Genetic Diversity in Honey Bee Colonies Enhances Productivity and Fitness

Heather R. Mattila* and Thomas D. Seeley

Honey bee queens mate with many males, creating numerous patrilines within colonies that are genetically distinct. The effects of genetic diversity on colony productivity and long-term fitness are unknown. We show that swarms from genetically diverse colonies (15 patrilines per colony) founded new colonies faster than swarms from genetically uniform colonies (1 patriline per colony). Accumulated differences in foraging rates, food storage, and population growth led to impressive boosts in the fitness (i.e., drone production and winter survival) of genetically diverse colonies. These results further our understanding of the origins of polyandry in honey bees and its benefits for colony performance.

One of the central challenges for understanding the evolution of sociality in bees, ants, and wasps (Order Hymenoptera) is the phenomenon of polyandry, or multiple mating with different males by queens (*1*). Selection for polyandry is unexpected because it generates intracolonial genetic diversity, which erodes high levels of relatedness among female offspring, thereby hindering the evolution of altruistic behavior toward kin. Nevertheless, polyandry occurs repeatedly in social insects (*2*) and to an extreme degree in every species of honey bee (genus *Apis*) (*3*). Several hypotheses have been proposed to explain how the benefits of a genetically diverse work force could outweigh the costs of reduced altruism resulting from low within-colony relatedness (*4*). A popular hypothesis suggests that genetically diverse work forces may operate more efficiently (*5*) and, consequently, produce colonies with a fitness advantage over those with uniform gene pools. However, there is conflicting evidence that genetically diverse colonies perform tasks better as a collective than genetically uniform colonies do (*6*–*10*) and, furthermore, enhanced productivity of the work force has never been linked explicitly with colony-level fitness gains.

A honey bee colony propagates its genes in two ways: by producing reproductive males (drones) and by producing swarms, when a reproductive female (queen) and several thousand infertile females (workers) leave and establish a new nest. Swarming is costly and perilous; with limited resources and labor, a swarm must construct new comb, build a food reserve, and begin rearing workers to replace the aging work force. In temperate climates, newly founded colonies must operate efficiently because there is limited time to acquire the resources to support these activities. Colony founding is so difficult that only 20% of swarms survive their first year (*11*); most do not gather adequate food to fuel the colony throughout the winter and die of starvation.

With the challenges of successful colony founding in mind, we conducted a long-term study to compare the development of genetically diverse and genetically uniform colonies after a swarming event. Each genetically diverse colony (n = 12) had a queen that was instrumentally inseminated with sperm from a unique set of fifteen drones and each genetically uniform colony (n = 9) had a queen inseminated with a similar volume of sperm from a single drone. Drones were selected at random from a pool of over 1000 individuals collected from 11 drone-source colonies. To replicate the experience of feral colonies, swarms were created by forcing a queen and 1 kg of her worker offspring (~7700 bees) to cluster in a screened cage for three days, where they were fed sucrose solution ad libitum to simulate preswarming engorgement on honey. Each swarm was subsequently relocated to a combless hive that was similar to that preferred by colonies naturally (*12*). Colonies were founded on 11 June 2006, during the region's swarming season (*13*). Once swarms were in their new nest sites, we documented colony development by measuring comb construction, brood rearing, foraging activity, food storage, population size, and weight gain at regular intervals (*14*). Intracolonial genetic diversity improves disease resistance (*15*), therefore colonies were medicated throughout the study so that we could examine the effects of multiple patrilines on productivity and fitness with minimal interference from the effects of enhanced resistance to disease.

There were notable differences in the progress of genetically diverse and genetically uniform colonies during the early stages of colony founding. Colonies with genetically diverse worker populations built ~30% more comb than colonies with genetically uniform populations before construction leveled off after 2 weeks [(Fig. 1); repeated measures ANOVA; $F(1,19) = 25.7$, $P < 0.0001$ (colony type); $F(19,342) = 126.9$, $P < 0.0001$ (time); $F(19,342) = 31.8$, $P < 0.0001$ (interaction)]. During the second week of colony founding, we compared foraging rates (number of workers returning to hive per minute for all workers and for only those carrying pollen) between different combinations of randomly paired colonies (one colony from each treatment, n = 50 pairs per day) throughout five consecutive mornings. Genetically diverse colonies maintained foraging levels that were 27 to 78% higher than genetically uniform colonies on three of five mornings [(Fig. 2); paired t tests with Bonferroni adjustment; 20 June: $t(49) = 4.1$, $P = 0.0001$ and $t(49) = 5.7$, $P < 0.0001$; 21 June: $t(49) = 3.2$, $P = 0.002$ and $t(49) = 5.5$, $P < 0.0001$; 22 June: $t(49) = 5.2$, $P < 0.0001$ and $t(49) = 5.8$, $P < 0.0001$]. Moreover, after 2 weeks in their new nest site, genetically diverse colonies stockpiled 39% more food than genetically uniform colonies [mean 1390 ± 120 versus 990 ± 145 cm^2 comb per colony filled with food; t test; $t(19) = 2.1$, $P = 0.045$]. This difference was not because some colonies lacked space (genetically diverse and uniform colonies had mean 61 ± 1.1% and 66 ± 3.2% of comb empty, respectively); instead, it was likely a consequence of increased foraging activity in genetically diverse colonies. The magnitude of these differences in growth during the initial 2 weeks after colony founding is impressive, considering that work forces in genetical-

