crisis of honeybee disappearance (CCD Colony Collapse Disorder).

PI Schatz doing industrial outreach, e.g. invited big Tech Talk at Google on BeeSpace-catalyzed semantic searching in July 2007.

Special Requirements

Special reporting requirements: None

Change in Objectives or Scope: None

Animal, Human Subjects, Biohazards: None

Categories for which nothing is reported:

Any Book

BeeSpace Research and Education, 9/1/2007 – 8/31/2008

This year was the fourth of five. We made progress on all aspects of Research, both Biology and Informatics, and of Education, both training and outreach. These are outlined below. See the BeeSpace website <http://www.beespace.uiuc.edu> for more information, including software and slides, among other digital materials.

In brief, the Informatics released a major version of the analysis software and is developing a streamlined interface, the Biology published the first analysis from the expression pipeline and is beginning cross-experiment analysis, the Education hosted a major workshop with project scientists training high school students.

Informatics Research

The goal of the Informatics Research is to build BeeSpace, an interactive environment for functional analysis. More specifically, to interactively annotate gene functions using concept-based navigation of biological literature and gene-centered summarization. This year, we enhanced our v3 system beyond the Gene Summarizer to include a Gene Annotator. This transforms gene lists into concept lists that can be categorized into gene groups corresponding to similar functions. See software and documentation at <http://beespace.uiuc.edu/software.php>.

In more detail, the BeeSpace v3.5 contains the Gene Annotator, which in preliminary testing by our BeeSpace postdocs has identified gene groups that were not discoverable using the manual categorization with the Gene Ontology. This version has also been optimized so that dynamic indexing is done for all categorization, when running on our new parallel server, with 16 processors and 128 GB RAM. That is, the user can create a new space, consisting of a special collection of selected documents, which is automatically and dynamically indexed for subsequent clustering and categorizing.

The v3.6 contains the trained Gene Summarizer, which automatically produces functional sentences categorized into functional groups, given a gene and a space. It extracts relevant sentences from the space collection describing that gene and classifies these sentences into functional categories such as expression location and mutant phenotype. This research was published in the journal *Information Processing and Management*.

The new summarizer is trained for sentence categorization on biologist judgments of actual sentences from biomedical abstracts, such as our collections deriving from Medline and Biosis, rather than on the FlyBase curator sentences as before. We hosted training sessions where biologists tagged sentences as being relevant to a variety of different functional categories. We ran a training session with our collaborators who work on the flour beetle (*Tribolium*) at Kansas State University and another with the local biologists who work on the honey bee and related insects, some part of BeeSpace and some on other projects. The trained summarizer was highlighted in plenary talks at major specialty symposia on *Biological Curation* and on *Arthropod Genomics* (250 attendees).

We are continuing to enhance version 3 with a new Gene Annotator (v3.7) that will produce more precise concept lists from gene lists and will automatically categorize long concept lists into useful functional groups. As with the Gene Summarizer, it operates against whatever space collection the user specifies to generate its conceptual categorization of specified genes. During this period, we will also produce a final version 3 system (v3.8) with the databases being updated to keep the literature current.

Our analysis software has been heavily used by the local biologists on our project, who work directly with and are often directly funded by BeeSpace. It has become clear that the software has a much wider potential audience if it was differently packaged. For example, we have been working closely with the arthropod genomics research community and are co-organizers of the quarterly workshops of the Arthropod Base Consortium (ABC). These include members of the various genome database groups such as FlyBase, VectorBase, BeetleBase, and BeeBase.

We hosted the ABC workshop in December 2007 at the Institute for Genomic Biology. See slides of the presentations at http://www.beespace.uiuc.edu/groups_abc.php. We gave a series of well-attended demonstrations at the large symposium (250 attendees rather than 25) in Kansas City of the *Arthropod Genomics Symposium*. See slides and software and documentations at <http://www.beespace.uiuc.edu/agsmaterials.php>. To further serve the extended community of genome biologists, we will be distributing our software as an integrated part of the GMOD package (Generic Model Organism Database) <http://www.gmod.org> and are presenting our plan at the *Bioinformatics Open Source Conference* in Toronto in July 2008, as an accepted full presentation.

