

MAX-PLANCK INSTITUTE
FOR DEVELOPMENTAL BIOLOGY



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Curt Lively
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Dear Dr. Lively and Microbial Ecology/Evolution Search Committee,

Greetings. I wish to apply for the open Microbial Ecology/Evolution faculty position in your department. Please find enclosed my curriculum vitae, statement of research interests, and four publications. Three letters of reference have been requested.

At the Max-Planck Institute for Developmental Biology, I am using the social and developmental bacterium *Myxococcus xanthus* as a model system to study the ecology and evolution of microbial sociality. Recently, I have demonstrated the existence of genetically-based social conflict between cheating and altruistic genotypes of *M. xanthus* during social development (*Nature* 2000) and have documented the evolution of novel cooperative behavior (*Nature* 2003). Ongoing and future projects include additional experimental evolution studies and the study of natural populations.

My group's research reflects a novel approach to the study of microbial social evolution and behavioral ecology. I am confident that this work will attract sustained external funding and generate fruitful interdisciplinary collaborations. I look forward to the possibility of developing a fruitful research program at Indiana University.

Sincerely,


Gregory J. Velicer

Research Interests- Gregory J. Velicer

INTRODUCTION

Our research program investigates questions that intersect the fields of ecology, evolution, social behavior and prokaryotic development using the social myxobacteria as a group of model organisms. Laboratory evolution and comparative approaches are employed, the latter examining numerous natural isolates of *Myxococcus xanthus*. We seek to combine knowledge from both natural and lab-evolved populations to help understand the dynamics and genetics of social evolution under a variety of selective conditions. Collaborative genomic and theory projects are also being pursued.

Background

The myxobacteria are a monophyletic group of soil-dwelling predators that exhibit complex intercellular communication, cooperative predation, and sophisticated social development. As groups, they consume other microorganisms by secreting pools of antibiotics and enzymes that kill neighboring prey. In *M. xanthus*, both predation and development are facilitated by two distinct motility systems, one social in nature (requires cell-cell proximity) and one allowing movement of isolated cells. During starvation, *M. xanthus* sporulates via fruiting body formation. Cells aggregate at high-density focal points where fruiting bodies form and vegetative cells differentiate into spherical spores in a social process requiring multiple stage-specific intercellular signals.

Laboratory experimental evolution

Laboratory evolution experiments with *M. xanthus* are underway in multiple selective environments that favor improved fitness during predation, motility, development, or asocial growth in liquid. Most evolving populations descend from a single common ancestor, representing an extensive adaptive radiation into various laboratory environments. Samples from evolving populations are frozen at regular intervals, creating a systematic “fossil record” of all lineages. After extended evolution, evolved genotypes are examined at population, cellular and molecular levels to characterize evolutionary changes in social traits and their genetic basis.

Natural isolate comparisons

We have collected dozens of distinct myxobacterial species and hundreds of *M. xanthus* strains from locations around the world. Research interests with these samples include intra-specific variation of social phenotypes, intra- and inter-specific social interactions, mechanisms of kin-distinction, the phylogenies of important social genes, and the fine-scale spatial and genetic structure of natural populations.

Genomic and theory collaborations

Genomics: evolutionary genome comparison of two closely related bacterial predators (*M. xanthus* and *Bdellovibrio bacteriovorus*) that exhibit very different life-histories.

Social evolution theory: competitive dynamics of cheaters and altruists in cooperative bacteria.

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RECENT STUDIES

Evolution of genetic conflict in social development. Several genotypes that are defective at social development in pure culture have been shown to exploit their developmentally-proficient parental strains in mixed cultures. (Velicer *et al.* 2000, *Nature*).

Fates of competing cheater and wildtype genotypes. Several distinct cheater genotypes from the *Nature* study above were competed directly with their developmentally-proficient progenitor over several cycles of development and growth. Different genotypes showed distinct competitive fates, including cheater persistence with little disruption to wildtype population dynamics, cheater-induced population crashes followed by cheater persistence, and cheater-induced extinction events (Fiegna & Velicer 2003, *Proc Roy Soc London B*).