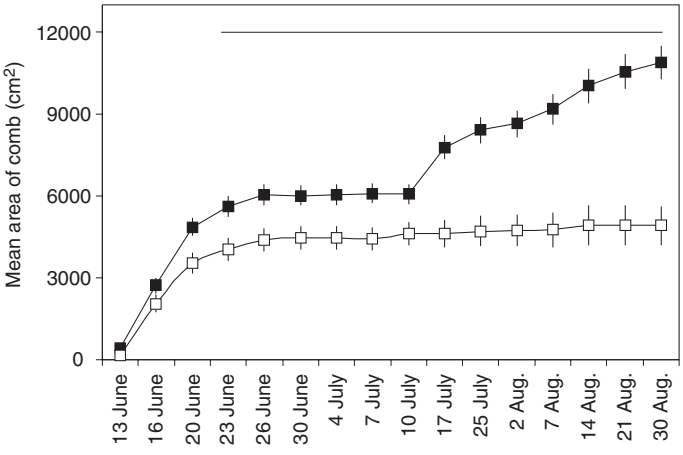


Fig. 1. Area of comb (means ± SEM) constructed by genetically diverse (■) and genetically uniform (□) colonies after occupying new nest sites on 11 June. Dates when groups differed significantly in comb area are indicated by a horizontal line (top).

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ly diverse and genetically uniform colonies were still similarly sized 1 month after founding [9 July comparison of worker populations; t test; $t(19) = 1.6$, $P = 0.12$].

One month after "swarming," there was an isolated and brief period when abundant forage became available (~9 to 21 July). At the start of this honey flow, genetically diverse colonies were already twice as heavy as genetically uniform colonies [(Fig. 3); repeated measures ANOVA; $F(1,19) = 39.9$, $P < 0.0001$ (colony type); $F(86,1373) = 237.0$, $P < 0.0001$ (time); $F(82,1373) = 17.4$, $P < 0.0001$ (interaction)]. Throughout the flow, genetically diverse colonies gained an average of 0.3 ± 0.05 kg/day per colony and increased their higher initial colony weight by 305%, whereas genetically uniform colonies gained only 0.09 ± 0.01 kg/day per colony and increased their lower colony weight by only 163% before resources waned (Fig. 3; comparison of mean daily weight gain during flow; paired t test; $t(11) = 3.9$, $P = 0.0007$). The influx of food sparked a resurgence in comb construction in genetically diverse colonies, however, comb area remained unchanged in genetically uniform colonies (Fig. 1).

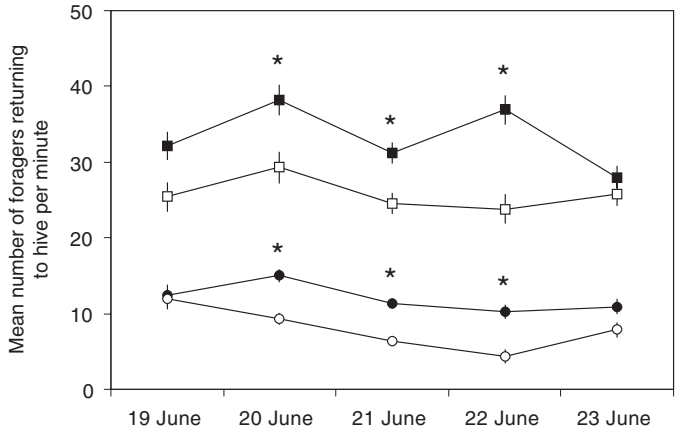


Fig. 2. Foraging rates (means ± SEM) of genetically diverse (■: all returning workers; ●: only workers carrying pollen) and genetically uniform (□: all returning workers; ○: only workers carrying pollen) colonies. Asterisks mark days when daily foraging rates differed significantly between groups.