To reach the extended scientific community, we are developing version 4 of the BeeSpace analysis system. This version has a greatly streamlined user interface, which we have designed in collaboration with our community of local biologists. During this period, we will produce a complete interface connected to some of the system functionality. A preliminary version will be released over the summer, and the system itself will be available to the general biological community during the next year.

The new interface is a single screen with multiple panes so that long interactive sessions are possible, without losing the context of where you are. Different spaces can be selected, then different categorizations can be made of selected documents using the dynamic indexing. That is, the particular space within the biological literature that corresponds to your exact problem can be easily and quickly located within an interactive session. Then functional analysis can be performed against this space, using the annotator and the summarizer. The Software page has a movie of the current mockup.

We are currently supporting 5 bioinformatics graduate students. coPI Zhai is supervising 2 of the students, Saurabh Sinha in Computer Science and Sheng Zhong in Bioengineering are each supervising 1, and the last will be entering the new interdisciplinary Informatics PhD Program next year, whose founding chair is PI Schatz. This year one of the previous students graduated and next year two more will graduate, who are the leads on the Gene Annotator (Xin He) and the Gene Summarizer (Xu Ling).

Biology Research

The goal of the Biology Research is to carefully dissect the relative contributions of nature and nurture for social behavior in the honey bee. In particular, we are experimentally measuring brain gene expression for important societal roles during normal behavior, with different experiments varying heredity (nature) and environment (nurture) for different societal roles, using the whole genome microarray.

This year, we have revised our experimental pipeline for expression microarrays and the biology experiments are emerging rapidly to be analyzed by the informatics. The analysis is using the Gene Annotator to supplement the Gene Ontology in discovering behavior function. We are focusing on Foraging and Defense, as symbolic of animal behavior for food and warfare. This may enable comparisons to higher organisms. The honey bee is a model for natural behavior and the samples were all field collected.

For Defense, we are dissecting nature via different races of bees (European, African) and nurture via different levels of threat (manipulations of alarm pheromones). For Foraging, our primary focus is on when a bee transitions her societal role from nurse to forager (age of onset of foraging). We are again dissecting nature via different races of bees and dissect nurture via social manipulations (e.g. manipulating food supply in the hive to create precocious foragers or overage nurses) and physiological manipulations (e.g. manipulating NPF with vitellogenin or JH Juvenile Hormone with octopamine).

In the first published analysis of nature dissection, species differences in honey bees for brain gene expression during communication prior to foraging onset were examined. The experiments and analyses were performed by a postdoctoral fellow (Moushumi Sen Sarma), who is now split between the Biology and the Informatics research, to enable her to closely advise the software developers on useful analysis functions. In the first published analysis of nurture dissection, effects of alarm pheromone on brain gene expression were examined. The experiments and analyses were performed by a postdoctoral fellow (Cedric Alaux) who is now supported full-time on the BeeSpace grant, using the revised expression pipeline.

The remainder of the nearly 20 experiments are underway, and more than half of the projected 2000 microarrays have been run through the revised expression pipeline. The required sample bees have all been collected, under natural behaviors with experimental variations for nature and for nurture. Detailed statistical analyses are in progress, which will then be fed into the Informatics pipeline to derive additional insights.

We have also been transferring the experimental and analytic techniques to attempt to understand the mass disappearance of honey bees, due to colony collapse disorder. These experiments use the gut rather than the brain as the source for microarray expression. A graduate student shared with May Berenbaum, chair of the NRC Pollinator Committee, is analyzing the results of genomic detection of bee disease rather than bee behavior. The expression pipeline developed with BeeSpace funds is being used for this purpose.

