CHEMICAL COMMUNICATION

The sex of scents

Mating in insects relies on pheromone production in just one of the sexes. A multidisciplinary study on the German cockroach identifies a gene that connects sex differentiation factors with the production of sexual pheromones in females only.

Xavier Belles

Jean-Baptiste Grenouille, the unloved protagonist of the novel 'Perfume: The Story of a Murderer' by Patrick Süskind[1], realizes that he does not give off any scent. Indeed, Grenouille cannot smell himself and neither can other people. Towards the middle of the story he creates an odour for his body and becomes accepted by society. The story is fictitious, but is grounded in reality. Scents play an important role in animal communication, and although in our species the language of smells has become much less prominent, other animals such as insects rely on scents — pheromones — for communication[2,3].Chemical communication in insects is based on volatile sex pheromones, as described in butterflies by the naturalist Jean-Henry Fabre at the end of the nineteenth century[4]. Females typically emit pheromones, which are received by males and trigger courting behaviours. Naturally, sex pheromones are produced in a sexually dimorphic manner, which is largely determined by sex differentiation genes. But how is the signal from these genes translated into the production of pheromones in one sex but not in the other? Writing in *Nature Ecology and Evolution*, Chen et al[5]., answer this question for one species of cockroach.

The authors study the German cockroach, *Blattella germanica*, which not only relies on volatile sex pheromones for finding a mate, but also on non-volatile contact sex pheromones that ensure species and sex recognition, and finally mate choice. The contact sex pheromones are produced by the female and act after the encounter with a male where the female and male rub their antennae, thereby stimulating the male to raise his wings upward, before the male turns around 180°, thus exposing the tergal gland to the female. The secretion of this gland stimulates the female to mount the male and feed, and in this position, the male clasps the female genitalia with his left phallomere and accomplishes mating[6] (Fig. 1).

Using a combination of approaches including behavioural, biochemical and genetic analyses, Chen et al. found a gene, *cytochrome P450 4 PC1* (*CYP4PC1*), that encodes a hydroxylase, which controls the rate-limiting step of contact sex pheromone production. This hydroxylase is expressed preferentially in the antennae, and only in females. The authors also unveil the role that sex differentiation genes play in the expression of *CYP4PC1*. The female