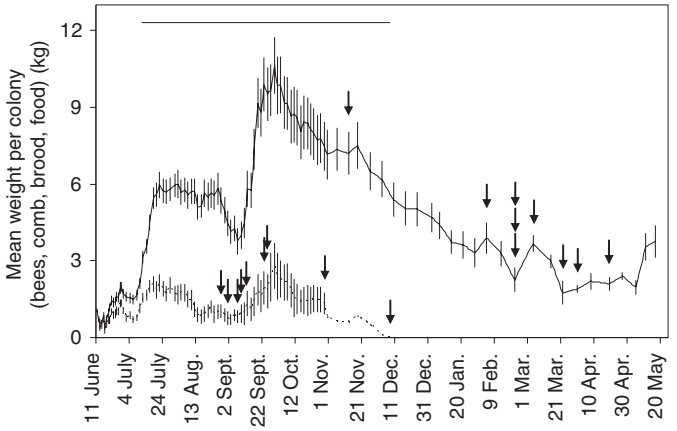


Fig. 3. Weight (means ± SEM) of genetically diverse (solid line) ($n = 12$) and genetically uniform (dashed line) ($n = 9$) colonies after occupying new nest sites on 11 June. Dates when groups differed significantly in weight are indicated by a horizontal line (top). Each arrow marks the death of a colony.

Production of new workers in genetically diverse colonies surpassed that of genetically uniform colonies within the first month of colony development [(Fig. 4); repeated measures ANOVA; $F(1,19) = 63.5$, $P < 0.0001$ (colony type); $F(11,174) = 37.4$, $P < 0.0001$ (time); $F(11,174) = 16.0$, $P < 0.0001$ (interaction)]. Brood rearing by workers increased continually in genetically diverse colonies until the end of August, whereas genetically uniform colonies produced consistently low numbers of workers over the same period (Fig. 4). Consequently, genetically diverse colonies had far larger worker populations by the end of August [mean $26,700 \pm 1830$ versus 5300 ± 2400 individuals per colony; t test; $t(17) = 7.1$, $P < 0.0001$]. These differences in post-founding development likely resulted from a combination of an enhanced capacity of multiple-patriline colonies to construct nest materials, to rear brood, and to acquire food (given comparable worker populations) and the momentum that this lent to the pace of colony growth, a pace that single-patriline colonies were not able to match despite having similar opportunities after a "swarming" event.

Colony size is closely tied to fitness; larger colonies produce more drones, have higher winter survival, and issue more swarms (*16*–*18*). Here, intracolonial genetic diversity resulted in considerably more populous and resource-rich colonies, which in turn affected their fitness. Genetically diverse colonies reared significantly more drones than genetically uniform colonies before brood rearing declined in September: mean 1910 ± 384 versus 240 ± 109 drones per colony [Fig. 4; t test; $t(19) = 3.7$, $P = 0.002$]. The larger, genetically diverse colonies also collected and stored more food than genetically uniform colonies and all survived a late-August cold period that starved and killed 50% of genetically uniform colonies (Fig. 3). The remaining genetically uniform colonies exhausted their food reserve and died by mid-December, whereas 25% of genetically diverse colonies survived to May (Fig. 3).

We have demonstrated that the productivity and fitness of honey bee colonies is enhanced by intracolonial genetic diversity. Our data confirm and extend trends toward increased growth reported in short-term studies of polyandrous colonies with low (≤6) numbers of patrilines (*6*, *7*). The benefits of a genetically diverse worker population are especially evident during colony founding when survival depends critically on

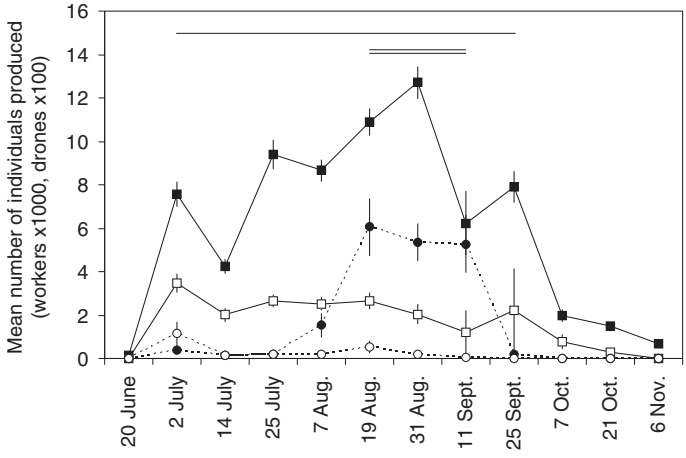


Fig. 4. Number (means ±SEM) of workers (solid lines) and drones (dashed lines) produced by genetically diverse (workers: ■; drones: ●) and genetically uniform (workers: □; drones: ○) colonies. A census of individuals in capped-pupae cells was made on each date; pupae counted at this time emerged as adults during the interval between that census and the next (*14*). Horizontal lines (workers: single line; drones: double line) mark periods when brood rearing differed significantly between groups.

successfully accomplishing a variety of pressing tasks. Given similar numbers of workers, environmental conditions, and need, newly founded colonies built comb faster, foraged more, and stored greater amounts of food when their work forces were comprised of many genetically distinct patrilines. Initial differences in labor productivity amplified growth rates over time and led to dramatic fitness gains for genetically diverse colonies (i.e., production of drones, colony growth, and survival). Thus, we expect intense selection favoring polyandry because intracolonial genetic diversity improves the productivity of the work force and increases colony fitness during the risky process of colony founding.