Localization of adaptive S-motility mutations and their effects on fitness and development. Specific loci responsible for the loss of S motility in several asocially-evolved lines have been identified. Mutations in these loci have been shown to increase asocial fitness and decrease developmental performance (Velicer *et al.* 2002, *J Bacteriol.*).

Evolution of novel cooperative behavior. From an asocial ancestor, laboratory populations of *M. xanthus* evolved new mechanisms of cooperative swarming (Yu & Velicer 2003, *Nature*).

CURRENT AND FUTURE RESEARCH

A. Laboratory Evolution Experiments

Social development

- **Evolution of developmental efficiency.** How does developmental efficiency (in terms of both sporulation rate and spore yield) change when evolving populations are subjected to serial alternation between development and growth? Do developmental cheaters arise and increase during evolution?
- **Co-evolution of cheaters and cooperators.** Mixed cheater/non-cheater populations undergoing co-evolution will be examined. Do the two subpopulations evolve enhanced cheating efficiency and/or the ability to suppress cheating, respectively?

Motility and predation

- **Evolution of searching vs. handling.** Searching components of predatory fitness are predicted to adapt relatively more during evolution in a low prey-density habitat, whereas handling components of predation are expected to improve more at high prey density.
- **Prey-type specialization.** Does specialized adaptation to one prey type result in improved general predatory fitness or rather decreased fitness on alternative prey types?
- **Predator-prey co-evolution.** Mixed cultures of *M. xanthus* and *E. coli* are to undergo long-term co-evolution in both liquid and structured environments, where *E. coli* grows on a carbon source not utilized by *M. xanthus*, and therefore the sole growth substrate for *M. xanthus* is *E. coli* itself. Evolved genotypes from multiple evolutionary time-points will be examined for evidence of an “arms race” between predator and prey.

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- **Evolution of social and adventurous motility.** Populations are evolving in multiple nutrient-agar environments (e.g. abundant vs. scarce nutrients, hard vs. soft agar). The two *M. xanthus* motility systems are predicted to adapt differently to distinct surface types.

B. Natural Isolate Studies

- **Cooperation and conflict.** The degree to which distinct natural strains of *M. xanthus* can undergo development together is being examined in pairwise mixtures of differentially marked strains. The relationship between co-development ability and genetic relatedness is also being examined.
- **Mechanisms of kin-distinction.** We seek to identify mechanisms of intra-specific social antagonism and cooperation between distinct strains of *M. xanthus*.
- **Evolutionary gene relationships.** Phylogenies of major developmental genes in the myxobacteria are to be constructed to explore their evolutionary relationships and the possible role of gene transfer in the evolution of myxobacterial developmental programs.
- **Predation range variation and prey defense.** Multiple *M. xanthus* strains and *Myxococcus* species will be compared in their predation ability on a variety of prey types and possible mechanisms of resistance to predation will be investigated in prey species that do not allow extensive *Myxococcus* growth.
- **Fine-scale genetic and social structure of natural populations.** Using spatially-structured isolates, we seek to characterize the fine-scale genetic diversity and social interactions among distinct *Myxococcus* strains that dwell in a common soil habitat.

C. Genomic and Theory Collaborations

Genomics/proteomics

In collaboration with Stephan C. Schuster (Genome Center Director, MPI-Tübingen) we have begun utilizing genomic and proteomic technologies to address evolutionary questions in the myxobacteria. Current projects include:

- **Evolutionary proteome changes.** Lab-evolved *M. xanthus* genotypes of particular interest are being examined for changes in their proteomes relative to their ancestor in their evolutionary environment.
- **Comparative genome analysis.** The *Bdellovibrio* predators of enteric bacteria have been classified as the closest relatives (along with sulfur/sulfate-reducing bacteria) to the myxobacteria based on 16S ribosomal DNA sequence, despite the radically distinct life-histories of these groups. The *B. bacteriovorus* genome has recently been completed at our institute's genome center and will be evolutionarily compared to the *M. xanthus* genome.

Social evolution theory

Theoretical modeling of competitive dynamics between cheater and altruist social strategies and corresponding empirical work is being pursued in collaboration with Sam P. Brown (CNRS Montpellier/Cambridge University).