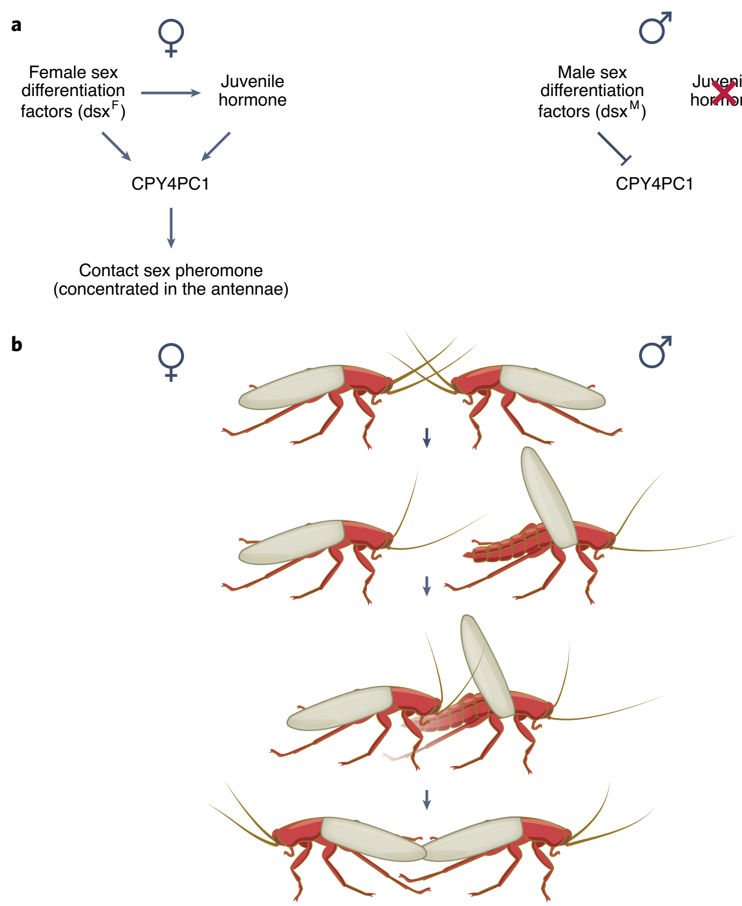

Fig. 1 | Mechanism that determines contact sex pheromone production in females, but not males, of the German cockroach. a, Chen et al[5]. show that the connection between sex differentiation factors and contact sex pheromones is established through CYP4PC1, the key enzyme that regulates the production of these pheromones. In the female, *CYP4PC1* expression is stimulated by female differentiation factors and by juvenile hormone, which is produced at very high levels in this sex. In the male, no contact sex pheromone is produced because male differentiation factors repress the expression of *CYP4PC1*, and there is practically no production of juvenile hormone. **b**, The contact sex pheromones concentrate in the female antennae. After encountering a male, the female rubs the antennae with those of the male thereby triggering the courtship sequence: the male raises his wings upward, exposing the tergal gland; then, the female feeds on the gland secretions and, taking advantage of the feeding position, the male accomplishes mating.

cockroach expresses two specific *doublesex* splicing isoforms: *dsx2* and *dsx3* (*dsx*^{F}), whereas the male expresses a single *doublesex* isoform, *dsx1* (*dsx*^{M}). The expression of *doublesex* isoforms is controlled by *transformer*, which is expressed by the female and encodes an RNA splicing factor[7]. When the authors depleted *transformer* in females, *dsx*^{F} was not activated, but *dsx*^{M} was activated instead. In those females, *CYP4PC1* expression fell by more than 80%, which resulted in lower production of contact sex pheromone precursors. When these females rubbed their antennae with those of a male, the male took longer than normal to respond by raising his wings. On the other hand, the depletion of *dsx*^{M} in males led them to court each other, exhibiting wing-raising, tergal secretion feeding and even attempts of mating with other males. Compared to controls, these *dsx*^{M}-depleted males produced substantial amounts of CYP4PC1 and produced more contact sex pheromone precursors. Going deeper into these observations, the authors found that the Dsx^{M} binds to the promoter region of *CYP4PC1* and represses its expression. This explains why there is no male–male sexual attraction in natural cockroach populations.

Another player that has a big role in the whole mechanism is the juvenile hormone. This is an important hormone, which in the adult female is needed to promote the production of huge amounts of yolk proteins required for oocyte development[8,9]. Consistent with this, the female produces much higher amounts of juvenile hormone than the male. The authors also found that juvenile hormone stimulates the expression of *CYP4PC1* and that this naturally happens in the females, which produce high hormone levels. In turn, Dsx^{F} factors stimulate the expression of *juvenile hormone acid methyl transferase*, a gene encoding the key enzyme that regulates juvenile hormone production.

Putting all the pieces of the puzzle together gives us a fascinatingly complex and accurate picture of the mechanisms behind male–female cockroach communication and mating. In short, the connection between sex differentiation factors and the contact sex pheromone is established through CYP4PC1. In the female, *CYP4PC1* expression is stimulated by Dsx^{F} factors and by juvenile hormone, which is produced at very high levels in this sex. In the male, no contact sex pheromone is produced because the Dsx^{M} factors inhibit the expression of *CYP4PC1*. In addition, males practically do not produce juvenile hormone, which could stimulate *CYP4PC1* expression (Fig. 1). This precise mechanism ensures that courtship takes place between the opposite sexes. How general is this mechanism? The case studied is very particular, with a contact pheromone consisting of a blend of hydrocarbon-derived components[10], the most abundant of which is 3,11-dimethylnonacosan-2-one[11]. In this case, the role of CYP4PC1 is central. As it regulates a key step in the synthesis of the compound, the modulation of its expression in each sex determines the sexual dimorphism of the contact sex pheromone production. In other species with similar pheromonal compounds and biology, a close mechanism might operate. In other pheromones, for example the volatile sex pheromones, the players could be different. But Chen et al. provide a general approach to unveil other mechanisms: find the key gene that regulates the production of the pheromone and determine if its expression is influenced by sexual factors and, eventually, by the juvenile hormone. While conceptually simple, this approach is technically complex and laborious. The work of Chen et al. paves the way for dissecting further mechanisms of chemical communication in insects and other animals. ❐

Xavier Belles ✉
Institute of Evolutionary Biology (CSIC-Universitat Pompeu Fabra), Barcelona, Spain.
✉*e-mail: xavier.belles@ibe.upf-csic.es*

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Competing interests

The author declares no competing interests.