Higher collective productivity of genetically diverse colonies may be rooted in a broader or more sensitive response from worker populations to changing conditions. The probability that a worker will engage in a task has been linked repeatedly to genotype [e.g. (*5*, *8*, *19*)]. Consequently, colonies with multiple patrilines would be expected to have worker populations that are able to respond to a broad range of task-specific stimuli and, as a group, should be able to provide appropriate, incremental responses to changes in these stimuli (*5*). The observation that intracolonial genetic diversity improved productivity in colonies is consistent with predictions made by models of division of labor that rely on genotypic differences in response thresholds among workers (*20*). Nevertheless, the extent to which genetically uniform colonies lagged behind genetically diverse colonies in the early stages of colony development was surprising, considering that colonies initially lacked comb and food reserves, and presumably, stimuli reflecting these needs could not have been greater. Actual response thresholds of workers are not well documented (*20*), and it is difficult to know how they are related to the productivity of individuals and the colony as a whole. For example, workers may vary genetically in the rate at which they perform a task once their response threshold is reached or they may not be "good" at tasks for which they have high thresholds (i.e., they lack physiological apparatuses or experience). Alternatively, thresholds may be so high for some tasks that behaviors are effectively missing from a worker's repertoire, thus multiple patrilines would contribute to the diversity of labor in a colony, rather than division of labor among workers.

A key advantage of intracolonial genetic diversity was revealed during infrequent periods when food resources were plentiful (~33 days during our study). Genetically diverse colonies gained weight at rates that far exceeded those of genetically uniform colonies (Fig. 3), whose sluggish foraging rates suggest that intracolonial genetic diversity enhances the discovery and exploitation of food resources by work forces, especially during periods when resources become suddenly and abundantly available. Intracolonial genetic diversity would result in more rapid mobilization of forager work forces if, by broadening the range of response thresholds in colonies, it increased the probability of having sufficient workers functioning as foragers and/or broadened the range of conditions over which foragers inspected, scouted, recruited to or were recruited/reactivated to food resources. Selection for polyandry would be strong if the genetic diversity that it bestows on colonies enhances the sophisticated mechanisms of honey bees for recruiting nest mates to food. Because successful colony founding by honey bees depends so heavily on rallying foragers and the swift accumulation of resources, this could explain, in concert with other benefits unrelated to worker productivity (*15*, *21*), the widespread occurrence of extreme polyandry in all honey bee species.

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Supporting Online Material

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Materials and Methods
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PDZ Domain Binding Selectivity Is Optimized Across the Mouse Proteome

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PDZ domains have long been thought to cluster into discrete functional classes defined by their peptide-binding preferences. We used protein microarrays and quantitative fluorescence polarization to characterize the binding selectivity of 157 mouse PDZ domains with respect to 217 genome-encoded peptides. We then trained a multidomain selectivity model to predict PDZ domain–peptide interactions across the mouse proteome with an accuracy that exceeds many large-scale, experimental investigations of protein-protein interactions. Contrary to the current paradigm, PDZ domains do not fall into discrete classes; instead, they are evenly distributed throughout selectivity space, which suggests that they have been optimized across the proteome to minimize cross-reactivity. We predict that focusing on families of interaction domains, which facilitates the integration of experimentation and modeling, will play an increasingly important role in future investigations of protein function.

Eukaryotic proteins are modular by nature, comprising both interaction and catalytic domains (*1*, *2*). One of the most frequently encountered interaction domains, the PDZ domain, mediates protein-protein interactions by binding to the C termini of its target proteins (*3*–*6*). Previous studies of peptide-binding selectivity have placed PDZ domains into discrete functional categories: Class I domains recognize the consensus sequence Ser/Thr-X-ψ-COOH, where X is any amino acid and ψ is hydrophobic; class II domains prefer ψ-X-ψ-COOH; and class III domains prefer Asp/Glu-X-ψ-COOH (*5*, *7*). More recent information has suggested that these designations are too restrictive and so additional classes have been proposed (*8*, *9*). The idea that domains fall into discrete categories, however, raises questions about functional overlap: Domains within the same class are more likely to cross-react with each other's ligands. To resolve this issue, we characterized and modeled PDZ domain selectivity on a genome-wide scale.

We began by cloning, expressing, and purifying most of the known PDZ domains encoded in

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