**Sex Determination in Honeybees**

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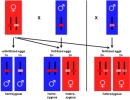
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In humans, sex is determined by the presence or absence of X or Y sex chromosomes. In honeybees, however, evolution has resulted in a very different and unique sex determination system.

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In honeybees (or honey bees), sex is normally determined by the fertilization or non-fertilization of eggs, rather than the presence or absence ofsex chromosomes. This mode of sex determination was first discovered by Johann Dzierzon, a Catholic priest, in 1845. Dzierzon reported that a virgin queen which has not taken a mating flight (the queens mate only while in free flight away from nest) produces only male progeny (Dzierzon*et al.,*1945). His report was the first rigorous description of a sex determination system, occurring more than 50 years before the discovery of sex chromosomes (McClung, 1902; Wilson, 1905). We now know that honey bees are not unique and that about 20% of animal species use ahaplodiploid mode of reproduction. In haplodiploid systems, male progeny normally develops from unfertilized eggs, which are haploid and have just one set of chromosomes. The fertilized honey bee eggs, which are diploid and have two sets of chromosomes, differentiate into queens and worker bees.

**Complementary Sex Determination**

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**[[View Full-Size Image](http://www.nature.com/scitable/topicpage/sex-determination-in-honeybees-2591764?scrlybrkr)Figure 1](http://www.nature.com/scitable/topicpage/sex-determination-in-honeybees-2591764?scrlybrkr)**

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**Figure 2:**

**Honeybee colony.**

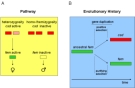
Inbreeding produces colonies with reduced numbers of progeny. Diploid male larvae homozygous at the sex determination locus (SDL) are consumed shortly after they hatch, resulting in empty cells on brood combs.

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In the years that followed the observation that honey bees lack sex chromosomes, investigators were surprised to discover that diploid males appeared in inbreedingstudies with honey bees. The presence of these diploid males suggested that neither the fertilization process nor the haploid or diploid state of the egg provides the primary signal for sex determination in honey bees (Mackensen, 1951). Since the appearance of diploid males was associated with inbreeding, investigators proposed a hypothesis of complementary sex determination, in which a single sex determination locus (SDL) determines the sexual fate (Whiting, 1933; Whiting, 1943). According to this hypothesis, fertilized eggs that are homozygous at SDL differentiate into diploid males, while fertilized eggs that are heterozygous at SDL develop into females. Fertile males are produced from the queen's unfertilized, haploid eggs, which are necessarily hemizygous at the SDL (Figure 1).Homozygosity at the SDL is lethal to males. The diploid males are eaten by worker bees shortly after they hatch from the egg. This results in a typical brood pattern in honey bee colonies that bee keepers refer to as shoot brood (Figure 2).

The isolation of the sex determination locus in honey bees led to the identification of the *complementary sex determiner* (*csd*) gene (Beye *et al*., 2003) (Figure 3A). The *csd*gene encodes a potential splicing factor that exists in at least 15 allelic variants that differ on average in ~3% of their amino acid residues (Hasselmann and Beye, 2004). The *csd*gene product is necessary for female development, because inactivation of *csd* gene product in female embryos causes a full switch into male development (Beye *et al*., 2003). The target of the *csd* gene product was recently identified as the *feminizer*(*fem*) gene (Hasselmann *et al*., 2008) (Figure 3A). The *fem* transcript is splicing differently in males and females, so that only female cells have a functional *fem* gene product. In males, splicing introduces a stop codon into the *fem* coding sequence.

**Evolution of Complementary Sex Determination**

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**[[View Full-Size Image](http://www.nature.com/scitable/topicpage/sex-determination-in-honeybees-2591764?scrlybrkr)Figure 3](http://www.nature.com/scitable/topicpage/sex-determination-in-honeybees-2591764?scrlybrkr)**

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The complementary mode of sex determination occurs in a variety of hymenopteran species, including bees, wasps and ants, but not all these species rely on products of the *csd* gene for sex determination. Comparison of gene orthologs in other bee and wasp species showed that the*csd*genearose recentlyby gene duplication within the honey bee lineage from a copy of the ancestral progenitor gene *feminizer* (*fem*) (Figure 3B). The *fem* gene remains a conserved component of sex determination pathways among insects. During the evolution of honey bees, the *fem* gene has become the target of *csd* activity (Figure 3A). The *csd* gene has most likely acquired its modern function by adaptive evolution. According to one model (Figure 3B) (Hasselmann *et al*., 2008), duplication of the ancestral sex-determining *fem* gene was followed by positive selection in one of the duplicates, favouring the presence of a new upstream signal that ultimately resulted in the novel sex determination system in the honey bees (Figure 3). The evolution of the *csd* gene is an example of how easily a new sex determination systems can arise by simple molecular changes of the existing genetic repertoire. The reduction of meiotic recombination that is observed at the sex determination locus of the honey bee may also indicate that the *csd* gene will gradually degenerate over time (Charlesworth *et al*., 2005), which would again facilitate the evolution and positive selection of alternative sex determination signals over evolutionary time scales in the honey bee lineage.

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