We are doing anatomical localization of gene expression, using in situ hybridization of whole bee brains. This plan is being executed at Wake Forest University by a postdoc (Rodrigo Velarde) under coPI Fahrbach who just earned a PhD at Illinois under coPI Robinson. The genes being localized were previously identified as important neuropeptides. This period we also graduated a student using the bee gene expression techniques to study wasp (Amy Toth); she published a paper in *Science* on this research. She will also be going to North Carolina as postdoc to join the bee research consortium; as a knowledgeable user of BeeSpace, she will be seeding this remote user group.

Education and Outreach

We are training students at many levels, concentrating on giving research experiences to small groups of focused persons. Our investigators and researchers are directly involved in education and outreach. Extensive photos and videos of our research activities are available on our website. Our overall strategy is to create a unique and useful collection of educational materials on biology and informatics, which are targeted at different audiences and which are freely available on our website.

At the Graduate level, we support 11 students in Biology and in Informatics, from entomology and neuroscience, computer science and animal science. The interdisciplinary interactions are facilitated by our new Institute for Genomic Biology. We also work closely with our early adopter community of biologists at other universities and research institutions. Our project coordinator Jim Buell is supporting the user community and educational activities; he is also finishing his dissertation in Educational Psychology under coPI Chip Bruce, using BeeSpace as example of inquiry learning.

Co-PI Robinson participated in a teacher training workshop organized by the College of Education and the Neuroscience Program, for which he serves as campus chair. He presented results from BeeSpace research as part of a lesson on how genomics can help educate students on the nature/nurture controversy.

At the Undergraduate Level, we have developed a new Bioinformatics for Beginners course based on BeeSpace. This was taught for the second time in Fall 2007 as a freshman honors class at Wake Forest University by coPI Fahrbach. The materials and examples during the course are derived directly from BeeSpace research, and both PI Schatz and coPI Robinson give lectures during the course via videoconference.

At the High School Level, each summer we are paying the biology teacher at University Laboratory High School to develop Beespace-related materials for use in his Field Biology course. The materials developed span a wide range of biological topics, and can be found on our website. The teacher (David Stone) is distributing these to other teachers in the regional school system throughout Champaign County Illinois.

We will be conducting a weeklong education workshop in July 2008 for fourteen University High School students. This is an expanded version of a workshop that BeeSpace piloted in summer 2007 with seven middle school-age learners. The 30-hour workshop will include in-depth learning about the genomic behavioral science behind BeeSpace, presentations by BeeSpace research scientists (Robinson, Fahrbach, Schatz), visits to the Bee Research Lab, evaluation of the Bioinformatics for Beginners educational materials, and use of the BeeSpace software to investigate the timely topic of Colony Collapse Disorder. We are employing a doctoral student who has been working for BeeSpace Biology (Nick Naeger) to introduce the learners to how project researchers are raising and answering questions about genetic bases for bee social behaviors, using tools like the honey bee genome microarray and RT-PCR. Morning workshop sessions will present scientific content relevant to BeeSpace biology and informatics.

The Uni High biology teacher mentioned above will lead the learners in using knowledge from the workshop to construct their own scientific investigations -- in preparation for entering major science project competitions, including ExploraVision sponsored by the National Science Teachers Association (for which Mr. Stone has previously coached 3 national contest winning teams). The entomology Ph.D. who led the 2007 pilot workshop (Katrina Lustofin) will be returning to coach the students.

This year, we set up a computer lab with donated computers and administration by our coordinator at both our collaborative outreach sites: Campus Middle School and University High School in Urbana Illinois. These are in active use for science education at K-12 level, and constitute a unique form of permanent outreach capability.

Special Requirements

Our funds from NSF were frontloaded, in that more money actually arrived in the first half of the grant than we requested. Because of this, we have underspent the funds and wish to push them forward into later years. The PI (Schatz) has significant experience in running large NSF systems projects and this pattern is quite typical. The planning years underspend, but the development years overspend, as the project ramps up with real systems and real users. So we appreciate the flexibility of NSF in permitting us to responsibly spend the funds as the needs of the project dictate, including the likely request for a no-cost extension after the formal end of the project in August 2009.